Intro to Organic Lab Techniques
A Microscale Approach

Pavia
Contents

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Experiments

1 Introduction to Microscale Laboratory 1
2 Solubility 12
3 Extraction 19
4 Chromatography 24
5 Simple and Fractional Distillation 31
6 Infrared Spectroscopy and Boiling-Point Determination 35
7 Electronic Effects of Substituents in Reactions; Acidity Constant Determination 40
8 Chemical Kinetics: Evidence for Nucleophilic Substitution Mechanisms 43
9 Nucleophilic Substitution Reactions: Competing Nucleophiles 51
10 Elimination Reactions: Dehydration and Dehydrohalogenation 61
11 An Oxidation Puzzle 68
12 Preparation of a C-4 or C-5 Acetate Ester 70

Techniques

Technique 1 74
Technique 2 90
Technique 3 97
Technique 4 105
Technique 5 112
Technique 7 121
Technique 9 138
Technique 10 144
Technique 12 154
Technique 13 175
Technique 14 181
Technique 15 193
Technique 19 204
Technique 20 222
Technique 22 234
Technique 24 252
Technique 25 258
EXPERIMENT 1

Introduction to Microscale Laboratory

This textbook discusses the important laboratory techniques of organic chemistry and illustrates many important reactions and concepts. In the traditional approach to teaching this subject, the quantities of chemicals used were on the order of 5–100 grams, and glassware was designed to contain up to 500 mL of liquid. This scale of experiment we might call a macroscale experiment. The approach used here, a microscale approach, differs from the traditional laboratory course in that nearly all the experiments use small amounts of chemicals. Quantities of chemicals used range from about 50 to 1000 milligrams (0.050–1.000 g), and glassware is designed to contain less than 25 mL of liquid. The advantages include improved safety in the laboratory, reduced risk of fire and explosion, and reduced exposure to hazardous vapors. This approach decreases the need for hazardous waste disposal, leading to reduced contamination of the environment. You will learn to work with the same level of care and neatness that has previously been confined to courses in analytical chemistry.

This experiment introduces the equipment and shows how to construct some of the apparatus needed to carry out further experiments. Detailed discussion of how to assemble apparatus and how to practice the techniques is found in Part Six (“The Techniques”) of this textbook. This experiment provides only a brief introduction, sufficient to allow you to begin working. You will need to read the techniques chapters for more complete discussions.

Microscale organic experiments require you to develop careful laboratory techniques and to become familiar with apparatus that is somewhat unusual, compared with traditional glassware. We strongly recommend that each student do Laboratory Exercises 1 and 2. These exercises will acquaint you with the most basic microscale techniques. To provide a strong foundation, we further recommend that each student complete most of Experiments 2 through 17 in Part One of this textbook before attempting any other experiments in the textbook.


HEATING METHODS

Aluminum Block

The most convenient means of heating chemical reactions on a small scale is to use an aluminum block. An aluminum block consists of a square of aluminum that has holes drilled into it. The holes are sized to correspond to the diameters of the most common vials and flasks that are likely to be heated. Often there is also a hole intended to accept the bulb of a thermometer, so that the temperature of the block can be monitored. However, this practice is not recommended. The aluminum block is heated by placing it on a hot plate. An aluminum block is shown in Figure 1. Note that the thermometer in this figure is not used to monitor the temperature of the block.
CAUTION

You should not use a mercury thermometer in direct contact with an aluminum block. If it breaks, the mercury will vaporize on the hot surface. Instead, use a non-mercury thermometer, a metal dial thermometer, or a digital electronic temperature-measuring device. See page 580.

It is recommended that an equipment kit contain two aluminum blocks, one drilled with small holes and able to accept the conical vials found in the glassware kit and another drilled with larger holes and able to accept small round-bottom flasks. The aluminum blocks can be made from inexpensive materials in a small mechanical shop, or they can be purchased from a glassware supplier.

Sand Baths

Another commonly used means of heating chemical reactions on a small scale is to use a sand bath. The sand bath consists of a Petri dish or a small crystallizing dish that has been filled to a depth of about 1 cm with sand. The sand bath is also heated by placing it on a hot plate. The temperature of the sand bath may be monitored by clamping a thermometer in position so that the bulb of the thermometer is buried in the sand. A sand bath, with thermometer, is shown in Figure 2.

Figure 1
Aluminum block with hot plate and reflux apparatus.
We recommend that an aluminum block, rather than a sand bath, be used as a heating source whenever possible. The aluminum block can be heated and cooled quickly, it is indestructible, and there are no problems with spillage of sand.

When precise control at lower temperatures (below about 80°C) is desired, a suitable alternative is to prepare a water bath. The water bath consists of a beaker filled to the required depth with water. The hot plate is used to heat the water bath to the desired temperature. The water in the water bath can evaporate during heating. It is useful to cover the top of the beaker with aluminum foil to diminish this problem.

**CONICAL REACTION VIALS**

One of the most versatile pieces of glassware contained in the microscale organic glassware kit is the **conical reaction vial**. This vial is used as a vessel in which organic reactions are performed. It may serve as a storage container. It is also used for extractions (see Technique 12). A reaction vial is shown in Figure 2.

The flat base of the vial allows it to stand upright on the laboratory bench. The interior of the vial tapers to a narrow bottom. This shape makes it possible to withdraw liquids completely from the vial, using a disposable Pasteur pipet. The vial has a screw cap, which tightens by means of threads.
cast into the top of the vial. The top also has a ground-glass inner surface. This ground-glass joint allows you to assemble components of glassware tightly.

The plastic cap that fits the top of the conical vial has a hole in the top. This hole is large enough to permit the cap to fit over the inner joints of other components of the glassware kit (see Fig. 4). A Teflon insert, or liner, fits inside the cap to cover the hole when the cap is used to seal a vial tightly. Notice that only one side of the liner is coated with Teflon; the other side is coated with a silicone rubber. The Teflon side generally is the harder side of the insert, and it will feel more slippery. The Teflon side should always face toward the inside of the vial. An O-ring fits inside the cap when the cap is used to fasten pieces of glassware together. The cap and its Teflon insert are shown in the expanded view in Figure 3.

**NOTE:** Do not use the O-ring when the cap is used to seal the vial.

You can assemble the components of the glassware kit into one unit that holds together firmly and clamps easily to a ring stand. Slip the cap from the conical vial over the inner (male) joint of the upper piece of glassware and fit a rubber O-ring over the inner joint. Then assemble the apparatus by fitting the inner ground-glass joint into the outer (female) joint of the reaction vial and tighten the screw cap to attach the entire apparatus firmly together. The assembly is illustrated in Figure 4.

The walls of the conical vials are made of thick glass. Heat does not transfer through these walls very quickly. This means that if the vial is subjected to rapid changes in temperature, strain building up within the glass walls of the vial may cause the glass to crack. For this reason, do not attempt to cool these vials quickly by running cold water on them. It is safer to allow them to cool naturally by allowing them to stand.

Although the conical vials have flat bottoms intended to allow them to stand up on the laboratory bench, this does not prevent them from falling over.

**NOTE:** It is good practice to store the vials standing upright inside small beakers.

The vials are somewhat top-heavy, and it is easy to upset them. The beaker will prevent the vial from falling over onto its side.
MEASUREMENT OF SOLIDS

Weighing substances to the nearest milligram requires that the weighings be done on a sensitive top-loading balance or an analytical balance.

NOTE: You must not weigh chemicals directly on balance pans.

Many chemicals can react with the metal surface of the balance pan and thus ruin it. All weighings must be made into a container that has been weighed previously (tared). This tare weight is subtracted from the total weight of container plus sample to give the weight of the sample. Some balances have a built-in compensating feature, the tare button, that allows you to subtract the tare weight of the container automatically, thus giving the weight of the sample directly. A top-loading and an analytical balance are shown in Figure 5.

Balances of this type are quite sensitive and expensive. Take care not to spill chemicals on the balance. It is also important to make certain that any spilled materials are cleaned up immediately.

MEASUREMENT OF LIQUIDS

In microscale experiments, liquid samples are measured using a pipet. When small quantities are used, graduated cylinders do not provide the accuracy needed to give good results. There are two common methods of delivering known amounts of liquid samples, automatic pipets and graduated pipets.

When accurate quantities of liquid reagents are required, the best technique...
is to deliver the desired amount of liquid reagent from the pipet into a container whose tare weight has been determined previously. The container, with sample, is then weighed a second time in order to obtain a precise value of the amount of reagent.

Automatic pipets may vary in design, according to the manufacturer. The following description, however, should apply to most models. The automatic pipet consists of a handle that contains a spring-loaded plunger and a micrometer dial. The dial controls the travel of the plunger and is the means used to select the amount of liquid that the pipet is intended to dispense. Automatic pipets are designed to deliver liquids within a particular range of volumes. For example, a pipet may be designed to cover the range from 10 to 100 \( \mu \text{L} \) (0.010 to 0.100 mL) or from 100 to 1000 \( \mu \text{L} \) (0.100 to 1.000 mL).

Automatic pipets must never be dipped directly into the liquid sample without a plastic tip. The pipet is designed so that the liquid is drawn only into the tip. The liquids are never allowed to come in contact with the internal parts of the pipet. The plunger has two \textbf{detent}, or “stop,” positions used to control the filling and dispensing steps. Most automatic pipets have a stiffer spring that controls the movement of the plunger from the first to the second detent position. You will find a greater resistance as you press the plunger past the first detent.

To use the automatic pipet, follow the steps as outlined here. These steps are also illustrated in Figure 6.

1. Select the desired volume by adjusting the micrometer control on the pipet handle.
2. Place a plastic tip on the pipet. Be certain that that tip is attached securely.
3. Push the plunger down to the first detent position. Do not press the plunger to the second position. If you press the plunger to the second detent, an incorrect volume of liquid will be delivered.
4. Dip the tip of the pipet into the liquid sample. Do not immerse the entire length of the plastic tip in the liquid. It is best to dip the tip only to a depth of about 1 cm.
5. Release the plunger slowly. Do not allow the plunger to snap back, or liquid may splash up into the plunger mechanism and ruin the pipet. Furthermore, rapid release of the plunger may cause air bubbles to be drawn into the pipet. At this point, the pipet has been filled.

6. Move the pipet to the receiving vessel. Touch the tip of the pipet to an interior wall of the container.

7. Slowly push the plunger down to the first detent. This action dispenses the liquid into the container.

8. Pause 1–2 seconds and then depress the plunger to its second detent position to expel the last drop of liquid. The action of the plunger may be stiffer in this range than it was up to the first detent.

9. Withdraw the pipet from the receiver. If the pipet is to be used with a different liquid, remove the pipet tip and discard it.

Automatic pipets are designed to deliver aqueous solutions with an accuracy of within a few percentage points. The amount of liquid actually dispensed varies, however, depending on the viscosity, surface tension, and vapor pressure of the liquid. The typical automatic pipet is very accurate with aqueous solutions but is not always as accurate with other liquids.

Dispensing Pumps

Some scientific supply catalogs offer a series of dispensing pumps. These pumps are useful in a microscale organic laboratory because they are simple to operate, easy to clean, chemically inert, and quite accurate. The interior
parts of dispensing pumps are made of Teflon, which renders them inert to most organic solvents and reagents. A dispensing pump is illustrated in Figure 7.

The first step in using a dispensing pump is to adjust the pump so that it dispenses the desired volume of liquid. Normally, the instructor will make this adjustment. Once the pump is adjusted correctly, it is a simple matter to dispense a liquid. Simply lift the head of the pump as far as it will travel. When you release the head, it will fall, and the liquid will issue from the spout. With viscous liquids, the head of the pump may not fall by itself. In such an instance, gently guide the head downward. After the liquid has been dispensed, you should touch the tip of the dispensing tube to an interior wall of the container in order to remove the last drop of liquid.

As with automatic pipets, dispensing pumps are designed to deliver aqueous solutions with an accuracy of within a few percentage points. The amount of liquid actually dispensed will vary, however, depending on the viscosity, surface tension, and vapor pressure of the liquid. You should always weigh the liquid to determine the amount accurately.

A less-expensive means of delivering known quantities of liquid is to use a graduated pipet. Graduated pipets should be familiar to those of you who have taken general chemistry or quantitative analysis courses. Because they are made of glass, they are inert to most organic solvents and reagents. Disposable serological pipets may be an attractive alternative to standard graduated pipets. The 2-mL size of disposable pipet represents a convenient size for the organic laboratory.

Never draw liquids into the pipets using mouth suction. A pipet bulb or a pipet pump, not a rubber dropper bulb, must be used to fill pipets. We recommend the use of a pipet pump. A pipet fits snugly into the pipet pump, and the pump can be controlled to deliver precise volumes of liquids.
Control of the pipet pump is accomplished by rotating a knob on the pump. Suction created when the knob is turned draws the liquid into the pipet. Liquid is expelled from the pipet by turning the knob in the opposite direction. The pump works satisfactorily with organic, as well as aqueous, solutions.

An alternative, and less expensive, approach is to use a rubber pipet bulb. Use of the pipet bulb is made more convenient by inserting a plastic automatic pipet tip into a rubber pipet bulb. The tapered end of the pipet tip fits snugly into the end of a pipet. Drawing the liquid into the pipet is made easy, and it is also convenient to remove the pipet bulb and place a finger over the pipet opening to control the flow of liquid.

The calibrations printed on graduated pipets are reasonably accurate, but you should practice using the pipets in order to achieve this accuracy. When accurate quantities of liquids are required, the best technique is to weigh the reagent that has been delivered from the pipet.

**LABORATORY EXERCISE 1**

**Option A, Automatic Pipet**

Accurately weigh a 3-mL conical vial, with screw cap and Teflon insert, on a balance. Determine its weight to the nearest milligram (nearest 0.001 g). Using the automatic pipet, dispense 0.500 mL of water into the vial, replace the cap assembly (with the insert arranged Teflon side down), and weigh the vial a second time. Determine the weight of water dispersed. Calculate the density of water from your results. Repeat the experiment using 0.500 mL of hexane. Dispose of any excess hexane in a designated waste container. Calculate the density of hexane from your data. Record the results in your notebook, along with your comments on any deviations from literature values that you may have noticed. At room temperature, the density of water is 0.997 g/mL, and the density of hexane is 0.660 g/mL.

**Option B, Dispensing Pump**

Accurately weigh a 3-mL conical vial, with screw cap and Teflon insert, on a balance. Determine its weight to the nearest milligram (nearest 0.001 g). Using a dispensing pump that has been adjusted to deliver 0.500 mL, dispense 0.500 mL of water into the vial, replace the cap assembly, and weigh the vial a second time. Determine the weight of water dispersed. Calculate the density of water from your results. Repeat the experiment using 0.500 mL of hexane. Dispose of any excess hexane in a designated waste container. Calculate the density of hexane from your data. Record the results in your notebook, along with your comments on any deviations from literature values that you may have noticed. See Option A for the density of water and of hexane.

**Option C, Graduated Pipet**

Accurately weigh a 3-mL conical vial, with screw cap and Teflon insert, on a balance. Determine its weight to the nearest milligram (nearest 0.001 g). Using a 1.0-mL graduated pipet, dispense 0.50 mL of water into the vial, replace the cap assembly, and weigh the vial a second time. Determine the weight of water dispensed. Calculate the density of water from your results. Repeat the experiment using 0.50 mL of hexane. Dispose of any excess hexane in a designated waste container. Calculate the density of hexane from your data. Record the results in your notebook along with your comments on any deviations from literature values that you may have noticed. See Option A for the density of water and of hexane.

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1 This technique was described in Deckey, G. “A Versatile and Inexpensive Pipet Bulb.” *Journal of Chemical Education*, 57 (July 1980): 526.
A convenient way of dispensing liquids when a great deal of accuracy is not required is to use a disposable pipet, or Pasteur pipet. Two sizes of Pasteur pipets are shown in Figure 8. Even though accurate calibration may not be required when these pipets are used, it is nevertheless handy to have some idea of the volume contained in the pipet. A crude calibration is, therefore, recommended.

**LABORATORY EXERCISE 2**

**Pipet Calibration**

On a balance, weigh 0.5 grams (0.5 mL) of water into a 3-mL conical vial. Select a short (5 ¼-inch) Pasteur pipet and attach a rubber bulb. Squeeze the rubber bulb before inserting the tip of the pipet into the water. Try to control how much you depress the bulb, so that when the pipet is placed into the water and the bulb is completely released, only the desired amount of liquid is drawn into the pipet. (This skill may take some time to acquire, but it will facilitate your use of a Pasteur pipet.) When the water has been drawn up, place a mark with an indelible marking pen at the position of the meniscus. A more durable mark can be made by scoring the pipet with a file. Repeat this procedure with 1.0 gram of water, and make a 1-mL mark on the same pipet.

Additional Pasteur pipets can be calibrated easily by holding them next to the pipet calibrated in Laboratory Exercise 2 and scoring a new mark on each pipet at the same level as the mark placed on the calibrated pipet. We recommend that several Pasteur pipets be calibrated at one time for use in future experiments.

**Extraction**

A technique frequently applied in purifying organic reaction products is **extraction**. In this method, a solution is mixed thoroughly with a second solvent. The second solvent is not miscible with the first solvent. When the two solvents are mixed, the dissolved substances (solute) distribute themselves between the two solvents until an equilibrium is established. When the mixing is stopped, the two immiscible solvents separate into two distinct layers. The solutes are distributed between the two solvents so that each solute is found in greater concentration in that solvent in which it is more soluble. Separation of the two immiscible solvent layers thus becomes a means of separating solutes from one another based on their relative solubilities in the two solvents.

In a common application, an aqueous solution may contain both inorganic and organic products. An organic solvent that is immiscible with water is added, and the mixture is shaken thoroughly. When the two solvent layers are allowed to form again, on standing, the organic solutes are
transferred to the organic solvent while the inorganic solutes remain in the aqueous layer. When the two layers separate, the organic and inorganic products also separate from one another. The separation, as described here, may not be complete. The inorganic materials may be somewhat soluble in the organic solvent, and the organic products may retain some water solubility. Nevertheless, reasonably complete separations of reaction products can be achieved by the extraction method.

For microscale experiments, the conical reaction vial is the glassware item used for extractions. Place the two immiscible liquid layers in the vial, and seal the top with a screw cap and a Teflon insert (Teflon side toward the inside of the vial). Shake the vial to provide thorough mixing between the two liquid phases. As the shaking continues, vent the vial periodically by loosening the cap and then tightening it again. After about 5 or 10 seconds of shaking, loosen the cap to vent the vial, retighten it, and allow the vial to stand upright in a beaker until the two liquid layers separate completely.

The two liquid layers are separated by withdrawing the lower layer using a disposable Pasteur pipet. This separation technique is illustrated in Figure 9. Take care not to disturb the liquid layers by allowing bubbles to issue from the pipet. Squeeze the pipet bulb to the required amount before introducing the pipet into the vial. Also take care not to allow any of the upper liquid layer to enter the pipet. The pointed shape of the interior of the conical vial makes it easy to remove all the lower layer without allowing it to be contaminated by some of the upper liquid layer. More precise control in the separation can be achieved by using a filter-tip pipet (see Technique 8, Section 8.6, p. 625).

Other Useful Techniques

The practice of organic chemistry requires you to master many more techniques than the ones described in this experiment. Those techniques included here are only the most elementary ones, those needed to get you
started in the laboratory. Additional techniques are described fully in Part Six of this textbook, and Experiments 2 through 17 expose you to the most important of them.

Some other practical hints need to be introduced at this point. The first of these involves manipulating small amounts of solid substances. The efficient transfer of solids requires a small spatula. We recommend that you have two microspatulas, similar to those shown in Figure 10, as part of your standard desk stock. The design of these spatulas permits the handling of milligram quantities of substances without undue spillage or waste. The larger style (see Fig. 10) is more useful when relatively large quantities of solid must be dispensed.

A clean work area is of utmost importance when working in the laboratory. The need for cleanliness is particularly great when working with the small amounts of materials characteristic of microscale laboratory experiments.

NOTE: You must read Technique 1 “Laboratory Safety.” In preventing accidents, there is no substitute for preparation and care.

With this final word of caution and advice, we hope you enjoy the learning experience you are about to begin. Learning the care and precision that microscale experiments require may seem difficult at first, but before long you will be comfortable with the scale of the experiments. You will develop much better laboratory technique as a result of microscale practice, and this added skill will serve you well.

**EXPERIMENT 2**

**Solubility**

**Solubility**

**Polarity**

**Acid-base chemistry**

**Critical-thinking application**

Having a good comprehension of solubility behavior is essential for understanding many procedures and techniques in the organic chemistry laboratory. For a thorough discussion of solubility, read the chapter on this concept
(Technique 10) before proceeding because an understanding of this material is assumed in this experiment.

In Parts A and B of this experiment, you will investigate the solubility of various substances in different solvents. As you are performing these tests, it is helpful to pay attention to the polarities of the solutes and solvents and to even make predictions based on this (see “Guidelines for Predicting Polarity and Solubility.”). The goal of Part C is similar to that of Parts A and B, except that you will be looking at miscible and immiscible pairs of liquids. In Part D, you will investigate the solubility of organic acids and bases. Section 10.2B will help you understand and explain these results.

**REQUIRED READING**

New: Technique 5  Measurement of Volume and Weight  
Technique 10  Solubility

**SUGGESTED WASTE DISPOSAL**

Dispose of all wastes containing methylene chloride into the container marked for halogenated waste. Place all other organic wastes into the non-halogenated organic waste container.

**NOTES TO THE INSTRUCTOR**

In Part A of the procedure, it is important that students follow the instructions carefully. Otherwise, the results may be difficult to interpret. It is particularly important that consistent stirring be done for each solubility test. This can be done most easily by using the larger-style microspatula shown in Figure 10 on page 13.

We have found that some students have difficulty performing Critical Thinking Application 2 (p. 17) on the same day that they complete the rest of this experiment. Many students need time to assimilate the material in this experiment before they can complete this exercise successfully. One approach is to assign Critical Thinking Applications from several technique experiments (for example, Experiments 1–3) to a laboratory period after students complete the individual technique experiments. This provides an effective way of reviewing some of the basic techniques.

**PROCEDURE**

**NOTE:** It is very important that you follow these instructions carefully and that consistent stirring be done for each solubility test.

**Part A. Solubility of Solid Compounds**

Place about 40 mg (0.040 g) of benzophenone into each of four dry test tubes.\(^1\) (Don’t try to be exact: You can be 1–2 mg off and the experiment will still work.) Label the test tubes and then add 1 mL of water to the first tube, 1 mL of methyl

\(^1\) Note to the instructor: Grind up the benzophenone flakes into a powder.
alcohol to the second tube, and 1 mL of hexane to the third tube. The fourth tube will serve as a control. Determine the solubility of each sample in the following way: Using the rounded end of a microspatula (the larger style on p. 13), stir each sample continuously for 60 seconds by twirling the spatula rapidly. If a solid dissolves completely, note how long it takes for the solid to dissolve. After 60 seconds (do not stir longer), note whether the compound is soluble (dissolves completely), insoluble (none of it dissolves), or partially soluble. You should compare each tube with the control in making these determinations. You should state that a sample is partially soluble only if a significant amount (at least 50%) of the solid has dissolved. If it is not clear that a significant amount of solid has dissolved, then state that the sample is insoluble. If all but a couple of granules have dissolved, state that the sample is soluble. An additional hint for determining partial solubility is given in the next paragraph. Record these results in your notebook in the form of a table, as shown on this page. For those substances that dissolve completely, note how long it took for the solid to dissolve.

Although the instructions just given should enable you to determine whether a substance is partially soluble, you may use the following procedure to confirm this. Using a Pasteur pipet, carefully remove most of the solvent from the test tube while leaving the solid behind. Transfer the liquid to another test tube and then evaporate the solvent by heating the tube in a hot water bath. Directing a stream of air or nitrogen gas into the tube will speed up the evaporation (see Technique 7, Section 7.10, p. 614). When the solvent has completely evaporated, examine the test tube for any remaining solid. If there is solid in the test tube, the compound is partially soluble. If there is no, or very little, solid remaining, you can assume that the compound is insoluble.

Now repeat the directions just given, substituting malonic acid and biphenyl for benzophenone. Record these results in your notebook.

<table>
<thead>
<tr>
<th>Organic Compounds</th>
<th>Solvents</th>
<th>Water (highly polar)</th>
<th>Methyl Alcohol (intermediate polarity)</th>
<th>Hexane (nonpolar)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzophenone</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malonic Acid</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biphenyl</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Part B. Solubility of Different Alcohols

For each solubility test (see table on p. 16), add 1 mL of solvent (water or hexane) to a test tube. Then add one of the alcohols, dropwise. Carefully observe what happens as you add each drop. If the liquid solute is soluble in the solvent, you may
see tiny horizontal lines in the solvent. These mixing lines indicate that solution is taking place. *Shake the tube after adding each drop.* While you shake the tube, the liquid that was added may break up into small balls that disappear in a few seconds. This also indicates that solution is taking place. Continue adding the alcohol with shaking until you have added a total of 20 drops. If an alcohol is partially soluble, you will observe that at first the drops will dissolve, but eventually a second layer of liquid (undissolved alcohol) will form in the test tube. Record your results (soluble, insoluble, or partially soluble) in your notebook in table form.

### Solvents

<table>
<thead>
<tr>
<th>Alcohols</th>
<th>Water</th>
<th>Hexane</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-Octanol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CH$_3$(CH$_2$)$_7$CH$_2$OH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-Butanol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CH$_3$CH$_2$CH$_2$CH$_2$OH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methyl alcohol</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CH$_3$OH</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Part C. Miscible or Immiscible Pairs

For each of the following pairs of compounds, add 1 mL of each liquid to the same test tube. Use a different test tube for each pair. Shake the test tube for 10–20 seconds to determine whether the two liquids are miscible (form one layer) or immiscible (form two layers). Record your results in your notebook.

- Water and ethyl alcohol
- Water and diethyl ether
- Water and methylene chloride
- Water and hexane
- Hexane and methylene chloride

#### Part D. Solubility of Organic Acids and Bases

Place about 30 mg (0.030 g) of benzoic acid into each of three dry test tubes. Label the test tubes and then add 1 mL of water to the first tube, 1 mL of 1.0 M NaOH to the second tube, and 1 mL of 1.0 M HCl to the third tube. Stir the mixture in each test tube with a microspatula for 10–20 seconds. Note whether the compound is soluble (dissolves completely) or is insoluble (none of it dissolves). Record these results in table form. Now take the tube containing benzoic acid and 1.0 M NaOH. With stirring add 6 M HCl dropwise until the mixture is acidic. Test the mixture with litmus or pH paper to determine when it is acidic. When it is acidic, stir the mixture for 10–20 seconds and note the result (soluble or insoluble) in the table.

Repeat this experiment using ethyl 4-aminobenzoate and the same three solvents. Record the results. Now take the tube containing ethyl 4-aminobenzoate and 1.0 M HCl. With stirring, add 6 M NaOH dropwise until the mixture is basic. Test the mixture with litmus or pH paper to determine when it is basic. Stir the mixture for 10–20 seconds and note the result.

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*Do not place the litmus or pH paper into the sample; the dye will dissolve. Instead, place a drop of solution from your spatula onto the test paper. With this method, several tests can be performed using a single strip of paper.*
Part E. Critical Thinking Applications

1. Determine by experiment whether each of the following pairs of liquids is miscible or immiscible.
   - Acetone and water
   - Acetone and hexane

   How can you explain these results, given that water and hexane are immiscible?

2. You will be given a test tube containing two immiscible liquids and a solid organic compound that is dissolved in one of the liquids. You will be told the identity of the two liquids and the solid compound, but you will not know the relative positions of the two liquids or in which liquid the solid is dissolved. Consider the following example, in which the liquids are water and hexane and the solid compound is biphenyl.

   a. Without doing any experimental work, predict where each liquid is (top or bottom) and in which liquid the solid is dissolved. Justify your prediction. You may want to consult a handbook such as The Merck Index or the CRC Handbook of Chemistry and Physics to determine the molecular structure of a compound or to find any other relevant information. Note that dilute solutions such as 1 M HCl are composed mainly of water.

   Biphenyl dissolved in hexane

   Water

3. The sample you are given may contain one of the following combinations of solid and liquids (the solid is listed first): fluorene, methylene chloride, water; triphenylmethanol, diethyl ether, water; salicylic acid, methylene chloride, 1 M NaOH; ethyl 4-aminobenzoate, diethyl ether, 1 M HCl; naphthalene, hexane, water; benzoic acid, diethyl ether, 1 M NaOH; p-aminoacetophenone, methylene chloride, 1 M HCl.
b. Now try to prove your prediction experimentally. That is, demonstrate which liquid the solid compound is dissolved in and the relative positions of the two liquids. You may use any experimental technique discussed in this experiment or any other technique that your instructor will let you try. In order to perform this part of the experiment, it may be helpful to separate the two layers in the test tube. This can be done easily and effectively with a Pasteur pipet. Squeeze the bulb on the Pasteur pipet and then place the tip of the pipet on the bottom of the test tube. Now withdraw only the bottom layer and transfer it to another test tube. Note that evaporating the water from an aqueous sample takes a very long time; therefore, this may not be a good way to show that an aqueous solution contains a dissolved compound. However, other solvents may be evaporated more easily (see p. 643). Explain what you did and whether or not the results of your experimental work were consistent with your prediction.

3. Add 0.025 g of tetraphenylcyclopentadienone to a dry test tube. Add 1 mL of methyl alcohol to the tube and shake for 60 seconds. Is the solid soluble, partially soluble, or insoluble? Explain your answer.

QUESTIONS

1. For each of the following pairs of solute and solvent, predict whether the solute would be soluble or insoluble. After making your predictions, you can check your answers by looking up the compounds in *The Merck Index* or the *CRC Handbook of Chemistry and Physics*. Generally, *The Merck Index* is the easier reference book to use. If the substance has a solubility greater than 40 mg/mL, you may conclude that it is soluble.

a. Malic acid in water

\[
\text{HO-C-CHCH}_2\text{C-OH}
\]

Malic acid

b. Naphthalene in water

[Diagram of Naphthalene]

c. Amphetamine in ethyl alcohol

[Diagram of Amphetamine]

d. Aspirin in water

[Diagram of Aspirin]

e. Succinic acid in hexane (*Note: The polarity of hexane is similar to petroleum ether.)*

[Diagram of Succinic acid]
f. Ibuprofen in diethyl ether

\[
\text{CH}_3 \text{CHCH}_2 \text{CH} = \text{COH} \quad \text{Ibuprofen}
\]

g. 1-Decanol (n-decyl alcohol) in water

\[
\text{CH}_3(\text{CH}_2)_8\text{CH}_2\text{OH} \quad \text{1-Decanol}
\]

2. Predict whether the following pairs of liquids would be miscible or immiscible:
   a. Water and methyl alcohol
   b. Hexane and benzene
   c. Methylene chloride and benzene
   d. Water and toluene

3. Would you expect ibuprofen (see 1f) to be soluble or insoluble in 1.0 \( M \) \( \text{NaOH} \)?
   Explain.

4. Thymol is very slightly soluble in water and very soluble in 1.0 \( M \) \( \text{NaOH} \). Explain.

5. Although cannabinol and methyl alcohol are both alcohols, cannabinol is very slightly soluble in methyl alcohol at room temperature. Explain.
Extraction is one of the most important techniques for isolating and purifying organic substances. In this method, a solution is mixed thoroughly with a second solvent that is \textit{immiscible} with the first solvent. (Remember that immiscible liquids do not mix; they form two phases, or layers.) The solute is extracted from one solvent into the other because it is more soluble in the second solvent than in the first.

The theory of extraction is described in detail in Technique 12, Sections 12.1–12.2, pp. 669–671. You should read these sections before continuing this experiment. Because solubility is the underlying principle of extraction, you may also wish to reread the introduction to the experiment on solubility.

Extraction is not only a technique used by organic chemists but it is also used to produce common products with which you are familiar. For example, vanilla extract, the popular flavoring agent, was originally extracted from vanilla beans using alcohol as the organic solvent. Decaffeinated coffee is made from coffee beans that have been decaffeinated by an extraction technique. This process is similar to the procedure in Experiment 3A of this experiment, in which you will extract caffeine from an aqueous solution.

The purpose of this experiment is to introduce the microscale technique for performing extractions and allow you to practice this technique. This experiment also demonstrates how extraction is used in organic experiments.
Distribution of a Solute between Two Immiscible Solvents

In this experiment, you will investigate how several different organic solids distribute themselves between water and methylene chloride. A solid compound is mixed with the two solvents until equilibrium is reached. The organic layer is removed, dried over anhydrous sodium sulfate, and transferred to a tared container. After evaporating the methylene chloride, the weight of the organic solid that was in the organic layer is determined. By finding the difference, the amount of solute in the aqueous layer can also be determined. The distribution coefficient of the solid between the two layers can then be calculated and related to the polarity of the solid and the polarities of the two liquids.

Three different compounds will be used: benzoic acid, succinic acid, and sodium benzoate. Their structures are given below. You should perform this experiment on one of the solids and share your data with two other students who worked with the other two solids. Alternatively, data from the entire class may be pooled and averaged.

**PROCEDURE**

Place 0.050 g of one of the solids (benzoic acid, succinic acid, or sodium benzoate) into a 5-mL conical vial. Add 2.0 mL of methylene chloride and 2.0 mL of water to the vial. Cap the vial and shake it as described in Experiment 4A for about 1 minute. Check for undissolved solid. Continue shaking the vial until all the solid is dissolved. After the layers have separated, transfer the bottom organic layer to another vial or a small test tube. Using the same procedure just described in Experiment 4A (see the section on “Drying the Organic Layers”), dry this organic layer over granular anhydrous sodium sulfate.

Transfer the dried methylene chloride solution with a clean, dry Pasteur pipet to a dry, preweighed conical vial, leaving the drying agent behind. Evaporate the methylene chloride by heating the vial in a hot water bath while directing a stream of dry air or nitrogen gas at the surface of the liquid. When the solvent is evaporated, remove the vial from the bath and dry the outside of the vial. When the vial has cooled to room temperature, weigh the vial to determine the amount of solid solute that was in the methylene chloride layer. Determine by difference the amount of the solid that was dissolved in the aqueous layer. Calculate the distribution
coefficient for the solid between methylene chloride and water. Because the volume of methylene chloride and water was the same, the distribution coefficient can be calculated by dividing the weight of solute in methylene chloride by the weight of solute in water.

**Optional Exercise**

Repeat the preceding procedure using 0.050 g of caffeine, 2.0 mL of methylene chloride, and 2.0 mL of water. Determine the distribution coefficient for caffeine between methylene chloride and water. Compare this to the literature value of 4.6.

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**EXPERIMENT 3B**

**How Do You Determine Which One Is the Organic Layer?**

A common problem that you might encounter during an extraction procedure is not knowing for sure which layer is organic and which is the aqueous one. Although the procedures in this textbook often indicate the expected relative positions of the two layers, not all procedures will give this information, and you should be prepared for surprises. Sometimes knowing the densities of the two solvents is not sufficient, because dissolved substances can significantly increase the density of a solution. It is very important to know the location of the two layers because usually one layer contains the desired product and the other layer is discarded. A mistake at this point in an experiment would be disastrous!

The purpose of this experiment is to give you some practice in determining which layer is aqueous and which layer is organic. One effective technique is to add a few drops of water to each layer after the layers have been separated. If the layer is water, then the drops of added water will dissolve in the aqueous layer and increase its volume. If the added water forms droplets or a new layer, then it is the organic layer.

**PROCEDURE**

Obtain three test tubes, each containing two layers. For each tube, you will be told the identity of the two layers, but you will not be told their relative positions. Determine experimentally which layer is organic and which layer is aqueous. Dispose of all these mixtures into the waste container designated for halogenated organic wastes. After determining the layers experimentally, look up the densities of the various liquids in a handbook to see if there is a correlation between the densities and your results.

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4 The three mixtures will likely be (1) water and n-butyl chloride, (2) water and n-butyl bromide, and (3) n-butyl bromide and saturated aqueous sodium bromide.
Use of Extraction to Isolate a Neutral Compound from a Mixture Containing an Acid or Base Impurity

In this experiment you will be given a solid sample containing an unknown neutral compound and an acid or base impurity. The goal is to remove the acid or base by extraction and isolate the neutral compound. By taking the melting point of the neutral compound, you will identify it from a list of possible compounds. There are many organic reactions in which the desired product, a neutral compound, is contaminated by an acid or base impurity. This experiment illustrates how extraction is used to isolate the product in this situation.

In Technique 10, “Solubility,” you learned that organic acids and bases can become ions in acid–base reactions (see “Solutions in Which the Solute Ionizes and Dissociates,”). Before reading on, review this material if necessary. Using this principle, it is possible to separate an acid or base impurity from a neutral compound. The following scheme, which shows how both an acid and a base impurity are removed from the desired product, illustrates how this is accomplished:

Flow chart showing how acid and base impurities are removed from the desired product.

The neutral compound can now be isolated by removing the water dissolved in the ether and evaporating the ether. Because ether dissolves a
relatively large quantity of water (1.5%), the water must be removed in two steps: In the first step, the ether solution is mixed with a saturated aqueous NaCl solution. Most of the water in the ether layer will be transferred to the aqueous layer in this step (see Technique 12, Section 12.9.) Finally, the remainder of the water is removed by drying the ether layer over anhydrous sodium sulfate. The neutral compound can then be isolated by evaporating the ether. In most organic experiments that use a separation scheme such as this, it would be necessary to perform a crystallization step to purify the neutral compound. However, in this experiment the neutral compound should be sufficiently pure at this point to identify it by melting point.

The organic solvent used in this experiment is ether. Recall that the full name for ether is diethyl ether. Because ether is less dense than water, this experiment will give you practice in performing extractions where the nonpolar solvent is less dense than water.

The following procedure details the removal of an acid impurity from a neutral compound and isolating the neutral compound. It contains an additional step that is not normally part of this kind of separation scheme: The aqueous layers from each extraction are segregated and acidified with aqueous HCl. The purpose of this step is to verify that the acid impurity has been removed completely from the ether layer. In the Optional Exercise, the sample contains a neutral compound with a base impurity; however, a detailed procedure is not given. If you are assigned this exercise, you must create a procedure by using the principles discussed in this introduction and by studying the following procedure for isolating the neutral compound from an acid impurity.

PROCEDURE

Isolating a Neutral Compound from a Mixture Containing an Acid Impurity. Add 0.150 g of an unknown mixture\(^2\) to a screw-cap centrifuge tube. Add 4.0 mL of ether to the tube and cap it. Shake the tube until all the solid dissolves completely.

Add 2.0 mL of 1.0 M NaOH to the tube and shake for 30 seconds. Let the layers separate. Remove the bottom (aqueous) layer, and place this in a test tube labeled “1st NaOH extract.” Add another 2.0-mL portion of 1.0 M NaOH to the centrifuge tube and shake for 30 seconds. When the layers have separated, remove the aqueous layer and put this in a test tube labeled “2nd NaOH extract.”

With stirring, add 6 M HCl dropwise to each of the two test tubes containing the NaOH extracts until the mixture is acidic. Test the mixture with litmus or pH paper to determine when it is acidic. Observe the amount of precipitate that forms. What is the precipitate? Does the amount of precipitate in each tube indicate that all the acid impurity has been removed from the ether layer containing the unknown neutral compound?

The drying procedure for an ether layer requires the following additional step compared to the procedure for drying a methylene chloride layer (see Technique 12, Section 12.9, “Saturated Salt Solution,” p. 680). To the ether layer in the

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\(^2\) The mixture contains 0.100 g of one of the neutral compounds given in the list on page 39 and 0.050 g of benzoic acid, the acid impurity.
centrifuge tube, add 2.0 mL of saturated aqueous sodium chloride. Shake for 30 seconds and let the layers separate. Remove and discard the aqueous layer.

With a clean, dry Pasteur pipet, transfer the ether layer (without any water) to a clean, dry test tube. Now dry the ether layer over granular anhydrous sodium sulfate (see Technique 12, Section 12.9, “Drying Procedure with Anhydrous Sodium Sulfate,”).

Transfer the dried ether solution with a clean, dry Pasteur pipet to a dry, preweighed test tube, leaving the drying agent behind. Evaporate the ether by heating the tube in a hot water bath. This should be done in a hood and can be accomplished more rapidly if a stream of dry air or nitrogen gas is directed at the surface of the liquid (see Technique 7, Section 7.10). When the solvent has evaporated, remove the test tube from the bath and dry the outside of the tube. Once the tube has cooled to room temperature, weigh it to determine the amount of solid solute that was in the ether layer. Obtain the melting point of the solid and identify it from the following list:

<table>
<thead>
<tr>
<th>Melting Point</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluorenone 82–85°C</td>
</tr>
<tr>
<td>Fluorene 116–117°C</td>
</tr>
<tr>
<td>1,2,4,5-Tetrachlorobenzene 139–142°C</td>
</tr>
<tr>
<td>Triphenylmethanol 162–164°C</td>
</tr>
</tbody>
</table>

Optional Exercise: Isolating a Neutral Compound from a Mixture Containing a Base Impurity. Obtain 0.150 g of an unknown mixture containing a neutral compound and a base impurity. Develop a procedure for isolating the neutral compound, using the preceding procedure as a model. After isolating the neutral compound, obtain the melting point and identify it from the list of compounds given above.

**EXPERIMENT 4**

**Chromatography**

**Thin-layer chromatography**

**Column chromatography**

**Following a reaction with thin-layer chromatography**

Chromatography is perhaps the most important technique used by organic chemists to separate the components of a mixture. This technique involves the distribution of the different compounds or ions in the mixture between two phases, one of which is stationary and the other moving. Chromatography works on much the same principle as solvent extraction. In extraction, the components of a mixture are distributed between two solvents according to their relative solubilities in the two solvents. The separation process in chromatography depends on differences in how strongly the components of the mixture are adsorbed to the stationary phase and how soluble they are in the moving phase. These differences depend primarily on the relative polarities of the components in the mixture.
There are many types of chromatographic techniques, ranging from thin-layer chromatography, which is relatively simple and inexpensive, to high-performance liquid chromatography, which is very sophisticated and expensive. In this experiment, you will use two of the most widely used chromatographic techniques: thin-layer and column chromatography. The purpose of this experiment is to give you practice in performing these two techniques, to illustrate the principles of chromatographic separations, and to demonstrate how thin-layer and column chromatography are used in organic chemistry.

**REQUIRED READING**

New: Technique 19  Column Chromatography  
Technique 20  Thin-Layer Chromatography

**SPECIAL INSTRUCTIONS**

Many flammable solvents are used in this experiment. Use Bunsen burners for making micropipets in a part of the lab that is separate from where the solvents are being used. The thin-layer chromatography should be performed in the hood.

**SUGGESTED WASTE DISPOSAL**

Dispose of methylene chloride in the container designated for halogenated organic wastes. Dispose of all other organic solvents in the container for nonhalogenated organic solvents. Place the alumina in the container designated for wet alumina.

**NOTES TO THE INSTRUCTOR**

The column chromatography should be performed with activated alumina from EM Science (No. AX0612-1). The particle sizes are 80–200 mesh, and the material is Type F-20. The alumina should be dried overnight in an oven at 110°C and stored in a tightly sealed bottle. Alumina more than several years old may need to be dried for a longer time at a higher temperature.

For thin-layer chromatography (TLC), use flexible silica gel plates from Whatman with a fluorescent indicator (No. 4110 222). If the TLC plates have not been purchased recently, they should be placed in an oven at 100°C for 30 minutes and stored in a desiccator until used. If you use different alumina or different thin-layer plates, try out the experiment before using it with a class. Other materials than those specified here may give different results from those indicated in this experiment.

Grind up the fluorenone flakes into smaller pieces for easier dispensing.
EXPERIMENT 4A

**Thin-Layer Chromatography**

In this experiment, you will use thin-layer chromatography (TLC) to separate a mixture of three compounds: fluorene, fluorenol, and fluorenone:

![Molecular structures of fluorene, fluorenol, and fluorenone](image)

Based on the results with known samples of these compounds, you will determine which compounds are found in an unknown sample. Using TLC to identify the components in a sample is a common application of this technique.

**PROCEDURE**

**Preparing the TLC Plate**

Technique 20 describes the procedures used for thin-layer chromatography. Use an 10 cm × 5.3 cm TLC plate (Whatman Silica Gel Plates No. 4410 222). These plates have a flexible backing but should not be bent excessively. They should be handled carefully or the adsorbent may flake off them. Also, they should be handled only by the edges; the surface should not be touched. Using a lead pencil (not a pen), lightly draw a line across the plate (short dimension) about 1 cm from the bottom (see figure). Using a centimeter ruler, move its index about 0.6 cm in from the edge of the plate and lightly mark off five 1-cm intervals on the line. These are the points at which the samples will be spotted.

Prepare five micropipets to spot the plate. The preparation of these pipets is described and illustrated in Technique 20, Section 20.4, page 782. Prepare a TLC development chamber with methylene chloride (see Technique 20, Section 20.5, p. 784). A beaker covered with aluminum foil or a wide-mouth, screw-cap bottle is a suitable container to use (see Fig. 20.4, p. 783). The backing on the TLC plates is thin, so if it touches the filter paper liner of the development chamber at any point, solvent will begin to diffuse onto the absorbent surface at that point. To avoid this, be sure that the filter paper liner does not go completely around the inside of the container. A space about 2.5 inches wide must be provided. (Note: This development chamber will also be used for Parts C and D in this experiment.)
On the plate, starting from left to right, spot fluorene, fluorenol, fluorenone, the unknown mixture, and the standard reference mixture, which contains all three compounds. For each of the five samples, use a different micropipet to spot the sample on the plate. The correct method of spotting a TLC plate is described in Technique 20, Section 20.4, page 782. Take up part of the sample in the pipet (don’t use a bulb; capillary action will draw up the liquid). Apply the sample by touching the pipet lightly to the thin-layer plate. The spot should be no larger than 2 mm in diameter. It will usually be sufficient to spot each sample once or twice. If you need to spot the sample more than once, allow the solvent to evaporate completely between successive applications and spot the plate in exactly the same position each time. Save the samples in case you need to repeat the TLC.

Developing the TLC Plate
Place the TLC plate in the development chamber, making sure that the plate does not come in contact with the filter paper liner. Remove the plate when the solvent front is 1–2 cm from the top of the plate. Using a lead pencil, mark the position of the solvent front. Set the plate on a piece of paper towel to dry. When the plate is dry, place the plate in a jar containing a few iodine crystals, cap the jar, and warm it gently on a hot plate until the spots begin to appear. Remove the plate from the jar and lightly outline all the spots that became visible with the iodine treatment. Using a ruler marked in millimeters, measure the distance that each spot has traveled relative to the solvent front. Calculate the $R_f$ values for each spot (see Technique 20, Section 20.9, p. 787). Explain the relative positions of the three compounds in terms of their polarities. Identify the compound or compounds that are found in the unknown mixture. At the instructor’s option, submit the TLC plate with your report.

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1. Note to the instructor: The individual compounds and the reference mixture containing all three compounds are prepared as 2% solutions in acetone. The unknown mixture may contain one, two, or all three of the compounds dissolved in acetone.

2. After you have developed the plate and seen the spots, you will be able to tell if you need to rerun the TLC plate. If the spots are too faint to see clearly, you need to spot the sample more. If any of the spots show tailing (see pp. 772–773), then less sample is needed.
Selecting the Correct Solvent for Thin-Layer Chromatography

In Experiment 4A, you were told what solvent to use for developing the TLC plate. In some experiments, however, it will be necessary to determine an appropriate development solvent by experimentation (Technique 20, Section 20.6). In this experiment, you will be instructed to try three solvents for separating a pair of related compounds that differ slightly in polarity. Only one of these solvents will separate the two compounds enough so that they can be easily identified. For the other two solvents, you will be asked to explain, in terms of their polarities, why they failed.

**PROCEDURE**

**Preparation**

Your instructor will assign you a pair of compounds to run on TLC, or you will select your own pair. You will need to obtain about 0.5 mL of three solutions: one solution of each of the two individual compounds and a solution containing both compounds. Prepare three thin-layer plates in the same way as you did in Experiment 5A, except that each plate should be 10 cm × 3.3 cm. When you mark them with a pencil for spotting, make three marks 1 cm apart. Prepare three micropipets to spot the plates. Prepare three TLC development chambers as you did in Experiment 5A, with each chamber containing one of the three solvents suggested for your pair of compounds.

**Developing the TLC Plate**

On each plate, spot the two individual compounds and the mixture of both compounds. For each of the three samples, use a different micropipet to spot the sample on the plates. Place each TLC plate in one of the three development chambers, making sure that the plate does not come in contact with the filter paper liner. Remove each plate when the solvent front is 1–2 cm from the top of the plate. Using a lead pencil, mark the position of the solvent front. Set the plate on a piece of paper towel to dry. When the plate is dry, observe it under a short-wavelength UV lamp, preferably in a darkened hood or a darkened room. With a pencil, lightly outline any spots that appear. Next, place the plate in a jar containing a few iodine crystals, cap the jar, and warm it gently on a hot plate until the spots begin to appear. Remove the plate from the jar and lightly outline all the spots that became visible with the iodine treatment. Using a ruler marked in millimeters, measure the distance that each spot has traveled relative to the solvent front. Calculate the $R_f$ values for each spot. At the instructor’s option, submit the TLC plates with your report.

Which of the three solvents resolved the two compounds successfully? For the two solvents that did not work, explain, in terms of their polarities, why they failed.

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*Note to the instructor: Possible pairs of compounds are given in the following list. The two compounds to be resolved are given first, followed by the three developing solvents to try: (1) benzoin and benzil; acetone, methylene chloride, hexane; (2) vanillin and vanillyl alcohol; acetone, 50% toluene–50% ethyl acetate, hexane; (3) diphenylmethanol and benzophenone; acetone, 70% hexane–30% acetone, hexane. Each compound in a pair should be prepared individually and as a mixture of the two compounds. Prepare all of them as 1% solutions in acetone.*
EXPERIMENT 4C

Column Chromatography

The principles of column chromatography are similar to those of thin-layer chromatography. The primary difference is that the moving phase in column chromatography travels downward, whereas in TLC the solvent ascends the plate. Column chromatography is used more often than TLC to separate relatively large amounts of compounds. With column chromatography, it is possible to collect pure samples of the separated compounds and perform additional tests on them.

In this experiment, fluorene and fluorenone will be separated by column chromatography using alumina as the adsorbent. Because fluorenone is more polar than fluorene, fluorenone will be absorbed to the alumina more strongly. Fluorene will elute off the column with a nonpolar solvent hexane, whereas fluorenone will not come off until a more polar solvent (30% acetone–70% hexane) is put on the column. The purities of the two separated compounds will be tested by TLC and melting points.

PROCEDURE

Advance Preparation

Before running the column, assemble the following glassware and liquids. Obtain four dry test tubes (16 x 100 mm) and number them 1 through 4. Prepare two dry Pasteur pipets with bulbs attached. Place 2.0 mL of hexane, 2.0 mL of acetone, and 2.0 mL of a solution of 70% hexane–30% acetone (by volume) into three Erlenmeyer flasks. Clearly label and stopper each flask. Place 0.3 mL of a solution containing fluorene and fluorenone into a small test tube. Stopper the test tube. Prepare one 10 cm x 3.3 cm TLC plate with four marks for spotting. Use the same TLC development chamber with methylene chloride that you used in Part A. Prepare four micropipets to spot the plates.

Prepare a chromatography column packed with alumina. Place a loose plug of cotton in a Pasteur pipet (5½-inch) and push it gently into position using a glass rod (see figure for the correct position of the cotton). Do not ram the cotton tightly, because this may result in the solvent flowing through the column too slowly. Using a file, score the Pasteur pipet about 1 cm below the cotton plug. To break the tip off the pipet, put your thumbs together at the place on the pipet that you scored and push quickly with both thumbs.

CAUTION

Wear gloves or use a towel to protect your hands from being cut while breaking the pipet.

5 Note to the instructor: This solution should be prepared for the entire class by dissolving 0.3 g of fluorene and 0.3 g of fluorenone in 9.0 mL of a mixture of 5% methylene chloride–95% hexane. Store this solution in a closed container to prevent evaporation of solvent. This will provide enough solution for 20 students, assuming little spillage or other types of waste.
Add 1.25 g of alumina (EM Science, No. AX0612-1) to the pipet while tapping the column gently with your finger. When all the alumina has been added, tap the column with your finger for several seconds to ensure that the alumina is tightly packed. Clamp the column in a vertical position so that the bottom of the column is just above the height of the test tubes you will be using to collect the fractions. Place test tube 1 under the column.

Running the Column

Using a Pasteur pipet, add 3 mL of hexane to the column. The column must be completely moistened by the solvent. Drain the excess hexane until the level of hexane reaches the top of the alumina. Once hexane has been added to the alumina, the top of the column must not be allowed to run dry. If necessary, add more hexane.

NOTE: It is essential that the liquid level not be allowed to drain below the surface of the alumina at any point in this procedure.

When the level of the hexane reaches the top of the alumina, add the solution of fluorene and fluorenone to the column using a Pasteur pipet. Begin collecting the eluent in test tube 2. Just as the solution penetrates the column, add 1 mL of hexane and drain until the surface of the liquid has reached the alumina. Add another 1 mL of hexane. As fluorene elutes off the column, some solvent will evaporate, leaving solid fluorene on the tip of the pipet. Using a Pasteur pipet, dissolve this solid off the column with a few drops of acetone. It may be necessary to do this several times, and the acetone solution is also collected in tube 2.

After you have added all the hexane, change to the more polar solvent (70% hexane–30% acetone). When changing solvents, do not add the new solvent until the last solvent has nearly penetrated the alumina. The yellow band (fluorenone) should now move down the column. Just before the yellow band reaches the bottom of the column, place test tube 3 under the column. When the eluent becomes colorless again, place test tube 4 under the column and stop the procedure.

Tube 2 should contain fluorene and tube 3, fluorenone. Test the purities of these two samples using TLC. You must spot the solution from tube 2 several times in order to apply enough sample on the plate to be able to see the spots. On the plate, also spot a reference solution containing fluorene and fluorenone. After developing the plate and allowing it to dry, visualize the spots with iodine. What do the TLC results indicate about the purities of the two samples?

Using a warm water bath (40–60°C) and a stream of nitrogen gas or air, evaporate the solvent from test tubes 2 and 3. As soon as all the solvent has evaporated from each of the tubes, remove them from the water bath. There may be a yellow oil in tube 3, but it should solidify when the tube cools to room temperature. If it does not, cool the tube in an ice-water bath and scratch the bottom of the test tube with a glass stirring rod or a spatula. Determine the melting points of the fluorene and fluorenone. The melting point of fluorene is 116–117°C and of fluorenone is 82–85°C.

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As an option, students may prepare a microfunnel from a 1-mL disposable plastic pipet. The microfunnel is prepared by (1) cutting the bulb in half with a scissors and (2) cutting the stem at an angle about 1⁄2 inch below the bulb. This funnel can be placed in the top of the column (Pasteur pipet) to aid in filling the column with alumina or with the solvents (see page 764).

Sometimes the fluorenone also moves through the column with hexane. Therefore, be sure to change to test tube 3 if the yellow band starts to emerge from the column.
QUESTIONS

1. Each of the solvents given should effectively separate one of the following mixtures by TLC. Match the appropriate solvent with the mixture that you would expect to separate well with that solvent. Select your solvent from the following: hexane, methylene chloride, or acetone. You may need to look up the structures of solvents and compounds in a handbook.
   a. 2-Phenylethanol and acetophenone
   b. Bromobenzene and o-xylene
   c. Benzoic acid, 2,4-dinitrobenzoic acid, and 2,4,6-trinitrobenzoic acid

2. The following questions relate to the column chromatography experiment performed in Experiment 5D.
   a. Why does the fluorene elute first from the column?
   b. Why was the solvent changed in the middle of the column procedure?

3. Consider the following errors that could be made when running TLC. Indicate what should be done to correct the error.
   a. A two-component mixture containing 1-octene and 1,4-dimethylbenzene gave only one spot with an \( R_f \) value of 0.95. The solvent used was acetone.
   b. A two-component mixture containing a dicarboxylic acid and tricarboxylic acid gave only one spot with an \( R_f \) value of 0.05. The solvent used was hexane.
   c. When a TLC plate was developed, the solvent front ran off the top of the plate.

EXPERIMENT 5
Simple and Fractional Distillation
(Semimicroscale Procedure)

PROCEDURE

You should work in pairs on this experiment. Each pair of students will be assigned an unknown mixture containing equal volumes of two of the liquids from the table on p. 49. One student should perform a simple distillation on the mixture, and the other person should perform a fractional distillation.

Apparatus

Assemble the appropriate distillation apparatus (see figures). Carefully notice the position of the thermometer in these figures. The bulb of the thermometer must be placed well below the sidearm or it will not read the temperature correctly. (In order to monitor the temperature most accurately, use a partial immersion mercury thermometer.) If performing the fractional distillation, pack the air condenser uniformly with 0.8–0.9 g of stainless steel cleaning pad material. Do not pack the material too tightly at any one place in the condenser.

CAUTION

You should wear heavy cotton gloves when handling the stainless steel cleaning pad. The edges are very sharp and can easily cut into the skin.
Wrap the glass section of the air condenser between the two plastic caps with plastic tubing as described in Notes to the Instructor. Alternatively, use the method with a cotton pad (see Notes to the Instructor). Hold the pad in place with tape or twist tie.

For either the simple or fractional distillation, place a boiling stone into the 10-mL round-bottom flask. Also add 7.0 mL of the unknown mixture (measured with a 10-mL graduated cylinder) to the flask. Use a hot plate and an aluminum block for heating.

**Distillation**

These instructions apply to both the simple and fractional distillations. Start circulating the cooling water in the condenser and adjust the heat so that the liquid boils rapidly. During the initial stages of the distillation, continue to maintain a rapid boiling rate. As the hot vapors rise, they will gradually heat up the glassware and, in the case of the fractional distillation, the fractionating column as well. Because the mass of glass and other materials is fairly large, it will take 10–20 minutes of heating before the distillation temperature begins to rise rapidly and approaches the boiling point of the distillate. (Note that this may take longer for the fractional distillation.) When the temperature begins to level off, you should soon see drops of distillate falling into the graduated cylinder.
Now you will probably need to turn down the heat control to achieve the desired rate of distillation. In addition, it may be helpful to raise the round-bottom flask slightly above the aluminum block for a minute or so to cool the mixture more quickly. You should also begin recording the distillation temperature as a function of the total volume of distillate collected. Beginning at a volume of 0.5 mL, record the temperature at every 0.5-mL interval, as determined by the volume of distillate in the 10-mL graduated cylinder. After you have collected 1.0 mL of distillate, remove the 10-mL graduated cylinder and collect the next two drops of distillate in a 3-mL conical vial. Label the vial “1-mL sample.” Cap the vial tightly; otherwise, the more volatile component will evaporate more rapidly, and the composition of the mixture will change. Resume collecting the distillate in the graduated cylinder. As the distillation temperature increases, you may need to turn up the control to maintain the same rate of distillation. Continue to record the temperature and volume data. When you have collected a total of 4.5 mL of distillate, take another small sample of distillate in a second 3-mL conical vial. (If the total volume of distillate that you can collect is less than 4.5 mL, take the last two drops.) Cap the vial.
and label it “4.5-mL sample.” Then continue the distillation until there is a small amount (about 0.5 mL) of liquid remaining in the distilling flask.

**NOTE:** Do not distill to dryness! A dry flask may crack if it is heated too hot.

The best way to stop the distillation is to turn off the hot plate and immediately raise the entire distillation apparatus off the aluminum block.

### Distillation Curve

Using the data you collected for the distillation temperature and the total volume of distillate, construct separate graphs for the simple and fractional distillations. Plot the volume in 0.5-mL increments on the x-axis and the temperature on the y-axis. Comparing the two graphs should make clear that the fractional distillation resulted in a better separation of the two liquids. Using the graph for the fractional distillation, estimate the boiling points of the two components in your mixture by noting the two regions on the graph where the temperatures leveled off. From these approximate boiling points, try to identify the two liquids in your mixture (see table on p. 49). Note that the observed boiling point for the first component may be somewhat higher than the actual boiling point, and the observed boiling point for the second component may be somewhat lower than the actual boiling point. The reason is that the fractionating column may not be efficient enough to completely separate all of the pairs of liquids in this experiment. Therefore, it may be easier to identify the two liquids in your mixture from the gas chromatograph, as described in the next section.

### Gas Chromatography

Gas chromatography is an instrumental method that separates the components of a mixture based on their boiling points. The lower boiling component passes through the column first, followed by the higher boiling components. The actual length of time required for a compound to pass through the column is called the **retention time** of that compound. As each component comes off the column, it is detected, and a peak is recorded that is proportional in size to the amount of the compound that was put on the column.

Gas chromatography can be used to determine the compositions of the two samples that you collected in 3-mL conical vials. The instructor or a laboratory assistant may either make the sample injections or allow you to make them. In the latter case, your instructor will give you adequate instructions beforehand. A reasonable sample size is 2.5 μL. Inject the sample into the gas chromatograph and record the gas chromatogram. Depending on how effectively the two compounds were separated by the distillation, you may see one or two peaks. The lower boiling component has a shorter retention time than the higher boiling one. Your instructor may provide you with the actual retention times for each compound so that you can identify each peak with more certainty.

Once the gas chromatogram has been obtained, determine the relative areas of the two peaks (Technique 22, Section 22.12, p. 810). You can calculate this by triangulation, or the instrument may do this electronically. In either case, you should divide each area by a response factor to account for differences in how the detector responds to the different compounds. Calculate the percentages of the two compounds in both samples. Compare these results for the simple and fractional distillations.
The ability to identify organic compounds is an important skill that is frequently used in the organic laboratory. Although there are several spectroscopic methods and many chemical and physical tests that can be used for identification, the goal of this experiment is to identify an unknown liquid using infrared spectroscopy and a boiling-point determination. Both methods are introduced in this experiment.

Many of the unknown liquids used for this experiment are flammable; therefore, do not use any flames in the laboratory. Also, be careful when handling all of the liquids because many of them are potentially toxic.

This experiment can be performed individually, with each student working on one unknown. However, the opportunity to learn is greater if students work in groups of three. In this case, each group is assigned three unknowns. Each student in the group obtains an infrared spectrum and performs a boiling-point determination on one of the unknowns. Subsequently, the student shares this information with the other two students in the group. Then each student analyzes the collective results for the three unknowns and writes a laboratory report based on all three unknowns. Your instructor will inform you whether you should work alone or in groups.
SUGGESTED WASTE DISPOSAL

If you have not identified the unknown by the end of the laboratory period, you should return the unknown liquid to your instructor in the original container in which it was issued to you. If you have identified the compound, dispose of it in either the container for halogenated waste or the one for nonhalogenated waste, whichever is appropriate.

NOTES TO THE INSTRUCTOR

If you choose to have students work in groups of three, be sure to assign unknowns that differ both in structure and functional group, with at least one aromatic compound in each set. If the experiment is performed early in the year, students may have some difficulty in finding the structures of the compounds that are in the list of possible unknowns, and they will need help. For each unknown, structures will be needed for several of the possible compounds. In fact, compounds with boiling points as much as 5°C higher should be considered because student-determined boiling points are frequently low. This will depend on the method used and the skill of the person performing the technique. The Merck Index, the CRC Handbook of Chemistry and Physics, and the lecture textbook can all be helpful in determining these structures. Technique 4, “How to Find Data for Compounds: Handbooks and Catalogs,” provides helpful information for students just beginning to use handbooks. The nuclear magnetic resonance (NMR) portion of the experiment is optional. We suggest that access to the NMR be granted only after a plausible solution has been tendered. If you do not have an NMR, there are several online databases where you can obtain a printed copy of the spectrum to hand to students.

For the boiling-point determination, it is best to use partial immersion mercury thermometers for most methods. The results are generally better with mercury thermometers than with nonmercury ones, and if you use partial immersion mercury thermometers, you do not need to perform a stem correction.
PROCEDURE

Part A. Infrared Spectrum

Obtain the infrared spectrum of your unknown liquid (Technique 25, Section 25.2, p. 834). If you are working in a group, provide copies of your spectrum for everyone in your group. Identify the significant absorption peaks by labeling them right on the spectrum, and include the spectrum in your laboratory report. Absorption peaks corresponding to the following groups should be identified:

- C—H (sp$^3$)
- C—H (sp$^2$)
- C—H (aldehyde)
- O—H
- C=O
- C=C (aromatic)
- C—O
- C—X (if applicable)
- N—H

Part B. Boiling-Point Determination

Perform a boiling-point determination on your unknown liquid (Technique 13, Section 13.2, p. 695). Your instructor will indicate which method to use. Depending on the method used and the skill of the person performing the technique, boiling points can sometimes be slightly inaccurate. When experimental boiling points are inaccurate, it is more common for them to be lower than the literature value. The difference may be as much as 5°C, especially for higher-boiling liquids. Your instructor may be able to give you more guidance about what level of accuracy you can expect.

Part C. Analysis and Report

Using the structural information from the infrared spectrum and the boiling point of your unknown, identify this liquid from the list of compounds on page 60. If you are working in a group, you will need to do this for all three compounds. In order to make use of the structural information determined from the infrared spectrum, you will need to know the structures of the compounds that have boiling points close to the value you experimentally determined. You may need to consult The Merck Index or the CRC Handbook of Chemistry and Physics. It may also be helpful to look up these compounds in the index of your lecture textbook. If there is more than one compound that fits the infrared spectrum and is within a few degrees of the experimental boiling point, you should list all of these in your laboratory report.

In your laboratory report, include (1) the infrared spectrum with the significant absorption peaks identified right on the spectrum, (2) the experimental boiling point for your unknown, and (3) your identification of the unknown. Explain your justifications for making this identification and write out the structure of this compound.
### List of possible unknown liquids

<table>
<thead>
<tr>
<th>Compound</th>
<th>BP (°C)</th>
<th>Compound</th>
<th>BP (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetone</td>
<td>56</td>
<td>Butyl acetate</td>
<td>127</td>
</tr>
<tr>
<td>2-Methylpentane</td>
<td>62</td>
<td>2-Hexanone</td>
<td>128</td>
</tr>
<tr>
<td><em>sec</em>-Butylamine</td>
<td>63</td>
<td>Morpholine</td>
<td>129</td>
</tr>
<tr>
<td>Isobutyraldehyde</td>
<td>64</td>
<td>3-Methyl-1-butanol</td>
<td>130</td>
</tr>
<tr>
<td>Methanol</td>
<td>65</td>
<td>Hexanal</td>
<td>130</td>
</tr>
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<td>Isobutylamine</td>
<td>69</td>
<td>Chlorobenzene</td>
<td>132</td>
</tr>
<tr>
<td>Hexane</td>
<td>69</td>
<td>2,4-Pentanediione</td>
<td>134</td>
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<tr>
<td>Vinyl acetate</td>
<td>72</td>
<td>Cyclohexylamine</td>
<td>135</td>
</tr>
<tr>
<td>1,3,5-Trifluorobenzene</td>
<td>75</td>
<td>Ethylbenzene</td>
<td>136</td>
</tr>
<tr>
<td>Butanal</td>
<td>75</td>
<td><em>p</em>-Xylene</td>
<td>138</td>
</tr>
<tr>
<td>Ethyl acetate</td>
<td>77</td>
<td>1-Octanol</td>
<td>138</td>
</tr>
<tr>
<td>Butyamine</td>
<td>78</td>
<td>Propionic acid</td>
<td>141</td>
</tr>
<tr>
<td>Ethanol</td>
<td>78</td>
<td>Decanal</td>
<td>142</td>
</tr>
<tr>
<td>2-Butanone</td>
<td>80</td>
<td>4-Heptanone</td>
<td>144</td>
</tr>
<tr>
<td>Cyclohexane</td>
<td>81</td>
<td>2-Ethyl-1-butanol</td>
<td>146</td>
</tr>
<tr>
<td>Isopropyl alcohol</td>
<td>82</td>
<td><em>N</em>-Methylcyclohexylamine</td>
<td>148</td>
</tr>
<tr>
<td>Cyclohexene</td>
<td>83</td>
<td>2,2,2-Trichloroethanol</td>
<td>151</td>
</tr>
<tr>
<td>Isopropyl acetate</td>
<td>85</td>
<td>2-Heptanone</td>
<td>151</td>
</tr>
<tr>
<td>Triethylamine</td>
<td>89</td>
<td>Heptanal</td>
<td>153</td>
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<tr>
<td>3-Methylbutanal</td>
<td>92</td>
<td>Isobutyric acid</td>
<td>154</td>
</tr>
<tr>
<td>3-Methyl-2-butane</td>
<td>94</td>
<td>Bromobenzene</td>
<td>156</td>
</tr>
<tr>
<td>1-Propanol</td>
<td>97</td>
<td>Cyclohexanone</td>
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</tr>
<tr>
<td>Heptane</td>
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<td>Dibutylamine</td>
<td>159</td>
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<tr>
<td><em>tert</em>-Butyl acetate</td>
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<td>Cyclohexanol</td>
<td>160</td>
</tr>
<tr>
<td>2,2,4-Trimethylpentane</td>
<td>99</td>
<td>Butyric acid</td>
<td>162</td>
</tr>
<tr>
<td>2-Butanol</td>
<td>99</td>
<td>Furfural</td>
<td>162</td>
</tr>
<tr>
<td>Formic acid</td>
<td>101</td>
<td>Diisobutyl ketone</td>
<td>168</td>
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<tr>
<td>2-Pentanone</td>
<td>101</td>
<td>Furfuryl alcohol</td>
<td>170</td>
</tr>
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<td>2-Methyl-2-butanol</td>
<td>102</td>
<td>Octanal</td>
<td>171</td>
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<tr>
<td>Pentanal</td>
<td>102</td>
<td>Decane</td>
<td>174</td>
</tr>
<tr>
<td>3-Pentanone</td>
<td>102</td>
<td>Isovaleric acid</td>
<td>176</td>
</tr>
<tr>
<td>Propyl acetate</td>
<td>102</td>
<td>Limonene</td>
<td>176</td>
</tr>
<tr>
<td>Piperidine</td>
<td>106</td>
<td>1-Heptanol</td>
<td>176</td>
</tr>
<tr>
<td>2-Methyl-1-propanol</td>
<td>108</td>
<td>Benzaldehyde</td>
<td>179</td>
</tr>
<tr>
<td>1-Methylcyclohexene</td>
<td>110</td>
<td>Cycloheptanone</td>
<td>181</td>
</tr>
<tr>
<td>Toluene</td>
<td>111</td>
<td>1,4-Diethylbenzene</td>
<td>184</td>
</tr>
<tr>
<td><em>sec</em>-Butyl acetate</td>
<td>111</td>
<td>Iodobenzene</td>
<td>186</td>
</tr>
<tr>
<td>Pyridine</td>
<td>115</td>
<td>1-Octanol</td>
<td>195</td>
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<tr>
<td>4-Methyl-2-pentanone</td>
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<td>Methyl benzoate</td>
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<td>2-Ethylbutanal</td>
<td>117</td>
<td>Methyl phenyl ketone</td>
<td>202</td>
</tr>
<tr>
<td>Methyl 3-methylbutanoate</td>
<td>117</td>
<td>Benzy alcohol</td>
<td>204</td>
</tr>
<tr>
<td>Acetic acid</td>
<td>118</td>
<td>4-Methylbenzaldehyde</td>
<td>204</td>
</tr>
<tr>
<td>1-Butanol</td>
<td>118</td>
<td>Ethyl benzoate</td>
<td>212</td>
</tr>
<tr>
<td>Octane</td>
<td>126</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The Hammett equation, discovered empirically, indicates a simple relationship between the logarithms of the equilibrium, or rate, constants for various reactions of substituted aromatic compounds and two constants, one characteristic of the substituent and one characteristic of the type of reaction.

\[
\log \left( \frac{K}{K_0} \right) = \sigma \rho
\]

In the equation, \( K \) represents the equilibrium (or rate) constant for some reaction of a specific substituted benzene derivative; \( K_0 \) represents the equilibrium (or rate) constant for the parent compound (substituent = hydrogen); \( \rho \) (rho) is the reaction constant; and \( \sigma \) (sigma) the substituent constant.

For the ionization of benzoic acids in water at 25°C, the value of \( \rho \) is defined as 1.00.

\[
\text{Z-COOH} + \text{H}_2\text{O} \xrightleftharpoons[K][\rho \equiv 1.00]{\text{K}} \text{Z-COO}^- + \text{H}_3\text{O}^+
\]

Thus, measurement of the acidity constant for various substituted benzoic acids will lead to a direct determination of the \( \sigma \) constant, the value of which is proportional to the electron-donating or -withdrawing ability of the substituent group on the ring.

In the following experiments you will determine and interpret the values of sigma for several substituents.

**A. Titration**

Prepare dilute solutions (about 0.01 M) of benzoic acid, \( m \)- and \( p \)-hydroxybenzoic acids, and \( p \)-chlorobenzoic acid in 50% (by volume) aqueous ethanol. Place about 25 mL of each acid solution in a 100-mL beaker having a magnetic stirring bar, and titrate slowly with approximately 0.05 M sodium hydroxide in 50% (by volume) aqueous ethanol. Neither the concentration of the sodium hydroxide solution nor those for the aromatic acid solutions need to be known accurately. Follow the titration by means
of a pH meter (glass and calomel electrodes) and prepare a plot such as that shown in Figure E41.1 for each acid. Record the temperature at which the titrations were run.

**EXERCISE**

1. Why isn’t it necessary to determine the exact concentrations of the acid or basic solutions? (*Hint: See Part B.*)

**B. Acidity Constant Determination**

If we consider the dissociation equilibrium for an acid, it becomes apparent that at the point of half-neutralization, the pH of the medium will be numerically equal to the pK of the acid.

\[
\frac{\text{(ArCOO}^-\text{)(H}_3\text{O}^+)}{\text{(ArCOOH)}} = K \\
\log \frac{\text{(ArCOO}^-\text{)}}{\text{(ArCOOH)}} + \log(\text{H}_3\text{O}^+) = \log K
\]

At half-neutralization \(\log[\text{(ArCOO}^-\text{)/(ArCOOH)}] = 0\), so that after multiplying each side of the resulting equation by \(-1\), we obtain

\[-\log (\text{H}_3\text{O}^+) = -\log K\]

or

\[\text{pH} = \text{pK}\]
From the titration curve from each acid, construct parallel lines \( a \) and \( b \) tangential to the initial and final portions of the curve and construct line \( c \). Drop a perpendicular line \( e \) from the midpoint of line \( c \) to the abscissa in order to find the volume of base needed for complete neutralization. Determine the pH corresponding to that point on the curve directly above one-half of the volume of base needed for complete neutralization. This will be the pK of the acid in this solvent system.

If difficulty is encountered in determining the exact equivalence point, an alternative method can be used in which the ordinate of the graph is the rate of change of the pH with base addition (\( \Delta \text{pH}/\Delta \text{base} \)) and the abscissa is the volume of base added (mL). The value of \( \Delta \text{pH}/\Delta \text{base} \) is easily obtained by taking the difference in pH between two data points and dividing it by the amount of base solution added between those same two points. The curve thus produced will have a maximum at the volume of added base, which corresponds to the equivalence point.

From the value \( \rho = 1.46 \) for substituted benzoic acid ionizations in 50% (vol.) aqueous ethanol (in contrast to the value of 1.00 for water), calculate the \( \sigma \) values of each of the substituents.

**EXERCISES**

2. Why might you expect \( \sigma_m \) and \( \sigma_p \) values for the same substituent to be different?

3. The value of \( \sigma \) for hydrogen is 0.0 by definition. What is the general interpretation of values that are more negative than that for hydrogen? More positive?

4. Comment briefly on each of the \( \sigma \) values that you have obtained. Which substituent constants reflect mostly inductive effects? Which reflect a combination of resonance and inductive effects? What can you tell about the electronic nature of a substituent if the \( \text{meta} \) and \( \text{para} \) \( \sigma \) values have opposite signs? Is the value for the \( \text{para} \) hydroxyl group consistent with your knowledge of the electronegativity of oxygen? Explain.

5. Would you expect the value of \( \sigma \) for the \( \text{meta} \) chloro group to be more or less positive than that for the \( \text{para} \) chloro group? Explain.
Continuous changes in the concentrations of reactants and products are observed during the course of chemical reactions. Thus, as an irreversible reaction proceeds, we find that the concentration of each reactant decreases until that of the limiting reagent becomes zero, at which point the reaction stops. Simultaneously, the concentration of the product increases from zero to its maximum value when the reaction is complete. How fast these concentrations change as a function of time is determined by the reaction rate for a chemical transformation.

The field of chemical kinetics involves investigation of the interplay of factors and variables influencing the rates of reactions. Because chemical kinetics provide great insight into the nature and details of reaction mechanisms, it is hard to overstate the importance of this area of research. Indeed, kinetic studies have provided some of the most important evidence in support of the $S_N1$ and $S_N2$ mechanisms (Sec. 14.2).

To simplify our discussion of kinetics, let’s first assume that the reactions are irreversible and then consider the mathematical expressions or rate laws governing these classes of reaction. To do so, we need only examine the rate-determining step for the particular type of substitution. In the case of an $S_N1$ reaction, this step is the formation of a carbocation from the precursor $R–L$ (Eq. 14.2). The rate of the overall reaction is then proportional only to the concentration of substrate, as expressed in Equation 14.24. We see that the rate is first order in the concentration of $R–L$, expressed as $[R–L]^1$, and zeroth order in that of $Nu$: that is $[Nu:]^0$, which means that the rate is independent of its concentration. Adding the two exponents for the concentration gives the overall order of the $S_N1$ reaction, which is seen to be first order. A simplified version of the rate law is seen in Equation 14.25, and this is the form in which it is normally written.

$$\text{Rate of reaction} = k_1[R–L]^1[Nu:]^0$$  \hspace{1cm} (14.24)

$$\text{Rate of reaction} = k_1[R–L]$$ \hspace{1cm} (14.25)

For $S_N2$ reactions, the rate-determining step involves attack by the nucleophile, $Nu$: on the substrate $R–L$ (Eq. 14.2). The corresponding rate law is shown in Equation 14.26, wherein the rate is seen to be proportional to the concentrations of $R–L$ and $Nu$: Both concentrations are taken to the first power, so the rate of the reaction is said to be second order overall.

$$\text{Rate of reaction} = k_2[R–L][Nu:]$$ \hspace{1cm} (14.26)

Both $k_1$ and $k_2$ (Eqs. 14.24–14.26) are rate constants or proportionality factors that relate the rate of reaction and the concentrations of reactants; the subscripts “1” and “2” indicate that they are for unimolecular and bimolecular processes, respectively. Rate constants may have different units: that for $k_1$ is $(\text{time})^{-1}$ whereas that for $k_2$ is $(\text{concentration})^{-1} (\text{time})^{-1}$.

As compared to their $S_N2$ relatives, $S_N1$ reactions are somewhat easier to study experimentally, and calculations of their rate constants are easier. Consequently you will be performing quantitative measurements of the kinetics of an $S_N1$ rather than $S_N2$ reaction in the procedure of this section.
Kinetic Study of an SN1 Reaction

Because an SN1 reaction is a first-order reaction, the rate of the reaction is linearly dependent on the concentration of the reactant R–L (Eq. 14.24). For example, doubling the concentration doubles the rate. A graph of rate versus concentration thus yields a straight line whose slope is \( k_1 \).

When the R–L is being consumed in a first-order reaction, its concentration decreases exponentially with time. If \( C_0 \) is the initial concentration of the substrate at time \( t = 0 \) (\( t_0 \)) and \( C \) is its concentration at any elapsed time \( t \), where \( t \) is measured in a unit of time, typically seconds or minutes. The relationship among these variables is given by Equation 14.27. This equation may be rewritten as shown in Equations 14.28 and 14.29.

\[
C_t = C_0 e^{-k_1 t} \quad (14.27) \\
k_1 t = \ln \left( \frac{C_0}{C_t} \right) \quad (14.28) \\
k_1 t = 2.303 \log \left( \frac{C_0}{C_t} \right) \quad (14.29)
\]

If the initial concentration, \( C_0 \), of R–L is known and if its concentration, \( C_t \), is measured at various time intervals, \( t \), while the reaction is proceeding, the rate constant may be determined in the following ways.

1. The values of \( C_0 \), \( C_t \), and \( t \) measured at each point during the reaction are substituted into Equation 14.28 or 14.29, which is then solved for \( k_1 \). This produces several values of \( k_1 \), which may then be averaged. The correct rate constant is not easily obtained by this method because the average value will be determined without bias, that is, without compensating for any measurements that may be incorrect due to experimental error.

2. A better method for calculating \( k_1 \) from experimental data is to plot either \( (C_0/C_t) \) or \( \log (C_0/C_t) \) versus \( t \). A straight line is then drawn so that it lies closest to the largest number of points on the graph and is called the “best fit.” This line is drawn with bias in that it purposely gives more “weight” to the majority of points lying close to the line; those lying farther from the line are taken to be less reliable and thus are given less “weight.” The slope of the line is the rate constant \( k_1 \) if natural logarithms are used (Eq. 14.28) or \( k_1 / 2.303 \) if log\text{10} are used (Eq. 14.29). Alternatively, a least-squares analysis may be performed on the data using commercially available software such as Cricket Graph\textsuperscript{TM} to obtain the slope of the line; this eliminates the human element in defining where the line should be drawn. You should consult with your instructor if this technique is to be used.

The discussion and experiments presented below illustrate methods of studying chemical kinetics and determining the effects of structure on reactivity, exemplified by the solvolysis of tertiary alkyl halides. The term “solvolysis” describes a substitution reaction in which the solvent, HOS, functions as the nucleophile (Eq. 14.30). In principle, solvolyses may be performed in any nucleophilic solvent such as water (hydrolysis), alcohols (alcoholysis), and carboxylic acids (for example, acetolysis with acetic acid). However, a practical limitation in choosing a solvent is the solubility of the substrate in the solvent because the reaction mixture must be homogeneous; if it is not, surface effects at the interface of the phases will make the kinetic results difficult to interpret and probably nonreproducible as well. In the experiment described here, you will explore solvolyses in mixtures of 2-propanol and water.
You will need to measure the quantities $C_0$, $C_i$, and $t$ in order to determine $k_1$. The procedure we’ll use to measure $C_t$ depends on the fact that a molecule of acid, H–X, is produced for each molecule of alkyl halide that reacts (Eq. 14.30). Thus, you may monitor the progress of the reaction by determining the concentration of hydrogen ion, $[H^+]$, produced as a function of time: At any time $t$, $[H^+] = C_0 - C_i$ so that $C_t$ is defined by Equation 14.31.

\[
C_t = C_0 - [H^+]
\]  

(14.31)

The value of $[H^+]$ is determined experimentally by withdrawing an accurately measured sample, referred to as an aliquot, from the reaction mixture and “quenching” it in a quantity of 98% 2-propanol sufficient to prevent further solvolysis; the solvolysis does not proceed at a measurable rate when so little water is present. The elapsed time $t$ is simply the time that the aliquot was removed minus the time $t_0$ that the reaction was started. The aliquot is titrated with base to yield $[H^+]$. If $C_0$ is known, $C_t$ may then be calculated from Equation 14.31.

The value of $C_0$ can be determined in two different ways. (1) A solution of defined molarity of the alkyl halide in the solvent mixture to be used may be prepared by accurately measuring the mass of alkyl halide and the volume of solvent. (2) A more reliable and easier procedure is to allow the solvolysis to go to completion, at which time all the alkyl halide will have reacted. Accurate titration of an aliquot of this mixture is the “infinity point,” the point at which $[H^+]_\infty = C_0$. Equation 14.31 may then be transformed to Equation 14.32.

\[
C_t = [H^+]_\infty - [H^+]
\]  

(14.32)

It is not necessary to use a standardized solution of base for the titrations so long as the same basic solution is used for all the titrations you perform and the volume of the aliquots withdrawn are identical. Furthermore, it is unnecessary to calculate $[H^+]$ for each aliquot, because the value is directly proportional to the volume of basic solution required to titrate the acid that has formed according to Equation 14.30. Using this fact, and Equation 14.32, allows Equation 14.29 to be rewritten as Equation 14.33.

\[
2.303 \log \left( \frac{\text{mL of NaOH}_0}{\text{mL of NaOH}_t} \right) = k_1 t
\]  

(14.33)

A variety of factors influence the rate of $S_{N1}$ reactions, and the experimental procedures you will perform allow you to investigate some of them. These include the influence of solvent and the structure of the alkyl halide undergoing solvolysis, as discussed below. Additional factors affecting reaction rates include temperature and the nature of $L_\text{r}$, the leaving group; exploration of these is possible in the Optional Discovery Experiments provided.

1. **Solvent Composition.** The nature of the solvent is expected to affect the rate of an $S_{N1}$ reaction because formation of ions occurs in the rate-determining step (Eq. 14.2). Based on your understanding of the principles of solvation, you would predict that more polar solvents would accelerate the rate of the reaction. You will test this hypothesis with experiments that use various mixtures of 2-propanol and water for the solvolysis.
2. Alkyl Group. Tertiary alkyl halides may be used in solvolyses with confidence that the reactions are proceeding by the SN1 mechanism. Two compounds that allow you to examine the possible effects of the structure of the alkyl group on reaction rates are 2-chloro-2-methylpropane (tert-butyl chloride) and 2-chloro-2-methylbutane (tert-pentyl chloride).

The composition of the reaction mixture formed in an SN1 reaction affects neither the rate of the reaction nor the value of the rate constant because the products all arise from a common intermediate, namely a carbocation, that is formed in the rate-determining step (Eq. 14.2). Thus, the four products that are likely to be formed in the solvolysis of 2-chloro-2-methylpropane in aqueous 2-propanol may individually be formed at different rates because of the differing values of the rate constants, \( k_a - k_d \), and of the concentrations of the reagents that react with the carbocation. Nevertheless, the overall rate of the reaction is defined by the ionization that produces the carbocation and chloride ion and has the rate constant \( k_1 \) (Scheme 14.1).

Scheme 14.1

![Scheme 14.1](image)

**Experimental Procedures**

**Kinetics of Solvolysis of 2-Chloro-2-methylbutane**

**Purpose** To investigate the effect of various factors on the rates of SN1 reactions.

**Safety Alert**

Avoid contact of the aqueous solutions with your skin as they may dry it out and/or cause chemical burns. Wash any affected areas with copious amounts of water.
Preparation

Miniscale Procedure

Prepare a table in your notebook for recording (1) the solvent(s) that have been assigned to you and their volume(s); (2) the mass or volume of alkyl halide to be used; (3) the time, \( t_0 \), at which the kinetic run is initiated; (4) the temperature of the reaction mixture; (5) the results of a “blank” titrimetric determination; (6) a series of times, \( t \), at which aliquots are withdrawn; and (7) the initial and final buret readings observed in the titration of each aliquot.

Apparatus

A 10-mL and a 100-mL graduated cylinder, 50-mL buret, a 25-mL beaker, 10-mL volumetric pipet, thermometer, one 125-mL and three 250-mL Erlenmeyer flasks, a 10-mm \( \times \) 75-mm test tube, disposable pipet, timer, apparatus for magnetic stirring.

Setting Up

Using a graduated cylinder, accurately measure 100 mL of your assigned solvent into a 250-mL Erlenmeyer flask equipped with a well-fitting rubber stopper. Measure and record the temperature of this solution. Place 80 mL of 98% 2-propanol in a second flask for use in quenching the solvolysis. Prepare 125–150 mL of approximately 0.04 M sodium hydroxide solution in a third flask. Stopper the flask with a well-fitting rubber stopper.

Set up the buret, and after rinsing it with a small amount of the 0.04 M sodium hydroxide solution, fill it with this solution, ensuring that all air bubbles are out of the tip, and cover the top with a test tube or beaker to minimize absorption of carbon dioxide from the air.

Put about 2 mL of phenolphthalein indicator solution in the test tube and have it and a dropper available for use in each titration. Connect a short length of rubber tubing to the nearest aspirator or vacuum line. This will be used to draw air through the volumetric pipet for a minute or two after each sampling in order to dry it before taking the next sample. Have a timer available that may be read to at least the nearest minute.

This experiment requires that a series of quantitative measurements be performed in a relatively short time. You should be prepared to work rapidly and carefully in order to maintain a high standard of accuracy. Buret readings should be made to the nearest 0.02 mL if possible, although precision within 0.05 mL will normally be satisfactory. Time measurements should be made at least to the nearest minute.

Reaction

Initiate the kinetic run by adding about 1 g of the alkyl halide to the solvent mixture. The alkyl halide may either be weighed out or be measured with a 1-mL pipet. Swirl the mixture gently to obtain homogeneity. Record the time of addition as \( t_0 \). Keep the flask tightly stoppered to avoid evaporation that would change the concentration of the mixture.

While waiting to make the first measurement, determine a “blank” correction for the solvent as follows. Using a graduated cylinder, measure a 10-mL portion of your assigned solvent into the 125-mL Erlenmeyer flask. Next add 20 mL of 98% 2-propanol and 4–5 drops of phenolphthalein to the flask and titrate the stirred solution with aqueous base until a faint pink color persists for 30 sec. In this and all other titrations, use a white background below the titration flask to assist you in detecting color. You may also wish to accentuate the lower edge of the meniscus in the buret by holding dark paper or some other dark object just below it to make
the graduations on the buret easier to read. The blank correction will probably be no more than 0.05–0.15 mL. Dispose of the titrated solution as specified in “Wrapping It Up.” Rinse the flask with water and then with a small amount of 98% 2-propanol so it is ready for further use.

At regular intervals, use the volumetric pipet to remove a 10-mL aliquot from the reaction mixture, and quench the reaction by adding the aliquot to 10 mL of 98% 2-propanol contained in the 125-mL Erlenmeyer flask. Be sure to note the time of addition of the aliquot, probably best taken as the time at which one-half of it has been added. Titrate the solution with base to the phenolphthalein endpoint just as you did in the blank determination.

The suggested approximate times for taking aliquots under various conditions are as follows:

1. 50% 2-propanol/water and 2-chloro-2-methylpropane: 10, 20, 35, 50, 75, and 100 min.
2. 55% 2-propanol/water and 2-chloro-2-methylpropane: 15, 30, 50, 75, 100, and 135 min.
3. 60% 2-propanol/water and 2-chloro-2-methylpropane: 20, 40, 70, 100, 130, and 170 min.
4. 50% 2-propanol/water and 2-chloro-2-methylbutane: 10, 20, 30, 40, 50, and 60 min.
5. 55% 2-propanol/water and 2-chloro-2-methylbutane: 15, 30, 45, 60, 80, 110, and 140 min.
6. 60% 2-propanol/water and 2-chloro-2-methylbutane: 20, 40, 60, 80, 100, and 120 min.

At room temperature, the fastest of these solvolyses requires about 4 h to reach 99.5% completion, and the slowest requires over 12 h. Therefore it is easiest to wait until the next laboratory period to perform the infinity titration that is necessary to obtain $C_0$. Stopper the reaction flask tightly to avoid evaporation and store it in your desk. Be sure to save at least 30 mL of the sodium hydroxide solution in a tightly stoppered flask so that it will be available for the infinity titration.

**Analysis** Obtain IR spectra of the starting materials and compare them. Compute the desired rate constants, $k_1$, by the following sequence of steps.

1. Using the buret readings, determine by difference the number of milliliters of sodium hydroxide solution used in each titration. Apply the blank correction to all values by subtracting it from each volume and use these corrected values in your calculations. Determine the elapsed time at which each aliquot was withdrawn from the reaction mixture. Apply Equation 14.33 by calculating the log term for each kinetic point, multiplying that value by 2.303, and plotting the resulting number (ordinate) vs. elapsed time (abscissa) in hours. Draw the best straight line through the points. Determine the slope of the line; this slope is the rate constant $k_1$. Alternatively, analyze your experimental data using least-squares techniques to obtain the rate constant.

2. Using the same data and Equation 14.31, calculate the value of $k_1$ separately for each kinetic point. Compare the average of these values with the rate constant obtained graphically. Also compare this average with each of the values that were averaged. In your laboratory report for this experiment, specify
which procedure, graphical or averaging, allows you most easily to identify a point that is likely in error.

3. Equation 14.34 provides the half-life, $t_{1/2}$, the time necessary for one-half of the original alkyl halide to react. Calculate the half-life of your reaction using the value of $k_1$ obtained from the graph. Then reexamine your experimental data to determine whether about one-half of the total volume of NaOH used in the infinity titration had been consumed by the end of the first half-life of the reaction. If not, an error has been made in the calculations, and they should be rechecked.

$$T_{1/2} = \frac{0.693}{k_1}$$ (14.34)

**Effect of Temperature on Rates of Solvolysis**

Temperature changes affect the rates of reactions, the rough rule of thumb being that the rate doubles for each rise of 10 °C. You may explore this effect by comparing solvolysis rates at room temperature and at 0 °C. Based on the experimental procedure of this section, design and execute a protocol for measuring the rate of solvolysis of either 2-chloro-2-methylpropane or 2-chloro-2-methylbutane at 0 °C. You should consider the effect of solvent polarity on the rate of the reaction so that the conditions you propose to use will allow measurable amounts of solvolysis to occur during the time period you have available for removing aliquots for titration. Consult with your instructor before performing your proposed procedure.

**Effect of Leaving Group on Rates of Solvolysis**

Because the bond between the carbon atom and the leaving group, L, in R–L is broken in the rate-determining step of an SN reaction, you might expect that the rate of the reaction would be dependent on the nature of L. You may investigate this possibility by comparing the rates of solvolysis of alkyl bromides with those of alkyl chlorides. Based on the experimental procedure of this section, design and execute a protocol for measuring the rate of solvolysis of 2-bromo-2-methylpropane at room temperature. Consult with your instructor before performing your proposed procedure.

**WRAPPING IT UP**

Although you normally should not dispose of solutions containing organic halides by pouring them down the drain, it is acceptable to do so in this case because of the small quantities of the alkyl halides being used and their facile solvolysis. Make the solvolysis solution strongly basic and allow it to remain in your desk until the next laboratory period. Neutralize the basic solution and flush it down the drain using copious amounts of water.

**EXERCISES**

1. Why does the titration endpoint color fade after 30–60 sec?
2. You covered the top of the buret with a test tube or beaker to protect its contents from air. Why was a rubber or cork stopper not used instead?
3. In the kinetics experiment you performed, individual aliquots were quenched by adding them to 98% 2-propanol. Why does this stop the solvolysis?

4. Suppose the reaction flask was left unstoppered until the following laboratory period when the infinity titration was performed. Would the calculated rate constant have been larger or smaller than the “correct” value if some evaporation of solvent had occurred during this time?

5. Derive Equation 14.33 from Equation 14.29. (Hint: Set up the concentrations $C_0$ and $C_t$ in terms of moles/liter for the volume of NaOH used in each titration, and recognize the fact that $[\text{OH}^-] = [\text{H}^+]$. Substitute these values into Equation 14.29, and cancel out constants that appear in the new equation.)

6. Give the possible advantages for using an infinity titration and Equation 14.33 for analyzing your data instead of calculating concentrations of the alkyl halide and using Equation 14.29 for the analysis. Be sure to consider the alternatives for obtaining $C_0$.

7. Equation 14.34 gives the half-life, $t_{1/2}$, of a reaction, which is defined as the time required for a reaction to reach 50% completion. This equation applies to any first-order reaction, including radioactive disintegration. Show how Equation 14.34 may be derived from Equation 14.29. (Hint: When the reaction is 50% complete, $C_t = 1/2 C_0$.)

8. List the possible errors involved in the determination of rate constants by the procedure you used and state the relative importance of each.

9. Refer to Scheme 14.1 and predict the ratio of 2-methyl-2-butanol:tert-amyl isopropyl ether expected if the solvent for the reaction were equimolar in water and 2-propanol and $k_c = 5k_d$. 


Nucleophilic Substitution Reactions: Competing Nucleophiles

Nucleophilic substitution
Heating under reflux
Extraction
Refractometry
Gas chromatography
NMR spectroscopy

The purpose of this experiment is to compare the relative nucleophilicities of chloride ions and bromide ions toward each of the following alcohols: 1-butanol (n-butyl alcohol), 2-butanol (sec-butyl alcohol), and 2-methyl-2-propanol (t-butyl alcohol). The two nucleophiles will be present at the same time in each reaction, in equimolar concentrations, and they will be competing for substrate.

In general, alcohols do not react readily in simple nucleophilic displacement reactions. If they are attacked by nucleophiles directly, hydroxide ion, a strong base, must be displaced. Such a displacement is not energetically favorable and cannot occur to any reasonable extent:

\[ X^- + ROH \rightarrow R-X + OH^- \]

To avoid this problem, you must carry out nucleophilic displacement reactions on alcohols in acidic media. In a rapid initial step, the alcohol is protonated; then water, a stable molecule, is displaced. This displacement is energetically favorable, and the reaction proceeds in high yield:

\[ ROH + H^+ \rightleftharpoons R-OH \]

\[ X^- + R-OH \rightarrow R-X + H_2O \]

Once the alcohol is protonated, it reacts by either the S_N1 or the S_N2 mechanism, depending on the structure of the alkyl group of the alcohol. For a brief review of these mechanisms, consult the chapters on nucleophilic substitution in your lecture textbook.
You will analyze the products of the three reactions in this experiment by a variety of techniques to determine the relative amounts of alkyl chloride and alkyl bromide formed in each reaction. That is, using equimolar concentrations of chloride ions and bromide ions reacting with 1-butanol, 2-butanol, and 2-methyl-2-propanol, you will try to determine which ion is the better nucleophile. In addition, you will try to determine for which of the three substrates (reactions) this difference is important and whether an $S_N1$ or $S_N2$ mechanism predominates in each case.

**REQUIRED READING**

**Review:** Techniques 1 through 6

- Technique 7  Reaction Methods, Section 7.2, 7.4, 7.5, and 7.8
- Technique 12  Extractions, Separations, and Drying Agents, Sections 12.5, 12.9, and 12.11
- Technique 22  Gas Chromatography
- Technique 24  Refractometry

Before beginning this experiment, review the appropriate chapters on nucleophilic substitution in your lecture textbook.

**SPECIAL INSTRUCTIONS**

Each student will carry out the reaction with 2-methyl-2-propanol. Your instructor will also assign you either 1-butanol or 2-butanol. By sharing your results with other students, you will be able to collect data for all three alcohols. You should begin this experiment with Experiment 9A. During the lengthy reflux period, you will be instructed to go on to Experiment 9B. When you have prepared the product of that experiment, you will return to complete Experiment 9A. To analyze the results of both experiments, your instructor will assign specific analysis procedures in Experiment 9C that the class will accomplish.

The solvent–nucleophile medium contains a high concentration of sulfuric acid. Sulfuric acid is corrosive; be careful when handling it.

In each experiment, the longer your product remains in contact with water or aqueous sodium bicarbonate, the greater the risk that your product will decompose, leading to errors in your analytical results. Before coming to class, prepare so that you know exactly what you are supposed to do during the purification stage of the experiment.
SUGGESTED WASTE DISPOSAL

When you have completed the three experiments and all the analyses have been completed, discard any remaining alkyl halide mixture in the organic waste container marked for the disposal of halogenated substances. All aqueous solutions produced in this experiment should be disposed of in the container for aqueous waste.

NOTES TO THE INSTRUCTOR

The solvent–nucleophile medium must be prepared in advance for the entire class. Use the following procedure to prepare the medium.

This procedure will provide enough solvent–nucleophile medium for about 10 students (assuming no spillage or other types of waste). Place 100 g of ice in a 500-mL Erlenmeyer flask and carefully add 76 mL concentrated sulfuric acid. Carefully weigh 19.0 g ammonium chloride and 35.0 g ammonium bromide into a beaker. Crush any lumps of the reagents to powder and then, using a powder funnel, transfer the halides to an Erlenmeyer flask. Carefully add the sulfuric acid mixture to the ammonium salts a little at a time. Swirl the mixture vigorously to dissolve the salts. It will probably be necessary to heat the mixture on a steam bath or a hot plate to achieve total solution. Keep a thermometer in the mixture and make sure that the temperature does not exceed 45°C. If necessary, you may add as much as 10 mL of water at this stage. Do not worry if a few small granules do not dissolve. When solution has been achieved, pour the solution into a container that can be kept warm until all students have taken their portions. The temperature of the mixture must be maintained at about 45°C to prevent precipitation of the salts. Be careful that the solution temperature does not exceed 45°C, however. Place a 20-ml calibrated pipet fitted with a pipet helper in the mixture. The pipet is always left in the mixture to keep it warm.

Be certain that the tert-butyl alcohol has been melted before the beginning of the laboratory period.

The gas chromatograph should be prepared as follows: column temperature, 100°C; injection and detector temperature, 130°C; carrier gas flow rate, 50 mL/min. The recommended column is 8 feet long, with a stationary phase such as Carbowax 20M. If you wish to analyze the products from the reaction of tert-butyl alcohol (Exp. 21B) by gas chromatography, be sure that the tert-butyl halides do not undergo decomposition under the conditions set for the gas chromatograph. tert-Butyl bromide is susceptible to elimination.

When analyzing the product from the reaction of tert-butyl alcohol by refractometry, it is easy for students to make mistakes in reading the refractive index. It is therefore advisable for students to practice first by analyzing a known liquid.
EXPERIMENT 9A

Competitive Nucleophiles with 1-Butanol or 2-Butanol

PROCEDURE

Apparatus
Assemble an apparatus for reflux using a 20-mL round-bottom flask, a reflux condenser, and a drying tube, as shown in the figure. Loosely insert dry glass wool into the drying tube and then add water dropwise onto the glass wool until it is partially moistened. The moistened glass wool will trap the hydrogen chloride and hydrogen bromide gases produced during the reaction. As an alternative, you can use an external gas trap as described in Technique 7, Section 7.7, Part B, page 608. Do not place the round-bottom flask into the aluminum block until the reaction mixture has been added to the flask. Six Pasteur pipets, two 3-mL conical vials with Teflon cap liners, and a 5-mL conical vial with a Teflon liner should also be assembled for use. All pipets and vials should be clean and dry.

CAUTION
The solvent–nucleophile medium contains a high concentration of sulfuric acid. This liquid will cause severe burns if it touches your skin.

Preparation of Reagents
If a calibrated pipet fitted with a pipet helper is provided, you may adjust the pipet to 10 mL and deliver the solvent–nucleophile medium directly into your 20-mL round-bottom flask (temporarily placed in a beaker for stability). Alternatively, you may use a warm 10-mL graduated cylinder to obtain 10.0 mL of the solvent–nucleophile medium. The graduated cylinder must be warm in order to prevent precipitation of the salts. Heat it by running hot water over the outside of the cylinder or by putting it in the oven for a few minutes. Immediately pour the mixture into the round-bottom flask. With either method, a small portion of the salts in the flask may precipitate as the solution cools. Do not worry about this; the salts will redissolve during the reaction.
Reflux

Assemble the apparatus shown in the figure. Using the following procedure, add 0.75 mL of 1-butanol (n-butyl alcohol) or 0.75 mL of 2-butanol (sec-butyl alcohol), depending on which alcohol you were assigned, to the solvent-nucleophile mixture contained in the reflux apparatus. Dispense the alcohol from the automatic pipet or dispensing pump into a 10-mL beaker. Remove the drying tube and, with a 9-inch Pasteur pipet, dispense the alcohol directly into the round-bottom flask by inserting the Pasteur pipet into the opening of the condenser. Also add an inert boiling stone. Replace the drying tube and start circulating the cooling water. Lower the reflux apparatus so that the round-bottom flask is in the aluminum block, as shown in the figure. Adjust the heat so that this mixture maintains a gentle boiling action. For 1-butanol, the aluminum block temperature should be about 140°C, and for 2-butanol, the temperature should be about 120°C. Be careful to adjust the reflux ring, if one is visible, so that it remains in the lower fourth of the condenser. Violent boiling will cause loss of product. Continue heating the reaction mixture containing 1-butanol for 75 minutes. Heat the

1 Do not use calcium carbonate–based stones or Boileezers, because they will partially dissolve in the highly acidic reaction mixture.
mixture containing 2-butanol for 60 minutes. During this heating period, go on to Experiment 9B and complete as much of it as possible before returning to this procedure.

**Purification**

When the period of reflux has been completed, discontinue heating, lift the apparatus out of the aluminum block, and allow the reaction mixture to cool. Do not remove the condenser until the flask is cool. Be careful not to shake the hot solution as you lift it from the heating block or a violent boiling and bubbling action will result; this could allow material to be lost out the top of the condenser. After the mixture has cooled for about 5 minutes, immerse the round-bottom flask (with condenser attached) in a beaker of cold tap water (no ice) and wait for this mixture to cool down to room temperature.

There should be an organic layer present at the top of the reaction mixture. Add 0.75 mL of pentane to the mixture and gently swirl the flask. The purpose of the pentane is to increase the volume of the organic layer so that the following operations are easier to accomplish. Using a Pasteur pipet, transfer most (about 7 mL) of the bottom (aqueous) layer to another container. Be careful that all of the top organic layer remains in the boiling flask. Transfer the remaining aqueous layer and the organic layer to a 3-mL conical vial, taking care to leave behind any solids that may have precipitated. Allow the phases to separate and remove the bottom (aqueous) layer using a Pasteur pipet.

**NOTE:** For the following sequence of steps, be certain to be well prepared. If you find that you are taking longer than 5 minutes to complete the entire extraction sequence, you probably have affected your results adversely!

Add 1.0 mL of water to the vial and gently shake this mixture. Allow the layers to separate and remove the aqueous layer, which is still on the bottom. Extract the organic layer with 1–2 mL of saturated sodium bicarbonate solution and remove the bottom aqueous layer.

**Drying**

Using a clean dry Pasteur pipet, transfer the remaining organic layer into a small test tube (10 × 75 mm) and dry over anhydrous granular sodium sulfate (see Technique 12, Section 12.9, page 680). Transfer the dry halide solution with a clean, dry Pasteur pipet to a small, dry conical vial, taking care not to transfer any solid. The preferred method of storage is to use a Teflon stopper that has been secured tightly with a plastic cap. It is helpful to cover the stopper and cap with Parafilm (on the outside of the stopper and cap). Alternatively, you may use a screw-cap vial with a Teflon liner. Be sure the cap is screwed on tightly. Again, it is a good idea to cover the cap with Parafilm. Do not store the liquid in a container with a cork or a rubber stopper, because these will absorb the halides. If it is necessary to store the sample overnight, store it in a refrigerator. This sample can now be analyzed by as many of the methods in Experiment 21C as your instructor indicates. However, it cannot be analyzed by refractometry because of the presence of pentane.
EXPERIMENT 9B

Competitive Nucleophiles with 2-Methyl-2-Propanol

PROCEDURE

Place 6.0 mL of the solvent–nucleophile medium into a 15-mL centrifuge tube, using the same procedure described in the “Preparation of Reagents” section at the beginning of Experiment 21A. Place the centrifuge tube in cold tap water and wait until a few crystals of ammonium halide salts just begin to appear. Using an automatic pipet or dispensing pump, transfer 1.0 mL of 2-methyl-2-propanol (tert-butyl alcohol, mp 25°C) to the 15-mL centrifuge tube. Replace the cap and make sure that it doesn’t leak.

CAUTION

The solvent–nucleophile mixture contains concentrated sulfuric acid.

Shake the tube vigorously, venting occasionally, for 5 minutes (use gloves). Any solids that were originally present in the centrifuge tube should dissolve during this period. After shaking, allow the layer of alkyl halides to separate (10–15 minutes at most). A fairly distinct top layer containing the products should have formed by this time.

CAUTION

tert-Butyl halides are volatile and should not be left in an open container any longer than necessary.

Slowly remove most of the bottom aqueous layer with a Pasteur pipet and transfer it to a beaker. After waiting 10–15 seconds, remove the remaining lower layer in the centrifuge tube, including a small amount of the upper organic layer to be certain that the organic layer is not contaminated by any water.

NOTE: For the following purification sequence, be certain to be well prepared. If you find that you are taking longer than 5 minutes to complete the entire sequence, you probably have affected your results adversely!

Using a dry Pasteur pipet, transfer the remainder of the alkyl halide layer into a small test tube (10 × 75 mm) containing about 0.05 g of solid sodium bicarbonate. As soon as the bubbling stops and a clear liquid is obtained, transfer it with a Pasteur pipet into a small, dry conical vial, taking care not to transfer any solid. The preferred method of storage is to use a Teflon stopper that has been secured tightly with a plastic cap. It is helpful to cover the stopper and cap with Parafilm (on the outside of the stopper and cap). Alternatively, you may use a screw-cap vial with a Teflon liner. Be sure the cap is screwed on tightly. Again, it
is a good idea to cover the cap with Parafilm. Do not store the liquid in a container with a cork or a rubber stopper, because these will absorb the halides. If it is necessary to store the sample overnight, store it in a refrigerator. This sample can now be analyzed by as many of the methods in Experiment 21C as your instructor indicates. When you have finished this procedure, return to Experiment 21A.

**Experiment 9C**

**Analysis**

**Procedure**

The ratio of 1-chlorobutane to 1-bromobutane, 2-chlorobutane to 2-bromobutane, or tert-butyl chloride to tert-butyl bromide must be determined. At your instructor’s option, you may do this by one of three methods: gas chromatography, refractive index, or NMR spectroscopy. The products obtained from the reactions of 1-butanol and 2-butanol, however, cannot be analyzed by the refractive index method (they contain pentane). The products obtained from the reaction of tert-butyl alcohol may be difficult to analyze by gas chromatography because the tert-butyl halides sometimes undergo elimination in the gas chromatograph.¹

**Gas Chromatography²**

The instructor or a laboratory assistant may either make the sample injections or allow you to make them. In the latter case, your instructor will give you adequate instruction beforehand. A reasonable sample size is 2.5 µL. Inject the sample into the gas chromatograph and record the gas chromatogram. The alkyl chloride, because of its greater volatility, has a shorter retention time than the alkyl bromide.

Once the gas chromatogram has been obtained, determine the relative areas of the two peaks (Technique 22, Section 22.12). If the gas chromatograph has an integrator, it will report the areas. Triangulation is the preferred method of determining areas, if an integrator is not available. Record the percentages of alkyl chloride and alkyl bromide in the reaction mixture.

**Refractive Index**

Measure the refractive index of the product mixture (Technique 24). It is easy to make mistakes in reading the scale on some refractometers. Therefore, it is advisable to measure the refractive index of a known liquid before analyzing your mixture. To determine the composition of the mixture, assume a linear relation between

₁*Note to the Instructor:* If pure samples of each product are available, check the assumption used here that the gas chromatograph responds equally to each substance. Response factors (relative sensitivities) are easily determined by injecting an equimolar mixture of products and comparing the peak areas.

²*Note to the Instructor:* To obtain reasonable results for the gas chromatographic analysis of the tert-butyl halides, it may be necessary to supply the students with response factor correction (Technique 22, Section 22.13, p. 813).
the refractive index and the molar composition of the mixture. At 20°C the refractive indices of the alkyl halides are

- tert-butyl chloride: 1.3877
- tert-butyl bromide: 1.4280

If the temperature of the laboratory room is not 20°C, the refractive index must be corrected. Add 0.0004 refractive index unit to the observed reading for each degree above 20°C and subtract the same amount for each degree below this temperature. Record the percentages of alkyl chloride and alkyl bromide in the reaction mixture.

A 60-MHz NMR spectrum of 1-chlorobutane and 1-bromobutane, sweep width 250 Hz (no pentane in sample).

A 60-MHz spectrum of tert-butyl chloride and tert-butyl bromide, sweep width 250 Hz.
1. Draw complete mechanisms that explain the resultant product distributions observed for the reactions of tert-butyl alcohol and 1-butanol under the reaction conditions of this experiment.

2. Which is the better nucleophile, chloride ion or bromide ion? Try to explain this in terms of the nature of the chloride ion and the bromide ion.

3. What is the principal organic by-product of these reactions?

4. A student left some alkyl halides (RC1 and RBr) in an open container for several minutes. What happened to the composition of the halide mixture during that time? Assume that some liquid remains in the container.

5. What would happen if all the solids in the nucleophile medium were not dissolved? How might this affect the outcome of the experiment?

6. What might have been the product ratios observed in this experiment if an aprotic solvent such as dimethyl sulfoxide had been used instead of water?

7. Explain the order of elution you observed while performing the gas chromatography for this experiment. What property of the product molecules seems to be the most important in determining relative retention times?

8. Does it seem reasonable to you that the refractive index should be a temperature-dependent parameter? Try to explain.

9. When you calculate the percentage composition of the product mixture, exactly what kind of “percentage” (i.e., volume percent, weight percent, mole percent) are you dealing with?

10. When a pure sample of tert-butyl bromide is analyzed by gas chromatography, two components are usually observed. One of them is tert-butyl bromide and the other one is a decomposition product. As the temperature of the injector is increased, the amount of the decomposition product increases and the amount of tert-butyl bromide decreases.

   (a) What is the structure of the decomposition product?

   (b) Why does the amount of decomposition increase with increasing temperature?

   (c) Why does tert-butyl bromide decompose much more easily than tert-butyl chloride?
Elimination Reactions: Dehydration and Dehydrohalogenation

Dehydration
Dehydrobromination
Collection of gaseous products
Gas chromatography
Regiochemistry
Zaitsev’s Rule

Alkenes can be prepared by elimination reactions such as the dehydration of alcohols and the dehydrobromination of alkyl bromides. Dehydration reactions follow an E1 mechanistic pathway, whereas dehydrobromination occurs by an E2 mechanism. In this experiment, you will study both methods for preparing alkenes.

In the first reaction, an alcohol undergoes dehydration in the presence of strong acid to form an alkene. In many cases, alcohols give a mixture of alkenes, including cis and trans isomers. For example, 2-butanol gives a mixture of 1-butene, cis-2-butene, and trans-2-butene. The class will study the dehydration of 1-butanol and 2-butanol. The general reaction for dehydration is the following:

\[
\begin{align*}
R-\text{C}-\text{C}-\text{R} + \text{H}_2\text{SO}_4 & \xrightarrow{\text{H}_3\text{PO}_4} R-\text{C}=\text{C}-\text{R} + \text{H}_2\text{O} \\
\text{H} & \quad \text{heat}
\end{align*}
\]

The second reaction is an example of a dehydrobromination reaction conducted in the presence of potassium hydroxide dissolved in ethanol. You will study the dehydrobromination of 1-bromobutane and 2-bromobutane. The general reaction for dehydrobromination is the following:

\[
\begin{align*}
R-\text{C}-\text{C}-\text{R} + \text{KOH} & \xrightarrow{\text{CH}_3\text{CH}_2\text{OH}} R-\text{C}=\text{C}-\text{R} + \text{KBr} + \text{H}_2\text{O} \\
\text{H} & \quad \text{heat}
\end{align*}
\]

The products of the dehydration and dehydrobromination reactions, which are gases at room temperature, can be analyzed by gas chromatography. For each reaction, the relative percentages of the alkenes can then be calculated. Using your knowledge of the mechanisms of dehydration and dehydrobromination, and by applying Zaitsev’s Rule, you should be able to explain the regiochemistry of these reactions.
REQUIRED READING

Review: Techniques 5, 6, and 22

New: Technique 7 — Reaction Methods, Section 7.9

Before beginning this experiment, review the appropriate chapters on elimination reactions in your lecture textbook. Pay special attention to dehydration of alcohols, dehydrohalogenation of alkyl halides, E1 and E2 reactions, and Zaitsev’s Rule.

SPECIAL INSTRUCTIONS

These experiments can be conveniently scheduled with another experiment because the time required for each experiment is 30–45 minutes. By scheduling these experiments over two laboratory periods, the waiting time for the gas chromatograph will also be minimized. You may be given a choice of doing one of the reactions in this experiment, or your instructor may assign one to you. In either case, you will need to share your results with other students so that you can write the laboratory report.

SUGGESTED WASTE DISPOSAL

Dispose of all halide wastes in the halogenated waste container. The alcohol mixtures from the dehydration reactions should be placed in the container designated for that purpose.

NOTES TO THE INSTRUCTOR

Because of the logistics involved, consider pairing students for this experiment. This experiment was designed to use a specific apparatus for collecting the products (see figure in this experiment). Depending on the type of glassware used by your students, it may be necessary to modify the apparatus described here. See Technique 7, Section 7.9, for possible modifications. You might find it useful to prepare the gas-collection apparatus in advance of the class and to reuse it in future classes. It is particularly difficult to insert sections of Pasteur pipets into the plastic tubing, and this should be prepared for the students in order to avoid accidents. It is also recommended to keep the 16 × 90-mm sections of glass tubing used for collecting gases.

A Gow-Mac model 69-350 or another traditional type of thermal conductivity gas chromatograph may be prepared as follows: column, injector, detector, and outlet should be at room temperature; carrier gas flow rate, 20 mL/min. An 8-foot column containing 20% DC-710 gives good separation. Retention times: 1-butene, 7 min; trans-2-butene, 8 min; and cis-2-butene, 9 min.

Conditions for a Hewlett Packard model 5890 with thermal conductivity detector are as follows: 6-foot × ¼-inch column filled with 3% SP-2100 (a methyl silicone) on 100/120 Supelcoport, available from Supelco; oven temperature cryogenically cooled to −20°C with CO2; helium carrier gas flow rate, 14.1 mL/min; detector temperature, 101°C; injector temperature, 40°C; column head pressure, 17 psi. A capillary gas chromatographic column is
not recommended. Packed columns, such as the one indicated, work better. A Hewlett Packard model 3393A Integrator may be set at attenuation 3; chart speed 2; area rejection 0; threshold 0; peak width 0.04. Retention times: 1-butene, 1.4 min; trans-2-butene, 1.6 min; and cis-2-butene, 1.8 min. The percentages of alkenes obtained from each reaction are listed in the Instructor’s Manual.

Determine in advance how much gaseous sample to inject into your gas chromatograph. The syringe mentioned in the experimental procedure works well with the Gow-Mac chromatograph. With the Hewlett Packard chromatograph, a 5-μL sample works well. It is recommended that you use a gas-tight syringe for small samples.

**PROCEDURE**

**Apparatus**

Assemble the apparatus shown in the figure, but do not connect the conical vial to the thermometer adapter (see individual experiments for the size of the conical vial needed). The section of the Pasteur pipet that fits into the thermometer adapter is prepared from a 5 3⁄4-inch Pasteur pipet. Your instructor may have prepared the gas-collecting equipment for you. If a collection device is unavailable, then break off the wide end of the pipet about 1 inch from where the constriction begins. Connect the narrow end of the Pasteur pipet to the 1⁄32-inch flexible plastic tubing. Heat the plastic tubing briefly above a flame before attaching it to the Pasteur pipet. This helps to soften and expand the tubing. While the tubing is still soft, twist it until it is firmly attached to the Pasteur pipet.

**CAUTION**

Accidental cuts or gouges to the skin may occur if the plastic tubing is not softened prior to attachment.

Insert the wide end of the Pasteur pipet into the thermometer adapter. Use a tight-fitting O-ring to create a better seal around the section of the Pasteur pipet and tighten the cap on the thermometer adapter. Be sure the connection between the pipet and the thermometer adapter is gas-tight. If there is a leak, you will not collect any gaseous products.

Make a mark on both the test tube and the glass tube corresponding to a volume of 4 mL. This can be done by inserting a rubber septum into the 16 mm (O.D.) glass tube and then filling each tube with 4 mL of water. Using a water-resistant marking pen, mark each tube at the level of the water. Fill a 400-mL beaker with water. Place one end of the flexible plastic tubing into the beaker so that it points slightly upward. (You may want to hold it in position by wrapping the plastic tubing with wire or by inserting the plastic tubing into a section of glass tubing bent into a U shape.) Now fill the test tube completely with water and, while holding your thumb over the opening, invert the test tube and place the open end into the beaker. Once the tube is in the water, you can release your thumb and allow the test tube to rest on the bottom of the beaker. Lift the test tube slightly and position it over the end of the plastic tubing without allowing air to enter the test tube. Repeat this filling operation with the glass tube sealed by the rubber septum, but do not insert the flexible tubing into it. The test tube
will be used to collect the first 2–4 mL of gas, which will consist mainly of air. Then insert the flexible tubing into the open end of the glass tube to collect the gaseous products.

Proceed to Experiment 24A or 24B and adjust the temperature of the aluminum block or sand bath to the temperatures listed in that experiment.

**EXPERIMENT 20A**

**Dehydration of 1-Butanol and 2-Butanol**

**PROCEDURE**

Adjust the aluminum block or sand bath to the following initial temperatures, depending on which alcohol you are using:

- 140°C for 1-butanol
- 80°C for 2-butanol

To a 3-mL conical vial, add 0.20 mL of either 1-butanol or 2-butanol and a magnetic spin vane. Using the graduated pipet provided, add 0.30 mL of the mixture...
of concentrated phosphoric acid and concentrated sulfuric acid to the vial. Stir the mixture for a few seconds.

Connect the thermometer adapter to the vial and place the vial in the aluminum block or sand bath as shown in the figure. If you are using a sand bath, secure the assembly with a clamp. Stir the mixture and increase the heat slowly until 4 mL of gas (mainly air) are collected in the inverted test tube. Carefully remove the test tube from the flexible tubing and place the glass tube with the rubber septum over the flexible tubing. Continue heating the reaction mixture (increasing the temperature if necessary) until you collect 4–5 mL of the gaseous products. It should not be necessary to heat the reaction mixture much above 170°C for 1-butanol or 100°C for 2-butanol.

**CAUTION**

Before turning the heat down or removing the vial from the heating device, you must first remove the flexible tubing from both the gas-collection tube and water bath or disconnect the thermometer adapter from the conical vial. Otherwise, water may be sucked back into the vial as the reaction mixture cools. Be sure to leave the tube containing the product in the water when you perform this operation.

With minimal delay, analyze your gaseous mixture on the gas chromatograph. Using a 1-mL syringe, remove about 0.5 mL of gaseous product by injecting the needle through the rubber septum. (Note: Your instructor may want you to use a different type of syringe or different amount of gaseous sample: see Notes to the Instructor.) With assistance from the instructor or lab assistant, analyze this sample on the gas chromatograph. The order of elution will be 1-butene, trans-2-butene, and cis-2-butene.

Once the gas chromatograph has been obtained, determine the relative amounts of the products (see Technique 22, Section 22.12, p. 810). Triangulation is the preferred method of determining the relative areas under the peaks (use a millimeter ruler). Record the percentage of the three alkenes in the product.

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**EXPERIMENT 10B**

**Dehydrobromination of 1-Bromobutane and 2-Bromobutane**

**PROCEDURE**

Adjust the aluminum block or sand bath to the following initial temperatures, depending on which bromoalkane you are using:

- 90°C for 1-bromobutane
- 80°C for 2-bromobutane

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* The acid mixture should be prepared for the entire class by mixing 6.0 mL of concentrated phosphoric acid and 3.0 mL of concentrated sulfuric acid. This mixture will provide enough acid for 20 students, assuming little spillage or other types of waste. Dispense this mixture with a graduated pipet and bulb.
Dehydrobromination of 1-Bromobutane

Using the graduated pipet provided, add 3.0 mL of an ethanolic potassium hydroxide solution\(^2\) to a 5-mL conical vial. Avoid getting any of the base on the ground-glass joint. Put a thin layer of stopcock grease on the ground-glass joint of the thermometer adapter. Add 0.32 mL of 1-bromobutane and a spin vane to the vial. (Alternatively, at your instructor’s option, use 3.0 mL of 1 M potassium tert-butoxide solution and 0.32 mL of 1-bromobutane.\(^3\) Attach the thermometer adapter to the vial and place this assembly in an aluminum block or sand bath as shown in the figure. If using a sand bath, clamp the apparatus to hold it more securely.

While stirring, slowly increase the temperature of the heating source until gas begins to collect in the test tube. Continue heating the reaction mixture at this temperature or slightly higher until about 2 mL of gas (mainly air) are collected in the test tube. Carefully remove the test tube from the flexible tubing and place the glass tube with the rubber septum over the flexible tubing. Continue to heat the reaction mixture until you collect 4 mL of gaseous product in the tube or until gas evolution ceases. Ethanolic potassium hydroxide produces less gaseous product than the reaction with potassium tert-butoxide. With minimal delay, analyze your gaseous mixture on the gas chromatograph, as described in Experiment 24.

CAUTION

Before turning down the heat or removing the heating source, you must first remove the flexible tubing from both the gas collection tube and water bath or disconnect the thermometer adapter from the conical vial. Otherwise, water may be sucked back into the vial. Be sure to leave the tube containing the product in the water when you perform this operation.

Dehydrobromination of 2-Bromobutane

Using the graduated pipet provided, add 2.0 mL of an ethanolic potassium hydroxide solution\(^2\) to a 3-mL conical vial. Put a thin layer of stopcock grease on the ground-glass joint of the thermometer adapter. Add 0.16 mL of 2-bromobutane and a spin vane to the vial. Attach the thermometer adapter to the vial and place this assembly in an aluminum block or sand bath as shown in the figure. If using a sand bath, clamp the apparatus to hold it more securely.

While stirring, slowly increase the temperature of the heating source until gas begins to collect in the test tube. Continue heating the reaction mixture at this temperature or slightly higher until 2 mL of gas (mainly air) are collected in the tube. Carefully remove the test tube from the flexible tubing and place the glass tube with the rubber septum over the flexible tubing. Continue to heat the reaction mixture until 4–5 mL of gaseous product are collected in the tube.

CAUTION

Read the caution statement on page 208 before turning down the heat.

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\(^2\) To prepare enough solution for 20 students (assuming little spillage or other types of waste), add 15.0 g of potassium hydroxide to 50.0 mL of 95% ethanol. Stir the mixture until the potassium hydroxide is completely dissolved. Dispense this solution with a graduated pipet and bulb.

\(^3\) The 1 M potassium tert-butoxide in 2-methyl-2-propanol is available from Aldrich Chemical Co., catalog number 33,134-1. Dispense this solution with a graduated pipet and bulb. The reagent is extremely moisture-sensitive and must be kept tightly stoppered when not in use.
With minimal time delay, analyze your gaseous mixture on the gas chromatograph, as described in Experiment 24A. Determine the percentages of three alkenes produced by the dehydrobromination of 2-bromobutane.

REFERENCES


QUESTIONS

1. Give the mechanism for the dehydration of 1-butanol. Why might you expect that the dehydration of 2-butanol would produce a similar composition of alkenes?
2. Give the mechanism for the dehydrobromination of 1-bromobutane in the presence of either potassium tert-butoxide or alcoholic potassium hydroxide.
3. Why is there a big difference in the regioselectivity of the dehydration of 1-butanol compared with the dehydrobromination of 1-bromobutane?
4. Explain the order of elution you observed while performing the gas chromatography for this experiment. What property of the product molecules seems to be the most important in determining the relative retention times?
5. What alkenes (including *cis* and *trans* isomers) would be produced by the dehydration of the following alcohols? Where possible, predict the relative amounts of each product according to Zaitsev’s Rule.
   (a) 3-Pentanol
   (b) 2-Methyl-2-butanol
   (c) 1-Butanol
   (d) 2-Methyl-1-butanol
6. What alkenes (including *cis* and *trans* isomers) would be produced by the dehydrobromination of the following alkyl bromides? Where possible, predict the relative amounts of each product according to Zaitsev’s rule?
   (a) 2-Bromo-2-methylbutane
   (b) 1-Bromobutane
   (c) 2-Bromo-2,3-dimethylbutane
   (d) 3-Bromopentane
An Oxidation Puzzle

Oxidation of alcohols
Infrared spectroscopy
Critical thinking application

Sodium hypochlorite in acetic acid is an oxidizing agent capable of oxidizing alcohols to the corresponding aldehydes or ketones. In this experiment, you will oxidize a diol, 2-ethyl-1,3-hexanediol (1) and then use infrared spectroscopy to determine which of the alcohol functional groups was oxidized.

You will determine whether the oxidation occurred selectively (and which functional group was oxidized) or whether both functional groups were oxidized at the same time. The possible outcomes of the oxidation are shown in the figure. If only the primary alcohol is oxidized, the aldehyde (2) will be formed; if only the secondary alcohol is oxidized, the ketone (3) will be the product. If both alcohol functional groups are oxidized, compound (4) will be observed. Your assignment will be to use infrared spectroscopy to determine the structure of the product and decide which of these three possible outcomes actually takes place.

REQUIRED READING

Review: Techniques 12 and 25

SPECIAL INSTRUCTIONS

Glacial acetic acid is corrosive; it can cause burns on the skin and on mucous membranes in the nose and mouth. Its vapors are also hazardous. Dispense it in the hood and use personal protective equipment. Avoid contact with skin, eyes, and clothing. Sodium hypochlorite emits chlorine gas, which is a respiratory and eye irritant. Dispense it in a fume hood.

SUGGESTED WASTE DISPOSAL

All aqueous solutions should be collected in a container specially marked for aqueous wastes. Place organic liquids in the container designated for nonhalogenated organic waste. Note that your instructor may establish a different method of collecting wastes in this experiment.

PROCEDURE

Dispense 0.5 mL of 2-ethyl-1,3-hexanediol into a tared 10-mL Erlenmeyer flask. An automatic pipet is a useful device to dispense this quantity of diol. Reweigh the flask to determine the weight of diol added. Add 3 mL of glacial acetic acid; also add a magnetic stirring bar. Have a thermometer available to monitor the temperature of the reaction.

Place the mixture in an ice bath on a magnetic stirrer. While the mixture is stirring, slowly add 3 mL of a 6% aqueous sodium hypochlorite solution to the mixture. Be careful not to allow the reaction temperature to rise above 30°C by controlling the rate of addition. Allow the solution to stir for 1 hour. In order to determine whether or not there is excess hypochlorite, test the solution periodically by placing a drop of the reaction mixture on a strip of potassium iodide starch test paper. A blue-black color indicates that there is an excess of hypochlorite. If there is no color change, add an additional 0.5 mL of sodium hypochlorite solution, stir for several minutes, and repeat the starch-iodide test. Continue this process until the paper turns blue-black.

When the reaction is complete, pour the mixture into 10–15 mL of an ice–salt mixture. Extract the mixture with three 5-mL portions of diethyl ether. It may be convenient to perform this extraction in a 15-mL centrifuge tube rather than in a separatory funnel (see Technique 12, Section 12.6, p. 677, for a description of this method). Collect the ether extracts and wash them with two 3-mL portions of saturated aqueous sodium carbonate solution, followed by two 3-mL portions of 5% aqueous sodium hydroxide. The ether layer should appear basic when tested with a moistened piece of red litmus paper. If it is not, wash the ether layer with an additional 3-mL portion of 5% aqueous sodium hydroxide.

Dry the ether layer over magnesium sulfate. Decant or filter the dried solution into a tared 25-mL filter flask and remove the solvent under reduced pressure (Technique 7, Section 7.10, p. 611). Determine the infrared spectrum of the residue as a pure liquid sample (Technique 25, Section 25.2, p. 834).
Preparation of a C-4 or C-5 Acetate Ester

**Esterification**

**Separatory funnel**

**Conventional distillation**

In this experiment, we prepare an ester from acetic acid and a C-4 or a C-5 alcohol. This experiment is a conventional-scale preparation, but it is similar to the microscale preparation of isopentyl acetate, which is described in Experiment 13. However, for the experiment, either your instructor will assign, or you will pick, one of the following C-4 or C-5 alcohols to react with acetic acid:

1. 1-Butanol (n-butyl alcohol)
2. 2-Butanol (sec-butyl alcohol)
3. 2-Methyl-1-propanol (isobutyl alcohol)
4. Cyclopentanol
5. 1-Pentanol (n-pentyl alcohol)
6. 2-Pentanol
7. 3-Pentanol
8. 3-Methyl-1-butanol
9. 3-Pentanol
10. Cyclopentanol
11. 3-Methyl-1-butanol
12. (isopentyl alcohol)

If an NMR spectrometer is available, your instructor may wish to give you one of these alcohols as an unknown, leaving it to you to determine which alcohol was issued. For this purpose, you could use the infrared and NMR spectra, as well as the boiling points of the alcohol and its ester.

**REQUIRED READING**

Review: Essay

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**Esters—Flavors and Fragrances**

Experiment 13

Techniques 12, 13, and 14

**SPECIAL INSTRUCTIONS**

Be careful when dispensing sulfuric and glacial acetic acids. They are corrosive and will attack your skin if you make contact with them. If you get one of these acids on your skin, wash the affected area with large amounts of running water for 10–15 minutes.

If you select 2-butanol, reduce the amount of concentrated sulfuric acid to 0.5 mL. Also reduce the heating time to 60 minutes or less. Secondary alcohols have a tendency to give a significant percentage of elimination in strongly acidic solutions. Some of the alcohols may undergo elimination, leading to the formation of some low-boiling material (alkenes). In addition, cyclopentanol forms some dicyclopentyl ether, a solid.
SUGGESTED WASTE DISPOSAL

Any aqueous solutions should be placed in the container designated for dilute aqueous waste. Place any excess ester in the nonhalogenated organic waste container.

NOTES TO THE INSTRUCTOR

The sulfuric acid used as a catalyst in this reaction may be replaced with Dowex 50WX8-100 cationic exchange resin (sulfonate groups).

The purity of the esters can be determined by gas chromatography. It is recommended that a gas chromatogram of each of the starting alcohols be performed prior to determining the gas chromatogram of the esters. In this way, the peak corresponding to the parent alcohol can be identified by its retention time and the percentage of unreacted alcohol in the sample can be obtained. Approximate gas chromatography conditions for a GowMac Series 580 instrument with an ½-inch OV-1 column: 0.5 μL sample; flow rate, 27 mL/min; column temperature, 82°C; injector temperature, 170°C; detector temperature, 180°C; detector current, 200 mA.

PROCEDURE

Apparatus
Assemble a reflux apparatus on top of your hot plate using a 20- or 25-mL round-bottom flask and a water-cooled condenser (refer to Fig. 7.6A, p. 601, but use a round-bottom flask instead of the conical vial). To control vapors, place a drying tube packed with calcium chloride on top of the condenser. Use a hot plate and the aluminum block with the larger set of holes for heating.

Reaction Mixture
Weigh (tare) an empty 10-mL graduated cylinder and record its weight. Place approximately 5.0 mL of your chosen alcohol in the graduated cylinder and reweigh it to determine the weight of alcohol. Disconnect the round-bottom flask from the reflux apparatus and transfer the alcohol into it. Do not clean or wash the graduated cylinder. Using the same graduated cylinder, measure approximately 7.0 mL of glacial acetic acid (MW = 60.1, d = 1.06 g/mL) and add it to the alcohol already in the flask. Using a calibrated Pasteur pipet, add 1 mL of concentrated sulfuric acid (0.5 mL if you have chosen 2-butanol), mixing immediately (swirl), to the reaction mixture contained in the flask. Add a corundum boiling stone or stirring bar and reconnect the flask. Do not use a calcium carbonate (marble) boiling stone, because it will dissolve in the acidic medium.
Reflux
Start water circulating in the condenser and bring the mixture to a boil. Continue heating under reflux for 60–75 minutes. Be sure to stir the mixture if you are using a stirring bar instead of a boiling stone. Then disconnect or remove the heating source and let the mixture cool to room temperature.

Extractions
Disassemble the apparatus and transfer the reaction mixture to a separatory funnel (60 or 125 mL) placed in a ring attached to a ring stand. Be sure the stopcock is closed and, using a funnel, pour the mixture into the top of the separatory funnel. Also be careful to avoid transferring the boiling stone (or stirring bar), or you will need to remove it after the transfer. Add 10 mL of water, stopper the funnel, and mix the phases by careful shaking and venting (Section 12.7 and Fig. 12.9). Allow the phases to separate and then uncap the funnel and drain the lower aqueous layer through the stopcock into a beaker or other suitable container. Next, extract the organic layer with 5 mL of 5% aqueous sodium bicarbonate just as you did previously with water. Extract the organic layer once again, this time with 5 mL of saturated aqueous sodium chloride.

Drying
Transfer the crude ester to a clean, dry, 25-mL Erlenmeyer flask and add approximately 1.0 g of anhydrous sodium sulfate. Cork the mixture and let it stand for 10–15 minutes while you prepare the apparatus for distillation. If the mixture does not appear dry (the drying agent clumps and does not “flow,” the solution is cloudy, or drops of water are obvious), transfer the ester to a new, clean, dry, 25-mL Erlenmeyer flask and add a new 0.5-g portion of anhydrous sodium sulfate to complete the drying.

Distillation
Assemble a distillation apparatus using your smallest round-bottom flask to distill from (Fig. 14.10, p. 713, but insert a water condenser as shown on p. 714). Use a hot plate with an aluminum block to heat. Preweigh (tare) and use a 5-mL conical vial to collect the product. (It might be wise to have a second tared 5-mL conical vial handy in case you fill the first one.) Immerse the collection flask in a beaker of ice to ensure condensation and to reduce odors. If your alcohol is not an unknown, you can look up its boiling point in a handbook; otherwise, you can expect your ester to have a boiling point between 95 and 150°C. Continue distillation until only 1 or 2 drops of liquid remain in the distilling flask. Record the observed boiling-point range in your notebook.

Yield Determination
Weigh the product and calculate the percentage yield of the ester. At the option of your instructor, determine the boiling point using one of the methods described in Section 13.2, page 695.
Spectroscopy
At your instructor’s option, obtain an infrared spectrum using salt plates (Technique 25, Section 25.2). Compare the spectrum with the one reproduced in Experiment 13. The spectrum of your ester should have similar features to the one shown. Interpret the spectrum and include it in your report to the instructor. You may also be required to determine and interpret the proton and carbon-13 NMR spectra (Technique 26, Section 26.1 and Technique 27, Section 27.1). Submit your sample in a properly labeled vial with your report.

Gas Chromatography (Optional)
At your instructor’s option, perform a gas chromatographic analysis of your ester. Either your instructor will provide a gas chromatogram of your starting alcohol or you will be asked to determine one at the same time that you do the analysis of your ester. Using both chromatograms, identify the alcohol and ester peaks and calculate the percentage of unreacted alcohol (if any) still remaining in your sample. Is there any evidence of a product from a competing elimination reaction? Attach the chromatograms to your notebook or your final report, and be sure to include a discussion of the results in your report.

QUESTIONS
1. One method of favoring the formation of an ester is to add excess acetic acid. Suggest another method, involving the right-hand side of the equation, that will favor the formation of the ester.
2. Why is the mixture extracted with sodium bicarbonate? Give an equation and explain its relevance.
3. Why are gas bubbles observed?
4. Using your alcohol, determine which starting material is the limiting reagent in this procedure. Which reagent is used in excess? How great is the molar excess (how many times greater)?
5. Outline a separation scheme for isolating your pure ester from the reaction mixture.
6. Interpret the principal absorption bands in the infrared spectrum of your ester or, if you did not determine the infrared spectrum of you ester, do this for the spectrum of isopentyl acetate on page 107. (Technique 25 may be of some help.)
7. Write a mechanism for the acid-catalyzed esterification that uses your alcohol and acetic acid. You may need to consult the chapter on carboxylic acids in your lecture textbook.
8. Tertiary alcohols do not work well in the procedure outlined for this experiment; they give a different product from what you might expect. Explain this and draw the expected product from 2-methyl-2-propanol (t-butyl alcohol).
9. Why is glacial acetic acid designated as “glacial”? (Hint: Consult a handbook of physical properties.)
Laboratory Safety

In any laboratory course, familiarity with the fundamentals of laboratory safety is critical. Any chemistry laboratory, particularly an organic chemistry laboratory, can be a dangerous place in which to work. Understanding potential hazards will serve you well in minimizing that danger. It is ultimately your responsibility, along with your laboratory instructor’s, to make sure that all laboratory work is carried out in a safe manner.

1.1 Safety Guidelines

It is vital that you take necessary precautions in the organic chemistry laboratory. Your laboratory instructor will advise you of specific rules for the laboratory in which you work. The following list of safety guidelines should be observed in all organic chemistry laboratories.

A. Eye Safety

Always Wear Approved Safety Glasses or Goggles. It is essential to wear eye protection whenever you are in the laboratory. Even if you are not actually carrying out an experiment, a person near you might have an accident that could endanger your eyes. Even dishwashing can be hazardous. We know of cases in which a person has been cleaning glassware only to have an undetected piece of reactive material explode, throwing fragments into the person’s eyes. To avoid such accidents, wear your safety glasses or goggles at all times.

Learn the Location of Eyewash Facilities. If there are eyewash fountains in your laboratory, determine which one is nearest to you before you start to work. If any chemical enters your eyes, go immediately to the eyewash fountain and flush your eyes and face with large amounts of water. If an eyewash fountain is not available, the laboratory will usually have at least one sink fitted with a piece of flexible hose. When the water is turned on, this hose can be aimed upward, and the water can be directed into the face, working much as an eyewash fountain does. To avoid damaging the eyes, the water flow rate should not be set too high, and the water temperature should be slightly warm.

B. Fires

Use Care with Open Flames in the Laboratory. Because an organic chemistry laboratory course deals with flammable organic solvents, the danger of fire is frequently present. Because of this danger, DO NOT SMOKE IN THE LABORATORY. Furthermore, use extreme caution when you light matches or use any open flame. Always check to see whether your neighbors on either side, across the bench, and behind you are using flammable solvents. If so, either wait or move to a safe location, such as a fume hood, to use your open flame. Many flammable organic substances are the source of dense vapors that can travel for some distance down a bench. These vapors present a fire danger, and you should be careful because the source of those vapors may be far away from you. Do not use the bench sinks to dispose of flammable solvents. If your bench has a trough running along it, pour only
water (no flammable solvents!) into it. The troughs and sinks are designed to carry water—not flammable materials—from the condenser hoses and aspirators.

*Learn the Location of Fire Extinguishers, Fire Showers, and Fire Blankets.*

For your own protection in case of a fire, you should immediately determine the location of the nearest fire extinguisher, fire shower, and fire blanket. You should learn how to operate these safety devices, particularly the fire extinguisher. Your instructor can demonstrate this.

If there is a fire, the best advice is to get away from it and let the instructor or laboratory assistant take care of it. DON’T PANIC! Time spent in thought before action is never wasted. If it is a small fire in a container, it can usually be extinguished quickly by placing a wire-gauze screen with a ceramic fiber center or, possibly, a watch glass over the mouth of the container. It is good practice to have a wire screen or watch glass handy whenever you are using a flame. If this method does not extinguish the fire and if help from an experienced person is not readily available, then extinguish the fire yourself with a fire extinguisher.

Should your clothing catch on fire, DO NOT RUN. Walk *purposefully* toward the fire shower station or the nearest fire blanket. Running will fan the flames and intensify them.

**C. Organic Solvents: Their Hazards**

*Avoid Contact with Organic Solvents.* It is essential to remember that most organic solvents are flammable and will burn if they are exposed to an open flame or a match. Remember also that on repeated or excessive exposure, some organic solvents may be toxic, carcinogenic (cancer causing), or both. For example, many chlorocarbon solvents, when accumulated in the body, result in liver deterioration similar to cirrhosis caused by excessive use of ethanol. The body does not easily rid itself of chlorocarbons, nor does it detoxify them; they build up over time and may cause future illness. Some chlorocarbons are also suspected of being carcinogens. MINIMIZE YOUR EXPOSURE. Long-term exposure to benzene may cause a form of leukemia. Do not sniff benzene, and avoid spilling it on yourself. Many other solvents, such as chloroform and ether, are good anesthetics and will put you to sleep if you breathe too much of them. They subsequently cause nausea. Many of these solvents have a synergistic effect with ethanol, meaning that they enhance its effect. Pyridine causes temporary impotence. In other words, organic solvents are just as dangerous as corrosive chemicals, such as sulfuric acid, but manifest their hazardous nature in other, more subtle ways.

*If you are pregnant,* you may want to consider taking this course at a later time. Some exposure to organic fumes is inevitable, and any possible risk to an unborn baby should be avoided.

Minimize any direct exposure to solvents and treat them with respect. The laboratory room should be well ventilated. Normal cautious handling of solvents should not result in any health problem. If you are trying to evaporate a solution in an open container, you must do the evaporation in the hood. Excess solvents should be discarded in a container specifically intended for waste solvents, rather than down the drain at the laboratory bench. A sensible precaution is to wear gloves when working with solvents. Gloves made from polyethylene are inexpensive and provide good protection. The disadvantage of polyethylene gloves is that they are slippery. Disposable surgical gloves provide a better grip on glassware and other equipment, but they do not offer...
as much protection as polyethylene gloves. Nitrile gloves offer better protection.

**Do Not Breathe Solvent Vapors.** In checking the odor of a substance, be careful not to inhale very much of the material. The technique for smelling flowers is not advisable here; you could inhale dangerous amounts of the compound. Rather, a technique for smelling minute amounts of a substance is used. Pass a stopper or spatula moistened with the substance (if it is a liquid) under your nose. Or hold the substance away from you and waft the vapors toward you with your hand. But never hold your nose over the container and inhale deeply!

The hazards associated with organic solvents you are likely to encounter in the organic laboratory are discussed in detail beginning on page 554. If you use proper safety precautions, your exposure to harmful organic vapors will be minimized and should present no health risk.

**Safe Transportation of Chemicals.** When transporting chemicals from one location to another, particularly from one room to another, it is always best to use some form of secondary containment. This means that the bottle or flask is carried inside another, larger container. This outer container serves to contain the contents of the inner vessel in case a leak or breakage should occur. Scientific suppliers offer a variety of chemical-resistant carriers for this purpose.

**D. Waste Disposal**

**Do Not Place Any Liquid or Solid Waste in Sinks; Use Appropriate Waste Containers.** Many substances are toxic, flammable, and difficult to degrade; it is neither legal nor advisable to dispose of organic solvents or other liquid or solid reagents by pouring them down the sink.

The correct disposal method for wastes is to put them in appropriately labeled waste containers. These containers should be placed in the hoods in the laboratory. The waste containers will be disposed of safely by qualified persons using approved protocols. Specific guidelines for disposing of waste will be determined by the people in charge of your laboratory and by local regulations. Two alternative systems for handling waste disposal are presented here. For each experiment that you are assigned, you will be instructed to dispose of all wastes according to the system that is in operation in your laboratory.

In one model of waste collection, a separate waste container for each experiment is placed in the laboratory. In some cases, more than one container, each labeled according to the type of waste that is anticipated, is set out. The containers will be labeled with a list that details each substance that is present in the container. In this model, it is common practice to use separate waste containers for aqueous solutions, organic halogenated solvents, and other organic nonhalogenated materials. At the end of the laboratory class period, the waste containers are transported to a central hazardous materials storage location. These wastes may be later consolidated and poured into large drums for shipping. Complete labeling, detailing each chemical contained in the waste, is required at each stage of this waste handling process, even when the waste is consolidated into drums.

In a second model of waste collection, you will be instructed to dispose of all wastes in one of the following ways:

**Nonhazardous solids.** Nonhazardous solids such as paper and cork can be placed in an ordinary wastebasket.
**Broken glassware.** Broken glassware should be put into a container specifically designated for broken glassware.

**Organic solids.** Solid products that are not turned in or any other organic solids should be disposed of in the container designated for organic solids.

**Inorganic solids.** Solids such as alumina and silica gel should be put in a container specifically designated for them.

**Nonhalogenated organic solvents.** Organic solvents such as diethyl ether, hexane, and toluene, or any solvent that does not contain a halogen atom, should be disposed of in the container designated for nonhalogenated organic solvents.

**Halogenated solvents.** Methylene chloride (dichloromethane), chloroform, and carbon tetrachloride are examples of common halogenated organic solvents. Dispose of all halogenated solvents in the container designated for them.

**Strong inorganic acids and bases.** Strong acids such as hydrochloric, sulfuric, and nitric acid will be collected in specially marked containers. Strong bases such as sodium hydroxide and potassium hydroxide will also be collected in specially designated containers.

**Aqueous solutions.** Aqueous solutions will be collected in a specially marked waste container. It is not necessary to separate each type of aqueous solution (unless the solution contains heavy metals); rather, unless otherwise instructed, you may combine all aqueous solutions into the same waste container. Although many types of solutions (aqueous sodium bicarbonate, aqueous sodium chloride, and so on) may seem innocuous and it may seem that their disposal down the sink drain is not likely to cause harm, many communities are becoming increasingly restrictive about what substances they will permit to enter municipal sewage-treatment systems. In light of this trend toward greater caution, it is important to develop good laboratory habits regarding the disposal of all chemicals.

**Heavy metals.** Many heavy-metal ions such as mercury and chromium are highly toxic and should be disposed of in specifically designated waste containers.

Whichever method is used, the waste containers must eventually be labeled with a complete list of each substance that is present in the waste. Individual waste containers are collected, and their contents are consolidated and placed into drums for transport to the waste-disposal site. Even these drums must bear labels that detail each of the substances contained in the waste.

In either waste-handling method, certain principles will always apply:

- Aqueous solutions should not be mixed with organic liquids.
- Concentrated acids should be stored in separate containers; certainly they must never be allowed to come into contact with organic waste.
- Organic materials that contain halogen atoms (fluorine, chlorine, bromine, or iodine) should be stored in separate containers from those used to store materials that do not contain halogen atoms.

In each experiment in this textbook, we have suggested a method of collecting and storing wastes. Your instructor may opt to use another method for collecting wastes.
E. Use of Flames
Even though organic solvents are frequently flammable (for example, hexane, diethyl ether, methanol, acetone, and petroleum ether), there are certain laboratory procedures for which a flame must be used. Most often, these procedures involve an aqueous solution. In fact, as a general rule, use a flame to heat only aqueous solutions. Heating methods that do not use a flame are discussed in detail in Technique 6, starting on page 589. Most organic solvents boil below 100°C, and an aluminum block, heating mantle, sand bath, or waterbath may be used to heat these solvents safely. Common organic solvents are listed in Technique 10, Table 10.3, page 643. Solvents marked in the table with boldface type will burn. Diethyl ether, pentane, and hexane are especially dangerous because, in combination with the correct amount of air, they may explode.

Some commonsense rules apply to using a flame in the presence of flammable solvents. Again, we stress that you should check to see whether anyone in your vicinity is using flammable solvents before you ignite any open flame. If someone is using a flammable solvent, move to a safer location before you light your flame. Your laboratory should have an area set aside for using a burner to prepare micropipets or other pieces of glassware.

The drainage troughs or sinks should never be used to dispose of flammable organic solvents. They will vaporize if they are low boiling and may encounter a flame farther down the bench on their way to the sink.

F. Inadvertently Mixed Chemicals
To avoid unnecessary hazards of fire and explosion, never pour any reagent back into a stock bottle. There is always the chance that you may accidently pour back some foreign substance that will react explosively with the chemical in the stock bottle. Of course, by pouring reagents back into the stock bottles, you may introduce impurities that could spoil the experiment for the person using the stock reagent after you. Pouring things back into bottles is not only a dangerous practice but also an inconsiderate one. Thus, you should not take more chemicals than you need.

G. Unauthorized Experiments
Never undertake any unauthorized experiments. The risk of an accident is high, particularly if the experiment has not been completely checked to reduce hazards. Never work alone in the laboratory. The laboratory instructor or supervisor must always be present.

H. Food in the Laboratory
Because all chemicals are potentially toxic, avoid accidentally ingesting any toxic substance; therefore, never eat or drink any food while in the laboratory. There is always the possibility that whatever you are eating or drinking may become contaminated with a potentially hazardous material.

I. Clothing
Always wear closed shoes in the laboratory; open-toed shoes or sandals offer inadequate protection against spilled chemicals or broken glass. Do not wear your best clothing in the laboratory because some chemicals can make holes in or permanent stains on your clothing. To protect yourself and your clothing, it is advisable to wear a full-length laboratory apron or coat.
When working with chemicals that are very toxic, wear some type of gloves. Disposable gloves are inexpensive, offer good protection, provide acceptable “feel,” and can be bought in many departmental stockrooms and college bookstores. Disposable latex surgical or polyethylene gloves are the least expensive type of glove; they are satisfactory when working with inorganic reagents and solutions. Better protection is afforded by disposable nitrile gloves. This type of glove provides good protection against organic chemicals and solvents. Heavier nitrile gloves are also available.

Finally, hair that is shoulder length or longer should be tied back. This precaution is especially important if you are working with a burner.

J. First Aid: Cuts, Minor Burns, and Acid or Base Burns

If any chemical enters your eyes, immediately irrigate the eyes with copious quantities of water. Tempered (slightly warm) water, if available, is preferable. Be sure that the eyelids are kept open. Continue flushing the eyes in this way for 15 minutes.

In case of a cut, wash the wound well with water unless you are specifically instructed to do otherwise. If necessary, apply pressure to the wound to stop the flow of blood. If you are assisting someone else, prudence dictates that you wear gloves in order to avoid contact with the blood of another person. Minor burns caused by flames or contact with hot objects may be soothed by immediately immersing the burned area in cold water or cracked ice until you no longer feel a burning sensation. Applying salves to burns is discouraged. Severe burns must be examined and treated by a physician. For chemical acid or base burns, rinse the burned area with copious quantities of water for at least 15 minutes.

If you accidentally ingest a chemical, call the local poison control center for instructions. Do not drink anything until you have been told to do so. It is important that the examining physician be informed of the exact nature of the substance ingested.

1.2 Right-to-Know Laws

The federal government and most state governments now require that employers provide their employees with complete information about hazards in the workplace. These regulations are often referred to as Right-to-Know Laws. At the federal level, the Occupational Safety and Health Administration (OSHA) is charged with enforcing these regulations.

In 1990, the federal government extended the Hazard Communication Act, which established the Right-to-Know Laws, to include a provision that requires the establishment of a Chemical Hygiene Plan at all academic laboratories. Every college and university chemistry department should have a Chemical Hygiene Plan. Having this plan means that all the safety regulations and laboratory safety procedures should be written in a manual. The plan also provides for the training of all employees in laboratory safety. Your laboratory instructor and assistants should have this training.

One of the components of Right-to-Know Laws is that employees and students have access to information about the hazards of any chemicals with which they are working. Your instructor will alert you to dangers to which you need to pay particular attention. However, you may want to seek additional information. Two excellent sources of information are labels on the bottles that come from a chemical manufacturer and Material Safety Data Sheets (MSDSs). The MSDSs are also provided by the manufacturer and must be kept available for all chemicals used at educational institutions.
A. Material Safety Data Sheets

Reading an MSDS for a chemical can be a daunting experience, even for an experienced chemist. MSDSs contain a wealth of information, some of which must be decoded to understand. The MSDS for methanol is shown on pages 550-554. Only the information that might be of interest to you is described in the paragraphs that follow.

Section 1. The first part of Section 1 identifies the substance by name, formula, and various numbers and codes. Most organic compounds have more than one name. In this case, the systematic (or International Union of Pure and Applied Chemistry [IUPAC]) name is methanol, and the other names are common names or are from an older system of nomenclature. The Chemical Abstract Service Number (CAS No.) is often used to identify a substance, and it may be used to access extensive information about a substance found in many computer databases or in the library.

Section 3. The Baker SAF-T-DATA System is found on all MSDSs and bottle labels for chemicals supplied by J. T. Baker, Inc. For each category listed, the number indicates the degree of hazard. The lowest number is 0 (very low hazard), and the highest number is 4 (extreme hazard). The Health category refers to damage involved when the substance is inhaled, ingested, or absorbed. Flammability indicates the tendency of a substance to burn. Reactivity refers to how reactive a substance is with air, water, or other substances. The last category, Contact, refers to how hazardous a substance is when it comes in contact with external parts of the body. Note that this rating scale is applicable only to Baker MSDSs and labels; other rating scales with different meanings are also in common use.

Section 4. This section provides helpful information for emergency and first aid procedures.

Section 6. This part of the MSDS deals with procedures for handling spills and disposal. The information could be very helpful, particularly if a large amount of the chemical was spilled. More information about disposal is also given in Section 13.

Section 8. Much valuable information is found in Section 8. To help you understand this material, some of the more important terms used in this section are defined:

Threshold Limit Value (TLV). The American Conference of Governmental Industrial Hygienists (ACGIH) developed the TLV: This is the maximum concentration of a substance in air that a person should be exposed to on a regular basis. It is usually expressed in ppm or mg/m³. Note that this value assumes that a person is exposed to the substance 40 hours per week, on a long-term basis. This value may not be particularly applicable in the case of a student performing an experiment in a single laboratory period.

Permissible Exposure Limit (PEL). This has the same meaning as TLV; however, PELs were developed by OSHA. Note that for methanol, the TLV and PEL are both 200 ppm.
Section 10. The information contained in Section 10 refers to the stability of the compound and the hazards associated with mixing of chemicals. It is important to consider this information before carrying out an experiment not previously done.

Section 11. More information about the toxicity is given in this section. Another important term must first be defined:

**Lethal Dose, 50% Mortality (LD$_{50}$).** This is the dose of a substance that will kill 50% of the animals administered a single dose. Different means of administration are used, such as oral, intraperitoneal (injected into the lining of the abdominal cavity), subcutaneous (injected under the skin), and application to the surface of the skin. The LD$_{50}$ is usually expressed in milligrams (mg) of substance per kilogram (kg) of animal weight. The lower the value of LD$_{50}$, the more toxic the substance. It is assumed that the toxicity in humans will be similar.

Unless you have considerably more knowledge about chemical toxicity, the information in Sections 8 and 11 is most useful for comparing the toxicity of one substance with another. For example, the TLV for methanol is 200 ppm, whereas the TLV for benzene is 10 ppm. Clearly, performing an experiment involving benzene would require much more stringent precautions than an experiment involving methanol. One of the LD$_{50}$ values for methanol is 5628 mg/kg. The comparable LD$_{50}$ value of aniline is 250 mg/kg. Clearly, aniline is much more toxic, and because it is easily absorbed through the skin, it presents a significant hazard. It should also be mentioned that both TLV and PEL ratings assume that the worker comes in contact with a substance on a repeated and long-term basis. Thus, even if a chemical has a relatively low TLV or PEL, it does not mean that using it for one experiment will present a danger to you. Furthermore, by performing experiments using small amounts of chemicals and with proper safety precautions, your exposure to organic chemicals in this course will be minimal.

Section 16. Section 16 contains the National Fire Protection Association (NFPA) rating. This is similar to the Baker SAF-T-DATA (discussed in Section 3), except that the number represents the hazards when a fire is present. The order here is Health, Flammability, and Reactivity. Often, this is presented in graphic form on a label (see figure). The small diamonds are often color coded: blue for Health, red for Flammability, and yellow for Reactivity. The bottom diamond (white) is sometimes used to display graphic symbols denoting unusual reactivity, hazards, or special precautions to be taken.
B. Bottle Labels

Reading the label on a bottle can be a helpful way of learning about the hazards of a chemical. The amount of information varies greatly, depending on which company supplied the chemical.

Apply some common sense when you read MSDSs and bottle labels. Using these chemicals does not mean you will experience the consequences that can potentially result from exposure to each chemical. For example, an MSDS for sodium chloride states, “Exposure to this product may have serious adverse health effects.” Despite the apparent severity of this cautionary statement, it would not be reasonable to expect people to stop using sodium chloride in a chemistry experiment or to stop sprinkling a small amount of it (as table salt) on eggs to enhance their flavor. In many cases, the consequences described in MSDSs from exposure to chemicals are somewhat overstated, particularly for students using these chemicals to perform a laboratory experiment.

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**METHYL ALCOHOL**

1. **Product Identification**
   - Synonyms: Wood alcohol; methanol; carbinol
   - CAS No: 67-56-1
   - Molecular Weight: 32.04
   - Chemical Formula: CH₃OH
   - Product Codes: J.T. Baker: 5217, 5370, 5704, 5807, 5811, 5842, 5869, 9049, 9063, 9066, 9067, 9069, 9070, 9071, 9073, 9075, 9076, 9077, 9091, 9093, 9096, 9097, 9098, 9263, 9893
   - Mallinckrodt: 3004, 3006, 3016, 3017, 3018, 3024, 3041, 3701, 4295, 5160, 8814, H080, H488, H603, V079, V571

2. **Composition/Information on Ingredients**
   - Ingredient: Methyl Alcohol
   - CAS No: 67-56-1
   - Percent: 100%
   - Hazardous: Yes

3. **Hazards Identification**

   **Emergency Overview**
   
   POISON! DANGER! VAPOR HARMFUL, MAY BE FATAL OR CAUSE BLINDNESS IF SWALLOWED. HARMFUL IF INHALED OR ABSORBED THROUGH SKIN. CANNOT BE MADE NONPOISONOUS. FLAMMABLE LIQUID AND VAPOR. CAUSES IRRITATION TO SKIN, EYES AND RESPIRATORY TRACT. AFFECTS THE LIVER.
J.T. Baker SAF-T-DATA™ Ratings
(Provided here for your convenience)

<table>
<thead>
<tr>
<th>Health:</th>
<th>Flammability:</th>
<th>Reactivity:</th>
<th>Contact:</th>
</tr>
</thead>
<tbody>
<tr>
<td>3 - Severe (Poison)</td>
<td>4 - Extreme (Flammable)</td>
<td>1 - Slight</td>
<td>1 - Slight</td>
</tr>
</tbody>
</table>

Lab Protection Equip: GOOGLES & SHIELD; LAB COAT & APRON; VENT HOOD; PROPER GLOVES; CLASS B EXTINGUISHER

Storage Color Code: Red (Flammable)

Potential Health Effects

Inhalation:
A slight irritant to the mucous membranes. Toxic effects exerted upon nervous system, particularly the optic nerve. Once absorbed into the body, it is very slowly eliminated. Symptoms of overexposure may include headache, drowsiness, nausea, vomiting, blurred vision, blindness, coma, and death. A person may get better but then worse again up to 30 hours later.

Ingestion:

Skin Contact:
Methyl alcohol is a defatting agent and may cause skin to become dry and cracked. Skin absorption can occur; symptoms may parallel inhalation exposure.

Eye Contact:
Irritant. Continued exposure may cause eye lesions.

Chronic Exposure:
Marked impairment of vision and enlargement of the liver has been reported. Repeated or prolonged exposure may cause skin irritation.

Aggravation of Pre-existing Conditions:
Persons with pre-existing skin disorders or eye problems or impaired liver or kidney function may be more susceptible to the effects of the substance.

4. First Aid Measures

Inhalation:
Remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Call a physician.

Ingestion:
Induce vomiting immediately as directed by medical personnel. Never give anything by mouth to an unconscious person.

Skin Contact:
Remove any contaminated clothing. Wash skin with soap or mild detergent and water for at least 15 minutes. Get medical attention if irritation develops or persists.

Eye Contact:
Immediately flush eyes with plenty of water for at least 15 minutes, lifting lower and upper eyelids occasionally. Get medical attention immediately.

5. Fire Fighting Measures

Fire:
Flash point: 12°C (54°F) CC
Autoignition temperature: 464°C (867°F)
Flammable limits in air % by volume:
LEL: 7.3; UEL: 36
Flammable.

Explosion:
Above flash point, vapor-air mixtures are explosive within flammable limits noted above. Moderate explosion hazard and dangerous fire hazard when exposed to heat, sparks or flames. Sensitive to static discharge.

Fire Extinguishing Media:
Water spray, dry chemical, alcohol foam, or carbon dioxide.

Special Information:
In the event of a fire, wear full protective clothing and NIOSH-approved self-contained breathing apparatus with full facepiece operated in the pressure demand or other positive pressure mode. Use water spray to blanket fire, cool fire exposed containers, and to flush non-ignited spills or vapors away from fire. Vapors can flow along surfaces to distant ignition source and flash back.

6. Accidental Release Measures

Ventilate area of leak or spill. Remove all sources of ignition. Wear appropriate personal protective equipment as specified in Section 8. Isolate hazard area. Keep unnecessary and unprotected personnel from entering. Contain and recover liquid when possible. Use non-sparking tools and equipment. Collect liquid in an appropriate container or absorb with an inert material (e.g., vermiculite, dry sand, earth), and place in a chemical waste container. Do not use combustible materials, such as saw dust. Do not flush to sewer.

J. T. Baker SOLUSORB® solvent adsorbent is recommended for spills of this product.
7. Handling and Storage

Protect against physical damage. Store in a cool, dry well-ventilated location, away from any area where the fire hazard may be acute. Outside or detached storage is preferred. Separate from incompatibles. Containers should be bonded and grounded for transfers to avoid static sparks. Storage and use areas should be No Smoking areas. Use non-sparking type tools and equipment, including explosion proof ventilation. Containers of this material may be hazardous when empty since they retain product residues (vapors, liquid); observe all warnings and precautions listed for the product.

8. Exposure Controls/Personal Protection

Airborne Exposure Limits:
For Methyl Alcohol:
- OSHA Permissible Exposure Limit (PEL): 200 ppm (TWA)
- ACGIH Threshold Limit Value (TLV): 200 ppm (TWA), 250 ppm (STEL) skin

Ventilation System:
A system of local and/or general exhaust is recommended to keep employee exposures below the Airborne Exposure Limits. Local exhaust ventilation is generally preferred because it can control the emissions of the contaminant at its source, preventing dispersion of it into the general work area. Please refer to the ACGIH document, "Industrial Ventilation, A Manual of Recommended Practices", most recent edition, for details.

Personal Respirator (NIOSH Approved)
If the exposure limit is exceeded, wear a supplied air, full-facepiece respirator, airlined hood, or full-facepiece self-contained breathing apparatus.

Skin Protection:
Rubber or neoprene gloves and additional protection including impervious boots, apron, or coveralls, as needed in areas of unusual exposure.

Eye Protection:
Use chemical safety goggles. Maintain eye wash fountain and quick-drench facilities in work area.

9. Physical and Chemical Properties

Appearance: Boiling Point:
Clear, colorless liquid. 64.5°C (148°F)

Odor: Melting Point:
Characteristic odor. -98°C (-144°F)

Solubility: Vapor Density (Air=1):
Misible in water. 1.1

Specific Gravity: Vapor Pressure (mm Hg):
0.8 97 @ 20°C (68°F)

pH: Evaporation Rate (BuAc=1):
No information found. 5.9

% Volatiles by volume @ 21°C (70°F): 100

10. Stability and Reactivity

Stability:
Stable under ordinary conditions of use and storage.

Hazardous Decomposition Products:
May form carbon dioxide, carbon monoxide, and formaldehyde when heated to decomposition.

Hazardous Polymerization:
Will not occur.

Incompatibilities:
Strong oxidizing agents such as nitrates, perchlorates or sulfuric acid. Will attack some forms of plastics, rubber, and coatings. May react with metallic aluminum and generate hydrogen gas.

Conditions to Avoid:
Heat, flames, ignition sources and incompatibles.

11. Toxicological Information

Methyl Alcohol (Methanol) Oral rat LD50: 5628 mg/kg; inhalation rat LC50: 64000 ppm/4H; skin rabbit LD50: 15800 mg/kg; Implantation data-standard Draize test: skin, rabbit: 20mg/24 hr. Moderate; eye, rabbit: 100 mg/24 hr. Moderate; Investigated as a mutagen, reproductive effector.

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>NTP Carcinogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methyl Alcohol (87-56-1)</td>
<td>No</td>
</tr>
</tbody>
</table>
12. Ecological Information

Environmental Fate:
When released into the soil, this material is expected to readily biodegrade. When released into the soil, this material is expected to leach into groundwater. When released into the water, this material is expected to have a half-life between 1 and 10 days. When released into water, this material is expected to readily biodegrade. When released into the air, this material is expected to exist in the aerosol phase with a short half-life. When released into the air, this material is expected to be readily degraded by reaction with photochemically produced hydroxyl radicals. When released into air, this material is expected to have a half-life between 10 and 30 days. When released into the air, this material is expected to be readily removed from the atmosphere by wet deposition.

Environmental Toxicity:
This material is expected to be slightly toxic to aquatic life.

13. Disposal Considerations

Whatever cannot be saved for recovery or recycling should be handled as hazardous waste and sent to a RCRA approved incinerator or disposed in a RCRA approved waste facility. Processing, use or contamination of this product may change the waste management options. State and local disposal regulations may differ from federal disposal regulations.

Dispose of container and unused contents in accordance with federal, state and local requirements.

14. Transport Information

Domestic (Land, D.O.T.)
- Proper Shipping Name: METHANOL
- Hazard Class: 3
- UN/NA: UN1230
- Packing Group: II
- Information reported for product/size: 350LB

International (Water, I.M.O.)
- Proper Shipping Name: METHANOL
- Hazard Class: 3.2, 6.1
- UN/NA: UN1230
- Packing Group: II
- Information reported for product/size: 350LB

15. Regulatory Information

--- Chemical Inventory Status ---

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>TSCA</th>
<th>EC</th>
<th>Japan</th>
<th>Australia</th>
<th>Korea</th>
<th>DSL</th>
<th>NDLS</th>
<th>Phill.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methyl Alcohol (67-56-1)</td>
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<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>

--- Federal, State & International Regulations ---

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>RQ</th>
<th>TPQ</th>
<th>List</th>
<th>Chemical Cat.</th>
<th>CERCLA</th>
<th>-SCARA-</th>
<th>-SARA 302-</th>
<th>-SARA 313-</th>
<th>-RCRA-</th>
<th>-TSCA-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methyl Alcohol (67-56-1)</td>
<td>RQ</td>
<td>TPQ</td>
<td>List</td>
<td>Chemical Cat.</td>
<td>CERCLA</td>
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<td>8(d)</td>
<td>8(d)</td>
<td>8(d)</td>
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</table>

Chemical Weapons Convention: No
TSCA 12(b): No
CDTA: No
SARA 311/312: Acute: Yes Chronic: Yes Fire: Yes Pressure: No Reactivity: No (Pure / Liquid)

Australian Hazchem Code: 2PE
Australian Poison Schedule: S6
WHMIS: This MSDS has been prepared according to the hazard criteria of the Controlled Products Regulations (CPR) and the MSDS contains all of the information required by the CPR.

16. Other Information

NFPA Ratings:
Health: 1 Flammability: 3 Reactivity: 0

Label Hazard Warning:
POISON! DANGER! VAPOR HARMFUL. MAY BE FATAL OR CAUSE BLINDNESS IF SWALLOWED. HARMFUL IF INHALED OR ABSORBED THROUGH SKIN. CANNOT BE MADE NONPOISONOUS. FLAMMABLE LIQUID AND VAPOR. CAUSES IRRITATION TO SKIN, EYES AND RESPIRATORY TRACT. AFFECTS THE LIVER.

Label Precautions:
Keep away from heat, sparks and flame. Keep container closed. Use only with adequate ventilation. Wash thoroughly after handling. Avoid breathing vapor. Avoid contact with eyes, skin and clothing.
1.3 Common Solvents

Most organic chemistry experiments involve an organic solvent at some step in the procedure. A list of common organic solvents follows, with a discussion of toxicity, possible carcinogenic properties, and precautions that you should use when handling these solvents. A tabulation of the compounds currently suspected of being carcinogens appears at the end of Technique 1.

**Acetic Acid.** Glacial acetic acid is corrosive enough to cause serious acid burns on the skin. Its vapors can irritate the eyes and nasal passages. Care should be exercised not to breathe the vapors and not to allow them to escape into the laboratory.

**Acetone.** Relative to other organic solvents, acetone is not very toxic. It is flammable, however. Do not use acetone near open flames.

**Benzene.** Benzene can damage bone marrow, it causes various blood disorders, and its effects may lead to leukemia. Benzene is considered a serious carcinogenic hazard. It is absorbed rapidly through the skin and also poisons the liver and kidneys. In addition, benzene is flammable. Because of its toxicity and its carcinogenic properties, benzene should not be used in the laboratory; you should use some less dangerous solvent instead. Toluene is considered a safer alternative solvent in procedures that specify benzene.

**Carbon Tetrachloride.** Carbon tetrachloride can cause serious liver and kidney damage, as well as skin irritation and other problems. It is absorbed rapidly through the skin. In high concentrations, it can cause death as a result of respiratory failure. Moreover, carbon tetrachloride is suspected of being a carcinogenic material. Although this solvent has the advantage of being non-flammable (in the past, it was used on occasion as a fire extinguisher), it causes health problems, so it should not be used routinely in the laboratory. If no reasonable substitute exists, however, it must be used in small quantities,
as in preparing samples for infrared (IR) and nuclear magnetic resonance (NMR) spectroscopy. In such cases, you must use it in a hood.

**Chloroform.** Chloroform is similar to carbon tetrachloride in its toxicity. It has been used as an anesthetic. However, chloroform is currently on the list of suspected carcinogens. Because of this, do not use chloroform routinely as a solvent in the laboratory. If it is occasionally necessary to use chloroform as a solvent for special samples, then you must use it in a hood. Methylene chloride is usually found to be a safer substitute in procedures that specify chloroform as a solvent. Deuterchloroform, CDCl₃, is a common solvent for NMR spectroscopy. Caution dictates that you should treat it with the same respect as chloroform.

**1,2-Dimethoxyethane (Ethylene Glycol Dimethyl Ether or Monoglyme).** Because it is miscible with water, 1,2-dimethoxyethane is a useful alternative to solvents such as dioxane and tetrahydrofuran, which may be more hazardous. 1,2-Dimethoxyethane is flammable and should not be handled near an open flame. On long exposure of 1,2-dimethoxyethane to light and oxygen, explosive peroxides may form. 1,2-Dimethoxyethane is a possible reproductive toxin.

**Dioxane.** Dioxane has been used widely because it is a convenient, water-miscible solvent. It is now suspected, however, of being carcinogenic. It is also toxic, affecting the central nervous system, liver, kidneys, skin, lungs, and mucous membranes. Dioxane is also flammable and tends to form explosive peroxides when it is exposed to light and air. Because of its carcinogenic properties, it is no longer used in the laboratory unless absolutely necessary. Either 1,2-dimethoxyethane or tetrahydrofuran is a suitable, water-miscible alternative solvent.

**Ethanol.** Ethanol has well-known properties as an intoxicant. In the laboratory, the principal danger arises from fires because ethanol is a flammable solvent. When using ethanol, take care to work where there are no open flames.

**Ether (Diethyl Ether).** The principal hazard associated with diethyl ether is fire or explosion. Ether is probably the most flammable solvent found in the laboratory. Because ether vapors are much denser than air, they may travel along a laboratory bench for a considerable distance from their source before being ignited. Before using ether, it is important to be sure that no one is working with matches or any open flame. Ether is not a particularly toxic solvent, although in high enough concentrations it can cause drowsiness and perhaps nausea. It has been used as a general anesthetic. Ether can form highly explosive peroxides when exposed to air. Consequently, you should never distill it to dryness.

**Hexane.** Hexane may be irritating to the respiratory tract. It can also act as an intoxicant and a depressant of the central nervous system. It can cause skin irritation because it is an excellent solvent for skin oils. The most serious hazard, however, comes from its flammability. The precautions recommended for using diethyl ether in the presence of open flames apply equally to hexane.
**Ligroin.** See Hexane.

**Methanol.** Much of the material outlining the hazards of ethanol applies to methanol. Methanol is more toxic than ethanol; ingestion can cause blindness and even death. Because methanol is more volatile, the danger of fires is more acute.

**Methylene Chloride (Dichloromethane).** Methylene chloride is not flammable. Unlike other members of the class of chlorocarbons, it is not currently considered a serious carcinogenic hazard. Recently, however, it has been the subject of much serious investigation, and there have been proposals to regulate it in industrial situations in which workers have high levels of exposure on a day-to-day basis. Methylene chloride is less toxic than chloroform and carbon tetrachloride. It can cause liver damage when ingested, however, and its vapors may cause drowsiness or nausea.

**Pentane.** See Hexane.

**Petroleum Ether.** See Hexane.

**Pyridine.** Some fire hazard is associated with pyridine. However, the most serious hazard arises from its toxicity. Pyridine may depress the central nervous system; irritate the skin and respiratory tract; damage the liver, kidneys, and gastrointestinal system; and even cause temporary sterility. You should treat pyridine as a highly toxic solvent and handle it only in the fume hood.

**Tetrahydrofuran.** Tetrahydrofuran may cause irritation of the skin, eyes, and respiratory tract. It should never be distilled to dryness because it tends to form potentially explosive peroxides on exposure to air. Tetrahydrofuran does present a fire hazard.

**Toluene.** Unlike benzene, toluene is not considered a carcinogen. However, it is at least as toxic as benzene. It can act as an anesthetic and damage the central nervous system. If benzene is present as an impurity in toluene, expect the usual hazards associated with benzene. Toluene is also a flammable solvent, and the usual precautions about working near open flames should be applied.

You should not use certain solvents in the laboratory because of their carcinogenic properties. Benzene, carbon tetrachloride, chloroform, and dioxane are among these solvents. For certain applications, however, notably as solvents for infrared or NMR spectroscopy, there may be no suitable alternative. When it is necessary to use one of these solvents, use safety precautions and refer to the discussions in Techniques 25–28.

Because relatively large amounts of solvents may be used in a large organic laboratory class, your laboratory supervisor must take care to store these substances safely. Only the amount of solvent needed for a particular experiment should be kept in the laboratory. The preferred location for bottles of solvents being used during a class period is in a hood. When the solvents are not being used, they should be stored in a fireproof storage cabinet for solvents. If possible, this cabinet should be ventilated into the fume hood system.
1.4 Carcinogenic Substances

A carcinogen is a substance that causes cancer in living tissue. The usual procedures for determining whether a substance is carcinogenic is to expose laboratory animals to high dosages over a long period. It is not clear whether short-term exposure to these chemicals carries a comparable risk, but it is prudent to use these substances with special precautions.

Many regulatory agencies have compiled lists of carcinogenic substances or substances suspected of being carcinogenic. Because these lists are inconsistent, compiling a definitive list of carcinogenic substances is difficult. The following common substances are included in many of these lists.

<table>
<thead>
<tr>
<th>Substance</th>
<th>Substances</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetamide</td>
<td>4-Methyl-2-oxetanone (β-butyrolactone)</td>
</tr>
<tr>
<td>Acrylonitrile</td>
<td>1-Naphthylamine</td>
</tr>
<tr>
<td>Asbestos</td>
<td>2-Naphthylamine</td>
</tr>
<tr>
<td>Benzene</td>
<td>N-Nitroso compounds</td>
</tr>
<tr>
<td>Benzidine</td>
<td>2-Oxetanone (β-propiolactone)</td>
</tr>
<tr>
<td>Carbon tetrachloride</td>
<td>Phenacetin</td>
</tr>
<tr>
<td>Chloroform</td>
<td>Phenylhydrazine and its salts</td>
</tr>
<tr>
<td>Chromic oxide</td>
<td>Polychlorinated biphenyl (PCB)</td>
</tr>
<tr>
<td>Coumarin</td>
<td>Progesterone</td>
</tr>
<tr>
<td>Diazomethane</td>
<td>Styrene oxide</td>
</tr>
<tr>
<td>1,2-Dibromoethane</td>
<td>Tannins</td>
</tr>
<tr>
<td>Dimethyl sulfate</td>
<td>Testosterone</td>
</tr>
<tr>
<td>p-Dioxane</td>
<td>Thioacetamide</td>
</tr>
<tr>
<td>Ethylene oxide</td>
<td>Thiourea</td>
</tr>
<tr>
<td>Formaldehyde</td>
<td>o-Toluidine</td>
</tr>
<tr>
<td>Hydrazine and its salts</td>
<td>Trichloroethylene</td>
</tr>
<tr>
<td>Lead (II) acetate</td>
<td>Vinyl chloride</td>
</tr>
</tbody>
</table>

REFERENCES


Useful Safety-Related Internet Addresses

Interactive Learning Paradigms, Inc.
This is an excellent general site for MSDS sheets. The site lists chemical manufacturers and suppliers. Selecting a company will take you directly to the appropriate place to obtain an MSDS sheet. Many of the sites listed require you to register in order to obtain a MSDS sheet for a particular chemical. Ask your departmental or college safety supervisor to obtain the information for you.

Acros Chemicals and Fisher Scientific

Alfa Aesar

Eastman Kodak

EMD Chemicals (formerly EM Science) and Merck

J. T. Baker and Mallinckrodt Laboratory Chemicals

National Institute for Occupational Safety and Health (NIOSH) has an excellent website that includes databases and information resources, including links:

Sigma, Aldrich and Fluka

VWR Scientific Products

2 TECHNIQUE 2

The Laboratory Notebook, Calculations, and Laboratory Records

It is important that you do some advance preparation for all laboratory work. Presented here are some suggestions about what specific information you should try to obtain in your advance studying. Because much of this information must be obtained while preparing your laboratory notebook, the two subjects, advance study and notebook preparation, are developed simultaneously.

An important part of any laboratory experience is learning to maintain complete records of every experiment undertaken and every item of data
obtained. Far too often, careless recording of data and observations has resulted in mistakes, frustration, and lost time due to needless repetition of experiments. If reports are required, you will find that proper collection and recording of data can make your report writing much easier.

Because organic reactions are seldom quantitative, special problems result. Frequently, reagents must be used in large excess to increase the amount of product. Some reagents are expensive, and, therefore, care must be used in measuring the amounts of these substances. Often, many more reactions take place than you desire. These extra reactions, or side reactions, may form products other than the desired product. These are called side products. For all these reasons, you must plan your experimental procedure carefully before undertaking the actual experiment.

### 2.1 The Notebook

For recording data and observations during experiments, use a bound notebook. The notebook should have consecutively numbered pages. If it does not, number the pages immediately. A spiral-bound notebook or any other notebook from which the pages can be removed easily is not acceptable, because the possibility of losing the pages is great.

All data and observations must be recorded in the notebook. Paper towels, napkins, toilet tissue, or scratch paper tend to become lost or destroyed. It is bad laboratory practice to record information on such random and perishable pieces of paper. All entries must be recorded in permanent ink. It can be frustrating to have important information disappear from the notebook because it was recorded in washable ink or pencil and could not survive a flood caused by the student at the next position on the bench. Because you will be using your notebook in the laboratory, the book will probably become soiled or stained by chemicals, filled with scratched-out entries, or even slightly burned. That is expected and is a normal part of laboratory work.

Your instructor may check your notebook at any time, so you should always have it up to date. If your instructor requires reports, you can prepare them quickly from the material recorded in the laboratory notebook.

### 2.2 Notebook Format

**A. Advance Preparation**

Individual instructors vary greatly in the type of notebook format they prefer; such variation stems from differences in philosophies and experience. You must obtain specific directions from your own instructor for preparing a notebook. Certain features, however, are common to most notebook formats. The following discussion indicates what might be included in a typical notebook.

It will be helpful and you can save much time in the laboratory if for each experiment you know the main reactions, the potential side reactions, the mechanism, and the stoichiometry and you understand fully the procedure and the theory underlying it before you come to the laboratory. Understanding the procedure by which the desired product is to be separated from undesired materials is also important. If you examine each of these topics before coming to class, you will be prepared to do the experiment efficiently. You will have your equipment and reagents already prepared when they are to be used. Your reference material will be at hand when you need it. Finally, with your time efficiently organized, you will be able to take advantage of long reaction or reflux periods to perform other tasks, such as doing shorter experiments or finishing previous ones.
For experiments in which a compound is synthesized from other reagents, that is, preparative experiments, it is essential to know the main reaction. To perform stoichiometric calculations, you should balance the equation for the main reaction. Therefore, before you begin the experiment, your notebook should contain the balanced equation for the pertinent reaction. Using the preparation of isopentyl acetate, or banana oil, as an example, you should write the following:

\[
\begin{align*}
\text{CH}_3\text{C}(-\text{OH}) + \text{CH}_3\text{C}-\text{CH}-\text{CH}_2-\text{CH}_2-\text{OH} & \xrightarrow{\text{H}^+} \\
\text{Acetic acid} & \quad \text{Isopentyl alcohol} \\
\text{CH}_3\text{C}(-\text{O})-\text{CH}_2-\text{CH}_2-\text{CH}-\text{CH}_3 + \text{H}_2\text{O} & \\
\text{Isopentyl acetate} & 
\end{align*}
\]

Also enter in the notebook the possible side reactions that divert reagents into contaminants (side products), before beginning the experiment. You will have to separate these side products from the major product during purification.

You should list physical constants such as melting points, boiling points, densities, and molecular weights in the notebook when this information is needed to perform an experiment or to do calculations. These data are located in sources such as the CRC Handbook of Chemistry and Physics, The Merck Index, Lange’s Handbook of Chemistry, or Aldrich Handbook of Fine Chemicals. Write physical constants required for an experiment in your notebook before you come to class.

Advance preparation may also include examining some subjects, information not necessarily recorded in the notebook, that should prove useful in understanding the experiment. Included among these subjects are an understanding of the mechanism of the reaction, an examination of other methods by which the same compound might be prepared, and a detailed study of the experimental procedure. Many students find that an outline of the procedure, prepared before they come to class, helps them use their time more efficiently once they begin the experiment. Such an outline might well be prepared on some loose sheet of paper rather than in the notebook itself.

Once the reaction has been completed, the desired product does not magically appear as purified material; it must be isolated from a frequently complex mixture of side products, unreacted starting materials, solvents, and catalysts. You should try to outline a separation scheme in your notebook for isolating the product from its contaminants. At each stage, you should try to understand the reason for the particular instruction given in the experimental procedure. This not only will familiarize you with the basic separation and purification techniques used in organic chemistry but also will help you understand when to use these techniques. Such an outline might take the form of a flowchart. For example, see the separation scheme for isopentyl acetate (Figure 2.1). Careful attention to understanding the separation,
besides familiarizing you with the procedure by which the desired product is separated from impurities in your particular experiments, may prepare you for original research in which no experimental procedure exists.

In designing a separation scheme, note that the scheme outlines those steps undertaken once the reaction period has been concluded. For this reason, the represented scheme does not include steps such as the addition of the reactants (isopentyl alcohol and acetic acid) and the catalyst (sulfuric acid) or the heating of the reaction mixture.

For experiments in which a compound is isolated from a particular source and is not prepared from other reagents, some information described in this section will not be applicable. Such experiments are called isolation experiments. A typical isolation experiment involves isolating a pure compound from a natural source. Examples include isolating caffeine from tea or isolating cinnamaldehyde from cinnamon. Although isolation experiments require somewhat different advance preparation, this advance study may include looking up physical constants for the compound isolated and outlining the isolation procedure. A detailed examination of the separation scheme is important here because it is the heart of such an experiment.

B. Laboratory Records

When you begin the actual experiment, keep your notebook nearby so you will be able to record those operations you perform. When working in the laboratory, the notebook serves as a place in which to record a rough
transcript of your experimental method. Data from actual weighings, volume measurements, and determinations of physical constants are also noted. This section of your notebook should not be prepared in advance. The purpose is not to write a recipe but rather to record what you did and what you observed. These observations will help you write reports without resorting to memory. They will also help you or other workers repeat the experiment in as nearly as possible the same way. The sample notebook pages found in Figures 2.2 and 2.3 illustrate the type of data and observations that should be written in your notebook.

When your product has been prepared and purified, or isolated if it is an isolation experiment, record pertinent data such as the melting point or boiling point of the substance, its density, its index of refraction, and the conditions under which spectra were determined.

C. Calculations

A chemical equation for the overall conversion of the starting materials to products is written on the assumption of simple ideal stoichiometry. Actually, this assumption is seldom realized. Side reactions or competing reactions will also occur, giving other products. For some synthetic reactions, an equilibrium state will be reached in which an appreciable amount of starting material is still present and can be recovered. Some of the reactant may also remain if it is present in excess or if the reaction was incomplete. A reaction involving an expensive reagent illustrates another reason for needing to know how far a particular type of reaction converts reactants to products. In such a case, it is preferable to use the most efficient method for this conversion. Thus, information about the efficiency of conversion for various reactions is of interest to the person contemplating the use of these reactions.

The quantitative expression for the efficiency of a reaction is found by calculating the yield for the reaction. The theoretical yield is the number of grams of the product expected from the reaction on the basis of ideal stoichiometry, with side reactions, reversibility, and losses ignored. To calculate the theoretical yield, it is first necessary to determine the limiting reagent. The limiting reagent is the reagent that is not present in excess and on which the overall yield of product depends. The method for determining the limiting reagent in the isopentyl acetate experiment is illustrated in the sample notebook pages shown in Figures 2.2 and 2.3. You should consult your general chemistry textbook for more complicated examples. The theoretical yield is then calculated from the expression

\[
\text{Theoretical yield} = \frac{\text{moles of limiting reagent}(\text{ratio})(\text{molecular weight of product})}{100}
\]

The ratio here is the stoichiometric ratio of product to limiting reagent. In preparing isopentyl acetate, that ratio is 1:1. One mole of isopentyl alcohol, under ideal circumstances, should yield 1 mole of isopentyl acetate.

The actual yield is simply the number of grams of desired product obtained. The percentage yield describes the efficiency of the reaction and is determined by

\[
\text{Percentage yield} = \frac{\text{Actual yield}}{\text{Theoretical yield}} \times 100
\]
THE PREPARATION OF ISOPENTYL ACETATE (BANANA OIL)

MAIN REACTION

\[
\begin{align*}
\text{CH}_3\text{COH} + \text{CH}_3\text{CHCH}_2\text{CH}_2\text{OH} & \xrightarrow{\text{H}^+} \text{CH}_3\text{COCH}_2\text{CH}_2\text{CHCH}_3 + \text{H}_2\text{O} \\
\text{ACETIC ACID} & \quad \text{ISOPENTYL ALCOHOL} & \quad \text{ISOPENTYL ACETATE}
\end{align*}
\]

<table>
<thead>
<tr>
<th>TABLE OF PHYSICAL CONSTANTS</th>
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<th>(\text{BP} )</th>
<th>DENSITY</th>
<th>(\text{g/mL} )</th>
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</thead>
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<td>132\text{°C}</td>
<td>0.813</td>
<td>\text{g/mL}</td>
</tr>
<tr>
<td>\text{ACETIC ACID}</td>
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<td>118</td>
<td>1.06</td>
<td></td>
</tr>
<tr>
<td>\text{ISOPENTYL ALCOHOL}</td>
<td>130.2</td>
<td>142</td>
<td>0.876</td>
<td></td>
</tr>
</tbody>
</table>

SEPARATION SCHEME

DATA AND OBSERVATIONS

0.70 mL of isopentyl acetate was added to a preweighed 50 mL conical vial:

\[
\begin{align*}
\text{VIAL} + \text{ALCOHOL} & = 25.524 \text{ g} \\
\text{VIAL} & = 24.955 \text{ g} \\
0.569 \text{ g} & = \text{ISOPENTYL ALCOHOL}
\end{align*}
\]

Acetic acid (1.4 mL) and 3 drops of concentrated \(\text{H}_2\text{SO}_4\) (using a Pasteur pipet) were also added to the conical vial along with a small boiling stone. A water-cooled condenser, topped with a drying tube containing a loose plug of glass wool, was attached to the vial. The reaction mixture was refluxed in an aluminum block (about 155°) for 75 min and then cooled to room temperature. The color of the reaction mixture was brownish-yellow.

Figure 2.2
A sample notebook, page 1.
Calculation of the theoretical yield and percentage yield can be illustrated using hypothetical data for the isopentyl acetate preparation:

\[
\text{Theoretical yield} = (6.45 \times 10^{-3} \text{ mol isopentyl alcohol}) \left( \frac{1 \text{ mol isopentyl acetate}}{1 \text{ mol isopentyl alcohol}} \right) \left( \frac{130.2 \text{ g isopentyl acetate}}{1 \text{ mol isopentyl acetate}} \right)
\]

\[
= 0.840 \text{ g isopentyl acetate}
\]

\[
\text{Percentage yield} = \frac{0.354 \text{ g}}{0.840 \text{ g}} \times 100 = 42.1\%
\]

Figure 2.3
A sample notebook, page 2.
Laboratory Glassware: Care and Cleaning

Because your glassware is expensive and you are responsible for it, you will want to give it proper care and respect. If you read this chapter carefully and follow the procedures presented here, you may be able to avoid some unnecessary expense. You may also save time because cleaning problems and replacing broken glassware are time-consuming.

If you are unfamiliar with the equipment found in an organic laboratory or are uncertain about how such equipment should be treated, this chapter provides some useful information. It includes topics such as cleaning glassware, caring for glassware when using corrosive or caustic reagents, and assembling components from your organic laboratory kit. At the end of this section are illustrations and names of most of the equipment you are likely to find in your drawer or locker.

Glassware can be cleaned easily if you clean it immediately. It is good practice to do your “dishwashing” right away. With time, organic tarry materials left in a container begin to attack the surface of the glass. The longer you wait to clean glassware, the more extensively this interaction will have progressed. Cleaning is then more difficult because water will no longer wet the surface of the glass as effectively. If you can’t wash your glassware immediately after use, soak the dirty pieces in soapy water. A half-gallon plastic container is convenient for soaking and washing glassware. Using a plastic container also helps prevent the loss of small pieces of equipment used in microscale techniques.

Various soaps and detergents are available for washing glassware. They should be tried first when washing dirty glassware. Organic solvents can also be used because the residue remaining in dirty glassware is likely to be soluble in some organic solvent. After the solvent has been used, the conical vial or flask probably will have to be washed with soap and water to remove the residual solvent. When you use solvents in cleaning glassware, use caution, because the solvents are hazardous (see Technique 1). Use fairly small amounts of a solvent for cleaning purposes. Usually 1–2 mL will be sufficient. Acetone is commonly used, but it is expensive. Your wash acetone can be used effectively several times before it is “spent.” Once your acetone is spent, dispose of it as your instructor directs. If acetone does not work, other organic solvents such as methylene chloride or toluene can be used.

CAUTION

Acetone is very flammable. Do not use it around flames.

For troublesome stains and residues that adhere to the glass despite your best efforts, use a mixture of sulfuric acid and nitric acid. Cautiously add about 20 drops of concentrated sulfuric acid and 5 drops of concentrated nitric acid to the flask or vial.
CAUTION
You must wear safety glasses when you are using a cleaning solution made from sulfuric acid and nitric acid. Do not allow the solution to come into contact with your skin or clothing. It will cause severe burns on your skin and create holes in your clothing. The acids may also react with the residue in the container.

Swirl the acid mixture in the container for a few minutes. If necessary, place the glassware in a warm waterbath and heat cautiously to accelerate the cleaning process. Continue heating until any sign of a reaction ceases. When the cleaning procedure is completed, decant the mixture into an appropriate waste container.

CAUTION
Do not pour the acid solution into a waste container that is intended for organic wastes.

Rinse the piece of glassware thoroughly with water and then wash with soap and water. For most common organic chemistry applications, any stains that survive this treatment are not likely to cause difficulty in subsequent laboratory procedures.

If the glassware is contaminated with stopcock grease (unlikely with the glassware recommended in this book), rinse the glassware with a small amount (1–2 mL) of methylene chloride. Discard the rinse solution into an appropriate waste container. Once the grease is removed, wash the glassware with soap or detergent and water.

The easiest way to dry glassware is to let it stand overnight. Store conical vials, flasks, and beakers upside down on a piece of paper towel to permit the water to drain from them. Drying ovens can be used to dry glassware if they are available, and if they are not being used for other purposes. Rapid drying can be achieved by rinsing the glassware with acetone and air-drying it or placing it in an oven. First, thoroughly drain the glassware of water. Then rinse it with one or two small portions (1–2 mL) of acetone. Do not use any more acetone than is suggested here. Return the used acetone to a waste acetone container for recycling. After you rinse the glassware with acetone, dry it by placing it in a drying oven for a few minutes or allow it to air-dry at room temperature. The acetone can also be removed by aspirator suction. In some laboratories, it may be possible to dry the glassware by blowing a gentle stream of dry air into the container. (Your laboratory instructor will indicate if you should do this.) Before drying the glassware with air, make sure that the air line is not filled with oil. Otherwise, the oil will be blown into the container, and you will have to clean it again. It is not necessary to blast the acetone out of the glassware with a wide-open stream of air; a gentle stream of air is just as effective and will not startle other people in the room.

Do not dry your glassware with a paper towel unless the towel is lint-free. Most paper will leave lint on the glass that can interfere with subsequent procedures performed in the equipment. Sometimes it is not necessary to dry a piece of equipment thoroughly. For example, if you are going to place water or an aqueous solution in a container, it does not need to be completely dry.
3.3 Ground-Glass Joints

It is likely that the glassware in your organic kit has standard-taper ground-glass joints. For example, the air condenser in the figure consists of an inner (male) ground-glass joint at the bottom and an outer (female) joint at the top. Each end is ground to a precise size, which is designated by the symbol $T$ followed by two numbers. A common joint size in microscale glassware is $T14/10$. The first number indicates the diameter (in millimeters) of the joint at its widest point, and the second number refers to its length (see Figure 3.1). One advantage of standard-taper joints is that the pieces fit together snugly and form a good seal. In addition, standard-taper joints allow all glassware components with the same joint size to be connected, thus permitting the assembly of a wide variety of apparatus. One disadvantage of glassware with ground-glass joints, however, is that it is expensive.

Some pieces of glassware with ground-glass joints also have threads cast into the outside surface of the outer joints (see top of air condenser in Figure 3.1). The threaded joint allows the use of a plastic screw cap with a hole in the top to fasten two pieces of glassware together securely. The plastic cap is slipped over the inner joint of the upper piece of glassware, followed by a rubber O-ring (see Figure 3.2). The O-ring should be pushed down so that it fits snugly on top of the ground-glass joint. The inner ground-glass joint is then fitted into the outer joint of the bottom piece of glassware. The screw cap is tightened without excessive force to attach the entire apparatus firmly together. The O-ring provides an additional seal that makes this joint airtight. With this connecting system, it is unnecessary to use any type of grease to seal the joint. The O-ring must be used to obtain a good seal and to lessen the chances of breaking the glassware when you tighten the plastic cap.

It is important to make sure no solid or liquid is on the joint surfaces. Such material will lessen the efficiency of the seal, and the joints may leak. The presence of solid particles could cause the ground-glass joints to break when

**Figure 3.1**
Illustration of $T14/10$ inner and outer joints showing dimensions.

**Figure 3.2**
A microscale standard-taper joint assembly.
the plastic cap is tightened. Also, if the apparatus is to be heated, material caught between the joint surfaces will increase the tendency for the joints to stick. If the joint surfaces are coated with liquid or adhering solid, you should wipe them with a cloth or lint-free paper towel before assembling. The most important thing you can do to prevent ground-glass joints from becoming “frozen,” or stuck together, is to disassemble the glassware as soon as possible after a procedure is completed. Even when this precaution is followed, ground-glass joints may become stuck tightly together. The same is true of glass stoppers in bottles or conical vials. Because microscale glassware is small and fragile, it is relatively easy to break a piece of glassware when trying to pull two pieces apart. If the pieces do not separate easily, you must be careful when you try to pull them apart. The best way is to hold the two pieces, with your hands touching, as close as possible to the joint. With a firm grasp, try to loosen the joint with a slight twisting motion (do not twist very hard). If this does not work, try to pull your hands apart without pushing sideways on the glassware.

If it is not possible to pull the pieces apart, the following methods may help. A frozen joint can sometimes be loosened if you tap it gently with the wooden handle of a spatula. Then, try to pull it apart as already described. If this procedure fails, you may try heating the joint in hot water or a steam bath. If this heating fails, the instructor may be able to advise you. As a last resort, you may try heating the joint in a flame. You should not try this unless the apparatus is hopelessly stuck, because heating by flame often causes the joint to expand rapidly and crack or break. If you use a flame, make sure the joint is clean and dry. Heat the outer part of the joint slowly, in the yellow portion of a low flame, until it expands and breaks away from the inner section. Heat the joint very slowly and carefully or it may break.

Glassware that has been used for reactions involving strong bases such as sodium hydroxide or sodium alkoxides must be cleaned thoroughly immediately after use. If these caustic materials are allowed to remain in contact with the glass, they will etch the glass permanently. The etching makes later cleaning more difficult because dirt particles may become trapped within the microscopic surface irregularities of the etched glass. Furthermore, the glass is weakened, so the lifetime of the glassware is shortened. If caustic materials are allowed to come into contact with ground-glass joints without being removed promptly, the joints will become fused, or “frozen.” It is extremely difficult to separate fused joints without breaking them.

Care must be taken when assembling the glass components into the desired apparatus. Always remember that Newtonian physics applies to chemical apparatus, and unsecured pieces of glassware are certain to respond to gravity. You should always clamp the glassware securely to a ring stand. Throughout this textbook, the illustrations of the various glassware arrangements include the clamps that attach the apparatus to a ring stand. You should assemble your apparatus using the clamps as shown in the illustrations.

The plastic screw caps used to join two pieces of glassware together can also be used to cap conical vials (see Figure 3.3) or other openings. A Teflon insert, or liner, fits inside the cap to cover the hole when the cap is used to seal a vial. Only one side of the liner is coated with Teflon. This side should
always face toward the inside of the vial. (Note that the O-ring is not used when the cap is used to seal a vial.) To seal a vial, it is necessary to tighten the cap firmly but not too tightly. It is possible to crack the vial if you apply too much force. Some Teflon liners have a soft backing materials (silicone rubber) that allows the liner to compress slightly when the cap is screwed down. It is easier to cap a vial securely with these liners without breaking the vial than with liners that have a harder backing materials.

*Alternative types of distillation equipment are shown.

**Figure 3.4**

*Components of a microscale organic kit.*
3.8 Attaching Rubber Tubing to Equipment

When you attach rubber tubing to the glass apparatus or when you insert glass tubing into rubber stoppers, first lubricate the rubber tubing or the rubber stopper with either water or glycerin. Without such lubrication, it can be difficult to attach rubber tubing to the side arms of items of glassware such as condensers and filter flasks. Furthermore, glass tubing may break when it is inserted into rubber stoppers. Water is a good lubricant for most purposes. Do not use water as a lubricant when it might contaminate the reaction. Glycerin is a better lubricant than water and should be used when there is considerable friction between the glass and rubber. If glycerin is the lubricant, be careful not to use too much.

3.9 Description of Equipment

The components of the organic kit recommended for use in this textbook are given in Figures 3.4–3.7. Notice that most of the joints in these pieces of glassware are 14/10, and all the outer joints are threaded. The organic kits used in your laboratory may have different joint sizes, or some of the outer joints may not be threaded. In particular, some older organic kits contain a number of pieces of glassware with 7/10 joints. These kits will work as well with the experiments in this book as the glassware recommended in the figures. In addition, there are microscale kits containing glassware that is connected without the use of ground-glass joints. The experiments in this book can also be performed with these glassware kits. Modifications with organic kits not containing the recommended glassware are discussed in the Technique chapters and in some of the experiments.

Figures 3.4–3.7 include glassware and equipment that are commonly used in the organic laboratory. Your glassware and equipment may vary slightly from the pieces shown on this spread and on the following pages.

**Figure 3.5**

Optional pieces of microscale glassware. Note: The optional pieces of equipment shown in this figure are not part of the standard microscale kit. They must be purchased separately.
Figure 3.6
Equipment commonly used in the organic laboratory.
Figure 3.7
Equipment commonly used in the organic laboratory.
How to Find Data for Compounds: Handbooks and Catalogs

The best way to find information quickly on organic compounds is to consult a handbook. We will discuss the use of the CRC Handbook of Chemistry and Physics, Lange's Handbook of Chemistry, The Merck Index, and the Aldrich Handbook of Fine Chemicals. Complete citations to these handbooks are provided in Technique 29. Depending on the type of handbook consulted, the following information may be found:

- Name and common synonyms
- Formula
- Molecular weight
- Boiling point for a liquid or melting point for a solid
- Beilstein reference
- Solubility data
- Density
- Refractive index
- Flash point
- Chemical Abstracts Service (CAS) Registry Number
- Toxicity data
- Uses and synthesis

4.1 CRC Handbook of Chemistry and Physics

This is the handbook that is most often consulted for data on organic compounds. Although a new edition of the handbook is published each year, the changes that are made are often minor. An older copy of the handbook will often suffice for most purposes. In addition to the extensive tables of properties of organic compounds, the CRC Handbook includes sections on nomenclature and ring structures, an index of synonyms, and an index of molecular formulas.

The nomenclature used in this book most closely follows the Chemical Abstracts system of naming organic compounds. This system differs, but only slightly, from standard IUPAC nomenclature. Table 4.1 lists some examples of how some commonly encountered compounds are named in this handbook. The first thing you will notice is that this handbook is not like a dictionary. Instead, you must first identify the parent name of the compound of interest. The parent names are found in alphabetical order. Once the parent name is identified and found, then you look for the particular substituent or substituents that may be attached to this parent.

For most compounds, it is easy to find what you are looking for as long as you know the parent name. Alcohols are, as expected, named by IUPAC nomenclature. Notice in Table 4.1 that the branched-chain alcohol, isopentyl alcohol, is listed as 1-butanol, 3-methyl.

Esters, amides, and acid halides are usually named as derivatives of the parent carboxylic acid. Thus, in Table 4.1, you find ethyl propanoate listed...
under the parent carboxylic acid, propanoic acid. If you have trouble finding a particular ester under the parent carboxylic acid, try looking under the alcohol part of the name. For example, isopentyl acetate is not listed under acetic acid, as expected, but instead is found under the alcohol part of the name (see Table 4.1). Fortunately, this handbook has a Synonym Index that nicely locates isopentyl acetate for you in the main part of the handbook.

Once you locate the compound by its name, you will find the following useful information:

<table>
<thead>
<tr>
<th>Name of Organic Compound</th>
<th>Location in CRC Handbook</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-Chloropentane</td>
<td>Pentane, 1-chloro-</td>
</tr>
<tr>
<td>1,4-Dichlorobenzene</td>
<td>Benzene, 1,4-dichloro-</td>
</tr>
<tr>
<td>4-Chlorotoluene</td>
<td>Benzene, 1-chloro-4-methyl-</td>
</tr>
<tr>
<td>Ethanoic acid</td>
<td>Acetic acid</td>
</tr>
<tr>
<td>tert-Butyl acetate (ethanoate)</td>
<td>Acetic acid, 1,1-dimethylethyl ester</td>
</tr>
<tr>
<td>Ethyl propanoate</td>
<td>Propanoic acid, ethyl ester</td>
</tr>
<tr>
<td>Isopentyl alcohol</td>
<td>1-Butanol, 3-methyl-</td>
</tr>
<tr>
<td>Isopentyl acetate (banana oil)</td>
<td>1-Butanol, 3-methyl-, acetate</td>
</tr>
<tr>
<td>Salicylic acid</td>
<td>Benzoic acid, 2-hydroxy-</td>
</tr>
<tr>
<td>Acetylsalicylic acid (aspirin)</td>
<td>Benzoic acid, 2-acetyloxy-</td>
</tr>
</tbody>
</table>

under the parent carboxylic acid, propanoic acid. If you have trouble finding a particular ester under the parent carboxylic acid, try looking under the alcohol part of the name. For example, isopentyl acetate is not listed under acetic acid, as expected, but instead is found under the alcohol part of the name (see Table 4.1). Fortunately, this handbook has a Synonym Index that nicely locates isopentyl acetate for you in the main part of the handbook.

Once you locate the compound by its name, you will find the following useful information:

<table>
<thead>
<tr>
<th>CRC number</th>
<th>This is an identification number for the compound. You can use this number to find the molecular structure located elsewhere in the handbook. This is especially useful when the compound has a complicated structure.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name and synonym</td>
<td>The Chemical Abstracts name and possible synonyms.</td>
</tr>
<tr>
<td>Mol. form.</td>
<td>Molecular formula for the compound.</td>
</tr>
<tr>
<td>Mol. wt.</td>
<td>Molecular weight.</td>
</tr>
<tr>
<td>CAS RN</td>
<td>Chemical Abstracts Service Registry Number. This number is useful for locating additional information on the compound in the primary chemical literature (see Technique 29, Section 29.11).</td>
</tr>
<tr>
<td>mp/°C</td>
<td>Melting point of the compound in degrees Celsius.</td>
</tr>
<tr>
<td>bp/°C</td>
<td>Boiling point of the compound in degrees Celsius. A number without a superscript indicates that the recorded boiling point was obtained at 760 mm Hg pressure (atmospheric pressure). A number with a superscript indicates that the boiling point was obtained at reduced pressure. For example, an entry of 234; 12216 would indicate that the compound boils at 234°C at 760 mm Hg and 122°C at 16 mm Hg pressure.</td>
</tr>
<tr>
<td>Den/g cm^{-3}</td>
<td>Density of a liquid. A superscript indicates the temperature in degrees Celsius at which the density was obtained.</td>
</tr>
</tbody>
</table>
Refractive index determined at a wavelength of 589 nm, the yellow line in a sodium lamp (D line). A superscript indicates the temperature at which the refractive index was obtained (see Technique 24).

Solubility

<table>
<thead>
<tr>
<th>Solubility classification</th>
<th>Solvent abbreviations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 = insoluble</td>
<td>ace = acetone</td>
</tr>
<tr>
<td>2 = slightly soluble</td>
<td>bz = benzene</td>
</tr>
<tr>
<td>3 = soluble</td>
<td>chl = chloroform</td>
</tr>
<tr>
<td>4 = very soluble</td>
<td>EtOH = ethanol</td>
</tr>
<tr>
<td>5 = miscible</td>
<td>eth = ether</td>
</tr>
<tr>
<td>6 = decomposes</td>
<td>hx = hexane</td>
</tr>
</tbody>
</table>

Beil. ref. Beilstein reference. An entry of 4-02-00-00157 would indicate that the compound is found in the fourth supplement in Volume 2, with no subvolume, on page 157 (see Technique 29, Section 29.10 for details on the use of Beilstein).

Merck No. Merck Index number in the 11th edition of the handbook. These numbers change each time a new edition of The Merck Index is issued.

Examples of sample handbook entries for isopentyl alcohol (1-butanol, 3-methyl) and isopentyl acetate (1-butanol, 3-methyl, acetate) are shown in Table 4.2.

4.2 Lange’s Handbook of Chemistry

This handbook tends not to be as available as the CRC Handbook, but it has some interesting differences and advantages. Lange’s Handbook has synonyms listed at the bottom of each page, along with structures of more complicated molecules. The most noticeable difference is in how compounds are named. For many compounds, the system lists names as they would appear in a dictionary. Table 4.3 lists examples of how some commonly encountered compounds are named in this handbook. Most often, you do not need to identify the parent name. Unfortunately, Lange’s Handbook frequently uses common names that are becoming obsolete. For example, propionate is used rather than propanoate. Nevertheless, this handbook often names compounds as a practicing organic chemist would tend to name them. Notice how easy it is to find the entries for isopentyl acetate and acetylsalicylic acid (aspirin) in this handbook.

Table 4.2 Properties of isopentyl alcohol and isopentyl acetate as listed in the CRC Handbook

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Synonym</td>
<td>Mol. Wt.</td>
<td>mp/°C</td>
<td>bp/°C</td>
<td>den/g cm⁻³</td>
<td>nD</td>
</tr>
<tr>
<td>3627</td>
<td>1-Butanol, 3-methyl</td>
<td>C₅H₁₂O₂</td>
<td>123-51-3</td>
<td>5081</td>
<td>4-01-00-01677</td>
<td>ace 4; eth 4; EtOH 4</td>
</tr>
<tr>
<td></td>
<td>Isopentyl alcohol</td>
<td>88.15</td>
<td>-117.2</td>
<td>131.1</td>
<td>0.8104²⁰</td>
<td>1.4053²⁰</td>
</tr>
<tr>
<td>3631</td>
<td>1-Butanol, 3-methyl,</td>
<td>C₇H₁₄O₂</td>
<td>123-92-2</td>
<td>4993</td>
<td>4-02-00-00157</td>
<td>H₂O 2; EtOH 5; eth 5; ace 3</td>
</tr>
<tr>
<td></td>
<td>acetate</td>
<td>130.19</td>
<td>-78.5</td>
<td>142.5</td>
<td>0.876¹⁵</td>
<td>1.4000²⁰</td>
</tr>
<tr>
<td></td>
<td>Isopentyl acetate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Once you locate the compound by its name, you will find the following useful information:

- **Lange’s number**: This is an identification number for the compound.
- **Name**: See examples in Table 4.3.
- **Formula**: Structures are drawn out. If they are complicated, then the structures are shown at the bottom of the page.
- **Formula weight**: Molecular weight of the compound.
- **Beilstein reference**: An entry of 2, 132 would indicate that the compound is found in Volume 2 of the main work on page 132. An entry of 3, 188 would indicate that the compound is found in Volume 3 of the second supplement on page 188 (see Technique 29, Section 29.10 for details on the use of *Beilstein*).
- **Density**: Density is usually expressed in units of g/mL or g/cm³. A superscript indicates the temperature at which the density was measured. If the density is also subscripted, usually 4/H₁₁₀, it indicates that the density was measured at a certain temperature relative to water at its maximum density, 4/C. Most of the time you can simply ignore the subscripts and superscripts.
- **Refractive index**: A superscript indicates the temperature at which the refractive index was determined (see Technique 24).
- **Melting point**: Melting point of the compound in degrees Celsius. When a “d” or “dec” appears with the melting point, it indicates that the compound decomposes at the melting point. When decomposition occurs, you will often observe a change in color of the solid.
- **Boiling point**: Boiling point of the compound in degrees Celsius. A number without a superscript indicates that the recorded boiling point was obtained at 760 mm Hg pressure (atmospheric pressure). A number with a
superscript indicates that the boiling point was obtained at reduced pressure. For example, an entry of \(102^{11}\text{mm}\) would indicate that the compound boils at 102°C at 11 mm Hg pressure.

Flash point

This number is the temperature in degrees Celsius at which the compound will ignite when heated in air and a spark is introduced into the vapor. There are a number of different methods that are used to measure this value, so this number varies considerably. It gives a crude indication of flammability. You may need this information when heating a substance with a hot plate. Hot plates can be a serious source of trouble because of the sparking action that can occur with switches and thermostats used in hot plates.

Solubility in 100 parts solvent

Parts by weight of a compound that can be dissolved in 100 parts by weight of solvent at room temperature. In some cases, the values given are expressed as the weight in grams that can be dissolved in 100 mL of solvent. This handbook is not consistent in describing solubility. Sometimes gram amounts are provided, but in other cases the description will be more vague, using terms such as soluble, insoluble, or slightly soluble.

<table>
<thead>
<tr>
<th>Solvent abbreviations</th>
<th>Solubility characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>acet = acetone</td>
<td>i = insoluble</td>
</tr>
<tr>
<td>bz = benzene</td>
<td>s = soluble</td>
</tr>
<tr>
<td>chl = chloroform</td>
<td>sls = slightly soluble</td>
</tr>
<tr>
<td>aq = water</td>
<td>vs = very soluble</td>
</tr>
<tr>
<td>alc = ethanol</td>
<td>misc = miscible</td>
</tr>
<tr>
<td>eth = ether</td>
<td></td>
</tr>
<tr>
<td>HOAc = acetic acid</td>
<td></td>
</tr>
</tbody>
</table>

Examples of sample handbook entries for isopentyl alcohol (3-methyl-1-butanol) and isopentyl acetate are shown in Table 4.4.

4.3 The Merck Index

*The Merck Index* is a useful book because it has additional information not found in the other two handbooks. This handbook, however, tends to emphasize medicinally related compounds, such as drugs and biological compounds, although it also lists many other common organic compounds. It is not revised each year; new editions are published in five- or six-year cycles. It does not contain all of the compounds listed in *Lange’s Handbook* or the

<table>
<thead>
<tr>
<th>No.</th>
<th>Name</th>
<th>Formula</th>
<th>Formula Weight</th>
<th>Beilstein Reference</th>
<th>Density</th>
<th>Refractive Index</th>
<th>Melting Point</th>
<th>Boiling Point</th>
<th>Flash Point</th>
<th>Solubility in 100 Parts Solvent</th>
</tr>
</thead>
<tbody>
<tr>
<td>m155</td>
<td>3-methyl-1-butanol</td>
<td>(CH₂)₂CHCH₂CH₂OH</td>
<td>88.15</td>
<td>1, 392</td>
<td>0.8129₄</td>
<td>1.4085₁₅</td>
<td>−117.2</td>
<td>132.0</td>
<td>45</td>
<td>2 aq; misc alc, bz, chl, eth, HOAc</td>
</tr>
<tr>
<td>i80</td>
<td>Isopentyl acetate</td>
<td>CH₃COOCH₂CH₂CH(CH₃)₂</td>
<td>130.19</td>
<td>2, 132</td>
<td>0.876₇₄</td>
<td>1.4007₂₀</td>
<td>−78.5</td>
<td>142.0</td>
<td>80</td>
<td>0.25 aq; misc alc, eth</td>
</tr>
</tbody>
</table>
CRC Handbook. However, for the compounds listed, it provides a wealth of useful information. The handbook will provide you with some or all of the following data for each entry.

- Merck number, which changes each time a new edition is issued
- Name, including synonyms and stereochemical designation
- Molecular formula and structure
- Molecular weight
- Percentages of each of the elements in the compound
- Uses
- Source and synthesis, including references to the primary literature
- Optical rotation for chiral molecules
- Density, boiling point, and melting point
- Solubility characteristics, including crystalline form
- Pharmacology information
- Toxicity data

One of the problems with looking up a compound in this handbook is trying to decide the name under which the compound will be listed. For example, isopentyl alcohol can also be named as 3-methyl-1-butanol or isoamyl alcohol. In the 12th edition of the handbook, it is listed under the name isopentyl alcohol (#5212) on page 886. Finding isopentyl acetate is even a more challenging task. It is located in the handbook under the name isoamyl acetate (#5125) on page 876. Often, it is easier to look up the name in the name index or to find it in the formula index.

The handbook has some useful appendices that include the CAS registry numbers, a biological activity index, a formula index, and a name index that also includes synonyms. When looking up a compound in one of the indexes, you need to remember that the numbers provided are compound numbers, rather than page numbers. There is also a useful section on organic name reactions that includes references to the primary literature.

The *Aldrich Handbook* is actually a catalog of chemicals sold by the Aldrich Chemical Company. The company includes in its catalog a large body of useful data on each compound that it sells. Because the catalog is reissued each year at no cost to the user, you should be able to find an old copy when the new one is issued. As you are mainly interested in the data on a particular compound and not the price, an old volume is perfectly fine. Isopentyl alcohol is listed as 3-methyl-1-butanol, and isopentyl acetate is listed as isoamyl acetate in the *Aldrich Handbook*. The following are some of the properties and information listed for individual compounds.

- Aldrich catalog number
- Name: Aldrich uses a mixture of common and IUPAC names. It takes a bit of time to master the names. Fortunately, the catalog does a good job of cross-referencing compounds and has a very good molecular formula index.
- CAS Registry Number
- Structure
- Synonym
- Formula weight
Boiling point/melting point
Index of refraction
Density
*Beilstein* reference
*Merck* reference
Infrared spectrum reference to the Aldrich Library of FT-IR spectra
NMR spectrum reference to the Aldrich Library of $^{13}$C and $^1$H FT-NMR spectra
Literature references to the primary literature on the uses of the compound
Toxicity
Safety data and precautions
Flash point
Prices of chemicals

### 4.5 Strategy for Finding Information: Summary

Most students and professors find *The Merck Index* and *Lange’s Handbook* easier and more “intuitive” to use than the CRC Handbook. You can go directly to a compound without rearranging the name according to the parent or base name followed by its substituents. Another great source of information is the *Aldrich Handbook*, which contains those compounds that are easily available from a commercial source. Many compounds are found in the *Aldrich Handbook* that you may never find in any of the other handbooks. The Sigma–Aldrich Web site (http://www.sigmaaldrich.com/) allows you to search by name, synonym, and catalog number.

### Problems

1. Using *The Merck Index*, find and draw structures for the following compounds:
   a. atropine
   b. quinine
   c. saccharin
   d. benzo[a]pyrene
   e. itaconic acid
   f. adrenosterone
   g. chrysanthemic acid (chrysanthemumic acid)
   h. cholesterol
   i. Vitamin C (ascorbic acid)

2. Find the melting points for the following compounds in the CRC Handbook, Lange’s Handbook, or the Aldrich Handbook:
   a. biphenyl
   b. 4-bromobenzoic acid
   c. 3-nitrophenol

3. Find the boiling point for each compound in the references listed in problem 2:
   a. octanoic acid at reduced pressure
   b. 4-chloroacetoephone at atmosphere and reduced pressure
   c. 2-methyl-2-heptanol

4. Find the index of refraction $n_D$ and density for the liquids listed in problem 3.

5. Using the *Aldrich Handbook*, report the specific rotations for the enantiomers of camphor.

6. Read the section on carbon tetrachloride in *The Merck Index* and list some of the health hazards for this compound.
Measurement of Volume and Weight

Special care must be taken when working with small amounts of liquid or solids. In the typical microscale experiment, a student will use from 10 to 1000 mg of a liquid or solid. Specially designed microscale equipment will be used for these small-scale reactions. You may not be used to working with such small quantities, but after a while you will adjust to “thinking small.”

**Liquids** to be used for an experiment will usually be found in small containers in a hood. For experiments in this book, an automatic pipet, dispensing pump, or calibrated pipet will be used for measuring the volume of a liquid. It is critical that *limiting reactants* be weighed for accuracy purposes. *Do not calculate the weight using densities!* Measurement of a small volume of a liquid is subject to a large experimental error when converted to a weight using the density of a liquid. To determine the weight of a liquid when dealing with limiting reactants, preweigh the container before adding the liquid to the container and then reweigh the container after adding the liquid. This gives an *exact weight* and avoids the experimental error involved in using densities to calculate weights when working with smaller amounts of a liquid. For *nonlimiting* liquid reactants, you may calculate the weight of the liquid from the volume you have delivered using the density of the liquid and the following equation:

$$\text{Weight (g)} = \text{density (g/mL)} \times \text{volume (mL)}$$

**Solids** may be found near the balance. When an accurate measurement is required, solids must be weighed on a balance that reads to the nearest milligram (0.001 g) or tenth of a milligram (0.0001 g). To weigh a solid, place your conical vial or round-bottom flask in a small beaker and take these with you to the balance. Place a piece of paper that has been folded once on the balance pan. The folded paper will enable you to pour the solid into the conical vial or flask without spilling. Use the larger of your two spatulas (p. 49) to aid the transfer of the solid to the paper. Never weigh directly into a conical vial or flask and never pour, dump, or shake a material from a bottle. While still at the balance, carefully transfer the solid from the paper to your vial or flask. The vial or flask should be in a beaker while transferring the solid. The beaker traps any material that fails to make it into the container. It also supports the vial or flask so that it does not fall over. It is not necessary to obtain the exact amount specified in the experimental procedure, and trying to be exact requires too much time at the balance. For example, if you obtained 0.140 g of a solid, rather than the 0.136 g specified in a procedure, you could use it, but the actual amount weighed should be recorded in your notebook. Use the amount you weighed to calculate the theoretical yield, if this solid is the limiting agent.

Careless dispensing of liquids and solids is a hazard in any laboratory. When reagents are spilled, you may be subjected to an unnecessary health or fire hazard. In addition, you may waste expensive chemicals, destroy balance pans and clothing, and damage the environment. Always clean up any spills immediately.
When available, an automatic pipet increases the speed of transfer of liquids from reagent bottles. These pipets are expensive and must be shared by the entire laboratory. A number of types of units are available commercially. We describe the use of the continuously adjustable automatic pipet. This type of pipet can be adjusted for any volume within its defined range using a three- or four-digit readout. Several types of adjustable automatic pipets are shown in Figure 5.1. The typical laboratory may have several units available: one 10–100 µL (0.01–0.10 mL) pipet for smaller volumes, and two 100–1000 µL (0.10–1.00 mL) pipets for larger volumes. Disposable tips are available for each of these units and are color coded: yellow and blue for the small and large units, respectively. The automatic pipet is accurate with aqueous solutions, but it is not as accurate with organic liquids.

In most cases, the instructor will adjust the pipet so that it will deliver the desired volume. It will be placed in a convenient location near the reagent bottle, usually in a hood, and students will reuse the tip. Your instructor will give directions for the correct use of the automatic pipet. Students must practice using the automatic pipet by following the instructions given on pages 7–8. Remember that the automatic pipet is expensive and must be handled carefully. To protect the unit, you must always use a tip on the end of the pipet. Liquid must be drawn only into this plastic tip and never up into the unit itself. If this happens, you should notify your laboratory instructor immediately. Keep the pipet upright and immerse the tip just below the surface of the liquid. Automatic pipets should never be used with corrosive liquids, such as sulfuric acid or hydrochloric acid.

5.2 Dispensing Pumps

Dispensing pumps may be used in place of automatic pipets when larger amounts (more than 0.1 mL) of liquids are being dispensed in the laboratory.
The pumps are simple to operate, chemically inert, and accurate. Because the plunger assembly is made of Teflon, the dispensing pump may be used with most corrosive liquids and organic solvents. Dispensing pumps come in a variety of sizes, but the 1-, 2-, and 5-mL sizes are most useful in the microscale organic laboratory. The pump is attached to a bottle containing the liquid being dispensed. The liquid is drawn up from this reservoir into the pump assembly through a piece of inert plastic tubing.

Dispensing pumps are somewhat more difficult to adjust to the proper volume than automatic pipets. Normally, the instructor or assistant will carefully adjust the unit to deliver the proper amount of liquid. As shown in Figure 5.2, the plunger is pulled up as far as it will travel to draw in the liquid from the glass reservoir. To expel the liquid from the spout into a container, slowly guide the plunger down. With low-viscosity liquids, the weight of the plunger will expel the liquid. With more viscous liquids, however, you may need to push the plunger gently to deliver the liquid into a container. Remove the last drop of liquid on the end of the spout by touching the tip on the interior wall of the container. When the liquid being transferred is a limiting reagent or when you need to know the weight precisely, you should weigh the liquid to determine the amount accurately.

As you pull up the plunger, look to see if the liquid is being drawn up into the pump unit. Some volatile liquids may not be drawn up in the expected manner, and you will observe an air bubble. Air bubbles are commonly observed when the pump has not been used for a while. The air bubble can be removed from the pump by dispensing and discarding several volumes of liquid to “reprime” the dispensing pump. Also check to see if the spout is filled completely with liquid. An accurate volume will not be dispensed unless the spout is filled with liquid before you lift up the plunger.

5.3 Graduated Pipets

A suitable alternative to an automatic pipet or a dispensing pump is the graduated serological pipet. These glass pipets are available commercially in a number of sizes. “Disposable” pipets may be used many times and discarded only when the graduations become too faint to be seen. A good assortment of these pipets consists of the following:

- 0.50-mL pipets calibrated in 0.01-mL divisions (5/10 in 1/100 mL)
- 1.00-mL pipets calibrated in 0.01-mL divisions (1 in 1/100 mL)
- 2.00-mL pipets calibrated in 0.01-mL divisions (2 in 1/100 mL)

Liquids may be measured and transferred using a graduated pipet and a pipet pump. The style of pipet pump shown in Figure 5.3A is available in four sizes. The 2-mL size (blue) works well with the range of pipets previously indicated. To fill the pipet, one simply rotates the knurled wheel forward so that the piston moves upward. The liquid is discharged by slowly turning the wheel backward until the proper amount of liquid has been expelled. The top of the pipet must be inserted securely into the pump and held there with one hand to obtain an adequate seal. The other hand is used to load and release the liquid.

The pipet pump shown in Figure 5.3B may also be used with graduated pipets. The knob is turned counterclockwise to draw in the liquid, and then the liquid is released by turning the knob clockwise. With this style of pipet, the top of the pipet is held securely by a rubber O-ring, and it is easily handled with one hand. You should be certain that the pipet is held securely by
the O-ring before using it. Disposable pipets may not fit tightly in the O-ring, because they often have smaller diameters than nondisposable pipets.

A syringe may be used as a pipet pump, as shown in Figure 5.3C. In the design shown here, a 1- or 2-mL syringe is attached to the graduated pipet using a short piece of plastic tubing. The liquid is drawn up into the pipet when the plunger is pulled up, and it is expelled when the plunger is pushed down.

Excellent results may be obtained with graduated pipets if you transfer by difference between marked calibrations and avoid transferring the entire contents of the pipet. When expelling the liquid, be sure to touch the tip of the pipet to the inside of the container before withdrawing the pipet. Graduated pipets are commonly used when dispensing corrosive liquids, such as sulfuric acid or hydrochloric acid. The pipet will be supplied with a bulb or pipet pump.

Pipets may be obtained in a number of styles, but only three types will be described here (Figure 5.4). One type of graduated pipet is calibrated “to deliver” (TD) its total capacity when the last drop is blown out. This style of pipet, shown in Figure 5.4A is probably the most common type of graduated pipet in use in the laboratory; it is designated by two rings at the top.
Of course, one does not need to transfer the entire volume to a container. To deliver a more accurate volume, you should transfer an amount less than the total capacity of the pipet using the graduations on the pipet as a guide.

Another type of graduated pipet is shown in Figure 5.4B. This pipet is calibrated to deliver its total capacity when the meniscus is located on the last graduation mark near the bottom of the pipet. For example, the pipet shown in the Figure 5.4B delivers 10.0 mL of liquid when it has been drained to the point where the meniscus is located on the 10.0-mL mark. With this type of pipet, you must not drain the entire pipet or blow it out. In contrast, notice that the pipet shown in Figure 5.4A has its last graduation at 0.90 mL. The last 0.10-mL volume is blown out to give the 1.00-mL volume.

A nongraduated volumetric pipet is shown in Figure 5.4C. It is easily identified by the large bulb in the center of the pipet. This pipet is calibrated so that it will retain its last drop after the tip is touched on the side of the container. It must not be blown out. These pipets often have a single colored band at the top that identifies it as a “touch-off” pipet. The color of the band

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**Figure 5.4**

*Pipets.*
is keyed to its total volume. This type of pipet is commonly used in analytical chemistry.

5.4 Pasteur Pipets

The Pasteur pipet is shown in Figure 5.5A with a 2-mL rubber bulb attached. There are two sizes of pipets: a long one (9 inch) and a short one (5½ inch). It is important that the pipet bulb fit securely. You should not use a medicine dropper bulb, because of its small capacity. A Pasteur pipet is an indispensable piece of equipment for the routine transfer of liquids. It is also used for separations (Technique 12). Pasteur pipets may be packed with cotton for use in gravity filtration (Technique 8) or packed with an adsorbent for small-scale column chromatography (Technique 19). Although they are considered disposable, you should be able to clean them for reuse as long as the tip remains unchipped.

A Pasteur pipet may be supplied by your instructor for dropwise addition of a particular reagent to a reaction mixture. For example, concentrated sulfuric acid is often dispensed in this way. When sulfuric acid is transferred, take care to avoid getting the acid into the rubber or latex dropper bulb. It is best to avoid the rubber dropper bulb entirely by using one-piece transfer pipets made entirely of polyethylene. These plastic pipets are available in 1- or 2-mL sizes. They come from the manufacturers with approximate calibration marks stamped on them (Fig. 5.5B).

Pipets may be calibrated for use in operations where the volume does not need to be known precisely. Examples include measurement of solvents needed for extraction and for washing a solid obtained following crystallization. It is suggested that you calibrate several 5½-inch pipets following
the procedure given on page 11. A calibrated Pasteur pipet is shown in Figure 5.5C. Your instructor may provide you with a calibrated Pasteur pipet and bulb for transferring liquids where an accurate volume is not required. The pipet may be used to transfer a volume of 1.5 mL or less. You may find that the instructor has taped a test tube to the side of the storage bottle. The pipet is stored in the test tube with that particular reagent.

In general, Pasteur pipets should not be used to measure volumes of reagents needed for organic reactions, because they are not accurate enough for this purpose. In some cases, however, your instructor may have available a calibrated pipet for transferring nonlimiting reagents that may damage an automatic pipet. For example, a calibrated Pasteur pipet may be used with concentrated acids.

NOTE: You should not assume that a certain number of drops equals a 1-mL volume. The common rule that 20 drops equal 1 mL does not hold true for a Pasteur pipet!

A Pasteur pipet may be packed with cotton to create a filter-tip pipet as shown in Figure 5.5D. This pipet is prepared by the instructions given in Technique 8, Section 8.6, page 625. Pipets of this type are useful in transferring volatile solvents during extractions and in filtering small amounts of solid impurities from solutions.

5.5 Syringes

Syringes may be used to add a pure liquid or a solution to a reaction mixture. They are especially useful when anhydrous conditions must be maintained. The needle is inserted through a septum, and the liquid is added to the reaction mixture. Although syringes come in a number of sizes, we will use a 1-mL unit in this textbook. Caution should be used with disposable syringes because they often use solvent-soluble rubber gaskets on the plungers. A syringe should be cleaned carefully after each use by drawing acetone or another volatile solvent into it and expelling the solvent with the plunger. Repeat this procedure several times to clean the syringe thoroughly. Draw air through the barrel with an aspirator to dry the syringe.

Syringes are usually supplied with volume graduations inscribed on the barrel. Large-volume syringes are not accurate enough to be used for measuring liquids in microscale experiments. A small microliter syringe, however, such as that used in gas chromatography, delivers a precise volume.

5.6 Graduated Cylinders

Graduated cylinders are used to measure relatively large volumes of liquids where accuracy is not required. For example, you could use a 10-mL graduated cylinder to obtain about 2 mL of a solvent for a crystallization procedure. You should use an automatic pipet, dispensing pump, or a graduated pipet for accurate transfer of liquids in microscale work. Use a clean and dry Pasteur pipet to transfer the liquid from the storage container into the graduated cylinder. Do not attempt to pour the liquid directly into the cylinder from the storage bottle or you may spill the fluid. Some instructors may want you to pour some of the liquid into a beaker first and then use a Pasteur pipet to transfer the liquid to a graduated cylinder. Remember that you should not take more than you need. Excess material should never be returned to the storage bottle. Unless you can convince someone else to take it, it must be poured into the appropriate waste container. You should be frugal in estimating amounts needed.
Conical vials, beakers, and Erlenmeyer flasks all have graduations inscribed on them. Beakers and flasks can be used to give only a crude approximation of the volume. They are much less precise than graduated cylinders for measuring volume. In some cases, a conical vial may be used to estimate volumes. For example, the graduations are sufficiently accurate for measuring a solvent needed to wash a solid obtained on a Hirsch funnel after a crystallization. You should use an automatic pipet, dispensing pump, or graduated transfer pipet for accurate measurement of liquids.

Solids and some liquids will need to be weighed on a balance that reads to at least the nearest milligram (0.001 g). A top-loading balance (see Fig. 5.6) works well if the balance pan is covered with a plastic draft shield. The shield has a flap that opens to allow access to the balance pan. An analytical balance (see Fig. 5.7) may also be used. This type of balance will weigh to the nearest tenth of a milligram (0.0001 g) when provided with a glass draft shield.

Modern electronic balances have a tare device that automatically subtracts the weight of a container or a piece of paper from the combined weight to give the weight of the sample. With solids, it is easy to place a piece of paper on the balance pan, press the tare device so that the paper appears to have zero weight, and then add your solid until the balance gives the weight you desire. You can then transfer the weighed solid to a container. You should always use a spatula to transfer a solid and never pour material from a bottle. In addition, solids must be weighed on paper and not directly on the balance pan. Remember to clean any spills.
With liquids, you should weigh the conical vial to determine the tare weight, transfer the liquid with an automatic pipet, dispensing pump, or graduated pipet into the vial, and then reweigh it. With liquids, it is usually necessary to weigh only the limiting reagent. The other liquids may be transferred using an automatic pipet, dispensing pump, or graduated pipet. Their weights can be calculated by knowing the volumes and densities of the liquids.

**Problems**

1. What measuring device would you use to measure the volume under each of the conditions described below? In some cases, there may be more than one answer to the question.
   a. 5 mL of a solvent needed for a crystallization
   b. 0.76 mL of a liquid needed for a reaction
   c. 1 mL of a solvent needed for an extraction

2. Assume that the liquid used in part (b) is a limiting reagent for a reaction. What should you do after measuring the volume?

3. Calculate the weight of a 0.25-mL sample of each of the following liquids:
   a. Diethyl ether (ether)
   b. Methylene chloride (dichloromethane)
   c. Acetone

4. A laboratory procedure calls for 0.146 g of acetic anhydride. Calculate the volume of this reagent needed in the reaction.

5. Criticize the following techniques:
   a. A 100-mL graduated cylinder is used to measure accurately a volume of 2.8 mL.
   b. A one-piece polyethylene transfer pipet (Figure 5.6B) is used to transfer precisely 0.75 mL of a liquid that is being used as the limiting reactant.
   c. A calibrated Pasteur pipet (Figure 5.6C) is used to transfer 25 mL of a solvent.
   d. The volume markings on a 100-mL beaker are used to transfer accurately 5 mL of a liquid.
   e. An automatic pipet is used to transfer 10 mL of a liquid.
   f. A graduated cylinder is used to transfer 0.126 mL of a liquid.
   g. For a small-scale reaction, the weight of a liquid limiting reactant is calculated from its density and volume.
Technique 7

Reaction Methods

The successful completion of an organic reaction requires the chemist to be familiar with a variety of laboratory methods. These methods include operating safely, assembling the apparatus, heating and stirring reaction mixtures, adding liquid reagents, maintaining anhydrous and inert conditions in the reaction, and collecting gaseous products. Several techniques that are used in bringing a reaction to a successful conclusion are discussed here.

7.1 Assembling the Apparatus

Care must be taken when assembling the glass components into the desired apparatus. You should always remember that Newtonian physics applies to chemical apparatus, and unsecured pieces of glassware are certain to respond to gravity.

Assembling an apparatus in the correct manner requires that the individual pieces of glassware be connected to each other securely and the entire apparatus be held in the correct position. This can be accomplished by using **adjustable metal clamps** or a combination of adjustable metal clamps and **plastic joint clips**.

Two types of adjustable metal clamps are shown in Figure 7.1. Although these two types of clamps can usually be interchanged, the extension clamp is more commonly used to hold round-bottom flasks in place, and the three-finger clamp is frequently used to clamp condensers. Both types of clamps must be attached to a ring stand using a clamp holder, shown in Figure 7.1C.

**A. Securing Macroscale Apparatus Assemblies**

It is possible to assemble an apparatus using only adjustable metal clamps. An apparatus used to perform a distillation is shown in Figure 7.2. It is held together securely with three metal clamps. Because of the size of the apparatus and its geometry, the various clamps would likely be attached to three different ring stands. This apparatus would be somewhat difficult to assemble because it is necessary to ensure that the individual pieces stay together while securing and adjusting the clamps required to hold the entire apparatus in place. In addition, one must be careful not to bump any part of the apparatus or the ring stands after the apparatus is assembled.

A more convenient alternative is to use a combination of metal clamps and plastic joint clips. A plastic joint clip is shown in Figure 7.3A. These clips

![Figure 7.1](image_url)
are easy to use (they just clip on), will withstand temperatures up to 140°C, and are durable. They hold together two pieces of glassware that are connected by ground-glass joints, as shown in Figure 7.3B. These clips come in different sizes to fit ground-glass joints of different sizes, and they are color coded for each size.

When used in combination with metal clamps, the plastic joint clips make it much easier to assemble most apparatus securely. There is less chance of dropping the glassware while assembling the apparatus, and once the apparatus is set up, it is more secure. Figure 7.4 shows the same distillation apparatus held in place with adjustable metal clamps and plastic joint clips.

To assemble this apparatus, first connect all of the individual pieces using the plastic clips. The entire apparatus is then connected to the ring stands using the adjustable metal clamps. Note that only two ring stands are required and the wooden blocks are not needed.

**B. Securing Microscale Apparatus Assemblies**

The glassware in most microscale kits is made with standard-taper ground joints. The most common joint size is $\frac{1}{2}$ 14/10. Some microscale glassware with ground-glass joints also has threads cast into the outside surface of the outer joints (see top of air condenser in Figure 7.5). The threaded joint allows the use of a plastic screw cap with a hole in the top to fasten two pieces of glassware together securely. The plastic cap is slipped over the inner joint of the upper piece of glassware, followed by a rubber O-ring (see Figure 7.5). The O-ring should be pushed down so that it fits snugly on top of the ground-glass joint. The inner ground-glass joint is then fitted into the outer joint of the bottom piece of glassware. The screw cap is tightened, without excessive force, to attach the entire apparatus firmly together. The O-ring provides an additional seal that makes
this joint airtight. With this connecting system, it is unnecessary to use any type of grease to seal the joint. The O-ring must be used to obtain a good seal and to lessen the chances of breaking the glassware when you tighten the plastic cap.

Microscale glassware connected in this fashion can be assembled easily. The entire apparatus is held together securely, and usually only one metal clamp is required to hold the apparatus onto a ring stand.

7.2 Heating under Reflux

Often we wish to heat a mixture for a long time and to leave it untended. A reflux apparatus (see Figure 7.6) allows such heating. It also keeps the solvent from being lost by evaporation. A condenser is attached to the reaction vial or boiling flask.

Choice of Condenser. The condenser used in a reflux apparatus can be either of two types. An air condenser is simply a long tube. The surrounding air removes heat from the vapors within the tube and condenses them to liquid. A water-jacketed condenser consists of two concentric tubes with the outer cooling tube sealed onto the inner tube. The vapors rise within the inner tube, and water circulates through the outer tube. The circulating water removes heat from the vapors and condenses them. The air condenser is suitable for use with high-boiling liquids or with small quantities of material that are being heated gently. The water-jacketed condenser must be used when the vapors are difficult to condense, usually because the
substance is volatile, or when vigorous boiling action is desired. In either case, the condenser prevents the vapors from escaping. Glassware assemblies using both air and water-jacketed condensers are shown in Figure 7.6A. The figure also shows a typical macroscale apparatus for heating large quantities of material under reflux (Fig. 7.6B).

When a water-jacketed condenser is used, the direction of the water flow should be such that the condenser will fill with cooling water. The water should enter the bottom of the condenser and leave from the top. The water should flow fast enough to withstand any changes in pressure in the water lines, but it should not flow any faster than absolutely necessary. An excessive flow rate greatly increases the chance of a flood, and high water pressure may force the hose from the condenser. Cooling water should be flowing before heating is begun! If the water is to remain flowing overnight, it is advisable to fasten the rubber tubing securely with wire to the condenser. If a flame is used as a source of heat, it is wise to use a wire gauze beneath the flask to provide an even distribution of heat from the flame. In most cases, an aluminum block, a sand bath, water bath, heating mantle, or steam bath is preferred over a flame.

**Stirring.** When heating a solution, always use a magnetic stirrer or a boiling stone (see Sections 7.3 and 7.4) to keep the solution from “bumping.”
Rate of Heating. If the heating rate has been correctly adjusted, the liquid being heated under reflux will travel only partway up the condenser tube before condensing. Below the condensation point, solvent will be seen running back into the flask; above it, the interior of the condenser will appear dry. The boundary between the two zones will be clearly demarcated, and a reflux ring or a ring of liquid will appear there. The reflux ring can be seen in Figure 7.6B. In heating under reflux, the rate of heating should be adjusted so that the reflux ring is no higher than a third to half the distance to the top of the condenser. With microscale experiments, the quantities of vapor rising in the condenser frequently are so small that a clear reflux ring cannot be seen. In those cases, the heating rate must be adjusted so that the liquid boils smoothly but not so rapidly that solvent can escape the condenser. With such small volumes, the loss of even a small amount of solvent can affect the reaction. With large-scale reactions, the reflux ring is much easier to see, and one can adjust the heating rate more easily.

Tended Reflux. It is possible to heat small amounts of a solvent under reflux in an Erlenmeyer flask. With gentle heating, the evaporated solvent will condense in the relatively cold neck of the flask and return to the solution. This technique (see Fig. 7.7) requires constant attention. The flask must be swirled frequently and removed from the heating source for a short period if the boiling becomes too vigorous. When heating is in progress, the reflux ring should not be allowed to rise into the neck of the flask.

How Do I Know How Hot to Heat It? A common problem that inexperienced students encounter when they assemble an apparatus for heating under reflux is that it is difficult to decide what temperature setting to use for heating the contents of a vial or flask to the desired temperature. This problem becomes more acute when the students attempt to reproduce the temperatures that are specified in the laboratory procedures of a textbook.

First, you should understand that the temperatures specified are only approximate suggestions. The actual temperature required to carry out a particular procedure must be determined for each student and each apparatus. When you see a temperature stipulated, consider it as nothing more than a guide. You will have to make adjustments to suit your own situation.

Second, you must always pay attention to what is going on in your reaction flask. If the temperature of your aluminum block or sand bath equals the suggested temperature, but the solution in your flask is not boiling, you clearly will have to increase the temperature of the heating device. Remember that what really matters is what is going on in the flask, not what the textbook says! The external temperature, as measured by a thermometer placed into the heating device, is not the important temperature. Far more critical is the temperature inside the flask, which may be considerably lower than the external temperature.

When a solution is heated, there is a danger that it may become superheated. When this happens, very large bubbles sometimes erupt violently from the solution; this is called bumping. Bumping must be avoided because of the risk that material may be lost from the apparatus, that a fire may start, or that the apparatus may break.

Magnetic stirrers are used to prevent bumping because they produce turbulence in the solution. The turbulence breaks up the large bubbles that
A magnetic stirring system consists of a magnet that is rotated by an electric motor. The rate at which this magnet rotates can be adjusted by a potentiometric control. A small magnet, which is coated with a nonreactive material such as Teflon or glass, is placed in the flask. The magnet within the flask rotates in response to the rotating magnetic field caused by the motor-driven magnet. The result is that the inner magnet stirs the solution as it rotates. A common type of magnetic stirrer includes the stirring system within a hot plate. This type of hot plate/stirrer permits one to heat the reaction and stir it simultaneously. In order for the magnetic stirrer to be effective, the contents of the flask being stirred should be placed as close to the center of the hot plate as possible and not offset.

For macroscale apparatus, magnetic stirring bars of various sizes and shapes are available. For microscale apparatus, a magnetic spin vane is often used. It is designed to contain a tiny bar magnet and to have a shape that conforms to the conical bottom of a reaction vial. A small Teflon-coated magnetic stirring bar works well with very small round-bottom boiling flasks. Small stirring bars of this type (often sold as “disposable” stirring bars) can be obtained cheaply. A variety of magnetic stirring bars is illustrated in Figure 7.8.

There is also a variety of simple techniques that may be used to stir a liquid mixture in a centrifuge tube or conical vial. A thorough mixing of the components of a liquid can be achieved by repeatedly drawing the liquid into a Pasteur pipet and then ejecting the liquid back into the container by pressing sharply on the dropper bulb. Liquids can also be stirred effectively by placing the flattened end of a spatula into the container and twirling it rapidly.

7.4 Boiling Stones

A boiling stone, also known as a boiling chip or Boileezer, is a small lump of porous material that produces a steady stream of fine air bubbles when it is heated in a solvent. This stream of bubbles and the turbulence that accompanies it break up the large bubbles of gases in the liquid. In this way, it reduces the tendency of the liquid to become superheated, and it promotes the smooth boiling of the liquid. The boiling stone decreases the chances for bumping.

Two common types of boiling stones are carborundum and marble chips. Carborundum boiling stones are more inert, and the pieces are usually
small, suitable for most applications. If available, carborundum boiling stones are preferred for most purposes. Marble chips may dissolve in strong acid solutions, and the pieces are larger. The advantage of marble chips is that they are cheaper.

Because boiling stones act to promote the smooth boiling of liquids, you should always make certain that a boiling stone has been placed in a liquid before heating is begun. If you wait until the liquid is hot, it may have become superheated. Adding a boiling stone to a superheated liquid will cause all the liquid to try to boil at once. The liquid, as a result, would erupt entirely out of the flask or froth violently.

As soon as boiling ceases in a liquid containing a boiling stone, the liquid is drawn into the pores of the boiling stone. When this happens, the boiling stone no longer can produce a fine stream of bubbles; it is spent. You may have to add a new boiling stone if you have allowed boiling to stop for a long period.

Wooden applicator sticks are used in some applications. They function in the same manner as boiling stones. Occasionally, glass beads are used. Their presence also causes sufficient turbulence in the liquid to prevent bumping.

Liquid reagents and solutions are added to a reaction by several means, some of which are shown in Figure 7.9. For microscale experiments, the simplest approach is simply to add the liquid to the reaction by means of a Pasteur pipet. This method is shown in Figure 7.9A. In this technique, the system is open to the atmosphere. A second microscale method, shown in Figure 7.9B, is suitable for experiments in which the reaction should be kept isolated from the atmosphere. In this approach, the liquid is kept in a hypodermic syringe. The syringe needle is inserted through a rubber septum, and the liquid is added dropwise from the syringe. The septum seals the apparatus from the atmosphere, which makes this technique useful for reactions that are conducted under an atmosphere of inert gas or where anhydrous conditions must be maintained. As an alternative, the rubber septum may be replaced by a cap and Teflon insert or liner. A disadvantage of the Teflon insert, however, is that the insert may no longer form an effective seal after being punctured by the needle.

The most common type of assembly for macroscale experiments is shown in Figure 7.9C. In this apparatus, a separatory funnel is attached to the side arm of a three-necked round-bottom flask. The separatory funnel must be equipped with a standard-taper, ground-glass joint to be used in this manner. The liquid is stored in the separatory funnel (which is called an addition funnel in this application) and is added to the reaction. The rate of addition is controlled by adjusting the stopcock. When it is being used as an addition funnel, the upper opening must be kept open to the atmosphere. If the upper hole is stoppered, a vacuum will develop in the funnel and will prevent the liquid from passing into the reaction vessel. Because the funnel is open to the atmosphere, there is a danger that atmospheric moisture can contaminate the liquid reagent as it is being added. To prevent this outcome, a drying tube (see Section 7.6) is attached to the upper opening of the addition funnel. The drying tube allows the funnel to maintain atmospheric pressure without allowing the passage of water vapor into the reaction.

Figure 7.9D shows an alternative type of addition funnel that is useful for reactions that must be maintained under an atmosphere of inert gas. This is the pressure-equalizing addition funnel. With this glassware, the upper
opening is stoppered. The side arm allows the pressure above the liquid in the funnel to be in equilibrium with the pressure in the rest of the apparatus, and it lets the inert gas flow over the top of the liquid as it is being added.

With certain reactions, atmospheric moisture must be prevented from entering the reaction vessel. A **drying tube** can be used to maintain anhydrous conditions within the apparatus. Two types of drying tubes are shown in Figure 7.10. The typical drying tube is prepared by placing a small, loose plug of glass wool or cotton into the constriction at the end of the tube nearest the ground-glass joint or hose connection. The plug is tamped gently.

### Figure 7.9
*Methods of adding liquid reagents to a reaction.*
with a glass rod or piece of wire to place it in the correct position. A drying agent, typically calcium sulfate ("Drierite") or calcium chloride (see Technique 12, Section 12.9, p. 680), is poured on top of the plug to the approximate depth shown in Figure 7.10. Another loose plug of glass wool or cotton is placed on top of the drying agent to prevent the solid material from falling out of the drying tube. The drying tube is then attached to the flask or condenser.

Air that enters the apparatus must pass through the drying tube. The drying agent absorbs any moisture from air passing through it so that air entering the reaction vessel has had the water vapor removed from it.

Figure 7.10
Drying tubes.

7.8 Capturing Noxious Gases

Many organic reactions involve the production of a noxious gaseous product. The gas may be corrosive, such as hydrogen chloride, hydrogen bromide, or sulfur dioxide, or it may be toxic, such as carbon monoxide. The safest way to avoid exposure to these gases is to conduct the reaction in a ventilated hood where the gases can be safely drawn away by the ventilation system.

In many instances, however, it is safe and efficient to conduct the experiment on the laboratory bench, away from the hood. This is particularly true when the gases are soluble in water. Some techniques for capturing noxious gases are presented in this section.

A. Drying Tube Method

Microscale experiments have the advantage that the amounts of gases produced are small. Hence, it is easy to trap them and prevent them from escaping into the laboratory. You can take advantage of the water solubility of corrosive gases such as hydrogen chloride, hydrogen bromide, and sulfur dioxide. A simple technique is to attach the drying tube (see Fig. 7.10B) to the top of the reaction vial or condenser. The drying tube is filled with moistened glass wool. The moisture in the glass wool absorbs the gas, preventing its
escape. To prepare this type of gas trap, fill the drying tube with glass wool and then add water dropwise to the glass wool until it has been moistened to the desired degree. Moistened cotton can also be used, although cotton will absorb so much water that it is easy to plug the drying tube.

When using glass wool in a drying tube, moisture from the glass wool must not be allowed to drain from the drying tube into the reaction. It is best to use a drying tube that has a constriction between the part where the glass wool is placed and the neck, where the joint is attached. The constriction acts as a partial barrier preventing the water from leaking into the neck of the drying tube. Make certain not to make the glass wool too moist.

B. External Gas Traps

Another approach to capturing gases is to prepare a trap that is separate from the reaction apparatus. The gases are carried from the reaction to the trap by means of tubing. There are several variations on this type of trap. One method that works well for microscale experiments is to place a thermometer adapter (Technique 14, Fig. 14.9A, p. 712) into the opening in the reaction apparatus. A Pasteur pipet is inserted upside down through the adapter, and a piece of fine flexible tubing is fitted over the narrow tip. It may be helpful to break the Pasteur pipet before using it for this purpose so that only the narrow tip and a short section of the barrel are used. The other end of the flexible tubing is placed through a large plug of moistened glass wool in a test tube. The water in the glass wool absorbs the water-soluble gases. This method is shown in Figure 7.12.

Figure 7.12
Microscale external gas trap. (The inset shows an expanded view of an alternative fitting, using a syringe needle and a rubber septum.)
A variation on the Pasteur pipet method uses a hypodermic syringe needle inserted upside down (from the inside) through a rubber septum, which has been fitted over the opening at the top of the reaction apparatus. Flexible tubing, fitted over the syringe needle, leads to a trap such as the one using wet glass wool described previously. This variation is also shown in Figure 7.12.

Another alternative to the apparatus shown in Figure 7.12 is to use a multipurpose adapter in place of the thermometer adapter (p. 712). The flexible tubing can be attached directly to the side arm of the multipurpose adapter, thus connecting the apparatus to the gas trap. If the multipurpose adapter is used for this purpose, the upper opening of the adapter must be closed; this is accomplished most easily by inserting a piece of glass rod or a short piece of glass tubing sealed at one end into the opening and tightening the fittings around it.

With large-scale reactions, a trap using an inverted funnel placed in a beaker of water is used. A piece of glass tubing, inserted through a thermometer adapter attached to the reaction apparatus, is connected to flexible tubing. The tubing is attached to a conical funnel. The funnel is clamped in place inverted over a beaker of water. The funnel is clamped so that its lip almost touches the water surface, but is not placed below the surface of the water. With this arrangement, water cannot be sucked back into the reaction if the pressure in the reaction vessel changes suddenly. This type of trap can also be used in microscale applications. An example of the inverted-funnel type of gas trap is shown in Figure 7.13.

![Figure 7.13](image)

*An inverted-funnel gas trap.*
C. Removal of Noxious Gases Using an Aspirator

An aspirator can be used to remove noxious gases from the reaction. The simplest approach is to clamp a disposable Pasteur pipet so that its tip is placed well into the condenser atop the reaction vessel. An inverted funnel clamped over the apparatus can also be used. The pipet or funnel is attached to an aspirator with flexible tubing. A trap should be placed between the pipet or funnel and the aspirator. As gases are liberated from the reaction, they rise into the condenser. The vacuum draws the gases away from the apparatus. Both types of systems are shown in Figure 7.14. In the special case in which the noxious gases are soluble in water, connecting a water aspirator to the pipet or funnel removes the gases from the reaction and traps them in the flowing water without the need for a separate gas trap.

7.9 Collecting Gaseous Products

In Section 7.8, means of removing unwanted gaseous products from the reaction system were examined. Some experiments produce gaseous products that you must collect and analyze. Methods to collect gaseous products are all based on the same principle. The gas is carried through tubing from the reaction to the opening of a flask or a test tube, which has been filled with water and is inverted in a container of water. The gas is allowed to bubble into the inverted collection tube (or flask). As the collection tube fills with gas, the water is displaced into the water container. If the collection tube is graduated, as in a graduated cylinder or a centrifuge tube, you can monitor the quantity of gas produced in the reaction.

If the inverted gas-collection tube is constructed from a piece of glass tubing, a rubber septum can be used to close the upper end of the container. This type of collection tube is shown in Figure 7.15. A sample of the gas can
be removed using a syringe equipped with a needle. The gas that is re-
moved can be analyzed by gas chromatography (see Technique 22).

Many of the glassware kits for microscale experiments contain a special,
all-glass, capillary gas-delivery tube. The tube is attached to the top of the
reaction apparatus by means of a ground-glass joint, and the open end of
the capillary tubing is placed into an inverted, water-filled flask or test tube,
clamped over a waterbath. An example of a microscale kit gas-delivery tube
is shown in Figure 7.16A. This type of tube is an efficient means of collect-
ing gases. A disadvantage, however, is that it is expensive and relatively
easy to break.

A simpler, less expensive approach is to use flexible tubing of a fine di-
ameter to lead the gases from the reaction vessel to the collecting container.
One method is to place a hypodermic syringe needle, point upward,
through a rubber septum. The septum is attached to the top of the reaction
apparatus, and a piece of fine flexible tubing is fitted over the end of the nee-
dle. The free end of the tubing is placed in the waterbath, underneath the
opening of the water-filled collection container. The gases bubble into the
container, where they are collected. This alternative apparatus is shown in
Figure 7.15 and also as an inset in Figure 7.16B.

Another alternative, which may also be used with larger-scale experi-
ments, is to place a piece of glass tubing or the tip of a Pasteur pipet through
a thermometer adapter. The thermometer adapter is attached to the top of the
reaction apparatus, and flexible tubing is attached to the piece of glass
tubing. The free end of the tubing is positioned in the opening of the water-
filled collection vessel, as described previously. This variation is also shown
as an inset in Figure 7.16. As an option, you may attach a second piece of
glass tubing to the free end of the flexible hose. This piece of glass tubing
sometimes makes it easier to fix the open end in the proper position in the
opening of the collection flask.

7.10 Evaporation of Solvents
In many experiments, it is necessary to remove excess solvent from a solu-
tion. An obvious approach is to allow the container to stand unstoppered in
the hood for several hours until the solvent has evaporated. This method is generally not practical, however, and a quicker, more efficient means of evaporating solvents must be used. Figures 7.17 and 7.18 show several methods of removing solvents by evaporation. Figure 7.17 depicts microscale methods; Figure 7.18 is devoted to large-scale procedures.

**NOTE:** It is good laboratory practice to evaporate solvents in the hood.

**Microscale Methods.** A simple means of evaporating a solvent is to place a conical vial in a warm waterbath or a warm sand bath. The heat from the waterbath or sand bath will warm the solvent to a temperature where it can
evaporate within a short time. The heat from the waterbath or sand bath can be adjusted to provide the best rate of evaporation, but the liquid should not be allowed to boil vigorously. The evaporation rate can be increased by allowing a stream of dry air or nitrogen to be directed into the vial (Fig. 7.17A). The moving gas stream will sweep the vapors from the vial and accelerate the evaporation. As an alternative, a vacuum can be applied above the vial to draw away solvent vapors (Fig. 7.17B and 7.17C).

A convenient waterbath suitable for microscale methods can be constructed by placing the aluminum collars, which are generally used with aluminum heating blocks into a 150-mL beaker (Fig. 7.17A). In some cases, it may be necessary to round off the sharp edges of the collars with a file in order to allow them to fit properly into the beaker. Held by the aluminum collars, the conical vial will stand securely in the beaker. This assembly can be filled with water and placed on a hot plate for use in the evaporation of small amounts of solvent.

Aluminum heating blocks placed on a hot plate can also be used for the evaporation of solvents (Fig. 7.17B). You must be careful, however, not to allow the aluminum block to become too hot, or the sample may decompose thermally.
During a crystallization procedure, you often must remove excess solvent from the solution. If a Craig tube is being used for the crystallization, the excess solvent can be removed directly from the Craig tube (see Technique 11, Section 11.4, p. 656). The Craig tube is placed in a warm waterbath or warm sand bath. Alternatively, the Craig tube can be placed into one of the small holes of an aluminum block. A microspatula is placed into the Craig tube, and it is twirled rapidly as the solvent evaporates (Fig. 7.17D). The twirling spatula acts in the same manner as a boiling stone; it prevents bumping and accelerates the evaporation.

Commercially available evaporation stations may be useful when a large number of evaporations must be performed at the same time. This type of equipment consists of several holders for vials or flasks. At each position, a piece of tubing equipped with a metal tip is used to direct a stream of air into the vessel. A waterbath is used to heat all the containers simultaneously.

**Larger-Scale Methods.** On a large scale, these evaporation methods can also be applied to standard-sized glassware. Solvents can be evaporated from solutions in Erlenmeyer flasks by adapting the techniques described previously. An Erlenmeyer flask can be placed on a source of heat, and the solvent can be removed by evaporation under a gas stream or a vacuum. Sources of heat that can be used with Erlenmeyer flasks include sand and steam baths and hot plates. A solution can also be placed in a side arm test tube or a filter flask, which is attached to a source of vacuum. A wooden stick or a piece of a melting point capillary is often placed in the solution, and the flask or test tube is swirled over the source of heat to reduce the possibility of bumping. The methods are illustrated in Figure 7.18.

![Figure 7.19](image)

*Figure 7.19*  
*A rotary evaporator.*
PROBLEMS

1. What is the best type of stirring device to use for stirring a reaction that takes place in the following type of glassware?
   a. A conical vial
   b. A 10-mL round-bottom flask
   c. A 250-mL round-bottom flask

2. Should you use a drying tube for the following reaction? Explain.

$$\text{CH}_3\text{C}\equiv\text{OH} + \text{CH}_3\text{CH} = \text{CH} - \text{CH}_2\text{OH} \rightarrow \text{CH}_3\text{C} = \text{O} - \text{CH}_2\text{CH}_2\text{CH} - \text{CH}_3 + \text{H}_2\text{O}$$

3. For which of the following reactions should you use a trap to collect noxious gases?
   a. $\text{O} \text{C} = \text{OH} + \text{SOCl}_2 \xrightarrow{\text{heat}} \text{O} \text{C} = \text{Cl} + \text{SO}_2 + \text{HCl}$
   b. $\text{O} \text{C} = \text{Cl} + \text{CH}_3\text{CH}_2\text{OH} \rightarrow \text{O} \text{C} = \text{O} - \text{CH}_2\text{CH}_3 + \text{HCl}$
   c. $\text{C}_12\text{H}_22\text{O}_11 + \text{H}_2\text{O} \rightarrow 4\text{CH}_3\text{CH}_2\text{OH} + 4\text{CO}_2$ (Sucrose)
   d. $\text{CH}_3\text{C} = \text{NH} + \text{H}_2\text{O} \xrightarrow{\text{base}} \text{CH}_3\text{C} = \text{O} + \text{NH}_3$

4. Criticize the following techniques:
   a. A reflux is conducted with a stopper in the top of the condenser.
   b. Water is passed through the reflux condenser at the rate of 1 gallon per minute.
   c. No water hoses are attached to the condenser during a reflux.
   d. A boiling stone is not added to the round-bottom flask until the mixture is boiling vigorously.
   e. To save money, you decide to save your boiling stones for another experiment.
   f. The reflux ring is located near the top of the condenser in a reflux setup.
   g. A rubber O-ring is omitted when the water condenser is attached to a conical vial.
   h. A gas trap is assembled with the funnel in Figure 7.13, completely submerged in the water in the beaker.
   i. Powdered drying agent is used rather than granular material.
   j. A reaction involving hydrogen chloride is conducted on the laboratory bench and not in a hood.
   k. An air-sensitive reaction apparatus is set up as shown in Figure 7.6.
   l. Air is used to evaporate solvent from an air-sensitive compound.
Physical Constants of Solids: 
The Melting Point

9.1 Physical Properties

The physical properties of a compound are those properties that are intrinsic to a given compound when it is pure. A compound may often be identified simply by determining a number of its physical properties. The most commonly recognized physical properties of a compound include its color, melting point, boiling point, density, refractive index, molecular weight, and optical rotation. Modern chemists would include the various types of spectra (infrared, nuclear magnetic resonance, mass, and ultraviolet-visible) among the physical properties of a compound. A compound’s spectra do not vary from one pure sample to another. Here, we look at methods of determining the melting point. Boiling point and density of compounds are covered in Technique 13. Refractive index, optical rotation, and spectra are also considered separately.

Many reference books list the physical properties of substances. You should consult Technique 4 for a complete discussion on how to find data for specific compounds. The works most useful for finding lists of values for the nonspectroscopic physical properties include

- The Merck Index
- The CRC Handbook of Chemistry and Physics
- Lange’s Handbook of Chemistry
- Aldrich Handbook of Fine Chemicals

Complete citations for these references can be found in Technique 29 (p. 942). Although the CRC Handbook has good tables, it adheres strictly to IUPAC nomenclature. For this reason, it may be easier to use one of the other references, particularly The Merck Index or the Aldrich Handbook of Fine Chemicals, in your first attempt to locate information (see Technique 4).

9.2 The Melting Point

The melting point of a compound is used by the organic chemist not only to identify the compound but also to establish its purity. A small amount of material is heated slowly in a special apparatus equipped with a thermometer or thermocouple, a heating bath or heating coil, and a magnifying eyepiece for observing the sample. Two temperatures are noted. The first is the point at which the first drop of liquid forms among the crystals; the second is the point at which the whole mass of crystals turns to a clear liquid. The melting point is recorded by giving this range of melting. You might say, for example, that the melting point of a substance is 51–54°C. That is, the substance melted over a 3-degree range.

The melting point indicates purity in two ways. First, the purer the material, the higher its melting point. Second, the purer the material, the narrower its melting-point range. Adding successive amounts of an impurity to a pure substance generally causes its melting point to decrease in proportion to the amount of impurity. Looking at it another way, adding impurities
Figure 9.1 is a graph of the usual melting-point behavior of mixtures of two substances, A and B. The two extremes of the melting range (the low and high temperature) are shown for various mixtures of the two. The upper curves indicate the temperatures at which all the sample has melted. The lower curves indicate the temperature at which melting is observed to begin. With pure compounds, melting is sharp and without any range. This is shown at the left- and right-hand edges of the graph. If you begin with pure A, the melting point decreases as impurity B is added. At some point, a minimum temperature, or eutectic, is reached, and the melting point begins to increase to that of substance B. The vertical distance between the lower and upper curves represents the melting range. Notice that for mixtures that contain relatively small amounts of impurity (<15%) and are not close to the eutectic, the melting range increases as the sample becomes less pure. The range indicated by the lines in Figure 9.1 represents the typical behavior.

We can generalize the behavior shown in Figure 9.1. Pure substances melt with a narrow range of melting. With impure substances, the melting range becomes wider, and the entire melting range is lowered. Be careful to note, however, that at the minimum point of the melting-point–composition curves, the mixture often forms a eutectic, which also melts sharply. Not all binary mixtures form eutectics, and some caution must be exercised in assuming that every binary mixture follows the previously described behavior. Some mixtures may form more than one eutectic; others might not form even one. In spite of these variations, both the melting point and its range are useful indications of purity, and they are easily determined by simple experimental methods.
9.3 Melting-Point Theory

Figure 9.2 is a phase diagram describing the usual behavior of a two-component mixture \((A + B)\) on melting. The behavior on melting depends on the relative amounts of \(A\) and \(B\) in the mixture. If \(A\) is a pure substance (no \(B\)), then \(A\) melts sharply at its melting point \(t_A\). This is represented by point \(A\) on the left side of the diagram. When \(B\) is a pure substance, it melts at \(t_B\); its melting point is represented by point \(B\) on the right side of the diagram. At either point \(A\) or point \(B\), the pure solid passes cleanly, with a narrow range, from solid to liquid.

In mixtures of \(A\) and \(B\), the behavior is different. Using Figure 9.2, consider a mixture of 80% \(A\) and 20% \(B\) on a mole-per-mole basis (that is, mole percentage). The melting point of this mixture is given by \(t_M\) at point \(M\) on the diagram. That is, adding \(B\) to \(A\) has lowered the melting point of \(A\) from \(t_A\) to \(t_M\). It has also expanded the melting range. The temperature \(t_M\) corresponds to the upper limit of the melting range.

![Figure 9.2](image)

A phase diagram for melting in a two-component system.

Lowering the melting point of \(A\) by adding impurity \(B\) comes about in the following way. Substance \(A\) has the lower melting point in the phase diagram shown, and if heated, it begins to melt first. As \(A\) begins to melt, solid \(B\) begins to dissolve in the liquid \(A\) that is formed. When solid \(B\) dissolves in liquid \(A\), the melting point is depressed. To understand this, consider the melting point from the opposite direction. When a liquid at a high temperature cools, it reaches a point at which it solidifies, or “freezes.” The temperature at which a liquid freezes is identical to its melting point. Recall that the freezing point of a liquid can be lowered by adding an impurity. Because the freezing point and the melting point are identical, lowering the freezing point corresponds to lowering the melting point. Therefore, as more impurity is added to a solid, its melting point becomes lower. There is, however, a limit to how far the melting point can be depressed. You cannot dissolve an infinite amount of the impurity substance in the liquid. At some point, the liquid will become saturated with the impurity substance. The solubility of \(B\) in \(A\) has an upper limit. In Figure 9.2, the solubility limit of \(B\) in liquid \(A\) is reached at point \(C\), the eutectic point. The melting point of the mixture cannot be lowered below \(t_C\), the melting temperature of the eutectic.

Now consider what happens when the melting point of a mixture of 80% \(A\) and 20% \(B\) is approached. As the temperature is increased, \(A\) begins...
to “melt.” This is not really a visible phenomenon in the beginning stages; it happens before liquid is visible. It is a softening of the compound to a point at which it can begin to mix with the impurity. As A begins to soften, it dissolves B. As it dissolves B, the melting point is lowered. The lowering continues until all B is dissolved or until the eutectic composition (saturation) is reached. When the maximum possible amount of B has been dissolved, actual melting begins, and one can observe the first appearance of liquid. The initial temperature of melting will be below $t_A$. The amount below $t_A$ at which melting begins is determined by the amount of B dissolved in A but will never be below $t_C$. Once all B has been dissolved, the melting point of the mixture begins to rise as more A begins to melt. As more A melts, the semisolid solution is diluted by more A, and its melting point rises. While all this is happening, you can observe both solid and liquid in the melting-point capillary. Once all A has begun to melt, the composition of the mixture M becomes uniform and will reach 80% A and 20% B. At this point, the mixture finally melts sharply, giving a clear solution. The maximum melting-point range will be $t_C - t_M$, because $t_A$ is depressed by the impurity B that is present. The lower end of the melting range will always be $t_C$; however, melting will not always be observed at this temperature. An observable melting at $t_C$ comes about only when a large amount of B is present. Otherwise, the amount of liquid formed at $t_C$ will be too small to observe. Therefore, the melting behavior that is actually observed will have a smaller range, as shown in Figure 9.1.

9.4 Mixture Melting Points

The melting point can be used as supporting evidence in identifying a compound in two different ways. Not only may the melting points of the two individual compounds be compared but a special procedure called a mixture melting point may also be performed. The mixture melting point requires that an authentic sample of the same compound be available from another source. In this procedure, the two compounds (authentic and suspected) are finely pulverized and mixed together in equal quantities. Then the melting point of the mixture is determined. If there is a melting-point depression or if the range of melting is expanded by a large amount compared to that of the individual substances, you may conclude that one compound has acted as an impurity toward the other and that they are not the same compound. If there is no lowering of the melting point for the mixture (the melting point is identical with those of pure A and pure B), then A and B are almost certainly the same compound.
Melting points are usually determined by heating the sample in a piece of thin-walled capillary tubing (1 mm × 100 mm) that has been sealed at one end. To pack the tube, press the open end gently into a pulverized sample of the crystalline material. Crystals will stick in the open end of the tube. The amount of solid pressed into the tube should correspond to a column no more than 1–2 mm high. To transfer the crystals to the closed end of the tube, drop the capillary tube, closed end first, down a ¼-m length of glass tubing, which is held upright on the desktop. When the capillary tube hits the desktop, the crystals will pack down into the bottom of the tube. This procedure is repeated if necessary. Tapping the capillary on the desktop with fingers is not recommended because it is easy to drive the small tubing into a finger if the tubing should break.

Some commercial melting-point instruments have a built-in vibrating device that is designed to pack capillary tubes. With these instruments, the sample is pressed into the open end of the capillary tube, and the tube is placed in the vibrator slot. The action of the vibrator will transfer the sample to the bottom of the tube and pack it tightly.

Three types of electrically heated melting-point instruments are illustrated in Figure 9.4. In each case, the melting-point tube is filled as described in Section 9.5 and placed in a holder located just behind the magnifying eyepiece. The apparatus is operated by moving the switch to the ON position, adjusting the potentiometric control dial for the desired rate of heating, and observing the sample through the magnifying eyepiece. The temperature is read from a thermometer or, in the most modern instruments, from a digital display attached to a thermocouple. Your instructor will demonstrate and explain the type used in your laboratory.

Most electrically heated instruments do not heat or increase the temperature of the sample linearly. Although the rate of increase may be linear in the early stages of heating, it usually decreases and leads to a constant temperature at some upper limit. The upper-limit temperature is determined by the setting of the heating control. Thus, a family of heating curves is usually obtained for various control settings, as shown in Figure 9.5. The four hypothetical curves shown (1–4) might correspond to different control settings. For a compound melting at temperature \( t_1 \), the setting corresponding to curve 3 would be ideal. In the beginning of the curve, the temperature is increasing too rapidly to allow determination of an accurate melting point, but after the change in slope, the temperature increase will have slowed to a more usable rate.

If the melting point of the sample is unknown, you can often save time by preparing two samples for melting-point determination. With one sample, you can rapidly determine a crude melting-point value. Then repeat the experiment more carefully using the second sample. For the second determination, you already have an approximate idea of what the melting-point temperature should be, and a proper rate of heating can be chosen.
When temperatures above 150°C are measured, thermometer errors can become significant. For an accurate melting point with a high-melting solid, you may wish to apply a stem correction to the thermometer as described in Technique 13, Section 13.4. An even better solution is to calibrate the thermometer as described in Section 9.9.
PROBLEMS

1. Two substances, A and B, have the same melting point. How can you determine if they are the same without using any form of spectroscopy? Explain in detail.

2. Using Figure 9.5, determine which heating curve would be most appropriate for a substance with a melting point of about 150°C.

3. What steps can you take to determine the melting point of a substance that sublimes before it melts?

4. A compound melting at 134°C was suspected to be either aspirin (mp 135°C) or urea (mp 133°C). Explain how you could determine whether one of these two suspected compounds was identical to the unknown compound without using any form of spectroscopy.

5. An unknown compound gave a melting point of 230°C. When the molten liquid solidified, the melting point was redetermined and found to be 131°C. Give a possible explanation for this discrepancy.

10 TECHNIQUE 10

Solubility

The solubility of a solute (a dissolved substance) in a solvent (the dissolving medium) is the most important chemical principle underlying three basic techniques you will study in the organic chemistry laboratory: crystallization, extraction, and chromatography. In this discussion of solubility, you will gain an understanding of the structural features of a substance that determine its solubility in various solvents. This understanding will help you to predict solubility behavior and to understand the techniques that are based on this property. Understanding solubility behavior will also help you understand what is going on during a reaction, especially when there is more than one liquid phase present or when a precipitate is formed.

10.1 Definition of Solubility

Although we often describe solubility behavior in terms of a substance being soluble (dissolved) or insoluble (not dissolved) in a solvent, solubility can be described more precisely in terms of the extent to which a substance is soluble. Solubility may be expressed in terms of grams of solute per liter (g/L) or milligrams of solute per milliliter (mg/mL) of solvent. Consider the solubilities at room temperature for the following three substances in water:

- Cholesterol 0.002 mg/mL
- Caffeine 22 mg/mL
- Citric acid 620 mg/mL

In a typical test for solubility, 40 mg of solute is added to 1 mL of solvent. Therefore, if you were testing the solubility of these three substances, cholesterol would be insoluble, caffeine would be partially soluble, and
citric acid would be soluble. Note that a small amount (0.002 mg) of cholesterol would dissolve. It is unlikely, however, that you would be able to observe this small amount dissolving, and you would report that cholesterol is insoluble. On the other hand, 22 mg (55%) of the caffeine would dissolve. It is likely that you would be able to observe this, and you would state that caffeine is partially soluble.

When the solubility of a liquid solute in a solvent is described, it is sometimes helpful to use the terms **miscible** and **immiscible**. Two liquids that are miscible will mix homogeneously (one phase) in all proportions. For example, water and ethyl alcohol are miscible. When they are mixed in any proportion, only one layer will be observed. When two liquids are miscible, it is also true that either one of them will be completely soluble in the other one. Two immiscible liquids do not mix homogeneously in all proportions, and under some conditions they will form two layers. Water and diethyl ether are immiscible. When mixed in roughly equal amounts, they will form two layers. However, each liquid is slightly soluble in the other one. Even when two layers are present, a small amount of water will be soluble in the diethyl ether, and a small amount of diethyl ether will be soluble in the water. Furthermore, if only a small amount of either one is added to the other, it may dissolve completely, and only one layer will be observed. For example, if a small amount of water (less than 1.2% at 20°C) is added to diethyl ether, the water will dissolve completely in the diethyl ether, and only one layer will be observed. When more water is added (more than 1.2%), some of the water will not dissolve, and two layers will be present.

Although the terms **solubility** and **miscibility** are related in meaning, it is important to understand that there is one essential difference. There can be different degrees of solubility, such as slightly, partially, very, and so on. Unlike solubility, miscibility does not have any degrees—a pair of liquids is either miscible or it is not.

### 10.2 Predicting Solubility Behavior

A major goal of this section is to explain how to predict whether a substance will be soluble in a given solvent. This is not always easy; even for an experienced chemist. However, guidelines will help you make a good guess about the solubility of a compound in a specific solvent. In discussing these guidelines, it is helpful to separate the types of solutions we will be looking at into two categories: solutions in which both the solvent and the solute are covalent (molecular) and ionic solutions, in which the solute ionizes and dissociates.

#### A. Solutions in Which the Solvent and Solute Are Molecular

A useful generalization in predicting solubility is the widely used rule “Like dissolves like.” This rule is most commonly applied to polar and nonpolar compounds. According to this rule, a polar solvent will dissolve polar (or ionic) compounds, and a nonpolar solvent will dissolve nonpolar compounds.

The reason for this behavior involves the nature of intermolecular forces of attraction. Although we will not be focusing on the nature of these forces, it is helpful to know what they are called. The force of attraction between polar molecules is called **dipole–dipole interaction**; between nonpolar
molecules, forces of attraction are called van der Waals forces (also called London or dispersion forces). In both cases, these attractive forces can occur between molecules of the same compound or different compounds. Consult your lecture textbook for more information on these forces.

To apply the rule “Like dissolves like,” you must first determine whether a substance is polar or nonpolar. The polarity of a compound is dependent on both the polarities of the individual bonds and the shape of the molecule. For most organic compounds, evaluating these factors can become quite complicated because of the complexities of the molecules. However, it is possible to make some reasonable predictions just by looking at the types of atoms that a compound possesses. As you read the following guidelines, it is important to understand that although we often describe compounds as being polar or nonpolar, polarity is a matter of degree, ranging from nonpolar to highly polar.

Guidelines for Predicting Polarity and Solubility

1. All hydrocarbons are nonpolar.
   Examples:

   \[
   \begin{align*}
   &\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3 \\
   &\text{CH}_3\text{CCH}_3 \\
   \end{align*}
   \]

   Hexane  
   Benzene

   Hydrocarbons such as benzene are slightly more polar than hexane because of their pi (\(\pi\)) bonds, which allow for greater van der Waals or London attractive forces.

2. Compounds possessing the electronegative elements oxygen or nitrogen are polar.
   Examples:

   \[
   \begin{align*}
   &\text{CH}_3\text{CCH}_3 \quad \text{CH}_3\text{CH}_2\text{OH} \quad \text{CH}_3\text{COCH}_2\text{CH}_3 \\
   &\text{CH}_3\text{CH}_2\text{NH}_2 \quad \text{CH}_3\text{CH}_2\text{OCH}_2\text{CH}_3 \quad \text{H}_2\text{O} \\
   \end{align*}
   \]

   Acetone  Ethyl alcohol  Ethyl acetate
   Ethylamine  Diethyl ether  Water

   The polarity of these compounds depends on the presence of polar C=O, C\(\equiv\)O, OH, NH, and CN bonds. The compounds that are most polar are capable of forming hydrogen bonds (see Guideline 6) and have NH or OH bonds. Although all these compounds are polar, the degree of polarity ranges from slightly polar to highly polar. This is due to the effect on polarity of the shape of the molecule and size of the carbon chain and whether the compound can form hydrogen bonds.

3. The presence of halogen atoms, even though their electronegativities are relatively high, does not alter the polarity of an organic compound in a significant way. Therefore, these compounds are only slightly polar.
The polarities of these compounds are more similar to those of hydrocarbons, which are nonpolar, than to that of water, which is highly polar.

**Examples:**

4. When comparing organic compounds within the same family, note that adding carbon atoms to the chain decreases the polarity. For example, methyl alcohol (CH₃OH) is more polar than propyl alcohol (CH₃CH₂CH₂OH). The reason is that hydrocarbons are nonpolar, and increasing the length of a carbon chain makes the compound more hydrocarbon-like.

5. Compounds that contain four or fewer carbons and also contain oxygen or nitrogen are often soluble in water. Almost any functional group containing these elements will lead to water solubility for low-molecular-weight (up to C₄) compounds. Compounds having five or six carbons and containing one of these elements are often insoluble in water or have borderline solubility.

6. As mentioned earlier, the force of attraction between polar molecules is dipole–dipole interaction. A special case of dipole–dipole interaction is hydrogen bonding. Hydrogen bonding is a possibility when a compound possesses a hydrogen atom bonded to a nitrogen, oxygen, or fluorine atom. The bond is formed by the attraction between this hydrogen atom and a nitrogen, oxygen, or fluorine atom in another molecule. Hydrogen bonding may occur between two molecules of the same compound or between molecules of different compounds:

![Hydrogen bond](image)

Hydrogen bonding is the strongest type of dipole–dipole interaction. When hydrogen bonding between solute and solvent is possible, solubility is greater than one would expect for compounds of similar polarity that cannot form hydrogen bonds. Hydrogen bonding is very important in organic chemistry, and you should be alert for situations in which hydrogen bonding may occur.

7. Another factor that can affect solubility is the degree of branching of the alkyl chain in a compound. Branching of the alkyl chain in a compound lowers the intermolecular forces between the molecules. This
is usually reflected in a greater solubility in water for the branched compound than for the corresponding straight-chain compound. This occurs simply because the molecules of the branched compounds are more easily separated from one another.

8. The solubility rule ("Like dissolves like") may be applied to organic compounds that belong to the same family. For example, 1-octanol (an alcohol) is soluble in the solvent ethyl alcohol. Most compounds within the same family have similar polarity. However, this generalization may not apply if there is a substantial difference in size between the two compounds. For example, cholesterol, an alcohol with a molecular weight (MW) of 386.64, is only slightly soluble in methanol (MW 32.04). The large hydrocarbon component of cholesterol negates the fact that they belong to the same family.

9. The stability of the crystal lattice also affects solubility. Other things being equal, the higher the melting point (the more stable the crystal) is, the less soluble the compound. For instance, \( p \)-nitrobenzoic acid (mp 242°C) is, by a factor of 10, less soluble in a fixed amount of ethanol than the \( o \)- (mp 147°C) and \( m \)- (mp 141°C) isomers.

You can check your understanding of some of these guidelines by studying the list given in Table 10.1, which is given in order of increasing polarity. The structures of these compounds are given on pages 639–640.

This list can be used to make some predictions about solubility, based on the rule "Like dissolves like." Substances that are close to one another on this list will have similar polarities. Thus, you would expect hexane to be soluble in methylene chloride but not in water. Acetone should be soluble in ethyl alcohol. On the other hand, you might predict that ethyl alcohol would be insoluble in hexane. However, ethyl alcohol is soluble in hexane because ethyl alcohol is somewhat less polar than methyl alcohol or water.

<table>
<thead>
<tr>
<th>Table 10.1</th>
<th>Compounds in increasing order of polarity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increasing Polarity</td>
<td></td>
</tr>
<tr>
<td>Aliphatic hydrocarbons</td>
<td>Hexane (nonpolar)</td>
</tr>
<tr>
<td>Aromatic hydrocarbons (( \pi ) bonds)</td>
<td>Benzene (nonpolar)</td>
</tr>
<tr>
<td>Halocarbons</td>
<td>Methylene chloride (slightly polar)</td>
</tr>
<tr>
<td>Compounds with polar bonds</td>
<td>Diethyl ether (slightly polar)</td>
</tr>
<tr>
<td></td>
<td>Ethyl acetate (intermediate polarity)</td>
</tr>
<tr>
<td></td>
<td>Acetone (intermediate polarity)</td>
</tr>
<tr>
<td>Compounds with polar bonds and hydrogen bonding</td>
<td>Ethyl alcohol (intermediate polarity)</td>
</tr>
<tr>
<td></td>
<td>Methyl alcohol (intermediate polarity)</td>
</tr>
<tr>
<td></td>
<td>Water (highly polar)</td>
</tr>
</tbody>
</table>
This last example demonstrates that you must be careful in using the guidelines on polarity for predicting solubilities. Ultimately, solubility tests must be done to confirm predictions until you gain more experience.

The trend in polarities shown in Table 10.1 can be expanded by including more organic families. The list in Table 10.2 gives an approximate order for the increasing polarity of organic functional groups. It may appear that there are some discrepancies between the information provided in these two tables. The reason is that Table 10.1 provides information about specific compounds, whereas the trend shown in Table 10.2 is for major organic families and is approximate.

### B. Solutions in Which the Solute Ionizes and Dissociates

Many ionic compounds are highly soluble in water because of the strong attraction between ions and the highly polar water molecules. This also applies to organic compounds that can exist as ions. For example, sodium acetate consists of Na<sup>+</sup> and CH<sub>3</sub>COO<sup>−</sup> ions, which are highly soluble in water. Although there are some exceptions, you may assume that all organic compounds that are in the ionic form will be water soluble.

The most common way by which organic compounds become ions is in acid–base reactions. For example, carboxylic acids can be converted to water-soluble salts when they react with dilute aqueous NaOH:

\[
\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{COH} + \text{NaOH (aq)} \rightarrow \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CO}\text{− Na}^+ + \text{H}_2\text{O}
\]

The water-soluble salt can then be converted back to the original carboxylic acid (which is insoluble in water) by adding another acid (usually
aqueous HCl) to the solution of the salt. The carboxylic acid precipitates out of solution.

Amines, which are organic bases, can also be converted to water-soluble salts when they react with dilute aqueous HCl:

\[
\text{Water-insoluble amine} \quad + \quad \text{HCl (aq)} \quad \rightarrow \quad \text{Water-soluble salt}
\]

This salt can be converted back to the original amine by adding a base (usually aqueous NaOH) to the solution of the salt.

### 10.3 Organic Solvents

Organic solvents must be handled safely. Always remember that organic solvents are all at least mildly toxic and that many are flammable. You should become thoroughly familiar with laboratory safety (see Technique 1, pp. 542–558).

The most common organic solvents are listed in Table 10.3 along with their boiling points. Solvents marked in boldface type will burn. Ether, pentane, and hexane are especially dangerous; if they are combined with the correct amount of air, they will explode.

The terms **petroleum ether** and **ligroin** are often confusing. Petroleum ether is a mixture of hydrocarbons with isomers of formulas \( \text{C}_5\text{H}_{12} \) and \( \text{C}_6\text{H}_{12} \).

### Table 10.3 Common organic solvents

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Bp (°C)</th>
<th>Solvent</th>
<th>Bp (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocarbons</td>
<td></td>
<td>Ethers</td>
<td></td>
</tr>
<tr>
<td>Pentane</td>
<td>36</td>
<td>Ether (diethyl)</td>
<td>35</td>
</tr>
<tr>
<td>Hexane</td>
<td>69</td>
<td>Dioxane(^a)</td>
<td>101</td>
</tr>
<tr>
<td>Benzene(^a)</td>
<td>80</td>
<td>1,2-Dimethoxyethane</td>
<td>83</td>
</tr>
<tr>
<td>Toluene</td>
<td>111</td>
<td>Others</td>
<td></td>
</tr>
<tr>
<td>Hydrocarbon mixtures</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Petroleum ether</td>
<td>30–60</td>
<td>Acetic acid</td>
<td>118</td>
</tr>
<tr>
<td>Ligroin</td>
<td>60–90</td>
<td>Acetic anhydride</td>
<td>140</td>
</tr>
<tr>
<td>Chlorocarbons</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methylene chloride</td>
<td>40</td>
<td>Pyridine</td>
<td>115</td>
</tr>
<tr>
<td>Chloroform(^a)</td>
<td>61</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbon tetrachloride(^a)</td>
<td>77</td>
<td>Dimethylformamide</td>
<td>153</td>
</tr>
<tr>
<td>Alcohols</td>
<td></td>
<td>Dimethylsulfoxide</td>
<td>189</td>
</tr>
<tr>
<td>Methanol</td>
<td>65</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ethanol</td>
<td>78</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Isopropyl alcohol</td>
<td>82</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

\(^a\)Suspect carcinogen (see p. 557).
C₆H₁₄ predominating. Petroleum ether is not an ether at all because there are no oxygen-bearing compounds in the mixture. In organic chemistry, an ether is usually a compound containing an oxygen atom to which two alkyl groups are attached. Figure 10.1 shows some of the hydrocarbons that appear commonly in petroleum ether. It also shows the structure of ether (diethyl ether). Use special care when instructions call for either ether or petroleum ether; the two must not become accidentally confused. Confusion is particularly easy when one is selecting a container of solvent from the supply shelf.

Ligroin, or high-boiling petroleum ether, is like petroleum ether in composition except that compared with petroleum ether, ligroin generally includes higher-boiling alkane isomers. Depending on the supplier, ligroin may have different boiling ranges. Whereas some brands of ligroin have boiling points ranging from about 60°C to about 90°C, other brands have boiling points ranging from about 60°C to about 75°C. The boiling-point ranges of petroleum ether and ligroin are often included on the labels of the containers.
1. For each of the following pairs of solutes and solvent, predict whether the solute would be soluble or insoluble. After making your predictions, you can check your answers by looking up the compounds in *The Merck Index* or the *CRC Handbook of Chemistry and Physics*. Generally, *The Merck Index* is the easier reference book to use. If the substance has a solubility greater than 40 mg/mL, you may conclude that it is soluble.

a. Malic acid in water

\[
\text{HO-}C\text{-CHCH}_{2}\text{-C-OH}
\]

b. Naphthalene in water

\[
\text{CH}\text{-CHCH}_{2}\text{-OH}
\]

c. Amphetamine in ethyl alcohol

\[
\text{CH}_{3}\text{-CH}_{2}\text{-CHCH}_{3}
\]

d. Aspirin in water

\[
\text{HO-}C\text{-CHCH}_{2}\text{-CH(OH)}\text{-CH}_{3}\text{-C-OH}
\]

e. Succinic acid in hexane (Note: the polarity of hexane is similar to that of petroleum ether.)

\[
\text{HO-}C\text{-CHCH}_{2}\text{-C-OH}
\]

f. Ibuprofen in diethyl ether

\[
\text{CH}_{3}\text{CHCH}_{2}\text{-CH-CH-OH}
\]
g. 1-Decanol (n-decyl alcohol) in water

CH$_3$(CH$_2$)$_9$CH$_2$OH

1-Decanol

2. Predict whether the following pairs of liquids would be miscible or immiscible:
   a. Water and methyl alcohol
   b. Hexane and benzene
   c. Methylene chloride and benzene
   d. Water and toluene

![Toluene](image1)

E. Ethyl alcohol and isopropyl alcohol

CH$_3$CHCH$_3$

Isopropyl alcohol

3. Would you expect ibuprofen (see problem 1f) to be soluble or insoluble in 1.0 M NaOH? Explain.

4. Thymol is very slightly soluble in water and very soluble in 1.0 M NaOH. Explain.

![Thymol](image2)

5. Although cannabinol and methyl alcohol are both alcohols, cannabinol is very slightly soluble in methyl alcohol at room temperature. Explain.

![Cannabinol](image3)

6. What is the difference between the compounds in each of the following pairs?
   a. Ether and petroleum ether
   b. Ether and diethyl ether
   c. Ligroin and petroleum ether
**PART A. THEORY**

12.1 Extraction

Transferring a solute from one solvent into another is called *extraction*, or, more precisely, liquid–liquid extraction. The solute is extracted from one solvent into the other because the solute is more soluble in the second solvent than in the first. The two solvents must not be *miscible* (mix freely), and they must form two separate *phases*, or layers, in order for this procedure to work. Extraction is used in many ways in organic chemistry. Many natural products (organic chemicals that exist in nature) are present in animal and plant tissues having high water content. Extracting these tissues with a water-immiscible solvent is useful for isolating natural products. Often, diethyl ether (commonly referred to as “ether”) is used for this purpose. Sometimes alternative water-immiscible solvents such as hexane, petroleum ether, ligroin, and methylene chloride are used. For instance, caffeine, a natural product, can be extracted from an aqueous tea solution by shaking it successively with several portions of methylene chloride.

A generalized extraction process that uses a conical vial is illustrated in Figure 12.1. The first solvent contains a mixture of black and white molecules (Fig. 12.1A). A second solvent that is not miscible with the first is added.

---

**Figure 12.1**

The extraction process.

A. Solvent 1 contains a mixture of molecules (black and white).

B. After shaking with solvent 2 (shaded), most of the white molecules have been extracted into the new solvent. The white molecules are more soluble in the second solvent, whereas the black molecules are more soluble in the original solvent.

C. With removal of the lower phase with a Pasteur pipet, the black and white molecules have been partially separated.
After the vial is capped and shaken, the layers separate. In this example, the second solvent is less dense, so it becomes the top layer (Fig. 12.1B). Because of differences in physical properties, the white molecules are more soluble in the second solvent, whereas the black molecules are more soluble in the first solvent. Most of the white molecules are in the upper layer, but there are some black molecules there, too. Likewise, most of the black molecules are in the lower layer. However, there are a few white molecules in this lower phase. A Pasteur pipet may be used to remove the lower layer (Fig. 12.1C). In this way, a partial separation of black and white molecules has been achieved. In this example, notice that it was not possible to effect a complete separation with one extraction. This is a common occurrence in organic chemistry. Many organic substances are soluble in both water and organic solvents.

Water can be used to extract or “wash” water-soluble impurities from an organic reaction mixture. To carry out a “washing” operation, you add water to the reaction mixture contained in a conical vial. After capping the vial and shaking it, you allow the organic layer and the aqueous (water) layer to separate from each other in the vial. A water wash removes highly polar and water-soluble materials, such as sulfuric acid, hydrochloric acid, or sodium hydroxide from the organic layer. A water wash can also be used to remove water-soluble and low-molecular-weight compounds, such as ethanol or acetic acid, from the organic layer. The washing operation helps purify the desired organic compound present in the original reaction mixture.

12.2 Distribution Coefficient

When a solution (solute A in solvent 1) is shaken with a second solvent (solvent 2) with which it is not miscible, the solute distributes itself between the two liquid phases. When the two phases have separated again into two distinct solvent layers, an equilibrium will have been achieved such that the ratio of the concentrations of the solute in each layer defines a constant. The constant, called the distribution coefficient (or partition coefficient) $K$, is defined by

$$K = \frac{C_2}{C_1}$$

where $C_1$ and $C_2$ are the concentrations at equilibrium, in grams per liter or milligrams per milliliter of solute A in solvent 1 and in solvent 2, respectively. This relationship is a ratio of two concentrations and is independent of the actual amounts of the two solvents mixed. The distribution coefficient has a constant value for each solute considered and depends on the nature of the solvents used in each case.

Not all the solute will be transferred to solvent 2 in a single extraction unless $K$ is very large. Usually it takes several extractions to remove all the solute from solvent 1. In extracting a solute from a solution, it is always better to use several small portions of the second solvent than to make a single extraction with a large portion. Suppose that, as an illustration, a particular extraction proceeds with a distribution coefficient of 10. The system consists of 50 mg of organic compound dissolved in 1.00 mL of water (solvent 1). In this illustration, the effectiveness of three 0.50-mL extractions with ether (solvent 2) is compared with one 1.50-mL extraction with ether. In the first 0.50-mL extraction, the amount extracted into the ether layer is given by the
following calculation. The amount of compound remaining in the aqueous phase is given by \( x \).

\[
K = 10 = \frac{C_2}{C_1} = \frac{(50.0 - x)}{0.50} \frac{mg}{mL \text{ ether}} = \frac{x}{0.10} \frac{mg}{mL \text{ water}}; \quad 10 = \frac{(50.0 - x)(1.00)}{0.50x}
\]

\[
5.0x = 50.0 - x
\]

\[
6.0x = 50.0
\]

\[
x = 8.3 \text{ mg remaining in the aqueous layer}
\]

\[
50.0 - x = 41.7 \text{ mg in the ether layer}
\]

As a check on the calculation, it is possible to substitute the value 8.3 mg for \( x \) in the original equation and demonstrate that the concentration in the ether phase divided by the concentration in the water phase equals the distribution coefficient.

\[
\frac{(50.0 - x)}{0.50} \frac{mg}{mL \text{ ether}} = \frac{41.7}{0.50} \frac{mg}{mL} = \frac{83 \text{ mg/mL}}{8.3 \text{ mg/mL}} = 10 = K
\]

The second extraction with another 0.50-mL portion of fresh ether is performed on the aqueous phase, which now contains 8.3 mg of the solute. The amount of solute extracted is given by the calculation shown in Figure 12.2. Also shown in the figure is a calculation for a third extraction with another 0.50-mL portion of ether. This third extraction will transfer 1.2 mg of solute into the ether layer, leaving 0.2 mg of solute remaining in the water layer. A total of 49.8 mg of solute will be extracted into the combined ether layers, and 0.2 mg will remain in the aqueous phase.

Figure 12.3 shows the result of a single extraction with 1.50 mL of ether. As shown there, 46.9 mg of solute was extracted into the ether layer, leaving 3.1 mg of compound in the aqueous phase. One can see that three successive 0.50-mL ether extractions (Fig. 12.2) succeeded in removing 2.9 mg more solute from the aqueous phase than using one 1.50-mL portion of ether (Fig. 12.3). This differential represents 5.8% of the total material.

### 12.3 Choosing an Extraction Method and a Solvent

Three types of apparatus are used for extractions: conical vials, centrifuge tubes, and separatory funnels. These are shown in Figure 12.4. Conical vials may be used with volumes of less than 4 mL; volumes of up to 10 mL may be handled in centrifuge tubes. A centrifuge tube equipped with a screw cap is particularly useful for extractions. The separatory funnel is used in large-scale reactions. Each type of equipment is discussed in a separate section.

Before using a conical vial for an extraction, make sure that the capped conical vial does not leak when shaken. To do this, place some water in the conical vial, place the Teflon liner in the cap, and screw the cap securely onto the conical vial. Shake the vial vigorously and check for leaks. Conical vials that are used for extractions must not be chipped on the edge of the vial or they will not seal adequately. If there is a leak, try tightening the cap
or replacing the Teflon liner with another one. Sometimes it helps to use the silicone rubber side of the liner to seal the conical vial. Some laboratories are supplied with Teflon stoppers that fit into the 5-mL conical vials. You may find that this stopper eliminates leakage.

When shaking the conical vial, do it gently at first in a rocking motion. When it is clear that an emulsion will not form (see Section 12.10, p. 684), you can shake it more vigorously.

In some cases, adequate mixing can be achieved by spinning your microspatula for at least 10 minutes in the conical vial. Another technique of mixing involves drawing up the mixture into a Pasteur pipet and squirting it rapidly back into the vial. Repeat this process for at least 5 minutes to obtain an adequate extraction.

If you are using a screw-cap centrifuge tube, put some water in the tube, cap it, and shake it vigorously to check for leaks. If the centrifuge tube leaks, try replacing the cap with another one. If available in the laboratory, a vortex mixer may be used to mix the phases. A vortex mixer works well with a variety of containers, including small flasks, test tubes, conical vials, and centrifuge tubes. You start the mixing action on a vortex mixer by holding the test tube or other container on one of the pads. The unit mixes the sample by high-frequency vibration.

Most extractions consist of an aqueous phase and an organic phase. In order to extract a substance from an aqueous phase, an organic solvent that

---

**Figure 12.2**

*The result of extraction of 50.0 mg of compound in 1.00 mL of water by three successive 0.50-mL portions of ether.*

*Compare this result with that of Figure 12.3.*

---

\[
K = 10 = \frac{8.3 - x}{0.50} = \frac{x}{1.00}
\]

\[x = 1.4 \text{ mg remaining in water}
6.9 \text{ mg in ether}\]

\[
K = 10 = \frac{1.4 - x}{0.50} = \frac{x}{1.00}
\]

\[x = 0.2 \text{ mg remaining in water}
1.2 \text{ mg in ether}\]
Start

50.0 mg compound in 1.00 mL water

Extraction

K = \frac{50.0 - x}{1.50} = \frac{x}{1.00}

10 = \frac{(50 - x)(1.00)}{1.50}

15.0x = 50.0 - x
16.0x = 50.0

x = 3.1 mg in water
50.0 - x = 46.9 mg in ether

Finish

(50.0 - 3.1) = 46.9 mg compound in 1.50 mL ether
3.1 mg compound left in 1.00 mL water

Figure 12.3

The result of extraction of 50.0 mg of compound in 1.00 mL of water with one 1.5-mL portion of ether. Compare this result with that of Figure 12.2.

Conical vial  
Centrifuge tubes  
Separatory funnel

Figure 12.4

Apparatus used for extraction.

is not miscible with water must be used. Table 12.1 lists a number of the common organic solvents that are not miscible with water and are used for extraction.

Those solvents that have a density less than that of water (1.00 g/mL) will separate as the top layer when shaken with water. Those solvents that have a greater density than water will separate into the lower layer. For instance, diethyl ether ($d = 0.71$ g/mL) when shaken with water will form the upper layer, whereas methylene chloride ($d = 1.33$ g/mL) will form the lower layer. When an extraction is performed, slightly different methods are used when you wish to separate the lower layer (whether it is the aqueous layer or the organic layer) than when you wish to separate the upper layer.

Table 12.1  Densities of common extraction solvents

<table>
<thead>
<tr>
<th>Solvent</th>
<th>Density (g/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ligroin</td>
<td>0.67–0.69</td>
</tr>
<tr>
<td>Diethyl ether</td>
<td>0.71</td>
</tr>
<tr>
<td>Toluene</td>
<td>0.87</td>
</tr>
<tr>
<td>Water</td>
<td>1.00</td>
</tr>
<tr>
<td>Methylene chloride</td>
<td>1.330</td>
</tr>
</tbody>
</table>
PART B. MICROSCELE EXTRACTION

12.4 The Conical Vial—Separating the Lower Layer

The 5-mL conical vial is the most useful piece of equipment for carrying out extractions on a microscale level. In this section, we consider the method for removing the lower layer. A concrete example would be the extraction of a desired product from an aqueous layer using methylene chloride (d = 1.33 g/mL) as the extraction solvent. Methods for removal of the upper layer are discussed in the next section.

NOTE: Always place a conical vial in a small beaker to prevent the vial from falling over.

Removing the Lower Layer. Suppose that we extract an aqueous solution with methylene chloride. This solvent is denser than water and will settle to the bottom of the conical vial. Use the following procedure, which is illustrated in Figure 12.5, to remove the lower layer.

1. Place the aqueous phase containing the dissolved product into a 5-mL conical vial (Fig. 12.5A).
2. Add about 1 mL of methylene chloride, cap the vial, and shake the mixture gently at first in a rocking motion and then more vigorously when it is clear that an emulsion will not form. Vent or unscrew the cap.

Figure 12.5
Extraction of an aqueous solution using a solvent denser than water: methylene chloride.
slightly to release the pressure in the vial. Allow the phases to separate completely so that you can detect two distinct layers in the vial. The organic phase will be the lower layer in the vial (Fig. 12.5B). If necessary, tap the vial with your finger or stir the mixture gently if some of the organic phase is suspended in the aqueous layer.

3. Prepare a Pasteur filter-tip pipet (Technique 8, Section 8.6, p. 625) using a 5½-inch pipet. Attach a 2-mL rubber bulb to the pipet, depress the bulb, and insert the pipet into the vial so that the tip touches the bottom (Fig. 12.5C). The filter-tip pipet gives you better control in removing the lower layer. In some cases, however, you may be able to use a Pasteur pipet (no filter tip), but considerably more care must be taken to avoid losing liquid from the pipet during the transfer operation. With experience, you should be able to judge how much to squeeze the bulb to draw in the desired volume of liquid.

4. Slowly draw the lower layer (methylene chloride) into the pipet in such a way that you exclude the aqueous layer and any emulsion (Section 12.10) that might be at the interface between the layers (Fig. 12.5D). Be sure to keep the tip of the pipet squarely in the V at the bottom of the vial.

5. Transfer the withdrawn organic phase into a dry test tube or another dry conical vial if one is available. It is best to have the test tube or vial located next to the extraction vial. Hold the vials in the same hand between your index finger and thumb, as shown in Figure 12.6. This avoids messy and disastrous transfers. The aqueous layer (upper layer) is left in the original conical vial (Fig. 12.5E).

In performing an actual extraction in the laboratory, you would extract the aqueous phase with a second 1-mL portion of fresh methylene chloride to achieve a more complete extraction. Steps 2–5 would be repeated, and the organic layers from both extractions would be combined. In some cases, you may need to extract a third time with yet another 1-mL portion of methylene chloride. Again, the methylene chloride would be combined with the other extracts. The overall process would use three 1-mL portions of methylene chloride to transfer the product from the water layer into methylene chloride. Sometimes you will see the statement “extract the aqueous phase with three 1-mL portions of methylene chloride” in an experimental procedure. This statement describes in a shorter fashion the process described previously. Finally, the methylene chloride extracts will contain some water and must be dried with a drying agent as indicated in Section 12.9.

In this example, we extracted water with the heavy solvent methylene chloride and removed it as the lower layer. If you were extracting a light solvent (for instance, diethyl ether) with water, and you wished to keep the water layer, the water would be the lower layer and would be removed using the same procedure. You would not dry the water layer, however.

In this section, we consider the method used when you wish to remove the upper layer. A concrete example would be the extraction of a desired product from an aqueous layer using diethyl ether (d = 0.71 g/mL) as the extraction solvent. Methods for removing the lower layer were discussed previously.

NOTE: Always place a conical vial in a small beaker to prevent the vial from falling over.
Removing the Upper Layer. Suppose we extract an aqueous solution with diethyl ether (ether). This solvent is less dense than water and will rise to the top of the conical vial. Use the following procedure, which is illustrated in Figure 12.7, to remove the upper layer.

1. Place the aqueous phase containing the dissolved product in a 5-mL conical vial (Fig. 12.7A).

2. Add about 1 mL of ether, cap the vial, and shake the mixture vigorously. Vent or unscrew the cap slightly to release the pressure in the vial. Allow the phases to separate completely so that you can detect two distinct layers in the vial. The ether phase will be the upper layer in the vial (Fig. 12.7B).

3. Prepare a Pasteur filter-tip pipet (Technique 8, Section 8.6, p. 625) using a 5%-inch pipet. Attach a 2-mL rubber bulb to the pipet, depress the bulb, and insert the pipet into the vial so that the tip touches the bottom. The filter-tip pipet gives you better control in removing the lower layer. In some cases, however, you may be able to use a Pasteur pipet.
(no filter tip), but considerably more care must be taken to avoid losing liquid from the pipet during the transfer operation. With experience, you should be able to judge how much to squeeze the bulb to draw in the desired volume of liquid. Slowly draw the lower aqueous layer into the pipet. Be sure to keep the tip of the pipet squarely in the V at the bottom of the vial (Fig. 12.7C).

4. Transfer the withdrawn aqueous phase into a test tube or another conical vial for temporary storage. It is best to have the test tube or vial located next to the extraction vial. This avoids messy and disastrous transfers. Hold the vials in the same hand between your index finger and thumb as shown in Fig. 12.6. The ether layer is left behind in the conical vial (Fig. 12.7D).

5. The ether phase remaining in the original conical vial should be transferred with a Pasteur pipet into a test tube for storage and the aqueous phase returned to the original conical vial (Fig. 12.7E).

In performing an actual extraction, you would extract the aqueous phase with another 1-mL portion of fresh ether to achieve a more complete extraction. Steps 2–5 would be repeated, and the organic layers from both extractions would be combined in the test tube. In some cases, you may need to extract the aqueous layer a third time with yet another 1-mL portion of ether. Again, the ether would be combined with the other two layers. This overall process uses three 1-mL portions of ether to transfer the product from the water layer into ether. The ether extracts contain some water and must be dried with a drying agent as indicated in Section 12.9.

12.6 The Centrifuge Tube

A screw-cap centrifuge tube may be employed instead of a conical vial for separations (Fig. 12.4). Before using the centrifuge tube, be sure to check it for leaks as indicated in Section 12.3. You should use the same extraction and separation procedures described in Sections 12.4 and 12.5. You may also use a “regular” (nonscrew-cap) centrifuge tube for extractions, although it will be necessary to cork the tube before shaking it. Because a regular centrifuge tube will probably leak around the cork, it is best to mix the contents with a vortex mixer (Section 12.3) to avoid shaking the tube. If an emulsion has formed after mixing or shaking, you can use a centrifuge to aid in the separation of the layers (Section 12.10). Once the layers have separated, it is easy to use a Pasteur pipet to withdraw the lower layer from the tapered bottom of the centrifuge tube.

12.7 The Separatory Funnel

The separatory funnel is often used in large-scale reactions. This apparatus is illustrated in Figure 12.8. To fill the separatory funnel, support it in an iron ring attached to a ring stand. Cut pieces of rubber tubing and attach them to the iron ring to cushion the separatory funnel as shown in Figure 12.8. This protects the funnel against possible breakage.

When beginning an extraction, the first step is close the stopcock. (Don’t forget!) Using a powder funnel (wide bore) placed in the top of the separatory funnel, fill it with both the solution to be extracted and the extraction
solvent. Swirl the funnel gently by holding it by its upper neck, and then stopper it. Pick up the separatory funnel with two hands and hold it as shown in Figure 12.9. Hold the stopper in place firmly because the two immiscible liquids will build pressure when they mix, and this pressure may force the stopper out of the separatory funnel. To release this pressure, vent the funnel by holding it upside down (hold the stopper securely) and slowly open the stopcock. Usually the rush of vapors out of the opening can be heard. Continue shaking and venting until the “whoosh” is no longer audible. Now continue shaking the mixture gently for about one minute. This can be done by inverting the funnel in a rocking motion repeatedly or, if the formation of an emulsion is not a problem (see Section 12.10, p. 684), by shaking the funnel more vigorously for less time.

NOTE: There is an art to shaking and venting a separatory funnel correctly, and it usually seems awkward to the beginner. The technique is best learned by observing a person, such as your instructor, who is thoroughly familiar with the separatory funnel’s use.

When you have finished mixing the liquids, place the separatory funnel in the iron ring and remove the top stopper immediately. The two immiscible solvents separate into two layers after a short time, and they can be separated from each other by draining most of the lower layer through the stopcock. A common error is to try to drain the separatory funnel without removing the top stopper. Under this circumstance, the funnel will not drain, because a partial vacuum is created in the space above the liquid.
adhering to the inner glass surfaces of the separatory funnel can drain down. Open the stopcock again and allow the remainder of the lower layer to drain until the interface between the upper and lower phases just begins to enter the bore of the stopcock. At this moment, close the stopcock and remove the remaining upper layer by pouring it from the top opening of the separatory funnel.

**NOTE:** To minimize contamination of the two layers, the lower layer should always be drained from the bottom of the separatory funnel and the upper layer poured out from the top of the funnel.

When methylene chloride is used as the extracting solvent with an aqueous phase, it will settle to the bottom and be removed through the stopcock. The aqueous layer remains in the funnel. A second extraction of the remaining aqueous layer with fresh methylene chloride may be needed.

With a diethyl ether (ether) extraction of an aqueous phase, the organic layer will form on top. Remove the lower aqueous layer through the stopcock and pour the upper ether layer from the top of the separatory funnel. Pour the aqueous phase back into the separatory funnel and extract it a second time with fresh ether. The combined organic phases must be dried using a suitable drying agent (Section 12.9) before the solvent is removed.

For microscale procedures, a 60- or 125-mL separatory funnel is recommended. Because of surface tension, water has a difficult time draining from the bore of smaller funnels. Funnels larger than 125 mL are simply too large for microscale experiments, and a good deal of material is lost in “wetting” their surfaces.

**PART D. ADDITIONAL EXPERIMENTAL CONSIDERATIONS: MICROSCALE AND MACROSCEALE**

12.8 How Do You Determine Which One Is the Organic Layer?

A common problem encountered during an extraction is trying to determine which of the two layers is the organic layer and which is the aqueous (water) layer. The most common situation occurs when the aqueous layer is on the bottom in the presence of an upper organic layer consisting of ether, ligroin, petroleum ether, or hexane (see densities in Table 12.1). However, the aqueous layer will be on the top when you use methylene chloride as a solvent (again, see Table 12.1). Although a laboratory procedure may frequently identify the expected relative positions of the organic and aqueous layers, sometimes their actual positions are reversed. Surprises usually occur in situations in which the aqueous layer contains a high concentration of sulfuric acid or a dissolved ionic compound, such as sodium chloride. Dissolved substances greatly increase the density of the aqueous layer, which may lead to the aqueous layer being found on the bottom even when coexisting with a relatively dense organic layer such as methylene chloride.

**NOTE:** Always keep both layers until you have actually isolated the desired compound or until you are certain where your desired substance is located.

To determine if a particular layer is the aqueous one, add a few drops of water to the layer. Observe closely as you add the water to see where it goes.
If the layer is water, then the drops of added water will dissolve in the aqueous layer and increase its volume. If the added water forms droplets or a new layer, however, you can assume that the suspected aqueous layer is actually organic. You can use a similar procedure to identify a suspected organic layer. This time, try adding more of the solvent, such as methylene chloride. The organic layer should increase in size, without separation of a new layer, if the tested layer is actually organic.

When performing an extraction procedure on the microscale level, you can use the following approach to identify the layers. When both layers are present, it is always a good idea to think carefully about the volumes of materials that you have added to the conical vial. You can use the graduations on the vial to help determine the volumes of the layers in the vial. If, for example, you have 1 mL of methylene chloride in a vial and you add 2 mL of water, you should expect the water to be on top because it is less dense than methylene chloride. As you add the water, watch to see where it goes. By noting the relative volumes of the two layers, you should be able to tell which is the aqueous layer and which is the organic layer. This approach can also be used when performing an extraction procedure using a centrifuge tube. Of course, you can always test to see which layer is the aqueous layer by adding one or two drops of water, as described previously.

After an organic solvent has been shaken with an aqueous solution, it will be “wet”; that is, it will have dissolved some water even though its solubility with water is not great. The amount of water dissolved varies from solvent to solvent; diethyl ether represents a solvent in which a fairly large amount of water dissolves. To remove water from the organic layer, use a drying agent. A drying agent is an anhydrous inorganic salt that acquires waters of hydration when exposed to moist air or a wet solution:

$$\text{Insoluble} \quad \text{Na}_2\text{SO}_4(\text{s}) \quad \text{Anhydrous drying agent}$$

$$\text{Insoluble} \quad \text{Na}_2\text{SO}_4 \cdot n\text{H}_2\text{O} (\text{s}) \quad \text{Hydrated drying agent}$$

The insoluble drying agent is placed directly into the solution, where it acquires water molecules and becomes hydrated. If enough drying agent is used, all of the water can be removed from a wet solution, making it “dry,” or free of water.

The following anhydrous salts are commonly used: sodium sulfate, magnesium sulfate, calcium chloride, calcium sulfate (Drierite), and potassium carbonate. These salts vary in their properties and applications. For instance, not all will absorb the same amount of water for a given weight, nor will they dry the solution to the same extent. Capacity refers to the amount of water a drying agent absorbs per unit weight. Sodium and magnesium sulfates absorb a large amount of water (high capacity), but magnesium sulfate dries a solution more completely. Completeness refers to a compound’s effectiveness in removing all the water from a solution by the time equilibrium has been reached. Magnesium ion, a strong Lewis acid, sometimes causes rearrangements of compounds such as epoxides. Calcium chloride is a good drying agent but cannot be used with many compounds containing oxygen or nitrogen because it forms complexes. Calcium chloride absorbs methanol and ethanol in addition to water, so it is useful for removing these materials when they are present as impurities. Potassium carbonate is a
base and is used for drying solutions of basic substances, such as amines. Calcium sulfate dries a solution completely but has a low capacity.

Anhydrous sodium sulfate is the most widely used drying agent. The granular variety is recommended because it is easier to remove the dried solution from it than from the powdered variety. Sodium sulfate is mild and effective. It will remove water from most common solvents, with the possible exception of diethyl ether, in which case a prior drying with saturated salt solution may be advised (see p. 684). Sodium sulfate must be used at room temperature to be effective; it cannot be used with boiling solutions. Table 12.2 compares the various common drying agents.

**Drying Procedure with Anhydrous Sodium Sulfate.** In experiments that require a drying step, the instructions are usually given in the following way: dry the organic layer (or phase) over granular anhydrous sodium sulfate (or some other drying agent). More specific instructions, such as the amount of drying agent to add, usually will not be given, and you will need to determine this each time that you perform a drying step. The drying procedure consists of four steps:

1. Remove the organic layer from any visible water.
2. Add the appropriate amount of granular anhydrous sodium sulfate (or other drying agent).
3. Allow a drying period during which dissolved water is removed from the organic layer by the drying agent.
4. Separate the dried organic layer from the drying agent.

More specific instructions are given below for both microscale and macroscale procedures. The only differences between these two procedures is that they are intended for different volumes of liquid and they require different glassware. The microscale procedure is generally for volumes up to

<table>
<thead>
<tr>
<th>Table 12.2 Common drying agents</th>
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<tr>
<td><strong>Acidity</strong></td>
</tr>
<tr>
<td>Magnesium sulfate</td>
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<tr>
<td>Sodium sulfate</td>
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<tr>
<td>Calcium chloride</td>
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<tr>
<td>Calcium sulfate (Drierite)</td>
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<tr>
<td>Potassium carbonate</td>
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<tr>
<td>Potassium hydroxide</td>
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<tr>
<td>Molecular sieves (3 or 4 Å)</td>
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*aAmount of water removed per given weight of drying agent.
*bRefers to amount of H$_2$O still in solution at equilibrium with drying agent.
*cRefers to rate of action (drying).
about 5 mL, and the macroscale procedure is usually appropriate for volumes of 5 mL or greater.

A. Microscale Drying Procedure

Step 1. (Removal of Visible Water). Before attempting to dry an organic layer, check closely to see that there are no visible signs of water. If there is a separate layer of water (top or bottom), droplets or a globule of water floating in the organic layer, or water droplets clinging to the sides of the container, then transfer the organic layer with a dry Pasteur pipet to a dry container, usually a conical vial or test tube, before adding any drying agent. If there is any doubt about whether water is present, it is advisable to make a transfer to a dry container. Performing this step when necessary may save time later in the drying procedure and result in a greater recovery of the desired substance.

Step 2. (Addition of Drying Agent). Each time a drying procedure is performed, it is necessary to determine how much granular anhydrous sodium sulfate (or other drying agent) should be added. This will depend on the total volume of the organic phase and how much water is dissolved in the solvent. Nonpolar organic solvents such as methylene chloride or hydrocarbons (hexane, pentane, etc.) can dissolve relatively small amounts of water and generally require less drying agent, whereas more polar organic solvents such as ether and ethyl acetate can dissolve more water, and more drying agent will be required. Begin by adding one spatulaful of granular anhydrous sodium sulfate (or other drying agent) from the V-grooved end of a microspatula (smaller microspatula on page 13) into the solution. If all the drying agent “clumps,” add another spatulaful of sodium sulfate. To determine if the drying agent has clumped, it is helpful to stir the mixture with a clean, dry spatula or to rapidly swirl the container. If any portion of the drying agent flows freely on the bottom of the container when stirred or swirled, then you can assume that enough of the drying agent has been added. Otherwise, you must continue adding one spatulaful of drying agent at a time until it is clear that the drying agent has stopped clumping. Stir or swirl the mixture after adding each spatulaful of the drying agent. For small amounts of liquid (less than 5 mL), about 1–6 microspatulafuls of drying agent will usually be required. However, the actual amount must be determined by experimentation, as just described. It is best to use a slight excess of drying agent; but if too great an excess is used, the recovery may be poor because some of the solution always adheres to the solid drying agent after the liquid is separated from the drying agent (Step 4). Take care not to add so much drying agent that all of the liquid is absorbed (disappears). If you do this you will have to add additional solvent to recover your product from the drying agent!

Step 3. (Drying Period). Stopper or cap the container and let the solution dry for at least 15 minutes.

NOTE: It is important that you stopper or cap the container to prevent evaporation and exposure to atmospheric moisture.

Stir the mixture occasionally with a spatula during the drying period. The mixture is dry if it appears clear (not cloudy) and shows the common
signs of a dry solution given in Table 12.3. Note that a “clear” solution may be colorless or colored. If the solution remains cloudy after treatment with the first batch of drying agent, add more drying agent and repeat the drying procedure. However, if a water layer forms or if drops of water are visible, transfer the organic layer to a dry container before adding fresh drying agent, as described in Step 2. It will also be necessary to repeat the 15-minute drying step described in Step 3.

Step 4. (Removal of Liquid from Drying Agent). When the organic phase is dry, use a dry Pasteur pipet or a dry filter-tip pipet (Technique 8, Section 8.6, p.625) to remove the dried organic layer from the drying agent and transfer the solution to a dry conical vial or test tube. Be careful not to transfer any of the drying agent when performing this step. Rinse the drying agent with a small amount of fresh solvent and transfer this additional solvent to the vial containing the dried organic layer. To isolate the desired material, remove the solvent by evaporation using heat and a stream of air or nitrogen (Technique 7, Section 7.10, p.611).

An alternative method of drying a small volume of organic phase is to pass it through a filtering pipet (Technique 8, Section 8.1C, p.618) that has been packed with a small amount (about 2 cm) of drying agent. Again, the solvent is removed by evaporation.

B. Macroscale Drying Procedure

To dry a large amount of organic liquid (greater than about 5 mL), follow the same four steps just described for the “Microscale Drying Procedure.” The main differences are that an Erlenmeyer flask is used rather than a test tube or conical vial and more drying agent will be required. The size of the Erlenmeyer flask is not critical, but it’s best that the flask not be filled more than half full with the solution being dried.

Step 1. (Removal of Visible Water). Refer to Step 1 above for instructions. If the amount of water is large, it may be best to separate the layers using a separatory funnel. If visible water must be removed in this step, place the separated organic layer in a clean, dry Erlenmeyer flask.

Step 2. (Addition of Drying Agent). Refer to Step 2 in the “Microscale Drying Procedure” for the basic instructions. Read these instructions carefully. The only difference is that in this macroscale procedure, more drying agent will be required. A common guideline is to add enough granular anhydrous sodium sulfate (or other drying agent) to give a 1- to 3-mm layer on the bottom of the flask, depending on the volume of the solution. However, it is best to add the
drying agent in small portions, as described above. In this procedure, use the larger microspatula shown in the figure (p. 13) to add the drying agent. Generally, an appropriate portion to add each time is about 0.5–1.0 g.

**Step 3. (Drying Period).** The instructions are the same as for Step 3 in the "Microscale Drying Procedure."

**Step 4. (Removal of Liquid from Drying Agent).** When the solution is dry, the drying agent should be removed by using decantation (pouring carefully to leave the drying agent behind). Transfer the liquid to a dry Erlenmeyer flask. If the volume of liquid is relatively small (less than 10 mL), it may be easier to complete this step by using a dry Pasteur pipet or a dry filter-tip pipet (Technique 8, Section 8.6, p. 625) to remove the dried organic layer. With granular sodium sulfate, decantation is easy to perform because of the size of the drying-agent particles. If a powdered drying agent, such as magnesium sulfate, is used, it may be necessary to use gravity filtration (Technique 8, Section 8.1B, p. 618) to remove the drying agent. Finally, to isolate the desired material, remove the solvent by distillation (Technique 14, Section 14.3, p. 707) or evaporation (Technique 7, Section 7.10, p. 611).

**Saturated Salt Solution.** At room temperature, diethyl ether (ether) dissolves 1.5% by weight of water, and water dissolves 7.5% of ether. Ether, however, dissolves a much smaller amount of water from a saturated aqueous sodium chloride solution. Hence, the bulk of water in ether, or ether in water, can be removed by shaking it with a saturated aqueous sodium chloride solution. A solution of high ionic strength is usually not compatible with an organic solvent and forces separation of it from the aqueous layer. The water migrates into the concentrated salt solution. The ether phase (organic layer) will be on top, and the saturated sodium chloride solution will be on the bottom \( (d = 1.2 \text{ g/mL}) \). After removing the organic phase from the aqueous sodium chloride, dry the organic layer completely with sodium sulfate or with one of the other drying agents listed in Table 12.2.

**12.10 Emulsions**

An emulsion is a colloidal suspension of one liquid in another. Minute droplets of an organic solvent are often held in suspension in an aqueous solution when the two are mixed or shaken vigorously; these droplets form an emulsion. This is especially true if any gummy or viscous material was present in the solution. Emulsions are often encountered in performing extractions. Emulsions may require a long time to separate into two layers and are a nuisance to the organic chemist.

Fortunately, several techniques may be used to break a difficult emulsion once it has formed.

1. Often an emulsion will break up if it is allowed to stand for some time. Patience is important here. Gently stirring with a stirring rod or spatula may also be useful.

2. If one of the solvents is water, adding a saturated aqueous sodium chloride solution will help destroy the emulsion. The water in the organic layer migrates into the concentrated salt solution.

3. With microscale experiments, the mixture may be transferred to a centrifuge tube. The emulsion will often break during centrifugation. Remember to place another tube filled with water on the opposite side of the centrifuge to balance it. The two tubes should weigh the same.
4. Adding a small amount of a water-soluble detergent may also help. This method has been used in the past for combating oil spills. The detergent helps to solubilize the tightly bound oil droplets.

5. Gravity filtration (see Technique 8, Section 8.1, p. 616) may help to destroy an emulsion by removing gummy polymeric substances. With large volumes, you might try filtering the mixture through a fluted filter (Technique 8, Section 8.1B, p. 618) or a piece of cotton. With small-scale reactions, a filtering pipet may work (Technique 8, Section 8.1C, p. 618). In many cases, once the gum is removed, the emulsion breaks up rapidly.

6. If you are using a separatory funnel, you might try to use a gentle swirling action in the funnel to help break an emulsion. Gently stirring with a stirring rod may also be useful.

When you know through experience that a mixture may form a difficult emulsion, you should avoid shaking the mixture vigorously. When using conical vials for extractions, it may be better to use a magnetic spin vane for mixing and not shake the mixture at all. When using separatory funnels, extractions should be performed with gentle swirling instead of shaking or with several gentle inversions of the separatory funnel. Do not shake the separatory funnel vigorously in these cases. It is important to use a longer extraction period if the more gentle techniques described in this paragraph are being employed. Otherwise, you will not transfer all the material from the first phase to the second one.

In nearly all synthetic experiments undertaken in the organic laboratory, a series of operations involving extractions is used after the actual reaction has been concluded. These extractions form an important part of the purification. Using them, you separate the desired product from unreacted starting materials or from undesired side products in the reaction mixture. These extractions may be grouped into three categories, depending on the nature of the impurities they are designed to remove.

The first category involves extracting or “washing” an organic mixture with water. Water washes are designed to remove highly polar materials, such as inorganic salts, strong acids or bases, and low-molecular-weight, polar substances including alcohols, carboxylic acids, and amines. Many organic compounds containing fewer than five carbons are water soluble. Water extractions are also used immediately following extractions of a mixture with either acid or base to ensure that all traces of acid or base have been removed.

The second category concerns extraction of an organic mixture with a dilute acid, usually 1–2 M hydrochloric acid. Acid extractions are intended to remove basic impurities, especially such basic impurities as organic amines. The bases are converted to their corresponding cationic salts by the acid used in the extraction. If an amine is one of the reactants or if pyridine or another amine is a solvent, such an extraction might be used to remove any excess amine present at the end of a reaction.

\[
\text{RNH}_2 + \text{HCl} \rightarrow \text{RNH}_3^+ \text{Cl}^- \\
(\text{water-soluble ammonium salt})
\]

Cationic ammonium salts are usually soluble in the aqueous solution, and they are thus extracted from the organic material. A water extraction may be
used immediately following the acid extraction to ensure that all traces of the acid have been removed from the organic material.

The third category is extraction of an organic mixture with a dilute base, usually 1 M sodium bicarbonate, although extractions with dilute sodium hydroxide can also be used. Such basic extractions are intended to convert acidic impurities, such as organic acids, to their corresponding anionic salts. For example, in the preparation of an ester, a sodium bicarbonate extraction might be used to remove any excess carboxylic acid that is present.

\[
\text{RCOOH} + \text{NaHCO}_3 \rightarrow \text{RCOO}^-\text{Na}^+ + \text{H}_2\text{O} + \text{CO}_2
\]

\((pK_a \sim 5)\)

(water-soluble carboxylate salt)

Anionic carboxylate salts, being highly polar, are soluble in the aqueous phase. As a result, these acid impurities are extracted from the organic material into the basic solution. A water extraction may be used after the basic extraction to ensure that all the base has been removed from the organic material.

Occasionally, phenols may be present in a reaction mixture as impurities, and removing them by extraction may be desired. Because phenols, although they are acidic, are about 10^5 times less acidic than carboxylic acids, basic extractions may be used to separate phenols from carboxylic acids by a careful selection of the base. If sodium bicarbonate is used as a base, carboxylic acids are extracted into the aqueous base, but phenols are not. Phenols are not sufficiently acidic to be deprotonated by the weak base bicarbonate. Extraction with sodium hydroxide, on the other hand, extracts both carboxylic acids and phenols into the aqueous basic solution because hydroxide ion is a sufficiently strong base to deprotonate phenols.

\[
\text{R}^-\text{OH} + \text{NaOH} \rightarrow \text{R}^-\text{Na}^+ + \text{H}_2\text{O}
\]

\((pK_a \sim 10)\)

(water-soluble salt)

Mixtures of acidic, basic, and neutral compounds are easily separated by extraction techniques. One such example is shown in Figure 12.10. The original compounds are dissolved in ether.

Organic acids or bases that have been extracted can be regenerated by neutralizing the extraction reagent. This would be done if the organic acid or base were a product of a reaction rather than an impurity. For example, if a carboxylic acid has been extracted with the aqueous base, the compound can be regenerated by acidifying the extract with 6 M HCl until the solution becomes just acidic, as indicated by litmus or pH paper. When the solution becomes acidic, the carboxylic acid will separate from the aqueous solution. If the acid is a solid at room temperature, it will precipitate and can be purified by filtration and crystallization. If the acid is a liquid, it will form a separate layer. In this case, it would usually be necessary to extract the mixture with ether or methylene chloride. After removing the organic layer and drying it, the solvent can be evaporated to yield the carboxylic acid.

In the example shown in Figure 12.10, you also need to perform a drying step at (3) before isolating the neutral compound. When the solvent is ether, you should first extract the ether solution with saturated aqueous sodium chloride to remove much of the water. The ether layer is then dried over a drying agent such as anhydrous sodium sulfate. If the solvent were
methylene chloride, it would not be necessary to do the step with saturated sodium chloride.

When acid–base extractions are performed, it is common practice to extract a mixture several times with the appropriate reagent. For example, if you were extracting a carboxylic acid from a mixture, you might extract the mixture three times with 2-mL portions of 1 M NaOH. In most published experiments, the procedure will specify the volume and concentration of extracting reagent and the number of times to do the extractions. If this information is not given, you must devise your own procedure. Using a carboxylic acid as an example, if you know the identity of the acid and the approximate amount present, you can actually calculate how much sodium hydroxide is needed. Because the carboxylic acid (assuming it is monoprotic) will react with sodium hydroxide in a 1:1 ratio, you would need the same number of moles of sodium hydroxide as there are moles of acid. To ensure that all the carboxylic acid is extracted, you should use about a twofold excess of the base. From this, you could calculate the number of milliliters of base needed. This should be divided into two or three equal portions, one portion for each extraction. In a similar fashion, you could calculate the amount of 5% sodium bicarbonate required to extract an acid or the amount of 1 M HCl required to extract a base. If the amount of organic acid or base is not known, then the situation is more difficult. A guideline that sometimes works is to do two or three extractions so that the total volume of the extracting reagent is approximately equal to the volume of the organic layer. To test this procedure, neutralize the aqueous layer from the last extraction. If a precipitate or cloudiness results, perform another extraction and test again. When no precipitate forms, you know that all the organic acid or base has been removed.
For some applications of acid–base extraction, an additional step, called \textit{backwashing} or \textit{back extraction}, is added to the scheme shown in Figure 12.10. Consider the first step, in which the carboxylic acid is extracted by sodium bicarbonate. This aqueous layer may contain some unwanted neutral organic material from the original mixture. To remove this contamination, backwash the aqueous layer with an organic solvent such as ether or methylene chloride. After shaking the mixture and allowing the layers to separate, remove and discard the organic layer. This technique may also be used when an amine is extracted with hydrochloric acid. The resulting aqueous layer is backwashed with an organic solvent to remove unwanted neutral material.

\textbf{PROBLEMS}

1. Suppose solute A has a distribution coefficient of 1.0 between water and diethyl ether. Demonstrate that if 4.0 mL of a solution of 0.20 g of A in water were extracted with two 1.0-mL portions of ether, a smaller amount of A would remain in the water than if the solution were extracted with one 2.0-mL portion of ether.

2. Write an equation to show how you could recover the parent compounds from their respective salts (1, 2, and 4) shown in Figure 12.10.

3. Aqueous hydrochloric acid was used \textit{after} the sodium bicarbonate and sodium hydroxide extractions in the separation scheme shown in Figure 12.10. Is it possible to use this reagent earlier in the separation scheme to achieve the same overall result? If so, explain where you would perform this extraction.

4. Using aqueous hydrochloric acid, sodium bicarbonate, or sodium hydroxide solutions, devise a separation scheme using the style shown in Figure 12.10 to separate the following two-component mixtures. All the substances are soluble in ether. Also indicate how you would recover each of the compounds from its respective salts.
   \textbf{a.} Give two different methods for separating this mixture.

\begin{center}
\begin{tikzpicture}
  \node (a) at (0,0) {\text{OH}};
  \node (b) at (-2,-1) {\text{(CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{)}_3\text{N}};
  \node (c) at (2,-1) {\text{Br}};
  \node (d) at (2,-2) {\text{Br}};
  \draw (a) -- (b);
  \draw (b) -- (c);
  \draw (b) -- (d);
\end{tikzpicture}
\end{center}

\textbf{b.} Give two different methods for separating this mixture.

\begin{center}
\begin{tikzpicture}
  \node (a) at (0,0) {\text{O}};
  \node (b) at (-2,-1) {\text{C}};
  \node (c) at (-2,-2) {\text{OH}};
  \node (d) at (2,-1) {\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}};
  \node (e) at (2,-2) {\text{CH}_3\text{CH}_2\text{OH}};
  \draw (a) -- (b);
  \draw (b) -- (c);
  \draw (b) -- (d);
  \draw (b) -- (e);
\end{tikzpicture}
\end{center}

\textbf{c.} Give one method for separating this mixture.

\begin{center}
\begin{tikzpicture}
  \node (a) at (0,0) {\text{OH}};
  \node (b) at (-2,-1) {\text{Br}};
  \node (c) at (2,-1) {\text{O}};
  \node (d) at (2,-2) {\text{OH}};
  \node (e) at (-2,-2) {\text{Br}};
  \draw (a) -- (b);
  \draw (b) -- (e);
  \draw (c) -- (d);
  \draw (d) -- (e);
\end{tikzpicture}
\end{center}
5. Solvents other than those in Table 12.1 may be used for extractions. Determine the relative positions of the organic layer and the aqueous layer in a conical vial or separatory funnel after shaking each of the following solvents with an aqueous phase. Find the densities for each of these solvents in a handbook (see Technique 4, p. 574).
   a. 1,1,1-Trichloroethane
   b. Hexane

6. A student prepares ethyl benzoate by the reaction of benzoic acid with ethanol using a sulfuric acid catalyst. The following compounds are found in the crude reaction mixture: ethyl benzoate (major component), benzoic acid, ethanol, and sulfuric acid. Using a handbook, obtain the solubility properties in water for each of these compounds (see Technique 4, p. 574). Indicate how you would remove benzoic acid, ethanol, and sulfuric acid from ethyl benzoate. At some point in the purification, you should also use an aqueous sodium bicarbonate solution.

7. Calculate the weight of water that could be removed from a wet organic phase using 50.0 mg of magnesium sulfate. Assume that it gives the hydrate listed in Table 12.2.

8. Explain exactly what you would do when performing the following laboratory instructions:
   a. “Wash the organic layer with 1.0 mL of 1 M aqueous sodium bicarbonate.”
   b. “Extract the aqueous layer three times with 1-mL portions of methylene chloride.”

9. Just prior to drying an organic layer with a drying agent, you notice water droplets in the organic layer. What should you do next?

10. What should you do if there is some question about which layer is the organic one during an extraction procedure?

11. Saturated aqueous sodium chloride ($d = 1.2 \text{ g/mL}$) is added to the following mixtures in order to dry the organic layer. Which layer is likely to be on the bottom in each case?
   a. Sodium chloride layer or a layer containing a high-density organic compound dissolved in methylene chloride ($d = 1.4 \text{ g/mL}$)
   b. Sodium chloride layer or a layer containing a low-density organic compound dissolved in methylene chloride ($d = 1.1 \text{ g/mL}$)
TECHNIQUE 13

Physical Constants of Liquids: The Boiling Point and Density

PART A. BOILING POINTS AND THERMOMETER CORRECTION

13.1 The Boiling Point

As a liquid is heated, the vapor pressure of the liquid increases to the point at which it just equals the applied pressure (usually atmospheric pressure). At this point, the liquid is observed to boil. The normal boiling point is measured at 760 mm Hg (760 torr), or 1 atm. At a lower applied pressure, the vapor pressure needed for boiling is also lowered, and the liquid boils at a lower temperature. The relation between applied pressure and temperature of boiling for a liquid is determined by its vapor pressure–temperature behavior. Figure 13.1 is an idealization of the typical vapor pressure–temperature behavior of a liquid.

Because the boiling point is sensitive to pressure, it is important to record the barometric pressure when determining a boiling point if the determination is being conducted at an elevation significantly above or below sea level. Normal atmospheric variations may affect the boiling point, but they are usually of minor importance. However, if a boiling point is being monitored during the course of a vacuum distillation (Technique 16) that is being performed with an aspirator or a vacuum pump, the variation from the atmospheric value will be especially marked. In these cases, it is important to know the pressure as accurately as possible.

As a rule of thumb, the boiling point of many liquids drops about 0.5°C for a 10-mm decrease in pressure when in the vicinity of 760 mm Hg. At lower pressures, a 10°C drop in boiling point is observed for each halving of the pressure. For example, if the observed boiling point of a liquid is 150°C at 10 mm pressure, then the boiling point would be about 140°C at 5 mm Hg.

A more accurate estimate of the change in boiling point with a change of pressure can be made by using a nomograph. In Figure 13.2, a nomograph

Figure 13.1
The vapor pressure–temperature curve for a typical liquid.
is given, and a method is described for using it to obtain boiling points at various pressures when the boiling point is known at some other pressure.

Several experimental methods of determining boiling points are available. Selecting a method depends on how much liquid is available and the availability of specific apparatus. In either microscale or macroscale experiments in which 0.3–0.5 mL of liquid is available, the semimicroscale direct method is usually most reliable. If less material is available, it will be necessary to perform either the semimicroscale or microscale inverted capillary method. With practice, these methods can be reliable, too. With larger quantities in both microscale and macroscale experiments, the boiling point can be observed best while performing a distillation.

**Semimicroscale Direct Method.** The apparatus for this method is shown in Figure 13.3. With this method, the bulb of the thermometer can be immersed in vapor from the boiling liquid for a period long enough to allow it to equilibrate and give a good temperature reading. A 13-mm × 100-mm test tube works well in this procedure. Use 0.3–0.5 mL of liquid and a small, inert carborundum (black) boiling stone. This method works best with a partial
immersion (76 mm) mercury thermometer (see Section 13.3, p. 700). It is not necessary to perform a stem correction with this type of thermometer.

Place the bulb of the thermometer as close as possible to the boiling liquid without actually touching it. The best heating device is a hot plate with either an aluminum block or a sand bath.1

While you are heating the liquid, it is helpful to record the temperature at 1-minute intervals. This makes it easier to keep track of changes in the temperature and to know when the liquid has reached the boiling point. The liquid must boil vigorously, such that you see a reflux ring above the bulb of the thermometer and drops of liquid condensing on the sides of the test tube. Note that with some liquids, the reflux ring will be faint, and you must looked closely to see it. The boiling point is reached when the temperature reading on the thermometer has remained constant at its highest observed value for 2–3 minutes. It is usually best to turn the heat control on the hot plate to a relatively high setting initially, especially if you are starting with a cold hot plate and aluminum block or sand bath. If the temperature begins to level off at a relatively low temperature (less than about 100°C) or if the reflux ring reaches the immersion ring on the thermometer, you should turn down the heat-control setting immediately.

Two problems can occur when you perform this boiling-point procedure. The first is much more common and occurs when the temperature appears to be leveling off at a temperature below the boiling point of the liquid. This is more likely to happen with a relatively high-boiling liquid (boiling points greater than about 150°C) or when the sample is not heated sufficiently. The best way to prevent this problem is to heat the sample more strongly. With high-boiling liquids, it may be helpful to wait for the temperature to remain constant for 3–4 minutes to make sure that you have reached the actual boiling point.

The second problem, which is rare, occurs when the liquid evaporates completely, and the temperature inside the dry test tube may rise higher than the actual boiling point of the liquid. This is more likely to happen with low-boiling liquids (boiling point less than 100°C) or if the temperature on the hot plate is set too high for too long. To check for this possibility, observe the amount of liquid remaining in the test tube as soon as you have finished with the procedure. If there is no liquid remaining, it is possible that the highest temperature you observed is greater than the boiling point of the liquid. In this case, you should repeat the boiling-point determination, heating the sample less strongly or using more sample.

Depending on the skill of the person performing this technique, boiling points may be slightly inaccurate. When experimental boiling points are inaccurate, it is more common for them to be lower than the literature value, and inaccuracies are more likely to occur for higher-boiling liquids. With higher-boiling liquids, the difference may be as much as 5°C. Carefully following the previous instructions will make it more likely that your experimental value will be close to the literature value.

1 Note to the Instructor: The aluminum block should have a hole drilled in it that goes all the way through the block and is just slightly larger than the outside diameter of the test tube. A sand bath can be conveniently prepared by adding 40 mL of sand to a 150-mL beaker or by using a heating mantle partially filled with sand. For additional comments about these heating methods, see the Instructor’s Manual, Experiment 7, “Infrared Spectroscopy and Boiling-Point Determination.”
With smaller amounts of material, you can carry out a microscale or semimicroscale determination of the boiling point by using the apparatus shown in Figure 13.4.

Semimicroscale Inverted Capillary Method. To carry out the semimicroscale determination, attach a piece of 5-mm glass tubing (sealed at one end) to a thermometer with a rubber band or a thin slice of rubber tubing. The liquid whose boiling point is being determined is introduced with a Pasteur pipet into this piece of tubing, and a short piece of melting-point capillary (sealed at one end) is dropped in with the open end down. The whole unit is then placed in a Thiele tube. The rubber band should be placed above the level of the oil in the Thiele tube; otherwise, the band may soften in the hot oil. When positioning the band, keep in mind that the oil will expand when heated. Next, the Thiele tube is heated in the same fashion as described in Technique 9, Section 9.6, page 631, for determining a melting point. Heating is continued until a rapid and continuous stream of bubbles emerges from the inverted capillary. At this point, you should stop heating. Soon, the stream of bubbles slows down and stops. When the bubbles stop, the liquid enters the capillary tube. The moment at which the liquid enters the capillary tube corresponds to the boiling point of the liquid, and the temperature is recorded.

Microscale Inverted Capillary Method. In microscale experiments, there often is too little product available to use the semimicroscale method just described. However, the method can be scaled down in the following manner.
The liquid is placed in a 1-mm melting-point capillary tube to a depth of about 4–6 mm (see Figure 13.4B). Use a syringe or a Pasteur pipet that has had its tip drawn thinner to transfer the liquid into the capillary tube. It may be necessary to use a centrifuge to transfer the liquid to the bottom of the tube. Next, prepare an appropriately sized inverted capillary, or bell.

The easiest way to prepare a bell is to use a commercial micropipet, such as a 10-μL Drummond “microcap.” These are available in vials of 50 or 100 microcaps and are inexpensive. To prepare the bell, cut the microcap in half with a file or scorer and then seal one end by inserting it a small distance into a flame, turning it on its axis until the opening closes.

If microcaps are not available, a piece of 1-mm open-end capillary tubing (same size as a melting-point capillary) can be rotated along its axis in a flame while being held horizontally. Use your index fingers and thumbs to rotate the tube; do not change the distance between your two hands while rotating. When the tubing is soft, remove it from the flame and pull it to a thinner diameter. When pulling, keep the tube straight by moving both your hands and your elbows outward by about 4 inches. Hold the pulled tube in place a few moments until it cools. Using the edge of a file or your fingernail, break out the thin center section. Seal one end of the thin section in the flame; then break it to a length that is about one and one-half times the height of your sample liquid (6–9 mm). Be sure the break is done squarely. Invert the bell (open end down), and place it in the capillary tube containing the sample liquid. Push the bell to the bottom with a fine copper wire if it adheres to the side of the capillary tube. A centrifuge may be used if you prefer. Figure 13.5 shows the construction method for the bell and the final assembly.

Place the microscale assembly in a standard melting-point apparatus (or a Thiele tube if an electrical apparatus is not available) to determine the boiling point. Heating is continued until a rapid and continuous stream of bubbles emerges from the inverted capillary. At this point, stop heating. Soon, the stream of bubbles slows down and stops. When the bubbles stop, the liquid enters the capillary tube. The moment at which the liquid enters the capillary tube corresponds to the boiling point of the liquid, and the temperature is recorded.

**Explanation of the Method.** During the initial heating, the air trapped in the inverted bell expands and leaves the tube, giving rise to a stream of bubbles. When the liquid begins boiling, most of the air has been expelled; the bubbles of gas are due to the boiling action of the liquid. Once the heating is stopped, most of the vapor pressure left in the bell comes from the vapor of the heated liquid that seals its open end. There is always vapor in equilibrium with a heated liquid. If the temperature of the liquid is above its boiling point, the pressure of the trapped vapor will either exceed or equal the atmospheric pressure. As the liquid cools, its vapor pressure decreases. When the vapor pressure drops just below atmospheric pressure (just below the boiling point), the liquid is forced into the capillary tube.

**Difficulties.** Three problems are common to this method. The first arises when the liquid is heated so strongly that it evaporates or boils away. The second arises when the liquid is not heated above its boiling point before heating is discontinued. If the heating is stopped at any point below the actual boiling point of the sample, the liquid enters the bell immediately, giving an apparent boiling point that is too low. Be sure you observe a
continuous stream of bubbles, too fast for individual bubbles to be distin-
guished, before lowering the temperature. Also be sure the bubbling action
decreases slowly before the liquid enters the bell. If your melting-point ap-
paratus has fine enough control and fast response, you can actually begin
heating again and force the liquid out of the bell before it becomes com-
pletely filled with the liquid. This allows a second determination to be per-
fomed on the same sample. The third problem is that the bell may be so
light that the bubbling action of the liquid causes the bell to move up the
capillary tube. This problem can sometimes be solved by using a longer
(heavier) bell or by sealing the bell so that a larger section of solid glass is
formed at the sealed end of the bell.

When measuring temperatures above 150°C, thermometer errors can
become significant. For an accurate boiling point with a high-boiling liquid,
you may wish to apply a stem correction to the thermometer, as described
in Section 13.3, or to calibrate the thermometer, as described in Technique 9,
Section 9.9, page 635.

Microscale or Macroscale–Distillation Method. When you have large quan-
tities of material, you can simply record the boiling point (or boiling range) as
viewed on a thermometer while performing a simple distillation (see Tech-
nique 14). When this method is used to determine a boiling point, it is best
to use a partial immersion mercury thermometer for more accurate readings.

PROBLEMS

1. Using the pressure–temperature alignment chart in Figure 13.2, answer the follow-
ing questions.
   a. What is the normal boiling point (at 760 mm Hg) for a compound that boils at
      150°C at 10 mm Hg pressure?
   b. At what temperature would the compound in (a) boil if the pressure were
      40 mm Hg?
   c. A compound was distilled at atmospheric pressure and had a boiling point
      of 285°C. What would be the approximate boiling range for this compound at
      15 mm Hg?

2. Calculate the corrected boiling point for nitrobenzene by using the method given in
   Section 13.3. The boiling point was determined using an apparatus similar to that
   shown in Figure 13.3. Assume that a total immersion thermometer was used. The
   observed boiling point was 205°C. The reflux ring in the test tube just reached up to
   the 0°C mark on the thermometer. A second thermometer suspended alongside the
   test tube, at a slightly higher level than the one inside, gave a reading of 35°C.
3. Suppose that you had calibrated the thermometer in your melting-point apparatus against a series of melting-point standards. After reading the temperature and converting it using the calibration chart, should you also apply a stem correction? Explain.

4. The density of a liquid was determined by the automatic pipet method. A 100-µL automatic pipet was used. The liquid had a mass of 0.082 g. What was the density in grams per milliliter of the liquid?

5. During the microscale boiling-point determination (see p. 697) of an unknown liquid, heating was discontinued at 154°C and the liquid immediately began to enter the inverted bell. Heating was begun again at once, and the liquid was forced out of the bell. Heating was again discontinued at 165°C, at which time a rapid stream of bubbles emerged from the bell. On cooling, the rate of bubbling gradually diminished until the liquid reached a temperature of 161°C and entered and filled the bell. Explain this sequence of events. What was the boiling point of the liquid?

14 TECHNIQUE 14

Simple Distillation

Distillation is the process of vaporizing a liquid, condensing the vapor, and collecting the condensate in another container. This technique is useful for separating a liquid mixture when the components have different boiling points or when one of the components will not distill. It is one of the principal methods of purifying a liquid. Four basic distillation methods are available to the chemist: simple distillation, vacuum distillation (distillation at reduced pressure), fractional distillation, and steam distillation. This technique chapter will discuss simple distillation. Vacuum distillation will be discussed in Technique 16. Fractional distillation will be discussed in Technique 15, and steam distillation will be discussed in Technique 18.

14.1 The Evolution of Distillation Equipment

There are probably more types and styles of distillation apparatus than exist for any other technique in chemistry. Over the centuries, chemists have devised just about every conceivable design. The earliest known types of distillation apparatus were the alembic and the retort (Fig. 14.1). They were
used by alchemists in the Middle Ages and the Renaissance and probably even earlier by Arabic chemists. Most other distillation equipment has evolved as variations on these designs.

Figure 14.1 shows several stages in the evolution of distillation equipment as it relates to the organic laboratory. It is not intended to be a complete history; rather, it is representative. Up until recent years, equipment based on the retort design was common in the laboratory. Although the retort itself was still in use early in the twentieth century, it had evolved by that time into the distillation flask and water-cooled condenser combination. This early equipment was connected with corks. By 1958, most introductory laboratories were beginning to use “organic lab kits” that included glassware connected by standard-taper glass joints. The original lab kits contained large 24/40 joints. Within a short time, they became smaller, with 19/22 and even 14/20 joints. These later kits are still being used today in many organic courses. Small-scale variations of these kits are also used today by chemical researchers, but they are too expensive to use in an introductory laboratory. Instead, the “microscale” equipment you
are using in this course is coming into common use. This equipment has ISO 14/10 standard-taper joints, threaded outer joints with screwcap connectors, and an internal O-ring. The distillation apparatus in microscale kits is designed for work with small amounts of material, and it is different from the more traditional larger-scale equipment. It is perhaps more closely related to the alembic design than to that of the retort. Because both types of equipment are in use today, after we describe microscale equipment, we will also show the equivalent large-scale apparatus used to perform distillation.

In the traditional distillation of a pure substance, vapor rises from the distillation flask and comes into contact with a thermometer that records its temperature. The vapor then passes through a condenser, which reliquefies the vapor and passes it into the receiving flask. The temperature observed during the distillation of a pure substance remains constant throughout the distillation so long as both vapor and liquid are present in the system (see Fig. 14.2A). When a liquid mixture is distilled, often the temperature does not remain constant but increases throughout the distillation. The reason for this is that the composition of the vapor that is distilling varies continuously during the distillation (see Fig. 14.2B).

For a liquid mixture, the composition of the vapor in equilibrium with the heated solution is different from the composition of the solution itself. This is shown in Figure 14.3, which is a phase diagram of the typical vapor-liquid relationship for a two-component system (A + B).

On this diagram, horizontal lines represent constant temperatures. The upper curve represents vapor composition, and the lower curve represents liquid composition. For any horizontal line (constant temperature), like that shown at $t$, the intersections of the line with the curves give the compositions of the liquid and the vapor that are in equilibrium with each other at that temperature. In the diagram, at temperature $t$, the intersection of the curve at X indicates that liquid of composition $W$ will be in equilibrium with vapor of composition $Z$, which corresponds to the intersection at Y. Composition is given as a mole percentage of A and B in the mixture. Pure A, which boils at temperature $t_A$, is represented at the left. Pure B, which boils at temperature $t_B$, is represented on the right. For either pure A or pure B, the vapor and liquid curves meet at the boiling point. Thus, either pure A or pure B will distill at a constant temperature ($t_A$ or $t_B$). Both the vapor and the

14.2 Distillation Theory

Figure 14.2
Three types of temperature behavior during a simple distillation. A. A single pure component. B. Two components of similar boiling points. C. Two components with widely differing boiling points. Good separations are achieved in A and C.
liquid must have the same composition in either of these cases. This is not the case for mixtures of A and B.

A mixture of A and B of composition W will have the following behavior when heated. The temperature of the liquid mixture will increase until the boiling point of the mixture is reached. This corresponds to following line WX from W to X, the boiling point of the mixture \( t \). At temperature \( t \) the liquid begins to vaporize, which corresponds to line XY. The vapor has the composition corresponding to Z. In other words, the first vapor obtained in distilling a mixture of A and B does not consist of pure A. It is richer in A than the original mixture but still contains a significant amount of the higher-boiling component B, even from the very beginning of the distillation. The result is that it is never possible to separate a mixture completely by a simple distillation. However, in two cases it is possible to get an acceptable separation into relatively pure components. In the first case, if the boiling points of A and B differ by a large amount (>100 degrees) and if the distillation is carried out carefully, it will be possible to get a fair separation of A and B. In the second case, if A contains a fairly small amount of B (<10%), a reasonable separation of A from B can be achieved. When the boiling-point differences are not large and when highly pure components are desired, it is necessary to perform a fractional distillation. Fractional distillation is described in Technique 15, in which the behavior during a simple distillation is also considered in detail. Note only that as vapor distills from the mixture of composition W (Fig. 14.3), it is richer in A than is the solution. Thus, the composition of the material left behind in the distillation becomes richer in B (moves to the right from W toward pure B in the graph).

A mixture of 90% B (dotted line on the right side in Fig. 14.3) has a higher boiling point than at W. Hence, the temperature of the liquid in the distillation flask will increase during the distillation, and the composition of the distillate will change (as is shown in Fig. 14.3B).

When two components that have a large boiling-point difference are distilled, the temperature remains constant while the first component distills. If the temperature remains constant, a relatively pure substance is being distilled. After the first substance distills, the temperature of the

Figure 14.3
Phase diagram for a typical liquid mixture of two components.
vapors rises, and the second component distills, again at a constant temperature. This is shown in Figure 14.2C. A typical application of this type of distillation might be an instance of a reaction mixture containing the desired component A (bp 140°C) contaminated with a small amount of undesired component B (bp 250°C) and mixed with a solvent such as diethyl ether (bp 36°C). The ether is removed easily at low temperature. Pure A is removed at a higher temperature and collected in a separate receiver. Component B can then be distilled, but it usually is left as a residue and not distilled. This separation is not difficult and represents a case where simple distillation might be used to advantage.

**14.3 Microscale Equipment**

Most large-scale distillation equipment requires the distilled liquid to travel a long distance from the distillation flask, through the condenser, to the receiving flask. When working at the microscale level, a long distillation path must be avoided. With small quantities of liquid, there are too many opportunities to lose all the sample. The liquid will adhere to, or wet, surfaces and get lost in every little nook and cranny of the system. A system with a long path also has a large volume, and a small amount of liquid may not produce enough vapor to fill it. Small-scale distillation requires a “short path” distillation. In order to make the distilling path as short as possible, the Hickman head has been adopted as the principal receiving device for most microscale distilling operations.

**The Hickman Head.** Two types of Hickman head (also called a Hickman “still”) are shown in Figure 14.4. One of these variations has a convenient opening, or port, in the side, making removal of liquid that has collected in it easier. In operation, the liquid to be distilled is placed in a flask or vial attached to the bottom joint of the Hickman head and heated. If desired, you can attach a condenser to the top joint. Either a magnetic spin vane or a boiling stone is used to prevent bumping. Some typical assemblies are shown in Figures 14.5 and 14.7. The vapors of the heated liquid rise upward and are cooled and condensed on either the walls of the condenser or, if no condenser is used, on the inside walls of the Hickman head itself. As liquid drains downward, it collects in the circular well at the bottom of the still.

**Collecting Fractions.** The liquid that distills is called the **distillate.** Portions of the distillate collected during the course of a distillation are called **fractions.** A small fraction (usually discarded) collected before the distillation is begun in earnest is called a **forerun.** The well in a Hickman head can contain anywhere from 1 to 2 mL of liquid. In the style with the side port, fractions may be removed by opening the port and inserting a Pasteur pipet (Fig. 14.6C). The unported head works equally well, but the head is emptied from the top by using a Pasteur pipet (Fig. 14.6A). If a condenser or an internal thermometer is used, the distilling apparatus must be partially disassembled to remove liquid when the well fills. In some stills, the inner diameter of the head is small, and it is difficult to reach in at an angle with the pipet and make contact with the liquid. To remedy this problem, you may be able to use the longer (9-inch) Pasteur pipet instead of the shorter (5 3⁄4-inch) one. The longer pipet has a much longer narrow section (tip) and can adapt more effectively to the required angle. The disadvantage of the longer tip is that you are more likely to break it off inside the still. You may prefer to modify a short pipet by bending its tip slightly in a flame (Fig. 14.6B).
Choice of Condenser. If you are careful (slow heating) or if the liquid to be distilled has a high boiling point, it many not be necessary to use a condenser with the Hickman head (Fig. 14.7). In this case, the liquid being distilled must condense on the cooler sides of the head itself without any being lost through evaporation. If the liquid has a low boiling point or is very volatile, a condenser must be used. With very volatile liquids, a water-cooled condenser must be used; however, an air-cooled condenser may suffice for less demanding cases. When using a water condenser, remember that water should enter the lower opening and exit from the upper one. If the hoses carrying the water in and out are connected in reverse fashion, the water jacket of the condenser will not fill completely.

Sealed Systems. Whenever you perform a distillation, be sure the system you are heating is not sealed off completely from the outside atmosphere.
During a distillation, the air and vapors inside the system will both expand and contract. If pressure builds up inside a sealed system, the apparatus may explode. In performing a distillation, you should leave a small opening at the far end of the system. If water vapor could be harmful to the substances being distilled, a calcium chloride drying tube may be used to protect the system from moisture. Carefully examine each system discussed to see how an opening to the outside is provided.

External Monitoring of Temperature. The simple assembly using the Hickman head shown in Figure 14.5 does not monitor the temperature inside the apparatus. Instead, the temperature is monitored externally with a thermometer placed in an aluminum block.

**CAUTION**

You should not use a mercury thermometer with an aluminum block. If it breaks, the mercury will vaporize on the hot surface. Instead, use a nonmercury glass thermometer, a metal dial thermometer, or a digital electronic temperature-measuring device.

---

**Figure 14.6**

Removing fractions.
External monitoring of the temperature has the disadvantage that the exact temperature at which liquid distills is never known. In many cases, this does not matter or is unavoidable, and the boiling point of the distilled liquid can be checked later by performing a microboiling-point determination (Technique 13, Section 13.2, p. 695).

As a rule, there is at least a 15-degree difference in temperature between the temperature of the aluminum block or sand bath and that of the liquid in the heated distillation vial or flask. However, the magnitude of this difference cannot be relied on. Keep in mind that the liquid in the vial or flask may be at a different temperature than the vapor that is distilling. In many procedures in this text, the approximate temperature of the heating device will be given instead of the boiling point of the liquid involved. Because this method of monitoring the temperature is rather approximate, you will need to make the actual heater setting based on what is supposed to be occurring in the vial or flask.

**Internal Monitoring of Temperature.** When you wish to monitor the actual temperature of a distillation, a thermometer must be placed inside the apparatus. Figures 14.7 and 14.8 show distillation assemblies that use an internal thermometer. The apparatus in Figure 14.7A represents the simplest possible distillation assembly. It does not use a condenser, and the

---

**Figure 14.7**

*Basic microscale distillation (internal monitoring of temperature).*

External monitoring of the temperature has the disadvantage that the exact temperature at which liquid distills is never known. In many cases, this does not matter or is unavoidable, and the boiling point of the distilled liquid can be checked later by performing a microboiling-point determination (Technique 13, Section 13.2, p. 695).

As a rule, there is at least a 15-degree difference in temperature between the temperature of the aluminum block or sand bath and that of the liquid in the heated distillation vial or flask. However, the magnitude of this difference cannot be relied on. Keep in mind that the liquid in the vial or flask may be at a different temperature than the vapor that is distilling. In many procedures in this text, the approximate temperature of the heating device will be given instead of the boiling point of the liquid involved. Because this method of monitoring the temperature is rather approximate, you will need to make the actual heater setting based on what is supposed to be occurring in the vial or flask.

**Internal Monitoring of Temperature.** When you wish to monitor the actual temperature of a distillation, a thermometer must be placed inside the apparatus. Figures 14.7 and 14.8 show distillation assemblies that use an internal thermometer. The apparatus in Figure 14.7A represents the simplest possible distillation assembly. It does not use a condenser, and the
thermometer is suspended from a clamp. It is possible to add either an air or a water condenser to this basic assembly (Fig. 14.7B) and maintain internal monitoring of the temperature.

In the arrangement shown in Figure 14.8, a thermometer adapter is used. A thermometer adapter (Fig. 14.9A) provides a convenient way of holding a thermometer in place. The Claisen head is used to provide an opening to the atmosphere, thereby avoiding a sealed system. With the Claisen head, a drying tube may be used to protect the system from atmospheric moisture.

If protection from atmospheric moisture is not required, the multipurpose adapter may be used. The multipurpose adapter (Fig. 14.9B) replaces both the thermometer adapter and the Claisen head. With this adapter, the necessary opening to the atmosphere is provided by the side arm. The threaded joint holds the thermometer in place.

Carefully notice the position of the thermometer in Figures 14.7 and 14.8. The bulb of the thermometer must be placed in the stem of the Hickman

Figure 14.8
Basic microscale distillation using thermometer adapter (internal monitoring of temperature).
head, just below the well, or it will not read the temperature correctly. The distillation temperature can be monitored most accurately by using a partial immersion mercury thermometer (see Technique 13, Section 13.3, p. 700).

NOTE: It is good practice to monitor the temperature internally whenever possible.

**Boiling Stones or Stirring.** A boiling stone should be used during distillation in order to prevent bumping. As an alternative, the liquid being distilled may be rapidly stirred. A triangular spin vane of the correct size should be used when distilling from a conical vial, whereas a stirring bar should be used when distilling from a round-bottom flask.

**Size of Distillation Flask.** As a rule, the distillation flask or vial should not be filled to more than two thirds of its total capacity. This allows room for boiling and stirring action, and it prevents contamination of the distillate by bumping. A flask that is too large should also be avoided. With too large a flask, the holdup is excessive; the holdup is the amount of material that cannot distill because some vapor must fill the empty flask.

**Assembling the Apparatus.** You should not grease the joints when assembling the apparatus. Ungreased joints seal well enough to allow you to perform a simple distillation. Stopcock grease can introduce a serious contaminant into your product.

**Rate and Degree of Heating.** Take care not to distill too quickly. If you vaporize liquid at a rate faster than it can be recondensed, some of your product may be lost by evaporation. On the other hand, you should not distill too slowly. This may also lead to loss of product because there is a longer period during which vapors can escape. Carefully examine your apparatus during distillation to monitor the position of either a reflux ring or a wet appearance on the surface of the glass. Either of these indicates the place at which condensation is occurring. The position at which condensation occurs should be well inside the Hickman head. Be sure that liquid is collecting in
the well. If all the surfaces are shiny (wet) and there is no distillate, you are losing material.

**NOTE:** A slower rate of heating also helps to avoid bumping.

If you are using a sand bath, material may be lost because the hot sand bath radiates too much heat upward and warms the Hickman still. If you believe this to be the case, it can often be remedied by placing a small square of aluminum foil over the top of the sand bath. Make a tear from one edge to the center of the foil to wrap it around the apparatus.

When you wish to distill quantities of liquid that are larger than 2–3 mL, different equipment is required. Most manufacturers of microscale equipment make two pieces of conventional distillation equipment sized to work with the 14/10 microscale kit components. These two pieces, the **distillation head** and the **bent vacuum adapter**, are not provided in student microscale kits but must be purchased separately. Figure 14.10 shows a semimicroscale assembly using these components. Note that the bulb of the thermometer must be placed below the side arm if it is to be bathed in vapor and give a correct temperature reading. This apparatus assumes that a condenser is not necessary; however, you could easily insert one between the distilling head and the bent vacuum adapter. This insertion would produce a completely traditional distillation apparatus but would use microscale equipment. (See Figure on p. 714.) A distillation apparatus constructed from a “macroscale” organic laboratory kit is shown in Figure 14.11. This type of equipment is being used today in organic laboratories that have not converted to microscale. Electrically regulated **heating mantles** are often used with this equipment.

**Figure 14.10**
Semimicroscale distillation (*requires special pieces).
1. Using Figure 14.3, answer the following questions.
   a. What is the molar composition of the vapor in equilibrium with a boiling liquid that has a composition of 60% A and 40% B?
   b. A sample of vapor has the composition 50% A and 50% B. What is the composition of the boiling liquid that produced this vapor?
2. Use an apparatus similar to that shown in Figure 14.10 and assume that the round-bottom flask holds 10 mL and that the Claisen head has an internal volume of about 2 mL in the vertical section. At the end of a distillation, vapor would fill this volume, but it could not be forced through the system. No liquid would remain in the distillation flask. Assuming this holdup volume of 12 mL, use the ideal gas law and assume a boiling point of 100°C (760 mm Hg) to calculate the number of microliters of liquid ($d = 0.9$ g/mL, $MW = 200$) that would recondense into the distillation flask on cooling.
3. Explain the significance of a horizontal line connecting a point on the lower curve with a point on the upper curve (such as line XY) in Figure 14.3.
4. Using Figure 14.3, determine the boiling point of a liquid having a molar composition of 50% A and 50% B.
5. What is the approximate difference between the temperature of a boiling liquid in a conical vial and the temperature read on an external thermometer when both are placed on an aluminum block?
6. Where should the thermometer bulb be located for internal monitoring in
a. a distillation apparatus using a Hickman head?
b. a large-scale distillation using a Claisen head with a water condenser placed beyond it?

7. Under what conditions can a good separation be achieved with a simple distillation?

---

**Fractional Distillation**

Simple distillation, described in Technique 14, works well for most routine separation and purification procedures for organic compounds. When boiling-point differences of components to be separated are not large, however, fractional distillation must be used to achieve a good separation.

**PART A. FRACTIONAL DISTILLATION**

15.1 Differences between Simple and Fractional Distillation

When an ideal solution of two liquids, such as benzene (bp 80°C) and toluene (bp 110°C), is distilled by simple distillation, the first vapor produced will be enriched in the lower-boiling component (benzene). However, when that initial vapor is condensed and analyzed, the distillate will not be pure benzene. The boiling-point difference of benzene and toluene (30°C) is too small to achieve a complete separation by simple distillation. Following the principles outlined in Technique 14, Section 14.2 (pp. 705–707), and using the vapor–liquid composition curve given in Figure 15.1, you can see what would happen if you started with an equimolar mixture of benzene and toluene.

Following the dashed lines shows that an equimolar mixture (50 mole % benzene) would begin to boil at about 91°C and, far from being 100% benzene, the distillate would contain about 74 mole % benzene and 26 mole % toluene. As the distillation continued, the composition of the undistilled liquid would move in the direction of A' (there would be increased toluene due to removal of more benzene than toluene), and the corresponding vapor would contain a progressively smaller amount of benzene. In effect, the temperature of the distillation would continue to increase throughout the distillation (as in Figure 14.2B, p. 705), and it would be impossible to obtain any fraction that consisted of pure benzene.

Suppose, however, that we are able to collect a small quantity of the first distillate that was 74 mole % benzene, and to redistill it. Using Figure 15.1, we can see that this liquid would begin to boil at about 84°C and would give an initial distillate containing 90 mole % benzene. If we were experimentally able to continue taking small fractions at the beginning of each distillation and redistill them, we would eventually reach a liquid with a composition of nearly 100 mole % benzene. However, because we only took a small amount of material at the beginning of each distillation, we would have lost most of the material we started with. To recapture a reasonable amount of benzene, we would have to process each of the fractions left behind in the same way as our early fractions. As each of them was partially distilled, the material advanced would become progressively richer in benzene, whereas...
that left behind would become progressively richer in toluene. It would require thousands (maybe millions) of such microdistillations to separate benzene from toluene.

Obviously, the procedure just described would be very tedious; fortunately, it need not be performed in usual laboratory practice. Fractional distillation accomplishes the same result. You simply have to use a column inserted between the distillation flask and the receiver (Hickman head), as shown in Figure 15.2. This fractionating column is filled, or packed, with a suitable material such as a stainless steel sponge. This packing allows a mixture of benzene and toluene to be subjected continuously to many vaporization–condensation cycles as the material moves up the column. With each cycle within the column, the composition of the vapor is progressively enriched in the lower-boiling component (benzene). Nearly pure benzene (bp 80°C) finally emerges from the top of the column, condenses, and passes into the receiving head or flask. This process continues until all the benzene is removed. The distillation must be carried out slowly to ensure that numerous vaporization–condensation cycles occur. When nearly all the benzene has been removed, the temperature begins to rise, and a small amount of a second fraction, which contains some benzene and toluene, may be collected. When the temperature reaches 110°C, the boiling point of pure toluene, the vapor is condensed and collected as the third fraction. A plot of boiling point versus volume of condensate (distillate) would resemble Figure 15.3. This separation would be much better than that achieved by simple distillation (Figure 15.1).

15.2 Vapor–Liquid Composition Diagrams

A vapor–liquid composition-phase diagram like the one in Figure 15.4 can be used to explain the operation of a fractionating column with an ideal solution of two liquids, A and B. An ideal solution is one in which the two liquids are chemically similar, miscible (mutually soluble) in all proportions, and do not interact. Ideal solutions obey Raoult’s Law. Raoult’s Law is explained in detail in Section 15.3.

The phase diagram relates the compositions of the boiling liquid (lower curve) and its vapor (upper curve) as a function of temperature. Any horizontal line drawn across the diagram (a constant-temperature line) intersects the diagram in two places. These intersections relate the vapor composition to
the composition of the boiling liquid that produces that vapor. By convention, composition is expressed either in mole fraction or in mole percentage. The mole fraction is defined as follows:

\[
\text{Mole fraction A} = N_A = \frac{\text{moles A}}{\text{moles A} + \text{moles B}}
\]

\[
\text{Mole fraction B} = N_B = \frac{\text{moles B}}{\text{moles A} + \text{moles B}}
\]

\[
N_A + N_B = 1
\]

\[
\text{Mole percentage A} = N_A \times 100
\]

\[
\text{Mole percentage B} = N_B \times 100
\]

The horizontal and vertical lines shown in Figure 15.4 represent the processes that occur during a fractional distillation. Each of the horizontal lines ($L_1V_1, L_2V_2$, etc.) represents the vaporization step of a given
vaporization–condensation cycle and represents the composition of the vapor in equilibrium with liquid at a given temperature. For example, at 63°C a liquid with a composition of 50% A (L₃ on the diagram) would yield vapor of composition 80% A (V₃ on diagram) at equilibrium. The vapor is richer in the lower-boiling component A than the original liquid was.

Each of the vertical lines (V₁L₂, V₂L₃, etc.) represents the condensation step of a given vaporization–condensation cycle. The composition does not change as the temperature drops on condensation. The vapor at V₃, for example, condenses to give a liquid (L₄ on the diagram) of composition 80% A with a drop in temperature from 63°C to 53°C.

In the example shown in Figure 15.4, pure A boils at 50°C and pure B boils at 90°C. These two boiling points are represented at the left- and right-hand edges of the diagram, respectively. Now consider a solution that contains only 5% of A but 95% of B. (Remember that these are mole percentages.) This solution is heated (following the dashed line) until it is observed to boil at L₁ (87°C). The resulting vapor has composition V₁ (20% A, 80% B). The vapor is richer in A than the original liquid, but it is by no means pure A. In a simple distillation apparatus, this vapor would be condensed and passed into the receiver in a very impure state. However, with a fractionating column in place, the vapor is condensed in the column to give liquid L₂ (20% A, 80% B). Liquid L₂ is immediately revaporized (bp 78°C) to give a vapor of composition V₂ (50% A, 50% B), which is condensed to give liquid L₃. Liquid L₃ is revaporized (bp 63°C) to give vapor of composition V₃ (80% A, 20% B), which is condensed to give liquid L₄. Liquid L₄ is revaporized (bp 53°C) to give vapor of composition V₄ (95% A, 5% B). This process continues to V₅, which condenses to give nearly pure liquid A. The fractionating process follows the stepped lines in the figure downward and to the left.

As this process continues, all of liquid A is removed from the distillation flask or vial, leaving nearly pure B behind. If the temperature is raised, liquid B may be distilled as a nearly pure fraction. Fractional distillation will
have achieved a separation of A and B, a separation that would have been nearly impossible with simple distillation. Notice that the boiling point of the liquid becomes lower each time it vaporizes. Because the temperature at the bottom of a column is normally higher than the temperature at the top, successive vaporizations occur higher and higher in the column as the composition of the distillate approaches that of pure A. This process is illustrated in Figure 15.5, where the composition of the liquids, their boiling points, and the composition of the vapors present are shown alongside the fractionating column.

Two liquids (A and B) that are miscible and that do not interact form an ideal solution and follow Raoult’s Law. The law states that the partial vapor pressure of component A in the solution \( P_A \) equals the vapor pressure of pure A \( P_A^\circ \) times its mole fraction \( N_A \) (Eq. 1). A similar expression can be written for component B (Eq. 2). The mole fractions \( N_A \) and \( N_B \) were defined in Section 15.2.

\[
\text{Partial vapor pressure of A in solution} = P_A = (P_A^\circ)(N_A) \quad [1]
\]

\[
\text{Partial vapor pressure of B in solution} = P_B = (P_B^\circ)(N_B) \quad [2]
\]

\( P_A^\circ \) is the vapor pressure of pure A, independent of B. \( P_B^\circ \) is the vapor pressure of B, independent of A. In a mixture of A and B, the partial vapor pressures are added to give the total vapor pressure above the solution (Eq. 3). When the total pressure (sum of the partial pressures) equals the applied pressure, the solution boils.

\[
P_{\text{total}} = P_A + P_B = P_A^\circ N_A + P_B^\circ N_B \quad [3]
\]

The composition of A and B in the vapor produced is given by Equations 4 and 5.

\[
N_A \text{ (vapor)} = \frac{P_A}{P_{\text{total}}} \quad [4]
\]

\[
N_B \text{ (vapor)} = \frac{P_B}{P_{\text{total}}} \quad [5]
\]

Several problems involving applications of Raoult’s Law are illustrated in Figure 15.6. Note, particularly in the result from Equation 4, that the vapor is richer \((N_A = 0.67)\) in the lower-boiling (higher vapor pressure) component A than it was before vaporization \((N_A = 0.50)\). This proves mathematically what was described in Section 15.2.

The consequences of Raoult’s Law for distillations are shown schematically in Figure 15.7. In Part A, the boiling points are identical (vapor pressures the same), and no separation is attained regardless of how the distillation is conducted. In Part B, a fractional distillation is required, whereas in Part C a simple distillation provides an adequate separation.

When a solid B (rather than another liquid) is dissolved in a liquid A, the boiling point is increased. In this extreme case, the vapor pressure of B is negligible, and the vapor will be pure A no matter how much solid B is added. Consider a solution of salt in water:

\[
P_{\text{total}} = P_{\text{water}}^\circ N_{\text{water}} + P_{\text{salt}}^\circ N_{\text{salt}}
\]

\[
P_{\text{salt}}^\circ = 0
\]

\[
P_{\text{total}} = P_{\text{water}}^\circ N_{\text{water}}
\]
Consider a solution at 100°C where \( N_A = 0.5 \) and \( N_B = 0.5 \).

1. What is the partial vapor pressure of A in the solution if the vapor pressure of pure A at 100°C is 1020 mm Hg?

   \[ P_A = P^\circ_A N_A = (1020)(0.5) = 510 \text{ mm Hg} \]

2. What is the partial vapor pressure of B in the solution if the vapor pressure of pure B at 100°C is 500 mm Hg?

   \[ P_B = P^\circ_B N_B = (500)(0.5) = 250 \text{ mm Hg} \]

3. Would the solution boil at 100°C if the applied pressure were 760 mm Hg?

   \[ \text{Yes. } P_{\text{total}} = P_A + P_B = (510 + 250) = 760 \text{ mm Hg} \]

4. What is the composition of the vapor at the boiling point?

   \[ N_A (\text{vapor}) = \frac{P_A}{P_{\text{total}}} = \frac{510}{760} = 0.67 \]
   \[ N_B (\text{vapor}) = \frac{P_B}{P_{\text{total}}} = \frac{250}{760} = 0.33 \]

**Figure 15.6**

*Sample calculations with Raoult’s Law.*

![Diagram](image)

**Figure 15.7**

*Consequences of Raoult’s Law.* (A) Boiling points (vapor pressures) are identical—no separation. (B) Boiling point somewhat lower for A than for B—requires fractional distillation. (C) Boiling point much lower for A than for B—simple distillation will suffice.

A solution whose mole fraction of water is 0.7 will not boil at 100°C, because \( P_{\text{total}} = (760)(0.7) = 532 \text{ mm Hg} \) and is less than atmospheric pressure. If the solution is heated to 110°C, it will boil because \( P_{\text{total}} = (1085)(0.7) = 760 \text{ mm Hg} \). Although the solution must be heated to 110°C to boil it, the vapor is pure water and has a boiling-point temperature of 100°C. (The vapor pressure of water at 110°C can be looked up in a handbook; it is 1085 mm Hg.)
A common measure of the efficiency of a column is given by its number of theoretical plates. The number of theoretical plates in a column is related to the number of vaporization–condensation cycles that occur as a liquid mixture travels through it. Using the example mixture in Figure 15.4, if the first distillate (condensed vapor) had the composition at $L_2$ when starting with liquid of composition $L_1$, the column would be said to have one theoretical plate. This would correspond to a simple distillation, or one vaporization–condensation cycle. A column would have two theoretical plates if the first distillate had the composition at $L_3$. The two-theoretical-plate column essentially carries out “two simple distillations.” According to Figure 15.4, five theoretical plates would be required to separate the mixture that started with composition $L_1$. Notice that this corresponds to the number of “steps” that need to be drawn in the figure to arrive at a composition of 100% A.

Most columns do not allow distillation in discrete steps, as indicated in Figure 15.4. Instead, the process is continuous, allowing the vapors to be continuously in contact with liquid of changing composition as they pass through the column. Any material can be used to pack the column as long as it can be wetted by the liquid and as long as it does not pack so tightly that vapor cannot pass.

The approximate relationship between the number of theoretical plates needed to separate an ideal two-component mixture and the difference in boiling points is given in Table 15.1. Notice that more theoretical plates are required as the boiling-point differences between the components decrease. For instance, a mixture of A (bp 130°C) and B (bp 166°C) with a boiling-point difference of 36°C would be expected to require a column with a minimum of five theoretical plates.

Several types of fractionating columns are shown in Figure 15.8. The Vigeux column, shown in Part A, has indentations that incline downward at angles of 45 degrees and are in pairs on opposite sides of the column. The projections into the column provide increased possibilities for condensation and...
for the vapor to equilibrate with the liquid. Vigreux columns are popular in cases where only a small number of theoretical plates are required. They are not very efficient (a 20-cm column might have only 2.5 theoretical plates), but they allow for rapid distillation and have a small holdup (the amount of liquid retained by the column). A column packed with a stainless steel sponge is a more effective fractionating column than a Vigreux column, but not by a large margin. Glass beads, or glass helices, can also be used as a packing material, and they have a slightly greater efficiency. The air condenser or the water condenser can be used as an improvised column if an actual fractionating column is unavailable. If a condenser is packed with glass beads, glass helices, or sections of glass tubing, the packing must be held in place by inserting a small plug of stainless steel sponge into the bottom of the condenser.

The most effective type of column is the spinning-band column. In the most elegant form of this device, a tightly fitting, twisted platinum screen or a Teflon rod with helical threads is rotated rapidly inside the bore of the column (Fig. 15.9). A spinning-band column that is available for microscale work is shown in Figure 15.10. This spinning-band column has a band about 2–3 cm in length and provides 4–5 theoretical plates. It can separate 1–2 mL of a mixture with a 30°C boiling-point difference. Larger research models of this spinning-band column can provide as many as 20 or 30 theoretical plates and can separate mixtures with a boiling-point difference of as little as 5–10°C.

Manufacturers of fractionating columns often offer them in a variety of lengths. Because the efficiency of a column is a function of its length, longer columns have more theoretical plates than shorter ones. It is common to express efficiency of a column in a unit called HETP, the Height of a column that is Equivalent to one Theoretical Plate. HETP is usually expressed in units of cm/plate. When the height of the column (in centimeters) is divided by this value, the total number of theoretical plates is specified.
When a fractional distillation is performed, the column should be clamped in a vertical position. The distillation should be conducted as slowly as possible, but the rate of distillation should be steady enough to produce a constant temperature reading at the thermometer.

Many fractionating columns must be insulated so that temperature equilibrium is maintained at all times. Additional insulation will not be required for columns that have an evacuated outer jacket, but those that do not can benefit from being wrapped in insulation.

A microscale air condenser can be converted to a column by packing it with a piece of stainless steel sponge. The simplest form of insulation is Tygon tubing that has been split lengthwise. Select a piece with an inner diameter that just matches or is slightly smaller than the diameter of the fractionating column so that it will fit snugly.

**CAUTION**

Cut the tubing to the correct length and then slit it with a sharp scissors. Do not use a razor blade or knife. Tygon tubing is difficult to cut; it is a nonslip substance and will “grab” even a single-edged razor blade in a way that can give you a nasty cut. See Experiment 6, page 52, for complete instructions.

Glass wool and aluminum foil (shiny side in) are often used for insulation. You can wrap the column with glass wool and then use a wrapping of the aluminum foil to keep it in place. An especially effective method is to make an insulation blanket by placing a layer of glass wool or cotton between two rectangles of aluminum foil, placed shiny side in. The sandwich is bound together with duct tape. This blanket, which is reusable, can be wrapped around the column and held in place with twist ties or tape.

The reflux ratio is defined as the ratio of the number of drops of distillate that return to the distillation flask compared to the number of drops of distillate collected. In an efficient column, the reflux ratio should equal or exceed the number of theoretical plates. A high reflux ratio ensures that the column will achieve temperature equilibrium and achieve its maximum efficiency. This ratio is not easy to determine; in fact, it is impossible to determine when using a Hickman head, and it should not concern a beginning student. In some cases, the throughput, or rate of takeoff, of a column may
be specified. This is expressed as the number of milliliters of distillate that can be collected per unit of time, usually as mL/min.

**Microscale Apparatus.** The apparatus shown in Figure 15.2 is the one you are most likely to use in the microscale laboratory. If your laboratory is one of the better-equipped ones, you may have access to spinning-band columns like those shown in Figure 15.10. The distillation temperature can be monitored most accurately by using a partial immersion mercury thermometer (see Technique 13, Section 13.3, page 700).

**Macroscale Apparatus.** Figure 15.11 illustrates a fractional distillation assembly that can be used for larger-scale distillations. It has a glass-jacketed column that is packed with a stainless steel sponge. This apparatus would be common in situations where quantities of liquid in excess of 10 mL were to be distilled.
PROBLEMS

1. In the accompanying chart are approximate vapor pressures for benzene and toluene at various temperatures.

<table>
<thead>
<tr>
<th>Temp (°C)</th>
<th>mm Hg</th>
<th>Temp (°C)</th>
<th>mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzene</td>
<td></td>
<td>Toluene</td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>120</td>
<td>30</td>
<td>37</td>
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<td>50</td>
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<td>50</td>
<td>95</td>
</tr>
<tr>
<td>60</td>
<td>390</td>
<td>60</td>
<td>140</td>
</tr>
<tr>
<td>70</td>
<td>550</td>
<td>70</td>
<td>200</td>
</tr>
<tr>
<td>80</td>
<td>760</td>
<td>80</td>
<td>290</td>
</tr>
<tr>
<td>90</td>
<td>1010</td>
<td>90</td>
<td>405</td>
</tr>
<tr>
<td>100</td>
<td>1340</td>
<td>100</td>
<td>560</td>
</tr>
</tbody>
</table>

a. What is the mole fraction of each component if 3.9 g of benzene C₆H₆ is dissolved in 4.6 g of toluene C₇H₈?

b. Assuming that this mixture is ideal—that is, it follows Raoult’s Law—what is the partial vapor pressure of benzene in this mixture at 50°C?

c. Estimate to the nearest degree the temperature at which the vapor pressure of the solution equals 1 atm (bp of the solution).

d. Calculate the composition of the vapor (mole fraction of each component) that is in equilibrium in the solution at the boiling point of this solution.

e. Calculate the composition in weight percentage of the vapor that is in equilibrium with the solution.

2. Estimate how many theoretical plates are needed to separate a mixture that has a mole fraction of B equal to 0.70 (70% B) in Figure 15.4.

3. Two moles of sucrose are dissolved in 8 moles of water. Assume that the solution follows Raoult’s Law and that the vapor pressure of sucrose is negligible. The boiling point of water is 100°C. The distillation is carried out at 1 atm (760 mm Hg).

a. Calculate the vapor pressure of the solution when the temperature reaches 100°C.

b. What temperature would be observed during the entire distillation?

c. What would be the composition of the distillate?

d. If a thermometer were immersed below the surface of the liquid of the boiling flask, what temperature would be observed?

4. Explain why the boiling point of a two-component mixture rises slowly throughout a simple distillation when the boiling-point differences are not large.

5. Given the boiling points of several known mixtures of A and B (mole fractions are known) and the vapor pressures of A and B in the pure state (Pᴬ and Pᴮ) at these same temperatures, how would you construct a boiling-point-composition phase diagram for A and B? Give a stepwise explanation.

6. Describe the behavior on distillation of a 98% ethanol solution through an efficient column. Refer to Figure 15.12.

7. Construct an approximate boiling-point-composition diagram for a benzene–methanol system. The mixture shows azeotropic behavior (see Table 15.3). Include on the graph the boiling points of pure benzene and pure methanol and the boiling point of the azeotrope. Describe the behavior on distillation of a mixture that is initially rich in benzene (90%) and then for a mixture that is initially rich in methanol (90%).
The most modern and sophisticated methods of separating mixtures that the organic chemist has available all involve chromatography. Chromatography is defined as the separation of a mixture of two or more compounds or ions by distribution between two phases, one of which is stationary and the other moving. Various types of chromatography are possible, depending on the nature of the two phases involved: solid–liquid (column, thin-layer, and paper), liquid–liquid, (high-performance liquid), and gas–liquid (vapor–phase) chromatographic methods are common.

All chromatography works on much the same principle as solvent extraction (Technique 12). Basically, the methods depend on the differential solubilities or adsorptivities of the substances to be separated relative to the two phases between which they are to be partitioned. In this chapter, column chromatography, a solid–liquid method, is considered. Thin-layer chromatography is examined in Technique 20; high-performance liquid chromatography is discussed in Technique 21; and gas chromatography, a gas–liquid method, is discussed in Technique 22.

19.1 Adsorbents

Column chromatography is a technique based on both adsorptivity and solubility. It is a solid–liquid phase-partitioning technique. The solid may be almost any material that does not dissolve in the associated liquid phase; the solids used most commonly are silica gel, SiO$_2$·xH$_2$O, also called silicic acid, and alumina, Al$_2$O$_3$·xH$_2$O. These compounds are used in their powdered or finely ground forms (usually 200 to 400 mesh).\(^1\)

Most alumina used for chromatography is prepared from the impure ore bauxite Al$_2$O$_3$·xH$_2$O + Fe$_2$O$_3$. The bauxite is dissolved in hot sodium hydroxide and filtered to remove the insoluble iron oxides; the alumina in the ore forms the soluble amphoteric hydroxide Al(OH)$_4$. The hydroxide is precipitated by CO$_2$, which reduces the pH, as Al(OH)$_3$. When heated, the Al(OH)$_3$ loses water to form pure alumina Al$_2$O$_3$.

\[
\begin{align*}
\text{Bauxite (crude)} & \rightarrow \text{Al(OH)}_4^{-}(aq) + \text{Fe}_2\text{O}_3 \text{ (insoluble)} \\
\text{Al(OH)}_4^{-}(aq) + \text{CO}_2 & \rightarrow \text{Al(OH)}_3 + \text{HCO}_3^- \\
2 \text{Al(OH)}_3 & \rightarrow \text{Al}_2\text{O}_3(s) + 3 \text{H}_2\text{O}
\end{align*}
\]

Alumina prepared in this way is called basic alumina because it still contains some hydroxides. Basic alumina cannot be used for chromatography of compounds that are base sensitive. Therefore, it is washed with acid to neutralize the base, giving acid-washed alumina. This material is unsatisfactory unless it has been washed with enough water to remove all the acid; on being so washed, it becomes the best chromatographic material, called

---

\(^1\) The term *mesh* refers to the number of openings per linear inch found in a screen. A large number refers to a fine screen (finer wires more closely spaced). When particles are sieved through a series of these screens, they are classified by the smallest mesh screen that they will pass through. Mesh 5 would represent a coarse gravel, and mesh 800 would be a fine powder.
neutral alumina. If a compound is acid-sensitive, either basic or neutral alumina must be used. You should be careful to ascertain what type of alumina is being used for chromatography. Silica gel is not available in any form other than that suitable for chromatography.

19.2 Interactions

If powdered or finely ground alumina (or silica gel) is added to a solution containing an organic compound, some of the organic compound will adsorb onto or adhere to the fine particles of alumina. Many kinds of intermolecular forces cause organic molecules to bind to alumina. These forces vary in strength according to their type. Nonpolar compounds bind to the alumina using only van der Waals forces. These are weak forces, and nonpolar molecules do not bind strongly unless they have extremely high molecular weights. The most important interactions are those typical of polar organic compounds. Either these forces are of the dipole–dipole type or they involve some direct interaction (coordination, hydrogen bonding, or salt formation). These types of interactions are illustrated in Figure 19.1, which for convenience shows only a portion of the alumina structure. Similar interactions occur with silica gel. The strengths of such interactions vary in the approximate order:

Salt formation > coordination > hydrogen-bonding > dipole–dipole > van der Waals

Strength of interaction varies among compounds. For instance, a strongly basic amine would bind more strongly than a weakly basic one (by coordination). In fact, strong bases and strong acids often interact so strongly that they dissolve alumina to some extent. You can use the following rule of thumb:

NOTE: The more polar the functional group, the stronger the bond to alumina (or silica gel).

A similar rule holds for solubility. Polar solvents dissolve polar compounds more effectively than nonpolar solvents; nonpolar compounds are dissolved best by nonpolar solvents. Thus, the extent to which any given solvent can wash an adsorbed compound from alumina depends almost directly on the relative polarity of the solvent. For example, although a ketone adsorbed on alumina might not be removed by hexane, it might be removed
completely by chloroform. For any adsorbed material, a kind of distribution equilibrium can be envisioned between the adsorbent material and the solvent. This is illustrated in Figure 19.2.

The distribution equilibrium is dynamic, with molecules constantly adsorbing from the solution and desorbing into it. The average number of molecules remaining adsorbed on the solid particles at equilibrium depends both on the particular molecule (RX) involved and the dissolving power of the solvent with which the adsorbent must compete.

19.3 Principle of Column Chromatographic Separation

The dynamic equilibrium mentioned previously, and the variations in the extent to which different compounds adsorb on alumina or silica gel, underlie a versatile and ingenious method for separating mixtures of organic compounds. In this method, the mixture of compounds to be separated is introduced onto the top of a cylindrical glass column (Fig. 19.3) packed, or filled, with fine alumina particles (stationary solid phase). The adsorbent is continuously washed by a flow of solvent (moving phase) passing through the column.

Initially, the components of the mixture adsorb onto the alumina particles at the top of the column. The continuous flow of solvent through the column elutes, or washes, the solutes off the alumina and sweeps them down the column. The solutes (or materials to be separated) are called eluates or elutants, and the solvents are called eluents. As the solutes pass down the column to fresh alumina, new equilibria are established among the adsorbent, the solutes, and the solvent. The constant equilibration means that different compounds will move down the column at differing rates, depending on their relative affinity for the adsorbent on one hand and for the solvent on the other. Because the number of alumina particles is large, because they are closely packed, and because fresh solvent is being added continuously, the number of equilibrations between adsorbent and solvent that the solutes experience is enormous.

As the components of the mixture are separated, they begin to form moving bands (or zones), each band containing a single component. If the column is long enough and the other parameters (column diameter, adsorbent, solvent, and flow rate) are correctly chosen, the bands separate from one another, leaving gaps of pure solvent in between. As each band (solvent and solute) passes out the bottom of the column, it can be collected.
before the next band arrives. If the parameters mentioned are poorly chosen, the various bands either overlap or coincide, in which case either a poor separation or no separation at all is the result. A successful chromatographic separation is illustrated in Figure 19.4.

Figure 19.4
Sequence of steps in a chromatographic separation.
The versatility of column chromatography results from the many factors that can be adjusted. These include

1. Adsorbent chosen
2. Polarity of the solvents chosen
3. Size of the column (both length and diameter) relative to the amount of material to be chromatographed
4. Rate of elution (or flow)

By careful choosing of the conditions, almost any mixture can be separated. This technique has even been used to separate optical isomers. An optically active solid-phase adsorbent was used to separate the enantiomers.

Two fundamental choices for anyone attempting a chromatographic separation are the kind of adsorbent and the solvent system. In general, nonpolar compounds pass through the column faster than polar compounds because they have a smaller affinity for the adsorbent. If the adsorbent chosen binds all the solute molecules (both polar and nonpolar) strongly, they will not move down the column. On the other hand, if too polar a solvent is chosen, all the solutes (polar and nonpolar) may simply be washed through the column, with no separation taking place. The adsorbent and the solvent should be chosen so that neither is favored excessively in the equilibrium competition for solute molecules.²

A. Adsorbents

In Table 19.1, various kinds of adsorbents (solid phases) used in column chromatography are listed. The choice of adsorbent often depends on the types of compounds to be separated. Cellulose, starch, and sugars are used for polyfunctional plant and animal materials (natural products) that are

<table>
<thead>
<tr>
<th>Adsorbent</th>
<th>Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paper</td>
<td></td>
</tr>
<tr>
<td>Cellulose</td>
<td></td>
</tr>
<tr>
<td>Starch</td>
<td></td>
</tr>
<tr>
<td>Sugars</td>
<td></td>
</tr>
<tr>
<td>Magnesium silicate</td>
<td></td>
</tr>
<tr>
<td>Calcium sulfate</td>
<td></td>
</tr>
<tr>
<td>Silicic acid</td>
<td></td>
</tr>
<tr>
<td>Silica gel</td>
<td></td>
</tr>
<tr>
<td>Florisil</td>
<td></td>
</tr>
<tr>
<td>Magnesium oxide</td>
<td></td>
</tr>
<tr>
<td>Aluminum oxide</td>
<td></td>
</tr>
<tr>
<td>Activated charcoal</td>
<td></td>
</tr>
</tbody>
</table>

² Often the chemist uses thin-layer chromatography (TLC), which is described in Technique 20, to arrive at the best choices of solvents and adsorbents for the best separation. The TLC experimentation can be performed quickly and with extremely small amounts (microgram quantities) of the mixture to be separated. This saves significant time and materials. Technique 20 describes this use of TLC.
very sensitive to acid–base interactions. Magnesium silicate is often used for separating acetylated sugars, steroids, and essential oils. Silica gel and Florisil are relatively mild toward most compounds and are widely used for a variety of functional groups—hydrocarbons, alcohols, ketones, esters, acids, azo compounds, amines. Alumina is the most widely used adsorbent and is obtained in the three forms mentioned in Section 19.1: acidic, basic, and neutral. The pH of acidic or acid-washed alumina is approximately 4. This adsorbent is particularly useful for separating acidic materials such as carboxylic acids and amino acids. Basic alumina has a pH of 10 and is useful in separating amines. Neutral alumina can be used to separate a variety of nonacidic and nonbasic materials.

The approximate strength of the various adsorbents listed in Table 19.1 is also given. The order is only approximate, and therefore it may vary. For instance, the strength, or separating abilities, of alumina and silica gel largely depend on the amount of water present. Water binds tightly to either adsorbent, taking up sites on the particles that could otherwise be used for equilibration with solute molecules. If one adds water to the adsorbent, it is said to have been deactivated. Anhydrous alumina or silica gel is said to be highly activated. High activity is usually avoided with these adsorbents. Use of the highly active forms of either alumina or silica gel, or of the acidic or basic forms of alumina, can often lead to molecular rearrangement or decomposition in certain types of solute compounds.

The chemist can select the degree of activity that is appropriate to carry out a particular separation. To accomplish this, highly activated alumina is mixed thoroughly with a precisely measured quantity of water. The water partially hydrates the alumina and thus reduces its activity. By carefully determining the amount of water required, the chemist can have available an entire spectrum of possible activities.

B. Solvents

In Table 19.2, some common chromatographic solvents are listed, along with their relative ability to dissolve polar compounds. Sometimes a single

<table>
<thead>
<tr>
<th>Table 19.2 Solvents (eluents) for chromatography</th>
</tr>
</thead>
<tbody>
<tr>
<td>Petroleum ether</td>
</tr>
<tr>
<td>Cyclohexane</td>
</tr>
<tr>
<td>Carbon tetrachloride*</td>
</tr>
<tr>
<td>Toluene</td>
</tr>
<tr>
<td>Chloroform*</td>
</tr>
<tr>
<td>Methylene chloride</td>
</tr>
<tr>
<td>Diethyl ether</td>
</tr>
<tr>
<td>Ethyl acetate</td>
</tr>
<tr>
<td>Acetone</td>
</tr>
<tr>
<td>Pyridine</td>
</tr>
<tr>
<td>Ethanol</td>
</tr>
<tr>
<td>Methanol</td>
</tr>
<tr>
<td>Water</td>
</tr>
<tr>
<td>Acetic acid</td>
</tr>
</tbody>
</table>

*Increasing polarity and “solvent power” toward polar functional groups

*Suspected carcinogens.
Table 19.3 Elution sequence for compounds

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Order of elution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrocarbons</td>
<td>Fastest (will elute with nonpolar solvent)</td>
</tr>
<tr>
<td>Olefins</td>
<td></td>
</tr>
<tr>
<td>Ethers</td>
<td></td>
</tr>
<tr>
<td>Halocarbons</td>
<td></td>
</tr>
<tr>
<td>Aromatics</td>
<td></td>
</tr>
<tr>
<td>Ketones</td>
<td>Order of elution</td>
</tr>
<tr>
<td>Aldehydes</td>
<td></td>
</tr>
<tr>
<td>Esters</td>
<td></td>
</tr>
<tr>
<td>Alcohols</td>
<td></td>
</tr>
<tr>
<td>Amines</td>
<td></td>
</tr>
<tr>
<td>Acids, strong bases</td>
<td>Slowest (need a polar solvent)</td>
</tr>
</tbody>
</table>

Solvent can be found that will separate all the components of a mixture. Sometimes a mixture of solvents can be found that will achieve separation. More often, you must start elution with a nonpolar solvent to remove relatively nonpolar compounds from the column and then gradually increase the solvent polarity to force compounds of greater polarity to come down the column, or elute. The approximate order in which various classes of compounds elute by this procedure is given in Table 19.3. In general, nonpolar compounds travel through the column faster (elute first), and polar compounds travel more slowly (elute last). However, molecular weight is also a factor in determining the order of elution. A nonpolar compound of high molecular weight travels more slowly than a nonpolar compound of low molecular weight, and it may even be passed by some polar compounds.

Solvent polarity functions in two ways in column chromatography. First, a polar solvent will better dissolve a polar compound and move it down the column faster. Therefore, as already mentioned, one usually increases the polarity of the solvent during column chromatography to wash down compounds of increasing polarity. Second, as the polarity of the solvent increases, the solvent itself will displace adsorbed molecules from the alumina or silica and take their place on the column. Because of this second effect, a polar solvent will move all types of compounds, both polar and nonpolar, down the column at a faster rate than a nonpolar solvent.

When the polarity of the solvent has to be changed during a chromatographic separation, some precautions must be taken. Rapid changes from one solvent to another are to be avoided (especially when silica gel or alumina is involved). Usually, small percentages of a new solvent are mixed slowly into the one in use until the percentage reaches the desired level. If this is not done, the column packing often “cracks” as a result of the heat liberated when alumina or silica gel is mixed with a solvent. The solvent solvates the adsorbent, and the formation of a weak bond generates heat.

\[
\text{Solvent} + \text{alumina} \rightarrow \text{(alumina} \cdot \text{solvent)} + \text{heat}
\]

Often, enough heat is generated locally to evaporate the solvent. The formation of vapor creates bubbles, which forces a separation of the
column packing; this is called **cracking**. A cracked column does not produce a good separation, because it has discontinuities in the packing. The way in which a column is packed or filled is also very important in preventing cracking.

Certain solvents should be avoided with alumina or silica gel, especially with the acidic, basic, and highly active forms. For instance, with any of these adsorbents, acetone dimerizes via an aldol condensation to give diacetone alcohol. Mixtures of esters **transesterify** (exchange their alcoholic portions) when ethyl acetate or an alcohol is the eluent. Finally, the most active solvents (pyridine, methanol, water, and acetic acid) dissolve and elute some of the adsorbent itself. Generally, try to avoid going to solvents more polar than diethyl ether or methylene chloride in the eluent series (Table 19.2).

**C. Column Size and Adsorbent Quantity**

The column size and the amount of adsorbent must also be selected correctly to separate a given amount of sample well. As a rule of thumb, the amount of adsorbent should be 25 to 30 times, by weight, the amount of material to be separated by chromatography. Furthermore, the column should have a height-to-diameter ratio of about 8:1. Some typical relations of this sort are given in Table 19.4.

Note, as a caution, that the difficulty of the separation is also a factor in determining the size and length of the column to be used and in the amount of adsorbent needed. Compounds that do not separate easily may require longer columns and more adsorbent than specified in Table 19.4. For easily separated compounds, a shorter column and less adsorbent may suffice.

**D. Flow Rate**

The rate at which solvent flows through the column is also significant in the effectiveness of a separation. In general, the time the mixture to be separated remains on the column is directly proportional to the extent of equilibration between stationary and moving phases. Thus, similar compounds eventually separate if they remain on the column long enough. The time a material remains on the column depends on the flow rate of the solvent. If the flow is too slow, however, the dissolved substances in the mixture may diffuse faster than the rate at which they move down the column. Then the bands grow wider and more diffuse, and the separation becomes poor.

**Table 19.4** Size of column and amount of adsorbent for typical sample sizes

<table>
<thead>
<tr>
<th>Amount of Sample (g)</th>
<th>Amount of Adsorbent (g)</th>
<th>Column Diameter (mm)</th>
<th>Column Height (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.01</td>
<td>0.3</td>
<td>3.5</td>
<td>30</td>
</tr>
<tr>
<td>0.10</td>
<td>3.0</td>
<td>7.5</td>
<td>60</td>
</tr>
<tr>
<td>1.00</td>
<td>30.0</td>
<td>16.0</td>
<td>130</td>
</tr>
<tr>
<td>10.00</td>
<td>300.0</td>
<td>35.0</td>
<td>280</td>
</tr>
</tbody>
</table>
The most critical operation in column chromatography is packing (filling) the column with adsorbent. The column packing must be evenly packed and free of irregularities, air bubbles, and gaps. As a compound travels down the column, it moves in an advancing zone, or band. It is important that the leading edge, or front, of this band be horizontal, or perpendicular to the long axis of the column. If two bands are close together and do not have horizontal band fronts, it is impossible to collect one band while completely excluding the other. The leading edge of the second band begins to elute before the first band has finished eluting. This condition can be seen in Figure 19.5. There are two main reasons for this problem. First, if the top surface edge of the adsorbent packing is not level, nonhorizontal bands result. Second, bands may be nonhorizontal if the column is not held in an exactly vertical position in both planes (front to back and side to side). When you are preparing a column, you must watch both these factors carefully.

Another phenomenon, called streaming or channeling, occurs when part of the band front advances ahead of the major part of the band. Channeling occurs if there are any cracks or irregularities in the adsorbent surface or any irregularities caused by air bubbles in the packing. A part of the advancing front moves ahead of the rest of the band by flowing through the channel. Two examples of channeling are shown in Figure 19.6.

19.5 Packing the Column: Typical Problems

The following methods are used to avoid problems resulting from uneven packing and column irregularities. These procedures should be followed carefully in preparing a chromatography column. Failure to pay close attention to the preparation of the column may well affect the quality of the separation.

Preparation of a column involves two distinct stages. In the first stage, a support base on which the packing will rest is prepared. This must be done so that the packing, a finely divided material, does not wash out of
the bottom of the column. In the second stage, the column of adsorbent is deposited on top of the supporting base.

A. Preparing the Support Base

For microscale applications, select a Pasteur pipet (5½-inch) and clamp it upright (vertically). To reduce the amount of solvent needed to fill the column, break off most of the tip of the pipet. Place a small ball of cotton in the pipet and tamp it into position using a glass rod or a piece of wire. Take care not to plug the column totally by tamping the cotton too hard. The correct position of the cotton is shown in Figure 19.7. A microscale chromatography column is packed by one of the dry pack methods described in Part B of this section.

B. Depositing the Adsorbent

Dry Pack Method 1. To fill a microscale column, fill the Pasteur pipet (with the cotton plug, prepared as described in Section A) about half full with solvent. Using a microspatula, add the solid adsorbent slowly to the solvent in the column. As you add the solid, tap the column gently with a pencil, a finger, or a glass rod. The tapping promotes even settling and mixing and gives an evenly packed column free of air bubbles. As the adsorbent is added, solvent flows out of the Pasteur pipet. Because the adsorbent must not be allowed to dry during the packing process, you must use a means of controlling the solvent flow. If a piece of small-diameter plastic tubing is available, it can be fitted over the narrow tip of the Pasteur pipet. The flow rate can then be controlled using a screw clamp. A simple approach to controlling the flow rate is to use a finger over the top of the Pasteur pipet, much as you control the flow of liquid in a volumetric pipet. Continue adding the adsorbent slowly, with constant tapping, until the level of the adsorbent has reached the desired level. As you pack the column, be careful not to let the column run dry. The final column should appear as shown in Figure 19.7.

Dry Pack Method 2. An alternative dry pack method for microscale columns is to fill the Pasteur pipet with dry adsorbent, without any solvent. Position a plug of cotton in the bottom of the Pasteur pipet. The desired
amount of adsorbent is added slowly, and the pipet tapped constantly, until the level of adsorbent has reached the desired height. Figure 19.7 can be used as a guide to judge the correct height of the column of adsorbent. When the column is packed, added solvent is allowed to percolate through the adsorbent until the entire column is moistened. The solvent is not added until just before the column is to be used.

**NOTE:** This method is not recommended for use with silica gel or for experiments where a careful separation is required.

This method is useful when the adsorbent is alumina, but it does not produce satisfactory results with silica gel. Even with alumina, poor separations can arise due to uneven packing, air bubbles, and cracking, especially if a solvent that has a highly exothermic heat of solvation is used.

As with microscale columns, the procedures described in this section should be followed carefully in preparing a semimicroscale or conventional-scale column. Failure to pay close attention to the details of these procedures may adversely affect the quality of the separation.

Again, preparation of a column involves two distinct stages: preparation of the support base and filling the column with adsorbent.

### A. Preparing the Support Base

**Semimicroscale Columns.** An alternative apparatus for small-scale column chromatography is a commercial column, such as the one shown in Figure 19.8. This type of column is made of glass and has a solvent-resistant plastic stopcock at the bottom. The stopcock assembly contains a filter disc to support the adsorbent column. An optional upper fitting, also made of solvent-resistant plastic, serves as a solvent reservoir. The column shown in Figure 19.8 is equipped with the solvent reservoir. This type of column is available in a variety of lengths, ranging from 100 to 300 mm. Because the column has a built-in filter disc, it is not necessary to prepare a support base before the adsorbent is added.

**Macroscale Columns.** For large-scale applications, clamp a chromatography column upright (vertically). The column (Figure 19.3, page 758) is a piece of cylindrical glass tubing with a stopcock attached at one end. The stopcock usually has a Teflon plug because stopcock grease (used on glass plugs) dissolves in many of the organic solvents used as eluents. Stopcock grease in the eluent will contaminate the eluates.

Instead of a stopcock, attach a piece of flexible tubing to the bottom of the column, with a screw clamp used to stop or regulate the flow (Fig. 19.9). When a screw clamp is used, care must be taken that the tubing used is not dissolved by the solvents that will pass through the column during the experiment. Rubber, for instance, dissolves in chloroform, benzene, methylene chloride, toluene, or tetrahydrofuran (THF). Tygon tubing dissolves

---

3 **Note to the Instructor:** With certain organic solvents, we have found that the “solvent-resistant” plastic stopcock may tend to dissolve! We recommend that instructors test their equipment with the solvent that they intend to use before the start of the laboratory class.
(actually, the plasticizer is removed) in many solvents, including benzene, methylene chloride, chloroform, ether, ethyl acetate, toluene, and THF. Polyethylene tubing is the best choice for use at the end of a column because it is inert with most solvents.

Next, the column is partially filled with a quantity of solvent, usually a nonpolar solvent like hexane, and a support for the finely divided adsorbent is prepared in the following way. A loose plug of glass wool is tamped down into the bottom of the column with a long glass rod until all entrapped air is forced out as bubbles. Take care not to plug the column totally by tamping the glass wool too hard. A small layer of clean white sand is formed on top of the glass wool by pouring sand into the column. The column is tapped to level the surface of the sand. Any sand adhering to the side of the column is washed down with a small quantity of solvent. The sand forms a base that supports the column of adsorbent and prevents it from washing through the stopcock. The column is packed in one of two ways: by the slurry method or by the dry pack method.

B. Depositing the Adsorbent

**Slurry Method.** The slurry method is not recommended as a microscale method for use with Pasteur pipets. On a very small scale, it is too difficult to pack the column with the slurry without losing the solvent before the packing has been completed. Microscale columns should be packed by the dry pack method, as described in Section 19.6.

In the slurry method, the adsorbent is packed into the column as a mixture of a solvent and an undissolved solid. The slurry is prepared in a separate container (Erlenmeyer flask) by adding the solid adsorbent, a little at a time, to a quantity of the solvent. This order of addition (adsorbent added to solvent) should be followed strictly because the adsorbent solvates and liberates heat. If the solvent is added to the adsorbent, it may boil away almost as fast as it is added due to heat evolved. This will be especially true if ether or another low-boiling solvent is used. When this happens, the final mixture will be uneven and lumpy. Enough adsorbent is added to the solvent, and mixed by swirling the container, to form a thick but flowing slurry. The container should be swirled until the mixture is homogenous and relatively free of entrapped air bubbles.

For a standard-sized column, the procedure is as follows. When the slurry has been prepared, the column is filled about half full with solvent, and the stopcock is opened to allow solvent to drain slowly into a large beaker. The slurry is mixed by swirling and is then poured in portions into the top of the draining column (a wide-necked funnel may be useful here). Be sure to swirl the slurry thoroughly before each addition to the column. The column is tapped constantly and gently on the side during the pouring operation with the fingers or with a pencil fitted with a rubber stopper. A short piece of large-diameter pressure tubing may also be used for tapping. The tapping promotes even settling and mixing and gives an evenly packed column free of air bubbles. Tapping is continued until all the material has settled, showing a well-defined level at the top of the column. Solvent from the collecting beaker may be re-added to the slurry if it becomes too thick to be poured into the column at one time. In fact, the collected solvent should be cycled through the column several times to ensure that settling is complete and that the column is firmly packed. The downward flow of solvent
tends to compact the adsorbent. You should take care never to let the column “run dry” during packing. There should always be solvent on top of the absorbent column.

**Dry Pack Method 1.** In the first of the dry pack methods introduced here, the column is filled with solvent and allowed to drain *slowly*. The dry adsorbent is added, a little at a time, while the column is tapped gently with a pencil, finger, or glass rod.

**Semimicroscale Columns** The procedure to fill a commercial semimicroscale column is essentially the same as that used to fill a Pasteur pipet (Section 19.6). The commercial column has the advantage that it is much easier to control the flow of solvent from the column during the filling process, because the stopcock can be adjusted appropriately. It is not necessary to use a cotton plug or to deposit a layer of sand before adding the adsorbent. The presence of the fritted disc at the base of the column acts to prevent adsorbent from escaping from the column.

**Macroscale Columns** A plug of cotton is placed at the base of the column, and an even layer of sand is formed on top (see p. 758). The column is filled about half full with solvent, and the solid adsorbent is added carefully from a beaker while the solvent is allowed to flow slowly from the column. As the solid is added, the column is tapped as described for the slurry method in order to ensure that the column is packed evenly. When the column has the desired length, no more adsorbent is added. This method also produces an evenly packed column. Solvent should be cycled through this column (for macroscale applications) several times before each use. The same portion of solvent that has drained from the column during the packing is used to cycle through the column.

**Dry Pack Method 2.** In this method, the column is filled with dry adsorbent without any solvent. When the desired amount of adsorbent has been added, solvent is allowed to percolate through the column.

**Semimicroscale Columns** The Dry Pack Method 2 is similar to that described for Pasteur pipets (Section 19.6), except that the plug of cotton is not required. The flow rate of solvent through the column can be controlled using the stopcock, which is part of the column assembly (see Fig. 19.8).

**Macroscale Columns** Macroscale columns can also be packed by a dry pack method that is similar to the microscale methods described in Section 19.6. The disadvantages described for the microscale method also apply to the macroscale method. This method is not recommended for use with silica gel or alumina, because the combination leads to uneven packing, air bubbles, and cracking, especially if a solvent that has a highly exothermic heat of solvation is used.

The solvent (or solvent mixture) used to pack the column is normally the least polar elution solvent that can be used during chromatography. The compounds to be chromatographed are not highly soluble in the solvent. If they were, they would probably have a greater affinity for the solvent than for the adsorbent and would pass right through the column without equilibrating with the stationary phase.
The first elution solvent, however, is generally not a good solvent to use in preparing the sample to be placed on the column. Because the compounds are not highly soluble in nonpolar solvents, it takes a large amount of the initial solvent to dissolve the compounds, and it is difficult to get the mixture to form a narrow band on top of the column. A narrow band is ideal for an optimum separation of components. For the best separation, therefore, the compound is applied to the top of the column undiluted if it is a liquid or in a very small amount of highly-polar solvent if it is a solid. Water must not be used to dissolve the initial sample being chromatographed, because it reacts with the column packing.

In adding the sample to the column, use the following procedure. Lower the solvent level to the top of the adsorbent column by draining the solvent from the column. Add the sample (either a pure liquid or a solution) to form a small layer on top of the adsorbent. A Pasteur pipet is convenient for adding the sample to the column. Take care not to disturb the surface of the adsorbent. This is best accomplished by touching the pipet to the inside of the glass column and slowly draining it so as to allow the sample to spread into a thin film, which slowly descends to cover the entire adsorbent surface. Drain the pipet close to the surface of the adsorbent. When all the sample has been added, drain this small layer of liquid into the column until the top surface of the column just begins to dry. Then add a small layer of the chromatographic solvent carefully with a Pasteur pipet, again being careful not to disturb the surface. Drain this small layer of solvent into the column until the top surface of the column just dries. Add another small layer of fresh solvent, if necessary, and repeat the process until it is clear that the sample is strongly adsorbed on the top of the column. If the sample is colored and the fresh layer of solvent acquires some of this color, the sample has not been properly adsorbed. Once the sample has been properly applied, you can protect the level surface of the adsorbent by carefully filling the top of the column with solvent and sprinkling clean, white sand into the column so as to form a small protective layer on top of the adsorbent. For microscale applications, this layer of sand is not required.

Separations are often better if the sample is allowed to stand a short time on the column before elution. This allows a true equilibrium to be established. In columns that stand for too long, however, the adsorbent often compacts or even swells, and the flow can become annoyingly slow. Diffusion of the sample to widen the bands also becomes a problem if a column is allowed to stand over an extended period. For small-scale chromatography, using Pasteur pipets, there is no stopcock, and it is not possible to stop the flow. In this case, it is not considered necessary to allow the column to stand.

Solvents for analytical and preparative chromatography should be pure reagents. Commercial-grade solvents often contain small amounts of residue, which remains when the solvent is evaporated. For normal work, and for relatively easy separations that take only small amounts of solvent, the residue usually presents few problems. For large-scale work, commercial-grade solvents may have to be redistilled before use. This is especially true for hydrocarbon solvents, which tend to have more residue than other solvent types. Most of the experiments in this laboratory manual have been designed to avoid this particular problem.
One usually begins elution of the products with a nonpolar solvent, such as hexane or petroleum ether. The polarity of the elution solvent can be increased gradually by adding successively greater percentages of either ether or toluene (for instance, 1, 2, 5, 10, 15, 25, 50, 100%) or some other solvent of greater solvent power (polarity) than hexane. The transition from one solvent to another should not be too rapid in most solvent changes. If the two solvents to be changed differ greatly in their heats of solvation in binding to the adsorbent, enough heat can be generated to crack the column. Ether is especially troublesome in this respect because it has both a low boiling point and a relatively high heat of solvation. Most organic compounds can be separated on silica gel or alumina using hexane–ether or hexane–toluene combinations for elution and following these by pure methylene chloride. Solvents of greater polarity are usually avoided for the various reasons mentioned previously. In microscale work, the usual procedure is to use only one solvent for the chromatography.

The flow of solvent through the column should not be too rapid or the solutes will not have time to equilibrate with the adsorbent as they pass down the column. If the rate of flow is too low or stopped for a period, diffusion can become a problem—the solute band will diffuse, or spread out, in all directions. In either of these cases, separation will be poor. As a general rule (and only an approximate one), most macroscale columns are run with flow rates ranging from 5 to 50 drops of effluent per minute; a steady flow of solvent is usually avoided. Microscale columns made from Pasteur pipets do not have a means of controlling the solvent flow rate, but commercial microscale columns are equipped with stopcocks. The solvent flow rate in this type of column can be adjusted in a manner similar to that used with larger columns. To avoid diffusion of the bands, do not stop the column and do not set it aside overnight.

For a microscale chromatography, the portion of the Pasteur pipet above the adsorbent is used as a reservoir of solvent. Fresh solvent, as needed, is added by means of another Pasteur pipet. When it is necessary to change solvent, the new solvent is also added in this manner. In some cases, the chromatography may proceed too slowly; the rate of solvent flow can be accelerated by attaching a rubber dropper bulb to the top of the Pasteur pipet column and squeezing gently. The additional air pressure forces the solvent through the column more rapidly. If this technique is used, however, care must be taken to remove the rubber bulb from the column before releasing it. Otherwise, air may be drawn up through the bottom of the column, destroying the column packing.

When large quantities of solvent are used in a chromatographic separation, it is often convenient to use a solvent reservoir to forestall having to add small portions of fresh solvent continually. The simplest type of reservoir, a feature of many columns, is created by fusing the top of the column to a round-bottom flask (Fig. 19.10A). If the column has a standard-taper joint at its top, a reservoir can be created by joining a standard-taper separatory funnel to the column (Fig. 19.10B). In this arrangement, the stopcock is left open, and no stopper is placed in the top of the separatory funnel. A third common arrangement is shown in Figure 19.10C. A separatory funnel is filled with solvent; its stopper is wetted with solvent and put firmly in place. The funnel is inserted into the empty filling space at the top of the chromatographic column, and the stopcock is opened. Solvent flows out of
the funnel, filling the space at the top of the column until the solvent level is well above the outlet of the separatory funnel. As solvent drains from the column, this arrangement automatically refills the space at the top of the column by allowing air to enter through the stem of the separatory funnel. Some microscale columns, such as that shown in Figure 19.8, are equipped with a solvent reservoir that fits onto the top of the column. It functions just like the reservoirs described in this section.

19.11 Monitoring the Column

It is a happy instance when the compounds to be separated are colored. The separation can then be followed visually and the various bands collected separately as they elute from the column. For the majority of organic compounds, however, this lucky circumstance does not exist, and other methods must be used to determine the positions of the bands. The most common method of following a separation of colorless compounds is to collect \textit{fractions} of constant volume in preweighed flasks, to evaporate the solvent from each fraction, and to reweigh the flask plus any residue. A plot of fraction number versus the weight of the residues after evaporation of solvent gives a plot like that in Figure 19.11. Clearly, fractions 2 through 7 (Peak 1) may be combined as a single compound, and so can fractions 8 through 11 (Peak 2) and 12 through 15 (Peak 3). The size of the fractions

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure19_10}
\caption{Various types of solvent-reservoir arrangements for chromatographic columns.}
\end{figure}
collected (1, 10, 100, or 500 mL) depends on the size of the column and the ease of separation.

Another common method of monitoring the column is to mix an inorganic phosphor into the adsorbent used to pack the column. When the column is illuminated with an ultraviolet light, the adsorbent treated in this way fluoresces. However, many solutes have the ability to quench the fluorescence of the indicator phosphor. In areas in which solutes are present, the adsorbent does not fluoresce, and a dark band is visible. In this type of column, the separation can also be followed visually.

Thin-layer chromatography is often used to monitor a column. This method is described in Technique 20 (Section 20.10, p. 789). Several sophisticated instrumental and spectroscopic methods, which we shall not detail, can also monitor a chromatographic separation.

19.12 Tailing

When a single solvent is used for elution, an elution curve (weight versus fraction) like that shown as a solid line in Figure 19.12 is often observed. An ideal elution curve is shown by dashed lines. In the nonideal curve, the compound is said to be tailing. Tailing can interfere with the beginning of a curve or a peak of a second component and lead to a poor separation. One way to avoid this is to increase the polarity of the solvent constantly while eluting. In this way, at the tail of the peak, where the solvent polarity is increasing, the compound will move slightly faster than at the front and allow the tail to squeeze forward, forming a more nearly ideal band.

19.13 Recovering the Separated Compounds

In recovering each of the separated compounds of a chromatographic separation when they are solids, the various correct fractions are combined and evaporated. If the combined fractions contain sufficient material, they may be purified by recrystallization. If the compounds are liquids, the correct fractions are combined, and the solvent is evaporated. If sufficient material has been collected, liquid samples can be purified by distillation. The combination of chromatography–crystallization or chromatography–distillation usually yields very pure compounds. For microscale applications, the amount of sample collected is too small to allow a purification by crystallization or distillation. The samples that are obtained after the solvent has

Figure 19.11
Typical elution graph.
been evaporated are considered to be sufficiently pure, and no additional purification is attempted.

**Figure 19.12**
*Elution curves: One ideal and one “tails.”*

**PROBLEMS**

1. A sample was placed on a chromatography column. Methylene chloride was used as the eluting solvent. No separation of the components in the sample was observed. What must have been happening during this experiment? How would you change the experiment to overcome this problem?

2. You are about to purify an impure sample of naphthalene by column chromatography. What solvent should you use to elute the sample?

3. Consider a sample that is a mixture composed of biphenyl, benzoic acid, and benzyl alcohol. Predict the order of elution of the components in this mixture. Assume that the chromatography uses a silica column, and the solvent system is based on cyclohexane, with an increasing proportion of methylene chloride being added as a function of time.

4. An orange compound was added to the top of a chromatography column. Solvent was added immediately, with the result that the entire volume of solvent in the solvent reservoir turned orange. No separation could be obtained from the chromatography experiment. What went wrong?

5. A yellow compound, dissolved in methylene chloride, is added to a chromatography column. The elution is begun using petroleum ether as the solvent. After 6 L of solvent had passed through the column, the yellow band still had not traveled down the column appreciably. What should be done to make this experiment work better?

6. You have 0.50 g of a mixture that you wish to purify by column chromatography. How much adsorbent should you use to pack the column? Estimate the appropriate column diameter and height.

7. In a particular sample, you wish to collect the component with the highest molecular weight as the first fraction. What chromatographic technique should you use?

8. A colored band shows an excessive amount of tailing as it passes through the column. What can you do to rectify this problem?

9. How would you monitor the progress of a column chromatography when the sample is colorless? Describe at least two methods.
Thin-Layer Chromatography

Thin-layer chromatography (TLC) is a very important technique for the rapid separation and qualitative analysis of small amounts of material. It is ideally suited for the analysis of mixtures and reaction products in microscale experiments. The technique is closely related to column chromatography. In fact, TLC can be considered simply column chromatography in reverse, with the solvent ascending the adsorbent, rather than descending. Because of this close relationship to column chromatography, and because the principles governing the two techniques are similar, Technique 19, on column chromatography, should be read first.

20.1 Principles of Thin-Layer Chromatography

Like column chromatography, TLC is a solid–liquid partitioning technique. However, the moving liquid phase is not allowed to percolate down the adsorbent; it is caused to ascend a thin layer of adsorbent coated onto a backing support. The most typical backing is a glass plate, but other materials are also used. A thin layer of the adsorbent is spread onto the plate and allowed to dry. A coated and dried plate of glass is called a thin-layer plate or a thin-layer slide. (The reference to slide comes about because microscope slides are often used to prepare small thin-layer plates.) When a thin-layer plate is placed upright in a vessel that contains a shallow layer of solvent, the solvent ascends the layer of adsorbent on the plate by capillary action.

In TLC, the sample is applied to the plate before the solvent is allowed to ascend the adsorbent layer. The sample is usually applied as a small spot near the base of the plate; this technique is often referred to as spotting. The plate is spotted by repeated applications of a sample solution from a small capillary pipet. When the filled pipet touches the plate, capillary action delivers its contents to the plate, and a small spot is formed.

As the solvent ascends the plate, the sample is partitioned between the moving liquid phase and the stationary solid phase. During this process, you are developing, or running, the thin-layer plate. In development, the various components in the applied mixture are separated. The separation is based on the many equilibrations the solutes experience between the moving and the stationary phases. (The nature of these equilibrations was thoroughly discussed in Technique 19, Sections 19.2 and 19.3, pp. 757–759.) As in column chromatography, the least polar substances advance faster than the most polar substances. A separation results from the differences in the rates at which the individual components of the mixture advance upward on the plate. When many substances are present in a mixture, each has its own characteristic solubility and adsorptivity properties, depending on the functional groups in its structure. In general, the stationary phase is strongly polar and strongly binds polar substances. The moving liquid phase is usually less polar than the adsorbent and most easily dissolves...
substances that are less polar or even nonpolar. Thus, substances that are the most polar travel slowly upward, or not at all, and nonpolar substances travel more rapidly if the solvent is sufficiently nonpolar.

When the thin-layer plate has been developed, it is removed from the developing tank and allowed to dry until it is free of solvent. If the mixture that was originally spotted on the plate was separated, there will be a vertical series of spots on the plate. Each spot corresponds to a separate component or compound from the original mixture. If the components of the mixture are colored substances, the various spots will be clearly visible after development. More often, however, the “spots” will not be visible because they correspond to colorless substances. If spots are not apparent, they can be made visible only if a visualization method is used. Often, spots can be seen when the thin-layer plate is held under ultraviolet light; the ultraviolet lamp is a common visualization method. Also common is the use of iodine vapor. The plates are placed in a chamber containing iodine crystals and left to stand for a short time. The iodine reacts with the various compounds adsorbed on the plate to give colored complexes that are clearly visible. Because iodine often changes the compounds by reaction, the components of the mixture cannot be recovered from the plate when the iodine method is used. (Other methods of visualization are discussed in Section 20.7.)

20.2 Commercially Prepared TLC Plates

The most convenient type of TLC plate is prepared commercially and sold in a ready-to-use form. Many manufacturers supply glass plates precoated with a durable layer of silica gel or alumina. More conveniently, plates are also available that have either a flexible plastic backing or an aluminum backing. The most common types of commercial TLC plates are composed of plastic sheets that are coated with silica gel and polyacrylic acid, which serves as a binder. A fluorescent indicator may be mixed with the silica gel. The indicator renders the spots due to the presence of compounds in the sample visible under ultraviolet light (see Section 20.7). Although these plates are relatively expensive when compared with plates prepared in the laboratory, they are far more convenient to use, and they provide more consistent results. The plates are manufactured quite uniformly. Because the plastic backing is flexible, they have the additional advantage that the coating does not flake off the plates easily. The plastic sheets (usually 8 in. by 8 in. square) can also be cut with a pair of scissors or paper cutter to whatever size may be required.

If the package of commercially prepared TLC plates has been opened previously, or if the plates have not been purchased recently, they should be dried before use. Dry the plates by placing them in an oven at 100°C for 30 minutes, and store them in a desiccator until they are to be used.

20.4 Sample Application: Spotting the Plates

Preparing a Micropipet

To apply the sample that is to be separated to the thin-layer plate, one uses a micropipet. A micropipet is easily made from a short length of thin-walled capillary tubing like that used for melting-point determinations, but open at both ends. The capillary tubing is heated at its midpoint with a microburner and rotated until it is soft. When the tubing is soft, the heated portion of the
tubing is drawn out until a constricted portion of tubing 4–5 cm long is formed. After cooling, the constricted portion of tubing is scored at its center with a file or scorer and broken. The two halves yield two capillary micropipets. Figure 20.3 shows how to make such pipets.

**Spotting the Plate**

To apply a sample to the plate, begin by placing about 1 mg of a solid test substance, or one drop of a liquid test substance, in a small container such as a watch glass or a test tube. Dissolve the sample in a few drops of a volatile solvent. Acetone or methylene chloride is usually a suitable solvent. If a solution is to be tested, it can often be used directly. The small capillary pipet, prepared as described, is filled by dipping the pulled end into the solution to be examined. Capillary action fills the pipet. Empty the pipet by touching it lightly to the thin-layer plate at a point about 1 cm from the

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1. Rotate in flame until soft.
2. Remove from flame and pull.
3. Score lightly in center of pulled section.
4. Break in half to give two pipets.

**Figure 20.3**

*Construction of two capillary micropipets.*

**Figure 20.4**

*Spotting the plate with a drawn capillary pipet.*
bottom (Fig. 20.4). The spot must be high enough that it does not dissolve in the developing solvent. It is important to touch the plate very lightly and not to gouge a hole in the adsorbent. When the pipet touches the plate, the solution is transferred to the plate as a small spot. The pipet should be touched to the plate very briefly and then removed. If the pipet is held to the plate, its entire contents will be delivered to the plate. Only a small amount of material is needed. It is often helpful to blow gently on the plate as the sample is applied. This helps to keep the spot small by evaporating the solvent before it can spread out on the plate. The smaller the spot formed, the better the separation obtainable. If needed, additional material can be applied to the plate by repeating the spotting procedure. You should repeat the procedure with several small amounts, rather than apply one large amount. The solvent should be allowed to evaporate between applications. If the spot is not small (about 2 mm in diameter), a new plate should be prepared. The capillary pipet may be used several times if it is rinsed between uses. It is repeatedly dipped into a small portion of solvent to rinse it and touched to a paper towel to empty it.

As many as three spots may be applied to a microscope-slide TLC plate. Each spot should be about 1 cm from the bottom of the plate, and all spots should be evenly spaced, about 1 cm apart. The spots should be positioned at least 1 cm from the edges of the plate. Due to diffusion, spots often increase in diameter as the plate is developed. To keep spots containing different materials from merging and to avoid confusing the samples, do not place more than three spots on a single plate. Larger plates can accommodate many more samples.

20.5 Developing (Running) TLC Plates

Preparing a Development Chamber
A convenient development chamber for microscope-slide TLC plates can be made from a 4-oz wide-mouthed jar. An alternative development chamber can be constructed from a beaker, using aluminum foil to cover the opening. The inside of the jar or beaker should be lined with a piece of filter paper, cut so that it does not quite extend around the inside of the jar. A small vertical opening (2–3 cm) should be left in the filter paper for observing the development. Before development, the filter paper inside the jar or beaker should be thoroughly moistened with the development solvent. The solvent-saturated liner helps to keep the chamber saturated with solvent vapors, thereby speeding the development. Once the liner is saturated, the level of solvent in the bottom of the development chamber is adjusted to a depth of about 5 mm, and the chamber is capped (or covered with aluminum foil) and set aside until it is to be used. A correctly prepared development chamber (with slide in place) is shown in Figure 20.5.
Developing the TLC Plate

Once the spot has been applied to the thin-layer plate and the solvent has been selected (see Section 20.5), the plate is placed in the chamber for development. The plate must be placed in the chamber carefully so that none of the coated portion touches the filter paper liner. In addition, the solvent level in the bottom of the chamber must not be above the spot that was applied to the plate, or the spotted material will dissolve in the pool of solvent instead of undergoing chromatography. Once the plate has been placed correctly, replace the cap on the developing chamber and wait for the solvent to advance up the plate by capillary action. This generally occurs rapidly, and you should watch carefully. As the solvent rises, the plate becomes visibly moist. When the solvent has advanced to within 5 mm of the end of the coated surface, the plate should be removed, and the position of the solvent front should be marked immediately by scoring the plate along the solvent line with a pencil. The solvent front must not be allowed to travel beyond the end of the coated surface. The plate should be removed before this happens. The solvent will not actually advance beyond the end of the plate, but spots allowed to stand on a completely moistened plate on which the solvent is not in motion expand by diffusion. Once the plate has dried, any visible spots should be outlined on the plate with a pencil. If no spots are apparent, a visualization method (Section 20.7) may be needed.

The development solvent used depends on the materials to be separated. You may have to try several solvents before a satisfactory separation is achieved. Because microscope slides can be prepared and developed rapidly, an empirical choice is usually not hard to make. A solvent that causes all the spotted material to move with the solvent front is too polar.
One that does not cause any of the material in the spot to move is not polar enough. As a guide to the relative polarity of solvents, consult Table 19.2 in Technique 19 (p. 761). Figure 20.6 shows three TLC plates run with different solvents. As can be seen, if the solvent is too polar, the spots tend to run near the top of the plate, and the separation is poor. If the solvent is not sufficiently polar, the spots do not travel very far; again, the separation is poor. The ideal solvent choice allows the spots to travel well up the plate but allows for a clean separation.

Methylene chloride and toluene are solvents of intermediate polarity and good choices for a wide variety of functional groups to be separated. For hydrocarbon materials, good first choices are hexane, petroleum ether (ligroin), or toluene. Hexane or petroleum ether with varying proportions of toluene or ether gives solvent mixtures of moderate polarity that are useful

Figure 20.6
TLC plates showing the effects of solvent polarity on a separation. The three spots on each plate are indicated by M for a two-component mixture, A for a standard sample of substance A, and B for a standard sample of substance B. (a) Solvent of low polarity: poor separation. (b) Solvent of high polarity: poor separation. (c) Solvent of intermediate polarity: clean separation.

Figure 20.7
Concentric ring method of testing solvents.
for many common functional groups. Polar materials may require ethyl acetate, acetone, or methanol.

A rapid way to determine a good solvent is to apply several sample spots to a single plate. The spots should be placed a minimum of 1 cm apart. A capillary pipet is filled with a solvent and gently touched to one of the spots. The solvent expands outward in a circle. The solvent front should be marked with a pencil. A different solvent is applied to each spot. As the solvents expand outward, the spots expand as concentric rings. From the appearance of the rings, you can judge approximately the suitability of the solvent. Several types of behavior experienced with this method of testing are shown in Figure 20.7.

20.7 Visualization Methods

It is fortunate when the compounds separated by TLC are colored because the separation can be followed visually. More often than not, however, the compounds are colorless. In that case, the separated materials must be made visible by some reagent or some method that makes the separated compounds visible. Reagents that give rise to colored spots are called visualization reagents. Methods of viewing that make the spots apparent are visualization methods.

The visualization reagent used most often is iodine. Iodine reacts with many organic materials to form complexes that are either brown or yellow. In this visualization method, the developed and dried TLC plate is placed in a 4-oz wide-mouth screw-cap jar along with a few crystals of iodine. The jar is capped and gently warmed on a steam bath or a hot plate at low heat. The jar fills with iodine vapors, and the spots begin to appear. When the spots are sufficiently intense, the plate is removed from the jar and the spots are outlined with a pencil. The spots are not permanent. Their appearance results from the formation of complexes the iodine makes with the organic substances. As the iodine sublimes off the plate, the spots fade. Hence, they should be marked immediately. Nearly all compounds except saturated hydrocarbons and alkyl halides form complexes with iodine. The intensities of the spots do not accurately indicate the amount of material present, except in the crudest way.

The second most common method of visualization is by an ultraviolet (UV) lamp. Under UV light, compounds often look like bright spots on the plate. This often suggests the structure of the compound: Certain types of compounds shine very brightly under UV light because they fluoresce.

Another method that provides good results involves adding a fluorescent indicator to the adsorbent used to coat the plates. A mixture of zinc and cadmium sulfides is often used. When treated in this way and held under UV light, the entire plate fluoresces. However, dark spots appear on the plate where the separated compounds are seen to quench this fluorescence.

In addition to the preceding methods, several chemical methods are available that either destroy or permanently alter the separated compounds through reaction. Many of these methods are specific for particular functional groups.
Alkyl halides can be visualized if a dilute solution of silver nitrate is sprayed on the plates. Silver halides are formed. These halides decompose if exposed to light, giving rise to dark spots (free silver) on the TLC plate.

Most organic functional groups can be made visible if they are charred with sulfuric acid. Concentrated sulfuric acid is sprayed on the plate, which is then heated in an oven at 110°C to complete the charring. Permanent spots are thus created.

Colored compounds can be prepared from colorless compounds by making derivatives before spotting them on the plate. An example of this is the preparation of 2,4-dinitrophenylhydrazones from aldehydes and ketones to produce yellow and orange compounds. You may also spray the 2,4-dinitrophenylhydrazine reagent on the plate after the ketones or aldehydes have separated. Red and yellow spots form where the compounds are located. Other examples of this method are using ferric chloride for visualizing phenols and using bromoresol green for detecting carboxylic acids. Chromium trioxide, potassium dichromate, and potassium permanganate can be used for visualizing compounds that are easily oxidized. p-Dimethylaminobenzaldehyde easily detects amines. Ninhydrin reacts with amino acids to make them visible. Numerous other methods and reagents available from various supply outlets are specific for certain types of functional groups. These visualize only the class of compounds of interest.

20.9 The Rf Value

Thin-layer chromatography conditions include

1. Solvent system
2. Adsorbent
3. Thickness of the adsorbent layer
4. Relative amount of material spotted

Under an established set of such conditions, a given compound always travels a fixed distance relative to the distance the solvent front travels. This ratio of the distance the compound travels to the distance the solvent travels is called the Rf value. The symbol Rf stands for “retardation factor,” or “ratio-to-front,” and it is expressed as a decimal fraction:

\[ Rf = \frac{\text{distance traveled by substance}}{\text{distance traveled by solvent front}} \]

When the conditions of measurement are completely specified, the Rf value is constant for any given compound, and it corresponds to a physical property of that compound.

The Rf value can be used to identify an unknown compound, but like any other identification based on a single piece of data, the Rf value is best confirmed with some additional data. Many compounds can have the same Rf value, just as many compounds have the same melting point.
It is not always possible, in measuring an $R_f$ value, to duplicate exactly the conditions of measurement another researcher has used. Therefore, $R_f$ values tend to be of more use to a single researcher in one laboratory than they are to researchers in different laboratories. The only exception to this is when two researchers use TLC plates from the same source, as in commercial plates, or know the exact details of how the plates were prepared. Nevertheless, the $R_f$ value can be a useful guide. If exact values cannot be relied on, the relative values can provide another researcher with useful information about what to expect. Anyone using published $R_f$ values will find it a good idea to check them by comparing them with standard substances whose identity and $R_f$ values are known.

To calculate the $R_f$ value for a given compound, measure the distance that the compound has traveled from the point at which it was originally spotted. For spots that are not too large, measure to the center of the migrated spot. For large spots, the measurement should be repeated on a new plate, using less material. For spots that show tailing, the measurement is made to the “center of gravity” of the spot. This first distance measurement is then divided by the distance the solvent front has traveled from the same original spot. A sample calculation of the $R_f$ values of two compounds is illustrated in Figure 20.8.

![Figure 20.8](image)

Sample calculation of $R_f$ values.

$R_f$ (compound 1) = \frac{22}{65} = 0.34 \quad R_f$ (compound 2) = \frac{50}{65} = 0.77
Thin-layer chromatography has several important uses in organic chemistry. It can be used in the following applications:

1. To establish that two compounds are identical
2. To determine the number of components in a mixture
3. To determine the appropriate solvent for a column-chromatographic separation
4. To monitor a column-chromatographic separation
5. To check the effectiveness of a separation achieved on a column, by crystallization or by extraction
6. To monitor the progress of a reaction

In all these applications, TLC has the advantage that only small amounts of material are necessary. Material is not wasted. With many of the visualization methods, less than a tenth of a microgram ($10^{-7}$ g) of material can be detected. On the other hand, samples as large as a milligram may be used. With preparative plates that are large (about 9 in. on a side) and have a relatively thick coating of adsorbent (>500 μm), it is often possible to separate from 0.2 to 0.5 g of material at one time. The main disadvantage of TLC is that volatile materials cannot be used, because they evaporate from the plates.

Thin-layer chromatography can establish that two compounds suspected to be identical are in fact identical. Simply spot both compounds side by side on a single plate and develop the plate. If both compounds travel the same distance on the plate (have the same $R_f$ value), they are probably identical. If the spot positions are not the same, the compounds are definitely not identical. It is important to spot compounds on the same plate. This is especially important with hand-dipped microscope slides. Because they vary widely from plate to plate, no two plates have exactly the same thickness of adsorbent. If you use commercial plates, this precaution is not necessary, although it is nevertheless a good idea.

Thin-layer chromatography can establish whether a sample is a single substance or a mixture. A single substance gives a single spot no matter what solvent is used to develop the plate. On the other hand, the number of components in a mixture can be established by trying various solvents on a mixture. A word of caution should be given. It may be difficult, in dealing with compounds of very similar properties, isomers for example, to find a solvent that will separate the mixture. Inability to achieve a separation is not absolute proof that a sample is a single pure substance. Many compounds can be separated only by multiple developments of the TLC slide with a fairly nonpolar solvent. In this method, you remove the plate after the first development and allow it to dry. After being dried, it is placed in the chamber again and developed once more. This effectively doubles the length of the slide. At times, several developments may be necessary.

When a mixture is to be separated, you can use TLC to choose the best solvent to separate it if column chromatography is contemplated. You can try various solvents on a plate coated with the same adsorbent as will be used in the column. The solvent that resolves the components best will probably work well on the column. These small-scale experiments are quick, use very little material, and save time that would be wasted by attempting to separate the entire mixture on the column. Similarly, TLC plates can monitor a column. A hypothetical situation is shown in Figure 20.9.
A solvent was found that would separate the mixture into four components (A–D). A column was run using this solvent, and 11 fractions of 15 mL each were collected. Thin-layer analysis of the various fractions showed that Fractions 1–3 contained Component A; Fractions 4–7, Component B; Fractions 8–9, Component C; and Fractions 10–11, Component D. A small amount of cross-contamination was observed in Fractions 3, 4, 7, and 9.

In another TLC example, a researcher found a product from a reaction to be a mixture. It gave two spots, A and B, on a TLC slide. After the product was crystallized, the crystals were found by TLC to be pure A, whereas the mother liquor was found to have a mixture of A and B. The crystallization was judged to have purified A satisfactorily.

Finally, it is often possible to monitor the progress of a reaction by TLC. At various points during a reaction, samples of the reaction mixture are taken and subjected to TLC analysis. An example is given in Figure 20.10. In this case, the desired reaction was the conversion of A to B. At the beginning...

Figure 20.9
Monitoring a column.

Figure 20.10
Monitoring a reaction.
of the reaction (0 hr), a TLC slide was prepared that was spotted with pure A, pure B, and the reaction mixture. Similar slides were prepared at 0.5, 1, 2, and 3 hours after the start of the reaction. The slides showed that the reaction was complete in 2 hours. When the reaction was run longer than 2 hours, a new compound, side product C, began to appear. Thus, the optimum reaction time was judged to be 2 hours.

**PROBLEMS**

1. A student spots an unknown sample on a TLC plate and develops it in dichloromethane solvent. Only one spot, for which the $R_f$ value is 0.95, is observed. Does this indicate that the unknown material is a pure compound? What can be done to verify the purity of the sample?

2. You and another student were each given an unknown compound. Both samples contained colorless material. You each used the same brand of commercially prepared TLC plate and developed the plates using the same solvent. Each of you obtained a single spot of $R_f = 0.75$. Were the two samples necessarily the same substance? How could you prove unambiguously that they were identical using TLC?

3. Consider a sample that is a mixture composed of biphenyl, benzoic acid, and benzyl alcohol. The sample is spotted on a TLC plate and developed in a dichloromethane–cyclohexane solvent mixture. Predict the relative $R_f$ values for the three components in the sample. Hint: See Table 19.3.

4. Calculate the $R_f$ value of a spot that travels 5.7 cm, with a solvent front that travels 13 cm.

5. A student spots an unknown sample on a TLC plate and develops it in pentane solvent. Only one spot, for which the $R_f$ value is 0.05, is observed. Is the unknown material a pure compound? What can be done to verify the purity of the sample?

6. A colorless unknown substance is spotted on a TLC plate and developed in the correct solvent. The spots do not appear when visualization with a UV lamp or iodine vapors is attempted. What could you do in order to visualize the spots if the compound is
   a. An alkyl halide
   b. A ketone
   c. An amino acid
   d. A sugar
Gas Chromatography

Gas chromatography is one of the most useful instrumental tools for separating and analyzing organic compounds that can be vaporized without decomposition. Common uses include testing the purity of a substance and separating the components of a mixture. The relative amounts of the components in a mixture may also be determined. In some cases, gas chromatography can be used to identify a compound. In microscale work, it can also be used as a preparative method to isolate pure compounds from a small amount of a mixture.

Gas chromatography resembles column chromatography in principle, but it differs in three respects. First, the partitioning processes for the compounds to be separated are carried out between a moving gas phase and a stationary liquid phase. (Recall that in column chromatography the moving phase is a liquid and the stationary phase is a solid adsorbent.) A second difference is that the temperature of the gas system can be controlled because the column is contained in an insulated oven. And third, the concentration of any given compound in the gas phase is a function of its vapor pressure only. Because gas chromatography separates the components of a mixture primarily on the basis of their vapor pressures (or boiling points), this technique is also similar in principle to fractional distillation. In microscale work, it is sometimes used to separate and isolate compounds from a mixture; fractional distillation would normally be used with larger amounts of material.

Gas chromatography (GC) is also known as vapor-phase chromatography (VPC) and as gas–liquid partition chromatography (GLPC). All three names, as well as their indicated abbreviations, are often found in the literature of organic chemistry. In reference to the technique, the last term, GLPC, is the most strictly correct and is preferred by most authors.
The apparatus used to carry out a gas–liquid chromatographic separation is generally called a gas chromatograph. A typical student-model gas chromatograph, the GOW-MAC model 69-350, is illustrated in Figure 22.1. A schematic block diagram of a basic gas chromatograph is shown in Figure 22.2. The basic elements of the apparatus are apparent. In short, the sample is injected into the chromatograph, and it is immediately vaporized in a heated injection chamber and introduced into a moving stream of gas, called the carrier gas. The vaporized sample is then swept into a column filled with particles coated with a liquid adsorbent. The column is contained in a temperature-controlled oven. As the sample passes through the column, it is subjected to many gas–liquid partitioning processes, and the components are separated. As each component leaves the column, its presence is detected by an electrical detector that generates a signal that is recorded on a strip chart recorder.

Many modern instruments are also equipped with a microprocessor, which can be programmed to change parameters, such as the temperature of the oven, while a mixture is being separated on a column. With this capability, it is possible to optimize the separation of components and to complete a run in a relatively short time.

The heart of the gas chromatograph is the column. There are two types in common use: packed and capillary columns.
Packed Columns. These columns are usually constructed of stainless steel tubing with diameters of \( \frac{1}{8} \) in. (3 mm) or \( \frac{1}{4} \) in. (6 mm) and lengths of from 4 to 12 feet. The column is packed with a liquid or low melting solid as the stationary phase distributed on a solid support material. The stationary phase must be relatively nonvolatile, that is, it should have a low vapor pressure and a high boiling point. Some typical stationary phases used with packed columns are listed in Table 22.1. Typical support materials are shown in Table 22.2. The most common support material consists of diatomaceous earth (Chromosorb).

Packed columns are bought from commercial sources or may sometimes be made in the laboratory by researchers. Basically, you dissolve one of the stationary phases listed in Table 22.1 in methylene chloride. Then you add the support material to the solution followed by removal of the solvent on a rotary evaporator (see Technique 7, Section 7.11, page 615 and Figure 7.19, p. 614). The evaporation process evenly distributes the stationary phase onto the support material and yields a dry solid. In the final step, the solid consisting of the stationary phase coated on the support material, is packed into the stainless steel tubing as evenly as possible. After plugging the ends of the tubing with glass wool to prevent the solid from coming out, the tubing is rolled into a coil that will fit into the oven of the gas chromatograph with the two ends connected to the gas entrance and exit ports (see Figure 22.2).

The selection of the packed column depends on the application. If one wants to separate nonpolar compounds that vary only by boiling point, one often uses one of the polydimethyl siloxanes (methyl silicones) columns such as SE-30 or DC-200. For more polar compounds, chemists will select a silicone column that has attached methyl and phenyl groups on the silicone polymer (DC-710). Separating even more polar compounds calls for a polyethylene glycol (carbowax) column or a column packed with diethylene glycol.
Increasing polarity

Table 22.1  *Typical stationary phases*

<table>
<thead>
<tr>
<th>Type</th>
<th>Composition</th>
<th>Maximum Temperature (°C)</th>
<th>Typical Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apiezon L</td>
<td>Hydrocarbon mixtures</td>
<td>250–300</td>
<td>Hydrocarbons</td>
</tr>
<tr>
<td>(M, N, etc.)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SE-30</td>
<td>Methyl silicone rubber</td>
<td>350</td>
<td>General applications</td>
</tr>
<tr>
<td>DC-200</td>
<td>Like silicone oil, but cross-linked</td>
<td>225</td>
<td>Aldehydes, ketones, halocarbons</td>
</tr>
<tr>
<td>DC-710</td>
<td>R&lt;sub&gt;3&lt;/sub&gt;Si-O-Si-O-Si&lt;sub&gt;n&lt;/sub&gt;O&lt;sub&gt;2&lt;/sub&gt;SiR&lt;sub&gt;3&lt;/sub&gt;</td>
<td>300</td>
<td>General applications</td>
</tr>
<tr>
<td>Carbowaxes</td>
<td>Polyether</td>
<td>Up to 250</td>
<td>Alcohols, ethers, halocarbons</td>
</tr>
<tr>
<td>(400–20M)</td>
<td>HO-(CH&lt;sub&gt;2&lt;/sub&gt;CH&lt;sub&gt;2&lt;/sub&gt;-O)&lt;sub&gt;n&lt;/sub&gt;-CH&lt;sub&gt;2&lt;/sub&gt;CH&lt;sub&gt;2&lt;/sub&gt;OH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DEGS</td>
<td>Diethylene glycol succinate</td>
<td>200</td>
<td>General applications</td>
</tr>
</tbody>
</table>

succinate (DEGS). Chemists will need to carefully note the maximum temperature that can be employed with the columns (Table 22.1). Above the specified temperature, the liquid phase itself will begin to “bleed” off the column.

Packed columns are cheaper to buy and can separate larger quantities of material than capillary columns. Packed columns, however, are not as
efficient in separating materials, especially with compounds with very similar polarities or boiling points.

**Capillary Columns.** Many gas chromatographs sold today use capillary columns rather than packed columns. Capillary columns are made of very thin fused-silica with an inner diameter of about 0.25 mm. Typically the columns are very long, often 25 meters up to 100 meters in length. The stationary phase is coated as a film on the inner surface with a thickness of about 0.25 μm. The film is bonded to the silica and cross-linked to improve thermal stability and to help prevent bleeding of the stationary phase from the column. Most of the capillary columns do not have any support material in them.

The liquid stationary phases used with capillary columns are similar to those used in packed columns. The most common stationary phases are polysiloxanes (silicones) that contain various substituents that modify the polarity of the phase. Polymethyl siloxane (methyl silicone) is nonpolar. Replacing methyl groups with increasing numbers of phenyl substituents increases the polarity of the silicone. For example, J&W DB-I, or a similar stationary phase sold by other companies, has the same properties as methyl silicone (SE-30 or DC-200) and is used with nonpolar compounds that separate by boiling point differences. For other applications, a J&W DB-5 may be used. This silicone consists of a material with 95% methyl and 5% phenyl substituents on the silicone. A DB-17 column has 50% phenyl groups replacing methyl groups, and would have a medium polarity (similar to DC-710). J&W DB-wax is used to separate much more polar compounds and is similar to diethylene glycols (carbowax). Chiral capillary columns are also available that can separate enantiomers (Section 22.8).

Because of the length and small diameter of capillary columns, there is increased interaction between the compounds in the mixture and the stationary phase. Capillary columns are, therefore, much more efficient in separating compounds with similar properties than with packed columns, but only if a dilute solution of a mixture of compounds is injected into the column. In order to obtain a satisfactory separation, you must dissolve about 1 drop of a mixture in about 2 mL of a solvent such as methylene chloride or pentane. About 1 μL of this dilute sample is injected onto the column. In contrast, 1 to 10 μL of an undiluted sample can often be analyzed on a packed column without overloading the column. These expensive capillary columns must be purchased from commercial companies specializing in their manufacture. Sensible researchers would never try to make their own capillary columns!

In the final step, the liquid-phase-coated support material is packed into the tubing as evenly as possible. The tubing is bent or coiled so that it fits into the oven of the gas chromatograph with its two ends connected to the gas entrance and exit ports.

Selection of a liquid phase usually revolves about two factors. First, most of them have an upper temperature limit above which they cannot be used. Above the specified limit of temperature, the liquid phase itself will

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1 Many companies supply capillary columns: J&W (Alltech), Supelco, HP, Chrompack, and Quadrex are some of the suppliers. Comparison of chemical compositions, polarities and applications may be made by consulting: http://www.quadrexcorp.com/new/columns.htm
begin to “bleed” off the column. Second, the materials to be separated must be considered. For polar samples, it is usually best to use a polar liquid phase; for nonpolar samples, a nonpolar liquid phase is indicated. The liquid phase performs best when the substances to be separated 

Most researchers today buy packed columns from commercial sources, rather than pack their own. A wide variety of types and lengths is available. Alternatives to packed columns are Golay or glass capillary columns of diameters 0.1–0.2 mm. With these columns, no solid support is required, and the liquid is coated directly on the inner walls of the tubing. Liquid phases commonly used in glass capillary columns are similar in composition to those used in packed columns. They include DB-1 (similar to SE-30), DB-17 (similar to DC-710), and DB-WAX (similar to Carbowax 20M). The length of a capillary column is usually very long, typically 50–100 ft. Because of the length and small diameter, there is increased interaction between the sample and the stationary phase. Gas chromatographs equipped with these small-diameter columns are able to separate components more effectively than instruments using larger packed columns.

22.3 Principles of Separation

After a column is selected and installed, the carrier gas (usually helium, argon, or nitrogen) is allowed to flow through the column supporting the liquid phase. The mixture of compounds to be separated is introduced into the carrier gas stream, where its components are equilibrated (or partitioned) between the moving gas phase and the stationary liquid phase (Figure 22.3). The latter is held stationary because it is adsorbed onto the surfaces of the support material.

The sample is introduced into the gas chromatograph by a microliter syringe. It is injected as a liquid or as a solution through a rubber septum into a heated chamber, called the injection port, where it is vaporized and mixed with the carrier gas. As this mixture reaches the column, which is heated in a controlled oven, it begins to equilibrate between the liquid and

![Figure 22.3](image-url)

*The separation process.*
gas phases. The length of time required for a sample to move through the column is a function of how much time it spends in the vapor phase and how much time it spends in the liquid phase. The more time it spends in the vapor phase, the faster it gets to the end of the column. In most separations, the components of a sample have similar solubilities in the liquid phase. Therefore, the time the different compounds spend in the vapor phase is primarily a function of the vapor pressure, and the more volatile component arrives at the end of the column first, as illustrated in Figure 22.3. By selecting the correct temperature of the oven and the correct liquid phase, the compounds in the injected mixture travel through the column at different rates and are separated.

Several factors determine the rate at which a given compound travels through a gas chromatograph. First of all, compounds with low boiling points will generally travel through the gas chromatograph faster than compounds of higher boiling points. This because the column is heated, and low-boiling compounds always have higher vapor pressures than compounds of higher boiling point. In general, therefore, for compounds with the same functional group, the higher the molecular weight, the longer the retention time. For most molecules, the boiling point increases as the molecular weight increases. If the column is heated to a temperature that is too high, however, the entire mixture to be separated is flushed through the column at the same rate as the carrier gas, and no equilibration takes place with the liquid phase. On the other hand, at too low a temperature, the mixture dissolves in the liquid phase and never revaporizes. Thus, it is retained on the column.

The second factor, the rate of flow of the carrier gas, is important. The carrier gas must not move so rapidly that molecules of the sample in the vapor phase cannot equilibrate with those dissolved in the liquid phase. This may result in poor separation between components in the injected mixture. If the rate of flow is too slow, however, the bands broaden significantly, leading to poor resolution (see Section 22.8).

The third factor is the choice of liquid phase used in the column. The molecular weights, functional groups, and polarities of the component molecules in the mixture to be separated must be considered when a liquid phase is being chosen. One generally uses a different type of material for hydrocarbons, for instance, than for esters. The materials to be separated should dissolve in the liquid. The useful temperature limit of the liquid phase selected must also be considered.

The fourth factor, the length of the column, is also important. Compounds that resemble one another closely, in general, require longer columns than dissimilar compounds. Many kinds of isomeric mixtures fit into the “difficult” category. The components of isomeric mixtures are so much alike that they travel through the column at very similar rates. You need a longer column, therefore, to take advantage of any differences that may exist.

All factors that have been mentioned must be adjusted by the chemist for any mixture to be separated. Considerable preliminary investigation is often required before a mixture can be separated successfully into its components by gas chromatography. Nevertheless, the advantages of the technique are many.

First, many mixtures can be separated by this technique when no other method is adequate. Second, as little as 1–10 μL (1 μL = 10⁻⁶ L) of a mixture can be separated by this technique. This advantage is particularly important
when working at the microscale level. Third, when gas chromatography is coupled with an electronic recording device (see following discussion), the amount of each component present in the separated mixture can be estimated quantitatively.

The range of compounds that can be separated by gas chromatography extends from gases, such as oxygen (bp $-183^\circ$C) and nitrogen (bp $-196^\circ$C), to organic compounds with boiling points over $400^\circ$C. The only requirement for the compounds to be separated is that they have an appreciable vapor pressure at a temperature at which they can be separated and that they be thermally stable at this temperature.

22.6 Monitoring the Column (The Detector)

To follow the separation of the mixture injected into the gas chromatograph, it is necessary to use an electrical device called a detector. Two types of detectors in common use are the thermal conductivity detector (TCD) and the flame-ionization detector (FID).

The thermal conductivity detector is simply a hot wire placed in the gas stream at the column exit. The wire is heated by constant electrical voltage. When a steady stream of carrier gas passes over this wire, the rate at which it loses heat and its electrical conductance have constant values. When the composition of the vapor stream changes, the rate of heat flow from the wire, and hence its resistance, changes. Helium, which has a higher thermal conductivity than most organic substances, is a common carrier gas. Thus, when a substance elutes in the vapor stream, the thermal conductivity of the moving gases will be lower than with helium alone. The wire then heats up, and its resistance decreases.

A typical TCD operates by difference. Two detectors are used: one exposed to the actual effluent gas and the other exposed to a reference flow of carrier gas only. To achieve this situation, a portion of the carrier gas stream is diverted before it enters the injection port. The diverted gas is routed through a reference column into which no sample has been admitted. The detectors mounted in the sample and reference columns are arranged so as to form the arms of a Wheatstone bridge circuit, as shown in Figure 22.4.

![Figure 22.4](image)

Typical thermal conductivity detector.
As long as the carrier gas alone flows over both detectors, the circuit is in balance. However, when a sample elutes from the sample column, the bridge circuit becomes unbalanced, creating an electrical signal. This signal can be amplified and used to activate a strip chart recorder. The recorder is an instrument that plots, by means of a moving pen, the unbalanced bridge current versus time on a continuously moving roll of chart paper. This record of detector response (current) versus time is called a **chromatogram**. A typical gas chromatogram is illustrated in Figure 22.5. Deflections of the pen are called **peaks**.

When a sample is injected, some air (CO\(_2\), H\(_2\)O, N\(_2\), and O\(_2\)) is introduced along with the sample. The air travels through the column almost as rapidly as the carrier gas; as it passes the detector, it causes a small pen response, thereby giving a peak, called the **air peak**. At later times (\(t_1\), \(t_2\), \(t_3\)), the components also give rise to peaks on the chromatogram as they pass out of the column and past the detector.

In a flame-ionization detector, the effluent from the column is directed into a flame produced by the combustion of hydrogen, as illustrated in Figure 22.6. As organic compounds burn in the flame, ion fragments are produced that collect on the ring above the flame. The resulting electrical signal is amplified and sent to a recorder in a similar manner to a TCD, except that a FID does not produce an air peak. The main advantage of the FID is that it is more sensitive and can be used to analyze smaller quantities of sample. Also, because a FID does not respond to water, a gas chromatograph with this detector can be used to analyze aqueous solutions. Two disadvantages are that it is more difficult to operate and the detection process destroys the sample. Therefore, an FID gas chromatograph cannot be used to do preparative work, which is often desired in the microscale laboratory.

**Figure 22.5**

*Typical chromatogram.*
22.7 Retention Time

The period following injection that is required for a compound to pass through the column is called the **retention time** of that compound. For a given set of constant conditions (flow rate of carrier gas, column temperature, column length, liquid phase, injection port temperature, carrier), the retention time of any compound is always constant (much like the $R_f$ value in thin-layer chromatography, as described in Technique 20, Section 20.9, p. 787). The retention time is measured from the time of injection to the time of maximum pen deflection (detector current) for the component being observed. This value, when obtained under controlled conditions, can identify a compound by a direct comparison of it with values for known compounds determined under the same conditions. For easier measurement of retention times, most strip chart recorders are adjusted to move the paper at a rate that corresponds to time divisions calibrated on the chart paper. The retention times ($t_1$, $t_2$, $t_3$) are indicated in Figure 22.5 for the three peaks illustrated.

Most modern gas chromatographs are attached to a “data station,” which uses a computer or a microprocessor to process the data. With these instruments, the chart often does not have divisions. Instead, the computer prints the retention time, usually to the nearest 0.01 minute, above each peak.

22.9 Poor Resolution and Tailing

The peaks in Figure 22.5 are well **resolved**. That is, the peaks are separated from one another, and between each pair of adjacent peaks the tracing returns to the **baseline**. In Figure 22.8, the peaks overlap, and the resolution is not good. Poor resolution is often caused by using too much sample, too high a column temperature, too short a column, a liquid phase that does not discriminate well between the two components, a column with too large a diameter, or, in short, almost any wrongly adjusted parameter. When peaks are poorly resolved, it is more difficult to determine the relative amount of each component. Methods for determining the relative percentages of each component are given in Section 22.12.

Another desirable feature illustrated by the chromatogram in Figure 22.5 is that each peak is symmetrical. A common example of an unsymmetrical peak is one in which **tailing** has occurred, as shown in Figure 22.9. Tailing
usually results from injecting too much sample into the gas chromatograph. Another cause of tailing occurs with polar compounds, such as alcohols and aldehydes. These compounds may be temporarily adsorbed on column walls or areas of the support material that are not adequately coated by the liquid phase. Therefore, they do not leave in a band, and tailing results.

22.12 Quantitative Analysis
The area under a gas-chromatograph peak is proportional to the amount (moles) of compound eluted. Hence, the molar percentage composition of a mixture can be approximated by comparing relative peak areas. This method
of analysis assumes that the detector is equally sensitive to all compounds eluted and that it gives a linear response with respect to amount. Nevertheless, it gives reasonably accurate results.

The simplest method of measuring the area of a peak is by geometrical approximation, or triangulation. In this method, you multiply the height $h$ of the peak above the baseline of the chromatogram by the width of the peak at half of its height $w_{1/2}$. This is illustrated in Figure 22.13. The baseline is approximated by drawing a line between the two side arms of the peak. This method works well only if the peak is symmetrical. If the peak has tailed or is unsymmetrical, it is best to cut out the peaks with scissors and weigh the pieces of paper on an analytical balance. Because the weight per area of a piece of good chart paper is reasonably constant from place to place, the ratio of the areas is the same as the ratio of the weights. To obtain a percentage composition for the mixture, first add all the peak areas (weights). Then, to calculate the percentage of any component in the mixture, divide its individual area by the total area and multiply the result by 100. A sample calculation is illustrated in Figure 22.14. If peaks overlap (see Fig. 22.8), either the gas-chromatographic conditions must be readjusted to achieve better resolution of the peaks or the peak shape must be estimated.

Figure 22.13
Triangulation of a peak.

Figure 22.14
Sample percentage composition calculation.
There are various instrumental means, which are built into recorders, of detecting the amounts of each sample automatically. One method uses a separate pen that produces a trace that integrates the area under each peak. Another method employs an electronic device that automatically prints out the area under each peak and the percentage composition of the sample.

Most modern data stations label the top of each peak with its retention time in minutes. When the trace is completed, the computer prints a table of all the peaks with their retention times, areas, and the percentage of the total area (sum of all the peaks) that each peak represents. Some caution should be used with these results because the computer often does not include smaller peaks and occasionally does not resolve narrow peaks that are so close together that they overlap. If the trace has several peaks and you would like the ratio of only two of them, you will have to determine their percentages yourself using only their two areas or instruct the instrument to integrate only these two peaks.

For the experiments in this textbook, we have assumed that the detector is equally sensitive to all compounds eluted. Compounds with different functional groups or with widely varying molecular weights, however, produce different responses with both TCD and FID gas chromatographs. With a TCD, the responses are different because not all compounds have the same thermal conductivity. Different compounds analyzed with a FID gas chromatograph also give different responses because the detector response varies with the type of ions produced. For both types of detectors, it is possible to calculate a response factor for each compound in a mixture. Response factors are usually determined by making up an equimolar mixture of two compounds, one of which is considered to be the reference. The mixture is separated on a gas chromatograph, and the relative percentages are calculated using one of the methods described previously. From these percentages you can determine a response factor for the compound being compared to the reference. If you do this for all the components in a mixture, you can then use these correction factors to make more accurate calculations of the relative percentages for the compounds in the mixture.

To illustrate how response factors are determined, consider the following example. An equimolar mixture of benzene, hexane, and ethyl acetate is prepared and analyzed using a flame-ionization gas chromatograph. The peak areas obtained are

<table>
<thead>
<tr>
<th>Compound</th>
<th>Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hexane</td>
<td>831158</td>
</tr>
<tr>
<td>Ethyl acetate</td>
<td>1449695</td>
</tr>
<tr>
<td>Benzene</td>
<td>966463</td>
</tr>
</tbody>
</table>

In most cases, benzene is taken as the standard, and its response factor is defined to be equal to 1.00. Calculation of the response factors for the other components of the test mixture proceeds as follows:

<table>
<thead>
<tr>
<th>Component</th>
<th>Response Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hexane</td>
<td>831158/966463 = 0.86</td>
</tr>
<tr>
<td>Ethyl acetate</td>
<td>1449695/966463 = 1.50</td>
</tr>
<tr>
<td>Benzene</td>
<td>966463/966463 = 1.00 (by definition)</td>
</tr>
</tbody>
</table>

Notice that the response factors calculated in this example are molar response factors. It is necessary to correct these values by the relative molecular weights of each substance to obtain weight response factors.

When you use a flame-ionization gas chromatograph for quantitative analysis, it is first necessary to determine the response factors for each
component of the mixture being analyzed, as just shown. For a quantitative analysis, it is likely that you will have to convert molar response factors into weight response factors. Next, the chromatography experiment using the unknown samples is performed. The observed peak areas for each component are corrected using the response factors in order to arrive at the correct weight percentage of each component in the sample. The application of response factors to correct the original results of a quantitative analysis will be illustrated in the following section.

A. Gas Chromatograms and Data Tables

Most modern gas chromatography instruments are equipped with computer-based data stations. Interfacing the instrument with a computer allows the operator to display and manipulate the results in whatever manner might be desired. The operator thus can view the output in a convenient form. The computer can display the actual gas chromatogram and display the integration results. It can even display the result of two experiments simultaneously, making a comparison of parallel experiments convenient.

Figure 22.15 shows a gas chromatogram of a mixture of hexane, ethyl acetate, and benzene. The peaks corresponding to each substance can be seen; the peaks are labeled with their respective retention times.

<table>
<thead>
<tr>
<th>RETENTION TIME (MINUTES)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hexane</td>
</tr>
<tr>
<td>Ethyl acetate</td>
</tr>
<tr>
<td>Benzene</td>
</tr>
<tr>
<td>2.959</td>
</tr>
<tr>
<td>3.160</td>
</tr>
<tr>
<td>3.960</td>
</tr>
</tbody>
</table>

We can also see that there is a very small amount of an unspecified impurity, with a retention time of about 3.4 minutes.

Figure 22.16 shows part of the printed output that accompanies the gas chromatogram. It is this information that is used in the quantitative analysis of the mixture. According to the printout, the first peak has a retention time of 2.954 minutes (the difference between the retention times that appear as labels on the graph and those that appear in the data table are not significant). The computer has also determined the area under this peak (422,373 counts). Finally, the computer has calculated the percentage of the first substance (hexane) by determining the total area of all the peaks in the chromatogram (1,227,054 counts) and dividing that into the area for the hexane peak. The result is displayed as 34.4217\%.

B. Application of Response Factors

If the detector responded with equal sensitivity to each of the components of the mixture, the data table shown in Figure 22.16 would contain the complete quantitative analysis of the sample. Unfortunately, as we have seen (Section 22.12), gas chromatography detectors respond more sensitively to some substances than they do to others. To correct for this discrepancy, it is necessary to apply corrections that are based on the response factors for each component of the mixture.
The method for determining the response factors was introduced in Section 22.12. In this section, we will see how this information is applied in order to obtain a correct analysis. This example should serve to demonstrate the procedure for correcting raw gas chromatography results when response factors are known. According to the data table, the reported peak area for the first (hexane) peak is 422,373 counts. The response factor for hexane was previously determined to be 0.86. The area of the hexane peak is thus corrected as follows:

\[
\frac{422,373}{0.86} \approx 491,000
\]

Notice that the calculated result has been adjusted to reflect a reasonable number of significant figures.
The areas for the other peaks in the gas chromatogram are corrected in a similar manner:

- Hexane: $422,373/0.86 = 491,000$
- Ethyl acetate: $204,426/1.50 = 136,000$
- Benzene: $600,255/1.00 = 600,000$

Total peak area: $1,227,000$

Using these corrected areas, the true percentages of each component can be easily determined:

<table>
<thead>
<tr>
<th>Composition</th>
<th>Area Ratio</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hexane</td>
<td>491,000</td>
<td>40.0%</td>
</tr>
<tr>
<td>Ethyl acetate</td>
<td>136,000</td>
<td>11.1%</td>
</tr>
<tr>
<td>Benzene</td>
<td>600,000</td>
<td>48.9%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>1,227,000</strong></td>
<td><strong>100.0%</strong></td>
</tr>
</tbody>
</table>

C. Determination of Relative Percentages of Components in a Complex Mixture

In some circumstances, one may wish to determine the relative percentages of two components when the mixture being analyzed may be more complex and may contain more than two components. Examples of this situation might include the analysis of a reaction product where the laboratory worker might be interested in the relative percentages of two isomeric products when the sample might also contain peaks arising from the solvent, unreacted starting material, or some other product or impurity.
The example provided in Figures 22.15 and 22.16 can be used to illustrate the method of determining the relative percentages of some, but not all, of the components in the sample. Assume we are interested in the relative percentages of hexane and ethyl acetate in the sample but not in the percentage of benzene, which may be a solvent or an impurity. We know from the previous discussion that the corrected relative areas of the two peaks of interest are as follows:

<table>
<thead>
<tr>
<th>Relative Area</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hexane</td>
</tr>
<tr>
<td>Ethyl acetate</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

We can determine the relative percentages of the two components simply by dividing the area of each peak by the total area of the two peaks:

<table>
<thead>
<tr>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hexane</td>
</tr>
<tr>
<td>Ethyl acetate</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

A recently developed variation on gas chromatography is gas chromatography–mass spectrometry, also known as GC–MS. In this technique, a gas chromatograph is coupled to a mass spectrometer (see Technique 28). In effect, the mass spectrometer acts as a detector. The gas stream emerging from the gas chromatograph is admitted through a valve into a tube, where it passes over the sample inlet system of the mass spectrometer. Some of the gas stream is thus admitted into the ionization chamber of the mass spectrometer.

The molecules in the gas stream are converted into ions in the ionization chamber, and thus the gas chromatogram is actually a plot of time versus ion current, a measure of the number of ions produced. At the same time that the molecules are converted into ions, they are also accelerated and passed through the mass analyzer of the instrument. The instrument, therefore, determines the mass spectrum of each fraction eluting from the gas chromatography column.

A drawback of this method involves the need for rapid scanning by the mass spectrometer. The instrument must determine the mass spectrum of each component in the mixture before the next component exits from the column so that the spectrum of one substance is not contaminated by the spectrum of the next fraction.

Because high-efficiency capillary columns are used in the gas chromatograph, in most cases compounds are completely separated before the gas stream is analyzed. The typical GC–MS instrument has the capability of obtaining at least one scan per second in the range of 10–300 amu. Even more scans are possible if a narrow range of masses is analyzed. Using capillary columns, however, requires the user to take particular care to ensure that the sample does not contain any particles that might obstruct the flow of gases through the column. For this reason, the sample is carefully filtered through a very fine filter before the sample is injected into the chromatograph.
With a GC–MS system, a mixture can be analyzed and results obtained that resemble very closely those shown in Figures 22.15 and 22.16. A library search on each component of the mixture can also be conducted. The data stations of most instruments contain a library of standard mass spectra in their computer memory. If the components are known compounds, they can be identified tentatively by a comparison of their mass spectrum with the spectra of compounds found in the computer library. In this way, a “hit list” can be generated that reports on the probability that the compound in the library matches the known substance. A typical printout from a GC–MS instrument will list probable compounds that fit the mass spectrum of the component, the names of the compounds, their CAS Nos. (see Technique 29, Section 29.11, p. 952), and a “quality” or “confidence” number. This last number provides an estimate of how closely the mass spectrum of the component matches the mass spectrum of the substance in the computer library.

A variation on the GC–MS technique includes coupling a Fourier-transform infrared spectrometer (FT–IR) to a gas chromatograph. The substances that elute from the gas chromatograph are detected by determining their infrared spectra rather than their mass spectra. A new technique that also resembles GC–MS is high-performance liquid chromatography–mass spectrometry (HPLC–MS). An HPLC instrument is coupled through a special interface to a mass spectrometer. The substances that elute from the HPLC column are detected by the mass spectrometer, and their mass spectra can be displayed, analyzed, and compared with standard spectra found in the computer library built into the instrument.

**Problems**

1. **a.** A sample consisting of 1-bromopropane and 1-chloropropane is injected into a gas chromatograph equipped with a nonpolar column. Which compound has the shorter retention time? Explain your answer.

   **b.** If the same sample were run several days later with the conditions as nearly the same as possible, would you expect the retention times to be identical to those obtained the first time? Explain.

2. Using triangulation, calculate the percentage of each component in a mixture composed of two substances, A and B. The chromatogram is shown in Figure 22.17.

![Figure 22.17](A chromatogram for problem 2.)
3. Make a photocopy of the chromatogram in Figure 22.17. Cut out the peaks and weigh them on an analytical balance. Use the weights to calculate the percentage of each component in the mixture. Compare your answer to what you calculated in problem 2.

4. What would happen to the retention time of a compound if the following changes were made?
   a. Decrease the flow rate of the carrier gas
   b. Increase the temperature of the column
   c. Increase the length of the column

TECHNIQUE 24

Refractometry

The **refractive index** is a useful physical property of liquids. Often, a liquid can be identified from a measurement of its refractive index. The refractive index can also provide a measure of the purity of the sample being examined. This is accomplished by comparing the experimentally measured refractive index with the value reported in the literature for an ultrapure sample of the compound. The closer the measured sample’s value to the literature value, the purer the sample.

24.1 The Refractive Index

The refractive index has as its basis the fact that light travels at a different velocity in condensed phases (liquids, solids) than in air. The refractive index \( n \) is defined as the ratio of the velocity of light in air to the velocity of light in the medium being measured:

\[
 n = \frac{V_{\text{air}}}{V_{\text{liquid}}} = \frac{\sin \theta}{\sin \phi}
\]

It is not difficult to measure the ratio of the velocities experimentally. It corresponds to \((\sin \theta / \sin \phi)\), where \( \theta \) is the angle of incidence for a beam of light striking the surface of the medium and \( \phi \) is the angle of refraction of the beam of light within the medium. This is illustrated in Figure 24.1.
The refractive index for a given medium depends on two variable factors. First, it is temperature dependent. The density of the medium changes with temperature; hence, the speed of light in the medium also changes. Second, the refractive index is wavelength dependent. Beams of light with different wavelengths are refracted to different extents in the same medium and give different refractive indices for that medium. It is usual to report refractive indices measured at 20°C, with a sodium discharge lamp as the source of illumination. The sodium lamp gives off yellow light of 589-nm wavelength, the so-called sodium D line. Under these conditions, the refractive index is reported in the following form:

\[ n_{D}^{20} = 1.4892 \]

The superscript indicates the temperature, and the subscript indicates that the sodium D line was used for the measurement. If another wavelength is used for the determination, the D is replaced by the appropriate value, usually in nanometers (1 nm = 10^{-9} m).

Notice that the hypothetical value reported has four decimal places. It is easy to determine the refractive index to within several parts in 10,000. Therefore, \( n_{D} \) is a very accurate physical constant for a given substance and can be used for identification. However, it is sensitive to even small amounts of impurity in the substance measured. Unless the substance is purified extensively, you will not usually be able to reproduce the last two decimal places given in a handbook or other literature source. Typical organic liquids have refractive index values between 1.3400 and 1.5600.

### 24.2 The Abbé Refractometer

The instrument used to measure the refractive index is called a refractometer. Although many styles of refractometer are available, by far the most common instrument is the Abbé refractometer. This style of refractometer has the following advantages:

1. White light may be used for illumination; the instrument is compensated, however, so that the index of refraction obtained is actually that for the sodium D line.
2. The prisms can be temperature controlled.
3. Only a small sample is required (a few drops of liquid using the standard method or about $5 \mu L$ using a modified technique).

A common type of Abbé refractometer is shown in Figure 24.2.

The optical arrangement of the refractometer is complex; a simplified diagram of the internal workings is given in Figure 24.3. The letters $A$, $B$, $C$, and $D$ label corresponding parts in both Figures 24.2 and 24.3. A complete description of refractometer optics is too difficult to attempt here, but Figure 24.3 gives a simplified diagram of the essential operating principles.

Using the standard method, introduce the sample to be measured between the two prisms. If it is a free-flowing liquid, it may be introduced into a channel along the side of the prisms, injected from a Pasteur pipet. If it is a viscous sample, the prisms must be opened (they are hinged) by lifting the upper one; a few drops of liquid are applied to the lower prism with a Pasteur pipet or a wooden applicator. If a Pasteur pipet is used, take care not to touch the prisms because they become scratched easily. When the prisms are closed, the liquid should spread evenly to make a thin film. With highly volatile samples, the remaining operations must be performed rapidly. Even when the prisms are closed, evaporation of volatile liquids can readily occur.

Next, turn on the light and look into the eyepiece $D$. The hinged lamp is adjusted to give the maximum illumination to the visible field in the eyepiece. The light rotates at pivot $A$. 

\[ \text{Figure 24.2} \]
\begin{center}
Abbé refractometer (Bausch and Lomb Abbé 3L).
\end{center}
Rotate the coarse and fine adjustment knobs at B until the dividing line between the light and dark halves of the visual field coincides with the center of the crosshairs (Figure 24.4). If the crosshairs are not in sharp focus, adjust the eyepiece to focus them. If the horizontal line dividing the light and dark areas appears as a colored band, as in Figure 24.5, the refractometer shows chromatic aberration (color dispersion). This can be adjusted with knob C drum (Figure 24.3). This knurled knob rotates a series of prisms, called Amici prisms, that color-compensate the refractometer and cancel out dispersion. Adjust the knob to give a sharp, uncolored division between the light and dark segments. When you have adjusted everything correctly (as in Figure 24.4B), read the refractive index. In the instrument described here, press a small button on the left side of the housing to make the scale visible in the eyepiece. In other refractometers, the scale is visible at all times, frequently through a separate eyepiece.
Occasionally, the refractometer will be so far out of adjustment that it may be difficult to measure the refractive index of an unknown. When this happens, it is wise to place a pure sample of known refractive index in the instrument, set the scale to the correct value of refractive index, and adjust the controls for the sharpest line possible. Once this is done, it is easier to measure an unknown sample. It is especially helpful to perform this procedure prior to measuring the refractive index of a highly volatile sample.

**NOTE:** There are many styles of refractometer, but most have adjustments similar to those described here.

In the procedure just described, several drops of liquid are required to obtain the refractive index. In some experiments, you may not have enough sample to use this standard method. It is possible to modify the procedure so that a reasonably accurate refractive index can be obtained on about 5 μL of liquid. Instead of placing the sample directly onto the prism, you apply the sample to a small piece of lens paper. The lens paper can be conveniently cut with a handheld paper punch, and the paper disc (0.6-cm diameter) is placed in the center of the bottom prism of the refractometer. To avoid scratching the prism, use forceps or tweezers with plastic tips to handle the disc. About 5 μL of liquid is carefully placed on the lens paper using a microliter syringe. After closing the prisms, adjust the refractometer as described previously and read the refractive index. With this method, the horizontal line dividing the light and dark areas may not be as sharp as it is in the absence of the lens paper. It may also be impossible to eliminate color dispersion completely. Nonetheless, the refractive index values determined by this method are usually within 10 parts in 10,000 of the values determined by the standard procedure.

In using the refractometer, you should always remember that if the prisms are scratched, the instrument will be ruined.

**NOTE:** Do not touch the prisms with any hard object.

This admonition includes Pasteur pipets and glass rods. When measurements are completed, the prisms should be cleaned with ethanol or petroleum ether. Moisten soft tissues with the solvent and wipe the prisms gently. When the solvent has evaporated from the prism surfaces, the prisms should be locked together. The refractometer should be left with the prisms closed to avoid collection of dust in the space between them. The instrument should also be turned off when it is no longer in use.

---

1 In order to cut the lens paper more easily, place several sheets between two pieces of heavier paper, such as that used for file folders.
24.5 Temperature Corrections

Most refractometers are designed so that circulating water at a constant temperature can maintain the prisms at 20°C. If this temperature-control system is not used or if the water is not at 20°C, a temperature correction must be made. Although the magnitude of the temperature correction may vary from one class of compound to another, a value of 0.00045 per degree Celsius is a useful approximation for most substances. The index of refraction of a substance decreases with increasing temperature. Therefore, add the correction to the observed \( n_D \) value for temperatures higher than 20°C and subtract it for temperatures lower than 20°C. For example, the reported \( n_D \) value for nitrobenzene is 1.5529. One would observe a value at 25°C of 1.5506. The temperature correction would be made as follows:

\[
 n_{D}^{20} = 1.5506 + 5(0.00045) = 1.5529
\]

PROBLEMS

1. A solution consisting of isobutyl bromide and isobutyl chloride is found to have a refractive index of 1.3931 at 20°C. The refractive indices at 20°C of isobutyl bromide and isobutyl chloride are 1.4368 and 1.3785, respectively. Determine the molar composition (in percent) of the mixture by assuming a linear relation between the refractive index and the molar composition of the mixture.

2. The refractive index of a compound at 16°C is found to be 1.3982. Correct this refractive index to 20°C.
Infrared Spectroscopy

Almost any compound having covalent bonds, whether organic or inorganic, will be found to absorb frequencies of electromagnetic radiation in the infrared region of the spectrum. The infrared region of the electromagnetic spectrum lies at wavelengths longer than those associated with visible light, which includes wavelengths from approximately 400 nm to 800 nm (1 nm = 10⁻⁹ m) but at wavelengths shorter than those associated with radio waves, which have wavelengths longer than 1 cm. For chemical purposes, we are interested in the vibrational portion of the infrared region. This portion includes radiations with wavelengths (λ) between 2.5 μm and 15 μm (1 μm = 10⁻⁶ m). The relation of the infrared region to other regions included in the electromagnetic spectrum is illustrated in Figure 25.1.

As with other types of energy absorption, molecules are excited to a higher energy state when they absorb infrared radiation. The absorption of the infrared radiation is, like other absorption processes, a quantized process. Only selected frequencies (energies) of infrared radiation are absorbed by a molecule. The absorption of infrared radiation corresponds to energy changes on the order of 8–40 kJ/mole (2–10 kcal/mole). Radiation in this energy range corresponds to the range encompassing the stretching and bending vibrational frequencies of the bonds in most covalent molecules. In the absorption process, those frequencies of infrared radiation that match the natural vibrational frequencies of the molecule in question are absorbed, and the energy absorbed increases the amplitude of the vibrational motions of the bonds in the molecule.

Most chemists refer to the radiation in the vibrational infrared region of the electromagnetic spectrum by units called wavenumbers (ν). Wavenumbers are expressed in reciprocal centimeters (cm⁻¹) and are easily computed by taking the reciprocal of the wavelength (λ) expressed in centimeters. This unit has the advantage, for those performing calculations, of being directly proportional to energy. Thus, the vibrational infrared region of the spectrum extends from about 4000 cm⁻¹ to 650 cm⁻¹ (or wavenumbers).

Figure 25.1
A portion of the electromagnetic spectrum showing the relation of vibrational infrared radiation to other types of radiation.
Wavelengths ($\mu m$) and wavenumbers ($cm^{-1}$) can be interconverted by the following relationships:

\[
\text{cm}^{-1} = \frac{1}{(\mu m)} \times 10,000
\]
\[
\mu m = \frac{1}{(cm)^{-1}} \times 10,000
\]

**PART A. SAMPLE PREPARATION AND RECORDING THE SPECTRUM**

### 25.1 Introduction

To determine the infrared spectrum of the compound, one must place the compound in a sample holder or cell. In infrared spectroscopy, this immediately poses a problem. Glass, quartz, and plastics absorb strongly throughout the infrared region of the spectrum (any compound with covalent bonds usually absorbs) and cannot be used to construct sample cells. Ionic substances must be used in cell construction. Metal halides (sodium chloride, potassium bromide, silver chloride) are commonly used for this purpose.

**Sodium Chloride Cells.** Single crystals of sodium chloride are cut and polished to give plates that are transparent throughout the infrared region. These plates are then used to fabricate cells that can be used to hold liquid samples. Because sodium chloride is water soluble, samples must be dry before a spectrum can be obtained. In general, sodium chloride plates are preferred for most applications involving liquid samples. Potassium bromide plates may also be used in place of sodium chloride.

**Silver Chloride Cells.** Cells may be constructed of silver chloride. These plates may be used for liquid samples that contain small amounts of water, because silver chloride is water insoluble. However, because water absorbs in the infrared region, as much water as possible should be removed, even when silver chloride is used. Silver chloride plates must be stored in the dark. They darken when exposed to light, and they cannot be used with compounds that have an amino functional group. Amines react with silver chloride.

**Solid Samples.** The easiest way to hold a solid sample in place is to dissolve the sample in a volatile organic solvent, place several drops of this solution on a salt plate, and allow the solvent to evaporate. This dry film method can be used only with modern FT-IR spectrometers. The other methods described here can be used with both FT-IR and dispersion spectrometers. A solid sample can also be held in place by making a potassium bromide pellet that contains a small amount of dispersed compound. A solid sample may also be suspended in mineral oil, which absorbs only in specific regions of the infrared spectrum. Another method is to dissolve the solid compound in an appropriate solvent and place the solution between two sodium chloride or silver chloride plates.

### 25.2 Liquid Samples—NaCl Plates

The simplest method of preparing the sample, if it is a liquid, is to place a thin layer of the liquid between two sodium chloride plates that have been ground flat and polished. This is the method of choice when you need to
determine the infrared spectrum of a pure liquid. A spectrum determined by this method is referred to as a neat spectrum. No solvent is used. The polished plates are expensive because they are cut from a large, single crystal of sodium chloride. Salt plates break easily, and they are water soluble.

**Preparing the Sample.** Obtain two sodium chloride plates and a holder from the desiccator where they are stored. Moisture from fingers will mar and occlude the polished surfaces. Samples that contain water will destroy the plates.

**NOTE:** The plates should be touched only on their edges. Be certain to use a sample that is dry or free from water.

Add 1 or 2 drops of the liquid to the surface of one plate and then place the second plate on top. The pressure of this second plate causes the liquid to spread out and form a thin capillary film between the two plates. As shown in Figure 25.2, set the plates between the bolts in a holder and place the metal ring carefully on the salt plates. Use the hex nuts to hold the salt plates in place.

**NOTE:** Do not overtighten the nuts or the salt plates will cleave or split.

---

1 Use a Pasteur pipet or a short length of microcapillary tubing. If you use the microcapillary tubing, it can be filled by touching it into the liquid sample. When you touch it (lightly) to the salt plate, it will empty. Be careful not to scratch the plate.
Tighten the nuts firmly, but do not use any force to turn them. Spin them with the fingers until they stop; then turn them just another fraction of a full turn, and they will be tight enough. If the nuts have been tightened carefully, you should observe a transparent film of sample (a uniform wetting of the surface). If a thin film has not been obtained, either loosen one or more of the hex nuts and adjust them so that a uniform film is obtained or add more sample.

The thickness of the film obtained between the two plates is a function of two factors: (1) the amount of liquid placed on the first plate (1 drop, 2 drops, and so on) and (2) the pressure used to hold the plates together. If more than 1 or 2 drops of liquid have been used, the amount will probably be too much, and the resulting spectrum will show strong absorptions that are off the scale of the chart paper. Only enough liquid to wet both surfaces is needed.

If the sample has a very low viscosity, the capillary film may be too thin to produce a good spectrum. Another problem you may find is that the liquid is so volatile that the sample evaporates before the spectrum can be determined. In these cases, you may need to use the silver chloride plates discussed in Section 25.3 or a solution cell described in Section 25.6. Often, you can obtain a reasonable spectrum by assembling the cell quickly and running the spectrum before the sample runs out of the salt plates or evaporates.

**Determining the Infrared Spectrum.** Slide the holder into the slot in the sample beam of the spectrophotometer. Determine the spectrum according to the instructions provided by your instructor. In some cases, your instructor may ask you to calibrate your spectrum. If this is the case, refer to Section 25.8.

**Cleaning and Storing the Salt Plates.** Once the spectrum has been determined, demount the holder and rinse the salt plates with methylene chloride (or dry acetone). (Keep the plates away from water!) Use a soft tissue, moistened with the solvent, to wipe the plates. If some of your compound remains on the plates, you may observe a shiny surface. Continue to clean the plates with solvent until no more compound remains on the surfaces of the plates.

**CAUTION**

Avoid direct contact with methylene chloride. Return the salt plates and holder to the desiccator for storage.

---

25.3 Liquid Samples—AgCl Plates

The minicell shown in Figure 25.3 may also be used with liquids. The cell assembly consists of a two-piece threaded body, an O-ring, and two silver chloride plates. The plates are flat on one side, and there is a circular depression (0.025 mm or 0.10 mm deep) on the other side of the plate. An advantage of using silver chloride plates is that they may be used with wet samples or

---

2 The Wilks Mini-Cell liquid sample holder is available from the Foxboro Company, 151 Woodward Avenue, South Norwalk, CT 06856. We recommend the AgCl cell windows with 0.10-mm depression rather than the 0.025-mm depression.
solutions. A disadvantage is that silver chloride darkens when exposed to light for extended periods. Silver chloride plates also scratch more easily than salt plates and react with amines.

Preparing the Sample. Silver chloride plates should be handled in the same way as salt plates. Unfortunately, they are smaller and thinner (about like a contact lens) than salt plates, and care must be taken not to lose them! Remove them from the light-tight container with care. It is difficult to tell which side of the plate has the slight circular depression. Your instructor may have etched a letter on each plate to indicate which side is the flat one. To determine the infrared spectrum of a pure liquid (neat spectrum), select the flat side of each silver chloride plate. Insert the O-ring into the cell body as shown in Figure 25.3, place the plate into the cell body with the flat surface up, and add 1 drop or less of liquid to the plate.

NOTE: Do not use amines with AgCl plates.

Place the second plate on top of the first with the flat side down. The orientation of the silver chloride plates is shown in Figure 25.4A. This arrangement is used to obtain a capillary film of your sample. Screw the top of the minicell into the body of the cell so that the silver chloride plates are held firmly together. A tight seal forms because AgCl deforms under pressure.

Other combinations may be used with these plates. For example, you may vary the sample path length by using the orientations shown in Figures 25.4B and C. If you add your sample and the 0.10-mm depression of one plate and cover it with the flat side of the other one, you obtain a path length of 0.10 mm (Figure 25.4B). This arrangement is useful for analyzing
volatile or low-viscosity liquids. Placement of the two plates with their depressions toward each other gives a path length of 0.20 mm (Figure 25.4C). This orientation may be used for a solution of a solid (or liquid) in carbon tetrachloride (Section 25.6B).

**Determining the Spectrum.** Slide the V-mount holder shown in Figure 25.3 into the slot on the infrared spectrophotometer. Set the cell assembly in the V-mount holder and determine the infrared spectrum of the liquid.

**Cleaning and Storing the AgCl Plates.** Once the spectrum has been determined, the cell assembly holder should be demounted and the AgCl plates rinsed with methylene chloride or acetone. Do not use tissue to wipe the plates, because they scratch easily. AgCl plates are light sensitive. Store the plates in a light-tight container.

A simple method for determining the infrared spectrum of a solid sample is the dry film method. This method is easier than the other methods described here, it does not require any specialized equipment, and the spectra are excellent.\(^3\) The disadvantage is that the dry film method can be used only with modern FT-IR spectrometers.

To use this method, place about 5 mg of your solid sample in a small, clean test tube. Add about 5 drops of methylene chloride (or diethyl ether, pentane, or dry acetone), and stir the mixture to dissolve the solid. Using a Pasteur pipet (not a capillary tube), place several drops of the solution on the face of a salt plate. Allow the solvent to evaporate; a uniform deposit of your product will remain as a dry film coating the salt plate. Mount the salt plate on a V-shaped holder in the infrared beam. Note that only one salt plate is used; the second salt plate is not used to cover the first. Once the salt plate is positioned properly, you may determine the spectrum in the normal manner. With this method, it is very important that you clean your material off the salt plate. When you are finished, use methylene chloride or dry acetone to clean the salt plate.

The methods described in this section can be used with both FT-IR and dispersion spectrometers.

**A. KBr Pellets**

One method of preparing a solid sample is to make a potassium bromide (KBr) pellet. When KBr is placed under pressure, it melts, flows, and seals the sample into a solid solution, or matrix. Because potassium bromide does not absorb in the infrared spectrum, a spectrum can be obtained on a sample without interference.

**Preparing the Sample.** Remove the agate mortar and pestle from the desiccator for use in preparing the sample. (Take care of them; they are expensive.) Grind 1 mg (0.001 g) of the solid sample for 1 minute in the agate mortar. At this point, the particle size will become so small that the surface of the

---

solid appears shiny. Add 80 mg (0.080 g) of powdered potassium bromide and grind the mixture for about 30 seconds with the pestle. Scrape the mixture into the middle with a spatula and grind the mixture again for about 15 seconds. This grinding operation helps to mix the sample thoroughly with the KBr. You should work as rapidly as possible because KBr absorbs water. The sample and KBr must be finely ground, or the mixture will scatter the infrared radiation excessively. Using your spatula, heap the mixture in the center of the mortar. Return the bottle of potassium bromide to the desiccator where it is stored when it is not in use.

The sample and potassium bromide should be weighed on an analytical balance the first few times that a pellet is prepared. After some experience, you can estimate these quantities quite accurately by eye.

Making a Pellet Using a KBr Handpress. Two methods are commonly used to prepare KBr pellets. The first method uses the handpress apparatus shown in Figure 25.5.4 Remove the die set from the storage container. Take extreme care to avoid scratching the polished surfaces of the die set. Place the anvil with the shorter die pin (lower anvil in Figure 25.5) on a bench. Slip the collar over the pin. Remove about one fourth of your KBr mixture with a spatula and transfer it into the collar. The powder may not cover

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4 KBr Quick Press unit is available from Wilmad Glass Company, Inc., Route 40 and Oak Road, Buena, NJ 08310.
the head of the pin completely, but do not be concerned about this. Place the
anvil with the longer die pin into the collar so that the die pin comes into
contact with the sample. Never press the die set unless it contains a sample.

Lift the die set carefully by holding onto the lower anvil so that the col-
lar stays in place. If you are careless with this operation, the collar may
move enough to allow the powder to escape. Open the handle of the hand-
press slightly, tilt the press back a bit, and insert the die set into the press.
Make sure that the die set is seated against the side wall of the chamber.
Close the handle. It is imperative that the die set be seated against the side
wall of the chamber so that the die is centered in the chamber. Pressing the
die in an off-centered position can bend the anvil pins.

With the handle in the closed position, rotate the pressure dial so that
the upper ram of the handpress just touches the upper anvil of the die as-
sembly. Tilt the unit back so that the die set does not fall out of the hand-
press. Open the handle and rotate the pressure dial clockwise about one-
half turn. Slowly compress the KBr mixture by closing the handle. The
pressure should be no greater than that exerted by a very firm handshake.
Do not apply excessive pressure or the dies may be damaged. If in doubt,
rotate the pressure dial counterclockwise to lower the pressure. If the han-
dle closes too easily, open the handle, rotate the pressure dial clockwise, and
compress the sample again. Compress the sample for about 60 seconds.

After this time, tilt the unit back so that the die set does not fall out of the
handpress. Open the handle and carefully remove the die set from the unit.
Turn the pressure dial counterclockwise about one full turn. Pull the die set
apart and inspect the KBr pellet. Ideally, the pellet should appear clear like
a piece of glass, but usually it will be translucent or somewhat opaque.
There may be some cracks or holes in the pellet. The pellet will produce a
good spectrum, even with imperfections, as long as light can travel through
the pellet. Clean the dies using the procedure outlined on page 841.

Making a Pellet with a KBr Minipress. The second method of preparing a
pellet uses the minipress apparatus shown in Figure 25.6. Obtain a ground
KBr mixture as described in “Preparing the Sample” and transfer a portion
of the finely ground powder (usually not more than half) into a die that
compresses it into a translucent pellet. As shown in Figure 25.6, the die con-
sists of two stainless steel bolts and a threaded barrel. The bolts have their
ends ground flat. To use this die, screw one of the bolts into the barrel, but
not all the way; leave one or two turns. Carefully add the powder with a

![Figure 25.6](image.png)

*Figure 25.6*

*Making a KBr pellet with a minipress.*
spatula into the open end of the partly assembled die and tap it lightly on the benchtop to give an even layer on the face of the bolt. While keeping the barrel upright, carefully screw the second bolt into the barrel until it is finger tight. Insert the head of the bottom bolt into the hexagonal hole in a plate bolted to the benchtop. This plate keeps the head of one bolt from turning. The top bolt is tightened with a torque wrench to compress the KBr mixture. Continue to turn the torque wrench until you hear a loud click (the ratchet mechanism makes softer clicks) or until you reach the appropriate torque value (20 ft-lb). If you tighten the bolt beyond this point, you may twist the head off one of the bolts. Leave the die under pressure for about 60 seconds; then reverse the ratchet on the torque wrench or pull the torque wrench in the opposite direction to open the assembly. When the two bolts are loose, hold the barrel horizontally and carefully remove the two bolts. You should observe a clear or translucent KBr pellet in the center of the barrel. Even if the pellet is not totally transparent, you should be able to obtain a satisfactory spectrum as long as light passes through the pellet.

**Determining the Infrared Spectrum.** To obtain the spectrum, slide the holder appropriate for the type of die that you are using into the slot on the infrared spectrophotometer. Set the die containing the pellet in the holder so that the sample is centered in the optical path. Obtain the infrared spectrum. If you are using a double-beam instrument, you may be able to compensate (at least partially) for a marginal pellet by placing a wire screen or attenuator in the reference beam, thereby balancing the lowered transmittance of the pellet. An FT-IR instrument will automatically deal with the low intensity if you select the “autoscale” option.

**Problems with an Unsatisfactory Pellet.** If the pellet is unsatisfactory (too cloudy to pass light), one of several things may have been wrong:

1. The KBr mixture may not have been ground finely enough, and the particle size may be too big. The large particle size creates too much light scattering.
2. The sample may not be dry.
3. Too much sample may have been used for the amount of KBr taken.
4. The pellet may be too thick; that is, too much of the powdered mixture was put into the die.
5. The KBr may have been “wet” or have acquired moisture from the air while the mixture was being ground in the mortar.
6. The sample may have a low melting point. Low-melting solids not only are difficult to dry but also melt under pressure. You may need to dissolve the compound in a solvent and run the spectrum in solution (Section 25.6).

**Cleaning and Storing the Equipment.** After you have determined the spectrum, punch the pellet out of the die with a wooden applicator stick (a spatula should not be used as it may scratch the dies). Remember that the polished faces of the die set must not be scratched or they become useless. After the pellet has been punched out, wash all parts of the die set or minipress with warm water. Then rinse the parts with acetone and dry them using a Kimwipe. Check with your instructor to see if there are additional
instructions for cleaning the die set. Return the dies to the storage container. Wash the mortar and pestle with water, dry them carefully with paper towels, and return them to the desiccator. Return the KBr powder to its desiccator.

B. Nujol Mulls

If an adequate KBr pellet cannot be obtained or if the solid is insoluble in a suitable solvent, the spectrum of a solid may be determined as a **Nujol mull**. In this method, finely grind about 5 mg of the solid sample in an agate mortar with a pestle. Then add 1 or 2 drops of Nujol mineral oil (white) and grind the mixture to a very fine dispersion. The solid is not dissolved in the Nujol; it is actually a suspension. This mull is then placed between two salt plates using a rubber policeman. Mount the salt plates in the holder in the same way as for liquid samples (Section 25.2).

Nujol is a mixture of high-molecular-weight hydrocarbons. Hence, it has absorptions in the C—H stretch and CH₂ and CH₃ bending regions of the spectrum (Figure 25.7). Clearly, if Nujol is used, no information can be obtained in these portions of the spectrum. In interpreting the spectrum, you must ignore these Nujol peaks. It is important to label the spectrum immediately after it was determined, noting that it was determined as a Nujol mull. Otherwise, you might forget that the C—H peaks belong to Nujol and not to the dispersed solid.

A. Method A—Solution between Salt (NaCl) Plates

For substances that are soluble in carbon tetrachloride, a quick and easy method for determining the spectra of solids is available. Dissolve as much solid as possible in 0.1 mL of carbon tetrachloride. Place 1 or 2 drops of the solution between sodium chloride plates in precisely the same manner as used for pure liquids (Section 25.2). The spectrum is determined as described for pure liquids using salt plates (Section 25.2). You should work as

![Figure 25.7](image-url)

*Infrared spectrum of Nujol (mineral oil).*
quickly as possible. If there is a delay, the solvent will evaporate from between the plates before the spectrum is recorded. Because the spectrum contains the absorptions of the solute superimposed on the absorptions of carbon tetrachloride, it is important to remember that any absorption that appears near 800 cm\(^{-1}\) may be due to the stretching of the C–Cl bond of the solvent. Information contained to the right of about 900 cm\(^{-1}\) is not usable in this method. There are no other interfering bands for this solvent (see Figure 25.8), and any other absorptions can be attributed to your sample. Chloroform solutions should not be studied by this method because the solvent has too many interfering absorptions (see Figure 25.9).

**Figure 25.8**
*Infrared spectrum of carbon tetrachloride.*

**Figure 25.9**
*Infrared spectrum of chloroform.*
CAUTION

Carbon tetrachloride is a hazardous solvent. Work under the hood!

Carbon tetrachloride, besides being toxic, is suspected of being a carcinogen. In spite of the health problems associated with its use, there is no suitable alternative solvent for infrared spectroscopy. Other solvents have too many interfering infrared absorption bands. Handle carbon tetrachloride carefully to minimize the adverse health effects. The spectroscopic-grade carbon tetrachloride should be stored in a glass-stoppered bottle in a hood. A Pasteur pipet should be attached to the bottle, possibly by storing it in a test tube taped to the side of the bottle. All sample preparation should be conducted in a hood. Rubber or plastic gloves should be worn. The cells should also be cleaned in the hood. All carbon tetrachloride used in preparing samples should be disposed of in an appropriately marked waste container.

B. Method B—AgCl Minicell

The AgCl minicell described in Section 25.3 may be used to determine the infrared spectrum of a solid dissolved in carbon tetrachloride. Prepare a 5–10% solution (5–10 mg in 0.1 mL) in carbon tetrachloride. If it is not possible to prepare a solution of this concentration because of low solubility, dissolve as much solid as possible in the solvent. Following the instructions given in Section 25.3, position the AgCl plates as shown in Figure 25.4C to obtain the maximum possible path length of 0.20 mm. When the cell is tightened firmly, the cell will not leak.

As indicated in method A, the spectrum will contain the absorptions of the dissolved solid superimposed on the absorptions of carbon tetrachloride. A strong absorption appears near 800 cm\(^{-1}\) for C—Cl stretch in the solvent. No useful information may be obtained for the sample to the right of about 900 cm\(^{-1}\), but other bands that appear in the spectrum will belong to your sample. Read the safety material provided in method A. Carbon tetrachloride is toxic, and it should be used under a hood.

NOTE: Care should be taken in cleaning the AgCl plates. Because AgCl plates scratch easily, they should not be wiped with tissue. Rinse them with methylene chloride and keep them in a dark place. Amines will destroy the plates.

C. Method C—Solution Cells (NaCl)

The spectra of solids may also be determined in a type of permanent sample cell called a solution cell. (The infrared spectra of liquids may also be determined in this cell.) The solution cell, shown in Figure 25.10, is made from two salt plates, mounted with a Teflon spacer between them to control the thickness of the sample. The top sodium chloride plate has two holes drilled in it so that the sample can be introduced into the cavity between the two plates. These holes are extended through the face plate by two tubular extensions designed to hold Teflon plugs, which seal the internal chamber and prevent evaporation. The tubular extensions are tapered so that a syringe body (Luer lock without a needle) will fit snugly into them from the outside. The cells are thus filled from a syringe; usually, they are held upright and filled from the bottom entrance port.
These cells are expensive, and you should try either method A or B before using solution cells. If you do need them, obtain your instructor’s permission and receive instruction before using the cells. The cells are purchased in matched pairs, with identical path lengths. Dissolve a solid in a suitable solvent, usually carbon tetrachloride, and add the solution to one of the cells (sample cell) as described in the previous paragraph. The pure solvent, identical to that used to dissolve the solid, is placed in the other cell (reference cell). The spectrum of the solvent is subtracted from the spectrum of the solution (not always completely), and a spectrum of the solute is thus provided. For the solvent compensation to be as exact as possible and to avoid contamination of the reference cell, it is essential that one cell be used as a reference and that the other cell be used as a sample cell without ever being interchanged. After the spectrum is determined, it is important to clean the cells by flushing them with clean solvent. They should be dried by passing dry air through the cell.

Solvents most often used in determining infrared spectra are carbon tetrachloride (Figure 25.8), chloroform (Figure 25.9), and carbon disulfide (Figure 25.11). A 5–10% solution of solid in one of these solvents usually gives a good spectrum. Carbon tetrachloride and chloroform are suspected carcinogens; however, because there are no suitable alternative solvents, these compounds must be used in infrared spectroscopy. The procedure outlined on page 844 for carbon tetrachloride should be followed. This procedure serves equally well for chloroform.

**NOTE:** Before you use the solution cells, you must obtain the instructor’s permission and instruction on how to fill and clean the cells.
The instructor will describe how to operate the infrared spectrophotometer because the controls vary considerably, depending on the manufacturer, model of the instrument, and type. For example, some instruments involve pushing only a few buttons, whereas others use a more complicated computer interface system.

In all cases, it is important that the sample, the solvent, the type of cell or method used, and any other pertinent information be written on the spectrum immediately after the determination. This information may be important, and it is easily forgotten if not recorded. You may also need to calibrate the instrument (Section 25.8).

For some instruments, the frequency scale of the spectrum must be calibrated so that you know the position of each absorption peak precisely. You can recalibrate by recording a very small portion of the spectrum of polystyrene over the spectrum of your sample. The complete spectrum of polystyrene is shown in Figure 25.12. The most important of these peaks is at 1603 cm⁻¹; other useful peaks are at 2850 cm⁻¹ and 906 cm⁻¹. After you record the spectrum of your sample, substitute a thin film of polystyrene for the sample cell and record the tips (not the entire spectrum) of the most important peaks over the sample spectrum.

It is always a good idea to calibrate a spectrum when the instrument uses chart paper with a preprinted scale. It is difficult to align the paper properly so that the scale matches the absorption lines precisely. You often need to know the precise values for certain functional groups (for example, the carbonyl group). Calibration is essential in these cases.

With computer-interfaced instruments, the instrument does not need to be calibrated. With this type of instrument, the spectrum and scale are printed on blank paper at the same time. The instrument has an internal calibration that ensures that the positions of the absorptions are known precisely and that they are placed at the proper positions on the scale. With this
type of instrument, it is often possible to print a list of the locations of the major peaks, as well as to obtain the complete spectrum of your compound.

**PART B. INFRARED SPECTROSCOPY**

25.9 Uses of the Infrared Spectrum

Because every type of bond has a different natural frequency of vibration and because the same type of bond in two different compounds is in a slightly different environment, no two molecules of different structure have exactly the same infrared absorption pattern, or infrared spectrum. Although some of the frequencies absorbed in the two cases might be the same, in no case of two different molecules will their infrared spectra (the patterns of absorption) be identical. Thus, the infrared spectrum can be used to identify molecules much as a fingerprint can be used to identify people. Comparing the infrared spectra of two substances thought to be identical will establish whether or not they are in fact identical. If the infrared spectra of two substances coincide peak for peak (absorption for absorption), in most cases the substances are identical.

A second and more important use of the infrared spectrum is that it gives structural information about a molecule. The absorptions of each type of bond (N–H, C–H, O–H, C–X, C=O, C–O, C–C, C≡C, C≡N, and so on) are regularly found only in certain small portions of the vibrational infrared region. A small range of absorption can be defined for each type of bond. Outside this range, absorptions will normally be due to some other type of bond. Thus, for instance, any absorption in the range 3000 ± 150 cm⁻¹ will almost always be due to the presence of a CH bond in the molecule; an absorption in the range 1700 ± 100 cm⁻¹ will normally be due to the presence of a C=O bond (carbonyl group) in the molecule. The same type of range applies to each type of bond. The way these are spread out over the vibrational infrared is illustrated schematically in Figure 25.13. It is a good idea to remember this general scheme for future convenience.
The simplest types, or *modes*, of vibrational motion in a molecule that are infrared active, that is, give rise to absorptions, are the stretching and bending modes.

Other, more complex types of stretching and bending are also active, however. To introduce several words of terminology, the normal modes of vibration for a methylene group are shown below.

In any group of three or more atoms—at least two of which are identical—there are two modes of stretching or bending: the symmetric mode and asymmetric mode. Examples of such groupings are —CH$_3$, —CH$_2$—, —NO$_2$, —NH$_2$, and anhydrides (CO)$_2$O. For the anhydride, owing to asymmetric and symmetric modes of stretch, this functional group gives two absorptions in the C=O region. A similar phenomenon is seen for amino groups, where primary amines usually have two absorptions in the NH stretch region, whereas secondary amines R$_2$NH have only one absorption peak. Amides show similar bands. There are two strong N=O stretch peaks for a nitro group, which are caused by asymmetric and symmetric stretching modes.

**Figure 25.13**

*Approximate regions in which various common types of bonds absorb. (Bending, twisting, and other types of bond vibration have been omitted for clarity.)*

### 25.10 Modes of Vibration

The simplest types, or *modes*, of vibrational motion in a molecule that are infrared active, that is, give rise to absorptions, are the stretching and bending modes.

![Symmetric stretch (≈2850 cm$^{-1}$)](image)

![Asymmetric stretch (≈2925 cm$^{-1}$)](image)

**STRETCHING VIBRATIONS**

![Scissoring (≈1450 cm$^{-1}$)](image)

![Rocking (≈750 cm$^{-1}$)](image)

**IN-PLANE**

![Wagging (≈1250 cm$^{-1}$)](image)

![Twisting (≈1250 cm$^{-1}$)](image)

**OUT-OF-PLANE**

**BENDING VIBRATIONS**
The instrument that determines the absorption spectrum for a compound is called an infrared spectrophotometer. The spectrophotometer determines the relative strengths and positions of all the absorptions in the infrared region and plots this information on a piece of paper. This plot of absorption intensity versus wavenumber or wavelength is referred to as the infrared spectrum of the compound. A typical infrared spectrum, that of methyl isopropyl ketone, is shown in Figure 25.14.

The strong absorption in the middle of the spectrum corresponds to the carbonyl group. Note that the C=O peak is intense. In addition to the characteristic position of absorption, the shape and intensity of this peak are also unique to the C=O bond. This is true for almost every type of absorption peak; both shape and intensity characteristics can be described, and these characteristics often make it possible to distinguish the peak in a confusing situation. For instance, to some extent both C=O and C=C bonds absorb in the same region of the infrared spectrum:

\[
\begin{align*}
C=O & \quad 1850–1630 \text{ cm}^{-1} \\
C=C & \quad 1680–1620 \text{ cm}^{-1}
\end{align*}
\]

However, the C=O bond is a strong absorber, whereas the C=C bond generally absorbs only weakly. Hence, a trained observer would not normally interpret a strong peak at 1670 cm\(^{-1}\) to be a carbon–carbon double bond or a weak absorption at this frequency to be due to a carbonyl group.

The shape of a peak often gives a clue to its identity as well. Thus, although the NH and OH regions of the infrared overlap,

\[
\begin{align*}
\text{OH} & \quad 3650–3200 \text{ cm}^{-1} \\
\text{NH} & \quad 3500–3300 \text{ cm}^{-1}
\end{align*}
\]

OH usually gives a sharp absorption peak (absorbs a very narrow range of frequencies), and OH, when it is in the NH region, usually gives a broad
absorption peak. Primary amines give two absorptions in this region, whereas alcohols give only one.

Therefore, while you are studying the sample spectra in the pages that follow, you should also notice shapes and intensities. They are as important as the frequency at which an absorption occurs, and you must train your eye to recognize these features. In the literature of organic chemistry, you will often find absorptions referred to as strong (s), medium (m), weak (w), broad, or sharp. The author is trying to convey some idea of what the peak looks like without actually drawing the spectrum. Although the intensity of an absorption often provides useful information about the identity of a peak, be aware that the relative intensities of all the peaks in the spectrum are dependent on the amount of sample that is used and the sensitivity setting of the instrument. Therefore, the actual intensity of a particular peak may vary from spectrum to spectrum, and you must pay attention to relative intensities.

To extract structural information from infrared spectra, you must know the frequencies or wavelengths at which various functional groups absorb. Infrared correlation tables present as much information as is known about where the various functional groups absorb. The books listed at the end of this chapter present extensive lists of correlation tables. Sometimes, the absorption information is given in a chart, called a correlation chart. A simplified correlation table is given in Table 25.1.

Although you may think assimilating the mass of data in Table 25.1 will be difficult, it is not if you make a modest start and then gradually increase your familiarity with the data. An ability to interpret the fine details of an infrared spectrum will follow. This is most easily accomplished by first establishing the broad visual patterns of Figure 25.13 firmly in mind. Then, as a second step, a “typical absorption value” can be memorized for each of the functional groups in this pattern. This value will be a single number that can be used as a pivot value for the memory. For instance, start with a simple aliphatic ketone as a model for all typical carbonyl compounds. The typical aliphatic ketone has carbonyl absorption of 1715 ± 10 cm⁻¹. Without worrying about the variation, memorize 1715 cm⁻¹ as the base value for carbonyl absorption. Then learn the extent of the carbonyl range and the visual pattern of how the different kinds of carbonyl groups are arranged throughout this region. See, for instance, Figure 25.27 (p. 860), which gives typical values for carbonyl compounds. Also learn how factors such as ring size (when the functional group is contained in a ring) and conjugation affect the base values (that is, in which direction the values are shifted). Learn the trends—always remembering the base value (1715 cm⁻¹). It might prove useful as a beginning to memorize the base values in Table 25.2 for this approach. Notice that there are only eight values.

In analyzing the spectrum of an unknown, concentrate first on establishing the presence (or absence) of a few major functional groups. The most conspicuous peaks are C=O, O−H, N−H, C−O, C≡C, C=, C≡N, and NO₂. If they are present, they give immediate structural information. Do not try to analyze in detail the CH absorptions near 3000 cm⁻¹; almost all compounds have these absorptions. Do not worry about subtleties of the exact
### Table 25.1  *A simplified correlation table*

<table>
<thead>
<tr>
<th>Type of Vibration</th>
<th>Frequency (cm(^{-1}))</th>
<th>Intensity(^{a})</th>
</tr>
</thead>
<tbody>
<tr>
<td>C—H</td>
<td>Alkanes (stretch)</td>
<td>3000–2850 s</td>
</tr>
<tr>
<td></td>
<td>—CH(_3) (bend)</td>
<td>1450 and 1375 m</td>
</tr>
<tr>
<td></td>
<td>—CH(_2) (bend)</td>
<td>1465 m</td>
</tr>
<tr>
<td></td>
<td>Alkenes (stretch)</td>
<td>3100–3000 m</td>
</tr>
<tr>
<td></td>
<td>(bend)</td>
<td>1700–1000 s</td>
</tr>
<tr>
<td></td>
<td>Aromatics (stretch)</td>
<td>3150–3050 s</td>
</tr>
<tr>
<td></td>
<td>(out-of-plane bend)</td>
<td>1000–700 s</td>
</tr>
<tr>
<td></td>
<td>Alkyne (stretch)</td>
<td>ca. 3300 s</td>
</tr>
<tr>
<td></td>
<td>Aldehyde</td>
<td>2900–2800 w</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2800–2700 w</td>
</tr>
<tr>
<td>C—C</td>
<td>Alkane</td>
<td>Not interpretatively useful</td>
</tr>
<tr>
<td>C=C</td>
<td>Alkene</td>
<td>1680–1600 m–w</td>
</tr>
<tr>
<td></td>
<td>Aromatic</td>
<td>1600–1400 m–w</td>
</tr>
<tr>
<td>C≡C</td>
<td>Alkyne</td>
<td>2250–2100 m–w</td>
</tr>
<tr>
<td>C≡O</td>
<td>Aldehyde</td>
<td>1740–1720 s</td>
</tr>
<tr>
<td></td>
<td>Ketone (acyclic)</td>
<td>1725–1705 s</td>
</tr>
<tr>
<td></td>
<td>Carboxylic acid</td>
<td>1725–1700 s</td>
</tr>
<tr>
<td></td>
<td>Ester</td>
<td>1750–1730 s</td>
</tr>
<tr>
<td></td>
<td>Amide</td>
<td>1700–1640 s</td>
</tr>
<tr>
<td></td>
<td>Anhydride</td>
<td>ca. 1810 s</td>
</tr>
<tr>
<td></td>
<td></td>
<td>ca. 1760 s</td>
</tr>
<tr>
<td>C—O</td>
<td>Alcohols, ethers, esters, carboxylic acids</td>
<td>1300–1000 s</td>
</tr>
<tr>
<td>O—H</td>
<td>Alcohol, phenols</td>
<td>3650–3600 m</td>
</tr>
<tr>
<td></td>
<td>Free</td>
<td>3400–3200 m</td>
</tr>
<tr>
<td></td>
<td>H-Bonded</td>
<td>3300–2500 m</td>
</tr>
<tr>
<td>N—H</td>
<td>Primary and secondary amines</td>
<td>ca. 3500 m</td>
</tr>
<tr>
<td>C≡N</td>
<td>Nitriles</td>
<td>2260–2240 m</td>
</tr>
<tr>
<td>N≡O</td>
<td>Nitro (R—NO(_2))</td>
<td>1600–1500 s</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1400–1300 s</td>
</tr>
<tr>
<td>C—X</td>
<td>Fluoride</td>
<td>1400–1000 s</td>
</tr>
<tr>
<td></td>
<td>Chloride</td>
<td>800–600 s</td>
</tr>
<tr>
<td></td>
<td>Bromide, iodide</td>
<td>&lt;600 s</td>
</tr>
</tbody>
</table>

\(^{a}\) s, strong; m, medium; w, weak.

### Table 25.2  *Base values for absorptions of bonds*

<table>
<thead>
<tr>
<th>Bond</th>
<th>Frequency (cm(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>O—H</td>
<td>3400 cm(^{-1})</td>
</tr>
<tr>
<td>N—H</td>
<td>3500 cm(^{-1})</td>
</tr>
<tr>
<td>C—H</td>
<td>3000 cm(^{-1})</td>
</tr>
<tr>
<td>C≡N</td>
<td>2250 cm(^{-1})</td>
</tr>
<tr>
<td>C≡C</td>
<td>2150 cm(^{-1})</td>
</tr>
<tr>
<td>C≡O</td>
<td>1715 cm(^{-1})</td>
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<tr>
<td>C≡O</td>
<td>1715 cm(^{-1})</td>
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<tr>
<td>C≡O</td>
<td>1650 cm(^{-1})</td>
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<tr>
<td>C≡O</td>
<td>1100 cm(^{-1})</td>
</tr>
</tbody>
</table>
type of environment in which the functional group is found. A checklist of
the important gross features follows:

1. Is a carbonyl group present?
The C=O group gives rise to a strong absorption in the region
1820–1600 cm\(^{-1}\). The peak is often the strongest in the spectrum and of
medium width. You can’t miss it.

2. If C=O is present, check the following types. (If it is absent, go to item 3.)
   - **Acids**: Is O—H also present?
     - **Broad** absorption near 3300–2500 cm\(^{-1}\) (usually
       overlaps C—H).
   - **Amides**: Is N—H also present?
     - Medium absorption near 3500 cm\(^{-1}\), sometimes a
double peak, equivalent halves.
   - **Esters**: Is C—O also present?
     - Medium intensity absorptions near 1300–1000 cm\(^{-1}\).
   - **Anhydrides**: Have **two** C=O absorptions near 1810 and 1760 cm\(^{-1}\).
   - **Aldehydes**: Is aldehyde C—H present?
     - Two weak absorptions near 2850 cm\(^{-1}\) and 2750 cm\(^{-1}\)
on the right side of C—H absorptions.
   - **Ketones**: The preceding five choices have been eliminated.

3. If C=O is absent
   - **Alcohols** or **Phenols**: Check for O—H.
     - **Broad** absorption near 3600–3300 cm\(^{-1}\).
     - Confirm this by finding C—O near 1300–1000 cm\(^{-1}\).
   - **Amines**: Check for N—H.
     - Medium absorption(s) near 3500 cm\(^{-1}\).
   - **Ethers**: Check for C—O (and absence of O—H) near
     1300–1000 cm\(^{-1}\).

4. Double bonds or aromatic rings or both
   - C=C is a **weak** absorption near 1650 cm\(^{-1}\).
   - Medium to strong absorptions in the region
     1650–1450 cm\(^{-1}\) often imply an aromatic ring.
   - Confirm the above by consulting the C—H region.
   - Aromatic and vinyl C—H occur to the left of 3000 cm\(^{-1}\)
     (aliphatic C—H occurs to the right of this value).

5. Triple bonds C≡N is a medium, sharp absorption near 2250 cm\(^{-1}\).
   - C≡C is a weak but sharp absorption near 2150 cm\(^{-1}\).
   - Check also for acetylenic C—H near 3300 cm\(^{-1}\).

6. Nitro groups **Two** strong absorptions near 1600–1500 cm\(^{-1}\) and
   1390–1300 cm\(^{-1}\).

7. Hydrocarbons None of the above is found.
   - Main absorptions are in the C—H region near
     3000 cm\(^{-1}\).
     - Very simple spectrum, only other absorptions are near
       1450 cm\(^{-1}\) and 1375 cm\(^{-1}\).

The beginning student should resist the idea of trying to assign or inter-
pret every peak in the spectrum. You simply will not be able to do this. Con-
centrate first on learning the principal peaks and recognizing their presence
or absence. This is best done by carefully studying the illustrative spectra in
the section that follows.
NOTE: In describing the shifts of absorption peaks or their relative positions, we have used the phrases “to the left” and “to the right.” This was done to simplify descriptions of peak positions. The meaning is clear because all spectra are conventionally presented left to right from 4000 to 600 cm\(^{-1}\).

A. Alkanes

The spectrum is usually simple, with a few peaks.

C—H Stretch occurs around 3000 cm\(^{-1}\).

1. In alkanes (except strained ring compounds), absorption always occurs to the right of 3000 cm\(^{-1}\).

2. If a compound has vinylic, aromatic, acetylenic, or cyclopropyl hydrogens, the CH absorption is to the left of 3000 cm\(^{-1}\).

CH\(_2\) Methylene groups have a characteristic absorption at approximately 1450 cm\(^{-1}\).

CH\(_3\) Methyl groups have a characteristic absorption at approximately 1375 cm\(^{-1}\).

C—C Stretch—not interpretatively useful—has many peaks.

The spectrum of decane is shown in Figure 25.15.

B. Alkenes

=C—H Stretch occurs to the left of 3000 cm\(^{-1}\).

=CH—H Out-of-plane (oop) bending occurs at 1000–650 cm\(^{-1}\).

The C—H out-of-plane absorptions often allow you to determine the type of substitution pattern on the double bond, according to the number of absorptions and their positions. The correlation chart in Figure 25.16 shows the positions of these bands.

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Figure 25.15
Infrared spectrum of decane (neat liquid, salt plates).
Conjugation moves C—C stretch to the right. Symmetrically substituted bonds, as in 2,3-dimethyl-2-butene, do not absorb in the infrared region (no dipole change). Highly substituted double bonds are often vanishingly weak in absorption.

The spectra of 4-methylcyclohexene and styrene are shown in Figures 25.17 and 25.18.
C. Aromatic Rings

- C=H Stretch is always to the left of 3000 cm⁻¹.
- C=H Out-of-plane (oop) bending occurs at 900 to 690 cm⁻¹.

The C–H out-of-plane absorptions often allow you to determine the type of ring substitution by their numbers, intensities, and positions. The correlation chart in Figure 25.19A indicates the positions of these bands.

The patterns are generally reliable—they are most reliable for rings with alkyl substituents and least reliable for polar substituents.

**Ring Absorptions (C=≡C).** There are often four sharp absorptions that occur in pairs at 1600 cm⁻¹ and 1450 cm⁻¹ and are characteristic of an aromatic ring. See, for example, the spectra of anisole (Figure 25.23), benzonitrile (Figure 25.26), and methyl benzoate (Figure 25.35).

There are many weak combination and overtone absorptions that appear between 2000 cm⁻¹ and 1667 cm⁻¹. The relative shapes and numbers of these peaks can be used to determine whether an aromatic ring is monosubstituted or di-, tri-, tetra-, penta-, or hexa-substituted. Positional isomers can also be distinguished. Because the absorptions are weak, these bands are best observed by using neat liquids or concentrated solutions. If the compound has a high-frequency carbonyl group, this absorption overlaps the weak overtone bands, so no useful information can be obtained from analyzing this region. The various patterns that are obtained in this region are shown in Figure 25.19B.

The spectra of styrene and o-dichlorobenzene are shown in Figures 25.18 and 25.20.

D. Alkynes

- C≡H Stretch is usually near 3300 cm⁻¹, sharp peak.
- C≡C Stretch is near 2150 cm⁻¹, sharp peak.
Conjugation moves $\text{C=}=\text{C}$ stretch to the right.
Disubstituted or symmetrically substituted triple bonds give either no absorption or weak absorption.

E. Alcohols and Phenols

$\text{O}—\text{H}$  Stretch is a sharp peak at 3650–3600 cm$^{-1}$ if no hydrogen bonding takes place. (This is usually observed only in dilute solutions.) If there is hydrogen bonding (usual in neat or concentrated solutions), the absorption is broad and occurs more to the right at 3500–3200 cm$^{-1}$, sometimes overlapping $\text{C—H}$ stretch absorptions.

$\text{C}—\text{O}$  Stretch is usually in the range of 1300–1000 cm$^{-1}$. Phenols are like alcohols. The 2-naphthol shown in Figure 25.21 has some molecules hydrogen bonded and some free. The spectrum of 4-methylcyclohexanol is shown in Figure 25.22. This alcohol, which was determined neat, would also have had a free OH spike to the left of this hydrogen-bonded band if it had been determined in dilute solution.
F. Ethers

C—O  The most prominent band is due to C—O stretch at 1300–1000 cm⁻¹. Absence of C=O and O—H bands is required to be sure C—O stretch is not due to an alcohol or ester. Phenyl and vinyl ethers are found in the left portion of the range, aliphatic ethers in the right. (Conjugation with the oxygen moves the absorption to the left.)

The spectrum of anisole is shown in Figure 25.23.
G. Amines

N—H Stretch occurs in the range of 3500–3300 cm\(^{-1}\). Primary amines have two bands typically 30 cm\(^{-1}\) apart. Secondary amines have one band, often vanishingly weak. Tertiary amines have no NH stretch.

C—N Stretch is weak and occurs in the range of 1350–1000 cm\(^{-1}\).

N—H Scissoring bending mode occurs in the range of 1640–1560 cm\(^{-1}\) (broad). An out-of-plane bending absorption can sometimes be observed at about 800 cm\(^{-1}\).

The spectrum of \(n\)-butylamine is shown in Figure 25.24.
H. Nitro Compounds

N≡O Stretch is usually two strong bands at 1600–1500 cm\(^{-1}\) and 1390–1300 cm\(^{-1}\).

The spectrum of nitrobenzene is shown in Figure 25.25.

I. Nitriles

C≡N Stretch is a sharp absorption near 2250 cm\(^{-1}\).

Conjugation with double bonds or aromatic rings moves the absorption to the right.

The spectrum of benzonitrile is shown in Figure 25.26.
The carbonyl group is one of the most strongly absorbing groups in the infrared region of the spectrum. This is mainly due to its large dipole moment. It absorbs in a variety of compounds (aldehydes, ketones, acids, esters, amides, anhydrides, and acid chlorides) in the range of 1850–1650 cm$^{-1}$. In Figure 25.27, the normal values for the various types of carbonyl groups are compared. In the sections that follow, each type is examined separately.

K. Aldehydes

C═O Stretch at approximately 1725 cm$^{-1}$ is normal. Aldehydes seldom absorb to the left of this value. Conjugation moves the absorption to the right.

C—H Stretch, aldehyde hydrogen (—CHO), consists of weak bands at about 2750 cm$^{-1}$ and 2850 cm$^{-1}$. Note that the CH stretch in alkyl chains does not usually extend this far to the right.

The spectrum of an unconjugated aldehyde, nonanal, is shown in Figure 25.28, and the conjugated aldehyde, benzaldehyde, is shown in Figure 25.29.
L. Ketones

C=O  Stretch at approximately at 1715 cm\(^{-1}\) is normal.
Conjugation moves the absorption to the right.
Ring strain moves the absorption to the left in cyclic ketones
(see Figure 25.30).

The spectra of methyl isopropyl ketone and mesityl oxide are shown in Figures 25.14 and 25.31. The spectrum of camphor, shown in Figure 25.32, has a carbonyl group that has been shifted to a higher frequency because of ring strain (1745 cm\(^{-1}\)).

Figure 25.28
Infrared spectrum of nonanal (neat liquid, salt plates).

Figure 25.29
Infrared spectrum of benzaldehyde (neat liquid, salt plates).
M. Acids

O—H \hspace{1em} \text{Stretch, usually very broad (strongly hydrogen bonded) at 3300–2500 cm}^{-1}, \text{ often interferes with C—H absorptions.}

C═O \hspace{1em} \text{Stretch, broad, 1730–1700 cm}^{-1}. \text{ Conjugation moves the absorption to the right.}

C—O \hspace{1em} \text{Stretch, in the range of 1320–1210 cm}^{-1}, \text{ is strong.}

The spectrum of benzoic acid is shown in Figure 25.33.
N. Esters (R—C—OR’)

C=O Stretch occurs at about 1735 cm\(^{-1}\) in normal esters.

1. Conjugation in the R part moves the absorption to the right.
2. Conjugation with the O in the R’ part moves the absorption to the left.
3. Ring strain (lactones) moves the absorption to the left.

C—O Stretch, two bands or more, one stronger than the others, is in the range of 1300–1000 cm\(^{-1}\).
The spectrum of an unconjugated ester, isopentyl acetate, is shown in Figure 25.34 (C=O appears at 1740 cm⁻¹). A conjugated ester, methyl benzoate, is shown in Figure 25.35 (C=O appears at 1720 cm⁻¹).

O. Amides

\[ \text{C=O} \] Stretch is at approximately 1670–1640 cm⁻¹.
Conjugation and ring size (lactams) have the usual effects.
\[ \text{N—H} \] Stretch (if monosubstituted or unsubstituted) is at 3500–3100 cm⁻¹.
Unsubstituted amides have two bands (−NH₂) in this region.
\[ \text{N—H} \] Bending around 1640–1550 cm⁻¹.

The spectrum of benzamide is shown in Figure 25.36.
P. Anhydrides

$C=O$ Stretch always has two bands: $1830-1800 \text{ cm}^{-1}$ and $1775-1740 \text{ cm}^{-1}$. Unsaturation moves the absorptions to the right. Ring strain (cyclic anhydrides) moves the absorptions to the left. $C=O$ Stretch is at $1300-900 \text{ cm}^{-1}$. The spectrum of cis-norbornene-5,6-endo-dicarboxylic anhydride is shown in Figure 25.37.
Q. Acid Chlorides

C=O Stretch occurs in the range 1810–1775 cm\(^{-1}\) in unconjugated chlorides. Conjugation lowers the frequency to 1780–1760 cm\(^{-1}\).

C–O Stretch occurs in the range 730–550 cm\(^{-1}\).

R. Halides

It is often difficult to determine either the presence or the absence of a halide in a compound by infrared spectroscopy. The absorption bands cannot be relied on, especially if the spectrum is being determined with the compound dissolved in CCl\(_4\) or CHCl\(_3\) solution.

C–F Stretch, 1350–960 cm\(^{-1}\).

C–Cl Stretch, 850–500 cm\(^{-1}\).

C–Br Stretch, to the right of 667 cm\(^{-1}\).

C–I Stretch, to the right of 667 cm\(^{-1}\).

The spectra of the solvents, carbon tetrachloride and chloroform, are shown in Figures 25.8 and 25.9, respectively.

REFERENCES


PROBLEMS

1. Comment on the suitability of running the infrared spectrum under each of the following conditions. If there is a problem with the conditions given, provide a suitable alternative method.

   a. A neat spectrum of liquid with a boiling point of 150°C is determined using salt plates.

   b. A neat spectrum of a liquid with a boiling point of 35°C is determined using salt plates.

   c. A KBr pellet is prepared with a compound that melts at 200°C.

   d. A KBr pellet is prepared with a compound that melts at 30°C.

   e. A solid aliphatic hydrocarbon compound is determined as a Nujol mull.
f. Silver chloride plates are used to determine the spectrum of aniline.
g. Sodium chloride plates are selected to run the spectrum of a compound that contains some water.

2. Indicate how you could distinguish between the following pairs of compounds by using infrared spectroscopy.

a. CH₃CH₂CH₂C≡CH₃  CH₃CH₂CH₂CH₃
b. CH₃CH₂COCH₂CH₃  CH₃CH₂COCH₃
c. CH₃CH₂NCH₂CH₃  CH₃CH₂CH₂CH₃NH₂
d. CH₃CH₂COCH₂CH₃  CH₃CH₂CH₂OCH₃
e. CH₃CH₂COH  CH₃CH₂CH₃OH
f. 

  CH₃
  CH₃

g. CH₃CH₂CH≡CH₂  CH₃CH≡CHCH₃ (trans)
h. CH₃CH₂CH₂C≡CH  CH₃CH₂CH₂CH≡CH₂
i. 

  CH₃
  NH₂

j. CH₃CH₂CH₂CH₂COH  CH₃CH₂CH₂COCH₃
k. CH₃CH₂CH₂CH₂CH₃  CH₂=CHCH₂CH₂CH₂CH₃
l. CH₃CH₂CH₂CH₂C≡CH  CH₃CH₂CH₂C≡CH₃