3. Extraction

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Vocabulary:

Miscible	Two or more compounds, which dissolve in one another to form a homogenous solution.
Aqueous	contains water.
Organic	non-aqueous (does not contain water), usually hydrophobic.
Emulsion	No separation of the organic and aqueous layers (usually cloudy).
Partition coefficient	the same as the distribution coefficient. It is the relationship between the solubility ratios of two different layers for a compound, which is soluble in both solvents.
Workup	is a generic term used for any step or series of steps performed at the end of a reaction to isolate and/or purify the product. It may include filtration, extraction, and/or chromatography.

Background

What is extraction? There are several listings for extraction in the American Heritage Dictionary (p. 466) but in its simplest form, extraction is the separation of something from another. There are numerous examples in our everyday lives. Vanilla extract is used in cooking. The essence of perfume is extracted from flowers and plants, for example. For the organic chemist, extraction is part of the normal work up of a reaction. Sometimes, it is referred to an aqueous workup in the text or manuscript. We wash the organic reaction mixture with water (acidic, neutral and/or basic) to remove any byproducts or inorganic material.

There are three basic types of extraction: liquid/liquid, acid/base and solid/liquid. We will be performing the first two types of extraction in this experiment. First, we have to understand how to choose a solvent for extraction. A couple of things we have to consider are polarity and density of the solvent. The polarity of the solvent is important because "like dissolves like." So if the extraction is from an aqueous solution, we do not want a solvent that is miscible with water. Thus during the extraction two layers are formed, aqueous and organic. It is important to know the density of the solvent so that we can predict which one is the organic layer. Most chlorinated solvents have densities greater than water (>1 g/mL). Aromatic (toluene, benzene - any compound which contains a benzene ring), aliphatic compounds (hexanes), and ethers have densities less than one. They would float on the top of the water layer. When in doubt, add a drop of water and observe which layer it joins.

A. Partition Coefficient of an Organic Acid. Sometimes we run into compounds, which are soluble in organic as well as aqueous solvents. Such compounds dissolve in each layer when these solvents are placed in contact with each other. A measure of this equilibrium is the partition or distribution coefficient, *k,* which is defined for a compound (A), a pair of solvents (including water (W) and a solvent (S)), and a certain temperature. It can be calculated as follows (where C stands for concentration):

$$k = C_{\text{A in S}} \div C_{\text{A in W}}$$

This relation can be approximated with (where Sol is the solubility in g/100mL):

$$k = Sol_{\text{A in S}} \div Sol_{\text{A in W}}$$

For example, compound A has a solubility of 6 g/ 100 mL in diethyl ether and a solubility of 3 g/ 100 mL in water, therefore *k* is equal to

$$k = 6\text{ g/100 mL} \div 3\text{ g/100 mL} = 2$$

Let's assume that you have prepared a solution of 3 g of A in 100 mL of water and then extracted (washed) the water layer with 100 mL of diethyl ether. How much material remains in the water layer? Let x be the grams of A in the ether layer. Then:

$$k = 2 = x\text{ g /100 mL ether} \div (3 - x)\text{ g /100 mL water}$$
$$2(3 - x) = x$$
$$6 - 2x = x$$
$$6 = 3x$$
$$x = 2$$
$$3 - x = 3 - 2 = 1\text{ g (which is the mass of A left in the water layer)}$$

Now, let's assume that the extraction was carried out with two 50 mL portions of diethyl ether instead of a single 100 mL portion. The calculation is in two steps:

$k = 2 = x$ g /50 mL ether ÷ $(3 - x)$ g /100 mL water
$2(3 - x) = 2x$
$3 - x = x$
$3 = 2x$
$x = 1.5$ g
$3 - x = 3 - 1.5 = 1.5$ g (which is the mass of A left in the water layer)

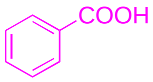
For the next aliquot of 50 mL:

$k = 2 = x$ g /50 mL ether ÷ $(1.5 - x)$ g /100 mL water
$2(1.5 - x) = 2x$
$1.5 - x = x$
$1.5 = 2x$
$x = 0.75$ g
$1.5 - x = 1.5 – 0.75 = 0.75$ g (which is the mass of A left in the water layer)

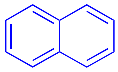
It is clear that multiple extractions are more efficient than single extractions. When working up a reaction, organic chemists usually extract/wash three times.

B – D. Acid/Base Extraction. Another typical extraction is acid/base. A Brønsted acid is a proton (H^+) donor; whereas a Brønsted base is a proton (H^+) acceptor. Let's consider the separation of a strong organic acid, an organic base, and a neutral organic compound. From general chemistry you know about strong and weak mineral acids, but in organic chemistry we consider carboxylic acids as strong organic acids. These carboxylic acids have pK_as in the range from 1.83-6.0. Remember there is a tenfold increase in acidity for every pK_a unit.

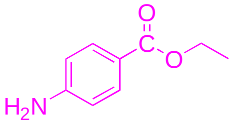
Physical properties and structures of reagents in this experiment.



benzoic acid
$C_7H_6O_2$
MW 122.12
mp 122-123 °C
pK_a = 4.19



naphthalene
$C_{10}H_8$
MW 128.17
mp 80-82 °C

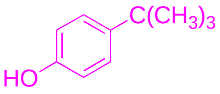


4-aminobenzoic acid ethyl ester
$C_9H_{11}NO_2$
MW 165.19
mp 88-90 °C
pK_b = 4.0 for conj. acid

NaOH
sodium hydroxide

HCl
hydrochloric acid

$(CH_3)_3C\text{-}O\text{-}CH_3$
tert-butyl methyl ether
bp 55-56 °C d 0.741



4-*tert*-butyl phenol
$C_{10}H_{14}O$
MW 150.22
mp 98-101 °C
pK_b = 10.16

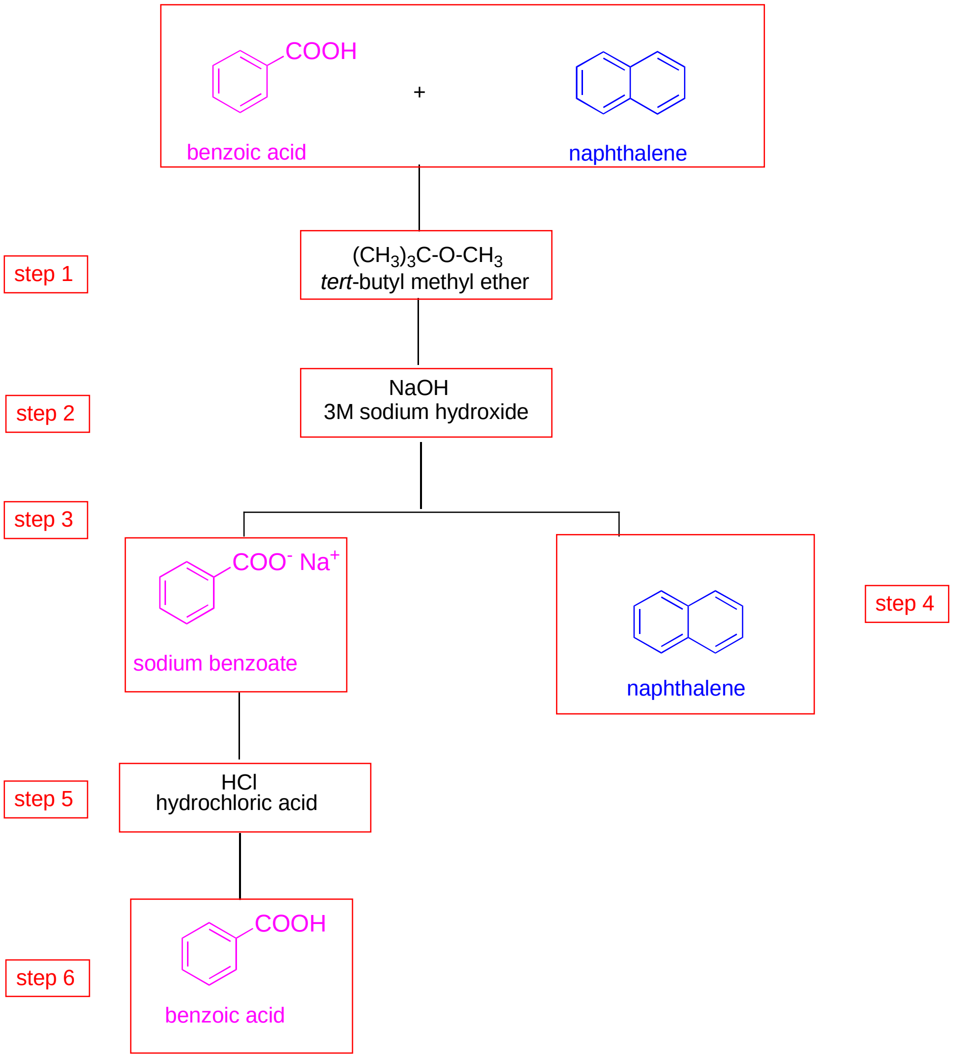
CH_2Cl_2
dichloromethane
(methylene chloride)
bp 40 °C
d 1.325

$CH_3CH_2\text{-}O\text{-}CH_2CH_3$
diethylether (ether)
bp 34.6 °C
d 0.708

$(CH_3)_3C\text{-}O\text{-}C(CH_3)_3$
di-*tert*-butylether
(butyl ether)
bp 142-143 °C d 0.764

B. Extraction of a strong organic acid from a neutral organic compound (Scheme 1)

The separation of benzoic acid from naphthalene is depicted in Scheme 1.



The 1st step is to dissolve the two compounds in an organic solvent like *tert*-butyl methyl ether. Dichloromethane (CH_2Cl_2) can also used but the densities of the two different organic solvents are different. The densities of chlorinated hydrocarbons are greater than that of water ($d > 1$ g/mL), whereas the densities of ethers are less than that of water ($d < 1$ g/mL).

In the 2nd step, a base, sodium hydroxide solution, is added to the solution. Since benzoic acid is a "strong" organic acid, a weak base, such as sodium bicarbonate, can also be used. To insure that the organic acid is completely transferred into the aqueous layer, this layer is tested using pH paper. A drop of the aqueous layer is dropped onto a piece of pH paper until the paper tests positive for base. Remember basic solutions turn pH paper blue. It is important to mix the solution after each addition of base.

There are two layers formed upon addition of the basic solution to the organic solution, because the organic solvent (*tert*-butyl methyl ether) is not miscible in the basic aqueous layer. In step 3, the different layers are separated from one another. Since *tert*-butyl methyl ether is less dense than the aqueous layer, this layer is removed and treated further in steps 5 and 6.

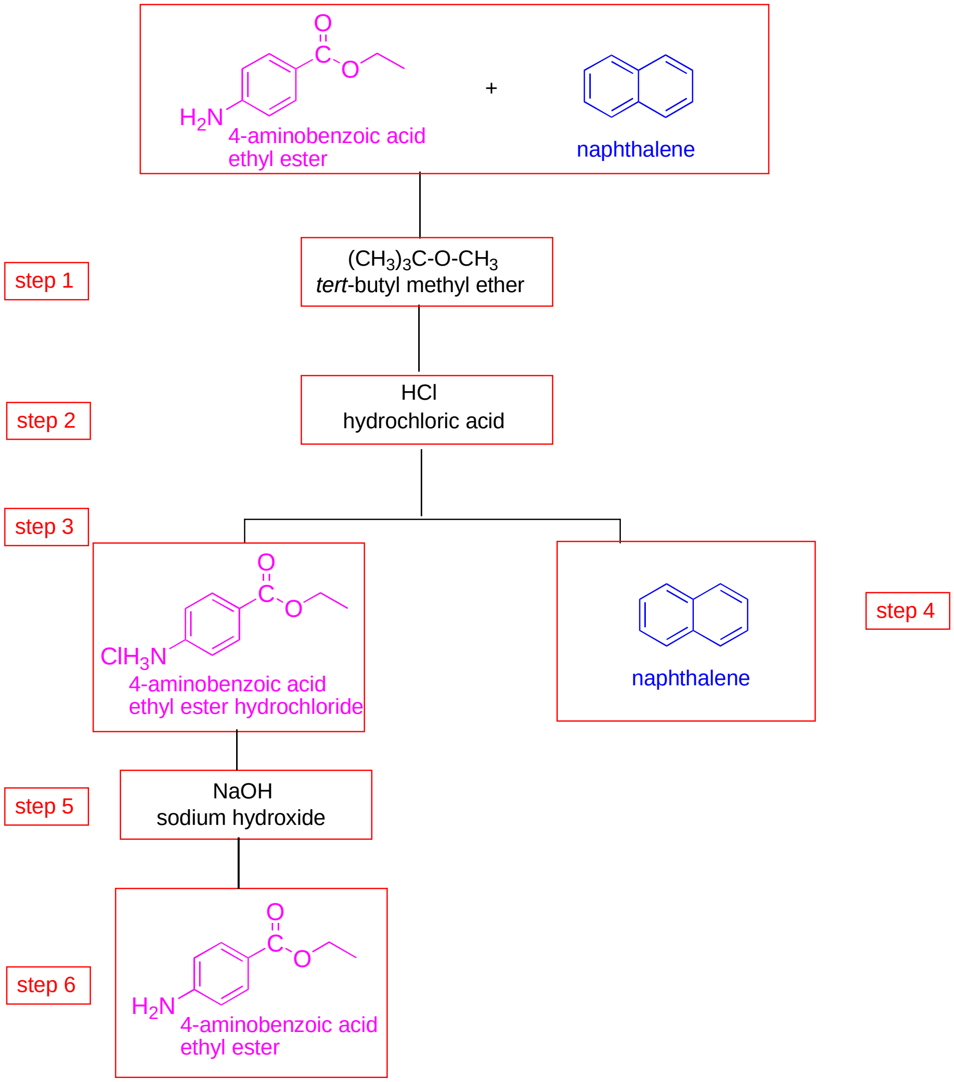
In step 4, the organic layer containing the compound (naphthalene) is dried using a drying agent like calcium chloride or sodium sulfate pellets. Any time an organic layer is washed or touches water, it must be dried using a drying agent. The solvent is then removed with a pipette to another tube and isolated after removal of *tert*-butyl methyl ether via evaporation with heat.

In step 5, the sodium benzoate is neutralized and acidified (protonated) to regenerate benzoic acid, which precipitates from the aqueous solution. The pH of the solution is tested with pH paper. In this case, acidic solutions turn the pH paper red.

In step 6, the benzoic acid can be isolated by vacuum filtration.

C. Extraction of an organic base from a neutral organic compound (Scheme 2)

The separation of 4-aminobenzoic acid ethyl ester from naphthalene is depicted in Scheme 2.



The 1st step is to dissolve the two compounds in *tert*-butyl methyl ether.

In the 2nd step, an acid, hydrochloric acid, is added to the solution. To insure that the organic base is completely transferred into the aqueous layer, this layer is tested using pH paper. A drop of the aqueous layer is dropped onto a piece of pH paper until the paper tests positive for acid. It is important to mix the solution after each addition of acid.

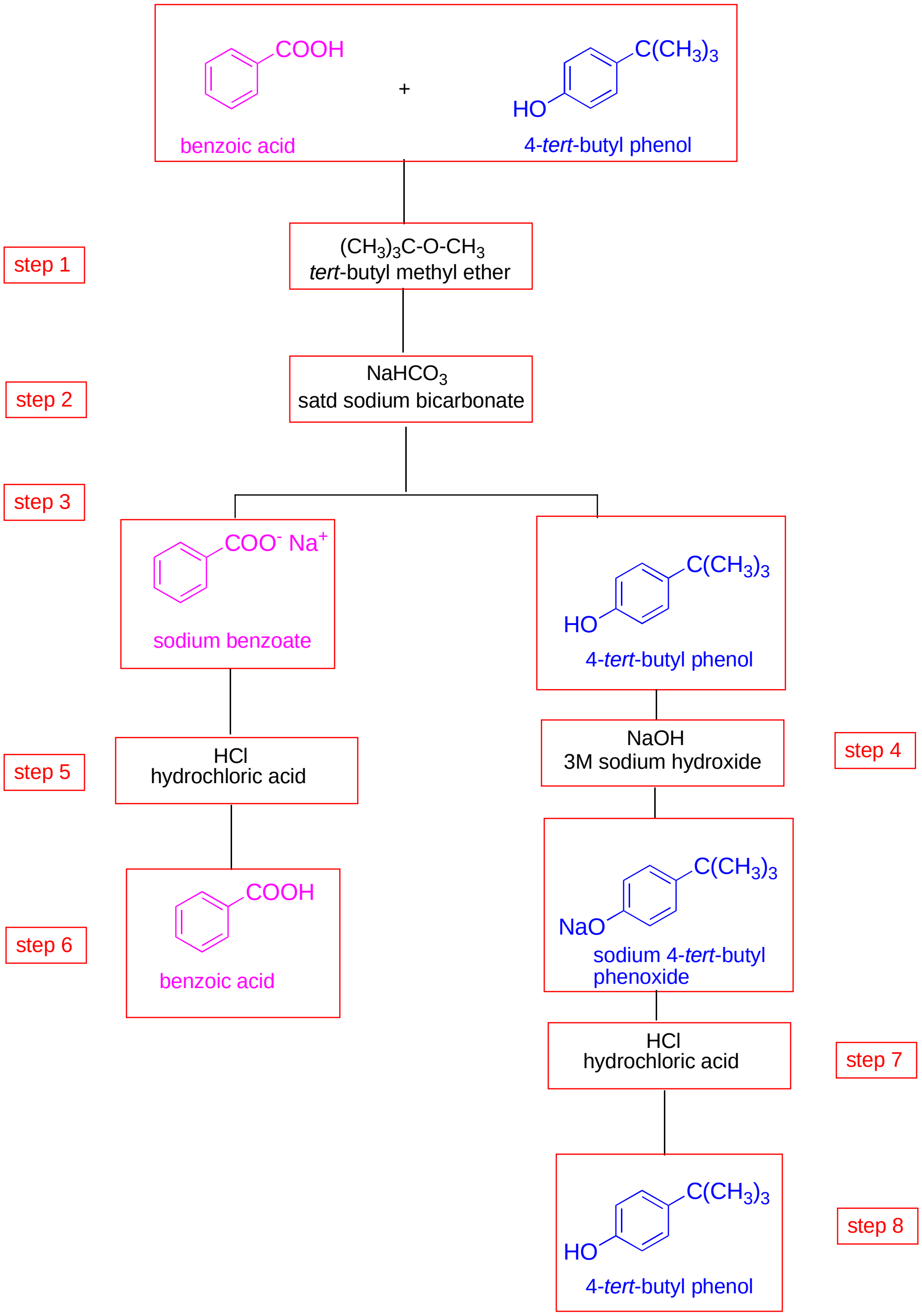
There are two layers formed upon addition of the acidic solution to the organic solution, because the organic solvent (*tert*-butyl methyl ether) is not miscible in the acidic aqueous layer. In step 3, the different layers are separated from one another. Since *tert*-butyl methyl ether is less dense than the aqueous layer, this layer is removed and treated further in steps 5 and 6.

In step 4, the organic layer containing the compound (naphthalene) is dried using calcium chloride or sodium sulfate pellets. The solvent is then removed with a pipette to another tube and isolated after removal of *tert*-butyl methyl ether via evaporation with heat.

In step 5, the 4-aminobenzoic acid ethyl ester hydrochloride is neutralized (deprotonated) to regenerate organic base, which precipitates from the aqueous solution. The pH of the solution is tested with pH paper.

In step 6, the 4-aminobenzoic acid ethyl ester can be isolated by vacuum filtration.

D. Extraction of a strong acid from a weak acid (Scheme 3)



The 1st step is to dissolve the two compounds in *tert*-butyl methyl ether.

In the 2nd step, a weak base, saturated sodium bicarbonate solution, is added to the solution. Since benzoic acid is a "strong" organic acid, this weak base only reacts with the strong acid not the weak acid. To insure that the organic acid is completely transferred into the aqueous layer, this layer is tested using pH paper. A drop of the aqueous layer is dropped onto a piece of pH paper until the paper tests positive for base. Remember basic solutions turn pH paper blue. It is important to mix the solution after each addition of base.

There are two layers formed upon addition of the basic solution to the organic solution, because the organic solvent (*tert*-butyl methyl ether) is not miscible in the basic aqueous layer. In step 3, the different layers are separated from one another. Since *tert*-butyl methyl ether is less dense than the aqueous layer, this layer is removed and treated further in steps 5 and 6.

In step 4, the organic layer containing the weak acid, the phenol, is treated with sodium hydroxide (ionizing the acid to a salt and driving it into the water layer) yielding sodium 4-*tert*-butyl phenoxide. This compound is further treated in steps 7 and 8.

In step 5, the sodium benzoate is neutralized and acidified (protonated) to regenerate benzoic acid, which precipitates from the aqueous solution. The pH of the solution is tested with pH paper. In this case, acidic solutions turn the pH paper red.

In step 6, the benzoic acid can be isolated by vacuum filtration.

The sodium 4-*tert*-butyl phenoxide is neutralized and acidified (protonated) to regenerate benzoic acid, which precipitates from the aqueous solution (steps 7 and 8). The pH of the solution is tested with pH paper. In this case, acidic solutions turn the pH paper red.

After completing this experiment, you should understand and/or perform the following.

1) extraction process.
2) write your own extraction scheme for separation of a strong acid, a weak acid, a base and a neutral compound.
3) acid/base and testing of it with pH paper.
4) role of the drying agent.
5) densities of solvents.

Hint for notebook:
You may want to put both the flowchart and procedure on the same page so that you keep focused on where you are and what you are doing.

This procedure has been adapted from the microscale procedure described in M*acroscale and Microscale Organic Chemistry Experiments* by Kenneth L. Williamson.

Experiment

A. Partition Coefficient of an Organic Acid.

Weigh approximately 0.25 g of benzoic acid and place into a small reaction tube. Dissolve the solid in exactly 4 mL of *tert*-butyl methyl ether. Add exactly 6 mL of water, cap the tube and shake for 2 minutes. Let the mixture stand until two layers have formed. Note in your lab notebook which layer is the organic layer and which layer is the aqueous layer. Gently unscrew the cap to vent any pressure buildup. Remove the aqueous layer with a pipette and discard. Add small amounts of sodium sulfate until the organic layer is dry. Remove the ether with a pipette and filter through your small powder funnel lined with a piece of 70 mm filter paper into **a pre-weighed vial**. Wash the sodium sulfate with about 2 mL of ether. Remove the ether with a pipette and filter through the powder funnel. Add a boiling stick and evaporate off the ether in the hood on a hot plate under low heat. When the vial has cooled to room temperature, weigh the beaker.

B. Extraction of an Acid from a Neutral.

Label two different reaction tubes. Weigh approximately 0.25 g of the acid/neutral mixture (benzoic acid/naphthalene) and transfer it into a small reaction tube. Dissolve the solid in exactly 4 mL of *tert*-butyl methyl ether. Wash the organic solution twice with two 1 mL portions of 3 M sodium hydroxide, followed by one 1 mL of water. Combine all of the aqueous layers during the process making sure that you know the organic and aqueous layers.

> **B1. Organic layer.** Dry the organic layer with sodium sulfate and filter off the drying agent into **a pre-weighed vial**. Wash the drying agent using about 2 mL of *tert*-butyl methyl ether. Then, add a boiling stick and concentrate the organic layer to dryness in the hood. When the vial has cooled to room temperature, weigh the vial.
>
> **B2. Aqueous layer.** To the combined aqueous layers, add 3 M hydrochloric acid dropwise with stirring between additions until the pH is acidic. This will be determined using pH paper. Filter the resulting solid and wash with water. Weigh the solid.

C. Extraction of a Base from a Neutral.

Label two different reaction tubes. Weigh approximately 0.25 g of the base/neutral mixture (4-aminobenzoic acid ethyl ester/naphthalene) and transfer it into a small reaction tube. Dissolve the solid in exactly 4 mL of *tert*-butyl methyl ether. Wash the organic solution twice with two 2 mL portions of 3 M hydrochloric acid, followed by one 1 mL of water. Combine all of the aqueous layers during the process making sure that you know the organic and aqueous layers.

C1. Organic layer. Dry the organic layer with sodium sulfate and filter off the drying agent into **a pre-weighed vial**. Wash the drying agent using about 2 mL of *tert*-butyl methyl ether. Then, add a boiling stick and concentrate the organic later to dryness in the hood. When the vial has cooled to room temperature, weigh the vial.

C2. Aqueous layer. To the combined aqueous layers, add 3 M sodium hydroxide dropwise with stirring between additions until the pH is basic. This will be determined using pH paper. Filter the resulting solid and wash with water. Weigh the solid.

D. Extraction of a Strong Acid from a Weak Acid.

Label three different reaction tubes. Weigh approximately 0.25 g of the strong/ weak acid mixture (benzoic acid/4-tert-butyl phenol) and transfer it into a small reaction tube (tube #1). Dissolve the solid in exactly 4 mL of tert-butyl methyl ether.

D1. Organic Layer. Wash the organic solution twice with two 1 mL portions of saturated sodium bicarbonate, followed by one 1 mL of water. Place all extractions in a separate reaction tube (tube #2).

D2. Organic Layer. Wash the organic solution twice with two 1 mL portions of 3M sodium hydroxide, followed by one 1 mL of water. Place all extractions in a separate reaction tube (tube #3). Discard the organic layer.

D3. Aqueous Layer ($NaHCO_3$). To the second reaction tube (tube #2), add 3M hydrochloric acid dropwise with stirring between additions until the pH is acidic. This will be determined using pH paper. Filter the resulting solid and wash with water. Weigh the solid. Note which aqueous layer the solid came from in your lab notebook.

D4. Aqueous Layer (NaOH). To the third reaction tube (tube #3), add 3M hydrochloric acid dropwise with stirring between additions until the pH is acidic. This will be determined using pH paper. Filter the resulting solid and wash with water. Weigh the solid. Note which aqueous layer the solid came from in your lab notebook.