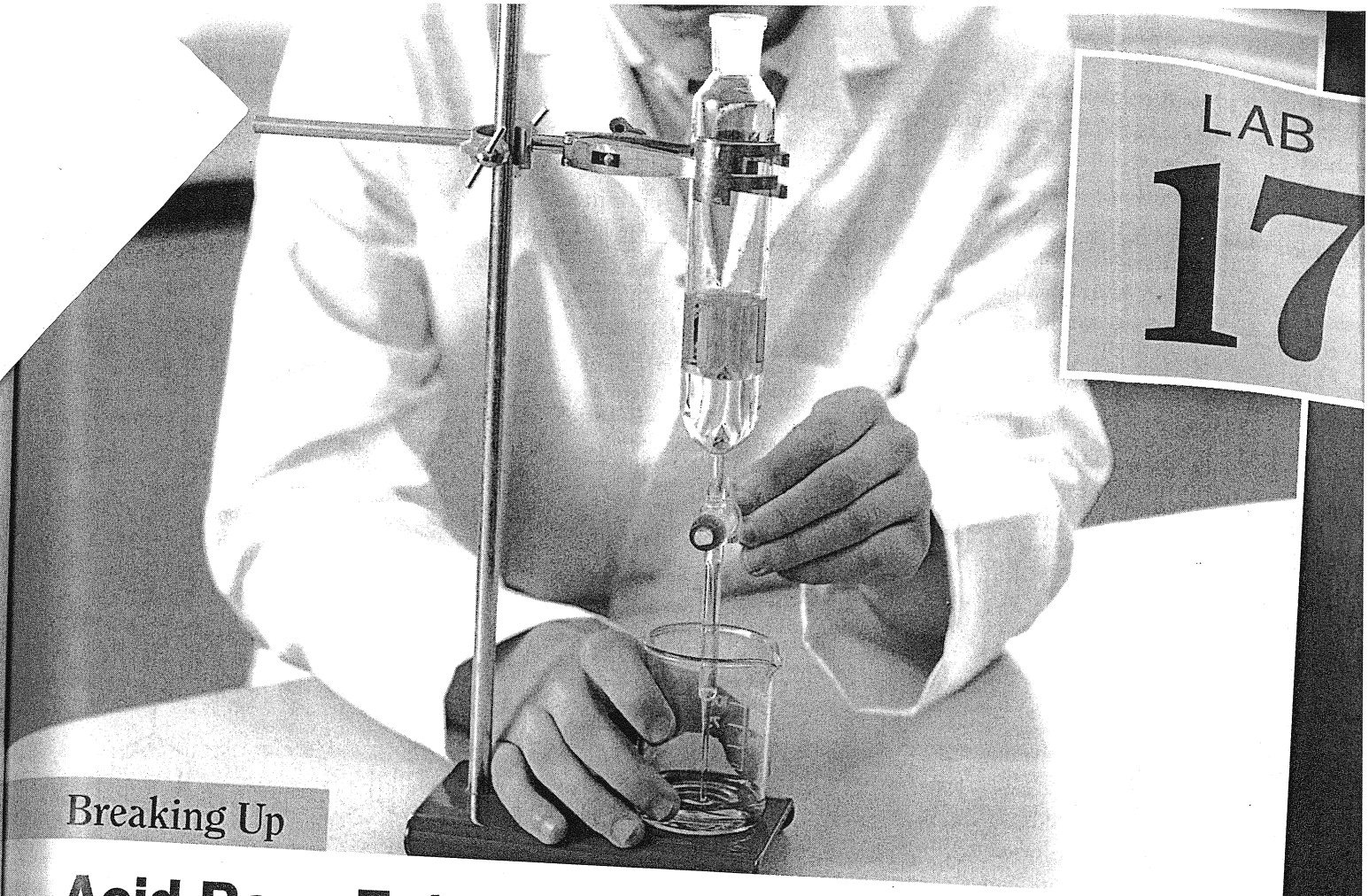


LAB 17

Breaking Up

Acid-Base Extraction

Objectives

After completing this lab you should be able to:

- Describe and perform the technique of liquid-liquid extraction.
- Explain how acid-base chemistry may be used to alter the solubility of compounds.
- Separate components of a mixture using acid-base extraction.
- Purify a solid by a simple recrystallization.
- Evaluate the purity of a substance by melting point analysis.

Extraction is the process of selectively transferring one component of a mixture into a different phase. Laboratory extractions typically exploit differences in solubilities, and there are a variety of extraction techniques that may be used to achieve different goals. For example, liquid-solid extraction is used to make coffee. Caffeine and the various flavors in coffee beans are extracted from the solid into the liquid phase by hot water. Similarly, many important pharmaceuticals were first discovered by liquid-solid extraction from various types of plants, and some are still produced in large quantities by this method.

Liquid-liquid extraction may be used to separate molecules that have significantly different solubilities in two liquids that are **immiscible** (such as oil and water). When the two liquids are shaken together and then allowed to separate into layers, compounds selectively migrate, or **partition**, into the solvent layer in which they are more soluble. For example, when water and dichloromethane are mixed and then allowed to settle, two layers will form because the solvents are not miscible with one another. The dichloromethane will be the bottom layer

because it is denser than water. If a solution of bromine in water is shaken with dichloromethane, the bromine will be extracted into the dichloromethane because the nonpolar molecule is more soluble in the relatively nonpolar solvent. Upon standing, the two solvents separate, and the reddish-brown color of the bromine will be observed only in the lower (dichloromethane) layer (Fig. 17.1).

The separation of acidic and basic compounds may be achieved using acid-base extraction, which involves using an acid-base reaction to chemically alter the solubility of a compound. In this lab, you will use acid-base extraction to separate a mixture of two pain relief medications.

Certain commercial pain relievers are mixtures of acetylsalicylic acid (aspirin) and acetaminophen (the active ingredient in Tylenol®). The structures of these compounds are shown in Figure 17.2. As you might expect, both compounds are soluble in organic solvents, such as ethyl acetate.

Despite their similar solubility properties, acetylsalicylic acid and acetaminophen have significantly different acid-base properties, which may be exploited to separate a commercial mixture of the two. Acetylsalicylic acid contains an acidic carboxylic acid functional group, and shaking an ethyl acetate solution of the mixture with an aqueous base (e.g., $NaHCO_3$) causes an acid-base reaction that produces a water-soluble aspirin salt (Fig.17.3). Acetaminophen is not acidic and does not react with the base. As a result, the ionic aspirin salt migrates to the aqueous solution while the acetaminophen remains dissolved in the ethyl acetate. Since ethyl acetate and water are not miscible with each other, these two solutions may be separated, providing a simple means of separating the two pharmaceuticals.

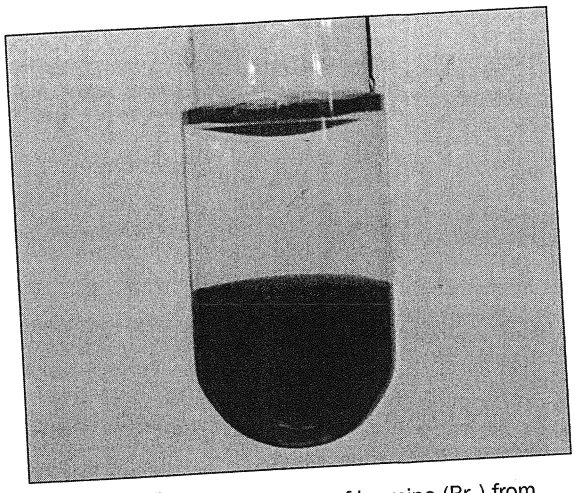


FIGURE **17.1** Extraction of bromine (Br_2) from water with dichloromethane. After shaking a mixture of Br_2 in water with dichloromethane, the immiscible solvents separate into layers. The nonpolar, reddish-brown Br_2 is extracted into the denser, nonpolar dichloromethane layer.

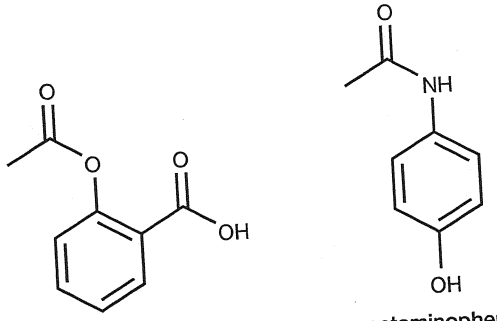
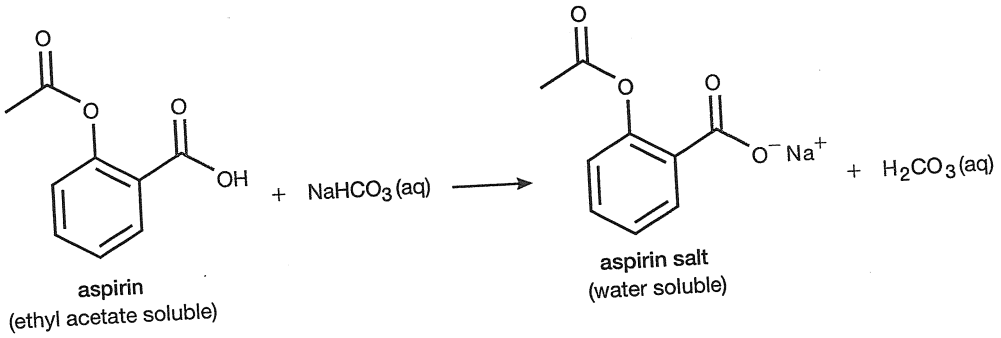


FIGURE **17.2** Structures and melting points of acetylsalicylic acid and acetaminophen.



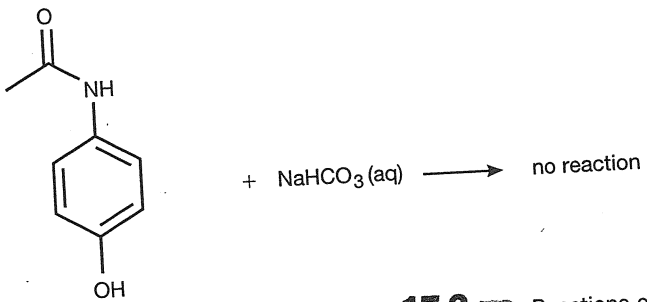


FIGURE **17.3** Reactions of acetylsalicylic acid and acetaminophen with a base. The products have different solubilities and are easily separated from each other.

The procedure you will use to separate and purify the acetylsalicylic acid and acetaminophen is outlined in Figure 17.4. Once the aqueous and ethyl acetate layers are separated, the ethyl acetate will be extracted a second time to ensure that all of the acetylsalicylic acid has been removed. The acetaminophen may be isolated directly from the ethyl acetate layer by evaporation of the solvent. However, the recovered acetaminophen will be a crude solid that may be contaminated with impurities. This solid will be further purified by dissolving it in hot water, cooling the solution, and allowing the acetaminophen crystals to reform slowly, a process called **recrystallization.** To isolate the acetylsalicylic acid, the combined aqueous layers will be acidified by the addition of hydrochloric acid (HCl). This will convert the carboxylate salt back into acetylsalicylic acid, which precipitates in a cold solution because it is insoluble in water.

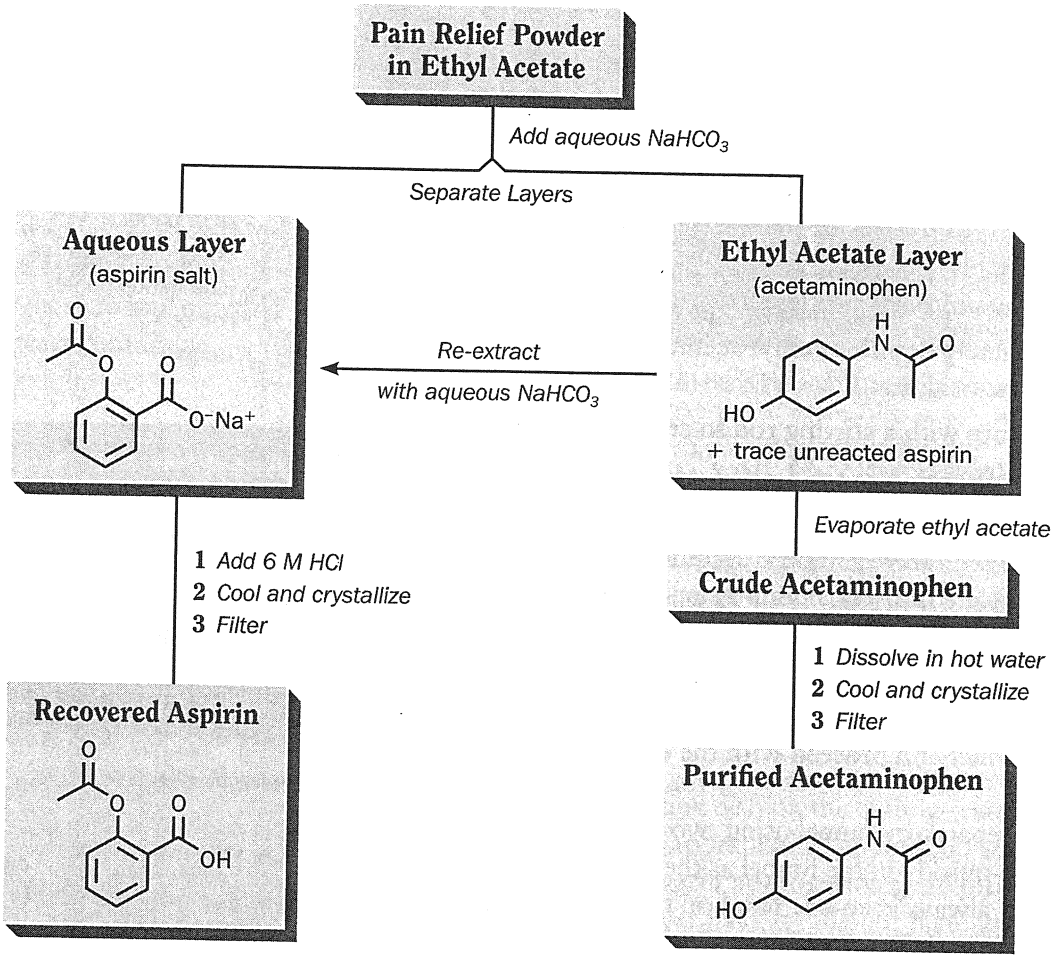


FIGURE **17.4** Extraction flow chart for the separation of an acetylsalicylic acid/acetaminophen mixture.

You will evaluate the effectiveness of your extraction by calculating the percent recovery of each drug from the original sample. The formula for this calculation is given in the following equation.

Equation 1

$$\textit{percent recovery} = \frac{\textit{mass of drug recovered}}{\textit{mass of drug in commercial sample}} \times 100$$

You also will confirm the identities of the solids you obtain by measuring their melting points and comparing them to the literature values for acetylsalicylic acid and acetaminophen (Fig. 17.2). Although melting points are usually reported as single values, they are actually measured as a range over which a substance is in equilibrium between the solid and liquid state. The melting of a pure substance occurs over a very narrow range (generally less than 1.0°C). Impurities cause a lowering and broadening of a substance's melting point. Thus, it is possible to assess purity of a sample by comparing the measured melting point range to the value reported in the literature.

Procedure

Acid-Base Extraction of a Commercial Pain Reliever

1. Set up a ring stand and with a separatory funnel as shown in Figure 17.5.
2. Obtain a sample of commercial pain relief powder. On the data sheet, page 249, record the total quantity of acetylsalicylic acid and acetaminophen in your sample according to the package label.
3. Add the contents of both packages to a 125 mL beaker.
4. Add approximately 25 mL of ethyl acetate and 25 mL of saturated $NaHCO_3$ to the beaker.
5. Swirl the mixture with a stirring rod to ensure that the powder completely dissolves.
6. Check that the stopcock of the separatory funnel is closed and then pour the solution into the funnel.
7. To ensure complete transfer of your sample, rinse the beaker with a few milliliters of ethyl acetate and add this to your separatory funnel. Next, rinse the beaker with a few milliliters of the saturated $NaHCO_3$ solution and add this to your separatory funnel.
8. Stopper the funnel and proceed with the extraction by following these steps:
   a. Pick up the separatory funnel using two hands. Note that pressure will build up quickly in the funnel as the two liquids mix, so it is a good idea to always keep one hand on the stopper (Fig. 17.6A).
   b. To vent the funnel (Fig. 17.6B), turn it upside down and slowly open the stopcock. This will relieve any pressure build up.
   c. Close the stopcock and swirl the mixture in the funnel several times. Immediately vent the funnel to relieve any pressure.
   d. Repeat the swirling/venting steps several times, gradually shaking the contents more vigorously until strong pressure ceases to build up in the funnel.
   e. When you have finished mixing, place the funnel back in the ring stand and immediately remove the stopper.
   f. After a short time, the two immiscible liquids will partition into layers, with the less dense layer (ethyl acetate) on top. Separate the layers by slowly draining the lower layer through the bottom of the funnel into a 125 mL Erlenmeyer flask. Stop draining once the boundary layer just enters the stopcock.

- ☐ Ring stand
- ☐ Iron ring
- ☐ Separatory funnel
- ☐ Glass stir rod
- ☐ 50 mL beakers
- ☐ 125 mL beaker
- ☐ 50 mL Erlenmeyer flasks
- ☐ 125 mL Erlenmeyer flask
- ☐ 250 mL beaker
- ☐ Hot plate
- ☐ Evaporating dish
- ☐ Büchner funnel with rubber adapter
- ☐ Vacuum flask with tubing
- ☐ Watch glasses (2)
- ☐ Filter paper
- ☐ Scoopula or spatula
- ☐ Blue litmus paper
- ☐ Forceps
- ☐ Tongs

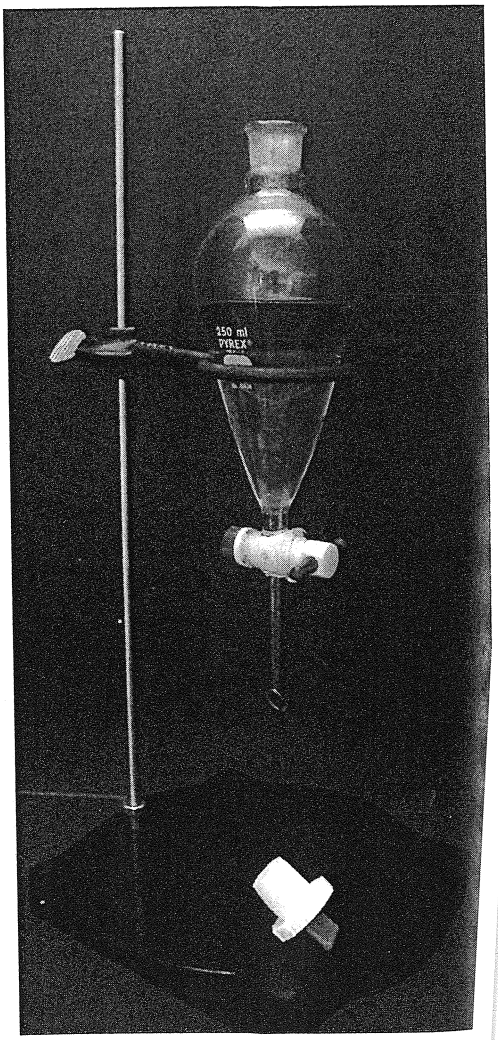


FIGURE **17.5** Separatory funnel apparat for extraction.

9 In order to ensure complete extraction of the aspirin from the ethyl acetate layer, add about 10 mL of saturated $NaHCO_3$ to the ethyl acetate solution in the separatory funnel and repeat step 8. The bottom (aqueous) layer may be collected in the same flask you used to collect the first aqueous extract.

10 Once you have removed the second portion of aqueous extract, pour the ethyl acetate layer out of the open top of the funnel into a 50 mL beaker. You should now have two solutions: an aqueous extract containing acetylsalicylic acid and an ethyl acetate extract containing acetaminophen.

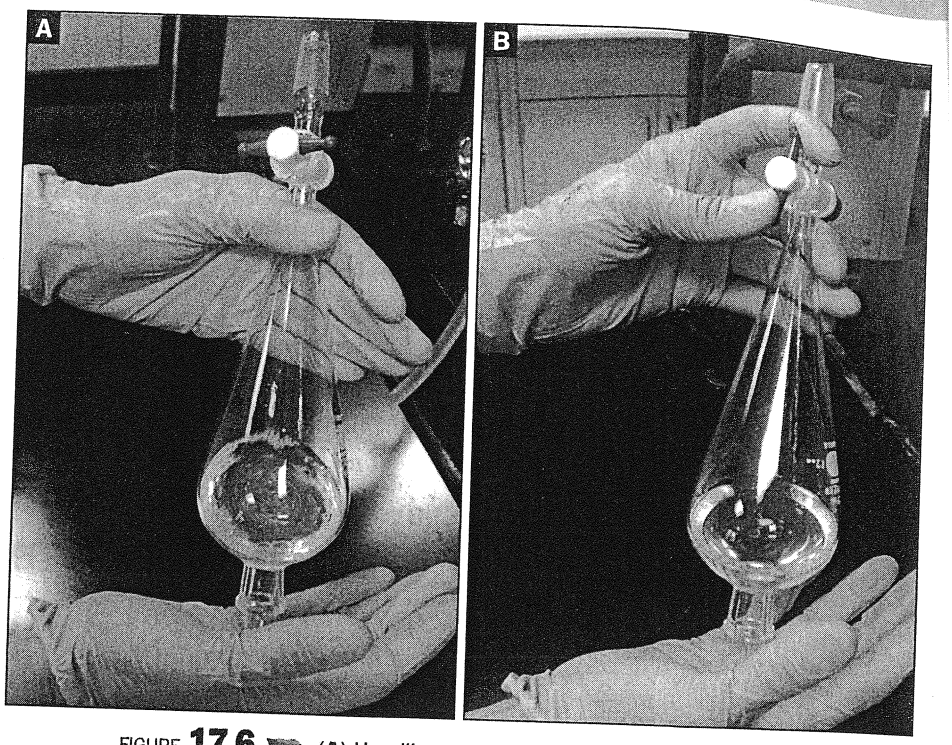


FIGURE **17.6** (**A**) Handling and (**B**) venting a separatory funnel.

TECHNIQUE TIP

If lab time is a concern, your instructor may direct you to divide the tasks of recovering the separated compounds. One lab partner may proceed with the isolation and purification of acetaminophen (Part B) while the other proceeds simultaneously with the isolation and purification of acetylsalicylic acid (Part C). You will both need a boiling-water bath in a 250 mL beaker at various points throughout the isolation processes.

Part B: Isolation and Purification of Acetaminophen

1 In a fume hood, prepare a boiling-water bath on a hot plate by filling a 250 mL beaker about two-thirds full of water.

2 Record the mass of an evaporating dish on your data sheet, page 249.

3 Pour the ethyl acetate solution into the pre-weighed evaporating dish.

4 Place the evaporating dish on the boiling-water bath and allow the ethyl acetate to evaporate until you obtain solid acetaminophen. While you wait, warm approximately 10 mL of distilled water in a 50 mL Erlenmeyer flask on the hot plate to just below the boiling point.

⚠ SAFETY NOTE

Steam from the boiling-water bath can cause severe burns. Use tongs to remove the evaporating dish and exercise caution!

5 When the ethyl acetate has evaporated, remove the dish with tongs. Dry and reweigh the evaporating dish containing the crude acetaminophen and record this value on the data sheet. Calculate the mass of crude acetaminophen you recovered, and record your results on the data sheet.

6 Use a scoopula or spatula to scrape the solid into a dry 50 mL beaker. To recrystallize the acetaminophen, add approximately 1 mL of the hot distilled water to the solid. Add a boiling stick to the beaker and place it on a warm hot plate. Continue to add 1 mL portions of hot distilled water to the beaker until the solid completely dissolves. Do not add more than 6 mL of water. If solid still remains after you have added 6 mL of boiling water, your instructor may add a few drops of methanol to complete the dissolution process.

7 Once all the solid is dissolved, allow the hot solution to cool slowly to room temperature and then chill it in an ice-water bath to ensure that the maximum amount of acetaminophen recrystallizes from the solution. Add about 15 mL of distilled water to a separate 50 mL Erlenmeyer flask and chill this in the ice-water bath as well. You will use this water to wash your isolated crystals.

8 While the acetaminophen is cooling, set up the suction filtration apparatus illustrated in Figure 17.7. Fit a vacuum flask with a rubber adapter and a Büchner funnel, and attach a vacuum hose from the port on the vacuum flask to the vacuum source.

9 When the acetaminophen crystals are completely cooled, place a piece of filter paper in the Büchner funnel, wet it with distilled water, and turn on the vacuum. This should seal the filter paper to the bottom of the funnel.

10 Slowly pour the solution of acetaminophen crystals into the funnel. The liquid will be pulled through the funnel, leaving the crystals on the filter paper. Wash any remaining crystals from the flask into the funnel with about 10 mL of the ice-cold distilled water.

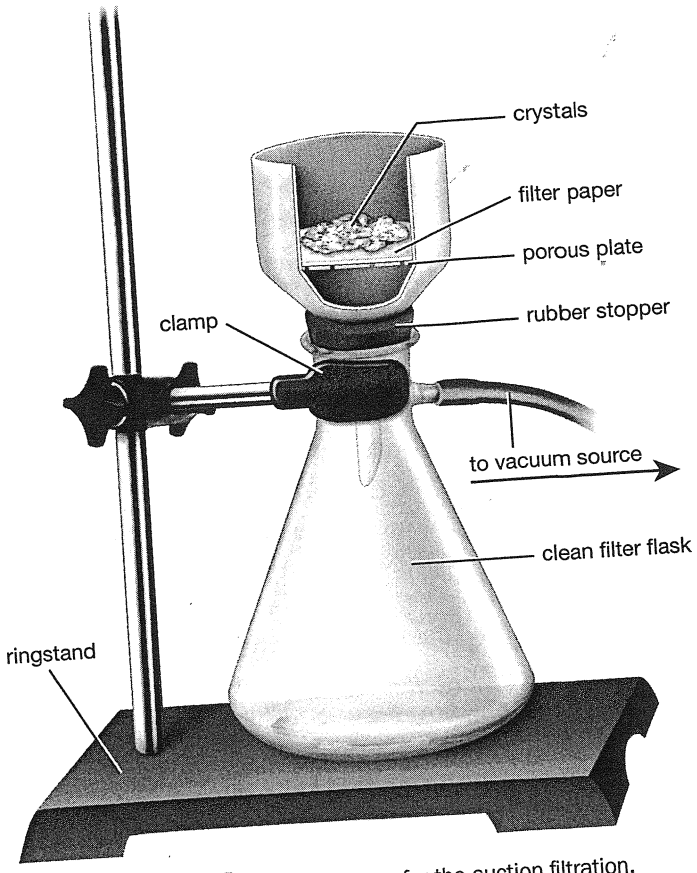


FIGURE **17.7** Apparatus for the suction filtration.

11 Allow the crystals to dry under suction for about 5 minutes. While the crystals are drying, weigh a large watch glass and record the mass on the data sheet, page 249. Also, ensure that the water bath on the hot plate is boiling gently.

12 After 5 minutes of drying the acetaminophen under suction, break the filter vacuum by pulling the hose off of the vacuum flask. Carefully scrape all of your crystals onto the pre-weighed watch glass.

13 Place the watch glass on top of the hot-water bath in order to further dry the acetaminophen. After about 10 minutes, the crystals should be fully dried.

14 Use tongs to remove the watch glass from the heat and dry the bottom with a paper towel.

15 On the data sheet, record the mass of the watch glass with the dried acetaminophen. Calculate the mass of the purified acetaminophen you isolated, and record your results on the data sheet.

⚠ SAFETY NOTE

Steam from the boiling-water bath can cause severe burns. Use tongs to remove the evaporating dish and exercise caution!

16 Obtain the melting point of your acetaminophen as directed by your instructor.

17 Dispose of the acetaminophen and the liquid in the filter flask as directed by your instructor.

18 Calculate the percent recovery of purified acetaminophen based on the sample quantity indicated on the package label, and record your results on the data sheet.

Part C: Isolation of Acetylsalicylic Acid

1 Place the aqueous extract containing acetylsalicylic acid in an ice-water bath. Also, add approximately 10 mL of distilled water to a separate 50 mL Erlenmeyer flask and chill it in the ice-water bath.

⚠ SAFETY NOTE

Hydrochloric acid is a corrosive strong acid. **Handle with caution!**

2 To the aqueous extract, add a total of approximately 8 mL of 6 M HCl in 1 mL increments. These incremental additions will minimize bubbling that may occur as the acid reacts with the $NaHCO_3$.

3 After you have added the 8 mL of HCl, check the acidity of the solution by using your glass rod to dab a drop onto blue litmus paper. If the solution is acidic, the blue paper will turn red. If the solution is not yet acidic, add more HCl in 1 mL increments until the litmus paper indicates that your solution is no longer basic.

4 When the litmus paper indicates that the solution is acidic, add 10 more drops of the 6 M HCl to ensure that all of the acetylsalicylic acid has been precipitated.

5 Assemble the suction filtration apparatus illustrated in Figure 17.7. Fit a vacuum flask with a rubber adapter and a Büchner funnel. Attach a vacuum hose from the port on the vacuum flask to the vacuum source.

6 Place a piece of filter paper in the Büchner funnel, wet it with distilled water, and turn on the vacuum. This should seal the filter paper to the bottom of the funnel.

7 Slowly pour the mixture of solid acetylsalicylic acid into the funnel. The liquid will be pulled through the funnel, leaving the crystals on the filter paper. Wash any remaining crystals from the flask into the funnel with about 10 mL of the ice-cold distilled water.

8 Allow the crystals to dry under suction for about 5 minutes. While the crystals are drying, weigh a large watch glass and record the mass on the data sheet, page 250. Also, use a half-filled 250 mL beaker to make a boiling-water bath on the hot plate.

9 After 5 minutes of drying the acetylsalicylic acid under suction, break the filter vacuum by pulling the hose off of the vacuum flask. Carefully scrape all of your crystals onto the pre-weighed watch glass.

10 Place the watch glass on top of the hot-water bath to further dry the solid. After about 10 minutes, the crystals should be fully dried.

11 Use tongs to remove the watch glass from the heat and dry the bottom with a paper towel.

12 Reweigh the watch glass with dried acetylsalicylic acid to calculate the mass of purified acetylsalicylic acid you recovered, and record the results on the data sheet. 1

13 Obtain the melting point of your acetylsalicylic acid as directed by your instructor.

14 Dispose of the acetylsalicylic acid and the liquid in the filter flask as directed by your instructor.

15 Calculate the percent recovery of purified acetylsalicylic acid based on the quantity indicated on the label, and record the results on the data sheet.

Name _____

Lab Partner _____

Lab Section _____ Date _____

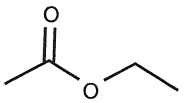
PRELABORATORY EXERCISE

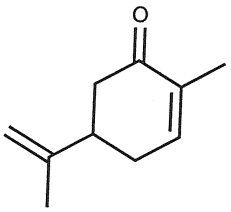
17

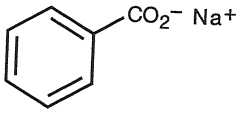
1 Why is it impossible to perform a liquid-liquid extraction using H_2O and CH_3OH as the two solvents?

2 Suppose a mixture of two immiscible solvents formed separate layers upon standing. Name the physical property of the solvents you would look up to determine which solvent formed each layer and describe how this property would help you.

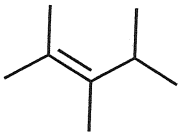
3 Consider the mixture of compounds below. Circle the compounds you would expect to partition into the ethyl acetate layer if this mixture was subjected to an extraction using water and ethyl acetate as the two solvents.

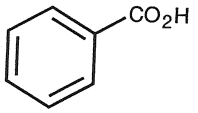




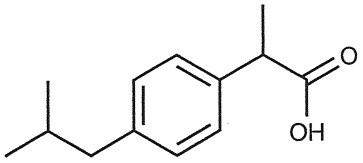


KBr





4 Use the structure of ibuprofen to answer the following questions.

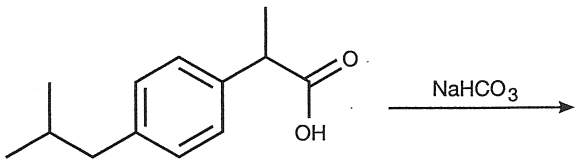


Ibuprofen

a Would you expect ibuprofen to be soluble in water or an organic solvent like ethyl acetate? Explain.

_____

b In the box provided, draw the structure of the product obtained upon reaction of ibuprofen with aqueous sodium bicarbonate.



Ibuprofen

c Would the product you drew in part (b) be soluble in ethyl acetate or water? Explain.

_____

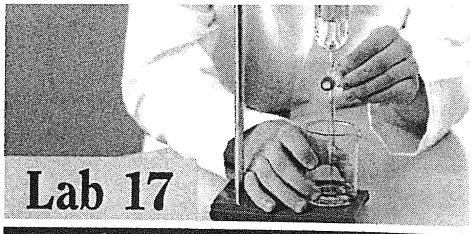
d What kind of reagent should you add to the product you drew in part (b) in order to regenerate ibuprofen?

_____

Name _____

Lab Partner _____

Lab Section _____ Date _____



Lab 17 DATA SHEET

Part A: Acid-Base Extraction of Commercial Pain Reliever

Total mass of acetylsalicylic acid according to label _____

Total mass of acetaminophen according to label _____

Part B: Isolation of Acetaminophen

Mass of evaporating dish _____

Mass of evaporating dish + crude acetaminophen _____

Calculated mass of crude acetaminophen _____

Mass of watch glass _____

Mass of watch glass + purified acetaminophen _____

Calculated mass of purified acetaminophen _____

Melting point of purified acetaminophen _____

Percent recovery of purified acetaminophen _____

Show calculation:

Part C: Isolation of Acetylsalicylic Acid

Mass of watch glass _____

Mass of watch glass + acetylsalicylic acid _____

Calculated mass of recovered acetylsalicylic acid _____

Melting point of recovered acetylsalicylic acid _____

Percent recovery of acetylsalicylic acid _____

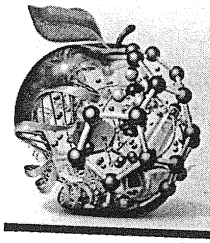
Show calculation:

17

Name _____

Lab Partner _____

Lab Section _____ Date _____



LAB 17 REFLECTIVE EXERCISES

1 What percent of the acetylsalicylic acid and acetaminophen in the commercial pain reliever were you able to recover? Based on your data, was your recovered material pure? Explain your answer.

2 What are some reasons that your measured melting points for acetaminophen and acetylsalicylic acid might not exactly equal the literature values for these substances?

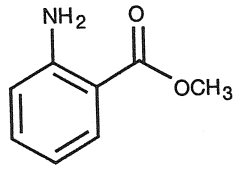
3 What was the purpose of recrystallizing the acetaminophen you recovered from the ethyl acetate extraction?

4 During a recrystallization, the solid is dissolved in a very hot solvent and the crystals are produced by cooling the solution in an ice-water bath. Why is it necessary to operate at these temperature extremes during these two steps?

5 Why did the procedure direct you to isolate the acetaminophen and acetylsalicylic acid crystals by vacuum filtration rather than a simple gravity filtration?

6 Would you have been able to separate the acetylsalicylic acid and acetaminophen if you had performed the extraction using a mixture of aqueous H_2SO_4 and ethyl acetate rather aqueous $NaHCO_3$ and ethyl acetate? Explain your answer.

7 The flavor of grapes is partly due to the compound methyl anthranilate, shown below. Suppose you soaked grapes in ethyl acetate in order to extract their flavoring agents. What type of solvent might you use to extract the methyl anthranilate from the other compounds in the ethyl acetate solution? To justify your answer, draw the structure of the compound produced when methyl anthranilate is exposed to the extraction solvent you choose.



methyl anthranilate