



Chapter One: An Overview. Part 1

1.1 INTRODUCTION

The laboratory component of a course in organic chemistry has an important role in developing and augmenting your understanding of the subject matter. The theoretical concepts, functional groups, and reactions presented in the lecture part of the course may seem abstract at times, but they are more understandable as a result of the experiments you perform. The successes, challenges, and, yes, frustrations associated with the “hands-on” experience gained in the laboratory, as you gather and interpret data from a variety of reactions, provide a sense of organic chemistry that is nearly impossible to communicate in formal lectures. For example, it is one thing to be told that the addition of bromine (Br_2) across the π -bond of most alkenes is a rapid process at room temperature. It is quite another to personally observe the *immediate* decoloration of a reddish solution of bromine in dichloromethane ($\text{Br}_2/\text{CH}_2\text{Cl}_2$) as a few drops of it are added to cyclohexene. The principles developed in the lectures will help you to predict what reaction(s) should occur when various reagents are combined in experimental procedures and to understand the mechanistic course of the process(es). Performing reactions allows you to test and verify the principles presented in lecture.

Of course, the laboratory experience in organic chemistry has another important function beyond reinforcing the concepts presented in lecture—to introduce you to the broad range of techniques and procedures that are important to the successful practice of experimental organic chemistry. You will learn how to handle a variety of chemicals safely and how to manipulate apparatus properly, talents that are critical to your success as a student of the chemical sciences. Along with

becoming more skilled in the technical aspects of laboratory work, you should also develop a proper scientific approach to executing experiments and interpreting the results. By reading and, more importantly, *understanding* the concepts of this chapter, you will be better able to achieve these valuable goals.

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.

There is little question that one of the most important abilities that you, the aspiring organic chemist, can bring to the laboratory is a sound knowledge of how to perform experimental work safely. But just knowing *how* to work safely is insufficient! You must also make a *serious* commitment to follow standard safety protocols. In other words, having the knowledge about safety is useless if you do not put that knowledge into practice. What you actually do in the laboratory will determine whether you and your labmates are working in a safe environment.

Chemistry laboratories are potentially dangerous because they commonly house flammable liquids, fragile glassware, toxic chemicals, and equipment that may be under vacuum or at pressures above atmospheric. They may also contain gas cylinders that are under high pressure. The gases themselves may or may not be hazardous—for example, nitrogen is not, whereas hydrogen certainly is—but the fact that their containers are under pressure makes them so. Imagine what might happen if a cylinder of nitrogen fell and ruptured: you could have a veritable rocket on your hands, and, if the tank contained hydrogen, the “rocket” might even come equipped with a fiery tail! This is another way of saying *all* substances are hazardous under certain conditions.

Fortunately the laboratory need be no more dangerous than a kitchen or bathroom, but this depends on you *and* your labmates practicing safety as you work. Should you observe others doing anything that is unsafe, let them know about it in a friendly manner. Everyone will benefit from your action. We'll alert you repeatedly to the possible dangers associated with the chemicals and apparatus that you will use so that you can become well trained in safe laboratory practice. Mastery of the proper procedures is just as important in the course as obtaining high yields of pure products, and carefully reading our suggestions will assist you in achieving this goal. Some safety information will be contained in the text describing a particular experiment or in the experimental procedure itself. It will also appear in highlighted sections titled “Safety Alert.” These are designed to draw your special attention to aspects of safety that are of particular importance. We urge you to read these sections carefully and follow the guidelines in them carefully. You will then be fully prepared to have the fun and fulfillment of the laboratory experience.

1.1 Safety Guidelines

We highlight here, in the form of a Safety Alert, some general aspects regarding safe practices in the laboratory.

SAFETY ALERT



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, as 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 thinking before acting 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 problems. 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 should be 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 in Section 1.3. If you use proper safety precautions, your exposure to harmful organic vapors will be minimized and should present no health risks.

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 particular 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. Most organic solvents boil below 100°C, and an aluminum block, heating mantle, sand bath, or water bath may be used to heat these solvents safely. Common organic solvents are listed in Technique 10, Table 10.3. 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 common-sense 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 accidentally 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 also introduce impurities that could spoil the experiment for the person using the stock reagent after you. Pouring reagents back into bottles is not only a dangerous practice, but 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.

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.

FIRE

Your first consideration is to remove yourself from any danger, *not to extinguish the fire*. *If it is possible to do so without endangering yourself*, turn off any burners and remove containers of flammable solvents from the immediate area to prevent the fire from spreading. For the most effective use of a fire extinguisher, direct its nozzle toward the *base* of the flames. Burning oil may be put out with an extinguisher classified for use on "ABC" type fires.

If your clothing is on fire, DO NOT RUN; rapid movement will only fan the flames. Roll on the floor to smother the fire and to help keep the flames away from your head. Your neighbors can help to extinguish the flames by using fire blankets, laboratory coats, or other items that are immediately available. Do not hesitate to aid your neighbor if he or she is involved in such an emergency; a few seconds delay may result in serious injury. A laboratory shower, *if close by*, can be used to extinguish burning clothing, as can a carbon dioxide extinguisher, which must be used with care until the flames are extinguished *and only if the flames are not near the head*.

If burns are minor, apply a burn ointment. In the case of serious burns, do not apply any ointment; seek professional medical treatment at once.

CHEMICAL BURNS

Areas of the skin with which corrosive chemicals have come in contact should be immediately and thoroughly washed with soap and warm water. If the burns are minor, apply burn ointment; for treatment of more serious burns, see a physician.

Bromine burns can be particularly serious. These burns should first be washed with soap and warm water and then thoroughly soaked with 0.6 M sodium thiosulfate solution for three hours. Apply cod liver oil ointment and a dressing; see a physician.

If chemicals, in particular corrosive or hot reagents, come in contact with the eyes, immediately *flood* the eyes with water *from the nearest outlet*. A specially designed eyewash fountain is useful if available in the laboratory. *Do not touch the eye*. The eyelid as well as the eyeball should be washed with water for several minutes. In all instances where sensitive eye tissue is involved in such an accident, consult an ophthalmologist as soon as possible.

CUTS

Minor cuts may be treated by ordinary first-aid procedures; seek professional medical attention for serious cuts. If severe bleeding indicates that an artery has been severed, attempt to stop the bleeding with compresses and pressure; a tourniquet should be applied only by those who have received first-aid training. Arrange for emergency room treatment at once.

A person who is injured severely enough to require a physician's treatment *should be accompanied* to the doctor's office, or infirmary, even if he or she claims to be all right. Persons in shock, particularly after suffering burns, are often more seriously injured than they appear to be.

Personal Attire

1. *Do not wear shorts or sandals in the laboratory;* the laboratory is *not* a beach! Proper clothing gives protection against chemicals that may be spilled accidentally. It is advisable to wear a laboratory coat, but in any case, the more skin that is protected by clothing the better.
2. *Always wear safety glasses or goggles in the laboratory.* This applies even when you are writing in your laboratory notebook or washing glassware, since nearby workers may have an accident. It is best *not* to wear contact lenses in the laboratory. Even if you are wearing eye protection, chemicals may get into your eyes, and you may not be able to get the contact lenses out before damage has occurred. Should you have to wear corrective glasses while working in the laboratory, make certain that the lenses are shatterproof. Wearing goggles over such glasses is recommended because the goggles give additional protection from chemicals entering your eyes from the sides of the lenses.
3. *Wear latex gloves when working with particularly hazardous chemicals.* Some reagents are especially hazardous if they come into contact with your skin. The ones you are most likely to encounter in the organic laboratory are concentrated acids and bases, and bromine and its solutions. Check with your instructor whenever you are uncertain whether you should be wearing gloves when handling reagents.

General Considerations

1. *Become familiar with the layout of the laboratory room.* Locate the exits from the room and the fire extinguishers, fire blankets, eyewash fountains, safety showers, and first-aid kits in and near your workspace. Consult with your instructor regarding the operation and purpose of each of the safety-related devices.
2. *Find the nearest exits from your laboratory room to the outside of the building.* Should evacuation of the building be necessary, use stairways rather than elevators to exit. Remain calm during the evacuation, and walk rather than run to the exit.
3. *Become knowledgeable about basic first-aid procedures.* The damage from accidents will be minimized if first aid is applied promptly. Read the section "First Aid in Case of an Accident" on the inside front cover of this book.
4. *Never work alone in the laboratory.* In the event of an accident, you may need the immediate help of a coworker. Should you have to work in the laboratory outside of the regularly scheduled periods, do so only with the express permission of your instructor and in the presence of at least one other person.

Before using any chemical, read the label twice and take into consideration the information on the safety pictogram symbols. Some of the safety pictogram symbols are shown in the figure below.



Know your GHS symbols



Harmful chemicals

GHS Labels



Oxidizers - Can burn without air, or can intensify fire in combustible materials.



Explosives - May explode if exposed to fire, heat, shock, friction.



Corrosives - May cause skin burns and permanent eye damage.



Gasses Under Pressure - Gas released may be very cold. Gas container may explode if heated.



Flammable if exposed to ignition sources, sparks, heat. Some substances may give off flammable gases.



Toxic to aquatic organisms and may cause long lasting effects in the environment.



Toxic material which may cause life threatening effects even in small amounts and with short exposure.



May cause serious and prolonged health effects on short or long term exposure.



Irritant - May cause irritation (redness, rash) or less serious toxicity

Figure: Some safety pictogram symbols.

2 TECHNIQUE 2

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 nonflammable (in the past, it was used on occasion as a fire extinguisher), it can cause 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. Deuterochloroform, CDCl_3 , 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. Upon long exposure of 1,2-dimethoxyethane to light and oxygen, explosive peroxides may form. 1,2-Dimethoxyethane is also 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 very 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

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.

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

The Laboratory Notebook, Calculations, and Laboratory Records

In the Introduction to this book, we mentioned the importance of advance preparation for 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 very 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. Very 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 of 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

1.2 PREPARING FOR THE LABORATORY

A common misconception students have about performing experiments is that it is much like cooking; that is, you merely follow the directions given—the “recipe”—and the desired product or data will result. Such students enter the laboratory expecting to follow the experimental procedure in a more or less rote manner. This unfortunate attitude can lead to inefficiencies, accidents, and minimal educational benefit and enjoyment from the laboratory experience.

To be sure, cooking is somewhat analogous to performing experiments. The successful scientist, just like a five-star chef, is a careful planner, a diligent worker, a keen observer, and is fully prepared for failures! Experiments may not work despite your best efforts, just as a cake may fall even in the hands of a premier pastry chef.

The correct approach to being successful in the laboratory is *never* to begin any experiment until you understand its overall purpose and the reasons for each operation that you are to do. This means that you must *study*, not *just read*, the entire experiment *prior* to arriving at the laboratory. Rarely, if ever, can you complete the necessary preparation in five or ten minutes, which means that you should not wait until just before the laboratory period begins to do the studying, thinking, and writing that are required. *Planning* how to spend your time in the laboratory is the key to efficient completion of the required experiments. Your performance in the laboratory will benefit enormously from proper advance work, and so will your grade!

The specific details of what you should do before coming to the laboratory will be provided by your instructor. However, to help you prepare in advance, we have developed a set of Pre-Lab Exercises for each of the experimental procedures we describe. These exercises are Web-based and are found at the URL given in the margin; you should bookmark this URL, as you will be visiting it frequently while preparing for each experimental procedure. In addition, the icon shown in the margin will appear whenever Web-based material is available.

Your instructor may require you to submit answers to the Pre-Lab Exercises for approval before authorizing you to proceed with the assigned experiments. Even if you are not required to submit the exercises, though, you will find that working them *prior* to the laboratory period will be a valuable educational tool to self-assess your understanding of the experiments to be performed.

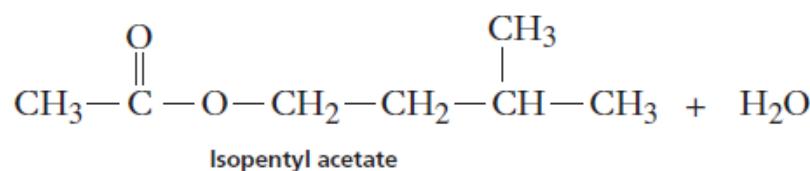
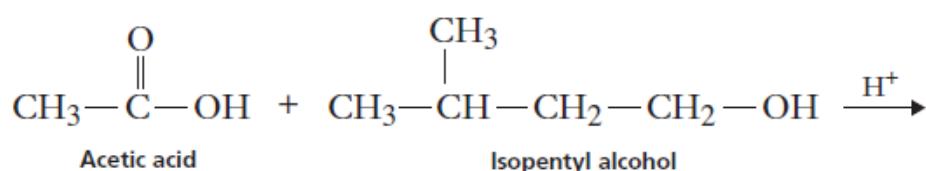
You undoubtedly will be required to maintain a laboratory notebook, which will serve as a complete, accurate, and neat record of the experimental work that you do. Once more, your instructor will provide an outline of what specific information should appear in this notebook, but part of what is prescribed will probably necessitate advance preparation, which will further enhance your ability to complete the experiments successfully. The laboratory notebook is a *permanent record* of your accomplishments in the course, and you should take pride in the quality and completeness of its contents!

A. Advance Preparation (Pre-Lab)

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 very 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 very 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:



Also, before beginning the experiment enter in the notebook the possible side reactions that divert reagents into contaminants (side products). 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 the *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 could very 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 (see 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.

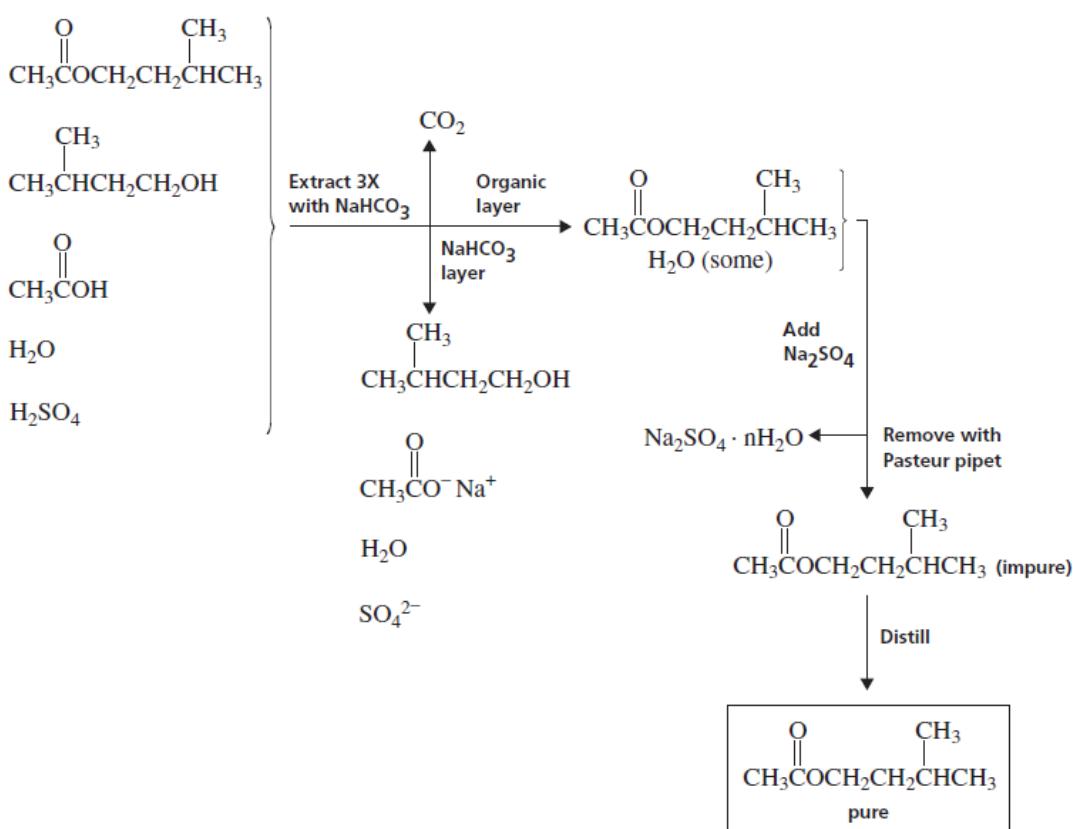


Figure 2.1 Separation scheme for isopentyl acetate.

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 very important here because it is the heart of such an experiment.

1.3 WORKING IN THE LABORATORY

You should be aware that experimental organic chemistry is *potentially* dangerous, because many of the chemicals used are toxic and/or highly flammable, and most of the procedures require the use of glassware that is easily broken. Careless handling of these chemicals and sloppy assembly of apparatus are sources of danger not only to you but also to those working near you. You should *not* be afraid of the chemicals and equipment that you will be using, but you *should* treat them with the respect and care associated with safe experimental practices. To facilitate this, there is an emphasis on the proper handling of chemicals and apparatus throughout the textbook, and the importance of paying particular attention to these subjects *cannot* be overemphasized. In a sense, laboratory safety is analogous to a chain, which is only as strong as its weakest link: the possibility that an accident will occur is only as great as the extent to which unsafe practices are followed. In other words, if you and your labmates adhere to proper laboratory procedures, the risk of an accident will be minimized.

It is important that you follow the experimental procedures in this textbook closely. There is a good reason why each operation should be performed as it is described, although that reason may not be immediately obvious to you. Just as it is risky for a novice chef to be overly innovative when following a recipe, it is *dangerous* for a beginning experimentalist to be “creative” when it comes to modifying the protocol that we’ve specified. As you gain experience in the organic laboratory, you may wish to develop alternative procedures for performing a reaction or purifying a desired product, but *always* check with your instructor *before* trying any modifications.

Note that rather detailed experimental procedures are given early in the textbook, whereas somewhat less detailed instructions are provided later on. This is because many of the basic laboratory operations will have become familiar to you in time and need not be spelled out. It is hoped that this approach to the design of procedures will decrease your tendency to think that you are essentially following a recipe in a cookbook. Moreover, many of the experimental procedures given in the literature of organic chemistry are relatively brief and require the chemist to "fill in the blanks," so it is valuable to gain some initial experience in figuring out some details on your own.

Most of your previous experience in a chemistry laboratory has probably required that you measure quantities precisely, using analytical balances, burets, pipets, and other precise measuring devices . Indeed, if you have done quantitative inorganic analysis, you know that it is often necessary to measure weights to the third or fourth decimal place and volumes to at least the first. Experiments in organic chemistry that are performed at the microscale level, that is, experiments in which less than about 1 mL of the principal reagents is used and the amounts of solvents are less than 2 or 3 mL, also require relatively precise measuring of quantities. For example, if you are to use 0.1 g of a reagent and your measuring device only allows measuring to the nearest 0.1 g, you could easily have as much as about 0.15 g or as little as 0.05 g of the reagent. Such deviations from the desired quantity represent significant *percentage* errors in measurement and can result in serious errors in the proportions of reagents involved in the reaction. Consequently, weights should be accurate to within about 0.01 g and volumes to within about 0.1 mL. This requires the use of appropriate analytical balances and graduated pipets.

Experiments being performed at the miniscale level, which we define as involving 1–5 g of reagents and usually less than about 25 mL of solvent, normally do not require such precise measuring. Weighing reagents to the nearest tenth of a gram is usually satisfactory, as is measuring out liquids in graduated cylinders, which are accurate to \pm 10%. For example, if you are directed to use 20 mL of diethyl ether as solvent for a reaction, the volume need *not* be 20.0 mL. In fact, it probably will make little difference to the success of the reaction whether anywhere from 15–25 mL of the solvent is added. This is not to say that care need not be exercised in measuring out the amounts of materials that you use. Rather, it means that valuable time need not be invested in making these measurements highly precise.

We've inserted markers in the form of stars (\star) in many of the experimental procedures in this textbook. These indicate places where the procedure can be interrupted without affecting the final outcome of the experiment. These markers are designed to help you make the most efficient use of your time in the laboratory. For example, you may be able to start a procedure at a point in the period when there is insufficient time to complete it but enough time to be able to work through to the location of a star; you can then safely store the reaction mixture and finish the sequence during the next laboratory period. We've *not* inserted stars at every possible stopping point but only at those where it is not necessarily obvious that interruption of the procedure will have no effect on the experimental results. Consult your instructor if in doubt about whether a proper stopping point has been reached.

As noted above, a *carefully* written notebook and *proper* safety procedures are important components of an experimental laboratory course. These aspects are discussed further in the following two sections.

1.4 THE LABORATORY NOTEBOOK

One of the most important characteristics of successful scientists is the habit of keeping a complete and understandable record of the experimental work that has been done. Did a precipitate form? Was there a color change during the course of the reaction? At what temperature was the reaction performed, and for how long did the reaction proceed? Was the reaction mixture homogeneous or heterogeneous? On what date(s) was the work performed? These are observations and data that may seem insignificant at the time but may later prove critical to the interpretation of an experimental result or to the ability of another person to reproduce your work. All of them belong in a properly kept laboratory notebook. We make suggestions for such a document in the following two sections. Your instructor may specify other items to be included, but the list we give is representative of a good notebook.

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, your 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.

1.5 GENERAL PROTOCOL FOR THE LABORATORY NOTEBOOK

1. Use a *bound* notebook for your permanent laboratory record to minimize the possibility that pages will be lost. If a number has not been printed on each page, do so manually. Some laboratory notebooks are designed with pairs of identically numbered pages so that a carbon copy of all entries can be made. The duplicate page can then be removed and submitted to your instructor or put in a separate place for safekeeping. Many professional scientists use this type of notebook.
2. Reserve the first page of the notebook for use as a title page, and leave several additional pages blank for a Table of Contents.
3. Use as the main criterion for what should be entered in the notebook the rule that the record should be sufficiently complete so that anyone who reads it will know exactly what you did and will be able to repeat the work in precisely the way you originally did it.
4. Record all experimental observations and data in the notebook *as they are obtained*. Include the *date* and, if appropriate, the *time* when you did the work. In a legal sense, the information entered into the notebook *at the time of performance* constitutes the primary record of the work, and it is important for you to follow this principle. Many patent cases have been determined on the basis of dates and times recorded in a laboratory notebook. One such example is described in the Historical Highlight at the end of this chapter.

5. Make all entries in ink, and *do not delete anything you have written* in the notebook. If you make a mistake, cross it out and record the correct information. Using erasers or correction fluid to modify entries in your notebook is unacceptable scientific practice!

Do not scribble notes on odd bits of paper with the intention of recording the information in your notebook later. Such bad habits only lead to problems, since the scraps of paper are easily lost or mixed up. They are also inefficient, since transcribing the information to your notebook means that you must write it a second time. This procedure can also result in errors if you miscopy the data.

Finally, do not trust your memory with respect to observations that you have made. When the time comes to write down the information, you may have forgotten a key observation that is critical to the success of the experiment.

6. Unless instructed to do otherwise, do not copy *detailed* experimental procedures that you have already written elsewhere in your notebook; this consumes valuable time. Rather, provide a specific reference to the source of the detailed procedure and enter a *synopsis* of the written procedure that contains enough information that (1) you need not refer to the source while performing the procedure and (2) another chemist will be able to *duplicate* what you did. For example, when performing an experiment from this textbook, give a reference to the page number on which the procedure appears, and detail any *variations* made in the procedure along with the reason(s) for doing so.
7. Start the description of each experiment on a new page titled with the name of the experiment. The recording of data and observations from several different procedures on the same page can lead to confusion, both for yourself and for others who may read your notebook.

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:

$$\text{Theoretical yield} = (\text{moles of limiting reagent})(\text{ratio})(\text{molecular weight of product})$$

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

$$\text{Percentage yield} = \frac{\text{Actual yield}}{\text{Theoretical yield}} \times 100$$

Main Reaction

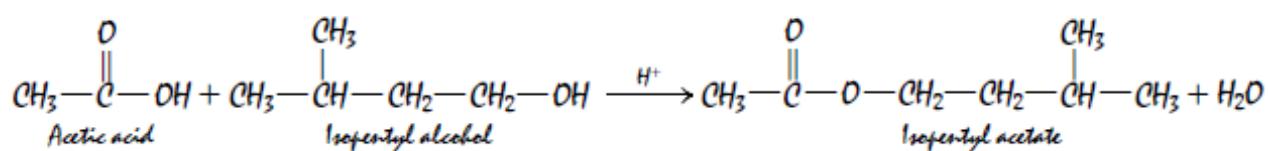


Table of Physical Constants

	MW	BP	Density
Isopentyl alcohol	88.2	132°C	0.813 g/ml
Acetic acid	60.1	118	1.06
Isopentyl acetate	130.2	142	0.876

Separation Scheme

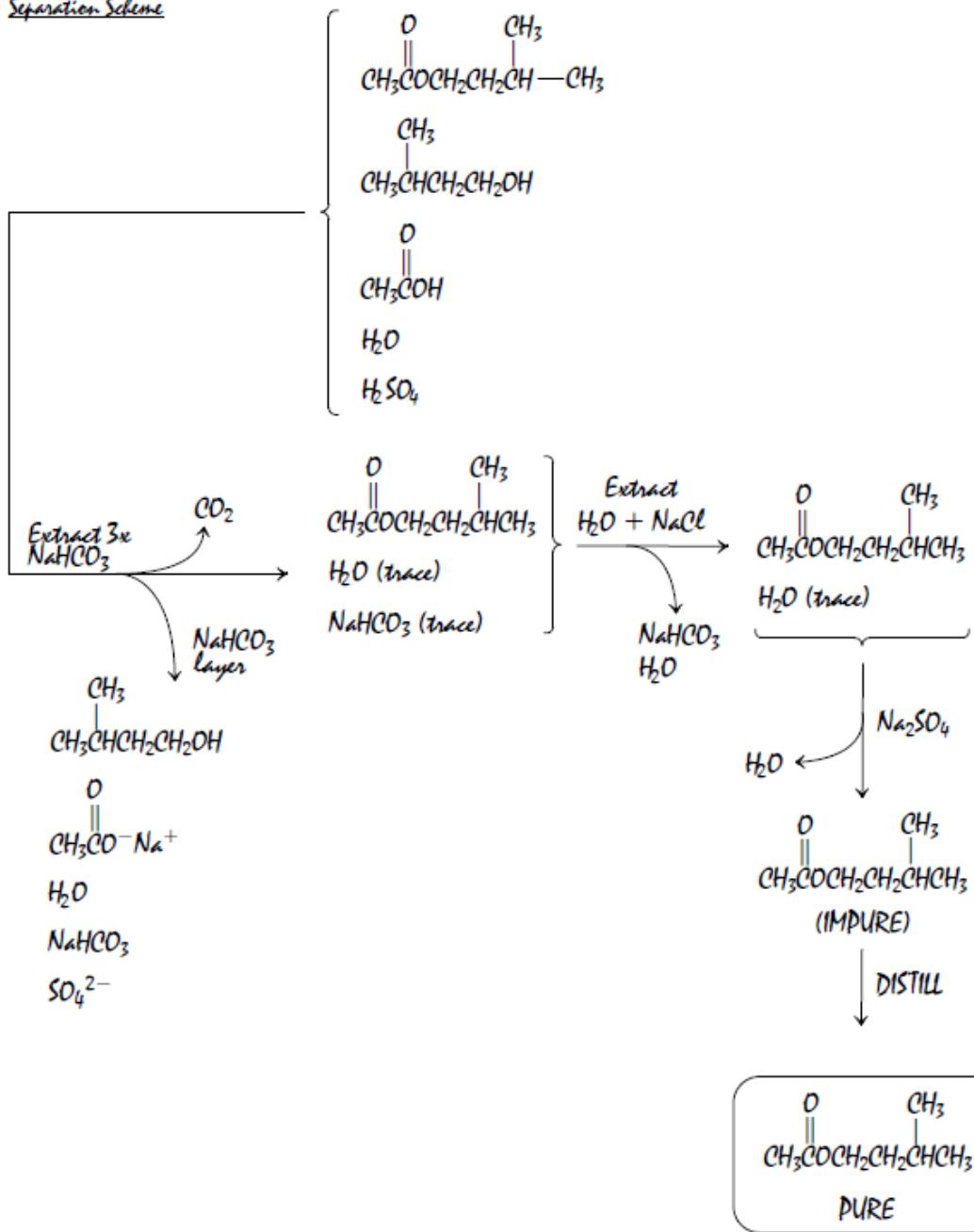


Figure 2.2 A sample notebook, page 1.

Data and Observations

7.5 mL of isopentyl alcohol was added to a pre-weighed 50-mL round-bottomed flask:

Flask + alcohol	139.75 g
Flask	133.63 g
6.12 g isopentyl alcohol	

Glacial acetic acid (10 mL) and 2 mL of concentrated sulfuric acid were also added to the flask, with swirling, along with several boiling stones. A water-cooled condenser was attached to the flask. The reaction was allowed to boil, using a heating mantle, for about one hour. The color of the reaction mixture was brownish-yellow.

After the reaction mixture had cooled to room temperature, the boiling stones were removed, and the reaction mixture was poured into a separatory funnel. About 30 mL of cold water was added to the separatory funnel. The reaction flask was rinsed with 5 mL of cold water, and the water was also added to the separatory funnel. The separatory funnel was shaken, and the lower aqueous layer was removed and discarded. The organic layer was extracted twice with two 10–15-mL portions of 5% aqueous sodium bicarbonate. During the first extraction, much CO₂ was given off, but the amount of gas evolved was markedly diminished during the second extraction. The organic layer was a light yellow in color. After the second extraction, the aqueous layer turned red litmus blue. The bicarbonate layers were discarded, and the organic layer was extracted with a 10–15-mL portion of water. A 2–3 mL portion of saturated sodium chloride solution was added during this extraction. When the aqueous layer had been removed, the upper, organic phase was transferred to a 15-mL Erlenmeyer flask. 2 g of anhydrous magnesium sulfate was added. The flask was stoppered, swirled gently, and allowed to stand for 15 mins.

The product was transferred to a 25-mL round-bottomed flask, and it was distilled by simple distillation. The distillation continued until no liquid could be observed dripping into the collection flask. After the distillation, the ester was transferred to a pre-weighed sample vial.

Sample vial + product	9.92 g
Sample vial	6.11 g
3.81 g isopentyl acetate	

The product was colorless and clear. The observed boiling point obtained during the distillation, was 140°C. An IR spectrum was obtained of the product.

Calculations

Determine limiting reagent:

$$\text{isopentyl alcohol } 6.12 \text{ g} \left(\frac{1 \text{ mol isopentyl alcohol}}{88.2 \text{ g}} \right) = 6.94 \times 10^{-2} \text{ mol}$$

$$\text{acetic acid: (10 mL)} \left(\frac{1.06 \text{ g}}{\text{mL}} \right) \left(\frac{1 \text{ mol acetic acid}}{60.1 \text{ g}} \right) = 1.76 \times 10^{-1} \text{ mol}$$

Since they react in a 1:1 ratio, isopentyl alcohol is the limiting reagent. Theoretical yield:

$$(6.94 \times 10^{-2} \text{ mol isopentyl alcohol}) \left(\frac{1 \text{ mol isopentyl acetate}}{1 \text{ mol isopentyl alcohol}} \right) \left(\frac{130.2 \text{ g isopentyl acetate}}{1 \text{ mol isopentyl acetate}} \right)$$
$$= 9.03 \text{ g isopentyl acetate}$$

$$\text{Percentage yield} = \frac{3.81 \text{ g}}{9.03 \text{ g}} \times 100 = 42.2\%$$

Figure 2.3 A sample notebook, page 2.

Calculation of the theoretical yield and percentage yield can be illustrated using hypothetical data for the isopentyl acetate preparation:

$$\text{Theoretical yield} = (6.94 \times 10^{-2} \text{ mol isopentyl alcohol}) \left(\frac{1 \text{ mol isopentyl acetate}}{1 \text{ mol isopentyl alcohol}} \right)$$

$$\times \left(\frac{130.2 \text{ g isopentyl acetate}}{1 \text{ mol isopentyl acetate}} \right) = 9.03 \text{ g isopentyl acetate}$$

$$\text{Actual yield} = 3.81 \text{ g isopentyl acetate}$$

$$\text{Percentage yield} = \frac{3.81 \text{ g}}{9.03 \text{ g}} \times 100 = 42.2\%$$

For experiments that have the principal objective of isolating a substance such as a natural product rather than preparing and purifying some reaction product, the **weight percentage recovery** and not the percentage yield is calculated. This value is determined by

$$\text{Weight percentage recovery} = \frac{\text{Weight of substance isolated}}{\text{Weight of original material}} \times 100$$

Thus, for instance, if 0.014 g of caffeine was obtained from 2.3 g of tea, the weight percentage recovery of caffeine would be

$$\text{Weight percentage recovery} = \frac{0.014 \text{ g caffeine}}{2.3 \text{ g tea}} \times 100 = 0.61\%$$

2.3 Laboratory Reports

Various formats for reporting the results of the laboratory experiments may be used. You may write the report directly in your notebook in a format similar to the sample notebook pages included in this section. Alternatively, your instructor may require a more formal report that is not written in your notebook. When you do original research, these reports should include a detailed description of all the experimental steps undertaken. Frequently, the style used in scientific periodicals such as *Journal of the American Chemical Society* is applied to writing laboratory reports. Your instructor is likely to have his or her own requirements for laboratory reports and should describe the requirements to you.

2.4 Submission of Samples

In all preparative experiments and in some isolation experiments, you will be required to submit to your instructor the sample of the substance you prepared or isolated. How this sample is labeled is very important. Again, learning a correct method of labeling bottles and vials can save time in the laboratory, because fewer mistakes will be made. More importantly, learning to label properly can decrease the danger inherent in having samples of material that cannot be identified correctly at a later date.

Solid materials should be stored and submitted in containers that permit the substance to be removed easily. For this reason, narrow-mouthed bottles or vials are not used for solid substances. Liquids should be stored in containers that will not let them escape through leakage. Be careful not to store volatile liquids in containers that have plastic caps, unless the cap is lined with an inert material such as Teflon. Otherwise, the vapors from the liquid are likely to contact the plastic and dissolve some of it, thus contaminating the substance being stored.

On the label, print the name of the substance, its melting or boiling point, the actual and percentage yields, and your name. An illustration of a properly prepared label follows:

Isopentyl Acetate
BP 140°C
Yield 3.81 g (42.2%)
Joe Schmedlock

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 section 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 chemistry laboratory or are uncertain about how such equipment should be treated, this section provides some useful information, such as how to clean and care for glassware when using corrosive or caustic reagents. At the end of this section are illustrations that show and name most of the equipment you are likely to find in your drawer or locker.

3.1 Cleaning Glassware

Glassware can be cleaned easily if you clean it immediately after use. 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. If you wait, cleaning is more difficult, because water will no longer wet the surface of the glass as effectively. If you cannot wash your glassware immediately after use, soak the dirty pieces of glassware 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.

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. After the solvent has been used, the glass item probably will have to be washed with soap and water to remove the residual solvent. When you use solvents to clean glassware, use caution, because the solvents are hazardous (see Technique 1). Use fairly small amounts of a solvent for cleaning purposes. Usually less than 5 mL (or 1–2 mL for microscale glassware) 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 water bath and heat it cautiously to accelerate the cleaning process. Continue heating the glassware 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 it 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, 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.

3.2 Drying Glassware

The easiest way to dry glassware is to let it stand overnight. Store 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 an acetone waste 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. 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 Claisen head in Figure 3.1 consists of an inner (male) ground-glass joint at the bottom and two outer (female) joints at the top. Each end is ground to a precise size, which is designated by the symbol \ddagger followed by two numbers. A common joint size in many macroscale organic glassware kits is $\ddagger 19/22$. 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 apparatuses. One disadvantage of glassware with ground-glass joints, however, is that it is expensive.

3.4 Connecting Ground-Glass Joints

It is a simple matter to connect pieces of macroscale glassware using standard-taper ground-glass joints. Figure 3.2B illustrates the connection of a condenser to a round-bottom flask. At times, however, it may be difficult to secure the connection so that it does not come apart unexpectedly. Figure 3.2A shows a plastic clip that serves to secure the connection. Methods to secure ground-glass connections with macroscale apparatus, including the use of plastic clips, are covered in Technique 7.

It is important to make sure no solid or liquid is on the joint surfaces. Either of these will decrease the efficiency of the seal, and the joints may leak. With microscale glassware, the presence of solid particles could cause the ground-glass joints to break when 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 the surfaces with a cloth or a lint-free paper towel before assembling.

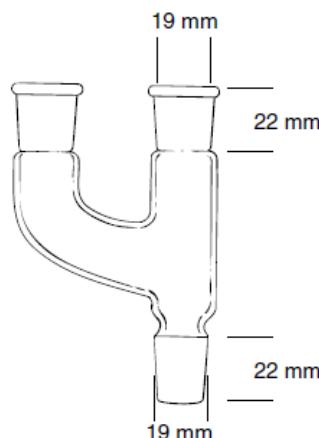


Figure 3.1 Illustration of inner and outer joints, showing dimensions. A Claisen head with # 19/22 joints.

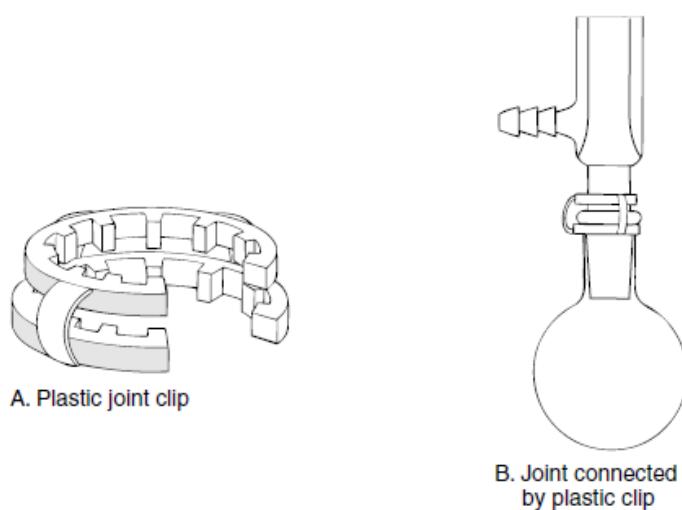


Figure 3.2 Connection of ground-glass joints. The use of a plastic clip (A) is also shown (B).

3.5 Capping Flasks, Conical Vials, and Openings

The sidearms in two-necked or three-necked round-bottom flasks can be capped using the #19/22 ground-glass stoppers that are part of a normal macroscale organic kit. Figure 3.3 shows such a stopper being used to cap the sidearm of a three-necked flask.

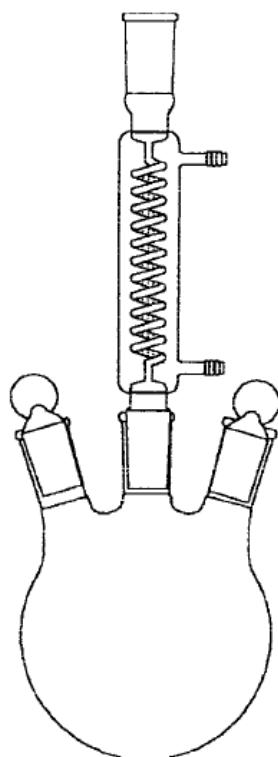


Figure 3.3 Capping a sidearm with a #19/22 stopper.

3.6 Separating Ground-Glass Joints

When ground-glass joints become “frozen” or stuck together, you are faced with the often vexing problem of separating them. The techniques for separating ground-glass joints, or for removing stoppers that are stuck in the openings of flasks and vials, are the same for both macroscale and microscale glassware.

The most important thing you can do to prevent ground-glass joints from becoming frozen 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 certain items of microscale glassware may be small and very 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 both 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 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 separates from the inner section. Heat the joint very slowly and carefully, or it may break.

3.7 Etching Glassware

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.

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 sidearms 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

Figures 3.4 and 3.5 include examples of glassware and equipment that are commonly used in the organic laboratory. Your glassware and equipment may vary slightly from the pieces shown.



25-mL Round-bottom
boiling flask



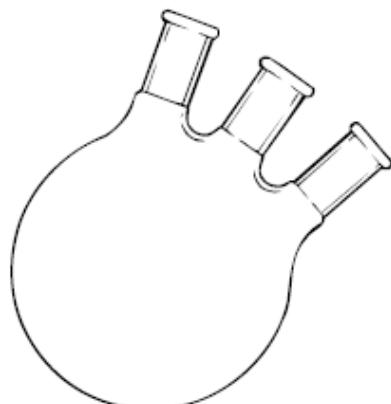
50-mL Round-bottom
boiling flask



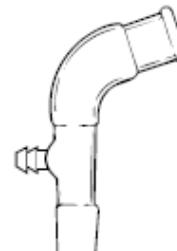
100-mL Round-bottom
boiling flask



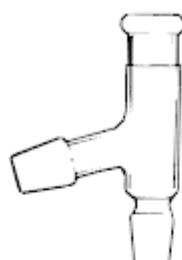
250-mL Round-bottom
boiling flask



500-mL Three-necked
round-bottom flask



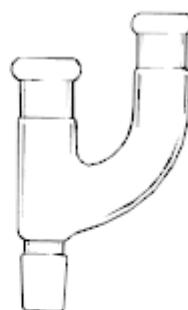
Vacuum
adapter



Distillation
head



Stopper



Claisen head



Thermometer
adapter (with
rubber fitting)

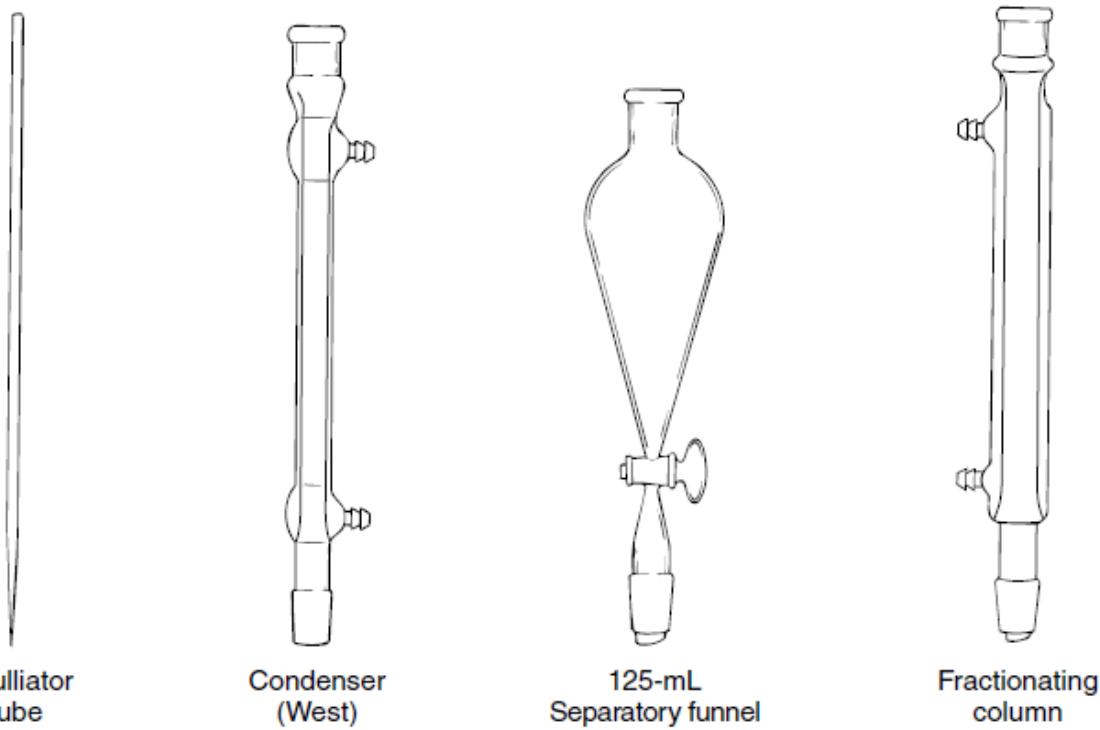
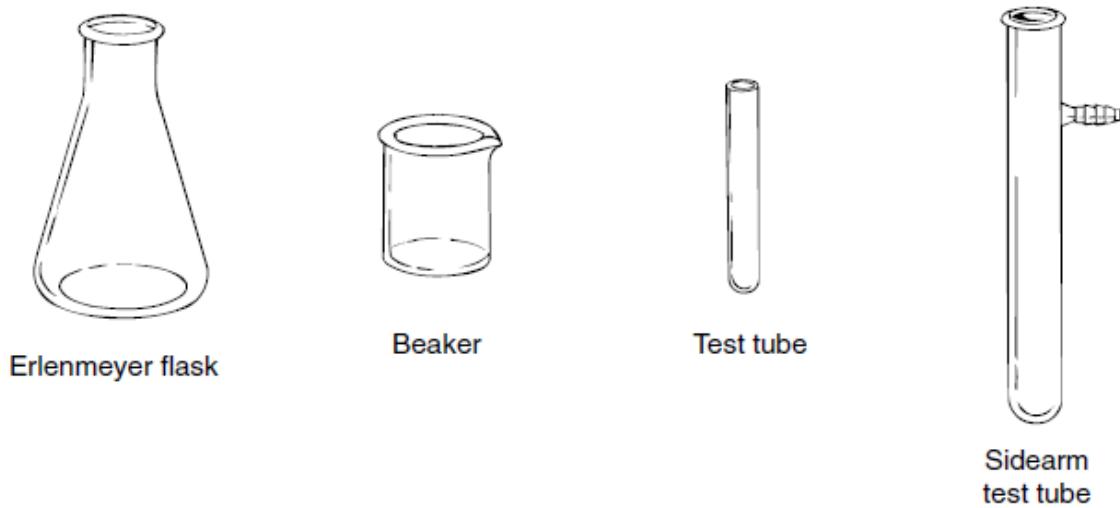
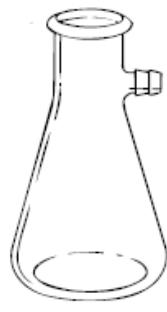


Figure 3.4 Components of the macroscale organic laboratory kit.





Filter flask



Hirsch funnel



Neoprene adapter



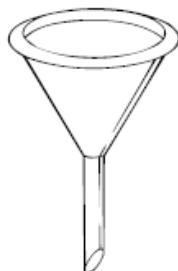
Pasteur pipets



Pipet bulb



Rubber septum



Conical funnel



Centrifuge tube

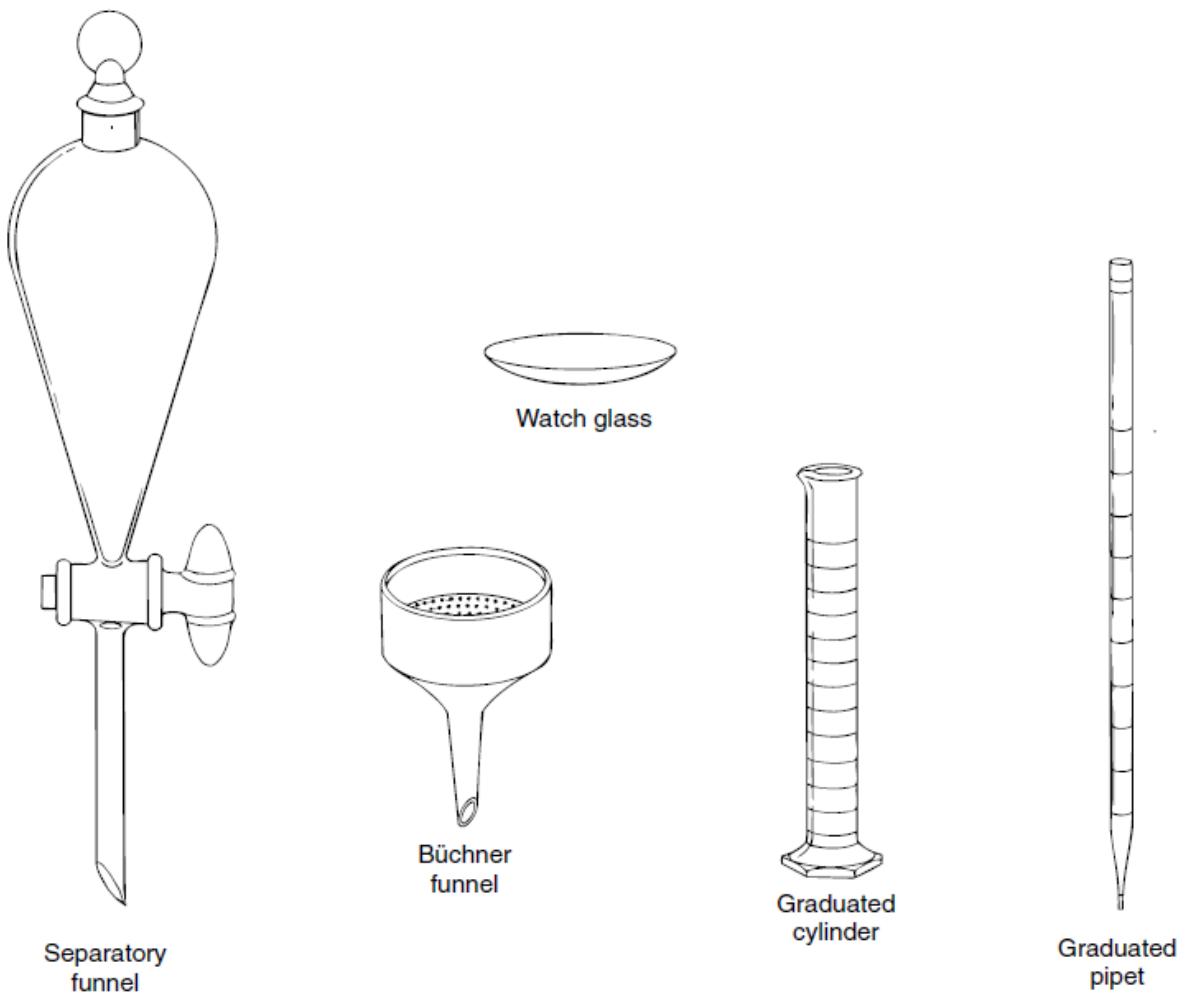
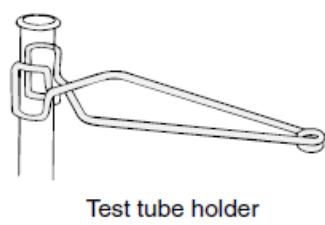


Figure 3.5 Equipment commonly used in the organic chemistry laboratory.



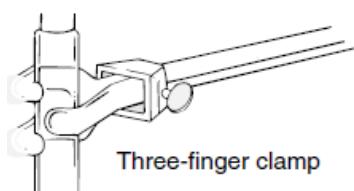
Test tube holder



Test tube brush



Spin Bar



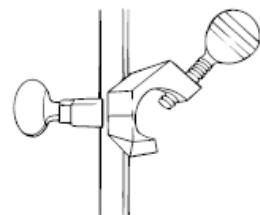
Three-finger clamp



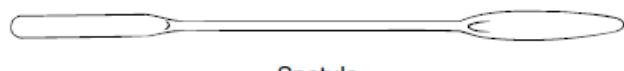
Forceps



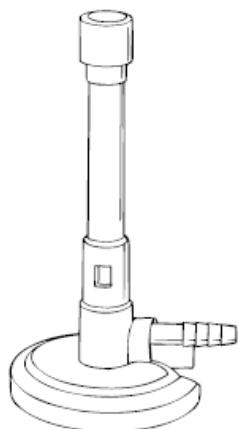
Syringe



Clamp holder



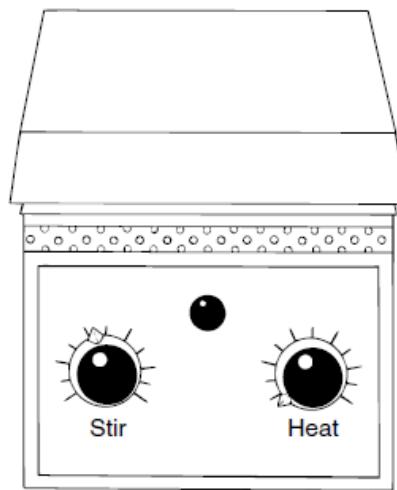
Spatula



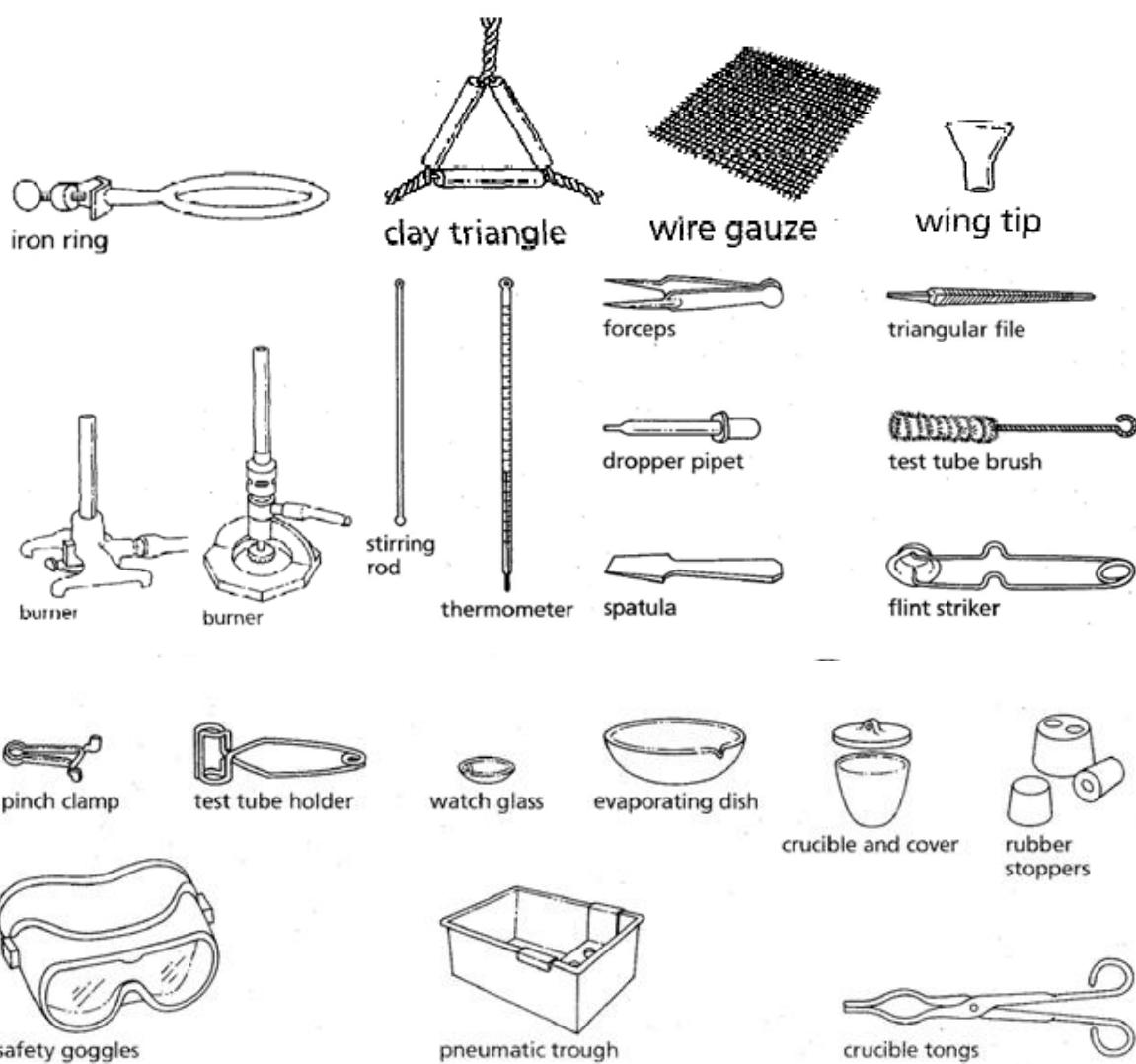
Microburner



Drying tube



Hot plate / Stirrer





These GOGGLES are used to protect your eyes from broken glass, chemicals and flames.



A WATCHGLASS can be used as a beaker cover, but you can also place small amounts of chemicals on it and then heat it (for example, to evaporate some water from a wet chemical).



A FUNNEL is used with filter paper to remove undissolved solids from a liquid mixture. It also can be used to help pour a liquid into a container that has a small opening (for example, a volumetric flask).



"A" is the STIRRING ROD, which is used to stir combinations of chemicals. You can also pour liquid down along it (as you pour it into another container) to keep it from splashing out. "B" is the RUBBER POLICEMAN. It is put on the end of the stirring rod, and it keeps the glass rod from scratching a glass beaker or other container.



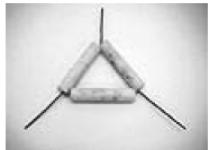
This all-purpose UTILITY CLAMP can be used to hold many lab equipment items when it is attached to a ring stand. For example: test tubes, hoses, erlenmeyer flasks, burets.



This BURET CLAMP is used to hold a buret. The clamp is attached to a ring stand.



The EVAPORATING DISH is used as a container for heating, usually when you want to evaporate a liquid from some chemicals.



The CLAY TRIANGLE is a frame which can support a container. For example, it can hold a crucible during heating or can hold a funnel during filtering.



LAB TONGS can be used to hold or pick up many items, but work best as tongs for picking up a hot evaporating dish.

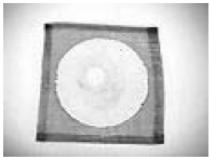
CRUCIBLE TONGS are designed up pick up and hold a crucible.



BEAKER TONGS are best used to hold a hot beaker.



HOT HANDS are a chemist's "hot pot holder". They are used to pick up hot glassware.



WIRE GAUZE can be used to support a container (such as a beaker or flask) during heating. When the bunsen burner flame is beneath it, the wire gauze helps to spread the flame (and heat) out evenly over the container.



The RING CLAMP is attached to the ring stand, and is used as a support. For example, it might be used to hold a funnel during filtering.



A TEST TUBE CLAMP holds a test tube during heating.



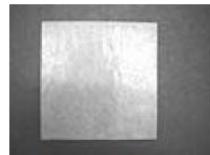
A RUBBER STOPPER with no holes is used as a "plug" for a test tube or flask. When the stopper has a hole in it, a piece of tubing can be inserted in it (see "A" and "C").



A TEST TUBE is used as a container to hold chemicals during heating or other reactions, and the TEST TUBE RACK supports the test tubes.



A SPOT PLATE has a number of small "wells". Chemicals are placed into the small wells, and the reaction can be observed as it takes place in the "well".



WEIGHING PAPER looks and feels like waxed paper. It is used with the balance so that the chemicals are placed on the paper instead of directly on the balance.



Weighing paper is folded before it is used (folded into quarters).



FORCEPS are used to pick up small items in the laboratory



The CHEMICAL SPATULA is used to transfer chemicals. Use these instead of your fingers!!



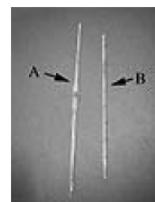
A THERMOMETER is used to measure temperature. We use celsius in the chemistry lab.



The PIPET BULB is used to fill a pipet with liquid.



A WASH BOTTLE is used to rinse glassware in the chemistry lab. It is NOT used to rinse your eyes!



Pipets are used to measure liquid. "A" is a VOLUMETRIC PIPET. Volumetric pipets are used to measure one amount only. For example, a 25 mL volumetric pipet is used to measure 25 mL only, and no other amount. "B" is a GRADUATED PIPET. Graduated pipets have a lot of lines drawn on it so that you can measure many different amounts.



A SEPARATORY FUNNEL is a glass container. A mixture of liquids can be poured into it and allowed to separate.



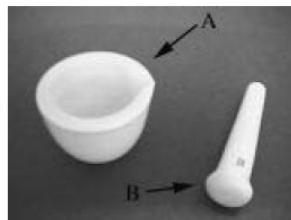
The ERLLENMEYER FLASK is a container which gives only approximate measurements of volume. It is usually used as a mixing vessel or a container for heating.



The FLORENCE FLASK is used to hold a liquid during heating.



This round-bottom flask is very similar to a florence flask.



The MORTAR is the dish, and the PESTLE is the grinder. They are used to crush or grind up chemicals.



The GRADUATED CYLINDER is used to measure the volume of liquids in mL.



The BEAKER doesn't measure the volume of liquids very accurately. It is usually used as a container for mixing or holding chemicals.



The VOLUMETRIC FLASK is used the measure one specific volume of liquid (kind of like a volumetric pipet).



The HYDROMETER floats or sinks when placed into a liquid which is related to the density of the liquid.



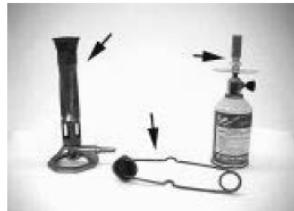
The CONDUCTIVITY TESTER is used to measure whether an object conducts electricity or not.



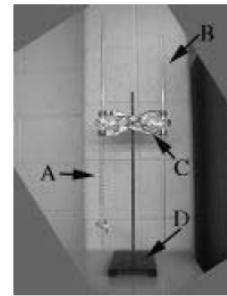
The THISTLE TUBE is a special type of funnel.



The MAGNETIC STIR BAR is a magnet covered with teflon.



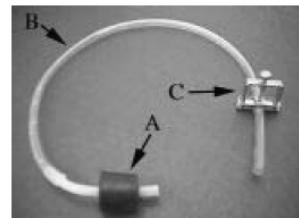
The FLINT LIGHTER is used to ignite the flame of a BUNSEN BURNER. The gas collects inside the small cup, and the spark created ignites the gas.



The RING STAND offers the support, and the buret clamp is holding a BURET (A) and a GAS COLLECTION TUBE (B). Although these look very similar, the buret is a glass tube open at both ends. There is a valve at the bottom and it is used to dispense liquids (kind of like a drink machine at McDonalds). The gas collection tube is closed at the top so that gases can collect inside and we can measure the volume of gas.



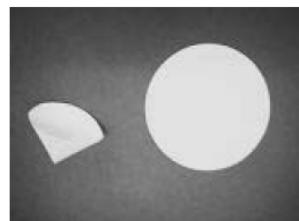
The DROPPER PIPET is a medicine dropper and just dispenses small drops of liquid.



The RUBBER TUBING has a rubber stopper at one end and a PINCH CLAMP at the other end. The pinch clamp can close the hose if necessary.



The CRUCIBLE and its COVER are used to hold small amounts of chemicals during heating at high temperatures, especially if you want to keep oxygen out of the reaction (just put the cover on the crucible).



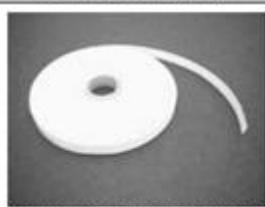
FILTER PAPER is used to separate a mixture. It feels like thick coffee filter paper and has very small holes in it. It is folded into a "cone" shape.



The FILTERING FLASK has a side-arm which is connected to a low pressure source. It is used for Vacuum filtration or Flash Chromatography



This HOT PLATE is used as a heat source.



CHROMATOGRAPHY PAPER is used to separate a mixture. It comes in rolls, but we use only short pieces.



CHROMATOGRAPHIC TANK or CHROMATOGRAPHIC CHAMBER is used to perform Thin Layer Chromatography or Paper Chromatography.



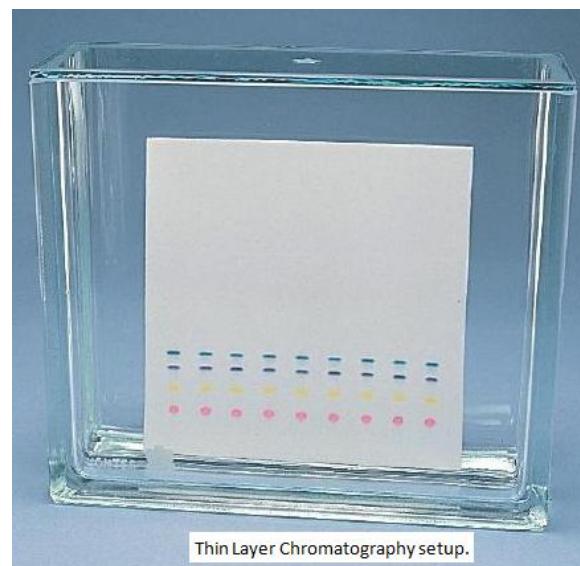
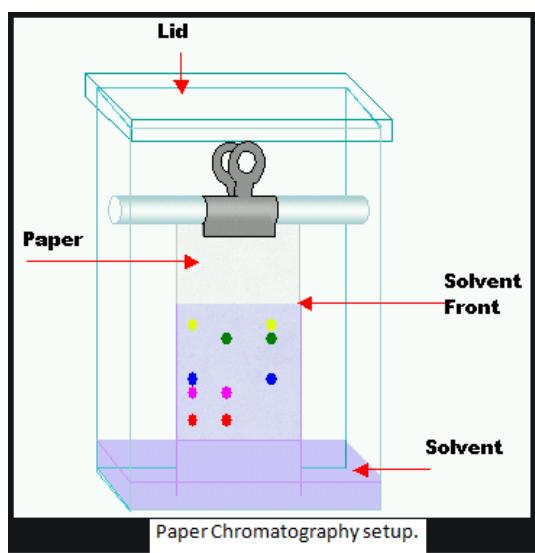
Columns used to perform Column Chromatography.

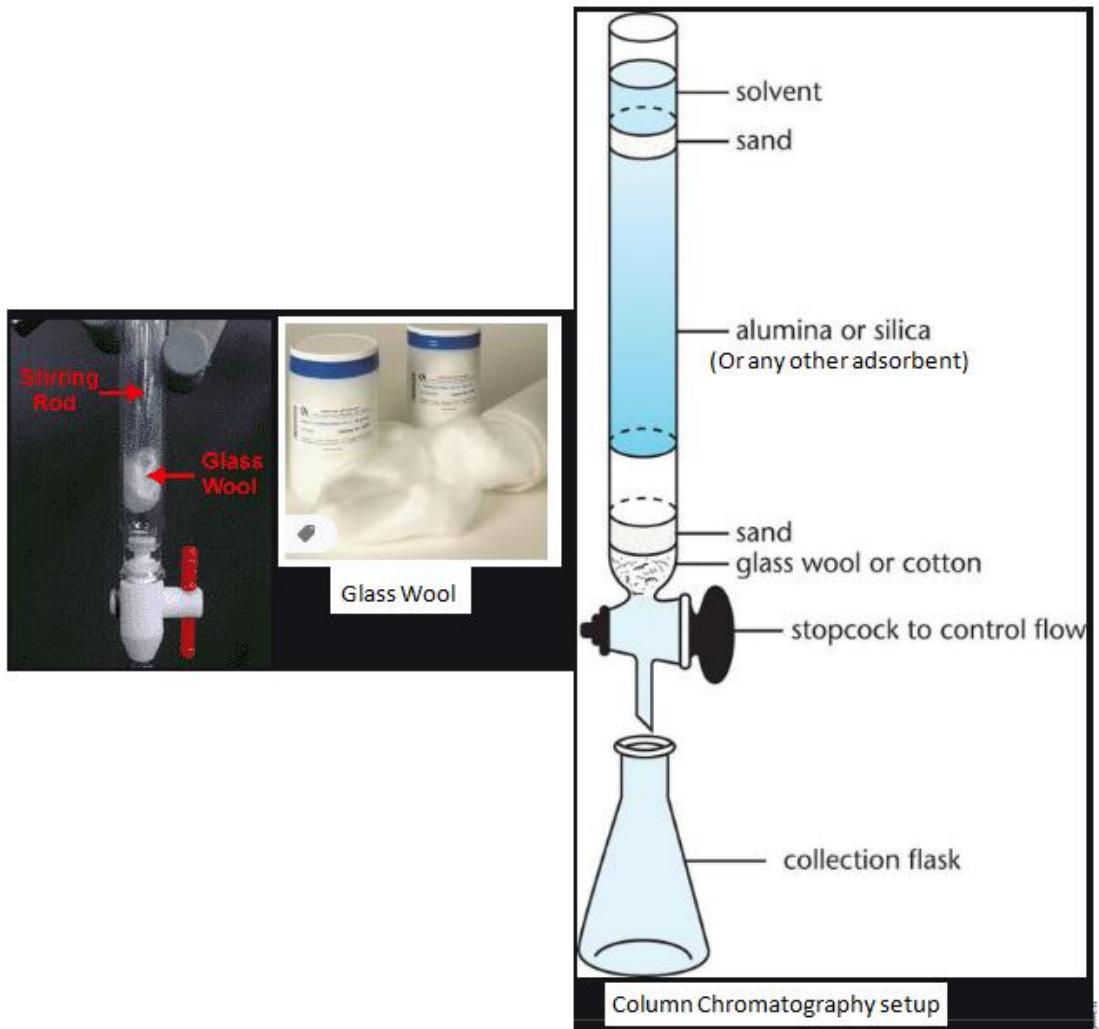


TLC Spotting Capillary Tubes used for TLC spotting.



TLC Plates are used to perform TLC.





Measurement of Volume and Weight



Figure 5.1 Graduated cylinder.

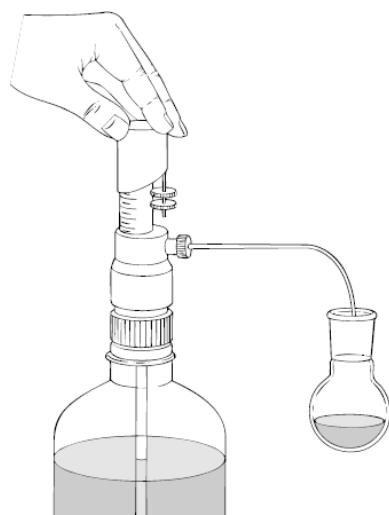


Figure 5.2 Use of a dispensing pump.

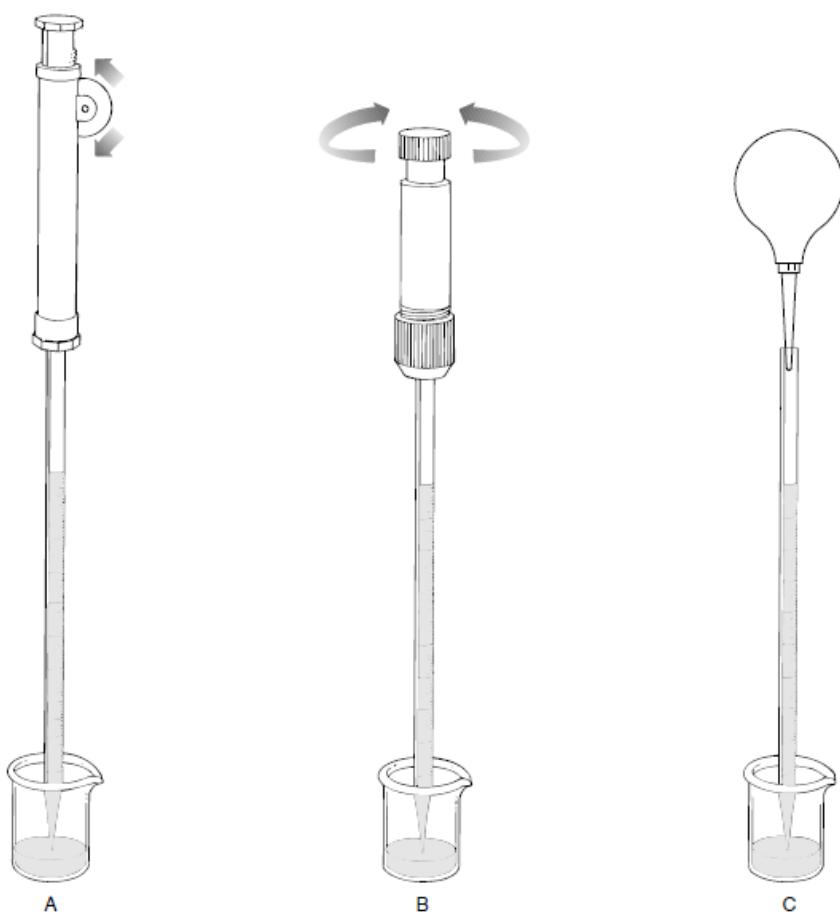


Figure 5.3 Pipet pumps (A, B) and a pipet bulb (C).

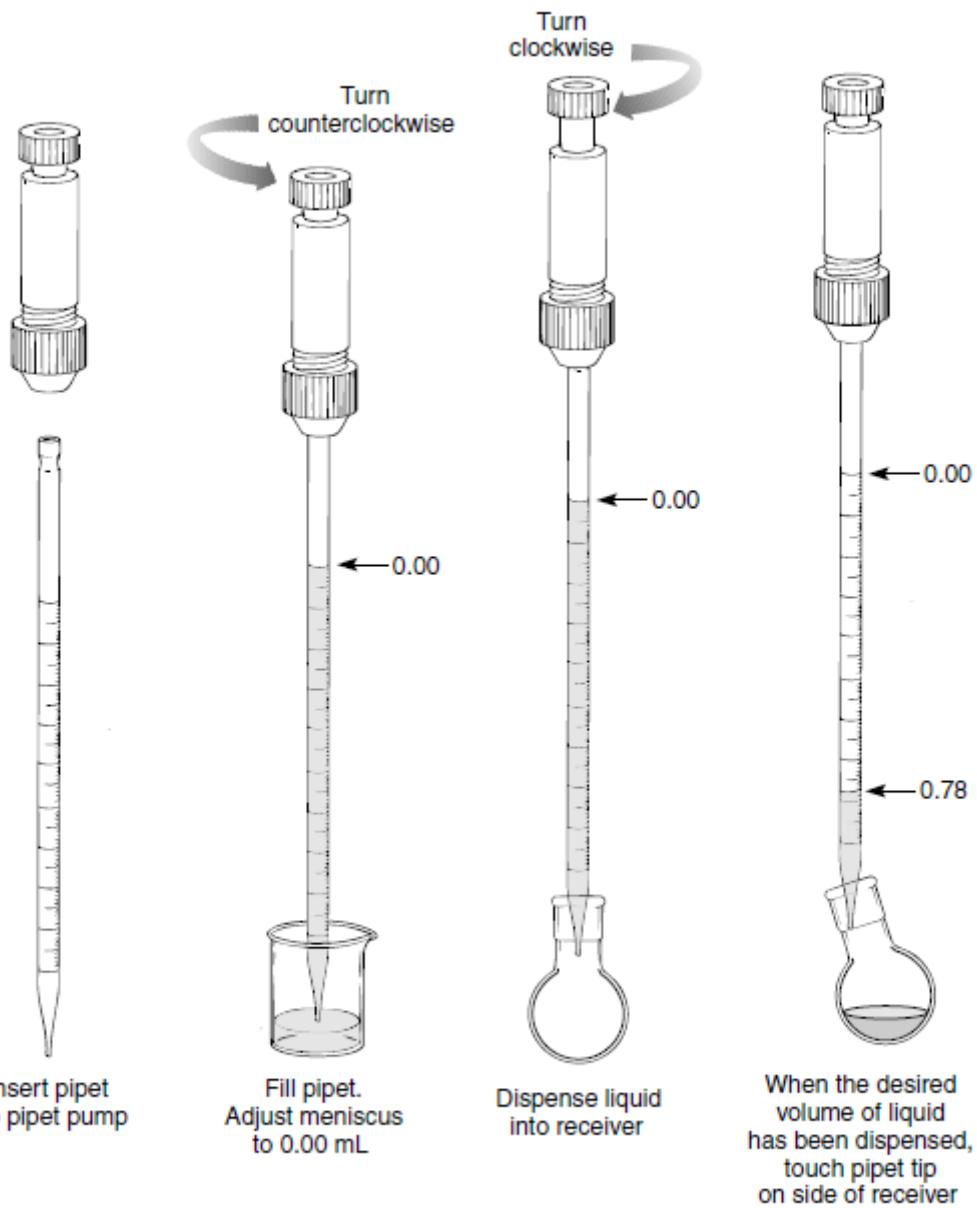


Figure 5.4 Use of a graduated pipet. (The figure shows, as an illustration, the technique required to deliver a volume of 0.78 mL from a 1.00-mL pipet.)

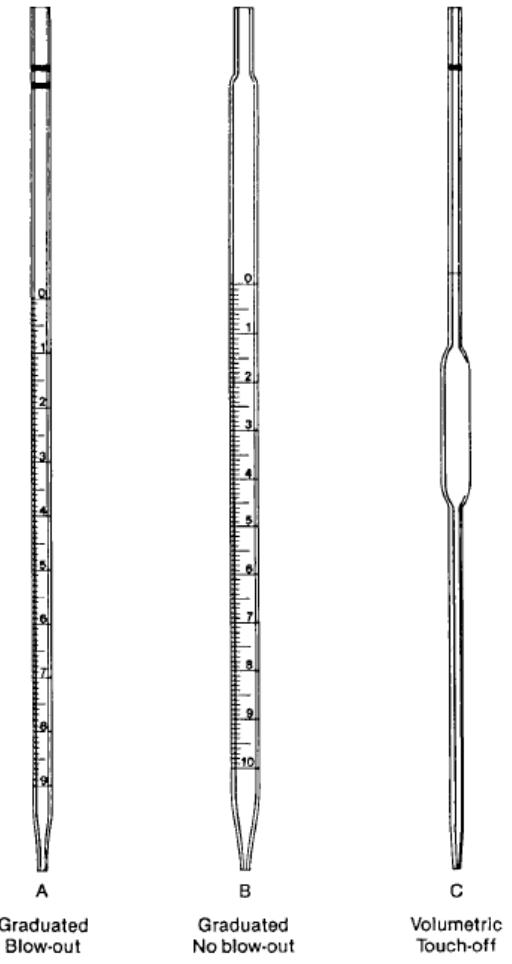


Figure 5.5 Pipets.

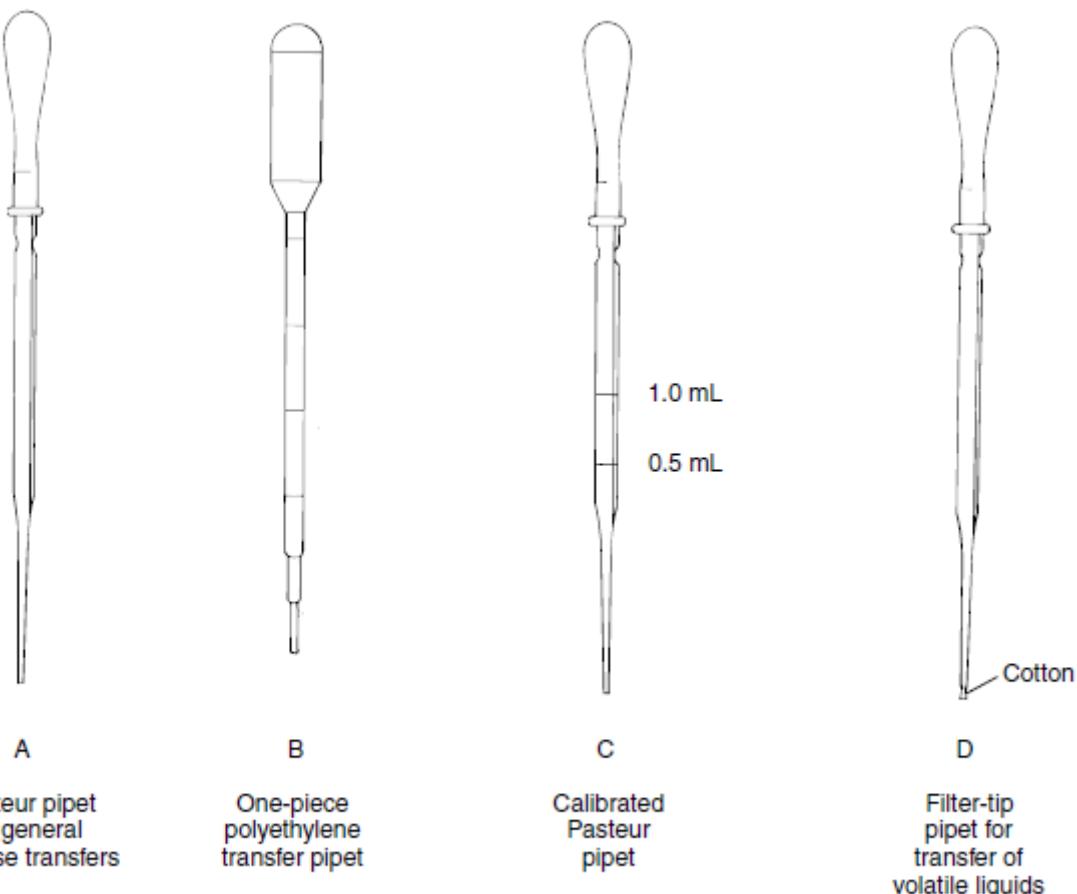


Figure 5.6 Pasteur (A, C, D) and transfer pipets (B).

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. Caution should be used with some disposable syringes, as 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. Remove the plunger and draw air through the barrel with an aspirator to dry the syringe.

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

Plastic or glass syringes (Fig. 2.11) are often used to deliver liquids into reaction mixtures. Syringes marked with gradations showing the amount of liquid contained in them normally have an accuracy of volumetric measurement on the order of $\pm 5\%$, although the syringes originally designed for use in gas chromatography and those having volumes of $500 \mu\text{L}$ or less are more accurate. The

needles on syringes are either fixed (Fig. 2.11a) or demountable (Fig. 2.11b, c). With the latter style of syringe, needles having various gauges can be affixed to the barrel. Removing and attaching the needles often require twisting the base of the needle to disengage it from or engage it to the barrel; this type of syringe is shown in Figure 2.11b. Otherwise, the needle simply slides on or off the plastic or ground-glass tip of the barrel (Fig. 2.11c).

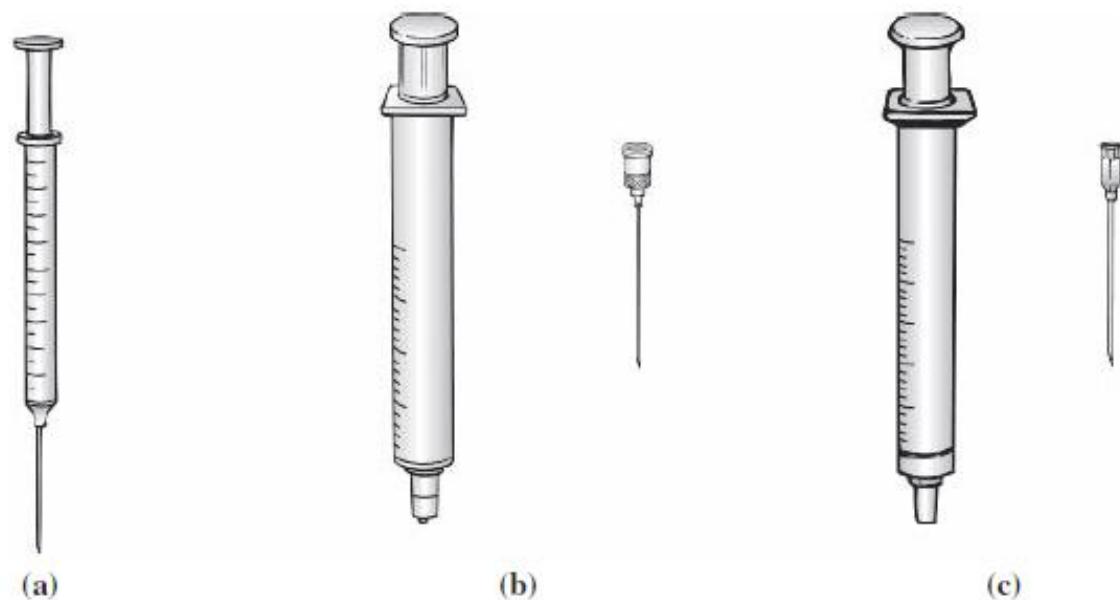


Figure 2.11

Fixed and demountable syringes:

- (a) *fixed needle;*
- (b) *demountable, locking;*
- (c) *demountable, nonlocking.*

Syringes are commonly used in the laboratory to transfer solutions or liquid reagents to reactions being performed under anhydrous conditions. The apparatus is usually fitted with a rubber septum, and the syringe needle is used to pierce the septum to deliver the liquid. You must be careful when inserting the needle into the septum to avoid bending it. The danger of bending can be minimized by supporting the sides of the needle with two fingers as you insert it into the septum.

A syringe is a sharp-pointed instrument, so you should be careful handling it. *Never* point an assembled syringe at yourself or anyone else, and do not leave needles pointed upward. You might get more than a simple needle prick as a result. You should clean a syringe immediately after use. This is done by pulling acetone or some other low-boiling solvent into the barrel and expelling it into an appropriate container. The rinsing should be repeated several times, whereupon the syringe should be dried by pumping the plunger to pull air through it or by attaching the barrel of the syringe to a water aspirator.

5.6 Automatic Pipets

Automatic pipets are commonly used in microscale organic laboratories and in biochemistry laboratories. Several types of adjustable automatic pipets are shown in Figure 5.7. The automatic pipet is very accurate with aqueous solutions, but it is not as accurate with organic liquids. These pipets are available in different sizes and can deliver accurate volumes ranging from 0.10 mL to 1.0 mL. They are very expensive and must be shared by the entire laboratory. Automatic pipets should never be used with corrosive liquids, such as sulfuric acid or hydrochloric acid. *Always use the pipet with a plastic tip.*

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 10–100 μL (0.010–0.100 mL) or 100–1000 μL (0.100–1.000 mL).

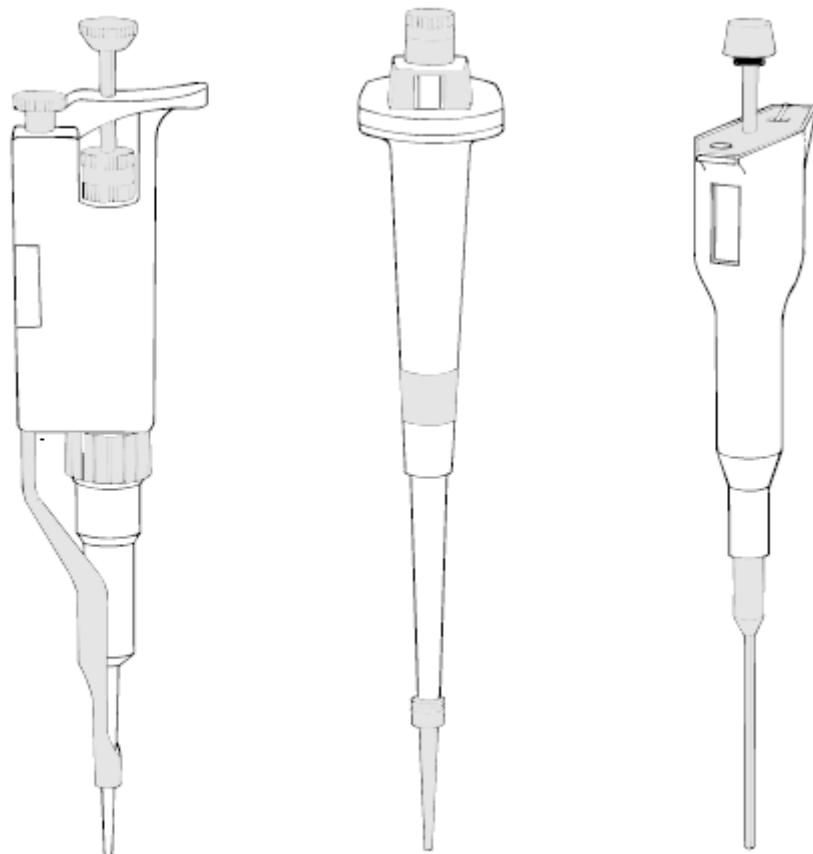


Figure 5.7 The adjustable automatic pipet.

5.7 Measuring Volumes with Conical Vials, Beakers, and Erlenmeyer Flasks

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 in microscale experiments.

5.8 Balances

Solids and some liquids will need to be weighed on a balance that reads to at least the nearest milligram (0.001 g) for microscale experiments or to at least the nearest decigram (0.01 g) for macroscale experiments. A top-loading balance (see Figure 5.8) 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 Figure 5.9) 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.

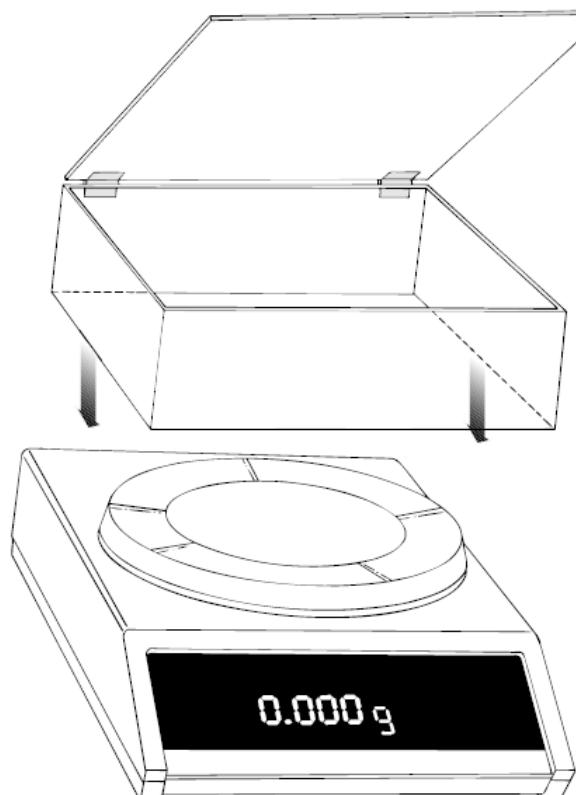


Figure 5.8 A top-loading balance with a plastic draft shield.

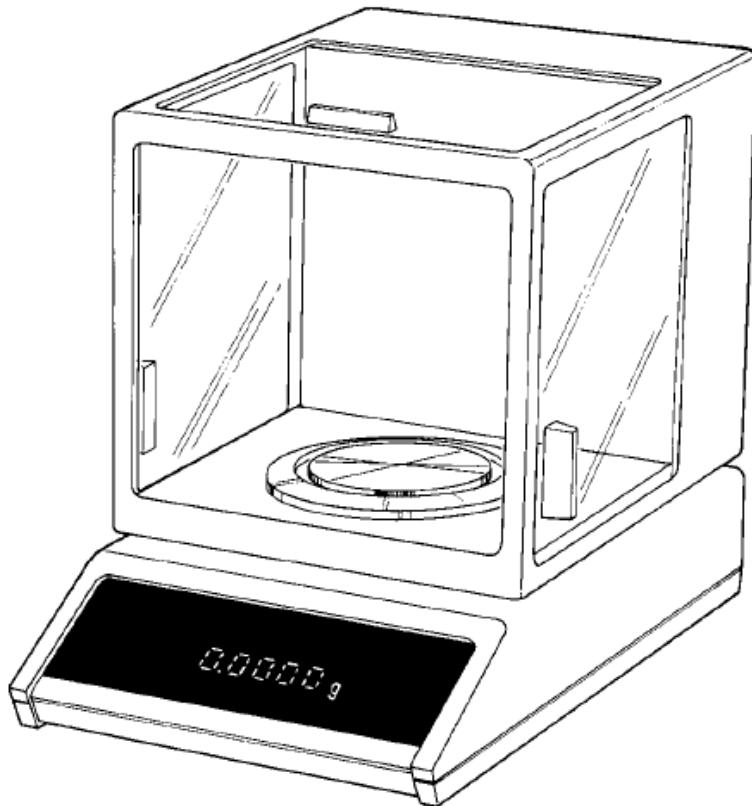


Figure 5.9 An analytical balance with a glass draft shield.

With liquids, you should weigh the flask to determine the tare weight; transfer the liquid with a graduated cylinder, dispensing pump, or graduated pipet into the flask; and then reweigh it. With liquids, it is usually necessary to weigh only the limiting reagent. The other liquids may be transferred using a graduated cylinder, dispensing pump, or graduated pipet. Their weights can be calculated by knowing the volumes and densities of the liquids.

Heating and Cooling Methods

Most organic reaction mixtures need to be heated in order to complete the reaction. In general chemistry, you used a Bunsen burner for heating because nonflammable aqueous solutions were used. In an organic chemistry laboratory, however, the student must heat nonaqueous solutions that may contain *highly flammable* solvents. You *should not heat organic mixtures with a Bunsen burner* unless you are directed to do so by your laboratory instructor. Open flames present a potential fire hazard. Whenever possible you should use one of the alternative heating methods, as described in the following sections.

Heating Methods

Heating is an important laboratory technique that is used in a variety of situations. For example, many chemical reactions require heating to proceed at a reasonable rate. Heating is also used to purify liquids by distillation, to remove volatile solvents during the work-up of a reaction, and to dissolve solids when purifying solid products by recrystallization.

Two general rules regarding heating are noted here. (1) Whatever device is being used to heat a liquid or solid, you must arrange the apparatus so that the heating source can be *rapidly* removed to prevent accidents that may occur by overheating. This normally means that the heating source is mounted on a ring clamp or a lab jack, either of which allows for quick removal of the device if necessary. (2) As a rule, the *safest* way to heat organic solvents is with a *flameless* heat source in a hood. This practice not only minimizes the chance of fire, but it also avoids filling the room with solvent vapors.

Heating with electrical devices is generally the method of choice in the organic laboratory, since it is much safer than using open flames. These devices are usually comprised of two essential components: (1) a resistance element that converts electrical into thermal energy, and (2) a variable transformer for controlling the voltage across the element. They differ, however, in the medium used to transfer heat from the element to the experimental apparatus. For example, air and oil are the heat transfer agents for a heat gun and an oil bath, respectively.

Although we describe below how burners are properly used for heating purposes, the experimental procedures in this textbook focus on *flameless* heating devices. Burners can be substituted for such devices in most cases, but not all. *Consult with your instructor if you have any questions regarding the suitability of substituting flames for other heating devices.*

Burners

Most chemistry laboratories are supplied with natural gas to fuel various types of burners. A burner provides the convenience of a rapid and reasonably inexpensive source of heat. However, many organic substances, especially solvents such as ether and hexane, are highly flammable, and you should always exercise

good judgment when considering the use of a burner for heating volatile organic compounds. *Before using a burner to heat anything in the laboratory, consult with your instructor for the proper precautions and directions.* If an alternative mode of heating is available, choose it in preference to a burner. *Never use a burner to heat flammable materials in open containers such as beakers or Erlenmeyer flasks, because a fire may result.*

There are a number of situations in the laboratory where burners are appropriate heating sources. They may be used to heat Thiele tubes in the determination of melting or boiling points of organic substances and to heat a water bath to obtain and maintain temperatures from ambient to about 80 °C. When volatile solvents are not being used in the laboratory, burners may be safely substituted for heat guns to dry apparatus so a reaction may be conducted under anhydrous conditions

. On occasion, you will need a burner to bend glass tubing or to fashion a piece of glass apparatus. Burners can also be used to heat aqueous solutions that do not contain flammable substances or to heat higher-boiling liquids that are completely contained in round-bottom flasks either fitted with a reflux condenser

or equipped for distillation . In these instances, it is important to lubricate the joints of the apparatus with a hydrocarbon or silicone grease to minimize the danger of leaking vapors and reduce the likelihood of the joints freezing.

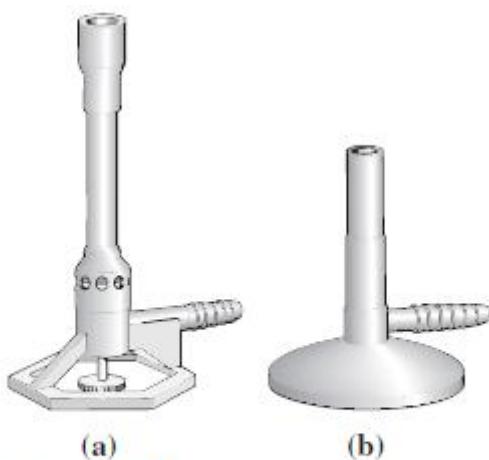


Figure 2.22

Laboratory burners: (a) Bunsen burner; (b) microburner.

You must be aware of what others are doing in the laboratory. Although you might be using a burner to perform a completely safe operation, someone nearby may be working with a very volatile, flammable solvent, some of which can creep along the bench top for several feet! These vapors or others in the room may be ignited explosively by an open flame.

Two common types of laboratory burners are pictured in Figure 2.22. The classic Bunsen burner, named after its inventor, is shown in Figure 2.22a. The needle valve at the bottom of the burner serves as a fine adjustment of the gas flow, and turning the barrel of the burner regulates the air flow; adjustment of gas and air flow provides control of the flame. In the microburner in Figure 2.22b, the air flow is adjusted at the baffle at the bottom of the burner, and the gas flow is adjusted at the gas valve on the laboratory bench.

Heating a flask with a burner may produce “hot spots” if most of the heat is applied to a small area on the bottom of the flask. Hot spots can lead to severe bumping, since the heat must be dispersed throughout the liquid by convection or by means of the turbulence caused by boiling. Hot spots can easily be avoided by holding the burner and slowly moving the flame over the bottom of the flask. Alternatively, a piece of wire gauze, which diffuses the heat reaching the flask, may be placed between the flame and the flask; the gauze is supported with an iron ring.

6.1 Heating Mantles

A useful source of heat for most macroscale experiments is the heating mantle, illustrated in Figure 6.1. The heating mantle shown here consists of a ceramic heating shell with electric heating coils embedded within the shell. The temperature of a heating mantle is regulated with the heat controller. Although it is difficult to monitor the actual temperature of the heating mantle, the controller is calibrated so that it is fairly easy to duplicate approximate heating levels after one has gained some experience with this apparatus. Reactions or distillations requiring relatively high temperatures can be easily performed with a heating mantle. For temperatures in the range of 50–80°C, you should use a water bath (see Section 6.3) or a steam bath (see Section 6.8).

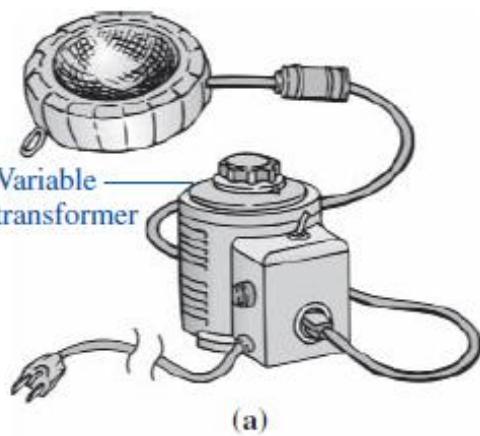
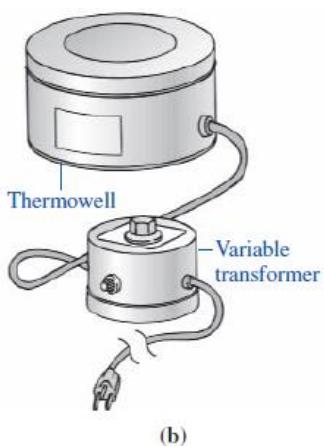
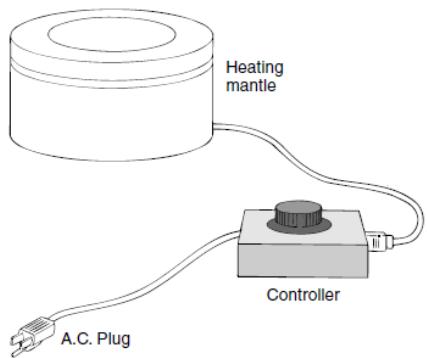


Figure 6.1 A heating mantle.

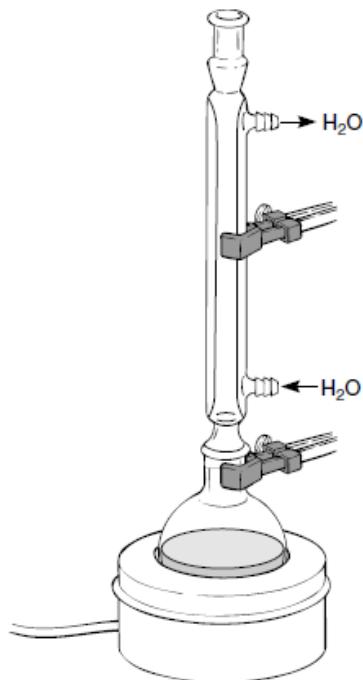


Figure 6.2 Heating with a heating mantle.

Figure 2.23

(a) Woven-glass heating mantle. (b) Heating mantle with ceramic core.

In the center of the heating mantle shown in Figure 6.1 is a well that can accommodate round-bottom flasks of several different sizes. Some heating mantles, however, are designed to fit only specific sizes of round-bottom flasks. Some heating mantles are also made to be used with a magnetic stirrer so that the reaction mixture can be heated and stirred at the same time. Figure 6.2 shows a reaction mixture being heated with a heating mantle.

Heating mantles are very easy to use and safe to operate. The metal housing is grounded to prevent electrical shock if liquid is spilled into the well; however, flammable liquids may ignite if spilled into the well of a hot heating mantle.

CAUTION



You should be very careful to avoid spilling liquids into the well of the heating mantle. The surface of the ceramic shell may be very hot and could cause the liquid to ignite.

Raising and lowering the apparatus is a much more rapid method of changing the temperature within the flask than changing the temperature with the controller. For this reason, the entire apparatus should be clamped above the heating mantle so that it can be raised if overheating occurs. Some laboratories may provide a lab jack or blocks of wood that can be placed under the heating mantle. In this case, the heating mantle itself is lowered and the apparatus remains clamped in the same position.

There are two situations in which it is relatively easy to overheat the reaction mixture. The first situation occurs when a larger heating mantle is used to heat a relatively small flask. You should be very careful when doing this. Many laboratories provide heating mantles of different sizes to prevent this from happening. The second situation occurs when the reaction mixture is first brought to a boil. To bring the mixture to a boil as rapidly as possible, the heat controller is often turned up higher than it will need to be set in order to keep the mixture boiling. When the mixture begins boiling very rapidly, turn the controller to a lower setting and raise the apparatus until the mixture boils less rapidly. As the temperature of the heating mantle cools down, lower the apparatus until the flask is resting on the bottom of the well.

6.2 Hot Plates

Hot plates are a very convenient source of heat; however, it is difficult to monitor the actual temperature, and changes in temperature occur somewhat slowly. Care must be taken with flammable solvents to ensure against fires caused by "flashing" when solvent vapors come into contact with the hot-plate surface. Never evaporate large quantities of a solvent by this method; the fire hazard is too great.

Some hot plates *heat constantly* at a given setting. They have no thermostat, and you will have to control the temperature manually, either by removing the container being heated or by adjusting the temperature up or down until a balance point is found. Some hot plates have a thermostat to control the temperature. A good thermostat will maintain a very even temperature. With many hot plates, however, the temperature may vary greatly (>10–20°C), depending upon whether the heater is in its "on" cycle or its "off" cycle. These hot plates will have a cycling (or oscillating) temperature, as shown in Figure 6.3. They, too, will have to be adjusted continually to maintain even heat.

Some hot plates also have built-in magnetic stirring motors that enable the reaction mixture to be stirred and heated at the same time. Their use is described in Section 6.5.

6.3 Water Bath with Hot Plate/Stirrer

A hot-water bath is a very effective heat source when a temperature below 80°C is required. A beaker (250-mL or 400-mL) is partially filled with water and heated on a hot plate. A thermometer is clamped into position in the water bath. You may need to cover the water bath with aluminum foil to prevent evaporation, especially at higher temperatures. The water bath is illustrated in Technique 6, Figure 6.4. A mixture can be stirred with a magnetic stir bar (see Technique 7, Section 7.3). A hot-water bath has some advantage over a heating mantle in that the temperature in the bath is uniform. In addition, it is sometimes easier to establish a lower temperature with a water bath than with other heating devices. Finally, the temperature of the reaction mixture will be closer to the temperature of the water, which allows for more precise control of the reaction conditions.

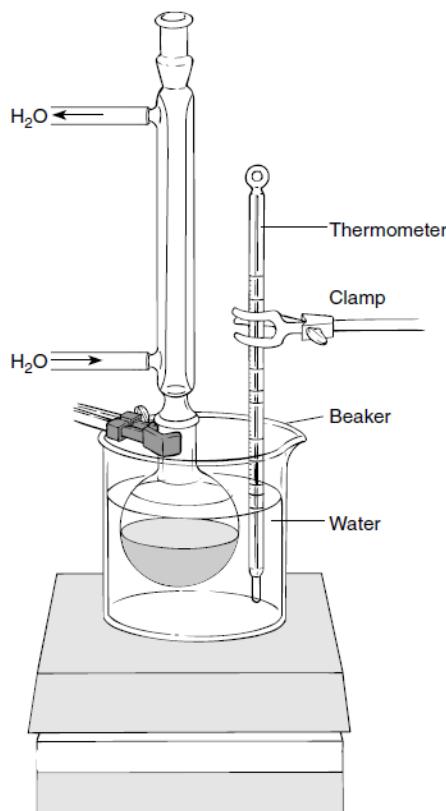


Figure 6.4 A water bath with a hot plate/stirrer.

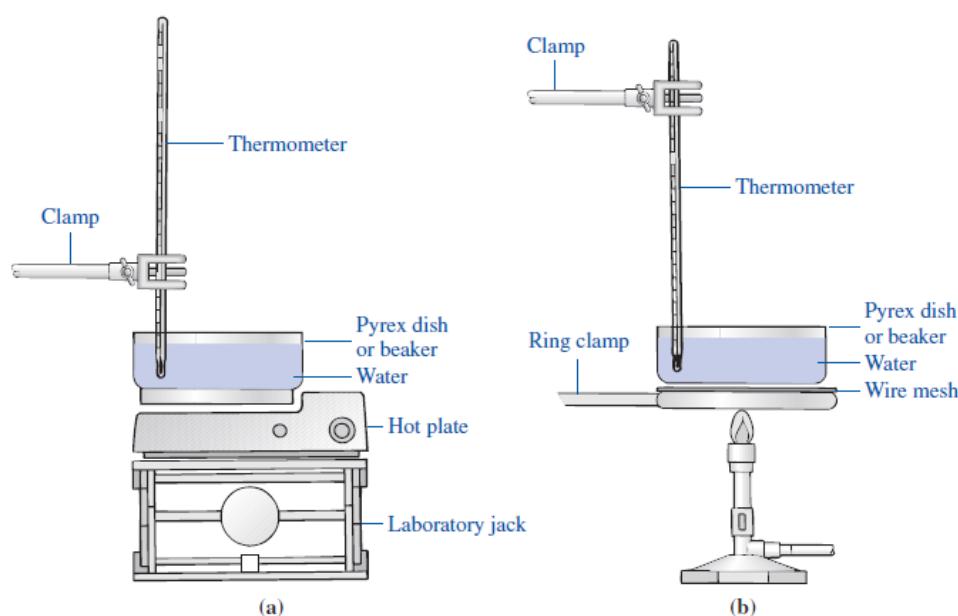


Figure 2.29
Water bath: (a) heated by hot plate; (b) heated by Bunsen burner.

6.4 Oil Bath with Hot Plate/Stirrer

In some laboratories, oil baths may be available. An oil bath can be used when carrying out a distillation or heating a reaction mixture that needs a temperature above 100°C. An oil bath can be heated most conveniently with a hot plate, and a *heavy-walled* beaker provides a suitable container for the oil.¹ A thermometer is clamped into position in the oil bath. In some laboratories, the oil may be heated electrically by an immersion coil. Because oil baths have a high heat capacity and heat slowly, it is advisable to heat the oil bath partially before the actual time at which it is to be used.

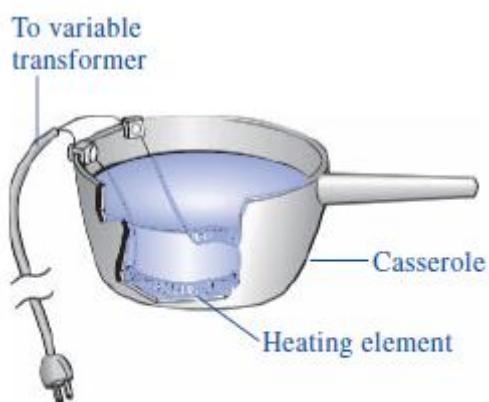


Figure 2.24
Electrically heated oil bath.

In some laboratories, oil baths may be available. An oil bath can be used when carrying out a distillation or heating a reaction mixture that needs a temperature above 100°C. An oil bath can be heated most conveniently with a hot plate, and a *heavy-walled* beaker provides a suitable container for the oil.¹ A thermometer is clamped into position in the oil bath. In some laboratories, the oil may be heated electrically by an immersion coil. Because oil baths have a high heat capacity and heat slowly, it is advisable to heat the oil bath partially before the actual time at which it is to be used.

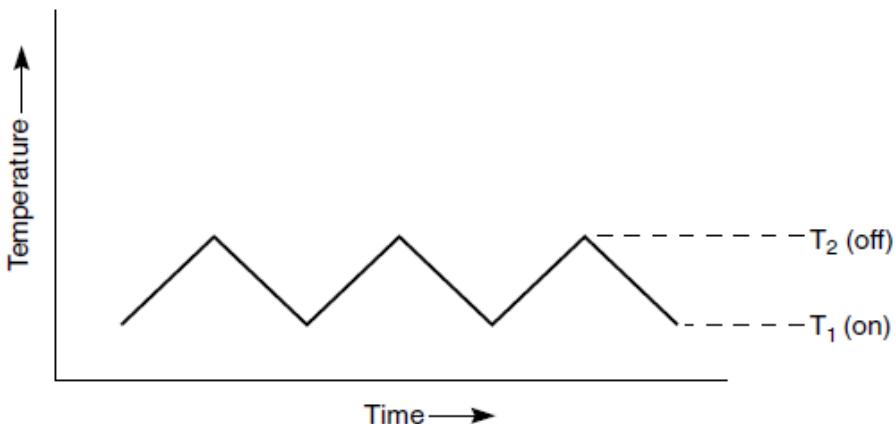


Figure 6.3 Temperature response for a hot plate with a thermostat.

¹It is very dangerous to use a thin-walled beaker for an oil bath. Breakage due to heating can occur, spilling hot oil everywhere!

An oil bath with ordinary mineral oil cannot be used above 200–220 °C. Above this temperature, the oil bath may “flash,” or suddenly burst into flame. A hot oil fire is not extinguished easily. If the oil starts smoking, it may be near its flash temperature; discontinue heating. Old oil, which is dark, is more likely to flash than new oil. Also, hot oil causes bad burns. Water should be kept away from a hot oil bath, because water in the oil will cause it to splatter. Never use an oil bath when it is obvious that there is water in the oil. If water is present, replace the oil before using the heating bath. An oil bath has only a finite lifetime. New oil is clear and colorless but, after extended use, becomes dark brown and gummy from oxidation.

Besides ordinary mineral oil, a variety of other types of oils can be used in an oil bath. Silicone oil does not begin to decompose at as low a temperature as does mineral oil. When silicone oil is heated high enough to decompose, however, its vapors are far more hazardous than mineral oil vapors. The polyethylene glycols may be used in oil baths. They are water-soluble, which makes cleaning up after using an oil bath much easier than with mineral oil. One may select any one of a variety of polymer sizes of polyethylene glycol, depending on the temperature range required. The polymers of large molecular weight are often solid at room temperature. Wax may also be used for higher temperatures, but this material also becomes solid at room temperature. Some workers prefer to use a material that solidifies when not in use because it minimizes both storage and spillage problems.

Some inconveniences are also encountered using oil baths. If the volume of heating liquid is fairly large, it may take a while to reach the desired bath temperature. The maximum temperature that may be safely attained in an oil bath is limited by the type of heating liquid being used. Silicone oils are more expensive but are generally preferable to mineral oils because they can be heated to 200–275 °C without reaching the **flash point**, the temperature at which a liquid can burst into flame, and without thickening through decomposition. Mineral oil should *not* be heated above about 200 °C because it will begin to smoke, and there is the potential danger of flash ignition of the vapors. Water must *not* be present in mineral and silicone oils, since at temperatures of about 100 °C, the water will boil, spattering hot oil. If water drops are present in the oil, change the heating fluid and clean and dry the container before refilling it.

A minor nuisance associated with oil baths is removing the film of mineral or silicone oils, both of which are water-insoluble, from the outer surface of the flask. This is best done by wiping the flask using a *small* amount of hexane or dichloromethane on a paper towel prior to washing the flask with soap and water.

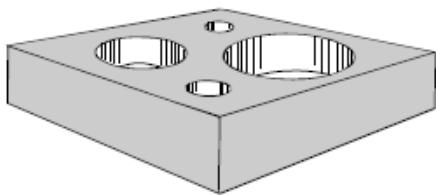
6.5 Aluminum Block with a Hot Plate/Stirrer

Although aluminum blocks are most commonly used in microscale organic chemistry laboratories, they can also be used with the smaller round-bottom flasks used in macroscale experiments.² The aluminum block shown in Figure 6.5A can be used to hold 25-, 50-, or 100-mL round-bottom flasks, as well as a thermometer. Heating will occur more rapidly if the flask fits all the way into the hole; however, heating is also effective if the flask only partially fits into the hole. The aluminum block with smaller holes, as shown in Figure 6.5B, is designed for microscale glassware. It will hold a conical vial, a Craig tube or small test tubes, and a thermometer.

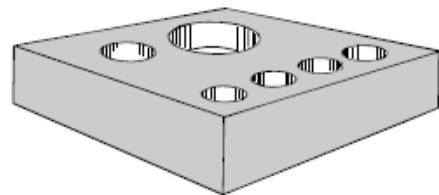
There are several advantages to heating with an aluminum block. The metal heats very quickly, high temperatures can be obtained, and you can cool the aluminum rapidly by removing it with crucible tongs and immersing it in cold water. Aluminum blocks are also inexpensive or can be fabricated readily in a machine shop.

Figure 6.6 shows a reaction mixture being heated with an aluminum block on a hot plate/stirrer unit. The thermometer in the figure is used to determine the temperature of the aluminum block. *Do not use a mercury thermometer:* use a thermometer containing a liquid other than mercury or use a metal dial thermometer that can be inserted into a smaller-diameter hole drilled into the side of the block.³ Make sure that the thermometer fits loosely in the hole, or it may break. Secure the thermometer with a clamp.

To avoid the possibility of breaking a glass thermometer, your hot plate may have a hole drilled into the metal plate so that a metal dial thermometer can be inserted into the unit (see Figure 6.7A). These metal thermometers, such as the one shown in Figure 6.7B, can be obtained in a number of temperature ranges. For example, a 0–250°C thermometer with 2-degree divisions can be obtained at a reasonable price. Also shown in Figure 6.7 (inset) is an aluminum block with a small hole drilled into it so that a metal thermometer can be inserted. An alternative to the metal thermometer is a digital electronic temperature measuring device that can be inserted into the aluminum block or hot plate. It is strongly recommended that mercury thermometers be avoided when measuring the surface temperature of the hot plate or aluminum block. If a mercury thermometer is broken on a hot surface, you will introduce toxic mercury vapors into the laboratory. Nonmercury thermometers filled with high-boiling colored liquids are available as alternatives.



A. Large holes for 25-, 50-, or 100-mL round-bottom flasks



B. Small holes for Craig tube, 3-mL and 5-mL conical vials, and small test tubes

Figure 6.5 Aluminum heating blocks.

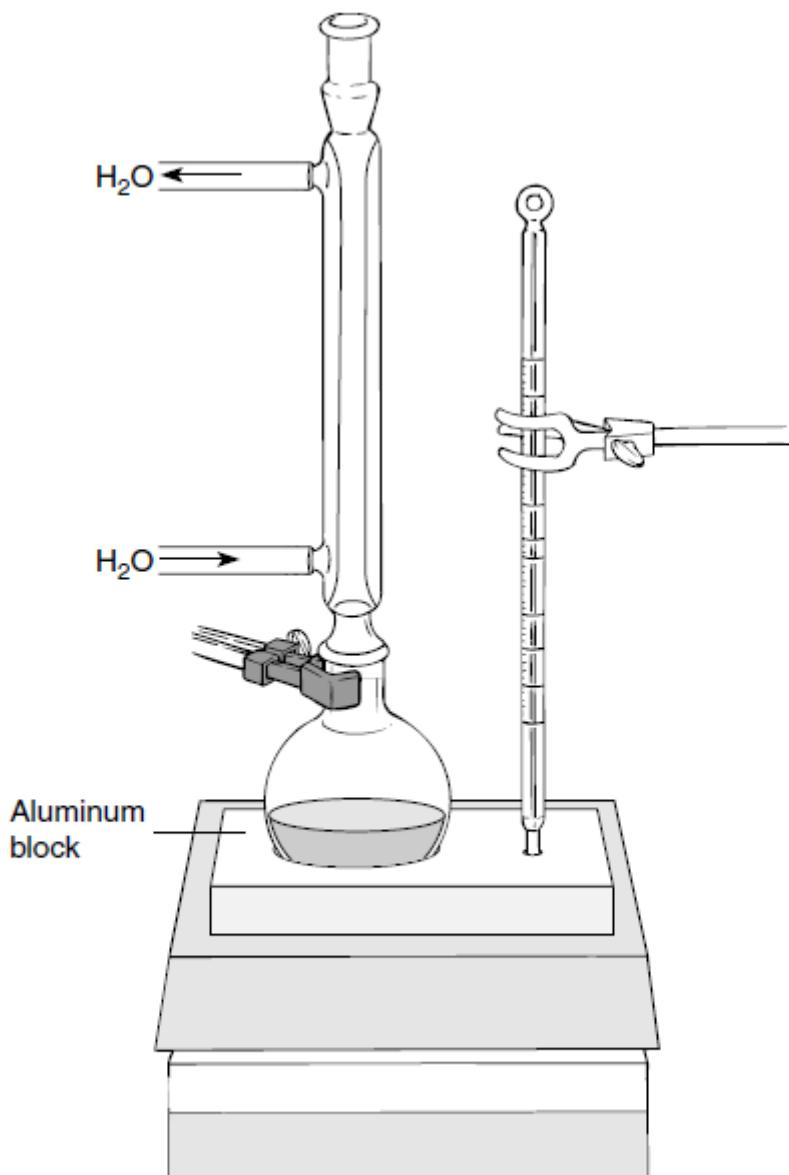


Figure 6.6 Heating with an aluminum block.

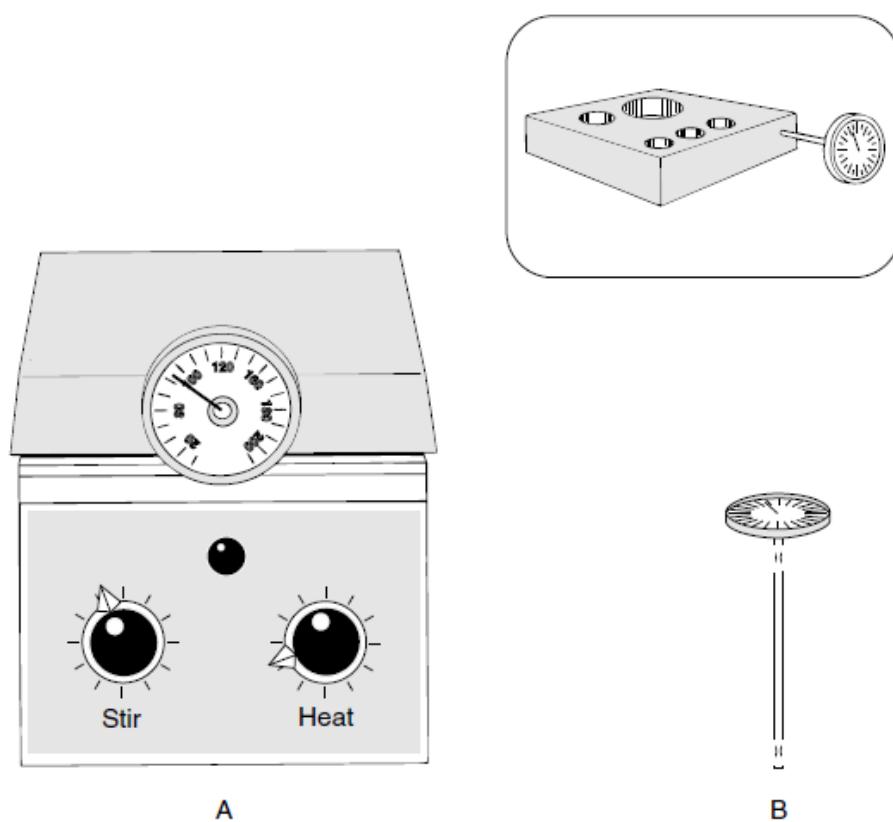


Figure 6.7 Dial thermometers.

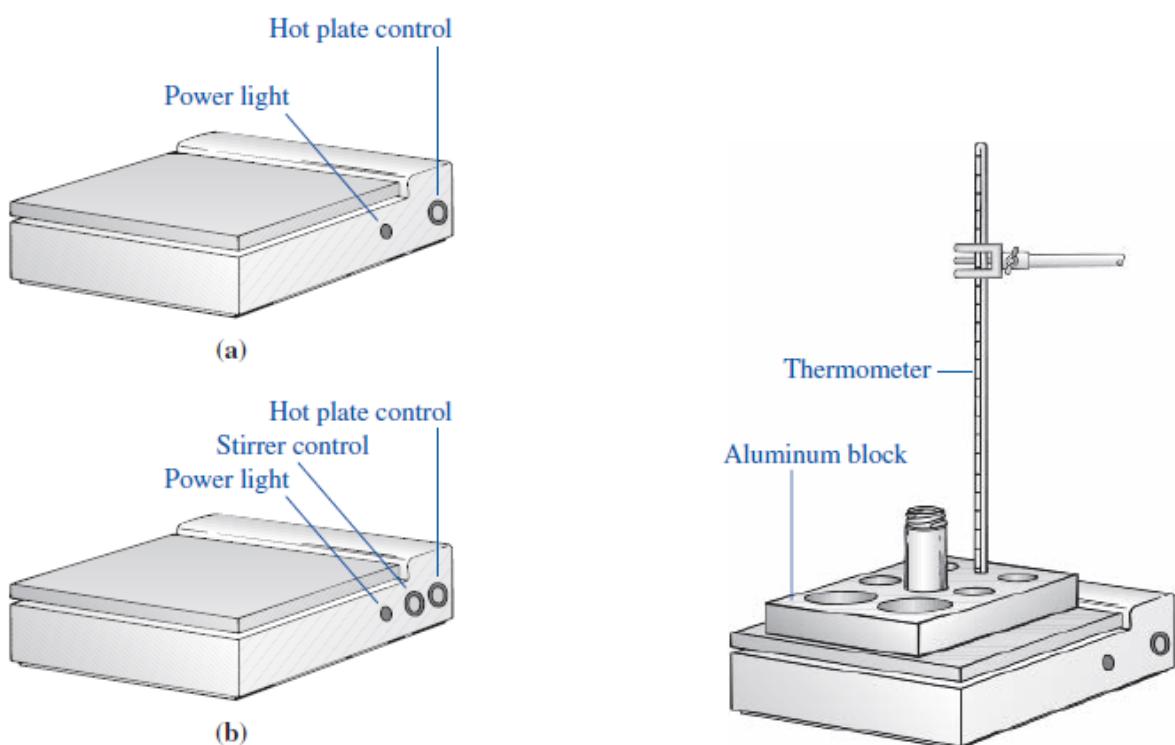


Figure 2.25
(a) Hot plate. (b) Stirring hot plate.

Figure 2.26
Aluminum block with conical vial in place.

As already mentioned, aluminum blocks are often used in the microscale organic chemistry laboratory. The use of an aluminum block to heat a microscale reflux apparatus is shown in Figure 6.8. The reaction vessel in the figure is a conical vial, which is used in many microscale experiments. Also shown in Figure 6.8 is a split aluminum collar that may be used when very high temperatures are required. The collar is split to facilitate easy placement around a 5-mL conical vial. The collar helps to distribute heat further up the wall of the vial.

You should first calibrate the aluminum block so that you have an approximate idea where to set the control on the hot plate to achieve a desired temperature. Place the aluminum block on the hot plate and insert a thermometer into the small hole in the block. Select five equally spaced temperature settings, including the lowest and highest settings, on the heating control of the hot plate. Set the dial to the first of these settings and monitor the temperature recorded on the thermometer. When the thermometer reading arrives at a constant value,⁴ record this final temperature, along with the dial setting. Repeat this procedure with the remaining four settings. Using these data, prepare a calibration curve for future reference.

It is a good idea to use the same hot plate each time, as it is very likely that two hot plates of the same type may give different temperatures with identical settings. Record in your notebook the identification number printed on the unit that you are using to ensure that you always use the same hot plate.

For many experiments, you can determine what the approximate setting on the hot plate should be from the boiling point of the liquid being heated. Because the temperature inside the flask is lower than the aluminum block temperature, you should add at least 20°C to the boiling point of the liquid and set the aluminum block at this higher temperature. In fact, you may need to raise the temperature even higher than this value in order to bring the liquid to a boil.

Many organic mixtures need to be stirred as well as heated to achieve satisfactory results. To stir a mixture, place a magnetic stir bar (see Technique 7, Figure 7.8A) in a round-bottom flask containing the reaction mixture as shown in Figure 6.9A. If the mixture is to be heated as well as stirred, attach a water condenser as shown in Figure 6.6. With the combination hot plate/stirrer unit, it is possible to stir and heat a mixture simultaneously. With conical vials, a magnetic spin vane must be used to stir mixtures (see Technique 7, Figure 7.8B). This is shown in Figure 6.9B. More uniform stirring will be obtained if the flask or vial is placed in the aluminum block so that it is centered on the hot plate. Mixing may also be achieved by boiling the mixture. A boiling stone (see Technique 7, Section 7.4) must be added when a mixture is boiled without magnetic stirring.

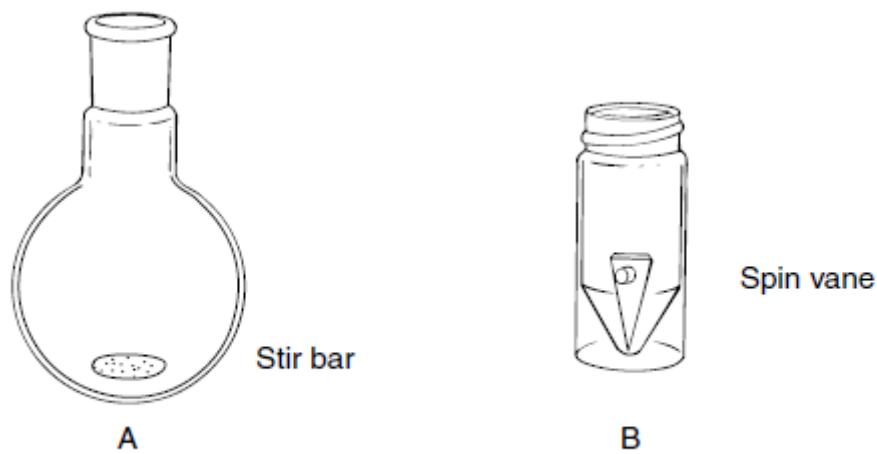


Figure 6.9 Methods of stirring in a round-bottom flask or conical vial.

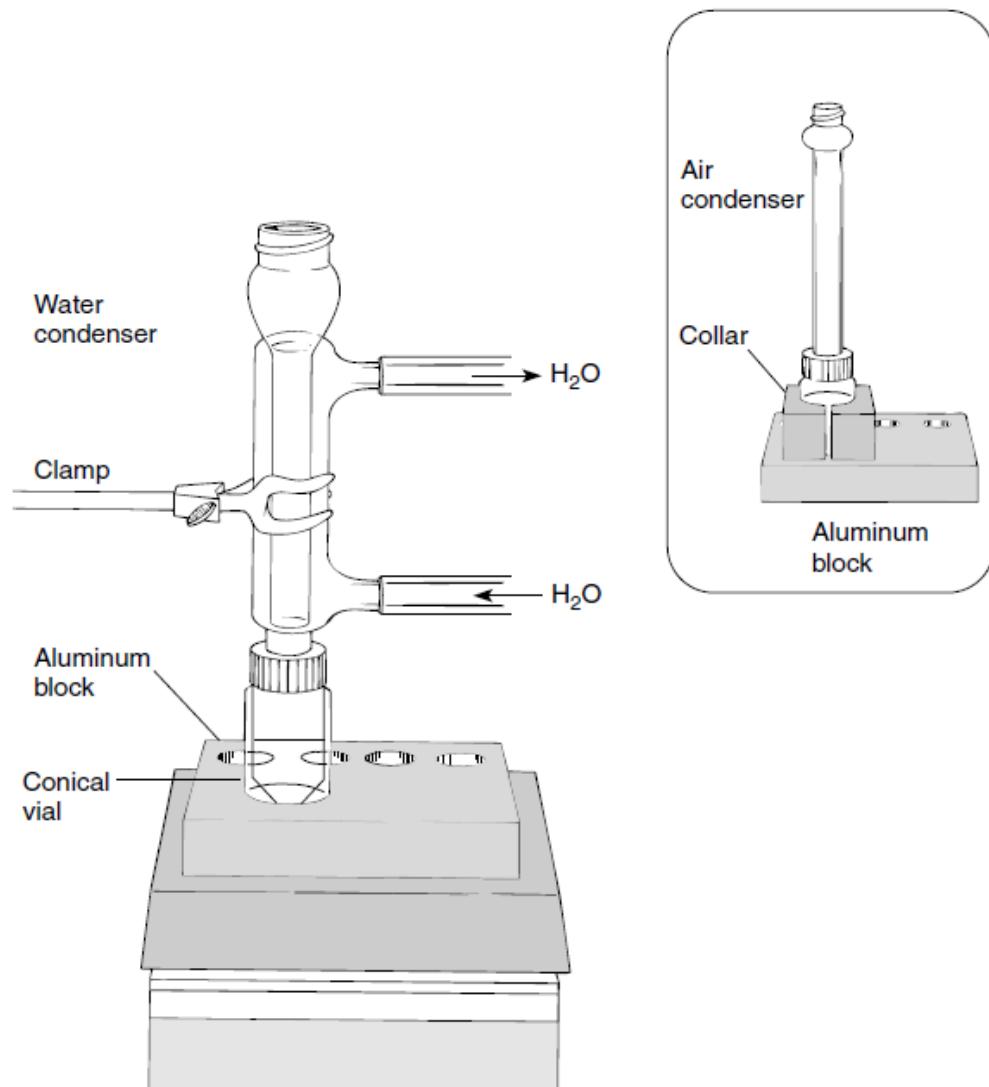


Figure 6.8 Heating with an aluminum block (microscale).

6.6 Sand Bath with Hot Plate/Stirrer

The sand bath is used in some microscale laboratories to heat organic mixtures. It can also be used as a heat source in some macroscale experiments. Sand provides a clean way of distributing heat to a reaction mixture. To prepare a sand bath for microscale use, place about a 1-cm depth of sand in a crystallizing dish and then set the dish on a hot plate/stirrer unit. The apparatus is shown in Figure 6.10. Clamp the thermometer into position in the sand bath. You should calibrate the sand bath in a manner similar to that used with the aluminum block (see previous section). Because sand heats more slowly than an aluminum block, you will need to begin heating the sand bath well before using it.

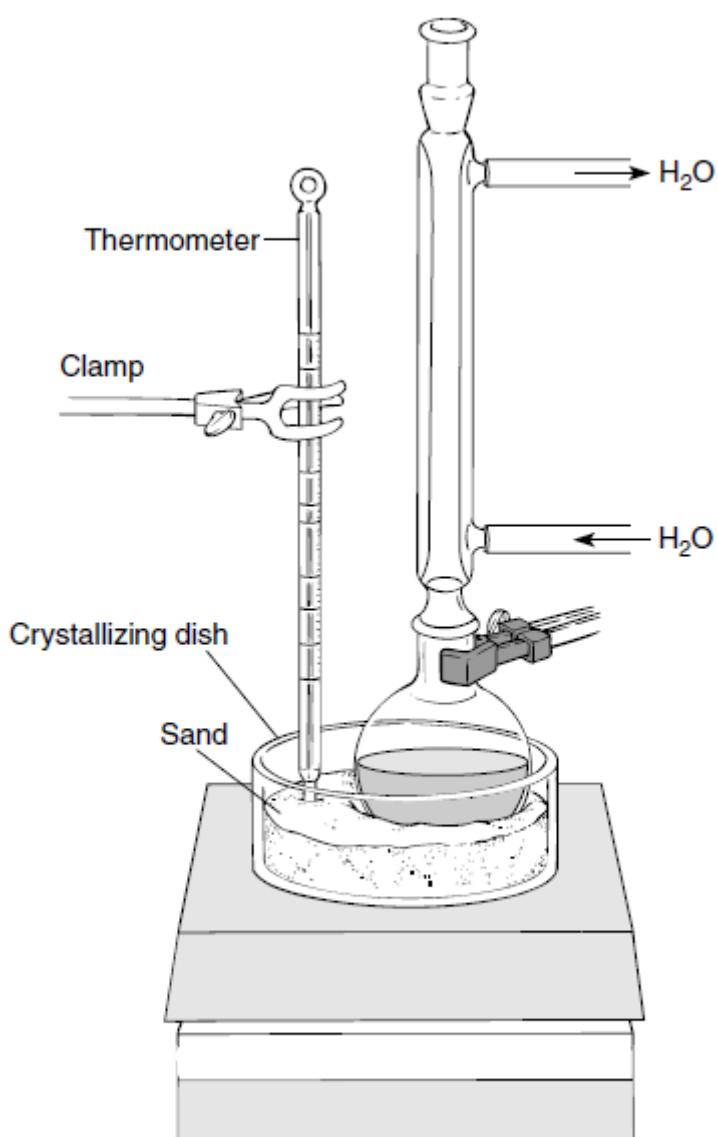


Figure 6.10 Heating with a sand bath.

Do not heat the sand bath much above 200°C, or you may break the dish. If you need to heat at very high temperatures, you should use a heating mantle or an aluminum block rather than a sand bath. With sand baths, it may be necessary to cover the dish with aluminum foil to achieve a temperature near 200°C. Because of the relatively poor heat conductivity of sand, a temperature gradient is established within the sand bath. It is warmer near the bottom of the sand bath and cooler near the top for a given setting on the hot plate. To make use of this gradient, you may find it convenient to bury the flask or vial in the sand to heat a mixture more rapidly. Once the mixture is boiling, you can then slow the rate of heating by raising the flask or vial. These adjustments may be made easily and do not require a change in the setting on the hot plate.

6.7 Flames

The simplest technique for heating mixtures is to use a Bunsen burner. Because of the high danger of fires, however, the use of a Bunsen burner should be strictly limited to those cases for which the danger of fire is low or for which no reasonable alternative source of heat is available. A flame should generally be used only to heat aqueous solutions or solutions with very high boiling points. You should always check with your instructor about using a burner. If you use a burner at your bench, great care should be taken to ensure that others in the vicinity are not using flammable solvents.

In heating a flask with a Bunsen burner, you will find that using a wire gauze can produce more even heating over a broader area. The wire gauze, when placed under the object being heated, spreads the flame to keep the flask from being heated in one small area only.

Bunsen burners may be used to prepare capillary micropipets for thin-layer chromatography or to prepare other pieces of glassware requiring an open flame. For these purposes, burners should be used in designated areas in the laboratory and not at your laboratory bench.

6.8 Steam Baths

The steam cone or steam bath is a good source of heat when temperatures around 100°C are needed. Steam baths are used to heat reaction mixtures and solvents needed for crystallization. A steam cone and a portable steam bath are shown in Figure 6.11. These methods of heating have the disadvantage that water vapor may be introduced, through condensation of steam, into the mixture being heated. A slow flow of steam may minimize this difficulty.

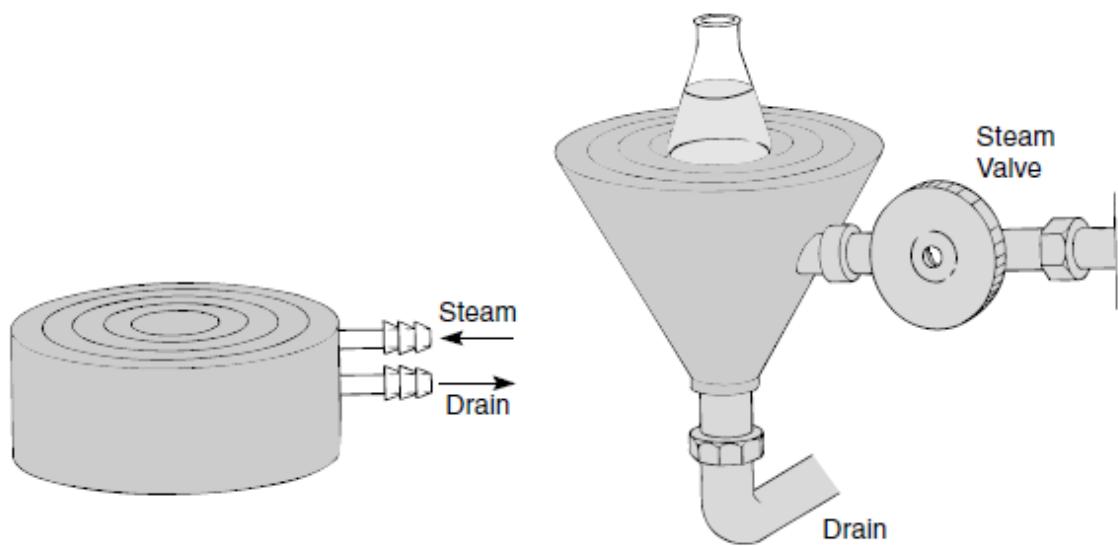


Figure 6.11 A steam bath and a steam cone.

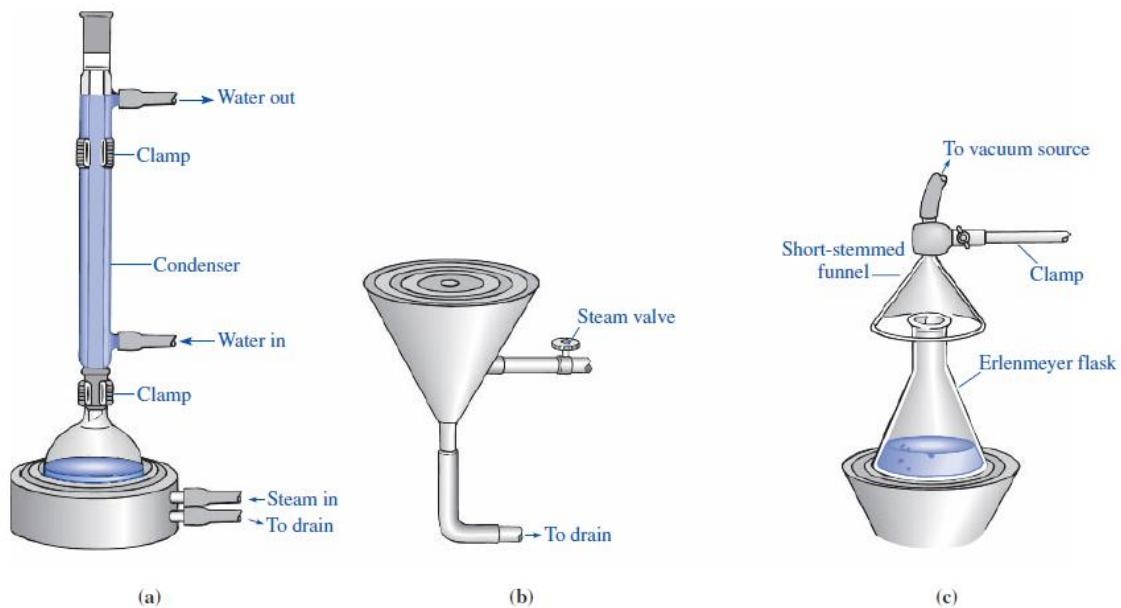


Figure 2.30

(a) Steam bath being used to heat a reaction mixture. (b) Steam cone. (c) Heating an Erlenmeyer flask on a steam cone, with a funnel attached to vacuum source for removing vapors.

Because water condenses in the steam line when it is not in use, it is necessary to purge the line of water before the steam will begin to flow. This purging should be accomplished before the flask is placed on the steam bath. The steam flow should be started with a high rate to purge the line; then the flow should be reduced to the desired rate. When using a portable steam bath, be certain that condensate (water) is drained into a sink. Once the steam bath or cone is heated, a slow steam flow will maintain the temperature of the mixture being heated. There is no advantage to having a Vesuvius on your desk! An excessive steam flow may cause problems with condensation in the flask. This condensation problem can often be avoided by selecting the correct place at which to locate the flask on top of the steam bath.

The top of the steam bath consists of several flat concentric rings. The amount of heat delivered to the flask being heated can be controlled by selecting the correct sizes of these rings. Heating is most efficient when the largest opening that will still support the flask is used. Heating large flasks on a steam bath while using the smallest opening leads to slow heating and wastes laboratory time.

Heat Gun

A useful device for heating apparatus, but not reaction mixtures, is a heat gun (Fig. 2.27), which is essentially a high-powered hair dryer. It is particularly useful for drying assembled apparatus, as this eliminates the need to use a flame. The stream of hot air from the heat gun is directed at the apparatus to drive atmospheric moisture out through an open port, which, after the entire apparatus is heated, is then fitted with a drying tube so that air is dried as it enters the cooling apparatus. A slow stream of dry nitrogen gas may be introduced during the heating process to help expel moisture from the apparatus. A drying tube or some other device such as a bubbler containing mineral oil must then be attached to the apparatus to prevent intrusion of atmospheric moisture as the apparatus cools and during the course of the reaction itself. For best results, you should start heating of the apparatus at a point most distant from the open port and work toward the opening.



Figure 2.27
Heat gun.

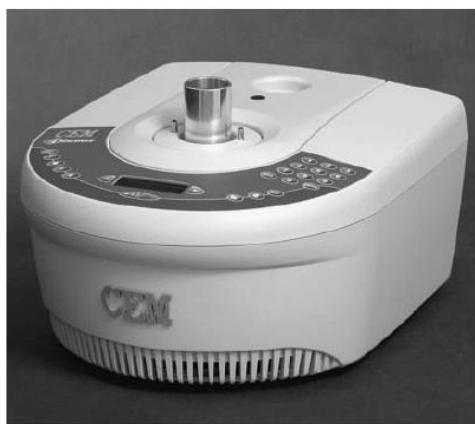
The temperature of the air stream emerging from a heat gun is commonly from 300 to 500 °C, far higher than that of the typical hand-held hair dryer. Consequently, you must use the heat gun prudently when drying apparatus held by plastic-containing devices such as Keck clips or clamps with rubber- or vinyl-coated jaws, because the plastic can melt.

You should never point a heat gun in the direction of another person. Moreover, when using this device, you should be certain that there are no light-weight objects such as your starting material or reaction product in the vicinity that might become airborne on the powerful jet of air produced.

Microwave Ovens

Microwave ovens are attaining wider application as a heating source for organic reactions. Although these ovens rely upon the same technology as the microwave oven you may use at home to heat water or food, the ones used in the laboratory have been specially modified so they can be operated safely with organic solvents. Such ovens are explosion-proof and allow precise temperature control and uniformity of heating throughout the cavity of the oven. A number of commercial models that have a wide range of capacities and capabilities are available, and two different types are depicted in Figure 2.31. Some models feature temperature and pressure-feedback control, whereas others have modular accessories that allow for automated synthesis. Simple ovens are relatively inexpensive and are found in a number of academic laboratories, but more sophisticated models can be rather expensive and are normally found only in industrial laboratories.

The transfer of microwave energy to a molecule is extremely fast and results from the direct interaction of a molecule with the high-frequency, oscillating electric component of the microwave field. Because the absorption of microwave energy depends on the polarity of the molecule, the reactant molecules in an organic reaction often absorb microwave energy better than the solvent. This preferential transfer of microwave energy to the reacting molecules results in an *instantaneous temperature increase*, which cannot be measured because of its short lifetime and molecular nature, and a rapid reaction then ensues. Reactions that may require hours of heating in an oil bath may be completed in a matter of minutes in a microwave oven.



(a)



(b)

Figure 2.31

Commercial microwave reactors: (a) CEM Benchmate microwave synthesis instrument (courtesy of CEM Corporation); (b) CEM MARSXpress high throughput microwave system (courtesy of CEM Corporation).

organic reaction often absorb microwave energy better than the solvent. This preferential transfer of microwave energy to the reacting molecules results in an *instantaneous temperature increase*, which cannot be measured because of its short lifetime and molecular nature, and a rapid reaction then ensues. Reactions that may require hours of heating in an oil bath may be completed in a matter of minutes in a microwave oven.

The use of microwave ovens as heat sources not only drastically reduces the heating times of organic reactions, but the reactions often proceed more efficiently and selectively than when conduction heating methods are used. This is because microwave energy is transferred uniformly and almost simultaneously to the entire sample, thus eliminating any hot spots that may result in side reactions. If sealed reaction vessels are used, superheating can be easily achieved, so reactions that might be otherwise difficult to induce can be performed with relative ease. Another benefit to using microwave heating in synthesis is that less solvent is required than for traditional heating methods.

Reactions heated in a microwave oven do not necessarily require special apparatus. For example, they can be conducted in vessels that range from simple laboratory glassware such as an Erlenmeyer flask covered with a watchglass to flasks of various shapes that are fitted with standard-taper glass joints (Fig. 2.32a). Specially designed pressure vessels can also be used. A number of tubes can also be mounted on a rotor so that multiple reactions can be conducted simultaneously (Fig. 2.32b).



(a)



(b)

Figure 2.32

Reaction vessels: (a) assorted shapes of standard-taper ground glassware and sealable glass tubes (courtesy CEM Corporation); (b) array of special reaction tubes for multiple, simultaneous reactions (courtesy of CEM Corporation).

6.9 Cold Baths

At times, you may need to cool an Erlenmeyer flask or round-bottom flask below room temperature. A cold bath is used for this purpose. The most common cold bath is an ice bath, which is a highly convenient source of 0°C temperature. An ice bath requires water along with ice to work well. If an ice bath is made up of only ice, it is not a very efficient cooler because the large pieces of ice do not make good contact with the flask. Enough water should be present with ice so that the flask is surrounded by water but not so much that the temperature is no longer maintained at 0°C. In addition, if too much water is present, the buoyancy of a flask resting in the ice bath may cause it to tip over. There should be enough ice in the bath to allow the flask to rest firmly.

For temperatures somewhat below 0°C, you may add some solid sodium chloride to the ice-water bath. The ionic salt lowers the freezing point of the ice so that temperatures in the range of 0 to –10°C can be reached. The lowest temperatures are reached with ice-water mixtures that contain relatively little water.

A temperature of –78.5°C can be obtained with solid carbon dioxide or dry ice. However, large chunks of dry ice do not provide uniform contact with a flask being cooled. A liquid such as isopropyl alcohol is mixed with small pieces of dry ice to provide an efficient cooling mixture. Acetone and ethanol can be used in place of isopropyl alcohol. Be careful when handling dry ice because it can inflict severe frostbite. Extremely low temperatures can be obtained with liquid nitrogen (–195.8°C).

2.11 STIRRING METHODS

Heterogeneous reaction mixtures must be stirred to distribute the reactants uniformly and facilitate chemical reactions. Stirring also ensures thermal equilibration whenever the contents of a flask are being heated or cooled. If a mixture is boiling, the associated turbulence is usually sufficient to provide reasonable mixing; however, stirring a boiling mixture is an alternative to using boiling stones to maintain smooth boiling action and avoid bumping. Stirring is most effectively achieved using magnetic or mechanical stirring devices, but swirling is often sufficient.

Swirling

The simplest means of mixing the contents of a flask is swirling, which is accomplished by manually rocking the flask with a circular motion. If a reaction mixture must be swirled, carefully loosen the clamp(s) that support the flask and attached apparatus, and swirl the contents periodically during the course of the reaction. If the entire apparatus is supported by clamps attached to a single ring stand, the clamp(s) attached to the flask do not have to be loosened. Make sure all the clamps are tight, pick up the ring stand, and gently move the entire assembly in a circular motion to swirl the contents of the flask.

Magnetic Stirring

The simplest means of mixing the contents of a flask is swirling, which is accomplished by manually rocking the flask with a circular motion. If a reaction mixture must be swirled, carefully loosen the clamp(s) that support the flask and attached apparatus, and swirl the contents periodically during the course of the reaction. If the entire apparatus is supported by clamps attached to a single ring stand, the clamp(s) attached to the flask do not have to be loosened. Make sure all the clamps are tight, pick up the ring stand, and gently move the entire assembly in a circular motion to swirl the contents of the flask.

Magnetic Stirring

Magnetic stirring is the most common technique for mixing the contents of a flask in the undergraduate laboratory. The equipment consists of a magnetic stirrer, which houses a large bar magnet that is spun by a variable-speed motor, and a stirbar (Fig. 2.33) that is contained in a round-bottom flask or conical vial. The metallic core of the stirbar is usually coated with a chemically inert substance such as Teflon, although glass is sometimes used for stirbars.

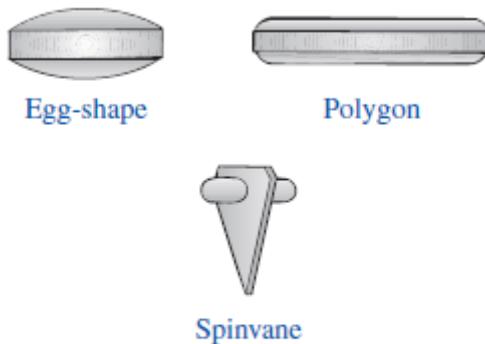


Figure 2.33

Magnetic stirbars and a spinvane.

The stirbar is normally placed in the flask or vial *before* any other materials, such as solvents or reagents. In the case of introducing stirbars into a flask, you should *not* simply drop the stirbar into the flask, because you might crack or break it. Rather, tilt the flask and let the stirbar gently slide down the side.

A flat-bottom container such as a beaker or Erlenmeyer flask may be placed directly on top of the stirrer (Fig. 2.34a), whereas a round-bottom flask or a conical vial must be clamped above the stirrer (Fig. 2.34b). A flask containing a stirbar should be *centered* on the magnetic stirrer so that the stirbar rotates smoothly and does not wobble. As the stirrer motor turns, the stirbar rotates in phase with the motor-driven magnet. The stirring rate may be adjusted using the control dial on the stirring motor, but excessive speed should be avoided because it often causes the stirbar to wobble or "jump" rather than to rotate smoothly. Because the shapes of a conical vial and a stirbar are matched, wobbling is not a problem. Nonetheless, the stirring rate must still be adjusted to minimize splashing.

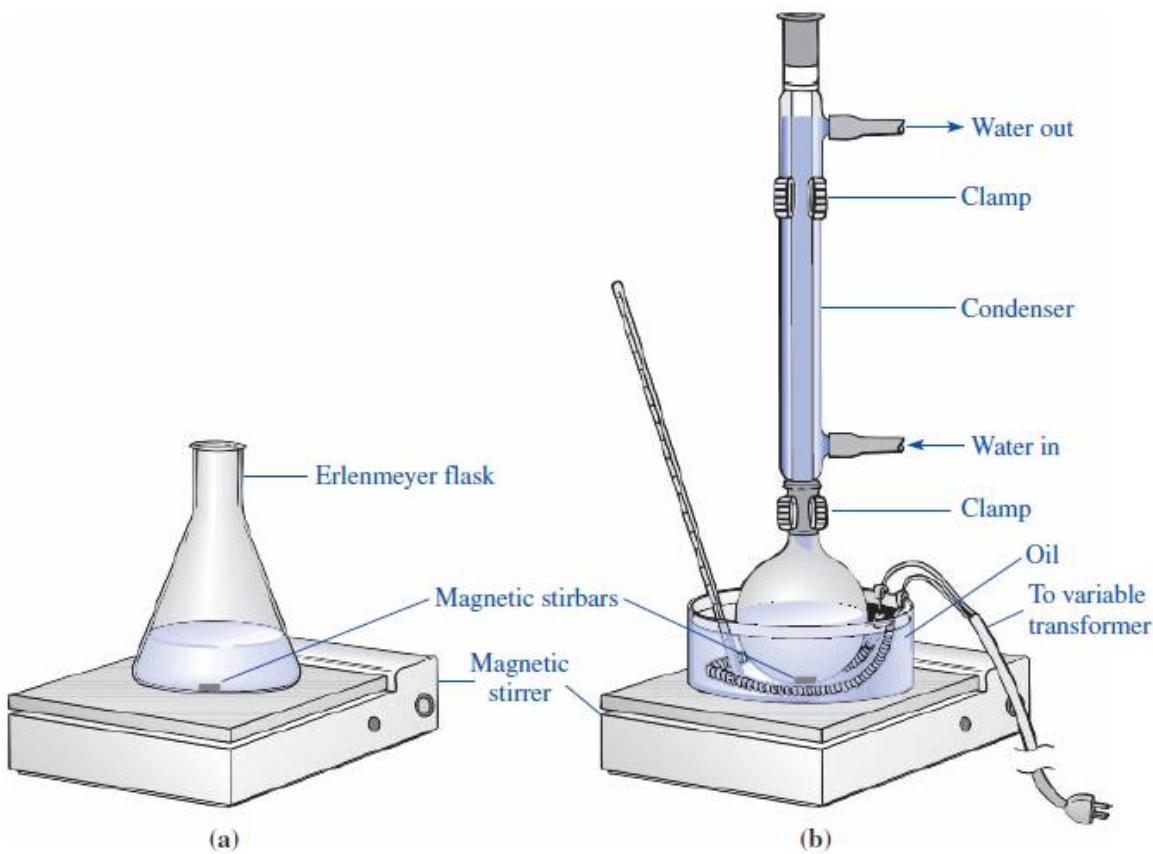


Figure 2.34

- (a) *Magnetic stirring of the contents of Erlenmeyer flask.*
- (b) *Using a heating source with magnetic stirring of reaction mixture.*

The use of magnetic stirring in conjunction with heating is illustrated in Figure 2.34b. This figure depicts apparatus in which the contents of a reaction vessel are simultaneously being heated and magnetically stirred, a common operation in the organic laboratory. A large stirbar or paper clip is used to stir the bath itself; this maintains a homogeneous temperature throughout the heating fluid. Other heating devices such as a sand bath, aluminum block, or heating mantle can be used as well, although monitoring of the heating source is more difficult with a mantle.

shaft to facilitate cleaning, and different-sized paddles can be used according to the size of the flask. The glass shaft and the inner bore of the standard-taper bearing are ground to fit each other precisely. A cup at the top of the bearing is used to hold a few drops of silicone or mineral oil, which lubricates the shaft and provides an effective seal.

The stirrer shaft is connected to the motor with a short length of heavy-walled rubber tubing that is secured with twisted copper wire or a hose clamp. The motor and shaft *must* be carefully aligned to avoid wear on the glass surfaces of the shaft and bearing and to minimize vibration of the apparatus that could result in breakage. The bearing is held in place in the flask with either a rubber band or a clamp so that it does not work loose while the motor is running. The rate of stirring is controlled by varying the speed of the motor with either a built-in or separate variable transformer.

Various operations can be performed while using mechanical stirring. For example, the flask in Figure 2.35 is a three-neck, standard-taper, round-bottom flask that is equipped with an addition funnel and a condenser. This apparatus could be used in cases where dropwise addition of a reagent to a stirred and heated reaction mixture is required.

Mechanical Stirring

Thick mixtures and large volumes of fluids are most efficiently mixed using a mechanical stirrer; a typical set-up is depicted in Figure 2.35. A variable-speed, explosion-proof, electric motor drives a stirring shaft and paddle that extend into the flask containing the mixture to be stirred. The motor should have high torque, so that it has sufficient power to turn the shaft and stir highly viscous mixtures. The stirrer shaft is usually constructed of glass, and the paddle, which agitates the contents of the flask, is constructed of an inert material such as stainless steel, Teflon, or glass. A glass paddle must be used to stir reaction mixtures containing active metals such as sodium or potassium. The paddle is easily removed from the shaft to facilitate cleaning, and different-sized paddles can be used according to the size of the flask. The glass shaft and the inner bore of the standard-taper bearing are ground to fit each other precisely. A cup at the top of the bearing is used to hold a few drops of silicone or mineral oil, which lubricates the shaft and provides an effective seal.

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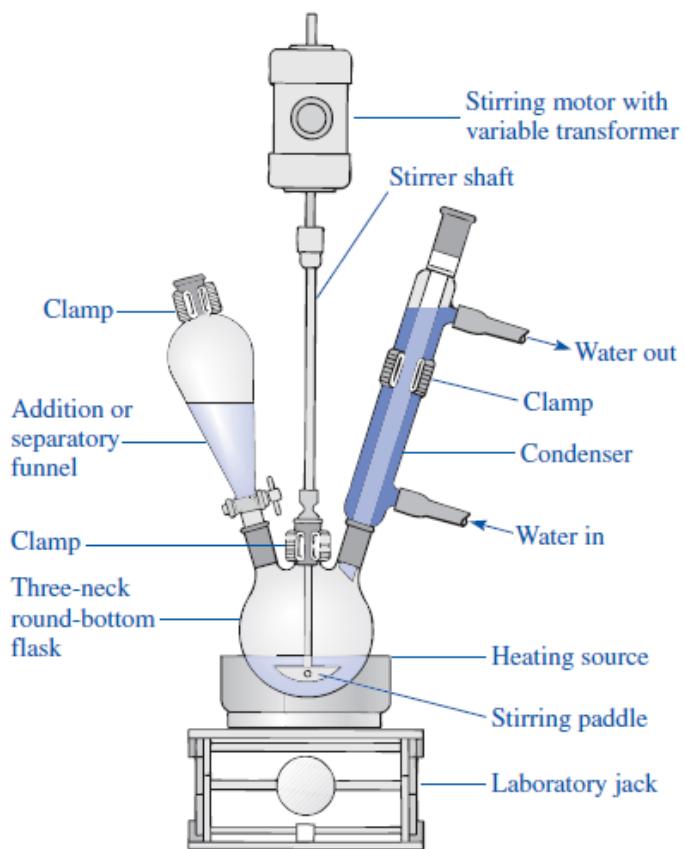


Figure 2.35
Flask equipped with mechanical stirring.

2.12 CENTRIFUGATION

Centrifugation is a useful technique to facilitate the separation of two immiscible phases. The procedure simply involves spinning a sample in one or more tubes at high speed in a bench-top centrifuge (Fig. 2.36). It is important to balance the centrifuge before spinning to avoid vibrating the centrifuge during spinning. For example, if the sample to be centrifuged is placed in a single centrifuge tube, you should then fill a second tube with an equal volume of solvent and place this tube opposite the sample tube in the centrifuge. After the sample has been spun, the phases may be separated by decantation or by removing a liquid phase with a Pasteur or filter-tip pipet.

Centrifugation is sometimes more effective than filtration for removing suspended solid impurities in a liquid, especially when the particles are so fine they would pass through a filter paper. It may also be used for Craig tube filtration during a microscale recrystallization. Centrifugation will also aid in separating the organic and aqueous layers when performing an extraction, especially when emulsions are formed.

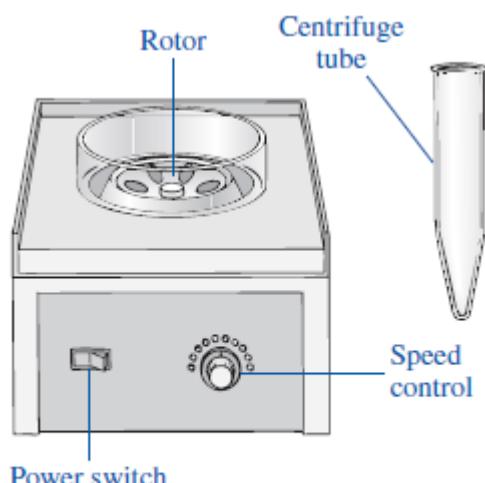


Figure 2.36

Centrifuge with centrifuge tube.

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 that the entire apparatus is 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.

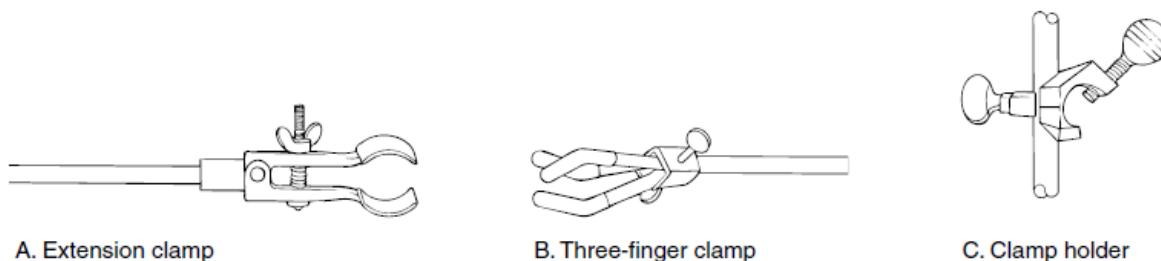


Figure 7.1 Adjustable metal clamps.

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 very careful not to bump any part of the apparatus or the ring stands after the apparatus is assembled.

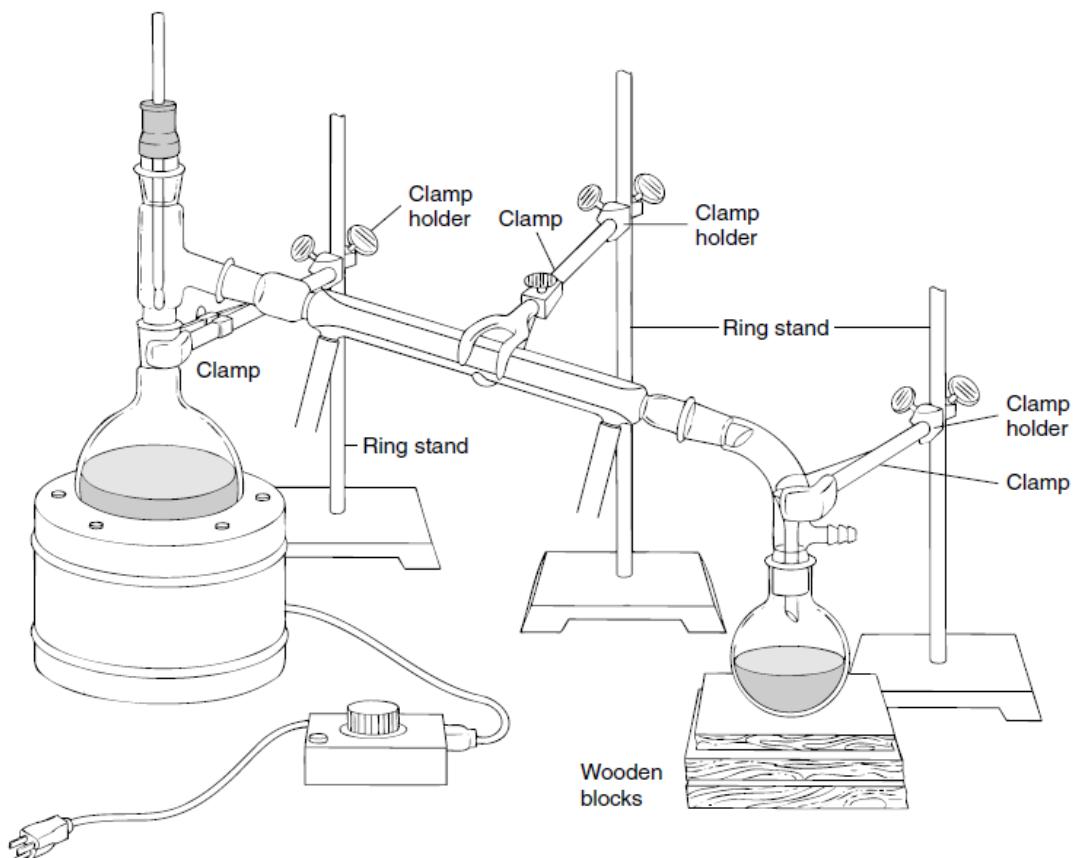


Figure 7.2 Distillation apparatus secured with metal clamps.

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 are very easy to use (they just clip on), will withstand temperatures up to 140°C, and are quite 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 in a secure manner. 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 both adjustable metal clamps and plastic joint clips.

To assemble this apparatus, first connect all of the individual pieces together 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.

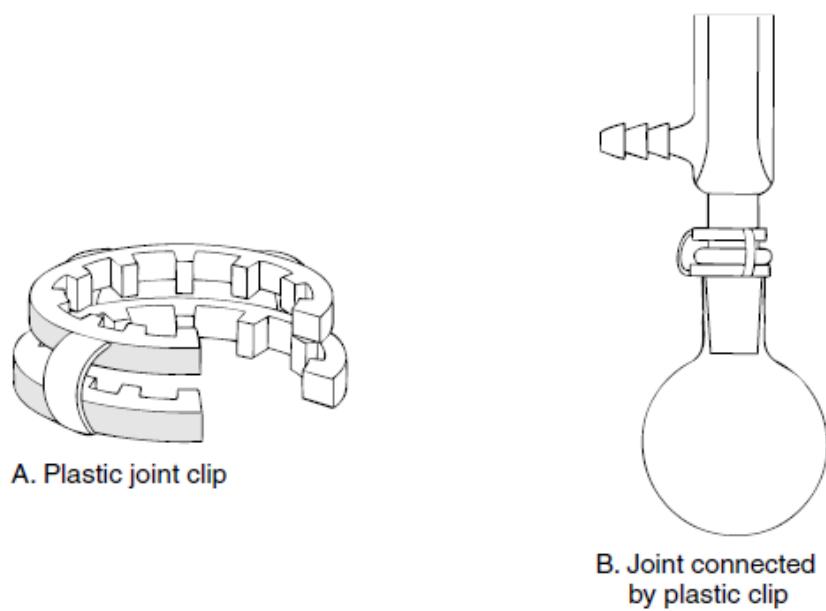


Figure 7.3 Plastic joint clip.

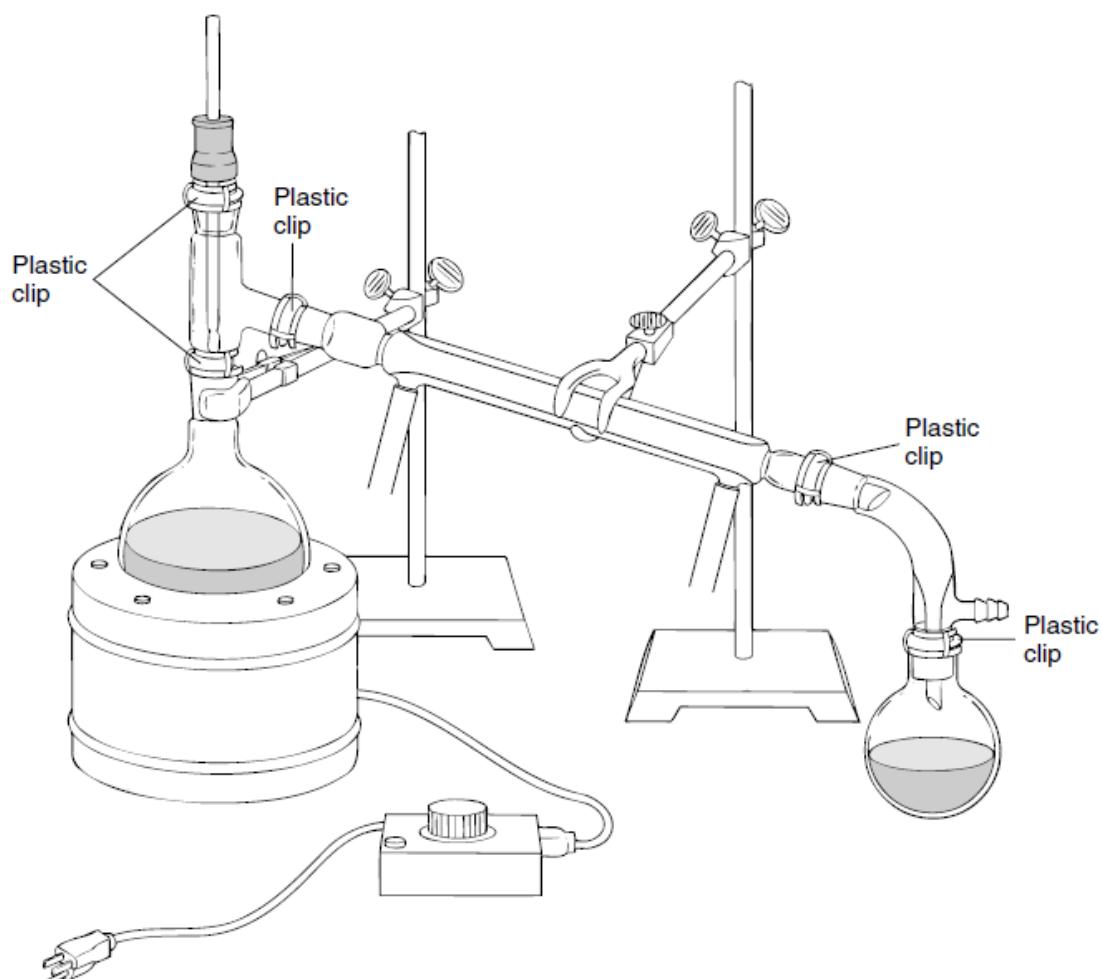


Figure 7.4 Distillation apparatus secured with metal clamps and plastic joint clips.

B. Securing Microscale Apparatus Assemblies

The glassware in most microscale kits is made with standard-taper ground joints. The most common joint size is $\frac{1}{4}$ 14/10. Some microscale glassware with ground-glass joints also has threads cast into the outside surface of the outer joints (see the top of the 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 together in this fashion can be assembled very easily. The entire apparatus is held together securely, and usually only one metal clamp is required to hold the apparatus onto a ring stand.

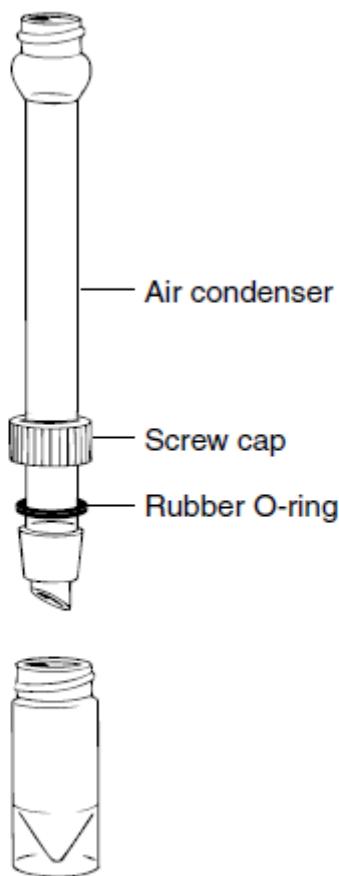


Figure 7.5 A microscale standard-taper joint assembly.

7.2 Heating Under Reflux

Often we wish to heat a mixture for a long time and to leave it unattended. A reflux apparatus (see Figure 7.6) allows such heating. The liquid is heated to a boil, and the hot vapors are cooled and condensed as they rise into the water-jacketed condenser. Therefore, very little liquid is lost by evaporation, and the mixture is kept at a constant temperature, the boiling point of the liquid. The liquid mixture is said to be heating under reflux.

Condenser. The water-jacketed condenser shown in Figure 7.6 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. Figure 7.6 also shows a typical microscale apparatus for heating small quantities of material under reflux (see Figure 7.6B).

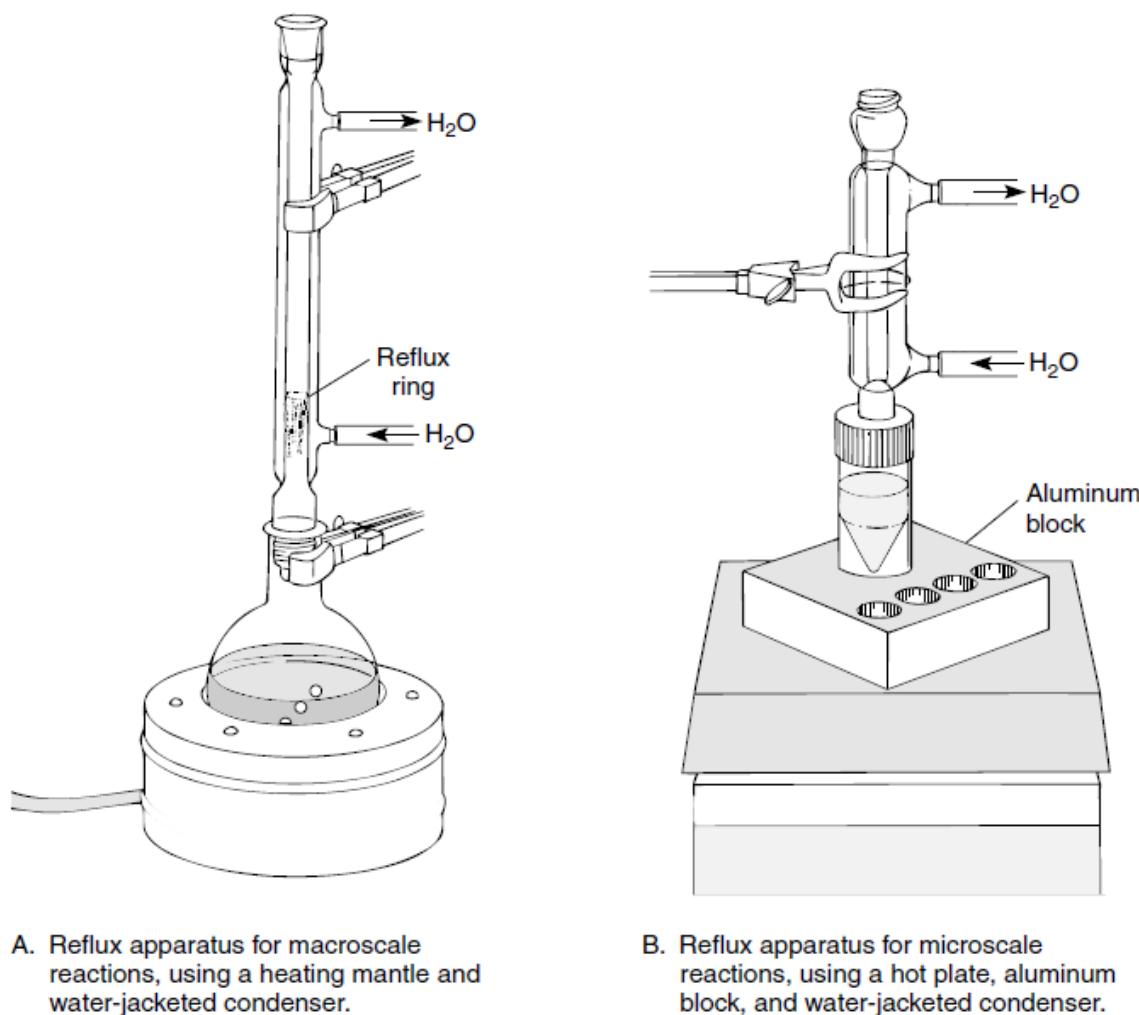


Figure 7.6 Heating under reflux.

When using a water-jacketed condenser, make sure that the direction of the water flow is 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, a heating mantle, water bath, oil bath, aluminum block, sand bath, 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" (see next section).

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 7.6A. In heating under reflux, the rate of heating should be adjusted so that the reflux ring is no higher than a third to half of 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 macroscale 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. By heating gently, the evaporated solvent will condense in the relatively cold neck of the flask and return to the solution. This technique (see Figure 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.

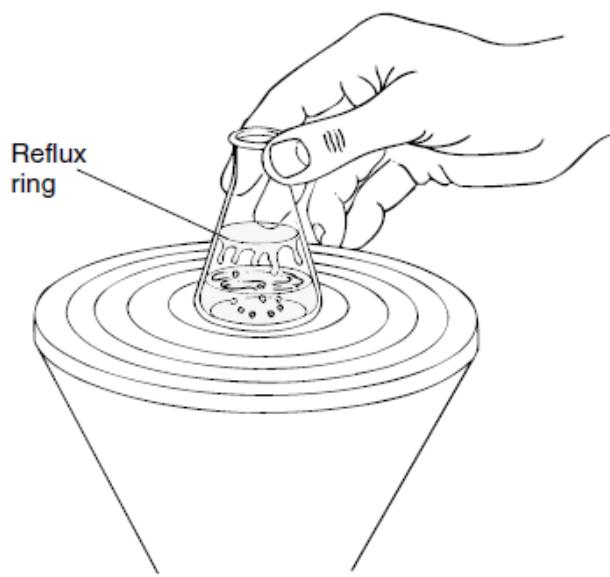


Figure 7.7 Tended reflux of small quantities on a steam cone (this can also be done with a hot plate).

7.3 Stirring Methods

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 form in boiling solutions. An additional purpose for using a magnetic stirrer is to stir the reaction to ensure that all the reagents are thoroughly mixed. 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 very 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 very 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.

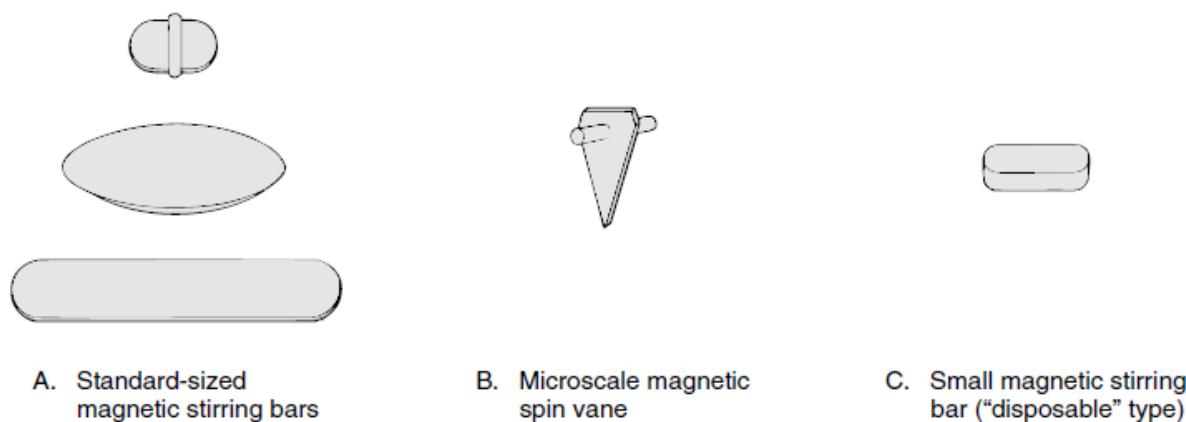


Figure 7.8 Magnetic stirring bars.

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 quite 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.

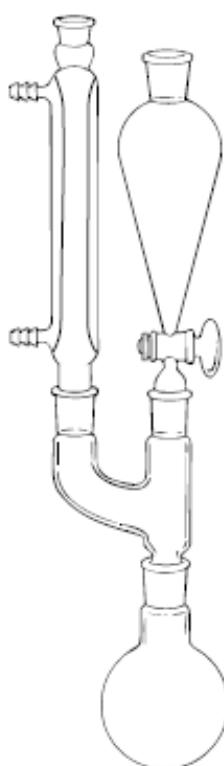
Wooden applicator sticks are used in some applications. They function in the same manner as boiling stones. Occasionally, glass beads are used. Their presence also causes sufficient turbulence in the liquid to prevent bumping.

7.5 Addition of Liquid Reagents

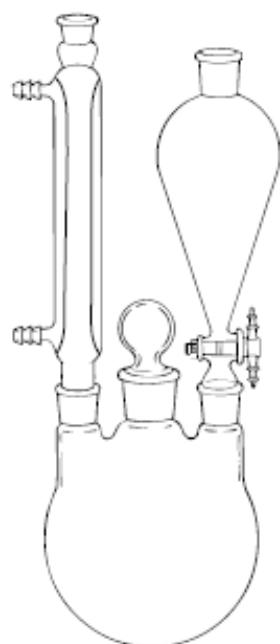
Liquid reagents and solutions are added to a reaction by several means, some of which are shown in Figure 7.9. The most common type of assembly for macroscale experiments is shown in Figure 7.9A. In this apparatus, a separatory funnel is attached to the sidearm of a Claisen head adapter. The separatory 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) may be 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. For reactions that are particularly sensitive to moisture, it is also advisable to attach a second drying tube to the top of the condenser.

tions 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 sidearm allows the pressure above the liquid in the funnel to be in equilibrium with the pressure in the rest of the apparatus, and it allows the inert gas to flow over the top of the liquid as it is being added.

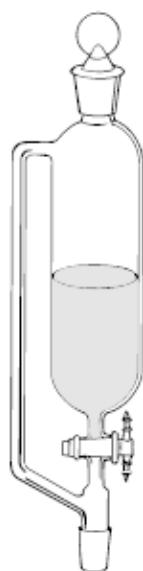
With either type of macroscale addition funnel, you can control the rate of addition of the liquid by carefully adjusting the stopcock. Even after careful adjustment, changes in pressure can occur, causing the flow rate to change. In some cases, the stopcock can become clogged. It is important, therefore, to monitor the addition rate carefully and to refine the adjustment of the stopcock as needed to maintain the desired rate of addition.



A. Macroscale equipment, using a separatory funnel as an addition funnel.



B. Macroscale, for larger amounts.



C. A pressure-equalizing addition funnel



D. Addition with a hypodermic syringe inserted through a rubber septum

Figure 7.9 Methods for adding liquid reagents to a reaction.

A fourth method, shown in Figure 7.9D, is suitable for use in microscale and some macroscale 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 drop-wise 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 in which anhydrous conditions must be maintained. The drying tube is used to protect the reaction mixture from atmospheric moisture.

7.6 Drying Tubes

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 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), 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.

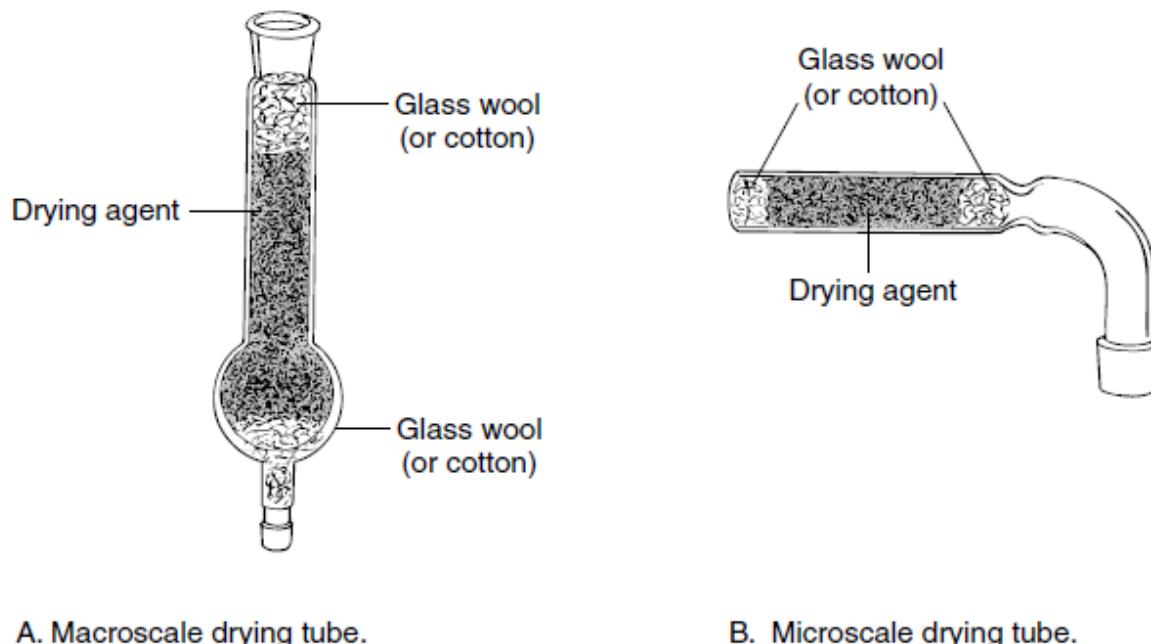


Figure 7.10 Drying tubes.

7.7 Reactions Conducted under an Inert Atmosphere

Some reactions are very sensitive to oxygen and water vapor present in air and require an inert atmosphere in order to obtain satisfactory results. The usual reactions in which it is desirable to exclude air often include organometallic reagents, such as organomagnesium or organolithium reagents, where water vapor and oxygen (air) react with these compounds. The most common inert gases available in a laboratory are nitrogen and argon, which are available in gas cylinders. Nitrogen is probably the gas most often used to carry out reactions under an inert atmosphere, although argon has a distinct advantage because it is denser than air. This allows the argon to push air away from the reaction mixture.

When laboratories are not equipped with individual gas lines to benches or hoods, it is very useful to supply nitrogen or argon to the reaction apparatus using a balloon assembly (shown in Figure 7.11). Your instructor will provide you with the apparatus.

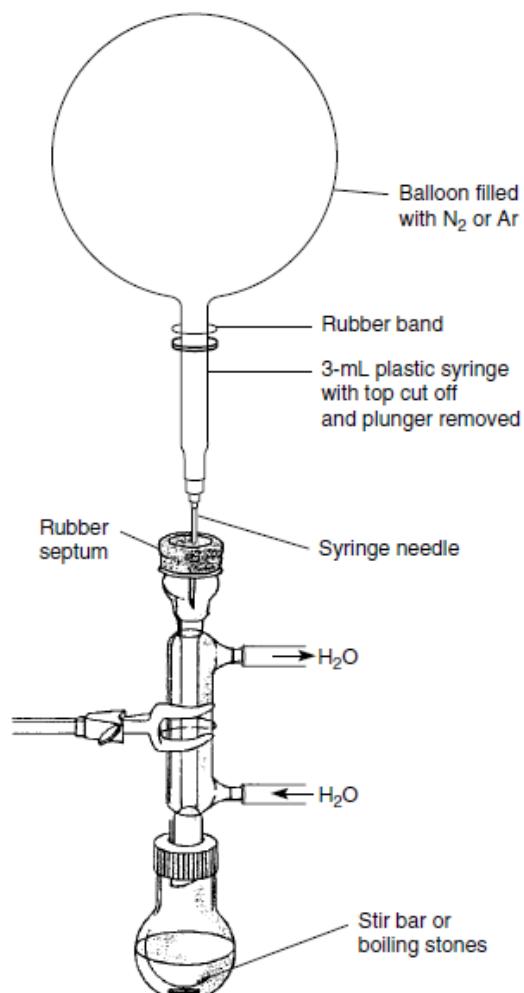


Figure 7.11 Conducting a reaction under an inert atmosphere using a balloon assembly.

Construct the balloon assembly by cutting off the top of a 3-mL disposable plastic syringe. Attach a small balloon snugly to the top of the syringe, securing it with a small rubber band that has been doubled to hold the balloon securely to the body of the syringe. Attach a needle to the syringe. Fill the balloon with the inert gas through the needle using a piece of rubber tubing attached to the gas source. When the balloon has been inflated to 2–3 inches in diameter, quickly pinch off the neck of the balloon while removing the gas source. Now push the needle into a rubber stopper to keep the balloon inflated. It is possible to keep an assembly like this filled with inert gas for several days without the balloon deflating.

Before you start the reaction, you may need to dry your apparatus thoroughly in an oven. Add all reagents carefully to avoid water. The following instructions are based on the assumption that you are using an apparatus consisting of a round-bottom flask equipped with a condenser. Attach a rubber septum to the top of your condenser. Now flush the air out of the apparatus with the inert gas. It is best not to use the balloon assembly for this purpose, unless you are using argon (see next paragraph). Instead, remove the round-bottom flask from the apparatus and, with the help of your instructor, flush it with the inert gas using a Pasteur pipet to bubble the gas through the solvent and reaction mixture in the flask. In this way, you can remove air from the reaction assembly prior to attaching the balloon assembly. Quickly reattach the flask to the apparatus. Pinch off the neck of the balloon between your fingers, remove the rubber stopper, and insert the needle into the rubber septum. The reaction apparatus is now ready for use.

When argon is employed as an inert gas, you can use the balloon assembly to remove air from the reaction apparatus in the following way. Insert the balloon assembly into the rubber septum as previously described. Also insert a second needle (no syringe attached) through the septum. The pressure from the balloon will force argon down the reflux condenser (argon is denser than air) and push the less dense air out through the second syringe needle. When the apparatus has been thoroughly flushed with argon, remove the second needle. Nitrogen does not work as well with this method because it is less dense than air and it will be difficult to remove the air that is in contact with the reaction mixture in the round-bottom flask.

For reactions conducted at room temperature, you can remove the condenser shown in Figure 7.11. Attach the rubber septum directly to the round-bottom flask and insert the needle of an argon-filled balloon assembly through the rubber septum. To flush the air out of the reaction flask, insert a second syringe needle into the rubber septum. Any air present in the flask will be flushed out through this second syringe needle, and the air will be replaced with argon. Now remove the second needle, and you have a reaction mixture free of air.

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 quite 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. External Gas Traps

One 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. With macroscale 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 7.12.

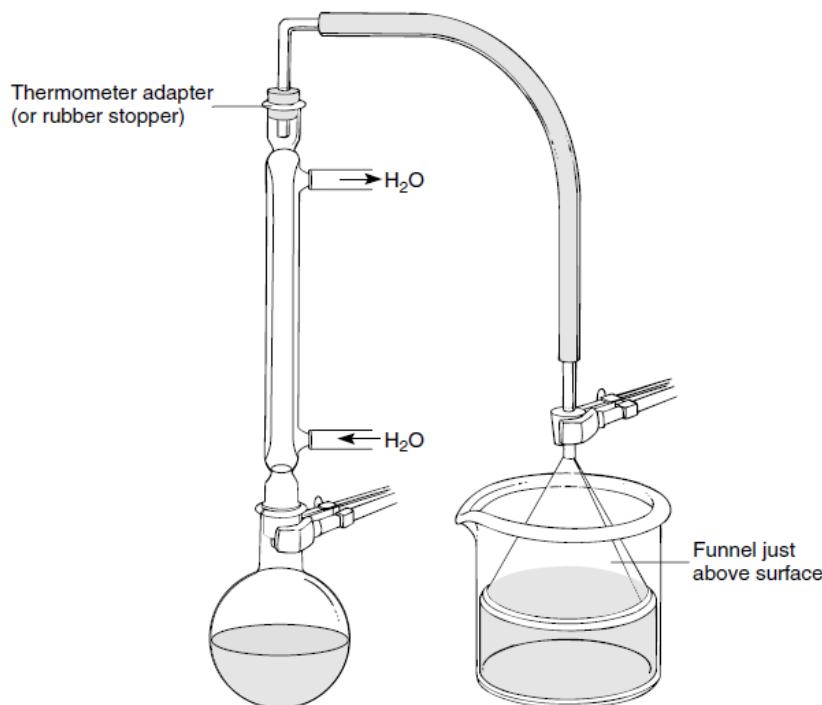


Figure 7.12 An inverted-funnel gas trap.

One method that works well for macroscale and microscale experiments is to place a thermometer adapter into the opening in the reaction apparatus. A Pasteur pipet is inserted upside down through the adapter, and a piece of flexible tubing is fitted over the narrow tip. It might 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 7.13.

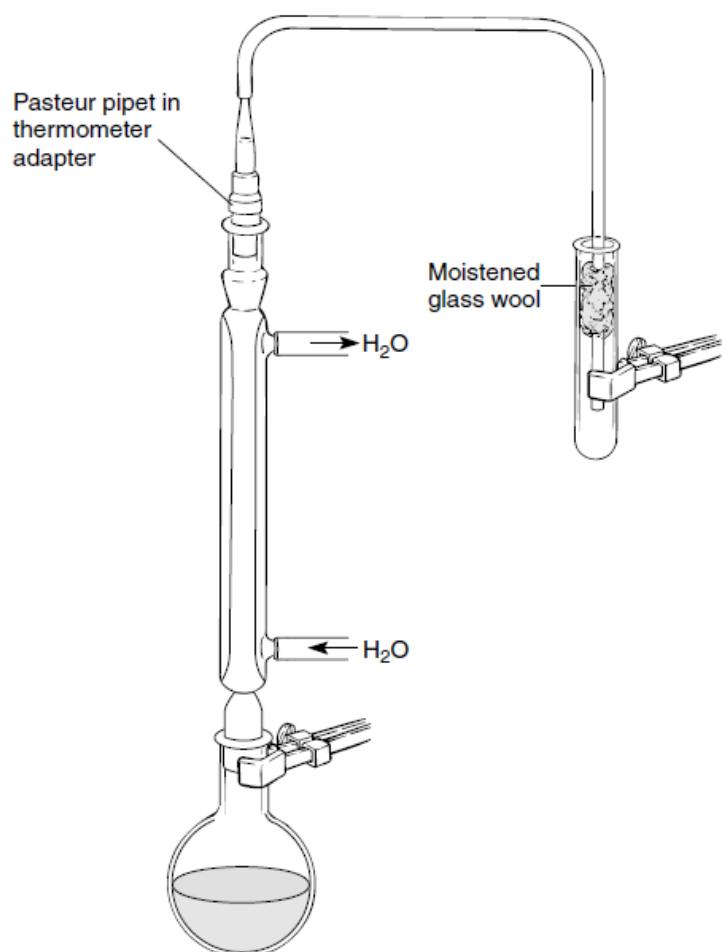


Figure 7.13 An external gas trap.

B. Drying-Tube Method

Some macroscale and most microscale experiments have the advantage that the amounts of gases produced are very small. Hence, it is easy to trap them and prevent them from escaping into the laboratory room. 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 Figure 7.10) to the top of the reaction flask 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 (see Figure 7.10B). 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. When it is necessary to use the drying tube shown in Figure 7.10A as a gas trap and it is essential that water not be allowed to enter the reaction flask, the modification shown in Figure 7.14 should be used. The rubber tubing between the thermometer adapter and the drying tube should be heavy enough to prevent crimping.

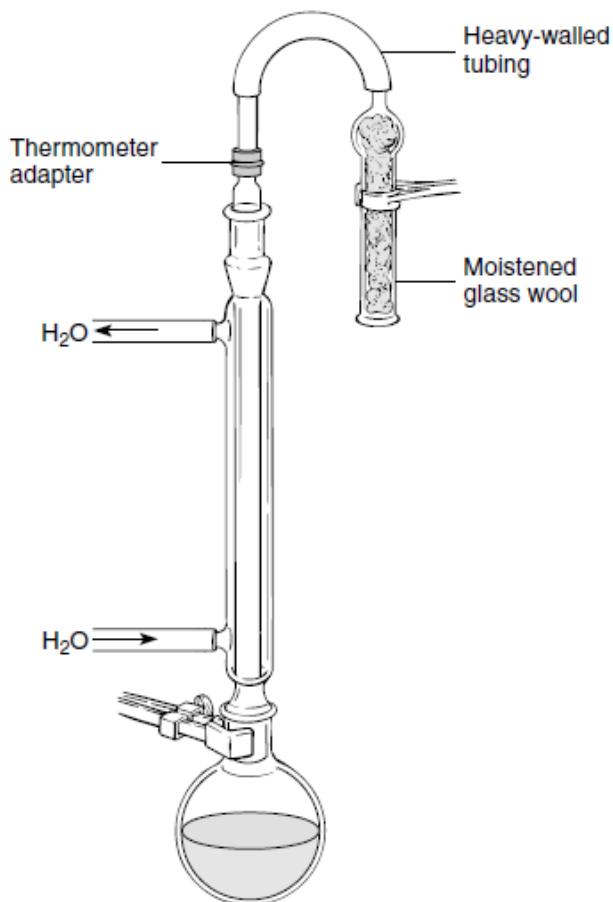


Figure 7.14 A drying tube used to capture evolved gases.

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 flask. 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 7.15. 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.

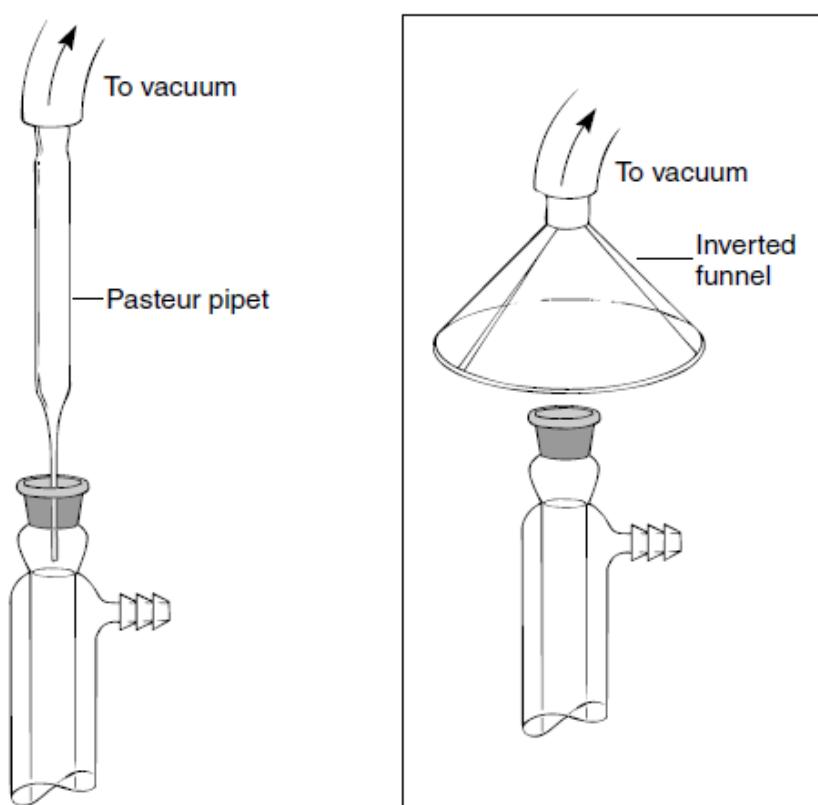


Figure 7.15 Removal of noxious gases under vacuum. (The inset shows an alternative assembly, using an inverted funnel in place of the Pasteur pipet.)

7.9 Collecting Gaseous Products

In Section 7.8, means for 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 7.16. A sample of the gas can be removed using a gas-tight syringe equipped with a needle. The gas that is removed can be analyzed by gas chromatography (see Technique 22).

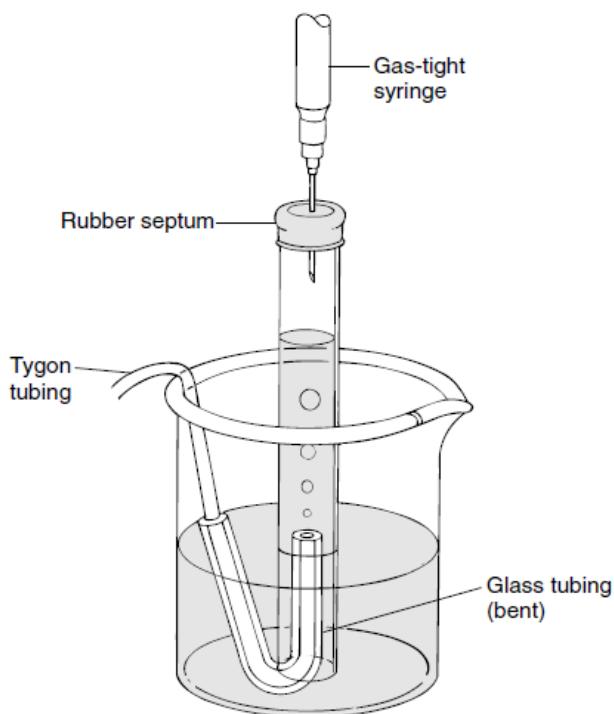


Figure 7.16 A gas collection tube, with rubber septum.

In Figure 7.16, a piece of glass tubing is attached 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 tube or flask. The other end of the flexible tubing is attached to a piece of glass tubing or a Pasteur pipet that has been inserted into a thermometer adapter.

7.10 Evaporation of Solvents

In many experiments, it is necessary to remove excess solvent from a solution. 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.

CAUTION



You must always evaporate solvents in the hood.

A. Large-Scale Methods

A large-scale method to remove excess solvent is to evaporate the solvent from an open Erlenmeyer flask (Figures 7.17A and B). Such evaporation must be conducted in a hood, because many solvent vapors are toxic or flammable. A boiling

stone must be used. A gentle stream of air directed toward the surface of the liquid will remove vapors that are in equilibrium with the solution and accelerate the evaporation. A Pasteur pipet connected by a short piece of rubber tubing to the compressed air line will act as a convenient air nozzle (see Figure 7.17A). A tube or an inverted funnel connected to an aspirator may also be used (see Figure 7.17B). In this case, vapors are removed by suction. It is better to use an Erlenmeyer flask than a beaker for this procedure because deposits of solid will usually build up on the sides of the beaker where the solvent evaporates. The refluxing action in an Erlenmeyer flask does not allow this buildup. If a hot plate is used as the heat source, care must be taken with flammable solvents to ensure against fires caused by "flashing," when solvent vapors come into contact with the hot-plate surface.

It is also possible to remove low-boiling solvents under reduced pressure (see Figure 7.17C). In this method, the solution is placed in a filter flask, along with a wooden applicator stick or a short length of capillary tubing. The flask is stoppered, and the sidearm is connected to an aspirator (by a trap), as described in Technique 8, Section 8.3. Under reduced pressure, the solvent begins to boil. The wooden stick or capillary tubing serves the same function as a boiling stone. By this method, solvents can be evaporated from a solution without using much heat. This technique is often used when heating the solution might decompose thermally-sensitive substances. The method has the disadvantage that when low-boiling solvents are used, solvent evaporation cools the flask below the freezing point of water. When this happens, a layer of frost forms on the outside of the flask. Because frost is insulating, it must be removed to keep evaporation proceeding at a reasonable rate. Frost is best removed by one of two methods: either the flask is placed in a bath of warm water (with constant swirling) or it is heated on the steam bath (again with swirling). Either method promotes efficient heat transfer.

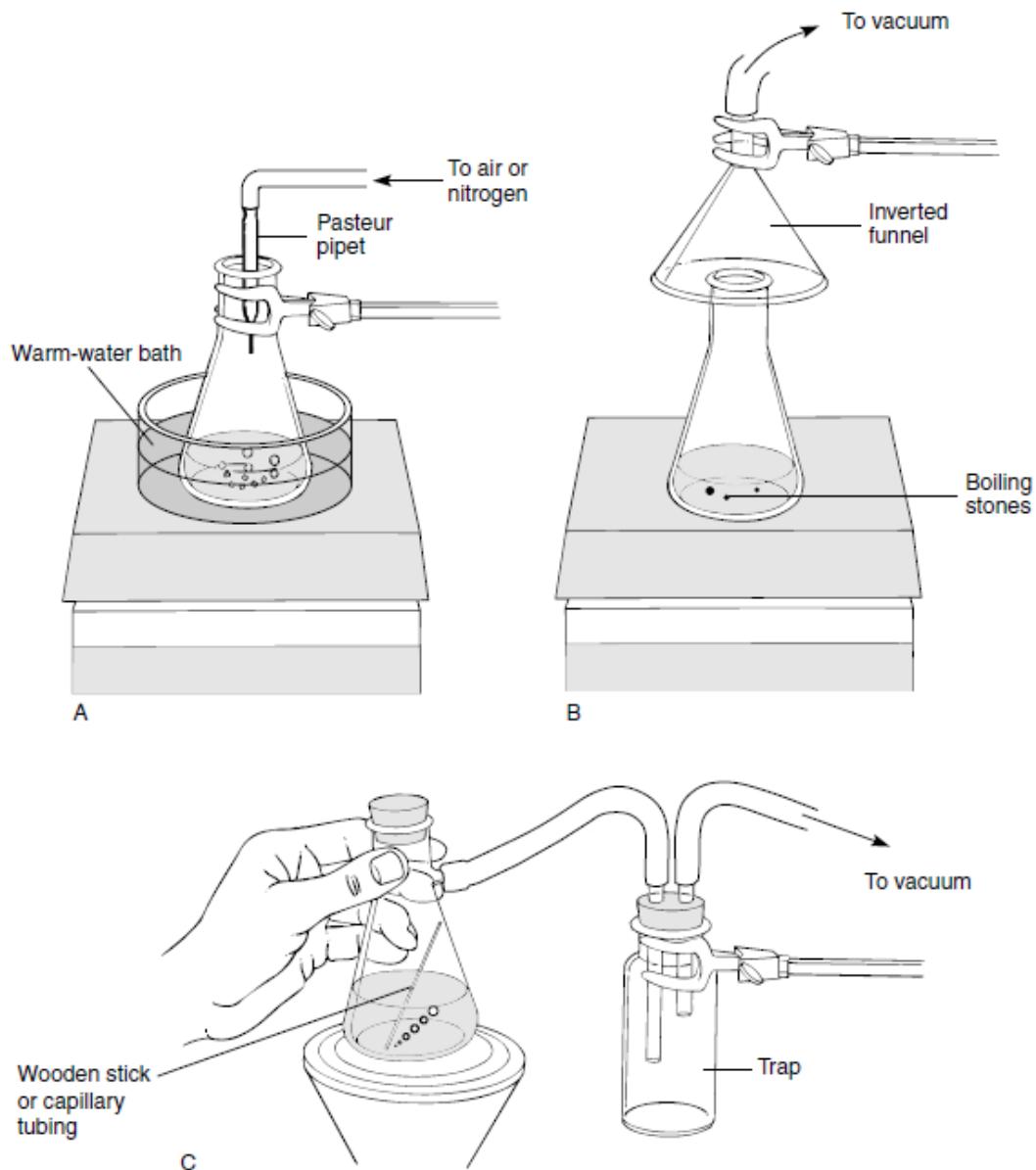


Figure 7.17 Evaporation of solvents (heat source can be varied among those shown).

Large amounts of a solvent should be removed by distillation (see Technique 14). *Never evaporate ether solutions to dryness*, except on a steam bath or by the reduced-pressure method. The tendency of ether to form explosive peroxides is a serious potential hazard. If peroxides should be present, the large and rapid temperature increase in the flask once the ether evaporates could bring about the detonation of any residual peroxides. The temperature of a steam bath is not high enough to cause such a detonation.

B. Small-Scale Methods

A simple means of evaporating a small amount of solvent is to place a centrifuge tube in a warm-water bath. The heat from the water bath will warm the solvent to a temperature at which it can evaporate within a short time. The heat from the water 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 centrifuge tube (see Figure 7.18A). The moving gas stream will sweep the vapors from the tube and accelerate the evaporation. As an alternative, a vacuum can be applied above the tube to draw away solvent vapors.

A convenient water bath 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 (see Figure 7.18B). 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.

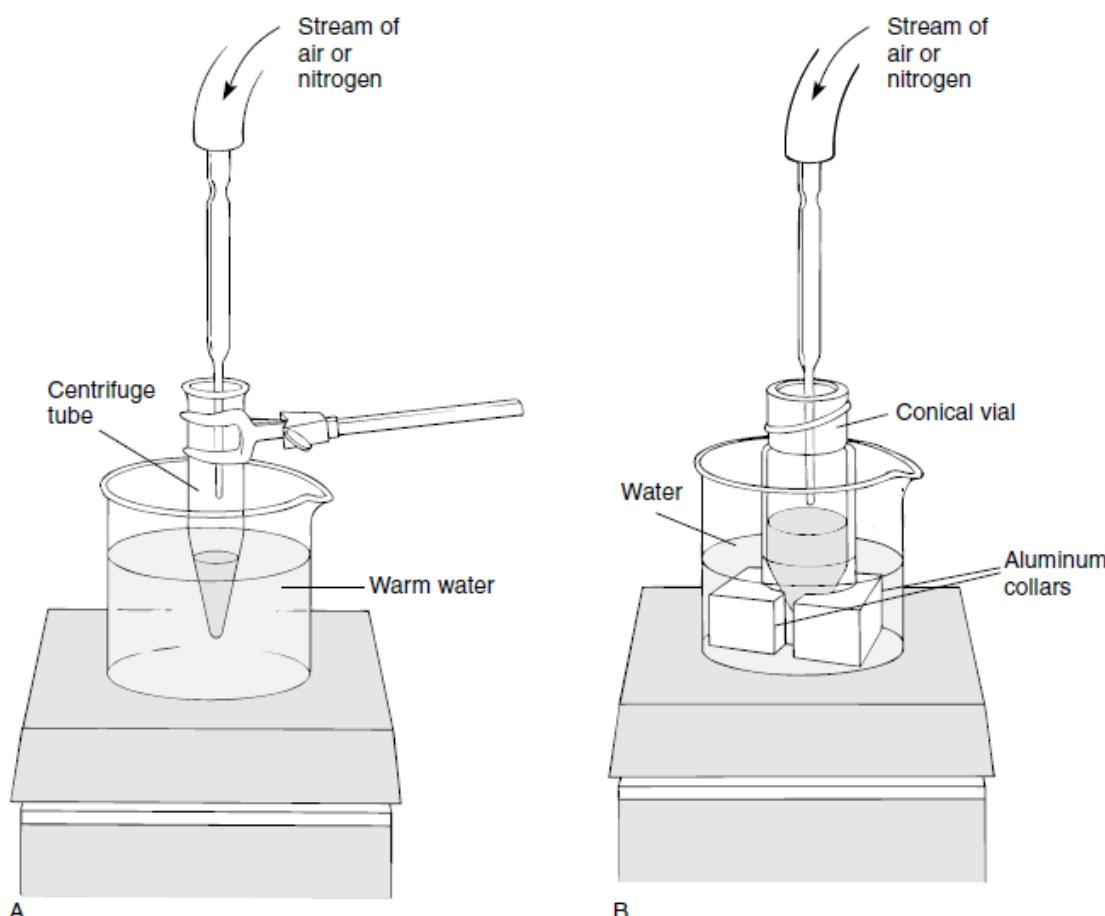


Figure 7.18 Evaporation of solvents (small-scale methods).

7.11 Rotary Evaporator

In some organic chemistry laboratories, solvents are evaporated under reduced pressure using a **rotary evaporator**. This is a motor-driven device that is designed for rapid evaporation of solvents, with heating, while minimizing the possibility of bumping. A vacuum is applied to the flask, and the motor spins the flask. The rotation of the flask spreads a thin film of the liquid over the surface of the glass, which accelerates evaporation. The rotation also agitates the solution sufficiently to reduce the problem of bumping. A water bath can be placed under the flask to warm the solution and increase the vapor pressure of the solvent. One can select the speed at which the flask is rotated and the temperature of the water bath to attain the desired evaporation rate. As the solvent evaporates from the rotating flask, the vapors are cooled by the condenser, and the resulting liquid collects in the flask. The product remains behind in the rotating flask. A complete rotary evaporator assembly is shown in Figure 7.19. If the coolant is sufficiently cold, virtually all of the solvent can be recovered and recycled. This is a good example of *Green Chemistry*.

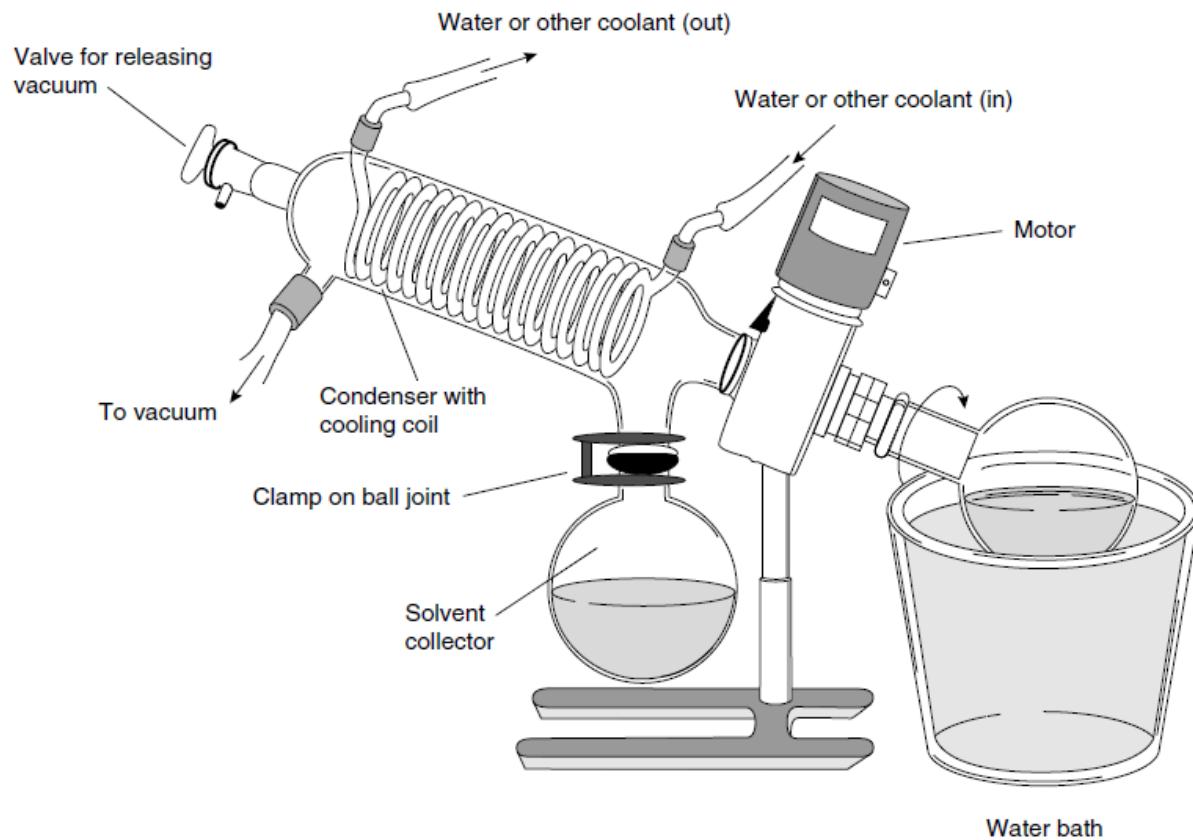


Figure 7.19 A rotary evaporator.

7.12 Microwave-Assisted Organic Chemistry

We are all familiar with the use of a microwave oven in the kitchen and its particular advantages. Cooking food in a microwave oven is much faster than in a conventional oven. Microwave cooking is much simpler, does not require as much crockery, and energy is not wasted in heating the container.

All of these advantages can also be applied to the chemistry laboratory. It is possible to conduct chemical reactions in much less time than with ordinary laboratory methods. Since the mid-1980s, chemists have been working on developing methods to apply microwave heating to chemical synthesis. Microwave-assisted organic chemical methods, or microwave chemistry, have gained wide acceptance, especially in industrial and research laboratories. Microwave heating is able to heat

the chemical reagents without wasting energy in heating their container. In "green chemistry" applications, it allows the chemist to perform chemical reactions using less energy, in less time, often using water as a solvent, and often without using any solvent at all.

There does not seem to be general agreement as to the mechanism of microwave heating. The arguments are too complex to be included here. A basic understanding is possible, however. Microwave radiation is a form of *electromagnetic radiation*; this means that microwave radiation consists of oscillating electric and magnetic fields. When an oscillating electric field passes through a medium that contains polar or ionic substances, these molecules will attempt to orient themselves or oscillate in response to the electric field. Because these molecules are bound to surrounding molecules in the medium, however, their motions are restricted, and they cannot respond completely to the oscillations of the electric field. This causes a non-equilibrium condition that results in an elevated instantaneous temperature in the immediate microscopic region surrounding the molecules that are being affected. As this localized temperature increases, molecules are activated above the required energy-of-activation threshold. Rates of reactions are dependent upon temperature; as the localized temperature increases, the molecules in that microscopic region will react faster.

Chemists first tried using domestic kitchen microwave ovens to speed up chemical reactions. They found that they were able to accelerate reactions, increase yields, and initiate otherwise impossible reactions. The results were often unsatisfactory, however, owing to uneven heating, lack of reproducibility, and the possibility of explosions. The power output of a typical kitchen microwave oven cannot be adjusted. The oven cycles between periods of full power and periods of zero power.

This means that the amount of microwave energy being transmitted into an experiment cannot be controlled precisely.

In recent years, companies have developed state-of-the-art microwave reaction systems to overcome these deficiencies. A modern reaction system, such as the one shown in Figure 7.20, has a specially-designed vessel that focuses the microwave energy for efficient heating. Such systems are often equipped with automatic stirring and computer controls. Often a pressure control system may be included; this allows one to conduct a reaction at elevated temperature and pressure in the presence of volatile solvents or reagents. An automated sample changer is a useful accessory; this allows the chemist to conduct a series of repeated experiments without having to spend time watching the system.



Figure 7.20 A microwave reaction system.

Papers describing the advantages of microwave chemistry are appearing with increasing frequency in the chemical literature. Examples of experiments that can be conducted using microwave reaction systems include esterifications, condensation reactions, hydrogenations, cycloadditions, and even peptide syntheses. Besides offering a versatile method of chemical synthesis, microwave reaction systems also include the advantages that many of the reactions can be conducted in water, rather than in harmful organic solvents, or even in the complete absence of solvent. This capability makes microwave chemistry an important tool in "green chemistry."

8

TECHNIQUE 8*Filtration*

Filtration is a technique used for two main purposes. The first is to remove solid impurities from a liquid. The second is to collect a desired solid from the solution from which it was precipitated or crystallized. Several different kinds of filtration techniques are commonly used: two general methods include gravity filtration and vacuum (or suction) filtration. Two techniques specific to the microscale laboratory are filtration with a filter-tip pipet and filtration with a Craig tube. The various filtration techniques and their applications are summarized in Table 8.1. These techniques are discussed in more detail in the following sections.

TABLE 8.1 Filtration Methods

Method	Application	Section
Gravity filtration		
Filter cones	The volume of liquid to be filtered is about 10 mL or greater, and the solid collected in the filter is saved.	8.1A
Fluted filters	The volume of liquid to be filtered is greater than about 10 mL, and solid impurities are removed from a solution; often used in crystallization procedures.	8.1B
Filtering pipets	Used with volumes less than about 10 mL to remove solid impurities from a liquid.	8.1C
Decantation	Although not a filtration technique, decantation can be used to separate a liquid from large, insoluble particles.	8.1D
Vacuum filtration		
Büchner funnels	Primarily used to collect a desired solid from a liquid when the volume is greater than about 10 mL; used frequently to collect the crystals obtained from crystallization.	8.3
Hirsch funnels	Used in the same way as Büchner funnels, except the volume of liquid is usually smaller (1–10 mL).	8.3
Filtering media		
Filter-tip pipets	May be used to remove a small amount of solid impurities from a small volume (1–2 mL) of liquid; also useful for pipetting volatile liquids, especially in extraction procedures.	8.6
Craig tubes	Used to collect a small amount of crystals resulting from crystallizations in which the volume of the solution is less than 2 mL.	8.7
Centrifugation	Although not strictly a filtration technique, centrifugation may be used to remove suspended impurities from a liquid (1–25 mL).	8.8

8.1 Gravity Filtration

The most familiar filtration technique is probably filtration of a solution through a paper filter held in a funnel, allowing gravity to draw the liquid through the paper. Because even a small piece of filter paper will absorb a significant volume of liquid, this technique is useful only when the volume of mixture to be filtered is greater than 10 mL. For many macroscale and microscale procedures, a more suitable technique, which also makes use of gravity, is to use a Pasteur (or disposable) pipet with a cotton or glass wool plug (called a filtering pipet).

A. Filter Cones

This filtration technique is most useful when the solid material being filtered from a mixture is to be collected and used later. The filter cone, because of its smooth sides, can easily be scraped free of collected solids. Because of the many folds, fluted filter paper, described in the next section, cannot be scraped easily. The filter cone is likely to be used in experiments only when a relatively large volume (greater than 10 mL) is being filtered and when a Büchner or Hirsch funnel (see Section 8.3) is not appropriate.

The filter cone is prepared as indicated in Figure 8.1. It is then placed into a funnel of an appropriate size. With filtrations using a simple filter cone, solvent may form seals between the filter and the funnel and between the funnel and the lip of the receiving flask. When a seal forms, the filtration stops because the displaced air has no possibility of escaping. To avoid the solvent seal, you can insert a small piece of paper, a paper clip, or some other bent wire between the funnel and the lip of the flask to let the displaced air escape. As an alternative, you can support the funnel by a clamp fixed *above* the flask rather than placed on the neck of the flask. A gravity filtration using a filter cone is shown in Figure 8.2.

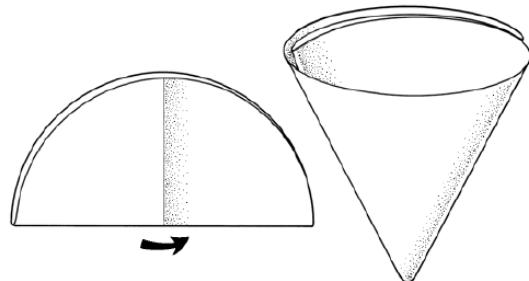


Figure 8.1 Folding a filter cone.

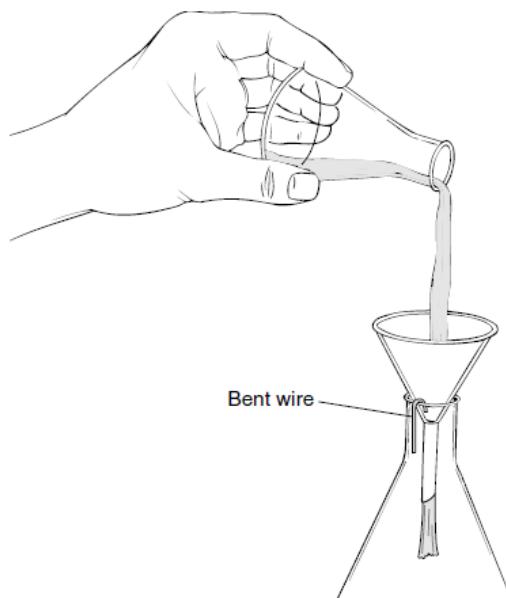


Figure 8.2 Gravity filtration with a filter cone.

B. Fluted Filters

This filtration method is also most useful when filtering a relatively large amount of liquid. Because a fluted filter is used when the desired material is expected to remain in solution, this filter is used to remove undesired solid materials, such as dirt particles, decolorizing charcoal, and undissolved impure crystals. A fluted filter is often used to filter a hot solution saturated with a solute during a crystallization procedure.

The technique for folding a fluted filter paper is shown in Figure 8.3. An advantage of a fluted filter is that it increases the speed of filtration in two ways. First, it increases the surface area of the filter paper through which the solvent seeps; second, it allows air to enter the flask along its sides to permit rapid pressure equalization. If pressure builds up in the flask from hot vapors, filtering slows down. This problem is especially pronounced with filter cones. The fluted filter tends to reduce this problem considerably, but it may be a good idea to clamp the funnel above the receiving flask or to use a piece of paper, paper clip, or wire between the funnel and the lip of the flask as an added precaution against solvent seals.

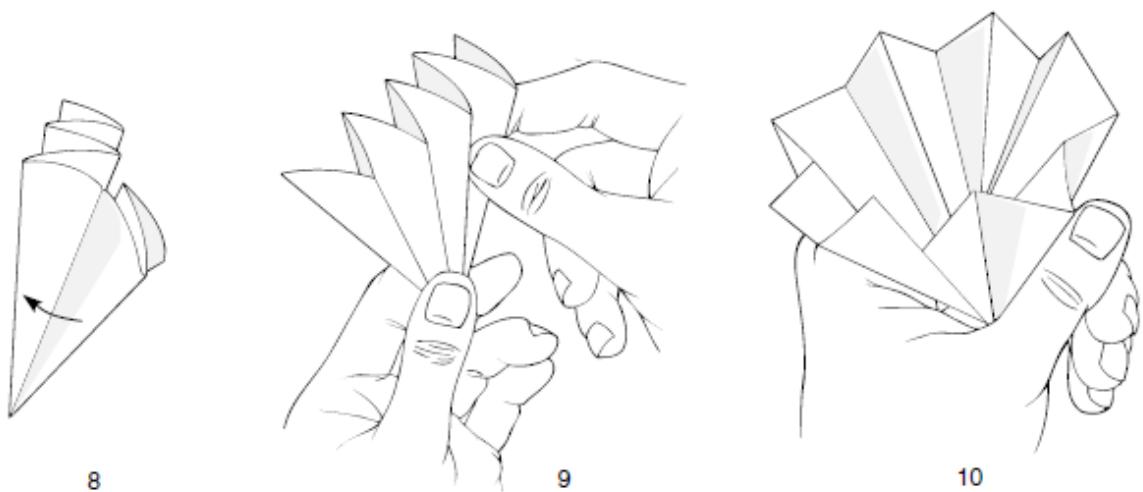
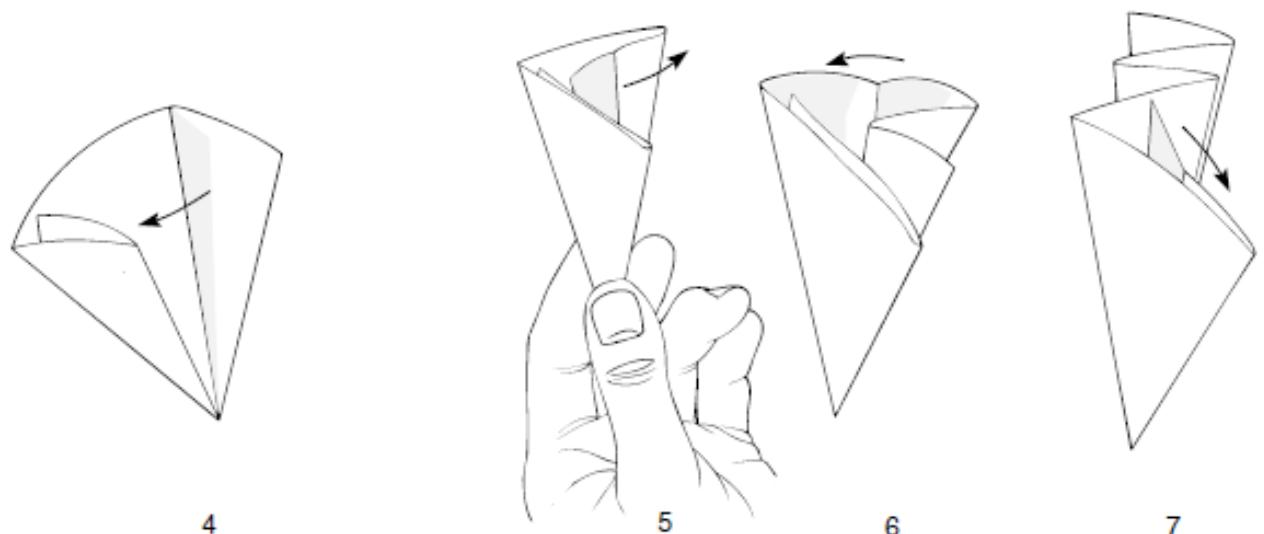
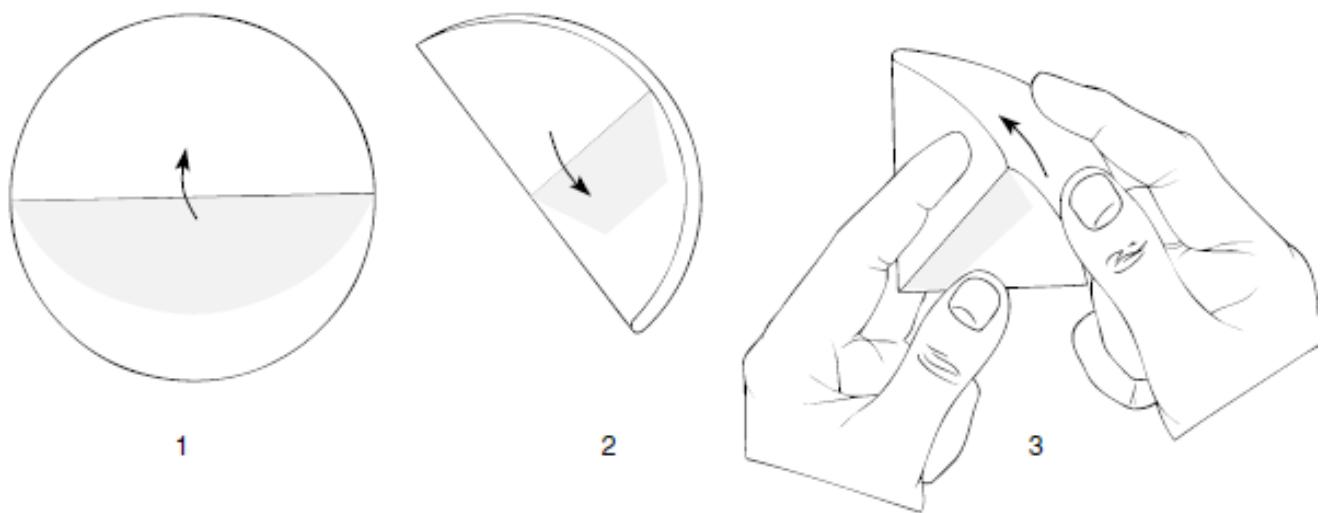


Figure 8.3 Folding a fluted filter paper, or origami at work in the organic chemistry laboratory.

Filtration with a fluted filter is relatively easy to perform when the mixture is at room temperature. However, when it is necessary to filter a hot solution saturated with a dissolved solute, a number of steps must be taken to ensure that the filter does not become clogged by solid material accumulated in the stem of the funnel or in the filter paper. When the hot, saturated solution comes in contact with a relatively cold funnel (or a cold flask, for that matter), the solution is cooled and may become supersaturated. If crystallization then occurs in the filter, either the crystals will fail to pass through the filter paper or they will clog the stem of the funnel.

To keep the filter from clogging, use one of the following four methods. The first is to use a short-stemmed or stemless funnel. With these funnels, it is less likely that the stem of the funnel will become clogged by solid material. The second method is to keep the liquid to be filtered at or near its boiling point at all times. The third way is to preheat the funnel by pouring hot solvent through it before the actual filtration. This keeps the cold glass from causing instantaneous crystallization. And fourth, it is helpful to keep the filtrate (filtered solution) in the receiver hot enough to continue boiling *slightly* (by setting it on a hot plate, for example). The refluxing solvent heats the receiving flask and the funnel stem and washes them clean of solids. This boiling of the filtrate also keeps the liquid in the funnel warm.

C. Filtering Pipets

A filtering pipet is a microscale technique most often used to remove solid impurities from a liquid with a volume less than 10 mL. It is important that the mixture being filtered be at or near room temperature because it is difficult to prevent premature crystallization in a hot solution saturated with a solute.

To prepare this filtration device, a small piece of cotton is inserted into the top of a Pasteur (disposable) pipet and pushed down to the beginning of the lower constriction in the pipet, as shown in Figure 8.4. It is important to use enough cotton to collect all the solid being filtered; however, the amount of cotton used should not be so large that the flow rate through the pipet is significantly restricted. For the same reason, the cotton should not be packed too tightly. The cotton plug can be pushed down gently with a long thin object such as a glass stirring rod or a wooden applicator stick. It is advisable to wash the cotton plug by passing about 1 mL of solvent (usually the same solvent that is to be filtered) through the filter.

In some cases, such as when filtering a strongly acidic mixture or when performing a very rapid filtration to remove dirt or impurities of large particle size from a solution, it may be better to use glass wool in place of the cotton. The disadvantage in using glass wool is that the fibers do not pack together as tightly, and small particles will pass through the filter more easily.

To conduct a filtration (with either a cotton or glass wool plug), the filtering pipet is clamped so that the filtrate will drain into an appropriate container. The mixture to be filtered is usually transferred to the filtering pipet with another Pasteur pipet. If a small volume of liquid is being filtered (less than 1 mL or 2 mL), it is advisable to rinse the filter and plug with a small amount of solvent after the last of the filtrate has passed through the filter. The rinse solvent is then combined

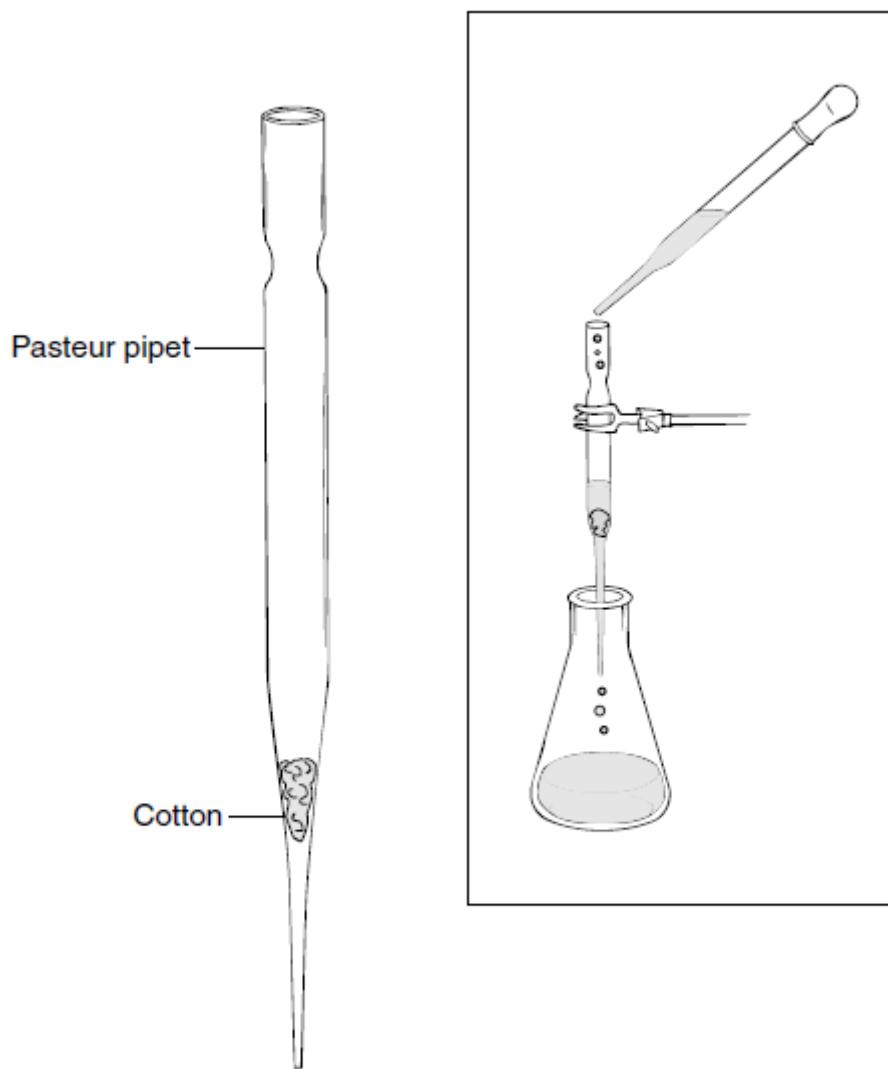


Figure 8.4 A filtering pipet.

with the original filtrate. If desired, the rate of filtration can be increased by gently applying pressure to the top of the pipet using a pipet bulb.

Depending on the amount of solid being filtered and the size of the particles (small particles are more difficult to remove by filtration), it may be necessary to put the filtrate through a second filtering pipet. This should be done with a new filtering pipet rather than with the one already used.

D. Decantation

It is not always necessary to use filter paper to separate insoluble particles. If you have large, heavy, insoluble particles, with careful pouring you can decant the solution, leaving behind the solid particles that will settle to the bottom of the flask. The term *decant* means “to carefully pour out the liquid, leaving the insoluble particles behind.” For example, boiling stones or sand granules in the bottom of an Erlenmeyer flask filled with a liquid can easily be separated in this way. This procedure is often preferred over filtration and usually results in a smaller loss of material. If there are a large number of particles and they retain a significant amount of the liquid, they can be rinsed with solvent and a second decantation performed. The term *decant* was coined in the wine industry, where it is often necessary to let the wine settle and then carefully pour it out of the original bottle into a clean one, leaving the “must” (insoluble particles) behind.

8.2 Filter Paper

Many kinds and grades of filter paper are available. The paper must be correct for a given application. In choosing filter paper, you should be aware of its various properties. **Porosity** is a measure of the size of the particles that can pass through the paper. Highly porous paper does not remove small particles from solution; paper with low porosity removes very small particles. **Retentivity** is a property that is the opposite of porosity. Paper with low retentivity does not remove small particles from the filtrate. The speed of filter paper is a measure of the time it takes a liquid to drain through the filter. Fast paper allows the liquid to drain quickly; with slow paper, it takes much longer to complete the filtration. Because all these properties are related, fast filter paper usually has a low retentivity and high porosity, and slow filter paper usually has high retentivity and low porosity.

Table 8.2 compares some commonly available qualitative filter paper types and ranks them according to porosity, retentivity, and speed. Eaton–Dikeman (E&D), Schleicher and Schuell (S&S), and Whatman are the most common brands of filter paper. The numbers in the table refer to the grades of paper used by each company.

TABLE 8.2 Some Common Qualitative Filter Paper Types and Approximate Relative Speeds and Retentivities

Fine	High	Slow	Type (by number)			
			Speed	E&D	S&S	Whatman
Porosity ↓	Retentivity ↓	Speed ↓	Very slow	610	576	5
Coarse	Low	Fast	Slow	613	602	3
			Medium	615	597	2
			Fast	617	595	1
			Very fast	—	604	4

8.3 Vacuum Filtration

Vacuum, or suction, filtration is more rapid than gravity filtration and is most often used to collect solid products resulting from precipitation or crystallization. This technique is used primarily when the volume of liquid being filtered is more than 1–2 mL. With smaller volumes, use of the Craig tube (see Section 8.7) is the preferred technique. In a vacuum filtration, a receiver flask with a sidearm, a filter flask, is used. For macroscale laboratory work, the most useful sizes of filter flasks range from 50 mL to 500 mL, depending on the volume of liquid being filtered. For microscale work, the most useful size is a 50-mL filter flask. The sidearm is connected by *heavy-walled* rubber tubing to a source of vacuum. Thin-walled tubing will collapse under vacuum, due to atmospheric pressure on its outside walls, and will seal the vacuum source from the flask. Because this apparatus is unstable and can tip over easily, it must be clamped, as shown in Figure 8.5.

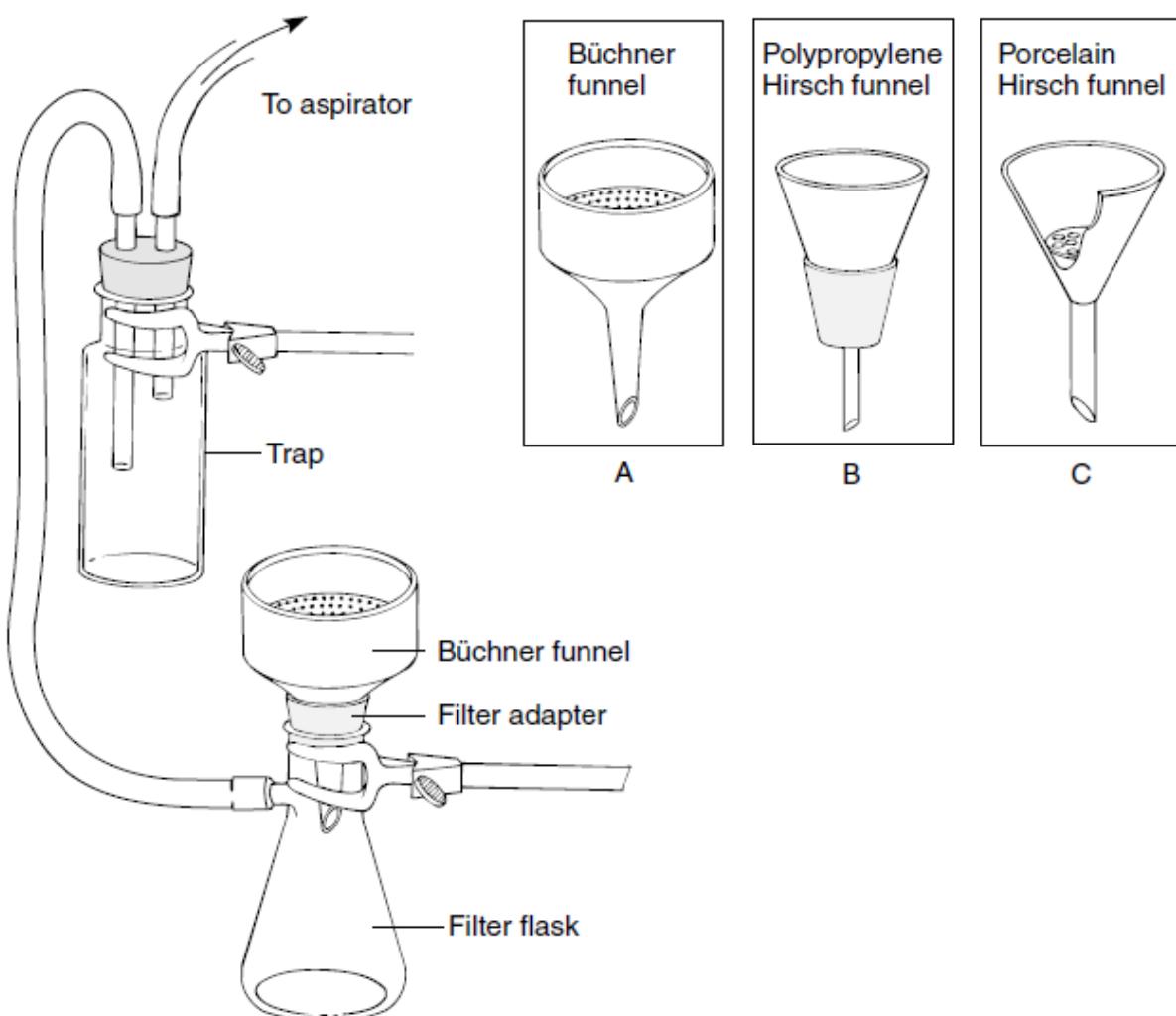


Figure 8.5 Vacuum filtration.

CAUTION



It is essential that the filter flask be clamped.

Two types of funnels are useful for vacuum filtration, the Büchner funnel and the Hirsch funnel. The Büchner funnel is used for filtering larger amounts of solid from solution in macroscale applications. Büchner funnels are usually made from polypropylene or porcelain. A Büchner funnel (see Figures 8.5 and 8.5A) is sealed to the filter flask by a rubber stopper or a filter (neoprene) adapter. The flat bottom of the Büchner funnel is covered with an unfolded piece of circular filter paper. To prevent the escape of solid materials from the funnel, you must be certain that the filter paper fits the funnel exactly. It must cover all the holes in the bottom of the funnel, but not extend up the sides. Before beginning the filtration, it is advisable to moisten the paper with a small amount of solvent. The moistened filter paper adheres more strongly to the bottom of the funnel and prevents the unfiltered mixture from passing around the edges of the filter paper.

The Hirsch funnel, which is shown in Figures 8.5B and C, operates on the same principle as the Büchner funnel, but it is usually smaller, and its sides are sloped rather than vertical. The Hirsch funnel is used primarily in microscale experiments. The polypropylene Hirsch funnel (see Figure 8.5B) is sealed to a 50-mL filter flask by a small section of Gooch tubing or a one-hole rubber stopper. This Hirsch funnel has a built-in adapter that forms a tight seal with some 25-mL filter flasks without the Gooch tubing. A polyethylene fritted disk fits into the bottom of the funnel. To prevent the holes in this disk from becoming clogged with solid material, the funnel should always be used with a circular filter paper that has the same diameter (1.27 cm) as the polyethylene disk. With a polypropylene Hirsch funnel, it is also important to moisten the paper with a small amount of solvent before beginning the filtration.

The porcelain Hirsch funnel is sealed to the filter flask with a rubber stopper or a neoprene adapter. In this Hirsch funnel, the filter paper must also cover all the holes in the bottom but must not extend up the sides.

Because the filter flask is attached to a source of vacuum, a solution poured into a Büchner funnel or Hirsch funnel is literally “sucked” rapidly through the filter paper. For this reason, vacuum filtration is generally not used to separate fine particles such as decolorizing charcoal, because the small particles would likely be pulled through the filter paper. However, this problem can be alleviated, when desired, by the use of specially prepared filter beds (see Section 8.4).

8.4 Filtering Media

It is occasionally necessary to use specially prepared filter beds to separate fine particles when using vacuum filtration. Often, very fine particles either pass right through a paper filter or clog it so completely that the filtering stops. This is avoided by using a substance called Filter Aid, or Celite. This material is also called diatomaceous earth because of its source. It is a finely divided inert material derived from the microscopic shells of dead diatoms (a type of phytoplankton that grows in the sea).

CAUTION



Diatomaceous earth is a lung irritant. When using Filter Aid, take care not to breathe the dust.

Filter Aid will not clog the fiber pores of filter paper. It is slurried, mixed with a solvent to form a rather thin paste, and filtered through a Hirsch or Büchner funnel (with filter paper in place) until a layer of diatoms about 2–3 mm thick is formed on top of the filter paper. The solvent in which the diatoms were slurried is poured from the filter flask, and, if necessary, the filter flask is cleaned before the actual filtration is begun. Finely divided particles can now be suction-filtered through this layer and will be caught in the Filter Aid. This technique is used for removing impurities, not for collecting a product. The filtrate (filtered solution) is the desired material in this procedure. If the material caught in the filter were the desired material, you would have to try to separate the product from all those diatoms! Filtration

with Filter Aid is not appropriate when the desired substance is likely to precipitate or crystallize from solution.

In microscale work, it may sometimes be more convenient to use a column prepared with a Pasteur pipet to separate fine particles from a solution. The Pasteur pipet is packed with alumina or silica gel, as shown in Figure 8.6.

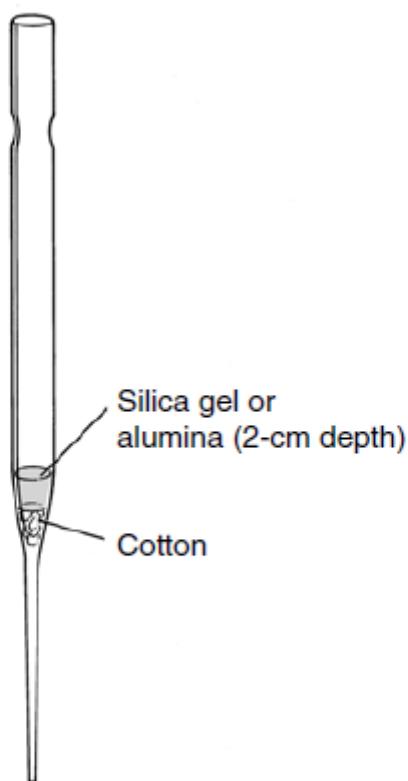


Figure 8.6 A Pasteur pipet with filtering media.

8.5 The Aspirator

The most common source of vacuum (approximately 10–20 mmHg) in the laboratory is the water aspirator, or “water pump,” illustrated in Figure 8.7. This device passes water rapidly past a small hole to which a sidearm is attached. The water pulls air in through the sidearm. This phenomenon, called the Bernoulli effect, causes a reduced pressure along the side of the rapidly moving water stream and creates a partial vacuum in the sidearm.

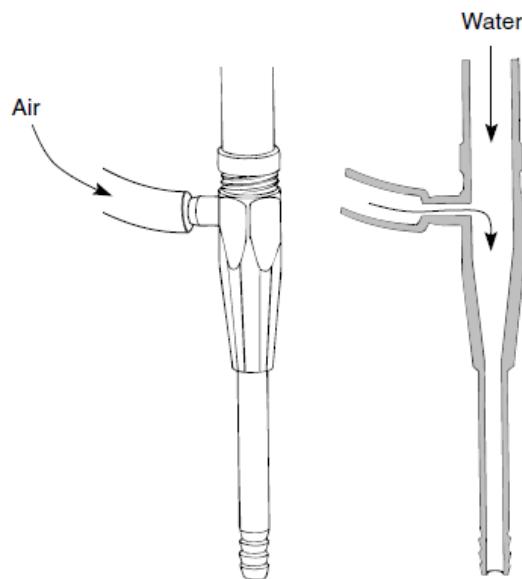


Figure 8.7 An aspirator.

NOTE: The aspirator works most effectively when the water is turned on to the fullest extent.

A water aspirator can never lower the pressure beyond the vapor pressure of the water used to create the vacuum. Hence, there is a lower limit to the pressure (on cold days) of 9–10 mmHg. A water aspirator does not provide as high a vacuum in the summer as in the winter, due to this water-temperature effect.

A trap must be used with an aspirator. One type of trap is illustrated in Figure 8.5. Another method for securing this type of trap is shown in Figure 8.8. This simple holder can be constructed from readily available material and can be placed anywhere on the laboratory bench. Although not often needed, a trap can prevent water from contaminating your experiment. If the water pressure in the laboratory drops suddenly, the pressure in the filter flask may suddenly become lower than the pressure in the water aspirator. This would cause water to be drawn from the aspirator stream into the filter flask and contaminate the filtrate or even the material in the filter. The trap stops this reverse flow. A similar flow will occur if the water flow at the aspirator is stopped before the tubing connected to the aspirator sidearm is disconnected.

NOTE: Always disconnect the tubing before stopping the aspirator.

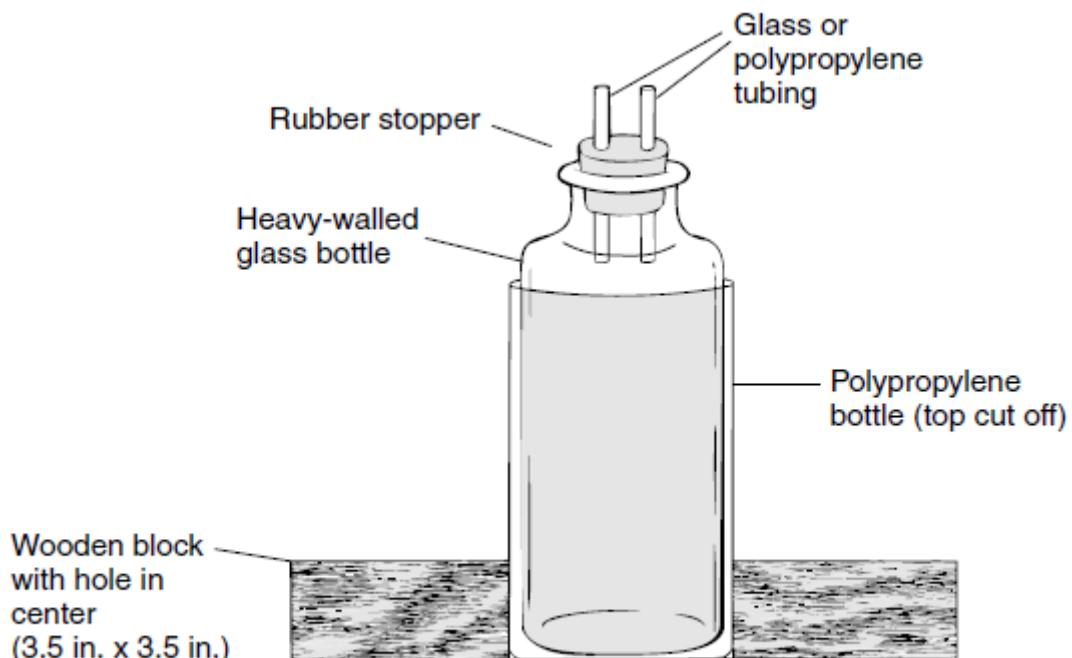


Figure 8.8 A simple aspirator trap and holder.

If a “backup” begins, disconnect the tubing as rapidly as possible before the trap fills with water. Some chemists like to fit a stopcock into the stopper on top of the trap. A three-hole stopper is required for this purpose. With a stopcock in the trap, the system can be vented before the aspirator is shut off. Then water cannot back up into the trap.

Aspirators do not work well if too many people use the water line at the same time because the water pressure is lowered. Also, the sinks at the ends of the lab benches or the lines that carry away the water flow may have a limited capacity for draining the resultant water flow from too many aspirators. Care must be taken to avoid floods.

8.6 Filter-Tip Pipet

The filter-tip pipet, illustrated in Figure 8.9, has two common uses. The first is to remove a small amount of solid, such as dirt or filter paper fibers, from a small volume of liquid (1–2 mL). It can also be helpful when using a Pasteur pipet to transfer a highly volatile liquid, especially during an extraction procedure (see Technique 12, Section 12.5).

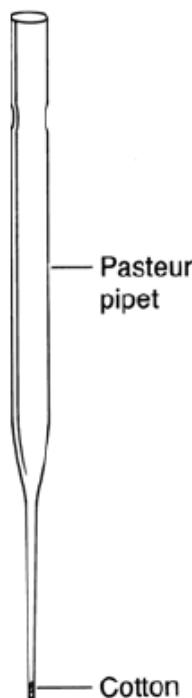


Figure 8.9 A filter-tip pipet.

Preparing a filter-tip pipet is similar to preparing a filtering pipet, except that a much smaller amount of cotton is used. A *very tiny* piece of cotton is loosely shaped into a ball and placed into the large end of a Pasteur pipet. Using a wire with a diameter slightly smaller than the inside diameter of the narrow end of the pipet, push the ball of cotton to the bottom of the pipet. If it becomes difficult to push the cotton, you have probably started with too much cotton; if the cotton slides through the narrow end with little resistance, you probably have not used enough.

To use a filter-tip pipet as a filter, the mixture is drawn up into the Pasteur pipet using a pipet bulb and then expelled. With this procedure, a small amount of solid will be captured by the cotton. However, very fine particles, such as activated charcoal, cannot be removed efficiently with a filter-tip pipet, and this technique is not effective in removing more than a trace amount of solid from a liquid.

Transferring many organic liquids with a Pasteur pipet can be a somewhat difficult procedure for two reasons. First, the liquid may not adhere well to the glass. Second, as you handle the Pasteur pipet, the temperature of the liquid in the pipet increases slightly, and the increased vapor pressure may tend to "squirt" the liquid out the end of the pipet. This problem can be particularly troublesome when separating two liquids during an extraction procedure. The purpose of the cotton plug in this situation is to slow the rate of flow through the end of the pipet so you can control the movement of liquid in the Pasteur pipet more easily.

8.7 Craig Tubes

The Craig tube, illustrated in Figure 8.10, is used primarily to separate crystals from a solution after a microscale crystallization procedure has been performed .

Although it may not be a filtration procedure in the traditional sense, the outcome is similar. The outer part of the Craig tube is similar to a test tube, except that the diameter of the tube becomes wider part of the way up the tube, and the glass is ground at this point so that the inside surface is rough. The inner part (plug) of the Craig tube may be made of Teflon or glass. If this part is glass, the end of the plug is also ground. With either a glass or a Teflon inner plug, there is only a partial seal where the plug and the outer tube come together. Liquid may pass through, but solid will not. This is the place where the solution is separated from the crystals.

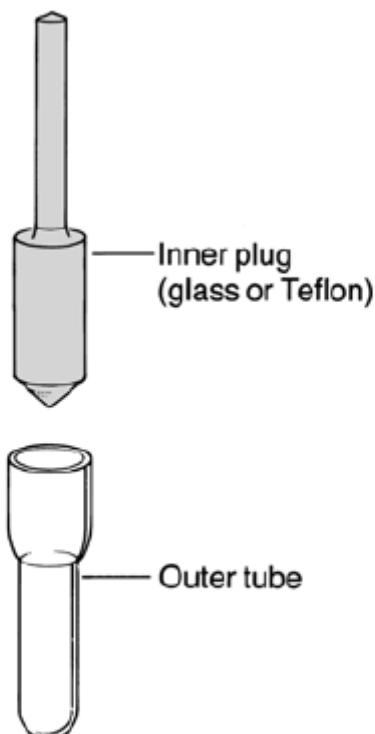


Figure 8.10 A Craig tube (2 mL).

After crystallization has been completed in the outer Craig tube, replace the inner plug (if necessary) and connect a thin copper wire or strong thread to the narrow part of the inner plug, as indicated in Figure 8.11A. While holding the Craig tube in an upright position, place a plastic centrifuge tube over the Craig tube so that the bottom of the centrifuge tube rests on top of the inner plug, as shown in Figure 8.11B. The copper wire should extend just below the lip of the centrifuge tube and is now bent upward around the lip of the centrifuge tube. This apparatus is then turned over so that the centrifuge tube is in an upright position. The Craig tube is spun in a centrifuge (be sure it is balanced by placing another tube filled with water on the opposite side of the centrifuge) for several minutes until the mother liquor (solution from which the crystals grew) goes to the bottom of the centrifuge tube and the crystals collect on the end of the inner plug (see Figure 8.11C). Depending on the consistency of the crystals and the speed of the centrifuge, the crystals may spin down to the inner plug, or (if you are unlucky) they may remain at the other end of the Craig tube.¹ If the latter situation occurs, it may be helpful to centrifuge the Craig tube longer or, if this problem is anticipated, to stir the crystal-and-solution mixture with a spatula or stirring rod before centrifugation.

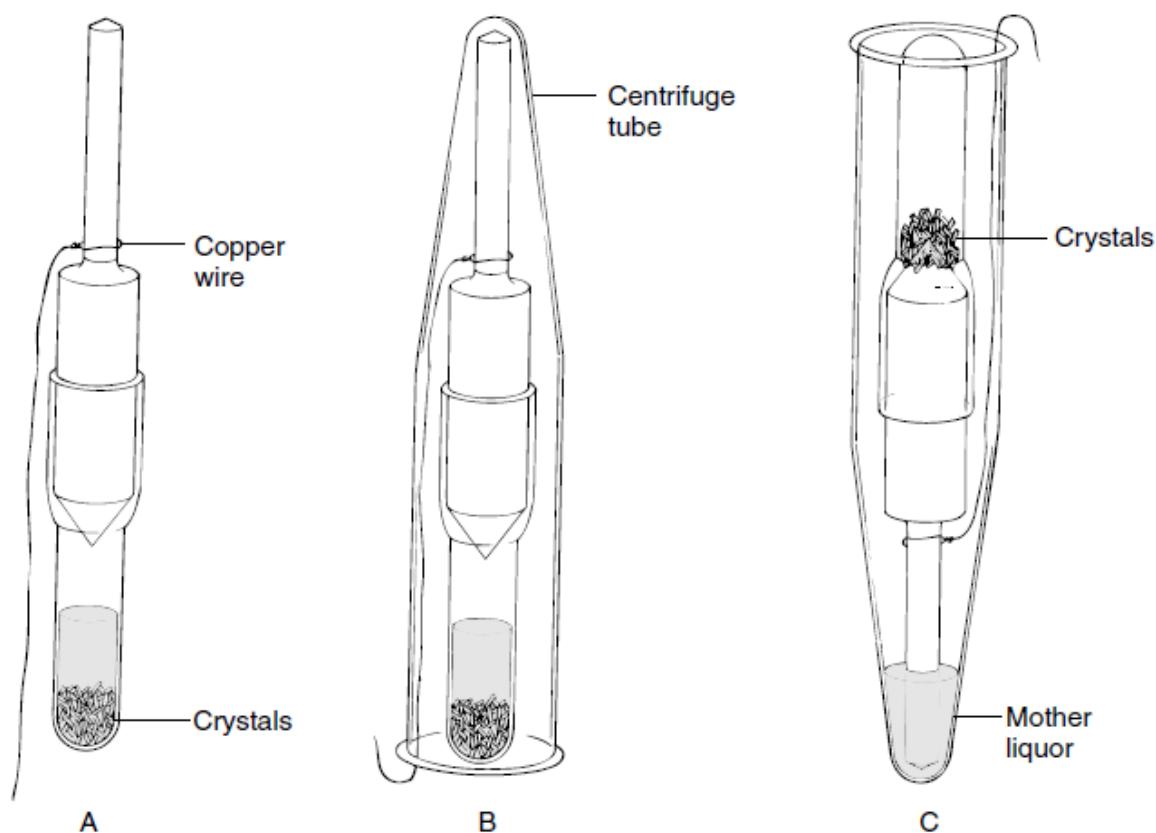


Figure 8.11 Separation with a Craig tube.

Using the copper wire, then pull the Craig tube out of the centrifuge tube. If the crystals are collected on the end of the inner plug, it is now a simple procedure to remove the plug and scrape the crystals with a spatula onto a watch glass, a clay plate, or a piece of smooth paper. Otherwise, it will be necessary to scrape the crystals from the inside surface of the outer part of the Craig tube.

8.8 Centrifugation

Sometimes, centrifugation is more effective than conventional filtration techniques in removing solid impurities. Centrifugation is particularly effective in removing suspended particles, which are so small that the particles would pass through most filtering devices. Centrifugation may also be useful when the mixture must be kept hot to prevent premature crystallization while the solid impurities are removed.

Centrifugation is performed by placing the mixture in one or two centrifuge tubes (be sure to balance the centrifuge) and centrifuging for several minutes. The supernatant liquid is then decanted (poured off) or removed with a Pasteur pipet.

9

TECHNIQUE 9

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.

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. Although the *CRC Handbook* has very 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 lowers the freezing point. The freezing point, a colligative property, is simply the melting point (solid → liquid) approached from the opposite direction (liquid → solid).

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.

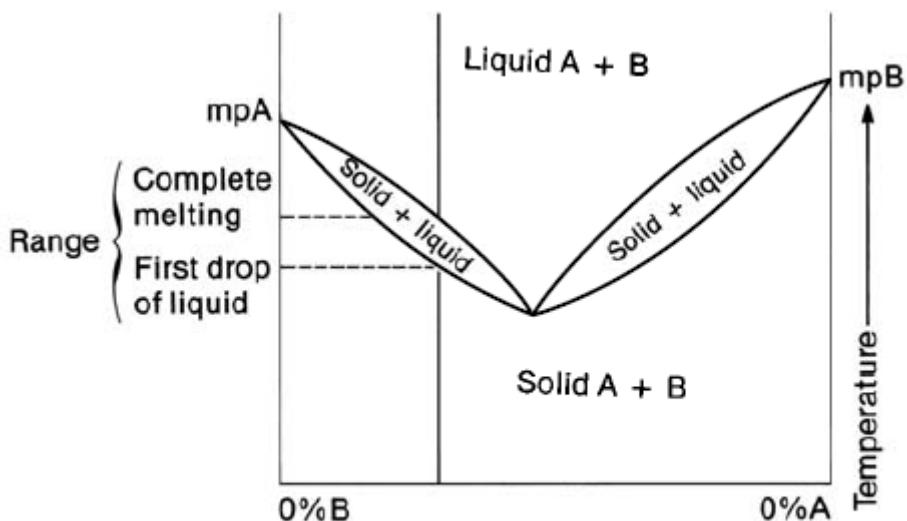


Figure 9.1 A melting-point–composition curve.

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.

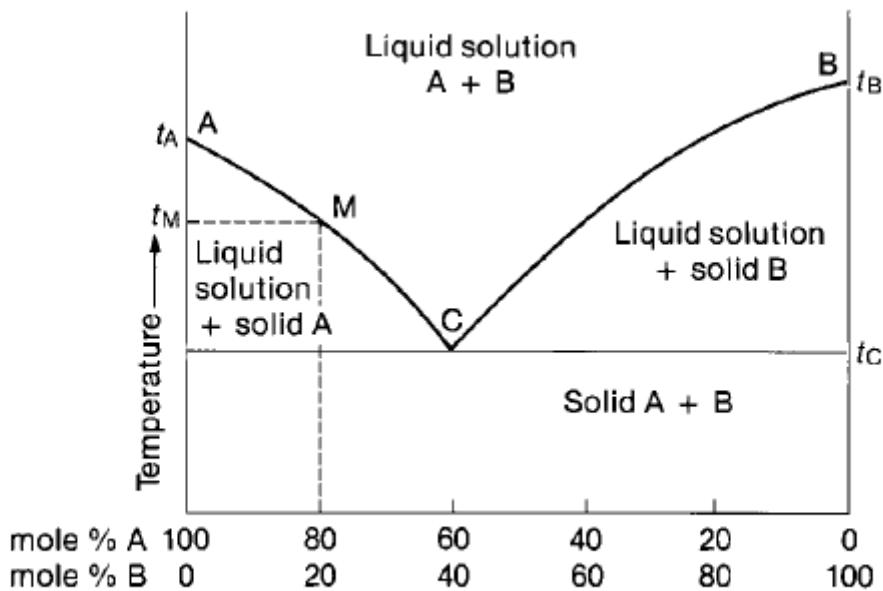


Figure 9.2 A phase diagram for melting in a two-component system.

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.

9.5 Packing the Melting-Point Tube

Melting points are usually determined by heating the sample in a piece of thin-walled capillary tubing ($1\text{ mm} \times 100\text{ mm}$) 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 $\frac{2}{3}\text{-m}$ 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.

9.6 Determining the Melting Point—The Thiele Tube

There are two principal types of melting-point apparatus available: the Thiele tube and commercially available, electrically heated instruments. The Thiele tube, shown in Figure 9.3, is the simpler device and was once widely used. It is a glass tube designed to contain a heating oil (mineral oil or silicone oil) and a thermometer to which a capillary tube containing the sample is attached. The shape of the Thiele tube allows convection currents to form in the oil when it is heated. These currents maintain a uniform temperature distribution through the oil in the tube. The sidearm of the tube is designed to generate these convection currents and thus transfer the heat from the flame evenly and rapidly throughout the oil. The sample, which is in a capillary tube attached to the thermometer, is held by a rubber band or a thin slice of rubber tubing. It is important that this rubber band be above the level of the oil (allowing for expansion of the oil on heating) so that the oil does not soften the rubber and allow the capillary tubing to fall into the oil. If a cork or a rubber stopper is used to hold the thermometer, a triangular wedge should be sliced in it to allow pressure equalization.

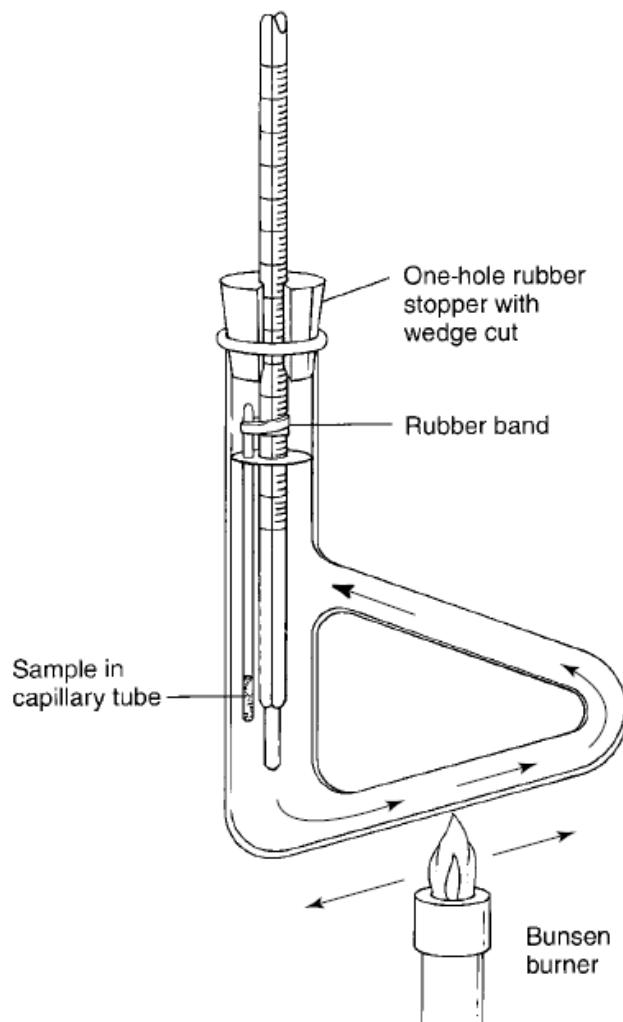


Figure 9.3 A Thiele tube.

The Thiele tube is usually heated by a microburner. During the heating, the rate of temperature increase should be regulated. Hold the burner by its cool base and, using a low flame, move the burner slowly back and forth along the bottom of the arm of the Thiele tube. If the heating is too fast, remove the burner for a few seconds and then resume heating. The rate of heating should be *slow* near the melting point (about 1°C per minute) to ensure that the temperature increase is not faster than the rate at which heat can be transferred to the sample being observed. At the melting point, it is necessary that the mercury in the thermometer and the sample in the capillary tube be at temperature equilibrium.

9.7 Determining the Melting Point—Electrical Instruments

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.

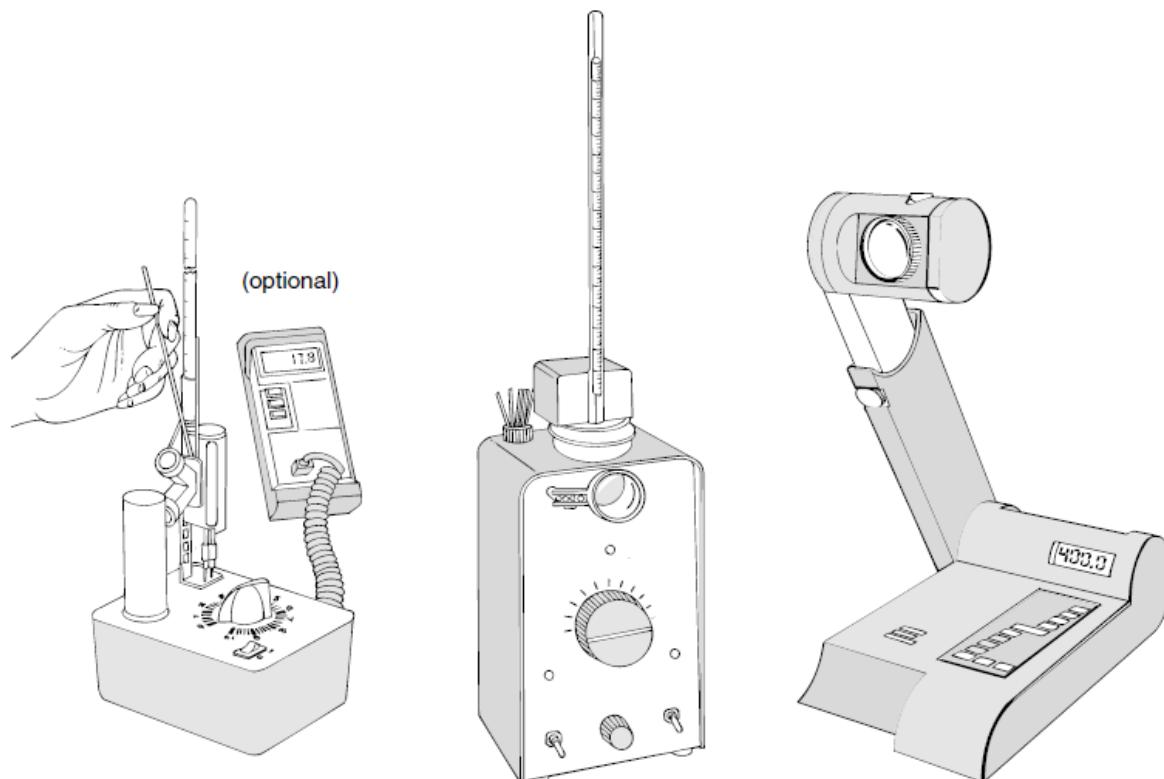


Figure 9.4 Melting-point apparatus.

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.

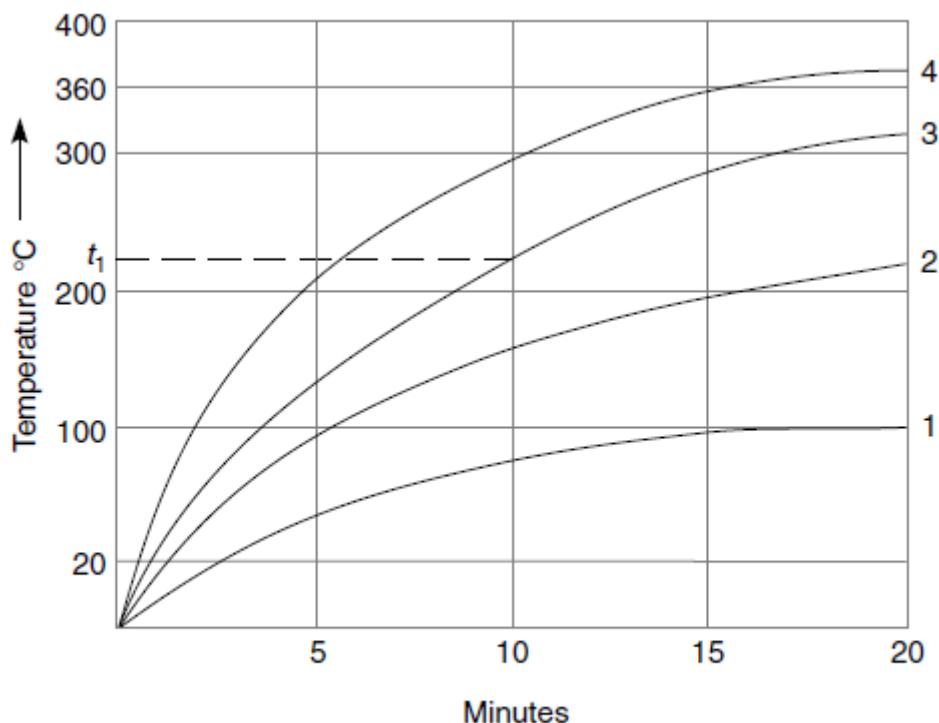


Figure 9.5 Heating-rate curves.

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 measuring temperatures above 150°C, 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.

An even better solution is to calibrate the thermometer as described in Section 9.9.

9.8 Decomposition, Discoloration, Softening, Shrinkage, and Sublimation

Many solid substances undergo some degree of unusual behavior before melting. At times it may be difficult to distinguish these types of behavior from actual melting. You should learn, through experience, how to recognize melting and how to distinguish it from decomposition, discoloration, and, particularly, softening and shrinkage.

Some compounds decompose on melting. This decomposition is usually evidenced by discoloration of the sample. Frequently, this decomposition point is a reliable physical property to be used in lieu of an actual melting point. Such decomposition points are indicated in tables of melting points by placing the symbol *d* immediately after the listed temperature. An example of a decomposition point is thiamine hydrochloride, whose melting point would be listed as 248°*d*, indicating that this substance melts with decomposition at 248°C. When decomposition is a result of reaction with the oxygen in air, it may be avoided by determining the melting point in a sealed, evacuated melting-point tube.

Figure 9.6 shows two simple methods of evacuating a packed tube. Method A uses an ordinary melting-point tube, and method B constructs the melting-point tube from a disposable Pasteur pipet. Before using method B, be sure to determine that the tip of the pipet will fit into the sample holder in your melting-point instrument.

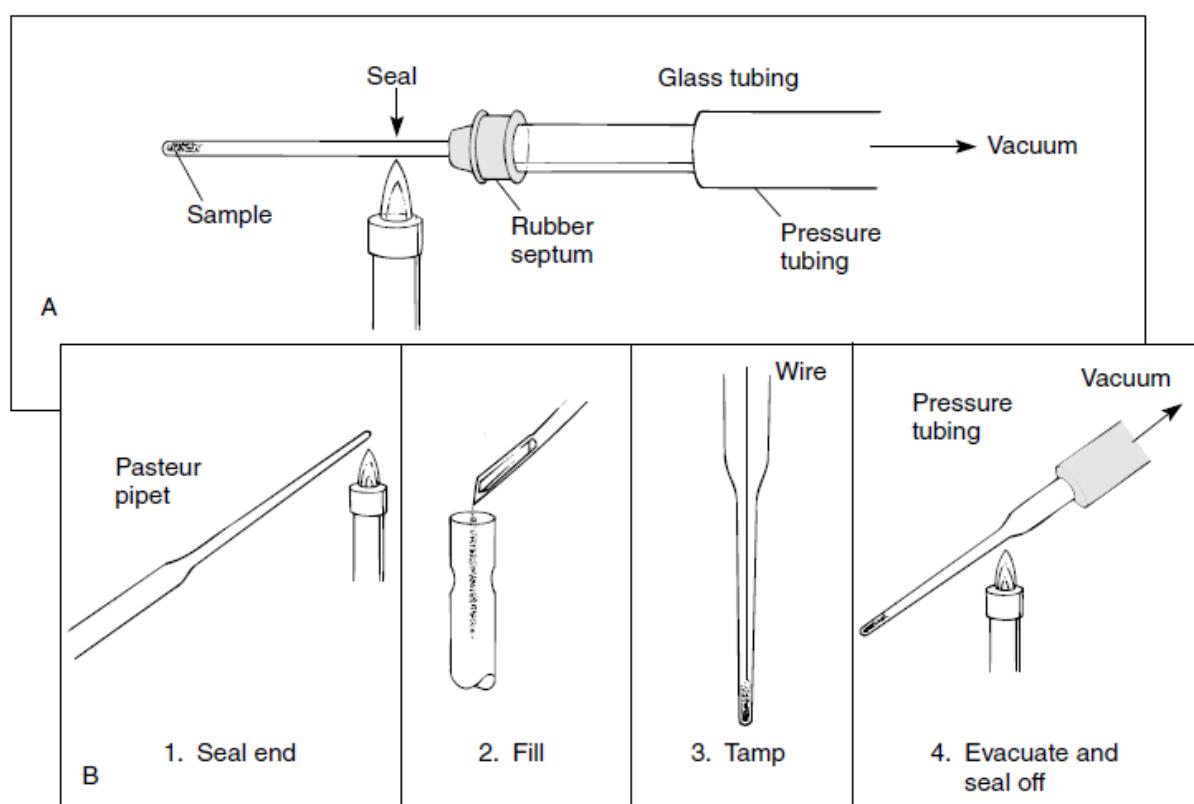


Figure 9.6 Evacuation and sealing of a melting-point capillary.

Method A

In method A, a hole is punched through a rubber septum using a large pin or a small nail, and the capillary tube is inserted from the inside, sealed end first. The septum is placed over a piece of glass tubing connected to a vacuum line. After the tube is evacuated, the upper end of the tube may be sealed by heating and pulling it closed.

Method B

In method B, the thin section of a 9-inch Pasteur pipet is used to construct the melting-point tube. Carefully seal the tip of the pipet using a flame. Be sure to hold the tip *upward* as you seal it. This will prevent water vapor from condensing inside the pipet. When the sealed pipet has cooled, the sample may be added through the open end using a microspatula. A small wire may be used to compress the sample into the closed tip. (If your melting-point apparatus has a vibrator, it may be used in place of the wire to simplify the packing.) When the sample is in place, the pipet is connected to the vacuum line with tubing and evacuated. The evacuated sample tube is sealed by heating it with a flame and pulling it closed.

Some substances begin to decompose *below* their melting points. Thermally unstable substances may undergo elimination reactions or anhydride formation reactions during heating. The decomposition products formed represent impurities in the original sample, so the melting point of the substance may be lowered due to their presence.

It is normal for many compounds to soften or shrink immediately before melting. Such behavior represents not decomposition, but a change in the crystal structure or a mixing with impurities. Some substances "sweat," or release solvent of crystallization, before melting. These changes do not indicate the beginning of melting. Actual melting begins when the first drop of liquid becomes visible, and the melting range continues until the temperature is reached at which all the solid has been converted to the liquid state. With experience, you soon learn to distinguish between softening, or "sweating," and actual melting. If you wish, the temperature of the onset of softening or sweating may be reported as a part of your melting-point range: 211°C (softens), 223–225°C (melts).

Some solid substances have such a high vapor pressure that they sublime at or below their melting points. In many handbooks, the sublimation temperature is listed along with the melting point. The symbols *sub*, *subl*, and sometimes *s* are used to designate a substance that sublimes. In such cases, the melting-point determination must be performed in a sealed capillary tube to avoid loss of the sample. The simplest way to accomplish sealing a packed tube is to heat the open end of the tube in a flame and pull it closed with tweezers or forceps. A better way, although more difficult to master, is to heat the center of the tube in a small flame, rotating it about its axis and keeping the tube straight until the center collapses. If this is not done quickly, the sample may melt or sublime while you are working. With the smaller chamber, the sample will not be able to migrate to the cool top of the tube that may be above the viewing area. Figure 9.7 illustrates the method.

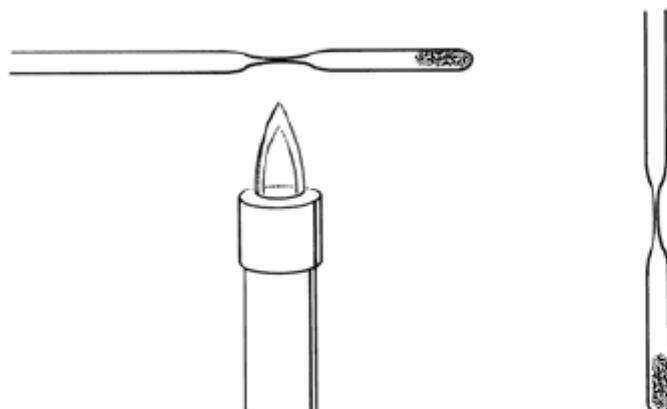


Figure 9.7 Sealing a tube for a substance that sublimes.

9.9 Thermometer Calibration

When a melting-point or boiling-point determination has been completed, you expect to obtain a result that exactly duplicates the result recorded in a handbook or in the original literature. It is not unusual, however, to find a discrepancy of several degrees from the literature value. Such a discrepancy does not necessarily indicate that the experiment was incorrectly performed or that the material is impure; rather, it may indicate that the thermometer used for the determination was slightly in error. Most thermometers do not measure the temperature with perfect accuracy.

To determine accurate values, you must calibrate the thermometer that is used. This calibration is done by determining the melting points of a variety of standard substances with the thermometer. A plot is drawn of the observed temperature vs. the published value of each standard substance. A smooth line is drawn through the points to complete the chart. A correction chart prepared in this way is shown in Figure 9.8. This chart is used to correct any melting point determined with that particular thermometer. Each thermometer requires its own calibration curve. A list of suitable standard substances for calibrating thermometers is provided in Table 9.1. The standard substances, of course, must be pure in order for the corrections to be valid.

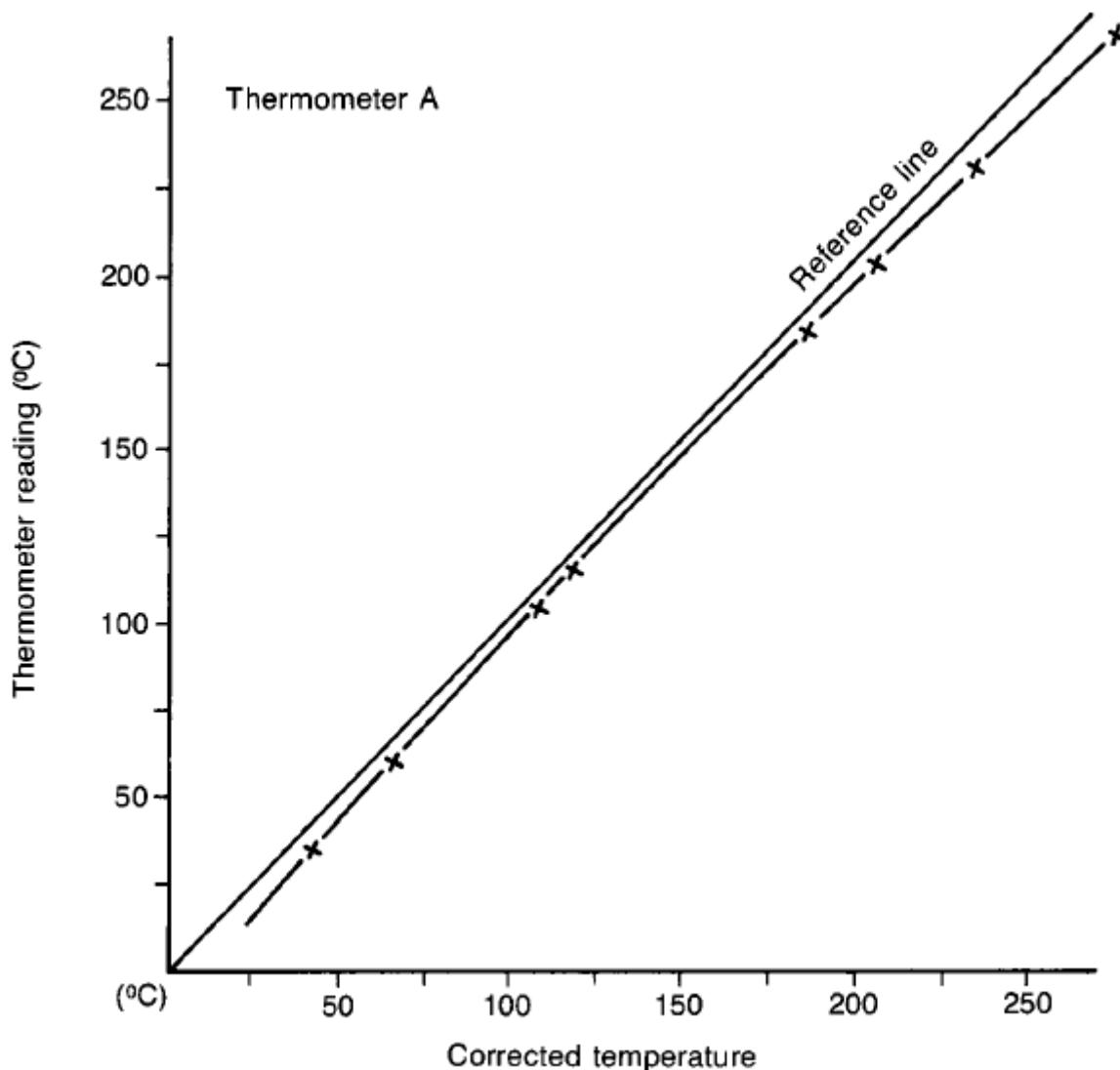


Figure 9.8 A thermometer-calibration curve.

TABLE 9.1 Melting-Point Standards

Compound	Melting Point (°C)
Ice (solid–liquid water)	0
Acetanilide	115
Benzamide	128
Urea	132
Succinic acid	189
3,5-Dinitrobenzoic acid	205

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 very 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.

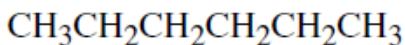
The reason for this behavior involves the nature of intermolecular forces of attraction. Although we will not be focusing on the nature of these forces, it is helpful to know what they are called. The force of attraction between polar molecules is called **dipole-dipole interaction**; between nonpolar 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.

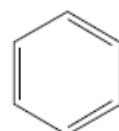
Guidelines for Predicting Polarity and Solubility

1. All hydrocarbons are nonpolar.

Examples:



Hexane

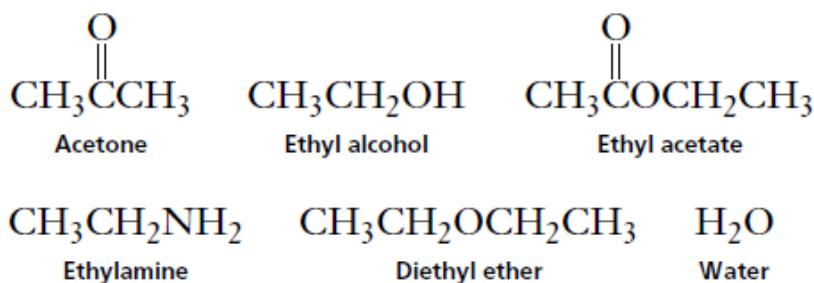


Benzene

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

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

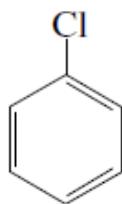
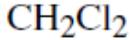
Examples:



The polarity of these compounds depends on the presence of polar C—O, C=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 of 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.

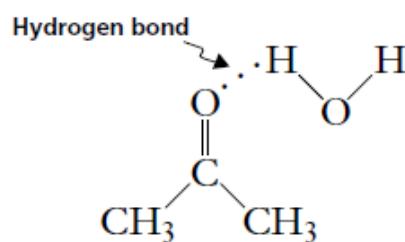
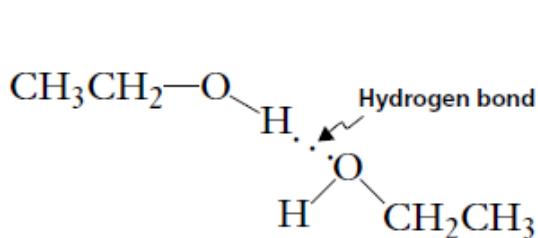
Examples:



Methylene chloride (dichloromethane) Chlorobenzene

4. When comparing organic compounds within the same family, note that adding carbon atoms to the chain decreases the polarity. For example, methyl alcohol (CH_3OH) is more polar than propyl alcohol ($\text{CH}_3\text{CH}_2\text{CH}_2\text{OH}$). 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 C_4) 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 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. Almost all organic compounds that are in the ionic form are water soluble (see next section B - Solutions in Which the Solute Ionizes and Dissociates).
10. The stability of the crystal lattice also affects solubility. Other things being equal, the higher the melting point (the more stable the crystal), 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 *ortho* (mp 147°C) and *meta* (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 above.

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. 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.

TABLE 10.1 Compounds in Increasing Order of Polarity

	Increasing Polarity
Aliphatic hydrocarbons	
Hexane (nonpolar)	
Aromatic hydrocarbons (π bonds)	
Benzene (nonpolar)	
Halocarbons	
Methylene chloride (slightly polar)	
Compounds with polar bonds	
Diethyl ether (slightly polar)	
Ethyl acetate (intermediate polarity)	
Acetone (intermediate polarity)	
Compounds with polar bonds and hydrogen bonding	
Ethyl alcohol (intermediate polarity)	
Methyl alcohol (intermediate polarity)	
Water (highly polar)	

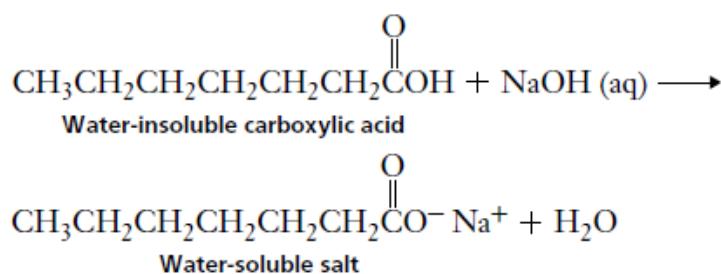
TABLE 10.2 Solvents in Increasing Order of Polarity**Increasing Polarity (Approximate)**

RH	Alkanes (hexane, petroleum ether)
ArH	Aromatics (benzene, toluene)
ROR	Ethers (diethyl ether)
RX	Halides ($\text{CH}_2\text{Cl}_2 > \text{CHCl}_3 > \text{CCl}_4$)
RCOOR	Esters (ethyl acetate)
RCOR	Aldehydes, ketones (acetone)
RNH ₂	Amines (triethylamine, pyridine)
ROH	Alcohols (methanol, ethanol)
RCONH ₂	Amides (N,N-dimethylformamide)
RCOOH	Organic acids (acetic acid)
H ₂ O	Water

B. Solutions in Which the Solute Ionizes and Dissociates

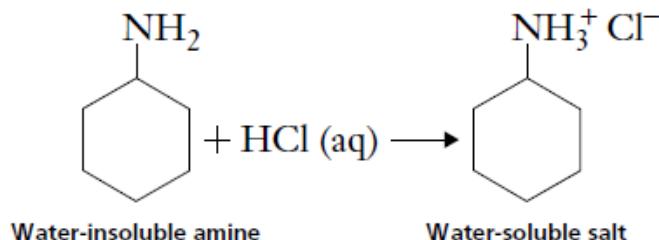
Many ionic compounds are highly soluble in water because of the strong attraction between ions and the highly polar water molecules. This also applies to organic compounds that can exist as ions. For example, sodium acetate consists of Na^+ and CH_3COO^- ions, which are highly soluble in water. Although 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:



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:



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).

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.

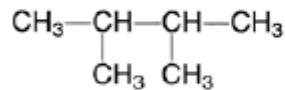
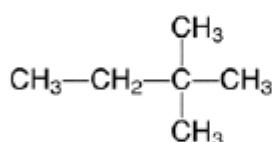
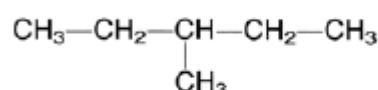
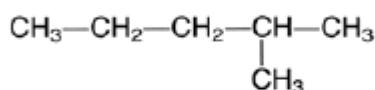
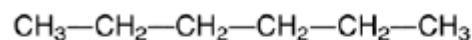
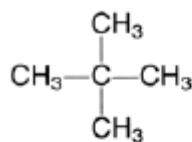
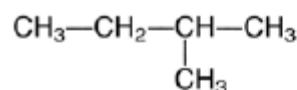
TABLE 10.3 Common Organic Solvents

Solvent	Bp (°C)	Solvent	Bp (°C)
Hydrocarbons		Ethers	
Pentane	36	Ether (diethyl)	35
Hexane	69	Dioxane ^a	101
Benzene ^a	80	1,2-Dimethoxyethane	83
Toluene	111	Others	
Hydrocarbon mixtures		Acetic acid	118
Petroleum ether	30–60	Acetic anhydride	140
Ligroin	60–90	Pyridine	115
Chlorocarbons		Acetone	56
Methylene chloride	40	Ethyl acetate	77
Chloroform ^a	61	Dimethylformamide	153
Carbon tetrachloride ^a	77	Dimethylsulfoxide	189
Alcohols			
Methanol	65		
Ethanol	78		
Isopropyl alcohol	82		

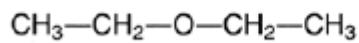
Note: Boldface type indicates flammability.

^aSuspect carcinogen.

The terms petroleum ether and ligroin are often confusing. Petroleum ether is a mixture of hydrocarbons with isomers of formulas C_5H_{12} and C_6H_{14} 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 commonly appear 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.



Petroleum ether
(a mixture of
alkanes)



Diethyl ether
(sometimes called
just "ether")

Figure 10.1 A comparison between "ether" (diethyl ether) and "petroleum ether."

Recrystallization: Purification of Solids

In most organic chemistry experiments, the desired product is first isolated in an impure form. If this product is a solid, the most common method of purification is recrystallization. The general technique involves dissolving the material to be recrystallized in a *hot* solvent (or solvent mixture) and cooling the solution slowly. The dissolved material has a decreased solubility at lower temperatures and will separate from the solution as it is cooled.

Recrystallization is an equilibrium process and produces very pure material. A small seed crystal is formed initially, and it then grows layer by layer in a reversible manner. In a sense, the crystal "selects" the correct molecules from the solution. In precipitation, the crystal lattice is formed so rapidly that impurities are trapped within the lattice. Therefore, any attempt at purification with too rapid a process should be avoided. Because the impurities are usually present in much smaller amounts than the compound being recrystallized, most of the impurities will remain in the solvent even when it is cooled. The purified substance can then be separated from the solvent and from the impurities by filtration.

The method of recrystallization described here is called **macroscale recrystallization**. This technique, which is carried out with an Erlenmeyer flask to dissolve the material and a Büchner funnel to filter the crystals, is normally used when the weight of solid to be recrystallized is more than 0.1 g. Another method, which is performed with a Craig tube, is used with smaller amounts of solid. Referred to as **microscale recrystallization**, this technique is discussed briefly in Section 11.4.

When the macroscale recrystallization procedure described in Section 11.3 is used

When the macroscale recrystallization procedure described in Section 11.3 is used with a Hirsch funnel, the procedure is sometimes referred to as a **semi-microscale recrystallization**. This procedure is commonly used in microscale work when the amount of solid is greater than 0.1 g or in macroscale work when the amount of solid is less than about 0.5 g.

PART A. THEORY

11.1 Solubility

The first problem in performing a recrystallization is selecting a solvent in which the material to be recrystallized shows the desired solubility behavior. In an ideal case, the material should be sparingly soluble at room temperature and yet quite soluble at the boiling point of the solvent selected. The solubility curve should be steep, as can be seen in line A of Figure 11.1. A curve with a low slope (line B) would not cause significant recrystallization when the temperature of the solution was lowered. A solvent in which the material is very soluble at all temperatures (line C) also would not be a suitable recrystallization solvent. The basic problem in performing a recrystallization is to select a solvent (or mixed solvent) that provides a steep solubility-vs.-temperature curve for the material to be recrystallized. A solvent that allows the

behavior shown in line A is an ideal recrystallization solvent. It should also be mentioned that solubility curves are not always linear, as they are depicted in Figure 11.1. This figure represents an idealized form of solubility behavior. The solubility curve for sulfanilamide in 95% ethyl alcohol, shown in Figure 11.2, is typical of many organic compounds and shows what solubility behavior might look like for a real substance.

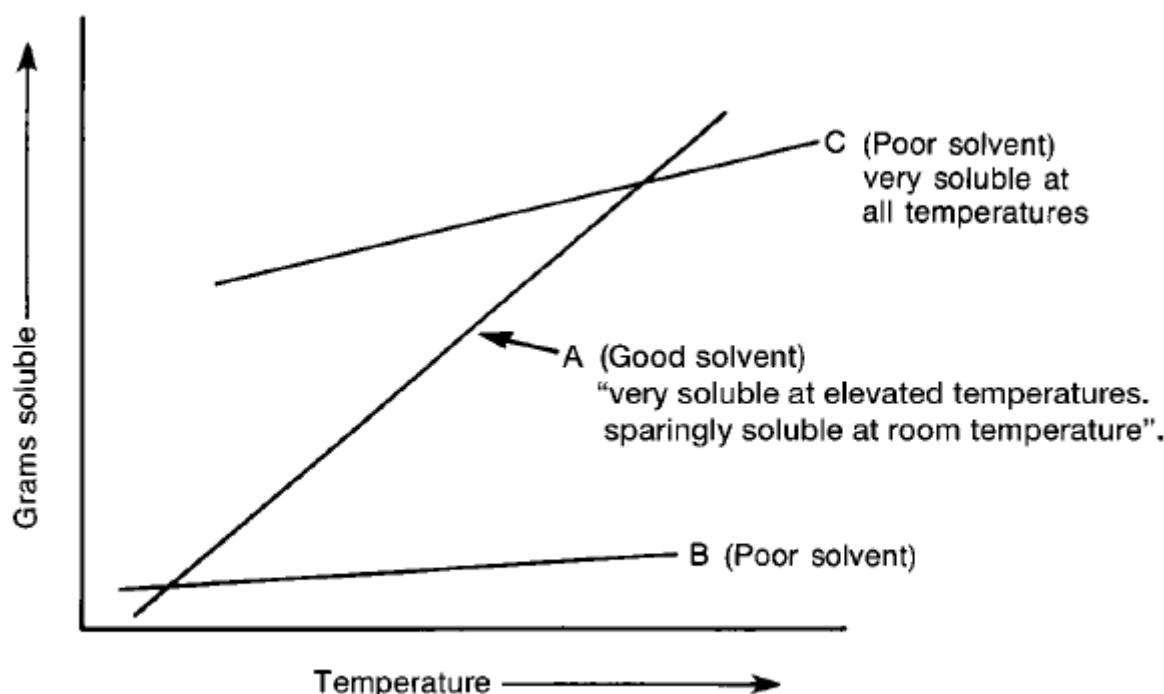


Figure 11.1 Graph of solubility vs. temperature.

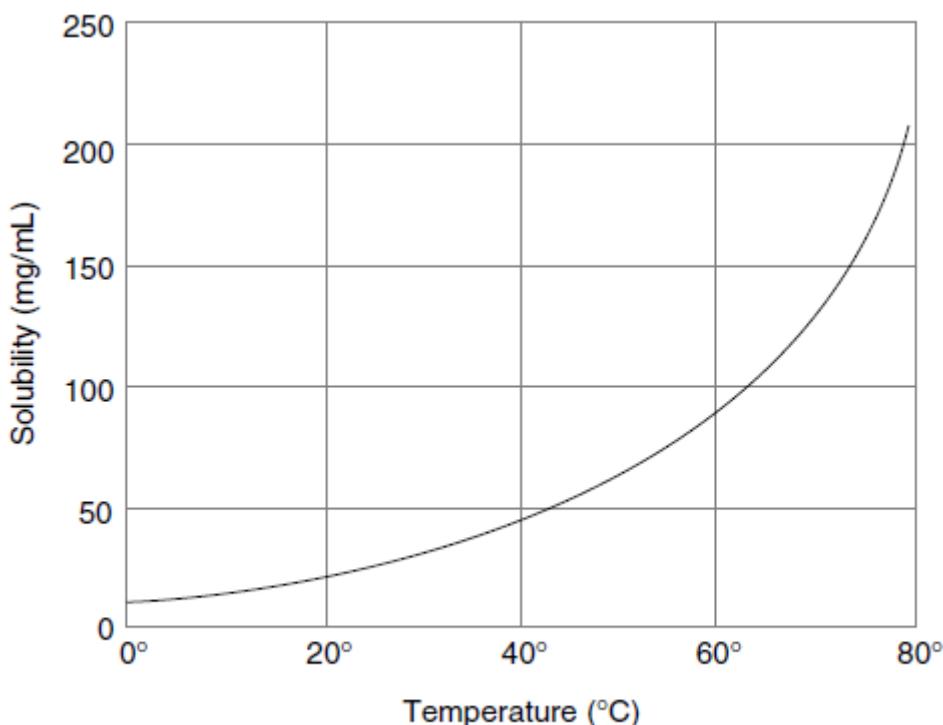


Figure 11.2 Solubility of sulfanilamide in 95% ethyl alcohol.

The solubility of organic compounds is a function of the polarities of both the solvent and the solute (dissolved material). A general rule is “Like dissolves like.” If the solute is very polar, a very polar solvent is needed to dissolve it; if the solute is nonpolar, a nonpolar solvent is needed. Applications of this rule are discussed extensively in Technique 10, Section 10.2, and in Technique 11, Section 11.5.

11.2 Theory Of Recrystallization

A successful recrystallization depends on a large difference between the solubility of a material in a hot solvent and its solubility in the same solvent when it is cold. When the impurities in a substance are equally soluble in both the hot and the cold solvent, an effective purification is not easily achieved through recrystallization. A material can be purified by recrystallization when both the desired substance and the impurity have similar solubilities, but only when the impurity represents a small fraction of the total solid. The desired substance will recrystallize on cooling, but the impurities will not.

For example, consider a case in which the solubilities of substance A and its impurity B are both 1 g/100 mL of solvent at 20°C and 10 g/100 mL of solvent at 100°C. In the impure sample of A, the composition is 9 g of A and 2 g of B. In the calculations for this example, it is assumed that the solubilities of both A and B are unaffected by the presence of the other substance. To make the calculations easier to understand, 100 mL of solvent are used in each recrystallization. Normally, the minimum amount of solvent required to dissolve the solid would be used.

At 20°C, this total amount of material will not dissolve in 100 mL of solvent. However, if the solvent is heated to 100°C, all 11 g dissolve. The solvent has the capacity to dissolve 10 g of A *and* 10 g of B at this temperature. If the solution is cooled to 20°C, only 1 g of each solute can remain dissolved, so 8 g of A and 1 g of B recrystallize, leaving 2 g of material in the solution. This crystallization is shown in Figure 11.3. The solution that remains after a recrystallization is called the **mother liquor**. If the process is now repeated by treating the crystals with 100 mL of fresh solvent, 7 g of A will recrystallize again, leaving 1 g of A and 1 g of B in the mother liquor. As a result of these operations, 7 g of pure A are obtained, but with the loss of 4 g of material (2 g of A plus 2 g of B). Again, this second recrystallization step is illustrated in Figure 11.3. The final result illustrates an important aspect of recrystallization—it is wasteful. Nothing can be done to prevent this waste; some A must be lost along with the impurity B for the method to be successful. Of course, if the impurity B were *more* soluble than A in the solvent, the losses would be reduced.

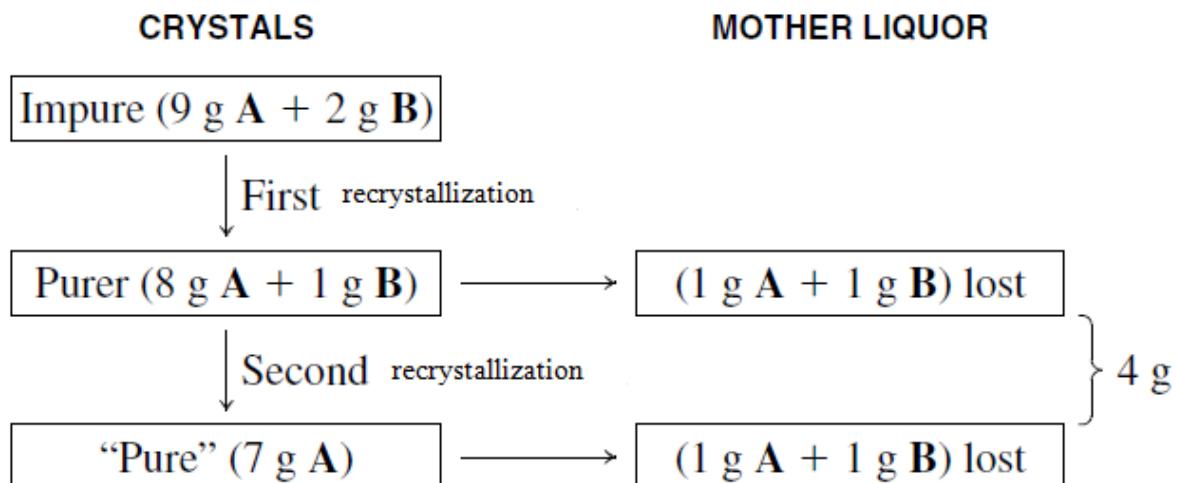


Figure 11.3 Purification of a mixture by recrystallization

Losses could also be reduced if the impurity were present in *much smaller* amounts than the desired material.

Note that in the preceding case, the method operated successfully because A was present in substantially larger quantity than its impurity B. If there had been a 50–50 mixture of A and B initially, no separation would have been achieved. In general, a recrystallization is successful only if there is a *small* amount of impurity. As the amount of impurity increases, the loss of material must also increase. Two substances with nearly equal solubility behavior, present in equal amounts, cannot be separated. If the solubility behavior of two components present in equal amounts is different, however, a separation or purification is frequently possible.

As illustrated in this example, a second crystallization results in purer crystals, but the yield is lower.

In some experiments, you will be instructed to cool the recrystallizing mixture in an ice-water bath before collecting the crystals by filtration. Cooling the mixture increases the yield by decreasing the solubility of the substance; however, even at this reduced temperature, some of the product will be soluble in the solvent. It is not possible to recover all your product in a recrystallization procedure even when the mixture is cooled in an ice-water bath. A good example of this is illustrated by the solubility curve for sulfanilamide shown in Figure 11.2. The solubility of sulfanilamide at 0°C is still significant, 14 mg/mL.

The recrystallization technique described in this section is used when the weight of solid to be crystallized is more than 0.1 g. There are four main steps in a macroscale recrystallization :

1. Dissolving the solid
2. Removing insoluble impurities (when necessary)
3. Crystallizing
4. Collecting and drying

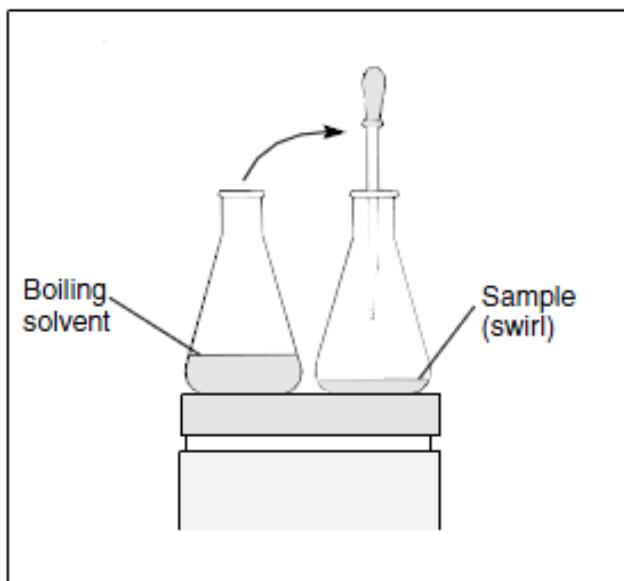
These steps are illustrated in Figure 11.4. An Erlenmeyer flask of an appropriate size must be chosen. It should be pointed out that a microscale crystallization with a Craig tube involves the same four steps, although the apparatus and procedures are somewhat different (see Section 11.4).

A. Dissolving the Solid

To minimize losses of material to the mother liquor, it is desirable to *saturate* the boiling solvent with solute. This solution, when cooled, will return the maximum possible amount of solute as crystals. To achieve this high return, the solvent is brought to its boiling point, and the solute is dissolved in the *minimum amount* (!) of *boiling solvent*. For this procedure, it is advisable to maintain a container of boiling solvent (on a hot plate). From this container, a small portion (about 1–2 mL) of the solvent is added to the Erlenmeyer flask containing the solid to be recrystallized, and this mixture is heated while swirling occasionally until it resumes boiling.

CAUTION

Do not heat the flask containing the solid until after you have added the first portion of solvent.



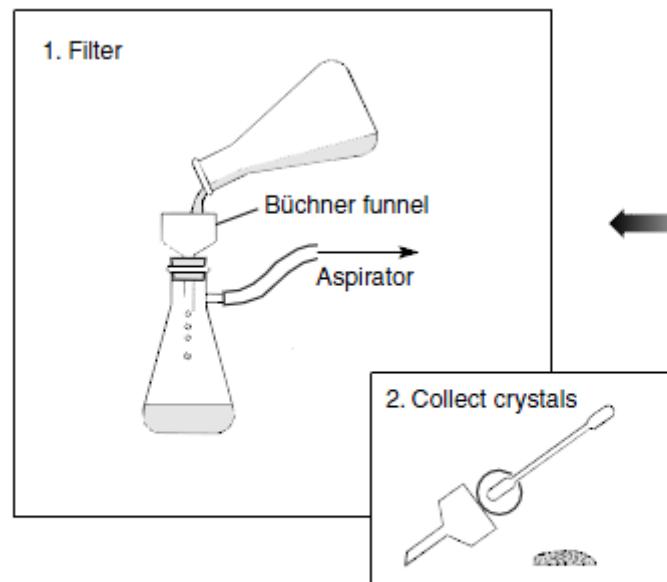
For options, see Figure 11.5.

- A. Decantation
- B. Fluted filter
- C. Filtering pipet

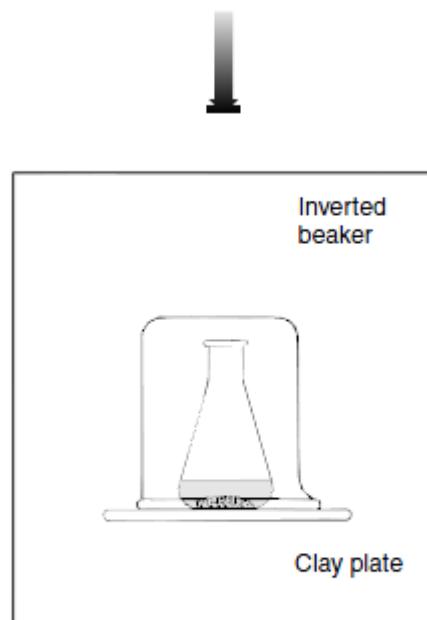
(Use A, B, or C, or omit.)

Step 1 Dissolve the solid by adding small portions of hot solvent.

Step 2 (Optional) Remove insoluble impurities if necessary.



Step 4 Collect crystals with a Büchner funnel.



Step 3 Set aside to cool and crystallize.

Figure 11.4 Steps in a macroscale recrystallization (no decolorization).

If the solid does not dissolve in the first portion of boiling solvent, then another small portion of boiling solvent is added to the flask. The mixture is swirled and heated again until it resumes boiling. If the solid dissolves, no more solvent is added. But if the solid has not dissolved, another portion of boiling solvent is added, as before, and the process is repeated until the solid dissolves. It is important to stress that the portions of solvent added each time are small, so only the *minimum* amount of solvent necessary for dissolving the solid is added. It is also important to emphasize that the procedure requires the addition of solvent to solid.

You must never add portions of solid to a fixed quantity of boiling solvent. By this latter method, it may be impossible to determine when saturation has been achieved. This entire procedure should be performed fairly rapidly, or you may lose solvent through evaporation nearly as quickly as you are adding it, and this procedure will then take a very long time. This is most likely to happen when using highly volatile solvents such as methyl alcohol or ethyl alcohol. The time from the first addition of solvent until the solid dissolves completely should not be longer than 15–20 minutes.

Comments on This Procedure for Dissolving the Solid

1. One of the most common mistakes is to add too much solvent. This can happen most easily if the solvent is not hot enough or if the mixture is not stirred sufficiently. If too much solvent is added, the percentage recovery will be reduced; it is even possible that no crystals will form when the solution is cooled. If too much solvent is added, you must evaporate the excess by heating the mixture. A nitrogen or air stream directed into the container will accelerate the evaporation process (see Technique 7, Section 7.10).
2. It is very important not to heat the solid until you have added some solvent. Otherwise, the solid may melt and possibly form an oil or decompose, and it may not crystallize easily (see Section 11.5).
3. It is also important to use an Erlenmeyer flask rather than a beaker for performing the crystallization. A beaker should not be used because the large opening allows the solvent to evaporate too rapidly and allows dust particles to get in too easily.

4. In some experiments, a specified amount of solvent for a given weight of solid will be recommended. In these cases, you should use the amount specified rather than the minimum amount of solvent necessary to dissolve the solid. The amount of solvent recommended has been selected to provide the optimum conditions for good crystal formation.
5. Occasionally, you may encounter an impure solid that contains small particles of insoluble impurities, pieces of dust, or paper fibers that will not dissolve in the hot crystallizing solvent. A common error is to add too much of the hot solvent in an attempt to dissolve these small particles, not realizing that they are insoluble. In such cases, you must be careful not to add too much solvent.
6. It is sometimes necessary to decolorize the solution by adding activated charcoal or by passing the solution through a column containing alumina or silica gel. A decolorization step should be performed only if the mixture is *highly* colored and it is clear that the color is due to impurities and not due to the actual color of the substance being crystallized. If decolorization is necessary, it should be accomplished before the following filtration step.

B. Removing Insoluble Impurities

It is necessary to use one of the following three methods only if insoluble material remains in the hot solution or if decolorizing charcoal has been used.

CAUTION

Indiscriminate use of the procedure can lead to needless loss of your product.

Decantation is the easiest method of removing solid impurities and should be considered first. If filtration is required, a filtering pipet is used when the volume of liquid to be filtered is less than 10 mL, and you should use gravity filtration through a fluted filter when the volume is 10 mL or greater. These three methods are illustrated in Figure 11.5, and each is discussed below.

Decantation. If the solid particles are relatively large in size or they easily settle to the bottom of the flask, it may be possible to separate the hot solution from the impurities by carefully pouring off the liquid, leaving the solid behind. This is accomplished most easily by holding a glass stirring rod along the top of the flask and tilting the flask so that the liquid pours out along one end of the glass rod into another container. A technique similar in principle to decantation, which may be easier to perform with smaller amounts of liquid, is to use a preheated Pasteur pipet to remove the hot solution. With this method, it may be helpful to place the tip of the pipet against the bottom of the flask when removing the last portion of solution. The small space between the tip of the pipet and the inside surface of the flask prevents solid material from being drawn into the pipet. An easy way to preheat the pipet is to draw up a small portion of hot *solvent* (not the *solution* being transferred) into the pipet and expel the liquid. Repeat this process several times.

Fluted Filter. This method is the most effective way to remove solid impurities when the volume of liquid is greater than 10 mL or when decolorizing charcoal has been used . You should first add a

small amount of extra solvent to the hot mixture. This action helps prevent crystal formation in the filter paper or the stem of the funnel during the filtration. The funnel is then fitted with a fluted filter and installed at the top of the Erlenmeyer flask to be used for the actual filtration. It is advisable to place a small piece of wire between the funnel and the mouth of the flask to relieve any increase in pressure caused by hot filtrate.

The Erlenmeyer flask containing the funnel and fluted paper is placed on top of a hot plate (low setting). The liquid to be filtered is brought to its boiling point and poured through the filter in portions. (If the volume of the mixture is less than 10 mL, it may be more convenient to transfer the mixture to the filter with a pre-heated Pasteur pipet.) It is necessary to keep the solutions in both flasks at their boiling temperatures to prevent premature crystallization. The refluxing action of the filtrate keeps the funnel warm and reduces the chance that the filter will clog with crystals that may have formed during the filtration. With low-boiling solvents, be aware that some solvent may be lost through evaporation. Consequently, extra solvent must be added to make up for this loss. If crystals begin to form in the filter during filtration, a minimum amount of boiling solvent is added to redissolve the crystals and to allow the solution to pass through the funnel. If the volume of liquid being filtered is less than 10 mL, a small amount of hot solvent should be used to rinse the filter after all the filtrate has been collected. The rinse solvent is then combined with the original filtrate.

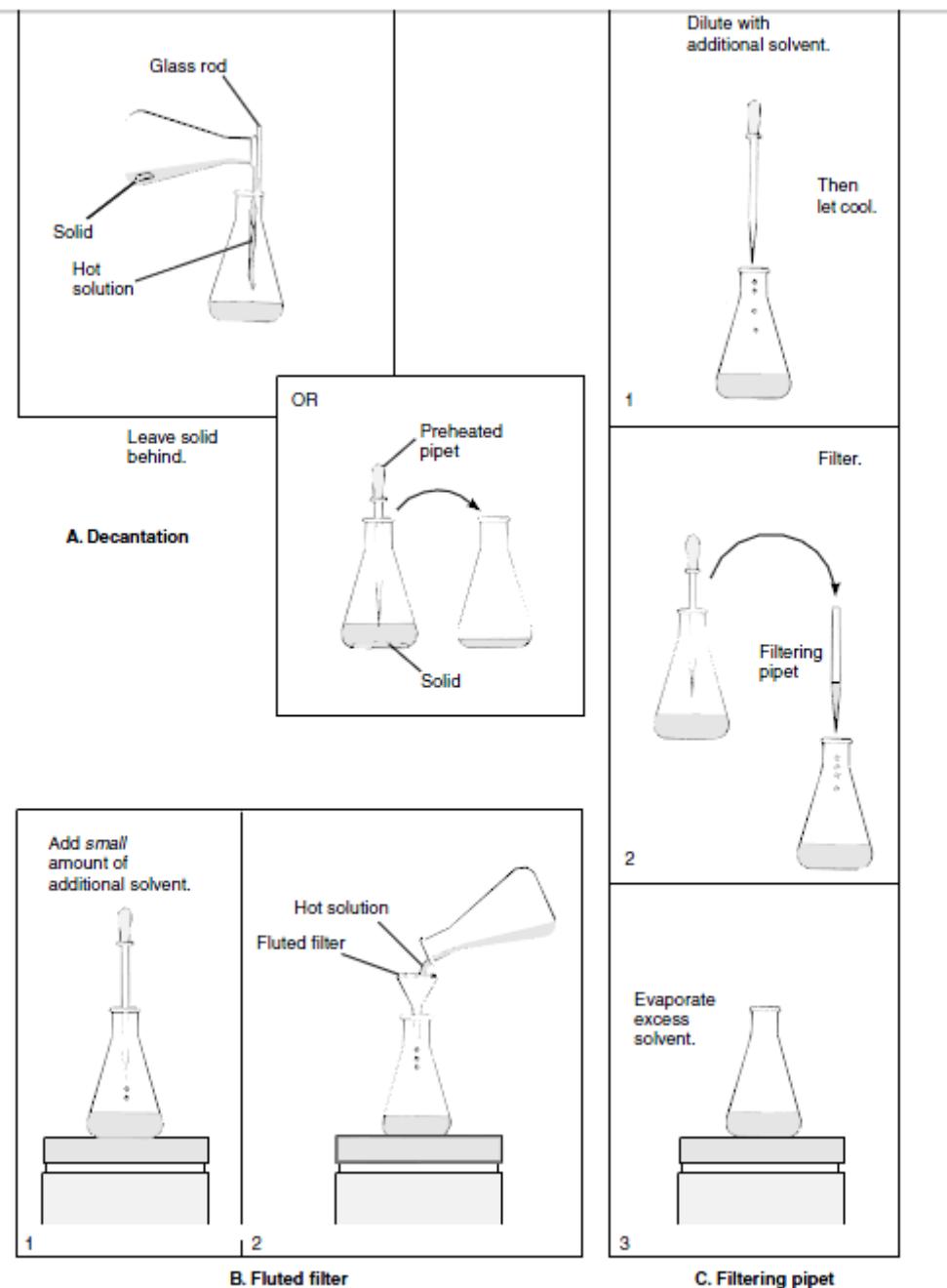


Figure 11.5 Methods for removing insoluble impurities in a macroscale recrystallization

After the filtration, it may be necessary to remove extra solvent by evaporation until the solution is once again saturated at the boiling point of the solvent

Filtering Pipet. If the volume of solution after dissolving the solid in hot solvent is less than 10 mL, gravity filtration with a filtering pipet may be used to remove solid impurities. However, using a filtering pipet to filter a hot solution saturated with solute can be difficult without premature recrystallization. The best way to prevent this from occurring is to add enough solvent to dissolve the desired product at room temperature (be sure not to add too much solvent) and perform the filtration at room temperature, as described in Technique 8, Section 8.1C. After filtration, the excess solvent is evaporated by boiling until the solution is saturated at the boiling point of the mixture (see Technique 7, Section 7.10). If powdered decolorizing charcoal was used, it will probably be necessary to perform two filtrations with a filtering pipet to remove all of the charcoal, or a fluted filter can be used.

C. recrystallization

An Erlenmeyer flask, not a beaker, should be used for recrystallization. The large open top of a beaker makes it an excellent dust catcher. The narrow opening of the Erlenmeyer flask reduces contamination by dust and allows the flask to be stoppered if it is to be set aside for a long period. Mixtures set aside for long periods must be stoppered after cooling to room temperature to prevent evaporation of solvent. If all of the solvent evaporates, no purification is achieved, and the crystals originally formed become coated with the dried contents of the mother liquor.

Even if the time required for crystallization to occur is relatively short, it is advisable to cover the top of the Erlenmeyer flask with a small watch glass or inverted beaker to prevent evaporation of solvent while the solution is cooling to room temperature.

The chances of obtaining pure crystals are improved if the solution cools to room temperature slowly. When the volume of solution is 10 mL or less, the solution is likely to cool more rapidly than is desired. This can be prevented by placing the flask on a surface that is a poor heat conductor and covering the flask with a beaker to provide a layer of insulating air. Appropriate surfaces include a clay plate or several pieces of filter paper on top of the laboratory bench. It may also be helpful to use a clay plate that has been warmed slightly on a hot plate or in an oven.

After crystallization has occurred, it is sometimes desirable to cool the flask in an ice-water bath. Because the solute is less soluble at lower temperatures, this will increase the yield of crystals.

If a cooled solution does not crystallize, it will be necessary to induce crystallization. Several techniques are described in Section 11.8A.

D. Collecting and Drying

After the flask has been cooled, the crystals are collected by vacuum filtration through a Büchner (or Hirsch) funnel.

The crystals should be washed with a small amount of *cold* solvent to remove any

mother liquor adhering to their surface. Hot or warm solvent will dissolve some of the crystals. The crystals should then be left for a short time (usually 5–10 minutes) in the funnel, where air, as it passes, will dry them free of most of the solvent. It is often wise to cover the Büchner funnel with an oversized filter paper or towel during this air drying. This precaution prevents accumulation of dust in the crystals. When the crystals are nearly dry, they should be gently scraped off the filter paper (so paper fibers are not removed with the crystals) onto a watch glass or clay plate for further drying (see Section 11.9).

The four steps in a macroscale recrystallization are summarized in Table 11.1.

TABLE 11.1 Steps in a Macroscale recrystallization

A. Dissolving the Solid

1. Find a solvent with a steep solubility-vs.-temperature characteristic (done by trial and error using small amounts of material or by consulting a handbook).
2. Heat the desired solvent to its boiling point.
3. Dissolve the solid in a minimum of boiling solvent in a flask.
4. If necessary, add decolorizing charcoal or decolorize the solution on a silicagel or alumina column.

B. Removing Insoluble Impurities

1. Decant or remove the solution with a Pasteur pipet.
2. Alternatively, filter the hot solution through a fluted filter, a filtering pipet, or a

filter-tip pipet to remove insoluble impurities or charcoal.

NOTE: If no decolorizing charcoal has been added or if there are no undissolved particles, Part B should be omitted.

C. Crystallizing

1. Allow the solution to cool.
2. If crystals appear, cool the mixture in an ice-water bath (if desired) and go to Part D. If crystals do not appear, go to the next step.
3. Inducing crystallization.
 - a. Scratch the flask with a glass rod.
 - b. Seed the solution with original solid, if available.
 - c. Cool the solution in an ice-water bath.
 - d. Evaporate excess solvent and allow the solution to cool again.

D. Collecting and Drying

1. Collect crystals by vacuum filtration using a Büchner funnel.
2. Rinse crystals with a small portion of cold solvent.
3. Continue suction until crystals are nearly dry.
4. Drying (three options).
 - a. Air-dry the crystals.
 - b. Place the crystals in a drying oven.
 - c. Dry the crystals under a vacuum.

PART C. MICROSCALE RECRYSTALLIZATION

11.4 Microscale recrystallization

In many microscale experiments, the amount of solid to be recrystallized is small enough (generally less than 0.1 g) that a Craig tube is the preferred method for recrystallization. The main advantage of the Craig tube is that it minimizes the number of transfers of solid material, thus resulting in a greater yield of crystals. Also, the separation of the crystals from the mother liquor with the Craig tube is very efficient, and little time is required for drying the crystals. The steps involved are, in principle, the same as those performed when a recrystallization is accomplished with an Erlenmeyer flask and a Büchner funnel.

The solid is transferred to the Craig tube, and small portions of hot solvent are added to the tube while the mixture is stirred with a spatula and heated. If there are any insoluble impurities present, they can be removed with a filter-tip pipet. The inner plug is then inserted into the Craig tube and the hot solution is cooled slowly to room temperature. When the crystals have formed, the Craig tube is placed into a centrifuge tube, and the crystals are separated from the mother liquor by centrifugation. The crystals are then scraped off the end of the inner plug or from inside the Craig tube onto a watch glass or piece of paper. Minimal drying will be necessary (see Section 11.9).

PART D. ADDITIONAL EXPERIMENTAL CONSIDERATIONS MACROSCALE AND MICROSCALE

11.5 Selecting a Solvent

A solvent that dissolves little of the material to be recrystallized when it is cold but a great deal of the material when it is hot is a good solvent for recrystallization. Quite often, correct recrystallization solvents are indicated in the experimental procedures that you will be following. When a solvent is not specified in a procedure, you can determine a good recrystallization solvent by consulting a handbook or making an educated guess based on polarities, both discussed in this section. A third approach, involving experimentation, is discussed in Section 11.6.

With compounds that are well known, the correct recrystallization solvent has already been determined through the experiments of earlier researchers. In such cases, the chemical literature can be consulted to determine which solvent should be used. Sources such as *The Merck Index* or the *CRC Handbook of Chemistry and Physics* may provide this information.

For example, consider naphthalene, which is found in *The Merck Index*. It states under the entry for naphthalene: "Monoclinic prismatic plates from ether." This statement means that naphthalene can be recrystallized from ether. It also gives the type of crystal structure. Unfortunately, the crystal structure may be given without reference to the solvent. Another way to determine the best solvent is by looking at solubility-vs.-temperature data. When this is given, a good solvent is one in which the solubility of the compound increases significantly as the temperature increases.

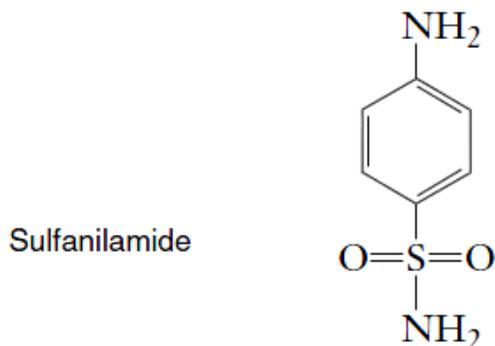
Sometimes, the solubility data will be given for only cold solvent and boiling solvent. This should provide enough information to determine whether this would be a good solvent for recrystallization.

In most cases, however, the handbooks will state only whether a compound is soluble or not in a given solvent, usually at room temperature. Determining a good solvent for recrystallization from this information can be somewhat difficult. The solvent in which the compound is soluble may or may not be an appropriate solvent

for recrystallization. Sometimes, the compound may be too soluble in the solvent at all temperatures, and you would recover very little of your product if this solvent were used for recrystallization. It is possible that an appropriate solvent would be the one in which the compound is nearly insoluble at room temperature because the solubility-vs.-temperature curve is very steep. Although the solubility information may give you some ideas about what solvents to try, you will most likely need to determine a good recrystallizing solvent by experimentation as described in Section 11.6.

When using *The Merck Index* or *Handbook of Chemistry and Physics*, you should be aware that alcohol is frequently listed as a solvent. This generally refers to 95% or 100% ethyl alcohol. Because 100% (absolute) ethyl alcohol is more expensive than 95% ethyl alcohol, the cheaper grade is usually used in the chemistry laboratory. Another solvent frequently listed is benzene. Benzene is a known carcinogen, so it is rarely used in student laboratories. Toluene is a suitable substitute; the solubility behavior of a substance in benzene and toluene is so similar that you may assume any statement made about benzene also applies to toluene.

Another way to identify a solvent for recrystallization is to consider the polarities of the compound and the solvents. Generally, you would look for a solvent that has a polarity somewhat similar to that of the compound to be recrystallized. Consider the compound sulfanilamide, shown in the figure. There are several polar bonds in sulfanilamide, the NH and the SO bonds. In addition, the NH₂ groups and the oxygen



atoms in sulfanilamide can form hydrogen bonds. Although the benzene ring portion of sulfanilamide is nonpolar, sulfanilamide has an intermediate polarity because of the polar groups. A common organic solvent of intermediate polarity is 95% ethyl alcohol. Therefore, it is likely that sulfanilamide would be soluble in 95% ethyl alcohol because they have similar polarities. (Note that the other 5% in 95% ethyl alcohol is usually a substance such as water or isopropyl alcohol, which does not alter the overall polarity of the solvent.) Although this kind of analysis is a good first step in determining an appropriate solvent for recrystallization, without more information it is not enough to predict the shape of the solubility curve for the temperature-vs.-solubility data (see Figure 11.1). Therefore, knowing that sulfanilamide is soluble in 95% ethyl alcohol does not necessarily mean that this is a good solvent for recrystallizing sulfanilamide. You would still need to test the solvent to see if it is appropriate. The solubility curve for sulfanilamide (see Figure 11.2) indicates that 95% ethyl alcohol is a good solvent for recrystallizing this substance.

When choosing a recrystallization solvent, do not select one whose boiling point is higher than the melting point of the substance (solute) to be recrystallized. If the boiling point of the solvent is too high, the substance may come out of solution as a liquid rather than a crystalline solid. In such a case, the solid may oil out. Oiling out occurs when upon cooling the solution to induce crystallization, the solute begins to come out of solution at a temperature above its melting point. The solute will then come out of solution as a liquid. Furthermore, as cooling continues, the substance may still not crystallize; rather, it will become a supercooled liquid. Oils may eventually solidify if the temperature is lowered, but often they will not actually crystallize. Instead, the solidified oil will be an amorphous solid or a hardened mass. In this case, purification of the substance will not have occurred as it does when the solid is crystalline. It can be very difficult to deal with oils when trying to obtain a pure substance. You must try to redissolve them and hope that the substance will crystallize with slow, careful cooling. During the cooling period, it may be helpful to scratch the glass container where the oil is present with a glass stirring rod that has not been fire polished. Seeding the oil as it cools with a small sample of the original solid is another technique that is sometimes helpful in working with difficult oils. Other methods of inducing crystallization are discussed in Section 11.8.

One additional criterion for selecting the correct recrystallization solvent is the volatility of that solvent. Volatile solvents have low boiling points or evaporate easily. A solvent with a low boiling point may be removed from the crystals through evaporation without much difficulty. It will be difficult to remove a solvent with a high boiling point from the crystals without heating them under vacuum. On the other hand, solvents with very low boiling points are not ideal for recrystallizations. The recovery will not be as great with low-boiling solvents because they cannot be heated past the boiling point. Diethyl ether ($\text{bp} = 35^\circ\text{C}$) and methylene chloride ($\text{bp} = 41^\circ\text{C}$) are not often used as recrystallization solvents.

Table 11.2 lists common recrystallization solvents. The solvents used most commonly are listed in the table first.

TABLE 11.2 Common Solvents for Crystallization

	Boils (°C)	Freezes (°C)	Soluble in H ₂ O	Flammability
Water	100	0	+	—
Methanol	65	*	+	+
95% Ethanol	78	*	+	+
Ligroin	60–90	*	—	+
Toluene	111	*	—	+
Chloroform**	61	*	—	—
Acetic acid	118	17	+	+
Dioxane**	101	11	+	+
Acetone	56	*	+	+
Diethyl ether	35	*	Slightly	++
Petroleum ether	30–60	*	—	++
Methylene chloride	41	*	—	—
Carbon tetrachloride**	77	*	—	—

* Lower than 0°C (ice temperature).

** Suspected carcinogen.

11.6 Testing Solvents for Crystallization

When the appropriate solvent is not known, select a solvent for recrystallization by experimenting with various solvents and a very small amount of the material to be recrystallized. Experiments are conducted on a small test tube scale before the entire quantity of material is committed to a particular solvent. Such trial-and-error methods are common when trying to purify a solid material that has not been previously studied.

Procedure

1. Place about 0.05 g of the sample in a test tube.
2. Add about 0.5 mL of solvent at room temperature and stir the mixture by rapidly twirling a microspatula between your fingers. If all (or almost all) of the solid dissolves at room temperature, then your solid is *probably* too soluble in this solvent and little compound would be recovered if this solvent were used. Select another solvent.
3. If none (or very little) of the solid dissolves at room temperature, heat the tube carefully and stir with a spatula. (A hotwater bath is perhaps better than an aluminum block because you can more easily control the temperature of the hot-water bath. The temperature of the hot-water bath should be slightly higher than the boiling point of the solvent.) Add more solvent dropwise, while continuing to heat and stir. Continue adding solvent until the solid dissolves, but do not add more than about 1.5 mL (total) of solvent. If all of the solid dissolves, go to step 4. If all of the solid has not dissolved by the time you have added 1.5 mL of solvent, this is probably not a good solvent. However, if most of the solid has dissolved at this point, you might try adding a little more solvent. Remember to heat and stir at all times during this step.
4. If the solid dissolves in about 1.5 mL or less of boiling solvent, then remove the test tube from the heat source, stopper the tube, and allow it to cool to room temperature. Then place it in an ice-water bath. If a lot of crystals come out, this is most likely a good solvent. If crystals do not come out, scratch the sides of the tube with a glass stirring rod to induce crystallization. If crystals still do not form, this is probably not a good solvent.

Comments about This Procedure

1. Selecting a good solvent is something of an art. There is no perfect procedure that can be used in all cases. You must think about what you are doing and use some common sense in deciding whether to use a particular solvent.
2. Do not heat the mixture above the melting point of your solid. This can occur most easily when the boiling point of the solvent is higher than the melting point of the solid. Normally, do not select a solvent that has a higher boiling point than the melting point of the substance. If you do, make certain that you do not heat the mixture beyond the melting point of your solid.

11.7 Decolorization

Small amounts of highly colored impurities may make the original recrystallization solution appear colored; this color can often be removed by decolorization, either by using activated charcoal (often called Norit) or by passing the solution through a column packed with alumina or silica gel. A decolorizing step should be performed only if the color is due to impurities, not due to the color of the desired product, and if the color is significant. Small amounts of colored impurities will remain in solution during crystallization, making the decolorizing step unnecessary. The use of activated charcoal is described separately for macroscale and microscale crystallizations, and the column technique, which can be used with both crystallization techniques, is then described.

A. Macroscale—Powdered Charcoal

As soon as the solute is dissolved in the minimum amount of boiling solvent, the solution is allowed to cool slightly, and a small amount of Norit (powdered charcoal)

is added to the mixture. The Norit adsorbs the impurities. When performing a recrystallization in which the filtration is performed with a fluted filter, you should add powdered Norit because it has a larger surface area and can remove impurities more effectively. A reasonable amount of Norit is what could be held on the end of a microspatula, or about 0.01–0.02 g. If too much Norit is used, it will adsorb product as well as impurities. A small amount of Norit should be used, and its use should be repeated if necessary. (It is difficult to determine if the initial amount added is sufficient until after the solution is filtered, because the suspended particles of charcoal will obscure the color of the liquid.) Caution should be exercised so that the solution does not froth or erupt when the finely divided charcoal is added. The mixture is boiled with the Norit for several minutes and then filtered by gravity, using a fluted filter, and the recrystallization is carried forward as described in Section 11.3.

The Norit preferentially adsorbs the colored impurities and removes them from the solution. The technique seems to be most effective with hydroxylic solvents. In using Norit, be careful not to breathe the dust. Normally, small quantities are used so that little risk of lung irritation exists.

B. Microscale—Pelletized Norit

If the crystallization is being performed in a Craig tube, it is advisable to use pelletized Norit. Although this is not as effective in removing impurities as powdered Norit, it is easier to remove, and the amount of pelletized Norit required is more easily determined because you can see the solution as it is being decolorized. Again, the Norit is added to the hot solution (the solution should not be boiling) after the solid has dissolved. This should be performed in a test tube rather than in a Craig tube.

About 0.02 g is added, and the mixture is boiled for a minute or so to see if more Norit is required. More Norit is added, if necessary, and the liquid is boiled again. It is important not to add too much pelletized Norit because the Norit will also adsorb some of the desired material, and it is possible that not all of the color can be removed no matter how much Norit is added. The decolorized solution is then removed with a preheated filter-tip pipet (see Technique 8, Section 8.6) to filter the mixture and transferred to a Craig tube for crystallization as described in Section 11.4.

C. Decolorization on a Column

The other method for decolorizing a solution is to pass the solution through a column containing alumina or silica gel. The adsorbent removes the colored impurities while allowing the desired material to pass through

If this technique is used, it will be necessary to dilute the solution with additional solvent to prevent crystallization from occurring during the process. The excess solvent must be evaporated after the solution is passed through the column, and the recrystallization procedure is continued as described in Sections 11.3 or 11.4.

11.8 Inducing Crystallization

If a cooled solution does not crystallize, several techniques may be used to induce crystallization. Although identical in principle, the actual procedures vary slightly when performing macroscale and microscale recrystallizations.

A. Macroscale

In the first technique, you should try scratching the inside surface of the flask vigorously with a glass rod that *has not been* fire polished. The motion of the rod should

be vertical (in and out of the solution) and should be vigorous enough to produce an audible scratching. Such scratching often induces crystallization, although the effect is not well understood. The high-frequency vibrations may have something to do with initiating crystallization; or perhaps—a more likely possibility—small amounts of solution dry by evaporation on the side of the flask, and the dried solute is pushed into the solution. These small amounts of material provide “seed crystals,” or nuclei, on which crystallization may begin.

A second technique that can be used to induce crystallization is to cool the solution in an ice bath. This method decreases the solubility of the solute.

A third technique is useful when small amounts of the original material to be recrystallized are saved. The saved material can be used to “seed” the cooled solution. A small crystal dropped into the cooled flask often will start the crystallization—this is called **seeding**.

If all of these measures fail to induce crystallization, it is likely that too much solvent was added. The excess solvent must then be evaporated
and the solution allowed to cool.

B. Microscale

The strategy is basically the same as described for macroscale recrystallizations. Scratching vigorously with a glass rod *should be avoided*, however, because the Craig tube is fragile and expensive. Scratching *gently* is allowed.

Another measure is to dip a spatula or glass stirring rod into the solution and allow the solvent to evaporate so that a small amount of solid will form on the surface of the spatula or glass rod. When placed back into the solution, the solid will seed the solution. A small amount of the original material, if some was saved, may also be used to seed the solution.

A third technique is to cool the Craig tube in an ice-water bath. This method may also be combined with either of the previous suggestions.

If none of these measures is successful, it is possible that too much solvent is present, and it may be necessary to evaporate some of the solvent
and allow the solution to cool again.

11.9 Drying Crystals

The most common method of drying crystals involves allowing them to dry in air. Several different methods are illustrated in Figure 11.6 below. In all three methods, the crystals must be covered to prevent accumulation of dust particles. Note that in each method, the spout on the beaker provides an opening so that solvent vapor can escape from the system. The advantage of this method is that heat is not required, thus reducing the danger of decomposition or melting; however, exposure to atmospheric moisture may cause the hydration of strongly hygroscopic materials. A hygroscopic substance is a substance that absorbs moisture from the air.

Another method of drying crystals is to place the crystals on a watch glass, a clay plate, or a piece of absorbent paper in an oven. Although this method is simple, some possible difficulties deserve mention. Crystals that sublime readily should not be dried in an oven because they might vaporize and disappear. Care should be taken that the temperature of the oven does not exceed the melting point of the crystals. Remember that the melting point of crystals is lowered by the presence of solvent; allow for this melting-point depression when selecting a suitable oven temperature. Some materials decompose on exposure to heat, and they should not be dried in an oven. Finally, when many different samples are being dried in the same oven, crystals might be lost due to confusion or reaction with another person's sample. It is important to label the crystals when they are placed in the oven.

A third method, which requires neither heat nor exposure to atmospheric moisture, is drying *in vacuo*. Two procedures are illustrated in Figure 11.7.

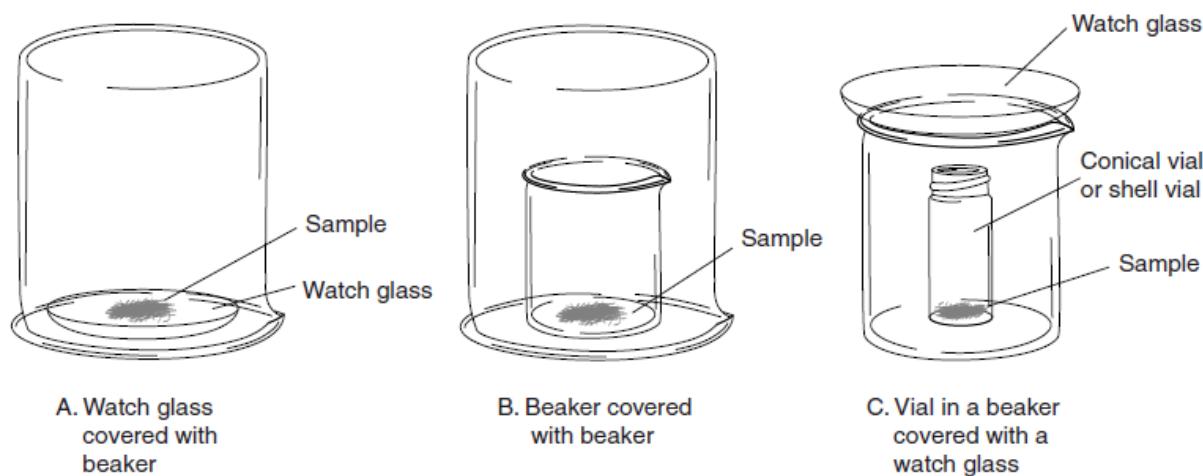


Figure 11.6 Methods for drying crystals in air.

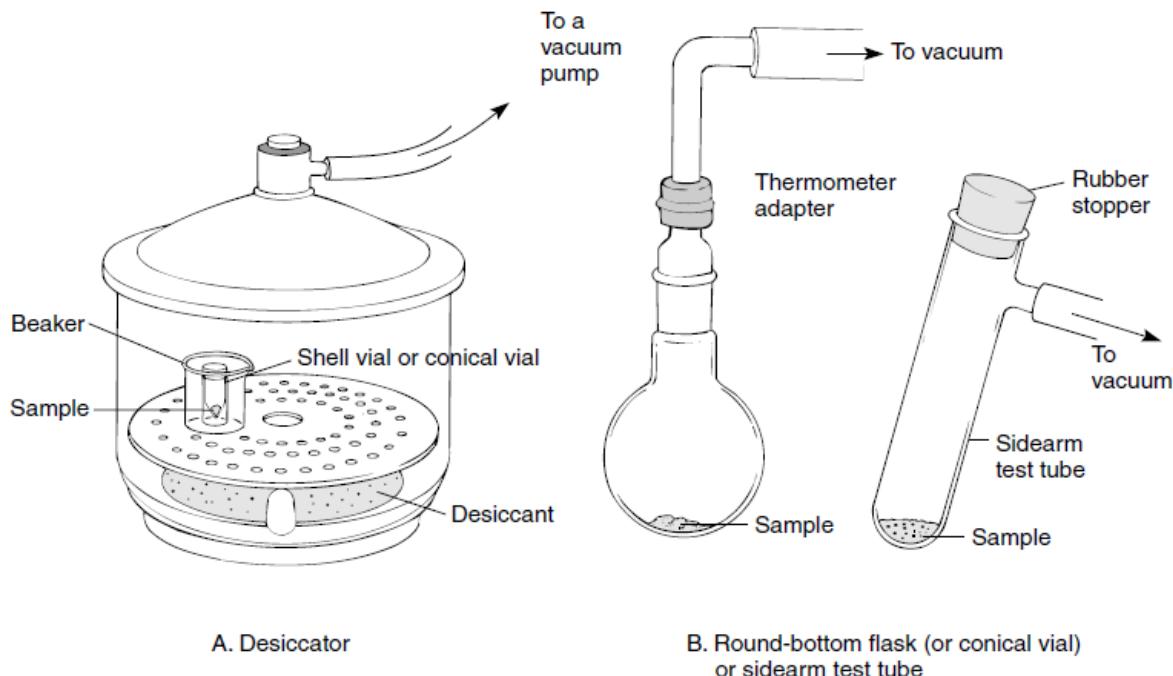


Figure 11.7 Methods for drying crystals in vacuum.

Procedure A

In this method, a desiccator is used. The sample is placed under vacuum in the presence of a drying agent. Two potential problems must be noted. The first deals with samples that sublime readily. Under vacuum, the likelihood of sublimation is increased. The second problem deals with the vacuum desiccator itself. Because the surface area of glass that is under vacuum is large, there is some danger that the desiccator could implode. A vacuum desiccator should never be used unless it has been placed within a protective metal container (cage). If a cage is not available, the

desiccator can be wrapped with electrical or duct tape. If you use an aspirator as a source of vacuum, you should use a water trap .

Procedure B

This method can be accomplished with a round-bottom flask and a thermometer adapter equipped with a short piece of glass tubing, as illustrated in Figure 11.7B. In microscale work, the apparatus with the round-bottom flask can be modified by replacing the round-bottom flask with a conical vial. The glass tubing is connected by vacuum tubing to either an aspirator or a vacuum pump. A convenient alternative, using a sidearm test tube, is also shown in Figure 11.7B. With either apparatus, install a water trap when an aspirator is used.

11.10 Mixed Solvents

Often, the desired solubility characteristics for a particular compound are not found in a single solvent. In these cases, a mixed solvent may be used. You simply select a first solvent in which the solute is soluble and a second solvent, miscible with the first, in which the solute is relatively insoluble. The compound is dissolved in a minimum amount of the boiling solvent in which it is soluble. Following this, the second hot solvent is added to the boiling mixture, dropwise, until the mixture barely becomes cloudy. The cloudiness indicates precipitation. At this point, more of the first solvent should be added. Just enough is added to clear the cloudy mixture. At that point, the solution is saturated, and as it cools, crystals should separate. Common solvent mixtures are listed in Table 11.3.

It is important not to add an excess of the second solvent or to cool the solution too rapidly. Either of these actions may cause the solute to oil out, or separate as a viscous liquid. If this happens, reheat the solution and add more of the first solvent.

TABLE 11.3 Common Solvent Pairs for Recrystallization

Methanol–water	Ether–acetone
Ethanol–water	Ether–petroleum ether
Acetic acid–water	Toluene–ligroin
Acetone–water	Methylene chloride–methanol
Ether–methanol	Dioxane ^a –water

^aSuspected carcinogen.

LIQUID-LIQUID EXTRACTIONS, SEPARATIONS, AND DRYING AGENTS

PART A. THEORY

12.1 Liquid-liquid 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 the 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 the solution successively with several portions of methylene chloride.

A generalized extraction process, using a specialized piece of glassware called a **separatory funnel**, is illustrated in Figure 12.1. The first solvent contains a

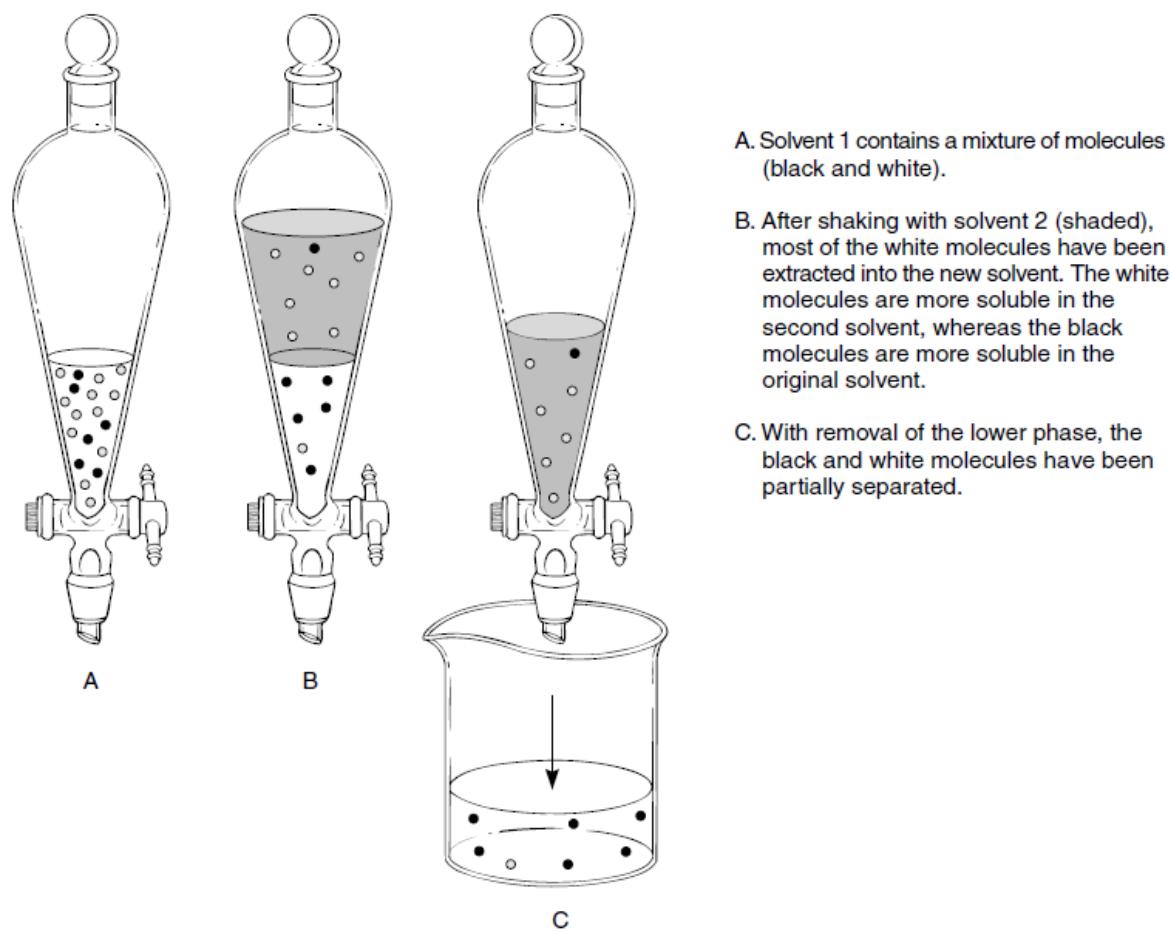


Figure 12.1 The extraction process.

mixture of black-and-white molecules (see Figure 12.1A). A second solvent that is not miscible with the first is added. After the separatory funnel is capped and shaken, the layers separate. In this example, the second solvent (shaded) is less dense than the first, so it becomes the top layer (see Figure 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 still a few white molecules in this lower phase. The lower phase may be separated from the upper phase by opening the stopcock at the bottom of the separatory funnel and allowing the lower layer to drain into a beaker (see Figure 12.1C). In this example, notice that it was not possible to effect a complete separation of the two types of molecules with a single extraction. This is a common occurrence in organic chemistry.

Many 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 and an immiscible organic solvent to the reaction mixture contained in a separatory funnel. After stoppering the funnel and shaking it, you allow the organic layer and the aqueous (water) layer to separate. A water wash removes highly polar and water-soluble materials, such as sulfuric acid, hydrochloric acid, and sodium hydroxide, from the organic layer. The washing operation helps to 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 of 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 of 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, as an illustration, a particular extraction proceeds with a distribution coefficient of 10. The system consists of 5.0 g of organic compound dissolved in 100 mL of water (solvent 1). In this illustration, the effectiveness of three 50-mL extractions with ether (solvent 2) is compared with one 150-mL extraction with ether. In the first 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 .

$$K = 10 = \frac{C_2}{C_1} = \frac{\left(\frac{5.0 - x}{50} \frac{\text{g}}{\text{mL ether}} \right)}{\left(\frac{x}{100} \frac{\text{g}}{\text{mL H}_2\text{O}} \right)}; \quad 10 = \frac{(5.0 - x)(100)}{50x}$$

$$500x = 500 - 100x$$

$$600x = 500$$

$x = 0.83$ g remaining in the aqueous phase

$5.0 - x = 4.17$ g in the ether layer

As a check on the calculation, it is possible to substitute the value 0.83 g for x in the original equation and demonstrate that the concentration in the ether layer divided by the concentration in the water layer equals the distribution coefficient.

$$\frac{\left(\frac{5.0 - x}{50} \frac{\text{g}}{\text{mL ether}} \right)}{\left(\frac{x}{100} \frac{\text{g}}{\text{mL H}_2\text{O}} \right)} = \frac{\frac{4.17}{50}}{\frac{0.83}{100}} = \frac{0.083 \text{ g/mL}}{0.0083 \text{ g/mL}} = 10 = K$$

The second extraction with another 50-mL portion of fresh ether is performed on the aqueous phase, which now contains 0.83 g 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 50-mL portion of ether. This third extraction will transfer 0.12 g of solute into the ether layer, leaving 0.02 g of solute remaining in the water layer. A total of 4.98 g of solute will be extracted into the combined ether layers, and 0.02 g will remain in the aqueous phase.

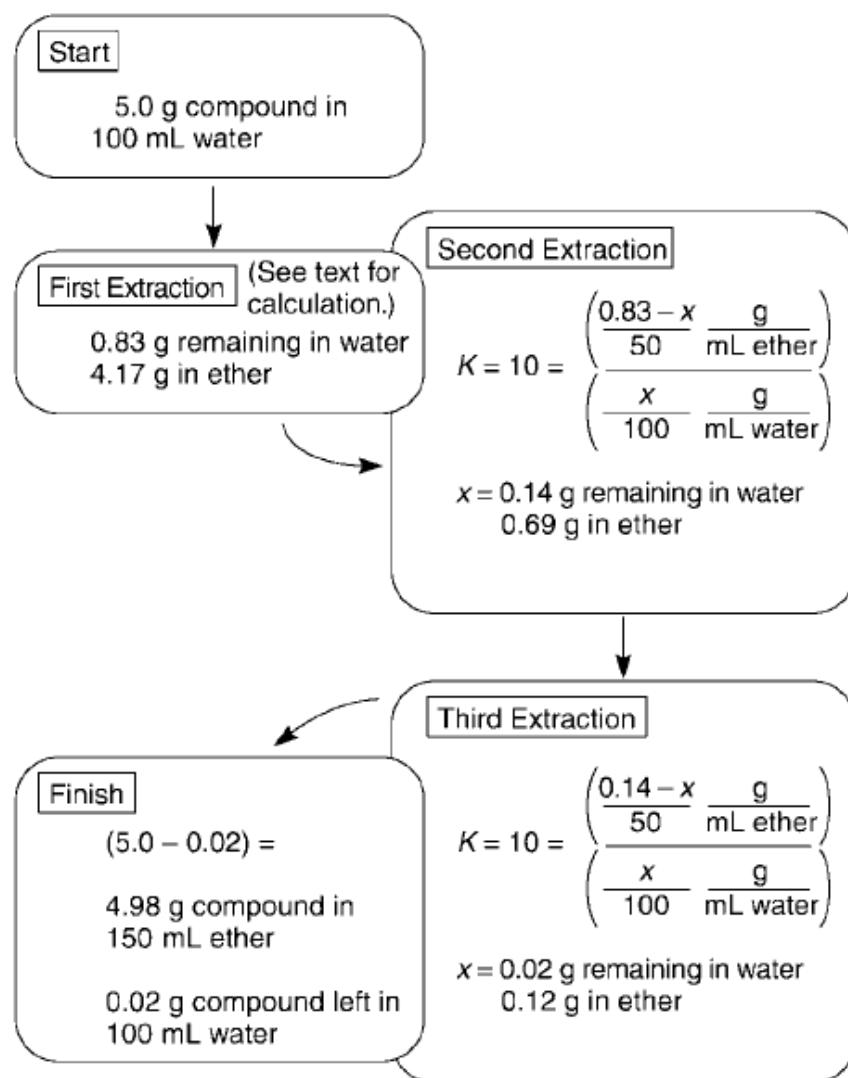


Figure 12.2 The result of extraction of 5.0 g of compound in 100 mL of water by three successive 50-mL portions of ether. Compare this result with that of Figure 12.

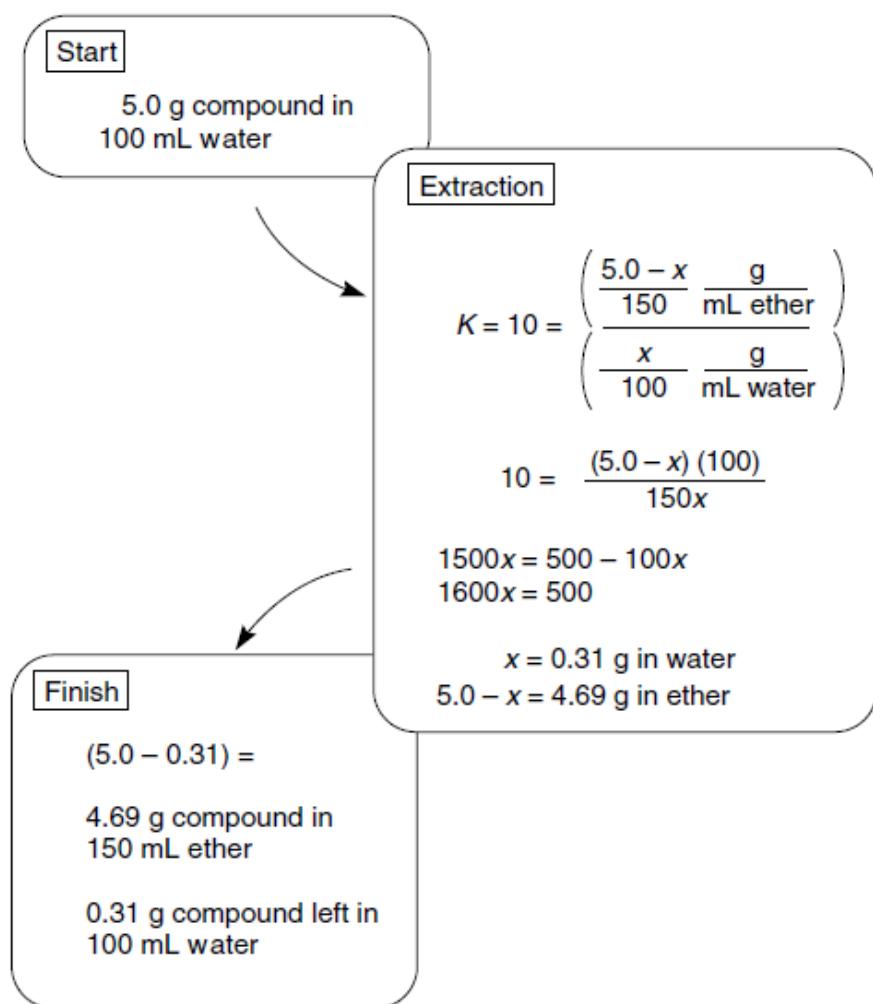


Figure 12.3 The result of extraction of 5.0 g of compound in 100 mL of water with one 150-mL portion of ether. Compare this result with that of Figure 12.2.

Figure 12.3 shows the result of a *single* extraction with 150 mL of ether. As shown there, 4.69 g of solute were extracted into the ether layer, leaving 0.31 g of compound in the aqueous phase. Three successive 50-mL ether extractions (see Figure 12.2) succeeded in removing 0.29 g more solute from the aqueous phase than using one 150-mL portion of ether (see Figure 12.3). This differential represents 5.8% of the total material.

NOTE: Several extractions with smaller amounts of solvent are more effective than one extraction with a larger amount of solvent.

12.3 Choosing an Extraction Method and a Solvent

Three types of apparatus are used for extractions: conical vials, centrifuge tubes, and separatory funnels (see 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. Conical vials and centrifuge tubes are most often used in microscale experiments, although a centrifuge tube may also be used in some macroscale applications. The separatory funnel is used with larger volumes of liquid in macroscale experiments. The separatory funnel is discussed in Part B and the conical vial and centrifuge tube are discussed in Part C.

TABLE 12.1 Densities of Common Extraction Solvents

Solvent	Density (g/mL)
Ligroin	0.67–0.69
Diethyl ether	0.71
Toluene	0.87
Water	1.00
Methylene chloride	1.330

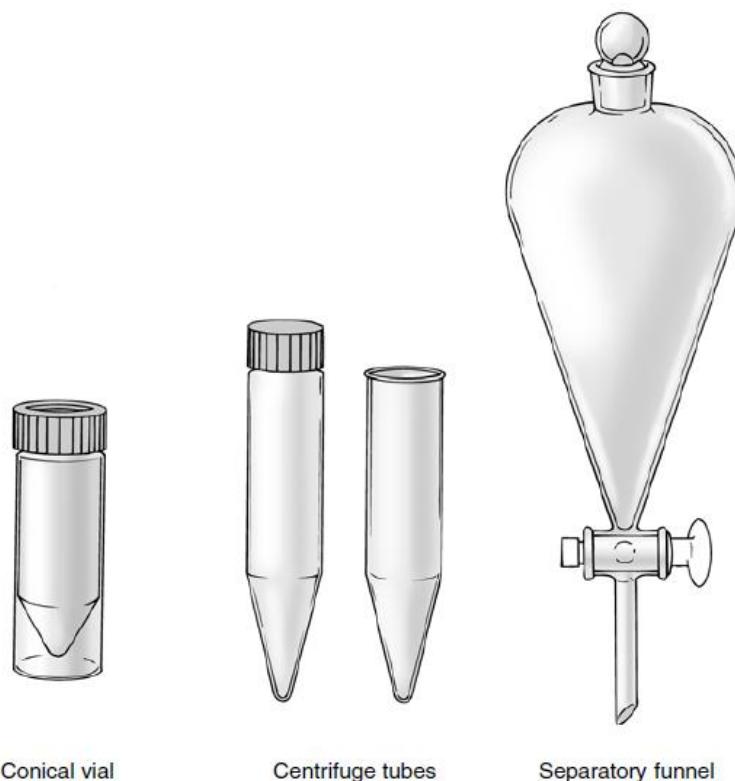


Figure 12.4 The apparatus used in extraction.

Most extractions consist of an aqueous phase and an organic phase. To extract a substance from an aqueous phase, you must use an organic solvent that is not miscible with water. Table 12.1 lists a number of the common organic solvents that are not miscible with water and are used for extractions.

Solvents that have a density less than that of water (1.00 g/mL) will separate as the top layer when shaken with water. Solvents that have a density greater than that of 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 to separate the lower layer (whether or not it is the aqueous layer or the organic layer) than to separate the upper layer.

PART B. MACROSCALE EXTRACTION

12.4 The Separatory Funnel

A separatory funnel is illustrated in Figure 12.5. It is the piece of equipment used for carrying out extractions with medium to large quantities of material. To fill the separatory funnel, support it in an iron ring attached to a ring stand. Since it is easy to break a separatory funnel by “clanking” it against the metal ring, pieces of rubber tubing are often attached to the ring to cushion the funnel, as shown in Figure 12.5. These are short pieces of tubing cut to a length of about 3 cm and slit open along their length. When slipped over the inside of the ring, they cushion the funnel in its resting place.

When beginning an extraction, first close the stopcock. (Don’t forget!) Using a powder funnel (wide bore) placed in the top of the separatory funnel, fill the funnel with both the solution to be extracted and the extraction solvent. Swirl the funnel gently

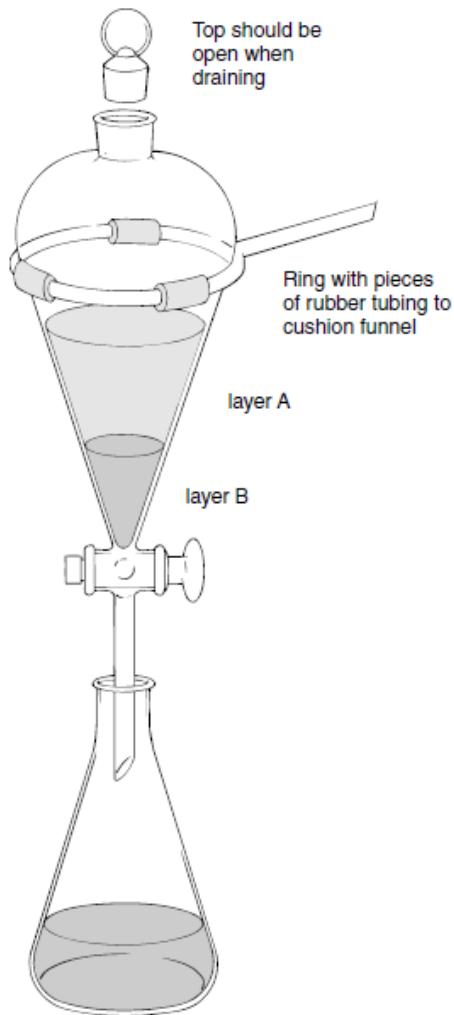


Figure 12.5 A separatory funnel.

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 12.6. 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 1 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), by shaking the funnel more vigorously for less time.

NOTE: There is an art to shaking and venting a separatory funnel correctly, and this technique 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 one another by draining most of the lower layer through the stopcock.¹ Allow a few minutes to pass so that any of the lower phase 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.



Figure 12.6 The correct way of shaking and venting a separatory funnel.

¹A 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 in the space above the liquid.

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 (see Section 12.9) before the solvent is removed.

The usual macroscale procedure requires the use of a 125-mL or 250-mL separatory funnel. For microscale procedures, a 60-mL or 125-mL separatory funnel is recommended. Because of surface tension, water has a difficult time draining from the bore of smaller funnels.

PART C. MICROSCALE EXTRACTION

12.5 The Conical Vial—Separating the Lower Layer

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), 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 the mixture up 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.

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 ($d = 1.33 \text{ g/mL}$) 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 12.7, to remove the lower layer.

1. Place the aqueous phase containing the dissolved product into a 5-mL conical vial (see Figure 12.7A).
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 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 (see Figure 12.7B). 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 (see Technique 8, Section 8.6) using a $5\frac{3}{4}$ -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 (see Figure 12.7C). 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 (see Section 12.10) that might be at the interface between the layers (see Figure 12.7D). 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 12.8. This avoids messy and disastrous transfers. The aqueous layer (upper layer) is left in the original conical vial (see Figure 12.7E).

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.

NOTE: If an organic solvent has been extracted with water, it should be dried with a drying agent (see Section 12.9) before proceeding.

- A. The aqueous solution contains the desired product.
- B. Methylene chloride is used to extract the aqueous phase.
- C. The Pasteur filter-tip pipet is placed in the vial.
- D. The lower organic layer is removed from the aqueous phase.
- E. The organic layer is transferred to a dry test tube or conical vial. The aqueous layer remains in the original extraction vial.

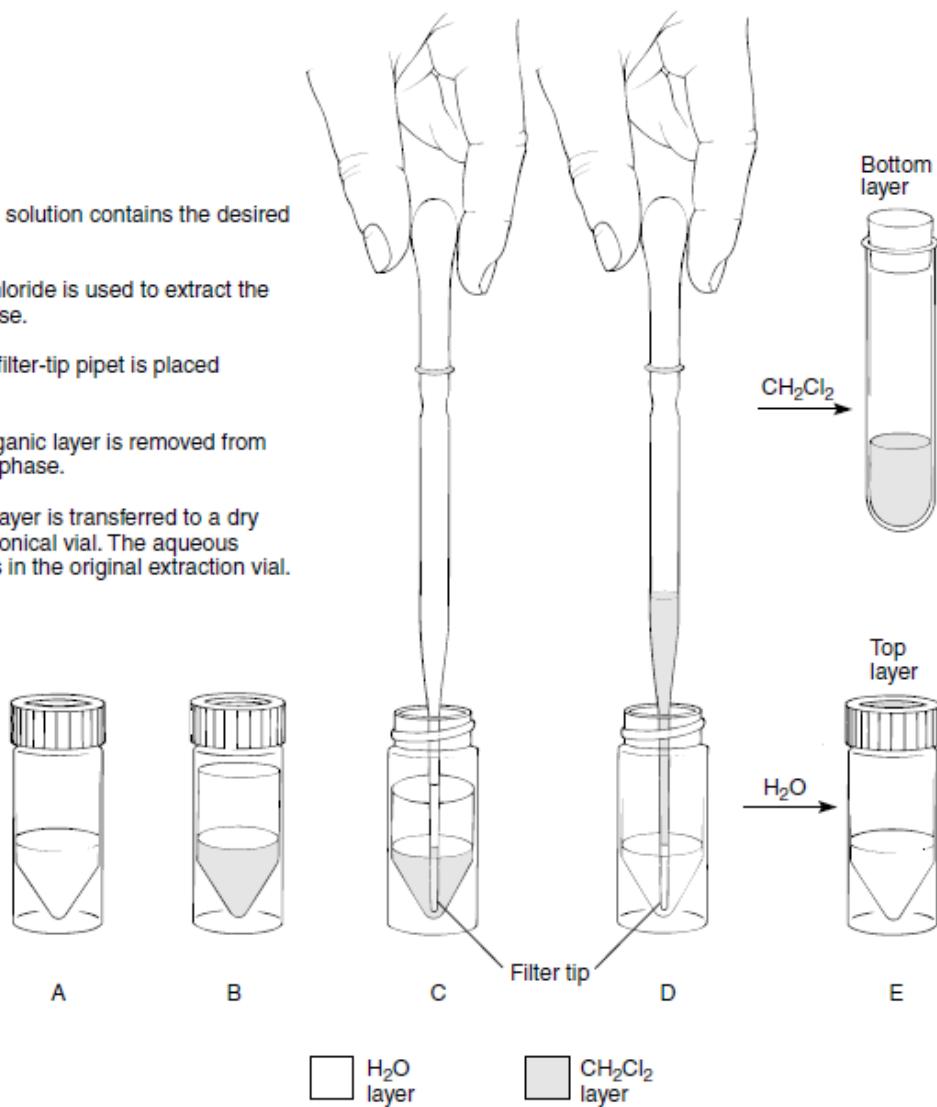


Figure 12.7 Extraction of an aqueous solution using a solvent denser than water: methylene chloride.

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.

12.6 The Conical Vial—Separating the Upper Layer

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 ($d = 0.71 \text{ g/mL}$) as the extraction solvent. Methods for removing the lower layer were discussed previously.

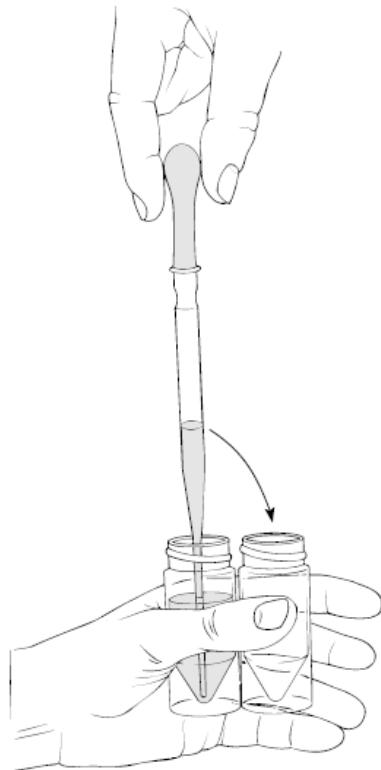


Figure 12.8 Method for holding vials while transferring liquids.

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 12.9, to remove the upper layer.

1. Place the aqueous phase containing the dissolved product in a 5-mL conical vial (Figure 12.9A).
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 (see Figure 12.9B).
3. Prepare a Pasteur filter-tip pipet (see Technique 8, Section 8.6) using a $5\frac{3}{4}$ -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 (see Figure 12.9C).

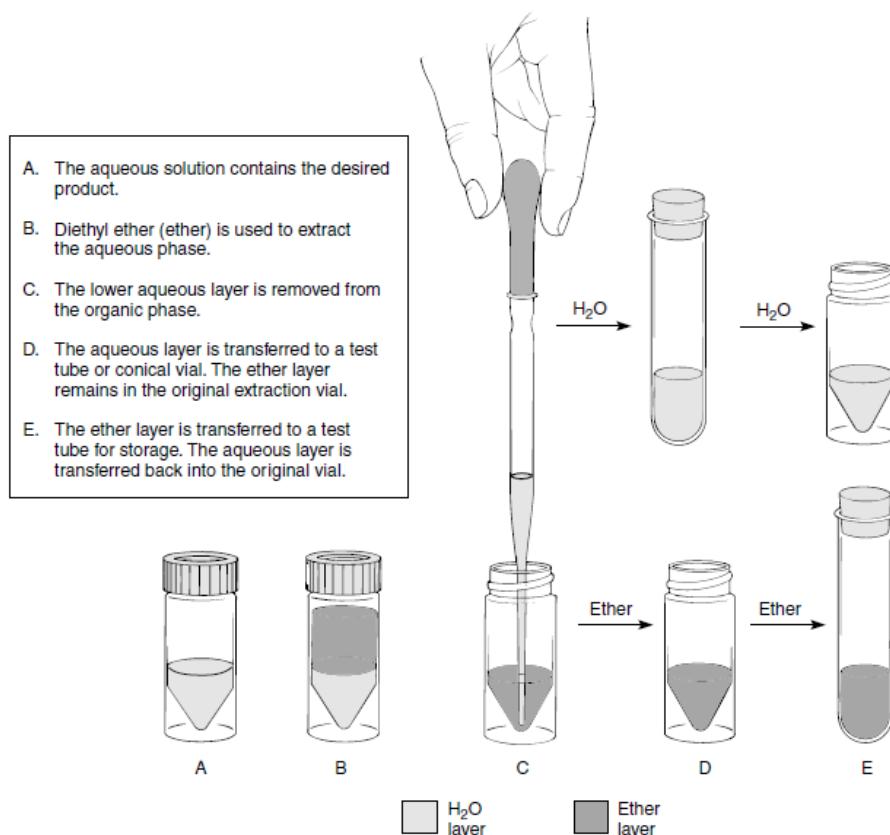


Figure 12.9 Extraction of an aqueous solution using a solvent less dense than water: diethyl ether.

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 Figure 12.8. The ether layer is left behind in the conical vial (see Figure 12.9D).
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 (see Figure 12.9E).

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.

12.7 The Screw-Cap Centrifuge Tube

If you require an extraction that uses a larger volume than a conical vial can accommodate (about 4 mL), a centrifuge tube can often be used. A centrifuge tube can also be used instead of a separatory funnel for some macroscale applications in which the total volume of liquid is less than about 12 mL. A commonly available size of centrifuge tube has a volume of about 15 mL and is supplied with a screw cap. In performing an extraction with a screw-cap centrifuge tube, use the same procedures outlined for the conical vial (see Sections 12.5 and 12.6). As is the case for a conical vial, the tapered bottom of the centrifuge tube makes it easy to withdraw the lower layer with a Pasteur pipet.

NOTE: A centrifuge tube has a great advantage over other methods of extraction. If an emulsion (Section 12.10) forms, you can use a centrifuge to aid in the separation of the layers.

You should check the capped centrifuge tube for leaks by filling it with water and shaking it vigorously. If it leaks, try replacing the cap with a different one. A **vortex mixer**, if available, provides an alternative to shaking the tube. In fact, 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 neoprene pads. The unit mixes the sample by high-frequency vibration.

PART D. ADDITIONAL EXPERIMENTAL CONSIDERATIONS: MACROSCALE AND MICROSCALE

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

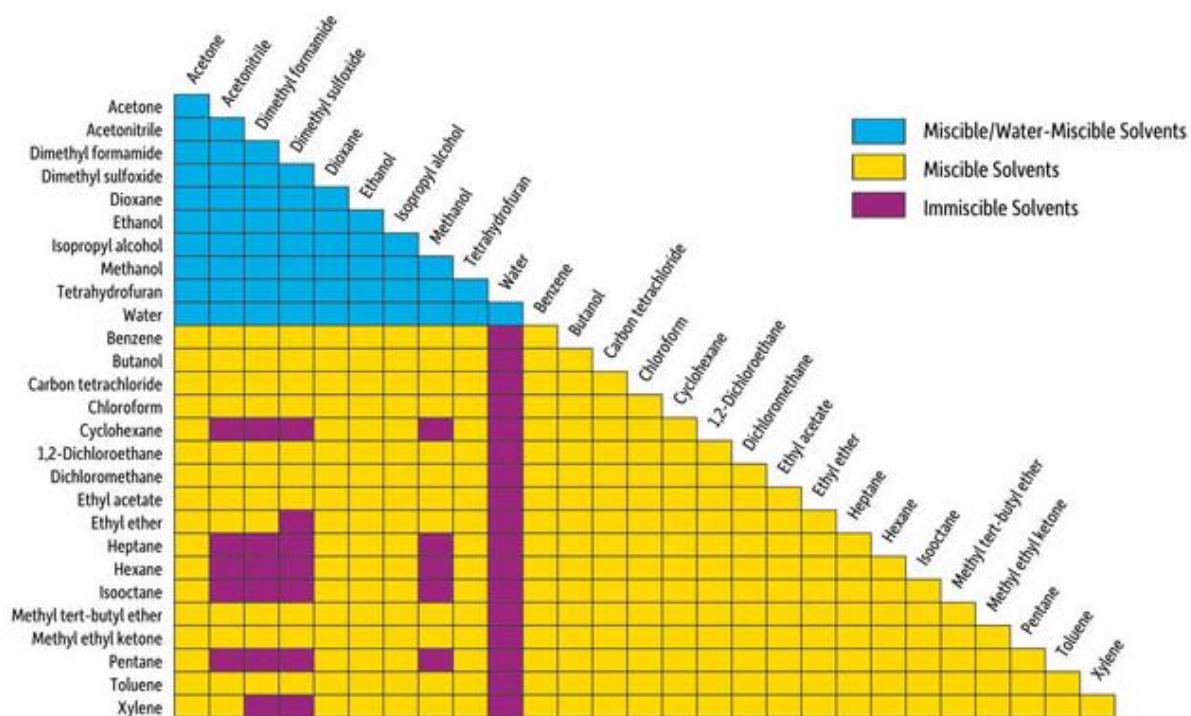
A common problem encountered during an extraction is trying to determine which of the two layers is the organic layer and which is the aqueous (water) layer. The most common situation occurs when the aqueous layer is on the bottom in the presence of an upper organic layer consisting of ether, ligroin, 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.

Solvent Miscibility and Solubility



12.9 Drying Agents

Drying a reagent, solvent, or product is a task that must be performed at some stage of nearly every reaction conducted in the organic chemistry laboratory. The techniques of drying solids and liquids are described in this and the following sections.

Drying Agents and Desiccants

Most organic liquids are distilled at the end of the purification process, and any residual moisture that is present may react with the compound during the distillation; water may also co- or steam-distill with the liquid and contaminate the distillate. In order to remove these small traces of moisture before distillation, drying agents, sometimes called desiccants, are used. There are two general requirements for a drying agent: (1) neither it nor its hydrolysis product may react chemically with the organic liquid being dried, and (2) it must be *completely* and *easily* removed from the dry liquid. A drying agent should also be efficient so that the water is removed in a reasonably short period of time.

Some commonly used drying agents and their properties are listed in Table 2.1. These desiccants function in one of two ways: (1) the drying agent interacts *reversibly* with water by the process of adsorption or absorption (Eq. 2.1), or (2) it reacts irreversibly with water by serving as an acid or a base.

With drying agents that function by reversible hydration, a certain amount of water will remain in the organic liquid in equilibrium with the hydrated drying agent. The lesser the amount of water left at equilibrium, the greater the efficiency of the desiccant. A drying agent that forms a hydrate (Eq. 2.1) must be *completely* removed by gravity filtration or by decantation before the dried liquid is distilled, since many hydrates decompose with loss of water at temperatures above 30–40 °C.



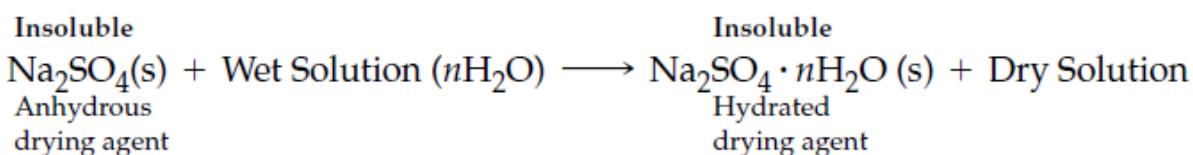
Drying agents that remove water by an irreversible chemical reaction are very efficient, but they are generally more expensive than other types of drying agents. Such drying agents are sometimes more difficult to handle and are normally used to remove *small* quantities of water from reagents or solvents prior to a chemical reaction. For example, phosphorus pentoxide, P_2O_5 , removes water by reacting vigorously with it to form phosphoric acid (Eq. 2.2). Desiccants such as calcium hydride (CaH_2) and sodium (Na) metal also react vigorously with water. When CaH_2 or Na metal is used as a drying agent, hydrogen gas is evolved, and appropriate precautions must be taken to vent the hydrogen and prevent buildup of this highly flammable gas.



Of the drying agents listed in Table 2.1, *anhydrous* calcium chloride, sodium sulfate, and magnesium sulfate will generally suffice for the needs of this introductory laboratory course. Both sodium sulfate and magnesium sulfate have high capacities and absorb a large amount of water, but magnesium sulfate dries

a solution more completely. Calcium chloride has a low capacity, but it is a more efficient drying agent than magnesium sulfate. Do *not* use an unnecessarily large quantity of drying agent when drying a liquid, since the desiccant may adsorb or absorb the desired organic product along with the water. Mechanical losses on filtration or decantation of the dried solution may also become significant. The amount of drying agent required depends upon the quantity of water present, the capacity of the drying agent, and the amount of liquid to be dried.

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:



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. 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 macroscale and microscale 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 about 5 mL, and the macroscale procedure is usually appropriate for volumes of 5 mL or greater.

TABLE 12.2 Common Drying Agents

	Acidity	Hydrated	Capacity ^a	Completeness ^b	Rate ^c	Use
Magnesium sulfate	Neutral	$\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$	High	Medium	Rapid	General
Sodium sulfate	Neutral	$\text{Na}_2\text{SO}_4 \cdot 7\text{H}_2\text{O}$ $\text{Na}_2\text{SO}_4 \cdot 10\text{H}_2\text{O}$	High	Low	Medium	General
Calcium chloride	Neutral	$\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$ $\text{CaCl}_2 \cdot 6\text{H}_2\text{O}$	Low	High	Rapid	Hydrocarbons Halides
Calcium sulfate (Drierite)	Neutral	$\text{CaSO}_4 \cdot \frac{1}{2}\text{H}_2\text{O}$ $\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$	Low	High	Rapid	General
Potassium carbonate	Basic	$\text{K}_2\text{CO}_3 \cdot 1\frac{1}{2}\text{H}_2\text{O}$ $\text{K}_2\text{CO}_3 \cdot 2\text{H}_2\text{O}$	Medium	Medium	Medium	Amines, esters, bases, ketones
Potassium hydroxide	Basic	—	—	—	Rapid	Amines only
Molecular sieves (3 or 4 Å)	Neutral	—	High	Extremely high	—	General

^aAmount of water removed per given weight of drying agent.^bRefers to amount of H_2O still in solution at equilibrium with drying agent.^cRefers to rate of action (drying).