

## RECRYSTALLIZATION, FILTRATION AND MELTING POINT

Recrystallization is one of the main purification methods for solid compounds on virtually any scale, from mg to kg to tons. From the experimental point of view, the process of recrystallization comes down to a few basic steps:

- a) the solid is heated to reflux or near reflux of a solvent in a minimum amount of the appropriate solvent to produce a saturated solution;
- b) in case there is an insoluble residue, the hot solution is filtered to produce a homogeneous solution and to remove the insoluble impurities;
- c) the homogeneous solution (or filtrate) is allowed to cool slowly to room or sub-ambient temperature to produce crystals;
- d) the crystals are filtered off and washed with a small amount of COLD solvent, and subsequently dried to yield the solid, which should have a higher degree of purity than the original sample.

The rationale for each step is fairly straightforward:

It is known that the solubility of most compounds in a given solvent will increase at elevated temperatures. Therefore heating is used to dissolve the sample. It is also known that the solubility near the boiling point greatly increases, therefore it is imperative to bring the solution to a boil. Furthermore, it is important to keep the volume of the solvent to the minimum, since recrystallizations from dilute solutions usually lead to poor yields of recovery of the material, if any. In this light, initially the smallest possible amount of solvent is added, and the solution is heated. If the majority of the solid remains undissolved, additional amounts of solvent (in small portions) can be carefully added.

During the cooling step, the molecules of a given compound will be assembling into aggregates with the molecules that have a similar nature. These aggregates will grow in size and eventually will be deposited from solution to form a solid with a particular crystal lattice. Other types of molecules that are not capable of engaging in the same types of interactions with the above aggregates (and/or possess a different size, shape) will be excluded from the solid and, ideally, will remain in the solution. Thus, a separation of one type of molecules from the others can be achieved.

Drying of the crystals (either in air at room temperature, or heated below the melting point, or in vacuo) will rid of the solvent molecules to produce the desired compound in a purer form than the initial solid. The drying step is usually done either on air over a prolonged period of time or under a vacuum. For air- and moisture-sensitive materials, the drying should be done under vacuum, and the solid should be stored in a desiccator.

### **Solvent selection:**

Obviously, the most crucial step is the choice of an appropriate solvent. There are few empirical rules that can be used as a guide to select a proper solvent, but for the most parts, the selection of the optimal recrystallization solvent is a trial and error method.

Rule #1: Like dissolves like.

Rule #2: The solid should be insoluble or only sparingly soluble in a cold solvent (room temperature or 0 °C usually refers to a cold solvent), and completely soluble in a hot solvent. (This is an ideal behavior, which is rarely observed.)

Rule #3: The impurities should have a different solubility profile in the particular solvent than the compound of interest.

Rule #4: The melting point of the compound should be higher than the boiling point of the solvent

Rule #5: Given the choice of solvents, the one with a lower boiling point will be a better option.

The structures and boiling points of some of the most commonly solvents used for the recrystallizations are given in Figure 1.

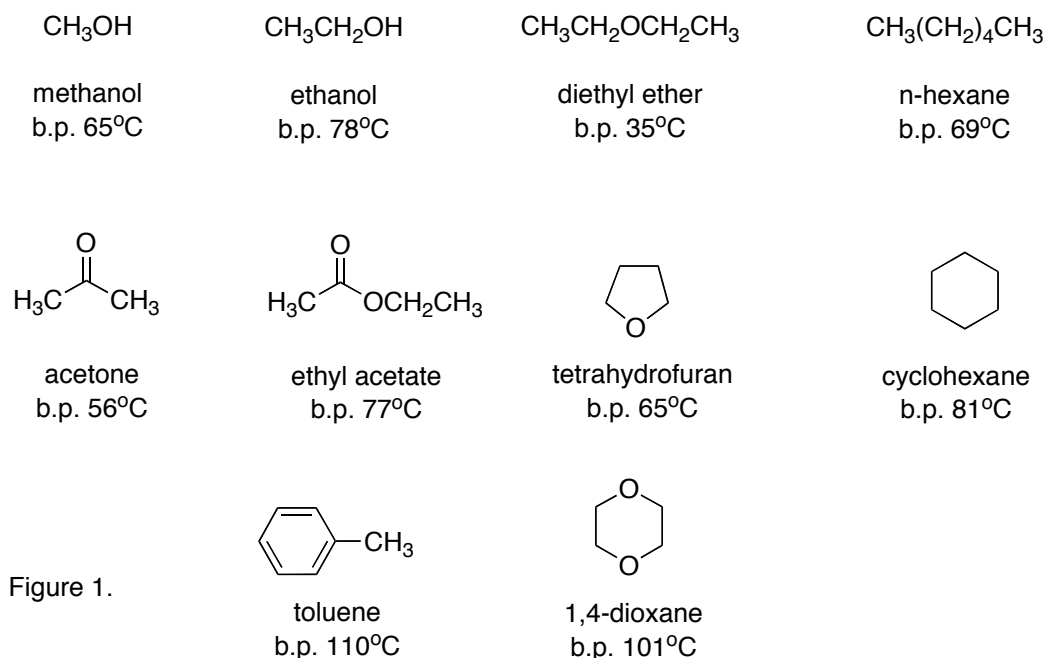


Figure 1.

Literature sources should be consulted for choosing solvents for recrystallization of known compounds. In cases where an unknown compound needs to be purified by recrystallization, testing of its solubility should be conducted before carrying out the recrystallization. Small amounts of solid (usually a few crystals) are placed in small test tubes and about 1 mL of the solvent is added. Immediate formation of the solution renders the solvent ineffective for the subsequent crystallizations. If the immediate dissolution does not take place, the test tube is shaken, and then it is gently heated. If the dissolution of the solvent does take place, the solvent can be considered suitable for the subsequent crystallization. If the solid still did not dissolve, an additional 1 mL of the solvent is added, the test tube is again shaken and heated. The presence of the solid indicates that the solid is insoluble in the given solvent. Table 1 can be used as a guide for initial selection of the recrystallization solvent.

Table 1.

<b>Compound class</b>	<b><i>Soluble in:</i></b>
Hydrocarbons	<i>Hydrocarbons, halogen-containing</i>
Halogen containing hydrocarbons	<i>hydrocarbons ethers</i>
Ethers	
Esters	<i>Esters</i>
Nitro-containing compounds	
Nitriles	<i>Alcohols, ethers</i>
Ketones	
Aldehydes	
Amines	<i>Alcohols, water</i>
Alcohols	
Carboxylic acids	
Salts	<i>Water</i>

In many instances, a mixture of solvents must be used for recrystallization ("mixed solvent" system). Usually, two solvents, which are completely miscible with each other over a wide temperature range, are used: one in which the compound is quite or completely soluble even at ambient temperature, and the second solvent in which the compound is insoluble. Two approaches can be applied:

1. The compound is first completely dissolved in a hot solvent in which it is soluble, removed from the heat source and the other solvent is added until cloudiness starts to appear. This is the sign of the beginning of crystal formation. At this point the mixture should be reheated to obtain a homogeneous, *i.e.*, clear, solution, and allowed to cool to produce the crystals.
2. The compound is added to the solvent in which it is insoluble, and the heterogeneous mixture is heated to a near boil, removed from the heat, and the second solvent is added in small portions. The mixture is reheated after each addition of the second solvent. This procedure is continued until all compound is dissolved.

In the above cases, the amounts of both solvents should be kept to the minimum to a) avoid the unnecessary use of too much solvent, and b) recrystallization from dilute solution is very inefficient. Moreover, it is desirable that the boiling points of the two solvents should be fairly close to each other, such that their ratio would not significantly change during the heating cycles.

The following is the list of commonly used solvent mixtures:

ethanol – water, acetone – water, ethyl acetate – hexane, toluene – heptane.

It is a good practice to weigh out the amount of recrystallized material, and approximately measure the amount of the solvent. This will allow to quantitatively estimate the efficiency of the recrystallization process as well as it will be possible to rapidly reproduce the recrystallization, if necessary.

### **Decolorizing agents**

On a number of occasions, the presence of highly colored impurities (even in the amount of < 1% of the total weight of the sample) will significantly contribute to the color of the compound. Colored impurities can be removed by the addition of decolorizing carbon (charcoal) to the hot, yet not boiling, solution. The charcoal has a very fine surface, which is filled with air. Once it is placed in a solution, the air is displaced by the solvent molecules; at boiling temperatures, the displacement process is extremely rapid, which usually results in frothing of the solution and usually leads to the loss of the compound and potential injury. After the charcoal is added, the solution is heated at or near the boiling point for several minutes, while continuously being swirl to avoid bumping. Subsequently the charcoal is removed by gravity filtration, and the filtrate is allowed to cool to yield the crystalline material.

It should be pointed out that both the molecules of the desired compound and the molecules of the impurities are absorbed on the decolorizing carbon. Also, the use of decolorizing carbon is not specific for colored impurities, although due to the electronic features of colored compounds, they tend to have a higher affinity towards charcoal than the non-colored ones. However, it is much easier to detect the removal of colored impurities than those that are not colored. Therefore, the application of too much of the decolorizing agent will lead to a loss of the material, and generally should be avoided.

## FILTRATION

After the crystallization is finished, the crystals should be separated from the liquid. In principle, the supernatant solution can be decanted from the solid. However, a loss of the solid as well as an incomplete removal of the liquid, which might contain the impurities, will take place. A better technique to separate the solid from the liquid is by filtration. Fundamentally, filtration is a process that involves passing the suspension of the solid in the liquid through a membrane that is permeable only to a liquid. The filtrate, often called “mother solution” or “mother liquor”, is collected in a separate receiving flask, whereas the solid remains on the membrane. The membrane can be made of any inert material, as long as it is permeable to the solvent; and it can be of any shape. The most common one, and the one, which will be used routinely throughout this course, is filter paper. Cotton or glass wool are other permeable flexible membranes that can be used to filter fairly large solid particles from the solutions.

### Gravity filtration

This technique is mostly used to remove impurities, drying or decolorizing agents. The set-up for the gravity filtration is very simple (Figure 2), and it features a filter paper, a funnel, ring clamp and a receiving container, usually a beaker or an Erlenmeyer flask are used. The proper folding of the filter paper is shown in Figure 3. The folding of the filter paper provides an enhanced surface area as it insures a rapid filtration.

In gravity filtration, the filter can usually be employed dry (no need to wet it with a solvent). Obviously, when gravity filtration is used to remove a drying agent, the filter should NEVER be wetted with water!

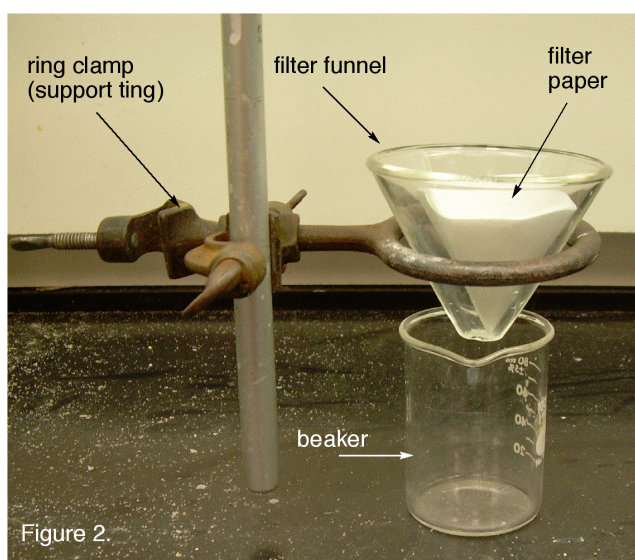


Figure 2.

It should be kept in mind that the filter paper itself can also absorb small, but significant amounts of solvent. Therefore, the filter paper should always be rinsed with additional amount of the fresh (cold) solvent to rid of the mother solution, which can contain the impurities.

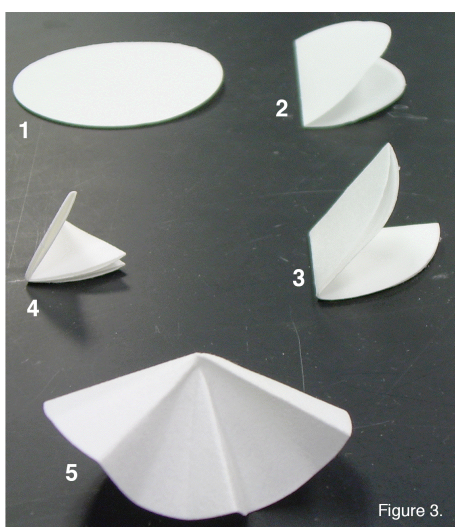


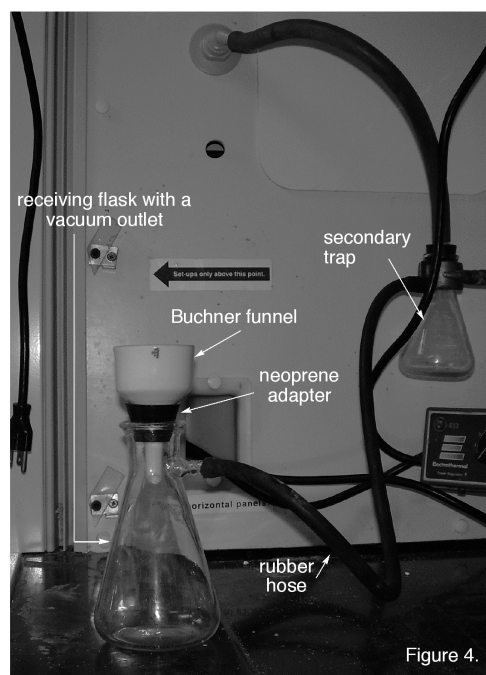
Figure 3.

### Vacuum filtration

This technique is usually used to collect solids from the solvents after either precipitation or recrystallization. A set-up for vacuum filtration (Figure 4) is more elaborate than that for the gravity filtration. It consists of a Buchner funnel, equipped with a flat round piece of a filter paper, neoprene adapter, a receiving flask with a vacuum outlet, which is connected to the vacuum trap (usually a second vacuum filter flask) to prevent an incidental flow of liquid to the vacuum pump. Similar to the gravity filtration, the filter paper on the Buchner funnel should be wetted before starting the filtration. The solid on the filter paper should be washed with additional amounts of the cold, pure solvent to remove the mother solution. At this stage, the vacuum can be released, and the solvent is allowed to pass through

the filter paper by gravity. This assures a closer contact of the solid with solvent and aids in removing the residual mother solution. The vacuum can be reapplied after most of the liquid passed through the funnel to completely dry the solid.

Vacuum filtration should not be used for filtering hot solutions. During filtration some of the solvent is evaporated, which cools down the solution. Since application of vacuum will enhance the rate of solvent evaporation, the solution will cool off much faster than at ambient pressure. This can lead to premature crystallization of the solid on the filter paper. The clogging of the filter paper will occur, which will significantly slow down the filtration process. It will also lead to the contamination of the solid, since the solubility of impurities can decrease at lower temperatures as well.



## MELTING POINT

Physical properties, such as melting point, boiling point, density, refractive index, etc are used extensively for the identification and characterization of organic compounds. The compound can be considered pure, if its physical properties are not changed after several rounds of purification either by recrystallization, sublimation, distillation, etc.

Melting point is a temperature at which the solid and liquid phases of the compound are in the equilibrium. In other words, the melting point is a point at which a solid undergoes a transition to a liquid. The melting point is one of the main physical constants of a solid substance. In general, a melting point refers to a temperature range. A sharp melting point (within  $\leq 1\text{-}2\text{ }^{\circ}\text{C}$  range – this of course depends on how high the melting point is) will be indicative of a pure sample. The purer the sample, the narrower the melting point. The melting–cooling cycle can be repeated many times without a significant change of the melting point range. A chemical decomposition might have taken place, if large, *i.e.*,  $> 2\text{-}3\text{ }^{\circ}\text{C}$ , deviations are observed during the second heating cycle. A melting point of the pure sample depends on the strength of the crystal lattice. Therefore, small amounts of impurities, which are capable of disrupting the crystal lattice, will lead to lowering of the melting point of the sample as compared to the melting point of the pure sample. Such change is also accompanied by the increase of the melting point range, which may significantly exceed  $2^{\circ}\text{C}$  limit. For the majority of cases, the impurity will lower the melting point and broaden the range. However, there are some cases, when an increase of the melting point is observed.

Impurity can be classified as any substance that differs from the main compound with respect to chemical composition, physical state, etc. For example: solvent molecules that are not removed from the sample after the crystallization, by-products that are produced in the chemical reaction, decomposed compound due to storage or handling conditions, just to name a few.

A good indication of the purity of the compound can be established by admixing the sample with the standard, whose purity has been established by other means. If there is no change in the melting point of a compound taken alone and in a mixture, the compound can be considered pure. This approach can also be used in establishing the identity and purity of two

samples with the same melting points: equal amounts of both samples should be thoroughly mixed, and if their melting points are unchanged, both samples can be considered identical. If the melting point of the mixture changes – the two samples are not identical. However, isomorphous compounds, which are different in their chemical compositions might not lead to deviations of the melting points in their mixtures.

A number of organic compounds decompose below or at their melting point. This process is accompanied by a color change (usually dark brown) and/or gas evolution. In such cases, the temperature of decomposition is used as a physical constant. The decomposition point depends strongly on the rate at which the sample is heated, and therefore in many cases cannot be precisely reproduced.

There is a correlation between the structure of a compound and its melting point. It has been noted that more symmetric compounds will have higher melting point than their non-symmetric homologues. Furthermore, the presence of functional groups capable of forming intermolecular hydrogen bonds will lead to higher melting points as opposed to compounds featuring groups that promote intramolecular hydrogen bonds.

#### Procedure for the melting point determination:

Finely ground and completely dried (water or solvents are impurities) solid is placed into a capillary tube, which is sealed from one end (Figure 5A). Large chunks of solid should not be used for the melting point determination, because a non-uniform heat transfer is likely to take place and contribute to the incorrect readings. The solid should be placed on a clean watch glass. The open end of the capillary tube is dipped into the solid, and the solid is shaken into the bottom of the capillary tube by carefully dropping the capillary through a long glass or plastic tube, which rests on the bench (Figure 5B). Repeat this process several times to assure that solid is tightly packed in the capillary, *i.e.*, there are no air-holes. Usually 2-3 mm of the solid will be sufficient for the melting point determination. For the compounds that are known to sublime, the open end of the capillary tube should be sealed before the melting point is taken. Fluffy solids are difficult to pack in the melting point capillary tubes. In this case, a fine wire, with a diameter smaller than the capillary should be used to pack the sample. The packed capillary is placed into the melting point apparatus (Figure 5C).

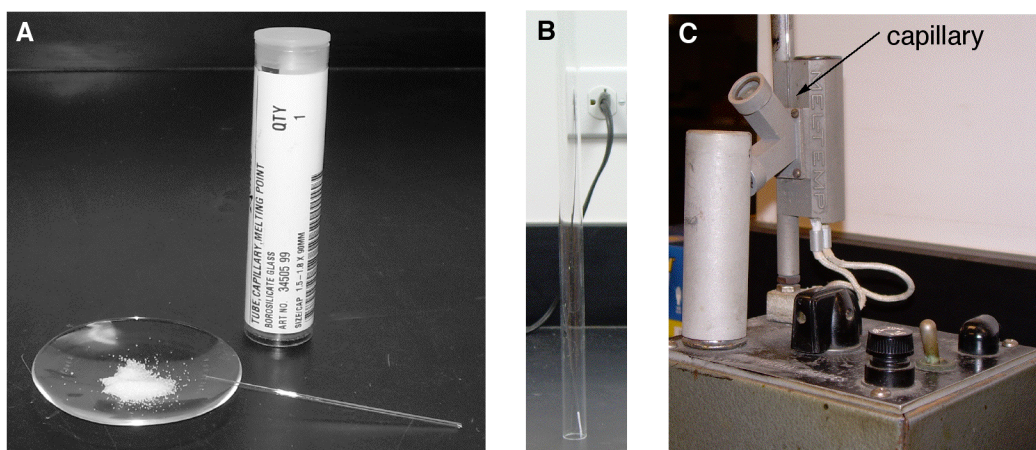


Figure 5.



The melting point apparatus, Mel-Temp, is shown in Figure 6. The capillary is placed into the holder of the metal block, and the phase transition of the sample is visually monitored through a magnifying glass upon heating. Since the melting point is a range, the lower limit will be the temperature at which some of the crystals start to melt, *i.e.*, there are only a few drops of the liquid phase that are visible, and the upper limit is the temperature at which no solid phase remains in the capillary. The accuracy of melting point should usually be within 0.5°C. It is imperative to slowly heat up the sample, 1-2 °C / min. A rapid increase in temperature will result in high level of inaccuracy of the melting point determination. In this instance, it is easier to record a lower melting point than the true melting point, since the reading of the thermometer lags behind the temperature of the heating block. The melting point measurement can be repeated one or two more times with the same capillary, once the capillary and the metal block of the Mel-Temp apparatus reached ambient or cooler (10-20 °C) temperature below the melting point range. The sample is not recovered from the capillary. The capillary should be disposed into a broken-glass container.

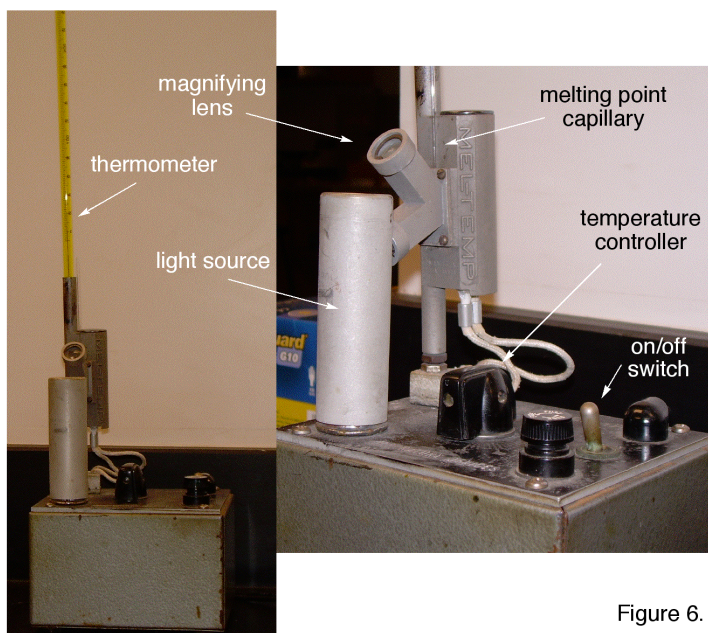


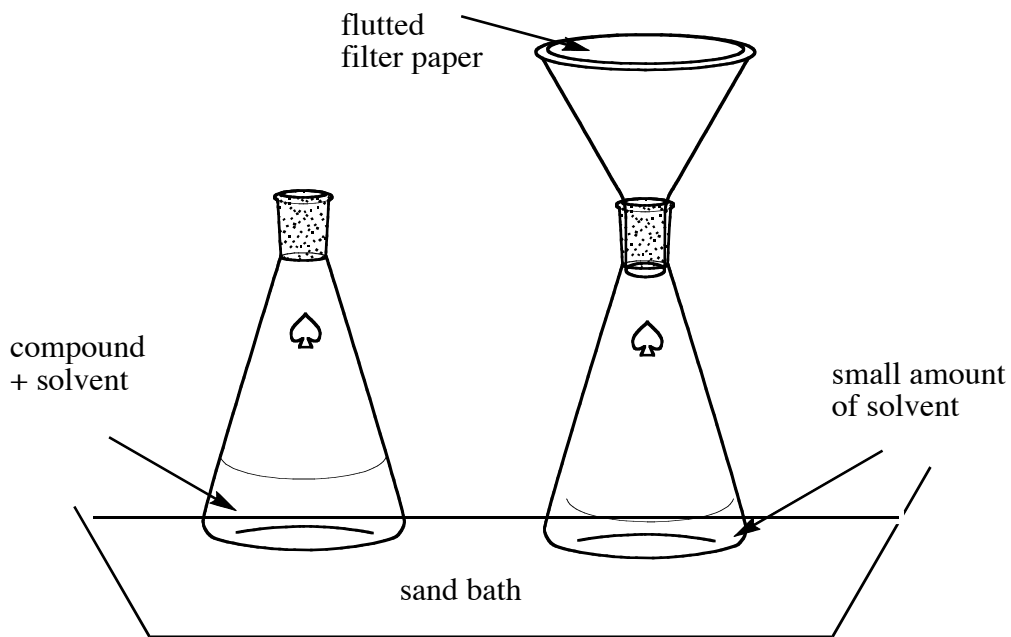
Figure 6.

### Thermometer calibration:

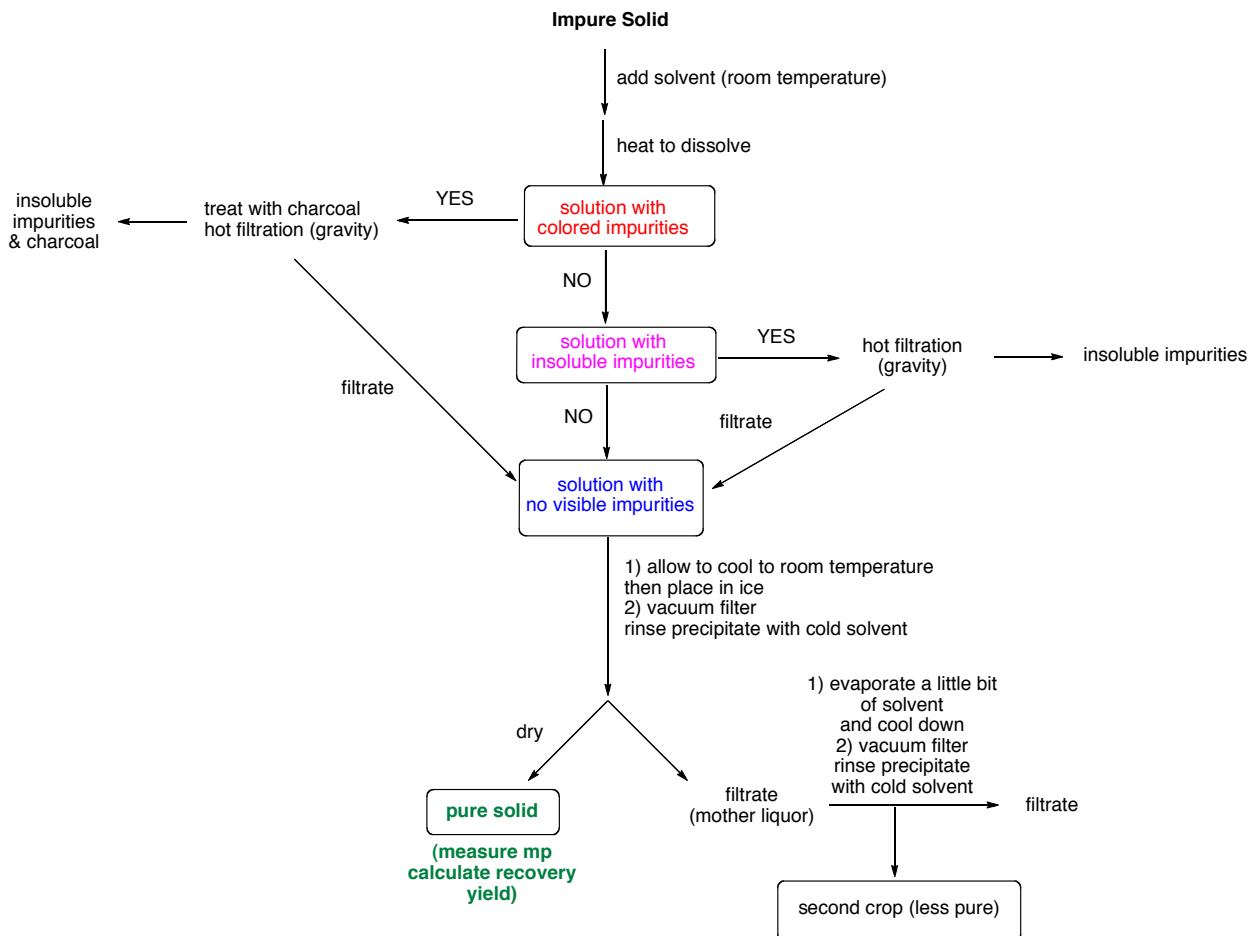
The accuracy of the melting point depends strongly on the quality and the calibration of the thermometer. Calibration of a thermometer is accomplished with the use of a set of known standards. It is important to perform a calibration over a range of temperature, since the error varies over different temperatures, and it is unlikely that a linear correlation will be observed. By plotting an actual melting point *versus* the Mel-Temp reading will result in a curve, which can be used to correct all the measured melting points of synthesized and/or purified compounds. This curve is valid only for this specific thermometer.

The melting point of a compound that is measured without the calibration curve will be reported as an “uncorrected melting point.” If the calibration curve is used, the melting point of the compound will be reported as “corrected melting point.” In the majority of literature accounts, however, uncorrected melting points are reported.

## HOT FILTRATION SETUP



## RECRYSTALLIZATION FLOW CHART





## PROBLEMS

1. A student had 1.00 g of an impure solid, which had to be purified by recrystallization. The student used 50ml of the appropriate solvent to carry on the recrystallization. In the end 0.77 g of the solid was isolated. What is the efficiency (i.e., yield) of recrystallization process?
2. For recrystallizations you generally need to use an Erlenmeyer flask or a test tube. Propose a reason or two, why would not be advisable to use a beaker as recrystallization container.
3. Is there any good reason, why one should not vacuum filter hot solutions? Briefly justify.
4. List major step in identifying suitable recrystallization solvents.
5. What is the reason for charcoal during recrystallizations? Could you use charcoal as a stand lone step, i.e., not in a recrystallization experiment?
6. For a filtration of hot solutions, would you rather use a stemless funnel or the one with a stem? Briefly explain your answer.
7. Often, inaccurate melting points are recorded when the heating of the melting point apparatus is too rapid. Under such circumstances, would the recorded melting point be higher or lower than the true melting point?
8. Why it is important to tightly pack the melting point capillary tube?
9. Why do you need to use finely powdered sample to measure the melting point?