Procedure for Establishing Distribution. Repeat the identical procedures carried out in Experiment [4A], but replace the 600 μL of water with 600 μL of 10% sodium bicarbonate solution. A good estimate of the efficiency of the conversion of benzoic acid to the sodium salt of the acid, which because of its ionic character is found almost exclusively in the aqueous phase, can be made by recovering any unreacted acid from the methylene chloride layer and using the distribution coefficient established in Experiment [4A]. Also, be sure to obtain a melting point of any recovered residue (assumed above to be benzoic acid) from the organic phase, since contamination of free acid by the acid salt can be detected by this measurement. Sodium benzoate has a melting point above 300 °C, whereas benzoic acid melts near 122 °C.

Test for a Carboxylic Acid. As illustrated in the above reaction, when a carboxylic acid comes in contact with a solution containing bicarbonate ion, carbon dioxide is generated. Once saturation of the solution by carbon dioxide occurs, bubbles of carbon dioxide gas are observed to form in the liquid phase. This effervescence may be used as a qualitative test for the presence of the carboxylic acid functional group in an unknown substance.

Place 1–2 mL of 10% sodium or potassium bicarbonate on a small watch glass. Add the pure acid, one drop from a Pasteur pipet if the sample is a liquid (~5 mg if it is a solid), to the bicarbonate solution. Evolution of bubbles (CO_2) from the mixture indicate the presence of an acid.

Perform the above test for the presence of carboxyl groups on several organic acids, such as acetic, benzoic, propanoic, or chloroacetic acid.

EXPERIMENT [4C]

Solvent Extraction II: A Three-Component Mixture; An Example of the Separation of an Acid, a Base, and a Neutral Substance

Purpose. This exercise investigates how solvent extraction techniques can be applied effectively to problems that require the separation of mixtures of organic acids, bases, and neutral compounds in the research or industrial laboratory.

Prior Reading

Chapter 3: Experimental Apparatus
- Pasteur Filter Pipet (pp. 26–27)
- Automatic Delivery Pipet (pp. 27–28)
- Weighing of Solids in Milligram Quantities (p. 29)

Technique 4: Solvent Extraction
- Liquid–Liquid Extraction (p. 60)
- Drying of the Wet Organic Layer (pp. 67–68)
- Separation of Acids and Bases (pp. 65–66)
- Salting Out (p. 66)

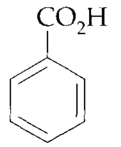
DISCUSSION

As implied in the discussions of Experiments [4A] and [4B], the solubility characteristics of organic acids in water can be shown to be highly dependent on the pH of the solution. By extending this extraction approach to include organic bases, it has been possible to develop a general procedure for the separation of mixtures of organic acids, bases, and neutral substances.

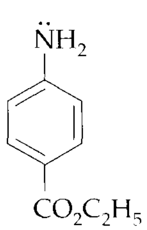
NOTE. Refer to Technique 4, p. 66 for a chart outlining the procedure.

The components of the mixture to be separated in this experiment are benzoic acid, ethyl 4-aminobenzoate (a base), and 9-fluorenone (a neutral compound, which may be prepared in Experiment [33A]).

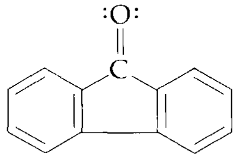
COMPONENTS



Benzoic acid



Ethyl 4-aminobenzoate



9-Fluorenone

EXPERIMENTAL PROCEDURE

Estimated time of experiment: 2.5 h.

Physical Properties of Reactants

Compound	MW	Amount	mmol	mp (°C)	bp (°C)	d
Benzoic acid	122.1	50 mg	0.41	122		
Ethyl 4-aminobenzoate	165.19	50 mg	0.31	89		
9-Fluorenone	180.22	50 mg	0.27	84		
Diethyl ether	74.12	4 mL			35	0.7184
3 M HCl		4 mL				
3 M NaOH		4 mL				
6 M HCl						
6 M NaOH						

NOTE. In carrying out the separation, you should keep a record or flow chart of your procedure (as suggested in the prior reading assignment) in your laboratory notebook. You should also be particularly careful to label all flasks.

HOOD

Reagents and Equipment. Weigh and add to a stoppered or capped 15-mL centrifuge tube the following: 50 mg (0.41 mmol) of benzoic acid, 50 mg (0.31 mmol) of ethyl 4-aminobenzoate, and 50 mg (0.27 mmol) of 9-fluorenone. Now, in the **hood,** add 4 mL of diethyl ether using a 10-mL graduated cylinder for the transfer. The solids may be dissolved by either stirring with a glass rod or mixing on a Vortex mixer (capped vial).

Separation of the Basic Component. Cool the solution in an ice bath. Now, using a calibrated Pasteur pipet, add 2 mL of 3 M HCl dropwise to the cooled solution with swirling. Cap and thoroughly mix the resulting two-phase system for several minutes (a Vortex mixer works well). Vent carefully and after the layers have separated remove the bottom (aqueous) layer using a Pasteur filter pipet and transfer this phase to a **labeled,** 10-mL Erlenmeyer flask.

Repeat this step with an additional 2 mL of the 3 M acid solution. As before, transfer the aqueous layer to the same labeled Erlenmeyer flask. Stopper or cap this flask. *Save the ether solution.* The aqueous acidic solution is to be used in the next step.

NOTE. A small amount of crystalline material may form at the interface between the layers. A second extraction generally dissolves this material.

Isolation of Ethyl 4-Aminobenzoate: The Basic Component. To the aqueous acidic solution, separated and set aside in the previous step, add 6 M NaOH dropwise until the solution is distinctly alkaline to litmus paper. Cool the flask in an ice bath for about 10–15 min. Collect the solid precipitate that forms in the basic solution by reduced-pressure filtration using a Hirsch funnel. Wash the precipitate with two 1-mL portions of distilled water. Air-dry the washed microcrystals by spreading them on a clay plate, filter paper, or in a vacuum drying oven. Weigh the material and calculate the percent recovery. Obtain the melting point of the dry ethyl 4-aminobenzoate and compare your result to the literature value. This material is used as a topical anesthetic.

Separation of the Acidic Component. Add 2 mL of 3 M NaOH to the ether solution that was set aside earlier in the experiment. At this point, if necessary, add additional ether (~1–2 mL) so that the volume of the organic layer is at least equal to, or somewhat larger than, that of the aqueous phase. This adjustment in volume should allow an efficient distribution to take place when the two phases are mixed. Then carry out the extraction as before, allow the layers to separate, and finally transfer the bottom aqueous basic layer to a **labeled,** 10-mL Erlenmeyer flask.

Repeat this routine and again remove the aqueous layer and transfer it to the same Erlenmeyer flask. Stopper this flask (containing the extracted aqueous basic phase) and set it aside for later use.

Separation of the Neutral Component. Wash (extract) the remaining ether solution contained in the centrifuge tube with two 1-mL portions of water. Separate the lower aqueous layer in each sequence. *Save the aqueous wash layer temporarily; it will be discarded at the very end of the experiment. (It is good practice to never discard any layer until you have recovered or accounted for all of the material.)* Now add about 300 mg of anhydrous granular sodium sulfate to the wet ether (ether saturated with water) solution. Cap the tube and set it aside while working up the alkaline extraction solution. This procedure will allow sufficient time for the traces of moisture to be removed from the ether solution by hydration of the insoluble drying agent. If the sodium sulfate initially forms large clumps, you may add a further quantity of the anhydrous salt.

Isolation of Benzoic Acid: The Acidic Component. Add 6 M HCl dropwise to the aqueous alkaline solution, which was separated and set aside earlier, until the solution becomes distinctly acidic to litmus paper. Then cool the flask in an ice bath for about 10 min. If only a small amount (10–25 mg) of precipitate is obtained on acidification, add a small amount of a saturated aqueous solution of sodium chloride (salting out effect; see Prior Reading assignment) to help promote further precipitation of the benzoic acid. Collect the precipitated benzoic acid by filtration under reduced pressure using a Hirsch funnel. Wash (rinse) the filter cake (precipitated acid) with two 1-mL portions of cold distilled water. Dry the solid product using one of the techniques described earlier for ethyl 4-aminobenzoate. Weigh the dry benzoic acid and calculate your percent recovery.

Obtain a melting point of this material and compare your result to the literature value.

Isolation of 9-Fluorenone: The Neutral Component. Use a Pasteur filter pipet to transfer the dried ether solution collected earlier to a tared 10-mL Erlenmeyer flask containing a boiling stone. Rinse the drying agent with an additional 1 mL of ether and combine the ether wash with the anhydrous organic phase.

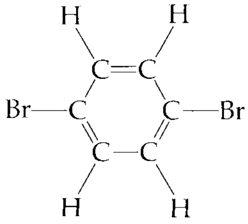
Concentrate the ether solution on a warm sand bath using a *slow* stream of nitrogen gas in the **hood.** Obtain the weight of the residue (9-fluorenone) after removal of the solvent and calculate the percent recovery. Obtain a melting point of the material and compare your result to the literature value.

HOOD

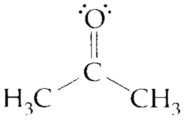
QUESTIONS

6-21. Explain why diethyl ether would be expected to be a satisfactory solvent for the straight-chain hydrocarbons hexane and heptane.

6-22. The solubility of *p*-dibromobenzene in benzene is 80 μg/100 μL at 25 °C. Would you predict the solubility of this compound to be greater, less, or approximately the same in acetone solvent at this temperature? Explain.



p-Dibromobenzene



Acetone

6-23. Each of the solvents listed below are used in experiments in this text to extract organic compounds from aqueous solutions.

(a) Methylene chloride
(b) Pentane
(c) Toluene
(d) Diethyl ether

Will the organic phase be the upper or lower layer when each of these solvents is mixed with water? Explain your answer for each case.

6-24. A 36-mg sample of an organic compound (MW = 84) is dissolved in 10 mL of water. This aqueous solution is extracted with 5.0 mL of hexane. Separation and analysis of the aqueous phase shows that it now contains 12 mg of the organic compound. Calculate the partition coefficient for the compound.

6-25. A qualitative method often used to determine whether an organic compound contains oxygen is to test its solubility in concentrated sulfuric acid. Almost all oxygen-containing compounds are soluble in this acid. Explain.

6-26. In the discussion of multiple extractions (p. 59), it was suggested that in the example given you might extend the relationship to the next step by using one-third of the total quantity of the ether solvent in three portions. The reason for increasing the number of extractions was to determine whether this expansion would increase the efficiency of the process even further. To determine if this next step is worth the effort, perform the calculations for the extraction of 100 mg of P in 300 μL of water with three 100-μL portions of ether. Assume the partition coefficient is 3.5 (as before).

(a) Compare the amounts of P extracted from the water layer using one, two, or three extractions.
(b) Do you think that the additional amount of P extracted from the water layer using three extractions is justified? Might it be justified if P were valuable and you were working on the industrial scale of 100 kg of P in 3000 L of water?

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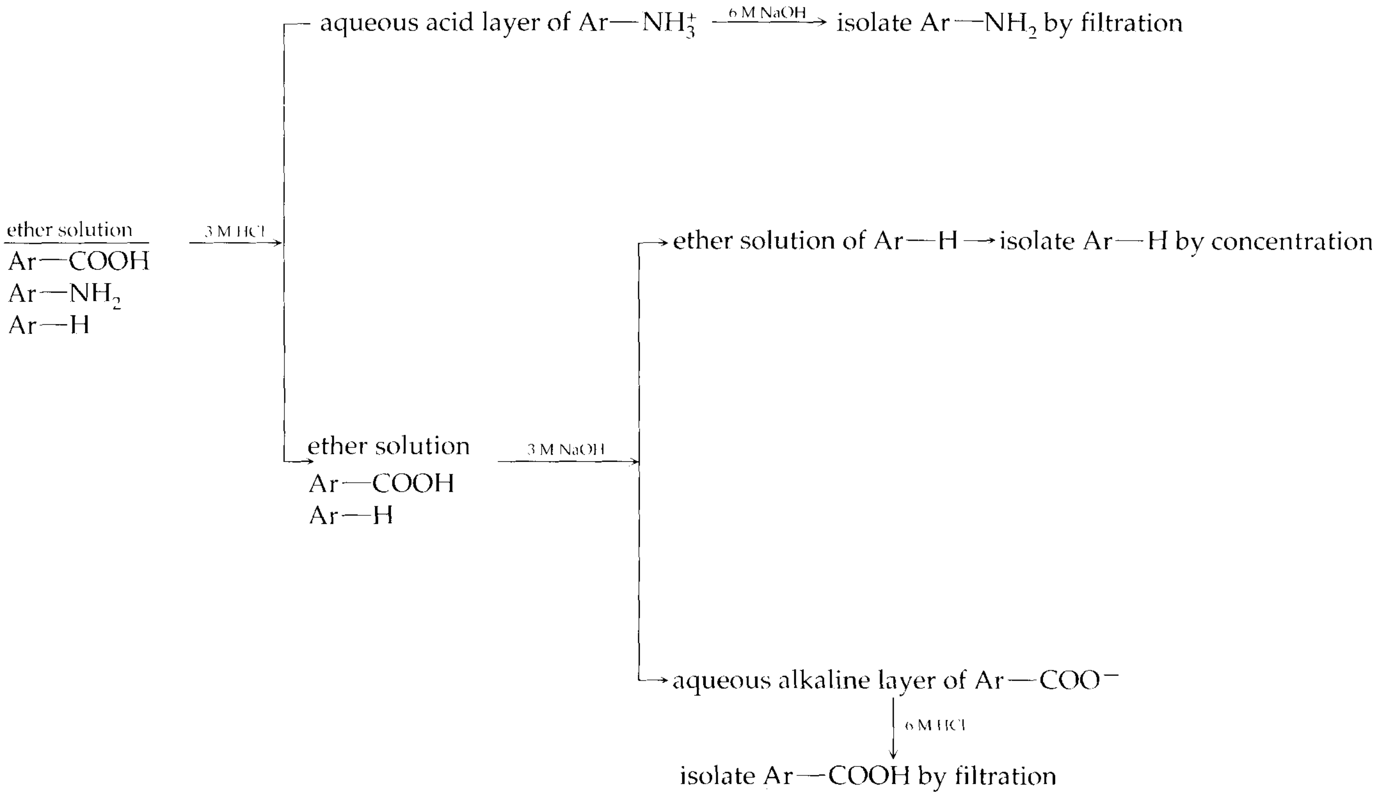
Extraction procedures can be used to separate mixtures of solids. For example, the flow chart below diagrams a sequence used to separate a mixture made up of an aromatic carboxylic acid ($ArCO_2H$), an aromatic base ($ArNH_2$), and a neutral aromatic compound (ArH). Aromatic compounds are discussed here simply because they are likely to be crystalline solids.



In this example, we assume that the organic acid and base are solids. If either or both were liquids, an additional extraction of the final acidic aqueous or alkaline solution with ether, followed by drying and concentration, would be required to isolate the acidic or basic component.

Salting Out. Most extractions in the organic laboratory involve water and an organic solvent. Many organic compounds have partial solubility in both solvents. To extract them from water, the partition coefficient (between the organic solvent and water) can be shifted in favor of the organic layer by saturating the water layer with an inorganic salt, such as sodium chloride. Water molecules prefer to solvate the polar ions (in this case sodium and chloride ions), and thus free the neutral organic molecules to migrate into the organic phase. Another way to think of this is to realize that the ionic solution is more polar than pure water, so the less polar organic molecules are less soluble than in pure water. Forcing an organic material out of a water solution by adding an inorganic salt is called *salting out.*

Salting out can also be effectively used for the *preliminary drying* of the wet organic layer that results from an extraction process. (Diethyl ether, in particular, can dissolve a fair amount of water.) Washing this organic layer with a saturated salt solution removes most of the dissolved water into the aqueous phase. This makes further drying of the organic phase with solid drying agents easier and much more effective (see Drying Agents below).