RECRYSTALLIZATION

A pure compound is a homogeneous sample consisting only of molecules having the same structure. However, substances believed to be pure on the basis of certain criteria may actually contain small amounts of contaminants. Indeed, the presence of impurities in what were believed to be pure compounds has sometimes led to incorrect structural assignments and scientific conclusions. The possibility of making such errors was of particular concern prior to the advent of the powerful chromatographic and spectral techniques that have been developed since the 1950s. It is now relatively easy for the chemist to purify solids and liquids and to demonstrate their purity.

A compound formed in a chemical reaction or extracted from some natural source is rarely pure when initially isolated. For example, a chemical transformation intended to produce a single product almost invariably yields a reaction mixture containing a number of contaminants. These may include the products of side reactions proceeding concurrently with the main reaction, unchanged starting materials, inorganic materials, and solvents. Unfortunately, even chemicals purchased commercially are not always pure, owing to the expense of the needed purification process or to decomposition that may occur during storage.

Recrystallization of solids is a valuable technique to master because it is one of the methods used most often for purification of solids. Other techniques for purifying solids include sublimation, extraction and chromatography. Nevertheless, even when one of these alternative methods of purification has been used, the solid material thus isolated may still be recrystallized to achieve the highest possible state of purity.

The process of recrystallization involves dissolution of the solid in an appropriate solvent at an elevated temperature and the subsequent re-formation of the crystals upon cooling, so that any impurities remain in solution. This technique, called solution re crystallization, is discussed here. An alternative approach involves melting the solid in the absence of solvent and then allowing the crystals to re-form so that impurities are left in the melt. This method is seldom used in the organic laboratory because the crystals often form out of a viscous oil that contains the impurities and from which it is difficult to separate the desired pure solid. It is interesting to note, however, that this is the technique used to prepare the high-purity single crystals of silicon used in computer chips.

Almost all solids are *more* soluble in a hot than in a *cold* solvent, and solution crystallization takes advantage of this fact. Thus, if a solid is first dissolved in an amount of hot solvent insufficient to dissolve it when cold, crystals should form when the hot solution is allowed to cool. The extent of precipitation of the solid depends on the difference in its solubility in the particular solvent at temperatures between the extremes used. The upper extreme is determined by the boiling point of the solvent, whereas the lower limit is usually dictated by experimental convenience. For example, an ice-water bath is often used to cool the solution to 0 °C, whereas ice-salt and Dry Ice-acetone baths are commonly used to cool solutions to -20 °C and -78 °C, respectively. The solid should be recovered with greater efficiency at these temperatures, provided the solvent itself does not freeze.

If the impurities present in the original solid mixture have dissolved and *remain* dissolved after the solution is cooled, isolation of the crystals that have formed should *ideally* provide pure material. Alternatively, the impurities may not dissolve at all in the hot solution and may be removed by filtration *before* the solution is cooled. The crystals that subsequently form should be purer than the original solid mixture. Solution recrystallization is seldom quite so simple in practice, but these two idealized generalizations do outline the basic principles of the technique.

Even after a solid has been recrystallized, it may still not be pure. Thus, it is important to determine the purity of the sample, and one of the easiest methods to do this is by determining the melting point of the solid.

The technique of solution recrystallization involves the following steps:

1. Selection of an appropriate solvent.
2. Dissolution of the solid to be purified in the solvent near or at its boiling point.
3. Decolouration with an activated form of carbon, if necessary, to remove colored impurities and filtration of the hot solution to remove insoluble impurities and the decolorizing carbon.
4. Formation of crystalline solid from the solution as it cools.
5. Isolation of the purified solid by filtration.
6. Drying the crystals.

SOLVENT SELECTION

The choice of solvent is perhaps the most critical step in the process of recrystallization since the correct solvent must be selected to form a product of high purity and in good recovery or yield. Consequently a solvent should satisfy certain criteria for use in recrystallization: (a) The desired compound should be reasonably soluble in the *hot sol*vent, about 5 g/100 mL (5 mg/100 μL) being satisfactory, and insoluble or *nearly* insoluble in the *cold* solvent. Note that the reference temperature for determination of the solubility in "cold" solvent is often taken to be room temperature. This combination of solute and solvent will allow dissolution to occur in an amount of solvent that is not unduly large and will also permit recovery of the purified product in high yield. A solvent having this type of solubility properties as a function of temperature would be said to have a favorable temperature coefficient for the desired solute. (b) Conversely, the impurities should either be insoluble in the solvent at all temperatures *or* must remain at least moderately soluble in the cold solvent. In other words, if the impurities are soluble, the temperature coefficient for them must be *unfavorable;* otherwise the desired product *and* the impurities would both crystallize simultaneously from solution. (c) The boiling point of the solvent should be low enough so that it can readily be removed from the crystals. (d) The boiling point of the solvent should generally be lower than the melting point of the solid being purified. (e) The solvent should not react chemically with the substance being purified.

The chemical literature is a valuable source of information about solvents suitable for recrystallizing known compounds. If the compound has *not* been prepared before, it is necessary to resort to trial-and-error techniques to find an appropriate solvent for recrystallization. The process of selection can be aided by consideration of some generalizations about solubility characteristics for classes of solutes. Polar compounds are normally soluble in polar solvents and insoluble in nonpolar solvents, for example, whereas nonpolar compounds are more soluble in nonpolar solvents. Such characteristics are summarized by the adage, *"like dissolves like."* Of course, although a highly polar compound is unlikely to be soluble in a hot, nonpolar solvent, it *may* be very soluble in a cold, very polar solvent. In this case, a solvent of intermediate polarity *may* be the choice for a satisfactory recrystallization.

The solvents commonly used in recrystallizations range widely in polarity, a property measured by the dielectric constants (ε) listed in Table 1. Those solvents with dielectric constants in the range of 2-3 are considered nonpolar, and those with constants above 10 as polar. Solvents in the 3-10 range are of intermediate polarity. Of the various solvents listed, *petroleum ether* deserves special mention because of its confusing common name. This solvent does *not* contain the *ether* functional group at all; rather it is a mixture of volatile aliphatic hydrocarbons obtained from the refining of petroleum. The composition and boiling point of the mixture depends on the particular distillation "cut" obtained. Thus, the boiling range of this type of solvent is usually given, as in the description, "petroleum ether, bp 60-80 °C (760 Torr)."

Occasionally a *mixture* of solvents is required for satisfactory recrystallization of a solute. The mixture is usually comprised of only two solvents; one of these dissolves the solute even when cold and the other one does not.

Table 1. Common solvents.

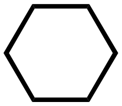
Solvent	Dielectric Constant (ε)	Boiling Point °C (760 Torr)	Freezing Point °C	Density g/mL	Water Soluble	Flammable
Petroleum ether	1.9	30-80			No	Yes
Pentane	1.84	36	-130	0.63	No	Yes
Hexane	1.89	69	-95	0.66	No	Yes
Heptane		98	-91	0.68	No	Yes
Ligroin	1.9	80-120			No	Yes
Heptane	1.9	98	-91	0.68	No	Yes
Octane	1.9	126	-57	0.70	No	Yes
Nonane	1.9	151	-51	0.72	No	Yes
Cyclohexane	1.965	80.7	6.6	0.78	No	Yes
1,4-Dioxane	2.21	101	11.8	1.03	Yes	Yes
Toluene	2.38	110.6	-95	0.87	No	Yes
Diethyl ether	4.34	34.5	-116	0.71	Slightly	Yes
Chloroform	4.81	61.7	-63.5	1.48	No	No
Ethyl acetate	6.02	77.1	-84	0.90	Yes	Yes
Tetrahydrofuran	7.60	65.6	-109	0.89	No	Yes
Dichloromethane	9.08	40.6	-95	1.33	No	No
Acetone	20.7	56	-95	0.79	Yes	Yes
Ethanol (95%)	24.6	78	-117	0.79	Yes	Yes
Methanol	32.6	65	-94	0.79	Yes	Yes
Water	78.5	100	0	1.00	n/a	No

$CH_3CH_2CH_2CH_2CH_3$

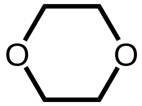
pentane

$CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_3$

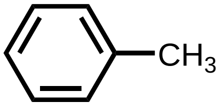
octane



cyclohexane



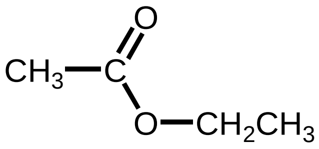
1,4-dioxane



toluene

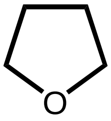
$CH_3CH_2{-}O{-}CH_2CH_3$

diethyl ether



$CH_3{-}C(=O){-}O{-}CH_2CH_3$

ethyl acetate



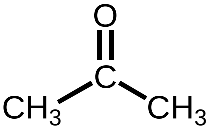
tetrahydrofuran

CH_2Cl_2

dichloromethane

$CHCl_3$

chloroform



$CH_3C(=O)CH_3$

acetone

$CH_3CH_2{-}OH$

ethanol

$CH_3{-}OH$

methanol

H_2O

water

Solvent Pairs. Sometimes no single satisfactory solvent can be found, so mixed solvents, or solvent pairs, are used. To use a solvent pair, one dissolves the crystals in the better solvent and adds the poorer solvent to the hot solution until it becomes cloudy, which means that the solution is saturated with the solute. The two solvents must be miscible with each other.

Common Solvent Pairs

Solvent 1 (more polar)		Solvent 2 (less polar)	
Solvent	Dielectric constant (ε)	Solvent	Dielectric constant (ε)
Water	78.3	Ethanol	24.3
Water	78.3	Acetone	20.7
Methanol	32.6	Dichloromethane	9.08
Ethanol	24.3	Acetone	20.7
Acetone	20.7	Diethyl ether	4.34
Acetone	20.7	Ligroin	1.9
Diethyl ether	4.34	Hexane	1.89
Ethyl acetate	6.02	Cyclohexane	1.965
Ethyl acetate	6.02	Ligroin	1.9
Dichloromethane	9.08	Ligroin	1.9
Toluene	2.38	Ligroin	1.9

DISSOLUTION

This step may involve the handling of relatively large volumes of volatile solvents. Although most solvents used in the organic laboratory are of relatively low toxicity, it is prudent to avoid inhaling their vapours.

Microscale Technique. The solid is weighed and placed in a test tube or small Erlenmeyer flask, with a few crystals of impure material being retained as "seeds" to induce crystallization. A boiling stone should be added to prevent bumping of the solution upon boiling. Alternatively, smooth boiling can be promoted by twirling a microspatula in the mixture.

A few drops of solvent, normally totaling no more than a milliliter are added, and the mixture is heated to the boiling point. Additional solvent, as needed, is added dropwise using a Pasteur pipette to the boiling mixture until the solid just dissolves. It is important to let boiling resume after each addition so that a minimum amount of solvent is used to effect dissolution; *using excessive amounts of solvent decreases the recovery of the solute.* If it necessary to perform a hot filtration, it is prudent to add an additional 2-5% of solvent to prevent premature crystallization during this operation.

If adding solvent fails to dissolve any more solid, it is likely that insoluble impurities are present. These can be removed by hot filtration. Thus, to avoid using too much solvent and risking poor recovery of the purified solute, you should observe the dissolution process *carefully.* This is particularly important when only a relatively small quantity of solid remains, as this may be the material that is insoluble.

The same general approach used for single-solvent dissolution is followed at the mini- and microscale levels when mixed solvents are employed. However, there are two options for effecting dissolution once the solvents have been selected. In one, the solid to be purified is first dissolved in a *minimum* volume of the hot solvent in which it is soluble; the second solvent is then added to the *boiling* solution until it turns cloudy. The cloudiness signals initial formation of crystals, caused by the fact that addition of the second solvent results in a solvent mixture in which the solute is less soluble. Finally, more of the first solvent is added *dropwise* until the solution clears.

Two further aspects of this option should be noted. First, the solution must be cooled slightly below the lower boiling point before the second solvent is added if this solvent has a boiling point *lower* than the first; otherwise the addition of this solvent could cause sudden and vigorous boiling of the mixture and hot solvent might spew from the apparatus. Second, hot filtration should be performed if needed *before* addition of the second solvent; this will prevent crystallization during the filtration step. A potential disadvantage of this method for mixed solvent recrystallization is that unduly large volumes of the second solvent may be required if excessive amounts of the initial solvent have been used.

In the second option, the solute is added to the solvent in which it is insoluble, and the mixture is heated near the boiling point of the solvent; the second solvent is then added in small portions until the solid just dissolves. As with recrystallization from a single solvent, it is generally wise to add 3-5% of additional solvent to prevent premature crystallization of the solute during hot filtration, if this step is necessary. The use of this approach to mixed solvent recrystallization also has the disadvantage that using too much of the first solvent will require the addition of undesirably large volumes of the second solvent.

DECOLOURATION AND HOT FILTRATION

After dissolution of the solid mixture, the solution may be colored. This signals the presence of impurities if the desired compound is known to be colorless. If the compound is colored, contaminants may alter the colour of the solution; for example, impurities should be suspected if the substance is yellow but the solution is green. Of course, the decolouration step is unnecessary if the solution is colorless.

Coloured impurities may often be removed by adding a small amount of decolourizing carbon to the hot, *but not boiling*, solution. Adding it to a boiling solution is likely to cause the liquid to froth over the top of the flask, resulting in the loss of product. After the decolourizing carbon is added, the solution is heated to boiling for a few minutes while being continuously stirred or swirled to prevent bumping.

Completely removing decolourizing carbon by hot filtration may be difficult if the powdered rather than the pelletized form is used, because the finely divided solid particles may pass through filter paper or the cotton of a Pasteur filtering pipette. If this occurs, the dark particles should be visible in the filtrate.

The following steps are recommended to assist in removing the decolourizing carbon during filtration. The hot decolorized solution is allowed to cool slightly below its boiling point, a small amount of a filter-aid such as Celite is added to *adsorb* the carbon, the mixture is briefly reheated to boiling, and then is subjected to hot filtration. It may be necessary to repeat this procedure if some of the decolourizing carbon still passes through the filter paper and remains in the filtrate.

This technique for decolourizing solutions works because coloured impurities as well as the compound being purified are adsorbed on the surface of the carbon particles. For electronic reasons, the coloured substances adsorb more strongly to the surface, and this factor, combined with the fact that the impurities are normally present in minor amounts, results in complete removal of the coloured contaminants. Of course, because the desired product itself is adsorbed by the decolourizing carbon, less of it will be recovered if too much carbon is added.

Insoluble impurities, including dust and decolorizing carbon, if used, are removed by gravity filtration of the hot solution; this step is not necessary if the hot solution is clear and homogeneous. Gravity filtration is normally preferred to vacuum filtration because the latter technique may cause cooling and concentration of the solution, owing to evaporation of the solvent, and this may result in premature crystallization. A short-stemmed or stemless glass funnel should be used to minimize crystallization in the funnel, and using fluted filter paper will minimize crystallization on the filter. To keep liquid from flowing over the top of the funnel, the top of the paper should not extend above the funnel by more than 1-2 millimeters.

CRYSTALLIZATION

The hot solution of solute is allowed to cool slowly to room temperature, and crystallization should occur. During cooling and crystallization, the solution should be protected from airborne contaminants by covering the opening with a piece of filter paper, an inverted beaker, or by loosely plugging it with a clean cork. Rapid cooling by immersing the flask in water or an ice-water bath is undesirable because the crystals formed tend to be very small, and their resulting large surface area may foster adsorption of impurities from solution. In this sense, the crystals are functioning like decolorizing carbon! Generally the solution should not be disturbed as it cools, since this also leads to production of small crystals. The formation of crystals larger than about 2 mm should be avoided because some of the solution may become occluded or trapped *within* the crystals. The drying of such crystals is more difficult, and impurities may be left in them. Should overly large crystals begin to form, brief, gentle agitation of the solution normally induces production of smaller crystals.

Failure of crystallization to occur after the solution has cooled somewhat usually means that either too much solvent has been used or that the solution is supersaturated. A supersaturated solution can usually be made to produce crystals by seeding. A crystal of the original solid is added to the solution to induce crystallization, which may then be quite rapid. If no solid is available and a volatile solvent is being used, it is sometimes possible to produce a seed crystal by immersing the tip of a glass stirring rod or metal spatula in the solution, withdrawing it, and allowing the solvent to evaporate. The crystals that form on the end of the rod or spatula are then reinserted into the solution to initiate crystallization. Alternatively, crystallization can often be induced by using a glass rod to rub the inside surface of the crystallization vessel *at* or *just above* the air/solution interface. This should be done carefully, as excessive force may scratch or break the vessel or result in a broken rod.

Occasionally the solute will separate from solution as an oil rather than a solid. This type of separation, which is sometimes called oiling out, is undesirable for purification of solutes because the oils usually contain significant amounts of impurities. Two general approaches are helpful in solving this problem: (1) Oils may persist on cooling with no evidence of crystallization. These may often be induced to crystallize by scratching the oil against the side of the flask with a glass stirring rod at the interface of the oil and the solution. If this fails, several small seed crystals of the original solid may be added to the oil, and the mixture allowed to stand for a period of time. Failure of these alternatives may necessitate separation of the oil from the solution and crystallization of it from another solvent. (2) Oils may form from the hot solution and then solidify to an amorphous mass at lower temperatures; in the meantime, crystals of the solute may precipitate from the mother liquor. Because the oil is not a pure liquid, the solid mass produced from it will be impure, as noted earlier. In a case such as this, the usual remedy is to reheat the entire mixture to affect dissolution, add a few milliliters of additional pure solvent, and allow the resulting solution to cool.

SIMPLE CRYSTALLIZATION

Simple crystallization works well with large quantities of material (100 mg and up).

Step 1. Place the solid in a small Erlenmeyer flask or test tube. A beaker is not recommended because the rapid and dangerous loss of flammable vapours of hot solvent occurs much more easily from the wide mouth of a beaker than from an Erlenmeyer flask. Furthermore, solid precipitate can rapidly collect on the walls of the beaker as the solution becomes saturated because the atmosphere above the solution is less likely to be saturated with solvent vapour in a beaker than in an Erlenmeyer flask.

Step 2. Add a minimal amount of solvent and heat the mixture to the solvent's boiling point in a sand bath. Stir the mixture by twirling a spatula between the thumb and index finger. A magnetic stir bar may be used if a magnetic stirring hot plate is used.

Step 3. Continue stirring and heating while adding solvent dropwise until all of the material has dissolved.

Step 4. Add a decolorizing agent (powdered charcoal, ~2% by weight; or better, activated-carbon pellets, ~0.1 % by weight), to remove coloured minor impurities and other resinous by-products.

Step 5. Filter (by gravity) the hot solution into a second Erlenmeyer flask (preheat the funnel with hot solvent). This removes the decolorizing agent and any insoluble material initially present in the sample.

Step 6. Evaporate enough solvent to reach saturation.

Step 7. Cool to allow crystallization (crystal formation will be better if this step takes place slowly). After the system reaches room temperature, cooling it in an ice bath may improve the yield.

FILTRATION AND SOLVENT REMOVAL

The crystalline product is isolated by filtration. The technique for doing this varies depending on the scale on which the crystallization was performed.

The solid product is isolated by vacuum filtration using a Büchner or Hirsch funnel and a clean, dry filter flask. The crystals normally are washed with a small amount of *pure, cold* solvent, with the vacuum off; the vacuum is then reapplied to remove as much solvent as possible from the filter cake. Care must be taken in this step to ensure that the filter paper is not lifted off the bed of the filter while the vacuum is off; this could result in loss of product when the vacuum is reapplied to remove the washes.

Further cooling of the filtrate, sometimes called the mother liquor, in an ice-water or ice salt bath may allow isolation of a second crop of crystals. The filtrate can also be concentrated by evaporating part of the solvent and cooling the residual solution. The crystals isolated as a second or even a third crop are likely to be less pure than those in the first. Consequently, the various crops should not be combined until their purity has been assessed by comparison of their melting points.

DRYING THE CRYSTALS

The final traces of solvent are removed by transferring the crystals from the filter paper of the Büchner or Hirsch funnel to a watch-glass or vial. Alternatively, solids may also be transferred to fresh pieces of filter or weighing paper for drying. This is a less desirable option, however, because fibers of paper may contaminate the product when it is ultimately transferred to a container for submission to your instructor. It is good practice to protect the crystals from airborne contaminants by covering them with a piece of filter paper or using loosely inserted cotton or a cork to plug the opening of the vessel containing the solid.

Removing the last traces of solvent from the crystalline product may be accomplished by air- or oven-drying. With the latter option, the temperature of the oven must be below the melting point of the product.

SOLVENT SELECTION

Although different criteria are used for defining solubility, plan to use the following definitions in this experiment: (a) soluble-20 mg of solute will dissolve in 0.5 mL of solvent; (b) slightly soluble-some but not all of the 20 mg of solute will dissolve in 0.5 mL of solvent; (c) insoluble-none of the solute appears to dissolve in 0.5 mL of solvent. *Be certain to record all your observations regarding solubilities in your notebook!*

Procedure

Apparatus Test tubes (10-mm × 75-mm), hot-water (80-100 °C).

For *known* compounds, place about 20 mg (a spatula-tip full) of the finely crushed solid in a test tube and add about 0.5 mL of water using a calibrated Pasteur pipette. Stir the mixture with a glass rod or spatula to determine whether the solid is soluble in water at room temperature. If the solid is not completely soluble at room temperature, warm the test tube in the hot-water or steam bath, and stir or swirl its contents to determine whether the solid is soluble in hot water.

If any of your solutes is soluble in the hot solvent but only slightly soluble or insoluble at room temperature, allow the hot solution to cool slowly to room temperature and compare the quantity, size, color, and form of the resulting crystals with the original solid material.

Repeat the solubility test for the solutes using 95% ethanol and then petroleum ether (b.p. 60-80 °C, 760 Torr). After completing these additional tests, record which of the three solvents you consider best suited for recrystallization of each of the solutes.

For *unknown* compounds, a *systematic* approach is important for determining their solubility, and the following protocol accomplishes this. The following solvents may be tried: water, ethanol, diethyl ether, and hexanes. Your instructor may also suggest other solvents to evaluate.

After selecting the solvents, obtain enough clean, dry test tubes so that there is one for each solvent to be tested. Place about 20 mg (a spatula-tip full) of the finely crushed unknown in each test tube and add about 0.5 mL of a solvent to a tube containing the solid. Stir each mixture and determine the solubility of the unknown in each solvent at room temperature. Use the definitions of *soluble*, *slightly soluble*, or *insoluble* given earlier.

If the unknown is insoluble in a particular solvent, warm the test tube in the hot-water. Stir or swirl the contents of the tube and note whether the *unknown* is soluble in hot solvent. If the solid is soluble in the hot solvent but only slightly soluble or insoluble at room temperature, allow the hot solution to cool to room temperature slowly. If crystals form in the cool solution, compare their quantity, size, color, and form with the original solid material and with those obtained from other solvents.

It is a good idea to test the solubility of a solute in a variety of solvents. Even though nice crystals may form in the first solvent you try, another one might prove better if it provides either better recovery or higher-quality crystals. To assist in determining the best solvent to use in recrystallizing an unknown, you should construct a table containing the solubility data you gather by the systematic approach described above.

If these solubility tests produce no clear choice for the solvent, mixed solvents might be considered. Review the discussion presented earlier in this section for the procedure for using a mixture of two solvents. Before trying any combinations of sol vent pairs, take about 0.2 mL of each pure solvent being considered and mix them to ensure that they are miscible in one another. If they are not, that particular combination **cannot** be used.

RECRYSTALLIZING IMPURE SOLIDS - PROCEDURES

1a. Benzoic Acid (*miniscale procedure*)

Apparatus Two 50-mL Erlenmeyer flasks, graduated cylinder, apparatus for magnetic stirring, vacuum filtration, and *flameless* heating.

Dissolution Place 1.0 g of impure benzoic acid in an Erlenmeyer flask equipped for magnetic stirring or with boiling stones. Measure 25 mL of water into the graduated cylinder and add a 10-mL portion of it to the flask. Heat the mixture to a gentle boil and continue adding water in 0.5-mL portions until no more solid appears to dissolve in the boiling solution. Record the total volume of water used; no more than 10 mL should be required. ***Caution:*** Because the sample may be contaminated with insoluble material, pay close attention to whether additional solid is dissolving as you add more solvent; if it is not, *stop adding solvent.*

Decolouration Pure benzoic acid is colourless, so a coloured solution indicates that treatment with decolourizing carbon is necessary. ***Caution:*** Do *not* add decolourizing carbon to a *boiling* solution ! Cool the solution slightly, add a spatula-tip full of carbon, and reheat to boiling for a few minutes. To aid in removing the finely divided carbon by filtration, allow the solution to cool slightly, add about 0.2 g of a filter-aid, and reheat.

Hot Filtration and Crystallization If there are insoluble impurities or decolorizing carbon in the solution, perform a hot filtration using a 50-mL Erlenmeyer flask to receive the filtrate. Rinse the empty flask with about 1 mL of *hot* water and filter this rinse into the original filtrate. If the filtrate remains colored, repeat the treatment with decolorizing carbon. Cover the opening of the flask with a piece of filter paper, an inverted beaker, or loose-fitting cork to exclude airborne impurities from the solution, and allow the filtrate to stand undisturbed until it has cooled to room temperature and no more crystals form. To complete the crystallization, place the flask in an ice-water bath for at least 15 min.

Isolation and Drying. Collect the crystals on a Büchner or Hirsch funnel by vacuum filtration and wash the filter cake with two small portions of cold water. Press the crystals as dry as possible on the funnel with a clean cork or spatula. Spread the benzoic acid on a watch-glass, protecting it from airborne contaminants with a piece of filter paper, and air-dry it at room temperature or in an oven. Be certain that the temperature of the oven is below the melting point of the product!

Analysis Determine the melting points of the crude and recrystallized benzoic acid, the weight of the latter material, and calculate your percent recovery using the following equation.

$$\text{Percent recovery} = \frac{\text{Amount recovered (mg)}}{\text{Amount dissolved (mg)}} \times 100\ \%$$

1b. Benzoic Acid (*microscale procedure*)

Apparatus A 10-mm × 75-mm test tube, Pasteur filtering and filter-tip pipettes, apparatus for Craig tube filtration and *flameless* heating.

Dissolution Place 100 mg of benzoic acid in the test tube. Add 1 mL of water to the tube and heat the mixture to a gentle boil. To aid in dissolution, stir the mixture vigorously with a spatula while heating; stirring also prevents bumping and possible loss of material from the test tube. If needed, add more solvent in 0.1-0.2 mL increments to dissolve any remaining solid. Bring the mixture to boiling and continue stirring after each addition. Once all the solid has dissolved, add an additional 0.1-0.2-mL portion of solvent to ensure that the solute remains in solution during transfer of the hot solution.

Caution: Because the sample may be contaminated with insoluble material, pay close attention to whether additional solid is dissolving as you add more solvent. If it is not, *stop adding solvent*. Record the approximate total volume of solvent used.

Decolouration If the solution is coloured and the recrystallized product is known or suspected to be colourless, treatment with decolourizing carbon is necessary. ***Caution: Do not*** add decolourizing carbon to a boiling solution! Cool the solution slightly, add a half of a spatula-tip full of powdered or, preferably, a pellet or two of decolourizing carbon, and reheat to boiling for a few minutes.

Hot Filtration and Crystallization Preheat a Pasteur filtering pipette by pulling hot solvent into the pipette. Then transfer the hot solution into this pipette with a Pasteur pipette or filter-tip pipette that has also been preheated with solvent, using the tared Craig tube as the receiver for the filtrate. If decolourizing carbon or other insoluble matter appears in the Craig tube, pass the solution through the filtering pipette a second, and if necessary, a third time. Concentrate the clear solution in the Craig tube to the point of saturation by heating it to boiling. Rather than using a boiling stone to prevent super-heating and possible bumping, continually stir the solution with a spatula while heating. The saturation point will be signaled by the appearance of cloudiness in the solution and/or the formation of crystals on the spatula at the air/liquid interface. When this occurs, add solvent dropwise at the boiling point until the cloudiness is discharged. Then remove the tube from the heating source, cap the tube with a loose plug of cotton to exclude air-borne impurities, and allow the solution to cool to room temperature. If necessary, induce crystallization by gently scratching the surface of the tube at the air/liquid interface or by adding seed crystals, if these are available. To complete crystallization, cool the tube in an ice-water bath for at least 15 min.

Isolation and Drying *Affix* a wire holder to the Craig tube and, using the wire as a hanger, invert the apparatus in a centrifuge tube. Remove the solvent by centrifugation, carefully dissemble the Craig tube, and scrape any crystalline product clinging to its upper section into the lower part. Protect the product from airborne contaminants by plugging the opening of the tube with cotton or by covering it with a piece of filter paper held in place with a rubber band. Air-dry the crystals to constant weight either at room temperature or in an oven. Be certain that the temperature of the oven is below the melting point of the product!

Analysis Determine the melting points of the crude and recrystallized benzoic acid, the weight of the latter material, and calculate your percent recovery using the following equation.

$$\text{Percent recovery} = \frac{\text{Amount recovered (mg)}}{\text{Amount dissolved (mg)}} \times 100\,\%$$

2. Unknown Compound

Apparatus A 10-mm × 75-mm test tube, Pasteur filtering and filter-tip pipettes, apparatus for Craig tube filtration and *flameless* heating.

Dissolution In a fume-hood, place 100 mg of the unknown in the test tube and dissolve it in a minimum amount of boiling solvent you selected on the basis of solubility tests. ***Caution:*** Because the sample may be contaminated with insoluble material, pay close attention to whether additional solid is dissolving as you add more solvent; if it is not, *stop adding solvent.* Then add 0.1 mL of additional solvent to ensure that premature crystallization will not occur during subsequent transfers. Record the total volume of solvent used.

Continue the procedure by following the directions for *Decolouration*, *Hot Filtration and Crystallization*, and *Isolation and Drying* given for benzoic acid; however, if you are not using water, use the solvent in which you dissolved the unknown.

Analysis Determine the melting points of the crude and recrystallized unknown, the weight of the latter material, and calculate your percent recovery using the following equation.

$$\text{Percent recovery} = \frac{\text{Amount recovered (mg)}}{\text{Amount dissolved (mg)}} \times 100\,\%$$

3. Mixed-Solvent Crystallization

Apparatus A 10-mm × 75-mm test tube, Pasteur filtering and filter-tip pipettes, apparatus for Craig tube filtration and *flameless* heating.

Dissolution Place 100 mg of benzoic acid or acetanilide in the test tube. Add 0.2 mL of 95% ethanol and heat the mixture to a gentle boil. If necessary, continue to add 95% ethanol dropwise by Pasteur pipette until a homogeneous solution is obtained. *Caution:* Because the sample may be contaminated with insoluble material, pay close attention to whether additional solid is dissolving as you add more solvent; if it is not, *stop adding solvent.* Once all the solid has dissolved, add an additional 0.1-0.2-mL portion of solvent to ensure that the solute remains in solution during transfer of the hot solution a Craig tube and, if necessary, decolorize the solution according to the directions in Part 1 for benzoic acid.

Hot Filtration and Crystallization Preheat a Pasteur filtering pipette by pulling hot solvent into the pipette. Then transfer the hot solution into this pipette with a Pasteur pipette or filter-tip pipette that has also been preheated with solvent, using the tared Craig tube as the receiver for the filtrate. If decolorizing carbon or other insoluble matter appears in the Craig tube, pass the solution through the filtering pipette a second, and if necessary, a third time.

Reheat the decolorized solution to boiling and add water dropwise from a Pasteur pipette until the boiling solution remains cloudy or precipitate forms. Rather than using a boiling stone to prevent superheating and possible bumping, continually stir the solution with a microspatula while heating. Then add a drop or two of 95% ethanol to restore homogeneity. Remove the tube from the heating source, cap the tube with a loose plug of cotton to exclude airborne impurities, and allow the solution to cool to room temperature. Follow the same directions as given for benzoic acid in Part 1 to complete both this stage of the procedure and *Isolation and Drying.*

Analysis Determine the melting points of the crude and recrystallized product, the weight of the latter material, and calculate your percent recovery using the following equation.

$$\text{Percent recovery} = \frac{\text{Amount recovered (mg)}}{\text{Amount dissolved (mg)}} \times 100\,\%$$

MELTING POINTS

The melting point of a solid is defined as the temperature at which the solid and liquid phases are in equilibrium. The time necessary to obtain such an equilibrium value is not practical for organic chemists; therefore, the melting-point range of temperatures between the first sign of melting and the complete melting of the solid is taken. A *narrow range* indicates high purity of the sample, whereas a *broad range* usually indicates an impure sample.

To determine a melting-point range, a small sample of the solid in close contact with a thermometer is heated in an oil bath or metal heating block so that the temperature rises at a slow, controlled rate. As the thermal energy imparted to the substance becomes sufficient to overcome the forces holding the crystals together, the substance melts. The rate of heating should be controlled so that the melting range is as narrow as possible. The temperature is recorded when the first melting appears and when the last solid disappears. A sharp melting point is generally accepted to have a range of 1 to 2°C. Impurities will usually cause the melting-point range to become wider and melting to occur at lower temperatures than that of a pure compound. A familiar example of this is the lowering of the melting point of ice by the addition of salt. This phenomenon results from the fact that both the liquid and solid are in equilibrium with the vapour. An impurity dissolved in the substance lowers the vapour pressure of the liquid, causing the solid to melt and restore the equilibrium among the three phases. The amount of lowering will depend on several factors, among which are the molal freezing point lowering constant (K_t), the concentration, and whether the solute is ionic or not. A typical curve for the lowering of the melting point of substance A by added amounts of substance B is shown in Figure 1.

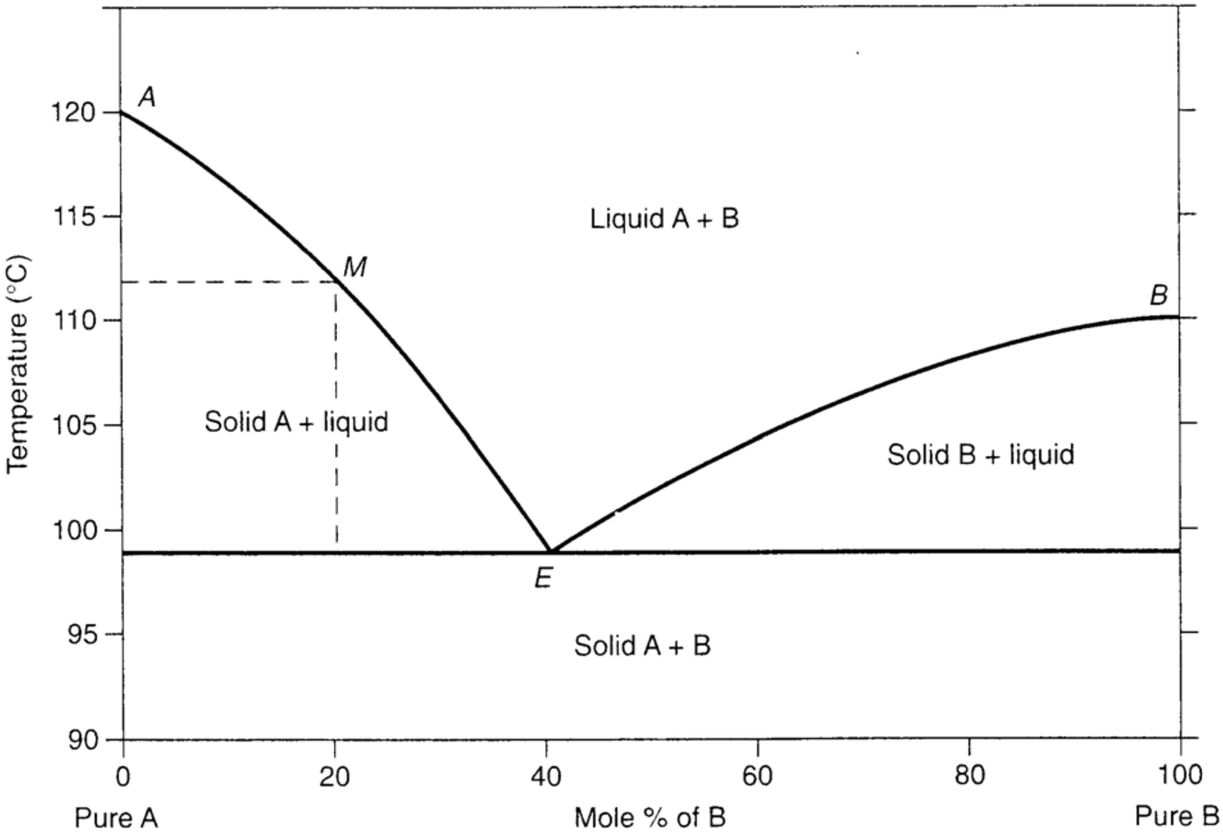


Figure 1. Solid-liquid phase diagram for a mixture of two compounds.

The melting point of pure **A** is 120°C and that of **B** is 110°C. The upper curves connecting points A with E and *E* with B are the boundary above which mixtures of **A** and **B** of any composition are completely melted. The lower horizontal line through point *E* is a boundary representing the temperature (99°C) below which the sample is completely solid at any composition. In the areas between these phase boundaries are mixtures of one or the other pure solids plus liquid.

A sample of composition M for example, will show a melting point range between the temperature at M (112°C) and that at line *E (99°C)*. Point *E*, where the lines intersect, is called the eutectic point. At this composition (known as the eutectic composition, 40% **B**) the mixture would melt sharply at *99°C*.

At the eutectic point, *E*, both solid components can exist in equilibrium with a liquid solution of that particular composition. In a broad sense, one might consider the liquid at the eutectic point to be a saturated solution of either solute ***A*** in solvent ***B*** or, solute ***B*** in solvent ***A***. Cooling of the eutectic liquid will bring about crystallization (freezing) of both ***A*** and ***B*** at a constant temperature, the *eutectic temperature* and at a constant composition, the *eutectic* composition.

To evaluate the effect of an impurity on the melting point **range**, consider the effect of heating a mixture of ***A*** with an amount of impurity, ***B***, less than the eutectic concentration (e.g. 20%). To establish the range we must know where the mixture will begin to melt! When heat is applied, the temperature of the solid mixture will rise; no changes in the physical state of the system will occur until the eutectic temperature is reached. At that temperature, assuming that the heating can be controlled sufficiently that equilibrium conditions are ensured, appropriate numbers of molecules of A and B already in contact at the crystal/crystal interfaces will *melt* to form a liquid phase of eutectic composition (in this case 60/40). As heating is continued more A and B will melt at the eutectic composition and the eutectic temperature, until all of B (the minor component) is entirely melted leaving only solid A in equilibrium with the eutectic liquid. On further heating, the remaining solid A will begin to melt. This, however, will raise the percentage of A in the liquid above the eutectic composition. Since the partial vapour pressure due to A in the liquid is thereby increased, the temperature (melting point!) at which solid A is in equilibrium with the liquid must also rise. In this fashion, melting will continue, at progressively increasing temperatures (represented by the curve EM in Figure 1) until the last trace of solid A becomes liquid at temperature M. Hence, if perfect equilibrium conditions were maintained, the melting point range for such a mixture would be from E, the eutectic temperature, to M.

Similarly, if we were to consider a solid mixture with a composition to the right of point E in Figure 1, we would speak of a compound B with impurity A and the rising temperature during the melting process would follow curve E B.

In theory, then, for any solid compound containing a relatively small amount of impurity, melting will begin at the eutectic temperature and be complete at some temperature lower than the melting point of the pure compound. Moreover, if the concentration of the impurity were increased, the upper limit of the melting would be lowered and therefore the melting range decreased !

In practice, however, equilibrium conditions are almost never achieved and, moreover, it is extremely difficult to detect the initial melting or eutectic condition. If only a very small amount of impurity is present (which is most often the case) the temperature may rise several degrees above the eutectic temperature before sufficient liquid phase accumulates to be visible to the human eye. Nevertheless, the temperature at which the last crystal disappears can be determined quite accurately.

Because of the inherent variabilities, if two students tested the same impure preparation, one might find a higher *initial* melting temperature but both should find the same *final* melting temperature.

Therefore, as actually observed, a nearly pure solid compound tends to show a narrow melting range with an upper limit near the true melting point whereas a rather impure compound usually shows a broader melting range with the maximum temperature considerably below the true melting point.

It is clear from further consideration of Figure 1 that the effect of an impurity is not directly dependent on its own melting point. Thus, for example, a solid impurity whose melting point is higher than that of the compound will still depress the latter's melting point (at least in amounts less than that of the eutectic composition). It should also be noted that a sample whose composition is exactly that of the eutectic exhibit a sharp melting point, melting completely at the eutectic temperature. Thus a eutectic mixture may sometimes be mistaken for a pure compound.

Such infrequent occurrences may be identified by adding a small amount of either component (assuming one knows what the components are!) and observing that the melting point rises. Finally, the eutectic point is not limited to mixture compositions around 50/50 (60/40 in the arbitrary example shown in Figure 1) but may in principle occur at any composition depending only on the specific properties of the particular components.

OTHER VARIATIONS IN MELTING BEHAVIOUR

On heating, some compounds undergo partial or complete decomposition before the melting point is reached. A compound which decomposes before its melting point, or melts with decomposition, often exists as a solid/liquid mixture over a wider temperature range than a normal melting point and the actual range observed depends, even more strongly than usual, on the rate of heating. For example, for those substances which decompose as the sample melts, the liquid phase becomes increasingly contaminated with decomposition products which depress the melting point. Slow heating, therefore, tends to give a melting point below that obtained by faster heating. Sometimes, however, these decomposition points are sharp enough to be useful for identification and should be recorded as such, e.g., mp 200-203°C (dec.).

It was noted earlier that the melting point is depressed only by impurities soluble in the liquid melt. Fortunately, completely insoluble impurities are seldom encountered, but nevertheless may usually be recognized by a cloudy or turbid melt. More frequent (but still rare) is the occurrence of *'solid solutions'* of the impurity in the crystals of the pure compound and even occasionally, of "compound formation" by interaction of the two components in the liquid melt. In such instances, the eutectic diagrams are much more complex than that depicted in Figure 1 with the result that in some cases the melting point is actually elevated by the impurity. Even for an '*ideal*' system, the eutectic composition may contain so little of component **B**, that even a fairly small amount of **B** as an impurity may actually raise the observed melting point of compound **A**.

More detailed explanations of such systems are available in more advanced books on laboratory techniques or in standard physical chemistry texts.

The phase diagram in Figure 1 represents a simple or limiting case in which no solution of **B** in **A** or **A** in **B** occurs in the solid phase. More complex phase diagrams are possible, in which a solid solution does occur or in which there are two eutectic points with a maximum between them, corresponding to the formation of a complex or compound between the two components. Even in these cases, the melting point of the pure compound is generally lowered by the presence of a second component.

The number of exceptions to the rule is small, and chemists are generally safe in using melting point determinations as criteria for purity of known compounds. However, the use of melting points as criteria of purity for unknown substances must be tempered by the knowledge that exceptions do exist.

MELTING POINT BEHAVIOUR

Many solids undergo some degree of decomposition or unusual behaviour prior to melting. There may be changes in appearance of the sample, such as loss of luster or darkening, before the sample actually begins to melt. Some compounds melt with decomposition, as evidenced by bubbling or formation of a dark char. In such cases, the observed melting point (or decomposition point) frequently depends on the rate of heating.

Often compounds begin to soften, shrink, or appear moist before melting. These changes are not the beginning of melting and are sometimes referred to as sintering; the actual melting begins when the first drop of liquid is visible and is completed when the last solid disappears.

If a compound is appreciably volatile, determination of the melting point may be accompanied by sublimation, wherein the solid vaporizes and disappears before it melts. With a capillary tube, sublimation can be prevented by sealing the top of the tube after filling it. On an open block, the sample will seem to shrink into an increasingly small circle and may disappear before melting occurs. It may be possible to observe the melting point by using a larger than normal sample and placing it on the block at a temperature not too far below the expected melting point.

PRACTICAL APPLICATIONS OF MELTING POINT BEHAVIOUR

In addition to its fundamental importance as a characteristic physical constant or "fingerprint" of a specific substance, the melting point can serve a number of useful roles:

(i) Monitoring of Purification Techniques

Typically, solid reaction products are impure and hence have low melting points over broad ranges. As the purity of the product increases, the melting point rises and becomes sharper. Thus, the effectiveness of each stage in any given purification process (most commonly, recrystallization) can be assessed by a simple melting point determination after each step. If a particular technique does not achieve an improvement in the melting point it should be abandoned and another substituted. Purification is continued (best by a combination of methods) until the same, sharp melting point is found after two successive steps.

(ii) Compound Identification: "Mixed" Melting Point Determination

Once a compound has been tentatively identified by its melting point and other information, the exclusion of other possible compounds of similar melting point can be accomplished through a mixture ("mixed") melting point determination with an authentic sample. This is best presented in the form of an example: A research worker has prepared a compound, X, which he believes might be 2-fluorobenzoic acid, m.p. 122°. There are however, several compounds with approximately the same melting point, including simple benzoic acid. If a sample of compound X is mixed intimately with an equivalent amount of an authentic sample of 2-fluoro-benzoic acid and the melting point of this mixture is depressed below that of either compound X or pure 2-fluorobenzoic acid, then the latter must be acting as an impurity and one can safely conclude that compound X is not 2-fluorobenzoic acid. If, however, the mixture melting point is essentially identical with that of each component individually, then compound X may be assumed to be 2-fluorobenzoic acid pending comparison of other properties. It should be noted that one can eliminate possibilities by this method with far more certainty than one can elect them.

(iii) Molecular Weight Determination

It was noted earlier, that in dilute, 'ideal' solutions, the depression of the melting (or freezing) point of a solvent is directly proportional to the mole fraction of the solute. Hence, determination of the melting point depression caused by the addition of a known weight of an unidentified, but pure, substance to a suitable 'solvent', provides a simple and effective method for determining the molecular weight of the unknown compound. Camphor, with its very large "molal freezing point depression constant" and its high solvent power in the molten state, is the most generally used 'solvent' for this purpose - the method is known as the Rast Molecular Weight Determination.

MIXTURE MELTING POINTS

In identifying an unknown, a useful practice is to take the melting point of the unknown and, at the same time, to take that of a mixture of the unknown and a known compound suspected to be the same as the unknown. If the known and unknown samples are the same substance, there will be no depression of the melting point; however, if they are different, a depression of the melting point will occur. To make sure that the mixture was not one of the exceptions mentioned above, another ratio of known to unknown should be melted.

To prepare a sample for determination of mixture melting point, place approximately equal amounts of the two compounds on a piece of glassine paper or a watch glass and mix them together. Then crush the crystals to a powder and grind them thoroughly with a spatula. When the pile of crystals is spread out to a thin layer, scrape the powder together and grind again. Fill the melting point capillary in the usual way and fill other capillaries with samples of the two individual compounds that have been ground to the same degree of fineness. Place all three samples together, with the mixture in the middle, in the bath or block and observe the melting points simultaneously. The temperature can be raised rapidly to about 20° below the expected melting point, then more slowly.

APPARATUS

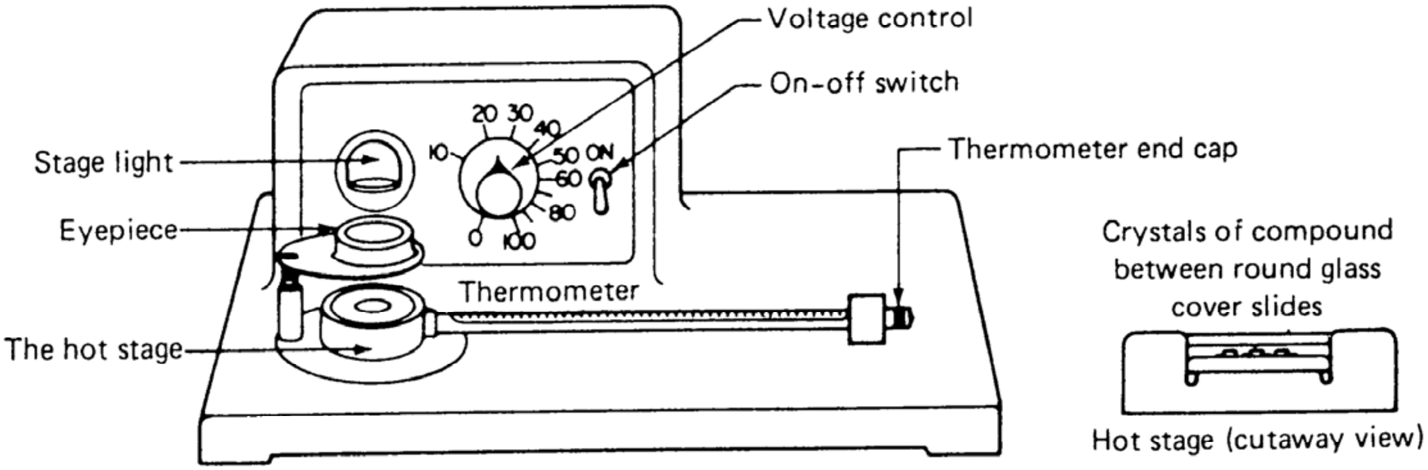
In its simplest terms, the determination of a melting point requires measurement of the temperature range over which liquid and solid coexist while the temperature of a sample of the solid is slowly raised under conditions which allow for uniform distribution of heat throughout the sample. The various types of apparatus which have been developed differ primarily in whether the sample is heated directly or contained in a glass capillary tube or between two glass disks, whether the heating medium is a fluid or a metal block and whether the source of heat is a simple Bunsen burner or a variable electric heater.

With the most precise, sophisticated apparatus (and most expensive !), the Köfler Block, a microscope is used to observe a tiny crystal of the solid placed directly on the surface of a metal block which is heated electrically.

The more common technique, employed in most laboratories on a routine basis, is the **capillary tube method** or a **hot stage** melting point instrument**.** The Fisher-Johns apparatus is an example of a **hot stage** melting point instrument. This is the type of the melting point apparatus you are going to use in this laboratory.

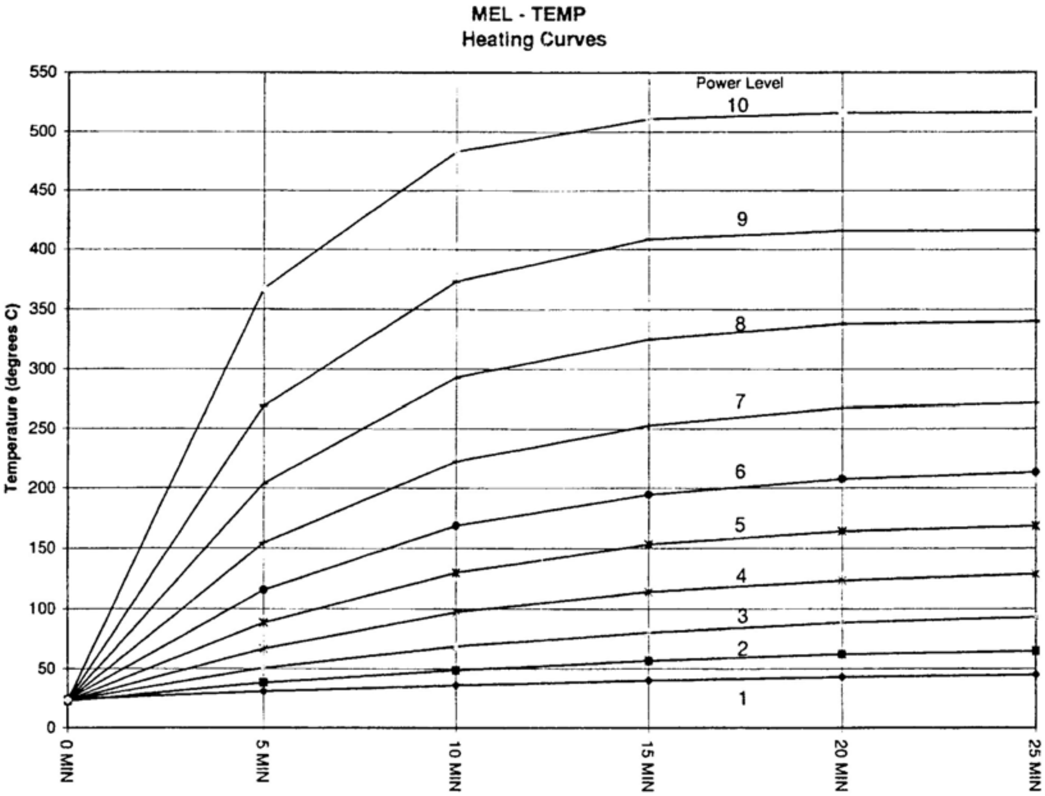
The Fisher-Johns Melting Point Apparatus

The Fisher-Johns apparatus is an example of a **hot stage** melting point instrument. The sample is placed between two round microscope cover slides (thin windows of glass) on a heating block.



Operation of the Fisher-Johns apparatus

1. Do not assume that the unit is cold. That is a good way to get burned.
2. Keep your fingers off the cover slides. Use tweezers or hold them by edges only.
3. Place a clean round glass cover slide in the well on the hot stage. Never melt any samples directly on the metal stage. Ever!
4. Put a few crystals on the glass. Not too many. As long as you can see them melt, you are all right.
5. Put another cover slide on top of the crystals to make a sandwich.
6. Set the voltage control to zero if it is not already there.
7. Turn on-off switch to ON. The light source should illuminate the sample. If not, call for help!
8. Now science turns into art. Set the voltage control to any convenient setting. The point is to get up to within 20°C of the supposed melting point. Yes, that is right. If you have no idea what the melting point is, it may require several runs as you keep skipping past the point with a temperature rise of 5 - 10°C per minute. A convenient setting is 40. This is just a suggestion, not an article of faith.
9. After you have melted a sample, let it cool, and remove the sandwich of sample and cover slides. Throw it away into an appropriate waste container.
10. Once you have an idea of the melting point (or looked it up in a handbook, or you were told), get afresh sample, and bring the temperature up quickly at about 5 -10° C per minute to within 20°C of this approximate melting point. Then turn down the voltage control to get a 2°C per minute rise. Patience!
11. When the first crystals just start to melt, record the temperature. When the last crystal just disappears, record the temperature. If both points appear to be the same, either the sample is extremely pure, or the temperature rise was too fast.
12. Turn the on-off switch to OFF. Now set the voltage control to zero.
13. Let the stage cool, then remove the sandwich.



ERRORS

The principal sources of error are inaccurate calibration of the thermometer and non-uniform distribution of heat to and within the solid sample.

The thermometer used in measuring melting points is only as accurate as the manufacturer has made it and handling has allowed it to remain! Moreover, particularly at higher temperatures, inaccurate readings are obtained because the long exposed stem is at a much lower temperature than the bulb of the thermometer. For these reasons, when a given melting point apparatus is to be used repeatedly with the same thermometer, it is good practice to calibrate the thermometer with a number of pure, standard compounds having sharp melting points. Appropriate corrections are then recorded on a graph attached to the instrument.

A finite time is required for the transfer of heat from the heating bath or block not only to the mercury of the thermometer but also, through the glass walls of the capillary tube and throughout the crystalline mass of the solid sample. If the apparatus is heated too rapidly, the temperature of the bath may rise several degrees during the time lags required for conduction of heat to the rest of the system. The most accurate results are obtained, therefore, only by a very slow, uniform rate of heating. At the melting point the temperature rise should not be greater than 1°C per minute. This may seem extraordinarily slow, but it is necessary in order for heat from the heating block to be transferred equally to the sample and to the thermometer.

From experience you know the rate at which ice melts. Consider doing a melting point experiment on an ice cube. Because water melts at 0°C, you would begin a few degrees below zero. To observe the true melting point of the ice cube, you would need to raise the temperature extraordinarily slowly. The ice cube would appear to begin to melt at 0°C and, if you waited for temperature equilibrium to be established, it would all be melted at 0.5 °C. If you were impatient and raised the temperature too rapidly, the ice might appear to melt over the range 0 to 20°C. Similarly, melting points determined in capillaries will not be accurate if the rate of heating is too fast. The rate of heating is the most important factor in obtaining accurate melting points. Heat no faster than 1°C per minute.