Chem 355 Jasperse RECRYSTALLIZATION

Background:

Impurities often contaminate organic compounds, whether they have been synthesized in the laboratory or isolated from natural sources. Recrystallization is the most important method for removing impurities from solid organic compounds. It is suitable for both small scale (<0.5 g) and large scale (>100g) work. **The basic recrystallization plan is to dissolve an impure solid in a hot solvent, then cool the solution so that the desired molecules recrystallize while the impurities remain in solution**. Subsequent filtration separates the solid crystal from the liquid solvent.

The dependence of solubility on temperature is key. Solubility of sample in solvent will always be higher at high temperature, but will decrease at low temperature. A solvent that can fully dissolve a solid while hot may thus become saturated as the temperature is reduced, resulting in crystal formation. Soluble impurities stay in solution because they are not concentrated enough to saturate the solution. However, even when the solvent is cold, at least some (if not all) of the desired compound will remain dissolved and will be lost during filtration.

The choice of solvent for a recrystallization is crucial. For a successful recrystallization **the dissolving power of the solvent must be "mediocre", neither too good nor too bad**. Why?

- If the solvent is too good, then even when the solvent is cold the sample will remain dissolved and you won't be able to harvest any crystals.
- If the solvent is too bad, then even when the solvent is hot it still won't be able to dissolve the sample, and the impurities won't be freed from the original sample.
- An effective solvent must be mediocre, good enough to dissolve the sample at high temperature (so that the impurities are freed), but weak enough so that at least some of your sample crystallizes out after cooling (so that you get at least some yield harvested.)

Necessary sources of mass loss: The yield for a recrystallization can never be 100%. Why not? Because while the chilled solvent is saturated and should release some crystals, at least some of your desired material will remain dissolved in the cold solvent and will be lost when the crystals and solvent are separated. **The primary necessary source of mass loss is to the solvent.** Obviously additional mass will be lost to physical handling, and some of the lost mass is simply the impurities that you wanted to lose. (But normally the mass of impurities is only a few percent or less.)

Unnecessary sources of mass loss: While losing mass to the solvent is inevitable, unnecessary losses to solvent are common and should be avoided. Some unnecessary losses to solvent result from the following:

- Using too much solvent. The more solvent that you use, the more sample will remain in the solvent even after cooling.
- Inadequate warming. If you don't warm your solvent to boiling temperature, you will not benefit from it's maximum dissolving ability, and will need to use extra solvent to make up for it. The unnecessary extra solvent will retain additional sample even after cooling.
- Inadequate cooling. If you don't cool below room temperature, for example, more sample will remain dissolved than if you cool to 0ºC.
- Excessive washing by solvent. Not only surface impurities but also some crystal will be lost when you wash your crystals. (There is usually some sort of happy medium required, because some rinsing is usually required).
- Choosing a poor solvent in the first place. If your solvent is too good, even after cooling it will still retain much or all of the sample.

Ideal: Use a Minimum of Hot Solvent so that you are at the Saturated/Dissolved Borderline at the Boiling Point. In order to maximize your purity, you'd like to use enough solvent to dissolve the crystals and keep the impurities in solution even after cooling. In order to maximize your yield, you'd like to minimize the amount of solvent used so that as little as possible sample remains in solution after cooling. The best way to accomplish both goals is to use enough solvent so that it can dissolve everything while hot, but to use no more than the minimum required so as to maximize yield after cooling. The minimum required is when your solution is just barely at the saturation point while boiling hot. Use just enough solvent so that the material is just barely soluble, or is just a little cloudy to show that it's just barely saturated.

Four Ways To Achieve Just-Barely-Saturated/Just-Barely-Dissolved Borderline. In all cases, heat to just barely gently boiling.

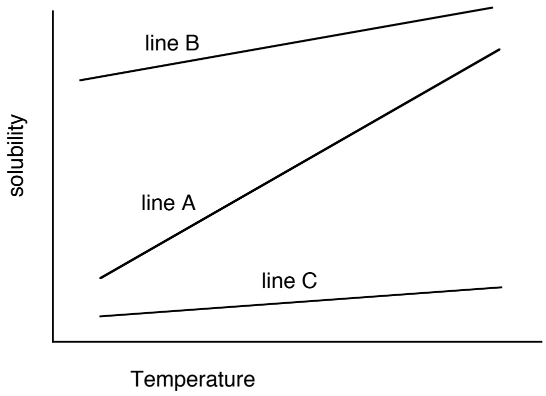
- Add more hot solvent (if solubility is too low)
- Add some superior solvent (if solubility is too low)
- Boil solvent away (if solubility is too high)
- Add 'bad solvent' (if solubility is too high) that will reduce the solubility

Mixed Solvents Often it's difficult to find a single solvent that is appropriately "mediocre". Frequently it's easier to work with a solvent mixture. If the dissolving power of your initial solvent is too strong, you can add some bad solvent to reduce the dissolving power. As a solvent with poor dissolving properties is added, the overall dissolving power of the solvent gets worse and worse. Eventually, the saturation point should be reached. This is often the most convenient way to do recrystallizations.

Alternatively, if the dissolving power of your initial solvent ends up being not high enough, you can add a superior solvent to get the solid fully dissolved.

- A very common "mixed solvent" combination involves an alcohol as the "good solvent" and water as the "bad solvent". This is effective because many organics are hydrophobic. By adding water, you can rapidly reduce their solubility.
- When mixed solvents are used, it is essential that both are co-soluble with each other. Trying to add water as the "bad solvent" to a hydrocarbon solvent like hexane or toluene fails, because the water simply forms a separate layer and doesn't actually do anything.

Choosing a Solvent As discussed previously, you don't want too good a solvent (line B) or too bad a solvent (line C). And you'd like a solvent with as sharp as possible a dependence of solubility on temperature (line A), so that it's pretty soluble hot but not very soluble cold. Trial and error experimentation is often required for finding a suitable solvent. Like-dissolves-like considerations can sometimes provide helpful guidance as to which solvents might be too good, or which might be hopelessly bad. For somewhat polar molecules containing oxygen or nitrogen atoms, alcohol/water or alcohol/pentanone mixed solvents are frequently a fine choice. The boiling point of the solvent is also worth considering. A relatively high boiling point is good because it allows a large temperature differential between boiling hot solvent and the chilled solvent. Diethyl ether, for example, boils at only 35ºC, so the solubility of a sample isn't likely to drop as much upon cooling from 35ºC to 0ºC as if water is used, where the hot/cold difference could be 100ºC. On the other hand, you don't want to use a solvent whose boiling point is so high that the sample will simply melt when the solvent is heated to boiling. It's also easier to dry the crystals if the solvent isn't too high boiling, so that it evaporates easily and won't depress the melting range.



Summary of the four criteria for selecting a recrystallizing solvent:

1. compound being purified must be insoluble in the solvent at room temperature
2. compound must be soluble in the boiling solvent
3. solvent's boiling point must be lower than the compound's melting point
4. an abundant quantity of crystals must be recoverable from the cool solvent

Crystallization Summary

1. **Choosing the Solvent.** "Like dissolves like." Some common solvents are water, methanol, ethanol, ligroin, and toluene. When you use a solvent pair, dissolve the solute in the better solvent and add the poorer solvent to the hot solution until saturation occurs. Some common solvent pairs are ethanol-water, diethyl ether-ligroin, toluene-ligroin, and t-butyl methyl ether-hexane.
2. **Dissolving the solute.** To the crushed or ground solute in an Erlenmeyer flask, add solvent, add a boiling stick, and heat the mixture to boiling. Add more solvent as necessary to obtain a hot, saturated solution. (Do not use a beaker, because the large mouth allows solvent evaporation to be too fast and uncontrolled.)
3. **Filtering suspended solids (if necessary).** If it is necessary to remove suspended solids, dilute the hot solution slightly to prevent crystallization from occurring during filtration. Filter the hot solution. Add solvent if crystallization begins in the funnel. Concentrate the filtrate to obtain a saturated solution.
4. **Crystallizing the solute.** Let the hot saturated solution cool spontaneously to room temperature. Do not disturb the solution. Slow cooling gives the best crystals. Cooling while clamped in the air, or while standing on a watch glass that is resting on your round-bottomed flask holder is a good way to do it. Put a watch glass or inverted beaker over the top of your flask so that solvent doesn't evaporate away while still hot. Then cool it in ice. If crystallization does not occur, scratch the insides of the container, add seed crystals, or for many solvents add ice chip(s).
5. **Collecting and washing the crystals.** Collect the crystals using a Hirsch funnel (<0.2 grams) or a Buchner funnel (>0.2 g), a filter flask, and aspirator suction. Place a filter paper on the surface, wet the filter paper with solvent, and apply suction to make sure the paper seals. Break the vacuum, add crystals and liquid, and apply vacuum. After solvent disappears, break vacuum, add cold wash solvent, apply vacuum, and repeat until crystals are clean and filtrate comes through clear. The wash solvent is normally either a small amount of an ice-cold portion of the main recrystallization solvent, or else a somewhat "worse" solvent (although it shouldn't normally be a totally "bad" solvent). For example, if 80% ethanol/water is used for a recrystallization, it would be common to wash with 60% ethanol/water to avoid dissolving much crystal.
6. **Drying the product**. Aspirate the sample for as long as is convenient. Press the product on the filter to remove solvent. Then remove it from the filter, squeeze it between sheets of filter paper to remove more solvent, and spread it on a watch glass to dry
7. **Analyzing the product.** Take a melting point of the final product. But since incomplete drying will contaminate the crystal and depress the melting point, it is normally best to wait for 15 hours or more before doing so.

PART 1: Macroscale Recrystallization of Phthalic Acid from Water

Weight out about 1 g of pthalic acid. (Record exact mass). Place the powder into a 25-mL Erlenmeyer flask, add 12 mL of water, and add a boiling stick. (The stick facilitates even boiling and prevents "bumping" explosions). Heat on a hot plate until the water begins to boil gently. (Avoid a hard boil. If much of your solvent boils away, the sample will either not dissolve in the first place or will not be able to remain dissolved). Once the solution has reached the boiling point and the sample has dissolved, remove it from the hot plate and move it onto a watch glass suspended on a round-bottomed flask holder (cork ring or rubber ring). (A convenient way to transfer a hot flask is to get a wet paper towel to hold it with, and transfer it by hand.) Remove the boiling stick and cover the top of the flask with an inverted 50-mL beaker. (This is to prevent further hot solvent from evaporating away.) The reason you don't want to put your flask on the bench top is that heat transfer will be too fast and it will cool too quickly, resulting in inferior and less pure crystals. Allow the flask to cool until it is no longer hot to the touch. (10 minutes.) Then place it in an ice bath so that it gets as cold as possible and the smallest necessary amount of desired product stays in solution. (5 minutes).

Collect the crystals using a Buchner funnel. (See picture below, and instructions on page 17 of this handout). Make sure you have a filter flask (with an arm on the side for attaching the tubing), that you have a rubber adapter between the flask and the Buchner funnel, and that you put filter paper onto the funnel. With the Buchner funnel on top plus the tube, the flask will be top-heavy and will very easily tip over. To avoid this, you should clamp it to keep it secure (see picture). Attach the tubing to the vacuum, and turn the vacuum on full blast to get maximum suction, and to hold the filter paper tight. Pour your crystals and solvent onto the paper. Use a micro-spatula with a bent-hook and perhaps additional cold water to try to get all of your crystals into the Buchner funnel. Rinse the crystals with a ~5mL of ice-cold water. (Pour this into your original flask first to help rinse out some residual crystals there, before pouring it through your Buchner funnel.) Break the vacuum before you add the rinse solvent; this allows all of the crystals in the Buchner funnel to be exposed to the rinse solvent. Let the solution stand for at least 20 seconds, then reapply the vacuum and pull the solvent through again. Maintain vacuum for at least ten minutes, and preferably longer if you are doing something else. It should run for at least ten minutes if you want to get final mass and melting point today; if it hasn't been dried accurately residual solvent will inflate the mass reading but depress the melting range.

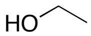
After allowing time to dry, weigh the crystals, record your final mass and calculate your % yield, and take a melting range for the final product. The melting point can be taken today, or sometime during the week. (The range should fall somewhere in the 190-220 area. So set the melting apparatus high enough, maybe at 6 or so, so that it doesn't take forever to warm up. If a previous user has been on the melting machine, so long as the temperature has cooled below 160° it should be cool enough for the next student to get on and get started.)

PART II: Recrystallization Experimement 3.1.

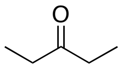
SOLVENTS

H_2O

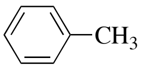
water ("W")



ethanol ("A")
("A" for "alcohol"!)

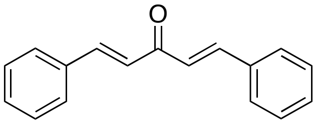


pentanone ("P")

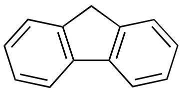


toluene ("T")

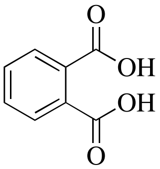
SOLUTES



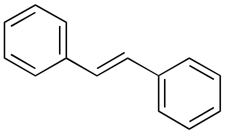
dibenzalacetone ("D")



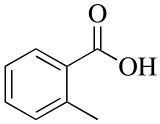
fluorene ("F")



phthalic acid ("P")



stilbene ("S")



o-toluic acid ("T")

Overview: For each of 5 solutes, you will screen its solubility in each of the 4 different solvents shown above: water, ethanol, 3-pentanone, and toluene. (5 x 4 = 20 tests/test tubes!) The big idea is that for each of the solutes, you should be able to decide which of the solvents would be suitable for carrying out a recrystallization. Repeat tests as needed.

Procedure: Add about 70 mL of hot tap water to a 150-mL beaker, and heat it on a hot plate (set around 6, maybe, to start?) to a gentle boil (just barely boiling). It will take a little while for the water to heat up, so start this before you'll actually need the hot water bath.

For each solute you will test the four solvents. It works best to try all four solvents for a given solute before beginning with the next solute.

For each solute: weight out about 0.16 g of the solute, and divide it into four roughly equal piles. Place these into four test tubes (about 40mg per tube). The easiest way to do this is to weigh it first, divide it on weighing paper, push the portions onto separate pieces of weighing paper, and then pour those portions into your test tubes. (Note: If the solid is "chunky", try to crush it before putting it into the test tubes to facilitate solubility.)

Then add 1 mL of each of the four solvents. (Be sure to label your test tubes adequately!) Stir with a wooden stick for 20-60 seconds. Record the results ("s" = soluble, "i" = insoluble, "ss" = slightly soluble.) For those that don't dissolve at room temperature, place the test tube into the hot water bath (2 minutes) and record the results again. If it still doesn't dissolve, add another 1mL of solvent to the hot solution, continue heating for another two minutes, and repeat your observation. (Sometimes more solvent will enable something to dissolve that wouldn't dissolve in a lesser amount of solvent.) (Note: There is no point in heating a test tube with something that dissolved already at low temp; things never "undissolve" at higher temperature!) Record all your observations.

- **Summary**: This is the standard process for finding which solvents are suitable for recrystallizing a particular solid.
- **What constitutes a suitable solvent**? If your results are "s" (soluble) even at room temperature, the solvent is unsuitable because it's too good. You'll never be able to harvest any crystals. If your results are "i" (insoluble) even at high temperature, the solvent is unsuitable because it's too bad. You'll never be able to free the impurities. The ideal solvent should be "i" (or perhaps "ss") at room temperature but then "s" at high temperature, so that you can both free the impurities (at high temperature) but also recover crystals (at low temperature).

RECRYSTALLIZATION REPORT Name:

Report requirements (Part 1):

1. Report your initial mass, your mass recovery, and your % yield.

2. Report your dry melting range.

3. Explain <u>very briefly</u> why dissolving and then reforming crystals can improve their purity.

4. Explain <u>very briefly</u> why recrystallization can never result in 100% mass recovery (even if you used perfectly pure material).

5. Explain <u>very briefly</u> why mass recovery is greater if you cool to 0°C rather than merely room temperature.

6. Explain <u>very briefly</u> why mass recovery is reduced if you use an excess amount of boiling solvent.

7. Explain <u>very briefly</u> why washing product crystals with excessive amounts of solvent, especially warm solvent, can result in reduced mass recovery.

8. Given:
    - The solubility of **X** at 100ºC in water is 18.0 g/100 mL water.
    - The solubility of **X** at 0ºC in water is 3.6 g/100 mL water.

How many mL of boiling water would be required to dissolve 25g of **X**? If that solution was then cooled down to 0ºC, how many grams of **X** could then crystallize out? What would be the maximum yield recovery for **X?**

9. An ideal recrystallization solvent is able to fully dissolve a solute only when hot, but not when cold.

- Why is a solvent that can dissolve the solute even when it is cold useless for recrystallizations?

- Why is a solvent that can't dissolve the solute even when hot useless for recrystallizations?

Report requirements (Part 2):

Fill out the table below. Convenient standard abbreviations are “i” = insoluble and “s” = soluble. (Sometimes “ss” = slightly soluble may also be useful, if it’s clear something is dissolving somewhat, but not completely.) (Don’t worry about distinguishing “insoluble” from “slightly soluble”.

Beside the names for the five solutes, write down which (if any) of the solvents would be appropriate for recrystallization. (It’s possible that none of the solvents screened will look good for a particular substrate, and it’s also possible that several will.)

Recrystallization Solute/Solvent Sheet Chem 355

	WATER ("W")			PROPANOL ("A")			3-PENTANONE ("P")			TOLUENE ("T")		
Solute	RT	Hot	Extra Solvent	RT	Hot	Extra Solvent	RT	Hot	Extra Solvent	RT	Hot	Extra Solvent
"D" Dibenzalacetone												
"F" Fluorene												
"P" (Pthallic Acid)												
"S" Silbene												
"T" o-Toluic Acid												

Standard abbreviatons: "I" = insoluble, "ss" = slightly soluble, "s" = soluble

Which solvents (if any) would be appropriate for the recrystallization of the following substrates? There may be more
Make sure that your answers are consistent with the observations in the table above.

"D"
Dibenzalacetone

"F"
Fluorene

"P"
(Pthallic Acid)

"S"
Silbene

"T"
o-Toluic Acid