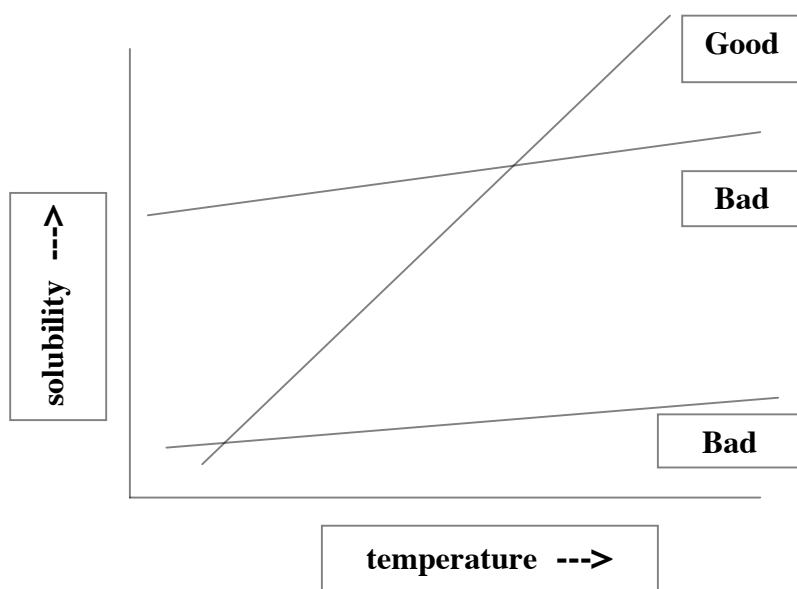


## Recrystallization.

Recrystallization is the primary method for purifying solid organic compounds. Compounds obtained from natural sources or from reaction mixtures almost always contain impurities. The impurities may include some combination of insoluble, soluble, and colored impurities. To obtain a pure compound these impurities must be removed. Each is removed in a separate step in the recrystallization procedure.

To understand the recrystallization process, solubility behavior must first be considered. It is often stated that "like dissolves like". More correctly, it should be stated that, "compounds having similar structural features will be soluble in one another". Some obvious structural features that may affect solubility include polarity and the ability to hydrogen bond. For example, a compound having just a few carbons and an alcohol functional group (FG) would be expected to be soluble in solvents that have a few carbons and an alcohol FG or in some other polar solvent, and to be less soluble in nonpolar solvents. Conversely an alkane would be expected to show the opposite solubility behavior. In most cases though it is not as simple as this. If for example a compound has lots of carbons and hydrogens (> 6 C's) and just one alcohol group, the solubility will be dominated more by the alkyl part of the molecule than by the alcohol part, and the compound will show a solubility behavior more like that of an alkane. For known compounds it is useful to consider the structure of the compound when choosing a recrystallization solvent. An educated guess can save some time. Usually however, the structure of a compound may not be known so the solvent must be chosen by carrying out solubility tests.

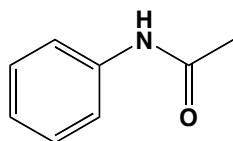
The first part of this experiment involves carrying out solubility tests on known compounds. Later on such solubility tests will be used to find a suitable recrystallization solvent for an unknown compound. A compound usually exhibits one of three general solubility behaviors: (1), the compound has a high solubility in both hot and cold solvent, (2), the compound has a low solubility in both hot and cold solvent, and (3), the compound has a high solubility in hot solvent and a low solubility in cold solvent. Solvents which exhibit the first two behaviors are not useful for recrystallizing a compound. A solvent showing the third behavior, that is, high solubility at high temperatures and low solubility at low temperatures, is one that is suitable for use as a recrystallization solvent.



Consider the three different types of impurities that may be present in a sample: soluble, insoluble, and colored. In theory, insoluble impurities can be removed from a compound fairly easily. The compound is

dissolved in a solvent, the solution is filtered to remove the insoluble impurities, and the solvent evaporated to produce the solid compound. The insoluble impurities are left behind in the filter paper. Colored impurities can be removed in a similar way but with an additional step. The solid is dissolved in a solvent, activated charcoal is added, the solution is filtered as before, and the solvent is evaporated to produce the solid compound. The charcoal, which has adsorbed the colored impurities, is left behind in the filter paper. The third type of impurity, the soluble impurity, cannot be filtered out because it has solubility characteristics similar to those of the desired compound (hence the name soluble impurity). To remove soluble impurities, first, by doing solubility tests, a suitable solvent is chosen (high solubility in hot solvent, low solubility in cold solvent). The soluble impurities are then removed as follows: the desired compound along with the soluble impurities are dissolved in a MINIMUM of near-BOILING solvent. The solution is then allowed to cool slowly and without interruption. As the solution cools, the solubility of the compound (and of the soluble impurities) decreases, the solution becomes saturated with the desired compound, and the compound begins to crystallize. Because formation of crystals is a highly selective process that usually excludes foreign molecules, only crystals of the desired compound form. Because the soluble impurities are present in smaller amounts, the solution never becomes saturated with the impurities, so the impurities remain in solution even after the solution has cooled. Removing the solution from the crystals thus removes the solvent and the soluble impurities from the desired crystals. A final rinse with a MINIMUM of ICE-COLD solvent followed by its removal cleans off any residual soluble impurities clinging to the surface of the desired crystals. After allowing the solvent to evaporate, pure crystals of desired compound should remain. The weight and usually the MP of the crystals would be determined, and along with the % recovery, would be included in the report.

In practice, by following a set procedure, the same solvent is used throughout the whole recrystallization process, and the impurities are removed one by one. Note that in any recrystallization some of the desired product is sacrificed and the recovery will be less than 100%. This is because even at the lower temperatures the desired compound has some finite solubility in the recrystallization solvent and is thus lost when solvent and soluble impurities are removed. To illustrate this, look at the solubility of acetanilide in water.



Acetanilide

Solubility in 100 mL water

0.5 g at 10°C; 5 g at 99°C

If 5 g were dissolved in 100 mL of water at 99° and then allowed to cool to 10°, 4.5 g would crystallize out and 0.5 g would remain in solution. The recovery then would be 90%. The 10% remaining in solution would be lost.

Recrystallization summary. For our recrystallizations you may assume that only soluble impurities are present. The six steps used here to recrystallize a compound are, (1) carry out solubility tests to determine a suitable solvent; (2) dissolve the solute in a minimum of near-boiling solvent; (3) allow the solution to cool slowly and undisturbed to room temperature (RT) then possibly to ice temperature; (4) collect the crystals by filtration; (5) rinse the crystals with a minimum amount of ice-cold solvent; and (6) allow the crystals to dry.

What can go wrong in a recrystallization? Care must be taken at each step to obtain good results, which can be measured by % recovery and purity of the desired compound. Fortunately, for most of the recrystallizations done in this course, for various reasons, colored impurities and insoluble impurities will not be present. Removing soluble impurities will thus be the focus of most recrystallizations done here. Recrystallizations require careful technique and practice. Some loss, resulting from transferring solids from

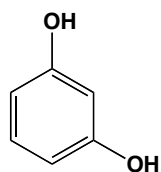
one container to another and leaving a little material behind, cannot be avoided. Such losses should however be minimized as much as possible by using careful technique. Also, because of the finite solubility of the solid in the recrystallization solvent, even at low temperatures, any unnecessary prolonged contact with recrystallization solvent, especially if the solvent is not ice-cold will result in loss of product. For that reason, the following problems commonly occur: if too much solvent is added in the recrystallization, a poor or no yield of crystals will result. If the solid is dissolved below the boiling point of the solution, too much solvent will be needed, resulting in a poor yield. If too much rinse solvent or rinse solvent that is not chilled to ice temperature is used, some of the product will be redissolved and lost. In summary, to obtain optimal results, a MINIMUM of near-BOILING solvent should be used for the recrystallization, and a MINIMUM of ICE-COLD solvent should be used for the rinse. Occasionally crystals will not form, even though the saturation point has been reached. If a recrystallization solution has been allowed to cool and crystals have not formed, it may be due to a condition known as supersaturation. If this happens, you may induce crystallization by scratching the inside of the glass tube just below the surface of liquid using a glass stirring rod. The tiny scratch provides a rough surface on which the crystallization may begin. The same result could be obtained by adding a small "seed" crystal of that substance, assuming a small amount of solid had been saved.

### **Procedure. Recrystallization – Part 1.** (rev 6/10)

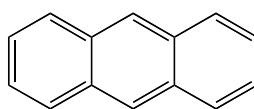
Because recrystallizations will be used throughout this course it is vital that you understand the principles behind it and learn to do it correctly from the start. In later experiments you will not be given detailed instructions for recrystallizations. You will simply be told to recrystallize a compound. A good recrystallization solvent is one in which the solid has a very high solubility at high temperatures and a very low solubility at low temperatures. Refer to the flow chart shown on the last page of this handout. Note the distinction between melting and dissolving. Melting is the process that converts a solid to a liquid by supplying heat. Dissolving is the process that homogeneously disperses a solid into a solvent.

Include in your prelab outline, the separate recrystallization steps noted above, along with the purpose of each. Photos of the recrystallization procedure are shown on the course website.

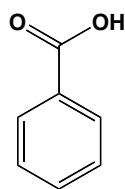
(1.) Solubility tests. Remember: sand baths take time to heat up so whenever a procedure calls for the use of a sand bath, the first thing to do upon entering the lab is to turn the controller on to a setting of just under 40% (NEVER HIGHER). Always turn the heater off before you leave for the day. You will test the solubility of four compounds - resorcinol, anthracene, benzoic acid, and 4-amino-1-naphthalenesulfonic acid, sodium salt - using water, toluene, and hexane (actually a mixture mainly composed of isomeric hexanes, sometimes called ligroin) as the solvents.



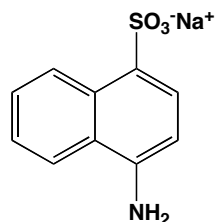
Resorcinol



Anthracene



Benzoic Acid



4-Amino-1-naphthalenesulfonic acid, sodium salt

Use about 10 mg of each compound for the tests. It is not necessary to use a balance to measure out the solids accurately. Samples of about 10 mg of solid in a reaction tube will be on display near the compounds. Simply use an amount which approximates that. To avoid spilling the solid, use the scoopula and the plastic funnel from the kit to help transfer the solid to the tube. The solvent does not have to be measured exactly either. Use a disposable pipet to add solvent and the calibrations on the reaction tube to measure the amount. This level of accuracy is enough for qualitative tests such as these and will be done often in certain microscale experiments, where accuracy is not essential. To heat solutions in a reaction tube, use the sand bath as the heat source and a boiling stick to promote smooth boiling. Failure to use a boiling stick will result in superheating of the solution followed by bumping of the solution out of the tube. In heating a tube with a sand bath, the temperature of the tube is controlled by adjusting the depth to which it is immersed in the sand. Use care in heating low-boiling solvents such as hexane on the sandbath. Such solvents evaporate easily. Note that hexane and toluene are flammable. Never point the heating tube at yourself or at anyone else because the tube contents may become overheated and shoot out of the tube.

Test solubilities as follows: First see if 10 mg of the compound is soluble in 0.25 mL of the solvent at room temperature (RT). After adding solvent always flick the tube with a finger to swirl the contents and to help ensure complete mixing, and give it 30 sec to dissolve. If the solid completely dissolves, it is considered to be very soluble at RT, in which case nothing more has to be done with that solid/solvent combination. If the compound is insoluble at RT, heat the tube to the BP of the solution. If the compound is still insoluble at the BP (give it 30 sec), it is considered to have a very low solubility at all temperatures, in which case nothing more has to be done with that solid/solvent combination. If it seems that some of it has dissolved in 0.25 mL of boiling solvent, add another 0.25 mL and reheat it to see if it will all dissolve. If the compound has dissolved in boiling solvent (either 0.25 or 0.5 mL), cool the tube in cold water to see if crystallization occurs. Scratching the reaction tube with a glass stirring rod at the air-liquid interface may be necessary to induce crystallization. If crystals form, redissolve the solid by heating and allow the tube to cool more slowly, without cooling in cold water. Slow cooling may allow larger crystals to form. If the crystals are large enough, record the crystal form (e.g., needles, plates, prisms). The relative amount of the crystals, compared to the starting amount, should be noted.

In the same way, test the four solid compounds in each of the three solvents. The most efficient strategy is to test one compound with the three solvents before going on to the next compound. A table such as that shown below should be made to summarize results. In the write-up include a discussion of any structure-solubility correlations that you observe (see the separate handout on Structure-Property Relationships).

**Sample solubility table:**

		<u>sol of ~ 10 mg of compound A</u>					
		<u>in ~0.25 mL solvent</u>			<u>in ~ 0.5 mL solvent</u>		
		<u>cold</u>	<u>hot</u>	<u>observations</u>	<u>cold</u>	<u>hot</u>	<u>observations</u>
<u>HOH</u>	<u>insol</u>	sol		needles on cooling/good yield	-	-	-
<u>toluene</u>	<u>insol</u>	sl sol		plates on cooling/good yield	<u>insol</u>	sol	plates on cooling/gd yield
<u>ligroin</u>	<u>insol</u>	<u>insol</u>		-	-	-	-

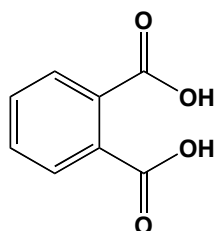
sol of ~ 10 mg compound B (prepare a table as for compound A)

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Dispose of all solutions in the ORGANIC LIQUID WASTE container in the hood. Place used boiling sticks into the “boiling stick” waste container in the hood, NOT into the trash. Being environmentally responsible: Minimize the number of Pasteur pipets being used. It is usually not necessary to dispose of a pipet after each

use. For example, if you have just transferred an aqueous solution with a pipet and you are going to transfer another aqueous solution, simply rinse the pipet with water, if necessary, and use it again.

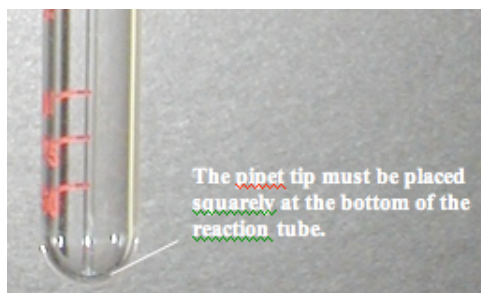
(2.) Recrystallization of Phthalic Acid. Into a reaction tube, using a plastic funnel to make a clean transfer, weigh about 60 mg of phthalic acid accurately (it can be 55 mg or 65 mg but measure the amount exactly). The approximate amount of HOH needed can be calculated from the data given below. The exact amount will be determined empirically. Add about half the amount of water that you calculated to the phthalic acid and bring the solution to boiling (boiling stick). Continue adding the HOH dropwise at the boiling point (BP), allowing some time for the solid to dissolve after each addition, until the last drop of HOH dissolves the last amount of solid (at the BP). Clamp the tube to a ring stand and observe the solution as it cools to RT, undisturbed. If large crystals do not form upon cooling, simply reheat the solution to redissolve the solid, then allow the solution to cool slowly again. Cool the tube further in ice to obtain a maximum yield.



Solubility per 100 mL of water:  
0.54 g at 14°C; 18 g at 99°C

Phthalic Acid

Filtration using the pipet method. This will be done many times over the course of the semester so it is important to learn to do it correctly. This method of separating crystals from a solution can be done only if the crystals are large enough so that they do not get sucked up into the pipet. If the crystals are too small, another method, suction filtration, must be used. This will be described later on. With the pipet method, to prevent crystals from going into the pipet, it is essential to make a tight seal between the pipet and the bottom of the reaction tube, as shown in the photo. Look also at the photos of the recrystallization procedure on the course website.



This can be done by stirring the crystals with the pipet to loosen them, and while expelling some air from the pipet beneath the solution to suspend the crystals above the bottom of the tube, push (not too hard) the pipet down onto the bottom of the reaction tube. With the pipet in place, draw solution up into the pipet. If this method is done correctly, very little solid will be drawn up into the pipet and a clean filtration will be accomplished. Use this method to separate the solution from the phthalic acid crystals. Generally the filtrate should be saved in another tube until it is certain that it is no longer needed. To remove further amounts of solution that may be left behind, tap the tube on a soft surface (such as a notebook) and repeat the pipet filtration. Using several drops of ice-cold water, rinse the crystals while keeping the tube cold in an ice bath, and remove the rinse water with the pipet as before. Rinsing with fresh solvent removes impurities clinging to the surface of the crystals. After removing as much water as possible with the pipet, use the curved end of the spatula to scrape as much of the solid as possible out onto a tared (pre-weighed) piece of filter paper. Because water evaporates slowly, the crystals must be left to dry at least overnight before weighing. Leave

this open in a safe place in your drawer so that the crystals can dry completely by the next day or so, at which time they can be weighed, and a % recovery determined. The tube can also be left to dry and any product remaining in it can be scraped out and combined with the material on the filter paper. Before you dispose of any sample, have your instructor examine it. Do not try to determine the MP of phthalic acid – it decomposes before melting. (In case you want to know, it loses water at the MP to form an anhydride.) **Waste:** dispose of the water filtrates in the ORGANIC LIQUID WASTE container. When finished with the phthalic acid, place it into the Solid Waste container.

**BEFORE YOU LEAVE THE LAB:** turn off the sand bath, turn off the air if used, put away your equipment and lock your drawer, clean up your work areas, close the fume hood sash completely and ask your TA for her or his signature. In general, please try to keep the lab is as good condition as you found it. If you see caps off of bottles, replace the caps. If you see spilled chemicals, clean them up or at least report it to your TA.

A note on morning hours. Sometimes, as in this experiment, before a sample can be accurately weighed it must be left to dry at least overnight. So that you may finish and write up an experiment before the next lab period, the lab will be open at certain hours during the morning for simple things such as weighings and melting point determinations to be done. Schedules and rules for use of the morning hours are posted on the web site and are posted at the entrance to the lab. Be sure that you know the schedules and the rules. Use of morning hours is however a CONVENIENCE, NOT a REQUIREMENT. Many students have schedules that do not allow them to attend any morning hours. In such cases, these students will do the weighings during their next lab period and submit the report later that day or if necessary the next day. Most people however will make use of the morning hours, which will make things less stressful for everyone during the next lab period. The few of those who cannot will have no problem finishing up at the next lab period.

Drying to constant weight. To be certain that a solid is dry, it must be weighed, left to dry for some period of time, then weighed again. If the sample does not lose weight, it can be considered to be dry. Because water evaporates very slowly, solids recrystallized from water must be left at least overnight to dry. Solids recrystallized from most common organic solvents dry more quickly and are often dry within an hour. Note that solvent remaining in the solid will affect not only the weight of the solid but its MP range as well.

Being environmentally responsible: Minimizing waste - cleaning reaction tubes: once the contents of a tube is disposed of in the correct waste container in the hood, the tube should be washed using soap, water, and a brush. If the tube must be used immediately, and if it must be free of water, rinse it with a SMALL amount of acetone (several drops a few separate times), drain the acetone into the ORGANIC LIQUID WASTE container in the hood, and turn the tube upside down to drip dry. DO NOT FILL the tubes with acetone - this creates excessive waste and is unnecessary- use just a little to rinse the tube. If the glassware must be dried quickly, use the compressed air in the hoods. (Use a gentle airflow only.). Remember to always minimize the chemical waste generated in the lab.

Conserve pipets. Do not throw away a pipet after each use unless it cannot be easily cleaned. If a pipet is used to measure a volatile (low-boiling) solvent, let the pipet dry after use and use it again. If an aqueous solution is measured, rinse with water and allow it to dry for future use. Minimize waste. **The yellow pipet bulbs can be used indefinitely and should not be thrown away.**

## Postlab Questions

- 1.) Draw a solubility (y) vs temperature (x) plot showing the three common solubility behaviors and indicate which one is that of a good recrystallization solvent.
- 2.) Briefly describe how soluble impurities are separated from the desired compound, at the molecular level.
- 3.) Using the information given in the handout, how many mL of boiling water are required to dissolve 4.2 g of phthalic acid?
- 4.) If the resulting solution in Problem 3.) were cooled to 14° C, how many g of phthalic acid would crystallize out? What would be the percent recovery?
- 5.) What structural property of 4-amino-1-naphthalenesulfonic acid, sodium salt makes it very soluble in water?

### FLOW CHART FOR RECRYSTALLIZATION

