



CHM 2210L

SEPARATION OF AN ACID-NEUTRAL MIXTURE

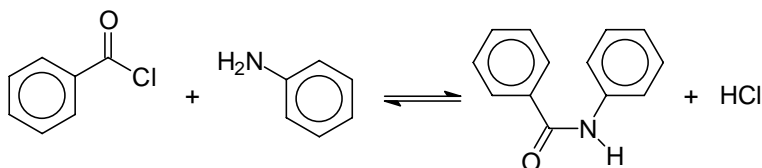


THE PROBLEM TO BE INVESTIGATED:

The acidic and neutral components of a mixture will be separated and purified by classical methods involving **extraction** and **recrystallization** procedures. The components will be identified by melting point determinations.

BACKGROUND INFORMATION:

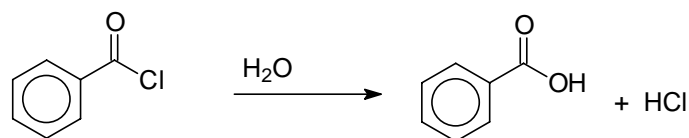
From your experiences in the **CHM 2210** laboratory, you may have noted that it is generally quite easy to carry out the conversion of one organic compound to another. The problems arise when one attempts the isolation and purification of the desired material. Techniques used include chromatography, fractional distillation, fractional crystallization, and extraction procedures. This last procedure is extremely general when attempting to isolate components with differing pK_a values. The overall procedure is so commonly used that it is frequently described in chemical journals as "*...working up a reaction in the usual manner*" rather than presenting a detailed description of the process. For example, let us consider the reaction of benzoyl chloride with aniline to form **N-phenylbenzamide**.¹



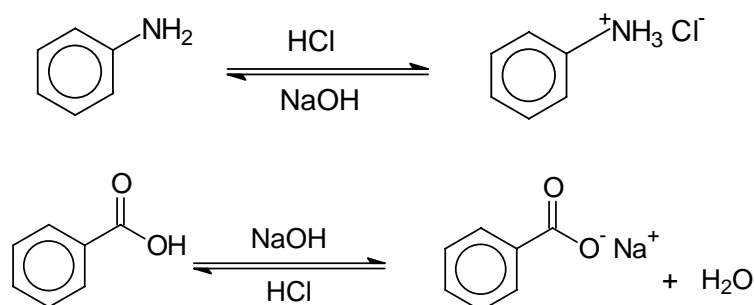
After allowing the reaction to stand for a period of time in some solvent (perhaps with an acid or base catalyst), the reaction is quenched by addition of ice/water. Ideally, the product should crystallize from the mixture. We can then isolate our product by suction filtration, recrystallize to constant melting point, and we are through. Unfortunately, *life is not always this kind to us*. Either nothing crystallizes, or products "oil" from the solution. We could throw the reaction mixture away and start over, hoping that this time we will be blessed with good results, or we could "work it up in the usual manner."

We begin by realizing that everything in the reaction mixture should dissolve in either an organic solvent (diethyl ether, methyl *t*-butyl ether, chloroform, toluene, *etc.*) or in water. Note that water is not miscible with the organic solvents cited. In a separatory funnel, two layers would form and we could discard the aqueous layer which carries with it any inorganic materials or traces of organic acids or bases. Considering the reaction above, we would now have the organic materials - unreacted aniline, the amide, and benzoic acid resulting from hydrolysis of benzoyl chloride - dissolved in the organic layer.

¹ In CHM 2210L, a similar experiment using acetic anhydride and aniline was performed.



To separate the basic amine and the acidic carboxylic acid from the neutral amide, we take advantage of acid-base reactions and the water solubility of the resulting salts at room temperature. Addition of aqueous acid (10% HCl) to the organic layer will convert the residual aniline to water-soluble anilinium chloride. Discarding this acidic aqueous layer discards the unwanted aniline. Addition of aqueous base (10% NaOH) converts the benzoic acid to water-soluble sodium benzoate.



Again, separation of the layers leaves only the desired amide dissolved in the ether in the separatory funnel. A wash with a saturated sodium chloride solution removes most of the residual water-soluble acid or base. Drying the ether layer over anhydrous magnesium sulfate or sodium sulfate completes the preliminaries. The drying agent is removed by decanting or filtering. The organic solvent is removed by evaporation (or distillation). At this time, recrystallization usually provides a pure sample.

The process just described could be easily modified to allow isolation of the acidic material and/or/instead of the neutral. If the acidic aqueous layer were now made basic (add NaOH), aniline would be regenerated from anilinium hydrochloride. The aniline would be insoluble in the aqueous media and could be separated from it; for example, by extraction with ether. If the basic aqueous layer containing sodium benzoate were now acidified (HCl), benzoic acid (insoluble in water) would precipitate and could be collected by suction filtration. Therefore, this "working-up in the usual manner" is a general technique for separating materials with different pK_a 's. As a rule, carboxylic acids will generally react with even the weak base, sodium bicarbonate (NaHCO_3). Phenols, as well as carboxylic acids, dissolve in the stronger base, sodium hydroxide. Amines are the only compounds basic enough to dissolve in hydrochloric acid. ***All other organic compounds are essentially neutral.*** See figure below for a graphical representation of a flow diagram for separation of a mixture of a neutral compound, a phenol, an amine, and a carboxylic acid.

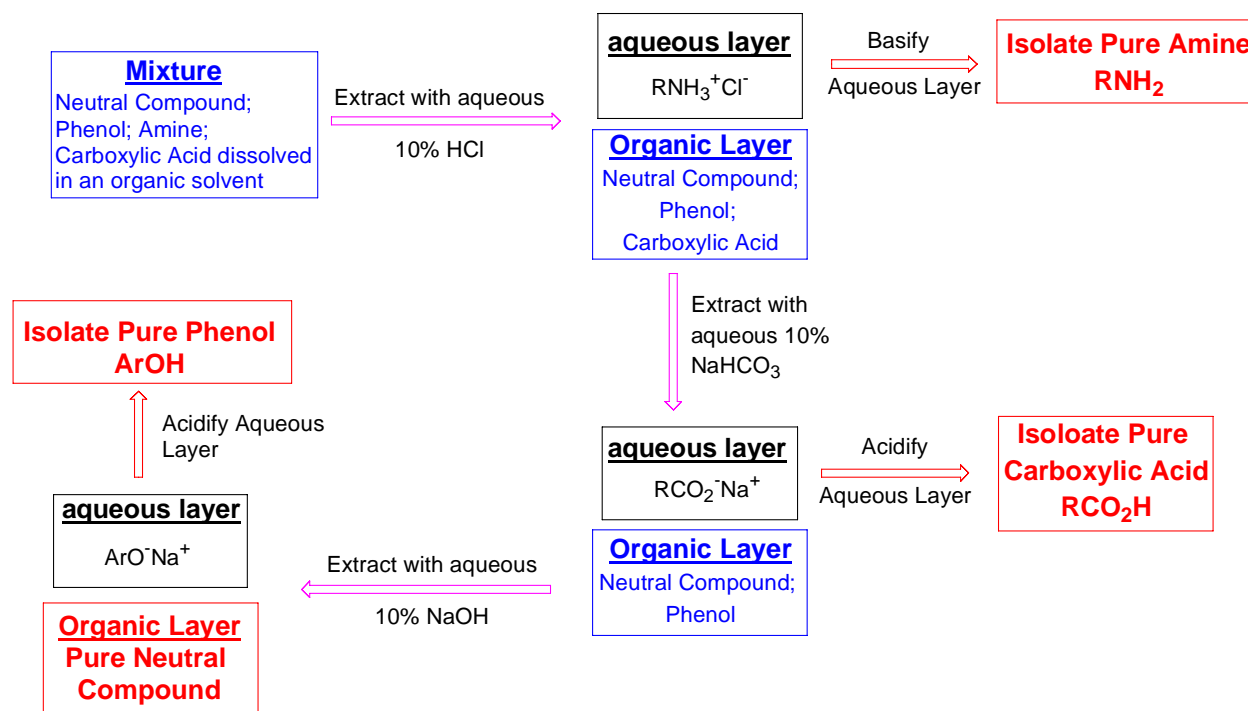


Figure 1. Graphical Representation of an extraction scheme based on acid-base chemistry

THE NATURE OF THIS INVESTIGATION:

In this experiment, you will obtain 4.0 g of a mixture containing **2.0 g of acidic** material and **2.0 g of neutral** material. Each 2.0 g portion will contain 1.8 g of a major component which is to be purified and identified, and 0.2 g of impurity which is to be removed and rejected. The mixtures will be composed as follows:

Acidic Mixtures

Major Component	MP °C	Impurity	MP °C
Cinnamic Acid	134	Glutaric Acid	95-98
o-Chlorobenzoic Acid	140	Glutaric Acid	95-98
m-Nitrobenzoic acid	140	Glutaric Acid	95-98
2-Chloro-5-nitrobenzoic acid	165	Glutaric Acid	95-98
p-t-butylbenzoic acid	162-165	Glutaric Acid	95-98

Neutral Mixtures

Major Component	MP °C	Impurity	MP °C
Methyl m-nitrobenzoate	78	Napthalene	80
p-Dibromobenzene	89	p-Dichlorobenzene	53
m-Dinitrobenzene	90	2,4-Dinitrotoluene	70
Acenaphthene	94	Napthalene	80
Acetanilide	114	Benzamide	128

In each case the impurity selected is very similar in chemical type to the major component while having a lower melting point. Accordingly, this impurity will have a greater solubility in any solvent than will the major component. Crystallization will necessarily change the composition in the desired direction.

You will first separate the acidic mixture from the neutral mixture by extraction from ether solution with a base, followed by isolation of these mixtures. From your two mixtures, you will then crystallize to constant melting points (see **Helpful Hints**) your purified compounds. Of those compounds listed in the tables, decide which compounds are eligible, and use mixture melting points with those compounds for final identification. (Be sure you realize that your mixture may contain any one of the four acidic major components along with any of the four neutral ones.)

PROCEDURE

Part I. Separation by Neutralization and Extraction

Obtain a 4.0 g sample of your acid-neutral mixture, note the number and then dissolve it in a small Erlenmeyer flask with a total of 20 mL of ether (methyl *t*-butyl ether will be provided), pouring the solution directly into your separatory funnel. Use an additional 5 mL of ether to rinse the bottle and funnel, pouring the rinse solution into the separatory funnel.

Caution: Low boiling ethers are the most easily ignited of the common solvents. No flames or hot plates should be in the immediate vicinity. Also, all aqueous HCl and NaOH solutions should be treated as dangerous.

A. The Acidic Fraction:

Add to the ethereal solution 20 mL of 10% sodium hydroxide solution, and shake the funnel gently for 2 minutes, remembering to release the pressure in the funnel frequently. (**Caution: The high vapor pressure of ethers will increase the pressure inside the stoppered separatory funnel when shaken!!**) If the aqueous solution is colorless or nearly so, use pH paper to find if the aqueous layer is still sufficiently basic. Draw off the aqueous layer and save it in a 50 mL Erlenmeyer flask. If the solution is not basic, add an additional 10 mL of the 10% sodium hydroxide solution to the separatory funnel, shake as before, and save both portions of aqueous solution in a 50 mL Erlenmeyer flask.

To the ethereal solution in the funnel, add 5 mL of water and shake briefly. Separate and add this aqueous washing liquid to the previously collected aqueous material. Then transfer the organic layer to a dry 50 mL Erlenmeyer flask.

Without rinsing the separatory funnel, add to it the combined aqueous material, as well as the rinse from the flask (*ca.* 1-2 mL of water) along with an additional 10 mL of ether. Shake the mixture, and then slowly run **only** the aqueous layer into a 150 mL beaker containing 6 mL of concentrated hydrochloric acid (or more if it was necessary to add a second portion of base) and 3 mL of water, stirring during the addition - use pH paper to ensure the solution is acidic. Shake the ether layer (some traces of water may remain) in the separatory funnel with 3 mL of brine solution. After discarding the aqueous wash, combine the ether layer with the bulk of the ethereal solution, add 3 g of anhydrous MgSO_4 or Na_2SO_4 , and let the solution stand with occasional swirling for 15-30 minutes.

Meanwhile cool the suspension of precipitated acid to 15-20 °C, collect and wash well in the usual fashion (suction: Büchner funnel and COLD water). Set the material aside for through air drying on a watch glass or piece of filter paper. Finally, weigh the dry acid mixture and determine its melting point, preparatory to recrystallization.

B. The Neutral Fraction:

Decant the dried ethereal solution (or filter it, if necessary) into a 125 mL Erlenmeyer flask, using 1-2 mL of ether for rinsing. Add a boiling chip and remove the ether by evaporation. Stop when 5-8 mL remains. Carefully pour the solution into a tared 25 mL Erlenmeyer flask, using 2-3 mL of ether for rinsing.

Evaporate the remaining ether using a hot water bath (metal pan with small layer of water), observing caution in not charring the solid. The resulting neutral mixture should crystallize on cooling (some scratching may be necessary). The last traces of ether may be removed by using the aspirator to suck air through the flask or by applying full suction through the use of a glass tube and one-hole stopper (caution!) finally letting the material dry completely by standing on a piece of paper or on a glass, the latter particularly if the mixture is sticky. Obtain the weight of this neutral mixture and determine the melting point.

Part II. Selective Crystallization of a Compound from a Mixture

Transfer the desired mixture to a 25 mL, 50 mL, or 125 mL Erlenmeyer flask, selecting among these sizes according to the amount of solvent you think may be needed. (Don't plan to have the liquid level above the lower half of the conical part of the flask.) **Erlenmeyer flasks are always to be used for crystallization unless a good and specific reason exists for using a different container in a given instance.** (Beakers are unsatisfactory for crystallization or for any operation involving the boiling of organic liquids or solutions; they are awkward to hold when hot and hard to swirl; loss by evaporation and the resulting fire hazard are needlessly great; crust forms on the surface and wall; the material on the walls tending to "creep"; it is impossible to tell when a solution is truly saturated.

- A.** Use of a Single Solvent. Add enough solvent to the flask to just cover the solids, and heat the mixture to boiling, using an appropriate means of heating. If any lumps are left, crush them with the end of a stirring rod that has been flattened (by heating and pressing onto an asbestos board). Add more solvent in small portions until an approximately saturated solution is obtained. Don't hesitate to shift (with rinsing) to a larger flask should this prove advisable. Let the solution stand undisturbed except for scratching or possible seeding with a trace of the original mixture.

These directions assume that the solute melts at a temperature at least 15-20° above the boiling point of the solvent selected. If this is not the case, saturate the solution at an appropriate lower temperature.

If care has been taken in the earlier steps of the isolation, there should be present no insoluble matter. If undissolved particles remain, ask your instructor for advice. This experiment intentionally aims to avoid filtration of a hot solution and the use of decolorizing charcoal.

When the mixture has cooled nearly to room temperature, cool it in ice, and collect, wash, and dry

the product. Determine the melting point of the material, weigh it, and then repeat the crystallization using proportionate amounts of the same solvent (unless you now think a different solvent would be preferable).

- B.** Use of a solvent pair. If the use of a single solvent seems impractical, place the mixture in a 50 mL Erlenmeyer flask, add about 5 mL of the overly effective solvent, and heat the mixture to boiling. Now add the other member of the pair in small portions (use a disposable pipet) to the boiling solution until a little solid (or oil) separates and will not redissolve on boiling. Clear the solution by adding a few drops of the more potent solvent. Let the flask cool in the usual fashion, finally collecting the product, as in the case above.

There are two hazards to avoid; the *first* is that already mentioned, the *unfavorable melting point/boiling point relationship* and the *second* is peculiar to the *use of solvent pairs*. If a compound is very soluble in one solvent and somewhat soluble in the other, and if too much of the first solvent is used there is no amount of the second solvent which can give a saturated solution. A point is first reached at which enough of the second solvent itself has been used to dissolve the compound without assistance from the more potent solvent. This situation is recognizable by the failure of solid to precipitate on the addition of a relatively large amount of the second solvent.

For this experiment, methanol or ethanol (neat or with added water) should serve as a good recrystallizing solvent. The "solvent pair" is a mixture (of varying proportions) of alcohol-water.

OVERVIEW

1. Dissolve solid in the minimum amount of alcohol using heat to help minimize the amount
2. Remove flask from heat and allow to cool to room temperature.
3. Chill solution in an ice-water bath and allow crystallization to occur. If crystallization occurs, skip to step 7.
4. If no crystallization occurs, add water carefully until cloudiness persists. Use squirts, followed by dropwise addition later.
5. Reheat until solution becomes clear.
6. Remove from heat, add seed crystals upon cooling in ice-water bath (if desired), and allow solution to cool slowly.
7. Collect crystals.

Steps 1-3 describe a single solvent recrystallization, see Part A for details. Adding Steps 4-6 to the procedure transforms the method to that of a solvent pair, i.e. methanol-water, as described in detail in Part B.

Part III. Mixture Melting Points.

Your second crystallization of each mixture should have given a product melting within a degree of the value obtained after the first crystallization. (If such is not the case, consult your instructor as to the advisability of doing a third crystallization). Consulting the melting point data for the four possible compounds in each case, decide which ones should be tested by a mixture melting point determination.

Take very small and roughly equal amounts of your compound and an appropriate known substance, crush and mix the combined sample very thoroughly, and then determine the melting point in the usual fashion. Repeat with each of the substances that were possible choices. You should obtain broad and depressed melting points in all but one case.

THE LABORATORY REPORT:

In this experiment there are three main considerations. In order of decreasing importance, these are: *(i)* the correct identification of the substances, *(ii)* the purity of the isolated materials, and *(iii)* the amounts of material recovered. Bottle your final samples, label them using the recommended identification system. Include all of usual data except the percentage yield; substitute the word "Recovery" for "Yield".

Helpful Hints - Acid-Neutral Mixture

- * The melting (or, boiling) point is always recorded as a range (initial and final).
- * The choice of a single solvent should meet the following criteria: (i) dissolves solid when warm or at its boiling point, but precipitates solid when cooled and (ii) bp generally lower than mp of solid.
- * In the case of a solvent pair, the "overly effective" or "potent (strong)" solvent represents the chosen solvent in which the solid to be crystallized is *readily* soluble at (or near) room temperature. The co-solvent is chosen because it is miscible with the "potent" solvent. Crystallization or recrystallization with a solvent pair necessitates dissolving the solid in a minimum amount of the potent solvent followed by the addition of the "weaker solvent" to the point of cloudiness which indicates precipitation. Heating to clarify the solution once again (more of the strong solvent may be necessary), allowing the solution to cool slowly, and seeding the solution will normally result in crystalline formation.
- * Common solvent pairs used in our laboratories are: (i) alcohol (either methanol or ethanol) - water, (ii) acetone - water, (iii) acetic acid - water, (iv) ether - methanol, and (v) ether - hexanes.
- * Some of the common solvents, with properties of dielectric constant (ϵ), bp, and solubility in water, are listed in the table below. With the exception of water, all are flammable and should be treated with caution.



Summary Guideline for Acid-Neutral Report



The following should be recorded in your laboratory notebook:

Unknown Number: _____

Acid Component

Name: _____ Structure

Gross weight: _____

Tare weight: _____

Net weight: _____

% recovery = $100 \times \frac{\text{_____}}{1.8 \text{ g}} =$

mp: expected: _____

found: _____

Mixture: _____

Neutral Component

Name: _____ Structure

Gross weight: _____

Tare weight: _____

Net weight:: _____

% recovery = $100 \times \frac{\text{_____}}{1.8 \text{ g}} =$

mp: expected: _____

found: _____

Mixture: _____



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QUESTIONS



1. Provide and label all possible structures of the major and minor components of the acidic and neutral mixtures.
2. Although acetic acid - water may be used as a "solvent pair", why are dilute solutions of an inorganic acid/water (or, inorganic base/water) avoided in recrystallization attempts? [**Hint:** see McMurry: sections **21.7**, **21.8**. Consider functional-group possibilities.]
3. Supposing one of your unknown neutrals is 2,4-dinitroiodobenzene and you are using a 1:1 mixture of ethanol and water to recrystallize your compound, the solid material obtained after your experiment has an unacceptable melting point range (more than 10 degrees). Explain, using equations, what may have happened. [**Hint:**see McMurry: section **16.9**]
4. Using a flow diagram, show the separation of a mixture containing *p*-bromoacetanilide, *N*-cyclopentyl-*N*-methyl-*N*-propylamine and *m*-nitrophenol. Specify the organic solvent and aqueous solutions to be used for the separation. Provide the exact acid-base reaction that occurs during each step of the separation.