2.2 RECRYSTALLIZATION

Crystallization is the deposition of crystals from a solution or melt of a given material. During the process of crystal formation, a molecule will tend to become attached to a growing crystal composed of the same type of molecules because of a better fit in a crystal lattice for molecules of the same structure than for other molecules. If the crystallization process is allowed to occur under near-equilibrium conditions, the preference of molecules to deposit on surfaces composed of like molecules will lead to an increase in the purity of the crystalline material. Thus the process of recrystallization is one of the most important methods available to the chemist for the purification of solids. Additional procedures can be incorporated into the recrystallization process to remove impurities. These include filtration to remove undissolved solids and adsorption to remove highly polar impurities.

Recrystallization depends on the differential solubility of a substance in a hot and a cold solvent. It is desirable that the solubility of the substance be high in the hot solvent and low in the cold solvent to facilitate the recovery of the starting material. The solution remaining after crystals have deposited is known as the *mother liquor*. The proper choice of solvent is critical and may require trial tests with small quantities of the material in a variety of solvents or solvent pairs (combinations of two solvents).

Solvents used in recrystallizations should be relatively low-boiling so that solvent adhering to the crystals can be readily removed by evaporation. If structural characteristics of the compound to be recrystallized are known, the adage "like dissolves like" should be kept in mind; polar compounds are more soluble in polar solvents, and nonpolar compounds are more soluble in nonpolar solvents. Some common solvents used in recrystallization are listed in Table 2.1.

Recrystallization Procedure

The solvent, or solvent pair, to be used in the recrystallization of a substance is chosen in the following manner. A small amount of the substance is placed in a small test tube and a few drops of solvent are added. The test tube is gently heated to see if the sample dissolves in the heated solvent. In general, one should first use a nonpolar solvent, for example, hexane or petroleum ether. If the sample does not dissolve, try

TABLE 2.1 Common Solvents* for Recrystallization Listed in Order of Decreasing Polarity

Solvent	bp (°C)	Useful for	Common Cosolvents
Water	100	Salts, amides, some carboxylic acids	Acetone, methanol, ethanol
Methanol	65	General use	Water, diethyl ether, benzene
Ethanol	78	General use	Water, diethyl ether, benzene
Acetone	56	General use	Water, hexane
Ethyl acetate	77	General use	Hexane
Dichloromethane	40	General use, low-melting compounds	Ethanol, hexane
Diethyl ether	35	General use, low-melting compounds	Methanol, ethanol, hexane
Chloroform†	61	General use	Ethanol, hexane
Toluene	111	Aromatic compounds	
Benzene†	80	Aromatic compounds	Ethanol, diethyl ether, ethyl acetate
Hexane (or petroleum ether)	69	Hydrocarbons	All solvents on this list except water and methanol

* For additional information on organic solvents see Section 1.15.

† Not recommended for general use because of health hazard (Sections 1.15.3 and 1.15.6).

using a more polar solvent such as ethanol or acetone. Should the sample completely dissolve in any solvent, chill the solution to see whether crystals will form. (Sometimes it is necessary to chill the solution using a Dry Ice-acetone bath in order to cause crystallization.) If no crystals appear, the material is too soluble in that solvent, and that solvent should not be used for the recrystallization. If no single solvent provides suitable results, a mixture of two solvents can be employed, one of the solvents being a good solvent for the sample, and the other being a poor solvent for the sample. The sample is first dissolved in the solvent in which the sample is most soluble, and then small portions of the other solvent are added until a cloudiness is formed upon addition of the second solvent. A small amount of the better solvent is added to remove the cloudiness, and the solution is allowed to cool. The correct proportion of the two solvents must be determined by trial and error. Once the proper solvent has been chosen, the remainder of the sample is recrystallized.

For gram- or multigram-scale recrystallizations, the material to be recrystallized is placed in a suitable container such as an Erlenmeyer flask. Solvent is added slowly, maintaining a gentle reflux of the solvent in the flask, until no more of the material dissolves. Occasionally, highly insoluble materials may be present in the sample, which, regardless of the amount of solvent added, will not dissolve. When it appears that no more material dissolves, the addition of further solvent is stopped.

If the sample is colored, a small amount of activated carbon (charcoal) can be added to adsorb highly polar, generally colored contaminants. The addition of activated carbon must be carried out with great care, for if the saturated solution has become superheated, the addition of the finely divided charcoal will induce violent boiling with the possible loss of material. The solution should be below its boiling

point before the addition of the activated carbon. After the addition of the charcoal, the mixture is gently boiled for about 30 seconds while rapidly swirling or stirring to avoid the rapid boiling (bumping) of the solution. The solids are allowed to settle to the bottom of the container. Any change in the color of the solution is noted. If the color of the solution has decreased, an additional amount of activated carbon is added and the process is repeated until no further change in color is noted.

CAUTION: Be very careful when recrystallizing highly polar or colored compounds in order to avoid a great excess of the activated carbon that may cause a considerable loss of material.

The hot, saturated solution is filtered through a hot, solvent-saturated filter that is kept warm, by refluxing the solvent, to prevent the premature formation of crystals (see Figure 2.1). The filter is washed with a small amount of the hot solvent, and the volume of the solution is reduced by boiling until a saturated solution is again attained. When removing the activated carbon by filtration it is often necessary to use a filter aid, for example Celite, to remove all of the very small particles of the activated carbon completely. Suction filtration techniques are generally employed when such a filter aid is used to decrease the filtering time (Section 2.1.2). The filter aid is added to the solution just prior to filtering; the solution is quickly mixed with the filter aid and poured into the filter, or the hot solution is filtered through a preformed layer of the filter aid in the funnel.

The rate of crystal growth from the saturated solution is critical. Too rapid a precipitation rate does not allow equilibrium conditions to exist, and the very slow precipitation with the formation of large crystals often leads to extensive solvent inclusion in the crystals. The hot, saturated solution should be allowed to cool at a rate between the two extremes. This can generally be accomplished by allowing the solution to cool on the bench top, followed by chilling in an ice bath. Occasionally, with low-boiling solvents such as ether or pentane, it may be desirable to chill the sample in a Dry Ice-acetone bath to induce crystal growth. In such cases the collection funnel should be chilled prior to filtration by pouring a portion of chilled solvent through the filter funnel.

Some materials tend to "oil out" as a liquid instead of forming crystals. This usually occurs when the melting point of the material is below the temperature at which a saturated solution is attained. Additional solvent should be added, maintaining a clear solution, until crystals finally begin to form. If crystals are reluctant to form, scratching the side of the container with a glass stirring rod or adding a seed crystal will generally induce crystallization. The crystals are then collected by suction filtration and washed with a small portion of cold solvent to remove any adhering mother liquor. When using filter paper to collect the sample, care should be taken in removing the sample from the paper to avoid dislodging any fibers of the paper, which may contaminate the sample. These fibers may interfere with subsequent elemental or spectral analysis.

The recrystallization of small quantities of materials can be carried out in small test tubes or centrifuge tubes. Centrifuge tubes are the most convenient in that the crystalline mass can be forced to the bottom of the tube and the mother liquors

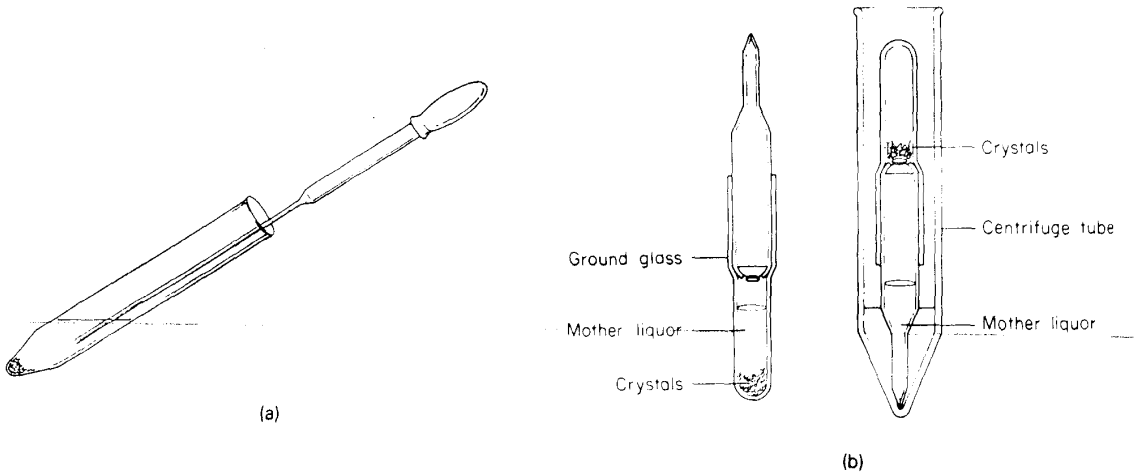

Figure 2.4 Illustrations showing the use of a centrifuge tube (a) and a Craig tube (b) for recrystallization. In (a), the crystals have been centrifuged to the bottom of the tube and the solvent is being removed with a disposable pipette. In (b), the Craig tube in which the crystals have formed (left) is placed in a centrifuge tube and the mother liquor is forced from the Craig tube by centrifugation (right).

removed by a capillary pipette (see Figure 2.4). The crystalline mass can then be washed with several small quantities of cold solvent and then removed from the tube to be dried.

The recrystallization of milligram quantities of material can be conveniently carried out using a Craig tube (see Figure 2.4). The Craig tube consists of an outer part in which the material to be recrystallized is dissolved in the solvent. The inner piece has a ground glass area that forms a seal with the outer part. The inner part is inserted and the contents of the Craig tube are allowed to cool to induce crystallization. After crystallization is completed, the Craig tube is placed upside down in a centrifuge tube and centrifuged. The spinning of the centrifuge forces the mother liquors through a sintered glass frit in the inner part of the apparatus. After centrifugation the inner tube is removed and adhering crystals are scraped off into the outer part of the apparatus. A small amount of cold solvent can be added to the crystals to wash away any adhering mother liquor, and then removed by the use of a disposable pipette.

The crystalline material obtained in the procedure outlined above is thoroughly dried to remove adhering solvent. Many compounds can be dried by allowing the samples to set in the open air (care must be exercised to protect the sample from contamination). Hygroscopic compounds or compounds recrystallized from high-boiling solvents must be dried in a vacuum drying apparatus (e.g., a vacuum dessicator, Section 1.14.2). The entire recrystallization procedure should be repeated until a constant melting point of relatively narrow range is obtained (see Section 3.2 on melting points for the details of melting-point determinations).