

4. Crystallization

A. Background

Crystallization is one of several available techniques available to purify organic compounds. Unlike other techniques, however, crystallization is specific to the purification of solids. Crystallization relies on the fact that most solids are more soluble in a hot solvent versus a cooled solvent. One of the most challenging aspects of crystallization is finding a suitable solvent. It is necessary to find a solvent or solvent mixture that completely dissolves the substance when hot. This same solvent should not, however, dissolve the substance when cold. Additionally, impurities should be soluble in the solvent regardless of whether the solvent is hot or cold. The crystallization process can be repeated until you have reached the desired purity level for your sample. Repeated crystallization is termed recrystallization.

Choosing a Suitable Solvent

- The solvent should be relatively volatile so that it can be removed easily from the sample. If the solvent has a low volatility, it will stick to the crystals and be very difficult to remove completely.
- The solvent must not have too low of a boiling point; otherwise there won't be a large enough temperature difference between the hot and cold state.
- The solvent should have a boiling point that is at least 10 °C above the melting point of your solid sample. If the boiling point of the solvent is too close to the melting point of the sample, the solid may "oil out" of the solution.
- It is best to avoid highly toxic solvents such as carbon tetrachloride.
- Solvent polarity is also a factor in determining the solubility of your sample. Polar solvents are best for polar compounds, while non-polar solvents tend to be best for nonpolar compounds.
- If a mixed solvent system is used, the two solvents must be miscible (i.e. they must form a homogeneous mixture).

Table 1 lists some common solvents used in the organic chemistry lab. The compounds are organized by dielectric constant, ϵ . When we refer to a solvent as polar, we mean that it has a high dielectric constant. Solvent polarity is the result of many molecules acting together. When an individual molecule is referred to as polar, we are talking about that molecule's dipole moment. A polar molecule will not necessarily result in a highly polar solvent (solvent with a high dielectric constant).

Mixed Solvent Systems

In the event that a solid is too soluble in one solvent, but too insoluble in a second solvent, a mixed solvent system (solvent-pair) might be useful. A solvent mixture may give the appropriate solvent properties for a successful crystallization. The solvents in the mixed system must be miscible – meaning they form a homogenous solution on mixing. Figure 1 provides a solvent miscibility chart that you can use to find an appropriate solvent pair. Typically, you should dissolve your sample in the better solvent first. While keeping the solution hot, the second solvent is added until you are very near the crystallization point.

Some commonly used solvent-pairs include: water-ethanol; ethyl acetate-hexane; toluene-hexane; and dichloromethane-hexane.

Table 1: Common Laboratory Solvents

Solvent	Structure	Boiling Point (°C)	Dielectric Constant, ϵ
Water	H-O-H	100	78
Methanol	H ₃ C-OH	64.6	33
Ethanol	H ₃ C-CH ₂ OH	78.5	25
Acetone	(CH ₃) ₂ C=O	56.2	21
Dichloromethane	Cl-CH ₂ -Cl	39.8	8.9
Ethyl Acetate	EtO-C=OCH ₃	77.1	6.0
Chloroform	HCCl ₃	61.7	4.8
Diethyl Ether	Et-O-Et	34.6	4.3
Toluene	Ph-CH ₃	110.6	2.38
Hexane	CH ₃ (CH ₂) ₄ CH ₃	69	1.89
Pentane	CH ₃ (CH ₂) ₃ CH ₃	36.1	1.84

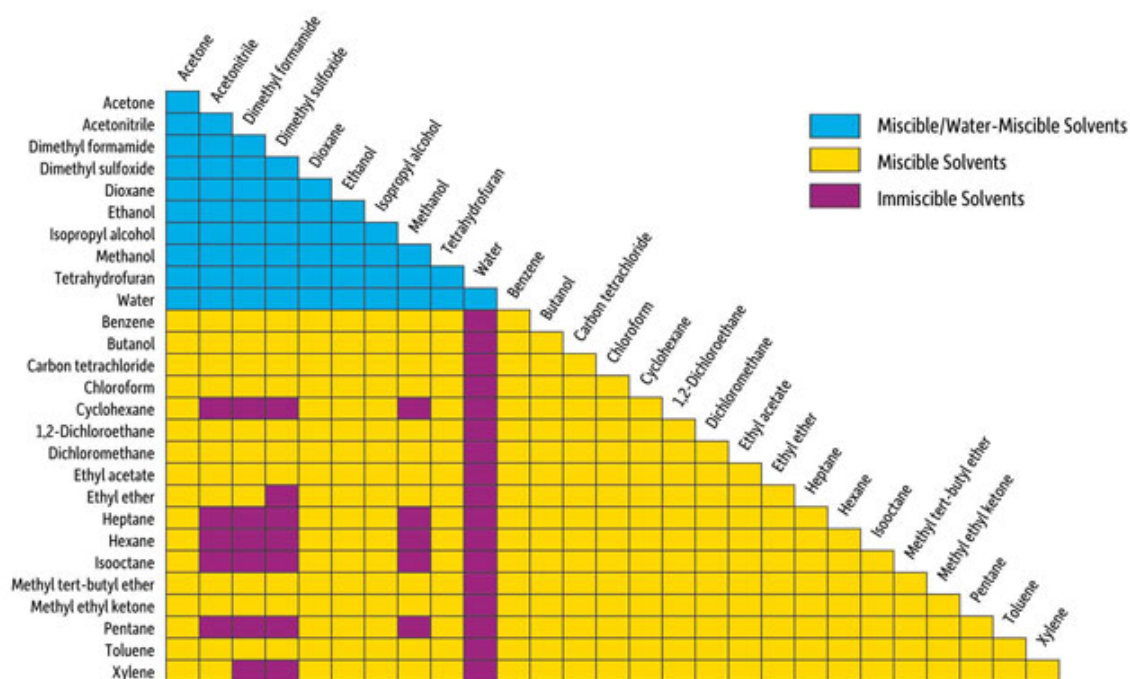


Chart courtesy of Restek Corporation, Bellefonte, PA

Figure 1. Solvent Miscibility Chart

Insoluble Impurities

Certain impurities may be insoluble in the solvent system being used for crystallization. This is not a problem. The most important thing is that your desired compound is soluble in the crystallization solvent when hot. In order to remove insoluble impurities, a hot gravity filtration can be employed. The hot filtration assembly is shown in figure 2.

A fluted filter should be placed in a stemless glass funnel, which is then placed on top of an Erlenmeyer flask. The Erlenmeyer flask should contain a few mL of the recrystallization solvent. A wire should be placed between the glass funnel and the flask to prevent the formation of a seal. If a seal forms, the vapors cannot escape the flask and gravity filtration will cease. The filtration assembly should be heated on a hotplate to the boiling point of the solvent. The hot solvent vapors will saturate the filtration assembly. The filtration assembly must be kept hot during the entire filtration process. Once the filtration assembly is sufficiently hot, you can filter your hot solution containing the dissolved solid. You should try to perform the filtration as quickly as possible. During each pour, do not fill the filter more than $\frac{3}{4}$ full. Return the solution flask to the hot-plate between each pour. Once filtration is complete, you can wash the filter down with a small amount of hot solvent to re-dissolve any product that solidified on the filter paper or the funnel. Following the filtration step, if your filtrate is not free of all solids, you will need to re-filter.

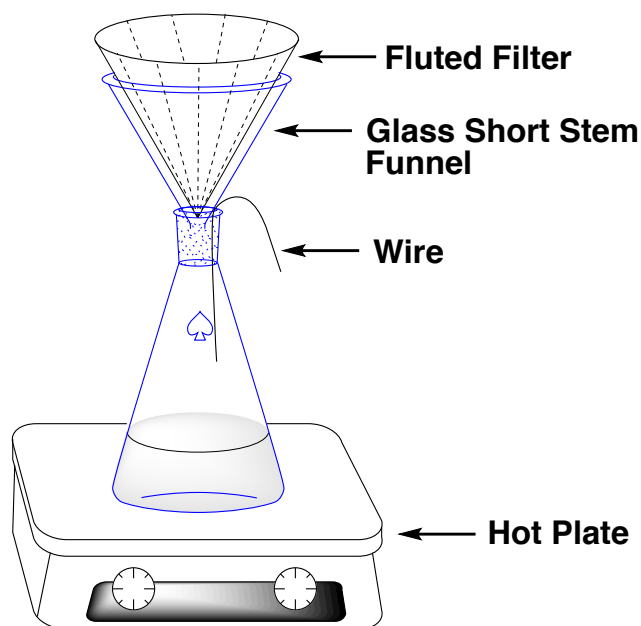


Figure 2. Hot Filtration Assembly

Colored Impurities

A colored compound could indicate the presence of impurities or your compound may simply be colored. If you are certain your compound should be colorless or is the wrong color, activated charcoal (decolorizing carbon) can be used to remove the colored impurity. Activated charcoal is a finely divided porous form of carbon with a large available surface area. Colored molecules are typically very large and polar. These molecules tend to stick to the surface of the activated charcoal.

To remove a colored impurity, add a small amount (pea size or less) of the activated charcoal to your heated solution. Do not add too much, else your desired compound may also stick to the carbon and be lost. Stir or swirl the solution with heating to disperse the activated charcoal. Be careful because activated charcoal can cause the solution to froth. Once finished, the activated charcoal can be removed from the solution during the hot filtration step. Following the filtration, inspect the solution carefully to ensure no specks of charcoal are remaining in the solution.

Inducing Crystallization

In some cases, even after cooling the solution, crystallization may not spontaneously occur. There are a few techniques that you can employ to induce crystallization.

- Gently tapping the flask with your finger is often enough to create a disturbance in the system resulting in initiation of crystallization.
- If tapping doesn't work, you can insert a glass rod into the flask and scratch the walls of the glass flask. Caution: Use care when scratching the flask as the stirring rod is glass and can break easily.
- Seeding is useful if you have some crystals of the pure compound available. In this case, you can add a few seed crystals to the flask, which will provide a surface for crystallization to begin.

If all of these methods fail, you may simply have too much solvent. If this is the case, you will need to evaporate off some of your solvent. As a rule of thumb, start by evaporating ~1/2 of the solvent. Allow the flask to slowly cool once again and see if crystallization occurs. If not, you may need to evaporate additional solvent.

Oiling Out

Occasionally a compound may separate from the solvent as an insoluble liquid or oil. If that happens, you should reheat the solution until the oil dissolves completely. Oftentimes a slower cooling process can prevent "oiling out" during the second go around. If "oiling out" occurs again, it may be necessary to add a bit more of the better solvent. Keep in mind that the boiling point of your solvent(s) should be at least 10 °C above the melting point of your sample.

Microscale Crystallization

If you are working with a relatively small amount of material (10-100 mg), a microscale recrystallization is often easier and provides a better percent recovery of product. In a microscale crystallization, the crude product is placed in a Craig tube and the solvent is added to the Craig tube with heating in order to dissolve the product. Once the product is dissolved, the Craig tube containing the solution is cooled until crystallization occurs. The crystals are subsequently collected by centrifugation of the Craig tube assembly (figure 3).

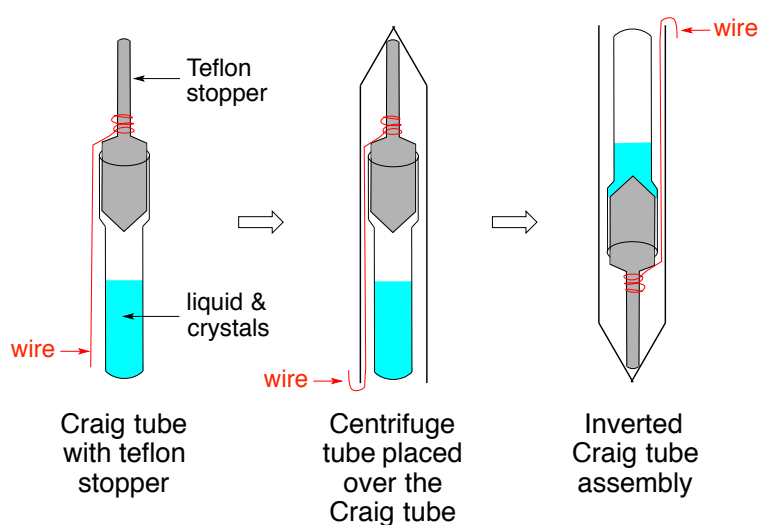
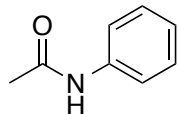


Figure 3. Craig Tube Setup

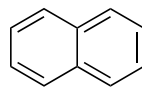
B. Experimental Procedure

The experimental procedure for this lab consists of the following:

- First, a macroscale crystallization will be performed on 1 g of impure acetanilide.
- Second, a microscale crystallization will be performed on 100 mg of naphthalene.
- Following the experiment, you will calculate the percent recovery and determine the melting point of each product.



acetanilide



naphthalene

1. Macroscale Crystallization

In the first part of the procedure, one gram of acetanilide will be purified by recrystallization. For this experiment, the recrystallization solvent will be water.

Weigh out approximately 1 gram of impure acetanilide into a clean 50 mL Erlenmeyer flask. Be sure to record the exact weight sample in your notebook. Also, save a small portion of impure acetanilide for later melting point analysis. Add approximately 20 mL (or less) of water and a boiling chip to the Erlenmeyer flask and heat the mixture until it boils. Swirl the flask periodically to aid in dissolution of the acetanilide. If molten acetanilide appears in the bottom of the flask, it is necessary to add more water. **Use caution when handling the hot flask!**

Once the sample has completely dissolved, remove the flask from the heat. Add a small amount of additional water (1-2 mL) along with a small portion of activated charcoal. Frothing will occur if the activated charcoal is added to the boiling solution. Once the charcoal is suspended in the solution add a small amount of Celite (150-200 mg). Celite is a common filter aid used in organic chemistry. Its addition will help prevent any charcoal particles from escaping through the filter paper.

Next, filter the solution using a hot filtration assembly. The hot filtration assembly should contain about 4 mL of water heated to a boil. Following the filtration, you can use a few mL of water to help remove any remaining material from the first flask.

If you have increased the solution volume much beyond 20 mL, you will need to boil off some of the solvent prior to crystallization. Once you have reached an appropriate solvent volume, remove the flask from heat, cover the mouth of the flask with a piece of foil, and allow the solution to cool to room temperature slowly. Do not disturb the flask while it is cooling. If crystallization doesn't occur during the cooling, use one of the methods described above to induce crystallization. Once crystallization is complete, cool the solution in an ice bath for approximately 15 min.

Finally, the crystals can be collected by vacuum filtration using a Hirsch funnel filtration assembly (figure 4). Clamp a filter flask in place to keep it from falling over. This flask can then be connected to the house vacuum line using thick walled tubing. Next, place the Hirsch funnel and rubber adaptor into the filter flask. Add a small circle of filter paper to the funnel, wet it with some water, and seat it by applying the vacuum. With the vacuum being continuously applied, pour the solution containing your crystals into the Hirsch funnel. 2-3 mL of ice water can be used to help remove the final traces of product from the flask. Leave the vacuum on for a few

minutes to aid in drying the crystals. The crystals should then be transferred to a weighed watch glass or vial and allowed to dry open to the air until the following lab period.

After the experiment the following data should be collected and analyzed.

1. Determine the mass of pure product isolated and calculate the percent recovery.

$$\% \text{ Recovery} = \frac{\text{mass of material recovered (in g)}}{\text{mass of material you started with (in g)}} \times 100$$

2. Determine the melting point of the pure acetanilide crystals that you isolated.
3. Determine the melting point of the impure acetanilide that you started with.

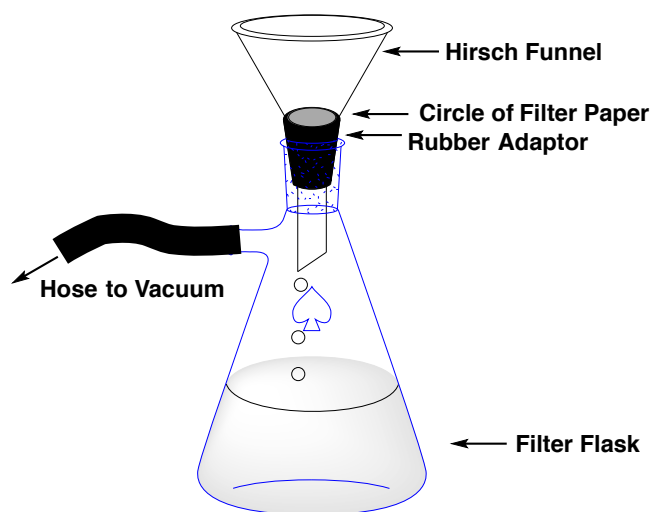


Figure 4. Hirsch Filtration Assembly

2. Microscale Crystallization

In the second part of this experiment you will recrystallize ~100 mg of naphthalene and collect the pure crystals using a Craig tube assembly as described in the introduction.

The dissolution of impure solid and subsequent crystallization will take place in a Craig tube. The Craig tube can not be easily heated directly on the hot-plate so a boiling water bath is necessary. The boiling water bath can be prepared using a 100 mL beaker filled half way with water. Set this up first then do the subsequent steps while you wait for the water to boil. Weigh approximately 100 mg of naphthalene into the Craig tube (record the exact value in your notebook). Add 3-4 drops of 95% ethanol and place the Craig tube into the boiling water bath. Continue to add ethanol dropwise with stirring until the naphthalene dissolves. Next, remove the Craig tube from the water bath and allow it to cool slowly as shown in figure 5. The outer beaker helps ensure slow cooling, which results in larger crystal growth.

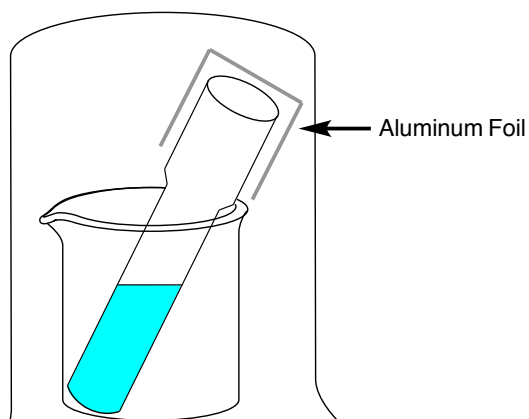


Figure 5. Craig Tube Crystallization Setup

Once crystals have formed, they can be collected by centrifugation. Be sure the centrifuge is counter balance. Your TA will discuss proper technique for set up and operation of the centrifuge. Following centrifugation, the crystals should be relatively dry. The crystals can be scraped onto a weighed watch glass or into a weighed vial. After a few minutes of drying, the following data should be obtained:

1. Determine the mass of pure naphthalene isolated and calculate the percent recovery.
2. Determine the melting point of the pure naphthalene crystals that you isolated.
3. Determine the melting point of the impure naphthalene that you started with.

Naphthalene sublimates readily so make sure it is stored in a tightly capped vial.

Dispose of all chemical waste in the properly labeled waste containers.

C. Pre-Lab Questions

1. Consider each of the following solvent pairs and determine if the pair would be a good crystallization solvent mixture. Explain why or why not.
 - (a) water-hexane
 - (b) water-methanol
 - (c) pentane-diethyl ether
 - (d) toluene-hexane
2. Dimethylsulfoxide (DMSO, bp 189 °C) is an excellent organic solvent, but is not routinely employed in crystallization. Explain.
3. If you perform a recrystallization on 435 mg of impure benzoic acid and recover 360 mg of crystals, what is the percent recovery?

4. Acetanilide has a solubility in water of 0.54 g/100 mL at 25 °C and 5.0 g/100 mL at 100 °C.
 - a. What is the minimum volume of hot water necessary to dissolve 1.0 g of acetanilide?
 - b. Approximately how much acetanilide will remain dissolved when the solution is cooled to room temperature?
 - c. What can you do to further decrease the amount of acetanilide dissolved in the water?
5. What will happen if the centrifuge is not properly balanced?

D. Post-Lab Questions

1. List some advantages as well as disadvantages to using the Craig tube crystallization technique.
2. What was the purpose of using activated charcoal in this experiment? Did you notice any differences before and after the addition of the activated charcoal?
3. Describe the purpose of each of the following as they apply to recrystallization.
 - a. Seed crystals
 - b. Boiling stones
 - c. Celite
4. Why must the acetanilide be completely dry before obtaining its melting point?
5. Why does slow, controlled cooling generally give better crystals than rapid cooling?
6. How do you know if you happen to use too much recrystallization solvent? If you encounter this problem, what can you do?
7. Why do you think a stemless funnel was used rather than a long stem funnel during the gravity filtration step?
8. How do the melting points of the impure acetanilide and the recrystallized acetanilide compare?