

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

Recrystallization

History and Commercial 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 ppm (parts per million) range.ⁱⁱ Recrystallization techniques are an important tool to achieve high purity products.ⁱⁱⁱ

Laboratory Application

1. Chemists recrystallize solid samples to purify them--that is, to separate molecules of impurities from molecules of a desired substance.
2. A recrystallization solvent should, ideally, have the following properties:
 - Does not dissolve the compound to be purified when cold
 - Does dissolve the compound when hot
 - Has 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 hot solvent, then the solution is cooled to precipitate the solid and turn the desired material back into crystals leaving the impurities still dissolved in the solution behind. The crystals are then isolated. The overall purpose is to separate impurities from the desired 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 that doesn't dissolve the compound when cold, but does when hot. (These properties of the solvent make the recrystallization process possible.)

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

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

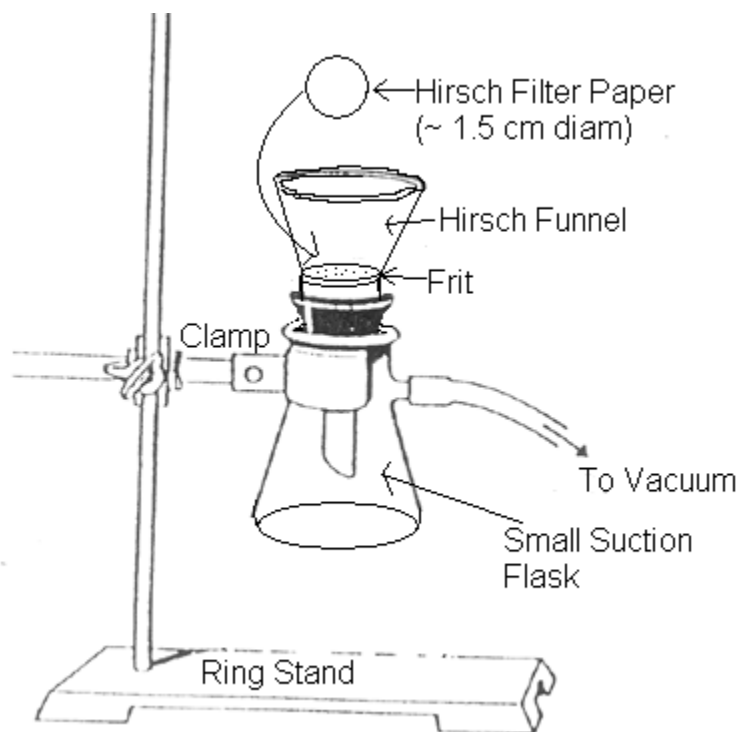
If charcoal was added, filter the resulting solution while it is still hot. (This step separates two kinds of impurities from the substance you want. The charcoal binds with the colored molecules. When filtering the charcoal coated with impurities is removed along with particles of impurities that didn't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

Cool the solution and obtain crystals of your desired compound. (Soluble impurities will remain in solution.)

Perform suction filtration to isolate the solid compound. (The soluble impurities and most of the recrystallization solvent are separated 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. Here is the setup needed for the suction filtration.



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 crystallized material into the funnel. Let the vacuum run for a few minutes to dry the solid, before removing the funnel and extracting the dry recrystallized solid.

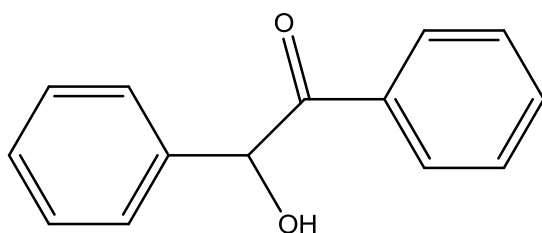
5. Here is the information about the behavior of samples when they melt that was given in the previous set of notes:

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).

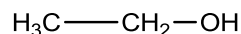
Samples containing soluble impurities have a melting point range that is broader and lower than the melting point range of a pure sample. Example: Pure substance, 121-122°; same substance when impure, 112-117°.

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).

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



Benzoin
Lit. M.P. 136-138°C



Ethanol
Lit. B.P. 78.3°C

7. The safety notes for this experiment begin with the same Mel-Temp comments given in the previous set of notes.

The Mel-Temp apparatus, especially the top portion, can get very hot during the experiment, and you won't be able to tell by looking. Handle the Mel-Temps with care.

You'll be using thermometers. These 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.

The Mel-Temp is an electrical apparatus. Notify your instructor if its wires are frayed or exposed, and don't splash water on it.

Ensure a boiling chip or a boiling stick is contained within both the beaker of water and the reaction tube or test tube of ethanol before beginning to heat.

Liquids heated without a nucleation center (boiling stick or chip) can superheat, boil all at once, and shoot out of a test tube. This rapid boiling is called 'bumping'.

Never look down the 'barrel' of a heated test tube or reaction tube. Do not overfill a heated tube. Half full or less is a proper volume of a test tube to be heated. Additional good lab technique associated with heating liquids may be found at the following web site

<http://crscientific.com/properheating2.html>

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.

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

7. The equation for the percent recovery from a recrystallization experiment (or any other experiment) is:

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

8. 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.

If you use too little solvent, not all of your crystals will dissolve in the hot solvent, and they'll retain some impurities.

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.

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)

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

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