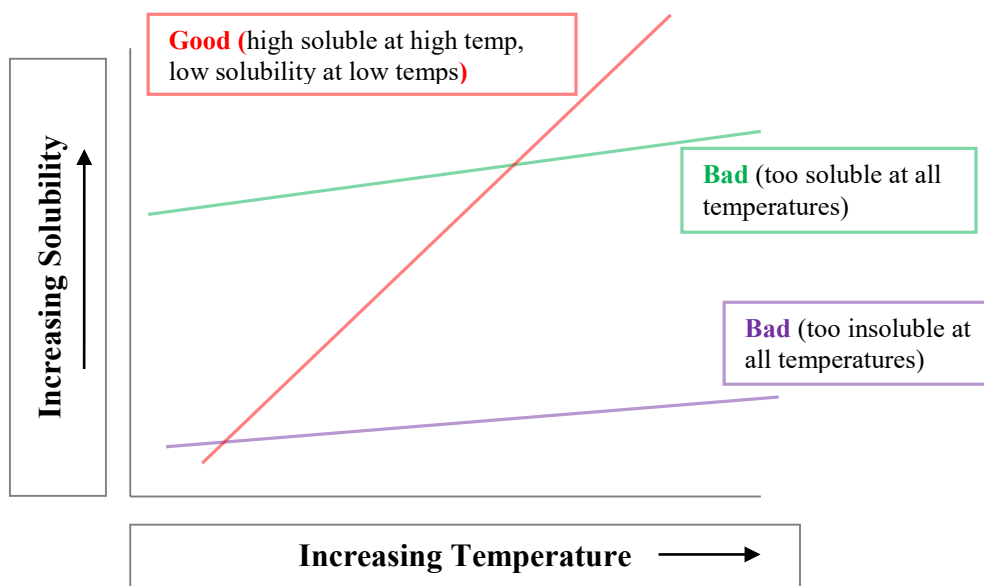


Recrystallization¹

Recrystallization is the most convenient method for purifying organic compounds that are solids at room temperature. 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 type of impurity 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 can 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. However, in most cases it is not as simple as this. If, for example, a compound has an abundance 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.

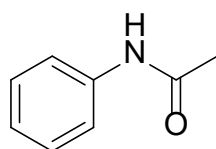
The first part of this experiment involves carrying out solubility tests on known compounds. Later on such solubility tests will be used to find a suitable recrystallization solvent for an unknown compound. A compound usually exhibits one of three general solubility behaviors: (1) the compound has a high solubility in both hot and cold solvent (green), (2) the compound has a low solubility in both hot and cold solvent (purple) and (3) the compound has a high solubility in hot solvent and a low solubility in cold solvent (red). 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, sparingly solubility at room temperature, and low solubility (or insoluble) at reduced temperatures, is one that is suitable for use as a recrystallization solvent.



¹ revised 3/2020

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, the following strategy can be utilized: 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 or at 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 removal of this solvent, 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 mass and the MP of the crystals would be determined, and along with the % recovery, this data would be included in the report.

In practice, by following a set procedure, the same solvent is used throughout the entire 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.



Solubility in 100 mL water
0.5 g at 10°C; 5 g at 99°C

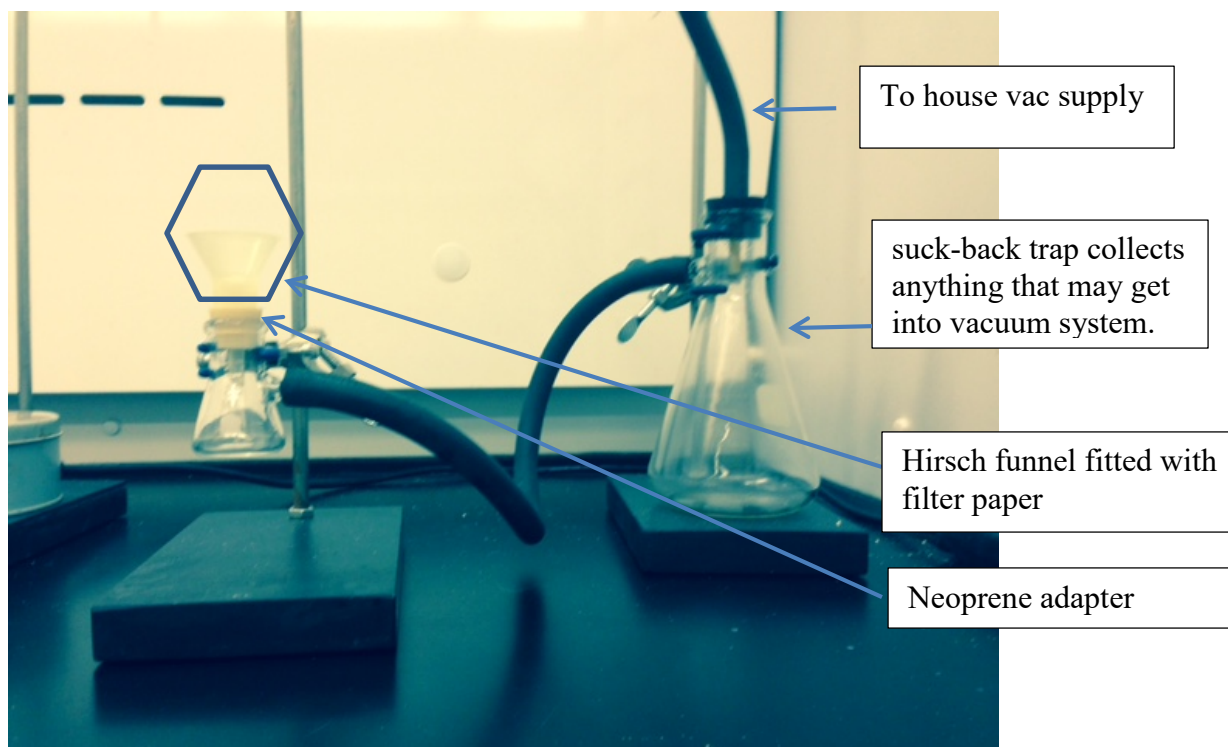
Acetanilide

If 5 g were dissolved in 100 mL of water at 99 °C and then allowed to cool to 10 °C, 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 or at 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, due to the finite solubility of the solid in the recrystallization solvent, even at low temperatures, any unnecessary prolonged contact with the 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.

Suction filtration: Isolation of the solid. There are many filtration methods to isolate a solid from a liquid: pipet (used later in a different experiment), gravity, and best of all, suction. We will utilize suction filtration, so it is the only one described here. In this method, the number of transfers from one container to another is kept to a minimum, thereby minimizing loss of material. An advantage of suction filtration is that the solution is completely separated from the solid, and can be allowed to dry with briskly passing air, so drying time is often shorter. The photo below shows the set-up:



The procedure for setting up a suction filtration is described below.

1. Clamp the 25-mL filter flask (Erlenmeyer flask with a tapered side-arm) to the ringstand as shown above.
2. Add the neoprene adapter (tapered neck piece) and plastic Hirsch funnel with a piece of filter paper.
3. Make sure the vacuum is working by turning on the knob; place a finger over the black tubing. You will know if it is working.
4. Connect the thick-walled vacuum tubing from the suck-back trap to side arm of flask.
 - a. the trap prevents anything from mistakenly entering the vacuum system.
5. Turn on vacuum 'full blast', until knob stops.
6. Actual filtration described in the experimental procedure.

Important: Because we will utilize recrystallizations throughout this course, it is vital that you understand the principles behind the process 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 by interfering with the intermolecular forces that allow a compound to be in its solid state.

Note: Hot plates and aluminum blocks take time to heat up so whenever a procedure calls for the use of a hot plate, the first thing to do upon entering the lab is turn the hot plate on and set the temperature. Because of the heat loss experienced by the blocks, the temperature typically needs to be set to over 200 °C. This will vary by experiment. Your TA should let you know what temperature to set the hot plate to. Keep in mind the temperature of the hot plate IS NOT the temperature of your boiling solvent. Always turn the temperature down and switch off the hot plate before you leave for the day.

Include in your prelab outline, the separate recrystallization steps noted above, along with the purpose of each.

Prelab: You may either print out your prelab and bring it with you to lab, or bring your computer. Your TA will grade it on the spot before you begin the experiment. For the in lab observations, you may use scratch paper and record later in your ELN, or bring your computer and record directly in your ELN.

Postlab Report: Make sure to use the non-formal postlab report template on the course website!

Experimental Procedure

Part 1: Solvent determination of your unknown.

- a. Turn on hot plate and adjust the temperature ~225°C upon entering the lab. Your TA will assign your unknown.
- b. Your goal is to determine the best recrystallization solvent for your unknown. Available solvents are water, methanol, pure ethanol, 70% ethanol in water, hexanes or toluene. (hexanes is a mixture of hydrocarbons mainly composed of isomeric hexanes) (see section f for specific procedure).
 - a. You must use all solvents available to determine which is best after you have analyzed data.

- b. You will use this information in part three of this lab, so **look for a solvent that produces the highest recovery and the most well-formed crystals.**
- c. Exact amounts are not required, but be careful not to use too much solid or solvent.
- You will be using 10 mg of unknown to do the solubility tests. Use the sample on the solvent bench to see how much ~10 mg is. Do not weigh it.
 - To avoid spilling, use the scoopula and the plastic funnel to help transfer the solid to the tube.
 - Add solvents using a disposable pipet, and use the calibrations on the reaction tube to measure the amount. Note the first line on the reaction tube is 0.5 mL. You will start with 0.25 mL, so approximately halfway to the first line.
- d. To heat solutions in a reaction tube, use the hot plate with aluminum block as the heat source and use a boiling stick to promote smooth boiling (**handle tube with your test-tube tongs**). Failure to use a boiling stick will result in superheating of the solution followed by bumping of the solution out of the tube.
- e. In heating a tube with the aluminum block, the temperature of the tube is controlled by the temperature of the hot plate, the amount of surface area of the tube in contact with the block, and by adjusting the depth to which the tube is inserted into the block.
- Use care in heating low-boiling solvents such as hexanes. Such solvents evaporate easily. Note that hexanes 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. Always work in the hood and **DO NOT PUT YOUR HEAD IN THE HOOD!!**
- f. Determine the best solvent as follows:
- First see if 10 mg of your unknown 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 seconds (s) 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 unknown/solvent combination. It can be disposed.
 - 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 30s or so), it is considered to have a very low solubility at all temperatures, in which case nothing more has to be done with that unknown/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 mL or 0.5 mL), cool the tube slowly to room temperature, then place it on ice. While the sample is cooling, perform the same procedure with the next solvent. 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.
 - You will record your data in your ELN using a table (example format below). Note that your table will have additional entries for the other solvents not listed in these tables. Also note that you may not have an entry for the 0.5 mL table for a solvent that didn't require additional solvent added.

Table 1. Solubility using 0.25 mL solvent.

Solvent	Cold	Hot	Observations
Water	Insoluble	Soluble	Needles on Cooling

Table 2. Solubility using 0.50 mL solvent.

PhCH ₃	Insoluble	Slightly Soluble	Precipitates on cooling
-------------------	-----------	------------------	-------------------------

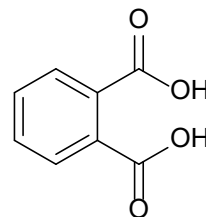
Solvent	Cold	Hot	Observations
Water	Insoluble	Insoluble	N/A
PhCH ₃	Insoluble	Soluble	Precipitates on cooling

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.

In the next part, you will recrystallize phthalic acid from water. Consider it a “practice” run for part 3.

Part 2: Macroscale Recrystallization of Phthalic Acid

- Weigh out 325 +/- 10 mg of phthalic acid. Place into a 10 mL Erlenmeyer flask.
 - Make sure to record the actual amount that you used.
- Add 5-6 mL of DI H₂O (about half-full) to a clean and dry test tube. Add a boiling stick.
- Place the tube into the appropriately sized drilled hole in the aluminum block and allow the water to boil. You may clamp the tube with a small 3-prong clamp.
 - If the water doesn't boil after some time, make sure its lowered all the way down into the well, and/or turn up the heat on the hot plate.
- Carefully add the boiling (or near boiling) water *dropwise* via a Pasteur pipet to the flask containing phthalic acid and keep the flask warm by allowing it to rest on top of the flat surface of the block. Do not put it into one of the wells. Don't heat the phthalic acid on the block until you've added some water, otherwise the phthalic acid will decompose.
- Keep adding water dropwise while the flask sits on top of the block.
 - Swirl flask very gently on top of the block using the test tube holder.
- Add more solvent if needed; maybe this time down the inside edge of the flask to remove the phthalic acid that adheres itself to the glass.
- By now, complete dissolution should take place. If you see solid form while it is still being kept warm, too much has evaporated. Add a few drops more, gently swirl and remove (use test tube holder) and let cool, unaided, to room temperature (rt). Don't bother it! Place it on a book, or just something other than the hood surface (it's cold and may induce precipitation, which is NOT what you want).
 - If procedure is performed correctly, crystallization should start almost immediately.
- While waiting for the solution to cool . . .
 - set up a suction filtration apparatus as described above. *Do not turn on vac just yet.*
 - add DI H₂O (~ 6-7 mL) to your other 10 mL Erlenmeyer flask and get it cooling in an ice bath.
- Once cooled to rt, place solution into another ice bath to induce further crystallization. Let cool for 5-10 minutes.
- Gently stir crystals with a micro-spatula.
- Wet filter paper with 2-3 drops of ice-cold solvent and turn on house vac knob 'full blast.'
 - Wetting the filter paper prevents it from rising when your solution is poured over it.
- Pour solution onto filter paper.
- To aid in transfer of crystals, simultaneously rinse with ~ 1 mL (pipet about a third full) of ice-cold solvent and pour onto filter paper. This is known as *quantitative transfer*.



Phthalic Acid

Solubility per
1 mL of water:
5.4 mg at 14 °C (cold);
180 mg at 99 °C

- a. It may be helpful to rinse flask with solvent at almost the angle you would pour it out!
- b. Rinsing may be done 1-2 additional times without significant loss of product. You should be able to get all crystals out within 1-2 rinses/washes.
- n. There is no need to perform additional washes after rinsing as above.
- o. Let dry under suction 5 - 10 minutes.
- p. Add your crystals to a **tared piece of filter paper** and place directly into your drawer. Dry at least overnight.
- q. Record final weight and % recovery. Place your purified phthalic acid into the container provided by your TA. Do not put in solid waste. It is recycled. *Go Green!*

Part 3: Purification of an Unknown.

- a. You will now recrystallize your unknown using the best solvent determined in part one.
- b. Recrystallize 250 mg +/- 10 mg of your unknown exactly as you did in part 2 with phthalic acid. **Record the exact mass used.**
- c. Note, that if you are using a solvent that is more volatile than water, especially hexanes, you will want to turn down the temperature of your hot plate. Remember, a sample recrystallized from water must be allowed to dry at least overnight.
- d. Once the recrystallized sample has dried to constant weight, obtain a mass, percent recovery, and determine the MP. (CAUTION: always turn off the melting point apparatus after use).
- e. While you are waiting for your sample to dry on the funnel, obtain a melting point of the impure unknown for comparison to your purified sample.

Identify your Unknown

Using the MP of the purified sample, identify your unknown by checking the list of possible compounds shown below. Note that if the crystals are not completely dry, a MP depression may be observed. It may be useful to confirm your identification by considering other physical properties such as solubility behavior and color (consult structure-property relationships handout on course website). Chemfinder.com or a web search may be helpful for physical properties of compounds. As part of the report, draw the structure of your unknown and comment on its structural features and how they might affect solubility (consult aforementioned handout).

Your results table should contain the % recovery (mass recovered/mass used), MP of your purified sample, MP of the impure unknown for comparison, and the identity of your unknown. You should discuss all these aspects in the discussion section of your report.

BEFORE YOU LEAVE THE LAB: turn off the hot plate, turn off the air if used, put away your equipment and clean up your work areas, close the fume hood sash completely, and ask your TA for their signature. In general, please try to keep the lab in as good of a 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 limited-use hours: Sometimes before a sample can be accurately weighed, it must be left overnight to dry. So that you may finish and write up an experiment before the next lab period, the lab will be open at certain hours for simple things such as weighings and melting point determinations. The time of these varies from semester to semester, so it is important that you check the course website for the current schedule. Be sure that you know this schedule and the rules. Use of limited-use hours is a REQUIREMENT when your work cannot be completed in your regularly scheduled lab. We imagine that all students have schedules that will allow them to attend at least one of the limited-use hours sessions. The LAST melting point must be started no later than 30 minutes before the scheduled end time. You will be asked to leave promptly at the end of the

session, even if your sample isn't finished. The labs will be locked, so to gain access go to the orange entrance and the TA on duty will let you in. DO NOT LET OTHER STUDENTS IN FROM ANOTHER ENTRANCE!

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 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.

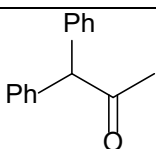
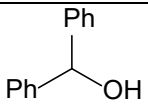
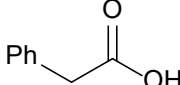
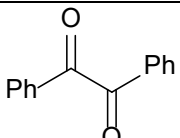
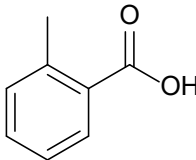
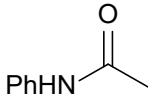
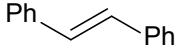
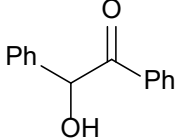
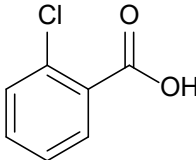
Being environmentally responsible: Minimizing waste—cleaning reaction tubes: once the contents of a tube are disposed of in the correct waste container in the hood, the tube should be washed using soap, water, and a brush. If the tube must be used immediately, and if it must be free of water, rinse it 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 until corroded, at which point they generally become "crunchy."

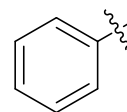
Postlab Questions

- 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 this handout, how many mL of boiling water are required to dissolve 4.2 g of phthalic acid?
- 4.) If the resulting solution in question 3 was cooled to 14° C, how many grams of phthalic acid would crystallize out? What would be the percent recovery?
- 5.) What structural property of sodium 4-amino-1-naphthalenesulfonate makes it very soluble in water? You will have to look up the structure of this compound and comment on why it is water-soluble. Simply stating that it's polar will get no credit.

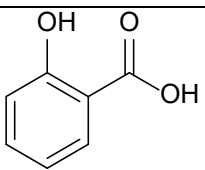
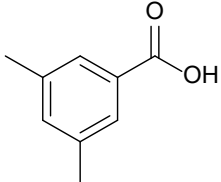
Possible Unknowns

Compound	Structure	MP (°C)
1,1-diphenylacetone		61
benzhydrol		69
phenylacetic acid		77
α -methyladipic acid	$\text{CO}_2\text{HCH}_2\text{CH}(\text{CH}_3)(\text{CH}_2)_2\text{CO}_2\text{H}$	85
benzil		95-96
o-toluic acid		105
acetanilide		115-116
<i>trans</i> -stilbene		124-125
benzoin		133-134
2-chlorobenzoic acid		142

Note: 'Ph' =



Values here may differ slightly from those on the Melting Point list because you have purified the compounds. Melting point values here are from the CRC Handbook, 54th edition.

adipic acid	$\text{CO}_2\text{H}(\text{CH}_2)_4\text{CO}_2\text{H}$	152
salicylic acid		159
3,5-dimethylbenzoic acid		166