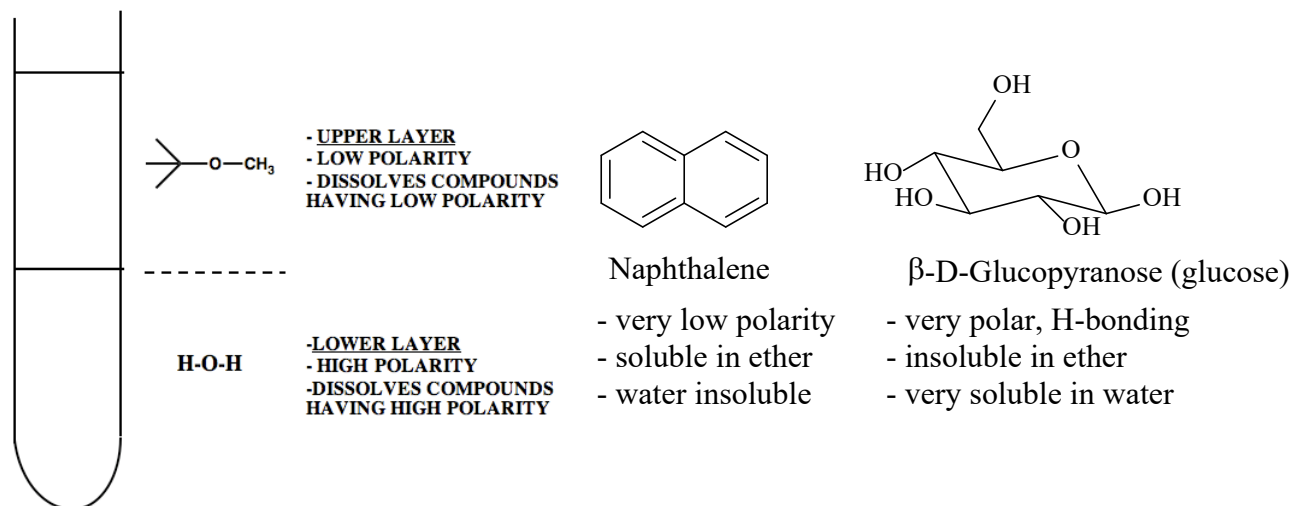


Acid-Base Extraction.¹

Extraction involves dissolving a compound or compounds either (1) from a solid into a solvent or (2) from a solution into another solvent. A familiar example of the first case is making a cup of tea or coffee: the soluble flavor, odor chemicals, and caffeine are extracted from the solid tea leaves or ground coffee beans into hot water (the solvent). Insoluble plant material is left behind in the tea bag or coffee filter. An example of case (2) is an experiment that is often done in an introductory organic lab: an organic solvent is used to extract the caffeine from an aqueous tea or coffee solution, leaving the more water-soluble compounds behind in the aqueous solution. This is, in fact, how decaffeinated tea and coffee were industrially produced for many years.

An acid-base extraction is a modification of case (2): a solvent-solvent extraction. Before looking at what makes this an acid-base extraction, first consider solvent-solvent extractions in general. A requirement of a solvent-solvent extraction is that the two solvents be mostly immiscible. That is, a mixture of the two solvents will separate into two layers (think of oil and water). It is important to note that the upper layer is that which is less dense. For example, a mixture of *tert*-butyl methyl ether and water will separate into two layers, with the ether layer (density = 0.74 g/mL) on top of the water layer (density = 1.0 g/mL). Note that in almost every case, one of the solvents is water, or some other aqueous solution. The other solvent is an organic solvent that is mostly immiscible with water. Examples include *tert*-butyl methyl ether, hexanes, and dichloromethane. The organic solvent must also be volatile (easily evaporated) so it can be removed by evaporation at the end of the process.

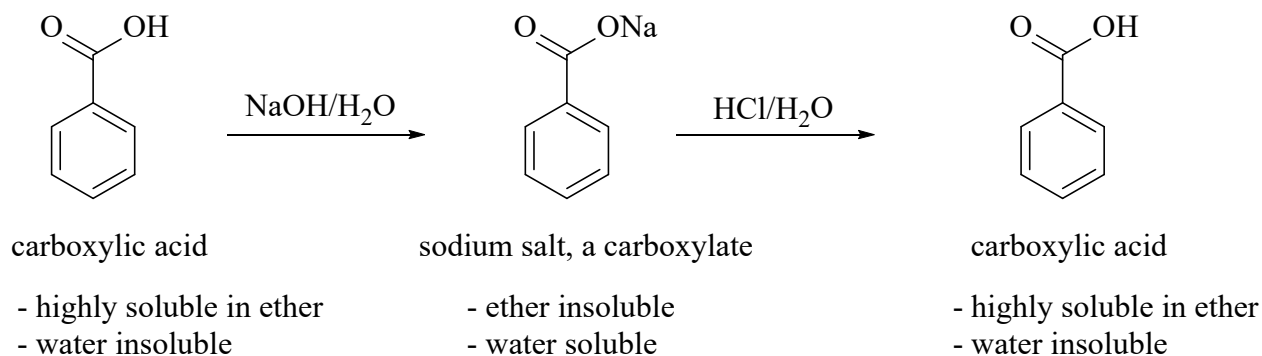


As an example of a separation that could be accomplished by using a solvent-solvent extraction, consider a mixture of two solid compounds: naphthalene and glucose (shown above).

If a mixture of naphthalene and glucose was dissolved in *tert*-butyl methyl ether and mixed well with water, the glucose would mostly dissolve in the lower water phase (phase = layer) and the naphthalene would mostly dissolve in the upper ether phase. The two phases can then be physically separated using a pipet and placed into two separate tubes. The water and ether can then be evaporated to yield the separated solid compounds. In a nut shell, this is an extraction.

¹ Revised 03/2020

An acid-base extraction operates on the same principle, but can provide a further level of fine-tuning. If one or more of the compounds in the mixture to be separated is acidic or basic, the solubilities of these acidic and basic components can be manipulated to our advantage by utilizing simple acid-base reactions. Using such manipulation, an acidic or basic compound that may be ether soluble and water insoluble can be changed to be ether insoluble and water soluble by carrying out an acid-base reaction. The solubilities of acidic and basic compounds can thus be changed at will. Once the layers are separated as mentioned before, the neutral acid or base can be regenerated by yet another acid-base reaction. An example of such a manipulation of solubilities is shown below for a carboxylic acid.

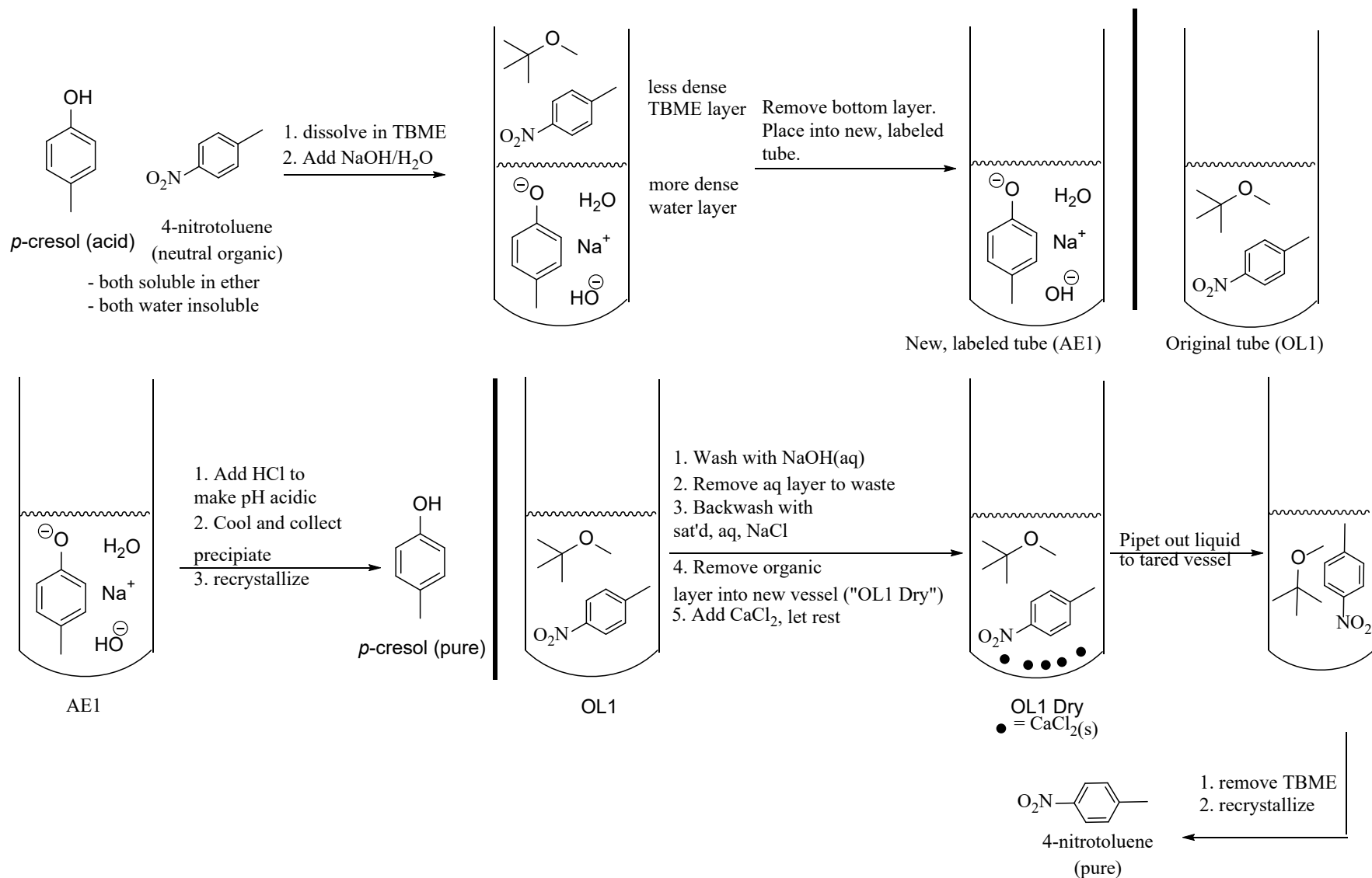


In this experiment, a mixture of a carboxylic acid and a neutral compound (an organic compound with no appreciably acidic protons) will be separated by an acid-base extraction (see scheme 1 below). The separated compounds will be purified by recrystallization and further identified by their melting points. A general scheme for the separation is given below. Note that instead of using sodium hydroxide as the base, sodium bicarbonate is used. A strong base such as sodium hydroxide is not necessary in this particular case.

The mixture is dissolved in ether and mixed thoroughly with aqueous sodium bicarbonate. The layers are allowed to separate and each is worked up separately. Dissolved water is removed from the ether solution using a drying procedure and the ether is evaporated to yield the solid neutral compound. This can then be recrystallized to yield pure solid neutral compound.

The basic aqueous solution is neutralized with concentrated HCl to yield the carboxylic acid, which, because of its water insolubility, precipitates out. This can be collected, recrystallized and allowed to dry to yield pure carboxylic acid.

Scheme 1. The acid-base extraction of *p*-cresol (an acidic phenol) and para-nitrotoluene (a neutral organic compound).



This is an EXAMPLE chart. You are using a carboxylic acid, not a phenol as depicted here, and NaHCO₃ as your base, NOT NaOH!

Neutralization of the carboxylic acid salt and excess sodium bicarbonate with concentrated hydrochloric acid: It is critical to add an amount of HCl necessary to completely neutralize the base, otherwise the yield of carboxylic acid will suffer. To be certain that neutralization is complete, a slight excess of HCl is added. The amount of HCl needed is calculated as follows: 1.15 mL of saturated aqueous sodium bicarbonate is used in the extraction. This determines the amount of HCl needed. A saturated aqueous solution of sodium bicarbonate is 1 M (1 mole/liter). Concentrated HCl is 12 M. Because HCl reacts with sodium bicarbonate in a 1:1 molar ratio, it follows that 1 mL of saturated aqueous sodium bicarbonate would be neutralized with 1/12 mL of concentrated HCl. If 1.15 mL of sat'd aq sodium bicarbonate has to be neutralized, how much HCl is needed? First, how many moles of sodium bicarbonate is present in 1.15 mL of a sat'd aq solution?

$$1 \text{ mol/L} \times 0.00115 \text{ L} = 0.00115 \text{ mol (1.15 mmol) sodium bicarbonate}$$

Therefore, 0.00115 mol of HCl is needed for neutralization. How many mL of HCl then is needed?

$0.00115 \text{ mol} / 12 \text{ mol/L} = 0.000096 \text{ L} = 0.096 \text{ mL}$ or, rounded off, about 0.1 mL. Thus 1.15 mL of sat'd aq sodium bicarbonate is neutralized by about 0.1 mL of conc HCl. With our pipets, there are about 30 drops in one mL of conc HCl. This translates into about 3 drops of HCl, a very small amount, indeed.

Drying the organic solvent: The organic solvent containing the neutral compound also contains some dissolved water. If the solvent were evaporated at this point, the resulting solid neutral compound would be wet with water and would consequently be a gooey mess that would take a long time to dry. A drying procedure is therefore necessary to remove small traces of water before the solvent is evaporated. This procedure consists of two steps: (1) thoroughly mixing the solution with sat'd NaCl(aq) (saturated salt solution, AKA brine) and discarding the aqueous layer (this is a preliminary drying step that removes most of the water and is known as **backwashing**), and (2) adding a solid inorganic drying agent. This strongly binds to the remaining traces of water dissolved in the organic solvent by allowing it to remain in contact with the solution for several minutes. The next step is then separating the solution from the solid drying agent. The solvent can then be removed by evaporation, leaving behind the solid neutral compound.

Very often in the synthesis of a compound, or in the isolation of a compound from a natural source, acid-base extractions are used to either directly isolate a desired acidic or basic compound, or to remove acidic or basic impurities. Extraction, recrystallization, and distillation are some of the most important separation and purification techniques in organic chemistry.

The Experiment

This experiment combines techniques learned in previous experiments (recrystallization, MP) with a new technique: extraction. The separation is based on the acid/base properties of the substances in the mixture. To understand the principles behind the separation, it is essential that you understand the acid/base chemistry involved and why each chemical species is soluble or insoluble in each layer.

Part of pre-lab outline:

This experiment is confusing due to constantly going back and forth from tube to tube. To help you understand what is going on, **draw a stepwise flow-chart** (see scheme 1) using structures, clearly showing each step in the process, as well as showing the chemical species present in each layer at each step. **Your flow-chart must use benzoic acid and naphthalene** as the organic species and **any reagents used in the actual experiment**.

This flow chart should provide a clear outline of all the steps in the process and should therefore enable you to follow the experiment more easily.

Do not ignore this requirement. Your TA will ask you to leave without having completed this flow-chart.

Mixing the layers: In extractions, it is important to **mix the two solvents well**. On the micro scale, this can be accomplished by drawing a portion of the lower layer up into a pipet and expelling it forcefully, but carefully, back into the tube, through the upper layer, and doing this repeatedly for about three minutes. The mixture is then allowed to separate into two layers. Normally, in separating the layers in a microscale extraction, the lower layer is carefully removed from the upper layer with a pipet, and transferred to another tube. The upper layer is typically not removed from the lower layer because it is very difficult to get a clean and complete separation in this way. (One exception to this rule is in drawing off the upper layer of backwash in the procedure below.)

Photos of the extraction technique are shown on the course website.

In an extraction such as this one, it is important to keep track of the different solutions at each step. There will be two main solutions throughout this extraction procedure: an aqueous layer and an ether layer. Label all tubes carefully and know exactly what chemical species is in each tube. Know which layer is which. Think carefully about each step and don't rush. This will help you to better understand what you are doing and why, and will help to decrease the possibility of error. What physical property of the solvents determines which will be the top or bottom layer? A careful chemist does not throw anything away until they are certain of its identity, so save each layer in a separate tube until the final products have clearly been obtained.

In this experiment, an acid-base extraction will be used to separate a mixture containing about equal parts of an unknown carboxylic acid and an unknown neutral compound. The unknown compounds will be identified by MP. The possible compounds are shown at the end of this handout.

Experimental Procedure: Your TA will assign an unknown mixture to you.

Step 1: Dissolution of Solids and Extraction

- Dissolve about 0.250 g (± 0.01 g, but weigh it exactly) of the mixture in 4 mL of *tert*-butyl methyl ether (TBME) in a test-tube labeled OL1 (organic layer 1). If something does not dissolve, add a small amount of ethyl acetate to facilitate dissolution of the solids.
- Add 2 mL of saturated aqueous sodium bicarbonate (NaHCO_3) and mix layers thoroughly. Incomplete mixing of layers means not all of your acid will be deprotonated and will still be in the organic solvent. **MIX THOROUGHLY!!!**
- Allow layers to separate and remove, via pipet, the lower layer into a clean, labeled test-tube called AE1 (aq extracts 1) and set aside for use later.

Step 2: The TBME, OL1

- Add to OL1 another small (~ 0.25 mL) portion of sat'd $\text{NaHCO}_{3(\text{aq})}$. This is called “**extracting**.”). Remove lower aqueous layer and add to AE1.
- Add to OL1 about 1 mL of sat'd $\text{NaCl}_{(\text{aq})}$ (This is called washing) and place the aqueous layer (lower) into a test-tube called "for waste". This removes most of the water dissolved in the ether.
- With a clean, dry pipet, carefully transfer OL1 to a clean dry vial, leaving behind any water clinging to the side of the tube.
- Add a few drops of fresh ether to tube OL1 and add to the new vial (a transfer rinse).
- Add anhydrous CaCl_2 in small amounts, **GENTLY** swirl the contents (do not stir with spatula or any other item), until the pellets no longer clump together. Label as "OL1 Dry." Set aside as the CaCl_2 requires ample time to fully dehydrate the solution.

Step 3: Back to AE1

- Add to AE1 about 0.5 mL TBME. This is known as backwashing and is used to remove a negligible amount of neutral compound that may contaminate the aqueous layer. With a backwash, you will need to **remove the small amount of upper ether layer**. This ether backwash contains minute, negligible amounts of neutral compound, therefore, place it into "for waste."
- Slowly and carefully, neutralize AE1 with *just enough* concentrated HCl, one drop at a time with stirring, to make the pH acidic (2-3). Use the indicator paper available to monitor pH. Too fast an addition will result in product bubbling out the top due to liberated $\text{CO}_2(\text{g})$. An excess of HCl is necessary as maximum yield is obtained at low pH. If no solid is present, it is likely that you have not added enough HCl or have not mixed the solution well.
- After maximum precipitation occurs, recrystallize solid directly in the tube:
 - Place AE1 into warm aluminum block with a boiling stick added. Allow to dissolve, remove stick.
 - Cool to rt
 - Cool further in an ice-bath.
- Isolate solid via suction filtration.
- Dry the solid to a constant weight (overnight), and determine its MP.

Continue on . . .

Step 4: Back to OL1 Dry

- Use a pipet to separate the ether from the drying agent and transfer the ether to a clean, dry, *pre-weighed Erlenmeyer flask*. Do a transfer rinse with fresh TBME.
- Evaporate the ether by passing a stream of air GENTLY over the solution in the hood while warming the tube with your hand. Caution: if the stream of air is too fast, or if you get the air tube too close to the solution, you may force it out of the tube and lose product.
- Weigh crude product by difference.
- Recrystallize crude product from hexanes (a mixture mainly made up of isomeric hexanes). (What is the correct amount of solvent to use in a recrystallization and what will result if too much is added?). **DO YOU REMEMBER HOW TO DO A PROPER RECRYSTALLIZATION?**
- Isolate solid via suction filtration. Allow it to dry to constant weight (hexanes evaporates quickly). Weigh the dry neutral compound and determine its MP.

Step 5: Final Work

- Report the % recovery of each compound (assume a 1:1 original mixture of unknowns).
- Identify each using MPs (possible compounds and MPs at the end of this document).
- Store the products on filter paper and save for inspection by your TA.

Things to watch out for:

- Mix layers well – if not, complete separation (or deprotonation in first step) will not occur and products will be contaminated.
- Acidification of the aqueous layer – not enough acid, low or no yield – not mixed well after adding acid – low or no yield.
- Recrystallization – too much solvent, low or no yield – add solvent at the BP in small portions until solid dissolves – allow time between additions.
- It is easy to mix tubes up – be sure to label them well as described in the procedure.

Note: Most samples need time to dry. You must make use of limited-use lab hours to obtain melting points and complete weighings. Check the course website for the current times the lab is open for this.

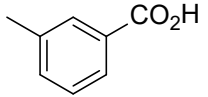
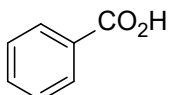
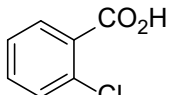
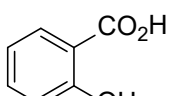
WASTE DISPOSAL: Combine all liquid wastes, including washes and filtrates, and put them into the Organic Liquid Waste container in the waste hood. Put the calcium chloride drying agent into the labeled evaporating dish in the waste hood. When finished with the products, place them into the Solid Waste container in the hood.

BEFORE YOU LEAVE THE LAB: turn off the hot plate, Mel-Temp, vacuum, and air. Clean and put away your equipment. Clean up your work areas, close the fume hood sash completely, and ask your TA for their signature. If you see caps off bottles, take care of it. If you see spilled chemicals, clean them up.

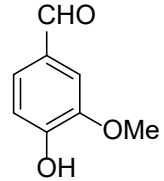
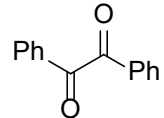
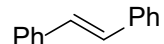
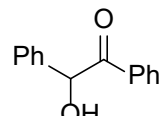
Postlab Questions

- 1.) In this experiment, if the carboxylic acid is benzoic acid, how many moles of benzoic acid are present (assume an equal portion of each component)? How many moles of sodium bicarbonate are contained in 1 mL of a saturated aqueous sodium bicarbonate? Is the amount of sodium bicarbonate sufficient to react with all of the benzoic acid?
- 2.) To isolate the benzoic acid from the bicarbonate solution, the bicarbonate solution is acidified with concentrated HCl. What volume of acid is required to neutralize the bicarbonate?
- 3.) The ether solution is extracted with saturated aqueous sodium chloride. What is the purpose of this?
- 4.) A mixture of benzoic acid and a neutral nonpolar compound is dissolved in ether and mixed thoroughly with aqueous sodium bicarbonate. What is the organic chemical species that is present in the ether layer? In the aqueous layer?
- 5.) Construct a flow chart that follows the separation of a mixture of 2-nitrophenol (an organic acid not used in this experiment with a $pK_a = 7.26$) and anthracene (neutral organic). Use scheme 1 as a template. Your reagents available are the same ones used in this lab.

Possible Carboxylic Acids:

Compound	Structure	melting point (°C)
3-toluic acid		112
benzoic acid		122
2-chlorobenzoic acid		142
salicylic acid		159

Possible Neutral Compounds:

Compound	Structure	melting point (°C)
vanillin		81
benzil		96
<i>trans</i> -stilbene		125
benzoin		135