

Reminder: These notes are meant to supplement, not replace, the laboratory manual.

Recrystallization

History and Application:

Recrystallization is a very common and useful method to purify solid organic materials. This purification method is commonly used in the pharmaceutical industry where the consistent manufacture of high purity drugs is of utmost importanceⁱ. Pharmaceutical companies need to tightly control the contaminants present in drugs for human consumption, some impurities are regulated at the parts per million (ppm) range.ⁱⁱ Recrystallization is an important technique to obtain high purity organic solids.ⁱⁱⁱ

Safety Considerations

Whenever heating a liquid always ensure the vessel contains a nucleation center. This can be a boiling stone, boiling stick, or stir bar. As a substance approaches its boiling point (where the vapor pressure of the liquid equals room pressure), microscopic vapor bubbles of that substance form. If no nucleation center is present, these can increase in concentration until they coalesce all at one, which will look as though the entire container boils at once, and the partially vaporized hot contents may spray out of the vessel ejecting the liquid material. This is called bumping and the source of the reported “exploding water in microwave” phenomena. The water is not in fact exploding. The presence of a nucleation center will allow a smooth boil. Always have a nucleation center in any vessel of heated liquid; this includes beakers, test tubes and reaction tubes.

Never look down the ‘barrel’ of a heated test tube or reaction tube. Do not overfill a tube to be heated with liquid. A proper level of liquid is 2/3 full or less.

The Mel-Temp apparatus, especially the cylindrical portion, gets very hot while taking a melting point measurement. Handle the Mel-Temps with care.

Thermometers are fragile--handle them carefully, especially when you’re installing them in the Mel-Temp apparatus. Do not place a hot thermometer on a cool lab bench. Do not remove the thermometer and shake it to cool the Mel-Temp. This has no effect on the temperature of the Mel-Temp.

All of the compounds in the experiment are at least slightly toxic. Ethanol is extremely flammable. Breathing ethanol vapor will cause central nervous system depression, disorientation and possible loss of consciousness.

1. Chemists recrystallize solid samples to purify them-that is, to remove impurities from a solid material.
2. A recrystallization solvent should, ideally, have the following properties:
 - Have a low solubility of the compound to be purified when the solvent is cold
 - Have a high solubility of the compound to be purified when the solvent is hot
 - Have a relatively low boiling point for easy evaporation from the purified compound
 - Does not react with the compound being purified

3. Recrystallization is a process in which impure crystals are dissolved in a minimum amount of hot solvent, then the solution is cooled to lower the solubility of the material and precipitate the solid, turning it back into crystals and leaving the impurities still dissolved in the solution. The crystals are then isolated. The overall purpose is to separate impurities from the desired solid substance thereby purifying the target compound. The practical process of recrystallization can be described in seven steps, as follows. The reason for each step is given in parentheses.

First, choose a solvent. (For this experiment, the recrystallization solvent has been chosen for you.) This solvent must not have a high solubility of the compound when cold, but does have a high solubility when hot. (This allows the solid to first be dissolved in hot liquid, then upon cooling to precipitate the solid. These solvent properties make the recrystallization process possible.) The solvent also cannot chemically react with the material to be purified. Lastly, the solvent should have a reasonably low boiling point ($<120^{\circ}\text{C}$) to ensure the solvent can be evaporated or otherwise easily removed from the isolated product.

Add hot solvent just until all of the compound you are trying to purify dissolves. (This makes the impurities that were locked inside the impure crystals dissolve in the solvent and available for removal.)

If colored impurities are present, add decolorizing charcoal. (The colored molecules are adsorbed onto the surface of the charcoal pellets.) If the starting material is not colored, this step is skipped.

If charcoal was added, or other insoluble materials are present, filter the resulting solution while it is still hot. (This step separates two kinds of impurities from the substance you want. The charcoal binds with the colored molecules. When filtering the charcoal coated with impurities is removed along with particles of impurities that didn't dissolve in the hot solvent to begin with.) If charcoal was not added, and other insoluble impurities are not present, this step is not necessary.

Cool the solution. The desired material should precipitate from the cool solution due to lower solubility in cold solvent. (Most if not all of the soluble impurities will remain in solution.)

Separate the solid compound from the solvent. This can be done by gravity filtration, suction filtration or another method of removing the solvent from the solid. (The soluble impurities and most of the recrystallization solvent are taken away from the desired compound in this step.)

Dry the isolated crystals. (This removes the remainder of the recrystallization solvent, which is an impurity.)

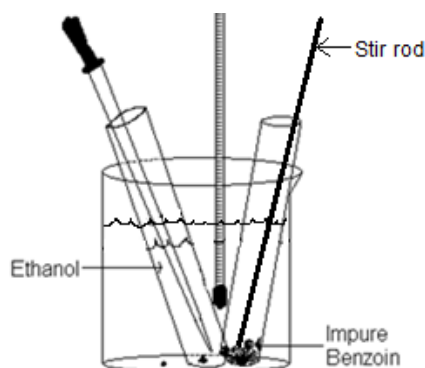
4. In this experiment, the starting mixture is not colored; hence decolorizing charcoal will not be used. Hot filtration will not be needed.

5. Benzoic acid is being recrystallized from ethanol. This is a good choice because the solubility of benzoic acid in ethanol changes dramatically with temperature.

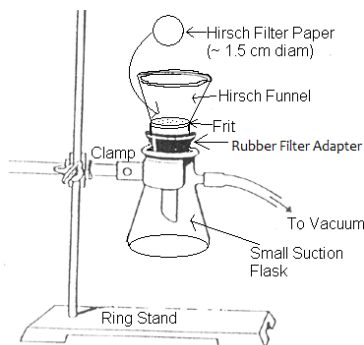
Temperature of Ethanol	Solubility of benzoic acid in 100 mL Ethanol
20 °C	0.86 ^{iv}
70°C	9.0 g ^v
78° C	12.8 g ^{vi}

Therefore at 78°C, each 0.1 g will need at least 0.8 mL of boiling ethanol (or 1.1 mL at 70° C). ^{vii}.

6. Here is what the set up on the hot plate should look like. Place about 2-3 inches of ethanol, a pipette and a boiling stone in one clean test tube. Place your solid, a glass stir bar and boiling stone in another test tube. Place both in the beaker of water also containing a boiling stone. When the temperature reaches 60°C or above begin to pipette ethanol from the test tube into the test tube containing the solid. Shake or stir vigorously. Continue to add ethanol with constant stirring just until all of the solid dissolves. Do not add any additional solvent after all of the solid has dissolved.



7. Here is the setup needed for the suction filtration. Hirsch funnels use 1.5 cm filter paper. Ensure your Hirsch funnel has a frit installed (that you cannot see directly through the funnel, and a small porous frit is in place.) In subsequent labs where larger amounts of product have been recrystallized the filtration will take place using a Buchner funnel, filter paper, and a larger suction flask. (Watch the video on Hirsch funnel use for clarification.)



The filter paper in the Hirsch funnel catches the crystals of your desired compound, allowing the soluble impurities and almost all of the solvent to go through.

Be sure the vacuum is on and the filter paper is in place before pouring the crystalized material into the funnel. Let the vacuum run for a few minutes to dry the solid before removing the funnel and extracting the solid.

8. Here is the information about the behavior of samples when they melt that was given in the melting point experiment:

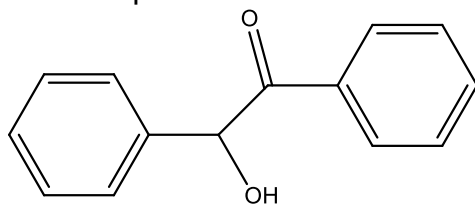
Pure samples melt over a narrow range, close to the literature value of the melting point (when the literature value is correct, which it usually is).

Samples containing soluble impurities have a melting point range that is usually broader and lower than the melting point range of a pure sample.

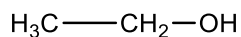
Example: Pure substance, 121-122°; same substance when impure, 112-117°.

Samples containing insoluble impurities have a melting range similar to that of a pure sample (except that you might see particles of the impurity floating around after all of your compound has melted).

9. There are no actual reactions in this experiment. The materials are not undergoing a chemical reaction they are simply being dissolved and then precipitated. The structures of the compounds you will use in this experiment are:



Benzoin
Lit. M.P.^{viii}. 134-137°C



Ethanol
Lit. B.P. 78.3°C

10. The starting benzoin is very impure and may start to melt well below 100°C. The purity of the recrystallized material, and the success of the recrystallization, will be assessed by how much the melting point range narrows from the starting impure benzoin melting point range, and how close it comes to the literature value of the pure material.
11. The amount of recovered material will be assessed by calculating a percent recovery.

$$\text{Percent Recovery} = \frac{\text{mass of compound recovered}}{\text{starting mass of compound}} \times 100\%$$

Since the starting benzoin contains impurities and the purpose of the recrystallization is to remove impurities, a percent recovery of 100% would signal a failed recrystallization. The 'perfect' percent recovery value is based on the amount of impurities present in the starting material. It is common not to know the exact level of impurities present.

Notes for topics that may be included in quizzes given after the experiment:

12. Here are the effects of some procedure changes and errors in the recrystallization process. Your instructor may ask about other changes and errors.

If you use too much solvent, less of the compound you're trying to purify recrystallizes (more remains in solution), and you'll get a low percent recovery. This does not impact the purity of the recovered material.

If you use too little solvent, not all of your crystals will dissolve in the hot solvent, and they will retain some impurities. The purity will decrease and the percent yield will increase slightly.

Slower cooling tends to give larger more pure crystals.

Faster cooling results in smaller crystals of lower purity.

Plunging hot liquid directly in ice water forces very rapid cooling and traps impurities within the crystal lattice.

REFERENCES

ⁱ FDA Good Manufacturing Practices

<http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm124740.htm> (December 26, 2010)

ⁱⁱ US Pharmacopeia <http://www.usp.org/referenceStandards/> (December 26, 2010)

ⁱⁱⁱ S. Rohani, *Front. Chem. Eng. China* 2010, 4(1): 2–9

<http://www.springerlink.com/content/rgu257r2051774r7/fulltext.pdf>

^{iv} Open Notebook Science Solubility, <http://xsrv7.oru.edu/~alang/onsc/solubility/allsolvents.php?solute=benzoin> (accessed September 25, 2013)

^v *J. Chem. Eng. Data*, Article ASAP

DOI: 10.1021/acs.jced.7b00238

Publication Date (Web): August 22, 2017 (Accessed September 15, 2017)

^{vi} *Organic Syntheses, Coll. Vol. 1, p.94 (1941); Vol. 1, p.33 (1921).*

<http://www.orgsyn.org/orgsyn/orgsyn/prepcontent.asp?prep=cv1p0094> . (September 25, 2013)

^{vii} *Organic Syntheses, Coll. Vol. 1, p.94 (1941); Vol. 1, p.33 (1921).*

<http://www.orgsyn.org/orgsyn/orgsyn/prepcontent.asp?prep=cv1p0094> . (September 25, 2013)

^{viii} CRC Handbook of Chemistry and Physics, 65th Ed, CRC Press, 1985, p C-159

Revised: March 16, 2022, S. L. Weaver