Shriner
Hermann
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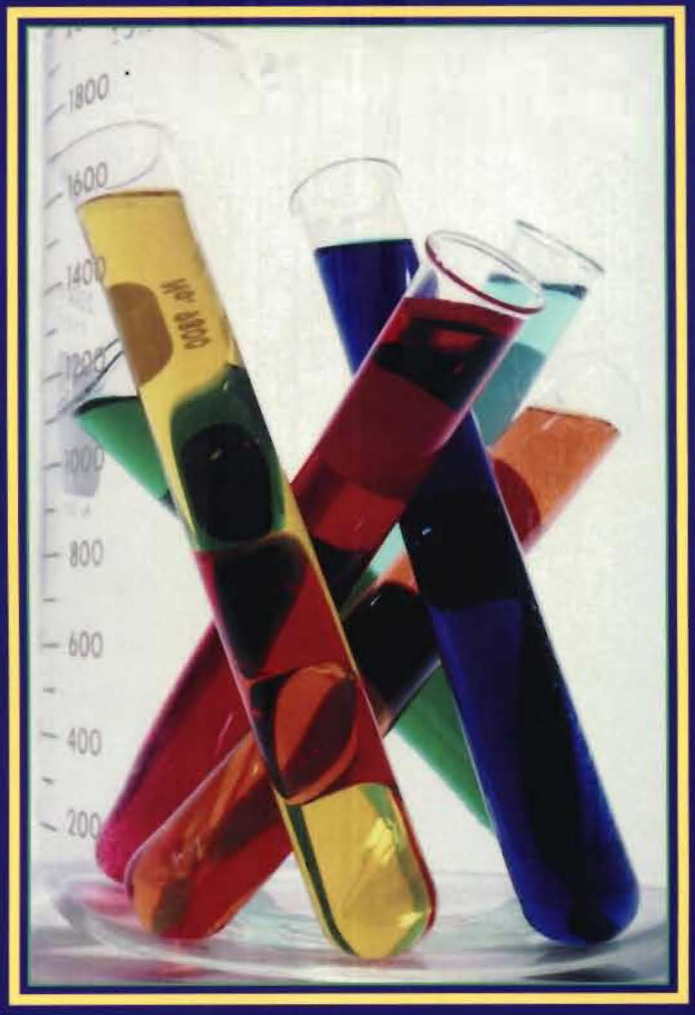
Fuson

The Systematic Identification of Organic Compounds



Eighth Edition

8TH EDITION

The Systematic Identification of Organic Compounds

RALPH L. SHRINER

CHRISTINE K. F. HERMANN

TERENCE C. MORRILL

DAVID Y. CURTIN

REYNOLD C. FUSON

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Preface

Ralph Shriner and Reynold Fuson wrote the first edition of "The Identification of Organic Compounds" in 1935. In those days, students had to identify organic compounds by solubility tests, physical properties, elemental tests, classification tests, and by preparing a derivative. The classification tests, the derivative experiments, and the derivative tables were expanded in the second edition in 1940 and in the third edition in 1948. The solubility tables were also redrawn in the third edition. David Curtin was added as author in the fourth edition in 1956. The title of the book was changed, in the fourth edition, to "The Systematic Identification of Organic Compounds." Infrared spectroscopy was added, with correlation tables. A discussion of ultraviolet spectroscopy was added. Raman spectroscopy and nuclear magnetic resonance spectroscopy were mentioned as "show promise of becoming increasingly important."

In the fifth edition, in 1964, 712 new entries were added to the original 2000 entries in the derivative tables. In the preface to this edition, proton magnetic resonance was considered second in importance to infrared spectroscopy. Proton nuclear magnetic resonance, including chemical shifts, peak areas, and spin-spin coupling, was described. Terence Morrill wrote the majority of the sixth edition, in 1980. Ralph Shriner provided the well-tried and chemical tests, in addition to providing advice from years of teaching organic chemistry and qualitative organic analysis. The chemical tests, the preparation of derivatives, and spectroscopy were combined into one large chapter. More infrared spectra and proton nuclear magnetic resonance spectra were included. The discussion of carbon-13 nuclear magnetic resonance spectroscopy, including spectra, was in a later chapter.

The seventh edition, in 1998, was written by Terence Morrill and Christine Hermann. Spectroscopy, the classification tests, and the preparation of derivatives were separated into three chapters. An introduction section was added to each set of functional groups in the classification tests and preparation of derivatives chapters. Cleaning up instructions were added at the end of each experiment. Many new drawings of apparatus were included. Almost all of these drawings were done by Christine Hermann's husband, Richard Hermann. The derivative tables were greatly expanded. A solutions manual was written to accompany this book.

The eighth edition of the book promises to continue the great tradition of qualitative organic chemistry. All of the photographs are new. Chromatography, which had been previously in several chapters, is now combined into Chapter 4. Chapter 4 also contains the separation of mixtures, based upon extractions, and distillation techniques. Spectroscopy is now divided into three chapters. Chapter 6 describes NMR spectrometry, including DEPT, COSY, and HETCOR. IR spectrometry is discussed in Chapter 7. Chapter 8 discusses mass spectrometry and ultraviolet spectrometry. Chapters 6, 7, 8, and 11 contain all new spectra. More problems have been added throughout the book. A solutions manual is available that contains the answers to all of the problems.

I am grateful to the following chemists for contributing their time and ideas to this edition: Andrew Bressette (Berry College), Earl Alley (Mississippi State University), Theodore Snider (Cameron University), Francis Smith (King's College), Robert Cunico (Northern Illinois University), John Allison (Michigan State University), F. Lamar Setliff (University of Arkansas at Little Rock), Daniell Mattern (University of Mississippi), and Charles Garner (Baylor University). Darrell Koza

(Eastern Connecticut State University) offered several suggestions for new classification tests.

Several chemists contributed spectra to this edition of the book. They are also acknowledged in the figure legend of each spectrum. Thomas Glass (Virginia Tech) and Geno Iannoccone (Virginia Tech) contributed several NMR spectra for this edition. Vernon Miller (Roanoke College) contributed mass spectra. Terra Hosp (Radford University) contributed IR spectra and tested the new classification tests in the laboratory. I would also like to thank Daniel Traficante (NMR Concepts) for teaching a course in NMR Interpretation that I attended while writing this book. I owe a special debt of gratitude to my husband, Richard Hermann, for his patience during the preparation of this manuscript.

This book could not have been published without David Harris and Deborah Brennan, Chemistry Editors at Wiley, and Catherine Donovan, Editorial Program Assistant at Wiley.

In summary, I hope that I have provided a book that is useful in the identification of organic compounds. I would appreciate input from faculty, students, and professional chemists on the value of the book and any comments about the book.

Christine K. F. Hermann
Radford University

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The Systematic Identification of Organic Compounds

CHAPTER 1

Introduction

1.1 SYSTEMATIC IDENTIFICATION OF ORGANIC COMPOUNDS: THE NEED FOR ORGANIC QUALITATIVE ANALYSIS

Qualitative organic chemistry has been in use since long before the advent of modern spectroscopy. Modern spectroscopic techniques have assisted the chemist by providing spectra that can be interpreted to give more detail of the interaction between atoms and functional groups. Some students have difficulty identifying structures using exclusively nuclear magnetic resonance (NMR) spectra, infrared spectra, and mass spectra. The information obtained through chemical tests allows the student to narrow down the possible functional groups. Additionally, by taking a course in qualitative organic chemistry, a student is given the freedom of selecting, for himself or herself, the particular chemical tests that are needed to identify a compound.

In roughly two dozen chapters of a standard organic text, the student encounters many chemical reactions. Literally millions of different organic compounds have been synthesized. Chemical companies sell thousands of compounds, and industrial-scale production generates thousands of different compounds on various scales. Characterization of organic compounds can be done by a handful of physical and chemical observations if it is done in a systematic manner. The list of more common and more readily available chemicals is much smaller than the millions that are possible.

In this text we have focused our attention on an even smaller list of compounds that can be used as "unknowns." The melting point–boiling point tables give a very accurate idea of the focus of this book. Instructors using this book may very well use other references (CRC reference volumes,[1] the Aldrich Company catalog, etc.) for a more extensive list of possibilities for "unknown" compounds.

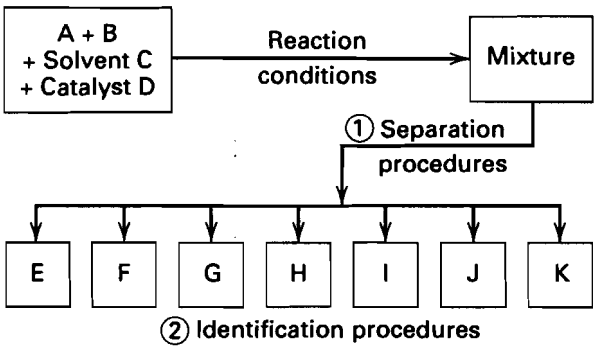
Organic chemists are often confronted with either of the following extreme situations:

1. Determination of the identity of a compound that has no prior history. This is often the case for a natural-products chemist who must study a very small amount of sample isolated from a plant or animal. A similar situation applies to the forensic chemist who analyzes very small samples related to a lawsuit or crime.
2. The industrial chemist or college laboratory chemist who must analyze a sample that contains a major *expected* product and minor products, all of which could be expected from a given set of reagents and conditions. It is entirely possible that such a sample with a well-documented history will allow one to have a properly preconceived notion as to how the analysis should be conducted.

[1]For example, *Handbook of Tables for Organic Compound Identification*, 3rd ed., edited by Z. Rappaport (CRC Press, Boca Raton, FL, 1967).

The theory and technique for identifying organic compounds constitute an essential introduction to research in organic chemistry. This study organizes the accumulated knowledge concerning physical properties, structures, and reactions of thousands of carbon compounds into a systematic, logical identification scheme. Although its initial aim is the characterization of previously known compounds, the scheme of attack constitutes the first stage in the elucidation of structure of newly prepared organic compounds.

If, for example, two known compounds A and B are dissolved in a solvent C, a catalyst D is added, and the whole subjected to proper reaction conditions of temperature and pressure, a mixture of new products plus unchanged starting materials results.



Immediately two questions arise:

1. What procedure should be chosen to separate the mixture into its components?
2. How are the individual compounds (E through K) to be definitely characterized? Which ones are unchanged reactants? Which compounds have been described previously by other chemists? Finally, which products are new?

These two problems are intimately related. Separations of organic mixtures use both chemical and physical processes and are dependent on the structures of the constituents.

The present course of study focuses on the systematic identification of individual compounds first. The specific steps are given in Chapter 2. Physical properties are described in Chapter 3. The use of these principles for devising efficient procedures for the separation of mixtures is outlined in Chapter 4. Solubility techniques are described in Chapter 5. Spectroscopy methods are discussed in Chapters 6 through 8. The practical laboratory methods are given in Chapters 9 and 10.

In recent years the question of scale has become an issue. Scale has always been a focal point for qualitative analysis. The issue has been recognized at an even earlier point in the chemistry curriculum, and a very large number of colleges now incorporate some sort of microscale approach into their sophomore organic courses. (Here we loosely define microscale chemistry as the use of tens of milligrams of organic compound in a procedure, while macroscale reactions employ tens of grams.) Organic qualitative analysis has always been a test-tube subject and thus should philosophically be in tune with the microscale revolution. We have left most of our experiments at the scale of the past editions of this text and thus many chemistry instructors may wish to scale down. We anticipate that scaling down to 1/2, 1/5, or 1/10 of the cited amount should be very straightforward in most cases, and thus scale is the option of the course coordinator. The only warning is that certain reactions (for example, conversion of a

carboxylic acid to an amide or of an alcohol to a 3,5-dinitrobenzoate) are notoriously sensitive to the purity of the reagents. Thus a larger-scale reaction is likely desirable here.

Cleanup and Waste Disposal

A related, and in some ways bigger, issue is that of waste disposal. The trend at most colleges in recent years is to have waste disposal done by a licensed company under contract with the college. Most instructors are not qualified to dispose of waste and thus they can only provide cleanup guidelines. We have attempted to prepare this edition with that in mind. It is usually the job of the instructor to provide containers for waste disposal (it is now very rare that a chemical can be washed down the sink). Waste disposal vessels are usually labeled as to their use, such as solids vs. liquids and inorganic vs. organic compounds. In some cases a special vessel is provided for especially toxic wastes such as halogenated organic compounds. Moreover, there are usually special containers for glass (especially broken glass) objects. There may be places to recycle paper, and finally there are simple trash cans for garbage. Thus there is usually a classification decision for every act of discarding material. Most importantly, the students should receive instructions from their lab instructor that are in accord with local regulations.

1.2 SUGGESTIONS TO STUDENTS AND INSTRUCTORS

Schedule

An exact time schedule applicable to all schools cannot be set because of the varied use of semester, quarter, trimester, and summer session terms of instruction. However, for a semester of 15 weeks, two 3-hr laboratory periods per week plus one "lab lecture" per week works well. Modification can be made to adapt the course to individual schools.

Lecture Material

The first lecture should describe the course overview as outlined in Chapter 2. Next, a review of spectroscopic techniques, including operating instructions, should be discussed (Chapters 6 through 8). Physical properties (Chapter 3), including melting point and boiling point, should be described next. Recrystallization (Section 3.4) and separation of mixtures (Chapter 4) could be explained. It is not necessarily to lecture on all of the experiments and procedures (Chapters 9 and 10), but an introduction to the most common tests should be discussed.

After the first one or two unknowns have been completed, it will be valuable to work some of the problems of Chapter 11 in class and discuss the structure correlation with chemical reactions and spectral data. It is the instructor's choice whether or not to make the *Solutions Manual* available to the students.

Laboratory Work—Unknowns

By use of spectroscopic data and chemical reactions it is possible for students to work out six to eight single compounds and two mixtures (containing two or three components each) in a 15-week semester.

To get a rapid start and illustrate the systematic scheme, it may be useful to give a titratable acid to each student for a first unknown. The student is told that the substance is titratable and that he or she is to get the elemental analysis, melting or

boiling point, and neutralization equivalent and to calculate the possible molecular weights.[2] Then, if the unknown contains halogen or nitrogen, the student is to select and try three or four (but no more) classification tests. Next, a list of possible compounds with derivatives is prepared by consulting the table of acids (Appendix II). One derivative is made and turned in with the report (see pp. 17–21). This first unknown should be completed in two 3-h laboratory periods.

Since many schools run organic qualitative analysis in a lab course connected to the second semester (or last term) of the traditional sophomore course, the decision about how to order the functional groups possible for the unknown may very well depend upon the order of coverage of these groups in the lecture course.

The other unknowns should be selected so as to provide experience with compounds containing a wide variety of functional groups.

It is often desirable to check the student's progress after the preliminary tests, solubility classification, and elemental analyses have been completed. This checking procedure is highly recommended for the first one or two unknowns for each student.

Purity of Unknowns Although every effort is made to provide samples of compounds with a high degree of purity, students and instructors should recognize that many organic compounds decompose or react with oxygen, moisture, or carbon dioxide when stored for a considerable time. Such samples will have wide melting or boiling point ranges, frequently lower than the literature values. Hence, for each unknown the student should make a preliminary report of the observed value for melting or boiling point. The instructor should verify these data and if necessary tell the student to purify the sample by recrystallization or distillation and to repeat the determination of the physical constant in question. This avoids waste of time and frustration from conflicting data. (Read also pp. 25–37.)

Amounts of Unknowns As a general guide, the following amounts are suggested:

Unknown No. 1, a titratable acid, 4 g of a solid or 10 mL of a liquid

Unknown No. 2, 3 g of a solid or 8 mL of a liquid

Unknown No. 3, 2 g of a solid or 5 mL of a liquid

Unknown No. 4, 1 g of a solid or 5 mL of a liquid

Mixtures should contain 4–5 g of each component. *Note:* If repurification of a sample is required, an additional amount should be furnished to the student.

The amounts listed above are essentially macroscale unknowns; use of analytical techniques and instrumentation such as thin-layer chromatography and gas chromatography may very well allow sample sizes of unknowns to be ca. 20% of that listed above. *In such cases—that is, for microscale samples—it is imperative that chemical test and derivatization procedures described in Chapters 9 and 10 be scaled down correspondingly.*

Toward the end of the term, when the student's laboratory technique has been perfected and facility in interpreting reactions has been obtained, it is possible to work with still smaller samples of compounds by using smaller amounts of reagents in the classification tests and by using a smaller scale in the derivatization procedure.

[2]Alternatively, the student can be given a compound with mass spectral data or elemental analyses (% C, H, N, O, . . .).

Timesaving Hints

It is important to plan laboratory work in advance. This can be done by getting the elemental analyses, physical constants, solubility behavior, and infrared and NMR spectra on several unknowns during one laboratory period. This information should be carefully recorded in the notebook and then reviewed (along with the discussion in each of these steps) the evening before the next laboratory period. A list of a few selected classification tests to be tried is made and carried out in the laboratory the next day. In some cases a preliminary list of possible compounds and desirable derivatives can be made. It is important to note that few of the 47 classification tests should be run on a given compound. It should not be necessary to make more than two derivatives; usually one derivative will prove to be unique. The object is to utilize the sequence of systematic steps outlined in Chapter 2 in the most efficient manner possible.

The instructor should guide the students so that the correct identification results by a process of logical deductive reasoning. Once the structure of the unknown is established, understanding of the test reactions and spectra becomes clear. Practice in this phase of reasoning from laboratory observations to structure is facilitated by early guidelines in Chapter 11. One method for developing this ability is for the instructor to write a structural formula on the chalkboard and ask the students to predict the solubility behavior and to select the appropriate classification tests.

To tie together the identification work in this course with actual research, the instructor can select a few typical examples of naturally occurring compounds, such as nicotine, D-ribose, quinine, penicillin G, and vitamin B_1, and review the identifying reactions used to deduce these structures. The recent literature also furnishes examples of the value of infrared, ultraviolet, and NMR spectra in establishing structures. Knowledge of the mechanisms of the reactions used for classification tests and for preparing derivatives requires an understanding of the functional groups and their electronic structures.

Throughout this book, references to original articles, monographs, and reference works are given. Many of these will not be used during a one-semester course. However, the citations have been selected to furnish valuable starting sources for future work and are of great use in senior and graduate research.

The use of this manual will be greatly facilitated by the preparation of a set of index tabs for each chapter and parts of chapters. The time spent in preparing the index tabs is more than recovered in speeding up the location of experiments for functional groups, derivatization procedures, and tables of derivatives.

1.3 LABORATORY SAFETY

At all times, the instructor and students should observe safety rules. They should always wear safety glasses in the laboratory and should become familiar with emergency treatment.

Laboratories are places of great responsibility. Careful practice and mature behavior can prevent most mishaps. The following are all very important. Treating the lab with respect makes it far less dangerous.

Eye Protection Goggles or safety glasses must be worn at all times. Eyeglasses, with shatterproof glass, are inadequate without goggles or safety glasses. Side shields are required for all protective eyewear.

Shoes Shoes that completely cover the feet are required in the laboratory.

Protective Clothing A protective apron or lab coat is recommended in the laboratory. If any chemical is spilled on your skin or clothing, it must be washed off immediately.

Food and Drink Food and beverage are strictly prohibited in the laboratory. Do not taste or smell any chemical.

No Unauthorized Experiments Do not perform any unauthorized experiments. Chemicals, supplies, or equipment must not be removed from the laboratory. All experiments must be approved by the instructor.

Smoking Smoking is prohibited in the laboratory.

Personal Items No bookbags, coats, books (except the lab book), or laptop computers should be brought into the laboratory. Ask your instructor where these items can be stored while you are in the laboratory. Bring in only the items that are needed during the laboratory period. These items can be damaged by the chemicals in the laboratory.

Use of Equipment Do not use any equipment until the instructor has shown you how to use it.

Glassware Do not use any broken, chipped, or cracked glassware. Get replacement glassware from your instructor.

Bench Cleanup At the end of the laboratory period, put away all equipment, clean the laboratory bench, and wash your hands.

Use of Chemicals Take only the amount that is needed. Leave all bottles in their proper places. Place the lids on the bottles after use. Clean up all spilled chemicals immediately.

Careful Reading of Labels A Material Safety Data Sheet is available for each chemical in the laboratory. Ask your instructor where the paper copies are located. Material Safety Data Sheets are also available on the web. Many chemical companies have posted this information. Use web search engines to locate this information. Students are encouraged to obtain this information prior to using the chemical in the laboratory. The safety, health, and fire precautions are the most important information to locate. Special instructions for the handling of certain reagents may be posted by the instructor.

Waste Disposal In recent years, the rules regarding waste disposal have become more rigidly defined. Reagents are never poured down the sink. Containers for chemical wastes are provided in the laboratory. Different containers are needed for different types of waste chemicals, such as chlorinated hydrocarbons, hazardous materials, and metals. All reagents in the waste container are listed on the container.

Fume Hoods Most laboratories provide fume hood areas or bench-top fume hoods. Always use these. If you think the hoods are not turned on, bring this to the attention of your instructor. Often students are provided with simple methods of testing hood efficiency, and these should be used periodically. Safety regulations usually prohibit storage of toxic substances in hoods, and fume cupboards for such compounds are normally available.

Gloves Most laboratories provide boxes of gloves. Modern gloves are quite manageable and allow for handling of equipment with some agility. Gloves have their place and can certainly protect your hands from obnoxious odors or chemicals that can cause allergic responses. But they are not a license for sloppy technique. Moreover, they often are easily penetrated by some compounds. Due care is still required.

Compressed Gas Cylinders Compressed gas cylinders, especially those that are nearly as tall as an adult, can be dangerous if not clamped to the bench top. Gas cylinders containing inert gases such as nitrogen or helium may well be around the lab. Cylinders containing chlorine or more toxic reagents should be stored in a fume cupboard.

Safety Equipment The location of safety equipment should be made known to you. Moreover, you should know if and when you should use these.

Most of the following items should be readily available in the chemistry laboratory; items on this list or their description may vary due to local safety regulations:

Fire blanket
Fire extinguisher
Eye-wash fountain
Shower
First aid kit
Washes for acid or base (alkali) burns

Accident Reporting All accidents should be reported. The manner in which they should be reported will be provided by the instructor. It is also important that someone accompany an injured person who is sent out of the laboratory for special care; if the injured person should faint, the injury could easily become compounded.

Medical treatment, except in the simplest of cases, is usually not the responsibility of the instructor. Very simple, superficial wounds can be cleaned and bandaged by the instructor. But any reasonably serious treatment is the job of a medical professional. The student should be sent to the college medical center accompanied by someone from the chemistry department. In all labs, the instructor should provide the students with instructions that are consistent with local regulations.

Explosion Hazards of Common Ethers

A number of violent explosions due to accidental detonation of peroxides, which can build up in common ether solvents, have been reported. These ethers include diethyl ether, diisopropyl ether, dioxane, and tetrahydrofuran. Apparently the greatest hazard exists when ethers have been exposed to air, especially for extended periods of time. Each ether container should be labeled with the date that it is opened. Check with your instructor if this date is several months old. The danger is enhanced when the ethers are concentrated—for example, by distillation. *Any ether solvent that displays a precipitate or that seems to be more viscous than usual may well contain peroxides; do not handle such samples and report their condition to your instructor IMMEDIATELY.* The situation described here involve ether samples that are not acceptable for laboratory use.

There are a number of qualitative tests for the presence of peroxides in ethers; two are described here. **Do not carry out these procedures without permission from**

your instructor. Your instructor may decide that ether peroxide tests are not necessary if fresh ether is used.

Procedure A: Ferrous Thiocyanate Test for Peroxide
Use only a freshly prepared solution. Combine 5 mL of 1% ferrous ammonium sulfate, 0.5 mL of 0.5 M sulfuric acid, and 0.5 mL of 0.1 M ammonium thiocyanate. Add a trace of zinc dust, if necessary, to decolorize the solution. Shake this solution with an equal quantity of the solvent to be tested. If peroxides are present, a red color will develop.

Procedure B. Potassium Iodide Test for Peroxides
Add 1 mL of a freshly prepared 10% solution of potassium iodide to 10 mL of ethyl ether in a 25-mL glass-stoppered cylinder of colorless glass protected from light. View the glass cylinder transversely against a white background. Observe the color. The appearance of a yellow color indicates the presence of peroxides. Shake 9 mL of ethyl ether with 1 mL of a saturated solution of potassium iodide. A yellow color indicates the presence of more than 0.005% peroxide. Purify or discard the ether if a yellow color is present.

Removal of Peroxides from Ethers
Ferrous sulfate can be used to remove peroxides from ethers. In the hood, treat each liter of ether with 40 g of 30% aqueous ferrous sulfate. *The reaction may be vigorous and produce heat if the ethers contain appreciable amounts of peroxide.* The ether can be dried with magnesium sulfate and distilled.

A simple method for removing peroxides from high-quality ether samples, without the need for the distillation or appreciable loss of ether, consists of percolating the solvent through a column of Dowex-1 ion exchange resin. Use a column of alumina to remove peroxides and traces of water from ethyl ether, butyl ether, dioxane, and hydrocarbons. Use this method also to remove peroxides from tetrahydrofuran, decahydronaphthalene (decalin), 1,2,3,4-tetrahydronaphthalene (tetralin), cumene, and isopropyl ether.

CHAPTER 2

Identification of Unknowns

There are two ways in which the information outlined in this chapter can be applied. The first way is the exercise wherein a student is asked to identify a compound already described in the literature. The second way is the characterization of a new compound.

The following directions are intended as a guide in the process of identifying an unknown. Good laboratory technique dictates that students keep their own careful and systematic records of observations. The preparation of such records will, however, be greatly simplified by following the suggested sequence of operations.

We shall begin by assuming that the student has a sample, in hand, that is one compound. This compound has probably been characterized in the literature. If the sample is made of more than one major component, Chapter 4 on separation techniques should be consulted.

The sample is given a preliminary examination, including determining its melting point or boiling point. An ignition test may be performed. The unknown is tested for the presence of nitrogen, sulfur, chlorine, bromine, iodine, or fluorine. Solubility tests are then used to simplify the list of possible functional groups. Infrared (IR), ^{1}H nuclear magnetic resonance (NMR), and ^{13}C NMR spectra are obtained on the unknown. A mass spectrum may be a reasonable option. The student should consult with the instructor to confirm that the spectra are of acceptable quality. The solubility tests and the spectra are then interpreted, leading to the identification of any functional group(s) present. Two or more classification tests should be run to confirm or deny the presence of any proposed functional group(s). Once the presence of a particular functional group is confirmed, then look in the derivative tables (Appendix II) under the type of functional group. The derivative tables are organized by boiling point or melting point of the functional groups. A list of possible structures for the unknown can then be proposed. The instructor may select unknowns that are not in the derivative tables. More classification tests may be done to further restrict the choices. Preparation of one or two derivatives is the final confirmation of the identity of the unknown.

In Figure 2.1, a systematic approach to the identification of an unknown sample is illustrated using a flowchart format. The melting point or boiling point, the solubility class, the IR spectrum, and the NMR spectrum were determined or obtained for the unknown prior to the first instruction in this chart. In this example, its solubility class was found to be class N. The possibilities for this solubility class include alcohols, aldehydes, ketones, esters with one functional group and more than five but fewer than nine carbons, ethers with fewer than eight carbons, epoxides, alkenes, alkynes, and aromatic compounds. Then, by referring to the IR spectrum, the NMR spectra, and the results of relevant classification tests, the functional group in the compound can be identified.

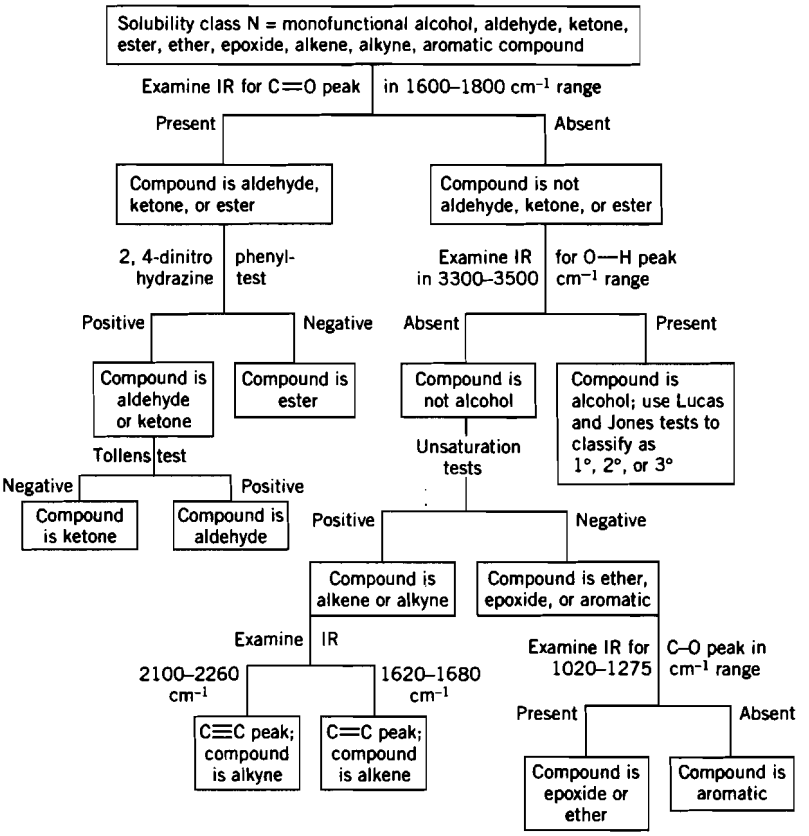


Figure 2.1 Example of a systematic approach to the identification of an unknown in solubility class N.

Next, the melting point or boiling point of the unknown is compared with the list of compounds in Appendix II.

In Figure 2.2, an unknown with a solubility class of S_1 is analyzed in a similar manner. The S_1 solubility class includes monofunctional alcohols, aldehydes, ketones, esters, nitriles, and amides with five carbons or less. An elemental test is useful in this analysis, since it will determine the presence or absence of the nitrile or amide.

To further illustrate the concept of identifying a compound, let us apply these techniques to an actual unknown. The melting point of the unknown was determined to be 80°C. In the elemental tests with sodium fusion (pp. 53–60), the unknown did not produce a black solid with lead sulfide; thus sulfur is absent. With 2-nitrobenzaldehyde and 1,2-dinitrobenzene in 2-methoxyethanol, a blue-purple compound was formed, showing that nitrogen is present. No precipitate was formed upon treatment of the sodium fusion filtrate with silver nitrate. Therefore halogen is absent.

Following the solubility procedures in Chapter 5 (pp. 114–115), the unknown was found to be insoluble in water and insoluble in 5% sodium hydroxide. A definitive result was not obtained when 5% hydrochloric acid was used. Thus the unknown would be classified as B, MN, N, or I. The solubility class B includes aliphatic amines with eight or more carbons, anilines, and some ethers. The solubility class MN includes miscellaneous neutral compounds containing nitrogen or sulfur and having more than five carbon atoms. The solubility class N includes alcohols, aldehydes, ketones, and esters

with one functional group and more than five but fewer than nine carbon atoms, ethers, epoxides, alkenes, alkynes, or aromatic compounds containing deactivating groups. Saturated hydrocarbons, haloalkanes, other deactivated aromatic compounds, and diaryl ethers are included in solubility class I.

In the ^{1}H NMR spectrum, a strong singlet at δ 2.77 ppm probably indicates an isolated methyl or methylene group. A multiplet in the range of δ 7.6–8.8 ppm shows that the unknown is an aromatic compound. The integration ratio of the singlet to the multiplet was 3:4, suggesting a disubstituted benzene ring and supporting the methyl group proposed above. In the IR spectrum, meta substitution on an aromatic ring is shown by peaks at 745 and 765 cm^{-1}.

Since a flowchart for solubility class N is presented in Figure 2.1, we can use it to assist us in the identification of the unknown. The presence of a strong carbonyl peak at 1670 cm^{-1} shows that the unknown is probably an aldehyde, a ketone, or an ester. The fact that this IR band is at less than 1700 cm^{-1} implies that the carbonyl group is conjugated with the benzene ring. A yellow-orange solid formed in the 2,4-dinitrophenylhydrazone test indicates that the compound is an aldehyde or a ketone. The Tollens test failed to produce a silver mirror, thus suggesting elimination of an aldehyde as a possibility. As a confirmation, the IR spectrum is examined for two peaks in the range of 2695–2830 cm^{-1} that correspond to the C—H stretch of an aldehyde. These peaks are absent in the IR spectrum of the unknown, confirming that the compound is not an aldehyde. The absence of a peak in the ^{1}H NMR spectrum in the range

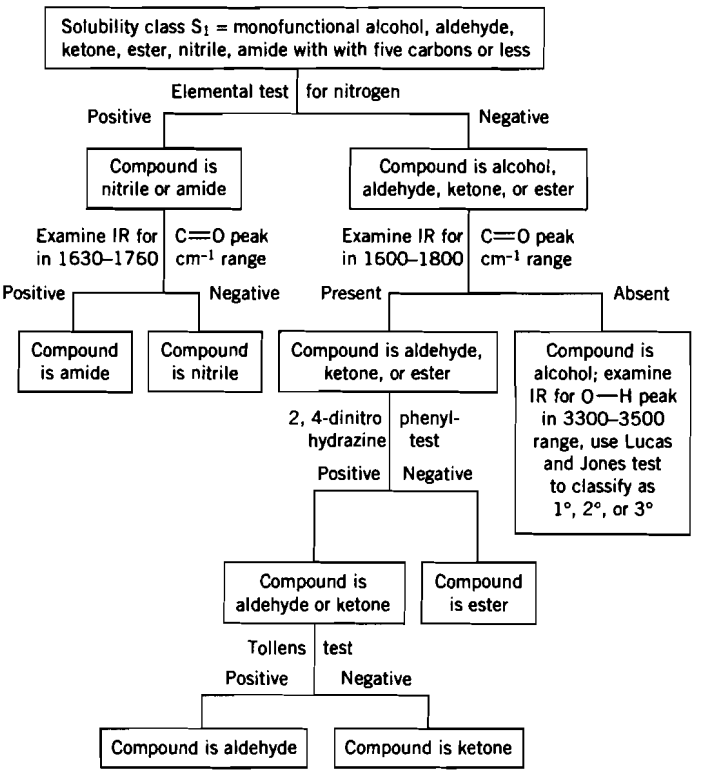


Figure 2.2 Example of a systematic approach to the identification of an unknown in solubility class S_1.

of δ 9.0–10.5, corresponding to the proton attached to the carbonyl in an aldehyde, also indicates that the unknown is not an aldehyde.

From the above information, we know that the compound is an aromatic compound containing nitrogen. In the ^{1}H NMR spectrum, a singlet at δ 2.77 ppm indicates the presence of an isolated methyl group. The classification tests confirm the presence of a ketone. The IR spectrum suggests meta substitution, but if a group meta to the methyl substituent is present, this group does not contain hydrogens since no other hydrogens are seen on the NMR spectrum. The positive test for nitrogen, however, suggests that this group may be something like a nitrile group or a nitro group.

In the IR spectrum, nitriles show a C≡N stretch in the range of 2220–2260 cm^{-1} and nitro compounds show two N(=O)$_2$ bands in the ranges of 1259–1389 and 1499–1661 cm^{-1}. In the IR spectrum of the unknown, there are no peaks in the 2200 cm^{-1} range, but peaks at 1350 and 1545 cm^{-1} indicate the presence of a nitro group.

At this time, the derivative tables (Appendix II) are consulted under the headings of ketone and nitro to find any compounds with this melting point that match the criteria above. The compounds listed below are ketones and nitro compounds that have a melting point in the range of 75–85°C.

Compound	*mp (°C)*
1-Naphthyl phenyl ketone	76
2-Benzoylfuryl methyl ketone	76
2-Naphthoxy-2-propanone	78
4-Phenylcyclohexanone	78
4-Chlorobenzophenone	78
1,4-Cyclohexanedione	79
1,3-Diphenyl-1,3-propadione	81
3-Nitroacetophenone	81
4-Bromobenzophenone	82
Fluorenone	83

The only compound that contains both a keto group and a nitro group is 3-nitroacetophenone.

Other strategies are possible. The derivative tables can be consulted earlier in the process. Chemical tests for the nitro group can be used. Other tests for the carbonyl group, such as semicarbazide, are possible. The 2,4-dinitrophenylhydrazine result already suggests that derivatives are possible. In summary, there are often a number of reasonable ways to deduce the structure.

The following sections only briefly outline each technique. Therefore the student should consult later chapters for a more thorough discussion.

2.1 PRELIMINARY EXAMINATION

[Refer to Chapter 3, pp. 22–24.] Note whether the substance is homogeneous, and record its physical state (solid or liquid), color, and odor. The student should not directly sniff the substance but merely note whether an odor is noticeable during general laboratory operations.

Thin-Layer and Gas Chromatography

[Refer to Chapter 4, pp. 86–90 and 90–99, respectively.] Simple thin-layer chromatography (TLC) and gas chromatography (GC) are very simple and direct methods of purity determination. TLC and GC analyses are optional; consult with your instructor. Observation of only a single developed spot on a thin-layer chromatogram (after using solvents of differing polarity), a single peak on a gas chromatogram, and a sharp melting point all lend strong support to a sample's purity. If the sample is a liquid or a solid, TLC should always be attempted. If the sample is a liquid, GC could be tried as well. Gas chromatography of reasonably volatile solids is also possible.

2.2 PHYSICAL PROPERTIES

[Refer to Chapter 3, pp. 25–37.] If the unknown is a solid, determine its melting point (pp. 25–30). If the melting point range encompasses more than 2.0°C, the compound should be recrystallized. Some pure compounds may not have a sharp melting point, especially if they undergo decomposition, such as turning dark, at or near the temperatures used for the melting point determination. If the unknown is a liquid or a very low melting solid, determine its boiling point (pp. 30–37); the range of this constant should not exceed 5.0°C except for extremely high boiling compounds. Distillation is recommended if the boiling point range indicates extensive contamination by a wide boiling point range, if the compound is heterogeneous, or if it appears to be discolored. Distillation at reduced pressure may be necessary for those compounds that show evidence of decomposition in the boiling point test.

As mentioned earlier, a sharp melting point is strong support for sample purity.[1] Narrow boiling point ranges do not, however, always indicate sample purity. Specific gravity (sp gr, pp. 38–42) was used in the past when NMR and IR spectroscopy were unavailable for structure determination. Occasionally specific gravity might be used for very inert compounds (e.g., certain hydrocarbons); in these situations, it might be one of the first steps in structure determination. Refractive index (pp. 42–45) values can be easily obtained and are of value in the identification of the unknown. NMR and IR spectroscopy have reduced the need for refractive index for initial structure determination.

2.3 MOLECULAR WEIGHT DETERMINATION

Molecular weight is normally very useful in determining organic structure; a reasonable estimate of the molecular formula can be postulated from the molecular weight. Mass spectrometry, discussed in Chapter 8, gives molecular weights for a wide range of organic compounds.[2] Molecular weights may also be obtained from neutralization equivalents (Procedure 1, p. 357) and saponification equivalents (Procedure 35, p. 404). These techniques apply to specific functional groups (Chapter 10).

[1]Sharp melting points are misleading; these do not, however, occur very frequently.

[2]Alternatively, instructors may feel compelled to provide the student with mass spectral data, molecular weights from colligative properties, or % C, H, N data in order to allow the student to have the experience of interpreting these data and applying them to structural determination.

2.4 MOLECULAR FORMULA DETERMINATION

[Consult Chapter 3, pp. 53–60] Simple "wet" or "test-tube" tests can be used to determine the presence of certain elements in the compound.

The compound should be tested for the presence of nitrogen, sulfur, chlorine, bromine, iodine, and fluorine (pp. 55–60). If a residue was noted in the ignition test, the student can identify the metal that it contains by inorganic qualitative methods.

Control Experiments

Results may be difficult to interpret, particularly if the student is unfamiliar with the procedure for decomposing the compound or with interpretation of the elemental tests. In this case, control experiments on a known compound should be carried out at the same time that the unknown is tested. The compound to be used for the control experiment should, of course, contain nitrogen, sulfur, and a halogen. A compound such as 4-bromobenzenesulfonamide is a good choice for the control experiments of this nature.

If mass spectrometry is available, an attempt should be made to determine the molecular formula of the organic compound from the cluster of peaks in the area of the molecular ion in the mass spectrum; these peaks are due to the isotopic contributions of elements in the molecular ion. Mass spectral data can also be used to determine the presence and number of elements in the molecule that make unusually large or unusually small contributions to peaks in the molecular ion cluster (Chapter 8).

Combustion analysis and other quantitative techniques for measuring elemental composition are useful in determining the structure of organic compounds; these procedures are generally not carried out in organic qualitative analysis labs, but the data from such procedures may be made available by the instructor.

The next stage in structural determination involves two steps. First, the student should determine the solubility (Chapter 5) to allow the placing of the unknown compound in a general structural class. Second, the student should determine the exact structure of the compound by detailed interpretation of the spectra (Chapters 6 through 8), by chemical tests (Chapter 9), and ultimately by chemical derivatization (Chapter 10).

2.5 SOLUBILITY TESTS

[Refer to Chapter 5, pp. 111–135.] Using the solubility chart in Figure 5.1 (p. 113), determine the solubility of the unknown in water, ether, 5% hydrochloric acid, 5% sodium hydroxide solution, 5% sodium bicarbonate solution, and/or cold concentrated sulfuric acid (pp. 114–115). If the classification is doubtful, repeat the tests with control compounds that will give positive solubility tests and compounds that will give negative solubility tests. Compare the results of these tests with your unknown.

We also recommend solubility studies in various organic solvents; results of these studies will be useful in choosing solvents for spectral analyses, for chromatographic analyses, and for purification by recrystallization.

When testing the solubility of the compound in water, the reaction to litmus (or other indicator paper) and phenolphthalein of the solution or suspension should be determined.

When the solubility behavior of the unknown has been determined, compose a list of the chemical classes to which the compound may belong. The results of these tests should agree with the information obtained from the IR and NMR spectra.

Preliminary Report

To avoid loss of time through mistaken observations, it is recommended at this point that the student consult with the instructor concerning the correct interpretation of the physical constants, elemental composition, and solubility behavior.

2.6 INFRARED, NUCLEAR MAGNETIC RESONANCE, AND MASS SPECTRA ANALYSES

Infrared and nuclear magnetic resonance spectroscopy are crucial to organic structural determination. Infrared analysis (Chapter 7) is an excellent functional group probe, which can be used in conjunction with the functional group chemical tests. Use of both IR and chemical tests *may* lead to structural diagnosis. Nuclear magnetic resonance (Chapter 6) also aids in the structure determination. NMR is essentially a method of determining the relative positions and numbers of spin-active nuclei. Both ^{1}H and ^{13}C NMR spectra can yield useful information concerning the types of protons or carbons present, such as aromatic or aliphatic; the number of adjacent protons (for ^{1}H NMR); and the number of protons attached to a particular carbon. Once some preliminary structures are chosen, mass spectrometry (Chapter 8) can be used to narrow down the choices by utilization of fragmentation patterns and molecular weight.

Interim Results

After interpretation of solubility results and IR and NMR analyses (recalling all results in the preliminary report), the student can usually propose one or more reasonable structures and subsequently proceed to the final characterization. Note that the instructor may well wish to review the student's interim results before the final characterization is attempted.

The final characterization stage involves application of the "wet" classification tests and detailed scrutiny of the NMR, IR, and perhaps the mass spectra, culminating in the derivatization of the compound; all of these steps are outlined below and discussed in detail in Chapters 6 through 10.

2.7 CLASSIFICATION TESTS

[Refer to Chapter 9, pp. 247–350.] From the evidence that has been accumulated, the student must deduce what functional group or groups are most likely to be present in the unknown and test for them by means of suitable classification reagents. About 47 of the most important of these are mentioned in Chapter 9, where directions for their use may also be found. In Table 9.1 these tests are arranged according to the functional groups for which they are most useful.

The student is strongly advised against carrying out unnecessary tests, since they are not only a waste of time but also increase the possibility of error. For example, it would be pointless to begin the functional group tests of a basic nitrogen-containing compound by testing for keto or alcohol groups. On the other hand, tests that can be expected to give information about the amino group are clearly indicated.

Several of the tests for ketones and aldehydes are, in general, easier to carry out and more reliable than tests for other oxygen functions. It is advisable, therefore, in the classification of a neutral compound suspected of containing oxygen, to begin with the carbonyl tests, especially when IR analysis has indicated the presence of a carbonyl group.

In this book we have provided directions on how to interpret IR, NMR, and mass spectra and have also included sample spectra of most of the typical organic functional groups. For additional aid in interpreting the spectra of these compounds, organic and instrumental analysis texts should be consulted.

After deducing the structure of an unknown compound, or perhaps a few possible structures, derivatization should be carried out to confirm this structure. Although the melting point of the derivative may be sufficient to allow correct choice of the identity of the unknown, it may also be useful to characterize the derivative by chemical and spectral means, in a similar manner to the procedure used for the characterization of the unknown.

2.8 PREPARATION OF A SATISFACTORY DERIVATIVE

[Refer to Chapter 10, pp. 351–441.] After the solubility tests, the NMR spectrum, the IR spectrum, and perhaps the mass spectrum and the elemental tests, the student should propose a list of possible compounds for the unknown sample. These possible compounds may contain a number of structural differences. More classification tests may be needed to confirm or deny the existence of particular functional groups. Other characteristic properties, such as specific gravity, refractive index, optical rotation, or neutralization equivalent, may also be desirable. The final confirmation for the identity of the unknown can be accomplished by the preparation of derivatives. An index to derivatization procedures by functional group class is listed in Table 10.1. The melting points of these derivatives are listed in Appendix II.

Properties of a Satisfactory Derivative

1. A satisfactory derivative is one that is easily and quickly made, readily purified, and gives a well-defined melting point. This generally means that the derivative must be a solid, because in the isolation and purification of small amounts of material, solids afford greater ease of manipulation. Also, melting points are more accurately and more easily determined than boiling points. The most suitable derivatives melt above 50°C but below 250°C. Most compounds that melt below 50°C are difficult to crystallize, and a melting point above 250°C is undesirable because of possible decomposition, as well as the fact that the standard melting point apparatus does not go higher than 250°C.
2. The derivative must be prepared by a reaction that results in a high yield. Procedures accompanied by rearrangements and side reactions are to be avoided.
3. The derivative should possess properties distinctly different from those of the original compound. Generally, this means that there should be a marked difference between its melting point and that of the parent substance.
4. The derivative chosen should be one that will single out one compound from among all the possibilities. Hence the melting points of the derivatives to be compared should differ from each other by at least 5°C.

For example, hexanoic anhydride (bp 257°C) and heptanoic anhydride (bp 258°C) would have very similar NMR and IR spectra. The amide derivatives, melting at 100°C and 96°C, respectively, are too similar to be useful. However, the anilide derivatives, hexananilide (mp 95°C) and heptananilide (mp 71°C), could be used to easily distin-

guish the two compounds. Consult Chapter 10 and select a suitable derivative from those suggested.

When determining the physical constants for a compound, considerable latitude must be allowed for experimental error. Thus, if the boiling point is very high or the melting point is very low, the range between the observed constant and the ones listed in the book must be extended somewhat beyond 5°C. Other constants such as specific gravity (pp. 38–42), refractive index (pp. 42–45), and neutralization equivalents (p. 357) may be used, with proper allowance for experimental error, to exclude compounds from the list of possibilities. A complete list of possible compounds with all of the derivatives for each should be compiled.

Examination of the list of possibilities often suggests that additional functional group tests need to be performed. For example, if a list of possible nitro compounds contains a nitro ketone, carbonyl tests may be valuable, especially if the IR spectrum is consistent with the presence of a carbonyl group.

If this text does not describe a useful procedure for the preparation of a derivative, a literature search can be made for more procedures. The most direct way to make a thorough search for a particular compound is to look for the molecular formula in the literature as described in Chapter 12.

2.9 MIXTURES

[Refer to Chapter 4, pp. 65–110.] At some time during the course, one or more mixtures may be assigned. After obtaining the mixture from the instructor, proceed with the separation according to the methods outlined in Chapter 4. The mixture may contain a volatile component which can be removed by heating the mixture on a steam bath. This volatile component would then be identified. In dealing with a mixture of unknown composition, it is inadvisable to attempt distillation at temperatures higher than 150°C.

When the components of the mixture have been separated, identify each according to the procedure followed for simple unknowns.

2.10 REPORT FORM

After the identification of an unknown has been completed, the results should be reported on special forms supplied by the instructor. The following report is an example illustrating the information to be reported. In the summary of the NMR data, abbreviations such as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and b (broad) are used. All spectra, as well as copies of literature (fingerprint) spectra, must be included with the report. Each report should be accompanied by a vial containing the derivative. A separate report should be written up for each component in a mixture. Please note that report forms at different schools may vary.

EXAMPLE OF A REPORT FORM

Compound *2-Amino-4-nitrotoluene* Name *John Smith*

Unknown Number *2* Date *March 17, 2004*

1. Physical Examination:
   (a) Physical state *Solid*
   (b) Color *Yellow*

(c) Odor _____

(d) Ignition test *Yellow flame, no residue*

(e) TLC _____

(f) GC _____

2. Physical Constants:

(a) mp: observed *107–108°C* ; corrected *109–110°C*

(b) bp: observed _____ ; corrected _____

3. Elemental Analysis:

F –, Cl –, Br –, I –, N +, S –,

Metals *None*

4. Solubility Tests:

H_2O	ether	NaOH	$NaHCO_3$	HCl	H_2SO_4
–		–		+	

Reaction to litmus: _____

Reaction to phenolphthalein: _____

Solubility class: *B*

Possible compounds: *Aliphatic amines with eight or more carbons, anilines (one phenyl group attached to nitrogen), some ethers*

5. Molecular Weight Determination: *150 ± 4 (freezing point depression, in camphor)*

6. IR Spectrum (attach to end of report):

Solvent: *KBr pellet*

Significant Frequencies (cm^{-1})	Inferences
3300–3400 (2 bands)	*$-NH_2$ primary*
1500, 1600	*C=C aromatic*
1260, 1550	*$-NO_2$*
2870	*C—H aliphatic*

7. NMR Spectrum (attach to end of report):

   Solvent: *$CDCl_3$/DMSO-d_6*

δ	Integration	Type of Peak (s, d, t, q, m)	Inferences
2.20	*3H*	*s*	*$ArCH_3$*
4.70	*2H*	*bs*	*aromatic —NH_2*
6.9–7.6	*3H*	*m*	*aromatic*

8. Mass Spectrum (attach to end of report):

M/Z Ratio	Inferences

9. Preliminary Classification Tests:

Reagent	Results	Inference
Hinsberg	*NaOH: clear solution; HCl: ppt*	*Primary amine*
Nitrous acid	*Orange ppt with 2-naphthol*	*Primary aromatic amine*

Functional group indicated by these tests:

Primary aromatic amine

10. Preliminary Examination of the Literature:

Possible Compounds	mp or bp (°C)	Suggestions for Further Tests
4-Aminoacetophenone	*106*	*Test for methyl ketone needed*
2-Amino-4-nitrotoluene	*107*	*Test for nitro group needed*
2-Naphthylamine	*112*	
3-Nitroaniline	*114*	*Test for nitro group needed*
4-Amino-3-nitrotoluene	*116*	*Test for nitro group needed*
		Run UV spectrum

11. Further Classification and Special Tests:

Reagent	Results	Inference
2,4-Dinitrophenylhydrazine	*No ppt*	*Not 4-amino-acetophenone*
Iodine and sodium hydroxide	*No iodoform*	*Not a methyl ketone*
Zinc and ammonium chloride; followed by Tollens reagent	*Silver mirror*	*Nitro group present*

12. Probable Compounds:

	Useful Derivatives and Their mp, NE, etc.		
Name	Benzene-sulfonamide (mp °C)	Acetamide (mp °C)	Phenol (mp °C)
2-Amino-4-nitrotoluene	*172*	*150*	*118*
3-Nitroaniline	*136*	*155*	*97*
4-Amino-3-nitrotoluene	*102*	*96*	*32*

13. Preparation of Derivatives:

Name of Derivative	Observed mp (°C)	Reported mp (°C)
Benzenesulfonamide	*170–171*	*172*
2-Hydroxy-4-nitrotoluene	*116–117*	*118*

14. Special Comments:

4-Amino-3-nitrotoluene has been reported to be hydrolyzed to 4-hydroxy-3-nitrotoluene [Neville and Winther, *Ber.* 1882, *15,* 2893]. *The unknown gave only starting material under these conditions. The unknown was converted to the phenol by the method reported by* Ullmann and Fitzenkam, *Ber.,* 1905, *38,* 3790.

15. Literature Used:

Additional References:

Pouchert, Charles J. *The Aldrich Library of* ^{1}H *and* ^{13}C *NMR Spectra* (Aldrich Chemical Company, Milwaukee, 1993).

CHAPTER 3

Preliminary Examination, Physical Properties, and Elemental Analysis

The investigator begins at this point when he or she has in hand a sample that is believed to be primarily one compound; if the investigator believes that the sample contains more than one component, Chapter 4 on separations should be consulted. The assumption that predominantly one component is present may be based on (1) the instructor's guidance, (2) the method of synthesis, (3) the method of isolation, and/or (4) chromatographic or other analytical results.

This chapter contains four major portions. The first (Sections 3.1 and 3.2) deals with the usual simple physical properties and the second (Sections 3.2–3.3) with more detailed and specialized methods of characterization. The simple properties include physical state, color, odor, and ignition tests (Section 3.1), and the simple physical constants (Section 3.2: melting point, boiling point, and, less frequently, specific gravity and index of refraction). In most teaching environments those two sections represent the bottom line of chemical characterization.

The third major portion involves the purification of the sample through recrystallization (Section 3.4) if the sample is a solid. The next portion involves the identification and quantification of the elements present. Qualitative elemental analysis (Section 3.5) is used to determine the presence of nitrogen, sulfur, and halogen. If the compound's empirical formula is determined (by combustion analysis, as described in Section 3.6) and the molecular weight is known, then the molecular formula can be determined.

3.1 PRELIMINARY EXAMINATION

3.1.1 Physical State

Note whether the unknown substance is a liquid or a solid. The tables of constants (Appendix II) are subdivided on the basis of phase. In addition, insofar as the phase relates to the solubility and volatility, an aid to the choice of purification method is provided. Liquids are usually purified by distillation (Section 4.2.1, pp. 67–71) or by gas chromatography (Section 4.4.2, pp. 90–99); solids are purified by recrystallization (Section 3.4, pp. 49–52) or by sublimation (Section 4.2.3, pp. 75–76).

3.1.2 Color

Note the color of the original sample as well as any change in color that may occur during the determination of the boiling point (Section 3.2.2, pp. 30–37), during

distillation (Section 4.2.1, pp. 67–73), or after chromatographic separation (Section 4.4, pp. 84–110).

The color of some compounds is due to impurities; frequently these are produced by the slow oxidation of the compound by oxygen in the air. Aniline, for example, is usually reddish brown, but a freshly distilled sample is colorless.

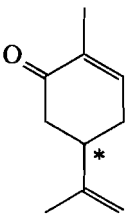
Many liquids and solids are definitely colored because of the presence of chromophoric groups in the molecule. Many nitro compounds, quinones, azo compounds, stable carbocations and carbanions, and compounds with extended conjugated systems are colored. If an unknown compound is a stable, colorless liquid or a white crystalline solid, this information is valuable because it excludes chromophoric functional groups as well as many groups that would become chromophores by oxidation.

3.1.3 Odor

We cannot in good conscience recommend that you examine the odor of an organic compound by direct inhalation. Frequently organic compounds have at least some degree of toxicity, and their uses are often regulated. The odor of many organic compounds will, however, quickly become evident during the course of normal handling; when that happens, you should make note of it.

It is not possible to describe odor in a precise manner, but some basic facts are well known. Amines often have a distinctly fishy smell and thus they frequently are easily identified. Some amines have common or trivial names that suggest odors; for example, cadavarine and putrescine. Thiols (or mercaptans) and organic sulfides (thioethers) are easily detected by their rotten egg smell, an odor that you may have encountered when dealing with hydrogen sulfide. Carboxylic acids of low molecular weight have distinct and noxious odors: acetic acid yields the bad smell in vinegar, while butanoic (or butyric) acid has the smell of unwashed gym socks. Esters usually have pleasant smells that are often characterized as fruity. For example, 3-methylbutyl ethanoate (isopentyl or isoamyl acetate) is often referred to as "banana oil." Hydrocarbons can have very different smells: naphthalene has been used as mothballs, and thus the odor should be recognizable; pinenes are components of turpentine, and therefore they have the odor of paint thinner. Benzaldehyde, nitrobenzene, and benzonitrile all have odors that have been described as "cherry-like" or the odor of "bitter almonds." The origins of some organic compounds suggest distinct smells; for example, eugenol (from cloves), coumarin (from lavender oil and sweet clover), and methyl salicylate (oil of wintergreen). Other compound classes have distinguishable but less pronounced odors. Thus aldehydes are different from ketones, and both are different from alcohols. Phenols also have unique odors, and isonitriles have very disagreeable odors.

The theory of odor is certainly dependent upon stereochemistry. A pertinent case is that of carvone: the (+), or dextrorotatory, stereoisomer has an odor quite consistent with the fact that it can be isolated from caraway or dill seeds. On the other hand, the (−), or levorotatory, form is a major component of spearmint.



carvone

Toxicity information is usually available on the bottle label and in catalogs such as that available from Aldrich Chemical Co. All labs must provide *MSD* sheets describing the toxicity of any organic compound used in that laboratory. The *Merck Index* can also be consulted for more information.

3.1.4 Ignition Test

Procedure

Place a 10-mg sample of the substance in a porcelain crucible lid (or any piece of porcelain) and bring the sample to the edge of a flame to determine flammability. Heat the sample gently over a low flame, behind a safety shield. Heat the sample until ignition has occurred. Note (1) the flammability and nature of the flame (is the compound explosive?); (2) whether the compound is a solid, whether it melts, and the manner of its melting; (3) the odor of the gases or vapors evolved (*caution!*); and (4) the residue left after ignition. Will it fuse? If a residue is left, allow the lid to cool. Add a drop of distilled water. Test the solution with litmus paper. Add a drop of 10% hydrochloric acid. Note whether a gas evolves. Perform a flame test, with a platinum wire, on the hydrochloric acid solution to determine the metal present.

Discussion

Many liquids burn with a characteristic flame that assists in determining the nature of the compound. Thus, an aromatic hydrocarbon (which has a relatively high carbon content) burns with a yellow, sooty flame. Aliphatic hydrocarbons burn with flames that are yellow but much less sooty. As the oxygen content of the compound increases, the flame becomes more and more clear (blue). If the substance is flammable, the usual precautions must be taken in subsequent manipulation of the compound. This test also shows whether the melting point of a solid should be taken and indicates whether the solid is explosive.

If an inorganic residue[1] is left after ignition, it should be examined for metallic elements. A few simple tests will often determine the nature of the metal present.[2] If the flame test indicates sodium, a sample of the compound should be ignited on a platinum foil instead of a porcelain crucible cover. (Why?)

3.1.5 Summary and Applications

The tests in this section are extremely useful for decisions as to whether further purification is necessary and as to what type of purification procedures should be used. If various tests in this section indicate that the compound is very impure, recrystallization (Section 3.4) or chromatography is almost certainly required. Although liquids are very often easily analyzed by gas chromatography (Section 4.4.2), those that leave residues upon ignition should *not* be injected into the gas chromatograph.

[1]A "residue" becomes identifiable with a little experience. A residue is more than a small streak of blackened remains; the amount should correspond to a reasonable percentage of the original sample. The control samples cited earlier containing metal (sodium, barium) ions should be ignited as a reference.

[2]Consult a book on inorganic qualitative analysis.

3.2 DETERMINATION OF PHYSICAL PROPERTIES

3.2.1 Melting Points and Freezing Points

The melting point of a compound is the temperature range at which the solid phase changes to liquid. Since this process is frequently accompanied by decomposition, the value may be not an equilibrium temperature but a temperature of transition from solid to liquid only. If the ignition test indicates that a solid melts easily (25–300°C), the melting point should be determined by Procedure A. For higher melting point ranges (300–500°C), use special equipment. If a melting point determination by Procedure A indicates definite decomposition or transition from one crystalline state to another, Procedure B is recommended. Compounds melting between 0°C and 25°C may be analyzed by the freezing point method described on p. 29.

Melting points for a large number of compounds and their derivatives are listed in this book. Frequently a small amount of impurity will cause a depression (and broadening) of the observed melting point. Thus the procedure of determining melting points of mixtures described below is strongly recommended. If, for any of a number of reasons, one has a compound that is contaminated by minor amounts of impurities, the section on recrystallization should be consulted (see Section 3.4).

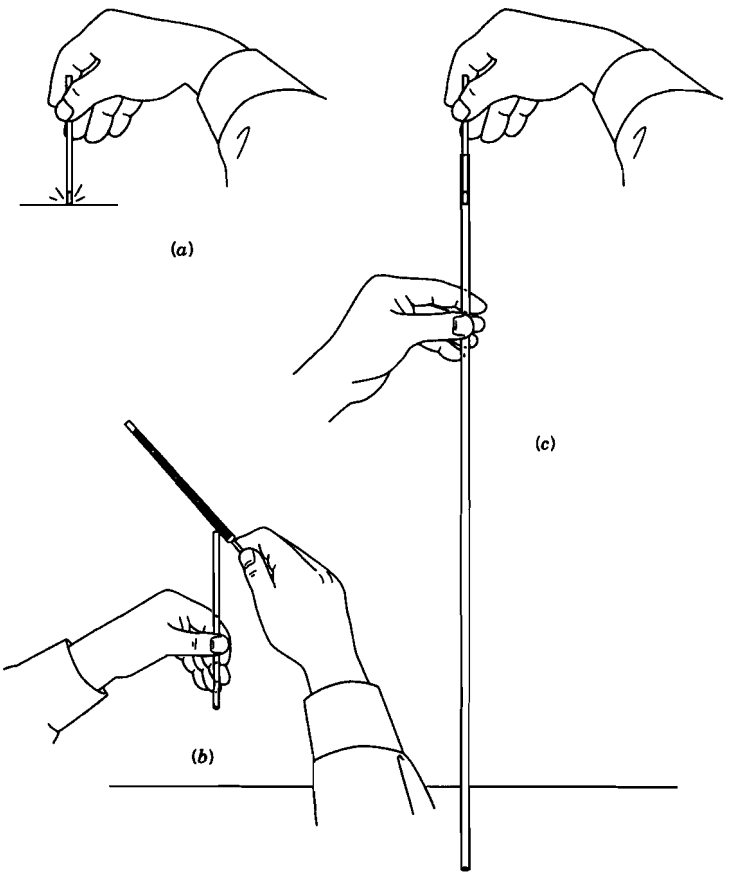


Figure 3.1 Charging (*a*) and packing (*b*, *c*) capillary melting point tubes.

Procedure A

For melting point determinations, many commercial melting point capillary tubes are available. These tubes are typically 1.1–1.8 mm wide and 90–100 mm long. One end is sealed. Use a new melting point capillary tube for each melting point. Place a small amount of the sample, approximately one-half of a spatula, on a hard, clean surface such as a watch glass. Tap the open end of the capillary tube into the sample until a few crystals are in the tube (Figure 3.1*a*). Hold the capillary tube vertically, open end up, and tap it gently on the counter so that the crystals pack to the bottom. If necessary, rub it with a file or a coin with a milled edge (Figure 3.1*b*) or drop it through a glass tube (Figure 3.1*c*) to move the crystals to the bottom. The capillary tube should contain 2–3 mm of sample. Use the capillary tube in melting point apparatuses such as the Thomas–Hoover melting point apparatus (Figure 3.2), a Thiele tube (Figure 3.3), or a Mel-Temp melting point apparatus (Figure 3.4).

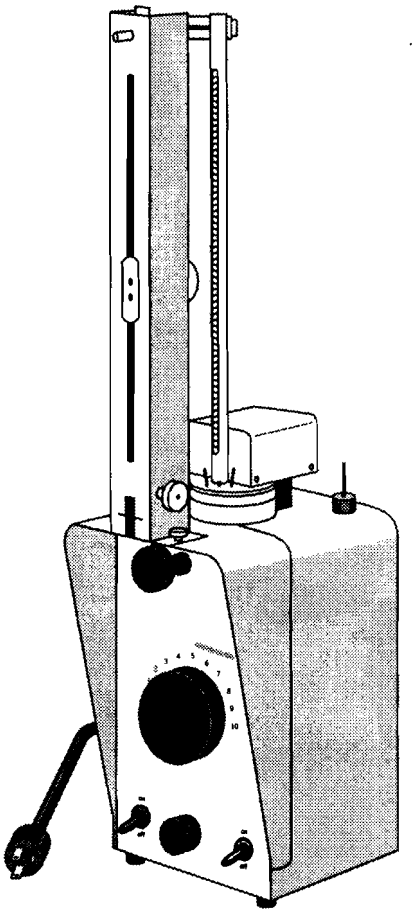


Figure 3.2 Thomas–Hoover Uni-Melt melting point apparatus.

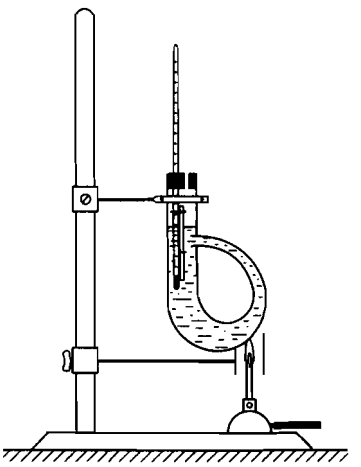


Figure 3.3 Thiele tube melting point apparatus.

Another type of melting point apparatus is the Fisher–Johns apparatus (Figure 3.5). This apparatus has an electrically heated aluminum block fitted with a thermometer reading to 300°C. Place the sample between two 18-mm microscope cover glasses. Place the cover glasses in the depression of the aluminum block. Regulate the temperature

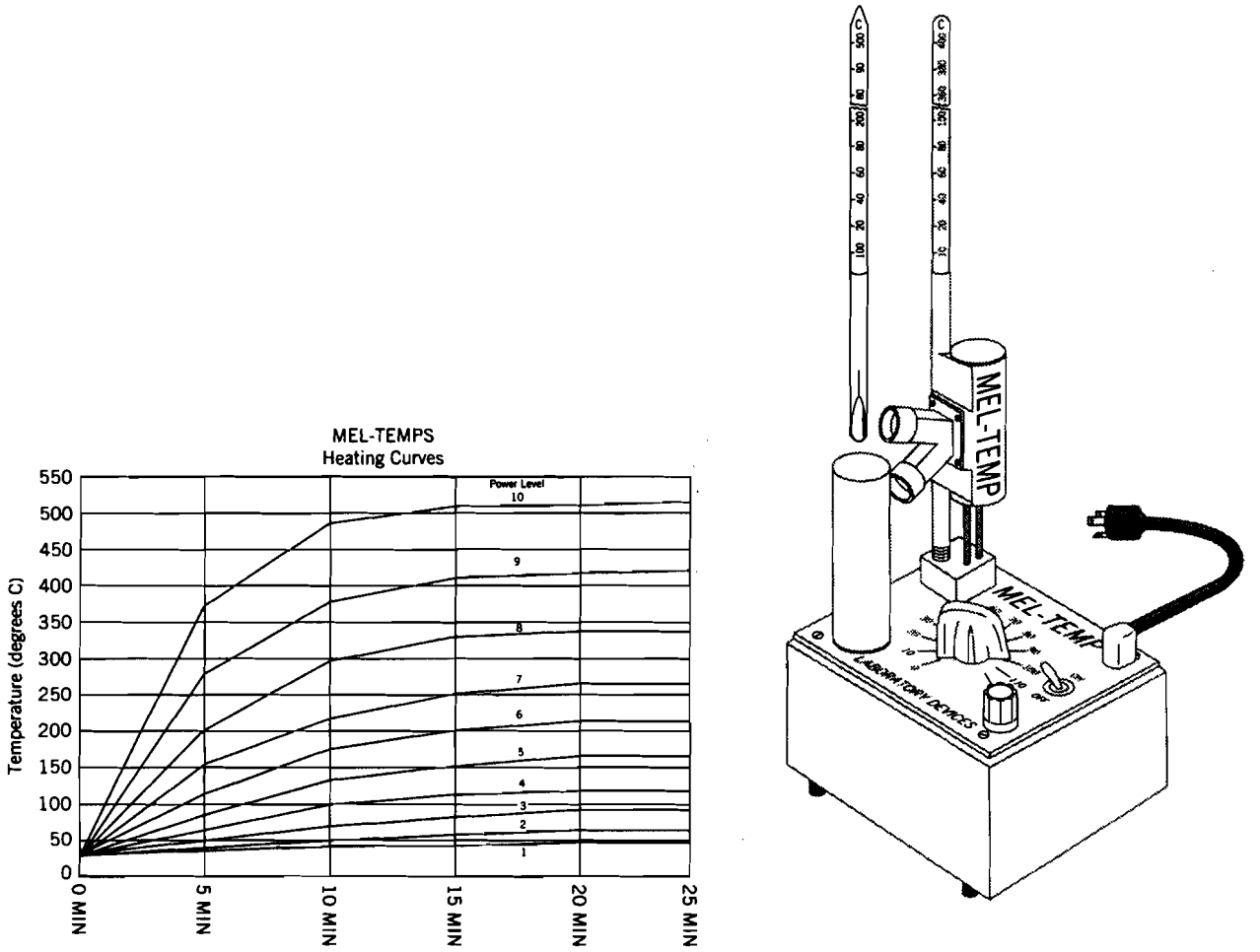


Figure 3.4 Barnstead–Thermolyne Mel-Temp melting point apparatus. [Graph supplied by Barnstead International. Used with permission.]

with the variable transformer. Observe the melting point with the aid of the illuminator and the magnifying glass. Prepare a calibration curve for the instrument by reference to known compounds as described below.

It is often timesaving to run a preliminary melting point determination, raising the temperature of the bath very rapidly. After the approximate melting point is known, raise the temperature to within 5°C of the approximate value and then proceed slowly as described above. Use a fresh sample of the compound for each melting point determination.

Corrected Melting Points

The thermometer should always be calibrated by observing the melting points of several pure compounds (Table 3.1). If care is taken to use the same apparatus and thermometer in all melting point determinations, it is convenient and timesaving to prepare a calibration curve such as that shown in Figure 3.6. The observed melting point of the standard compound is plotted against the corrected value, and a curve, *DA*, is drawn

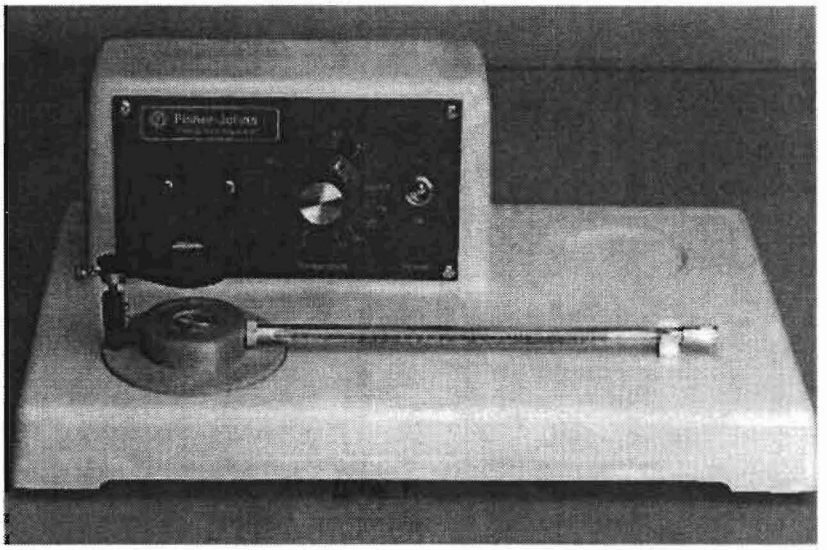


Figure 3.5 Fisher–Johns melting point apparatus. [Reproduced with permission of Fisher Scientific.]

TABLE 3.1 Melting Point Standards

mp (corr.) (°C)		mp (corr.) (°C)	
0	Ice	187	Hippuric acid
53	*p*-Dichlorobenzene	200	Isatin
90	*m*-Dinitrobenzene	216	Anthracene
114	Acetanilide	238	1,3-Diphenylurea
121	Benzoic acid	257	Oxanilide
132	Urea	286	Anthraquinone
157	Salicylic acid	332	*N,N'*-Diacetylbenzidine

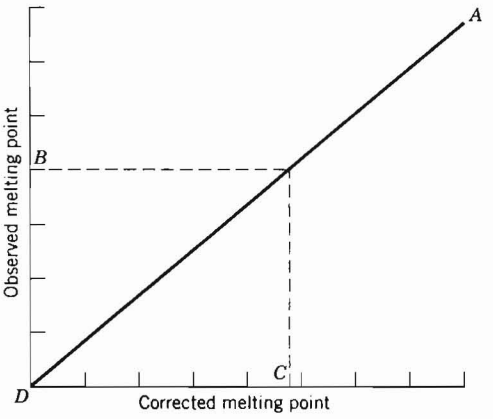


Figure 3.6 Melting point calibration curve.

through these points. In subsequent determinations the observed value, *B*, is projected horizontally to the curve and then vertically down to give the corrected value, *C*. Such a calibration curve includes corrections for inaccuracies in the thermometer and stem correction. The thermometer should be calibrated by observing the melting points of several pure compounds.

It is important to record the melting point range of an unknown compound, because this is an important index of purity. A large majority of pure organic compounds melt within a range of 0.5°C or melt with decomposition over a narrow range of temperature (about 1°C). If the melting point range or decomposition range is wide, the compound should be recrystallized from a suitable solvent and the melting or decomposition point determined again. Some organic compounds, such as amino acids, salts of acids or amines, and carbohydrates, melt with decomposition over a considerable range of temperature.

Mixture Melting Points

The "mixed melting point" method provides a means of testing for the identity of two solids (which should, of course, have identical melting points) by examination of the melting point behavior of a mechanical mixture of the two. In general, a mixture of samples of nonidentical compounds shows a melting point depression. Although the use of mixed melting points is valuable at certain points of the identification procedure, a mixed melting point of an unknown with a known sample from the side shelf will not be accepted in this course as proof of the structure.

A few pairs of substances when mixed show no melting point depression, but more frequently the failure to depress may be observed only at certain compositions. It requires little additional effort to measure the melting points of mixtures of several compositions if the following method is used.

Make small piles of approximately equal sizes of the two components (A and B) being examined. Mix one-half of pile A with one-half of pile B. Now separate the mixture of A and B into three equal parts. To the first add the remainder of component A, and to the third, the remainder of component B. It is seen that three mixtures with the compositions 80% A, 20% B; 50% A, 50% B; and 20% A, 80% B are obtained. The melting points of all three mixtures may be measured at the same time by any of the preceding procedures.

Freezing Points

Place 5–10 mL of the liquid in an ordinary test tube fitted with a thermometer and a wire stirrer made of copper, nickel, or platinum. Fasten the tube in a slightly larger test tube by means of a cork and cool them in an ice or ice–salt bath or an acetone–dry ice bath (Figure 3.7). Stir the liquid vigorously. As soon as crystals begin to form, remove the tubes from the bath. Continue the vigorous stirring and read the temperature on the thermometer. The freezing point is the temperature reached after the initial supercooling effect has disappeared. The temperature of the cooling bath should not be too far below the freezing point of the compound. The freezing points of most organic liquids are only approximate due to the relatively large amount of sample.

The presence of impurities in the sample can lead to a freezing point depression. This colligative property is discussed, in much detail, in general chemistry textbooks.

A more elaborate apparatus for determining freezing points (down to −65°C) has been described.[3]

[3]R. J. Curtis and A. Dolenga, *J. Chem. Educ.*, *52*, 201 (1975).

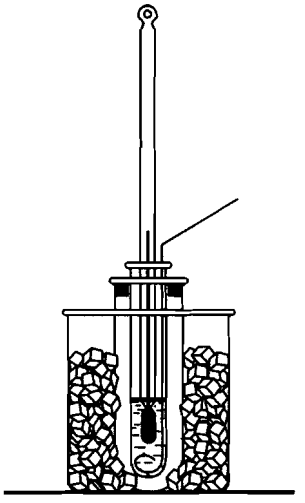


Figure 3.7 Simple freezing point apparatus.

3.2.2 Boiling Points

The use of boiling points (bp) for compound identification was introduced in Chapter 2 (p. 13).

Procedure A

Set up a simple distillation as illustrated in Figure 3.8. Add a few boiling chips and 10 mL of the unknown liquid. Insert the thermometer so that the top of the mercury bulb is just below the side arm. If necessary, wrap the distilling head in glass wool to prevent heat loss. Heat the liquid to boiling using a sand bath (illustrated in Figure 3.8),

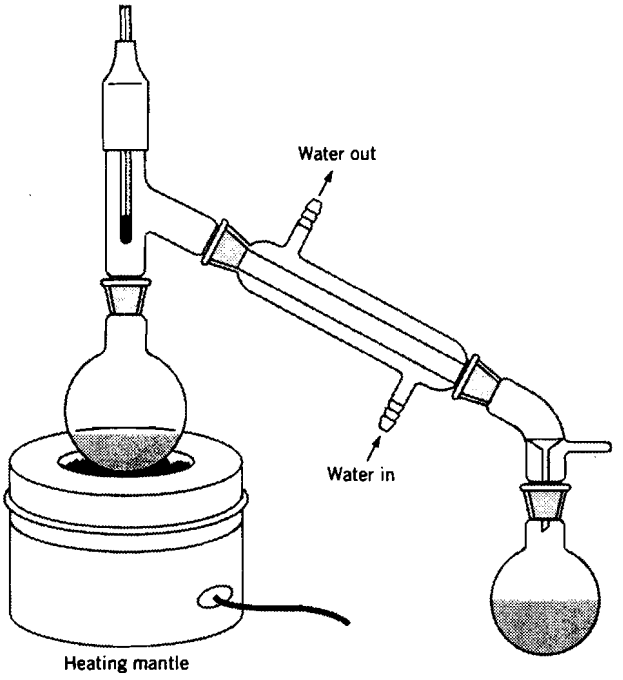


Figure 3.8 A small-scale simple distillation apparatus. Sand has been used to fill in the well.

a heating mantle, a heating block, or a Bunsen burner. For liquids with low boiling points, use steam or a hot-water bath. Distill the liquid at as uniform a rate as possible. Change the receiver, without interruption of the distillation, after the first 2–3 mL of liquid has been collected. Collect the next 5–6 mL in a dry receiver. Record the boiling point range during the distillation of the second portion of the liquid.

Great care should be exercised against overrelying upon boiling point as a criterion of purity or a basis for identity. Atmospheric pressure variations have a significant effect upon boiling point. Many organic liquids are hygroscopic, and some decompose on standing. Generally the first few milliliters of distillate will contain any water or more volatile impurities, and the second fraction will consist of the pure substance. If the boiling point range is large, the liquid should be refractionated through a suitable column (see Chapter 4 pp. 68–70).

The boiling point determined by the distillation of a small amount of liquid as described above is frequently in error. Unless special care is taken, the vapor may be superheated; also, the boiling points observed for high-boiling liquids may be too low because of the time required for the mercury in the thermometer bulb to reach the temperature of the vapor. The second fraction collected above should be used for a more accurate boiling point determination by Procedure B below. *Portions of the main fraction should also be used for the determination, as far as possible, of all subsequent chemical, spectral, and physical tests.*

Procedure B

Place a thermometer 1–1.5 cm above approximately 0.5 mL of the liquid in a test tube (Figure 3.9). Slowly heat the liquid to boiling so that the thermometer bulb is immersed in the vapor. Allow the temperature to remain at a constant value for 30 sec. This value is the boiling point of the liquid. This technique is also useful for determining the boiling point of some low-melting solids provided they are thermally stable.

Figure 3.9 Boiling point determination: Procedure B.

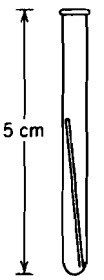


Figure 3.10 Micro boiling point tube.

Procedure C

Set up a micro boiling point tube (Figure 3.10). Use a 5-cm test tube for the outer tube. Add two drops of the unknown liquid. Place an inverted sealed capillary tube inside the

test tube. Place the micro boiling point tube in a Thiele tube (Figure 3.3). Raise the temperature until a rapid and continuous stream of bubbles comes out of the small capillary tube and passes through the liquid. Remove the heat and allow the Thiele tube to cool. Note the temperature at the instant bubbles cease to come out of the capillary and immediately before the liquid enters it. Record this temperature as the boiling point of the liquid.

Procedure D

The ultramicro boiling point determination procedure uses a glass bell inside of a melting point tube. Use a purchased glass bell or prepare one by heating 3-mm O.D. Pyrex glass tubing and drawing it out very thin so that it will fit inside of a melting point capillary tube (Figure 3.11*a*). Fuse the drawn tube at one end (Figure 3.11*b*) to give the bell sufficient weight. Inject the melting point capillary tube with 3–4 μL of the unknown liquid, using a 10-μL syringe. Insert the glass bell, with the open end down, into the melting point capillary tube (Figure 3.11*c*). If necessary, centrifuge the liquid and the glass bell to the bottom of the capillary tube. Place the entire unit in a standard melting point apparatus. Measure the boiling point by rapidly raising the temperature to 15–20°C below the boiling point of the liquid, which was estimated by a preliminary run on the unknown. Slow the heating rate to an increase of 2°C/min and continue this rate until a fine stream of bubbles is emitted from the end of the bell. Adjust the heat so that the temperature drops. Record the boiling point at the point when the last bubble collapses. This procedure may be repeated on the same sample.

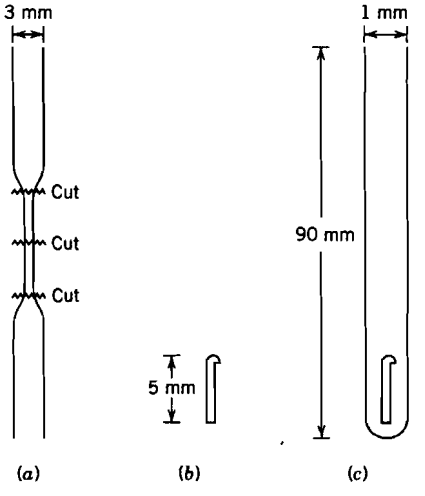


Figure 3.11 Ultramicro boiling point. (*a*) Preparation of a small glass bell; (*b*) the completed glass bell with a fused tip; (*c*) the glass bell in a capillary melting point tube. [From a description by Mayo, Pike, Butcher, and Meredith, *J. Chem. Educ.*, 62 (12), 1114–1115 (1985).]

Effect of Pressure on Boiling Point

At the time the boiling point is being determined, the atmospheric pressure should be recorded. Table 3.2 illustrates the magnitude of such barometric "corrections" of boiling point for pressures that do not differ from 760 mm by more than about 30 mm.

These corrections are applied in the following equation:

$$\text{corr bp} = \text{obs bp} + \frac{760 - \text{obs pressure}}{10 \text{ mm}} \left\{ \left(\frac{\Delta \text{ factor}}{\Delta T_1} \times \Delta T_2 \right) + \text{original factor} \right\}$$

TABLE 3.2 Boiling Point Changes per Slight Pressure Change

bp (°C)	bp (K)	Correction in °C for 10-mm Difference in Pressure: Nonassociated[a] Liquids	Correction in °C for 10-mm Difference in Pressure: Associated[a] Liquids
50	323	0.38	0.32
100	373	0.44	0.37
150	423	0.50	0.42
200	473	0.56	0.46
300	573	0.68	0.56
400	673	0.79	0.66
500	773	0.91	0.76

[a]Associated liquids are those liquids that have substantial intermolecular associations due to hydrogen bonding; an example is methanol.

where

corr bp = corrected boiling point
obs bp = observed boiling point
obs pressure = observed pressure
Δ factor = difference in correction
ΔT_1 = difference in boiling points
ΔT_2 = observed boiling point − lowest of two boiling points
original factor = lowest of two corrections

Example Problem

Calculate the corrected boiling point of a compound that has an observed boiling point of 125°C at 700 mm pressure.

ANSWER

Since the problem did not state whether the compound was associated or nonassociated, both equations will be shown.

For a nonassociated liquid, the corrected bp is calculated as shown below:

$$\text{corr bp} = 125°\text{C} + \frac{760 - 700 \text{ mm}}{10 \text{ mm}} \left\{ \left(\frac{0.50 - 0.44}{150 - 100} \times 125 - 100 \right) + 0.44 \right\}$$

$$= 127.8°\text{C}$$

For an associated liquid, a slightly different answer is obtained:

$$\text{corr bp} = 125°\text{C} + \frac{760 - 700 \text{ mm}}{10 \text{ mm}} \left\{ \left(\frac{0.42 - 0.37}{150 - 100} \times 125 - 100 \right) + 0.37 \right\}$$

$$= 127.4°\text{C}$$

Problems

1. Calculate the corrected boiling point for an aromatic halide that had an observed boiling point of 167°C at 650 mm Hg. Give the name and structure of the compound. (*Hint:* Use Appendix II).
2. Calculate the corrected boiling point for an alcohol that contained halogen and that had an observed boiling point of 180°C at 725 mm Hg. Give the name and structure of the compound.
3. Using the pressure–temperature nomograph in Appendix I, give the corrected bp of a compound that has a bp of 120°C at 10 mm.
4. Give the bp of a compound at 25 mm that has a corrected bp of 250°C.

Azeotropes

In some cases, a two- or three-component mixture will distill at one constant temperature and cannot be separated into its components through distillation. These mixtures are examples of azeotropes. The vapor of the azeotrope has the same composition as the boiling liquid.

It is evident that small deviations in pressure from 760 mm, such as 5 mm, may be neglected in ordinary work.

Investigators working in laboratories at high altitudes[4] and low barometric pressures have found it convenient to determine a set of empirical corrections to be added to observed boiling points in order to get boiling points at 760 mm. The corrections are obtained by distilling a number of different types of compounds with different boiling points. The difference between the boiling point recorded in the literature and the observed boiling point gives the correction.

Nomographs for boiling point versus pressure data of organic compounds have been devised; these charts are useful for vacuum distillations. An example is provided in Appendix I.

In order to give an idea of the change in boiling point with pressure, the data on three pairs of nonassociated and associated compounds are given in Table 3.3. The tem-

[4]At the top of Mt. Evans in Colorado, water boils at 81°C (average pressure 460–470 mm; altitude 14,200 ft). Water boiling at the University of Colorado (ca. 5000 ft) will have a temperature of about 90°C.

TABLE 3.3 Boiling Points (°C) at Reduced Pressures

	Pressure in Millimeters of Mercury (torr)					
Compound	760	700	650	600	550	ΔT^a
Heptane	98	96	94	91	88	10
1-Propanol	97	95	93	91	89	8
Iodobenzene	188	185	182	179	175	13
Pentanoic acid	186	183	180	178	175	11
Fluorene	298	294	290	286	282	16
2-Naphthol (β-naphthol)	295	292	288	284	280	15

[a]$\Delta T = bp_{760} - bp_{550}$.

peratures are given to the nearest whole degree. The data indicate that, as the pressure is reduced, the boiling point of an associated compound does not fall off as much as the boiling point of a nonassociated liquid.

Correlations of Boiling Point with Structure

The boiling points of the members of a given homologous series increase as the series is ascended. The boiling points rise in a uniform manner, as shown in Figure 3.12, but the increment per CH_2 group is not constant, being greater at the beginning of the series than for the higher members (Table 3.4).

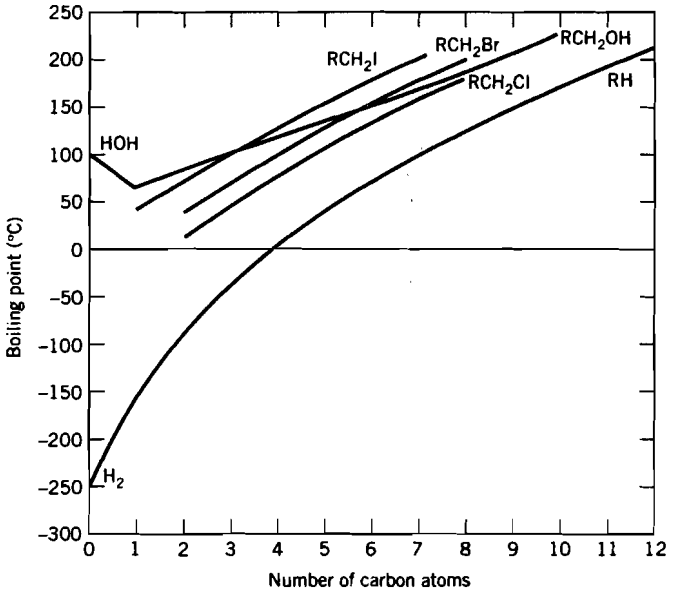


Figure 3.12 Relationship between boiling point and molecular weight.

If a hydrogen atom of a saturated hydrocarbon (alkane) is replaced by another atom or group, an elevation of the boiling point results. Thus alkyl halides, alcohols, aldehydes, ketones, acids, and so on boil higher than the hydrocarbons with the same carbon skeleton.

If the group introduced is of such a nature that it promotes association, a very marked rise in boiling point occurs. This effect is especially pronounced in the alcohols (Figure 3.12) and acids because of hydrogen bonding. For example, the difference in boiling point between propane (nonassociated) and 1-propanol (associated) is 142°C—a difference far greater than the change in molecular weight would indicate. As more hydroxyl groups are introduced, the boiling point rises, but the change is not as great as that caused by the first hydroxyl group. Nevertheless, the increment per hydroxyl group is much greater than the increment per methylene group (Tables 3.4 and 3.5).

If the hydroxyl groups are converted to ether linkages, the association due to hydrogen bonds is prevented and the boiling point drops. The following series illustrates this effect:

	CH_2OH	$CH_2OC_2H_5$	$CH_2OC_2H_5$	$CH_2OC_2H_5$
	$CHOH$	$CHOH$	$CHOH$	$CHOC_2H_5$
	CH_2OH	CH_2OH	$CH_2OC_2H_5$	$CH_2OC_2H_5$
bp(°C):	+290	+230	+191	+185

TABLE 3.4 Boiling Point and Chain Length for Straight-Chain Alkanes

	bp (°C)	Δ^a
Pentane	36	
		32
Hexane	68	
		30
Heptane	98	
		27
Octane	125	
		24
Nonane	149	
		24
Decane	173	
		21
Undecane	194	
		21
Dodecane	215	

[a]Δ = change in boiling point for addition of one methylene group.

TABLE 3.5 Boiling Point and Hydroxyl Group Substitution

	$CH_3CH_2CH_3$	$CH_3CH_2CH_2OH$	$CH_2OHCH_2CH_2OH$	$CH_2OHCHOHCH_2OH$
bp(°C)	−45	+97	+216	+290
Δ/OH(°C)		142	119	74

A comparison of oxygen derivatives with their sulfur analogs also shows that association is a more potent factor than molecular weight. The thiol (RSH) compounds are associated only slightly and hence boil lower than their oxygen analogs, even though the former have higher molecular weights than the latter.

	bp (°C)		bp (°C)
HOH	100	HSH	−62
CH_3OH	66	CH_3SH	+6
CH_3COOH	119	CH_3COSH	93

Ethers and thio ethers are not associated, and hence the alkyl sulfides boil higher than the ethers because they have higher molecular weights:

	bp (°C)		bp (°C)
$(CH_3)_2O$	−24	$(CH_3)_2S$	+38
$(C_2H_5)_2O$	+35	$(C_2H_5)_2S$	+92

These data on sulfur and oxygen compounds, and on hydrocarbons, alkyl chlorides, bromides, and iodides illustrate the general rule that replacement of an atom by an atom of higher atomic weight causes a rise in the boiling point, provided that no increase or decrease in the extent of association takes place as a result of this substitution.

Just as with solubility relationships (Chapter 5, pp. 119–120), branching of the chain and position of the functional group influence the boiling point. The saturated aliphatic alcohols (Table 3.6) serve to illustrate the following generalizations:

TABLE 3.6 Alcohol Boiling Point and Branching

Primary Alcohols		Secondary Alcohols		Tertiary Alcohols	
Structure	bp(°C)	Structure	bp(°C)	Structure	bp(°C)
CH_3OH	66				
CH_3CH_2OH	78				
$CH_3CH_2CH_2OH$	97	$CH_3\underset{\displaystyle OH}{\underset{\vert}{C}}HCH_3$	83		
$CH_3CH_2CH_2CH_2OH$	118	$CH_3CH_2\underset{\displaystyle OH}{\underset{\vert}{C}}HCH_3$	100	$CH_3-\underset{\displaystyle OH}{\underset{\vert}{\overset{\displaystyle CH_3}{\overset{\vert}{C}}}}-CH_3$	83
$CH_3\underset{\displaystyle CH_3}{\underset{\vert}{C}}HCH_2OH$	108				
$CH_3CH_2CH_2CH_2CH_2OH$	138	$CH_3CH_2CH_2\underset{\displaystyle OH}{\underset{\vert}{C}}HCH_3$	120		
$CH_3\underset{\displaystyle CH_3}{\underset{\vert}{C}}HCH_2CH_2OH$	132	$CH_3CH_2\underset{\displaystyle OH}{\underset{\vert}{C}}HCH_2CH_3$	116		
$CH_3-\underset{\displaystyle CH_3}{\underset{\vert}{\overset{\displaystyle CH_3}{\overset{\vert}{C}}}}-CH_2OH$	113	$CH_3\underset{\displaystyle CH_3}{\underset{\vert}{C}}H-\underset{\displaystyle OH}{\underset{\vert}{C}}HCH_3$	114	$CH_3CH_2-\underset{\displaystyle OH}{\underset{\vert}{\overset{\displaystyle CH_3}{\overset{\vert}{C}}}}-CH_3$	102

1. Among isomeric alcohols, the straight-chain isomer has the highest boiling point.
2. If comparisons are made of alcohols of the same type, the greater the branching of the chain, the lower the boiling point.
3. A comparison of the boiling points of isomeric primary, secondary, and tertiary alcohols shows that primary alcohols boil higher than secondary alcohols, which, in turn, boil higher than tertiary alcohols provided that isomeric alcohols with the same maximum chain length are compared.

A knowledge of the boiling points of some simple compounds is frequently of value in excluding certain types of compounds. The following simple generalizations are helpful.

1. An organic chloro compound that boils below 132°C must be aliphatic. If it boils above 132°C, it may be either aliphatic or aromatic. This follows from the fact that the simplest of aryl halides, chlorobenzene, boils at 132°C.
2. Similarly, an organic bromo compound that boils below 157°C or an iodo compound that boils below 188°C must be aliphatic. Other bromo and iodo compounds may be either aliphatic or aromatic.

3.2.3 Specific Gravity

The use of specific gravity in compound identification can be a useful fingerprint. Recall that specific gravity (sp gr), for substance 2, is defined as

$$\text{sp gr}_{T_1}^{T_2} = \frac{w_2}{w_1}$$

where w_2 = weight of a precise volume of substance 2 (the unknown)

w_1 = weight of precisely the same volume of substance 1 (usually water)

T_2, T_1 = the temperatures of these substances.

The density (d) of substance 2 can be obtained from

$$d_2 = \left(\text{sp gr}_{T_1}^{T_2}\right)_2 (d_1)_{T_1}$$

where $(d_1)_{T_1}$ = the density of water (or other reference substance) at temperature T_1

d_2 = the density of substance 2 at temperature T_2.

Such densities are available from standard chemistry handbooks.

Specific gravity may be determined by means of a small pycnometer.

Procedure

If a small pycnometer with a capacity of 1–2 mL is not available, use one of the two pycnometers shown in Figures 3.13 and 3.14.

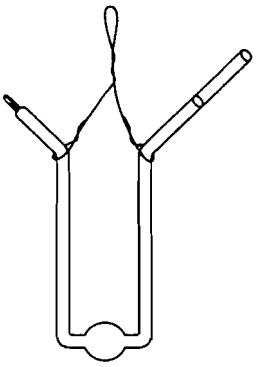


Figure 3.13 Micropycnometer.

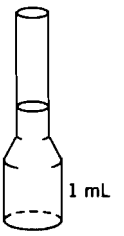


Figure 3.14 Specific gravity bulb (small volumetric flask).

Bend a piece of capillary tubing to an U-shape (Figure 3.13), with a small bulb blown in the middle and one end drawn out to a fine capillary. Make a small scratch on the other vertical piece at the same height as the tip of the capillary. Suspend the pycnometer with a fine Nichrome, aluminum, or platinum wire. Weigh the empty pycnometer to ±0.1 mg. Fill the pycnometer with water to a point beyond the mark and suspend it in a constant-temperature bath at about 20°C. After 10 min, adjust the amount of liquid by holding a piece of filter paper to the capillary tip until the meniscus in the open arm coincides with the mark. Remove the pycnometer from the water bath, dry the outside, and weigh it.

A commercial 1.00-mL volumetric flask (Figure 3.14) can also be used. Determine the weight of the empty flask. Fill it with distilled water and suspend it by a wire in a constant-temperature bath at about 20°C. Adjust the level of the water with a pipet. Remove the flask from the water bath, dry the outside, and weigh it.

Fill the pycnometer or the 1.00-mL volumetric flask with the unknown liquid and determine its weight at the same constant temperature. Calculate the specific gravity of the unknown liquid using the equation shown below:

$$\text{sp gr}_{20}^{20} = \frac{\text{weight of sample}}{\text{weight of water}}$$

Care must be taken that the sample used for this determination is pure. It is best to use a portion of the center fraction collected from distillation or a gas chromatographic collection corresponding to a single peak (Chapter 4, pp. 90–99). Sometimes it is necessary to determine the density with reference to that of water at 4°C. This may be done by means of the factor 0.99823:

$$\text{sp gr}_{4}^{20} = \frac{\text{weight of sample}}{\text{weight of water}} \times 0.99823$$

Another micropycnometer has been described.[5]

Problem

5. An ester has a corrected boiling point of 225°C. In a 1-mL pycnometer, the weight of the sample was 0.989 g and the weight of water was 0.834 g. Calculate sp gr_{20}^{20} and sp gr_{4}^{20}. Give the name and structure of the compound.

Discussion

The specific gravity of a liquid may often be used to exclude certain compounds from the list of possibilities. It varies with the composition as well as the structure of the compound.

Hydrocarbons are usually lighter than water. As a given homologous series of hydrocarbons is ascended, the specific gravity of the members increases, but the increment per methylene radical gradually diminishes. Curves I, II, and III in Figure 3.15 show the change in density for the alkanes, 1-alkenes, and 1-alkynes. It will be noted that the specific gravity of the acetylenic hydrocarbon is greater than that of the corresponding olefin, which in turn is more dense than the alkane hydrocarbon with the same number of carbon atoms. The position the unsaturated linkage occupies also influences the density. Moving the double bond nearer the middle of the molecule causes an increase in the specific gravity. The data in Table 3.7 illustrate this change.

The replacement of one atom by another of higher atomic weight usually increases the density. Thus curve IV, which represents the specific gravities of the normal alkyl chlorides, lies above the curves of the hydrocarbons. It will be noted that the alkyl chlorides are lighter than water and that the specific gravities *decrease* as the number of carbon atoms is increased.

The rather limited data on the alkyl fluorides are shown by curve V. The graph is interesting because it reveals only a very slight change in density as the number of carbon atoms is increased.

Curves VI and VII show that the specific gravities of the primary alkyl bromides and iodides are greater than 1.0 and that in these homologous series the specific gravity decreases as the number of carbon atoms is increased. The slopes of curves IV, VI, and VII are decreasing because the halogen atom constitutes a smaller and smaller percentage of the molecule as the molecular weight is increased by increments of

[5]M. M. Singh, Z. Szafran, and R. M. Pike, *J. Chem. Educ., 70,* A36 (1993).

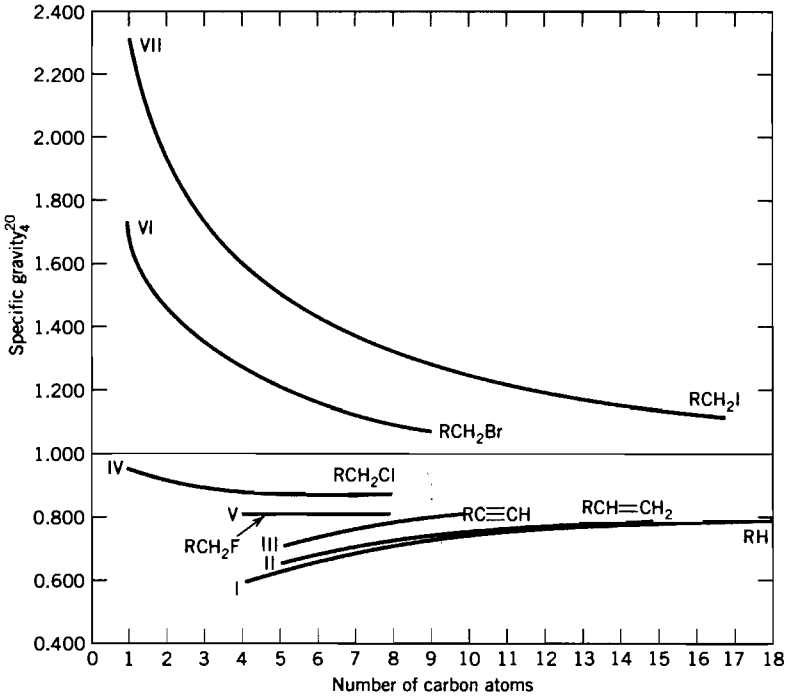


Figure 3.15 Relationship between specific gravity and molecular weight.

TABLE 3.7 Specific Gravity and Double Bond Position

Name	Compound	sp gr
1-Pentene	$CH_2=CHCH_2CH_2CH_3$	0.645_4^{25}
2-Pentene	$CH_3CH=CHCH_2CH_3$	0.651_4^{25}
1,4-Pentadiene	$CH_2=CHCH_2CH=CH_2$	0.659_4^{20}
1,3-Pentadiene	$CH_2=CHCH=CHCH_3$	0.696_4^{20}
2,3-Pentadiene	$CH_3CH=C=CHCH_3$	0.702_4^{20}
1-Hexene	$CH_2=CHCH_2CH_2CH_2CH_3$	0.673_4^{20}
2-Hexene	$CH_3CH=CHCH_2CH_2CH_3$	0.681_4^{20}
3-Hexene	$CH_3CH_2CH=CHCH_2CH_3$	0.722_4^{20}

methylene units. The relative positions of the curves show that the specific gravity increases in the order

$$RH < RF < RCl < RBr < RI$$

provided that comparisons are made on alkyl halides with the same carbon skeleton and of the same class. Similar relationships are exhibited by secondary and tertiary chlorides, bromides, and iodides.

The specific gravities of aryl halides also arrange themselves in order of increasing weight of the substituent (Table 3.8).

An increase in the number of halogen atoms present in the molecule increases the specific gravity. Compounds containing two or more chlorine atoms or one chlorine

TABLE 3.8 Boiling Point and Specific Gravity of Aryl Halides

Compound	bp(°C)	sp gr_4^{20}
Benzene	79.6	0.878
Fluorobenzene	86	1.024
Chlorobenzene	132	1.107
Bromobenzene	156	1.497
Iodobenzene	188	1.832

atom together with an oxygen atom or an aryl group will generally have a specific gravity greater than 1.000 (Table 3.9).

TABLE 3.9 Specific Gravity Change per Number of Chlorine or Oxygen Atoms

Compound	sp gr	Compound	sp gr
Benzyl chloride	1.1026_4^{15}	Carbon tetrachloride	1.595_4^{20}
Benzal chloride[a]	1.2557_4^{14}	Ethylene chlorohydrin	1.213_4^{20}
Benzotrichloride	1.3800_{20}^{20}	Chloroacetone	1.162_4^{16}
Methylene chloride	1.336_4^{20}	Methyl chloroacetate	1.235_{20}^{20}
Chloroform	1.4984_4^{15}		

[a]Benzylidene chloride, $C_6H_5CHCl_2$.

The introduction of functional groups containing oxygen causes an increase in the specific gravity. The curves in Figure 3.16 represent the change in specific gravity of some of the common types of compounds. The ethers (curve VIII) are the lightest of all the organic oxygen compounds. The aliphatic alcohols (curve IX) are heavier than the ethers but lighter than water. The specific gravity of the alcohols becomes greater than 1.0 if a chlorine atom (ethylene chlorohydrin), a second hydroxyl (ethylene glycol), or an aromatic nucleus (benzyl alcohol) is introduced. The dip in curve IX is due to the fact that methanol is more highly associated than ethanol. The amines (curve X) are not as dense as the alcohols and are less associated. Association also causes the specific gravity of formic acid and acetic acid to be greater than 1.000; the higher liquid fatty acids are lighter than water (curve XI).

The simple esters (curve XII) and aldehydes (RCHO) are lighter than water, whereas esters of polybasic acids (curve XIII) and halogenated, keto, or hydroxy esters are heavier than water. Introduction of the aromatic ring may also cause esters to be heavier than water. Examples of esters of these types that are heavier than water are phenyl acetate, methyl benzoate, benzyl acetate, ethyl salicylate, butyl oxalate, triacetin, isopropyl tartrate, and ethyl citrate. Since the hydrocarbons are lighter than water, it is to be expected that esters containing long hydrocarbon chains will show a correspondingly diminished specific gravity.

In general, compounds containing several functional groups—especially those groups that promote association—will have a specific gravity greater than 1.0. Merely noting whether a compound is lighter or heavier than water gives some idea of its complexity. This is of considerable value in the case of neutral liquids. If the compound contains no halogen and has a specific gravity less than 1.0, it probably does not contain more than a single functional group in addition to the hydrocarbon or ether portion. If the compound is heavier than water, it is probably polyfunctional.

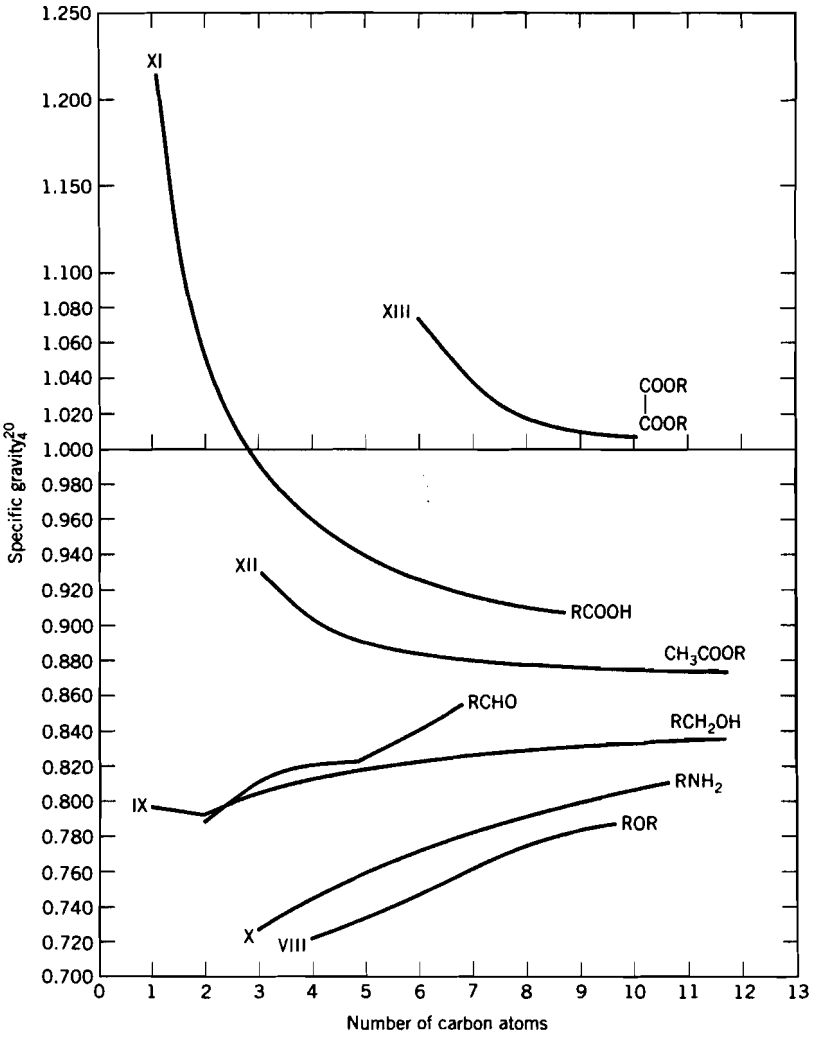


Figure 3.16 Relationship between specific gravity and molecular weight (linear compounds).

3.2.4 Index of Refraction of Liquids

The refractive index of a liquid is equal to the ratio of the sine of the angle of incidence of a ray of light in air to the sine of the angle of refraction in the liquid (Figure 3.17). The ray of light undergoes changes in wave velocity ($v_{air} \longrightarrow v_{liquid}$) and in direction at the boundary interface, and these changes are dependent on temperature (T) and wavelength (λ) of light. Direct measurements of the angles of incidence and refraction are not feasible; hence optical systems have been devised that are dependent on the critical angle of reflection at the boundary of the liquid with a glass prism of known refractive index.

The Abbe-3L benchtop refractometer,[6] illustrated in Figure 3.18, is the most common type of refractometer used in colleges and universities. Other popular models in-

[6]The Abbe-3L benchtop refractometer is available from Thermo Spectronic, Rochester, NY 14625.

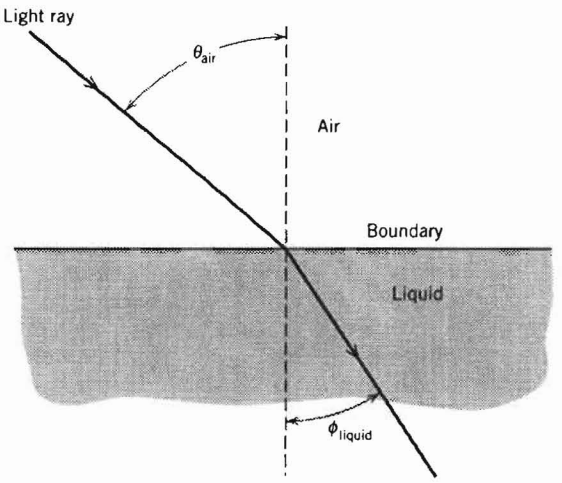


Figure 3.17 Refraction of light:

$$n_\lambda^T = \frac{\sin \theta_{air}}{\sin \phi_{liquid}} = \frac{v_{air}}{v_{liquid}}$$

n = index of refraction

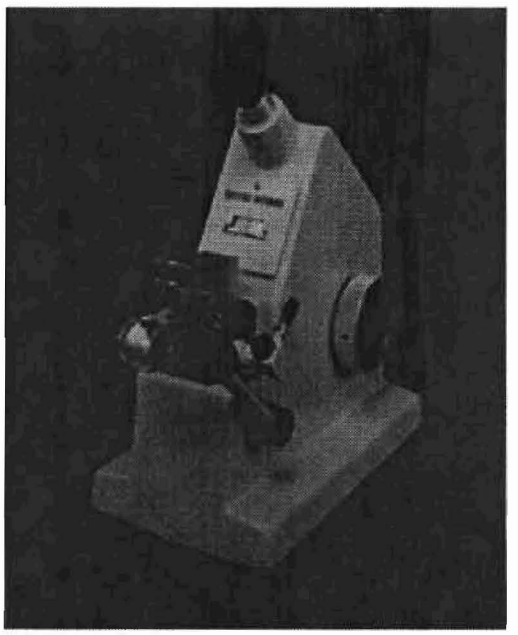


Figure 3.18 An Abbe-3LTM benchtop refractometer. [Used with permission from Thermo Spectronic US, Rochester, NY.]

clude the Leica Abbe Mark II Plus refractometer,[7] the Atago Model DR-A1 Digital Abbe refractometer,[8] and the Arias Digital Abbe refractometer.[9] Refractive indices can be measured from a minimum range of 1.3200 to 1.7000, with an accuracy of ±0.1% or ±0.0001 for refractive index. The temperature compensation range, at a minimum, ranges from 15°C to 40°C. A schematic drawing of the Leica Auto Abbe refractometer is illustrated in Figure 3.19.

[7]The Leica Abbe Mark II Plus refractometer is available from Leica Microsystems Inc, Depew, NY 14043.

[8]The Atago Model DR-A1 Digital Abbe refractometer is available from RL Instruments, Northbridge, MA 01534.

[9]The Arias Digital Abbe refractometer is available from Misco, Cleveland, OH 44122.

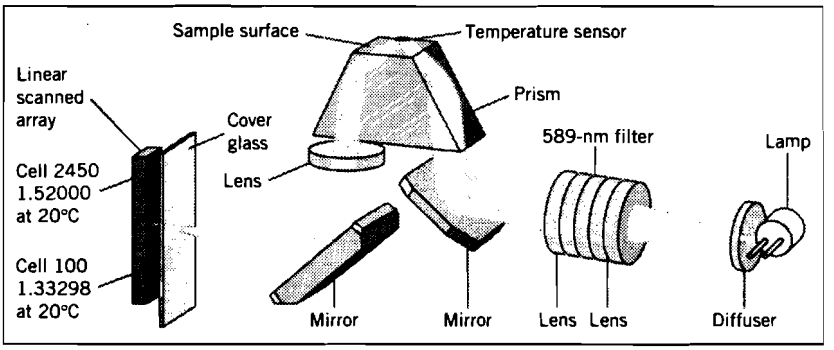


Figure 3.19 A schematic drawing of the Leica Auto Abbe refractometer. [Used with permission from Leica Microsystems, Buffalo, NY.]

Procedure

Place a drop of the sample on the prism. Close the cover. While looking through the eyepiece, rotate the adjustment knob until the dividing line between the light and dark halves coincides with the center of the crosshairs (Figure 3.20). Record the refractive index and the temperature. If the refractive index is measured at 20°C, it is recorded in the following form:

$$n_D^{20} = 1.4357$$

At other temperatures, a correction factor is added, with "obs refractive index" as the observed refractive index and "obs temp" as the observed temperature:

$$n_D^{20} = \text{obs refractive index} + [(\text{obs temp} - 20)(0.00045)]$$

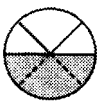


Figure 3.20 Correct adjustment of the light and dark halves coinciding with the center of the crosshairs for determining refractive index.

Problem

6. Calculate the corrected refractive index of a liquid that has an observed refractive index of 1.430 at 35°C.

Clean the prisms with a cotton swab that has been dipped in toluene or petroleum ether for water-insoluble compounds. Do not use acetone. Use distilled water to remove water-soluble compounds. Use extreme care so that the prisms are not scratched. Avoid metal or glass applicators, and use only clean, absorbent, dust-free cotton to clean the prisms. Manuals for operating procedures should be consulted for variations in operating procedures.

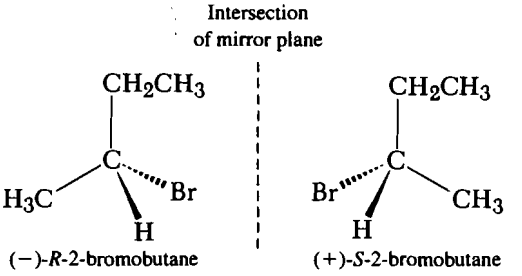
Discussion

The values for density and refractive index are useful in excluding certain compounds from consideration in the identification of an unknown. Care must be taken, however, that the sample is pure. It is best to determine these physical constants on a middle cut from distillation or a gas chromatography collection.

This constant can also serve as a final check on an unknown after its identity and structure have been established. They are of value in research work for checking structures. This checking is accomplished by comparing the observed refractive index to the literature value.

3.3 OPTICAL ROTATION

Stereochemistry is chemistry caused by structural differences due to variations in spatial arrangements of atoms and groups in a pair of molecules. A molecular structure that does not possess an internal mirror plane is called chiral (possesses "handedness"). A chiral compound has the potential of being optically active. The compound 2-bromobutane is a simple example of a chiral compound. Its structure reveals one stereocenter (a carbon center bearing four different substituents) at C-2. Thus 2-bromobutane can exist in two different forms called enantiomers:



Enantiomers are stereoisomers (isomers that have the same structural connectivity) that are nonsuperimposable mirror images. The *R* and *S* forms of 2-bromobutane have identical IR spectra, NMR spectra, boiling points, densities, and chromatographic retention times. They differ only in their abilities to rotate plane-polarized light (and thus only in their optical rotations, or optical activity). The *R* enantiomer rotates plane-polarized light 12° in the negative (or levorotatory) direction and the *S* enantiomer rotates plane-polarized light 12° in the positive (or dextrorotatory) direction. The terms *R* and *S* refer to the three-dimensional absolute configurations of the two forms of 2-bromobutane as defined by the Cahn–Ingold–Prelog notation (this is described in detail in organic lecture texts). Thus for 2-bromobutane the *R* isomer is also the (−) isomer and the other is the *S*-(+)-isomer. These two forms of 2-bromobutane thus have optical activity that is measurable on a polarimeter as described below. Configuration (*R* or *S*) does not necessarily correspond to a particular rotation. For example, a molecule with the *R* configuration can have either a positive (+) or negative (−) rotation.

The optical rotation is determined only if the list of possible compounds contains optically active substances.

3.3.1 Preparation of the Solution

Procedure

Accurately weigh 0.25 g of the compound and dissolve it in 25 mL of solvent in a volumetric flask. The commonly used solvents are water, ethanol, and chloroform. The solution should be clear, with no suspended particles of dust or filter paper. If the solution is not clear, recrystallize the original compound or prepare 50 mL of the solution and filter it. Discard the first 25 mL of the filtrate; use the last 25 mL in the polarimeter.

3.3.2 Filling the Polarimeter Tube

Procedure

Screw the cap on the end of the polarimeter tube. Hold the tube vertically and pour in the solution until the tube is full and the rounded meniscus extends above the end of the tube. Slide the glass plate over the end of the tube so that no air bubbles are caught. Screw on the brass cap.

Precautions

1. Place a rubber washer between the glass plate and the brass cap. Do not place any washers between the glass end plate and the glass tube. This is a glass-to-glass contact.
2. Do not screw on the ends too tightly. Screw on the ends enough to make a firm, leak-proof joint. If the ends are screwed on too tightly, the glass end plates will be strained and a rotation will be observed with nothing in the tube at all. For substances with low readings, loosen the caps and tighten them again between readings.

3.3.3 The Use of the Polarimeter

One type of polarimeter is the PerkinElmer Model 341 polarimeter. A schematic is shown in Figure 3.21.

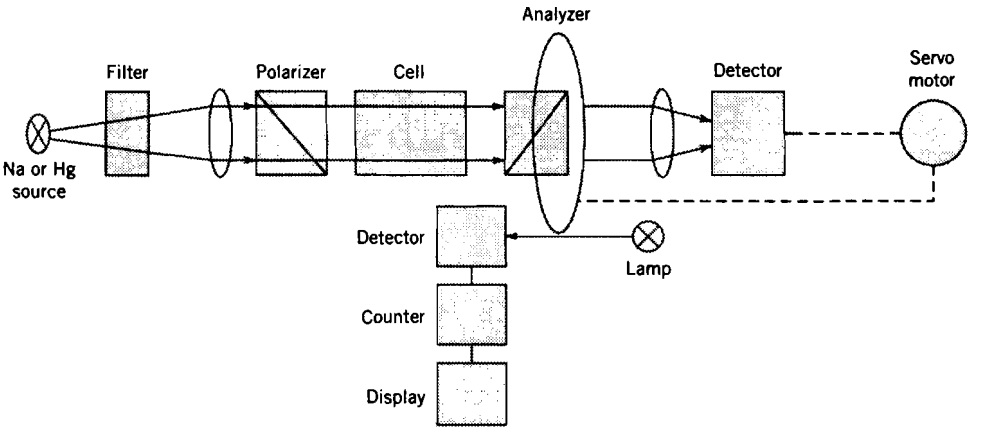


Figure 3.21 Functional principle of a PerkinElmer 341 polarimeter. [Used with permission from Perkin-Elmer Instruments]

Procedure

Select the desired wavelength for the sample. Place the filled polarimeter tube into the sample tube holder. On the manual polarimeter, adjust the analyzer until the maximum amount of light is transmitted. This adjustment is done automatically on the electronic polarimeter. Read the observed rotation.

The sodium or mercury light passes through the polarizer. The polarizer allows only one plane of polarized light to be emitted. The light passes through the sample cell. If an optical active compound is present, then the plane of polarized light is rotated. After the sample cell, the light passes through the analyzer. The analyzing filter is adjusted

until the maximum amount of light is transmitted. The difference, in degrees, between the polarizer and the analyzer is the observed rotation of the sample.

3.3.4 Expression of Results

The specific rotation of a substance is calculated by one of the following formulas:

For pure liquids:	*For solutions:*
$[\alpha]_D^{25^\circ} = \frac{\alpha}{ld}$	$[\alpha]_D^{25^\circ} = \frac{\alpha}{lc}$

where

$[\alpha]_D^{25^\circ}$ = specific rotation at 25°C (using the D line of sodium)

α = observed rotation

l = length of tube (decimeters)

d = density in g/mL

c = grams per mL of solution

It should be noted that the specific rotation may be quite sensitive to the nature of the solvent and, in certain cases, even to the concentration of the substance being examined. The wavelength of the light used for measurement can also affect not only the magnitude but also the sign of rotation. Attention should be paid, therefore, to the exact conditions under which a rotation reported in the literature was measured.

The following is the correct way to report specific rotation:

$$[\alpha]_{546}^{25^\circ} = -40 \pm 0.3^\circ \qquad (c = 5.44 \text{ g/100 mL water})$$

The preceding relationship refers to a specific rotation determined at 25°C, in water, with light of a wavelength of 546 nm, at a concentration of 5.44 g/100 mL of solution. It is necessary to determine the observed rotation, α, at two different concentrations. In the simplest cases, observed rotations will be decreased by the same factor as the concentration decrease; for example,

α	*Concentration*
−50°	x
−5.0°	$0.1x$
0.50°	$0.01x$

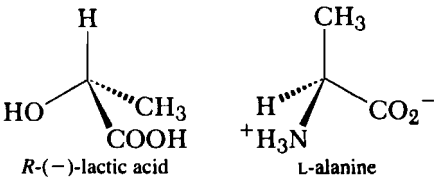
Thus in such a case the $[\alpha]$ determined from all three experiments will be the same, and one has in hand a value of $[\alpha]$ that can be safely compared to literature values of $[\alpha]$ determined at other concentrations. In this way the value of $[\alpha]$ in such simple cases can be used to confirm the identity of the compound of interest. If the value of $[\alpha]$ has been determined upon a liquid sample using no solvent, the specific rotation should be reported as follows:

$$[\alpha]_D^{25^\circ} = +40^\circ \text{ (neat)}$$

PROBLEM

7. A solid carbohydrate has a decomposition point of 187°C. A solution of this compound was prepared by dissolving 5 g in 50 mL of water. This solution gave an observed rotation of 6.65° in a 10-cm tube. Calculate the specific rotation. Give the name of the carbohydrate.

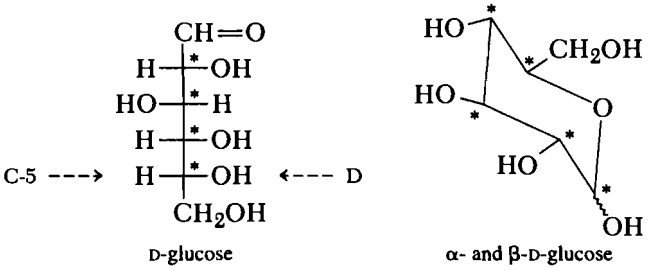
As described earlier, the existence of a single stereocenter (also called chiral or asymmetric center) in a compound such as 2-bromobutane can cause optical activity. Other commonly encountered organic compounds with one stereocenter include



R-(−)-lactic acid L-alanine

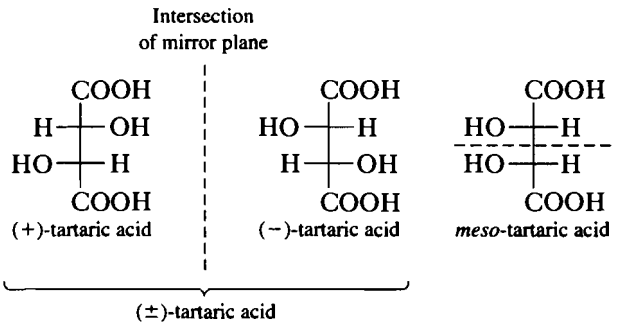
The L designation used above for alanine refers to its absolute configuration (here the L form has the *S* configuration). The enantiomer of L-alanine would be D-alanine (the D and L notation for absolute configuration is frequently encountered for amino acids and carbohydrates, and is less general than *R* and *S* notation). The L notation is not to be confused with *l*, which stands for levorotatory, or (−), rotation of plane-polarized light. In like manner, D absolute configuration is not the same as *d* rotation. In fact it is not uncommon to find that a D stereoisomer has *l*, or (−), rotation!

Chiral compounds with more than one stereocenter are common. Glucose, for example, has four stereocenters when acyclic and five when cyclic.



D-glucose α- and β-D-glucose

Tartaric acid exists in three stereoisomeric forms, (+), (−), and *meso*.



The *meso* form shows no optical activity; although it has two stereocenters, the effects of these two centers cancel, resulting in an optically inactive (or achiral) compound. The lack of activity is not surprising in view of the fact that this compound bears a *meso* plane (the intersection of which is illustrated by the dotted line). Since this *meso* plane is an internal mirror plane, this compound by definition is achiral and thus optically inactive.

3.3.5 Optical Purity

In introducing optically active compounds above, we have discussed compounds that are one enantiomer (e.g., *S*-2-bromobutane) or the other (*R*-2-bromobutane). Clearly, mixtures are possible, and one of the more well known cases is that of a racemic mixture (50% one enantiomer, 50% the other). Mixtures other than 50/50 are, of course, also possible. Optical purity is defined as

$$\% \text{ ee} = \frac{[\alpha]_{\text{obs}}}{[\alpha]} \times 100$$

Here $[\alpha]_{\text{obs}}$ is the specific rotation observed for the mixture of interest and $[\alpha]$ is the specific rotation for a sample of just one enantiomer. The specific rotations should be carried out at the same temperature and concentration and in the same solvent. The resulting enantiomeric excess can be related to the solution composition as follows: A 2-bromobutane sample of $+12°$ is clearly 100% (*S*)-(+) form. If a sample of $-6°$ rotation is isolated, the enantiomeric excess is

$$\% \text{ ee} = \frac{[\alpha]_{\text{obs}}}{[\alpha]} \times 100 = \frac{-6°}{-12°} \times 100 = 50\% \text{ ee}$$

The composition of the mixture of $-6°$ rotation can be calculated on a 100-molecule basis: 50 molecules (50%) give rise to the $-6°$ rotation and have the *R* configuration. Since the remaining 50 molecules have no net optical activity, they must have the composition of a racemic mixture, and thus there must be 25 *S* and 25 *R* molecules in this mixture. Thus the entire mixture has 25 *S* molecules and 50 + 25 = 75 *R* molecules.

3.4 RECRYSTALLIZATION

Recrystallization depends on the decreased solubility of a solid in a solvent, or mixture of solvents, at lower temperature. Thus, one should be familiar with the theory of solubility (pp. 115–120) in order to understand better the theory of recrystallization.

Recrystallization procedures can be quite complex. Standard laboratory textbooks for organic chemistry usually have exercises to introduce these procedures. In this section, recrystallization principles will be discussed that may be useful in solving recrystallization problems in the more unpredictable situations involved in organic qualitative analysis.

Table 3.10 and Table 3.11 list a variety of recrystallization solvents or solvent pairs. Even if the correct solvent or solvent pair cannot be found in Table 3.10 or Table 3.11, the tables should give an idea as to what general class of solvent or solvent pairs is appropriate. For example, if a phenylurethane derivative does not recrystallize from petroleum ether, then petroleum ether–toluene might work.

Procedure for a Single Solvent

Select a solvent so that the sample is five times as soluble in the hot solvent as in the cold solvent. Place the solid, oil, or semisolid sample in a small amount of solvent. Add one or two boiling chips. Heat the solution on a hot plate until the sample dissolves completely. If necessary, add more solvent, a little at a time, to completely dissolve the sample. Use the minimum amount of solvent needed to dissolve the sample. If undissolved solid remains, even with additional solvent, then filter or decant the boiling solution into another flask. The undissolved solid remains in the filter paper or in the

TABLE 3.10 Common Solvents for Recrystallization of Standard Functional Classes

Sample to Be Recrystallized	Solvent[a]	Solvent bp(°C)	Co-Solvent Possibilities
1. Acid anhydride	Methylene chloride	40	Ether, toluene, hydrocarbons
2. Acid chloride	Methylene chloride	40	See line 1
3. Acid chloride	Chloroform[b]	61.7	Hydrocarbons
4. Amide	Acetic acid	118	Water
5. Amide	Dioxane	102	Water, toluene, hydrocarbons
6. Amide	Water	100	Acetone, alcohols, dioxane, acetonitrile
7. Aromatic	Toluene	111	Ether, ethyl acetate, hydrocarbons
8. Bromo compound	Acetone	56	Water, ether, hydrocarbons
9. Bromo compound	Ethyl alcohol	78	Water, hydrocarbons, ethyl acetate
10. Carboxylic acid	Acetic acid	118	See line 4
11. Carboxylic acid	Water	100	See line 6
12. Complex	Toluene	111	See line 7
13. Ester	Ethyl acetate	77	Ether, hydrocarbons, toluene
14. Ester	Ethyl alcohol	78	See line 9
15. General	Acetone	56	See line 8
16. General	Chloroform[b]	61.7	See line 3; also ethyl alcohol
17. General	Ethyl acetate	77	See line 13
18. General	(Ethyl) ether	34.5	Acetone, hydrocarbons, ethyl acetate, toluene, methylene chloride
19. General	Methylene chloride	40	Ethyl alcohol, hydrocarbons
20. General	Ethyl alcohol	78	See line 9; bromo compounds
21. Hydrocarbon	Toluene	111	See line 7
22. Hydrocarbon	Hexane	69	Any but acetonitrile, acetic acid, water
23. Low-melting compound	Ether	34.5	See line 18
24. Low-melting compound	Methylene chloride	40	See line 19
25. Nitro compound	Acetone	56	See line 8
26. Nitro compound	Ethyl alcohol	78	See line 9
27. Nonpolar compound	Methylene chloride	40	See line 1
28. Osazone	Acetone	56	See line 8
29. Polar compound	Acetonitrile	81.6	Water, ether, toluene
30. Salt	Acetic acid	118	See line 4
31. Salt	Water	100	See line 6
32. Sugar	Methyl cellosolve		Water, toluene, ether

[a]More details on these and other solvents, especially with regard to solvent toxicity, flammability, and practical handling comments, may be found in A. J. Gordon and R. A. Ford, *The Chemists' Companion* (Wiley, New York, 1972), pp. 442–443. **Caution: Remember that many of these solvents, of which benzene is an important example, are toxic.**

[b]In revising earlier forms of this table, toluene has been substituted for benzene and methylene chloride (dichloromethane) for carbon tetrachloride. Methylene chloride is also a possible alternative for chloroform.

TABLE 3.11 Solvents and Solvent Pairs for Recrystallization of Common Derivatives

Derivative	Solvent or Solvent System[a]
Acetate	Methanol; ethanol
Amide	Methanol; ethanol
Anilide	Methanol–water; ethanol
Benzoate	Methanol; ethanol
Benzyl ester	Methanol–water; ethanol
Bromo compound	Acetone–alcohol; methanol; ethanol
3,5-Dinitrobenzoate	Methanol; ethanol
3,5-Dinitrophenylurethane	Petroleum ether–toluene
Ester	Ethyl acetate; methanol; ethanol
Hydrazone	Methanol–water; ethanol
α-Naphthylurethane	Petroleum ether
p-Nitrobenzyl ester	Methanol–water; ethanol
Nitro compound	Methanol; ethanol; acetone–alcohol
p-Nitrophenylurethane	Petroleum ether–toluene
Osazone	Acetone–alcohol
Phenylurethane	Petroleum ether
Picrate	Toluene; ethanol; methanol–water
Quaternary ammonium salt	Ethyl acetate; isopropyl ether
Semicarbazone	Ethanol; methanol–water
Sulfonamide	Methanol–water; ethanol
Sulfonyl chloride	Chloroform; methylene chloride
p-Toluidide	Methanol; ethanol
Xanthylamide	Dioxane–water

[a]See footnote *a* in Table 3.10.

bottom of the original flask. Allow the solution to cool to room temperature. In the "ideal" case, uniform crystals slowly appear. When the solution becomes cloudy or a few crystals appear, chill the solution in an ice bath. Wait until there is a transparent layer of liquid above the layer of crystals before isolating the crystals. Depending on the amount of crystals, isolate the crystals by filtering the solution through a Hirsch funnel or a Buchner funnel. Check the crystals for purity (mp, GC, NMR, or TLC, etc).

Procedure for a Solvent Pair

Dissolve the sample in a minimum amount of hot solvent in which the sample is more soluble. While it is still heating, add the second solvent dropwise until a faint cloudiness persists after stirring. Allow the solution to cool to room temperature. After the solution becomes cloudy or a few crystals appear, chill the solution in an ice bath. Wait until there is a transparent layer of liquid above the layer of crystals before isolating the crystals. Isolate the crystals by filtering the solution through a Hirsch funnel or a Buchner funnel. Check the crystals for purity.

Removal of Highly Colored Impurities

If the sample is highly colored, there is a possibility that it contains highly colored impurities. Check with your instructor to see if the color is due to impurities. To remove a highly colored impurity, dissolve the sample in a hot solvent in which it is readily

soluble. Add a small amount of decolorizing charcoal so that the solution turns black. Pour the boiling solution through filter paper into another flask. Remove the solvent, by boiling or evaporation, and proceed with the directions for either a single solvent or solvent pair.

Oil Formation

Frequently, recrystallization attempts will result in oil formation rather than the desired solid. An oil is recognized by the formation of a second layer. The formation of an oil may be due to the fact that the sample is impure. If there is reason to believe this, dissolve the sample in a solvent in which it is readily soluble and treat with decolorizing charcoal as described above.

Additional Suggestions

Oils may persist, even after repeated purifications. This may be due to the fact that the sample is inherently difficult to crystallize or that the last traces of impurity must be removed by recrystallization. If an oil persists or crystals are reluctant to form, the following techniques may be tried.

1. Shake the flask several times. Sometimes this gives enough momentum to start the formation of crystals.
2. Provide a site for crystal nucleation to initiate the recrystallization process. Scratch the inside surface of the flask or add a boiling stone to initiate crystallization.
3. Add a small seed of pure sample during recrystallization. Add the seed of crystal after the solution has been supersaturated and allowed to cool to room temperature but has not yet produced crystals.
4. Lower the temperature to decrease the solubility of the sample, not to freeze the solvent or sample. An increase in the solvent volume by 20–30% can be used effectively to require a lower temperature for crystal formation. The following conditions produce increasingly lower temperatures. See Appendix I for additional chilling solutions.
   Room temperature
   Refrigeration
   Ice-water bath
   Refrigerator freezer or salted ice bath
   Dry ice–acetone
   Liquid nitrogen

Be careful not to confuse frozen solvent or frozen amorphous oils with crystals; frozen oils will melt and form oils at room temperature.

Sometimes it is necessary to stir the neat oil sample—for example, with a stirring rod—to induce crystallization. This stirring can be done in contact with the mother liquor. Seeding can also be used. In some cases, a long period of stirring is needed to induce crystallization.

Problems

8. List a solvent or solvent combination that can be used to recrystallize an acid anhydride.
9. List a solvent or solvent combination that can be used to recrystallize a benzoate.

3.5 QUALITATIVE ELEMENTAL ANALYSIS

Organic chemists do not usually use chemical tests for carbon, hydrogen, and oxygen. It is often valuable, however, to determine the existence of other elements, such as nitrogen, sulfur, fluorine, chlorine, bromine, and iodine. The detection of these elements, by means of chemical tests, is usually straightforward. Many of these chemical tests are quite sensitive, so all aqueous solutions should be *carefully* prepared using only distilled or deionized water. Samples that show indications of explosive character in the ignition test (1) should not be analyzed by the sodium fusion procedure or (2) should be analyzed by a smaller-scale procedure than that described below. Compounds that are known to react explosively with molten sodium are nitroalkanes, organic azides, diazo esters, diazonium salts, and some aliphatic polyhalides such as chloroform or carbon tetrachloride. ***Safety glasses, with side shields, must be worn at all times when any procedure or experiment is being conducted. The safety of other members of the class must be taken into account and therefore care must be taken so that reaction flasks are not pointed toward others in the lab.***

Controls should be run for all tests that leave the slightest doubt about the decisiveness of the results; for example, if you are unsure about the validity of the observations associated with a positive nitrogen test run on an unknown, the same test should be carried out on a compound that is known to contain nitrogen. A sample of 4-bromobenzenesulfonamide is recommended as a control. This sample can be decomposed by sodium and analyzed for nitrogen, bromine, and sulfur by the procedures described below. It may even be advantageous to run a control on a compound that is known *not* to contain the element of interest; observations associated with this control allow one to draw conclusions about tests yielding negative results or about the purity of the reagents involved.

Knowledge of the elemental composition of an organic compound being studied is essential for the following reasons. Such knowledge aids in the selection of the appropriate classification experiments, which serve as tests for functional groups (Chapter 9), and in the selection of procedures for the preparation of derivatives (Chapter 10). Additionally, NMR spectra (Chapter 6), IR spectra (Chapter 7), and mass spectra (Chapter 8) can be interpreted so that the structure of the unknown is determined.

Almost all the elements listed in the periodic table can be a part of an organic compound. In this text we will, however, be concerned with detection of only a few of the elements more commonly found in organic compounds; detection of the other elements is a subject that is discussed in other courses, such as one on instrumental analysis that covers atomic absorption and other instrumental procedures. For an introduction to the identification of "unknown" organic compounds, it is recommended that the possible elements be limited to C, H, P, N, S, F, Cl, Br, and I. A few of the most common salts, such as those containing Na, K, and Ca, might also be included.

3.5.1 Fusion of Organic Compounds with Sodium

$$\text{C, H, O, N, S, X} \xrightarrow{\text{Na}} \begin{cases} \text{NaX} \\ \text{NaCN} \\ \text{Na}_2\text{S} \end{cases}$$

X = halogen

The unknowns can be treated with sodium to form the sodium fusion filtrate according to one of the following three procedures. The filtrate is then used for determination of the presence of sulfur, nitrogen, and halogen. A compound such as

4-bromobenzenesulfonamide can be used as a control for a positive test for bromine, sulfur, and nitrogen. ***The first time that the student prepares the sodium fusion filtrate, it must be done under supervision. It is imperative that the preparation of the sodium fusion filtrate be done in the hood.***

Procedure A[10]

Support a small test tube (approximately 100 × 13 mm) made of *soft* glass (not Pyrex or Kimax) in a vertical position with a clamp from which the rubber has been removed. With a knife, cut a cube piece of *clean* sodium metal about 4 mm on an edge and place it in the test tube. ***Prior to placing the sodium in the test tube, rinse the sodium metal with a small amount of hexane to remove all traces of kerosene, the liquid in the container of sodium. Rinse the knife, and any other utensils that were in contact with the sodium, with hexane. Add ethanol dropwise to the hexane washings until all of the sodium reacts.*** Heat the lower part of the test tube until the sodium melts and sodium vapors rise in the test tube. Next, remove the heat and add one-third of a mixture of 100 mg of the compound, mixed with 50 mg of powdered sucrose.[11] Heat the test tube. Add the mixture and heat the test tube for a second and third time. Heat the bottom of the tube to a dull red. Cool the test tube, and add 1 mL of ethanol to dissolve any unreacted sodium. Heat the test tube to a dull red again and, while still hot, drop it into a small beaker containing 20 mL of distilled water (*caution!*). During the heating, alcohol vapors may ignite at the mouth of the tube; this should not affect the analysis. Break up the test tube with a stirring rod, and heat the solution to boiling. Filter the solution. Use the filtrate, which should be colorless, for the specific tests for various elements described below after Procedure C.

Procedure B

Place 10 mg or 10 μL of the unknown and a freshly cut, pea-size (about 50-mg) piece of sodium metal (*caution!*) into a small (100 × 13 mm) Pyrex or Kimax glass test tube, following the precautions used in Procedure A. Heat the test tube until the bottom is a glowing red. Allow the glowing and charred residue to cool to room temperature. Add a few drops of ethanol, with stirring, to ensure decomposition of all remaining elemental sodium. Repeat until no further bubbles of hydrogen gas are evolved. Add 2 mL of water to this solution. Heat and filter the solution. Use the filtrate, which should be colorless, for the specific element tests outlined after Procedure C. Repeat the entire procedure on a fresh sample if there is any indication of incomplete fusion (for example, the presence of color).

Procedure C[12]

Place a small Pyrex or Kimax glass test tube (100 × 13 mm), containing 500 mg of sodium–lead alloy, in a vertical position. Heat the test tube with a flame until sodium vapors rise in the tube. ***Do not heat the test tube or its contents to redness.*** Add

[10]K. N. Campbell and B. K. Campbell, *J. Chem. Educ.*, 27, 261 (1950).

[11]Powdered sugar (sucrose) is sold in supermarkets as "confectioner's sugar." It typically contains 97% sucrose and 3% starch. The mixture of the unknown and powdered sugar provides a charring and reducing action so that compounds containing nitrogen, such as amides, nitrosos, azos, hydrazos, and heterocyclic rings, produce sodium cyanide. Sulfur compounds, such as sulfides, sulfoxides, sulfones, sulfonamides, and heterocyclic sulfur compounds, produce sodium sulfide.

[12]J. A. Vinson and W. T. Grabowski, *J. Chem. Educ.*, 54, 187 (1977).

four to six drops, or about 10 mg, of the unknown directly onto the sodium without getting any of the sample on the walls of the test tube. If the unknown is a volatile liquid with a boiling point of less than 100°C, then mix 50 mg of powdered sucrose with the unknown prior to its addition into the test tube. Heat the reaction mixture gently to initiate the reaction. Remove the flame until the reaction ceases, then heat the test tube and its contents to redness for 2 min. Allow the test tube to cool to room temperature. Add 3 mL of water and heat the test tube gently for 2 min. Filter the reaction mixture while still warm. Rinse the test tube with 2 mL of water and filter the rinsings. Combine these filtrates together and use them for the specific tests described below.

Note: If a sharp explosion occurs when the initial portion of the unknown is heated with the sodium, stop the procedure. Add 0.5 g of fresh unknown, 5 mL of acetic acid, and 0.5 g of zinc dust to the sample. *Caution: Do not heat too strongly, as compounds such as low-molecular-weight amine acetates may be lost by evaporation.* After dissolving most of the zinc, evaporate the mixture to dryness and decompose the entire residue by Procedure A, B, or C.

Cleaning Up Place the sodium fusion solutions from Procedures A, B, or C, which remain after the elemental tests are completed, in the aqueous solution container. Place the hexane washings, after they have been in the hood for an hour with sufficient ethanol to consume any residual sodium, in the organic solvent container.

Additional methods have been published to form the fusion solution. One method[13] involves the formation of a calcium oxide–zinc fusion. Repeated attempts in our laboratories gave unsatisfactory results. The oxygen flask method[14–16] yields a liquid that can be used for elemental analysis.

Specific Tests for Elements

Use the sodium fusion filtrate, obtained by Procedures A, B, or C, in the experiments below to test for the presence of sulfur, nitrogen, or halogen.

Sulfur

Use either of the following procedures to test for the presence of sulfur.

Procedure (a) for Sulfur Acidify 1 mL of the sodium fusion filtrate with acetic acid. Add two drops of 1% lead acetate solution. A black precipitate of lead sulfide indicates the presence of sulfur in the unknown.

$$Na_2S + \underset{\text{lead acetate}}{Pb(OCCH_3)_2} \longrightarrow \underset{\text{(black precipitate)}}{PbS} + 2CH_3CONa$$

Procedure (b) for Sulfur Add 2 drops of 2% sodium nitroprusside to 1 mL of the sodium fusion filtrate. A deep blue-violet color indicates the presence of sulfur.

$$Na_2S + \underset{\text{sodium nitroprusside}}{Na_2Fe(CN)_5NO} \longrightarrow \underset{\text{(blue-violet)}}{Na_4[Fe(CN)_5NOS]} + 2NaOH$$

[13]C. H. Snyder, J. P. Sickels, and C. J. Del Valle, *J. Chem. Educ.*, *50*, 72 (1977).

[14]R. Thomas, *J. Chem. Educ.*, 59, 690 (1982).

[15]R. D. Guthrie and I. D. Jenkins, *J. Chem. Educ.*, *57*, 226 (1980).

[16]C. H. Boulton, *Educ. in Chem.*, *10*, 231 (1973).

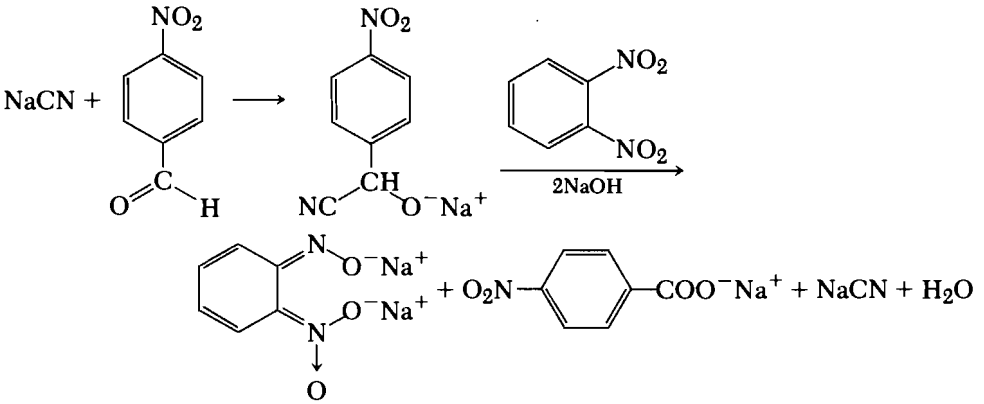
Controls Test these procedures with benzenesulfonamide (positive test) and toluene (negative test).

Cleaning Up Place the solutions from both tests for sulfur in the aqueous solution container.

Nitrogen

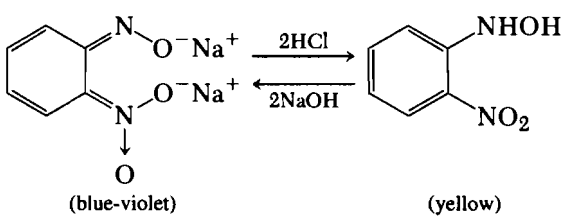
The presence of nitrogen can be detected using any of the procedures below. The use of these elemental tests, in combination with data obtained from the classification tests, can give definite information as to the type of functional group that contains nitrogen. Such classification tests include the treatment of the unknown with sodium hydroxide, which can determine the presence of an amide (Experiments 2c, 2d, and 18), amine (Experiments 5, 6, 19–23), nitrile (Experiment 2c, 18), or nitro compound (Experiment 42–44).

Procedure (a) for Nitrogen[17] In a small test tube, combine 1 mL of 1.5% 4-nitrobenzaldehyde in 2-methoxyethanol solution, 1 mL of 1.7% 1,2-dinitrobenzene in 2-methoxyethanol solution, and two drops of 2% sodium hydroxide solution. Add two drops of the sodium fusion filtrate. A positive test for nitrogen is the appearance of a deep–blue-purple compound. The deep-purple compound is due to a dianion produced when sodium cyanide, which is formed from nitrogen in the original compound, undergoes reaction with 4-nitrobenzaldehyde and 1,2-dinitrobenzene.



A yellow or tan solution is a negative test. This test for nitrogen is more sensitive than the Prussian blue test described in the fifth or earlier editions of this text.

This test is valid in the presence of NaX (X = halogen) or Na_2S; in other words, it is reliable even if the original unknown also contains halogen or sulfur. The products of the above reactions provide the explanation as to why this test is especially sensitive. Acidification of the solution of the purple dianion results in a yellow solution of 2-nitrophenylhydroxylamine (an acid–base indicator).



[17]G. G. Guilbault and D. N. Kramer, *Anal. Chem.*, *38*, 834 (1966); D. N. Kramer and G. G. Guilbault, *J. Org. Chem.*, *31*, 1103 (1966).

Procedure (b) for Nitrogen Add two drops of a 10% ammonium polysulfide solution to 2 mL of the sodium fusion filtrate, and evaporate the mixture to dryness in a steam bath or hot-water bath. Add 5 mL of a 5% hydrochloric acid solution, and warm the solution. Filter the solution. Add three drops of 5% ferric chloride solution to the filtrate. The presence of a red color indicates that nitrogen was present in the original unknown.

$$\underset{}{NaCN} + \underset{\substack{\text{ammonium}\\\text{polysulfide}}}{(NH_4)_2S_X} \longrightarrow NaSCN + (NH_4)_2S_{X-1}$$

$$6NaSCN + FeCl_3 \longrightarrow \underset{\text{(red)}}{Na_3Fe(SCN)_6} + 3NaCl$$

Procedure (c) for Nitrogen Using 5% sodium hydroxide solution, adjust the pH of 1 mL of the sodium fusion filtrate to pH 13. Add two drops of saturated ferrous ammonium sulfate solution and two drops of 30% potassium fluoride solution. Boil gently for 30 sec. Acidify the hot solution carefully by adding 30% sulfuric acid dropwise until the iron hydroxide just dissolves. The appearance of the characteristic precipitate of Prussian blue indicates the presence of nitrogen.

Isolate and wash the precipitate on white filter paper to better observe the color. If no precipitate is observed but a blue or greenish-blue solution is obtained, then the original sodium decomposition was not complete.

Controls Test these procedures with benzenesulfonamide (positive test) and toluene (negative test).

Cleaning Up Place all solutions in the aqueous solution container.

Halogens

Use the tests listed below to check for the presence and identity of halogens. Use the data from these tests, in conjunction with the classification tests of ethanolic silver nitrate (Experiment 35) and sodium iodide (Experiment 36), to determine the specific halogen and whether the halogen is primary, secondary, tertiary, or aromatic.

Unless otherwise stated, determine the acidity of a solution by placing a drop, with a stirring rod, of the solution on red or blue litmus paper. The solution is acidic when the litmus paper turns red and basic when the litmus paper turns blue.

Procedure (a) for Presence of a Halogen Beilstein's test is a very general test to see if any halogen is present. For this test, make a small loop in the end of a copper wire and heat the wire with the Bunsen burner until the flame is no longer green. Cool the wire. Dip the loop in a little of the *original* unknown compound and heat it in the edge of the flame. A green flame indicates halogen and is not sustained for very long.

This test is extremely sensitive *but should always be cross-checked* by the silver nitrate test described below because minute traces of impurities containing halogen may produce a green flame. Another drawback of this test is the possibility of highly volatile liquids evaporating completely prior to the wire becoming sufficiently hot to cause decomposition, thus resulting in a possible false-negative result.

Also, certain nitrogen compounds not containing halogen cause a green color to be imparted to the flame; among them are quinoline and pyridine derivatives, nitrogen-containing organic acids, urea, and copper cyanide. Some inorganic compounds also give green flames.

Procedure (b) for One Halogen—Chlorine, Bromine, or Iodine *In the hood,* acidify 2 mL of the sodium fusion filtrate with 5% nitric acid in a small test tube. Boil gently for a few minutes to expel any hydrogen cyanide or hydrogen sulfide that might be present due to nitrogen or sulfur contained in the original compound.

$$NaCN + HNO_3 \longrightarrow HCN\uparrow + NaNO_3$$
$$Na_2S + 2HNO_3 \longrightarrow H_2S\uparrow + 2NaNO_3$$

Cool the solution. If any precipitation occurs at this point, filter the solution. Add three drops of 0.1 M silver nitrate solution to the liquid. An immediate heavy formation of a solid indicates the presence of chlorine, bromine, or iodine. Silver chloride is white, silver bromide is pale yellow, and silver iodide is yellow. Since silver fluoride is soluble in water, it cannot be detected by this test. If only a faint turbidity is produced, it is probably due to the presence of impurities in the reagents or in the test tube.

$$NaCl + AgNO_3 \longrightarrow \underset{\text{(white)}}{AgCl(s)} + NaNO_3$$
$$NaBr + AgNO_3 \longrightarrow \underset{\text{(pale yellow)}}{AgBr(s)} + NaNO_3$$
$$NaI + AgNO_3 \longrightarrow \underset{\text{(yellow)}}{AgI(s)} + NaNO_3$$

If a silver halide is present, then continue to add sufficient 0.1 M silver nitrate until precipitation ceases. Isolate the precipitate by filtration.

Silver chloride, silver bromide, and silver iodide have different solubilities in 5% ammonium hydroxide. Add 2 mL of 5% ammonium hydroxide to the solid. Silver chloride is soluble in ammonium hydroxide due to the formation of $Ag(NH_3)_2Cl$. Silver bromide is slightly soluble because it only partially forms its salt. Silver iodide does not undergo reaction with the ammonium hydroxide and thus remains insoluble.

$$AgCl + 2NH_4OH \longrightarrow Ag(NH_3)_2^+ Cl(aq)^- + 2H_2O$$

Procedure (c) for One Halogen—Bromine, Iodine, or Chlorine[18] Acidify 2 mL of the sodium fusion filtrate with 5% nitric acid. Add 10 drops of a 1.0% aqueous potassium permanganate solution and shake the solution for 2 min. Add 25 mg of oxalic acid to barely decolorize the solution. Add 1 mL of methylene chloride and again shake the mixture. Observe the color of the bottom methylene chloride layer against a white background. A brown color indicates that bromine is present. A purple color indicates the presence of iodine. If the methylene chloride layer is colorless, then chlorine is the halogen present.

Procedure (d) for Bromine and/or Iodine, or Chlorine Acidify 3 mL of the sodium fusion filtrate with 10% sulfuric acid and boil the solution for a few minutes. Cool the solution to room temperature. Add 1 mL of methylene chloride, followed by a drop of 5.25% sodium hypochlorite.[19] View the color of the solution against a white background. The production of a purple color in the bottom methylene chloride layer indicates the presence of iodine.

$$2NaI + Cl_2(H_2O) \longrightarrow 2NaCl + \underset{\text{(purple)}}{I_2(CH_2Cl_2)}$$

[18]D. W. Mayo, R. M. Pike, and P. K. Trumper, *Microscale Organic Chemistry with Multistep and Multiscale Syntheses*, 4th ed. (Wiley, New York, 2000).

[19]A source of 5.25% sodium hypochlorite is household bleach.

Add 5.25% sodium hypochlorite, drop by drop. Shake the solution after each addition. The purple will gradually disappear and be replaced by a reddish-brown color if bromine is present.

$$\underset{\text{(purple)}}{I_2(CH_2Cl_2)} + Cl_2(H_2O) \longrightarrow \underset{\text{(colorless)}}{2ICl}$$

$$2NaBr + Cl_2(H_2O) \longrightarrow 2NaCl + \underset{\text{(reddish brown)}}{Br_2(CH_2Cl_2)}$$

If a positive test was obtained in Procedure (b), but neither bromine nor iodine is present according to the results obtained in this procedure, then chlorine is the halogen present. The chlorine does not produce a color when in solution in methylene chloride. One of the procedures listed below should be used to confirm the presence of chlorine.

Procedure (e) for More Than One Halogen—Chlorine, Bromine, and Iodine Acidify 10 mL of the sodium fusion filtrate with 10% sulfuric acid. Boil the solution for a few minutes. Cool the solution to room temperature. Add 0.5 mL of methylene chloride. Add three drops of a 20% sodium nitrite solution. A purple color indicates iodine. If iodine is present, then add 5 mL of 20% sodium nitrite and extract the iodine with 5 mL of methylene chloride. Next, boil the solution for a minute. Cool the solution. To 1 mL of this solution, add 0.5 mL of methylene chloride and two drops of 5.25% sodium hypochlorite. A brown color indicates the presence of bromine. Dilute the remaining 9 mL of the acidified solution to 60 mL with water. Add 2 mL of concentrated sulfuric acid, followed by 0.5 g of potassium persulfate ($K_2S_2O_8$). Boil the solution for 5 min. Cool the mixture. Add three drops of 0.1 M silver nitrate solution. A white precipitate indicates chlorine.

Procedure (f) for Bromine To 3 mL of the sodium fusion filtrate in a test tube, add 3 mL of acetic acid and 0.1 g of lead dioxide. Place a piece of filter paper, moistened with a 1% solution of fluorescein, over the mouth of the test tube and heat the contents of the tube to boiling. If bromide is present in the solution, brown vapors cause the yellow fluorescein to turn pink, owing to the formation of eosin. Chlorides and cyanides do not interfere with this test. Iodides produce a brown color.

Procedure (g) for Iodine Acidify 2 mL of the sodium fusion filtrate with 2 M nitric acid. Add 1 mL of a 5% mercury(II) chloride solution. The formation of a yellow solid, which changes to orange-red upon standing for a few minutes, indicates the presence of iodine.

Procedure (h) for Chlorine in the Presence of Nitrogen, Sulfur, Bromine, and Iodine *In a hood,* acidify 2 mL of the sodium fusion filtrate with 5% nitric acid. Boil to expel any hydrogen cyanide and hydrogen sulfide that might be present. Add sufficient 0.1 M silver nitrate to precipitate completely all of the halogens as silver halides, and isolate the precipitate by filtration. If both nitrogen and sulfur have been determined to be present, add 6 mL of concentrated nitric acid to the precipitate and boil the solution for 10 min. This treatment results in the reaction of any silver thiocyanate that may be present. Dilute the resulting mixture to 6 mL of distilled water and filter. Isolate the solid. Boil the precipitate of silver halides with 4 mL of 0.1% sodium hydroxide for 2 min. Filter the solution. Acidify the filtrate with 5% nitric acid and add three drops of 0.1 M silver nitrate. A white precipitate indicates the presence of chlorine.

Procedure (i) for Fluorine Acidify 2 mL of the sodium fusion solution with glacial acetic acid and boil the solution. Cool the solution. Place one drop of the solution on a piece of zirconium–alizarin test paper. A yellow color on the red paper indicates the presence of fluorine. Prepare the test paper by dipping a piece of filter paper into a solution composed of 3 mL of 1% ethanolic alizarin solution and 2 mL of a 0.4% solution of zirconium chloride (or nitrate). Dry the red filter paper and, immediately before use, moisten it with a drop of 50% acetic acid.

Procedure (j) for Fluorine Acidify 4 mL of the stock solution with acetic acid. Heat the solution to boiling. Cool the solution. Add four drops of saturated calcium chloride solution. If fluorine is present, a gelatinous precipitate of calcium chloride will form after several hours.

Controls Test these procedures with chlorobenzene (positive test for chlorine), bromobenzene (positive test for bromine), iodobenzene (positive test for iodine), fluorobenzene (positive test for fluorine), 4-bromobenzenesulfonamide (positive test for bromine in the presence of nitrogen and sulfur), and toluene (negative test).

Cleaning Up Filter off the silver, mercury, and lead salts and place them in the hazardous solid waste container. Place the methylene chloride layers in the halogenated organic solvent container. Neutralize the aqueous layers with sodium bicarbonate, if acidic, or 5% hydrochloric acid, if basic, and place them in the aqueous solution container.

3.6 QUANTITATIVE ELEMENTAL ANALYSIS

3.6.1 Combustion and Related Analyses

Quantitative analytical data are routinely reported for confirmation of structure of new organic compounds; these data are extremely useful for structure determination of unknown compounds. Such microanalyses are usually determined by commercial firms[20] equipped with combustion or other appropriate analytical equipment. Unknown samples must be checked for purity by thin-layer chromatography (Section 4.4.1, pp. 86–90) and/or gas chromatography (Section 4.4.2, pp. 90–99) after they have been recrystallized (Section 3.4, pp. 49–52) or distilled (Section 4.2, pp. 67–75). The unknown can be dried to remove residual solvents in an Abderhalden drying pistol (Figure 3.22). A small amount of material is spread thinly in a porcelain boat or on glazed weighing paper. The sample can also be placed in a small vial with a high-quality laboratory tissue held around the mouth of the container with a rubber band. The container is then placed in the horizontal portion of the drying pistol.

The drying bulb of the drying pistol is charged with fresh, anhydrous drying agent. For removal of water, the drying agent can be phosphorus pentoxide or, less efficiently, calcium sulfate or calcium chloride. The entire system is then evacuated with a vacuum pump. The speed at which the sample loses the solvent may be increased by allowing toluene or xylene to reflux up from the lower flask; the sample must be stable and have a melting point higher than the boiling point of the solvent. If it is believed that hydrocarbon solvents are present in the sample, wax shavings are used instead of the

[20]Quantitative analyses of C, H, N, S, P, and X are determined by Galbraith Analytical Laboratories, Knoxville, TN; Baron Consulting, Milford, CT; Huffman Laboratories, Golden, CO; and Atlantic Microlab, Norcross, GA.

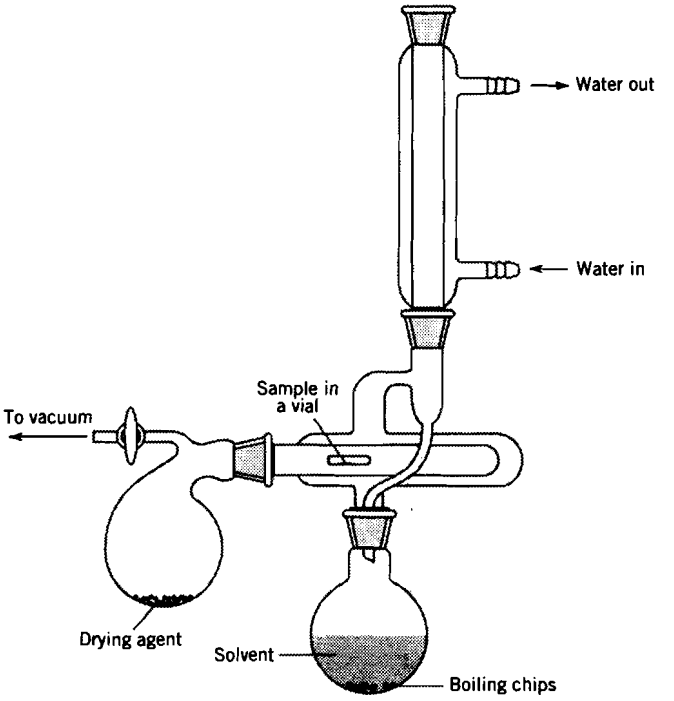


Figure 3.22 Abderhalden drying pistol.

desiccant. Samples can be examined under a magnifying lens for filter paper fibers or other extraneous material.

Normally 5 mg of the sample is needed for carbon and hydrogen analysis and another 5 mg for each additional analysis for other atoms such as sulfur, halogen, or deuterium. Oxygen analyses are not generally obtained; percent of oxygen is normally obtained by the difference in percentages. Confirmation of a molecular formula is satisfactory when the calculated and experimentally determined percentages agree within ±0.4%; for example:

Calculated for $C_{13}H_{16}O$:	C, 82.93; H, 8.57
Observed:	C, 82.87; H, 8.67

When the molecular formula is unknown prior to the analysis, the empirical formula can be determined by combustion. The molecular formula can then be calculated if the molecular weight is known.

Two methods[21] are used in order to determine the amounts of carbon, hydrogen, and nitrogen in a sample. In one method[22] of elemental determination, the sample is combusted in pure oxygen. The products, in a stream of helium gas, are passed over suitable reagents to completely oxidize the products. The products from the combustion are carbon dioxide (from carbon), water (from hydrogen), and nitrogen oxides (from nitrogen). In a reduction tube, the nitrogen oxides are reduced to molecular nitrogen. The resulting mixture is swept over three thermal conductivity detectors. Water is

[21]Private communication with Paul Rosenberg, Fisons Pharmaceuticals, Rochester, NY.

[22]The first method is based on a CE-440 elemental analyzer manufactured by Exeter Analytical, Chelmsford, MA.

removed between the first and second detectors with an adsorption trap, which determines the amount of hydrogen. Between the second and third detectors, the carbon dioxide is removed by a trap; the amount of carbon is determined. The remaining sample, which contains nitrogen, passes through a thermal conductivity cell. The output signal is compared to a reference signal of pure helium. For the determination of oxygen, the entire combustion is done only in the presence of helium. The sample passes through a pyrolysis tube containing platinized carbon to yield carbon monoxide and is then oxidized to carbon dioxide in a tube containing copper oxide. The carbon dioxide is removed by a trap and the amount measured. For sulfur determination, a tube containing tungsten oxide is used to combust the sulfur to sulfur dioxide. Silver oxide is used to absorb the sulfur dioxide.

Another manufacturer[23] separates the combustion products, from an oxidation/reduction reactor, on a gas chromatograph connected to a thermal conductivity detector. Carbon, hydrogen, nitrogen, and sulfur are easily determined on this instrument. The instrument is easily adapted for the determination of oxygen.

To determine the amount of halogen present, the sample is combusted in a Schöniger micro combustion flask. The combustion products are titrated with mercuric nitrate to a diphenylcarbazone colorimetric end point.

For example, 11.55 mg of a compound produced 16.57 mg of carbon dioxide and 5.09 mg of water from combustion. Another 5.12 mg of the same compound was found to contain 1.97 mg of chlorine. The molecular weight had been previously determined to be 368.084 g/mole by another method.

The mg of C is determined by multiplying the weight of CO_2 by the ratio of the atomic weight of carbon to the molecular weight of carbon dioxide (C/CO_2). The percentage of C is then calculated by the ratio of mg of C to the total weight of the sample.

$$\text{mg C} = 16.57 \text{ mg } CO_2 \times \frac{12.011\ (C)}{44.010\ (CO_2)}$$

$$= 4.52 \text{ mg C in original sample}$$

$$\% \text{ C} = \frac{4.52}{11.55} \times 100 = 39.13\% \text{ C}$$

The mg of H is determined by multiplying the weight of H_2O by the ratio of the atomic weight of two hydrogens to the molecular weight of water ($2H/H_2O$). The percentage of H is determined by the ratio of mg of H to the total weight of the sample.

$$\text{mg H} = 5.09 \text{ mg } H_2O \times \frac{2.016\ (2H)}{18.015\ (H_2O)}$$

$$= 0.57 \text{ mg H in original sample}$$

$$\% \text{ H} = \frac{0.57}{11.55} \times 100 = 4.935\% \text{ H}$$

Since 1.97 mg of Cl was found in 5.12 mg of sample, then the percentage of chlorine can be determined by the ratio of mg of Cl to the weight of the sample used for the analysis.

$$\% \text{ Cl} = \frac{1.97}{5.12} \times 100 = 38.48\% \text{ Cl}$$

[23]The second method is based on a organic elemental analyzer manufactured by CE Instruments, which is now part of ThermoFinnigan, San Jose, CA.

The percentage of oxygen is determined by the difference.

$$\% \text{ O} = 100 - (39.13 + 4.94 + 38.48)$$
$$= 17.45\% \text{ O}$$

Each percentage is then divided by the atomic weight of that element to obtain the ratio of the elements.

$$\text{C} = \frac{39.13}{12.011} = 3.258$$

$$\text{H} = \frac{4.94}{1.008} = 4.901$$

$$\text{Cl} = \frac{38.48}{35.453} = 1.085$$

$$\text{O} = \frac{17.45}{16.000} = 1.091$$

The ratios are then divided by the lowest ratio (in this example, 1.085). If a fraction is obtained that is not close to a whole number, then all of the ratios are multiplied by whatever integer is necessary to obtain whole-number ratios. For example, if one of the ratio numbers contains a 0.2, then all of the ratios are multiplied by 5. With a 0.25, all are multiplied by 4; with a 0.33, all are multiplied by 3; and with a 0.5, all ratios are multiplied by 2.

$$\text{C} = \frac{3.258}{1.085} = 3.003;\ 3.003 \times 2 \approx 6$$

$$\text{H} = \frac{4.901}{1.085} = 4.517;\ 4.517 \times 2 \approx 9$$

$$\text{Cl} = \frac{1.085}{1.085} = 1.000;\ 1.000 \times 2 \approx 2$$

$$\text{O} = \frac{1.091}{1.085} = 1.005;\ 1.005 \times 2 \approx 2$$

Thus the empirical formula is $C_6H_9Cl_2O_2$, with an empirical weight of 184.042 g/mole. The formula weight, which had been previously determined to be 368.084 g/mole, is then divided by the empirical weight to obtain the number of empirical units, n. Then multiply the subscripts of the empirical formula by n to obtain the molecular formula.

$$\frac{368.084}{184.0542} = n \approx 2$$

$$C_{6\times2}H_{9\times2}Cl_{2\times2}O_{2\times2} = C_{12}H_{18}Cl_4O_4 = \text{molecular formula}$$

The empirical formula could not possibly be the molecular formula because all compounds containing only carbons, hydrogens, oxygens, and halogens must have an even number of hydrogens plus halogens.

From the molecular formula, the number of rings and/or pi bonds can be determined. The unsaturation number is calculated by the formula

$$\text{U} = \text{C} + 1 - \frac{1}{2}\text{X} + \frac{1}{2}\text{Y}$$

where

U = the unsaturation number

C = the number of carbons

X = the number of hydrogens plus halogens

Y = the number of nitrogens plus phosphorus

Oxygen and sulfur do not change the number of unsaturations and thus do not appear in the formula.

U can be interpreted as follows:

U = 0: no double bonds, no triple bonds, no rings

U = 1: one double bond *or* one ring

U = 2: two double bonds *or* two rings *or* one double bond and one ring *or* one triple bond

U = 3: three double bonds *or* three rings *or* two double bonds and one ring *or* two rings and one double bond *or* one triple bond and one ring *or* one triple bond and one double bond

U = 4: usually a benzene ring

U = 5: benzene plus one double bond *or* one ring

For example, for the formula $C_9H_{11}NO$, the unsaturation number is $9 + 1 - \frac{1}{2}(11) + \frac{1}{2}(1) = 5$.

PROBLEMS

10. 13.66 mg of a compound produced 10.71 mg of carbon dioxide and 3.28 g of water. Another 4.86 g of the same compound yielded 3.46 g of bromine. The molecular weight is 673.72 g/mole. Calculate the percentages of carbon, hydrogen, bromine, and oxygen in the sample. Determine the empirical formula and the molecular formula of the compound.

11. Calculate the unsaturation number and give the interpretation for the following formulas.

a. $C_6H_{12}O$

b. $C_5H_{10}Cl_2$

c. $C_7H_{13}N$

d. $C_{12}H_{10}$

3.6.2 Formula Determination by Mass Spectrometry

A sample of sufficient thermal stability and volatility to result in a measurable molecular ion should yield the molecular weight by mass spectrometry. Tables[24] have been published that correlate molecular weights to four decimal places with molecular formulas. Also, certain elements, such as bromine, chlorine, and sulfur, have distinctive patterns in a mass spectrum. This information is discussed in detail in Chapter 8.

[24]R. M. Silverstein and F. X. Webster, *Spectometric Identification of Organic Compounds*, 6th ed. (Wiley, New York, 1998), pp. 45–65.

CHAPTER 4

Separation of Mixtures

The identification of the components of a mixture involves, first, a separation into individual components and, second, the characterization of each of the latter according to the procedures outlined in Chapter 9. It is very rarely possible to identify the constituents of a mixture without separation. The separation of the compounds in a mixture should be as nearly quantitative as possible in order to give some idea of the actual percentage of each component. It is far more important, however, to carry out the separation in such a manner that each compound is obtained in a pure form, because this renders the individual identifications much easier.

The method of separation chosen should be such that the compounds are obtained as they existed in the original mixture. Derivatives of the original compounds are not very useful unless they may be readily reconverted into the original compounds. This criterion of separation is necessary because the identification of a compound rests ultimately on agreement between physical constants of the original and of a derivative with similar data obtained from the literature.

The history of a mixture will frequently furnish sufficient information to indicate the group to which the mixture belongs and hence the general mode of separation to be used.

In recent years the field of analytical separation has been extensively developed and widely applied by organic chemists. It is thus necessary to be aware of the nature of the many techniques available in order to be able to choose the one which is most appropriate for the mixture in hand. There are a number of separation problems which frequently occur for the organic chemist. In one common situation the mixture is comprised of a number of components, all of reasonable purity and all of substantial proportion. Another type of separation is the isolation of a single component from large amounts of unreacted starting material or from undesired side products; these side products frequently are simply intractable tars or polymeric materials. We should try to place each new separation problem into one of these two categories in order to be able to select the most efficient separation approach.

Before selecting a separation procedure, the preliminary tests outlined in Section 4.1 should be carried out. As these tests are performed, one should constantly be concerned with the following:

1. Will the sample survive the separation procedure? That is, are the components of the mixture stable under the conditions of the procedure?
2. Is this the easiest and most efficient way to carry out the separation?

Thermal stability is always of concern. Stability of the sample under the conditions of the separation procedure may not be known until the separation is attempted. Compounds which are thermally unstable to the heat required for distillation at atmospheric pressure should be distilled at reduced pressure. Extractions and column

chromatography do not involve heat and thus may be appropriate for samples which cannot be distilled. However, some samples may decompose because of chemical reactions with acid or base in extractions or with chromatographic packing or support in column chromatography. A TLC test (pp. 86–90) is a fast and useful check for sample durability under chromatographic conditions.

4.1 PRELIMINARY EXAMINATIONS OF MIXTURES

1. Note the physical state. Take advantage of existing separations. If a solid is suspended in a liquid, remove the solid by filtration and examine it separately. If two immiscible liquids are present, separate them and examine them separately.
2. Determine the solubility of the mixture in water. Classify the mixture according to Figure 5.1 (p. 113) and Table 5.1 (p. 112).
3. With liquid mixtures, evaporate 2 mL of the solution to dryness on a watch glass or porcelain crucible cover and note the presence or absence of a residue. Apply the ignition test (Section 3.1.4, p. 24) to the residue or 0.1 g of the liquid or solid.
4. In liquid samples, determine the presence of water by (a) determining the miscibility of the solution with ether, (b) using the anhydrous copper sulfate test, or (c) using the distillation test for water.

   In the copper sulfate test, add a small sample of anhydrous copper sulfate to the liquid. If the solution turns blue, it is indicative of the presence of water, indicating the copper sulfate has absorbed the water. The distillation test is the most reliable and is carried out in the following manner: Place 5 mL of the liquid and 5 mL of anhydrous toluene in the distilling flask of a distillation apparatus. Heat the mixture gently with a flame until distillation occurs. Collect 2 mL of the distillate. Add 5 mL of toluene to the distillate. The presence of two layers or distinct drops suspended in toluene indicates the presence of water. If the solution is only cloudy, traces of water are indicated.
5. If water is absent, determine the presence of a volatile solvent by placing 1.0 mL of the mixture in a distilling flask in a simple distillation apparatus. Place the distilling flask in a beaker of water and heat the water to boiling. Any liquid that distills under these conditions is classified as a volatile solvent. Examine the distillate, which may be a mixture of readily volatile compounds, and the residue in the flask separately.

   It frequently happens that distillation of a water soluble mixture yields a volatile solvent and a water insoluble residue. The separation of such a mixture is therefore carried out by removing all of the volatile solvent. The residue is then treated as a water insoluble mixture.

   If the residue after distillation is a water soluble liquid, it is best not to remove the solvent at this stage because the separation is usually not quantitative.

   If, however, the residue after distillation is a water insoluble solid and the removal of the solvent seems quantitative, then remove all of the volatile solvent and examine the distillate and the residue separately.

   If water is present, no such separation should be attempted.
6. Determine the reaction of an aqueous solution or suspension of the mixture to litmus and to phenolphthalein. If the mixture is distinctly acidic, titrate 1 mL (of a known exact weight) of the solution in 2.5 mL of water or ethanol with a standardized 0.1 M sodium hydroxide solution to determine whether

considerable amounts of free acid are present or whether the acidity is due to traces of acids formed by hydrolysis of esters. Perform the titration in an ice-cold solution, and take the first pink color of phenolphthalein as the end point. Obtain an IR spectrum of a mixture to reveal the presence of several carboxylic acid groups.

7. Acidify 2 mL of the mixture with 5% hydrochloric acid, and cool the solution. Note the evolution of a gas or the formation of a precipitate. Add 5% sodium hydroxide solution to the solution until the solution is basic and note the result.
8. Make 2 mL of the mixture basic with 5% sodium hydroxide solution. Note the separation of an oil or solid, the liberation of ammonia, and/or any color change. Heat the solution just to boiling and then cool. Compare the odor with that of the original mixture. The presence of esters is often indicated by a change in odor. Next, add 5% hydrochloric acid until the solution is acidic and note the result.
9. In the case of water insoluble mixtures, perform an elemental analysis (Chapter 3, pp. 53–60). If water or a large amount of a volatile solvent is present in a water insoluble mixture, omit the elemental analysis of the mixture. If the water soluble mixture is composed of solids, perform an elemental analysis.
10. If water is absent, cautiously determine the effect of the following classification reagents: (a) metallic sodium (Experiment 5, p. 262); (b) acetyl chloride (Experiment 6, p. 264).
11. Determine the action of the following classification reagents on an aqueous solution or suspension of the original mixture: (a) bromine water (Experiment 46, p. 326); (b) potassium permanganate solution (Experiment 38, p. 328); (c) ferric chloride solution (Experiment 45, p. 345); (d) alcoholic silver nitrate solution (Experiment 35, p. 320); (e) fuchsin–aldehyde reagent (Experiment 17, p. 284); and (f) 2,4-dinitrophenylhydrazine (Experiment 12, p. 278).

    At this stage of the examination, the results of the foregoing tests are summarized and as much information as possible is deduced from the behavior of the mixture. The preliminary study will show the group in which the mixture should be classified and will, therefore, indicate which of the following procedures should be used in its separation.

4.2 DISTILLATION AND SUBLIMATION

An introduction to simple distillation has been given on pages 30–31 (Section 3.2.2); in these earlier treatments simple sample purification and boiling point measurement were discussed. Other more sophisticated distillation techniques are also available for sample purification. Several of these methods will be discussed in the following sections.

Sublimation is a technique in which a solid is heated and vaporized, without passing through the liquid phase. The gas is then condensed and collected as a solid.

4.2.1 Distillation

For amounts from a few milligrams to 5 g, with appropriate variation of the sizes of the distillation flask and the receiver bulb, the Kugelrohr distillation apparatus (Figure 4.1) can be used. A converted coffee pot can be used as the heat source. The reciprocating motor moves the glassware back and forth so that the compound does not bump over. A vacuum pump is used as the source of the vacuum. The great advantage of this apparatus is its ability to apply good vacuums, sometimes as low as 0.1 mm Hg (torr),

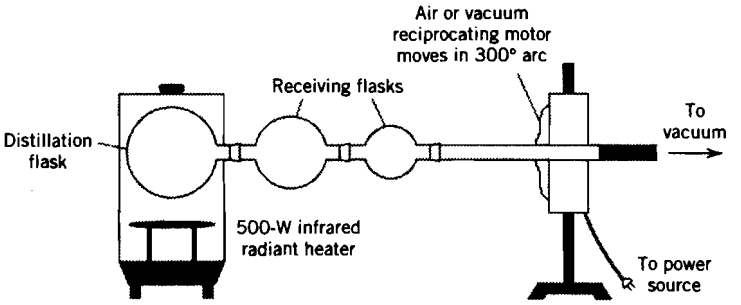


Figure 4.1 Kugelrohr distillation apparatus.

especially when the glassware is composed of only one piece rather than of a number of fitted pieces with many possibilities for leaks. An ice bath or dry ice–acetone bath is used to condense the material into the center receiver. The Kuglerohr apparatus is best for only purifying a product, therefore leaving impurities behind.

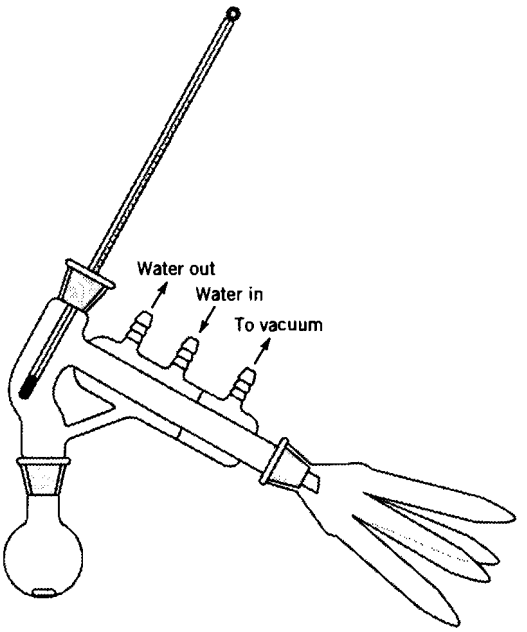


Figure 4.2 Short-path distillation apparatus with stirbar.

For larger amounts up to 50 mL of material, a short-path distillation apparatus (Figure 4.2) is used. The short-path process allows distillation of materials such as low-melting solids for which long exposure to elevated temperatures could be detrimental.

A Hickman–Hinkle distillation (Figure 4.3) and a microscale distillation apparatus (Figure 4.4) can be used to distill 0.5–2.0 mL of a sample. An air condenser is used for condensation of the liquid.

In order to improve the efficiency of a distillation, a column (Figure 4.5) can be placed between the vessel to be heated and the condenser tube. Frequently, the column is a condenser filled with glass beads or steel wool to provide increased surface area and/or increase cooling surfaces. Alternatively, the column may contain coils or glass indentations such as those in Vigreux columns (Figure 4.5*a*), which are available

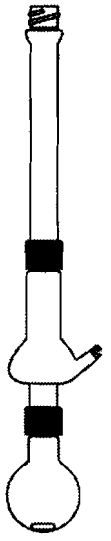


Figure 4.3
Hickman–Hinkle still head with a round-bottom flask, air condenser, and stirbar.

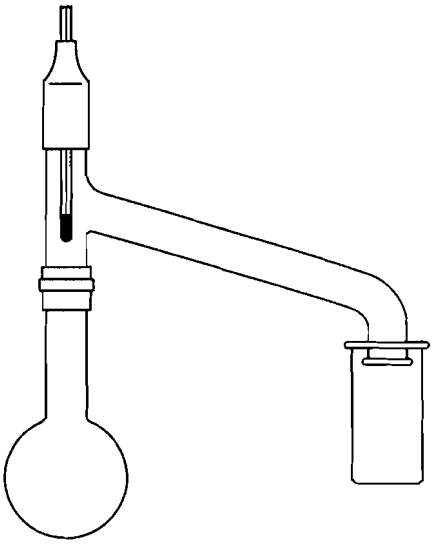


Figure 4.4 Microscale distillation apparatus.

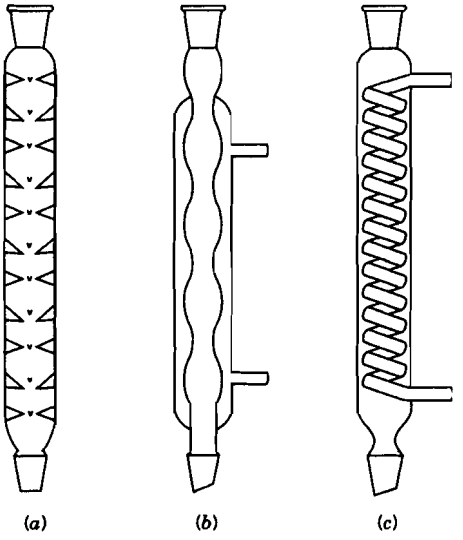


Figure 4.5 Distillation columns and condensers: (*a*) Vigreux column, (*b*) Allihn condenser, (*c*) coiled condenser.

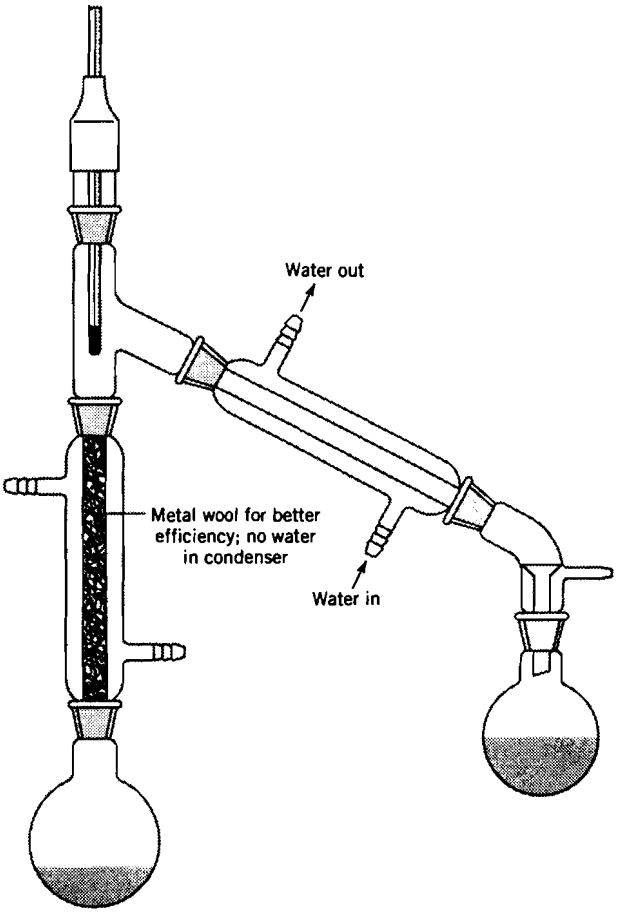


Figure 4.6 A fractional distillation apparatus.

in some commercial condensers. In any case, this vertical column is not surrounded by a jacket of water as typically found in the traditional condenser.

A fractional distillation apparatus (Figure 4.6) uses the vertical column in addition to the condenser. With this distillation apparatus, compounds with a difference in their boiling points of 5–10°C or more can be efficiently separated.

The spinning band apparatus, shown in a microscale form in Figure 4.7, allows a very efficient distillation because of the large number of theoretical plates provided for the distillate.

Frequently the result of a more efficient distillation apparatus is that the distilling compound remains on the vertical column for a longer time. To avoid heat loss, the column should be externally insulated with glass wool, cotton, or aluminum foil.

A Hickman flask (Figure 4.8) is another microscale approach to distilling small amounts of compound. The distilling flask, Vigreux column, and condenser are all one

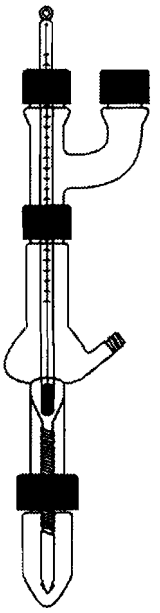


Figure 4.7 Microscale spinning band column.

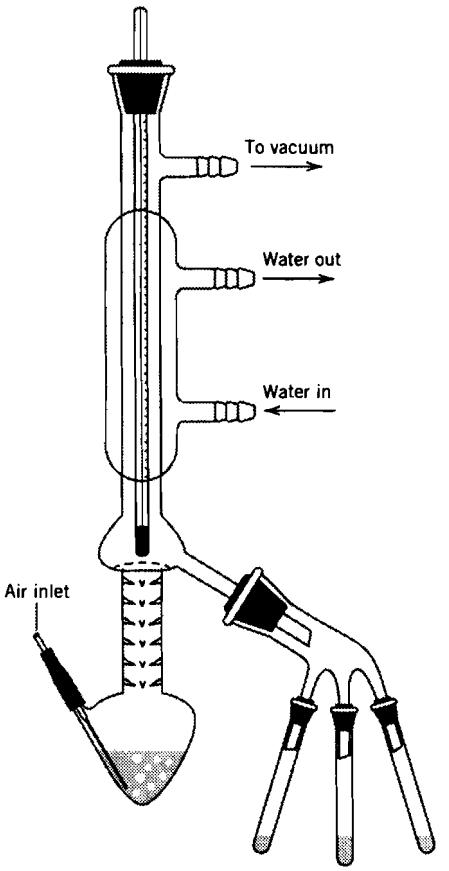


Figure 4.8 Hickman flask.

piece of glass in this particular apparatus. Normally a stopper is placed in the lower side tube of the Hickman flask. If a vacuum distillation is to be done, a small pipet is placed through the side tube to create a small stream of bubbles going through the compound. The distilled fractions are collected using test tubes attached to a cow adaptor.

In order to distill liquids and solids of low volatility which might be somewhat heat sensitive, a vacuum distillation apparatus (Figure 4.9) can be used. In this apparatus, the Vigreux column and the condenser are one piece of glass. The stopcocks are used to regulate pressure in the apparatus. An air inlet is optional. A laboratory aspirator can provide a vacuum of 15 mm Hg (torr), and a good vacuum pump can yield a range of 0.01–15 mm Hg (torr) for vacuum distillations.

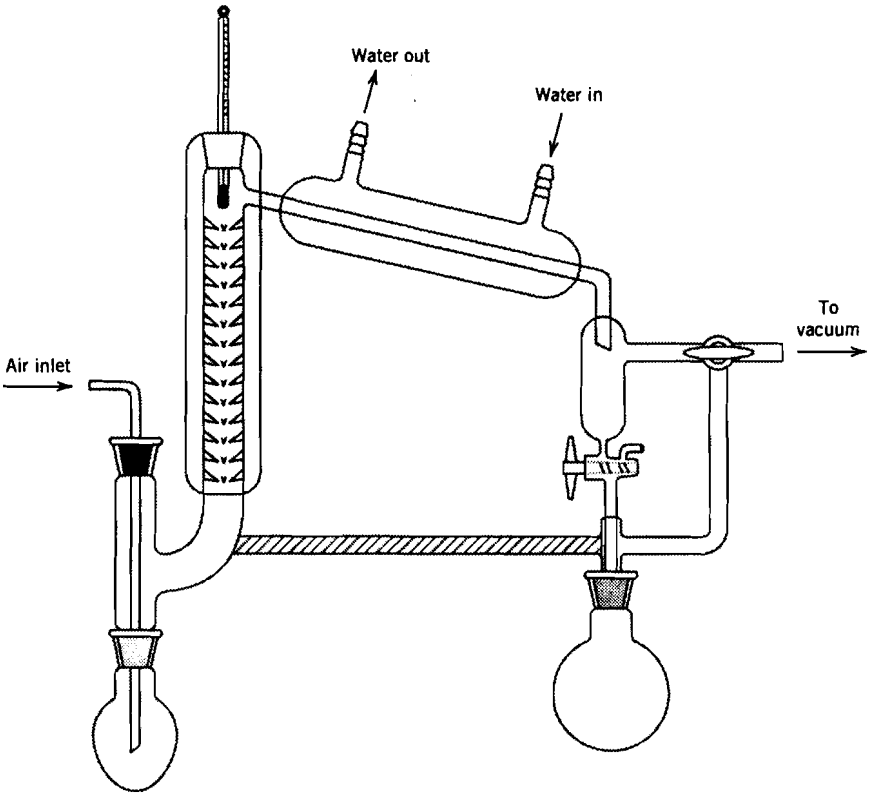


Figure 4.9 Vacuum distillation apparatus. Another option involves the replacement of the air inlet with a glass stopper and the addition of a stirbar.

An important aspect in distillation is the method of heating the distilling pot. For volatile liquids, a steam bath is used. Baths containing oils or other involatile, inert substances (see Liquid Media for Heating Baths, Appendix I, p. 529) can be used; such hot liquids provide a very even method of heat application and can be used to higher temperatures (ca. 250–400°C). Heating mantles attached to Variacs can be used for heat application; use of such mantles allows one to avoid the messy oils used for external heating.

Sand baths (Figure 4.10), in which sand is placed in a small heating mantle (manufactured by Thermowell), and aluminum blocks (Figure 4.11), which have concave spaces for flasks, are popular as heating devices, particularly in microscale applications. Flaked graphite can be substituted for the sand. The heating mantles for the sand baths are controlled with a Variac. The aluminum blocks are heated by placing them on a hot-plate stirrer.

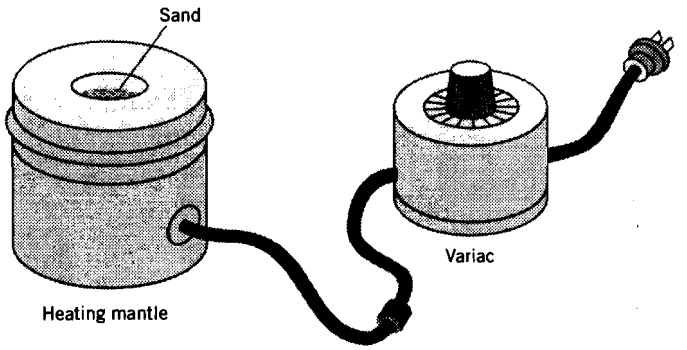


Figure 4.10 Sand bath with Variac.

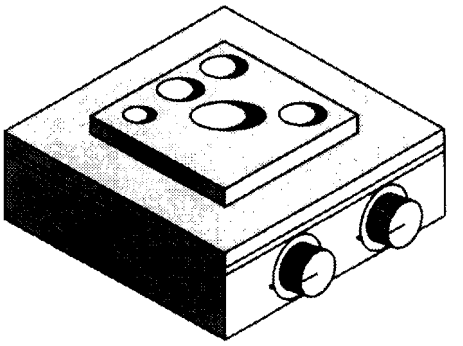


Figure 4.11 Aluminum block on hot-plate stirrer.

Frequently, an organic chemist is concerned with removal of volatile solvents from a solution during the workup of a reaction. A rotary evaporator ("rotovap", Figure 4.12)

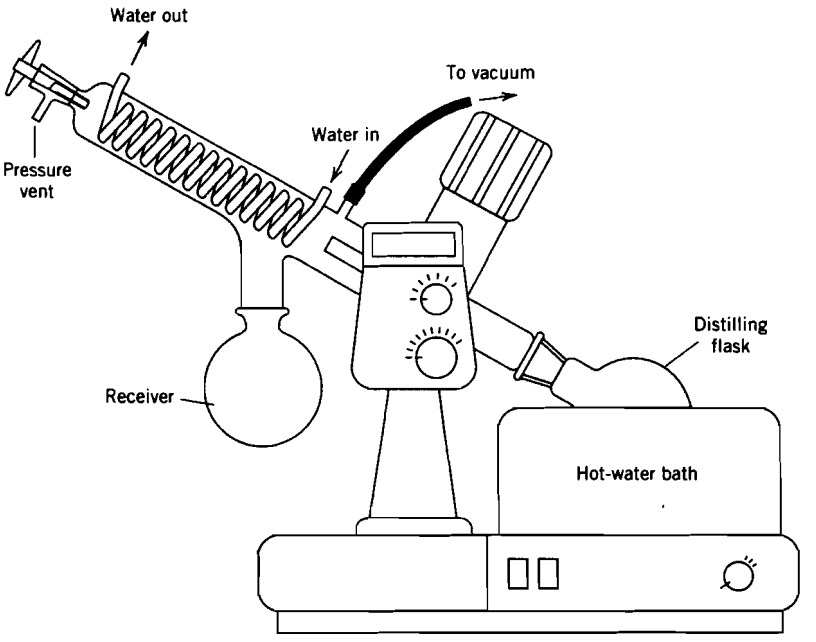


Figure 4.12 A rotary evaporator.

is useful for solvent removal. The distilling flask is spun to increase the surface area, to increase the rate of evaporation, and to prevent bumping of the solution. The vacuum lowers the boiling point of the liquid. A hot-water bath serves as a source of heat. The solvent is distilled into the receiver, leaving the product in the distilling flask.

4.2.2 Steam Distillation

Steam distillation is a technique whereby a compound of relatively low volatility can be purified by co-distilling it with water. This distillation occurs because both of the liquid components contribute to the vapor pressure and thus the distillation can be carried out at a temperature slightly less than 100°C at 760 mm Hg (torr). The distillation is actually carried out by simply forcing steam through a vessel containing the mixture and collecting the distillate with a water-cooled condenser (Figure 4.13). An alternate way to the steam inlet is to heat the flask with a bunsen burner and add water, via an addition funnel, to maintain a constant volume in the flask.

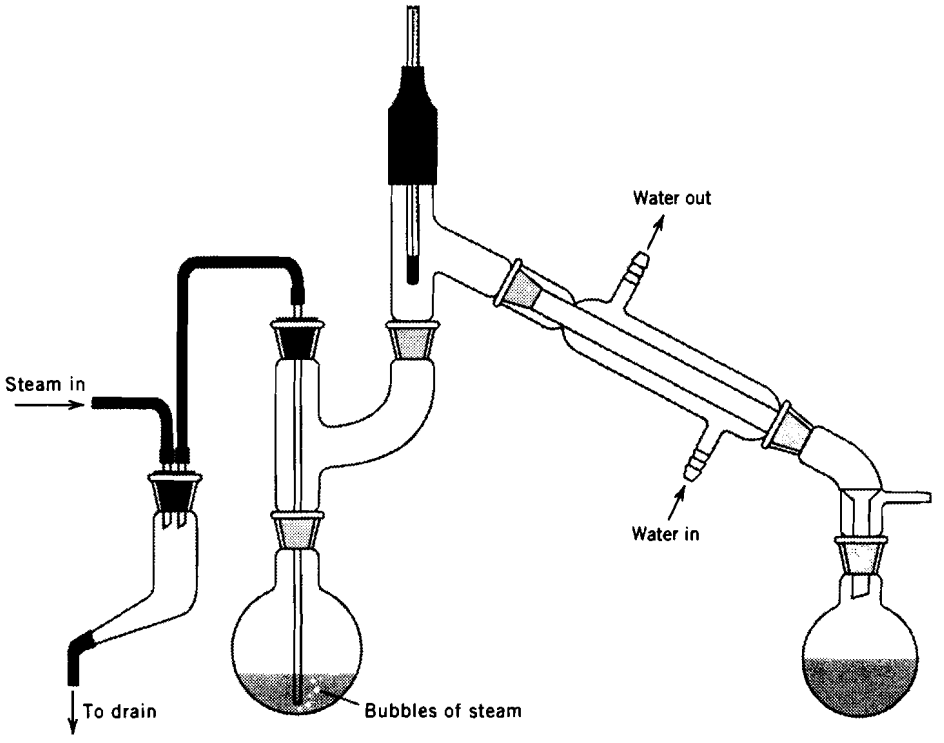


Figure 4.13 Steam distillation apparatus (macroscale).

A difference in polarity sufficient to permit separation by steam distillation is generally provided by a second functional group in the molecule. Polyfunctional compounds are normally more polar and thus have a higher boiling point than monofunctional com-

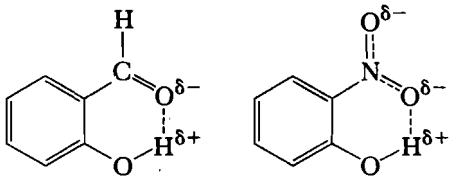
pounds. Thus, monohydroxy alcohols can be separated from dihydroxy and polyhydroxy alcohols by this scheme. Similarly, simple acids, amines, and many other volatile compounds can be separated from the corresponding di- and polyfunctional compounds. Moreover, the additional group or groups need not be the same as the original. Amino acids, hydroxy acids, nitro acids, keto acids, keto alcohols, and cyano ketones are rarely volatile with steam. In fact, it is a general rule that the presence in a molecule of two or more functional (polar) groups will render a compound nonvolatile. Table 4.1 shows which types of compounds are volatile with steam and which are not. Acetic acid and

TABLE 4.1 Solubility and Steam Distillation

Solubility	Types of Compounds	Volatility	Volatility with Steam
Soluble in water and ether (S_A, S_B, S_1)	Low-molecular-weight alcohols, aldehydes, ketones, acids, esters, amines, nitriles, acid chlorides	Readily distill. Many compounds boil below 100°C	Volatile with steam
Soluble in water but insoluble in ether (S_2)	Polyhydroxy alcohols, diamines, carbohydrates, amine salts, metal salts, polybasic acids; hydroxy aldehydes, ketones, and acids; amino acids	Low volatility. With certain exceptions these compounds cannot be distilled at atmospheric pressure	Not volatile with steam
Insoluble in water but soluble in NaOH and $NaHCO_3$ (A_1)	High-molecular-weight acids; negatively substituted phenols	Low volatility	Usually not volatile, but there are some exceptions
Insoluble in water and $NaHCO_3$ but soluble in NaOH (A_2)	Phenols, sulfonamides of primary amines, primary and secondary nitro compounds; imides, thiophenols	High boiling points; many cannot be distilled	Usually not volatile
Insoluble in water but soluble in dilute HCl (B)	Amines containing not more than one aryl group attached to nitrogen; hydrazines	High boiling points	Many are volatile with steam
Insoluble in water, dilute NaOH, and HCl, but contain elements other than carbon, hydrogen, oxygen, and the halogens (MN)	Nitro compounds (*tert*), amides, negatively substituted amines; sulfonamides of secondary amines; azo and azoxy compounds; alkyl or aryl cyanides, nitrites, nitrates, sulfates, phosphates	High boiling points; many cannot be distilled	Some are volatile with steam
Insoluble in water, dilute NaOH, and HCl, but soluble in H_2SO_4 (N)	Alcohols, aldehydes, ketones, esters, unsaturated compounds	High boiling compounds	Usually volatile with steam
Insoluble in water, dilute NaOH, dilute HCl, and H_2SO_4 (I)	Aromatic and aliphatic hydrocarbons and their halogen derivatives	Volatile	Volatile with steam

oxalic acid, ethyl alcohol and ethylene glycol, benzoic acid and 1,2-benzenedicarboxylic acid are mixtures that illustrate the point. In each pair the first named can be removed by steam distillation, whereas the other remains behind.

A very interesting group of exceptions to the multiple function rule is found in the aromatic series. 2-Hydroxybenzaldehyde, 2-nitrophenol, and many other *ortho*-disubstituted benzene derivatives are volatile with steam. The explanation for this apparently anomalous loss of polar character is found in the observation that *all these exceptional compounds are capable of intermolecular hydrogen-bonded forms.* These forms tend not to associate with the water and are thus relatively volatile. The hydrogen-bonded structures of 2-hydroxybenzaldehyde and 2-nitrophenol are shown below.



Another valuable use of steam distillation is the separation of reaction products from solvents such as *N,N*-dimethylformamide (DMF) and dimethyl sulfoxide (DMSO). DMF and DMSO are good solvents for carrying out many reactions, but their high boiling points (as well as other properties) make their removal from the reaction mixture a very difficult process when conducted by other procedures. Neither DMSOn or DMF is volatile in a steam distillation. Thus in many cases we may merely dilute a reaction mixture with water and remove the products or the unreacted starting materials by steam distillation.

4.2.3 Sublimation

Occasionally compounds may be purified by sublimation. In a sublimation apparatus (Figure 4.14), a cold finger is placed inside another container containing a side arm. The outer container may consist of a special type of glassware or may be as simple as

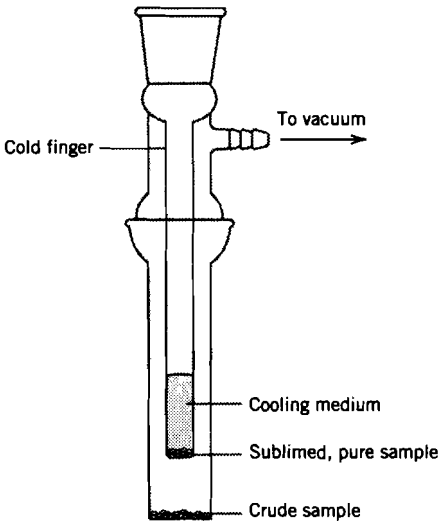


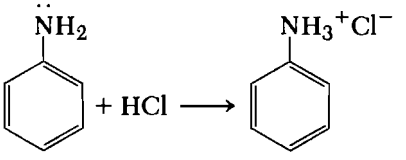
Figure 4.14 Sublimation apparatus.

a test tube or Erlenmeyer flask with a side arm. Ice, dry ice, or a dry ice–acetone slurry is placed inside the cold finger. The material to be sublimed is placed on the bottom of the inside of the outer container. Frequently, the apparatus is attached to vacuum. Heat is applied externally, usually in the form of an oil or sand bath. Successful sublimation of material from the crude mixture will result in the formation of crystals on the bottom outside of the cold finger. It may be necessary to interrupt the sublimation periodically and scrape the solid off the surface of the cold finger.

Before attempting sublimation on a compound, look up the boiling point to see if the compound sublimes instead of boiling. The abbreviation "sub" indicates that the compound will sublime. Caffeine and camphor are examples of such compounds.

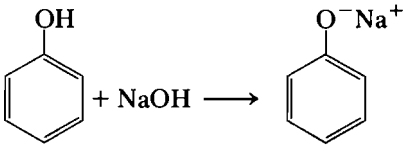
4.3 EXTRACTIONS: SEPARATIONS BASED UPON SALT FORMATION

The basic principle of this technique can be made clear by reference to simple examples. The separation of aniline from toluene is effected by extraction with dilute hydrochloric acid. The aniline goes into the aqueous layer as its salt, aniline hydrochloride. Whereas aniline is very soluble in toluene and virtually insoluble in water, its hydrochloride salt, because of its polar nature, is soluble in water and insoluble in toluene.



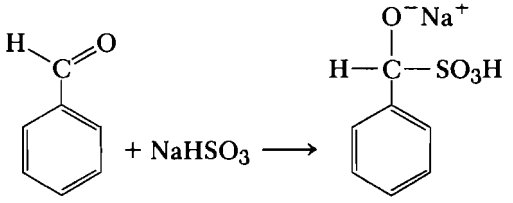
water soluble
toluene insoluble

Similarly, phenol is removed from toluene by shaking the mixture with a dilute sodium hydroxide solution. The phenol is transformed into its anionic form, sodium phenoxide, whose highly polar character makes it insoluble in toluene and soluble in water.



water soluble
toluene insoluble

Benzaldehyde may be separated by a similar scheme. In this case the mixture is shaken with an aqueous solution of sodium bisulfite which converts the aldehyde into its bisulfite derivative. This is a typical salt and therefore insoluble in toluene but soluble in water.



water soluble
toluene insoluble

In each of these examples the original acid, base, or aldehyde is easily recovered by decomposition of the salt by familiar methods.

If the compounds to be separated are water soluble to any considerable degree, extraction methods usually have little value. Steam distillation, however, can generally be used instead. For example, a mixture of acetic acid and cyclohexanone can be separated by adding enough alkali to transform the acid to sodium acetate and steam distilling the mixture. The ketone will be removed in the distillate while the salt, being nonvolatile, remains behind. Acidification with phosphoric acid regenerates the organic acid, which can now be distilled with steam.

Diethylamine can be separated from 1-butanol in a similar manner. Phosphoric acid is added in sufficient amount to neutralize the amine. Steam distillation will now remove the alcohol, and the amine can be recovered by adding dilute sodium hydroxide solution to the residue and repeating the steam distillation.

$$(CH_3CH_2)_2NH + CH_3CH_2CH_2CH_2OH \xrightarrow{H_3PO_4}$$

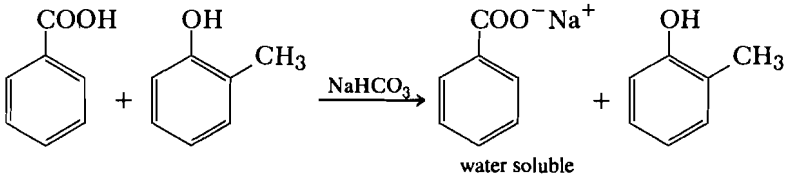
$$(CH_3CH_2)_2NH_2^+ H_2PO_4^- + \underset{\text{volatile with steam}}{CH_3CH_2CH_2CH_2OH}$$

$$\xrightarrow{\text{dilute NaOH}} (CH_3CH_2)_2NH$$

Another useful method for establishing a marked difference in the polar character of the components is illustrated by the separation of mixtures of primary amines from tertiary amines. Acetylation or benzoylation converts the primary amine to a *neutral* amide. Extraction with dilute hydrochloric acid will then remove the tertiary amine and leave the amide behind. The amide can be reconverted to the original amine by hydrolysis.

A very similar principle is involved in the Hinsberg method (Chapter 9, p. 291) of separating and characterizing primary and secondary amines. The sulfonamide from the primary amine forms a salt with alkali and thus can be removed by extraction with dilute sodium hydroxide solution.

A general method can be developed for separating acidic compounds differing in acidity. Strong acids form salts when treated with sodium bicarbonate and can be extracted with this reagent. Thus, if a mixture of 2-methylphenol and benzoic acid is shaken with a dilute solution of sodium bicarbonate, the carboxylic acid passes into the water layer as sodium benzoate, leaving the less acidic 2-methylphenol (*o*-cresol) behind.



If a mixture contains more than two compounds, combinations of the following methods frequently lead to satisfactory separations. The necessary condition for successful separation is that *the components be such that a wide polarity difference exists or can be induced between any two of them.*

In practice, mixtures fall into two categories, depending on whether they are soluble in water. These two types will be considered separately.

4.3.1 Extraction of Water Insoluble Mixtures

After the removal of any volatile solvent one of the following procedures may be used for the separation of the compounds of a water insoluble mixture. For these procedures to work effectively, no component of the mixture can be soluble in water.

These procedures are used after the water solubility test on page 114. These procedures, as described below, assume that all possible fractions are obtained. Of course, if the mixture does not contain certain types of compounds, then those fractions will not be obtained.

Procedure A: Water Insoluble Mixtures (Figure 4.15)
Mix 5 g of the mixture with 15 mL of diethyl ether. Separate any insoluble compounds (Residue 1) on a filter and wash with two 5-mL portions of diethyl ether. Add the ether washings to the original ether solution (Organic Layer 1). Extract this layer with three 5-mL portions of 5% hydrochloric acid solution. If a solid amine hydrochloride separates

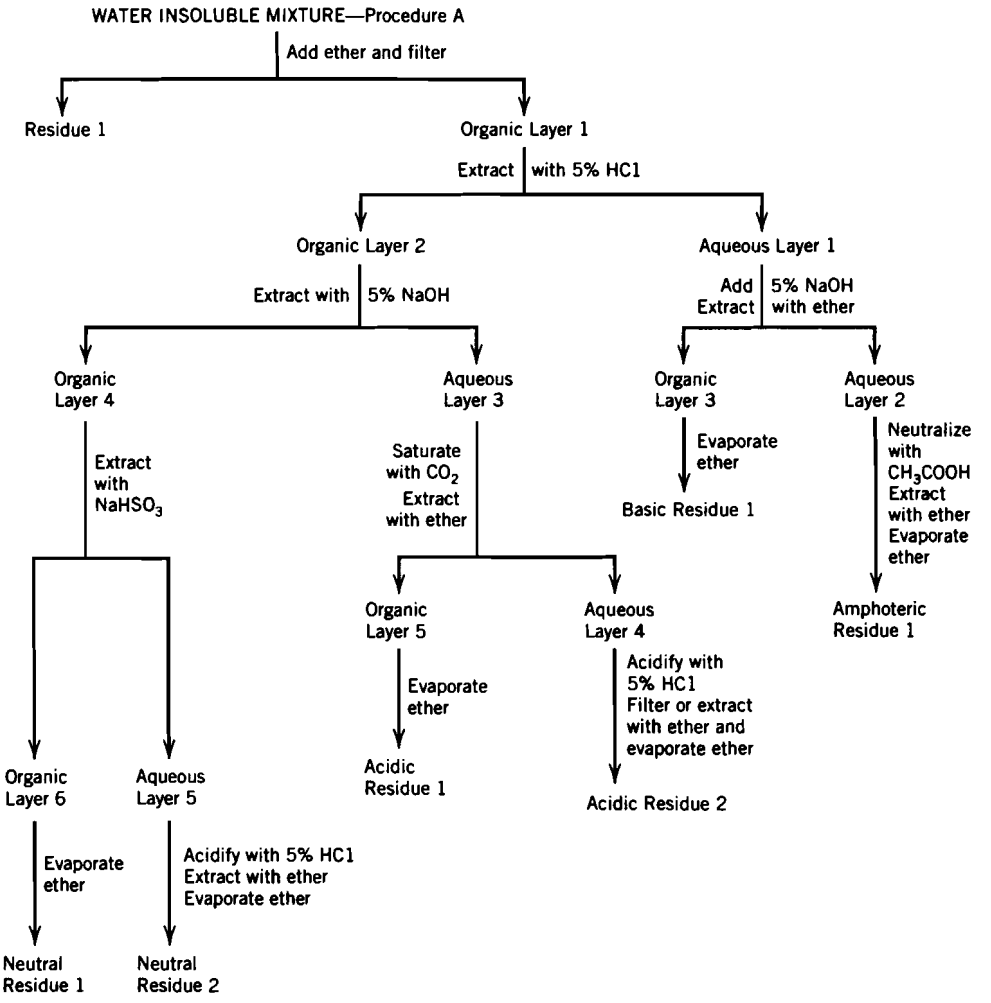


Figure 4.15 Separation of a water insoluble mixture as described in Procedure A.

during this extraction, add water until the amine hydrochloride dissolves. Combine the acidic aqueous layers (Aqueous layer 1). Place the ether layer (Organic layer 2) aside.

Make the aqueous layer (Aqueous layer 1) basic with 5% sodium hydroxide solution. Extract the resulting mixture with three 5-mL portions of diethyl ether. Separate the layers into the aqueous layer (Aqueous layer 2) and the organic layer (Organic layer 3). Dry the ether layer (Organic layer 3) with anhydrous sodium sulfate. Distill off the ether. The residue is composed of bases (Basic residue 1).

Carefully neutralize the remaining aqueous layer (Aqueous layer 2) with acetic acid. Extract the solution with five 5-mL portions of diethyl ether to recover any amphoteric compounds. Evaporate the ether to leave the amphoteric compounds (Amphoteric residue 1).

Extract the ether layer (Organic layer 2) with three 5-mL portions of 5% sodium hydroxide solution. If an emulsion occurs, add more water and a few crystals of sodium chloride to aid in the separation of the layers. Combine the basic aqueous layers (Aqueous layer 3). Set aside the ether layer (Organic layer 4).

Saturate the combined basic aqueous layers (Aqueous layer 3) with carbon dioxide (dry ice) by slowly adding small pulverized dry ice chunks, with caution, until the aqueous layer is no longer basic. Test with pH paper. Extract any weak acids with three 5-mL portions of diethyl ether. Combine the ether layers (Organic layer 5). Distill off the ether from the ether layers (Organic layer 5) to yield the weak acids (Acidic residue 1).

Acidify the remaining aqueous layer (Aqueous layer 4) with 5% hydrochloric acid. Isolate the stronger acids (Acidic residue 2) by filtration or by extraction with three 5-mL portions of diethyl ether, followed by evaporation of the ether.

Extract the ether layer (Organic layer 4) with four 5-mL portions of 40% aqueous sodium bisulfite. Separate the aqueous layer (Aqueous layer 5) and the ether layer (Organic layer 6). Place the ether layer (Organic layer 6) aside. Add 7 mL of 5% hydrochloric acid to the combined bisulfite aqueous layers (Aqueous layer 5) . Extract the solution with three 5-mL portions of ether. Remove the ether by distillation to leave behind a residue (Neutral residue 2).

Distill off the ether from the ether layer (Organic layer 6) to leave behind a residue (Neutral residue 1).

Frequently, the extent of the procedure given above in Procedure A is not needed. A more abbreviated version is described in Procedure B.

Procedure B: Water Insoluble Mixtures (Figure 4.16)

Mix 5 g of the mixture with 15 mL of diethyl ether. Extract the resulting mixture with three 5-mL portions of 5% hydrochloric acid solution. Separate the layers into the aqueous layer (Aqueous layer 1) and the organic layer (Organic layer 1).

Make the combined aqueous layers (Aqueous layer 1) alkaline with 5% sodium hydroxide solution. Extract the resulting solution with three 5-mL portions of diethyl ether. Dry the ether layer with sodium sulfate and distill off the ether. The residue (Basic residue 1) is composed of bases.

Extract the ether layer (Organic layer 1) with three 5-mL portions of 5% sodium hydroxide solution. Set aside the remaining ether layer (Organic layer 2). Acidify the combined basic aqueous layers (Aqueous layer 2) with 5% hydrochloric acid solution. Isolate the acid by filtration or by extraction with three 5-mL portions of ether, followed by evaporation of the ether (Acidic residue 1).

Extract the ether layer (Organic layer 2) with four 5-mL portions of 40% sodium bisulfite solution. Separate the layers into the organic layer (Organic layer 3) and

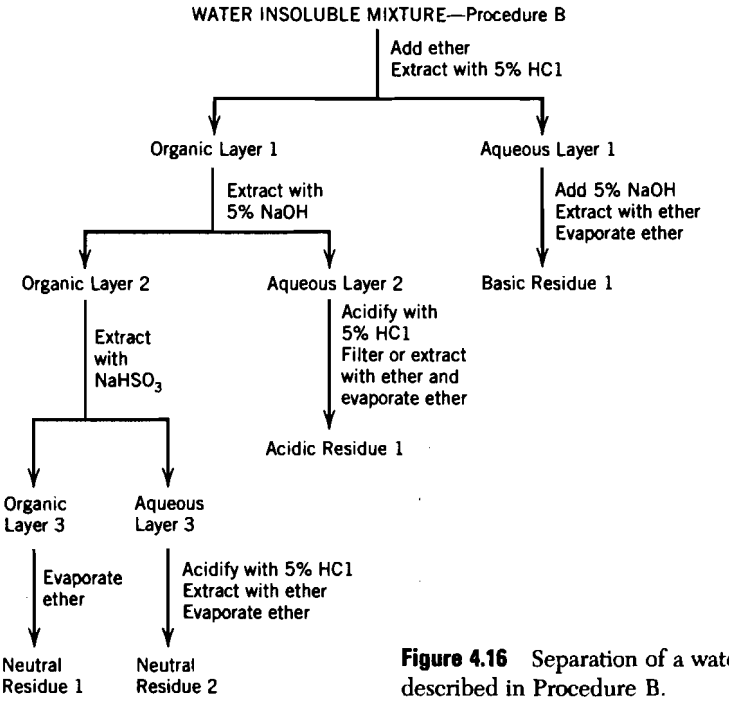


Figure 4.16 Separation of a water insoluble mixture as described in Procedure B.

the aqueous layer (Aqueous layer 3). Add 7 mL of 5% hydrochloric acid solution to the aqueous layer (Aqueous layer 3) and extract with three 5-mL portions of ether. Remove the ether by distillation to leave behind a residue (Neutral residue 2).

Distill off the ether from the ether layer (Organic layer 3) to leave behind a residue (Neutral residue 1).

Cleaning Up For Procedures A and B, place the ether in the organic solvents container. Neutralize any aqueous filtrate before placing it into the aqueous solution container.

▸ Problems

1. Show the equations for the formation of each salt at each step using Procedure B starting from a mixture of chlorobenzene, *N,N*-dimethylaniline, 2-naphthol, and 2-methoxybenzaldehyde.
2. A mixture of benzaldehyde, 4-butylaniline, 4-ethylphenol, and 4-propylbenzoic acid is subjected to the extraction procedure outlined in Procedure A (Figure 4.15). Where is each compound isolated and what are the reactions?
3. Although glucose is water soluble, its place of isolation in Figure 4.15 is predictable. Where would it be?

4.3.2 Extraction of Water Soluble Mixtures

If all components of the mixture are water soluble, steam distillation is the best method for the separation of the components. However, it may prove to be unsatisfactory if the

mixture is not chosen carefully. Too often the components of the mixture, when improperly chosen, undergo reaction with each other or with boiling aqueous acid or alkali during steam distillation. Thus extraction, which does not involve heating of the mixture, would be preferable.

Procedure C: Water Soluble Mixtures (Figure 4.17)

Place 5 mL of the mixture in a 125-mL round-bottom flask setup for a steam distillation (Figure 4.13). Collect 5–6 mL of the distilled solution (Distillate 1). Place the remainder of the solution (Residue 1) in an evaporating dish and remove the water by means of a steam bath. Remove the last traces of water with a rotary evaporator (Figure 4.12).

Acidify the distilled solution (Distillate 1) with phosphoric acid. Steam distill the solution. Collect 5 mL of the distilled compound (Distillate 2). Make the residue (Residue 2) left in the distilling flask basic with 5% sodium hydroxide solution. Extract the resulting mixture with three 5-mL portions of diethyl ether. Distill off the ether to yield a base (Basic residue 1).

Make the distilled solution (Distillate 2) just slightly basic with 5% sodium hydroxide solution and steam distill the mixture. Collect 5 mL of the distillate (Distillate 3).

Make the solution (Residue 3) left in the flask acidic with phosphoric acid and then extract it with three 5-mL portions of diethyl ether. Combine the ether layers and distill off the ether to yield the acid (Acid residue 1).

Saturate the distilled solution (Distillate 3) with potassium carbonate. Separate the layers. Save the upper layer (Organic layer 1) and apply the classification tests to this layer.

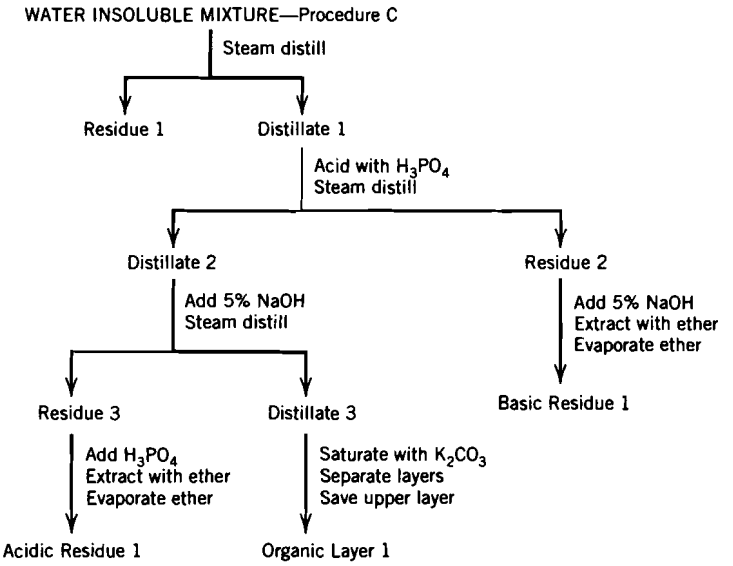


Figure 4.17 Separation of a water soluble mixture as described in Procedure C.

Cleaning Up For Procedure C, place the ether in the organic solvents container. Neutralize any aqueous filtrate before placing it into the aqueous solution container.

➤ PROBLEM

4. Show the equations for the formation of each salt at each step using Procedure C starting from a mixture of lactic acid, piperidine, acetic acid, and 2-propanol.

Hydrolysis of esters would occur using Procedure C. If the presence of an ester is indicated by odor or by change of color in the preliminary tests, then the procedure may be modified to use a milder base as described in Procedure D.

Procedure D: Water Soluble Mixture Containing Esters (Figure 4.18)
Saturate 5 mL of the mixture with potassium carbonate to yield an upper organic layer (Organic layer 1) and an aqueous layer (Aqueous layer 1). Neutralize the organic layer (Organic layer 1) with 5% sulfuric acid solution, using methyl orange as an indicator. Steam distill the resulting mixture. The solution (Residue 1) remaining in the flask contains the amine salts.

Saturate the distillate (Distillate 1) with potassium carbonate. Separate the upper layer (Organic layer 2), which contains the neutral compounds, from the aqueous layer (Aqueous layer 2).

Acidify the original aqueous layer (Aqueous layer 1) with phosphoric acid and filter it. The precipitate (Solid 1) contains acidic compounds. Steam distill the filtrate (Filtrate 1). The distilled solution (Distillate 2) contains acidic compounds.

Evaporate the residue (Residue 2) to dryness and extract with hot ethanol solution to yield an alcohol solution of acids (Solution 1).

If the mixture contains no acidic constituents, start the separation at the same point as the treatment of the first organic layer (Organic layer 1). In such a case, the first residue (Residue 1) from the steam distillation contains acidic compounds in addition to the amine sulfates. Separate it by the first method given.

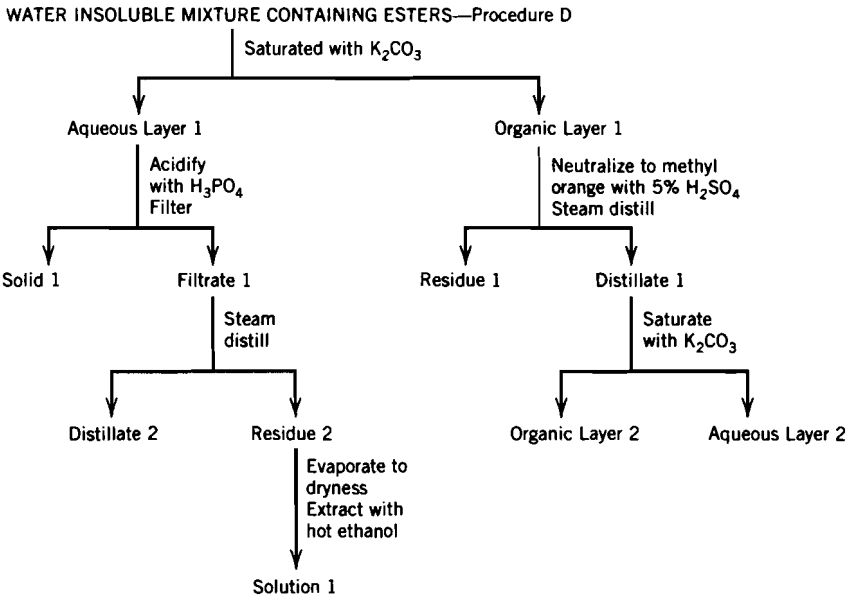


Figure 4.18 Separation of a water soluble mixture containing esters as described in Procedure D.

Cleaning Up The aqueous filtrate is neutralized and placed in the aqueous solution container.

This modified procedure may also be used with mixtures containing acids and alcohols; it provides no opportunity for esterification to take place.

The next three examples (Figures 4.19, 4.20, and 4.21) illustrate the separation of various types of mixtures.

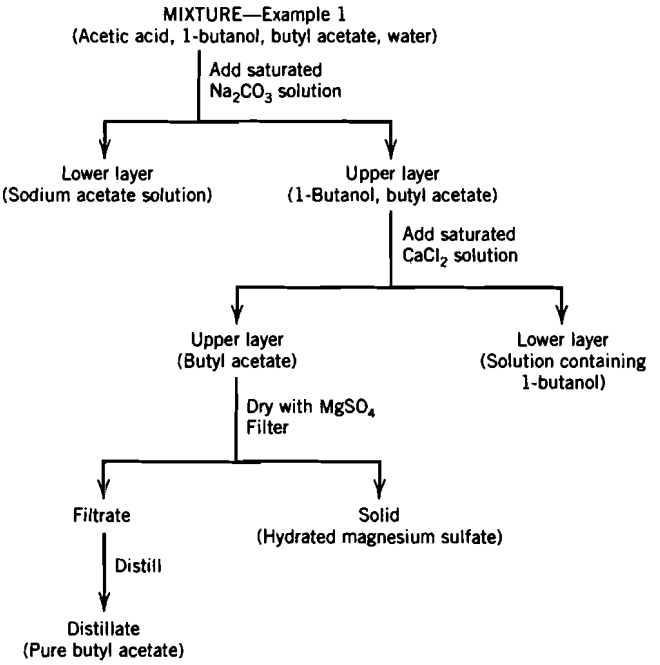


Figure 4.19 Separation of a mixture, Example 1.

Problems

5. Diagram a satisfactory procedure for the separation of the following mixtures and the identification of each component.
   a. Water, 2-propanol, anilinium sulfate, 2-methylpropanoic acid.
   b. Chloroform, aniline, *N,N*-diethylaniline, benzoic acid, naphthalene.
   c. Toluene, diphenylamine, quinoline, nitrobenzene.
   d. 2-Hydroxytoluene, 2-hydroxybenzoic acid, *N*-methylaniline, 4-aminotoluene, styrene.
   e. Carbon tetrachloride, 2-hydroxybenzaldehyde, benzaldehyde, triphenylmethanol, benzyl alcohol.
   f. Diethyl ether, 3-pentanone, diethylamine, acetic acid.
   g. Cyclohexane, 4-methylaniline, toluene, 3-hydroxytoluene, 2-chloro-4-aminobenzoic acid.
6. An instructor mixed the following compounds in the order named and gave out the mixture as an unknown: 2-methyl-2-propanol (2.47 g), benzyl alcohol (3.6 g), benzaldehyde (3.53 g), acetyl chloride (5.2 g), acetophenone (4.0 g),

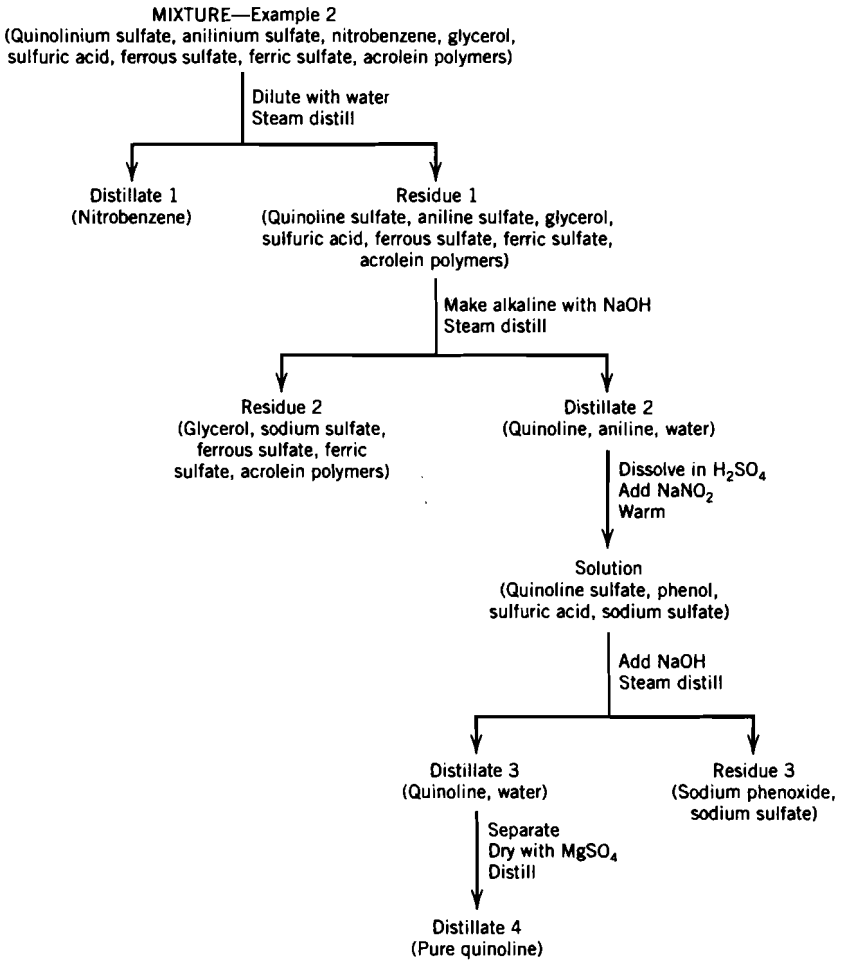


Figure 4.20 Separation of a mixture, Example 2.

N,N-dimethylaniline (28.2 g). What might the student expect to find? Diagram a possible separation of the actual components after the mixture has stood for a week (assume complete reactions).

4.4 CHROMATOGRAPHY

Chromatography is the separation of the components of a mixture by the selective distribution of the components between a mobile phase and a stationary phase. The linguistic origin of the word *chromatography* is based on the idea of color (from the Greek words *chroma* meaning "color" and *graphy* meaning "written"). Early chromatography was carried out on paper using colored derivatives of naturally occurring compounds.

The mobile phase is a liquid or a gas and carries the compounds along a column. The stationary phase may be composed of various types of materials, for example, silica gel in column chromatography. The ability to separate various components of a mixture of organic compounds is based on selective and preferential absorption of these components in the mobile phase by the stationary phase.

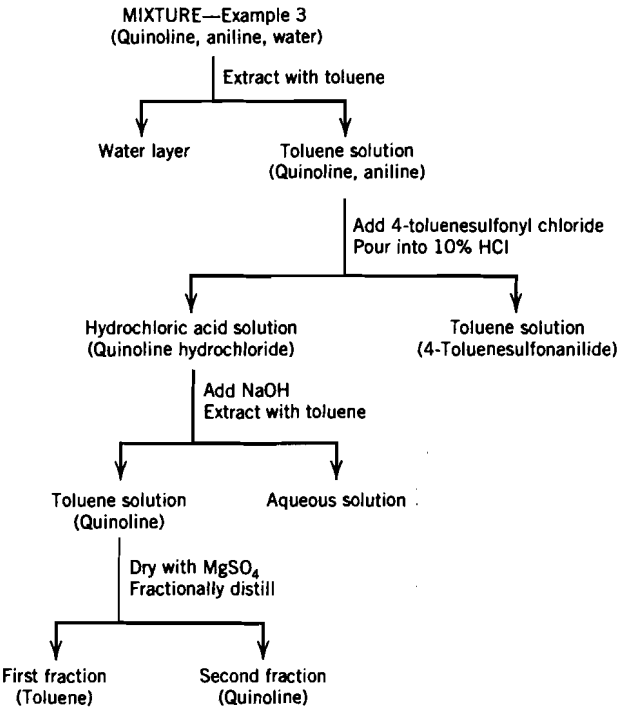


Figure 4.21 Separation of a mixture, Example 3.

Organic chemists are interested in two major classes of chromatography: gas chromatography (GC) and liquid chromatography (LC). Gas chromatography is useful for relatively volatile and thermally stable organic compounds. This method involves a gaseous mobile phase, which is usually helium or, less frequently, nitrogen. The stationary phase is either a liquid adsorbed on a solid support, an organic compound bonded to a solid support, a solid, or a nonvolatile liquid.

Liquid chromatography uses a liquid mobile phase, which is usually a common organic solvent. The stationary phase may consist of a liquid adsorbed onto a solid support, an organic species spread over a solid support, a solid, or a resin. Examples of liquid chromatography are column chromatography, high-performance liquid chromatography (HPLC), and thin layer chromatography (TLC).

In choosing to use either or both GC and LC, the following should be considered before making a decision.

Gas Chromatography

1. The sample should be volatile and reasonably stable to heat. Specifically, the compound must be stable enough to survive the conditions necessary to convert it to the gas phase.
2. Simple gas chromatographs are inexpensive, are easy to operate, and give results rapidly.

Liquid Chromatography

1. With the simple gravity flow columns, the separation of the components is time consuming. Rapid analyses are carried out with HPLC and flash chromatography.

2. A small percentage of organic compounds may react with the stationary phase of some columns. Proper choice of conditions, in order to prevent undesirable side reactions, allows virtually any organic compound to be analyzed by LC.
3. Flash and other types of column chromatography are fairly cheap; HPLC has a much higher initial cost, because of the high-quality pumps and column packings that are necessary.

4.4.1 Thin-Layer Chromatography

Thin-layer chromatography (TLC) is perhaps the most rapid, easiest, and most often applied method for assessing the purity (complexity, and often the nature) of organic compounds. In TLC, the immobile phase is a thin layer of adsorbent spread over a sheet of glass or plastic. Calcium sulfate or an organic polymer serves to bind the adsorbent to the sheet. A small amount of sample is placed near the bottom of the slide, and this spotted slide is placed on end in a container with a shallow layer of solvent; the distance to which the solvent moves the compound up the chromatogram sheet is dependent on the ability of the compound to adhere to this adsorbent system, as well as many other factors. More often than not, adsorbent–solvent systems can be found to separate most components of a given mixture. This procedure is especially useful for compounds that are heat sensitive or nonvolatile, that is, those compounds that are not amenable to boiling point or gas chromatographic determination.

Compounds can be detected on TLC sheets in various ways. The simplest is to use a low-power hand-held UV light. This procedure requires the use of TLC adsorbent that has been mixed with a fluorescent indicator. In such cases the eluted compounds will appear as dark spots because they block out the fluorescent indicator. Other procedures are described below, including methods involving *p*-anisaldehyde and involving phosphomolybdic acid, both of which are much more sensitive than fluorescent indicators.

Procedure

Commercial sheets, precoated with alumina (Al_2O_3) or silica gel ($SiO_2 \cdot x\ H_2O$), are available. If the UV light will be used as a visualization method, then use TLC plates containing a fluorescent indicator.

If fine capillary tubes are not available, then prepare them from melting point tubes that have both ends open. Adjust the flame on the bunsen burner until there are two distinct blue flames. Using the smaller of the two flames, heat the middle of the melting point tube while slowly rotating the tube (Figure 4.22). Once the tube becomes flexible, pull it toward you and immediately pull it apart. Do not pull the tube while it is in the flame because doing so will seal the ends of the tube. Two TLC capillary tubes are formed from each melting point capillary tube.

Select a solvent by testing out the sample in various solvents. Dissolve a small sample of the unknown in different flasks containing solvents of different polarity (Table 4.2). Place the end of the TLC capillary tube in the solution and allow some of the solution to be drawn into the tube by capillary action. Touch the TLC chromatography plate with the end of the tube (Figure 4.23). When the solvent circle has reached its final position, a useful solvent will have moved the sample ring to a position about 0.3–0.5 that of the solvent circle radius. If the sample ring is too large, try a less polar solvent. If the sample ring is too small, try a more polar solvent. If no solvent information is available, chloroform and solvents of similar polarity can be tried first.

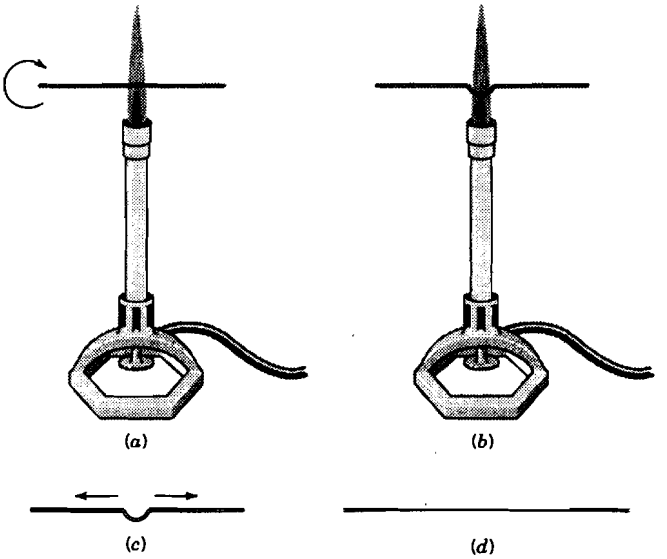


Figure 4.22 Preparation of a TLC capillary tube. (*a*) While rotating the tube, heat the melting point capillary tube in the smaller of the two flames. (*b*) Heat the melting point capillary tube until the middle section is flexible. (*c*) Pull the melting point capillary tube out of the flame and immediately pull it apart. (*d*) The finished TLC capillary tube before breaking it in the middle.

TABLE 4.2 Chromatographic Solvents[a]

Petroleum ether	
Cyclohexane	
Carbon tetrachloride	
Benzene	Increasing polarity[b]
Methylene chloride	
Chloroform (alcohol free)	
Ethyl ether	
Ethyl acetate	
Pyridine	
Acetone	
1-Propanol	
Ethanol	
Methanol	
Water	
Acetic acid	

[a]Mixtures of two or more solvents can be used as developing solvents in chromatographic separations.

[b]Polarity, in this context, is meaningful only for chromatography and is not necessarily the same as polarity as measured by, for example, dielectric constant.

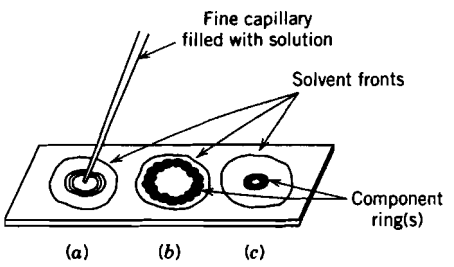


Figure 4.23 Determination of solvent for thin-layer chromatography. (*a*) Good development. (*b*) Overdeveloped. (*c*) Underdeveloped.

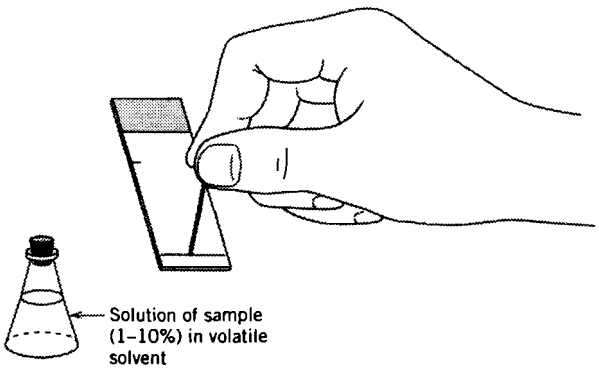


Figure 4.24 Preparation for TLC.

Once the solvent is selected, then the TLC plate can be prepared. Prepare a solution (1–10%) of the sample in the solvent. On the powder side of the TLC plate, draw a pencil line about 1 cm from the bottom and 1 cm from the top. Touch the TLC capillary tube onto the surface of the solution and allow some of the solution to rise into the tube through capillary action. Spot the plate by touching the tube to a position on only one pencil line (Figure 4.24). Limit the number and size of the drop by placing a finger on the top of the capillary tube.

In the development chamber, place a folded piece of filter paper along the side. Saturate the filter paper with the solvent, and add enough solvent so there is 5 mm of solvent in the bottom. Place the TLC plate, spotted side down, into the chamber so that the lower pencil line is above the solvent. Lean the plastic side against the glass and do not allow the filter paper to touch it (Figure 4.25). Place a lid on the development chamber. Allow the solvent to climb up the plate until the solvent front is at the top pencil line. Remove the plate from the development chamber and allow it to dry. Circle any spots that are visible.

If the TLC plate contained the fluorescent indicator, place the TLC plate under ultraviolet light. *Do not look directly at the UV light as it can cause eye damage.* Mark any dark spots by circling them. The dark spots are observed where the sample spots block out the fluorescent indicator. Alternately, place the developed TLC plate in an enclosed chamber with iodine crystals (Figure 4.26). Slightly heat the development chamber on a steam bath. Nearly all compounds, except alkanes and aliphatic halides, form iodine charge-transfer complexes. The formation of these complexes is reversible, so the position of the dark spot should be marked quickly. Another visualization

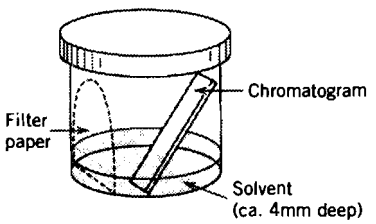


Figure 4.25 Chromatographic development unit.

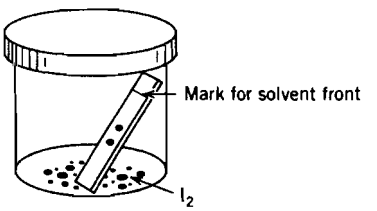


Figure 4.26 Iodine TLC spot-marking chamber.

technique involves spraying the TLC plate with sulfuric acid to cause the colorless compounds to darken by charring. This method is a sample destructive technique.

A very sensitive method for detecting compounds involves use of a spray containing *p*-anisaldehyde. TLC plates should be made of glass. If plastic sheets are used, a test should be run to see if the sheets can survive the heating conditions. The adsorbent should not contain the fluorescent indicator. Prepare the solution by combining, with cooling, 9 mL of 95% ethanol with 0.5 mL of concentrated sulfuric acid and two drops of glacial acetic acid. Slowly add 0.5 mL of *p*-anisaldehyde. Spray the solution on the developed plates and bake the plates to dryness on a hot plate until the dark spots develop.

Another procedure involves the use of 5% phosphomolybdic acid. Spray the developed plates with 5% phosphomolybdic acid. This method does not suffer from interference from indicators mixed into the silica gel.

If commercial chromatographic sheets are not available, glass plates are easily prepared. Prepare a slurry of adsorbent (35 g of silica gel G in 100 mL of chloroform or 60 g of alumina in 100 mL of 67 vol%/33 vol% chloroform/methanol). Stir the slurry thoroughly; dip a pair of back-to-back plates (e.g., standard microscope slides) into the slurry and slowly withdraw them. Wipe excess adsorbent from the edges and separate the plates. Wipe adsorbent from the back of the plates and allow them to dry (ca. 5 min). Such plates may be used immediately or stored in a desiccator.

Discussion

Development of different chromatograms (alumina, silica gel, silica acid) of the same sample that clearly yield only a single spot in a variety of solvents is a very good indication of purity. In addition, the identity of an unknown can be supported (but not completely proved; why not?) by comparison of spot positions of known and unknown materials (Figure 4.27). Figure 4.27 also implies how the progress of a reaction can be monitored. The most common method of reporting TLC results is by the R_f value (Figure 4.28) in a specific solvent on a specific type of chromatographic sheet:

$$R_f = \frac{\text{distance spot of interest has moved from origin } (b)}{\text{distance solvent front has moved from origin } (a)}$$

Alternatively, the results may be reported as R_x, where

$$R_x = \frac{\text{distance spot of interest has moved from the origin}}{\text{distance spot of reference compound has moved from the origin}}$$

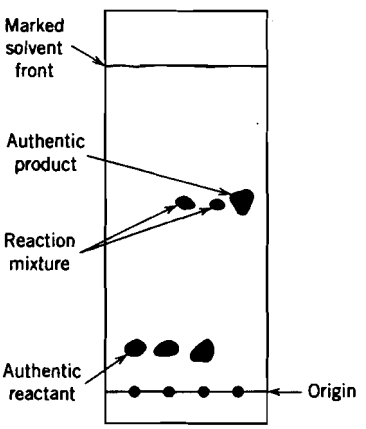


Figure 4.27 Thin-layer chromatogram; reaction mixture analysis.

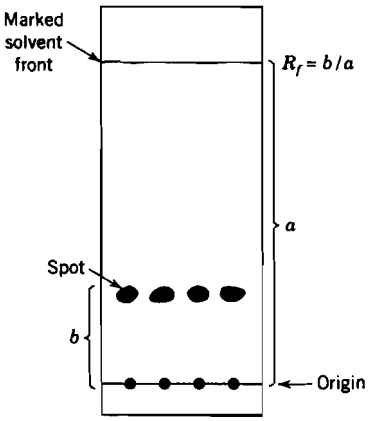


Figure 4.28 Determination of R_f value on the TLC chromatogram.

Information obtained from TLC is useful for solvent and adsorbent choices in (preparative-scale) column chromatography.

4.4.2 Gas Chromatography

Gas chromatography (GC) is the technique of separating compounds that have been converted to the gas phase on the basis of their boiling points or of their polarity differences. Liquid samples can be directly injected onto the GC instrument; solids must be dissolved in a solvent, and they can be analyzed only if they are sufficiently volatile. Liquid samples are frequently injected as solutions. Samples upon injection are subjected to a very hot injection port which immediately converts them to the gas phase. A carrier gas (usually helium) transports the gases into a heated column which is internally coated with a stationary phase. A primary driving force for separation of organic components by GC is simple boiling point differences: higher-boiling compounds are eluted more slowly. Boiling point differences are of substantial importance even for the so-called polarity-based columns described below. There are two major classifications of columns: nonpolar and polar. Nonpolar columns separate components almost completely by boiling point differences; that is, the higher-boiling compounds are eluted more slowly (have longer retention times). Polar columns separate components at least to some degree on the basis of differences in dipole–dipole interactions between each component and the stationary phase. The stationary phase is thus a material that separates components by selective attraction (selective adsorption). More polar compounds are held back longer (have longer retention times) and less polar compounds elute more rapidly (have shorter retention times). Isolated compounds are passed through a detector, and the detector responses are converted to peak shapes on an electronic recorder. Part of this process involves computer-based conversion of the detector's analog signal to a digitized format. Retention times of the components can be used to identify them (knowns can be injected to measure standard retention times), and relative peak areas are used to measure the amount of each compound.

Gas chromatography is useful for purity determinations and component analysis of sufficiently volatile organic compounds. Observation of a single, large peak in a variety of GC determinations (various columns, temperatures, etc.) for a given sample is a strong indication of its purity. Samples must thus be thermally stable to volatilization conditions for GC analysis.

A simplified schematic diagram of a gas chromatograph is shown in Figure 4.29. A specific gas chromatograph is shown in Figure 4.30. The instrument consists of the following:

1. A tank of carrier gas (see point 1), which is usually helium (or, less frequently, nitrogen). Helium is used because it is inert and has a high thermal conductivity.
2. A method of controlling the gas flow. This usually involves a valve on the tank (points 1 and 2) and a regulator on the instrument (point 3).
3. An injection port (see point 4). This is a metal cap, with a hole over a piece of rubber or plastic material that can be pierced with a syringe.
4. A heated column (see point 5). This is a metal or glass tube that contains the solid support and stationary phase. This "column" is coiled to fit in the heated compartment and is connected from the injection port to the detector.
5. A detector (see point 6). The two most common detectors are of the thermal conductivity and flame ionization types. The thermal conductivity detector measures changes, at a filament, in the conductivity of the carrier gas as a function of sample content; this change is electrically passed on to the recorder (see point 7). Thermal conductivity (TC) detectors are used on instruments that employ packed columns. Flame ionization detection (FID) measures sample content by burning the eluted sample in a small hydrogen flame, followed by determining the amount of ions so produced. Detection by flame ionization detection is frequently used on instruments that are equipped with capillary columns.
6. Recorder (see point 7). The analog signal from the detector is converted to digital output on an electronic recorder in the form of peaks (Figure 4.31). As described earlier, the chromatogram occurs as a series of these peaks. The retention times are used to identify compounds, and the peak areas are used to

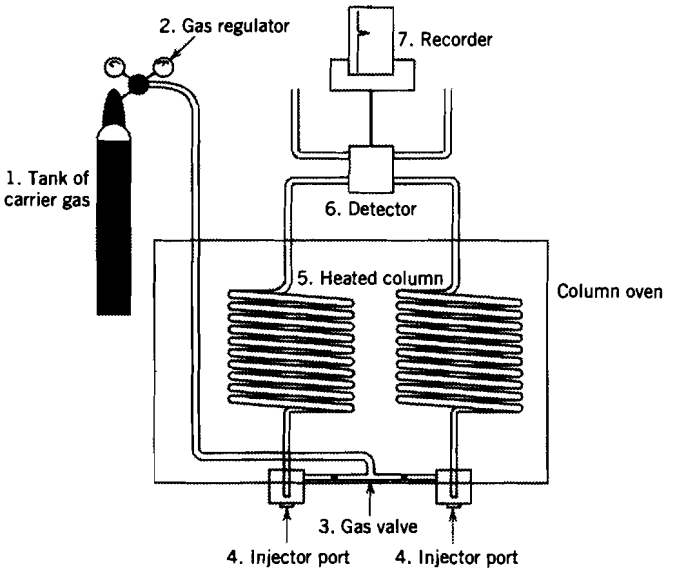


Figure 4.29 A schematic diagram of a gas chromatograph.

Figure 4.30 GOW-MAC series fundamental gas chromatograph. (Series 350 Gas Chromatograph, courtesy of GOW-MAC Instrument Co, Bethlehem, PA USA.)

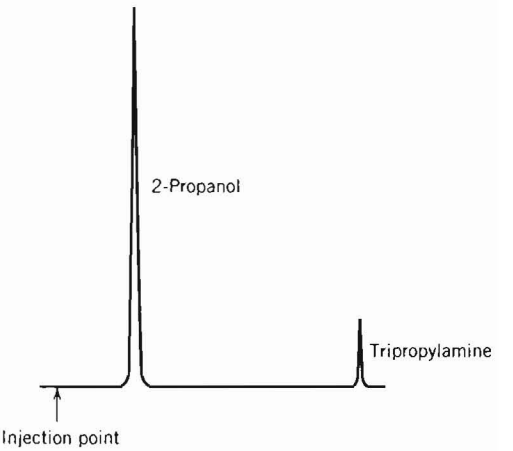


Figure 4.31 Gas chromatogram.

measure the amounts of the various compounds in the sample. The retention time of a component is taken as the time at which the maximum for the peak occurs relative to the time of injection (or relative to the retention time of some volatile standard).

There are two major categories of GC instrument based upon the sizes of columns employed. One type uses "packed" columns, which are typically 3–6 mm in width and 1–5 m long. The other type uses open tubular or capillary columns 0.10–0.70 mm in width and 15–100 m long. Commonly the widths are in the 0.20–0.53-mm range. The latter, capillary technique, is much more efficient and is the method of choice for analytical work. The former, packed-column method, is used when preparative-scale collections are required.

Since capillary GC instruments are so sensitive, they are often fitted with a splitter which functions to make the sample concentration much more lean when it is introduced onto the column. For example if 1 μL (1×10^{-6} L) of a 1% solution of compound is used, a typical splitter setting might be such that only 1/40th of the vaporized sample is allowed to pass onto the column.

Capillary GC involves the use of open tubular columns (Figure 4.32) whose walls are made of fused silica (SiO_2) of 15–100 m length. These columns have inside diameters of 0.10–0.70 mm (typical columns are in the 0.20–0.53-mm range), and they are frequently coated internally with a stationary phase adsorbent that is 0.1–5 μm ($\mu m = 10^{-6}$ m) thick. There are three categories of stationary phase coatings (Figure 4.32*c*): simple wall coatings (WCOT), coatings dispersed on porous solid support (SCOT) to increase adsorbent surface area, and a dispersion of porous solid particles on the inside wall (PLOT; e.g., Zeolite particles are used to separate gases). Stationary adsorbent phases may be modified by chemical cross-linking or by chemical bonding to the solid support to reduce loss by bleeding. Detectors for capillary GC are either FID or electron-capture detectors (ECD), since these are more sensitive, reliable, and reproducible than TC detection—especially for the small sample sizes that can be used on these columns. Since FID and ECD detection is destructive and since the sample size is much smaller than with packed columns, capillary GC is restricted to analytical procedures. Preparative-scale operations are normally carried out on packed columns.

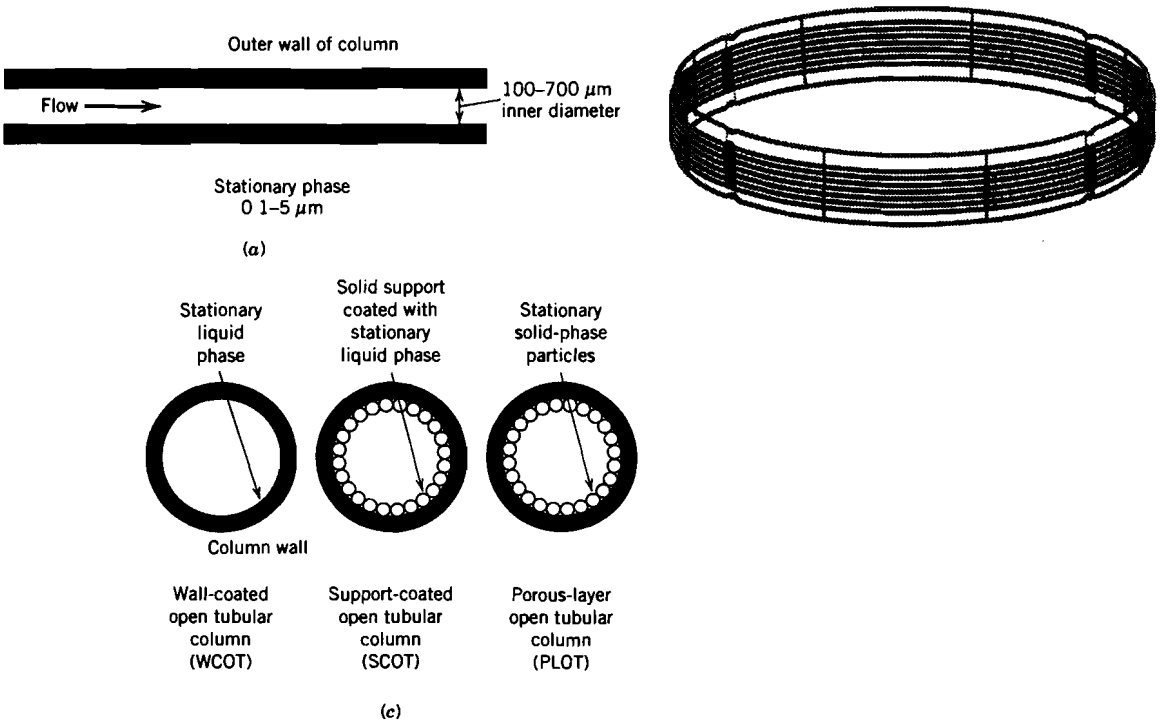


Figure 4.32 (*a*) Typical dimensions of open tubular column for gas chromatography. (*b*) Aluminum-clad fused silica chromatography column. (*c*) Cross-sectional views of wall-coated, support-coated, and porous-layer columns.

There are several advantages to capillary GC (compared to packed-column GC):

1. Very accurate analyses are quickly attained on very small samples.
2. Since capillary columns contain so little stationary phase, column "bleed" is normally not a serious problem. Thus the loss of packing materials as columns age is not nearly as serious as with packed columns, which contain much larger

amounts of stationary phase. As volatile materials bleed off, they can be confused with samples of compounds of interest with similar retention times.

A wide array of stationary phases are available for GC, and a number of these have been listed in Figure 4.33. The choice of stationary phase used is based upon the polarity of the compound being analyzed (Table 4.3) and on the temperature that is required. The polarity of compounds classified in Table 4.3 ranges from polar to nonpolar in four stages. For example, if the analysis is to be conducted on alkanes of low molecular weight (and thus high volatility), squalene can be used. Polar organic compounds such as carboxylic acids, which frequently have very low volatility, require a stationary phase such as XE-60.

Capillary GC has become very common, and its great sensitivity and reliability make it the method of choice for analytical work. Packed-column GC is very useful where it is desirable to collect larger, preparative-scale samples and it can be used for analytical work, keeping in mind its limited sensitivity.

Carrier Gas

To begin instrument operation, check to see if there is helium flow before turning on the filament current. *Failure to have an inert gas around the detector filament could result in the destruction of the filament of a thermal conductivity detector.* Check the flow by checking the tank and instrument gas gauges *and* the detector exit port with a bubble meter. The pressure of the carrier gas entering the gas chromatograph is usually 10–50 psi, with a resulting flow rate of 10–150 mL/min. Allow about 30 min for the instrument to reach a steady state before checking the flow rate.

Column Temperature

The column temperature is usually set so that it is slightly below the temperature of the highest-boiling component. This temperature should *always* be below the upper limit recommended for the stationary phase. Typical columns temperatures are 50–200°C. Sample stability should influence the temperatures chosen. The temperature is selected so that there is good resolution between the peaks without long retention times.

A ramp column temperature can be used in some applications, such as complex mixtures. Ramping refers to the practice of using regular increases in column temperatures over time to allow GC analysis in a minimum length of time. A typical ramp might mean that the column is increased from 100°C to 150°C at a rate of 5°C a minute. This could be done so that the main components of interest, if more volatile, could be analyzed at 100°C before ramping, and then the elevated temperature would drive off less volatile side products, clearing the column of all injected materials. If a ramping procedure is to be used, the initial and final temperatures, the start and stop times of the ramp, and the heating rate must be programmed.

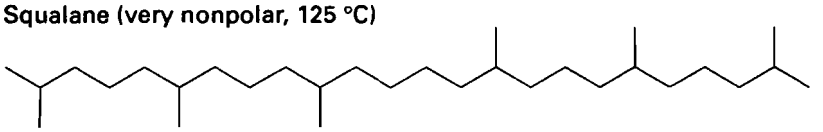
Injector and Detector Temperatures

The detector and the injector blocks should be heated continuously. These blocks come to temperature very slowly, over 1 to 2 h, and are usually several tens of degrees warmer than the column. Usually the temperature of the inlet system and the detector is 20–30°C higher than that of the column. Typical detector and injector temperatures are 250°C.

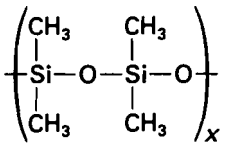
Filament Current

The current is usually between 100 mA and 200 mA.

Squalane (very nonpolar, 125 °C)



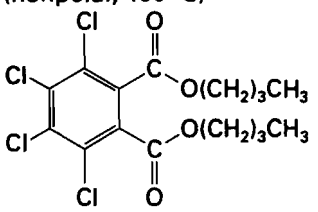
SE-30 (very nonpolar, 350 °C)



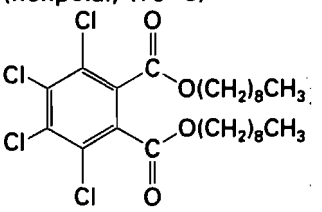
Apiezon (very nonpolar, 275–300 °C)

various alkane greases

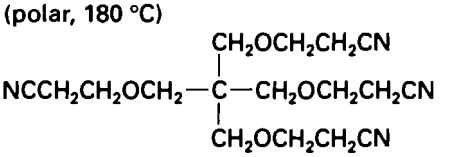
Dibutyl tetrachlorophthalate
(nonpolar, 150 °C)



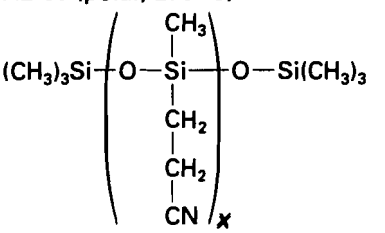
Dinonyl tetrachlorophthalate
(nonpolar, 175 °C)



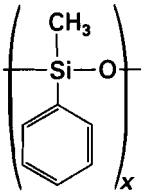
Tetracyanoethyl pentaerythritol
(polar, 180 °C)



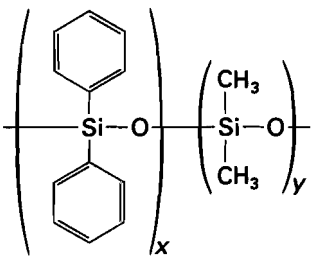
XE-60 (polar, 275 °C)



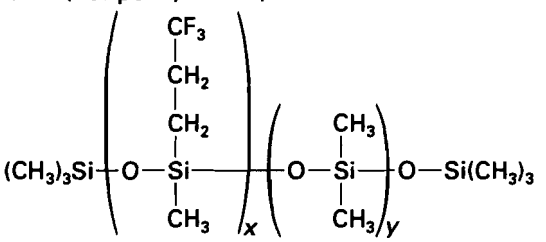
OV-17 (nonpolar, 325 °C)



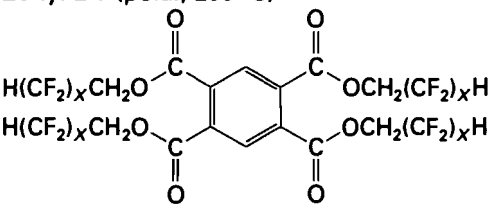
SE-54 and OV-73 (nonpolar, 325 °C)



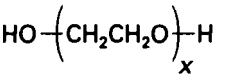
QF-1 (nonpolar, 250 °C)



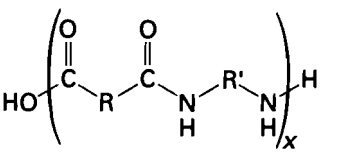
Zonyl E-7 (polar, 200 °C)



Carbowax 20M
(very polar, 250 °C)



Versamid 900
(very polar, 275 °C)



DEGS (diethylene glycol succinate)
(nonpolar, 190 °C)

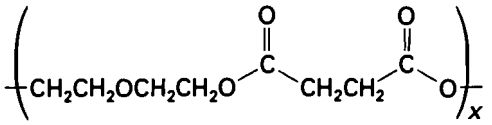


Figure 4.33 Common stationary phases. See polarity classifications in Table 4.3.

TABLE 4.3 Polarity Classifications of Organic Compounds for GC Analysis[a]

Very Nonpolar (VNP)
- Saturated hydrocarbons
- Olefins
- Aromatic hydrocarbons
- Alkyl halides
- Thioalcohols (mercaptans)
- Thioethers

Nonpolar (NP)
- Ethers
- Aldehydes, ketones
- Esters
- Tertiary amines
- Nitro compounds with no α-hydrogens
- Nitriles with no α-hydrogens

Polar (P)
- Alcohols
- Carboxylic acids
- Primary (1°) and secondary (2°) amines
- Oximes
- Nitro compounds with α-hydrogens
- Nitriles with α-hydrogens

Very Polar (VP)
- Polyhydroxy compounds (alcohols, carbohydrates)
- Amino alcohols
- Hydroxy acids
- Polyprotic acids
- Polyphenols

[a]More details can be found in D. C. Harris, *Quantitative Chemical Analysis*, 6th ed. (Freeman, New York, 2003).

Sample Injection

The sample is injected using a microsyringe (Figure 4.34). For a packed column or thermal conductivity gas chromatograph, 1 μL or 10–100 μL of a 1–10% solution in a volatile liquid of the sample is injected into one of the ports. For preparatory gas chromatography, 20–80 μL or 50 mg can be separated into pure components. Too much sample will cause the column to be overloaded and the peaks merged together.

The plunger of the syringe must have some pressure on it at all times during injection. If moderate pressure has not been maintained on the plunger during the injection, the plunger can be blown out of the barrel of the syringe due to the high pressure from the vaporization of the sample.

During injection, the needle of the syringe punctures a rubber or silicon septum located at the head of the inlet system. The sample is *quickly* injected into the gas chromatograph; a prolonged injection results in poorer resolution.

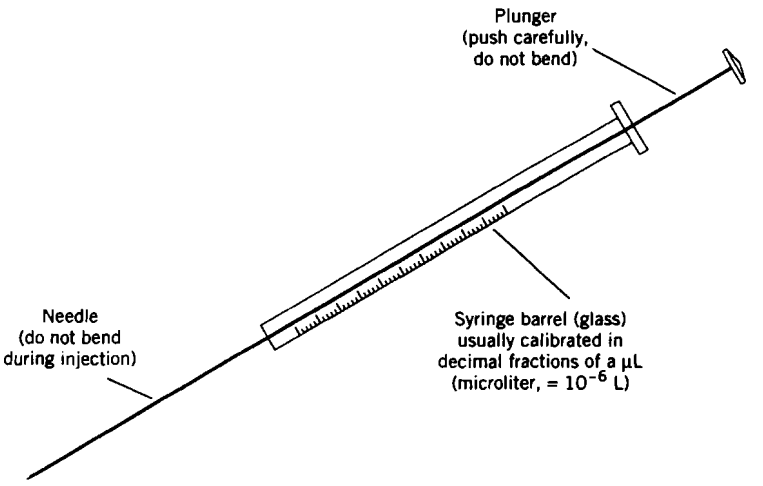


Figure 4.34 Syringe.

Obtaining the Chromatogram

The chart pen is zeroed and the recorder started at the time of injection. The chart is marked at the moment of injection. A record should be made of the column size and type used, the column temperature, gas flow rate, and other details. As the peaks are recorded, attenuation changes may need to be made so that the top of the peak can be observed.

Interpretation of the Chromatogram

Retention time is taken as the time from the injection until the time that the peak maximum is obtained (Figure 4.35). The area of each peak is roughly calculated by

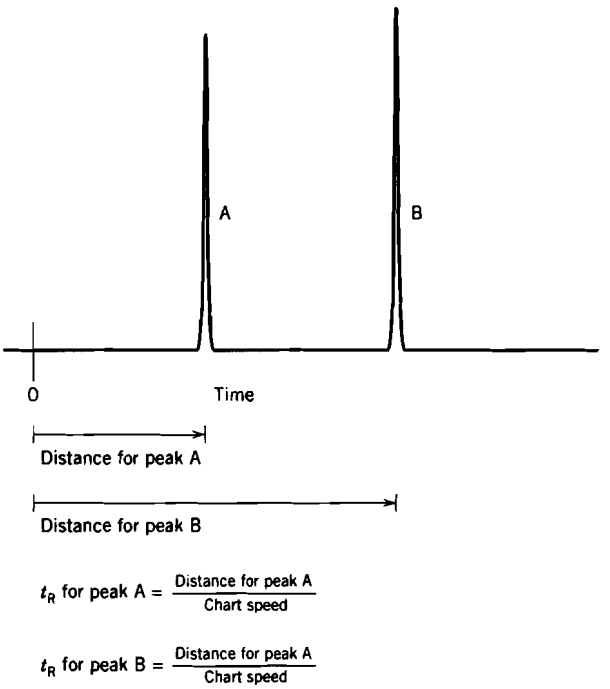
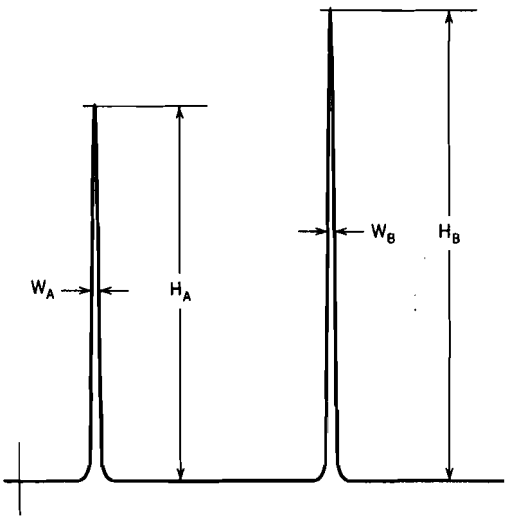


Figure 4.35 Calculation of retention time. [From C. K. F. Hermann, *J. Chem. Educ.*, *73*, 852–853 (1996). Copyright © 1996 by the Division of Chemical Education, American Chemical Society, used with permission.]

multiplying the height of the peak by the width of the peak, which is measured at half the height (Figure 4.36). The molar percent of a component is determined by dividing the area of the peak by the total area of all peaks combined and multiplying this number by 100. For thermal conductivity detectors, the relative peak area corresponds to a weight percentage, not a molar percentage.



Area of peak A = height A × width A (measured at half height)

Area of peak B = height B × width B (measured at half height)

$$\text{Percent composition of peak A} = \frac{\text{Area of peak A}}{\text{Area of peak A + peak B}} \times 100$$

$$\text{Percent composition of peak B} = \frac{\text{Area of peak B}}{\text{Area of peak A + peak B}} \times 100$$

Figure 4.36 Calculation of peak area and molar percent composition. [From C. K. F. Hermann, *J. Chem. Educ.*, 73, 852–853 (1996). Copyright © 1996 by the Division of Chemical Education, American Chemical Society, used with permission.]

Collection Devices

To carry out a preparative-scale collection from a gas chromatograph, a proper collection device must be available. A number of commercial, automatic devices are available; some are built into the chromatograph or are available as separate units.

Several types of collection devices are illustrated in Figure 4.37. Care must be exercised in the choice of a coolant. Some compounds, when collected at their condensation temperatures, which are far too low, will form an aerosol that cannot be easily condensed in the collection device. Centrifuge tubes are handy for collection when small samples require spinning down after collection.

Turning Off the Gas Chromatograph

Consult your laboratory instructor for the instructions on turning off the gas chromatograph.

Discussion

Retention times are characteristic of the compound of interest. One should avoid precise quantitative comparisons to literature retention values; too many parameters have to be reproduced to justify such correspondence. However, injection of an unknown mixed with an authentic sample of the suspected compound resulting in a single, sharp

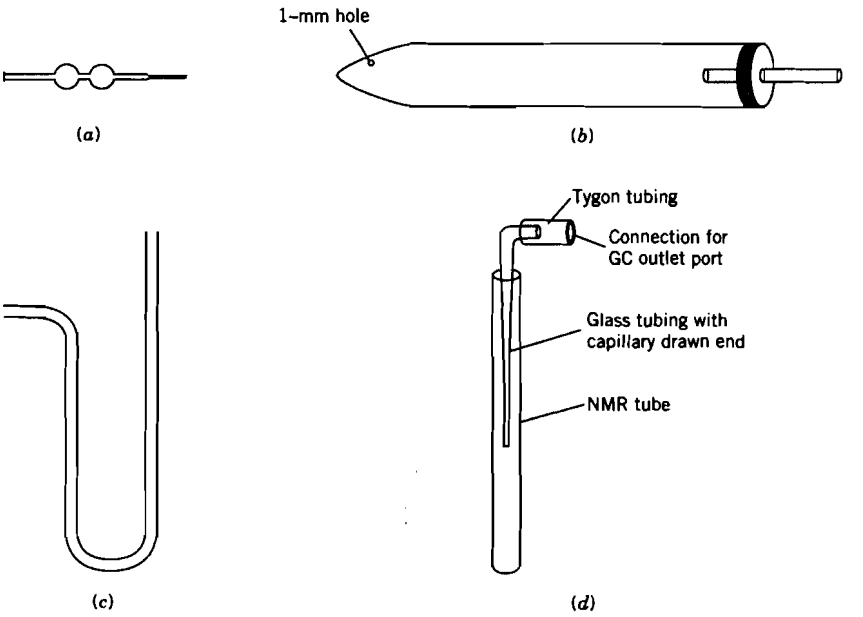


Figure 4.37 Collection devices for GC: (*a*) capillary size; (*b*) centrifuge tube; (*c*) bent piece of glass; (*d*) with an NMR tube as the receiver. All can be placed in an ice bath for volatile compounds. [Figure 4.37*d* is used with permission from A. R. Bressette, *J. Chem. Educ.*, *78*, 366–367; copyright © 2001, Division of Chemical Education, Inc.]

peak is strong support for the identity of one of the components. The mixture should be analyzed on both polar and nonpolar GC columns. Reaction progress (reactant, product, side product quantities, etc.) as well as purity can be monitored by gas chromatography.

Samples collected directly from GC are usually very pure and can be analyzed directly; for example, the sample can be washed with $CDCl_3$ solvent directly into a NMR tube. For many compounds, it is *necessary* that they be collected from the gas chromatograph and analyzed quickly so that the physical constants and other characteristics determined from these samples are accurate. The samples collected can be checked for purity by reinjecting a small sample into the GC.

Problems

7. For each of the following mixtures, suggest a separation technique and explain a basis for your choice.
   a. 1-octanol, 2-octanol, and 3-methyl-2-heptanol
   b. aniline, benzamide, and 4-methylphenol (*p*-cresol)
   c. ethyl benzoate, propyl benzoate, and butyl benzoate
8. It is common to convert carboxylic acids to esters before conducting separation analysis. Explain why this is important when using GC and LC.

4.4.3 Column Chromatography

Column chromatography is directly applicable to preparative-scale separations and purifications because, in principle, we can simply choose the size of the column and its

contents to fit the amount of the sample to be fractionated. This approach usually takes a time commitment of many hours with the classical gravity flow columns. Flash chromatography is a type of column chromatography in which air pressure is applied to the top of the column to push the solvent through the column at a much faster rate. With this method, mixtures can be separated in a very short period of time. *It is imperative that a knowledge of thin-layer chromatography characteristics of a sample be known before column chromatography is employed.*

An illustration of the separation of a mixture in column chromatography is seen in Figure 4.38. The most polar compound, signified by dark circles, is more strongly adsorbed than the least polar compound, signified by light circles. Thus the least polar compound is eluted first from the column.

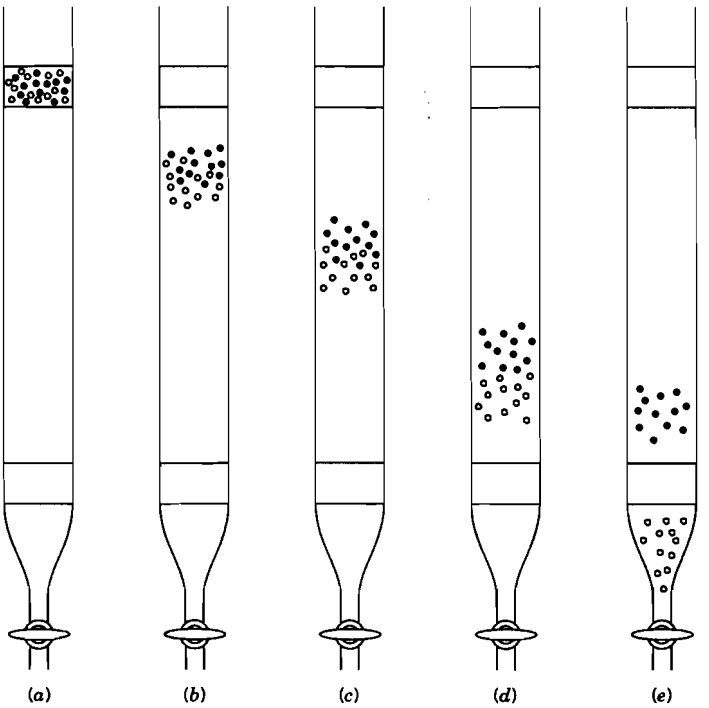


Figure 4.38 Illustration of separating a mixture in chromatography: (*a*) initial placement of the mixture; (*b*) components of mixture begin to elute downward; (*c*)–(*d*) components are separating; (*e*) least polar component (light circles) is eluting first.

Types of Columns

A variety of chromatography columns (Figure 4.39) are available commercially. A small piece of Teflon tubing with a pinch clamp is attached to the bottom of the plain chromatographic column (Figure 4.39*a*) to regulate flow rate. Some columns come with a filter disk (fritted glass) above the stopcock (Figure 4.39*c*). Teflon stopcocks are recommended over glass stopcocks to avoid contamination by the grease from the glass stopcock. Burets and Pasteur pipets are used as columns when chromatographing microscale amounts of material.

A common alternative to the reservoir already built into the column is a separatory funnel. The separatory funnel would only be used with gravity columns. The separatory funnel, filled with solvent and closed at the stopcock and stoppered at the top, is

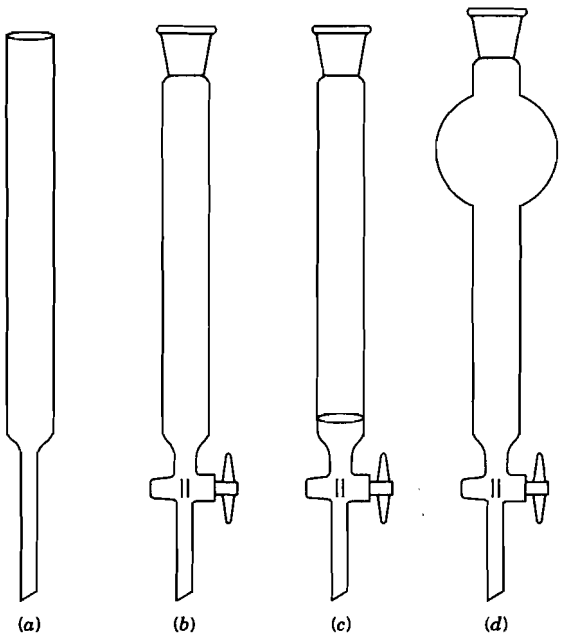


Figure 4.39 Chromatography columns: (*a*) plain; (*b*) with a ground glass joint at top; (*c*) with a fritted disk; (*d*) with a solvent reservoir.

hung such that the lower tip is under the surface of the solvent in the column. If the stopcock of the *stoppered* stopcock is opened, solvent will drip out of the funnel into the column whenever the solvent in the column drops below the tip of the funnel. This will supply a constant solvent head on the column until the contents of the separatory funnel are depleted. This method works best only if the stopcock hole is greater than 2 mm.

(a) Slurry Packed Columns

In the slurry packed column, the solvent is used to pack the column.

Column Construction Figure 4.40 illustrates a completed packed column. *LC (liquid column chromatography) columns are always packed the day they are to be used.* Push a small glass wool plug down to the bottom of the column. Place the column in a ring stand in a vertical position. Place the sand on top of the glass wool plug to a depth of about 1 cm. Tap the column gently to level the sand. Use TLC to determine the choice of the elution solvents. Fill the column halfway with the proper elution solvent or solvent mixture.

Weigh 30 g of absorbent per gram of mixture. The most commonly used adsorbents are silica gel and alumina. Silica gel is more commonly used and is especially favorable for sensitive compounds.

Prepare a slurry of the adsorbent and the solvent and *gently* pour on top of the solvent. Tap the column gently and drain the solvent slowly as the slurry is added so that the adsorbent is evenly packed. The solvent may be reused. *It is crucial that the adsorbent is never allowed to dry out; drying creates air bubbles in the adsorbent and results in poor separation due to solvent channeling.* Once all of the adsorbent has been added to the column and it has been leveled by gentle tapping, then slowly place 1 cm of sand on the top of the sand. Level the sand. Drain the solvent until it is halfway down the top sand layer.

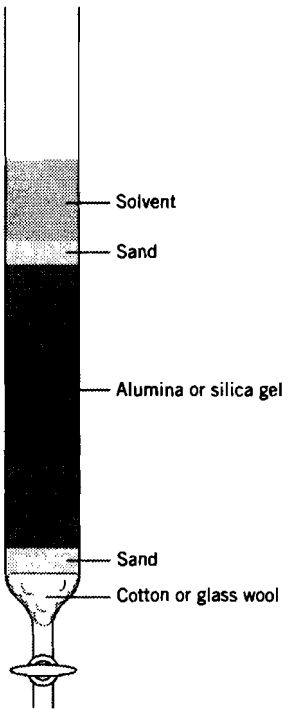


Figure 4.40 Packed chromatography column.

Use of the Packed Chromatography Column Weigh the dried mixture to be analyzed. Dissolve this mixture in a minimum amount of solvent; use heat only if necessary. Using a pipet, transfer the solution onto the surface of the sand as gently as possible.

In those cases where it is very difficult to dissolve the sample in the solvent to be used for the column, the sample can be dissolved in a minimum amount of polar but volatile solvent and dispersed on a quantity of the adsorbent. Use 5 g of adsorbent per 1 g of sample. Remove the volatile solvent by placing this mixture in a rotary evaporator at a low temperature. When dried, evenly distribute the dispersion on top of the partially packed column. Cover the packed column with 1 cm of sand. This method is superior to pipetting a solution of the mixture in a very polar solvent directly onto the top layer of sand.

Carefully fill the rest of the column with the solvent, including the reservoir. Allow the liquid to drip from the bottom of the column at a rate of about one drop per second. Allow solvent to pass through the column until all pertinent sample bands are eluted.

During the course of the chromatographic elution, the solvent composition can be varied through a range of increasing polarities. This is recommended only if several components of a mixture need to be separated and isolated. For instance, the following solvent combinations of increasing polarity may be used on one particular column:

100% hexane, 0% ethyl acetate

80% hexane, 20% ethyl acetate

60% hexane, 40% ethyl acetate

40% hexane, 60% ethyl acetate

20% hexane, 80% ethyl acetate

0% hexane, 100% ethyl acetate

In the cases in which the solvent polarity is changing, treat the column 10–20 mL of solvent per gram of adsorbent before changing polarity; this normally amounts to two to four fractions. Changing solvent polarity too abruptly may result in poor resolution between components of the mixture.

Collect the eluted liquid in regular volume increments, using test tubes or Erlenmeyer flasks. Monitor the elution of colored sample visually. Monitor colorless samples with TLC or GC, usually with fluorescent-sensitive sheets and looking at the plates under an ultraviolet light. Similar fractions are combined. Evaporate off the solvent by using a rotary evaporator using as little heat as possible.

Monitor the total mass of all compounds eluted and compare to the mass of the mixture originally placed on the column. A good mass balance will not be obtained in those cases where substantial amounts of intractable tars are held behind near the top of the column.

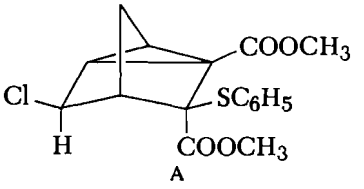
Determine the purity of the fractions by TLC or GC. The identity of the components can be determined by NMR, IR, or mass spectrometry.

Band resolution problems such as streaking and unevenness can occur with column chromatography. Possible causes include impure solvents, channeled columns resulting from uneven adsorbent packing, contaminated adsorbent, or decomposition of the sample on the column. If the column has been packed too tightly, the elution flow may not reach the desired flow of one drop per second.

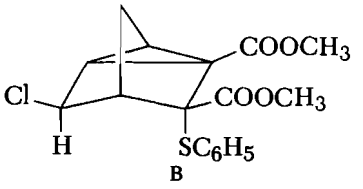
(b) Dry Column Chromatography

Dry column chromatography[1–4] provides several improvements over traditional column chromatography. These include the high degree of component resolution and that it is faster than traditional column chromatography. Another important characteristic is the near-quantitative applicability of TLC results to the dry column analysis.

The tremendous potential of dry column chromatography is shown by the separation of isomeric compounds A and B on silica gel. This is quite impressive when one realizes that compounds A and B have only very slight structural differences.



A



B

In dry column chromatography, the column is prepared dry without the use of solvent and developed just once with a single volume of solvent, in contrast to the slurry method and multiple volumes of solvent in traditional column chromatography.

[1]B. Loev and M. M. Goodman, *Chem Ind.*, 2026 (1967).

[2]*Progress in Separation and Purification*, Vol. 3, edited by E. S. Perry and C. J. Van Oss (Wiley, New York, 1970), pp. 73–95.

[3]J. M. Bohen, M. M. Joullie, F. A. Kaplan, and B. Loev, *J. Chem. Educ.*, *50*, 367 (1973).

[4]B. Loev, P. E. Bender, and R. Smith, *Synthesis*, 362 (1973).

TABLE 4.4 Activity of Alumina with 4-Aminoazobenzene

R_f of Dye	Brockmann Activity Grade	Percent of Water
0.00	I	0
0.12	II	3
0.24	III	6
0.46	IV	8
0.54	V	10

Adsorbent Careful control of the moisture content of the adsorbent is crucial to the dry column as well as other types of chromatography. Commercial and well-defined grades of adsorbent must be deactivated to match the TLC conditions. In the dry column, silica gel should contain 15% water and alumina should contain 3–6% water.

Check the percent water in the adsorbent by using known published procedures.[5] Determine the activity of the adsorbent by using Tables 4.4 and 4.5. Prepare the deactivated adsorbent by adding the appropriate quantity of water and rotate the mixture in a rotary evaporator for 3 h without heat. Check the percent of water again.

TABLE 4.5 Activity of Silica Gel with 4-*N,N*-Dimethylaminoazobenzene or 1,4-Di-*p*-toluidinoanthraquinone

R_f of Dye	Brockmann Activity Grade	Percent of Water
0.15	I	0
0.22	II	3
0.33	—	6
0.44	—	9
0.55	—	12
0.65	III	15

A fluorescent column adsorbent is extremely useful for monitoring the development of bands of colorless compounds. Band progress can be monitored by observing the column under a hand-held UV lamp and noting those bands on the column which have the fluorescence *blocked out.*

Column Preparation for a Glass Column A glass column cannot be used with a fluorescent column adsorbent since glass blocks the UV light. The size of the column chosen depends directly on the preliminary TLC results; the more difficult the separation, the larger the column. Compounds which are reasonably mobile with an R_f separation of 0.3 are usually involved in typical separations. The weight of the mixture and the column width are factors in choosing the correct height for the adsorbent (Figure 4.41). For instance, a 6.0-g sample with an average separation would need a 2-in.-thick column with a height of 12 in. of alumina. More efficiency is gained by using samples of 50–75% of the column capacity; for example, 3.0–4.5 g of the average mixture described above would be more efficiently separated than would 6.0 g.

These amounts correspond to a requirement of roughly 70 g of adsorbent per gram of mixture for average separations and of about 300 g of adsorbent per gram of mixture for difficult separations. The decreased capacity of grams of mixture per column

[5]H. Brockman and H. Schodder, *Ber., 74b,* 73 (1941).

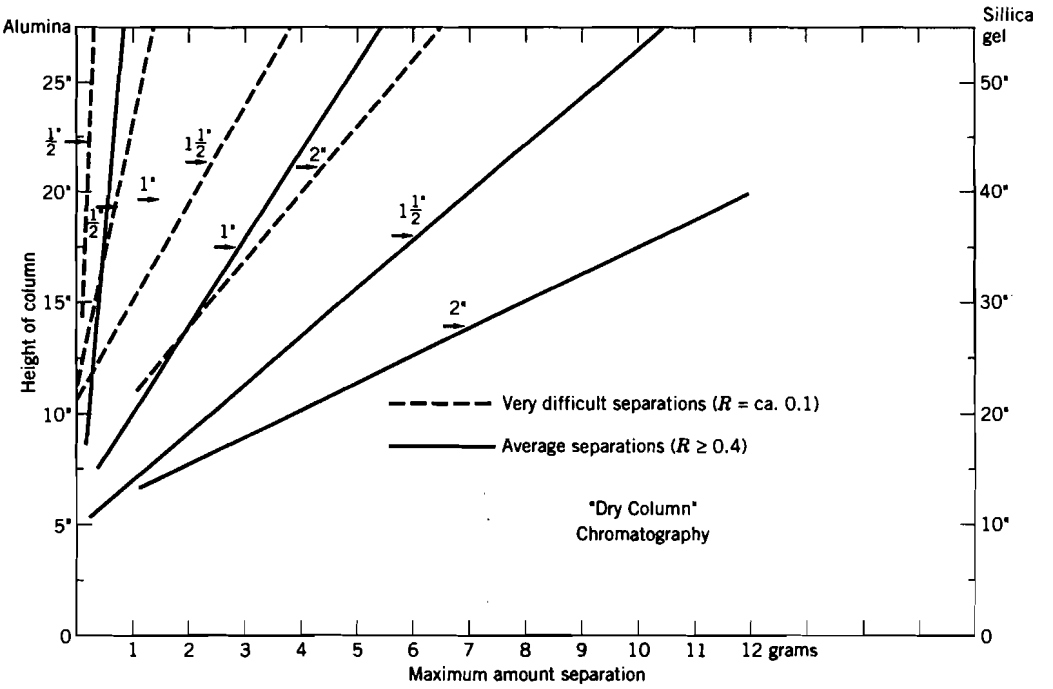


Figure 4.41 Graph for determining diameter and height of a dry column necessary to separate specified weights of mixtures. [The experimental procedure on which this graph is based is described in B. Loev and M. M. Goodman, *Chem. Ind.*, 2026 (1967); reproduced with permission.]

height for silica gel compared to alumina is due largely to the fact that silica gel is about one-half as dense as alumina.

A standard glass column may be used (Figure 4.39). If a fritted disk is not present in the column, then place a small piece of glass wool in the bottom of the column.

The stopcock in the column should be left open during packing in order to minimize the trapping of air in the adsorbent. *Slowly* pour dry adsorbent into the column while gently tapping the column, preferably with something less dense than glass such as a cork ring.

Column Preparation for a Nylon Column For this separation, the nylon tubing must be transparent to UV light.

Cut a piece of nylon tubing that is longer than the length needed for the column (Figure 4.41). Seal one end with heat using a hot flat iron or a hand sealer, or fold the end a few times and staple it shut. Place a small piece of glass tubing at the bottom of the tube. Make two or three small holes at the bottom to prevent air pocket formation during the packing of the column. Add one-third of the adsorbent rapidly and tap the bottom end of the tube two or three times on the bench top from a height of 6 in. to compact the adsorbent. Repeat two times until all of the adsorbent has been added. A properly packed column is quite sturdy and can be supported by a single clamp.

Use of the Dry Column Mixtures are placed on the dry column in a minimum amount of the eluting solvent or on the adsorbent as described above for traditional column chromatography.

The solvent used for the column should ideally be one solvent and not a solvent mixture. The best solvent for the separation is determined by TLC. Approximate solvent amounts are shown in Table 4.6. Solvent should be added such that a constant head of 3–5 cm is maintained on top of the adsorbent; this can be done by placing a stoppered separatory funnel containing the solvent just above the top layer of sand. The quantity of the solvent required is enough to wet the entire column but not to drip out the bottom. *As soon as the solvent has reached the bottom, solvent addition should be halted; development is complete.*

TABLE 4.6 Volume of Solvent for Development of Various Sizes of Dry Chromatographic Columns

Column Size (in.)	Solvent Volume (mL)
20 × 0.5	20
20 × 1.0	90
20 × 1.5	300
20 × 2.0	500

With colored compounds the division between individual compounds is obvious. If the compounds are colorless and a fluorescent mixture has been used for an adsorbent, these divisions should be marked under UV light. The nylon column and its contents are then sliced cleanly and the separated units of adsorbent are extracted with methanol or diethyl ether to remove the desired components.

If a glass column is used, the column is inverted and the end of the column is attached to an air line. With a small amount of air pressure passing through the open stopcock, the contents of the column are carefully laid out in a pan in order to avoid mixing the separated components. The adsorbent is sliced into separate pieces and these pieces are extracted with methanol or diethyl ether.

Using the dry column technique, columns as long as 6 ft have been packed and mixtures of mass of up to 50 g have been separated.

(c) Flash Chromatography

Traditional column chromatography (LC) typically takes many hours. Flash chromatography allows separations of samples weighing 0.01–10.0 g in less than 15 min elution time[6] and produces separation similar to those obtained from TLC. In flash chromatography, the column is pressurized with a flow control adaptor attached to the top of the column to pressure the column (Figure 4.42). The flow control adaptor is attached to an air line at a medium pressure. The stopcock on this adaptor is adjusted so that the air flow is not too strong.

Solvent System A low-viscosity solvent system must be used for flash chromatography. The chosen solvent system should produce an R_f value centered around 0.35 on the TLC for the components to be effectively separated.

Column Construction After selection of a column of the correct size (Table 4.7), it is packed using either the slurry method (pp. 101–103) or the dry column method (pp. 103–106). The amount of silica gel used should be approximately 50 times the weight of the mixture to be separated.

[6]W. Still, M. Kahn, and A. Mitra, *J. Org. Chem.*, *43* (14), 2923 (1978).

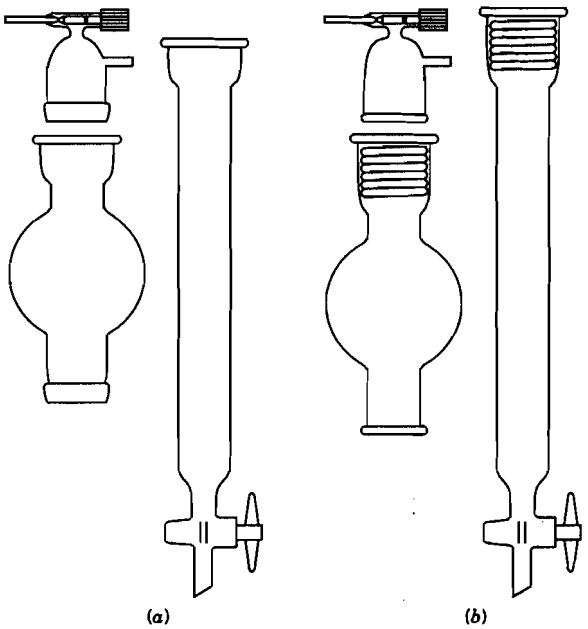


Figure 4.42 Flash chromatography columns: (*a*) with joints, (*b*) with thread connectors. Both types are available with or without the fritted disk.

TABLE 4.7 Column Diameter Needed for Flash Chromatography[a]

Column Diameter (mm)	Vol of Eluant[b] (mL)	Sample: Typical Loading (mg)		Typical Fraction Size (mL)
		$\Delta R_f \geq 0.2$	$\Delta R_f \geq 0.1$	
10	100	100	40	5
20	200	400	160	10
30	400	900	360	20
40	600	1600	600	30
50	1000	2500	1000	50

[a]The experimental procedure on which this table is based is described in W. C. Still, M. Kahn, and A. Mitra, *J. Org. Chem.*, *43* (14), 2923 (1978); reproduced with permission.

[b]Typical volume of eluant required for packing and elution.

If the dry column method is used, the column is filled with solvent above the dry adsorbent and the flow controller is attached. The inert gas line is attached to the inlet tube below the stopcock. The gas is barely turned on and the stopcock is slowly closed until a flow rate of 2 in./min is achieved. The solvent is replenished as needed until the adsorbent is saturated with the solvent and no air bubbles are present.

Use of the Flash Chromatography Column Once the column is prepared, the sample added (p. 102), and the column filled with solvent, the flow controller is attached to the top of the column. A flow rate of 2 in./min is maintained until all components have been eluted, replenishing the solvent as needed until the components are eluted.

The total amount of solvent used for the separation is roughly 7–10 times, in mL, of the silica gel, in grams. The column is not allowed to run dry at any time.

The size of the fractions is one-third to one-sixth, in mL, of the amount of the silica gel, in grams. If the column is packed properly, one fraction should be collected every 10–20 sec.

A simple modification of flash chromatography uses a balloon as a reservoir of pressurized gas attached with glass tubing to a one-hole stopper which is placed on the top of the column.[7]

(d) Microscale Column Chromatography[8]

Microscale column chromatography uses either a Pasteur pipet or a 50-mL titration buret (Figure 4.43) for chromatographing mixtures.

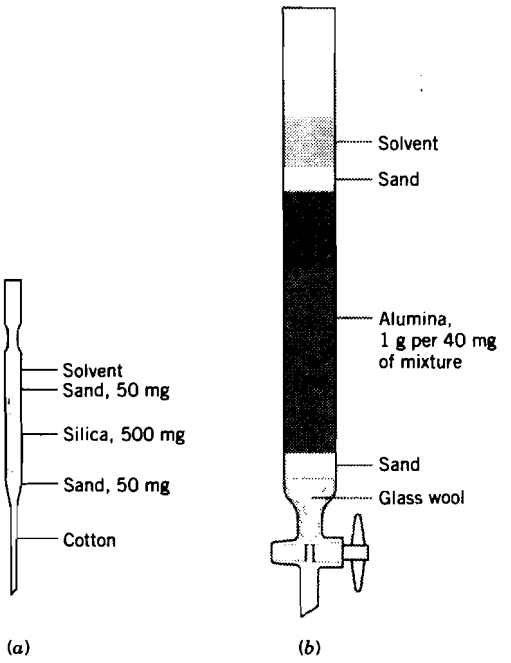


Figure 4.43 Microscale chromatography columns: (*a*) from a Pasteur pipet; (*b*) from a buret. [Figure 4.43*a* is from James W. Zubrick, *The Organic Chem Lab Survival Manual*, 4th ed. (Wiley, New York, 1997). Reprinted by permission of John Wiley and Sons, Inc., New York.]

Pasteur Pipet Chromatography Column The Pasteur pipet is used to separate mixtures of 10–100 mg and is packed dry. The cotton is placed in the Pasteur buret, followed by 50 mg of sand. Only 500 mg of dry adsorbent is needed in the Pasteur pipet. The adsorbent is topped with another 50 mg of sand. The column is moistened with the solvent prior to use. No stopcock or clamp is attached to the bottom of the Pasteur pipet.

Buret Chromatography Column A 50-mL titration buret, shortened to 10 cm above the stopcock, is used to separate mixtures of 50–200 mg and is packed as a slurry column. One centimeter of sand is used before and after the adsorbent. One gram of adsorbent is used for each 40 mg of mixture to be chromatographed.

[7]W. J. Thompson and B. A. Hansen, *J. Chem. Educ.*, *61* (7), 645 (1981).

[8]D. W. Mayo, R. M. Pike, and P. K. Trumper, *Microscale Organic Laboratory with Multistep and Multiscale Syntheses*, 3rd ed. (Wiley, New York, 1994), pp. 99–100.

Using the Microscale Chromatography Columns The microscale columns are used the same day they are prepared and are used in the same manner as the larger-scale columns. Once moistened, they should not be allowed to run dry.

4.4.4 High-Performance Liquid Chromatography (HPLC)

High-performance liquid chromatography (HPLC), sometimes called high-pressure liquid chromatography, attacks problems associated with traditional column chromatography with great success.[9]

In traditional LC chromatography the stationary phase consists of a particle size which is large relative to that used in HPLC. In order to speed the diffusion of sample into the stationary phase, *very fine particles* of stationary phase are used in HPLC. These particles are on the order of a few micrometers in size. The small size of such fine particles produces a new problem, such as potentially slow flow rates; pressures well above atmospheric pressure are necessary to push the mobile phase through tightly packed columns of fine particles. Pumps delivering thousands of pounds per square inch push mobile phases through columns of very fine particles. Detectors that differentiate samples by refractive index, by UV absorption, and by fluorescence are commonly used.

High-performance liquid chromatography offers the advantage of high speed, reusable columns, automatic and continuous solvent addition, reproducible programmed gradients of solvents, and automatic and continuous monitoring of the eluted samples. Less than 1 mg of sample is commonly analyzed. Preparative-scale instruments separate between several milligrams and a few grams of sample. The main disadvantage of preparative-scale separations is that large amounts of solvents are used.

Solvent System In the schematic (Figure 4.44), the apparatus is equipped with one or more glass or steel solvent reservoirs. The solvent may be heated or stirred, or the

[9]Consult Chapter 12 for analytical chemistry books that explain this method in detail.

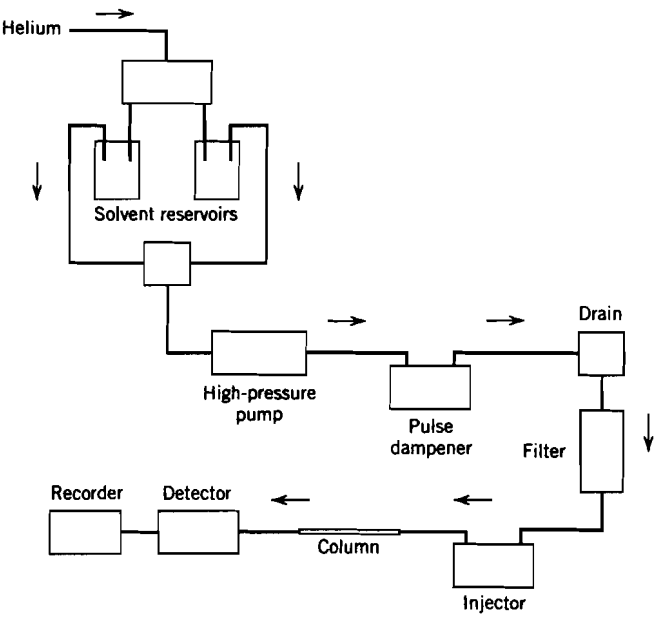


Figure 4.44 Schematic of a high-performance liquid chromatography column.

solvent reservoirs may contain attachments inlets for inert gases for solvent degassing. The presence of dissolved gases results in poorer resolution of the peaks.

Pumps The pump for the HPLC instrument must be pulseless and able to generate reproducible flow rates. The pump must be able to drive the mobile phase through long, narrow columns which are packed with very fine particles and to generate pressures up to 6000 psi and a solvent flow of 0.1–10 mL/min.

Sample Introduction The sample is introduced into the system via a syringe. A sampling loop is the most common method of sample introduction. The sample is injected into a small loop. As a lever is moved, the loop is closed off from the outside and the solvent is allowed to pass through the loop, thus introducing the sample into the system.

Columns Columns for HPLC are usually constructed from stainless steel tubing. Fittings and plugs must be inert and should not detract from the homogeneity of the flow. Analytical columns range in length from 10 to 150 cm long. The inside diameters vary from 1 to 20 mm. Columns of less than 8 mm are difficult for a novice to pack. The dimensions of a preparative LC column are typically 30 cm by 5 cm.

Silica is the most common type of packing material. The silica may be coated with a thin organic film, which is chemically bonded to the surface of the silica. By using a reverse-phase type of adsorbent, compounds may be separated on the basis of nonpolar–nonpolar interactions rather than polar–polar interactions.

Detectors The most commonly used detector for HPLC is an ultraviolet spectrophotometer or a refractometer. Other detectors such as infrared and electrochemical have also been used. The spectrophotometers are considered to be much more versatile and can detect a wider range of compounds. By using a refractometer, changes in the solvent refractive index can be detected.

Analysis of Chromatograms The retention times and percent composition of each component are determined from the chromatogram. The retention times are calculated by dividing the distance by the chart speed (Figure 4.35). The distance is measured from the zero time mark, when the sample is injected, to the top of the peak. The zero time mark can be made by moving the pen on the recorder up and down before the sample is injected into the column. The chart speed is determined by looking at the recorder. The units of the chart speed may be in cm/min or mm/min. Care must be taken so that the units cancel out properly, leaving behind only the unit of time.

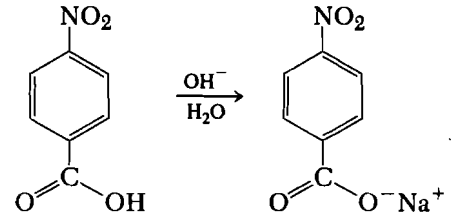
CHAPTER 5

Classification of Organic Compounds by Solubility

In this chapter we begin the process of determining the structural composition of organic compounds. Elemental composition obtained in Chapter 3 can be of use here. Both solubility and spectrometric analyses (Chapters 6, 7, and 8) often lead to the same kinds of structural deduction. Deductions based upon interpretation of simple solubility tests can be extremely useful in organic structure determination.

Before proceeding, the difference between solubility and a chemical reaction must be ascertained. In some cases, a chemical reaction is accompanied by a change in color or heat or by the formation of a precipitate. Solubility involves the formation of one layer, if the compounds are miscible, or two layers, if the compounds are immiscible.

The solubility of organic compounds can be divided into two major categories: solubility in which a chemical reaction is the driving force, for example, the following acid–base reaction,



4-nitrobenzoic acid
water insoluble

sodium 4-nitrobenzoate
water soluble

and solubility in which simple miscibility is the only mechanism involved, such as dissolving ethyl ether in carbon tetrachloride. Although the two solubility sections below are interrelated, the first section deals primarily with the identification of functional groups and the second with the determination of solvents to be used in recrystallizations, spectral analyses, and chemical reactions.

5.1 SOLUBILITY IN WATER, AQUEOUS ACIDS AND BASES, AND ETHER

Three kinds of information can often be obtained about an unknown substance by a study of its solubilities in water, 5% sodium hydroxide solution, 5% sodium bicarbonate solution, 5% hydrochloric acid solution, and cold concentrated sulfuric acid. First, the presence of a functional group is often indicated. For instance, because hydrocarbons are insoluble in water, the mere fact that an unknown is partially soluble in water indicates that a polar functional group is present. Second, solubility in certain solvents often leads to more specific information about the functional group. For example, benzoic

acid is insoluble in a polar solvent, water, but is converted by 5% sodium hydroxide solution to a salt, sodium benzoate, which is readily water soluble. In this case, then, the solubility in 5% sodium hydroxide solution of a water insoluble unknown is a strong indication of an acidic functional group. Finally, certain deductions about molecular size and composition may sometimes be made. For example, in many homologous series of monofunctional compounds, the members with fewer than about five carbon atoms are water soluble, whereas the higher homologs are insoluble.

Compounds are first tested for solubility in water. In considering solubility in water, a substance is arbitrarily said to be "soluble" if it dissolves to the extent of 3.3 g/100 mL of solvent. This standard is dictated by the limitations inherent in the method employed, which depends on rough semiquantitative visual observations, as will be seen. Care is needed in interpreting the classifications of "soluble" and "insoluble" in other references because different standards for solubility may have been followed.

If the compound is soluble in water, then it is tested for solubility in ether. If the compound is insoluble in ether, then it is in solubility class S_2. Solubility in ether indicates that the compound is in solubility classes S_A, S_B, or S_1. The aqueous solutions of the ether soluble compounds are then tested with pH paper to narrow down the choices. No more solubility tests are needed at this point if the compound is soluble in water.

However, if the compound is not soluble in water, then it is tested for solubility in 5% sodium hydroxide solution. Acidic compounds are identified by their solubility in 5% sodium hydroxide solution. Strong and weak acids (solubility classes A_1 and A_2; see Table 5.1 and Figure 5.1) are differentiated by their solubility or lack of solubility in 5% sodium bicarbonate solution. Once the compound is identified as an acid and its solubility class determined, then no more solubility tests are needed.

TABLE 5.1 Organic Compounds Comprising the Solubility Classes of Figure 5.1[a]

S_2	Salts of organic acids (RCO_2Na, RSO_3Na); amine hydrochlorides (RNH_3Cl); amino acids ($R-\underset{\displaystyle NH_3^+}{\underset{\vert}{CH}}-CO_2^-$); polyfunctional compounds with hydrophilic functional groups: carbohydrates (sugars), polyhydroxy compounds, polybasic acids, etc.
S_A	Monofunctional carboxylic acids with five carbons or fewer; arylsulfonic acids.
S_B	Monofunctional amines with six carbons or fewer.
S_1	Monofunctional alcohols, aldehydes, ketones, esters, nitriles, and amides with five carbons or fewer.
A_1	Strong organic acids: carboxylic acids with more than six carbons; phenols with electron-withdrawing groups in the *ortho* and/or *para* position(s); β-diketones (1,3-diketones).
A_2	Weak organic acids: phenols, enols, oximes, imides, sulfonamides, thiophenols, all with more than five carbons; β-diketones (1,3-diketones); nitro compounds with α-hydrogens.
B	Aliphatic amines with eight or more carbons; anilines (only one phenyl group attached to nitrogen); some ethers.
MN	Miscellaneous neutral compounds containing nitrogen or sulfur and having more than five carbon atoms.
N	Alcohols, aldehydes, ketones, esters with one functional group and more than five but fewer than nine carbons, ethers, epoxides, alkenes, alkynes, some aromatic compounds (especially those with activating groups).
I	Saturated hydrocarbons, haloalkanes, aryl halides, other deactivated aromatic compounds, diaryl ethers.

[a]Acyl halides and carboxylic acid anhydrides have not been classified because of their high reactivity.

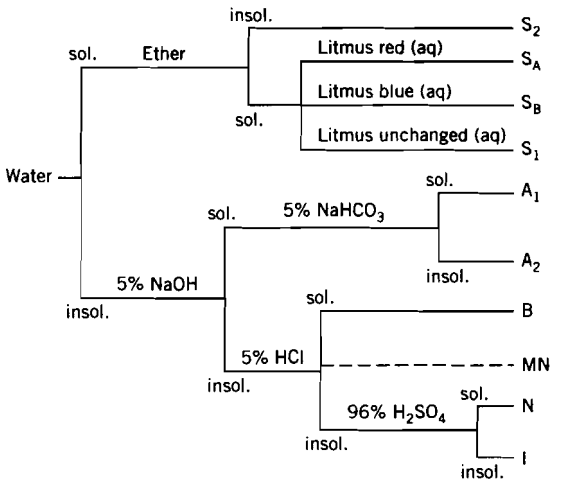


Figure 5.1 Classification of organic compounds by solubility: determination in water, acids, bases, and ethers (see Table 5.1 for compounds comprising each class). sol. = soluble, insol. = insoluble; litmus is red at pHs below 4.5 and blue above 8.3.

For compounds that are insoluble in water and subsequently insoluble in 5% sodium hydroxide, the solubility in 5% hydrochloric acid solution is determined. Compounds that behave as bases in aqueous solution are detected by their solubility in 5% hydrochloric acid solution (solubility class B). If the compound is identified as a base, then additional solubility tests are not needed.

Many compounds that are neutral toward 5% hydrochloric acid solution behave as bases in more acidic solvents such as concentrated sulfuric acid. In general, compounds containing sulfur or nitrogen have an atom with an unshared pair of electrons and would be expected to dissolve in a strong acid. No additional information would be gained, therefore, by determining such solubility; for this reason, when the elemental analysis has shown the presence of sulfur or nitrogen, no solubility tests beyond those for acidity and basicity in aqueous solution are carried out. Compounds that contain nitrogen or sulfur and are neutral in aqueous acid or base are placed in solubility class MN.

Compounds that are insoluble in water, 5% sodium hydroxide solution, and 5% hydrochloric acid solution, but soluble in 96% sulfuric acid solutions, are classified in solubility class N. The solubility in 96% sulfuric acid indicates the presence of an oxygen atom or of a reactive hydrocarbon function such as a double or triple bond or an easily sulfonated aromatic ring.

Compounds that are insoluble in water, 5% sodium hydroxide solution, 5% hydrochloric acid solution, and 96% sulfuric acid solution are placed in solubility class I (inert compounds).

When solubility in 5% acid or base is being considered, the significant observation to be made is not whether the unknown is soluble to the extent of 3% or to any arbitrary extent but, rather, whether it is significantly more soluble in aqueous acid or base than in water. This increased solubility is a positive test for a basic or acidic functional group.

It is very important to follow the flowchart illustrated in Figure 5.1. Unnecessary tests give confusing results.

Directions for determining the solubility class of an unknown compound are given below, followed by an explanation of the solubility of various types of compounds.

Problem

1. Give the solubility class and the possible types of compounds for the solubilities listed below.
   a. The unknown compound was insoluble in water, 5% NaOH, and 5% HCl, but soluble in 96% H_2SO_4.
   b. The unknown compound was soluble in water and ether and was unchanged with litmus.
   c. The unknown compound was insoluble in water and 5% $NaHCO_3$, but soluble in 5% NaOH.

5.1.1 Determination of Solubilities

Procedure for Water Solubility

Place 0.05 mL (approximately one drop) or 25 mg of the compound in a small test tube, and add 0.75 mL of water in small portions. Shake vigorously after the addition of each portion of solvent, being careful to keep the mixture at room temperature. If the compound dissolves completely, record it as soluble.

Powder all solids to increase the rate of dissolving of the solid. If the solid appears to be insoluble in water or ether, it is sometimes advisable to heat the mixture gently. If the solid dissolves with heating, the solution is cooled to room temperature and is shaken to prevent supersaturation. The cooled solution is then "seeded" with a crystal of the solid. Care should be taken in weighing the sample; it should weigh 25 mg ± 1 mg.

Measure all liquids with a graduated pipet that permits the accurate measurement of the liquid. When two colorless liquid phases lie one above the other, it is often possible to overlook the boundary between them and thus to see only one phase. This mistake can generally be avoided by shaking the test tube vigorously when a liquid unknown seems to have dissolved in the solvent. If two phases are present, the solution will become cloudy. In the rare cases where two colorless phases have the same refractive index, the presence of a second phase will escape detection even if this precaution is taken.

Cleaning Up Place the test solutions in the aqueous solution container.

Procedure for Testing with Litmus Paper

Dissolve 0.05 mL (approximately one drop) or 25 mg of the compound in 0.75 mL of water. Using a stirring rod, place a drop of this aqueous solution on both red and blue litmus paper. If both litmus papers turn red, the compound has a solubility class of S_A. If both litmus papers turn blue, the compound has a solubility class of S_B. If both litmus papers remain their original color, the compound has a solubility class of S_1.

Compounds with a $pK_a < 8$ will fall in class S_A (see Table 5.1 and Figure 5.1). Compounds with a $pK_b < 9$ will fall in class S_B. Consequently, phenols with pK_a of about 10 give aqueous solutions too weakly acidic (pH about 5) to turn litmus paper red. Litmus is red at pHs below 4.5 and blue above 8.3. For similar reasons, an aromatic amine such as aniline is too weak a base (pK_b 9.4) to turn litmus blue in aqueous solution. Although more refined procedures can be developed using a pH-indicating paper, it is preferable to rely more on the tests discussed in Chapter 9.

Cleaning Up Place the test solutions in the aqueous solution container.

Procedure for Ether Solubility
Place 0.05 mL (approximately one drop) or 25 mg of the compound in a small test tube, and add 0.75 mL of diethyl ether in small portions. Shake vigorously after the addition of each portion of solvent, being careful to keep the mixture at room temperature. If the compound dissolves completely, record it as soluble.

Cleaning Up Place the test solution in the organic solvent container.

Procedure for Solubility in Aqueous Acid or Base
To test for solubility in aqueous acid or base, thoroughly shake a mixture of 0.05 mL (approximately one drop) or 25 mg of the unknown compound with 0.75 mL of 5% sodium hydroxide solution, 5% sodium bicarbonate solution, or 5% hydrochloric acid solution. Separate (filter if necessary) the aqueous solution from any undissolved unknown, and *neutralize* it with acid and base. Examine the solution very carefully for any sign of separation of the original unknown. Even a cloudy appearance of the neutralized filtrate is a positive test.

When solubility in acid or alkali is being determined, heat should *not* be applied because it might cause hydrolysis to occur. If the mixture is shaken thoroughly, the time required for the unknown to dissolve should not be more than 1 to 2 min.

Often it is possible to utilize a single portion of unknown for tests with several different solvents. Thus, if the compound is found to be insoluble in water, a fairly accurate measure of its solubility in 5% sodium hydroxide solution can be obtained by adding about 0.25 mL of a 20% solution of sodium hydroxide to a mixture of the compound in 0.75 mL of water. The resulting 1.0 mL of solvent will then contain a 5% solution of sodium hydroxide. If the substance is very insoluble, it may often be recovered and used subsequently for the hydrochloric acid test. Although it is possible to conserve the unknown in this manner, it is recommended that a fresh unknown sample be used for each test.

Cleaning Up Place the test solutions in the aqueous solution container.

Procedure for Solubility in Concentrated Acid
Place 0.6 mL of concentrated sulfuric acid in a test tube, and add 0.05 mL (approximately one drop) or 25 mg of the unknown compound. For purposes of solubility classification, unknowns that react with sulfuric acid to produce heat and/or color changes should be classified as soluble, even if the sample does not appear to dissolve.

Cleaning Up Carefully neutralize the test solution with 10% sodium hydroxide solution and place the test solution in the aqueous solution container.

5.1.2 Theory of Solubility

Polarity and Solubility
When a solute dissolves, its molecules or ions become distributed more or less randomly among those of the solvent. In crystalline sodium chloride, for example, the average distance between sodium and chloride ions is 2.8 Å. In a 1 M solution the solvent has interspersed itself in such a way that sodium and chloride ions are about 10 Å apart. The difficulty of separating such ions is indicated by the high melting point (800°C) and boiling point (1413°C) of pure sodium chloride. Another indication of the importance of solvent is the fact that sodium chloride readily forms ions in water, while it takes several hundred kilocalories per mole to form ions from sodium chloride in the solid state.

The *dielectric constant* is the measure of the ability of the solvent to separate ionic charges. The dielectric constant of the solvent is related to the polarity of the solvent. Dielectric constants of some organic solvents are listed in Table 5.2. A compound with a high dielectric constant is a polar solvent; a compound with a low dielectric solvent is a nonpolar solvent. It is not surprising that water, with a high dielectric constant of 80, facilitates the separation of sodium and chloride ions and dissolves sodium chloride readily, whereas both hexane (dielectric constant 1.9) and diethyl ether (dielectric constant 4.4) are extremely poor solvents for ionic salts. Water molecules positioned between two ions (or the charged plates of a condenser) are actually small dipoles, which orient themselves end to end in such a way as to partially neutralize the ionic charges and thus stabilize the system. An assumption might be made that the solvating ability and dielectric constant are related. However, this is not entirely the case. A high dielectric constant is required but is not the only characteristic of an effective ion solvent. For example, hydrogen cyanide, with a dielectric constant of 116, is a very poor solvent for salts such as sodium chloride. Although the situation is quite complex, one major factor responsible for the efficiency of water and other hydroxylic solvents is their ability to form hydrogen bonds with the solute.

TABLE 5.2 Dielectric Constants of Common Organic Solvents

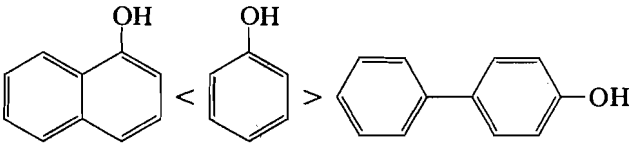
Compound	Dielectric Constants
Hydrogen cyanide	116
Formamide	111
Water	80
Formic acid	58
Dimethyl sulfoxide	47.8
Acetonitrile	37.5
N,N-Dimethylformamide	37
Methanol	32.6
Hexamethylphosphortriamide	30
Ethanol	24.3
Acetone	20.7
Methylene chloride	9
Tetrahydrofuran	7.6
Acetic acid	6.2
Ethyl acetate	6
Chloroform	4.8
Diethyl ether	4.4
Benzene	2.3
Carbon tetrachloride	2.2
Hexane	1.9

The high dielectric constant and hydrogen-bonding ability of water, which combine to make it a good solvent for salts, also make it a poor solvent for nonpolar substances. In pure water, molecules are oriented in such a way that positive and negative centers are adjacent. Attempting to dissolve a nonpolar substance such as hexane in a solvent such as water is analogous to separating unlike charges in a medium of low dielectric constant. As a general rule, a polar solvent may be expected to readily dissolve only polar solutes, and nonpolar solvent only nonpolar solutes. This generalization has been summarized more succinctly as "like dissolves like."

Table 5.1, related to Figure 5.1, lists the solubility class of various types of compounds. A discussion of the solubility trends of compounds appears below.

Since most organic molecules have both a polar and a nonpolar entity, it can be deduced that its solubility would depend on the balance between the two parts. As the percentage of the hydrocarbon portion increases, the properties of the compounds approach those of the parent hydrocarbons. As a result, water solubility decreases and ether solubility increases. A similar change in solubility occurs as the number of aromatic hydrocarbon residues in the molecule increases. Thus 1-naphthol and 4-hydroxybiphenyl are less soluble in water than phenol:

Water Solubility



1-naphthol phenol 4-hydroxybiphenyl

The phenyl group, when present in aliphatic acids, alcohols, aldehydes, and similar compounds, has an effect on water solubility approximately equivalent to a four-carbon aliphatic unit. Benzyl alcohol, for example, is about as soluble in water as 1-pentanol, and 3-phenylpropanoic (hydrocinnamic) acid exhibits a solubility similar to that of heptanoic acid:

Water Solubility

$$\underset{\text{benzyl alcohol}}{C_6H_5CH_2OH} \approx \underset{\text{1-pentanol}}{CH_3CH_2CH_2CH_2CH_2OH}$$

$$\underset{\substack{\text{3-phenylpropanoic acid}\\ \text{(dihydrocinnamic acid)}}}{C_6H_5CH_2CH_2COOH} \approx \underset{\text{heptanoic acid}}{CH_3CH_2CH_2CH_2CH_2CH_2COOH}$$

The solubility of a substance is a measure of the equilibrium between the substance in its solid state and the substance, or its ions, in solution. Such an equilibrium is affected not only by the solvent–solute interactions previously discussed but also by the intermolecular forces present in the pure solute. These forces are independent of the polarity or other properties of the solvent, and their relative strengths may be estimated by a comparison of melting and boiling points, since these processes involve a separation of molecules that is somewhat related to the separation that occurs on solution.

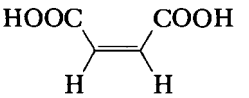
The dicarboxylic acids illustrate the inverse relationship of melting point and solubility. The data in Table 5.3 show that each member with an even number of carbon atoms melts at a higher temperature than either the immediately preceding or following acid containing an odd number of carbon atoms. The intracrystalline forces in the members with an even number of carbon atoms evidently are greater than in those with an odd number of carbons. Since the solubility limit for solids is generally set at 3.3 g/100 mL of water, it is evident that hexanedioic acid (adipic acid, six carbons) is water insoluble but heptanedioic acid (pimelic acid, seven carbons) is water soluble.

The relationship of high melting point and low solubility is further illustrated by the isomers *cis*- and *trans*-2-butenedioic acid (maleic and fumaric acids). *trans*-2-Butenedioic acid sublimes at 200°C and is insoluble in water. *cis*-2-Butenedioic acid melts at 130°C and is soluble in water. Among *cis-trans* isomers, the *cis* form generally is the more soluble. Similarly, with polymorphous substances such as benzophenone,[1] the lower melting forms possess the higher solubilities.

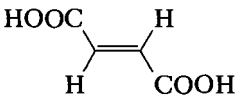
[1]Benzophenone occurs in at least four crystalline forms.

TABLE 5.3 Water Solubility of Dicarboxylic Acids, HOOC—$(CH_2)_{x-2}$—COOH

Number (x) of Carbon Atoms	mp (°C)	Solubility (g/100 g of Water at 20°C)
Even number of carbon atoms		
Ethanedioic acid (2) (oxalic acid)	189	9.5
Butanedioic acid (4) (succinic acid)	185	6.8
Hexanedioic acid (6) (adipic acid)	153	2
Octanedioic acid (8) (suberic acid)	140	0.16
Decanedioic acid (10) (sebacic acid)	133	0.10
Odd number of carbon atoms		
Propanedioic acid (3) (malonic acid)	135	73.5
Pentanedioic acid (5) (glutaric acid)	97	64
Heptanedioic acid (7) (pimelic acid)	103	5
Nonanedioic acid (9) (azelaic acid)	106	0.24

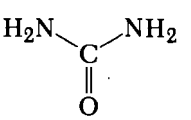


cis-2-butenedioic acid
(maleic acid)
Z-isomer

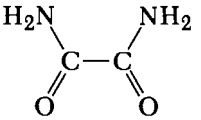


trans-2-butenedioic acid
(fumaric acid)
E-isomer

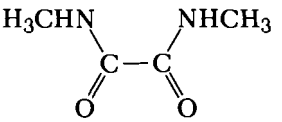
The diamides of dicarboxylic acids constitute another group of compounds for which the melting point is a valuable index of the forces present in the crystals. Urea (mp 132°C) is water soluble. On the other hand, ethanediamide (oxalic acid diamide) has a quite high melting point of 420°C and a low solubility in water. Substitution of methyl groups for the hydrogen atoms of the amide group lowers the melting point by reducing intermolecular hydrogen bonding and increases the solubility in water; *N*,*N*′-dimethylethanediamide and *N*,*N*,*N*′,*N*′-tetramethylethanediamide are water soluble. Hexanediamide is water insoluble, whereas its *N*,*N*,*N*′,*N*′-tetramethyl derivative is water soluble.



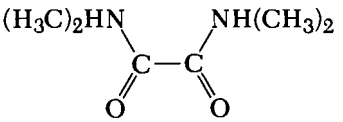
urea
mp 132°C



ethanediamide
mp 420°C

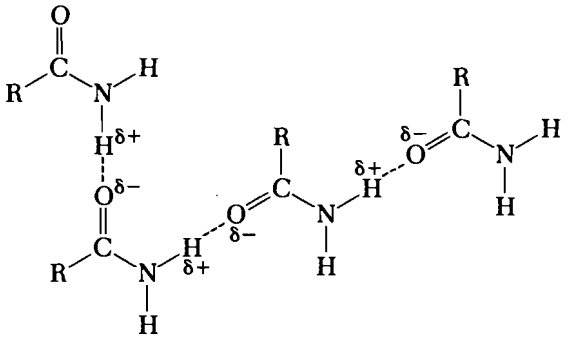


N,*N*′-dimethylethanediamide
mp 217°C

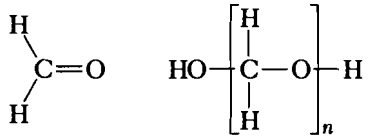


N,*N*,*N*′,*N*′-tetramethylethanediamide
mp 80°C

Regarding water solubility, amides of the type $RCONH_2$ and RCONHR agree with the general rule that the borderline compounds contain about five carbon atoms (above). However, *N,N*-dialkylamides ($RCONR_2$), which have lower melting points than the corresponding unsubstituted amides, are much more soluble in water. The water solubility limit for the *N,N*-dialkylamides is in the range of nine to ten carbon atoms. Amides having the group $—CONH_2$ may act both as acceptors and as donors in forming hydrogen bonds. Intermolecular hydrogen bonding cannot occur with the *N,N*-disubstituted amides ($RCONR_2$), and hence their state of molecular aggregation is low, as indicated by their lower melting points and higher solubilities.



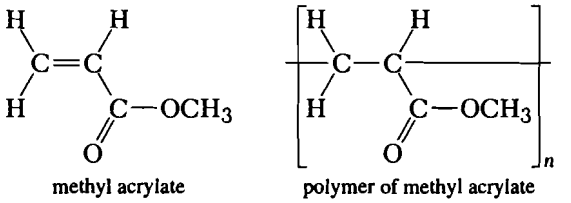
In general, an increase in *molecular weight* leads to an increase in intermolecular forces in a solid and decreased solubility. Therefore, polymers and other compounds of high molecular weight generally exhibit low solubilities in both water and ether. Thus formaldehyde is readily soluble in water, whereas paraformaldehyde is insoluble.



formaldehyde (methanal) water soluble

paraformaldehyde water insoluble

Methyl acrylate is soluble in water, but its polymer is insoluble. The fact that a pi bond is lost upon polymerization may also affect solubility.



methyl acrylate

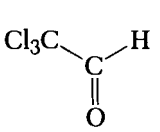
polymer of methyl acrylate

Glucose is soluble in water, but its polymers (starch, glycogen, and cellulose) are insoluble. Fibrous proteins are insoluble in water, but globular proteins are soluble in water. Many amino acids are soluble in water, but their condensation polymers, the proteins, are usually insoluble. The tendency of certain proteins, dextrins, and starches to form colloidal dispersions may lead to inaccurate conclusions regarding their solubility.

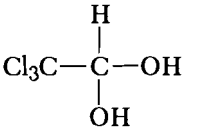
Another method of increasing the molecular weight of a molecule is by the substitution of halogens for hydrogens. The result is a lower water solubility of the halogenated compound.

The five-carbon upper limit for water solubility follows from a very general principle—that increased structural similarity of the solute and the solvent is accompanied by an increase in solubility. Since water is a polar solvent, compounds that are water soluble contain polar functional groups. As a homologous series is ascended, the nonpolar hydrocarbon part of the molecule increases while the polar function remains essentially unchanged, thus resulting in a decrease in solubility in polar solvents such as water.

The tendency of certain oxygen-containing compounds to form hydrates also contributes to water solubility. The stability of these hydrates is therefore a factor in determining water and ether solubility. Compounds such as 2,2,2-trichloroethanal probably owe their solubility in water to hydrate formation.

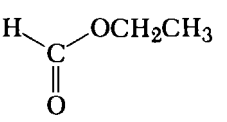


2,2,2-trichloroethanal
(chloral)

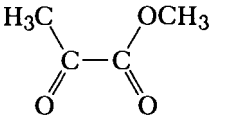


2,2,2-trichloroethanalhydrate
(chloral hydrate)

Low molecular weight esters of methanoic (formic) and 2-oxopropanoic (pyruvic) acids are hydrolyzed by water at room temperature, as indicated by the fact that the aqueous layer becomes distinctly acid to litmus.



ethyl methanoate
(ethyl formate)



methyl 2-oxopropanoate
(methyl pyruvate)

Effect of Chain Branching on Solubility

Since branching of the hydrocarbon chain lowers the boiling points of the lower homologous series, such as the hydrocarbons and alcohols, an assumption can be made that branching also lowers intermolecular forces and decreases intermolecular attraction. Therefore, a compound having a branched chain is more soluble than the corresponding straight-chain compound. This is a general rule and is particularly useful in connection with simple aliphatic compounds. For example, the solubility of an *iso* compound differs widely from that of its normal isomer and is close to that of the next-lower normal member of the same homologous series. The effects of chain branching are shown in Table 5.4.

The position of the functional group in the carbon chain also affects solubility. For example, 3-pentanol is more soluble than 2-pentanol, which in turn is more soluble than 1-pentanol. When the branching effect is combined with the position of the functional group toward the center of the molecule, as in the case of 2-methyl-2-butanol, a very marked increase in solubility is noted. *Normally, the more compact the structure, the greater the solubility, provided that comparisons are made on compounds containing the same functional group(s) and molecular weight.*

5.1.3 Theory of Acid–Base Solubility

Effect of Structure on Acidity and Basicity

In general, the problem of deciding whether a water insoluble unknown should dissolve in dilute acid or base is primarily a matter of estimating its approximate acid or base

TABLE 5.4 Water Solubility of Various Organic Compounds

Type of Compound	Soluble	Borderline	Insoluble
Acid	2,2-Dimethylpropanoic acid (C_5) (pivalic acid)	3-Methylbutanoic acid (C_5) (isovaleric acid)	Pentanoic acid (C_5) (valeric acid)
Acid chloride	2-Methylpropanoyl chloride (C_4) (isobutyryl chloride)	Butanoyl chloride (C_4) (butyryl chloride)	
Alcohol	2,2-Dimethyl-1-propanol (C_5) (neopentyl alcohol)	3-Methyl-2-butanol (C_5)	1-Pentanol (C_5) (amyl alcohol)
Amide	2-Methylpropanamide (C_4) (isobutyramide)	Butanamide (C_4) (butyramide)	
Ester	1-Methylethyl ethanoate (C_5) (isopropyl acetate)	Propyl ethanoate (C_5) (propyl acetate)	
Ketone	3-Methyl-2-butanone (C_5) (isopropyl methyl ketone)	2-Pentanone (C_5) (methyl propyl ketone)	
Nitrile		2-Methylpropanenitrile (C_4) (isobutyronitrile)	Butanenitrile (C_4) (butyronitrile)

strength. In doing this, we must be concerned with the structural features that will stabilize the organic anion, A^-, and position the following equilibrium[2] farther to the right:

$$HA \rightleftharpoons H^+ + A^-$$

that is, we increase the magnitude of K_a, where

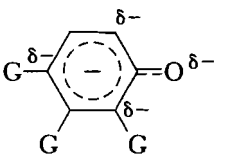
$$K_a = \frac{[H^+][A^-]}{[HA]}$$

or decrease the magnitude of $pK_a = \log(1/K_a) = -\log K_a$.

The two principal effects influencing structural control of acid–base strength are electronic and steric.

Electronic Effects on Acidity and Basicity

Extensive studies have been done on the correlation of structure with acid or base strength of substituted organic compounds. These effects have been rationalized[3] on an electronic basis; thus the *para* and *ortho* positions of aromatic compounds are more sensitive to electronic influences than are the *meta* positions:

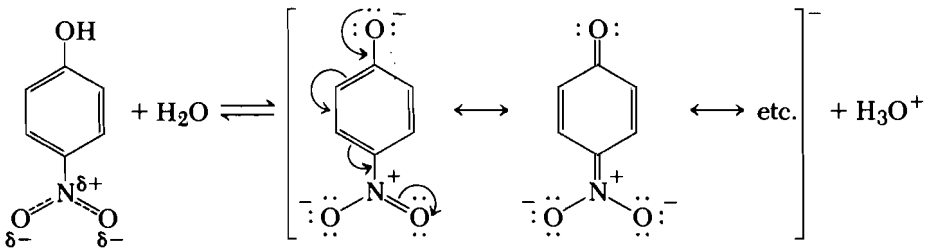


The *ortho* and *para* positions are centers of partial negative charge and thus these centers respond to substitution by polar groups; *ortho*-substitution considerations are sometimes hindered by steric factors.

[2] H^+ is used interchangeably with H_3O^+.

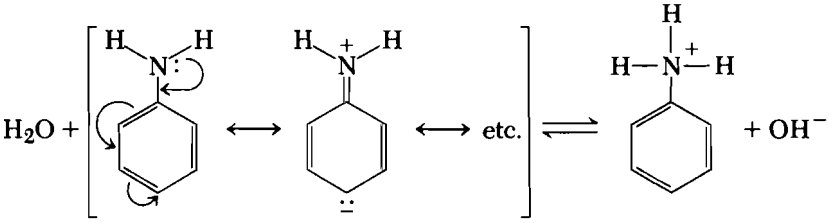
[3] Consult any book on theoretical organic chemistry, such as M. B. Smith and J. March, *Advanced Organic Chemistry*, 5th ed. (Wiley-Interscience, New York, 2000).

Most carboxylic acids have dissociation constants in water, at 25°C, of 1×10^{-6} or greater and therefore are readily soluble in 5% sodium hydroxide solution. Phenols, with a dissociation constant of 1×10^{-10}, are less acidic. Phenols are soluble in strongly basic sodium hydroxide solution, but insoluble in 5% sodium bicarbonate solution.[4] However, the substitution of certain functional groups onto the ring may have a profound effect on their acidity. Thus 2- and 4-nitrophenol have dissociation constants of about 6×10^{-8}. The introduction of an *ortho* or *para* nitro group onto the ring increases the acidity of phenol by a factor of about 600. Therefore, the addition of two nitro groups, such as in 2,4-dinitrophenol, increases the acidity to such an extent that the compound is soluble in 5% sodium bicarbonate solution. The acidity-increasing effect of the nitro group is due to stabilization of the phenoxide anion by further distribution of the negative charge on the nitro group.



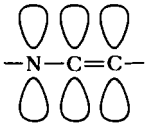
A similar increase in acidity is observed when a halogen is substituted onto phenol. Thus an *ortho* bromine atom increases the acidity of phenol by a factor of about 30 and a *para* bromine atom by a factor of about 5. The presence of more halogens increases solubility so that a compound such as 2,4,6-tribromophenol is a sufficiently strong acid to dissolve in 5% sodium bicarbonate solution. The increase in acidity can be explained by inductive effects.

Similar electronic influences affect the basicity of amines. Aliphatic amines in aqueous solution have basicity constants, K_b, of about 1×10^{-3} or 1×10^{-4}, which is approximately the basicity constant of ammonia, 1×10^{-5}. Introduction of a conjugated phenyl group[5] lowers the basicity by about 6 orders of magnitude, for example, aniline has a K_b of 5×10^{-10}. The phenyl ring stabilizes the free amine by resonance and also decreases the basicity of nitrogen inductively.

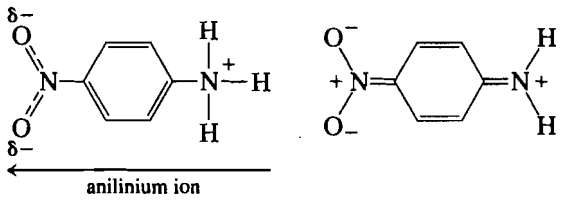


[4]The K_a of 2,4-dinitrophenol is about 10^{-4}.

[5]The nonbonded electron pair on nitrogen is said to be conjugated with formal "double" bonds of the benzene ring; for example, it possesses an —N—C=C unit with overlapping orbitals.



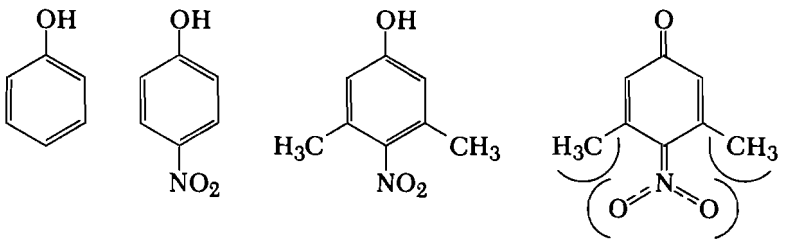
A second phenyl substituent decreases the basicity to such an extent that the amine is no longer measurably basic in water. For example, diphenylamine is insoluble in 5% hydrochloric acid solution. Substitution of a nitro group on the phenyl ring of aniline lowers the base strength because this electron-withdrawing group destabilizes the anilinium ion, the conjugate acid, while stabilizing the free base.



Steric Effects on Acidity and Basicity

The *ortho*-disubstituted phenols have reduced solubility in aqueous alkali, and the term *cryptophenol* has been used to emphasize this characteristic. Claisen's alkali (35% potassium hydroxide in methanol–water) has been used to dissolve such hindered phenols. An extreme example is 2,4,6-tri-*t*-butylphenol, which fails to dissolve in either aqueous sodium hydroxide or Claisen's alkali. It can be converted to a sodium salt only by treatment with sodium in liquid ammonia or sodium amide. 2,4,6-Tri-*t*-butylaniline shows similar behavior. It is such a weak base that the pK_a of the conjugate acid is too low to be measured in aqueous solution. 2,6-Di-*t*-butylpyridine is a significantly weaker base than is dimethylpyridine. It has been suggested that the weakening of the base strengths of the *ortho*-disubstituted amines is due to the steric strain created about the protonated nitrogen atom. Thus, the instability of the 2,6-di-*t*-butylphenoxide ion and of the other hindered ammonium ions mentioned is probably due primarily to the steric interference with the solvation of ions.

Steric strain may either increase or decrease the acidity of carboxylic acids. For example, substitution of alkyl groups on the *a*-carbon atom of acetic acid tends to decrease acidity by destabilizing the conjugate base through steric inhibition by solvation. *Ortho*-disubstituted benzoic acids, on the other hand, are appreciably stronger than the corresponding *para* isomers. The *ortho* substituents cause the carboxyl group to be out of the plane of the ring, disrupting resonance overlap between the carboxylate group and the ring, thus resulting in greater destabilization of the acid than of the anion.[6] This latter case is an example of a second kind of steric effect, which is commonly referred to as *steric inhibition of resonance*. Although 4-nitrophenol is about 2.8 pK_a units stronger than phenol, 3,5-dimethyl-4-nitrophenol is only about 1.0 pK_a units stronger.



pK_a at 25°C:	9.99	7.21	8.24	A

[6]More details on this can be found in a physical organic book such as T. H. Lowry and K. S. Richardson, *Mechanism and Theory of Organic Chemistry*, 3rd ed. (Benjamin Cummings, New York, 1987). (Also see footnote 3.)

Part of the effect of the two methyl groups, in reducing the acidity of the nitrophenol, seems to be due to steric inhibition of resonance in the anion. Thus, structure A requires coplanarity or near coplanarity of all of the nitro group's atoms and the aromatic ring. Such coplanarity is inhibited by the presence of the methyl groups in the ion.

5.1.4 Solubility in Water

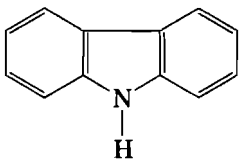
Water, being a polar solvent, is a poor solvent for hydrocarbons. The presence of double bonds, triple bonds, or aromatic rings does not affect the polarity greatly and such substances are not appreciably different from alkanes in their water solubility. The introduction of halogen atoms changes the water solubility. As a halogen is substituted for a hydrogen, the water solubility decreases. Salts are extremely polar and are usually water soluble (class S_2).

As might be expected, acids and amines generally are more soluble than nonpolar compounds. The amines are highly soluble owing to their tendency to form hydrogen bonds with water molecules. This is consistent with the fact that the solubility of amines decreases as the basicity decreases. It also explains the observation that many tertiary amines are more soluble in cold than in hot water. At lower temperatures, the solubility of the hydrate is involved, whereas at higher temperatures, the hydrate is unstable and the solubility measured is that of the free amine.

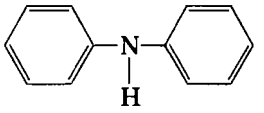
Monofunctional ethers, esters, ketones, aldehydes, alcohols, nitriles, amides, acids, and amines may be considered together with respect to water solubility. *In most homologous series of this type, the longest chain with appreciable water solubility will be reached at about five carbons.*

5.1.5 Solubility in 5% Hydrochloric Acid Solution

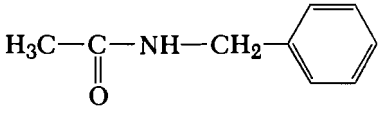
Primary, secondary, and tertiary aliphatic amines form polar ionic salts with hydrochloric acid. Aliphatic amines are readily soluble in 5% hydrochloric acid solution and are placed in class B if water insoluble. The presence of conjugated aryl groups decreases the basicity of the nitrogen atom. For example, primary aromatic amines, although more weakly basic than primary aliphatic amines, are soluble in 5% hydrochloric acid solution. However, diphenylamine, triphenylamine, and carbazole are insoluble in 5% hydrochloric acid solution. Arylalkylamines, such as benzylamines, containing not more than one aryl group, are soluble in 5% hydrochloric acid solution.



carbazole



diphenylamine

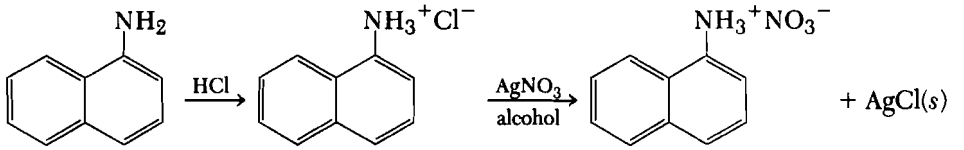


N-benzylacetamide

Disubstituted amides ($RCONR_2$) of sufficiently high molecular weight to be water insoluble are soluble in 5% hydrochloric acid solution. Simple amides ($RCONH_2$)[7] and most monosubstituted amides (RCONHR) are neutral compounds. *N*-Benzylacetamide, however, is a basic compound.

[7]Amides are generally comparable to water in basicity, and small structural changes, such as alkylation, need change their K_b by only ~10^2 to move them into the "basic" category.

Amines may undergo reaction with 5% hydrochloric acid solution to form *insoluble* hydrochlorides, which may lead to errors in classification. For example, certain arylamines, such as 1-aminonaphthalene, form hydrochlorides that are sparingly soluble in 5% hydrochloric acid solution. By warming the mixture slightly and diluting it with water, it may make the compound soluble. The appearance of a solid will indicate if the amine has undergone a change. In order to decide doubtful cases, the solid should be separated and its melting point compared with that of the original compound. A positive halogen test with alcoholic silver nitrate would indicate formation of a hydrochloride.



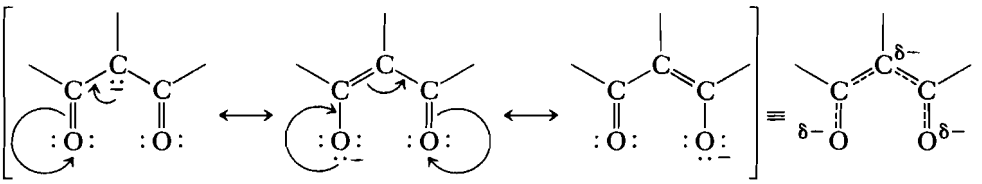
1-aminonaphthalene (α-naphthylamine) — 1-aminonaphthalene hydrochloride

Another useful technique is to dissolve the suspected base in ether and treat that with 5% hydrochloric acid solution with shaking. Formation of a solid at the interface of the two layers indicates the presence of a basic amine.

5.1.6 Solubility in 5% Sodium Hydroxide and 5% Sodium Bicarbonate Solutions

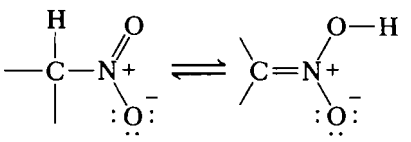
A list of the various types of organic acids is given in Table 5.5. The reasoning behind most of these classifications can be understood in terms of the stability due to structural features of the conjugate base anion.

Aldehydes and ketones are sufficiently acidic to react with aqueous alkali to yield anions which serve as reaction intermediates in such reactions as the aldol condensation. They are far too weakly acidic, however, to dissolve to any measurable extent in 5% sodium hydroxide solution. When two carbonyl groups are attached to the same carbon atom, as they are in acetoacetic esters, malonic esters, and 1,3-diketones, the acidity increases sharply because of the added stabilization of the anion, since the negative charge is distributed over the two oxygen atoms as well as the central carbon atom.



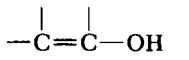
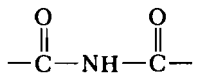
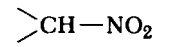
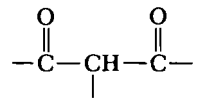
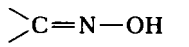
Although 1,3-dicarbonyl compounds are approximately as acidic as the phenols, the rate of proton removal from carbon may be relatively slow; as a result, the rate of solution of such compounds may be so slow that they appear to be, at first, insoluble in 5% base.

Nitro compounds have a tautomeric form, the *aci* form, which is approximately as acidic as the carboxylic acids. The *aci* form of nitroethane has a K_a of 3.6×10^{-5}.



aci form

TABLE 5.5 Solubility Classes of Various Organic Acids

Name	General Structure	Solubility Class[a]
Carboxylic acids	RCO_2H	A_1
Sulfonic acids	RSO_3H	A_1
Sulfinic acids	RSO_2H	A_1
Enols		A_2
Imides		A_2
Nitro[b]		A_2
Arenesulfonamides[c]	$ArSO_2NHR$	A_2
β-Dicarbonyl compounds[d] (1,3-diketones)		A_2[d]
Oximes		A_2

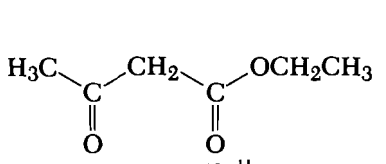
[a]Borderline cases are named in Table 5.6.

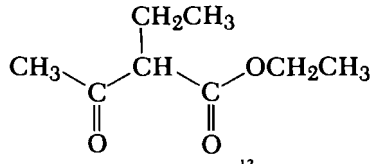
[b]Primary (RCH_2NO_2) and secondary (R_2CHNO_2) nitroalkanes only.

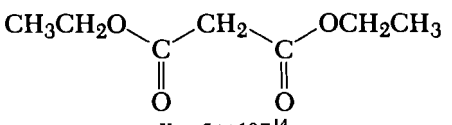
[c]The acidity of the N—H proton is utilized in the Hinsberg test (Experiment 19). This category also includes sulfonamides of ammonia and other sulfonamides of primary amines.

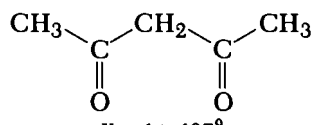
[d]Highly electronegative groups, e.g., trifluoromethyl, on the carbonyl group can move these compounds into class A_1.

The presence of one nitro group confers sufficient acidity on a substance to make the compound soluble in 5% sodium hydroxide solution. For example, nitroethane has a K_a of about 3.5×10^{-9}. This value should be compared to the K_a values for the following 1,3-dicarbonyl compounds:

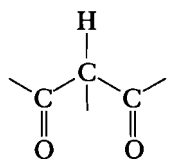




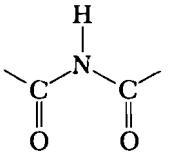




Just as the grouping



is acidic, so is the imide grouping,



Imides are soluble in 5% sodium hydroxide solution but not in 5% sodium bicarbonate solution. A 4-nitrophenyl group makes the —CONH— function weakly acidic in aqueous solution. Thus 4-nitroacetanilide[8] dissolves in 5% sodium hydroxide solution but not in 5% sodium bicarbonate solution. Sulfonamides show the same solubility trends in base as 4-nitroacetanilide. Oximes, which have a hydroxyl group attached to a nitrogen atom, display similar solubility behavior.

Esters with five or six carbon atoms that are almost completely soluble in water may be hydrolyzed by continued shaking with 5% sodium hydroxide solution.[9] The alkali should not be heated and the solubility or insolubility should be recorded after 1–2 min.

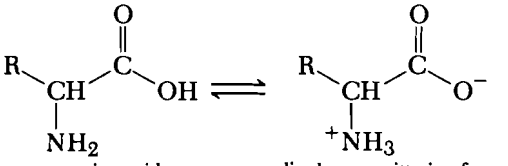
Monoesters of dicarboxylic acids are soluble in 5% sodium bicarbonate solution. These esters are rapidly hydrolyzed, even with weak aqueous bases such as 5% sodium bicarbonate solution.

Fatty acids containing 12 or more carbon atoms react with the alkali slowly, forming salts which are commonly referred to as soaps. The mixture is not homogeneous but, instead, consists of an opalescent colloidal dispersion which foams when shaken. Once this behavior has been observed, it is easily recognized.

Certain of the sodium salts of highly substituted phenols are insoluble in 5% sodium hydroxide solution. Certain phenols which are very insoluble in water may precipitate due to hydrolysis and, hence, appear to be insoluble in alkali.

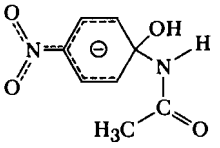
5.1.7 Solubility of Amphoteric Compounds

Compounds containing both an acidic and a basic group are referred to as amphoteric. Low molecular weight amino acids exist largely as dipolar salts. They are soluble in water and may yield solutions which produce a neutral litmus in aqueous solutions (class S_2).



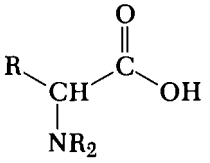
an amino acid — dipolar or zwitterion form

[8]Compounds of this type may also form adducts (Meisenheimer complexes) by bonding hydroxide to the carbon bearing the amide group:

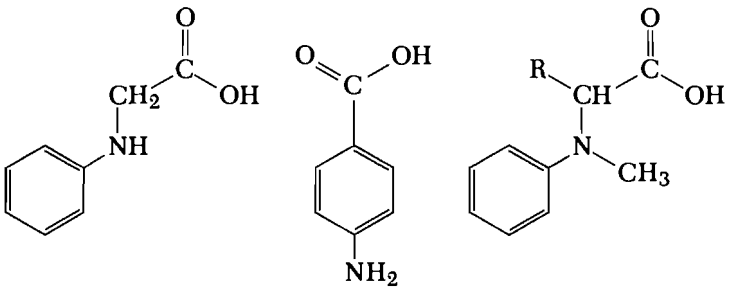


[9]Use of lithium hydroxide in place of sodium hydroxide will often yield water soluble salts.

The water insoluble amphoteric compounds act both as bases and as strong or weak acids, depending on the relative basicity of the amino group, since its basicity determines the extent to which the acidic group will be neutralized by salt formation. If the α-amino group contains only aliphatic substituents with no hydrogens directly attached to the nitrogen, the compounds will dissolve in 5% hydrochloric acid and 5% sodium hydroxide solutions, but not in 5% sodium bicarbonate solution (class A_2 or B):



The presence of an aryl group on the nitrogen atom, however, diminishes its basicity, so that such compounds are soluble even in 5% sodium bicarbonate solution. This is illustrated by the following compounds (class A_1 and B):



If two aryl groups are attached to the nitrogen atom, the compound is not basic. Its solubility classification is that of a strong acid (class A_1):

$$(C_6H_5)_2NCH_2COOH$$

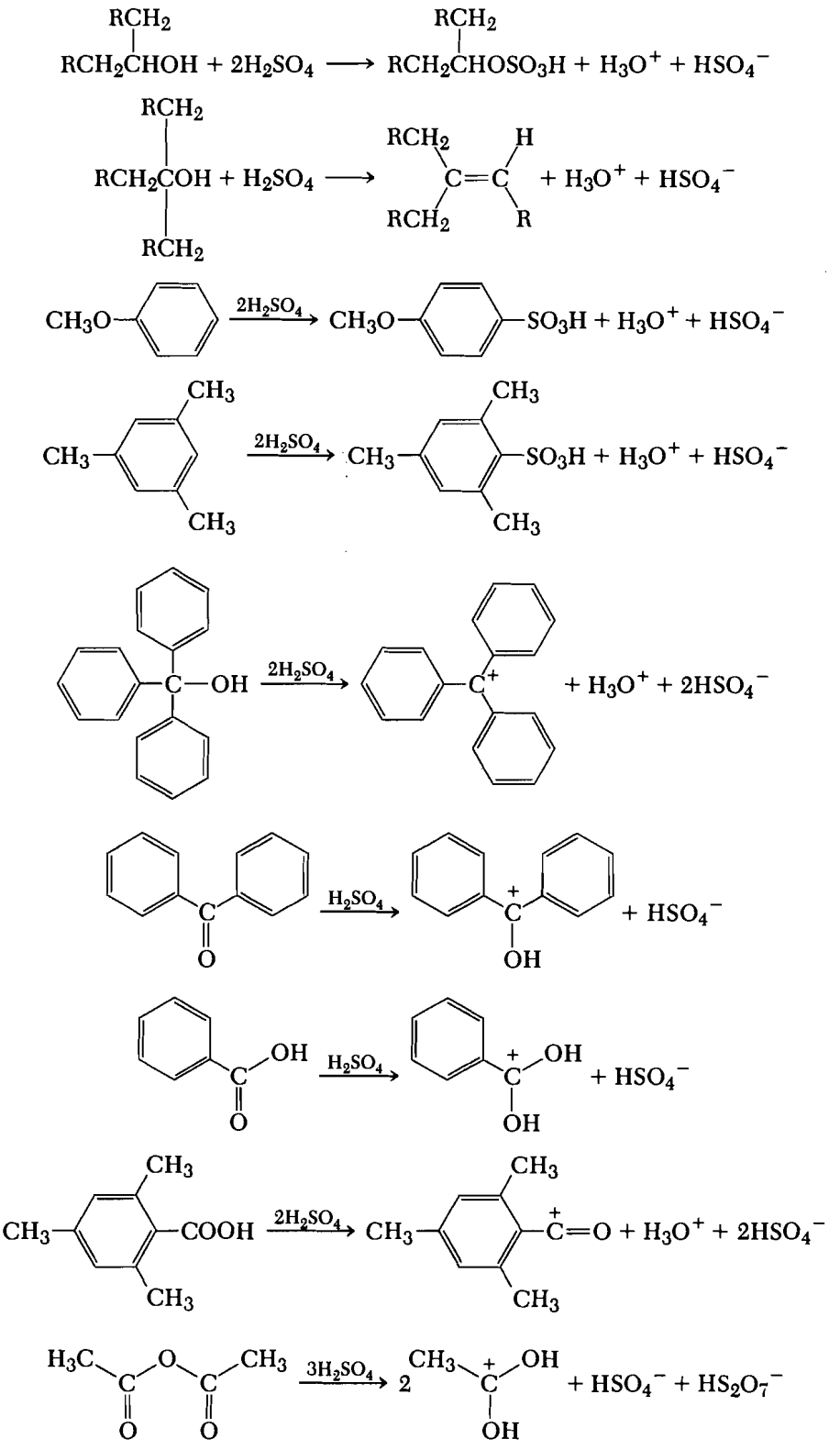
5.1.8 Solubility in Cold, Concentrated Sulfuric Acid

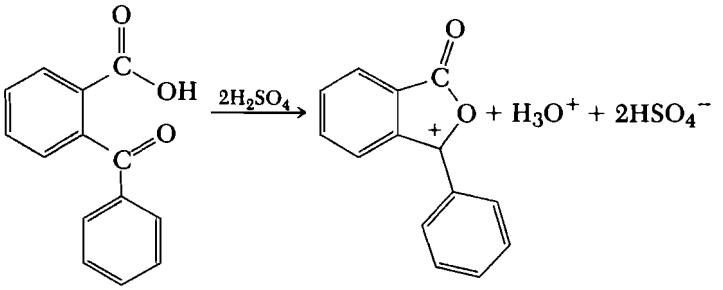
Cold, concentrated sulfuric acid is used with neutral, water insoluble compounds containing no elements other than carbon, hydrogen, and oxygen. If the compound is unsaturated, is readily sulfonated, or possesses a functional group containing oxygen, it will dissolve in cold, concentrated sulfuric acid. This is frequently accompanied by a reaction such as sulfonation, polymerization, dehydration, or addition of the sulfuric acid to olefinic or acetylenic linkages. In many cases, however, the solute may be recovered by dilution with ice water. The following examples illustrate some of the more common reactions:

$$RCH{=}CHR + H_2SO_4 \longrightarrow [RCH_2{-}\overset{+}{C}HR] \xrightarrow{HSO_4^-} RCH_2\underset{\displaystyle OSO_3H}{\underset{|}{C}}HR$$

$$RCH_2OH + 2H_2SO_4 \longrightarrow RCH_2OSO_3H + H_3O^+ + HSO_4^-$$

The water arising from sulfate ester formation is converted to the hydronium ion by concentrated sulfuric acid.





Alkanes, cycloalkanes, and their halogen derivatives are insoluble in sulfuric acid. Simple aromatic hydrocarbons and their halogen derivatives do not undergo sulfonation under these conditions and are also insoluble in sulfuric acid. However, the presence of two or more alkyl groups[10] on the aromatic ring permits the compound to be sulfonated quite easily. Therefore, polyalkylbenzenes such as 1,2,3,5-tetramethylbenzene (isodurene) and 1,3,5-trimethylbenzene (mesitylene) dissolve rather readily in sulfuric acid. Occasionally the solute may react in such a manner as to yield an insoluble product. A few high molecular weight ethers, such as phenyl ether, undergo sulfonation so slowly at room temperature that they may not dissolve.

Many secondary and tertiary alcohols are dehydrated readily by concentrated sulfuric acid to give olefins which subsequently undergo polymerization. The resulting polymers are insoluble in cold, concentrated sulfuric acid and will form a distinct layer on top of the acid. Benzyl alcohol and other similar alcohols react with concentrated sulfuric acid, resulting in a colored precipitate.

In summary, a student should not conclude that formation of a black tarry substance means that a compound is insoluble in sulfuric acid. The original compound must have dissolved to induce a reaction, and the precipitate arises from formation of a new compound.

5.1.9 Borderlines Between Solubility Classes

In Table 5.6 are listed a number of compounds selected in such a way as to show the position of the most important of the various borderlines between solubility classes with respect to the number of carbons present in the compound. These compounds have been grouped, so far as is possible, according to their chemical nature. Within each group an attempt has been made to include the borderline members together with one or more members on either side of their respective borderlines. Thus, the table shows 1-butanol to be in class S_1; it follows that the other butanols and all lower homologs are also in this class. Similarly, since 3-methyl-1-butanol is in class N, it follows that 1-pentanol and all higher alcohols are in this class as well.

Although it is often possible to predict the solubility class of a particular compound solely by reference to its structural formula, there are many cases where this would result in an incorrect prediction. Sometimes, it is difficult to classify a compound by solubility, since many compounds, as shown in Table 5.6, occupy borderline positions.

[10]Other activating groups often facilitate sulfonation.

TABLE 5.6 Borderlines Between Solubility Classes

Compound	Solubility Class(es)
Alcohols	
1-Butanol (butyl alcohol)	S_1
2-Methyl-2-propanol (*t*-butyl alcohol)	S_1
3-Methyl-2-butanol	S_1–N
3-Methyl-1-butanol (isopentyl alcohol)	S_1–N
Benzyl alcohol	N
Cyclopentanol (cyclopentyl alcohol)	N
Aldehydes	
2-Methylpropanal (isobutyraldehyde)	S_1
Butanal (butyraldehyde)	S_1–N
3-Methylbutanal (isovaleraldehyde)	N
Amides	
Methanamide (formamide)	S_1–S_2
Ethanamide (acetamide)	S_1–S_2
Propanamide (propionamide)	S_1–S_2
2-Methylpropanamide (isobutyramide)	S_1–S_2
Butanamide (butyramide)	S_1–MN
Methananilide (formanilide)	S_1–MN
Ethananilide (acetanilide)	MN
Amines	
Diethylamine	S_B
3-Methylbutylamine (isopentylamine)	S_B
Pentylamine	S_B
Benzylamine	S_B
Piperidine	S_B
Cyclohexylamine	S_B
Dipropylamine	S_B–B
Dibutylamine	B
Aniline	B
Tripropylamine	B
Carboxylic acids	
Chloroethanoic acid (chloroacetic acid)	S_A
Butanoic acid (butyric acid)	S_A
2-Chloropropanoic acid (α-chloropropionic acid)	S_A
trans-2-Butenoic acid (crotonic acid)	S_A
3-Methylbutanoic acid (isovaleric acid)	S_A–A_1
Pentanoic acid (valeric acid)	A_1
Esters	
Ethyl ethanoate (ethyl acetate)	S_1–N
Methyl propanoate (methyl propionate)	S_1
Propyl methanoate (propyl formate)	S_1
2-Methylethyl ethanoate (isopropyl acetate)	S_1
Propyl ethanoate (propyl acetate)	S_1–N
Methyl 2-methylpropanoate (methyl isobutyrate)	S_1–N
Butyl methanoate (butyl formate)	S_1–N
Methyl 3-methylbutanoate (methyl isovalerate)	N
1-Methylpropyl ethanoate (*sec*-butyl acetate)	N
Butyl ethanoate (butyl acetate)	N
Benzyl ethanoate (benzyl acetate)	N
Ethyl octanoate (ethyl caprylate)	N
Ethyl benzoate	N

(Continued)

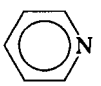
TABLE 5.6 *(Continued)*

Dimethyl carbonate	S_1–N
Diethyl ethanedioate (ethyl oxalate)	S_1–N
Dimethyl propanedioate (methyl malonate)	S_1–N
Diethyl carbonate	S_1–N
Diethyl butanedioate (ethyl succinate)	N
Diethyl 1,2-benzenedicarboxylate (ethyl phthalate)	N
Diethyl propanedioate (ethyl malonate)	N
Dibutyl carbonate	N
Dibutyl ethanedioate (butyl oxalate)	N
Ethers	
Ethyl methyl ether	S_1
Diethyl ether	S_1–N
Ethyl 1-methylethyl ether (ethyl isopropyl ether)	S_1–N
Di-1-methylethyl ether (isopropyl ether)	N
Dibutyl ether	N
Hydrocarbons (aromatic)	
1,3,5-Trimethylbenzene (mesitylene)	N
1,2,3,5-Tetramethylbenzene (isodurene)	N
(1-Methylethyl) toluene (cymene)	I
1,4-Dimethylbenzene (*p*-xylene)	N–I
Diphenylmethane	N–I
1,3-Dimethylbenzene (*m*-xylene)	N–I
1,2-Dimethylbenzene (*o*-xylene)	N–I
Naphthalene	I
Ketones	
Butanone (ethyl methyl ketone)	S_1
3-Methyl-2-butanone (isopropyl methyl ketone)	S_1
2-Pentanone (methyl propyl ketone)	S_1–N
3,3-Dimethyl-2-butanone (pinacolone)	S_1–N
3-Pentanone (diethyl ketone)	S_1–N
Cyclopentanone	S_1
Cyclohexanone	S_1–N
Acetophenone	N
5-Nonanone (dibutyl ketone)	N
Benzil	N
Benzophenone	N
Nitriles	
Propanenitrile (propionitrile)	S_1
2-Methylpropanenitrile (isobutyronitrile)	S_1–MN
Butanedinitrile (succinonitrile)	S_1–S_2–MN
Pentanedinitrile (glutaronitrile)	S_2–MN
Butanenitrile (butyronitrile)	MN
Nitro compounds	
Nitromethane	S_1A_2
Nitroethane	A_2
Nitrobenzene	MN
Phenols	
Hydroquinone	S_A
Chlorohydroquinone	S_A–A_2
1,3,5-Trihydroxybenzene (phloroglucinol)	S_2–A_2
Phenol	S_A–A_2

5.2 SOLUBILITY IN ORGANIC SOLVENTS

The solubility of organic compounds in organic solvents should be determined in order to plan a variety of laboratory operations. A range of solvents, useful to the organic chemist, is tabulated in Table 5.7. These solvents are useful for running organic reactions, for dissolving substrates for spectral analyses (Chapters 6, 7, and 8), and for standard laboratory maintenance such as cleaning glassware. Virtually all of the solvents listed, as well as mixtures of these and other solvents, are useful for column chromatography (Chapter 4, pp. 99–109) and thin-layer chromatography (Chapter 4,

TABLE 5.7 Common Organic Solvents[a]

Name	Structure	Common Use (Code)[b]	Dielectric Constant (25°C)
Acetone[a]	$CH_3-\overset{\overset{O}{\|}}{C}-CH_3$	C, R, NMR[d]	21
Acetonitrile	CH_3CN	R, UV, NMR[d]	36
Benzene[e]	C_6H_6	R, NMR[d]	4.2
Carbon disulfide	CS_2	R, IR, NMR	2.6
Carbon tetrachloride[c]	CCl_4	R, IR, UV, NMR	2.2
Chloroform[c]	$CHCl_3$	All five[d]	4.7
N,N-Dimethylformamide	$H-\overset{\overset{O}{\|}}{C}-N(CH_3)_2$	R, NMR[d], R	37
Dimethyl sulfoxide (DMSO)	$CH_3-\overset{\overset{O}{\|}}{S}-CH_3$	NMR[d], R	49
Ethanol[c]	CH_3CH_2OH	R, UV, C, NMR[d]	24
(Ethyl) ether[c]	$(CH_3CH_2)_2O$	R, C	4
Hexane	$CH_3(CH_2)_4CH_3$	UV, C, R	2.0
Methanol	CH_3OH	R, UV, NMR[d], C	33
Methylene chloride	CH_2Cl_2	R, C, IR, NMR[d]	9
Pyridine		R, NMR[d]	12
Tetrahydrofuran		R, NMR[d]	7.3
(Water)	(H_2O)	(All five)[d]	(78.5)

[a]The IR and NMR (proton) spectra of many of these compounds may be found in the Sadtler collection and in R. M. Silverstein and Francis X. Webster, *Spectrometric Identification of Organic Compounds*, 6th ed. (Wiley, New York, 1998).

[b]C = glassware cleaning; R = reaction medium; solvents to dissolve samples for spectral analysis are denoted IR, NMR, or UV.

[c]Preliminary solubility analysis should employ these solvents.

[d]Deuterated solvents, e.g., acetone-d_6 = CD_3COCD_3, are available for determination of proton magnetic resonance spectra.

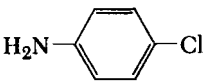
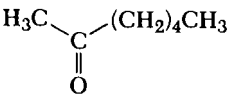
[e]Toluene can be substituted to reduce toxicity problems.

pp. 86–90), for recrystallizations (Chapter 3, pp. 49–52), and for extractions during the workup of reaction products. The sample can be readily recovered by evaporation from virtually all of these solvents except *N*,*N*-dimethylformamide (DMF) and dimethyl sulfoxide (DMSO). Since all of the solvents listed in Table 5.7 are used for a variety of purposes, they are often encountered as impurities in samples of interest.

Procedure

Carry out solubility tests in organic solvents using the simple procedure described for water solubilities on page 114. Use 10 mg or 10 μL of compound per 0.5 mL of solvent for an NMR sample and 50 mg or 15 μL of compound per 1 mL of solvent for an IR sample. For FTIR, the lower concentration levels can be used.

Example

Structure and Name	***Expected Solubility Behavior and Class***
 4-chloroaniline	Insoluble in water because it has six carbon atoms and a chlorine atom. It is basic, only one aryl group being attached to the amino group, and hence is insoluble in 5% sodium hydroxide solution but soluble in 5% hydrochloric acid solution, thus in solubility class B.
 2-heptanone	Insoluble in water because it has more than five carbon atoms. Since it is a neutral compound, containing only carbon, hydrogen, and oxygen, it is soluble in cold, concentrated sulfuric acid, thus in solubility class N.

Problems

2. Tabulate the structure, name, and solubility behavior of the following compounds.
   a. 1-chlorobutane
   b. 4-methylaniline
   c. 1-nitroethane
   d. alanine
   e. benzophenone
   f. benzoic acid
   g. hexane
   h. 4-methylbenzyl alcohol
   i. ethylmethylamine
   j. propoxybenzene
   k. propanal
   l. 1,3-dibromobenzene
   m. propanoic acid
   n. benzenesulfonamide
   o. 1-butanol
   p. methyl propanoate
   q. 4-methylcyclohexanone
   r. 4-aminobiphenyl
   s. 4-methylacetophenone
   t. naphthalene
   u. phenylalanine
   v. benzoin
   w. 4-hydroxybenzenesulfonic acid
3. Arrange the following compounds in the approximate order of their basicity toward 5% hydrochloric acid solution.
   a. benzanilide
   b. pentylamine
   c. diphenylamine
   d. benzylamine
   e. 4-methylaniline
   f. butanamide
4. List the solubility class(es) for each compound in problem 3.
5. Arrange each group of compounds in the order of increasing solubility in water.
   a. methanol, isopropyl alcohol, ethanol, 1-butanol
   b. butane, 1,4-butanediol, 1-butanol

c. 1-butanol, 2-methyl-2-propanol, 2-butanol
d. ammonium butanoate, 3-pentanone, benzaldehyde, trimethylamine

6. List the solubility class(es) for each compound in problem 5.

7. Arrange the following compounds in the approximate order of decreasing reactivity.

a. *meso*-tartaric acid
b. 2-naphthol
c. benzohydroxamic acid
d. 4-toluenesulfonic acid
e. 4-toluenesulfonamide
f. 2-bromo-6-nitrophenol
g. octadecanamide
h. saccharin
i. benzyl phenyl ketone (deoxybenzoin)
j. 1-naphthoic acid

CHAPTER 6

Nuclear Magnetic Resonance Spectrometry

This is the first of three chapters that discuss the usefulness of spectroscopy. Organic compounds can be quickly characterized through spectrometric methods. The amount of compound that is needed is so small that synthetic chemists can rapidly prepare sufficient compound for complete structure determination. Nowadays, depending upon the instrument, milligram or microgram amounts are all that are needed for characterization of a compound. The advent of Fourier transform methods in the area of IR and NMR spectrometry, as well as computer manipulation of data, has decreased the amount of time needed to obtain well-resolved spectra.

Even with recent technique advances, the fundamental role of each instrument remains the same:

Nuclear magnetic resonance (NMR) spectrometry (this chapter). Method for structure determination by analysis of the relative positions of carbons and hydrogens

Infrared (IR) spectrometry (Chapter 7). Method for functional group analysis

Mass spectrometry (Chapter 8). Source of molecular weight and molecular formula

6.1 THEORY OF NUCLEAR MAGNETIC RESONANCE

From the 1950s to the present, nuclear magnetic resonance has gone from a method used for structure determination at a minimal level to applications in medicine such as magnetic resonance imaging. With higher magnetic fields and computer technology, more detailed information about a compound can be quickly obtained.

In the presence of a magnetic field, $\mathbf{B}_0$, certain nuclei are distributed between two states of different energies. The Pauli exclusion principle allows two electrons in the same orbital or energy level only if they have opposite spins, $+\frac{1}{2}$ and $-\frac{1}{2}$.

Similarly, nuclei can have spins and certain nuclei have two spin states, $+\frac{1}{2}$ and $-\frac{1}{2}$. Nuclei with either an odd number of neutrons or an odd number of protons have a nuclear spin that gives rise to an NMR signal. Examples of nuclei that give rise to NMR signals are ^{1}H, ^{2}H, ^{11}B, ^{13}C, ^{14}N, ^{15}N, ^{17}O, ^{19}F, ^{31}P, ^{35}Cl, and ^{37}Cl. Nuclei that have an even number of both protons and neutrons cannot produce an NMR signal. Examples of nuclei that do not yield NMR signals are ^{12}C, ^{16}O, and ^{32}S.

A rotating nuclei is similar to a bar magnet (Figure 6.1). In the absence of a magnetic field, the fields of the individual nuclei are randomly oriented (Figure 6.2*a*). When a

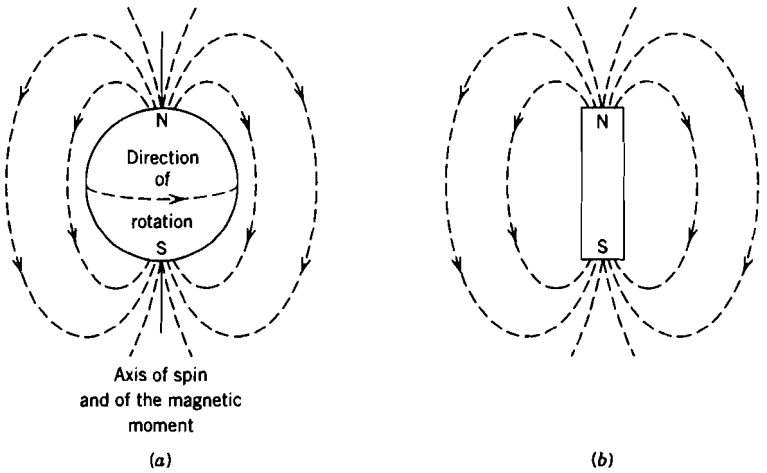


Figure 6.1 (*a*) The magnetic field associated with a spinning proton. (*b*) The spinning proton resembles a tiny magnet.

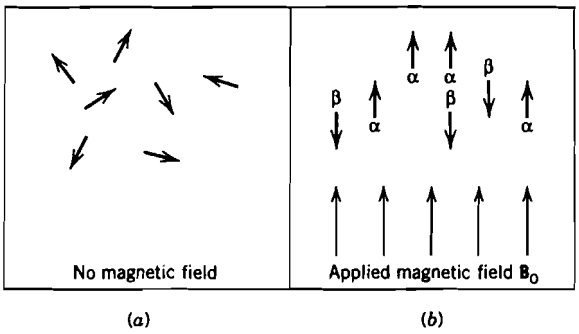
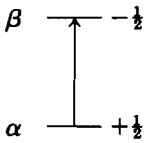


Figure 6.2 (*a*) In the absence of a magnetic field, the magnetic moments of protons (represented by arrows) are randomly oriented. (*b*) When an external magnetic field ($\mathbf{B}_0$) is applied, the protons orient themselves. Some are aligned with the applied field (α spin state) and some against it (β spin state).

magnetic field ($\mathbf{B}_0$) is applied (Figure 6.2*b*), the nuclei are oriented aligned with the field (α, lower energy) or against the field (β, higher energy). At room temperature in the presence of the applied magnetic field ($\mathbf{B}_0$), there is a very slight excess, on the order of parts per million, of the nuclei in the lower energy state (α) compared to the nuclei in the higher energy state (β). This distribution between the states, known as a Boltzmann distribution, is a type of equilibrium.

When the nuclei are distributed between two energy states, the energy required to excite the nuclei from the lower α energy to the higher β energy can be measured.



It is the energy of this transition, ΔE, that is characteristic of a given nucleus. In the equation

$$\Delta E = h\nu$$

ΔE is proportional to ν, the radio frequency radiation, since h is Planck's constant.

The radio frequency (ν) can be introduced by either a continuous-wave (CW) method of energy or a pulse of radiation. The CW method was used in the early NMR spectrometers. The Fourier transform (FT) method is used in all modern NMR spectrometers.

In the CW spectrometers, there are two ways of obtaining a signal. In one method, the magnetic field is held constant while the radio frequency changes. In the second method, the radio frequency is held constant while the magnetic field changes.

Very few CW spectrometers are still in use. These have been replaced by the FT NMR spectrometers. In FT, an intense, broad pulse of radiation activates all of the nuclei in a molecule to the higher β state. These activated nuclei are then allowed to decay back to the ground α state. This decay signal (called a free induction decay or time domain signal) is mathematically converted to a frequency domain spectrum. This data are stored in a computer. Faster spectral accumulation is possible. Repetitive storage of large numbers of signals allows signal reinforcement, which produces a more intense spectrum with a higher signal-to-noise ratio. The signal-to-noise ratio increases by the square root of the number of acquisitions (for example, 64 acquisitions would give rise to an eight-fold increase in signal-to-noise). Very small samples of 1–5 mg can be analyzed.

The energy difference between the spin states depends on the strength of the applied magnetic field. With a weaker applied field, the energy required for the transition is less. With a stronger applied field, the energy is much greater (Figure 6.3).

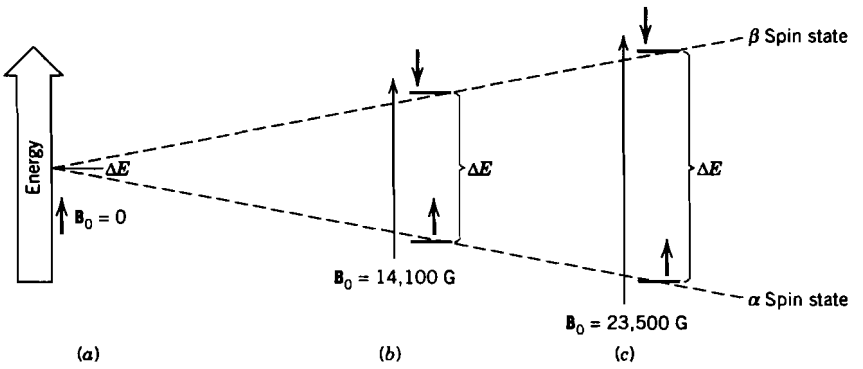


Figure 6.3 The energy difference between the two spin states of a proton depends on the strength of the applied external field, $\mathbf{B}_0$. (*a*) If there is no applied field ($\mathbf{B}_0 = 0$), there is no energy difference between the two states. (*b*) In a magnetic field of approximately 14,100 G, the energy difference corresponds to that of electromagnetic radiation of 60×10^6 Hz (60 MHz). (*c*) With a magnetic field of approximately 23,500 G, the energy difference corresponds to the electromagnetic radiation of 100×10^6 Hz (100 MHz).

6.1.1 Chemical Shift

The signal positions are known as chemical shifts. Chemical shift is defined as the difference, in ppm, between the frequency of the proton being observed compared to the frequency of tetramethylsilane (TMS). Tetramethylsilane, $(CH_3)_4Si$, is used as the internal standard and has a chemical shift of $\delta = 0.0$. Chemical shifts (δ) are calculated by measuring the frequency (ν = cycles per second, or hertz = Hz) of interest relative

to the frequency of the internal standard, ν_{TMS}, divided by the frequency of the instrument (ν_0, in megahertz, MHz = 10^6 Hz).

$$\delta = [(\nu - \nu_{TMS}) \times 10^6]/\nu_0$$

If a signal occurs at 60 Hz on a 60-MHz instrument, the chemical shift is

$$\delta = [(60 \text{ Hz} - 0) \times 10^6]/60 \text{ MHz} = 1.00$$

If this signal is a singlet or a well-defined multiplet, it will occur exactly at δ 1.00 on instruments of field strengths of 100, 300, 500, or 600 MHz. This is because the chemical shift measured in δ has been adjusted for the instrument strength. For example, this signal would be at δ 1.00 on an instrument of field strength 300 MHz, and the shift in frequency units would be 300 Hz.

6.1.2 Shielding and Deshielding

Protons in different chemical environments are shielded by different amounts. A proton is deshielded when the induced field reinforces the applied field. For example, the induced field from the protons in benzene reinforces the applied field (Figure 6.4*a*). As a result, these protons are deshielded and their chemical shifts are at a higher value of δ.

A proton is shielded when the induced field opposes the applied field. For example, the induced field from the protons in acetylene opposes the applied field (Figure 6.4*b*). These protons are shielded and their chemical shifts are at a lower value of δ.

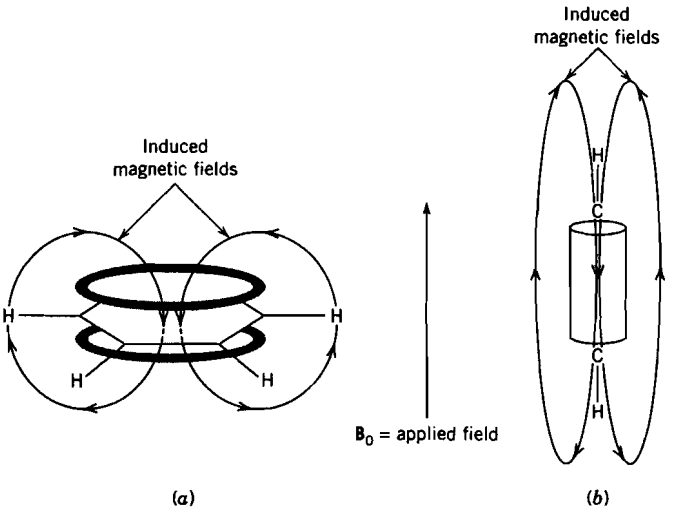


Figure 6.4 In benzene (*a*), the induced field reinforces the applied field and the protons are deshielded. In acetylene (*b*), the induced field opposes the applied field and the protons are shielded.

6.2 PREPARATION OF THE SAMPLE

The sample must be in fairly pure form before the NMR spectra are obtained. The sample needs to be dissolved in a minimal amount of a deuterated solvent (Tables 6.1 and 6.2). The solution must be homogeneous. Paramagnetic substances must be

TABLE 6.1 ^{1}H Chemical Shifts of Common NMR Solvents

Solvent	Group	δ	Multiplicity[1]
Acetic acid-d_4	Methyl	2.03	5
	Hydroxyl	11.53	1
Acetone-d_6	Methyl	2.05	5
Acetonitrile-d_3	Methyl	1.94	5
Benzene-d_6	Methine	7.16	1
Chloroform-d	Methine	7.27	1
Cyclohexane-d_{12}	Methylene	1.38	1
1,2-Dichloroethane-d_4	Methylene	3.69	1
Diethyl ether-d_{10}	Methyl	1.07	m
	Methylene	3.34	m
Dimethylformamide-d_7	Methyl	2.75	5
	Methyl	2.92	5
	Amide	8.03	1
Dimethylsulfoxide-d_6	Methyl	2.5	5
1,4-Dioxane-d_8	Methylene	3.53	m
Ethanol-d_6	Methyl	1.11	m
	Methylene	3.56	1
	Hydroxyl	5.26	1
Methanol-d_4	Methyl	3.31	5
	Hydroxyl	4.84	1
Methylene chloride-d_2	Methylene	5.32	3
Nitrobenzene-d_5	Methylene (H-3, H-5)	7.5	b
	Methylene (H-4)	7.67	b
	Methylene (H-2, H-6)	8.1	b
Nitromethane-d_3	Methyl	4.33	5
Pyridine-d_5	Methylene (H-3, H-5)	7.20	1
	Methylene (H-4)	7.58	1
	Methylene (H-2, H-6)	8.74	1
Tetrahydrofuran-d_8	Methylene (H-3, H-4)	1.73	1
	Methylene (H-2, H-5)	3.58	1
Toluene-d_8	Methyl	2.09	5
	Methine (H-2, H-6)	6.98	m
	Methine (H-4)	7.00	1
	Methine (H-3, H-5)	7.09	m
Trifluoroacetic acid-d_1	Hydroxyl	11.5	1
2,2,2-Trifluoroethanol-d_3	Methylene	3.88	(4 × 3)
	Hydroxyl	5.02	1
Water-d_2	Hydroxyl	4.8	1

[1]b = broad, m = multiplet.

excluded to prevent line broadening. If needed, the sample may be filtered through glass wool in a Pasteur pipet. The NMR tubes (Figure 6.5) must be completely dry. This is done by heating the NMR tubes in an oven overnight. Place a specified amount of solution in the NMR tube, according to your instructor's guidelines.

Tetramethylsilane (TMS), $(CH_3)_4Si$, is used an internal standard for obtaining NMR spectra. The NMR spectrometer is calibrated to TMS, which has a chemical shift of

TABLE 6.2 ^{13}C Chemical Shifts of Common NMR Solvents

Solvent	Group	δ	Multiplicity	J_{C-D}
Acetic acid-d_4	Methyl	20.1	7	20.0
	Carbonyl	178.4	1	
Acetone-d_6	Methyl	29.9	7	20.0
	Carbonyl	206.0	13	0.9
Acetonitrile-d_3	Methyl	1.3	7	21.0
	Nitrile	118.2	1	
Benzene-d_6	Methine	128.3	3	24.2
Carbon disulfide		192.8		
Carbon tetrachloride		96.7		
Chloroform-d	Methine	77.0	3	32.0
Cyclohexane-d_{12}	Methylene	26.4	5	19.0
Dimethylformamide-d_7	Methyl	30.1	7	21.0
	Methyl	35.2	7	21.0
	Amide	162.7	3	29.4
Dimethylsulfoxide-d_6	Methyl	39.5	7	21.0
1,4-Dioxane-d_8	Methylene	66.7	5	21.9
Ethanol-d_6	Methyl	17.3	7	19.1
	Methylene	56.8	5	22.0
Methanol-d_4	Methyl	49.1	7	21.4
Methylene chloride-d_2	Methylene	54.0	5	27.2
Nitrobenzene-d_5	Methine (C-2, C-6)	123.2	3	26
	Methine (C-3, C-5)	129.7	3	25
	Methine (C-4)	134.9	3	24.5
	Substituted C-1	148.6	1	
Nitromethane-d_3	Methyl	60.5	7	22.0
Pyridine-d_5	Methine (C-3, C-5)	123.8	3	25.0
	Methine (C-4)	135.7	3	24.5
	Methine (C-2, C-6)	150.4	3	27.5
Tetrahydrofuran-d_8	Methylene(C-3, C-4)	25.4	5	20.5
	Methylene(C-2, C-5)	67.5	5	22.1
Toluene-d_8	Methyl	20.4	7	19.0
	Methine (C-4)	125.2	3	24.0
	Methine (C-3, C-5)	128.2	3	24.0
	Methine (C-2, C-6)	129.1	3	23
	Methine (C-1)	137.6	1	
Trifluoroacetic acid-d_1	Trifluoromethyl	116.6	4	28.3
	Carbonyl	164.2	4	44
2,2,2-Trifluoroethanol-d_3	Methylene	61.5	(4 × 5)	22
		126.4	4	

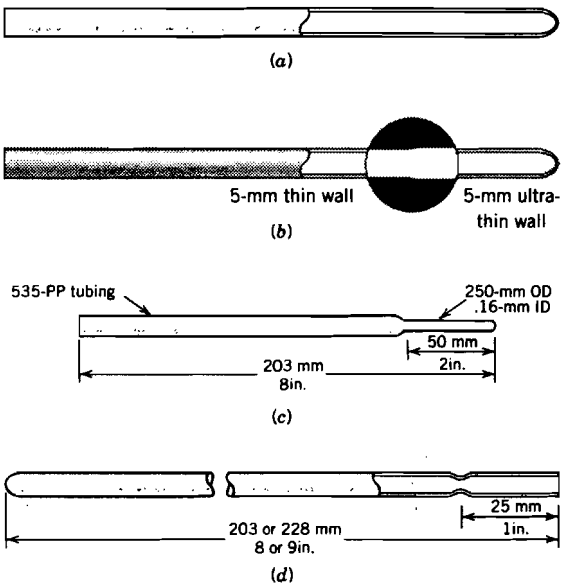


Figure 6.5 Different types of NMR tubes. (*a*) Ultra-thin NMR tube. (*b*) Step-down ultra-thin NMR tube. (*c*) Bruker microprobe. (*d*) Constricted NMR tube. [Courtesy of WILMAD-LABGLASS. Design/art direction by Mark Gray. Used with permission.]

δ = 0.00. TMS is usually added to the bottle of deuterated solvent. Check with your instructor.

6.3 PROTON SPECTRA

Four important types of information are needed for the interpretation of proton NMR spectra:

1. The number of different signals indicates how many different types of protons are present.
2. The chemical shift of each signal indicates the electronic environment.
3. The intensity, or integration, of each signal indicates the number of protons for each signal.
4. The splitting of each signal indicates the number of adjacent protons.

Chemical shift, integration, and splitting will be discussed in detail in the following sections. All NMR spectra, unless otherwise stated, were obtained on an EFT-60 NMR spectrometer with a Varian 60-MHz permanent magnet.[1]

6.3.1 Chemical Shift

Shielding and deshielding effects will change the chemical shift of a proton. As illustrated in Table 6.3, the aromatic protons are deshielded and are seen at a higher chemical

[1]The upgrade of the Varian EM-360 NMR spectrometer to an EFT-60 NMR spectrometer with a Varian 60-MHz permanent magnet was supported by Radford University, Radford, Virginia, and the National Science Foundation under Grant No. 0088222.

TABLE 6.3 Proton Magnetic Resonance Frequencies

Type of Proton		Chemical Shift (δ, ppm)
1° Alkyl	$RC\underline{H}_3$	0.8–1.0
2° Alkyl	$R_2C\underline{H}_2$	1.2–1.4
3° Alkyl	$R_3C\underline{H}$	1.4–1.7
Allylic	$R_2C{=}CC\underline{H}_3$ (R)	1.6–1.9
Benzylic	$ArC\underline{H}_3$	2.2–2.5
Alkyl chloride	$RC\underline{H}_2Cl$	3.6–3.8
Alkyl bromide	$RC\underline{H}_2Br$	3.4–3.6
Alkyl iodide	$RC\underline{H}_2I$	3.1–3.3
Alkyl fluoride	$RC\underline{H}_2F$	4.0–4.5
Ether	$ROC\underline{H}_2R$	3.3–3.9
Ester	$RCOOC\underline{H}_2R$	3.3–3.9
Alcohol	$HOC\underline{H}_2R$	3.3–4.0
Ketone	$RCC\underline{H}_3$ (O)	2.1–2.6
Ester	$RC\underline{H}_2COOR$	2.1–2.6
Aldehyde	$RC\underline{H}$ (O)	9.0–10.0
Vinylic	$R_2C{=}C\underline{H}_2$	4.6–5.0
Vinylic	$R_2C{=}C\underline{H}$ (R)	5.2–5.7
Aromatic	$Ar\underline{H}$	6.0–9.5
Acetylenic	$RC{\equiv}C\underline{H}$	2.5–3.1
Alcohol hydroxyl	$RO\underline{H}$	0.5–6.0
Carboxylic	$RCOO\underline{H}$	10–13
Phenolic	$ArO\underline{H}$	4.5–7.7
Amino	$RN\underline{H}_2$	1.0–5.0
Amide	$RCN\underline{H}R$ (O)	5.0–9.0

shift. The acetylenic protons are shielded and are seen at a lower chemical shift. Tables listing chemical shifts should be used only as guidelines, since additional functional groups in the structure may yield more shielding and deshielding effects.

The value for a methine or methylene can be predicted by using a method that was proposed by Shoolery.[2] In Shoolery's method, only functional groups that are directly attached (α position) to the methine or methylene are included in the calculations. More accurate calculations can be done if effects from substituents that are farther away are included. Beauchamp and Marquez[3] proposed equations for calculating the chemical shifts of sp^3-hybridized methyl, methylene, and methine protons, adding

[2]J. N. Shoolery, *Technical Information Bulletin*, 2 (3) (Varian Associates: Palo Alto, CA, 1959).

[3]P. S. Beauchamp and R. Marquez, *J. Chem. Educ.*, *74*, 1483 (1997).

TABLE 6.4 Hydrogen Chemical Shift Correction Factors for Groups on sp^3-Hybridized Carbons

α = directly attached substituent
β = once-removed substituent
γ = twice-removed substituent

Substituent	α	β	γ
R—	0.0	0.0	0.0
$R_2C{=}C(R)-$	0.8	0.2	0.1
R—C≡C—	0.9	0.3	0.1
Ar—	1.4	0.4	0.1
F—	3.2	0.5	0.2
Cl—	2.2	0.5	0.2
Br—	2.1	0.7	0.2
I—	2.0	0.9	0.1
HO—	2.3	0.3	0.1
RO—	2.1	0.3	0.1
$R_2C{=}C(R)-CO-$	2.5	0.4	0.2
ArO—	2.8	0.5	0.3
RCO—	2.8	0.5	0.1
ArCO—	3.1	0.5	0.2
$ArSO_3$—	2.8	0.4	0.0
H_2N—	1.5	0.2	0.1
RCNH—	2.1	0.3	0.1
O_2N—	3.2	0.8	0.1
HS—	1.3	0.4	0.1
RS—	1.3	0.4	0.1
HC—	1.1	0.4	0.1
RC—	1.2	0.3	0.0
ArC—	1.7	0.3	0.1
HOC—	1.1	0.3	0.1
ROC—	1.1	0.3	0.1

(Continued)

TABLE 6.4 *(Continued)*

$H_2NC(=O)-$	1.0	0.3	0.1
$ClC(=O)-$	1.8	0.4	0.1
$N\equiv C-$	1.1	0.4	0.2
$RS(=O)-$	1.6	0.5	0.3
$RS(=O)(=O)-$	1.8	0.5	0.3

Source: From P. S. Beauchamp and R. Marquez, *J. Chem. Educ.*, *74* (12), 1483–1485 (1997). Copyright © 1997, Division of Chemical Education, Inc; used with permission.

in the electronic effects of groups that are in the β and γ positions. These equations are described below. Correction factors for functional groups in the α, β, and γ positions are listed in Table 6.4.

For a hydrogen on a carbon that has only a functional group attached to the methyl, the chemical shift can be calculated as follows:

$$\delta_{\text{H in } CH_3} = 0.9 + \alpha$$

$$\underset{\alpha}{H_3C-}$$

If the methyl is attached to other carbons in the β and γ positions, then the electronic effects of these substituents are taken into account in the following equation. Correction factors for any functional groups in the β and γ positions are added into the calculation.

$$\delta_{\text{H in } CH_3} = 0.9 + \Sigma(\beta + \gamma)$$

$$\underset{\beta\ \ \gamma}{H_3C-C-C-}$$

Chemical shifts for a methylene and a methine can be calculated using the following equations:

$$\delta_{\text{H in } CH_2} = 1.2 + \Sigma(\alpha + \beta + \gamma)$$

$$\underset{\alpha\ \ \ \beta\ \ \gamma}{-CH_2-C-C-}$$

$$\delta_{\text{H in CH}} = 1.5 + \Sigma(\alpha + \beta + \gamma)$$

$$\underset{\alpha\ \ \beta\ \ \gamma}{-\overset{|}{CH}-C-C-}$$

The proton chemical shifts of 2-chloropropanoic acid (Figure 6.6) can be calculated using these methods. Hydrogen ***a*** has a chlorine and a carboxylic group on the β carbon, giving a calculated chemical shift of δ 1.7(0.9 + 0.5 + 0.3) [observed chemical shift = δ 1.71]. Hydrogen ***b*** has a chlorine and a carboxylic acid on the α carbon, giving

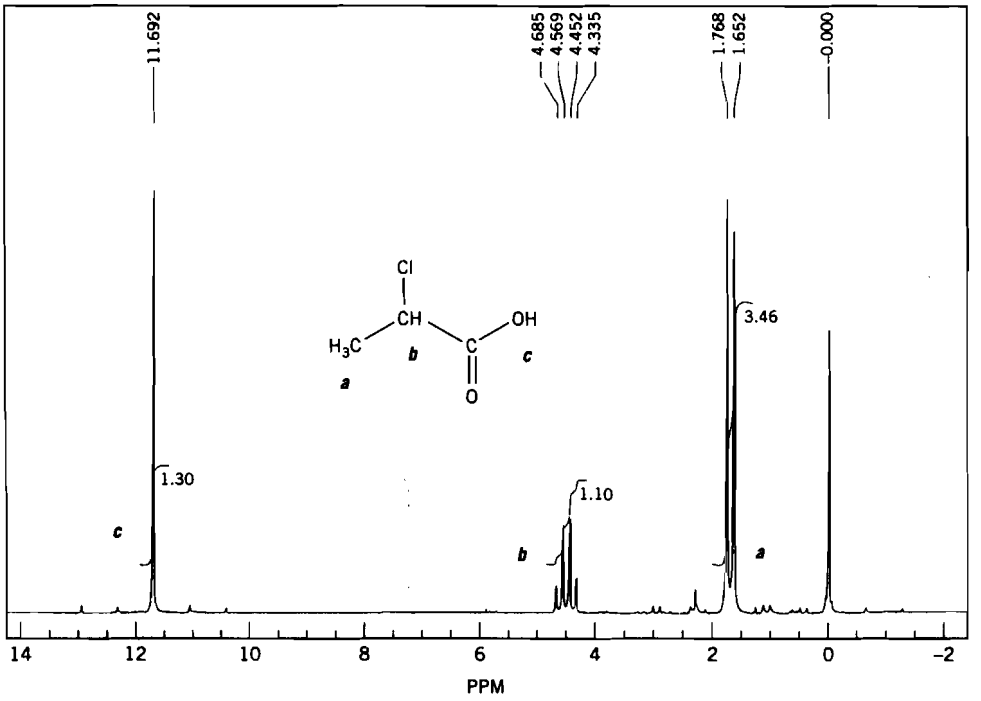
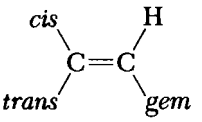


Figure 6.6 ^{1}H NMR spectrum of 2-chloropropanoic acid. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

a calculated chemical shift of δ 4.9(1.5 + 2.2 + 1.2) [observed chemical shift = δ 4.51]. The agreement between the calculated and the experimental is quite good using this procedure. The reliability of this method is decreased if there are many substitutent groups on the carbons.

Pascual, Meier, and Simon[4] proposed a method for predicting the chemical shift of hydrogens attached to alkenes. Correction factors for the electronic effects of other groups at the *cis*, *trans*, and *gem* positions are added to a value of δ 5.28. The values for groups in these positions are listed in Table 6.5.

$$\delta_H = 5.28 + \Sigma(cis + trans + gem)$$



Each hydrogen attached to the alkene for styrene (Figure 6.7) can be identified. The observed proton chemical shifts were measured in the middle of each splitting pattern. Hydrogen ***a*** has only a *trans* group, giving a calculated chemical shift of δ 5.18(5.28 − 0.10) [observed chemical shift = δ 5.08]. Hydrogen ***b*** has only a *cis* group, yielding a calculated chemical shift of δ 5.65(5.28 + 0.37) [observed chemical shift = δ 5.58]. Hydrogen **c** has only a *gem* group, producing a calculated chemical shift of

[4]C. Pascual, J. Meier, and W. Simon, *Helv. Chim. Acta.*, *49*, 164 (1966).

TABLE 6.5 Hydrogen Chemical Shift Correction Factors for Groups on Alkenes

Substituent	*gem*	*cis*	*trans*
H—	0.0	0.0	0.0
Alkyl—	0.44	−0.26	−0.29
Cycloalkenyl—	0.71	−0.33	−0.30
$ROCH_2$—	0.67	−0.02	−0.07
ICH_2—	0.67	−0.02	−0.07
$RSCH_2$—	0.53	−0.15	−0.15
$BrCH_2$—	0.72	0.12	0.07
$ClCH_2$—	0.72	0.12	0.07
H_2NCH_2— (NHR, NR_2)	0.66	−0.05	−0.23
RC≡C—	0.50	0.35	0.10
N≡C—	0.23	0.78	0.58
H_2C=CH— (unconjugated) (H or R)	0.98	−0.04	−0.21
H_2C=CH— (conjugated) (H or R)	1.26	0.08	−0.01
RC(=O)— (unconjugated)	1.10	1.13	0.81
RC(=O)— (conjugated)	1.06	1.01	0.95
HOC(=O)— (unconjugated)	1.00	1.35	0.74
HOC(=O)— (conjugated)	0.69	0.97	0.39
ROC(=O)— (unconjugated)	0.84	1.15	0.56
ROC(=O)— (conjugated)	0.68	1.02	0.33
HC(=O)—	1.03	0.97	1.21
H_2NC(=O)— (NHR, NR_2)	1.37	0.93	0.35

(Continued)

TABLE 6.5 *(Continued)*

Substituent	*gem*	*cis*	*trans*
ClC(=O)—	1.10	1.41	0.99
RO— (R = unconjugated)	1.18	−1.06	−1.28
RO— (R = conjugated)	1.14	−0.65	−1.05
RCO—	2.09	−0.40	−0.67
C_6H_5—	1.35	0.37	−0.10
Cl—	1.00	0.19	0.03
Br—	1.04	0.40	0.55
R_2N— (R = unconjugated)	0.69	−1.19	−1.31
R_2N— (R = conjugated)	2.30	−0.73	−0.81
RS—	1.00	−0.24	−0.04
RSO_2—	1.58	1.15	0.95

Source: From C. Pascual, J. Meier, and W. Simon, *Helv. Chim. Acta.*, *49*, 165 (1966). Used with permission.

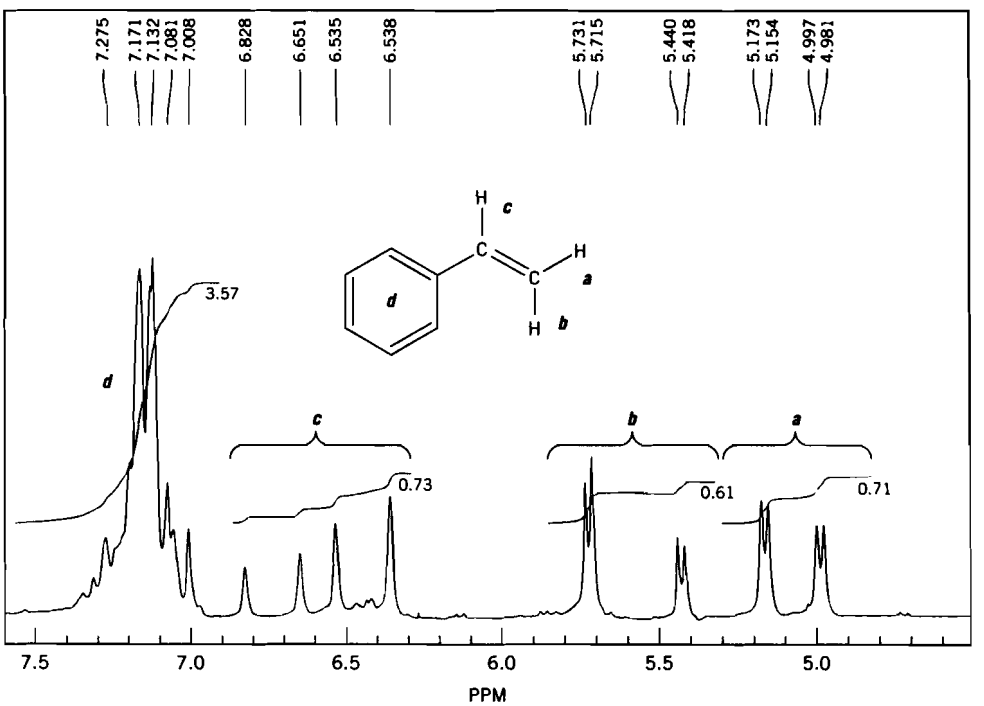
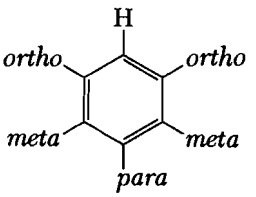


Figure 6.7 ^{1}H NMR spectrum of styrene. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

δ 6.63(5.28 + 1.35) [observed chemical shift = δ 6.59]. The agreement between the chemical shifts is fairly close.

In some cases, the aromatic hydrogens can be distinguished. The chemical shifts of the aromatic protons can be calculated by adding correction factors for any non-hydrogen group to the value of δ 7.27 for the unsubstituted benzene. These values are listed in Table 6.6.

$$\delta_H = 7.27 + \Sigma(ortho + meta + para)$$



The chemical shifts of protons on aromatic carbons can be calculated for acetophenone (Figure 6.8) using these methods. Hydrogens ***b*** have the acetyl group in the *meta* position, giving a calculated chemical shift of δ 7.36 (7.27 + 0.09) [observed chemical shift = δ 7.24 − 7.48]. Hydrogen **c** has the acetyl group in the *para* position, producing a calculated chemical shift of δ 7.57 (7.27 + 0.30) [observed chemical shift = δ 7.24 − 7.48]. Hydrogens ***d*** have the acetyl group in the *ortho* position, yielding a calculated chemical shift of δ 7.91 (7.27 + 0.64) [observed chemical shift = δ 7.83 − 7.99]. The agreement between the calculated and the observed chemical shifts is reasonable.

6.3.2 Integration

Integration is defined as the area underneath each signal. This area is proportional to the number of hydrogens contributing to that signal. In most instances, the student will not have available the chemical formula of the unknown compound. To calculate the number of hydrogens per signal, first add up all of the integration values. Divide each area by the total area. Divide by the lowest number and multiply by the same factor to get all of the numbers to whole values. If there are three signals, the following equations are used.

$$\text{area a} + \text{area b} + \text{area c} = \text{total area}$$

$$\frac{\text{area a}}{\text{total area}} = \text{ratio for area a}$$

$$\frac{\text{area b}}{\text{total area}} = \text{ratio for area b}$$

$$\frac{\text{area c}}{\text{total area}} = \text{ratio for area c}$$

These equations can be applied to the proton NMR spectra of acetophenone (Figure 6.8):

$$6.94 + 6.87 + 4.78 = 18.62$$

$$(a)\ \frac{6.94}{18.62} = 0.373 \qquad \frac{0.373}{0.257} = 1.45 \times 2 = 2.90$$

TABLE 6.6 Hydrogen Chemical Shift Correction Factors for Groups on Substituted Benzenes

Substituent	*ortho*	*meta*	*para*
CH_3—	−0.17	−0.09	−0.18
CH_3CH_2—	−0.15	−0.06	−0.18
$(CH_3)_2CH$—	−0.14	−0.09	−0.18
$(CH_3)_3C$—	0.01	−0.10	−0.24
CH_2=CH—	0.00	0.00	0.00
HC≡C—	0.20	0.00	0.00
C_6H_5—	0.18	0.00	0.08
CF_3—	0.25	0.25	0.25
$ClCH_2$—	0.00	0.01	0.00
Cl_2CH—	0.10	0.06	0.10
Cl_3C—	0.80	0.20	0.20
$HOCH_2$—	−0.10	−0.10	−0.10
$ROCH_2$—	0.00	0.00	0.00
NH_2CH_2—	0.00	0.00	0.00
RS—	−0.03	0.00	0.00
F—	−0.30	−0.02	−0.22
Cl—	0.02	−0.06	−0.04
Br—	0.22	−0.13	−0.03
I—	0.40	−0.26	−0.03
HO—	−0.50	−0.14	−0.40
RO—	−0.27	−0.08	−0.27
RCO— (O)	−0.22	0.00	0.00
$ArSO_3$—	−0.26	−0.05	0.00
HC— (O)	0.58	0.21	0.27
RC— (O)	0.64	0.09	0.30
HOC— (O)	0.80	0.14	0.20
ROC— (O)	0.74	0.07	0.20
ClC— (O)	0.83	0.16	0.30
N≡C—	0.27	0.11	0.30
H_2N—	−0.75	−0.24	−0.63
R_2N—	−0.60	−0.10	−0.62
RCNH— (O)	0.33	0.03	−0.10
^+H_3N—	0.63	0.25	0.25
O_2N—	0.95	0.17	0.33
O=C=N—	−0.20	−0.20	−0.20

Source: From R. S. Macomber, *A Complete Guide to Modern NMR Spectroscopy* (Wiley, New York, 1998). Copyright © 1998, John Wiley and Sons, New York; used with permission.

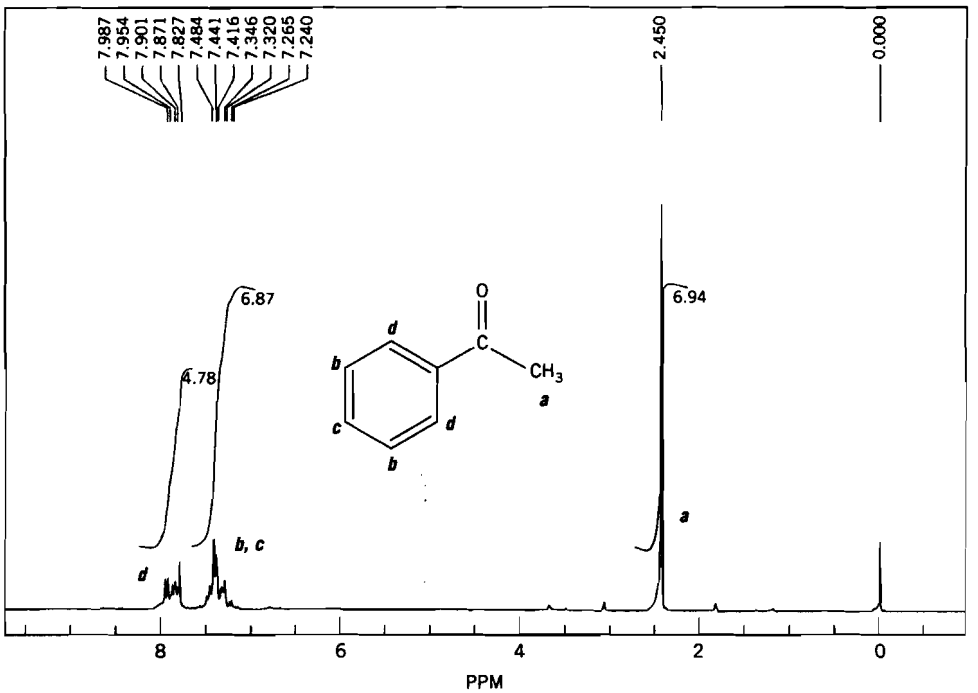
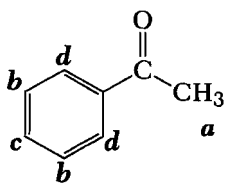


Figure 6.8 ^{1}H NMR spectrum of acetophenone. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

$$(b, c)\ \frac{6.87}{18.62} = 0.369 \qquad \frac{0.369}{0.257} = 1.44 \times 2 = 2.88$$

$$(d)\ \frac{4.78}{18.62} = 0.257 \qquad \frac{0.257}{0.257} = 1 \times 2 = 2$$

The calculations are in agreement with the structure below.



6.3.3 Splitting

When two protons are in close proximity to one another, the magnetic field of each proton affects protons on adjacent carbons. This magnetic effect results in the splitting of the signal into multiple peaks and is known as spin-spin splitting.

In Figure 6.9, protons H_A see proton H_B as aligned with or against the applied field. Since there are only two ways of drawing this (one arrow aligned and one arrow against), the result is that H_A is split into a doublet and each peak of the doublet is approximately the same height.

Proton H_B sees protons H_A as aligned with or against the applied field, as seen in Figure 6.10. With this type of system, proton H_B is split into a triplet. The middle peak

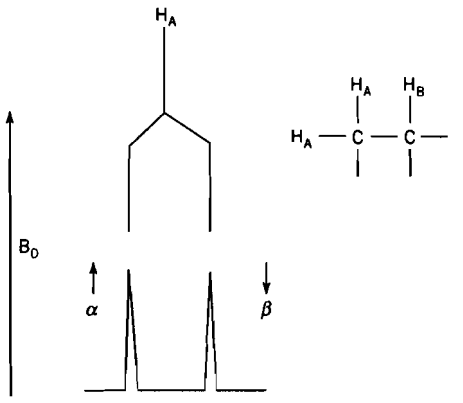


Figure 6.9 H_A sees H_B as aligned with or against the applied field. Therefore, H_A is split into a doublet by H_B.

is twice as high as the outer peaks, since the middle peak consists of one α and one β alignment.

If proton H_B is adjacent to three protons H_A, as seen in Figure 6.11, then proton H_B is split into a quartet. The middle two peaks are three times the size of the outer two peaks because there are three combinations of α and β alignments.

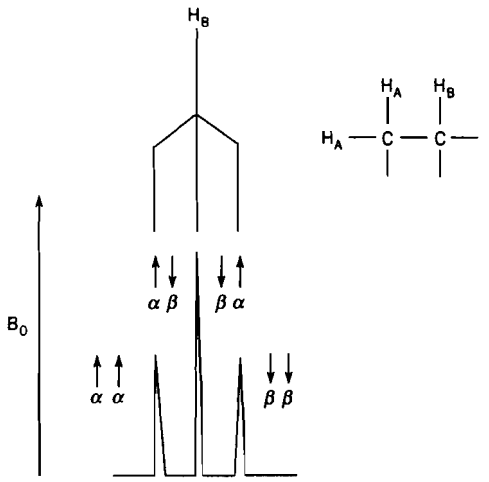


Figure 6.10 H_B sees H_A as aligned with or against the applied field. Since there are two possibilities of the arrangements of α and β together, the middle peak is twice as high as the outer peaks. As a result, H_B is split into a triplet by H_A.

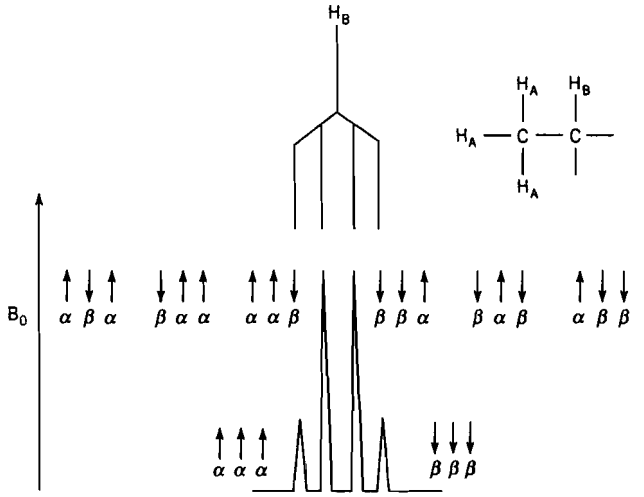


Figure 6.11 H_B sees H_A as aligned with or against the applied field. Since there are three possibilities of the arrangements of α and β, the middle peak is three times as high as the outer peaks. As a result, H_B is split into a quartet by H_A.

Spin-spin splitting can be predicted using first-order rules. The multiplicity expected for a signal can be predicted from the $n + 1$ rule, which is a simple first-order rule. The first-order rule applies to nuclei of spin $\frac{1}{2}$ such as ^1H, ^{13}C, and ^{19}F. That is, a given magnetically active nucleus coupled by n equivalent neighbors should appear as an $n + 1$ multiplet. Thus, 1, 2, 3, 4, 5, 6, . . . neighbors give rise to a signal containing $n + 1 = 2$ (doublet, d), 3 (triplet, t), 4 (quartet, q), 5 (quintet, quin), 6 (sextet, sext), 7 (septet, sept), . . . lines. The theoretical measure of the line composition in multiplets

arises from the coefficients of the expanded polynomial, as seen in Pascal's triangle (Figure 6.12). In simple terms, the number of peaks, within a signal, is equal to the number of hydrogens on the adjacent carbons plus one. On a spectrum, the number of peaks, within a signal, minus one is equal to the number of hydrogens on adjacent carbons.

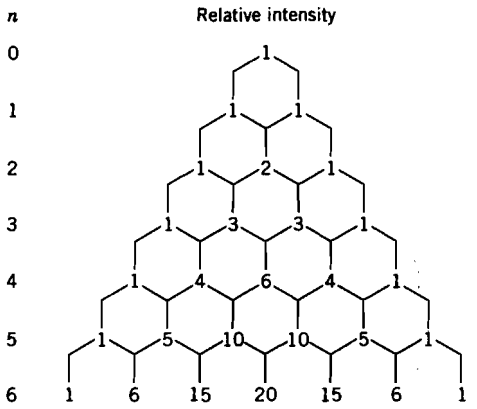


Figure 6.12 Pascal's triangle. Relative order of first-order multiplicities; n = number of equivalent coupling nuclei of spin $\frac{1}{2}$ (e.g., protons).

Both integration and splitting can be used to identify a compound from the proton NMR spectrum. The integration of the signals is calculated to be in a 3 : 2 : 2 : 1 ratio for the NMR spectrum in Figure 6.13.

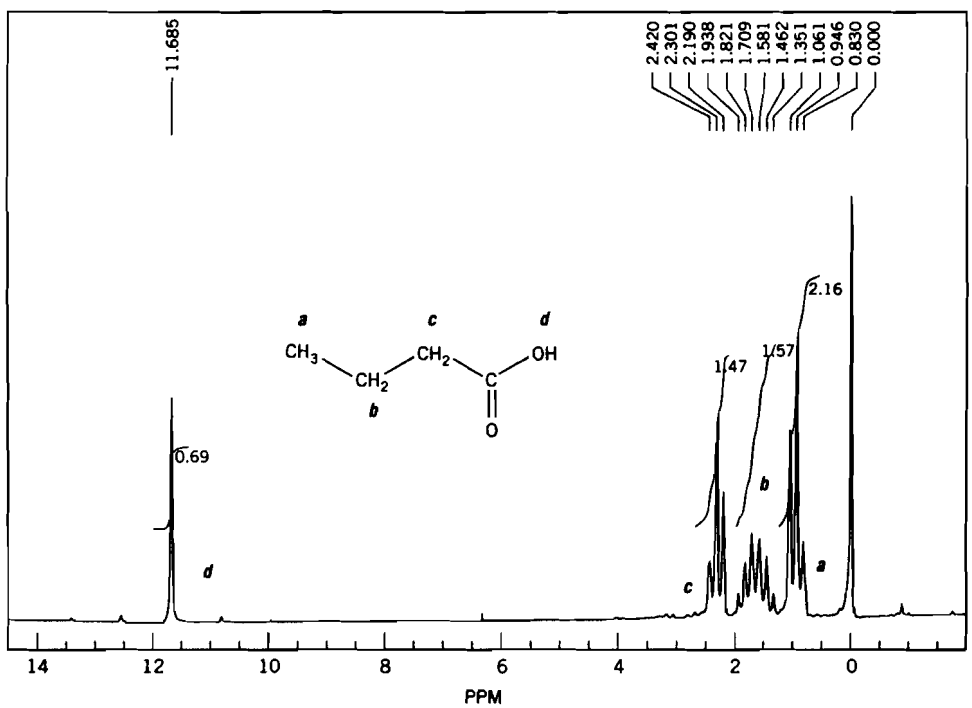


Figure 6.13 ^{1}H NMR spectrum of butanoic acid. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

The splitting and integration can be summarized as follows.

	Chemical Shift	*Splitting*	*Integration*	*Interpretation*
(a)	0.95	t	3 H	CH_3 adjacent to CH_2
(b)	1.65	sext	2 H	CH_2 adjacent to 5 H
(c)	2.3	t	2 H	CH_2 adjacent to CH_2
(d)	11.68	s	1 H	OH isolated

The first part of the interpretation is based upon the integration. The second part of the interpretation is the splitting minus one. By using Table 6.3, signal ***d*** is identified as an —OH of a carboxylic acid. The only possible answer is butanoic acid.

The distance between the individual peaks of a signal is known as the coupling constant, J. The coupling constant is useful in determining which protons are splitting each other. For example, if H_A is adjacent to H_B and the protons split each other, then the coupling constants within the signal for H_A would be equal to the coupling constants within the signal for H_B.

In the proton NMR spectrum of 2-propanol (Figure 6.14), the coupling constant is approximately 0.1 ppm or 6 Hz (0.1 ppm × 60 MHz, the size of the magnet) between the individual peaks of each multiplet. A more detailed drawing is shown in Figure 6.15. Since the coupling constants are the same, it illustrates that the hydrogens (2 CH_3) giving rise to the doublet are splitting the hydrogen (CH), giving rise to the septet.

In the NMR spectra of compounds such as alcohols, carboxylic acids, phenols, or amines, the OH or NH signal is usually a broad singlet. The broad singlet results from the OH or NH undergoing a rapid exchange.

$$R_aOH_a + R_bOH_b \rightleftarrows R_aOH_b + R_bOH_a$$

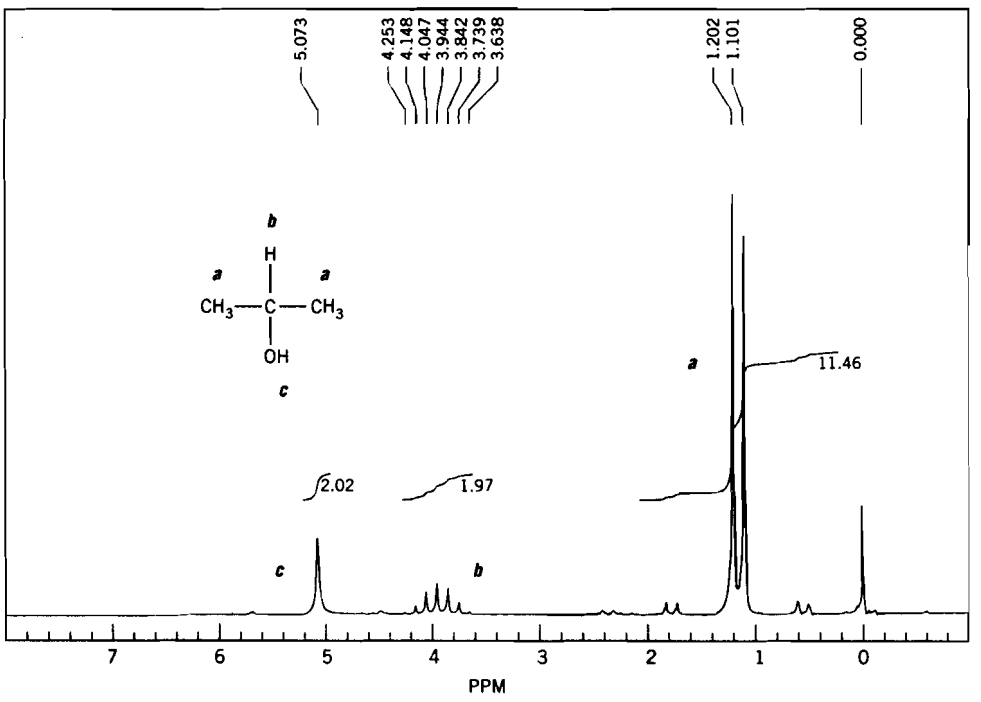


Figure 6.14 ^1H NMR spectrum of 2-propanol. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

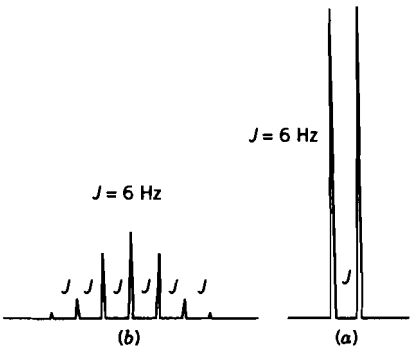


Figure 6.15 The coupling constant, J, between the peaks of the doublet (a) is equal to the coupling constant, J, between the peaks of the septet (b) in 2-propanol. The NMR spectrum is shown in Figure 6.14.

This exchange is rapid enough that the hydroxylic or amino hydrogen cannot experience coupling with nearby protons on carbon. The nearby protons do not experience coupling by the OH proton. This proton exchange occurs in ($CDCl_3$) deuterochloroform. The NMR spectra of 2-propanol (Figure 6.14) was obtained neat and the exchange occurs. In DMSO-d_6 and acetone-d_6, the OH and NH are coupled with the nearby protons and splitting of these protons is seen. A number of factors strongly affect the ^1H NMR spectra of exchangeable hydrogens:

1. Concentration (dilution shifts the OH to a lower chemical shift)
2. Acid catalysis (changes the positions and shapes of the OH peak)
3. Temperature (an increase enhances the rate of exchange)
4. D_2O exchange (causes the OH peak to disappear and replaces it with a HOD peak at $\delta \cong 4.5$)

▶ 6.4 CARBON-13 SPECTRA

Three important types of information are needed for the interpretation of carbon-13 NMR spectra:

1. The number of different signals indicates how many different types of carbons are present.
2. The chemical shifts of each signal indicate the electronic environment.
3. Using DEPT, each signal is identified as CH_3, CH_2, CH, or C.

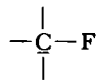
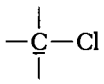
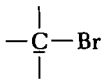
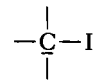
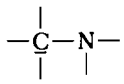
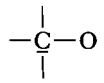
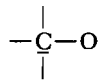
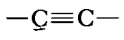
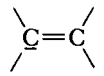
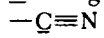
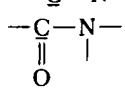
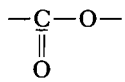
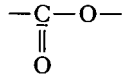
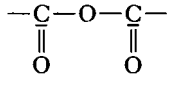
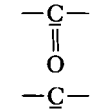
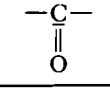
Chemical shift and splitting will be discussed in detail in the following sections. Peak areas are not necessarily correlated to the number of carbons giving rise to each signal. Usually carbon atoms with two or three hydrogens give the strongest signals, while carbons with no hydrogens give the weakest signals.

The most effective method of identifying a signal as CH_3, CH_2, CH, or C is DEPT (distortionless enhancement by polarization transfer). This method will be discussed in Section 6.5.

6.4.1 Chemical Shift

In Table 6.7, chemical shift ranges for carbons are listed. This table is to be used as a guideline. It is more accurate to predict the chemical shift by calculations.

TABLE 6.7 Carbon-13 Magnetic Resonance Frequencies

Type of Carbon		Chemical Shift (δ, ppm)
1° Alkyl	RCH_3	5–40
2° Alkyl	RCH_2R	15–55
3° Alkyl	$RCHR_2$	25–60
Alkyl fluoride		70–80
Alkyl chloride		40–50
Alkyl bromide		30–40
Alkyl iodide		5–15
Amine		10–70
Alcohol		45–90
Ether		55–90
Alkyne		60–90
Alkene		100–170
Aryl	C in ring	90–160
Nitriles		105–130
Amides		150–180
Carboxylic acids		160–185
Esters		150–185
Anhydrides		145–175
Aldehydes		175–220
Ketones		180–220

The carbon-13 chemical shifts for unsubstituted alkanes is given in Table 6.8. Use Table 6.8 for the hydrocarbon portion, then add in substituent effects from Table 6.9.

$$\delta_C = \delta_{C \text{ in hydrocarbon}} + \Sigma(\alpha + \beta + \gamma)$$

The chemical shifts for the alkane carbons in butanoic acid (Figure 6.16) can be calculated using these methods. Since the —COOH is located on one end of the structure, the linear (n) values will be used. The first values are from Table 6.8 for propane. Next, values from Table 6.9 are added in. The —COOH is in the γ position for carbon ***a***, β position for carbon ***b***, and α position for carbon ***c***. Carbon ***a*** has a calculated chemical shift of δ 13.6(15.6 − 2) [observed chemical shift = δ 12.29]. Carbon ***b*** has a calculated chemical shift of δ 19.1(16.1 + 3) [observed chemical shift = δ 17.24]. Carbon ***c*** has a calculated chemical shift of δ 36.6(15.6 + 21) [observed chemical shift = δ 34.88].

If several functional groups are added in, the chemical shifts are inaccurate due to the cumulative effects of the substituents.

The chemical shifts for the carbons in 2-chloropropanoic acid (Figure 6.17) can be calculated. The values for ethane (Table 6.8) are used. From Table 6.9, both the —Cl and —COOH are in the β position for carbon ***a*** and in the α position for carbon ***b***. Carbon ***a*** has a calculated chemical shift of δ 19.9(5.9 + 11 + 3) [observed chemical

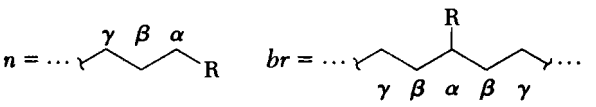
TABLE 6.8 Chemical Shifts of Carbons in Straight- and Branched-Chain Alkanes[a]

Compound	C-1	C-2	C-3	C-4	C-5
Straight chain					
Methane	−2.1				
Ethane	5.9	5.9			
Propane	15.6	16.1	15.6		
Butane	13.2	25.0	25.0	13.2	
Pentane	13.7	22.6	34.5	22.6	13.7
Hexane	13.9	22.9	32.0	32.0	22.9
Heptane	13.9	23.0	32.4	29.5	32.4
Octane	14.0	23.0	32.4	29.7	29.7
Nonane	14.0	23.1	32.4	29.8	30.1
Decane	14.1	23.0	32.4	29.9	30.3
Branched chain					
Isobutane	24.3	25.2			
Isopentane	22.0	29.9	31.8	11.5	
Isohexane	22.5	27.8	41.8	20.7	14.1
Neopentane	31.5	27.9			
Neohexane	28.9	30.4	36.7	8.7	
3-Methylpentane	11.3	29.3	36.7		
			18.6[b]		
2,3-Dimethylbutane	19.3	34.1			
2,2,3-Trimethylbutane	27.2	32.9	38.1	15.9	
3,3-Dimethylpentane	6.8	25.1	36.1		
	4.4[b]				

[a]From D. G. Grant and E. G. Paul, *J. Amer. Chem. Soc., 86,* 2984 (1964); J. D. Roberts, F. J. Weigert, J. I. Kroschwitz, and H. J. Reich, *J. Amer. Chem. Soc., 92,* 1338 (1970); H. Spiescke and W. G. Scheider, *J. Chem. Phys., 36,* 722 (1961).

[b]Branch methyl carbon. Chemical shifts in ppm downfield from TMS. Since these are obtained from spectra using various internal standards (TMS, benzene, CS_2), the error in shift position is at least 0.2 ppm.

TABLE 6.9 Carbon-13 Shift Effect Due to Replacement of H by Functional Groups (R) in Alkanes



	α		β		
R	*n*	*br*	*n*	*br*	γ^a
CH_3	+9	+6	+10	+8	−2
COOH	+21	+16	+3	+2	−2
COO^-	+25	+20	+5	+3	−2
COOR	+20	+17	+3	+2	−6
COCl	+33	+28		+2	
COR	+30	+24	+1	+1	−2
CHO	+31		+0		−2
Phenyl	+23	+17	+9	+7	−2
OH	+48	+41	+10	+8	−5
OR	+58	+51	+8	+5	−4
OCOR	+51	+45	+6	+5	−3
NH_2	+29	+24	+11	+10	−5
NH_3^+	+26	+24	+8	+6	−5
NHR	+37	+31	+8	+6	−4
NR_2	+42		+6		−3
NO_2	+63	+57	+4	+4	
CN	+4	+1	+3	+3	−3
SH	+11	+11	+12	+11	−4
SR	+20		+7		−3
F	+68	+63	+9	+6	−4
Cl	+31	+32	+11	+10	−4
Br	+20	+25	+11	+10	−3
I	−6	+4	+11	+12	−1

n = straight-chain compounds, *br* = branched-chain compounds.

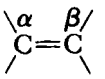
[a]The effect of the γ position is virtually the same for straight- and branched-chain compounds.

Source: From F. W. Wehrli, A. P. Marchand, and S. Wehrli, *Interpretation of Carbon-13 NMR Spectra*, 2nd ed. (Wiley, New York, 1988). © John Wiley and Sons Limited; used with permission.

shift = δ 20.80]. Carbon ***b*** has a calculated chemical shift of δ 57.9(5.9 + 31 + 21) [observed chemical shift = δ 51.87].

The chemical shifts of carbons in alkenes can be calculated using the equation below with Table 6.10.

$$\delta_C = 123.3 + \Sigma(\alpha + \beta)$$



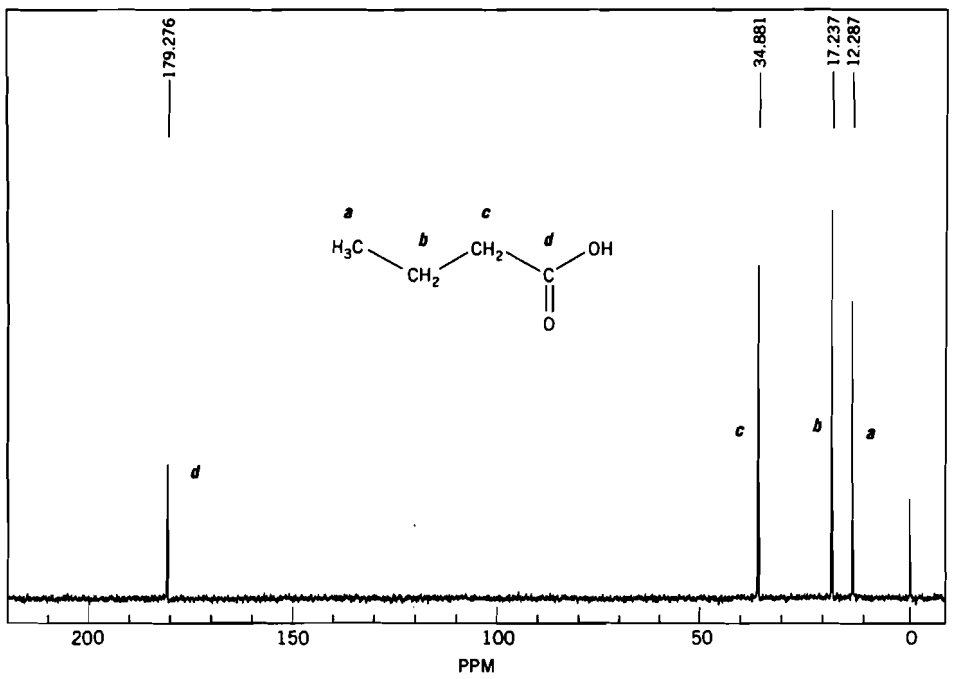


Figure 6.16 ^{13}C NMR spectrum of butanoic acid. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

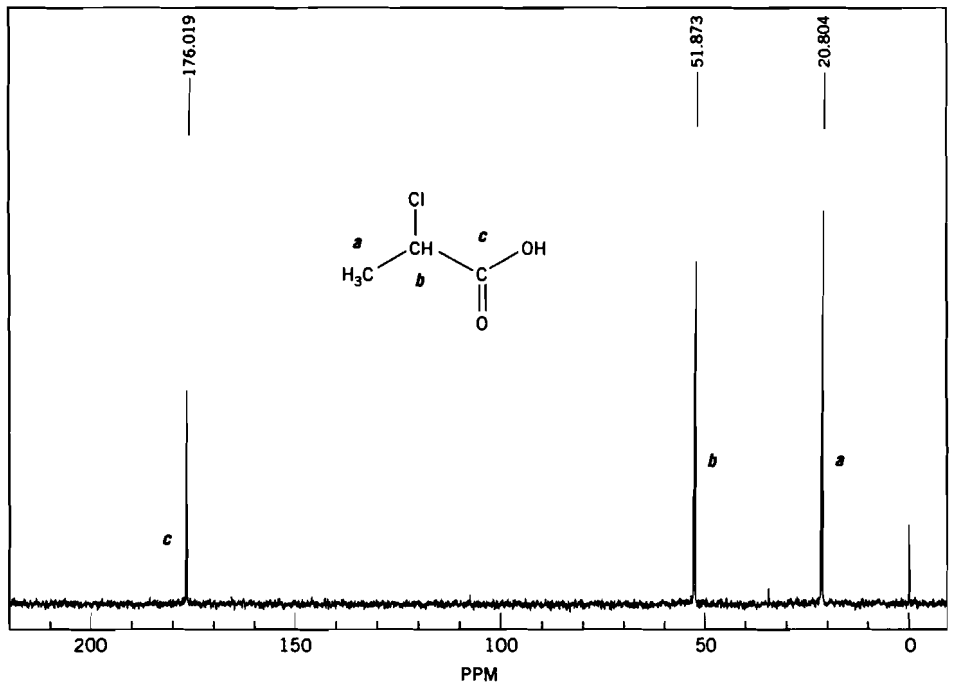


Figure 6.17 ^{13}C NMR spectrum of 2-chloropropanoic acid. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

TABLE 6.10 Carbon-13 Chemical Shift Correction Factors for Groups on Alkenes.

Substituent	α	β
H—	0.0	0.0
CH_3—	12.9	−7.4
CH_3CH_2—	17.2	−9.8
$CH_3CH_2CH_2$—	15.7	−8.8
$(CH_3)_2CH$—	22.7	−12.0
$CH_3CH_2CH_2CH_2$—	14.6	−8.9
$(CH_3)_3C$—	26.0	−14.8
$ClCH_2$—	10.2	−6.0
$BrCH_2$—	10.9	−4.5
ICH_2—	14.2	−4.0
$HOCH_2$—	14.2	−8.4
$CH_3CH_2OCH_2$—	12.3	−8.8
CH_2=CH—	13.6	−7.0
HC≡C—	−6.0	5.9
phenyl-	12.5	−11.0
F—	24.9	−34.3
Cl—	2.8	−6.1
Br—	−8.6	−0.9
I—	−38.1	7.0
HO—	25.7	−35.3
CH_3O—	29.4	−38.9
CH_3CH_2O—	28.8	−37.1
$CH_3CH_2CH_2CH_2O$—	28.1	−40.4
$CH_3C(=O)$—	18.4	−26.7
$(CH_3)_2N$—	28.0	−32.0
$(CH_3)_3\overset{+}{N}$—	19.8	−10.6
N-pyrrolidonyl—	6.5	−29.2
O_2N—	22.3	−0.9
NC—	−15.1	14.2
CN—	−3.9	−2.7
CH_3CH_2S—	9.0	−12.8
CH_2=$CHSO_2$—	14.3	7.9
HC(=O)—	15.3	14.5
$CH_3C(=O)$—	13.8	4.7
HOC(=O)—	5.0	9.8
$CH_3CH_2OC(=O)$—	6.3	7.0

(Continued)

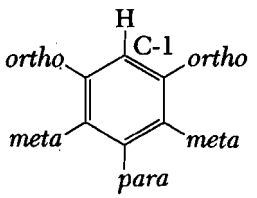
TABLE 6.10 *(Continued)*

ClC(=O)—	8.1	14.0
$(CH_3)_3Si$—	16.9	6.7
Cl_3Si—	8.7	16.1

Source: From E. Pretsch, P. Buehlmann, and C. Affolter, *Structure Determination of Organic Compounds* (Springer-Verlag, Heidelberg, 2000), p 83. Used with permission.

The chemical shifts of aromatic carbons can be predicted with the equation below and Table 6.11.

$$\delta_C = 128.7 + \Sigma(\text{C-1} + \textit{ortho} + \textit{meta} + \textit{para})$$



All of the signals in the carbon NMR spectrum of styrene (Figure 6.18) can be identified, using the equations above.

The alkene carbon attached to the benzene ring is α to the phenyl group and has a calculated chemical shift of δ 135.8(123.3 + 12.5) [observed chemical shift = δ 136.44,

TABLE 6.11 Effect of Substituents on the C-13 Shift of Benzene Ring Carbons[a]

	Position			
Substituent	C-1	*ortho*	*meta*	*para*
—Br	−5.5	+3.4	+1.7	−1.6
$-CF_3$	−9.0	−2.2	+0.3	+3.2
$-CH_3$	+8.9	+0.7	−0.1	−2.9
—CN	−15.4	+3.6	+0.6	+3.9
—C≡C—H	−6.1	+3.8	+0.4	−0.2
1,4-di—C≡C—H	−5.6	+3.8	—	—
$-COCF_3$	−5.6	+1.8	+0.7	+6.7
$-COCH_3$	+9.1	+0.1	0.0	+4.2
—COCl	+4.6	+2.4	0.0	+6.2
—CHO	+8.6	+1.3	+0.6	+5.5
—COOH	+2.1	+1.5	0.0	+5.1
$-CO_2CH_3$	+2.0	+1.2	−0.1	+4.8
$-COC_6H_5$	+9.4	+1.7	−0.2	+3.6
—Cl	+6.2	+0.4	+1.3	−1.9
—F	+34.8	−12.9	+1.4	−4.5
—H	0.0	—	—	—

(Continued)

TABLE 6.11 *(Continued)*

Substituent	Position			
	C-1	*ortho*	*meta*	*para*
—NCO	+5.7	−3.6	+1.2	−2.8
—NH_2	+18.0	−13.3	+0.9	−9.8
—NO_2	+20.0	−4.8	+0.9	+5.8
—OCH_3	+31.4	−14.4	+1.0	−7.7
—OH	+26.9	−12.7	+1.4	−7.3
—C_6H_5	+13.1	−1.1	+0.4	−1.2
—SH	+2.3	+1.1	+1.1	−3.1
—SCH_3	+10.2	−1.8	+0.4	−3.6
—SO_2NH_2	+15.3	−2.9	+0.4	+3.3
—O (oxyanion)	+39.6	−8.2	+1.9	−13.6
—OC_6H_5	+29.2	−9.4	+1.6	−5.1
—$OCOCH_3$ (acetoxy)	+23.0	−6.4	+1.3	−2.3
—$N(CH_3)_2$	+22.6	−15.6	+1.0	−11.5
—$N(CH_2CH_3)_2$	+19.9	−15.3	+1.4	−12.2
—$NH(C{=}O)CH_3$	+11.1	−9.9	+0.2	−5.6
—CH_2OH	+12.3	−1.4	−1.4	−1.4
—I	−32.0	+10.2	+2.9	+1.0
—$Si(CH_3)_3$	+13.4	+4.4	−1.1	−1.1
—$CH{=}CH_2$	+9.5	−2.0	+0.2	−0.5
—COCl	+5.8	+2.6	+1.2	+7.4
—CHO	+9.0	+1.2	+1.2	+6.0
—$COCH_2CH_3$	+7.6	−1.5	−1.5	+2.4
—$COCH(CH_3)_2$	+7.4	−0.5	−0.5	+4.0
—$COC(CH_3)_3$	+9.4	−1.1	−1.1	+1.7

[a]Data obtained in various solvents (CCl_4, neat, DMF = *N,N*-dimethylformamide) with various internal standards (TMS, CS_2). A positive value means a downfield shift, negative means an upfield shift. Estimated error is ±0.5 ppm. Chemical shift of unsubstituted benzene is 128.7 ppm.

carbon ***e***]. The other alkene carbon is β to the phenyl group and has a calculated chemical shift of δ 112.3(123.3 − 11) [observed chemical shift = δ 112.71, carbon ***a***].

The aromatic carbons are calculated according to the functional groups in *ortho, meta,* and *para* positions. The C-1 carbon has a calculated chemical shift of δ 138.2(128.7 + 9.5) [observed chemical shift = δ 137.02, carbon ***f***]; the carbon *ortho* to the alkene group has a calculated chemical shift of δ 126.7(128.7 − 2.0) [observed chemical shift = δ 125.63, carbon ***b***]; the carbon *meta* to the alkene group has a calculated chemical shift of δ 128.9(128.7 + 0.2) [observed chemical shift = δ 127.83, carbon ***d***]; and the carbon *para* to the alkene group has a calculated chemical shift of δ 128.2(128.7 − 0.5) [observed chemical shift = δ 127.05, carbon ***c***].

6.4.2 Splitting

Nowadays, all carbon-13 NMR spectra are run decoupled. Decoupling removes all of the splitting between carbon and hydrogen. If the spectra were run coupled, then a

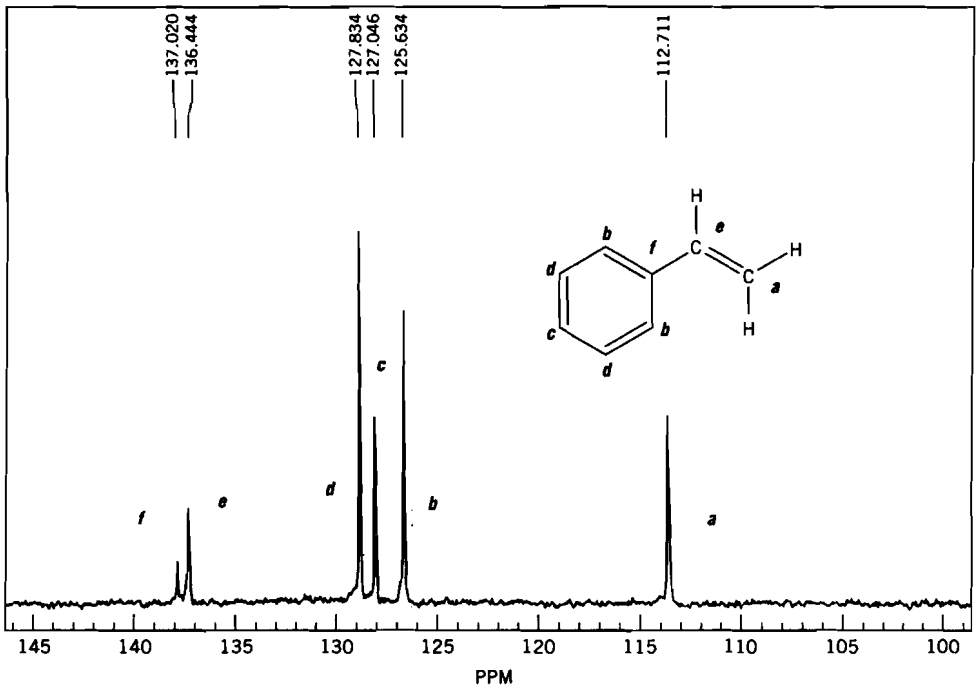
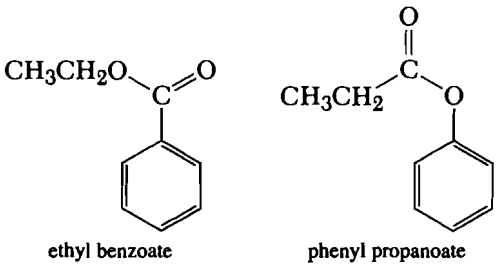


Figure 6.18 ^{13}C NMR spectrum of styrene. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

CH_3 would show up as a quartet, a CH_2 would show up as a triplet, a CH would show up as a doublet, and a C would show up as a singlet. This type of information is obtained from DEPT spectra, which is described in Section 6.5.

A problem-solving format is applied to deduce the structure of a compound by NMR analysis using the ^1H NMR spectrum (Figure 6.19) and ^{13}C NMR spectra (Figure 6.20) for an unknown ester of formula $C_9H_{10}O_2$. An unsaturation number (see Section 3.6.1, pp. 63–64) of $5[U = 9 + 1 - \frac{1}{2}(10) + \frac{1}{2}(0)]$ yields the interpretation of benzene plus a double bond or a ring. If it is known that the compound is an ester, then the ester is attached to the benzene ring.

An ethyl group is very obvious in the ^1H NMR spectrum (Figure 6.19), with a triplet at δ 1.28 and a quartet centered at δ 4.31. The integration gives 3H for the triplet, 2H for the quartet, 3H for the first set of aromatic peaks (δ 7.24 – 7.43), and 2H for the second set of aromatic peaks (δ 7.99 – 8.15). The 5 H integration in the aromatic region indicates a monosubstituted benzene. The structure must be either phenyl propanoate or ethyl benzoate.



ethyl benzoate phenyl propanoate

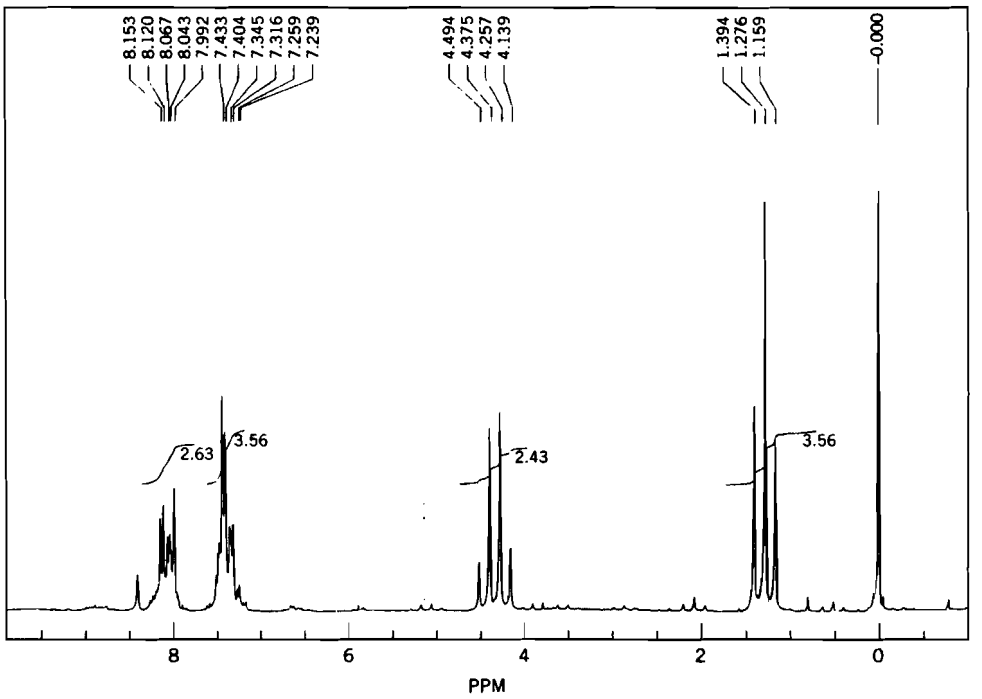
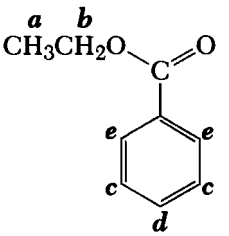


Figure 6.19 ^{1}H NMR spectrum of unknown ester, $C_9H_{10}O_2$. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

According to calculations described in Section 6.3.1 and Table 6.4, the methylene group has a calculated chemical shift of δ 4.3(1.2 + 3.1) in ethyl benzoate and a calculated chemical shift of δ 2.3(1.2 + 1.1) in phenyl propanoate. The quartet for the CH_2 has a chemical shift centered at δ 4.31 (hydrogens ***b***), so the structure must be ethyl benzoate. The CH_3 is centered at δ 1.28 (hydrogens ***a***). From Table 6.6, the hydrogens *ortho* to the ester (hydrogens ***e***) have a calculated chemical shift of δ 8.01(7.27 + 0.74) [observed chemical shift = δ 7.99 − 8.15], the *meta* hydrogens (hydrogens ***c***) have a calculated chemical shift of δ 7.34(7.27 + 0.07) [observed chemical shift = δ 7.24 − 7.43], and the *para* hydrogens (hydrogen ***d***) have a calculated chemical shift of δ 7.49(7.27 + 0.20) [observed chemical shift = δ 7.24 − 7.43].



The ^{13}C NMR spectrum (Figure 6.20) is analyzed next. From the equation in Section 6.4.1 and Tables 6.8 and 6.9, the CH_2 (carbon ***b***) has a calculated chemical shift of δ 56.9(5.9 + 51) [observed chemical shift = δ 60.43] and the CH_3, (carbon ***a***) has a calculated chemical shift of δ 11.9(5.9 + 6) [observed chemical shift = δ 13.81]. For

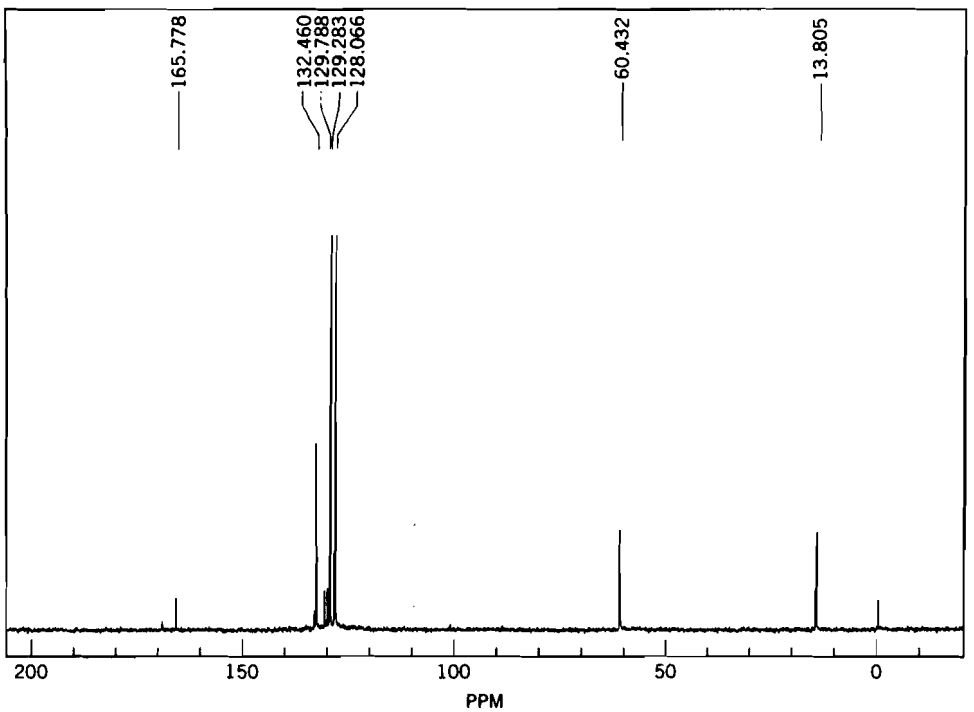
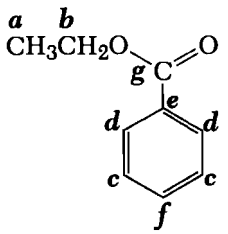


Figure 6.20 ^{13}C NMR spectrum of unknown ester, $C_9H_{10}O_2$. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

the aromatic carbons (Table 6.11), the calculated chemical shifts of the substituted carbon (carbon ***e***) is δ 130.7(128.7 + 2.0) [observed chemical shift = δ 129.79], the *ortho* carbons (carbons ***d***) are δ 129.9(128.7 + 1.2) [observed chemical shift = δ 129.28], the *meta* carbons (carbons ***c***) are δ 128.6(128.7 − 0.1)[observed chemical shift = δ 128.07], and the *para* carbon (carbon ***f***) is δ 133.5(128.7 + 4.8) [observed chemical shift = δ 132.46]. The carbonyl carbon (carbon ***g***) has an observed chemical shift at δ 165.78.



The next problem is a compound of formula $C_9H_{11}NO_2$. The unsaturation number gives a value of 5[U = 9 + 1 − $\frac{1}{2}$(11) + $\frac{1}{2}$(1)], which probably indicates a benzene ring plus a double bond or ring. Integration from the ^1H NMR spectrum (Figure 6.21) indicates 3H(δ 1.29), 2H(δ 4.24), 2H(δ 5.92), 2H(δ 6.66), and 2H(δ 7.74). The triplet and quartet, with the integration of 3H and 2H, are indicative of an ethyl group. The two doublets (δ 6.66 and δ 7.74) in the aromatic range show that the structure is a *para*-disubstituted aromatic ring. The broad singlet at δ 5.97 can be either an —OH, —NH,

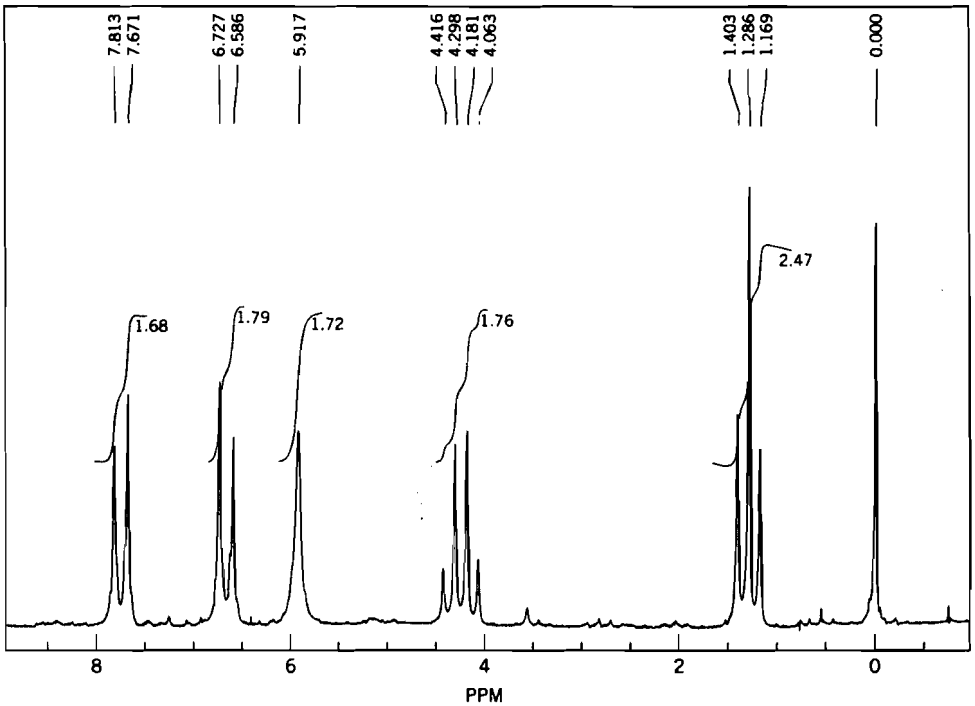
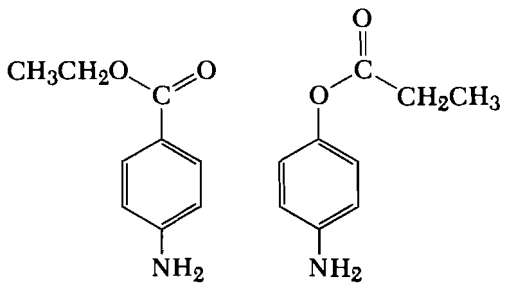


Figure 6.21 ^{1}H NMR spectrum of unknown compound, $C_9H_{11}NO_2$. [Compound courtesy of the Department of Chemistry, Roanoke College, Salem, Virginia. Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

or $-NH_2$. Given that the integration is 2H, it should be an NH_2. Two structures are possible:



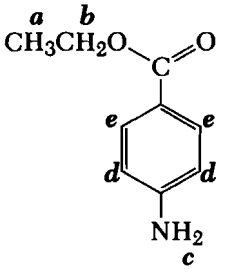
ethyl 4-aminobenzoate (benzocaine)

4-aminophenyl propanoate

From the calculations described in Section 6.3.1 and Table 6.4, the methylene group has a calculated chemical shift of δ 4.3(1.2 + 3.1) in benzocaine and a calculated chemical shift of δ 2.3(1.2 + 1.1) in 4-aminophenyl propanoate. The quartet for the CH_2 (hydrogens ***b***) has a chemical shift centered at δ 4.24, so the compound must be benzocaine. The triplet of the CH_3 (hydrogens ***a***) has a calculated chemical shift at δ 1.3 (0.9 + 0.4) [observed chemical shift = δ 1.29].

From Table 6.6, the hydrogens *ortho* to the ester (hydrogens ***d***) have a calculated chemical shift of δ 7.77(7.27 + 0.74 − 0.24) [observed chemical shift = δ 7.74], and the

hydrogens *ortho* to the amino group (hydrogens ***e***) have a calculated chemical shift of δ 6.59(7.27 + 0.07 − 0.75) [observed chemical shift = δ 6.66].



The ^{13}C NMR spectrum (Figure 6.22) is analyzed next. From the equation in Section 6.4.1 and Tables 6.8 and 6.9, the CH_2 (carbons ***b***) has a calculated chemical shift of δ 56.9(5.9 + 51) [observed chemical shift = δ 59.29] and the CH_3 (carbons ***a***) has a calculated chemical shift of δ 11.9(5.9 + 6) [observed chemical shift = δ 14.08]. For the aromatic carbons (Table 6.11), the calculated chemical shift of the carbon substituted with the ester (carbon ***d***) is δ 120.9(128.7 + 2.0 − 9.8) [observed chemical shift = 116.20], the carbons *ortho* to the ester (carbons ***e***) are δ 130.8(128.7 + 1.2 + 0.9) [observed chemical shift = δ 130.90], the carbons *ortho* to the amino group (carbon ***c***) are δ 115.3(128.7 − 13.3 − 0.1) [observed chemical shift = δ 112.52], and the carbon substituted with the amino group (carbon ***f***) is δ 151.5(128.7 + 18.0 + 4.8) [observed

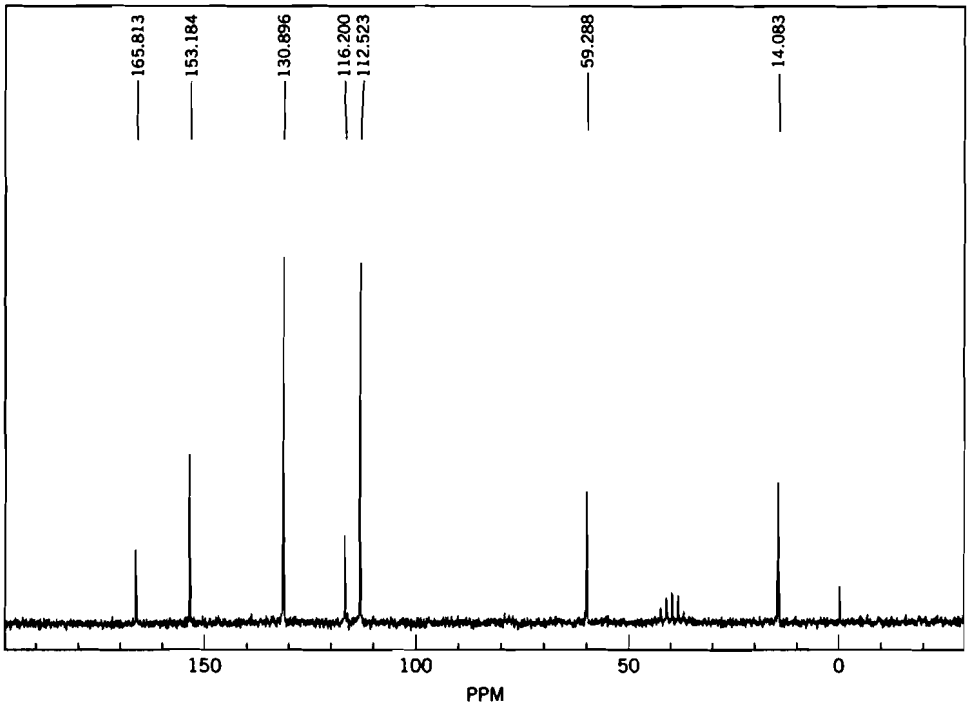
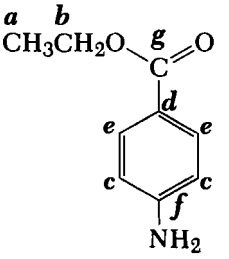


Figure 6.22 ^{13}C NMR spectrum of unknown compound, $C_9H_{11}NO_2$. [Compound courtesy of the Department of Chemistry, Roanoke College, Salem, Virginia. Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

chemical shift = δ 153.18]. The observed chemical shift of the carbonyl carbon is at δ 165.81.



Problem

1. Identify all of the peaks in the ^{1}H NMR (Figure 6.23) and ^{13}C NMR (Figure 6.24) spectra of a compound with a formula of C_3H_6BrCl. Give the structure. By using the methods described thus far, calculate the chemical shift of each hydrogen and carbon.

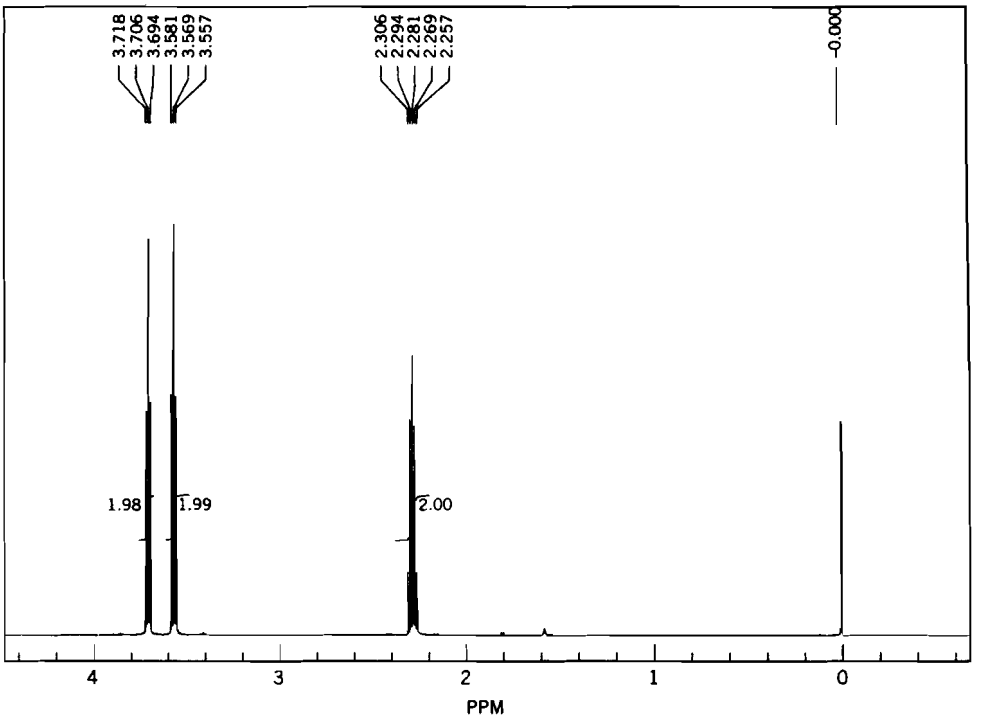


Figure 6.23 Problem 1 ^{1}H NMR spectrum of unknown compound, C_3H_6BrCl. The spectrum was obtained on a JEOL Eclipse 500 spectrometer. [Spectrum courtesy of Geno Iannaccone, Department of Chemistry, Virginia Tech, Blacksburg, Virginia. Used with permission.]

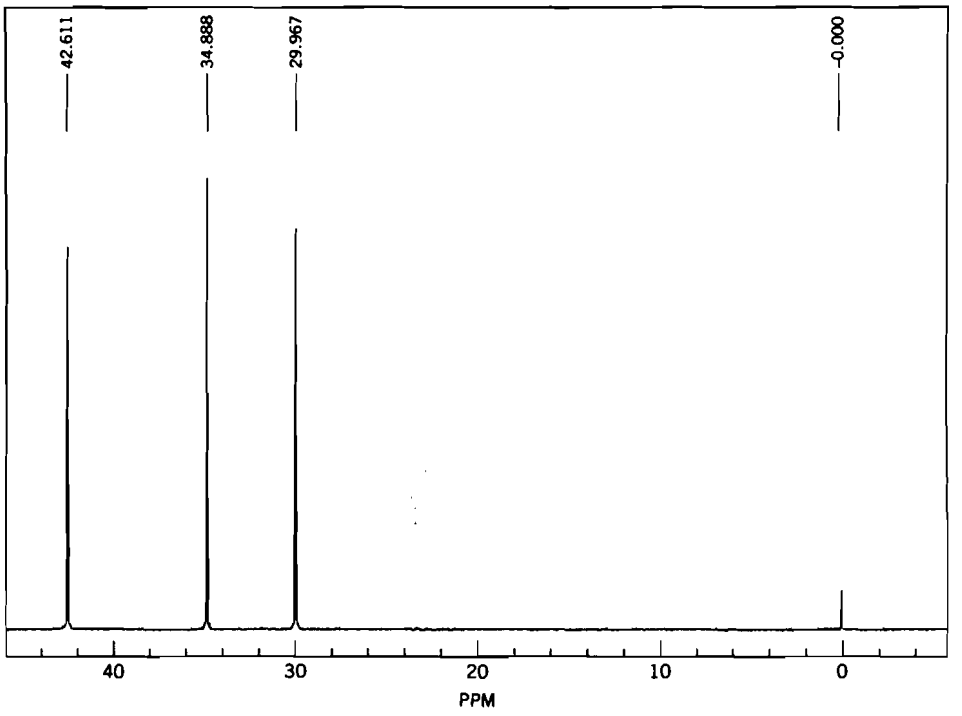


Figure 6.24 **Problem 1** ^{13}C NMR spectrum of unknown compound, C_3H_6BrCl. The spectrum was obtained on a JEOL Eclipse 500 spectrometer. [Spectrum courtesy of Geno Iannaccone, Department of Chemistry, Virginia Tech, Blacksburg, Virginia. Used with permission.]

6.5 DEPT

In a distortionless enhancement by polarization transfer (DEPT) spectrum, CH_3, CH_2, CH, and C can be distinguished. A proton pulse is set at 45°, 90°, and 135° in three separate experiments (Figure 6.25). DEPT spectra are presented in two basic ways. In one type of DEPT spectra, the methyls are positive at 135°, zero at 90°, and positive at 45°; methylenes are negative at 135°, zero at 90°, and positive at 45°; and the methines are positive at 135°, positive at 90°, and positive at 45°. In a second type of DEPT spectra, separate spectra are obtained for the methyls, methylenes, and methines.

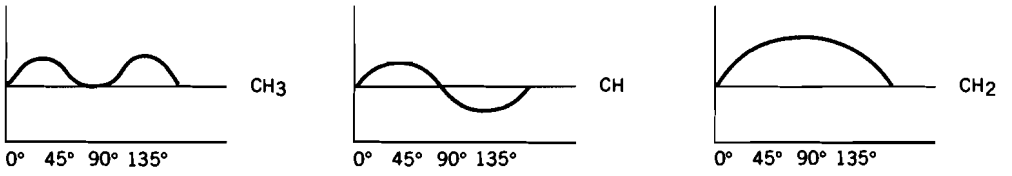


Figure 6.25 DEPT signal as a function of the variable pulse angle.

The DEPT spectrum of benzocaine is shown in Figure 6.26. On this type of DEPT spectrum, the 135° spectrum is on the top, the 90° spectrum is in the middle, and the

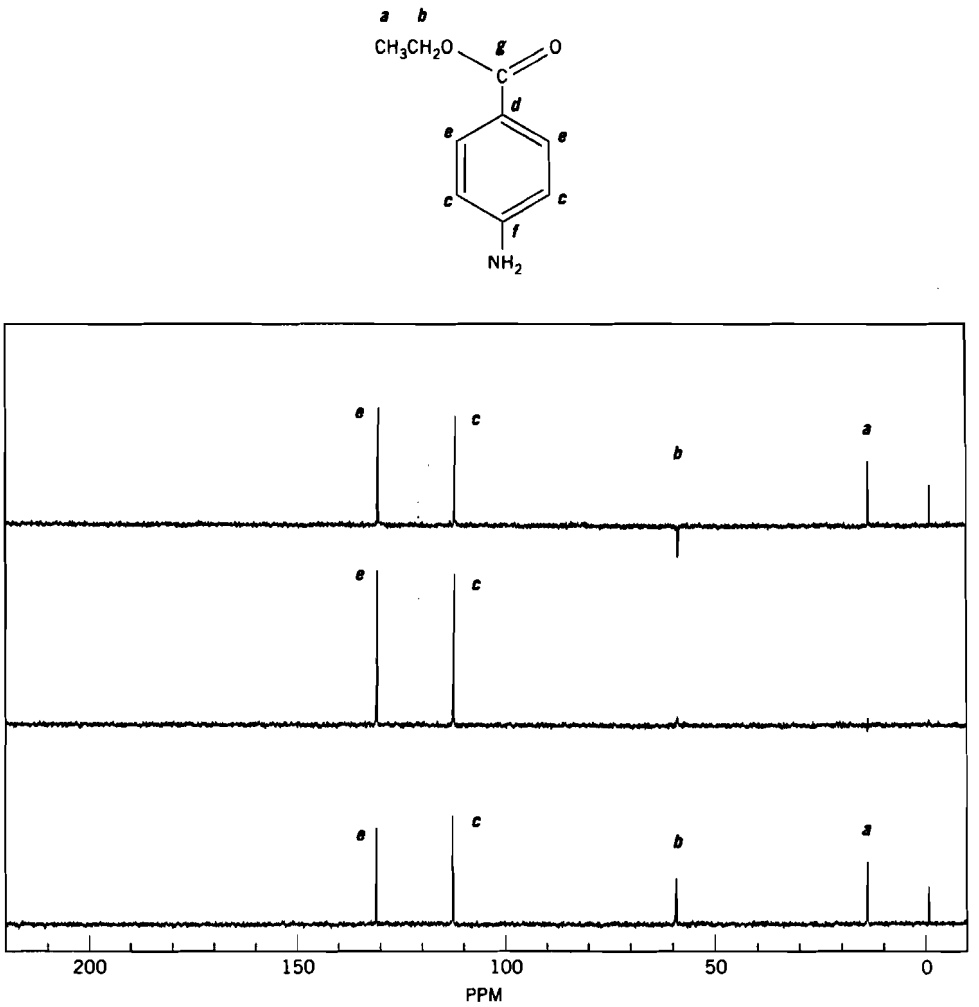


Figure 6.26 DEPT spectrum of benzocaine. [Compound courtesy of the Department of Chemistry, Roanoke College, Salem, Virginia. Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

45° spectrum is on the bottom. This spectrum should be compared with the ^{13}C NMR spectrum in Figure 6.22. In the ^{13}C NMR spectrum, there are peaks at δ 14.08, δ 59.29, δ 112.52, δ 116.20, δ 130.90, δ 153.18, and δ 165.81. The peak at δ 14.08 (carbons ***a***) is identified as a CH_3, since the peaks are positive in the top and bottom spectra. The peak at δ 59.29 (carbons ***b***) is identified as a CH_2, since the peak is negative in the top spectrum and positive in the bottom spectrum. The peaks at δ 112.52 (carbons ***c***) and δ 130.90 (carbons ***e***) are identified as CH, since the peak is positive in all three spectra. The peaks at δ 116.20 (carbon ***d***), δ 153.18 (carbon ***f***), and δ 165.81 (carbon ***g***) are not present because these carbons do not contain any hydrogens.

The DEPT spectrum of butanoic acid is shown in Figure 6.27. From the ^{13}C NMR spectrum (Figure 6.16), peaks are present at δ 12.29, δ 17.24, δ 34.88, and δ 179.28. By using the DEPT spectrum, the peak at δ 12.29 (carbon ***a***) is identified as a CH_3; the peaks at δ 17.24 (carbon ***b***) and δ 34.88 (carbon ***c***) are CH_2; and the peak at δ 179.28 (carbon ***d***) is a C.

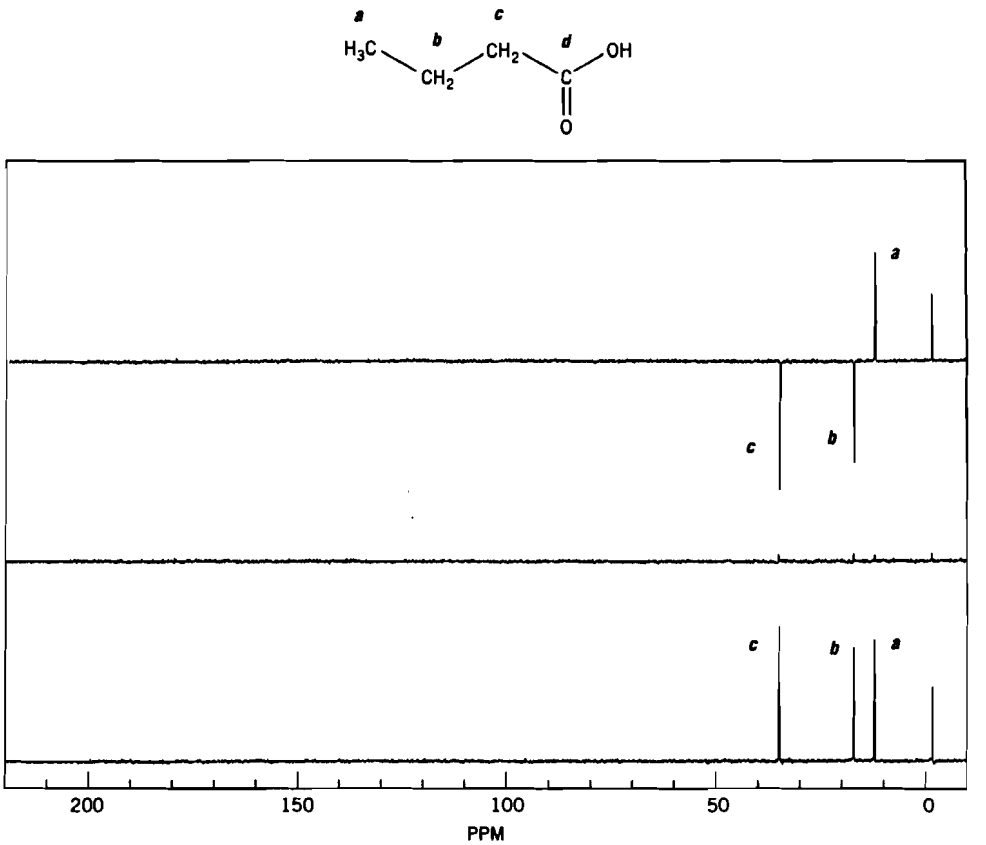


Figure 6.27 DEPT spectrum of butanoic acid. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

▶ Problems

2. Calculate the unsaturation number and list possibilities for a compound with a formula of $C_5H_{12}O$. Give the structure and identify all of the peaks in the ^{13}C (Figure 6.28) and DEPT (Figure 6.29) spectra. Calculate the carbon chemical shifts.
3. Calculate the unsaturation number and list possibilities for a compound with a formula of $C_4H_{10}O_2$. Give the structure and identify all of the peaks in the ^{1}H (Figure 6.30), ^{13}C (Figure 6.31), and DEPT (Figure 6.32) spectra. Calculate the hydrogen and carbon chemical shifts.
4. Calculate the unsaturation number and list possibilities for a compound with a formula of $C_5H_{10}O$. Give the structure and identify all of the peaks in the ^{1}H (Figure 6.33), ^{13}C (Figure 6.34), and DEPT (Figure 6.35) spectra. Calculate the hydrogen and carbon chemical shifts.

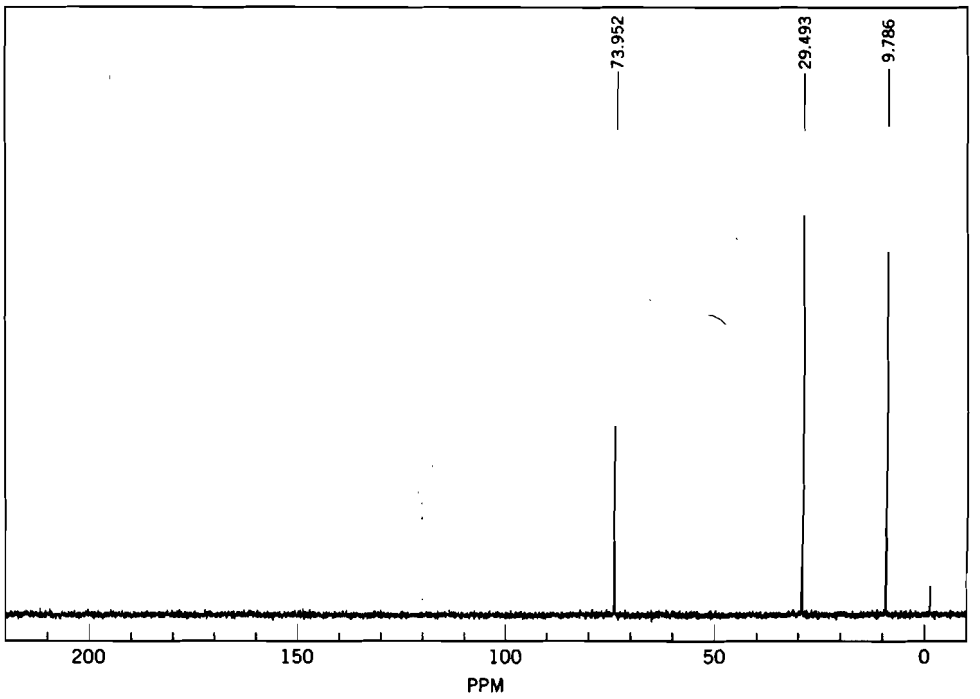


Figure 6.28 **Problem 2** ^{13}C NMR spectrum of unknown compound, $C_5H_{12}O$. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

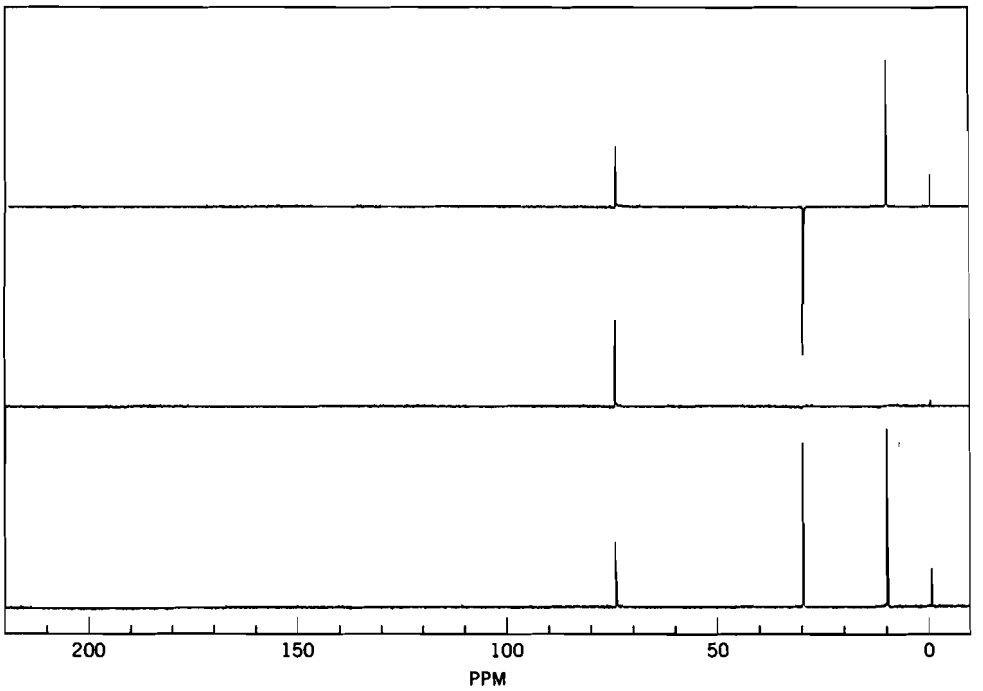


Figure 6.29 **Problem 2** DEPT spectrum of unknown compound, $C_5H_{12}O$. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

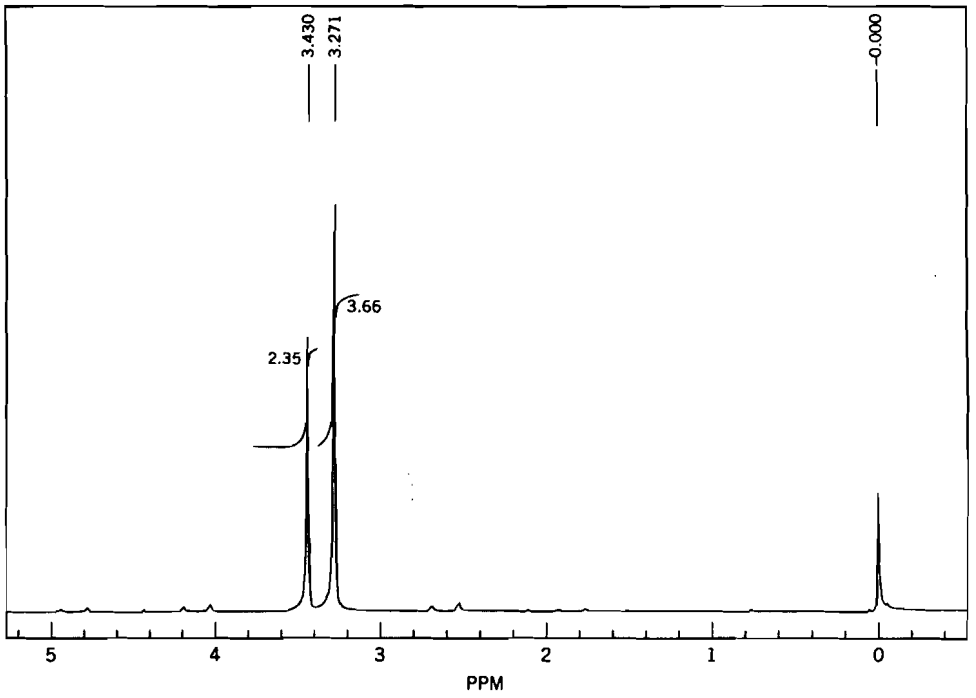


Figure 6.30 **Problem 3** ^{1}H NMR spectrum of unknown compound, $C_4H_{10}O_2$. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

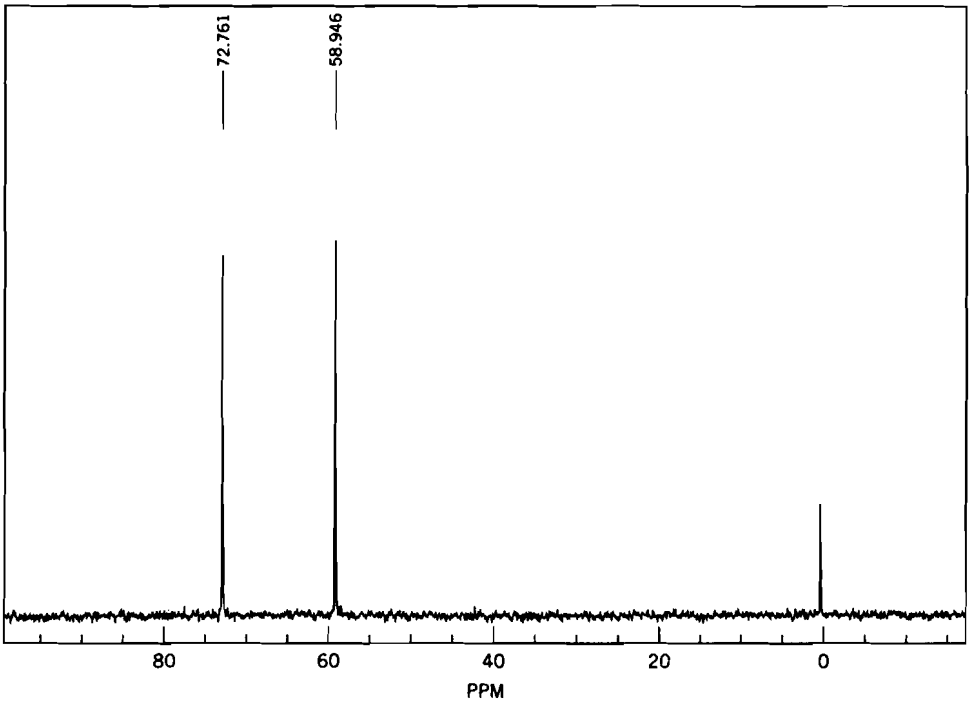


Figure 6.31 **Problem 3** ^{13}C NMR spectrum of unknown compound, $C_4H_{10}O_2$. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

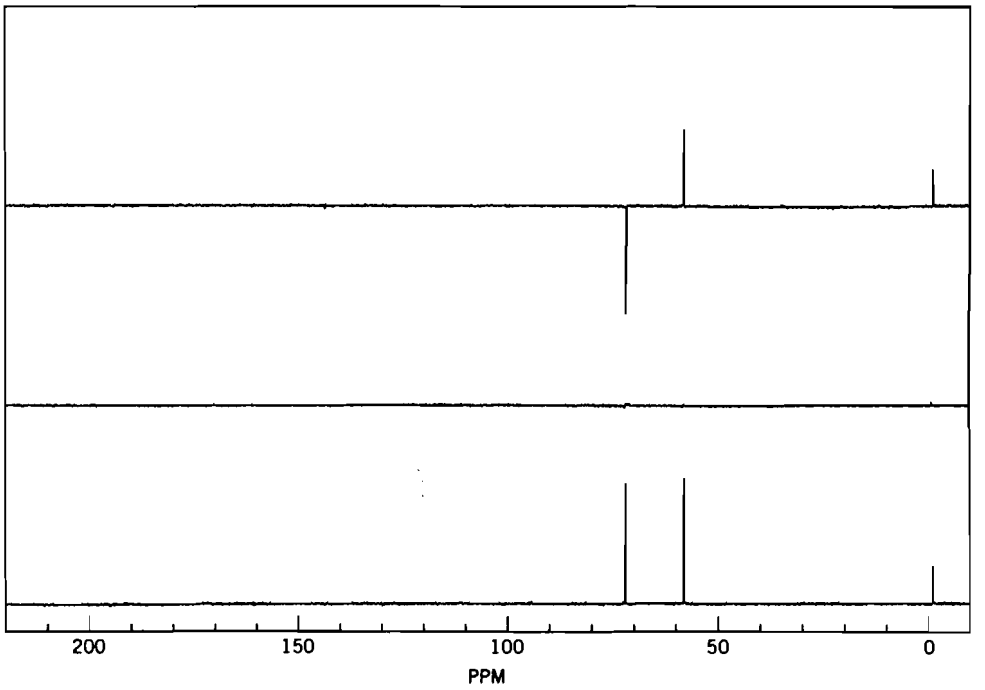


Figure 6.32 **Problem 3** DEPT spectrum of unknown compound, $C_4H_{10}O_2$. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

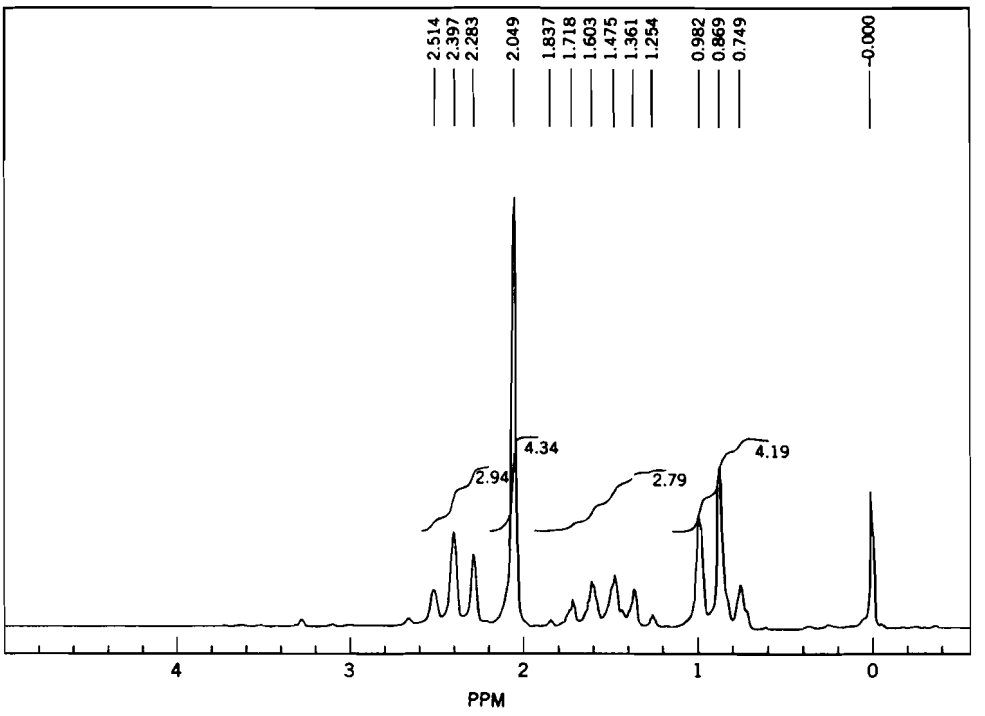


Figure 6.33 **Problem 4** ^1H NMR spectrum of unknown compound, $C_5H_{10}O$. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

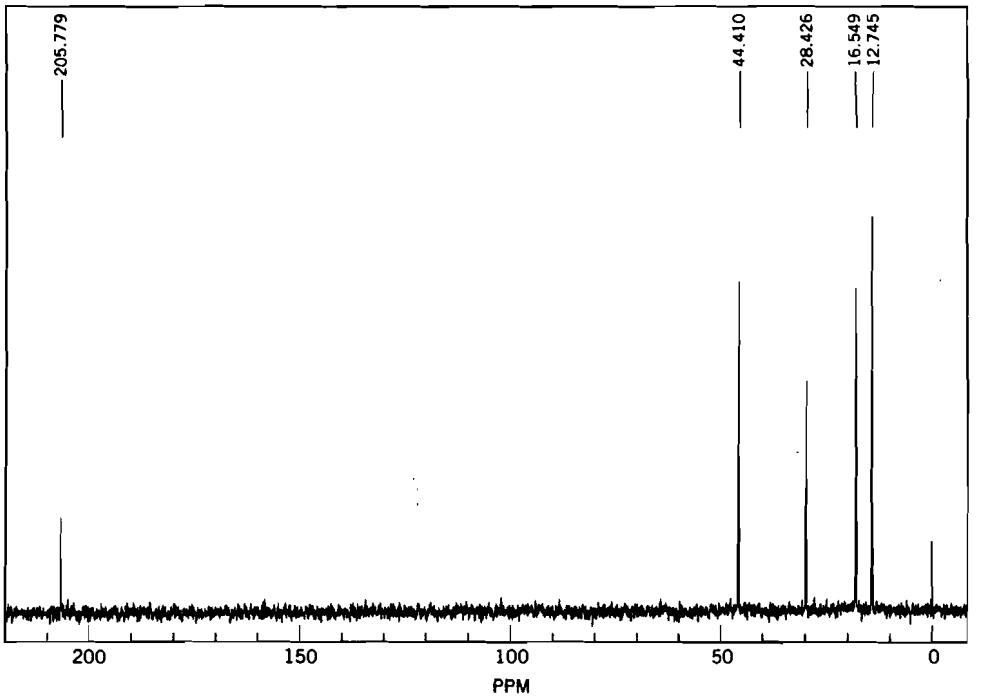


Figure 6.34 **Problem 4** ^{13}C NMR spectrum of unknown compound, $C_5H_{10}O$. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

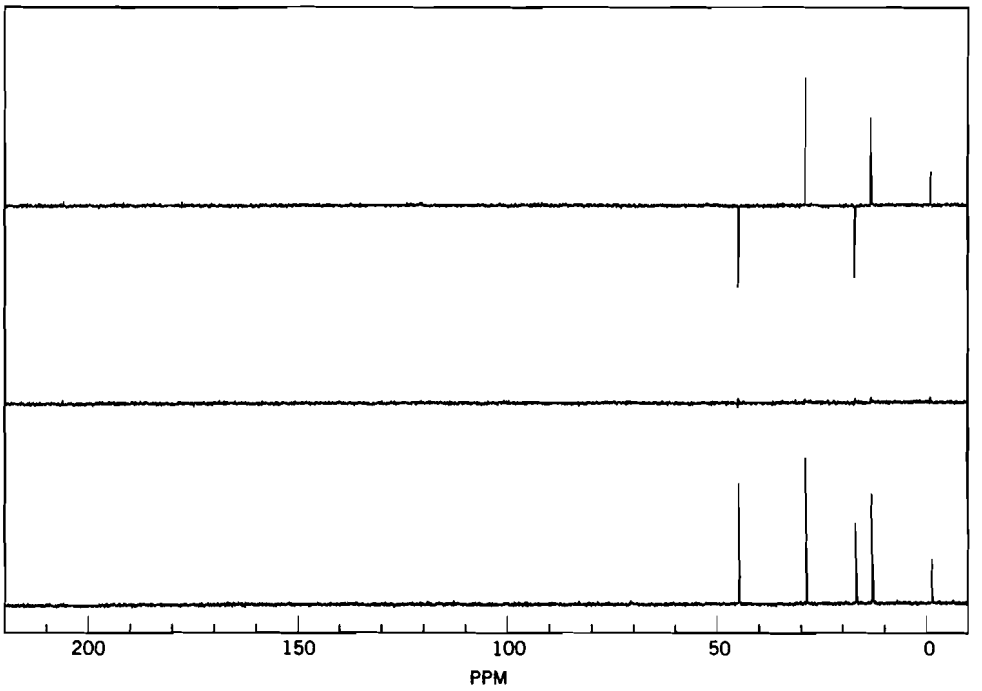


Figure 6.35 **Problem 4** DEPT spectrum of unknown compound, $C_5H_{10}O$. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

6.6 COSY

Homonuclear shift correlation spectroscopy (COSY) indicates which hydrogens are coupled to other hydrogens. Each axis is a one-dimensional ^{1}H NMR spectrum. The diagonal (upper right to lower left) indicates the correlation of a signal with itself, so these spots are ignored. The off-diagonal signals provide the useful information. Examination of a COSY spectrum (Figure 6.36) reveals that the upper left and lower right spots are symmetrical from the diagonal. These off-diagonal peaks are correlated to each other to see which protons are adjacent to each other.

In the COSY spectrum of butanoic acid (Figure 6.36), the ^{1}H NMR spectrum (Figure 6.13) can be seen on the top and left axes. Chemical shifts are on the right and bottom axes. The data can be placed in tabular form and then compared with the structure:

	(c) 2.30	*(b)* 1.65	*(a)* 0.95
(a) 0.95		x	
(b) 1.65	x		
(c) 2.30			

Hydrogen ***a*** is adjacent to hydrogen ***b***, and hydrogen ***b*** is adjacent to hydrogen ***c***. This correlation agrees with the identification of the hydrogens done in Section 6.3.3.

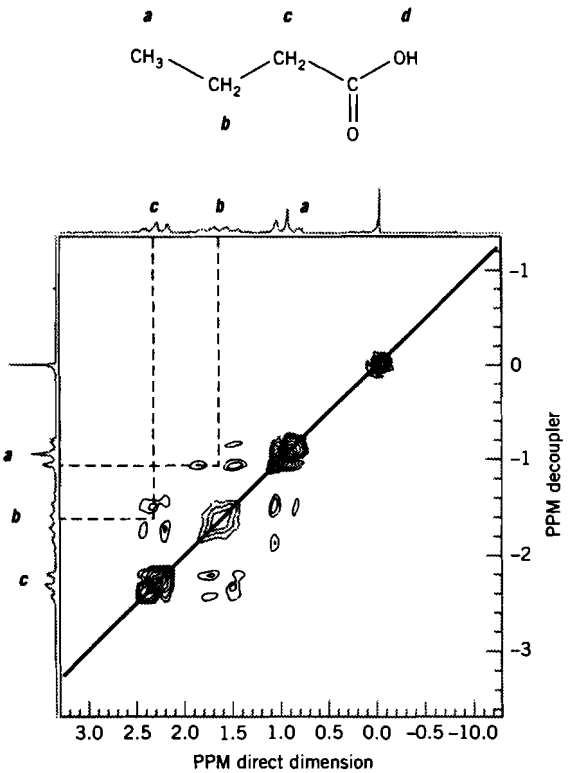


Figure 6.36 COSY spectrum of butanoic acid. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

From the COSY spectrum of benzocaine (Figure 6.37), the following correlations can be determined. Hydrogen ***a*** is adjacent to hydrogen ***b*** and hydrogen ***d*** is adjacent to hydrogen ***e***. This correlation agrees with the identification of the hydrogens done in Section 6.4.2.

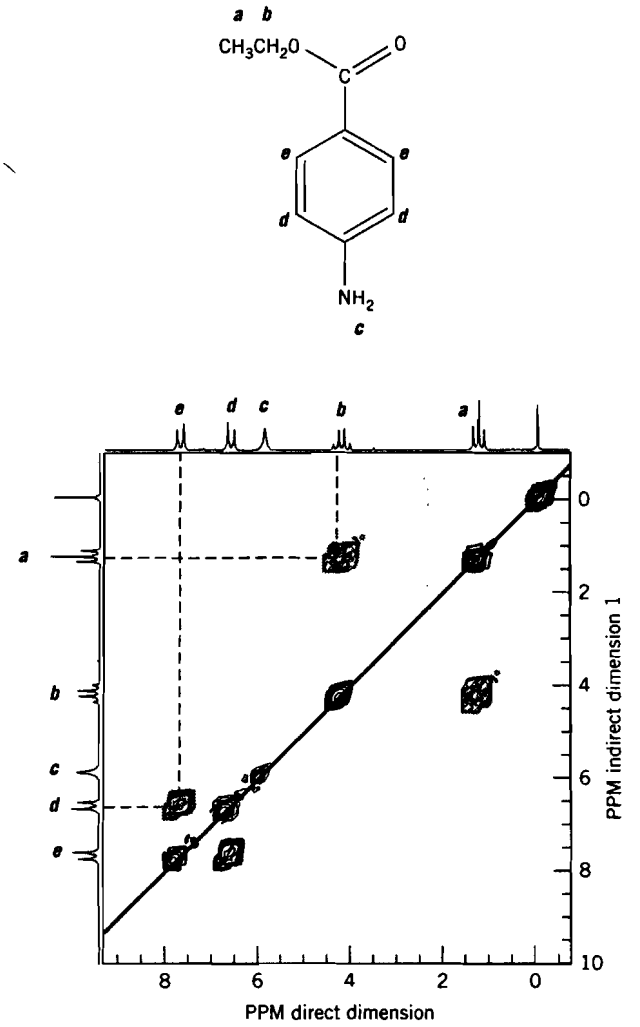


Figure 6.37 COSY spectrum of benzocaine. [Compound courtesy of the Department of Chemistry, Roanoke College, Salem, Virginia. Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

6.7 HETCOR

Heteronuclear correlation spectroscopy (HETCOR) gives the correlation between protons and carbons that are directly attached to each other. The ^{13}C NMR spectrum is shown along the top, and the ^{1}H NMR spectrum is shown along the left side. The chemical shifts for carbon are shown along the bottom, and the chemical shifts for hydrogen are shown along the right side. An equivalent type of 2-D NMR spectroscopy is heteronuclear multiple quantum coherence (HMQC). In HMQC, the ^{1}H NMR spectrum is along the top, with the proton chemical shift along the bottom, the ^{13}C NMR spectrum along the left side, and the carbon chemical shift along the right side. Both HETCOR and HMQC give the same information.

Dashed lines can be drawn to correlate the ^1H NMR spectrum with the ^{13}C NMR spectrum, as shown in the HETCOR spectrum of butanoic acid (Figure 6.38). The results are summarized as follows:

	^{13}C *(c)* 34.88	*(b)* 17.24	*(a)* 12.29
^1H			
(a) 0.95			x
(b) 1.65		x	
(c) 2.30	x		

Hydrogens ***a*** are attached to carbon ***a***, hydrogens ***b*** are attached to carbon ***b***, and hydrogens ***c*** are attached to carbon ***c***.

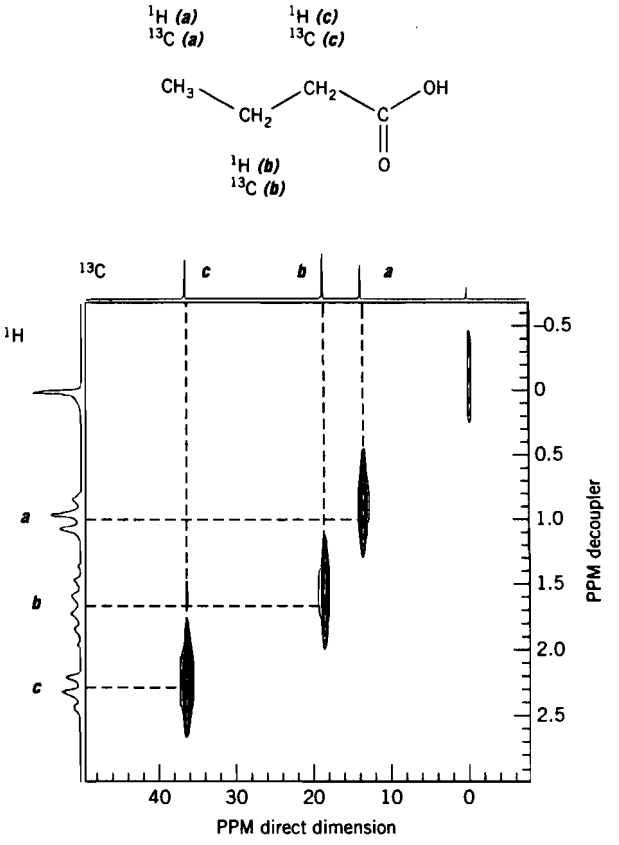


Figure 6.38 HETCOR spectrum of butanoic acid. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

From the HETCOR spectrum of benzocaine (Figure 6.39), the following correlations can be determined. Hydrogens ***a*** are attached to carbon ***a***, hydrogens ***b*** are attached

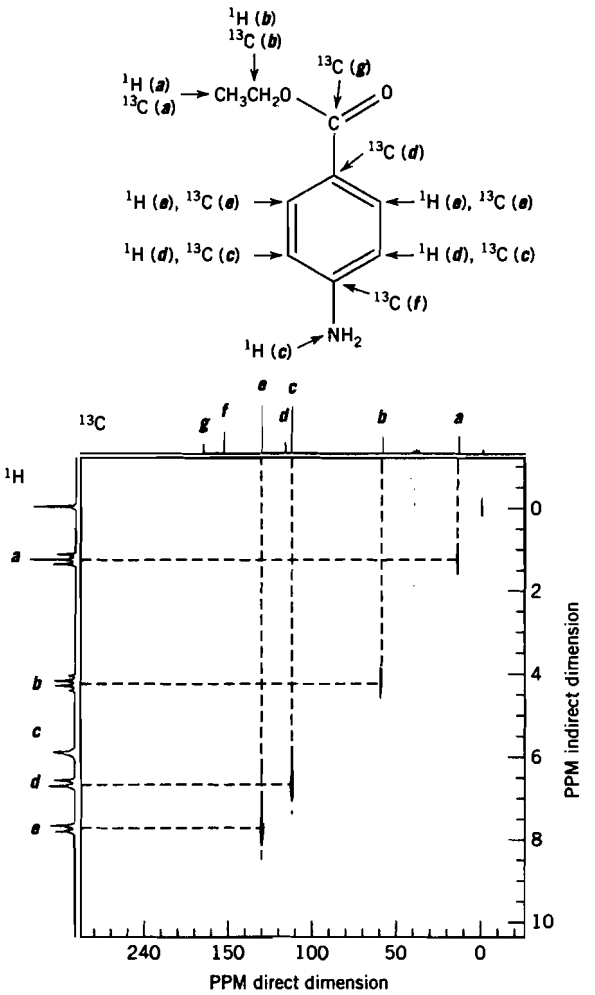


Figure 6.39 HETCOR spectrum of benzocaine. [Compound courtesy of the Department of Chemistry, Roanoke College, Salem, Virginia. Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

to carbon ***b***, hydrogens ***d*** are attached to carbons ***c***, and hydrogens ***e*** are attached to carbons ***e***. Hydrogens ***c*** are an amino group and are not attached to a carbon. Carbons ***d***, ***f***, and ***g*** do not have any hydrogens attached to them.

The next problem incorporates all of the spectra discussed so far. A compound with a formula of $C_5H_8O_2$ gave the spectra shown in Figures 6.40 through 6.46. The unsaturation number is calculated to be $2[U = 5 + 1 - \frac{1}{2}(8) + \frac{1}{2}(0)]$, which may be two double bonds, two rings, a triple bond, or a ring plus a double bond. Tables can be made up for each spectra and the tables combined to deduce a structure.

The ^1H NMR data are summarized from Figures 6.40 through 6.42 and Table 6.3:

	chemical shift	splitting	integration	interpretation
(a)	1.90	d of d	3H	CH_3, allylic
(b)	3.70	s	3H	CH_3, —OR of ester
(c)	5.54	5 peaks	1H	CH, alkene
(d)	6.04	6 peaks	1H	CH, alkene

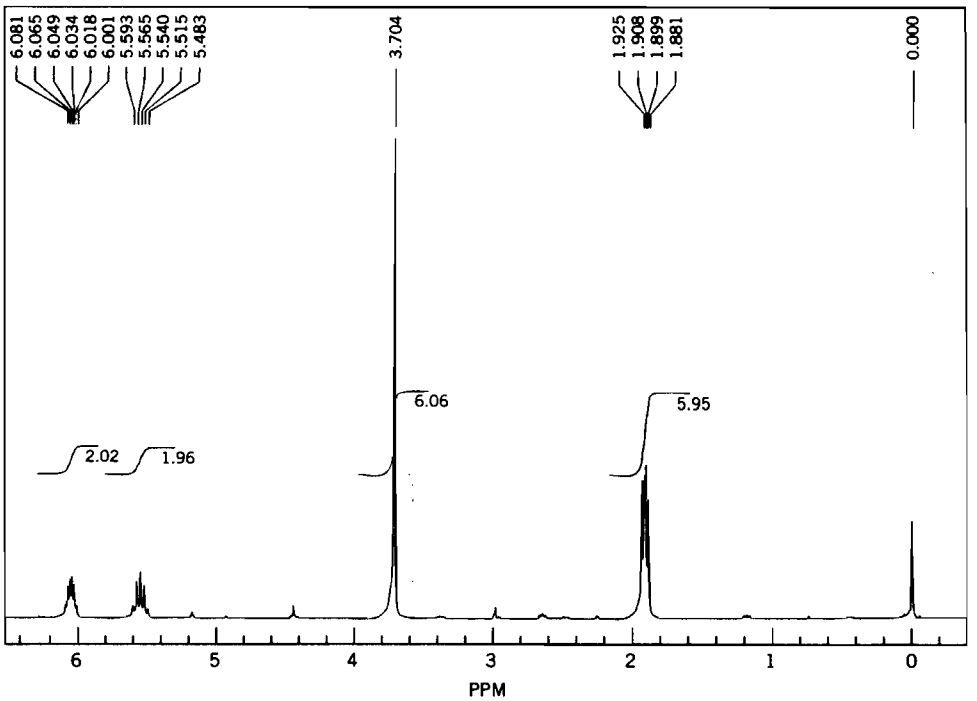


Figure 6.40 ^{1}H NMR spectrum of unknown compound, $C_5H_8O_2$. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

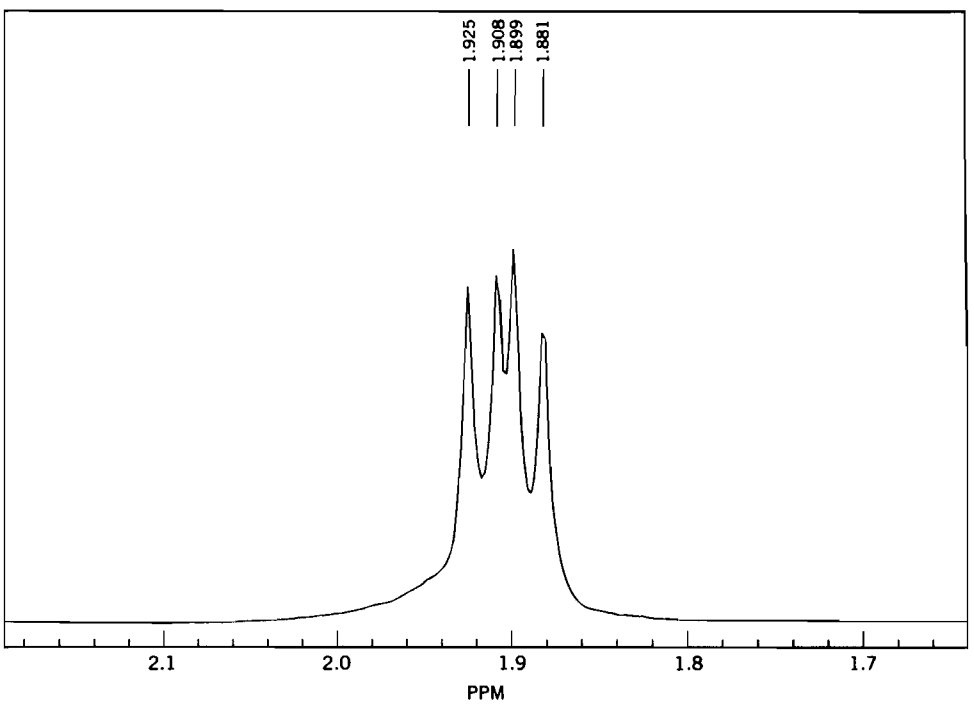


Figure 6.41 Expanded region of δ 1.7 to 2.1 for ^{1}H NMR spectrum of unknown compound, $C_5H_8O_2$. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

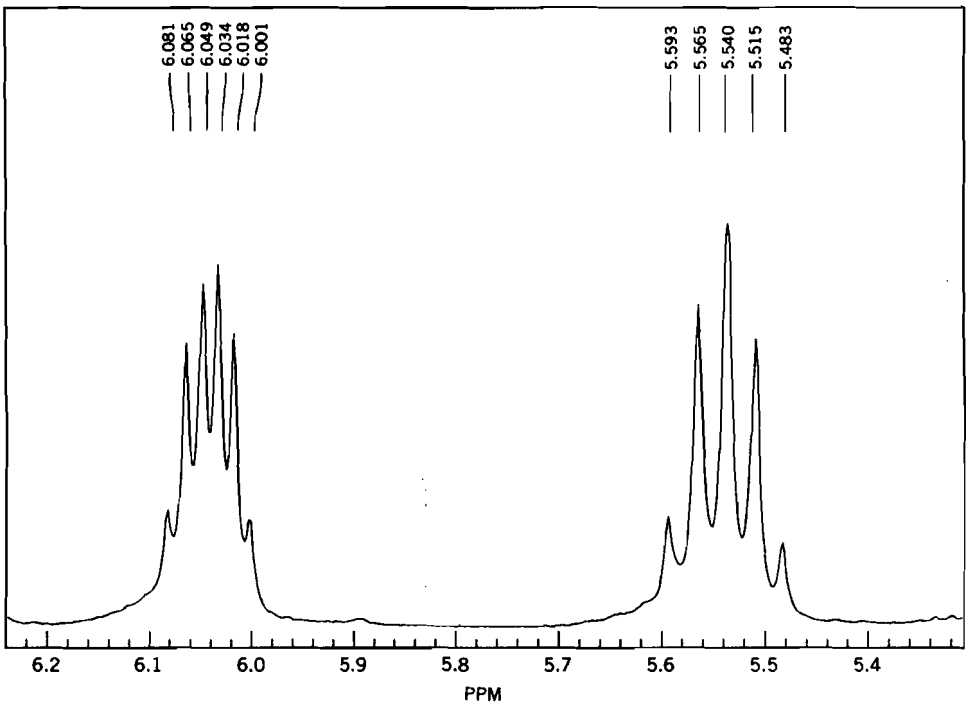


Figure 6.42 Expanded region of δ 5.4 to 6.2 for ^{1}H NMR spectrum of unknown compound, $C_5H_8O_2$. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

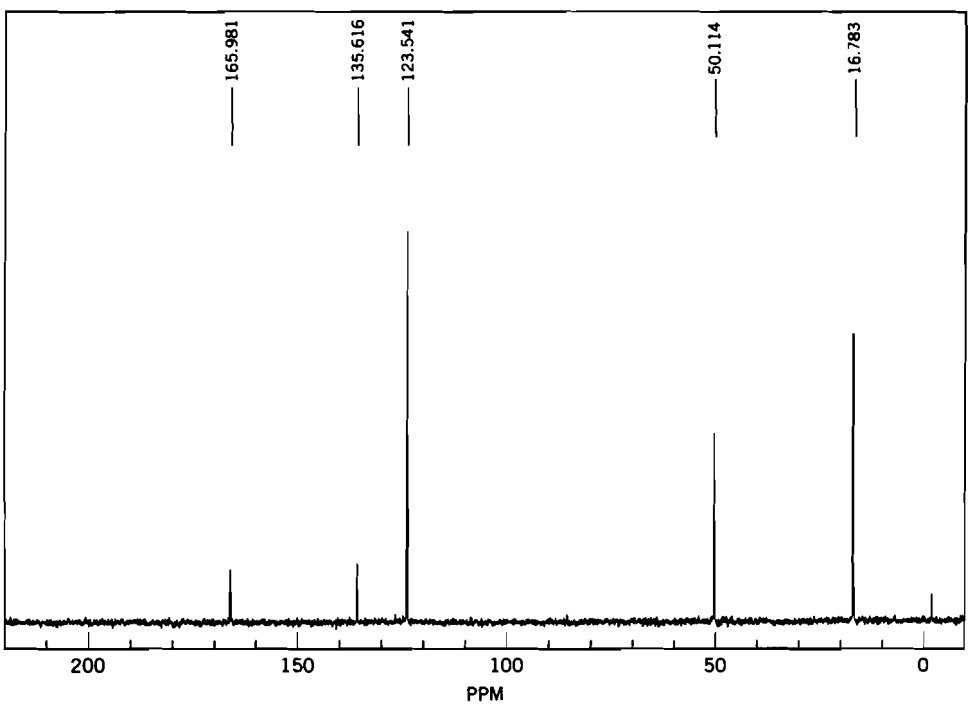


Figure 6.43 ^{13}C NMR spectrum of unknown compound, $C_5H_8O_2$. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

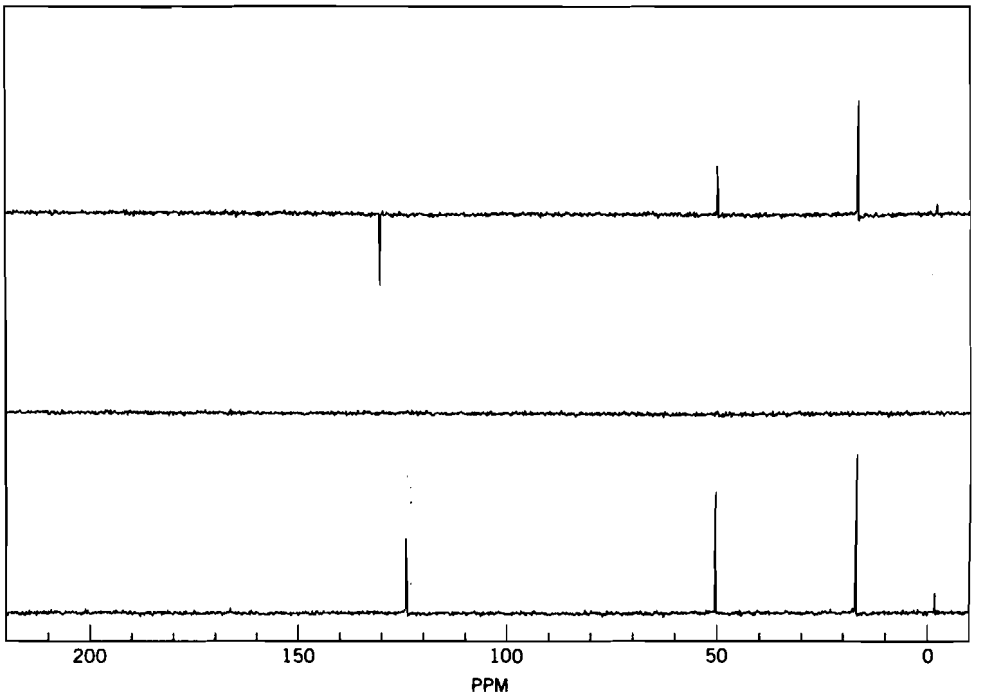


Figure 6.44 DEPT spectrum of unknown compound, $C_5H_8O_2$. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

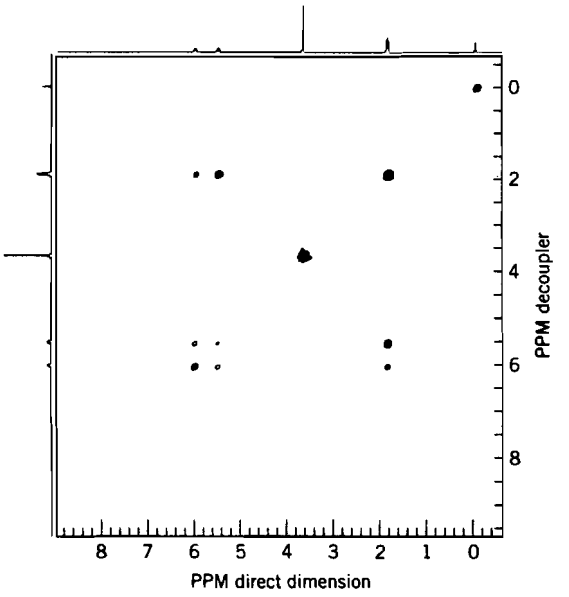


Figure 6.45 COSY spectrum of unknown compound, $C_5H_8O_2$. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

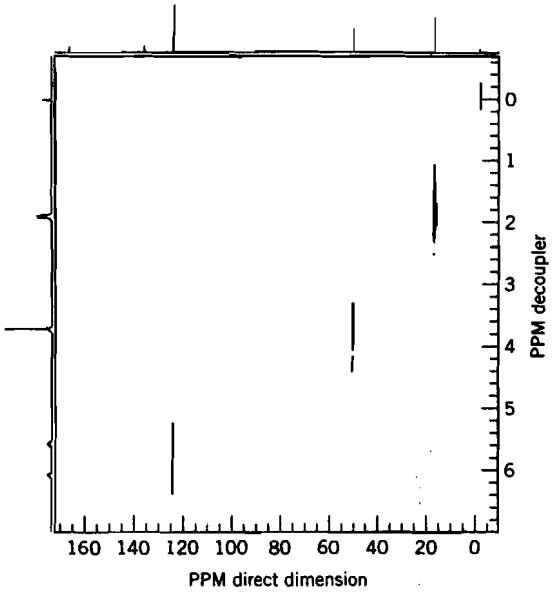


Figure 6.46 HETCOR spectrum of unknown compound, $C_5H_8O_2$. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

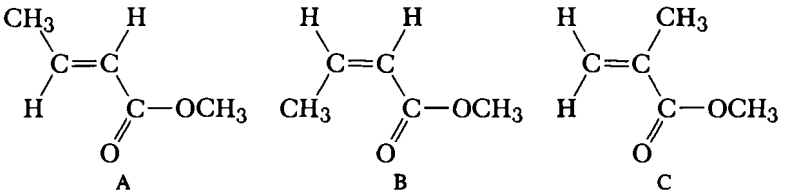
The ^{13}C NMR data are summarized from Figures 6.43 and 6.44 and Table 6.7:

	chemical shift	DEPT	interpretation
(a)	16.78	CH_3	alkyl
(b)	50.11	CH_3	C next to O
(c)	123.54	CH_2	alkene
(d)	135.62	C	alkene
(e)	165.98	C	ester

From the COSY spectrum (Figure 6.45), hydrogens ***a*** are adjacent to hydrogens ***c*** and ***d***, and hydrogen ***c*** is adjacent to hydrogen ***d***.

From the HETCOR spectrum (Figure 6.46), hydrogens ***a*** are attached to carbon ***a***, hydrogens ***b*** are attached to carbon ***b***, hydrogens ***c*** and ***d*** are attached to carbon ***c***.

From the data, the structure must contain an alkene and an ester; the ester has a methyl next to the oxygen. Three structures are possible:

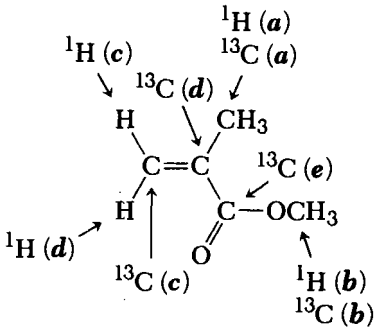


The HETCOR and the DEPT indicate the presence of a CH_2 that is part of an alkene carbon and another alkene carbon that has no hydrogens attached to it. Structure C, methyl methacrylate, must be the structure. The chemical shifts of the alkene hydrogens are calculated by using Table 6.5. The hydrogen (hydrogen ***c***) that is *cis* to the methyl has a calculated chemical shift of δ 5.58(5.28 − 0.26 + 0.56) [observed chemical shift = δ 5.54], and the hydrogen (hydrogen ***d***) that is *cis* to the ester has a calculated chemical shift of δ 6.14(5.28 − 0.29 + 1.15) [observed chemical shift = δ 6.04]. The

CH_3 attached directly to the alkene is split by both hydrogens ***c*** and ***d*** into a doublet of doublets. Hydrogens ***c*** and ***d*** are split by the CH_3 and are split by each other.

The chemical shifts of the alkene carbons are determined by using Table 6.10. The unsubstituted carbon (carbon ***c***) has a calculated chemical shift of δ 122.9 (123.3 − 7.4 + 7.0) [observed chemical shift = δ 123.54]; the substituted carbon (carbon ***d***) has a calculated chemical shift of δ 142.5(123.3 + 12.9 + 6.3) [observed chemical shift = δ 135.62].

The labeled structure is shown below.



6.8 2-D INADEQUATE

Incredible natural abundance double-quantum transfer experiment (2-D INADEQUATE) spectra shows the connectivity between adjacent carbons. The ^{13}C NMR spectrum and the carbon chemical shifts are along the left. If two carbons are adjacent to each other, then spots appear vertically. To make full use of this technique, the ^{13}C NMR and the DEPT spectra must be obtained first.

From the ^{13}C (Figure 6.47) and DEPT (Figure 6.48) spectra of limonene, there are six alkyl carbons and four alkene carbons. In this particular type of DEPT spectrum, the methyls show up only in the top spectrum, the methylenes appear only in the second spectrum, the methines appear only in the third spectrum, and the ^{13}C NMR spectrum is included for reference as the bottom spectrum. The alkyl carbons are at chemical shifts of δ 20.82 (CH_3, carbon ***a***); δ 23.51 (CH_3, carbon ***b***); δ 28.04 (CH_2, carbon ***c***); δ 30.71 (CH_2, carbon ***d***); δ 30.94 (CH_2, carbon ***e***); and δ 41.23 (CH, carbon ***f***). The alkene carbons are at chemical shifts of δ 108.52 (CH_2, carbon ***g***); δ 120.80 (CH, carbon ***h***); δ 133.62 (C, carbon ***i***); and δ 150.08 (C, carbon ***j***).

From the 2-D INADEQUATE spectrum (Figure 6.49), a spot aligned below two chemical shifts indicates that those carbons are connected to each other. A chart, similar to the HETCOR and the COSY spectra, can be drawn. From this data, the carbons on the structure can be drawn. The top part of the table corresponds to the chemical shift for the top spot, and the left part of the table corresponds to the chemical shift for the bottom spot.

	(j) 150.08	(i) 133.62	(h) 120.80	(g) 108.52	(f) 41.23	(e) 30.94	(d) 30.71	(c) 28.04	(b) 23.51	(a) 20.82
(a) 20.82										
(b) 23.51										
(c) 28.04										
(d) 30.71								x		
(e) 30.94										
(f) 41.23						x		x		
(g) 108.52										
(h) 120.80						x				
(i) 133.62			x				x		x	
(j) 150.08				x	x					x

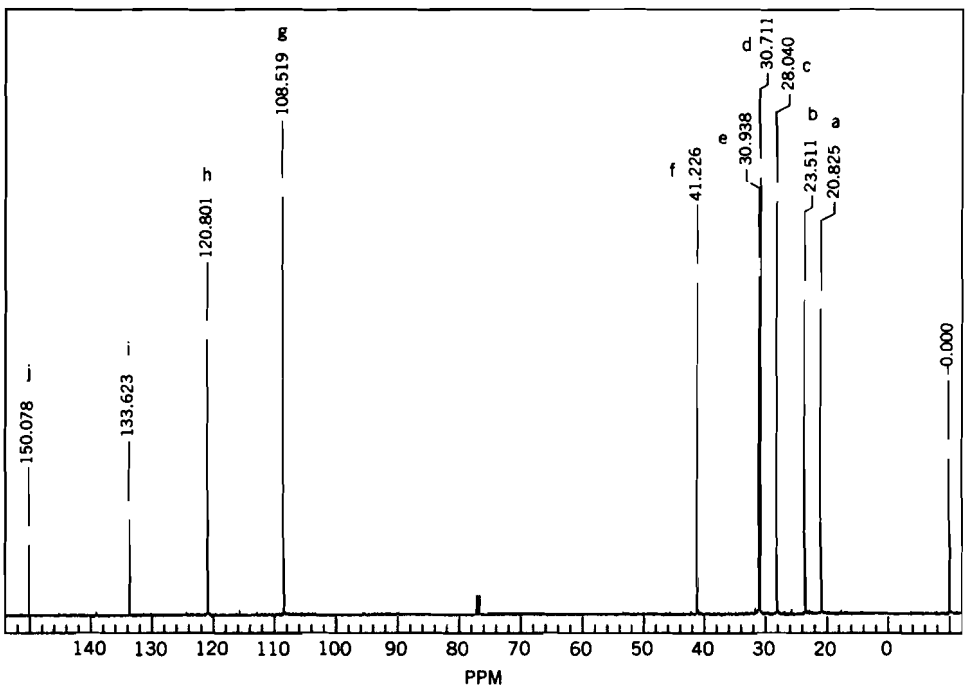


Figure 6.47 ^{13}C NMR spectrum of limonene. The spectrum was obtained on a Varian Unity 400 spectrometer. [Spectrum courtesy of Tom Glass, Department of Chemistry, Virginia Tech, Blacksburg, Virginia. Used with permission.]

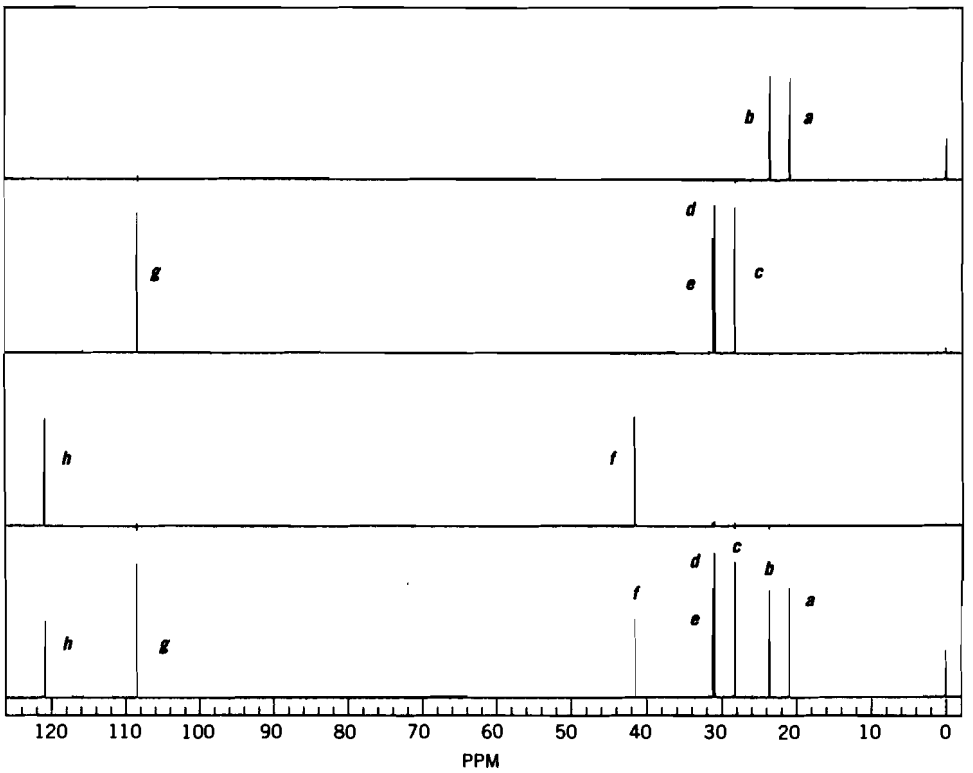


Figure 6.48 DEPT spectrum of limonene. The spectrum was obtained on a Varian Unity 400 spectrometer. [Spectrum courtesy of Tom Glass, Department of Chemistry, Virginia Tech, Blacksburg, Virginia. Used with permission.]

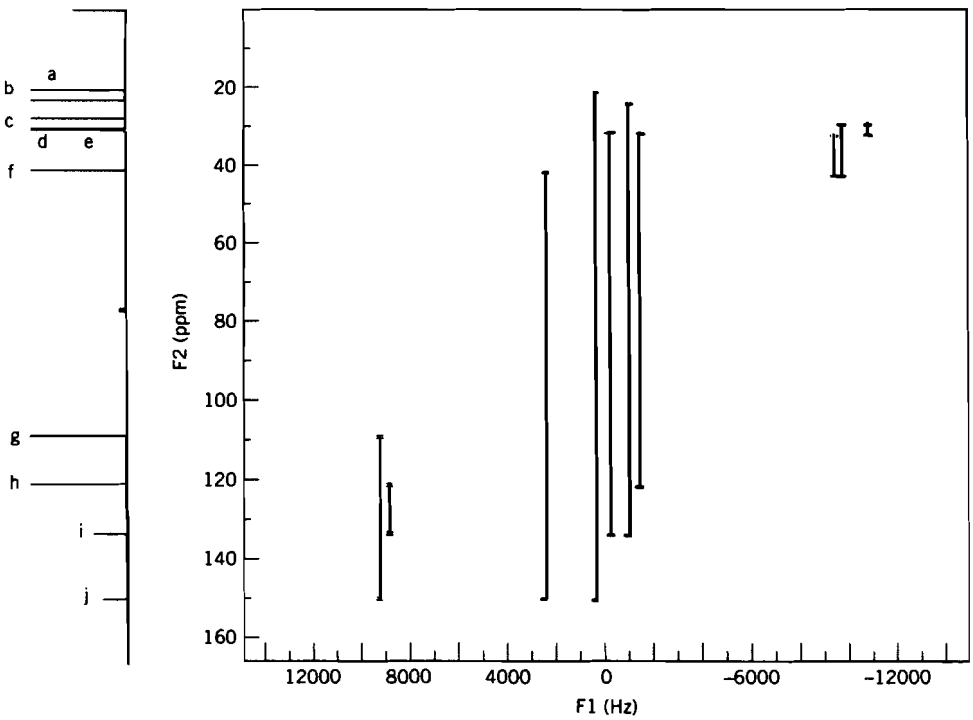
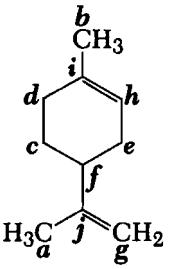


Figure 6.49 2-D INADEQUATE spectrum of limonene. The spectrum was obtained on a Varian Unity 400 spectrometer. [Spectrum courtesy of Tom Glass, Department of Chemistry, Virginia Tech, Blacksburg, Virginia. Used with permission.]

Putting the pieces together, it is best to start with a carbon whose position is known. Carbon ***g*** (CH_2) is attached to carbon ***j*** (C). Carbon ***j*** (C) is attached to carbons ***a*** (CH_3) and ***f*** (CH). Carbon ***f*** (CH) is attached to carbons ***c*** (CH_2) and ***e*** (CH_2). Carbon ***e*** (CH_2) is attached to carbon ***h*** (CH). Carbon ***h*** (CH) is attached to carbon ***i*** (C). Carbon ***d*** (CH_2) is between carbons ***c*** (CH_2) and ***i*** (C). Carbon ***i*** (C) is also attached to carbon ***b*** (CH_3).



▶ Problems

5. Calculate the unsaturation number and list possibilities for a compound with a formula of C_8H_9NO. Give the structure and identify all of the signals in the ^1H (Figure 6.50), ^{13}C (Figure 6.51), and DEPT (Figure 6.52) spectra. Give a table for the HETCOR (Figure 6.53) spectrum. Calculate the hydrogen and carbon chemical shifts.
6. Calculate the unsaturation number and list possibilities for a compound with a formula of $C_{10}H_{12}O_2$. Give the structure and identify all of the signals in the ^1H

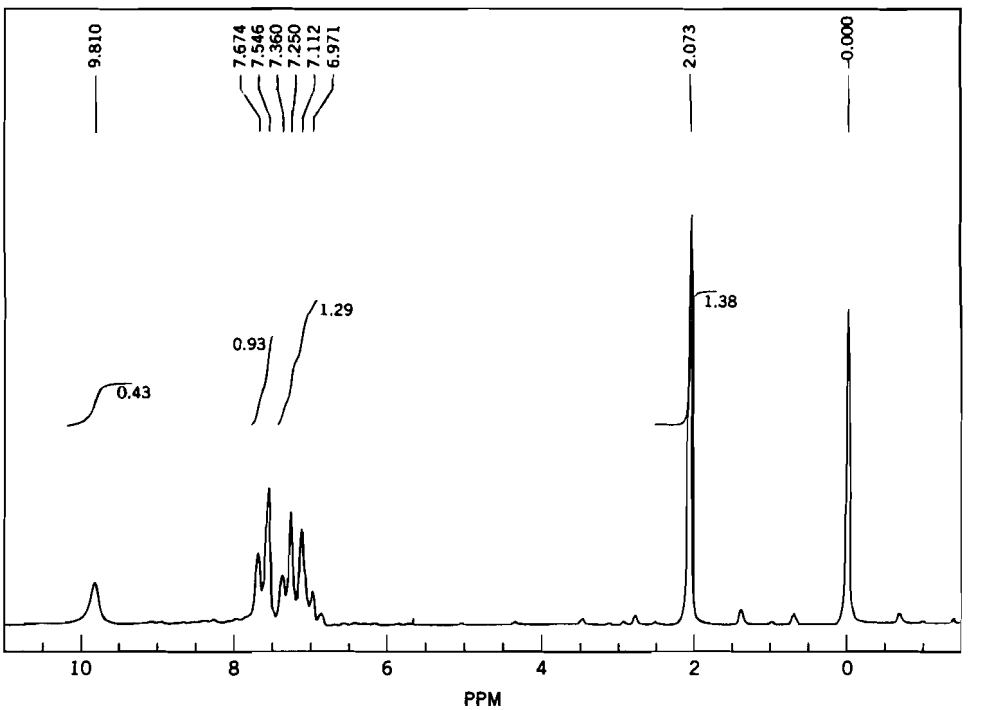


Figure 6.50 **Problem 5** ^1H NMR spectrum of unknown compound, C_8H_9NO. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

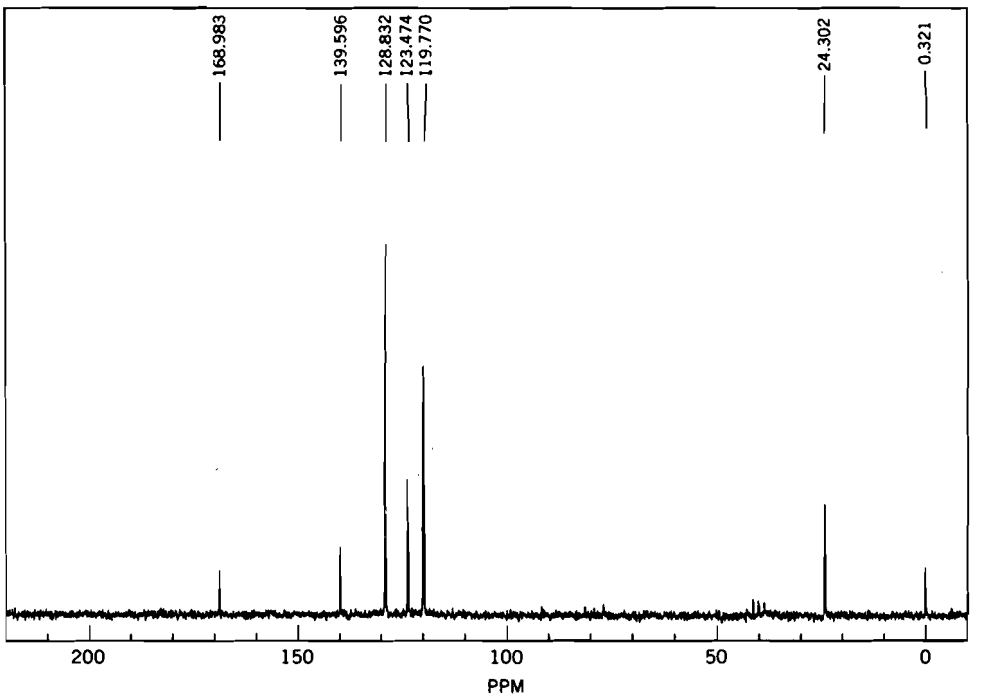


Figure 6.51 **Problem 5** ^{13}C NMR spectrum of unknown compound, C_8H_9NO. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

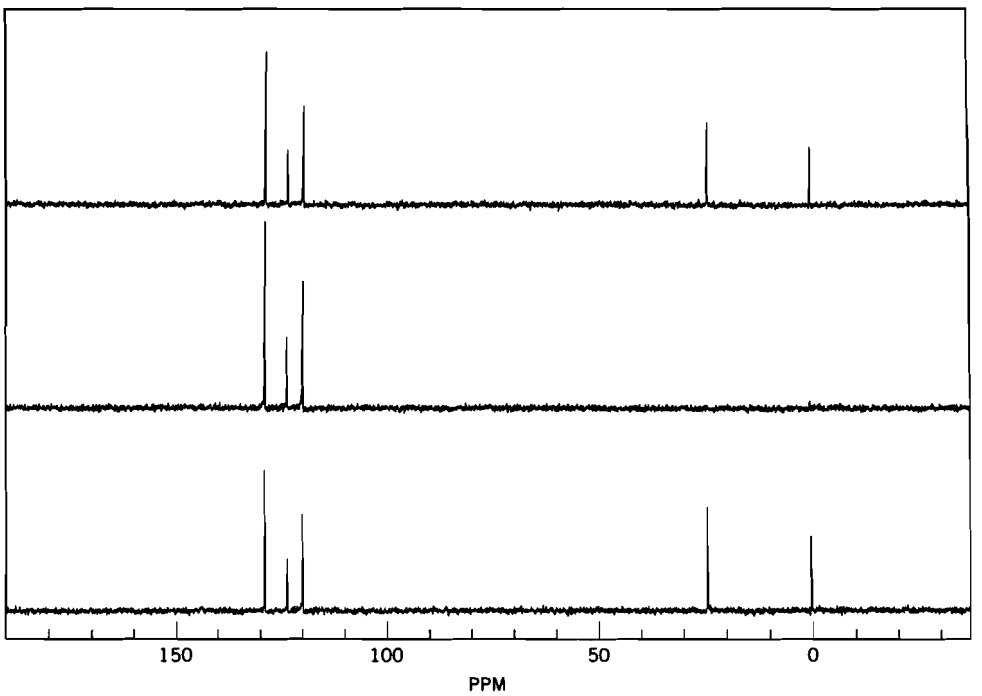


Figure 6.52 **Problem 5** DEPT spectrum of unknown compound, C_8H_9NO. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

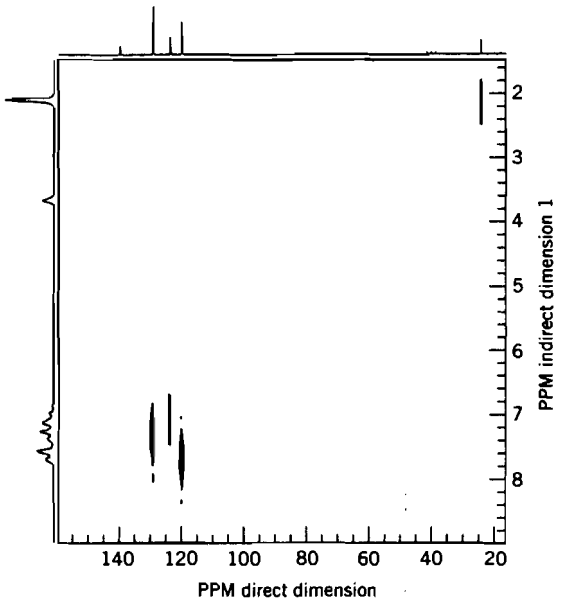


Figure 6.53 **Problem 5** HETCOR spectrum of unknown compound, C_8H_9NO. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

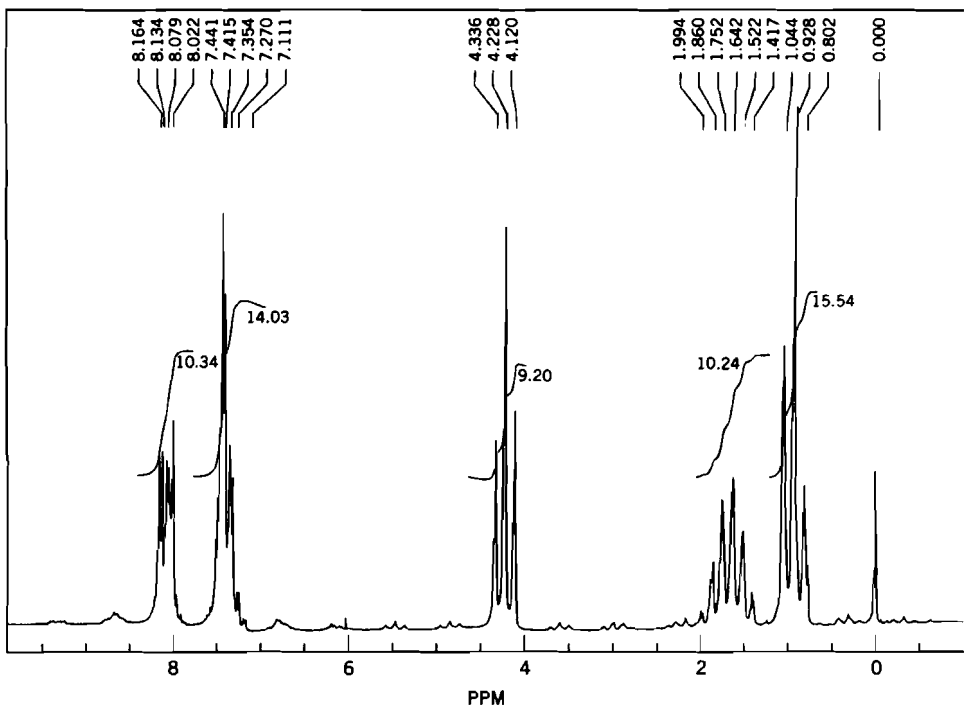


Figure 6.54 **Problem 6** ^1H NMR spectrum of unknown compound, $C_{10}H_{12}O_2$. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

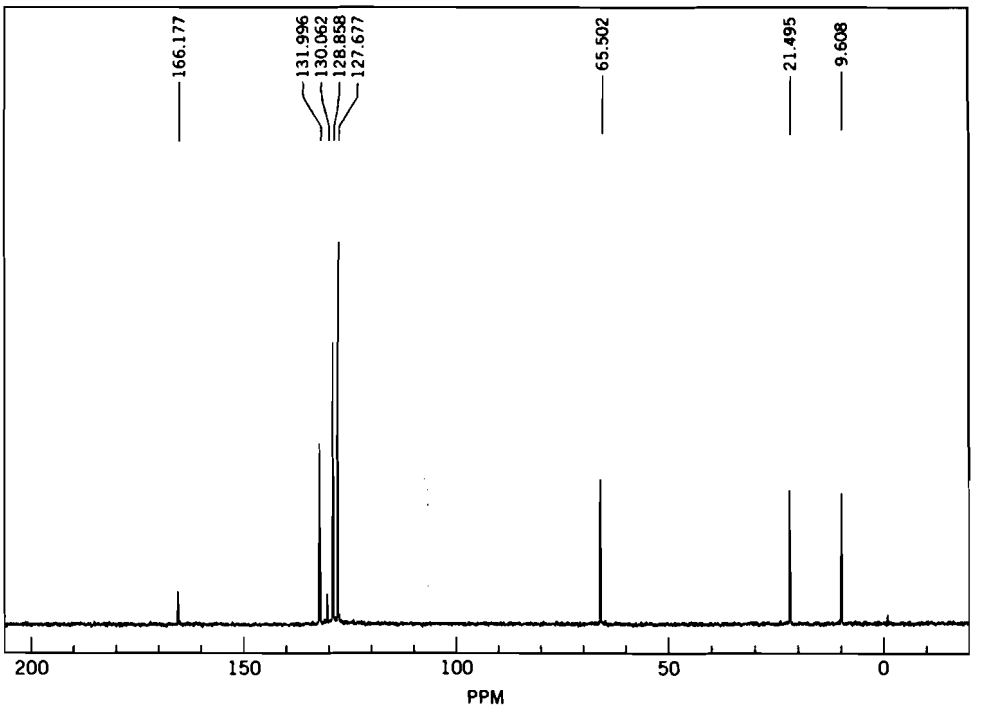


Figure 6.55 **Problem 6** ^{13}C NMR spectrum of unknown compound, $C_{10}H_{12}O_2$. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

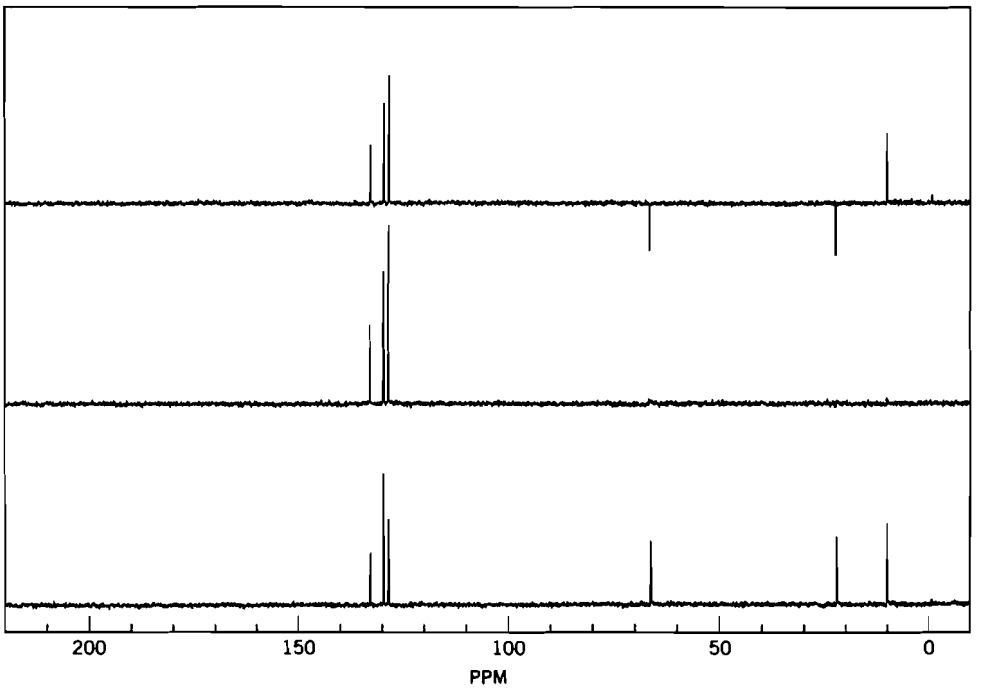


Figure 6.56 **Problem 6** DEPT spectrum of unknown compound, $C_{10}H_{12}O_2$. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

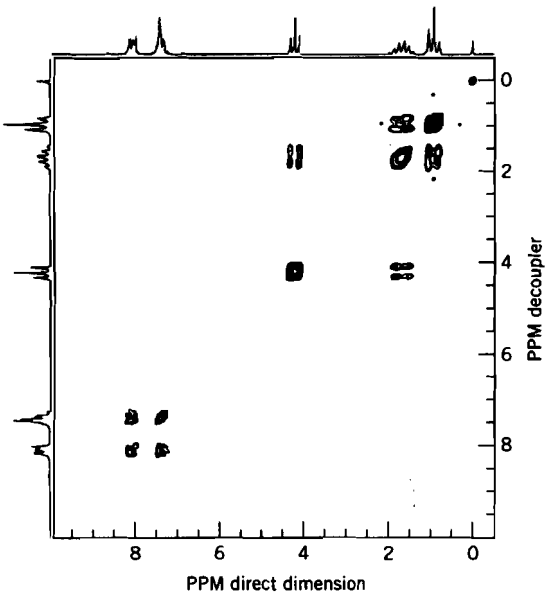


Figure 6.57 Problem 6 COSY spectrum of unknown compound, $C_{10}H_{12}O_2$. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

(Figure 6.54),^{13}C (Figure 6.55), and DEPT (Figure 6.56) spectra. Give a table for the COSY (Figure 6.57) and HETCOR (Figure 6.58) spectra. Calculate the hydrogen and carbon chemical shifts.

7. Calculate the unsaturation number and list possibilities for a compound with a formula of $C_{10}H_{13}NO_2$. Give the structure and identify all of the signals in the ^{1}H (Figure 6.59), ^{13}C (Figure 6.60), and DEPT (Figure 6.61) spectra. Give a table for the COSY (Figure 6.62) and HETCOR (Figure 6.63) spectra. Calculate the hydrogen and carbon chemical shifts.

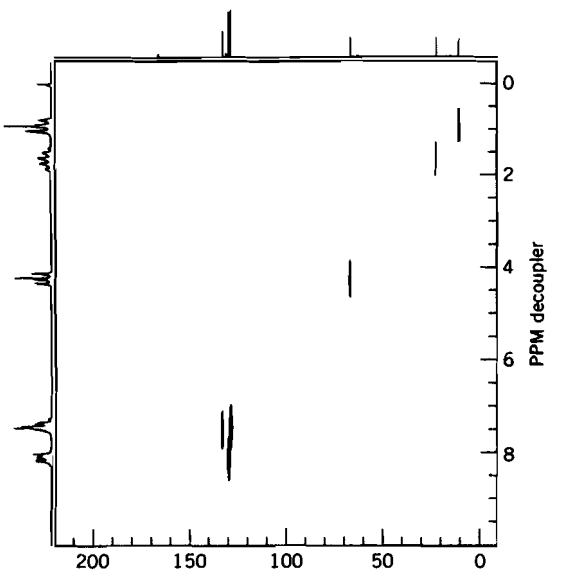


Figure 6.58 Problem 6 HETCOR spectrum of unknown compound, $C_{10}H_{12}O_2$. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

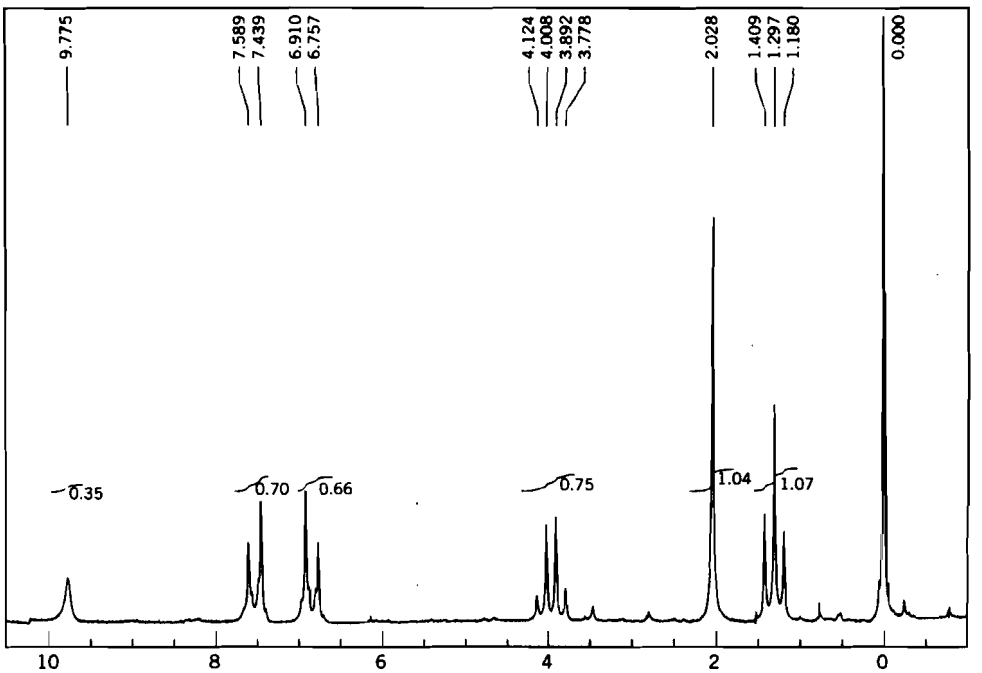


Figure 6.59 **Problem 7** ^{1}H NMR spectrum of unknown compound, $C_{10}H_{13}NO_2$. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

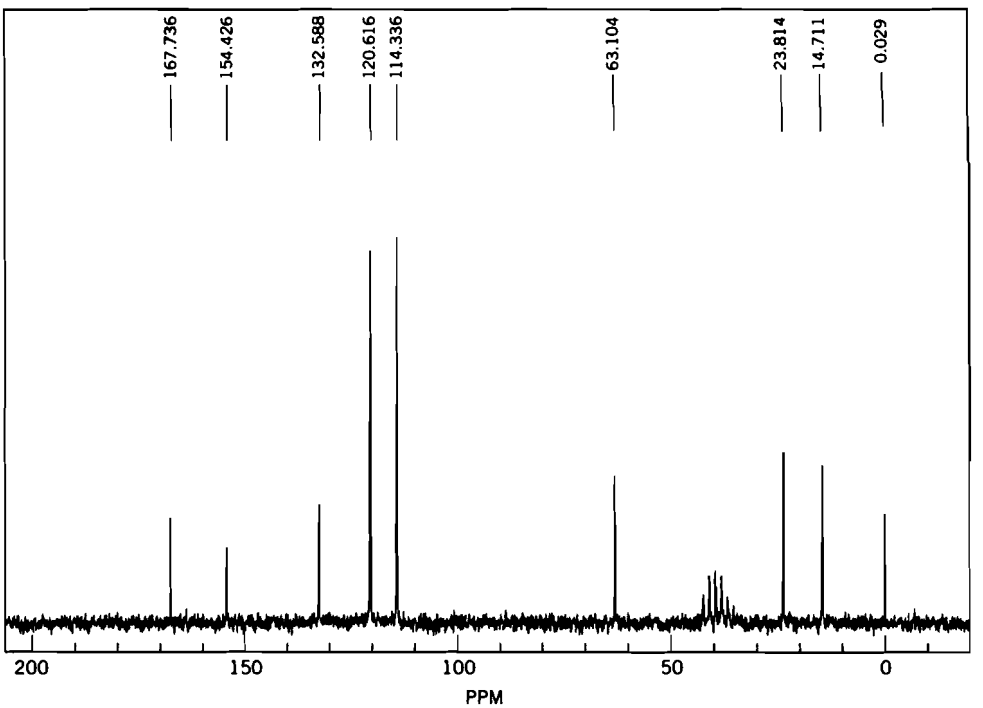


Figure 6.60 **Problem 7** ^{13}C NMR spectrum of unknown compound, $C_{10}H_{13}NO_2$. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

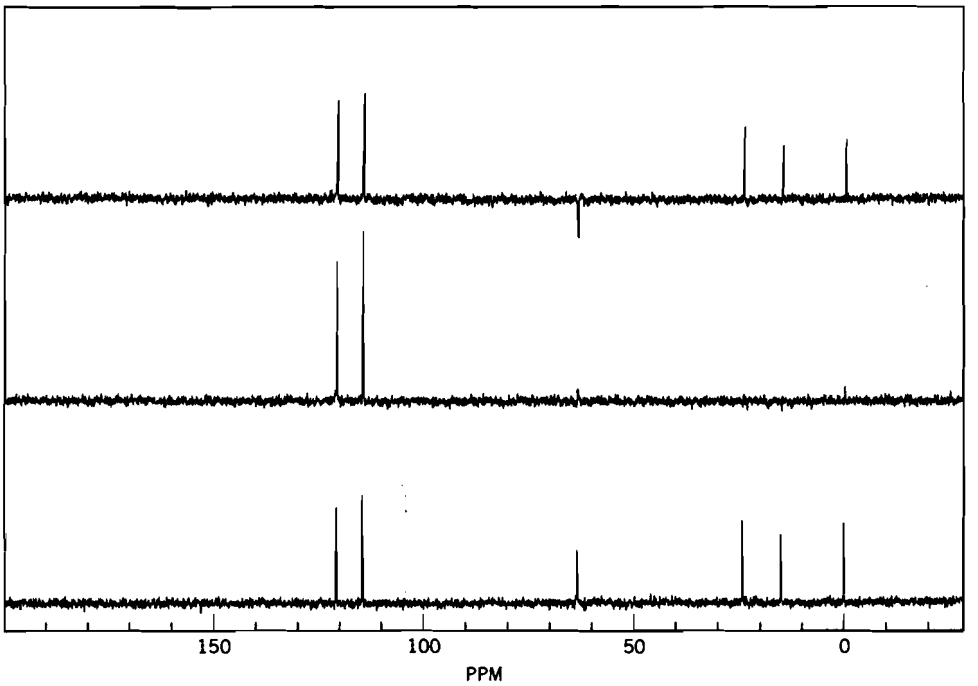


Figure 6.61 **Problem 7** DEPT spectrum of unknown compound, $C_{10}H_{13}NO_2$. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

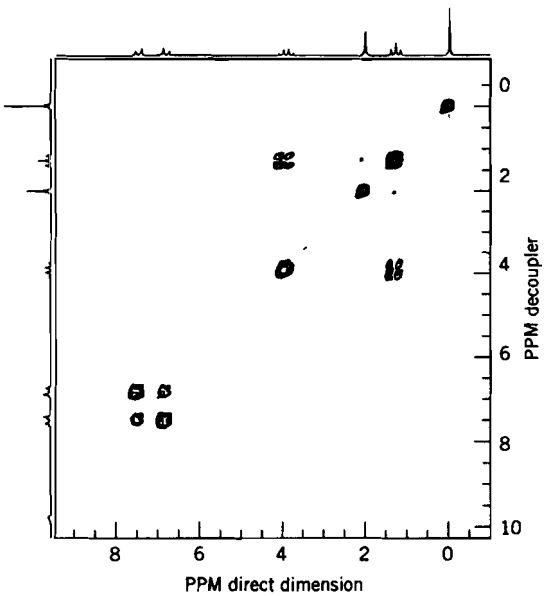


Figure 6.62 **Problem 7** COSY spectrum of unknown compound, $C_{10}H_{13}NO_2$. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

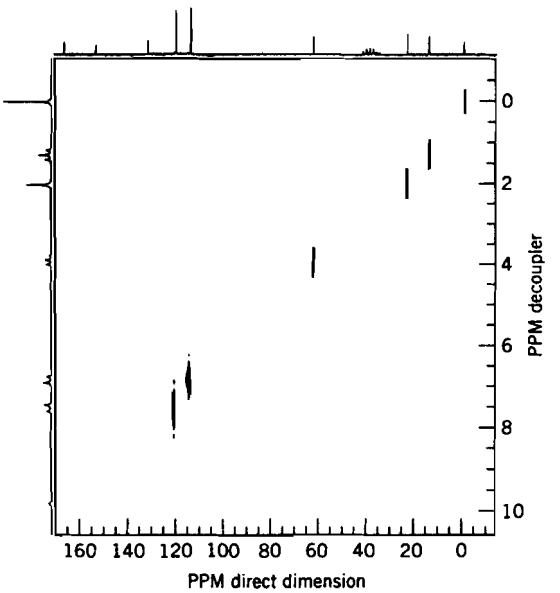


Figure 6.63 **Problem 7** HETCOR spectrum of unknown compound, $C_{10}H_{13}NO_2$. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

CHAPTER 7

Infrared Spectrometry

Infrared (IR) spectrometry gives additional information about a compound's structure. In NMR spectrometry, the relationship of carbons and hydrogens to each other is determined. IR spectrometry aids in the identification of functional groups.

7.1 THEORY OF INFRARED SPECTROMETRY

A beam of electromagnetic radiation of wavelengths shorter than visible light is absorbed by an organic compound when this beam has an energy corresponding to that of the vibrating organic bond.

In infrared spectrometry, energy (ΔE) and frequency (ν) are related through Planck's constant, $h(6.6242 \times 10^{-27}$ erg sec).

$$\Delta E = h\nu$$

Frequently, wavenumber, $\bar{\nu}$, rather than frequency, ν, is used to describe the magnitude of IR radiation.

$$\Delta E = h\bar{\nu}$$

It is now routine to supply IR band positions in wavenumbers, but years ago wavelength (λ) in μm (micrometers, 10^{-6} m)—or, earlier, μ (microns, also 10^{-6} m)—was used. The equation for wavelength and energy is:

$$\Delta E = hc/\lambda$$
$$hc/\lambda = hc\bar{\nu}$$

Wavelength (in μm) and wavenumber (cm^{-1}) are related by the following equation:

$$10{,}000/\lambda = \bar{\nu}$$

The IR spectrum contains the wavenumbers from 4000 to 600 or 400 cm^{-1}. Fourier transform (FT) IR spectrometers offer a number of advantages over the older IR spectrometers. Since the data are collected and stored in a digitized form in the computer, they can be easily manipulated, transported, and displayed. Spectra can be added or subtracted, and this technique is useful for subtracting the solvent spectrum from a spectrum of a sample in that solvent. FT IR instruments are faster, more sensitive, and more accurate when compared to the older spectrometers. In an FT IR spectrometer, all of the infrared frequencies are measured simultaneously instead of individually, as was the case in older IR instruments.

A schematic diagram of an FT IR spectrometer is depicted in Figure 7.1. The infrared energy from the laser passes through an aperture that controls the amount of infrared energy emitted. The infrared beam is split into two optical beams by the beam

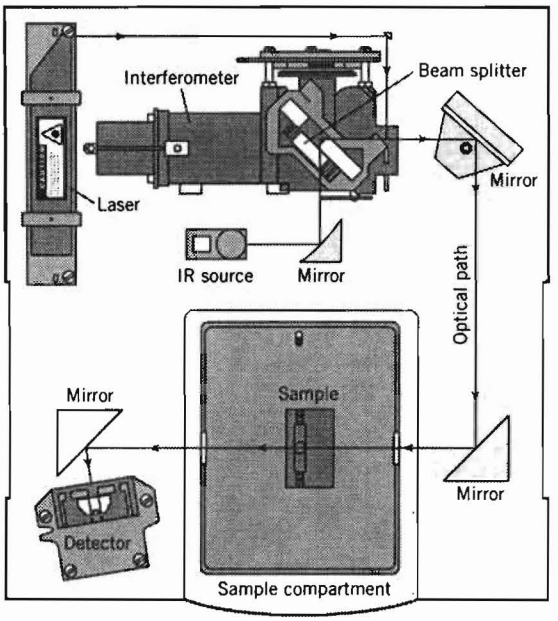
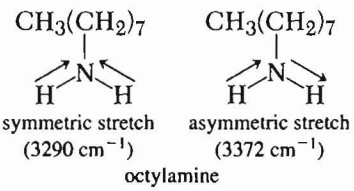


Figure 7.1 Schematic of an FT IR spectrometer. [Courtesy of Thermo Nicolet, Madison, WI. Used with permission.]

splitter in the interferometer. The beam splitter can be a partially coated mirror that can be manipulated to alternately let the radiation pass toward either the fixed mirror or the movable mirror. The movable mirror is carefully incrementally adjusted so that the path length is regularly varied. The signals are recombined at the beam splitter. The difference between the path lengths results in a difference between the two wavelengths of energy. The differences produce an interferogram. The interferogram has information about every infrared signal coming from the source, and thus all frequencies are measured simultaneously. When the difference between the two wavelengths is an even-integer multiple of the invariant beam's wavelength, constructive interference results. If the difference between the two wavelengths is an odd-integer multiple of one-quarter of the invariant beam's wavelength, destructive interference results. The interferogram then passes through the sample and then to the detector. The signal from the detector cannot be interpreted directly; it undergoes a Fourier transformation, a very complex mathematical procedure. The resulting signal is printed as an infrared spectrum.

Infrared spectra contain different types of absorption for the same bond. The different types are depicted in Figure 7.2.

Examples of stretching and bending are shown below. In octyl amine, the two hydrogens both move away from the nitrogen (symmetric stretch) or one toward and one away (asymmetric stretch).



Symmetric and asymmetric in-plane bending occurs in 2-methylpropene, as do symmetric and asymmetric out-of-plane bending.

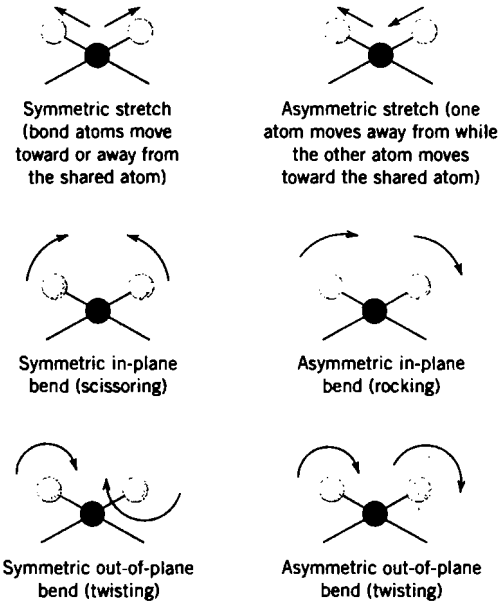
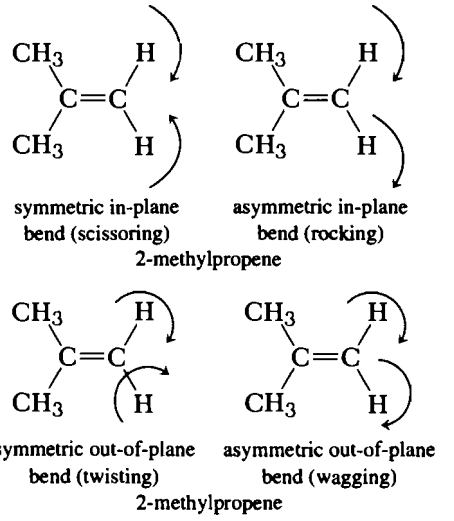


Figure 7.2 Various types of vibrational modes.



7.2 PREPARATION OF THE SAMPLE

Compounds that are subjected to IR analysis should be pure. Solids should be samples from recrystallization or from chromatography. Liquids should be samples from distillation or from gas chromatographic separation.

Liquids can be examined as a thin film between two salt plates. The salt plates can be individual salt disks (Figure 7.3), in a demountable cell (Figure 7.4), or in a sealed cell (Figure 7.5). The spectrum of a compound dissolved in a nonpolar organic solvent, such as carbon tetrachloride, is least distorted due to associations caused by solvent–solute or sample–sample aggregates. The wavenumbers for the absorption of

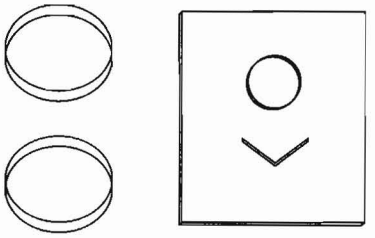
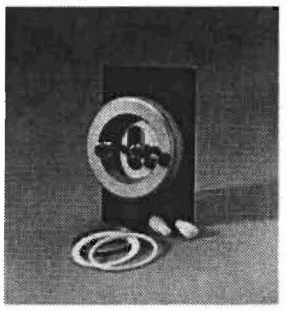
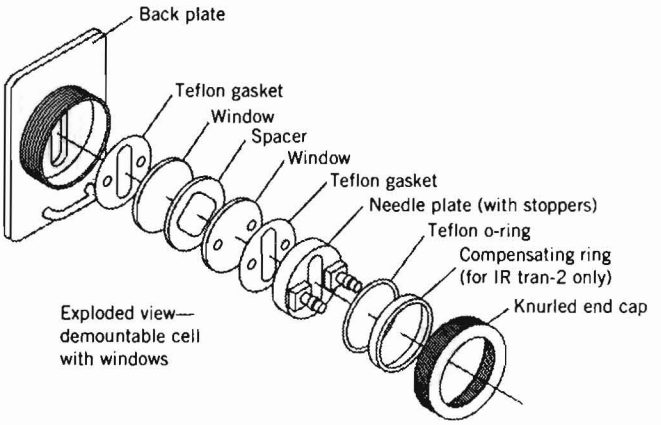


Figure 7.3 Salt plates and sample holder. A drop is placed between the salt plates and in the sample holder.





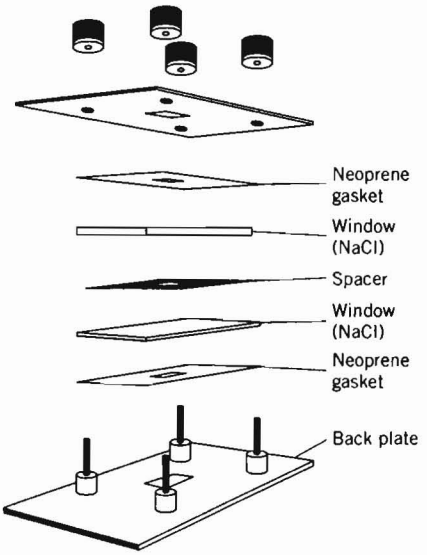


Figure 7.4 Two types of demountable cells for IR analysis of liquids. Assembly procedure: (1) Place bottom gasket and lower NaCl plates in the middle of the plate. (2) Place spacer on lower window and add one or two drops of sample. (3) Place upper plate, top gasket, and front plate on the cell; carefully tighten nuts until the sample is evenly dispersed between the plates. *Do not overtighten the nuts, as this may break the salt plate.* [(*a*) is courtesy of Aldrich Chemical Company, Milwaukee, WI. Used with permission.]

standard IR solvents and mulls are given in Figure 7.6. Mulls do not involve substantial miscibility of the substrate in the solvent; intermolecular associations, such as intermolecular hydrogen bonding, may persist in such samples. From the standpoint of lack of absorption by the supporting medium, potassium bromide pellets are the most desirable. Preparation of these pellets requires careful technique.

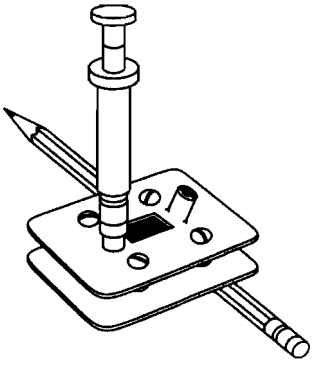


Figure 7.5 Correct way to fill a sealed cell.

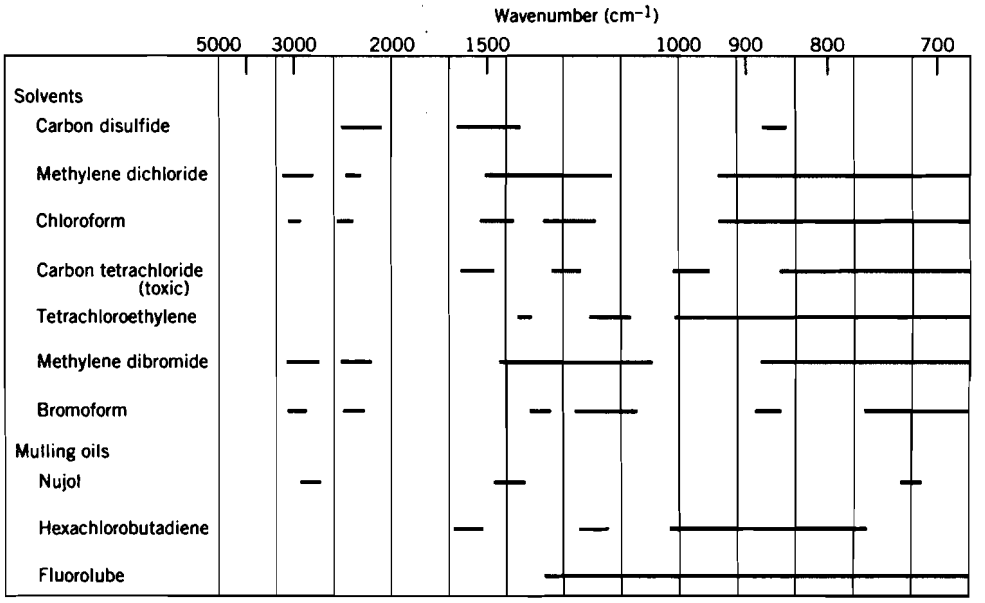


Figure 7.6 Transparent regions of IR solvents and mulling oils. The open regions for the solvents are those in which the solvent transmits more than 25% of the incident light at 1-mm thickness. The open regions for the mulling oils indicate transparency of thin films.

Procedure

Warm up the instrument sufficiently. Take the spectrum of the cell plates and store in the background file. This allows moisture in the air to be subtracted out from the spectrum. If possible, liquid samples should be analyzed neat, without any solvent. If a mull is preferred, blend 1% of the sample (liquid or solid) in the mulling solvent or oil by thoroughly mashing the mixture with an agate mortar and pestle. Usually 1 mg of sample in 100 mg of mulling medium is sufficient. Place one or two drops of the pure liquid sample or mixture between the individual salt plates and place in the sample holder (Figure 7.3) or assemble the demountable cell (Figure 7.4). Liquids can also be injected into the sealed cell (Figure 7.5). Touch only the edges of the salt plates. Do not clean the salt plates with water, since it will ruin them. Wipe the salt plates with a nonabrasive

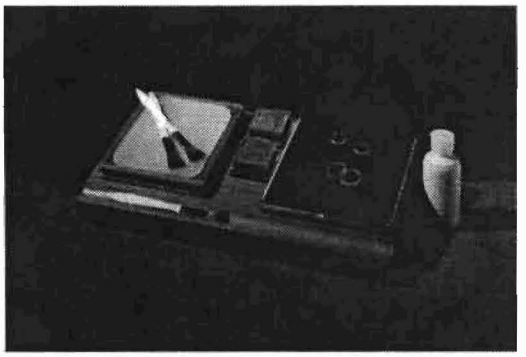


Figure 7.7 Crystal-polishing kit for grinding, polishing, and buffing salt plates. [Courtesy of Aldrich Chemical Company, Milwaukee, Wisconsin. Used with permission.]

tissue to remove the sample. Polish the salt plates, if needed, with a crystal-polishing kit such as the one shown in Figure 7.7. Polishing will remove minor scratches and cloudiness on the salt plate.

Solid samples must be mixed with either a mulling solvent or mulling oil, as described above, or mixed with a solid salt, such as potassium bromide. For best results, use FT IR quality potassium bromide that has been oven-dried and stored in a dessicator. Prepare a mixture of 1 mg of solid to 100 mg of potassium bromide. Tighten one of the bolts in the cell (Figure 7.8) or place the bolt in the nut (Figure 7.9). Place a fine layer of the solid mull into cell. Insert the other bolt (Figures 7.8 and 7.9), keeping the apparatus upright. Tighten the bolts with two wrenches or a vise and a wrench (Figure 7.8) or with the Handi-Press (Figure 7.9). In either apparatus, remove the bolts slowly. If a transparent solid salt layer is present, then attempt to obtain the IR spectrum. If the layer is not transparent or has holes in it, start over again. Clean the apparatus thoroughly using a nonabrasive tissue. The flat side of each bolt must be smooth so that a good pellet can be made. Consult your instructor as to the correct way to remove any rust or corrosive on the bolts.

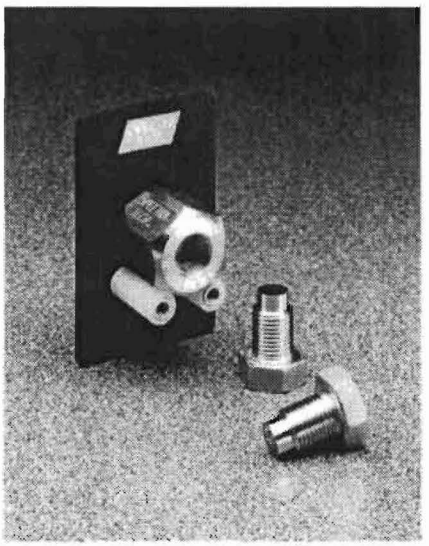


Figure 7.8 Econo-Press kit. [Courtesy of Aldrich Chemical Company, Milwaukee, Wisconsin. Used with permission.]

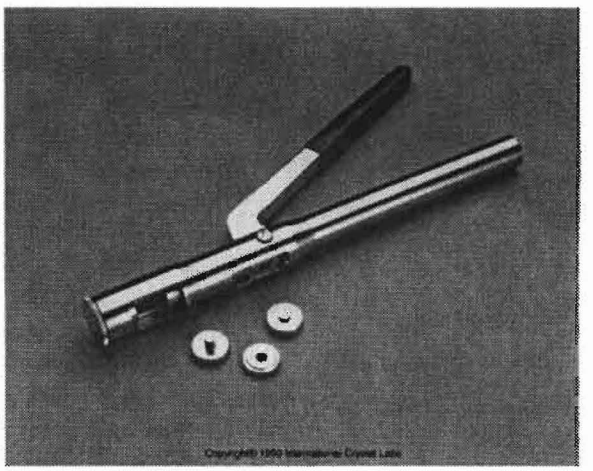


Figure 7.9 Qwik Handi-Press kit. [Courtesy of Aldrich Chemical Company, Milwaukee, Wisconsin. Used with permission.]

Obtain directions from the instructor as to the procedure for operating the IR spectrometer and manipulating the spectrum.

Improving the IR Spectrum

The IR spectrum can be improved prior to printing a copy. Adjust the peaks until they almost fill the vertical area. If the peaks are flat on the side opposite from the baseline, then rerun the spectrum with less sample. If very few peaks are visible, and these can be identified as mulling medium, or the peaks are very small after adjustment, then rerun the spectrum with more sample. With a mull or a pellet, a higher ratio of sample to mulling medium may be required. With an unknown sample, record the wavenumbers of all peaks. Using only dry equipment and dry chemicals will minimize the appearance of water absorptions at 3000–3800 cm^{-1} (O—H stretching) and 1520–1750 cm^{-1} (O—H bending).

7.3 FUNCTIONAL GROUP IDENTIFICATION

The IR spectrum can be broken down into three major regions:

1. The functional group region (1600–4000 cm^{-1}) is the region in which most functional groups absorb. Most of these absorptions are at least of moderate intensity, and many are quite strong. Organic chemists rarely if ever report absorbance or transmittance of IR spectra quantitatively. Bands are only identified as strong (s), moderate (m), or weak (w). Morever, the functional group region is relatively free from overlap or other interferences.
2. The fingerprint region (1000–1600 cm^{-1}) is often quite complex. This region is often used for band-by-band comparison of the spectrum of a known compound to the spectrum of an unknown compound in order to identify the compound. Only strong bands associated with the C—O stretching of alcohols, esters, and other oxygen-containing molecules are easily assigned.
3. The aromatic region (675–900 cm^{-1}) is useful for identifying the number and relative positions of groups on a benzene ring. The out-of-plane C—H bonds occur in this region. If polar substituents are substituted on the benzene ring, this estimation falls.

Figure 7.10 can be used to make a preliminary identification of a compound's functional group. The Colthup chart (Figure 7.11) provides much more detail. A listing of the wavenumbers is given in Table 7.1.

The position of a band depends upon a number of characteristics of a bond. The higher the bond order, the higher the wavenumber for the stretching vibration for a bond. For example, for carbon–carbon bonds, triple bond stretching occurs at 2100–2260 cm^{-1}, double bond stretching at 1620–1680 cm^{-1}, and single bonds are lost in the fingerprint region. Carbonyl groups have bond stretching at 1630–1850 cm^{-1}, and C—O stretching is usually 1000–1300 cm^{-1}.

Another factor that is important is band intensity. Fundamental vibrations give more intense bands when the vibration causing the band results in a significant change of the dipole moment for the molecule. This accounts for the weakness of absorptions for the nonpolar carbon–carbon bonds of alkanes. Highly polar carbonyl groups give rise to a strong absorption in the area of 1630–1850 cm^{-1}.

At this point, IR spectra of common organic compounds will be described. Important peaks for a particular functional group will be mentioned.

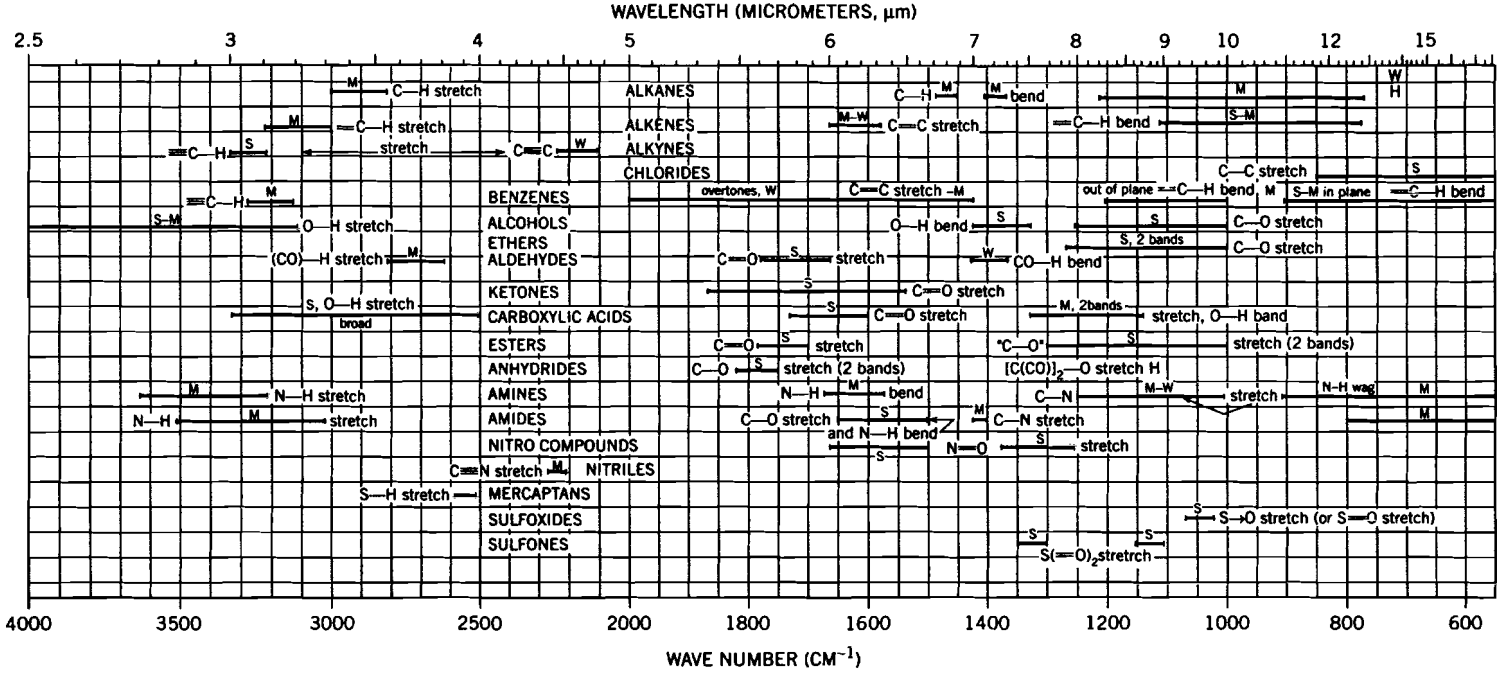


Figure 7.10 Correlation of infrared absorption with organic functional groups. Rows below the first row show only unique bands for the new functional group. For example, the alkene row shows only bands due to the double bond and does not show the C—H absorption bands for the saturated side chains.

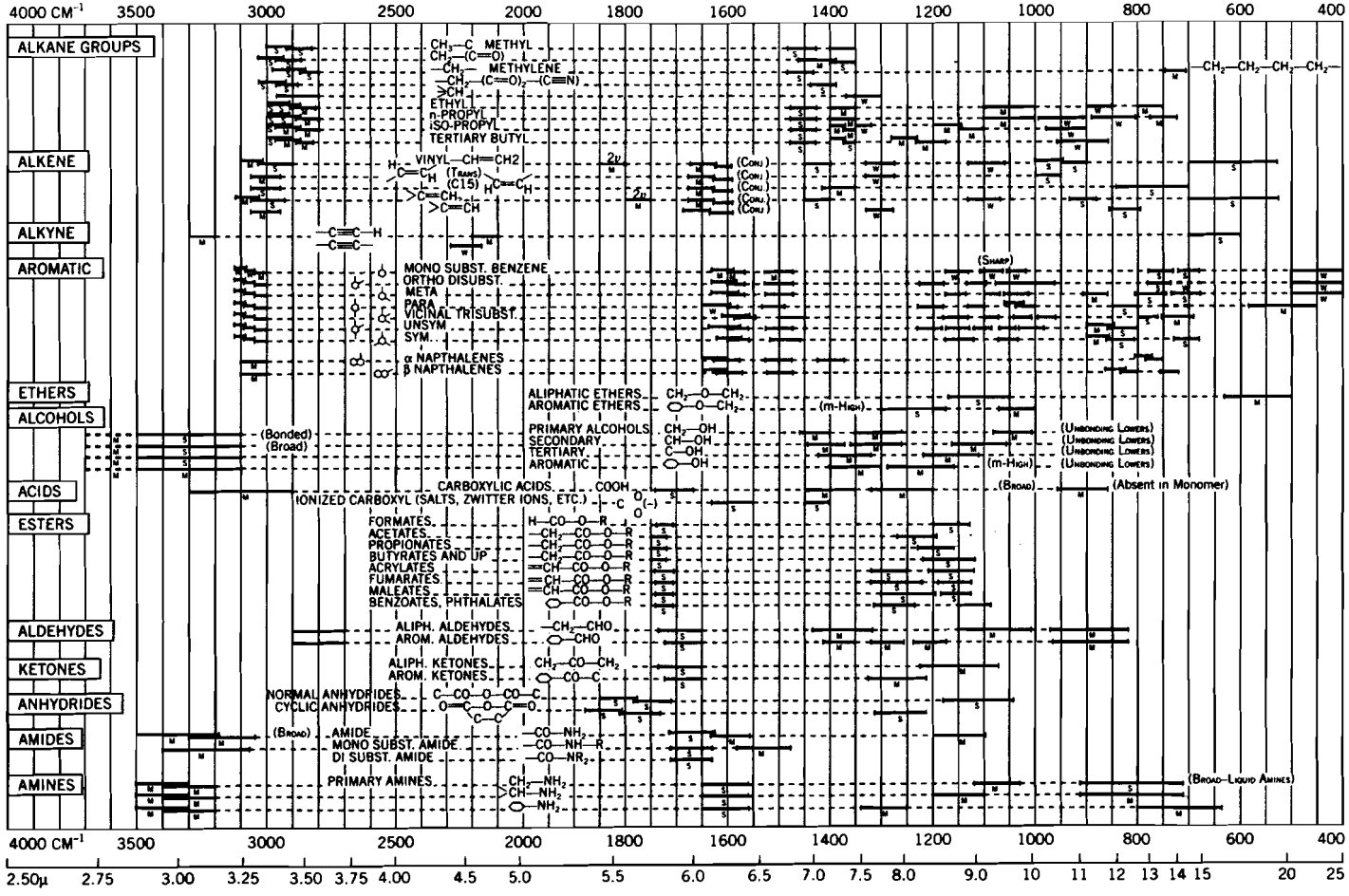


Figure 7.11 Colthup chart correlating infrared absorption with organic functional groups.

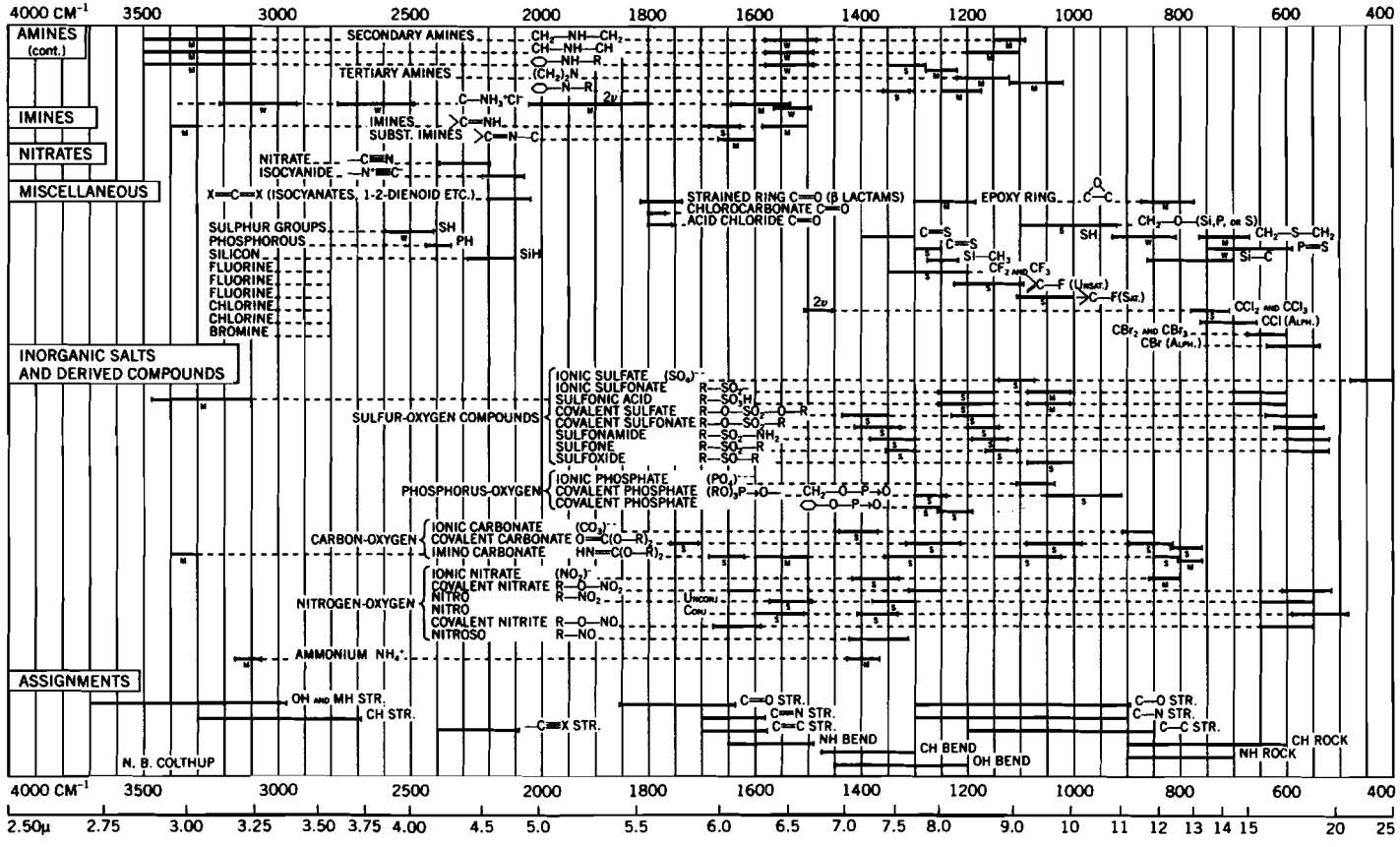


Figure 7.11 *(Continued)*

TABLE 7.1 Characteristic Infrared Absorption Frequencies

Bond	Compound Type	Frequency Range, cm^{-1}
	Hydrocarbons	
C—H stretching	Alkanes	2840–3000
	—CH_3	2872 & 2962 (s)
	—CH_2	2853 & 2926
	—CH (3°)	2890 (w)
	—CH_2 & —CH (cyclic)	2990–3100
	Alkyl	2853–2962 (m–s)
	Alkenes	3010–3095 (m)
	Alkynes (RC≡CH)	3267–3333 (s)
	Aromatic	3000–3100
C—H bending	Alkanes	
	—CH_3	1375 & 1450
	—CH_2	1465 & 1150–1350
	—CH_2 (straight chain ≥ 7 C)	720
	—$CH(CH_3)_2$	1365–1370, 1380–1385 (s, d), & 919–922 (w)
	—$C(CH_3)_3$	1370 (s), 1385–1395 (m), & 926–932 (w)
	cyclohexane	1452
	cyclopentane	1455
	cyclopropane	1442
	Alkenes	
	cis disubstituted, vinyl	1416
	Alkynes	
	(RC≡CH, HC≡CH)	610–700 (s, b) & 1220–1370 (w, b)
C—H out-of-plane bending	Alkenes	650–1000 (s)
	$RCH{=}CH_2$	905–915 (s) & 985–995 (s)
	$R_2C{=}CH_2$	885–895 (s)
	RCH=CHR (*cis*)	665–730 (s)
	RCH=CHR (*trans*)	960–980 (s)
	$R_2C{=}CHR$	790–840 (m)
	Allenes $=CH_2$	850
	Aromatic	675–900 (s)
	monosubstituted	690–710 (s) & 730–770 (s)
	o-disubstituted	735–770 (s)
	m-disubstituted	680–725 (s) & 750–810 (s)
	p-disubstituted	800–840 (s)
C—H in-plane bending	Alkenes	
	$=CH_2$	1416
	Aromatic	1000–1300
C=C stretching	Alkenes	1620–1680 (v)
	unconjugated	1640–1667 (m, w)
	$RCH{=}CH_2$	1638–1648
	$R_2C{=}CH_2$	1648–1658 (m)
	RCH=CHR (*cis*)	1626–1662 (v)
	RCH=CHR (*trans*)	1668–1678 (v)
	$R_2C{=}CHR$	1665–1675 (m)

(Continued)

TABLE 7.1 Characteristic Infrared Absorption Frequencies

Bond	Compound Type	Frequency Range, cm^{-1}
	$R_2C{=}CR_2$	1665–1675 (w)
	$-CH{=}CF_2$	1754
	$-CF{=}CF_2$	1786
	cyclopropene	1641
	cyclobutene	1566
	α-substituted cyclobutene	1641
	conjugated	1600 & 1650
	conjugated with an aromatic ring	1625
	cumulated	1900–2000
	Aromatic	1400–1500 & 1585–1600
C≡C stretching	Alkynes	2100–2260 (w)
	symmetrical	no band
	RC≡CH	2100–2140
	RC≡CR (unsymmetrical)	2190–2260
	Alcohols and phenols	
O—H stretching	Alcohols, phenols (vapor phase or very dilute solution)	3584–3650 (s)
	Alcohols, phenols	3200–3550 (b, s)
C—O stretching	Alcohols	1000–1260 (s)
	1°	
	α-unsaturated and/or α-branched	<1050
	saturated	1050–1085
	2°	
	alicyclic 7- or 8-membered ring, α-unsaturated and α-branched, or di-α-unsaturated	<1050
	alicylic 5- or 6-membered ring, α-unsaturated	1050–1085
	saturated	1087–1124
	highly symmetrical	1124–1205
	3°	
	highly α-unsaturated	<1050
	α-unsaturated or cyclic	1087–1124
	saturated	1124–1205
	Phenols	1180–1260 & 1330–1390
O—H bending	Alcohols	1330–1420
	1°, 2°	1330 & 1420
	3°	1330–1420 (one band)
	Alcohols, phenols (liquid)	650–769 (b)
	Ethers, epoxides, and peroxides	
C—O stretching	Ethers	
	aliphatic	1085–1150 (s, usually 1125)
	aliphatic, with branching adjacent to O	1114–1170 (t)
	aryl alkyl	1020–1075 & 1200–1275

(Continued)

TABLE 7.1 *(Continued)*

Bond	Compound Type	Frequency Range, cm^{-1}
	vinyl	1020–1075 & 1200–1225
	Peroxides	
	alkyl, aryl	1176–1198
	Epoxides	750–840, 810–950 & 1250 (one band each)
C=C stretching	Ethers	
	vinyl	1610–1660 (d)
C—H stretching	Epoxides	2990–3050
C=O stretching	Peroxides	
	acyl, aroyl	1754–1818 (two bands)
	Ketones and aldehydes	
C=O stretching	Ketones	1680–1750 (s)
	saturated aliphatic (neat)	1715 (s)
	aliphatic	1705–1720
	aliphatic & aryl	1680–1700
	α,β-unsaturated	1665–1680
	α,β-unsaturated or aryl	1666–1685 (s)
	β-diketones	1580–1640 (b, s)
	quinones	
	both C=O in 1 ring	1655–1690 (s)
	C=O in 2 rings	1635–1655 (s)
	acyclic α-chloro	1725 & 1745
	cyclohexanone	1715 (s)
	cyclopentanone	1751 (s)
	cyclobutanone	1775 (s)
	Aldehydes	1690–1740 (s)
	aliphatic	1720–1740 (s)
	α,β-unsaturated	1680–1690 (s)
	aryl	1695–1715 (s)
C=O stretching and bending	Ketones	1100–1300 (m)
	aliphatic	1100–1230
O—H stretching	Ketones	
	enolic	2700–3000 (b, shallow)
C—H stretching	Aldehydes	2695–2830 (two m bands, usually at 2720)
	o-substituted aromatic	2900
C—H bending	Aldehydes	1390 (w)
	Carboxylic acids and anions	
O—H stretching	Carboxylic acids	2500–3300 (b, s) (center at 3000)
C=O stretching	Carboxylic acids	1710–1780 (s)
	saturated aliphatic monomers	1760 (s)
	dimerized saturated aliphatic	1706–1720 (s)
	aliphatic	1700–1725 (s)
	α,β-unsaturated	1690–1715 (s)
	aryl	1680–1700 (s)
	α,β-unsaturated, aryl	1680–1710 (s)
	Carboxyl anions	1550–1630

(Continued)

TABLE 7.1 *(Continued)*

Bond	Compound Type	Frequency Range, cm^{-1}
C=O stretching	Carboxylic anions	1550–1650 (s) & 1400 (w)
C—O stretching	Carboxylic acids	1210–1320
	dimers	1280–1315
O—H bending	Carboxylic acids	1395–1440 (m)
	Esters and lactones	
C=O stretching	Esters	
	saturated aliphatic	1735–1750 (s)
	formates, benzoates, α,β-unsaturated	1715–1730 (s)
	vinyl	1776 (s)
	phenyl	1770 (s)
	oxalates, α-keto	1740–1755 (s)
	β-keto	1650 (s)
	aliphatic	1735–1750 (s)
	aromatic	1715–1730 (s)
	δ-Lactones	
	saturated	1735–1750 (s)
	α,β-unsaturated	1750 (s)
	β,δ-unsaturated	1800 (s)
	α-Pyrones	1715–1775 (two bands)
	τ-Lactones	1760–1795
C—O stretching	Esters	1000–1300
	saturated, except for acetates	1163–1210 (s)
	acetates of saturated alcohols	1240
	vinyl acetates, phenyl acetates	1140–1190
	of α,β-unsaturated acids	1160–1300
	of aromatic acids	1250–1310
	of 1° ROH	1031–1064
	of 2° ROH	1100
	aromatic esters of 1° ROH	1111
	methyl esters of fatty acids	1175 (s), 1205, & 1250 (3-band pattern)
	Lactones	1111–1250
	Acid halides	
C=O stretching	Unconjugated acid chlorides	1785–1815 (s)
	Aromatic acid chlorides	1770–1800 (s) & 1735–1750 (w)
	Acid chlorides	1780–1850
	Acid bromides	1812
	Acid fluorides	1869
	Acid anhydrides	
C=O stretching	Anhydrides	
	saturated acyclic	1750 & 1818
	conjugated acyclic	1720 & 1775
	aliphatic	1740–1790 & 1800–1850
	aromatic	1730–1780 & 1780–1860

(Continued)

TABLE 7.1 *(Continued)*

Bond	Compound Type	Frequency Range, cm^{-1}
C—O stretching	Anhydrides	
	unconjugated straight chain	1047 (s)
	cyclic	909–952 & 1176–1299
	acetic	1125
	Amides	
N—H stretching	Amides	
	1°	
	(dilute solutions)	3400 (m) & 3520 (m)
	(solid samples)	3180 & 3350
	2°	
	(dilute solutions)	3400–3500
	(concentrated solutions)	3060–3330
	Lactams	3200 (s)
C=O stretching	Amides	1630–1690 (s)
	1°	
	(solid samples)	1650 (s)
	(dilute solutions)	1690 (s)
	2°	
	(solid samples)	1640
	(dilute solutions)	1680
	anilides	1700
	3°	1630–1680
	Lactams (≥ 6-membered)	1650
	γ-Lactams	1700–1750
	β-Lactams	1730–1760
N—H bending	Amides	1515–1650 & 666–800 (b, m)
	1°	
	(mulls and pellets)	1620–1655
	(dilute solutions)	1590–1620
	2° acyclic	
	(solid samples)	1515–1570
	(dilute solutions)	1510–1550
	Lactams	700–800 (b)
C—N stretching	1° Amides	1400
	Amines and salts of amines	
N—H stretching	Amines	3300–3500 (m)
	1°	3300–3500 (2 bands)
	(dilute solutions)	3400 (w) & 3500 (w) (2 bands)
	aliphatic (neat)	3250–3330 & 3330–3400
	2°	3310–3350 (w) (1 band)
	3°	3300–3500 (no bands)
	Amine salts	
	ammonium	3030–3300 (b, s) & 1709–2000
	1°	2800–3000 (b, s) & 2000–2800 (m)
	2°	2700–3000 (s) & 2000 (m)
	3°	2250–2700
	4°	no bands

(Continued)

TABLE 7.1 *(Continued)*

Bond	Compound Type	Frequency Range, cm^{-1}
N—H bending	Amines	
	1°	1580–1650 (m or s)
	2°	
	aliphatic	undetected
	aromatic	1515
	1°, 2° (liquid samples)	666–909
	Amine salts	
	ammonium	1429 (b, s)
	1°	1504–1550 & 1575–1600
	2°	1560–1620
C—N stretching	Amines	
	1°, 2°, 3° aliphatic	1020–1250 (m, w)
	1° aromatic	1250–1340 (s)
	2° aromatic	1280–1350 (s)
	3° aromatic	1310–1360 (s)
	Amino acids and salts of amino acids	
N—H stretching	Free 1° amino acids	2600–3100 (b, s)
	Hydrochloride salts of amino acids	2380–3333 (s)
	Sodium salts of amino acids	3200–3400
N—H bending	Free 1° amino acids	1485–1550 (s), 1610–1660 (w) & 2000–2222 (m)
	Hydrochloride salts of amino acids	1481–1550 (s) & 1590–1610 (w)
C=O stretching	Free 1° amino acid	1590–1600 (s) & 1400 (w)
	Sodium salts of amino acids	1590–1600 (s) & 1400 (w)
O—C=O stretching	Hydrochloride salts of amino acids	1190–1220 (s)
C=O stretching	α-Amino acid hydrochlorides	1730–1755 (s)
	Other amino acid hydrochlorides	1700–1730 (s)
O—H stretching	Hydrochloride salts of amino acids	2380–3333 (s)
	Compounds with C≡N, C=N, —N=C=O, —N=C=S groups	
C≡N stretching	Nitriles	2220–2260 (m)
	aliphatic	2240–2260
	aromatic, conjugated	2222–2240
	Isocyanides, isocyanates, thiocyanates, isothiocyanates	2000–2273
C=N stretching	Imines, oximes, thiazoles, iminocarbonates, guanidines	1471–1689
	Compounds with nitrogen–oxygen bonds	
N–O stretching	Nitro compounds	1259–1389 & 1499–1661(s)
	nitroalkanes	1372 & 1550
	conjugated aliphatic, aromatic	1290–1360 & 1500–1550

(Continued)

TABLE 7.1 *(Continued)*

Bond	Compound Type	Frequency Range, cm^{-1}
N—O stretching	Nitrates	1255–1300 (s) & 1625–1660 (s)
	Nitrites	750–850 (s)
N=O stretching	Nitrates	833–870
	Nitrites	
	cis isomer	1610–1625 (s)
	trans isomer	1650–1680 (s)
	Nitroso compounds	
	monomeric, tertiary	
	aliphatic	1539–1585
	aromatic	1495–1511
N-O bending	Nitrates	690–763
C—N stretching	Nitroaromatics	870
	Organic halogen compounds	
C—X stretching	Chlorides	
	aliphatic	550–850 (s)
	aryl	1089–1096 (s)
	Bromides	515–690 (s)
	Iodides	500–600 (s)
	Fluorides	730–1400 (s)
	monofluoroalkanes	1000–1100 (s)
	$—CF_2—$, $—CF_3$	1120–1350 (s)
	aryl	1100–1250 (s)
	Organic sulfur compounds	
S—H stretching	Aliphatic mercaptans, thiophenols	2550–2600 (w)
	Thioketos	2415 (b)
C—S stretching	Sulfides	600–700 (w)
S—S stretching	Disulfides	400–500 (w)
C=S stretching	Thiocarbonyls	1020–1250
	Thiobenzophenones	1207–1224
	Compounds containing sulfur–oxygen bonds	
S=O stretching	Organic sulfoxides	1030–1070 (s)
	Sulfones	1120–1160 (s) & 1300–1350 (s)
	Sulfonyl chlorides	1177–1204 (s) & 1380–1410 (s)
	Sulfonamides	1155–1170 (s) & 1335–1370 (s)
	Covalent sulfonates	1168–1195 (s) & 1335–1372 (d, s)
	Organic sulfates	1185–1200 (s) & 1380–1415 (s)
	Sulfonic acids	1150–1165 (s) & 1342–1350 (s)
	Sulfonate salts	1055 (s) & 1175 (s)
N—H stretching	Sulfonamides	
	1°	3247–3300 (s) & 3330–3390 (s)
	2°	3265 (s)
	Silicon compounds	
Si—H stretching		2200
Si—H bending		800–950
SiO—H stretching		3200–3700
Si—O stretching		830–1110 (s)

(Continued)

TABLE 7.1 *(Continued)*

Bond	Compound Type	Frequency Range, cm^{-1}
Si—X stretching	Si—F	800–1000
	Si—Cl	below 666
	Phosphorus compounds	
P=O stretching	Phosphine oxides	
	aliphatic	1150
	aromatic	1190
	Phosphate esters	1250–1299
P—O stretching	P—OH bonds	910–1040 (s)
	P—O—P bonds	700 (w), 870–1000 (s)
	P—O—C bonds	
	aliphatic	770–830 (s), 970–1050 (s)
	aromatic	855–994(s), 1160–1260 (s)
	Heteroaromatic compounds	
C—H stretching	Pyridines, pyrazines, pyrroles, furans, thiophenes	3003–3077
N—H stretching	Heteroaromatics	3220–3500
	Pyrroles, indoles	
	(dilute solution)	3495
	(conc solution)	3400
ring stretching	Heteroaromatics	1300–1600
C—H out-of-plane bending	Pyridines	
	2-substituted	746–752 & 740–781
	3-substituted	712–715 & 789–810
	4-substituted	709–775 & 794–820
	Furans	
	2-substituted	
	($CHCl_3$)	780–835, 884, & 925
	(liquid)	725–780, 875–890, & 915–960
	(solid)	723–750 & 793–821, 860–887 & 906–955
	3-substituted	
	(liquid)	741 & 870–885
	Thiophenes	
	2-substituted ($CHCl_3$)	803–843, 853, & 925
	3-substituted (liquid)	755
	Pyrrole	
	2-acyl	755 & 740–774

Abbreviations: s = strong, m = moderate, w = weak, d = doublet, b = broad, v = variable, t = triplet.

Source: Compiled from R. M. Silverstein and F. X. Webster, *Spectrometric Identification of Organic Compounds*, 6th ed. (Wiley, New York, 1998); T. W. G. Solomons and C. Fryhle, *Organic Chemistry*, 7th ed. upgrade (Wiley, New York, 2001).

Nujol, a commercially available compound used to prepare mulls, is a viscous oil composed of long-chain saturated hydrocarbons. The IR spectrum (Figure 7.12) shows typical C—H stretching at 2919 cm^{-1} and C—H bending at 1372 and 1461 cm^{-1} for a hydrocarbon. In other compounds with substantial hydrocarbon character, the peaks should be seen.

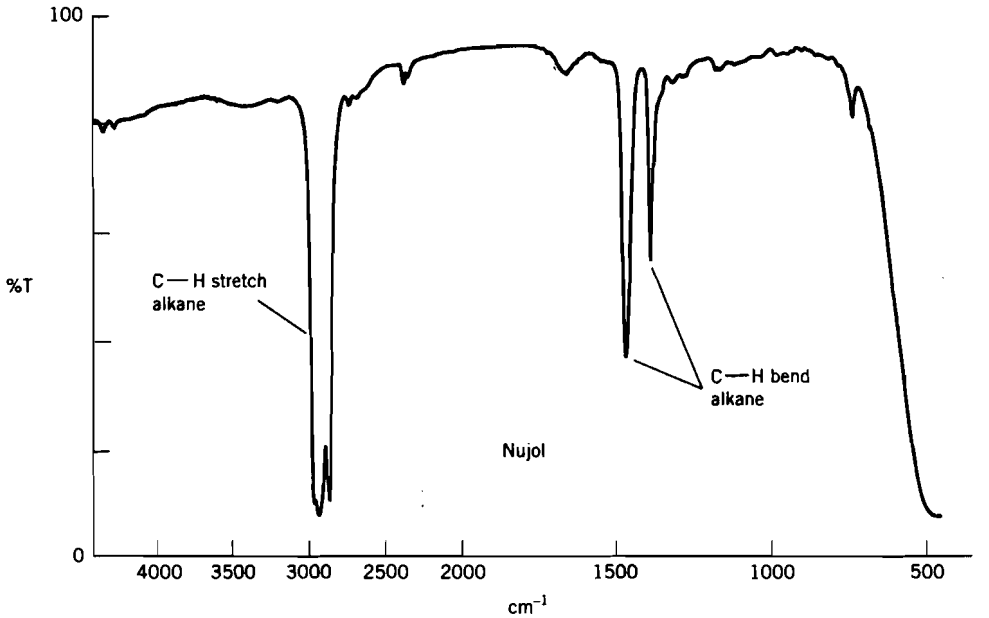


Figure 7.12 IR spectrum of Nujol. [Spectrum courtesy of Terra Hosp, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

Cyclohexene has many of the same features as a hydrocarbon and has the additional bands due to a carbon–carbon double bond. In Figure 7.13, a C=C stretching for a *cis* RCH=CHR at 1648 cm^{-1} and a C—H out-of-plane bending for a *cis* RCH=CHR at 720 cm^{-1} confirm the presence of a *cis* group. To confirm the identity of an alkene, there are always the same kind of alkene peaks for C=C stretching and C—H out-of-plane bending for the alkene. The only exception would be for a $R_2C{=}CR_2$, since there is no C—H bending. For cyclohexene, a band indicative of a double bond is found at 3019 cm^{-1} due to a C—H stretch of an alkene. Other peaks include a C—H stretch for an alkene at 3019 cm^{-1} and C—H stretch for an alkene at 2931 cm^{-1}.

The IR spectrum of 1-heptyne (Figure 7.14) indicates the presence of a carbon–carbon triple bond with a C≡C stretching at 2120 cm^{-1}. At this wavelength, a terminal alkyne is present. Unsymmetrical alkynes would have a peak for C≡C stretching at 2190–2260 cm^{-1}, and symmetrical alkynes do not show a peak in this range. Additional peaks indicating the presence of a terminal alkyne include C—H bending at 625 and 1255 cm^{-1} and C—H stretching at 3307 cm^{-1}. The compound does not have an isopropyl group or a *tert*-butyl group due to the lack of a peak in the 1365–1370 cm^{-1} range and another peak in the 1380–1395 cm^{-1} range.

Substituted benzene rings have distinctive patterns at 1667–2000 cm^{-1} (Figure 7.15). These weak bands are due to overtones of aromatic bands. Such use of this region to identify substitution patterns can be difficult since these bands are weak, and strong bands, such as carbonyl bands, can obscure the overtone patterns.

The IR spectrum of a simple aromatic hydrocarbon, 1,3-dimethylbenzene, *m*-xylene, is shown in Figure 7.16. The C—H stretch region contains the C—H stretching for the aromatic at 3013 cm^{-1} and the C—H stretching for the alkane at 2907 cm^{-1}. As compared with Figure 7.15, the aromatic overtone bands in the 1667–2000 cm^{-1} range agree with *meta* substitution. From Table 7.1, the compound is confirmed with *meta*

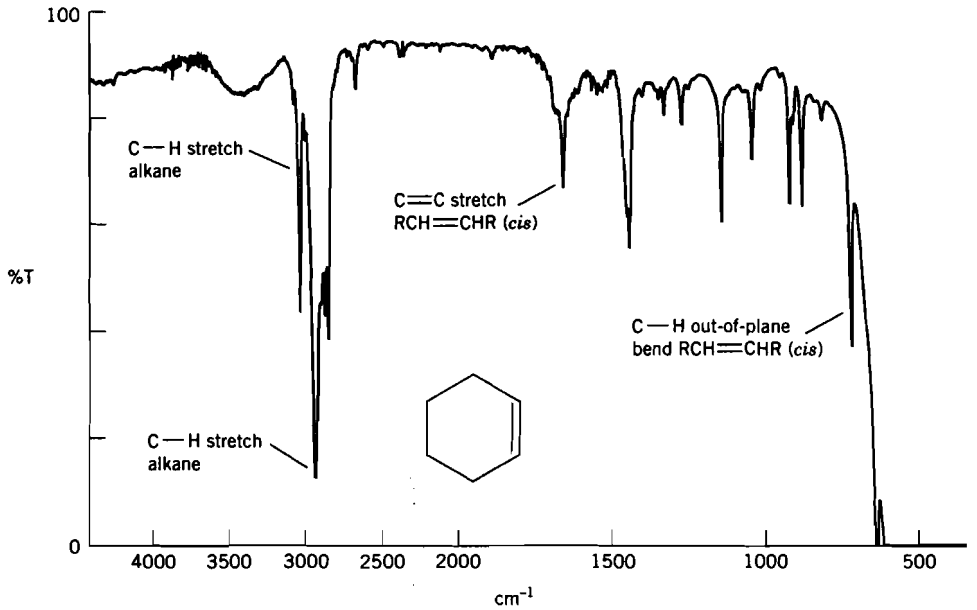


Figure 7.13 IR spectrum of cyclohexene. [Spectrum courtesy of Terra Hosp, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

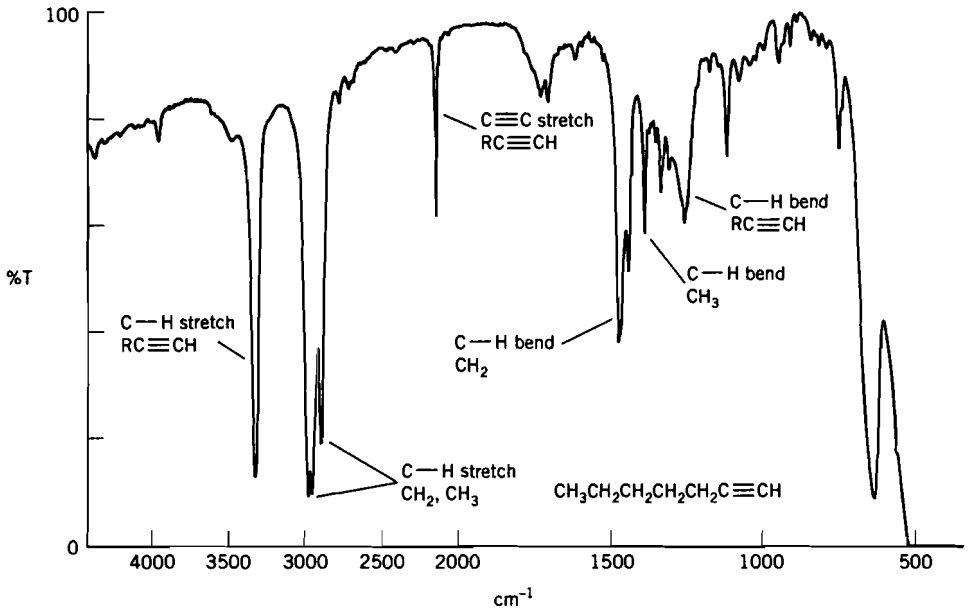


Figure 7.14 IR spectrum of 1-heptyne. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

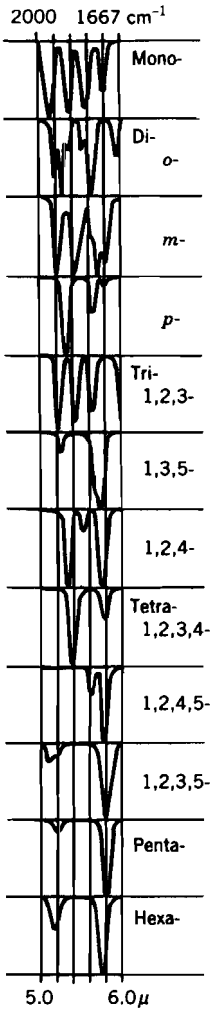


Figure 7.15 Schematic representation of the 1667–2000 cm^{-1} IR region for benzene substitution. [From J. R. Dyer, *Applications of Absorption Spectroscopy of Organic Compounds* (Prentice-Hall, Upper Saddle River, NJ, 1965) © 1965, p. 52. Reprinted by permission of Prentice-Hall, Inc., Upper Saddle River, New Jersey]

substitution with two peaks for the C—H out-of-plane bending at 685 and 767 cm^{-1}. C=C stretching for an aromatic compound occurs at 1490 and 1613 cm^{-1}.

The IR spectrum of methanol is shown in Figure 7.17. The O—H stretching of the alcohol is centered at 3366 cm^{-1}. A sharp, strong C—O stretching is seen at 1026 cm^{-1}. The peak at 1408 cm^{-1} is due to the O—H bending.

In the IR spectrum of 3-methylphenol (*m*-cresol) (Figure 7.18), a strong O—H stretching is centered at 3319 cm^{-1}, a C—O stretching for the phenol is at 1267 and 1337 cm^{-1}, and an O—H bending for the phenol is at 691 cm^{-1}. *Meta* disubstitution on the aromatic ring is indicated by C—H out-of-plane bending at 691 and 773 cm^{-1}. The C=C stretching for the aromatic is at 1484 and 1590 cm^{-1}.

In the IR spectrum of diethyl ether (Figure 7.19), there is no O—H stretching or bending. A strong C—O stretching is seen for the aliphatic ether at 1137 cm^{-1}.

Beginning with the IR spectrum of acetone (Figure 7.20), various types of carbonyl compounds will be described. A C=O stretching at 1713 cm^{-1} indicates the presence of an aliphatic ketone. Ring strain in cyclic ketones moves this band to a higher

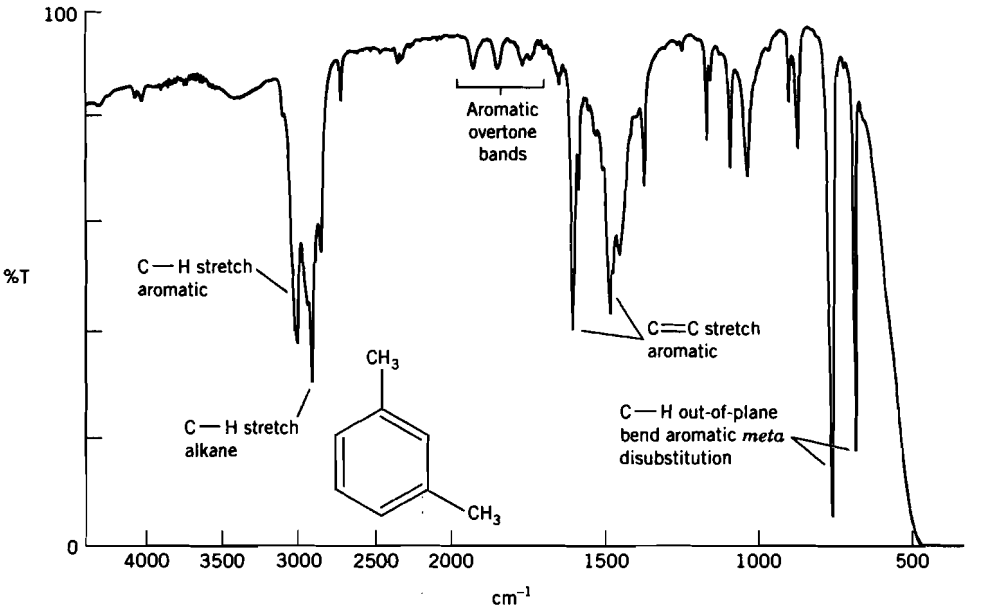


Figure 7.16 IR spectrum of *m*-xylene. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, VA. Used with permission.]

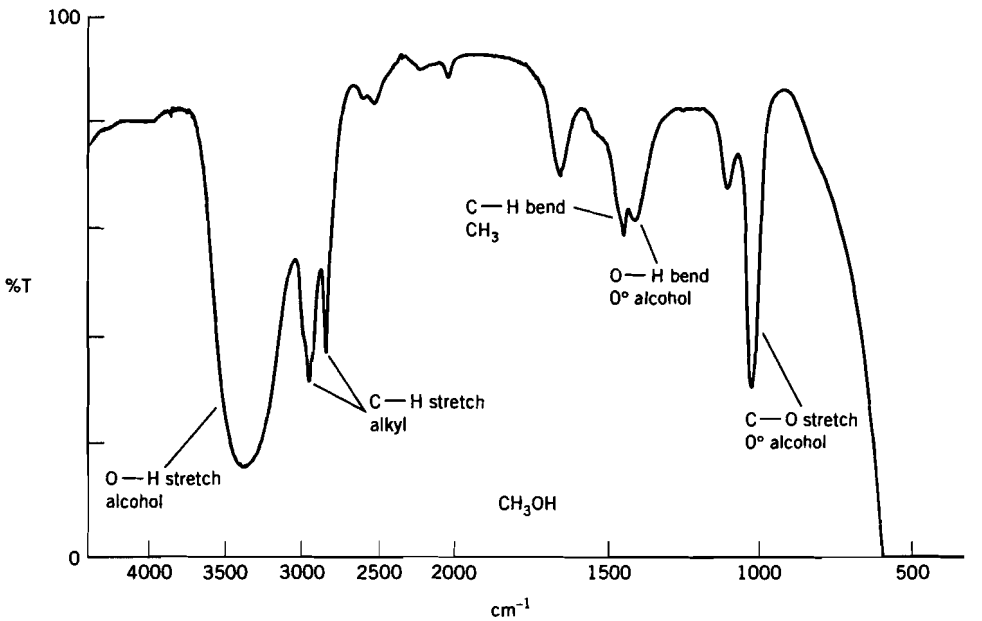


Figure 7.17 IR spectrum of methanol. [Spectrum courtesy of Terra Hosp, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

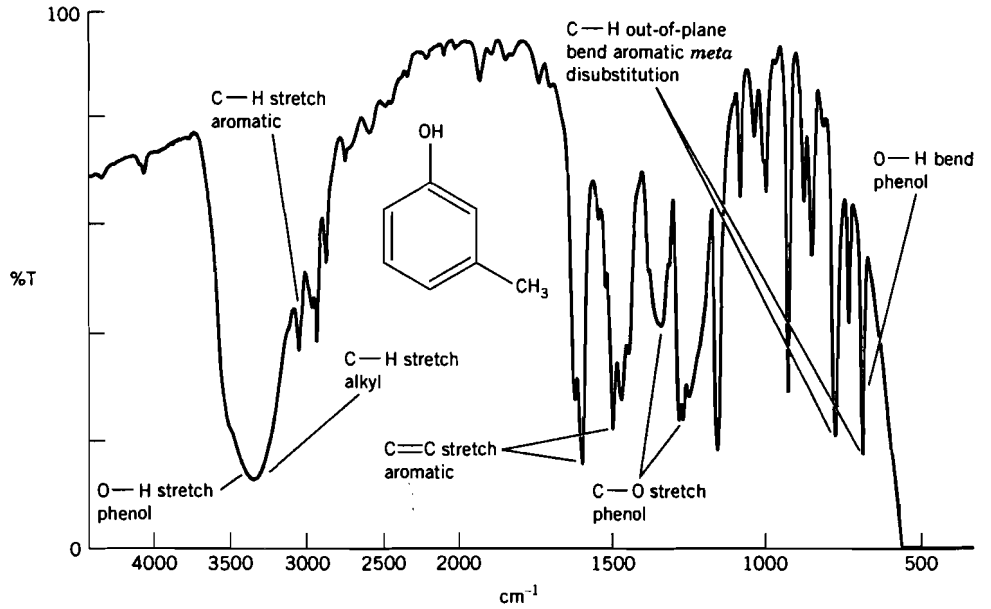


Figure 7.18 IR spectrum of *m*-cresol. [Spectrum courtesy of Terra Hosp, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

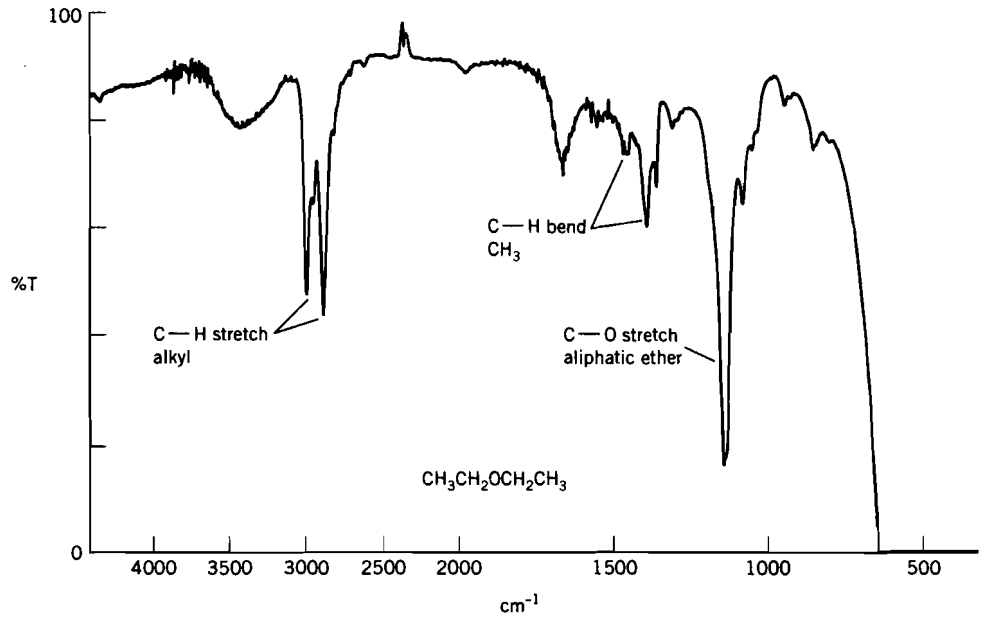


Figure 7.19 IR spectrum of diethyl ether. [Spectrum courtesy of Terra Hosp, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

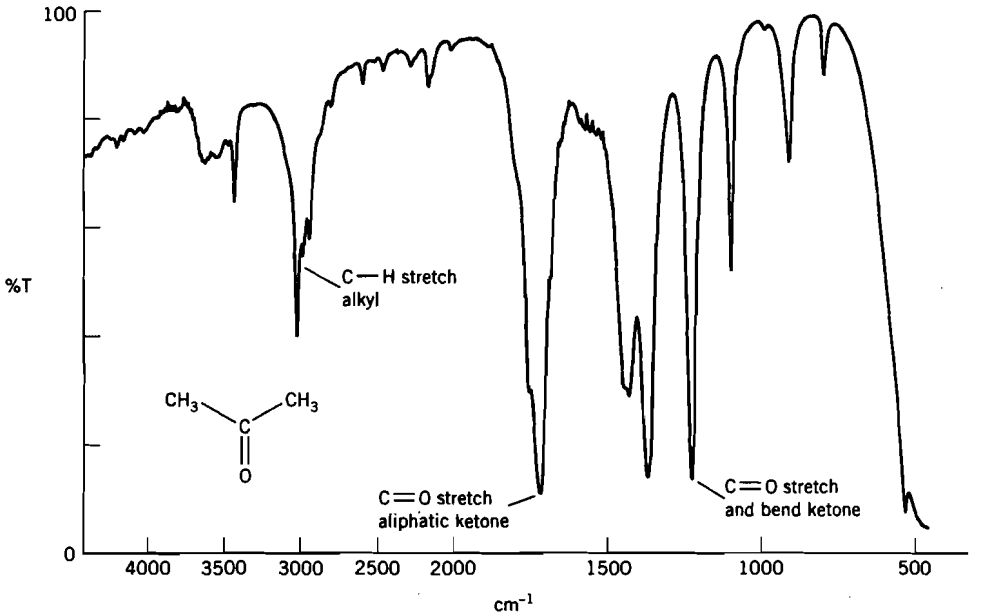


Figure 7.20 IR spectrum of acetone. [Spectrum courtesy of Terra Hosp, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

wavenumber; conjugation with a C=C or aromatic ring unit moves the band to lower wavenumbers. Also present is C=O stretching and bending for a ketone at 1213 cm^{-1}.

Acetophenone (Figure 7.21) gives a C=O stretching for an aliphatic and aryl ketone at 1684 cm^{-1}, which is a lower wavenumber than for simple aliphatic ketones. Other peaks are C=O stretching and bending for a ketone at 1260 cm^{-1} and C—H out-of-plane bending for a monosubstituted aromatic at 691 and 756 cm^{-1}.

Aldehydes are distinguished from ketones by the additional presence of two bands in the 2695–2830 cm^{-1} range. This aldehydic C—H stretching appears at 2731 and 2831 cm^{-1} in benzaldehyde (Figure 7.22). The C=O stretching for the aryl aldehyde is indicated by a peak at 1696 cm^{-1}. A weak C—H bending for the aldehyde is present at 1390 cm^{-1}.

Carboxylic acids are identified by both a C=O stretching and an O—H stretching. For propanoic acid (Figure 7.23), the O—H stretching centered at 3000 cm^{-1} and the C=O stretching at 1713 cm^{-1} are both broad because the —OH group is hydrogen bonded to the hydroxyl group of another molecule. Additional carboxylic acid peaks are indicated by the C—O stretching at 1237 cm^{-1} and the O—H bending at 1414 cm^{-1}. The peak around 3000 cm^{-1} is actually both the very broad O—H stretching and the sharper C—H stretching for an alkane.

Esters can be identified from a carboxylic acid due to the lack of O—H stretching around 3000 cm^{-1}, but esters still have a strong C=O stretching. In the IR spectrum of ethyl acetate (Figure 7.24), a strong C=O stretching is observed at 1743 cm^{-1} for an aliphatic ester as well as C—O stretching for the acetate portion at 1238 cm^{-1} and for the alkoxy portion at 1047 cm^{-1}.

The IR spectrum of another carboxylic acid derivative, benzoyl chloride, is shown in Figure 7.25. Fermi resonance causes the C=O stretching to appear as two peaks: one at 1731 cm^{-1} and one at 1778 cm^{-1}. A C—Cl stretching band occurs at 873 cm^{-1}.

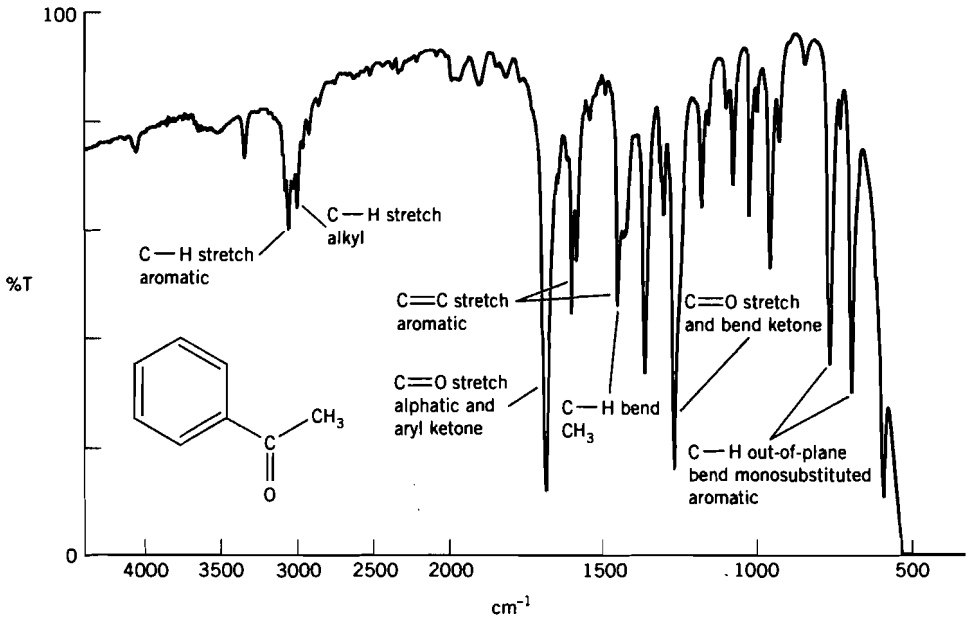


Figure 7.21 IR spectrum of acetophenone. [Spectrum courtesy of Terra Hosp, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

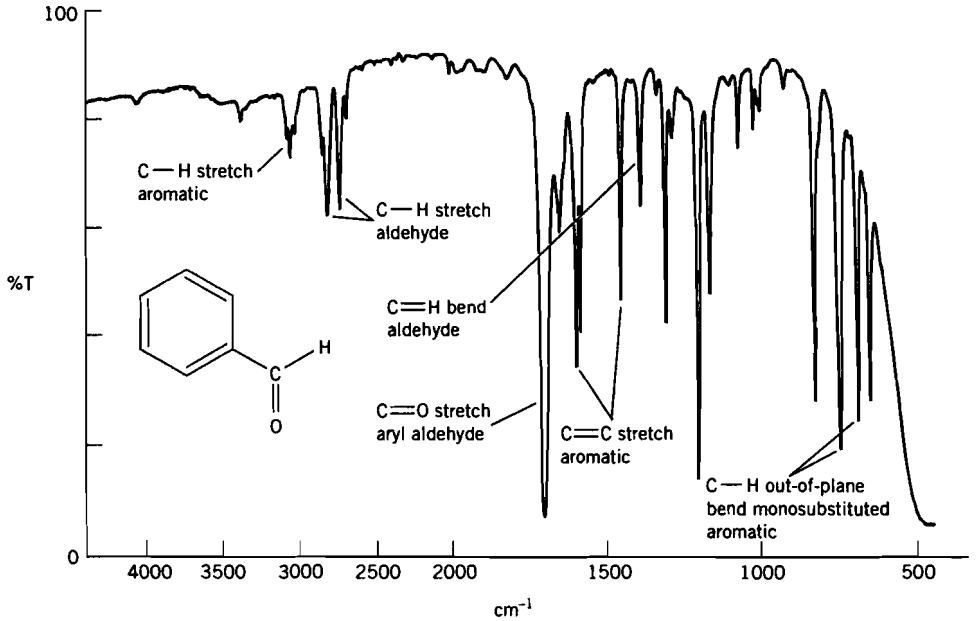


Figure 7.22 IR spectrum of benzaldehyde. [Spectrum courtesy of Terra Hosp, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

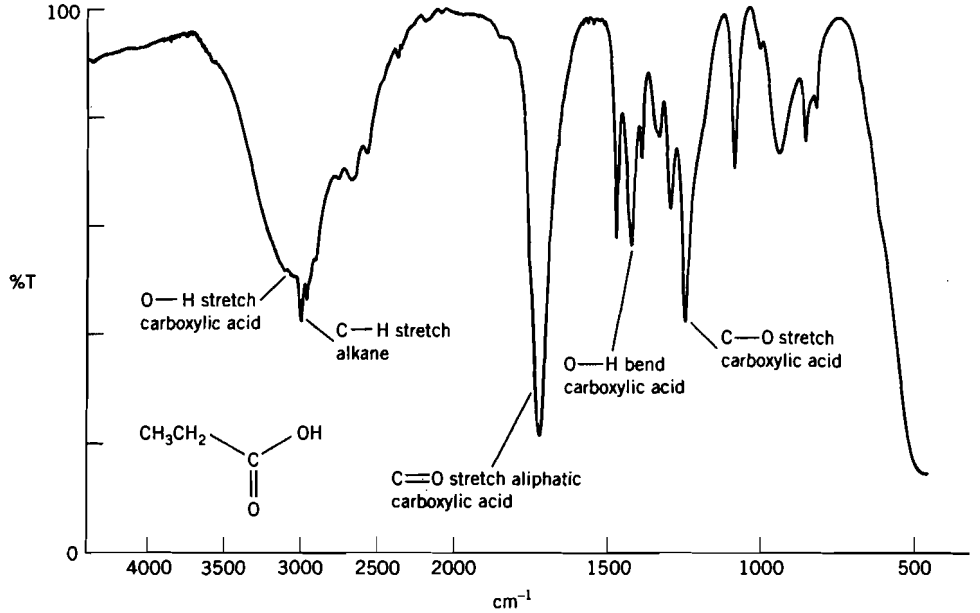


Figure 7.23 IR spectrum of propanoic acid. [Spectrum courtesy of Terra Hosp, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

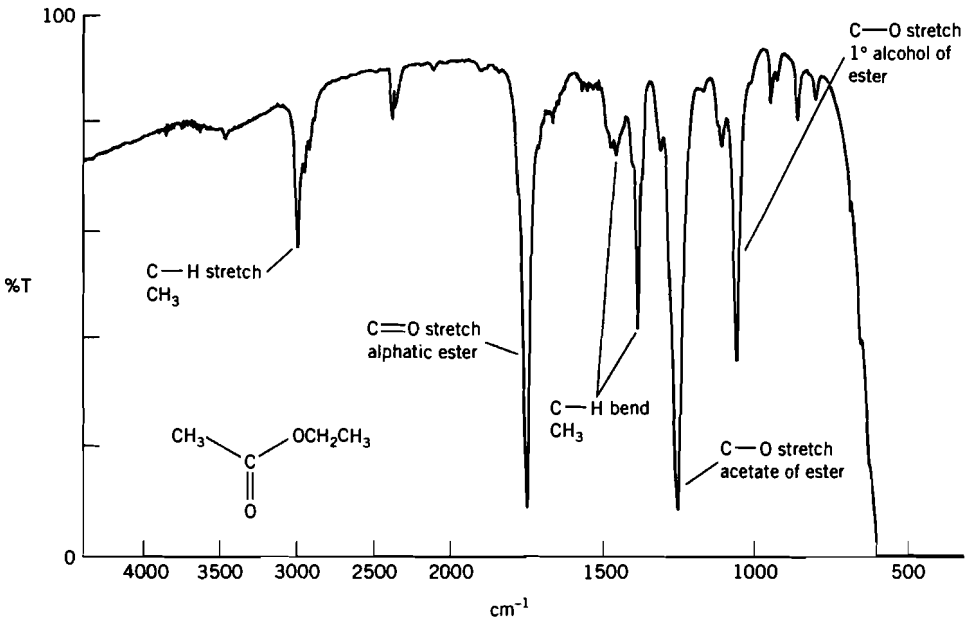


Figure 7.24 IR spectrum of ethyl acetate. [Spectrum courtesy of Terra Hosp, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

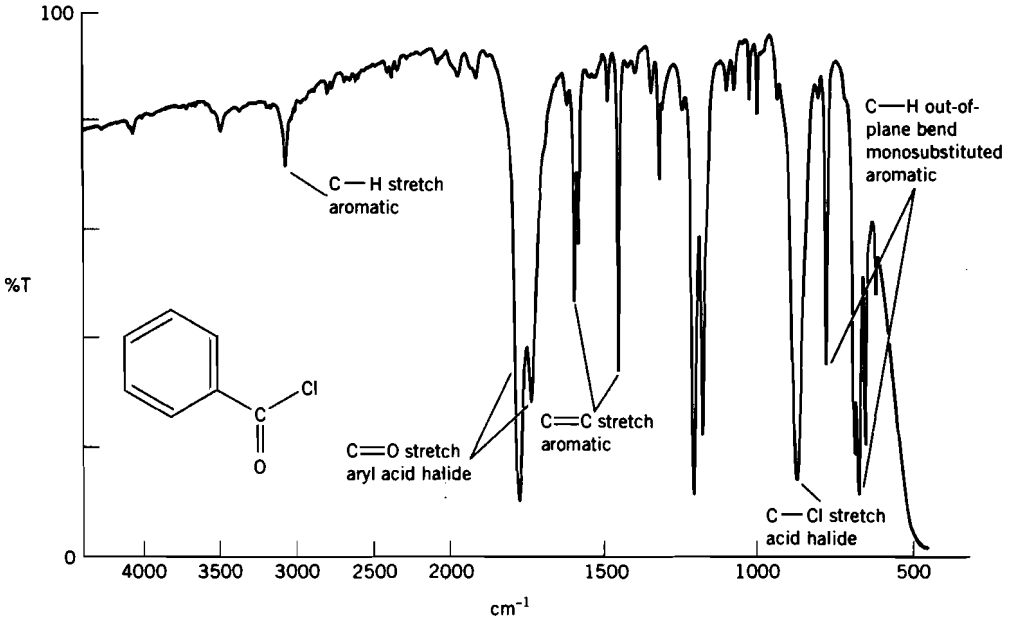


Figure 7.25 IR spectrum of benzoyl chloride. [Spectrum courtesy of Terra Hosp, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

The structure of an anhydride provides a symmetry relationship between the carbonyl groups that permits asymmetric and symmetric coupling. This results in a pair of bands for the C=O stretching, as seen in the IR spectrum of acetic anhydride (Figure 7.26). The C=O stretching appears as both an asymmetric band at 1825 cm^{-1} and a symmetric band at 1754 cm^{-1}. The C—O stretching for acetic anhydride appears at 1125 cm^{-1}.

An amide C=O stretching appears at lower wavenumbers than the examples already discussed. In the IR spectrum of *N,N*-dimethylformamide (Figure 7.27), the C=O stretching is at 1672 cm^{-1}. Because *N,N*-dimethylformamide is a tertiary amide, no N—H stretching or N—H bending signals are present. Secondary amides have one signal for N—H stretching, and primary amides have two signals for N—H stretching. The C—N stretching for the amide is at 1388 cm^{-1}.

Primary and secondary amines are identified by the number of bands in the 3300–3500 cm^{-1} range due to N—H stretching. Primary amines have two bands, secondary amines have one band, and tertiary amines have no bands. In the IR spectrum of aniline (Figure 7.28), the coupled N—H stretching appears at 3354 and 3436 cm^{-1}. The N—H bending is at 1613 cm^{-1}, and C—N stretching is at 1272 cm^{-1}. The C—N stretching of amines is difficult to find and is rarely, if ever, used for structure determination.

The IR spectrum of diethyl amine (Figure 7.29) illustrates an example of a secondary amine with only one band for N—H stretching at 3283 cm^{-1}. The C—N stretching for this aliphatic amine appears at 1138 cm^{-1}.

Nitriles are very distinctive, with a peak for C≡N stretching near 2200 cm^{-1}. In the IR spectrum of acetonitrile (Figure 7.30), strong C≡N stretching appears at 2249 cm^{-1}.

Nitrobenzene contains a functional group that shows a coupled pair of IR bands for the N–O stretching at 1343 and 1519 cm^{-1} in the IR spectrum (Figure 7.31). The C—N stretching for the nitroaromatic is at 860 cm^{-1}. The remainder of the IR spectrum is largely due to the benzene ring. Below 800 cm^{-1}, the bands are of little use here for

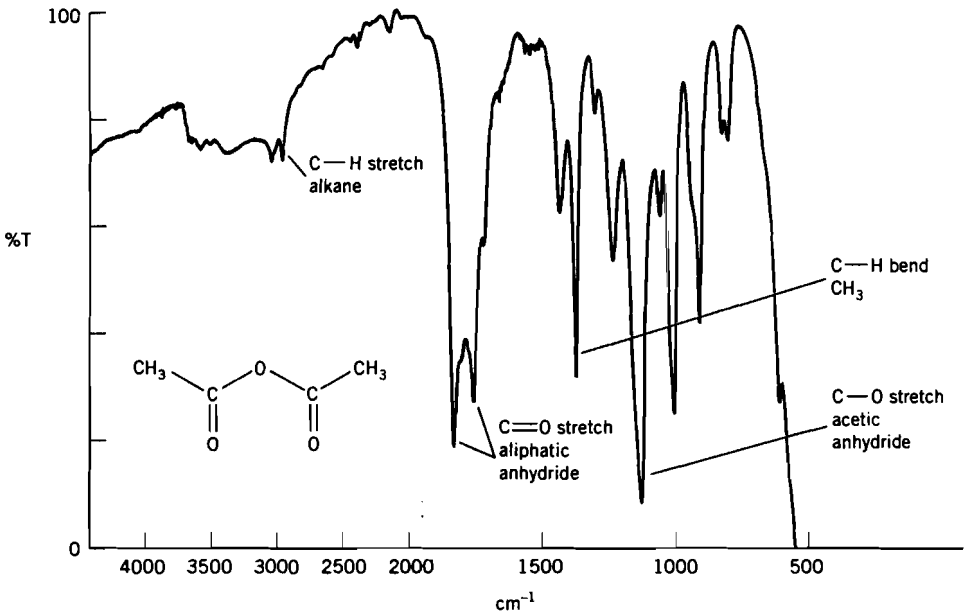


Figure 7.26 IR spectrum of acetic anhydride. [Spectrum courtesy of Terra Hosp, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

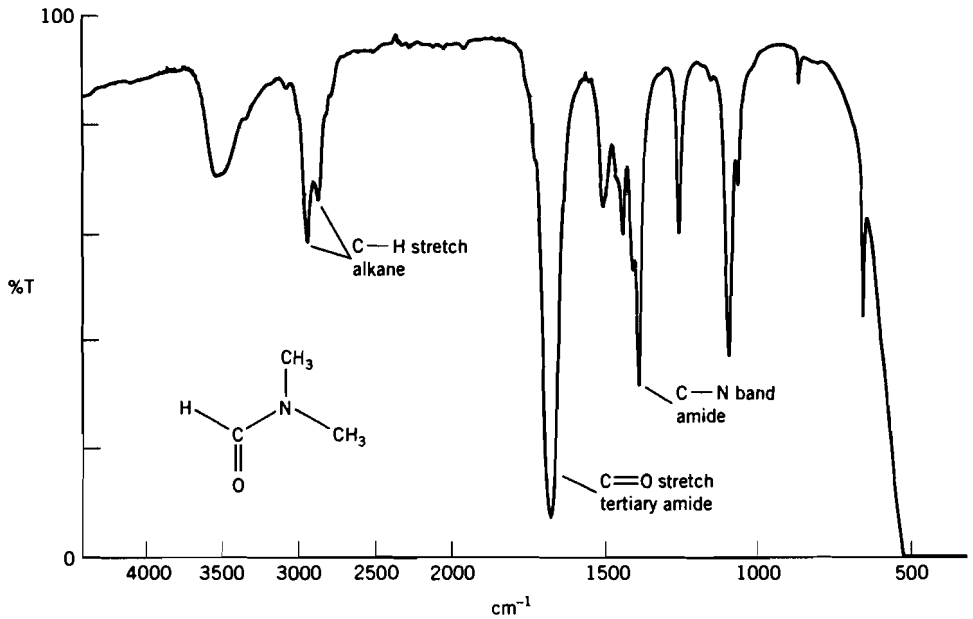


Figure 7.27 IR spectrum of *N,N*-dimethylformamide. [Spectrum courtesy of Terra Hosp, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

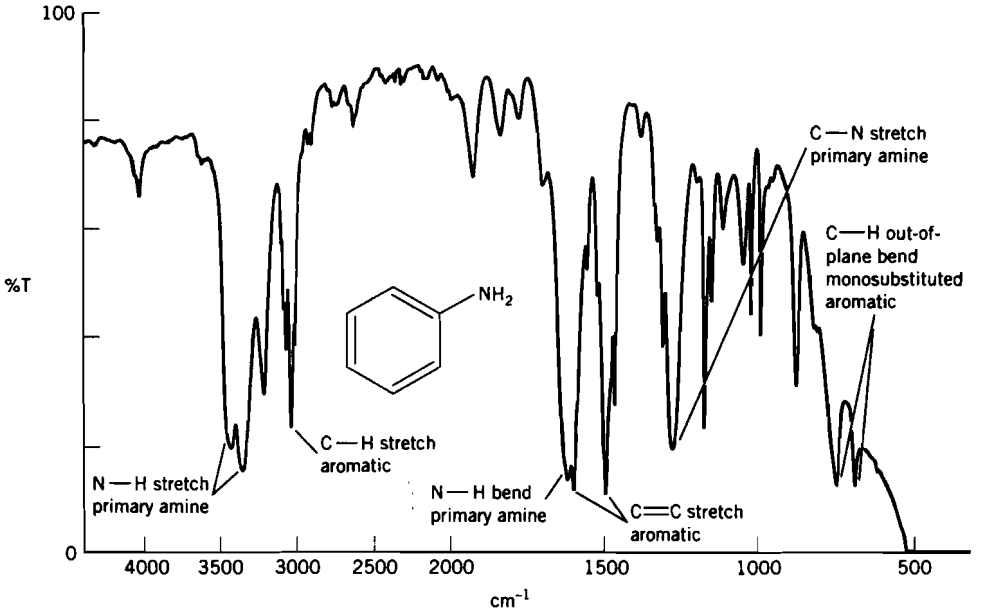


Figure 7.28 IR spectrum of aniline. [Spectrum courtesy of Terra Hosp, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

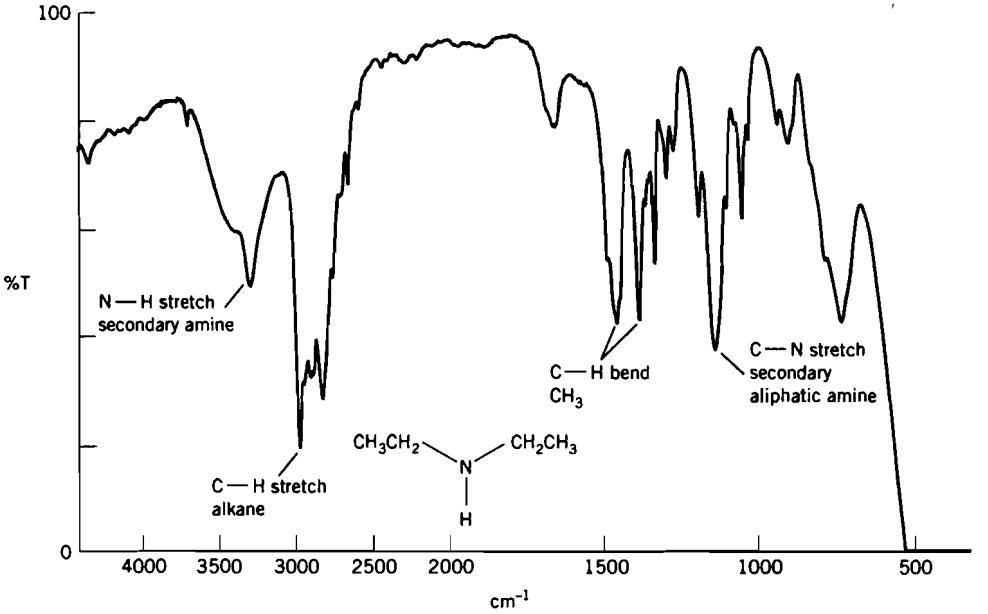


Figure 7.29 IR spectrum of diethyl amine. [Spectrum courtesy of Terra Hosp, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

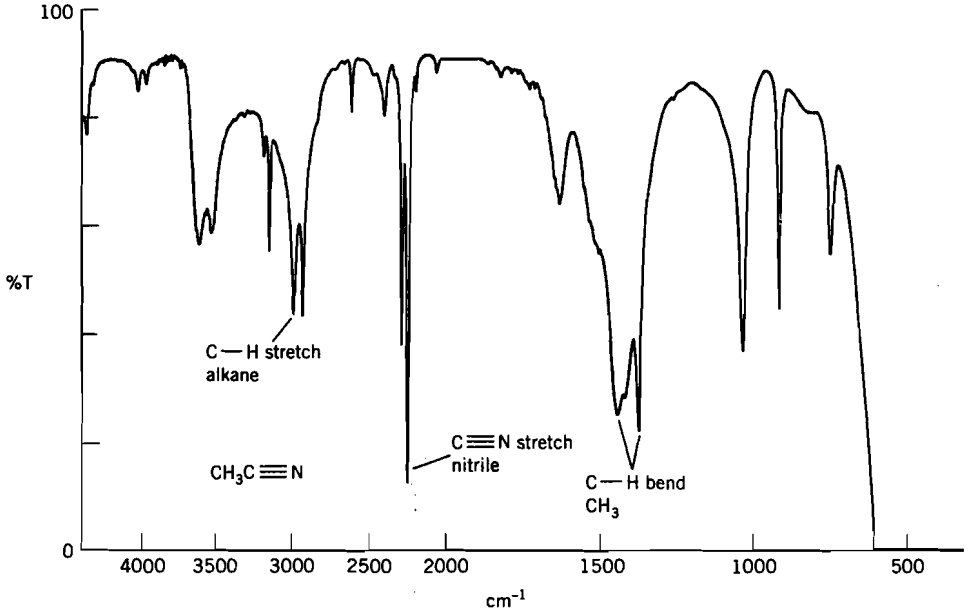


Figure 7.30 IR spectrum of acetonitrile. [Spectrum courtesy of Terra Hosp, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

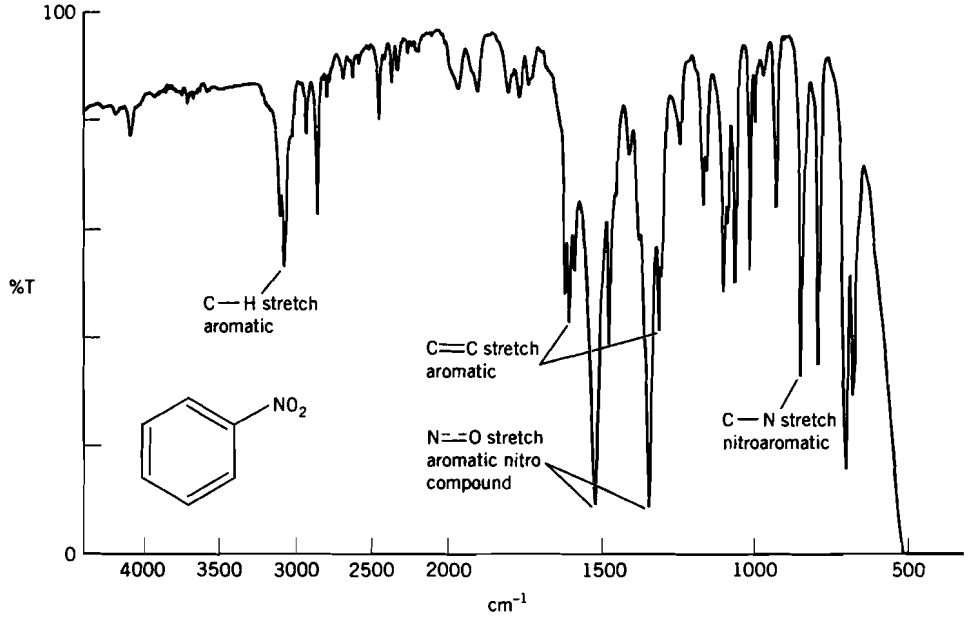


Figure 7.31 IR spectrum of nitrobenzene. [Spectrum courtesy of Terra Hosp, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

determination of the number and the relative positions of the ring substituents. Many of these bands are due to the interaction of the polar nitro group with the out-of-plane bending vibrations of the C—H of the aromatic.

The IR spectrum of chloroform (Figure 7.32) shows the presence of chlorine and can be used for reference when solution spectra are run using this compound as a solvent. The C—Cl stretching is visible at 756 cm^{-1}.

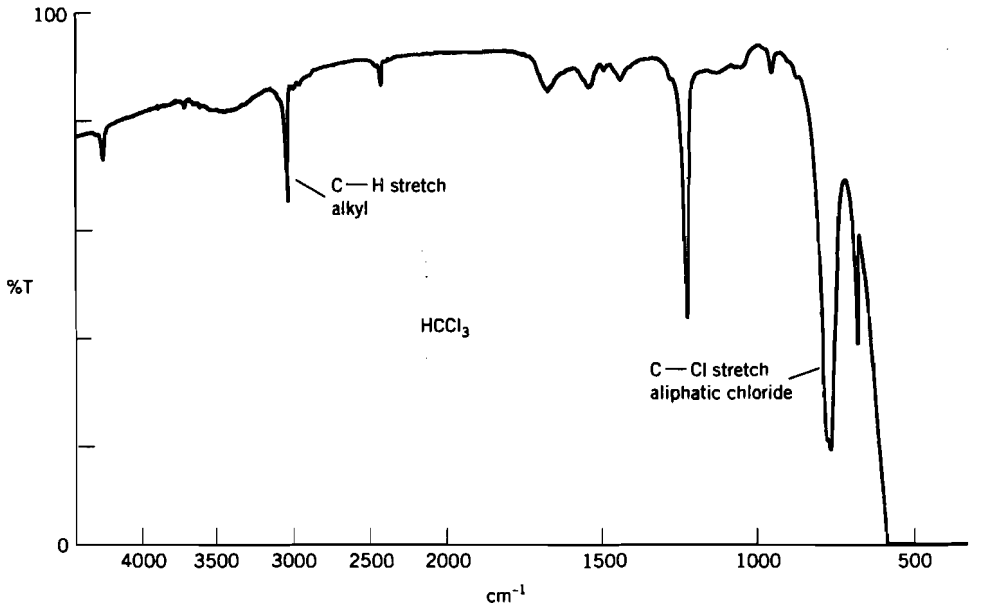
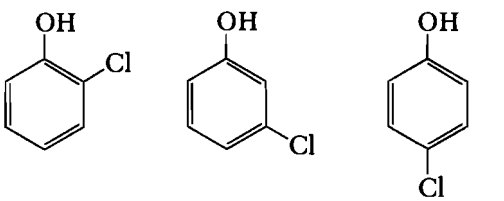


Figure 7.32 IR spectrum of chloroform. [Spectrum courtesy of Terra Hosp, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

Once an IR spectrum has been taken for an unknown compound, then begin looking for major stretching and bending peaks. A very large peak in the 3200–3500 cm^{-1} range indicates the presence of an alcohol or phenol. Another strong peak is C=O stretching, which is in the range of 1630–1850 cm^{-1}. Moderate bands in the 3300–3500 cm^{-1} range could be indicative of N—H stretching. A peak around 2200 cm^{-1} could possibly be a nitrile. If a compound is aromatic, then aromatic peaks would appear in the NMR spectra. Multiple techniques can be used in identifying an unknown compound.

In Figure 7.33, there is an indication of an alcohol or phenol with a band at 3506 cm^{-1}. This unknown compound does not have a carbonyl group since there is no strong peak in the 1630–1850 cm^{-1} range. A sharp peak at 3072 cm^{-1} is probably C—H stretching for an alkene or aromatic compound. With a formula of C_6H_5ClO, the unsaturation number is 4 [$U = 6 + 1 - \frac{1}{2}(6) + \frac{1}{2}(0)$]. Interpretation of this value gives a prediction of an aromatic compound. The only possibilities are 2-chlorophenol, 3-chlorophenol, and 4-chlorophenol.



2-chlorophenol 3-chlorophenol 4-chlorophenol

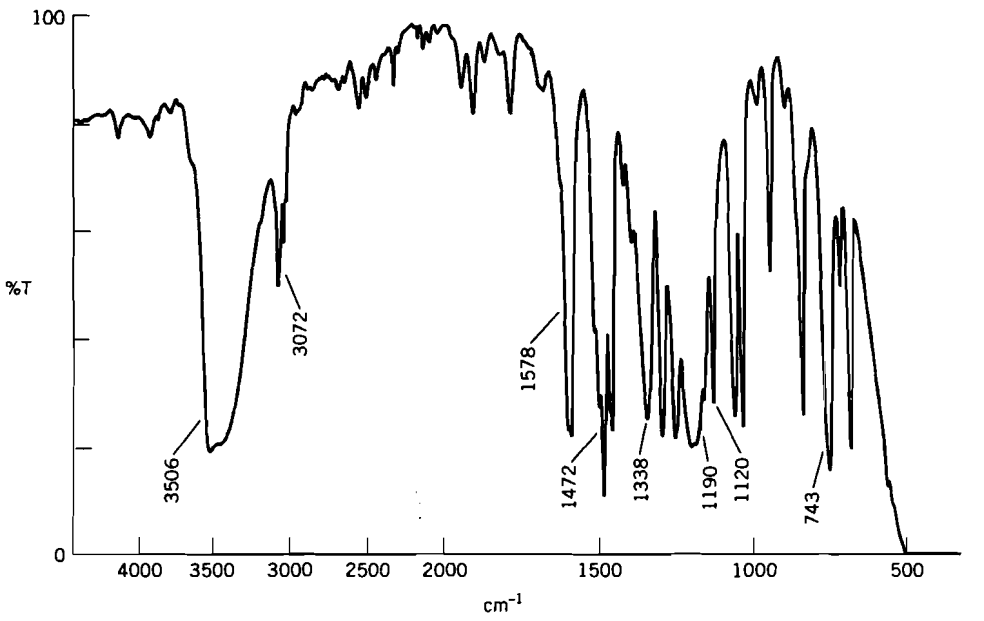


Figure 7.33 IR spectrum of unknown compound of formula C_6H_5ClO. [Spectrum courtesy of Terra Hosp, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

These three structures can be distinguished by using C—H out-of-plane bending. The closest match is an *o*-disubstituted aromatic with a signal at 743 cm^{-1}. The only possibility is 2-chlorophenol. Most of the bands are identified as follows:

frequency	bond	compound type
743	C—H out-of-plane bend	*o*-disubstituted aromatic
3506	O—H stretch	phenol
1190 and 1338	C—O stretch	phenol
743	O—H bend	phenol
3072	C—H stretch	aromatic
1472 and 1578	C=C stretch	aromatic
1120	C—Cl stretch	aryl chloride

Problems

For each of the following problems, calculate the unsaturation number and give the interpretation. List the labeled wavenumbers in tabular form and identify the bond and compound type. Give the name and the structure.

1. Unknown compound of formula C_4H_9NO (Figure 7.34). Identify wavenumbers 1390, 1649, 1660, 2985, 3201, and 3354 cm^{-1}.
2. Unknown compound of formula $C_4H_{10}O$ (Figure 7.35). Identify wavenumbers 1102, 1326, 1373, 1455, 2872, 2919, 2955, and 3342 cm^{-1}.
3. Unknown compound of formula C_7H_7Br (Figure 7.36). Identify wavenumbers 591, 797, 1484, 1596, 2919, and 3013 cm^{-1}.
4. Unknown compound of formula C_4H_8O (Figure 7.37). Identify wavenumbers 1173, 1375, 1455, 1713, and 2978 cm^{-1}.

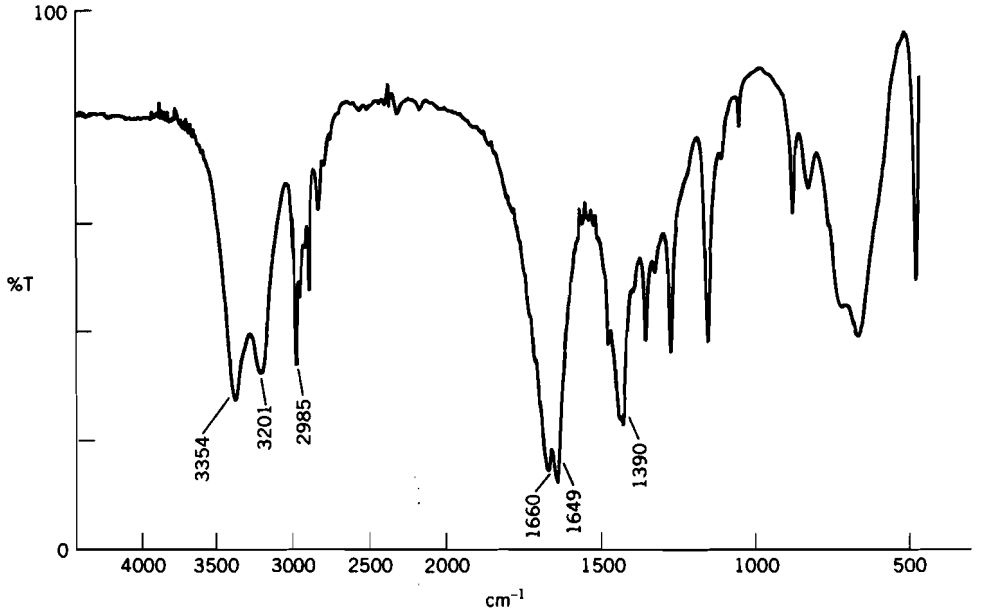


Figure 7.34 Problem 1 IR spectrum of unknown compound of formula C_4H_9NO. [Spectrum courtesy of Terra Hosp, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

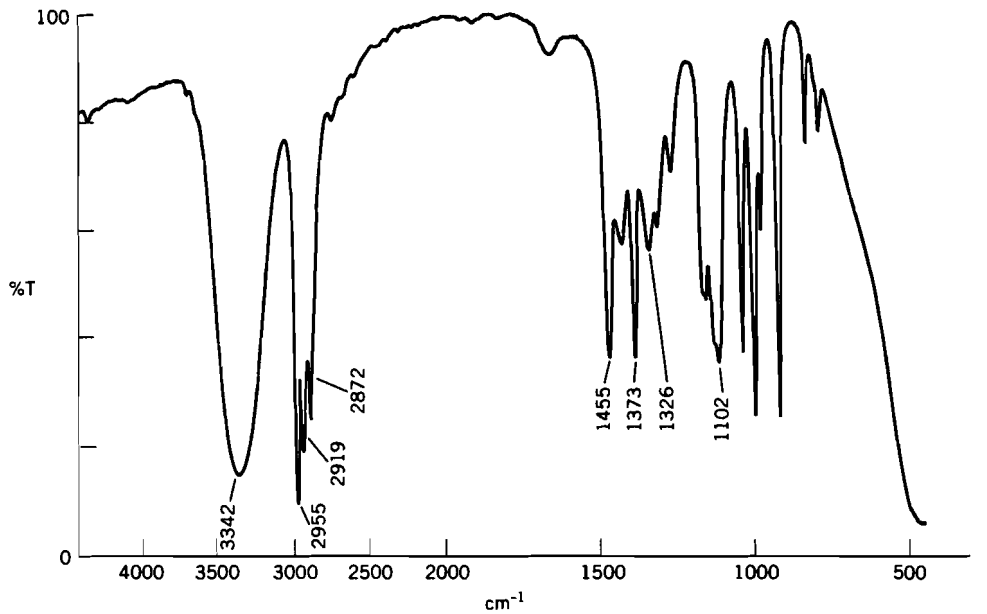


Figure 7.35 Problem 2 IR spectrum of unknown compound of formula $C_4H_{10}O$. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

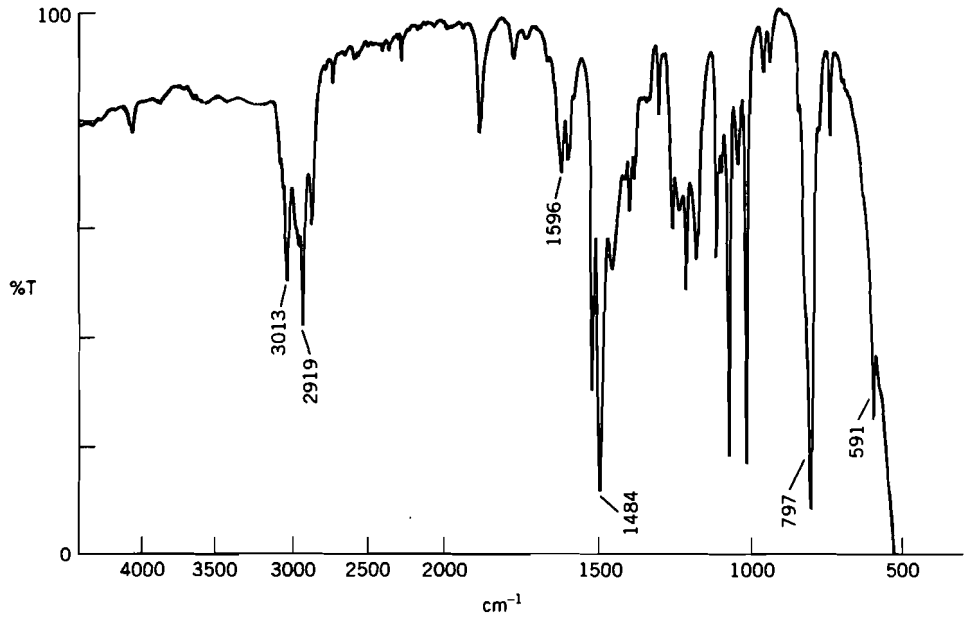


Figure 7.36 **Problem 3** IR spectrum of unknown compound of formula C_7H_7Br. [Spectrum courtesy of Terra Hosp, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

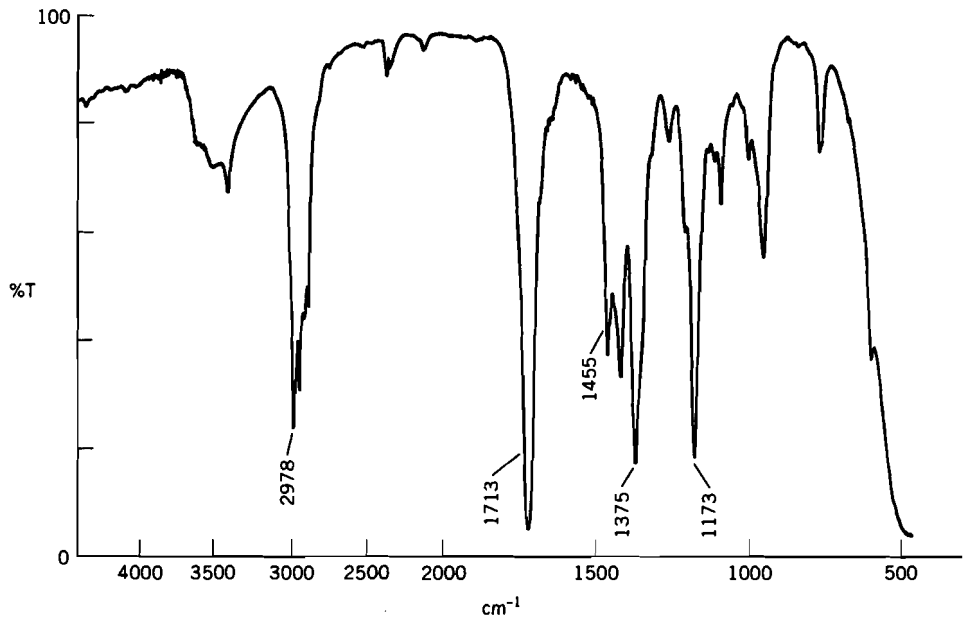


Figure 7.37 **Problem 4** IR spectrum of unknown compound of formula C_4H_8O. [Spectrum courtesy of Terra Hosp, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

CHAPTER 8

Mass Spectrometry

8.1 THEORY OF MASS SPECTROMETRY

Mass spectrometry is of lesser importance than NMR and IR spectroscopy. Many qualitative organic courses require only IR and NMR spectroscopy for compound identification. A few will require a mass spectrum of an unknown compound.

Mass spectrometry can analyze a variety of pure samples. Solid samples can be placed on the tip of a rod, which is then inserted into the vacuum chamber through a vacuum-tight seal. The solid is sublimed or vaporized in the presence of heat. Gases and liquids are introduced directly into the vacuum chamber through a syringe.

If a sample is impure, it must be separated into its individual components prior to analysis by mass spectrometry. Separation is necessary since a mixture will generate many overlapping peaks and a pure compound may generate many peaks. The most common method of separating a mixture is gas chromatography. A sample is injected into the gas chromatograph. A chromatogram is generated that shows the individual components. An individual component is then selected for analysis with the mass spectrometer. Other methods of separation include liquid chromatography, supercritical fluid chromatography, and capillary electrophoresis. Each of these methods can be interfaced with a mass spectrometer.

For a compound to be analyzed in a mass spectrometer, it must be in the gaseous state. Solids and liquids are vaporized with heat. The vapors are then bombarded with a beam of electrons. In the electron ionization mass spectrometer (Figure 8.1), positive ions are accelerated through the accelerating plates. The magnet field separates the ions by their mass-to-charge ratio (m/z). Since the charge (z) is usually $+1$, a direct measure of the particle is obtained. By varying the magnetic field, the abundance of each mass is detected. A detector then records the mass-to-charge ratio and this information is given as a mass spectrum.

The compound may be ionized in several ways. Besides the electron ionization, described above, the compound may be ionized by *chemical ionization.* A reagent gas such as methane, isobutane, or ammonia is ionized by electron impact. These ions react with the sample molecules to produce ions. *Electrospray ionization* generates ions directly from solution. A spray of charged droplets is created by the application of a high potential difference. This method can produce multiply charged ions that increase with increasing molecular weight. The *atmospheric pressure chemical ionization* contains a heated vaporizer that aids in the vaporization of the compound. A corona discharge is used to create ions under atmospheric pressure. In *matrix-assisted laser desorption ionization,* the compound is dissolved in a solution containing an excess of the matrix compound, which absorbs at a laser wavelength. The solution is placed on the laser target. A pulse UV radiation of this mixture produces a plasma from the vaporization of both the matrix and the compound. The compound is dissolved in a liquid matrix such

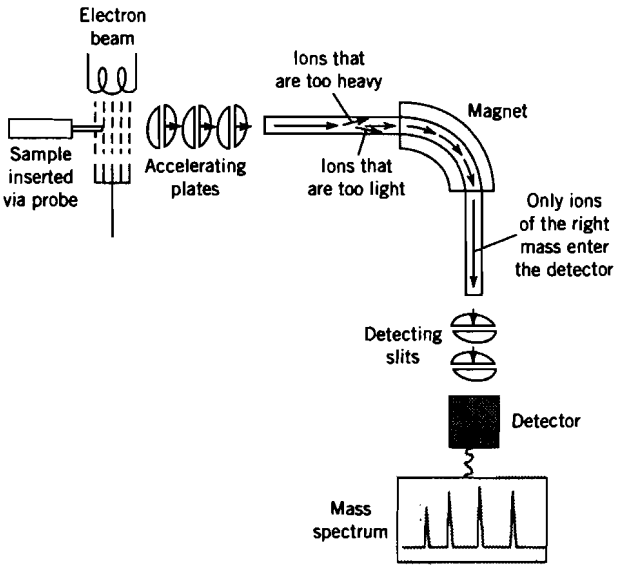


Figure 8.1 A diagram of an electron ionization mass spectrometer.

as glycerol or *m*-nitrobenzyl alcohol in the *fast atom bombardment*. The mixture is placed on a probe and bombarded with a high-energy beam of cesium ions or xenon atoms that desorb molecular ions and fragments from the compound. In *inductively coupled plasma*, the sample is injected into gaseous ions that are produced by the inductive coupling of high energy to argon. The sample droplets are vaporized and ionized.

Many other types of mass analyzers are available. In a *double-focusing mass spectrometer*, a magnetic field provides directional focusing. The ions are then subjected to an electrical field that is perpendicular to the magnetic field. A *quadrupole mass filter* contains four parallel rods. Ions enter from one end and are subjected to both direct current and radio frequency voltage on the rods. The only ions that are recorded are the ions that are able to pass beside the poles without striking the poles. Scanning of the masses is performed by varying the direct current and the radio frequency voltage while maintaining their ratios. In *quadrupole ion storage*, the ions are stored temporarily in an ion trap. The ions are released to the detector sequentially by scanning the electric field to eject the ions sequentially in increasing mass-to-charge ratio. A burst of ions is emitted from a source in a *time-of-flight mass analyzer*. The ions are separated by their different flight times over a known distance. A *Fourier transform–ion cyclotron resonance* traps the ions in a cubic cell in the presence of a constant magnetic field. The ions assume a cyclotron motion under the influence of a constant radio frequency voltage. The electric field is varied and when resonance is reached, a signal is detected. A *tandem mass spectrometer* generates additional fragments from a selected ion and then mass analyzes the fragments.

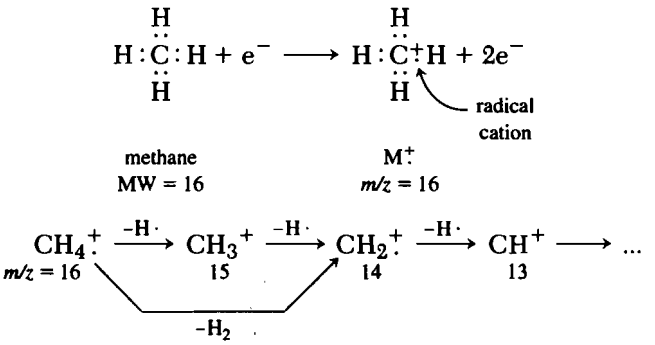
8.2 CLEAVAGE REACTIONS

When an electron strikes a neutral molecule, that molecule may be ionized by the loss of one electron.

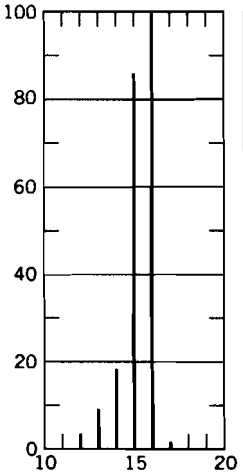
$$M + e^- \longrightarrow M^{+\cdot} + 2e^-$$

The *molecular ion*, $M^{+\cdot}$, is formed when the original molecule loses one electron and becomes positive. The molecular ion is also a radical cation. A negligible mass change occurs, but the chemistry of the molecule is very different.

The formation of the molecular ion is illustrated with methane. The molecular ion can then undergo bond cleavage and a number of fragmentation routes are possible.



In Figure 8.2, the peaks are seen at 16, 15, 14, and 13, corresponding to the four species in the above equation.



m/z	Intensity
12	2.6
13	8.6
14	17.1
15	85.6
16	100.0
17	1.15

Figure 8.2 Mass spectrum of CH_4 in both bar graph and tabular form.

In a mass spectrum, the tallest peak is the *base peak*. The base peak is usually not the same as the molecular ion.

In unit-resolution mass spectrometry (mass to the nearest whole number), the cluster of peaks of successive mass numbers usually observed in the region of the molecular ion is due to the significant abundance of more than one isotope of one of more of the elements in a compound (Table 8.1). The molecular ion is composed of atoms of the most abundant isotopes. For methane, the isotopes would be ^{12}C and ^{1}H. Contributions are made to the smaller peaks of higher mass in this cluster by molecules composed of the less abundant isotopes (for methane, ^{13}C and ^{2}H).

To appreciate the significance of the isotopes of carbon and hydrogen (Table 8.1), it might be tempting to write the structure of an *m/z* ratio of 16 as $^{12}C_1{}^{1}H_4$, rather than simply CH_4. For the more abundant isotopes, the nuclide does not need to be labeled. The exception to this rule is for the case of bromine and chlorine; these particular

TABLE 8.1 Isotope Abundances Based on the Common Isotope Set at 100%

Element			Abundance (%) M + 1		Abundance (%) M + 2	
Hydrogen	^{1}H	100	^{2}H	0.0115		
Carbon	^{12}C	100	^{13}C	1.08		
Nitrogen	^{14}N	100	^{15}N	0.369		
Oxygen	^{16}O	100	^{17}O	0.0381	^{18}O	0.205
Fluorine	^{19}F	100				
Silicon	^{28}Si	100	^{29}Si	5.08	^{30}Si	3.35
Phosphorus	^{31}P	100				
Sulfur	^{32}S	100	^{33}S	0.800	^{34}S	4.52
Chlorine	^{35}Cl	100			^{37}Cl	32.0
Bromine	^{79}Br	100			^{81}Br	97.3
Iodine	^{127}I	100				

nuclides need to be identified. The greatest contribution to the *m/z* peak is from $^{13}C_1{}^{1}H_4$, as seen in Table 8.2. Minor contributions are seen from substituting a deuterium atom for any one of the four hydrogen atoms in methane. Peaks from species containing minor isotopes of more than two elements are usually too weak to make significant contributions to the mass spectrum.

The M + 1 and M + 2 peaks compared to that of the M peak at 100 can be used to determine the molecular formula of a compound. This is based on the molecular formula and the known natural abundances of the isotopes. Tables of M + 1 and M + 2 peak intensities for all possible formulas of a given molecular weight can be used to determine the molecular formula for a compound. The following equations give general guidelines for predicting the intensities of the M + 1 and the M + 2 peaks:

$$\%\,[M+1] = [1.08 \times nC] + [0.0115 \times nH] + [0.369 \times nN] + [0.0381 \times nO] + [5.08 \times nSi] + [0.800 \times nS]$$

TABLE 8.2 Isotope Abundance Aspects of Methane (CH_4)

Possible Molecular Species	Nominal Mass	Nuclide	Abundance Relative to the Most Abundant Isotope
$^{12}C^{1}H_4$	16	^{12}C	100[a]
$^{13}C^{1}H_4$	17	^{13}C	1.08
$^{12}C^{1}H_3{}^{2}H_1$	17	^{2}H	0.0115
$^{14}C^{1}H_4$	18	^{14}C	[b]
$^{12}C^{1}H_2{}^{2}H_2$	18	—	—
$^{12}C^{1}H_3{}^{3}H_1$	18	^{3}H	[b]
$^{12}C^{1}H_1{}^{2}H_3$	19	—	—
$^{12}C^{2}H_4$	20	—	—
$^{13}C^{2}H_4$	Highly improbable	—	—

[a]Arbitrary standard; set at 100%.

[b]Radioactive isotope; abundance varies with time and is negligible for mass spectral considerations.

$$\% [M + 2] = \left[\frac{(1.08 \times nC)^2}{200}\right] + [0.205 \times nO] + [3.35 \times n\text{Si}] + [4.52 \times nS] + [32.0 \times n\text{Cl}] + [97.3 \times n\text{Br}]$$

where

n = number of that type of atom

For a molecular ion of 28, C_2H_4, CO, and N_2 are possibilities. Using the equations above, the abundances of the M + 1 and M + 2 peaks can be calculated.

The calculation of M + 1 and M + 2 peaks is shown below for C_2H_4, with only C and H shown in the calculations:

$$\% [M + 1] = [1.08 \times 2] + [0.0115 \times 4] = 2.21$$

$$\% [M + 2] = \left[\frac{(1.08 \times 2)^2}{200}\right] = 0.0233$$

The values for M + 1 and M + 2 peaks are different for CO, again showing only the C and the O values:

$$\% [M + 1] = [1.08 \times 1] + [0.0381 \times 1] = 1.12$$

$$\% [M + 2] = \left[\frac{(1.08 \times 1)^2}{200}\right] + [0.205 \times 1] = 0.211$$

The M + 1 peak for N_2 is shown below. The M + 2 value for N_2 is 0.00, since there is no value for N in the equation.

$$\% [M + 1] = [0.369 \times 2] = 0.738$$

These values are in good agreement with the observed values shown in Table 8.3.

TABLE 8.3 Masses and Isotope Abundance Ratios for Combinations of C, H, N, and O Corresponding to Mass 28

Formula	*m/z* Ratio	M + 1	M + 2
C_2H_4	28.0313	2.28	0.01
CO	27.9949	1.15	0.20
N_2	28.0062	0.74	0.00

PROBLEMS

1. Calculate the M + 1 and M + 2 peaks for C_3H_4O, C_4H_8, and $C_2H_4N_2$.
2. Calculate the M + 1 and M + 2 peaks for $C_6H_{12}Br_2$, $C_6H_{12}BrCl$, and $C_6H_{12}Cl_2$.

High-resolution mass spectrometry is far superior for determining the molecular formula of a compound. High-resolution mass spectra are obtained when both an electric field and a magnetic field are used to obtain the spectrum. As shown in Table 8.3, C_2H_4 has an exact mass of 28.0313, from 2 × 12.0000 (the exact mass of ^{12}C) plus 4 × 1.00783 (the exact mass of ^{1}H). Similarly, CO has an exact mass of 27.9949, obtained from the sum of 12.0000 (the exact mass of the nuclide ^{12}C) plus 15.99491 (the exact mass of the nuclide ^{16}O). The exact mass of N_2 is 28.0062, or 2 × 14.00307 (the exact mass of ^{14}N). If an experimental value of 27.9938 is obtained, this value is in better

agreement with CO than with C_2H_4 or N_2. High-resolution results with at least three or four significant figures beyond the decimal point are quite common. In using high-resolution mass spectrometry, the exact mass of the most abundant isotope must be used, not the elemental mass from the periodic table. Each atomic weight listed on the periodic table is a weighted average of all the isotopes.

In Table 8.4, the exact masses of the isotopes are listed. These values can be used in calculating the exact molecular weight of the compound. From Table 8.1, the ^{37}Cl isotope would be approximately one-third the height of the ^{35}Cl isotope. This is based on Table 8.4, where chlorine atoms consist of 75.78% of ^{35}Cl and 24.22% of ^{37}Cl, which is a 3:1 ratio. The ^{79}Br isotope is approximately in the same abundance as the ^{81}Br isotope, as seen in both Table 8.1 and Table 8.4. Bromine exists as 50.69% of ^{79}Br and 49.31% of ^{81}Br. Polyhalogen compounds (Br and/or Cl) have more complex patterns, as seen in the bar graphs in Figure 8.3.

TABLE 8.4 Exact Masses of Isotopes

Element	Atomic Weight[a]	Nuclide	Isotopic Composition[b]	Mass[c]
Hydrogen	1.00794	^{1}H	99.9885	1.00783
		D (^{2}H)	0.0115	2.01410
Carbon	12.0107	^{12}C	98.93	12.00000
		^{13}C	1.07	13.00336
Nitrogen	14.0067	^{14}N	99.632	14.00307
		^{15}N	0.368	15.00010
Oxygen	15.9994	^{16}O	99.757	15.99491
		^{17}O	0.038	16.99914
		^{18}O	0.205	17.99916
Fluorine	18.9984032	^{19}F	100	18.99840
Silicon	28.0855	^{28}Si	92.2297	27.97693
		^{29}Si	4.6832	28.97649
		^{30}Si	3.0872	29.97377
Phosphorus	30.973761	^{31}P	100	30.97376
Sulfur	32.065	^{32}S	94.93	31.97207
		^{33}S	0.76	32.97146
		^{34}S	4.29	33.96787
Chlorine	35.453	^{35}Cl	75.78	34.96888
		^{37}Cl	24.22	36.96590
Bromine	79.904	^{79}Br	50.69	78.91834
		^{81}Br	49.31	80.91629
Iodine	126.90447	^{127}I	100	126.90447

[a]From T. B. Coplen, *Pure Appl. Chem.*, *73* (4), 667–683 (2001).

[b]From K. J. R. Rosman and P. D. P. Taylor, *Pure Appl. Chem.*, *70* (1), 217–235 (1998).

[c] From H. Xiaolong, Z. Chunmei, Z. Youxiang, and Z. Zhixiang (China Nuclear Data Center, Beijing, China); T. V. Golashvili, H. Lbov, and A. Demidov (Atominform, Moscow, Russia); and V. P. Chechev (V. G. Khlopin Radium Institute, St. Petersburg, Russia).

Table 8.5 summarizes some distinguishing characteristics of certain elements in a mass spectrum.

To explain the fragmentation pattern in a mass spectrum, think of the molecule being hit with the electrons and then either becoming a molecular ion or breaking apart into fragments. Some of these fragmentation patterns are fairly simple; others involve additional reactions or rearrangements. Cleavage is favored at branch sites that lead to

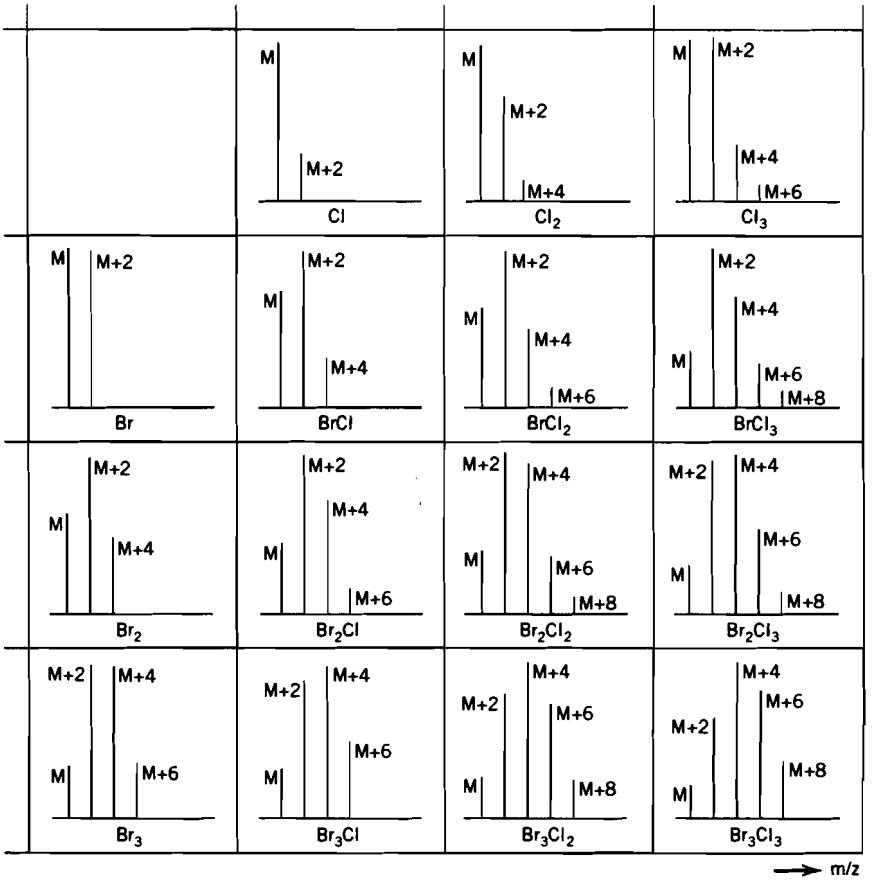


Figure 8.3 Peaks in molecular ion region of bromo and chloro compounds. Contributions due to C, H, N, and O are usually small compared to those due to Br and Cl.

TABLE 8.5 Distinguishing Elements in a Mass Spectrum

Element	Distinguishing Characteristic
N	Odd M^+
S	Large M + 2 (about 4%)
Cl	M + 2 one-third as large as M^+
Br	M + 2 as large as M^+
I	Small M + 1 and M + 2

more substituted carbocations and radicals. The best way to explain the *m/z* charge ratios is through the use of examples.[1]

The mass spectrum of hexane (Figure 8.4) shows that the molecular ion (*m/z* 86) is split into a pentyl cation (*m/z* 71) and a methyl radical.

$$\left[CH_3CH_2CH_2CH_2CH_2\text{-}CH_3\right]^{+\cdot} \longrightarrow CH_3CH_2CH_2CH_2CH_2^{+} + \cdot CH_3$$

hexane radical cation, $M^{+\cdot}$ *m/z* 86 — pentyl cation, *m/z* 71 — methyl radical, not detected

[1]All spectra were obtained on a gas chromatograph–mass spectrometer. The GC is an HP 5890 Series II model. The MS is an HP 5971 mass selective detector.

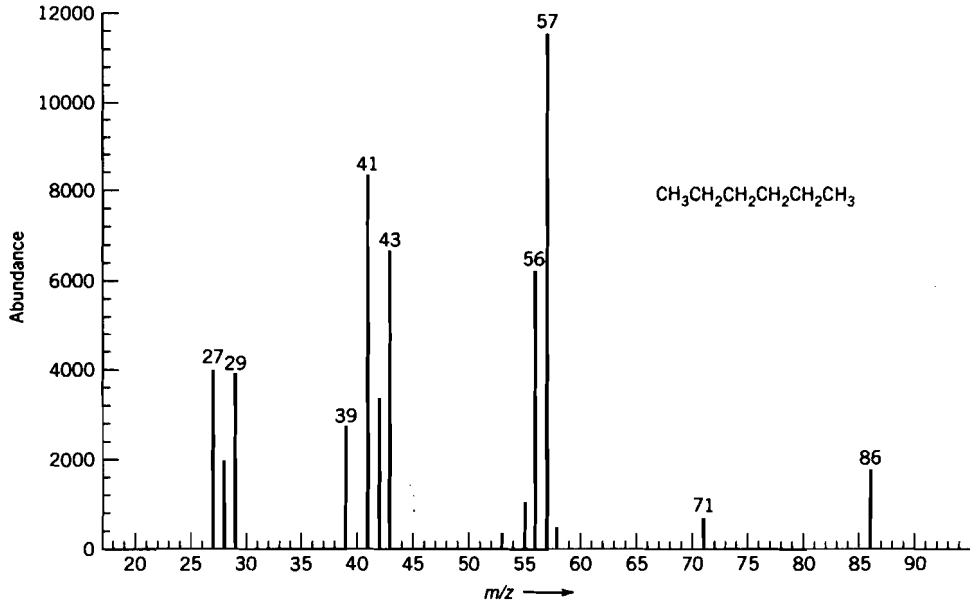


Figure 8.4 Mass spectrum of hexane. [Spectrum courtesy of Vernon Miller, Department of Chemistry, Roanoke College, Salem, Virginia. Used with permission.]

A pentyl radical and a methyl cation could also be created from this cleavage:

$$\left[CH_3CH_2CH_2CH_2CH_2\text{-}CH_3\right]^{+\cdot} \longrightarrow CH_3CH_2CH_2CH_2CH_2\cdot + {}^{+}CH_3$$

hexane radical cation	pentyl radical	methyl cation
$M^{+\cdot}$ *m/z* 86	not detected	not detected

Fragmentation can also occur to form a butyl cation (*m/z* 57) and an ethyl radical or a butyl radical and an ethyl cation (*m/z* 29). The butyl cation is the base peak, since it is the tallest peak in the spectrum.

$$\left[CH_3CH_2CH_2CH_2\text{-}CH_2CH_3\right]^{+\cdot} \longrightarrow CH_3CH_2CH_2CH_2{}^{+} + \cdot CH_2CH_3$$

hexane radical cation	butyl cation	ethyl radical
$M^{+\cdot}$ *m/z* 86	*m/z* 57	not detected

$$\left[CH_3CH_2CH_2CH_2\text{-}CH_2CH_3\right]^{+\cdot} \longrightarrow CH_3CH_2CH_2CH_2\cdot + {}^{+}CH_2CH_3$$

hexane radical cation	butyl radical	ethyl radical
$M^{+\cdot}$ *m/z* 86	not detected	*m/z* 29

Hexane can undergo a symmetrical cleavage to yield a propyl cation (*m/z* 43) and a propyl radical:

$$\left[CH_3CH_2CH_2\text{-}CH_2CH_2CH_3\right]^{+\cdot} \longrightarrow CH_3CH_2CH_2{}^{+} + \cdot CH_2CH_2CH_3$$

hexane radical cation	propyl cation	propyl radical
$M^{+\cdot}$ *m/z* 86	*m/z* 43	not detected

As seen in Figure 8.5, 1-bromobutane (*m/z* 136, 138) can be fragmented to the bromide cation (*m/z* 79, 81) and the butyl radical or the bromide radical and the butyl cation (*m/z* 57). As described earlier, peaks containing bromide are very distinctive, since the M + 2 peak is approximately the same size as the M peak. The butyl cation is the base peak.

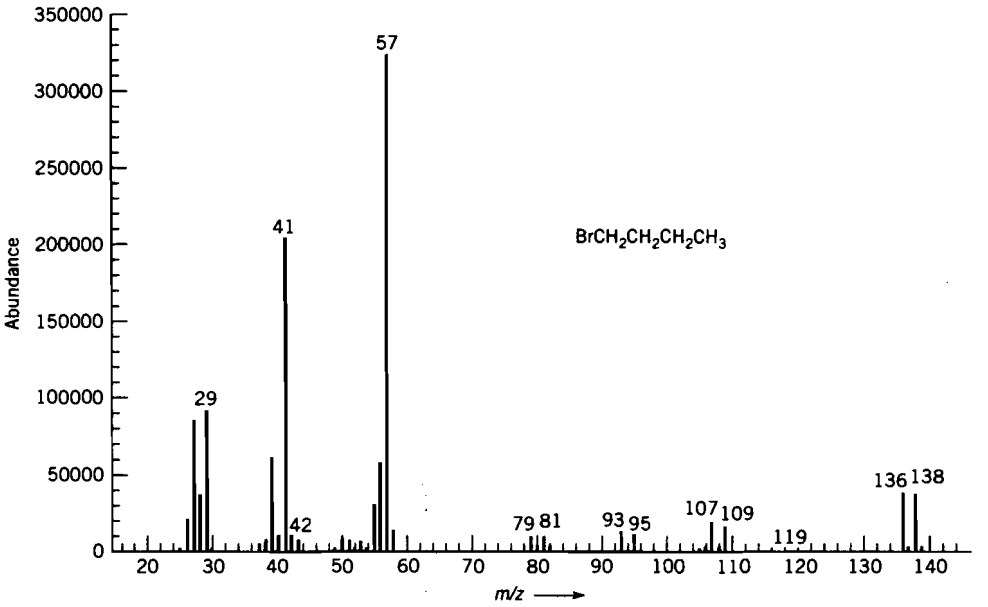


Figure 8.5 Mass spectrum of 1-bromobutane. [Spectrum courtesy of Vernon Miller, Department of Chemistry, Roanoke College, Salem, Virginia. Used with permission.]

$$\underset{\substack{\text{1-bromobutane radical cation}\\ M^{+\cdot}\ m/z\ 136, 138}}{\left[Br\text{-}CH_2CH_2CH_2CH_3\right]^{+\cdot}} \longrightarrow \underset{\substack{\text{bromide cation}\\ m/z\ 79, 81}}{Br^+} + \underset{\substack{\text{butyl radical}\\ \text{not detected}}}{\cdot CH_2CH_2CH_2CH_3}$$

$$\underset{\substack{\text{1-bromobutane radical cation}\\ M^{+\cdot}\ m/z\ 136, 138}}{\left[Br\text{-}CH_2CH_2CH_2CH_3\right]^{+\cdot}} \longrightarrow \underset{\substack{\text{bromide radical}\\ \text{not detected}}}{Br\cdot} + \underset{\substack{\text{butyl cation}\\ m/z\ 57}}{{}^+CH_2CH_2CH_2CH_3}$$

Fragmentation can occur between carbon-1 and carbon-2 to produce a bromomethyl cation (*m/z* 93, 95) and a propyl radical. The formation of a bromomethyl radical and a propyl cation (*m/z* 43) is not a highly favored reaction, since the peak at *m/z* 43 is very small.

$$\underset{\substack{\text{1-bromobutane radical cation}\\ M^{+\cdot}\ m/z\ 136, 138}}{\left[BrCH_2\text{-}CH_2CH_2CH_3\right]^{+\cdot}} \longrightarrow \underset{\substack{\text{bromomethyl cation}\\ m/z\ 93, 95}}{BrCH_2^+} + \underset{\substack{\text{propyl radical}\\ \text{not detected}}}{\cdot CH_2CH_2CH_3}$$

$$\underset{\substack{\text{1-bromobutane radical cation}\\ M^{+\cdot}\ m/z\ 136, 138}}{\left[BrCH_2\text{-}CH_2CH_2CH_3\right]^{+\cdot}} \longrightarrow \underset{\substack{\text{bromomethyl radical}\\ \text{not detected}}}{BrCH_2\cdot} + \underset{\substack{\text{propyl cation}\\ m/z\ 43}}{{}^+CH_2CH_2CH_3}$$

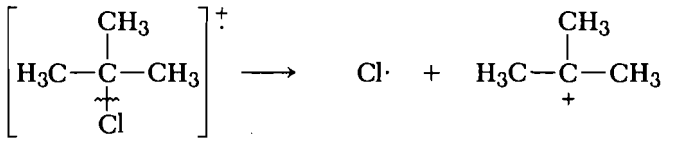
The last fragmentation is a cleavage between carbon-2 and carbon-3. This produces a bromoethyl cation (*m/z* 107, 109) and an ethyl radical or a bromoethyl radical and an ethyl cation (*m/z* 29).

$$\underset{\substack{\text{1-bromobutane radical cation}\\ M^{+\cdot}\ m/z\ 136, 138}}{\left[BrCH_2CH_2\text{-}CH_2CH_3\right]^{+\cdot}} \longrightarrow \underset{\substack{\text{bromoethyl cation}\\ m/z\ 107, 109}}{BrCH_2CH_2^+} + \underset{\substack{\text{ethyl radical}\\ \text{not detected}}}{\cdot CH_2CH_3}$$

$$\left[BrCH_2CH_2\text{-}CH_2CH_3\right]^{+\cdot} \longrightarrow BrCH_2CH_2\cdot + {}^{+}CH_2CH_3$$

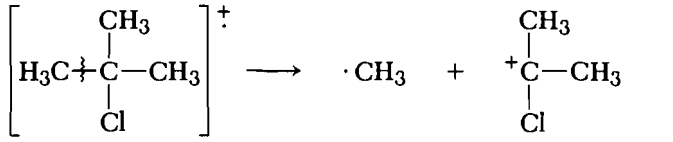
1-bromobutane radical cation, $M^{+\cdot}$ *m/z* 136, 138 — bromoethyl radical, not detected — ethyl cation, *m/z* 29

2-Chloro-2-methylpropane (Figure 8.6) also yields a very distinctive pattern in the mass spectrum. For peaks containing chlorine, the M + 2 peak is approximately one-third as large as the M peak. The molecular ion is not seen in the spectrum. 2-Chloro-2-methylpropane (*m/z* 92, 94) can be cleaved at the chlorine to yield the chloride radical and a *tert*-butyl cation (*m/z* 57). The *tert*-butyl cation is the base peak. The formation of a chloride cation and a *tert*-butyl radical is not a very favored reaction, since there are no peaks for the chloride cation at both *m/z* 35 and 37.



2-chloro-2-methylpropane, $M^{+\cdot}$ *m/z* 92, 94 — chloride radical, not seen — *tert*-butyl cation, *m/z* 57

Fragmentation of a methyl from 2-chloro-2-methylpropane yields a methyl radical and a 2-chloropropyl cation (*m/z* 77, 79). The formation of a methyl cation and a 2-chloropropyl radical is not favored.



2-chloro-2-methylpropane, $M^{+\cdot}$ *m/z* 92, 94 — methyl radical, not seen — 2-chloropropyl cation, *m/z* 77, 79

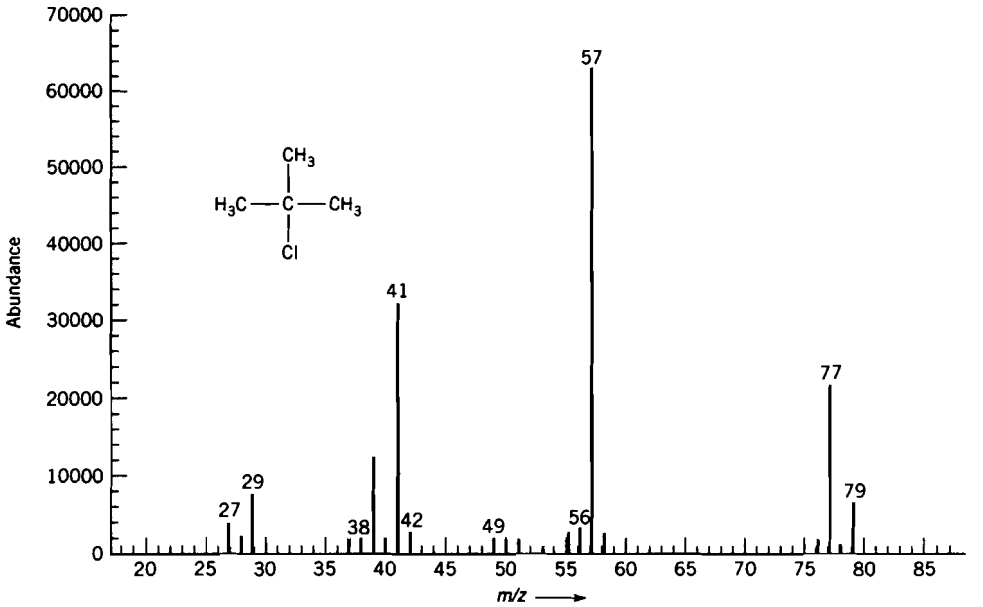


Figure 8.6 Mass spectrum of 2-chloro-2-methylpropane. [Spectrum courtesy of Vernon Miller, Department of Chemistry, Roanoke College, Salem, Virginia. Used with permission.]

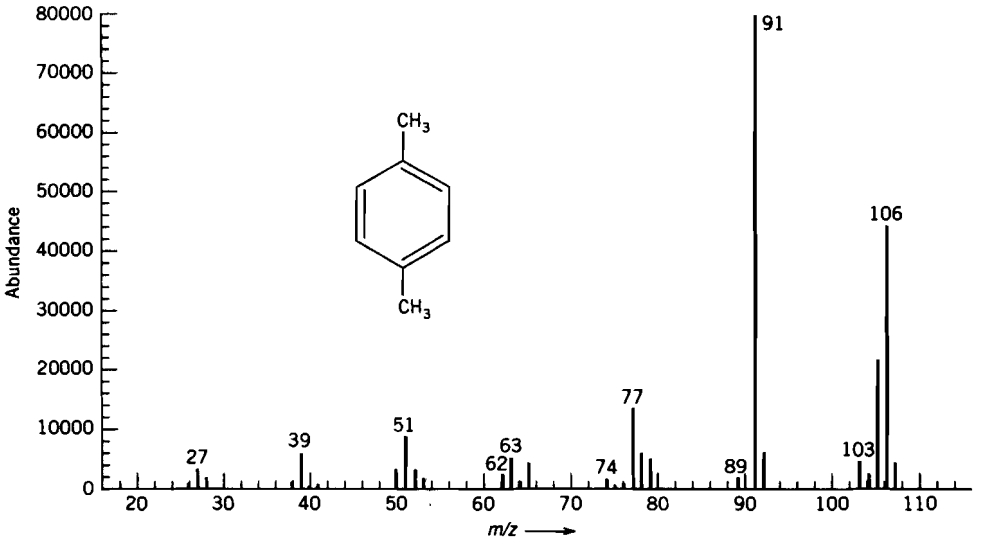
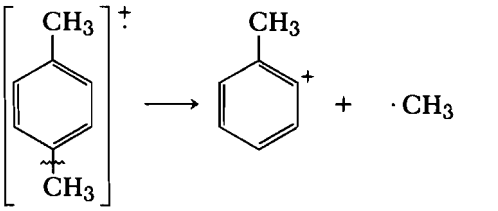
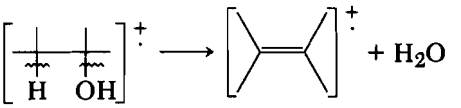


Figure 8.7 Mass spectrum of *p*-xylene. [Spectrum courtesy of Vernon Miller, Department of Chemistry, Roanoke College, Salem, Virginia. Used with permission.]

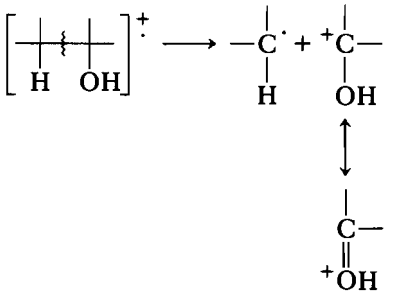
In Figure 8.7, *p*-xylene (*m/z* 106) can lose one methyl to yield a benzyl cation (*m/z* 91) and a methyl radical. The benzyl cation is the base peak.



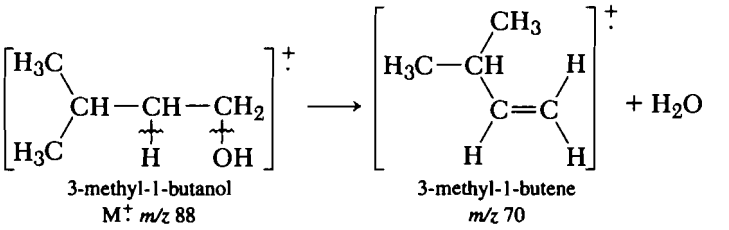
Alcohols can undergo dehydration to yield an alkene.



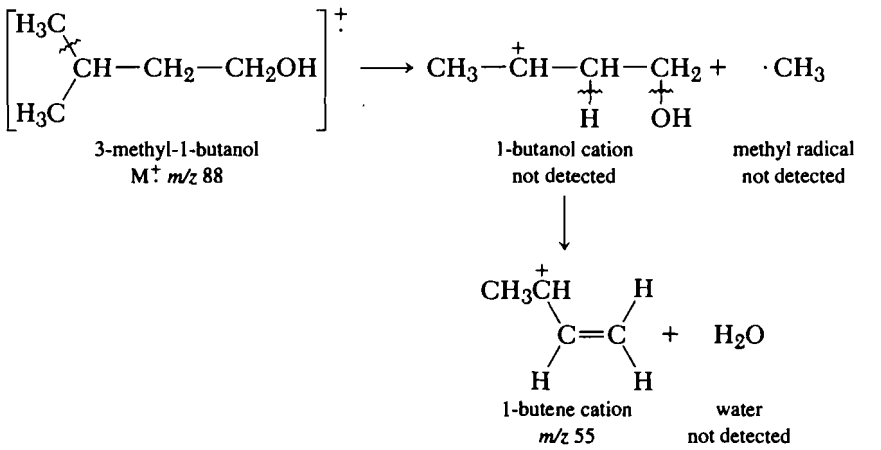
Alcohols can also undergo cleavage to produce a carbocation, which rearranges to a more stable species:



In Figure 8.8, 3-methyl-1-butanol (*m/z* 88) can dehydrate to form 3-methyl-1-butene (*m/z* 70). The molecular ion at *m/z* 88 is not visible since it dehydrates so easily.



3-Methyl-1-butanol can fragment to lose a methyl, with the remaining fragment then losing water. The 1-butene cation (*m/z* 55) is the base peak.



Fragmentation can also occur between carbon-2 and carbon-3, resulting in the isopropyl cation (*m/z* 43) and the ethanol radical or the isopropyl radical and the ethanol cation (*m/z* 45). The ethanol cation can lose water to form an ethene cation (*m/z* 27).

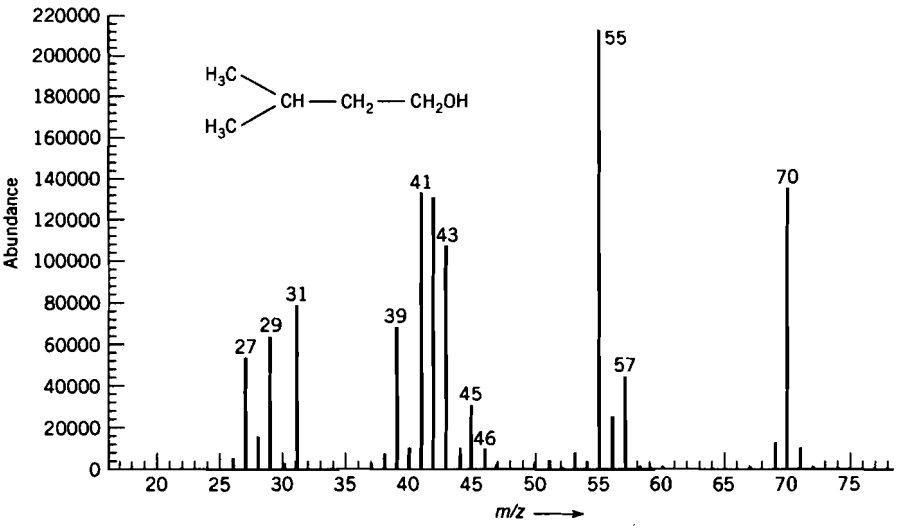
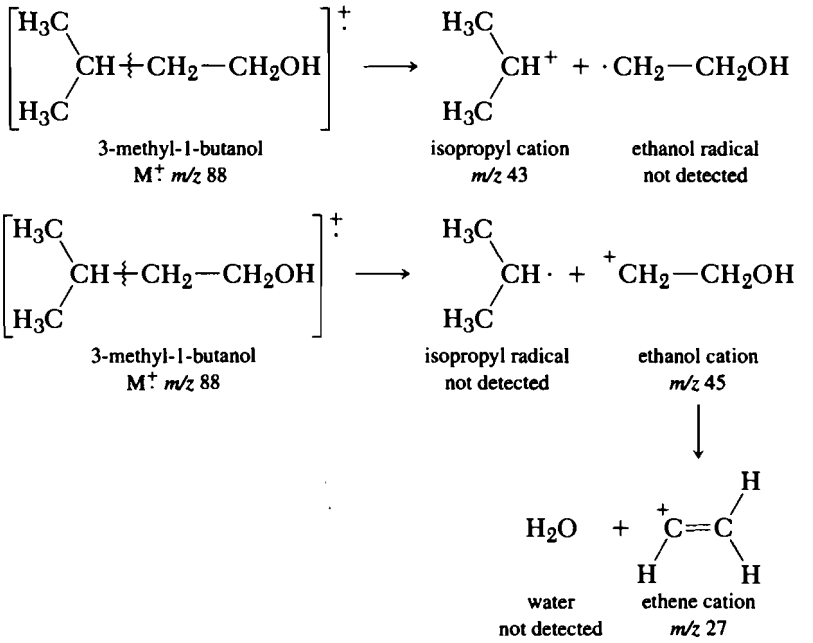
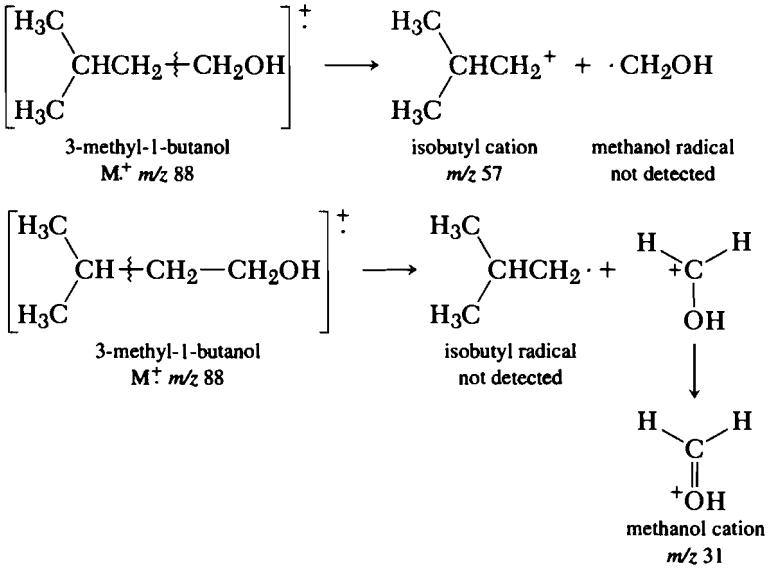


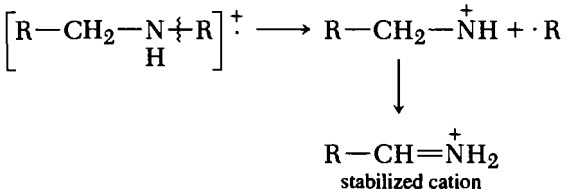
Figure 8.8 Mass spectrum of 3-methyl-1-butanol. [Spectrum courtesy of Vernon Miller, Department of Chemistry, Roanoke College, Salem, Virginia. Used with permission.]

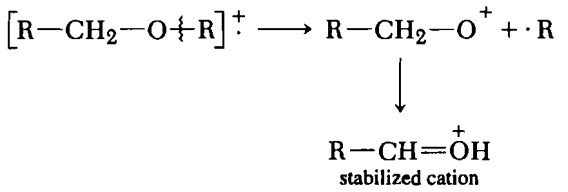


Fragmentation occurs between carbon-1 and carbon-2 to produce an isobutyl cation (*m/z* 57) and a methanol radical or an isobutyl radical and a methanol cation (*m/z* 31).

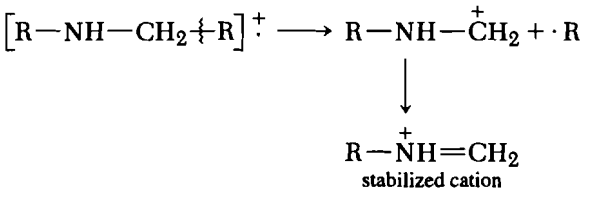


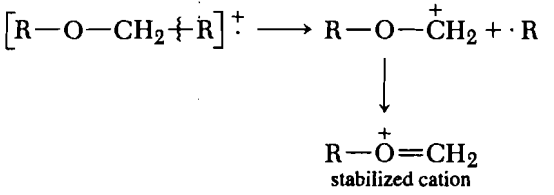
Both amines and ethers undergo a similar type of fragmentation reaction. If the fragmentation occurs next to a nitrogen or oxygen, then electron rearrangement may occur to form either an iminium ion or an oxonium ion.



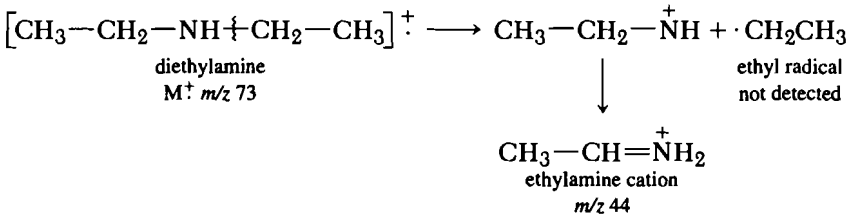


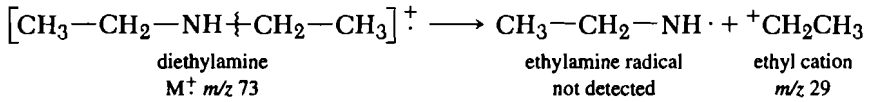
Additional stabilized cations may be formed from α-cleavage.



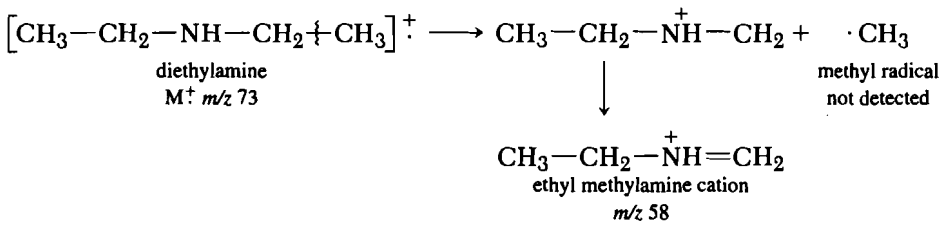


Diethylamine (*m/z* 73) can fragment between the nitrogen and carbon, as seen in Figure 8.9. This fragmentation can yield an ethylamine cation (*m/z* 44) and an ethyl radical or an ethylamine radical and an ethyl cation (*m/z* 29).





Alpha cleavage can also occur within the ethyl group to yield an ethyl methylamine cation (*m/z* 58) and a methyl radical. The ethyl methylamine cation is the base peak.



Compounds containing carbonyl groups may fragment next to the carbonyl. Electron delocalization occurs to yield an acylium ion.

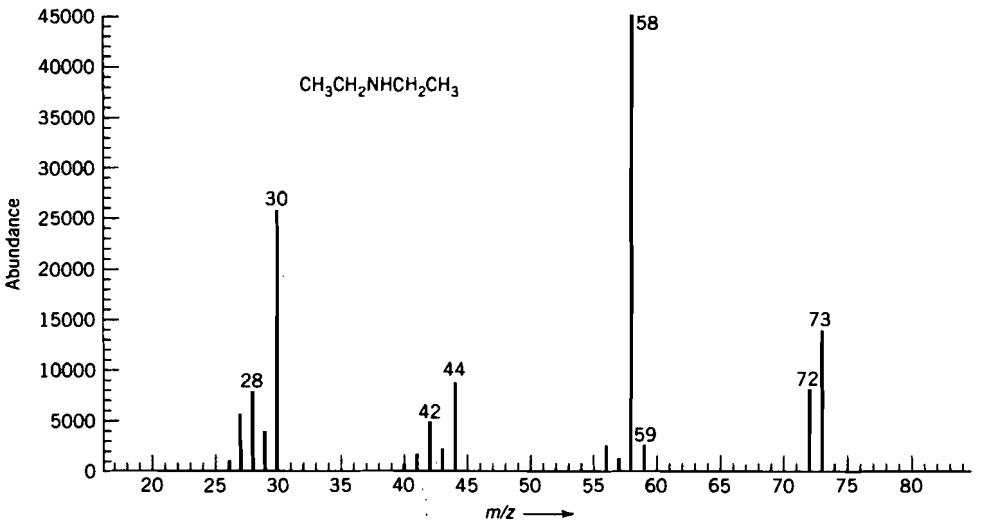
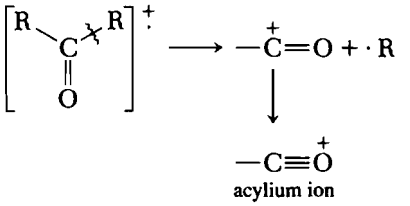
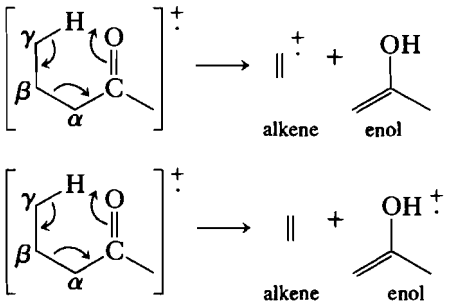


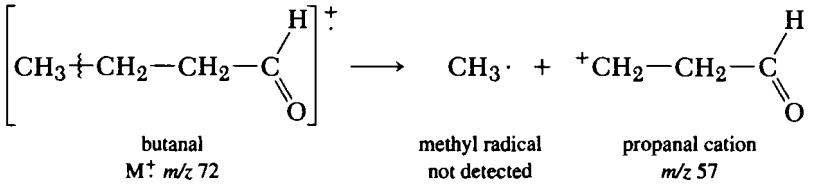
Figure 8.9 Mass spectrum of diethylamine. [Spectrum courtesy of Vernon Miller, Department of Chemistry, Roanoke College, Salem, Virginia. Used with permission.]



McLafferty rearrangement occurs in carbonyl compounds only if the γ(gamma) carbon contains a hydrogen. In the mass spectrum, peaks from the alkene and enol would occur.



As seen in Figure 8.10, butanal (*m/z* 72) can fragment to form the methyl radical and the propanal cation (*m/z* 57).



Butanal can also fragment to yield an ethyl cation (*m/z* 29) and an ethanal radical or an ethyl radical and an ethanal cation (*m/z* 43).

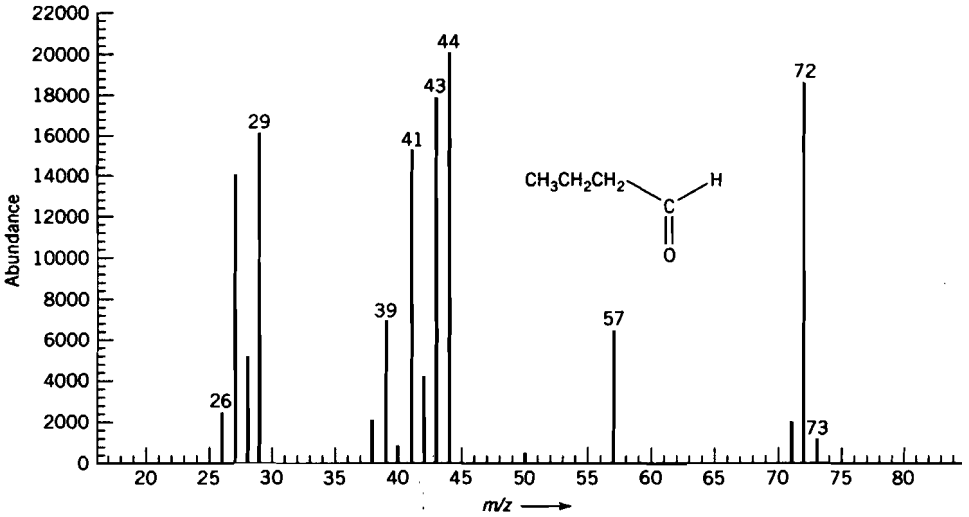
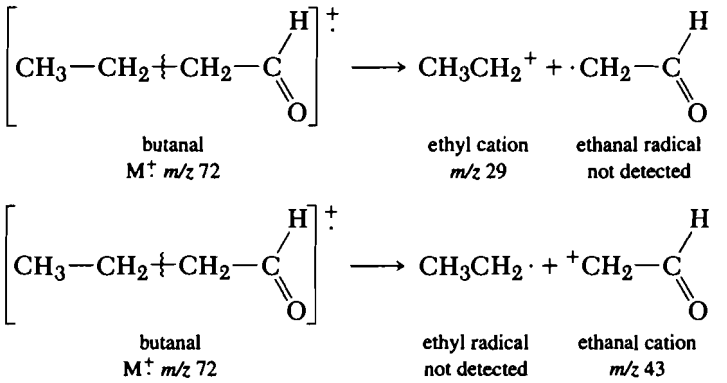
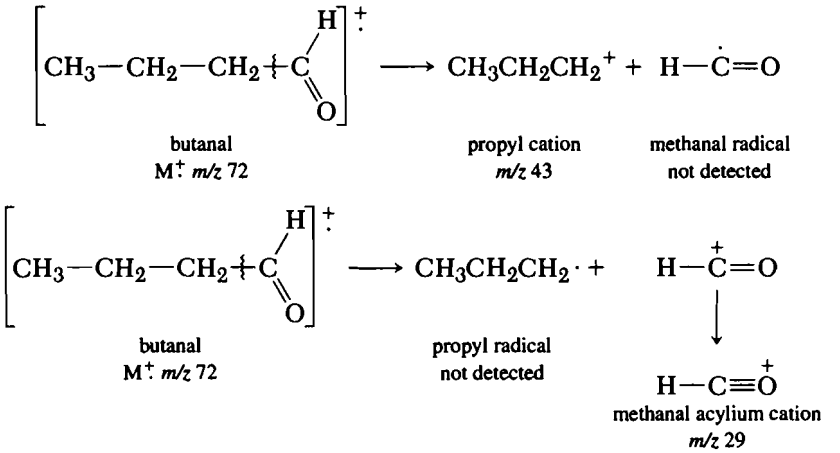


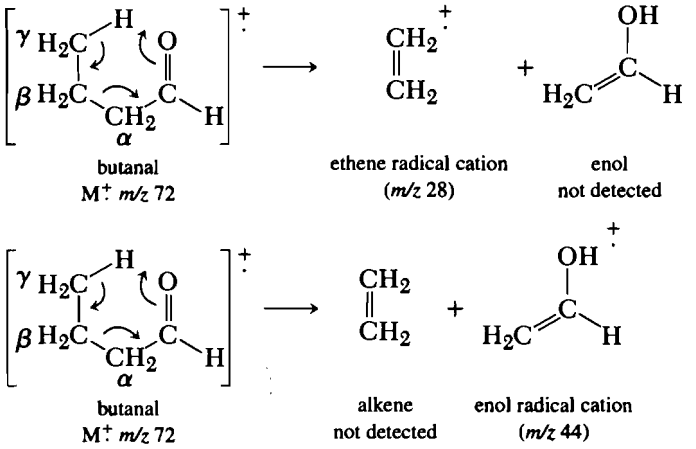
Figure 8.10 Mass spectrum of butanal. [Spectrum courtesy of Vernon Miller, Department of Chemistry, Roanoke College, Salem, Virginia. Used with permission.]



As illustrated below, butanal can fragment to the propyl cation (*m/z* 43) and the methanal radical or the propyl radical and the methanal acylium cation (*m/z* 29).



Since butanal contains a γ hydrogen, McLafferty rearrangement produces two products—the ethene (*m/z* 28) radical cation and the enol radical cation (*m/z* 44). The enol radical cation is the base peak.



Problems

3. Give the structures for the peaks indicated by the *m/z* of 27, 29, 31, 41, 43, 45, 56, 57, and 74 for the mass spectrum of 1-butanol (Figure 8.11). Identify the base peak and the molecular ion.
4. Give the structures for the peaks indicated by the *m/z* of 28, 43, 58, 71, and 86 for the mass spectrum of 2-pentanone (Figure 8.12). Identify the base peak and the molecular ion.
5. Give the structures for the peaks indicated by the *m/z* of 31, 57, 73, and 88 for the mass spectrum of methyl *t*-butyl ether (Figure 8.13). Identify the base peak and the molecular ion.

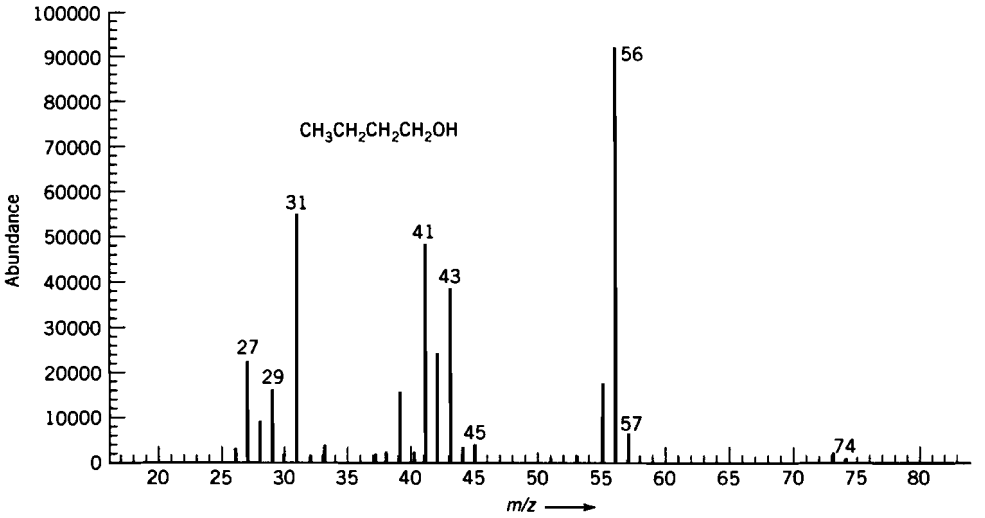


Figure 8.11 Problem 3 Mass spectrum of 1-butanol. [Spectrum courtesy of Vernon Miller, Department of Chemistry, Roanoke College, Salem, Virginia. Used with permission.]

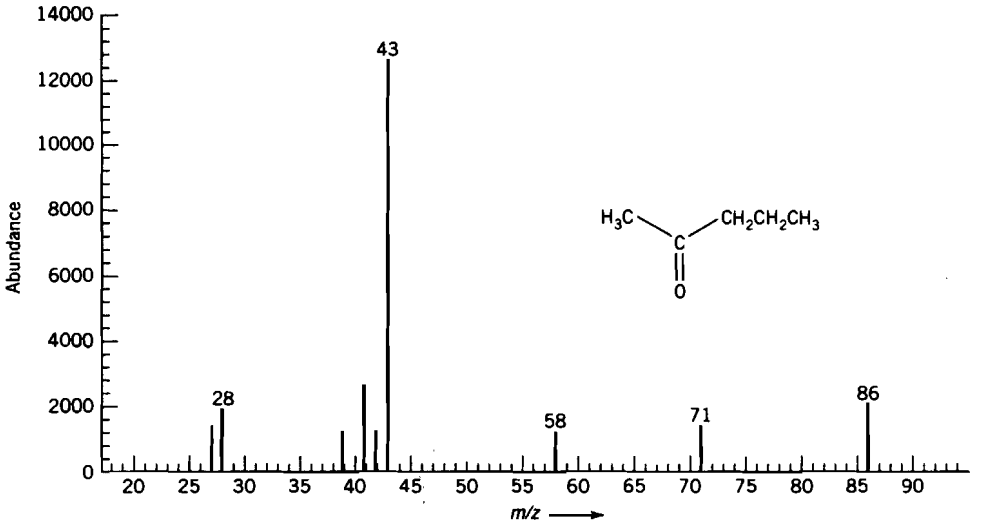


Figure 8.12 **Problem 4** Mass spectrum of 2-pentanone. [Spectrum courtesy of Vernon Miller, Department of Chemistry, Roanoke College, Salem, Virginia. Used with permission.]

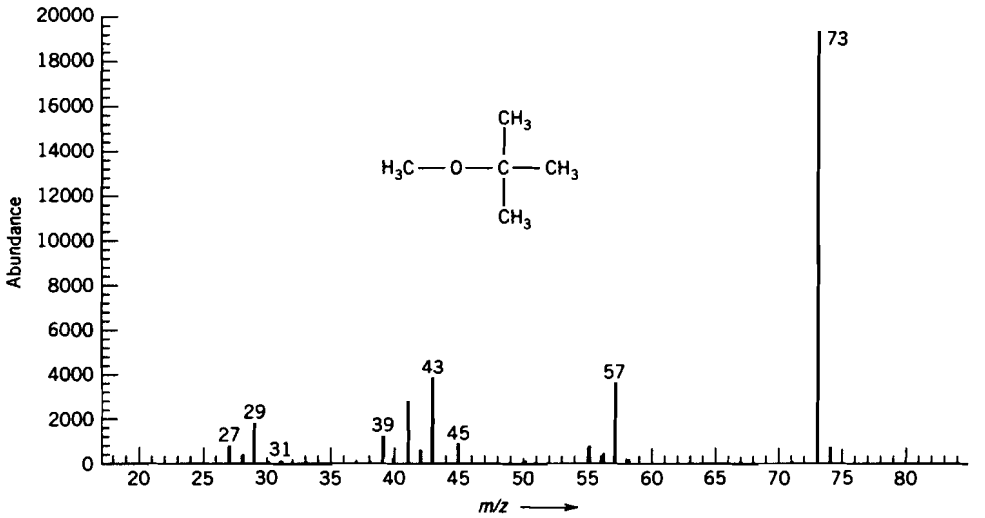


Figure 8.13 **Problem 5** Mass spectrum of methyl *t*-butyl ether. (Spectrum courtesy of Vernon Miller, Department of Chemistry, Roanoke College, Salem, Virginia. Used with permission.]

6. Give the structures for the peaks indicated by the *m/z* of 29, 43, 71, 93, 95, 107, 109, 150, and 152 for the mass spectrum of 1-bromopentane (Figure 8.14). Identify the base peak and the molecular ion.

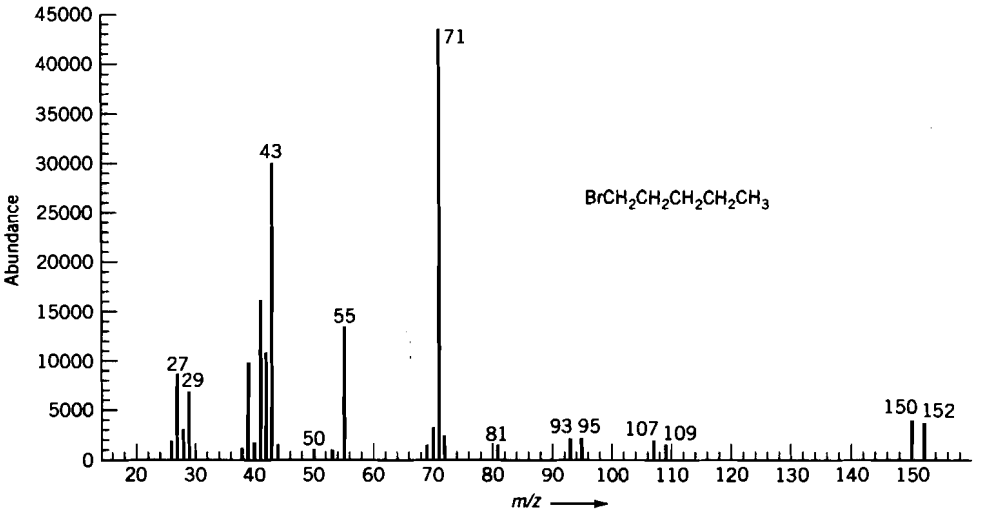


Figure 8.14 Problem 6 Mass spectrum of 1-bromopentane. [Spectrum courtesy of Vernon Miller, Department of Chemistry, Roanoke College, Salem, Virginia. Used with permission.]

CHAPTER 9

Chemical Tests for Functional Groups

As a result of earlier purity (Chapter 3), physical (Chapter 3), spectral (Chapter 6, 7, 8), and solubility tests (Chapter 5), the student probably has a reasonable idea regarding the identity of the unknown compound; it is, however, virtually certain that additional, thorough characterization is in order. A very large proportion of organic compounds lend themselves to final characterization by the chemical tests described in this chapter.

Despite the tremendous importance and ease of spectral analyses, chemical tests are indispensable to complete characterization. These "wet" tests are commonly used as a method of functional group and compound identification.

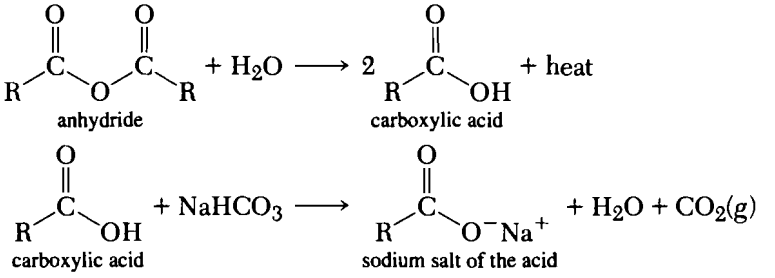
The classification tests are organized in two tables. Table 9.1 lists the tests alphabetically by the name of the functional group. Table 9.2 lists the classification tests alphabetically by the name of the test.

Each experiment contains a ***Cleaning Up***[1] procedure. If the same procedure applies to all parts of the experiment, then it is listed only once—at the end of the experiment and before the discussion.

If a more microscale approach is desired, users of this book may wish to scale down some experiments by multiplying the amount of reagent used by 1/2, 1/5, or 1/10.

9.1 ACID ANHYDRIDES

The presence of acid anhydrides in an unknown sample can be demonstrated by several tests. Many acid anhydrides are rapidly converted by water to the corresponding carboxylic acids (Experiment 1, p. 252). Large aliphatic anhydrides and aromatic anhydrides are not readily hydrolyzed with water. The presence of the carboxylic acid is detected by the addition of sodium bicarbonate, which results in the evolution of carbon dioxide gas, the sodium salt of the acid, and water.



[1]The ***Cleaning Up*** procedures are based on information found in K. L. Williamson, *Macroscale and Microscale Organic Experiments*, 3rd ed. (Houghton Mifflin, Boston, MA, 1999) and *Prudent Practices for Disposal of Chemicals from Laboratories* (National Academy Press, Washington, DC, 1983).

TABLE 9.1 Classification Tests, Listed by Functional Group

Functional Group	Classification Test	Experiment Number	Page
Acid anhydrides	Hydrolysis	1	252
	Hydroxamic acid test	2b	253
	Ester formation (Schotten–Baumann reaction)	3a	256
	Anilide formation	4	258
Acyl halides	Hydrolysis	1	252
	Hydroxamic acid test	2b	253
	Ester formation (Schotten–Baumann reaction)	3a	256
	Anilide formation	4	258
	Silver nitrate (ethanolic)	35	320
Alcohols	Sodium detection of active hydrogen	5	262
	Detection of active hydrogen with acetyl chloride	6	264
	Ceric ammonium nitrate	7	265
	Chromic anhydride (chromium trioxide, Jones oxidation)	8	268
	Hydrochloric acid/zinc chloride (Lucas test)	9	269
	TCICA Test	10	271
	Iodoform test	11	273
Aldehydes	2,4-Dinitrophenylhydrazine	12	278
	Hydroxylamine hydrochloride	13	280
	Sodium bisulfite addition complex	14	281
	Chromic anhydride (chromic trioxide, Jones oxidation)	8	268
	Tollens test	15	283
	TCICA test	10	271
	Purpald test	16	284
	Fuchsin–aldehyde reagent (Schiff's reagent)	17	284
	Periodic acid oxidation	27	308
	Benedict's solution	28	310
	Fehling's solution	29	311
Amides	Hydroxamic acid test	2c, 2d	254
	Sodium hydroxide hydrolysis	18	287
Amines	Sodium detection of active hydrogen	5	262
	Detection of active hydrogen with acetyl chloride	6	264
	Benzenesulfonyl chloride (Hinsberg's method)	19	291
	Nitrous acid	20	294
	Nickel chloride, carbon disulfide, and ammonium hydroxide	21	300
	Nickel chloride and 2-hydroxy-5-nitrobenzaldehyde	22	301
	Sodium hydroxide treatment	23	302
Amino acids	Ninhydrin test	24	303
	Copper complex formation	25	304
	Nitrous acid	20e	297
Carbohydrates	Sodium detection of active hydrogen	5	262
	Detection of hydrogen with acetyl chloride	6	264
	Tollens test	15	283
	Borax test	26	308
	Periodic acid oxidation	27	308
	Benedict's solution	28	310
	Fehling's solution	29	311
	Osazones	30	313
	TCICA test	10	271

(Continued)

TABLE 9.1 *(Continued)*

Functional Group	Classification Test	Experiment Number	Page
Carboxylic acids	Sodium bicarbonate test	31	314
	Ester formation	3b	256
	Silver nitrate (ethanolic)	35	320
Esters	Hydroxamic acid test	2b	253
	Hydroiodic acid (Zeisel's alkoxy method)	34	318
Ethers	Ferrox test	32	316
	Iodine test	33	317
	Hydroiodic acid (Zeisel's alkoxy method)	34	318
Halides	Silver nitrate (ethanolic)	35	320
	Sodium iodide test	36	323
Hydrocarbons—Alkanes			325
Hydrocarbons—Alkenes	Iodine test	33	325
	Bromine solution	37	326
	Potassium permanganate solution	38	328
Hydrocarbons—Alkynes	Bromine solution	37	326
	Potassium permanganate solution	38	328
	Sodium detection of active hydrogen	5	262
Hydrocarbons—Aromatic	Fuming sulfuric acid	39	334
	Azoxybenzene and aluminum chloride	40	336
	Chloroform and aluminum chloride	41	337
Ketones	2,4-Dinitrophenylhydrazine	12	278
	Hydroxylamine hydrochloride	13	280
	Sodium bisulfite addition complex	14	281
	Iodoform test	11	273
	Periodic acid oxidation	27	308
	Benedict's test	28	310
	Fehling's test	29	311
Nitriles	Sodium hydroxide hydrolysis	18	287
	Hydroxamic acid test	2c	254
Nitro compounds	Ferrous hydroxide reduction	42	341
	Zinc and ammonium chloride reduction	43	342
	Sodium hydroxide treatment	44	342
Phenols	Sodium detection of active hydrogen	5	262
	Detection of active hydrogen with acetyl chloride	6	264
	Ceric ammonium nitrate	7	265
	Liebermann's nitroso reaction	20d	297
	Potassium permanganate solution	38	328
	Ferric chloride–pyridine reagent	45	345
	Bromine water	46	347
	TCICA test	10	271
Sulfonamides	Sodium hydroxide fusion	47	349
Sulfonic acids	Hydroxamic acid test	2e	255
Sulfonyl chlorides	Hydroxamic acid test	2e	255
	Silver nitrate (ethanolic)	35	320
	Sodium iodide test	36	323

TABLE 9.2 Experiments for Classification of Functional Groups

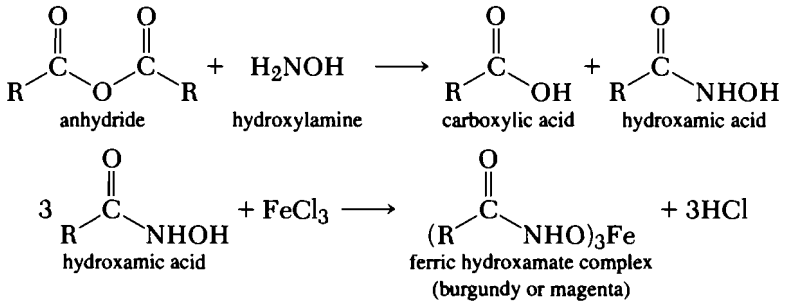
Classification Test	Experiment Number	Class Tested for	Page
Acetyl chloride	6	Alcohols	264
		Amines	
		Carbohydrates	
		Phenols	
Anilide formation	4	Acid anhydrides	258
		Acyl halides	
Azoxybenzene and aluminum chloride	40	Hydrocarbons—Aromatic	336
Benedict's solution	28	Aldehydes	310
		Carbohydrates	
		Ketones	
Benzenesulfonyl chloride (Hinsberg's method)	19	Amines	291
Borax test	26	Carbohydrates	308
Bromine solution	37	Hydrocarbons—Alkenes	326
		Hydrocarbons—Alkynes	
Bromine water	46	Phenols	347
Ceric ammonium nitrate	7	Alcohols	265
		Phenols	
Chloroform and aluminum chloride	41	Hydrocarbons—Aromatic	337
Chromic anhydride (chromium trioxide, Jones oxidation)	8	Alcohols	268
		Aldehydes	
Copper complex formation	25	Amino acids	304
2,4-Dinitrophenylhydrazine	12	Aldehydes	278
		Ketones	
Ester formation (Schotten–Baumann reaction)	3a	Acid anhydrides	256
		Acyl halides	
	3b	Carboxylic acids	256
Fehling's solution	29	Aldehydes	311
		Carbohydrates	
		Ketones	
Ferric chloride–pyridine reagent	45	Phenols	345
Ferrous hydroxide reduction	42	Nitro compounds	341
Ferrox test	32	Ethers	316
Fuchsin–aldehyde reagent (Schiff's reagent)	17	Aldehydes	284
Fuming sulfuric acid	39	Hydrocarbons—Aromatic	334
Hinsberg's method (benzenesulfonyl chloride)	19	Amines	291
Hydrochloric acid/zinc chloride (Lucas test)	9	Alcohols	269
Hydroiodic acid (Zeisel's alkoxy method)	34	Esters	318
		Ethers	
Hydrolysis	1	Acid anhydrides	252
		Acyl halides	252
Hydroxamic acid test	2b	Acid anhydrides	253
		Acyl halides	
	2c, 2d	Amides	254
	2b	Esters	253
	2c	Nitriles	254
	2e	Sulfonic acids	255
	2e	Sulfonyl chlorides	
Hydroxylamine hydrochloride	13	Aldehydes	280
		Ketones	
Iodine test	33	Ethers	317
		Alkenes	

(Continued)

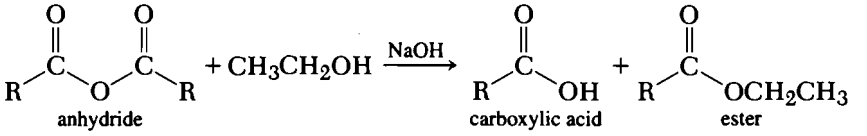
TABLE 9.2 *(Continued)*

Classification Test	Experiment Number	Class Tested for	Page
Iodoform test	11	Alcohols Ketones	273
Jones oxidation (chromic anhydride, chromium trioxide)	8	Alcohols Aldehydes	268
Liebermann's nitroso reaction	20d	Phenols	297
Lucas test (hydrochloric acid/zinc chloride)	9	Alcohols	269
Nickel chloride, carbon disulfide, and ammonium hydroxide	21	Amines	300
Nickel chloride and 2-hydroxy-5-nitrobenzaldehyde	22	Amines	301
Ninhydrin test	24	Amino acids	303
Nitrous acid	20	Amines	294
	20e	Amino acids	297
	20d	Phenols	297
Osazones	30	Carbohydrates	313
Periodic acid oxidation	27	Carbohydrates Aldehydes Ketones	308
Potassium permanganate solution	38	Hydrocarbons—Alkenes Hydrocarbons—Alkynes Phenols	328
Purpald test	16	Aldehydes	284
Schiff's reagent (Fuchsin–aldehyde reagent)	17	Aldehydes	284
Schotten–Baumann Reaction (Ester formation)	3a	Acid anhydrides Acyl halides	256
Silver nitrate (ethanolic)	35	Acyl halides Carboxylic acids Halides Sulfonyl chlorides	320
Sodium bicarbonate test	31	Carboxylic acids	314
Sodium bisulfite addition complex	14	Aldehydes Ketones	281
Sodium detection of active hydrogen	5	Alcohols Amines Carbohydrates Hydrocarbons—Alkynes Phenols	262
Sodium hydroxide fusion	47	Sulfonamides	349
Sodium hydroxide hydrolysis	18	Amides Nitriles	287
Sodium hydroxide treatment	23	Amines	302
	44	Nitro compounds	342
Sodium iodide test	36	Halides Sulfonyl chlorides	323
TCICA test	10	Alcohols Aldehydes Carbohydrates Phenols	271
Tollens test	15	Aldehydes Carbohydrates	283
Zeisel's alkoxy method (hydroiodic acid)	34	Esters Ethers	318
Zinc and ammonium chloride reduction	43	Nitro compounds	342

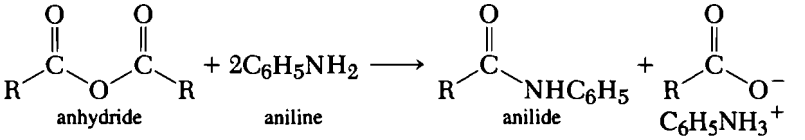
The hydroxamic acid test may be used to analyze for an acid anhydride (Experiment 2b, p. 253). The hydroxamic acid is treated with ferric chloride to form a ferric hydroxamate complex, which has a burgundy or magenta color.



Acid anhydrides react quickly with alcohols to form esters and carboxylic acids (Experiment 3a, p. 256). The esters form an upper layer in the presence of the basic aqueous layer.

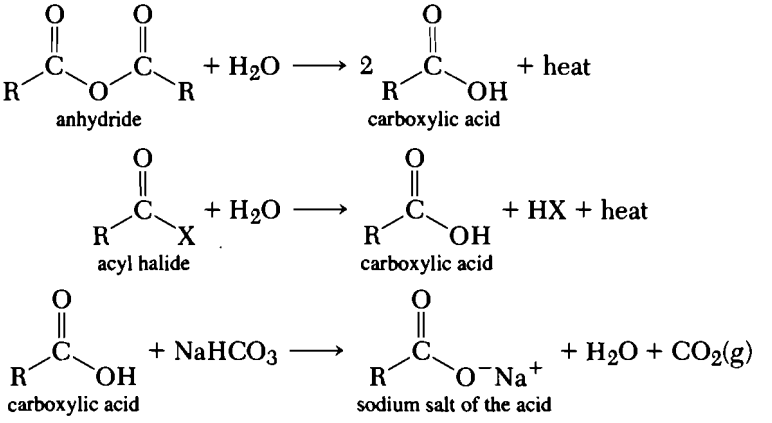


Anilides are formed from acid anhydrides and aniline (Experiment 4, p. 258). The anilides precipitate from the solution.



Experiment 1 Hydrolysis of Acid Anhydrides and Acyl Halides

The anhydride and acid chloride tests are closely related and Section 9.2 (p. 259) below discusses the latter.



Cautiously add a few drops or a few crystals of the unknown compound to 1 mL of water and touch the test tube to see if heat is evolved. If the test tube is warm, then the

test is positive for an acid anhydride or an acyl halide, since water will react with these compounds to form the carboxylic acid with the evolution of heat. Add 1 mL of methanol to dissolve the sample. Pour the solution into 1 mL of a saturated solution of sodium bicarbonate. Evolution of carbon dioxide gas is a positive test for the presence of the product carboxylic acid.

Controls Acetic anhydride and benzoyl chloride will give a positive test. Acetophenone will give a negative test.

Cleaning Up Place the reaction mixture in the aqueous solution container.

Discussion

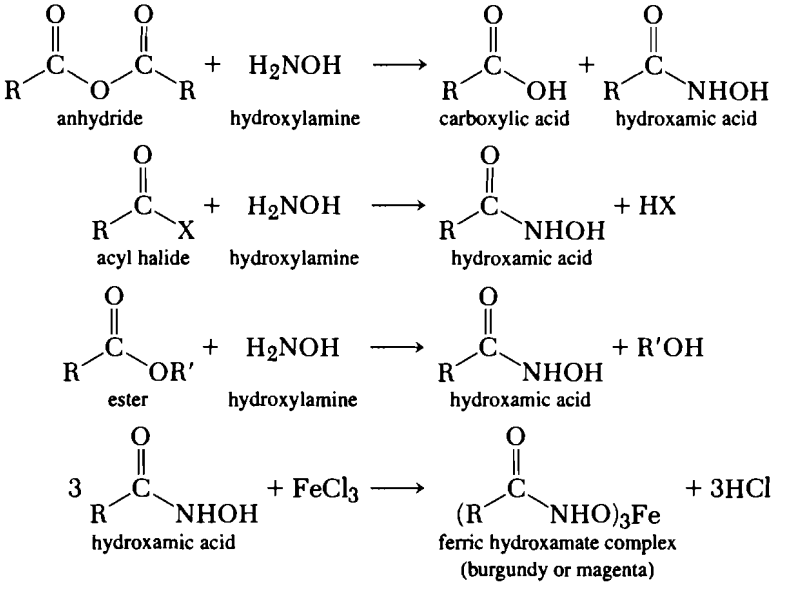
Higher aliphatic anhydrides and aromatic anhydrides are not readily hydrolyzed with water and thus may not give a positive test.

Experiment 2 Hydroxamic Acid Test

(a) Preliminary Test

Dissolve a drop or a few crystals of the compound to be tested in 1 mL of 95% ethanol and add 1 mL of 1 M hydrochloric acid. Note the color produced when one drop of 5% ferric chloride solution is added to the solution. If a definite orange, red, blue, or violet color is produced, the following test for the acyl group is not applicable and should be omitted. Too much hydrochloric acid prevents the development of colored complexes of many phenols and all enols.

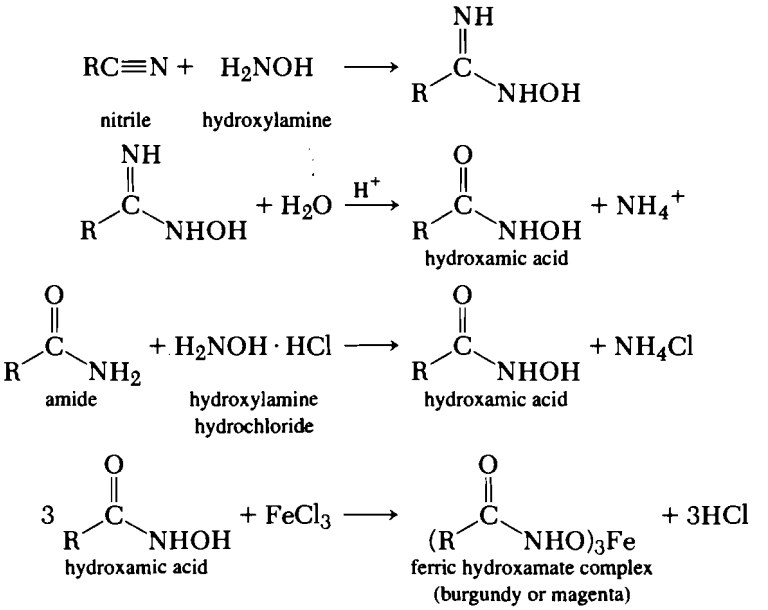
(b) Hydroxamic Acid Formation from Anhydrides, Acyl Halides, and Esters



Heat to boiling a mixture of one drop or about 40 mg of the compound, 1 mL of 0.5 M hydroxylamine hydrochloride in 95% ethanol, and 0.2 mL of 6 M sodium hydroxide. After the solution has cooled slightly, cautiously add 2 mL of 1 M hydrochloric acid. Anhydrides, acyl halides, and esters react with hydroxylamine to form the hydroxamic acid, as indicated in the above equations. If the solution is cloudy, add 2 mL of 95%

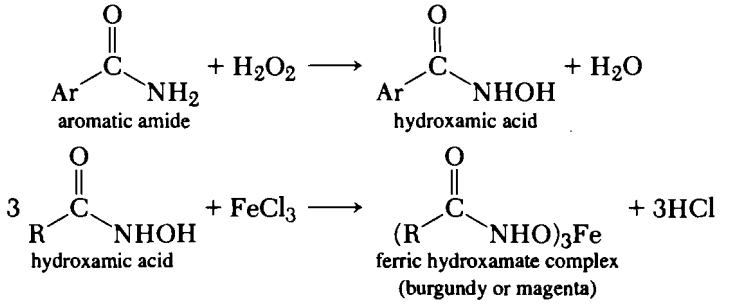
ethanol. Observe the color produced when one drop of 5% ferric chloride solution is added. If the color caused by the drop of ferric chloride solution does not persist, continue to add the ferric chloride solution dropwise until the observed color permeates the entire test solution. Compare the color with that produced in (a). A positive test will be a distinct burgundy or magenta color of the ferric hydroxamate complex, which is formed upon the reaction of the hydroxamic acid with the ferric chloride. Compare the color of this solution with the yellow observed when the original compound is tested with ferric chloride in the presence of acid.

(c) Hydroxamic Acid Formation from Nitriles and Amides



Add one drop or 30 mg of the compound dissolved in a minimum amount of propylene glycol to 2 mL of a 1 M hydroxylamine hydrochloride solution in propylene glycol. Add 1 mL of 1 M potassium hydroxide and boil the mixture gently for 2 min. Allow the mixture to cool to room temperature and add 0.5–1 mL of a solution of 5% alcoholic ferric chloride. A red to violet color constitutes a positive test. Yellow colors indicate negative tests, and brown colors or precipitates are indeterminate.

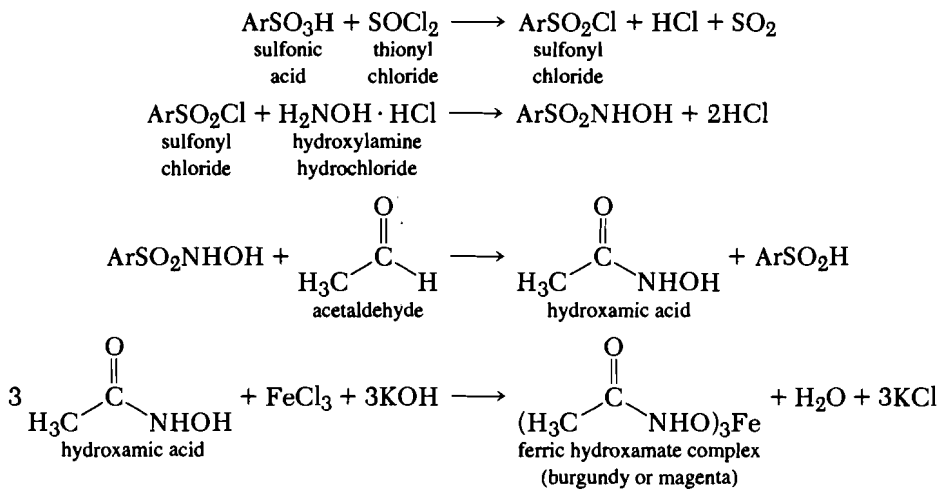
(d) Hydroxamic Acid Formation from Aromatic Primary Amides[2]



[2]N. D. Cheronis and J. B. Entrikin, *Semimicro Qualitative Organic Analysis*, 3rd ed. (Wiley, New York, 1965), p. 374.

This procedure tests for the presence of an aromatic primary amide, which would give a negative result when analyzed with experiment (c). Place 50 mg of the unknown in 5 mL of water. Add 0.5 mL of 3% hydrogen peroxide and two drops of 5% ferric chloride solution. Heat the solution to boiling. The hydrogen peroxide reacts with the aromatic amide to form the hydroxamic acid, which then reacts with the ferric chloride to form ferric hydroxamate complex. The characteristic magenta color should develop if the compound is an aromatic primary amide.

(e) Hydroxamic Acid Formation from Sulfonic Acids and Sulfonyl Chlorides[3]



To prepare the sulfonyl chloride from the sulfonic acid, combine five drops of thionyl chloride and 100 mg of the sulfonic acid in a test tube and heat in boiling water for 1 min. Allow the test tube to cool. To the test tube, add 0.5 mL of a saturated solution of hydroxylamine hydrochloride in methanol. Add a drop of acetaldehyde. The sulfonyl chloride undergoes the reaction with the hydroxylamine to form an intermediate, which, when treated with the acetaldehyde, forms the hydroxamate acid. Add dropwise a solution of 2 M potassium hydroxide in methanol until the solution is slightly basic when checked with pH paper. Heat the solution to boiling and then allow it to cool. Acidify the mixture by dropwise adding 0.5 M hydrochloric acid, until blue litmus paper turns red. Add a drop of 5% ferric chloride solution. Ferric chloride converts the hydroxamic acids to the ferric hydroxamate complex. The magenta color of the ferric hydroxamate complex is a positive result.

Sulfonyl chlorides can be treated directly with the hydroxylamine hydrochloride. Neutralize the salts of sulfonic acids with hydrochloric acid, then evaporate to dryness. Treat the residue with thionyl chloride as described above.

Controls Acetic anhydride, acetyl chloride, and ethyl acetate will give a positive test for (b). Acetonitrile and butanamide will give a positive test for (c). Benzamide will give a positive test for (d). Benzenesulfonyl chloride and benzenesulfonic acid will give a positive test for (e). Acetophenone and benzaldehyde will give a negative test for all experiments.

[3]N. D. Cheronis and J. B. Entrikin, *Semimicro Qualitative Organic Analysis* (Thomas Y. Cromwell Company, New York, 1947), p. 143.

Cleaning Up For all parts of Experiment 2, neutralize the reaction mixture with sodium carbonate until the foaming no longer occurs and place in the aqueous solution container.

Discussion

All esters of carboxylic acids, including polyesters and lactones, give definite magenta colors of varying degrees of intensity. Acid chlorides, acid anhydrides, and trihalo compounds such as trichloromethylbenzene and chloroform give positive magenta test results.

Formic acid produces a red color; with all other carboxylic acids the test is negative. Commercial lactic acid gives a positive test. Phthalic acid usually contains phthalic anhydride and thus gives a positive test.

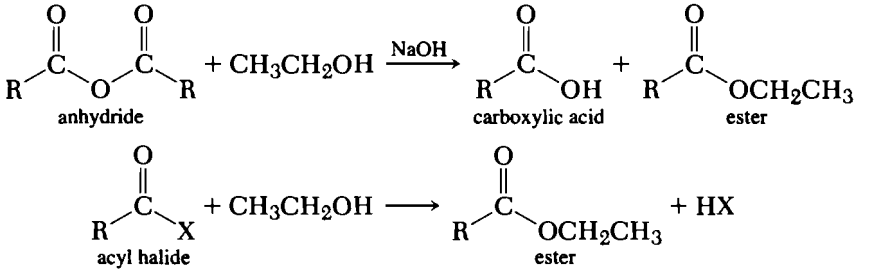
Primary or secondary nitro compounds give a positive test.

Most imides give positive tests, aliphatic amides and salicylamide give light magenta colors, and most nitriles give a negative test with procedure (b). For procedure (c), all common nitriles and amides give positive tests. Benzanilide, diacetylbenzidine, and certain sterically hindered amides fail to give a positive test. However, aromatic primary amides will give a positive result only with hydrogen peroxide in the presence of ferric chloride, as described in (d).

Aldehydes with no α-hydrogen atoms may give weakly positive tests; with other aldehydes and ketones the test is negative.

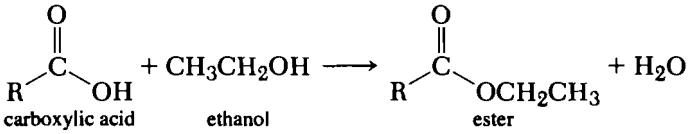
Experiment 3 Ester Formation

(a) The Schotten–Baumann Reaction



Place 0.5 mL of ethanol, 1 mL of water, and 0.2 mL or 0.20 g of the unknown compound in a small flask. To this solution add in portions, with vigorous shaking, 2 mL of 20% sodium hydroxide solution. Stopper the flask and shake the mixture for several minutes and then test the solution with litmus paper to make sure that it is still alkaline. The anhydrides and acyl halides will undergo a reaction with alcohols under basic conditions to form esters. Esters are both insoluble in water and less dense than water and thus will form a layer on top of the water.

(b) Esterification of a Carboxylic Acid



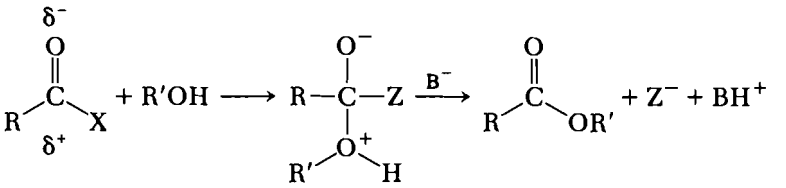
Warm a mixture of 0.20 g of the compound, 0.40 mL of absolute ethanol, and 0.20 mL of concentrated sulfuric acid over a steam bath or hot-water bath for 2 min. Pour the mixture slowly into an evaporating dish containing 2 mL of saturated sodium bicarbonate solution. A second layer should be formed. Carefully smell the mixture. The presence of a sweet, fruity smell in the product, where no such smell existed in the original unknown, indicates that the original compound was a carboxylic acid and the acid was esterified. Large-molecular-weight carboxylic acids produce esters that are odorless.

Controls Acetyl chloride and acetic anhydride will give a positive test for (a). Butanoic acid will give a positive test for (b). Acetophenone and acetone will give a negative test for both experiments.

Cleaning Up For both (a) and (b), place the ester layer in the organic solvent container. Neutralize the aqueous layer with 10% hydrochloric acid, and place in the aqueous solution container.

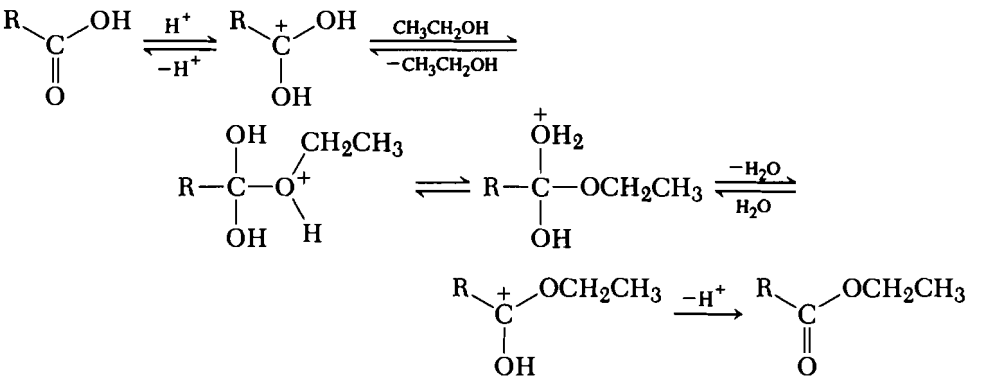
Discussion

The Schotten–Baumann reaction in (a) is of particular interest because it might be expected that the water and hydroxyl ion present could compete with the alcohol to be acylated and seriously reduce the yield of the product desired. The success of the reaction is probably due to a combination of circumstances. It generally occurs in a heterogeneous medium with the organic reagent and the unknown anhydride or acyl halide in the same phase. One could speculate that the organic reagents combine in the organic phase and that only acid–base neutralization takes place in the inorganic layer.

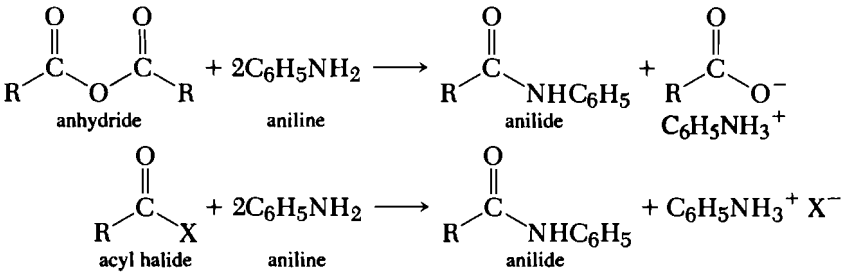


Experiment 3a, Z = O_2CR or halogen

The mechanism of the esterification carried out in (b) involves protonation as a method of enhancing the electrophilicity of the acid substrate toward nucleophilic attack by ethanol.



Experiment 4 Anilide Formation from Acid Anhydrides and Acyl Halides



(a)

Add a few drops or a few crystals of the unknown sample to 0.5 mL of aniline. Pour the mixture into 5 mL of water. A positive test is the precipitation of the solid anilide.

(b)

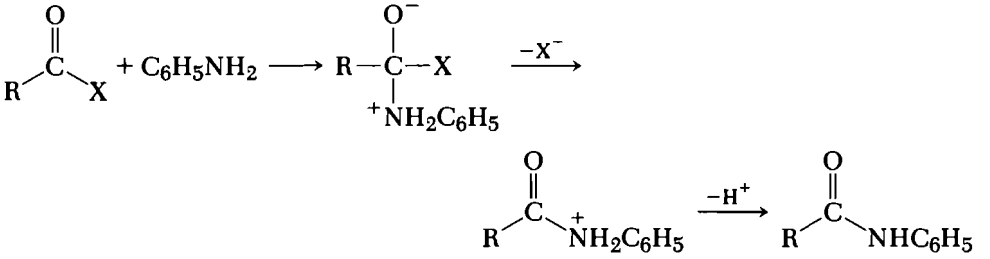
In a small flask, place 0.2 mL of aniline, 1 mL of water, and 0.2 mL or 0.2 g of the unknown. Add in portions, with vigorous shaking, 10 mL of 20% sodium hydroxide solution. Shake the mixture in a stoppered flask for several minutes, and then test the solution with litmus paper to make sure that it is still alkaline. A positive test is the formation of a precipitate.

Controls Acetic anhydride and acetyl chloride will give a positive test. Acetone and acetophenone will give a negative test.

Cleaning Up For both (a) and (b), filter off the solid and place in the organic nonhazardous solid waste container. Place the filtrate in the aqueous solution container.

Discussion

Anhydrides and acyl halides react with aniline to form anilides, which precipitate out of the solution. The mechanism involves the direct attack of the free amine (aniline) on the anhydride or acyl halide.

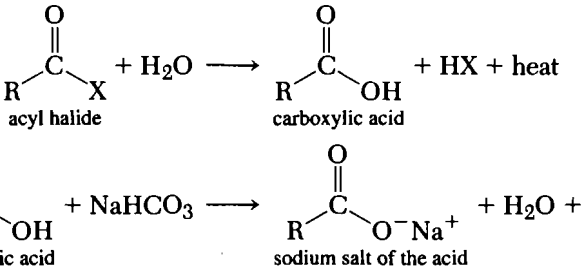


Problems

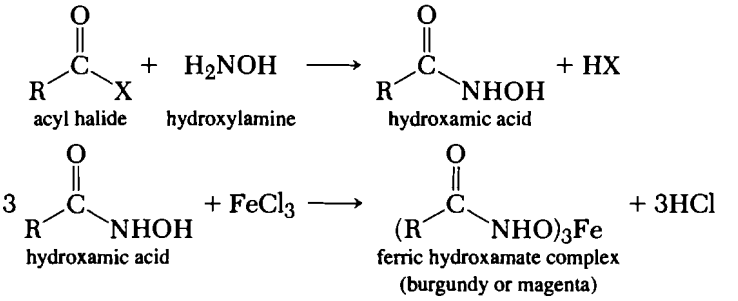
1. What is the role of the sodium hydroxide in Experiment 4b? (*Hint:* Note that the two equivalents of aniline have been used in the equations at the start of the experiment.)
2. Give the equations for the reaction of propanoyl chloride and propanoic acid with hydroxamic acid. Give another method of distinguishing between these two compounds.

9.2 ACYL HALIDES

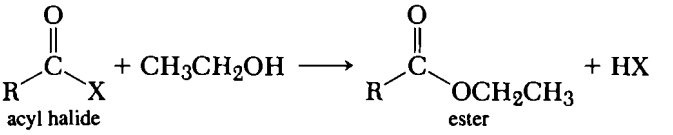
The same experiments that are used to the detect the presence of acid anhydrides can be used for acyl halides. Theory predicts that the acyl halides are more reactive. Acid halides can be hydrolyzed to carboxylic acids (Experiment 1, p. 252). Addition of sodium bicarbonate to the solution produces the observable evolution of carbon dioxide gas, the sodium salt of the acid, and water.



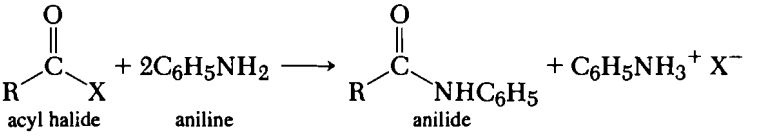
The hydroxamic acid test also will give a positive result for acid halides (Experiment 2b, p. 253). The acyl halide undergoes reaction with the hydroxylamine to form a hydroxamic acid, which is then treated with ferric chloride to form the magenta-colored ferric hydroxamate complex.



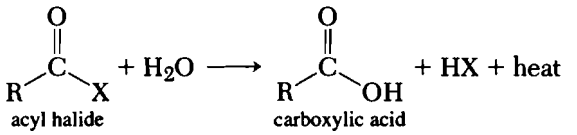
Acid halides undergo reaction with alcohols to form esters (Experiment 3a, p. 256). The esters form an upper layer with the basic aqueous layer.



Aniline undergoes reaction with acid halides to form anilides, which precipitate from the solution (Experiment 4, p. 258).



To distinguish between the acid anhydride and the acyl halide, the silver nitrate test for halides (Experiment 35, p. 320) is used. The acyl halide is hydrolyzed to form the carboxylic acid and hydrogen halide. The hydrogen halide undergoes reaction with silver nitrate to give an immediate precipitation of silver halide.



$$HX + AgNO_3 \longrightarrow AgX(s) + HNO_3$$

The more volatile acid halides can be detected merely by their obnoxious, lachrymatory odor. Do not smell compounds directly; however, some compounds such as volatile acid halides have distinctive odors that permeate the surroundings when the sample vial is opened.

Problem

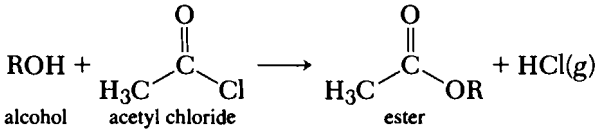
3. Why are the acyl halides generally more reactive than the anhydrides? (*Hint:* Write the mechanisms for the reaction of hydroxylamine with acetic anhydride and with acetyl chloride and discuss the leaving group ability of chloride vs. carboxylate.)

9.3 ALCOHOLS

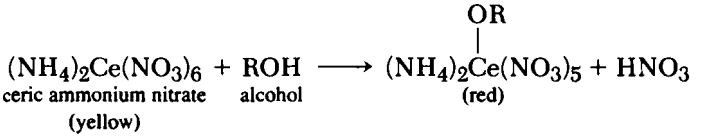
Several methods are available for the analysis of the hydroxyl group, the functional group present in alcohols. Sodium metal undergoes reaction with hydroxyl groups of many alcohols to liberate hydrogen gas and form the salt of the alcohol (Experiment 5, p. 262). The rate is highly variable and depends upon the alcohol structure.

$$\underset{\text{alcohol}}{2ROH} + 2Na \longrightarrow 2RO^-Na^+ + H_2(g)$$

Another method of detecting such an active hydrogen is by adding acetyl chloride to the alcohol to form the ester (Experiment 6, p. 264), which is less dense than the aqueous layer.

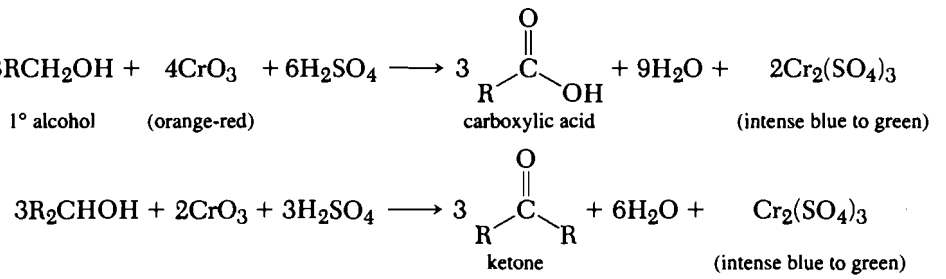


Another method of testing for the presence of the alcoholic hydrogen involves ceric ammonium nitrate (Experiment 7, p. 265). The yellow ceric ammonium nitrate forms a red organometallic compound with alcohols. Positive results are obtained from alcohols of 10 or fewer carbons.

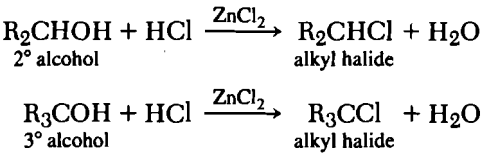


The Jones oxidation, in conjunction with the sodium metal test and the Lucas test, may be used to differentiate among primary (1°), secondary (2°), and tertiary (3°) alcohols. The Jones oxidation (Experiment 8, p. 268) only detects the presence of a hydroxyl substituent that is on a carbon bearing at least one hydrogen. Thus, only primary and secondary alcohols are oxidized to the corresponding carboxylic acids and ketones. Tertiary alcohols are not oxidized under these conditions. As the alcohol is oxidized, the

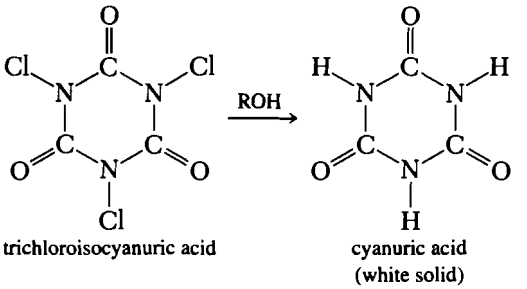
solution changes from an orange-red color from the Cr^{+6} ion, to a blue to green color from the Cr^{+3} ion.



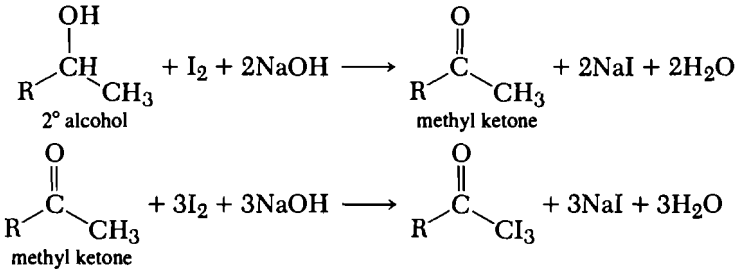
Substrates that easily give rise to cationic character at the carbon bearing the hydroxyl group undergo the Lucas test (Experiment 9, p. 269) readily. Therefore, only secondary (2°) and tertiary (3°) alcohols form the alkyl halide, which appears as a second liquid layer, tertiary alcohols being the most reactive. Primary (1°) alcohols undergo reaction with the zinc chloride and hydrochloric acid either negligibly slowly or not at all.

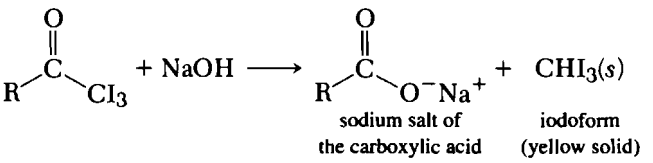


To distinguish between primary, secondary, and tertiary alcohols, the TCICA test (Experiment 10, p. 271) can be utilized. The trichloroisocyanuric acid is reduced to cyanuric acid, a white solid. Primary alcohols react in 1 to 15 min; secondary alcohols react in 0.1 to 1 min; tertiary alcohols do not react within 5 h.



The iodoform test (Experiment 11, p. 273) gives positive results for secondary alcohols in which a methyl group is attached to the carbon bearing the hydroxyl group. This type of alcohol is oxidized to a methyl ketone and under these basic conditions it forms a triiodo intermediate, which is then oxidized to the sodium salt of the acid and iodoform. Iodoform is a foul-smelling yellow precipitate.





Experiment 5 Sodium Detection of Active Hydrogen

$$2\text{ROH} + 2\text{Na} \longrightarrow 2\text{RO}^-\text{Na}^+ + \text{H}_2(g)$$
alcohol

$$2\text{RNH}_2 + 2\text{Na} \longrightarrow 2\text{RNH}^-\text{Na}^+ + \text{H}_2(g)$$
1° amine

$$2\text{R}_2\text{NH} + 2\text{Na} \longrightarrow 2\text{R}_2\text{N}^-\text{Na}^+ + \text{H}_2(g)$$
2° amine

$$\text{H—C}{\equiv}\text{C—H} + 2\text{Na} \longrightarrow \text{Na}^+{}^-\text{C—C}{\equiv}\text{C}^-\text{Na}^+ + \text{H}_2(g)$$
terminal alkyne

$$2\text{R—C}{\equiv}\text{C—H} + 2\text{Na} \longrightarrow 2\text{R—C}{\equiv}\text{C}^-\text{Na}^+ + \text{H}_2(g)$$
terminal alkyne

To 0.25 mL or 0.25 g of the sample, add small thin slices of freshly cut sodium until no more will dissolve. Evolution of hydrogen gas indicates the presence of an acidic hydrogen, such as a hydroxyl group in an alcohol, a hydrogen attached to the nitrogen in a primary or secondary amine, or a hydrogen in a terminal alkyne. Cool the solution, and observe. Add an equal volume of ether. Another positive test is the formation of the solid salt. Prior to testing, dry liquid samples with calcium sulfate. Any residual water will undergo reaction with the sodium. This test may be applied to solid compounds or very viscous liquids by dissolving them in an inert solvent such as anhydrous ligroin or toluene.

The order of reactivity of alcohols with sodium is known to decrease with increasing size of the alkyl portion of the molecule. This test is subject to many limitations, and the results should be interpreted with caution.

Controls Methanol and diethyl amine will give a positive test. Acetophenone and hexane will give a negative test.

Cleaning Up Add enough ethanol dropwise to the solution until all of the sodium has reacted. Allow to stand for 1 h. Dilute the reaction mixture with 10 mL of water, neutralize with 10% hydrochloric acid, and place in the aqueous solution container.

Discussion

This reagent is used in testing *neutral* compounds for the presence of groups that contain easily replaceable hydrogen atoms. Functional groups containing a hydrogen atom attached to oxygen, nitrogen, or sulfur may react with sodium to liberate hydrogen.

$$2\text{ROH} + 2\text{Na} \longrightarrow 2\text{RO}^-\text{Na}^+ + \text{H}_2(g)$$
alcohol

$$2\text{RNH}_2 + 2\text{Na} \longrightarrow 2\text{RNH}^-\text{Na}^+ + \text{H}_2(g)$$
1° amine

$$2\text{R}_2\text{NH} + 2\text{Na} \longrightarrow 2\text{R}_2\text{N}^-\text{Na}^+ + \text{H}_2(g)$$
2° amine

$$2\text{RSH} + 2\text{Na} \longrightarrow 2\text{RS}^-\text{Na}^+ + \text{H}_2(g)$$
sulfide

This test is most useful with alcohols of intermediate molecular weight, such as those containing from three to eight carbon atoms. Lower alcohols are difficult to obtain in anhydrous condition. The presence of traces of moisture causes the test to be positive. Alcohols of high molecular weight undergo reaction slowly with sodium, and the evolution of hydrogen gas is often so slow as to make the test of little value. Metallic sodium, when cut in moist air, adsorbs water on its surface so that, when placed in a perfectly dry solvent such as benzene, it gives off hydrogen gas produced by the interaction of the metal with the adsorbed moisture.

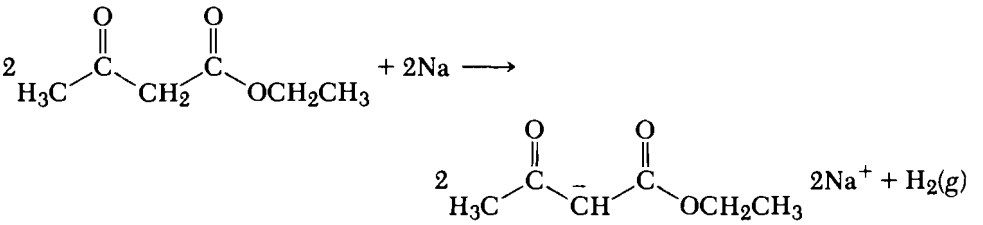
Hydrogen atoms attached to the carbon are not displaced by metals unless there are adjacent functional groups that activate the hydrogen atoms. Compounds with active methine groups, such as acetylene or monosubstituted acetylenes, undergo reaction with sodium.

$$\underset{\text{terminal alkyne}}{H{-}C{\equiv}C{-}H} + 2Na \longrightarrow Na^+{}^-C{-}C{\equiv}C^-Na^+ + H_2(g)$$

$$2R{-}\underset{\text{terminal alkyne}}{C{\equiv}C{-}H} + 2Na \longrightarrow 2R{-}C{\equiv}C^-Na^+ + H_2(g)$$

Frequently the hydrogen produced is not observed, as this hydrogen undergoes reaction with unsaturated functional groups as rapidly as it is produced.

A methylene group, adjacent to an activating group or between two activating groups, possesses hydrogen atoms that may be displaced by sodium. This hydrogen may also be difficult to observe due to its subsequent reaction with unsaturation in the original organic compound.



Reactive methyl groups are present in certain compounds, especially methyl ketones such as acetone and acetophenone. These react with sodium to give the sodium derivative of the ketone and a mixture of products formed by reducing and condensation. For example, acetone yields sodium acetonide, sodium isopropoxide, sodium pinacolate, mesityl oxide, and phorone.

Metallic sodium is thus a useful reagent for detecting the types of reactive hydrogen compounds that are not sufficiently active to produce hydrogen ions in an ionizing solvent. It is obviously unnecessary and dangerous to try the action of sodium on compounds known to be acids.

Structural effects upon acidity are complex. It is well known that liquid samples of alcohols follow this order of reactivity:

$$CH_3OH > CH_3CH_2OH > (CH_3)_2CHOH > (CH_3)_3COH$$

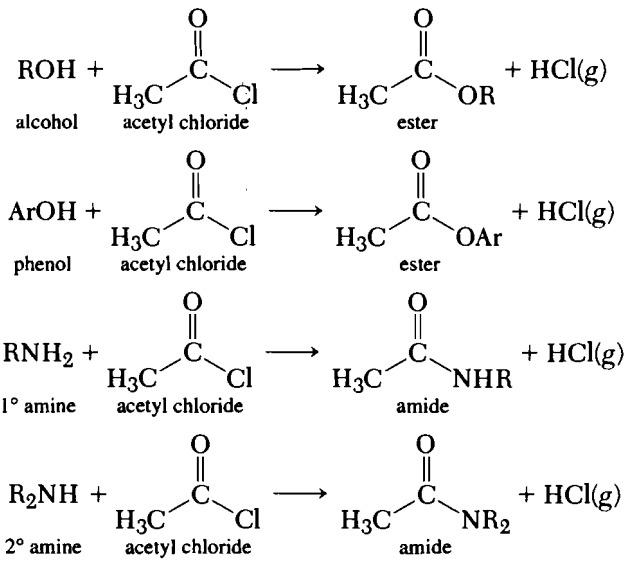
In the gas phase, the reverse order applies. It has been suggested that larger alkyl groups stabilize the alkoxide ion by polarization, while bulky groups about the oxygen destabilize solvation.

Problems

4. Predict the action of sodium on phenol, benzoic acid, oximes, nitromethane, and benzenesulfonamide. Why is this test never used with these compounds? What effect would the presence of moisture have on this test?
5. What is the principal defect of metallic sodium as a classification reagent?

The "active" hydrogen of the hydroxyl group can often be detected by another procedure, involving the use of acid halides, described in Experiment 6.

Experiment 6 Detection of Active Hydrogen with Acetyl Chloride



Perform this test in the hood. Add drop by drop 0.2 mL of acetyl chloride to 0.2 mL or 0.2 g of the unknown. Evolution of heat and hydrogen chloride gas is a positive test. To destroy any unreacted acetyl chloride, allow the mixture to stand for a minute or two and the pour it cautiously into 1 mL of water. Alcohols and phenols react with acetyl chloride to form esters, which is indicated by the formation of a top layer in the flask. Primary and secondary amines react with acetyl chloride to form amides, which precipitate from the solution.

Controls Methanol and diethyl amine will give a positive test. Acetophenone and hexane will give a negative test.

Cleaning Up Separate the organic layer and place in the organic solvent container. Neutralize the aqueous layer with sodium carbonate and place in the aqueous solution container.

Discussion

Primary and secondary alcohols form esters, while tertiary alcohols form primarily the alkyl chloride, due to the reaction of the liberated hydrogen chloride on another molecule of the alcohol.

Only primary and secondary amines will react with acetyl chloride to form amides. However, some low-molecular-weight amides are water soluble. Many substituted anilines, especially those with nitro groups in the *ortho* and *para* position relative to the amino group, do not react with acetyl chloride. Tertiary amines do not have an active hydrogen and, therefore, give a negative result with acetyl chloride.

Problem

6. Explain the difference in reactivity of the primary, secondary, and tertiary alcohols with the acetyl chloride.

Experiment 7 Ceric Ammonium Nitrate

$$\underset{\substack{\text{ceric ammonium nitrate}\\(\text{yellow})}}{(NH_4)_2Ce(NO_3)_6} + \underset{\text{alcohol}}{ROH} \longrightarrow \underset{\text{(red)}}{(NH_4)_2Ce(NO_3)_5(OR)} + HNO_3$$

(a) For Water-Soluble Compounds

Add four to five drops of a liquid unknown or 0.1–0.2 g of a solid to 1 mL of the ceric ammonium nitrate reagent. Mix thoroughly and note whether the yellow color of the reagent changes to red. Alcohols react with the reagent to form a red alkoxy cerium(IV) compound. If a red color develops, watch the solution carefully and note the time for the mixture to become colorless. If no change is noted in 15 min, stopper the test tube and allow to stand several hours or overnight. Also note whether bubbles of carbon dioxide are liberated.

(b) For Water-Insoluble Compounds

Add 2 mL of dioxane[4] to 1 mL of the ceric ammonium nitrate reagent. If a red color develops or if the solution becomes colorless, purify the dioxane. If the mixture remains yellow or is only a light orange-yellow, it may be used to test water-insoluble compounds. Divide the 6 mL of the solution in half, reserving 3 mL for observation as a control. To the other 3 mL of the dioxane containing reagent, add four to five drops of a liquid unknown or 0.1–0.2 g of a solid. Mix thoroughly and make the same observations as in (a).

Controls Methanol, 2-propanol, glycerol, and glucose will give a positive test for (a). 1-Heptanol, benzyl alcohol, and (±)-mandelic acid will give a positive test for (b). Acetophenone and hexane will give a negative test.

Ceric Ammonium Nitrate Reagent

Add 1.3 mL of concentrated nitric acid to 40 mL of distilled water and then dissolve 10.96 g of yellow ceric ammonium nitrate in the dilute nitric acid solution. After the solid has dissolved, dilute to 50 mL. The test is carried out at room temperature (20–25°C).

[4]The dioxane should be checked with ceric nitrate solution to be sure that it does *not* give a positive test. The dioxane sold as "histological grade" is usually pure enough so that it may be used. Pure dioxane does not give a red complex. Commercial dioxane sometimes contains glycols or antioxidants as preservatives and must be purified.

Hot solutions (50–100°C) of Ce(IV) oxidize many types of organic compounds. This reagent is usable for about a month.

Cleaning Up For (a) and (b), place the reaction mixture in the aqueous solution container.

(c) Alternate Experiment for Water Insoluble Compounds

To prepare the reagent, dissolve 0.43 g of ceric ammonium nitrate in 2 mL of acetonitrile. Add about 0.1 g of the unknown compound to the reagent in a test tube. Stir the mixture with a glass rod and heat just to boiling. In 1–6 min the color will change from yellow to red. Even cholesterol, $C_{27}H_{45}OH$, gives a red to orange color. The red color disappears as oxidation of the alcohol group takes place.

Cleaning Up Treat the reaction mixture from (c) with 1 mL of 10% sodium hydroxide. Neutralize the solution with 10% hydrochloric acid and place in the aqueous solution container.

Discussion

The ceric ammonium nitrate reagent forms red complexes with primary, secondary, and tertiary alcohols of up to 10 carbons. Also, all types of glycols, polyols, carbohydrates, hydroxy acids, hydroxy aldehydes, and hydroxy ketones give red solutions. Phenols give a brown color or precipitate.

$$\underset{\substack{\text{ceric ammonium nitrate}\\(\text{yellow})}}{(NH_4)_2Ce(NO_3)_6} + \underset{\text{phenol}}{ArOH} \longrightarrow \underset{\text{(brown or black)}}{(NH_4)_2Ce(OAr)(NO_3)_5} + HNO_3$$

The red cerium(IV) compound has been shown to be the intermediate for the oxidation of alcohols by Ce(IV) solutions. Hence, *a second phase* of this test involves the disappearance of the red color due to oxidation of the coordinated alcohol and reduction of the colored Ce(IV) complex to the colorless Ce(III) complex. Thus a positive test includes successively the formation, and then the disappearance of the red color, assuming the oxidation step occurs within a reasonable time (see Table 9.3).

The overall sequence of reactions for a primary alcohol is as follows:

$$\text{(a)}\quad \underset{\text{(yellow)}}{(NH_4)_2Ce(NO_3)_6} + RCH_2OH \longrightarrow \underset{\text{(red)}}{(NH_4)_2Ce(OCH_2R)(NO_3)_5} + HNO_3$$

$$\text{(b)}\quad \underset{\text{(red)}}{(NH_4)_2Ce(OCH_2R)(NO_3)_5} \longrightarrow RCH_2O\cdot + \underset{\text{(colorless)}}{(NH_4)_2Ce(NO_3)_5} + HNO_3$$

$$\text{(c)}\quad \underset{\text{(yellow)}}{RCH_2O\cdot + (NH_4)_2Ce(NO_3)_6} \longrightarrow \underset{\text{(colorless)}}{R{-}C(=O){-}H} + (NH_4)_2Ce(NO_3)_5 + HNO_3$$

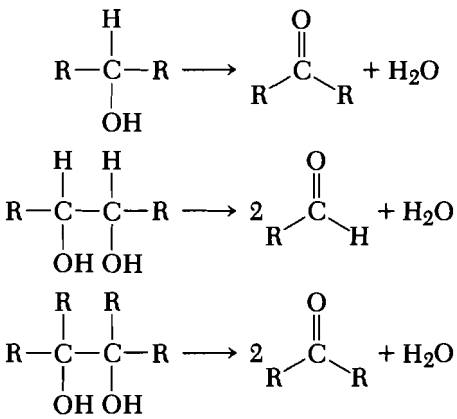
The rates of the oxidation steps (b and c) depend upon the structure of the hydroxy compound.

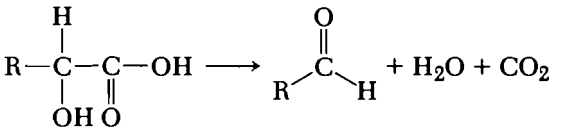
TABLE 9.3 Approximate Times for Reduction of Red Ce(IV) Complexes at 20°C to Colorless Ce(III) Nitrato Anion with Oxidation of Alcohols to Aldehydes or Ketones

Compound	Time[a]	Compound	Time[a]
Primary alcohols		**Diols, triols, . . . , polyols**	
Allyl alcohol	6 min	Pinacol	5 sec
Methyl cellosolve	1.2 hr	Mannitol	38 sec
1-Propanol	3.6 hr	2,3-Butanediol	1 min
Benzyl alcohol	4.0 hr	Glycerol	10 min
1-Butanol	4.1 hr	Propylene glycol	15 min
2-Methyl-1-propanol	4.1 hr	Diethylene glycol	3 hr
1-Heptanol	5.0 hr	Ethylene glycol	5 hr
Ethanol	5.5 hr	1,4-Butanediol	1 hr
Methanol	7.0 hr	1,4-Butynediol	36 min
2-Methyl-1-butanol	7.0 hr	1,4-Butenediol (mostly *cis*)	3 min
1-Decanol	12.0 hr		
Secondary alcohols		**Carbohydrates**	
Cyclohexanol	3.7 hr	Glucose	1 min
2-Propanol	6.0 hr	Fructose	30 sec
2-Butanol	9.0 hr	Galactose	1 min
2-Pentanol	17.0 hr	Lactose	5 min
2-Octanol	16.0 hr	Maltose	8 min
Diphenylcarbinol	12.0 hr	Sucrose	12 min
		Cellulose—insoluble—no red	
		Starch—insoluble—no red	
Tertiary alcohols		**Hydroxy acids**	
tert-Butyl alcohol	>48 hr	Lactic acid	15 sec + CO_2
tert-Pentyl alcohol	>48 hr	Malic acid	30 sec + CO_2
3-Methyl-3-hydroxy-1-butyne	36 hr	Tartaric acid	1 min + CO_2
		Mandelic acid	1 min + CO_2
		Citric acid	1 min + CO_2
		Hydroxy ketones	
		3-Hydroxy-2-butanone	15 sec
		3-Methyl-3-hydroxy-2-butanone	10 sec

[a]Variations in time of consideration can be expected due to variable size of reagent drops and to the age of the reagent.

The products from other hydroxylic compounds are listed below:





Among simple hydroxy compounds, methanol gives the deepest red color. As the molecular weight of the alcohols increases, the color becomes less intense and somewhat brownish red.

A red color is produced by aqueous 40% formaldehyde (formalin). This is due to methanol present in the solution. Acetaldehyde frequently gives a red color due to the presence of 3-hydroxybutanal, acetaldol. Alternatively, these aldehydes may hydrate in aqueous solution to form gem diols, $RCH(OH)_2$, which may be the species that are oxidized.

Negative tests are indicated by the absence of the red complex with retention of the yellow color of the reagent. All pure aldehydes, ketones, saturated and unsaturated acids, ethers, esters, and dibasic and tribasic acids produce a negative test. The dibasic acids, oxalic and malonic, do *not* give a red color but do reduce the yellow Ce(IV) to colorless Ce(III) solutions.

Basic aliphatic amines cause precipitation of white ceric hydroxide. If the amines are dissolved in dilute nitric acid, thus forming the amine nitrate, and this solution is treated with the ceric reagent, no red color develops provided that there are no alcoholic hydroxyl groups present in addition to the amino groups. If alcoholic groups are present, then dilute nitric acid solutions of such compounds do give red colors. For example, dilute nitric acid solutions of these compounds

$$HOCH_2CH_2NH_2 \qquad (HOCH_2CH_2)_2NH \qquad (HOCH_2CH_2)_3N$$

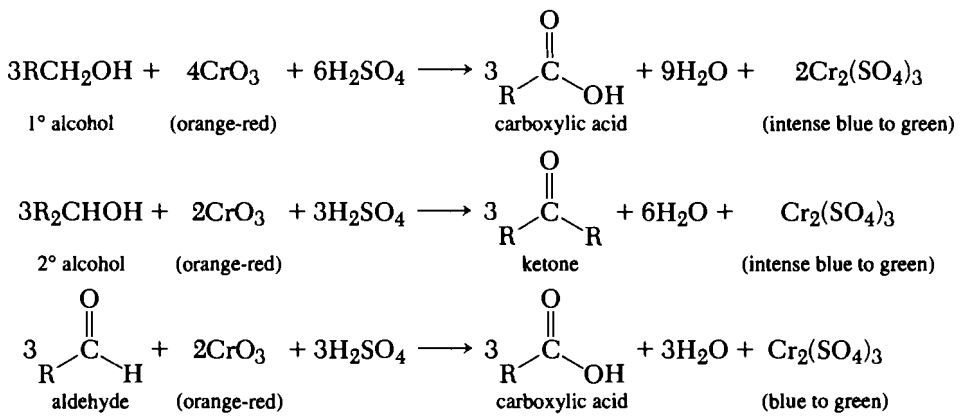
all give positive tests.

Alcohols containing halogens give positive tests. For example, $ClCH_2CH_2OH$, $BrCH_2CH_2OH$, $ClCH_2CH_2CH_2OH$, and $CH_3CHOHCH_2Cl$ form red complexes.

Very insoluble alcohols of high molecular weight such as 1-hexadecanol, triphenylmethanol, or benzipinacol fail to react even in the dioxane solutions and do not give a red color.

Long-chain alcohols, C_{12} through C_{18}, *will* give a positive test when added to an acetonitrile solution of ammonium hexanitratocerate at the boiling point, 82°C. Note that (c), listed above for water-insoluble compounds, is especially useful for such long-chain alcohols.

Experiment 8 Chromic Anhydride (Chromium Trioxide, Jones Oxidation)



To 1 mL of acetone in a small test tube, add one drop of the liquid or about 10 mg of a solid compound. Then add one drop of the Jones reagent and note the result *within 2 sec.* Run a control test on the acetone and compare the result. A positive test for primary or secondary alcohols consists in the production of an opaque suspension with a green to blue color. Tertiary alcohols give no visible reaction within 2 sec, the solution remaining orange in color. *Disregard* any changes after 2 sec.

Controls 1-Butanol, 2-propanol, and benzaldehyde will give a positive test. 2-Methyl-2-propanol, acetone, and acetophenone will give a negative test.

Jones Reagent
Pour a suspension of 25 g of chromic anhydride (CrO_3) in 25 mL of concentrated sulfuric acid, slowly with stirring into 75 mL of water. Cool the deep orange-red solution to room temperature before use.

Use a good grade of acetone. Some samples of acetone may become cloudy in appearance in 20 sec, but this does not interfere, providing the test solution becomes yellow. If the acetone gives a positive test, purify the acetone by adding a small amount of potassium permanganate and distill the mixture.

Cleaning Up Place the reaction mixture in the hazardous waste container.

Discussion
This test is a rapid method for distinguishing primary and secondary alcohols from tertiary alcohols. Positive tests are given by primary and secondary alcohols without restriction as to molecular weight. Even cholesterol ($C_{27}H_{46}O$) gives a positive test. Aldehydes give a positive test but would be detected by other classification experiments. Aldehydes produce the green color in 5–15 sec, with aliphatic aldehydes reacting more quickly than aromatic aldehydes. Ketones do not react. Olefins, acetylenes, amines, ethers, and ketones give negative tests within 2 sec provided that they are not contaminated with small amounts of alcohols. Enols may give a positive test, and phenols produce a dark-colored solution entirely unlike the characteristic green-blue color of a positive test.

Experiment 9 Hydrochloric Acid/Zinc Chloride (Lucas Test)

$$\underset{\text{2° alcohol}}{R_2CHOH} + HCl \xrightarrow{ZnCl_2} \underset{\text{alkyl halide}}{R_2CHCl} + H_2O$$

$$\underset{\text{3° alcohol}}{R_3COH} + HCl \xrightarrow{ZnCl_2} \underset{\text{alkyl halide}}{R_3CCl} + H_2O$$

(a)
To 0.2 mL or 0.2 g of the sample in a test tube add 2 mL of the Lucas reagent at 26–27°C. Stopper the tube and shake; then allow the mixture to stand. Note the time required for the formation of the alkyl chloride, which appears as an insoluble layer or emulsion.

Lucas Reagent
Dissolve 13.6 g (0.1 mole) of anhydrous zinc chloride in 10.5 g (0.1 mole) of concentrated hydrochloric acid, with cooling.

(b)

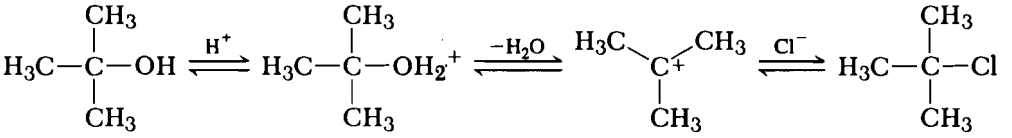
To 0.2 mL or 0.2 g of the alcohol in a test tube add 1.2 mL of concentrated hydrochloric acid. Shake the mixture, and allow it to stand. Observe carefully during the first 2 min.

Controls Note the time required for both (a) and (b) to take place with 1-butanol, 2-methyl-2-propanol, 2-pentanol, 1-propanol, 1-pentanol, allyl alcohol, and benzyl alcohol.

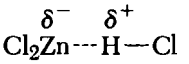
Cleaning Up Add sodium carbonate to the test solution until foaming no longer occurs and place the mixture in the aqueous solution container.

Discussion

The mechanism of the Lucas test is an S_N1-type process as follows:



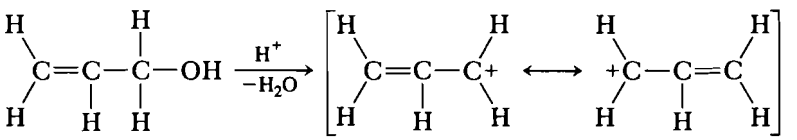
The role of the $ZnCl_2$ is to enhance the reactivity of the HCl by polar coordination:



Since the Lucas test depends on the appearance of the alkyl chloride as a second liquid phase, it is normally applicable only to alcohols that are soluble in the reagent. This limits the test in general to monofunctional alcohols lower than hexyl and certain polyfunctional molecules.

The reaction of alcohols with halogen acids is a displacement reaction in which the reactive species is the conjugate acid of the alcohol, $R—OH_2^+$, and is analogous to the replacement reactions of organic halides and related compounds with silver nitrate and iodide ion (Experiment 35, p. 320, and Experiment 36, pp. 323). The effects of structure on reactivity in these reactions are closely related. Thus primary alcohols do not react perceptibly with hydrochloric acid even in the presence of zinc chloride at ordinary temperatures. Chloride ion is too poor a nucleophilic agent to effect a concerted displacement reaction, and, additionally, the primary carbonium ion is too unstable to serve as an intermediate in the carbonium ion mechanism. Hydrogen bromide and hydrogen iodide, which have a greater nucleophilic reactivity, are also more reactive toward primary alcohols.

Tertiary alcohols react with concentrated hydrochloric acid so rapidly that the alkyl halide is visible within a few minutes at room temperature, first as a milky suspension and then as an oily layer. The acidity of the medium is increased by the addition of anhydrous zinc chloride, which is a strong Lewis acid, and, as a result, the reaction rate is increased. The high reactivity of tertiary alcohols is a consequence of the relatively great stability of the intermediate carbocation. Allyl alcohol, although a primary alcohol, yields a carbocation that is relatively stable because its charge is distributed equally on the two terminal carbon atoms.



As a result, allyl alcohol reacts rapidly with the Lucas reagent and the reaction is accompanied by the evolution of heat. Addition of ice water to the reaction results in the formation of the allyl chloride as a separate layer.

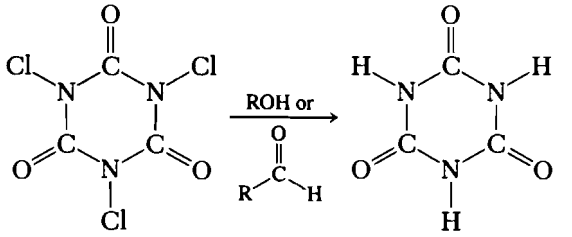
Secondary alcohols are intermediate in reactivity between primary and tertiary alcohols. Although they are not appreciably affected by concentrated hydrochloric acid alone, they react with it fairly rapidly in the presence of anhydrous zinc chloride. A cloudy appearance of the mixture is observed within 5 min, and in 10 min a distinct layer is usually visible.

For a more extended discussion of the effect of structure on reactivity in replacement reactions of this type, see the discussion of the silver nitrate test (Experiment 35, p. 320).

Problems

7. Write the structural formulas and names of the isomeric five-carbon saturated alcohols that were not used in this experiment. How would they react with this reagent?
8. How would you account for the difference in the behavior of allyl alcohol and 1-propanol? Benzyl alcohol and 1-pentanol?
9. List two tests, with the equations, that will give a positive test for butanal and 1-butanol.
10. List two tests, with the equations, that will distinguish between butanal and 1-butanol.

Experiment 10 TCICA Test



This procedure is a modification of existing published procedures.[5,6] Add 0.5 mL of TCICA solution in acetonitrile, one drop of 1 M hydrochloric acid, and three drops or 0.04 g of sample to a small test tube. Some solid samples may need to be dissolved in five drops of methanol. Note the time that the sample was added. Flick the test tube until a precipitate forms and record the time. ***TCICA solution is a strong oxidizing agent. Clean up any spills immediately with a dilute solution of sodium hydrogen sulfite.***

Controls Note the time of a positive reaction with ethanol, 2-propanol, 2-methyl-2-propanol, 3-pentanone, butanal, benzaldehyde, phenol, and cholesterol.

[5]G. A. Hiegel, C. Juska, and M. Kim, *J. Chem. Educ., 78,* 1105 (2001).

[6]G. A. Hiegel and A. K. Chaharmohal, *J. Chem. Educ., 74,* 423 (1997).

TCICA Reagent

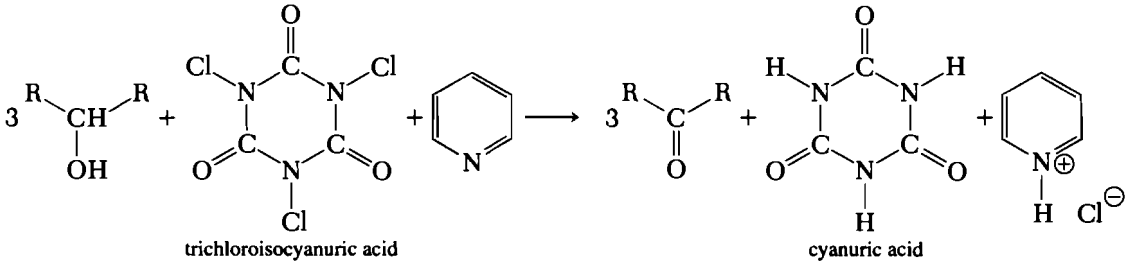
Dissolve 0.30 g of trichloroisocyanuric acid (TCICA) in 10 mL of acetonitrile. Other names for TCICA include 1,3,5-trichloro-1,3,5-triazine-2,4,6-(1H, 3H, 5H)-trione and trichloro-*sec*-triazinetrione. The TCICA can be obtained from a swimming pool store and ground up for use. The solution is stable for years when stored in a brown bottle.

Cleaning Up Add a few drops of 2-propanol or a few crystals of sodium hydrogen sulfite to the reaction flask to destroy any TCICA. Place in the aqueous waste container.

Discussion

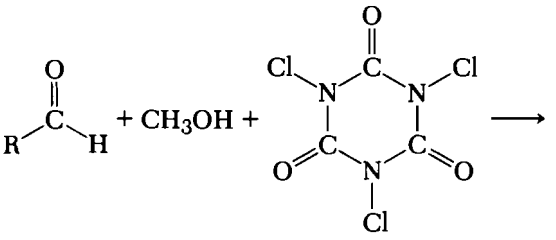
The existing published procedures (see footnotes 5 and 6) were modified to increase the amount of sample in order to speed up the reaction time. With the increased amount of sample,[7] primary alcohols react in 1–15 min; secondary alcohols react in 0.1–1 min; tertiary alcohols do not react within 5 h; ketones do not react within 4 h; aliphatic aldehydes react in 1–1.5 min; aromatic aldehydes react in 2–3 h; phenols react in 1–15 sec; sugars react in 1–5 min; and cholesterol reacts in 10–40 sec.

Trichloroisocyanuric acid has been used to prepare ketones from secondary alcohols.[8]

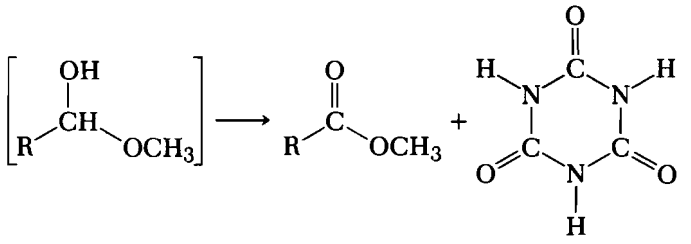


trichloroisocyanuric acid cyanuric acid

The reaction of the aldehyde, in the presence of methanol, with TCICA is believed to form an intermediate hemiacetal, which is then rapidly oxidized to the methyl ester.[9]



aldehyde trichloroisocyanuric acid



hemiacetal cyanuric acid

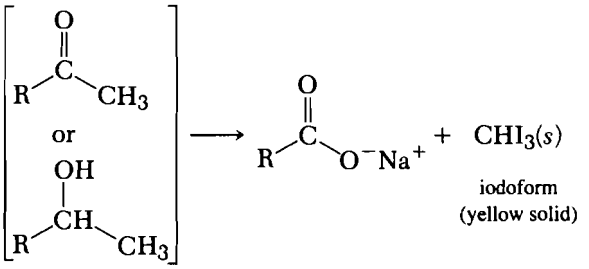
[7]Courtesy of Terra Hosp, Department of Chemistry and Physics, Radford University, Radford, Virginia.

[8]G. A. Hiegel and M. Nalbandy, *Synth. Commun.*, *22*, 1589 (1992).

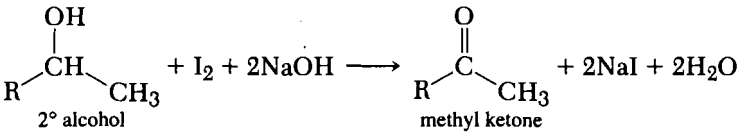
[9]G. A. Hiegel, C. D. Bayne, Y. Donde, G. S. Tamashiro, and L. A. Hiberath, *Synth Comm.*, *26*, 2633 (1996).

Experiment 11 Iodoform Test

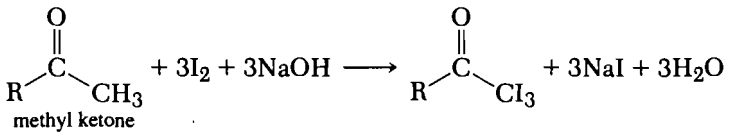
The iodoform is a test for methyl ketones and secondary alcohols that have a methyl group adjacent to the carbon bearing the hydroxyl group.



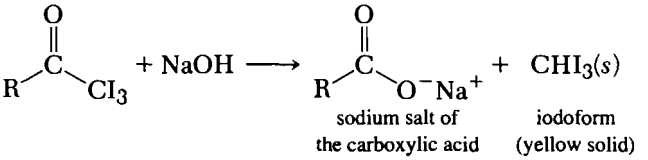
The alcohols are oxidized to the methyl ketones by the "iodine bleach."



Iodination occurs preferentially and completely on the methyl groups.



Cleavage produces the carboxylate salt and iodoform.



Place four drops of the liquid or 0.1 g of the solid to be tested in a test tube. Add 5 mL of dioxane[10] and shake until all the sample has gone into solution. Add 1 mL of 10% sodium hydroxide solution, and then slowly add the iodine–potassium iodide solution, with shaking, until a slight excess yields a definite dark color of iodine. If less than 2 mL of the iodine solution is decolorized, place the test tube in a water bath at a temperature of 60°C. If the slight excess of iodine already present is decolorized, continue the addition of the iodine solution (keep the iodine solution at 60°C), with shaking, until a slight excess of iodine solution again yields a definite dark color. Continue the addition of iodine until the dark color is not discharged by 2 min of heating at 60°C. Remove the excess of iodine by the addition of a few drops of 10% sodium hydroxide solution, with shaking. Now fill the test tube with water and allow to stand for 15 min. A positive test is indicated by the formation of a foul-smelling yellow precipitate (iodoform). Collect the precipitate by filtration and dry. Obtain the melting point. Iodoform (CHI_3) melts at 119–121°C (d) and has a distinctive foul odor. If the iodoform is reddish, dissolve in 3–4 mL of dioxane, add 1 mL of 10% sodium hydroxide solution, and shake until only a light lemon color remains. Dilute with water and filter.

[10]Dioxane is appropriate for water *insoluble* compounds; water soluble compounds may be treated by substituting 2 mL of water for the dioxane solvent.

Controls 2-Propanol, acetophenone, and acetone will give a positive test. Ethyl acetate and methanol will give a negative test. (Note that some lower commercial grades of methanol give misleading positive results due to impurities.)

Iodine–Potassium Iodide Solution

Add 20.0 g of potassium iodide and 10.0 g of iodine to 80.0 mL of water and stir until the reaction is complete.

$$I_2 + KI \xrightarrow{H_2O} KI_3$$

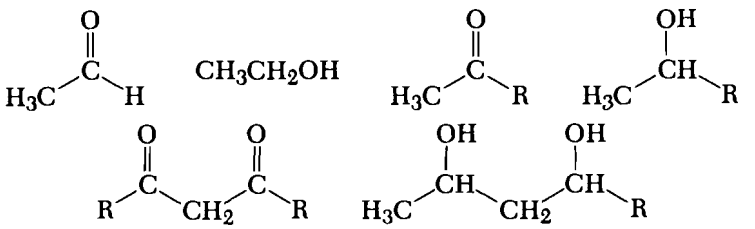
The solution is deep brown due to the triiodide anion (I_3^-).

Cleaning Up Add a few drops of acetone to the reaction mixture to destroy any unreacted iodine in potassium iodide solution. Remove the iodoform by suction filtration and place in the halogenated organic waste container. Place the filtrate in the aqueous solution container.

Discussion

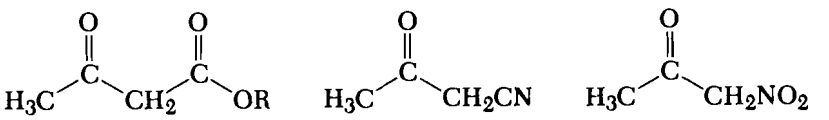
This test is positive for compounds that contain the grouping $CH_3\overset{\overset{O}{\|}}{C}-$, $ICH_2\overset{\overset{O}{\|}}{C}-$, $I_2CH\overset{\overset{O}{\|}}{C}-$ when joined to a hydrogen atom or to a carbon atom that does not have highly active hydrogens or groups that provide an excessive amount of steric hindrance. The test will, of course, also be positive for any compound that reacts with the reagent to give a derivative containing one of the requisite groupings. Conversely, compounds that contain one of the requisite groupings will not give iodoform if that grouping is destroyed by the hydrolytic action of the reagent before iodination is complete.

Following are the principal types of compounds that give a positive test:



R = any alkyl or aryl radical except an *ortho*-disubstituted aryl radical

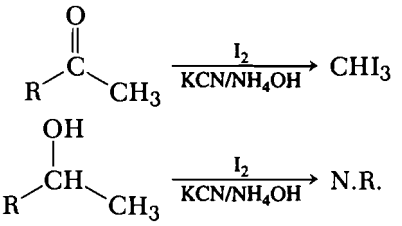
R, however, if large, will sterically inhibit this reaction. The test is negative for compounds of the following types:



In such compounds the reagent removes the acetyl group and converts it to acetic acid, which resists iodination.[11]

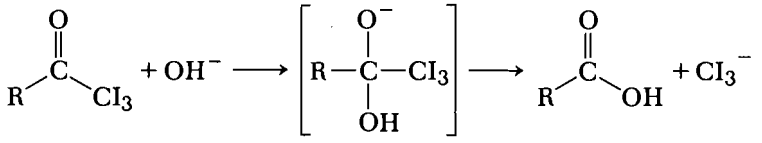
[11]For a general discussion of this test, see R. C. Fuson and B. A. Bull, *Chem. Rev.*, *15*, 275 (1934).

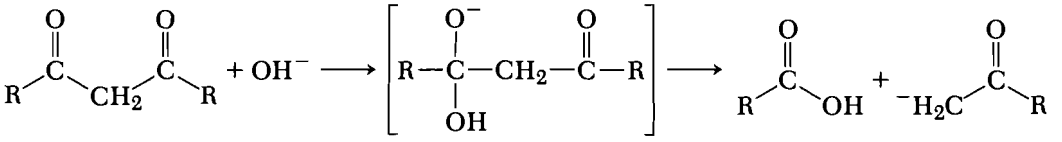
A modified reagent[12] has been suggested for distinguishing methyl ketones from methyl carbinols. It consists of a solution of 1 g of potassium cyanide, 4 g of iodine, and 6 mL of concentrated ammonium hydroxide in 50 mL of water. *Potassium cyanide is extremely toxic; use only with the instructor's permission. Do not mix with acid.*



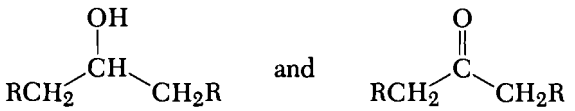
This reagent produces iodoform from methyl ketones but not from methyl carbinols.

The cleavage of trihalo ketones with base, exemplified by the second step of the iodoform test, is related to the reversal of the Claisen condensation. In each case the reaction can proceed because of the stability of the final anionic fragment:



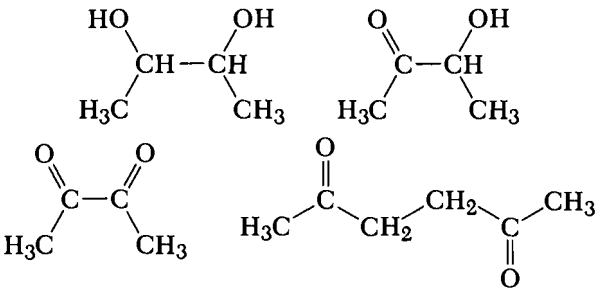


Secondary alcohols and ketones of the structures



do not produce iodoform, although they may undergo some halogenation on the methylene group adjacent to the carbonyl group. Occasionally commerical samples of diethyl ketone give a weak iodoform test. This is due to the presence of such impurities as 2-pentanone.

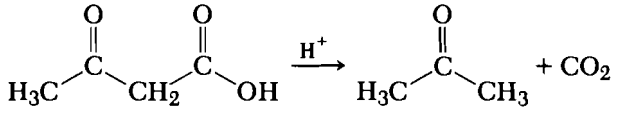
Bifunctional alcohols and ketones of the following types give positive iodoform tests:



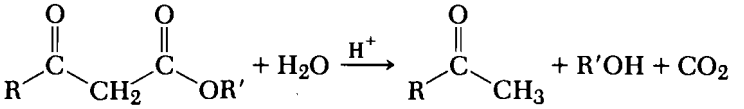
[12]E. Rothlin, *Arch. Escuela Farm. Fac. Ci. Med. Cordoba [R. A.] Secc. ci.*, *10*, 1 (1939); *C. A.*, *35*, 5091 (1941).

β-Keto esters do not produce iodoform by the test method, but their alkaline solutions do react with sodium hypoiodite.

Acetoacetic acid is unstable; acidic aqueous solutions decompose to give CO_2 and acetone.

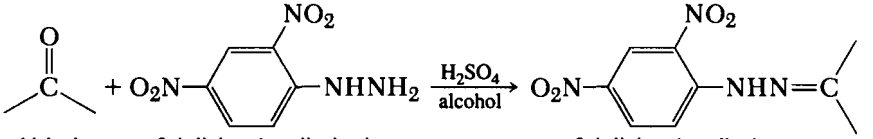


The acetone will give a positive iodoform test. This behavior is generally useful if a β-keto ester is one of the possibilities being considered, since these esters are hydrolyzed by boiling with 5% sulfuric acid (acid-induced retro condensation):

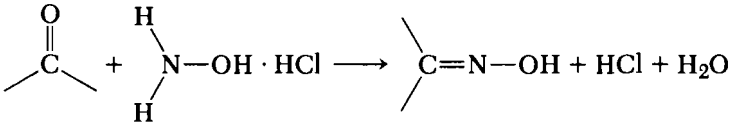


9.4 ALDEHYDES

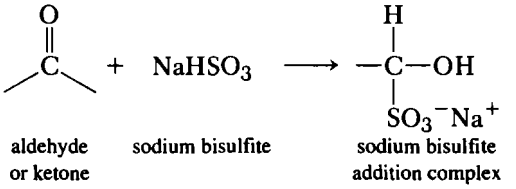
The reaction of aldehydes and ketones with 2,4-dinitrophenylhydrazine (Experiment 12, p. 278) to form the 2,4-dinitrophenylhydrazone probably represents the most studied and most successful of all qualitative tests and derivatizing procedures. In addition, the general details of the reaction serve as a model for a number of other chemical reactions (osazone, semicarbazone, oxime, and other arylhydrazone preparations). The 2,4-dinitrophenylhydrazone precipitates from the solution.



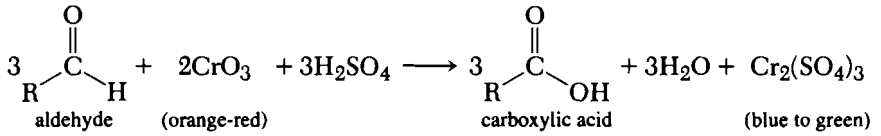
In the reaction of hydroxylamine hydrochloride with aldehydes (Experiment 13, p. 280), the formation of the oximes results in the liberation of hydrogen chloride, which can be detected by the change in color from orange to red of a pH indicator.



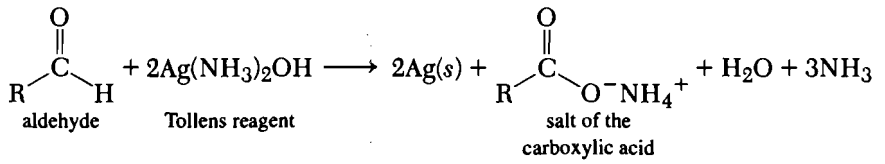
The precipitation of a bisulfite addition complex (Experiment 14, p. 281) is indicative of a variety of carbonyl compounds reacting with sodium bisulfite. This reaction is greatly inhibited by the steric constraints about the carbonyl group.



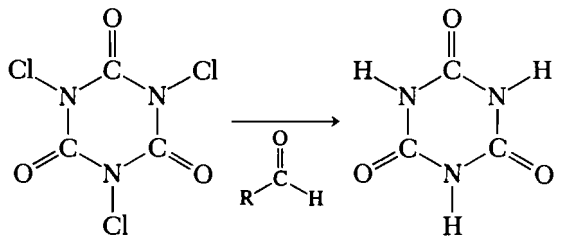
A simple chemical test for aldehydes involves the use of CrO_3 in Jones oxidation (Experiment 8, p. 268). As the aldehyde is oxidized to the carboxylic acid, the chromium is oxidized from a +3 oxidation state, which is an orange-red color, to a +6 oxidation state, which is a deep–blue-green color.



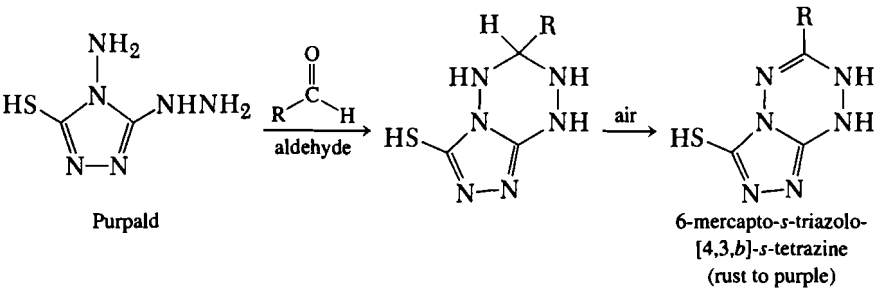
Aldehydes produce a silver mirror when mixed with Tollens reagent (Experiment 15, p. 283). As the aldehyde is oxidized to an acid, the silver is reduced from a +1 oxidation state to elemental silver and is deposited as a silver mirror or colloidal silver inside the reaction flask.



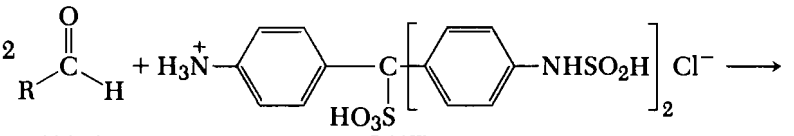
To distinguish between aliphatic and aromatic aldehydes, the TCICA test (Experiment 10, p. 271) can be utilized. The trichloroisocyanuric acid is reduced to cyanuric acid, a white solid. Aliphatic aldehydes react in 1–1.5 min and aromatic aldehydes react in 2–3 h.



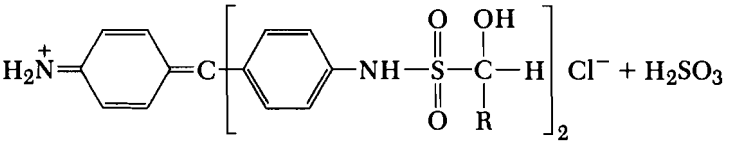
The Purpald test (Experiment 16, p. 284) is a rapid test for the detection of aldehydes. Aldehydes react with Purpald to yield a purple or rust-colored solution of 6-mercapto-*s*-triazolo-[4,3,*b*]-*s*-tetrazine.



Schiff's reagent (Experiment 17, p. 284) undergoes reaction with aldehydes to form a violet-purple solution.

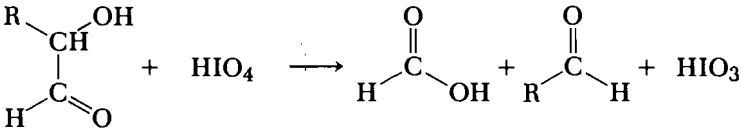


aldehyde — Schiff's reagent (colorless)



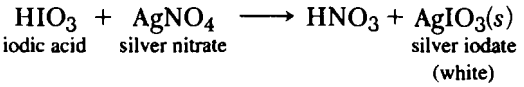
(violet-purple solution)

α-Hydroxy aldehydes are oxidized with periodic acid (Experiment 27, p. 308).



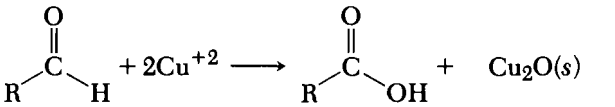
α-hydroxy aldehyde — periodic acid — carboxylic acid — aldehyde — iodic acid

The iodic acid produced above is detected with 5% silver nitrate solution. An immediate precipitation of silver iodate occurs.



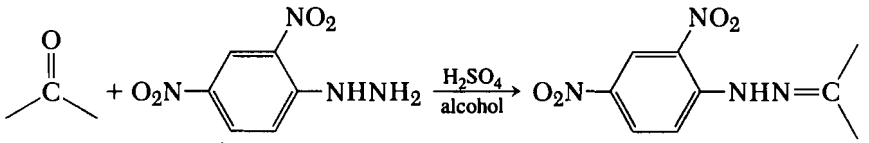
iodic acid — silver nitrate — silver iodate (white)

Benedict's solution (Experiment 28, p. 310) and Fehling's solution (Experiment 29, p. 311) will undergo reactions with aliphatic aldehydes but not with aromatic aldehydes. These reagents oxidize the aliphatic aldehyde to a carboxylic acid, and the copper in the reagent is reduced from +2 to +1. The copper(I) oxide precipitates as a red, yellow, or yellowish-green solid.



aldehyde — (blue) — carboxylic acid — (red, yellow, or yellowish green)

Experiment 12 2,4-Dinitrophenylhydrazine



aldehyde or ketone — 2,4-dinitrophenylhydrazine — 2,4-dinitrophenylhydrazone

Add a solution of one or two drops or about 50 mg of the compound to be tested in 2 mL of 95% ethanol to 3 mL of 2,4-dinitrophenylhydrazine reagent. Shake vigorously and, if no precipitate forms immediately, allow the solution to stand for 15 min. If needed, the precipitate can be recrystallized from ethanol.

Controls Butanal, acetophenone, and acetone will give a positive test. Ethyl acetate and methanol will give a negative test.

2,4-Dinitrophenylhydrazine Reagent[13]

Dissolve 3 g of 2,4-dinitrophenylhydrazine in 15 mL of concentrated sulfuric acid. Add the solution, with stirring, to 20 mL of water and 70 mL of 95% ethanol. Mix thoroughly and filter.

Cleaning Up Place the test solution in the hazardous waste container.

Discussion

Most aldehydes and ketones yield dinitrophenylhydrazones that are insoluble solids. The precipitate may be oily at first and become crystalline on standing. A number of ketones, however, give dinitrophenylhydrazones that are oils. For example, 2-decanone, 6-undecanone, and similar substances fail to form solid dinitrophenylhydrazones.

A further difficulty with the test is that certain allyl alcohol derivatives may be oxidized by the reagent to aldehydes or ketones, which then give a positive test. For example, the 2,4-dinitrophenylhydrazones of the corresponding carbonyl compounds have been obtained in yields of 10–25% from cinnamyl alcohol, 4-phenyl-3-buten-2-ol, and vitamin A_1. Benzhydryl alcohol was also found to be converted to benzophenone dinitrophenylhydrazone in low yield. Needless to say, there is always the further danger that an alcohol sample may be contaminated by enough of its aldehyde or ketone, formed by air oxidation, to give a positive test. If the dinitrophenylhydrazone appears to be formed in a very small amount, it may be desirable to carry out the reaction on the scale employed for the preparation of the derivative (Procedure 13, p. 372). The melting point of the solid should be checked to be sure it is different from that of 2,4-dinitrophenylhydrazine, mp 198°C.

If necessary, this hydrazone derivative can be recrystallized from a solvent such as ethanol. Recrystallization solvents containing reactive carbonyl groups, such as acetone, should not be used as they may result in the formation of another hydrazone.

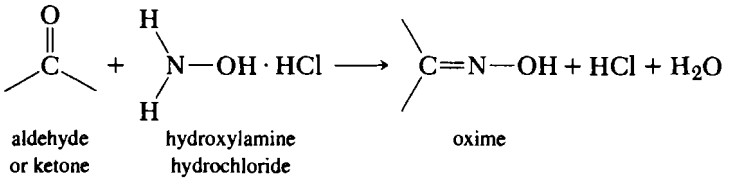
The color of a 2,4-dinitrophenylhydrazone may give an indication as to the structure of the aldehyde or ketone from which it is derived. The dinitrophenylhydrazones of aldehydes and ketones in which the carbonyl group is not conjugated with another functional group are yellow. Conjugation with a carbon–carbon double bond or with a benzene ring shifts the absorption maximum toward the visible and is easily detected by an examination of the ultraviolet spectrum.[14] However, this shift is also responsible for a change in color from yellow to orange-red. In general, a yellow dinitrophenylhydrazone may be assumed to be unconjugated. However, an orange or red color should be interpreted with caution, since it may be due to contamination by an impurity.

In difficult cases, it may be desirable to try the preparation of a dinitrophenylhydrazone in diethylene glycol dimethyl ether (diglyme), ethylene glycol monomethyl ether (glyme), DMF, or DMSO. Difficulty in the workup, due to removal of a nonvolatile solvent, can be encountered in these cases. Methanol can be used as an alternative to ethyl alcohol; the more volatile alcohol may, however, result in mixtures that are difficult to purify.

[13]This reagent is sometimes called "Brady's reagent."

[14]Z. Rappoport, and T. Sheradsky, *J. Chem. Soc. B*, 277 (1968); L. A. Jones, J. C. Holmes, and R. B. Seligman, *Anal. Chem.*, *28*, 191 (1956).

Experiment 13 Hydroxylamine Hydrochloride



(a) For Neutral Aldehydes

Add a drop or a few crystals of the compound to 1 mL of the Bogen or Grammercy indicator–hydroxylamine hydrochloride reagent. Note the color change. If no pronounced change occurs at room temperature, heat the mixture to boiling. A change in color from orange to red constitutes a positive test.

(b) For Acidic or Basic Aldehydes

Add about 0.2 g of the compound to 1 mL of the indicator solution. Adjust the color of the mixture so that it matches 1 mL of the Bogen or Grammercy indicator–hydroxylamine hydrochloride reagent in a separate test tube of the same size. This is done by adding a few drops of 1% sodium hydroxide or 1% hydrochloric acid solution. Then add the resulting solution to 1 mL of the Bogen or Grammercy indicator–hydroxylamine hydrochloride reagent and note whether a red color is produced.

Controls Butanal, benzophenone, and acetone will give a positive test for (a). 4-(*N*,*N*-Dimethylamino)benzaldehyde and salicylaldehyde will give a positive test for (b). Hexane and tartaric acid will give a negative test for both (a) and (b).

Bogen or Grammercy Universal Indicator–Hydroxylamine Hydrochloride Reagent

Add 0.3 mL of Bogen or Grammercy universal indicator to a solution of 500 mg of hydroxylamine hydrochloride in 100 mL of 95% ethanol. Grammercy indicator is getting increasingly difficult to find. Adjust the color of the solution to a bright-orange shade (pH 3.7–3.9) by adding 5% ethanolic sodium hydroxide or 5% ethanolic hydrochloric acid dropwise. The reagent is stable for several months.

Indicator Solution

Add 0.3 mL of either of the above solutions to 100 mL of 95% ethanol to make a solution of the indicator.

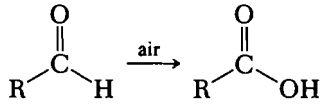
Cleaning Up Place the test solutions in the aqueous solution container.

Discussion

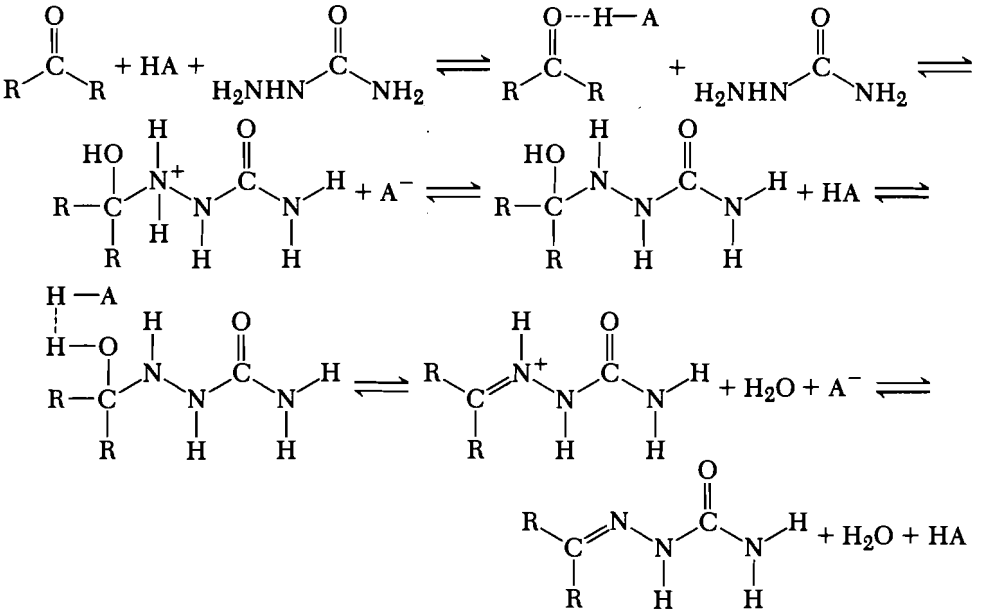
The change in color of the indicator is due to the hydrochloric acid liberated in the reaction of the carbonyl compound with hydroxylamine hydrochloride, with the oxime not being sufficiently basic to form a hydrochloride. All aldehydes and most ketones give an immediate change in color. Some higher-molecular-weight ketones such as benzophenone, benzil, benzoin, and camphor require heating. Sugars, quinones, and hindered ketones, such as 2-benzoylbenzoic acid, give a negative test.

Many aldehydes undergo autoxidation in the air and contain appreciable amounts of acids; hence the action of an aqueous solution or suspension on litmus must always

be determined. If the solution is acidic, (b) must be used; this is also true of compounds whose solubility behavior shows them to be acids or bases.



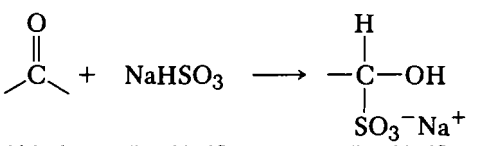
The mechanism of the reaction of carbonyl compounds with hydroxylamine is apparently very closely related to the mechanisms of the reaction with phenylhydrazine, dinitrophenylhydrazine, and semicarbazide. Semicarbazone formation is the reaction of this group that has been most thoroughly studied. The mechanism in aqueous solution, as catalyzed by the acid HA, is shown below:



The mechanism shows that the reaction is hindered by solutions that are either too acidic or too basic. Since the reaction requires both free semicarbazide and a proton source (HA), a strongly acidic solution depresses the reaction rate by converting virtually all of the semicarbazide to its inactive conjugate acid, whereas a strongly basic solution depresses the rate by converting the acid HA to its inactive conjugate base. The most favorable conditions are those in which the product of the concentrations of HA and $NH_2NHCONH_2$ is at a maximum.

The reaction is reversible. Although in relatively weakly acidic solutions the equilibrium may be made to lie far toward the right, strong acid removes semicarbazide by converting it to the conjugate acid and shifts the equilibrium toward the free ketone.

Experiment 14 Sodium Bisulfite Addition Complex



aldehyde or ketone — sodium bisulfite — sodium bisulfite addition complex

Add 1 mL of ethanol to 4 mL of a 40% aqueous sodium bisulfite solution to prepare an alcoholic solution of the sodium bisulfite. Separate any precipitated salt by decantation or filtration before using the reagent.

Place 1 mL of the reagent in a test tube and add 0.3 mL or 300 mg of the sample. Stopper the test tube and shake vigorously. Aldehydes and ketones react with sodium bisulfite to form a solid. The formation of a solid is a positive test.

Controls Acetone, benzaldehyde, heptanal, and acetophenone will give a positive test. Hexane and diethylamine will give a negative test.

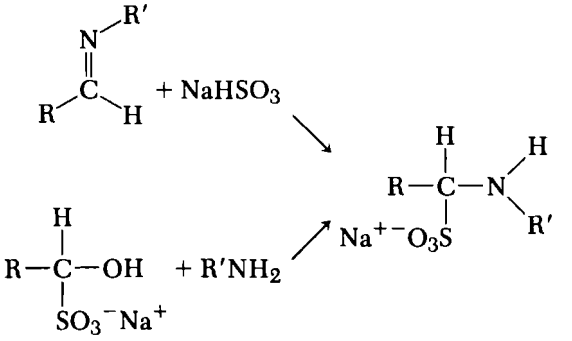
Cleaning Up Place the mixture in the aqueous solution container.

Discussion

The formation of bisulfite addition compounds, also known as α-hydroxyalkanesulfonates, is a general reaction of aldehydes. Most methyl ketones, low-molecular-weight cyclic ketones up to cyclooctanone, and certain other compounds having very active carbonyl groups behave similarly. Some methyl ketones, however, form the addition compounds slowly or not at all. Examples are aryl methyl ketones, pinacolone, and mesityl oxide. Cinnamaldehyde forms an addition compound containing two molecules of bisulfite.

The bisulfite addition compounds are in equilibrium with the carbonyl compound. These compounds are easily decomposed by either acids or alkalies to regenerate the original compounds, and thus they are stable only in neutral solutions. Compounds derived from low-molecular-weight carbonyl compounds are soluble in water. Another advantage of the bisulfite addition compounds is how easily they are purified.

The nitrogen analogs of aldehydes, imines (or Schiff bases), also undergo reaction with sodium bisulfite. The product is identical with that formed by the action of a primary amine on the aldehyde bisulfite compound.



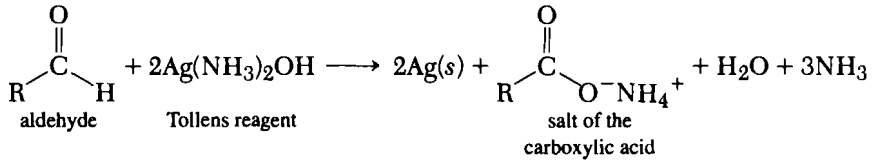
The carbon–sulfur bond in these compounds is reactive, with the sulfonate group being displaced by reactions with anions such as CN^-.

Problems

11. Suggest an explanation of the fact that cyclohexanone reacts with sodium bisulfite readily, whereas 3-pentanone does not.
12. What is the explanation of the failure of pinacolone to react? Compare the case with that of acetophenone.
13. Explain the behavior of cinnamaldehyde.

14. Why is an alcoholic solution of sodium bisulfite used? Try the test on acetone, using an aqueous solution.

Experiment 15 Tollens Test



Add one drop or a few crystals of the sample to the freshly prepared Tollens reagent. A positive test is the formation of silver metal or colloidal silver. If no reaction takes place in the cold, the solution should be warmed slightly on a steam bath or in a hot-water bath. However, excessive heating will cause the appearance of a false positive test by decomposition of the reagent.

Controls Formalin, acetone, and benzaldehyde will give a positive test. Hexane ethanol, and acetophenone will give a negative test.

Tollens Reagent

Clean a test tube with 10% sodium hydroxide. Add 2 mL of a 5% silver nitrate solution and a drop of 10% sodium hydroxide. Add 2% ammonia solution, drop by drop, with constant shaking, until the precipitate of silver oxide just dissolves. In order to obtain a sensitive reagent, it is necessary to avoid a large excess of ammonia.

This reagent should be prepared just before use and should not be stored, because the solution decomposes on standing and deposits a highly explosive precipitate.

Cleaning Up Pour the solution into a beaker. Add a few drops of 5% nitric acid to dissolve the silver mirror or colloidal silver. Combine all solutions. Make the solution acidic with 5% nitric acid, then neutralize with sodium carbonate. Add 5 mL of saturated sodium chloride solution to precipitate the silver as silver chloride. Isolate the silver chloride by filtration and place in the nonhazardous solid waste container. Place the filtrate in the aqueous solution container.

Problem

15. Would the presence of a reactive halogen atom interfere with this test?

Discussion

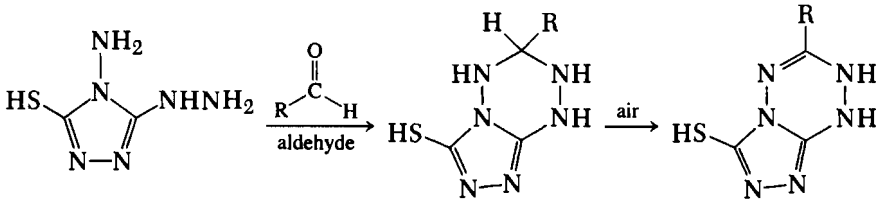
It should be noted that diphenylamine and aromatic amines, as well as 1-naphthols and certain other phenols, give a positive Tollens test. α-Alkoxy and α-dialkylamino ketones have been found to reduce ammoniacal silver nitrate. In addition, the stable hydrate of trifluoroacetaldehyde gives a positive test.

This test often results in a smooth deposit of silver metal on the inner surface of the test tube; hence the name the "silver mirror" test. In some cases, however, the metal forms merely as a granular gray or black precipitate, especially if the glass is not scrupulously clean.

The reaction is autocatalyzed by the silver metal and often involves an induction period of a few minutes.

False-negative tests are common with water insoluble aldehydes.

Experiment 16 Purpald Test[15]



Purpald

6-mercapto-*s*-triazolo-[4,3,*b*]-*s*-tetrazine (rust to purple)

Place 10 mg of Purpald®[16] (4-amino-5-hydrazino-1,2,4-triazole-3-thiol) and 0.2 mL (10 drops) of PTC solution in two test tubes. Add 1 mL of toluene to each test tube. Add two drops or 40 mg of the compound to one of the test tubes. Add 0.2 mL (10 drops) of 10% sodium hydroxide solution to each test tube. Stopper and shake vigorously. Note the changing colors. If the unknown is an aldehyde, the color will change from yellow to green to orange to deep rust. The control solution changes to a yellow color and then diffuses to the toluene layer. If no color change occurs within 5 min, then heat in a hot-water bath at 70°C for 2 min.

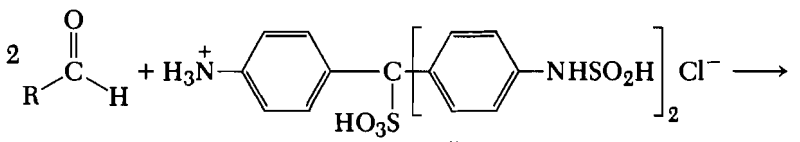
Controls Benzaldehyde and butanal will give a positive test. Diethyl ether and acetone will give a negative test.

PTC Solution
Prepare the phase transfer catalysis solution by dissolving 1 g of tri-*n*-caprylylmethylammonium chloride in 10 mL of toluene.

Cleaning Up Separate the layers. Place the organic layer in the organic solvents container and the aqueous layer in the aqueous solution container.

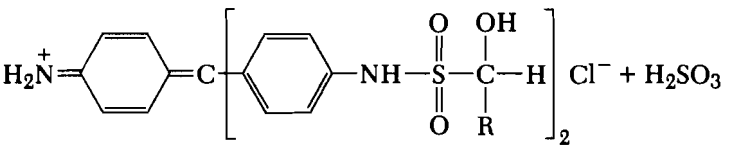
Discussion
False positives may occur with dioxane, 1,4-butanediol, and diethylamine.

Experiment 17 Fuchsin–Aldehyde Reagent (Schiff's Reagent)



aldehyde

Schiff's reagent (colorless)



(violet-purple solution)

[15]H. D. Durst and G. W. Gokel, *J. Chem Educ.*, 55, 206 (1978).

[16]Purpald is a registered trademark of Aldrich Chemical Co., Inc.

Place 2 mL of Schiff's reagent in a test tube and add two drops or a few crystals of the unknown. Shake the tube gently, and observe the color that is developed in 3–4 min. Aldehydes react with Schiff's reagent to form a complex which has a wine-purple color.

Controls Butanal and benzaldehyde will give a positive test. Acetophenone and acetone will give a negative test.

In this test, the reagent should not be heated and the solution tested should not be alkaline. When the test is used on an unknown, a simultaneous test on a known aldehyde and a known ketone should be performed for comparison.

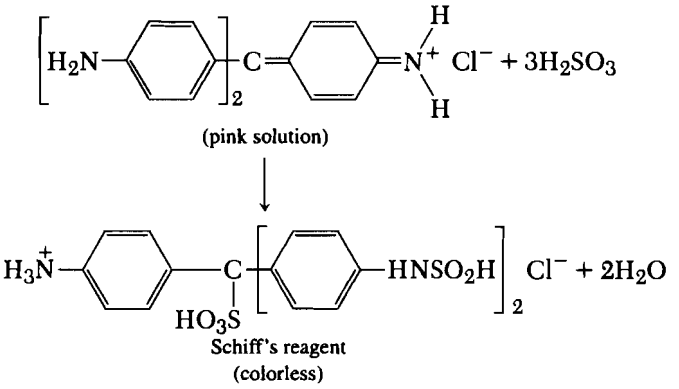
Schiff's Reagent

Dissolve 0.05 g of certified basic fuchsin (4-rosaline hydrochloride) in 50 mL of distilled water. Add 2 mL of saturated sodium bisulfite solution. After allowing the solution to sit for 1 h, add 1 mL of concentrated hydrochloric acid. Allow to stand overnight. This reagent is practically colorless and very sensitive.

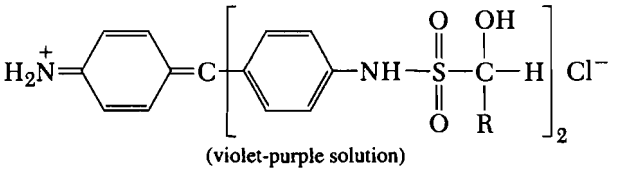
Cleaning Up Neutralize the test solution with sodium carbonate and place in the aqueous solution container.

Discussion

Fuchsin is a pink triphenylmethane dye that is converted to the colorless leucosulfonic acid by sulfurous acid. Apparently the reaction involves 1,6-addition of sulfurous acid to the quinoid nucleus of the dye.



The leucosulfonic acid is unstable and loses sulfurous acid when treated with an aldehyde, resulting in a violet-purple quinoid dye.



This violet-purple color is different from the color of the original fuchsin. It is not a light pink but has a blue cast bordering on a violet or purple. Some ketones and unsaturated compounds react with sulfurous acid to regenerate the pink color of the fuchsin. Therefore, the development of a light pink color in the reagent is not a positive test for aldehydes.

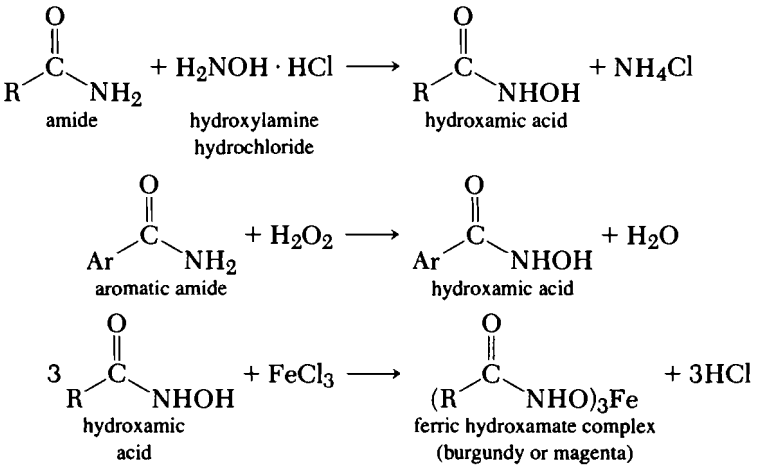
The fact that certain compounds cause the regeneration of the pink color of the original fuchsin has been made the basis of a test. When a specially prepared reagent is used and the reaction time is 1 hr, aldoses produce a pink color whereas ketoses and disaccharides, except maltose, do not. This modification of the Schiff test must be employed with caution, because many organic compound produce a pink color with the reagent when shaken in the air. Other compounds, such as α,β-unsaturated ketones, combine with sulfurous acid and thus reverse the first reaction given above.

PROBLEM

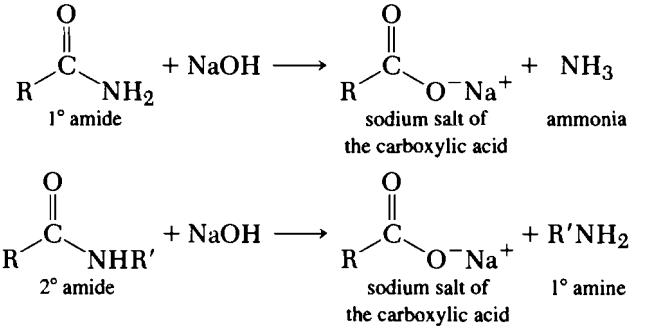
16. List two tests, with equations, that will distinguish between hexanal and 3-hexanone.

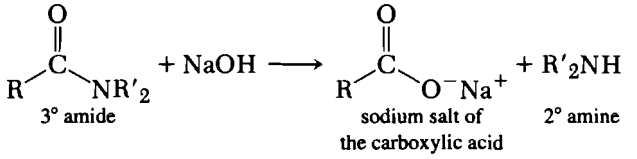
9.5 AMIDES

Aliphatic amides react with hydroxylamine hydrochloride to form hydroxamic acid (Experiment 2c, p. 254). Similarly, aromatic primary amides react with hydrogen peroxide to produce hydroxamic acid (Experiment 2d, p. 254). The hydroxamic acid then reacts with ferric chloride to form the ferric hydroxamate, which has a characteristic magenta color.

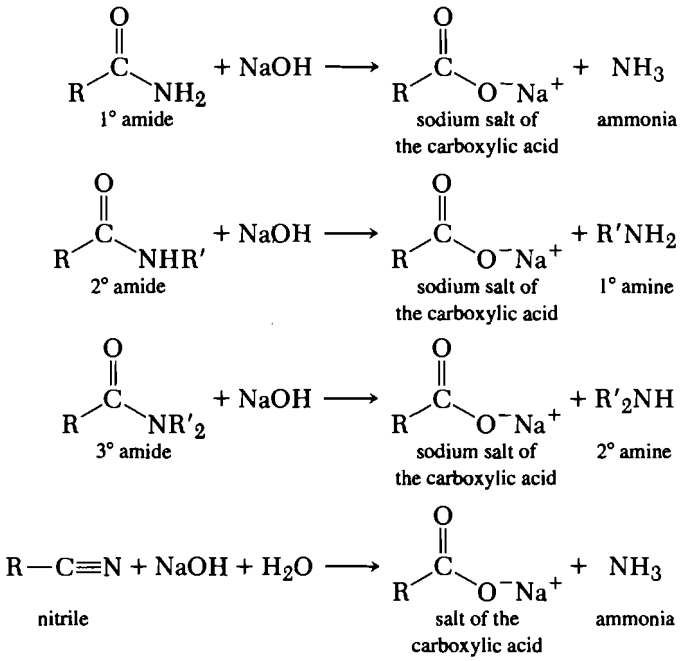


Amides can be hydrolyzed to yield the salt of the carboxylic acid and ammonia or amine (Experiment 18, p. 287). The presence of ammonia or a low-molecular-weight amine is detected with litmus paper.





Experiment 18 Sodium Hydroxide Hydrolysis of Amides and Nitriles



Add 0.2 g of the unknown in a test tube with 5 mL of 10% sodium hydroxide solution. Shake the mixture and note whether or not ammonia is evolved. Heat the solution to boiling and note the odor. Test the action of the vapor on either pink moist litmus paper or filter paper moistened with a copper sulfate solution. If ammonia or amine is being evolved, the litmus paper turns blue. Ammonia, which is evolved only from primary amines, will turn the copper sulfate solution on the filter paper blue. Nitriles and ammonium salts will also give a positive test with the copper sulfate.

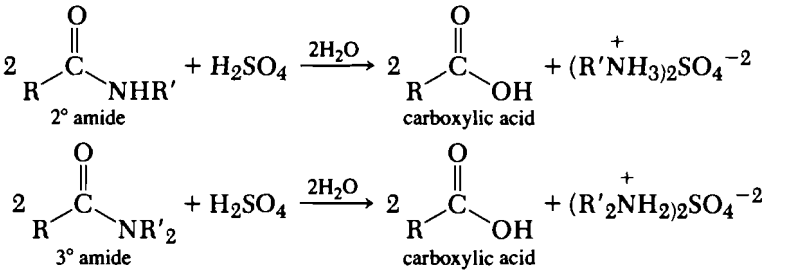
Controls Benzamide and benzonitrile will give a positive test. Hexane and acetone will give a negative test.

Cleaning Up Place the mixture in the aqueous solution container.

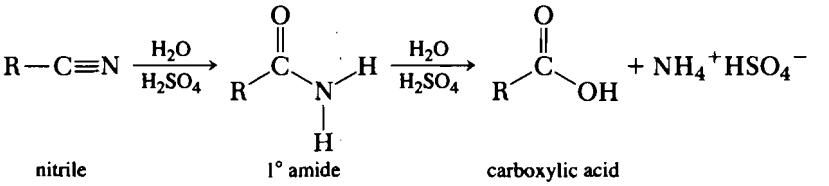
Discussion

The ammonia or amine that is the product of this alkaline hydrolysis may be characterized by the Hinsberg test (Experiment 19, p. 291).

Many substituted amides are hydrolyzed more easily by heating under reflux with 20% sulfuric acid.

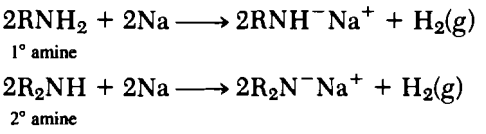


Nitriles, particularly cyanohydrins, are frequently hydrolyzed by acids. Treatment with concentrated hydrochloric acid, with heating, converts the nitriles to amides. The amides may be hydrolyzed further by diluting the mixture with water and heating for 0.5–2 h.

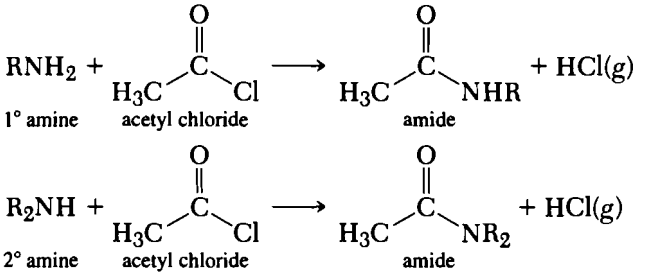


9.6 AMINES AND AMINE SALTS

The active hydrogen on primary and secondary amines undergoes reaction with sodium to form the salt and to liberate hydrogen gas (Experiment 5, p. 262). A tertiary amine does not undergo reaction, since it does not have an active hydrogen.



Primary and secondary amines react with acetyl chloride to produce amides, which often precipitate from the solution (Experiment 6, p. 264). This reaction is usually accompanied by the evolution of heat. Tertiary amines do not react with acetyl chloride due to the lack of a hydrogen on the nitrogen.



The Hinsberg test (Experiment 19, p. 291) can be used to distinguish among primary, secondary, and tertiary amines. Benzenesulfonyl chloride undergoes reaction with primary amines in basic solution to form the sodium salts of the sulfonamide, which are soluble in the reaction mixture. Acidification of the reaction mixture results in the precipitation of the sulfonamides.

$$\underset{\text{1° amine}}{RNH_2} + \underset{\substack{\text{benzenesulfonyl}\\\text{chloride}}}{C_6H_5SO_2Cl} + 2NaOH \longrightarrow \underset{\text{(soluble)}}{C_6H_5SO_2NR^-Na^+} + NaCl + 2H_2O$$

$$\downarrow H^+$$

$$\underset{\substack{\text{sulfonamide}\\\text{(insoluble)}}}{C_6H_5SO_2NHR}$$

Secondary amines, when treated with benzenesulfonyl chloride, yield the sulfonamides, which precipitate from the solution. Acidification of the solution does not dissolve the sulfonamide.

$$\underset{\text{2° amine}}{R_2NH} + \underset{\substack{\text{benzenesulfonyl}\\\text{chloride}}}{C_6H_5SO_2Cl} + NaOH \longrightarrow \underset{\substack{\text{sulfonamide}\\\text{(insoluble)}}}{C_6H_5SO_2NR_2} + NaCl + H_2O$$

$$\downarrow H^+$$

No Reaction

Tertiary amines undergo reaction with benzenesulfonyl chloride to produce quaternary ammonium sulfonate salts, which yield sodium sulfonates and insoluble tertiary amines in basic solution. Acidification of the reaction mixture results in the formation of sulfonic acids and soluble amine salts.

$$\underset{\text{3° amine}}{R_3N} + \underset{\substack{\text{benzenesulfonyl}\\\text{chloride}}}{C_6H_5SO_2Cl} \longrightarrow C_6H_5SO_2\overset{+}{N}R_3Cl^- \xrightarrow{2NaOH}$$

$$\underset{\text{(soluble)}}{C_6H_5SO_3^-Na^+} + \underset{\text{(insoluble)}}{NR_3} + NaCl + H_2O$$

$$\downarrow 2HCl$$

$$C_6H_5SO_3H + \underset{\text{(soluble)}}{R_3\overset{+}{N}HCl^-} + 2NaCl$$

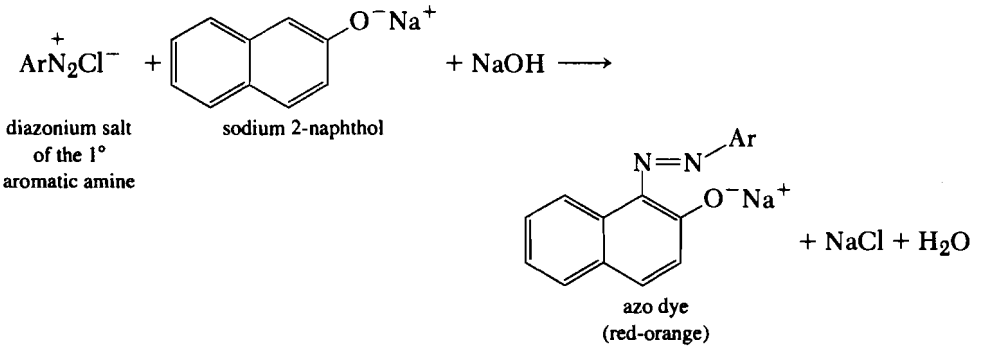
The reaction of amines with nitrous acid (Experiment 20, p. 294) classifies the amine not only as primary, secondary, or tertiary, but also as aliphatic or aromatic. Primary aromatic and aliphatic amines react with nitrous acid to form an intermediate diazonium salt. The aliphatic diazonium salts decompose spontaneously by rapid loss of nitrogen, particularly when the original amino group is attached to a secondary or tertiary carbon. Most aromatic diazonium salts are stable at 0°C but lose nitrogen slowly on warming to room temperature.

$$\underset{\substack{\text{1° aliphatic}\\\text{amine}}}{RNH_2} + \underset{\substack{\text{nitrous}\\\text{acid}}}{HONO} + 2HCl \longrightarrow \underset{\substack{\text{diazonium salt}\\\text{(unstable at 0°)}}}{[\overset{+}{R}N_2Cl^-]} \xrightarrow[\text{spontaneous}]{H_2O}$$

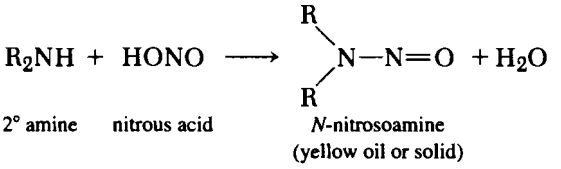
$$N_2(g) + ROH + RCl + ROR + \text{alkene}$$

$$\underset{\substack{\text{1° aromatic}\\\text{amine}}}{ArNH_2} + \underset{\substack{\text{nitrous}\\\text{acid}}}{HONO} + HCl \longrightarrow \underset{\substack{\text{diazonium salt}\\\text{(stable at 0°C)}}}{\overset{+}{A}rN_2Cl^-} \xrightarrow{H_2O} N_2(g) + ArOH + HCl$$

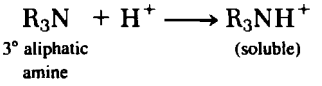
The diazonium salt of the primary aromatic amine reacts with sodium 2-naphthol to produce a red-orange azo dye.



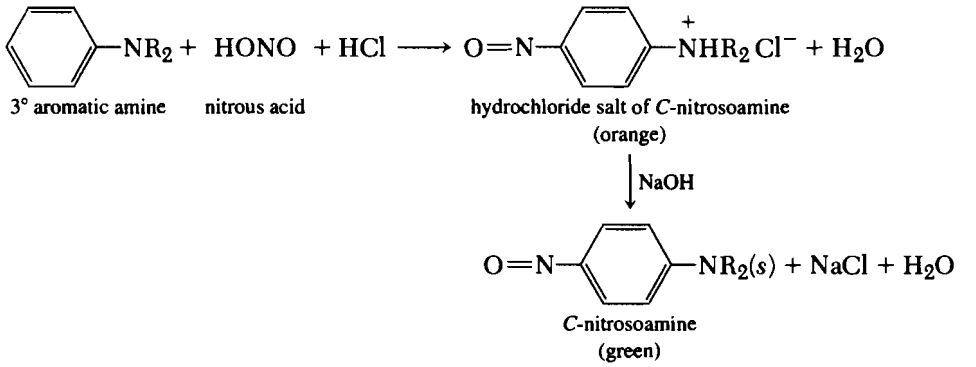
Secondary amines undergo a reaction with nitrous acid to form *N*-nitrosoamines, which are usually yellow solids.



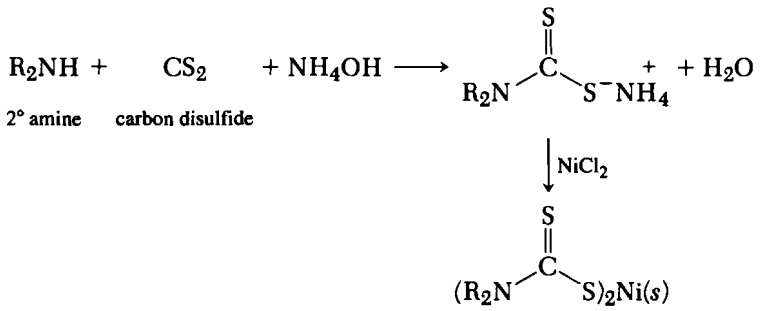
Tertiary aliphatic amines do not react with nitrous acid, but they form a soluble salt. The reaction mixture gives an immediate positive test on the starch–iodide paper for nitrous acid.



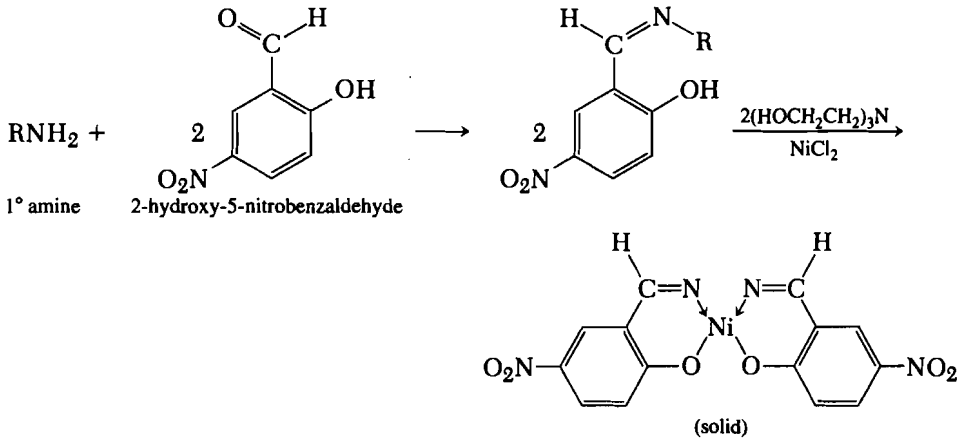
Tertiary aromatic amines react with nitrous acid to form the orange-colored hydrochloride salt of the *C*-nitrosoamine. Treating the solution with base liberates the blue or green *C*-nitrosoamine.



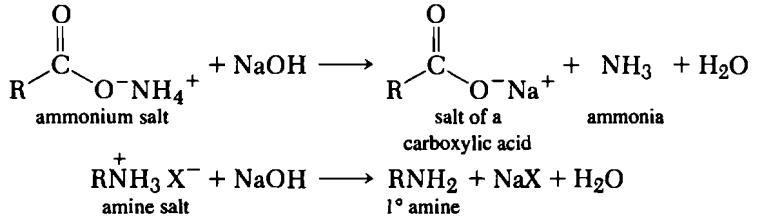
Secondary amines combine with carbon disulfide and ammonium hydroxide, followed by nickel chloride, to produce a solid product (Experiment 21, p. 300).



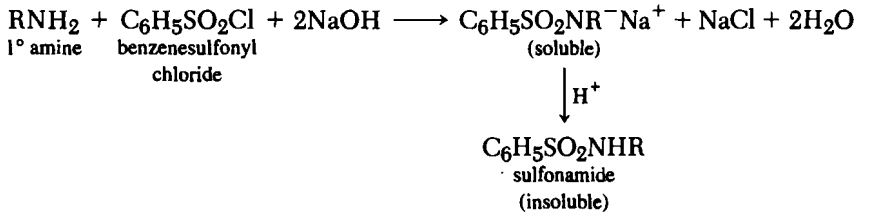
Primary aliphatic amines react quickly with 2-hydroxy-5-nitrobenzaldehyde, followed by nickel chloride, to form a precipitate within several minutes (Experiment 22, p. 301).

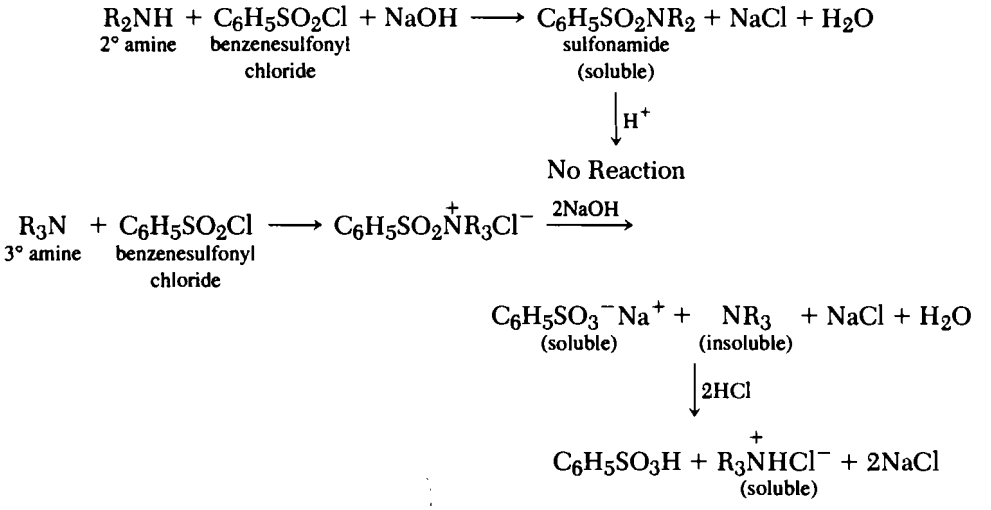


Amine salts can be detected by treating the salt with sodium hydroxide to liberate the ammonia or amine (Experiment 23, p. 302).



Experiment 19 Benzenesulfonyl Chloride (Hinsberg's Method for Characterizing Primary, Secondary, and Tertiary Amines)





To 0.3 mL or 300 mg of the unknown sample in a test tube, add 5 mL of 10% sodium hydroxide solution and 0.4 mL of benzenesulfonyl chloride. Stopper the test tube, and shake the mixture very vigorously. Test the solution to make sure that it is alkaline. After all the benzenesulfonyl chloride has reacted, cool the solution and separate the residue, if present, from the solution. Test the residue for solubility in 10% hydrochloric acid. If no residue remains, then treat the solution with 10% hydrochloric acid and observe whether a precipitate forms.

If all of the original compound dissolves in the base, no residue remains, and acidification produces a precipitate, the original unknown is a primary amine. Primary amines react with benzenesulfonyl chloride in basic solution to form the sodium salt of the sulfonamide, which is normally soluble in basic solution, but the sulfonamide precipitates upon acidification.

If a residue is formed and it is insoluble in acid, the original unknown is a secondary amine. Secondary amines undergo reaction with benzenesulfonyl chloride to precipitate the sulfonamide, and acidification does not result in any change.

If a residue is present that is soluble in acid, it indicates that the residue is the unreacted tertiary amine. Tertiary amines undergo reaction with benzenesulfonyl chloride to produce quaternary ammonium sulfonate salts, which yield sodium sulfonates and water-insoluble tertiary amines in basic solution. Acidification of the reaction mixture results in the formation of sulfonic acids and water-soluble amine salts. Any solid that is formed should be isolated and purified, and its melting point should be compared against the original amine.

If the amount of the solid is in sufficient quantity, it may be saved and used as a derivative for that unknown.

Controls Aniline, *N*-methylaniline, and *N*,*N*-dimethylaniline will give a positive test. Make note of all precipitate formation and dissolution and use melting points to check the identity of the compound as an amine or a sulfonamide.

Cleaning Up Isolate any solid by filtration and place in the organic nonhazardous solid waste container. If the original compound is identified as a primary or secondary amine, then dilute the solution with water and place in the aqueous solution container. If the unknown is a tertiary amine, then make the solution basic with 10% sodium

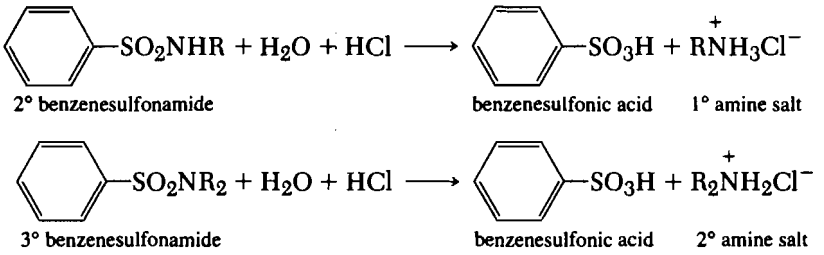
hydroxide and extract the amine with petroleum ether. Place the organic layer in the organic solvents container, and place the aqueous layer in the aqueous solution container.

Discussion

The sodium salts of certain sulfonamides of cyclohexyl through cyclodecylamine and certain high-molecular-weight amines are insoluble in 10% sodium hydroxide solution.[17] Usually they are soluble in water. Certain primary amines may yield alkali-insoluble disulfonyl derivatives. These may be hydrolyzed by boiling for 30 min with 5% sodium ethoxide in absolute ethanol.

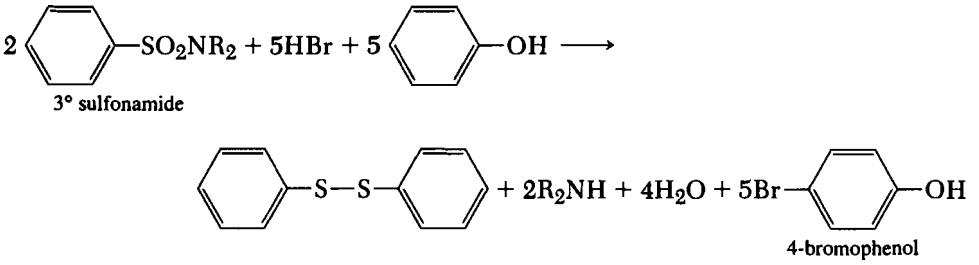
If the solution heats up considerably, cool it. Certain *N,N*-dialkylanilines produce a purple dye if the mixture becomes too hot. This may be prevented by carrying out the reaction at 15–20°C.

When the Hinsberg method is used to separate a mixture of amines, it is necessary to recover the pure individual amines. The benzenesulfonamides may be hydrolyzed as follows:



To hydrolyze the sulfonamide, heat 1.0 g of the sulfonamide with 10 mL of 25% hydrochloric acid under reflux. Sulfonamides of primary amines require 24–36 hr refluxing, whereas sulfonamides of secondary amines may be hydrolyzed in 10–12 hr. After the reaction is complete, cool the mixture, make it alkaline with 20% sodium hydroxide solution, and extract with three 5-mL portions of ether. Dry the ether, and remove the ether by distillation. Distill the resulting amine. With certain low- or high-boiling amines, recover the amine as the hydrochloride salt by passing dry hydrogen chloride gas through the dry ether solution.

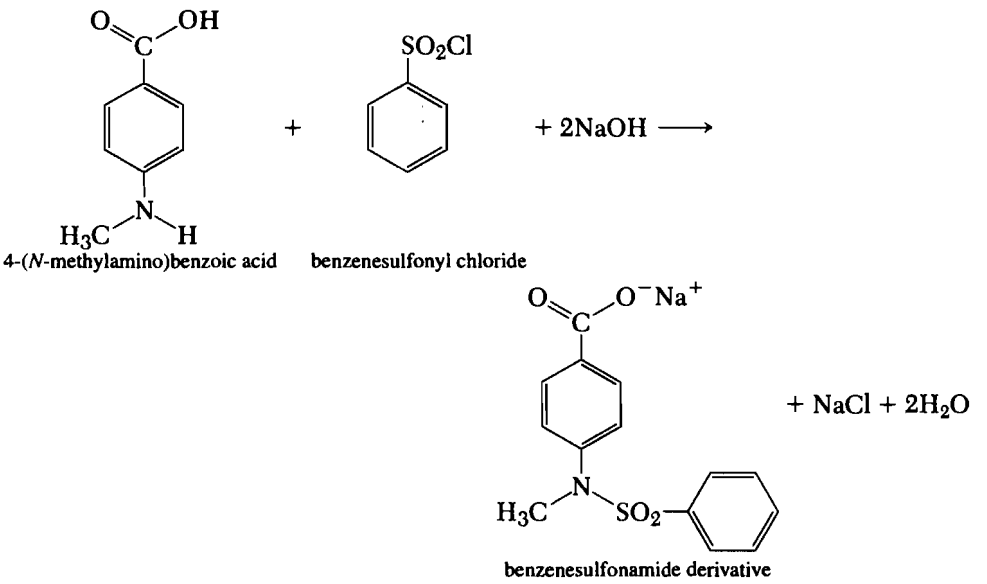
Many sulfonamides are hydrolyzed only with great difficulty; a more satisfactory procedure involves 48% hydrobromic acid and phenol.[18] Instead of a simple hydrolysis, this reaction is a reductive cleavage in which the hydrogen bromide is oxidized to bromine and the sulfonamide reduced to the disulfide. The primary purpose of the phenol is to remove the bromine by the formation of 4-bromophenol.



[17]P. E. Fanta and C. S. Wang, *J. Chem. Educ.*, *41*, 280 (1964). Certain primary amines may yield alkali-insoluble disulfonyl derivatives. These may be hydrolyzed by boiling for 30 min with 5% sodium ethoxide in absolute ethanol.

[18]H. R. Synder and R. E. Heckert, *J. Amer. Chem. Soc.*, *74*, 2006 (1952); H. R. Synder and H. C. Geller, *J. Amer. Chem. Soc.*, *74*, 4864 (1952).

Arylsulfonyl chlorides can be useful in characterizing primary and secondary amines. The Hinsberg method for separating amines is based on the fact that the sulfonamides of primary amines are soluble in alkali whereas those of secondary amines are not. Since tertiary amines do not give amides, the method provides a means of classifying and separating the three types of amines. However, the results of the Hinsberg test must not be used alone in classifying amines. The solubility of the original compound must also be considered. If the original compound is amphoteric, which means that it is soluble in both acids and alkalies, the Hinsberg method fails to distinguish among the types of amines. For example, 4-(*N*-methylamino)benzoic acid undergoes reaction with benzenesulfonyl chloride and alkali to give a *solution* of the sodium salt of the *N*-benzenesulfonyl derivative.



4-(*N*-methylamino)benzoic acid benzenesulfonyl chloride benzenesulfonamide derivative

Acidification of the solution precipitates the free acid. This observation, taken by itself, would incorrectly identify the original compound as a primary amine rather than a secondary amine.

Problem

17. Using the Hinsberg test and equations, show how propyl amine, diethylamine, and triethylamine can be separated.

Experiment 20 Nitrous Acid

(a) Diazotization

$$\underset{\text{sodium nitrite}}{NaNO_2} + HCl \longrightarrow \underset{\text{nitrous acid}}{HONO} + NaCl$$

$$\underset{\substack{1^\circ \text{ aliphatic} \\ \text{amine}}}{RNH_2} + \underset{\substack{\text{nitrous} \\ \text{acid}}}{HONO} + 2HCl \longrightarrow \underset{\substack{\text{diazonium salt} \\ \text{(unstable at 0°)}}}{[R\overset{+}{N}_2Cl^-]} \xrightarrow[\text{spontaneous}]{H_2O} N_2(g) + ROH + RCl + ROR + \text{alkene}$$

$$\underset{\substack{1^\circ \text{ aromatic}\\ \text{amine}}}{ArNH_2} + \underset{\substack{\text{nitrous}\\ \text{acid}}}{HONO} + HCl \longrightarrow \underset{\substack{\text{diazonium salt}\\ \text{(stable at 0°C)}}}{ArN_2^+Cl^-} \xrightarrow{H_2O} N_2(g) + ArOH + HCl$$

Dissolve 0.5 mL or 0.5 g of the sample in 1.5 mL of concentrated hydrochloric acid diluted with 2.5 mL of water, and cool the solution to 0°C in a beaker of ice. Dissolve 0.5 g of sodium nitrite in 2.5 mL of water, and add the solution dropwise, with shaking, to the cold solution of the amine hydrochloride. Continue the addition until the mixture gives a positive test for nitrous acid. Perform the test by placing a drop of the solution on starch–iodide paper; a blue color indicates the presence of nitrous acid. If the test is positive, move 2 mL of the solution to another test tube, warm gently, and examine for evolution of gas.

The observation of rapid bubbling or foaming as the aqueous sodium nitrite solution is added at 0°C indicates the presence of a primary aliphatic amine. The evolution of gas upon warming indicates that the amine is a primary aromatic amine, and the solution should be subjected to the coupling reaction (b).

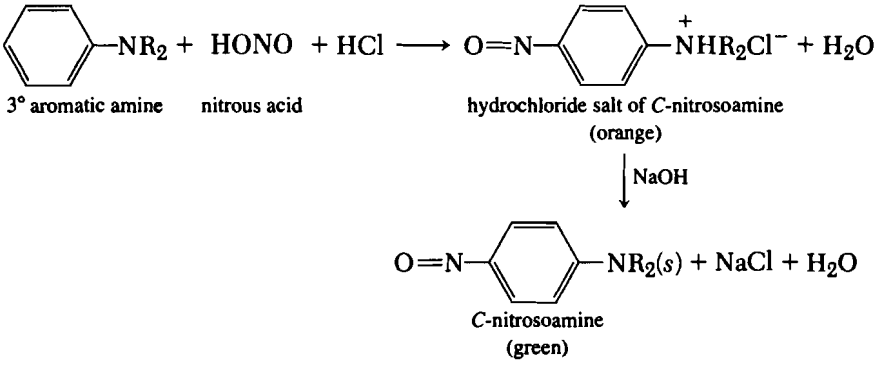
If a pale yellow oil or low-melting solid, which is the *N*-nitrosoamine, is formed with no evolution of gas, the original amine is a secondary amine. The oil or solid is isolated and treated under conditions of the Liebermann nitroso reaction (c) to provide confirmation of the presence of the *N*-nitrosoamine.

$$\underset{\substack{2^\circ \text{ amine}}}{R_2NH} + \underset{\substack{\text{nitrous acid}}}{HONO} \longrightarrow \underset{\substack{N\text{-nitrosoamine}\\ \text{(yellow oil or solid)}}}{\begin{matrix} R \\ \diagdown \\ N{-}N{=}O \\ \diagup \\ R \end{matrix}} + H_2O$$

An immediate positive test for nitrous acid with no evolution of gas indicates the presence of a tertiary aliphatic amine. The tertiary aliphatic amine is simply protonated to form a soluble salt under these conditions and does not react with the nitrous acid.

$$\underset{\substack{3^\circ \text{ aliphatic}\\ \text{amine}}}{R_3N} + H^+ \longrightarrow \underset{\text{(soluble)}}{R_3NH^+}$$

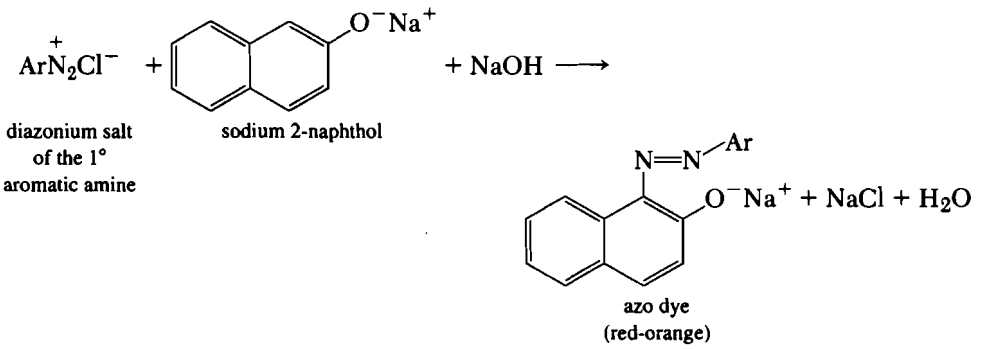
The reaction of a tertiary aromatic amine (an aniline) with nitrous acid produces a dark-orange solution or an orange crystalline solid, which is the hydrochloride salt of the *C*-nitrosoamine. Treating 2 mL of the solution with 10% sodium hydroxide or sodium carbonate solution will produce the bright-green or -blue nitrosoamine base. The nitrosoamine base can be isolated, purified, and characterized.



Cleaning Up If the compound is identified as a primary aromatic amine, then dilute the solution with 10 mL of water and then pass through 5 g of charcoal. Place the char-

coal in the nonhazardous waste container and place the aqueous solution in the aqueous solution container. If the unknown is identified as a primary aliphatic amine or tertiary aliphatic amine, dilute the solution with water and place in the aqueous solution container. For secondary amines and tertiary aromatic amines, isolate the nitrosoamines by filtration and place in the hazardous solid waste container. Neutralize the filtrates with 10% sodium hydroxide and place in the aqueous solution container.

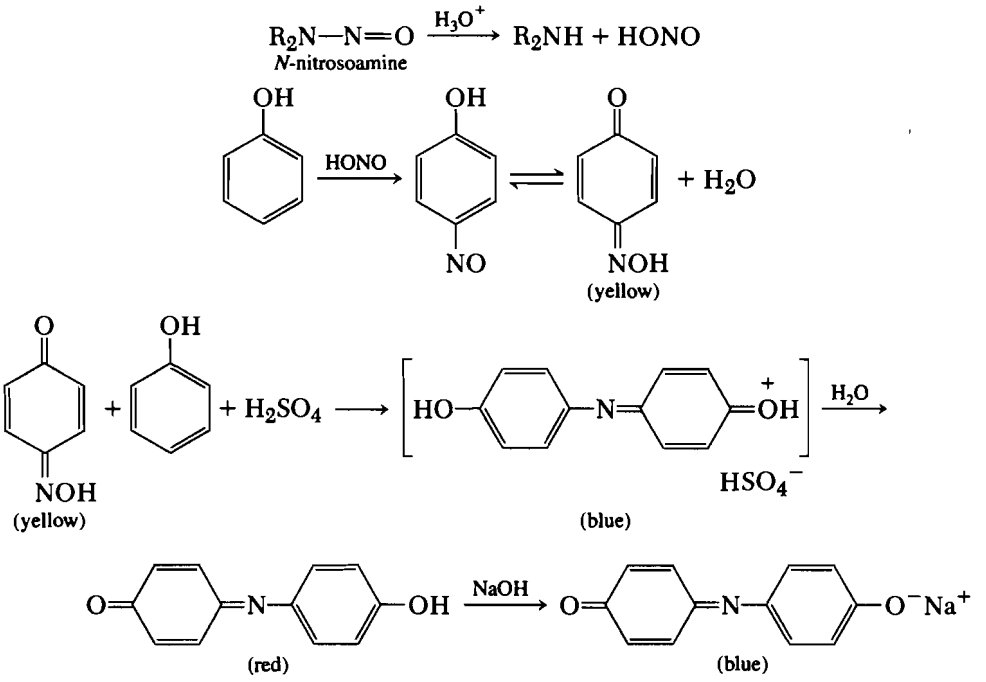
(b) Coupling



Add 2 mL of the cold diazonium solution to a solution of 0.1 g of 2-naphthol in 2 mL of 10% sodium hydroxide solution and 5 mL of water. The formation of the orange-red dye, with the evolution of gas only upon warming as noted in (a), indicates the original compound is a primary aromatic amine.

Cleaning Up Separate any solids by filtration and place in the organic nonhazardous solid waste container. Place the remaining liquid in the aqueous solution container.

(c) Liebermann's Nitroso Reaction



Add 0.05 g of the *N*-nitrosoamine, 0.05 g of phenol, and 2 mL of concentrated sulfuric acid to a test tube and warm gently for 20 sec. Cool the solution slightly. A blue color should develop, which changes to red when the solution is poured into 20 mL of ice water. Add 10% sodium hydroxide until the mixture is alkaline, and the blue color is produced again.

The *N*-nitrosoamine liberates nitrous acid in the presence of sulfuric acid. The nitrous acid then undergoes reaction with phenol to yield the yellow 4-nitrosophenol (quinone monoxime). The blue color observed in this reaction is due to phenolindophenol formed from the reaction of the initially produced 4-nitrosophenol (quinone monoxime) with excess phenol. This reaction is characteristic of phenols in which an *ortho* or *para* position is unsubstituted.

To run a comparative test in order to check the colors, the following procedure may be done. Add a crystal of sodium nitrite to 2 mL of concentrated sulfuric acid, and shake until dissolved. Add 0.1 g of phenol, and a blue color will appear. The solution is poured into 20 mL of ice water, and the color of the solution changes to red. Addition of 10% sodium hydroxide, until the mixture is alkaline, results in the return of the blue color.

Controls Aniline, *N*-methylaniline, triethylamine, and *N*,*N*-dimethylaniline will give a positive test for (a). The diazonium salt of aniline is then subjected to (b). The *N*-nitrosoamine of *N*-methylaniline is then subjected to (c). Acetophenone will give a negative test.

Cleaning Up If necessary, make the solution basic with 10% sodium hydroxide. Place the mixture in the aqueous solution container.

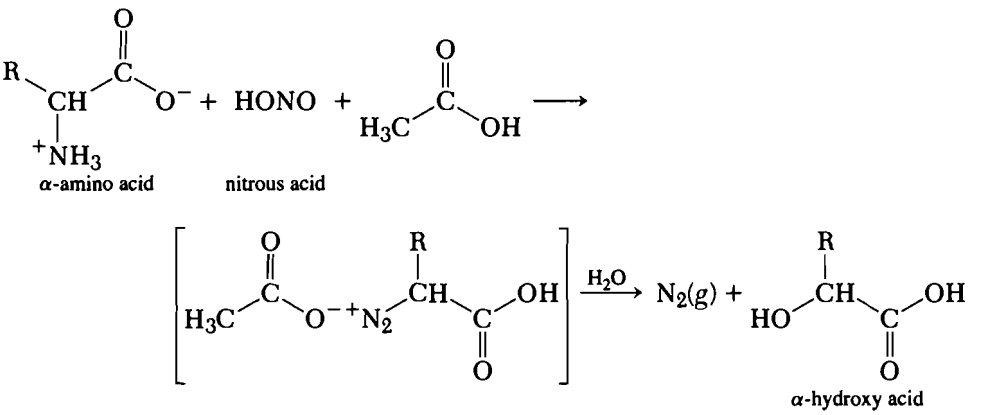
(d) Test for Phenols

To test for the presence of a phenol, a modification of Liebermann's test is used. Add a crystal of sodium nitrite to 2 mL of concentrated sulfuric acid, and shake until dissolved. Add 0.1 g of the unknown. A blue color indicates the presence of a phenol. Another indication of the presence of the phenol is the change of color of the solution to red when it is poured into 20 mL of ice water and the return of the blue color when the mixture becomes alkaline after the addition of 10% sodium hydroxide solution.

Controls Phenol will give a positive test. Acetone will give a negative test.

Cleaning Up Place the basic aqueous layer in the aqueous solution container.

(e) Test for α-Amino Acids



The procedure in (a) should be followed, except substitute acetic acid for hydrochloric acid. A positive test is the evolution of nitrogen gas. The α-amino acid reacts with the nitrous acid to form an intermediate, which decomposes to nitrogen gas and an α-hydroxy acid.

Controls Glycine will give a positive test. Acetone will give a negative test.

Cleaning Up Make the solution alkaline with 10% sodium hydroxide and place in the aqueous solution container.

Discussion

Reaction of Primary Amines Both aliphatic and aromatic primary amines react with nitrous acid to initially give the corresponding diazonium ions. The aliphatic diazonium compounds are so unstable that their existence has not been directly detected. Nitrogen gas, alcohol, olefin, and products of other displacement and carbocation reactions are formed.

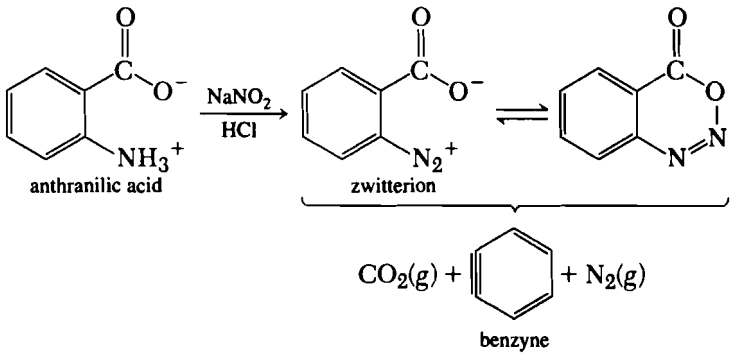
Aromatic diazonium salts, on the other hand, are generally stable in solution at 0°C. When heated in aqueous solution, they quickly lose nitrogen to give the aryl cation, Ar^+. This ion reacts rapidly with water to give phenol.

$$\underset{\substack{1^\circ \text{ aromatic}\\ \text{amine}}}{ArNH_2} + \underset{\substack{\text{nitrous}\\ \text{acid}}}{HONO} + HCl \longrightarrow \underset{\substack{\text{diazonium salt}\\ \text{(stable at 0°C)}}}{ArN_2^+Cl^-} \xrightarrow{H_2O} N_2(g) + ArOH + HCl$$

If allowed to dry, these compounds can be an explosion hazard, so the aryldiazonium ions should be used immediately upon preparation.

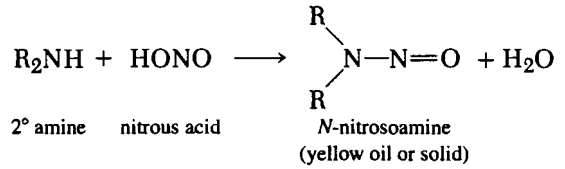
The coupling reaction between certain diazonium salts and phenols has been shown to involve reaction between diazonium ion and phenoxide ion.[19] If the solution is too acidic, the phenoxide ion is converted to phenol, and thus reaction is retarded; if the solution is too basic, the diazonium ion reacts with hydroxide ion to give diazotate, ArN_2O^-, which does not couple. The solution must, therefore, be properly buffered for a satisfactory coupling reaction.

The diazotization of anthranilic acid produces a zwitterion or a cyclic acyl diazotate. This compound is unstable and loses carbon dioxide and nitrogen to form a highly reactive benzyne intermediate. The reactive benzyne combines with ethanol to form phenetole, with diethyl maleate to form a substituted benzocyclobutene, and with anthracene to form triptycene. The best yields of products are obtained by carrying out the diazotization with amyl nitrite and the displacement reaction in an aprotic solvent such as methylene chloride, tetrahydrofuran, or acetonitrile. Again, the diazonium ion intermediate should be handled with care as it is an explosion hazard.

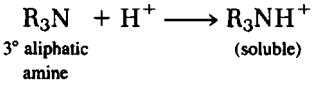


[19]C. K. Ingold, *Structure and Mechanism in Organic Chemistry*, 2nd ed. (Cornell University Press, Ithaca, NY, 1967), p. 387. See also N. A. Figero, *J. Chem. Educ.*, *43*, 142 (1966).

Reaction with Secondary Amines Both aliphatic and aromatic secondary amines react with nitrous acid to form *N*-nitroso compounds, commonly called nitrosoamines. ***Caution:*** *Many of these compounds are carcinogenic and should be handled carefully.* They are pale yellow oils or solids.

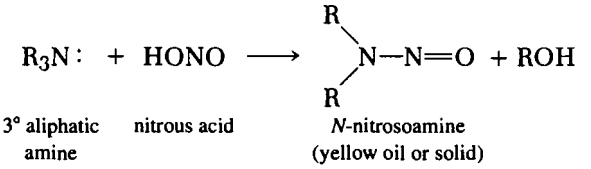


Reaction with Tertiary Amines The chemistry of the reaction of tertiary amines is quite complex.[20] Under certain conditions, it may appear that tertiary amines undergo no reaction; this is actually true only at low pH, low temperature, and dilute conditions. The amine is simply protonated to form salts under these mild conditions.

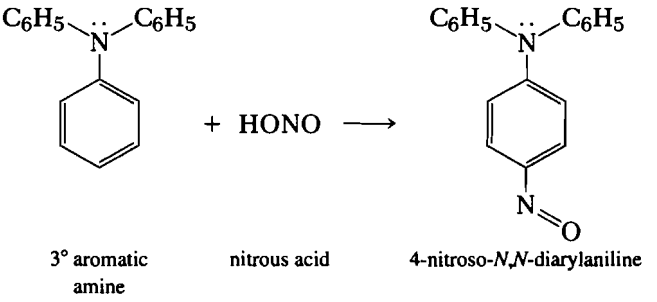


These salts can be recognized by their reaction with base to regenerate the original amine.

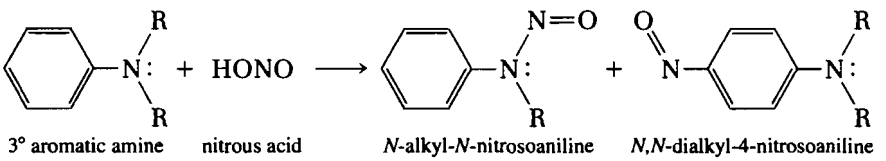
Under higher temperatures, less acidic conditions, and other conditions, a variety of reactions occur when tertiary amines are treated with nitrous acid. For aliphatic amines, *N*-nitrosoamines are formed.



For aromatic amines, *N*,*N*-diaryl-4-nitrosoanilines are produced.

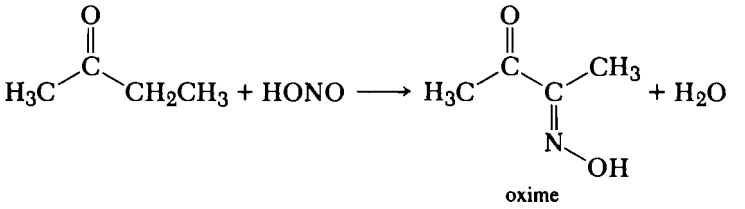


N-Alkyl-*N*-nitrosoanilines and *N*,*N*-dialkyl-4-nitrosoanilines are produced from alkylarylamines.



[20]G. E. Hein, *J. Chem. Educ.*, *40*, 181 (1963).

Although nitrous acid is useful for characterizing amines, other functional groups also react. A methylene group adjacent to a keto group is converted to an oximino group,[21] and alkyl mercaptans yield red *S*-alkyl thionitrites.

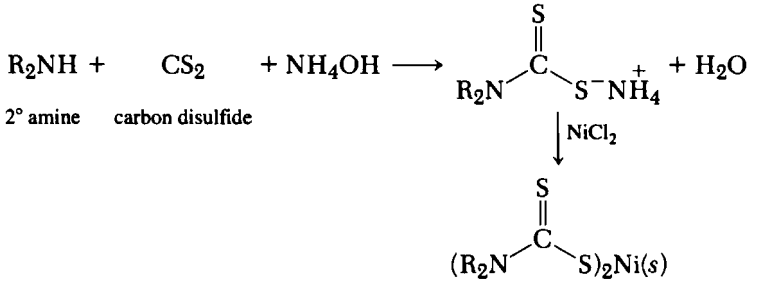


$$RCH_2SH + HONO \longrightarrow \underset{\substack{S\text{-alkyl thionitrite}\\(red)}}{RCH_2{-}S{-}N{=}O} + H_2O$$

Problem

18. Give the equations for the reaction of nitrous acid with propylamine, diethylamine, triethylamine, aniline, *N*-methylaniline, and *N*,*N*-dimethylaniline.

Experiment 21 Nickel Chloride, Carbon Disulfide, and Ammonium Hydroxide—Test for Secondary Aliphatic Amines



Prepare an aqueous solution of the unknown by adding one or two drops or 50 mg of the unknown to 5 mL of water. If necessary, add one or two drops of concentrated hydrochloric acid to dissolve the amine. Add 0.5–1 mL of concentrated ammonium hydroxide to 1 mL of the nickel chloride in carbon disulfide reagent in a test tube, followed by 0.5–1 mL of the amine solution. A definite precipitation indicates that the unknown is a secondary amine. A slight turbidity is an indication of a trace of a secondary amine as an impurity.

Controls *N*-Methylaniline will give a positive test. Aniline and triethylamine will give a negative test.

Nickel Chloride in Carbon Disulfide Reagent

Add an amount of carbon disulfide to 0.5 g of nickel chloride hexahydrate in 100 mL of water so that after the mixture has been shaken, a globule of carbon disulfide is left on the bottom of the bottle. If stored in a tightly stoppered bottle, the reagent is stable for long periods of time. When the undissolved carbon disulfide evaporates, more must be added.

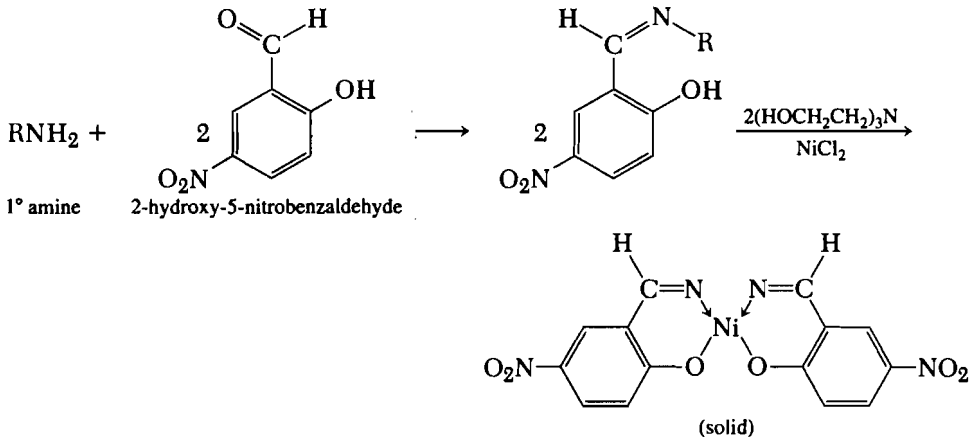
[21]W. L. Semon and V. R. Damrell, *Org. Syntheses Coll. Vol. II*, 204 (1943).

Cleaning Up Isolate the solid by suction filtration and place in the hazardous solid waste container. Place the liquid in the hazardous waste container.

Discussion

This test is given by all secondary amines but not by primary amines. *It is very sensitive, and many commercial samples of tertiary amines produce turbidity because of the presence of small amounts of secondary amines.* This is true of substituted pyridines, quinolines, and isoquinolines separated from coal-tar distillates.

Experiment 22 Nickel Chloride and 2-Hydroxy-5-Nitrobenzaldehyde—Test for Primary Amines



Add one or two drops or 50 mg of the compound to be tested to 5 mL of water. If necessary, add one or two drops of concentrated hydrochloric acid to dissolve the compound. Add 0.5 mL of the amine solution to 3 mL of the nickel chloride and 2-hydroxy-5-nitrobenzaldehyde reagent. An immediate, copious precipitate is produced by primary aliphatic amines, whereas primary aromatic amines usually require 2–3 min to give a definite precipitate. The appearance of a slight turbidity is not a positive test; it indicates that traces of primary amines may be present as impurities.

Controls Butylamine and aniline will give a positive test. Diethylamine and *N,N*-dimethylaniline will give a negative test.

Nickel Chloride and 2-Hydroxy-5-Nitrobenzaldehyde Reagent

Add a solution of 0.5 g of 2-hydroxy-5-nitrobenzaldehyde dissolved in 25 mL of water to 15 mL of triethanolamine. Then add 0.5 g of nickel chloride hexahydrate dissolved in 10 mL of water, and bring the total volume of the solution to 100 mL. If the triethanolamine contains ethanolamine, it may be necessary to add another 0.5 g of the aldehyde and remove the resulting precipitate by filtration.

Cleaning Up Isolate the solid by suction filtration and place in the hazardous solid waste container. Place the liquid in the hazardous waste container.

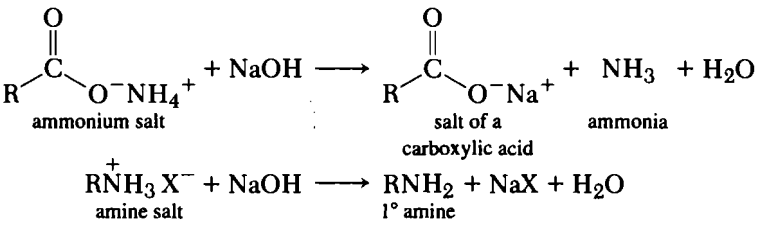
Discussion

This test is so sensitive that care must be taken in interpreting it. Only a definite precipitate produced in considerable quantity indicates a primary amine; a slight turbidity

is merely indicative of impurities. Care must be taken to use the amounts specified above since the addition of large amounts of solutions of secondary amines will also give a precipitate. Many commercial samples of secondary and tertiary amines contain traces of primary amines and produce a turbidity.

The test is given by all primary amines capable of forming the Schiff base with 2-hydroxy-5-nitrobenzaldehyde. Hydroxylamine and hydrazines substituted on only one nitrogen atom give positive tests. Amides do not give a precipitate. The test is not applicable to amino acids.

Experiment 23 Sodium Hydroxide Treatment of Ammonium Salts and Amine Salts



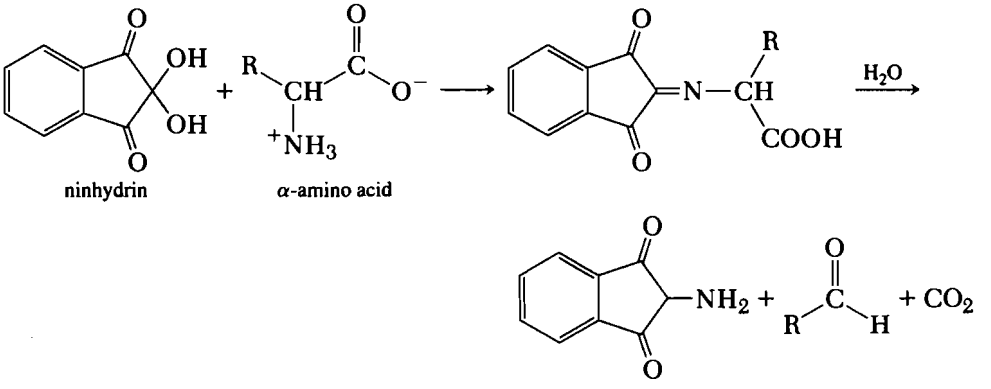
Place 5 mL of 10% sodium hydroxide solution in a test tube, add 0.2–0.4 g of the compound, and shake the mixture vigorously. Note the odor of ammonia or the formation of an oily layer of the amine. Moistened pink litmus paper placed in the vapor above the solution will turn blue if ammonia or a volatile amine is present.

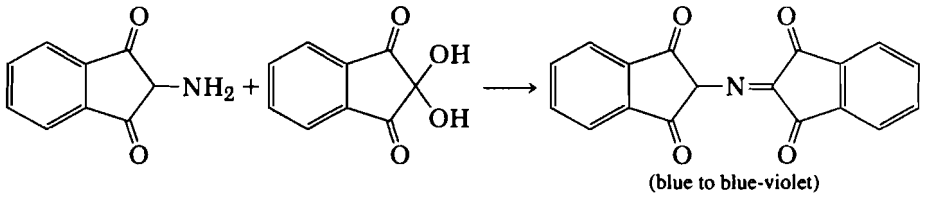
Controls Ammonium benzoate will give a positive test. Hexane will give a negative test.

Cleaning Up Separate any amine layer and place into the organic solvent container. Place the aqueous layer in the aqueous solution container.

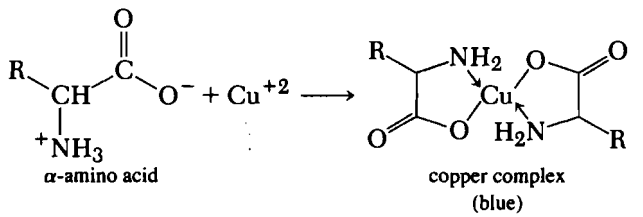
▶ 9.7 AMINO ACIDS

The ninhydrin test (Experiment 24, p. 303) is the chemical basis for the amino acid analyzer, and it can be used to distinguish between different types of amino acids. α-Amino acids and β-amino acids react with ninhydrin to give a positive test, which is a blue to blue-violet color.

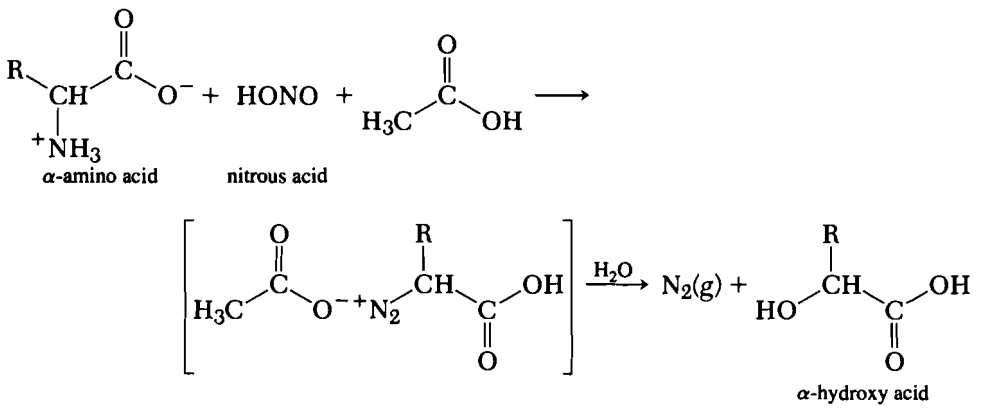




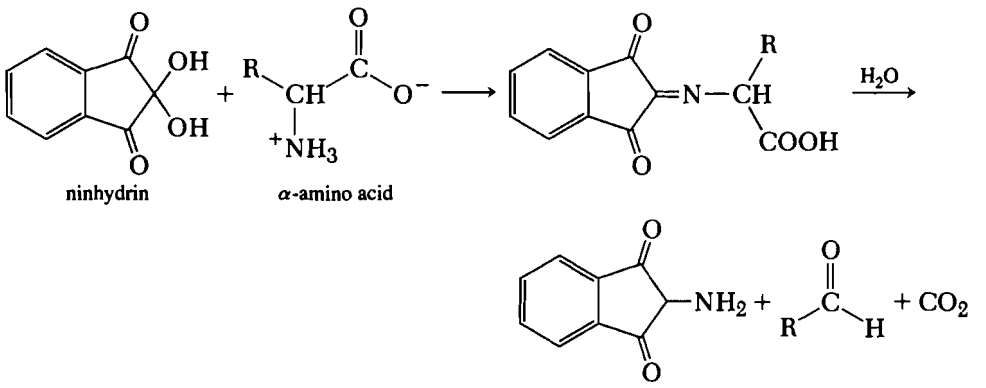
Copper complexes are formed from the reaction of α-amino acids with copper sulfate (Experiment 25, p. 304). A deep-blue color is produced, indicating the presence of the copper complex.

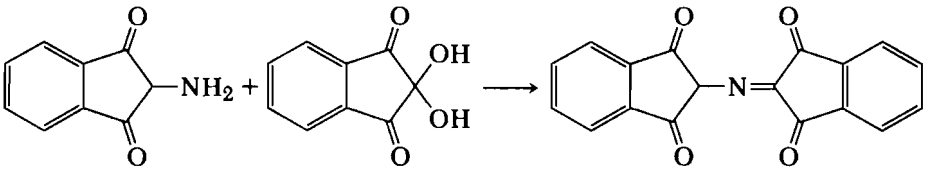


α-Amino acids combine with nitrous acid to produce an intermediate, which decomposes to form nitrogen gas and an α-hydroxy acid (Experiment 20e, p. 297).



Experiment 24 Ninhydrin Test





(blue to blue-violet)

Add 2 mg of the sample to 1 mL of a solution of 0.2 g of ninhydrin (1,2,3-indanetrione monohydrate) in 50 mL of water. Heat the test mixture to boiling for 15–20 sec. A blue to blue-violet color is given by α-amino acids and constitutes a positive test. Other colors (yellow, orange, red) are negative.

Controls Glycine and valine will give a positive test. Aniline and diethylamine will give a negative test.

Cleaning Up Place the mixture in the aqueous solution container.

Discussion

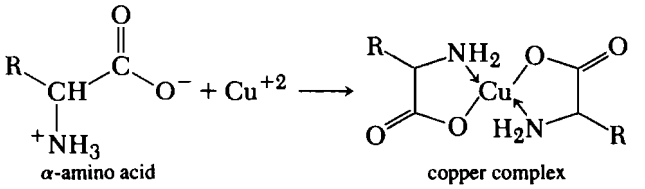
This reaction is important not only because it is a qualitative test but also because it is the source of the absorbing material that can be measured quantitatively by an automatic amino acid analyzer. This color reaction is also used to detect the presence and position of amino acids after paper chromatographic separation.

Proline, hydroxyproline, and 2-, 3-, and 4-aminobenzoic acids fail to give a blue color but produce a yellow color instead. Ammonium salts give a positive test. Some amines, such as aniline, yield orange to red colors, which is a negative test.

Problem

19. Give another name for ninhydrin.

Experiment 25 Copper Complex[22] Formation



α-amino acid

copper complex
(blue)

Dissolve a small amount of the compound in 1 mL of water. Add two drops of 1 M copper(II) sulfate. If a blue color is not formed immediately, then heat the test tube in a hot-water bath for 5 min. A moderate- to deep-blue liquid or a dark-blue solid is a positive test.

Controls Alanine, tyrosine, and lysine will give a positive test. Sucrose, aniline, and triethylamine will give a negative test.

[22]B. S. Furniss, A. J. Hannaford, P. W. G. Smith, and A. R. Tatchell, *Vogel's Textbook of Practical Organic Chemistry*, 5th ed. (Wiley, New York, 1991), p. 1230.

Cleaning Up Place the test solution in the aqueous solution container.

Discussion

Some α-amino acids are not very soluble in cold water. However, these amino acids are soluble in hot water and will give a positive test when the solution is heated. Aliphatic amines yield a blue precipitate. Anilines give a brown or green color, but other aromatic amines produce a blue-purple color.

A variety of tests are available that are specific for some amino acids (Table 9.4).

TABLE 9.4 Chemical Tests[a] for Amino Acids

Amino Acid Detected	Name of Reaction	Reagents	Color
Arginine	Sakaguchi reaction	α-Naphthol and sodium hypochlorite	Red
Cysteine	Nitroprusside reaction	Sodium nitroprusside in dil. NH_3	Red
Cysteine	Sullivan reaction	Sodium 1,2-naphthoquinone-4-sulfonate and sodium hydrosulfite	Red
Histidine, tyrosine	Pauly reaction	Diazotized sulfanilic acid in alkaline solution	Red
Tryptophan	Ehrlich reaction	*p*-Dimethylaminobenzaldehyde in conc. HCl	Blue
Tryptophan	Glyoxylic acid reaction (Hopkins–Cole reaction)	Glyoxylic acid in conc. H_2SO_4	Purple
Tyrosine	Folin–Ciocalteu reaction	Phosphomolybdotungstic acid	Blue
Tyrosine	Millon reaction	$HgNO_3$ in nitric acid with a trace of nitrous acid	Red
Tyrosine, tryptophan, phenylalanine	Xanthoproteic reaction	Boiling conc. nitric acid	Yellow

[a]A number of the experimental procedures for these tests are described in J. P. Greenstein and M. Winitz, *Chemistry of the Amino Acids* (Wiley, New York, 1961).

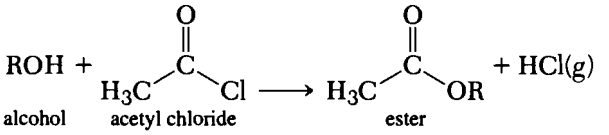
9.8 CARBOHYDRATES

Carbohydrates or polysaccharides are polyhydroxy aldehydes and ketones; within this broad category are simpler compounds called sugars. The word *carbohydrates* is derived historically from the idea "hydrates of carbon," that is, the general formula $C_n(H_2O)_n$; for example, glucose has the formula $C_6H_{12}O_6$. Sucrose (common table sugar) is consistent with another general formula, $C_n(H_2O)_m$, because it has the formula $C_{12}(H_2O)_{11}$. Carbohydrates do not have uniformly recognizable properties. These compounds are usually water-soluble solids that melt with decomposition; these characteristics correctly point toward the presence of a large number of highly polar functional groups in these molecules.

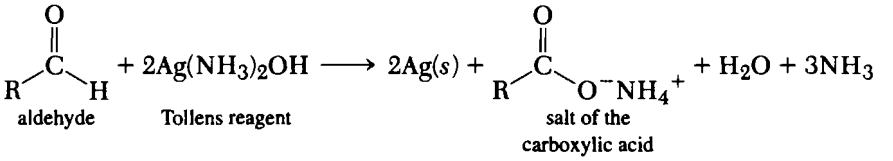
Sodium metal undergoes reaction with hydroxyl groups of many compounds to liberate hydrogen gas and form the salt of the alcohol (Experiment 5, p. 262).

$$\underset{\text{alcohol}}{2ROH} + 2Na \longrightarrow 2RO^-Na^+ + H_2(g)$$

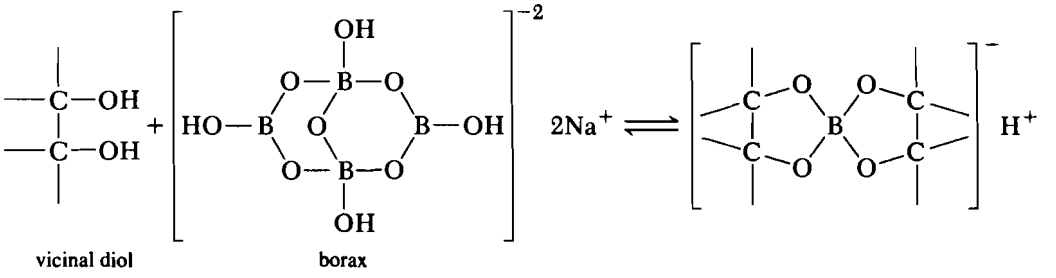
The presence of the hydroxyl group on a carbohydrate can be detected with acetyl chloride (Experiment 6, p. 264). The reaction of the hydroxyl group with the acetyl chloride yields an ester, which appears as another liquid layer.



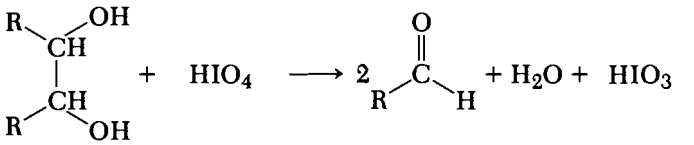
The Tollens test (Experiment 15, p. 283) can be used to test for the presence of the aldehyde group. The aldehyde functional group is oxidized to the salt of the carboxylic acid, with the silver ion being reduced to elemental silver, which is deposited as a coating inside the reaction flask.

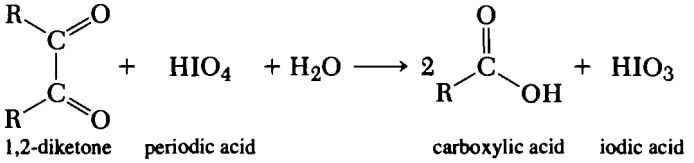


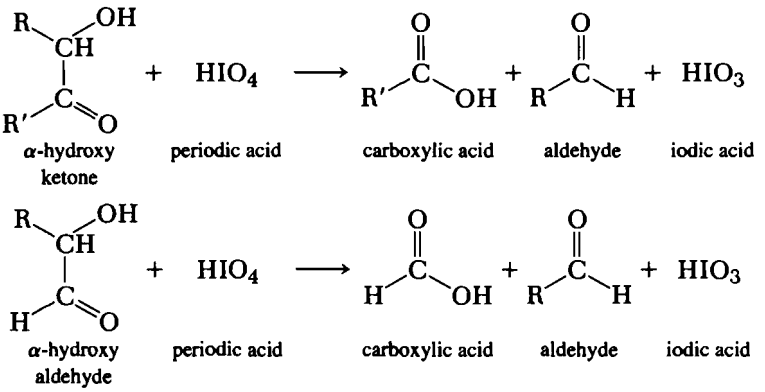
Vicinal diols can be detected with borax, sodium tetraborate decahydrate (Experiment 26, p. 308). Borax exists as $Na_2[B_4O_5(OH)_4] \cdot 8\ H_2O$. The resulting solution, with the addition of phenolphthalein indicator, is colorless at room temperature but yields a pink solution when warmed.



Vicinal diols, 1,2-diketones, α-hydroxy ketones, and α-hydroxy aldehydes are oxidized with periodic acid (Experiment 27, p. 308).



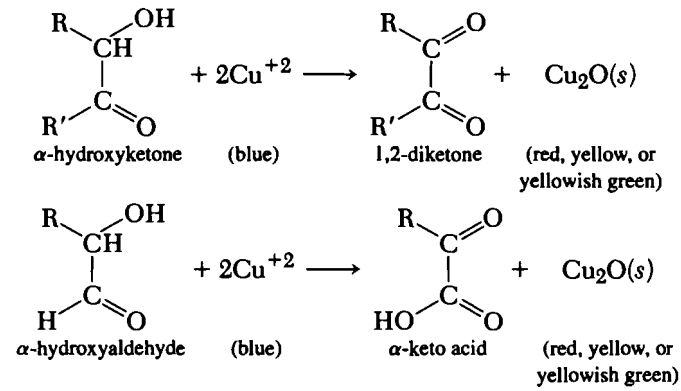




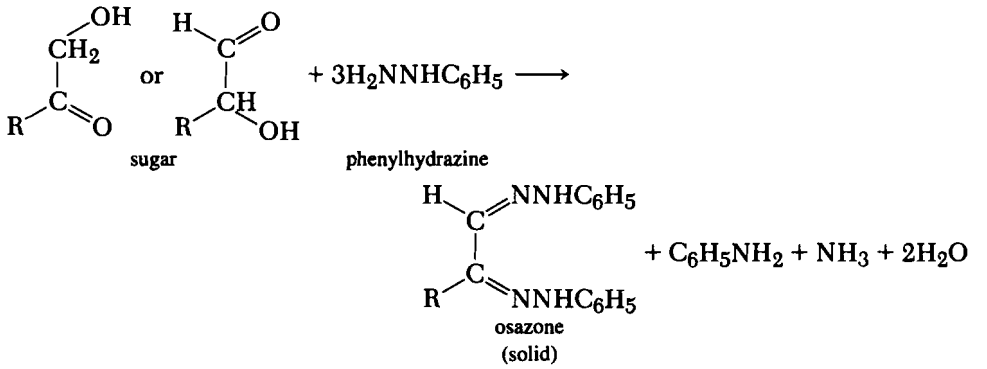
The iodic acid produced above is detected with 5% silver nitrate solution. An immediate precipitation of silver iodate occurs.

$$\underset{\text{iodic acid}}{HIO_3} + \underset{\text{silver nitrate}}{AgNO_3} \longrightarrow HNO_3 + \underset{\substack{\text{silver iodate}\\(\text{white})}}{AgIO_3(s)}$$

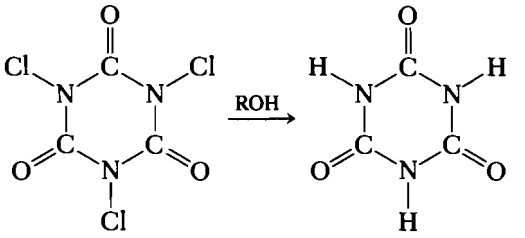
Benedict's solution (Experiment 28, p. 310) and Fehling's solution (Experiment 29, p. 311) will undergo reaction with reducing sugars such as α-hydroxy ketones and α-hydroxy aldehydes. The solution is initially a blue color from Cu^{+2} complex, but as the reaction proceeds, copper(I) oxide precipitates as a red, yellow, or yellowish-green solid.



The preparation of osazones (Experiment 30, p. 313) from sugars and phenylhydrazine along with the time required for the solid osazone to form can be used in distinguishing among the various sugars.

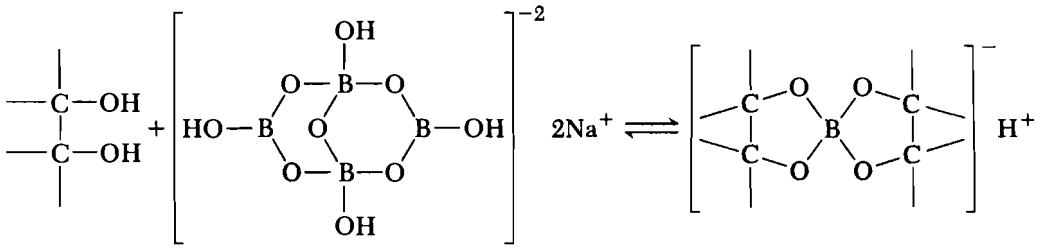


The TCICA test (Experiment 10, p. 271) can be used to detect sugars. The trichloroisocyanuric acid is reduced to cyanuric acid, a white solid. Sugars react in 1–5 min and cholesterol reacts in 10–40 sec.



trichloroisocyanuric acid — cyanuric acid (white solid)

Experiment 26 Borax Test



vicinal diol — borax

In a test tube, add a few drops of phenolphthalein to 0.5 mL of a 1% solution of borax. A pink solution is formed. Add a couple of drops or a few crystals of the unknown. If the pink color begins to fade after the unknown and the reagent have been mixed together, then continue to add small amounts of the unknown until the pink color fades completely. Place the test tube in a hot-water bath. If the pink color reappears on warming, and dissipates again on cooling, then the unknown is a polyhydric alcohol.

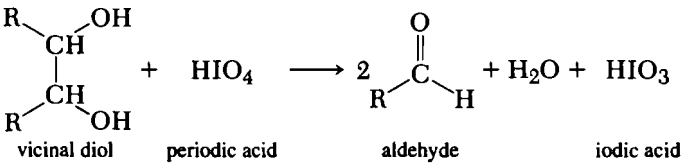
Controls Fructose, lactose, sucrose, and ethylene glycol will give a positive test. Hexane will give a negative test.

Cleaning Up Place the test solution with water in the aqueous solution container.

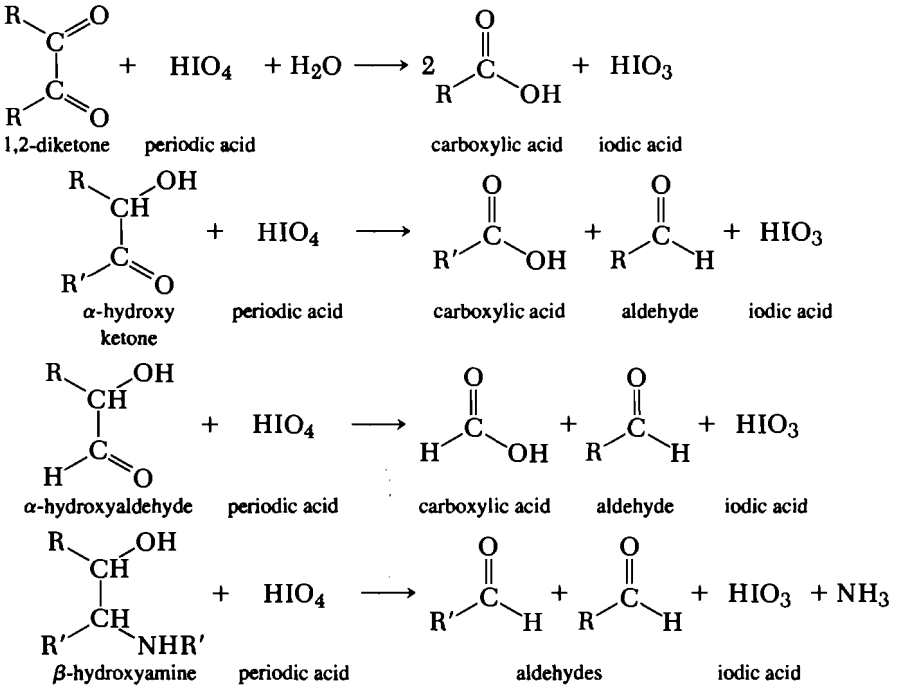
Discussion

Carbohydrates and 1,2-diols give a positive test.

Experiment 27 Periodic Acid Oxidation of Vicinal Diols and Related Compounds



vicinal diol — periodic acid — aldehyde — iodic acid



Place 2 mL of the periodic acid reagent in a small test tube, add one drop (no more) of concentrated nitric acid, and shake thoroughly. Then add one drop or a small crystal of the compound to be tested. Shake the mixture for 10–15 sec, and add one to two drops of 5% aqueous silver nitrate solution. The instantaneous formation of a *white* precipitate (silver iodate) indicates that the organic compound has been oxidized by the periodate, which is thereby reduced to iodate. This constitutes a positive test. Failure to form a precipitate, or the appearance of a brown precipitate that redissolves on shaking, constitutes a negative test.

$$\underset{\text{iodic acid}}{HIO_3} + \underset{\text{silver nitrate}}{AgNO_3} \longrightarrow HNO_3 + \underset{\substack{\text{silver iodate}\\(\text{white})}}{AgIO_3(s)}$$

Dioxane may be added to facilitate the reaction of water insoluble polyols.

Controls Ethylene glycol, glycerol, and glucose will give a positive test. Acetone and 2-propanol will give a negative test.

Periodic Acid Reagent
Dissolve 0.5 g of paraperiodic acid (H_5IO_6) in 100 mL of distilled water.

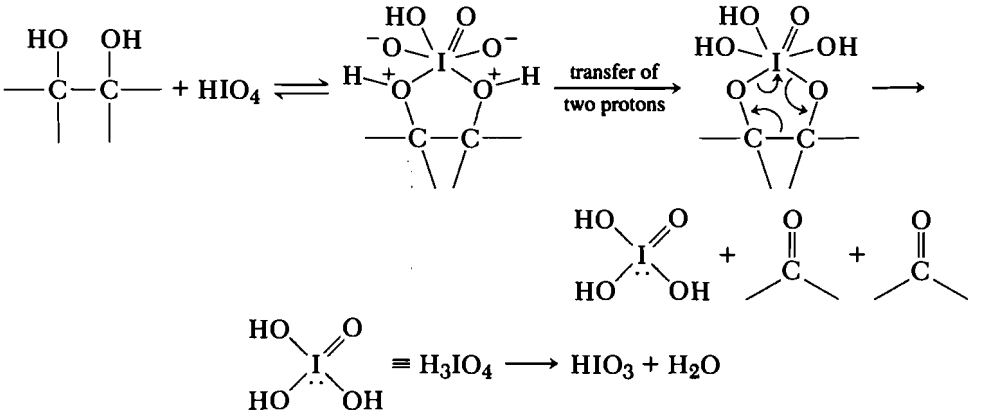
Cleaning Up Place the test solution in the aqueous solution container.

Discussion
Periodic acid has a very selective oxidizing action on 1,2-glycols, α-hydroxy aldehydes, α-hydroxy ketones, 1,2-diketones, α-hydroxy acids, and α-amino alcohols. The rate of the reaction decreases in the order mentioned. Under the conditions specified above, α-hydroxy acids sometimes give a negative test. β-Dicarbonyl compounds and other active methylene compounds also react.

It is important that the exact amounts of reagent and nitric acid be used. The test depends on the fact that silver iodate is only slightly soluble in dilute nitric acid, whereas silver periodate is very soluble. If too much nitric acid is present, however, the silver iodate will fail to precipitate.

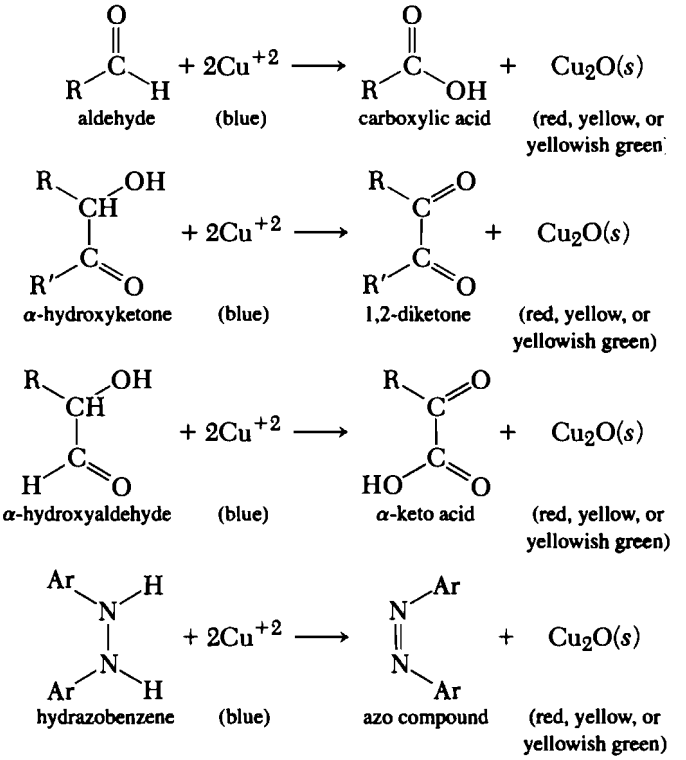
Olefins, secondary alcohols, 1,3-glycols, ketones, and aldehydes are not affected by periodic acid under the above conditions. The periodic acid test is best suited for water-soluble compounds.

The following mechanism has been proposed to account for the oxidation of vicinal diols:



Experiment 28 Benedict's Solution

Compounds Containing No Sulfur



$$\underset{\text{arylhydrazine}}{ArNHNH_2} + \underset{\text{(blue)}}{2Cu^{+2}} \longrightarrow ArH + \underset{\text{phenol}}{ArOH} + N_2(g) + \underset{\text{(red, yellow, or yellowish green)}}{Cu_2O(s)}$$

To a solution or suspension of 0.2 g of the compound in 5 mL of water, add 5 mL of Benedict's solution. Benedict's solution oxidizes a variety of compounds, with the corresponding reduction of Cu^{+2} to Cu^{+1}. The precipitation of the copper(I) oxide as a red, yellow, or yellowish-green solid is a positive test. If no precipitate is formed, heat the mixture to boiling and cool. Note whether any solid is formed.

To a solution of 0.2 g of sucrose in 5 mL of water, add two drops of concentrated hydrochloric acid and boil the solution for a minute. Cool the solution, neutralize the acid with dilute sodium hydroxide solution, and try the action of Benedict's solution. Explain the result.

Controls Butanal and benzoin will give a positive test. Acetone and 2-propanol will give a negative test.

Benedict's Solution

Heat a solution of 17.3 g of sodium citrate and 10.0 g of anhydrous sodium carbonate in 80.0 mL of water until the salts are dissolved. Add additional water to bring the volume up to 85.0 mL. Slowly pour a solution of 1.73 g of hydrated copper sulfate in 10.0 mL of water, with stirring, into the solution of the citrate and carbonate. Add additional water to bring the volume of the solution up to 100 mL.

Cleaning Up Remove the colored copper complex by suction filtration and place in the nonhazardous solid waste container. Place the filtrate in the aqueous solution container.

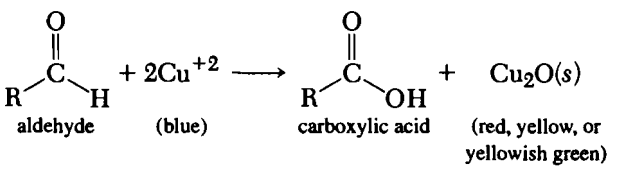
Discussion

Benedict's solution, which contains the copper bound in the complex anion, functions as a selective oxidizing agent. It was introduced as a reagent for reducing sugars to replace Fehling's solution, which is very strongly alkaline. Benedict's reagent will detect 0.01% of glucose in water. The color of the precipitate may be red, yellow, or yellowish green, depending on the nature and amount of the reducing agent present.

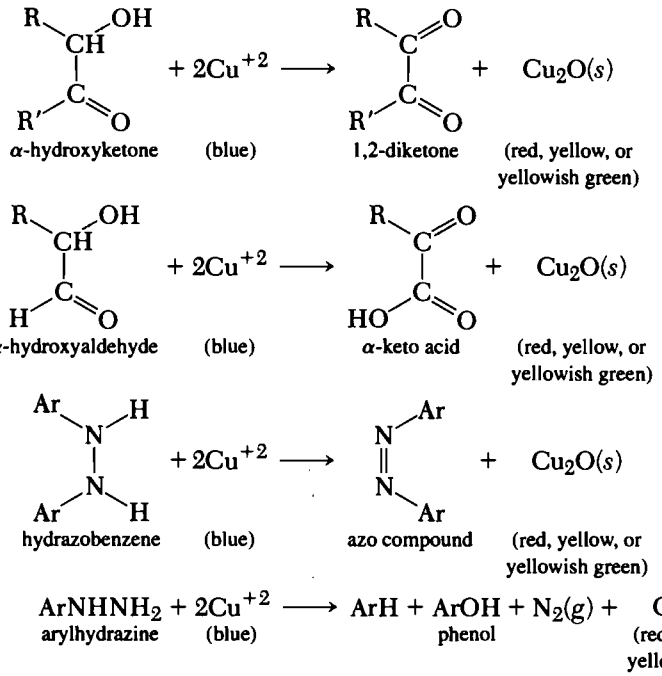
Benedict's reagent is reduced by α-hydroxy aldehydes, α-hydroxy ketones, and α-keto aldehydes. It does not oxidize simple aromatic aldehydes. Molecules containing only the alcohol functional group or only the keto group are not oxidized by Benedict's solution.

Hydrazine derivatives, as exemplified by phenylhydrazine and hydrazobenzene, are oxidized by this reagent. Other easily oxidizable systems, such as phenylhydroxylamine, aminophenol, and related photographic developers, also reduce Benedict's solution.

Experiment 29 Fehling's Solution



aldehyde (blue) carboxylic acid (red, yellow, or yellowish green)



To a solution of 0.2 g of the compound in 5 mL of water, add 5 mL of Fehling's solution and heat the mixture to boiling. Cool the solution. Fehling's solution oxidizes many compounds, and copper in the reagent is reduced from Cu^{+2} to Cu^{+1}. The precipitation of the copper(I) oxide as a red, yellow, or yellowish-green solid is a positive test.

Controls Butanal and benzoin will give a positive test. Acetone and 2-propanol will give a negative test.

Fehling's Solution

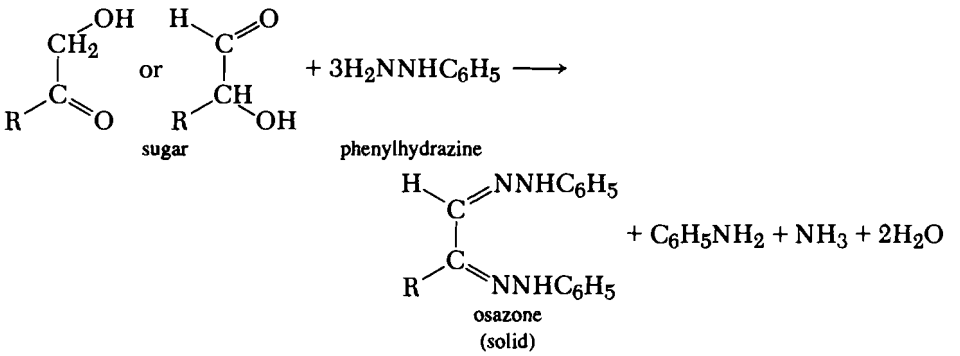
Mix 2.5 mL of the following two solutions immediately before use. *Fehling's solution #1:* Dissolve 8.65 g of hydrated copper sulfate crystals in 100 mL of water and dilute the solution to 125 mL. *Fehling's solution #2:* Dissolve 43.2 g of sodium potassium tartrate and 17.5 g of sodium hydroxide in 50 mL of water and dilute the solution to 125 mL.

Cleaning Up Remove the colored copper complex by suction filtration and place in the nonhazardous solid waste container. Place the filtrate in the aqueous solution container.

Discussion

Benedict's and Fehling's solutions serve as a test for reducing sugars. Nonreducing sugars are hydrolyzed by heating with a small amount of 10% hydrochloric acid, then neutralized with 10% sodium hydroxide. The resulting solution will then give a positive test with Benedict's and Fehling's solutions.

Experiment 30 Osazones



Place 0.2 g of the unknown sample in a test tube and add 0.4 g of phenylhydrazine hydrochloride, 0.6 g of crystallized sodium acetate, and 4 mL of distilled water. Place the test tube in a beaker of boiling water. Note the time that the test tube was immersed and, finally, the time of the precipitation.

After 20 min, remove the test tube from the hot-water bath and set it aside to cool. Pour a small amount of the liquid and solid on a watch glass. Tip the watch glass from side to side to spread out the crystals, and absorb some of the mother liquor with a piece of filter paper, taking care not to crush or break up the clumps of crystals. Examine the crystals under a low-power microscope (about 80 to 100×), and compare with photomicrographs.[23]

Controls Note the time that it takes for osazone formation with glucose, maltose, sucrose, and galactose.

The formation of tarry products due to oxidation of the phenylhydrazine may be prevented by the addition of 0.5 mL of saturated sodium bisulfite solution. This should be done before heating if it is desired to isolate the osazone and determine its melting point.

Cleaning Up Place the solid products in the organic nonhazardous solid waste container. Add 8 mL of 5.25% sodium hypochlorite (household bleach) to the filtrate. Heat the solution at 45–50° for 2 h to oxidize the amine. Dilute the solution with 10 mL of water and place in the aqueous solution container.

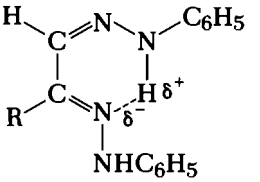
Discussion

The time required for the formation of the osazone can be a valuable aid in distinguishing among various sugars. The following figures are the times required for the osazone to precipitate from the hot solution: fructose, 2 min; glucose, 4–5 min; xylose, 7 min; arabinose, 10 min; galactose, 15–19 min; raffinose, 60 min; lactose, osazone soluble in hot water; maltose, osazone soluble in hot water; mannose, 0.5 min (hydrazone); sucrose, 30 min (owing to hydrolysis and formation of glucosazone).

Osazone formation involves hydrazone formation at C-1 of an aldose (or C-2 of a ketose) and oxidation of C-2 (or C-1) of an alcohol group to a ketone (or an aldehyde). The new carbonyl group is also converted to a hydrazone. It has been suggested that

[23]W. Z. Hassid and R. M. McCready, *Ind. Eng. Chem., Anal. Ed.*, *14*, 683 (1942).

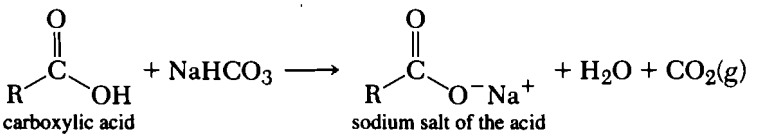
the reaction stops here (rather than further oxidation at C-3, etc.) due to the hydrogen-bonding stabilization of the osazone:



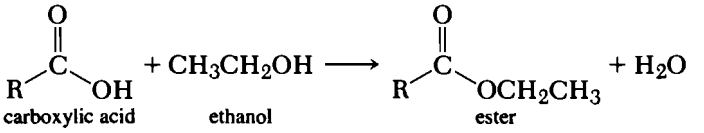
9.9 CARBOXYLIC ACIDS

Carboxylic acids are primarily identified by spectroscopy and solubility tests. However, a few classification tests can be used to confirm the presence of the carboxylic group.

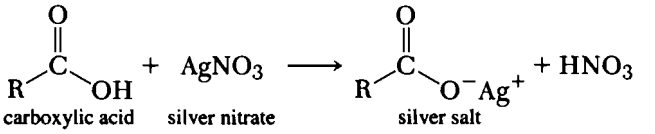
Carboxylic acids react with a sodium bicarbonate solution to form the carboxylate anion and carbon dioxide gas (Experiment 31, below).



Another test for carboxylic acids involve the esterification of the acid (Experiment 3b, p. 256). The ester forms another layer and has a sweet, fruity smell.



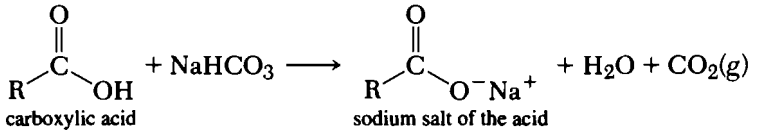
Silver nitrate reacts with carboxylic acids to form silver salts of the carboxylic acid (Experiment 35, p. 320). These silver salts are soluble in dilute nitric acid, whereas silver halides are insoluble in nitric acid.



Problem

20. Volatility contributes greatly to odor. Briefly explain why ethyl esters are normally more volatile than the corresponding carboxylic acids.

Experiment 31 Sodium Bicarbonate Test



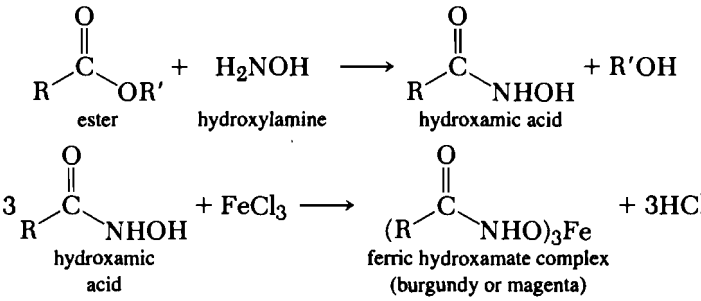
Dissolve a few drops or a few crystals of the unknown sample in 1 mL of methanol and slowly add to 1 mL of a saturated solution of sodium bicarbonate. Evolution of carbon dioxide gas is a positive test for the presence of the carboxylic acid.

Controls Benzoic acid and butanoic acid will give a positive test. Acetone and 2-propanol will give a negative test.

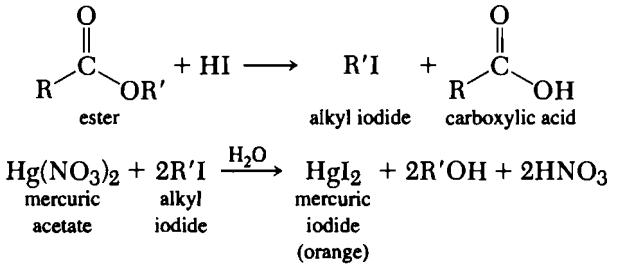
Cleaning Up Place the test solution in the aqueous solution container.

9.10 ESTERS

Esters characteristically have a sweet fruity smell. Esters combine with hydroxylamine to yield an alcohol and hydroxamic acid (Experiment 2b, p. 253). The solution is then treated with ferric chloride to produce the ferric hydroxamate complex, which has a characteristic burgundy or magenta color.

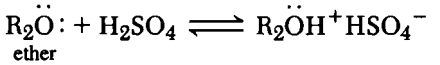


Esters are cleaved by hydroiodic acid (Experiment 34, p. 318) to form an alkyl iodide and a carboxylic acid. The alkyl iodide is treated with mercuric nitrate to yield mercuric iodide, which is an orange color.



9.11 ETHERS

Ethers are only a little more polar and slightly more reactive than either saturated hydrocarbons or alkyl halides. The ether oxygen can be protonated by concentrated sulfuric acid.



Caution: *Ethers form extremely explosive peroxides upon standing, especially when exposed to air and/or light. Liquid ether that shows solid precipitates should not be handled at all.*

Peroxides can be detected by treating the ether with starch–iodide paper that has been moistened with dilute hydrochloric acid; peroxides will cause the paper to turn blue. Methods of removing peroxides have been described.[24] Many laboratories have

[24]B. S. Furniss, A. J. Hannaford, P. W. G. Smith, and A. R. Tatchell, *Vogel's Textbook of Practical Organic Chemistry*, 5th ed. (Wiley, New York, 1991), p. 404.

substituted *t*-butyl methyl ether for diethyl ether because of the much greater peroxide danger for the latter.

Pure ethers are more likely to be initially diagnosed by their failure to undergo reactions rather than by their ability to undergo chemical reactions.

The ferrox test is used to distinguish ethers from hydrocarbons (Experiment 32, below). Ferric ammonium sulfate reacts with potassium thiocyanate to form iron hexathiocyanatoferrate, which reacts with oxygen-containing compounds to form a reddish-purple solution.

$$\underset{\text{ferric ammonium sulfate}}{2Fe(NH_4)_2(SO_4)_2} + \underset{\text{potassium thiocyanate}}{6KSCN} \longrightarrow \underset{\text{iron hexathiocyanatoferrate}}{Fe[Fe(SCN)_6]} + 3K_2SO_4 + (NH_4)_2SO_4$$

Ethers can be detected by the iodine test (Experiment 33, p. 317); as the ether undergoes reaction with iodine, the color of the solution changes from purple to tan.

$$\underset{\text{ether}}{R_2\ddot{O}:} + I_2 \longrightarrow R_2\ddot{O}: \longrightarrow I_2$$

Treatment of an ether with hydroiodic acid results in the cleavage of the ether (Experiment 34, p. 318). The alkyl iodide product is heated and its vapors undergo reaction with mercuric nitrate to form mercuric iodide, which is orange.

$$\underset{\text{ether}}{R'OR} + \underset{\text{hydroiodic acid}}{2HI} \longrightarrow \underset{\text{alkyl iodides}}{R'I + RI} + H_2O$$

$$\underset{\text{ether}}{ArOR} + \underset{\text{hydroiodic acid}}{HI} \longrightarrow \underset{\text{alkyl iodide}}{RI} + \underset{\text{phenol}}{ArOH}$$

$$\underset{\text{mercuric acetate}}{Hg(NO_3)_2} + 2\underset{\text{alkyl iodide}}{R'I} \xrightarrow{H_2O} \underset{\text{mercuric iodide (orange)}}{HgI_2} + 2R'OH + 2HNO_3$$

Experiment 32 Ferrox Test

$$\underset{\text{ferric ammonium sulfate}}{2Fe(NH_4)_2(SO_4)_2} + \underset{\text{potassium thiocyanate}}{6KSCN} \longrightarrow \underset{\text{iron hexathiocyanatoferrate}}{Fe[Fe(SCN)_6]} + 3K_2SO_4 + (NH_4)_2SO_4$$

Grind together, with a glass stirring rod, a crystal of ferric ammonium sulfate and a crystal of potassium thiocyanate. The iron hexathiocyanatoferrate that is formed sticks to the stirring rod.

In a test tube, dissolve 30 mg or three drops of the unknown in a minimal amount of toluene. Use the stirring rod with the iron hexathiocyanatoferrate solid to stir the unknown. If the solid dissolves and a reddish-purple color develops, the compound contains oxygen.

Controls Diethyl ether, and acetone will give a positive test. Phenol and hexane will give a negative test.

Cleaning Up Place the mixture in the hazardous waste container.

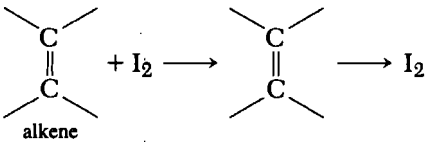
Discussion

Hydrocarbons, alkyl halides, diaryl ethers, and other high-molecular-weight ethers give a negative test. Most compounds in which the oxygen is in a carbonyl group that is in

conjugation with an aromatic ring or a double bond produce a negative test. Such compounds include cinnamic acid, aromatic acids, aromatic esters, aromatic anhydrides, and aromatic ketones. Phenols also give a negative test. However, aromatic aldehydes give a positive test. Other compounds that produce a positive test are aliphatic acids, aliphatic aldehydes, aliphatic ketones, aliphatic esters, aliphatic anhydrides, and aliphatic ethers.

This test should be used in conjunction with other tests. If the unknown produces a positive test but yields a negative test for an aldehyde (Experiments 8, p. 268; 12–17, pp. 278–284; 28–29, pp. 310–311), a ketone (Experiments 11–14, pp. 273–281), an ester (Experiment 2b, p. 253), a carboxylic acid (Experiments 3b, p. 256; 31, p. 314; 35, p. 320), or an anhydride (Experiments 1, p. 252; 2b, p. 253; 3a, p. 256; 4, p. 258), then the compound is an aliphatic or a low-molecular-weight ether.

Experiment 33 Iodine Test for Ethers and Unsaturated Hydrocarbons [25]



$$R_2\ddot{O}: + I_2 \longrightarrow R_2\ddot{O}: \longrightarrow I_2$$
ether

Add 0.25 mL or 0.25 g of the unknown sample to 0.5 mL of the iodine in methylene chloride solution. If an ether is present, the purple solution becomes tan in color. Aromatic hydrocarbons, saturated hydrocarbons, fluorinated hydrocarbons, and chlorinated hydrocarbons do not react. Unsaturated hydrocarbons produce a light-tan solid, while retaining the purple color of the iodine solution.

Controls Diethyl ether and cyclohexene will give a positive test. Cyclohexane and toluene will give a negative test.

Iodine in Methylene Chloride Solution
Add a couple of crystals of iodine to 100 mL of methylene chloride. Stopper the solution tightly.

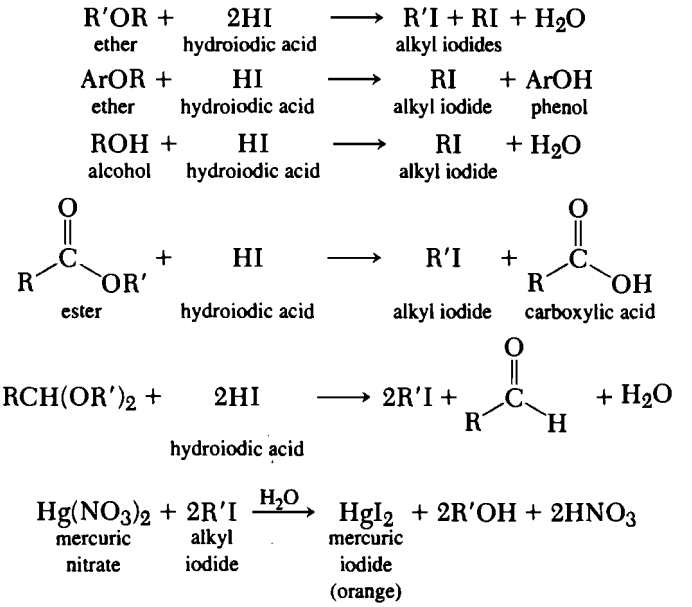
Cleaning Up Place the test solution in the halogenated organic waste container.

Discussion
Some compounds with nonbonded electron pairs or π-bonded electrons form charge-transfer complexes with iodine, yielding a brown solution. The brown color is from the iodine forming a π complex or charge transfer with the nonbonded or π electrons. These compounds are formed quickly and, sometimes, reversibly. Because they are often unstable, conclusions should be drawn on the results observed in a short period of time.

Some alcohols and ketones may also give a positive test. Thus, this test should be used in addition to other tests for compounds containing oxygen.

[25]D. J. Pasto, C. R. Johnson, and M. J. Miller, *Experiments and Techniques in Organic Chemistry* (Prentice-Hall, Englewood Cliffs, NJ, 1992), pp. 277–278.

Experiment 34 Hydroiodic Acid (Zeisel's Alkoxyl Method)



Do this reaction in the hood. Place about 0.1 g or 0.1 mL of the compound in a 16-by-150-mm test tube. Carefully add, by means of a pipet, 1 mL of glacial acetic acid and 1 mL of 57% hydroiodic acid (sp gr 1.7). Add a boiling chip, and insert into the mouth of the test tube a gauze plug as described below. Twist the gauze plug so as to make a good fit and push it down so that it is 4 cm from the mouth of the test tube. Gently push a small piece of nonabsorbent cotton on top of the plug by means of a glass rod so as to make a disk of cotton 2–3 mm thick. Fold a piece of filter paper 2 by 10 cm longitudinally, moisten it with a solution of mercuric nitrate, and place it on the cotton disk. Immerse the test tube to a depth of 4–5 cm in an oil bath that is kept at 120–130°C.

When the reaction mixture boils, vapors rise through the porous plug, which usually turns gray. The volatile alkyl halide, rising through the plugs, reacts with the mercuric nitrate to produce a light-orange or vermilion color due to the formation of the mercuric iodide. A positive test consists in the formation of an orange or vermilion color on the test paper within a 10-min heating period. A yellow color constitutes a negative or doubtful test.

Controls Anisole, methyl benzoate, and 1-butanol will give a positive test. Hexane and acetone will give a negative test.

Gauze Plugs

Add a solution of 0.10 g of lead acetate in 1.0 mL of water to 6.0 mL of 1 M sodium hydroxide solution and stir until the precipitate dissolves. Add a solution of 0.5 g of hydrated sodium thiosulfate in 1.0 mL of water. Add 0.5 mL of glycerol, and dilute the solution to 10.0 mL. Pipet 5 mL of this solution onto strips of double cheesecloth 2 by 45 cm. Dry the strips of cloth and roll them to fit the test tube.

Mercuric Nitrate Solution

Prepare 24.5 mL of a saturated solution of mercuric nitrate and add 0.5 mL of concentrated nitric acid. Mercury compounds are very toxic and require handling with special care.

Cleaning Up Place the gauze plugs and filter paper in the hazardous solid waste container. Place the test solution in the halogenated organic waste container.

Discussion

This test is based on the classic Zeisel method for quantitatively estimating the percentage of methoxyl or ethoxyl groups. Functional groups containing methyl, ethyl, 1-propyl, or 2-propyl radicals attached to oxygen are cleaved by the hydroiodic acid with the formation of a volatile alkyl halide. Alkoxy derivatives in which the group is butyl or larger are difficult to cleave, and the iodide is too high boiling to be volatilized. Some butoxy compounds give a positive test, but the procedure is not reliable (the boiling point of butyl iodide is 131°C).

This class reaction is most useful for ethers, esters, and acetals in which the groups are methyl or ethyl. Methanol, ethanol, 1-propanol, 2-propanol, and even higher alcohols such as 1-butanol and 3-methyl-1-butanol will also give a positive test. The test has been applied to numerous alkaloids and methylated sugars. The chief interference is caused by the presence of a sulfur-containing functional group that liberates hydrogen sulfide when heated with hydroiodic acid.

Some ethers may require a more vigorous reagent for cleavage. It is sometimes advantageous to use 2 mL of hydroiodic acid, 0.1 g of phenol, and 1 mL of propanoic anhydride for each 0.1 g of the sample.

Hydroiodic acid is a strong acid, and it protonates the ether; iodide ion nucleophilically displaces the protonated alkoxy group, giving alkyl iodide. This process is expected to predominate when the R groups are primary.

$$\underset{\text{ether}}{\text{ROR}} + \underset{\text{hydroiodic acid}}{\text{HI}} \longrightarrow \text{R}_2\overset{+}{\text{O}}\text{H} \xrightarrow{\text{I}^-} \text{RI} + \text{H}_2\text{O} \xrightarrow{\text{HI}} \text{R}\overset{+}{\text{O}}\text{H}_2 \xrightarrow{\text{I}^-} \text{RI} + \text{H}_2\text{O}$$

Problem

21. Modify the mechanism just above to explain how ethers with tertiary alkyl groups might be hydrolyzed.

9.12 HALIDES

Since aliphatic halides are often detected initially by qualitative halogen analysis, it should not be surprising that further characterization takes advantage of the wide range of processes by which halogens can be displaced. The two tests for displaceable halogens that are discussed below are complementary and are thus often very useful in classifying the structures of alkyl halides. The silver nitrate reaction proceeds by a carbocation (S_N1) process and the sodium iodide reaction by a direct displacement (S_N2). Thus the following reactivity order:

$$\begin{aligned} &\text{AgNO}_3\text{/ethanol test:} && \text{R}_3\text{CX} > \text{R}_2\text{CHX} > \text{RCH}_2\text{X} \\ &\text{NaI/acetone test:} && \text{R}_3\text{CX} < \text{R}_2\text{CHX} < \text{RCH}_2\text{X} \end{aligned}$$

In both the silver nitrate test (Experiment 35, p. 320) and the sodium iodide test (Experiment 36, p. 323), the halide is displaced from the alkyl halide to form an insoluble salt. The reaction of the alkyl halide with silver nitrate yields a silver halide precipitate.

$$\underset{\text{alkyl halide}}{\text{RX}} + \underset{\text{silver nitrate}}{\text{AgNO}_3} \xrightarrow{\text{CH}_3\text{CH}_2\text{OH}} \underset{\text{silver halide}}{\text{AgX}(s)} + \text{RONO}_2$$

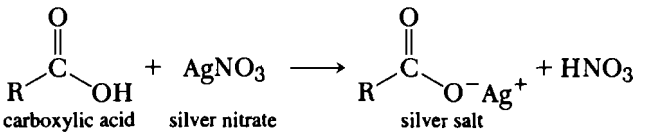
The sodium iodide test can be used to test for the presence of bromine or chlorine. Sodium halide precipitates from the solution.

$$\underset{\text{alkyl chloride}}{RCl} + \underset{\text{sodium iodide}}{NaI} \xrightarrow{\text{acetone}} \underset{\text{alkyl iodide}}{RI} + \underset{\text{sodium chloride}}{NaCl(s)}$$

$$\underset{\text{alkyl bromide}}{RBr} + \underset{\text{sodium iodide}}{NaI} \xrightarrow{\text{acetone}} \underset{\text{alkyl iodide}}{RI} + \underset{\text{sodium bromide}}{NaBr(s)}$$

Experiment 35 Silver Nitrate Solution (Ethanolic)

$$\underset{\text{alkyl halide}}{RX} + \underset{\text{silver nitrate}}{AgNO_3} \xrightarrow{CH_3CH_2OH} \underset{\text{silver halide}}{AgX(s)} + RONO_2$$



This reagent is useful for classifying compounds known to contain halogen. Add one drop or a couple of crystals of the unknown to 2 mL of the 2% ethanolic silver nitrate solution. If no reaction is observed after 5 min standing at room temperature, heat the solution to boiling and note whether a precipitate is formed. If there is a precipitate, note its color. Add two drops of 5% nitric acid, and note whether the precipitate dissolves. Silver halides are insoluble in dilute nitric acid; silver salts of organic acids are soluble.

Controls Note the time of the rate of reaction with benzoyl chloride, benzyl chloride, ethyl bromide, 2-bromobutane, 2-bromo-2-methylbutane, chloroform, and chloroacetic acid.

Cleaning Up Add a saturated solution of sodium chloride. Isolate the silver halide by filtration and place in the nonhazardous solid waste container. Place the filtrate in the aqueous solution container.

Discussion

Since alkyl halides often contain small amounts of isomeric impurities, it may be advisable in certain borderline cases to collect and dry the silver halide obtained from a weighed sample of the unknown. Generally an approximate value for the molecular weight can be arrived at from a consideration of its physical constants and from an inspection of the list of possibilities; the estimated theoretical yield of the silver halide can thus be compared with the amount obtained. If the observed yield amounts to only a few percent, the test is negative. An alkyl halide that gives only a small amount of silver halide because it reacts slowly may be distinguished from a mixture of an inert halide with a small amount of reactive impurity by collecting the halide initially precipitated and then testing the filtrate with more silver nitrate.

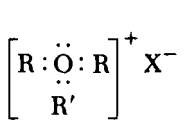
Many halogen-containing substances react with silver nitrate to give an insoluble silver halide, and the rate of this reaction is an index of the degree of reactivity of the halogen atom in question. This information is valuable because it permits certain deductions to be drawn concerning the structure of the molecule. Moreover, the identity of the halogen can sometimes be determined from the color of the silver halide (silver

chloride is white, silver bromide is pale yellow, and silver iodide is yellow), although impurities easily cause ambiguous results.

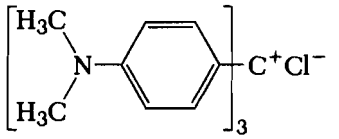
The most reactive halides are those that are ionic. Among organic compounds, the amine salts of the halogen acids constitute the most common examples.

$$[RNH_3]^+X^-$$

Less frequently encountered are oxonium salts and "carbonium" salts that contain ionic halogen.



R′ = alkyl, H



crystal violet

Aqueous solutions of these salts give an immediate precipitate of the silver halide with aqueous silver nitrate solution.

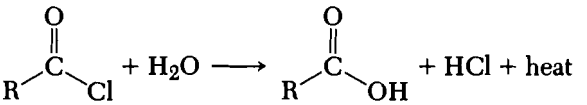
A summary of the results to be expected in the alcoholic silver nitrate test is given below.

I. The following water-soluble compounds give an immediate precipitate with aqueous silver nitrate.

1. Amine salts of halogen acids.

$$RNH_3^+Cl^- + Ag^+NO_3^- \longrightarrow AgX(s) + RNH_3^+NO_3^-$$

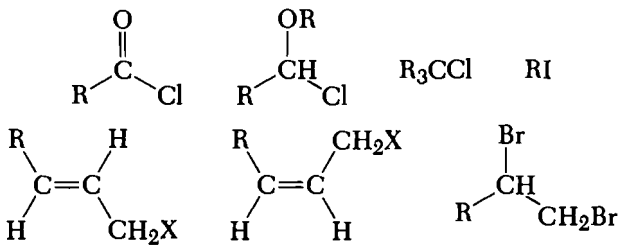
2. Oxonium salts.
3. Carbonium halides.
4. Low-molecular-weight acid chlorides. Many of these are easily hydrolyzed by water and produce the halide ion.



acyl halide carboxylic acid

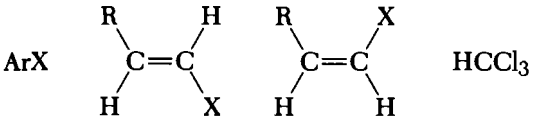
II. Water-insoluble compounds fall roughly into three groups with respect to their behavior toward alcoholic silver nitrate solutions.

1. Compounds in the first group give an immediate precipitation at room temperature.



2. The second group includes compounds that react slowly or not at all at room temperature but give a precipitate readily at higher temperatures.

3. A final group is made up of compounds that are usually inert toward hot alcoholic silver nitrate solutions.



In the reaction with silver nitrate, cyclohexyl halides exhibit a decreased reactivity when compared with the corresponding open-chain secondary halides. Cyclohexyl chloride is inactive, and cyclohexyl bromide is less reactive than 2-bromohexane, although it will give a precipitate with alcoholic silver nitrate. Similarly, 1-methylcyclohexyl chloride is considerably less reactive than acyclic tertiary chlorides. However, both 1-methylcyclopentyl and 1-methylcycloheptyl chloride are more reactive than the open-chain analogs.

Since, as emphasized above, reactivity toward alcoholic silver nitrate is often very different from reactivity toward sodium iodide in acetone (Experiment 36, p. 323), *both* tests should be used with any halogen compound.

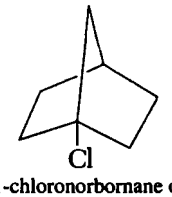
A major factor that contributes to the reactivity of an alkyl halide (RX) toward silver nitrate is the stability of the carbocation (R^+) that is formed. Specifically, the more stable the carbocation, the faster the reaction with ethanolic $AgNO_3$.

$$R{-}X \xrightarrow{Ag^+} R^{\delta+}\cdots X^{\delta-}\cdots Ag^{\delta+} \longrightarrow AgX + R^+$$

$$R^+ \xrightarrow{{}^-NO_3} R{-}ONO_2$$

Problems

22. Suggest a reason why $ClCH_2OR$ compounds should be reasonably reactive toward $AgNO_3$. (*Hint:* Resonance theory supports a stable, although primary, carbocation.)
23. Suggest reasons why benzyl chloride reacts faster than cyclohexylmethyl chloride.
24. Suggest a reason why vinyl and aryl halides are quite inert toward ethanolic $AgNO_3$.
25. The compound shown below is expected to be inert toward ethanolic $AgNO_3$, despite the fact that it is tertiary. Explain your reasoning.



1-chloronorbornane or
1-chlorobicyclo[2.2.1]heptane

Experiment 36 Sodium Iodide in Acetone Test

$$\underset{\text{alkyl chloride}}{RCl} + \underset{\text{sodium iodide}}{NaI} \xrightarrow{\text{acetone}} \underset{\text{alkyl iodide}}{RI} + \underset{\text{sodium chloride}}{NaCl(s)}$$

$$\underset{\text{alkyl bromide}}{RBr} + \underset{\text{sodium iodide}}{NaI} \xrightarrow{\text{acetone}} \underset{\text{alkyl iodide}}{RI} + \underset{\text{sodium bromide}}{NaBr(s)}$$

To 1 mL of the sodium iodide in acetone reagent in a test tube add two drops of the compound whose elemental analysis showed the presence of chlorine or bromine. If the compound is a solid, dissolve about 0.1 g in the smallest possible volume of acetone, and add the solution to the reagent. Shake the test tube, and allow the solution to stand at room temperature for 3 min. Note whether a precipitate is formed and also whether the solution turns reddish brown, because of the liberation of free iodine. If no change occurs at room temperature, place the test tube in a beaker of water at 50°C. Excessive heating causes loss of acetone and precipitation of sodium iodide, which can lead to false-positive results. At the end of 6 min, cool to room temperature and note whether a reaction has occurred.

Controls Note the time of the rate of reaction with benzoyl chloride, benzyl chloride, ethyl bromide, 2-bromobutane, 2-bromo-2-methylbutane, chloroform, and chloroacetic acid.

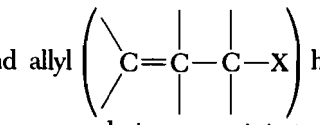
Sodium Iodide in Acetone Reagent
Dissolve 15 g of sodium iodide in 100 mL of acetone. The solution, colorless at first, becomes a pale lemon yellow. Keep the solution in a dark bottle and discard as soon as a definite red-brown color develops.

Cleaning Up Place the test solution in the aqueous solution container.

Discussion
This test is used to classify aliphatic chlorides and bromides as primary, secondary, or tertiary. This test depends on the fact that sodium chloride and sodium bromide are only very slightly soluble in acetone. As might be anticipated by a direct displacement (S_N2) process, the order of reactivity of simple halides is primary > secondary > tertiary. With sodium iodide, primary bromides give a precipitate of sodium bromide within 3 min at 25°C, whereas the chlorides give no precipitate and must be heated to 50°C in order to effect a reaction. Secondary and tertiary bromides react at 50°C, but the tertiary chlorides fail to react within the time specified. Tertiary chlorides will react if the test solutions are allowed to stand for a day or two. These results are consistent with the following S_N2 process.

$$R{-}X \xrightarrow{I^-} \left[I^{\delta-} \cdots C \cdots X^{\delta-} \right] \longrightarrow I{-}R$$

In the reaction with sodium iodide in acetone, cyclopentyl chloride undergoes reaction at a rate comparable with that of acyclic secondary chlorides, whereas the reaction with cyclohexyl chloride is considerably slower. Thus, cyclopentyl chloride and bromide, as well as similar compounds, fail to react appreciably with sodium iodide at 50° within 6 min.

Benzyl ($ArCH_2X$) and allyl  halides are extremely reactive toward sodium iodide in acetone and give a precipitate of sodium halide within 3 min at 25°C; the reason for this reactivity is discussed below.

Although triphenylmethylchloride would be expected to be too hindered to undergo a displacement reaction with iodide ion, it has been found to react much faster than benzyl chloride. However, the reaction is not a simple replacement to form trityl iodide, since the color of *iodine* is observed. This example emphasizes the care that needs to be taken in the interpretation of qualitative tests of this type. It must be remembered that members of a class of compounds under consideration may react with the same reagent in several ways and that for each kind of reaction the effect of structure on reactivity may be different.

Polybromo compounds such as bromoform and 1,1,2,2-tetrabromoethane undergo reaction with sodium iodide at 50°C to give a precipitate and liberate iodine. Carbon tetrabromide undergoes reaction at 25°C.

Sulfonyl bromides and chlorides give an immediate precipitate and also liberate free iodine. Presumably the iodine is formed by the action of sodium iodide on the sulfonyl iodide.[26]

$$ArSO_2X + NaI \longrightarrow ArSO_2I + NaX(s)$$
$$\downarrow NaI$$
$$ArSO_2Na + I_2$$

Benzenesulfonyl chlorides gave a 60% yield of sodium benzenesulfinate; other products obtained were diphenyl disulfone (27%) and phenyl thiosulfinate (10%).

Alkyl sulfonates also undergo reactions, producing the corresponding sodium sulfonates as precipitates. Groups (R) that give stable carbocations undergo S_N1 reactions; otherwise, S_N2 displacement can compete.

$$ArSO_2OR + NaI \longrightarrow ArSO_2ONa + RI$$

This reaction must be kept in mind in the event that one of the groups in the sulfonic ester contains halogen atoms.

1,2-Dichloro and 1,2-dibromo compounds not only give a precipitate of sodium chloride or bromide but also liberate free iodine.

$$\begin{matrix} & Br & Br & & & & \\ & | & | & & & & \\ RHC & - & CHR & + 2NaI & \longrightarrow & RHC{=}CHR & + 2NaBr + I_2 \end{matrix}$$

Stepwise:

$$\begin{matrix} I^- & & & & & & \\ \curvearrowright & & & & & & \\ & Br & & & & & \\ & | & & & & & \\ RHC & - & CHR & + 2NaI & \longrightarrow & RHC{=}CHR & + IBr + Br^- \\ & & | & & & & \\ & & Br\curvearrowleft & & & & \end{matrix}$$

$$IBr + I^- \longrightarrow I_2 + Br^-$$

[26]B. S. Furniss, A. J. Hannaford, P. W. G. Smith, and A. R. Tatchell, *Vogel's Textbook of Practical Organic Chemistry*, 5th ed. (Wiley, New York, 1991), p. 1234.

A comparison of ethylene halides gave the following results:

	ppt at 25°C
$BrCH_2CH_2Br$	1.5 min
$BrCH_2CH_2Cl$	3 min
$ClCH_2CH_2Cl$	none (ppt at 50°C in 2.5 min)

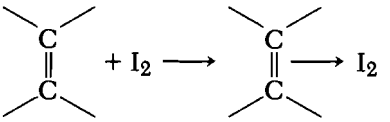
These results support the standard leaving group effects upon RX reactivity in S_N2 displacements: I > Br > Cl.

9.13 HYDROCARBONS—ALKANES

Alkanes are not usually characterized chemically because they are quite inert to most reactions discussed in this book. Since chemists usually rely heavily on physical and spectral characterization, we can use the lack of reaction to conclude that our compound is not in a more reactive class. This is consistent with the fact that alkanes fall into solubility class I.

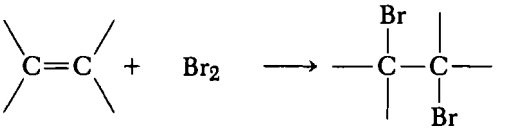
9.14 HYDROCARBONS—ALKENES

The carbon–carbon double bond of alkenes (olefins) can be detected very easily by chemical tests. Alkenes can be detected by the use of iodine (Experiment 33, p. 317). If an alkene is present, a tan solid is formed while retaining the purple solution of the iodine solution.



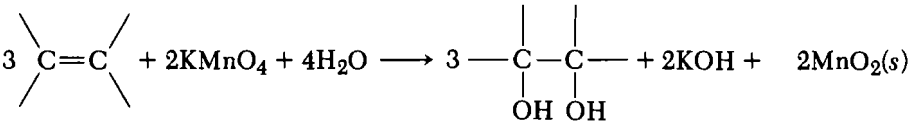
alkene

Addition across the double bond occurs in both the bromine test (Experiment 37, p. 326) and the potassium permanganate test (Experiment 38, p. 328). Since the ionic characters of the bromine and potassium permanganate reactions are very different, there is some complementary character between the two tests. For example, some alkenes bearing electron-withdrawing groups undergo rapid reaction with potassium permanganate but often slow or negligible reaction with bromine. Bromine adds across the carbon–carbon double bond, with dissipation of the brown-red bromine color.



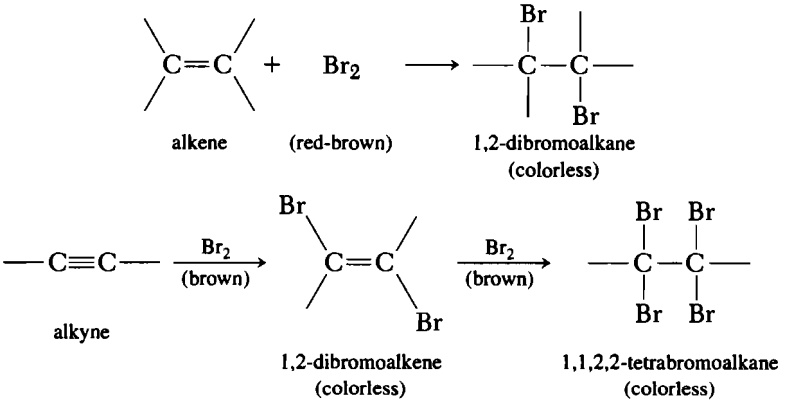
alkene (red-brown) 1,2-dibromoalkane (colorless)

Alkenes are oxidized to 1,2-diols with potassium permanganate, with reduction of the manganese from +7, which is purple, to +4, which is brown.



alkene (purple) 1,2-diol manganese dioxide (brown)

Experiment 37 Bromine Solution



In the hood, add 0.1 g or 0.2 mL of the unknown compound to 2 mL of methylene chloride, and add a 5% solution of bromine in methylene chloride drop by drop, with shaking, until the bromine color persists.

A positive test for a carbon–carbon double bond or triple bond involves the disappearance of the bromine color without the evolution of hydrogen bromide. If the bromine color is discharged and hydrogen bromide is evolved, then substitution has occurred on the unknown. Hydrogen bromide gas can be detected by placing moistened blue litmus paper across the mouth of the test tube and noting whether it turns red, indicating the presence of an acidic gas.

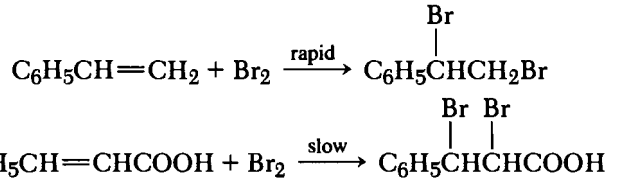
Controls 2-Pentene and cinnamic acid will give a positive test. Hexane, acetone, and acetophenone will give a negative test.

Cleaning Up Place the test solution in the hazardous waste container.

Discussion

This reagent is widely used to test for the presence of an olefinic or acetylenic linkage. It should be employed in conjunction with the potassium permanganate test (Experiment 38, p. 328). The methylene chloride–bromide solution has a shelf life of about a year. Fresh solutions should be made each year.

The evolution of hydrogen is, accordingly, accepted as evidence that the reaction is substitution rather than addition. When employed in detecting unsaturation, this reagent may lead to erroneous conclusions for two reasons. The first is that not all olefinic compounds take up bromine. The presence of electron-withdrawing groups on the carbon atoms of the ethylenic bond causes the addition to be slow and in extreme cases prevents the reaction. The following equations illustrate this point:

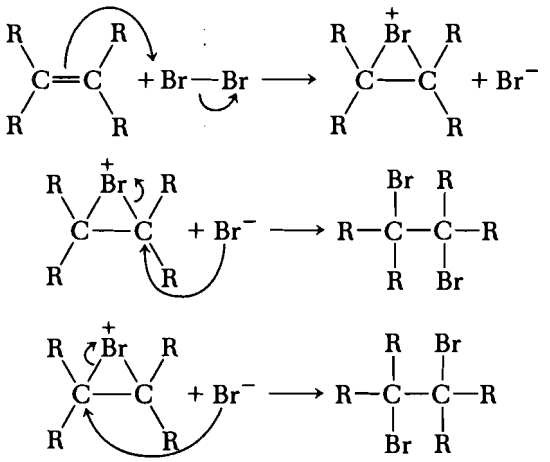


In some cases, electron-withdrawing groups may require the use of potassium permanganate to reveal the alkene double bond.

A positive test for unsaturation is one in which the bromine color is discharged *without the evolution of hydrogen bromide.*

When bromination is employed as a qualitative test, carbon tetrachloride has been the preferred solvent; it is, however, an unfortunate choice for a study of the mechanism of the reaction because in nonpolar solvents the reaction is complicated. The reaction is powerfully catalyzed by traces of water or acids and may be inhibited by oxygen. It could be anticipated that such effects would make it difficult to obtain reproducible results and so render uncertain the interpretation of any negative qualitative test.

In a nonpolar solvent, the addition reaction has been shown to be a two-stage process. The first is the reaction of the alkene with bromine to give a bromonium ion. The second is the attack of the bromine ion on either carbon of the three-member ring on the side away from the bromine. The final products contain the two bromine atoms on opposite sides, in an anti-orientation.

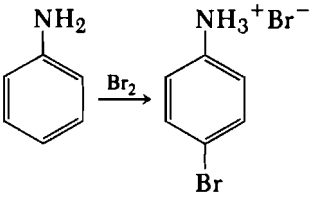


In a polar solvent such as water, the bromohydrin is the major product accompanied by the evolution of hydrogen bromide.

Substituents that help to stabilize the positively charged bromonium ion increase the rate; those that destabilize the positive ion retard the reaction. For example, substitution of an alkyl group on either of the doubly bonded carbon atoms in alkenes of the type $RCH{=}CH_2$ increases the rate of addition in acetic acid solution by a factor of 30–40. Attached carboxyl groups (COOH) slow the reaction.

Discharge of the bromine color *accompanied by the evolution of hydrogen bromide,* indicating that substitution has occurred, is characteristic of many compounds. In this category are enols, many phenols, and enolizable compounds. Ketones, like other carbonyl compounds, may exhibit an induction period because the hydrobromic acid liberated acts as a catalyst for the enolization step of the bromination. Simple esters do not give this test. Ethyl acetoacetate decolorizes the solution immediately, whereas ethyl malonate may require as much as a minute. A number of active methylene compounds that do not discharge the color at room temperature will readily give a positive test at 70°C. Among these substances are propanal and cyclopentanone. Benzyl cyanide, even at 70°C, may require several minutes.

Aromatic amines are exceptional because the first mole of hydrogen bromide is not evolved but reacts with the amine to produce a salt. For this reason this reaction could be mistaken for simple addition.



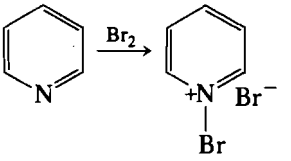
Benzylamine represents an unusual type that reacts readily with bromine. Substitution of the hydrogen atoms on the nitrogen atom appears to take place, followed by decomposition to benzonitrile:

$$3C_6H_5CH_2NH_2 + 2Br_2 \longrightarrow [C_6H_5CH_2NBr_2] + 2C_6H_5CH_2NH_3^+Br^-$$

$$\downarrow$$

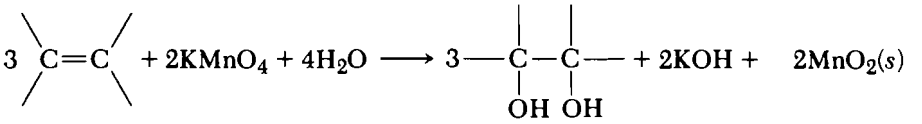
$$C_6H_5CN + 2HBr$$

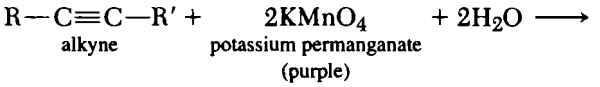
Certain tertiary amines such as pyridine form perbromides upon treatment with bromine:

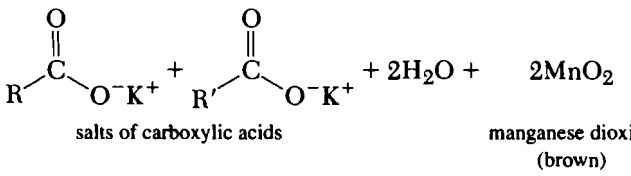


The bromine color is likewise discharged by aliphatic amines of all types.

Experiment 38 Potassium Permanganate Solution







(a) Baeyer Test—Aqueous Solutions

Add 0.1 g or 0.2 mL of the compound to 2 mL of water or ethanol. Add a 2% aqueous potassium permanganate solution drop by drop with shaking until the purple color of the permanganate persists.

If the permanganate color is not changed in 0.5–1 min, allow the tubes to stand for 5 min with occasional vigorous shaking. Do not be deceived by a slight reaction, which may be due to the presence of impurities.

The disappearance of the purple color and the formation of a brown suspension, which is manganese(II) oxide, at the bottom of the test tube is a positive indication for a carbon–carbon double or triple bond.

Controls 2-Pentene, benzaldehyde, allyl alcohol, and phenol will give a positive test. Hexane, acetone, and acetophenone will give a negative test.

Cleaning Up Place the test solution in the hazardous waste container.

(b) Phase Transfer Method Using Quaternary Ammonium Salts

Place 5 mL of the "purple benzene" reagent in a test tube and add one drop of distilled water and about 0.01 g of the unknown. Stopper the tube, shake, and then rock the tube back and forth holding it over a sheet of white paper to follow the change in color from purple to brown. The time required ranges from 30 sec to 5–15 min.

Controls 2-Pentene, cyclohexene, stilbene, and diphenylacetylene will give a positive test. Hexane, acetone, and acetophenone will give a negative test.

Compare the times required for these reactions against those for method A for the same compounds.

"Purple Benzene" Reagent

Prepare this reagent immediately prior to use. Dissolve 2 g of sodium chloride and 10 mg of potassium permanganate in 10 mL of distilled water. Place the solution in a 125-mL separatory funnel, and add 10 mL of benzene. *Note: Benzene is a known carcinogen. Use benzene in the hood, do not breathe the vapors, and avoid contact with the skin. Benzene is toxic; check with your instructor to see if a different solvent could be used.* Agitate the mixture gently, and allow the layers to separate. Note that the benzene layer is colorless; only the lower aqueous layer is purple. Next add 20 mg of tetrabutyl ammonium bromide to the mixture, agitate, and allow the layers to separate. The benzene layer should become deep purple due to the phase transfer of the permanganate anion along with the tetrabutyl ammonium cation from the aqueous layer into the benzene layer. The transfer is not complete; however, an equilibrium is established. Separate the layers and note the appearance of the purple benzene over 5 min. If the purple color changes to brown, the presence of impurities in the quaternary ammonium salt is indicated; prepare the reagent again after the quaternary salt is purified. Benzene is not oxidized by dilute permanganate at 20°C, since it is not olefinic but is aromatic.

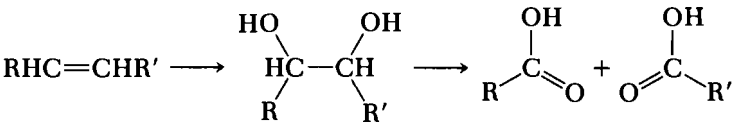
In addition to tetrabutyl ammonium bromide, tetrapentyl or tetrahexyl ammonium chloride or bromide may be used. Other long-chain quaternary ammonium halides have also been used.

Cleaning Up Place the benzene layer in the hazardous waste container for benzene. Place the aqueous layer in the aqueous solution container.

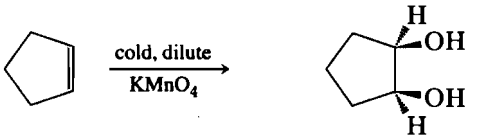
Discussion

Procedure (a) A solution of potassium permanganate is decolorized by compounds having ethylenic or acetylenic linkages. This is known as Baeyer's test for unsaturation.

In cold dilute solutions, the chief product of the action of potassium permanganate on an olefin is the glycol. If the reaction mixture is heated, further oxidation takes place, leading ultimately to cleavage of the carbon chain:

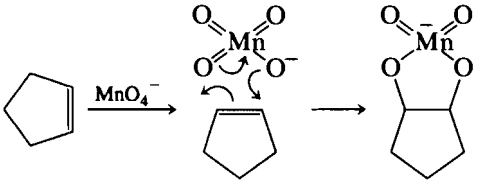


The mechanism for this dihydroxylation is well known and is supported by the fact that a *syn* addition takes place; that is, both hydroxyl groups are added from the same side.

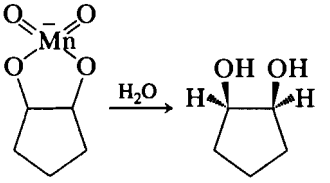


cyclopentene *cis*-1,2-dihydroxy-cyclopentanediol

This mechanism involves a concerted addition of two oxygen atoms of the permanganate ion to the face of the alkene.



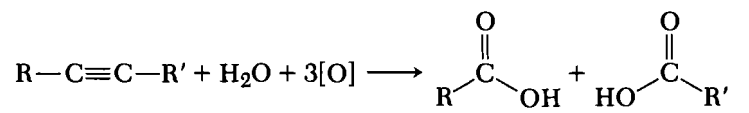
Hydrolysis of this bridged intermediate leaving the C—O bonds intact gives the *cis*-diol.



Although acetone rather than ethanol has sometimes been employed as a solvent for water-insoluble compounds, it has been found that certain carefully prepared olefins show a negative test in acetone but a positive one in ethanol. Ethanol does not react with neutral, dilute potassium permanganate at room temperature within 5 min.

Potassium permanganate in aqueous acetic acid has been used to distinguish among simple primary, secondary, and tertiary alcohols. Under the conditions of the test, primary and secondary alcohols undergo reaction but tertiary alcohols do not. In fact, *tert*-butyl alcohol can be a co-solvent for use in the Baeyer test. It is frequently used in place of ethanol or acetone above.

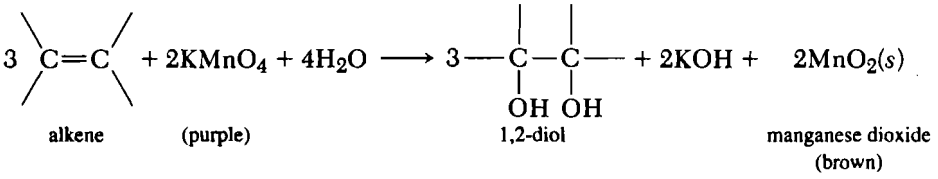
Acetylenic linkages are usually cleaved by oxidation and yield acids.



The speed with which unsaturated compounds decolorize potassium permanganate depends on the solubility of the organic compound. If the compound is very insoluble,

it is necessary to powder the compound and shake the mixture vigorously for several minutes or to dissolve the substance in a solvent unaffected by permanganate. A few tetrasubstituted olefins such as $C_6H_5CBr{=}CBrC_6H_5$ and $(C_6H_5)_2C{=}C(C_6H_5)_2$ fail to give positive tests with bromine in CCl_4 or the permanganate solutions above.

Inspection of the following equation shows that, as the reaction proceeds, the solution becomes alkaline:



It is necessary, however, to avoid using a solution that is strongly alkaline, as this changes the nature of the test. In sodium carbonate solution, even acetone gives a positive test. Frequently no actual precipitate of manganese dioxide is observed; the purple color gradually changes to a reddish brown.

However, the use of permanganate in neutral media is feasible. Thus, with zinc permanganate, the zinc hydroxide produced is only slightly soluble and the solution remains practically neutral. Also, it is possible to use potassium permanganate in the presence of magnesium sulfate to accomplish this objective. In this case, the hydroxyl ion is precipitated in the form of insoluble magnesium hydroxide.

The Baeyer test, though superior to the bromine test for unsaturated compounds, offers certain complications in its turn. All easily oxidizable substances give this test. Carbonyl compounds that decolorize bromine solutions generally give a negative Baeyer test. Acetone is a good example; although it decolorizes bromine solutions rapidly, it can be used as a solvent in the Baeyer test. Aldehydes give a positive Baeyer test; however, many of them, such as benzaldehyde and formaldehyde, do not decolorize bromine solutions. Formic acid and its esters, which have the O=CH— group, also reduce permanganate.

Alcohols form another important class of compounds that decolorize permanganate solutions but not bromine solutions. Pure alcohols do not give the test readily; however, they often contain impurities that are easily oxidized. Other types of compounds are also likely to contain slight amounts of impurities that may decolorize permanganate solutions. For this reason, the decolorization of only a drop of two of the permanganate solution cannot always be accepted as a positive test.

Phenols and arylamines also reduce permanganate solution and undergo oxidation to quinones; these may be further oxidized with an excess of the reagent to yield a series of oxidation products, among which are maleic acid, oxalic acid, and carbon dioxide.

Procedure (b) The phase transfer technique, using either long-chain quaternary ammonium salts or crown ethers, has become a valuable method for carrying out many types of reactions. For this qualitative Baeyer test, the use of the quaternary ammonium salts has given good results, whereas tests using samples of available crown ethers were erratic.

When a polar solvent such as water is placed in a flask with a nonpolar solvent such as benzene or another hydrocarbon, two layers will form; the less dense hydrocarbon layer will be the top layer. Normally, inorganic compounds such as $KMnO_4$ are highly ionic and polar, thus favoring the polar solvent. It is the role of the phase transfer catalyst to convert the inorganic reagent to a modified form that is soluble in the organic solvent.

Quaternary ammonium salts are very effective at this conversion and less expensive than crown ethers. One example is tetrabutyl ammonium bromide, $(CH_3CH_2CH_2CH_2)_4NBr$. The ionic character of this reagent causes it to be sufficiently soluble in the water layer, where it can undergo an ion exchange to form a new salt, $Q^+\ MnO_4^-$, which contains the permanganate oxidizing agent:

$$[Q^+ + Br^-] + [K^+ + MnO_4^-] \rightleftharpoons [Q^+ + MnO_4^-] + [K^+ + Br^-]$$

$$Q^+(aq) + MnO_4^-(aq) \rightleftharpoons \underset{\text{(nonpolar solvent)}}{Q^+MnO_4^-}$$

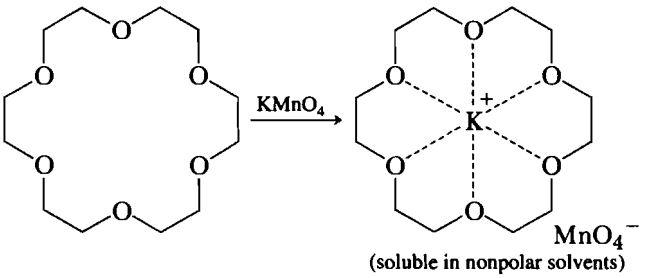
In the organic layer, the permanganate oxidizes the alkene to release the hydroxide and this transfers back into the aqueous layer to pick up more permanganate to repeat the cycle:

$$Q^+MnO_4^- + \text{>C=C<} \longrightarrow \text{—C(HO)—C(OH)—} + MnO_2 + Q^+OH^-$$

$$Q^+OH^- \xrightarrow[\text{transfer}]{\text{phase}} Q^+ + OH^-$$

$$[Q^+ + OH^-] + [K^+ + MnO_4^-] \rightleftharpoons [Q^+ + MnO_4^-] + [K^+ + OH^-]$$

In a similar way, crown ethers mask the K^+ ion to form complexes that are soluble in nonpolar solvents:



(soluble in nonpolar solvents)

Problems

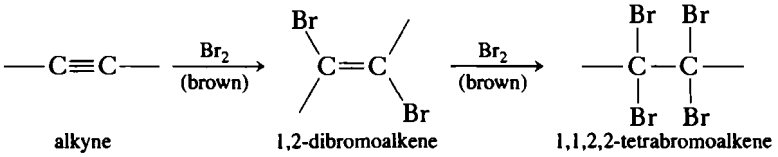
26. What functional groups respond to both the bromine and the permanganate tests?

27. Which of these tests is better for detecting the presence of multiple bonds? Explain.

28. In what instances is it helpful to use both reagents?

9.15 HYDROCARBONS—ALKYNES

Alkynes give a positive test with bromine (Experiment 37, p. 326) and potassium permanganate (Experiment 38, p. 328). Bromine adds across the carbon–carbon triple bond, with the bromine color of the solution dissipating. Potassium permanganate oxidizes alkynes to carboxylic acids, concurrently with the reduction of the manganese from an oxidation state of +7, a purple color, to +4, a brown color.



alkyne — 1,2-dibromoalkene (colorless) — 1,1,2,2-tetrabromoalkene (colorless)

$$\underset{\text{alkyne}}{R{-}C{\equiv}C{-}R'} + \underset{\substack{\text{potassium permanganate}\\(\text{purple})}}{2KMnO_4} + 2H_2O \longrightarrow \underset{\text{salts of carboxylic acids}}{R{-}\overset{O}{\overset{\|}{C}}{-}O^-K^+ + R'{-}\overset{O}{\overset{\|}{C}}{-}O^-K^+} + 2H_2O + \underset{\substack{\text{manganese dioxide}\\(\text{brown})}}{2MnO_2}$$

Terminal alkynes react with sodium to liberate hydrogen gas and form a salt (Experiment 5, p. 262).

$$\underset{\text{terminal alkyne}}{H{-}C{\equiv}C{-}H} + 2Na \longrightarrow Na^+\,{}^-C{-}C{\equiv}C^-\,Na^+ + H_2(g)$$

$$\underset{\text{terminal alkyne}}{2R{-}C{\equiv}C{-}H} + 2Na \longrightarrow 2R{-}C{\equiv}C^-\,Na^+ + H_2(g)$$

▶ PROBLEM

29. Give the equations for a test that will distinguish between 1-butyne and 2-butyne.

▶ 9.16 HYDROCARBONS—AROMATIC

If the results of preliminary chemical tests suggest aromatic character for an unknown, then a variety of tests can be used to chemically characterize this class of organic compound. Specifically, new substituents can be added onto the aromatic ring or existing substituents can be modified, such that the new compound may be more readily characterized. If the molecule already contains reactive chemical substituents (acids, amines, ethers, carbonyl compounds, etc.), the chemist is referred to other sections for that particular group.

The most vigorous test will be described first, and the tests that follow will be described in decreasing order of the severity of conditions. A few of the most inert aromatic compounds may remain unchanged after even the most vigorous test; characterization of those compounds may rely more on the spectral and physical tests than is usually the case.

Fuming sulfuric acid converts aromatic compounds to arylsulfonic acids (Experiment 39, p. 334). The aromatic compound dissolves completely with the evolution of heat.

$$\underset{\text{aromatic compound}}{ArH} \xrightarrow[SO_3]{H_2SO_4} \underset{\text{arylsulfonic acid}}{ArSO_3H} + \text{heat}$$

The reaction of aromatic compounds with azoxybenzene and aluminum chloride gives rise to 4-arylazobenzene, with the color of the solution or precipitate indicating particular functional groups (Experiment 40, p. 336).

$$\underset{\text{aromatic compound}}{ArH} + \underset{\text{azoxybenzene}}{\text{azoxybenzene}} \xrightarrow{AlCl_3} \underset{\substack{\text{4-arylazobenzene}\\(\text{colored complex})}}{[Ar{-}C_6H_4{-}N{=}N{-}C_6H_5]\,AlCl_3}$$

Aromatic compounds react with chloroform and aluminum chloride to produce triaryl carbocations in a variety of colors, dependent upon the functional groups on the aryl ring (Experiment 41, p. 337).

$$\underset{\text{aromatic compound}}{3ArH} + CHCl_3 \xrightarrow{AlCl_3} \underset{\text{triarylmethane}}{Ar_3CH} + 3HCl$$

$$\underset{\text{triarylmethane}}{Ar_3CH} + R^+ \longrightarrow \underset{\substack{\text{triaryl carbocation}\\ \text{(colored)}}}{Ar_3C^+} + RH$$

The triaryl carbocations are in solution as $Ar_3C^+\ AlCl_4^-$ salts and are responsible for the colors observed.

Experiment 39 Fuming Sulfuric Acid

$$\underset{\text{aromatic compound}}{ArH} \xrightarrow[SO_3]{H_2SO_4} \underset{\text{arylsulfonic acid}}{ArSO_3H} + \text{heat}$$

Caution: *Use this reagent with relatively inert compounds only, such as those compounds that do not dissolve in the solubility tests with concentrated sulfuric acid. Compounds for which preliminary tests indicate highly activating groups (OH, NH_2, etc.) may be decomposed violently by fuming sulfuric acid.*

This test must be done in a hood. Place 0.5 mL of 20% fuming sulfuric acid (*hazardous*) in a clean, dry test tube, and add 0.25 mL or 0.25 g of the unknown. Shake the mixture vigorously, and allow it to stand for a few minutes. A positive test for the presence of an aromatic ring is complete dissolution of the unknown, evolution of heat, and minimal charring.

Controls Benzene and bromobenzene will give a positive test. 1,2-Dibromoethane and cyclohexane will give a negative test.

Cleaning Up In the hood, pour the test solution into a large beaker containing 10 mL of water. Add sodium carbonate, a few crystals at a time, until the foaming ceases. Place the solution in the aqueous solution container.

Discussion

Before considering fuming sulfuric acid, some of the properties of sulfuric acid need to be reviewed. Concentrated sulfuric acid is a remarkable solvent in two respects. Its dielectric constant appears to be very much greater than that of many other compounds for which this property has been measured.[27] Thus, forces of attraction between dissolved ions are so small in dilute solution that activity coefficients may be taken as unity.

$$2H_2SO_4 \rightleftharpoons H_3SO_4^+ + HSO_4^-$$

The second unusual property is that, in addition to the autoprotolysis like that found in hydroxylic solvents (such as water), there is a self-dissociation resulting initially in the formation of sulfur trioxide and water. However, at the concentrations concerned, each

[27]R. J. Gillespie, E. D. Hughes, and C. K. Ingold, *J. Chem. Soc.*, 2473 (1950).

of these reacts essentially completely with sulfuric acid so that the overall equilibrium is as follows:

$$\begin{array}{rr} (1) & H_2SO_4 \rightleftharpoons H_2O + SO_3 \\ (2) & SO_3 + H_2SO_4 \rightleftharpoons HSO_3^+ + HSO_4^- \\ (3) & H_2O + H_2SO_4 \rightleftharpoons H_3O^+ + HSO_4^- \\ \hline & 3H_2SO_4 \rightleftharpoons HSO_3^+ + H_3O^+ + 2HSO_4^- \end{array}$$

Also:

$$H_2SO_4 + HSO_3^+ + HSO_4^- \rightleftharpoons H_3SO_4^+ + HSO_7^-$$

Concentrated sulfuric acid converts ethylene to ethyl hydrogen sulfate, but sulfuric acid containing added sulfur trioxide (fuming sulfuric acid) yields ethionic acid, as shown below. The reason for the difference between the two sets of conditions is understood if it is realized that 100% sulfuric acid contains sulfonating species such as SO_3 or HSO_3^+ in small concentration and therefore the sulfonating reagent fails to compete with proton addition, the first step in alkyl sulfate formation:

$$H_2C{=}CH_2 + H_2SO_4 \longrightarrow CH_3CH_2^+ + HSO_4^-$$

However, in fuming sulfuric acid, the addition of HSO_3^+, SO_3, or some other sulfonating agent to the double bond becomes important, so that the principal reaction is the following:

$$H_2C{=}CH_2 + HSO_3^+ \longrightarrow {}^+CH_2CH_2SO_3H$$

In each case the second step is the same: the reaction of the carbocation with the bisulfate ion.

$$CH_3CH_2^+ + HSO_4^- \longrightarrow \underset{\substack{\text{ethyl hydrogen}\\ \text{sulfate}}}{CH_3CH_2OSO_3H}$$

$${}^+CH_2CH_2OSO_3H + HSO_4^- \longrightarrow \underset{\text{ethionic acid}}{HO_3SOCH_2CH_2OSO_3H}$$

The first step in the formation of the ethionic acid is, at least formally, like the first step in aromatic substitution.

The action of fuming sulfuric acid on 1,2-dihalo compounds is complex. The mixture turns dark, and some free halogen is liberated. It seems probable that loss of hydrogen halide occurs followed by polymerization of the vinyl halide. For example, 1,2-dibromoethane probably undergoes the following changes.

$$BrH_2C{-}CH_2Br \longrightarrow H_2C{=}CHBr + HBr$$

$$n H_2C{=}CHBr \longrightarrow -\!\left(CH_2{-}\underset{\displaystyle Br}{\underset{|}{CH}}\right)_n\!-$$

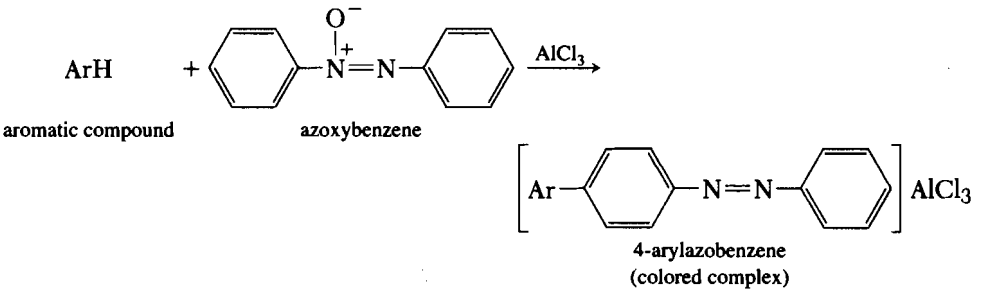
$$2HBr + H_2SO_4 \longrightarrow Br_2 + SO_2 + 2H_2O$$

Problems

30. Note that this test is useful only for compounds insoluble in sulfuric acid. Why?

31. Write equations for the reaction of sulfuric acid with 1-hexene. Compare the products of this reaction with those formed in your solubility test with concentrated sulfuric acid (pp. 128–130).

Experiment 40 Azoxybenzene and Aluminum Chloride



Place 0.5 mL or 0.4 g of the dry compound in a clean, dry test tube; add one crystal of azoxybenzene and about 25 mg of anhydrous aluminum chloride. Note the color. If no color is produced immediately, warm the mixture for a few minutes. Wait for up to 30 min to observe any color change. If the hydrocarbon is a solid, a solution of 0.5 g of it in 2 mL of dry carbon disulfide may be used.

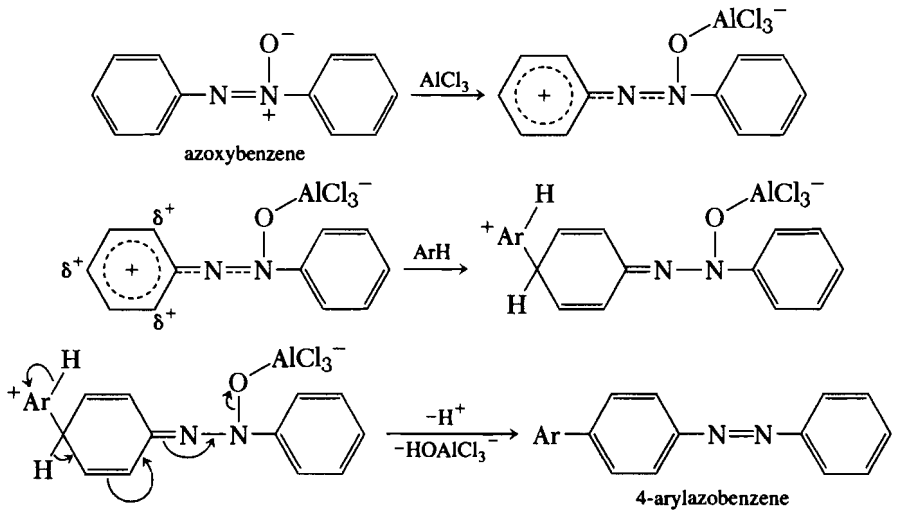
Controls Chlorobenzene and naphthalene give a positive test. Petroleum ether and ethyl bromide give a negative test.

Cleaning Up Place the reaction mixture in the organic solvent container.

Discussion

The color produced is due to an addition compound formed from the 4-arylazobenzene and aluminum chloride. Many oxygen functions interfere with this test and may give confusing color changes.

The 4-arylazobenzene is formed from the aromatic substitution of the aromatic compound by aluminum chloride, followed by the elimination of water and aluminum chloride:



Aromatic hydrocarbons and their halogen derivatives produce a deep-orange to dark-red color in solution or give a precipitate. Fused aromatic rings such as naphthalene, anthracene, and phenanthrene produce brown colors. Aliphatic hydrocarbons give no color or, at most, a pale yellow.

Experiment 41 Chloroform and Aluminum Chloride

$$\underset{\text{aromatic compound}}{3ArH} + CHCl_3 \xrightarrow{AlCl_3} \underset{\text{triarylmethane}}{Ar_3CH} + 3HCl$$

$$\underset{\text{triarylmethane}}{Ar_3CH} + R^+ \longrightarrow \underset{\substack{\text{triaryl carbocation}\\ \text{(colored)}}}{Ar_3C^+} + RH$$

Add 0.1 mL or 0.1 g of the unknown compound to 2 mL of dry chloroform in a test tube. Mix thoroughly, and incline the test tube so as to moisten the wall. Then add 0.5–1.0 g of anhydrous aluminum chloride so that some of the powder strikes the side of the test tube. Note the color of the powder on the side, as well as the solution.

Controls Biphenyl, chlorobenzene, toluene, and naphthalene give a positive test. Petroleum ether and hexane give a negative test.

Cleaning Up Place the test solution in the halogenated organic waste container.

Discussion

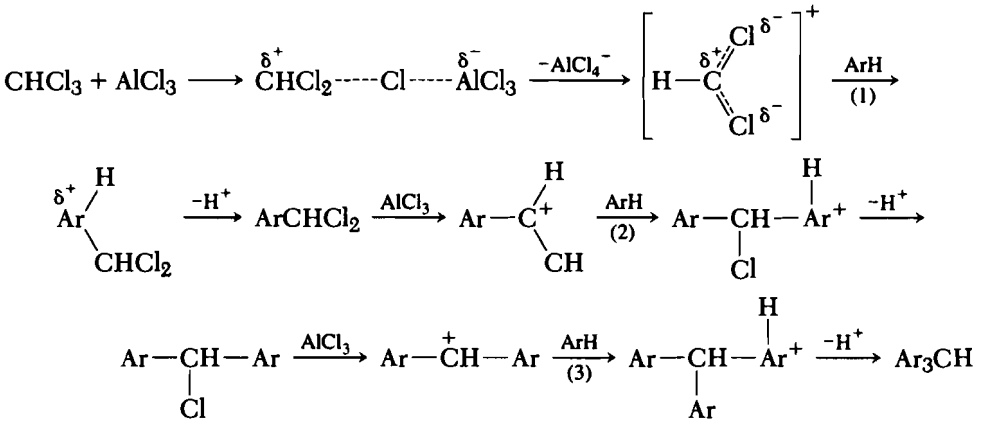
The colors produced by the reaction of aromatic compounds with chloroform and aluminum chloride are quite characteristic. Aliphatic compounds, which are insoluble in sulfuric acid, give no color or only a very light yellow. Typical colors produced are the following:

Compound	*Color*
Benzene and its homologs	Orange to red
Aryl halides	Orange to red
Naphthalene	Blue
Biphenyl	Purple
Phenanthrene	Purple
Anthracene	Green

With time the colors change to various shades of brown. Similar colors are obtained when chloroform is replaced by carbon tetrachloride.

Aromatic esters, ketones, amines, and other oxygen- or nitrogen-containing compounds may also give blue or green colors. This test should be used in conjunction with other tests to confirm the presence or absence of an aromatic structure.

The reaction begins as three successive (1–3 below) Friedel–Crafts reactions between the aromatic and chlorinated hydrocarbons. These alkylation reactions are promoted by the Lewis acid, aluminum chloride, and facilitated by positive delocalization by the chlorine and the aryl groups.



Partially substituted chlorides (e.g., Ar_2CHCl or $ArCHCl_2$) may undergo reaction with aluminum chloride to give mono or diaryl carbocations:

$$Ar_2CHCl + AlCl_3 \longrightarrow Ar_2CH^+ + AlCl_4^-$$

The hydride leaves from the triarylmethane to give rise to stable triaryl carbocation.

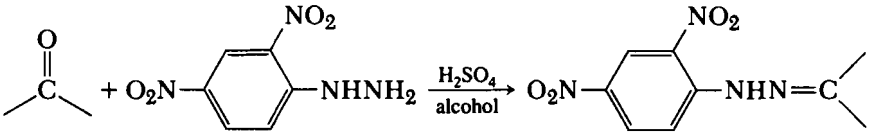
$$Ar_3CH + Ar_2CH^+ \longrightarrow \underset{\text{(colored)}}{Ar_3C^+} + Ar_2CH_2$$

▶ Problem

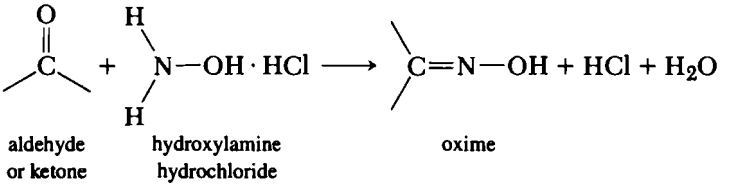
32. Propose a reason why tetraarylmethanes are not formed.

▶ 9.17 KETONES

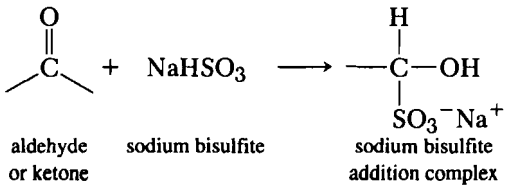
Many of the same reactions that are described above (Section 9.4, pp. 276–286) in the classification of aldehydes can also be used to classify ketones. The addition of 2,4-dinitrophenylhydrazine to ketones to precipitate the 2,4-dinitrophenylhydrazones (Experiment 12, p. 278) is probably the most useful of these reactions.



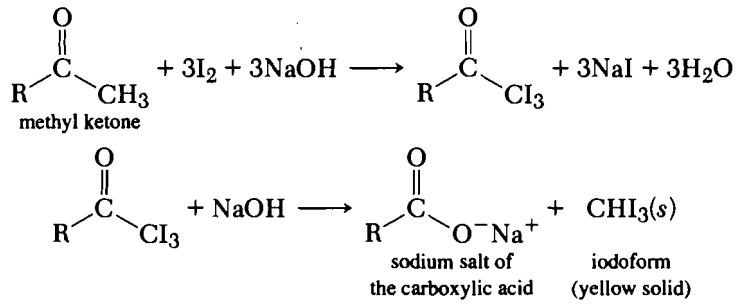
The reaction of hydroxylamine hydrochloride with ketones (Experiment 13, p. 280) produces oximes and results in the liberation of hydrogen chloride, which can be detected by an indicator.



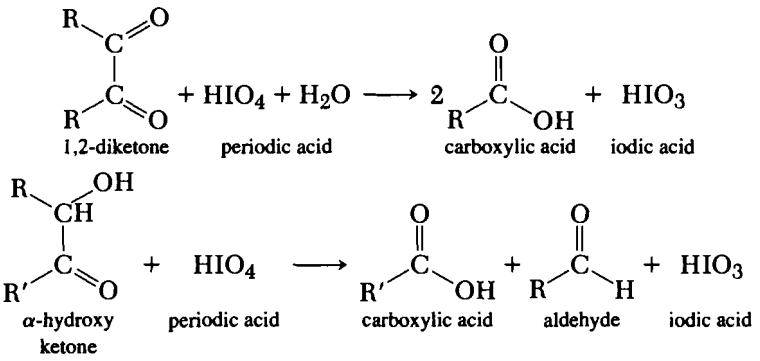
The precipitation of a bisulfite addition complex (Experiment 14, p. 281) is indicative of a variety of carbonyl compounds. This reaction is greatly influenced by the steric environment of the carbonyl group.



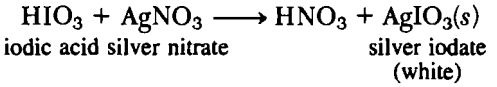
The iodoform test (Experiment 11, p. 273) will give positive results with methyl ketones. A positive test is indicated by the precipitation of iodoform, a foul-smelling yellow solid.



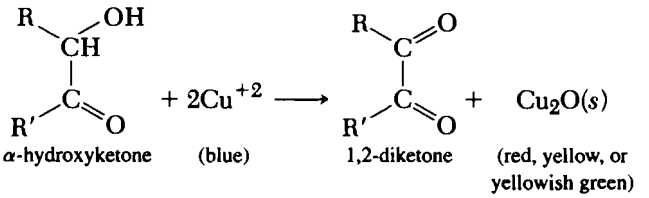
1,2-Diketones and α-hydroxy ketones are oxidized with periodic acid (Experiment 27, p. 308).



The iodic acid is detected with 5% silver nitrate solution. An immediate precipitation of silver iodate occurs.

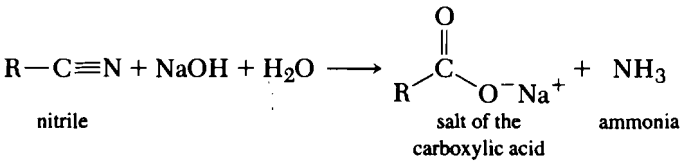


Benedict's solution (Experiment 28, p. 310) and Fehling's solution (Experiment 29, p. 311) will undergo reaction with reducing sugars such as α-hydroxy ketones. The solution is initially a blue color from Cu^{+2} complex, but as the reaction proceeds, copper(I) oxide precipitates as a red, yellow, or yellowish-green solid.

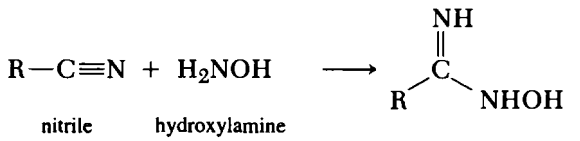


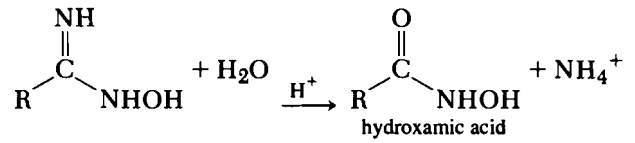
9.18 NITRILES

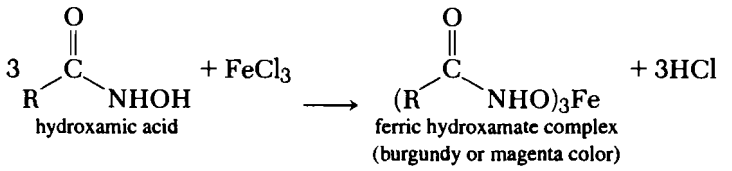
Nitriles can be hydrolyzed under basic conditions to yield the salt of the carboxylic acid and ammonia (Experiment 18, p. 287). The ammonia vapor is detected by litmus paper.



Nitriles, along with many other compounds, give a positive hydroxamic acid test (Experiment 2c, p. 254). The hydroxamic acid is detected with ferric chloride to form the ferric hydroxamate complex, which has a burgundy or magenta color.

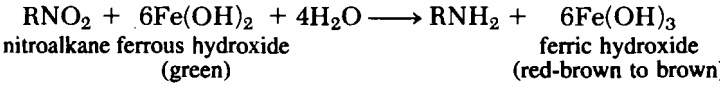






9.19 NITRO COMPOUNDS

The presence of a nitro group is detected in several different ways. In the ferrous hydroxide reduction (Experiment 42, p. 341), a positive test is noted by the change in color from green to red-brown or brown due to the oxidation of iron from +2 to +3.

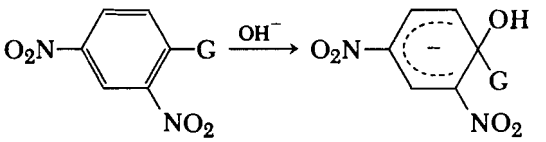


Of the nitro compounds, only tertiary aliphatic nitro compounds and aromatic nitro compounds are reduced by zinc and ammonium chloride (Experiment 43, p. 342) to the hydroxylamine. The hydroxylamine is then detected by the formation of metallic silver in the Tollens test (Experiment 15, p. 283).

$$\underset{\text{nitro compound}}{RNO_2} + 4[H] \xrightarrow[NH_4Cl]{Zn} \underset{\text{hydroxylamine}}{RNHOH} + H_2O$$

$$RNHOH + \underset{\text{Tollens reagent}}{2Ag(NH_3)_2OH} \longrightarrow RNO + 2H_2O + 2Ag(s) + 4NH_3$$

The number of nitro groups on an aromatic ring can be determined by the reaction of the unknown with sodium hydroxide (Experiment 44, p. 342). In the reaction with sodium hydroxide, the mononitro aromatic compounds yield no color change, dinitro aromatic compounds produce a bluish-purple color, and trinitro aromatic compounds give a red color. The color of the solution is due to a Meisenheimer complex.



Meisenheimer complex

Experiment 42 Ferrous Hydroxide Reduction

$$\underset{\text{nitroalkane}}{RNO_2} + \underset{\substack{\text{ferrous hydroxide}\\\text{(green)}}}{6Fe(OH)_2} + 4H_2O \longrightarrow RNH_2 + \underset{\substack{\text{ferric hydroxide}\\\text{(red-brown to brown)}}}{6Fe(OH)_3}$$

Add 10 mg of the compound to 1 mL of the ferrous sulfate reagent in a test tube, and then add 0.7 mL of the alcoholic potassium hydroxide reagent. Insert a glass tube so that it reaches the bottom of the test tube, and pass a stream of inert gas through the tube for about 30 sec in order to remove air. Stopper the tube quickly, and shake. Note the color of the precipitate after 1 min. A positive test is the formation of the red-brown to brown precipitate of iron(III) hydroxide.

Controls Nitrobenzene, 3-nitroaniline, and nitromethane will give a positive test. Ethanol and 2-propanol will give a negative test.

Ferrous Sulfate Reagent
Add 5.0 g of ferrous ammonium sulfate crystals to 100 mL of recently boiled, distilled water. Add 0.4 mL of concentrated sulfuric acid. Add an iron nail to retard air oxidation.

Alcoholic Potassium Hydroxide Reagent
Dissolve 3 g of potassium hydroxide in 3 mL of distilled water. Add this solution to 100 mL of 95% ethanol.

Cleaning Up Isolate the solid by filtration and place in the nonhazardous solid waste container. Neutralize the filtrate with 10% hydrochloric acid and place in the aqueous solution container.

Discussion
The red-brown to brown precipitate[28] of iron(III) hydroxide (ferric hydroxide) is formed by the oxidation of iron(II) hydroxide (ferrous hydroxide) by the nitro compound, which in turn is reduced to the primary amine. A negative test is indicated by a greenish

[28]W. M. Hearson and R. G. Gustavson, *Ind. Eng. Chem., Anal. Ed.*, 9, 352 (1937).

precipitate. In some cases partial oxidation may cause a darkening of the ferrous hydroxide.

Practically all nitro compound give a positive test in 30 sec. The speed with which the nitro compound is reduced depends on its solubility. 4-Nitrobenzoic acid, which is soluble in the alkaline reagent, gives a test almost immediately, whereas 2-nitronaphthalene must be shaken for 30 sec.

A positive test is also given by other compounds that oxidize ferrous hydroxide. Nitroso compounds, quinones, hydroxylamines, alkyl nitrates, and alkyl nitrites are in this group. Highly colored compounds cannot be tested.

Experiment 43 Zinc and Ammonium Chloride Reduction

$$\underset{\text{nitro compound}}{RNO_2} + 4[H] \xrightarrow[NH_4Cl]{Zn} \underset{\text{hydroxylamine}}{RNHOH} + H_2O$$

$$RNHOH + \underset{\text{Tollens reagent}}{2Ag(NH_3)_2OH} \longrightarrow RNO + 2H_2O + 2Ag(s) + 4NH_3$$

Dissolve 0.2 mL or 0.2 g of the unknown in 4 mL of 50% ethanol, and add 0.2 g of ammonium chloride and 0.2 g of zinc dust. Shake, and heat to boiling. Allow to stand for 5 min, filter, and test the action of the filtrate on Tollens reagent (Experiment 15, p. 283). A positive test with Tollens reagent is the formation of a black or gray precipitate, or a silver mirror.

Controls Nitrobenzene and 3-nitroaniline will give a positive test. Ethanol will give a negative test.

Cleaning Up Pour the solution into a beaker. Add a few drops of 5% nitric acid to dissolve the silver mirror or colloidal silver. Combine all solutions. Make the solution acidic with 5% nitric acid, then neutralize with sodium carbonate. Add 2 mL of saturated sodium chloride solution to precipitate the silver as silver chloride. Isolate the silver chloride by filtration and place in the nonhazardous solid waste container. Place the filtrate in the aqueous solution container.

Discussion

This test depends on the reduction of the unknown to a hydrazine, a hydroxylamine, or an aminophenol; all these compounds are oxidized by Tollens reagent.

This test cannot be applied if the original compound reduces Tollens reagent.

Tertiary aliphatic compounds and aromatic nitro compounds give a positive test. Nitroso, azoxy, and azo compounds are reduced with zinc and ammonium chloride, with the products being oxidized by the Tollens reagent.

Experiment 44 Treatment of Aromatic Nitro Compounds with Sodium Hydroxide

To 5 mL of 20% sodium hydroxide solution add 2 mL of ethanol and a drop or a crystal of the unknown, and shake vigorously. Note the color of the solution.

Alternatively, dissolve 0.1 g of the unknown in 10 mL of acetone and add, with shaking, 2–3 mL of 10% sodium hydroxide solution. Note the color of the solution.

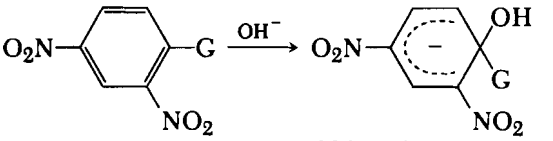
Controls Nitrobenzene and 1,3-dinitrobenzene will give a positive test. Ethanol will give a negative test.

Cleaning Up Place the test solution in the aqueous solution container.

Discussion

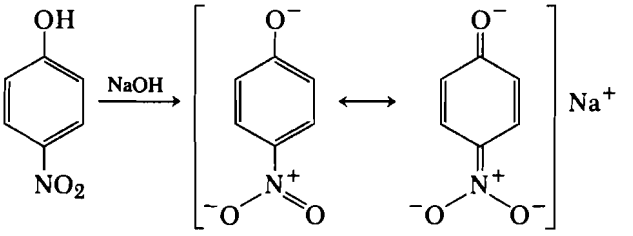
Mononitro benzene compounds give no color or a very light yellow with these reagents. If two nitro groups on the same ring are present, a bluish-purple color develops; the presence of three nitro groups produces a blood-red color. The presence of an amino, substituted amino, or hydroxyl group in the molecules inhibits the formation of the characteristic red and purple colors.

Polynitro compounds can form Meisenheimer complexes, which may lead to colored solution.



Meisenheimer complex

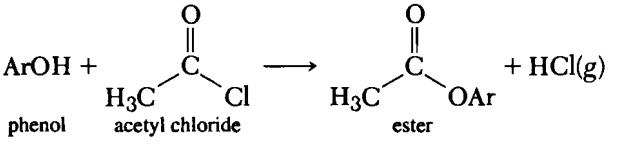
Nitrophenols can form highly conjugated and stable phenoxide anions that may be a source of color:



9.20 PHENOLS

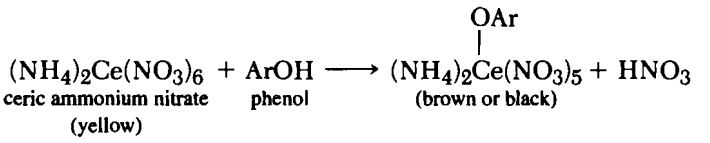
As with alcohols, the acidic hydrogen in a phenol can be detected with sodium (Experiment 5, p. 262) or acetyl chloride (Experiment 6, p. 264). Hydrogen gas is evolved with sodium, and an ester layer is formed with acetyl chloride.

$$\underset{\text{phenol}}{2ArOH} + 2Na \longrightarrow 2ArO^-Na^+ + H_2(g)$$



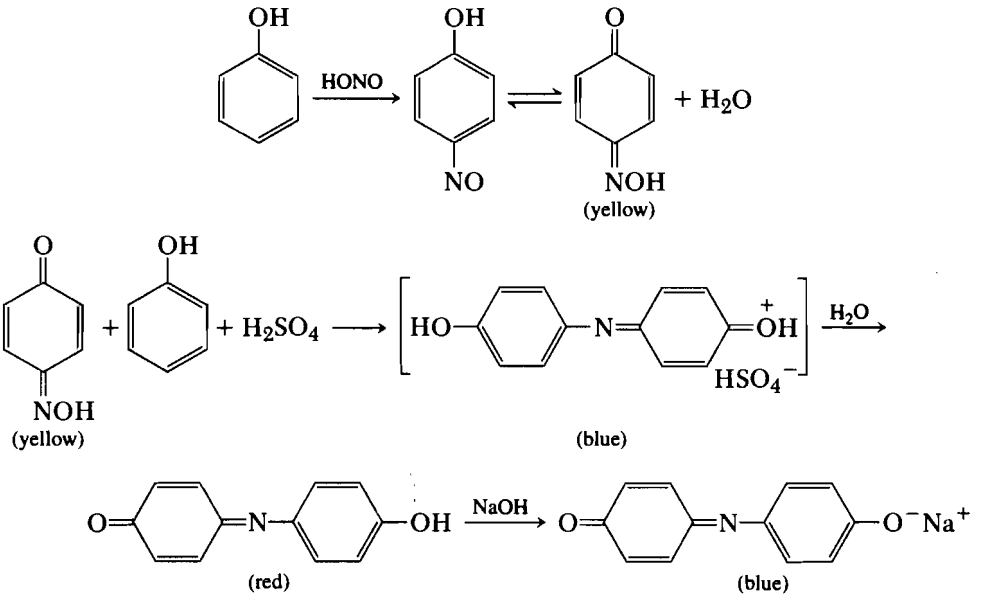
phenol acetyl chloride ester

Phenols undergo reaction with the yellow ceric ammonium nitrate (Experiment 7, p. 265) to produce brown or black products.

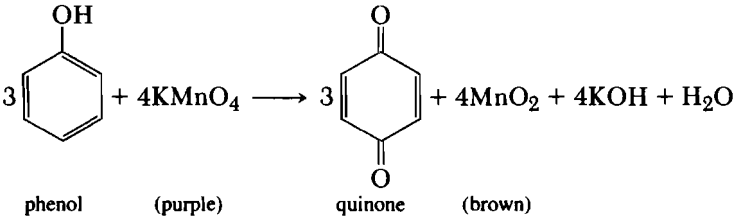


ceric ammonium nitrate (yellow) phenol (brown or black)

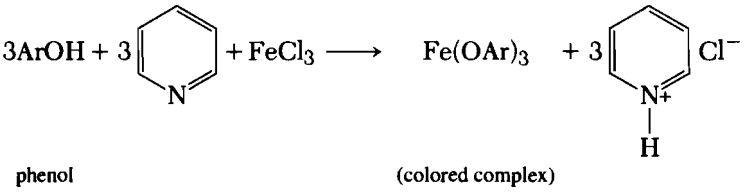
A modification of Liebermann's test (Experiment 20d, p. 297) can be used to test for the presence of a phenol. A blue intermediate is formed, which changes to red when diluted and blue when the solution is made basic.



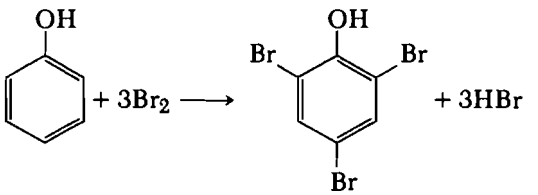
Phenols reduce potassium permanganate solutions and undergo oxidation to quinones; an excess of the reagent yields a series of oxidation products, including maleic acid, oxalic acid, and carbon dioxide (Experiment 38, p. 328). The manganese is reduced from +7, which gives a purple solution, to +4, which is brown.



Phenols can be detected by treatment with ferric chloride (Experiment 45, p. 345). The procedure using pyridine solvent has resulted in accurate results in 90% of the phenolic substrates tested; previous procedures using water or alcohol–water solvents had only a 50% success rate. The color of the solution changes immediately to blue, violet, purple, green, or red-brown.

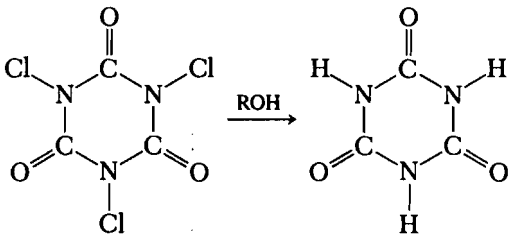


Since the aromatic nucleus of a phenol is substantially more reactive toward electrophilic aromatic substitution than benzene, bromination of phenols should be carried out under mild conditions (Experiment 46, p. 347). The discharge of the bromine color is a positive test.



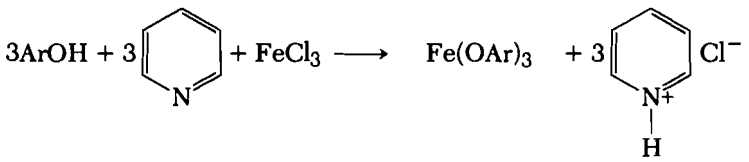
phenol — 2,4,6-tribromophenol

The TCICA test (Experiment 10, p. 271) can be utilized to identify aldehydes, alcohols, and phenols. The trichloroisocyanuric acid is reduced to cyanuric acid, a white solid. Phenols react in 1–15 sec.



trichloroisocyanuric acid — cyanuric acid (white solid)

Experiment 45 Ferric Chloride–Pyridine Reagent



phenol — (colored complex)

This test must be done in the hood. Add 30 to 50 mg of the solid unknown or four to five drops of the liquid unknown to 2 mL or pure chloroform in a clean, dry test tube. Stir the solution. If the unknown does not seem to dissolve, even partially, add an additional 2–3 mL of chloroform and warm gently. Cool to 25°C and add two drops of 1% solution of anhydrous ferric chloride in chloroform followed by three drops of pyridine. Shake the tube and note the color produced *immediately*. A positive test is shown by production of a blue, violet, purple, green, or red-brown solution. Frequently the colors change in a few minutes.

Controls Phenol, 4-cresol, 2-nitrophenol, and 3-bromophenol will give a positive test. Hexane and 2-propanol will give a negative test.

1% Ferric Chloride in Chloroform

Add 1 g of the black crystals of *anhydrous* ferric chloride to 100 mL of pure chloroform. Shake the mixture occasionally for about an hour, and allow to stand to permit the insoluble material to settle. Decant the pale-yellow solution into a screw-cap bottle fitted with a medicine dropper.

Cleaning Up Place the test solution in the halogenated organic waste container.

Discussion

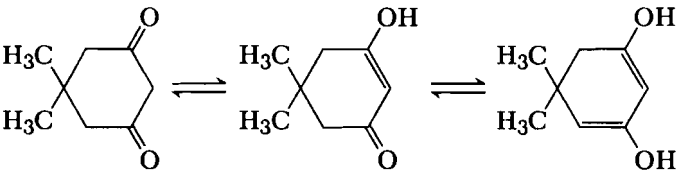
This reagent is useful for detecting compounds containing a hydroxyl group directly attached to an aromatic nucleus. Treatment of chloroform solutions of phenols, naphthols, and their ring-substituted derivatives with a chloroform solution of anhydrous ferric chloride and pyridine produces characteristic blue, violet, purple, green, or red-brown complexes.

Alcohols, ethers, aldehydes, acids, ketones, hydrocarbons, and their halogen derivatives give negative results of colorless, pale-yellow, or tan solutions.

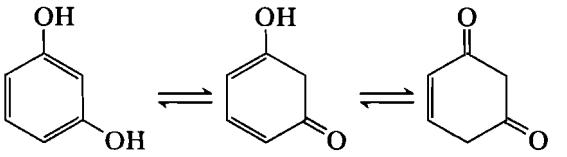
This method is especially valuable for substituted phenols and naphthols that are very insoluble in water. Even 2,4,6-trichlorophenol, 2,4,6-tribromophenol, nonylphenol, phenolphthalein, and thymolphthalein give positive tests provided that sufficient chloroform (about 5 mL) is used to get them into solution.

Phenolic compounds that have failed to give positive tests are picric acid, 2,6-di-*tert*-butylphenol, phenolsulfonic acid, naphtholsulfonic acid, hydroquinone, *dl*-tyrosine, 4-hydroxylphenylglycine, and 4-hydroxybenzoic acid. The 4-hydroxybenzoic acid gives a distinct yellow color, a negative result, whereas salicylic acid gives a violet color, a positive test. The esters of 4-hydroxybenzoic acid produce purple colors and 4-hydroxybenzaldehyde a violet-purple color.

It is of interest that 5,5-dimethyl-1,3-cyclohexandione (dimedon, methone) gives a beautiful purple color. Resorcinol gives a blue-violet color. Note that several of the tautomeric forms of these compounds are similar in structure to tautomeric forms of phenols.

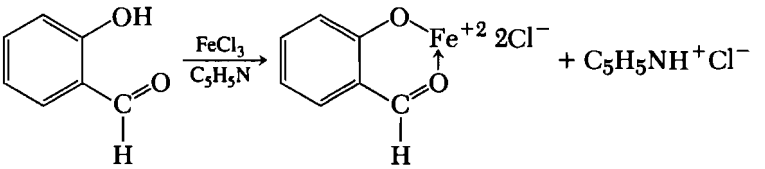


dimedon



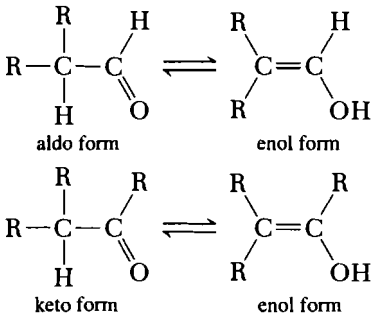
resorcinol

Salicylaldehyde forms a highly colored complex with ferric chloride:



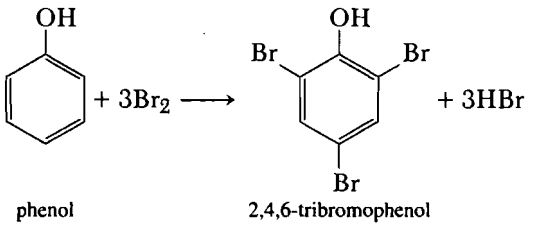
salicylaldehyde (colored complex)

In aqueous or aqueous alcoholic solutions, some enols, oximes, and hydroxamic acids produce red-, brown-, or magenta-colored complexes with *aqueous* ferric chloride. In aqueous solutions, aldehydes and ketones with α-hydrogens may tautomerize to the enol form, which will then give a violet-, red-, or tan-colored complex with the ferric chloride.



However, in this anhydrous chloroform test, these compounds give yellow or pale-tan solutions quite different from the phenols.

Experiment 46 Bromine Water



Dissolve 0.1 g of the unknown in 10 mL of water. Add bromine water drop by drop until the bromine color is no longer discharged. The discharge of the bromine color is a positive test. In some cases, a white precipitate (the brominated phenol) may also be formed.

Controls Phenol and aniline will give a positive test. Salicylic acid will give a negative test.

Cleaning Up Place the test solution in the halogenated organic waste container.

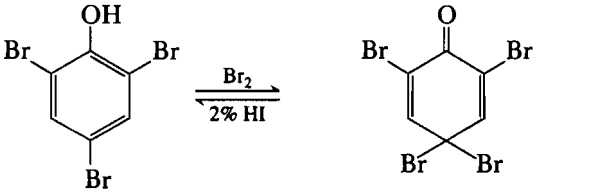
Discussion

It has been shown that, in the bromination of benzene and 2-nitroanisole with bromine water, the brominating agent operates by complex mechanisms.

Mercaptans are oxidized readily by bromine water to disulfides.

$$2RSH + Br_2 \longrightarrow RSSR + 2HBr$$

The advantage of bromine in water over bromine in carbon tetrachloride or methylene chloride is that the more polar solvent greatly increases the rate of bromination by the ionic mechanism. Of course, it is impossible with this solvent to observe the evolution of hydrogen bromide. An excess of bromine water converts tribromophenol to a yellow tetrabromo derivative, 2,4,4,6-tetrabromocyclohexadienone. The tetrabromo compound is readily converted to the tribromophenol by washing with 2% hydroiodic acid.



2,4,6-tribromophenol 2,4,4,6-tetrabromocyclohexadienone

Problems

33. Will tribromoaniline give a positive test? Explain your answer.
34. Could the decolorization of the bromine water result from the presence of an inorganic compound?
35. Is bromine hydrolyzed in water?
36. Explain the following order of reactivity toward electrophilic bromine: $C_6H_5O^- > C_6H_5OH >> C_6H_6$.

For more discussion of the reaction of bromine with organic compounds, consult Experiment 37, p. 326.

9.21 SULFONAMIDES, SULFONIC ACIDS, SULFONYL CHLORIDES

The presence of sulfonamides can be detected by fusing with sodium hydroxide (Experiment 47, p. 349) and testing for the evolution of amine or ammonia and of sulfur dioxide.

$$\underset{\text{sulfonamide}}{ArSO_2NH_2} + 2NaOH \longrightarrow ArONa + NaHSO_3 + \underset{\text{ammonia}}{NH_3(g)}$$

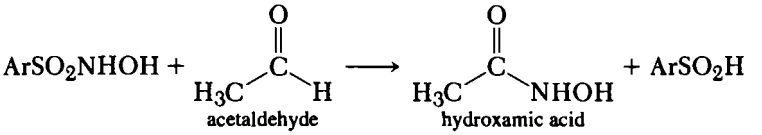
$$NaHSO_3 + HCl \longrightarrow \underset{\text{sulfur dioxide}}{SO_2(g)} + NaCl + H_2O$$

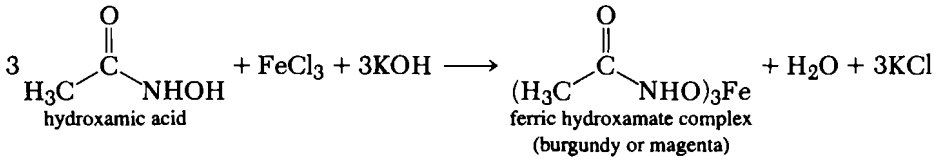
Sulfonic acids are structurally different from sulfuric acid only in that an organic group has been substituted for one hydroxyl group, and thus the high acid strength of sulfonic acids is not surprising. Sulfonic acids and their metal salts are usually soluble in water.

Sulfonyl chlorides and sulfonic acids can be detected through the hydroxamic acid test (Experiment 2e, p. 255). The sulfonyl chloride is produced from the sulfonic acid and thionyl chloride. The sulfonyl chloride is treated with hydroxylamine, which undergoes reaction with acetaldehyde to form the hydroxamic acid. The hydroxamic acid undergoes reaction with ferric chloride to form the ferric hydroxamate complex, which is a burgundy or magenta color.

$$\underset{\substack{\text{sulfonic}\\\text{acid}}}{ArSO_3H} + \underset{\substack{\text{thionyl}\\\text{chloride}}}{SOCl_2} \longrightarrow \underset{\substack{\text{sulfonyl}\\\text{chloride}}}{ArSO_2Cl} + HCl + SO_2$$

$$\underset{\substack{\text{sulfonyl}\\\text{chloride}}}{ArSO_2Cl} + \underset{\substack{\text{hydroxylamine}\\\text{hydrochloride}}}{H_2NOH \cdot HCl} \longrightarrow ArSO_2NHOH + 2HCl$$





The presence of the halogen in the sulfonyl halides can be detected by ethanolic silver nitrate solution (Experiment 35, p. 320). The sulfonyl halide is converted to the sulfonic ester and hydrogen halide. The halide ion reacts with the silver cation to form the insoluble silver halide.

$$\underset{\text{sulfonyl halide}}{RSO_2X} + CH_3CH_2OH \longrightarrow \underset{\text{sulfonyl ester}}{RSO_3CH_2CH_3} + HX$$

$$HX + AgNO_3 \longrightarrow AgX(s) + HONO_2$$

The halogen in sulfonyl bromides or chlorides can also be detected by sodium iodide in acetone (Experiment 36, p. 323), with the formation of the solid sodium chloride and the liberation of iodine.

$$ArSO_2X + NaI \longrightarrow ArSO_2I + NaX(s)$$

$$\downarrow \text{NaI}$$

$$ArSO_2Na + I_2$$

Experiment 47 Sodium Hydroxide Fusion of Sulfonamides

$$\underset{\text{sulfonamide}}{ArSO_2NH_2} + 2NaOH \longrightarrow ArONa + NaHSO_3 + \underset{\text{ammonia}}{NH_3(g)}$$

$$NaHSO_3 + HCl \longrightarrow \underset{\text{sulfur dioxide}}{SO_2(g)} + NaCl + H_2O$$

In a test tube, fuse 0.25 g of the unknown with 1.5 g of powdered sodium hydroxide by heating with a bunsen burner. Test the escaping gas for the presence of ammonia or amines by placing pink moist litmus paper in the test tube, being careful to avoid touching the sides of the test tube with the paper. If ammonia or amine is being evolved, the litmus paper turns blue.

Allow the test tube to cool. Add just enough distilled water to dissolve the sample. Acidify the solution with 2 M hydrochloric acid. Suspend a filter paper that has been covered with a paste of nickel(II) hydroxide over the test tube. Gently warm the test tube to speed up the production of sulfur dioxide. If sulfur dioxide is present, the green nickel(II) hydroxide is oxidized to gray-black nickel(IV) oxyhydrate.

A positive test for the presence of a sulfonamide is the evolution of both ammonia or amine and sulfur dioxide.

Nickel(II) Hydroxide Reagent

Prepare the nickel(II) hydroxide reagent immediately before use by slowly adding 1 M sodium hydroxide to 0.20 g of nickel(II) chloride until no more solid precipitates. Wash the precipitate with 10-mL portions of cold water until the washings are no longer basic. Moisten the nickel(II) hydroxide with water and apply as a paste to a strip of filter paper.

Controls Benzenesulfonamide will give a positive test. 2-Propanol will give a negative test.

Cleaning Up Place the solid nickel(II) hydroxide and the filter paper impregnated with the nickel(II) hydroxide solution in the hazardous solid waste container. Place the reaction mixture in the aqueous solution container.

Discussion

The sulfur dioxide undergoes reaction with the green nickel(II) hydroxide to yield black nickel(IV) oxyhydrate.[29]

$$\underset{\substack{\text{nickel(II) hydroxide}\\\text{(green)}}}{2Ni(OH)_2} + SO_2 \longrightarrow (NiOH)_2SO_3 + H_2O$$

$$(NiOH)_2SO_3 + O_2 \longrightarrow \underset{\substack{\text{nickel(IV) oxyhydrate}\\\text{(black)}}}{NiO(OH)_2} + NiSO_4$$

[29]F. Feigl, *Spot Tests in Organic Analysis* (Elsevier Scientific Publishing Company, New York, 1966), p. 87.

CHAPTER 10

The Preparation of Derivatives

Derivatization procedures have somewhat diminished in stature with the advent of spectroscopy. However, these procedures still provide both physical data and an insight into the chemistry of the unknown, especially when the possibilities for the identity of the unknown have similar boiling or melting points and similar spectra. Chemists should also remember that certain "derivatizations" are really "conversions" of one common organic compound into another. Conversion (e.g., oxidizing a secondary alcohol to a ketone) may yield a compound that should also be thoroughly characterized. Many derivatizations are really syntheses.

In this edition of the book, care was taken that, for a particular type of compound, both the procedure for preparing derivatives and the melting points of those derivatives are given.

A listing of derivatization procedures, listed by functional group, is given in Table 10.1.

As in Chapter 9, each procedure in this chapter contains a ***Cleaning Up*** procedure. Users of this book may wish to scale down some procedures by multiplying the amount of reagent used by 1/2, 1/5, or 1/10, bearing in mind that these experiments have not been tested in the smaller amounts.

In the derivative tables in Appendix II, compounds are listed only if they have two or more derivatives.

10.1 CARBOXYLIC ACIDS, ACID ANHYDRIDES, ACID HALIDES

One of the most useful pieces of information about a carboxylic acid is its *neutralization equivalent* (NE), which is obtained by quantitative titration with a standardized base (Procedure 1, p. 357). The molecular weight of the acid, within experimental error, is an integral (usually 1, 2, 3, etc.) multiple of the neutralization equivalent.

Acid anhydrides, acyl halides, and carboxylic acids can be derivatized by using some of the same procedures. Acid anhydrides and acyl halides can be hydrolyzed to the carboxylic acids or the sodium salts of the acid (Procedure 2, p. 358). Symmetrical anhydrides lead to just one kind of one carboxylic acid. Unsymmetrical anhydrides are far more difficult to characterize. If the acid is a solid, it will frequently serve as a derivative of anhydrides and acyl halides. Otherwise, the mixture of the sodium salt of the acid and sodium chloride obtained from the basic hydrolysis of the acyl halide may be used for preparing other solid derivatives such as amides (Procedure 4b, p. 361).

TABLE 10.1 Index to Characterization Procedures for Functional Group Classes

Compound	Derivative	Procedure	Page Number
Acid anhydrides	Acids	2	358
	Amides	3b	359
	Anilides	4c	362
	4-Toluidides	4c	362
Acyl halides	Acids	2	358
	Amides	3b	359
	Anilides	4c	362
	4-Toluidides	4c	362
Alcohols	Phenylurethanes	8	366
	1-Naphthylurethanes	8	366
	4-Nitrobenzoates	9	367
	3,5-Dinitrobenzoates	10	368
	Hydrogen 3-nitrophthalates	11	369
Aldehydes	Semicarbazones	12	372
	2,4-Dinitrophenylhydrazones	13	372
	4-Nitrophenylhydrazones	14	373
	Phenylhydrazones	14	373
	Oximes	15	374
	Dimedon derivatives	16	374
	Oxidation to an acid	17	375
Amides	9-Acylamidoxanthenes	18	379
	Hydrolysis to acids and amines	19	379
	4-Nitrobenzyl esters	19, then 5	379, 362
	4-Bromophenacyl esters	19, then 5	379, 362
	Acetamides	19, then 20a	379, 384
	Benzamides	19, then 20b or 20c	379, 384
Amines—1° and 2°	Acetamides	20a	384
	Benzamides	20b or 20c	384
	Benzenesulfonamides	21	386
	4-Toluenesulfonamides	21	386
	Phenylthioureas	22	387
	Amine hydrochlorides	26	389
Amines—3°	Chloroplatinates	23	387
	Methyl 4-toluenesulfonates	24a	388
	Methyl iodide	24b	388
	Picrate	25	388
	Amine hydrochlorides	26	389
Amino acids	4-Toluenesulfonamides	27	393
	Phenylureido acids	28	394
	Acetamides	20d	385
	Benzamides	20d	385
	3,5-Dinitrobenzamides	29	394
	2,4-Dinitroaniline derivatives	30	395
Carbohydrates	Phenylosazones	31	396
	4-Nitrophenylhydrazones	32	397
	4-Bromophenylhydrazones	32	397
	Acetates	33	398

(Continued)

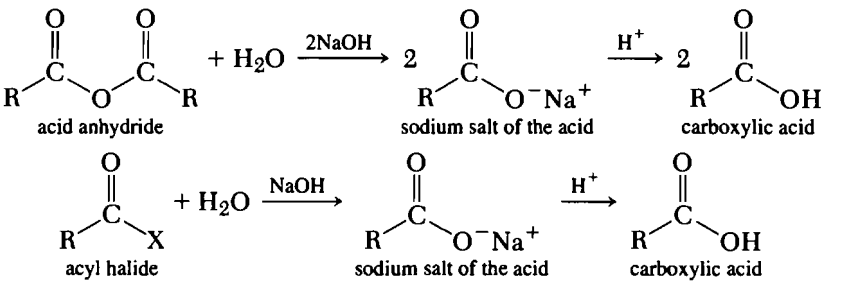
TABLE 10.1 *(Continued)*

Compound	Derivative	Procedure	Page Number
Carboxylic acids	Neutralization equivalent	1	357
	4-Toluidides	4a or 4b	360 or 361
	Anilides	4a or 4b	360 or 361
	4-Nitrobenzyl esters	5	362
	4-Bromophenacyl esters	5	362
	Amides	3a	359
	S-Benzylthiuronium salts	6	363
	Phenylhydrazides	7	364
Esters	Saponification and hydrolysis	34	401
	Saponification equivalent	35	404
	Amides	34, then 3a	401, 359
	4-Toluidides	36; 34, then 4a or 4b	406, 401, 360, 361
	3,5-Dinitrobenzoates	37	408
	N-Benzylamides	38	408
	Acid hydrazides	39	409
Ethers—Alkyl	3,5-Dinitrobenzoates	40	410
Ethers—Aromatic	Picrates	41	411
	Sulfonamides	42, then 43	412, 413
	Nitro derivatives	51	423
	Bromo derivatives	44	414
Halides—Alkyl	Anilides	46	417
	1-Naphthalides	46	417
	Alkylmercuric halides	45	416
	Alkyl 2-naphthyl ethers	47	417
	Alkyl 2-naphthyl ether picrates	48	418
	S-Alkylthiuronium picrates	49	419
Halides—Aromatic	Nitration	51	423
	Sulfonamides	42, then 43b	412, 413
	Oxidation	50	420
Hydrocarbons—Aromatic	Nitration	51	423
	Aroylbenzoic acids	52	424
	Picrates	41	411
Ketones	Semicarbazones	12	372
	2,4-Dinitrophenylhydrazones	13	372
	4-Nitrophenylhydrazones	14	373
	Phenylhydrazones	14	373
	Oximes	15	374
Nitriles	Hydrolysis of nitriles	53	427
	Amides	53, then 3a; 54	427, 359, 428
	Anilides	53, then 4	427, 360
	Reduction of nitriles	55	429
	Benzamides	55, then 20b or 20c	429, 384
	Benzenesulfonamides	55, then 21	429, 386
	Phenylthiourea	55, then 22	429, 387
	α-(Imidioylthio)acetic acid hydrochlorides	56	429
Nitro compounds	Reduction to amines	57	431
	Acetamides	57, then 20a	431, 384
	Benzamides	57, then 20b or 20c	431, 384
	Benzenesulfonamides	57, then 21	431, 386

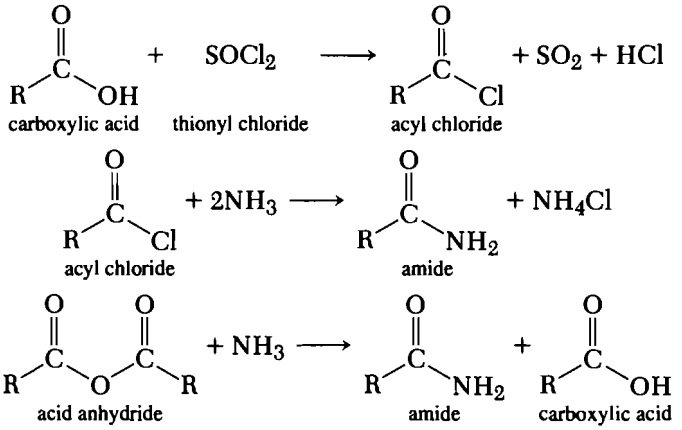
(Continued)

TABLE 10.1 *(Continued)*

Compound	Derivative	Procedure	Page Number
Phenols	Phenylurethanes	8 or 58	366, 433
	1-Naphthylurethanes	8 or 58	366, 433
	4-Nitrobenzoates	9	367
	3,5-Dinitrobenzoate	10	368
	Acetates	59	434
	Benzoates	9	367
	Aryloxyacetic acid	60	434
	Bromo derivatives	61	434
Sulfonamides	Sulfonic acids	64	438
	Sulfonyl chlorides	64, then 62	438, 437
	Sulfanilides	64, then 62, then 63	438, 437
			438
	N-Xanthylsulfonamides	65	439
Sulfonic acids	Sulfonyl chlorides	62	437
	Sulfonamides	62, then 43	437, 413
	Sulfanilides	62, then 63	437, 438
	Benzylthiuronium sulfonates	66	440
	4-Toluidine salts	67	440
Sulfonyl chlorides	Sulfonic acids	64	438
	Sulfonamides	43	413
	Sulfanilides	63	438

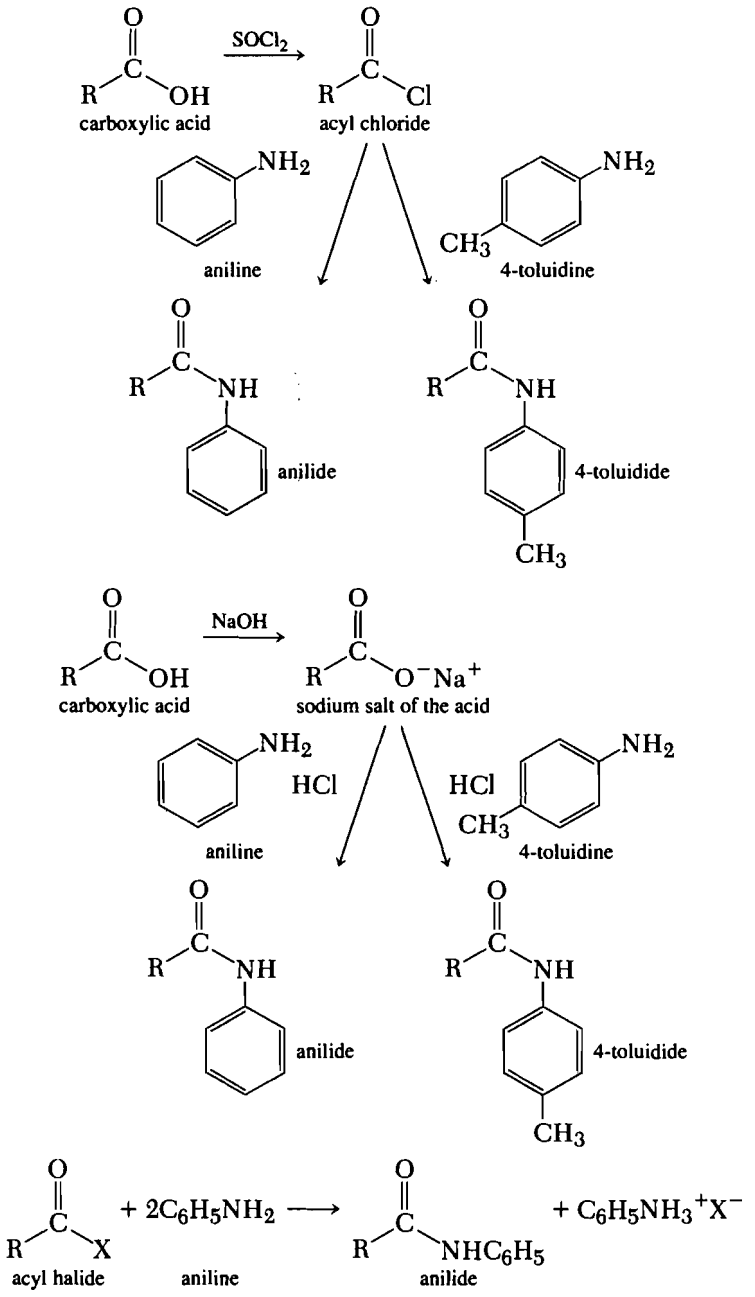


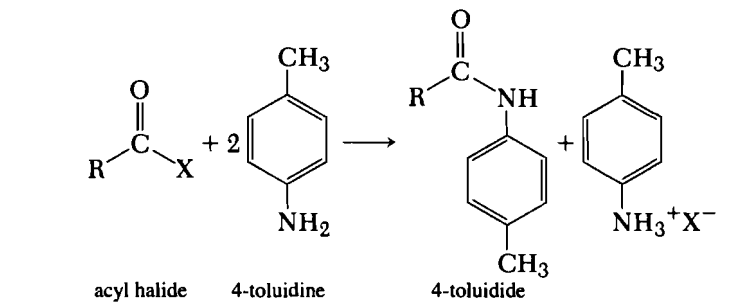
Acids may be converted to amides by reaction with thionyl chloride, followed by treatment of the intermediate acyl chloride with concentrated aqueous ammonia. Acid anhydrides undergo reaction with aqueous ammonia to yield amides and carboxylic acids (Procedure 3b, p. 359).

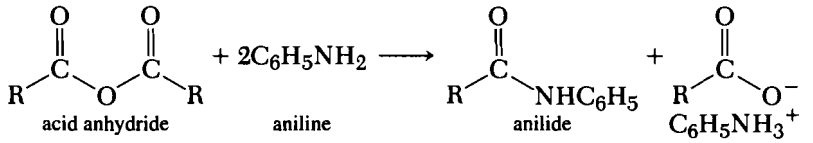


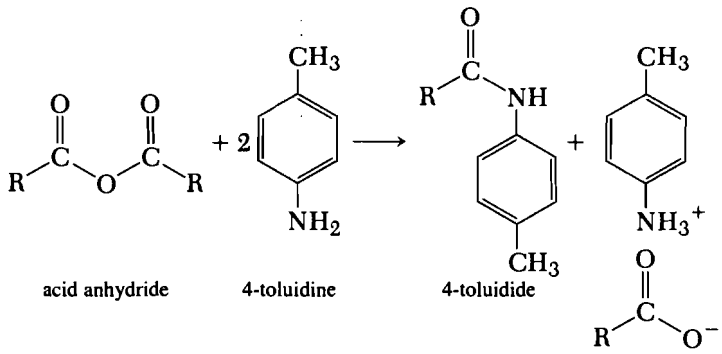
This method is particularly suitable if the amide is insoluble in water.

Anilides and 4-toluidides are excellent derivatives because of the ease with which they may be made and purified. They may be prepared from the free acid, the salt of the acid, the acyl halide, or the anhydride (Procedure 4, p. 360).

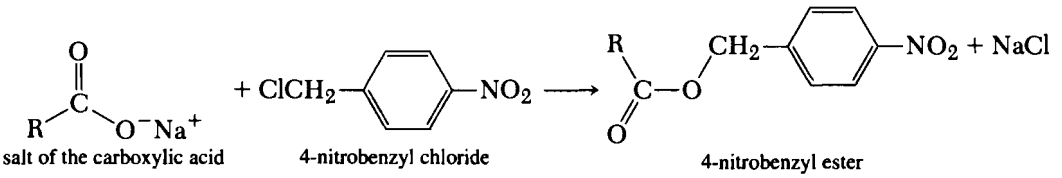


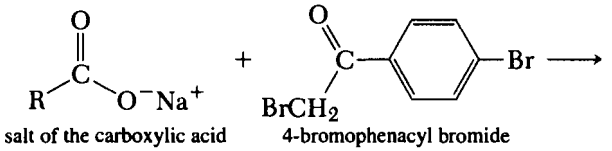


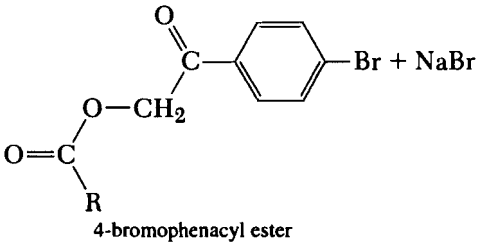




Solid esters furnish a useful means for characterizing the acids. Some methyl esters are solid, but it most cases the 4-nitrobenzyl or the 4-bromophenacyl esters are preferred. These are prepared by treating the salts of the acids with either 4-nitrobenzyl chloride or 4-bromophenacyl bromide (Procedure 5, p. 362).

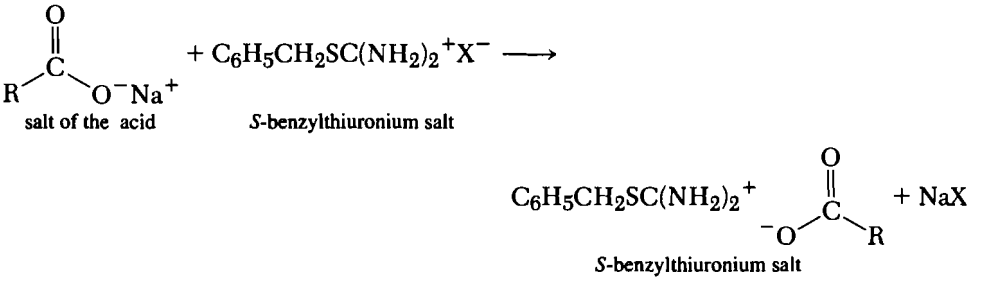




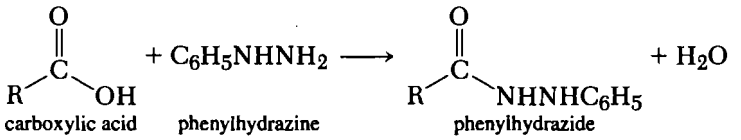


This method is particularly advantageous because it does not require an anhydrous sample of the acid.

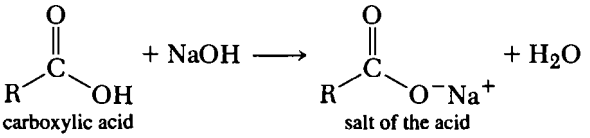
S-Benzylthiuronium halide undergoes reaction with the salt of the carboxylic acid to yield the corresponding *S*-benzylthiuronium salt (Procedure 6, p. 363).



The reaction products of phenylhydrazine and acids are also good derivatives. At the boiling point (243°C) of phenylhydrazine, simple unsubstituted aliphatic mono- and dibasic acids form phenylhydrazides (Procedure 7, p. 364).



Procedure 1 Neutralization Equivalents (NE) of Carboxylic Acids



Weigh a sample of the acid (about 0.2 g) to at least three figures on an analytical balance and dissolve the acid in 50 to 100 mL of water or ethanol. Heat the mixture, if necessary, to dissolve all the compound. Titrate this solution with a previously standardized sodium hydroxide solution having a molarity of about 0.1, using phenolphthalein or bromothymol blue as an indicator. Calculate the neutralization equivalent according to the formula listed below.

$$\text{neutralization equivalent} = \frac{\text{weight of the sample} \times 1000}{\text{volume of alkali (mL)} \times \text{M}}$$

The amount of alkali is the amount required to titrate to the end point.

Cleaning Up Place the mixture in the aqueous solution container.

Discussion

The molecular weight (MW) of an acid may be determined from the neutralization equivalent (NE) by multiplying that value by the number of acidic groups (x) in the molecule:

$$\text{MW} = x(\text{NE})$$

The change in medium, even from pure water to pure ethanol, affects the pK of both the organic acid and the indicator. For this reason, best results are obtained in water or aqueous ethanol with only enough ethanol to dissolve the organic acid. In absolute or 95% ethanol, it is often impossible to obtain a sharp end point with phenolphthalein. In such cases bromothymol blue should be employed as the indicator. Acids may also be titrated in a solvent composed of ethanol and benzene or toluene.

The neutralization equivalents should agree with the calculated values within ±1%. By using carefully purified and dried samples and good technique, the error may be reduced to ±0.3%.

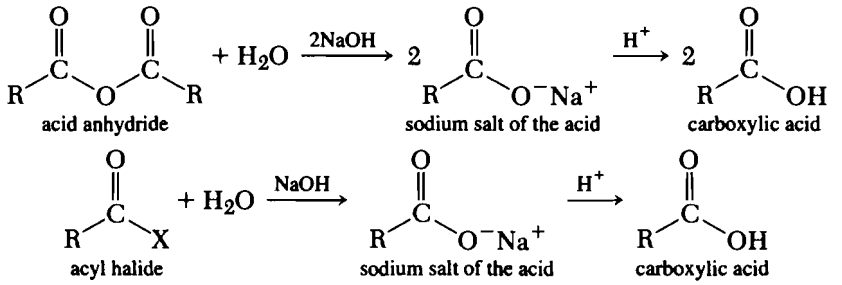
In order to give an accurate neutralization equivalent, the substance titrated must be pure and anhydrous. If the value obtained for the neutralization equivalent does not agree with the theoretical value, the compound should be recrystallized from a suitable solvent and carefully dried.

Amine salts of strong acids may be titrated by the same procedure.

❧ Problems

1. Calculate the neutralization equivalent of benzoic acid and of phthalic acid.
2. If an acid is not completely dried, will the neutralization equivalent be high or low?
3. Would the presence of an aromatic amino group interfere in the determination of the neutralization equivalent? What would be the effect of an aliphatic amino group?
4. What types of phenols may be titrated quantitatively?[1]
5. From a theoretical point of view, what should be the ionization constant of an acid in order that the acid may be titrated with phenolphthalein (see footnote 1)?

Procedure 2 Hydrolysis of Acid Anhydrides and Acyl Halides to Carboxylic Acids



Add 1 g of the acid anhydride or acyl halide to 5 mL of water in a small flask. To hydrolyze the acid anhydride or acyl halide, add 10% sodium hydroxide solution slowly until the solution is alkaline to litmus. Warm the flask gently for a few minutes. Acidify the resulting solution with 10% hydrochloric acid until it is acidic. Remove the insoluble

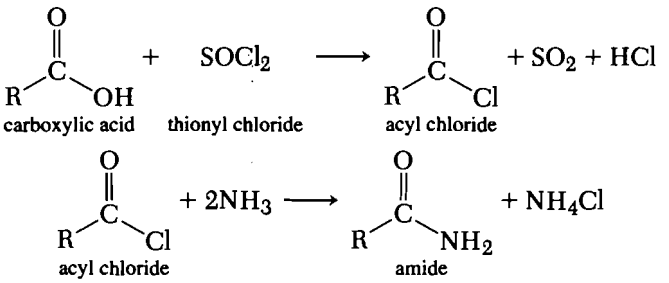
[1]An analytical book such as those cited in Chapter 12 should be consulted.

carboxylic acids by filtration. If no solid is obtained, neutralize the solution and evaporate to dryness. Use the resulting mixture of the sodium salt of the acid and sodium chloride for preparing anilides, 4-toluidides (Procedure 4, p. 360), or esters (Procedure 5, p. 362).

Cleaning Up Neutralize the filtrate with 10% sodium hydroxide and place in the aqueous solution container.

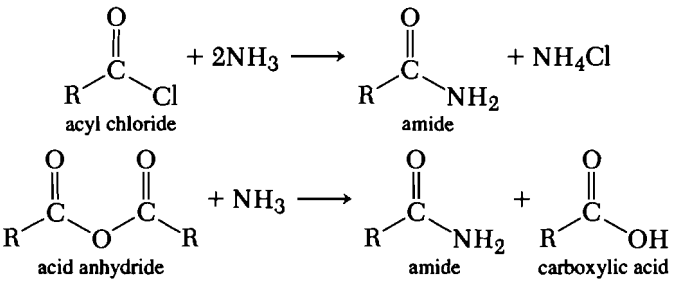
Procedure 3 Preparation of Amides

(a) From the Carboxylic Acid



Perform the entire procedure in the hood. Mix 1 g of the acid with 5 mL of thionyl chloride. Add one drop of *N*,*N*-dimethylformamide. Heat under reflux for 15–30 min. Pour the mixture cautiously into 15 mL of ice-cold, concentrated aqueous ammonia. Extract the solution with three 10-mL portions of methylene chloride. Isolate the methylene chloride layer and evaporate to dryness. Recrystallize the crude amide from ethanol.

(b) From the Acyl Halide or Acid Anhydride

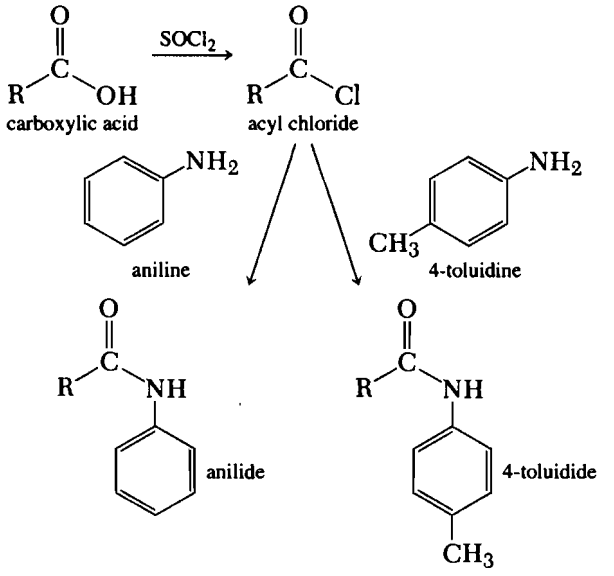


In the hood, add 1 g of the acyl halide or acid anhydride to 15 mL of concentrated aqueous ammonia. Extract the solution with three 10-mL portions of methylene chloride. Isolate the methylene chloride layer and evaporate to dryness. Recrystallize the crude amide from ethanol.

Cleaning Up Neutralize the filtrate with 10% hydrochloric acid and place in the aqueous solution container.

Procedure 4 Anilides and 4-Toluidides

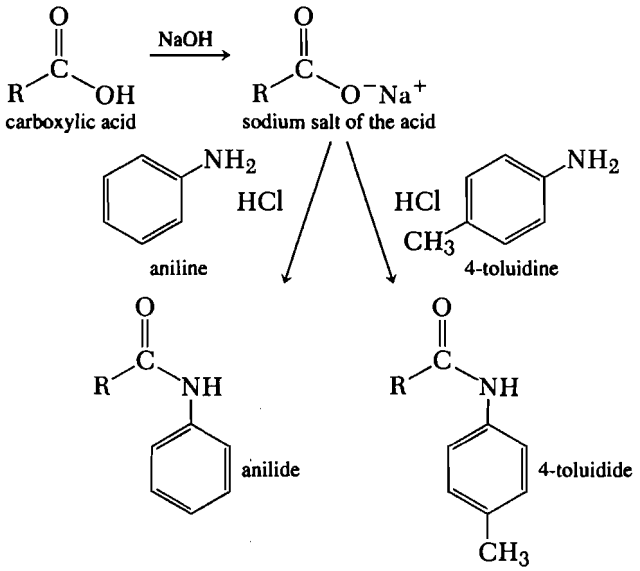
(a) From the Carboxylic Acid



Perform the experiment in the hood. Mix 1 g of the acid with 2 mL of thionyl chloride. Heat the mixture at reflux for 30 min. Cool the mixture, and add a solution of 1–2 g of aniline or 4-toluidine (4-aminotoluene) in 30 mL of benzene,[2] and heat the mixture in a hot-water bath or on a steam bath for 2 min. *Note: Benzene is a known carcinogen. Use benzene in the hood, do not breathe the vapors, and avoid contact with the skin.* Pour the benzene solution into a separatory funnel and wash successively with 2 mL of water, 5 mL of 5% hydrochloric acid, 5 mL of 5% sodium hydroxide solution, and 2 mL of water. In the hood, recover the benzene by distillation, using a steam bath, and recrystallize the resulting amide from water or ethanol.

[2]Benzene is highly toxic and should be used only with the instructor's permission. Other solvents such as toluene or tetrachloroethane may be substituted for benzene.

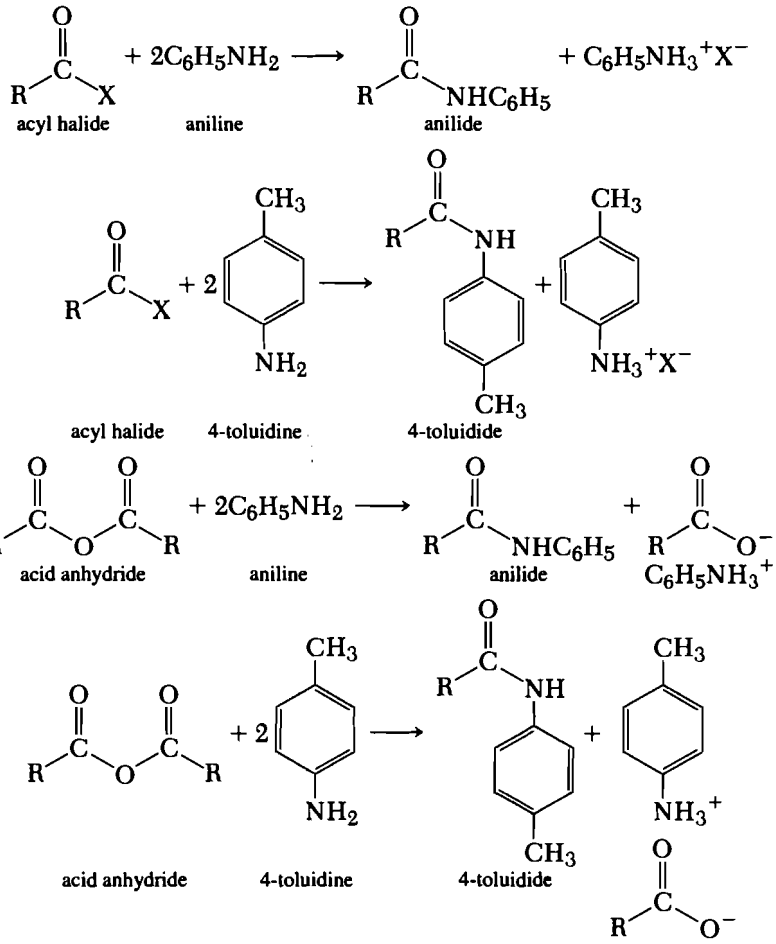
(b) From the Sodium Salt of the Carboxylic Acid



Place a mixture of 0.4 g of the dry powdered sodium salt of the acid, 0.5 mL of aniline or 4-toluidine (4-aminotoluene), and 0.15 mL of concentrated hydrochloric acid in a test tube. Place the test tube in an oil bath and heat the solution at a temperature between 150° and 160°C for 45–60 min. Remove the test tube and purify the product by one of the following methods.

1. If the acid under consideration has fewer than six carbon atoms, add 5 mL of 95% ethanol. Heat the solution to boiling and decant into 15 mL of hot water. Evaporate the resulting solution to a volume of 10–12 mL and cool in an ice bath. Isolate the crystals by filtration and recrystallize from a small amount of water or dilute ethanol.
2. If the acid contains six or more carbon atoms, powder the crude reaction product and wash with 15 mL of 5% hydrochloric acid and then with 15 mL of cold water. Add 30 mL of 95% ethanol, heat the solution to boiling, and then filter. Chill the filtrate in an ice bath, and remove the crystals of the amide by filtration. Recrystallize the product from aqueous ethanol.

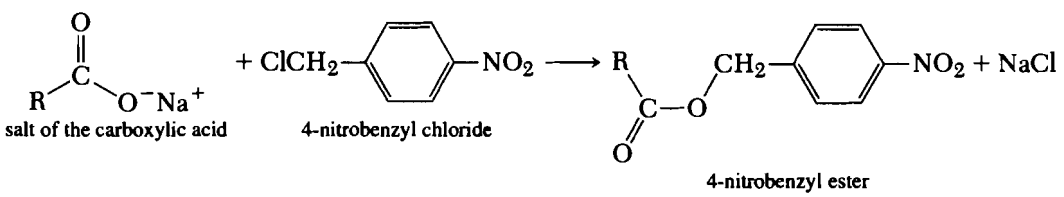
(c) From the Acid Halide or Anhydride

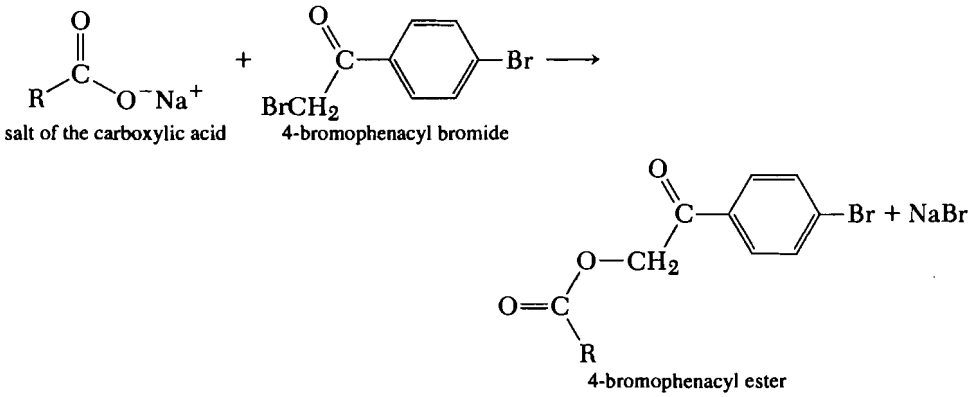


Mix 1 g of the acid halide or anhydride with 1 g of aniline or 4-toluidine (4-aminotoluene). Heat the mixture in a boiling water bath for 5 min. Add 5 mL of water. Heat the solution to boiling, then cool it. Recrystallize the anilide from ethanol or aqueous ethanol.

Cleaning Up Place benzene in the hazardous waste container for benzene and any unreacted amine in the aromatic organic solvent container. Neutralize the aqueous filtrate, if needed, with sodium carbonate, and place in the aqueous solution container.

Procedure 5 4-Nitrobenzyl and 4-Bromophenacyl Esters from Carboxylic Acids





Add 1 g of the acid to 5 mL of water and neutralize carefully with 10% sodium hydroxide solution. Add a little more of the acid, and continue the addition until the solution is just acid to litmus. If the original acid is obtained as a sodium salt, dissolve 1 g of the salt in 5–10 mL of water. If this solution is alkaline, add a drop or two of 10% hydrochloric acid. Add 10 mL of ethanol and 1 g of 4-nitrobenzyl chloride or 4-bromophenacyl bromide. *Caution! Phenacyl halides are lachrymators.* Heat the mixture under reflux for 1 hr if the acid is monobasic, 2 hr if dibasic, and 3 hr if tribasic. If a solid separates during reflux, then add a few more mL of ethanol. Cool the solution, and isolate the ester by filtration. Recrystallize the ester from ethanol.

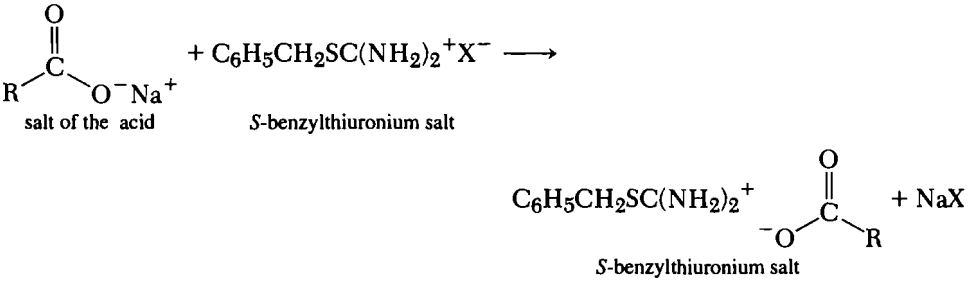
Cleaning Up Place any unreacted halide in the halogenated organic waste container. Place the aqueous filtrate in the aqueous solution container.

Discussion

In preparing derivatives with these reagents, care must be taken that the original reaction mixture is not alkaline. Alkalies cause hydrolysis of the phenacyl halides to phenacyl alcohols. In addition, 4-bromophenacyl bromide should not be used if considerable amounts of sodium chloride are present in the sodium salt of the acid.

Crown ethers can be used to improve the ease with which esters are formed. For example, potassium acetate will convert 1-bromoheptane to heptyl acetate in near-quantitative yield.[3]

Procedure 6 *S*-Benzylthiuronium Salts of Carboxylic Acids



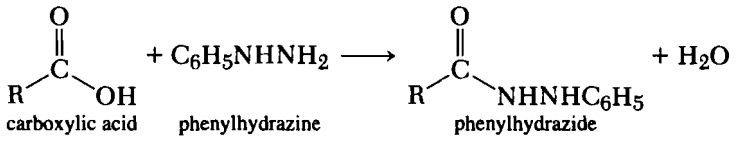
[3]G. Gokel and H. Durst, *Synthesis*, 178 (1976).

Add 0.3 g of the acid (or 0.5 g of the salt) to 3–4 mL of water. Add a drop of phenolphthalein indicator solution. Neutralize the solution by the dropwise addition of 5% sodium hydroxide solution. Avoid an excess of base. If too much base is used, add dilute hydrochloric acid until the solution is just a pale pink. Add a hot solution of 1 g of the benzylthiuronium chloride or bromide (prepared according to Procedure 49, p. 419, using benzyl chloride or benzyl bromide) in 10 mL of 95% ethanol to this aqueous solution of the sodium salt. Cool the mixture, and isolate the salt by filtration. A few salts (e.g., from formic acid) fail to precipitate, and part of the ethanol must be evaporated to obtain the salt.

The thiuronium salts of organic acids separate in a state of high purity and usually do not require crystallization. If necessary they may be recrystallized from a small amount of dioxane.

Cleaning Up Place the aqueous filtrate in the aqueous solution container.

Procedure 7 Phenylhydrazine and Phenylhydrazonium Salts from Carboxylic Acids



(a) With No Solvent

Dissolve 1 g of the acid in 2 mL of phenylhydrazine, and reflux the solution gently for 30 min. Cool the solution. Isolate the crystalline product filtration and wash with small quantities of toluene or ether until the crystals are white. When a large excess of phenylhydrazine is used, it is sometimes necessary to dilute the mixture with toluene in order to bring about precipitation of the product. Recrystallize the derivatives of the lower monobasic acids from hot toluene, and recrystallize the higher acids and dibasic acids from ethanol or ethanol–water mixtures. The derivatives obtained from dibasic acids by this method are bis-β-phenylhydrazides.

(b) Using Toluene as a Solvent

Mix 1 g of the acid with 2 mL of phenylhydrazine dissolved in 5 mL of toluene. If a white solid precipitates immediately, recrystallize it from ethanol. If no solid separates, heat the mixture under reflux for 30 min. Cool the solution. Isolate the product by filtration, wash with ether, and recrystallize from toluene or ethanol. Sulfonic acids, halogen-substituted aliphatic acids, and aliphatic dibasic acids yield salts by this procedure, whereas simple unsubstituted aliphatic acids give phenylhydrazides.

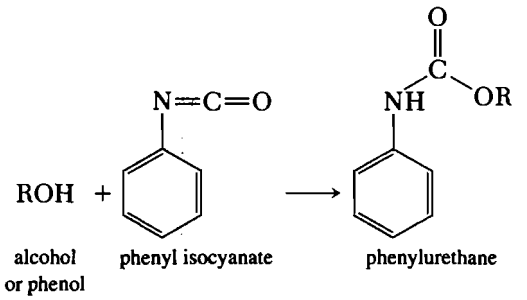
Cleaning Up Place the initial filtrates, any unreacted phenylhydrazine, and toluene filtrates in the aromatic organic solvent container. Place the ether filtrate in the organic solvent container. Dilute the ethanol filtrate with 10 mL of water and place in the aqueous solution container.

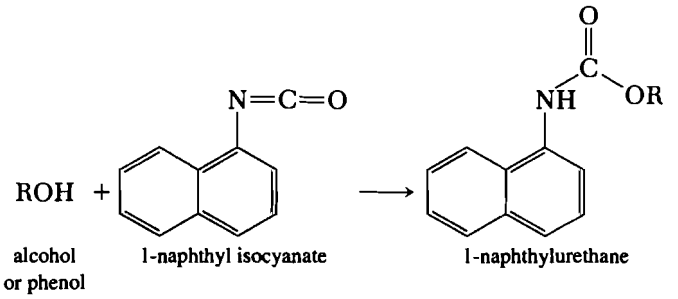
Problem

6. Give the equation for the reaction of butanoic acid with (a) 4-toluidine, (b) aniline, (c) 4-nitrobenzyl chloride, (d) 4-bromophenacyl bromide, (e) *S*-benzylthiuronium salt, and (f) phenylhydrazine.

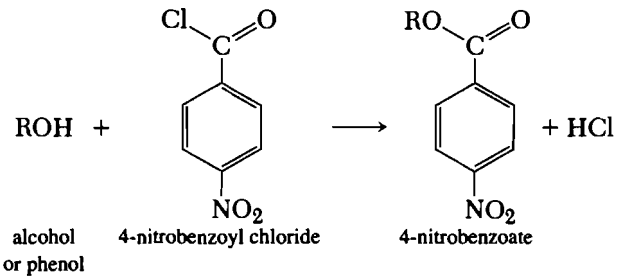
10.2 ALCOHOLS

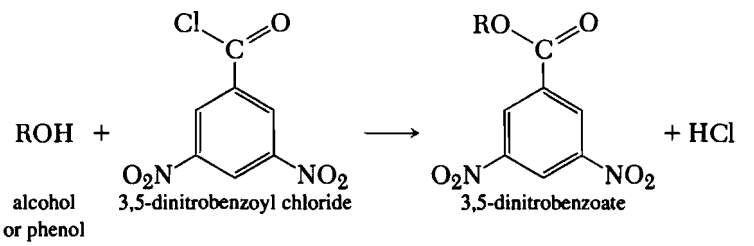
The most general derivatives of primary and secondary alcohols are the phenylurethanes and 1-naphthylurethanes. Urethane derivatives are prepared when the alcohol is treated with either phenyl isocyanate or naphthyl isocyanate (Procedure 8, p. 366).





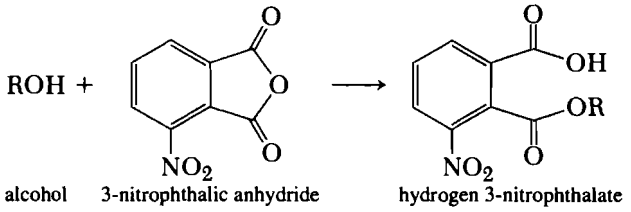
4-Nitrobenzoates (Procedure 9, p. 367) or 3,5-dinitrobenzoates (Procedure 10, p. 368) are easily prepared from the reaction of the alcohol with the corresponding acyl halide.



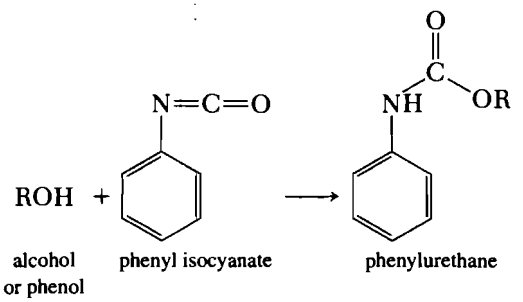


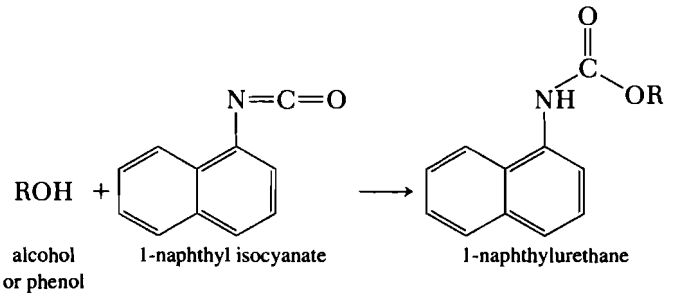
For water-soluble alcohols that are likely to contain traces of moisture, the 3,5-dinitrobenzoates are generally more satisfactory as derivatives than the urethanes.

The reaction of alcohols with 3-nitrophthalic anhydride produces hydrogen 3-nitrophthalate derivatives (Procedure 11, p. 369).



Procedure 8 Phenyl and 1-Naphthylurethanes of Alcohols and Phenols



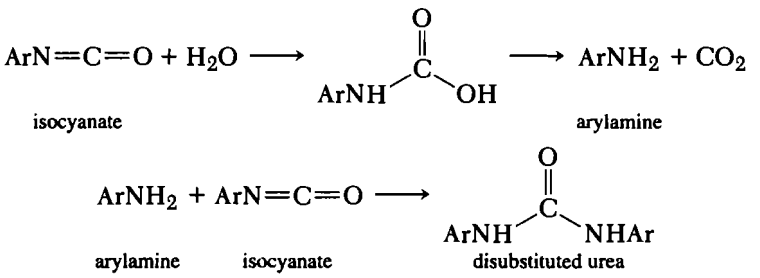


Place 1 g of the anhydrous alcohol or phenol in a test tube, and add 0.5 mL of phenyl isocyanate or 1-naphthyl isocyanate. *Caution! The isocyanates are lachrymators and should be stored in desiccators.* If the reactant is a phenol, catalyze the reaction by adding two to three drops of anhydrous pyridine or triethylamine. If a spontaneous reaction does not take place, stopper the solution loosely and warm it on a steam bath for 5 min. Cool the solution in a beaker of ice, and scratch the sides of the tube with a glass rod to induce crystallization. Purify the urethane by dissolving it in 5 mL of petroleum ether or carbon tetrachloride (*toxic*). Filter the hot solution to remove the unwanted urea by-product, and cool the filtrate in an ice bath. Isolate the crystals by filtration.

Cleaning Up Treat any unreacted phenyl isocyanate with an excess of 5.25% sodium hypochlorite (household bleach), dilute with 10 mL of water, and place in the aqueous solution container. Place the petroleum ether filtrate in the organic solvent waste container. Place the carbon tetrachloride filtrate in the halogenated organic waste container. Place the urea by-product in the hazardous waste container.

Discussion

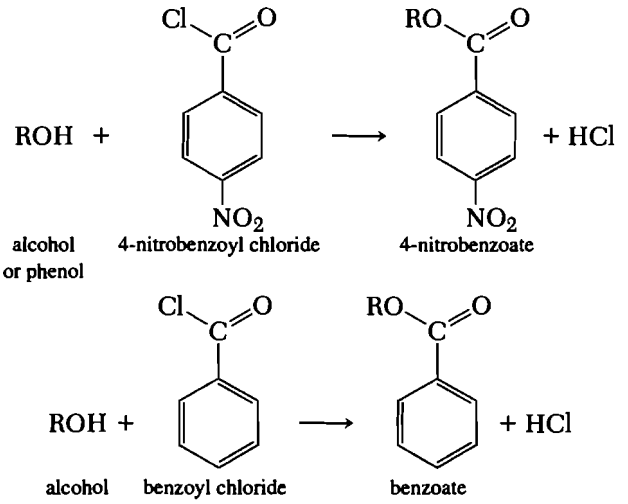
The presence of water as an impurity in the alcohol causes difficulty in obtaining the urethane. Water hydrolyzes the isocyanates to give arylamines, which combine with the excess reagent to produce disubstituted ureas.



The ureas are higher melting and less soluble than the corresponding urethanes; and ureas, even in small amounts, make the isolation and purification of the urethanes a matter of considerable difficulty. For this reason, this procedure is most useful for alcohols that are insoluble in water and, therefore, easily obtained in anhydrous conditions.

Urethanes can be obtained from tertiary alcohols only with great difficulty. The isocyanates cause dehydration to occur with the formation of the alkene and diarylurea.

Procedure 9 4-Nitrobenzoates of Alcohols and Phenols; Benzoates of Phenols



(a) With Pyridine

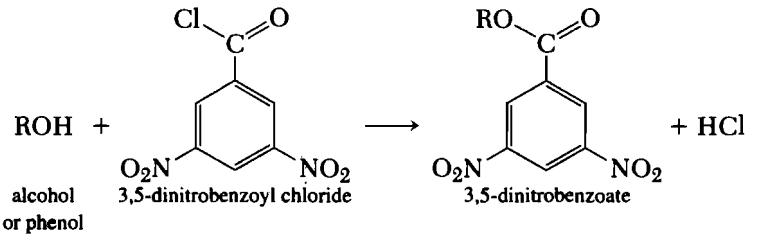
Dissolve 1 mL or 1 g of the alcohol or phenol in 3 mL of anhydrous pyridine, and add 0.5 g of 4-nitrobenzoyl or benzoyl chloride. After the initial reaction has subsided, warm the mixture over low heat for a minute and pour, with vigorous stirring, into 10 mL of water. Allow the precipitate to settle, and decant off the supernatant liquid. Stir the residue with 5 mL of 5% sodium carbonate solution. Remove the precipitate by filtration, and purify by recrystallization from ethanol.

(b) Without Pyridine

Mix 1 mL or 1 g of the alcohol or phenol with 0.5 g of 4-nitrobenzoyl or benzoyl chloride, and heat to boiling over low heat. Pour the mixture into 10 mL of water and purify as in (a).

Cleaning Up Place the organic layer in the organic solvent container. Place the aqueous layer in the aqueous solution container.

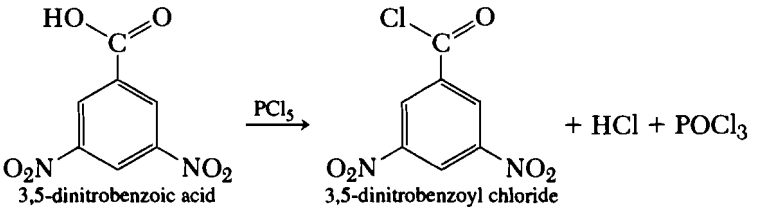
Procedure 10 3,5-Dinitrobenzoates of Alcohols and Phenols



(a) With Pyridine

Mix 0.5 g of 3,5-dinitrobenzoyl chloride with 1 mL or 0.8 g of the alcohol or phenol in a test tube. Add 4 mL of pyridine. Boil the mixture gently for 5 min. Add 10 mL of distilled water, and cool the solution in an ice bath until the product solidifies. Isolate the precipitate by filtration, wash with 10 mL of 2% sodium carbonate solution, and recrystallize from 5–10 mL of a mixture of ethyl alcohol and water of such composition that the ester will dissolve in the hot solution but will separate when the solution is cooled. Isolate the crystals by filtration and dry.

If 3,5-dinitrobenzoyl chloride is not available, it may be made by mixing 0.5 g of 3,5-dinitrobenzoic acid with 1 g of phosphorus pentachloride in a test tube. In the hood, warm the mixture gently to start the reaction. After the initial rapid reaction has subsided, heat the mixture for about 4 min at such a rate as to cause vigorous bubbling. Pour the hot liquid onto a watch glass, and allow to solidify. Isolate the solid material and use immediately for the preparation of the derivative as described above.



(b) With Pyridine and Tosyl Chloride[4]

In a small flask, add 95 mg of 4-toluenesulfonyl chloride (tosyl chloride) to a mixture of 106 mg of 3,5-dinitrobenzoic acid dissolved in 0.5 mL of dry pyridine. Stir the mixture vigorously and place in an ice bath. Once the mixture is cold, add 100 mg or 1 mL of the alcohol or phenol and stir the solution vigorously. Allow the mixture to cool in the ice bath for 10 min.

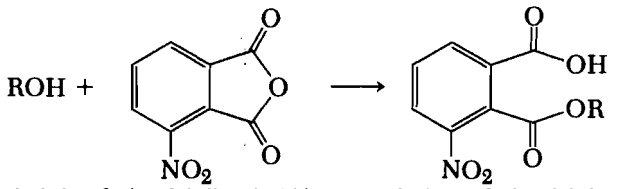
[4]R. F. Smith and G. M. Cristalli, *J. Chem. Educ.*, 72, A160 (1995).

Precipitate the alcohol derivatives by the addition of 2 mL of water. Isolate the product by suction filtration, wash with 1 mL of cold water, and recrystallize from ethanol.

Precipitate the phenol derivatives by the addition of 2 mL of 1 M sodium hydroxide solution. Isolate the derivative by vacuum filtration, and wash with 1 mL of cold water. Recrystallize the derivative by placing the product in 1 mL of boiling water, and add enough *N*,*N*-dimethylformamide to dissolve the solid. After dissolution occurs, chill the solution to reprecipitate the crystals. Isolate the crystals by suction filtration.

Cleaning Up Place the filtrate in the aqueous solution container.

Procedure 11 Hydrogen 3-Nitrophthalates of Alcohols



alcohol 3-nitrophthalic anhydride hydrogen 3-nitrophthalate

An extremely useful application of this derivative would be the determination of the neutralization equivalent (Procedure 1, p. 357) of such an acid ester; this could very possibly lead to an estimate of the molecular weight of this compound.

(a) Alcohols with Boiling Points Below 150°C

Heat, under reflux, a mixture of 0.4 g of 3-nitrophthalic anhydride and 0.5 mL or 0.4 g of the alcohol. Continue the heating for 5–10 min after the mixture liquifies. Cool the mixture, dilute with 5 mL of water, and heat to boiling. If solution is not complete, add an additional 5–10 mL of hot water. Cool the solution and allow the ester to crystallize. Sometimes the derivative separates as an oil and must be allowed to stand overnight to crystallize. Recrystallize the product once or twice from hot water.

(b) Alcohols with Boiling Points Above 150°C

Heat a mixture of 0.4 g of 3-nitrophthalic anhydride, 0.5 g of the alcohol, and 5 mL of dry toluene until all of the anhydride has dissolved, and then heat for 15 min more. Decant off the toluene and extract the residue twice with 5 mL of hot water. Dissolve the residual oil in 10 mL of 95% ethanol, and heat the solution to boiling. If the hot solution is not clear, filter it. Add water to the hot solution until a turbidity is produced that is cleared up with a drop or two of ethanol. Allow the solution to cool slowly; sometimes several days are needed for the solution to solidify. Isolate the crystals by filtration.

Cleaning Up Place the toluene in the aromatic organic solvent container. Neutralize the aqueous filtrate with sodium carbonate and place in the aqueous solution container.

Discussion

Many of the higher alkyl 3-nitrophthalates derived from the monoalkyl ethers of ethylene glycol and diethylene glycol separate as oils and must be allowed to stand several days

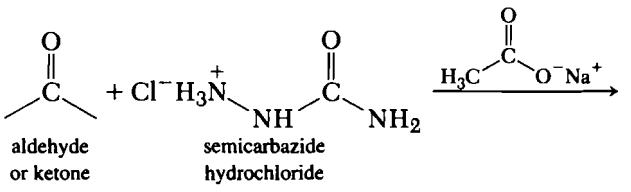
to solidify. Occasionally toluene may be substituted for the ethanol–water mixture for recrystallization. It is sometimes useful to determine the neutralization equivalent of the alkyl acid phthalate as well as the melting point.

Problem

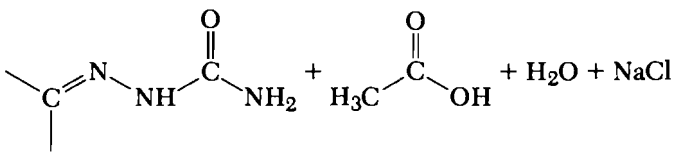
7. Give the equation for the reaction of 1-butanol with (a) phenyl isocyanate, (b) 1-naphthyl isocyanate, (c) 4-nitrobenzoyl chloride, (d) 3,5-dinitrobenzoyl chloride, and (e) 3-nitrophthalic anhydride.

10.3 ALDEHYDES AND KETONES

For low-molecular-weight, water-soluble aldehydes and ketones, it is often advantageous to prepare the semicarbazones from the reaction of the aldehyde or ketone with semicarbazide hydrochloride (Procedure 12, p. 372). All semicarbazones are solids and generally can be obtained nearly pure without recrystallization. Sometimes these derivatives form slowly, and care must be taken to allow sufficient time for the reaction to go to completion.

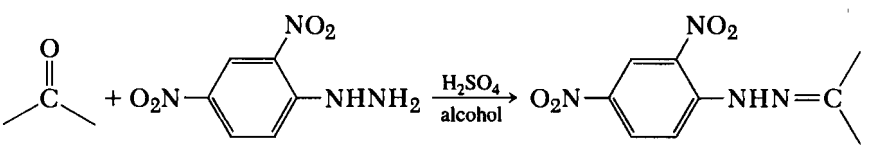


aldehyde or ketone — semicarbazide hydrochloride

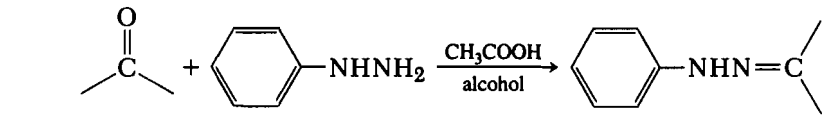


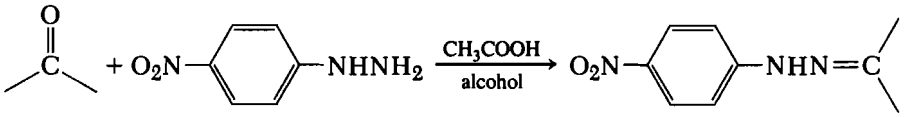
semicarbazone

The most useful derivatives of aldehydes are the 2,4-dinitrophenylhydrazones (Procedure 13, p. 372), phenylhydrazones (Procedure 14, p. 373), and 4-nitrophenylhydrazones (Procedure 14, p. 373). Of these, the 2,4-dinitrophenylhydrazones are recommended because they are most likely to be solids. Low-molecular-weight ketones may also be derivatized by 2,4-dinitrophenylhydrazones (Procedure 13, p. 372) or 4-nitrophenylhydrazones (Procedure 14, p. 373). For high-molecular-weight ketones, phenylhydrazones are suitable (Procedure 14, p. 373). The 2,4-dinitrophenylhydrazone, phenylhydrazone, and 4-nitrophenylhydrazone are prepared from the reaction of the aldehyde or ketone with 2,4-dinitrophenylhydrazine, phenylhydrazine, or 4-nitrophenylhydrazine, respectively.

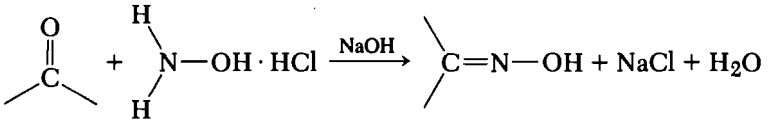


aldehyde or ketone — 2,4-dinitrophenylhydrazine — 2,4-dinitrophenylhydrazone

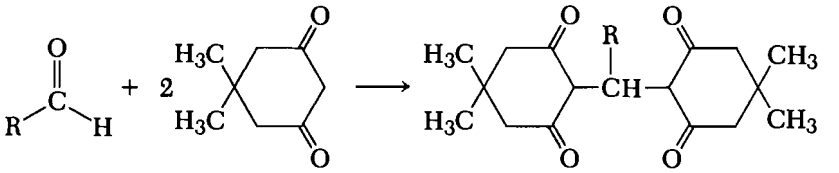




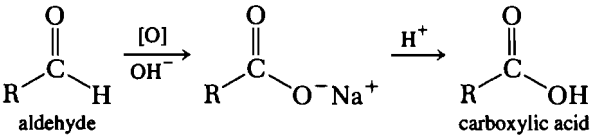
Oximes (Procedure 15, p. 374) are prepared from the reaction of the aldehyde or ketone with hydroxylamine hydrochloride. However, these derivatives are likely to melt lower than the corresponding 2,4-dinitrophenylhydrazones and semicarbazones. The reaction between carbonyl compound and hydroxylamine is reversible, and care must be taken to avoid unnecessary contact with strongly acidic solutions; under these conditions the oxime may be hydrolyzed to the original compound.



Aldehydes react with methone to yield dimedon derivatives (Procedure 16, p. 374).

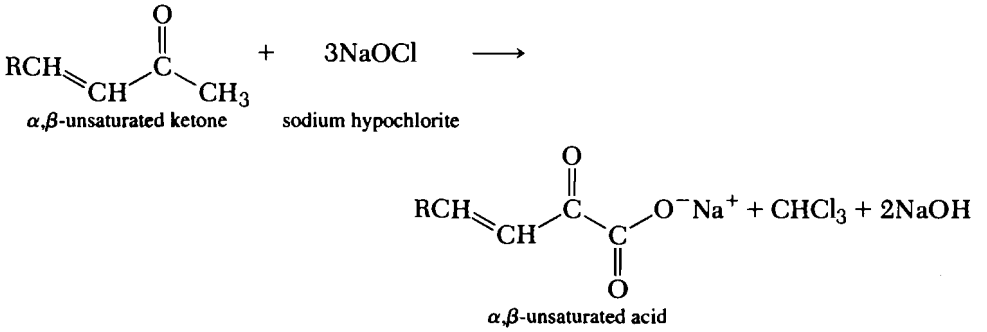


The CHO group in the aldehyde can be oxidized to a carboxylic acid (Procedure 17, p. 375); then the acid can be derivatized as described in Procedures 3 (p. 359), 4 (p. 360 or 361), and 5 (p. 362). Oxidizing agents such as potassium permanganate, hydrogen peroxide, and silver nitrate can be used.

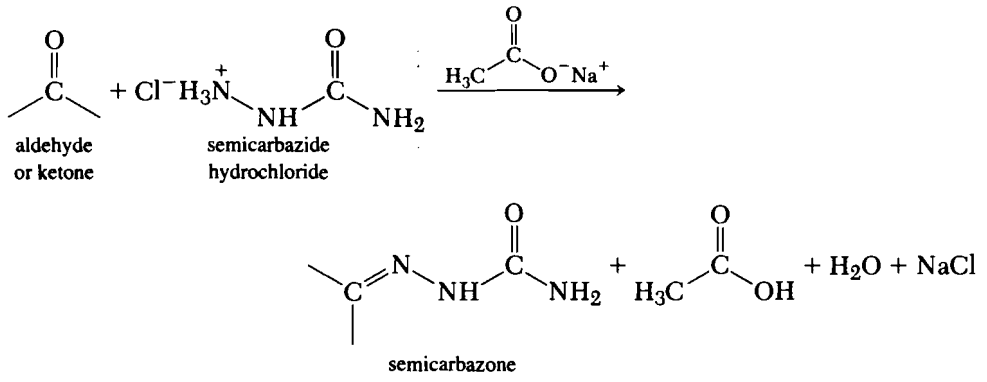


Methyl ketones may be oxidized to acids selectively by means of sodium hypochlorite.[5] This reagent is particularly useful for unsaturated methyl ketones because many other oxidizing agents attack the double bond.

[5]A. M. Van Arendonk and M. E. Cuperty, *J. Amer. Chem. Soc.*, 53, 3184 (1931); C. D. Hurd and C. L. Thomas, *J. Amer. Chem. Soc.*, 55, 1646 (1933).



Procedure 12 Semicarbazones of Aldehydes and Ketones



(a) For Water Soluble Compounds

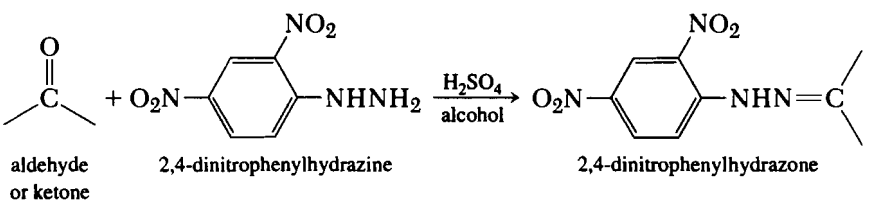
Dissolve 1 mL or 1 g of the aldehyde or ketone, 1 g of semicarbazide hydrochloride, and 1.5 g of sodium acetate in 10 mL of water in a test tube. Shake the mixture vigorously, and place the test tube in a beaker of boiling water for 5 min. Remove the test tube from the beaker, allow it to cool, and place it in a beaker of ice. Scratch the sides of the tube with a glass rod. Isolate the crystals of the semicarbazone by filtration, and recrystallize from water or 25 to 50% ethanol.

(b) For Water Insoluble Compounds

Dissolve 1 mL or 1 g of the aldehyde or ketone in 10 mL of ethanol. Add water until the solution is faintly turbid; remove the turbidity with a few drops of ethanol. Then add 1 g of semicarbazide hydrochloride and 1.5 g of sodium acetate, and from this point follow the procedure in (a).

Cleaning Up Combine the filtrates. Make the solution slightly acidic with 10% hydrochloride acid and place in the aqueous solution container.

Procedure 13 2,4-Dinitrophenylhydrazones of Aldehydes and Ketones



(a) In Ethanol

In a small flask, add 0.4 g of 2,4-dinitrophenylhydrazine to 2 mL of concentrated sulfuric acid. Add 3 mL of water dropwise, with swirling or stirring, until the 2,4-dinitrophenylhydrazine is dissolved. Add 10 mL of 95% ethanol.

Add the freshly prepared 2,4-dinitrophenylhydrazine solution to a mixture of 0.5 g of the aldehyde or ketone in 20 mL of 95% ethanol, and then allow the resulting mixture to stand at room temperature. Crystallization of the 2,4-dinitrophenylhydrazone usually occurs within 5–10 min. If no precipitate is formed, allow the mixture to stand overnight.

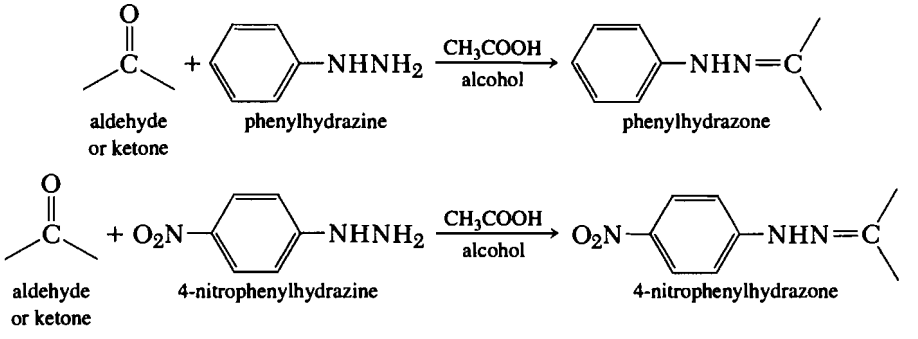
Recrystallize the 2,4-dinitrophenylhydrazone from 30 mL of 95% ethanol by heating on a steam bath. If the derivative dissolves immediately, add water slowly until the cloud point is reached or until a maximum of 5 mL of water is used. If the derivative does not dissolve, add ethyl acetate to the hot mixture until the derivative dissolves. Filter the hot solution through a fluted filter and allow to stand at room temperature until crystallization is complete (about 12 hr). Isolate the crystals by suction filtration.

(b) In Diethylene Glycol Dimethyl Ether (Diglyme)

Warm a solution of 0.17 g of 2,4-dinitrophenylhydrazine in 5 mL of diethylene glycol dimethyl ether (diglyme) and then allow to stand at room temperature for several days. Add 0.1 g of the carbonyl compound in 1 mL of 95% ethanol or in 1 mL of diethylene glycol dimethyl ether. Add three drops of concentrated hydrochloric acid. If there is not an immediate precipitation, dilute the solution with water and allow to stand. Isolate the crystals of 2,4-dinitrophenylhydrazine by suction filtration. Recrystallize as described in (a).

Cleaning Up Place any unreacted 2,4-dinitrophenylhydrazine in the hazardous waste container. Dilute the filtrate from (a) and the ethanol from recrystallization with 10 mL of water and place in the aqueous solution container. Place the filtrate from (b) in the organic solvent container.

Procedure 14 Phenylhydrazones and 4-Nitrophenylhydrazones of Aldehydes and Ketones

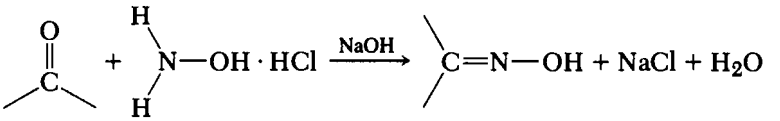


Heat to boiling a mixture of 0.5 mL of phenylhydrazine or 0.5 g of 4-nitrophenylhydrazine and 0.5 g of the aldehyde or ketone in 10–15 mL of ethanol. Add a drop of glacial acetic acid. Keep the mixture hot for a few minutes and add more ethanol, if necessary, to obtain a clear solution. Cool the solution, and isolate the hydrazone by filtration. Recrystallize from a small amount of ethanol.

If the derivative does not separate from the solution on cooling, heat the mixture to the boiling point, add water until the solution is cloudy, and then add a drop of two of ethanol to clarify it. After cooling, isolate the phenylhydrazone or 4-nitrophenylhydrazone by filtration. Recrystallize from a water–ethanol mixture.

Cleaning Up Place any unreacted 2,4-dinitrophenylhydrazine in the hazardous waste container. Place the filtrate in the aqueous solution container.

Procedure 15 Oximes of Aldehydes and Ketones



(a) In Pyridine

This procedure is used for water insoluble aldehydes and ketones. Heat, under reflux, for 2 hr on a steam bath or in a hot-water bath, a mixture of 1 g of the aldehyde or ketone, 1 g of hydroxylamine hydrochloride, 5 mL of pyridine, and 5 mL of absolute ethanol. Remove the solvents by distillation using a steam bath. Mix the residue thoroughly with 5 mL of cold water, and filter the mixture. Recrystallize the oxime from methanol, ethanol, or an ethanol–water mixture.

(b) In Water

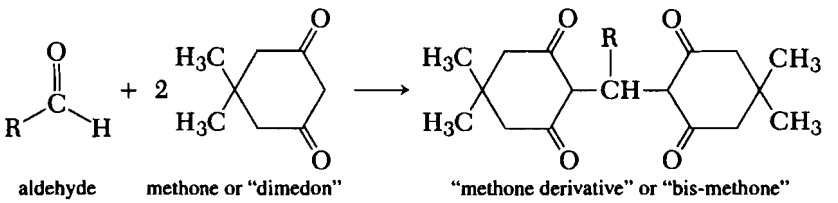
Dissolve 0.5 g of the hydroxylamine hydrochloride in 3 mL of water. Add 2 mL of 10% sodium hydroxide solution and 0.2 g of the aldehyde or ketone. If the carbonyl compound is water insoluble, add a minimal amount of ethanol to the mixture to give a clear solution. Warm the mixture on the steam bath for 10 min and cool in an ice bath. Scratch the sides of the flask with a glass rod to hasten crystallization. Add 2 mL of water. Recrystallize the product from water or dilute ethanol.

(c) For Larger or Cyclic Ketones

Certain cyclic ketones, such as camphor, require an excess of alkali and a longer time of heating. If a ketone fails to yield an oxime by (a) or (b), treat 0.5 g of the ketone with 0.5 g of hydroxylamine hydrochloride, 2 g of potassium hydroxide, and 10 mL of 95% ethanol. Heat the mixture under reflux for 2 hr and pour into 75 mL of water. Stir the suspension and allow to stand to permit the unchanged ketone to separate. Filter the solution, acidify with 10% hydrochloric acid, and allow to stand to permit the oxime to crystallize. Recrystallize the product from ethanol or an ethanol–water mixture.

Cleaning Up Place the distilled solvents from (a) in the organic solvent container. Place the filtrates in the aqueous solution container.

Procedure 16 Dimedon Derivatives of Aldehydes



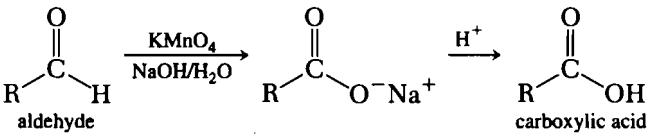
If the aldehyde is aliphatic, add a solution of 0.1 g of the aldehyde in 4 mL of 50% ethanol to 0.4 g of methone (dimedon). If the aldehyde is aromatic, add only 0.3 g of the methone. Add one drop of piperidine, and boil the mixture gently for 5 min. If the

hot solution is clear at the end of this time, add water dropwise until the solution just begins to turn cloudy. Chill the mixture. Separate the aldehyde bis-methone condensation product by filtration and wash with 2 mL of cold 50% ethanol. Recrystallize the derivative from mixtures of methanol and water.

Cleaning Up Place the filtrate in the aqueous solution container.

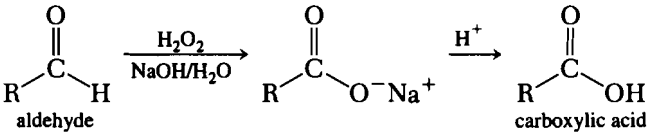
Procedure 17 Oxidation of an Aldehyde to an Acid

(a) Permanganate Method



Add a few drops of 10% sodium hydroxide solution to a solution or suspension of 1 g of the aldehyde in 10–20 mL of water. Add, dropwise, a saturated solution of potassium permanganate in water until a definite purple color remains after shaking the solution. Acidify the mixture with 10% sulfuric acid, and add sodium bisulfite until the permanganate and manganese dioxide have been converted to manganese sulfate, as evidenced by the loss of the purple color in the solution. Isolate the carboxylic acid by filtration and recrystallize from water or a water–acetone mixture. If the acid does not separate, recover it by extraction with three 15-mL portions of chloroform, methylene chloride, or diethyl ether. Dry the organic layer with magnesium sulfate, filter, and remove the organic solvent by distillation, using a steam bath, to leave the crude carboxylic acid.

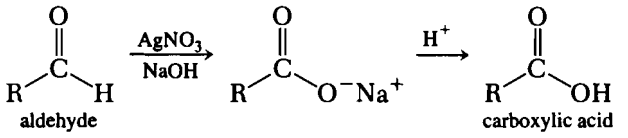
(b) Hydrogen Peroxide Method



Place, in a 250-mL flask, 10 mL of 5% sodium hydroxide solution and 15 mL of 3% hydrogen peroxide solution. Warm the solution to 65 –70°C, and add 0.5 g of the aldehyde. Shake the mixture and keep the temperature at 65°C for 15 min. If the aldehyde has not dissolved, add a few mL of ethanol. Add an additional 5 mL of hydrogen peroxide, and warm the mixture for 10 min more. Acidify the solution with 5% hydrochloric acid, and remove the acid by filtration.

If the acid is either a liquid or water soluble, it is best to make the solution neutral to phenolphthalein and evaporate to dryness.

(c) Silver(I) Oxide Method[6]



[6]S. C. Thomason and D. G. Kugler, *J. Chem. Educ.*, *45*, 546 (1968). These authors describe the use of silver(I) oxide and silver(II) oxide.

Dissolve 3.4 g of silver nitrate in 10 mL of distilled water in a 50-mL beaker. Add 10% sodium hydroxide solution dropwise with vigorous stirring until no further precipitation of silver oxide occurs (approximately 4 mL). Then add 1 g of the aldehyde with vigorous stirring and add an additional 5 mL of 10% sodium hydroxide solution. The reaction mixture usually warms up as the oxidation proceeds and the silver oxide is converted to metallic silver. Stir for 10–15 min. Remove the silver and unchanged silver oxide by filtration. Acidify the filtrate with 20% nitric acid and cool the solution in an ice bath. Isolate the precipitated solid carboxylic acid by filtration. If necessary, recrystallize the solid from a small amount of hot water or a 1:1 water–2-propanol mixture. If the acid is so soluble in water that it does not precipitate at the acidification step, extract with three 15-mL portions of chloroform, methylene chloride, or diethyl ether. Dry the organic layer with magnesium sulfate, filter, and remove the organic solvent by distillation, using a steam bath, to leave the crude carboxylic acid.

Cleaning Up Place the filtrate from (a) in the hazardous waste container. Place the recrystallization solvents from (a), (b), and (c) and the filtrate from (b) in the aqueous solution container. Place chloroform and diethyl ether from (a) and (c) in the organic solvent container. Place the silver and silver oxide from (c) in a beaker, make acidic with 5% nitric acid, and then neutralize with sodium carbonate. Add saturated sodium chloride solution to precipitate the silver chloride. Isolate the silver chloride by suction filtration and place in the nonhazardous solid waste container. Place the filtrate in the aqueous solution container.

Discussion

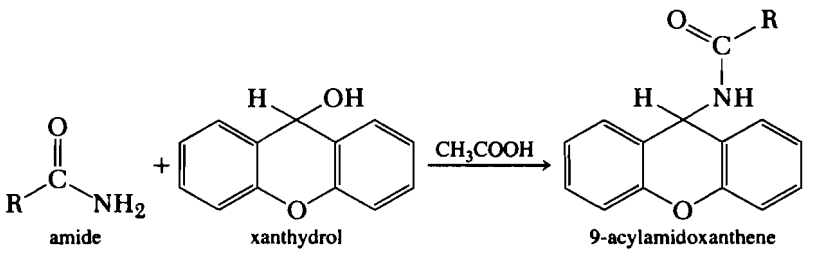
The carboxylic acids formed from these procedures are characterized by Procedures 3 through 7 (pp. 359–364).

Problem

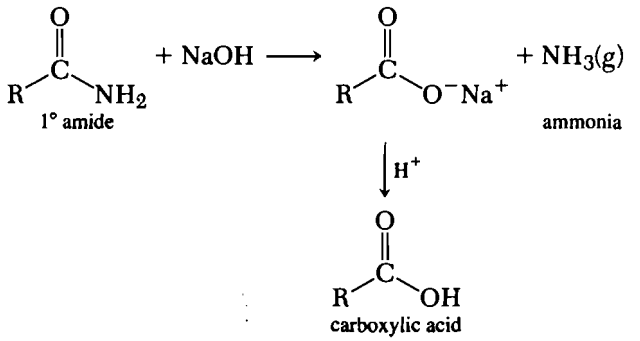
8. Give the equations for the reaction of 2-methylbenzaldehyde with (a) semicarbazide hydrochloride, (b) 2,4-dinitrophenylhydrazine, (c) 4-nitrophenylhydrazine, (d) phenylhydrazine, (e) hydroxylamine hydrochloride, and (f) dimedon.

10.4 AMIDES

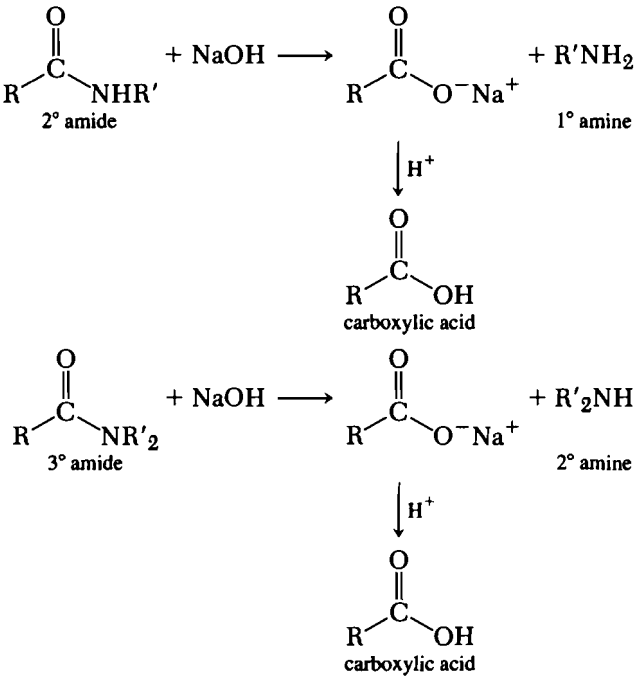
Xanthydrol reacts readily with unsubstituted amides and imides to form 9-acylamidoxanthenes (Procedure 18, p. 379). These are the only derivatives that are prepared directly from the amide.



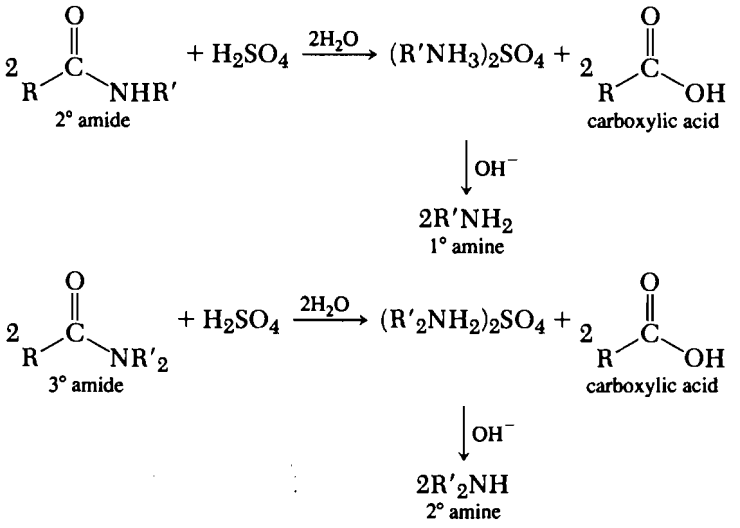
The most general method for chemically characterizing primary amides consists in hydrolyzing them with alkali to the salt of the carboxylic acid and ammonia (Procedure 19a, p. 379). Acidification of the salt produces a carboxylic acid. Either the salt or the acid can be characterized.



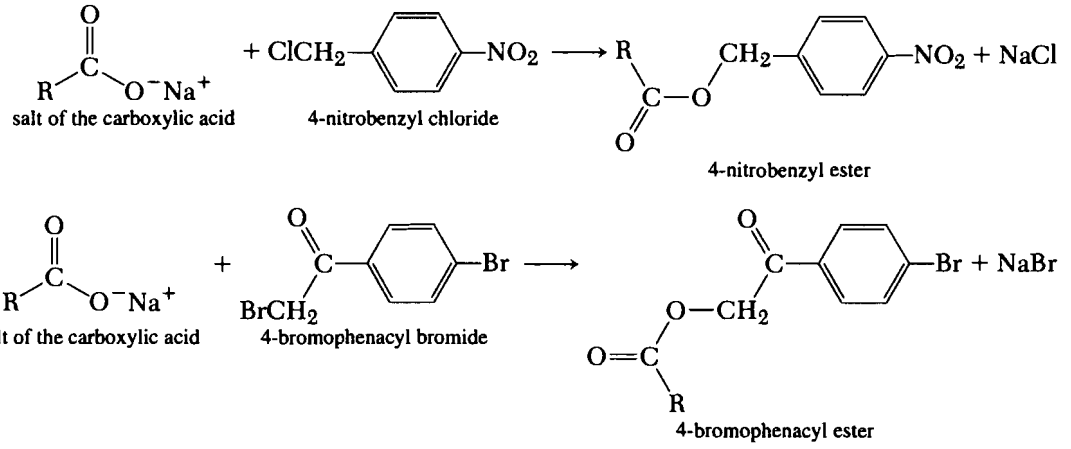
Hydrolysis of substituted amides yields carboxylic acids and primary or secondary amines instead of ammonia. The hydrolysis occurs faster in acidic conditions than in basic conditions. In basic hydrolysis, the amide is hydrolyzed to the amine and the salt of the carboxylic acid. The carboxylic acid is liberated by acidification (Procedure 19b, p. 380).



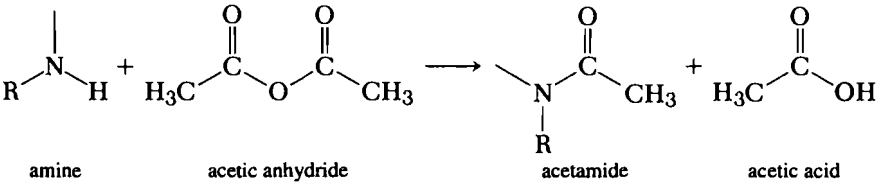
In acidic hydrolysis, the amide yields an ammonium salt and the carboxylic acid. The solution of the ammonium salts is made basic and the amine is liberated (Procedure 19c, p. 380).

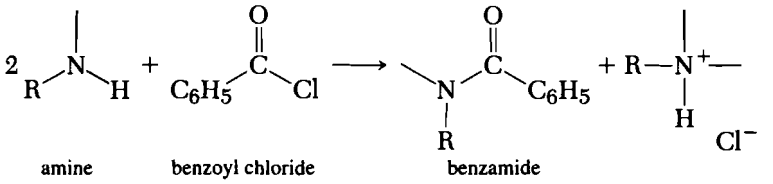


Once the carboxylic acid and the amine are isolated from the amide, derivatives of these compounds can be prepared. The 4-nitrobenzyl ester and the 4-bromophenacyl ester (Procedure 5, p. 362) are recommended as derivatives for the carboxylic acid.

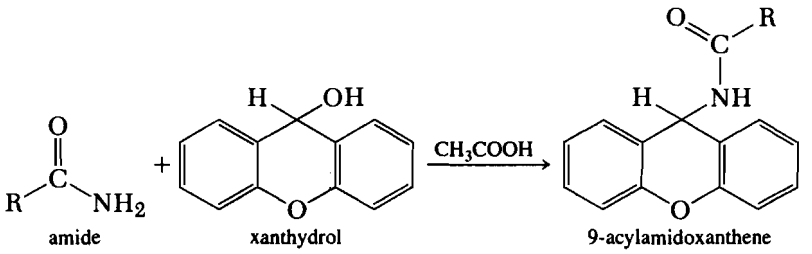


The acetamide (Procedure 20a, p. 384) and benzamide derivatives (Procedure 20b or 20c, p. 384) of the amine are also excellent derivatives. The acetamide is prepared by treating the amine with acetic anhydride. The benzamide is synthesized from the reaction of the amine with benzoyl chloride.





Procedure 18 9-Acylamidoxanthenes from Primary Amides and Imides



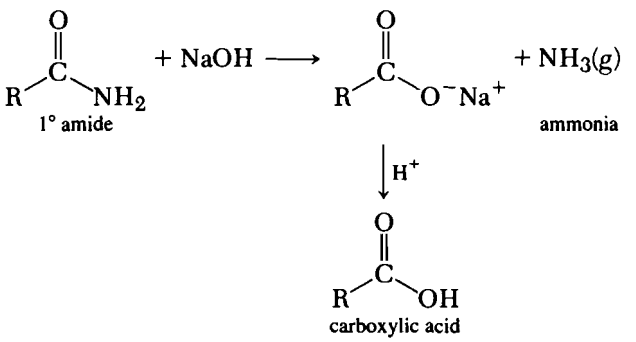
Dissolve 0.5 g of xanthydrol in 7 mL of glacial acetic acid. If the solution is not clear, allow to stand a few minutes or centrifuge. Decant the clear solution into a clean test tube. Add 0.5 g of the amide, and warm the mixture at 85°C in a beaker of water for 20–30 min. Upon cooling, isolate the acylamidoxanthene by filtration and recrystallize from a mixture of 2 parts of dioxane and 1 part water.

Some amides fail to dissolve in the acetic acid and may be converted to the derivative by using a mixture of 5 mL of ethanol, 2 mL of acetic acid, and 3 mL of water as the solvent for the reaction.

Cleaning Up Place the filtrate in the aqueous solution container.

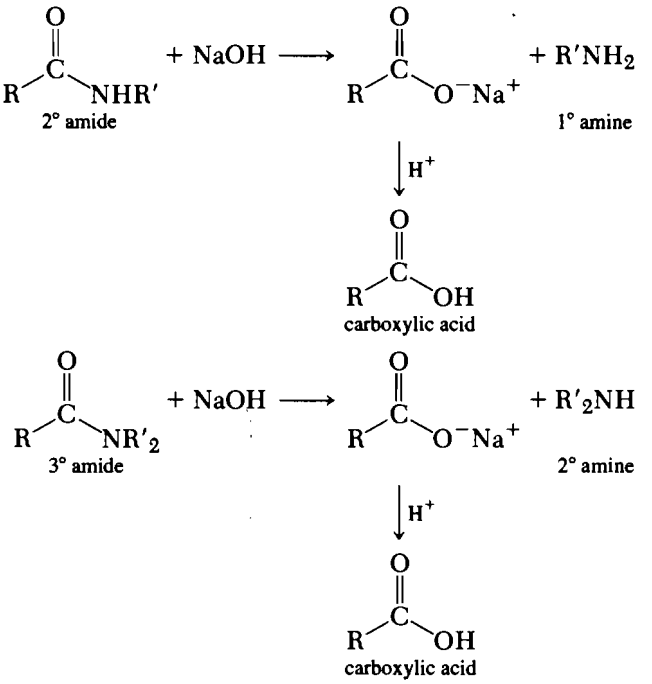
Procedure 19 Hydrolysis of Amides

(a) Basic Conditions—Primary Amides



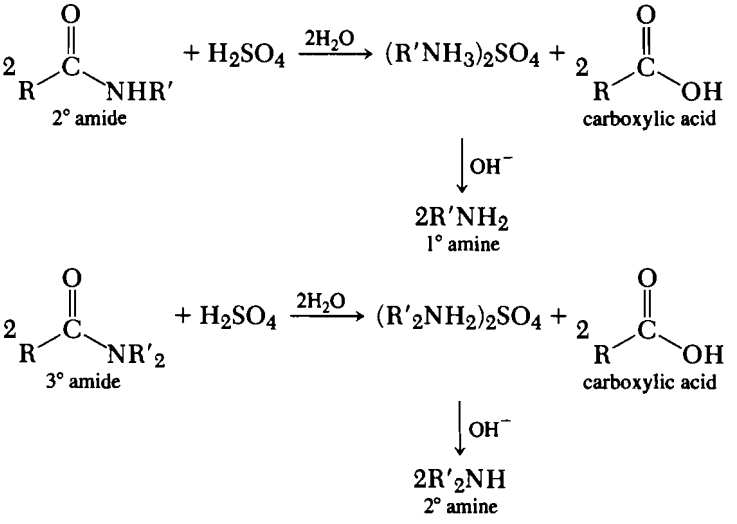
Heat for 30 min, under reflux, a mixture of 25 mL of 10% sodium hydroxide solution and 1.0 g of the amide. The odor of ammonia will be very apparent. Cool the aqueous solution in an ice bath, and add concentrated hydrochloric acid until the solution is acidic to litmus. Remove the solid carboxylic acid by filtration. If the carboxylic acid does not precipitate, extract the solution with three 15-mL portions of chloroform, methylene chloride, or diethyl ether. Dry the organic layer with magnesium sulfate, filter, and remove the organic solvent by distillation, using a steam bath, to leave the crude carboxylic acid.

(b) Basic Conditions—Substituted Amides



Heat for 1 hr, under reflux, a mixture of 25 mL of 10% sodium hydroxide solution and 1.0 g of the amide. Cool the solution. Extract the aqueous layer twice with 15 mL of ethyl ether. Dry the combined ether layers with magnesium sulfate, and then filter. Remove the ether by distillation, using a steam bath, to yield the primary or secondary amine. Cool the aqueous solution in an ice bath, and add concentrated hydrochloric acid until the solution is acidic to litmus. Remove the solid carboxylic acids by filtration. Extract volatile carboxylic acids with three 15-mL portions of chloroform, methylene chloride, or diethyl ether. Dry the organic layer with magnesium sulfate, filter, and remove the organic solvent by distillation, using a steam bath, to leave the crude carboxylic acid.

(c) Acidic Conditions—Substituted Amides



Heat 1 g of the amide with 20 mL of 20% sulfuric acid for 2 hr and cool the solution. Remove the carboxylic acid by filtration if insoluble in water. Extract water-soluble or liquid carboxylic acids with three 15-mL portions of chloroform, methylene chloride, or diethyl ether. Dry the organic layer with magnesium sulfate, filter, and remove the organic solvent by distillation, using a steam bath, to leave the crude carboxylic acid. Cool the solution, and add 20% sodium hydroxide solution until the solution is alkaline. Extract with two 15-mL portions of ethyl ether, dry the combined ether layers with magnesium sulfate, and filter. Remove the ether by distillation, using a steam bath, to yield the amine.

Cleaning Up Place the diethyl ether in the organic solvent container. Neutralize the acidic filtrates from (a) and (b) with sodium carbonate and the basic filtrate from (c) with 10% hydrochloric acid. Place these aqueous solutions in the aqueous solution container.

Discussion

A solid amine or carboxylic acid is purified by recrystallization and used as a derivative. Derivatives of any amine or carboxylic acid can also be prepared.

The carboxylic acid or the salt of the carboxylic acid can undergo reaction with 4-nitrobenzyl chloride to give the 4-nitrobenzyl ester or with 4-bromophenacyl bromide to yield the 4-bromophenacyl ester (Procedure 5, p. 362).

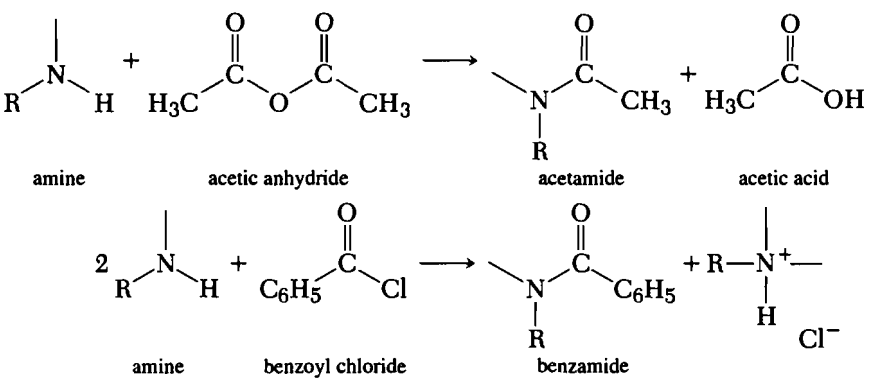
The amine can undergo reaction with acetic anhydride to yield the acetamide (Procedure 20a, p. 384) or with benzoyl chloride to produce the benzamide (Procedure 20b or 20c, p. 384).

Problems

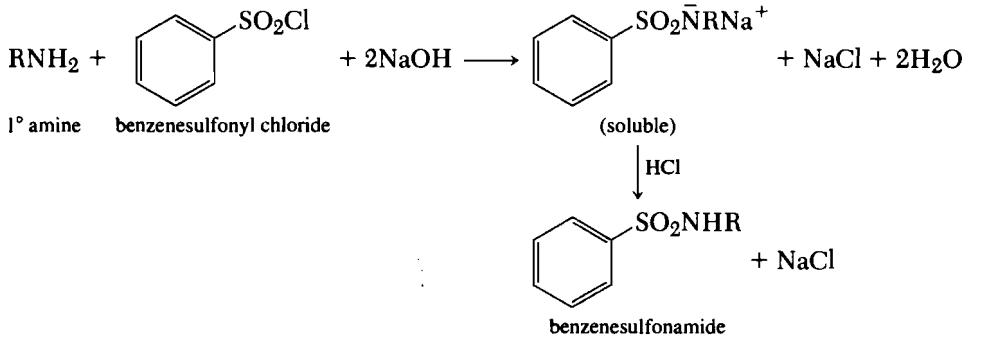
9. Give the equation for the reaction of heptanamide with xanthydrol.
10. Give the equation for the basic hydrolysis, followed by acidification, of *N*-methyl-*N*-phenylethanamide. Give the equations for the formation of the 4-nitrobenzyl ester and the 4-bromophenacyl ester derivatives. Give the equations for the formation of the acetamide and benzamide derivatives.

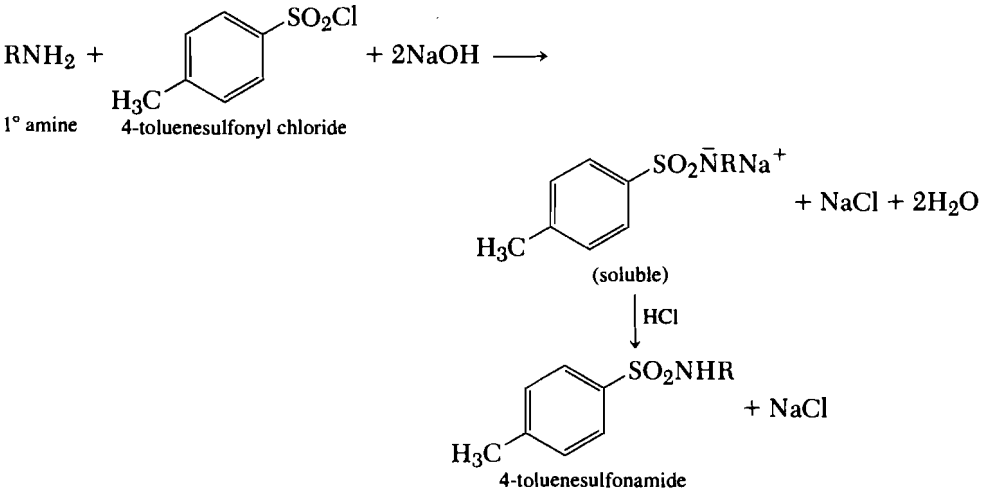
10.5 AMINES

The most useful derivatives of primary and secondary amines take advantage of their reactive N—H bond. The amides of acetic and benzoic acids (Procedure 20, p. 384) are conveniently prepared by treatment of the amine, respectively, with acetic anhydride or benzoyl chloride. Acetyl and benzoyl derivatives are known for most primary and secondary amines, and for this reason these derivatives are useful.

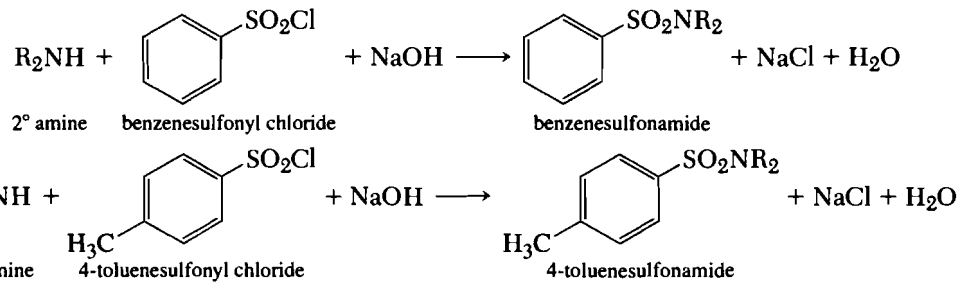


Arylsulfonamides are frequently used as derivatives. The benzenesulfonamides are frequently used, and their preparation is related to the Hinsberg method for classifying amines (compare Experiment 19, p. 291, and Procedure 21, p. 386). The reaction of a primary amine with alkaline benzenesulfonyl chloride or 4-toluenesulfonyl chloride produces the soluble salt of the arylsulfonamide. Acidification results in precipitation of the arylsulfonamide.

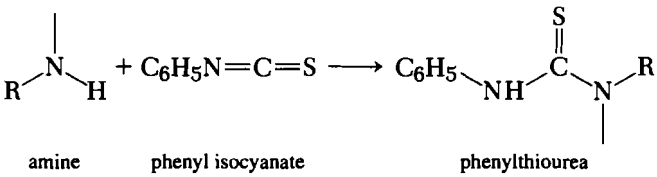




A secondary amine reacts with benzenesulfonyl chloride or 4-toluenesulfonyl chloride to give the arylsulfonamide, which is usually insoluble.



The phenylthioureas are especially valuable for characterizing low-molecular-weight, water-soluble amines. They are formed by treatment of amines with phenyl isothiocyanate (Procedure 22, p. 387).

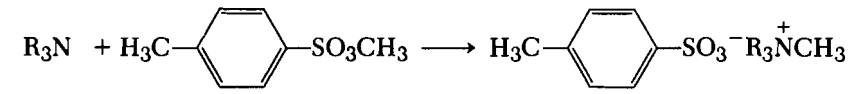


Tertiary amines vary so greatly in nature that no type of derivative has been found to be generally applicable.

Chloroplatinic salts (Procedure 23, p. 387) are prepared from the tertiary amine and chloroplatinic acid.

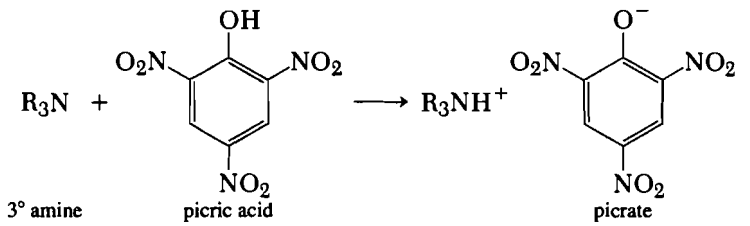
$$\underset{\text{3° amine}}{R_3N} + \underset{\text{chloroplatinic acid}}{H_2PtCl_6 \cdot 6H_2O} \xrightarrow[H_2O]{HCl} \underset{\text{chloroplatinic salt}}{R_3NH^+HPtCl_6^-}$$

Perhaps the most useful derivatives from tertiary amines are the quaternary ammonium salts formed by the reaction of the amine with methyl 4-toluenesulfonate (Procedure 24a, p. 388) or methyl iodide (Procedure 24b, p. 388).



$$\underset{\text{3° amine}}{R_3N} + \underset{\text{methyl iodide}}{CH_3I} \longrightarrow \underset{\text{quaternary salt}}{(R_3NCH_3)^+I^-}$$

Picric acid undergoes reaction with tertiary amines to yield the picrates (Procedure 25, p. 388).



Primary, secondary, and tertiary amines are readily converted to hydrochloride salts (Procedure 26, p. 389). These hydrochlorides are almost always easily purified solids with sharp melting points, which makes them useful for purposes of characterization. The amine hydrochlorides are prepared by passing hydrogen chloride gas through an ether solution of the amine.

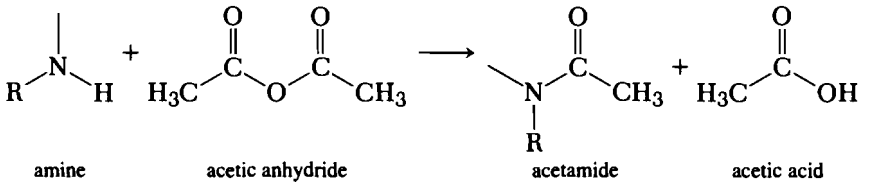
$$\underset{\text{1° amine}}{RNH_2} + HCl(g) \longrightarrow \underset{\text{amine hydrochloride}}{RNH_3^+\,Cl^-}$$

$$\underset{\text{2° amine}}{R_2NH} + HCl(g) \longrightarrow \underset{\text{amine hydrochloride}}{R_2NH_2^+\,Cl^-}$$

$$\underset{\text{3° amine}}{R_3N} + HCl(g) \longrightarrow \underset{\text{amine hydrochloride}}{R_3NH^+\,Cl^-}$$

Procedure 20 Substituted Amides from Amines

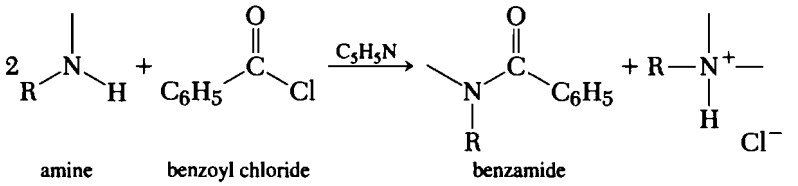
(a) Substituted Acetamides from Water-Insoluble Amines



Dissolve 0.5 g of the compound in 15 mL of 5% hydrochloric acid. Add a few chips of ice, then add 3 mL of acetic anhydride. Stir or swirl the mixture vigorously, and add a previously prepared solution of 2.5 g of sodium acetate trihydrate in 2.5 mL of water in one portion. If the product does not crystallize, chill the mixture overnight. Isolate the crystals by filtration.

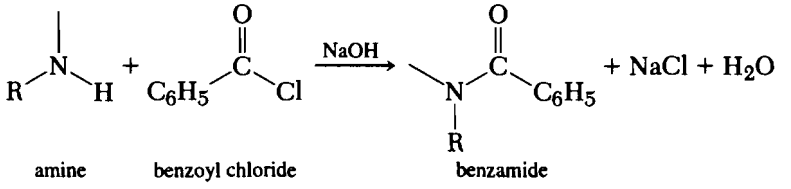
Recrystallize from cyclohexane or from a mixture of cyclohexane and benzene (see footnote 2, p. 360). Dry the acetamide thoroughly before recrystallization is attempted from these solvents. An ethanol–water mixture may also be used for recrystallization.

(b) Benzamides: Pyridine Method



Dropwise add 0.50 mL of benzoyl chloride to a solution of 0.5 g of the compound in 5 mL of dry pyridine and 10 mL of dry benzene (see footnote 2, p. 360). *Note: Benzene is a known carcinogen. Use benzene in the hood, do not breathe the vapors, and avoid contact with the skin.* Heat the resulting mixture in a water bath at 60–70°C for 30 min and then pour into 100 mL of water. Separate the benzene layer, and wash the aqueous layer once with 10 mL of benzene. Wash the combined benzene solutions successively with 10 mL of 5% hydrochloric acid, 10 mL of water, and 10 mL of 5% sodium carbonate solution. Dry the benzene layers with a little anhydrous magnesium sulfate. Remove the drying agent by filtration through a fluted filter, and remove the benzene by distillation to a volume of 3–4 mL. Stir 20 mL of hexane into the mixture. Isolate the crystalline benzamide by suction filtration and wash with hexane. Recrystallize from a mixture of cyclohexane and hexane or from a mixture of cyclohexane and ethyl acetate. Ethanol or aqueous ethanol may also be used with many compounds.

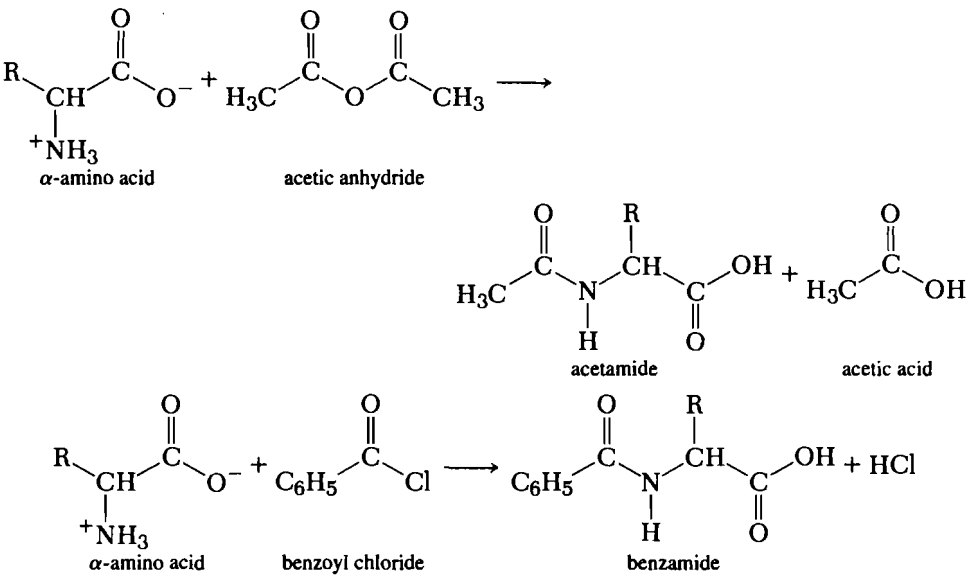
(c) Benzamides: Sodium Hydroxide Method



The regular procedure for the Schotten–Baumann reaction described under Experiment 3a (p. 256) may be used. Two modified procedures are described below.

1. Stir or shake a mixture of 20 mL of 5% sodium hydroxide solution, 5 mL of chloroform, 0.5 g of the compound, and 0.5 g of benzoyl chloride for about 20 min and then allow to stand for 12 hr. Separate the chloroform layer, and wash the aqueous layer with 10 mL of chloroform. Wash the combined chloroform solutions with water, dry with anhydrous magnesium sulfate, and evaporate to a volume of 2–3 mL. Stir 20 mL of hexane into the solution, and remove the derivative by filtration and wash with hexane.
2. Add 1 mL of the amine to a solution of 1 g of benzoyl chloride in 20 mL of dry benzene (see footnote 2, p. 360). *Note: Benzene is a known carcinogen. Use benzene in the hood, do not breathe the vapors, and avoid contact with the skin.* Reflux the resulting solution for 15 min and then allow to cool. Filter the solution, and wash the precipitate with 10 mL of warm benzene. Add the washings to the original filtrate. Wash the benzene solution with 10 mL of 2% sodium carbonate solution, with 10 mL of 2% hydrochloric acid (*Caution: foaming*), and with 10 mL of distilled water. Remove the benzene by distillation, and recrystallize the residue from 60% ethanol.

(d) Acetamides and Benzamides from Amino Acids



Acetamide

Dissolve 0.5 g of the compound in 15 mL of 5% hydrochloric acid. Add a few chips of ice, followed by 3 mL of acetic anhydride. Reflux the mixture for 1 hr and then allow to cool. Isolate the crystals by filtration and recrystallize the precipitate from 60% ethanol.

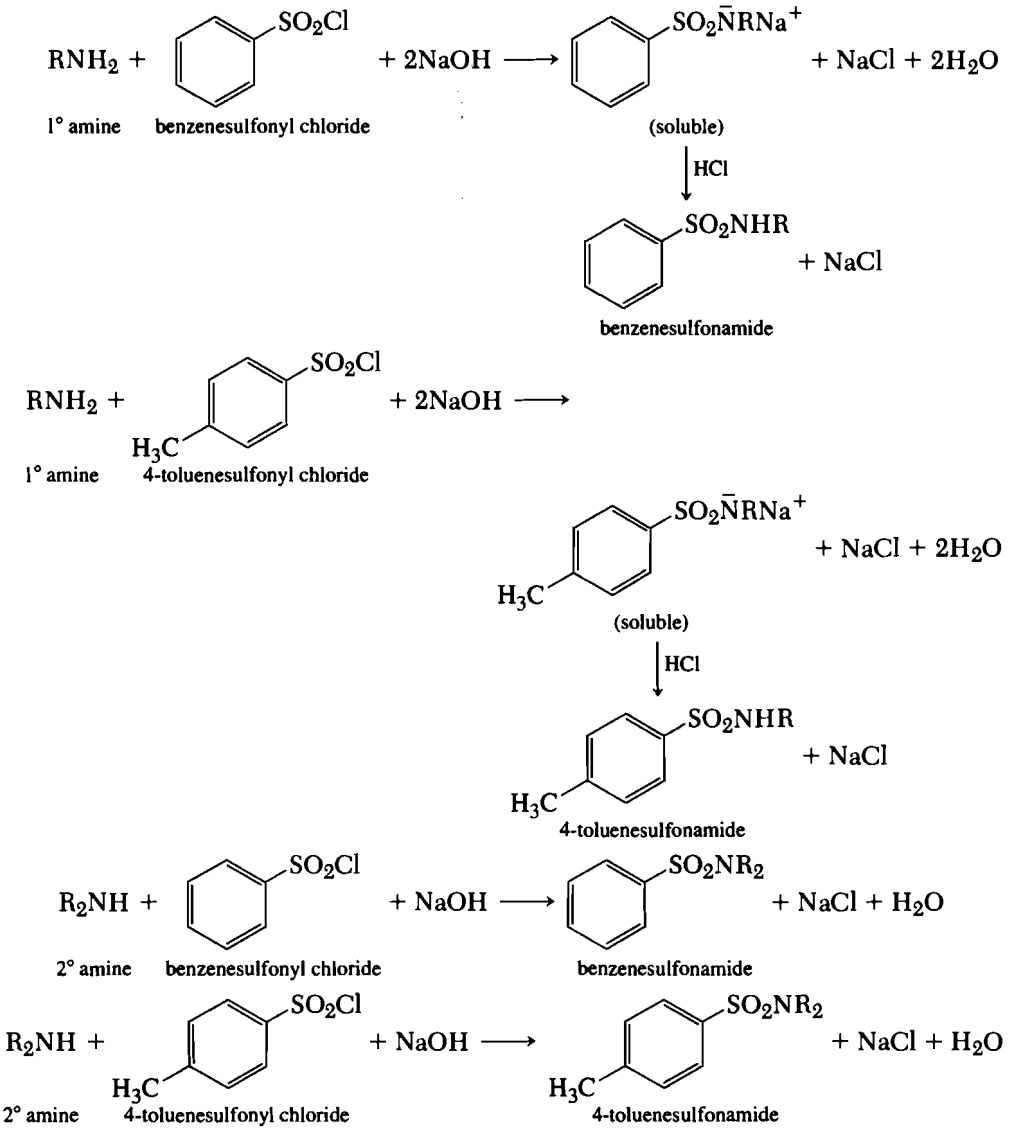
Benzamide

In a test tube, dissolve 0.5 g of the amino acid in 10 mL of 10% sodium bicarbonate solution. Add 1 g of benzoyl chloride. Stopper and shake the mixture vigorously, venting it periodically to allow the carbon dioxide gas to escape. When the odor of benzoyl chloride has disappeared, acidify the solution with 10% hydrochloric acid to a pH of 4.

Isolate the crystals by filtration and rinse the crystals with a small amount of diethyl ether to remove any benzoic acid. Recrystallize the product from 60% ethanol.

Cleaning Up Place the reaction filtrate from (a) in the aqueous solution container. Place the chloroform from (c) and (d) in the halogenated organic waste container. Place the distilled benzene in the hazardous waste container for benzene. Place the non-halogenated filtrates and other solvents in the organic solvent container. Place the ethanol–water recrystallization solvents in the aqueous solution container.

Procedure 21 Benzenesulfonamides and 4-Toluenesulfonamides from Primary and Secondary Amines (Hinsberg's Method)

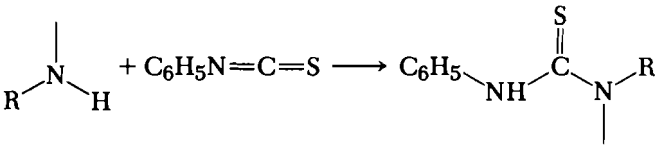


Add 17 mL of 10% sodium hydroxide solution and 2.0 g of benzenesulfonyl chloride or 4-toluenesulfonyl chloride to 1 mL or 1 g of the amine in a test tube. Stopper the test

tube, and shake the mixture very vigorously. Test the solution to make sure that it is alkaline. Cool the solution and acidify with 10% hydrochloric acid. Isolate the benzenesulfonamide by filtration and recrystallize from 95% ethanol.

Cleaning Up Place the filtrate in the aqueous solution container.

Procedure 22 Phenylthioureas from Amines



amine phenyl isocyanate phenylthiourea

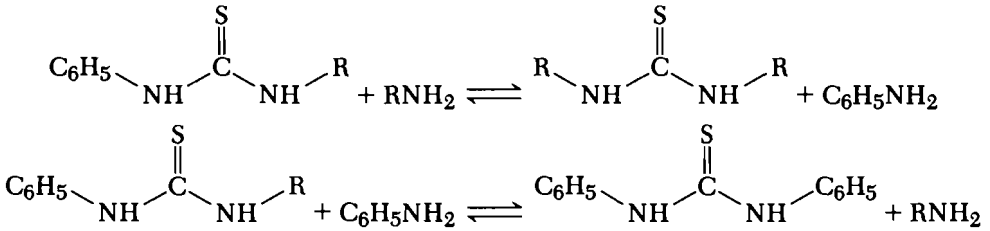
Mix equal amounts of the amine and phenyl isothiocyanate in a test tube and shake for 2 min. If no reaction occurs spontaneously, heat the mixture for 3 min over a low flame. *Caution! The isothiocyanates are lachrymators.* The aliphatic amines usually react immediately, whereas the aromatic amines require heating. Chill the mixture in a beaker of ice until the mass solidifies. Powder the solid and wash with petroleum ether and 50% ethanol in order to remove any excess of either reactant. Recrystallize the residue from 95% ethanol.

Cleaning Up Treat any unreacted phenyl isothiocyanate with an excess of 5.25% sodium hypochlorite (household bleach). Place the filtrates in the aqueous solution container.

Discussion

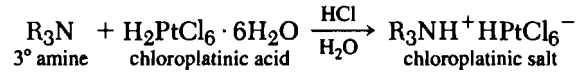
The reagent phenyl isothiocyanate is not sensitive to water; in fact, this reaction may be carried out with dilute aqueous solutions of the amines.

Occasionally the thiourea derivative reversibly undergoes a complicating disproportionation reaction with the original amine.



This complication is averted if long heating times are avoided.

Procedure 23 Chloroplatinate Salts from Tertiary Amines



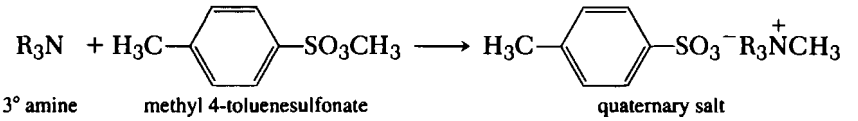
3° amine chloroplatinic acid chloroplatinic salt

With shaking, add 10 mL of a 25% aqueous solution of chloroplatinic acid ($H_2PtCl_6 \cdot 6H_2O$) to a solution of 0.5 g of the amine in 10 mL of 10% hydrochloric acid. Collect the crystalline chloroplatinate by filtration and wash with 10% hydrochloric acid. Recrystallize from ethanol containing a drop of concentrated hydrochloric acid to prevent hydrolysis.

Cleaning Up Place the filtrate in the hazardous waste container.

Procedure 24 Quaternary Ammonium Salts of Tertiary Amines

(a) Addition Product with Methyl 4-Toluenesulfonate

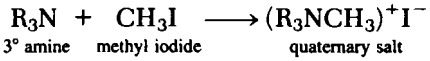


3° amine methyl 4-toluenesulfonate quaternary salt

Add 1 g of the amine to a solution of 2–3 g of methyl 4-toluenesulfonate in 10 mL of dry benzene (see footnote 2, p. 360). *Note: Benzene is a known carcinogen. Use benzene in the hood, do not breathe the vapors, and avoid contact with the skin.* Reflux the solution for 10–20 min and cool. Recrystallize the products by dissolving them in the least possible amount of boiling ethanol. Add ethyl acetate until precipitation starts, and cool the mixture. Isolate the product by filtration and quickly dry; determine the melting point immediately.

Cleaning Up Place the filtrate in the hazardous waste container for benzene.

(b) Addition Product with Methyl Iodide

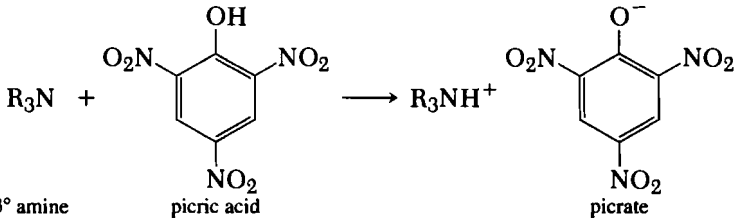


3° amine methyl iodide quaternary salt

Warm a mixture of 0.5 g of the amine and 0.5 mL of methyl iodide in a test tube over a low flame for a few minutes and then cool in an ice bath. *Note: Methyl iodide is a suspected cancer agent.* Scratch the tube with a glass rod to hasten crystallization. Purify the product by recrystallization from absolute ethanol, methanol, or ethyl acetate.

Cleaning Up Place the filtrate in the hazardous waste container.

Procedure 25 Picrates from Tertiary Amines



3° amine picric acid picrate

Note: Picric acid can explode if it is allowed to dry. Do not allow the reagent to dry out. Add a sample of the compound (0.3–0.5 g) to 10 mL of 95% ethanol. If the sample does not dissolve, shake the mixture until a saturated solution results and then filter. Add the filtrate to 10 mL of a saturated solution of picric acid (2,4,6-trinitrophenol) in 95% ethanol, and heat the solution to boiling. Allow the solution to cool slowly, and remove the yellow crystals of the picrate by filtration.

Most picrates are pure enough that recrystallization is usually not needed. *Caution: Some picrates explode when heated.* Certain picrates, especially those of hydrocarbons, dissociate when heated and consequently cannot be recrystallized. In such cases the original precipitate should be washed with a very small amount of ether and dried in preparation for the melting point determination. Use ethanol as a recrystallization solvent.

Cleaning Up Place the filtrate in the aqueous solution container.

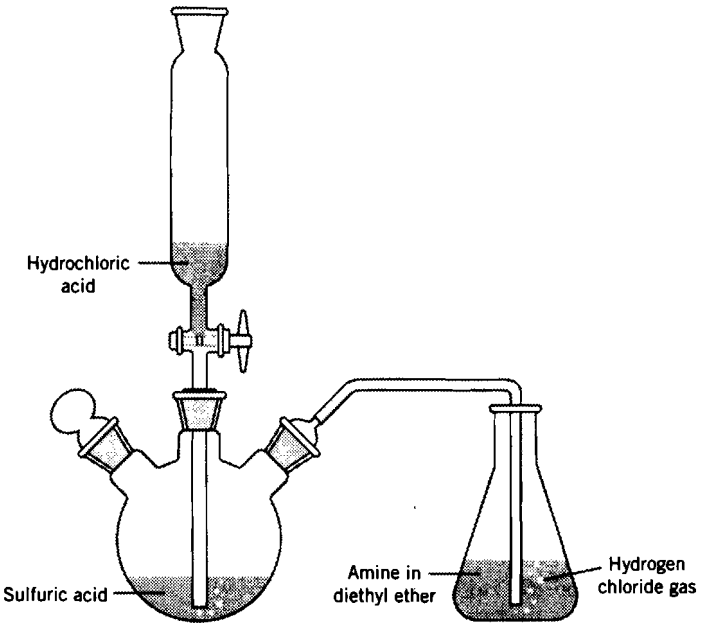


Figure 10.1 Apparatus for Procedure 26.

Procedure 26 Amine Hydrochloride Salts[7]

$$\underset{1^\circ \text{ amine}}{RNH_2} + HCl(g) \longrightarrow \underset{\text{amine hydrochloride}}{RNH_3{}^+Cl^-}$$

$$\underset{2^\circ \text{ amine}}{R_2NH} + HCl(g) \longrightarrow \underset{\text{amine hydrochloride}}{R_2NH_2{}^+Cl^-}$$

$$\underset{3^\circ \text{ amine}}{R_3N} + HCl(g) \longrightarrow \underset{\text{amine hydrochloride}}{R_3NH^+Cl^-}$$

Assemble a hydrogen chloride generator (Figure 10.1) in a fume hood using a three-neck 250-mL round-bottom flask equipped with a stoppered 100-mL pressure-equalizing addition funnel and a glass tube leading to a 250-mL Erlenmeyer flask. The addition funnel contains a long tube that is below the solution in the round-bottom flask. The glass tube connecting the two flasks is above the solution in the round-bottom flask but below the solution in the Erlenmeyer flask, so that the hydrogen chloride gas is bubbled through the reaction mixture. Add 50 mL of concentrated sulfuric acid to the round-bottom flask and place 30 mL of concentrated hydrochloric acid in the dropping funnel. Dissolve 1 g of the amine in 75 mL of anhydrous diethyl ether and place in the Erlenmeyer flask. Slowly add the hydrochloric acid to the sulfuric acid. The hydrogen chloride gas that is generated is bubbled into the ether solution. Care must be taken in the slow addition of the hydrochloric acid to the sulfuric acid so that no sulfuric acid is carried over into the amine solution. After the precipitate stops forming in the ether solution, filter the amine hydrochloride salt from the ether, wash with anhydrous ether, and recrystallize from a mixture of hexane and 2-propanol.

[7]Personal communication with Rogers Lambert, Professor Emeritus of Chemistry, Radford University, Radford, Virginia.

Cleaning Up Place the sulfuric acid–hydrochloric acid mixture in a 600-mL beaker and slowly add solid sodium carbonate until the foaming ceases. Place the solution in the aqueous solution container. Place the organic solvents and filtrates in the organic solvent container.

PROBLEMS

11. Give the equations for the reaction of cyclohexylamine with (a) acetic anhydride; (b) benzoyl chloride and pyridine; (c) benzenesulfonyl chloride and base, followed by acid, (d) 4-toluenesulfonyl chloride and base, followed by acid; (e) phenyl isothiocyanate, and (f) hydrochloric acid.
12. Give the equations for the reaction of *N,N*-dimethylaniline with (a) chloroplatinic acid, (b) methyl 4-toluenesulfonate, (c) methyl iodide, (d) picric acid, and (e) hydrochloric acid.

10.6 AMINO ACIDS

The melting points or decomposition points of amino acids are not exact. The values depend upon the rate of heating. Hence, in using these constants to prepare a list of possibilities, extra allowance must be made for their inaccuracy.

The α-amino acids occurring naturally in plants and animals or obtained from the acid or enzymatic hydrolysis of proteins and peptides are optically active (except glycine) and belong to the *configurational* L-series. The specific rotations are valuable constants for identification (Table 10.2).

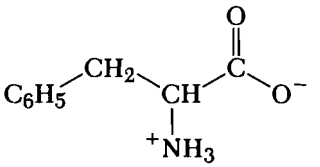
TABLE 10.2 Specific Rotations of α-Amino Acids[a]

Amino Acid Configuration	Solvent	C (g/100 mL)	Temp. (°C)	$[\alpha]_D$ (deg.)	R/S
L-Alanine	1.0 N HCl	5.8	15	+14.7	2(*S*)
L-Arginine	6.0 N HCl	1.6	23	+26.9	2(*S*)
L-Aspartic acid	6.0 N HCl	2.0	24	+24.6	2(*S*)
L-Cystine	1.0 N HCl	1.0	24	−214.4	2(*R*), 2′ (*R*)
L-Glutamic acid	6.0 N HCl	1.0	22	+31.2	2(*S*)
L-Histidine	6.0 N HCl	1.5	22	+13.0	2(*S*)
Hydroxy-L-proline	1.0 N HCl	1.3	20	−47.3	2(*S*), 4(*R*)
Allohydroxy-L-proline	Water	2.6	18	−58.1	2(*S*), 4(*S*)
L-Isoleucine	6.0 N HCl	5.1	20	+40.6	2(*S*), 3(*S*)
L-Alloisoleucine	6.0 N HCl	3.9	20	+38.1	2(*S*), 3(*R*)
L-Leucine	6.0 N HCl	2.0	26	+15.1	2(*S*)
L-Lysine	6.0 N HCl	2.0	23	+25.9	2(*S*)
L-Methionine	0.2 N HCl	0.8	25	+21.2	2(*S*)
L-Phenylalanine	5.4 N HCl	3.8	20	−7.1	2(*S*)
L-Proline	0.5 N HCl	0.6	20	−52.6	2(*S*)
L-Serine	1.0 N HCl	9.3	25	+14.4	2(*S*)
L-Threonine	Water	1.3	26	+28.4	2(*S*), 3(*R*)
L-Allothreonine	Water	1.6	26	+9.6	2(*S*), 3(*S*)
L-Tryptophan	Water	1.0	22	−31.5	2(*S*)
L-Tyrosine	6.3 N HCl	4.4	20	−8.6	2(*S*)
L-Valine	6.0 N HCl	3.4	20	+28.8	2(*S*)

[a]A leading reference for amino acids is *The Merck Index*, 12th ed. (Merck & Co., Rahway, NJ, 1996).

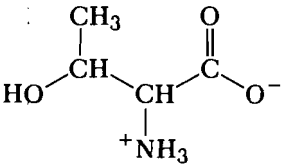
Amino acids can be divided into four general categories; this division is based on their acid–base and charge properties:

1. *Hydrophobic:* Amino acids that are substantially less water soluble than class 2, for example, phenylalanine,



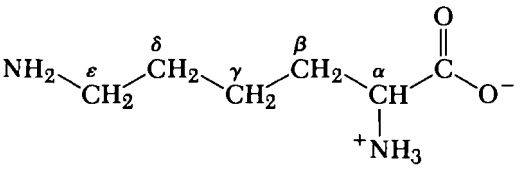
which is in solubility class $A_2(B)$, is virtually insoluble in water.

2. *Hydrophilic (polar, no net charge):* These amino acids have polar functional groups (OH) that, despite not having a positive or negative charge, are reasonably soluble in water, for example, threonine.



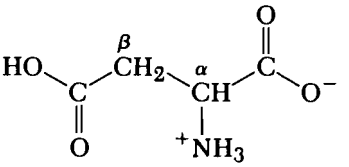
These compounds are differentiated from those in succeeding classes in that the polar groups are not appreciably acidic or basic (in the proton-transfer sense).

3. *Positively charged (basic):* Such amino acids have basic, usually nitrogenous, functions that are protonated at intracellular[8] pH. Lysine,



would also have its ε-amino group protonated under these conditions.

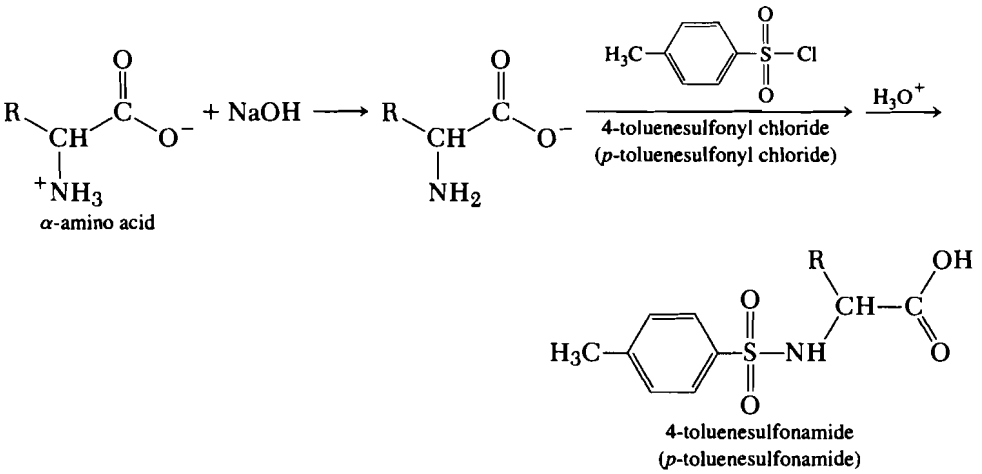
4. *Negatively charged (acidic):* These amino acids have an acidic, thus ionized, carboxyl group at intracellular pH. For example, the β-carboxyl group of aspartic acid,



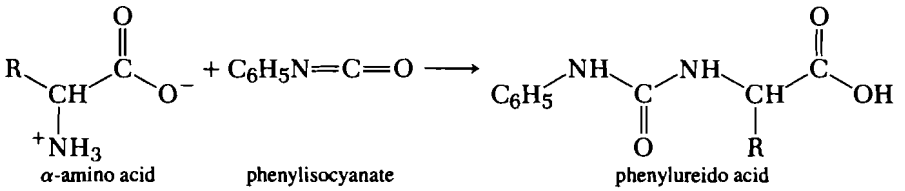
would also be ionized to a carboxylate group under these conditions.

Solid derivatives of the amino acids are usually obtained from reaction of the amino groups rather than the carbonyl groups. The Hinsberg reaction (Procedure 27, p. 393) furnishes good derivatives for a considerable number of the amino acids. In the Hinsberg reaction, 4-toluenesulfonyl chloride reacts with the amino acid to yield a 4-toluenesulfonamide.

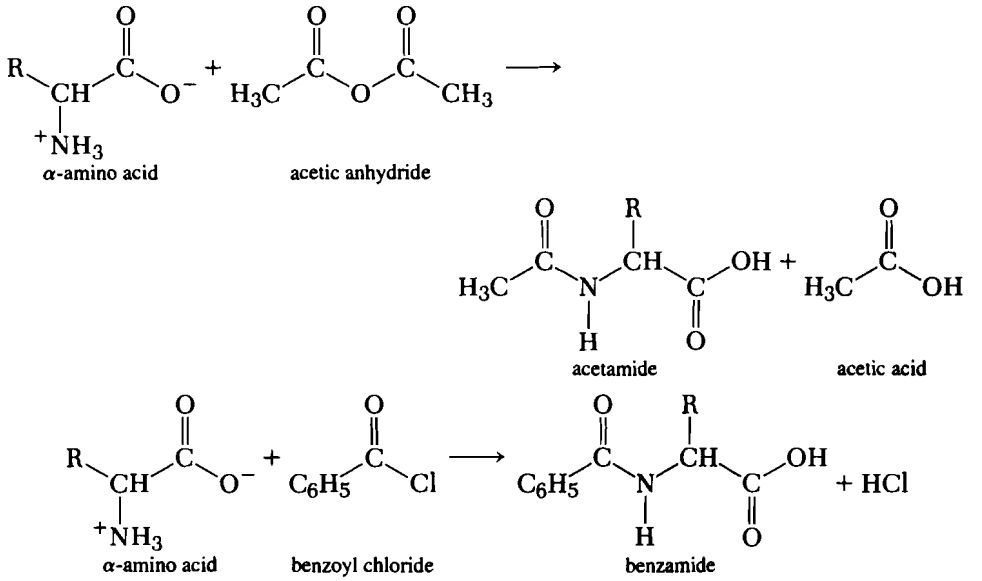
[8]Intracellular pH: 6.0–7.0.



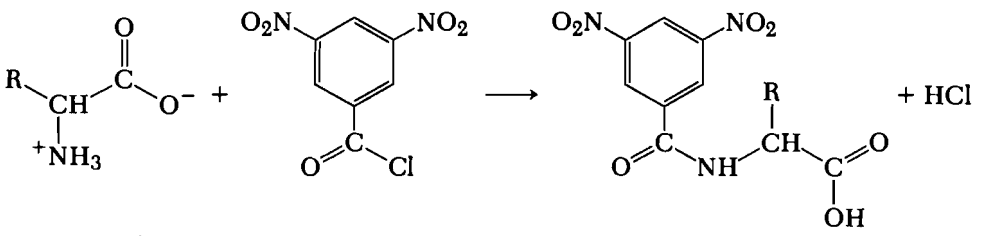
Phenyl isocyanate reacts with the amino acids to produce the corresponding substituted phenylureas, also known as phenylureido acids (Procedure 28, p. 394).



Procedures similar to ones used for the preparation of amides are used to synthesize acetamides and benzamides from amino acids (Procedure 20d, p. 385).

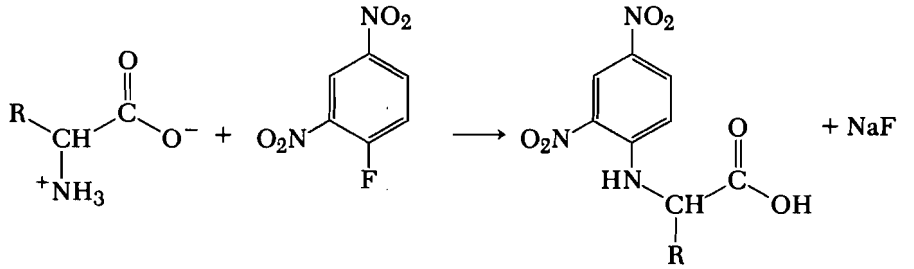


3,5-Dinitrobenzamides are prepared from treating the amino acid with 3,5-dinitrobenzoyl chloride in the presence of base (Procedure 29, p. 394).



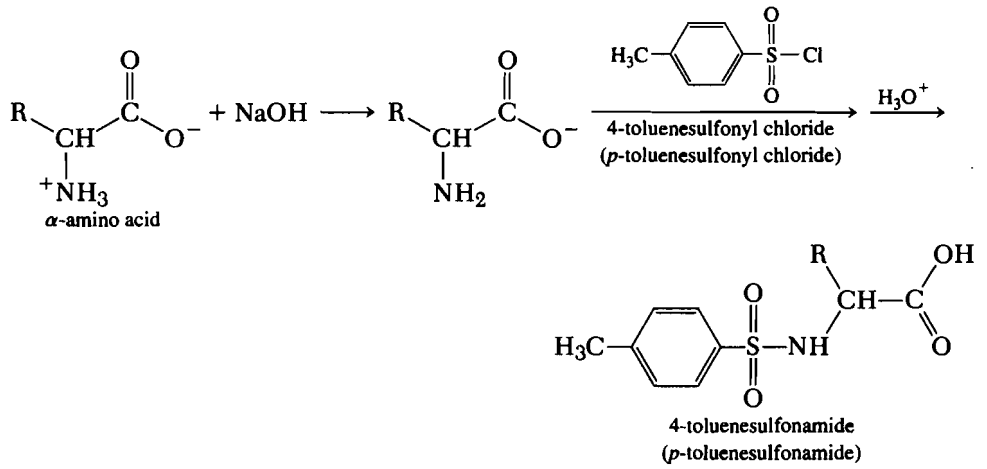
α-amino acid 3,5-dinitrobenzoyl chloride 3,5-dinitrobenzamide

The *N*-substituted 2,4-dinitroanilines obtained by the action of 2,4-dinitrofluorobenzene on amino acids (Procedure 30, p. 395) have found extensive use as derivatives of amino acids, peptides, and proteins.



α-amino acid 2,4-dinitrofluorobenzene (Sanger's reagent) *N*-substituted 2,4-dinitroaniline

Procedure 27 4-Toluenesulfonamides from Amino Acids



α-amino acid

4-toluenesulfonyl chloride (*p*-toluenesulfonyl chloride)

4-toluenesulfonamide (*p*-toluenesulfonamide)

Dissolve 1 g of the amino acid in 20 mL of 1 M sodium hydroxide solution. Add a solution of 2 g of 4-toluenesulfonyl chloride in 25 mL of diethyl ether. Shake the mixture mechanically or vigorously for 3–4 hr. Separate the ether layer, and acidify the aqueous layer to a pH of about 4 using 10% hydrochloric acid. Isolate the solid filtration and recrystallize from 4–5 mL of 60% ethanol. If an oil is obtained upon acidification, place the mixture in a refrigerator overnight to induce crystallization.

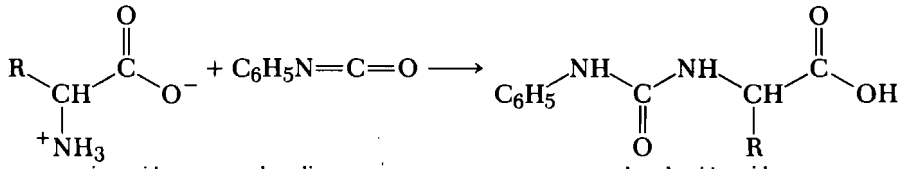
The sodium salts of the derivatives of phenylalanine and tyrosine are sparingly soluble in water and separate during the initial reaction. Acidify the resulting suspension.

The salts go into solution, and the mixture separates into two layers. The 4-toluenesulfonyl derivatives then crystallize from the ether layer. Remove the derivatives by filtration.

The derivatives of glutamic and aspartic acids, arginine, lysine, tryptophane, and proline crystallize with difficulty; other derivatives should be tried in the event that oils are produced.

Cleaning Up Place the ether layer in the organic solvent container. Neutralize the aqueous filtrate with sodium carbonate and place in the aqueous solution container.

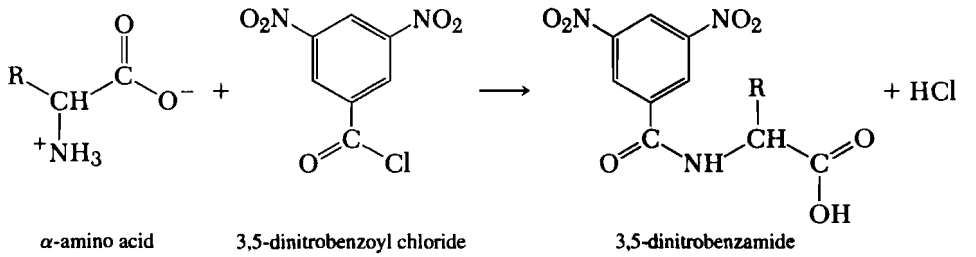
Procedure 28 Phenylureido Acids from Amino Acids[9]



Mix 1 g of the phenyl isocyanate and 0.5 g of the amino acid with 25 mL of 2% sodium hydroxide solution in a small Erlenmeyer flask. *Caution! Phenyl isocyanate is a lachrymator.* Shake the resulting mixture vigorously for 5 min. Leave it undisturbed for 30 min. Filter off any solid diarylurea, and acidify the filtrate with 5% hydrochloric acid to a pH of about 4. Wash the crystals with cold water, then recrystallize from water or ethanol.

Cleaning Up Treat any unreacted phenyl isocyanate with an excess of 5.25% sodium hypochlorite (household bleach), dilute with 10 mL of water, and place in the aqueous solution container. Neutralize the aqueous filtrate with sodium carbonate and place in the aqueous solution container.

Procedure 29 3,5-Dinitrobenzamides from Amino Acids[10]



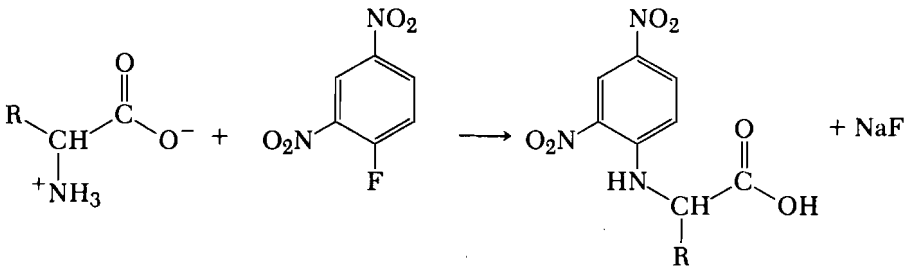
In a small flask, dissolve 1.0 g of the amino acid with 10 mL of 1 M sodium hydroxide. Next, add 1.6 g of powdered 3,5-dinitrobenzoyl chloride and shake the mixture vigorously until the acid chloride dissolves. Shake the solution for another 2 min and filter off any undissolved solids. Acidify the mixture to a pH of 4 with 5% hydrochloric acid. Isolate the 3,5-dinitrobenzamide by filtration and recrystallize from water or 50% ethanol.

Cleaning Up Make the aqueous layer slightly basic with sodium carbonate and place in the aqueous solution container.

[9]B. S. Furniss, A. J. Hannaford, P. W. G. Smith, and A. R. Tatchell, *Vogel's Textbook of Practical Organic Chemistry*, 5th ed. (Wiley, New York, 1989), p. 1281.

[10]B. S. Furniss, A. J. Hannaford, P. W. G. Smith, and A. R. Tatchell, *Vogel's Textbook of Practical Organic Chemistry*, 5th ed. (Wiley, New York, 1989), p. 1279.

Procedure 30 2,4-Dinitroaniline Derivatives of Amino Acids



α-amino acid | 2,4-dinitrofluorobenzene (Sanger's reagent) | *N*-substituted 2,4-dinitroaniline

Add a solution of 0.8 g of 2,4-dinitrofluorobenzene (*highly toxic*) in 5 mL of ethanol to a solution or suspension of 0.5 g of the amino acid in 10 mL of water and 1.0 g of sodium bicarbonate. Shake the mixture very vigorously and allow to stand at room temperature for an hour, with occasional vigorous shaking. Then, add 5 mL of saturated sodium chloride solution, and extract the mixture twice with 10 mL of ether to remove any remaining reactants. With vigorous stirring, pour the aqueous layer into 25 mL of cold 5% hydrochloric acid. This mixture should have a pH below 4. The product sometimes separates as an oil. Stir or scratch the inside of the flask to induce crystallization. Isolate the derivative by filtration, and recrystallize from 50% ethanol.

This procedure may be used for amines and for proteins or peptides with free primary amino groups on the chain or at the end.

Cleaning Up Place the ether layer in the organic solvent container. Neutralize the aqueous layer with sodium carbonate and place in the aqueous solution container.

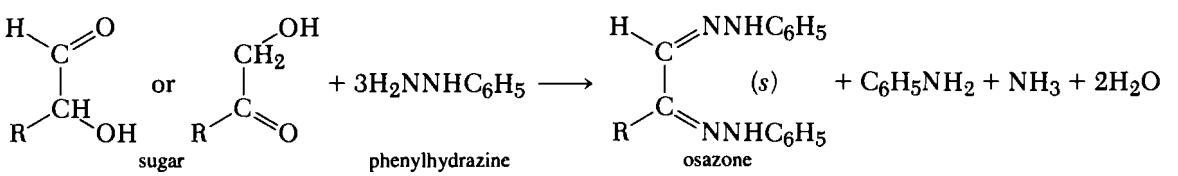
Problem

13. Give the equations for the reaction of glycine with (a) 4-toluenesulfonyl chloride, (b) phenyl isocyanate, (c) acetic anhydride, (d) benzoyl chloride, (e) 3,5-dinitrobenzoyl chloride, and (f) 2,4-dinitrofluorobenzene.

10.7 CARBOHYDRATES

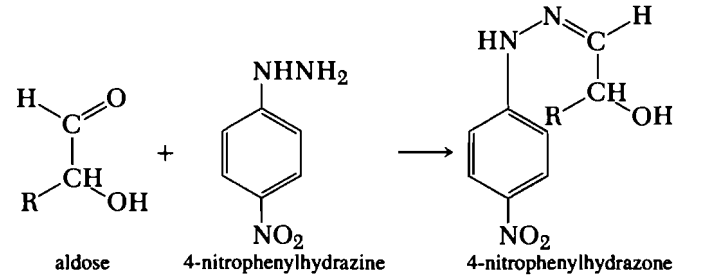
The osazones give useful information concerning the common sugars. The relative rates of formation of the osazones are significant. Since the melting points of the individual osazones often lie too close together to serve as a means of identification, the shapes of the crystals are usually checked against known photomicrographs.

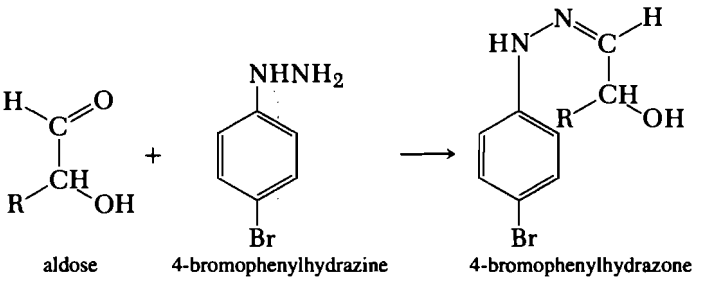
Treating the carbohydrate with at least three equivalents of phenylhydrazine produces the phenylosazone (Procedure 31, p. 396).

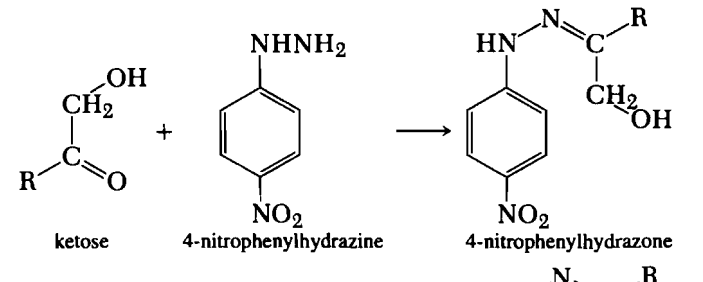


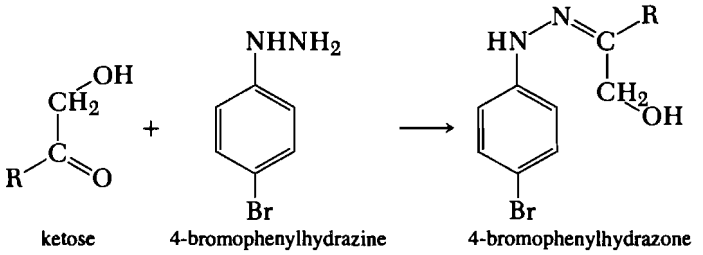
sugar (aldose or ketose) | phenylhydrazine | osazone

4-Nitrophenylhydrazones and 4-bromophenylhydrazones are prepared by reacting the carbohydrate with one equivalent of the substituted phenylhydrazine (Procedure 32, p. 397).



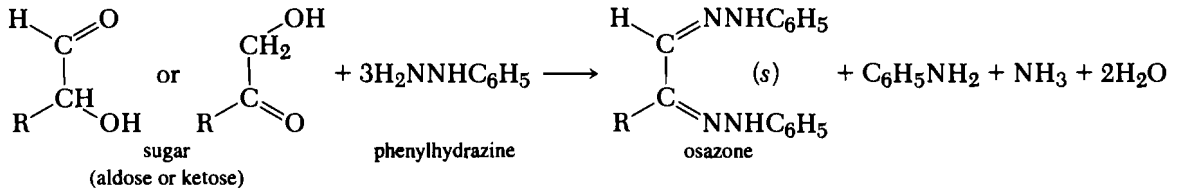






Acetates also make good derivatives for carbohydrates (Procedure 33, p. 398). Excess acetic anhydride is used so that all free hydroxyl groups are acetylated.

Procedure 31 Preparation of Osazones from Carbohydrates



Mix together 0.40 g of phenylhydrazine hydrochloride, 0.60 g of crystalline sodium acetate, and 4 mL of distilled water in a test tube. Add 0.20 g of the carbohydrate. Place the test tube in a beaker of boiling water and note the time of precipitation. Shake the test tube occasionally to avoid supersaturation.

After 20 min, remove the test tube from the hot-water bath and set it aside to cool. Place a small amount of the crystals and liquid on a watch glass, spreading out the crystals by tipping the watch glass from side to side. Absorb some of the mother liquor with a piece of filter paper, taking care not to crush or break up the crystals. Isolate the remainder of the crystals by filtration. Examine the crystals under a low-power microscope (about 80–100×), and compare with photomicrographs.[11]

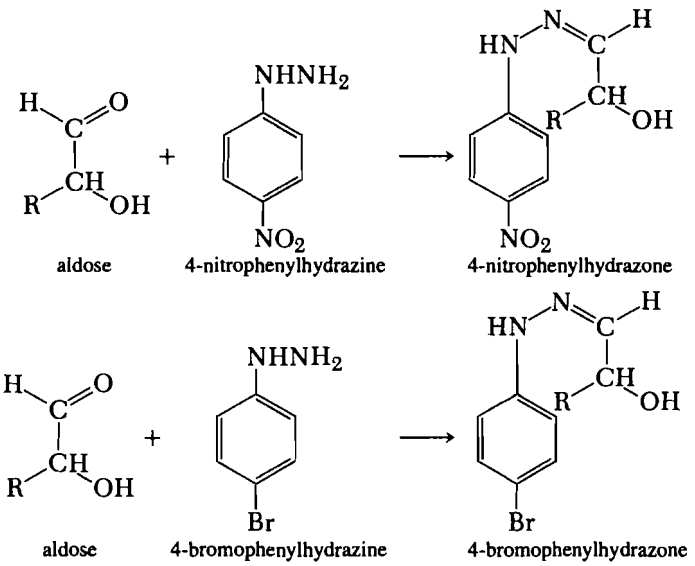
The formation of tarry products due to oxidation of the phenylhydrazine may be prevented by the addition of 0.5 mL of saturated sodium bisulfite solution prior to heating.

Cleaning Up Place the solid products in the organic nonhazardous solid waste container. Add 8 mL of 5.25% sodium hypochlorite (household bleach) to the filtrate. Heat the solution at 45–50° for 2 hr to oxidize the amine. Dilute the solution with 10 mL of water and place in the aqueous solution container.

Discussion

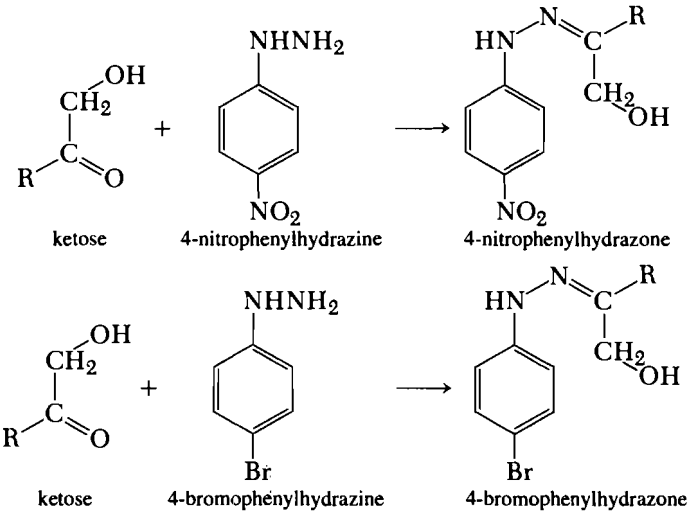
The times required for the formation of the osazone are discussed in Experiment 30 (p. 313) in Chapter 9.

Procedure 32 Substituted Phenylhydrazones from Carbohydrates[12]



[11]W. Z. Hassid and R. M. McCready, *Ind. Eng. Chem., Anal. Ed., 14*, 683 (1942).

[12]B. S. Furniss, A. J. Hannaford, P. W. G. Smith, and A. R. Tatchell, *Vogel's Textbook of Practical Organic Chemistry*, 5th ed. (Wiley, New York, 1989), p. 1247.



Place 0.25 g of the sugar, 3 mL of ethanol, and 0.25 g of 4-nitrophenylhydrazine or 4-bromophenylhydrazine in a test tube. Place the test tube in a hot-water bath and heat until no more reaction occurs. Cool the solution in an ice bath. Isolate the crystals by filtration, wash with a small amount of cold ethanol, and recrystallize from ethanol.

Cleaning Up Add 2 mL of 5.25% sodium hypochlorite (household bleach) to the filtrate. Heat the mixture for 2 hr to hydrolyze the amine, cool the mixture, and place in the aqueous solution container.

Procedure 33 Acetates of Polyhydroxy Compounds

This procedure is useful for enhancing the volatility of carbohydrates and related compounds.

(a) Without Pyridine

Mix 1 g of the anhydrous polyhydroxy compound with 0.5 g of powdered fused sodium acetate and 5 mL of acetic anhydride. Heat the mixture on a steam bath, with occasional shaking, for 2 hr. At the end of this time pour the warm solution, with vigorous stirring, into 30 mL of ice water. Allow the mixture to stand, with occasional stirring, until the excess of acetic anhydride has been hydrolyzed. Remove the crystals by filtration, wash with water, and recrystallize from ethanol.

(b) With Pyridine

Add 1 g of the polyhydroxy compound to 10 mL of anhydrous pyridine. Add 4 g of acetic anhydride, with shaking. After any initial reaction has subsided, reflux the solution for 3–5 min. Cool the mixture and pour into 25–35 mL of ice water. Isolate the acetyl derivative by filtration, wash with cold 2% hydrochloric acid, and then wash with water. Recrystallize from ethanol.

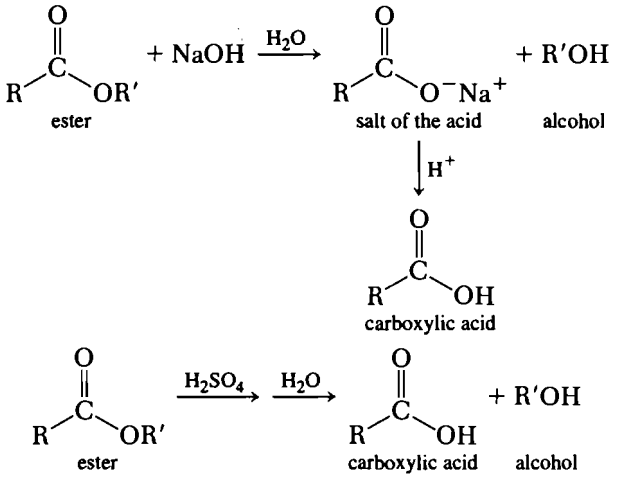
Cleaning Up Place the filtrates in the aqueous solution container.

Problem

14. Give the equations for the reaction of D-galactose with (a) three equivalents of phenylhydrazine, (b) 4-nitrophenylhydrazine, (c) 4-bromophenylhydrazine, and (d) excess acetic anhydride.

10.8 ESTERS

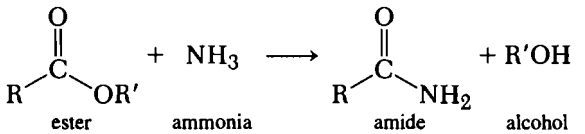
The most fundamental reaction of esters is the saponification reaction. Saponification converts an ester to an alcohol and the salt of a carboxylic acid (Procedure 34, p. 401). The carboxylic acid is liberated by acidification of the salt solution. Acid hydrolysis of the ester yields the carboxylic acid and the alcohol. Although the carboxylic acids and the alcohols can each be characterized, experience has shown that direct derivatization of the ester is a more efficient approach.



Saponification equivalents of esters (Procedure 35, p. 404) are extremely useful, especially for samples where previous molecular weight determinations were unsuccessful. The saponification equivalent is simply the equivalent weight of the ester determined by a titrimetric procedure; the procedure is conceptually similar to that used for carboxylic acids (Procedure 1, p. 357). Either the saponification equivalent or a small integral ($x = 1, 2, 3, \ldots$) multiple of the saponification equivalent, within experimental error, will be the molecular weight.

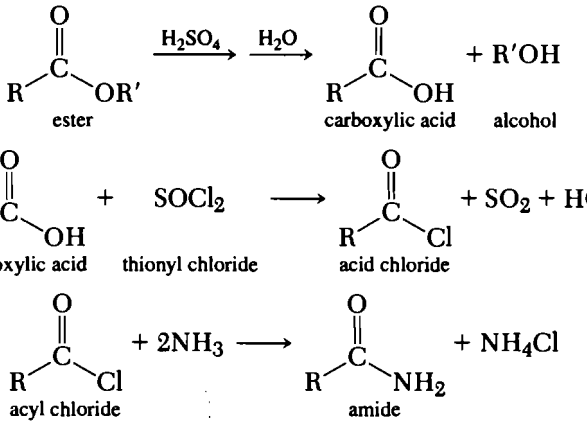
Because of difficulties involved in the separation and purification of the hydrolysis products, it is best to prepare ester derivatives by reactions using the original ester. Esters containing other functional groups may often be identified by reference to solid derivatives obtained by reactions such as halogenation of aromatic rings, nitration of aromatic rings, or acylation of alcoholic or phenolic hydroxy groups.

Some simple esters undergo reaction with aqueous or alcoholic ammonia to produce amide derivatives.

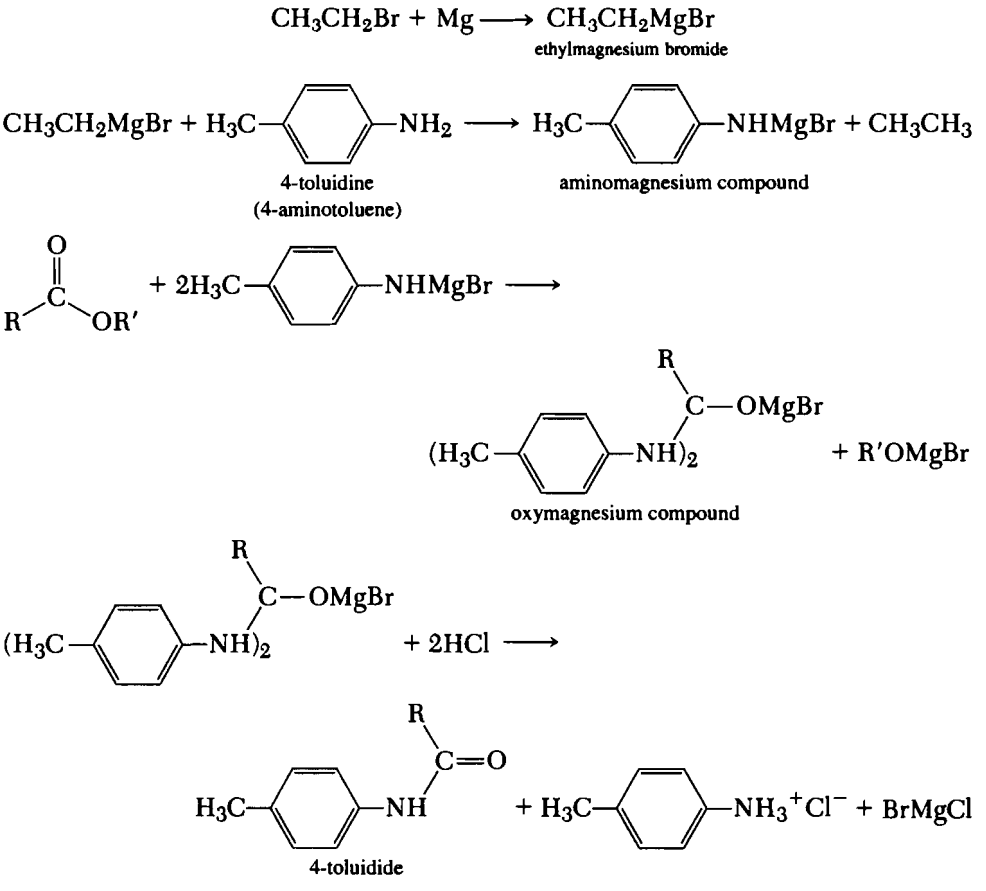


However, most esters must be heated under pressure in order to effect this reaction. A better way to prepare the amide would be to hydrolyze the ester (Procedure 34, p. 401),

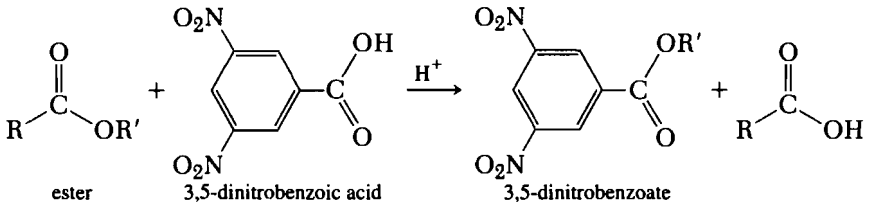
followed by treatment of the acid with thionyl chloride to form the acyl halide. The acyl halide is then treated with aqueous ammonia to form the amide (Procedure 3a, p. 359).



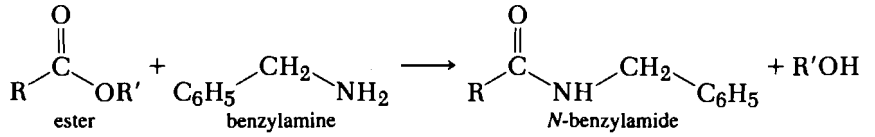
The 4-toluidide of the acidic portion of the ester may be obtained through a Grignard reaction (Procedure 36, p. 406). Ethyl magnesium bromide is prepared from ethyl bromide and magnesium. The 4-toluidine (4-aminotoluene) is converted by the ethyl Grignard compound to an aminomagnesium compound, which then undergoes reaction with the ester of interest. Hydrolysis of the resulting oxymagnesium compound yields the 4-toluidide derivative.



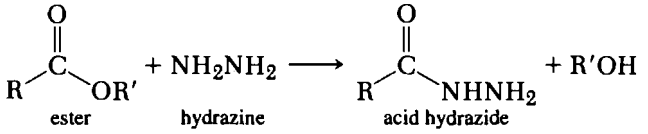
The 3,5-dinitrobenzoates, formed from the alcohol portion of a simple ester, are produced by effecting an interchange reaction between 3,5-dinitrobenzoic acid and the ester in the presence of concentrated sulfuric acid (Procedure 37, p. 408).



The reaction of esters with benzylamine in the presence of a little ammonium chloride yields *N*-benzylamides (Procedure 38, p. 408).

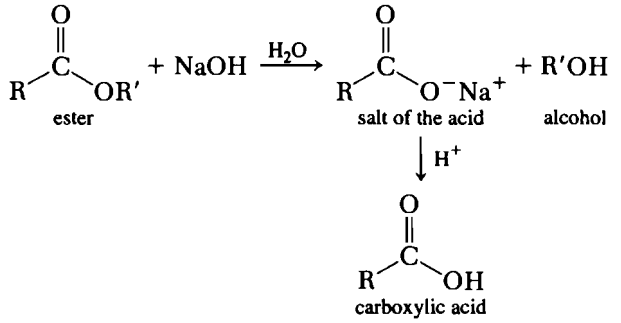


Hydrazine undergoes reaction readily with esters to produce acid hydrazides, which serve as satisfactory derivatives (Procedure 39, p. 409).



Procedure 34 Saponification and Hydrolysis of Esters

(a) Refluxing Water Solvent

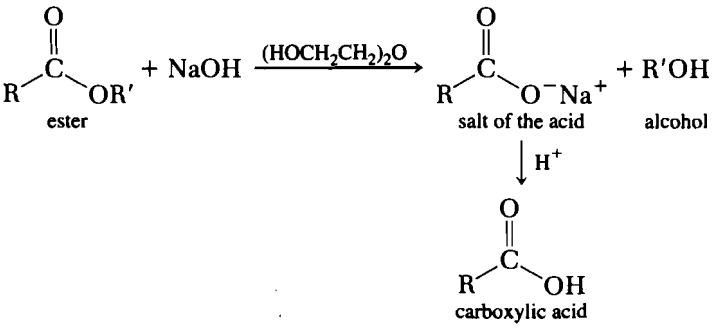


Place 12 mL of a 10% sodium hydroxide solution in a round-bottom flask fitted with a reflux condenser. Add 1 mL or 0.8 g of an ester and heat to boiling. Continue refluxing the solution until the ester layer or the characteristic odor disappears (about 1–2 hr). Rearrange the condenser for distillation. Distill about 2 mL, and saturate the distillate with potassium carbonate. Note the formation of two layers. The amount of sample required will obviously depend on the molecular weight of the alcohol to be isolated as well as on the molecular weight of the original ester. Isolate the alcohol layer from the aqueous layer.

Cool the residue in the flask, and acidify with 10% hydrochloric acid. Remove by suction filtration any solid acid that separates. Isolate liquid carboxylic acids by extraction

with three 15-mL portions of chloroform, methylene chloride, or diethyl ether. Dry the organic layer with magnesium sulfate, filter, and remove the organic solvent by distillation, using a steam bath, to leave the crude carboxylic acid.

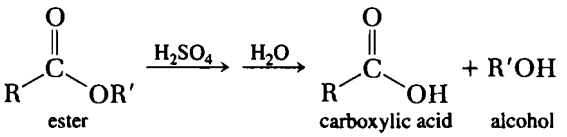
(b) Refluxing Diethylene Glycol



Place 3 mL of diethylene glycol, 0.5 g of potassium hydroxide pellets, and 0.5 mL of water in a small distilling flask. Heat the mixture, under reflux, over a low flame until the alkali has dissolved, and cool. Add 1 g of the ester, and mix thoroughly. Distill the mixture and place the receiving flask in an ice-water bath. Heat the flask over a small flame at first, and mix the contents by shaking. When only one liquid phase or one liquid and one solid phase are present, heat the mixture more strongly so that the alcohol distills.

The residue in the flask is either a solution or a suspension of the potassium salt of the acid derived from the ester. Add 10 mL of water and 10 mL of ethanol to the residue, and shake thoroughly. Add 3 M sulfuric acid until the solution is slightly acidic to phenolphthalein. Allow the mixture to stand about 5 min and then filter. Use the filtrate directly for the preparation of a derivative. If the original ester was so high-boiling that an accurate boiling point could not be obtained, it may be desirable to divide the filtrate in half and make two derivatives.

(c) Concentrated Sulfuric Acid



Dissolve 1 g of the sterically hindered ester in a minimum amount of 100% sulfuric acid and dilute the resulting solution with 20 mL of ice water. Remove the alcohol by distillation. Isolate the carboxylic acid by suction filtration and recrystallize.

Cleaning Up Place the aqueous layer from (a) and the solvent from (c) in the aqueous solution container. Neutralize the sulfuric acid from (c) with sodium carbonate and place in the aqueous solution container.

Discussion

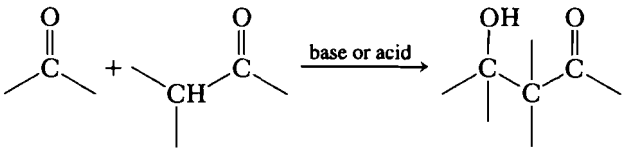
The carboxylic acids can be characterized further by the preparation of derivatives described in Procedures 3 (p. 359) and 4 (p. 360). The alcohols can also be isolated and characterized by derivatives.

Esters vary considerably in the ease with which they may be saponified. Most simple esters boiling below 110°C will be saponified completely by refluxing with 10% sodium hydroxide solution as described in (a). Esters boiling between 100 and 200°C require a longer time of 1–2 hr for complete saponification.

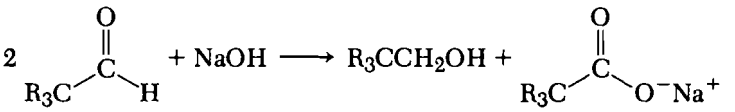
The hydrolysis of water-insoluble esters may be accelerated by the addition of 0.1 g of sodium lauryl sulfate to the alkali and the ester. Shake the mixture vigorously to emulsify the ester and then heat to reflux. Use a large flask because the emulsifying agent causes considerable foaming.

Very high boiling esters (above 200°C) that are insoluble in water hydrolyze slowly, and prolonged refluxing may result in the loss of a volatile alcohol. A solution of potassium hydroxide in diethylene glycol (bp 244°C) is used in (b). Diethylene glycol is not only an excellent solvent for esters but also permits the use of a higher reaction temperature, and all but high-boiling alcohols (boiling points over 180°C) can be distilled from the reaction mixture in a pure state.

Saponification represents the most useful procedure for characterizing esters. However, it must be remembered that hot concentrated base also affects other functional groups. Aldehydes that have α-hydrogen atoms undergo the aldol condensation:

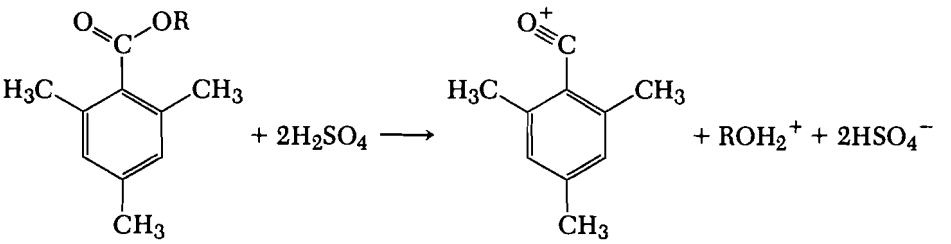


Aldehydes that have no α-hydrogen atoms undergo the Cannizzaro reaction and form an alcohol and the sodium salt of the acid:

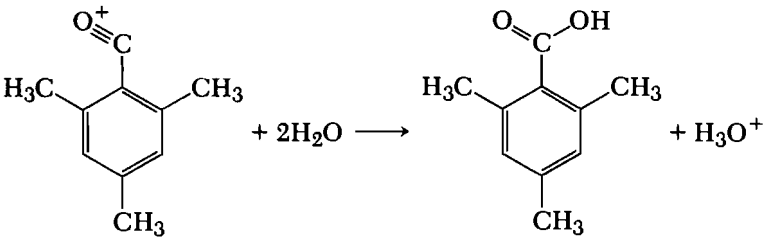


Polyfunctional compounds such as β-diketones and β-keto esters undergo cleavage under the influence of hot alkalies. The possibility of such interfering reactions is detected by means of other classification reagents, mentioned in Chapter 9, and emphasizes the fact that *a single classification reagent cannot be taken as proof of the presence of a certain functional group.* It is important to correlate all tests in attempting to draw conclusions concerning the structure of an unknown compound.

In (c), esters of sterically hindered acids undergo the following reaction with 100% sulfuric acid:



When water is added, the intermediate ion forms the acid:



Conversely, the sterically hindered acid may be converted readily to an ester by dissolving it in 100% sulfuric acid and treating the solution with the alcohol.

Unhindered esters do not undergo these reactions. They dissolve in 100% sulfuric acid and are recovered unchanged when the solution is poured into ice water.

Esters of sterically hindered acids and alcohols such as *tert*-butyl 2,4,6-trimethylbenzoate, though extremely resistant to hydrolysis by alkalies, may be hydrolyzed readily by boiling for 1 hr with 18% hydrochloric acid.[13]

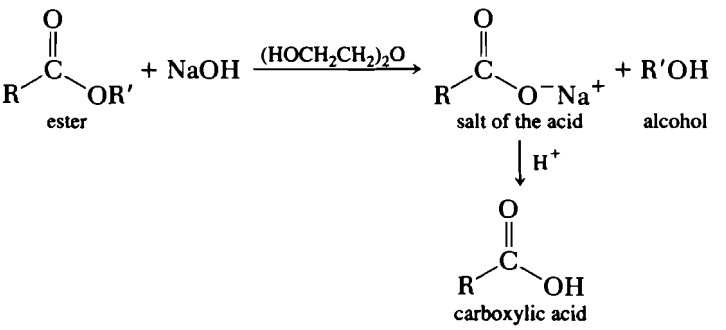
Problems

15. Describe the structural characteristics for esters in which Procedure 34a would be the most likely method.

16. Show by equations the products formed by the alkaline hydrolysis of (a) 4-phenylphenacyl acetate, (b) ethylene glycol dibenzoate, (c) dibutyl oxalate, (d) glycerol triacetate, and (e) diethyl phthalate. List a suitable procedure for detecting the products formed in these reactions.

Procedure 35 Saponification Equivalents (SE) of Esters

(a) Diethylene Glycol Method



Weigh a small round-bottom flask with three-figure accuracy. Add a sample of 0.4–0.6 g of the ester and weigh the flask again. The difference in weights is the exact weight of the ester, with three significant figures. Add exactly 10 mL of the potassium hydroxide in diethylene glycol reagent, measured from a buret.

Stopper the flask with a greased glass stopper and mix the ester thoroughly with the reagent for 10 min by constant rotation of the flask. Heat, under reflux, in an oil bath at a temperature of 70–80°C for 2–3 min with constant agitation during heating.

[13]S. G. Cohen and A. Schneider, *J. Amer. Chem. Soc.*, 63, 3382 (1941).

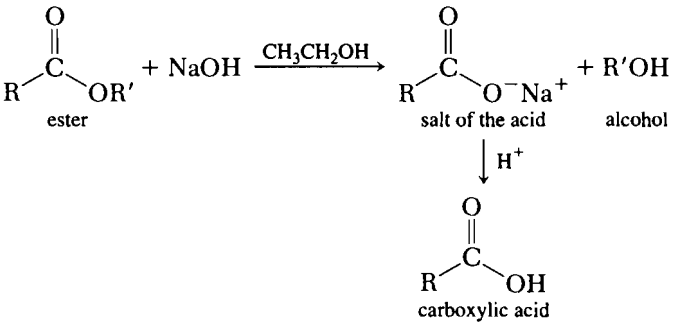
Remove the flask from the heating bath, stopper, and shake vigorously. Place the condenser on the flask and heat the mixture at 120–130°C for 3 min. Cool the flask and its contents to 80–90°C. Add 15 mL of distilled water through the condenser, rinsing down any condensation of alcohol or carboxylic acid vapors. Mix the contents of the flask thoroughly and allow to cool to room temperature.

Titrate the solution with 0.25 M hydrochloric acid that has been previously standardized to three-figure accuracy, using phenolphthalein as the indicator.

Potassium Hydroxide in Diethylene Glycol Reagent

Dissolve 3 g of potassium hydroxide pellets in 15 mL of diethylene glycol. Warm the mixture gently to complete dissolution. Use a thermometer for stirring, and do not heat the mixture above 130°C. Higher temperatures may cause the reagent to be colored. After all the solid has dissolved, pour the warm solution into 35 mL of diethylene glycol. Mix the solution thoroughly and allow to cool. The solution is approximately 1.0 M and is standardized to three significant figures by pipetting 10 mL in a flask, adding 10 mL of water, and titrating with 0.25 M hydrochloric acid solution that has been previously standardized to three-figure accuracy.

(b) Alcoholic Sodium Hydroxide Method



Determine the weight of a small round-bottom flask to three-figure accuracy. Add a sample of 0.2–0.4 g of the ester and weigh the flask again. The difference in weights is the exact weight of the ester with three significant figures. Add 15 mL of the alcoholic sodium hydroxide reagent, measured from a buret, to the flask. Heat the mixture gently under reflux for 1.25–1.5 hr. At the end of this time, allow it to cool slightly. Add 10 mL of distilled water through the condenser into the solution, rinsing down any condensation along the sides of the tube. Add two drops of phenolphthalein indicator to the flask and titrate the solution with 0.25 M hydrochloric acid that has been previously standardized with three-figure accuracy. The end point should be a faint pink.

Alcoholic Sodium Hydroxide Reagent

In the hood, dissolve 8 g of sodium in 250 mL of absolute ethanol; after the sodium has dissolved, add 25 mL of water. *Care must be taken when working with sodium. Only dry equipment is used to weigh out the sodium. Use a dry knife to expose the shiny metal; use only the shiny metal in any reaction. Place any equipment in a beaker; add ethanol slowly. Allow the beaker to sit in the hood for several hours before disposing of the liquid.* Standardize this solution to three-figure accuracy by titration against a weighed sample of pure potassium acid phthalate.

Cleaning Up Place the neutralized solution in the aqueous solution container. Place the contents of the beaker used in the disposal of waste sodium in the aqueous solution container.

Discussion

Calculate the saponification equivalent (SE) according to the following equation:

$$\text{saponification equivalent (SE)} = \frac{\text{weight of the sample (mg)}}{[\text{volume of alkali (mL)} \times M_{KOH}] - [\text{volume of acid (mL)} \times M_{HCl}]}$$

Complete saponification of esters that are insoluble in water is given by (a). Esters such as benzyl acetate, butyl phthalate, ethyl sebacate, butyl oleate, and glycol and glycerol esters are completely saponified.

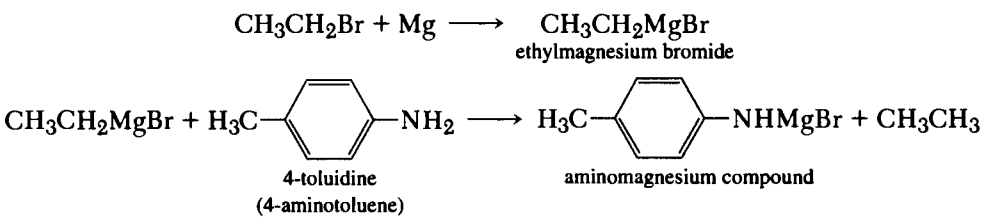
The ester must be *pure* and *anhydrous* in order to give an accurate saponification equivalent. The following precautions must be observed in order to obtain accurate results:

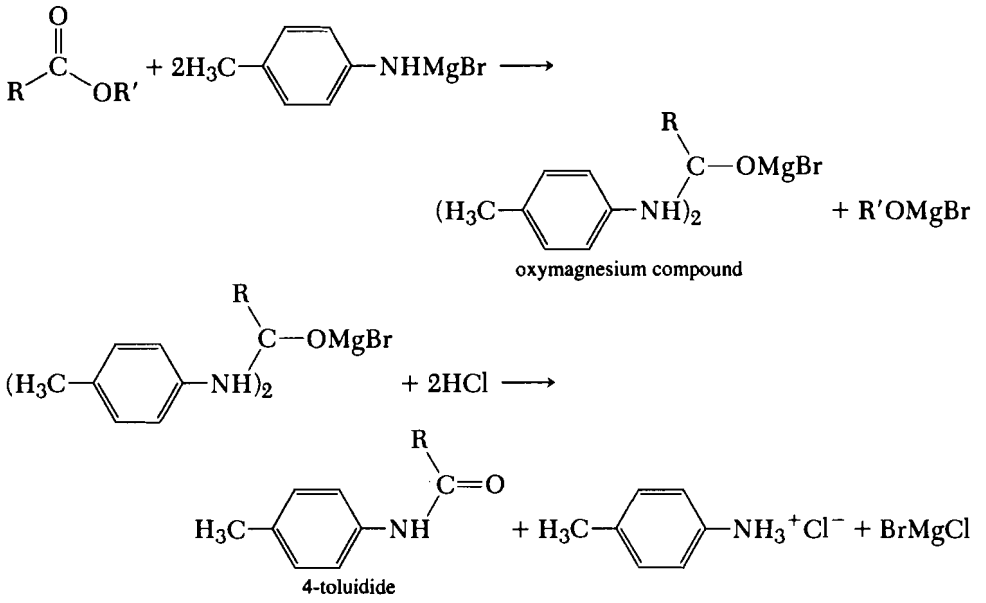
1. Standardize the alcoholic sodium hydroxide solution immediately before use and record its molarity (M).
2. Measure the standardized solutions accurately from a buret, because a slight error in the amount of alkali will cause a large error in the saponification equivalent. This is especially noticeable with high-molecular-weight esters.
3. Heating the mixture for 1.5 hr will saponify most esters. For some, a longer time (2–24 hr) may be necessary.
4. Lubricate the glassware lightly with stopcock grease prior to assembling. Hot alcoholic alkali will "freeze" two ground glass joints together within a few minutes if the grease is not present.
5. The end point should be a *faint* pink. This is the color assumed by phenolphthalein at a pH of 9, which represents the hydrogen ion concentration of solutions of the sodium salts of most organic acids.
6. The molecular weight of the ester is equal to x times the saponification equivalent, where x is the number of ester groups in the molecule.

Problems

17. Calculate the saponification equivalent (SE) value for (a) ethyl acetoacetate, (b) ethyl hydrogen phthalate, (c) diethyl propanedioate, (d) ethyl cyanoacetate, and (e) dibutyl phthalate.
18. What would happen if Procedure 35 were applied to benzaldehyde?
19. If an ester had already been partially hydrolyzed, what effect would this have on the saponification equivalent?

Procedure 36 4-Toluidides (4-Methylanilides) from Esters





Use dry glassware to prepare the Grignard reagent. Bake the glassware in the oven for a few hours prior to usage. Equip a 50-mL round-bottom flask with a Y-adapter, which holds a condenser and an addition funnel. Attach drying tubes to the condenser and addition funnel.

Weigh 0.5 g of magnesium and grind up a few of these magnesium turnings with a mortar and pestle. Place the magnesium in the round-bottom flask. Place 2.5 g (1.75 mL) of ethyl bromide and 15 mL of anhydrous diethyl ether in the addition funnel. Slowly add 0.5 mL of the ethyl bromide solution. It may take several minutes before the Grignard reaction actually begins, which is noticed by the appearance of bubbles. If no reaction begins, then add two drops of 1,2-dibromoethane to begin the reaction. Once the reaction has definitely begun, slowly add the remainder of the ethyl bromide dropwise. Allow the mixture to stand until the reaction has ceased. Almost all of the magnesium metal should have been consumed to form the Grignard reagent, thus leaving very little, if any, of the magnesium turnings in the reaction flask.

Place a solution of 2.2 g of 4-toluidine (4-methylaniline) dissolved in 10 mL of anhydrous diethyl ether in the addition funnel and slowly add to the ethylmagnesium bromide. After the vigorous evolution of ethane has ceased, add 1 g of the ester in 5 mL of anhydrous diethyl ether dropwise from the addition funnel.

After the addition of the ester solution is complete, heat the solution on a steam bath for 10 min. Transfer the reaction mixture into an Erlenmeyer flask and place the flask in an ice bath. Add 10% hydrochloric acid until the solution is acidic to litmus. Acidification hydrolyzes the Grignard reagent and makes an ammonium salt from the excess 4-toluidine. Separate the ether layer and dry it with magnesium sulfate. Remove the ether by distillation, using a steam bath. Recrystallize the resulting solid 4-toluidide from aqueous ethanol.

Cleaning Up Place the recovered ether in the organic solvent container. Neutralize the aqueous layer with sodium carbonate and place in the aqueous solution container.

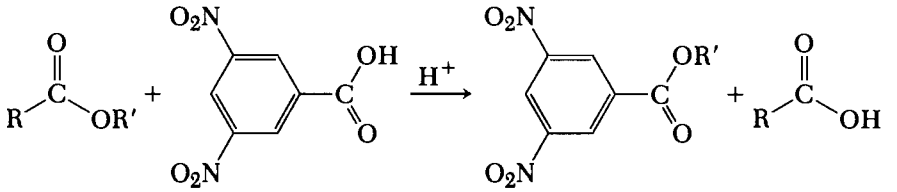
Discussion

Ethyl magnesium bromide is commercially available. Thus this sequence can be started with the second step.

Problem

20. Calculate the number of moles of magnesium and ethyl bromide used in the procedure above. Which is the limiting reagent—magnesium or ethyl bromide?

Procedure 37 3,5-Dinitrobenzoates from Esters

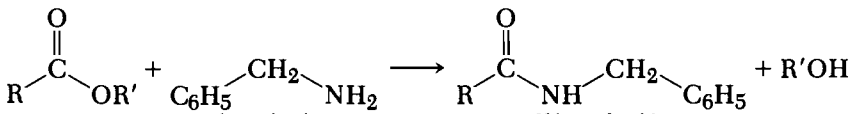


ester 3,5-dinitrobenzoic acid 3,5-dinitrobenzoate

Mix 1 mL or 0.9 g of the ester with 0.8 g of 3,5-dinitrobenzoic acid, and add one drop of concentrated sulfuric acid. If the original ester boiled below 150°C, heat the mixture gently under reflux. If the ester boiled above 150°C, heat the mixture in an oil bath at 150°C, with frequent stirring. The time required varies from 30 min to 1 hr, the longer time being used in those cases in which the 3,5-dinitrobenzoic acid fails to dissolve in about 15 min. Cool the mixture, add 15 mL of absolute diethyl ether, and extract the solution twice with two 10-mL portions of 5% sodium carbonate solution (*Caution: foaming*) to neutralize the sulfuric acid and remove unreacted 3,5-dinitrobenzoic acid. Wash the ether layer with 10 mL of water, and evaporate the solvent. Dissolve the residue in 3 mL of boiling ethanol. Filter the solution, and add water dropwise until the solution begins to get cloudy. Cool the mixture and stir to induce crystallization of the derivative.

Cleaning Up Place the filtrates in the aqueous solution container. Place any recovered ether in the organic solvent container.

Procedure 38 *N*-Benzylamides from Esters



ester benzylamine *N*-benzylamide

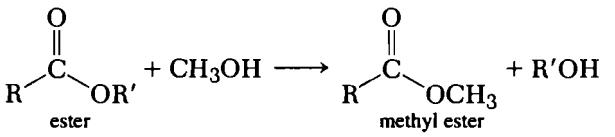
Heat a mixture of 1 g of the ester, 2 mL of benzylamine, and 0.1 g of powdered ammonium chloride for 1 hr in a small flask fitted with a reflux condenser. Cool the solution. Wash with 10 mL of water to remove excess benzylamine and to induce crystallization. Often the addition of a few drops of 10% hydrochloric acid will promote crystallization. Avoid an excess of hydrochloric acid, because it dissolves *N*-benzylamides. Occasionally the presence of unchanged ester may prevent crystallization. In that case, boil the solution for a few minutes with 10 mL of water in an evaporating dish in the hood to volatilize the ester. Isolate the solid amide by filtration, wash with a little ligroin, and recrystallize from a mixture of ethanol and water or of acetone and water.

With esters of alcohols higher than ethanol, heat for 30 min with 5 mL of absolute methanol in which a small piece of sodium (0.1 g) has been dissolved. At the end of the reflux period, evaporate the methanol and treat the residue by the above procedure.

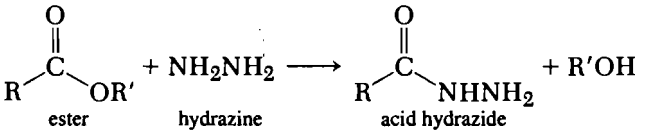
Cleaning Up Add 10% hydrochloric acid to the initial filtrate until the solution is slightly acidic. Combine all filtrates and place them in the aqueous solution container.

Discussion

The reaction proceeds well when R′ is methyl or ethyl. Esters of higher alcohols should be subjected to a preliminary methanolysis, followed by treatment with benzylamine.



Procedure 39 Acid Hydrazides from Esters



Wear gloves when handling hydrazine, since hydrazine is a carcinogen. Do this experiment in the hood. Mix 1 g of the methyl or ethyl ester and 1 mL of 85% hydrazine hydrate, and heat the mixture under reflux for 15 min. Add just enough absolute ethanol, through the top of the condenser, to obtain a clear solution. Heat the mixture under reflux for 2 hr, evaporate the alcohol, and cool the residue. Isolate the crystals of the hydrazide by filtration and recrystallize from water or a mixture of water and ethanol.

Higher esters must be subjected to methanolysis, as described in Procedure 38, above, before treatment with hydrazine.

Cleaning Up Combine all of the filtrates, dilute with 10 mL of water, and neutralize with sodium carbonate. Add 10 mL of 5.25% sodium hypochlorite (household bleach), and heat in a water bath at 50°C for 1 hr to oxidize any unreacted hydrazine. Dilute the mixture with 10 mL of water and place in the aqueous solution container.

Discussion

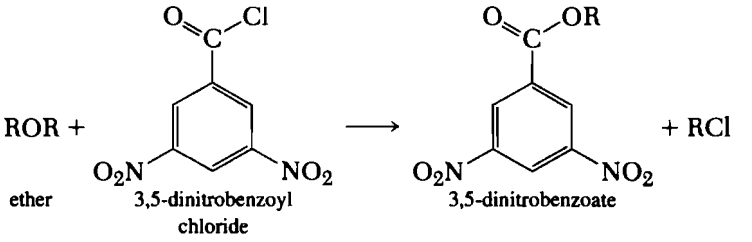
Esters of higher alcohols should be converted to methyl esters, prior to reacting with hydrazine.

Problem

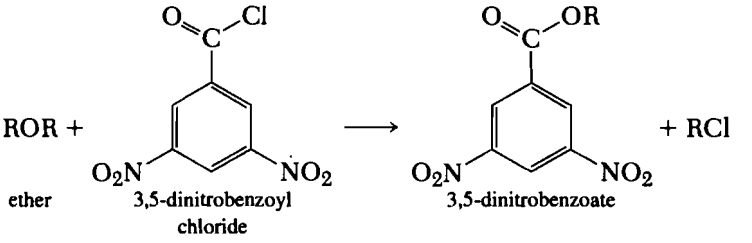
21. Give the equations for the formation from methyl propanoate of (a) the amide, (b) the 4-toluidide, (c) the 3,5-dinitrobenzoate, (d) the *N*-benzylamide, and (e) the hydrazide.

10.9 ETHERS—ALIPHATIC

Derivatives of symmetrical aliphatic ethers can be prepared by treating the ether with 3,5-dinitrobenzoyl chloride in the presence of zinc chloride (Procedure 40, p. 410). This method cleaves symmetrical ethers and forms the corresponding 3,5-dinitrobenzoate. The melting points of the 3,5-dinitrobenzoates can be found in the derivative tables under alcohols.



Procedure 40 Alkyl 3,5-Dinitrobenzoates from Ethers



Place 1 mL or 0.9 g of the ether, 0.15 g of anhydrous zinc chloride, and 0.5 g of 3,5-dinitrobenzoyl chloride in a small flask connected to a reflux condenser. Reflux the mixture for 1 hr and then cool. Add 10 mL of 5% sodium carbonate solution. Warm the mixture to 90°C in a water bath, cool, and filter. Wash the precipitate with 5 mL of 5% sodium carbonate solution and 10 mL of distilled water. Dissolve the residue in 10 mL of hot chloroform, and filter the solution while hot; cool the filtrate in an ice bath. Remove any precipitated ester by suction filtration. If the ester does not separate, evaporate the chloroform. Allow the residue to dry on a watch glass.

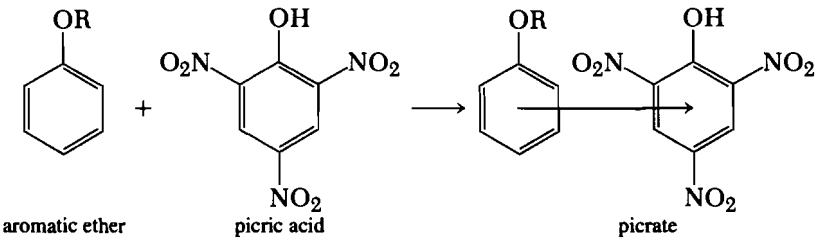
Cleaning Up Place the aqueous filtrates in the aqueous solution container. Place the chloroform filtrate in the halogenated organic waste container.

Problems

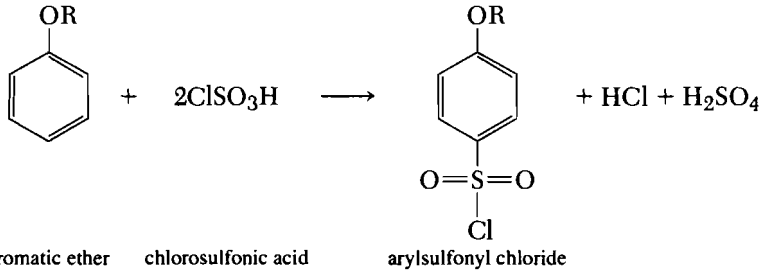
22. Describe the problem that would arise if an unsymmetrical ether such as ethyl methyl ether were subjected to 3,5-dinitrobenzoate derivatization.
23. Give the equation for the reaction of dipropyl ether with 3,5-dinitrobenzoyl chloride.

10.10 ETHERS—AROMATIC

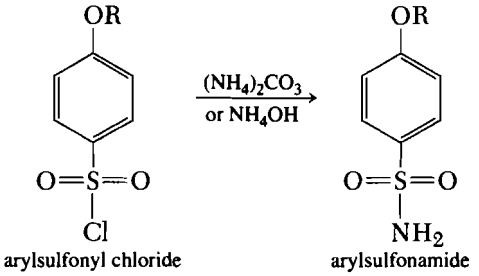
Picrates are used as derivatives of aromatic ethers (Procedure 41, p. 411). The picrates are prepared by the treatment of the aromatic ether with picric acid.



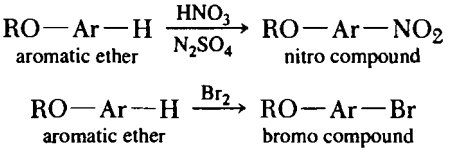
Aromatic ethers undergo reaction with chlorosulfonic acid at 0°C to produce arylsulfonyl chlorides (Procedure 42, p. 412).



Since the arylsulfonyl chlorides are usually oils or low-melting solids, they then undergo reaction with ammonium carbonate or ammonia to form the arylsulfonamides (Procedure 43, p. 413). Arylsulfonamides obtained in this way are useful derivatives.



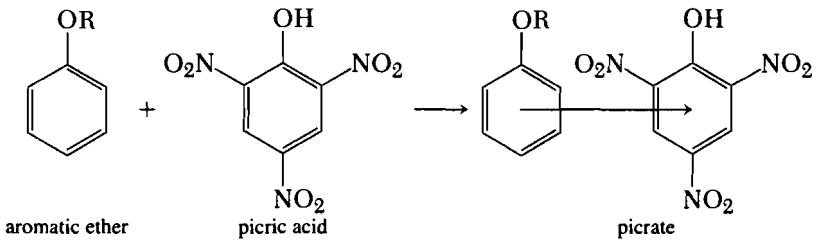
The derivatives of aromatic ethers that are employed most frequently are those obtained by nitration (Procedure 51, p. 423) and bromination (Procedure 44, p. 414).



The position of the nitro or bromo substituent on the aromatic ring depends upon the directing effect of the ether group and of the other groups that are attached to the aromatic ring. Frequently the bromo or the nitro group substitutes in more than one position on the aromatic ring.

The formation of picrate, nitro, and bromo compounds takes advantage of the ability of the aromatic ring to undergo attack by electron-deficient species.

Procedure 41 Picrates of Aromatic Ethers

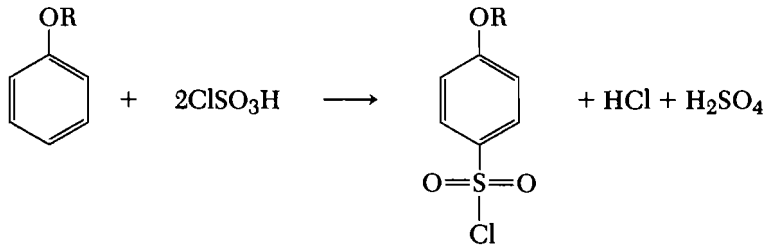


Add a solution of 0.5–1 g of the ether in 5 mL of chloroform to a boiling solution of 6 mL of picric acid in chloroform. *The picric acid may explode if it becomes dry; do not let the solvent evaporate.* Stir the mixture thoroughly, set aside, and allow to cool. Allow the mixture to stand. Determine the melting point immediately, because some picrates decompose.

Picric Acid in Chloroform
Dissolve 1 g of picric acid in 15 mL of chloroform. This solution is prepared by the instructor.

Cleaning Up Add 50 mL of water to the chloroform filtrate. Shake thoroughly and separate the layers. Pour the aqueous layer into the aqueous solution container. Place the chloroform layer in the halogenated organic waste container.

Procedure 42 Sulfonyl Chlorides from Aromatic Ethers



aromatic ether chlorosulfonic acid arylsulfonyl chloride

Caution: This reaction must be done in a hood. Place 1 g of the compound and 5 mL of dry chloroform in a clean, dry test tube. Cool in a beaker of ice to 0°C. Add 3 mL of chlorosulfonic acid dropwise, and after the initial evolution of the hydrogen chloride has subsided, remove the tube from the ice bath and allow to warm up to room temperature (about 20 min). Pour the contents of the tube into a 50-mL beaker full of cracked ice. Remove the chloroform layer and wash with water. Evaporate the chloroform, and recrystallize the residual sulfonyl chloride from low-boiling petroleum ether or chloroform.

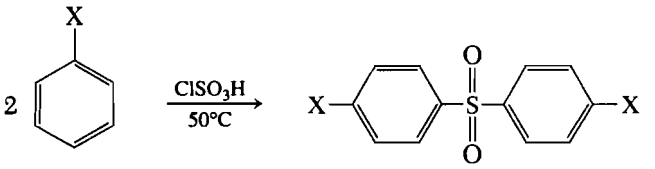
Cleaning Up Place any recovered chloroform in the halogenated waste container. Place the aqueous solution in the aqueous solution container. Place the recovered petroleum ether in the organic solvent container.

Discussion
Since the arylsulfonyl chlorides are usually oils or low-melting solids, they are used to form sulfonamide derivatives (Procedure 43, p. 413).

This procedure may also be used for the preparation of sulfonyl chlorides from most of the simple aryl halides and alkylbenzenes. For halotoluenes, warm the chloroform solution to 50°C for 10 min and then pour the mixture on cracked ice.

Polyhalogen derivatives require more drastic treatment. Carry out the sulfonation without any solvent, and warm the sulfonation mixture to 100°C for 1 hr under a reflux condenser.

Two other reactions may take place during the sulfonation. Fluorobenzene, iodobenzene, and 1,2-dibromobenzene yield the corresponding sulfones when treated with chlorosulfonic acid at 50°C in the absence of a solvent.

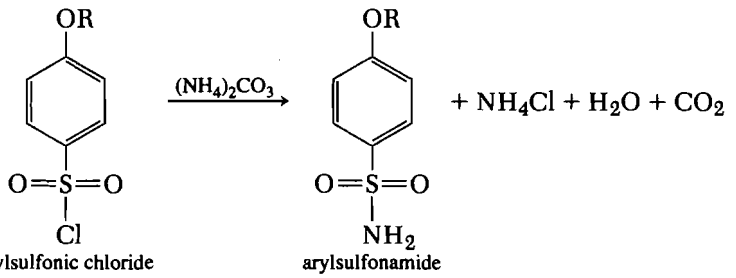


aryl halide chlorosulfonic acid

These sulfones are solids and will serve as derivatives. In other cases (for example, during Procedure 43, below), small amounts of sulfones may be produced; these are separable from the sulfonamide because they are insoluble in alkali. A second reaction is ring chlorination. This reaction takes place with 1,4-diiodobenzene and 1,2,4,5-tetrachlorobenzene. Unsatisfactory results are frequently obtained with aryl iodides.

Procedure 43 Sulfonamides from Aromatic Ethers

(a) With Ammonium Carbonate

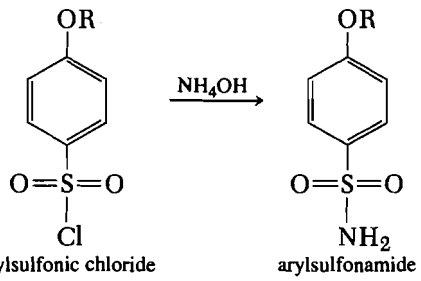


arylsulfonic chloride arylsulfonamide

Mix 0.5 g of the sulfonyl chloride with 2.0 g of dry powdered ammonium carbonate and heat at 100°C for 30 min. Cool the mixture and wash with three 10-mL portions of cold water.

Dissolve the crude sulfonamide in 10 mL of 5% sodium hydroxide solution, gentle heating being used if necessary, and filter the solution to remove any sulfone or chlorinated products. Acidify the filtrate with 5% hydrochloric acid. Isolate the sulfonamide by filtration. Recrystallize from dilute ethanol and dry at 100°C.

(b) With Ammonium Hydroxide



arylsulfonic chloride arylsulfonamide

Heat 0.5 g of the sulfonyl chloride with 5 mL of concentrated ammonium hydroxide for 10 min. Dilute the mixture with 10 mL of water, cool, and filter.

Purify the crude sulfonamide according to the directions given in (a).

Cleaning Up Pour the aqueous rinsings and filtrates from (a) and (b) into the aqueous solution container.

Discussion
This procedure, or the Hinsberg procedure (Procedure 21, p. 386), can be used to prepare *N*-substituted sulfonamides by using primary and secondary amines instead of ammonia.

Procedure 44 Bromination of Ethers

$$\underset{\text{aromatic ether}}{RO{-}Ar{-}H} \xrightarrow{Br_2} \underset{\text{bromo compound}}{RO{-}Ar{-}Br}$$

Dissolve 1 g of the compound in 15 mL of glacial acetic acid, and add 1–1.5 mL of liquid bromine. *Bromine is very toxic; measure bromine out in the hood and do the experiment in the hood.* Allow the mixture to stand for 15–30 min and then pour into 50–100 mL of water. Remove the bromo compound by filtration and purify by recrystallization from dilute ethanol. In some cases carbon tetrachloride may be substituted for acetic acid as the solvent. Distill the carbon tetrachloride, and recrystallize the residue. *Carbon tetrachloride is a known carcinogen. Do not allow any carbon tetrachloride to contact the skin.*

Cleaning Up Place the filtrates in the halogenated organic waste container.

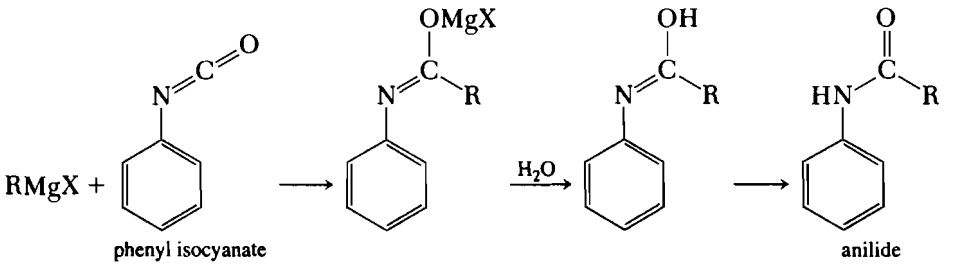
Problem

24. From 1,2-dimethoxybenzene, give the equations for the formation of (a) the picrate, (b) the sulfonamide (4-), (c) the nitro derivative (4-), and (d) the bromo derivative (4,5-).

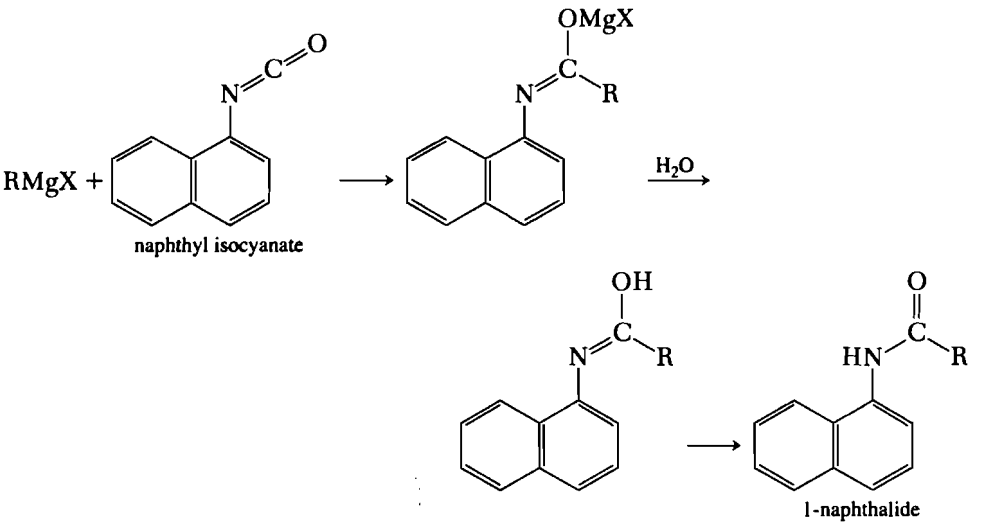
10.11 HALIDES—ALKYL

The best methods for making derivatives of alkyl and cycloalkyl halides depend on their conversion into the corresponding Grignard reagents. The anilides and 1-naphthalides, prepared from the Grignard reagents (Procedure 45, p. 416) by treatment with phenyl and 1-naphthyl isocyanate (Procedure 46, p. 417), respectively, are the derivatives most frequently used.

$$\underset{\text{alkyl halide}}{RX} + Mg \longrightarrow \underset{\substack{\text{alkylmagnesium halide}\\ \text{(Grignard reagent)}}}{RMgX}$$



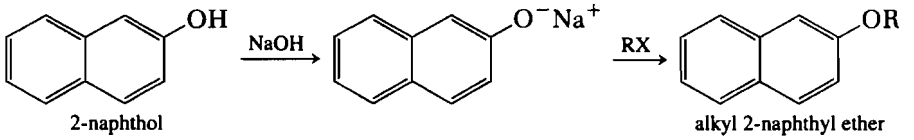
phenyl isocyanate anilide



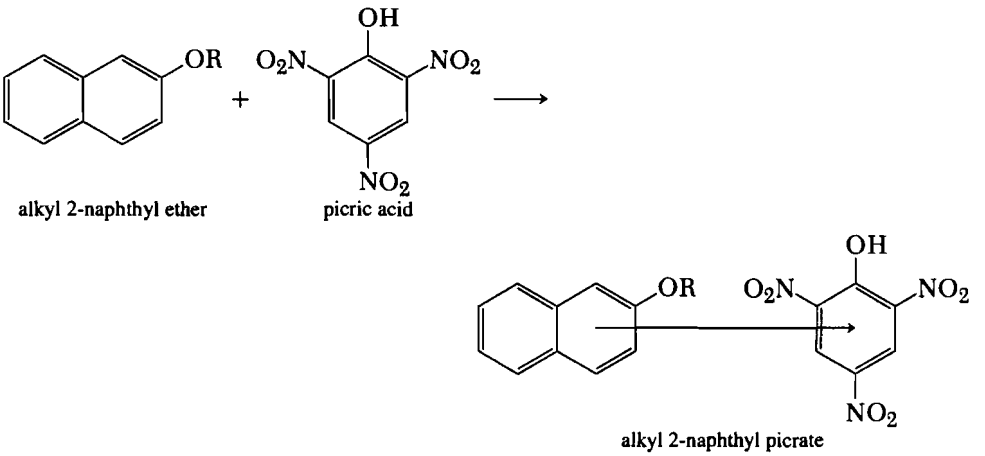
The Grignard reagent may be converted to the corresponding alkylmercuric halide by treatment with a mercuric halide (Procedure 45, p. 416).

$$\underset{\text{alkylmagnesium halide}}{RMgX} + \underset{\text{mercuric halide}}{HgX_2} \longrightarrow \underset{\text{alkylmercuric halide}}{RHgX} + MgX_2$$

Alkyl 2-naphthyl ethers are prepared by the reaction of the alkyl halides with 2-naphthol (Procedure 47, p. 417).

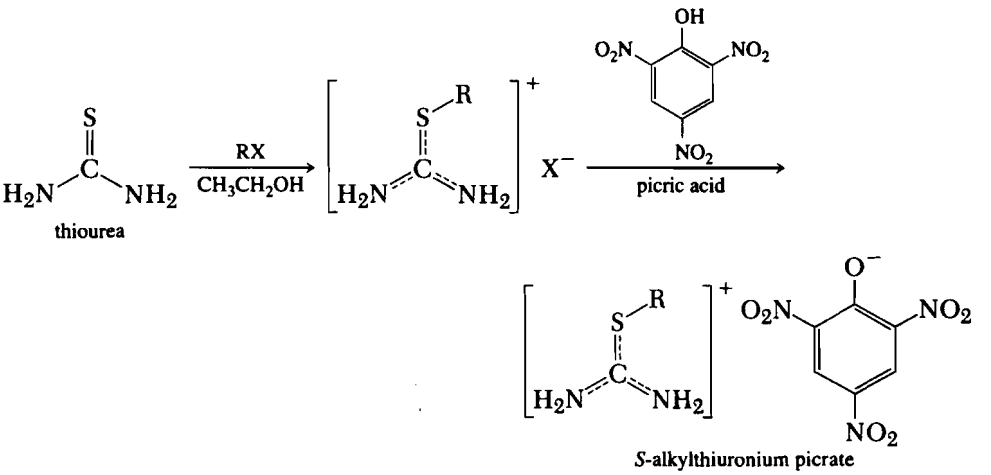


The alkyl 2-naphthyl ethers can then be treated with picric acid to form the alkyl 2-naphthyl ether picrates, which is another derivative (Procedure 48, p. 418).



S-Alkylthiuronium picrates are also derivatives of alkyl halides (Procedure 49, p. 419). These derivatives are prepared by the treatment of the alkyl halide to form

the intermediate, which is treated with picric acid to produce the *S*-alkylthiuronium picrate.



Derivatives of alkyl and cycloalkyl halides are particularly useful not only because these compounds are encountered frequently but also because they are readily made from alcohols, and so furnish an indirect way of identifying the alcohols. All the preceding methods are to be used with caution in view of the fact that rearrangements sometimes occur.

Procedure 45 Grignard Reagents and Alkylmercuric Halides

$$\underset{\text{alkyl halide}}{RX} + Mg \longrightarrow \underset{\substack{\text{alkylmagnesium halide}\\ \text{(Grignard reagent)}}}{RMgX}$$

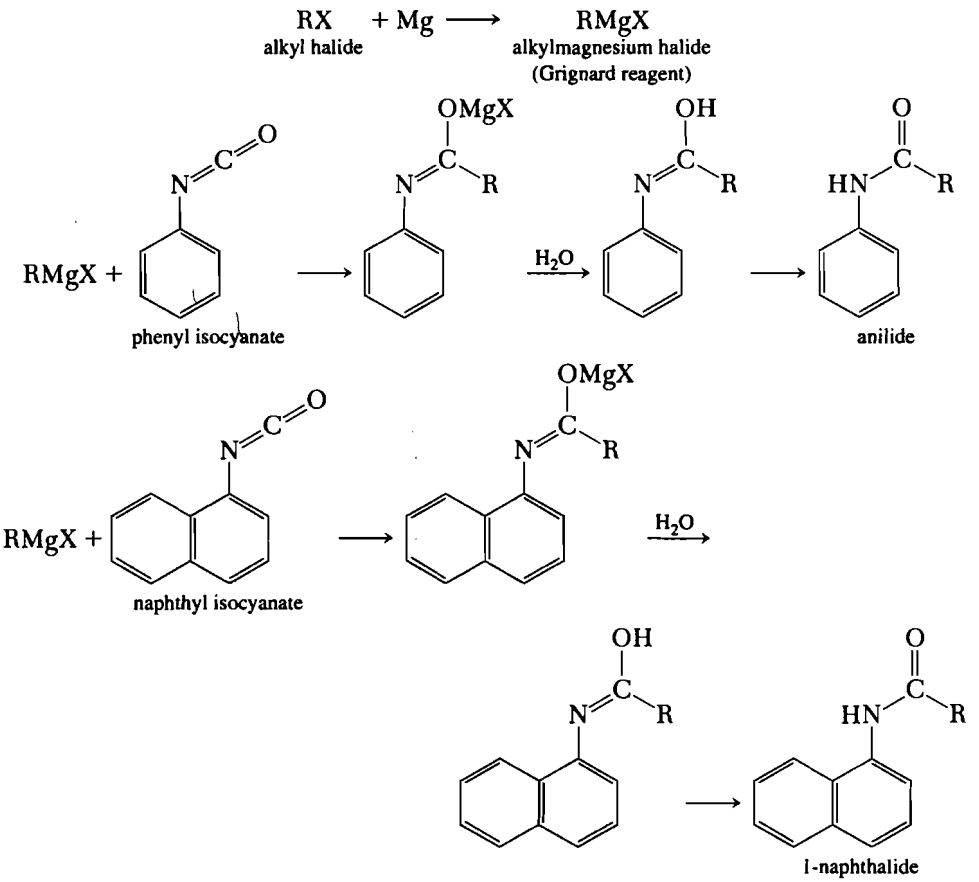
$$\underset{\substack{\text{alkylmagnesium}\\ \text{halide}}}{RMgX} + \underset{\substack{\text{mercuric}\\ \text{halide}}}{HgX_2} \longrightarrow \underset{\substack{\text{alkylmercuric}\\ \text{halide}}}{RHgX} + MgX_2$$

In a 50-mL round-bottom flask, prepare the Grignard reagent by treating 0.3 g of magnesium with 1 mL of the alkyl halide in 15 mL of dry diethyl ether, following the directions given in Procedure 36, p. 406.

When the reaction is complete, filter the solution through glass wool and allow the filtrate to flow into a test tube containing 4–5 g of mercuric chloride, bromide, or iodide, depending on the halogen in the original alkyl halide. Shake the reaction mixture vigorously, warm on a hot-water bath or steam bath for a few minutes, and remove the solvent by distillation, using a hot-water bath or steam bath. Boil the residue with 20 mL of 95% ethanol, and filter the solution. Dilute the filtrate with 10 mL of water and cool in an ice bath. Collect the alkylmercuric halide by filtration and recrystallize from 60% ethanol.

Cleaning Up Place the recovered ether in the organic solvent container. Distill off the ethanol from the filtrate, using a steam bath. Place the ethanol in the aqueous solution container. The liquid that remains after distillation may contain some mercuric halides. Place this liquid in the hazardous waste container.

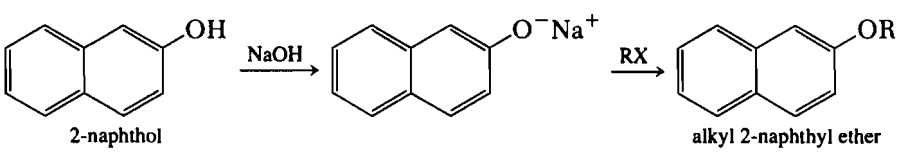
Procedure 46 Anilides and 1-Naphthalides



Prepare the Grignard reagent, as described in Procedures 45 and 36, pp. 416 and 406. Treat the Grignard reagent with 0.5 mL of phenyl or 1-naphthyl isocyanate dissolved in 10 mL of absolute diethyl ether. Shake the mixture and allow to stand for 10 min. Add 25 mL of 2% hydrochloric acid. Shake vigorously. Separate the ether layer and dry with magnesium sulfate. Distill off the ether, using steam as a source of heat. Recrystallize the residue from methanol, diethyl ether, or petroleum ether.

Cleaning Up Treat any unreacted phenyl isocyanate with an excess of 5.25% sodium hypochlorite (household bleach), dilute with 10 mL of water, and place in the aqueous solution container. Place the recovered ether and recrystallization solvents in the organic solvent container.

Procedure 47 Alkyl 2-Naphthyl Ethers from Alkyl Halides



Add 1 g of 2-naphthol and 1 g of the alkyl halide to a solution of 0.3 g of sodium hydroxide in 12 mL of ethanol. *2-Naphthol is a carcinogen and must be used only in the hood.* If the halide is a chloride, also add 0.25 g of potassium iodide. Heat the mixture under reflux for 30 min and pour into 40 mL of cold water. If the mixture is not distinctly alkaline to phenolphthalein, then add dropwise 10% sodium hydroxide solution as needed, and stir vigorously. Remove the alkyl 2-naphthyl ether by filtration and recrystallize from ethanol or an ethanol–water mixture.

Cleaning Up Place any unreacted alkyl halide in the halogenated organic waste container. Place the aqueous layer in the aqueous solution container.

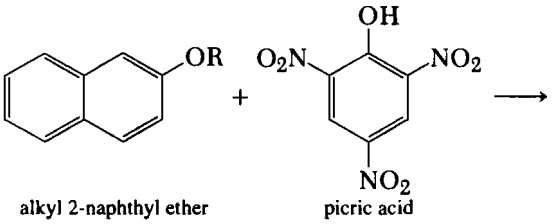
Discussion

Since the reaction is S_N2, the alkyl halide is restricted to primary and some secondary alkyl halides.

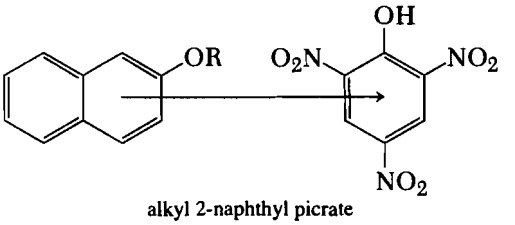
Problem

25. This procedure is occasionally useful for making derivatives of dihalides of the type $X(CH_2)_nX$. Potassium iodide must not be added if the compound is a 1,2-dihalide ($n = 2$). Why?

Procedure 48 Picrates of Alkyl 2-Naphthyl Ethers



alkyl 2-naphthyl ether picric acid



alkyl 2-naphthyl picrate

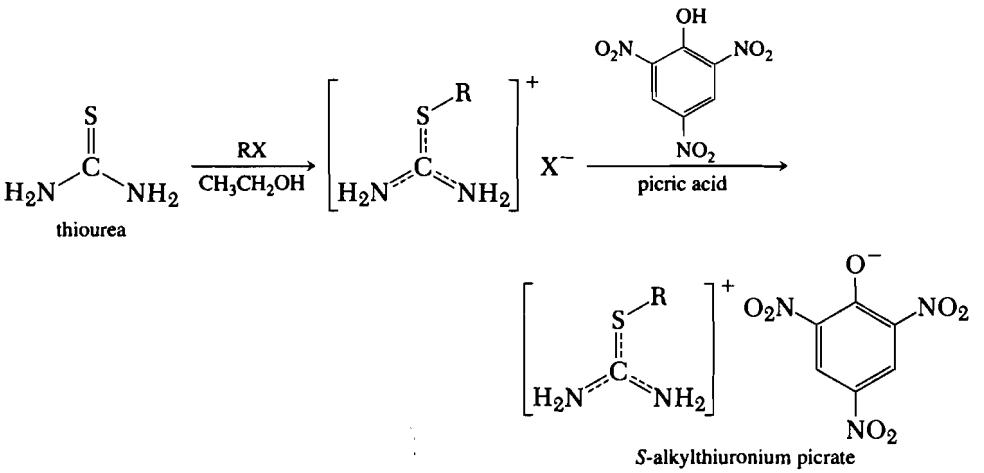
Dissolve the alkyl 2-naphthyl ether from Procedure 47, p. 417, in a minimum volume of hot ethanol. Add a hot solution of 6 mL of 20% picric acid in ethanol. *The picric acid may explode if it becomes dry; do not let the solvent evaporate.* Isolate the picrate by filtration and recrystallize from ethanol.

20% Picric Acid in Ethanol

Dissolve 1 g of picric acid in 5 mL of ethanol. The solution is prepared by the instructor.

Cleaning Up Pour the filtrates into the aqueous solution container.

Procedure 49 *S*-Alkylthiuronium Picrates from Alkyl Halides



Reflux a mixture of 0.5 powdered thiourea, 0.5 g of the alkyl halide, and 5 mL of 95% ethanol. The reflux time is dependent upon the type of alkyl halide: primary alkyl bromides and iodides, 10–20 min; secondary alkyl bromides and iodides, 2–3 hr; alkyl chlorides, with the addition of 1 g of potassium iodide, 50–60 min; and dihalides, 20–50 min.[14]

Add 6 mL of 10% picric acid in ethanol to the above solution, and heat the mixture at reflux until a clear solution is obtained. *The picric acid may explode if it becomes dry; do not let the solvent evaporate.* Cool the mixture. Isolate the *S*-alkylthiuronium picrate by filtration and recrystallize from ethanol.

10% Picric Acid in Ethanol
Dissolve 0.4 g of picric acid in 5 mL of ethanol. This solution is prepared by the instructor.

Cleaning Up Place the aqueous filtrate in the aqueous solution container.

Problem

26. From 1-bromo-2-methylpropane, give the equations for the formation of (a) the anilide, (b) the *N*-naphthalide, (c) the alkylmercuric bromide, (d) the alkyl 2-naphthyl ether, (e) the alkyl 2-naphthyl ether picrate, and (f) *S*-alkylthiuronium picrate.

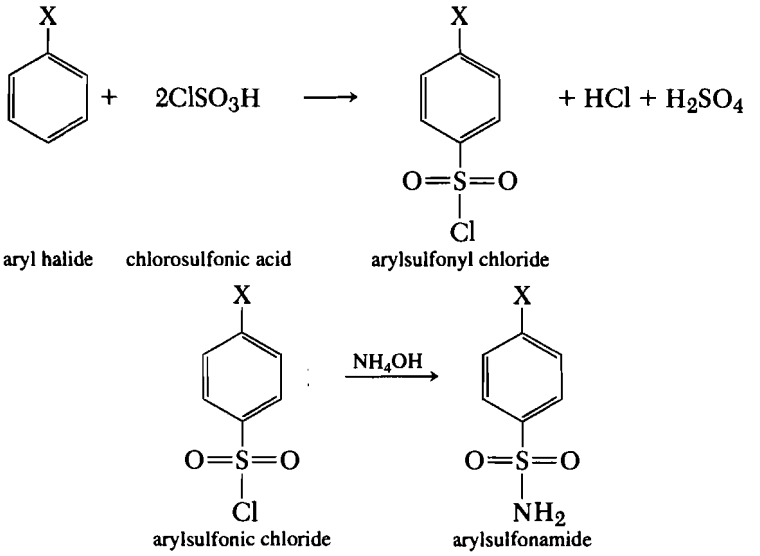
10.12 HALIDES—AROMATIC

Many excellent methods are available for making suitable derivatives of halogen derivatives of aromatic hydrocarbons. The most general method of these procedures is nitration (Procedure 51, p. 423). The aromatic ring is nitrated in the presence of nitric and sulfuric acid.

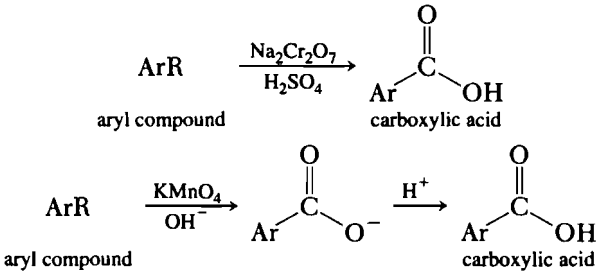
$$\underset{\text{aryl halide}}{X{-}Ar{-}H} \xrightarrow[H_2SO_4]{HNO_3} \underset{\text{nitro compound}}{X{-}Ar{-}NO_2}$$

[14]B. S. Furniss, A. J. Hannaford, P. W. G. Smith, and A. R. Tatchell, *Vogel's Textbook of Practical Organic Chemistry*, 5th ed. (Wiley, New York, 1989), p. 1253.

Aryl halides undergo reaction readily with chlorosulfonic acid to produce arylsulfonyl chlorides (Procedure 42, p. 412), which yield sulfonamides when treated with ammonia solution (Procedure 43b, p. 413).

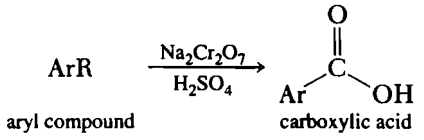


Many aryl halides contain other groups attached to the aromatic ring. Aryl halides containing side chains are frequently oxidized to the corresponding substituted aromatic acid (Procedure 50, below). Oxidizing agents such as sodium dichromate or potassium permanganate can be used.



Procedure 50 Oxidation of a Side Chain of an Aromatic Compound

(a) Dichromate Oxidation

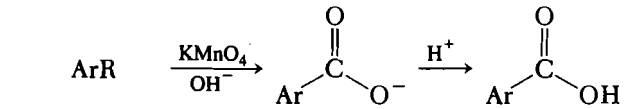


Place 8 mL of water, 3.5 g of sodium dichromate, and 1 g of the compound to be oxidized in a small round-bottom flask. Add 5 mL of concentrated sulfuric acid, attach the flask to a reflux condenser, and thoroughly shake the mixture. Heat the flask carefully until the reaction starts; then remove the flame and allow the flask to cool. After the mixture has ceased to boil from the heat of the reaction, heat it under reflux for 2 hr.

Cool the contents of the flask in an ice bath and pour into 15 mL of water. Isolate the precipitate by suction filtration. Mix the precipitate with 10 mL of 5% sulfuric acid, and warm the mixture on a steam bath with vigorous stirring. Cool the precipitate, isolate, and wash with 10 mL of cold water. Dissolve the precipitate in 10 mL of 5% sodium hydroxide solution, and filter. Pour the filtrate, with vigorous stirring, into 15 mL of cold 10% sulfuric acid. Collect the precipitate on a filter and wash with water. Purify by recrystallization from ethanol or 60% ethanol.

Cleaning Up Since the filtrate probably contains unreacted sodium dichromate, it must be treated. Add 10% sulfuric acid to the filtrate until the pH is 1. Slowly add solid sodium thiosulfate until the solution becomes a cloudy blue color. Neutralize with 10% sodium carbonate. Collect the precipitate of chromium hydroxide through Celite in a Buchner funnel. Place the Celite and the chromium hydroxide solid in the hazardous waste container for heavy metals. Place the filtrate in the aqueous solution container.

(b) Permanganate Oxidation



aryl compound carboxylic acid

Add 1 g of the compound to 80 mL of water containing 4 g of potassium permanganate. Add 1 mL of 10% sodium hydroxide solution, and heat under reflux for 3 hr. Allow to cool. Discharge the purple color by adding a small amount of sodium bisulfite. Remove the brown suspension of manganese dioxide by suction filtration through a Buchner funnel containing a thin layer of Celite (filter aid). Acidify the filtrate carefully with 10% sulfuric acid. Heat the mixture for 0.5 hr and cool. Collect the precipitated acid on a filter. Recrystallize from ethanol. If the acid is appreciably soluble in water, it may not separate from this dilute acid solution. In such a case, extract the acid with chloroform or diethyl ether. Remove the solvent by distillation and recrystallize the residue. A slight precipitate of silicic acid sometimes appears on acidification; hence it is important to recrystallize the acid before taking the melting point.

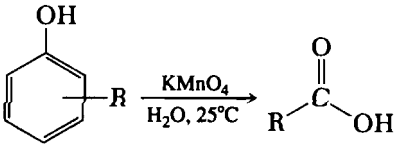
Cleaning Up Place the manganese dioxide in the hazardous waste container for heavy metals. Neutralize the aqueous filtrate with sodium carbonate and place in the aqueous solution container.

Discussion

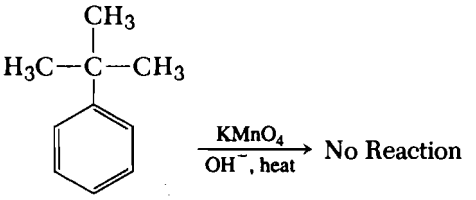
Aromatic hydrocarbons that have side chains may be oxidized to the corresponding acids. Aromatic acids having several carboxyl groups are sometimes difficult to oxidize, and for this reason the utility of the oxidation method is limited. If there are two side chains situated in adjacent positions on the ring, oxidation is recommended because the resulting acid (phthalic acid) is easy to identify. 1,2-Dialkylbenzenes, as well as compounds substituted on the 1,2-dialkyl chains, undergo complete oxidation with Cr(VI) (Procedure 50a, p. 420). The melting points of the acids from the oxidation of the alkylbenzenes may be obtained by reference to the tables in Appendix II.

Aromatic rings that are substituted with electron-withdrawing groups (nitro, halo, etc.) easily survive even the more vigorous oxidation procedures, whereas rings substituted with electron-donating groups may be oxidized on the ring more readily than on

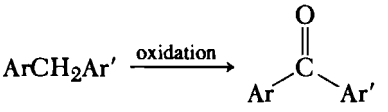
the side chain. For example, the oxidation of a substituted phenol can give the aliphatic acid in sufficient yield to be characterized.



It is clear that hydrogens α to the ring (benzylic hydrogens) facilitate this oxidation.



Substitution of a second aromatic ring onto the alkyl group can decrease the degree of oxidation.

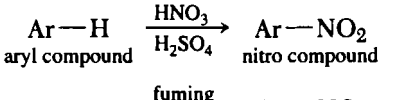


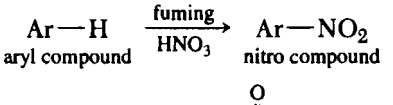
PROBLEM

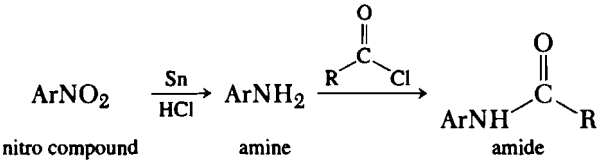
27. From 3,4-dichlorotoluene, give the equations for the formation of (a) the nitration product (6-), (b) the sulfonamide (6-), and (c) the oxidation product.

10.13 HYDROCARBONS—AROMATIC

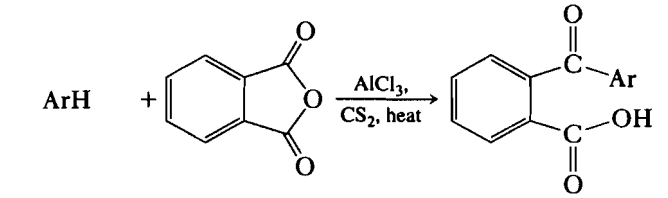
The most useful derivatives of aromatic hydrocarbons are usually those obtained by nitration (Procedure 51, p. 423). Nitration of the aromatic ring is effected by a combination of nitric and sulfuric acid or by fuming nitric acid. Highly alkylated nitrated benzenes can then be reduced to the amines (Procedure 57, p. 431), which are then acetylated or benzoylated to give mono- or diacetamino or benzamino derivatives (Procedure 20, p. 384).





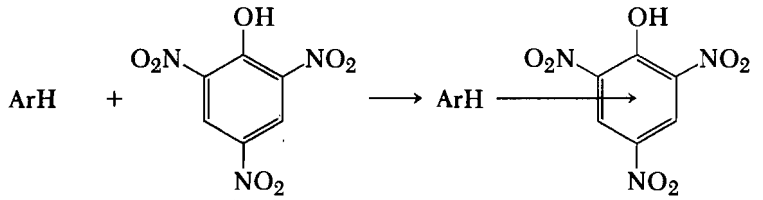


Aromatic hydrocarbons and their halogen derivatives undergo the Friedel–Crafts reaction with phthalic anhydride, producing aroylbenzoic acids in good yield (Procedure 52, p. 424).



aryl compound phthalic anhydride aroylbenzoic acid

Picric acid combines with some aromatic hydrocarbons to yield picrates (Procedure 41, p. 411). The stability of the picrates varies considerably; many of them dissociate readily into the original reactants.



aryl compound picric acid picrate

Procedure 51 Aromatic Nitration

The nitration of an aromatic compound, especially if it is an unknown substance, should be carried out with special precaution, because many of these compounds react violently. Try a small-scale test behind a shield first.

(a) With Nitric and Sulfuric Acids

$$\underset{\text{aryl compound}}{\text{Ar—H}} \xrightarrow[H_2SO_4]{HNO_3} \underset{\text{nitro compound}}{\text{Ar—NO}_2}$$

The nitro compound may be prepared by either method.

1. Add 1 g of the compound to 4 mL of concentrated sulfuric acid. Add 4 mL of concentrated nitric acid, drop by drop, with shaking after each addition. Connect the flask to a reflux condenser and keep in a beaker of water at 45°C for 5 min. Pour the reaction mixture on 25 g of cracked ice and isolate the precipitate by filtration. Recrystallize from 60% ethanol.
2. Place 4 mL of concentrated nitric acid in a 50-mL round-bottom flask and place in an ice bath. Add 4 mL of concentrated sulfuric acid dropwise. Add 1 g of the unknown a few drops at a time, with shaking after each addition. Reflux the solution and work up as described above.

(b) With Fuming Nitric Acid

$$\underset{\text{aryl compound}}{\text{Ar—H}} \xrightarrow[HNO_3]{\text{fuming}} \underset{\text{nitro compound}}{\text{Ar—NO}_2}$$

The procedure outlined above is followed, except use 4 mL of fuming nitric acid[15]

[15]This corresponds to highly concentrated (ca. 90%) nitric acid, sometimes called "white" or "yellow" fuming nitric acid; this is a powerful nitrating agent. It is not to be confused with "red" nitric acid, which contains dissolved NO_2 and is a vigorous oxidizing agent.

instead of concentrated nitric acid, and warm the mixture on a steam bath for 10 min. Occasionally, with compounds that are difficult to nitrate, substitute fuming sulfuric acid for the concentrated sulfuric acid.

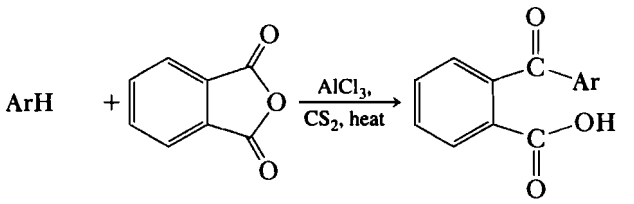
Cleaning Up Place the solution in a large beaker. Slowly dilute the filtrate with 20 mL of water, add sodium carbonate until the foaming ceases, and place in the aqueous solution container.

Discussion

Procedure (a) yields 1,3-dinitrobenzene from benzene or nitrobenzene and the 4-nitro derivative of chlorobenzene, bromobenzene, benzyl chloride, or toluene. Phenol, acetanilide, naphthalene, and biphenyl yield dinitro derivatives. It is best to employ (b) for halogenated benzenes because it produces dinitro derivatives that are easier to purify than the mononitro derivatives formed in (a). Mesitylene, the xylenes, and 1,2,4-trimethylbenzene yield trinitro derivatives.

Polynuclear aromatic hydrocarbons, which are easily oxidized, are not nitrated successfully by either procedure. Experiment 39, p. 334, should be used to determine the possibility of a polynuclear aromatic hydrocarbon. These compounds require mild conditions to nitrate without oxidative decomposition.

Procedure 52 Aroylbenzoic Acids from Aromatic Hydrocarbons



aryl compound phthalic anhydride aroylbenzoic acid

Add 2.4 g of anhydrous aluminum chloride to a solution of 1 g of the dry aromatic hydrocarbon and 1.2 g of phthalic anhydride in 10 mL of dry carbon disulfide. *Aluminum chloride is very hygroscopic and releases hydrogen chloride gas when it undergoes reaction with water.* Heat the mixture under a reflux condenser in a boiling water bath for 30 min and cool. Decant the carbon disulfide layer, and add 10 mL of concentrated hydrochloric acid and 10 mL of water to the residue. Add the acid slowly at first, cool with ice if necessary, and shake the final mixture thoroughly.

If the aroylbenzoic acid separates as a solid, collect it immediately on a filter and wash with cold water. If an oil separates, cool the mixture in an ice bath for some time to induce crystallization. If the product remains oily, decant the supernatant liquid and wash the oil with cold water. Boil the crude product for 1 min with 30 mL of 10% ammonium hydroxide solution to which has been added about 0.1 g of Norite. Filter the hot solution and cool. Add 25 g of crushed ice, and acidify the solution with concentrated hydrochloric acid. Remove the aroylbenzoic acid by filtration and recrystallize from dilute ethanol. If necessary, allow the product to stand overnight in order to obtain crystals.

Cleaning Up Place the carbon disulfide in the hazardous waste container. Neutralize the aqueous filtrates with sodium carbonate and place in the aqueous solution container.

Discussion

This procedure produces a derivative with a functional group that can be easily characterized. For example, the neutralization equivalent (Procedure 1, p. 357) of the acid may be determined; this will yield the molecular weight of the keto acid derivative. The molecular weight of the original aromatic compound may be calculated:

$$\text{molecular weight of ArH} = (\text{molecular weight of acid}) - 148$$

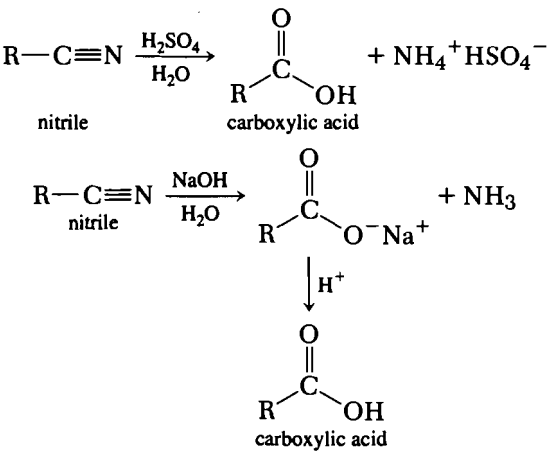
Problems

28. Explain the origin of the value 148 in the preceding formula.

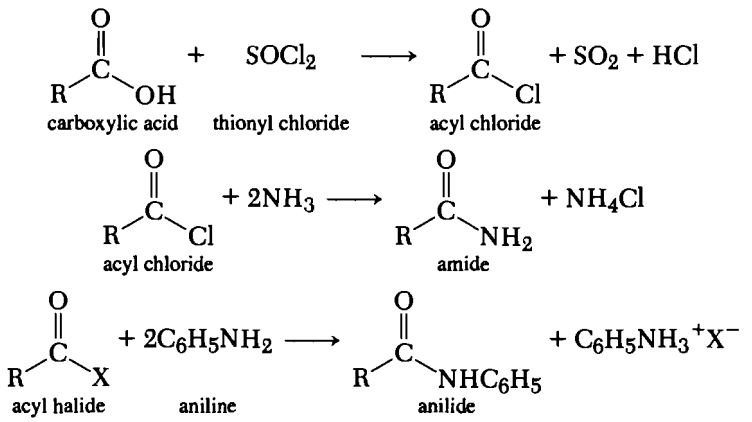
29. From ethylbenzene, give the equations for the formation of (a) the nitration product (2,4,6-), (b) the aroylbenzoic acid, and (c) the picrate.

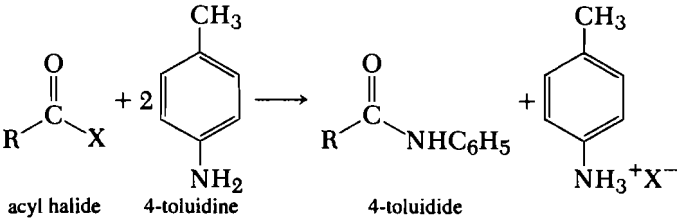
10.14 NITRILES

The nitriles may be hydrolyzed to the corresponding carboxylic acid by means of a mineral acid or an aqueous base (Procedure 53, p. 427).



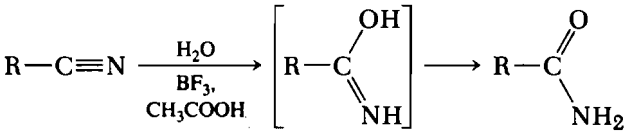
If the resulting acid is a solid, it serves as an excellent derivative. The carboxylic acid can be derivatized by preparing the acyl chloride, followed by treatment with ammonia, aniline, or 4-toluidine to form the amide (Procedure 3a, p. 359), the anilide, or 4-toluidide (Procedure 4a or 4b, p. 360 or 361), respectively.





acyl halide 4-toluidine 4-toluidide

Controlled hydrolysis of the nitrile with a boron trifluoride/acetic acid complex results in the corresponding amide (Procedure 54, p. 428). This procedure can be used instead of the several-step process listed above.

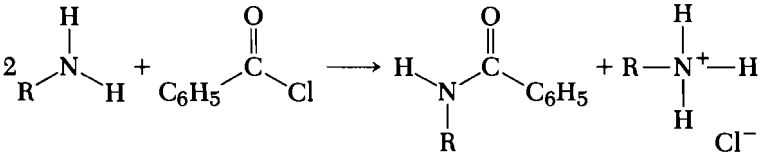


nitrile amide

Reduction of nitriles with sodium and an alcohol forms primary amines (Procedure 55, p. 429).

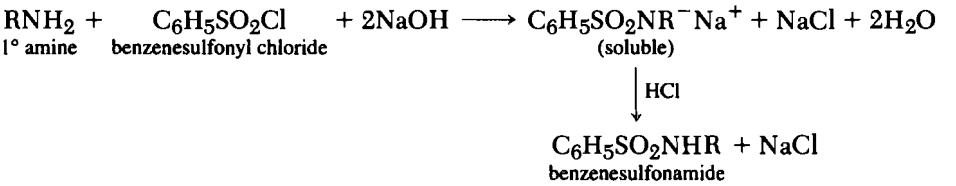
nitrile 1° amine

The primary amines can then be used to prepare the benzamide (Procedure 20b or 20c, p. 384), benzenesulfonamide (Procedure 21, p. 386), and phenylthiourea (Procedure 22, p. 387) derivatives. The benzamide is prepared from the reaction of the primary amine with benzoyl chloride.



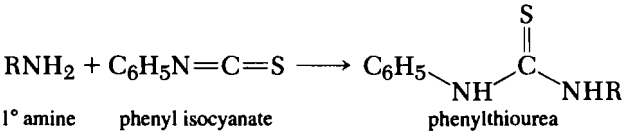
1° amine benzoyl chloride benzamide

Treatment of the primary amine with benzenesulfonyl chloride yields the benzamide.



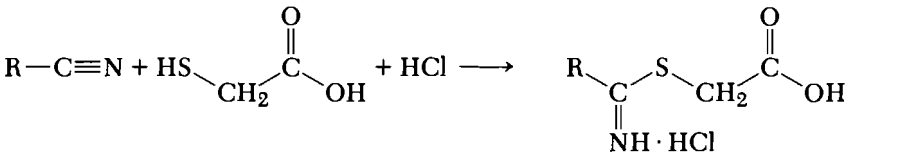
1° amine benzenesulfonyl chloride (soluble) benzenesulfonamide

The phenylthiourea is prepared by the reaction of the amine with phenyl isothiocyanate.



1° amine phenyl isocyanate phenylthiourea

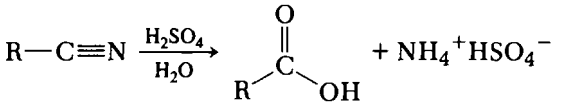
Mercaptoacetic acid (thioglycolic acid) condenses with nitriles in the presence of hydrogen chloride to produce α-(imidioylthio)acetic acid hydrochlorides (Procedure 56, p. 429).



nitrile thioglycolic acid α-(imidioylthio)acetic acid hydrochloride

Procedure 53 Hydrolysis of a Nitrile to a Carboxylic Acid

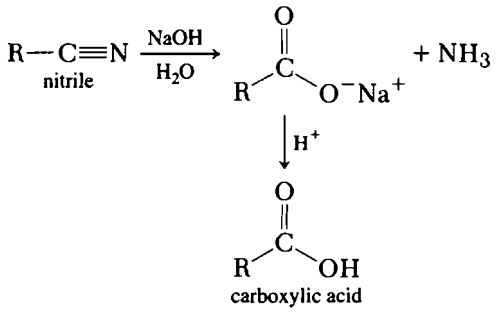
(a) Acidic Conditions for Aromatic Nitriles



nitrile carboxylic acid

Place 5 mL of 75% sulfuric acid and 0.2 g of sodium chloride in a small round-bottom flask fitted with a reflux condenser. Heat the flask to 150–160°C by means of an oil bath, and add 1 g of the nitrile dropwise through the top of the condenser, with vigorous shaking after the addition of each portion. Heat the mixture, with stirring, at 160°C for 30 min and at 190°C for another 30 min. Cool and pour on 20 g of cracked ice in a beaker. Isolate the precipitate by filtration. Add a slight excess of 10% sodium hydroxide solution to the precipitate, and remove any insoluble amide by filtration. Acidify the filtrate with 10% sulfuric acid to yield the carboxylic acid. Purify by recrystallization from an acetone–water mixture.

(b) Basic Conditions



Reflux 1 g of the nitrile with 5 mL of 40% sodium hydroxide for 1–3 hr, or until the evolution of ammonia ceases. Cool the mixture in an ice bath, and add 25% sulfuric acid slowly until the solution is acidic. Remove the insoluble carboxylic acids by filtration and recrystallize. If no solid is obtained, extract the solution three times with 15 mL of diethyl ether. Dry, filter, and concentrate the combined ether layers to yield the carboxylic acid.

Cleaning Up Neutralize the aqueous filtrates with sodium carbonate and place in the aqueous solution container. Place the recovered ether in the organic solvent container.

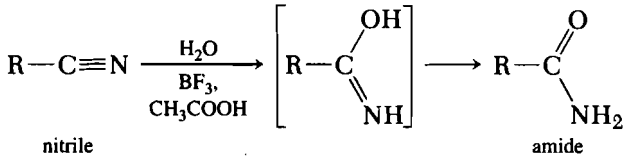
Discussion

The solid carboxylic acid may be used as a derivative. A solid or liquid carboxylic acid can be converted to an amide (Procedure 3, p. 359) or an anilide (Procedure 4a or 4b, p. 360 or 361).

Hydrochloric acid is more effective than sulfuric and for some nitriles. However, for nitriles that are difficult to hydrolyze, it is advisable to choose sulfuric acid because of its higher boiling point. The addition of a small amount of hydrochloric acid (as sodium chloride) increases the rate of reaction.

Prior to using (a), place a few drops or crystals of the sample in a test tube containing 0.2 mL of 75% sulfuric acid. In the hood, heat the sample to boiling. If charring occurs, (b) should be used.

Procedure 54 Controlled Hydration of a Nitrile to an Amide



nitrile amide

Place 1 g of the nitrile, 1.33 g of water, and 6.7 g of boron trifluoride/acetic acid complex[16] in a 100-mL flask fitted with a reflux condenser. Heat the mixture to 115–120°C in an oil bath for 10 min, and then cool in an ice bath to 15–20°C. Add a solution of 6 M sodium hydroxide slowly, keeping the temperature below 20°C, until the mixture is just alkaline to litmus paper. About 30–35 mL of the sodium hydroxide solution will be needed. Extract the cold solution with three 35-mL portions of 1:1 ethyl ether/ethyl acetate solvent. Dry the combined extracts with 1.5 g of anhydrous sodium sulfate and filter into a distilling flask. Using a hot-water bath as a source of heat, remove the ethyl ether/ethyl acetate solvent by distillation. Purify the residual amide by crystallization from water or a mixture of water and methanol. Dry the amide in a vacuum desiccator before the melting point is taken.

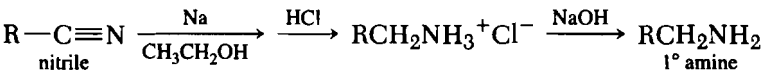
Cleaning Up Place the recovered ethyl ether/ethyl acetate mixture in the organic solvent container. Place the aqueous layer in the aqueous solution container.

Discussion

This controlled hydration of a nitrile to an amide may be accomplished in a short time in yields of 90–95% by use of boron trifluoride/acetic acid catalyst using a limited amount of water.[17]

Diamides (from dinitriles) may be extracted from the cold alkaline mixture more efficiently by use of three 100-mL portions of methylene chloride or chloroform.

Procedure 55 Reduction of Nitriles to Primary Amines



nitrile 1° amine

Place 20 mL of absolute ethanol and 1 g of an aliphatic nitrile or 2 g of an aromatic nitrile in a clean, dry, 100-mL round-bottom flask, fitted with a reflux condenser.

[16]The liquid complex, $BF_3 \cdot 2CH_3COOH$, may be purchased from the Aldrich Chemical Company or prepared according to the procedure described in L. F. Fieser and M. Feiser, *Reagents for Organic Synthesis* (Wiley, New York, 1967), p. 69 (1943).

[17]C. R. Hauser and D. S. Hoffenberg, *J. Org. Chem.*, *20*, 1448 (1955).

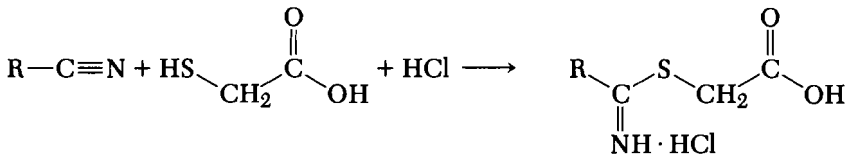
Through the top of the condenser, add 1.5 g of finely cut sodium slices as rapidly as possible without causing the reaction to become too vigorous. When the reduction is complete (10–15 min), cool the mixture to 20°C. Add 10 mL of concentrated hydrochloric acid dropwise through the condenser, with vigorous swirling of the contents of the flask. Test the reaction mixture to make certain it is acid to litmus. Rearrange the glassware to a distillation apparatus containing a Claisen adaptor and distill off 20 mL of ethanol and water. Cool the flask and contents. Fit a small dropping funnel containing 15 mL of 40% sodium hydroxide to the top of the Claisen adaptor. Attach tubing to the end of the vacuum adaptor, attached to the condenser, and place the other end so that it dips into 3 mL of water in a 50-mL Erlenmeyer flask. Add the alkali drop by drop, with shaking. The reaction is vigorous, and care must be exercised to avoid adding the alkali too fast. After all the alkali has been added, heat the mixture until the distillation of the amine is complete. Stop the distillation when the contents of the flask are very viscous.

Cleaning Up Rinse the initial distillate of ethanol and water into an aqueous solution container. Neutralize the aqueous layer with 10% hydrochloric acid and place in the aqueous solution container.

Discussion

The primary amine that is isolated from this reaction is then used to prepare derivatives such as a benzamide (Procedure 20b or 20c, p. 384), a benzenesulfonamide (Procedure 21, p. 386), or a phenylthiourea (Procedure 22, p. 387).

Procedure 56 α-(Imidioylthio)acetic Acids from Nitriles



nitrile thioglycolic acid α-(imidioylthio)acetic acid hydrochloride

Dissolve 1 g of the nitrile and 2.0 g of mercaptoacetic acid (thioglycolic acid) in 15 mL of absolute ethyl ether in a clean, dry test tube. Cool the solution in an ice bath and thoroughly saturate with dry hydrogen chloride. Prepare the hydrogen chloride gas as previously described (Procedure 26, p. 389). Dry the gas by passing it through a trap containing concentrated sulfuric acid. Tightly stopper the tube and keep in the ice bath or refrigerator until crystals of the derivative separate. Aliphatic nitriles form the addition compound in 15–30 min, whereas aromatic nitriles usually have to stand overnight in the refrigerator.

Remove the crystals by filtration, wash thoroughly with absolute ether, and place in a vacuum desiccator containing sulfuric acid in the bottom and small beakers of potassium hydroxide pellets and paraffin wax in the top. Determine the decomposition point in the melting point apparatus and the neutralization equivalent by titration with standard alkali, using thymol blue as the indicator.

Determination of the neutralization equivalent (Procedure 1, p. 357) can lead to the mass of the R group; one should keep in mind that there are two acid groups in such a derivative.

Cleaning Up Add 100 mL of 5.25% sodium hypochlorite (household bleach) to the aqueous filtrate. Heat the mixture at 45–50°C for 2 hr in a hot-water bath. At this point, all of the thioglycolic acid should have been oxidized. Place the mixture in the aqueous solution container.

PROBLEM

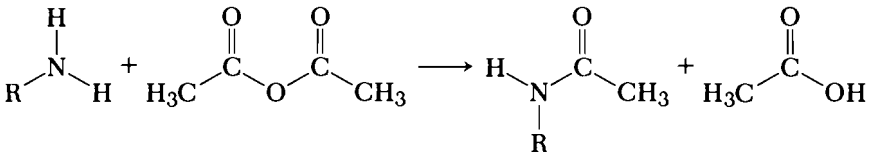
30. From benzonitrile, give the equations for the formation of (a) benzoic acid (two ways), (b) benzamide (two ways), (c) benzanilide, (d) 4-phenyltoluidide, (e) benzylamine, (f) *N*-benzylbenzamide, (g) *N*-benzylbenzenesulfonamide, (h) 1-benzyl-3-phenylthiourea, and (i) phenyl α-(imidioylthio)acetic acid hydrochloride.

10.15 NITRO COMPOUNDS

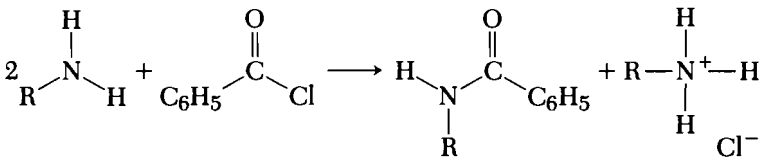
The reduction of nitro compounds in acidic media leads to the formation of primary (1°) amines (Procedure 57, p. 431).

$$\underset{\text{nitro compound}}{RNO_2} \xrightarrow[HCl]{Sn} RNH_3{}^+Cl^- \xrightarrow{NaOH} \underset{1° \text{ amine}}{RNH_2}$$

These primary amines can then be converted into suitable derivatives such as acetamides (Procedure 20a, p. 384), benzamides (Procedure 20b or 20c, p. 384), or benzenesulfonamides (Procedure 21, p. 386). The acetamide is prepared by the reaction of the amine with acetic anhydride.



The reaction of the amine with benzoyl chloride produces the benzamide.



Amines undergo reaction with benzenesulfonyl chloride to yield benzenesulfonamides.

$$\underset{1° \text{ amine}}{RNH_2} + \underset{\text{benzenesulfonyl chloride}}{C_6H_5SO_2Cl} + 2NaOH \longrightarrow \underset{\text{(soluble)}}{C_6H_5SO_2NR^-Na^+} + NaCl + 2H_2O$$

$$\downarrow HCl$$

$$\underset{\text{benzenesulfonamide}}{C_6H_5SO_2NHR} + NaCl$$

Procedure 57 Reduction of a Nitro Compound with Tin and Hydrochloric Acid

$$\underset{\text{nitro compound}}{RNO_2} \xrightarrow[HCl]{Sn} RNH_3{}^+Cl^- \xrightarrow{NaOH} \underset{1^\circ \text{ amine}}{RNH_2}$$

Add 1 g of the nitrogen-containing compound (nitro, nitroso, azo, azoxy, or hydrazo) to 2 g of granulated tin in a small round-bottom flask. Attach a reflux condenser. Add 20 mL of 10% hydrochloric acid, in small portions, to the mixture with vigorous shaking after each addition. Add 5 mL of ethanol to the mixture. Warm the mixture on the steam bath for 10 min. While still hot, decant the solution into 10 mL of water, and add sufficient 40% sodium hydroxide solution to dissolve the tin hydroxide. Extract the solution several times with 10-mL portions of ether. Dry the ether extract with magnesium sulfate, filter, and remove the ether by distillation. The residue that remains is the amine, which can then be made into other derivatives or recrystallized. Take a melting point if the amine is a solid.

Cleaning Up Neutralize the aqueous filtrate with 10% hydrochloric acid. Separate the tin hydroxide by filtration, and place in the nonhazardous solid waste container. Place the aqueous filtrate in the aqueous solution container. Place the recovered ether in the organic solvent container.

Discussion

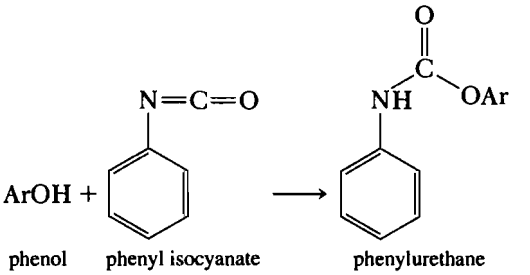
These primary amines can used to prepare derivatives such as acetamides (Procedure 20a, p. 384), benzamides (Procedure 20b or 20c, p. 384), or benzenesulfonamides (Procedure 21, p. 386).

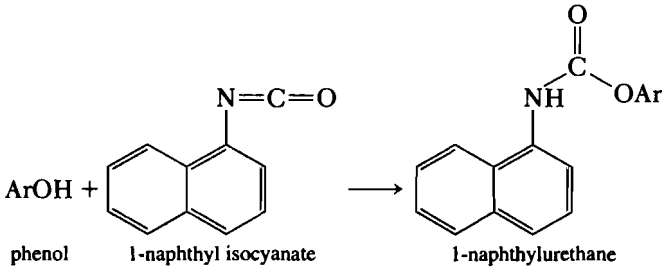
Problem

31. From 2,4-dichloro-1-nitrobenzene, give the equations for the formation of (a) *N*-(2,4-dichlorophenyl) acetamide, (b) *N*-(2,4-dichlorophenyl) benzamide, and (c) *N*-(2,4-dichlorophenyl) benzenesulfonamide.

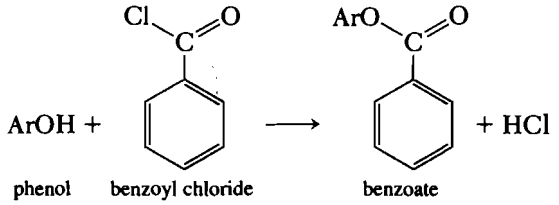
10.16 PHENOLS

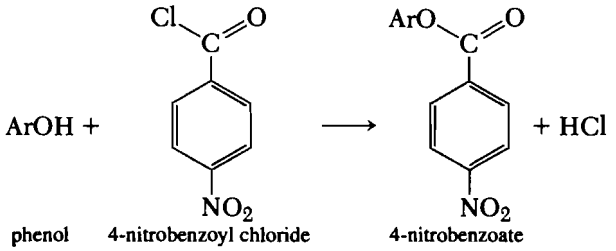
Phenols, like alcohols, yield urethanes when treated with isocyanates (Procedures 8 or 58, p. 366 or 433). Both the phenylurethanes and the 1-naphthylurethanes (α-naphthylurethanes) are generally useful derivatives in identifying phenols.

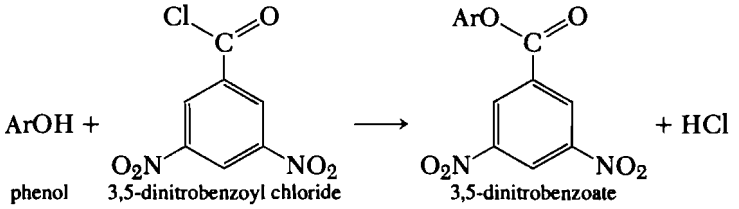




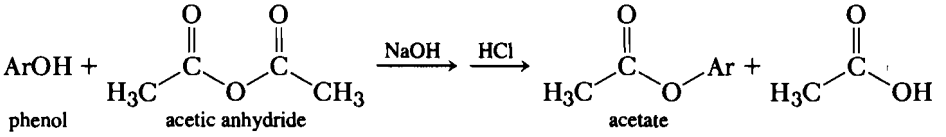
Benzoates (Procedure 9, p. 367), 4-nitrobenzoates (Procedure 9, p. 367), or 3,5-dinitrobenzoates (Procedure 10, p. 368) are easily prepared from the reaction of the phenol with the corresponding acyl halide.





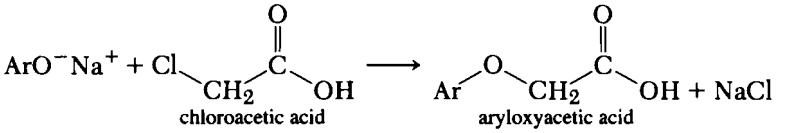


The acetates of monohydroxy aromatic compounds are usually liquids. Aromatic compounds containing two or more hydroxy groups, as well as substituted phenols, are frequently solids. Preparation of the acetates from phenols is done with acetic anhydride in basic media (Procedure 59, p. 434).



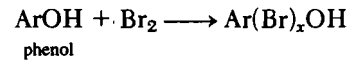
In the presence of alkali, phenols react readily with chloroacetic acid to give aryloxyacetic acids. These derivatives crystallize well from water and have proved to be exceedingly useful in characterization work (Procedure 60, p. 434).

$$\underset{\text{phenol}}{\text{ArOH}} + \text{NaOH} \longrightarrow \text{ArO}^{-}\text{Na}^{+}$$

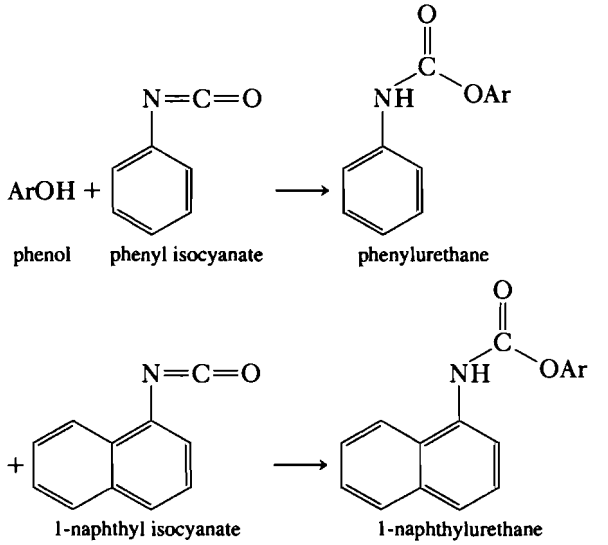


The aryloxyacetic acids can be compared not only by melting point determinations but also by their neutralization equivalents (Procedure 1, p. 357). Accurate determination of the neutralization equivalent can lead to an estimate of the total mass of substituents on the aryl ring.

Similar to its use as a qualitative test for phenols (Experiment 44, p. 414), bromine can be used to form derivatives of phenol (Procedure 61, p. 434). Since the phenolic ring is reactive toward such electrophilic reagents, every proton atom in an *ortho* or *para* position is displaced by bromine; in fact, bromine often substitutes for groups other than protons.



Procedure 58 Phenylurethanes and 1-Naphthylurethanes from Phenols



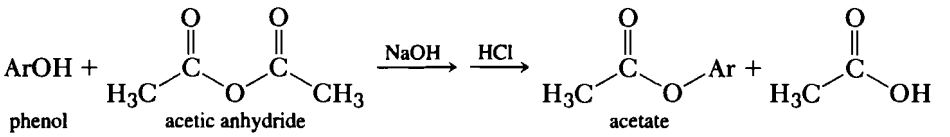
Add 1 drop of pyridine to a mixture of 0.5 g of the dry phenol and 0.5 mL of phenyl isocyanate or 1-naphthyl isocyanate in a dry 25-mL flask. Loosely stopper the flask with a plug of cotton and heat on a steam bath for 15 min. If the derivative does not solidify during this time, cool the flask and scratch the walls. When crystals have formed, add 10 mL of dry ethyl acetate. Heat the mixture on a steam bath and filter through a fluted filter. Add hexane until a turbidity or crystals are obtained. Allow crystallization to proceed overnight. Remove the product by filtration, wash with hexane, and air-dry.

If any water is present in the original sample or reagents, the product will be contaminated with *N,N'*-diphenylurea (mp 238°C) or *N,N'*-dinaphthylurea (mp 287°C). Warm the product with 10 mL of carbon tetrachloride and remove the insoluble

diphenylurea by filtration. Cool the filtrate to obtain the urethane. Occasionally the filtrate may have to be evaporated to 2–3 mL for the crystallization to occur.

Cleaning Up Treat any unreacted phenyl isocyanate or 1-naphthyl isocyanate with an excess of 5.25% sodium hypochlorite (household bleach) and place in the aqueous solution container. Place the organic solvents in the organic solvent container.

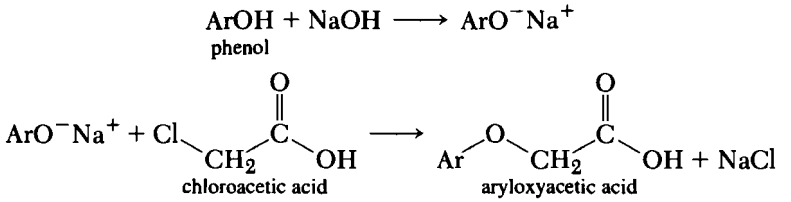
Procedure 59 Preparation of Acetates from Phenols



Dissolve 1 g of the phenol in 5 mL of 3 M sodium hydroxide solution. If the solution is not slightly basic, add 3 M sodium hydroxide as needed. Add 15 g of crushed ice quickly, followed immediately by 1.5 g (1.5 mL) of acetic anhydride. Shake the mixture vigorously for 1 min. If the acetate does not separate immediately, then add 10% sulfuric acid until the solution is acidic to litmus. Isolate the acetate by filtration and recrystallize from hot water or dilute ethanol.

Cleaning Up Place the filtrate in the aqueous solution container.

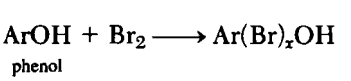
Procedure 60 Aryloxyacetic Acids of Phenols



Add 1.5 g of chloroacetic acid to a mixture of 1 g of the phenol in 5 mL of a 33% sodium hydroxide solution. Shake the mixture thoroughly, and add 1–5 mL of water, if necessary, in order to dissolve the sodium salt of the phenol. Heat the flask in a beaker of boiling water for 1 hr. Cool the solution, dilute with 10–15 mL of water, and acidify to a pH of 4 with 10% hydrochloric acid. Extract with 50 mL of ether. Wash the ether solution with 10 mL of cold water and then shake with 25 mL of 5% sodium carbonate solution. Acidify the solution with 10% hydrochloric acid (*Caution: foaming*). Isolate the aryloxyacetic acid by filtration and recrystallize from hot water.

Cleaning Up Place the ether layer in the organic solvent container. Neutralize the aqueous filtrate with sodium carbonate and place in the aqueous solution container.

Procedure 61 Bromination of Phenols



(a) With Bromine and Potassium Bromide

This reaction must be done in the hood. Add the potassium bromide and bromine solution slowly, with shaking, to a solution of 0.5 g of the phenol dissolved in water, ethanol,

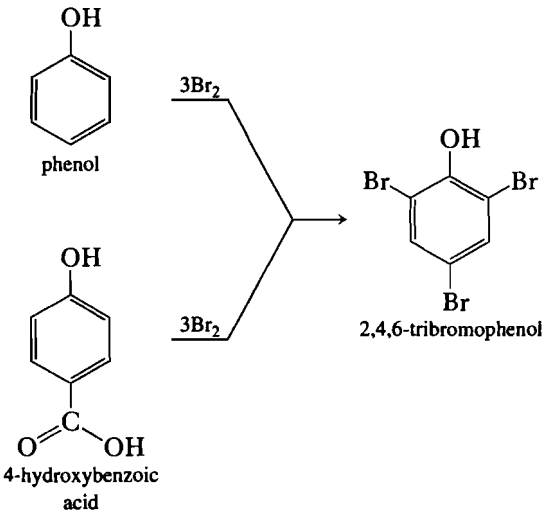
or dioxane until a yellow color persists. Add 25 mL of water, and shake the mixture vigorously to break up the lumps. Isolate the bromo derivative by filtration and wash with a dilute solution of sodium bisulfite. Recrystallize from ethanol or a water–ethanol mixture.

Potassium Bromide and Bromine Solution
Dissolve 15 g of potassium bromide in 100 mL of water and add 10 g of bromine. This solution is prepared by the instructor.

(b) With Bromine in Acetic Acid
This reaction must be done in the hood. Dissolve 1 g of the compound in 10–15 mL of acetic acid. Add 3 to 4 mL of bromine, dropwise, to 10–15 mL of acetic acid until the yellow to brown color of bromine persists. Allow the mixture to stand for 20 min. Pour the mixture into 75 mL of water. Isolate the solid product by suction filtration and rinse the product with 10 mL of cold water. Recrystallize from 60% ethanol.

Cleaning Up Extract the filtrates and any excess bromine in acetic acid solution with three 5-mL portions of methylene chloride to remove the unreacted bromine. Treat the methylene chloride extract with sufficient cyclohexene to discharge the bromine color and then place in the halogenated organic waste container. Place the aqueous layer in the aqueous solution container.

Discussion
Bromine reacts with both phenol and 4-hydroxybenzoic acid to form 2,4,6-tribromophenol.

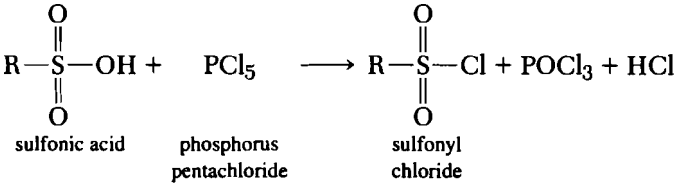


Problem

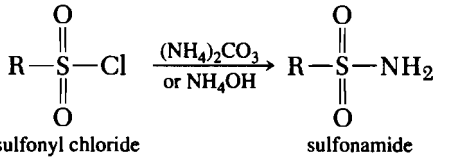
32. Give the equations for the reaction of 4-nitrophenol with (a) phenyl isocyanate, (b) 1-naphthyl isocyanate, (c) benzoyl chloride, (d) 4-nitrobenzoyl chloride, (e) 3,5-dinitrobenzoyl chloride, (f) acetic anhydride, (g) sodium hydroxide, followed by chloroacetic acid, and (h) bromine and potassium bromide.

10.17 SULFONIC ACIDS, SULFONYL CHLORIDES, SULFONAMIDES

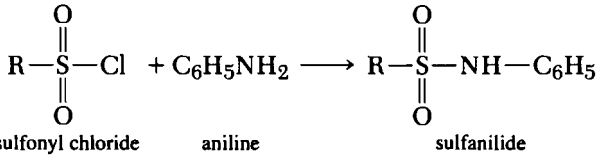
Sulfonic acids and their salts are converted into sulfonyl chlorides by heating with phosphorus pentachloride (Procedure 62, p. 437).



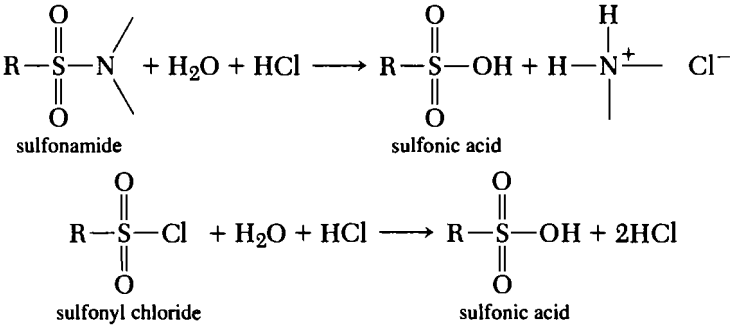
The sulfonyl chloride is rarely used as a derivative itself. The sulfonyl chloride undergoes reaction with aqueous ammonium carbonate or aqueous ammonia to obtain the sulfonamide (Procedure 43, p. 413).



The sulfanilide is prepared by reacting sulfonyl chloride with aniline (Procedure 63, p. 438).



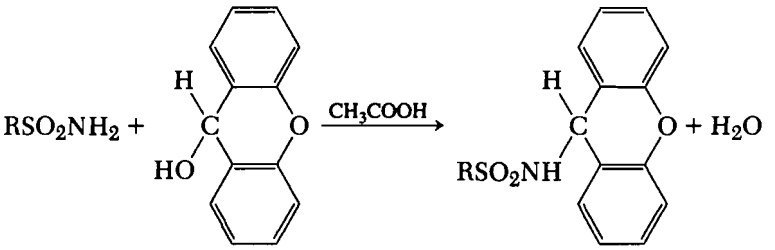
The sulfonamides and sulfonyl chlorides can be hydrolyzed to sulfonic acids under acidic conditions (Procedure 64, p. 438).



Sulfonic acids, from the sulfonamides, can then be treated with phosphorus pentachloride to produce the sulfonyl chloride (Procedure 62, p. 437), which is then used

as an intermediate in the preparation of other derivatives (Procedures 43 or 63, p. 413 or 438).

Primary sulfonamides react with xanhydrol to form *N*-xanthylsulfonamides, which are satisfactory derivatives (Procedure 65, p. 439).



Sulfonic acids and their salts readily react with *S*-benzylthiuronium chloride to give *S*-benzylthiuronium sulfonates. This reaction represents the shortest and most direct method for obtaining derivatives of these compounds (Procedure 66, p. 440).

$$RSO_3H + NaOH \longrightarrow RSO_3^-Na^+ + H_2O$$

sulfonic acid — sodium salt of sulfonic acid

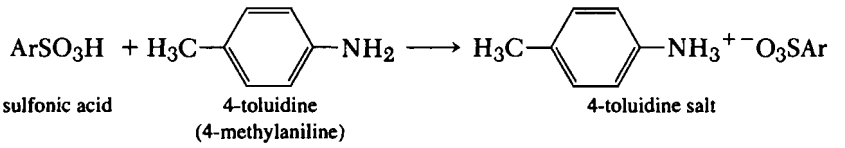
$$RSO_3^-Na^+ + [C_6H_5CH_2SC(NH_2)_2]^+Cl^- \longrightarrow$$

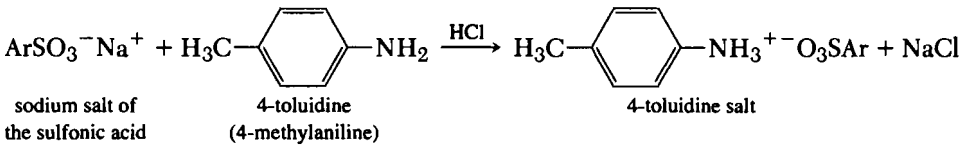
sodium salt of the sulfonic acid — *S*-benzylthiuronium chloride

$$[C_6H_5CH_2SC(NH_2)_2]^+RSO_3^- + NaCl$$

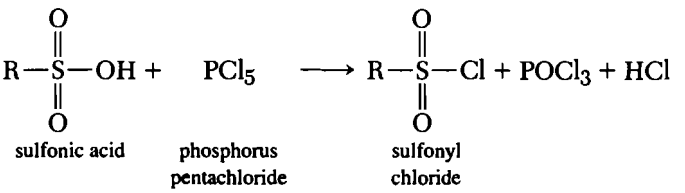
S-benzylthiuronium sulfonate

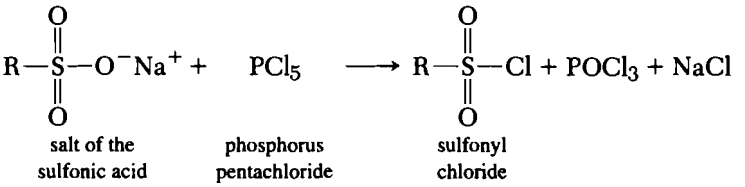
The 4-toluidine salts are prepared by treating the sulfonic acid with 4-toluidine or the sodium salt of the sulfonic acid with hydrochloric acid and 4-toluidine (Procedure 67, p. 440).





Procedure 62 Sulfonyl Chlorides from Sulfonic Acids and Their Salts

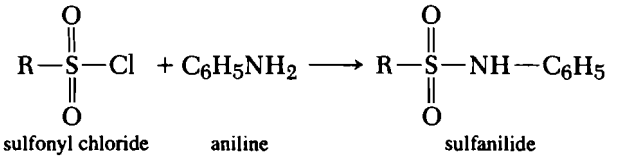




Mix 1 g of the dry sulfonic acid or the anhydrous salt with 2.5 g of phosphorus pentachloride in a clean, dry round-bottom flask. Attach a reflux condenser, and heat the flask in an oil bath at 150°C for 30 min. Cool the mixture. Add 10 mL of dry benzene (see footnote 2, p. 360). *Note: Benzene is a known carcinogen. Use benzene in the hood, do not breathe the vapors, and avoid contact with the skin.* Warm the mixture on a steam bath, and stir the solid mass thoroughly. Filter the solution through dry filter paper and wash the filtrate rapidly with two 10-mL portions of water. Separate the benzene layer, dry with calcium chloride, and remove the solvent by distillation, using a steam bath. Recrystallize solid sulfonyl chlorides from petroleum ether or chloroform. Liquid or recrystallized sulfonyl chlorides then can be used to prepare other derivatives, such as those described in Procedures 43 (p. 413) or 63 (p. 438).

Cleaning Up Place the recovered benzene in the hazardous waste container for benzene. Place the aqueous layer in the aqueous solution container.

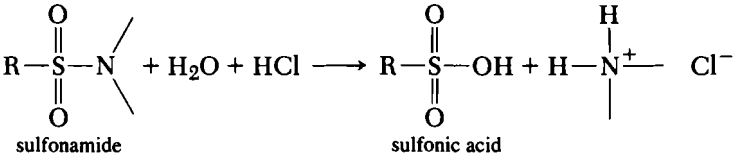
Procedure 63 Sulfanilides

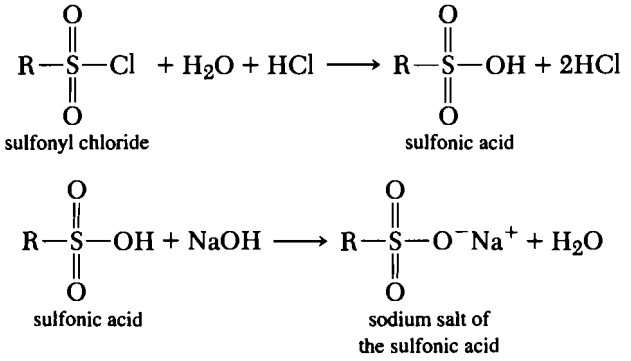


Heat a mixture of 1.0–1.5 g of the sulfonyl chloride in 10 mL of benzene (see footnote 2, p. 360) and 2.5 g of aniline under reflux for 1 hr. *Note: Benzene is a known carcinogen. Use benzene in the hood, do not breathe the vapors, and avoid contact with the skin.* Concentrate the solution to half its volume and chill. Isolate the solid by filtration, wash thoroughly with warm water, and recrystallize from ethanol. If the solid dissolves in warm water, then concentrate the original benzene filtrate and treat it as above to isolate the sulfanilide.

Cleaning Up Place the benzene filtrate in the hazardous waste container for benzene. Place the water and ethanol filtrates in the aqueous solution container.

Procedure 64 Hydrolysis of Sulfonamides and Sulfonyl Chlorides



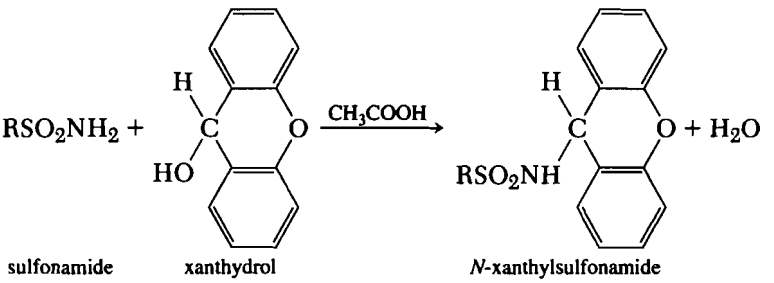


Heat, under reflux, 1 g of the compound with 10 mL of 25% hydrochloric acid. For unsubstituted sulfonamides or sulfonyl chlorides, the reaction is complete in 1–2 hr. Sulfonamides of primary amines require 24–36 hr refluxing, whereas sulfonamides of secondary amines may be hydrolyzed in 10–12 hr. After the reaction is complete, cool the mixture. Make the solution alkaline with 20% sodium hydroxide solution and extract with three 25-mL portions of diethyl ether. Dry the ether solution with magnesium sulfate, filter, and concentrate to yield the primary or secondary amine. With certain very low or very high boiling amines, it is often more convenient to recover them as hydrochlorides by passing dry hydrogen chloride gas into the dry ether solution (Procedure 26, p. 389). The amines can then be characterized by a suitable derivative (Procedures 20–22, pp. 384–387).

The aqueous layer contains the sodium salt of the sulfonic acid. Acidify the solution with 25% hydrochloric acid, and isolate the sulfonic acid by filtration. If no solid is formed, neutralize the solution with sodium bicarbonate and add an excess of sodium chloride. The solid that is formed contains the sodium salt of the sulfonic acid and sodium chloride. Recrystallize from ethanol. Filter the solution hot to remove the insoluble sodium chloride. Chill and isolate the sulfonate salt by filtration. Concentrate the ethanol to yield more of the sulfonate salt.

Cleaning Up Place the recovered ether in the organic solvent container. Place the aqueous layer in the aqueous solution container.

Procedure 65 *N*-Xanthylsulfonamides from Sulfonamides



Dissolve 0.2 g of xanthydrol in 10 mL of glacial acetic acid. If the mixture is not clear, filter or centrifuge, and add 0.2 g of the sulfonamide. Shake the mixture and allow to stand at room temperature until the derivative separates; this may require as long as

1.5 hr. Remove the *N*-xanthylsulfonamide by filtration and recrystallize from a dioxane–water mixture.

Cleaning Up Place the filtrates in the aqueous solution container.

Procedure 66 Benzylthiuronium Sulfonates

$$\underset{\text{sulfonic acid}}{RSO_3H} + NaOH \longrightarrow \underset{\substack{\text{sodium salt of}\\ \text{sulfonic acid}}}{RSO_3^-Na^+} + H_2O$$

$$\underset{\substack{\text{sodium salt of the}\\ \text{sulfonic acid}}}{RSO_3^-Na^+} + \underset{\text{S-benzylthiuronium chloride}}{[C_6H_5CH_2SC(NH_2)_2]^+Cl^-} \longrightarrow$$

$$\underset{\text{S-benzylthiuronium sulfonate}}{[C_6H_5CH_2SC(NH_2)_2]^+RSO_3^-} + NaCl$$

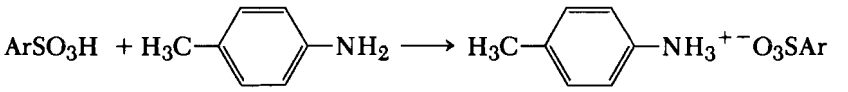
Dissolve 1 g of the sodium or potassium salt of the sulfonic acid in the smallest amount of water, heating if necessary. If the free sulfonic acid is the starting material, dissolve it in 2 M sodium hydroxide solution and neutralize any excess alkali with hydrochloric acid, using phenolphthalein as the indicator.

Dissolve 1 g of the benzylthiuronium chloride (see Procedure 49, p. 419, using benzyl chloride) in the smallest possible amount of water. Chill this solution and that of the sulfonate in an ice bath, mix, and shake thoroughly. Occasionally it is necessary to scratch the tube and cool in an ice bath to induce crystallization. Isolate the benzylthiuronium sulfonate crystals by filtration, wash with a little cold water, and recrystallize from 50% ethanol.

Cleaning Up Place the filtrate in the aqueous solution container.

Procedure 67 4-Toluidine Salts of Sulfonic Acid

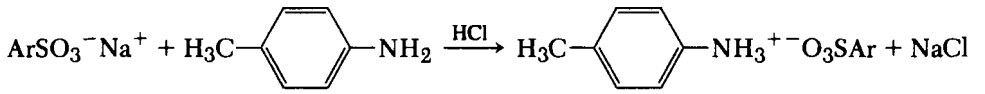
(a) From Free Sulfonic Acids



sulfonic acid — 4-toluidine (4-methylaniline) — 4-toluidine salt

Dissolve 1 g of the sulfonic acid in a minimum amount of boiling water and add 1 g of 4-toluidine. Add more water or additional sulfonic acid to obtain a clear solution. Cool the solution and scratch the flask to induce crystallization of the salt. Remove the salt by filtration and recrystallize from the minimum amount of water.

(b) From Soluble Salts of Sulfonic Acids



sodium salt of the sulfonic acid — 4-toluidine (4-methylaniline) — 4-toluidine salt

Dissolve 1 g of the sodium, potassium, or ammonium salt in a minimum amount of boiling water, and add 0.5 g of 4-toluidine and 1–2 mL of concentrated hydrochloric acid.

If a precipitate separates or if the 4-toluidine is not completely dissolved, add more hot water and a few drops of concentrated hydrochloric acid until a clear solution is obtained at the boiling point. Cool the solution, and scratch the walls of the flask to induce crystallization of the salt. Remove the product by filtration and recrystallize from a small amount of water or dilute ethanol.

Cleaning Up Make the filtrate basic with 10% sodium hydroxide solution. Extract with two 10-mL portions of diethyl ether. Place the ether layer in the organic solvent waste container. Place the aqueous layer in the aqueous solution container.

▶ Problems

33. From 4-methylbenzenesulfonamide, give the equations for the formation of (a) 4-methylbenzenesulfonic acid, (b) 4-methylbenzenesulfonyl chloride, (c) 4-methylbenzenesulfonanilide, and (d) *N*-xanthyl 4-methylbenzenesulfonamide.

34. Give the equations for the reaction of 4-bromobenzenesulfonic acid with (a) phosphorus pentachloride, (b) phosphorus pentachloride, followed by ammonium carbonate, (c) phosphorus pentachloride, followed by aniline, (d) sodium hydroxide, followed by *S*-benzylthiuronium chloride, and (e) 4-toluidine.

CHAPTER 11

Structural Problems—Solution Methods and Exercises

The laboratory examination of an organic compound results in the accumulation of the physical properties, elements present or absent, solubility, spectral data, and behavior toward certain classification reagents and in various special tests. All these observed facts must be correlated and interpreted in order to arrive at possible structural formulas for the compound in question. It is necessary to show what functional groups are present, to determine the nature of the nucleus to which they are attached, and to find the positions of attachment.

It is the purpose of this discussion to point out, by means of several specific examples, the mode of attack and reasoning involved in deducing information concerning the structure of a molecule from experimental data.

11.1 COMPOUNDS WITH STRUCTURES PREVIOUSLY DESCRIBED IN THE LITERATURE

The identification of these compounds does not require quantitative analysis for the elements present, molecular weight determination, or calculation of molecular formulas. The identification is based on the *matching* of the physical and chemical properties of the substance being studied and the data on its derivatives. The laboratory work in this course as described in the preceding chapters is concerned with these previously described compounds.

Two very helpful physical constants described in Chapter 10 are the neutralization equivalents of acids and bases and the saponification equivalents of esters. These numerical data, in conjunction with the solubility class and behavior toward reagents, frequently give valuable clues concerning the molecular structure of the compound. Their use may best be explained by reference to examples.

EXAMPLE 1 An organic acid has a neutralization equivalent of 45 ± 1.

As pointed out on page 357, the neutralization equivalent of an acid is dependent on the number of carboxyl groups in the molecule. If one carboxyl group is present, the neutralization equivalent is equal to the molecular weight. If the present compound is monobasic, its molecular weight[1]

[1]For purposes of illustration and calculation in this chapter, whole numbers have been used for the atomic weights of carbon, hydrogen, oxygen, nitrogen, and bromine. The actual atomic weights (which must be used in all precise quantitative analyses) differ from these rounded-off values by an amount less than the experimental error involved in the determination of the neutralization and saponification equivalents.

must be 44, 45, or 46. A carboxyl group weighs 45; hence, if the molecular weight were 45, nothing could be attached to the carboxyl group. A molecular weight of 44 is obviously impossible, but a molecular weight of 46 leaves a residue of 1 after the weight of the carboxyl radical is subtracted. Only one element has the atomic weight of 1; thus, formic acid (HCOOH) is one possibility.

However, the compound might be dibasic, in which event the molecular weight would be 90 ± 2. Two carboxyl groups equals $2 \times 45 = 90$. Hence, a possible residue of 0, 1, or 2 units remains. There are no bivalent atoms of this atomic weight, so the only possible dibasic acid is oxalic acid, in which the two carboxyl groups are united:

Thus, by assuming first a monobasic acid and then a dibasic acid, two possible structures have been deduced from the neutralization equivalent alone. In order to decide between the two, the physical state or the solubility class of the compound must be used. If this compound, with a neutralization equivalent of 45 ± 1, is a liquid, soluble in water and in pure ether (solubility group S_1), it must be formic acid. If it is a solid, soluble in water but insoluble in ether (group S_2), it is anhydrous oxalic acid.

Consideration of the molecular weights indicates in a similar fashion that the compound could not be tribasic (mol wt 135 ± 3) or tetrabasic (mol wt 180 ± 4).

EXAMPLE 2 **An acid (A) possessed a neutralization equivalent of 136 ± 1. It gave negative tests for halogen, nitrogen, and sulfur. It did not decolorize cold potassium permanganate solution; but when an alkaline solution of the compound was heated with this reagent for an hour and acidified, a new compound (B) was precipitated. This compound had a neutralization equivalent of 83 ± 1.**

First consider the compound B. Assume it to be monobasic.

$$\begin{aligned} \text{molecular weight} &= 83 \pm 1 \\ \text{less one } —\text{COOH} &= 45 \\ \text{residue} &= 38 \pm 1 \end{aligned}$$

This residue to which the carboxyl group is attached must be made up of some combination of carbon, hydrogen, and perhaps oxygen that is stable to hot potassium permanganate solution. Examination shows that this is not possible.

$$\begin{aligned} \text{residue} &= 38 \pm 1 \\ \text{three carbon atoms} &= 3 \times 12 = 36 \\ \text{remainder} &= 2 \pm 1 \end{aligned}$$

The residue might be C_3H, C_3H_2, or C_3H_3, none of which correspond to a compound that would be stable to permanganate. The alkane would require C_3H_8 as the parent compound, and the alkyl group would have to be $C_3H_7—$; similarly, the cycloalkane would have to be C_3H_6 and the cyclopropyl group, $C_3H_5—$.

The presence of oxygen in this residue is also excluded. If it is assumed to be present, the following figures are obtained:

$$\begin{aligned} \text{residue} &= 38 \pm 1 \\ \text{one oxygen atom} &= 16 \\ &22 \pm 1 \\ \text{one carbon atom} &= 12 \\ \text{remainder} &= 10 \pm 1 \end{aligned}$$

or

$$\begin{aligned} \text{residue} &= 38 \pm 1 \\ \text{two oxygen atoms} &= 32 \\ \text{remainder} &= 6 \pm 1 \end{aligned}$$

Neither of these remainders corresponds to any atom or group of atoms that forms a reasonable organic compound. For example, the former suggest $CH_{10}OCO_2H$ for the compound and the

latter, $H_6O_2CO_2H$, both of which are unreasonable. Thus, it is now safe to conclude that compound B *cannot be monobasic.*

$$\begin{aligned} \text{molecular weight} &= 2 \times 83 \pm 1 = 166 \pm 2 \\ \text{two carboxyl groups} &= \underline{\quad 90 \quad} \\ \text{residue} &= \quad 76 \pm 2 \end{aligned}$$

If this residue is saturated and aliphatic, it must be made up of $—CH_2—$ units.

$$\begin{aligned} \text{five } —CH_2— &= 5 \times 14 = 70 \\ \text{six } —CH_2— &= 6 \times 14 = 84 \end{aligned}$$

Neither of these corresponds to the weight of the residual radical, 76 ± 2.

A grouping that is stable to hot permanganate is the benzene nucleus. This is an arrangement of six CH groups or $6 \times 13 = 78$ = molecular weight of benzene itself. If two carboxyl groups are present, two of the hydrogen atoms are replaced and the residue becomes $78 - 2 = 76$. This value matches that calculated above for the residue, and hence a possible structure for B is $C_6H_4(COOH)_2$; that is, it may be one of the three phthalic acids.

The question now arises whether compound B could be tribasic. If so, we have the following values:

$$\begin{aligned} \text{molecular weight} &= 3 \times 83 \pm 1 = 249 \pm 3 \\ \text{three carboxyl groups} &= 3 \times 45 \quad = \underline{\quad 135 \quad} \\ \text{residue} &= \quad 114 \pm 3 \end{aligned}$$

Inspection shows that this residue cannot be aromatic because it does not correspond to one or more benzene rings. A benzene ring plus a side chain is excluded because the side chain would be oxidized by the permanganate. The value 114 ± 3 does correspond, however, to eight CH_2 groups ($8 \times 14 = 112$) within experimental error. Moreover, $C_8H_{15}(COOH)_3$, with a molecular weight of 246, falls within the limit of 249 ± 3. Although this tricarboxylic acid represents a possible structure for a compound with a molecular weight of 249 ± 3, it would be impossible to produce it from compound A, which has a neutralization equivalent of 136 ± 1.

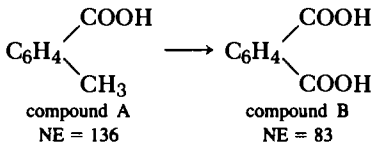
Let us assume that A is monobasic.

$$\begin{aligned} \text{molecular weight A} &= 136 \pm 1 \\ \text{one } —COOH &= \underline{\quad 45 \quad} \\ \text{residue} &= \quad 91 \pm 1 \end{aligned}$$

Since B has a C_6H_4 grouping stable to permanganate, this same group must also be present in A.

$$\begin{aligned} \text{residue} &= 91 \pm 1 \\ C_6H_4 &= \underline{\quad 76 \quad} \\ \text{remainder} &= 15 \pm 1 \end{aligned}$$

This remainder of 15 ± 1 corresponds to a methyl group that must be attached to the ring.



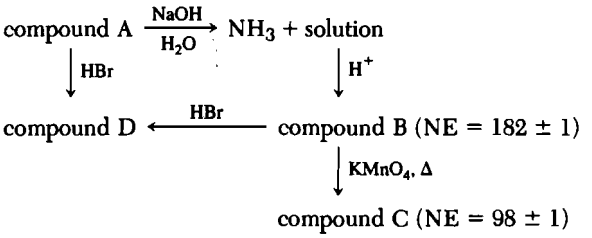
The original must be 2-, 3-, or 4-methylbenzoic acid (*o*-, *m*-, or *p*-toluic acid), each of which would give the reactions cited. Additional data such as a melting point, a derivative, or spectra are necessary to distinguish among them.

This example also illustrates the fact that oxidation almost invariably converts a compound with a given neutralization equivalent to a product that has a lower neutralization equivalent. This generalization follows naturally from the increase in the number of carboxyl groups or cleavage of the molecule into smaller fragments.

EXAMPLE 3

A colorless crystalline compound (A) gave a positive test for nitrogen but not for halogens or sulfur. It was insoluble in water, dilute acids, and alkalies. It produced a red-colored complex with ammonium hexanitratocerate reagent but did not react with phenylhydrazine. Compound A dissolved in hot sodium hydroxide solution with the liberation of ammonia and the formation of a clear solution. Acidification of this solution produced compound B, which contained no nitrogen and gave a neutralization equivalent of 182 ± 1. Oxidation of B by hot permanganate solution produced C, which had a neutralization equivalent of 98 ± 1. When either A or B was heated with hydrobromic acid for some time, a compound D separated. This compound contained bromine but no nitrogen. It gave a precipitate with bromine water and a violet color with ferric chloride, and it readily reduced dilute potassium permanganate. It was soluble in sodium bicarbonate solution.

These reactions may be summarized as follows.



The elimination of nitrogen from compound A by alkaline hydrolysis suggests the presence of a nitrile or amide grouping, because these functional groups liberate ammonia when they undergo hydrolysis.

$$RCN + NaOH + H_2O \longrightarrow RCOONa + NH_3$$
$$RCONH_2 + NaOH \longrightarrow RCOONa + NH_3$$

The imide grouping, —CONHCO—, which also liberates ammonia, is excluded by the fact that compound A is not soluble in sodium hydroxide solution. Since compound B contained no nitrogen, certain substituted anilines, such as 2,4-dinitroaniline, are excluded. The absence of nitrogen in B and the fact that it was acidic and not basic likewise eliminates a substituted urea, which also liberates ammonia when hydrolyzed.

$$RNHCONH_2 + H_2O \longrightarrow RNH_2 + CO_2 + NH_3$$

The positive red color with ammonium hexanitratocerate reagent suggests A is an alcohol; an amino or phenolic group is excluded by the fact that compound A is neutral. Further evidence for the presence of a hydroxyl group is furnished by the fact that compound D, produced from A by the action of hydrobromic acid, contained bromine.

$$ROH + HBr \longrightarrow RBr + H_2O$$

The properties of compound D strongly suggest the presence of a phenolic hydroxyl group. Ease of bromination, sensitivity to permanganate, and color with ferric chloride are properties characteristic of substituted phenols. This phenolic hydroxyl group was produced by the action of hydrobromic acid on some functional group present in A and B, because neither of these originally contained the phenol grouping. One type of compound that produces a phenol when treated with hydrobromic acid is an aryl alkyl ether.

$$ArOR + HBr \longrightarrow ArOH + RBr$$

If the alkyl group is small, it would be lost as alkyl bromide during the treatment with hydrobromic acid. Thus compounds A, B, and C probably contain such a mixed ether group

and also an aromatic nucleus, since the substituted phenol D contains one. The solubility of D in sodium bicarbonate solution is probably due to the presence of a carboxyl group, because both the nitrile and amide groups are hydrolyzed to carboxyl groups by acids as well as alkalies. Hence compound D is a hydroxybenzoic acid with the bromine attached to a side chain. This side chain must also be present in compound A with an alcoholic group in place of the bromine atom.

The neutralization equivalents of compounds B and C may now be considered. It will be noted that the neutralization equivalent of compound C, produced by permanganate oxidation, is lower than that of compound B, which acquired its acidic properties by a hydrolysis reaction only. This oxidation obviously affects the side chain, and compound C must have more carboxyl groups than B.

Assume compound C to be dibasic.

$$\begin{aligned} \text{molecular weight} = 2 \times 98 \pm 1 &= 196 \pm 2 \\ \text{two carboxyl groups} = 2 \times 45 &= \underline{\quad 90} \\ &\quad 106 \pm 2 \\ \text{one oxygen atom in ether linkage} &= \underline{\quad 16} \\ &\quad 90 \pm 2 \\ \text{benzene minus three hydrogen atoms } (C_6H_3) &= \underline{\quad 75} \\ \text{residue} &= 15 \pm 2 \end{aligned}$$

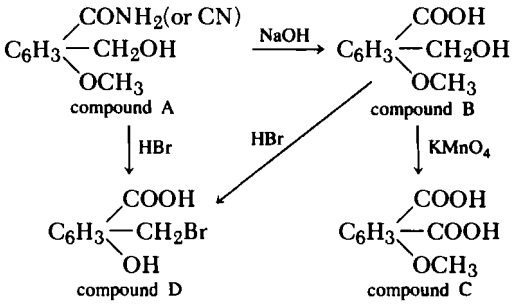
This residue of 15 corresponds to a CH_3— group, and hence the ether grouping must have been CH_3O—.

It is now necessary to find the length of the side chain to which the alcohol group in A and B is attached.

If C is dibasic, B is monobasic.

$$\begin{aligned} \text{NE} = \text{mol wt} &= 182 \pm 1 \\ \text{carboxyl group} &= \underline{\quad 45} \\ &\quad 137 \pm 1 \\ \text{methoxyl group} &= \underline{\quad 31} \\ &\quad 106 \pm 1 \\ \text{hydroxyl group} &= \underline{\quad 17} \\ &\quad 89 \pm 1 \\ \text{benzene nucleus } (C_6H_3) &= \underline{\quad 75} \\ \text{residue} &= 14 \pm 1 \end{aligned}$$

This residue represents the weight of the aliphatic side chain and obviously corresponds to —CH_2—. Hence, possible structures for A, B, C, and D are



This example illustrates the fact that a given reagent may affect more than one functional group. Thus, boiling hydrobromic acid affected three functional groups in compound A and two in compound B.

EXAMPLE 4

A liquid, with a boiling point of 248°C, gave no positive tests for sulfur, nitrogen, or halogen. The compound was insoluble in water, 5% sodium hydroxide, and 5% hydrochloric acid, but soluble in 96% sulfuric acid. The unknown gave an orange-red precipitate with 2,4-dinitrophenylhydrazine and a positive hydroiodic acid test. The oxime melted at 45°C. The IR, ^{1}H NMR, ^{13}C NMR, and DEPT spectra are shown in Figures 11.1 through 11.4.

The compound is in solubility class N, which includes alcohols, aldehydes, ketones, esters with one functional group and more than five but fewer than nine carbons, ethers, epoxides, alkenes, alkynes, and some aromatic compounds. A precipitate with the 2,4-dinitrophenylhydrazine test includes the presence of an aldehyde or ketone. A positive hydroiodic test indicates an ether.

The IR spectrum indicates the presence of an aryl aldehyde, a *p*-disubstituted compound, and an aryl alkyl ether.

Frequency	*Bond*	*Compound Type*
2825, 2731	C—H stretch	aldehyde
1690	C=O stretch	aryl aldehyde
1390	C—H bend	aldehyde
1020, 1260	C—O stretch	aryl alkyl ether
826	C—H out-of-plane bend	*p*-disubstituted aromatic
1502, 1596	C=C stretch	aromatic

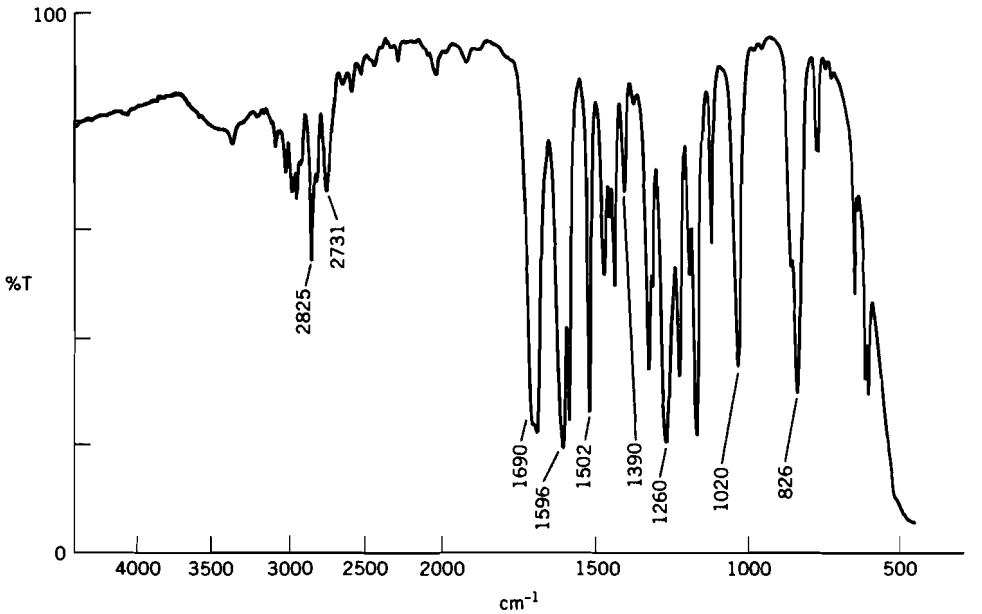


Figure 11.1 IR spectrum for Example 4. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

The ^{1}H NMR spectrum confirms the structure from the IR spectrum and gives the ether as a methyl ether.

	Chemical Shift	*Splitting*	*Integration*	*Interpretation*
(a)	3.79	s	3H	isolated CH_3
(b)	6.93	d	2H	CH adjacent to CH, aromatic
(c)	7.81	d	2H	CH adjacent to CH, aromatic
(d)	9.89	s	1H	CH isolated

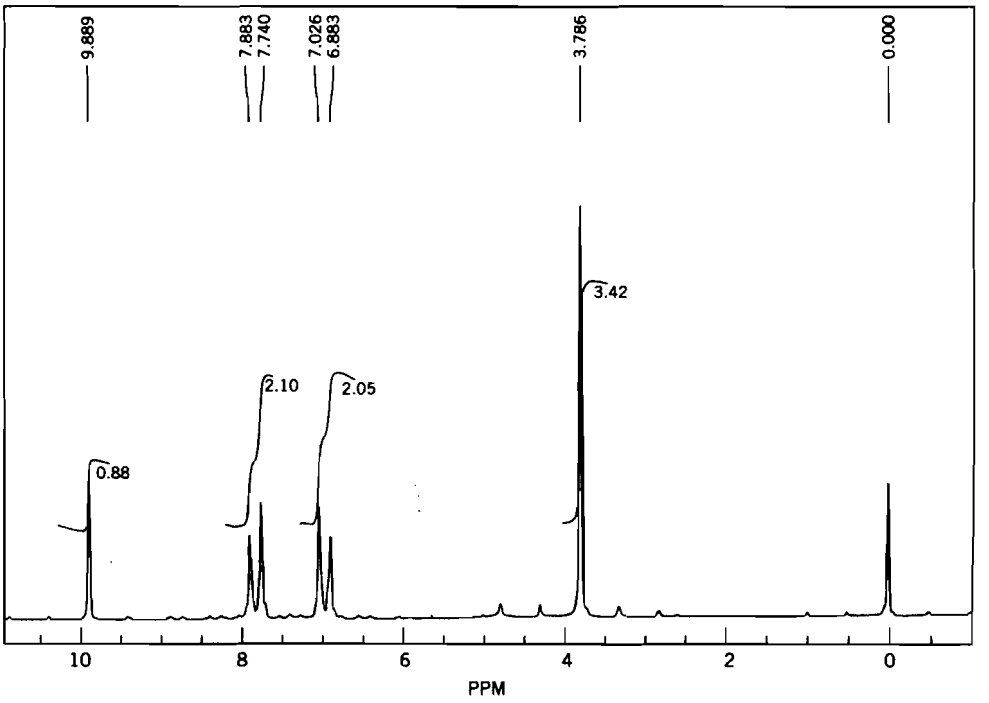


Figure 11.2 ^{1}H NMR spectrum for Example 4. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

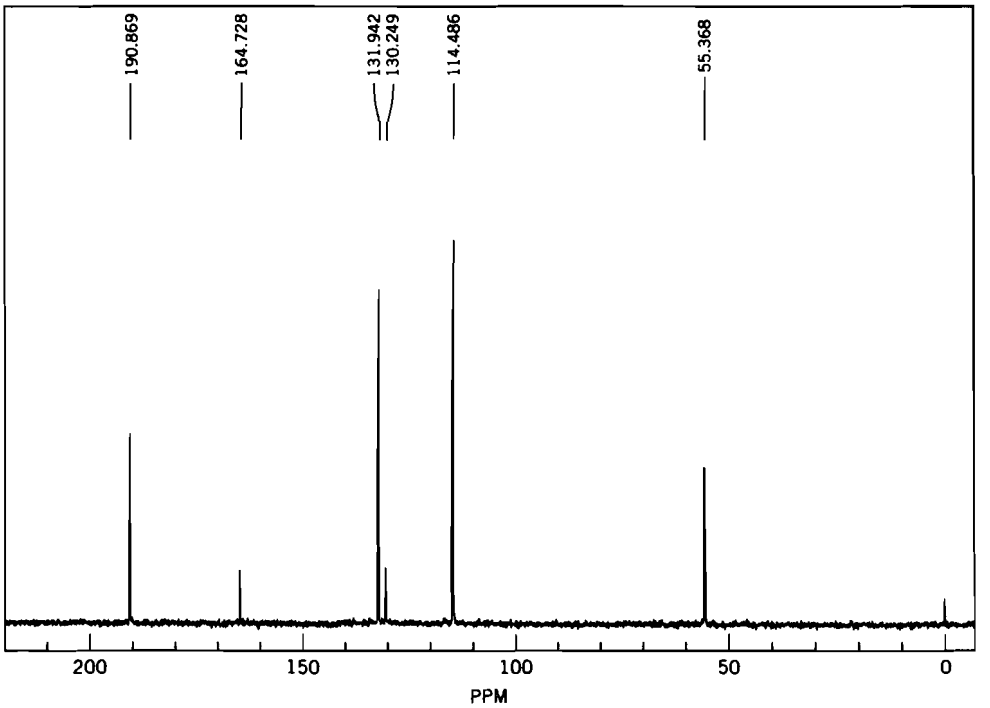


Figure 11.3 ^{13}C NMR spectrum for Example 4. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

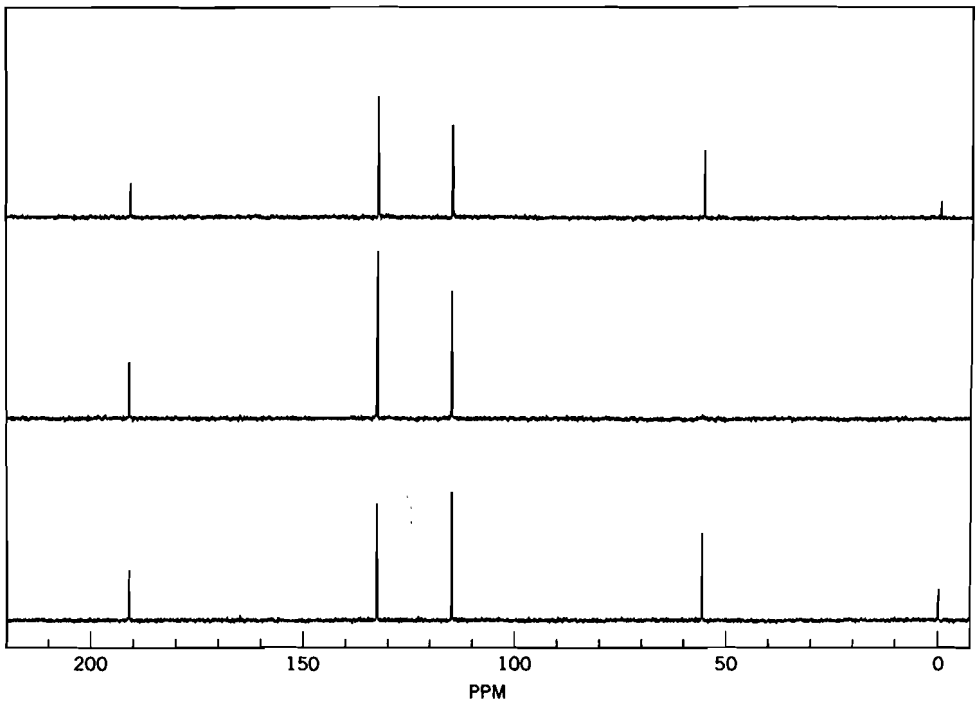
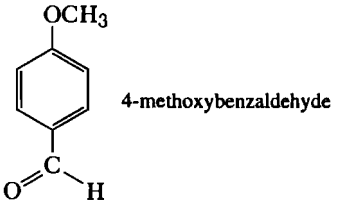


Figure 11.4 DEPT spectrum for Example 4. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

The ^{13}C NMR spectrum is additional confirmation of the structure.

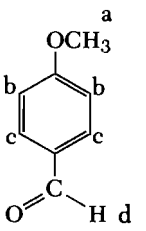
	Chemical Shift	*DEPT*	*Interpretation*
(a)	55.37	CH_3	ether
(b)	114.49	2CH	aromatic
(c)	130.25	C	aromatic
(d)	131.94	2CH	aromatic
(e)	164.73	C	aromatic
(f)	190.87	CH	aldehyde

From the IR and NMR spectra, the compound is a *p*-disubstituted aromatic compound. A methoxy group and an aldehyde group are *para* to each other. The only possible answer is *p*-methoxybenzaldehyde. This compound has an oxime derivative that melts at 45°C.

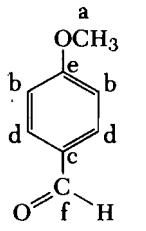


4-methoxybenzaldehyde

In the ^1H NMR spectra, the hydrogens *ortho* to the methoxy group would have a chemical shift of δ 7.21 (7.27 − 0.27 + 0.21) and the hydrogens *ortho* to the aldehyde group would have a chemical shift of δ 7.77 (7.27 − 0.08 + 0.58) (see Section 6.3.1).



In the ^{13}C NMR spectrum, the carbon attached to the methoxy group would have a chemical shift of δ 166.10 (128.7 + 31.4 + 6.0); the carbons *ortho* to the methoxy group would have a chemical shift of δ 115.5 (128.7 − 14.4 + 1.2); the carbons *ortho* to the aldehyde group would have a chemical shift of δ 130.9 (128.7 + 1.0 + 1.2); and the carbon attached to the aldehyde group would have a chemical shift of δ 130.0 (128.7 − 7.7 + 9.0) (see Section 6.4.1).



EXAMPLE 5

A liquid, with a boiling point of 104°C, gave no positive tests for sulfur, nitrogen, or halogen. The compound was insoluble in water, 5% sodium hydroxide, and 5% hydrochloric acid, but soluble in 96% sulfuric acid. The compound gave a negative test with 2,4-dinitrophenylhydrazine. It reacted with acetyl chloride, reacted with sodium, and formed a brown precipitate with potassium permanganate. The IR, ^1H NMR, ^{13}C NMR, and DEPT spectra are shown in Figures 11.5 through 11.8.

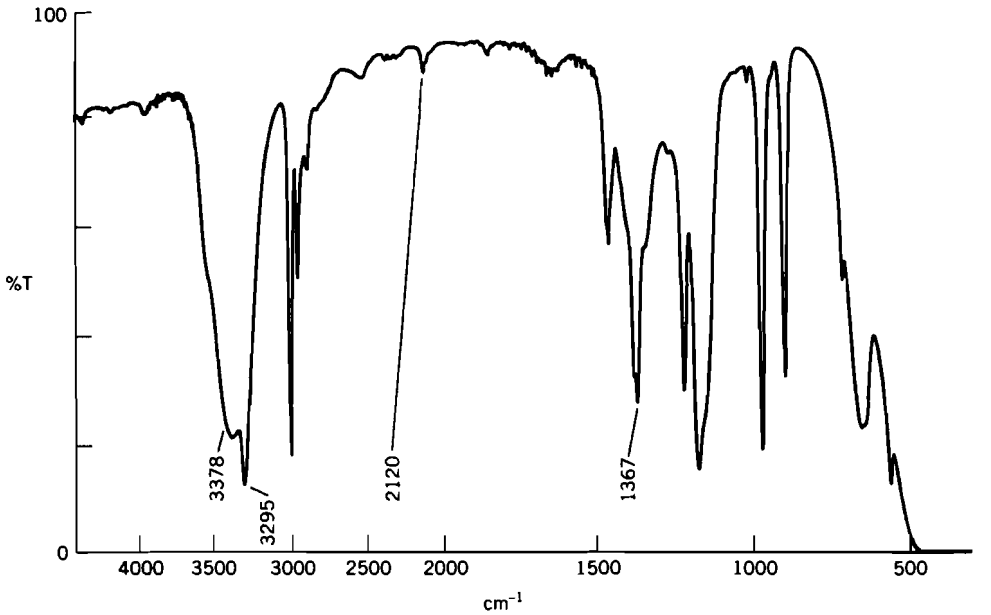


Figure 11.5 IR spectrum for Example 5. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

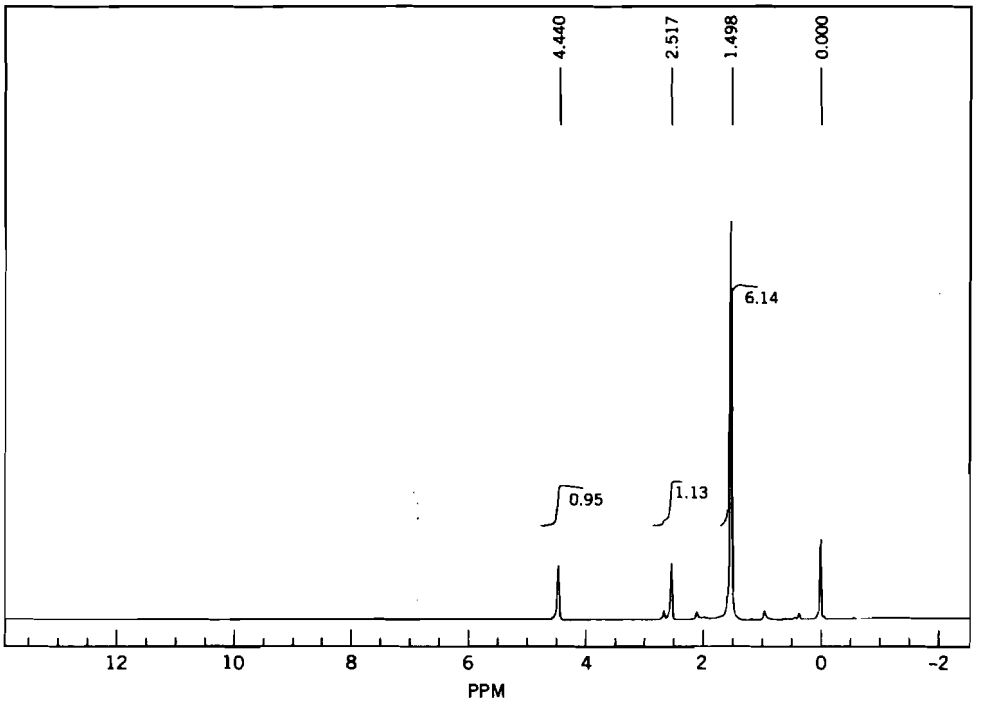


Figure 11.6 ^{1}H NMR spectrum for Example 5. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

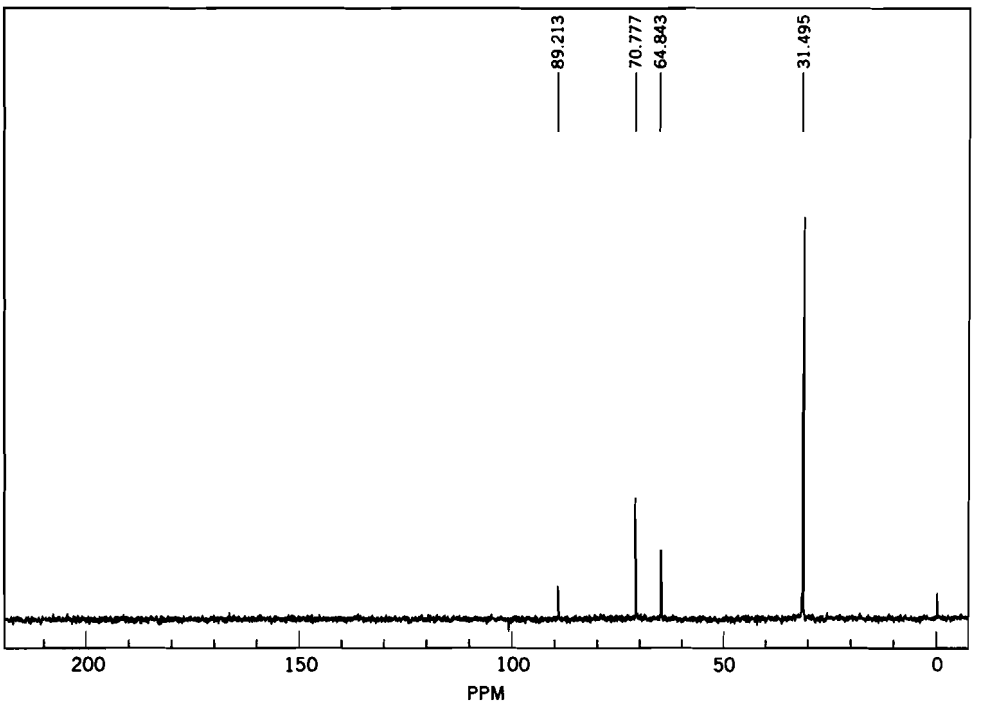


Figure 11.7 ^{13}C NMR spectrum for Example 5. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

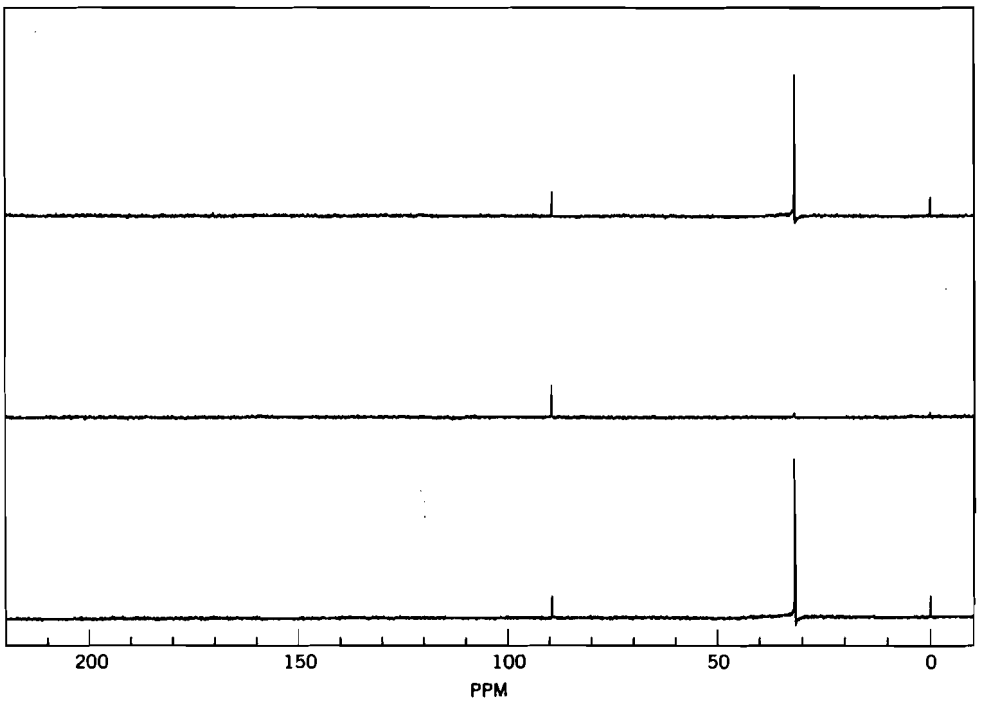


Figure 11.8 DEPT spectrum for Example 5. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

The compound is in solubility class N, which includes alcohols, aldehydes, ketones, esters with one functional group and more than five but fewer than nine carbons, ethers, epoxides, alkenes, alkynes, and some aromatic compounds. A negative test with 2,4-dinitrophenylhydrazine eliminates aldehydes and ketones as possibilities. A positive test with acetyl chloride, in the absence of nitrogen, indicates an alcohol. A positive test with sodium indicates an alcohol or alkyne. The reaction with potassium permanganate shows the presence of an alkene or alkyne.

The IR spectrum indicates an alcohol and a terminal alkyne.

Frequency	*Bond*	*Compound Type*
3378	O—H stretch	alcohol
1367	C—O stretch	3° alcohol
2120	C≡C stretch	alkyne
3295	C—H stretch	alkyne

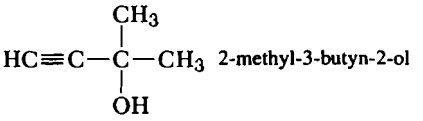
The ^{1}H NMR and ^{13}C NMR spectra also confirm the alkyne and alcohol.

	Chemical Shift	*Splitting*	*Integration*	*Interpretation*
(a)	1.50	s	6H	2 CH_3 isolated
(b)	2.52	s	1H	acetylenic
(c)	4.44	s	1H	alcoholic

The ^{13}C NMR spectrum is interpreted below.

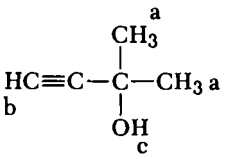
	Chemical Shift	*DEPT*	*Interpretation*
(a)	31.49	CH_3	alkyl
(b)	64.84	C	alcohol
(c)	70.78	C	alkyne
(d)	89.21	CH	alkyne

A terminal alkyne is indicated. Two methyl groups are attached to the carbon next to the alkyne carbon. The hydroxy group is attached to the same carbons as the methyl. The only possible answer is 2-methyl-3-butyn-2-ol.

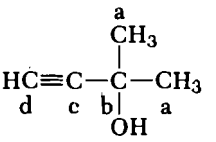


2-methyl-3-butyn-2-ol

The hydrogens can be labeled from the ^{1}H NMR spectrum.



The carbons can be labeled from the ^{13}C NMR spectrum.



EXAMPLE 6 **A compound had a boiling point of 102°C. The compound was soluble in water and ether; the litmus test of the aqueous solution was unchanged. The sodium fusion filtrate of the compound gave a yellow color with sodium nitroprusside; a yellow color with ammonium polysulfide, hydrochloric acid, and ferric chloride; and no precipitate with silver nitrate. It was mixed with ceric ammonium nitrate to give a yellow color. The compound did not react with sodium or acetyl chloride and gave a yellow color when treated with hydroxamic acid. The compound reacted with 2,4-dinitrophenylhydrazine to form a yellow solid. Treatment of the compound with Tollens test did not yield a silver mirror. The IR, ^{1}H NMR, ^{13}C NMR, and DEPT spectra are shown in Figures 11.9 through 11.12.**

The compound is in solubility class S_1, which includes monofunctional alcohols, aldehydes, ketones, esters, nitriles, and amides with five carbons or fewer. The tests with the sodium fusion filtrate indicate the absence of sulfur, the absence of nitrogen, and the absence of halogen. The compound is not an alcohol, since it gave a negative ceric ammonium nitrate test. The compound does not have an active hydrogen, as indicated by the negative sodium and negative acetyl chloride tests. The color of the hydroxamic acid shows that the compound is not an acid anhydride, an acyl halide, an amide, an ester, a nitrile, a sulfonic acid, or a sulfonyl chloride. The yellow solid with 2, 4-dinitrophenylhydrazine indicates that the compound is an aldehyde or a ketone. A negative Tollens test eliminates the aldehyde.

The IR spectrum confirms the presence of an aliphatic ketone.

Frequency	*Bond*	*Compound Type*
1713	C=O stretch	aliphatic ketone
1114	C=O stretch and bend	aliphatic ketone

The ^{1}H NMR spectrum indicates an ethyl group.

	Chemical Shift	*Splitting*	*Integration*	*Interpretation*
(a)	0.98	t	3H	CH_3 adjacent to CH_2
(b)	2.42	q	2H	CH_2 adjacent to CH_3

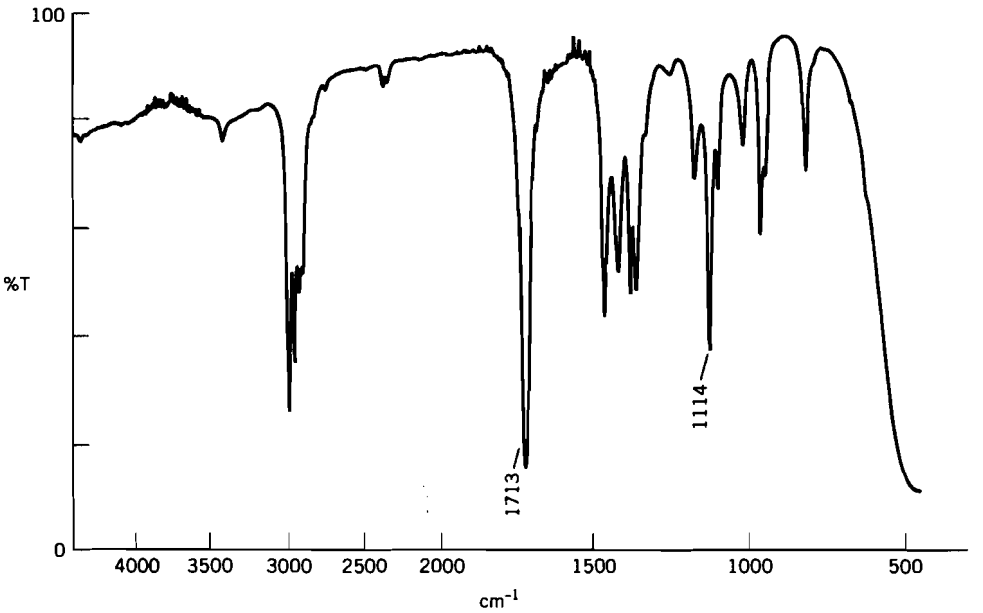


Figure 11.9 IR spectrum for Example 6. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

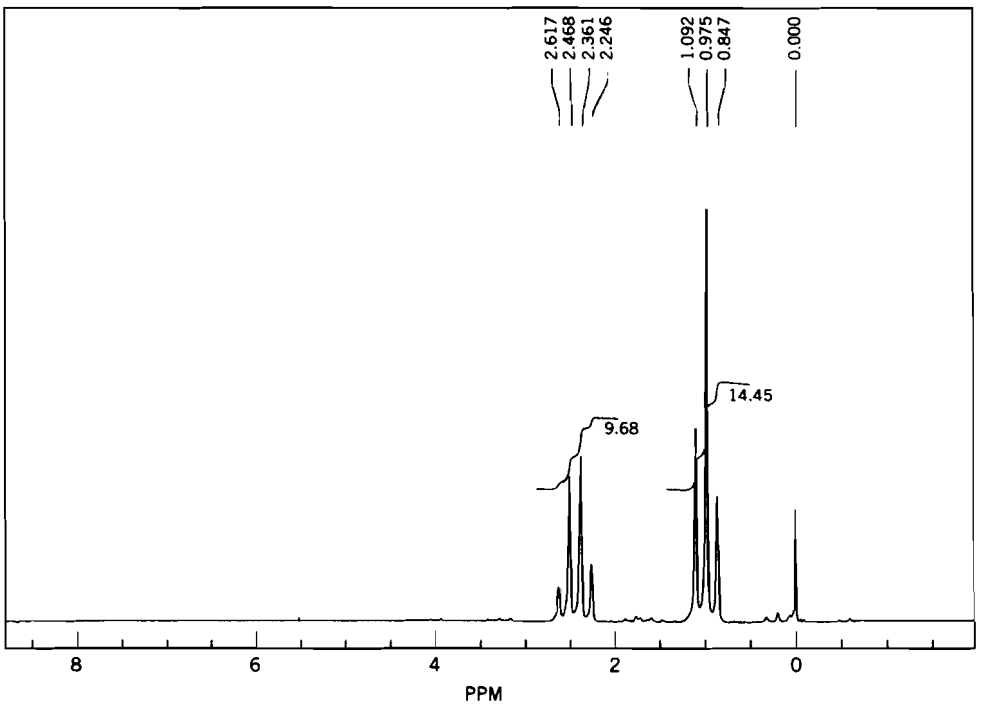


Figure 11.10 ^{1}H NMR spectrum for Example 6. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.)

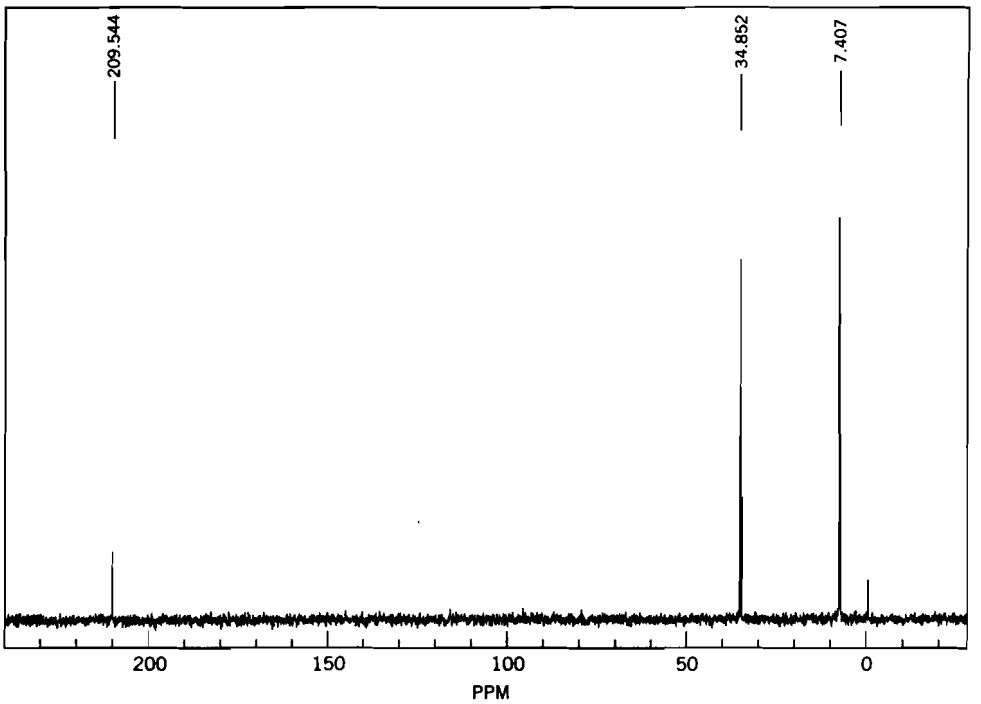


Figure 11.11 ^{13}C NMR spectrum for Example 6. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

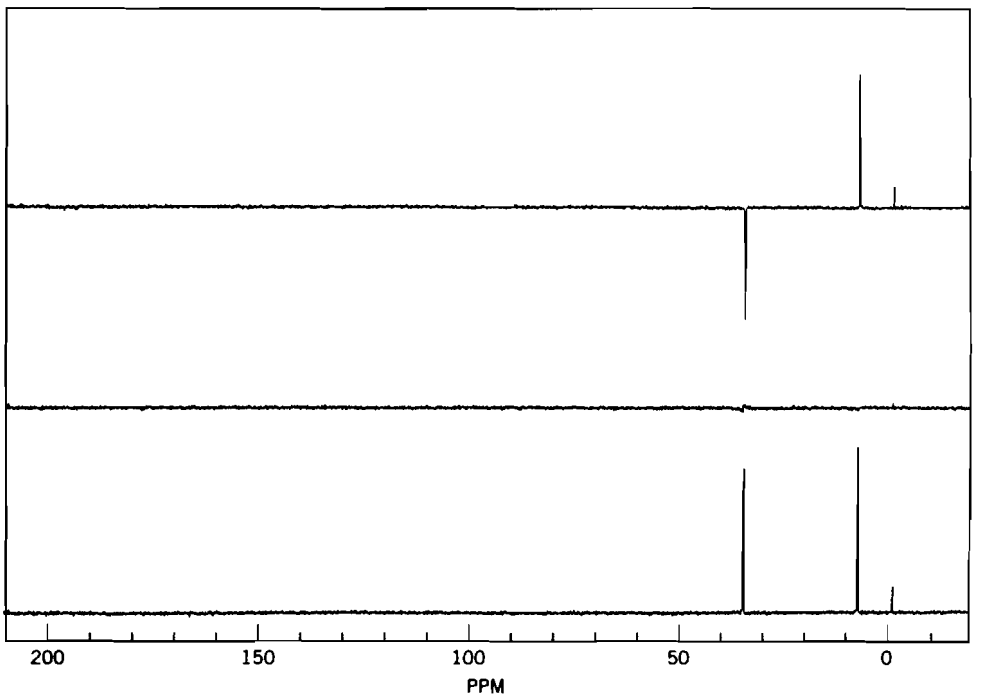
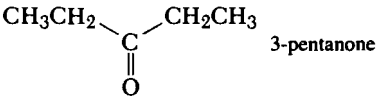


Figure 11.12 DEPT spectrum for Example 6. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

The ^{13}C NMR spectrum also indicates an ethyl group and a ketone.

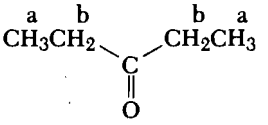
	Chemical Shift	*DEPT*	*Interpretation*
(a)	7.41	CH_3	alkyl
(b)	34.85	CH_2	alkyl
(c)	209.54	C	ketone

The only possibility is 3-pentanone.

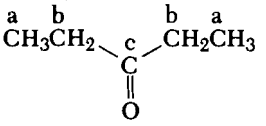


3-pentanone

The hydrogens are labeled as indicated from the ^1H NMR spectrum.



The carbons are identified from the ^{13}C NMR spectrum.



EXAMPLE 7 **An ester, containing only carbon, hydrogen, and oxygen, possessed a saponification equivalent of 74 ± 1.**

The first step is to work out the possibilities on the assumption that the molecule contains only one ester group. In that event the molecular weight is equal to the saponification equivalent. The type of formula for an ester is R—COO—R′, and therefore the first step is to subtract the weight of —COO— from the molecular weight.

$$\begin{aligned} \text{molecular weight} &= 74 \pm 1 \\ \text{—COO—} &= 44 \\ \text{residue} &= 30 \pm 1 \end{aligned}$$

This residue represents the combined weight of R and R′. In saturated esters[2] containing only carbon, hydrogen, and oxygen, this residue must always be equal to C_nH_{2n+2} and thus must always be an even number. Thus residual weights of 31 and 29 are impossible, and the value 30 represents the molecular weight of C_nH_{2n+2}. Mere inspection in this case shows that the hydrocarbon residue is C_2H_6, but the general approach is to solve for the value of n by multiplying its value by the atomic weights of the elements in the formula and setting this equal to the residual weight.

$$\begin{aligned} 12n + 1(2n + 2) &= 30 \\ 14n &= 28 \\ n &= 2 \end{aligned}$$

This residue of C_2H_6 represents the sum of R and R′, and it is now necessary to write the possibilities.

$$R + R' = C_2H_6 = H + C_2H_5 \textit{ or } CH_3 + CH_3$$

[2]In an olefinic ester, the residue is C_nH_{2n}; in an acetylenic ester, C_nH_{2n-2}.

Assuming that the compound was a monoester, we have two possibilities.

$HCOOC_2H_5$	CH_3COOCH_3
ethyl formate	methyl acetate

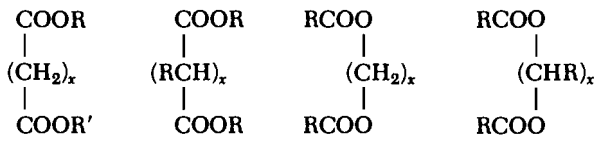
If two ester groups are present in the molecule, then the molecular weight is twice the saponification equivalent. Two ester groups will contain two —COO— combinations; hence

$$\begin{aligned} \text{molecular weight} &= 2 \times 74 \pm 1 = 148 \pm 2 \\ \text{two —COO—} &= 2 \times 44 = \underline{\quad 88 \quad} \\ \text{residue} &= \quad 60 \pm 2 \end{aligned}$$

The value of 60 ± 2 represents the summation of those portions of the molecule other than the two —COO— groups. Again, $C_nH_{2n+2} = 60 \pm 2$ and

$$12n + 1(2n + 2) = 60 \pm 2$$
$$14n = 58 \pm 2$$

Since n must be an integer, the only value of the right-hand side of the equation that will fulfill this requirement is 56, and hence $n = 4$. The residue must be C_4H_{10} and has to be divided among the various hydrocarbon radicals present in the type formulas for a compound with two ester groups. Some of the possible type formulas are the following.



Using these type formulas for esters of a dicarboxylic acid, or a dihydroxy alcohol, possible structures may now be written in which the four carbon atoms and ten hydrogen atoms are distributed properly in each of the above formulas.

This example illustrates the use of saponification equivalents in deducing possible structures. It also shows that a saponification equivalent is not quite so useful as the neutralization equivalent of an acid. It is always desirable to have some additional data concerning either the acid or alcohol or both produced by saponification of the ester in order to reduce the number of isomeric esters which possess the required saponification equivalent.

11.2 DETERMINATION OF THE STRUCTURE OF NEW COMPOUNDS NOT DESCRIBED IN THE CHEMICAL LITERATURE

Interpretation of Molecular Formulas

In research, quantitative analyses together with molecular weight determinations routinely yield the molecular formula of any unknown substance. Much information about possible functional groups can often be deduced from such information alone, and for this reason it is pertinent to consider the significance of the molecular formula.

A saturated hydrocarbon without any rings has the general formula C_nH_{2n+2}. Introduction of oxygen to give an alcohol, ether, acetal, or any other saturated acyclic compound does not change the carbon-to-hydrogen ratio, and the molecular formula is $C_nH_{2n+2}O_m$. The introduction of a double bond or a ring into a saturated molecule requires the removal of two hydrogen atoms, and the introduction of a triple bond involves the removal of four hydrogen atoms. By an examination of the carbon-to-hydrogen ratio, then, it is possible to draw conclusions concerning the possible number of multiple bonds or rings in a molecule.

For example, the substance C_3H_6O must have either one double bond (either olefinic or carbonyl) or one ring but cannot have a triple bond because it is only two

hydrogen atoms short of saturation. The compound $C_8H_{12}O$ must have three double bonds or three rings or some combination of double bonds, triple bonds, and rings that accounts for the three pairs of missing hydrogen atoms. It cannot contain a benzene ring, however, because such a ring requires a shortage from saturation of four pairs of hydrogen atoms. (Thus the possibility that the oxygen function is a phenolic hydroxyl group is immediately excluded.)

Furthermore, the introduction of a halogen atom into a saturated molecule necessitates the removal of one hydrogen atom, and consequently the general formula of a saturated acyclic monohalide is $C_nH_{2n+1}X$. On the other hand, introduction of a nitrogen atom to give an acyclic saturated amine also requires the addition of an extra hydrogen atom so that the formula is $C_nH_{2n+3}N$. A consequence of these generalizations, which is of value in deriving molecular formulas from the analyst's carbon and hydrogen determination, is that a molecule with no elements other than carbon, hydrogen, and oxygen must contain an even number of hydrogen atoms; an odd number of halogen or nitrogen atoms requires an odd number of hydrogen atoms; and an even number of halogen or nitrogen atoms requires an even number of hydrogen atoms. Thus a molecular formula such as $C_5H_{11}O_3$, calculated from analytical data, is obviously incorrect; the correct formula is likely either $C_5H_{10}O_3$ or $C_5H_{12}O_3$.

The unsaturation number equation (see Section 3.6.1) can be used to help derive a structure.

$$U = C + 1 - \tfrac{1}{2}X + \tfrac{1}{2}Y$$

where

U = the unsaturation number

C = the number of carbons

X = the number of hydrogens plus halogens

Y = the number of nitrogens plus phosphorus

Oxygen and sulfur do not change the number of unsaturations and thus do not appear in the formula.

This unsaturation number represents "missing pairs" of monovalent atoms that correspond to double bonds, triple bonds, and/or cyclic features in the structure of interest. This formula should be used with care when dealing with other than simple oxidation states of elements in the second and lower rows of the periodic table. For example, the unsaturation number for the formula C_3H_8OS is zero. Possible structures for this formula include the following:

$HOCH_2CH_2SCH_3$ $\quad$ $HOCH_2CH_2CH_2SH$ $\quad$ $CH_3\overset{\overset{O}{\|}}{S}CH_2CH_3$

The last formula, a sulfoxide, seems to present a contradiction. We can, however, include this if we visualize it in terms of its polar covalent resonance form:

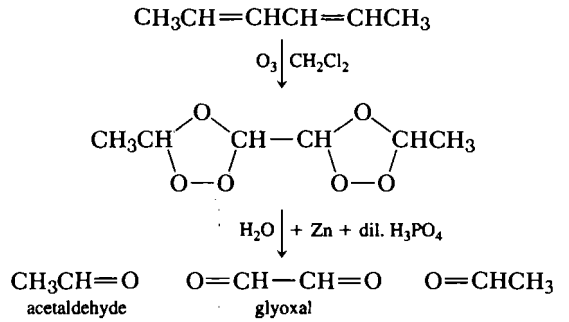
$$CH_3-\overset{\overset{O^-}{|}}{\underset{+}{S}}-CH_2-CH_3$$

Thus, all three structures would have an unsaturation number of zero.

EXAMPLE 8 A substance A has the formula C_6H_{10}. On hydrogenation over platinum under mild conditions it is converted to B (C_6H_{14}). When compound A was ozonized and the ozonide reductively

cleaved, two products, acetaldehyde and glyoxal, were formed. These known compounds were identified by means of their 2,4-dinitrophenylhydrazones.

The molecular formula (it has an unsaturation number of $6 - 5 + 1 = 2$) shows that the maximum number of double bonds and rings is two, or else there is one triple bond. Uptake of two moles of hydrogen indicates that there are, in fact, either two double bonds or one triple bond.[3] Ozonolysis to give two-carbon fragments suggests that the six-carbon skeleton originally present must have been cleaved at two points to give three two-carbon fragments rather than at one. This means that two double bonds rather than one triple bond must have been present. Finally, the probable arrangement of the three two-carbon pieces is as shown.



By considering the molecular formulas of several compounds and the reactions that produced then, one is frequently able to deduce possible formulas. The following example involves the deduction of a large amount of information from only a few clues.

EXAMPLE 9 **A neutral compound A ($C_{15}H_{14}O$) gave a negative Baeyer permanganate test and was not attacked by hydrogen bromide; it was oxidized to an acid B ($C_{14}H_{10}O_3$) by hot chromic acid solution.**

First, note that the oxidation has caused a *loss* of one carbon atom and four hydrogen atoms and a *gain* of two oxygen atoms. It is necessary to find a functional group or several groups that will do this. In this connection it is useful to tabulate the behavior of the common functional groups on oxidation, making a note of the gain and loss in composition. From the table below it will be noted that the oxidation of an ethyl side chain corresponds exactly to the oxidation of A to B; in both cases there are gains of two oxygen atoms and a loss of four hydrogen atoms and one carbon atom.

Functional Group	*Oxidation Product*	*Gain*	*Loss*	
RCHO	RCOOH	1O		
RCH_2OH	RCOOH	1O	2H	
R_2CHOH	R_2CO		2H	
$R_2C(OH)CH_3$	R_2CO		4H	1C
$RCH{=}CH_2$	RCOOH	2O	2H	1C
$RC{\equiv}CH$	RCOOH	2O		1C
$ArCH_2CH_2OH$	ArCOOH	1O	4H	1C
$ArCOCH_3$	ArCOOH	1O	2H	1C
$ArCH_3$	ArCOOH	2O	2H	
$ArCH_2CH_3$	ArCOOH	2O	4H	1C
ArC_nH_{2n+1}	ArCOOH	2O	$2n$ H	$(n-1)$C
Ar_2CHCH_3	Ar_2CO	1O	4H	1C
Ar_2CH_2	Ar_2CO	1O	2H	
From Example 9:				
(A) $C_{15}H_{14}O$	(B) $C_{14}H_{10}O_3$	2O	4H	1C

[3]Less frequently, hydrogen will add across a *strained* ring of a compound containing no multiple bonds.

Extracting an ethyl group from A ($C_{15}H_{14}O$) or a carboxyl group from B leaves a unit $C_{13}H_9O$. This unit is derived from some parent compound C ($C_{13}H_{10}O$) which is stable to oxidation.

The next question concerns the character of the functional group containing the oxygen atom. What functional groups containing only one oxygen atom are stable to oxidation? Consideration of various functional groups leads to the conclusion that the ether linkage is one possibility and that a properly substituted ketone is a second. Ketones with no hydrogen atoms on the α-carbon atoms are usually stable to oxidation. The most common examples are diaryl ketones.

The next step consists of considering the ratio of carbon to hydrogen in the compounds A and B and the hypothetical parent compound, C ($C_{13}H_{10}O$). These carbon and hydrogen atoms must be combined so that the resulting compound will be stable to oxidation. A completely saturated compound, C_nH_{2n+2}, would require a formula $C_{13}H_{28}$ for a 13-carbon-atom compound, C. Even allowing two hydrogen atoms as equivalent to the oxygen atom, it is obvious that the compound has no such ratio of carbon and hydrogen atoms. An alicyclic compound would require C_nH_{2n} or $C_{13}H_{26}$. Ordinary olefinic compounds and acetylenic compounds with enough double or triple bonds to lower the ratio of hydrogen to carbon are excluded by the stability to oxidation.

The only large class of compounds with such a low ratio of hydrogen to carbon atoms is aromatic in nature. Since benzene has six carbon atoms whereas the parent compound (C) has 13, the possibility of two benzene rings is suggested. This leaves one carbon atom to be accounted for.

Subtracting two phenyl groups, $(C_6H_5—)_2$, from compound C ($C_{13}H_{10}O$) leaves a residue of CO. It will be remembered that diaryl ketones are stable to oxidation. The parent compound (C) is evidently benzophenone, $C_6H_5COC_6H_5$, and the compounds A and B are probably

$$\underset{\substack{\text{compound A}\\ \text{(one of the isomers of}\\ \text{ethylbenzophenone)}}}{C_6H_5COC_6H_4CH_2CH_3} \longrightarrow \underset{\substack{\text{compound B}\\ \text{(one of the isomers of}\\ \text{benzoylbenzoic acid)}}}{C_6H_5COC_6H_4CO_2H}$$

11.3 PROBLEMS

The following problems are designed to give the student added experience in the types of reasoning illustrated by the examples above. It is important to seek the answers by systematic procedures, and students are urged to avoid a random attack on the problems.

After determining structures, all spectra need to be interpreted, following the procedures outlined in earlier chapters (see Chapters 6 and 7). The answers to these problems are available in the *Solutions Manual* that accompanies this text.

Problem Set 1

1. Three compounds (A–C) yield the solubilities and chemical tests described below. Assign a name from the list of three below to each of A–C.

   Compound A: insoluble in water; insoluble in sulfuric acid; sodium fusion, followed by silver nitrate treatment, gave a white precipitate.

   Compound B: insoluble in water; insoluble in sulfuric acid; sodium fusion, followed by silver nitrate treatment, gave no precipitate.

   Compound C: insoluble in water; soluble in sulfuric acid; sodium fusion, followed by silver nitrate treatment, gave no precipitate.

   Choices: chlorocyclohexane, diethyl ether, cyclohexane.

2. Five compounds (A–E) yield the solubilities and chemical tests described below. Assign a name from the list of five below to each of A–E.

Compound A: insoluble in water; did not decolorize bromine; did not react with acetyl chloride; did not form a precipitate with 2,4-dinitrophenylhydrazine; did not form a precipitate when treated with excess iodine in aqueous sodium hydroxide solution.

Compound B: insoluble in water; quickly decolorized bromine; did not react with acetyl chloride; did not form a precipitate with 2,4-dinitrophenylhydrazine; did not form a precipitate when treated with excess iodine in aqueous sodium hydroxide solution.

Compound C: soluble in water; gave a rapid reaction with acetyl chloride; did not form a precipitate with 2,4-dinitrophenylhydrazine; formed a yellow precipitate with a noxious odor when treated with excess iodine in aqueous sodium hydroxide solution.

Compound D: soluble in water; did not react with acetyl chloride; formed a yellow precipitate with 2,4-dinitrophenylhydrazine; formed a yellow precipitate with a noxious odor when treated with excess iodine in aqueous sodium hydroxide solution.

Compound E: soluble in water; reacted rapidly with acetyl chloride; did not form a precipitate with 2,4-dinitrophenylhydrazine; did not form a precipitate when treated with excess iodine in aqueous sodium hydroxide solution.

Choices: acetone, 2-methyl-2-propanol, cyclohexane, cyclohexene, ethanol.

3. Compounds A, B, and C had boiling points near 80°C. Compounds A, B, and C were soluble in water and ether, but their aqueous layers did not change the color of litmus paper. Yellow liquids were formed when compounds A, B, or C were treated with 2,4-dinitrophenylhydrazine. A gas was evolved when compounds A, B, and C were treated with acetyl chloride. Compounds A and B produced a blue-green color when treated with chromium trioxide; compound C yielded a red-orange color. Compound C reacted quickly with hydrochloric acid and zinc chloride to form a second layer, compound B reacted more slowly, and compound A did not react. What are the names and structures of these three compounds?

4. Compounds A, B, and C had boiling points near 158°C. Compounds A, B, and C were insoluble in water, 5% sodium hydroxide solution, 5% hydrochloric acid solution, and 96% sulfuric acid solution. Compounds A, B, and C produced a colorless/white solution when treated with chloroform and aluminum chloride. Compound A produced a white solid with silver nitrate, compound B produced a pale-yellow solid, and compound C produced a yellow solid. What are the names and structures of these three compounds?

5. Compounds A, B, and C had boiling points near 80°C. Compounds A, B, and C were soluble in water and ether, but their aqueous layers did not change the color of litmus paper. Compounds A, B, and C did not react with acetyl chloride, and they formed a yellow liquid with 2,4-dinitrophenylhydrazine. In their IR spectrum, there was no significant peak between 1600 and 1800; however, there was a large peak around 2250. Compound A reacted with bromine to give a colorless solution; compounds B and C yielded yellowish solutions. Compound B tested positive for a halogen; compounds A and C did not test positive for a halogen. What are the names and structures of these three compounds?

Problem Set 2

All of the answers in this problem set can be found in Appendix II. Interpret all classification tests and spectra. Give equations for the formation of any derivatives.

1. The compound had a boiling point of 176°C. The compound was insoluble in water, 5% sodium hydroxide solution, and 5% hydrochloric acid solution but soluble in 96% sulfuric acid solution. It gave negative tests with acetyl chloride, 2,4-dinitrophenylhydrazine, and bromine. The compound gave an orange color with chloroform and aluminum chloride. The IR, ^{1}H NMR, ^{13}C NMR, and DEPT spectra are shown in Figures 11.13 through 11.16.
2. A liquid had a boiling point of 260°C. The compound was insoluble in water, 5% sodium hydroxide solution, and 5% hydrochloric acid solution but soluble in 96% sulfuric acid solution. The compound gave off a gas with acetyl chloride and yielded a yellow liquid with 2,4-dinitrophenylhydrazine. The compound produced an orange color with hydroiodic acid. A 4-nitrobenzoate derivative was produced from the compound with a melting point of 95°C. The IR, ^{1}H NMR, ^{13}C NMR, and DEPT spectra are shown in Figures 11.17 through 11.20.
3. A liquid had a boiling point of 198°C. The compound was insoluble in water but soluble in 5% sodium hydroxide solution and 5% sodium bicarbonate solution. A gas was formed when the compound was mixed with sodium. When the compound was mixed with chromium trioxide, a blue color was formed. It yielded an oxime derivative with a melting point of 62°C and a phenylurethane derivative with a melting point of 134°C. The IR, ^{1}H NMR, ^{13}C NMR, and DEPT spectra are shown in Figures 11.21 through 11.24.

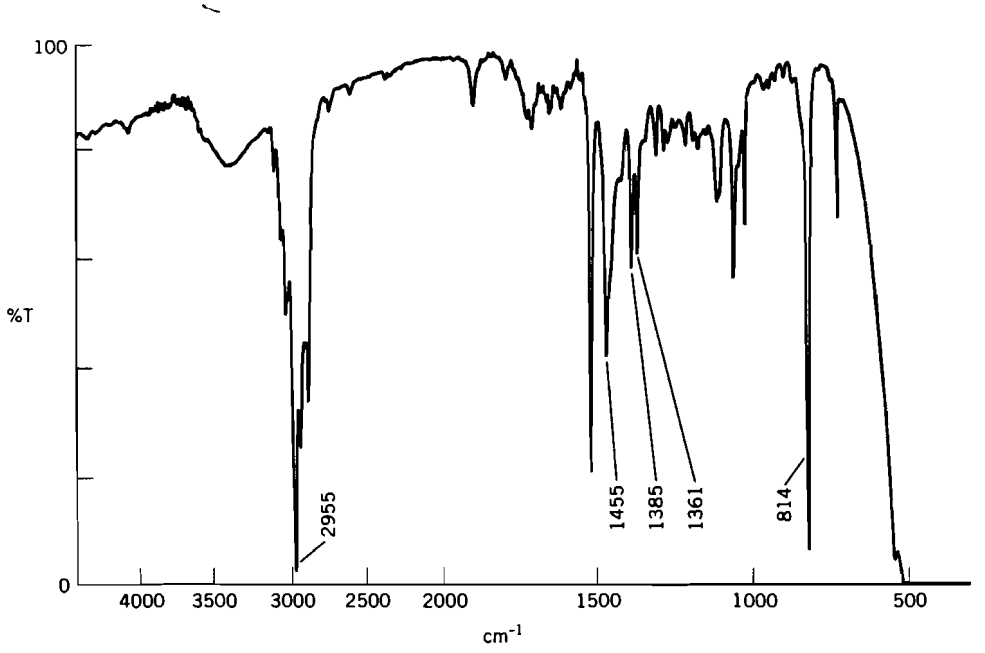


Figure 11.13 IR spectrum for Problem Set 2, Problem 1. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

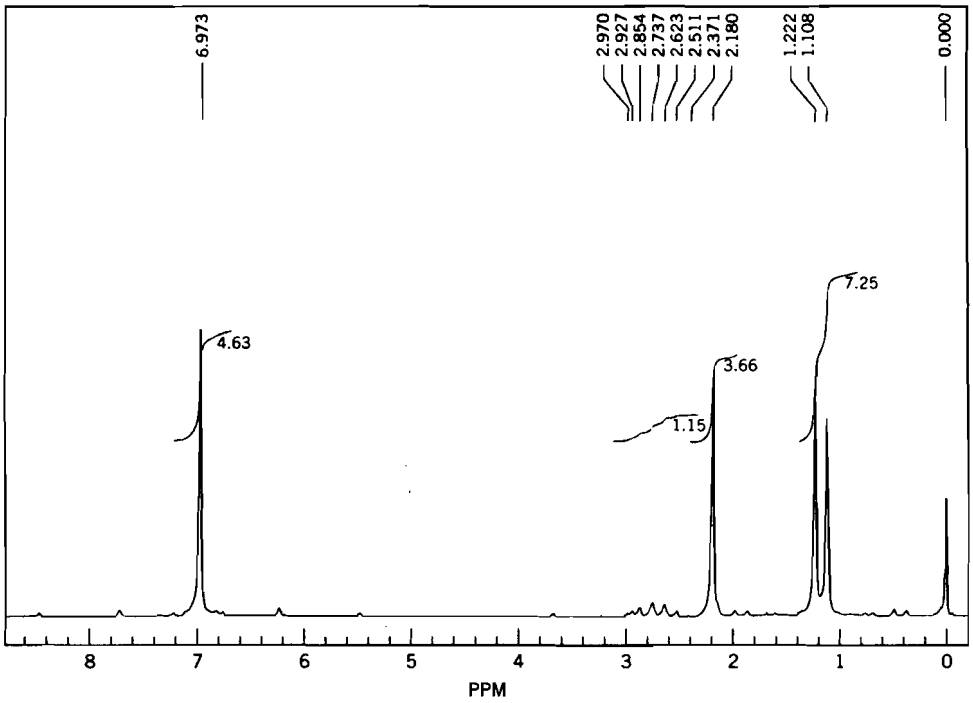


Figure 11.14 ^{1}H NMR spectrum for Problem Set 2, Problem 1. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

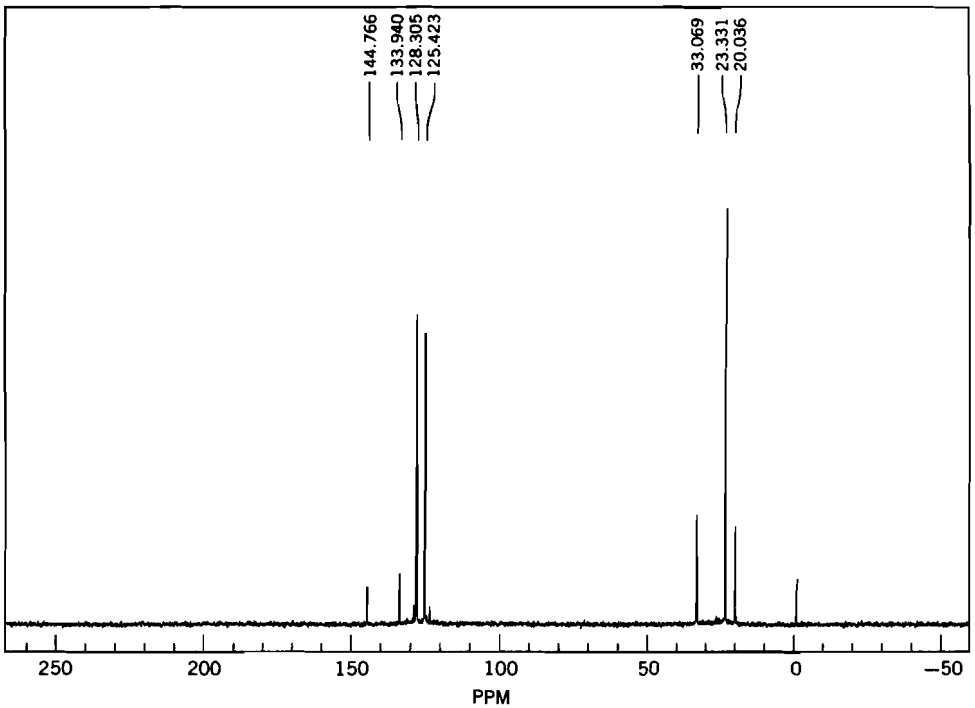


Figure 11.15 ^{13}C NMR spectrum for Problem Set 2, Problem 1. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

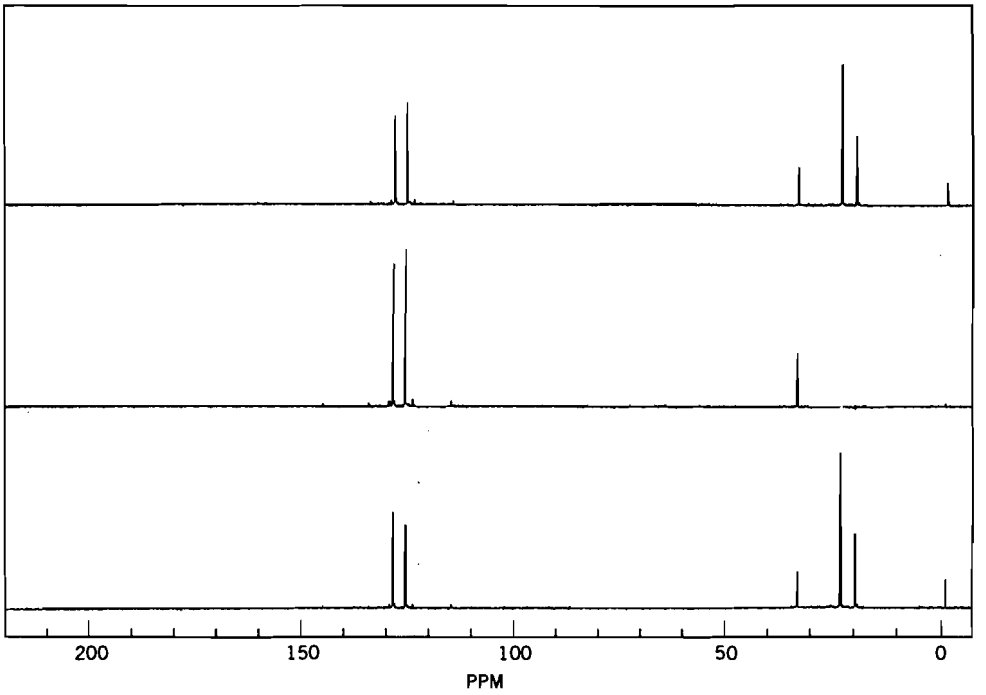


Figure 11.16 DEPT spectrum for Problem Set 2, Problem 1. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

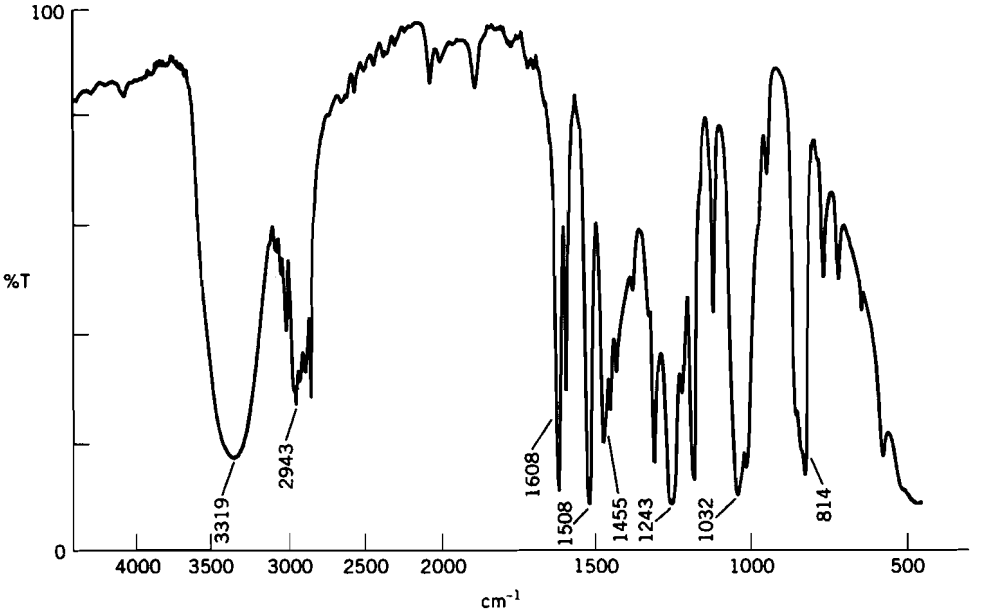


Figure 11.17 IR spectrum for Problem Set 2, Problem 2. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

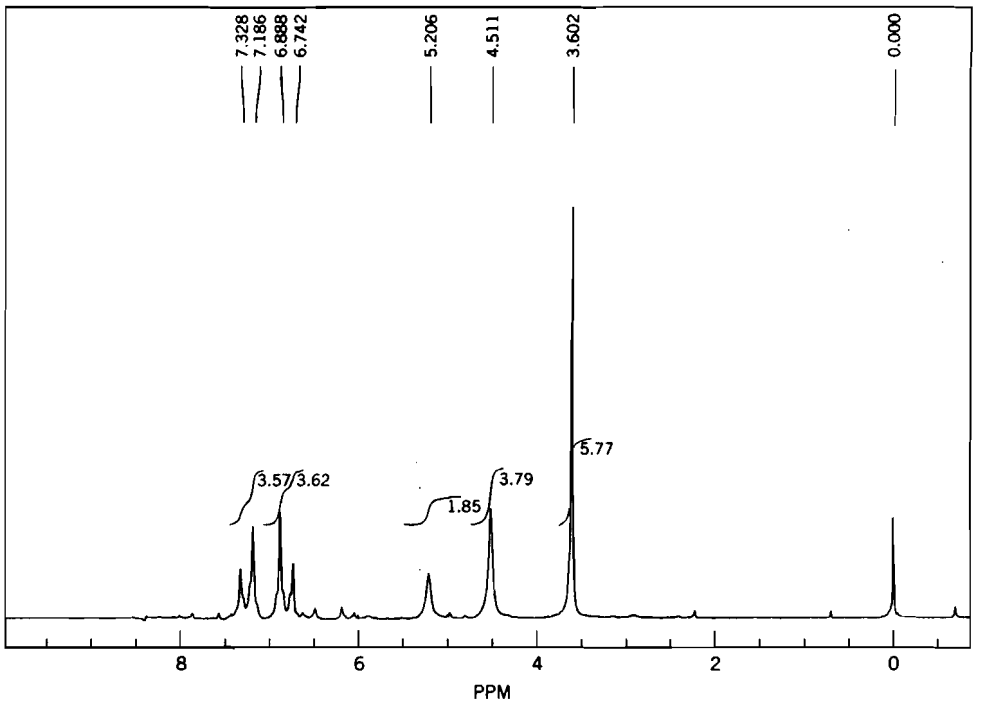


Figure 11.18 ^{1}H NMR spectrum for Problem Set 2, Problem 2. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

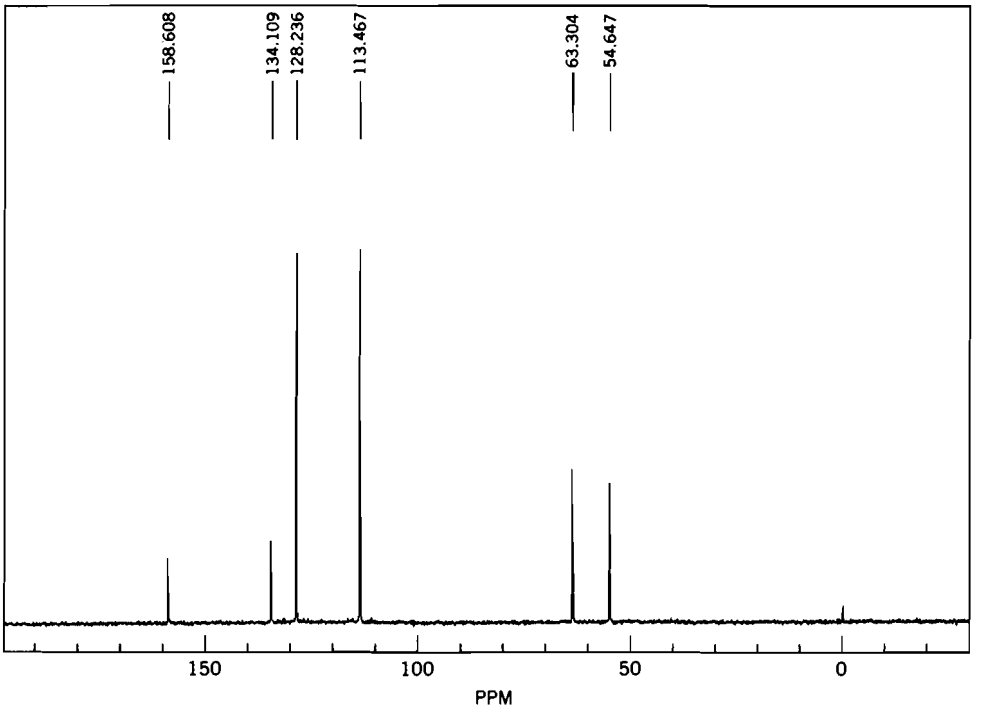


Figure 11.19 ^{13}C NMR spectrum for Problem Set 2, Problem 2. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

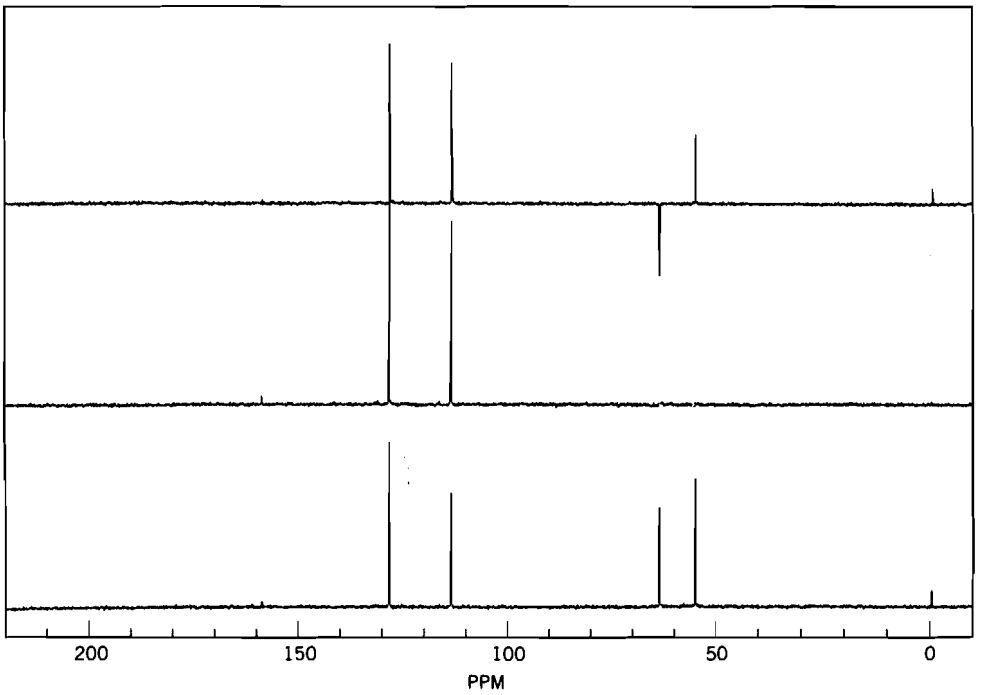


Figure 11.20 DEPT spectrum for Problem Set 2, Problem 2. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

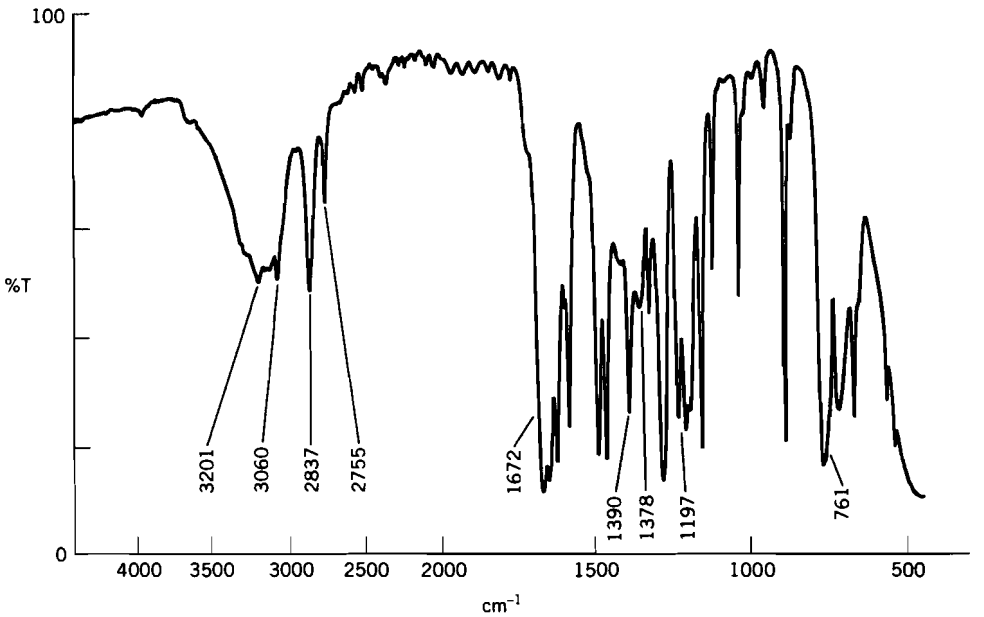


Figure 11.21 IR spectrum for Problem Set 2, Problem 3. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

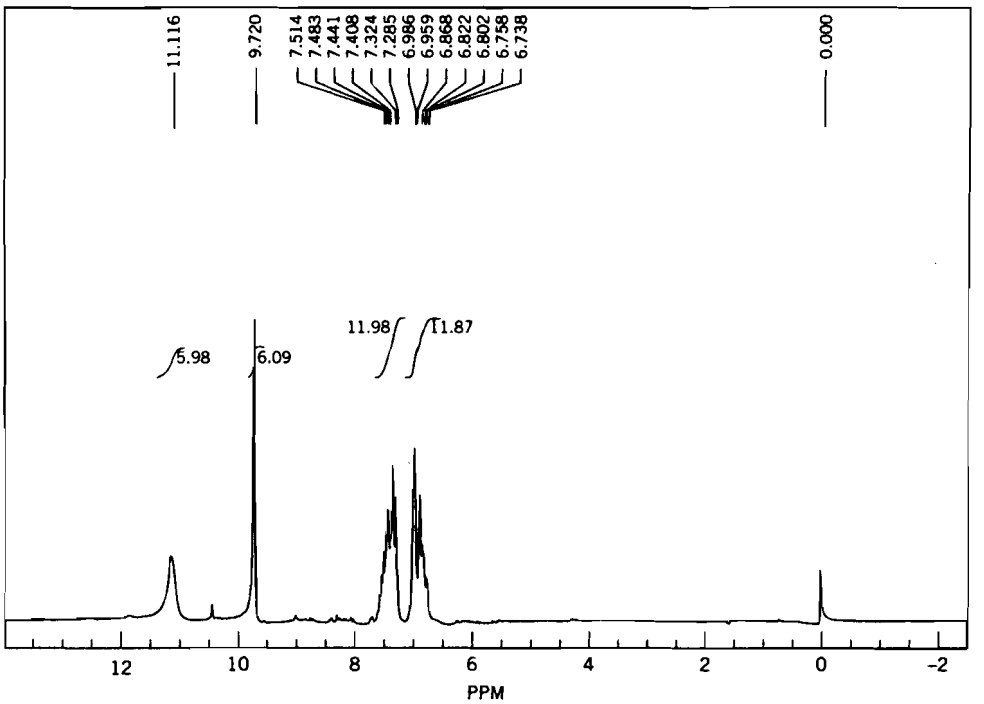


Figure 11.22 ^{1}H NMR spectrum for Problem Set 2, Problem 3. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

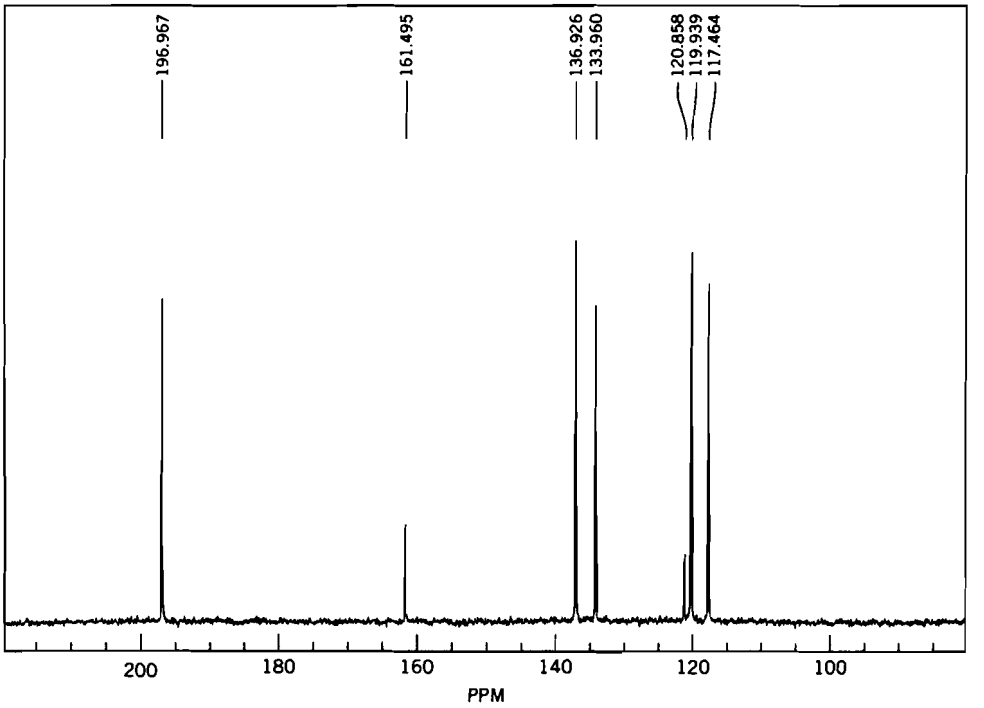


Figure 11.23 ^{13}C NMR spectrum for Problem Set 2, Problem 3. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

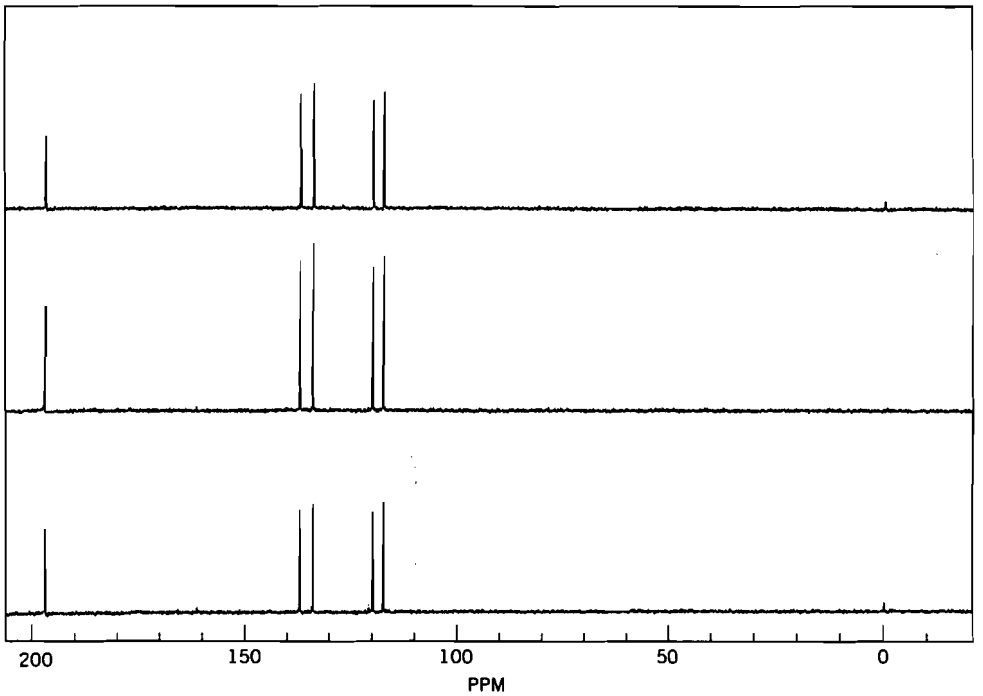


Figure 11.24 DEPT spectrum for Problem Set 2, Problem 3. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

4. A compound had a boiling point of 90°C. It was soluble in water and ether, but its aqueous solution changed litmus to blue. The compound did not react with acetyl chloride or sodium. Treatment of the compound with benzenesulfonyl chloride, followed by acidification, produced only soluble products. Reaction of the compound with picric acid yielded a derivative that melted at 174°C. The IR, ^{1}H NMR, ^{13}C NMR, and DEPT spectra are shown in Figures 11.25 through 11.28.
5. A liquid had a boiling point of 252°C. The compound was insoluble in water, 5% sodium hydroxide solution, and 5% hydrochloric acid solution but soluble in 96% sulfuric acid solution. The compound reacted with chromium trioxide to produce a blue color and with 2,4-dinitrophenylhydrazine to give an orange solid. Treatment of the compound with Tollens reagent produced a silver mirror. It did not react with sodium. It reacted with potassium permanganate to yield a brown suspension. The semicarbazone derivative melted at 213°C. The IR, ^{1}H NMR, ^{13}C NMR, and DEPT spectra are shown in Figures 11.29 through 11.32.
6. A liquid had a boiling point of 181°C. The compound was insoluble in water, 5% sodium hydroxide solution, and 5% hydrochloric acid solution but soluble in 96% sulfuric acid solution. The sodium fusion filtrate of the compound yielded a yellow color with ammonium polysulfide and ferric chloride, gave no precipitate with lead acetate, and did not give a precipitate with silver nitrate. The compound formed a white solid with sodium bisulfite and gave a red color with hydroxylamine and ferric chloride. The semicarbazone derivative melted at 134°C. The IR, ^{1}H NMR, ^{13}C NMR, DEPT, and HETCOR spectra are shown in Figures 11.33 through 11.37.

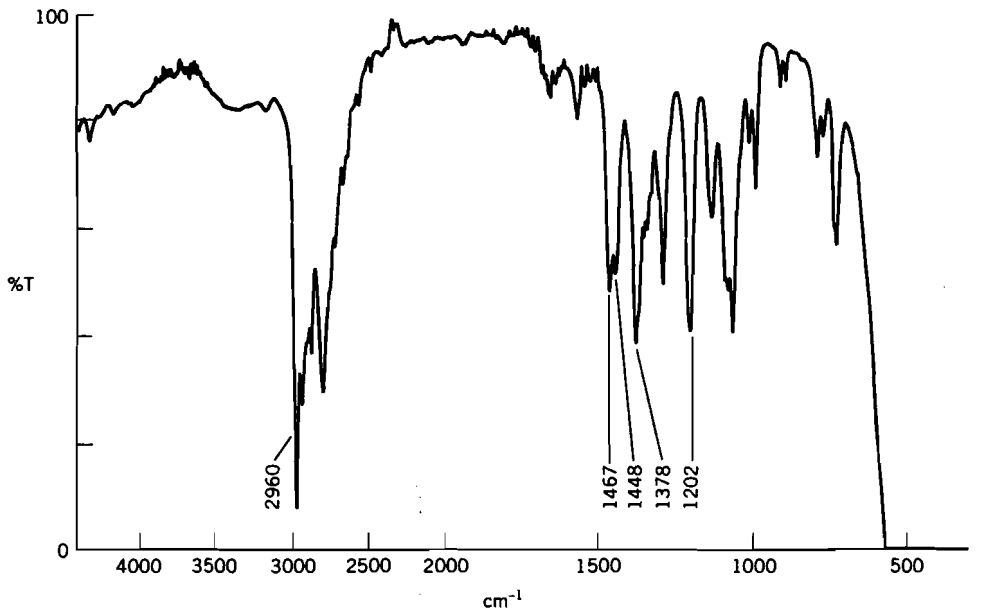


Figure 11.25 IR spectrum for Problem Set 2, Problem 4. [Spectrum courtesy of Terra Hosp, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

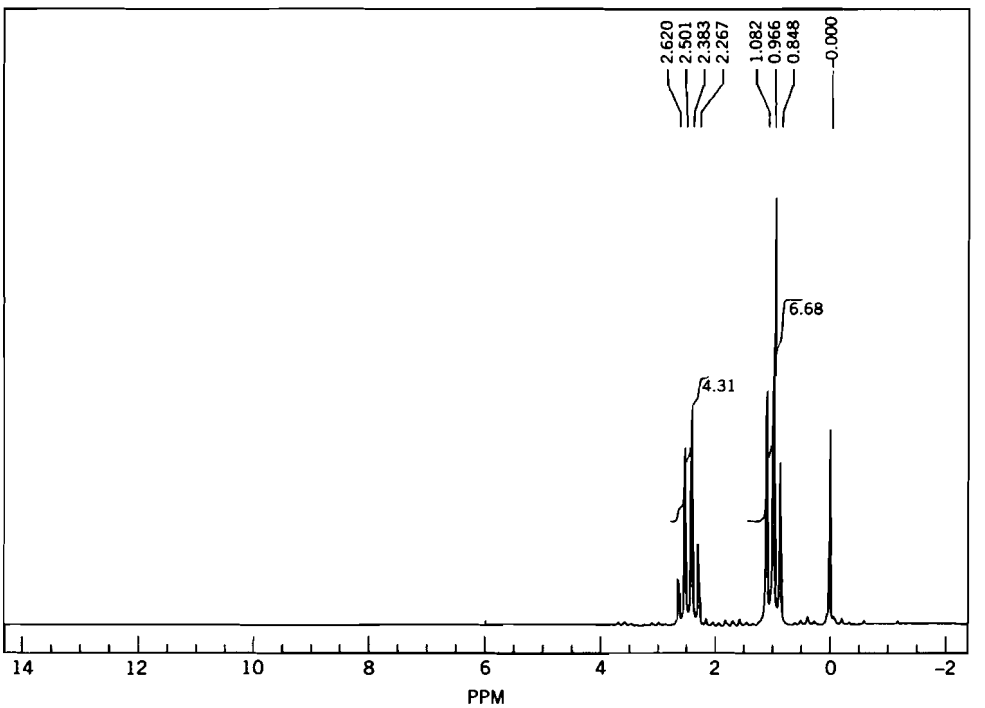


Figure 11.26 ^{1}H NMR spectrum for Problem Set 2, Problem 4. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

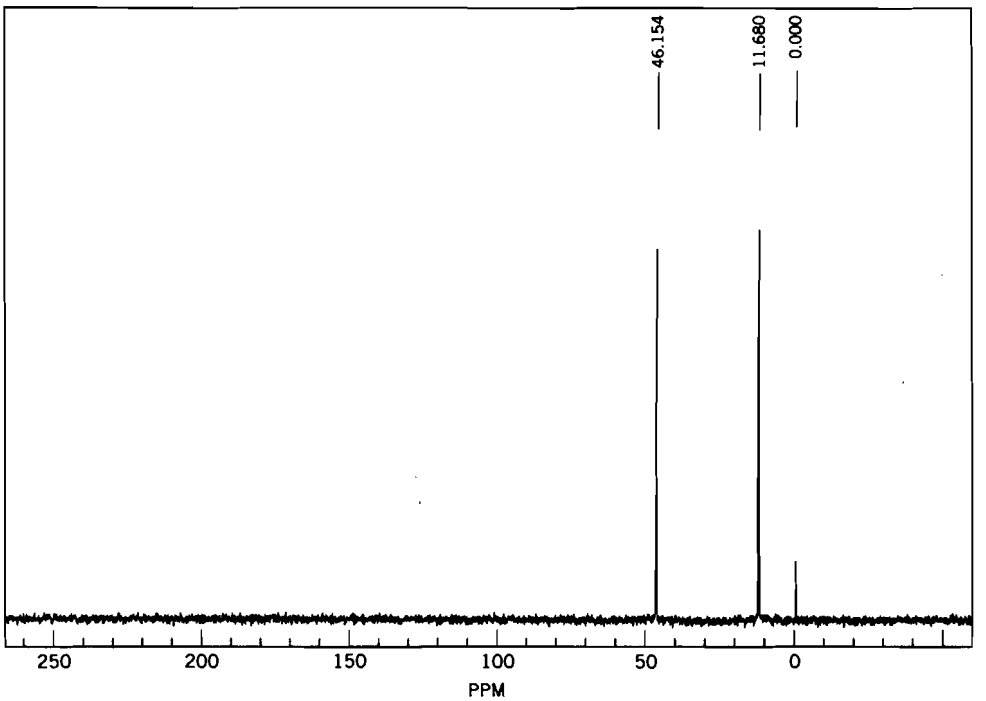


Figure 11.27 ^{13}C NMR spectrum for Problem Set 2, Problem 4. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

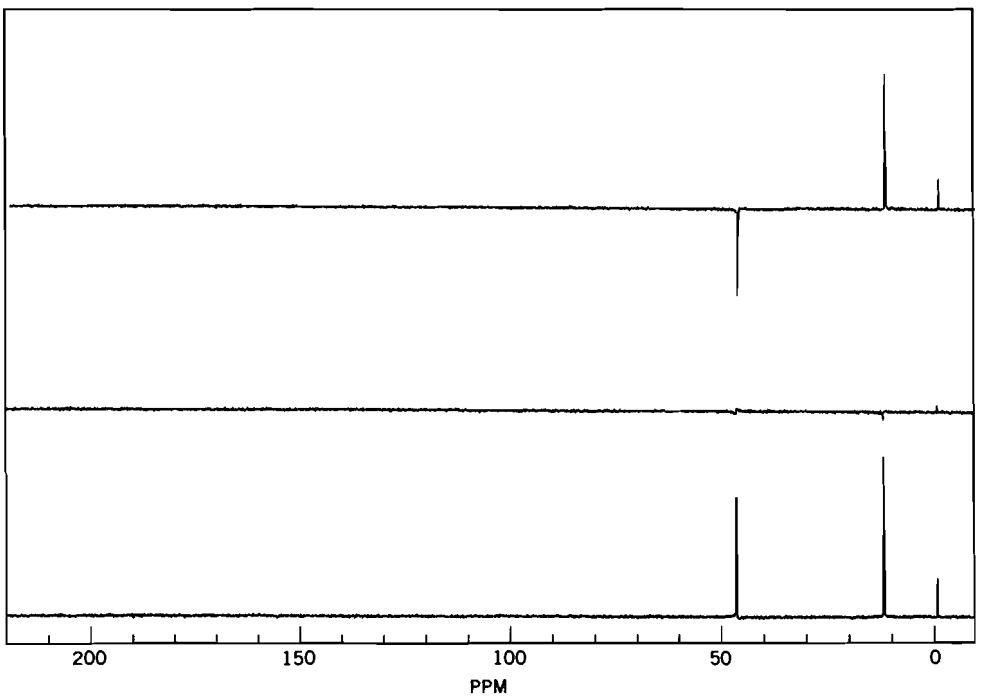


Figure 11.28 DEPT spectrum for Problem Set 2, Problem 4. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

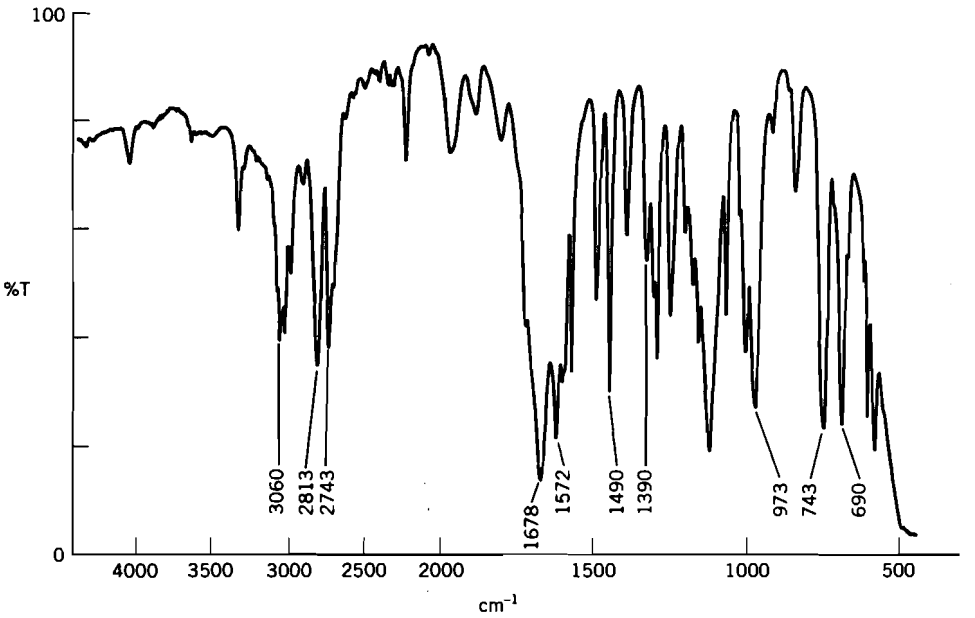


Figure 11.29 IR spectrum for Problem Set 2, Problem 5. [Spectrum courtesy of Terra Hosp, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

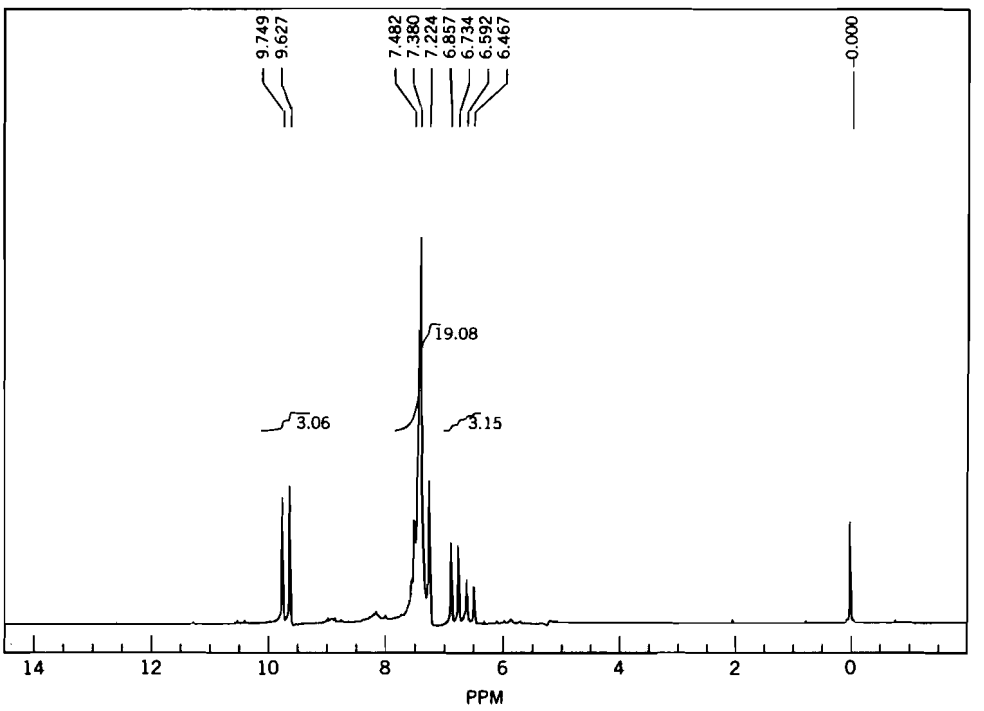


Figure 11.30 ^{1}H NMR spectrum for Problem Set 2, Problem 5. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

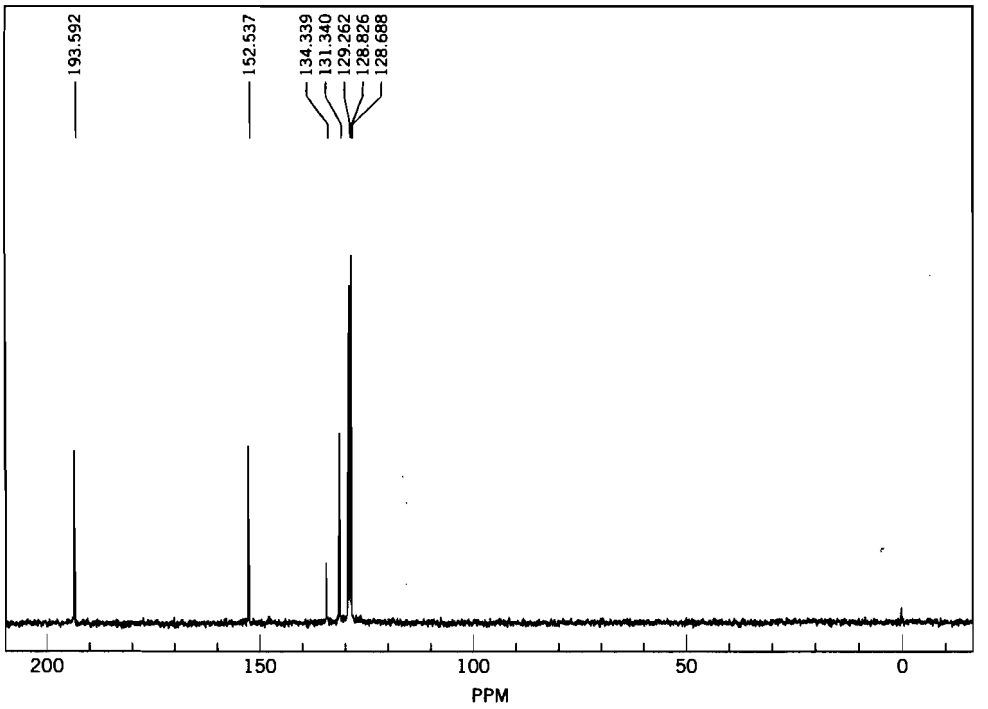


Figure 11.31 ^{13}C NMR spectrum for Problem Set 2, Problem 5. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

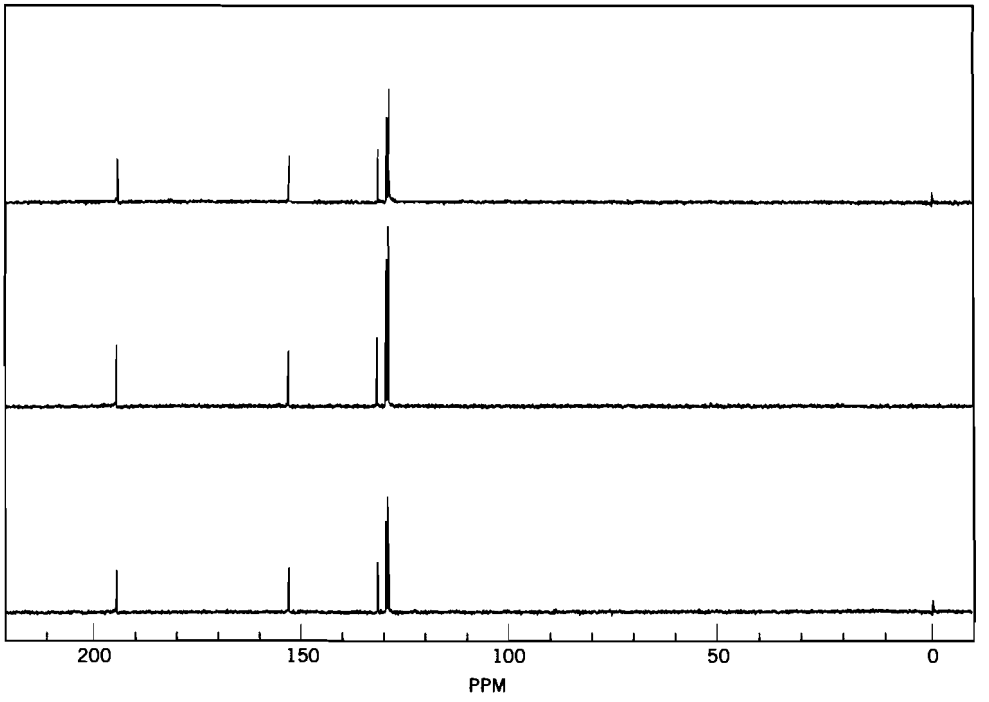


Figure 11.32 DEPT spectrum for Problem Set 2, Problem 5. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

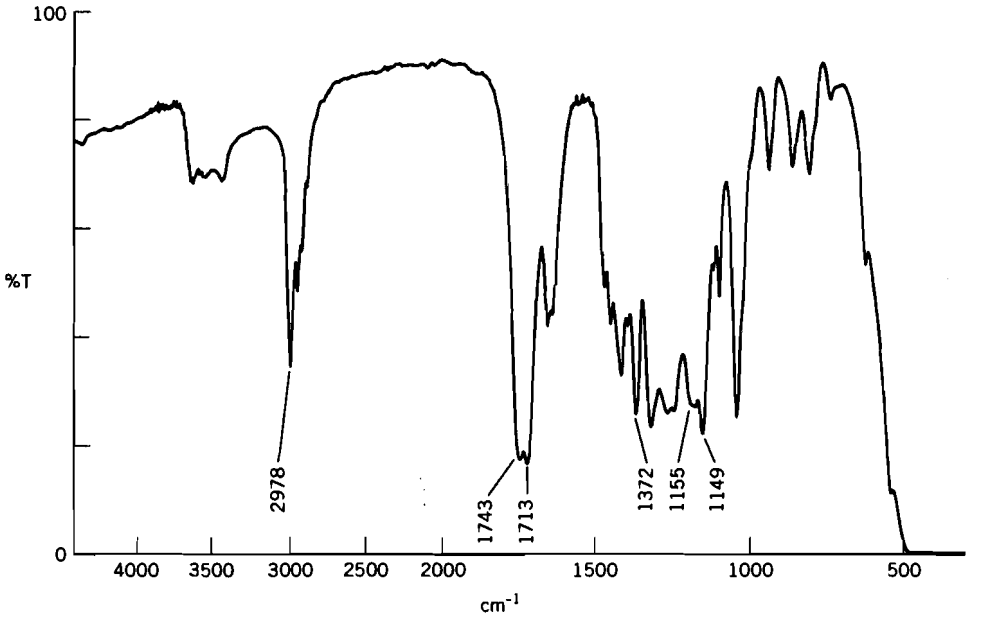


Figure 11.33 IR spectrum for Problem Set 2, Problem 6. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

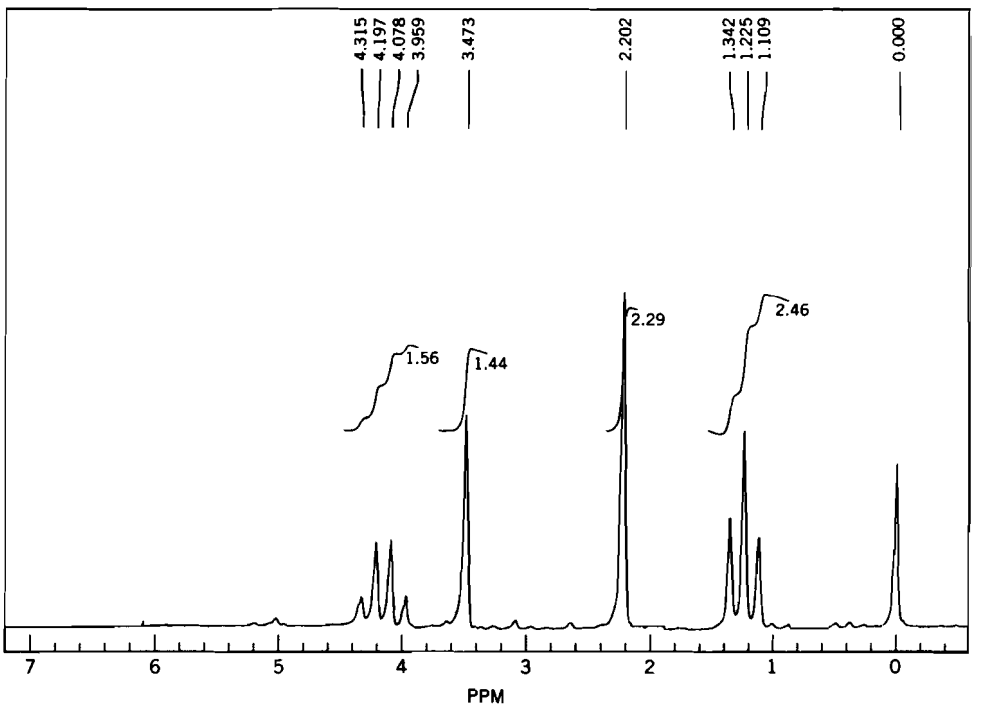


Figure 11.34 ^{1}H NMR spectrum for Problem Set 2, Problem 6. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

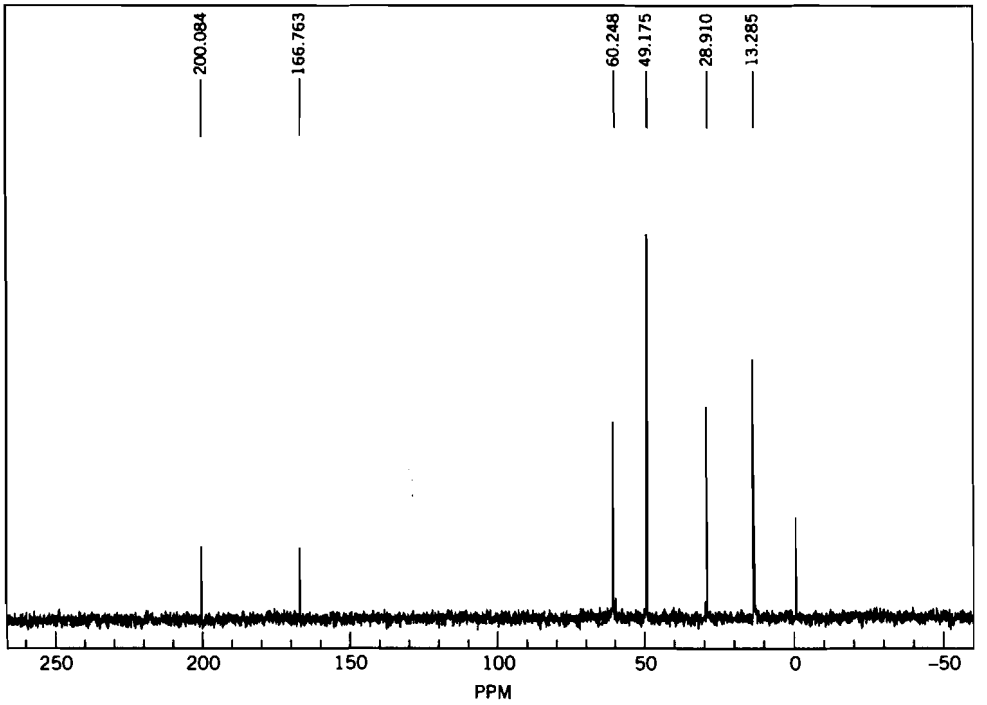


Figure 11.35 ^{13}C NMR spectrum for Problem Set 2, Problem 6. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

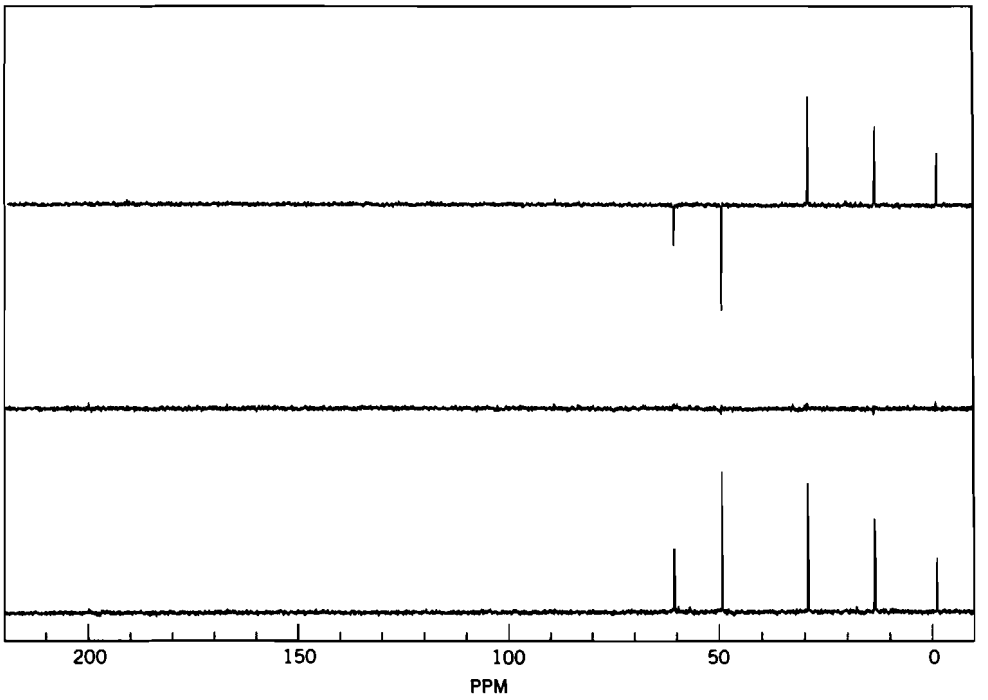


Figure 11.36 DEPT spectrum for Problem Set 2, Problem 6. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

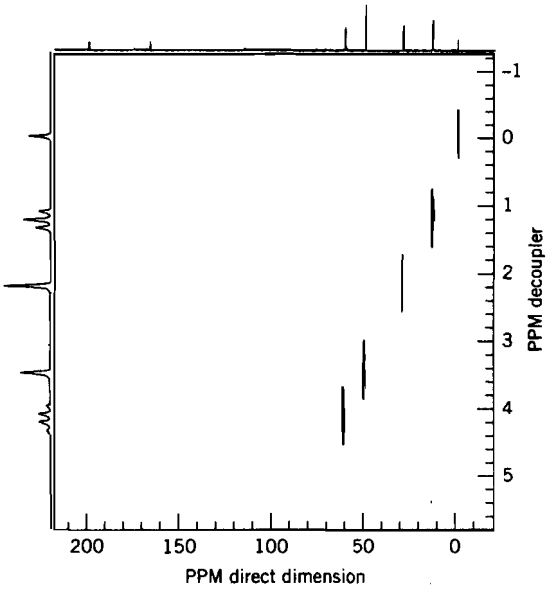


Figure 11.37 HETCOR spectrum for Problem Set 2, Problem 6. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

Problem Set 3

Interpret all classification tests and spectra. Give equations for the formation of any derivatives.

1. A liquid had a boiling point of 205°C. The compound was insoluble in water, 5% sodium hydroxide solution, and 5% hydrochloric acid solution but soluble in 96% sulfuric acid solution. It gave a blue color with Jones reagent, a colorless solution with Schiff's reagent, and no precipitate with sodium bisulfite. The compound reacted violently with sodium. The 3,5-dinitrobenzoate derivative melted at 112°C. The IR, ^{1}H NMR, ^{13}C NMR, and DEPT spectra are shown in Figures 11.38 through 11.41.
2. A liquid had a boiling point of 155°C. The compound was soluble in water and ether. The aqueous solution of the compound turned litmus red. When mixed with sodium bicarbonate solution, a gas was evolved. The compound formed an amide derivative that melted at 129°C. The IR, ^{1}H NMR, ^{13}C NMR, and DEPT spectra are shown in Figures 11.42 through 11.45.
3. A liquid had a boiling point of 158°C. The compound was insoluble in water, 5% sodium hydroxide solution, and 5% hydrochloric acid solution but soluble in 96% sulfuric acid solution. It gave a yellow liquid with 2,4-dinitrophenylhydrazine and did not react with acetyl chloride. The compound did not react with potassium permanganate or bromine. It gave a sulfonamide derivative that melted at 113°C. The IR, ^{1}H NMR, ^{13}C NMR, and DEPT spectra are shown in Figures 11.46 through 11.49.

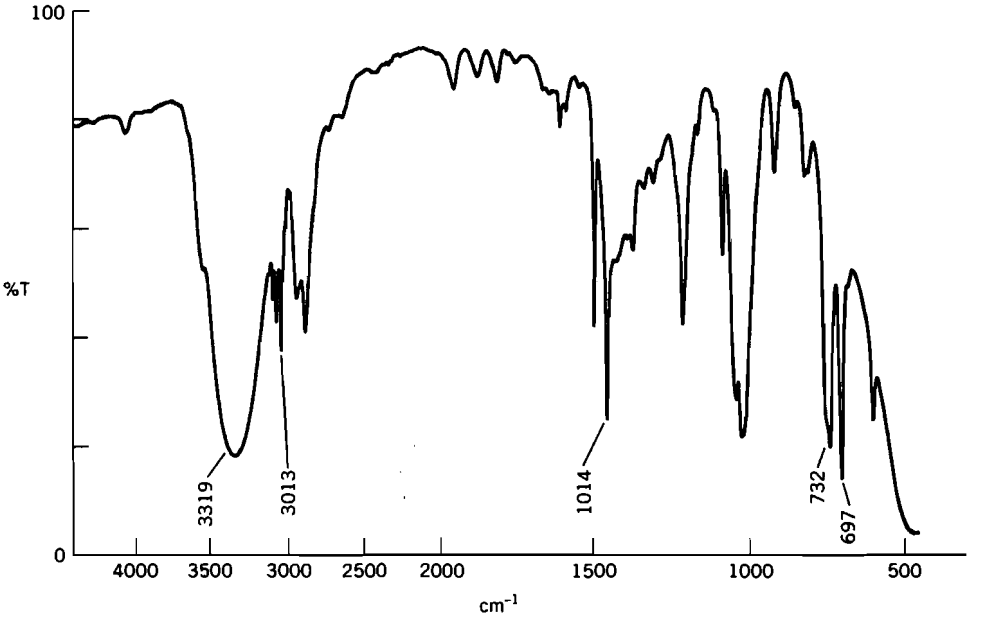


Figure 11.38 IR spectrum for Problem Set 3, Problem 1. (Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.)

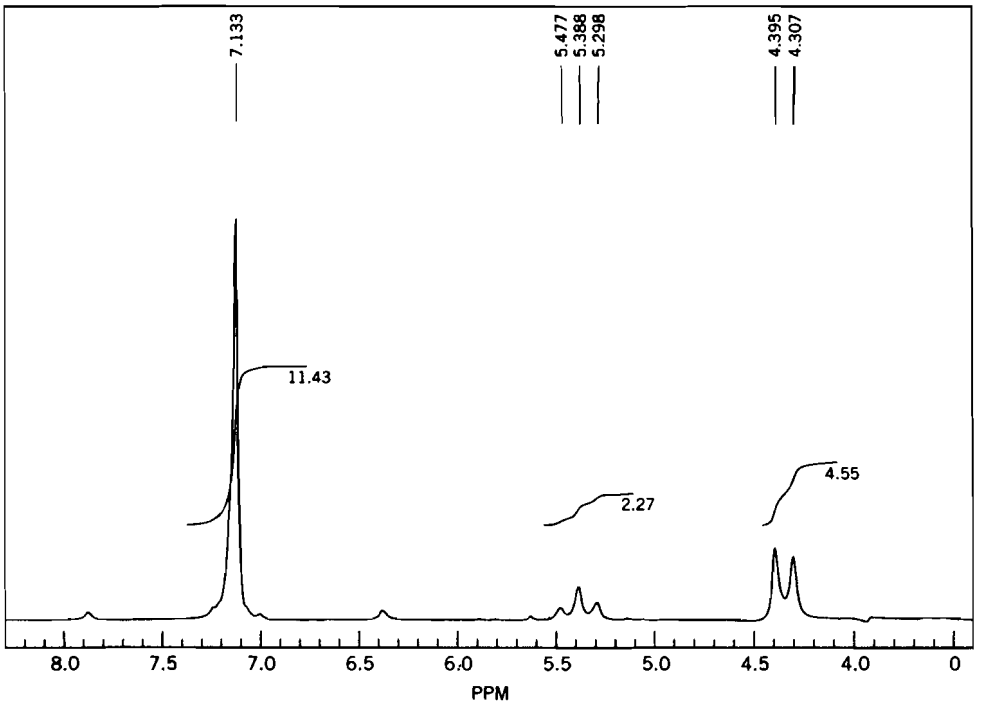


Figure 11.39 ^{1}H NMR spectrum for Problem Set 3, Problem 1. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

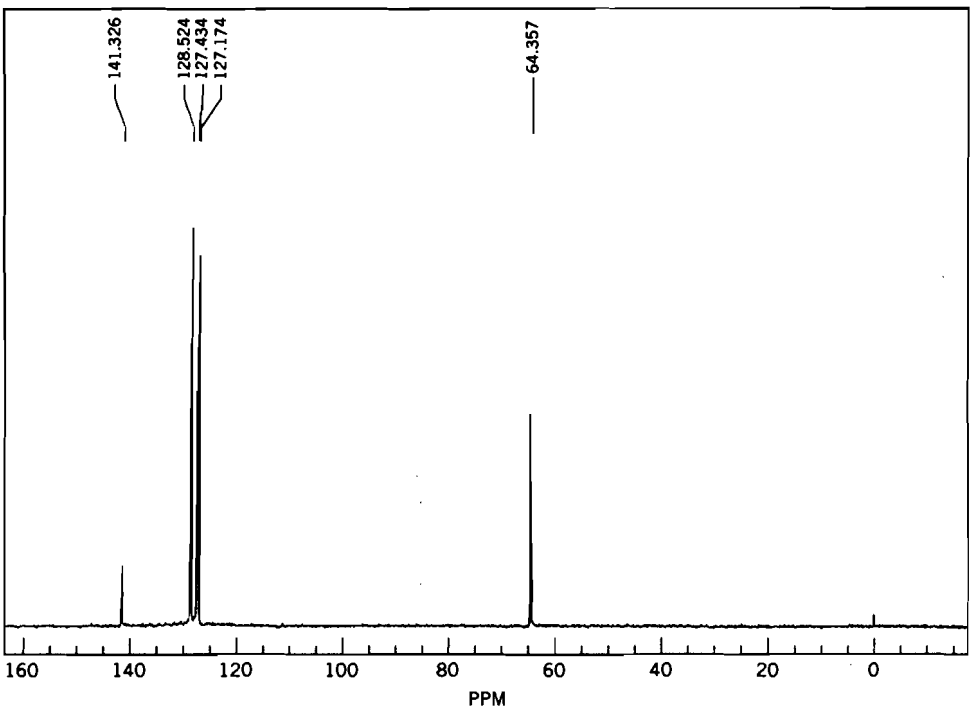


Figure 11.40 ^{13}C NMR spectrum for Problem Set 3, Problem 1. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

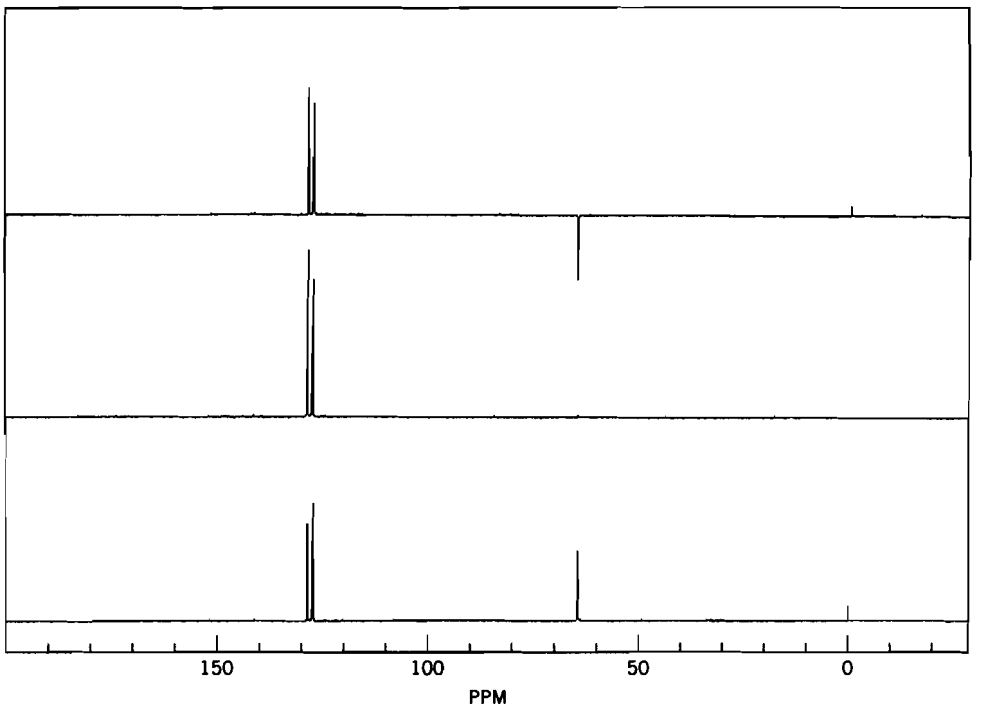


Figure 11.41 DEPT spectrum for Problem Set 3, Problem 1. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

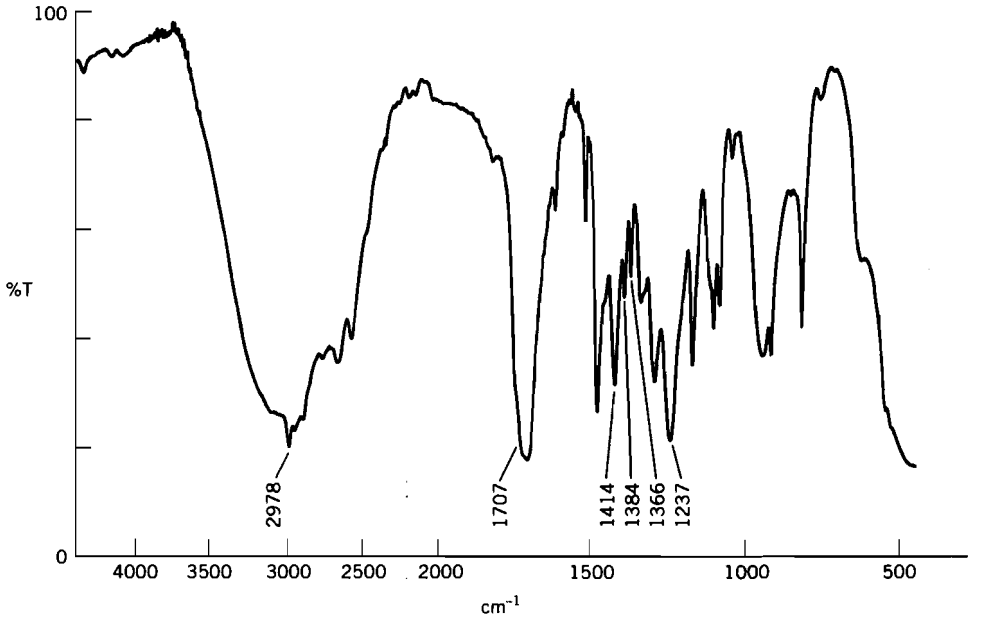


Figure 11.42 IR spectrum for Problem Set 3, Problem 2. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

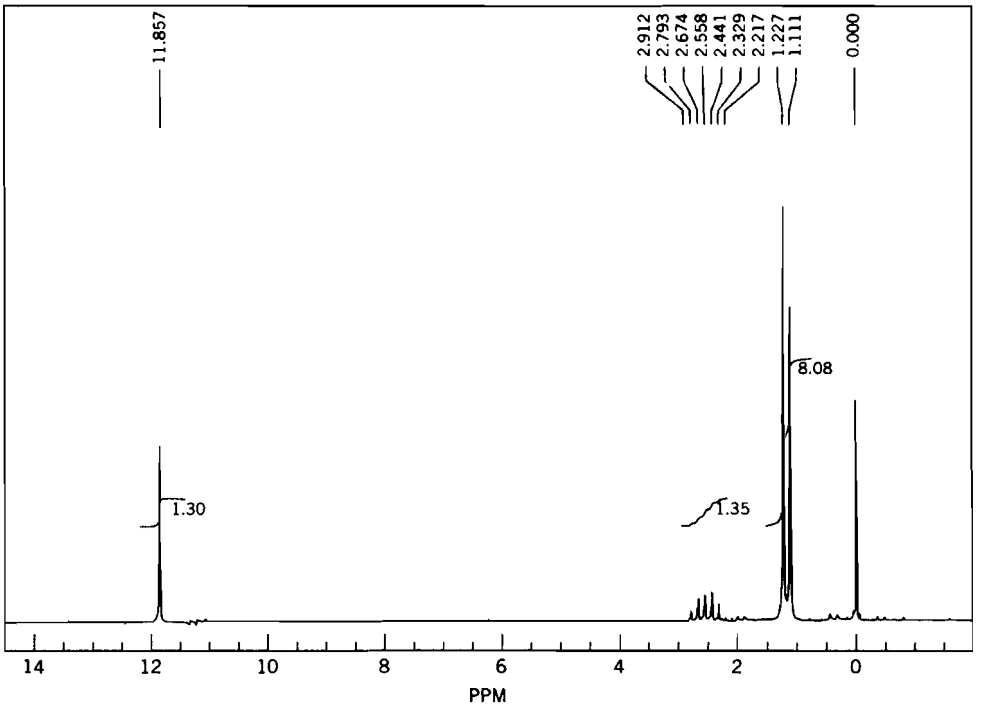


Figure 11.43 ^{1}H NMR spectrum for Problem Set 3, Problem 2. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

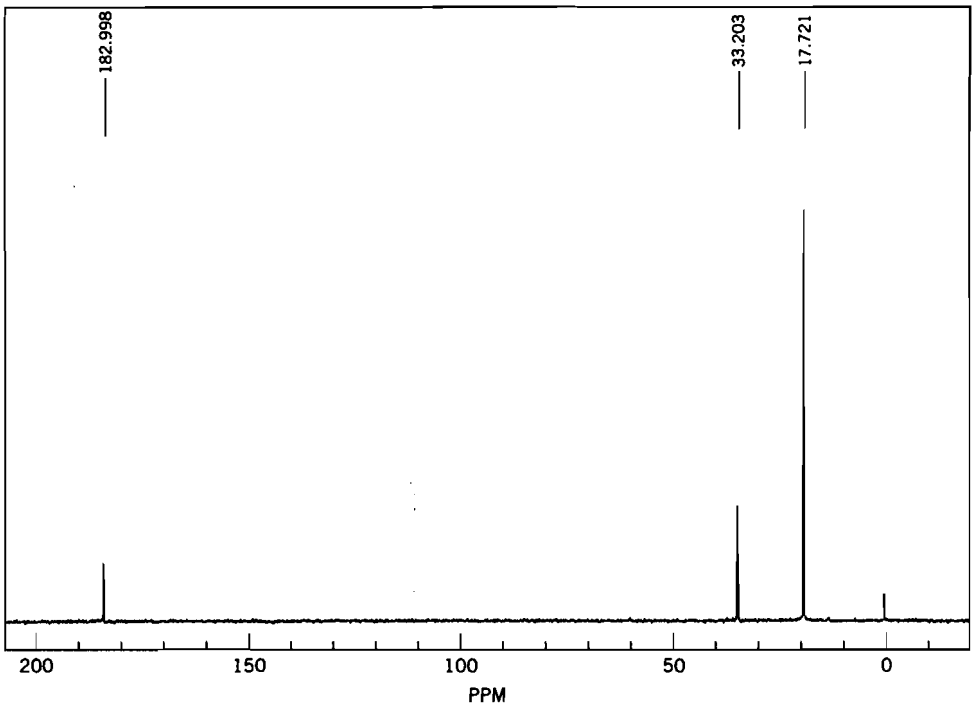


Figure 11.44 ^{13}C NMR spectrum for Problem Set 3, Problem 2. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

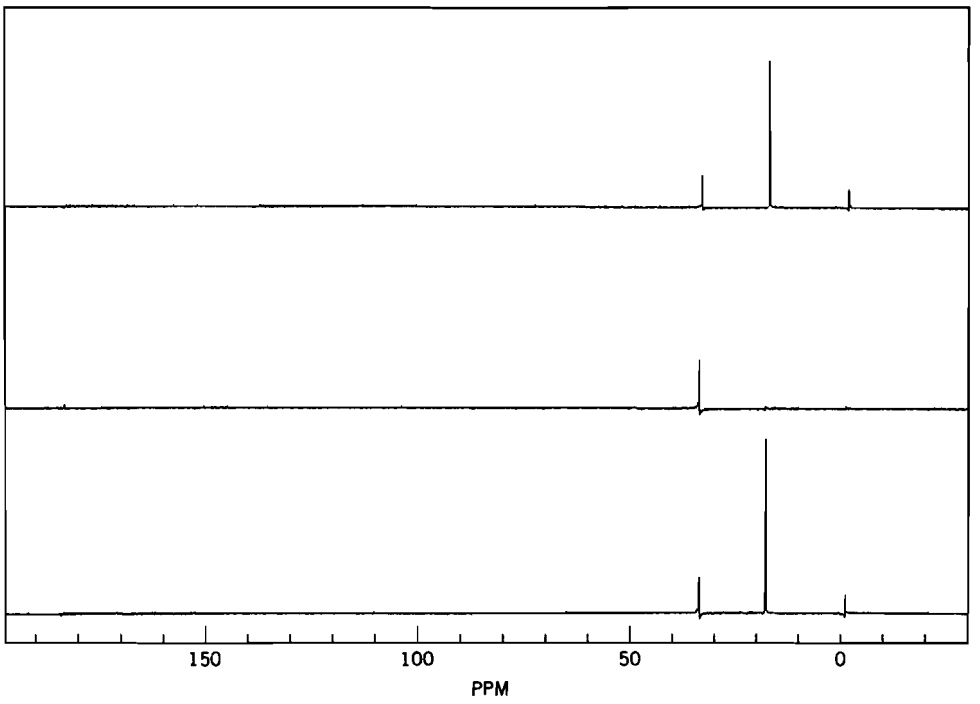


Figure 11.45 DEPT spectrum for Problem Set 3, Problem 2. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

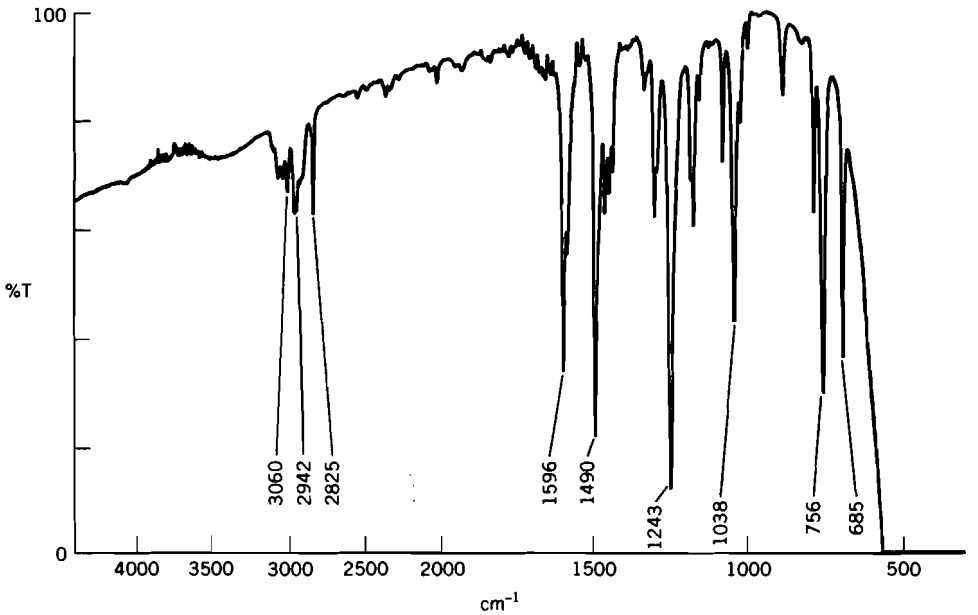


Figure 11.46 IR spectrum for Problem Set 3, Problem 3. [Spectrum courtesy of Terra Hosp, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

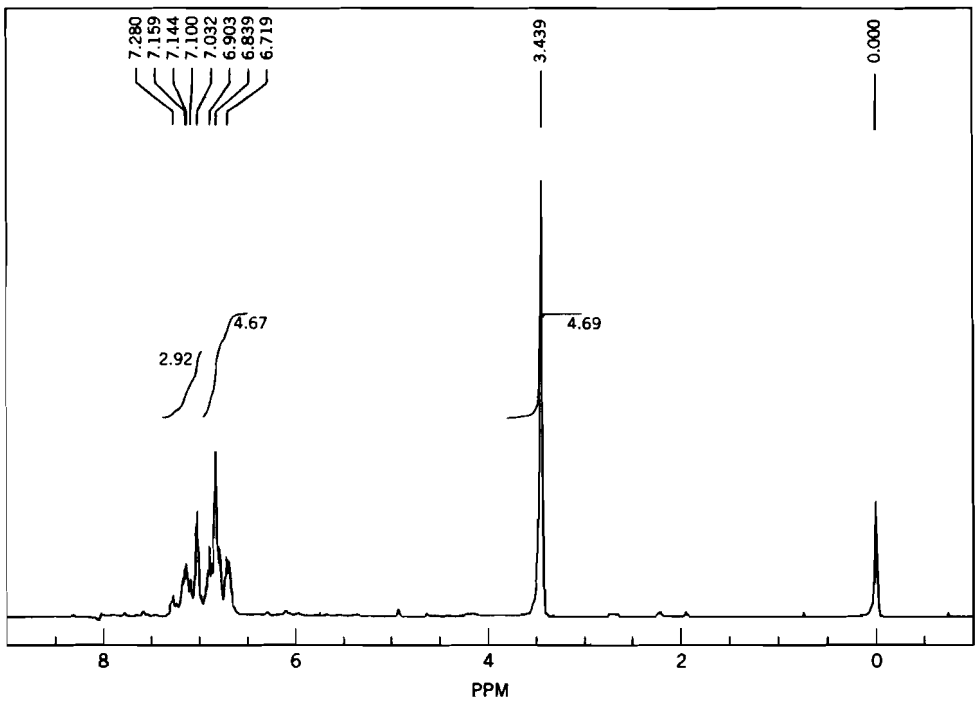


Figure 11.47 ^{1}H NMR spectrum for Problem Set 3, Problem 3. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

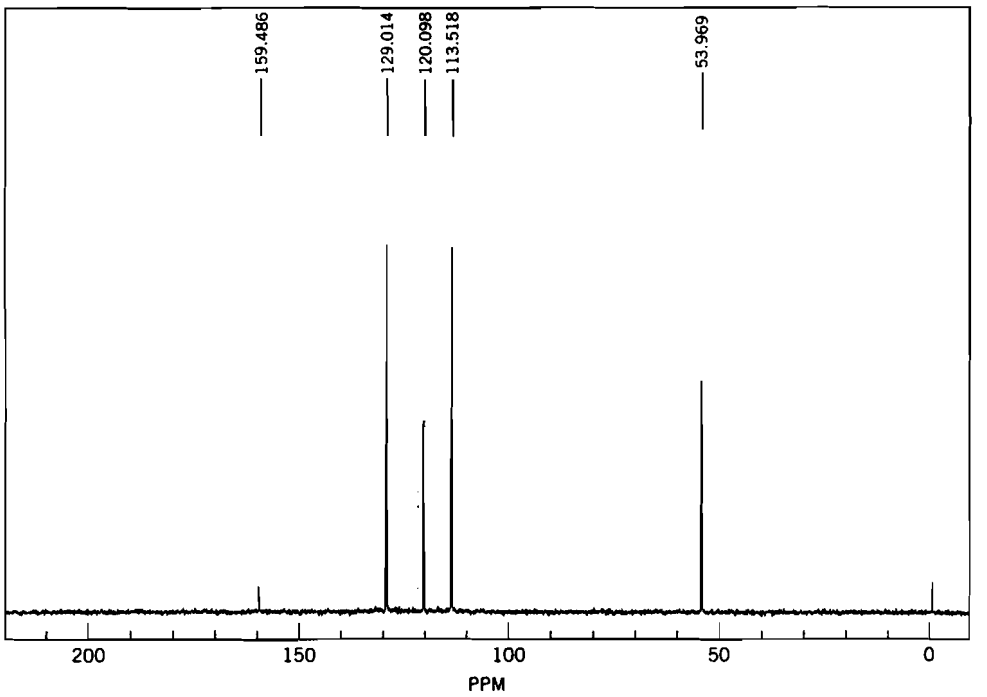


Figure 11.48 ^{13}C NMR spectrum for Problem Set 3, Problem 3. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

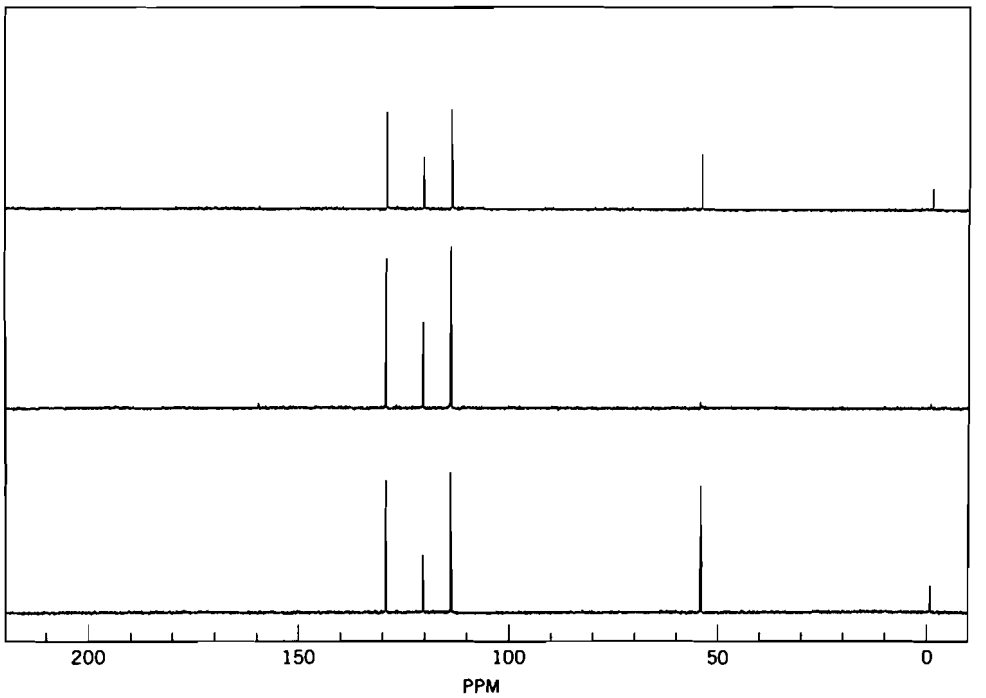


Figure 11.49 DEPT spectrum for Problem Set 3, Problem 3. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

4. A compound was insoluble in water, 5% sodium hydroxide solution, and 5% hydrochloric acid solution but soluble in 96% sulfuric acid solution. It did not react with 2,4-dinitrophenylhydrazine, acetyl chloride, or potassium thiocyanate. It reacted with bromine and potassium permanganate. The IR, ^{1}H NMR, ^{13}C NMR, DEPT, and HETCOR spectra are shown in Figures 11.50 through 11.54.
5. A compound was insoluble in water and 5% sodium hydroxide but soluble in 5% hydrochloric acid. It reacted with acetyl chloride to form a precipitate. Treatment of the compound with benzenesulfonyl chloride, followed by acidification, gave an insoluble product. The IR, ^{1}H NMR, ^{13}C NMR, and DEPT spectra are shown in Figures 11.55 through 11.58.
6. A compound was soluble in water and ether, and its aqueous solution turned litmus blue. It reacted with sodium to give a gas. The compound reacted with benzenesulfonyl chloride and base to give an insoluble product, which was unchanged with acidification. It reacted with nitrous acid to give a yellow solid. The IR, ^{1}H NMR, ^{13}C NMR, and DEPT spectra are shown in Figures 11.59 through 11.62.

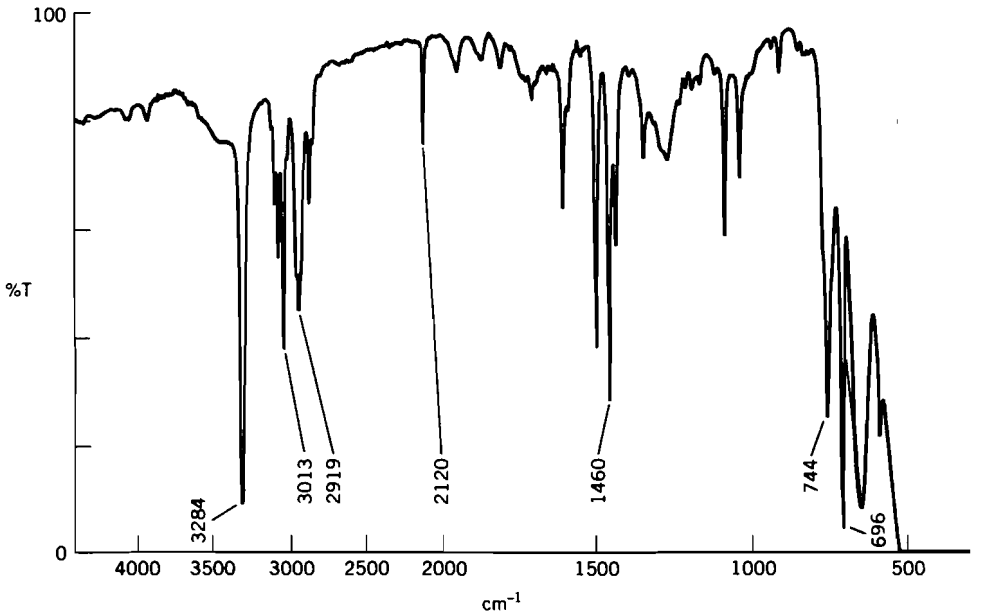


Figure 11.50 IR spectrum for Problem Set 3, Problem 4. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

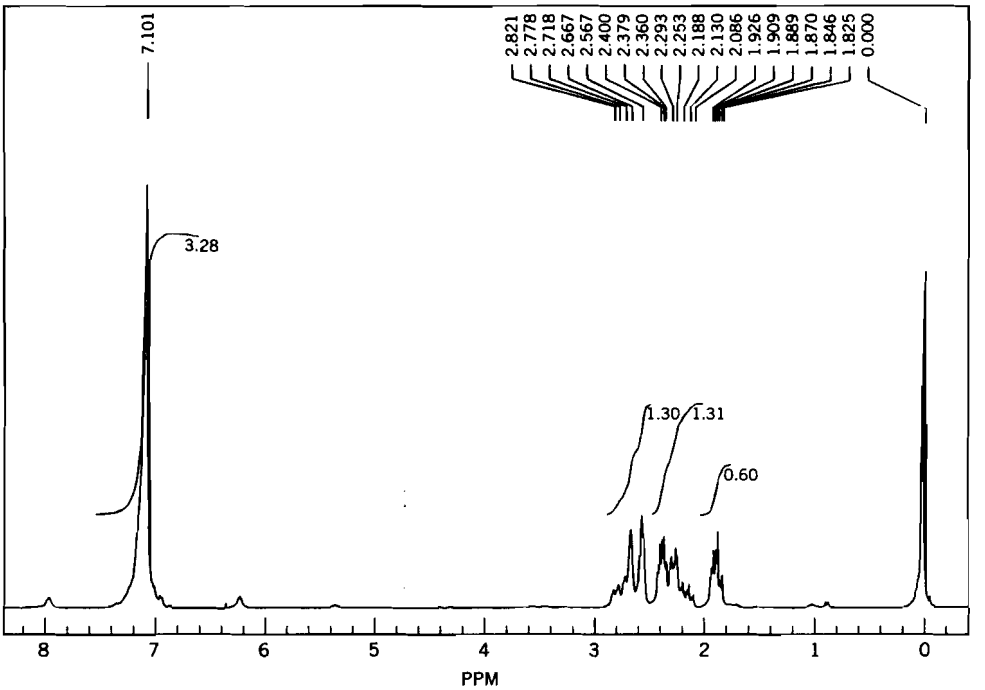


Figure 11.51 ^{1}H NMR spectrum for Problem Set 3, Problem 4. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

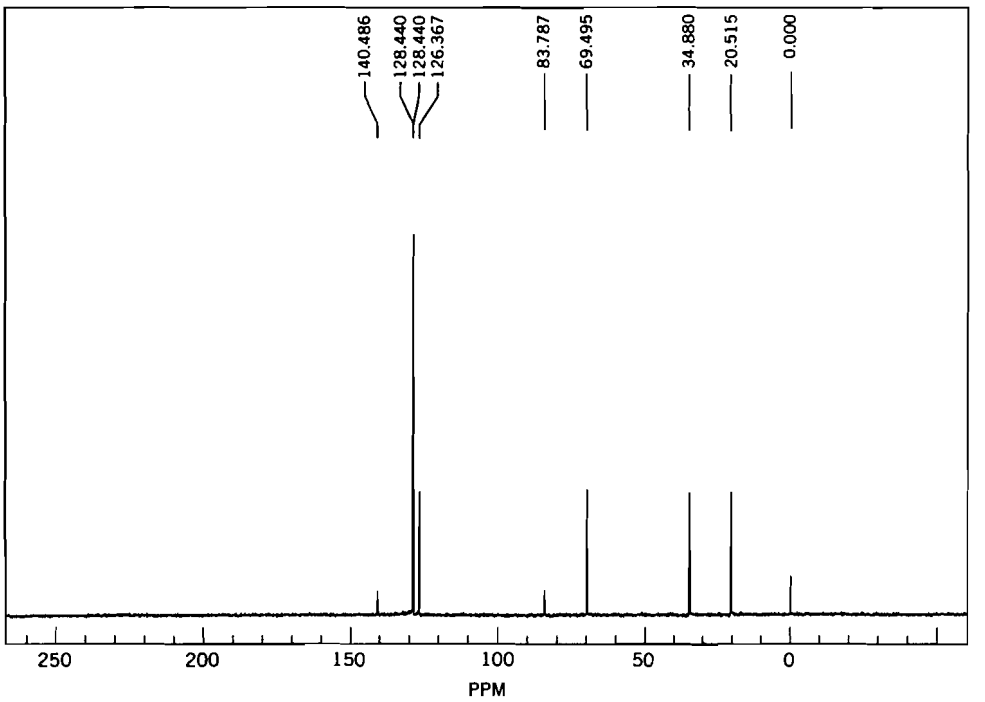


Figure 11.52 ^{13}C NMR spectrum for Problem Set 3, Problem 4. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

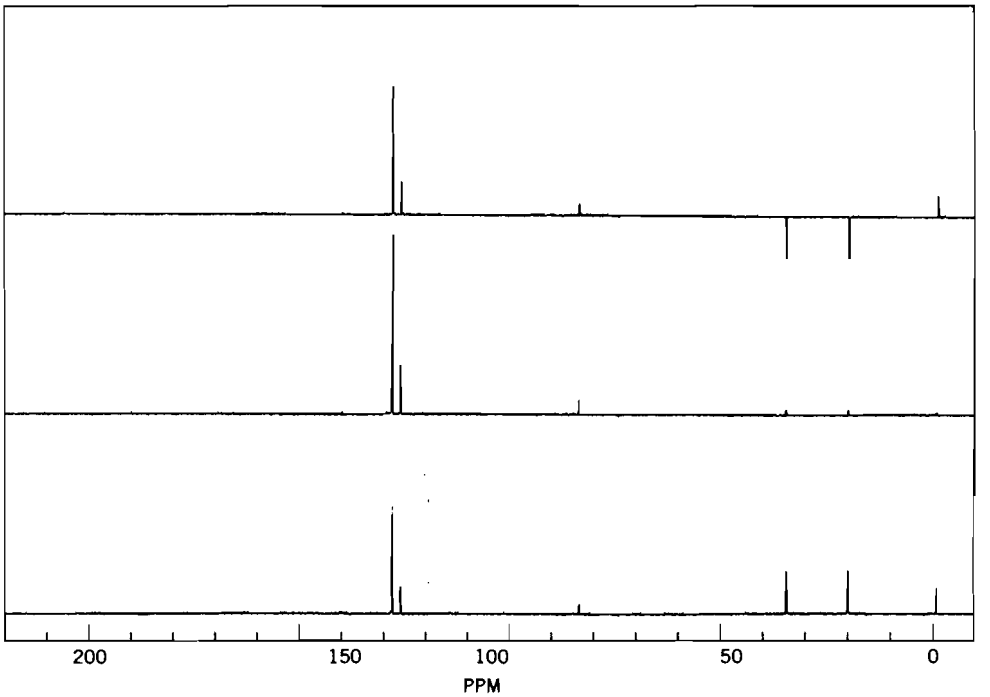


Figure 11.53 DEPT spectrum for Problem Set 3, Problem 4. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

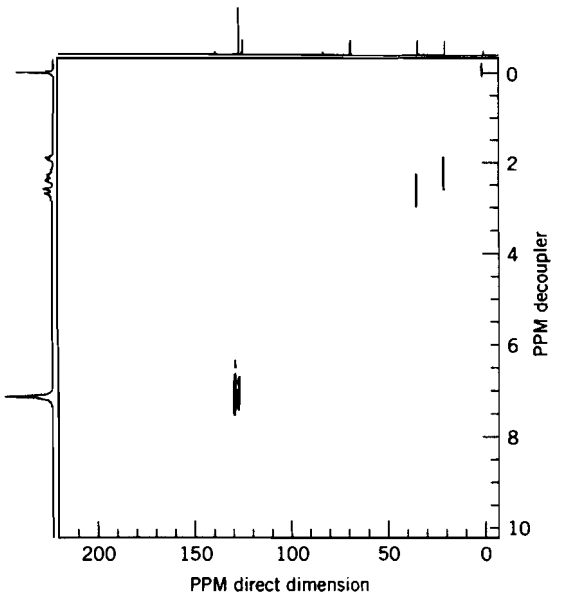


Figure 11.54 HETCOR spectrum for Problem Set 3, Problem 4. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

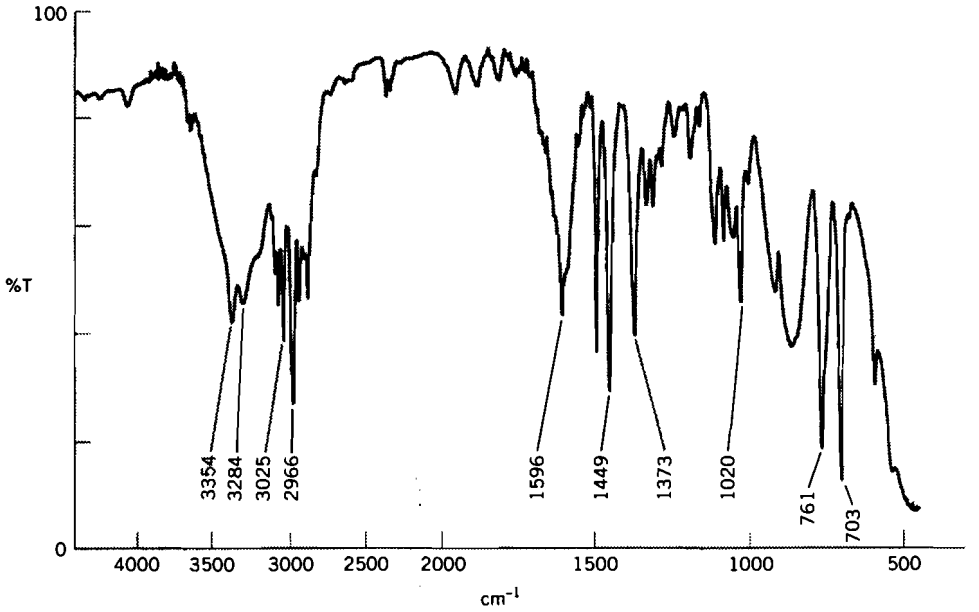


Figure 11.55 IR spectrum for Problem Set 3, Problem 5. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

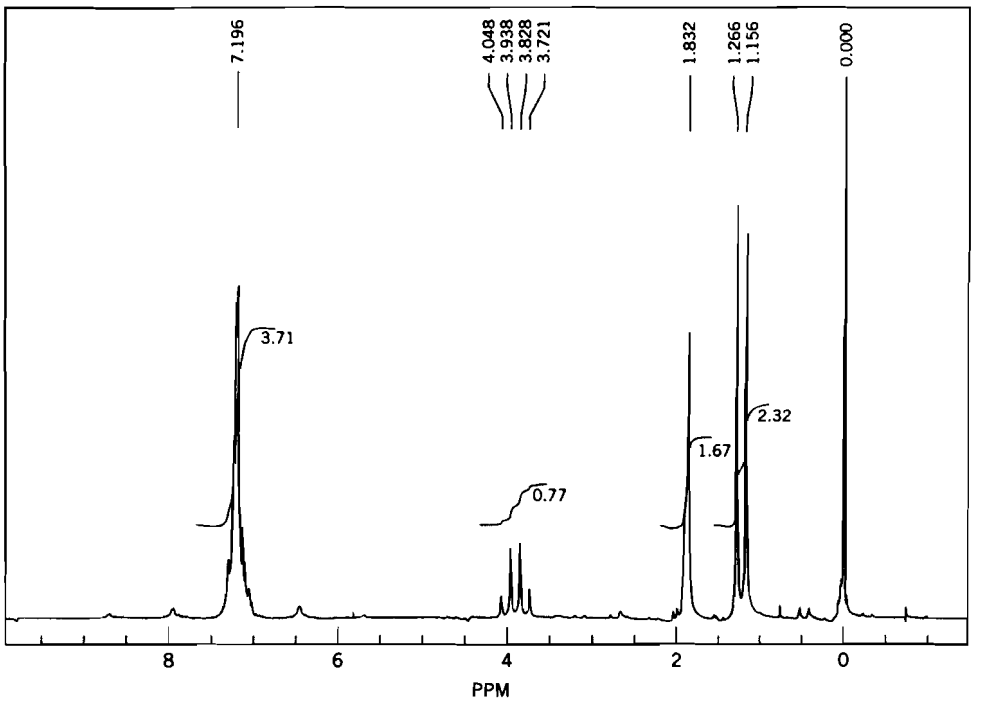


Figure 11.56 ^{1}H NMR spectrum for Problem Set 3, Problem 5. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

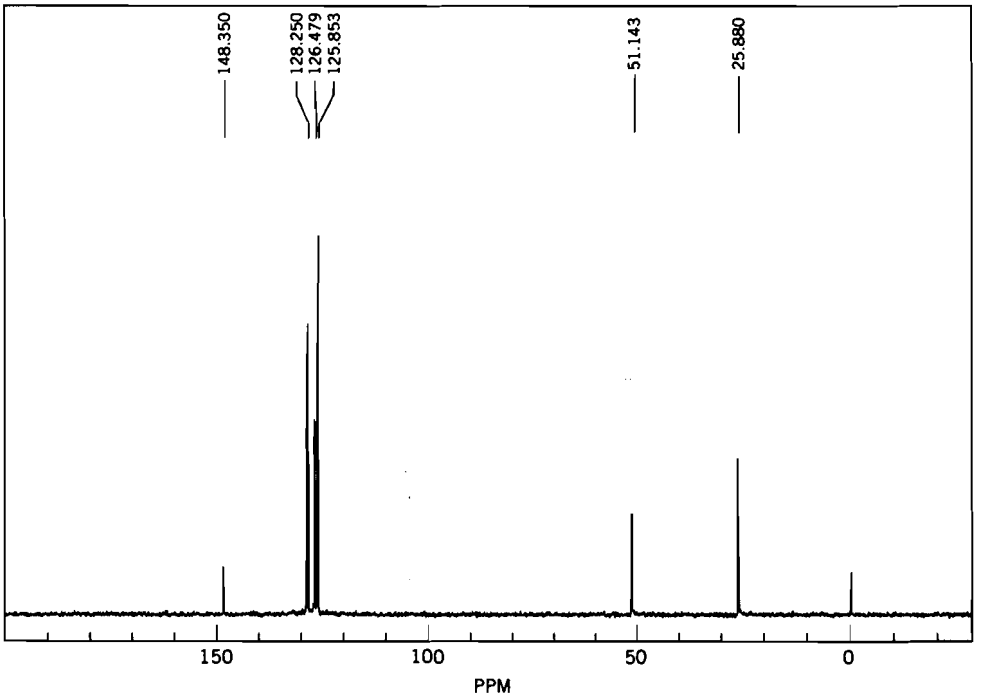


Figure 11.57 ^{13}C NMR spectrum for Problem Set 3, Problem 5. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

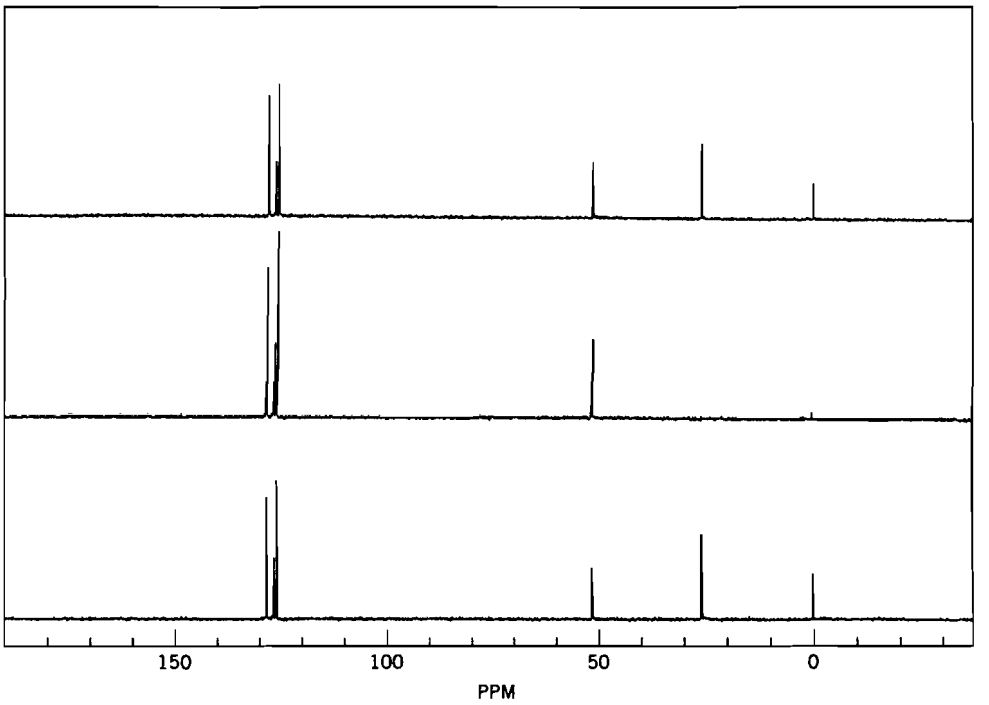


Figure 11.58 DEPT spectrum for Problem Set 3, Problem 5. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

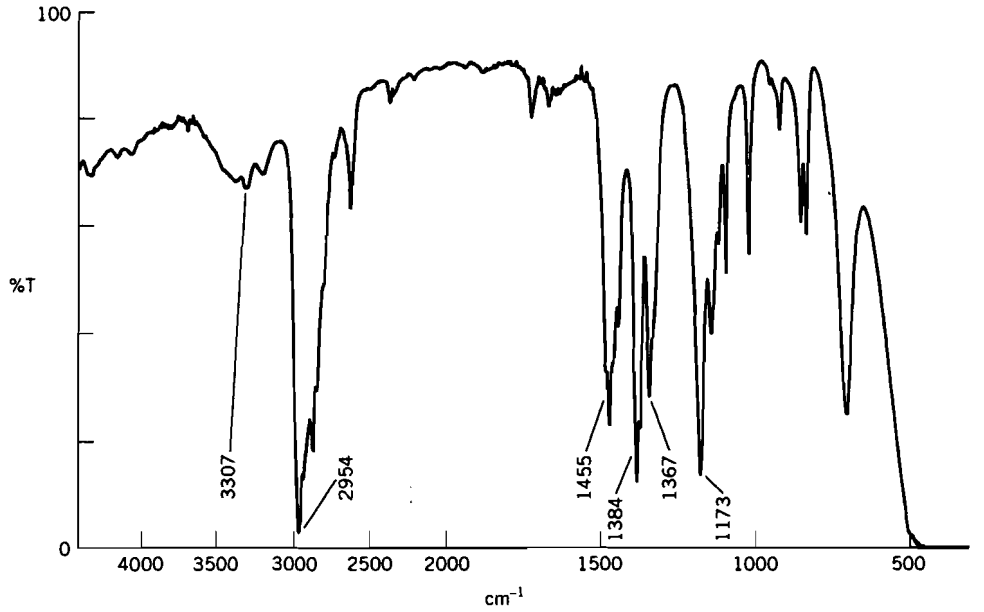


Figure 11.59 IR spectrum for Problem Set 3, Problem 6. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

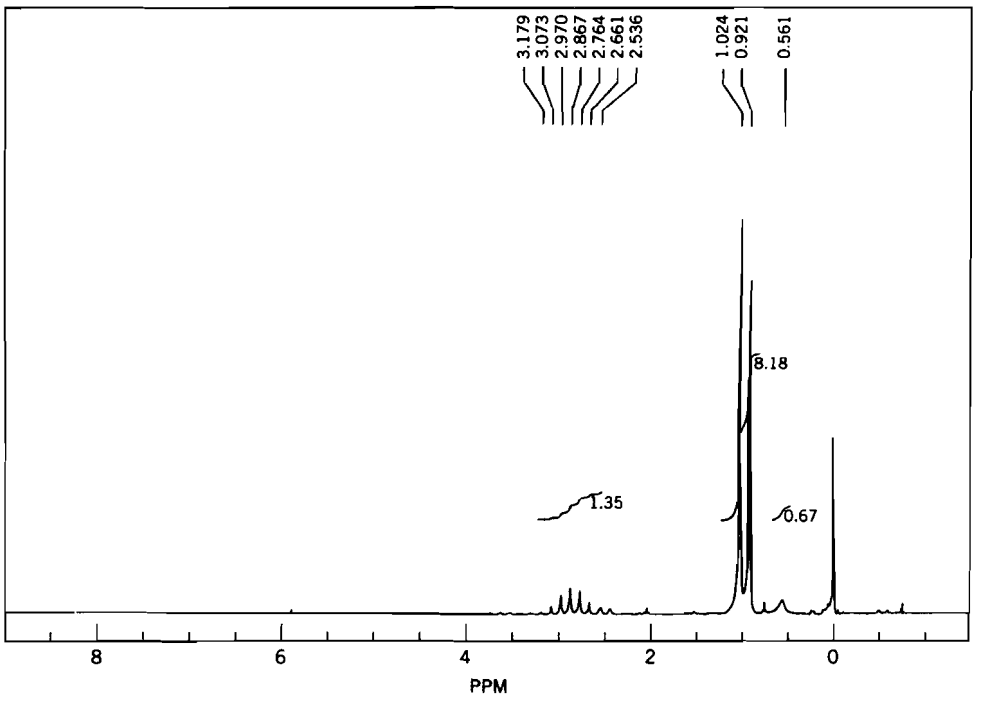


Figure 11.60 ^{1}H NMR spectrum for Problem Set 3, Problem 6. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

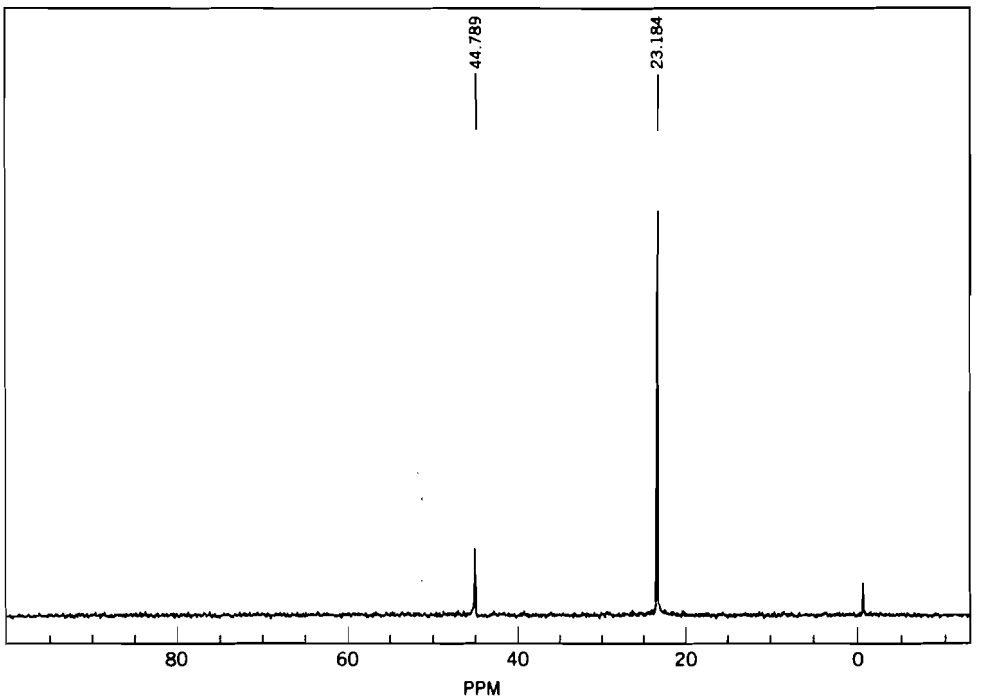


Figure 11.61 ^{13}C NMR spectrum for Problem Set 3, Problem 6. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

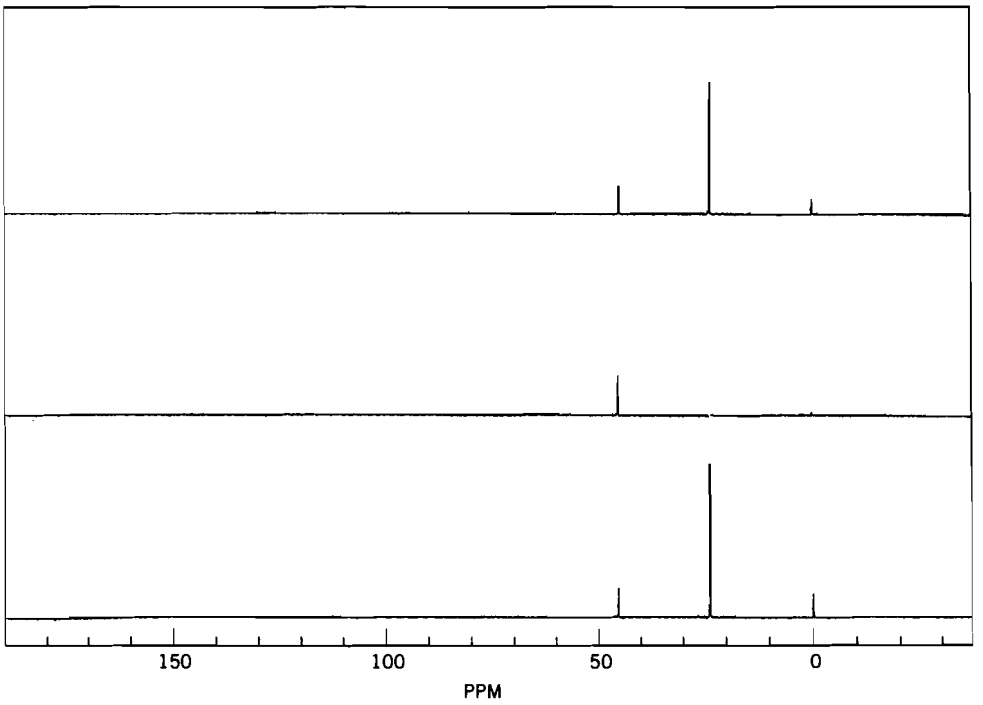


Figure 11.62 DEPT spectrum for Problem Set 3, Problem 6. [Spectrum courtesy of Christine K. F. Hermann, Department of Chemistry and Physics, Radford University, Radford, Virginia. Used with permission.]

Problem Set 4

1. A liquid had a boiling point of 146°C. It was insoluble in water, 5% sodium hydroxide solution, and 5% hydrochloric acid solution but soluble in 96% sulfuric acid solution. The reaction of the liquid with sodium did not yield any bubbles. A purple liquid resulted from mixing the liquid with potassium permanganate. Reaction of the liquid with 2,4-dinitrophenylhydrazine yielded a yellow solid with a melting point of 77°C.
2. A liquid had a boiling point of 184°C. It was soluble in water and ether. An aqueous solution of the compound did not change the color of litmus paper. The sodium fusion filtrate was treated with 10% ammonium polysulfide, 5% hydrochloric acid solution, and 5% ferric chloride to produce a red color. Reaction of the liquid with acetyl chloride did not yield any bubbles. When the liquid was mixed with 2,4-dinitrophenylhydrazine, a yellow liquid was produced. The benzamide derivative had a melting point of 80°C.
3. A liquid had a boiling point of 130°C. It was soluble in water and ether. An aqueous solution of the compound did not change the color of litmus paper. Treatment of the liquid with silver nitrate produced a white solid. When the liquid was mixed with 2,4-dinitrophenylhydrazine, a yellow liquid was produced. The liquid reacted with sodium to produce bubbles. The 4-nitrobenzoate derivative had a melting point of 54°C.
4. A solid had a melting point of 166°C. The solid was insoluble in water and 5% sodium bicarbonate solution but was soluble in 5% sodium hydroxide solution. The sodium fusion filtrate reacted with lead acetate to produce a black precipitate. The sodium fusion filtrate was treated with 10% ammonium polysulfide, 5% hydrochloric acid solution, and 5% ferric chloride to produce a red color. Reaction of the compound with ferrous hydroxide yielded a red-brown color. No reaction occurred when the compound was mixed with acetyl chloride. The solid reacted with aniline to yield a solid of melting point 125°C.
5. Compound A had a melting point of 170°C; it was insoluble in water and 5% sodium bicarbonate solution but soluble in 5% sodium hydroxide solution. Compound A reacted with sodium to form bubbles. The reaction of compound A with ceric ammonium nitrate produced a brown color. Compound A was mixed with silver nitrate to produce a transparent liquid. Treatment of compound A with benzenesulfonyl chloride yielded a soluble compound; acidification of the solution produced an insoluble compound. Compound A reacted with ferrous hydroxide to yield a green color. No bubbles were produced from a mixture of compound A with a 5% sodium bicarbonate solution. Compound A reacted with three equivalents of benzoyl chloride to yield compound B (mp 224°C). Explain all tests. Identify compounds A and B.
6. A compound had a melting point of 80°C and smelled like a flavoring. It was insoluble in water and 5% sodium bicarbonate solution but soluble in 5% sodium hydroxide solution. The sodium fusion test with lead acetate gave a colorless solution. The reaction of the compound with silver nitrate yielded no solid. The treatment with ceric ammonium nitrate gave a brown solution. The compound reacted with Jones reagent to give a blue-green color. It reacted with acetyl chloride to produce bubbles and with 2,4-dinitrophenylhydrazine to yield a yellow solid. Explain all tests and identify the compound.
7. Compound A had a melting point of 69°C; it was insoluble in water, 5% sodium hydroxide solution, and 5% hydrochloric acid solution but was soluble in 96%

sulfuric acid solution. Treatment of compound A with a potassium permanganate solution gave a purple liquid. A yellow liquid was formed when compound A was mixed with 2,4-dinitrophenylhydrazine. Compound A did not react with sodium. The proton NMR spectrum of compound A showed only aromatic peaks.

Compound A was heated with acid to form compounds B (mp 120°C) and C (mp 40°C). Compound B was insoluble in water but soluble in 5% sodium hydroxide solution and 5% sodium bicarbonate solution. Compound B reacted with a 5% sodium bicarbonate solution to form bubbles. Compound B gave no reaction with sodium but gave a yellow liquid with 2,4-dinitrophenylhydrazine.

Compound C was insoluble in water and 5% sodium bicarbonate solution but soluble in 5% sodium hydroxide solution. Compound C did not produce bubbles with 5% sodium bicarbonate solution but did produced bubbles with sodium. Compound C gave a green color with ferrous hydroxide.

Explain all tests. Identify Compounds A, B, and C.

8. A compound had a melting point of 58°C and was insoluble in water, 5% sodium hydroxide solution, and 5% hydrochloric acid solution but was soluble in 96% sulfuric acid solution. It was mixed with Jones reagent to yield an orange-red color. It did not produce bubbles with sodium. The compound was combined with Schiff reagent to give a colorless solution and with 2,4-dinitrophenylhydrazine to yield a yellow liquid. Mixing the compound with bromine gave a yellow-brown liquid. Treatment with hydroxamic acid and ferric chloride gave a yellow color. The compound reacted with ferric ammonium sulfate to give a reddish purple color.

Problem Set 5

Give the name and structure of all compounds. Give all reactions.

1. Compound A had a boiling point of 205°C; it was insoluble in water and 5% sodium hydroxide solution but soluble in 5% hydrochloric acid solution. Treatment of compound A with benzoyl chloride yielded compound B, which had a melting point of 60°C. Compound B was heated with base; the aqueous layer was acidified to yield compound C. Compound C had a melting point of 122°C. Compound C was treated with thionyl chloride to yield compound D. Compound D was reacted with 4-toluidine to give compound E. Compound E had a melting point of 158°C.
2. Compound A had a boiling point of 97°C. Compound A was soluble in water and ether; its aqueous solution did not change the color of litmus paper. The sodium fusion filtrate of compound A gave a yellow color with ammonium polysulfide, hydrochloric acid, and ferric chloride. Compound A reacted violently with acetyl chloride and gave a yellow liquid with 2,4-dinitrophenylhydrazine. Compound B had a boiling point of 80°C and gave a white solid with silver nitrate. Compound A reacted with compound B to yield compound C. Compound C had a boiling point of 123°C and a specific gravity of 0.902. Compound C was soluble in water and ether; its aqueous solution did not change the color of litmus paper. Compound C did not react with acetyl chloride or silver nitrate. Compound C produced a yellow liquid with 2,4-dinitrophenylhydrazine. Compound C was reacted with hydrazine to produce Compound D. Compound D had a melting point of 40°C.

3. Compound A had a melting point of 36°C. Compound A was insoluble in water and 5% sodium hydroxide solution. The solubility in 5% hydrochloric acid solution was inconclusive. The sodium fusion filtrate of compound A gave a black precipitate with lead acetate; a red color with ammonium polysulfide, hydrochloric acid, and ferric chloride; and a white solid with silver nitrate. Compound A was treated with water and acid to give compound B. Compound B had a melting point of 92°C. Compound B was treated with phosphorus pentachloride to give back compound A. Compound A reacted with ammonium hydroxide to produce compound C. Compound C had a melting point of 144°C.
4. A compound had a melting point of 185°C and was a common household substance. It was soluble in water but insoluble in ether. The compound reacted violently with acetyl chloride. When treated with three equivalents of phenylhydrazine, the compound yielded a solid product after 30 min. The sodium fusion filtrate of the compound gave a yellow color with ammonium polysulfide, hydrochloric acid, and ferric chloride.
5. A compound had a melting point of 170°C. It reacted violently with acetyl chloride. The reaction of the compound with ferric chloride–pyridine produced a colored complex. It was treated with ferrous hydroxide to give a brown precipitate. Mixing the compound with chromium trioxide yielded a yellow-orange liquid. The compound reacted with benzenesulfonyl chloride to yield a soluble product; acidification of this product produced an insoluble compound.
6. A compound had a melting point of 100°C. It reacted with bromine to yield a colorless solution. When the compound was treated with sodium bicarbonate solution, gas evolution occurred. The compound was combined with 2,4-dinitrophenylhydrazine solution to yield a yellow-orange solid. A Tollens test of the compound produced a colorless solution. Mixing it with chromium trioxide yielded a yellow-orange liquid.
7. A compound had a boiling point of 182°C. It reacted violently with acetyl chloride. A 2,4-dinitrophenylhydrazine test of the compound gave a yellow liquid. Treatment of the compound with chromium trioxide produced a blue-green color. It reacted with silver nitrate to give a white precipitate. The compound was treated with bromine to give a yellow solution.
8. A compound had a boiling point of 149°C. It reacted with bromine to yield a colorless solution. Treatment of the compound with potassium permanganate produced a brown blob. A 2,4-dinitrophenylhydrazine test of the compound gave a yellow solid. It reacted with a Tollens test to give a silver mirror and reacted with chromium trioxide to give a blue-green solution.

Problem Set 6

In the investigation of unknown compounds, the following types of behavior are observed frequently. Indicate in each instance the deductions which may be made as to the nature of the compound.

1. A yellow, neutral compound containing only carbon, hydrogen, and oxygen was changed to an acid by the action of hydrogen peroxide. The original yellow compound displayed a singlet in the ^{1}H NMR spectrum at $\approx \delta$ 9.0 ppm, as well as other signals.

2. A neutral compound reacted with phenylhydrazine to yield a product that differed from the expected phenylhydrazone by the elements of ethanol; that is, the condensation involved the elimination not only of the elements of water but also of those of ethanol.
3. A compound containing only carbon, hydrogen, and oxygen reacted with acetyl chloride but not with phenylhydrazine. Treatment with periodic acid converted it into a compound that reacted with phenylhydrazine but not with acetyl chloride.
4. A yellow, neutral compound formed a derivative with *o*-phenylenediamine. The original compound showed an IR band at 1710 cm^{-1}.
5. An alcohol gave a positive iodoform test and a negative Lucas test.
6. A neutral compound containing only carbon, hydrogen, and oxygen reacted with acetyl chloride but not with phenylhydrazine. Heating with mineral acids converted it to a compound that failed to react with acetyl chloride but that gave positive tests with phenylhydrazine and bromine in carbon tetrachloride. The ^1H NMR spectrum of the original compound showed only two singlets.
7. A nitrogen-containing compound gave a positive nitrous acid test for secondary amines, but its derivative with benzenesulfonyl chloride was soluble in alkalies.
8. A compound, when treated with excess ethanol and a trace of acid, was found to take up the elements of ethyl ether. One of the two possible classes of compounds that serve as an answer showed a ^1H NMR signal at ca. δ 9.0–10.0 before treatment; treatment moved this signal to ca. δ 5.0.
9. A neutral compound containing carbon, hydrogen, and oxygen underwent dimerization in an ethanolic solution of sodium cyanide. The IR spectrum of the reactant showed bands at ca. 2800 and 2700 cm^{-1}.
10. A basic compound failed to react with benzenesulfonyl chloride but yielded a derivative with nitrous acid. The original basic compound showed no appreciable IR bands near 3333 cm^{-1}. The product of nitrous acid treatment showed an IR band at ca. 1550 cm^{-1}.
11. An ester had a saponification equivalent of 59 $\pm$ 1. The ^1H NMR spectrum showed two singlets with an integration ratio of 3:1.
12. A solid water soluble acid had a neutralization equivalent of 54 $\pm$ 1. At temperatures above its melting point, the compound lost carbon dioxide and formed a new solid acid with a neutralization equivalent of 59 $\pm$ 1. The nonexchangeable protons of the original compound resulted in a multiplet ^1H NMR signal; the product formed upon heating showed the nonexchangeable protons as a singlet.
13. A water soluble acidic compound containing nitrogen and sulfur gave a neutralization equivalent of 142 $\pm$ 1. Addition of barium chloride to an aqueous solution produced a precipitate insoluble in acids. Alkali caused the separation of a basic compound. The hydrochloride of this basic compound had a neutralization equivalent of 130 $\pm$ 1. Both the first and last compounds (the acids) showed broad IR bands at ca. 3333–2500 cm^{-1}.
14. A water soluble compound containing nitrogen gave a neutralization equivalent of 73 $\pm$ 1 when titrated with standard hydrochloric acid and methyl red as the indicator. It formed a precipitate when treated with benzenesulfonyl chloride and sodium hydroxide solution. The original compound showed a

quartet (4H), a triplet (6H), and a broadened singlet (1H) in the ^{1}H NMR spectrum.

15. A 12-g sample of a compound, C_8H_8O, was treated with a carbon tetrachloride solution of bromine containing 60 g of bromine. Hydrobromic acid was evolved, and a quantitative determination showed that 16.2 g were liberated. After the reaction was complete, the solution was still red, and it was found that 12 g of bromine remained unused. Calculate the number of atoms of bromine per molecule that were introduced by substitution and, if addition also took place, the number of atoms of bromine which were added. Use Br = 80, H = 1, C = 12, O = 16. Also describe important NMR and IR features you would anticipate for both the reactant and the product; emphasize the important spectral changes expected as the result of the bromine treatment.

Problem Set 7

In solving the problems of this set and those in sets 8 and 9, follow the general procedure described in the sample problems above. Also, the sample report forms at the end of Chapter 2 are largely consistent with the information provided below. Make the customary allowances for experimental error in boiling points and melting points. Assign spectral data to structural features. Give equations for derivatives.

I. (1) White crystals, mp 117–118°C.

(2) Elemental analysis for X, N, S—negative. (X = halogen)

(3) Solubility—water (+).

(4) Classification tests:

$C_6H_5NHNH_2$—negative	CH_3COCl—positive
$KMnO_4$—positive	HIO_4—positive
Br_2 in CCl_4—negative	

Neutralization equivalent = 151 ± 1

(5) Derivative: *p*-Nitrobenzyl ester, mp 123°C.

(6) Spectra:

IR (mineral oil mull): 3333–2400 cm^{-1} (s, b); 1706 cm^{-1} (s); 1449, 1379, 1300, 1200, 1190, 943, 865, 730 cm^{-1} (all m).

^{1}H NMR (60 HMz, acetone): δ 5.22, 1H, s; δ 6.93–7.88, 7H, m.

II. (1) Colorless liquid, bp 259–261°C

(2) Elemental analysis for Br—positive; for Cl, I, N, S—negative.

(3) Solubility—water (−), NaOH (−), HCl (−), H_2SO_4 (+).

(4) Classification tests:

$H_2NOH \cdot HCl$—negative	$KMnO_4$—negative
CH_3COCl—negative	Br_2 in CCl_4—negative
$AgNO_3$—negative	NaI—negative

Hot sodium hydroxide—clear solution which on acidification gave white crystals, mp 250°C, containing bromine.

Saponification equivalent of the original compound = 229 ± 2.

(5) Derivatives:

(a) Treatment with hydrazine gave colorless crystals, mp 164°C.

(b) Treatment with 3,5-dinitrobenzoic acid and sulfuric acid gave pale-yellow crystals, mp 92°C.

III. (1) Brown liquid, bp 198–200°C.

(2) Elemental analysis for X, N, S—negative.

(3) Solubility—water (−), NaOH (+), $NaHCO_3$ (−).

(4) Classification tests:

CH_3COCl—positive Br_2 in H_2O—precipitate

$C_6H_5NHNH_2$—negative $FeCl_3$—violet

Ce(IV)—negative

(5) Derivative: Treatment with chloroacetic acid gave white crystals, mp 102–103°C.

(6) Spectra:

IR (neat): 3390 cm^{-1} (s, b); 1163, 935, 780, 690 cm^{-1} (all s).

^1H NMR (60 MHz, $CDCl_3$): δ 2.25, 3H, s; δ 5.67, 1H, s; δ 6.5–7.3, 4H, m.

IV. (1) Colorless liquid, bp 194–195°C.

(2) Elemental analysis for X, N, S—negative.

(3) Solubility—all (−).

(4) Classification tests:

$H_2SO_4 \cdot SO_3$—negative $Br_2 + CCl_4$—negative

$AlCl_3 + CHCl_3$—light yellow

(5) Derivatives: none.

sp $gr_4^{20} = 0.8963$ $n_D^{20} = 1.4811$

(6) Spectra:

Mass spectrometry: molecular formula of $C_{10}H_{18}$.

^{13}C NMR: δ 24.6 (CH_2), 29.6 (CH_2), and 36.9 (CH).

V. (1) White crystals, mp 187–188°C.

(2) Elemental analysis for X, N, S—negative.

(3) Solubility—water (+). Aqueous solution is acid to litmus.

(4) Classification tests:

$KMnO_4$—negative $C_6H_5NHNH_2$—negative

Br_2 in CCl_4—negative CH_3COCl—negative

Neutralization equivalent = 59

(5) Derivative: Heating with 4-bromophenacyl bromide gave white crystals, mp 209–210°C.

(6) Spectra:

IR (Nujol mull): 3333–3222 cm^{-1} (s, b); 1695, 1418, 1307, 1198, 913 cm^{-1} (all s).

^1H NMR (60 MHz, DMSO-d_6): δ 2.43, s; δ 11.80, bs; areas 2:1 (upfield singlet to downfield singlet). δ 11.80 shift is concentration dependent.

VI. (1) Reddish-brown solid, mp 72°C.

(2) Elemental analysis for N—positive; for X, S—negative.

(3) Solubility—water (−), NaOH (−), HCl (+). A solution of the compound in dilute hydrochloric acid was decolorized with Norit and alkali added. The compound purified in this manner melted at 73°C.

(4) Classification tests:

$KMnO_4$—positive	$C_6H_5SO_2Cl$ + NaOH—residue soluble in hydrochloric acid
Br_2 in CCl_4—precipitate	$Fe(OH)_2$—negative
Bromine water—precipitate	Tollens reagent—positive
$C_6H_5NHNH_2$—positive	

Hot sodium hydroxide decomposed the compound. After removal of a dark-brown solid by filtration, the filtrate was neutralized and a light-tan precipitate obtained. After recrystallization from a water–alcohol mixture, it melted with decomposition at 236–240°C. It was soluble in HCl and NaOH, insoluble in sodium bicarbonate. The original compound reacted with acetone and sodium hydroxide to give a yellow precipitate, mp 134–135°C.

(5) Derivatives:

Phenylhydrazone, mp 148°C.

Semicarbazone, mp 224°C.

(6) Spectra:

IR (Nujol mull): no absorption near 3333 cm^{-1}; absorptions at 1653 cm^{-1} (m) and 1587 cm^{-1} (s).

^1H NMR (60 MHz, $CDCl_3$) δ 3.05, 6H, s; δ 6.69, 2H, d; δ 7.71, 2H, d; δ 9.70, 1H, s.

Problem Set 8

1. A brown liquid (I) boiled at 193–195°C. It contained nitrogen but gave negative tests for sulfur and the halogens. It was insoluble in water but soluble in dilute acid. It did not react with acetyl chloride or benzenesulfonyl chloride. Treatment of a hydrochloric acid solution of the unknown compound with sodium nitrite, followed by neutralization, gave a compound (II) that melted at 164°C. Compound II was insoluble in alkalies but dissolved in boiling concentrated sodium hydroxide solution, with the liberation of a gas (III). This gas (III) was absorbed in water, and the aqueous solution was treated with phenyl isothiocyanate to form a compound (IV) with a melting point of 134–135°C. Careful acidification of the alkaline solution, followed by extraction, gave a compound (V) that melted at 125–126°C.

The ^1H NMR spectrum of compound V (60 MHz, acetone) showed δ 6.63, 2H, d; δ 7.67, 2H, d; δ 8.7, 1H, bs. The δ 8.7 signal was so broad as to be detectable only by electronic integration.

2. A colorless liquid was found to be soluble in water and in ether. It boiled at 94–96°C, and gave negative tests for the halogens, nitrogen, and sulfur. It reduced a dilute potassium permanganate solution, decolorized bromine in

carbon tetrachloride, reacted with acetyl chloride, and liberated hydrogen upon treatment with sodium. It did not give iodoform when treated with sodium hypoiodite and did not react with phenylhydrazine. Treatment with 3,5-dinitrobenzoyl chloride transformed it into a compound melting at 47–48°C.

The ^{1}H NMR spectrum of the original compound (60 MHz, $CDCl_3$) showed δ 3.58, 1H, s; δ 4.13, 2H, m; δ 5.13, 1H, m; δ 5.25, 1H, m; δ 6.0, 1H, 10 lines. The δ 3.58 signal showed a chemical shift that was concentration-dependent.

3. A yellow solid (I), melting at 113–114°C, contained nitrogen but no halogens, sulfur, or metals. It was insoluble in water and alkalies but soluble in dilute acids. The acid solution of I was treated with sodium nitrite in the cold and then boiled. The product (II) of this reaction separated when the solution was cooled. It contained nitrogen and melted at 95–96°C; it was insoluble in water and sodium bicarbonate solution but soluble in sodium hydroxide solution. The products obtained by treating compounds I and II with zinc and a boiling solution of ammonium chloride readily reduced Tollens reagent. The original compound (I) was treated with benzenesulfonyl chloride and alkali. Acidification of the resulting solution gave a compound (III) that melted at 135–136°C.

   The ^{1}H NMR spectrum of compound II (60 MHz, DMSO-d_6) showed δ 7.0–7.75, 4H, m; δ 9.8, 1H, s.

4. A colorless crystalline compound (I) melted at 186–187°C; it contained nitrogen but no halogens or sulfur. It was insoluble in water but soluble in dilute base and in dilute sodium bicarbonate solution. It gave a neutralization equivalent of 180 ± 2 but did not react with bromine in carbon tetrachloride, dilute potassium permanganate solution, acetyl chloride, or phenylhydrazine. It was treated for some time with boiling hydrochloric acid. When this reaction mixture was cooled, a compound (II) separated that melted at 120–121°C and gave a neutralization equivalent of 121 ± 1. The filtrate remaining after the removal of II was evaporated to dryness, and the residue (III) was purified by recrystallization. It contained nitrogen and chlorine, was rather hygroscopic, and decomposed when an attempt was made to determine is melting point. It was insoluble in ether, and its aqueous solution gave a precipitate with silver nitrate. A solution of III was treated with nitrous acid in the cold. A vigorous evolution of a gas was observed. Compound III was treated with benzenesulfonyl chloride and sodium hydroxide solution. Acidification of the resulting solution gave a new product (IV) that melted at 164–165°C.

   ^{1}H NMR spectra (60 MHz): I (NaOD, D_2O) showed δ 4.06, 2H, s; δ 4.77, HDO impurity, s; δ 7.5–8.0, 5H, m. II (CCl_4) showed δ 7.3–7.7, 3H, m; δ 8.0–8.25, 2H, m; δ 12.8, 1H, s. III (D_2O) showed δ 3.58, s; δ 4.9, HDO.

5. A colorless crystalline compound (I) melted at 168°C, with decomposition. It gave negative tests for nitrogen, halogens, sulfur, and metals. It was soluble in water but insoluble in ether. It reacted with acetyl chloride, decolorized permanganate solution, and reduced Fehling's solution and Tollens reagent. It reacted with phenylhydrazine to give a product (II) which melted, with decomposition, at 199–201°C. When I was warmed with concentrated nitric acid, a vigorous reaction took place, and a compound (III) separated when the reaction mixture was cooled. This compound (III) was insoluble in water but readily soluble in alkalies; it gave a neutralization equivalent of 104 ± 1. Compound III reacted with acetyl chloride but not with phenylhydrazine, and

it melted at about 212–213°C, with decomposition. If kept above its melting point for some time, it was converted into a new compound (IV) which melted at 132–133°C, after recrystallization. Compound IV was insoluble in water but soluble in sodium bicarbonate solution, and it gave a neutralization equivalent of 111 ± 1. Treatment of the sodium salt of IV with *p*-bromophenacyl bromide gave a compound (V) melting at 137–138°C.

The original compound (I) was optically active, having a specific rotation of +81°, but the degradation products III, IV, and V were optically inactive.

A solution of the sodium salt of IV (in D_2O) gave rise to these ^1H NMR signals: δ 6.59, 1H, m; δ 7.05, 1H, m; δ 7.64, 1H, m. A Nujol mull of IV gave these IR bands: 3100–2400 cm^{-1} (s); 1675 cm^{-1} (s); several bands in the 1667–1000 cm^{-1} region; 932 cm^{-1} (m); 885 cm^{-1} (m); 758 cm^{-1} (m).

Problem Set 9

1. A compound insoluble in water, sodium hydroxide, and hydrochloric acid but soluble in concentrated sulfuric acid and containing nitrogen melted at 68°C. When treated with tin and hydrochloric acid, it yielded a substance that reacted with benzenesulfonyl chloride to give an alkali-soluble derivative. When the original compound was treated with zinc and hot sodium hydroxide solution, it was converted to a new substance melting at 130°C.

   The product of the reaction with tin and hydrochloric acid was neutralized with base and then distilled. This distillate (in CCl_4) gave rise to the following ^1H NMR (60 MHz) spectrum: δ 3.32, 2H, s; δ 6.44, 2H, m; δ 6.6, 1H, m; δ 7.0, 2H, m.

2. A compound boiled at 166–169°C and contained sulfur but no nitrogen or halogen. It was insoluble in water but soluble in dilute sodium hydroxide solutions. Its sodium derivative reacted with 2,4-dinitrochlorobenzene to give a compound melting at 118–119°C. When allowed to stand in air, the original compound was slowly oxidized to a derivative melting at 60–61°C.

   The ^1H NMR spectrum of the air oxidation product (60 MHz, $CDCl_3$) showed only δ 7.2–7.7, m. The ^1H NMR spectrum of the original compound showed δ 3.39, 1H, s; δ 7.12, 5H, s.

3. A compound melted at 145–146°C and contained nitrogen but no halogen or sulfur. It was insoluble in water, dilute acids, and dilute alkalies. It was unaffected by treatment with tin and hydrochloric acid. When treated for a long time with hot sodium hydroxide solution, it reacted, forming an insoluble oil (I) (bp 200°C). The oil was soluble in dilute hydrochloric acid and reacted with acetyl chloride to give a solid (II) melting at 111–112°C. Acidification of the alkaline solution from which I was removed gave a solid melting at 120–121°C, whose neutralization equivalent was 122 ± 1.

   A ^1H NMR spectrum of the mp 120–121°C solid (60 MHz, $CDCl_3$) showed δ 7.4–7.7, 3H, m; δ 8.0–8.3, 2H, m; δ 12.8, 1H, s. The ^1H NMR spectrum of compound I (60 MHz, $CDCl_3$) showed: δ 2.15, 3H, s; δ 3.48, 2H, bs; δ 6.45–6.8, 2H, m; δ 6.8–7.15, 2H, m.

   Identify I and II and the original (mp 145–146°C) compound.

4. A compound boiled at 159–161°C and contained chlorine but no nitrogen or sulfur. It was insoluble in water, in dilute acids and alkalies, and in cold

concentrated sulfuric acid. It dissolved in fuming sulfuric acid. It gave no precipitate with hot alcoholic silver nitrate solution. Treatment with a hot solution of potassium permanganate caused the compound to dissolve slowly. The resulting solution, when acidified with sulfuric acid, gave a precipitate which melted at 138–139°C and had a neutralization equivalent of 157 ± 1.

A ^{1}H NMR spectrum of the original compound (60 MHz, $CDCl_3$) showed δ 2.37, 3H, s; δ 7.0–7.35, 4H, m. An IR spectrum of the material melting at 138–139°C (in a Nujol mull) showed bands at 3333–2381 cm^{-1} (s); 1678 cm^{-1} (s); several bands in the region 1587–1389 cm^{-1} (m); 1316 cm^{-1} (s); 1053, 1042 cm^{-1} (m); 913 cm^{-1} (bm); 742 cm^{-1} (s).

5. A colorless liquid boiled at 188–192°C. It contained only carbon, hydrogen, and oxygen. It was insoluble in water, dilute acids, and alkalies but dissolved readily in cold concentrated sulfuric acid. It did not react with phenylhydrazine or acetyl chloride and did not decolorize a carbon tetrachloride solution of bromine. Boiling alkalies dissolved it slowly. The resulting mixture was subjected to steam distillation. The distillate contained a compound which, when pure, boiled at 129–130°C and reacted with α-naphthyl isocyanate to give a derivative melting at 65–66°C. IR and ^{1}H NMR spectra were obtained from the bp 129–130°C material. The alkaline residue, left after the steam distillation, was acidified with phosphoric acid and steam-distilled. The distillate contained an acid which yielded an anilide melting at 108–109°C.

   Treatment of the original compound with lithium aluminum hydride (followed by the usual careful workup) resulted in only one compound, which showed NMR and IR spectra identical to those obtained from material of boiling point 129–130°C described above. The 60 MHz ^{1}H NMR spectrum showed: δ 0.92, 6H, d; δ 1.2–1.7, 3H, m; δ 2.13, 1H, bs; δ 3.63, 2H, t.

6. An unknown compound was a pink solid that melted at 109–112°C. Treatment with decolorizing carbon and recrystallization removed the color and brought the melting point to 112–114°C. The compound burned with a smoky flame and left no residue. Elemental analysis showed nitrogen to be present and sulfur and halogens to be absent. The compound was insoluble in water and dilute alkalies but dissolved in dilute acids. It reacted with benzenesulfonyl chloride to give a derivative that was soluble in alkali and melted at 101–102°C. The acetyl derivative melted at 132°C.

   Infrared bands for the original compound (5000–1250 cm^{-1} in $CHCl_3$, 1250–650 cm^{-1} in CS_2) were found at 3400, 3350, 3200, 3050, 1640, 1610, 1520, 1480, 1400, 1290, 1280, 1230, 1190, 1130, 970, 890, 870, 850, 820, 750, and 720 cm^{-1}.

Problem Set 10

For each of the problems in this and the following sets, give the structure of an organic compound which will fulfill the conditions stated and show by equations the changes it undergoes. Associate all major spectral bands with appropriate components of your answers.

1. An acid (A) containing only carbon, hydrogen, and oxygen had a neutralization equivalent of 103 ± 1. It gave a negative test with phenylhydrazine. Treatment with sulfuric acid converted it to a new acid (B) that decolorized permanganate

and bromine solutions and had a neutralization equivalent of 87 ± 1. The original acid (A) was transformed by hypoiodite to iodoform and a new acid (C), the neutralization equivalent of which was 52 ± 1.

The ^{1}H NMR spectrum of compound B (60 MHz, $CDCl_3$) showed δ 1.90, 3H, d of d (J = 8, 2 Hz); δ 5.83, 1H, d of q (J = 15, 2Hz); δ 7.10, 1H, m; δ 12.18, 1H, s.

2. An acid had a neutralization equivalent of 97. It could not be made to undergo substitution of bromine for hydrogen readily, even in the presence of phosphorus tribromide. Vigorous oxidation transformed it into a new acid whose neutralization equivalent was 83.

   The ^{1}H NMR spectrum of the second acid (60 MHz, $CDCl_3$) showed δ 8.08, s; δ 11.0, s; relative areas = 2:1 for the δ 8.08 to 11.0 signals.

3. An optically active hydrocarbon dissolved in cold, concentrated sulfuric acid, decolorized permanganate solutions, and readily absorbed bromine. Oxidation converted it to an acid containing the same number of carbon atoms as the parent substance and having a neutralization equivalent of 66. Mass spectrometry indicated the molecular ion of the hydrocarbon to be *m/z* 68.

4. A compound had a neutralization equivalent of 66. The substance was not affected by bromine in carbon tetrachloride, but heat transformed it into an acid whose neutralization equivalent was 88. The ^{1}H NMR spectrum of the latter acid (60 MHz, $CDCl_3$) showed δ 1.20, 6H, d; δ 2.57, 1H, septet; δ 12.4, 1H, bs.

5. A base had a neutralization equivalent of 121 ± 1. Vigorous oxidation converted it to an acid having a neutralization equivalent of 121 ± 1. The ^{1}H NMR spectrum of the acid (60 MHz, CCl_4) showed δ 7.52, 3H, m; δ 8.14, 2H, m; δ 12.82, 1H, s. The ^{1}H NMR spectrum of the base (60 MHz, $CDCl_3$) showed δ 0.91, 2H, s; δ 2.78, 4H, m; δ 7.23, 5H, s.

6. An acid whose neutralization equivalent was 166 was unaffected by bromine in carbon tetrachloride but gave a positive iodoform test.

7. A compound (A) gave negative tests for nitrogen, sulfur, and halogens. It was insoluble in water but dissolved in dilute sodium hydroxide solution. Compound A gave no color with ferric chloride and did not decolorize a solution of potassium permanganate. Treatment with concentrated hydrobromic acid converted A into two compounds. One was a compound (insoluble in all tests) containing bromine, which gave a precipitate with sodium iodide in acetone. The other was a new acid (B), which decolorized bromine solutions and gave a color with ferric chloride. Compound B contained no halogen. The neutralization equivalents of compounds A and B were, respectively, 180 ± 2 and 137 ± 1.

   The ^{1}H NMR spectrum of acid B (60 MHz, $CDCl_3$ containing DMSO-d_6) showed δ 6.84, 2H, d (J = 9 Hz); δ 7.86, 2H, d (J = 9 Hz); δ 8.2, 2H, bs.

8. An optically active acid had a molecular weight of 98.

9. A compound (I) gave a precipitate with 2,4-dinitrophenylhydrazine. Compound I was heated with 25% aqueous sodium hydroxide, and the mixture was partially distilled. The distillate contained a compound that reacted with sodium and gave a positive iodoform test. It gave a negative Lucas test. The residue from the distillation was acidified with phosphoric acid and the mixture steam-distilled. A volatile acid was isolated. Its *p*-bromophenacyl ester had a saponification number of 257 ± 1.

Mass spectral analysis of the original compound (I) gave rise to the following data (only peaks of intensity greater than or equal to 10% of the base peak are reported):

m/z	*Percent of Base*	*m/z*	*Percent of Base*
15	13.7	45	13.2
27	22.6	85	18.0
29	42.7	88	12.3
31	28.9	130	10.4
42	13.5	131	0.8
43	(100, base)		

The IR spectrum of a neat sample of compound I showed bands at 3000 cm^{-1} (m); 2933 cm^{-1} (w); 1715 cm^{-1} (s); 1634 cm^{-1} (w); 1408 cm^{-1} (w); 1364 cm^{-1} (m); 1316 cm^{-1} (s); 1250 cm^{-1} (s); 1149 cm^{-1} (s); 1042 cm^{-1} (s).

Problem Set 11

1. An acid (I) contained nitrogen and had a neutralization equivalent of 197 ± 2. Treatment with thionyl chloride followed by ammonium hydroxide converted I to a neutral compound (II) which reacted with an alkaline hypobromite solution to yield a basic compound (III). Hydrolysis of compound III produced a new compound (IV), soluble in both acids and bases and having a neutralization equivalent of 186 ± 2. Treatment of this compound with nitrous acid in the presence of sulfuric acid gave a clear solution. When copper cyanide was added to this solution, compound I was regenerated. Hydrolysis of I gave an acid (V) having a neutralization equivalent of 107 ± 1. Heat converted V into a neutral substance (VI), which could be reconverted to V by hydrolysis. Oxidation of compound IV gave a new acid (VII) having a neutralization equivalent of 71 ± 1.

   The ^1H NMR spectrum of structure I (60 MHz, $CDCl_3$ plus DMSO-d_6) showed the following signals (of area 1:1:1:1): δ 7.6, m; δ 7.9, m; δ 8.28, s; δ 11.8, bs. The δ 11.8 signal showed a concentration-dependent chemical shift. The two upfield multiplets, although complex, showed symmetry; the two signals were nearly mirror images of each other.

2. An unknown (I) was insoluble in water but soluble in both dilute acid and dilute alkali. It contained nitrogen and bromine. No satisfactory neutralization equivalent could be obtained. Treatment with acetic anhydride converted it into an acid (II) which gave a neutralization equivalent of 270 ± 3. When I was treated with cold nitrous acid, a gas was liberated and a compound (III) was produced which gave a neutralization equivalent of 230 ± 2. Compounds I, II, and III when vigorously oxidized gave the same product—a bromine-containing acid whose neutralization equivalent was found to be 199 ± 2.

   The ^1H NMR spectrum of the product of vigorous oxidation (60 MHz, $CDCl_3$ containing DMSO-d_6) showed δ 7.60, 2H, d; δ 7.95, 2H, d; δ 12.18, 1H, bs. The δ 12.8 signal showed a chemical shift which was concentration dependent.[4]

[4]The two doublets are separated from one another so much that the signal could be mistaken for a quartet centered at δ 7.75.

3. A solid ester (I) was saponified (saponification equivalent 173 ± 2), and the alkaline aqueous solution was evaporated nearly to dryness. The distillate was pure water. The residue was acidified and distilled; a colorless oil (II) was isolated. Substance II reacted with acetyl chloride and gave a violet color with ferric chloride solution. The residue from the distillation yielded a solid (III) which was alkali soluble. When III was heated above its melting point, it changed to IV; IV was dissolved by shaking with warm aqueous alkali, and the solution was acidified; the solid that separated was identical with III.

   The ^{1}H NMR spectrum of compound II (60 MHz, $CDCl_3$) showed δ 2.25, 3H, s; δ 5.67, 1H, s; δ 6.5–7.3, 4H, m. The δ 5.67 signal had a concentration-dependent chemical shift.

   The ^{1}H NMR spectrum of III (60 MHz, $CDCl_3$) showed δ 7.4–7.9, m, and δ 12.08, s; the singlet had an area one-half that of the multiplet. In addition, the chemical shift of the singlet was concentration dependent.

4. A solid (I) giving a positive test for nitrogen was soluble in water and insoluble in ether. Addition of cold alkali liberated a water soluble, ether soluble compound (II) which possessed an ammonia odor and reacted with benzenesulfonyl chloride to give a derivative insoluble in alkali. Addition of hydrochloric acid to a dilute aqueous solution of I gave a solid acid (III) which possessed a neutralization equivalent of 167 ± 2. After being boiled with zinc dust and ammonium chloride solution, it gave a compound (IV) that reduced Tollens reagent.

   The ^{1}H NMR spectrum of II (60 MHz, CCl_4) showed δ 0.53, 1H, s; δ 0.90, 6H, t, distorted; δ 1.2–1.7, 8H, m; δ 2.52, 4H, t.

   The ^{1}H NMR spectrum of III (60 MHz, $CDCl_3/CF_3CO_2H$) showed δ 7.77, 1H, t (J = 7 Hz); ca. δ 8.54, 2H, d of m (J = 7 Hz, ca. 2 Hz and smaller splittings); δ 8.96, 1H, t (J = ca. 2 Hz); δ 12.0, 1H, bs.

5. An optically active compound ($C_5H_{10}O$) was found to be slightly soluble in water. Its solubility was not increased appreciably by sodium hydroxide or hydrochloric acid. It gave negative tests with phenylhydrazine, Lucas reagent, and hypoiodite but decolorized solutions of bromine and permanganate. It reacted with acetyl chloride. Oxidation with permanganate converted it to an acid having a neutralization equivalent of 59 ± 1. When heated, the acid lost carbon dioxide and was converted to a new acid having a neutralization equivalent of 73 ± 1.

6. A compound (I) containing carbon, hydrogen, oxygen, and nitrogen was soluble in dilute sodium hydroxide solution and in dilute hydrochloric acid but insoluble in sodium bicarbonate solution. It reacted with an excess of acetic anhydride to give a product (II) which was insoluble in water, in dilute acids, and in dilute alkalies. Compound I decolorized bromine water; when I was dissolved in an excess of dilute hydrochloric acid and the cold solution was treated with sodium nitrite, a new product (III) separated without the evolution of nitrogen.

   The ^{1}H NMR spectrum of I (CF_3COOH) showed δ 3.31, 1H, bs; δ 3.65, 3H, s; δ 5.51, 1H, bs; δ 7.12, 2H, d (J = 10 Hz); δ 7.49, 2H, d (J = 10 Hz);

Problem Set 12

1. When a solid, $C_9H_6O_2$ (I), was heated with a dilute solution of potassium carbonate, it was converted to the potassium salt of an acid, $C_9H_8O_3$ (II). The salt

reverted to I when treated with acids. Compound I reacted with bromine in carbon tetrachloride to yield $C_9H_6O_2Br_2$ (III). When heated with a solution of sodium hydroxide, compound III gradually went into solution. Acidification of the solution precipitated a compound, $C_9H_6O_3$ (IV).

The ^{1}H NMR spectrum of acid II (60 MHz, $CDCl_3$ containing DMSO-d_6) showed δ 6.4–8.2, m; δ 10.3, very broad s. The δ 10.3 signal showed a chemical shift that was dependent on sample concentration; the area of this signal was one-third that of the δ 6.4–8.2 signal.

2. A compound, C_8H_8ONBr, when treated with boiling potassium hydroxide solution, gave the potassium salt of an acid, $C_8H_8O_3$, which was resolvable into (+) and (−) forms.

   A ^{1}H NMR spectrum of the acid of formula $C_8H_8O_3$ (60 MHz, acetone) showed δ 5.22, 1H, s; δ 7.2–7.7, 7H, m. The chemical shift of the δ 5.22 signal was not concentration dependent.

3. A compound, $C_{11}H_{12}O_4$ (I), reacted with hot sodium hydroxide solution to yield a salt, $C_{11}H_{13}O_5Na$ (II). Treatment of the salt with hot dilute sulfuric acid converted it to an acid, $C_9H_8O_4$ (III). Heat converted compound III to a high-melting compound, $C_{18}H_{12}O_6$ (IV).

4. A compound, $C_5H_8O_2$ (I), was changed to $C_5H_9O_2Cl$ (II) by treatment with boiling concentrated hydrochloric acid. Compound II reacted slowly with a solution of potassium hydroxide to yield $C_5H_9O_3K$ (III). This compound was converted into $C_5H_8O_3$ (IV) by treatment with an alkaline permanganate solution. Compound IV, when treated with a solution of sodium hypochlorite, was transformed into $C_4H_6O_4$ (V), an acid whose neutralization equivalent was 58 ± 1. This acid, when heated, gave $C_4H_4O_3$ (VI). When the aqueous solution of II was made exactly neutral with sodium hydroxide solution, the original compound (I) was slowly regenerated.

   The ^{1}H NMR spectrum of V (60 MHz, DMSO-d_6) showed only two singlets, one at δ 2.43 and the other at δ 11.8. The two singlets were of area 2:1, respectively, and the δ 11.8 signal was very broad.

5. A solid neutral compound had the formula $C_7H_7NO_3$. The ^{1}H NMR spectrum of this compound (60 MHz, CCl_4) showed δ 3.89, 3H, s; δ 6.91, 2H, d (J = 10 Hz); δ 8.12, 2H, d (J = 10 Hz).

6. A compound, $C_{16}H_{13}N$, formed salts with strong mineral acids. The salts were hydrolyzed by water. The ^{1}H NMR spectrum of this compound (in CCl_4) showed δ 5.61, 1H, bs; δ 6.60–7.55, 10H, m; δ 7.80, 2H, m.

7. A compound, $C_{14}H_{10}O$, gave $C_{13}H_{10}O_3$ when oxidized by alkaline permanganate. The original compound reacted with sodium to give $C_{14}H_9ONa$.

8. An acid of neutralization equivalent 57 was unaffected by bromine in carbon tetrachloride.

Problem Set 13

1. A liquid, $C_5H_4O_2$ (I), decolorized a permanganate solution and also reduced Tollens solution. When heated with an alkali cyanide, compound I dimerized. Treatment of compound I with excess ethanol in the presence of an acid catalyst converted it to a new substance, $C_9H_{14}O_3$.

   The ^{1}H NMR spectrum of compound I (60 MHz, $CDCl_3$) showed δ 6.63, 1H, d of d (J = 5, 2 Hz); δ 7.28, 1H, d (J = 5 Hz); δ 7.72, 1H, m; δ 9.67,

1H, s. The chemical shift position of the δ 9.67 signal was not concentration dependent.

2. A compound, $C_4H_4O_4$ (I), was soluble in dilute sodium hydroxide solution and when treated with bromine was converted into $C_4H_4Br_2O_4$ (II). Compound I was regenerated from II by treatment of the latter with zinc dust. Compound I was converted into compound III by hydrogenation in the presence of nickel. Compound III possessed a neutralization equivalent of 59 and lost a molecule of water when heated. The anhydride (IV) then reacted with benzene in the presence of aluminum chloride to give $C_{10}H_{10}O_3$ (V), which was soluble in alkali, reacted with phenylhydrazine, and was converted into benzoic acid by vigorous oxidation.

   The ^{1}H NMR spectrum of the compound of formula $C_{10}H_{10}O_3$ (60 MHz, $CDCl_3$) showed δ 2.8, 2H, t (J = 7 Hz); δ 3.3, 2H, t (J = 7 Hz); δ 7.2–7.6, 3H, m; δ 8.0, 2H, m; δ 11.7, 1H, s. The chemical shift of the δ 11.7 signal was concentration dependent.

3. A compound, $C_{11}H_{10}N_2$, was converted by vigorous oxidation to $C_{11}H_8N_2O$.

4. A compound, $C_5H_{10}O$, decolorized an alkaline solution of potassium permanganate but was not affected by bromine in carbon tetrachloride. The mass spectrum of this compound (bp 75°C) resulted in the following peaks of intensity greater than or equal to 5% of the base peak:

m/z	*Percent of Base*	*m/z*	*Percent of Base*
86	34	41	83
57	(100, base)	39	17
55	7	29	40
43	18	27	11

5. A compound, $C_{14}H_{12}O$, was converted by chromic acid oxidation into an acid whose neutralization equivalent was 226. The ^{1}H NMR spectrum of the oxidation product (60 MHz, $CDCl_3$ containing DMSO-d_6) showed δ 7.45–7.95, 7H, m; δ 8.19, 2H, d (J = 7 Hz); δ 10.8, 1H, bs.

6. A neutral compound, $C_{10}H_6O_4$ (I), when heated with a sodium hydroxide solution, was converted to the salt of an acid (II) having a neutralization equivalent of 209 ± 2. Compound I reacted with alkaline hydrogen peroxide to yield a new acid (III) having a neutralization equivalent of 111 ± 1.

   The ^{1}H NMR spectrum of compound I (60 MHz, $CDCl_3$) showed δ 6.64, 2H, d of d (J = 5 Hz, 2 Hz); δ 7.63, 2H, d (J = 5 Hz); δ 7.78, 2H, d (J = 2 Hz).

7. A compound, $C_{10}H_7NO_2$ (I), when treated with iron and hydrochloric acid, was converted into $C_{10}H_9N$ (II), which was soluble in dilute hydrochloric acid. By vigorous oxidation of I and II, $C_8H_5O_6N$ and $C_8H_6O_4$, respectively, were produced. Both oxidation products were soluble in alkali.

   The ^{1}H NMR spectrum of I (60 MHz, $CDCl_3$) showed a complex multiplet extending from δ 7.15 to δ 8.5. The product of oxidation of II, $C_8H_6O_4$, when heated, lost the elements of water.

Problem Set 14

1. A naturally occurring compound, $C_{10}H_{10}O_2$ (I), was found to be unreactive toward acetyl chloride and phenylhydrazine. Heating with potassium hydroxide, however, brought about isomerization. The isomer (II) also failed to react with

acetyl chloride and phenylhydrazine. Both isomers decolorized solutions of bromine and permanganate. Ozone converted isomer II to a compound (III) which formed a phenylhydrazone. Oxidation of compound II or III with alkaline potassium permanganate yielded an acid, $C_8H_6O_4$ (IV).

The ^1H NMR spectrum of I (60 MHz, $CDCl_3$) showed δ 3.30, 2H, d of m (J = 7 Hz, additional small splittings); δ 4.90, 1H, m; δ 5.15, 1H, m; δ 5.88, 2H, s; ca. δ 5.6–6.2, 1H, m (a wide band, highly split); δ 6.67, 3H, s (with small splittings).

2. A compound, $C_8H_5ClO_2$ (I), when heated with absolute alcohol, gave $C_{14}H_{20}O_4$ (II), which by oxidation with alkaline permanganate was converted after acidification into $C_8H_6O_4$. Treatment with aniline converted I into $C_{20}H_{16}N_2O$. The product of permanganate oxidation was converted by treatment with excess thionyl chloride to compound III, $C_8H_4Cl_2O_2$. Compound III yielded a ^1H NMR spectrum (60 MHz, $CDCl_3$) showing δ 7.72, 1H, t (J = 7 Hz); δ 8.33, 2H, t of d (J = 7, 2 Hz); δ 8.82, 1H, t (J = 2 Hz).

3. A compound, $C_8H_{14}O_3$ (I), was soluble in dilute sodium hydroxide solution. Phenylhydrazine converted I into $C_{12}H_{14}N_2O$ (II), and heating with 20% hydrochloric acid transformed I into $C_5H_{10}O$ (III). Compound III gave a crystalline precipitate when treated with semicarbazide but when treated with a solution of sodium hypoiodite gave no iodoform.

   The compound arising from semicarbazide treatment of III, when dissolved in $CDCl_3$, yielded a ^1H NMR spectrum (60 MHz) that showed δ 1.09, 6H, t; δ 2.26, 4H, q; δ 5.89, 2H, bs; δ 8.59, 1H, bs.

4. A compound, C_9H_7N (I), was converted by catalytic reduction into $C_9H_{11}N$ (II). When compound II was treated with an excess of methyl iodide followed by wet silver oxide and the reaction product heated, a compound, $C_{11}H_{15}N$ (III), was produced. This compound was converted (a) by vigorous oxidation into $C_8H_6O_4$ (IV); (b) by treatment with ozone and hydrolysis of the reaction product into $C_{10}H_{13}NO$ (V). The ozonization product yielded $C_{20}H_{26}N_2O_2$ (VI) when heated with a dilute solution of potassium cyanide. Compound VI was converted into IV by vigorous oxidation.

   Compound I (60 MHz, $CDCl_3$) yielded a ^1H NMR spectrum showing δ 7.25–8.1, 5H, m; δ 8.52, 1H, d (J = 7 Hz); δ 9.26, 1H, s.

5. A compound, $C_{10}H_{10}O$ (I), reacted with sodium to give a derivative, $C_{10}H_9ONa$, which gave I when treated with water. Treatment of compound I with cold 80% sulfuric acid in the presence of mercuric sulfate and then with water gave $C_{10}H_{12}O_2$ (II). This compound dissolved slowly in a solution of sodium hypochlorite, and by acidification of the solution $C_9H_{10}O_3$ (III) was obtained. Boiling 48% hydrobromic acid converted compound III into $C_8H_7BrO_2$ (IV), a compound transformed by vigorous oxidation into $C_8H_6O_4$.

   The ^1H NMR spectrum of the compound of formula $C_8H_6O_4$ (60 MHz, $CDCl_3$ containing DMSO-d_6) showed only two singlets of area 2:1 at, respectively, δ 8.08 and δ 11.0.

6. A compound having the molecular formula $C_{14}H_{12}$ was converted by permanganate oxidation into a derivative of molecular formula $C_{13}H_{10}O$, which was not affected by further treatment with permanganate.

   The ^1H NMR spectrum of the original compound (100 MHz, CCl_4) showed δ 5.35, 2H, s; δ 7.21, 10H, s (slightly distorted near the base).

7. An optically active compound, $C_9H_{13}N$, was converted by vigorous oxidation into an acid whose neutralization equivalent was 83. A closely related isomer of the original compound yielded a ^1H NMR spectrum (60 MHz, $CDCl_3$) which showed δ 0.95, 2H, s; δ 2.30, 3H, s; δ 2.5–3.0, 4H, m (8 lines, symmetrical); δ 7.05, 4H, s. Oxidation of this isomer (which was not optically active) resulted in the same acid as was obtained upon oxidation of the original compound.

8. A compound did not decolorize bromine water but reacted with sodium to give $C_8H_6O_3Na_2$. It had a neutralization equivalent of 152. This compound was not optically active, and vigorous oxidation converted it to an acid, $C_8H_6O_4$, of neutralization equivalent 82 ± 2. A ^1H NMR spectrum of this acid (60 MHz, $CDCl_3$ containing DMSO-d_6) showed δ 8.08, 4H, s; δ 11.0, 2H, bs.

Problem Set 15

1. A colorless, crystalline solid (I) contained nitrogen but no halogen or sulfur. It was soluble in water but insoluble in ether. Its aqueous solution was acidic and gave a neutralization equivalent of 123 ± 1. It was treated with sodium nitrite and hydrochloric acid. A gas evolved, one-third of which was soluble in potassium hydroxide solution. The solution from the nitrous acid treatment was evaporated to dryness; only sodium chloride, sodium nitrate, and sodium nitrite were left. Compound I was heated with dilute sodium hydroxide solution; ammonia was evolved, and the solution on acidification gave off a gas. Evaporation of this solution left only inorganic salts.

   The original compound was carefully neutralized with base under mild conditions to give a solid of melting point 135°C. The UV spectrum of this solid, in the presence of sodium hydroxide, showed no features above 220 nm. The solid resulted in the following spectra.

   Mass spectrum (only peaks of intensity greater than or equal to 10% of base are reported):

m/z	*Percent of Base*
60	(100, base)
44	60
43	18
28	17

   The IR spectrum showed peaks at 3450, 3350, 1690, 1640, 1600, 1470, 1160, 1050, 1000, 790, and 710 cm^{-1}.

2. An unknown compound containing carbon, hydrogen, oxygen, and nitrogen was insoluble in water, in dilute acids, and in dilute alkalies. It did not react with acetyl chloride or phenylhydrazine and was not easily reduced. When treated with hot aqueous alkali, the substance slowly dissolved. Distillation of this alkaline solution gave a distillate containing a compound which was salted out by means of potassium carbonate. This compound gave the iodoform test but no reaction with a hydrochloric acid solution of zinc chloride. The original alkaline solution (residue from the distillation) was acidified with sulfuric acid, and the solution was again distilled; a volatile acid was obtained in the distillate. This distillate reduced permanganate. The residual liquor from this second distillation was exactly neutralized, and a solid was obtained. This solid contained nitrogen and possessed a neutralization equivalent of 137 ± 1.

A 100-mg sample of the volatile acid (in 0.5 mL of CCl_4) yielded a ^1H NMR spectrum which showed δ 5.8–6.75, 3H, m; δ 12.4, 1H, s. The ^1H NMR spectrum of a 60-mg sample of the solid of neutralization equivalent 137 (dissolved in 0.5 mL of acetone) showed δ 6.55, 3H, s (shift position was concentration dependent); δ 6.75, 2H, d (J = 8 Hz); δ 7.83, 2H, d (J = 8 Hz). The compound that salted out with potassium carbonate showed, among other bands, one ^1H NMR signal whose chemical shift was concentration dependent and which appeared as a singlet when the analysis was done in a $CDCl_3$ solution and as a triplet (J = ca. 7 Hz) when done in a DMSO-d_6 solution.

3. An acid, $C_6H_8O_4$ (I), was converted into $C_6H_6O_2Cl_2$ (II) by phosphorus pentachloride. The chlorine derivative, when treated with benzene in the presence of anhydrous aluminum chloride, gave $C_{18}H_{16}O_2$ (III). This compound did not decolorize permanganate but decolorized a bromine solution and readily formed a dioxime. The dioxime rearranged under the influence of phosphorus pentachloride to yield $C_{18}H_{18}O_2N_2$ (IV), a compound which gave the original acid (I) when hydrolyzed.

   The ^1H NMR spectrum of compound I (60 MHz, CCl_4) showed δ 2.2–2.6, 4H, m; δ 3.90, 2H, t (distorted, J = ca. 7 Hz); δ 11.9, 2H, bs.

4. A compound (I) contained carbon, hydrogen, oxygen, nitrogen, and chlorine. It was soluble in water but insoluble in ether. The aqueous solution immediately gave a precipitate with silver nitrate. When the aqueous solution of I was exactly neutralized, a new compound (II) free from chlorine separated. It reacted with acetic anhydride to give an alkali soluble, acid insoluble compound (III) possessing a neutralization equivalent of 207 ± 2. Compound II reacted with benzenesulfonyl chloride to give an alkali soluble product and with nitrous acid without evolution of any gas even when heated. The product from the latter treatment still contained nitrogen and was soluble in alkalies and insoluble in acids. Vigorous oxidation of either I, II, or III gave a nitrogen-free acid, insoluble in water, and possessing a neutralization equivalent of 82 ± 2.

   The ^1H NMR spectrum of this nitrogen-free acid (60 MHz, $CDCl_3$ containing DMSO-d_6) showed δ 7.62, 1H, t (J = 7 Hz); δ 8.25, 2H, distorted doublet (J = ca. 2 Hz); δ 8.70, 1H, distorted s; δ 12.28, 2H, s.

5. A compound, $C_{10}H_6O_3$ (I), decolorized alkaline permanganate and reacted with hydroxylamine. It decomposed when distilled at ordinary pressure to give $C_9H_6O_2$ (II), a compound which yielded a monosodium derivative and was readily oxidized to $C_8H_6O_4$ (III). Compound III was an acid which, when heated with soda lime, was converted into $C_7H_6O_2$ (IV). Compound IV was decomposed by heating with dilute hydrochloric acid under pressure and yielded a weakly acidic compound having the formula $C_6H_6O_2$.

   The ^1H NMR spectrum of compound IV (60 MHz, $CDCl_3$) showed δ 5.90, 2H, s; δ 6.83, 4H, s (slight distortions at the bottom of this signal). The spectrum of compound III ($CDCl_3$) showed δ 6.00, 2H, s; δ 6.8, 1H, d (J = 7 Hz); δ 7.38, 1H, d (J = 2 Hz); δ 7.55, 1H, d of d (J = 7, 2 Hz); δ 7.6, 1H, bs. The chemical shift of the δ 7.6 signal was concentration dependent.

Problem Set 16

1. A compound (A) contained only carbon, hydrogen, and oxygen. It was insoluble in water, dilute acids, and dilute alkalies but dissolved in cold concentrated sulfuric acid. It gave negative tests with phenylhydrazine and acetyl chloride.

When heated with alkali and neutralized, it yielded an oil (B) and a volatile acid having a neutralization equivalent of 59 ± 1. Compound B reacted with acetyl chloride but not with phenylhydrazine. Treatment with a concentrated solution of hydrogen bromide transformed it into a bromine-containing compound (C) which gave positive tests with silver nitrate, ferric chloride, and bromine water.

Mild oxidation converted B to an acid (D) having a neutralization equivalent of 164 ± 2.

Treatment of acid D with ethyl alcohol and a trace of sulfuric acid resulted in compound E. The ^{1}H NMR spectrum of compound E (60 MHz, CCl_4) showed δ 1.35, t (J = 7 Hz); δ 1.40, t (J = 7 Hz); δ 3.8–4.5, 4H, 6 lines (relative intensities 1:3:4:4:3:1, spaced by ca. 7 Hz each); δ 6.79, 2H, d (J = 9 Hz); δ 7.89, 2H, d (J = 9 Hz). The signals at δ 1.35 and δ 1.40 had a combined area of 6H.

2. A compound (I), giving positive tests for nitrogen and chlorine, was insoluble in water and sodium bicarbonate solution but soluble in sodium hydroxide solution. A neutralization equivalent of 210 ± 2 was obtained. Compound I reacted with acetyl chloride but not with hot alcoholic silver nitrate. The acetyl derivative (II) had a neutralization equivalent of 253 ± 2. Boiling alkali liberated ammonia from I, and acidification of the resulting solution precipitated a new acid (III), which had a neutralization equivalent of 115 ± 1. Compound III contained chlorine but no nitrogen. When compound III was boiled with potassium permanganate solution, a new compound having the same solubility characteristics as I was produced which still contained chlorine and gave a neutralization equivalent of 81 ± 1.

Compound IV (neutralization equivalent 71) could be chlorinated to give the compound of neutralization equivalent 81; compound IV yielded a ^{1}H NMR spectrum (60 MHz, $CDCl_3$/DMSO-d_6) displaying δ 7.57, 1H, t (J = 7 Hz); δ 8.18, 2H, d (J = 7 Hz); δ 11.2, 3H, bs.

The IR spectrum of I (in Nujol) showed, among other bands, strong absorptions at 1779 cm^{-1} and 1712 cm^{-1}.

3. A neutral compound (A) was a colorless solid that gave negative tests for nitrogen, sulfur, and the halogens. It gave positive tests with phenylhydrazine and acetyl chloride. Mild oxidation converted it to a new compound, a yellow solid (B). The new compound (B) gave a positive test with phenylhydrazine but a negative test with acetyl chloride. Vigorous oxidation of B converted it into an acid (C) with a neutralization equivalent of 121 ± 1.

The ^{1}H NMR spectrum of compound A (60 MHz, $CDCl_3$) showed δ 4.5, 1H, bs; δ 5.9, 1H, bs; δ 7.2–7.5, 8H, m (the major part of which was a sharp singlet); δ 7.85, 2H, d of d.

4. A liquid (I) containing chlorine was insoluble in water, dilute hydrochloric acid, and dilute sodium hydroxide. It dissolved in cold concentrated sulfuric acid. It gave no precipitate with warm alcoholic silver nitrate and did not react with acetyl chloride. It gave a precipitate with phenylhydrazine but gave a negative Tollens test. When boiled with concentrated sodium hydroxide solution, compound (I) dissolved. The distillate from this alkaline solution gave a positive iodoform test. Acidification of the alkaline solution precipitated a compound (II) which contained chlorine and had a neutralization equivalent of 156 ± 1. Compound II was not affected by permanganate solution. After removal of compound II, a portion of the acidic filtrate was distilled, and the distillate was

found to be acid to litmus. The original compound (I) had a saponification equivalent of 113 ± 1. The acidic filtrate yielded a compound with a neutralization equivalent of 61 ± 1.

The ^{1}H NMR spectrum of compound II (60 MHz, $CDCl_3$/DMSO-d_6) showed δ 7.1–7.5, 3H, m (primarily a large singlet); δ 7.82, 1H, m; δ 9.0, 1H, bs.

5. A liquid had a saponification equivalent of 163 ± 1. Saponification yielded an oil, which gave a positive ferric chloride test, and an acid of neutralization equivalent 60 ± 1.

   The ^{1}H NMR spectrum of 49 mg of the oil (60 MHz) in 0.5 mL of CCl_4 showed δ 2.18, 6H, s; δ 5.73, 1H, s; δ 6.33, 2H, s; δ 6.45, 1H, s. Upon addition of more CCl_4, the δ 5.73 signal moved upfield.

Problem Set 17

1. An ether-insoluble compound (I), containing nitrogen, dissolved in water, giving an alkaline solution. Titration of this solution with standard acid gave a neutralization equivalent of 37 ± 1. Treatment of a cold solution of I with sodium nitrite and hydrochloric acid liberated a gas. The solution of NE = 37 was made distinctly alkaline, and benzoyl chloride was added. A neutral nitrogen-containing compound (II) separated. Compound II was shown by mass spectrometry to have a molecular weight of 282. When treatment of I with sodium nitrite and hydrochloric acid was followed by addition of benzoic anhydride, a neutral compound (III) was obtained which contained no nitrogen and had a saponification equivalent (SE) of 142 ± 1.

   The ^{1}H NMR spectrum of compound I (60 MHz, $CDCl_3$) showed δ 1.08, s; δ 1.58, quintet (J = 7 Hz, relative intensities 1:4:6:4:1); δ 2.75, t. The relative signal areas were, from high to low field, 2:1:2.

2. A colorless liquid (I) gave no tests for halogen, nitrogen, sulfur, or metals. It was insoluble in water, dilute hydrochloric acid, and dilute sodium hydroxide but soluble in cold concentrated sulfuric acid. It did not react with acetyl chloride or phenylhydrazine. It was boiled with dilute phosphoric acid, and an oil (II) separated when the solution was cooled. Compound II gave a precipitate with phenylhydrazine and with sodium bisulfite solution but did not react with acetyl chloride. When II was vigorously shaken with strong alkali, a compound (III) separated from the alkaline solution. This product (III) reacted with acetyl chloride but not with phenylhydrazine. Acidification of the alkaline solution gave IV, which had a neutralization equivalent of 136 ± 1. Strong oxidation of IV gave an acid (V) with a neutralization equivalent of 82 ± 1.

   The phosphoric acid solution, from which II was separated, was distilled. The distillate was saturated with potassium carbonate, and a compound (VI) was obtained. This compound reacted with sodium and acetyl chloride and gave a yellow precipitate with sodium hypoiodite. It did not react with Lucas reagent.

   The ^{1}H NMR spectrum of II (60 MHz, $CDCl_3$) showed δ 2.42, 3H, s; δ 7.18, 2H, d (J = 8 Hz); δ 7.66, 2H, d (J = 8 Hz); δ 9.81, 1H, s.

3. A colorless liquid (I) gave no tests for nitrogen, sulfur, or halogen. It was soluble in water and ether. It did not react with sodium, acetyl chloride, phenylhydrazine, or dilute permanganate solution. It did not decolorize bromine in carbon tetrachloride. When compound I was heated with an excess of hydro-

bromic acid, an oil (II) separated. This oil (II) contained bromine and readily gave a precipitate with alcoholic silver nitrate. It was insoluble in water, acids, and alkalies. After II was dried and purified, it was treated with magnesium in pure ether. A reaction occurred, with the liberation of a gas (III). No Grignard reagent could be detected. Treatment of II with alcoholic potassium hydroxide liberated a gas (IV). Both III and IV decolorized bromine water and reduced permanganate solutions. A careful examination of the action of hydrobromic acid on compound I showed that II was the only organic compound produced and that no gases were evolved during this reaction.

The mass spectrum of compound I showed peaks at *m/z* values (relative abundance) as follows: *m/z* 88 (65); *m/z* 89 (32); *m/z* 90 (3); and no peaks at higher mass. The ^{1}H NMR spectrum of I (60 MHz, $CDCl_3$) showed only a singlet at δ 3.69.

4. A compound (I) containing carbon, hydrogen, nitrogen, and oxygen was insoluble in acids and dilute alkalies. When heated for some time with hydrochloric acid, compound I yielded a solid acid (II) having a neutralization equivalent of 180 ± 1. When compound I was oxidized with potassium dichromate and sulfuric acid, it yielded a solid, nitrogen-containing acid (III) with a neutralization equivalent of 166 ± 1. Compound I reacted with benzaldehyde in the presence of alkalies to give a benzal derivative.

   When compound I was treated with tin (II) chloride and hydrogen chloride in dry ether and the resulting mixture was treated with water, a new compound (IV), whose molecular formula was C_8H_7N, resulted. Analysis showed IV to possess one active hydrogen atom. Compound IV was weakly basic and was resinified by acids.

   The ^{1}H NMR spectrum of I (60 MHz, $CDCl_3$) showed signals at δ 4.25, 2H, s; δ 7.5–8.0, 3H, m; δ 8.25, 1H, d (distorted slightly). The spectrum of II (60 MHz, $CDCl_3$ containing DMSO-d_6) showed δ 4.02, 2H, s; δ 7.3–7.65, 3H, m; δ 8.0, 1H, d (distorted); δ 11.2, 1H, bs. The spectrum of III (60 MHz, $CDCl_3$ containing DMSO-d_6) showed δ 7.5–8.0, 4H, m; δ 12.15, 1H, s. The spectrum of IV (60 MHz, $CDCl_3$) showed δ 6.38, 1H, m; δ 6.76, 1H, t (distorted); δ 6.95–7.10, 4H, m; δ 7.4–7.65, 1H, m.

Problem Set 18

1. A colorless, oily liquid (I) having an agreeable odor and containing only carbon, hydrogen, and oxygen reacted with phenylhydrazine but not with acetyl chloride, and it readily decolorized potassium permanganate solution. When it was treated with a concentrated sodium hydroxide solution and the reaction mixture acidified, two products were obtained: an oxygen-containing compound (II) which reacted with acetyl chloride, and an acid (III) which at 200°C lost carbon dioxide to yield an oxygen-containing compound (C_4H_4O). The latter decolorized permanganate solutions but did not react with sodium or phenylhydrazine. When compound I was warmed with potassium cyanide, a compound (IV) was produced. Compound IV gave positive acetyl chloride and phenylhydrazine tests and, on oxidation with periodic acid, was converted to the original compound (I) and to the acid (III).

   The ^{1}H NMR spectra of some of the above compounds showed the following signals.

Chemical Shift	*No. of Protons*	*Multiplicity*
Compound I in ($CDCl_3$)		
δ 6.63	1H	d of d (J = 5 Hz, 2 Hz)
δ 7.28	1H	d (J = 5 Hz)
δ 7.72	1H	m
δ 9.67	1H	s
Compound II (in $CDCl_3$)		
δ 2.83	1H	s (chemical shift concentration dependent)
δ 4.57	2H	s
δ 6.33	2H	m
δ 7.44	1H	m
Compound III (in DMSO-d_6)		
δ 6.56	1H	m
δ 7.20	1H	m
δ 7.65	1H	m
δ 12.18	1H	bs
Compound of formula C_4H_4O (in $CDCl_3$)		
δ 6.37	2H	t
δ 7.42	2H	t

2. A weakly acidic compound (I) contained nitrogen but no sulfur or halogens. It reacted with acetyl chloride but not with phenylhydrazine. When compound I was heated with dilute acids, a new compound (II) was obtained; it was isolated by distillation from the acid solution and saturation of the distillate with potassium carbonate. Compound II did not react with acetyl chloride or Tollens reagent but gave positive tests with phenylhydrazine and sodium bisulfite.

When compound I was warmed with phosphorus pentachloride and poured into water, a new compound (III) was obtained. Compound III still contained nitrogen but no halogen, was neutral, and was decomposed by alkalies. By the addition of benzoyl chloride to this alkaline solution an acid (IV) was obtained. It gave a neutralization equivalent of 220 ± 2. When compound IV was heated for some time with dilute acids and distilled, two products resulted. One (V) contained no nitrogen, was acidic, and gave a neutralization equivalent of 120 ± 2. The other proved to be identical with III. When III was treated with cold concentrated hydrochloric acid, a compound (VI) was obtained which contained nitrogen and chlorine and was soluble in water. It liberated a gas when treated with cold sodium nitrite solution.

The following ^1H NMR spectra were determined.

Chemical Shift	*No. of Protons*	*Multiplicity*
Compound I (in $CDCl_3$)		
δ 1.77	4H	m
δ 2.40	4H	m
δ 9.12	1H	bs
Compound III (in $CDCl_3$)		
δ 1.80	4H	m
δ 2.38	2H	m
δ 3.32	2H	m
δ 7.60	1H	bs

3. A compound (I) soluble in water but not in ether was decomposed by heat into a compound (II), which was insoluble in all tests, and a basic compound (III). When II and III were heated together, I was reformed. Both I and II gave a

precipitate immediately when treated with silver nitrate. Compound III did not give a benzenesulfonamide but yielded a nitroso derivative.

The following ^{1}H NMR spectra (60 MHz) were determined.

Chemical Shift	*No. of Protons*	*Multiplicity*
Compound I (D_2O; 80 mg/0.5 mL)		
δ 3.70	9H	s
δ 7.4	5H	m
Compound II ($CDCl_3$ solvent)		
δ 2.20	—	s
Compound III ($CDCl_3$ solvent)		
δ 2.85	6H	s
δ 6.4–6.7	3H	m
δ 7.10	2H	m

4. A neutral compound (I) gave positive tests for chlorine, bromine, and iodine. Alcoholic silver nitrate gave a white precipitate which was readily soluble in ammonia. Phenylhydrazine produced a precipitate, but acetyl chloride failed to react. When compound I was shaken with cold dilute alkali for some time, it dissolved. Acidification of the alkaline solution produced a compound (II) which gave positive tests for bromine and iodine and possessed a neutralization equivalent of 369 ± 3. When compound I was boiled with dilute alkali and then acidified, a compound (III) precipitated which gave a positive test for iodine. Compound III possessed a neutralization equivalent of 306 ± 3 and reacted with both phenylhydrazine and acetyl chloride. Treatment of I or II with sodium hypochlorite and acidification yielded an acid containing iodine and having a neutralization equivalent of 146 ± 1.

5. A neutral compound (A) contained bromine but no nitrogen or other halogens. It did not react with hot alcoholic silver nitrate solution, acetyl chloride, phenylhydrazine, or bromine in carbon tetrachloride. It dissolved in boiling sodium hydroxide solution, but the distillate from this alkaline solution contained no organic compounds. Acidification of the alkaline solution with phosphoric acid caused the precipitation of a compound (B) containing bromine and having a neutralization equivalent of 200 ± 2. Steam distillation of the acid solution gave a distillate that was repeatedly extracted with chloroform. Removal of the chloroform left a colorless liquid (C) which was purified by distillation. Compound C contained no bromine and was soluble in sodium bicarbonate solution. It had a neutralization equivalent of 102 ± 1. After removal of C, the solution remaining in the steam distillation flask was made distinctly alkaline, benzoyl chloride added, and the mixture shaken vigorously. A new compound (D) separated from the alkaline solution. Compound D contained no bromine and was neutral. It had a saponification equivalent of 135 ± 1.

The ^{1}H NMR spectra (60 MHz) of compounds B and C showed the following:

Chemical Shift	*No. of Protons*	*Multiplicity*
Compound B (in DMSO-d_6)		
δ 7.3	1H	bs (very broad)
δ 7.71	2H	d (distorted)
δ 7.90	2H	d (distorted)
Compound C (in CCl_4)		
δ 0.93	3H	t (distorted)
δ 1.2–1.8	4H	m
δ 2.31	2H	t
δ 11.7	1H	s

Problem Set 19

1. A compound (I) containing only carbon, hydrogen, and oxygen had a neutralization equivalent of 179 ± 1. When it was heated with aqueous sodium hydroxide and the reaction mixture was acidified with sulfuric acid, a solid (II) separated which was soluble in alkalies and had a neutralization equivalent of 138 ± 1. Compound II decolorized bromine water and gave a color with ferric chloride. Distillation of the filtrate from II yielded an acid (III) with a neutralization equivalent of 60 ± 1.

   The ^{1}H NMR spectrum of compound II (60 MHz, DMSO-d_6 plus $CDCl_3$) showed δ 6.7–7.0, 2H, m; δ 7.35, 1H, t of d (J = 9, 3 Hz); δ 7.75, 1H, d of d (J = 9, 3 Hz); δ 11.55, 2H, s.

2. A compound (I) containing nitrogen was insoluble in water and dilute alkalies but soluble in dilute hydrochloric acid. Treatment with benzenesulfonyl chloride and alkali gave a clear solution. Acidification of this solution produced a precipitate which dissolved in an excess of the acid. The original compound did not react with phenylhydrazine but was decomposed by boiling with hot sodium hydroxide solution. An oil (II) was separated from the alkaline solution (III). The oil still contained nitrogen and was soluble in dilute hydrochloric acid. Compound II reacted with acetyl chloride and sodium. When compound II was treated with benzenesulfonyl chloride and alkali, an oil remained that proved to be soluble in hydrochloric acid. Compound II was dissolved in ether and the solution saturated with hydrogen chloride; a solid compound (IV) separated. Compound IV was soluble in water and had a neutralization equivalent of 187 ± 1.

   Acidification of the alkaline solution (III) produced a precipitate (V) which dissolved in an excess of acid. Addition of sodium nitrite to a solution of V chilled in ice water gave a clear solution without the evolution of nitrogen. Addition of this solution to a solution of sodium 2-naphthoxide gave a red solution. Compound V gave a neutralization equivalent of 137 ± 1.

   Methylation (twice) of V followed by reduction gave II. The ^{1}H NMR spectrum of V (60 MHz, acetone) showed δ 6.55, 3H, bs; δ 6.76, 2H, d (J = 8 Hz); δ 7.83, 2H, d (J = 8 Hz).

3. A solid (I) gave tests for nitrogen, sulfur, and bromine. Solid (I) was soluble in water but insoluble in ether. It gave a neutralization equivalent of 221 ± 1. Addition of cold alkali caused an oil (II) to separate which contained bromine and nitrogen but no sulfur. Compound II reacted with benzenesulfonyl chloride and alkali to give a clear solution from which a compound (III) precipitated which contained bromine, nitrogen, and sulfur. Compound II did not give a precipitate with silver nitrate but decolorized both bromine water and dilute permanganate solution. Treatment of I with nitrous acid in the cold gave a solution without the evolution of any gas. This solution was poured into copper cyanide solution, and a compound (IV) separated. Compound IV still contained bromine and nitrogen but was insoluble in dilute acids and alkalies. When IV was boiled with dilute sulfuric acid for some time, it was converted to V. This compound no longer contained nitrogen but did contain bromine. It (V) was insoluble in water but soluble in dilute sodium hydroxide and in sodium bicarbonate. A neutralization equivalent of 200 ± 2 was obtained. Compound V did not react with silver nitrate or permanganate.

   The ^{1}H NMR spectrum of II (60 MHz, $CDCl_3$) showed δ 3.53, 2H, bs; δ 6.57, 2H, d (J = 9 Hz); δ 7.21, 2H, d (J = 9 Hz).

4. A pale-yellow crystalline compound (I), giving tests for nitrogen and bromine, was insoluble in water, acids, and alkalies. It did not react with phenylhydrazine, acetyl chloride, or cold dilute permanganate. Cold alcoholic silver nitrate did not react, but when the solution was boiled for some time, a precipitate of silver bromide formed. When compound I was heated with zinc and ammonium chloride solution and the mixture filtered, the filtrate was found to reduce Tollens reagent. Vigorous oxidation of I produced a new compound (II), still containing bromine and nitrogen, which was insoluble in hydrochloric acid but soluble in sodium bicarbonate solution. It had a neutralization equivalent of 145 ± 1.

   Treatment of compound I with tin and hydrochloric acid followed by alkali gave a new compound (III) which contained nitrogen and bromine and was soluble in dilute hydrochloric acid. Compound III gave a precipitate with bromine water, reacted with acetyl chloride, and gave a clear solution when treated with benzenesulfonyl chloride and alkali. Vigorous oxidation of III produced a white crystalline acid (IV). Compound IV gave no tests for bromine or nitrogen and had a neutralization equivalent of 82 ± 1.

   Compound IV, when heated, lost the elements of water. The ^{1}H NMR spectrum of III (60 MHz, $CDCl_3$) showed δ 3.96, 2H, bs; δ 6.45, 1H, d (J = 8 Hz); δ 7.25–7.75, 4H, m; δ 8.0–8.2, 1H, m.

5. A light-yellow neutral solid (I) contained chlorine but not nitrogen. It did not react with hot alcoholic silver nitrate, acetyl chloride, or bromine in carbon tetrachloride. It gave a precipitate with phenylhydrazine. Compound I was not attacked by cold alkalies, but when it was heated for some time with concentrated sodium hydroxide, a clear solution resulted. The distillate from this alkaline solution contained no organic compounds. Acidification of the alkaline solution with phosphoric acid gave a precipitate (II), which was removed by filtration. No organic compounds could be obtained from the filtrate by distillation or evaporation to dryness.

   Compound II contained chlorine, had a neutralization equivalent of 297 ± 2, and reacted with acetic anhydride to produce a compound (III) having a neutralization equivalent of 340 ± 3. Compound III did not react with bromine water, bromine in carbon tetrachloride, or phenylhydrazine.

   Vigorous oxidation of I with alkaline permanganate gave a very good yield of a product (IV) which contained chlorine and possessed a neutralization equivalent of 156 ± 1. No other oxidation product could be found.

   Vigorous oxidation of II or III with potassium dichromate and sulfuric acid also produced IV but in very poor yield.

   The ^{1}H NMR spectrum of IV (60 MHz, $CDCl_3$ plus DMSO-d_6) showed δ 7.37, 2H, d (J = 9 Hz); δ 7.45, 1H, bs; δ 7.81, 2H, d (J = 9 Hz). Treatment of the solution with deuterium oxide caused the δ 7.45 signal to disappear, leaving the two doublets.

Problem Set 20

1. An acid (I) was found to have a neutralization equivalent of 151 ± 2. Treatment in the cold with acetyl chloride converted it to a new acid (II) with a neutralization equivalent of 193 ± 2. Gentle oxidation of I with cold potassium permanganate solution transformed it to an acid (III) having a neutralization

equivalent of 149 ± 2. Compound III yielded a derivative with phenylhydrazine. Vigorous oxidation of I, II, or III yielded an acid (IV) having a neutralization equivalent of 122 ± 1.

The ^{1}H NMR spectrum of compound I (60 MHz, acetone) showed δ 5.22, 1H, s; δ 6.93–7.88, 7H, m. The IR spectrum of compound I (in a mineral oil mull) showed, among other bands, a strong band at 1706 cm^{-1} and a broad band at 3333–2400 cm^{-1}.

2. A compound (I) had a neutralization equivalent of 223. Vigorous oxidation converted it to a new acid (II) having a neutralization equivalent of 167. Treatment of I with zinc and hydrochloric acid gave an acid (III) with a neutralization equivalent of 179. Compounds I, II, and III were found to contain nitrogen.

   The ^{1}H NMR spectrum of compound II (60 MHz, $CDCl_3$ plus DMSO-d_6) showed δ 7.72, 1H, t (J = 8 Hz); δ 8.2–8.55, 2H, m; δ 8.71, 1H, t (J = 2 Hz); δ 12.98, 1H, s.

3. A sulfur-containing compound was soluble in strong alkalies but not in sodium bicarbonate solutions. Vigorous oxidation gave a sulfur-containing acid having a neutralization equivalent of 102 ± 1. When this compound was treated with superheated steam, a sulfur-free acid was formed.

   The ^{1}H NMR spectrum of 100 mg of the sulfur-free acid (in 0.5 mL of acetone-d_6) showed δ 7.00–7.75, 5H, m; δ 8.00, 1H, s. The δ 8.00 signal position had a chemical shift that was concentration dependent. The ^{1}H NMR spectrum of the original compound (60 MHz, $CDCl_3$) showed δ 2.29, 3H, s; δ 3.37, 1H, s; δ 7.02, 4H, s (somewhat broadened at the base).

4. A compound (I) containing chlorine gave positive tests with alcoholic silver nitrate, sodium hypoiodite solution, and acetyl chloride. Hydrolysis with sodium bicarbonate yielded a chlorine-free compound (II) which gave a positive iodoform test and was oxidized by periodic acid to a single compound (III). Compound III also gave a positive iodoform test.

5. A compound (A), containing only carbon, hydrogen, and oxygen, was found to react with acetyl chloride but not with phenylhydrazine. Oxidation with periodic acid converted it to a new compound (B) which reduced Tollens but not Fehling's reagent.[5] Treatment of B with potassium cyanide in aqueous ethanol converted it to a new compound (C) which gave positive tests with acetyl chloride and phenylhydrazine. Oxidation of C with Fehling's solution or nitric acid converted it to a yellow compound (D) which yielded a derivative with *o*-phenylenediamine. When D was treated with hydrogen peroxide, it yielded an acid (E) having a neutralization equivalent of 135 ± 1. Catalytic hydrogenation of C or D produced the original compound (A).

   The ^{1}H NMR spectrum of compound B (in $CDCl_3$) showed δ 2.42, 3H, s; δ 7.18, 2H, d (J = 10 Hz); δ 7.56, 2H, d (J = 10 Hz); δ 9.81, 1H, s.

6. A solid, neutral substance (A) contained nitrogen. It was recovered from attempted hydrolysis with dilute acids and bases. It gave negative tests with acetyl chloride, bromine in carbon tetrachloride, sodium hypoiodite solution, and Tollens reagent. It reacted slowly with dinitrophenylhydrazine and, after treatment with zinc and ammonium chloride, reduced Tollens reagent.

[5]See Bernhard Tollens, *Ber.*, *14*, 1950 (1881) and Ralph Daniels, Clyde Rush, and Ludwig Bauer. *J. Chem. Educ.*, *37*, 205 (1960).

When A was treated with hydroxylamine hydrochloride in pyridine, it was slowly converted to a new compound B. Substance B was treated with phosphorus pentachloride, which changed it to C. Boiling with acid converted C to D, a nitrogen-containing acid of neutralization equivalent 168 ± 2, and the salt of a base E. The hydrochloride of E had a neutralization equivalent (by titration with alkali) of 195 ± 2.

Acid D was treated with thionyl chloride, and the product was added to aqueous ammonia. The neutral substance so obtained was treated with bromine and sodium hydroxide solution. The product (F) was an acid soluble substance which, after treatment with hydrochloric acid and sodium nitrite, gave a color with 2-naphthol. Treatment of F with tin and hydrochloric acid produced G, a substance readily attacked by oxidizing agents.

Base E, obtained in the reaction with phosphorus pentachloride, reacted with sodium nitrite and dilute sulfuric acid. The resulting solution gave a color with 2-naphthol. Boiling the aqueous solution produced a nitrogen-free substance, H, which dissolved in aqueous alkali but not in aqueous sodium bicarbonate. Oxidation of either E or H produced an acid (neutralization equivalent 83) which was readily converted to an anhydride. Substance H did not undergo coupling with benzenediazonium solutions.

The ^{1}H NMR spectrum of compound F (60 MHz, $CDCl_3$ plus DMSO-d_6) showed δ 5.68, 2H, bs; δ 6.58, 2H, d (J = 10 Hz); δ 7.88, 2H, d (J = 10 Hz). The ^{1}H NMR spectrum of compound H (60 MHz, $CDCl_3$) showed δ 2.32, 3H, s; δ 5.12, 1H, bs; δ 7.1–7.55, 4H, m; δ 7.6–7.9, 1H, m; δ 8.0–8.2, 1H, m. The δ 5.12 signal moved to lower field upon addition of more compound H to the NMR tube.

CHAPTER 12

Chemical Literature

The chemical literature is important to a student undertaking organic qualitative analysis. First, a student must be able to find the melting and boiling points of organic compounds and the melting points of their derivatives. The chemical literature can be used to supplement the procedures found in this book. It simplifies a laboratory procedure when the melting point as well as the procedure for the preparation of a derivative of a *specific* compound are know *before* the derivative preparation is begun.

This chapter is not meant to be comprehensive. The purpose of this chapter is to provide supplemental information such that the identification of unknowns can be carried out efficiently. This discussion is arbitrarily broken down into the following categories.

Handbooks (Section 12.1)
Compendia (Section 12.2)
Spectral Collections (Section 12.3)
Journals (Section 12.4)
Abstracts and Indexes (Section 12.5)
Monographs (Section 12.6)

The student in a qualitative analysis course will likely focus on the first three sections: handbooks, compendia, and spectral collections. But because organic qualitative analysis often serves as a lead into undergraduate and graduate research, students who follow this path will find the sections on journals, abstracts and indexes, and monographs useful.

12.1 HANDBOOKS

One of the best-known handbooks is the *Handbook of Chemistry and Physics* (CRC Press, Boca Raton, FL). Organic chemists routinely use the table entitled "Physical Constants for Organic Compounds" for properties of organic compounds used in reactions. This table includes molecular weights, solubilities, boiling points, melting points, and density of most common organic compounds. The rest of the handbook contains other tables, including ones listing pK_a values for acids, properties of inorganic compounds, and so on. A new edition of the book comes out every year. Each year the data are revised. A CD-ROM version of the book is also available, as well as an online version (http://www.knovel.com/). Other handbooks include *Lange's Handbook of Chemistry* (McGraw-Hill, New York, 1999) and *Handbook of Physical Properties of Organic Chemicals* (Lewis Publishers, New York, 1997). The former includes listings of the properties of approximately 4,000 organic and 1,400 inorganic compounds; the latter lists more than 13,000 chemicals.

A very useful and inexpensive reference is the *Aldrich Catalog of Fine Chemicals*, published annually by the Aldrich Chemical Company, Milwaukee, Wisconsin. This catalog has alphabetical entries for more than 100,000 chemicals, including melting and/or boiling points, other physical properties, safety information, and references to Beilstein and other literature. There is also a molecular formula index.

One of the most useful books published is the *Merck Index* (Merck & Co., Whitehouse Station, NJ, 2001). It is available in hardback, on CD-ROM, and as an Internet subscription (http://products.camsoft.com/themerckindex.cfm). The physical, chemical, and physiological properties of a large number of compounds are listed, and although this book is very useful for pharmaceutical studies, it is not limited to that. Also included is detailed and expanded information on the hazards associated with many of these compounds.

A supplement to this text and to the *Handbook of Chemistry and Physics* is the *Handbook of Tables for Organic Compound Identification*, 3rd edition, edited by Z. Rappaport (CRC Press, Boca Raton, FL, 1967). This book provides melting points for many standard derivatives of organic compounds.

The web offers an easy way to find physical properties of a compound. ChemFinder.com (http://chemfinder.cambridgesoft.com/) gives the structure and physical properties of a compound. The Vermont SIRI MSDS Collection (http://hazard.com/msds/) lists Material Safety Data Sheets from many manufacturers.

12.2 COMPENDIA

Compendia are a useful support for laboratory work. One of the best known is Beilstein's *Handbook of Organic Chemistry*. This series of books was begun in the 1880s by Friedrich Beilstein. Every piece of information (synthetic methods and properties of organic compounds) is backed by a reference to the original literature, making it possible to check the data. Moreover, information is not incorporated in *Beilstein* until it has been evaluated. Corrections and updating are continually done. Since 1960, it has been published in English.

Beilstein has a main work (*das Hauptwerk*), which covers the literature up to 1909. Thereafter, time periods are covered by supplements (*Erganzungswerks*):

First supplement (*erstes Erganzungswerk*)	1910–1919
Second supplement (*zweites Erganzungswerk*)	1920–1929
Third supplement (*drittes Erganzungswerk*)	1930–1949
Fourth supplement (*viertes Erganzungswerk*)	1950–1959
Fifth supplement (*funf Erganzungswerk*)	1960–1979

Crossfine Beilstein (http://www.beilstein.com) is a subscription online database of *Beilstein* and contains all up-to-date *Beilstein* data. Abstracts of papers published since 1980 are available. For the *Beilstein* database, 180 journals are indexed. This online version contains more than 8 million compounds and more than 5 million chemical reactions.

The Dictionary of Organic Compounds, edited by J. Buckingham and F. Macdonald (9 volumes, Chapman & Hall/CRC, London, England, 1996) lists properties and derivatization procedures for more than 220,000 compounds. It is also available as a CD-ROM and on the Internet (http://www.chemnetbase.com/scripts/docweb.exe).

Rodd's Chemistry of Carbon Compounds has been published (Elsevier Publishing, New York) since 1964. *Second Supplements to the 2nd Edition of Rodd's Chemistry of Carbon Compounds* is the most current book. To date, the second edition of this series

consists of 71 volumes and more than 30,000 pages. It is organized in the same fashion as an organic text, but it is much more extensively developed.

Reagents for Organic Synthesis, by L. F. Fieser and M. Fieser, is a series of volumes published by Wiley. Volume 1, published in 1967, is the cornerstone edition and is a 1457-page listing of reagents, catalysts, solvents, and references for standard organic procedures. Extensive amounts of practical information are included, such as solvent drying techniques and physical constants. Currently, 21 volumes have been written.

Wiley also publishes two well-known series that are useful in the laboratory: *Organic Syntheses* and *Organic Reactions*. *Organic Syntheses* is a collection of organic preparations with the distinct advantage of having been checked. Annual volumes began in 1921 and published cumulative volumes include Collective Volume I (Annual Volumes 1–9, 1932), Collective Volume II (Annual Volumes 10–19, 1943), Collective Volume III (Annual Volumes 20–29, 1953), Collective Volume IV (Annual Volumes 30–39, 1963), Collective Volume V (Annual Volumes 40–49, 1973), Collective Volume VI (Annual Volumes 50–59, 1988), Collective Volume VII (Annual Volumes 60–64, 1990), and Collective Volume VIII (Annual Volumes 65–69, 1993). Seventy-nine volumes have been printed thus far. Submitted procedures are sent to scientists at other research laboratories for independent testing of procedures and yields. All procedures are extensively supplemented by notes that describe the practical handling of solvents, reagents, and starting materials. Literature references are provided, and procedures for preparing starting materials are cited.

Organic Reactions is a continuing series that has been published by Wiley since 1942. Each chapter describes a given reaction in detail, supported by literature references. Volume 61 was published in 2002.

12.3 SPECTRAL COLLECTIONS

The literature provides a wealth of spectral information. This information is presented in books that list tables of data and bound volumes of copies of spectra. Both have their uses, but it is often advantageous for students to see the actual spectra. This is especially true for infrared spectra, where peak shapes, as well as peak positions and intensities, are important characteristics for each compound.

When comparing spectra, it is important to be aware of the details of how the spectra were obtained, such as the type of spectrometer used and the sampling techniques. When comparing spectra for final identification, it is important to have both the unknown compound's spectrum and the reference spectrum for a known compound, hopefully under highly similar, if not identical, conditions. It is also important to know the solvent or mulling compound and where these signals occur.

There are two well-known and long-used compilations of spectra: the Aldrich collection and the Sadtler collection. Aldrich Chemical Company (Milwaukee, WI) publishes extensive collections of both infrared (IR) and nuclear magnetic resonance (NMR) spectra for many of the compounds sold by the Aldrich Chemical Company. The *Aldrich Library of FT-IR Spectra* (Aldrich Chemical Company, Milwaukee, WI, 1997) contains more than 18,000 spectra. The *Aldrich Library of* ^{13}C *and* ^{1}H *FT-NMR Spectra* (Aldrich Chemical Company, Milwaukee, WI, 1992) contains more than 12,000 spectra. The ^{13}C spectra were obtained from a 75-MHz spectrometer, and the ^{1}H NMR spectra were obtained from a 300-MHz spectrometer. The *Aldrich/ACD Library of FT-NMR Spectra* is an electronic reference book with more than 15,000 spectra, as well as physical properties. The *Aldrich FT-IR Condensed Phase Library, Edition 2* contains nearly 18,500 pure compounds and is available on CD-ROM. Both NMR and IR spectra

are available on the company's website (http://www.sigmaaldrich.com/). The Aldrich NMR and IR collections both provide certain advantages: the spectra of a large number of compounds with similar structures in a given molecular class are on the same page. For example, several spectra of saturated alcohols will be found on the same page. This allows the beginning student to obtain an overview of spectral information common to that structural class. It also provides a variety of related structures when completing a final structural assignment. The ^{1}H NMR spectra contain integration.

The Sadtler collections are available in the KnowItAll® Informatics System. In the KnowItAll® Informatics System, Bio-Rad Laboratories offers more than 220,000 IR spectra in its HaveItAll® IR database, more than 350,000 ^{13}C and 17,000 ^{1}H NMR spectra in its HaveItAll® NMR database, and more than 197,000 mass spectra in its HaveItAll® MS database. These databases are available on CD-ROM. At a cheaper price, there is a pay-as-you-go option.

The *NIST/EPA/NIH Mass Spectral Database* is available on CD-ROM and has nearly 130,000 mass spectra. This database is able to perform a standard quick search. Chemical structures are displayed with the spectra.

The *NIST Chemistry WebBook* (http://webbook.nist.gov/chemistry/) allows searching by formula, structure, CAS registry number, and structure. More than 8,700 IR spectra, 12,600 mass spectra, and 400 UV/Vis spectra are accessible in this database. Another online source for spectra is *SDBS—Integrated Spectral Data Base System for Organic Compounds* (http://www.aist.go.jp/RIODB/SDBS/). This database contains approximately 20,500 mass spectra, 13,700 ^{1}H NMR spectra, 11,800 ^{13}C NMR spectra, 47,300 IR spectra, 3,500 Raman spectra, and 2,000 ESR spectra.

12.4 JOURNALS

A journal paper is the initial formal report of laboratory research results. Sometimes these results may have already been presented in a presentation at an American Chemical Society meeting.

The general format for a paper can vary. The paper can be in complete paper form (historical background section, experimental section, results and discussion section, and references) or in the briefer form of a preliminary report (brief description of results, rather than an experimental section, and a only a very brief recounting of the history behind the project). *The Journal of Organic Chemistry* includes examples of both of these formats. All the papers described here are abstracted by *Chemical Abstracts* (see Section 12.5). An extensive list of journals and their abbreviations is provided below.

Acc. Chem. Res. (Accounts of Chemical Research) is a publication in which leading authors in certain areas of chemistry are invited to contribute a paper that is a review of an area in which the invited author is a leader. It is usually supported by a large number of references to primary publications.

Anal. Chem. (Analytical Chemistry) is a publication containing analytical results that frequently contain data useful to organic chemists.

Angew. Chem. Int. Ed., Eng. (Angewandte Chemie International Edition, English) is published in Germany but is in English. It contains review articles, papers, and brief communications in the area of organic chemistry.

Chem Ber. (Chemisch Berichte) is published in Germany, and articles appear in both German and English. At one time, this journal was published under the name *Ber. (Berichte)*.

J. Amer. Chem. Soc. (Journal of the American Chemical Society), published by the American Chemical Society, includes both complete papers and communications. It is intended for the entire chemistry community.

J. Chem. Soc. includes a variety of publications, such as *Journal of the Chemical Society*, for the British Chemical Society. *Perk. Trans. (Perkin Transactions) 1* & *2* publishes papers in, respectively, organic and physical organic chemistry. *Perkin 1* & *2* have merged to form *Organic and Biomolecular Chemistry*, effective December 2002. *Chem. Commun. (Chemical Communications)* is a British Chemical Society journal for brief communications in all areas of chemistry.

Science is edited by members of the National Academy of Sciences. It includes papers of high significance that cross interdisciplinary boundaries. It also includes articles describing current events in areas such as public policy in science.

Tet. Lett. (Tetrahedron Letters) contains brief papers in areas of organic chemistry of timely interest. Chemists must submit papers in camera-ready format, and such papers appear as direct reproductions in the journal. The papers are brief in scope, usually four pages double-spaced.

Zh. Org. Khim. (Zhurnal Organicheskoi Khimmi) is the journal of organic chemistry published in Russia and is available in both Russian and English.

The types of papers listed above are examples of primary literature. Many journals—for example, *Chemical Reviews*—include or are totally comprised of review papers. Review papers are descriptions of the contents of a large number of primary references; thus they normally survey and interrelate a much broader range of information than included in a single primary reference.

12.5 ABSTRACTS AND INDEXES

The best-known abstracting service is *Chemical Abstracts* (Chemical Abstracts Service, Columbus, OH). The publication includes all papers published within the broad domain of chemistry. In a year's time, there are 755,000 references listed, including 606,000 document references from 8,000 major scientific journals and 200,600 patent documents from 38 patent-granting organizations around the world.

A variety of indexes are available in *Chemical Abstracts*, including general subject indexes, patent indexes, key word indexes, author indexes, formula indexes, and chemical substance indexes. The general subject, patent, and author indexes have been published collectively since 1907, the formula indexes since 1920, and the chemical substance indexes since 1972. Collective indexes originally covered ten-year periods, but, because of the great increase in the number of papers published, they were reduced to five-year periods. Beginning with the eighth collective index (1967), an *Index Guide* has been published. The 14th Collective Index covers September 1997 through March 2002.

Chemical Abstracts Service[1] originated in 1895 when Arthur Noyes, a chemist at MIT, founded the *Review of American Chemical Research*. Noyes used this publication to publish summaries of American chemistry research papers because he felt that American chemists were not being recognized for their research.

The *Review of American Chemical Research* became a part the *Journal of the American Chemical Society* in 1897. The editor of the *Journal of the American Chemical*

[1]"The History of the Chemical Abstracts Service" was graciously provided from the Chemical Abstracts Service. The text in this book is paraphrased from the original document. Used with permission from CAS, a Division of the American Chemical Society.

Society was William A. Noyes, Sr, a relative of Arthur Noyes. He proposed that the American Chemical Society should investigate the possibility of publishing a journal whose emphasis was comprehensive abstracts for the field of chemistry. This was accomplished in 1906, when the American Chemical Society approved the publication of *Chemical Abstracts*. William Noyes was its first editor when it began publication in 1907.

Noyes was editor of *Chemical Abstracts* for the first two years of publication. At first, *Chemical Abstracts* was published through the National Bureau of Standards in Washington and then from the University of Illinois. The move was due to a change in jobs, since Noyes accepted the position of chair of the chemistry department at the University of Illinois. Austin Patterson became editor in 1909. William McPherson, head of the chemistry department at Ohio State University, invited Patterson to move the *Chemical Abstracts* to the Ohio State University campus. One advantage was that Patterson could be nearer the Patterson home in Xenia, Ohio. In 1914, Patterson resigned as editor due to poor health. John Miller was then editor for a brief period of time.

Evan J. Crane, an Ohio State University alumnus, became editor in 1915 and remained editor for 43 years. During the last two years, he also served as the director of the Chemical Abstracts Service. Under his leadership, he led *Chemical Abstracts* through difficult financial times and established it as a leader among scientific abstract services. The *Chemical Abstracts Indexes* grew to be a more important service than the abstracts.

For 60 years, the *Chemical Abstracts* editorial office remained at Ohio State University. In the early years, the four-member office was in a renovated classroom in the old chemistry building. After the McPherson Chemistry Building was built, the office moved there in 1928. A separate three-story building was necessary by the mid-1950s, since the staff had grown to 100. A fourth floor was added by 1960, since the staff had grown to 300. The building and the university's resources were beginning to be strained by the early 1960s.

Fifty acres, north of the Ohio State University campus, were purchased by the American Chemical Society in 1962 for the Chemical Abstracts Service. Construction of a four-story office building began immediately. By 1965, the Chemical Abstracts Service had moved into the new building. Another building was built in 1973.

Until 1956, the Chemical Abstracts Service was funded partly by dues paid by American Chemical Society members. In 1956, Chemical Abstracts Service was established as self-supporting through fees charged for the publications and services.

Well into the 1960s, the abstracts were written by volunteers, with the editing and indexing performed by a small full-time staff. Today, all work is done by a paid staff in Columbus, Berlin, or Tokyo. This shift to a paid staff was required so that the information would be available in a timely manner. The advent of the computer age also required that the information be available quickly. The Chemical Abstracts Service developed a computer-based system in the late 1960s to deal with the increasing volume of the chemical literature. This system consisted of three components. One component was comprised of an integrated, computer-assisted input of all information. Another component was a single database to organize all of the data. The last component consisted of a system that was user-friendly. The history of these systems is given below.

In 1961, *Chemical Titles* began publication by the Chemical Abstracts Service as the world's first periodical to be completely written, organized, and indexed on computer. It was also the first periodical to use the keyword-in-context indexing technique. A very important aspect of the Chemical Abstracts Service was the development of the *CAS*

Chemical Registry System, begun in 1965. A unique *CAS Registry Number* has been assigned for the structure and name of every chemical substance that has ever been indexed by the Chemical Abstracts Service. These *CAS Registry Numbers* are now used by manufacturers in the labeling of their chemicals and in publications.

CA Condensates was introduced in 1968 as the first computer-readable service to include all documents abstracted by the Chemical Abstracts Service. Bibliographic information, as well as natural language keyword indexing, was included. In the early 1970s, *CA Subject Index Alert* began as a biweekly computer file that contained parts of the vocabulary index entries that were being compiled for the semiannual indexes of *Chemical Abstracts.* In 1978, *CA Condensates* and the *Subject Index Alert* were combined into one system, the *CA Search.* Currently, *CA Search* is the most widely used file in the world and is the basis for several other online search services.

In the late 1960s, the Chemical Abstracts Services began to license the computer-readable files to many organizations for the purpose of local searches of files. Remote online access was available by the early 1970s. *CAS Online* was introduced in 1980 and initially provided only substructure search of the *CAS Chemical Registry* database. *CAS Online* was soon expanded to include the additional features of bibliographic, abstract, and index information.

Messenger was developed in the 1980s as a versatile software program that allowed searching in a variety of technical databases. *Messenger* was the foundation for the development of *STN International,* which is an online network with access to more than 200 international scientific and technical databases. *STN International* is a service offered jointly by the American Chemical Society; Fachinformationszentrum (FIZ) Energie, Physik, Mathematik; and the Japan Science and Technology Corporation. *STN International* links together the computers in Columbus, in Karlsruhe, Germany, and in Tokyo.

Besides *Chemical Abstracts,* there are several other chemical information services offered by Chemical Abstracts Services. *Chemistry Industry Notes* abstracts chemical business information. *CA Selects* and *CAS BioTech Updates* summarize information in selected abstracts. *Chemical Titles* lists the titles of articles from the mainstream chemical journals. *CAS Source Index* lists bibliographic information for more than 70,000 scientific publications.

The Chemical Abstracts Services offers access to many databases, such as the *CA File, CAplus, REGISTRY File, CAOLD File, CASREACT, MARPAT, CIN, CHEMLIST,* and *CHEMCATS. Chemical Abstracts,* as well as *CASSI* and the *CASurveyor,* are available on CD-ROM.

SciFinder, a research tool with access to the Chemical Abstracts databases, was released in October 1994. This online software program allows scientists to search chemical topics—from chemical structures to chemical-related literature—very easily. *SciFinder* provides access to more than 22 million abstracts, more than 20 million organic and inorganic substances, and more than 24 million sequences.

Recently Chemical Abstracts Services has developed several new search engines. *STN Easy* searches selected *STN* databases. *Chemical Patents Plus* allows retrieval of text and full-page images for all classes of U.S. patents since 1975. *FirstSearch CA Student Edition* is customized to serve the needs of undergraduate students. Today, the Chemical Abstracts Services is global in its databases and its users.

Science Citation Index (SCI) is an index that lists all publications in a given year referring to a paper published earlier. This is especially useful when there is a key paper describing a procedure that will be used by a large number of chemists who publish later. *SCI* provides access to cited references found in 3,700 science and technical

journals, with coverage of more than 100 disciplines. The *Science Citation Index Expanded* and the online version, *SciSearch,* cover more than 5,800 journals.

12.6 MONOGRAPHS

A variety of organic qualitative analysis texts have been published. *Semimicro Qualitative Organic Analysis: The Systematic Identification of Organic Compounds,* 3rd edition, by N. D. Cheronis, J. B. Entrikin, and E. M. Hodnett (Wiley, New York, 1965, reprinted by Krieger Publishing Company, Melbourne, FL, 1983), and *Identification of Organic Compounds: A Student's Text Using Semimicro Techniques,* by N. D. Cheronis and J. B. Entrikin (Wiley, New York, 1980), describe many useful wet chemical tests.

Organic Structure Determination, by D. J. Pasto (Prentice Hall, Upper Saddle River, NJ, 1969), provides chemical and spectroscopic methods of characterization of organic compounds. This book appeared in a greatly revised format as *Laboratory Text for Organic Chemistry: A Source Book of Chemical and Physical Techniques,* by D. J. Pasto (Prentice Hall, Upper Saddle River, NJ, 1979), and later as *Experiments and Techniques in Organic Chemistry,* by D. J. Pasto, C. R. Johnson, and M. J. Miller (Prentice Hall, Upper Saddle River, NJ, 1991).

Spectroscopic information can be obtained from a variety of sources. The text *Spectrometric Identification of Organic Compounds,* 6th edition, by R. M. Silverstein and F. X. Webster (Wiley, New York, 1998), describes mass spectrometry, infrared (IR) spectrometry, and nuclear magnetic resonance (NMR) spectrometry. The main focus of the text is organic structure determination. Discussions of topics begin with the assumption that they are new to the reader, and they are then developed to the intermediate level. Moreover, the text includes many structure determination problems and ample tables to solve these problems.

APPENDIX I

Handy Tables for the Organic Laboratory

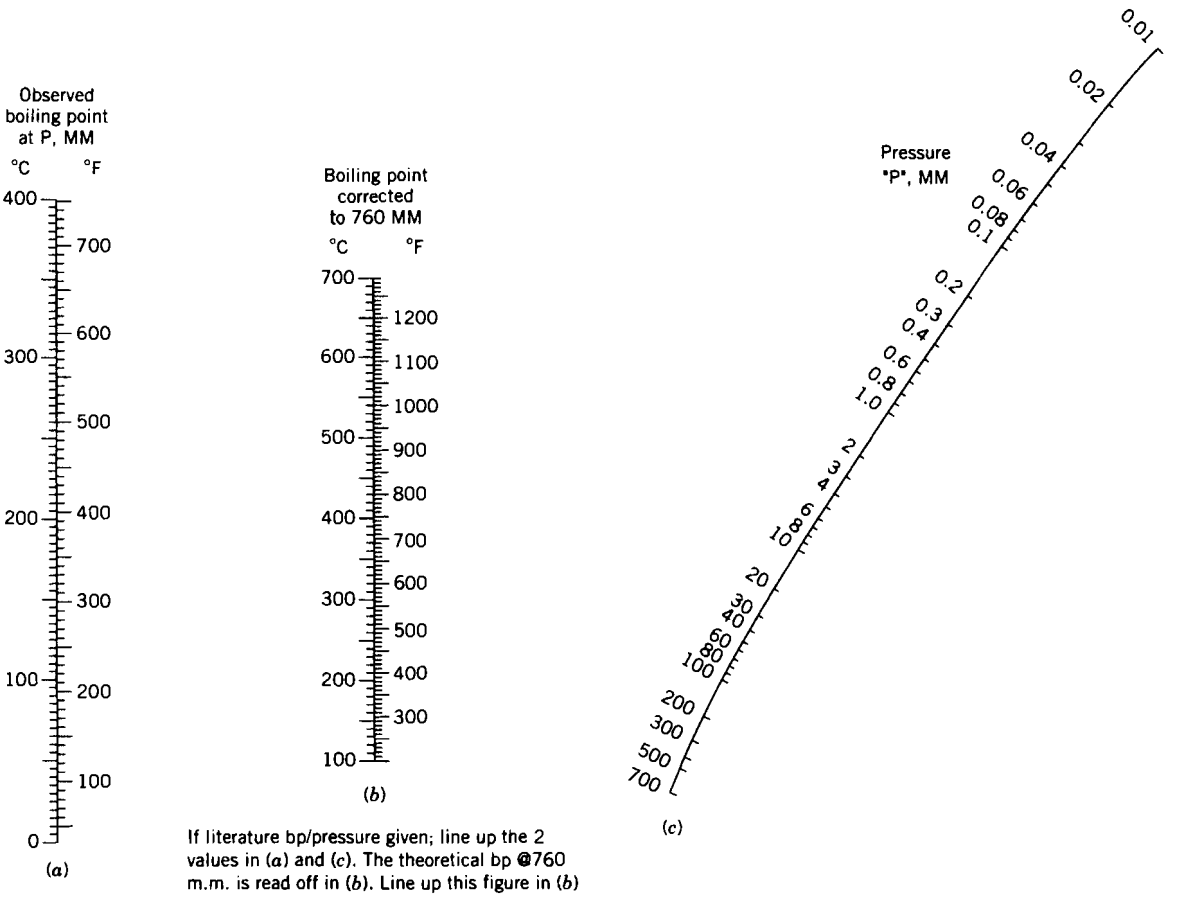
TABLE AI.1 Composition and Properties of Common Acids and Bases

	sp gr	Wt %	Moles per Liter	Grams/100 mL
Hydrochloric acid, conc	1.19	37	12.0	44.0
Constant-boiling (252 mL conc acid + 200 mL water, bp 110°)	1.10	22.2	6.1	24.4
10% (100 mL conc acid + 321 mL water)	1.05	10	2.9	10.5
5% (50 mL conc acid + 380 mL water)	1.03	5	1.4	5.2
1 N (41.5 mL conc acid diluted to 500 mL)	1.02	3.6	1	3.7
Hydrobromic acid, constant-boiling (bp 126°C)	1.49	47.5	8.8	70.8
Hydriodic acid, constant-boiling (bp 127°C)	1.7	57	7.6	97
Sulfuric acid, conc	1.84	96	18	177
10% (25 mL conc acid + 398 mL water)	1.07	10	1.1	10.7
1 N (13.9 mL conc acid diluted to 500 mL)	1.03	4.7	0.5	4.8
Nitric acid, conc	1.42	71	16	101
Sodium hydroxide, 10% solution	1.11	10	2.8	11.1
Ammonium hydroxide, conc	0.90	28.4	15	25.6
Phosphoric acid, conc (syrupy)	1.7	85	14.7	144

TABLE AI.2 Composition of Common Buffer Solutions

pH	Components
0.1	1 N Hydrochloric acid
1.1	0.1 N Hydrochloric acid
2.2	15.0 g Tartaric acid per liter (0.1 M solution)
3.9	40.8 g Potassium acid phthalate per liter
5.0	14.0 g KH phthalate + 2.7 g $NaHCO_3$ per liter (heat to expel carbon dioxide, then cool)
6.0	23.2 g KH_2PO_4 + 4.3 g Na_2HPO_4 (anhyd) per liter
7.0	9.1 g KH_2PO_4 + 18.9 g Na_2HPO_4 per liter
8.0	11.8 g Boric acid + 9.1 g Borax ($Na_2B_4O_7 \cdot 10H_2O$) per liter
9.0	6.2 g Boric acid + 38.1 g Borax per liter
10.0	6.5 g $NaHCO_3$ + 13.2 g Na_2CO_3 per liter
11.0	11.4 g Na_2HPO_4 + 19.7 g Na_3PO_4 per liter
12.0	24.6 g Na_3PO_4 per liter (0.15 M solution)
13.0	4.1 g Sodium hydroxide pellets per liter (0.1 M)
14.0	41.3 g Sodium hydroxide pellets per liter (1 M)

TABLE AI.3 Pressure–Temperature Nomograph for Vacuum Distillations



If literature bp/pressure given; line up the 2 values in (*a*) and (*c*). The theoretical bp @760 m.m. is read off in (*b*). Line up this figure in (*b*) with another pressure in (*c*) and the approximate corresponding bp can be read off in (*a*).

TABLE A1.4 Elution Solvents for Chromatography

Alumina Adsorbent		Silica Adsorbent
Fluoroalkanes	Increasing polarity[a] ↓	Fluoroalkanes
Pentane		Cyclohexane
Isooctane		Heptane
Petroleum ether (light)		Pentane
Hexane		Carbon tetrachloride
Cyclohexane		Carbon disulfide
Cyclopentane		Chlorobenzene
Carbon tetrachloride		Ethylbenzene
Carbon disulfide		Toluene
Xylene		
Diisopropyl ether		Benzene
Toluene		2-Chloropropane
1-Chloropropane		Chloroform
Chlorobenzene		Nitrobenzene
		Diisopropyl ether
Benzene		Diethyl ether
Ethyl bromide		Ethyl acetate
Diethyl ether		2-Butanol
Diethyl sulfide		
Chloroform		Ethanol
Methylene chloride		Water
Tetrahydrofuran		Acetone
1,2-Dichloroethane		Acetic acid
Ethyl methyl ketone		Methanol
1-Nitropropane		Pyruvic acid
Acetone		
1,4-Dioxane		
Ethyl acetate		
Methyl acetate		
1-Pentanol		
Dimethyl sulfoxide		
Aniline		
Diethylamine		
Nitromethane		
Acetonitrile		
Pyridine		
Butyl cellosolve		
2-Propanol		
1-Propanol		
Ethanol		
Methanol		
Ethylene glycol		
Acetic acid		

[a]The ability of a solvent to elute chromatographically depends on the compound being eluted as well as the adsorbent; thus, exceptions to these orders will be found. In general, however, as one goes down these lists, one finds solvents of increasing "polarity" which, in principle, more readily elute the more polar compounds.

TABLE AI.5 Salt–Ice Mixtures for Cooling Baths[a]

Substance	Initial Temperature (°C)	g Salt/100 g H_2O[b]	Final Temperature (°C)
Na_2CO_3	−I (ice)	20	−2.0
NH_4NO_3	20	106	−4.0
$NaC_2H_3O_2$	10.7	85	−4.7
NH_4Cl	13.3	30	−5.1
$NaNO_3$	13.2	75	−5.3
$Na_2S_2O_3 \cdot 5H_2O$	10.7	110	−8.0
$CaCl_2 \cdot 6H_2O$	−1 (ice)	41	−9.0
KCl	0 (ice)	30	−10.9
KI	10.8	140	−11.7
NH_4NO_3	13.6	60	−13.6
NH_4Cl	−1 (ice)	25	−15.4
NH_4NO_3	−1 (ice)	45	−16.8
NH_4SCN	13.2	133	−18.0
NaCl	−1 (ice)	33	−21.3
$CaCl_2 \cdot 6H_2O$	0 (ice)	81	−21.5
H_2SO_4 (66.2%)	0 (ice)	23	−25
NaBr	0 (ice)	66	−28
H_2SO_4 (66.2%)	0 (ice)	40	−30
C_2H_5OH(4°)	0 (ice)	105	−30
$MgCl_2$	0 (ice)	85	−34
H_2SO_4 (66.2%)	0 (ice)	91	−37
$CaCl_2 \cdot 6H_2O$	0 (ice)	123	−40.3
$CaCl_2 \cdot 6H_2O$	0 (ice)	143	−55

[a]Addition of the substance listed in the first column can, but does not always, lower the bath temperature to that listed in the last column. The final temperature may not be quite that low owing to insufficiently crushed ice, and so forth.

[b]H_2O means liquid water except where ice is listed parenthetically.

TABLE AI.6 Liquid Media for Heating Baths[a]

Medium	mp (°C)	bp (°C)	Range (°C)	Flash Point (°C)	Comments
H_2O (l)	0	100	0–80	None	Ideal in limited range
Ethylene glycol	−12	197	−10–180	115	Cheap; flammable; difficult to remove from apparatus
20% H_3PO_3, 80% H_3PO_4[b]	<20	—	20–250	None	Water soluble; nonflammable; corrosive; steam evolved at high temperature
Triethylene glycol	−5	287	0–250	156	Water soluble; stable
Glycerol	18	290	−20–260	160	Supercools; water soluble; viscous
Paraffin	~50	—	60–300	199	Flammable
Dibutyl phthalate	—	340	150–320	—	Viscous at low temperature
Wood's metal (50% Bi, 25% Pb, 12.5% Sn, 12.5% Cd)[b]	70	—	70–350	—	Oxidizes if used at >250° for long period of time
Tetracresyl silicate	<−48	~440	20–400	—	Noncorrosive; fire-resistant; expensive

[a]Range of useful temperatures for a bath which is open to the atmosphere; all of these baths except water should be used only in a hood.
[b]Wt %.

TABLE AI.7 Solvents for Extraction of Aqueous Solutions[a]

Solvent	bp (°C)	Flammability[b]	Toxicity[b]	Comments
Benzene	80.1	3	3	Prone to emulsion;[c] good for alkaloids and phenols from buffered solutions
2-Butanol	99.5	1	3	High boiling; good for highly polar water-soluble materials from buffered solution
Carbon tetrachloride	76.5	0	4	Easily dried; good for nonpolar materials
Chloroform	61.7	0	4	May form emulsion;[c] easily dried
Diethyl ether	34.5	4	2	Absorbs large amounts of water; good general solvent
Diisopropyl ether	69	3	2	May form explosive peroxides on long storage; good for acids from phosphate-buffered solutions
Ethyl acetate	77.1	3	1	Absorbs large amount of water; good for polar materials
Methylenechloride	40	0	1	May form emulsions;[c] easily dried
Pentane	36.1	4	1	Hydrocarbons easily dried;
Hexane	69	4	1	poor solvents for polar
Heptane	98.4	3	1	compounds

[a]Data in this table are taken mostly from A. J. Gordon and R. A. Ford, *The Chemists Companion* (Wiley-Interscience, New York, 1973).
[b]4 means most toxic or flammable, 4 > 3 > 2 > 1; 0 = nonflammable.
[c]*Emulsions* may form during the extraction of aqueous solutions by organic solvents, making good separation very difficult, if not impossible. Their formation is especially liable to occur if the solution is alkaline; addition of dilute sulfuric acid (if permissible) may break up such an emulsion. The following are general methods for breaking up emulsions: saturation of the aqueous phase with a salt (NaCl, Na_2SO_4, etc.); addition of several drops of alcohol or ether (especially when $CHCl_3$ is the organic layer); centrifugation of the mixture, one of the most successful techniques.

TABLE AI.8 Drying Agents of Moderate Strength for Organic Solvents

Drying Agent	Capacity[a]	Speed[b]	Comments
$CaSO_4$	$\frac{1}{2}H_2O$	Very fast (1)	Sold commercially as Drierite with or without a color indicator; very efficient. When dry, the indicator ($CoCl_2$) is blue but turns pink as it takes on H_2O (capacity $CoCl_2 \cdot 6H_2O$); useful in temperature range −50 to +86°C. Some organic solvents leach out, or change the color of $CoCl_2$ (acetone, alcohols, pyridine, etc.).
$CaCl_2$	$6H_2O$	Very fast (2)	Not very efficient; use only for hydrocarbons and alkyl halides (forms solvates, complexes, or reacts with many nitrogen and oxygen compounds).
$MgSO_4$	$7H_2O$	Fast (4)	Excellent general agent; very inert but may be slightly acidic (avoid with very acidic-sensitive compounds). May be soluble in some organic solvents.
Molecular sieve 4A	High	Fast (30)	Very efficient; predrying with a more common agent recommended. Sieve 3A also excellent.
Na_2SO_4	$10H_2O$	Slow (290)	Very mild, inefficient, slow, inexpensive, high capacity; good for gross predrying, but do not warm the solution.
K_2CO_3	$2H_2O$	Fast	Good for esters, nitriles, ketones, and especially alcohols; do not use with acidic compounds.
NaOH or KOH	Very high	Fast	Powerful, but used only with inert solutions in which agent is insoluble; especially good for amines.
H_2SO_4	Very high	Very fast	Very efficient, but use limited to saturated or aromatic hydrocarbons or halides (will remove olefins and other "basic" compounds).
Alumina (Al_2O_3) or silica gel (SiO_2)	Very high	Very fast	Especially good for hydrocarbons. Should be finely divided; can be reactivated after use by heating (300°C for SiO_2, 500°C for Al_2O_3).

[a]Moles of water per mole of agent (maximum).

[b]Relative rating. For first five entries, number in parentheses is relative drying speed for benzene—low number, rapid drying; order may change for slow agents with change in solvent. [B. Pearson and J. Ollerenshaw, *Chem. Ind.*, 370 (1966).]

TABLE A1.9 More Powerful Dehydrating Agents for Organic Liquids

Agent[a]	Products Formed with H_2O	Comments
Na	NaOH, H_2	Excellent for saturated hydrocarbons and ethers; do *not* use with any halogenated compounds.
CaH	$Ca(OH)_2$, H_2	One of the best agents; slower than $LiAlH_4$ but just as efficient and safer. Use for hydrocarbons, ethers, amines, esters, C_4 and higher alcohols (not C_1, C_2, C_3 alcohols). Do *not* use for aldehydes and active carbonyl compounds.
$LiAlH_4$	LiOH, $Al(OH)_3$, H_2	Use only with inert solvents [hydrocarbons, aryl (not alkyl) halides, ethers]; reacts with any acidic hydrogen and most functional groups (halo, carbonyl, nitro, etc.). Use caution; excess may be destroyed by slow addition of ethyl acetate.
BaO or CaO	$Ba(OH)_2$ or $Ca(OH)_2$	Slow but efficient; good mainly for alcohols and amines but should not be used with compounds sensitive to strong base.
P_2O_5	HPO_3, H_3PO_4, $H_4P_2O_7$	Very fast and efficient; very acidic. Predrying recommended. Use only with inert compounds (especially hydrocarbons, ethers, halides, acids, and anhydrides).

[a]The best dehydrating agents are those that react rapidly and irreversibly with water (and not with the solvent or solutes); they are also the most dangerous and should be used only after gross predrying with a less vigorous drying agent (see previous table). These agents are almost always used only to dry a solvent prior to and/or during distillation. Although $MgClO_4$ is one of the most efficient drying agents, it is *not* recommended because it can cause explosions if mishandled. [See D. R. Burfield, K.-H. Lee, and R. H. Smithers, *J. Org. Chem.*, *42*, 3060 (1977), for studies of desiccant efficiency.]

APPENDIX II

Tables of Derivatives

The tables on the following pages contain common organic compounds arranged according to classes. The compounds in each table are listed in the order of boiling points or melting points. Only compounds which have two or more solid derivatives are listed. This table of derivatives is not intended to be complete. One reason for this is the desirability of following the specific directions given in other literature for the conversion of a compound not listed on the table to its derivative. The use of such procedures will increase the student's chances of success, since the directions given in Chapter 10 are compromise directions designed to apply to as many compounds of a particular class as possible. There are obviously many cases in which these generalizations are unsatisfactory, and detailed directions which have been found to work for the particular compound must be utilized.

In describing compounds in the literature it is customary to give a *range* of a number of degrees for the boiling point or melting point. In order to keep the following tables from being too cumbersome, only the highest point of the boiling or melting point range is listed; this value is rounded to the nearest whole degree. Specific gravities are given for a temperature of 20°C referred to water at 4°C unless otherwise indicated. Refractive indices are given at 20° for the sodium D line.

Students should bear in mind that the value obtained for a melting point depends somewhat on the observer and on the method used in the determination. Thus, it often happens that the literature gives several different values for the same compound. In such cases the highest value has generally been chosen for the tables that follow. If the literature melting point values vary by a great amount, the different values are included.

TABLE AII.1 Acid Anhydrides (Liquids)

Name of Compound	bp (°C)	Derivative mp (°C)			
		Acid	Amide	Anilide	4-Toluidide
Trifluoroethanoic anhydride (trifluoroacetic anhydride)	39		75	88	
Ethanoic anhydride (acetic anhydride)	140	16	82	115	153
Propanoic anhydride (propionic anhydride)	168		81	106	126
2-Methylpropanoic anhydride (isobutyric anhydride)	182		128	105	108
2,2-Dimethylpropanoic anhydride (pivalic anhydride; trimethylacetic anhydride)	190	35	155	132	120
Butanoic anhydride (butyric anhydride)	198		116	96	75
Z-Butenedioic anhydride (maleic anhydride; *cis*-2-butenedioic anhydride)	198	130	181 (mono) 266 (di)	175 (mono) 187 (di)	142
Methyl Z-butenedioic anhydride (citraconic anhydride; methylmaleic anhydride; methyl *cis*-2-butenedioic anhydride)	214	92d	187d	175 (di) 153 (mono)	170 (mono)
3-Methylbutanoic anhydride (isovaleric anhydride)	215		137	110	107
Dichloroethanoic anhydride (dichloroacetic anhydride)	216d		98	118	153
Pentanoic anhydride (valeric anhydride)	218		106	63	74
2-Ethylbutanoic anhydride	229		112	127	116
E-2-Butenoic anhydride (crotonic anhydride; *trans*-2-butenoic anhydride)	248	72	161	118	132
(±)-Methylbutanedioic anhydride [(±)-methylsuccinic anhydride]	248	115	225	123; 159	164
Hexanoic anhydride (caproic anhydride)	257		100	95	75
Heptanoic anhydride	258		96	71	81
2-Methylpentanedioic anhydride (α-methylglutaric anhydride)	275			176	175
Cyclohexanecarboxylic anhydride (hexahydrobenzoic anhydride)	283	30	186		
Octanoic anhydride (caprylic anhydride)	285	16	110	57	70
4-Methyl-1,2-benzenedicarboxylic acid anhydride (4-methylphthalic anhydride)	295	152	188 (di)		
Z-1,3-Cyclohexanedicarboxylic acid anhydride (*cis*-hexahydroisophthalic anhydride)	304	189		299	

TABLE AII.2 Acid Anhydrides (Solids)

Name of Compound	mp (°C)	Derivative mp (°C)			
		Acid	Amide	Anilide	4-Toluidide
Z-9-Octadecenoic anhydride (oleic anhydride; *cis*-9-octadecenoic anhydride)	22		76	41	43
Decanoic anhydride (capric anhydride)	24	31	108	70	78
3-Ethyl-3-methylpentanedioic anhydride (β-ethyl-β-methylglutaric anhydride)	25	87		105	
Cyclohexanecarboxylic anhydride (hexahydrobenzoic anhydride)	25	30	186		
(±)-Methylbutanedioic anhydride [(±)-methylsuccinic anhydride]	37	115	225	123; 159	164
Undecanoic anhydride (hendecanoic anhydride)	37	30	103	71	80
2-Methylbenzoic anhydride (*o*-toluic anhydride)	39	105	143	125	144
3-Methylpentanedioic anhydride (β-methylglutaric anhydride)	41	87		200 (di) 121 (mono)	135
Bromoethanoic anhydride (bromoacetic anhydride)	42	50	91	131	
Dodecanoic anhydride (lauric anhydride)	42	44	110	78	87
Benzoic anhydride	42	122	130	163	158
E-2,3-Dimethylbutanedioic anhydride (*trans*-α,β-dimethylsuccinic anhydride)	43	208	238 (di) 167 (mono)		
Iodoethanoic anhydride (iodoacetic anhydride)	46	83	95	144	
Chloroethanoic anhydride (chloroacetic anhydride)	46	63	121	134	162
Tridecanoic anhydride	50	44	100	80	88
(±)-Phenylbutanedioic anhydride [(±)-phenylsuccinic anhydride]	54	168	210 (di) 159 (α) 145 (β)	222 (di) 175 (α) 171 (β)	175 (α) 169 (β)
Tetradecanoic anhydride (myristic anhydride)	54	54	107	84	93
Pentanedioic anhydride (glutaric anhydride)	56	97	176	224	218
Z-Butenedioic anhydride (maleic anhydride)	56	130	181 (mono) 266 (di)	175 (mono) 187 (di)	142
Hexadecanoic anhydride (palmitic anhydride)	64	63	107	90	98
Octanedioic anhydride (suberic anhydride)	65	144	127 (mono) 217 (di)	128 (mono) 186 (di)	219 (di)
2-Bromo-2-methylpropanoic anhydride (α-bromoisobutyric anhydride)	65	49	148	83	92
Heptadecanoic anhydride (margaric anhydride)	67	61	108		
Methylenebutanedioic anhydride (itaconic anhydride; methylenesuccinic anhydride)	68	165d	192	190	
Decanedioic anhydride (sebacic anhydride)	68	133	210 (di) 170 (mono)	201 (di) 122 (mono)	201
Octadecanoic anhydride (stearic anhydride)	70	70	109	95	102

(Continued)

TABLE AII.2 Acid Anhydrides (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)			
		Acid	Amide	Anilide	4-Toluidide
3-Methylbenzoic anhydride (*m*-toluic anhydride)	71	113	94	126	118
Phenylethanoic anhydride (phenylacetic anhydride)	72	77	156	118	136
2-Bromobenzoic anhydride	76	150	156		
2-Chlorobenzoic anhydride	79	142	142	118	131
cis-α-Methylglutaconic anhydride	85	118		148	
cis-β-Methylglutaconic anhydride	86	149		143	
Z-2,3-Dimethylbutanedioic anhydride (*cis*-α,β-dimethylsuccinic anhydride)	87	129	149 (mono) 244 (di)	222	
4-Methyl-1,2-benzenedicarboxylic anhydride (4-methylphthalic anhydride)	92	152	188 (di)		
3-Chlorobenzoic anhydride	95	158	134	122	
4-Methylbenzoic anhydride (*p*-toluic anhydride)	95	180	160	145	160
Diphenylethanoic anhydride (diphenylacetic anhydride)	98	148	168	180	172
4-Methoxybenzoic anhydride (*p*-anisic anhydride)	99	186	167	171	186
3-Phenylpentanedioic anhydride (β-phenylglutaric anhydride)	105	140		171	154
4-Ethoxybenzoic anhydride	108	198	202	170	
3,5-Dinitrobenzoic anhydride	109	205	183	234	
4-Nitro-1,2-benzenedicarboxylic anhydride (4-nitrophthalic anhydride)	119	165	200d	192	172
Butanedioic anhydride (succinic anhydride)	120	188	157 (mono) 260 (di); 242	148 (mono) 230 (di)	180 (mono) 255 (di)
3-Pyridinecarboxylic anhydride (nicotinic anhydride)	123	238	128	85	150
1,2-Benzenedicarboxylic anhydride (phthalic anhydride)	132	184; 206	149 (mono) 220 (di)	170 (mono) 255 (di)	160 (mono) 201 (di)
3-Iodobenzoic anhydride	134	187	187		
2-Naphthoic anhydride	135	185	193	172	192
2-Nitrobenzoic anhydride	135	146	176	158	
E-3-Phenyl-2-propenoic anhydride (*trans*-cinnamic anhydride)	136	133	148	153	168
E-(±)-Cyclohexanecarboxylic acid anhydride [*trans*-(±)-hexahydrophthalic anhydride]	140	221	196		
2-Carboxyphenylethanoic anhydride (homophthalic anhydride; 2-carboxyphenylacetic anhydride)	141	181	230 (2-) 185 (α)	231	
1-Naphthoic anhydride	146	162	205	163	
3-Bromobenzoic anhydride	149	155	155		
2,4-Dinitrobenzoic anhydride	160	183	203		

(Continued)

TABLE AII.2 Acid Anhydrides (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)			
		Acid	Amide	Anilide	4-Toluidide
3-Nitrobenzoic anhydride	160	140	143	154	162
3-Nitro-1,2-benzenedicarboxylic anhydride (3-nitrophthalic anhydride)	162	218	201d (di)	234 (di)	226 (di)
1,2-Naphthalic anhydride	169	175d	265d		
4-Nitrobenzoic anhydride	189	241	201	211	204
4-Chlorobenzoic anhydride	194	240	179	194	
β-phenylglutaconic anhydride	206	155	138	174	184
2,2′-Biphenyldicarboxylic acid anhydride (2,2′-diphenic anhydride)	217	229	191 (mono) 212 (di)	176 (mono) 230 (di)	
4-Bromobenzoic anhydride	218	251	189	197	
(+)-1,2,2-Trimethylcyclopentane-1,3-dicarboxylic acid anhydride (D-camphoric anhydride)	221	187	177 (mono)	210 (mono) 193 (di); 226 (di)	214 (α) 196 (β)
4-Iodobenzoic anhydride	228	270	218		
1,8-Naphthalenedicarboxylic anhydride	274	274		282	

TABLE AII.3 Acyl Halides (Liquids)

Name of Compound	bp (°C)	Derivative mp (°C)			
		Acid	Amide	Anilide	4-Toluidide
Ethanoyl fluoride (acetyl fluoride)	21		82	114	147
Propanoyl fluoride (propionyl fluoride)	46		81	106	126
Fluoroethanoyl fluoride (fluoroacetyl fluoride)	51	32	108		
Ethanoyl chloride (acetyl chloride)	55	16	82	115	153
Ethanedioic acid chloride (oxalyl chloride)	64	101	419d (di) 219 (mono)	246 (di) 148 (mono)	268 (di) 169 (mono)
Ethanedioic acid dibromide (oxalyl dibromide)	64	101	419d (di) 219 (mono)	254 (di) 148 (mono)	268 (di) 169 (mono)
Butanoyl fluoride (butyryl chloride)	67		115	96	75
Trichloroethanoyl fluoride (trichloroacetyl fluoride)	68	58	141	97	113
Fluoroethanoyl chloride (fluoroacetyl chloride)	73	32	108		
Chloroethanoyl fluoride (chloroacetyl fluoride)	75	63	120	137	162
Propenoic chloride (acrylyl chloride)	76		85	105	141
Propanoyl chloride (propionyl chloride)	80		81	106	126
Ethanoyl bromide (acetyl bromide)	81		82	115	147
2-Methylpropanoyl chloride (isobutyryl chloride)	92		129	105	108
2-Methylpropenoyl chloride (methacryl chloride)	95	16	102	87	
3-Butenoyl chloride (vinylacetyl chloride)	98		73	58	
Butanoyl chloride (butyryl chloride)	102		116	96	75
Propanoyl bromide (propionyl bromide)	103		81	106	126
2,2-Dimethylpropanoyl chloride (pivalyl chloride; trimethylacetyl chloride)	106	35	155	132	120
Dichloroethanoyl chloride (dichloroacetyl chloride)	108		98	118	153
Ethanoyl iodide (acetyl iodide)	108		82	114	147
Chloroethanoyl chloride (chloroacetyl chloride)	110	63	120	137	162
(±)-2-Chloropropanoyl chloride [(±)-α-chloropropionyl chloride]	111		80	92	124
Methoxyethanoyl chloride (methoxyacetyl chloride)	113		97	58	
3-Methylbutanoyl chloride (isovaleryl chloride)	115		135	110	107
(±)-2-Methylbutanoyl chloride [(±)-α-ethylmethylacetyl chloride]	116		112	110	93
Trichloroethanoyl chloride (trichloroacetyl chloride)	118	58	141	97	113
Acetylglycyl chloride	118	206	137		
E-2-Butenoyl chloride (*trans*-crotonyl chloride)	126	72	161	118	132
Propanoyl iodide (propionyl chloride)	127		81	106	126
Pentanoyl chloride (valeryl chloride)	127		106	63	74
Chloroethanoyl bromide (chloroacetyl bromide)	127	63	120	137	162
Bromoethanoyl bromide (bromoacetyl bromide)	127		91	131	
Butanoyl bromide (butyryl bromide)	128		115	96	75
Bromoethanoyl chloride (bromoacetyl chloride)	135	50	91	131	
2-Ethylbutanoyl chloride	139		112	127	116
3-Methylbutanoyl bromide (isovaleryl bromide)	140		135		107
Trichloroethanoyl bromide (trichloroacetyl bromide)	143	58	163	97	113
3-Chloropropanoyl chloride (β-chloropropionyl chloride)	144	42		119	121

(Continued)

TABLE AII.3 Acyl Halides (Liquids) *(Continued)*

Name of Compound	bp (°C)	Derivative mp (°C)			
		Acid	Amide	Anilide	4-Toluidide
4-Methylpentanoyl chloride (isocaproyl chloride)	147		121	112	63
Butanoyl iodide (butyryl iodide)	148		115	96	75
Bromoethanoyl bromide (bromoacetyl bromide)	150	50	91	131	
(±)-2-Bromobutanoyl chloride [(±)-α-bromobutyryl chloride]	152		112	98	92
2-Bromopropanoyl bromide (α-bromopropionyl bromide)	153		123	99	
Hexanoyl chloride (caproyl chloride)	153		100	95	75
(±)-2-Bromopropanoyl bromide [(±)-α-bromopropionyl bromide]	155	26	123	110	
Benzoyl fluoride	159		128	160	
E-2-Butenedioic acid chloride (fumaroyl chloride)	160	287	267	314	
2-Bromo-2-methylpropanoyl bromide (α-bromoisobutyryl bromide)	164	49	148	83	93
Furoyl chloride	174	134	143	124	107
Heptanoyl chloride (enanthoyl chloride)	176		96	71	81
Hexanoyl bromide (caproyl bromide)	176		100	95	75
Cyclohexane carboxylic acid chloride (hexahydrobenzoyl chloride)	184	30	185	144	
3-Fluorobenzoyl chloride	189; 204	124	130		
Butanedioic acid dichloride (succinyl dichloride)	190d	188	260	230	255
Heptanoyl chloride	193		96	65	81
4-Fluorobenzoyl chloride	193	183	155		
(±)-2-Bromo-3-methylbutanoyl bromide [(±)-α-bromoisovaleryl bromide]	194	44	133	116	124
Octanoyl chloride (capryloyl chloride)	196		110	57	70
Benzoyl chloride	197	122	130	163	158
Diethylpropanedioic acid chloride (diethylmalonyl chloride)	197	125	224		
2-Fluorobenzoyl chloride	206	127	116		
Phenylethanoyl chloride (phenylacetyl chloride)	210	76	157	118	136
2-Methylbenzoyl chloride (*o*-toluyl chloride)	212	105	142	125	144
Nonanoyl chloride (pelargonyl chloride)	215		99	57	84
Pentanedioic acid dichloride (glutaryl dichloride)	218	98	176	224	218
3-Methylbenzoyl chloride (*m*-toluyl chloride)	218	111	96	126	118
Benzoyl bromide	219	122	130	163	158
4-Chlorobenzoyl chloride	222	242	179	194	
3-Phenylpropanoyl chloride (hydrocinnamyl chloride; β-phenylpropionyl chloride)	225d	48	105; 82	98	135
3-Chlorobenzoyl chloride	225	158	134	122	
1,2-Benzenedicarboxylic acid difluoride (phthaloyl difluoride)	226	206	220	253	201
Phenoxyethanoyl chloride (phenoxyacetyl chloride)	226	99	102	101	
4-Methylbenzoyl chloride (*p*-toluyl chloride)	226	180	160	145	165
Decanoyl chloride (capryl chloride)	232	31	108	70	78
2-Chlorobenzoyl chloride	238	142	142	118	131

(Continued)

TABLE AII.3 Acyl Halides (Liquids) *(Continued)*

Name of Compound	bp (°C)	Derivative mp (°C)			
		Acid	Amide	Anilide	4-Toluidide
3-Bromobenzoyl chloride	243	155	155	136	
2-Bromobenzoyl chloride	245	150	156	141	
4-Bromobenzoyl chloride	247	253	190	197	
2-Methoxybenzoyl chloride (*o*-anisoyl chloride)	254	100	129	62; 131; 78	
E-3-Phenyl-2-propenoyl chloride (*trans*-cinnamoyl chloride)	258	133	148	151	168
4-Methoxybenzoyl chloride (*p*-anisyl chloride)	263	184	163	169	186
1,2-Benzenedicarboxylic acid chloride (phthaloyl chloride)	276	206	220	254 (di) 170 (mono)	201 (di) 155 (mono)
1,3-Benzenedicarboxylic acid chloride (isophthaloyl chloride)	276	347	280		
3-Nitrobenzoyl chloride	278	140	143	154	162
1-Chloronaphthalene (α-naphthyl chloride)	298	161	202		
2-Chloronaphthalene (β-naphthyl chloride)	306	185	192		

TABLE AII.4 Acyl Halides (Solids)

Name of Compound	mp (°C)	Derivative mp (°C)			
		Acid	Amide	Anilide	4-Toluidide
4-Chlorobenzoyl chloride	16	242	179	194	
Butanedioic acid chloride (succinyl chloride)	20	188	260 (di) 157 (mono)	230 (di) 148 (mono)	255 (di) 179 (mono)
1-Naphthoyl chloride	20	161	202	163	
2-Nitrobenzoyl chloride	20	146	174	155	
2-Hydroxybenzoyl chloride (salicyloyl chloride)	20	158	142	136	156
Octadecanoyl chloride (stearyl chloride)	23	71	109	33; 95	102
4-Methoxybenzoyl chloride (*p*-anisyl chloride)	26	184	163	169	186
3-Nitrobenzoyl chloride	35	140	143	153	
E-3-Phenyl-2-propenoyl chloride (*trans*-cinnamoyl chloride)	36	133	148	153	168
2-Iodobenzoyl chloride	40	162	184		
4-Bromobenzoyl bromide	42	253	189	197	
2-Naphthoyl chloride	43	185	192	171	191
3-Nitrobenzoyl bromide	43	140	143	154	162
1,3-Benzenedicarboxylic acid dichloride (isophthaloyl dichloride)	44	347	280	250	
2,4-Dinitrobenzoyl chloride	46	183	203		
4-Nitrophenylethanoyl chloride (*p*-nitrophenylacetyl chloride)	48	153	198	198	
E-3-Phenyl-2-propenoyl bromide (*trans*-cinnamoyl bromide)	48	133	148	153	168
2-Naphthoxyethanoyl chloride (β-naphthoxyacetyl chloride)	54	156	147	145	
Diphenylethanoyl chloride (diphenylacetyl chloride)	57	148	168	180	173
4-Iodobenzoyl bromide	60	270	217	210	
3,5-Dinitrobenzoyl bromide	60	205	183	234	
Z-Butenedioic acid chloride (maleyl chloride)	60	139	266 (di) 181 (mono)	187	142
4-Nitrobenzoyl bromide	64	241	201	211	203
E-3-(2-Nitrophenyl)-2-propenoyl bromide (*trans*-2-nitrocinnamoyl chloride)	65	240	185		
3,5-Dinitrobenzoyl chloride	74	205	183	234	
4-Nitrobenzoyl chloride	75	241	201	211	204
3-Nitronaphthaloyl chloride	77	218	201	234	226
1,2-Benzenedicarboxylic acid dibromide (phthaloyl dibromide)	80	206	220	253	201
4-Iodobenzoyl chloride	83	270	218	210	
1,4-Benzenedicarboxylic acid dichloride (terephthaloyl dichloride)	84		250	337	

(Continued)

TABLE AII.4 Acyl Halides (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)			
		Acid	Amide	Anilide	4-Toluidide
1-Hydroxy-2-naphthoyl chloride	85	195	202	154	
2,2′-Biphenyldicarboxylic acid dichloride (2,2′-diphenic acid dichloride)	94	229	212		
3-Hydroxy-2-naphthoyl chloride	95	222	217	243	221
2,2-Diphenylpropanoyl chloride (α,α-diphenylpropionyl chloride)	96	174	149		
2,5-Dihydroxybenzoyl chloride (gentisyl chloride)	98	200	218		
Phenanthrene-2-carboxylic acid chloride	101	260	243	218	
Phenanthrene-9-carboxylic acid chloride	102	252	232	218	
4-Phenylbenzoyl chloride (biphenyl-4-carbonyl chloride)	115	228	223		
Phenanthrene-3-carboxylic acid chloride	117	269	233	217	
E-3-(Nitrophenyl)-2-propenyl chloride (*trans*-nitrocinnamoyl chloride)	124	286	217		
9,10-Anthraquinone-2-carboxylic acid chloride	147	290	280	260	

TABLE AII.5 Alcohols (Liquids)

Name of Compound	bp (°C)	Derivative mp (°C)				
		Phenyl-urethane	1-Naphthyl-urethane	4-Nitro-benzoate	3,5-Dinitro-benzoate	Hydrogen 3-nitro-phthalate
Methanol (methyl alcohol)	66	47	124	96	109	153
Ethanol (ethyl alcohol)	78	52	79	57	94	158
2-Propanol (isopropyl alcohol)	83	88; 76	106	111	123	154
2-Methyl-2-propanol (*tert*-butyl alcohol)	83	136	101	116	142	
2-Propen-1-ol (allyl alcohol)	97	70	109	29	50	124
1-Propanol	97	57	80	35	75	146
2-Butanol (*sec*-butyl alcohol)	100	65	98	26	76	131
2-Methyl-2-butanol (*tert*-pentyl alcohol)	102	42	72	85	118	
2-Methyl-1-propanol (isobutyl alcohol)	108	86	104	69	88	183
2,2-Dimethyl-1-propanol (neopentyl alcohol)	113	144	100			
(±)-3-Methyl-2-butanol	114	68	112		76	127
3-Pentanol	116	49	71; 95	17	101	121
1-Butanol	118	63	71	70; 36	64	147
(±)-2-Pentanol (*sec*-amyl alcohol; *sec*-pentyl alcohol)	120		76	17	62	103
3,3-Dimethyl-2-butanol	120	78			107	
2,3-Dimethyl-2-butanol	120	66	101		111	
3-Methyl-3-pentanol	123	44	84	69	97; 63	
2-Methyl-2-pentanol	123	239			72	
2-Methoxyethanol (methyl cellosolve; ethylene glycol monomethyl ether)	125		113	51		129
2-Methyl-3-pentanol	128	50			85	151
2-Methyl-1-butanol	129	31	82		70	158
2-Chloroethanol (ethylene chlorohydrin)	131	51	101	56	95	98
(±)-4-Methyl-2-pentanol	132	143	88	26	65	166
3-Methyl-1-butanol (isoamyl alcohol; isopentyl alcohol)	132	57	68	21	62	166
3-Methyl-2-butanol	134		72		44	
2-Ethoxyethanol (ethyl cellosolve; ethylene glycol monomethyl ether)	135		68		75	121 (anhyd) 94 (monohyd)
3-Hexanol	136				77	127
2,2-Dimethyl-1-butanol	137	66	81			51
1-Pentanol (pentyl alcohol; amyl alcohol)	138	46	68	11	46	136
(±)-2-Hexanol	139		61	40	39	
2,4-Dimethyl-3-pentanol	140	95	99	155; 40	38	151
Cyclopentanol	141	133	118	62	115	
2,3-Dimethyl-1-butanol	145	29			52	
2-Methyl-1-pentanol	148		76		51	145
2-Ethyl-1-butanol	149		61		52	147
2-Bromoethanol	150	76	86		85	172

(Continued)

TABLE AII.5 Alcohols (Liquids) *(Continued)*

Name of Compound	bp (°C)	Derivative mp (°C)				
		Phenyl-urethane	1-Naphthyl-urethane	4-Nitro-benzoate	3,5-Dinitro-benzoate	Hydrogen 3-nitro-phthalate
2,2,2-Trichloroethanol	151	87	120	71	142	
4-Methyl-1-pentanol	153	48			72	140
3-Methyl-1-pentanol	154		40; 58		38	
(±)-4-Heptanol	156		80	35	64	
1-Hexanol	159	42	62		61	124
Cyclohexanol	160	82	129	50	113	160
(±)-2-Heptanol (*sec*-heptylalcohol)	160		54		49	
3-Chloro-1-propanol (trimethylene chlorohydrin)	161d	38	76		77	
(±)-*cis*-2-Methylcyclohexanol	165	94	155	56	99	
4-Hydroxy-4-methyl-2-pentanone	166			48	55	
(±)-*trans*-2-Methylcyclohexanol	167	105	155	65	115	
Furfuryl alcohol	172	45	130	76	81	
(±)-4-Methyl-1-hexanol	174		50			149
(±)-*cis*-3-Methylcyclohexanol	174	88	129	65	92	
(±)-*cis*-4-Methylcyclohexanol	174	119	160	94	134	
(±)-*trans*-4-Methylcyclohexanol	174	125	160	67	140	
(±)-*trans*-3-Methylcyclohexanol	175	94	122	58	98	
2-Butoxyethanol	176	62				121
1-Heptanol	176	68	62		48	127
1,3-Dichloro-2-propanol	176	73	115		129	
Tetrahydrofurfuryl alcohol	178	61	90	48	84	
(±)-2-Octanol	179	114	64	28	32	
Cyclohexylmethanol	182		110		96	
2,3-Dichloro-1-propanol	183	73	93	38		
2-Ethyl-1-hexanol	184	34	61			108
1,2-Propanediol (propylene glycol)	187	153		127	147	
3,5,5-Trimethyl-1-hexanol	193				62	150
2-(2-Methoxyethoxy)ethanol	194			92		92
1-Octanol	195	74	67		62	128
1,2-Ethanediol (ethylene glycol)	197	157	176	141	169	
(±)-2-Nonanol	198		56		43	
3,7-Dimethyl-1,6-octadien-3-ol (linalool)	199	66	53	70	135	
1-Phenylethanol	203	94	106	43	95	
Benzyl alcohol	205	78	134	86	113	183
(±)-1,3-Butanediol [(±)-1,3-butylene glycol]	208	123	184			
(±)-2-Decanol	211		69		44	
1-Nonanol	215	69	65	66	52	125
(−)-5-Methyl-2-(1-methylethyl)-cyclohexanol [(−)-menthol]	216	112	128	62	153	
1,3-Propanediol (trimethylene glycol)	216	137	164	119	164; 178	
1,7,7-Trimethyl-*exo*-hydroxybicyclo-[2.2.1]heptane (isoborneol)	216			129	138	130

(Continued)

TABLE AII.5 Alcohols (Liquids) *(Continued)*

Name of Compound	bp (°C)	Derivative mp (°C)				
		Phenyl-urethane	1-Naphthyl-urethane	4-Nitro-benzoate	3,5-Dinitro-benzoate	Hydrogen 3-nitro-phthalate
3-Methylbenzyl alcohol (α-hydroxy-3-xylene)	217		116	89	111	
2-Methylbenzyl alcohol (α-hydroxy-*o*-xylene)	219	79		101		
1-Phenyl-1-propanol	219		102	60		
2,3-Dibromo-1-propanol	219d		84		60	
1,3-Dibromo-2-propanol	219d	81		78		
2-Phenylethyl alcohol	219	79	119	62	108	123
α-Terpineol	221	113	152	139; 97	79	
1-Tetradecanol (myristic alcohol)	221			51	67	123
E-3,7-Dimethylocta-2,6-dien-1-ol	229			35	63	117
1-Decanol	231	60	73	30	63	123
1,4-Butanediol (tetramethylene glycol)	235	183	199	175		
3-Phenyl-1-propanol (hydrocinnamyl alcohol)	237	48		47	92	117
1,5-Pentanediol (pentamethylene glycol)	239	176	147	105		
1-Undecanol (1-hendecanol)	243	62	73	100; 30	55	123
Di-2-hydroxyethyl ether (diethylene glycol)	244		149; 122	151; 100 (di)	150	
2-Phenoxyethanol	245			63	105; 74	113
E-3-Phenyl-2-propen-1-ol (*trans*-cinnamyl alcohol)	257	91	114	78	121	
1-Dodecanol (lauryl alcohol)	259	74	80	45	60	124
4-Methoxybenzyl alcohol (*p*-anisyl alcohol)	259	93		94		
1,2,3-Propanetriol (glycerol; 1,2,3-trihydroxypropane)	290d	180	192	188	76	
Benzhydrol	297	140	136		141	
1-Heptadecanol	310		89	54	122	122
E-Octa-9-decen-1-ol (elaidyl alcohol)	333	57	71			

TABLE AII.6 Alcohols (Solids)

Name of Compound	mp (°C)	Derivative mp (°C)				
		Phenyl-urethane	1-Naphthyl-urethane	4-Nitro-benzoate	3,5-Dinitro-benzoate	Hydrogen 3-nitro-phthalate
1-Undecanol	16	62	73	30; 100	55	123
1-Phenyl-1-butanol	16		99	58		
1,2,3-Propanetriol (glycerol; 1,2,3-trihydroxypropane)	18	180	192	188	76	
2,2,2-Trichloroethanol	19	87	120	71	142	
1,4-Butanediol (tetramethylene glycol)	19	183	198	175		
1-Phenylethanol	20	92	106	43	95	
(±)-*E*-2-Methylcyclohexanol	21	105	155	65	115	
1-Dodecanol (lauryl alcohol)	25	74	80	45	60	124
Cyclohexanol	25	82	129	52	113	160
2-Methyl-2-propanol (*tert*-butyl alcohol)	25	136	101	116	142	
4-Methoxybenzyl alcohol (*p*-anisyl alcohol)	25	93		94		
2,4-Hexadien-1-ol	31	79			85	
1-Tridecanol	31			37		124
E-3-Phenyl-2-propen-1-ol (*trans*-cinnamyl alcohol)	33	91	114	78	121	
α-Terpineol	35				78	
E-Octa-9-decen-1-ol (elaidyl alcohol)	37	57	71			
1-Tetradecanol (myristyl alcohol)	39	74	82	51	67	124
2-Methylbenzyl alcohol (α-hydroxy-2-xylene)	39	79		101		
(−)-5-Methyl-2-(1-methylethyl)-cyclohexanol [(−)-menthol]	44	112	128	62	153	
1-Pentadecanol	44	72	72	46		123
(±)-α-Propylbenzyl alcohol	49		99	58		
1-Hexadecanol (cetyl alcohol)	50	73	82	58	66	122
2,2-Dimethyl-1-propanol (neopentyl alcohol)	53	144	100			
1-Heptadecanol	54		89	54	122	122
2-Butyne-1,4-diol	55	132			191	
4-Methylbenzyl alcohol (α-hydroxy-4-xylene)	60	79			118	
1-Octadecanol (stearyl alcohol)	60	80	89	64	66	119
Diphenylmethanol (benzhydrol)	69	140	139	132	142	
10-Nonadecanol (myricyl alcohol)	85	96	54			
(±)-Benzoin	137	165	140	123		
(−)-Cholesterol	148	168	160; 176	193		
(+)-1,7,7-Trimethyl-*endo*-3-hydroxy bicyclo[2.2.1]heptane [(+)-borneol]	212			153		154
(−)-1,7,7-Trimethyl-*endo*-3-hydroxy bicyclo[2.2.1]heptane [(−)-borneol]	212	138	127	137	154	

TABLE AII.7 Aldehydes (Liquids)

Name of Compound	bp (°C)	Derivative mp (°C)					
		Semicarbazone	2,4-Dinitrophenylhydrazone	4-Nitrophenylhydrazone	Phenylhydrazone	Oxime	Dimedon
Methanal (formaldehyde)	−21	169	167	182	145		191
Ethanal (acetaldehyde)	21	163	147; 169	129	63; 99	47	141
Propanal (propionaldehyde)	50	89; 154	155	125		40	156
Ethanedial (glyoxal)	50	270	328	311	180	178	228 (di) 186 (mono)
Propenal (acrolein)	52	171	165	151	52		192
2-Methylpropanal (isobutyraldehyde)	64	126	187	132			154
2-Methyl-2-propenal (α-methylacrolein)	74	198	206		74		
Butanal (butyraldehyde)	75	106; 96	125	95	95		142; 134
2,2-Dimethylpropanal (pivalaldehyde; trimethylacetaldehyde)	75	190	210	119		41	
Methoxyethanal (methoxyacetaldehyde)	92		125	115			
3-Methylbutanal (isovaleraldehyde)	93	107; 132	123	111		49	155
2-Methylbutanal (α-Methylbutyraldehyde)	93	105	121				
Trichloroethanal (chloral)	98	90d	131	131		56	
2-Butenal (crotonaldehyde)	103	200	196	186	56	119	184
Pentanal (valeraldehyde)	104		107; 98	74		52	105
Ethoxyethanal (ethoxyacetaldehyde)	106		117	114			
5-Hydroxymethylfurfural	114	195; 166	184	185	141	78; 108	
2-Methylpentanal (α-methylvaleraldehyde)	116	102	103				
2-Ethylbutanal (α-ethylbutyraldehyde)	117	99	134; 95				102
4-Methylpentanal	121	127	99				
2-Pentenal	125	180		123			
Hexanal (caproaldehyde)	131	108	107	80		51	109
3-Methyl-2-butenal (3-methylcrotonaldehyde)	135	223	186				
2-Methyl-2-pentenal (3-ethyl-2-methylacrolein)	137	207	159		60	49	
5-Methylhexanal	144	117	117				
3-Furaldehyde	144	211			150		
Tetrahydrofurfural	145	166	134; 204				123
1-Cyclopentenylmethanal (1-cyclopentenylformaldehyde)	146	208		188			

(Continued)

TABLE AII.7 Aldehydes (Liquids) *(Continued)*

Name of Compound	bp (°C)	Derivative mp (°C)					
		Semicarbazone	2,4-Dinitrophenylhydrazone	4-Nitrophenylhydrazone	Phenylhydrazone	Oxime	Dimedon
2-Hexenal	150	176		139			
Heptanal (heptaldehyde)	156	109	108	73		57	135; 103
2-Furancarboxaldehyde (furfural)	162	203	230; 212; 185	54; 154	98	92; 76	162d
1-Cyclohexanecarboxaldehyde (hexahydrobenzaldehyde)	162	176	172			91	
2-Ethylhexanal (α-ethylcaproaldehyde)	163	254d	121				
4-Cyclohexene-1-carboxaldehyde (1,2,3,6-tetrahydrobenzaldehyde)	165	154		163		76	
Butanedial (succinaldehyde)	170		280			172	
Octanal (caprylaldehyde)	171	101	106; 96	80		60	90
2-Ethylpentenal (2-ethyl-3-propylacrolein)	173	153	125				
3-Fluorobenzaldehyde	173			202	114	63	
4-Fluorobenzaldehyde	175			212	147	117; 86	
2-Fluorobenzaldehyde	175			205	90	63	
Benzaldehyde	179	222; 235	237	192; 236; 262	158	35; 130	195
5-Methylfurfural	187	211	212	130	148	112 (syn) 52 (anti)	
Pentanedial (glutaraldehyde)	189			169		178	
Nonanal (pelargonaldehyde)	190	100; 84	100			64	86
Phenylethanal (phenylacetaldehyde)	194	156; 163	121; 110	151	63; 102	103	165
2-Hydroxybenzaldehyde (salicylaldehyde)	197	231	252d	228	143	63	211
3-Methylbenzaldehyde (*m*-tolualdehyde)	199	213; 224	212; 194	157	84; 91	60	172
2-Methylbenzaldehyde (*o*-tolualdehyde)	200	208; 218	195	222	101; 111	49	167
4-Methylbenzaldehyde (*p*-tolualdehyde)	205	221; 234	239	201	114; 121	80; 110	
(+)-Citronellal	207	84	78				79
Decanal (capraldehyde)	209	102	104			69	92
3-Chlorobenzaldehyde	214	230	256	216	134	71	
2-Chlorobenzaldehyde	214	230; 146	209; 214	238; 249	86	76; 103	205d
Phenoxyethanal (phenoxyacetaldehyde)	215d	145			86	95	
4-Chlorobenzaldehyde	216	233	270; 254	239; 220	127	110 (α) 146 (β)	
2-Pyrrolecarboxaldehyde	219	184		183	139	164	

(Continued)

TABLE AII.7 Aldehydes (Liquids) *(Continued)*

Name of Compound	bp (°C)	Derivative mp (°C)					
		Semicarbazone	2,4-Dinitrophenylhydrazone	4-Nitrophenylhydrazone	Phenylhydrazone	Oxime	Dimedon
3-Phenylpropanal (hydrocinnamaldehyde)	224	127	149	123		97	
E-3,7-Dimethylocta-2,6-dien-1-al (geranial; citral)	229	164	116	195			
3-Methoxybenzaldehyde (*m*-anisaldehyde)	230	233d	218	171	76	40; 112	
2-Bromobenzaldehyde	230	214	203	240		102	
3-Bromobenzaldehyde	236	205	256	220	141	72	
2-(1-Methylethyl)benzaldehyde (cumaldehyde; *p*-isopropylbenzaldehyde)	236	211	245	190	129	52; 111	171
Dodecanal (lauraldehyde)	238	106	106	90		78	
2-Methoxybenzaldehyde (*o*-anisaldehyde)	246	215d	253	205		92	188
4-Methoxybenzaldehyde (*p*-anisaldehyde)	248	210	254d	161	121	45	145 (α) 65 (α') 133 (β)
3,4-Dichlorobenzaldehyde	248			277		122	
4-Ethoxybenzaldehyde (salicylaldehyde ethyl ether)	249	219				59	
E-3-Phenyl-2-propenal (*trans*-cinnamaldehyde)	252	215	255d	195	168	139 (β) 65 (α)	219; 161
4-Ethoxybenzaldehyde	255	208				157 (syn) 118 (anti)	
3,4-Methylenedioxybenzaldehyde (piperonal)	263	237	266d	200	106	112; 146	178; 193
3,4-Dimethoxybenzaldehyde (veratraldehyde)	285	177	265		121	95	
1-Naphthaldehyde	292	221	254	234	80	98	
Diphenylethanal (diphenylacetaldehyde)	316	162				120 (α) 106 (β)	

TABLE AII.8 Aldehydes (Solids)

Name of Compound	mp (°C)	Derivative mp (°C)					
		Semicarbazone	2,4-Dinitrophenylhydrazone	4-Nitrophenylhydrazone	Phenylhydrazone	Oxime	Dimedon
2-Chlorobenzaldehyde	11	230; 146	209; 214	238; 249	86	76; 103	205
3-Chlorobenzaldehyde	18	230	256	216	135	71; 118	
2,3,5,6-Tetramethylbenzaldehyde	20	270d				125	
2-Ethoxybenzaldehyde (salicylaldehyde ethyl ether)	22	219				59	
2-Bromobenzaldehyde	22	214	230	240		102	
Tetradecanal (myristaldehyde)	24	107	108	95		84	
Pentadecanal	25	107	107	95		86	
Hexadecanal (palmitaldehyde)	34	109	108	97		88	
1-Naphthaldehyde	34	221	254	224; 234	80	90; 98	
Phenylethanal (phenylacetaldehyde)	34	156; 163	121; 110	151	63; 102	103	165
5-Hydroxymethylfurfural	36	195; 166	184	185	141	78; 108	
2-Iodobenzaldehyde	37	206			79	108	
3,4-Methylenedioxybenzaldehyde (piperonal)	37	237	266d	200	106	112; 146	178; 193
2-Methoxybenzaldehyde (*o*-anisaldehyde)	38	215d	253	205		92	188
Phenoxyethanal (phenoxyacetaldehyde)	38	145			86	95	
Octadecanal (stearaldehyde)	38	119	110	101		89	
2-Aminobenzaldehyde	40	247	250	220	221	135	
4-(*N*,*N*-Diethylamino)benzaldehyde	41	214d	206		103	93	
2-Nitrobenzaldehyde	44	256	265; 250	263	156	103; 154	
3,4-Dichlorobenzaldehyde	44			277		122	
3,3-Diphenyl-2-propenal (β-phenylcinnamaldehyde)	44	215	196		173		
2,3-Dimethoxybenzaldehyde (veratraldehyde)	44	177	265		121	95	173
2,4,5-Trimethylbenzaldehyde	44	243			127		
Dodecanal (lauraldehyde)	45	106	106	90		78	
4-Chlorobenzaldehyde	48	233	270; 254	239; 220	127	110 (α) 146 (β)	
2-Pyrrolecarboxaldehyde	50	184		183	139	164	
4-Chloro-2-hydroxybenzaldehyde	53	212		257		155	
Quinoline-4-carboxaldehyde	53			262		182	
2-(2-Furyl)propenal [2-(2-furyl)acrolein]	54	220			132	111	
2,3-Dimethoxybenzaldehyde (veratraldehyde)	54	231	264d		138	99	
3-Chloro-2-hydroxybenzaldehyde (3-chlorosalicylaldehyde)	56	243				168	

(Continued)

TABLE AII.8 Aldehydes (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)					
		Semicarbazone	2,4-Dinitrophenylhydrazone	4-Nitrophenylhydrazone	Phenylhydrazone	Oxime	Dimedon
Isoquinoline-1-carboxaldehyde	56	197			172		
2-Hydroxy-5-methylbenzaldehyde (5-methylsalicylaldehyde)	56				149	105	
Trichloroethanal hydrate (chloral hydrate; trichloroacetaldehyde hydrate)	57	90	131			56	
4-Bromobenzaldehyde	57	229	128; 257	208	113	157 (syn) 111 (anti)	
3-Iodobenzaldehyde	57	226		212	155	62	
3-Nitrobenzaldehyde	58	246	293d	247	124	122	198
2,5-Dichlorobenzaldehyde	58				105	128	
2-Phenanthraldehyde	60	282				175	
4-Phenylbenzaldehyde	60	243	239		189	150	
3-Methoxy-1-naphthaldehyde	60	200		197		102	
2-Naphthaldehyde	61	245	270	230	206d; 218	156	
3,5-Dichlorobenzaldehyde	65				107	112	
5-Methoxy-1-naphthaldehyde	66	246		246		104	
Quinoline-2-carboxaldehyde	71			225; 250	204	188	
2,4-Dichlorobenzaldehyde	71		226	256		136	
4-Aminobenzaldehyde	72	153; 173			156	124	
4-(*N*,*N*-Dimethylamino)benzaldehyde	74	222	325; 237	182	148	185	
Quinoline-6-carboxaldehyde	76	239			185	191	
3,4,5-Trimethoxybenzaldehyde	78	220		202		84	
4-Iodobenzaldehyde	78	224	257	201	121		
3-Phenanthraldehyde	80	275				145	
4-Hydroxy-3-methoxybenzaldehyde (vanillin)	81	229; 240d	271d	228	105	122	198
2-Hydroxy-1-naphthaldehyde	82	240				157	
1,3-Benzenedicarboxaldehyde (isophthalaldehyde)	89				242	180	
3,4,5-Trichlorobenzaldehyde	91	254		342d	147		
2-Phenyl-2-oxoethanal (phenylglyoxal)	91	217d	296	310	152 (di)	129 (α) 168 (di)	
Quinoline-8-carboxaldehyde	95	239			176	115	
2,3-Diphenyl-2-propenal (α-phenylcinnamaldehyde)	95	195			126; 141	166	
3,5-Dichloro-2-hydroxybenzaldehyde (3,5-dichlorosalicylaldehyde)	96	227			153	196	
Benzaldehyde-2-carboxylic acid (*o*-formylbenzoic acid; phthalaldehyde acid)	99	202				120	

(Continued)

TABLE AII.8 Aldehydes (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)					
		Semicarbazone	2,4-Dinitrophenylhydrazone	4-Nitrophenylhydrazone	Phenylhydrazone	Oxime	Dimedon
3-Hydroxy-2-naphthaldehyde	100	>270			248	207d	
5-Chloro-2-hydroxybenzaldehyde	100	287			152	128	
9-Phenanthraldehyde	101	223		265		157	
9-Anthraldehyde	105	219			207	187	
4-Nitrobenzaldehyde	106	221	320d	249	159	133	190 (anti) 184 (syn)
5-Bromo-2-hydroxybenzaldehyde	106	297	292			126	
3-Hydroxybenzaldehyde	108	199	260d	222	131; 147	90	
2,3-Dihydroxybenzaldehyde	108	226		167			
2-Chloro-5-hydroxybenzaldehyde	112	236		251		147	
2-Ethoxy-1-naphthaldehyde	115	215			91		
4-Hydroxybenzaldehyde	117	224; 280	280d; 260	266	178; 184	72; 112	190
3-Hydroxy-2,4,6-trichlorobenzaldehyde	117			272		172	
1,4-Benzenedicarboxaldehyde (terephthalaldehyde)	118	225		281	154; 278	200	
4-Chloro-3-hydroxybenzaldehyde	121	239		227		126	
2,4-Dihydroxybenzaldehyde (β-resorcylaldehyde)	136	260d	286d; 302	285	160	192	226
3-Chloro-4-hydroxybenzaldehyde	139	210				145	
2-Chloro-3-hydroxybenzaldehyde	140	237		245		149	
2,4-Dichloro-3-hydroxybenzaldehyde	141			278		188	
(±)-2,3-Dihydroxypropanal [(±)-glyceraldehyde]	142	160d	167		132	118	203
2-Chloro-4-hydroxybenzaldehyde	148	214		284d		194	
3,4-Dihydroxybenzaldehyde (protocatechualdehyde)	154	230d	275d		176	157	145
3,5-Dichloro-4-hydroxybenzaldehyde	156	237				185	
Diphenylhydroxyacetaldehyde (diphenylglycolaldehyde)	163	242				124	
Benzaldehyde-3-carboxylic acid (*m*-formylbenzoic acid)	175	265			164	188d	
2-Hydroxybenzaldehyde-3-carboxylic acid (3-formylsalicylic acid)	179				188	193	
Pentachlorobenzaldehyde	203				153	201	
3,4,5-Trihydroxybenzaldehyde (gallaldehyde)	212d			236		200	
4-Hydroxybenzaldehyde-3-carboxylic acid (5-formylsalicylic acid)	249				219	179	
Benzaldehyde-4-carboxylic acid (*p*-formylbenzoic acid)	256			226	210		

TABLE AII.9 Amides (Liquids)

		Derivative mp (°C)					
			Acid			Amine	
Name of Compound	bp (°C)	9-Acyl-amido-xanthene	Acid	4-Nitro-benzyl ester	4-Bromo-phen-acyl-ester	Acet-amide	Benz-amide
N,*N*-Dimethylmethanamide (*N*,*N*-dimethylformamide)	153	184		31	140		41
N,*N*-Diethylmethanamide (*N*,*N*-diethylformamide)	178			31	140		42
N-Methylmethanamide (*N*-methylformamide)	185			31	140	28	80
Methanamide (formamide)	195	184		31	140		
N-Ethylmethanamide (*N*-ethylformamide)	199			31	140		71
N-Formylpiperidine	222			31	140		48
N-Acetylpiperidine	226		166	78	86		48
N-Methylmethananilide (*N*-methylformanilide)	251			31	140	102	63
N-Ethylmethananilide (*N*-ethylformanilide)	258			31	140	54	60
N-Propylmethananilide (*N*-propylformanilide)	267			31	140	47	
N-(2-Methylpropyl)methananilide (*N*-isobutylformanilide)	274			31	140		
N-(3-Methylbutyl)methananilide (*N*-isopentylformanilide)	286			31	140		

TABLE AII.10 Amides (Solids)

Name of Compound	mp (°C)	Derivative mp (°C)					
			Acid			Amine	
		9-Acyl-amido-xanthene	Acid	4-Nitro-benzyl ester	4-Bromo-phen-acyl-ester	Acet-amide	Benz-amide
Butananilide (butyranilide)	35				63	114	160
Z-9-Octadecenanilide (oleanilide)	41		16		46	114	160
N-Benzoylpiperidine (*N*-benzipiperidine)	48		122	89	119		48
Methananilide (formanilide)	50			31	140	114	160
N-Methyl-*N*-phenylethanamide (*N*-propylethananilide; *N*-propyl-*N*-phenylacetamide; *N*-propylacetanilide)	50		16	78	86	47	
Propanedioic acid monoamide (malonic acid monoamide; malonamic acid)	50		135	86 (di)			
N-Benzylhexanamide (*N*-benzylcaproamide)	53				72	60	105
N-Ethyl-*N*-phenylethanamide (*N*-ethylethananilide; *N*-ethyl-*N*-phenyl acetamide; *N*-ethylacetanilide)	54		17	78	86	54	60
N-Benzyl-3-methylbutanamide (*N*-benzylisovaleramide)	54			68	137	60	105
N-Methyl-*N*-(2-methylphenyl) ethanamide [*N*-methyl-*o*-acetotoluidide; *N*-acetyl-*N*-methyl-*o*-toluidine; *N*-methyl-*N*-(*o*-tolyl)acetamide]	56		17	78	86	56	66
Octananilide (caprylanilide)	57		16		67	114	160
Nonananilide (pelargonanilide)	57		12		69	114	160
N-Benzyl-*N*-phenylethanamide (*N*-benzyl ethananilide; *N*-benzyl-*N*-phenyl acetamide; *N*-benzylacetanilide)	58		17	78	86	58	107
Methoxyethananilide (methoxyacetanilide)	58					114	160
(±)-2-Hydroxypropananilide [(±)-lactanilide; (±)-β-hydroxypropionanilide]	59		18		113	114	160
N-Ethylbenzanilide	60		122	89	119	54	60
N-Benzylmethanamide (*N*-benzylformamide)	60			31	140	60	105
N-Benzylethanamide (*N*-benzylacetamide)	61		17	78	86	60	105
Pentananilide (valeranilide)	63				75	114	160
Z-13-Docosenanilide (erucanilide)	65		34		63	114	160

(Continued)

TABLE AII.10 Amides (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)					
			Acid			Amine	
		9-Acyl-amido-xanthene	Acid	4-Nitro-benzyl ester	4-Bromo-phen-acyl-ester	Acet-amide	Benz-amide
N-(3-Methylphenyl)ethanamide [*N*-acetyl-*m*-toluidine; *m*-aceto-toluidide; *N*-(*m*-tolyl)acetamide]	66		17	78	86	65	125
N-Methyl-*N*-(3-methylphenyl) ethanamide [*N*-methyl-*m*-acetotoluidide; *N*-acetyl-*N*-methyl-*m*-toluidine; *N*-methyl-*N*-(*m*-tolyl)acetamide]	66		17	78	86	66	125
Ethyl *N*-phenylethanedioic acid monoamide (ethyl oxanilate)	67					114	160
Benzindole	68		122	89	119	158	68
Heptanilide (enanthanilide)	70				72	114	160
Decananilide (capranilide)	70		31		60	114	160
Undecananilide (hendecananilide)	71		28; 16		68	114	160
N,*N*-Diphenylmethanamide (*N*,*N*-diphenylformamide)	73		8	31	140	101	180
3-Butenanilide (vinylacetanilide)	73					114	160
E-2-Methyl-2-butenamide (tiglamide)	76		65	64	68		
E-2-Methyl-2-butenanilide (tiglanilide)	77		65	64	68	114	160
4-Methylhexananilide	77					114	160
Dodecanilide (lauranilide)	78		44		76	114	160
(±)-2,3-Dimethylbutananilide	78					114	160
Pentadecananilide	78		52	40	77	114	160
E-13-Docosenanilide (brassidianilide)	79		60		94	114	160
(±)-2-Hydroxypropanamide [(±)-lactamide]	79		18		113		
N-(2-Ethoxyphenyl)ethanamide [*o*-acetophenetidide; *N*-acetyl-*o*-phenetidine; *N*-acetyl-2-ethoxyaniline; *N*-(*o*-ethoxyphenyl) acetamide]	79		17	78	86	79	104
Tridecananilide	80		43		75	114	160
Propanamide (propionamide)	81	214		31	63		
Ethanamide (acetamide)	82	245	17	78	86		
N-Methyl-*N*-(4-methylphenyl) ethanamide [*N*-methyl-*p*-acetotoluidide; *N*-acetyl-*N*-methyl-*p*-toluidine; *N*-methyl-*N*-(*p*-tolyl)acetamide]	83		17	78	86	83	
2-Bromo-2-methylpropananilide (α-bromoisobutyranilide)	83		49			114	160
Tetradecananilide (myristanilide)	84		54		81	114	160

(Continued)

TABLE AII.10 Amides (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)					
			Acid			Amine	
		9-Acyl-amido-xanthene	Acid	4-Nitro-benzyl ester	4-Bromo-phen-acyl-ester	Acet-amide	Benz-amide
2-Oxobutananilide (acetoacetanilide)	85					114	160
3-Pyridinecarboxylic acid anilide (nicotinanilide)	85 (dihyd)		238			114	160
N-(4-Propylphenyl)ethanamide [*p*-propylacetanilide; *p*-propylethananilide; *N*-(*p*-propylphenyl) acetamide]	87		17	78	86	87	115
Propylanilide (propiolanilide)	87		18			114	160
N-(3-Bromophenyl)ethanamide [*m*-bromoacetanilide; *m*-bromoethananilide; *N*-(*m*-bromophenyl) acetamide]	87		17	78	86	87	120; 136
(±)-3-Methylpentanilide	87					114	160
Butyl oxamate	88		190 (anhyd) 101 (hyd)	204 (di)			
N-(2-Chlorophenyl)ethanamide [*o*-chloroacetanilide; *o*-chloroethananilide; *N*-(*o*-chlorophenyl) acetamide]	88		17	78	86	87	99
(+)-13-(2-Cyclopentenyl) tridecananilide [(+)-chaulmoogranilide]	89		69			114	160
Hexadecananilide (palmitanilide)	90		63	43	86	114	160
Bromoethanamide (bromoacetamide)	91		50	88			
Z-*N*-Phenylbutenedioic acid imide (*N*-phenylmaleimide)	91		130	91 (di)	170; 190	114	160
Didecananilide (1-eicosananilide; arachidanilide)	92		77		89	114	160
(±)-2-Chloropropananilide [(±)-*a*-chloropropionanilide]	92					114	160
2,2-Dimethylbutanilide	92					114	160
Z-Butenedioic acid imide (maleimide)	93		130	91 (di)	170; 190		
N-(2-Nitrophenyl)ethanamide [*o*-nitro-acetanilide; *o*-nitroethananilide; *N*-(*o*-nitrophenyl)acetamide]	94		17	78	86	94	110
2-Ethylpentananilide	94					114	160
N-Methyl-*N*-(1-napththyl) ethanamide [*N*-methyl-*N*-(*α*-naphthyl)acetamide]	94		17	78	86	95	121
E-9-Octadecenamide (elaidamide)	94		51		65		
E-13-Docosenamide (transbrassidamide)	94		60		94		
Hexanilide (caproanilide)	95				72	114	160

(Continued)

TABLE AII.10 Amides (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)					
			Acid			Amine	
		9-Acyl-amido-xanthene	Acid	4-Nitro-benzyl ester	4-Bromo-phen-acyl-ester	Acet-amide	Benz-amide
Butananilide (butyranilide)	95			35	63	114	160
N-Benzylhexadecanamide (*N*-benzylpalmitamide)	95		63	43	86	60	105
Nonanedioic acid monoamide (azelaic acid monoamide)	95		106	44 (di)	131 (di)		
(±)-2-Methylpentanilide	95					114	160
Octadecananilide (stearanilide)	95		70		92	114	160
Heptanamide	96	155			72		
Semicarbazide	96					67 (mono) 138 (di)	172 (mono) 241 (di)
3-Methylbenzamide (*m*-toluamide)	97		113	87	108		
Trichloroethananilide (trichloroacetanilide)	97		58	80		114	160
N-(3-Ethoxyphenyl)ethanamide [*m*-acetophenetidide; *N*-acetyl-*m*-phenetidine; *N*-acetyl-3-ethoxyaniline; *N*-(*m*-ethoxyphenyl) acetamide]	97		17	78	86	37	103
N-Benzyloctadecanamide (*N*-benzylstearamide)	97		70		92	60	105
Hydroxyethananilide (glycolanilide; hydroxyacetanilide)	97		80	107	138	114	160
3-Phenylpropananilide (β-phenylpropionanilide; hydrocinnamanilide)	98		48	36	104	114	160
2-Hydroxy-2-methylpropanamide (α-hydroxyisobutyramide)	98		79	81	98		
2-Methylhexananilide	98					114	160
Phenoxyethananilide (phenoxyacetanilide)	99		100		149	114	160
Decanamide (capramide)	99	148	31		67		
N-(4-Methyl-2-nitrophenyl)ethanamide [4-methyl-2-nitroacetanilide; 4-methyl-2-nitroethananilide; *N*-(4-methyl-2-nitrophenyl) acetamide]	99		17	78	86	99	148
Nonanamide (pelargonamide)	99	148	12		69		
N-(3-Bromophenyl)ethanamide [*m*-bromo acetanilide; *m*-bromoethananilide; *N*-(*m*-bromophenyl)acetamide]	99		17	78	86	99	116
2-Bromopropananilide (α-bromopropionanilide)	99; 110		26			114	160
Tridecanamide	100		43		75		

(Continued)

TABLE AII.10 Amides (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)					
			Acid			Amine	
		9-Acyl-amido-xanthene	Acid	4-Nitro-benzyl ester	4-Bromo-phen-acyl-ester	Acet-amide	Benz-amide
Hexanamide (caproamide)	101	160			72		
N,N-Diphenylethanamide (*N,N*-diphenylacetamide)	101		17	78	86	101	180
N,N'-Diacetyl-1,3-diaminopropane - (*N,N'*-diacetyltrimethylenediamine)	101		17	78	86	126 (mono) 101 (di)	140 (mono) 147 (di)
Phenoxyethanamide (phenoxyacetamide)	101		100		149		
Methylurea	102	230				28	80
N-Methyl-*N*-phenylethanamide (*N*-methyl ethananilide; *N*-methyl-*N*-phenyl acetamide; *N*-methylacetanilide)	102		17	78	86	102	63
4-Oxopentananilide (levulinanilide)	102		35	61	84	114	160
Pentadecanamide	102		52	40	77		
Z-2-Butenanilide (isocrotonanilide)	102		15		81	114	160
Z-2-Butenamide (isocrotonamide)	102		15		81		
N-Benzoyl-3-ethoxyaniline [*m*-benzophenetidide; *N*-benzoyl-*m*-phenetidine; *N*-(*m*-ethoxyphenyl) benzamide]	103			89	119	97	103
N,N-Dicyclohexylethanamide (*N,N*-dicyclohexylacetamide)	103		17	78	86	103	153
Undecanamide (hendecanamide)	103		29; 16		68		
3,4-Dimethylbenzanilide	104		166			114	160
N-Benzoyl-2-ethoxyaniline [*N*-benzoyl-*o*-phenetidine; *o*-benzophenetidide; *N*-(*o*-ethoxyphenyl) benzamide]	104		122	89	119	97	103
2-Oxopropananilide (pyruvanilide)	104		14			114	160
N-Cyclohexylethanamide (*N*-cyclohexylacetamide)	104		17	78	86	104	149
N-(2-Propylphenyl)ethanamide [*o*-propylacetanilide; *o*-propylethananilide; *N*-(*o*-propylphenyl)acetamide]	105		17	78	86	105	119
2-Methylpropananilide (isobutyranilide)	105				77	114	160
N-(4-Butylphenyl)ethanamide [*p*-butylacetanilide; *p*-butylethananilide; *N*-(*p*-butylphenyl)acetamide]	105		17	78	86	105	126
Propenanilide (acrylanilide)	105		13			114	160
3-Phenylpropanamide (hydrocinnamamide; β-phenylpropionamide)	105	189	48	36	104		
Propananilide (propionanilide)	106			31	64	114	160

(Continued)

TABLE AII.10 Amides (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)					
			Acid			Amine	
		9-Acyl-amido-xanthene	Acid	4-Nitro-benzyl ester	4-Bromo-phen-acyl-ester	Acet-amide	Benz-amide
Pentanamide (valeramide)	106	167			75		
Hexadecanamide (palmitamide)	106	142	63	42	86		
N-Benzylbenzamide	106		122	89	119	60	105
N,N-Dimethyurea (*sym*-dimethylurea)	106					28	80
N-Benzylbenzanilide	107		122	89	119	58	107
Tetradecanamide (myristamide)	107		54		81		
Heptadecanamide (margaramide)	108		61	49	82		
4-Oxopentanamide (levulinamide)	108		35	61	84		
Nonanedioic acid (azelaic acid monoanilide)	108		107	144 (di)	131 (di)	114	160
N-(2-Iodophenyl)ethanamide [*o*-iodo-acetanilide; *o*-iodoethananilide; *N*-(*o*-iodophenyl)acetamide]	109		17	78	86	109	139
Octadecanamide (stearamide)	109	141	70		92		
Heptanedioic acid monoanilide (pimelic acid monoanilide)	109		105		137 (di)	114	160
Phenylpropynamide (phenylpropiolamide)	109		137	83			
Didecanamide (arachidamide)	109		77		89		
3-Methylbutananilide (isovaleranilide)	110				68	114	160
(±)-2-Methylbutananilide	110				55	114	160
Octanamide (caprylamide)	110	148	16		67		
N-(2-Ethylphenyl)ethanamide [*o*-ethyl-acetanilide; *o*-ethylethananilide; *N*-(*o*-ethylphenyl)acetamide]	111		17	78	86	111	147
4-Methylpentananilide (isocaproanilide)	112				77	114	160
N-(2-Methylphenyl)ethanamide [*N*-acetyl-*o*-toluidine; *o*-aceto-toluidide; *N*-(*o*-tolyl)acetamide]	112		17	78	86	111	146
N-Phenylethanamide (ethananilide; acetanilide; *N*-phenylacetamide)	114		17	78	86	114	160
N-Benzyl-*E*-2-butenamide (*N*-benzylcrotonamide)	114		72	67	96	60	105
Ethyl ethanedioic acid monoamide (ethyl oxamate)	114		189 (anhyd) 101 (dihyd)	204 (di)			71
Dihydroethanoic acid monoanilide (dihydroacetic acid monoanilide)	115		109			114	160
Butanamide (butyramide)	116	187			63		
2-Bromo-3-methylbutananilide (α-bromoisovaleranilide)	116		44			114	160
2-Chlorobenzanilide	118		142	106	106	114	160
Z-2-Butenanilide (crotonanilide)	118		72	67	96	114	160

(Continued)

TABLE AII.10 Amides (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)					
			Acid			Amine	
		9-Acyl-amido-xanthene	Acid	4-Nitro-benzyl ester	4-Bromo-phen-acyl-ester	Acet-amide	Benz-amide
Phenylethananilide (phenylacetanilide; *N*,2-diphenylethanamide; *N*,2-diphenylacetamide)	118		77	65	89	114	160
Dichloroethananilide (dichloroacetanilide)	118				99	114	160
N-Ethyl-*N*-(4-nitrophenyl)ethanamide [*N*-ethyl-*p*-nitroacetanilide; *N*-ethyl-*p*-nitroethananilide; *N*-ethyl-*N*-(*p*-nitrophenyl)acetamide]	118		17	78	86	119	98
1,3,5-Benzenetricarboxylic acid trianilide (trimesic acid trianilide)	120		380		197 (tri)	114	160
N-(3-Iodophenyl)ethanamide [*m*-iodo-acetanilide; *m*-iodoethananilide; *N*-(*m*-iodophenyl)acetamide]	120		17			119	157
Hydroxyethanamide (glycolamide; hydroxyacetamide)	120		80	107	138		
Chloroethanamide (chloroacetamide)	120	209	52; 56; 61		104		
4-Methylpentanamide (isocaproamide)	121	160			77		
2-Chlorophenoxyethananilide (*o*-chlorophenoxyacetanilide)	121		146			114	160
Decanedioic acid monoanilide (sebacic acid monoanilide)	122		33	74 (di)	147 (di)	114	160
Cyanoethanamide (cyanoacetamide)	123	223	66				
Furanilide	124		134	134	139	114	160
3-Chlorobenzanilide	125		158	107	116	114	160
4-Chlorophenoxyethananilide (*p*-chlorophenoxyacetanilide)	125		158		136	114	160
N-Benzoyl-3-methylaniline (*N*-benzoyl-*m*-toluidine; *m*-benzotoluidine; *N*-benzoyl-*m*-aminotoluene)	125		122	89	119	65	125
2-Methylbenzanilide (*o*-toluanilide)	125		108	91	57	114	160
1-Acetyl-2-phenylhydrazine (acetyl-β-phenylhydrazine)	126		17	78	86	128; 107 (di)	168; 177 (di)
3-Methylbenzanilide (*m*-toluanilide)	126		113	87	108	114	160
Butanedioic acid imide (succinimide)	126	247	185	88 (di)	211 (di)		
Z-2-Methyl-2-butenanilide (angelanilide)	126		46			114	160
2,4-Dihydroxybenzanilide (β-resorcylanilide)	127		217	189		114	160
2-Ethylbutanilide	127					114	160
Octanedioic acid monoamide (suberic acid monoamide)	127		144	85 (di)	144 (di)		

(Continued)

TABLE AII.10 Amides (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)					
			Acid			Amine	
		9-Acyl-amido-xanthene	Acid	4-Nitro-benzyl ester	4-Bromo-phen-acyl-ester	Acet-amide	Benz-amide
N-(4-Methoxyphenyl)ethanamide [*p*-methoxyacetanilide; *p*-methoxyethan anilide; *N*-(*p*-methoxyphenyl) acetamide]	127		17	78	86	130	157
Phenylpropynanilide (phenylpropiolanilide)	128		137	83		114	160
Octanedioic acid monoanilide (suberic acid monoanilide)	129		144	85 (di)	144 (di)	114	160
N-(2-Bromo-4-nitrophenyl)ethanamide [2-bromo-4-nitroacetanilide; 2-bromo-4-nitroethananilide; *N*-(2-bromo-4-nitrophenyl)acetamide]	129		17	78	86	129	160
2-Methylpropanamide (isobutyramide)	129	211			77		
2-Methoxybenzamide	129		101		113		
Benzamide	130	224	122	89	119		
Hexanedioic acid monoamide (adipic acid monoamide)	130		154	106	154		
2-Aminobenzanilide (anthranilanilide)	131		147			114	160
Bromoethananilide (bromoacetanilide)	131		50	88		114	160
2-Methoxybenzanilide	131		101		113	114	160
3-Pyridinecarboxylic acid anilide (nicotinanilide)	132		238			114	160
3,3-Dimethylbutanilide	132					114	160
N-(2,5-Dichlorophenyl)ethanamide [2,5-dichloroacetanilide; 2,5-dichloroethananilide; *N*-(2,5-dichlorophenyl)acetamide]	132		17	78	86	132	120
Propanedioic acid monoamide (malonic acid monoamide)	132		135	86 (di)		114	160
N-(2,4-Dimethylphenyl)ethanamide [2,4-dimethylacetanilide; 2,4-dimethylethananilide; *N*-(2,4-dimethylphenyl)acetamide]	133		17	78	86	133	190
2,2-Dimethylpropananilide (pivalanilide; trimethylacetanilide)	133		36		76	114	160
4-Chlorophenoxyethanamide (*p*-chlorophenoxyacetamide)	133		158		136		
N-(2-Napththyl)ethanamide [*N*-(β-naphthyl)acetamide]	134		17	78	86	132	162
3-Chlorobenzamide	134		158	107	116		
Chloroethananilide (chloroacetanilide)	134		61; 56; 52		104	114	160
2-Hydroxy-2-phenylethanamide [(±)-mandelamide]	134		118	124			

(Continued)

TABLE AII.10 Amides (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)					
			Acid			Amine	
		9-Acyl-amido-xanthene	Acid	4-Nitro-benzyl ester	4-Bromo-phen-acyl-ester	Acet-amide	Benz-amide
N-(4-Ethoxyphenyl)ethanamide [*N*-acetyl-4-ethoxyaniline; *p*-acetophenetidide; phenacetin; *N*-acetyl-*p*-phenetidine; *N*-(*p*-ethoxyphenyl)acetamide]	135		17	78	86	137	173
N-(2,3-Dimethylphenyl)ethanamide [2,3-dimethylacetanilide; 2,3-dimethylethananilide; *N*-(2,3-dimethylphenyl) acetamide]	135		17	78	86	135	189
Acetyl-2-hydroxybenzanilide (acetylsalicylanilide)	136		135	91		114	160
3-Bromobenzanilide	136		155	105	120	114	160
2-Hydroxybenzanilide (salicylanilide)	136		158	98	140	114	160
2-Hydroxy-2-methylpropananilide (α-hydroxyisobutyranilide)	136		79	81	98	114	160
3-Methylbutanamide (isovaleramide)	136	183			68		
N,*N*′-Diacetyl-1,4-diaminobutane (*N*,*N*′-diacetyltetra-methylenediamine)	137		17	78 (di)	86 (di)	137	177
N-Benzoyl-2-iodoaniline (benzo-*o*-iodoanilide)	139		122	89	119	109	139
N-(2,5-Dimethylphenyl)ethanamide [2,5-dimethylacetanilide; 2,5-dimethylethananilide; *N*-(2,5-dimethylphenyl)acetamide]	139		17	78	86	139	140
3-Aminobenzanilide	140		174			114	160
2-Iodobenzanilide	141		162	111	143	114	160
2-Bromobenzanilide	141		150	110	102	114	160
Trichloroethanamide (trichloroacetamide)	141		58	80			
3-Methylphenylurea (*m*-tolylurea)	142					65	125
2-Chlorobenzamide	142		142	106	106		
2-Hydroxybenzamide (salicylamide)	142		158	98	140		
Furamide	143	210	134	134	139		
3-Nitrobenzamide	143		140	141	132		
2-Methylbenzamide (*o*-toluamide)	143	200	108	91	57		
Iodoethananilide (iodoacetanilide)	144		83		114	160	
N-(3,5-Dimethylphenyl)ethanamide [3,5-dimethylacetanilide; 3,5-dimethylethananilide; *N*-(3,5-dimethylphenyl)acetamide]	144		17	78	86	144	136
N-Benzoyl-2-methylaniline (*o*-benzotoluidide; *N*-benzoyl-*o*-toluidine; *N*-benzoyl-*o*-aminotoluene)	144		122	89	119	111	146

(Continued)

TABLE AII.10 Amides (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)						
			Acid			Amine		
		9-Acyl-amido-xanthene	Acid	4-Nitro-benzyl ester	4-Bromo-phen-acyl-ester	Acet-amide	Benz-amide
N-(2,4-Dichlorophenyl)ethanamide [2,4-dichloroacetanilide; 2,4-dichloroethananilide; *N*-(2,4-dichlorophenyl)acetamide]	145		17	78	86	145	177
Cyclohexanecarboxanilide (hexahydrobenzanilide)	146		31			114	160
Diethylpropanedioic acid monoamide (diethylmalonic acid monoamide)	146		125	91 (di)			
Phenylurea	147	225				114	160
N,*N*′-Dibenzoyl-1,3-diaminopropane (*N*,*N*′-dibenzoyltrimethylenediamine)	147		122	89	119	126 (mono) 101 (di)	140 (mono) 147 (di)
N-Benzoyl-2-ethylaniline (benzo-*o*-ethylanilide)	147		122	89	119	111	147
4-Methylbenzanilide (*p*-toluanilide)	148		182	105	153	114	160
N-(2,4,6-Trichlorophenyl)ethanamide [2,4,6-trichloroacetanilide; 2,4,6-trichloroethananilide; *N*-(2,4,6-trichlorophenyl)acetamide]	148		17	78	86	148	172
E-3-Phenyl-2-propenamide (*trans*-cinnamide)	148		133	117	146		
Butanedioic acid monoanilide (succinic acid monoanilide)	149		185	88 (di)	211 (di)	114	160
N-Cyclohexylbenzamide	149		122	89	119	104	149
Benzylurea	149					60	105
1,2-Benzenedicarboxylic acid monoamide (phthalic acid monoamide)	149		206; 230	156 (di)	153 (di)		
2-Benzoylpropananilide (β-benzoylpropionanilide)	150		116			114	160
Ethylpropanedioic acid monoanilide (ethylmalonic acid monoanilide)	150		111	75		114	160
N-(4-Fluorophenyl)ethanamide [*p*-fluoroacetanilide; *p*-fluoroethananilide; *N*-(*p*-fluorophenyl)-acetamide]	152		17	78	86	152	185
(±)-2-Hydroxy-2-phenylethananilide [(±)-mandelanilide; (±)-2-hydroxy-2-phenylacetanilide; 2-hydroxy-*N*,2-diphenylacetamide; 2-hydroxy-*N*,2-diphenylethanamide]	152		118	124		114	160
Hexanedioic acid monoanilide (adipic acid monoanilide)	153		154	106	155	114	160
3-Phenyl-2-propenanilide (cinnamanilide)	153		133	118	146	114	160

(Continued)

TABLE AII.10 Amides (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)					
			Acid			Amine	
		9-Acyl-amido-xanthene	Acid	4-Nitro-benzyl ester	4-Bromo-phen-acyl-ester	Acet-amide	Benz-amide
N-(4-Methylphenyl)ethanamide [*N*-acetyl-*p*-toluidine; *p*-acetotoluidide; *N*-(*p*-tolyl)acetamide]	153		17	78	86	147	158
N-Methyl-*N*-(4-nitrophenyl) ethanamide [*N*-methyl-*p*-nitroacetanilide; *N*-methyl-*p*-nitroethananilide; *N*-methyl-*N*-(*p*-nitrophenyl)acetamide]	153		17	78	86	153	112
3,4-Dimethoxybenzanilide (veratranilide)	154		181			114	160
3-Nitrobenzanilide	154		140	141	132	114	160
2,2-Diphenyl-2-hydroxyethanamide (benzilamide; 2,2-diphenyl-2-hydroxyacetamide)	155		150	100	152		
2-Bromobenzamide	155		150	110	102		
Dibenzylethananilide (dibenzylacetanilide)	155		89			114	160
2-Nitrobenzanilide	155		146	112	107	114	160
3-Bromobenzamide	155		155	105	120		
N-(3-Nitrophenyl)ethanamide [*m*-nitroacetanilide; *m*-nitroethananilide; *N*-(*m*-nitrophenyl)acetamide]	155		17	78	86	155 (mono) 76 (di)	155 (mono) 150 (di)
N-Phenylbutanedioic acid imide (*N*-phenylsuccinimide)	156		185	88 (di)	211 (di)	114	160
Heptanedioic acid dianilide (pimelic acid dianilide)	156		105		137 (di)	114	160
Phenylethanamide (phenylacetamide)	157	196	77	65	89		
3-Hydroxybenzanilide	157		200	108	176	114	160
Butanedioic acid monoamide (succinic acid monoamide)	157		185	88 (di)	211 (di)		
2,2-Dimethylpropanamide (pivalamide; trimethylacetamide)	157		36		76		
Hydroxybutanedioic acid diamide (malamide; hydroxysuccinamide)	158		101	87 (mono) 125 (di)	179 (di)		
N-Benzoyl-4-methylaniline (*N*-benzoyl-*p*-toluidine; *p*-benzotoluidide; *N*-benzoyl-*p*-aminotoluene)	158		122	89	119	147	158
N-Acetylindole	158		17	78	86	158	68
N-(1-Naphthyl)ethanamide [*N*-(α-naphthyl)acetamide]	159		17	78	86	159	160

(Continued)

TABLE AII.10 Amides (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)					
			Acid			Amine	
		9-Acyl-amido-xanthene	Acid	4-Nitro-benzyl ester	4-Bromo-phen-acyl-ester	Acet-amide	Benz-amide
N-(2-Naphthyl)ethananilide [*N*-(β-naphthyl)acetanilide; *N*-(β-naphthyl)-*N*-phenylethanamide; *N*-(β-naphthyl)-*N*-phenylacetamide]	160		135			114	160
4-Methylbenzamide (*p*-toluamide)	160	225	180	105	153		
E-2-Butenamide (crotonamide)	161		72	67	96		
N-(1-Naphthyl)benzamide	161		122	89	119	159	160
N-(2-Naphthyl)benzamide	162		122	89	119	132	162
N-(4-Aminophenyl)ethanamide [*p*-aminoacetanilide; *p*-aminoethananilide; *N*-(*p*-aminophenyl) acetamide]	162		17	78	86	163 (mono) 304 (di)	128 (mono) 300 (di)
4-Hydroxybenzamide	162		215	182	192		
Benzanilide	163		122	89	119	114	160
1-Naphthanilide	164		162		136	114	160
2-Hydroxy-3,3,3-trichloropropananilide (trichlorolactanilide)	164		124			114	160
2-Benzoylbenzamide	165		128; 91 (hyd)	100			
3,4-Dihydroxybenzanilide (protocatechuanilide)	166		200			114	160
4-Methoxybenzamide (*p*-anisamide)	167		186	132	152		
Acetyl-2-aminobenzanilide (acetylanthranilanilide)	167		185			114	160
N-(4-Bromophenyl)ethanamide [*p*-bromo acetanilide; *p*-bromoethananilide; *N*-(*p*-bromophenyl)acetamide]	168		17	78	86	168	204
1-Benzoyl-2-phenylhydrazine (α-benzoyl-β-phenylhydrazine)	168		122	89	119	128	168
N-(4-Hydroxyphenyl)ethanamide [*p*-hydroxyacetanilide; *p*-hydroxyethananilide; *N*-(*p*-hydroxyphenyl)acetamide]	169		17	78	86	168 (mono) 150 (di)	217 (mono) 234 (di)
Propanedioic acid diamide (malonic acid diamide; malondiamide)	170	270	135	86 (di)			
3-Hydroxybenzamide	170		200	108	177		
Decanedioic acid monoamide (sebacic acid monoamide)	170		33	74 (di)	147 (di)		
Z-1,2,3-Propenetricarboxylic acid anilide (*cis*-aconitranilide)	170		125		186 (tri)	114	160
(±)-Phenylbutanedioic acid monoanilide [(±)-phenylsuccinic acid monoanilide]	170		168; 84 (anhyd)			114	160
4-Methoxybenzanilide (*p*-anisanilide)	171		186	132	152	114	160

(Continued)

TABLE A11.10 Amides (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)					
			Acid			Amine	
		9-Acyl-amido-xanthene	Acid	4-Nitro-benzyl ester	4-Bromo-phen-acyl-ester	Acet-amide	Benz-amide
4-Ethoxybenzanilide	172		198			114	160
2-Naphthylanilide	172		185			114	160
N,N'-Diacetyl-1,2-diaminoethane (*N,N'*-diacetylethylenediamine)	172		17	78	86	172 (di)	244 (di)
N-Benzoyl-2,4,6-trichloroaniline (benzo-2,4,6-trichloroanilide)	172		122	89	119	148	172
Nonanedioic acid diamide (azelaic acid diamide)	172		106	44 (di)	131 (di)		
Z-Butenedioic acid monoamide (maleic acid monoamide; maleamic acid)	173		138	91	190		
N-(4-Ethoxyphenyl)urea (*p*-phenethylurea)	173					137	173
N-Benzoyl-4-ethoxyaniline [*N*-benzoyl-*p*-phenetidine; *p*-benzophenetidide; *N*-(*p*-ethoxyphenyl)benzamide]	173		122	89	119	137	173
Heptanedioic acid diamide (pimelic acid diamide)	175		105		137 (di)		
Benzylanilide	175		150	100	152	114	160
(±)-Phenylbutanedioic acid monoanilide [(±)-phenylsuccinic acid monoanilide]	175		168; 84 (anhyd)			114	160
Z-Methylbutenedioic acid dianilide (citraconic acid dianilide; methylmaleic acid dianilide)	176		93; 22	71		114	160
Pentanedioic acid diamide (glutaric acid diamide)	176		98	69	140		
2-Nitrobenzamide	176		146	112	107		
2-Carboxyphenyl-2-oxoethanoic acid monoanilide (phthalonic acid monoanilide; 2-carboxyphenyl-2-oxoacetic acid monoanilide)	176		146			114	160
E-Methylbutenedioic acid diamide (mesaconic acid diamide)	177		205	134 (di)			
1,2,2-Trimethylcyclopentane-1,3-dicarboxylic acid monoamide (D-camphoric acid monoamide)	177		188	65			
N,N'-Dibenzoyl-1,4-diaminobutane (*N,N'*-dibenzoyltetra-methylenediamine)	177		122	89	119	137 (di)	177 (di)
N-(2,6-Dimethylphenyl)ethanamide [2,6-dimethylacetanilide; 2,6-dimethylethananilide; *N*-(2,6-dimethylphenyl)acetamide]	177		17	78	86	177	168

(Continued)

TABLE AII.10 Amides (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)					
			Acid			Amine	
		9-Acyl-amido-xanthene	Acid	4-Nitro-benzyl ester	4-Bromo-phen-acyl-ester	Acet-amide	Benz-amide
4-Cyanobenzanilide	179		219	189		114	160
N-Benzyl-1,2-benzenedicarboxylic acid amide (*N*-benzoylphthalamide)	179		206; 230	156 (di)	153 (di)	60	105
N-(4-Chlorophenyl)ethanamide [*p*-chloroacetanilide; *p*-chloroethananilide; *N*-(*p*-chlorophenyl)acetamide]	179		17	78	86	179	192
D-2,3-Dihydroxybutanedioic acid monoanilide (D-tartaric acid monoanilide)	180		171	163 (di)	204 (di)	114	160
1-Acetyl-2-methylurea (α-acetyl-β-methylurea)	180		17	78	86	28	80
Diphenylethananilide (diphenylacetanilide)	180		148			114	160
Z-Butenedioic acid diamide (maleic acid diamide)	181		137	91	170; 190		
4-Methylphenylurea (*p*-tolylurea)	182					147	158
N,N-Dimethylurea (*asym*-dimethylurea)	182	225; 250					41
N-Benzoylaminoethanamide (hippuramide; *N*-benzoylamino-acetamide)	183		187	136	151		
3,5-Dinitrobenzamide	183		205	157	159		
2-Iodobenzamide	184		162	111	143		
N-(4-Iodophenyl)ethanamide [*p*-iodo-acetanilide; *p*-iodoethananilide; *N*-(*p*-iodophenyl)acetamide]	184		17	78	86	184	222
N-Benzoyl-4-fluoroaniline (benzo-*p*-fluoroanilide)	185		122	89	119	152	185
N,N'-Diacetyl-2-diaminobenzene (*N,N'*-diacetyl-1,2-phenylenediamine)	185		17 (di)	78 (di)	86	185	301
3-(2-Nitrophenyl)-2-propenamide (2-nitrocinnamamide)	185		240	132	141		
E-2-Methyl-2-butenedioic acid dianilide (mesaconic acid dianilide)	186		204	134 (di)		114	160
Z-2-Chloro-2-butenedioic acid anilide (chlorofumaranilide)	186		192	139		114	160 (di)
3-Iodobenzamide	186		187	121	128		
Octanedioic acid dianilide (suberic acid dianilide)	187		144	85 (di)	144 (di)	114	160
Z-2-Butenedioic acid dianilide (maleic acid dianilide)	187		137	91 (di)	170; 190	114	160
Z-2-Butenedioic acid monoanilide (maleic acid monoanilide)	187		137	91 (di)	170; 190	114	160

(Continued)

TABLE AII.10 Amides (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)					
			Acid			Amine	
		9-Acyl-amido-xanthene	Acid	4-Nitro-benzyl ester	4-Bromo-phen-acyl-ester	Acet-amide	Benz-amide
Z-2-Methyl-2-butenedioic acid diamide (citraconic acid diamide)	187		93	71 (di)			
N-Benzoylaminoethanoic acid (hippuric acid; *N*-benzoylglycine; *N*-benzoylaminoacetic acid)	188		122	89	119	206	188
N,*N*-Diphenylurea (*asym*-diphenylurea)	189	180				101	180
1,2,3-Propanetricarboxylic acid dianilide (aconitic acid dianilide)	189		195		186 (tri)	114	160
4-Bromobenzamide	190		253	180			
(2*R*,3*S*)-2,3-Dihydroxybutanedioic acid diamide (*meso*-tartaric acid diamide)	190		140	93			
2-Methylenebutanedioic acid dianilide (itaconic acid dianilide; methylenesuccinic acid dianilide)	190		165	91	117	114 (di)	160 (di)
N,*N*′-Diacetyl-3-diaminobenzene (*N*,*N*′-diacetyl-3-phenylenediamine)	191		17	78	86	89 (mono) 191 (di)	125 (mono) 240 (di)
2-Methylenebutanedioic acid diamide (itaconic acid diamide; methylenesuccinic acid diamide)	192		165	91 (di)	117 (di)		
(2*R*,3*S*,4*R*,5*S*)-2,3,4,5-Tetrahydroxy-hexanedioic acid monoamide (mucic acid monoamide; galacratic acid monoamide)	192		214; 255	310	225		
4-Nitro-1,2-benzenedicarboxylic acid anilide (4-nitrophthalanilide)	192		165			114	160
2-Methylphenylurea (*o*-tolylurea)	192	228				111	146
N-Benzoyl-4-chloroaniline (benzo-*p*-chloroaniline)	192		122	89	119	179	192
D-1,2,2-Trimethylcyclopentane-1,3-dicarboxylic acid diamide (D-camphoric acid diamide)	193		188	66			
4-Chlorobenzanilide	194		243	130	126	114	160
2-Benzoylbenzanilide	195		128; 91 (hyd)	101		114	160
3-(3-Nitrophenyl)-2-propenamide (3-nitrocinnamamide)	196		199	174	178		
(2*S*,3*S*)-2,3-Dihydroxybutanedioic acid diamide (D-tartaric acid diamide)	196		171	163 (di)	204 (di)		
Hydroxybutanedioic acid dianilide (L-malanilide; hydroxysuccinanilide)	197		101	87 (mono) 125 (di)	179 (di)	114	160
4-Hydroxybenzanilide	198		215	182	192	114	160

(Continued)

TABLE AII.10 Amides (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)					
			Acid			Amine	
		9-Acyl-amido-xanthene	Acid	4-Nitro-benzyl ester	4-Bromo-phen-acyl-ester	Acet-amide	Benz-amide
N-[4-(Nitrophenyl)phenyl] ethanamide {*p*-nitrophenylacetanilide; *p*-nitrophenylethananilide; *N*-[*p*-(nitrophenyl)phenyl]-acetamide}	198		153		207	215	203
Cyanoethananilide (cyanoacetanilide)	199		66			114	160
2-Hydroxy-1,2,3-propanetricarboxylic acid trianilide (citric acid trianilide)	199		100; 153 (anhyd)	102 (tri)	148 (tri)	114	160
E-1,2,3-Propenetricarboxylic acid dianilide (aconitic acid dianilide)	200		125	186 (tri)	114	160	
2-Methylbutanedioic acid dianilide (methylsuccinic acid dianilide)	200		115			114	160
4-Nitrobenzamide	200	232	241	168	137		
3-Nitro-1,2-benzenedicarboxylic acid diamide (3-nitrophthalic acid diamide)	201		218	189			
Decanedioic acid dianilide (sebacic acid dianilide)	201		33	74 (di)	147 (di)	114	160
N-(2-Methyl-4-nitrophenyl)ethanamide [2-methyl-4-nitroacetanilide; 2-methyl-4-nitroethananilide; *N*-(2-methyl-4-nitrophenyl)acetamide]	202		17	78	86	202	
1-Naphthoamide	202		162		136		
2,4-Dinitrobenzamide	203		183	142	158		
D-1,2,2-Trimethylcyclopentane-1,3-dicarboxylic acid monoanilide (D-camphoric acid monoanilide)	204		188	66		114	160
N-Benzoyl-4-bromoaniline (benzo-4-bromoanilide)	204		122	89	119	168	204
N-Phenyl-1,2-benzenedicarboxylic acid imide (*N*-phenylphthalimide)	205		206; 230	156	153	114	160
3,4,5-Trihydroxybenzanilide (gallanilide)	207		254; 222	141	134	114	160
2-Carboxyphenyl-2-oxoethanoic acid dianilide (phthalonic acid dianilide; 2-carboxyphenyl-2-oxoacetic acid dianilide)	208		146			114	160
N-Benzoylaminoethananilide-(*N*-benzoylaminoacetanilide; hippuranilide)	208		187	136	151	114	160
Decanedioic acid diamide (sebacic acid diamide)	210		133	74 (di)	147 (di)		
4-Iodobenzanilide	210		270	141	146	114	160
4-Nitrobenzanilide	211		241	168	137	114	160
3,4-Dihydroxybenzamide (protocatechuamide)	212		200	188			
2,2′-Biphenyldicarboxylic acid diamide (2,2′-diphenic acid diamide)	212		233	187 (di)			

(Continued)

TABLE AII.10 Amides (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)					
			Acid			Amine	
		9-Acyl-amido-xanthene	Acid	4-Nitro-benzyl ester	4-Bromo-phen-acyl-ester	Acet-amide	Benz-amide
N-(4-Nitrophenyl)ethanamide [*p*-nitroacetanilide; *p*-nitroethananilide; *N*-(*p*-nitrophenyl)acetamide]	214		17	78	86	215	203
Ethylpropanedioic acid diamide (ethylmalonic acid diamide)	214		111	75			
2-Hydroxy-1,2,3-propanetricarboxylic acid triamide (citric acid triamide)	215		153	102 (tri)	148 (tri)		
3-Nitro-1,2-benzenedicarboxylic acid imide (3-nitrophthalimide)	216		218	189			
3-(4-Nitrophenyl)-2-propenamide (4-nitrocinnamamide)	217		285	186	191		
Octanedioic acid diamide (suberic acid diamide)	217		144	85	144		
4-Iodobenzamide	217		270	141	146		
Benzylpropanedioic acid dianilide (benzylmalonic acid dianilide)	217		121	120		114	160
Acetylurea	218		17	78	86		
sym-Di-(3-methylphenyl)urea (*sym*-di-*m*-tolylurea)	218					65	125
1,2-Benzenedicarboxylic acid diamide (phthalic acid diamide)	220		206; 230	156	153		
(2*R*,3*S*,4*R*,5*S*)-2,3,4,5-Tetrahydroxyhexanedioic acid diamide (mucic acid diamide)	220		214	310	225		
2,4-Dihydroxybenzamide (β-resorcylamide)	222		213	189			
(±)-Phenylbutanedioic acid dianilide [(±)-phenylsuccinic acid dianilide]	222		168; 84 (anhyd)			114	160
4-Cyanobenzamide	223		219	189			
Diethylpropanedioic acid diamide (diethylmalonic acid diamide)	224		125	91 (di)			
Pentanedioic acid dianilide (glutaric acid dianilide)	224		98	69 (di)	140 (di)	114	160
5-Nitro-2-hydroxybenzanilide (5-nitrosalicylanilide)	224		230			114	160
Benzylpropanedioic acid diamide (benzylmalonic acid diamide)	225		121	120 (di)			
D-1,2,2-Trimethylcyclopentane-1,3-dicarboxylic acid dianilide (D-camphoric acid dianilide)	226		188	66		114	160
(±)-2,3-Dihydroxybutanedioic acid monoamide [(±)-tartaric acid monoamide]	226		204	148			

(Continued)

TABLE AII.10 Amides (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)					
			Acid			Amine	
		9-Acyl-amido-xanthene	Acid	4-Nitro-benzyl ester	4-Bromo-phen-acyl-ester	Acet-amide	Benz-amide
Hexanedioic acid diamide (adipic acid diamide)	229		154	106	155		
Propanedioic acid dianilide (malonic acid dianilide)	230		135	86 (di)		114	160
Butanedioic acid dianilide (succinic acid dianilide)	230		185	88 (di)	211 (di)	114	160
2-Sulfobenzoic acid imide (saccharin)	230	199	206				
2,2′-Biphenyldicarboxylic acid anilide (2,2′-diphenanilide)	230		233	187 (di)		114	160
3,5-Dinitrobenzanilide	234		205	157	159	114	160
3-Nitro-1,2-benzenedicarboxylic acid dianilide (3-nitrophthalic acid dianilide)	234		218	189		114	160
(±)-2,3-Dihydroxybutanedioic acid monoanilide [(±)-tartaric acid monoanilide]	236		206			114	160
1,4-Benzenedicarboxylic acid monoanilide (terephthalic acid monoanilide)	237		300	264 (di)	225 (di)	114	160
N-Benzylpropenamide (*N*-benzylacrylamide)	237					60	105
1,2-Benzenedicarboxylic acid imide (phthalimide)	238	177	206; 230	89	119	232	204
N,N-Diphenylurea (*sym*-diphenylurea; carbanilide)	240					114	160
Hexanedioic acid dianilide (adipic acid dianilide)	241		154	106	155	114	160
N,N′-Dibenzoyl-1,2-diaminoethane (*N,N′*-dibenzoylethylenediamine)	244		122	89	119	172 (di)	244 (di)
3,4,5-Trihydroxybenzamide (gallamide)	245		254; 240	141	134		
3-Hydroxy-2-naphthanilide	249		223			114	160
N,N-Di-(2-methylphenyl)urea (*sym*-di-*o*-tolylurea)	250					111	146
1,2,3-Propanetricarboxylic acid trianilide (carballylic acid trianilide)	252		166			114	160
1,2-Benzenedicarboxylic acid dianilide (phthalic acid dianilide)	255		206; 230	156	153	114	160
N,N-Diphenylethanedioic acid dianilide (oxanilide; oxalic acid dianilide; ethanedioic acid dianilide)	257		189 (anhyd) 101 (dihyd)	204 (di)		114	160
Butanedioic acid diamide (succinic acid diamide)	260	275	185; 125	88 (di)	211 (di)		
(2*S*,3*S*)-2,3-Dihydroxybutanedioic acid dianilide (D-tartaric acid dianilide)	264		171	163	204	114	160

(Continued)

TABLE AII.10 Amides (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)					
			Acid			Amine	
		9-Acyl-amido-xanthene	Acid	4-Nitro-benzyl ester	4-Bromo-phen-acyl-ester	Acet-amide	Benz-amide
3-Pyridinecarboxylic acid anilide (nicotinanilide)	265 (anhyd)		238			114	160
E-2-Butenedioic acid diamide (fumaric acid diamide)	266		295; 200	151			
N,N-Di-(4-methylphenyl)urea (*sym*-di-*o*-tolylurea)	268					147	158
1,3-Benzenedicarboxylic acid monoamide (isophthalic acid monoamide)	280		348	203	179		
1,3-Benzenedicarboxylic acid diamide (isophthalic acid diamide)	280		348	203	179		
(2*R*,3*S*,4*R*,5*S*)-2,3,4,5-Tetrahydroxy-hexanedioic acid monoanilide (mucic acid monoanilide)	310		214; 255	310	225	114	160
N,N'-Diacetyl-1,4-diaminobenzene (*N,N'*-diacetyl-1,4-phenylenediamine)	310		17	78	86	163 (mono) 304 (di)	128 (mono) 300 (di)
E-2-Butenedioic acid dianilide (fumaric acid dianilide)	314		286; 295; 200			114	160
N,N'-Diacetyl-4,4'-diaminobiphenyl (*N,N'*-diacetylbenzidine)	317		17	78	86	199 (mono) 317 (di)	205 (mono) 352 (di)
1,4-Benzenedicarboxylic acid dianilide (terephthalic acid dianilide)	337		300	264 (di)	225 (di)		
N,N'-Dibenzoyl-4,4'-diaminobiphenyl (*N,N'*-dibenzoylbenzidine)	352		122	89	119	199 (mono) 317 (di)	205) (mono) 351 (di)
1,3,5-Benzenetricarboxylic acid triamide (trimesic acid triamide)	365		380		197		
Ethanedioic acid diamide (oxalic acid diamide)	419		190 (anhyd) 101 (dihyd)	204			

TABLE AII.11 Amines—Primary and Secondary (Liquids)

Name of Compound	bp (°C)	Derivative mp (°C)					
		Acetamide	Benzamide	Benzenesulfonamide	4-Toluenesulfonamide	Phenylthiourea	Amine hydrochloride
Methylamine	−6	28	80	30	77	113	
Dimethylamine	7		42	47	79	135	171
Ethylamine	19		71	58	63	106; 135	110
2-Aminopropane (isopropylamine)	33		100	26	51	101	
2-Methyl-2-aminopropane (*tert*-butylamine)	46	102	134		114	120	280
Propylamine	49		84	36	52	63	
Cyclopropylamine	50		99	120			100
Diethylamine	56		42	42	60	34	230
3-Aminopropene (allylamine)	58			39	64	98	
2-Aminobutane (*sec*-butylamine)	63		76	70	55	101	
2-Methylpropylamine (isobutylamine)	69		57	53	78	82	
Butylamine	77		42		65	65	195
3-Methylbutylamine (isopentylamine)	96				65	102	
Piperidine	106		48	94	103	101	
Dipropylamine	110			51		69	
1,2-Diaminoethane (ethylenediamine)	116	172	249	168	160; 360	102	330
(±)-2-Methylpiperidine	119		45		55		207
1,2-Diaminopropane	120	139 (di)	192 (di)		103		
2,6-Dimethylpiperidine	128		111	50			
Hexylamine	130		40	96		77	
Morpholine	130		75	119	147	136	175
Cyclohexylamine	134	104	149	89	87	148	207
1,3-Diaminopropane (trimethylenediamine)	136	126 (di); 101	147 (di)	96	148		
Piperazine	139	144 (di)	196 (di)	292 (di)	173 (mono)		83 (di)
Di-(2-methylpropyl)amine (diisobutylamine)	139	86		57		113	
1,4-Diaminobutane (tetramethylenediamine)	159	137 (di)	177 (di)		224 (di)	168	315 (di)
2-Fluoroaniline	176	80	113				
1,5-Diaminopropane (pentamethylenediamine; cadaverine)	180		135 (di)	119		148	
Aniline	184	114	163	112	103	54; 154	198
Benzylamine	185	65	106	88	116; 185	156	258
(±)-1-Phenylethylamine	187	57	120				158
4-Fluoroaniline	188	152	185				
1,2,3-Triaminopropane	190	202 (tri)	218 (tri)				
N-Methylaniline	194	103	63	79	95	87	123

(Continued)

TABLE AII.11 Amines—Primary and Secondary (Liquids) *(Continued)*

Name of Compound	bp (°C)	Derivative mp (°C)					
		Acetamide	Benzamide	Benzenesulfonamide	4-Toluenesulfonamide	Phenylthiourea	Amine hydrochloride
2-Phenylethylamine	198	114; 51	116	69	64	135	
2-Methylaniline (*o*-toluidine; *o*-aminotoluene)	200	112	146	124	110; 186	136	215
4-Methylaniline (*p*-toluidine; *p*-aminotoluene)	200	154	158	120	118	141	243
Nonylamine	201	35	49				
3-Methylaniline (*m*-toluidine; *m*-aminotoluene)	203	66	125	95	114; 172	94	228
N-Ethylaniline	205	55	60		88	89	176
1,6-Diaminohexane (hexamethylenediamine)	205	127 (di)	158 (di)	154 (di)			
3-Methylbenzylamine	207	240	150				208
2-Chloroaniline	208	88	99	129	105; 193	156	235
N,2-Dimethylaniline [*N*-methyl-*o*-toluidine; *o*-(*N*-methylamino)toluene]	208	56	66		120		
2-Methylbenzylamine	208	69	88				
4-Methylbenzylamine	208	108	137				
1-Phenylpropylamine	208		116	81			190
2-Amino-6-methylpyridine	209	90	90				155
N,4-Dimethylaniline [*N*-methyl-*p*-toluidine; *p*-(*N*-methyl)aminotoluene]	210	83	53	67	60	89	120
L-2-(1-Methylethyl)-5-methylcyclohexylamine (L-menthylamine)	212	145	157			135	
2,5-Dimethylaniline	215	139	140	138	119; 233	148	
2-Ethylaniline	216	112	147				
4-Ethylaniline	216	94	151		104	104	
2,4-Dimethylaniline	217	133	192	130	181	133; 152	
N-Ethyl-4-methylaniline [*N*-ethyl-*p*-toluidine; *p*-(*N*-ethylamino)toluene]	217		40	66	71		
2,6-Dimethylaniline	218	177	168		212	204	
2-Methoxyaniline	218	85	60		127		
N-Ethyl-2-methylaniline [*N*-ethyl-*o*-toluidine; *o*-(*N*-ethylamino)toluene]	218		72	62	75		
2-(*N*,*N*-Dimethylamino)aniline	219	72	51				
3,5-Dimethylaniline	220	144	145	136		153	
2,3-Dimethylaniline	222	136	189				254
N-Propylaniline	222	47		54		104	
2-Chloro-4-methylaniline (4-amino-3-chlorotoluene)	223	118	138	110	103		

(Continued)

TABLE AII.11 Amines—Primary and Secondary (Liquids) *(Continued)*

Name of Compound	bp (°C)	Derivative mp (°C)					
		Acetamide	Benzamide	Benzenesulfonamide	4-Toluenesulfonamide	Phenylthiourea	Amine hydrochloride
E-9-Aminobicyclo[4.4.0]decane (*trans*-9-aminodecalin)	223	183	149				
2-Propylaniline	224	105	119				173
2-Amino-3-methylpyridine	224	64	220				
2-Methoxyaniline (*o*-anisidine)	225	88	60; 84	89	127	136	
4-(1-Methylethyl)aniline (*p*-isopropylaniline; *p*-cumidine)	225	102	162				
4-Propylaniline	225	94	115				204
3,4-Dimethylaniline	226	99		118	154		
α-Methyl-α-phenylhydrazine	227	92	153	132			
4-(1,1-Dimethylethyl)aniline (*p*-*tert*-butylaniline)	228	173	140				274
Z-9-Aminobicyclo[4.4.0]decane (*cis*-9-aminodecalin)	228	127	147				
2-Bromoaniline	229	99	116			146	
2-Ethoxyaniline (*o*-phenetidine)	229	79	104	102	164	137	
2-Aminoindane	230	127	155				241
2,4,6-Trimethylaniline	232	216	204	137	167	193	
1,2,3,4-Tetrahydroisoquinoline	233	46	129	154			
2-Aminothiophenol	234	135 (di)	154 (di)				
4-(2-Methylpropyl)aniline (*p*-isobutylaniline)	235	127			137		
4-Aminoindane	236	126	136				
3-Chloroaniline	236	79	120	121	138; 210	124	
2-Bromo-4-methylaniline (4-amino-3-bromotoluene)	240	118	149			154	221
1-Aminoundecane (1-aminohendecane)	240	48	60				190
N-Butylaniline	241		56		56		
4-Chloro-2-methylaniline (2-amino-5-chlorotoluene)	241	140	172; 142	125	145		
2-Amino-4-(1-methylethyl)-toluene (5-isopropyl-2-methylaniline; 2-amino-*p*-cumene; *p*-cymidine)	242	71	102				207
Phenylhydrazine	243	128; 107 (di)	168; 177 (di)	148	151	172	
3-Chloro-2-methylaniline (2-amino-6-chlorotoluene)	245	159	173				
2-Chloro-6-methoxyaniline	246	123	135				
3-Ethoxyaniline (*m*-phenetidine)	248	97	103		157	138	
1,3-Di(aminomethyl)benzene (α,α′-diamino-*m*-xylene)	248	135	172				

(Continued)

TABLE AII.11 Amines—Primary and Secondary (Liquids) *(Continued)*

Name of Compound	bp (°C)	Derivative mp (°C)					
		Acetamide	Benzamide	Benzenesulfonamide	4-Toluenesulfonamide	Phenylthiourea	Amine hydrochloride
1,2,3,4-Tetrahydroquinoline	250		76	67			181
2-Bromoaniline	250	99	116		90	146; 161	
3-Methoxyaniline (*m*-anisidine)	251	81			68		168
3-Bromoaniline	251	88	136; 120			143; 97	
2,5-Dichloroaniline	251	132	120			166	
2-Aminoacetophenone	252	77	98		148		168d
4-Ethoxyaniline (*p*-phenetidine)	254	137	173	143	106	136	
3-Bromo-2-methylaniline (2-amino-6-bromotoluene)	255	163	177				
Dicyclohexylamine	255	103	153		119		
3-Bromo-4-methylaniline (4-amino-2-bromotoluene)	257	118	132				
4-(*N*-Methylamino)aniline [*N*-methyl-*p*-toluidine; *p*-(*N*-methylamino)aniline]	258	63	165				
Methyl 2-aminobenzoate (methyl anthranilate)	260	101	100	107			
4-(*N*,*N*-Diethylamino)aniline	261	104	172		112		
4-Butylaniline	261	105	126				
4-(*N*,*N*-Dimethylamino)aniline	262	133	228				
Ethyl 2-aminobenzoate (ethyl anthranilate)	266	61	98	93	112		
Di-(2-hydroxyethyl)amine (diethanolamine)	270			130	99		
3-(*N*,*N*-Dimethylamino)aniline	272	87; 69	164				
1-Amino-*N*-methylnaphthalene (*N*-methyl-α-naphthylamine)	293	95	121		164		
Ethyl 3-aminobenzoate	294	110	148; 114				
N-Benzylaniline	298	58	107	119	149	103	
2-Aminobiphenyl	299	121	86; 102				
Dibenzylamine	300		112	68	159		256
Diphenylamine	302	103	180	124	144	152	
1,1-Diphenylmethylamine (benzhydrylamine; α-amino-diphenylmethane)	304	147	172				
N-Benzylaniline	306	58	107	119	140		
2-Amino-*N*-methylnaphthalene (*N*-methyl-β-naphthylamine)	317	51	84	107	78		183
2,4′-Diaminobiphenyl	363	202	278				

TABLE AII.12 Amines—Primary and Secondary (Solids)

Name of Compound	mp (°C)	Derivative mp (°C)					
		Acetamide	Benzamide	Benzenesulfonamide	4-Toluenesulfonamide	Phenylthiourea	Amine hydrochloride
Ethyl 2-aminobenzoate (ethyl anthranilate)	13	61	98	92	112		
2,5-Dimethylaniline	15	142	140	138	119; 233	148	
3-Bromoaniline	18	88	136; 120			97; 143	
1,2,3,4-Tetrahydroquinoline	20		76	67			181
Dicyclohexylamine	20	103	153		119		
2-Aminoacetophenone	20	76	98		148		
Phenylhydrazine	23	128; 107 (di)	168; 177 (di)	148	151	172	
4-Aminostyrene	24	142	161				
Methyl 2-aminobenzoate (methyl anthranilate)	24	101	100	107			
4-Amino-2-bromotoluene (3-bromo-4-methylaniline)	26	118	132				
2-Bromo-4-methylaniline (4-amino-3-bromotoluene)	26	118	149			154	
2-Amino-3-methylpyridine	26	64	220				
2-Aminothiophenol	26	135 (di)	154 (di)				
1,4-Diaminobutane (putrescine; tetramethylenediamine)	27	137 (di)	177 (di)		224 (di)		315 (di)
4-Chloro-2-methylaniline (2-amino-5-chlorotoluene)	29	140	172; 142	125	145		
2-Bromoaniline	32	99	116		90	146; 161	
1-Amino-2-methylnaphthalene (2-methyl-α-naphthylamine)	32	188	180				
3-Iodoaniline	33	119	157		128		
2-Aminodibenzyl	33	117	166				198
3-Iodoaniline	33	119	157		128		
N,*N*′-Diphenylhydrazine (*asym*-diphenylhydrazine)	34	184	192				
1,4-Di(aminomethyl)-benzene (α,α′-diamino-1,4-dimethylbenzene)	35	194 (tetra)	193 (di)				
4-(*N*-Methylamino)aniline	36	63	165				
N-Benzylaniline	37	58	107	119	149	103	
5-Aminoindane	38	106	137				
2-Amino-5,6,7,8-tetrahydronaphthalene (2-aminotetralin)	38	107	167				
2-Amino-5-bromonaphthalene (5-bromo-β-naphthylamine)	38	165	109				
2,2-Diphenylethylamine	38	88	145				257
2-Iodo-4-methylaniline (4-amino-3-iodotoluene)	40	133	161				188

(Continued)

TABLE AII.12 Amines—Primary and Secondary (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)					
		Acetamide	Benzamide	Benzenesulfonamide	4-Toluenesulfonamide	Phenylthiourea	Amine hydrochloride
2-Chloro-4,6-dimethylaniline	40	206	148				
4-(*N*,*N*-Dimethylamino)aniline	41	133	228				
2-Amino-6-methylpyridine	41	90	90				155
1,6-Diaminohexane (hexamethylenediamine)	42	127 (di)	155 (di)	154 (di)			
4-Amino-3-methylbiphenyl	43	165	189				
2,4′-Diaminobiphenyl	45	202 (di)	278 (di)				
4-Methylaniline (*p*-toluidine; *p*-aminotoluene)	45	154	158	120	118	141	240
4-Aminobenzyl cyanide	46	97 (mono) 153 (di)	177				
4-Aminothiophenol	46	144	180				
1-(2-Aminophenyl)-1-propanone (2-aminopropiophenone)	47	71	130				
3,4-Dimethylaniline	49	99	118	118	154		256
Heptadecylamine	49	62	91				
2-Aminobiphenyl	49	121	86; 102				
2-Bromo-4,6-dimethylaniline	50	197	186				
2,5-Dichloroaniline	50	133	120			166	192
1-Aminooxindole	50	187	189				
1-Aminonaphthalene (α-naphthylamine)	50	160	161	167	157; 147	165	286
2-Amino-1-methylnaphthalene (1-methyl-β-naphthylamine)	51	189	222				
1-Amino-3-methylnaphthalene (3-methyl-α-naphthylamine)	52	176	189				
1-Amino-4-methylnaphthalene (4-methyl-α-naphthylamine)	52	167	239				234
Indole	52	158	68	254			
2-Aminodiphenylmethane	52	135	116				137
4-(*N*,*N*-Dimethylamino)aniline	53	131	228				
4-Aminobiphenyl (*p*-phenylaniline)	53	175; 120 (di)	233		255; 160		
Diphenylamine	54	103	180; 107	124	142	152	
2-Amino-5-bromobiphenyl	57	130	162				
4-Methoxyaniline (*p*-anisidine)	58	130	157	96	114	157; 171; 144	
1-Amino-7-methylnaphthalene (7-methyl-α-naphthylamine)	59	183	204				
4-Bromo-2-methylaniline (2-amino-5-bromotoluene)	59	157	115				
2-Amino-1-chloronaphthalene (1-chloro-β-naphthylamine)	59	147	98	131			

(Continued)

TABLE AII.12 Amines—Primary and Secondary (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)					
		Acetamide	Benzamide	Benzenesulfonamide	4-Toluenesulfonamide	Phenylthiourea	Amine hydrochloride
2-Aminoazobenzene	59	126	122				
2-Aminopyridine	60	71	169 (di); 87			216	
2-Iodoaniline	61	110	139				154
N-Phenyl-1-aminonaphthalene (*N*-phenyl-α-naphthylamine)	62	115	152				
4-Iodoaniline	62	184	222			153	
1-Amino-3-chloronaphthalene (3-chloro-α-naphthylamine)	62	197	162				219
2-Amino-4,4′-dimethylbiphenyl	63	119	96				
1,3-Diaminobenzene (1,3-phenylenediamine)	63	191 (di) 89 (mono)	240 (di) 125 (mono)	194	172		
2,4-Dichloroaniline	63	146	117	128	126		
3-Aminopyridine	64	133 (mono) 88 (di)	119				
2-Amino-5-methylnaphthalene (5-methyl-β-naphthylamine)	64	124	156				
2,5-Diaminotoluene	64	220 (di)	307	147 (2-mono)	150 (2-mono)		
9-Aminofluorene	64	262	261				255
4-Methylphenylhydrazine (*p*-tolylhydrazine)	65	130	146; 70 (mono)				
4-Aminobenzyl alcohol	65	188	150				217
N-Methyl-3-nitroaniline	66	95	156	83			
4-Bromoaniline	66	168	204	134	101; 141	148	
2-Amino-5-methylbenzophenone	66	159	118				
1,8-Diaminonaphthalene	66	312 (di)			207 (di)		
1-Amino-8-methylnaphthalene (8-methyl-α-naphthylamine)	68	184	196				
2,4,5-Trimethylaniline (pseudocumine)	68	162	167	136			
4-Iodoaniline	68	184	222			153	
1,2-Bis(2-aminophenyl)ethane (2,2′-diaminobenzyl)	68	249 (di)	255 (di)				
2-Amino-4-methylnaphthalene (4-methyl-β-naphthylamine)	68	173	195				
N-Methyl-3-nitroaniline	68	95	105; 155	83			
1-Amino-3-bromonaphthalene (3-bromo-α-naphthylamine)	70	174	166				247
8-Aminoquinoline	70	103	98		156		209
2-Nitroaniline	71	94	98; 110	104	115; 142	142	
3,4-Diaminotriphenylmethane	72	226 (di)	243 (di)				
4-Chloroaniline	72	179	193	122	96; 121	152	
4-Aminophenylurethane	74	202; 181	230				242

(Continued)

TABLE AII.12 Amines—Primary and Secondary (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)					
		Acetamide	Benzamide	Benzenesulfonamide	4-Toluenesulfonamide	Phenylthiourea	Amine hydrochloride
3-Nitro-2,4,6-trimethylaniline (3-nitromesidine)	75	191	169	163			
4-Aminodiphenylamine	75	158	203				
2,4-Dimethyl-6-nitroaniline	76	176	185				
2-Bromo-1,4-diaminobenzene	76	200 (di)	235 (di)				
4-Amino-2-nitrotoluene (4-methyl-3-nitroaniline)	78	148	172	160	164	145; 171	
2,4,6-Trichloroaniline	78	206	174	154			
1-Amino-5-methylnaphthalene (5-methyl-α-naphthylamine)	78	195	174				
1-Amino-*N*-(4-methylphenyl)-naphthalene [*N*-(*p*-tolyl)-α-naphthylamine]	79	124	140	83			
Di-(4-methylphenyl)amine (di-*p*-tolylamine)	79	88	125				
2,4-Dibromoaniline	79	146	134		134; 171		
2-Aminodiphenylamine	80	121 (mono)	136 (mono)				
2,4-Diaminophenol	80	222 (di) 182 (tri)	253 (di) 231				240 (di)
2,2′-Diaminobiphenyl	81	89 (mono) 161 (di)	159 (mono) 190 (di)				
3-Aminoacenaphthene	81	193	209				
2-Aminobenzyl alcohol	82	114 (mono)	199 (mono)				108
4-Chloro-3-methylaniline (5-amino-2-chlorotoluene)	83	91	119				
2,5-Dimethoxyaniline	83	91	85		80		
5-Chloro-2-methoxyaniline	84	104	78				
4-Aminotriphenylmethane	84	168	198				
1-Amino-3-iodonaphthalene (3-iodo-α-naphthylamine)	84	207	174				
N-Methyl-4-hydroxyaniline [*p*-(*N*-methylamino)phenol]	85	240; 97; 43 (mono)	175 (mono)		135 (mono)		
2-Aminophenanthrene	85	225	216				
3,4-Dimethoxyaniline (4-aminoveratrol)	86	133	177				
4-Aminobenzonitrile	86	205	170				
N-Methyl-2-hydroxyaniline [*o*-(*N*-methylamino)phenol]	87	150	150				
4-Aminoacenaphthene	87	176	196				
3-Aminophenanthrene	88	201	213				
4-Amino-3-methyl-1-phenylpyrazole	88	95	181				
3-Aminoethananilide (*m*-aminoacetanilide)	89	191			241		

(Continued)

TABLE AII.12 Amines—Primary and Secondary (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)					
		Acetamide	Benzamide	Benzenesulfonamide	4-Toluenesulfonamide	Phenylthiourea	Amine hydrochloride
3,4-Diaminotoluene (4-methyl-1,2-phenylenediamine)	90	210 (di); 95; 131 (mono)	264 (di)	179 (di)	140 (mono)		
2-Nitrophenylhydrazine	90	141 (di); 58	166				
2-Amino-3-nitrotoluene (2-methyl-6-nitroaniline)	91	157	167				
1-Chloro-2,4-diaminobenzene (4-chloro-1,3-phenylenediamine)	91	170 (mono) 243 (di)	178		215 (di)		
1-Amino-2,6-dimethylnaphthalene (2,6-dimethyl-α-naphthylamine)	91	211	220				
4-Iodo-2-methylaniline (2-amino-5-iodotoluene)	92	170; 162	184				
Ethyl 4-aminobenzoate (benzocaine)	92	110	148				
2-Amino-3-nitrotoluene (2-methyl-6-nitroaniline)	92	158	167				
3-Bromo-2-hydroxy-5-methylaniline (6-amino-2-bromo-4-methylphenol; 5-amino-3-bromo-4-hydroxytoluene)	93	129 (mono) 169 (di)	185 (mono) 166 (di)	157 (mono) 230 (di)			
4-Chloro-2,6-dibromoaniline	93	226	194				
3-Nitrophenylhydrazine	93	150 (di)	153 (di)				
7-Aminoquinoline	94	167	189				
2-Aminodibenzofuran	94	178; 83 (di)	201				
6-Chloro-2,4-dibromoaniline	95	227	192				
1,2-Diaminonaphthalene	95	234	291				
N-Ethyl-4-nitroaniline	96	119	98		107		
5-Amino-2-methylpyridine	96	126	111				218 (di)
2,4-Diiodoaniline	96	141; 171	181				
N-Methyl-2-hydroxyaniline [*p*-(*N*-methylamino)phenol]	96	64 (di)	160 (mono)				
1-Amino-8-nitronaphthalene (8-nitro-α-naphthylamine)	97	191		194			
2-Methyl-3-nitroaniline (2-amino-6-nitrotoluene)	97	158	168		122		
1-Amino-8-naphthol (8-hydroxy-α-naphthylamine)	97	181 (mono) 118 (di)	193 (mono) 206 (di)		189 (mono)		
3-Aminobenzyl alcohol	97	107 (mono)	115 (mono) 114 (di)				
2-Amino-4-methylpyridine	98	114; 103	114; 183 (di)	103			

(Continued)

TABLE AII.12 Amines—Primary and Secondary (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C) Acet-amide	Benz-amide	Ben-zene-sulfon-amide	4-Tolu-ene-sulfon-amide	Phenyl-thio-urea	Amine hydro-chlo-ride
2-Aminophenacyl alcohol	98	141 (mono)	167 (di)				
1,2-Diaminonaphthalene	98	234 (di)	291 (di)	215 (mono)			
5-Bromo-2-methoxyaniline	98	160	108				
2,4-Diaminotoluene (4-methyl-1,3-phenylenediamine)	99	224 (di)	224 (di)	178; 138 (mono) 192 (di)	192 (di) 160 (mono)		
3-Aminoacetophenone	99	129			130		
1,2-Diaminobenzene (1,2-phenylenediamine)	102	186 (di)	301 (di)	186	202; 260 (di)		
2-Amino-*N*-(4-methylphenyl)-naphthalene [*N*-(*p*-tolyl)-*β*-naphthylamine]	103	85	139				
3,4-Diaminobiphenyl	103	211; 155 (mono) 163 (di)	186; 221 (mono) 248 (di)				
Piperazine	104	134; 52 (mono) 144 (di)	191; 75 (mono) 196 (di)	282 (di)	173 (mono)		
2-Amino-8-nitronaphthalene (8-nitro-*β*-naphthylamine)	104	196	162				
3-Amino-4,4′-dimethylbiphenyl	105	157	161				230
1,3-Diamino-4,6-dimethylbenzene	105	165 (mono) 295 (di)	259 (di)				
2-Bromo-4-nitroaniline	105	129	160				
Triphenylmethylamine	105	208	162				
4-Aminophenanthrene	105	190	224				
2-Aminobenzophenone	106	72; 89	80				
3-Amino-6-phenylpyridine	106	149	201				
3-Amino-4-methylpyridine	106	84	81				180
4-Aminoacetophenone	106	167	205	128	203		
N-Methyl-9-aminophenanthrene (9-phenanthrylmethylamine)	107	185	167				
2-Amino-4-nitrotoluene (2-methyl-5-nitroaniline)	107	151	186	172			
N-Phenyl-2-aminonaphthalene (*N*-phenyl-*β*-naphthylamine)	108	93	148; 136; 111				
2-(4-Aminophenyl)ethyl alcohol	108	105	60 (mono) 136 (di)				171
5-Aminoacenaphthene	108	238 (mono) 122 (di)	210; 199				
2-Chloro-4-nitroaniline	108	139	161		164		
5-Aminoquinoline	110	178				204	
2,5-Diaminopyridine	110	290 (di)	230 (di)				

(Continued)

TABLE AII.12 Amines—Primary and Secondary (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C) Acet-amide	Benz-amide	Ben-zene-sulfon-amide	4-Tolu-ene-sulfon-amide	Phenyl-thio-urea	Amine hydro-chlo-ride
2-Aminobenzamide	111	177	215				
1,4-Diamino-2-iodobenzene	111	211	254				
4-Bromo-3-nitroaniline	111	104	138				
4-Bromo-2-nitroaniline	111	104	137				
2-Aminonaphthalene (β-naphthylamine)	112	134	162	102	133	129	260
4-Amino-3-methylbenzophenone	112	175	158				
4-Ethoxy-2-nitroaniline	113	104		72	94		
5-Bromo-2-hydroxy-3-methylaniline (2-amino-4-bromo-6-methylphenol; 3-amino-5-bromo-2-hydroxytoluene)	113	119 (mono) 200 (di)	195 (mono)				
1-Aminoethyl phenyl ketone (β-aminopropiophenone)	114	91	105				187
3-Nitroaniline	114	155	157 (mono) 76 (di)	136 150 (di)	139	160	
6-Aminoquinoline	114	138 (mono) 75 (di)	169	193			
Z-2,5-Dimethylpiperazine	114		152 (di)		147 (di)		
3-Aminocamphor	115	121	141				
3-Amino-2-phenylquinoline	116	124 (mono) 173 (di)	180				
5-Bromo-2-hydroxy-4-methylaniline (2-amino-4-bromo-5-methylphenol; 4-amino-2-bromo-5-hydroxytoluene)	116	199 (mono) 188 (di)	223 (mono)				
4-Methyl-2-nitroaniline (4-amino-3-nitrotoluene)	117	99	148	102	166; 146		171
4-Chloro-2-nitroaniline	117	104			110		
E-2,5-Dimethylpiperazine	118		229 (di)		225 (di)		
2-Methoxy-5-nitroaniline	118	176	161		128		
2-Amino-5', 4-dimethylazobenzene	119	157	135				
2,4,6-Tribromoaniline	119 (di)	127 232 (mono)	198				
1-Amino-5-nitronaphthalene (5-nitro-α-naphthylamine)	119	220		183			
5-Hydroxy-2,4,6-tribromoaniline (3-amino-2,4,6-tribromophenol)	119	136 (tri)			147		
1,4-Diaminonaphthalene	120	303 (di)	280 (di) 186 (mono)		188 (mono)		
2,2'-Diamino-4, 4'-dimethylbiphenyl	120	189 (di)	170 (di)				

(Continued)

TABLE AII.12 Amines—Primary and Secondary (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C) Acet-amide	Benz-amide	Ben-zene-sulfon-amide	4-Tolu-ene-sulfon-amide	Phenyl-thio-urea	Amine hydro-chlo-ride
2,6-Diaminopyridine	121	203 (di)	176 (di)				
Z-4,4′-Diaminostilbene	121	172 (di)	253 (di)				
3-Hydroxyaniline (*m*-aminophenol)	123	101 (di) 148 (mono)	153; 204 174 (mono)		157 (mono)	156	229
3,4,5-Tribromoaniline	123	256	210				
2,4-Dimethyl-5-nitroaniline	123	159	200	149	192		
4-Aminobenzophenone	124	153	152				
2-Amino-5-nitrobiphenyl	125	133			169		
2-Amino-1-nitronaphthalene (1-nitro-β-naphthylamine)	126	124	168	156	160		
4-Aminoazobenzene	126	146	211				
Hydrazobenzene	127	159 (mono) 105 (di)	126 (mono) 162 (di)				
4,4′-Diaminobiphenyl (benzidine)	127	317 (di) 199 (mono)	352 (di) 205 (mono)	232 (di)	243 (di)		
4-Amino-2-hydroxytoluene (3-hydroxy-4-methylaniline; 5-amino-2-methylphenol)	127	119 (mono)	164 (di)				
1-Amino-6-bromonaphthalene (6-bromo-α-naphthylamine)	128	192	218				
2-Methylaniline (*o*-toluidine; *o*-aminotoluene)	129	314	265				
4-Methoxy-2-nitroaniline	129	117	140				
4,4′-Diamino-3,3′-dimethylbiphenyl	129	103 (mono) 315 (di) 211 (tetra)	198 (mono) 265 (di)				
2,4-Diaminodiphenylamine	130	188 (mono)	213 (di)				
2-Aminocoumarin	130	202	173				
2-Methyl-4-nitroaniline (2-amino-5-nitrotoluene)	130	202	178	158	174		
2-Amino-4-chloropyridine	131	116	120 (mono) 165 (di)				
2-Aminobenzothiazole	132	186	186				
3,5-Dimethyl-2-hydroxyaniline (2-amino-4,6-dimethylphenol)	135	96 (mono)	154 (di)				
2-Hydroxy-5-methylaniline (2-amino-4-methylphenol; 3-amino-4-hydroxytoluene)	135	160 (mono) 145 (di)	191 (mono) 190 (di)				
2-Amino-3-methylnaphthalene (3-methyl-β-naphthylamine)	135	182	190				
(±)-2,2′-Diamino-6,6′-dimethylbiphenyl	136	205 (di)	182 (di)		163 (di)		

(Continued)

TABLE AII.12 Amines—Primary and Secondary (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)					
		Acetamide	Benzamide	Benzenesulfonamide	4-Toluenesulfonamide	Phenylthiourea	Amine hydrochloride
1,4-Diamino-2-nitrobenzene	137	162, 189 (mono) 186 (di)	236				
1-Aminophenanthrene	138	208	199				
4,4′-Diamino-3,3′-dimethoxybiphenyl (*o*-bianisidine)	138	242 (di)	236 (di)				
2-(4-Aminophenyl)quinoline	138	189 (mono) 154 (di)	234				
2-Methoxy-4-nitroaniline	140	154	150	181	175		
1-(4-aminophenyl)-1-propanone (4-aminopropiophenone)	140	161	190				
5-Amino-8-hydroxyquinoline	143	222 (mono) 207 (di)	205 (di)				
2-Amino-5-nitronaphthalene (5-nitro-β-naphthylamine)	144	186	182				
1-Amino-2-nitronaphthalene (2-nitro-α-naphthylamine)	144	199	175				
2-Aminobenzoic acid (anthranilic acid)	144	185	182	214	217		
2-Amino-4-hydroxytoluene (3-amino-4-methylphenol; 5-hydroxy-2-methylaniline)	144	178 (mono) 128 (di)		183 (mono)			
2,5-Dimethyl-4-nitroaniline	145	169		162	185		
4-Bromo-4′-bromobiphenyl	145	247			174		
1,4-Diaminobenzene (1,4-phenylenediamine)	147	304 (di) 163 (mono)	300, 338 (di) 128 (mono)	247 (di)	266 (di)		
4-Nitroaniline	148	216	203	139	191		
4,4′-Diamino-2,2′-dimethylazoxybenzene	148	281 (di)	290				
4-Bromo-3-hydroxyaniline (2-bromo-5-aminophenol)	150	212			136		
N-Methyl-4-nitroaniline	152	153	112	121			
4-Amino-2-chlorophenol (3-chloro-4-hydroxyaniline)	153	144 (mono) 124 (di)			117		
3-Aminobenzopyrazole	154	178 (di)	182 (di)				
(−)-2,2′-Diamino-6,6-dimethylbiphenyl	156	205 (di)	172 (di)				
3,3′-Diaminoazobenzene	156	272 (di)	286 (di)				
4-Nitrophenylhydrazine	157	205	193				
4-Aminopyridine	158	150	202				
4,4′-Diamino-3,3′-dimethyldiphenylmethane	159	224 (di) 119 (tetra)	215 (di)				

(Continued)

TABLE AII.12 Amines—Primary and Secondary (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)					
		Acetamide	Benzamide	Benzenesulfonamide	4-Toluenesulfonamide	Phenylthiourea	Amine hydrochloride
2-Amino-8-nitroquinoline	159	211	166				
2-Amino-4′-nitrobiphenyl	159	199			163		
3-Amino-2-methylquinoline	160	165	161				
1-Amino-4-hydroxy-3-nitronaphthalene (4-hydroxy-3-nitro-α-naphthylamine)	160	250	330				
1,3-Diamino-4-nitrobenzene	161	200 (mono) 246 (di)	222 (di)		169 (di)		
4-Amino-2-hydroxytoluene (3-hydroxy-4-methylaniline; 5-amino-2-methylphenol)	161	225 (mono) 133 (di)			112 (mono)		
2-Hydroxy-4-methylaniline (4-amino-3-hydroxytoluene; 2-amino-5-methylphenol)	162	171 (mono)	169 (mono) 162 (di)				
2-Amino-3,5-dimethylphenol (2,4-dimethyl-6-hydroxyaniline)	163	187 (mono) 88 (di)	211 (mono) 149 (di)				
4-Aminophenacyl alcohol	165	177, 130 (mono) 162 (di)	188 (mono)				
4-Amino-2-bromophenol (3-bromo-4-hydroxyaniline)	165	157 (mono)	185 (mono) 192 (di)				
4-Aminobenzenesulfonamide (sulfanilamide)	165	219 (mono) 254 (di)	284 (mono) 268 (di)	211			
2,7-Diaminonaphthalene	166	261 (di)	267 (di)				
4-Amino-3-nitrobiphenyl	167	132	143				
3,4-Diaminophenol	168	207 (di)	203 (di) 225 (tri)				
4-Amino-2-phenylquinoline	168	117 (di)	182				
2-Amino-4,6-dinitrophenol (picramic acid; 3,5-dinitro-2-hydroxyaniline)	169	201; 193	229; 300		191		
6-Aminocoumarin	170	217	173	159			
2,6-Dinitro-4-methylaniline (4-amino-3,5-dinitrotoluene)	172	195	186				
2-Hydroxyaniline (*o*-aminophenol)	174	201 (mono) 124 (di)	185; 165	141	139	146	
3-Aminobenzoic acid	174	250	248				
4,5-Dimethyl-2-hydroxyaniline (2-amino-4,5-dimethylphenol)	175	191 (mono) 157 (di)	196 (mono) 153 (di)				
4-Amino-2-methylphenol (5-amino-2-hydroxytoluene; 4-hydroxy-3-methylaniline)	175	103 (di) 179 (mono)	194 (di)		110 (mono)		

(Continued)

TABLE AII.12 Amines—Primary and Secondary (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C) Acet-amide	Benz-amide	Ben-zene-sulfon-amide	4-Tolu-ene-sulfon-amide	Phenyl-thio-urea	Amine hydro-chlo-ride
2-Amino-4-hydroxy-3-(1-methylethyl)toluene [6-aminothymol; 3-amino-4-methyl-2-(1-methylethyl)-phenol; 5-hydroxy-6-isopropyl-2-methylaniline]	179	74 (mono) 91 (tri)	179 (mono) 167 (di)				
4-Hydroxy-2-methylaniline (2-amino-5-hydroxytoluene; 4-amino-3-methylphenol)	179	130 (mono)	92 (mono)				215
1-Amino-3-hydroxynaphthalene (3-hydroxy-α-naphthylamine)	185	179 (mono)	309 (di)		137 (mono)		
4-Hydroxyaniline (*p*-aminophenol)	186	150 (di) 168 (mono)	234 (di) 217 (mono)	125	168 (di) 254; 142 (mono)	150	
6,6′-Diamino-3,3′-dimethyltriphenylmethane	186	217 (di)	196 (di)				
4-Aminobenzoic acid	187	252	278	212	223		
2,4-Dinitroaniline	188	121	202; 220		219		
2,4,6-Trinitroaniline (picramide)	190	230	196	211			
1-Amino-6-naphthol (6-hydroxy-α-naphthylamine)	190	218 (mono) 187 (di)	152 (mono) 223 (di)				
2-Amino-1,5-dinitronaphthalene (1,5-dinitro-β-naphthylamine)	191	201			182		
(±)-2,2′-Diamino-1,1′-dinaphthyl	193	236 (di)	235 (di)				
1-Amino-4-nitronaphthalene (4-nitro-α-naphthylamine)	195	190	224	158; 173	185		
1,2-Diamino-4-nitrobenzene	198	205 (mono) 195 (di)	235 (di)				
2,4-Dinitrophenylhydrazine	200	198	207				
4-Amino-4′-nitrobiphenyl	200	264; 240		174			
2-Amino-5-nitrobenzaldehyde	200	161			182		
2-Amino-7-hydroxynaphthalene (7-hydroxy-β-naphthylamine)	201	232 (mono) 156 (di)	246 (mono) 181 (di)				
4,4′-Diamino-1,1′-dinaphthyl	202	363 (di)	320 (di)				
3-Amino-5-phenylacridine	204	156	246				
1-Amino-2-methylanthraquinone	205	177 (mono) 206 (di)			218		
1-Amino-7-naphthol (7-hydroxy-α-naphthylamine)	207	165 (mono)	209 (mono) 208 (di)				
1-Amino-8-naphthol (8-hydroxy-α-naphthylamine)	207	165	208				
4,4′-Diamino-2,5,2′,5′-tetramethyltriphenylmethane	210	217 (di)	250 (di)				

(Continued)

TABLE AII.12 Amines—Primary and Secondary (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)					
		Acet-amide	Benz-amide	Ben-zene-sulfon-amide	4-Tolu-ene-sulfon-amide	Phenyl-thio-urea	Amine hydro-chlo-ride
5-Bromo-4-hydroxy-2-methylaniline(2-amino-4-bromo-5-hydroxytoluene; 4-amino-2-bromo-5-methylphenol)	215	172 (di)	229 (di)				
2-Hydroxy-6-nitroaniline (2-amino-3-nitrophenol)	216	172 (mono)			136 (mono)		
1-Amino-5-chloroanthraquinone	219	219	218				
2-Amino-10-hydroxyphenanthrene	221	182 (di)	225 (di)				
5-Amino-4-nitroacenaphthene	222	252	233				
5-Chloro-4-hydroxy-2-methylaniline (2-amino-4-chloro-5-hydroxytoluene; 4-amino-2-chloro-5-methylphenol)	225	162 (di)	220 (di)				
2-Amino-1,8-dinitronaphthalene (1,8-dinitro-β-naphthylamine)	226	238			221		
E-4,4′-Diphenylethene (*trans*-4,4′-diaminostilbene)	231	353 (di)	352 (di)				
2-Amino-3-naphthol (3-hydroxy-β-naphthylamine)	234	188 (di)	235 (mono)				
1-Amino-2,4-dinitronaphthalene (2,4-dinitro-α-naphthylamine)	242	259	252		166		
1-Amino-3-bromoanthraquinone	243	214			227		
Dibenzopyrrole (carbazole)	246	69	98		137		
1-Aminoanthraquinone	252	218	255		229		
3-Aminodibenzopyrrole (3-aminocarbazole)	254	217 (mono) 200 (di) 175 (tri)	250 (mono)				
1,8-Diaminoanthraquinone	262	284 (di)	324 (di)				
1,4-Diaminoanthraquinone	268	271 (di)	284 (di) 280 (mono)				
1,1′-Diamino-2,2′-dinaphthyl	281	230 (di)	278 (di)				
1,7-Diaminoanthraquinone	290	283 (di)	325 (di)				
1,6-Diaminoanthraquinone	292	295 (di)	275 (di)				
1-Amino-5-nitroanthraquinone	293	275	237				
2-Aminoanthraquinone	308	258 (di) 262 (mono)	228	271	304		
2-Amino-3-bromoanthraquinone	308	259; 217	279				

TABLE AII.13 Amines—Tertiary (Liquids)

Name of Compound	bp (°C)	mp (°C) of Derivative Formed Using				Derivative mp (°C)
		Chloroplatinic Acid	Methyl 4-toluenesulfonate	Methyl Iodide	Picric Acid	Amine Hydrochloride
Trimethylamine	3	242		230	216	278
N-Methylpyrrolidine	80	233			221	
Triethylamine	89			280	173	
1,2-Dimethylpyrrolidine	96	223			235	
1,3-Dimethylpyrrolidine	97	59			181; 115	
Pyridine	116	241; 262	139	118	167	
1,2,5-Trimethylpyrrolidine	116			310	163	
2-Dimethylaminodiethyl ether	121			165	121	
1-Methylpyrazole	127	198		190	148	
N-Ethylpiperidine	128	202			168	
2-Methylpyridine (α-picoline)	129	216; 195	150	230	169	
1,3-Dimethylpyrazole	136			256	138	
2-Methylpyrazine	137			130	133	
2,6-Dimethylpyridine (2,6-lutidine)	143	208		238	168	
4-Methylpyridine (γ-picoline)	143	231		152	167	
3-Methylpyridine (β-picoline)	144	202		92	150	
3-Chloropyridine	149	168			135	
2-Ethylpyridine	149	167			189	
Tripropylamine	156			208	117	
2,4-Dimethylpyridine (2,4-lutidine)	159	216		113	183	
2,5-Dimethylpyridine (2,5-lutidine)	160	194			169	
2-(Diethylamino)ethanol	161			249	79	
Tropidine	163	217		300	285	
2,3-Dimethylpyridine (2,3-lutidine)	164	195			188	
3,4-Dimethylpyridine (3,4-lutidine)	164	205			163	
3-Ethylpyridine	164	209			130	
4-Ethylpyridine	165	213			168	
Tropane	167	230			281	
2,4,5-Triethylpyridine	168	205			131	
3-Bromopyridine	170	175	156	165		
1,3,5-Trimethylpyrazole	170	191			147	
3,5-Dimethylpyridine (3,5-lutidine)	171	255			245	
2,4,6-Trimethylpyridine (γ-collidine)	172	223			156	
2,3,6-Trimethylpyridine	178	252			146	
2,3,5-Trimethylpyridine	184	228			183	
N,*N*,2-Trimethylaniline (*N*,*N*-dimethyl-*o*-toluidine)	185	193		210	122	156
N,*N*-Dimethylbenzylamine	185	192		179	93	
2,6-Dimethyl-4-ethylpyridine	186	210			120	
2,4-Diethylpyridine	188	171			100	

(Continued)

TABLE AII.13 Amines—Tertiary (Liquids) *(Continued)*

Name of Compound	bp (°C)	mp (°C) of Derivative Formed Using				Derivative mp (°C)
		Chloroplatinic Acid	Methyl 4-toluenesulfonate	Methyl Iodide	Picric Acid	Amine Hydrochloride
Methyl 2-pyridyl ketone	192	220		161	131	
2,3,4-Trimethylpyridine	193	259			164	
N,*N*-Dimethylaniline	193	173	161	228	163	90
3-Ethyl-4-methylpyridine	196	205; 234			150	
3,5-Dimethyl-2-ethylpyridine	198	189			152	
N-Ethyl-*N*-methylaniline	201			125	134	114
N,*N*,2,5-Tetramethylaniline	204	196			158	
N,*N*,2,4-Tetramethylaniline	205	219			124	
2-Chloro-*N*,*N*-diethylaniline	207			152	132	
N,*N*-Diethyl-2-methylaniline (*N*,*N*-diethyl-*o*-toluidine)	210			224	180	
N,*N*,4-Trimethylaniline (*N*,*N*-dimethyl-*p*-toluidine)	210		85	220	130	
3,4-Diethylpyridine	211	221			139	
Tributylamine	212			186	107	
N,*N*,3-Trimethylaniline (*N*,*N*-dimethyl-*m*-toluidine)	212			177	131	
Methyl 4-pyridyl ketone	214	205			130	
N,*N*-Diethylaniline	218			104	142	
N,*N*-Diethyl-4-methylaniline (*N*,*N*-diethyl-*p*-toluidine)	229			184	110	157
2,3,4,5-Tetramethylpyridine	234	210			172	
Quinoline	239	227	126	72 (hyd) 133 (anhyd)	203	
Isoquinoline	243	263	163	159	223	
(±)-Nicotine	243	280		219	218	
2-(*N*,*N*-Dimethylamino)benzaldehyde	244	206		164		
N,*N*-Dipropylaniline	245			156	261	
2-Ethylquinoline	246	188		180	148	
2-Methylquinoline (quinaldine)	247	228	161; 134	195	195	
L-Nicotine	248	275			218	
8-Methylquinoline	248			193	203	
1-Ethylisoquinoline	250	200			210	
2,4-Dimethyl-5,6,7,8-tetrahydroquinoline	250			157	144	195
2,8-Dimethylquinoline	252			221	180	
N-Methyl-2-pyridone	255	141			145	
3-Ethylisoquinoline	257	180			172	
6-Methylquinoline	258		154	219	234	
3-Methylquinoline	259	249		221	187	
3-Chloroquinoline	260			276	182	
5-Methylquinoline	260			105	213	

(Continued)

TABLE AII.13 Amines—Tertiary (Liquids) *(Continued)*

Name of Compound	bp (°C)	mp (°C) of Derivative Formed Using				Derivative mp (°C)
		Chloroplatinic Acid	Methyl 4-toluenesulfonate	Methyl Iodide	Picric Acid	Amine Hydrochloride
6-Chloroquinoline	262		143	248		
4-Methylquinoline (lepidine)	263	230		174	212	
4-Chloroquinoline	263	278			212	
2,6,8-Trimethylquinoline	265	207			189	207
7-Chloroquinoline	268	253		250		
2,4-Dimethylquinoline	269	229		265	194	
2-Phenylpyridine	269	204			175	
6,8-Dimethylquinoline	269	235			289	
N,*N*-Dibutylaniline	271		180		125	
4-Ethylquinoline	274	204		149	180	
3,5-Dimethyl-1-phenylpyrazole	275	186		190	103	
5,8-Dimethylquinoline	275	234			198	
6-Bromoquinoline	278			278	217	
2,6-Dimethylquinoline	280	238			237	
2,4,7-Trimethylquinoline	281	272		322	232	
4,7-Dimethylquinoline	283	227			224	
3,4-Dimethyl-1-phenylpyrazole	285	180			123	
8-Chloroquinoline	288	235		165		
8-Bromoquinoline	304	230		281		
6-Methoxyquinoline	305			236	305	
N-Benzyl-*N*-methylaniline	306			164	103; 127	
N-Benzyl-*N*-ethylaniline	312			161	117	

TABLE AII.14 Amines—Tertiary (Solids)

Name of Compound	mp (°C)	mp (°C) of Derivative Formed Using				Derivative mp (°C)
		Chloroplatinic Acid	Methyl 4-toluenesulfonate	Methyl Iodide	Picric Acid	Amine Hydrochloride
6-Bromoquinoline	19			278	217	
Isoquinoline	24		163	159	223	
2,8-Dimethylquinoline	27			221	180	
4-Chloroquinoline	31	278			212	
7-Chloroquinoline	32	253		250		
8-Iodoquinoline	36	251		200		
1,3,5-Trimethylpyrazole	37	191			147	
2,3-Dimethyl-5,6,7,8-tetrahydroquinoline	38			117	169	
7-Methylquinoline	39	224			237	
2,4,6-Trimethylquinoline	40 (hyd)			247; 225	201	272
6-Chloroquinoline	41		143	248		
2,4,8-Trimethylquinoline	42			229	193	
4-Chloro-2-methylquinoline	43			212	178	
5-Chloroquinoline	45	255		231; 172		
2,6,8-Trimethylquinoline	46	207			189	207
8-Methoxyquinoline	50			160	143	
4,8-Dimethylquinoline	55	226			217	
2,6-Dimethylquinoline	60		175	244	191	
N,N-Dimethyl-3-nitroaniline	60			205	119	
2,4,6-Trimethylquinoline	65 (anhyd)			247; 225	201	272
1,2-Dimethylbenzimidazole	65 (anhyd)			254	238	
2,3-Dimethylquinoline	69	230		218	231	
N,N-Dibenzylaniline	70			135	132	
3,4-Dimethylquinoline	74			191	215	290
8-Hydroxyquinoline	76			143	204	
Tribenzylamine	91			184	190	227
4,4′-Bis(dimethylamino)diphenylmethane	91			214 (di)	185 (mono) 178 (di)	
2,3,4-Trimethylquinoline	92	215		260	216	274
2,2′-Dipyridylamine	95	160			228	
1-Phenylisoquinoline	96	242			165	235
4-Iodoquinoline	97	185		251		
5-Iodoquinoline	100	263		245		
2,2′-Bisquinolylmethane	103			205	239, 210 (di)	

(Continued)

TABLE AII.14 Amines—Tertiary (Solids) *(Continued)*

Name of Compound	mp (°C)	mp (°C) of Derivative Formed Using				Derivative mp (°C)
		Chloroplatinic Acid	Methyl 4-toluenesulfonate	Methyl Iodide	Picric Acid	Amine Hydrochloride
Acridine	111			224	208	
1,2-Dimethylbenzimidazole	112 (anhyd)			254	238	
3,5-Dibromopyridine	112		219	274		
6,8′-Biquinolyl	148			126 (mono)	268	
2,7′-Biquinolyl	160			263	240	
7,7′-Biquinolyl	172			310 (mono)	300	
4,4′-Bis(dimethylamino)benzophenone (Michler's ketone)	174			105	156	
2,3′-Biquinolyl	176	278		286		
5-Hydroxyquinoline	224	230		224		240
4-Hydroxy-2-methylquinoline	232 (anhyd)	215		201 (anhyd)	200	
7-Hydroxyquinoline	235			251	245	
Hexamethylenetetramine	280		205	190	179	

TABLE AII.15 Amino Acids

Name of Compound	Decomposition Point (°C)	Derivative mp (°C)					
		4-Toluenesulfonamide	Phenylureido Acid	Acetamide	Benzamide	3,5-Dinitrobenzamide	2,4-Dinitroaniline Derivative
2-Aminophenylacetic acid	119			158	179		
N-Phenylglycine	127		195	124; 194	63		
3-(4-Aminophenyl)propanoic acid (4-aminohydrocinnamic acid)	132			143 (anhyd) 124 (hyd)	195		
(+)- or (−)-Ornithine	140		190		240 (mono) 189 (di)		
2-Aminobenzoic acid (anthranilic acid)	144	217	181	185	182	278	
E-3-(2-Aminophenyl)-2-propenoic acid (*trans*-2-aminocinnamic acid)	158			250 (mono) 158 (di)	193		
3-Aminobenzoic acid	174		270	250	248	270	
E-3-(4-Aminophenyl)-2-propenoic acid (*trans*-4-aminocinnamic acid)	176			260	274		
E-3-(3-Aminophenyl)-2-propenoic acid (*trans*-3-aminocinnamic acid)	183			237	229		
4-Aminobenzoic acid	188	223	300	252	278	290	
(+)- or (−)-Glutamic acid	198	117		187	138; 157		
4-Aminophenylacetic acid	200			170	206		
3-Aminopropanoic acid (β-alanine)	200	117	174		120; 165	202	146
(±)-Proline	203		170			217	181
(+)- or (−)-Arginine	207				298 (mono) 235 (di)	150	
(+)- or (−)-Glutamic acid	211	131		199	138	217	
Sarcosine	212	102	102	135	104	154	
β-Hydroxyvaline	218		182		153 (mono)		
(+)- or (−)-Lysine	224		184		235 (mono) 149 (di)	169	171
(+)- or (−)-Proline	224	133	170		156		138
(+)- or (−)-Asparagine	227	175	164		189	196	181
(±)-Glutamic acid	227	213			156		149
(+)- or (−)-Serine	228	213			171 (mono) 124 (di)	95	174
(±)-β-Hydroxynorvaline	230		156		170		
(±)-3-Amino-3-phenylpropanoic acid [(±)-β-aminohydrocinnamic acid]	231			161	196		

(Continued)

TABLE AII.15 Amino Acids *(Continued)*

Name of Compound	Decomposition Point (°C)	Derivative mp (°C) 4-Toluenesulfonamide	Phenylureido Acid	Acetamide	Benzamide	3,5-Dinitrobenzamide	2,4-Dinitroaniline Derivative
Glycine	232	150	163; 197	206	187	179	204
3-Aminosalicylic acid	235			215	189		
(±)-Threonine	235; 251	147			174 (di) 176 (mono); 150	145	178
(±)-Isoserine	246		184		151		
(±)-Serine	246	213	169		150; 171		201
4-Hydroxyphenylglycine	248			203 (mono) 175 (di)	117		
(+)- or (−)-Threonine	253				148		145
(±)-α-Aminophenylacetic acid	256			199	175		
(+)- or (−)-Cystine	260	205	117; 160		181 (di)	180	109
Glycylglycine	260	178	176		208	210	
(+)- or (−)-Aspartic acid	272	140	162		185		187
(±)-Methionine	272	105		114	151		117
(±)-Phenylalanine	273	135	182		188	93	186
(+)- or (−)-Hydroxyproline	274	153	175		100 (mono) 92 (di)		
(±)-Tryptophan	275	176			188	240	
(±)-Aspartic acid	280				165		196
(+)- or (−)-Methionine	283			99	150	95 (hyd) 150 (anhyd)	
5-Aminosalicylic acid	283			218 (mono) 184 (di)	252		
(+)- or (−)-Isoleucine	285	132	121		117		113
(+)- or (−)-Histidine	288; 253; 277	204			230 (mono); 249	189	233
(+)- or (−)-Tryptophan	290; 252	176; 104	166		183	233	221
(±)-Isoleucine	292	141	121		118		175
(±)-Alanine	295	139	190; 174		166	177	
(+)- or (−)-Alanine	297	139	168; 190		151		
(±)-Valine	298	110	164		132	158	184
(2*R*,3*S*)-2,3-Diaminosuccinic acid	306			235		212 (di, hyd)	
(+)-Norvaline	307			137	64		
(±)-2-Aminobutanoic acid	307		170		147	194	143
(+)- or (−)-Valine	315	149	147		127	158; 181	132
(±)-Tyrosine	318	226		148 (*N*-); 172 (di)	197	254	

(Continued)

TABLE AII.15 Amino Acids *(Continued)*

Name of Compound	Decomposition Point (°C)	Derivative mp (°C)					
		4-Toluenesulfonamide	Phenylureido Acid	Acetamide	Benzamide	3,5-Dinitrobenzamide	2,4-Dinitroaniline Derivative
(±) or (−)-Phenylalanine	320; 283	165	181		146	93	189
(±)-Leucine	332; 293		165	157	141	187	
(+)- or (−)-Leucine	337	124	115		107; 118	187	94
(+)- or (−)-Tyrosine	344	119 (di) 188 (mono)	104	172	211 (di) 166 (mono)		180

TABLE AII.16 Carbohydrates

Name of Compound	Decomposition Point (°C)	Specific Rotation in Water at 20°C	Time Required for Osazone Formation (min)	Derivative mp (°C)			
				Phenylosazone	4-Nitrophenylhydrazone	4-Bromophenylhydrazone	Acetate
Turanose (hydrate)	65	+27.3 ⟶ +75.8		220			141 (hepta)
1,3-Dihydroxyacetone	71 (monomer); 80 (dimer)			132	160		47
Melibiose (monohydrate)	85	+129.5		178			177 (β) 147 (α)
Gentiobiose (hydrated)	86	+9.5		164; 179			193 (β) 189 (α)
L-Ribose	87	+20.3 ⟶ +20.7		166		165	
α-D-Glucose (hydrated)	90	+47.7	4–5	205	88; 196	166	132 (β) 112 (α)
L-Rhamnose (hydrated)	94	−8.6 ⟶ +8.2		182; 222	191		
D-Ribose	95	−21.5		166		170	
Glycollic aldehyde	97			179			158 (mono)
β-Maltose (monohydrate)	101	+129.0		206			161 (β) 125 (α)
Levulose (D-fructose)	104	−92.0	2	210	176		109 (β) 70 (α)
α-L-Rhamnose (hydrated)	105	+9.4	9	190; 222	191		99
Lactic aldehyde	105			154	129		
L-Lyxose	106	+13.5		163	172	162	
D-Lyxose	107	+5.5 ⟶ −14.0		164	172	162	
D-Galactose (hydrated)	120	+81.7	15–19	201	154; 197	168	142 (β) 95 (α)
β-L-Rhamnose (anhydrous)	126	+9.1	9	222; 190		191	99
β-D-Allose	128	+0.58 ⟶ +14.41		178		145	
β-L-Allose	129	−1.9		165		145	
D-Talose	130	+30.0 ⟶ +20.6		201		205	
D-Threose	132	+29 ⟶ −19.6		164			114 (tri)
D-Mannose	132	+14.1	0.5	210	195	210	115 (β) 74 (α)
α-D-Mannoheptose	135	+85.05 ⟶ +68.64		200		208	106 (hexa) 140

(Continued)

TABLE AII.16 Carbohydrates *(Continued)*

Name of Compound	Decomposition Point (°C)	Specific Rotation in Water at 20°C	Time Required for Osazone Formation (min)	Derivative mp (°C)			
				Phenylosazone	4-Nitrophenylhydrazone	4-Bromophenylhydrazone	Acetate
D-Xylose	145	+18.7	7	164	155	128	141; 126 (β) 59 (α)
L-Fucose	145	−152.6 ⟶ −75.9		178	211	184	
α-D-Glucose (anhydrous)	146	+52.8	4–5	210	88; 196	166	132 (β) 112 (α)
β-D-Glucose	150	+18.7 ⟶ +52.7		210			132 (β)
Turanose (anhydrous)	157	+27.3 ⟶ +75.8		220			141 (hepta)
β-L-Arabinose	160	+104.0	9–10	166	186	155	86 (β) 96 (α)
L-Sorbose	164	−43.0	4	162			97
D,L-Arabinose	164			169		160	
Maltose (anhydrous)	165	+129.0		206			161 (β) 125 (α)
α-D-Galactose (anhydrous)	170	+81.7	15–19	201	154; 197	168	142 (β) 95 (α)
D-Glucoheptolose	171			210			112 (hexa)
Sucrose	185	+66.5	30	205			89; 70
L-Ascorbic acid	190	+49.0			262 (di)	170 (di)	
α-D-Glucoheptose	193	−20		195			135 (β) 164 (α)
Gentiobiose (anhydrous)	195	+9.5		164; 179			193 (β) 189 (α)
Lactose (hydrate)	203	+52.5			200		100 (β) 152 (α)
6-(β-D-Xyloside)-D-glucose (primeverose)	210	+24.1 ⟶ −3.3		220			216 (β)
Cellobiose	225	+35.0			200		192 (β) 230 (α)
Lactose (anhydrous)	233; 252	+52.5			200		100 (β) 152 (α)

TABLE AII.17 Carboxylic Acids (Liquids)

Name of Compound	bp (°C)	Derivative mp (°C)						
		4-Toluidide	Anilide	4-Nitrobenzyl Ester	4-Bromophenacyl Ester	Amide	*S*-Benzylthiuronium Salts	Phenylhydrazide
Trifluoroethanoic acid (trifluoroacetic acid)	72		91		74			
Thioethanoic acid (thioacetic acid)	93	131	76			115		
Methanoic acid (formic acid)	101	53	50	31	140		151	143
Ethanoic acid (acetic acid)	118	153	114	78	86	82	136	129
Propenoic acid (acrylic acid)	141	141	105			85		
Propanoic acid (propionic acid)	141	126	106	31	63	81	152	157
Propynoic acid (propiolic acid)	144d		87			62		
2-Methylpropanoic acid (isobutyric acid)	155	110	105		77	129	149	140
2-Methylpropenoic acid (methacrylic acid)	161		87			102		
Butanoic acid (butyric acid)	164	75	97	35	63	116	149	102
2,2-Dimethypropanoic acid (pivalic acid; trimethylacetic acid)	164	120	133		76	157		
2-Oxopropanoic acid (pyruvic acid)	165d	109; 130	104			125; 145		
Z-2-Butenoic acid (*cis*-crotonic acid; isocrotonic acid)	169	132	102		82	102		
3-Butenoic acid (vinylacetic acid)	169		58		60	73		
(±)-2-Methylbutanoic acid (ethylmethylacetic acid)	177	93	112		55	112		
3-Methylbutanoic acid (isovaleric acid)	177	109	110		68	137	159	
1-Heptyne-1-carboxylic acid (amylpropiolic acid)	180–220d	68				91		
3,3-Dimethylbutanoic acid (*tert*-butylacetic acid)	184	134	132			132		
Chloroethanoic acid (chloroacetic acid)	185	120	134		105			
2-Chloropropanoic acid (α-chloropropionic acid)	186	124	92			80		
Pentanoic acid (valeric acid)	186	74	63		75	106	156	109
2,2-Dimethylbutanoic acid (dimethylethylacetic acid)	190	83	92			103		
(±)-2,3-Dimethylbutanoic acid (isopropylmethylacetic acid)	192	113	78			132		
Dichloroethanoic acid (dichloroacetic acid)	194	153	125		99	98	178	

(Continued)

TABLE AII.17 Carboxylic Acids (Liquids) *(Continued)*

Name of Compound	bp (°C)	Derivative mp (°C)						
		4-Toluidide	Anilide	4-Nitrobenzyl Ester	4-Bromophenacyl Ester	Amide	*S*-Benzylthiuronium Salts	Phenylhydrazide
2-Ethylbutanoic acid (diethylacetic acid)	195	116	128	66		112		
(±)-2-Methylpentanoic acid	196	81	95			80		
(±)-3-Methylpentanoic acid	197	75	88			125		
Z-2-Methyl-2-butenoic acid (tiglic acid)	198	76	77	64	68			
4-Methylpentanoic acid (isocaproic acid; isobutylacetic acid)	200	63	112		79	121		144
Methoxyethanoic acid (glycolic acid methyl ester; methoxyacetic acid)	204		58			97		
Hexanoic acid (caproic acid)	205	75	95		72	101	159	98
2-Bromopropanoic acid (α-bromopropionic acid)	205	125	100			123		
Ethoxyethanoic acid (glycolic acid ethyl ester; ethoxyacetic acid)	207	32	95		105	82		
5-Methylhexanoic acid	207		75			103		
Bromoethanoic acid (bromoacetic acid)	208	91	131	88		91		
2-Ethylpentanoic acid (α-ethylpropylacetic acid)	209	129	94			105		
2-Methylhexanoic acid (butylmethylacetic acid)	210	85	98			73		
2-Bromobutanoic acid (α-bromobutyric acid)	217d	92	98	49		112		
4-Methylhexanoic acid	218		77			98		
Heptanoic acid	224	81	71		72	97		103
2-Ethylhexanoic acid	228	107	89			103		
Cyclohexanecarboxylic acid (hexahydrobenzoic acid)	233		146			186		
Octanoic acid (caprylic acid)	239	70	57		67	110	157	106
4-Oxopentanoic acid (levulinic acid; β-acetylpropionic acid)	250d	109	102	61	84	108		
Nonanoic acid (pelargonic acid)	254	84	57		69	101		
Decanoic acid (capric acid)	270	78	70		67	108		
2-Methyl-3-phenylpropanoic acid [(±)-α-methylhydrocinnamic acid; (±)-α-benzyl-propionic acid]	272	130; 116				108		

(Continued)

TABLE AII.17 Carboxylic Acids (Liquids) *(Continued)*

Name of Compound	bp (°C)	Derivative mp (°C)						
		4-Toluidide	Anilide	4-Nitrobenzyl Ester	4-Bromophenacyl Ester	Amide	*S*-Benzylthiuronium Salts	Phenylhydrazide
10-Undecenoic acid (undecylenic acid)	275	68	67			87	149	97
4-Oxohexanoic acid (4-acetylbutanoic acid; 4-acetobutyric acid)	275	123				114		
Undecanoic acid (undecylic acid; hendecanoic acid)	280	80	71		68	103		110
2-Phenylpropanoic acid (β-phenylpropionic acid)	280		92	36				
Z-9-Octadecenoic acid (oleic acid)	286	42	41		46	76		

TABLE AII.18 Carboxylic Acids (Solids)

Name of Compound	mp (°C)	Derivative mp (°C)						
		4-Toluidide	Anilide	4-Nitrobenzyl Ester	4-Bromophenacyl Ester	Amide	*S*-Benzylthiuronium Salts	Phenylhydrazide
Z-9-Octadecenoic acid (oleic acid)	16	43	41		46	76		
2-Methylpropenic acid (methacrylic acid)	16		87			106		
Ethanoic acid (acetic acid)	16	153	114	78	86	82	136	
Octanoic acid (caprylic acid)	16	70	57		67	110	157	
(±)-2-Hydroxypropanoic acid [(±)-lactic acid]	18	107	59		113	79	153	
Propynoic acid (propiolic acid)	18		87			62		
E-2-Methyl-2-pentanoic acid (*trans*-β-ethyl-α-methylacrylic acid)	24				91; 46	80		
10-Undecenoic acid	25	68	67			87	149	97
(±)-2-Bromopropanoic acid [(±)-α-Bromopropionic acid]	26	125	100			123		
Undecanoic acid (undecylic acid; hendecanoic acid)	29	80	71		68	103		
Cyclohexanecarboxylic acid (hexahydrobenzoic acid)	31		146			186		
Decanoic acid (capric acid)	32	78	70		67	108		105
Z-13-Docosenoic acid (erucic acid)	34	78	55		63	84		
4-Oxopentanoic acid (levulinic acid; β-acetylpropionic acid)	35	109	102	61	84	108		
2,2-Dimethylpropanoic acid (pivalic acid; trimethylacetic acid)	35	120	133		76	157		
2-Methyl-3-phenylpropanoic acid [(±)-α-methylhydrocinnamic acid; (±)-α-benzylpropionic acid]	37	130; 116				108		
Dodecanoic acid (lauric acid)	44	87	78		76	100	141	
Tridecanoic acid (tridecylic acid)	44	88	80		75	100		
(±)-2-Bromo-3-methylbutanoicacid [(±)-α-bromoisovaleric acid]	44	124	116			133		
E-2-Methyl-2-butenoic acid (angelic acid)	46		126			128		
3-Phenylpropanoic acid (hydrocinnamic acid; 3-phenylpropionic acid)	49	135	98	36	104	82; 105		

(Continued)

TABLE AII.18 Carboxylic Acids (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)						
		4-Toluidide	Anilide	4-Nitrobenzyl Ester	4-Bromophenacyl Ester	Amide	*S*-Benzylthiuronium Salts	Phenylhydrazide
2-Bromo-2-methylpropanoic acid (α-bromoisobutanoic acid)	49	93	83			148		
Bromoethanoic acid (bromoacetic acid)	50	91	131	88		91		
E-9-Octadecenoic acid (elaidic acid; *trans*-oleic acid)	51				65	94		
4-Phenylbutanoic acid (4-phenylbutyric acid)	52				58	84		
Pentadecanoic acid (pentadecylic acid)	52		78	40	77	103		
Tetradecanoic acid (myristic acid)	57	93	84		81	103	139	
Trichloroethanoic acid (trichloroacetic acid)	58	113	97	80		141	148	123
E-13-Docosenoic acid (brassidic acid)	59		78		94	94		
5-Phenylpentanoic acid	60		90			109		
Heptadecanoic acid (margaric acid)	61			49	83	108		
Z-3-Chloro-2-butenoic acid (β-chloroisocrotonic acid)	61		108			110		
Hexadecanoic acid (palmitic acid)	63	98	91	43	86	107	141	111
Chloroethanoic acid (chloroacetic acid)	63	162	137		105	121	160	111
Z-2-Methyl-2-butenoic acid (tiglic acid)	64	71	77	64	68	76		
Cyanoethanoic acid (cyanoacetic acid)	66		199			123		
D-13-(2-Cyclopentenyl) tridecanoic acid (chaulmoogric acid)	68	100	89			106		
3-Methyl-2-butenoic acid (β,β-dimethylacrylic acid)	68				104	107		
Octadecanoic acid (stearic acid)	71	102	96		92	109	143	115
E-2-Butenoic acid (*trans*-crotonic acid)	72	132	118	67	96	160	172	
Phenylethanoic acid (phenylacetic acid)	76	136	118	65	89	157	165	175
Didecanoic acid (eicosanic acid; arachidic acid)	77	96	92		89	109		

(Continued)

TABLE AII.18 Carboxylic Acids (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)						
		4-Toluidide	Anilide	4-Nitrobenzyl Ester	4-Bromophenacyl Ester	Amide	*S*-Benzylthiuronium Salts	Phenylhydrazide
2-Hydroxy-2-methylpropanoic acid (α-hydroxyisobutyric acid)	79	133	136	81	98	98		
Hydroxyethanoic acid (glycolic acid; hydroxyacetic acid)	80	143	97	107	142	120	146	
Docosanoic acid (behenic acid)	82		102			111		
2-Benzoylpropanoic acid (α-benzoylpropionic acid)	83		138			146		
Iodoethanoic acid (iodoacetic acid)	84		143			95		
Dibenzylethanoic acid (dibenzylacetic acid)	89	175	155			129		
2-Benzoylbenzoic acid	90		195	100		165		
Z-Methylbutenedioic acid (citraconic acid; methylmaleic acid)	93	171 (mono)	176 (di) 153 (mono)	71 (di)		187d (di)		
E-3-Chloro-2-butenoic acid (β-chlorocrotonic acid)	94		124			101		
2-Chlorophenylethanoic acid (2-chlorophenylacetic acid)	95	170	139			175		
1,3-Pentanedicarboxylic acid (glutaric acid)	98	218 (di)	224 (di)	69 (di)	137 (di)	176 (di)	161	
Phenoxyethanoic acid (phenoxyacetic acid)	100		101		149	101		
3-Carboxy-3-hydroxypentanedioic acid (monohydrate) [2-hydroxy-1,2,3-propanetricarboxylic acid; citric acid (monohydrate)]	100	189 (tri)	199 (tri)	102 (tri)	148 (tri)	215 (tri)		
2-Methoxybenzoic acid (o-anisic acid)	101		131; 78	113	113	129		
2-Hydroxybutanedioic acid (L-malic acid; hydroxysuccinic acid)	101	207 (di)	197 (di)	124 (di) 87 (mono)	179 (di)	157 (di) 102 (mono)	124	
Ethanedioic acid (dihydrate) [oxalic acid (dihydrate)]	101	268 (di) 169 (mono)	254 (di) 149 (mono)	204 (di)	252d	419d (di) 219 (mono)	198	
2-Butylpropanedioic acid (butylmalonic acid)	101		193 (di)			200 (di)		
3-Phenylpropanoic acid (benzylacetic acid)	104		108			113		
Heptanedioic acid (pimelic acid)	105	206 (di)	156 (di) 109 (mono)		137 (di)	175 (di)		
4-Chlorophenylethanoic acid (p-chlorophenylacetic acid)	106	190	165			175		

(Continued)

TABLE AII.18 Carboxylic Acids (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)						
		4-Toluidide	Anilide	4-Nitrobenzyl Ester	4-Bromophenacyl Ester	Amide	*S*-Benzylthiuronium Salts	Phenylhydrazide
Nonanedioic acid (azelaic acid)	106	202 (di)	187 (di) 108 (mono)	44 (di)	131 (di)	175 (di) 95 (mono)		
2-Phenylpropenoic acid (2-phenylacrylic acid; atropic acid)	107		134			122		
2-Methylbenzoic acid (*o*-toluic acid)	108	144	125	91	57	143	146	
D-1,2,2,3-Trimethylcyclohexene-6-carboxylic acid (D-campholic acid)	109		91			80; 90		
E-2-Chloro-3-phenyl-2-propenoic acid (*cis*-α-chloroallocinnamic acid; *cis*-2-chlorocinnamic acid)	111		139			134		
2-Ethylpropanedioic acid (ethylmalonic acid)	111		150	75		214 (di)		
3-Methylbenzoic acid (*m*-toluic acid)	113	118	126	87	108	97	140	
2-Bromopropanedioic acid (bromomalonic acid)	113d	217 (di)				181 (di)		
2-Methylbutanedioic acid (methylsuccinic acid; pyrotartaric acid)	115	164	200 (di) 159 (mono)			165 (mono) 225 (di)		
2-Phenoxypropanoic acid (2-phenoxypropionic acid)	116	115	119			133		
3-Benzoylpropanoic acid (β-benzoylpropionic acid)	116		150			125; 146		
2-Hydroxy-2-phenylethanoic acid (mandelic acid; 2-hydroxy-2-phenylacetic acid)	119	172	152	124	113	134	166	
2-Chloro-2,2-diphenylethanoic acid (2-chloro-2,2-diphenylacetic acid)	119		88			115		
1-Cyclopentenylcarboxylic acid	121	122	126					
2-Benzylpropanedioic acid (benzylmalonic acid)	121d		217 (di)	120 (di)		225 (di)		
Benzoic acid	122	158	163	89	119	130	167	168
(±)-*trans*-Camphenic acid [(±)-*trans*-camphene-camphoric acid]	123		165 (di)			232 (di)		
3,3,3-Trichloro-2-hydroxy-propanoic acid (3,3,3-trichlorolactic acid)	124		164			96		123

(Continued)

TABLE AII.18 Carboxylic Acids (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)						
		4-Toluidide	Anilide	4-Nitrobenzyl Ester	4-Bromophenacyl Ester	Amide	*S*-Benzylthiuronium Salts	Phenylhydrazide
Trichloroethanoic acid (trichloroacetic acid)	124		164			145		
2-Hydroxy-3-nitrobenzoic acid	125	165				145		
2,2-Diethylpropanedioic acid (diethylmalonic acid)	125			91 (di)		224 (di) 146 (mono)		
2,4-Dimethylbenzoic acid	127		141			181		
2-Benzoylbenzoic acid	128		195	100		165		
Z-Butenedioic acid (maleic acid)	132	142 (di)	187 (di) 198 (mono)	91 (di)	170; 190	153, 266 (di) 281 (mono) 181	163	
2,5-Dimethylbenzoic acid	132		140			186		
Z-2-Chloro-3-phenyl-2-propenoic acid (*cis*-β-chloroallocinnamic acid)	132	142	135			76		
Decanedioic acid (sebacic acid)	133	201 (di)	202 (di) 123 (mono)	72 (di)	147 (di)	210 (di) 170 (mono)	155	194
E-3-Phenyl-2-propenoic acid (*trans*-cinnamic acid)	133	168	153; 109	116	146	148	183	
2-Chloropropanedioic acid (chloromalonic acid)	133		118 (di)			170 (di)		
(±)-2-Hydroxy-2-phenylethanoic acid [(±)-mandelic acid; 2-hydroxy-2-phenylacetic acid]	134	172	152	124	113	134		
Furoic acid (pyromucic acid)	134	171; 108	124	134	139	143	211	
Propanedioic acid (malonic acid)	135d	253 (di) 156 (mono)	230 (di) 132 (mono)	86 (di)		170 (di) 110, 50 (mono)	147	194
1-Naphthaleneethanoic acid (α-naphthylacetic acid)	135		160		112	181		
2-Acetylbenzoic acid (aspirin; acetylsalicylic acid)	135		136	90		138	144	
1,5,5-Trimethylcyclopentene-2-carboxylic acid (β-campholytic acid)	135	114	104			130		
2,4-Hexadienoic acid (sorbic acid)	135 135		153 153		129 129	168 168		
3-Phenylpropynoic acid (phenylpropiolic acid)	137 137	142 142	126 126	83 83		102 102		
(±)-*cis*-Camphenic acid [(±)-*cis*-camphenecamphoric acid]	137		212 (di)			225 (di)		
E-2-Chloro-3-phenyl-2-propenoic acid (*trans*-α-chlorocinnamic acid)	138	116	118			122		

(Continued)

TABLE AII.18 Carboxylic Acids (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)						
		4-Toluidide	Anilide	4-Nitrobenzyl Ester	4-Bromophenacyl Ester	Amide	*S*-Benzylthiuronium Salts	Phenylhydrazide
2-Methylpropanedioic acid (methylmalonic acid)	138d	228; 214 (di) 145d (mono)	182	75		217		
2-Pyridinecarboxylic acid (2-picolinic acid)	138	104	76			107		
5-Chloro-2-nitrobenzoic acid	139		164			154		
(*R,S*)-2,3-Dihydroxybutanedioic acid (*meso*-tartaric acid)	140		194 (mono)	93		190 (di)		
3-Nitrobenzoic acid	141	162	154	141	137	143	163	
2-Chloro-4-nitrobenzoic acid	142		168			172		
4-Chloro-2-nitrobenzoic acid	142		131			172		
Z-3-Chloro-3-phenyl-2-propenoic acid (*trans*-β-chlorocinnamic acid)	142	125	128			118		
2-Chlorobenzoic acid	142	131	118	106	107	142; 202		
Octanedioic acid (suberic acid)	144	219 (di)	187 (di) 129 (mono)	85 (di)	144 (di)	216 (di) 127 (mono)		
2-Aminobenzoic acid (anthranilic acid)	144	151	131	205	172	109	149 149	
2,4,5-Trimethoxybenzoic acid (asaronic acid)	144		155			185		
2-Chlorophenoxyethanoic acid (*o*-chlorophenoxyacetic acid)	146		121			149		
2-Nitrobenzoic acid	146	203	155	112	107	176	159	
2-Carboxyphenyl-2-oxoethanoic acid [phthalonic acid (anhydrous); 2-carboxyphenyl-2-oxoacetic acid]	146		176 (mono) 208 (di)			179 (α) 155 (β)		
Diphenylethanoic acid (diphenylacetic acid)	148	173	180			168		
Oxodiethanoic acid (diglycolic acid; oxodiacetic acid)	148	148 (mono)	152 (di) 118 (mono)			135 (mono)		
N-Phenylethanedioic acid monoamide (*N*-Phenyloxalic acid monoamide; oxanilic acid)	149		154 (di)			228		
2-Bromobenzoic acid	150		141	110	102	155	171	
2-Hydroxy-2,2-diphenylethanoic acid (benzilic acid; 2-hydroxy-2,2-diphenylacetic acid)	150	190	175	100	152	155		
4-Nitrophenylethanoic acid (*p*-nitrophenylacetic acid)	153	210	198; 212		207	198		

(Continued)

TABLE AII.18 Carboxylic Acids (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)						
		4-Toluidide	Anilide	4-Nitrobenzyl Ester	4-Bromophenacyl Ester	Amide	*S*-Benzylthiuronium Salts	Phenylhydrazide
3-Carboxy-3-hydroxypentanedioic acid (anhydrous) [citric acid (anhydrous); 2-hydroxy-1,2,3-propanetricarboxylic acid]	153	189 (tri)	192 (tri)	102 (tri)	148 (tri)	215d (tri)		
2-Hydroxy-5-methylbenzoic acid (5-methylsalicylic acid)	153			147	142	178	185	
Hexanedioic acid (adipic acid)	154	241	241 (di) 153 (mono)	106	155	220 (di) 130 (mono)	163	209
3-Bromobenzoic acid	155		146; 136	105	126	155	168	
2-Hydroxybenzoic acid (salicylic acid)	158	156	136	98	140	142	148	
4-Chlorophenoxyethanoic acid (*p*-chlorophenoxyacetic acid)	158		125		136	133		
3-Chlorobenzoic acid	158		124	107	117	134	155	
2-Iodobenzoic acid	162		142	111	143; 110	110; 184		
1-Naphthoic acid	162		164		135	205		
2,4-Dichlorobenzoic acid	164	168	165; 153			194		
4-Nitro-1,2-benzenedicarboxylic acid (4-nitrophthalic acid)	165	172	192			200d		
2-Methylenebutanedioic acid (itaconic acid; methylenesuccinic acid)	165		190; 152 (mono)	91	117	192 (di)		
5-Bromo-2-hydroxybenzoic acid (5-bromosalicylic acid)	165		222			232		
3,4-Dimethylbenzoic acid	166		108			130		
1,2,3-Propanetricarboxylic acid (tricarballylic acid)	166		252 (tri)		138 (tri)	207d (tri)		
2-(±)-Phenylbutanedioic acid [(±)-phenylsuccinic acid]	167	175 (mono)	222 (di) 175 (mono)			211 (di) 159, 145 (mono)		
2,3-Dihydroxybutanedioic acid (D- or L-tartaric acid)	169		180; 194, 180 (mono) 264 (di)	163 (di)	216, 204 (di)	196 (di) 172 (mono)		240
2-Hydroxy-3-methylbenzoic acid (3-methylsalicylic acid)	169	164		99		112	204	
3,5-Dinitro-2-hydroxybenzoic acid (3,5-dinitrosalicylic acid)	173		181			197		
3-Aminobenzoic acid	174		140	201	190	111		
2-Hydroxy-4-methylbenzoic acid	177			175			165	
8-Bromo-1-naphthoic acid	178		151			180		
4-Methylbenzoic acid (*p*-toluic acid)	180	165	148	105	153	160	190	

(Continued)

TABLE AII.18 Carboxylic Acids (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)						
		4-Toluidide	Anilide	4-Nitrobenzyl Ester	4-Bromophenacyl Ester	Amide	S-Benzylthiuronium Salts	Phenylhydrazide
6-Bromo-3-nitrobenzoic acid	180		166			198		
3,4-Dimethoxybenzoic acid [veratric acid (anhydrous)]	181		166; 154		124	164		
N-Benzoyl-2-aminobenzoic acid (*N*-benzoylanthranilic acid; 2-benzaminobenzoic acid)	181		279			219		
4-Chloro-3-nitrobenzoic acid	182		131			156		
2,4-Dinitrobenzoic acid	183			142	158	204		
2-Naphthoic acid	185	192	173		211	195		
N-Acetyl-2-aminobenzoic acid (acetylanthranilic acid)	185		167			177		
2-Carboxyphenylethanoic acid (homophthalic acid; 2-carboxyphenylacetic acid)	185		232			228		
4-Methoxybenzoic acid (4-anisic acid)	186	186	171	132	152	167	185	
4-Aminobenzoic acid	186				200	114		
N-Benzoylaminoethanoic acid (hippuric acid; *N*-benzoylglycine; *N*-benzoylaminoacetic acid)	187		208	136	151	183		
3-Iodobenzoic acid	187			121	128	186		
Coumarin-3-carboxylic acid	187		250			236		
Butanedioic acid (succinic acid)	188	260 (di) 180 (mono)	230 (di) 149 (mono)	88 (di)	211 (di)	260 (di) 157 (mono)	154	210
1,2,2-Trimethylcyclopentane-1,3-dicarboxylic acid (D-camphoric acid)	188	196; 214	210, 196 (mono) 226 (di)	67		192 (di) 183 (mono)		
Ethanedioic acid (anhydrous) [oxalic acid (anhydrous)]	188	268 (di) 169 (mono)	246 (di) 148 (mono)			419 (di) 219 (mono)		
1,2,3,4-Butanetetracarboxylic acid	189		187			181 (di) 310 (tetra)		
2-Chlorobutenedioic acid (chlorofumaric acid)	192		186	139				
Coumarilic acid (coumarone-2-carboxylic acid)	193		159			159		
2,2-Dimethylpropanedioic acid (dimethylmalonic acid)	193			84		269 (di)		
1-Hydroxy-2-naphthoic acid	195		154			202		
E-1,2,3-Propenetricarboxylic acid (aconitic acid)	195		189 (di) 170 (mono)	76	186 (tri)	250d (tri)		
4-Ethoxybenzoic acid	198		172	110		202		

(Continued)

TABLE AII.18 Carboxylic Acids (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)						
		4-Toluidide	Anilide	4-Nitrobenzyl Ester	4-Bromophenacyl Ester	Amide	*S*-Benzylthiuronium Salts	Phenylhydrazide
E-3-(3-Nitrophenyl)-2-propenoic acid (*trans*-3-nitrocinnamic acid)	200			174	178	196		
3,4-Dihydroxybenzoic acid (protocatechuic acid)	200		167	188		212		
3-Hydroxybenzoic acid	201	163	157	108	176	170		
2-Methyl-*E*-butenedioic acid (mesaconic acid; methylfumaric acid)	204	212 (di) 196 (mono)	186 (di) 202, 163 (mono)	134 (di)		176 (di) 222 (mono)		
(±)-2,3-Dihydroxybutanedioic acid [(±)-tartaric acid]	204		236 (di)	147 (di)		226 (di)		
4-Bromo-3-nitrobenzoic acid	204		156			156		
3,5-Dinitrobenzoic acid	205		234	157	159	183		
1,2-Benzenedicarboxylic acid (phthalic acid)	208d	201 (di) 165, 150 (mono)	255 (di) 170 (mono)	155 (di)	153 (di)	220 (di) 149 (mono)	158	
E-3-(2-Hydroxyphenyl)-2-propenoic acid (*o*-coumaric acid; *trans*-2-hydroxycinnamic acid)	208			152		209d		
Ethanedioic acid monoamide (oxamic acid, oxalic acid monoamide)	210		149			419		
E-3-(2-Chlorophenyl)-2-propenoic acid (*trans*-2-chlorocinnamic acid)	212		176			168		
2,4-Dihydroxybenzoic acid (β-resorcylic acid)	213		127	189		222		
2,3,4,5-Tetrahydroxyhexanedioic acid (mucic acid; galactaric acid)	214d			310	225	220 (di) 192 (mono)		
4-Hydroxybenzoic acid	215	204	202	198; 182	191	162	145	
3-Nitro-1,2-benzenedicarboxylic acid (3-nitrophthalic acid)	218	226 (di)	234 (di)	190	166	201 (di)		
4-Cyanobenzoic acid	219		179	189		223		
3-Hydroxy-2-naphthoic acid	223	223	249			218		
4-Hydroxy-2-naphthoic acid	226	206				218		
Biphenyl-2,2′-dicarboxylic acid (diphenic acid)	229		230 (di) 176 (mono)	187 (di)		212 (di) 193 (mono)		
2-Hydroxy-5-nitrobenzoic acid (5-nitrosalicylic acid)	230		224			225		
4-Chloro-1-hydroxy-2-naphthoic acid	234	144	181					

(Continued)

TABLE AII.18 Carboxylic Acids (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)						
		4-Toluidide	Anilide	4-Nitrobenzyl Ester	4-Bromophenacyl Ester	Amide	*S*-Benzylthiuronium Salts	Phenylhydrazide
5-Bromo-2-hydroxy-3-methylbenzoic acid (5-bromo-2-hydroxy-3-toluic acid)	236		125			78		
1,2,3,4-Butanetetracarboxylic acid	237		168 (di)			169 (di)		
7-Bromo-1-naphthoic acid	237		202			247		
3-Pyridinecarboxylic acid (nicotinic acid)	238	150	85; 132; 265			128		
E-3-(2-Nitrophenyl)-2-propenic acid (*trans*-2-nitrocinnamic acid)	240			132	142	185		
4-Nitrobenzoic acid	241	204; 192	217	169	137	201	182	
4-Chlorobenzoic acid	243		194	130	126	179; 170		
7-Chloro-1-naphthoic acid	243		185			237		
2-Chloroquinoline-4-carboxylic acid (3-chlorocinchonic acid)	244		202			335; 278		
4-Bromobenzoic acid	253		197	139; 180		190		
3,4,5-Trihydroxybenzoic acid (gallic acid)	254d; 240d		207	141	134	245; 189		
3,4-Pyridinedicarboxylic acid (cinchomeronic acid)	260d		206 (di)			170, 200 (mono) 165 (di)		
4-Iodobenzoic acid	270		210	141	147	217		
5-Chloro-2-naphthoic acid	270		203			187		
1-Chloroanthraquinone-2-carboxylic acid	272		249			317		
2-Amino-3-phenylpropanoic acid (β-phenylalanine)	273			222		140		
E-3-(4-Nitrophenyl)-2-propenoic acid (*trans*-4-nitrocinnamic acid)	287			187	191	204; 217		
9,10-Anthraquinone-2-carboxylic acid	292		260			280		
9,10-Anthraquinone-1-carboxylic acid	294		289			280		
1,4-Benzenedicarboxylic acid (terephthalic acid)	300		337	263	225			
E-Butenedioic acid (fumaric acid)	302; 287		314 (di) 235 (mono)	151	256d	267d (di) 302	195	
1,3-Benzenedicarboxylic acid (isophthalic acid)	348; 300		250	215; 203	186	280	216	
1,3,5-Benzenetricarboxylic acid (trimesic acid)	350; 380		120d (tri)		197 (tri)	365d (tri)		

TABLE AII.19 Esters (Liquids)

Name of Compound	bp (°C)	sp gr	Derivative mp (°C)					
			Acid	Amide	4-Toluidide	3,5-Dinitrobenzoate	*N*-Benzylamide	Hydrazide
Methyl methanoate (methyl formate)	32	0.998_4^0 0.974			53	108	60	54
Ethyl methanoate (ethyl formate)	54	0.938; 0.922			53	93	60	54
Methyl ethanoate (methyl acetate)	57	0.958; 0.927	17	82	153	108	61	77
1-Methylethyl methanoate (isopropyl formate)	71	0.883; 0.873		53	123		60	54
Ethenyl ethanoate (vinyl acetate; ethenyl acetate)	72	0.9317_4^{20}	17	82	153		61	77
Ethyl ethanoate (ethyl acetate)	77	0.924; 0.901	17	82	153	93	61	77
Methyl propanoate (methyl propionate)	80	0.937; 0.915		81	126	108	44	40
Propyl methanoate (propyl formate)	81	0.918; 0.904			53	74	60	54
1,1-Dimethylethyl methanoate (*tert*-butyl formate)	83				53	142	60	54
2-Propenyl methanoate (allyl formate; 2-propenyl formate)	84	0.932_4^{17}; 0.946			53	50	60	54
Methyl propenoate (methyl acrylate)	85	0.977_4^0; 0.961_4^{19}		85	141	108		
1-Methylethyl ethanoate (isopropyl acetate)	91	0.917; 0.872	17	82	153	123	61	77
Methyl 2-methylpropanoate (methyl isobutyrate)	92	0.912_4^0; 0.888		129	109	108	87	104
1-Methylpropyl methanoate (*sec*-butyl formate)	97	0.882			53	76	60	54
1,1-Dimethylethyl ethanoate (*tert*-butyl acetate)	98	0.867	17	82	153	142	61	77
2-Methylpropyl methanoate (isobutyl formate)	98	0.905; 0.876			53	87	60	54
Ethyl difluoroethanoate (ethyl difluoroacetate)	99			52		93		
Ethyl propanoate (ethyl propionate)	99	0.912; 0.889		81	126	93	44	40
Methyl 2-methylpropenoate (methyl methacrylate)	101	0.936	17	106		108		
Ethyl propenoate (ethyl acrylate)	101	0.925_4^0; 0.914_4^{15}; 0.909		85	141	93		
Methyl 2,2-dimethylpropanoate (methyl pivalate; methyl trimethylacetate)	101	0.891_4^0	36	157	120	108		

(Continued)

TABLE AII.19 Esters (Liquids) *(Continued)*

Name of Compound	bp (°C)	sp gr	Derivative mp (°C)					
			Acid	Amide	4-Toluidide	3,5-Dinitrobenzoate	*N*-Benzylamide	Hydrazide
Propyl ethanoate (propyl acetate)	101	0.909; 0.883	17	82	153	74	61	77
Methyl butanoate (methyl butyrate)	102	0.919; 0.898		116	75	108	38	44
2-Propenyl ethanoate (allyl acetate; 2-propenyl acetate)	104	0.938; 0.928	17	82	153	50	61	77
Trimethyl orthomethanoate (trimethyl orthoformate)	105	0.974_4^{23}; 0.967			53	108		
Butyl methanoate (butyl formate)	107	0.911; 0.888			53	64	60	54
Methyl Z-2-butenoate (methyl isocrotonate)	108			102	132	108		
Ethyl 2-methylpropanoate (ethyl isobutyrate)	111	0.890; 0.869		129	109	93	87	104
Chloromethyl ethanoate (chloromethyl acetate)	111	1.195_4^{14}; 1.094_4^{15}	17	82	153		61	77
1-Methylethyl propanoate (isopropyl propionate)	111	0.893_4^0		81	126	123	44	40
1-Methylpropyl ethanoate (*sec*-butyl acetate)	112	0.870	17	82	153	76	61	77
Methyl 3-methylbutanoate (methyl isovalerate)	117	0.901; 0.881		137	107	108	54	68
2-Methylpropyl ethanoate (isobutyl acetate)	118	0.892; 0.871	17	82	153	87	61	77
Ethyl 2,2-dimethylpropanoate (ethyl pivalate; ethyl trimethylacetate)	118	0.855	35	157	120	93		
Ethyl 2-methylpropenoate (ethyl methacrylate)	118	0.911	16	106		93		
Methyl *E*-2-butenoate (methyl crotonate)	119	0.981_4^4; 0.946	72	118	132	108	114	
1-Methylethyl 2-methylpropanoate (isopropyl isobutyrate)	120	0.847_4^{21}		129	109	123	87	104
Ethyl butanoate (ethyl butyrate)	122	0.900; 0.879		116	75	93	38	44
Propyl propanoate (propyl propionate)	123	0.902; 0.881		81	126	74	44	40
2,2-Dimethylpropyl ethanoate (*tert*-amyl acetate; dimethylethylcarbinyl acetate; 2,2-dimethylpropyl acetate)	124	0.874_4^{19}	17	82	153	118	61	77
2-Propenyl propanoate (allyl propionate)	124	0.914		81	126	50	44	40

(Continued)

TABLE AII.19 Esters (Liquids) *(Continued)*

Name of Compound	bp (°C)	sp gr	Derivative mp (°C)					
			Acid	Amide	4-Toluidide	3,5-Dinitrobenzoate	*N*-Benzylamide	Hydrazide
3-Methylbutyl methanoate (isoamyl formate; isopentyl formate; 3-methylbutyl formate)	124	0.894; 0.882			53	61	60	54
Ethyl Z-2-butenoate (ethyl isocrotonate)	126	0.918	15	102	132	93		
Butyl ethanoate (butyl acetate)	126	0.902; 0.881	17	82	153	64	61	77
1,1-Dimethylethyl 2-methylpropanoate (*tert*-butyl isobutyrate)	127			129	109	142	87	104
1-Methylethyl butanoate (isopropyl butyrate)	128	0.879_4^0; 0.865_4^{13}		116	75	123	38	44
Methyl pentanoate (methyl valerate)	130	0.910; 0.885		106	74	108	42	
Methyl methoxyethanoate (methyl methoxyacetate)	130	1.051		97		108		
Methyl chloroethanoate (methyl chloroacetate)	132	1.238	61; 53	121	162	108		
Ethyl methoxyethanoate (ethyl methoxyacetate)	132	1.012_4^{15}		97		93		
Pentyl methanoate (amyl formate)	132	0.902; 0.885			53	46	60	54
1-Ethylpropyl ethanoate (diethylcarbinyl acetate; 1-ethylpropyl acetate)	133	1.401	17	82	153	101	61	77
1-Methylbutyl ethanoate (methylpropylcarbinyl acetate; 1-methylbutyl acetate)	133	0.869_4^{18}	17	82	153	62	61	77
2-Propenyl 2-methylpropanoate (allyl isobutyrate)	134			129	109	50	87	104
Ethyl 3-methylbutanoate (ethyl isovalerate)	135	0.865		137	107	93	54	68
Propyl 2-methylpropanoate (propyl isobutyrate)	135	0.884_4^0; 0.864		129	109	74	87	104
Methyl 2-hydroxy-2-methylpropanoate (methyl α-hydroxy isobutyrate)	137		79		133	108		
Methyl 2-oxopropanoate (methyl pyruvate)	138	1.154	14	125; 145	109; 130	108		
2-Methylpropyl propanoate (isobutyl propionate)	138	0.888		81	126	87	44	40
Ethyl *E*-2-butenoate (ethyl crotonate)	138	0.9175_4^{20}	72	160	132	93	114	

(Continued)

TABLE AII.19 Esters (Liquids) *(Continued)*

Name of Compound	bp (°C)	sp gr	Derivative mp (°C)					
			Acid	Amide	4-Toluidide	3,5-Dinitrobenzoate	*N*-Benzylamide	Hydrazide
2-Propenyl butanoate (allyl butyrate)	142	0.902		116	75	50	38	44
3-Methylbutyl ethanoate (isoamyl acetate; isopentyl acetate)	142	0.884; 0.867	17	82	153	61	61	77
1-Methylethyl 3-methylbutanoate (isopropyl isovalerate)	142	0.854_4^{17}		137	107	123	54	68
Propyl butanoate (propyl butyrate)	144	0.893; 0.872		116	75	74	38	44
2-Methoxyethyl ethanoate (ethylene glycol monomethyl ether acetate; 2-methoxyethyl acetate)	144	1.0067_{20}^{20}; 1.088	17	82	153		61	77
Methyl bromoethanoate (methyl bromoacetate)	144	1.657_4^{19}	50	91		108		
2-Chloroethyl ethanoate (2-chloroethyl acetate)	145	1.178	17	82	153		61	77
Methyl (±)-2-hydroxypropanoate [methyl (±)-lactate]	145	1.090_4^{19}	17	79	107	108		
Ethyl chloroethanoate (ethyl chloroacetate)	145	1.158; 1.150	61; 52	121	162	93		
1,1-Dimethylethyl butanoate (*tert*-butyl butyrate)	146			116	75	142	38	44
Triethyl orthomethanoate (triethyl orthoformate)	146	0.897			53	93		
Ethyl pentanoate (ethyl valerate)	146	0.8765_4^{20}		106	74	93	42	
Ethyl 2-chloropropanoate (ethyl α-chloropropionate)	146	1.087		80	124	93		
Butyl propanoate (butyl propionate)	147	0.895; 0.875		81	126	64	44	40
Benzyl chloroethanoate (benzyl chloroacetate)	147	1.222_4^4	61; 52	121	162	113		
Methyl ethoxyethanoate (methyl ethoxyacetate)	148	1.011_4^{15}		82	32	108		
2-Methylpropyl 2-methylpropanoate (isobutyl isobutyrate)	149	0.875		129	109	87	87	104
Pentyl ethanoate (amyl acetate)	149	0.896; 0.875	17	82	153	46	61	77
Ethyl 2-hydroxy-2-methylpropanoate (ethyl α-hydroxyisobutyrate)	150		79		133	93		

(Continued)

TABLE AII.19 Esters (Liquids) *(Continued)*

Name of Compound	bp (°C)	sp gr	Derivative mp (°C)					
			Acid	Amide	4-Toluidide	3,5-Dinitrobenzoate	*N*-Benzylamide	Hydrazide
Methyl hydroxyethanoate (methyl glycolate; methyl hydroxyacetate)	151	1.168_4^{18}	80	120	143	108	104	
Methyl hexanoate (methyl caproate)	151	0.904; 0.885		101	75	123	53	
1-Methylethyl pentanoate (isopropyl valerate)	153	0.858		106	74	61	42	
Ethyl (±)-2-hydroxypropanoate [ethyl (±)-lactate]	155	1.031_4^{19}	18	79	107	93		
Ethyl 2-oxopropanoate (ethyl pyruvate)	155	1.080_4^{14}; 1.055	14	125; 145	109; 130	93		
Propyl 3-methylbutanoate (propyl isovalerate)	156	0.864_8^{17}		137	107	74	54	68
Hexyl methanoate (hexyl formate)	156	0.898_0^0; 0.879			53	58	60	54
2-Methylpropyl butanoate (isobutyl butyrate)	157	0.888; 0.862		116	75	87	38	44
2-Ethoxyethyl ethanoate (ethylene glycol monoethyl ether acetate; 2-ethoxyethyl acetate)	158	0.9749_{20}^{20}; 0.970	17	82	153	73	61	77
Ethyl dichloroethanoate (ethyl dichloroacetate)	158	1.282		98	153	93		
Ethyl bromoethanoate (ethyl bromoacetate)	159	1.506	50	91		93		
Ethyl hydroxyethanoate (ethyl glycolate; ethyl hydroxyacetate)	160	1.0869_4^{15}; 1.082	80	120	143	93	104	
3-Methylbutyl propanoate (isoamyl propionate)	160	0.888; 0.870; 0.859		81	126	61	44	40
Ethyl 2-bromopropanoate (ethyl α-bromopropionate)	162	1.329; 1.524	26	123	125	93		
Cyclohexyl methanoate (cyclohexyl formate)	163	1.010; 0.994			53	113	60	54
2-Bromoethyl ethanoate (2-bromoethyl acetate)	163	1.524	17	82	153		61	77
Propyl pentanoate (propyl valerate)	167	0.8888_4^0; 0.870		106	74	74	42	
Butyl butanoate (butyl butyrate)	167	0.888; 0.869		116	75	64	38	44
Ethyl hexanoate (ethyl caproate)	168	0.889; 0.871		101	75	93	53	
Ethyl trichloroethanoate (ethyl trichloroacetate)	168	1.369_4^{15}; 1.380	58	141	113	93		

(Continued)

TABLE AII.19 Esters (Liquids) *(Continued)*

Name of Compound	bp (°C)	sp gr	Derivative mp (°C)					
			Acid	Amide	4-Toluidide	3,5-Dinitrobenzoate	*N*-Benzylamide	Hydrazide
(±)-1-Methylethyl 2-hydroxypropanoate [isopropyl (±)-lactate]	168	0.998	18	79	107	123		
Pentyl propanoate (amyl propionate)	169	0.876; 0.881		81	126	46	44	40
3-Methylbutyl 2-methylpropanoate (isoamyl isobutyrate; isopentyl isobutyrate)	169	0.876_4^0		129	109	61	87	104
2-Methylpropyl 3-methylbutanoate (isobutyl isovalerate)	171	0.853		137	107	87	54	68
Methyl heptanoate (methyl enanthate)	174	0.898; 0.880		96	81	108		
1,2-Ethanediol dimethanoate (ethylene glycol diformate; 1,2-ethanediol formate)	174	1.193_4^0; 1.229			53	46	60	54
1-Methylpropyl pentanoate (*sec*-butyl valerate)	174	0.860_4^{20}		106	74	76	42	
Cyclohexyl ethanoate (cyclohexyl acetate)	175	0.972_4^{19}	17	82	153	113	61	77
Butyl chloroethanoate (butyl chloroacetate)	175	1.081_4^{15}	61; 52	121	62	64		
Furfuryl ethanoate (furfuryl acetate)	177	1.1176_{20}^{20}	17	82	153	81	61	77
Heptyl methanoate (heptyl formate)	178	0.878			53	47	60	54
Hexyl ethanoate (hexyl acetate)	178	0.873	17	82	153	58	61	77
3-Methylbutyl butanoate (isoamyl butyrate; isopentyl butyrate)	179	0.882; 0.864		116	75	61	38	44
Ethyl 3-bromopropanoate (ethyl β-bromopropionate)	179	1.425	63	111		93		
2-Methylpropyl pentanoate (isobutyl valerate)	179	0.8625		106	74	87	42	
2-Hydroxyethyl methanoate (ethylene glycol monoformate; 2-hydroxyethyl formate)	180	1.199_4^{15}			53	46	60	54
Methyl 2-furoate (methyl pyromucate)	181	1.1786_4^{21}	134	143	171	108		80
Dimethyl propanedioate (dimethyl malonate, methyl malonate)	182	1.160_4^{15}; 1.119	135	106 (mono)	156 (mono) 170 (di)	108 253 (di)	142	154
Methyl cyclohexanecarboxylate (methyl hexahydrobenzoate)	183	0.995_4^{15}; 0.990	31	186		108		

(Continued)

TABLE AII.19 Esters (Liquids) *(Continued)*

Name of Compound	bp (°C)	sp gr	Derivative mp (°C)					
			Acid	Amide	4-Toluidide	3,5-Dinitrobenzoate	*N*-Benzylamide	Hydrazide
Ethyl hexadecanoate (ethyl palmitate)	185		63	107	98	93	95	111
Diethyl ethanedioate (diethyl oxalate; ethyl oxalate)	186	1.082	190 (anhyd) 101 (dihyd)	219 (mono) 419 (di)	169 (mono) 268 (di)	93	223	243
Pentyl butanoate (amyl butyrate)	186	0.8832_0^0; 0.866		116	75	46	38	44
Ethyl 2-methyl-3-oxobutanoate (ethyl methylacetoacetate)	187	1.024_4^{15}; 1.012		73		93		
Butyl pentanoate (butyl valerate)	187	0.868		106	74	64	42	
Propyl hexanoate (propyl caproate)	187	0.8844_0^0; 0.867		101	75	74	53	
Butyl 2-hydroxypropanoate (butyl lactate)	188	0.984_{20}^{20}	18	79	107	64		
2-Hydroxyethyl ethanoate (ethylene glycol monoacetate; 2-hydroxyethyl acetate)	189		17	82	153	46	61	77
Ethyl heptanoate (ethyl enanthate)	189	0.888; 0.869		97	81	93		
Hexyl propanoate (hexyl propionate)	190	0.870		81	126	58	44	40
3-Methylbutyl 3-methylbutanoate (isoamyl isovalerate; isopentyl isovalerate)	190	0.870		137	107	61	54	68
Methyl 2-ethyl-3-oxobutanoate (methyl ethylacetoacetate)	190	0.989		96		108		
1,2-Ethanediol diethanoate (ethylene glycol diacetate; 1,2-ethanediol diacetate)	190	1.128; 1.104	17	82	153	46	61	77
Heptyl ethanoate (heptyl acetate)	192	0.8891; 0.865	17	82	153	47	61	77
Cyclohexyl propanoate (cyclohexyl propionate)	193	0.9718_4^0		81	126	113	44	40
Di-(1-methylethyl) ethanedioate (diisopropyl oxalate; isopropyl oxalate)	194	1.010_4^{18}; 0.995	190 (anhyd) 101 (dihyd)	219 (mono) 419 (di)	169 (mono) 268 (di)	123	223	243
1-Methylheptyl ethanoate (*sec*-octyl acetate)	195	0.861_4^{19}	17	82	153	32	61	77
Methyl octanoate (methyl caprylate)	195	0.894; 0.878	16	57	70	108		

(Continued)

TABLE AII.19 Esters (Liquids) *(Continued)*

Name of Compound	bp (°C)	sp gr	Derivative mp (°C)					
			Acid	Amide	4-Toluidide	3,5-Dinitrobenzoate	*N*-Benzylamide	Hydrazide
2-Tetrahydrofurfuryl ethanoate (α-tetrahydrofurfuryl acetate)	195	1.0624_4^{25}	17	82	153	84	61	77
Dimethyl butenedioate (dimethyl succinate; methyl succinate)	196	1.120_4^{18}	185	157 (mono) 260d (di)	180 (mono) 256 (di)	108	206	168
Methyl 4-oxopentanoate (methyl levulinate)	196	1.068; 1.049	35	108	109	108		
Ethyl cyclohexanecarboxylate (ethyl hexahydrobenzoate)	196	0.967_4^{15}; 0.962	31	186		93		
Diethyl methylpropanedioate (diethyl methylmalonate; ethyl methylmalonate)	196	1.019_4^{15}	138	217	145 (mono) 228, 214 (di)	93 93		
Phenyl ethanoate (phenyl acetate)	197	1.081_4^{15}	17	82	153	146	61	77
Ethyl furoate (ethyl pyromucate)	197	1.117	134	143	171	93		80
Ethyl 2-ethyl-3-oxobutanoate (ethyl ethylacetoacetate)	198	0.972; 0.986		96		93		
Octyl methanoate (octyl formate)	199	0.8744			53	62	60	54
2-Ethyl-1-hexyl ethanoate (2-ethyl-1-hexyl acetate)	199	0.8733_{20}^{20}	17	82	153		61	77
Methyl benzoate	199	1.103; 1.089	122	130	158	108	106	112
Diethyl propanedioate (diethyl malonate; ethyl malonate)	199	1.077; 1.055	135	110 (mono) 170 (di)	156 (mono) 253 (di)	93	142	154
Methyl cyanoethanoate (methyl cyanoacetate)	200	1.0962_4^{25}	66	120		108	124	
Methyl *E*-2-methylbutenedioate (dimethyl mesaconate; methyl mesaconate)	203	1.0914; 1.120	205	222 (α) 174 (β) (mono) 177 (di)	196 (mono) 212 (di)	108		
Benzyl methanoate (benzyl formate)	203	1.081_4^{23}			53	133	60	54
Ethenyl benzoate (vinyl benzoate)	203	1.065	122	130	158		106	112
Cyclohexyl 2-methylpropanoate (cyclohexyl isobutyrate)	204	0.949_4^0		129	109	113	87	104

(Continued)

TABLE AII.19 Esters (Liquids) *(Continued)*

Name of Compound	bp (°C)	sp gr	Derivative mp (°C)					
			Acid	Amide	4-Toluidide	3,5-Dinitrobenzoate	*N*-Benzylamide	Hydrazide
Diethyl Z-butenedioate (diethyl maleate; ethyl maleate)	204	1.145_4^{15}	137	173 153 (mono) 181 (di)	142 (di)	108	150	
Ethyl 4-oxopentanoate (ethyl levulinate)	206	1.016	35	108	109	93		
Pentyl pentanoate (amyl valerate)	207	0.881_4^0		106	74	46	42	
2-Tetrahydrofurfuryl propanoate (α-tetrahydrofurfuryl propionate)	207			81	126	84	44	40
Butyl hexanoate (butyl caproate)	208	0.8653		101	75	64	53	
Hexyl butanoate (hexyl butyrate)	208	0.8652		116	75	58	38	44
2-Methylphenyl ethanoate (*o*-tolyl acetate; *o*-cresyl acetate)	208	1.048_4^{19}	17	82	153	135	61	77
Propyl heptanoate (propyl ethanthate)	208	0.866		97	81	74		
Ethyl octanoate (ethyl caprylate)	208	0.887	16	110	70	93		
Dimethyl methylenebutanedioate (dimethyl itaconate; methyl itaconate; dimethyl methylene-succinate; methyl methylenesuccinate)	208		165	192		108		
2-Methylpropyl heptanoate (isobutyl enanthate)	209	0.859		97	81	87		
1-Methylethyl 4-oxopentanoate (isopropyl levulinate)	209	0.987	34	108	109	123		
1,3-Propanediol diethanoate (trimethylene glycol diacetate; 1,3-diacetoxypropane; 1,3-propanediol diacetate)	210	1.070_4^{19}	17	82	153	178	61	77
Octyl ethanoate (octyl acetate)	210	0.885_4^0	17	82	153	62	61	77
Heptyl propanoate (heptyl propionate)	210	0.868		81	126	47	44	40
Dimethyl Z-methylbutenedioate (dimethyl citraconate; dimethyl *cis*-methylmaleate)	211	1.115	93	101		108		177
Propyl 2-furoate (propyl pyromucate)	211	1.0745_4^{26}	134	143	171	74		80
1,2-Ethanediol dipropanoate (ethylene glycol dipropionate)	211	1.045_4^{25}; 1.054_{15}^{15}		81	126	46	44	40

(Continued)

TABLE AII.19 Esters (Liquids) *(Continued)*

Name of Compound	bp (°C)	sp gr	Derivative mp (°C)					
			Acid	Amide	4-Toluidide	3,5-Dinitrobenzoate	*N*-Benzylamide	Hydrazide
Phenyl propanoate (phenyl propionate)	211	1.054_4^{15}		81	126	146	44	40
3-Methylphenyl ethanoate (*m*-tolyl acetate; *m*-cresyl acetate)	212	1.049	17	82	153	165	61	77
Cyclohexyl butanoate (cyclohexyl butyrate)	212	0.957_4^0		116	75	113	38	44
Ethyl benzoate	212	1.066; 1.047	122	130	158	93	106	112
4-Methylphenyl ethanoate (*p*-tolyl acetate; *p*-cresyl acetate)	213	1.050_4^{23}	17	82	153	189	61	77
Dipropyl ethanedioate (dipropyl oxalate; propyl oxalate)	214	1.038;	190 (anhyd)	219 (mono)	169 (mono)	74	223	243
		1.017	101 (dihyd)	419d (di)	268 (di)			
Methyl nonanoate (methyl pelargonate)	214	0.892		99	84	108		
Dimethyl pentanedioate (dimethyl glutarate; methyl glutarate)	214	1.0874	98	175 (di)	218 (di)	108	170	176
Ethyl 2,4-dioxopentanoate (ethyl acetopyruvate; ethyl aceto-2-oxopropanoate)	215	1.125	101	132		93		
Methyl 2-methylbenzoate (methyl *o*-toluate)	215	1.073_4^{15}; 1.061	108	143	144	108		124
2,6-Dimethylphenyl ethanoate (2,6-dimethylphenyl acetate)	216		17	82	153	159	61	77
Benzyl ethanoate (benzyl acetate)	217	1.062_4^{15}; 1.055	17	82	153	113	61	77
Diethyl butanedioate (diethyl succinate; ethyl succinate)	217	1.049_4^{15};	185	157 (mono)	180 (mono)	93	206	168
		1.0398		260d (di)	260 (di)			
Diethyl *E*-butenedioate (diethyl fumarate; ethyl fumarate)	218	1.047_4^{25};	287;	270,	234 (mono)		205	
		1.052	235;	302 (mono)	314 (di)			
			200	266d (di)				
2-Acetoxy-2′-ethoxydiethyl ether (diethylene glycol monoethyl ether acetate)	218	1.0114_{20}^{20}	17	82	153			
1-Methylethyl benzoate (isopropyl benzoate)	219	1.010_4^{24}	122	130	158	123	106	112

(Continued)

TABLE AII.19 Esters (Liquids) *(Continued)*

Name of Compound	bp (°C)	sp gr	Derivative mp (°C)					
			Acid	Amide	4-Toluidide	3,5-Dinitrobenzoate	*N*-Benzylamide	Hydrazide
Methyl phenylethanoate (methyl phenylacetate)	220	1.044_4^{16}; 1.068	77	156	136	108	122	
L-1,5-Dimethyl-1-ethenyl-4-hexenyl ethanoate (L-3,7-dimethyl-1,6-octadien-3-ol acetate; L-linalyl acetate; L-1,5-dimethyl-1-ethenyl-4-hexenyl acetate)	220	0.895	17	82	153		61	77
Methyl 3-methylbenzoate (methyl *m*-toluate)	221	1.066_4^{15}	113	97	118	108	75	97
Propyl 4-oxopentanoate (propyl levulinate)	221	0.9895_4^{20}	35	108	109	74		
Methyl 4-methylbenzoate (methyl *p*-toluate)	223		180	160	165	108	133	117
Methyl 2-hydroxybenzoate (methyl salicylate)	224	1.184_4^{20}	158	142	156	108	136	
Diethyl Z-butenedioate (diethyl maleate; ethyl maleate)	225	1.074_4^{15}; 1.066	137	173, 153 (mono) 181 (di)	142 (di)	93	150	
Diethyl (±)-2-hydroxypropanedioate [diethyl (±)-tartronate; ethyl (±)-tartronate; diethyl hydroxymalonate; ethyl hydroxymalonate]	225	1.152_4^{15}	158	198 (di) 196		93		
1-Methylpropyl 4-oxopentanoate (*sec*-butyl levulinate)	226	0.967	35	108	109	76		
Heptyl butanoate (heptyl butyrate)	226	0.8637		116	75	47	38	44
2,4-Dimethylphenyl ethanoate (2,4-dimethylphenyl acetate)	226	1.030_5^{15}	17	82	153	166	61	77
Pentyl hexanoate (amyl caproate)	226	0.863		101	75	46	53	
Butyl heptanoate (butyl enanthate)	226	0.864		97	81	64		
Hexyl pentanoate (hexyl valerate)	226	0.863		106	74	58	42	
Propyl octanoate (propyl caprylate)	226	0.8659	16	110	57	74		
Methyl 3-(2-furyl)propenoate [methyl β-(2-furyl)acrylate]	227			169		108		
Ethyl 2-methylbenzoate (ethyl *o*-toluate)	227	1.033_4^{21}	108	143	144	93		124

(Continued)

TABLE AII.19 Esters (Liquids) *(Continued)*

Name of Compound	bp (°C)	sp gr	Derivative mp (°C)					
			Acid	Amide	4-Toluidide	3,5-Dinitrobenzoate	*N*-Benzylamide	Hydrazide
Ethyl nonanoate (ethyl pelargonate)	227	0.866_4^{17}		99	84	93		
L-Methyl ethanoate (L-methyl acetate)	227	0.9185_4^{20}	17	82	153	153	61	77
Octyl propanoate (octyl propionate)	228	0.866		81	126	62	44	40
Diethyl methylenebutanedioate (diethyl itaconate; ethyl itaconate; diethyl methylenesuccinate; ethyl methylenesuccinate)	228	1.047	165	192 (di)		93		
Ethyl phenylethanoate (ethyl phenylacetate)	229	1.031	77	156	136	93	122	
Diethyl *E*-methylbutenedioate (diethyl mesaconate; ethyl mesaconate; diethyl methylfumarate; ethyl methylfumarate)	229	1.0453	205	222 (α) 174 (β) (mono) 177 (di)	196 (α) (mono) 212 (di)	93		
Di-(2-methylpropyl) ethanedioate (diisobutyl oxalate; isobutyl oxalate)	229	1.002_4^{14}; 0.974	190 (anhyd) 101 (dihyd)	219 (mono) 419d (di)	169 (mono) 268 (di)		223	243
2-Propenyl benzoate (allyl benzoate)	230	1.067_4^4; 1.052	122	130	158	50	106	112
2-Methylpropyl 4-oxopentanoate (isobutyl levulinate)	231	0.9677	35	108	109	87		
Propyl benzoate	231	1.025_4^{15}	122	130	158	74	106	112
Diethyl Z-methylbutenedioate (diethyl citraconate; ethyl citraconate; diethyl methylmaleate)	231	1.049	93	101		93		177
Methyl 3-chlorobenzoate	231		158	134		108		158
Methyl decanoate (methyl caprate)	232	0.876_4^{18}	32	108	78	108		
2-Phenylethyl ethanoate (β-phenylethyl acetate)	232	1.057_4^{22}	17	82	153	108	61	77
Ethyl 3-(2-furyl)propenoate [ethyl β-(2-furyl)acrylate]	232	1.089_4^{15}	141	169		93		
Diethyl pentanedioate (diethyl glutarate; ethyl glutarate)	234	1.022; 1.424	98	176 (di)	218 (di)	93	170	176
Ethyl 3-methylbenzoate (ethyl *m*-toluate)	234	1.0265_4^{21}	113	97	118	93	75	97
Ethyl 2-hydroxybenzoate (ethyl salicylate)	234	1.147_4^4; 1.125	158	142	156	93	136	

(Continued)

TABLE AII.19 Esters (Liquids) *(Continued)*

Name of Compound	bp (°C)	sp gr	Derivative mp (°C)					
			Acid	Amide	4-Toluidide	3,5-Dinitrobenzoate	*N*-Benzylamide	Hydrazide
Methyl 2-chlorobenzoate	234		144	142; 202	131 131	108 108		110 110
Ethyl 4-methylbenzoate (ethyl *p*-toluate)	235	1.027_4^{18}	180	160	165	93	133	117
Diethyl 2-bromopropanedioate (diethyl bromomalonate; ethyl bromomalonate)	235	1.426_{15}^{15}	113	181 (di)	217 (di)	93		
3,5-Dimethylphenyl ethanoate (3,5-dimethylphenyl acetate)	235		17	82	153	182	61	77
2,4,6-Trimethylphenyl ethanoate (mesityl acetate; 2,4,6-trimethylphenyl acetate)	236		17	82	153		61	77
1,2-Ethanediol dibutanoate (ethylene glycol dibutyrate)	237	1.0005		116	75	46	38	44
2,5-Dimethylphenyl ethanoate (2,5-dimethylphenyl acetate)	237	1.0264_4^{15}	17	82	153	137	61	77
Butyl 4-oxopentanoate (butyl levulinate)	238	0.9735	35	108	109	64		
Methyl 3-phenylpropanoate (methyl hydrocinnamate; methyl β-phenylpropionate)	239	1.0455_4^0	48	105; 82	135	108	85	
Diethyl 2-butylpropanedioate (diethyl butylmalonate; ethyl butylmalonate)	240	1.425		200 (di)		93		
Benzyl butanoate (benzyl butyrate)	240	1.033_4^{16}		116	75	113	38	44
2-Methoxyphenyl ethanoate (guaiacol acetate; *o*-methoxyphenyl acetate)	240	1.129_4^{25}	17	82	153	141	61	77
1-Methylethyl 2-hydroxybenzoate (isopropyl salicylate)	242	1.095_4^{19}; 1.073	158	142	156	123	136	
Dimethyl L-hydroxybutanedioate (dimethyl L-malate; methyl L-malate; dimethyl hydroxysuccinate; methyl hydroxysuccinate)	242	1.233	101	157 (di)	207 (di)	108	157	178
2-Methylpropyl benzoate (isobutyl benzoate)	242	1.002_4^{15}	122	130	158	87	106	112
Methyl 2-bromobenzoate	244		150	155		108		
Octyl butanoate (octyl butyrate)	244	0.863		116	75	62	38	44
Ethyl decanoate (ethyl caprate)	245	0.868_4^{18}	32	108	78	93		
Diethyl hexanedioate (diethyl adipate; ethyl adipate)	245	1.009	154	130 (mono) 220 (di)	241	93	189	171

(Continued)

TABLE AII.19 Esters (Liquids) *(Continued)*

Name of Compound	bp (°C)	sp gr	Derivative mp (°C)					
			Acid	Amide	4-Toluidide	3,5-Dinitrobenzoate	*N*-Benzylamide	Hydrazide
Methyl phenoxyethanoate (methyl phenoxyacetate)	245	1.150_4^{17}	99	102		108		
5-Methyl-2-(1-methylethyl)-phenyl ethanoate (thymyl acetate; 2-isopropyl-5-methylphenyl acetate)	245	1.009	17	82	153	103	61	77
Butyl octanoate (butyl caprylate)	245	0.8628	16	110	70	64		
Heptyl pentanoate (heptyl valerate)	245	0.8622		106	74	47	42	
Pentyl heptanoate (pentyl enanthate)	245	0.8623		97	81	46		
Hexyl decanoate (hexyl caproate)	245	0.8622	32	101	75	58		
Dibutyl ethanedioate (dibutyl oxalate; butyl oxalate)	246	1.010; 0.987	190 (anhyd) 101 (dihyd)	219 (mono) 419d (di)	169 (mono) 268 (di)	64	223	243
2-Acetoxy-2′-butyldiethyl ether (diethylene glycol monobutyl ether acetate)	246	0.9871_{20}^{20}	17	82	153			
2,4,5-Trimethylphenyl ethanoate (pseudomenyl acetate; 2,4,5-trimethylphenyl acetate)	246		17	82		153	61	77
2-Methylpropyl phenylethanoate (isobutyl phenylacetate)	247	0.999_4^{18}	77	156	136	87	122	
Ethyl 3-phenylpropanoate (ethyl hydrocinnamate; ethyl β-phenylpropionate)	247	1.0147	49	105; 82	135	93	85	
Dipropyl butenedioate (dipropyl succinate; propyl succinate)	248	1.016_4^4	185	157 (mono) 260d (di)	180 (mono) 256 (di)	74	206	168
Methyl 2-methoxybenzoate	248	1.157_4^{19}	101	129		108		
Methyl undecanylenate (methyl hendecanoate)	248	0.889_4^{15}	25	87		108		
3-Methylbutyl 4-oxopentanoate (isobutyl levulinate)	249	0.9614	35	108	109	62		
Butyl benzoate	250	1.000; 1.005	122	130	158	64	106	112
Propyl 2-hydroxybenzoate (propyl salicylate)	251	1.098_4^{15}	158	142	156	74	136	
2,2′-Diacetoxy diethyl ether (diethylene glycol diacetate)	251	1.108_{15}^{15}		82	153	149		
Ethyl phenoxyethanoate (ethyl phenoxyacetate)	251	1.104_4^{17}	99	102		93		

(Continued)

TABLE AII.19 Esters (Liquids) *(Continued)*

Name of Compound	bp (°C)	sp gr	Derivative mp (°C)					
			Acid	Amide	4-Toluidide	3,5-Dinitrobenzoate	*N*-Benzylamide	Hydrazide
Diethyl L-hydroxybutanedioate (diethyl L-malate; ethyl L-malate; diethyl hydroxysuccinate; ethyl hydroxysuccinate)	253	1.129	101	157 (di)	207 (di)	108	157	178
Pentyl 4-oxopentanoate (amyl levulinate)	253	0.9614	35	108	109	46		
Ethyl (±)-2-hydroxy-2-phenylethanoate [ethyl (±)-mandelate; ethyl (±)-2-hydroxy-2-phenylacetate]	254		120	134	172	93		
Butyl phenylethanoate (butyl phenylacetate)	254	0.996_4^{18}	77	156	136	64	122	
2-Methoxyethyl benzoate	255	1.0891_4^{25}	122	130	158		106	112
Methyl 4-methoxybenzoate (methyl *p*-anisate)	255		185	167	186	108	132	
Diethyl heptanedioate (diethyl pimelate; ethyl pimelate)	255	0.9945_4^{20}; 0.9929	105	175 (di)	206 (di)	93	154	182
Ethyl benzoylmethanoate (ethyl benzoylformate)	257	1.222_4^{25}	66	91		93		
1,2,3-Propanetriol triethanoate (glyceryl triacetate; 1,2,3-propanetriol triacetate; triacetin)	258	1.161_4^{15}	17	82	153		61	77
Pentyl octanoate (amyl caprylate)	260	0.8613	16	110	70	46		
2-Ethoxyethyl benzoate	261	1.058_{25}^{25}	122	130	158	78	106	112
Hexyl heptanoate (hexyl enanthate)	261	0.8611		97	81	58		
Heptyl hexanoate (heptyl caproate)	261	0.8611		101	75	47	53	
Ethyl 2-methoxybenzoate	261	1.112	101	129		93		
Octyl pentanoate (octyl valerate)	261	0.8615		106	74	62	42	
Methyl *E*-3-phenyl-2-propenoate (methyl cinnamate)	261		133	148	168	108	225	
2-Methylpropyl 2-hydroxybenzoate (isobutyl salicylate)	262	1.0639	158	142	156	87	136	
3-Methylbutyl benzoate (isoamyl benzoate; isopentyl benzoate)	262	1.004; 0.986	122	130	158	61	106	112
Ethyl 4-bromobenzoate	262					92		164

(Continued)

TABLE AII.19 Esters (Liquids) *(Continued)*

Name of Compound	bp (°C)	sp gr	Derivative mp (°C)					
			Acid	Amide	4-Toluidide	3,5-Dinitrobenzoate	*N*-Benzylamide	Hydrazide
D-Dimethyl 1,2,2-trimethylcyclopentane-1,3-dicarboxylate (dimethyl D-camphor; methyl D-camphor)	263	1.0747	188	176, 183 (mono) 193 (di)	214 (α) 196 (β)	108		
Ethyl undecylenate (ethyl hendecylenate)	264	0.8827_{15}^{15}		87		93		
Di-(2-methylpropyl) butanedioate (diisobutyl succinate; isobutyl succinate)	265	0.974	185	157 (mono) 260d (di)	180 (mono) 260 (di)	87	206	185
Di-(3-methylbutyl) ethanedioate (diisoamyl oxalate; isoamyl oxalate)	268	0.968_4^{11}; 0.961	190 (anhyd) 101 (dihyd)	219 (mono) 419d (di)	169 (mono) 268 (di)	61	223	243
Dimethyl octanedioate (dimethyl suberate; methyl suberate)	268	1.0198	144	127 (mono) 217 (di)	219 (di)	108		
Methyl dodecanoate (methyl laurate)	268	0.869_4^{19}	44	100	87	108	83	105
Ethyl 4-methoxybenzoate (ethyl *p*-anisate)	269	1.119_4^4; 1.1038	185	167	186	93	132	
Ethyl dodecanoate (ethyl laurate)	269	0.867_4^{13}	44	100	87	93	83	105
Ethyl *E*-3-phenyl-2-propenoate (ethyl cinnamate)	271	1.050	133	148	168	93	225	
Butyl 2-hydroxybenzoate (butyl salicylate)	272	1.074_4^{19}	158	142	156	64	136	
Dibutyl butanedioate (dibutyl succinate; butyl succinate)	274	0.976	185	157 (mono) 260d (di)	180 (mono) 260 (di)	64	206	168
Di-(1-Methylethyl) D-2,3-dihydroxybutanedioate (diisopropyl D-tartarate; isopropyl D-tartarate)	275			172 (mono) 196d (di)		123		
Di-(1-Methylethyl) (±)-2,3-dihydroxybutanedioate [diisopropyl (±)-tartarate; isopropyl (±)-tartarate]	275	1.1274	171	226		123	199	
Ethyl 4-ethoxybenzoate	275	1.076_4^{21}	170	202		93		
Octyl hexanoate (octyl caproate)	275	0.8603		101	75	62	53	
Ethyl 2-nitrobenzoate	275		146	176		93		
Heptyl heptanoate (heptyl enanthate)	277	0.8604		96	81	47		
Hexyl octanoate (heptyl caproate)	277	0.8603	16	110	70	58		
3-Methylbutyl 2-hydroxybenzoate (isoamyl salicylate; isopentyl salicylate)	278	1.065_4^{15}; 1.0535	158	143	156	61	136	

(Continued)

TABLE AII.19 Esters (Liquids) *(Continued)*

Name of Compound	bp (°C)	sp gr	Derivative mp (°C)					
			Acid	Amide	4-Toluidide	3,5-Dinitrobenzoate	*N*-Benzylamide	Hydrazide
2,4-Dihydroxybenzoic acid diethanoate (resorcinol diacetate; 2,4-dihydroxybenzoic acid diacetate)	278	1.180_4^{19}	17	82	153	201 (di)	61	77
Diethyl D-2,3-dihydroxybutanedioate (diethyl D-tartarate; ethyl D-tartarate)	280	1.2028		172 (mono) 196d (di)		93		
Diethyl octanedioate (diethyl suberate; ethyl suberate)	282	0.9822_4^{20}; 1.9807	144	127 (mono) 217 (di)	219 (di)	93		
2,4-Dihydroxybenzoic acid monoethanoate (resorcinol monoacetate; 2,4-dihydroxybenzoic acid monoacetate)	283		17	82	153	201 (di)	61	77
Dimethyl 1,2-benzenedicarboxylate (dimethyl phthalate; methyl phthalate)	283	1.196_4^{19}; 1.191	206	149 (mono) 220 (di)	150, 165 (mono) 201 (di)	108		
Ethyl 3,4-methylenedioxybenzoate (ethyl piperonylate)	286			169		93		
Diethyl 1,3-benzenedicarboxylate (diethyl isophthalate; ethyl isophthalate)	286	1.121	348	280 (mono) 280 (di)		93		
Dipropyl (±)-2,3-dihydroxybutanedioate [dipropyl (±)-tartarate; propyl (±)-tartarate]	286		171	226		74	199	
D-Diethyl 1,2,2-trimethylcyclopentane-1,3-dicarboxylate (diethyl D-camphor; ethyl D-camphor)	286	1.0298	188	176, 183 (mono) 193 (di)	214 (α) 196 (β)	93		
Dimethyl decanedioate (dimethyl sebacate; methyl sebacate)	286		133	170 (mono) 210 (di)	201 (di)	108	167	
1,2,3-Propanetriol tripropanoate (glyceryl tripropionate)	289	1.083_4^{19}	16	81	126		44	40
Heptyl octanoate (heptyl caprylate)	291	0.859		110	70	47		

(Continued)

TABLE AII.19 Esters (Liquids) *(Continued)*

Name of Compound	bp (°C)	sp gr	Derivative mp (°C)					
			Acid	Amide	4-Toluidide	3,5-Dinitrobenzoate	*N*-Benzylamide	Hydrazide
Octyl heptanoate (octyl enanthate)	291	0.860		97	81	62		
Diethyl nonanedioate (diethyl azelate; ethyl azelate)	291	0.9766_0^{15}; 0.973	107	95 (mono) 175 (di)	202 (di)	93		
Triethyl 2-hydroxy-1,2,3-tripropanecarboxylate (triethyl citrate)	294	1.137	153 (anhyd) 100 (hyd)	215 (tri)	189 (tri)	93	170	
Ethyl 3-nitrobenzoate	296		141	190		93	101	
Dipropyl D-2,3-dihydroxybutanedioate (dipropyl D-tartarate; propyl D-tartarate)	297	1.139		172 (mono) 196d (di)		74		
Di-(3-methylbutyl) butanedioate (diisoamyl succinate; isoamyl succinate)	297	0.961_4^{13}	185	157 (mono) 260d (di)	180 (mono) 260 (di)	61	206	168
Diethyl 1,2-benzenedicarboxylate (diethyl phthalate; ethyl phthalate)	298	1.117	206	149 (mono) 220 (di)	150, 165 (mono) 201 (di)	93		
Diethyl 2-benzylpropanoate (diethyl benzylmalonate; ethyl benzylmalonate)	300	1.077_4^{15}	117	225		93		
Methyl 2-aminobenzoate (methyl anthranilate)	300		146	109	151	93		
2-Tetrahydrofurfuryl benzoate (α-tetrahydrofurfuryl benzoate)	302	1.137_0^{20}	122	130	158	84	106	112
Diethyl 1,4-benzenedicarboxylate (diethyl terephthalate; ethyl terephthalate)	302	1.065_4^{19}		>225		93		
Di-(1-methylethyl)-1,2-benzenedicarboxylate (diisopropyl phthalate; isopropyl phthalate)	302	1.065_4^{19}	206	149 (mono) 220 (di)	150, 165 (mono) 201 (di)	123		
Ethyl 2-naphthoate	304			195	192	93		
Ethyl tetradecanoate (ethyl myristate)	306	0.865_4^{19}; 0.857_4^{25}	58	103	93	93	90	
Octyl octanoate (octyl caprylate)	307	0.859		110	70	62		

(Continued)

TABLE AII.19 Esters (Liquids) *(Continued)*

Name of Compound	bp (°C)	sp gr	Derivative mp (°C)					
			Acid	Amide	4-Toluidide	3,5-Dinitrobenzoate	*N*-Benzylamide	Hydrazide
Diethyl decanedioate (diethyl sebacate; ethyl sebacate)	307	0.965_4^{16}	133	170 (mono) 210 (di)	201 (di)	93	167	
2-Methylphenyl benzoate (*o*-tolyl benzoate)	307	1.114_4^{19}	122	130	158	138	106	112
Ethyl 1-naphthoate	309	1.127_{15}^{15}	162	205		93		
1,2,3-Propanetriol tributanoate (glyceryl tributyrate)	318	1.033_4^{17}		116	75		38	44
Dibutyl (±)-2,3-dihydroxybutanedioate [dibutyl (±)-tartarate; butyl (±)-tartarate]	320	1.0879_4^{18}	206 (anhyd) 204 (hyd)	226 (di)		64		
Benzyl 2-hydroxybenzoate (benzyl salicylate)	320		158	142	156	113	136	
Benzyl benzoate	323	1.114_4^{18}	122	130	158	113	106	112
Methyl tetradecanoate (methyl myristate)	323; 295	0.873_4^{19}	58	103	93	108	90	
Dibutyl 1,2-benzenedicarboxylate (dibutyl phthalate; butyl phthalate)	340	1.050_4^{19}	206	149 (mono) 220 (di)	150, 165 (mono) 201 (di)	64		
Dibutyl decanedioate (dibutyl sebacate; butyl sebacate)	345	0.9329_4^{15}	133	170 (mono) 210 (di)	201 (di)	64	167	
Di-(3-methylbutyl)-1,2-benzenedicarboxylate (diisoamyl phthalate; isoamyl phthalate)	349	1.024_4^{17}	206	149 (mono) 220 (di)	150, 165 (mono) 201 (di)	61		

TABLE AII.20 Esters (Solids)

Name of Compound	mp (°C)	Derivative mp (°C)					
		Acid	Amide	4-Toluidide	3,5-Dinitrobenzoate	*N*-Benzylamide	Hydrazide
Methyl dodecanoate (methyl laurate)	5	44	100	87	108	83	105
Ethyl 4-methoxybenzoate (ethyl *p*-anisate)	7	185	167	186	93	132	
Ethyl tetradecanoate (ethyl myristate)	11	58	103	93	93	90	
Diethyl D-2,3-dihydroxybutanedioate (diethyl D-tartarate; ethyl D-tartarate)	17		172 (mono) 196d (di)		93		
Dimethyl butanedioate (dimethyl succinate; methyl succinate)	19	185	157 (mono) 260 (di)	180 (mono) 260 (di)	108	206	168
Methyl tetradecanoate (methyl myristate)	19	58	103	93	108	90	
Ethyl 3,4-methylenedioxybenzoate (ethyl piperonylate)	19	229	169		93		
Diethyl D-2,3-dihydroxybutanedioate (diethyl D-tartarate; ethyl D-tartarate)	19		172 (mono) 196 (di)		93		
Phenyl propanoate (phenyl propionate)	20		81	126	146	44	40
Ethyl heptadecanoate (ethyl margarate)	21		108		93		
Methyl 3-chlorobenzoate	21	158	134		108		158
Benzyl benzoate	21	122	130	158	113	106	112
Dibutyl D-2,3-dihydroxybutanedioate (dibutyl D-tartarate; butyl D-tartarate)	22		172 (mono) 196 (di)		64		
3,4-Dimethylphenyl ethanoate (3,4-dimethyldiphenyl acetate)	22	17	82	153	182	61	77
3-Methylbutyl octadecanoate (isoamyl stearate; isopentyl stearate)	23	70	109	102	61	97	
Hexadecyl ethanoate (cetyl acetate; hexadecyl acetate)	24; 19	17	82	153	66	61	77
Ethyl hexadecanoate (ethyl palmitate)	24; 19	63	107	98	93	95	111
Methyl 2-aminobenzoate (methyl anthranilate)	24	146	109	151	93		
Dipropyl (±)-2,3-dihydroxybutanedioate [dipropyl (±)-tartarate; propyl (±)-tartarate]	25		226		74		
Methyl 3-(2-furyl)propenoate [methyl β-(2-furyl)acrylate]	27		169		108		

(Continued)

TABLE AII.20 Esters (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)					
		Acid	Amide	4-Toluidide	3,5-Dinitrobenzoate	*N*-Benzylamide	Hydrazide
Dimethyl decanedioate (dimethyl sebacate; methyl sebacate)	28	133	170 (mono) 210 (di)	201 (di)	108	167	
Butyl octadecanoate (butyl stearate)	28	70	109	102	64	97	
2-Methylpropyl octadecanoate (isobutyl stearate)	29; 23	70	109	102	87	97	
Methyl heptadecanoate (methyl margarate)	29		108		108		
Methyl hexadecanoate (methyl palmitate)	30	63	107	98	108	95	111
Pentyl octadecanoate (amyl stearate)	30	70	109	102	136	97	
Ethyl 2-nitrobenzoate	30	147	176		93		
Octadecyl ethanoate (octadecyl acetate)	32	17	82	153	66	61	77
Ethyl 2-naphthoate	32		195	192	93		
Methyl 3-bromobenzoate	32	155	155		108		
Methyl 4-methylbenzoate (methyl *p*-toluate)	33	180	160	165	108	133	117
5-Methyl-2-(1-methylethyl)phenyl benzoate (thymyl benzoate; 2-isopropyl-5-methylphenyl benzoate)	33	122	130	158	103	106	112
Di-(2-ethoxyethyl) 1,2-benzenedicarboxylate [di-(β-ethoxyethyl) phthalate]	33	208	149 (mono) 220 (di)	150, 165 (mono) 201 (di)	75	179	
Ethyl octadecanoate (ethyl stearate)	34	70	109	102	93	97	
Di-(1-methylethyl) (±)-2,3-dihydroxybutanedioate [diisopropyl (±)-tartarate; isopropyl (±)-tartarate]	34		226		123		
Ethyl furoate (ethyl pyromucate)	34	134	143	171	93		80
Diethyl 4-nitro-1,2-benzenedicarboxylate (diethyl 4-nitrophthalate; ethyl 4-nitrophthalate)	34	165	200	172 (mono)	93		
Ethyl 2,2-diphenyl-2-hydroxyethanoate (ethyl benzilate; ethyl 2,2-diphenyl-2-hydroxyacetate)	34		155	190	93		
2,4,5-Trimethylphenyl ethanoate (pseudocumenyl acetate; 2,4,5-trimethylphenyl acetate)	35	17	82	153		61	77

(Continued)

TABLE AII.20 Esters (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)					
		Acid	Amide	4-Toluidide	3,5-Dinitrobenzoate	*N*-Benzylamide	Hydrazide
Methyl 3-phenyl-2-propenoate (methyl cinnamate)	36	133	148	168	108	225	
Ethyl (±)-2-hydroxy-2-phenylethanoate [ethyl (±)-mandelate; ethyl (±)-2-hydroxy-2-phenylacetate]	37	120	134	172	93		
Dimethyl methylenebutanedioate (dimethyl itaconate; methyl itaconate; dimethyl methylenesuccinate; methyl methylenesuccinate)	38	165	192 (di)		108		
Dimethyl decanedioate (dimethyl sebacate; methyl sebacate)	38	133	170 (mono) 210 (di)	201 (di)	108	167	
Methyl octadecanoate (methyl stearate)	39	70	109	102	108	97	
Benzyl 3-phenyl-2-propenoate (benzyl cinnamate)	39	133	147	168	113	225	
Methyl dibenzylethanoate (methyl dibenzylacetate)	41		129	175	108		
Phenyl 2-hydroxybenzoate (phenyl salicylate; salol)	42	158	142	156	146	136	
Butanedioic acid monobenzyl ester (succinic acid monobenzyl ester)	42	185	157 (mono) 260 (di)	180 (mono) 260 (di)	113	168	206
Dibenzyl 1,2-benzenedicarboxylate (dibenzyl phthalate; benzyl phthalate)	43	208	149 (mono) 220 (di)	150, 165 (mono) 201 (di)	113	179	
Diethyl 1,4-benzenedicarboxylate (diethyl terephthalate; ethyl terephthalate)	44	380	>225		93	266	
3-Phenyl-2-propenyl 3-phenyl-2-propenoate (cinnamyl cinnamate)	44	133	148	168	121	225	
Ethyl 3-(2-nitrophenyl)-2-propenoate (ethyl 2-nitrocinnamate)	44	240	185		93		
Methyl 3-(2-chlorophenyl)-2-propenoate (methyl 2-chlorocinnamate)	44		168		108		
Diethyl 3-nitro-1,2-benzenedicarboxylate (diethyl 3-nitrophthalate; ethyl 3-nitrophthalate)	46	219	201 (di)	226 (di)	93		
Ethyl 3-nitrobenzoate	47	141	190		93	101	
Dicyclohexyl ethanedioate (dicyclohexyl oxalate; cyclohexyl oxalate)	47	190 (anhyd) 101 (dihyd)	219 (mono) 419d (di)	168 (mono) 268 (di)	113	223	243

(Continued)

TABLE AII.20 Esters (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)					
		Acid	Amide	4-Toluidide	3,5-Dinitrobenzoate	*N*-Benzylamide	Hydrazide
2-Phenylethyl 3-phenyl-2-propenoate (2-phenylethyl cinnamate)	48	133	148	168	108	225	
1-Naphthyl ethanoate (α-naphthyl acetate)	49	17	82	153	217	61	77
Methyl 4-methoxybenzoate (methyl *p*-anisate)	49	184	167	186	108	132	
Phenacyl ethanoate (benzoylcarbinyl acetate; phenacyl acetate)	49	17	82	153		61	77
Dibenzyl D-2,3-dihydroxybutanedioate (dibenzyl D-tartarate; benzyl D-tartarate)	50		172 (mono) 196 (di)		113		
Dibenzyl butanedioate (dibenzyl succinate; benzyl succinate)	52	185	157 (mono) 260 (di)	180 (mono) 260 (di)	113	206	168
Methyl 3,4-methylenedioxybenzoate (methyl piperonylate)	52		169		108		
Hexadecyl hexadecanoate (cetyl palmitate)	52	63	107	98	66	95	111
Furfuryl diethanoate (furfuryl diacetate)	52	17	82	153		61	77
1,2-Ethanediol di(dodecanoate) (ethylene glycol dilaurate)	52	44	100	87	169	83	105
Phenyl octadecanoate (phenyl stearate)	52	70	109	102	146	97	
Methyl (±)-2-hydroxy-2-phenylethanoate [methyl (±)-mandelate; methyl (±)-2-hydroxy-2-phenylacetate]	53	120	134	172	108		
Dimethyl 2-hydroxypropanedioate (dimethyl tartronate; methyl tartronate; dimethyl hydroxymalonate; methyl hydroxymalonate)	53		198 (di)		108		
Dimethyl ethanedioate (dimethyl oxalate; methyl oxalate)	54	190 (anhyd) 101 (dihyd)	219 (mono) 419d (di)	168 (mono) 268 (di)	108	223	243
3-Methylphenyl benzoate (*m*-tolyl benzoate)	55	122	130	158	165	106	112
Diethyl *R,S*-2,3-dihydroxybutanedioate (diethyl *meso*-tartarate; ethyl *meso*-tartarate)	55	140	190 (di)		93	205	
Ethyl 4-nitrobenzoate	56	239	201	204	93	142	
1-Naphthyl benzoate	56	122	130	158	217	106	112
Hexadecyl octadecanoate (cetyl stearate)	57	70	109	102	66	97	

(Continued)

TABLE AII.20 Esters (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)					
		Acid	Amide	4-Toluidide	3,5-Dinitrobenzoate	*N*-Benzylamide	Hydrazide
Di-(2-methylpropyl) (±)-2,3-dihydroxybutanedioate [diisobutyl (±)-tartarate; isobutyl (±)-tartarate]	58		226		87		
Ethyl diphenylethanoate (ethyl diphenylacetate)	58		168	173	93		
Ethyl 2-benzoylbenzoate	58		165		93		
Methyl diphenylethanoate (methyl diphenylacetate)	60		168	173	108		
Methyl 2-(4-methylphenyl)benzoate [methyl 2-(*p*-tolyl)benzoate]	61		176		108		
Dimethyl D-2,3-dihydroxybutanedioate (dimethyl D-tartarate; methyl D-tartarate)	62		172 (mono) 196 (di)		108		
1,2-Ethanediol di(tetradecanoate) (ethylene glycol dimyristate)	63	58	103	93	169	90	
Dimethyl 4-nitro-1,2-benzenedicarboxylate (dimethyl 4-nitrophthalate; methyl 4-nitrophthalate)	66	165	200	172 (mono)	108		
Dicyclohexyl 1,2-benzenedicarboxylate (dicyclohexyl phthalate; cyclohexyl phthalate)	66	208	149 (mono) 220 (di)	150, 165 (mono) 201 (di)	113	179	
Ethyl *N*-phenylethanedioic acid monoamide (ethyl oxalinate; ethyl *N*-phenyl oxalic acid monoamide)	67		228		93		
Dimethyl 1,3-benzenedicarboxylate (dimethyl isophthalate; methyl isophthalate)	68	347	280 (mono) 280 (di)		108		220
Ethyl 2-(4-methylphenyl)benzoate [ethyl 2-(*p*-tolyl)benzoate]	69		176		93		
Dimethyl 3-nitro-1,2-benzenedicarboxylate (dimethyl 3-nitrophthalate; methyl 3-nitrophthalate)	69	219	201 (di)	226 (di)	108		
Methyl 3-hydroxybenzoate	70	201	170	163	108	142	
Phenyl benzoate	71	122	130	158	146	106	112
1,2-Ethanediol di(hexadecanoate) (ethylene glycol dipalmitate)	71	63	107	98	169	95	111
2-Naphthyl ethanoate (α-naphthyl acetate)	71	17	82	153	210	61	77

(Continued)

TABLE AII.20 Esters (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)					
		Acid	Amide	4-Toluidide	3,5-Dinitrobenzoate	*N*-Benzylamide	Hydrazide
1,2,3-Propanetriol tri(octadecanoate) (glyceryl tristearate)	71	70	109	102		97	
4-Methylphenyl benzoate (*p*-tolyl benzoate)	71	122	130	158	189	106	112
Phenyl 3-phenyl-2-propenoate (phenyl cinnamate)	72	133	148	168	146	225	
1,2-Ethanediol dibenzoate (ethylene glycol dibenzoate)	73	122	130	158	169 (di)	106	112
Methyl *E*-3-(2-nitrophenyl)-2-propenoate (methyl 2-nitrocinnamate)	73	240	185		108		
Di(2-methylpropyl) D-2,3-dihydroxy butenedioate (diisobutyl D-tartarate; isobutyl D-tartarate)	74		172 (mono) 196 (di)		87		
Ethyl 3-hydroxybenzoate	74	201	170	163	93	142	
Diphenyl 1,2-benzenedicarboxylate (diphenyl phthalate; phenyl phthalate)	75	208	149 (mono) 220 (di)	150, 165 (mono) 201 (di)	146	179	
Methyl 3-hydroxy-2-naphthoate	75		228	223	108		
Methyl 2,2-diphenyl-2-hydroxyethanoate (methyl benzilate; methyl 2,2-diphenyl-2-hydroxyacetate)	75		155	190	108		
1,2,3-Propanetriol tribenzoate (glyceryl tribenzoate)	76	122	130	158		106	112
1,2-Ethanediol di(octadecanoate) (ethylene glycol distearate)	76	70	109	102	169 (di)	97	
Methyl 2-naphthoate	77		193	192	108		
Methyl 2-phenylbutanoate (methyl α-phenylbutyrate)	78		87		108		
Methyl 3-nitrobenzoate	78	141	143	162	108	101	
Trimethyl 2-hydroxy-1,2,3-propanetricarboxylate (trimethyl citrate; methyl citrate)	79	100	215 (tri)	189 (tri)	108	170	
Ethyl *E*-3-(3-nitrophenyl)-2-propenoate (ethyl 3-nitrocinnamate)	79	205	196		93		
Methyl 2-benzylbenzoate	80		165		108		
Dibenzyl 1,2-ethanedioate (dibenzyl oxalate; benzyl oxalate)	80	190 (anhyd) 101 (dihyd)	219 (mono) 419d (di)	169 (mono) 268 (di)	113	223	243
Methyl 4-bromobenzoate	81	252	190		108		163
1-Acetoxybenzyl phenyl ketone (benzoin acetate)	83		82	153			

(Continued)

TABLE AII.20 Esters (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)					
		Acid	Amide	4-Toluidide	3,5-Dinitrobenzoate	*N*-Benzylamide	Hydrazide
1,2-Diacetoxybenzene (catechol diacetate)	84	16	130	158	152 (di)		
Ethyl 3-hydroxy-2-naphthoate	85		218	223	93		
Dimethyl (±)-2,3-dihydroxybutanedioate [dimethyl (±)-tartarate; methyl (±)-tartarate]	90		226		108		
Di(2-methylphenyl) 1,2-ethanedioate (di-*o*-tolyl oxalate; *o*-tolyl oxalate)	91	190 (anhyd) 101 (dihyd)	219 (mono) 419d (di)	169 (mono) 268 (di)	138	223	243
Ethyl 3,5-dinitrobenzoate	94	207	183		93		
2-Naphthyl 2-hydroxybenzoate (β-naphthyl salicylate)	96	158	142	156	210	136	
Methyl 4-nitrobenzoate	96	239	201	204	108	142	
Propyl 4-hydroxybenzoate	96	213	162	204	123		
1,2,4-Triacetoxybenzene (hydroquinone triacetate)	97	17	82	153		61	77
Ethyl 3,5-dinitro-2-hydroxybenzoate (ethyl 3,5-dinitrosalicylate)	99		181		93		
Dimethyl *E*-butenedioate (dimethyl fumarate; methyl fumarate)	102	286	270; 302 (mono) 266 (di)		108	205	
Ethyl 5-nitro-2-hydroxybenzoate (ethyl 5-nitrosalicylate)	102		225		93		
Di-(3-methylphenyl) 1,2-ethanedioate (di-*m*-tolyl oxalate; *m*-tolyl oxalate)	105	190 (anhyd) 101 (dihyd)	219 (mono) 419d (di)	169 (mono) 268 (di)	165	223	243
1,3,5-Triacetoxybenzene (phloroglucinol triacetate)	106	16	82	153	162 (tri)	61	77
Diphenyl hexanedioate (diphenyl adipate; phenyl adipate)	106	152	130 (mono) 220 (di)	241	146	189	171
2-Naphthyl benzoate	107	122	130	158	210	106	112
Methyl 3,5-dinitrobenzoate	108	207	183		108		
Dimethyl *R,S*-2,3-dihydroxybutanedioate (dimethyl *meso*-tartarate; methyl *meso*-tartarate)	111	140	190 (di)		108	205	
Ethanedioic acid monoamide monoethyl ester (ethyl oxamate; oxalic acid monoamide monoethyl ester)	115		419d		93		
Ethyl 4-hydroxybenzoate	116	213	162	204	93		
2,4-Dihydroxyphenyl dibenzoate (resorcinol dibenzoate)	117	122	130	158	201	106	112

(Continued)

TABLE AII.20 Esters (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)					
		Acid	Amide	4-Toluidide	3,5-Dinitrobenzoate	*N*-Benzylamide	Hydrazide
Ethyl 3-nitro-2-hydroxybenzoate (ethyl 3-nitrosalicylate)	118		145		93		
Methyl 5-nitro-2-hydroxybenzoate (methyl 5-nitrosalicylate)	119		225		108		
Diphenyl butanedioate (diphenyl succinate; phenyl succinate)	121	185	157 (mono) 260 (di)	180 (mono) 260 (di)	149	206	168
Di-(4-methylphenyl) butanedioate (di-*p*-tolyl succinate; *p*-tolyl succinate)	121	185	157 (mono) 260 (di)	180 (mono) 260 (di)	189	206	168
Hydroquinone diethanoate (hydroquinone diacetate)	124	16	82	153	317	61	77
Methyl *E*-3-(3-nitrophenyl)-2-propenoate (methyl 3-nitrocinnamate)	124	205	196		108		
Methyl 3,5-dinitro-2-hydroxybenzoate (methyl 3,5-dinitrosalicylate)	127		181		108		
Methyl 4-hydroxybenzoate	131	213	162	204	108		
Methyl 3-nitro-2-hydroxybenzoate (methyl 3-nitrosalicylate)	132		145		108		
Triethyl 1,3,5-benzenetricarboxylate (triethyl trimesate)	133	380	365 (tri)		93		
Ethyl *E*-3-(4-nitrophenyl)-2-propenoate (ethyl 4-nitrocinnamate)	141	287	217		93		
Dimethyl 1,4-benzenedicarboxylate (dimethyl terephthalate; methyl terephthalate)	141	300	>225 (di)		108	266	
Trimethyl 1,3,5-benzenetricarboxylate (trimethyl trimesate)	144	380	365 (tri)		108		
Di(4-methylphenyl) 1,2-ethanedioate (di-*p*-tolyl oxalate; *p*-tolyl oxalate)	149	190 (anhyd) 101 (dihyd)	219 (mono) 419d (di)	169 (mono) 268 (di)	189	223	243
Methyl *E*-3-(4-nitrophenyl)-2-propenoate (methyl 4-nitrocinnamate)	161	287	217		108		
Diethyl 2,3,4,5-tetrahydroxyhexanedioate (diethyl mucate; ethyl mucate)	164		192 (mono) 220 (di)		93		
Dimethyl 2,3,4,5-tetrahydroxyhexanedioate (dimethyl mucate; methyl mucate)	167		192 (mono) 220 (di)		108		
Hydroquinone benzoate	204	122	130	158	317	106	112

TABLE AII.21 Ethers—Aromatic (Liquids)

Name of Compound	bp (°C)	sp gr	Derivative mp (°C)			
			Picrate	Sulfonamide	Nitro Derivative	Bromo Derivative
Methoxybenzene (anisole)	158	0.988	81 (4-)	113	87, 95 (2,4-)	61 (2,4-)
2-Methoxytoluene (*o*-cresol methyl ether; *o*-methylanisole; methyl *o*-tolyl ether)	171	0.966_4^0; 0.985	119	137(5-)	69 (3,5-); 64 (5-)	
Ethoxybenzene (phenetole)	172	0.979_4^4; 0.967	92	150 (4-)	59 (4-)	
4-Methoxytoluene (*p*-cresyl methyl ether; *p*-methylanisole; methyl *p*-tolyl ether)	176	0.987_4^0; 0.970	89	182 (3-)	122 (3,5-)	
3-Methoxytoluene (*m*-cresyl methyl ether; *m*-methylanisole; methyl *m*-tolyl ether)	177	0.985_4^4; 0.972	114	130 (6-)	92 (2,4,6-) 55 (2-)	
4-Ethoxytoluene (*p*-cresyl ethyl ether; ethyl *p*-tolyl ether)	192	0.949	111	138		
3-Ethoxytoluene (*m*-cresyl ethyl ether; ethyl *m*-tolyl ether)	192	0.949	115	111		
2-Ethoxytoluene (*o*-cresyl ethyl ether; ethyl *o*-tolyl ether)	192	0.953	118 (di)	149	51	
2-Chloro-1-methoxybenzene (*o*-chloroanisole)	195	1.191		130 (4-)	95 (4-)	
4-Chloro-1-methoxybenzene (*p*-chloroanisole)	200	1.185_4^{13}		151 (2-)	98 (2-)	
2-Methoxyphenol (guaiacol; catechol monomethyl ether)	205	1.129	87			116 (4,5,6-)
1,2-Dimethoxybenzene (veratole)	207	1.086_4^{15}	57	136 (4-)	95 (4-) 132 (4,5-)	93 (4,5-)
2-Chlorophenyl ethyl ether (*o*-chlorophenetole)	208			133	82	
Butyl phenyl ether	210	0.950	112	104		
4-Chloro-1-ethoxybenzene (*p*-chlorophenetole)	212	1.123_{20}^{20}		134	61	54 (2,6-)
1,3-Dimethoxybenzene (resorcinol dimethyl ether)	217	1.080_4^0; 1.055_{25}^{25}	58	167 (4-)	72 (2,4-) 157 (4,6-) 124 (2,4,6-)	140 (4,6-)
2-Bromo-1-methoxybenzene (*o*-bromoanisole)	218			140 (4-)	106 (4-)	
4-Bromo-1-methoxybenzene (*p*-bromoanisole)	223	1.494_4^9		148 (2-)	88 (2-)	
2-Bromophenyl ethyl ether (*o*-bromophenetole)	224			135 (4-)	98 (4-)	
1,2-Methylenedioxy-4-(2-propenyl)benzene (safrole)	233	1.096_4^{18}	105			108 (tri) 170 (penta) 51 (1,3,5-)
4-Bromophenyl ethyl ether (*p*-bromophenetole)	233			145	47	

(Continued)

TABLE AII.21 Ethers—Aromatic (Liquids) *(Continued)*

Name of Compound	bp (°C)	sp gr	Derivative mp (°C)			
			Picrate	Sulfonamide	Nitro Derivative	Bromo Derivative
1-Methoxy-4-propenylbenzene (anethole)	235	0.989_4^{28}	70			67 (di) 108 (tri)
1,3-Diethoxybenzene (resorcinol diethyl ether)	235		58; 109	184		69 (tri)
1,2,3-Trimethoxybenzene	241		81	123 (4,5,6-)	106 (5-)	74 (4,5,6-)
1,2-Dimethoxy-4-(2-propenyl)benzene (eugenol methyl ether)	244	1.055_4^{15}; 1.034	115			78 (tri)
Ethyl 2-iodophenyl ether (*o*-iodophenetole)	246	1.800	84		110 (tri)	
1,2-Methylenedioxy-4-propylbenzene (isosafrole)	248	1.125_4^{14}	75		53 (di) 110 (tri)	
Diphenyl ether	259	1.073	110	159 (4,4'-)	144 (4,4') 197 (2,2',4,4'-)	58 (4,4'-)
1,2-Dimethoxy-4-propenylbenzene (isoeugenol methyl ether)	264	1.0528	45		101 (di)	
Methyl 1-naphthyl ether (α-methoxynaphthalene)	271	1.096_4^{14}	113; 131	157 (4-)	80 (2-) 85(4-) 128 (2,4,5-)	46, 68 (mono) 55 (2,4-)
Ethyl 1-naphthyl ether (α-ethoxynaphthalene)	280	1.074; 1.060	100; 119	165 (4-)	84 (2-) 117 (4-) 149 (2,4,5-)	48 (4-)
Ethyl 2-naphthyl ether (β-ethoxynaphthalene)	282	1.064	44; 101	163		66 (1-) 94 (1,6-)
Benzyl ether	300	1.043	78			108 (di)
2-Naphthyl pentyl ether (amyl β-naphthyl ether)	328		67	159	135 (di)	58 (di)

TABLE AII.22 Ethers—Aromatic (Solids)

Name of Compound	mp (°C)	Derivative mp (°C)			
		Picrate	Sulfonamide	Nitro Derivative	Bromo Derivative
4-Chloro-1-ethoxybenzene (*p*-chlorophenetole)	21		134	54 (2,6-)	
1,2-Dimethoxybenzene (veratole)	22	57	136 (4-)	95(4-) 132 (4,5-)	93 (4,5-)
1-Methoxy-4-propenylbenzene (anethole)	22	70			67 (di) 108 (tri)
2-Naphthyl pentyl ether (amyl β-naphthyl ether)	25	67	159	135 (di)	58 (di)
Phenyl ether	28	110	159 (4,4′)	144 (4,4′-) 197 (2,2′,4,4′-)	58
2-Methoxyphenol (guaiacol; catechol monomethyl ether)	28	87			116 (4,5,6-)
Ethyl 2-naphthyl ether (β-ethoxynaphthalene)	37	44; 101	163		66 (1-) 94 (1,6-)
1,2-Diethoxybenzene (catechol diethyl ether)	43	71	163 (3,4-)	122 (tri)	
1,2,3-Trimethoxybenzene (pyrogallol trimethyl ether)	47	81	124 (2,3,4-)	106 (5-)	74 (4,5,6-)
1,4-Dimethoxybenzene (hydroquinone dimethyl ether)	57	119; 48	148 (2-)	72 (2-) 177 (2,3-) 202 (2,5-)	142 (di)
Methyl 2-naphthyl ether (β-methoxynaphthalene)	72	117	151 (8-)	128 (1-) 215 (1,6,8-)	63 (mono) 84 (1-) 78 (3-) 108 (6-)
Biphenylene oxide (dibenzofuran)	87	94		182 (3-) 245 (di)	
4-Methoxybiphenyl (4-biphenyl methyl ether; *p*-phenylanisole)	90		92 (3-) 138 (3,5-) 171 (3,4′-)	79 (3-) 144 (4′-) 134 (3,4′-) 87 (3,5-)	
1,2-Diphenoxyethane (ethylene glycol diphenyl ether)	98		229 (4,4′-)	215 (2′,4′-)	135 (4,4′-)

TABLE AII.23 Halides—Alkyl, Cycloalkyl, and Aralkyl (Liquids)

Name of Compound	bp (°C)	Derivative mp (°C)					
		Anilide	1-Naphthalide	Alkylmercuric Halide	Alkyl 2-naphthyl Ether	Alkyl 2-naphthyl Ether Picrate	*S*-Alkylthiuronium Picrate
Chlorides:							
Choroethane (ethyl chloride)	12	104	126	192	37	104	188
2-Chloropropane (isopropyl chloride)	36	104		97	41	95	196; 148
3-Chloropropene (allyl chloride)	45	114			16	99	155
1-Chloropropane (propyl chloride)	46	92	121	147	39	81	181
2-Chloro-2-methylpropane (*tert*-butyl chloride)	54	128	147	123			161
2-Chlorobutane (*sec*-butyl chloride)	68	108	129	39	34	86	190; 166
1-Chloro-2-methylpropane (isobutyl chloride)	69	110	126		33	85	174
1-Chlorobutane (butyl chloride)	78	63	112	128	33	67	180
1-Chloro-2,2-dimethylpropane (neopentyl chloride)	85	131		118			
2-Chloro-2-methylbutane (*tert*-pentyl chloride; *tert*-amyl chloride)	86	92	138				
(±)-2-Chloropentane	97	96	103				
3-Chloropentane	97	127	118				
1-Chloro-3-methylbutane (isopentyl chloride; isoamyl chloride)	100	108	111	86	28	94	179
1-Chloropentane (pentyl chloride; amyl chloride)	107	96	112	110	25	67	154
2-Chloro-2-methylpentane	113	74	118				
1-Chloro-3,3-dimethylbutane	115	139		133			
1-Chlorohexane (hexyl chloride)	134	69	106	125			157
Cyclohexyl chloride	143	146	188	164	116		
1-Chloroheptane (heptyl chloride)	160	57	95	120			142
Benzyl chloride	179	117	166		99	123	188
1-Chlorooctane (octyl chloride)	184	57	91	115; 151			134
1-Chloro-2-phenylethane (β-phenylethyl chloride)	190	97			70	84	139
1-Chlorohexadecane (cetyl chloride)	286			102			155
Bromides:							
Bromomethane (methyl bromide)	5	114	160	160; 172	72	118	224
Bromoethane (ethyl bromide)	38	104	126	198	37	104	188
2-Bromopropane (isopropyl bromide)	60	104		94	41	92	196; 148
3-Bromopropene (allyl bromide)	71	114			16	99	155
1-Bromopropane (propyl bromide)	71	92	121	138	40	81	181
2-Bromo-2-methylpropane (*tert*-butyl bromide)	72	128	147				151
2-Bromobutane (*sec*-butyl bromide)	91	108	129	39	34	86	190; 166
1-Bromo-2-methylpropane (isobutyl bromide)	91	109	126	56	33	84	174
1-Bromobutane (butyl bromide)	101	63	112	136	33	67	180

(Continued)

TABLE AII.23 Halides—Alkyl, Cycloalkyl, and Aralkyl (Liquids) *(Continued)*

Name of Compound	bp (°C)	Derivative mp (°C)					
		Anilide	1-Naphthalide	Alkylmercuric Halide	Alkyl 2-naphthyl Ether	Alkyl 2-naphthyl Ether Picrate	*S*-Alkylthiuronium Picrate
2-Bromo-2-methylbutane (*tert*-pentyl bromide; *tert*-amyl bromide)	108	92	138				
1-Bromo-3-methylbutane (isopentyl bromide; isoamyl bromide)	118	110	111	80	28	94	179
(±)-2-Bromopentane	118	93	104				
1-Bromopentane (pentyl bromide; amyl bromide)	129	96	112	127	25	67	154
1-Bromohexane (hexyl bromide)	157	69	106	119; 127			157
Cyclohexyl bromide	165	146	188	153	116		
1-Bromoheptane (heptyl bromide)	174	57	95	118			142
Benzyl bromide	198	117	166	119	99	123	188
1-Bromooctane (octyl bromide)	204	57	91	109			134
1-Bromo-2-phenylethane (2-phenylethyl bromide)	218	97		169	70	84	139
1-Bromononane	220			109			131
β-Bromostyrene	221	115	217	91			
Iodides:							
Iodomethane (methyl iodide)	43	114	160	152	72	118	224
Iodoethane (ethyl iodide)	73	104	126	186	37	104	188
2-Iodopropane (isopropyl iodide)	89	103		125	41	95	196; 148
1-Iodopropane (propyl iodide)	102	92	121	113	40	81	181
2-Iodo-2-methylpropane (*tert*-butyl iodide)	103	128	147				151
3-Iodopropene (allyl iodide)	103	114	121	112	16	99	155
2-Iodobutane (*sec*-butyl iodide)	120	108	129		34	86	190; 166
1-Iodo-2-methylpropane (isobutyl iodide)	120	109	125	72	33	84	174
2-Iodo-2-methylbutane (*tert*-pentyl iodide; *tert*-amyl iodide)	128	92	138				
1-Iodobutane (butyl iodide)	130	63	112	117	33	67	180
1-Iodo-3-methylbutane (isopentyl iodide; isoamyl iodide)	148	108	111	122	28	94	179
1-Iodopentane (pentyl iodide; amyl iodide)	156	96	112	110	25	67	154
Cyclohexyl iodide	179	146	188		116		
1-Iodohexane (hexyl iodide)	180	69	106	110			157
1-Iodoheptane (heptyl iodide)	204	57	95	103			142

TABLE AII.24 Halides—Aromatic (Liquids)

		Nitration Product		Sulfonamide		Oxidation	
Name of Compound	bp (°C)	Position	mp (°C)	Position	mp (°C)	Name of Product	mp (°C)
Fluorobenzene	85	4	27	4	125		
2-Fluorotoluene	114			5	105	2-Fluorobenzoic acid	127
3-Fluorotoluene	116			6	174	3-Fluorobenzoic acid	124
4-Fluorotoluene	117			2	141	4-Fluorobenzoic acid	182
Chlorobenzene	132	2,4	52	4	144		
Bromobenzene	157	2,4	75	4	166		
2-Chlorotoluene	159	3,5	63	5	128	2-Chlorobenzoic acid	141
3-Chlorotoluene	162	4,6	91	6	185	3-Chlorobenzoic acid	158
4-Chlorotoluene	162	2	38	2	143	4-Chlorobenzoic acid	242
		2,6	76				
1,3-Dichlorobenzene	173	4,6	103	4	182		
				2,4	180		
1,2-Dichlorobenzene	179	4,5	110	4	140		
				3,4	135		
2-Bromotoluene	182	3,5	82	5	146	2-Bromobenzoic acid	150
3-Bromotoluene	184	4,6	103	6	168	3-Bromobenzoic acid	155
4-Bromotoluene	185	2	47	2	165	4-Bromobenzoic acid	251
2-Chloro-1,4-dimethylbenzene	185	5	77	5	155		
		5,6	101				
1-Chloro-2,4-dimethylbenzene	192	6	42	6	192	4-Chloro-3-methylbenzoic acid	210
						4-Chlorobenzene-1,3-dicarboxylic acid (4-chloroisophthalic acid)	295
1-Chloro-3,4-dimethylbenzene	195	5	63	5	207		
2,6-Dichlorotoluene	199	3	50	3	204	2,6-Dichlorobenzoic acid	139
		3,5	121				
2,5-Dichlorotoluene	199	4	51			2,5-Dichlorobenzoic acid	154
		4,6	101				
2,4-Dichlorotoluene	200	3,5	104	5	176	2,4-Dichlorobenzoic acid	164
3,5-Dichlorotoluene	201	2	62			3,5-Dichlorobenzoic acid	188
		2,6	100				
3-Iodotoluene	204	4,6	108			3-Iodobenzoic acid	187
2-Chloro-1,3,5-trimethylbenzene	206	4,6	178		166	2-Chlorobenzene-1,3,5-tricarboxylic acid	285 (anhyd) 278 (hyd)
2,3-Dichlorotoluene	207	4	51			2,3-Dichlorobenzoic acid	163
		4,6	72				
3,4-Dichlorotoluene	209	6	64	6	190	3,4-Dichlorobenzoic acid	208
		2,6	92				
2-Iodobenzene	211	6	103			2-Iodobenzoic acid	162
1,3-Dibromobenzene	219	4	62	4	190		
		4,6	117				
1,2-Dibromobenzene	224	4,5	114	4	176		
1-Chloronaphthalene	259	4,5	180	4	186		
1-Bromonaphthalene	281	4	85	4	193		
3-Chlorobiphenyl	285	4,4′	203			3-Chlorobenzoic acid	158

TABLE AII.25 Halides—Aromatic (Solids)

		Nitration Product		Sulfonamide		Oxidation	
Name of Compound	mp (°C)	Position	mp (°C)	Position	mp (°C)	Name of Product	mp (°C)
4-Bromotoluene	28	2	47	6	165	4-Bromobenzoic acid	251
2,4,6-Trichlorotoluene	38	3	54			2,4,6-Trichlorobenzoic acid	161
		3,5	180				
2,3,4-Trichlorotoluene	41	5	60			2,3,4-Trichlorobenzoic acid	187
		6	60				
		5,6	141				
3,4,5-Trichlorotoluene	45	2	82			3,4,5-Trichlorobenzoic acid	203
		2,6	164				
2,3,5-Trichlorotoluene	46	4	59			2,3,5-Trichlorobenzoic acid	162
		6	59				
		4,6	150				
1,6-Dichloronaphthalene	48	4	119	4	216		
1,2,3-Trichlorobenzene	53	4	56	4	230		
		4,6	93				
1,4-Dichlorobenzene	53	2	56	2	186		
2-Chloronaphthalene	61	1,8	175		126		
				8	232		
1,3,5-Trichlorobenzene	63	2	68	2	212		
1,7-Dichloronaphthalene	64		139	4	226		
1,4-Dichloronaphthalene	68	8	92	6	244	3,6-Dichlorobenzene-1,2-dicarboxylic acid (3,6-dichlorophthalic acid)	194
2,4,5-Trichlorotoluene	82	3	90			2,4,5-Trichlorobenzoic acid	168
		3,6	227				
1,4-Dibromobenzene	89	2	84	2	195		
		2,5	84				
1,5-Dichloronaphthalene	107	8	142	3	204		
2,7-Dichloronaphthalene	115	mono	142	3	218		
1,3,5-Tribromobenzene	120	2,4	192	2	222		

TABLE AII.26 Hydrocarbons—Aromatic (Liquids)

Name of Compound	bp (°C)	sp gr	Nitration Product		Derivative mp (°C)	
			Position	mp (°C)	Aroyl-benzoic Acid	Picrate
Benzene	80	0.874	1,3	90	128	84
			1,3,5	122		
Toluene	111	0.881_4^4; 0.867	2,4	71	137	88
Ethylbenzene	136	0.876_4^{19}; 0.867	2,4,6	37	128	96
1,4-Dimethylbenzene (*p*-xylene)	138	0.866_4^4; 0.861	2,3,5	139	132; 148	90
1,3-Dimethylbenzene (*m*-xylene)	139	0.871_4^{12}; 0.864	2,4	83	126	91
			2,4,6	183	142	
1,2-Dimethylbenzene (*o*-xylene)	144	0.890_4^4; 0.880	4,5	71; 118	178; 167	88
1-Methylethylbenzene (isopropylbenzene; cumene)	153	0.875_4^4; 0.862	2,4,6	109	134	
Propylbenzene	159	0.861			125	103
1,3,5-Trimethylbenzene (mesitylene)	164	0.869_4^{10}; 0.865	2,4	86	212	97
			2,4,6	235		
1,2,4-Trimethylbenzene (pseudocumene)	169	0.895; 0.876	3,5,6	185	149	97
1-Methyl-4-(1-methylethyl)benzene (*p*-cymene; *p*-isopropyltoluene)	177	0.857	2,6	54	124	
			2,3,6	118		
1,3-Diethylbenzene	182	0.860	2,4,6	62	114	
1,2,3,5-Tetramethylbenzene (isodurene)	198	0.890	4,6	157; 181	213	
1,2,3,4-Tetramethylbenzene (prehnitene)	205	0.905	5,6	176		95
1,2,3,4-Tetrahydronaphthalene(tetralin)	207	0.971	5,7	95	155	
1,3,5-Triethylbenzene	218	0.863; 0.857_4^{20}	2,4,6	112	129	
2-Methylnaphthalene	241		1	81	190	116
1-Methylnaphthalene	245	1.001_4^{19}; 1.020	4	71	169	142
			4,5	143	68	

TABLE AII.27 Hydrocarbons—Aromatic (Solids)

Name of Compound	mp (°C)	Nitration Product		Derivative mp (°C)	
		Position	mp (°C)	Aroyl-benzoic Acid	Picrate
2-Methylnaphthalene	38	1	81	190	116
Pentamethylbenzene	54	6	154		131
Biphenyl	71	4,4′	237	225	
		2,2′,4,4′	150		
1,2,4,5-Tetramethylbenzene (durene)	80	3,6	207	264	95
Naphthalene	80	1	61	173	150
Acenaphthalene	96	5	101	200	162
Fluorene	117	2,7	199	228	87
		2	156		
Hexamethylbenzene	162		176		170
Dibiphenylenethylene (bifluroenylidene)	195		171		178
1,2-Benzphenanthrene (chrysene)	254			214	273

TABLE AII.28 Ketones (Liquids)

Name of Compound	bp (°C)	Derivative mp (°C)				
		Semicarbazone	2,4-Dinitrophenylhydrazone	4-Nitrophenylhydrazone	Phenylhydrazone	Oxime
Propanone (acetone)	56	190	128	152	42	59
2-Butanone (ethyl methyl ketone)	80	146	117	129		
3-Butyn-2-one (ethynyl methyl ketone)	86		181	143		
2,3-Butanedione (biacetyl)	88	235 (mono) 278 (di)	315 (di)	230 (mono)	134 (mono) 245 (di)	74 (mono) 246, 234 (di)
3-Methyl-2-butanone (isopropyl methyl ketone)	94	114	120	109		
2-Pentanone (methyl propyl ketone)	102	112	144	117		58
3-Pentanone (diethyl ketone)	102	139	156	144		69
3,3-Dimethyl-2-butanone (pinacolone; *tert*-butyl methyl ketone)	106	158	125	139		79
1-Methoxy-2-propanone (methoxymethyl methyl ketone)	115		163	111		
3-Benzoylpropanoic acid	116	181	191			
3-Methyl-2-pentanone (*sec*-butyl methyl ketone)	118	95	71			
4-Methyl-2-pentanone (isobutyl methyl ketone)	119	135	95	79		58
1-Chloro-2-propanone (chloroacetone)	119	164d	125	83		
2,4-Dimethyl-3-pentanone (diisopropyl ketone)	125	160; 149	98; 107			34
3-Hexanone (ethyl propyl ketone)	125	113	130			
2-Hexanone (butyl methyl ketone)	129	122	110	88		49
4-Methyl-3-penten-2-one (mesityl oxide)	130	164 (α) 134 (β)	203	134	142	49 (β)
Cyclopentanone	131	210	146	154	55	57
5-Hexen-2-one (allyl acetone)	132	102	108			
2,2,4-Trimethyl-3-pentanone (*tert*-butyl isopropyl ketone)	135	132				144
1-Bromo-2-propanone (bromoacetone)	136	135				36
Methyl 2-oxopropanoate (methyl pyruvate)	136	208	187			
4-Methyl-3-hexanone (*sec*-butyl ethyl ketone)	136	137	78			
4-Methyl-2-hexanone (ethyl isobutyl ketone)	136	152	75			
2-Methyl-3-hexanone (isopropyl propyl ketone)	136	119	97			
3-Methyl-1-penten-4-one	138	201				76
2,4-Pentanedione (acetylacetone)	139	107	122 (mono) 209 (di)	209		149 (di)

(Continued)

TABLE AII.28 Ketones (Liquids) *(Continued)*

Name of Compound	bp (°C)	Derivative mp (°C)				
		Semicarbazone	2,4-Dinitrophenylhydrazone	4-Nitrophenylhydrazone	Phenylhydrazone	Oxime
3-Hydroxy-3-methyl-2-butanone	140	165				87
D-3-Methylcyclopentanone	143	185				92 (α) 69 (β)
5-Methyl-2-hexanone (isopentyl methyl ketone)	144	143	95			
4-Heptanone (dipropyl ketone)	145	133	75			
1-Hydroxy-2-propanone (hydroxyacetone; acetol)	146	196	129	173	103	71
3-Hydroxy-2-butanone (acetoin)	148	185; 202	318		243d	
2-Heptanone (methyl pentyl ketone; amyl methyl ketone)	151	127	89	73	207	
Cyclohexanone	155	167	162	147	82	91
Ethyl 2-oxopropanoate (ethyl pyruvate)	155	206	155			
2-Methyl-3-cyclopentenone	161	220				127
2-Oxopropanoic acid (pyruvic acid)	165	222	218	220		
2-Methylcyclohexanone	166	197	137	132		43
4-Hydroxy-4-methyl-2-pentanone (diacetone alcohol)	166		159; 203	209		58
2,6-Dimethyl-4-heptanone (diisobutyl ketone)	168	126	92; 66			210
3-Methylcyclohexanone	170	180; 191	155	119	94	43
2,2-Dimethylcyclohexanone	170	201	142			
Methyl 3-oxobutanoate (methyl acetoacetate)	170	152	119			
6-Methyl-2-heptanone (isohexyl methyl ketone)	171	154	77			
4-Methylcyclohexanone	171	203	134	129	110	39
(±)-2,5-Dimethylcyclohexanone	173	122 (α) 173 (β)				111
2-Octanone (hexyl methyl ketone)	173	123	58	93		
2-Acetylfuran (2-furyl methyl ketone)	173	150	220	186	86	104
D-2,5-Dimethylcyclohexanone	174	177				98
Acetoxyacetone	175	145		144	60	
cis-2,4-Dimethylcyclohexanone	176	200				99
2,2,6-Trimethylcyclohexanone	179	209	141			
Cyclohexyl methyl ketone	180	177	140	154		60
Ethyl 3-oxobutanoate (ethyl acetoacetate)	181	133	93	218		
Cycloheptanone	182	163	148	137		23
cis-3,5-Dimethylcyclohexanone	183	203				74
5-Nonanone (dibutyl ketone)	187	90	41			
2,5-Dimethylcyclohexene-3-one	190	165				93; 169

(Continued)

TABLE AII.28 Ketones (Liquids) *(Continued)*

Name of Compound	bp (°C)	Derivative mp (°C)				
		Semicarbazone	2,4-Dinitrophenylhydrazone	4-Nitrophenylhydrazone	Phenylhydrazone	Oxime
2,5-Hexanedione (acetonylacetone)	194	185 (mono) 224 (di)	257 (di)	212 (di); 115	120 (di)	137 (di)
2-Nonanone (methyl octyl ketone)	194	120	56			
Fenchone	194	184	140			167
Methyl 4-oxopentanoate (methyl levulinate)	196	144	142	136	105; 96	
Cyclooctanone	196	167	163			
4-Fluoroacetophenone	196	219	235			80
(±)-2-Ethyl-5-methylcyclohexanone	197	181				80
1-Acetyl-4-methylcyclohexanone	197	159 (α) 175 (β)				59
2,6-Dimethyl-2,5-heptadiene-4-one (phorone; diisopropylideneacetone)	198	186; 221	118			48
2-Propylcyclohexanone	199	133				68
1-Acetylcyclohexene	200	220				59
Acetophenone (methyl phenyl ketone)	205	203	250	185	105	60
Ethyl 4-oxopentanoate (ethyl levulinate)	206	150	102	157	104	
L-Menthone	209	189	146		53	59
1,5-Dimethylcyclohexen-3-one	209	180			78	
2-Decanone (methyl octyl ketone)	209	124	74			
2-Acetylthiophene (methyl 2-thienyl ketone)	214	191		181	96	81
1,5,5-Trimethylcyclohexene-3-one (isophorone)	215	191; 200	130		68	80
1-Phenyl-2-propanone (benzyl methyl ketone)	216	200	156	145	87	70
2-Methylacetophenone (methyl *o*-tolyl ketone)	216	210	159			61
Propyl 2-pyridyl ketone	218				82	48
2-Hydroxyacetophenone (2-acetylphenol)	218	210	213		110	118
1-Phenyl-1-propanone (ethyl phenyl ketone; propiophenone)	220	174	191	147	147	54
Methyl 3-pyridyl ketone	220				137	113
3-Methylacetophenone (methyl *m*-tolyl ketone)	220	203	207			57
2-Methyl-1-phenyl-1-propanone (isopropyl phenyl ketone; isobutyrophenone)	222	181	163		73	61; 94
2,2-Dimethyl-1-phenyl-1-propanone (*tert*-butyl phenyl ketone; pivalophenone)	224	150	195			167

(Continued)

TABLE AII.28 Ketones (Liquids) *(Continued)*

Name of Compound	bp (°C)	Derivative mp (°C)				
		Semicarbazone	2,4-Dinitrophenylhydrazone	4-Nitrophenylhydrazone	Phenylhydrazone	Oxime
1-Phenyl-2-butanone (benzyl ethyl ketone)	226	135; 146	140			
4-Methylacetophenone (methyl *p*-tolyl ketone)	226	205	260	198	97	88
3-Chloroacetophenone	228	232		176	176	88
2-Undecanone (2-hendecanone; methyl nonyl ketone)	228	123	63	91		45
2-Chloroacetophenone	229	160; 179	206	215		113
Carvone	230	142; 163	193	175	110	72 (α) 57 (β); 94
1-Phenyl-1-butanone (phenyl propyl ketone; butyrophenone)	230	191	190		200	50
2,4-Dimethylacetophenone	235	187				64
4-Phenyl-2-butanone (methyl β-phenylethyl ketone)	235	142	128			87
3-Methyl-1-phenyl-1-butanone (isobutyl phenyl ketone; isovalerophenone)	236	210	240			76
4-Chloroacetophenone	236	204; 160; 146	231	239	114	95
3,5-Dimethylacetophenone	237			180		114
3-Methoxyacetophenone	240	196	189			
1-Phenyl-1-pentanone (butyl phenyl ketone; valerophenone)	242	166	166	162	162	52
2-Methoxyacetophenone (*o*-acetylanisole)	245	183			114	83; 97
3-Acetylpropanoic acid (levulinic acid)	246	187	206	175	108	46
2,4,5-Trimethylacetophenone	247	204				86
1-Phenyl-1-pentanone (butyl phenyl ketone; valerophenone)	248	166	166	162	162	52
5-Isopropyl-2-methylacetophenone (2-acetyl-*p*-cymene)	250	147	142			92
Diethyl 3-oxopentanedioate (ethyl acetonedicarboxylate)	250	94	86			
3,4-Dimethylacetophenone	251	234				85
Propyl 3-pyridyl ketone	252	170			182	
2-Aminoacetophenone	252	290			108	109
α-Tetralone	257	226	257	231		
4-Methoxyacetophenone	258	198	220; 232	196	142	87
Benzylidenepropanone (benzalacetone)	262	186	227	166	157	116
2-Tridecanone (methyl undecyl ketone)	263	126	69	102		57

(Continued)

TABLE AII.28 Ketones (Liquids) *(Continued)*

Name of Compound	bp (°C)	Derivative mp (°C)				
		Semicarbazone	2,4-Dinitrophenylhydrazone	4-Nitrophenylhydrazone	Phenylhydrazone	Oxime
1-Phenyl-1-hexanone (pentyl phenyl ketone; amyl phenyl ketone)	265	133	168			
1-Phenyl-1-heptanone (enanthophenone; hexyl phenyl ketone)	283	119		128		55
3-Phenylcyclohexanone	288	167				129
Methyl 1-naphthyl ketone (α-acetylnaphthalene)	302	289; 233	255		149	140
3-Methylphenyl phenyl ketone (phenyl *m*-tolyl ketone)	314		221			101
Phenyl 2-pyridyl ketone (2-benzoylpyridine)	317		199		136	150; 165
1,3-Diphenyl-2-propanone (dibenzyl ketone)	330	146; 126	100		129	125
1,3-Diphenyl-2-propene-1-one (dypnone; α-methylstyryl phenyl ketone)	345	151				134 (syn) 78 (anti)

TABLE AII.29 Ketones (Solids)

Name of Compound	mp (°C)	Derivative mp (°C)				
		Semicarbazone	2,4-Dinitrophenylhydrazone	4-Nitrophenylhydrazone	Phenylhydrazone	Oxime
2-Aminoacetophenone	20	290d			108	109
Acetophenone (methyl phenyl ketone)	20	203	250; 237	185	105	60
2-Chloroacetophenone	20	201	231	239	114	95
1-Phenyl-1-hexanone (pentyl phenyl ketone; amyl phenyl ketone)	25	133	168			
1-Phenyl-2-propanone (benzyl methyl ketone; phenylacetone)	27	199	156	145	87	70
2-Nitroacetophenone	27	210	154			117
2,6-Dimethyl-2,5-heptadiene-4-one (phorone)	28	186; 221	118			48
4-Methylacetophenone	28	205	260	198	97	88
2-Hydroxyacetophenone (*o*-acetylphenol)	28	210	212		110	118
2,6-Dimethyl-2,5-heptadiene-4-one (phorone; diisopropylideneacetone)	28	186; 221	112			48
2-Tridecanone (methyl undecyl ketone)	28	126	69	102		57
4-Cyclohexylcyclohexanone	31	216	137			105
2-Acetylfuran (2-furyl methyl ketone)	33	150	220	186	86	104
3-Acetylpropanoic acid (levulinic acid)	33	187	206	175	108	46
Methyl 1-naphthyl ketone (α-acetylnaphthalene)	34	235; 289	255		149	140
1,3-Diphenyl-2-propanone (dibenzyl ketone; 1,3-diphenylacetone)	35	146; 126	100		129	125
2,2,6,6-Tetramethyl-4-piperidone	35	220				153
1-(4-Chlorophenyl)-1-propanone (*p*-chloropropiophenone)	36	177	222			63
4-Methoxyacetophenone	38	198	220; 232	196	142	87
Furfuralacetone	39		241		132	
Propiopiperone (3,4-methylenedioxypropiophenone)	39	188			97	104
2-Hydroxybenzophenone	39; 153				155	143
4,4-Dimethylcyclohexanone	41	204			107	
Benzylidenepropane	41	186	227	166		
4-Phenyl-3-butene-2-one (benzalacetone)	41	187	227	166	157	116
1-Indanone (α-hydrindone)	42	239	258	235	135	146
2,4-Dichloroacetophenone	42	208				152
1-(3-Aminophenyl)-1-propanone (*m*-aminopropiophenone)	42	197				113

(Continued)

TABLE AII.29 Ketones (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)				
		Semicarbazone	2,4-Dinitrophenylhydrazone	4-Nitrophenylhydrazone	Phenylhydrazone	Oxime
4-Phenyl-3-buten-2-one (methyl styryl ketone)	42	198; 142	227	167	159	116; 87
2-Isopropyl-5-methyl-1,4-benzoquinone (thymoquinone)	45	202 (mono) 237 (di)	180[a] (mono) 162		93[a]	162 (mono)
1,3-Dichloropropanone (1,3-dichloroacetone)	45	120	133			
1-(4-Bromophenyl)-1-propanone (*p*-bromopropiophenone)	46	171				91
1-Phenyl-1-dodecanone (phenyl undecyl ketone; laurophenone)	47	95				64
1-(2-Aminophenyl)-1-propanone (*o*-aminopropiophenone)	47	190				89
Benzophenone (diphenyl ketone)	49	167	239	159	138	144
2,4,6-Heptanetrione (diacetylacetone)	49	203 (mono)			142 (di)	69 (di)
5-Phenoxy-2-pentanone (methyl 3-phenoxypropyl ketone)	50	110	110			
9-Heptadecanone (dioctyl ketone)	50			54		112
α-Bromoacetophenone (phenacyl bromide)	51	146	220			97
4-Bromoacetophenone	51	208	237	248	126	129
3,4-Dimethoxyacetophenone	51	218	207	227	131	140
Methyl 2-naphthyl ketone (β-acetylnaphthalene)	54	237	262		177	149
1-Chloro-4-phenyl-2-butanone (chloromethyl 2-phenylethyl ketone)	54	156	147			89
2-Benzoylthiophene (phenyl 2-thienyl ketone)	56	197				93
2-Nonadecanone (heptadecyl methyl ketone)	56	126				77
2-Chloro-1,4-benzoquinone	57	185d				184; 148d
2-Indanone	59	218		232		155
α-Chloroacetophenone (phenacyl chloride)	59	156	215			89
1-Phenyl-2-propanone (deoxybenzoin; benzyl phenyl ketone)	60	148	204	163	116	98
1-(2-Naphthyl)-1-propanone (ethyl β-naphthyl ketone)	60	202				133
4-Methylbenzophenone (phenyl *p*-tolyl ketone)	60	122	202		109	154; 136; 115
1-Phenyl-1,3-butadione (benzoylacetone; methyl phenacyl ketone)	61		151	101	153	

(Continued)

TABLE AII.29 Ketones (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)				
		Semicarbazone	2,4-Dinitrophenylhydrazone	4-Nitrophenylhydrazone	Phenylhydrazone	Oxime
1,1-Diphenyl-2-propanone (1,1-diphenylacetone)	61	170			131	165
1,3-Diphenyl-2-propene-1-one (benzalacetophenone; phenyl styryl ketone; chalone)	62	168; 180	248; 208		120	75; 140
4-Methoxybenzophenone (*p*-anisyl phenyl ketone)	63		180; 228	199	132; 90	116; 138
2-Phenylcyclohexanone	63	90	139			169
Benzoylformic acid (phenylglyoxylic acid)	66		197			127(α) 115(β)
2,2′-Dimethylbenzophenone (di-*o*-tolyl ketone)	67		190			105
2-Methyl-1,4-benzoquinone (*p*-toluquinone)	68	179 (mono) 240 (di)	128[a] 269 (di)		130[a]	135 (mono) 220d (di)
3,5-Dibromoacetophenone	68	268			110	
6-Phenyl-5-hexene-2,4-dione (cinnamalacetone)	68	186	223		180	153
12-Tricosanone (laurone; diundecyl ketone)	69	179				40
1,3-Dihydroxy-2-propanone (dihydroxyacetone)	72		278	160		84
3-Acetylphenanthrene	72	230				194
4-(4-Methoxyphenyl)-3-buten-2-one (4-methoxybenzalacetone; anisalacetone)	73		229			120
1,3-Diphenyl-1-propanone (benzylacetophenone)	73	144				87
9-Acetylphenanthrene	74	201				155
1-Naphthyl phenyl ketone	76	385	247			161
2-Benzoylfuryl methyl ketone	76	207			154	
2-Naphthoxy-2-propanone (β-naphthoxyacetone)	78	203			154	123
4-Phenylcyclohexanone	78	212; 229				110
4-Chlorobenzophenone	78		185		106	163; 106
1,4-Cyclohexanedione	79	222 (mono) 231 (di)	240			188
1,3-Diphenyl-1,3-propadione (dibenzoylmethane; benzoylacetophenone; phenacyl phenyl ketone)	81	205			105 (mono)	165 (mono)
3-Nitroacetophenone	81	259	232	135	135	132
4-Bromobenzophenone	82	350	230		126	117; 169

(Continued)

TABLE AII.29 Ketones (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)				
		Semicarbazone	2,4-Dinitrophenylhydrazone	4-Nitrophenylhydrazone	Phenylhydrazone	Oxime
Fluorene (diphenylene ketone; 9-oxofluorene)	83	234	284	269	152	196
α-Hydroxyacetophenone (phenacyl ketone)	86	146			112	70
4,4'-Dimethylbenzophenone (di-*p*-tolyl ketone)	95	144	229; 219		100	163
Benzil (dibenzoyl)	95	182 (mono) 244 (di)	189 (mono) 189 (di) 314 (di)	193 (mono) 290 (di) 192 (di)	134 (mono) 225 (di)	140 (mono) 237 (di)
3-Hydroxyacetophenone (*m*-acetylphenol)	96	191	261			
2,3-Dihydroxyacetophenone (3-acetylcatechol)	98	167				97
3-Aminoacetophenone	99	196				194; 148
3-Benzoylpropenoic acid (3-benzoylacrylic acid)	99	190			197	168d
2-Acetyl-1-hydroxynaphthalene	102	250			137	169
1,5-Diphenyl-4-pentene-1,3-dione (cinnamacetophenone)	102		222	135		
2-Methyl-1,4-naphthoquinone	106	178 (4-) 247 (di)	299d (mono)			160 (mono) 168 (di)
Benzoylnitromethane	106				106	96
4-Aminoacetophenone	106	250	267			148
α,4-Dibromoacetophenone (4-bromophenacyl bromide)	108		218			115
4-Hydroxyacetophenone (*p*-acetylphenol)	109	199	210; 225; 261		151	145
Piperonalacetone	111	217 (α) 168 (β)			163	186
1,5-Diphenyl-1,4-pentadien-3-one (dibenzalacetone; dibenzylidenepropanone)	112	190	180	173	153	144
1,4-Benzoquinone (quinone)	116	166, 178 (mono) 243 (di)	186 (mono) 231[a] (di) 240		152[a]	144 (mono) 240 (di)
3-Benzoylpropanoic acid	116	181	191			
α-Hydroxyacetophenone (phenacyl alcohol; benzoyl carbinol)	118	147			112	70
1,2-Naphthoquinone	120; 147	184 (mono)	162	251, 236 (mono)	138[a] (mono)	110, 164 (mono) 169 (di)
Acenaphthenone (1-oxoacenaphthene)	121				90	175; 184, 222 (di)

(Continued)

TABLE AII.29 Ketones (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)				
		Semicarbazone	2,4-Dinitrophenylhydrazone	4-Nitrophenylhydrazone	Phenylhydrazone	Oxime
4-Phenylacetophenone (*p*-acetylbiphenyl; methyl *p*-xenyl ketone)	121		242			187
1,4-Naphthoquinone (α-naphthoquinone)	125	247 (mono)	278[a] (mono) 198	279 (mono)	206[a] (mono)	198 (mono) 207 (di)
2,5-Dimethyl-1,4-benzoquinone (*p*-xylo-*p*-quinone)	125				124; 155	168 (mono) 272, 254 (di)
1,5-Di(4-methoxyphenyl)-3-pentanone (dianisalacetone)	129		83			148
4-(4-Hydroxy-3-methoxyphenyl)-3-buten-2-one(vanillidineacetone; 4-hydroxy-3-methoxystyryl methyl ketone)	130		230		128	
2,6-Dibromo-1,4-benzoquinone	131	225 (mono)				170 (mono)
4,4′-Dimethoxydibenzoyl (anisil; 4,4′-dimethoxybenzil)	133	255 (di)				133 (mono) 195, 217 (di)
Benzoylphenylmethanol (benzoin)	135	206d	245		159 (α) 106 (β)	152 (α) 99 (β)
3,4,5-Tibromoacetophenone	135	265			134	
Furoin	135		217		81	161 (α) 102 (β)
4-Hydroxybenzophenone (*p*-benzoylphenol)	135	194	244		144	152
2-Acetylphenanthrene	143	260			188	
1,9-Diphenyl-1,8-nonadien-3,5,7-trione (dicinnamalacetone)	144		196		166	
1,2-Naphthoquinone	146	184 (mono)		235	138	162 (2-) 109 (1-) 169 (di)
1,2-Dibenzoylethane	147		265 (di)		116 (mono) 179 (di)	204
2,4-Dihydroxyacetophenone (resacetophenone)	147	220	208; 218; 244		159	203
3,5-Dihydroxyacetophenone	148	206		237		
4,4′-Dichlorobenzophenone	148		240			135
Furil	165		215	199	184	100 (di)
Quinhydrone	171				152	161
2,3,4-Trihydroxyacetophenone (Gallacetophenone)	173	225	199			163
4,4′-Di-(dimethylamino)benzophenone (Michler's ketone)	174		273		175	233

(Continued)

TABLE AII.29 Ketones (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)				
		Semicarbazone	2,4-Dinitrophenylhydrazone	4-Nitrophenylhydrazone	Phenylhydrazone	Oxime
Diphenylene ketone oxide (xanthone)	174				152	161
(±)-Camphor	178	237; 248	164; 177	217	233	118
(+)-Camphor	179	238	177		233	118
3,4,5-Trihydroxyacetophenone	188	217		260		
7-Isopropyl-1-methyl-9,10-phenanthraquinone (retenequinone)	197	200		223	160	131
Camphorquinone	199	236 (α) 147	36 (mono) 190[a] (di)	239	170,[a] 190	170, 153, 115 (mono) 201, 248, 140 194 (di)
2,5-Dihydroxyacetophenone (quinacetophenone)	202			216		150
9,10-Phenanthrenequinone	208	220d (mono)	313d (mono) 162	245 (mono)	165[a] (mono)	158 (mono) 202 (di)
Ninhydrin (triketohydrindene hydrate)	243				208	201
Acenaphthenequinone	261	193 (mono) 271 (di)	222 (di)	247 (mono)	179 (mono) 219 (di)	230 (mono)
3-Bromo-9,10-phenanthraquinone	268	242 (mono)			177 (mono)	198 (mono) 212 (di)
Aceanthrenequinone (3,4-benzacenaphthenequinone)	270				203 (mono)	251 (mono)
9,10-Anthraquinone	286		183[a]		183	224 (mono)

[a]These melting points are those of the addition compounds of the quinones and substituted hydrazines. The products are not true hydrazones.

TABLE AII.30 Nitriles (Liquids)

Name of Compound	bp (°C)	Acid Derivative mp (°C)			Amine Derivative mp (°C)			Derivative mp (°C)
		Acid	Amide	Anilide	Benzamide	Benzenesulfonamide	Phenylthiourea	α-(Imidioylthio)-acetic Acid Hydrochloride
Propynenitrile (cyanoacetylene)	42	18	62	87				
Propenenitrile (acrylonitrile; vinyl cyanide)	78		85	105				
Fluoroethanenitrile (fluoroacetonitrile; fluoromethyl cyanide)	80	33	77					
Ethanenitrile (acetonitrile; methyl cyanide)	82		82	114	71	58	106; 135	115
Trichloroethanenitrile (trichloroacetonitrile; trichloromethyl cyanide)	86	58	141	97				
Propanenitrile (propionitrile; ethyl cyanide)	97		79	106	84	36	63	128
2,2-Dimethylpropanenitrile (trimethylacetonitrile; *tert*-butyl cyanide)	106	35	154	129				
2-Methylpropanenitrile (isobutyronitrile; isopropyl cyanide)	108		129	110	57	53	82	137
2-Chloro-2-methylpropanenitrile (2-chloroisobutyronitrile; α-chloroisopropyl cyanide)	116	31	70					
Butanenitrile (butyronitrile; propyl cyanide)	117		116	96	42	65	136	
E-2-Butenenitrile (*trans*-crotononitrile)	119	72	158	115		110		
3-Butenenitrile (vinylacetonitrile; allyl cyanide)	119		73	58		39	127; 57	
Methoxyethanenitrile (methoxyacetonitrile; methoxymethyl cyanide)	120		96	58				
2-Hydroxy-2-methylpropanenitrile (2-hydroxyisobutyronitrile; acetone cyanohydrin)	120	79	98	136				
2-Methylbutanenitrile (2-methylbutyronitrile; α-methylpropyl cyanide)	126		112	110				
Chloroethanenitrile (chloroacetonitrile; chloromethyl cyanide)	127	63	120	137				
3-Methylbutanenitrile (isovaleronitrile; isobutyl cyanide)	130		136	113			102	133

(Continued)

TABLE AII.30 Nitriles (Liquids) *(Continued)*

Name of Compound	bp (°C)	Acid Derivative mp (°C)			Amine Derivative mp (°C)			Derivative mp (°C)
		Acid	Amide	Anilide	Benz-amide	Ben-zene-sulfon-amide	Phenyl-thio-urea	α-(Imidi-oylthio)-acetic Acid Hydro-chloride
Z-2-Chloro-2-butenenitrile (2-chlorocrotononitrile)	136	99	212					
2,4-Pentadienonitrile	138	72	124					
2-Methyl-2-butenenitrile (2-methylcrotononitrile)	138	64	76	77				
2-Bromo-2-methylpropanenitrile (2-bromoisobutyronitrile; α-bromoisopropyl cyanide)	140	49	148	83				
2,3-Dicyanothiophene (thiophene-2,3-dicarbonitrile)	140	274	228 (di)					
Pentanenitrile (valeronitrile; butyl cyanide)	141		106	63			69	138
3,3-Dimethylpropenenitrile (3,3-dimethylacrylonitrile; β,β-dimethylvinyl cyanide)	142	70	108; 66	127			106	
2-Chlorobutanenitrile (2-chlorobutyronitrile; α-chloropropyl cyanide)	143		76	75				
2-Furancarbonitrile (α-furonitrile; 2-furyl cyanide)	147	134	142	124				
2-Methyl-3-oxobutanenitrile (2-methylacetoacetonitrile)	147	73	140					
Cyclobutanecarbonitrile (cyclobutyl cyanide)	150		155	113				
4-Methylpentanenitrile (isocapronitrile; isopentyl cyanide)	155		121	112				128
2-Methylhexanenitrile (2-methylcapronitrile; α-methylpentyl cyanide)	165		72	98				
Hexanenitrile (capronitrile; pentyl cyanide)	165		100	95	40	96	77	136
Z-Chlorobutenedinitrile (chlorofumaronitrile)	172	192		186 (di)				
3-Chlorobutanenitrile (3-chlorobutyronitrile; β-chloropropyl cyanide)	176	44		90				
3-Chloropropanenitrile (3-chloropropionitrile; β-chloroethyl cyanide)	178	41		119				
3-Cyanothiophene (thiophene-3-carbonitrile)	179; 205	138	180					

(Continued)

TABLE AII.30 Nitriles (Liquids) *(Continued)*

Name of Compound	bp (°C)	Acid Derivative mp (°C)			Amine Derivative mp (°C)			Derivative mp (°C)
		Acid	Amide	Anilide	Benzamide	Benzenesulfonamide	Phenylthiourea	α-(Imidioylthio)-acetic Acid Hydrochloride
5-Methylhexanenitrile (5-methylcapronitrile; isohexyl cyanide)	180		104	75				
2-Hydroxyethanenitrile (glycolonitrile; α-hydroxyacetonitrile formaldehyde cyanohydrin)	183	80	120	97				
(±)-2-Hydroxypropanenitrile [(±)-lactonitrile; α-hydroxypropionitrile; acetaldehyde cyanohydrin]	184		79	59				
Heptanenitrile (hexyl cyanide)	187		95	71			75	133
Benzonitrile (phenyl cyanide)	190	122	129	162	105	88	156	124
2-Cyanothiophene (thiophene-2-carbonitrile)	192	130; 192	180	140				
2-Octynenitrile	196		91	44				
4-Chlorobutanenitrile (4-chlorobutyronitrile; β-chloropropyl cyanide)	197	16	89	70				
2-Methylbenzonitrile (*o*-tolunitrile; *o*-tolyl cyanide)	205	104	142	125	88			
2,3,3-Trimethyl-1-cyclopentene-1-carbonitrile (β-campholytonitrile)	205; 225	135	130	104				
Octanenitrile (caprylnitrile; heptyl cyanide)	206; 199	16	110	57				134
1,1-Dicyanopropane (ethyl malononitrile)	206	112	216 (di)					
1,1-Dicyanobutane (propylmalonitrile)	210	96	184 (di)	198 (di)				
3-Methylbenzonitrile (*m*-tolunitrile; *m*-tolyl cyanide)	212	113	96	126				168
Cyclohexylethanenitrile (cyclohexylacetonitrile; cyclohexylmethyl cyanide)	215	33	172		81			
Dibenzylethanenitrile (dibenzylacetonitrile; dibenzylmethyl cyanide)	215	89	129	155				
2-Cyanopyridine (picolinonitrile; 2-pyridinecarbonitrile)	215		107	76				
4-Methylbenzonitrile (*p*-tolunitrile; *p*-tolyl cyanide)	218		165	148	137			181

(Continued)

TABLE AII.30 Nitriles (Liquids) *(Continued)*

Name of Compound	bp (°C)	Acid Derivative mp (°C)			Amine Derivative mp (°C)			Derivative mp (°C)
		Acid	Amide	Anilide	Benzamide	Benzenesulfonamide	Phenylthiourea	α-(Imidioylthio)-acetic Acid Hydrochloride
1,1-Dicyano-3-methylbutane (isobutylmalonitrile)	222	108	196 (di)					
Nonanenitrile (octyl cyanide)	224	15	99	57	49			
Z-2-Phenyl-2-butenenitrile (2-phenyl-2-crotononitrile)	226	136	99					
Phenylethanenitrile (phenylacetonitrile; benzyl cyanide)	234	77	157	118	116	69	135	146
Phenoxyethanenitrile (phenoxyacetonitrile; phenoxymethyl cyanide)	240	99	102					
3-Methylphenylethanenitrile (*m*-tolylacetonitrile; *m*-xylyl cyanide; *m*-tolylmethyl cyanide)	241	61	141					
4-Methylphenylethanenitrile (*p*-tolylacetonitrile; *p*-xylyl cyanide; *p*-tolylmethyl cyanide)	243	94	185		96			
4-(1-Methylethyl)benzonitrile (*p*-isopropylbenzonitrile; *p*-isopropylphenyl cyanide)	244	118	153; 133					
2-Methylphenylethanenitrile (*o*-tolylacetonitrile; *o*-xylyl cyanide; *o*-tolylmethyl cyanide)	244	89	161					
Decanenitrile (nonyl cyanide)	245	31	108	70				
3-Methyl-2-phenylbutanenitrile (3-methyl-2-phenylbutyronitrile; β-methyl-α-phenylpropyl cyanide)	249	62	112	133				
2-Chlorophenylethanenitrile (*o*-chlorobenzyl cyanide; *o*-chlorophenylacetonitrile)	251		175	139				
1,2-Dicyanopropane (methyl succinonitrile)	254	115	225 (di)	200 (di)	154			
1-Undecanenitrile (1-hendecanonitrile; decyl cyanide)	254	28	99	71				
2-Phenylpentanenitrile (2-phenylvaleronitrile; α-phenylbutyl cyanide)	255	58	85					
3-Phenyl-2-propenenitrile (cinnamonitrile)	256		153; 109	147				
2-Methoxybenzonitrile (*o*-methoxyphenylcyanide)	256		129	131				

(Continued)

TABLE AII.30 Nitriles (Liquids) *(Continued)*

Name of Compound	bp (°C)	Acid Derivative mp (°C)			Amine Derivative mp (°C)			Derivative mp (°C)
		Acid	Amide	Anilide	Benz-amide	Ben-zene-sulfon-amide	Phenyl-thio-urea	α-(Imidi-oylthio)-acetic Acid Hydro-chloride
3-Phenylpropanenitrile (3-phenylpropionitrile; β-phenylethyl cyanide)	261	49	105	98	58			
N-Cyano-*N*-methylaniline (*N*-methylanilinonitrile)	266	100	163					
4-Chlorophenylethanenitrile (*p*-chlorobenzyl cyanide; *p*-chlorophenylacetonitrile)	267		175	165				
3-(2-Chlorophenyl)propanenitrile [3-(*o*-chlorophenyl)propionitrile; β-(*o*-chlorophenyl)ethyl cyanide]	268	97	119					
1,3-Dicyano-2-methylpropane	271	79	176 (di)					
Dodecanenitrile (undecyl cyanide; lauronitrile)	277	44	110	78				
Pentanedinitrile (glutaronitrile; 1,3-dicyanopropane; trimethylene cyanide)	286	97	175	224	135 (di)	119	148	
Hexanedinitrile (adiponitrile; 1,4-dicyanobutane; tetramethylene cyanide)	295	153	220	239	158 (di)	154 (di)		
1-Naphthonitrile (1-cyanonaphthalene)	302				148			
Pentanedecanenitrile	322		102	78				

TABLE AII.31 Nitriles (Solids)

Name of Compound	mp (°C)	Acid Derivative mp (°C)			Amine Derivative mp (°C)	
		Acid	Amide	Anilide	Benzamide	Benzenesulfonamide
2-Cyanodiphenylmethane	19	117	163			
Tetradecanenitrile	20	54	103	82		
3-Phenyl-2-propenenitrile (cinnamonitrile)	20	133	153; 109	147		
3,3,3-Trichloropropenenitrile (trichloroacrylonitrile; trichlorovinyl cyanide)	20	76	98; 87	98		
(±)-2-Hydroxy-2-phenylethanenitrile [(±)-mandelonitrile; benzaldehyde cyanohydrin; 2-hydroxy-2-phenylacetonitrile; α-hydroxybenzyl cyanide]	22	119	134	152	149	
Pentanedecanenitrile	23	52	102	78		
2-Methoxybenzonitrile (*o*-methoxyphenyl cyanide)	25	101	129	131		
2-Chlorophenylethanenitrile (*o*-chlorophenylacetonitrile; *o*-chlorobenzyl cyanide)	25	95	175	139		
1,1-Dicyanoethane (methylmalonitrile)	26	138	217 (di)	182 (di)		
2-Cyanopyridine (picolinonitrile; 2-pyridinecarbonitrile)	26	137	107	76		
4-Methylbenzonitrile (*p*-tolunitrile; *p*-tolyl cyanide)	29	180	165	148	137	
D-2-Hydroxy-2-phenylethanenitrile (D-mandelonitrile; D-2-hydroxy-2-phenylacetonitrile; D-α-hydroxybenzyl cyanide)	29	133	123			
2-Bromophenylethanenitrile (*o*-bromophenylacetonitrile; *o*-bromobenzyl cyanide)	29	84	148			
4-Chlorophenylethanenitrile (*p*-chlorophenylacetonitrile; *p*-chlorobenzyl cyanide)	30	105	175	165		
Propanedinitrile (dicyanomethane; malonitrile; methylene cyanide)	30	135	170		140	96
Hexadecanenitrile	31	63	107	90		
Z-Butenedinitrile (maleonitrile; *cis*-1,2-dicyanoethylene; *cis*-1,2-dicyanoethene)	31	130	181	187	179 (di)	155 (di)
2,2-Dicyanopropane (dimethylmalonitrile)	32	193	269 (di)	204	152 (di)	

(Continued)

TABLE AII.31 Nitriles (Solids) *(Continued)*

Name of Compound	mp (°C)	Acid Derivative mp (°C)			Amine Derivative mp (°C)	
		Acid	Amide	Anilide	Benzamide	Benzenesulfonamide
2,2-Dimethylpropanenitrile (*tert*-butylacetonitrile; neopentyl cyanide)	33		132	131		
1-Naphthylethanenitrile (α-naphthylacetonitrile; α-naphthylmethyl cyanide)	33	131	154; 180			
4,4-Dicyanoheptane (dipropylmalononitrile)	34 (anhyd)	161	214 (di)	168 (di)	154 (di)	
Heptadecanenitrile	34	61	106		91	
2-Cyanopropanoic acid (2-cyanopropionic acid)	35	135; 120	206 (di)	182 (di); 214		
4-Fluorobenzonitrile (*p*-fluorophenyl cyanide)	35	183	155			
Indole-3-ethanenitrile (indole-3-acetonitrile)	36	165; 199	151	150	138	
1-Naphthonitrile (α-cyanonaphthalene)	37	162	202			148
3-Bromobenzonitrile (*m*-bromophenyl cyanide)	38	155	155		136	
2-(Phenylamino)butanenitrile [2-(*N*-anilino) butanenitrile; 2-(*N*-anilino)butyronitrile]	39	141	123	92		
E-3-(2-Chlorophenyl)-2-propenenitrile (*trans*-*o*-chlorocinnamonitrile)	40	212	168	176		
3-Chlorobenzonitrile (*m*-chlorophenyl cyanide)	41	158	134	125	214	
2-Chlorobenzonitrile (*o*-chlorophenyl cyanide)	43	141	142	118	117	
4-Chloro-2-hydroxy-2-phenylethanenitrile (4-chloromandelonitrile; 4-chloro-2-hydroxy-2-phenylacetonitrile; *p*-chloro-α-hydroxybenzyl cyanide)	43	122; 112	123			
Octadecanenitrile	43	70	109	95		
Nonadecanenitrile	43	69	110	96		
4-Cyanobutanoic acid (4-cyanobutyric acid)	45	98	183	222 (di)	105	
3,3-Dicyanopentane (diethylmalonitrile)	45	125	146 (mono) 224 (di)			
R,*S*-2,3-Dimethylbutanedinitrile (*meso*-2,3-dimethylsuccinonitrile)	46	209; 198	313 (di)	235 (di)		

(Continued)

TABLE AII.31 Nitriles (Solids) *(Continued)*

Name of Compound	mp (°C)	Acid Derivative mp (°C)			Amine Derivative mp (°C)	
		Acid	Amide	Anilide	Benzamide	Benzenesulfonamide
4-Aminophenylethanenitrile (*p*-aminophenylacetonitrile; 4-aminobenzyl cyanide)	46	199	162			
3-Bromo-4-methylbenzonitrile (3-bromo-4-tolunitrile; 3-bromo-4-tolyl cyanide)	47	140	137			
4-Bromophenylethanenitrile (*p*-bromophenylacetonitrile; *p*-bromobenzyl cyanide)	47	114	194			
2-(Phenylamino)ethanenitrile [*N*-anilinoacetonitrile; 2-(phenylamino)acetonitrile]	48	128	136	113		
3,3-Diphenylpropenenitrile (3,3-diphenylacrylonitrile; β-phenylcinnamonitrile; β,β-diphenylvinyl cyanide)	49	167		131		
3-Bromo-2-hydroxybenzonitrile (3-bromo-2-hydroxyphenyl cyanide)	50	184	165			
4,4-Dicyanoheptane (dipropylmalonitrile)	50 (hyd)	161	214 (di)	169 (di)	154 (di)	
3-Cyanopropanoic acid (3-cyanopropionic acid)	50	235	157 (mono) 269 (di)	149 (mono) 230 (di)	80	
Eicosanonitrile	50	77	109	92		
3-Cyanopyridine (nicotinonitrile)	50	232	122	85; 132	132	
2-(Phenylamino)pentanenitrile [2-(*N*-anilino) valeronitrile; 2-(*N*-anilino)butyl cyanide]	51	148	99			
E-2,3-Diphenylpropenenitrile (*trans*-2,3-diphenylacrylonitrile; *trans*-α,β-diphenylvinyl cyanide)	51	172	127	141		
2-Aminobenzonitrile (anthranilonitrile; *o*-aminophenyl cyanide)	51	147	111	131	167	
5-Cyanothiazole	53	218	186			
2-Bromobenzonitrile (*o*-bromophenyl cyanide)	53	150	156			
3-Aminobenzonitrile (*m*-aminophenyl cyanide)	54	174	79	114		
2-Iodobenzonitrile (*o*-iodophenyl cyanide)	55	162	184		154	
2,4,6-Trimethylbenzonitrile (2,4,6-trimethylphenyl cyanide)	55	155	188		154	

(Continued)

TABLE AII.31 Nitriles (Solids) *(Continued)*

Name of Compound	mp (°C)	Acid Derivative mp (°C)			Amine Derivative mp (°C)	
		Acid	Amide	Anilide	Benzamide	Benzenesulfonamide
2-Amino-2-phenylethanenitrile (α-aminobenzyl cyanide; 2-amino-2-phenylacetonitrile)	55	256	132		225 (di)	
Butanedinitrile (succinonitrile; 1,2-dicyanoethane; ethylene cyanide)	57	188	260	230	177	
2-Iodo-4-methylbenzonitrile (2-iodo-4-tolunitrile; 2-iodo-4-tolyl cyanide)	58	206	167			
(±)-2,3-Dimethylbutanedinitrile [(±)-2,3-dimethylsuccinonitrile; (±)-1,2-dicyano-1,2-dimethylethane]	59	135	149 (mono) 244 (di)	222 (di)		
4-Methoxybenzonitrile (p-methoxyphenyl cyanide)	62	186	163	169		
2-Chloro-4-methylbenzonitrile (2-chloro-4-tolunitrile; 2-chloro-4-tolyl cyanide)	62	156	182			
2,4-Dichlorobenzonitrile (2,4-dichlorophenyl cyanide)	62	164	194			
4-Methoxy-3-phenyl-2-propenenitrile (p-methoxycinnamonitrile)	64	170	186			
Bromopropanedinitrile (bromomalonitrile; bromomethylene cyanide)	66	113	181			
2-Naphthonitrile (β-cyanonaphthalene)	66	184	195			
2-Cyano-2-ethylbutanoic acid (diethylcyanoacetic acid)	66; 57	125	146 (mono) 224 (di)			
Cyanoethanoic acid (cyanoacetic acid)	66	136	170; 123	227; 198	120	
2-Chloro-3-methylbenzonitrile (2-chloro-3-tolunitrile; 2-chloro-3-tolyl cyanide)	67	132	124			
4-Chloro-2-methylbenzonitrile (4-chloro-2-tolunitrile; 4-chloro-2-tolyl cyanide)	67	172	183			
2-Cyanobenzyl cyanide (phenylmalononitrile; phenylmethylene cyanide)	69	153	233			
5-Bromo-2-methylbenzonitrile (5-bromo-2-tolunitrile; 5-bromo-2-tolyl cyanide)	70	187	170			
4-Hydroxyphenylethanenitrile (p-hydroxyphenylacetonitrile; p-hydroxybenzyl cyanide)	70	150	175			

(Continued)

TABLE AII.31 Nitriles (Solids) *(Continued)*

Name of Compound	mp (°C)	Acid Derivative mp (°C)			Amine Derivative mp (°C)	
		Acid	Amide	Anilide	Benzamide	Benzenesulfonamide
2-Methyl-6-nitrobenzonitrile (6-nitro-2-tolunitrile; 6-nitro-2-tolyl cyanide)	70	184	163			
3,4-Dichlorobenzonitrile (3,4-dichlorophenyl cyanide)	72	209	133			
2-Aminophenylethanenitrile (*o*-aminophenylacetonitrile; *o*-aminobenzyl cyanide)	72	119	93			
2,2-Diphenylpentanedinitrile (2,2-diphenylglutaronitrile; α,α-diphenyltrimethylene cyanide)	72	197; 183	144 (mono)			
1,2,2,3-Tetramethylcyclopentene-1-carbonitrile (campholic acid)	73	106	80	91	98	
2,2-Diphenylethanenitrile (2,2-diphenylacetonitrile; α-phenylbenzyl cyanide)	75	148	168	180	145	
4-Cyano-*N*,*N*-dimethylaniline	76	243	206	183		
Dicyanodimethylamine [bis(cyanomethyl)amine]	77	247; 225	143 (di)	141 (di)	166 (tri)	
4-Cyanobenzyl chloride (α-chloro-*p*-tolunitrile; α-chloro-*p*-tolyl cyanide)	80	203	173			
3-Methyl-6-nitrobenzonitrile (6-nitro-3-tolunitrile; 6-nitro-3-tolyl cyanide)	80	219	151			
3-Cyanobenzaldehyde (*m*-formylbenzonitrile)	81	175	190			
Benzoylethanenitrile (benzoylacetonitrile; benzoylmethyl cyanide)	81	104	113	108		
4-Cyanopyridine	83	315	156			
6-Chloro-2-methylbenzonitrile (6-chloro-2-tolunitrile; 6-chloro-2-tolyl cyanide)	83	102	167			
2,3,4,5-Tetrachlorobenzonitrile (2,3,4,5-tetrachlorophenyl cyanide)	84	195	208	197		
8-Cyanoquinoline	84	187	173			
3-Methyl-2-nitrobenzonitrile (2-nitro-3-tolunitrile; 2-nitro-3-tolyl cyanide)	84	223	192			
4-Aminobenzonitrile (*p*-cyanoaniline; *p*-aminophenyl cyanide)	86	188	183			

(Continued)

TABLE AII.31 Nitriles (Solids) *(Continued)*

Name of Compound	mp (°C)	Acid Derivative mp (°C)			Amine Derivative mp (°C)	
		Acid	Amide	Anilide	Benzamide	Benzenesulfonamide
Z-2,3-Diphenylpropenenitrile (*cis*-2,3-diphenylacrylonitrile; *cis*-α,β-diphenylvinyl cyanide)	86	138	168	179		
4-Cyanobiphenyl	86	228	223			
2-Naphthylethanenitrile (β-naphthylacetonitrile; β-naphthylmethyl cyanide)	86	142	200			
1-Cyano-2-phenylpropenenitrile (1-cyano-2-phenylacrylonitrile; benzalmalononitrile; 1-cyano-2-phenylvinyl cyanide)	87	196	190 (di)			
5-Bromo-2,4-dimethylbenzonitrile (5-bromo-2,4-dimethylphenyl cyanide)	90	181	198			
2,6-Dimethylbenzonitrile (2,6-dimethylphenyl cyanide)	91	116	139; 125			
2,4-Dibromobenzonitrile (2,4-dibromophenyl cyanide)	92	174	198			
2-(2-Nitrophenyl)propenenitrile [β-(2-nitrophenyl)acrylonitrile; β-(2-nitrophenyl)vinyl cyanide]	92	147 (*cis*) 240 (*trans*)	185			
2-(Phenylamino)propanenitrile [2-(*N*-anilino)propionitrile; 2-(*N*-anilino)ethyl cyanide]	92	162	144	127		
2-Methyl-2-(phenylamino)-propanenitrile [2-(*N*-anilo)-isobutyronitrile; 2-(*N*-anilino)isopropyl cyanide]	94	185	136	155		
3-Methyl-4-nitrobenzonitrile (4-nitro-3-tolunitrile; 4-nitro-3-tolyl cyanide)	94	134	177			
2-Cyanoquinoline	94	157	133			
E-Butenedinitrile (fumaronitrile; *trans*-1,2-dicyanoethene)	96	300	266	314		
4-Chlorobenzonitrile (*p*-chlorophenyl cyanide)	96	240	179	194	140	
4-Cyanopentanenitrile (4-cyanovaleric acid; 2-methylglutaromononitrile)	96	79	176 (di)			
3,5-Dibromobenzonitrile (3,5-dibromophenyl cyanide)	97	220	187			
9-Phenanthrylethanenitrile (9-phenanthrylacetonitrile)	97	224	252			

(Continued)

TABLE AII.31 Nitriles (Solids) *(Continued)*

Name of Compound	mp (°C)	Acid Derivative mp (°C)			Amine Derivative mp (°C)	
		Acid	Amide	Anilide	Benz-amide	Ben-zene-sulfon-amide
4-Chloro-2-nitrobenzonitrile (4-chloro-2-nitrophenyl cyanide)	98	142	172			
2-Hydroxybenzonitrile (*o*-cyanophenol; *o*-hydroxyphenyl cyanide)	98	159	133	135		
4-Cyanotriphenylmethane	100	165		196		
4-Methyl-3-nitrobenzonitrile (3-nitro-4-tolunitrile; 3-nitro-4-tolyl cyanide)	101	165	153			
4-Chloro-3-nitrobenzonitrile (4-chloro-3-nitrophenyl cyanide)	101	182	156	131		
2-Cyano-3-phenylpropanoic acid (2-cyano-3-phenylpropionic acid)	102; 75	121	225			
4-Cyanoquinoline	102	254	181			
2,3,3-Triphenylpropanenitrile (2,3,3-triphenylpropionitrile; α,β,β-triphenylethyl cyanide)	102	223	213			
3-Cyanophenanthrene	102	269	234	217		
4-Bromo-2,5-dimethylbenzonitrile (4-bromo-2,5-dimethylphenyl cyanide)	104	172	210			
3-Methyl-5-nitrobenzonitrile (5-nitro-3-tolunitrile; 5-nitro-3-tolyl cyanide)	105	174	165			
2,4-Dinitrobenzonitrile (2,4-dinitrophenyl cyanide)	105	183	204			
2-Methyl-4-nitrobenzonitrile (4-nitro-2-tolunitrile; 4-nitro-2-tolyl cyanide)	105	179	174			
6-Chloro-3-nitrobenzonitrile (6-chloro-3-nitrophenyl cyanide)	106	165	178			
5-Bromo-2-methyl-3-nitrobenzonitrile (5-bromo-3-nitro-2-tolunitrile; 5-bromo-3-nitro-2-tolyl cyanide)	107	226	235			
4-Methyl-2-nitrobenzonitrile (2-nitro-4-tolunitrile; 2-nitro-4-tolyl cyanide)	107	190	166			
3-Cyanoquinoline	108	275	199			
2-Cyanophenanthrene	109	260	243	218		
2-Methyl-3-nitrobenzonitrile (3-nitro-2-tolunitrile; 3-nitro-2-tolyl cyanide)	110	152	158			
2-Nitrobenzonitrile (*o*-nitrophenyl cyanide)	110	146	176	155		
4-Chloro-1-naphthonitrile (1-chloro-4-cyanonaphthalene)	110	224; 210	236			

(Continued)

TABLE AII.31 Nitriles (Solids) *(Continued)*

Name of Compound	mp (°C)	Acid Derivative mp (°C)			Amine Derivative mp (°C)	
		Acid	Amide	Anilide	Benzamide	Benzenesulfonamide
9-Cyanophenanthrene	111	257	233	218	167	
5-Cyanoacenaphthene (acenaphthene-5-carbonitrile)	111	219	198		184	149
4-Bromobenzonitrile (*p*-bromophenyl cyanide)	112	251	190		143	
4-Hydroxybenzonitrile (*p*-cyanophenol; *p*-hydroxyphenyl cyanide)	113	214	162 (hyd)	197		
2,4,5-Trimethoxybenzonitrile (2,4,5-trimethoxyphenyl cyanide)	114	144	185	155		
4-Nitrophenylethanenitrile (*p*-nitrophenylacetonitrile; *p*-nitrobenzyl cyanide)	116	153	198	198		
6-Bromo-3-nitrobenzonitrile (6-bromo-3-nitrophenyl cyanide)	117	180	198	166		
3-Nitrobenzonitrile (*m*-nitrophenyl cyanide)	118	140	143	154		
2-Hydroxyphenylethanenitrile (*o*-hydroxyphenylacetonitrile; *o*-hydroxybenzyl cyanide)	119	149	118			
4-Bromo-3-nitrobenzonitrile (4-bromo-3-nitrophenyl cyanide)	120	204	156			
4-Cyanoazobenzene	121	241	225			
2,6-Dicyanopyridine (dipicolonitrile)	123; 113	252; 228	302 (di)			
Dibromopropanedinitrile (dibromomalononitrile; dibromodicyanomethane; dibromomethylene cyanide)	124	147	206 (di)			
2-Cyanohexanoic acid	126	101	200 (di)	193 (di)		
1-Cyanoanthracene	126	245	260			
2,2,3-Triphenylpropanenitrile (2,2,3-triphenylpropionitrile; α,α,β-triphenylethyl cyanide)	126	162; 132	111			
1-Cyanophenanthrene	128	233	284	245		
5-Bromo-4-methyl-3-nitrobenzonitrile (5-bromo-3-nitro-4-tolunitrile; 5-bromo-3-nitro-4-tolyl cyanide)	130	206	171			
2,5-Dichlorobenzonitrile (2,5-Dichlorophenyl cyanide)	130	154	155			
2,3-Diphenylbutanenitrile (2,3-diphenylbutyronitrile; α,β-diphenylpropyl cyanide)	130	134; 186	174; 193			

(Continued)

TABLE AII.31 Nitriles (Solids) *(Continued)*

Name of Compound	mp (°C)	Acid Derivative mp (°C)			Amine Derivative mp (°C)	
		Acid	Amide	Anilide	Benz-amide	Ben-zene-sulfon-amide
5-Bromo-4-methyl-2-nitrobenzonitrile (5-bromo-2-nitro-4-tolunitrile; 5-bromo-2-nitro-4-tolyl cyanide)	132	203	191			
2-Hydroxy-3-nitrobenzonitrile (2-cyano-6-nitrophenol; 2-hydroxy-3-nitrophenyl cyanide)	133	148	155			
4-Nitro-1-naphthonitrile (1-cyano-4-nitronaphthalene)	133	221	218			
4-Acetamidobenzonitrile	133	185	177	168		
6-Cyanoquinoline	135	292	174			
3,5-Dichloro-2-hydroxybenzonitrile (3,5-dichloro-2-hydroxyphenyl cyanide)	139	223	209			
4-Cyano-2-phenylquinoline (2-phenyl-4-quinolinonitrile)	140	218	196	198		
3,3,3-Triphenylpropanenitrile (3,3,3-triphenylpropionitrile; β,β,β-triphenylethyl cyanide)	140	177	198			
1,2-Dicyanobenzene (phthalonitrile)	141	206	220 (di)	253 (di)	184 (di)	
8-Nitro-2-naphthonitrile (2-cyano-8-nitronaphthalene)	143	295; 288	218			
5-Chloro-2-cyanonaphthalene (5-chloro-2-cyanonaphthonitrile)	144	270	187	202		
5-Chloro-1-naphthonitrile (5-chloro-1-cyanonaphthalene)	145	245	239			
5-Bromo-1-naphthonitrile (1-bromo-5-cyanonaphthalene)	147	261	241			
4-Nitrobenzonitrile (*p*-nitrophenyl cyanide)	149	241	201	211		
2-Cyano-5-iodonaphthalene (5-iodo-2-naphthonitrile)	149	264	196	203		
2-Cyano-2-propylpentanamide (dipropylcyanoacetamide; 2-cyano-2-propylvaleramide)	153	161	214 (di)	169 (di)		
3-Chloro-4-hydroxybenzonitrile (3-chloro-4-hydroxyphenyl cyanide)	155	170	182			
2,6-Dibromobenzonitrile (2,6-dibromophenyl cyanide)	155	157	209			
5-Chloro-2,4-dinitrobenzonitrile (5-chloro-2,4-dinitrophenyl cyanide)	156	183	212	226		
4-Benzamidobenzonitrile (*N*-benzoylanthranilonitrile)	156	181	219	279		

(Continued)

TABLE AII.31 Nitriles (Solids) *(Continued)*

Name of Compound	mp (°C)	Acid Derivative mp (°C)			Amine Derivative mp (°C)	
		Acid	Amide	Anilide	Benzamide	Benzenesulfonamide
5-Bromo-2-hydroxybenzonitrile (5-bromo-2-hydroxyphenyl cyanide)	159	165	232	222		
(±)-2,3-Diphenylbutanedinitrile [(±)-2,3-diphenylsuccinonitrile; (±)-α,β-diphenylethylene cyanide]	160	183 (hyd)		173 (mono)		
2-Hydroxy-4-nitrobenzonitrile (2-cyano-5-nitrophenol; 2-hydroxy-4-nitrophenyl cyanide)	161	235	194			
1,3-Dicyanobenzene (isophthalonitrile)	162	347	280 (di)			
(±)-4-Cyano-3,4-diphenylbutanoic acid [(±)-4-cyano-3,4-diphenylbutyric acid; (±)-2,3-diphenylglutaromononitrile]	163	210	205 (mono)	202 (mono)		
2,3-Diphenyl-3-phenyl-2-propenenitrile (2,3-diphenylcinnamonitrile)	167	213	223			
5-Chloro-2-hydroxybenzonitrile (4-chloro-2-cyanophenol; 5-chloro-2-hydroxyphenyl cyanide)	167	172	226			
2-Cyano-2′-biphenylcarboxylic acid (2,2′-diphenic acid mononitrile; 2-carboxy-2′-cyanobiphenyl)	172	234	193 (mono) 212 (di)	183 (mono)		
5-Nitro-2-naphthonitrile (2-cyano-5-nitronaphthalene)	173	295	263			
2,3-Dicyanopyridine	176	229	169 (mono) 165 (di)			
2-Cyano-3-phenyl-2-propanoic acid (2-cyanocinnamic acid)	183	196	190 (di)			
1,2-Dicyanonaphthalene	190	175	265 (di)			
2-Cyanobenzoic acid	192	206	219 (di)	253 (di)	184 (di)	
2-Hydroxy-5-nitrobenzonitrile (2-cyano-4-nitrophenol; 2-hydroxy-5-nitrophenyl cyanide)	196	230	225			
5-Nitro-1-naphthonitrile (1-cyano-5-nitronaphthalene)	205	242	236			
3-Cyanobenzoic acid	217	345	280			
4-Cyanobenzoic acid	219	300		337 (di)		
1,4-Dicyanobenzene (terephthalonitrile)	222	300		337 (di)		
1,8-Dicyanonaphthalene	232	260	252 (di)			
1-Cyano-9,10-anthraquinone	247	294	280	289		

TABLE AII.32 Nitro Compounds (Liquids)

Name of Compound	bp (°C)	Acyl Derivative mp (°C) of Amine: Acetamide	Benzamide	Benzenesulfonamide
Nitroethene (nitroethylene)	99		71	58
Nitromethane	101	28	80	30
Nitroethane	114		71	58
1-Nitropropane	132		84	36
2-Nitrobutane	140		76	70
2-Methyl-1-nitropropane	141		58	53
2-Methyl-1-nitropropene (1-nitroisobutene)	158		57	53
1-Nitrohexane	193		40	96
Nitrocyclohexane	206	104	147	
Nitrobenzene	211	114	160	112
2-Nitrotoluene	224	111	146	124
1-Ethyl-2-nitrobenzene	224	112	147	
1,3-Dimethyl-2-nitrobenzene	226	177	168	
Phenylnitromethane	226	60	105	88
3-Nitrotoluene	233	65	125	95
1,4-Dimethyl-2-nitrobenzene	234	139	140	138
6-Chloro-2-nitrotoluene	238	159; 136	173	
1-Ethyl-4-nitrobenzene	241	94	151	
2,4-Dimethyl-1-nitrobenzene	246	133	192	130
2,3-Dimethyl-1-nitrobenzene (1,2-dimethyl-3-nitrobenzene)	250	135	189	
2,4-Dichloro-1-nitrobenzene	258	146	115	128
1-Isopropyl-4-methyl-2-nitrobenzene	264	71	102	
2-Methoxy-1-nitrobenzene (*o*-nitroanisole)	265	88	84; 60	89
1-(2-Methylpropyl)-4-nitrobenzene (*o*-*tert*-butylnitrobenzene)	267	170	136	
2-Ethoxy-1-nitrobenzene (*o*-nitrophenetole)	268	79	104	102

TABLE AII.33 Nitro Compounds (Solids)

Name of Compound	mp (°C)	Acyl Derivative mp (°C) of Amine: Acetamide	Benzamide	Benzenesulfonamide
3-Nitrotoluene	16		125	95
4-Fluoro-1-nitrobenzene	27	152	185	
2-Chloro-1-nitrobenzene	32	87	99	129
2,4-Dichloro-1-nitrobenzene	33	146	115	128
3-Ethoxy-1-nitrobenzene (*m*-nitrophenetole)	34	97	103	
2-Nitrobiphenyl	37	121	102	
6-Chloro-2-nitrotoluene	37	159; 136	173	
3-Iodo-1-nitrobenzene	38	119	157	
5-Nitroindane	40	106	137	
2-Bromo-1-nitrobenzene	43	99	116	
4-Nitroindane	44	126	136	
2-Nitro-1,3,5-trimethylbenzene (nitromesitylene)	44	217	204	
3-Chloro-1-nitrobenzene	44	78	120	121
2-Iodo-1-nitrobenzene	49	109	139	
1-Chloro-2,4-dinitrobenzene	52	142 (di)	178 (di)	
4-Methoxy-1-nitrobenzene (*p*-nitroanisole)	54	130	154	95
4-Nitrotoluene	54	147	158	120
2,5-Dichloro-1-nitrobenzene	54	132	120	
3-Bromo-1-nitrobenzene	56	87	120; 136	
1-Methyl-2-nitronaphthalene	59	189	222	
4-Ethoxy-1-nitrobenzene (*p*-nitrophenetole)	60	137	173	143
1-Nitronaphthalene	61	159	160	167
3,4-Dinitrotoluene	61	132 (mono) 210 (di)	194 (mono) 264 (di)	179 (di)
1-Methyl-8-nitronaphthalene	64	184	196	
2,4-Dinitrotoluene	72	224 (di)	224 (di)	138 (mono) 191 (di)
1-Methyl-4-nitronaphthalene	72	167	239	
5-Methyl-2-nitronaphthalene	72	124	156	
2-Nitronaphthalene	78	132	162	136; 102
2-Methyl-1-nitronaphthalene	81	188	180	
4-Nitrophenanthrene	81	190	224	
5-Methyl-1-nitronaphthalene	83	195	174	
4-Chloro-1-nitrobenzene	83	179	192	122
1,3-Dinitrobenzene	90	89 (mono) 191 (di)	125 (mono) 240 (di)	194
1,5-Dimethyl-2,4-dinitrobenzene	93	165 (mono) 295 (di)	259 (di)	
2,4′-Dinitrobiphenyl	93	202 (di)	278 (di)	

(Continued)

TABLE AII.33 Nitro Compounds (Solids) *(Continued)*

Name of Compound	mp (°C)	Acyl Derivative mp (°C) of Amine		
		Acet-amide	Benz-amide	Benzene-sulfon-amide
4-Chloro-1-methoxy-2-nitrobenzene (4-chloro-2-nitroanisole)	98	104	78	
2-Nitrophenanthrene	99	225	216	
1,2-Dinitronaphthalene	103	234 (di)	291 (di)	215 (mono)
5-Nitroacenaphthene	106	238	210; 199	
4-Nitrobiphenyl	114	171	230	
9-Nitrophenanthrene	117	208	199	
1,2-Dinitrobenzene	118	185 (di)	301 (di)	186
1-Nitro-2,4,6-tribromobenzene	125	232	198	
4-Bromo-1-nitrobenzene	126	168	204	134
2,2′-Dinitrobiphenyl	128	90 (mono) 161 (di)	160 (mono) 191 (di)	
1,4-Dinitronaphthalene	132	304 (di)	280 (di)	
3-Nitroacenaphthene	152	193	210	
1,6-Dinitronaphthalene	166	263 (di)	265 (di)	
3-Nitrophenanthrene	171	201	213	
1,4-Dinitrobenzene	173	163 (mono) 304 (di)	128 (mono) 300 (di)	247 (di)
4-Iodo-1-nitrobenzene	173	184	222	
9-Nitrofluorene	182	262	261	
2-Nitroanthraquinone	185	262	228	
1-Nitroanthraquinone	230	218	255	
2,7-Dinitronaphthalene	234	261 (di)	267 (di)	
4,4′-Dinitrobiphenyl	240	199 (mono) 317 (di)	205 (mono) 352 (di)	
1,6-Dinitroanthraquinone	257	295 (di)	275 (di)	
E-4,4′-Dinitro-1,2-diphenylethene (*trans*-4,4′-dinitrostilbene)	288	353 (di)	352 (di)	
1,7-Dinitroanthraquinone	295	283 (di)	325 (di)	
1,8-Dinitroanthraquinone	312	284 (di)	324 (di)	

TABLE AII.34 Phenols (Liquids)

Name of Compound	bp (°C)	Derivative mp (°C)							
		Phenylurethane	1-Naphthylurethane	4-Nitrobenzoate	3,5-Dinitrobenzoate	Acetate	Benzoate	Aryloxyacetic Acid	Bromo Derivative
2-Chlorophenol	176	121	120	115	143			145	49 (mono) 76 (di)
Phenol	183	126	133	127	146		69	99	95 (tri)
2-Methylphenol (*o*-cresol; *o*-hydroxytoluene)	192	143	142	94	138			152	56 (di)
2-Bromophenol	195		129					143	95 (tri)
2-Chloro-4-methylphenol (3-chloro-4-hydroxytoluene)	196							72	108
2-Hydroxybenzaldehyde (salicylaldehyde)	197	133		128		39		132	
4-Methylphenol (*p*-cresol; *p*-hydroxytoluene)	202	115	146	98	189		71	136	49 (di) 199 (tetra)
3-Methylphenol (*m*-cresol; *m*-hydroxytoluene)	203	125	128	90	165		55	103	84 (tri)
2-Methoxyphenol (guaiacol)	205	136	118	93	142		58	121	116 (tri)
2-Ethylphenol	207	144		57	108		39	141	
2,4-Dichlorophenol	210						96	140	140 (mono)
2,4-Dimethylphenol	212	112	135	105	165		38	142	179 (tri)
3-Chlorophenol	214		158	99	156		71	110	
2-Hydroxyacetophenone (*o*-acetylphenol)	215					89	88		
3-Ethylphenol	217	138		68			52	77	
4-Chlorophenol	217	149	166	171	186		89	156	34 (mono) 90 (di)
2-(2-Propenyl)phenol (2-allylphenol)	220	116						150	50 (mono)
2-Chloro-4,6-dimethylphenol	223	130		95					
Methyl 2-hydroxybenzoate (methyl salicylate)	224	117		128		52	92		
2-Propylphenol	226	111			96			100	
2-(1-Methylpropyl)-phenol (2-*sec*-butylphenol)	228	86						110	
4-Propylphenol	232	129			123		38		
Ethyl 2-hydroxybenzoate (ethyl salicylate)	234	100		108			87		

(Continued)

TABLE AII.34 Phenols (Liquids) *(Continued)*

Name of Compound	bp (°C)	Derivative mp (°C)							
		Phenyl-urethane	1-Naph-thyl-urethane	4-Nitro-ben-zoate	3,5-Di-nitro-ben-zoate	Acetate	Ben-zoate	Aryl-oxy-acetic Acid	Bromo Deriv-ative
3-Bromophenol	236		108				86	108	
2-Butylphenol	237				97	106		105	
2-Methyl-5-(1-methylethyl)-phenol (carvacrol; 5-isopropyl-2-methylphenol)	238	138	116	51	83			151	46 (mono)
2,4-Dibromophenol	239			184		36	98	153	95 (tri) 96 (mono)
3-Methoxyphenol (resorcinol monomethyl ether)	244		129					118	104 (tri)
4-Butylphenol	248	115		68	92		27; 127	81	
2-Methoxy-4-(2-propenyl)phenol (eugenol; 4-allyl-2-methoxyphenol)	255	96	122	81	131	30	70	81 (hyd) 100	118 (tetra)
2-Methoxy-4-(1-propenyl)phenol (isoeugenol)	267	118 (*cis*) 152 (*trans*)	150	109	158	80	68 (*cis*) 106 (*trans*)	94; 116	94 (di)

TABLE AII.35 Phenols (Solids)

Name of Compound	mp (°C)	Derivative mp (°C)							
		Phenyl-urethane	1-Naphthyl-urethane	4-Nitrobenzoate	3,5-Dinitrobenzoate	Acetate	Benzoate	Aryloxyacetic Acid	Bromo Derivative
4-Propylphenol	22	129			123		38		
4-Butylphenol	22	115		68	92		27; 127	81	
4-Pentylphenol (*p*-amylphenol)	23						52	90	
3-Propylphenol	26				75; 118			97	
2,4-Dimethylphenol	28	112	135	105	165		38	142	179 (tri)
2-Hydroxyacetophenone (*o*-acetylphenol)	28					89	88		
2-Methylphenol (*o*-cresol; 2-hydroxytoluene)	31	142	142	94	138			152	56 (di)
2-Methoxyphenol (guaiacol)	32		118	93	142		58	119	116 (tri)
3-Bromophenol	33		108				86	108	
3-Chlorophenol	33		158	99	156		71	110	
2-Bromo-4-chlorophenol	34						100	140	
4-Methylphenol (*p*-cresol; *p*-hydroxytoluene)	36	115	146	98	189		71	136	108, 199 (tetra) 49 (di)
4-Methyl-2-nitrophenol (4-hydroxy-3-nitrotoluene)	36				192		101		
2,4-Diethylphenol	38	171						68	
2,4-Dibromophenol	40			184		36	98	153	95 (tri) 96 (mono)
3-Ethoxyphenol (resorcinol monoethyl ether)	40			184			97		
3-Iodophenol	40	138		133	183	38	73	115	
3-Methyl-2-nitrophenol (3-hydroxy-2-nitrotoluene)	41					59	79		
Phenol	42	126	133	127	146		69	99	95 (tri)
Phenyl 2-hydroxybenzoate (phenyl salicylate)	42	112		111		99	81		
2-Iodophenol	43	122				101	34	135	
4-Chlorophenol	43	149	166	171	186		93	156	34 (mono) 90 (di)

(Continued)

TABLE AII.35 Phenols (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)							
		Phenyl-urethane	1-Naphthyl-urethane	4-Nitrobenzoate	3,5-Dinitrobenzoate	Acetate	Benzoate	Aryloxyacetic Acid	Bromo Derivative
2,4-Dichlorophenol	45				143		97	141	68 (mono)
2-Nitrophenol	45		113	141	142; 155	41	59	158	117 (di)
4-Ethylphenol	47	120	128	81	133		60	97	
3-Methyl-2,4,6-trichlorophenol	47					32	53		
4-Chloro-2-methylphenol (5-chloro-2-hydroxytoluene)	48						71	117	
2,6-Dimethylphenol	49		176		159		39	140	79 (mono)
5-Methyl-2-(1-methylethyl)phenol (thymol; 2-isopropyl-5-methylphenol)	52	107	160	70	103		33	149	55 (mono)
2,6-Dibromo-4-methylphenol (3,5-dibromo-4-hydroxytoluene)	54			141		67	95		
4-Methoxyphenol (*p*-hydroxyanisole; hydroquinone monomethyl ether)	56				166	32	87	112	
3-Methyl-6-nitrophenol (3-hydroxy-4-nitrotoluene)	56					48	77		
2,6-Dibromophenol	57						46	68	93 (mono)
4,6-Dibromo-2-methylphenol (3,5-dibromo-2-hydroxytoluene)	57			137			62		
3-Hydroxy-6-nitrobiphenyl	58			135	171				
3,5-Dihydroxytoluene (orcinol; 5-methylresorcinol)	58 (hyd)	154	160	214	190	25 (di)	88 (di)	217	104 (tri)
4-Chloro-5-methyl-2-(1-methylethyl)phenol (4-chloro-2-isopropyl-5-methylphenol)	60				129		72		
5,6,7,8-Tetrahydro-2-naphthol	62			113			96		
3,4-Dimethylphenol	65	120	142		182	22	59	163	171 (tri)
2-Methyl-1-naphthol	65					82	95		
3,4-Dihydroxytoluene (4-methylcatechol)	65	166 (di)					58 (di)	58 (di)	
4-Bromophenol	66	140	169	180	191	22	102;	157	95, 171 (tri)

(Continued)

TABLE AII.35 Phenols (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)							
		Phenyl-urethane	1-Naphthyl-urethane	4-Nitrobenzoate	3,5-Dinitrobenzoate	Acetate	Benzoate	Aryloxyacetic Acid	Bromo Derivative
4-Chloro-2-methylphenol (2-chloro-5-hydroxytoluene)	66		154				86		
4-Chloro-3-methylphenol (4-chloro-3-hydroxytoluene)	66		154				86	178	
4-Hydroxy-3-nitrobiphenyl	66					86	111		
2,4,6-Trichlorophenol	67		188				70		
4-Methyl-2,3,5-trichlorophenol (4-hydroxy-2,3,6-trichlorotoluene)	67					38	89		
2-Phenylphenol (2-hydroxybiphenyl)	68					63	76	107	
3,5-Dichlorophenol	68					38	55		189 (tri)
3,5-Dimethylphenol	68	151		109	195		24	111; 86 (hyd)	166 (tri)
2,3,5-Trichlorophenol	68						93	157	
2,4,5-Trichlorophenol	68						93	157	
2,4,6-Trichlorophenol	70			106	136		76	186	
2,4,6-Trimethylphenol (mesitol)	70	142					62	142	158 (di)
2,3,4,6-Tetrachlorophenol	70					66	108		
2,4,5-Trimethylphenol (pseudodocumenol)	71	110			179	35	63	132	35 (mono)
1-Chloro-2-naphthol	72					43	100		
2,4-Diiodophenol	72					71	98		
5-Chloro-2-methylphenol (4-chloro-2-hydroxytoluene)	74						54		190 (tri)
Ethyl 3-hydroxybenzoate	74					35	58		
2,5-Dimethylphenol	75	166	173	87	137		61	118	178 (tri)
5,6,7,8-Tetrahydro-1-naphthol	75					75	46		
2,3-Dimethylphenol	75	193		104				187	
8-Hydroxyquinoline	76			175		174	120		
4-Bromo-2,6-dinitrophenol	78					111	154		
4-Chloro-2-iodophenol	78	128				57	88		
2,3,4,6-Tetramethylphenol (isodurenol)	79	179					72		
4-Hydroxy-3-methoxybenzaldehyde (vanillin)	81	117				102	78	189	160 (mono)
3,5-Dibromophenol	81					53	77		

(Continued)

TABLE AII.35 Phenols (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)							
		Phenyl-urethane	1-Naphthyl-urethane	4-Nitro-benzoate	3,5-Dinitro-benzoate	Acetate	Benzoate	Aryloxy-acetic Acid	Bromo Derivative
3-Methyl-2,4,6-tribromophenol (3-hydroxy-2,4,6-tribromotoluene)	82					68	85		
4-(1,1,3,3-Tetramethylbutyl)phenol	84						82	103	
3-(Dimethylamino)phenol (3-hydroxydimethylaniline)	85					37	94		
3-Hydroxy-2-nitrobiphenyl	86					62	131		
2-Hydroxyphenylmethanol (saligenin; 2-hydroxybenzyl alcohol)	87						51, 85 (di)	120	
4,6-Dinitro-2-methylphenol (3,5-dinitro-2-hydroxytoluene)	87					96	135		
4-(Methylamino)phenol (4-hydroxy-*N*-methylaniline)	87					43	174	214	
2-Methyl-3,4,6-tribromophenol (6-hydroxy-2,3,5-tribromotoluene; 2-hydroxy-3,5,6-tribromotoluene)	91					77	85; 133		
4-(1,1-Dimethylpropyl)phenol (*p-tert*-amylphenol; *p-tert*-pentylphenol)	93	108					61		
4-Iodophenol	94	148				32	119	156	
1-Naphthol	94	178	152	143	217	49	56	194	105 (di)
2,4,6-Tribromophenol (bromol)	95		153	153	174	87	81	200	120 (tetra)
3-Bromo-4-hydroxybiphenyl	95					75	94		
2,3,5-Trimethylphenol	95	174				241	50		
2-Naphthyl 2-hydroxybenzoate (2-naphthyl salicylate; betol)	96	268				136			
3-Hydroxyacetophenone (*m*-acetylphenol)	96					45	53		
5-Iodo-2-nitrophenol	96					95	122		
3-Nitrophenol	97	129	167	174	159	56	95	156	91 (di)
2,3-Dibromo-5,6-dimethylphenol	97					78	153		
4-(1,1-Dimethylethyl)phenol (*p-tert*-butylphenol)	100	149	110				83	87	50 (mono) 67 (di)
2-Acetyl-1-naphthol	102					108	128		
3,5-Diiodophenol	104					79	93		

(Continued)

TABLE AII.35 Phenols (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)							
		Phenylurethane	1-Naphthylurethane	4-Nitrobenzoate	3,5-Dinitrobenzoate	Acetate	Benzoate	Aryloxyacetic Acid	Bromo Derivative
3-Hydroxy-4-nitrobiphenyl	105			157	199				
1,2-Dihydroxybenzene (catechol; pyrocatechol)	105	169 (di)	175	159 (mono) 170 (di)	152 (di)	58 (mono) 65 (di)	181, 84 (di)	138	193 (tetra)
2-Hydroxypyridine	107			120			42		
3,5-Dihydroxytoluene (orcinol; 5-methylresorcinol)	107 (anhyd)	154	160	214	190	25 (di)	88 (di)	217	104 (tri)
1,2-Dihydroxynaphthalene (1,2-naphthalenediol)	108					109 (di)	106 (di)	106 (di)	
1,2,3,4-Tetrahydroanthranol	108					109	142		
4-Methyl-5,6,7,8-tetrahydro-2-naphthol	108			116			89		
3-Hydroxybenzaldehyde	108	160					49; 38	148	
3-Methyl-2,4,6-trinitrophenol (3-hydroxy-2,4,6-trinitrotoluene)	110					135	140		
1,3-Dihydroxybenzene (resorcinol)	110	164 (di)	206	182 (di)	201 (di)	58	136 (mono) 117 (di)	175; 195	112 (di) 112 (tri)
2,2′-Dihydroxybiphenyl (2,2′-biphenol)	110	145 (di)				95 (di)	101 (di)		188 (di)
2-Bromo-1,4-dihydroxybenzene (bromohydroquinone)	110					72 (di)			186 (di)
4-Hydroxyacetophenone	110				138	54	134	177	
1-Methyl-2-naphthol	111					66	117		
1,3-Dihydroxy-2,4,6-tribromobenzene (2,4,6-tribromoresorcinol)	112					114 (mono) 108 (di)	120 (mono)		
4′,5-Dimethyl-2-hydroxyazobenzene	113					91	95		
4,4′-Dihydroxy-2,2′-dimethylbiphenyl	114					75 (di)	127 (di)		
2-Bromo-4-nitrophenol	114					62; 86	132		
4-Nitrophenol	114	156	151	159	188	83	143	187	142 (di)
2,4-Dinitrophenol	114			139		72	132	148	118 (mono)
4-Hydroxy-3-methoxybenzyl alcohol	115					51 (mono) 48 (di)	90 (mono) 121 (di)		

(Continued)

TABLE AII.35 Phenols (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)							
		Phenyl-urethane	1-Naphthyl-urethane	4-Nitro-benzoate	3,5-Dinitro-benzoate	Acetate	Benzoate	Aryloxy-acetic Acid	Bromo Derivative
1-Hydroxyfluorene	115					131	129		
4-Chloro-3,5-dimethylphenol	115						68	141	
3,5-Dimethyl-2,4-dinitrophenol	116					148	156		
4-Hydroxy-2′-nitrobiphenyl	116					122	157	161	
4-Hydroxybenzaldehyde	117						91	198	181 (di)
1,3,5-Trihydroxybenzene (phloroglucinol)	117 (hyd)	191 (tri)		283	162 (tri)	104 (tri)	185 (tri) 174		151 (tri)
2,4′-Dihydroxydiphenylmethane	118					70 (di)	108 (di)		
2-Bromo-4,6-dinitrophenol	119					105	94		
3,4-Dihydroxyacetophenone (4-acetylcatechol)	119					58 (mono) 91 (di)	118 (di)		
2-Chloro-5-nitrophenol	120					82	128		
9-Hydroxyanthracene	120					131	288		
2-Chloro-3-nitrophenol	121					51	94		
3-Aminophenol (*m*-hydroxyaniline)	122			143	179		153 (di)		
1,3-Dihydroxy-4-nitrobenzene (4-nitroresorcinol)	122					91 (di)	124, 189 (mono) 110 (di)		
2,4,6-Trinitrophenol (picric acid)	122			143		76			
2-Naphthol	123	156	157	169	210	72	107	95; 154	84 (mono)
2,3,4,5-Tetrabromophenol	123					111	133		226
3,4-Dimethyl-1-naphthol	123				224	91			
3,3′-Dihydroxybiphenyl (3,3′-biphenol)	124					83 (di)	92 (di)		
3-Iodo-4-nitrophenol	124					77	119		
2,5-Dihydroxytoluene (2-methylhydroquinone)	125					92 (mono) 49 (di)	120 (di)	153	84
(4-Hydroxyphenyl)methanol (4-hydroxybenzyl alcohol)	125					84 (mono) 75 (di)	89		
4-(Phenylmethyl)-1-naphthol (4-benzyl-1-naphthol)	126					88	103		

(Continued)

TABLE AII.35 Phenols (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)							
		Phenyl-urethane	1-Naphthyl-urethane	4-Nitro-benzoate	3,5-Dinitro-benzoate	Acetate	Benzoate	Aryloxy-acetic Acid	Bromo Derivative
Pentamethylphenol	126	215				273	127		
4-Chloro-3-nitrophenol	127					84	97		
1,3-Dibromo-2,4-dihydroxynaphthalene (1,3-dibromo-2,4-naphthalenediol)	129					148 (mono) 125 (di)			186
3-Methyl-4-nitrophenol (5-hydroxy-2-nitrotoluene)	129					34	74		
4-Hydroxy-3-nitroazobenzene	129					121	132		
Methyl 4-hydroxybenzoate	131	135				85	135		
4-Cyclohexylphenol	132	146		137	168	35	119		
1,2,3-Trihydroxybenzene (pyrogallol)	133	173 (tri)		230 (tri)	205 (tri)	173 (tri); 111 (di)	90 (tri); 108, 126 (di) 140 (mono)	198	158 (tri); 158 (di)
4,6-Dibromo-2-naphthol	135					128	129		
2,3-Dichloro-1,4-dihydroxynaphthalene)	135; 156					240 (di)	252 (di)		
4-Hydroxybenzophenone (*p*-benzoylphenol)	135					81	115; 95		
1,4-Dihydroxy-2,6-dinitrobenzene (2,6-dinitrohydroquinone)	136					96 (mono) 136 (di)	151 (mono)		
1,4-Dimethyl-2-naphthol	136					78	125		
5-Iodo-3-nitrophenol	136					110	101		
1,6-Dihydroxynaphthalene (1,6-naphthalenediol)	138					73 (di)	104 (di)		
2,6-Dibromo-3,4,5-trihydroxybenzoic acid (dibromogallic acid)	139					168 (di)	96 (di)		
2-Hydroxybenzamide (salicylamide)	139				224	138	143		
2-Hydroxy-2′-nitrobiphenyl	140			116	180		116		149 (di)
1,8-Dihydroxynaphthalene (1,8-naphthalenediol)	142		220			155 (di)	175 (di)		
4-Hydroxy-2-nitrobiphenyl	143					169	106		
3-Chloro-1-naphthol	143					69	119		

(Continued)

TABLE AII.35 Phenols (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)							
		Phenylurethane	1-Naphthylurethane	4-Nitrobenzoate	3,5-Dinitrobenzoate	Acetate	Benzoate	Aryloxyacetic Acid	Bromo Derivative
5-Methyl-2-(1-methylethyl)-1,4-dihydroxybenzene (thymoquinol; 2-isopropyl-5-methylhydroquinone)	143	233	148			75 (di)	142 (di)		
1,2,4-Trihydroxybenzene (hydroxyhydroquinone)	145					97 (tri)	120 (tri)		
1,3-Diphenyl-2,4′-dihydroxy-2-propen-1-one (2,4′-dihydroxychalcone)	145					95 (di)	120 (di)		
2,4-Dihydroxyacetophenone (4-acetylresorcinol; resacetophenone)	147					120, 74 (mono) 38 (di)	67, 107 (mono)		
3-Chloro-5-nitrophenol	147					84	78		
2-Chloro-4-hydroxybenzaldehyde	148					52	97		
1,3-Dihydroxy-2,4-dinitrobenzene (2,4-dinitroresorcinol)	148					120	184	155	
4-Hydroxypropiophenone (*p*-propionylphenol)	148					62	108		
9,10-Dihydroxyphenanthrene (9,10-phenanthrenediol)	148					170 (mono) 202 (di)	217 (di)		
4-Hydroxypyridine	149					150	81		
4-Hydroxyazobenzene	152					89	138		
2-Hydroxy-5-methylbenzoic acid (5-methylsalicylic acid)	153					152	155	185	
6-Hydroxybiphenyl-2-carboxylic acid	154					89	121; 150		
2-Azophenol (2,2′-dihydroxyazoxybenzene)	155					150 (di)	108 (di)		
E-3,5-Dihydroxy-1,2-diphenylethene (3,5-dihydroxystilbene; 3,5-stilbenediol)	156					101 (di)	151 (di)		
9-Hydroxyphenanthrene (9-phenanthrol)	158					78	100		
4,4′-Dihydroxydiphenylmethane	158					70 (di)	156 (di)		
2-Hydroxybenzoic acid (salicylic acid)	159			205		135	132	191	

(Continued)

TABLE AII.35 Phenols (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)							
		Phenyl-urethane	1-Naphthyl-urethane	4-Nitrobenzoate	3,5-Dinitrobenzoate	Acetate	Benzoate	Aryloxyacetic Acid	Bromo Derivative
2,4,6-Triiodophenol	159					181	156	137	
1,3-Diphenyl-2,2′-dihydroxy-2-propene-1-one (2,2′-dihydroxychalcone)	161						86 (di)	114 (di)	
4,4′-Dihydroxy-3,3′-dimethylbiphenyl	161						136 (di)	185	
3-Hydroxy-1,2-benzenedicarboxylic acid (3-hydroxyphthalic acid)	161						116	148	
1,2,3,4-Tetrahydroxybenzene (apionol; phenetrol)	161						142 (tetra)	192 (tetra)	
2,3-Dihydroxynaphthalene	162						105	152	
2-Hydroxy-3-methylbenzoic acid (3-methylsalicylic acid)	163						113		204
2,2′-Dihydroxy-6,6′-dimethylbiphenyl	164						87 (di)	136 (di)	
2-Methoxy-4-nitrophenol	165					158	188		
4-Hydroxybiphenyl (*p*-phenylphenol)	165	168				89	151	190	
2-Hydroxyphenanthrene (2-phenanthrol)	168					143	140		
1,5-Di-(2-hydroxyphenyl)-1,4-pentadiene-3-one	168					128 (di)	135		
3,3′-Dihydroxybenzophenone	170					90	102		
1,4-Dihydroxy-2-methylnaphthalene (2-methyl-1,4-naphthohydroquinone)	170					113 (di)	181		
5-Nitro-1-naphthol	171					114	109		
1,4-Dihydroxybenzene (hydroquinone)	172	207, 224 (di)	247	258 (di)	317 (di)	124 (di)	204 (di)	250	186 (di)
2,3,4-Trihydroxyacetophenone (gallacetophenone)	173					85 (tri)	118		
1,4-Dihydroxynaphthalene (1,4-naphthalenediol; 1,4-naphthohydroquinone)	176		220			130 (di)	169 (di)		
1,2-Dihydroxy-4-nitrobenzene (4-nitrocatechol)	176					98 (di)	156 (di)		
1,7-Dihydroxynaphthalene (1,7-naphthalenediol)	178	204		183		108 (di)	102 (di)		
9,10-Dihydroxyanthracene (9,10-anthradiol)	180					260 (di)	292 (di)		

(Continued)

TABLE AII.35 Phenols (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)							
		Phenyl-urethane	1-Naphthyl-urethane	4-Nitrobenzoate	3,5-Dinitrobenzoate	Acetate	Benzoate	Aryloxyacetic Acid	Bromo Derivative
4-Hydroxy-3-iodo-5-methoxybenzaldehyde (5-iodovanillin)	180					106	136		
3,3'-Dihydroxyazoxybenzene (3-azoxyphenol)	183					102 (di)	75 (di)		
N-Benzylidene-4-aminophenol	183					92	144		
4-Aminophenol (*p*-hydroxyaniline)	184				179	168	234		
4,6-Diacetyl-1,3-dihydroxybenzene (4,6-diacetylresorcinol; resodiacetophenone)	185					120 (di)	215 (mono) 118 (di)		
7-Hydroxy-4-methylcoumarin	186	156		143		150	160		
α,2,4-Trihydroxyacetophenone (2,4-dihydroxyphenyl hydroxymethyl ketone)	189					129 (tri)	200 (mono)		
2,7-Dihydroxynaphthalene (2,7-naphthalenediol)	190					172 (mono) 136 (di)	199 (mono) 139 (di)	149	
Pentachlorophenol	190					150	165	196	
1,5-Diacetyl-2,3,4-trihydroxybenzene	191					109 (di)	189 (tri)		
1,2-Dihydroxynaphthalene (1,2-naphthalenediol)	192					130 (di)	169 (di)		
1,2-Dihydroxy-3,4,5,6-tetrabromobenzene (tetrabromocatechol)	193					216 (di)	198 (di)		
6-Hydroxyquinoline	193						38	231	
3-Methyl-2,4,5,6-tetrabromophenol	194						166	154	
1,5-Dichloro-4,8-dihydroxynaphthalene	194						160 (mono) 154 (di)	158 (mono) 179 (di)	
Hexahydroxybenzene	200						203 (hexa)	313 (hexa)	
3-Hydroxybenzoic acid	200						131		206
Methyl 3,4,5-trihydroxybenzoate (methyl gallate)	201						120 (tri)	139 (tri)	
2,5-Dihydroxyacetophenone (2-acetylhydroquinone)	202						68 (di)	113 (di)	
4-Hydroxy-4'-nitrobiphenyl	203						139	210	

(Continued)

TABLE AII.35 Phenols (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)							
		Phenyl-urethane	1-Naphthyl-urethane	4-Nitro-benzoate	3,5-Dinitro-benzoate	Acetate	Benzoate	Aryloxy-acetic Acid	Bromo Derivative
3,5-Dimethoxy-4-hydroxybenzoic acid	205						191	232	
2,3,5-Trihydroxyacetophenone	207						107 (tri)	107 (tri)	
3,3′-Dihydroxyazobenzene (3-azophenol)	207						144 (di)	188 (di)	
2-Acetamidophenol (2-hydroxyacetanilide)	209						122	140	
4-Hydroxy-3-methoxybenzoic acid (vanillic acid)	210				141		110	178	
2,4-Dihydroxybenzoic acid	213						136 (di)	152	
4-Hydroxybenzoic acid	215						187	223	278
1,3-Dihydroxy-4,6-dinitrobenzene (4,6-dinitroresorcinol)	215				178 (di)		139 (di)	344 (di)	
4,4′-Dihydroxyazobenzene (4-azophenol)	216						119 (di)	212; 251 (di)	
2,5-Dimethyl-1,4-dihydroxybenzene (hydrophlorone; 2,5-dimethylhydroquinone)	217					117 (mono) 135 (di)	163 (mono) 159 (di)		
1,3,5-Trihydroxybenzene (phloroglucinol)	218 (anhyd)	191		283	162 (tri)	105 (tri)	185, 174 (tri) 126 (di) 196 (mono)	151 (tri)	
2,2′-Dihydroxy-1,1′-binaphthyl	218					109 (di)	204 (mono) 160 (di)		
2,6-Dihydroxynaphthalene (2,6-naphthalenediol)	218					175 (di)	215 (di)		
4-Hydroxy-4′-nitroazobenzene	220					147	195		
3-Hydroxy-2-naphthoic acid	222						184	204	
2,4,6-Trihydroxyacetophenone (acetylphloroglucinol)	222						103 (tri)	168, 211 (mono) 118 (tri)	

(Continued)

TABLE AII.35 Phenols (Solids) *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)							
		Phenyl-urethane	1-Naphthyl-urethane	4-Nitrobenzoate	3,5-Dinitrobenzoate	Acetate	Benzoate	Aryloxyacetic Acid	Bromo Derivative
4,4′-Dihydroxyazoxybenzene	224						163 (di)	200, 212 (mono) 190 (di)	
4-Hydroxybenzanilide (4-benzamidophenol)	227						171	235	
2,6-Dihydroxyphenanthrene (2,6-phenanthrenediol)	234						123 (di)	253 (di)	
5-Hydroxy-1-naphthoic acid	235						202	241	
3,5-Dihydroxybenzoic acid	236						160 (di)	227	
1,4-Dihydroxy-2,3,5,6-tetrachlorobenzene (tetrachlorohydroquinone)	237					245 (di)	233 (di)		
3-Hydroxynaphthoic acid	248					170	223		
2,3-Dihydroxyquinoline (2,3-quinolinediol)	258					211 (mono)	287 (mono) 46 (di)		
1,5-Dihydroxynaphthalene (1,5-naphthalenediol)	265					161 (di)	242 (di)		
Phenolphthalein	265	135 (di)				143 (di)	169 (di)		
4,4′-Dihydroxyphenol (4,4′-biphenol)	275					161 (di)	241 (di)	274	

TABLE AII.36 Sulfonamides

Name of Compound	mp (°C)	Derivative mp (°C)			
		Sulfonic Acid	Sulfonyl Chloride	Sulfonanilide	*N*-Xanthylsulfonamide
2,4,5-Trimethoxybenzenesulfonamide	76		130	170	
Methanesulfonamide	90	20		100	
2,6-Dimethylbenzenesulfonamide	96	98	39		
Hexadecane-1-sulfonamide (cetylsulfonamide)	97	54	54		
Benzylsulfonamide	105		93	102	188
4-Methylbenzenesulfonamide (*p*-toluenesulfonamide)	105 (dihyd)	105; 92	71	103	197
Pyridine-3-sulfonamide	111	357	144	145	
3-Methoxynaphthalene-2-sulfonamide	113		138	174	
2,6-Dimethylbenzenesulfonamide	113	98	39		
2-Phenylethane-1-sulfonamide	122	91	33	77	
4-Chloro-3-methylbenzenesulfonamide	128		65	92	
D-Camphor-10-sulfonamide	132	193	67	121; 88	
2-Fluoronaphthalene-6-sulfonamide	133	105 (hyd)	97	129	
3-Chloro-4-methylbenzenesulfonamide	134		38	96	
(±)-Camphor-8-sulfonamide	135	58	106		
Tetralin-6-sulfonamide	135		58	156	
3,5-Dimethylbenzenesulfonamide	135		94	129	
Indane-5-sulfonamide	136	92	47	129	
4-Methylbenzenesulfonamide (*p*-toluenesulfonamide)	139 (anhyd)	105; 92	71	103	197
2,4-Dimethylbenzenesulfonamide	139	62 (hyd)	34	110	188
7-Ethoxynaphthalene-2-sulfonamide	142		103	153	
2,4,6-Trimethylbenzenesulfonamide	142	78	57	109	203
D-Camphor-3-sulfonamide	143	77	88	124	
3,4-Dimethylbenzenesulfonamide	144	64	52		
4-Chlorobenzenesulfonamide	144	93; 69	53	104	
4-Methyl-3-nitrobenzenesulfonamide	145	92	36		
3-Bromocamphor-8-sulfonamide	145	196 (anhyd)	137		
2,5-Dimethylbenzenesulfonamide	148	48 (anhyd) 86 (hyd)	26		176
Naphthalene-1-sulfonamide	150	90	68	112; 152	
4,6-Dichloro-2,5-dimethylbenzenesulfonamide	150		81	175	
6-Methoxynaphthalene-1-sulfonamide	150		81	178	
8-Chloro-7-methoxynaphthalene-1-sulfonamide	153		137	196	
2-Carboxybenzenesulfonamide	154	69 (hyd) 134 (anhyd)	79; 40	195	
6-Ethoxynaphthalene-1-sulfonamide	154		118	195	
Benzenesulfonamide	156	66 (anhyd) 44 (monohyd)		112	206

(Continued)

TABLE AII.36 Sulfonamides *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)			
		Sulfonic Acid	Sulfonyl Chloride	Sulfonanilide	*N*-Xanthylsulfonamide
2-Chloro-5-methylbenzenesulfonamide	156	56		230	
2-Methylbenzenesulfonamide (*o*-toluenesulfonamide)	156	57	68	136	183
3-Bromocamphor-10-sulfonamide	157	48	65		
2,4-Dinitrobenzenesulfonamide	157	108 (hyd) 130 (anhyd)	102		
2-Methyl-4-nitrobenzenesulfonamide	157	130 (anhyd)	106		
Benzophenone-3,3′-disulfonamide	157		138 (di)	178 (di)	197
4-Methoxynaphthalene-2-sulfonamide	157		75	145	
2-Ethoxynaphthalene-1-sulfonamide	158		116	187	
2-Methoxynaphthalene-1-sulfonamide	159		121	197	
3-Nitrobenzylsulfonamide	159	74 (hyd)	100		
2-Nitrodiphenylamine-4-sulfonamide	162	220	157		
2-Ethoxybenzenesulfonamide	163		66	158	
4-Chloro-2-nitrobenzenesulfonamide	164	82	75	138	
3,6-Dichloro-2,5-dimethylbenzenesulfonamide	165		71	171	
4-Bromobenzenesulfonamide	166	103; 89	76	119	
3-Nitrobenzenesulfonamide	167	48	64	126	
3,4-Dimethoxybenzenesulfonamide	167	192	71		
4-Hydroxynaphthalene-1-sulfonamide	167	170		200	
Propane-1,3-disulfonamide	169	92 (di)	45 (di)	129 (di)	
4-Ethoxynaphthalene-1-sulfonamide	170		103	180	
3-Carboxybenzenesulfonamide	170	98 (hyd) 148 (anhyd)	20 (di)		
4-Methyl-2-nitrobenzenesulfonamide	170	141 (anhyd)	99		
2,4-Dimethyl-3-nitrobenzenesulfonamide	172	144 (anhyd)	96		
2,5-Dimethyl-3-nitrobenzenesulfonamide	173	128; 200	61	144	
4-Nitrodiphenylamine-2-sulfonamide	173		104	164	
3,4-Dibromobenzenesulfonamide	175	68 (anhyd)	34		
7-Chloronaphthalene-2-sulfonamide	176	118 (anhyd) 68 (tetrahyd)	87		
4-Methylnaphthalene-1-sulfonamide	177		81	158	
4-Nitrobenzenesulfonamide	180	95, 111	80	136, 171	
3-Chloro-2-methylbenzenesulfonamide	180	72	72		
2,4,5-Trimethylbenzenesulfonamide	181	112	62		
5-Chloro-4-methyl-2-nitrobenzenesulfonamide	181	128	99		
2,5-Dichlorobenzenesulfonamide	181	93	38	160	
2,4-Dichlorobenzenesulfonamide	182	86	55		
4-Iodobenzenesulfonamide	183		85	143	
4-Ethoxynaphthalene-2-sulfonamide	183		85	144	
5-Ethoxynaphthalene-1-sulfonamide	183		121	130	

(Continued)

TABLE AII.36 Sulfonamides *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)			
		Sulfonic Acid	Sulfonyl Chloride	Sulfon-anilide	*N*-Xan-thylsul-fonamide
6-Ethoxynaphthalene-2-sulfonamide	183		108	153	
Quinoline-8-sulfonamide	184	312	124		
5-Nitronaphthalene-2-sulfonamide	184	119	125		
4-Chloro-2,5-dimethylbenzenesulfonamide	185	100	50	155	
2-Carboxy-5-methylbenzenesulfonamide	185	190, 158 (anhyd)	59 (di)		
2,5-Dichlorobenzenesulfonamide	186	97	38	160	
2-Chloro-5-nitrobenzenesulfonamide	186	169 (hyd)	90		
2-Methyl-5-nitrobenzenesulfonamide	186	134 (dihyd)	47	148	
6-Chloro-3-nitrobenzenesulfonamide	186	169	90		
2,4-Dimethyl-5-nitrobenzenesulfonamide	187	132; 122	98		
2-Methyl-5-nitrobenzenesulfonamide	187	131	47	148	
4-Chloronaphthalene-1-sulfonamide	187	133	95	146	
8-Iodonaphthalene-1-sulfonamide	187		115	140	
2,4-Diaminobenzene-1,5-disulfonamide	187		275	236	
5-Methylnaphthalene-2-sulfonamide	189		122	250; 134	
6-Methoxynaphthalene-2-sulfonamide	189		93	120	
Phenanthrene-3-sulfonamide	190	176 (anhyd) 121 (monohyd) 89 (dihyd)	111		
2,4-Dibromobenzenesulfonamide	190	110 (anhyd)	79		
2-Nitrobenzenesulfonamide	191	70	68	115	
8-Nitronaphthalene-1-sulfonamide	191	115 (trihyd)	165	179	
4-Methylbenzene-2,4-disulfonamide	191		56	189	
2,5-Dimethyl-6-nitrobenzenesulfonamide	192	145 (anhyd)	110	182	
4-Carboxy-3-nitrobenzenesulfonamide	192 (mono)	111 (di)	160 (di)		
2-Nitrobenzenesulfonamide	193	70; 85	69	115	
Phenanthrene-9-sulfonamide	194	174 (anhyd) 134 (hyd)	127		
2-Carboxybenzenesulfonamide	194	69 (hyd) 134 (anhyd)	79; 40	195	
2,5-Dibromobenzenesulfonamide	195	128 (anhyd)	71		
5-Methoxynaphthalene-1-sulfonamide	195		120	157	
7-Methylnaphthalene-1-sulfonamide	196		96	164	
5-Fluoronaphthalene-1-sulfonamide	197	106 (hyd)	123		
2,5-Dimethyl-4-nitrobenzenesulfonamide	198	140	75	131	
Acenaphthene-3-sulfonamide	199	89	114	286	
3,4-Dicarboxybenzenesulfonamide	200	140 (monohyd)	170		
3,4-Dichloro-2, 5-dimethylbenzene-sulfonamide	201		62	157	
5-Amino-2-hydroxybenzenesulfonamide	202	100 (anhyd)		159	
4-Nitrobenzylsulfonamide	204	71	90	220	
4-Iodonaphthalene-1-sulfonamide	206		124	136	

(Continued)

TABLE AII.36 Sulfonamides *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)			
		Sulfonic Acid	Sulfonyl Chloride	Sulfon-anilide	*N*-Xan-thylsul-fonamide
4-Fluoronaphthalene-1-sulfonamide	206	100 (hyd)	86	144	
2,6-Dimethyl-4-hydroxybenzene-1,3-disulfonamide	208		119	207	
Fluorene-2-sulfonamide	213	155 (hyd)	164		
1-Nitronaphthalene-2-sulfonamide	214	105	121	202	
5-Methylbenzene-1,3-disulfonamide	216		94	153	
Naphthalene-2-sulfonamide	217	91	79	132	
4-Acetamidobenzenesulfonamide	219		149	214	
7-Methoxynaphthalene-2-sulfonamide	220		83	121	
Acenaphthene-5-sulfonamide	223		111	178	
8-Nitronaphthalene-2-sulfonamide	223	136 (monohyd)	169	173	
3-Chlorobenzene-1,5-disulfonamide	224	100	106		
2-Methylbenzene-1,4-disulfonamide	224		98	178 (di)	
4-Carboxy-3-nitrobenzenesulfonamide	226 (di)	111 (di)	160 (di)		
4-Methoxynaphthalene-1-sulfonamide	226		99	148	
5-Chloronaphthalene-1-sulfonamide	226		95	138	
3,4-Diiodobenzenesulfonamide	227	125	82		
8-Nitronaphthalene-2-sulfonamide	228	136 (anhyd)	169	173	
2,4,6-Tribromobenzenesulfonamide	228	64	64	222	
Benzene-1,3-disulfonamide	229		63	150	170
Biphenyl-4-sulfonamide	230		115	125	
2,4-Diiodobenzenesulfonamide	230	162 (anhyd)	78		
2-Carboxybenzenesulfonamide	230	69 (hyd) 134 (anhyd)	79; 40	195	199
5-Nitronaphthalene-1-sulfonamide	236		113	123	
4-Carboxybenzenesulfonamide	236 (di)	94 (hyd) 260 (anhyd)	57 (di)	252 (di)	
6-Hydroxynaphthalene-2-sulfonamide	237	167 (anhyd) 129 (hyd)		161	
4-Chloro-2-nitrobenzenesulfonamide	237	82	75	138	
4-Methylbenzene-1,2-disulfonamide	239		111	190	
4,5-Dimethylbenzene-1,3-disulfonamide	239		79	200	
4-Hydroxybenzene-1,3-disulfonamide	239	100 (di)	89 (di)	205 (di)	
4-Methoxybenzene-1,3-disulfonamide	240		86	209	
2,4,6-Trimethylbenzene-1,3-disulfonamide	244		125 (di)	151 (di)	
4,6-Dimethylbenzene-1,3-disulfonamide	249		130	196	
1-Chloronaphthalene-2-sulfonamide	250	133 (anhyd)	85	172	
Azobenzene-4,4′-disulfonamide	250	169 (anhyd)	222; 170 (di)		
Phenanthrene-2-sulfonamide	254	150	156	158	
Benzene-1,2-disulfonamide	254		143	241	
2-Amino-5-methylbenzene-1,3-disulfonamide	257	290 (di)	156 (di)	197 (di)	

(Continued)

TABLE AII.36 Sulfonamides *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)			
		Sulfonic Acid	Sulfonyl Chloride	Sulfon-anilide	*N*-Xan-thylsul-fonamide
2-Methylbenzene-1,3-disulfonamide	260		88	162	
Anthracene-2-sulfonamide	261		122	201	
Anthraquinone-2-sulfonamide	261		197	193	
Azoxybenzene-3,3′-disulfonamide	273	126	138		
Naphthalene-1,4-disulfonamide	273		166	179	
9,10-Dichloroanthracene-2-sulfonamide	279		221	248	
Benzene-1,4-disulfonamide	288		139	249	
2,5-Dimethyl-1,3-disulfonamide	295		81	174	
Naphthalene-1,6-disulfonamide	298	125 (anhyd)	129		
Biphenyl-4,4′-disulfonamide	300	72	203		
Naphthalene-1,5-disulfonamide	310	245 (di) (anhyd)	183 (di)	249 (di)	
2,5-Dimethyl-1,4-disulfonamide	310		164	223	
Benzene-1,3,5-trisulfonamide	315	100 (tri)	187 (tri)	237 (tri)	
Anthracene-1,5-disulfonamide	330		249 (di)	293 (di)	
Anthracene-1,8-disulfonamide	333		225	224	
Anthraquinone-1,8-disulfonamide	340	294	223	238	
Anthraquinone-1,5-disulfonamide	350	311 (anhyd)	270	270	

TABLE AII.37 Sulfonic Acids

Name of Compound	mp (°C)	Derivative mp (°C)				
		Sulfonyl Chloride	Sulfonamide	Sulfonanilide	Benzyl Thiuronium Salt	4-Toluidine Salt
Methanesulfonic acid	20		90	100		
Benzenesulfonic acid	44 (hyd)		156	112	148	205
3-Bromocamphor-10-sulfonic acid	48	65	157			
3-Nitrobenzenesulfonic acid	48	64	167	126	146	222
2,5-Dimethylbenzenesulfonic acid	48 (anhyd)	26	148		184	
Hexanedecane-1-sulfonic acid (cetylsulfonic acid)	54	54	97			
2-Methylbenzenesulfonic acid (2-toluenesulfonic acid)	57	68	156	136	170	204
(±)-Camphor-8-sulfonic acid	58	106	135			
Diphenylmethane-4,4′-disulfonic acid	59	124		178		
2,4-Dimethylbenzenesulfonic acid	62 (hyd)	34	139	110	146	
3,4-Dimethylbenzenesulfonic acid	64	52	144		208	
2,4,6-Tribromobenzenesulfonic acid	64	64	228	222		
Benzenesulfonic acid	66 (anhyd)		156	112	148	205
4-Chlorobenzenesulfonic acid	68	53	144	104	175	210
3,4-Dibromobenzenesulfonic acid	68	34	175			
7-Chloronaphthalene-2-sulfonic acid	68 (tetrahyd)	87	176			
2-Carboxybenzenesulfonic acid (*o*-sulfobenzoic acid)	69 (hyd)	79; 40	194; 154; 230	195	206	200
4-Nitrobenzylsulfonic acid	71	90	204	220		
3-Chloro-2-methylbenzenesulfonic acid	72	72	180			
Biphenyl-4,4′-disulfonic acid	72	203	300		171	330
3-Nitrobenzylsulfonic acid	74 (hyd)	100	159			
D-Camphor-3-sulfonic acid	77	88	143	124		197
2,4,6-Trimethylbenzenesulfonic acid	78	56	142	109		
4-Chloro-2-nitrobenzensulfonic acid	82	75	164; 237	138		
2-Nitrobenzenesulfonic acid	85	69	193	115		
2,4-Dichlorobenzenesulfonic acid	86	55	182			206
2,5-Dimethylbenzenesulfonic acid	86 (hyd)	26	148		184	
Phenanthrene-3-sulfonic acid	89 (dihyd)	111	190			222
Acenaphthene-3-sulfonic acid	89	114	199	286		
4-Bromobenzenesulfonic acid	90	76	166	119	170	216
Naphthalene-1-sulfonic acid	90	68	150	112; 152	137	181
2-Phenylethane-1-sulfonic acid	91	33	122	77		
Naphthalene-2-sulfonic acid	91	79	217	132	191	221
Indane-5-sulfonic acid	92	47	136	129		
4-Methyl-3-nitrobenzenesulfonic acid	92	36	144			131
4-Methylbenzenesulfonic acid (*p*-toluenesulfonic acid)	92	71	139 (anhyd) 105 (dihyd)	103	182	198
Propane-1,3-disulfonic acid	92d	45 (di)	169 (di)	129 (di)		
4-Chlorobenzenesulfonic acid	93	53	144	104	175	210
4-Carboxybenzenesulfonic acid (*p*-sulfobenzoic acid)	94 (hyd)	57 (di)	237 (di)	252 (di)	213	

(Continued)

TABLE AII.37 Sulfonic Acids *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)				
		Sulfonyl Chloride	Sulfonamide	Sulfonanilide	Benzyl Thiuronium Salt	4-Toluidine Salt
4-Nitrobenzenesulfonic acid	95	80	180	171		180
2,5-Dichlorobenzenesulfonic acid	97	38	186	160	170	248
2,6-Dimethylbenzenesulfonic acid	98	39	113; 96			
3-Carboxybenzenesulfonic acid	98 (hyd)	20	170 (di)		163	226
4-Chloro-2,5-dimethylbenzenesulfonic acid	100	50	185	155		
5-Amino-2-hydroxybenzenesulfonic acid	100 (anhyd)		202	159		
4-Fluoronaphthalene-1-sulfonic acid	100	86	206	144		
3-Chlorobenzene-1,5-disulfonic acid	100d	106	224			
Benzene-1,3,5-trisulfonic acid	100d	187	312	237		
4-Bromobenzenesulfonic acid	103	76	166	119	170	216
Ethanedisulfonic acid	104	95 (di)		69	202	270
2-Fluoronaphthalene-6-sulfonic acid	105 (hyd)	97	133	129	191	221
4-Methylbenzenesulfonic acid (*p*-toluenesulfonic acid)	105	71	139 (anhyd) 105 (dihyd)	103	182	198
1-Nitronaphthalene-2-sulfonic acid	105	121	214	202		
5-Fluoronaphthalene-1-sulfonic acid	106 (hyd)	123	197			
2,4-Dinitrobenzenesulfonic acid	108 (hyd)	102	157			
2,4-Dibromobenzenesulfonic acid	110 (anhyd)	79	190			
4-Nitrobenzenesulfonic acid	111	80	180	136; 171		180
4-Carboxy-3-nitrobenzenesulfonic acid (2-nitro-4-sulfobenzoic acid)	111	160 (di)	226 (di) 192 (mono)			
2,4,5-Trimethylbenzenesulfonic acid	112	62	181			
8-Nitronaphthalene-1-sulfonic acid	115 (trihyd)	165	192	179		
8-Iodonaphthalene-1-sulfonic acid	115	140	187			
7-Chloronaphthalene-2-sulfonic acid	118 (anhyd)	87	176			
5-Nitronaphthalene-2-sulfonic acid	119	125	184			
Anthraquinone-1,7-disulfonic acid	120 (hyd)	232	238			
Phenanthrene-3-sulfonic acid	121 (monohyd)	111	190			222
Naphthalene-2-sulfonic acid	122	79	217	132	191	221
3,4-Diiodobenzenesulfonic acid	125	82	227			
Naphthalene-1,6-disulfonic acid	125 (anhyd)	129	298		81; 235	315
Azoxybenzene-3,3′-disulfonic acid	126	138	273 (di)			
2,5-Dimethyl-3-nitrobenzenesulfonic acid	128	61	173	144		136
5-Chloro-4-methyl-2-nitrobenzenesulfonic acid	128	99	181			
2,5-Dibromobenzenesulfonic acid	128 (anhyd)	71	195			
6-Hydroxynaphthalene-2-sulfonic acid	129 (hyd)		237	161	217	248
2-Methyl-4-nitrobenzenesulfonic acid	130	106	157			
2,4-Dinitrobenzeneusulfonic acid	130 (anhyd)	102	157			
2,4-Dimethyl-5-nitrobenzenesulfonic acid	132	98	187			
4-Chloronaphthalene-1-sulfonic acid	133	95	187	146		
1-Chloronaphthalene-2-sulfonic acid	133 (anhyd)	85	250	172		
2-Methyl-5-nitrobenzenesulfonic acid	134 (dihyd)	47	186	148		257

(Continued)

TABLE AII.37 Sulfonic Acids *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)				
		Sulfonyl Chloride	Sulfon-amide	Sulfon-anilide	Benzyl Thiuro-nium Salt	4-Tolu-idine Salt
Phenanthrene-9-sulfonic acid	134 (hyd)	127	194			235
2-Carboxybenzenesulfonic acid (2-sulfobenzoic acid)	134 (anhyd)	79; 40	194; 154; 230	195	206	200
8-Nitronaphthalene-2-sulfonic acid	136 (hyd)	169	228	173		
3,4-Dicarboxybenzenesulfonic acid (phthalic acid-4-sulfonic acid)	140 (monohyd)	170	200			
2,5-Dimethyl-4-nitrobenzenesulfonic acid	140	75	198	131	144	
4-Methyl-2-nitrobenzenesulfonic acid	141 (anhyd)	99	170			
2,4-Dimethyl-3-nitrobenzenesulfonic acid	144 (anhyd)	96	172			
2,5-Dimethyl-6-nitrobenzenesulfonic acid	145 (anhyd)	110	192	182		159
3-Carboxybenzenesulfonic acid	148 (anhyd)	20	170 (di)		163	226
Phenanthrene-2-sulfonic acid	150	156	254	158		291
Fluorene-2-sulfonic acid	155 (hyd)	164	213			
5-Carboxy-2-methylbenzenesulfonic acid	158 (anhyd)	59	185			
2,4-Diiodobenzenesulfonic acid	167 (anhyd)	78	230			
6-Hydroxynaphthalene-2-sulfonic acid	167 (anhyd)		237	161	217	248
2-Chloro-5-nitrobenzenesulfonic acid	169 (hyd)	90	186			
Azobenzene-4,4′-disulfonic acid	169 (anhyd)	222, 170 (di)	250 (di)			
4-Hydroxynaphthalene-1-sulfonic acid	170		167	200	103	196
Phenanthrene-9-sulfonic acid	174 (anhyd)	127	194			235
Phenanthrene-3-sulfonic acid	176 (anhyd)	111	190			222
2-Carboxy-5-methylbenzenesulfonic acid	190	59 (di)	185			
2,4-Dimethoxybenzenesulfonic acid	192	71	167			
D-Camphor-10-sulfonic acid	193	67	132	121; 88	210	
3-Bromocamphor-8-sulfonic acid	196	137	145			
2,5-Dimethyl-3-nitrobenzenesulfonic acid	200	61	173		144	136
Anthraquinone-1,6-disulfonic acid	217	198		227d		
Anthraquinone-1-sulfonic acid	218	218		216	191	
2-Nitrodiphenylamine-4-sulfonic acid	220d	157	162			
Naphthalene-1,5-disulfonic acid	245 (anhyd)	183 (di)	310, 340 (di)	249 (di)	257	332
4-Carboxybenzenesulfonic acid (4-sulfobenzoic acid)	260 (anhyd)	57 (di)	236 (di)	252 (di)	213	
2-Amino-5-methylbenzene-1,4-disulfonic acid	290d	156 (di)	257 (di)	197 (di)		
Anthraquinone-1,8-disulfonic acid	294	223	> 340	238		
Anthraquinone-1,5-disulfonic acid	311 (hyd)	270	246	270		
Quinoline-8-sulfonic acid	312	124	184			
Pyridine-3-sulfonic acid	357		111	145		

TABLE AII.38 Sulfonyl Chlorides

Name of Compound	mp (°C)	Derivative mp (°C)		
		Sulfonic Acid	Sulfonamide	Sulfonanilide
2-Methylbenzenesulfonyl chloride (*o*-toluenesulfonyl chloride)	10	57	153	136
3-Methylbenzenesulfonyl chloride (*m*-toluenesulfonyl chloride)	12		108	96
Benzenesulfonyl chloride	14	66 (anhyd) 44 (monohyd)	156	110
3-Carboxybenzenesulfonyl chloride (*m*-sulfobenzoic acid)	20	98 (hyd) 148 (anhyd)	170 (di)	
2,5-Dimethylbenzenesulfonyl chloride	25	48 (anhyd) 86 (hyd)	148	
2-Phenylethane-1-sulfonyl chloride	33	91	122	77
2,4-Dimethylbenzenesulfonyl chloride	34	62 (hyd)	139	110
3,4-Dibromobenzenesulfonyl chloride	34	68 (anhyd)	175	
4-Methyl-3-nitrobenzenesulfonyl chloride	36	92	144	109
3-Chloro-4-methylbenzenesulfonyl chloride	38		134	96
2,5-Dichlorobenzenesulfonyl chloride	38	97	186	160
2,6-Dimethylbenzenesulfonyl chloride	39	98	96; 113	
2-Carboxybenzenesulfonyl chloride	40	69 (hyd) 134 (anhyd)	194 (anhyd) 154	195
Propane-1,3-disulfonyl chloride	45	92	169 (di)	129 (di)
2-Methyl-5-nitrobenzenesulfonyl chloride	47	134 (dihyd)	187	148
Indane-5-sulfonyl chloride	47	92	136	129
4-Chloro-2,5-dimethylbenzenesulfonyl chloride	50	100	185	155
3,4-Dimethylbenzenesulfonyl chloride	52	64	144	
4-Chlorobenzenesulfonyl chloride	53	69; 93	144	104
Hexane-1-sulfonyl chloride (cetyl sulfonyl chloride)	54	54	97	
2,4-Dichlorobenzenesulfonyl chloride	55	86	182	
4-Methylbenzene-1,3-disulfonyl chloride	56		191 (di)	189
2,4,6-Trimethylbenzenesulfonyl chloride	57	77	142	109
2-Chloro-5-methylbenzenesulfonyl chloride	56		156	230
4-Carboxybenzenesulfonyl chloride	57	94 (di) 260 (anhyd)	236 (di)	252 (di)
Tetralin-6-sulfonyl chloride	58		135	156
2-Carboxy-5-methylbenzenesulfonyl chloride	59	190; 158 (anhyd)	185	
2,4,5-Trimethylbenzenesulfonyl chloride	61	112	181	
2,5-Dimethyl-3-nitrobenzenesulfonyl chloride	61	200; 128	173	144
3,4-Dichloro-2,5-dimethylbenzenesulfonyl chloride	62		201	157
Benzene-1,3-disulfonyl chloride	63		229	150
3-Nitrobenzenesulfonyl chloride	64	48	167	126
2,4,6-Tribromobenzenesulfonyl chloride	64	64	228	222
4-Chloro-3-methylbenzenesulfonyl chloride	65		128	92
3-Bromocamphor-10-sulfonyl chloride	65	48	157	
2-Ethoxybenzenesulfonyl chloride	66		163	158

(Continued)

TABLE AII.38 Sulfonyl Chlorides *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)		
		Sulfonic Acid	Sulfonamide	Sulfonanilide
D-Camphor-10-sulfonyl chloride	67	193	132	121
Naphthalene-1-sulfonyl chloride	68	90	150	112; 152
2-Methylbenzenesulfonyl chloride (*o*-toluenesulfonyl chloride)	68	57	156	136
2-Nitrobenzenesulfonyl chloride	69	70; 85	193	115
4-Methylbenzenesulfonyl chloride (*p*-toluenesulfonyl chloride)	71	92; 105	138 (anhyd) 105 (dihyd)	103
2,4-Dimethoxybenzenesulfonyl chloride	71	192	167	
3,6-Dichloro-2,5-dimethylbenzenesulfonyl chloride	71		165	171
2,5-Dibromobenzenesulfonyl chloride	71	128 (anhyd)	195	
3-Chloro-2-methylbenzenesulfonyl chloride	72	72	180	
2,5-Dimethyl-4-nitrobenzenesulfonyl chloride	75	140	198	131
4-Chloro-2-nitrobenzenesulfonyl chloride	75		164; 237	138
4-Methoxynaphthalene-2-sulfonyl chloride	75		157	145
4-Bromobenzenesulfonyl chloride	76	103; 90	166	119
2,4-Diiodobenzenesulfonyl chloride	78	167 (anhyd)	230	
4,5-Dimethoxybenzene-1,3-disulfonyl chloride	79		239	200
Napthalene-2-sulfonyl chloride	79	91; 122	217	132
2,4-Dibromobenzenesulfonyl chloride	79	110 (anhyd)	190	
1,2-Dimethylbenzene-3,5-disulfonyl chloride	79		239	200
2-Carboxybenzenesulfonyl chloride	79	69 (hyd) 134 (anhyd)	194 (anhyd) 154; 230	195
4-Nitrobenzenesulfonyl chloride	80	95; 111	180	171; 136
6-Methoxynaphthalene-1-sulfonyl chloride	81		150	178
2,5-Dimethylbenzene-1,3-disulfonyl chloride	81		295	174
4,6-Dichloro-2,5-dimethylbenzenesulfonyl chloride	81		150	175
1-Methylnaphthalene-4-sulfonyl chloride	81		177	158
3,4-Diiodobenzenesulfonyl chloride	82	125	227	
7-Methoxynaphthalene-2-sulfonyl chloride	83		220	121
4-Iodobenzenesulfonyl chloride	85		183	143
1-Chloronaphthalene-2-sulfonyl chloride	85	133 (anhyd)	250	172
4-Ethoxynaphthalene-2-sulfonyl chloride	85		183	144
4-Fluoronaphthalene-1-sulfonyl chloride	86	100 (hyd)	206	144
4-Methoxybenzene-1,3-disulfonyl chloride	86		240	209
7-Chloronaphthalene-2-sulfonyl chloride	87	118 (anhyd) 68 (tetrahyd)	176	
D-Camphor-3-sulfonyl chloride	88	77	143	124
2-Methylbenzene-1,3-disulfonyl chloride	88		260	162
4-Hydroxybenzene-1,3-disulfonyl chloride	89	100	239 (di)	205 (di)
2-Chloro-5-nitrobenzenesulfonyl chloride	90	169 (hyd)	186	
4-Nitrobenzylsulfonyl chloride	90	71	204	220
6-Methoxynaphthalene-2-sulfonyl chloride	93		189	120
Benzylsulfonyl chloride	93		105	102

(Continued)

TABLE AII.38 Sulfonyl Chlorides *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)		
		Sulfonic Acid	Sulfonamide	Sulfonanilide
3,5-Dimethylbenzenesulfonyl chloride	94		135	129
Ethanedisulfonyl chloride	95	104		69
3-Methylbenzene-1,5-disulfonyl chloride	95		216	153
4-Chloronaphthalene-1-sulfonyl chloride	95	133	187	146
5-Chloronaphthalene-1-sulfonyl chloride	95		226	138
7-Methylnaphthalene-1-sulfonyl chloride	96		196	164
2,4-Dimethyl-3-nitrobenzenesulfonyl chloride	96	144 (anhyd)	172	
2-Fluoronaphthalene-6-sulfonyl chloride	97 (anhyd)	105	133	129
2-Methylbenzene-1,4-disulfonyl chloride	98		224 (di)	178 (di)
2,4-Dimethyl-5-nitrobenzenesulfonyl chloride	98	132	187	
5-Chloro-4-methyl-2-nitrobenzenesulfonyl chloride	99	128	181	
4-Methyl-2-nitrobenzenesulfonyl chloride	99	141 (anhyd)	170	
4-Methoxynaphthalene-1-sulfonyl chloride	99		226	148
3-Nitrobenzylsulfonyl chloride	100	74	159	
2,4-Dinitrobenzenesulfonyl chloride	102	108 (hyd) 130 (anhyd)	157	
4-Ethoxynaphthalene-1-sulfonyl chloride	103		170	180
7-Ethoxynaphthalene-2-sulfonyl chloride	103		142	153
4-Nitrodiphenylamine-2-sulfonyl chloride	104		173	164
3-Chlorobenzene-1,5-disulfonyl chloride	106	100	224	
(±)-Camphor-8-sulfonyl chloride	106	58	135	
2-Methyl-4-nitrobenzenesulfonyl chloride	106	130 (anhyd)	157	
6-Ethoxynaphthalene-2-sulfonyl chloride	108		183	153
2,5-Dimethyl-6-nitrobenzenesulfonyl chloride	110	145 (anhyd)	192	182
Phenanthrene-3-sulfonyl chloride	111	176 (anhyd) 121 (monohyd) 89 (dihyd)	190	
4-Methylbenzene-1,2-disulfonyl chloride	111		239	190
Acenaphthene-5-sulfonyl chloride	111		223	178
5-Nitronaphthalene-1-sulfonyl chloride	113		236	123
Acenaphthene-3-sulfonyl chloride	114	89	199	286
8-Iodonaphthalene-1-sulfonyl chloride	115		187	140
Biphenyl-4-sulfonyl chloride	115		230	125
2-Ethoxynaphthalene-1-sulfonyl chloride	116		158	187
6-Ethoxynaphthalene-1-sulfonyl chloride	118		154	195
2,6-Dimethyl-4-hydroxybenzene-1,3-disulfonyl chloride	119		208	207
5-Methoxynaphthalene-1-sulfonyl chloride	120		195	157
1-Iodonaphthalene-4-sulfonyl chloride	121		202	133
1-Nitronaphthalene-2-sulfonyl chloride	121	105	214	202
5-Ethoxynaphthalene-1-sulfonyl chloride	121		183	130
2-Methoxynaphthalene-1-sulfonyl chloride	121		159	197
5-Methylnaphthalene-2-sulfonyl chloride	122		189	250; 134
Anthracene-2-sulfonyl chloride	122		261	201

(Continued)

TABLE AII.38 Sulfonyl Chlorides *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)		
		Sulfonic Acid	Sulfonamide	Sulfonanilide
5-Fluoronaphthalene-1-sulfonyl chloride	123	106 (hyd)	197	
Quinoline-8-sulfonyl chloride	124	312	184	
Diphenylmethane-4,4′-disulfonyl chloride	124	59		178
4-Iodonaphthalene-1-sulfonyl chloride	124		206	136
5-Nitronaphthalene-2-sulfonyl chloride	125	119	184	
2,4,6-Trimethylbenzene-1,3-disulfonyl chloride	125		244 (di)	151 (di)
Phenanthrene-9-sulfonyl chloride	127	174 (anhyd) 134 (hyd)	194	
Naphthalene-1,6-disulfonyl chloride	129	125 (anhyd)	298	
2,4-Dimethylbenzene-1,5-disulfonyl chloride	129		249	196
2,4,5-Trimethoxybenzenesulfonyl chloride	130		76	170
8-Chloro-7-methoxynaphthalene-1-sulfonyl chloride	137		153	196
3-Bromocamphor-8-sulfonic chloride	137	196 (anhyd)	145	
Benzophenone-3,3′-disulfonyl chloride	138		157 (di)	178 (di)
Azoxybenzene-3,3′-disulfonyl chloride	138	126	273 (di)	
3-Methoxynaphthalene-2-sulfonyl chloride	138		113	174
Benzene-1,4-disulfonyl chloride	139		288	249
8-Iodonaphthalene-1-sulfonyl chloride	140	115	187	
Benzene-1,2-disulfonyl chloride	143		254	241
Pyridine-3-sulfonyl chloride	144	357	111	145
4-Acetamidobenzenesulfonyl chloride	149		219	214
2-Amino-5-methylbenzene-1,3-disulfonyl chloride	156		257 (di)	192 (di)
Phenanthrene-2-sulfonyl chloride	156	150	254	158
2-Nitrodiphenylamine-4-sulfonyl chloride	157	220	162	
4-Carboxy-3-nitrobenzenesulfonyl chloride	160 (di)	111 (dihyd)	226 (di) 192 (mono)	
Fluorene-2-sulfonyl chloride	164	155 (anhyd)	213	
2,5-Dimethylbenzene-1,4-disulfonyl chloride	164		310	223
8-Nitronaphthalene-1-sulfonyl chloride	165	115 (trihyd)	191	179
Naphthalene-1,4-disulfonyl chloride	166		273	179
8-Nitronaphthalene-2-sulfonyl chloride	169	136 (hyd)	228	173
3,4-Dicarboxybenzenesulfonyl chloride	170	140 (monohyd)	200	
Azobenzene-4,4′-disulfonyl chloride	170	169 (anhyd)	250 (di)	
Naphthalene-1,5-disulfonyl chloride	183	245 (anhyd) (di)	310; 340 (di)	249 (di)
Benzene-1,3,5-trisulfonyl chloride	187	100 (tri)	315 (tri)	237 (tri)
Anthraquinone-2-sulfonyl chloride	197		261	193
Anthraquinone-1,6-disulfonyl chloride	198	217		228
Biphenyl-4,4′-disulfonyl chloride	203	72	300	
Anthraquinone-1-sulfonyl chloride	218	218		216
9,10-Dichloroanthracene-2-sulfonyl chloride	221		279	248
Azobenzene-4,4′-disulfonyl chloride	222	169 (anhyd)	250 (di)	
Anthraquinone-1,8-disulfonyl chloride	223	294 (di)	340	238
Anthracene-1,8-disulfonyl chloride	225		333	224

(Continued)

TABLE AII.38 Sulfonyl Chlorides *(Continued)*

Name of Compound	mp (°C)	Derivative mp (°C)		
		Sulfonic Acid	Sulfonamide	Sulfonanilide
Anthraquinone-1,7-disulfonyl chloride	232	120 (hyd)		238
Anthracene-1,5-disulfonyl chloride	249		330 (di)	293 (di)
Anthraquinone-1,5-disulfonyl chloride	270	310 (hyd) (di)	246	270
2,4-Diaminobenzene-1,5-disulfonyl chloride	275		187	236
Anthraquinone-1,7-disulfonyl chloride	302	120 (hyd)		238

APPENDIX III

Equipment and Chemicals for the Laboratory

The following representative list of laboratory supplies suitable for a course in identification has been included in response to many inquiries. Variation from one laboratory to another in the equipment available may require much of the equipment here to be modified or omitted.

The suggested supplementary microscale kit is included for those colleges and universities that already incorporate microscale equipment into their courses.

AIII.1 APPARATUS

Individual Desk Equipment

It has been found convenient to assign each student a standard organic laboratory desk equipped with the usual apparatus required for the first year's work in organic preparations. This is supplemented by a special kit containing apparatus for carrying out classifications tests and preparation of derivatives on a small scale.

Suggested Locker Equipment

1 Beaker, 50 mL
1 Beaker, 100 mL
1 Beaker, 250 mL
1 Beaker, 400 mL
1 Beaker, 800 mL
2 Brushes, test tube and regular
1 Burner, bunsen
1 Burner, micro
1 Burner tip, wing top
1 Clamp, screw
1 Clamp, test tube
3 Cork rings, assorted
1 Cylinder, graduated, 10 mL
1 Cylinder, graduated, 100 mL
1 Flask, distilling, 10 mL
1 Flask, distilling, 25 mL
1 Flask, distilling, 50 mL
1 Flask, distilling, 100 mL
2 Flasks, Erlenmeyer, 25 mL
2 Flasks, Erlenmeyer, 50 mL
2 Flasks, Erlenmeyer, 125 mL
2 Flasks, Erlenmeyer, 250 mL
1 Flask, Erlenmeyer, 500 mL
1 Flask, filter, 125 mL
1 Flask, filter, 250 mL
2 Funnels, Buchner, 5.5 cm and 7.0 cm
1 Funnel, glass
2 Funnels, Hirsch
1 Funnel, powder
1 Goggles, pair

2 Rings—4 in. and 2 in.
Several 3-ft sections of tubing
2 Spatulas, 1 flat and 1 curved
1 Striker (burner lighter)
6 Test tubes, 13 × 100 mm
6 Test tubes, 16 × 150 mm
2 Test tube racks, to fit above test tubes
1 Thermometer, −5 to 360°C
1 Thermometer adaptor
1 Tongs, crucible
2 Watch glasses, small and large

Suggested Supplementary Kit

1 Condenser
1 Crucible, porcelain with cover
1 Desiccator, small
2 Distillation adapters, needed for a simple distillation
1 Flask, filter, 50 mL
1 Funnel, separatory, 125 mL
2 Magnetic stirring bars, small and large
2 NMR tubes
1 Pipet, graduated, 1 mL
1 Pipet, graduated, 10 mL
5 Pipets, disposable
2 Test tubes, side-arm, 15 × 125 mm
2 Test tubes, side-arm, 20 × 150 mm

Suggested Supplementary Microscale Kit

Aluminum block or sand bath with variae Claisen adapter
Condenser, air
Condenser, jacketed
Conical vials, 0.1 mL
Drying tube
GC collection tube
Hickman–Hinkle still
Needles
Recrystallization tubes, Craig, 2 and 3 mL
Round-bottom flask, 5 and 10 mL
Spin vane
Syringe
Teflon band (used with certain distillation equipment)
Thermometer
Thermometer adapter
Vials, 0.1, 3.0, and 5.0 mL
Vial, reaction

General Laboratory Equipment

Boiling stones
Clamps, assorted
1 Desiccator, large, vacuum, with vacuum pump
Distilled water
Filter paper, assorted
Glass tubing and rods, assorted
Gloves, disposable
Grease
Hot plate stirrers, one per student
Ice machine
Melting point apparatus, one for every five students
Melting point tubes
Mortars and pestles
1 Oven, drying
Pipets, automatic, assorted sizes—stored in a holder

Pipets, Beral (box)
Pipet tips to fit automatic pipets
1 Rack, drying
Ring stands, assorted
Thiele tubes

Special Laboratory Equipment

The following equipment should be kept free from corrosive fumes.

Balances, quantitative, one for every five students, minimum requirements, 1-mg to 100-g range
1 Gas chromatograph mass spectrometer (GC-MS)
1 Gravitometer
1 Fourier transform infrared (FT-IR) spectrophotometer
1 Fourier transform nuclear magnetic resonance (FT-NMR) spectrometer
1 Polarimeter with sodium lamp
1 Refractometer

Items Obtained by Temporary Loan from Instructor or Stockroom

Cylinder of dry nitrogen gas
Development chambers for TLC, such as wide-mouth jars
IR cells, salt plates, mulling oils, and calibration window
NMR solvents (CCl_4, $DCCl_3$, acetone-d_6, DMSO-d_6, D_2O)
Polarimeter tubes, one dm and two dm long
Syringes and needles for GC-MS
Thin-layer chromatography plates
UV lamp

Waste Containers Needed in the Laboratory

These containers should be conveniently located in a hood. Directions for the types of compounds to be placed in each container are discussed in the textbook.

Aqueous solution container
Aromatic organic solvent container
Halogenated organic waste container
Hazardous solid waste container
Hazardous waste container
Hazardous waste container for heavy metals
Nonhazardous solid waste container
Organic nonhazardous solid waste container
Organic solvent container

AIII.2 CHEMICALS NEEDED IN THE LABORATORY

The following compounds are useful for carrying out solubility and classification tests and for preparing the derivatives. It has been found convenient to provide a set of bottles of about 100-mL capacity, using small-mouth bottles for liquids and wide-mouth bottles for solids. Each reagent bottle should have a test tube taped to the side of the bottle that contains a disposable pipet or a spatula for the students to use with the reagent. By providing this for the students, the chemical is not wasted or contaminated with use. For a class of 20 students, 20–50 g of the reagent may be placed in the shelf bottles. The actual amounts needed per student will naturally vary with the nature of the unknowns, the intelligence with which the classification tests are selected, and the manipulative skill of the student. The bottles should be grouped according to the information on the Material Data Safety Sheets (MSDS), and these sheets should be available in the laboratory in a three-ring binder.

Organic Compounds

Acetaldehyde
Acetic anhydride
Acetone
Acetonitrile
Acetyl chloride
Alizarin
Aniline
Azoxybenzene
Benzene
Benzenesulfonyl chloride
Benzoyl chloride
Benzylamine
Benzyl bromide
Benzyl chloride
4-Bromophenacyl bromide
4-Bromophenylhydrazine
Carbon tetrachloride
Chloroacetic acid
Chloroform
Cyclohexane
Diethylene glycol
Diethylene glycol dimethyl ether (diglyme)
Diethyl ether
1,2-Dinitrobenzene
3,5-Dinitrobenzoic acid
3,5-Dinitrobenzoyl chloride
2,4-Dinitrofluorobenzene
2,4-Dinitrophenylhydrazine
Dioxane
95% Ethanol
100% Ethanol
Ethyl acetate
Ethyl bromide
Fluorescein
Fuchsin (*p*-rosaniline hydrochloride)
Glycerol
Hexane
Ligroin
Methanol
Methone (dimedon)
2-Methoxyethanol
Methylene chloride
Methyl iodide
Methyl 4-toluenesulfonate
2-Naphthol
1-Naphthyl isocyanate
Ninhydrin (1,2,3-indanetrione monohydrate)
4-Nitrobenzaldehyde
4-Nitrobenzoyl chloride
4-Nitrobenzyl chloride
4-Nitrophenylhydrazine
3-Nitrophthalic anhydride
5-Nitrosalicylaldehyde

Oxalic acid
Petroleum ether
Phenol
Phenylhydrazine
Phenyl isocyanate
Phenyl isothiocyanate
Phthalic anhydride
Picric acid
Piperidine
2-Propanol
Propylene glycol
Purpald (4-amino-5-hydrazino-1,2,4-triazole-3-thiol)
Pyridine
Sucrose
Thioglycolic acid (mercaptoacetic acid)
Thiourea
Toluene
4-Toluenesulfonyl chloride
4-Toluidine (4-methylaniline or 4-aminotoluene)
Trichloroisocyanuric acid
Tri-*n*-caprylylmethylammonium chloride
Triethanolamine
Triethylamine
Xanthydrol

Inorganic Compounds

Aluminum chloride
Ammonium carbonate
Ammonium chloride
Ammonium hexanitratocerate
Ammonium polysulfide
Borax
Boron trifluoride–acetic acid complex
Bromine
Calcium chloride
Calcium sulfate
Carbon disulfide
Ceric ammonium nitrate
Chloroplatinic acid
Chlorosulfonic acid
Chromic anhydride
Copper sulfate
Copper wire
Ferric ammonium sulfate
Ferric chloride (anhydrous)
Ferrous ammonium sulfate
85% Hydrazine
3% Hydrogen peroxide
Hydroxylamine hydrochloride
Iodine
Iron nails
Lead acetate
Lead dioxide
Magnesium
Magnesium sulfate
Mercuric bromide
Mercuric chloride
Mercuric iodide
Mercuric nitrate
Mercury(II) chloride
Nickel(II) chloride
Nickel chloride hexahydrate
Paraperiodic acid
Phenylhydrazine hydrochloride
Phosphorus pentachloride
Potassium acid phthalate
Potassium bromide
Potassium carbonate
Potassium cyanide
Potassium hydroxide
Potassium iodide
Potassium permanganate
Potassium persulfate
Potassium thiocyanate
Semicarbazide hydrochloride
Silver nitrate

- Sodium
- Sodium acetate
- Sodium acetate trihydrate
- Sodium bicarbonate
- Sodium bisulfite
- Sodium carbonate
- Sodium chloride
- Sodium citrate
- Sodium dichromate
- Sodium hydrogen sulfite
- Sodium hydroxide
- 5.25% Sodium hypochlorite (household bleach)
- Sodium iodide
- Sodium–lead alloy
- Sodium nitrite
- Sodium nitroprusside (disodium pentacyanonitrosoferrate III)
- Sodium potassium tartrate
- Sodium sulfate
- Sodium thiosulfate (hydrated)
- Tetrabutyl ammonium bromide
- Thionyl chloride
- Tin
- Zinc chloride
- Zinc dust
- Zirconium chloride or nitrate

Acids and Bases

These acids and bases should be kept in 250-mL bottles that are easily refilled from the larger bottles.

- Acetic acid
- Ammonium hydroxide
- Hydrochloric acid
- Hydroiodic acid (57%)
- Nitric acid
- Nitric acid (fuming)
- Phosphoric acid
- Sulfuric acid
- Sulfuric acid (20% fuming)

Solutions

Below is a listing of the various solutions needed in this textbook. The directions for the preparation of these solutions are given in Chapters 3, 5, 9, and 10 and in textbooks on qualitative and quantitative inorganic chemistry. These solutions should be stored in 100-mL reagent bottles. The bottles that contain the sodium hydroxide solutions should have a rubber stopper, since glass stoppers frequently get stuck on these bottles.

- 1% Ethanolic alizarin solution
- 2% Ammonia solution
- 5% Ammonium hydroxide solution
- 10% Ammonium hydroxide solution
- 10% Ammonium polysulfide solution
- Benedict's solution
- Bogen or Grammercy indicator—hydroxylamine hydrochloride reagent
- 1% Borax solution
- 5% Bromine in carbon tetrachloride
- Bromine water
- Saturated calcium chloride solution
- Ceric ammonium nitrate reagent
- 25% Chloroplatinic acid solution
- 1 M Copper sulfate solution
- 1.7% 1,2-Dinitrobenzene in 2-methoxyethanol
- 2,4-Dinitrophenylhydrazine reagent
- 50% Ethanol
- 60% Ethanol

Fehling's solution
1% Ferric chloride in chloroform
5% Alcoholic ferric chloride solution
5% Ferric chloride solution
Saturated ferrous ammonium sulfate
Ferrous sulfate reagent
1% Fluorescein solution
0.25 M Hydrochloric acid solution
0.5 M Hydrochloric acid solution
1 M Hydrochloric acid solution
2 M Hydrochloric acid solution
1% Hydrochloric acid solution
2% Hydrochloric acid solution
5% Hydrochloric acid solution
10% Hydrochloric acid solution
25% Hydrochloric acid solution
0.5 M Hydroxylamine hydrochloride in 95% ethanol
1 M Hydroxylamine hydrochloride in propylene glycol
Saturated hydroxylamine hydrochloride in methanol
Indicator solution
Iodine in methylene chloride solution
Iodine–potassium iodide solution
Jones reagent
1% Lead acetate solution
Lucas reagent
Mercuric nitrate solution
5% Mercury(II) chloride solution
Nickel chloride hexahydrate in carbon disulfide
Nickel chloride hexahydrate with 5-nitrosalicylaldehyde
2 M Nitric acid solution
5% Nitric acid solution
20% Nitric acid solution
1.5% 4-Nitrobenzaldehyde in 2-methoxyethanol
Periodic acid reagent
10% Phosphoric acid solution
Picric acid in chloroform
10% Picric acid in ethanol
20% Picric acid in ethanol
Saturated picric acid in 95% ethanol
Potassium bromide and bromine solution
30% Potassium fluoride solution
Alcoholic potassium hydroxide reagent
1 M Potassium hydroxide in diethylene glycol
1 M Potassium hydroxide solution
2 M Potassium hydroxide in methanol
1% Potassium permanganate solution
2% Potassium permanganate solution
Saturated potassium permanganate solution
PTC solution
Schiff's reagent
0.1 M Silver nitrate solution
2% Ethanolic silver nitrate solution
5% Silver nitrate solution
Saturated sodium bicarbonate solution
10% Sodium bisulfite solution
40% Sodium bisulfite solution
Saturated sodium bisulfite solution
2% Sodium carbonate solution
5% Sodium carbonate solution
10% Sodium carbonate solution
Saturated sodium chloride solution
Dilute sodium hydrogen sulfite solution
Alcoholic sodium hydroxide solution
0.1 M Sodium hydroxide solution (standardized)
1 M Sodium hydroxide solution
2 M Sodium hydroxide solution
3 M Sodium hydroxide solution
6 M Sodium hydroxide solution
0.1% Sodium hydroxide solution
1% Sodium hydroxide solution
2% Sodium hydroxide solution

5% Sodium hydroxide solution
5% Ethanolic sodium hydroxide solution
10% Sodium hydroxide solution
20% Sodium hydroxide solution
25% Sodium hydroxide solution
33% Sodium hydroxide solution
40% Sodium hydroxide solution
Sodium iodide in acetone
20% Sodium nitrite solution
2% Sodium nitroprusside solution
3 M Sulfuric acid solution
5% Sulfuric acid solution
10% Sulfuric acid solution
20% Sulfuric acid solution
25% Sulfuric acid solution
30% Sulfuric acid solution
75% Sulfuric acid solution
TCICA in acetonitrile
0.4% Zirconium chloride or nitrate solution

Indicators

Bogen Universal Indicator
Grammercy Universal Indicator
Phenolphthalein
Thymol blue
Zirconium–alizarin test paper

Other Items

Blue litmus paper
Celite
Cheesecloth
Congo red paper
Cotton
Cottonseed oil
Glass wool
Norite (charcoal)
Paraffin wax
Phenolphthalein paper
pH paper (1–14)
Red litmus paper
Starch–potassium iodide paper

AIII.3 UNKNOWNS

Compounds for use as unknowns should be carefully selected for purity; typical examples may be chosen from the tables in Appendix II but not necessarily limited to the compounds listed there. The unknowns should not exceed 3 g of a solid and 5 mL of a liquid. Mixtures should also contain no more than 3 g of each solid and 5 mL of each liquid. If microscale techniques are to be used for the preparation of derivatives, then these amounts can be cut down considerably.

As the technique of the students improves with experience toward the end of the quarter or semester, much smaller amounts of the unknowns may be given and the solubility, classification tests, and preparation of derivatives carried out on a much smaller scale (about one-tenth the amounts specified in the experiments and procedures).

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