Experiment 29

Aspirin Synthesis and Analysis

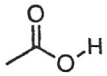
OBJECTIVES

- To synthesize aspirin
- To determine the purity of the synthesized aspirin or a commercial aspirin tablet

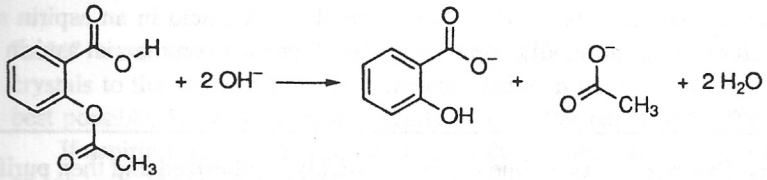
INTRODUCTION

Pure aspirin, acetylsalicylic acid, is both an organic **ester** and an **organic acid**. It is used extensively in medicine as a painkiller (analgesic) and as a fever-reducing drug (antipyretic). When ingested, acetylsalicylic acid remains intact in the acidic stomach, but in the basic medium of the upper intestinal tract, it **hydrolyzes** forming the salicylate and acetate ions.

Ester: a  *grouping of atoms in a molecule*

Organic acid: a  *grouping of atoms in a molecule*

Hydrolyzes: reacts with water



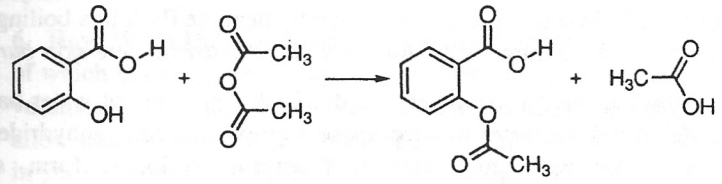
(29.1)

aspirin (acetylsalicylic acid) — salicylate ion — acetate ion

The analgesic action of aspirin is undoubtedly due to the salicylate ion; however, its additional physiological effects and biochemical reactions are still not thoroughly understood. It is known that salicylic acid has the same therapeutic effects as aspirin; however, it causes a more severe upset stomach than does aspirin.

Aspirin (molar mass of 180.2 g/mol) is prepared by reacting salicylic acid (molar mass of 138.1 g/mol) with acetic anhydride (molar mass of 102.1 g/mol). Aspirin is a weak **monoprotic acid**.

Monoprotic acid: a molecule that provides one proton for neutralization



(29.2)

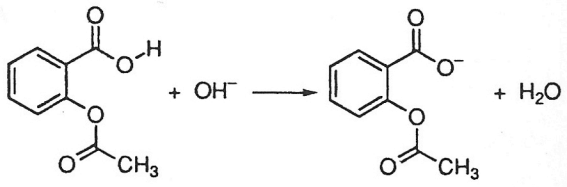
salicylic acid — acetic anhydride — aspirin (acetylsalicylic acid) — acetic acid

Qualitatively, the purity of an aspirin sample can be determined from its melting point. The melting point of a substance is essentially independent of atmospheric pressure, but it is always lowered by the presence of impurities (a colligative property

Aspirin is a leading commercial pain reliever, first synthesized in 1853.

of pure substances. See Experiment 20). The degree of lowering of the melting point depends on the nature and the concentration of the impurities.

Quantitatively, the purity of an aspirin sample can be determined by a simple acid–base titration. The acetylsalicylic acid reacts with hydroxide ion, from a standardized sodium hydroxide solution, accordingly.



(29.3)

The volume and molar concentration of a standardized NaOH solution titrate the acetylsalicylic acid to the phenolphthalein endpoint, where

volume of NaOH (L) × molar concentration of NaOH (mol/L) = mol NaOH (29.4)

According to Equation 29.3, one mole of OH^- reacts with one mole of acetylsalicylic acid; thus, the moles of acetylsalicylic acid in the prepared sample are known. Using the known molar mass of acetylsalicylic acid, the measured mass of the acid and the percent purity of the aspirin sample can be calculated:

$$\text{mol acetylsalicylic acid} \times \frac{180.2\ \text{g}}{\text{mol}} = \text{g acetylsalicylic acid} \quad (29.5)$$

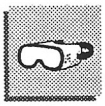
$$\%\ \text{purity} = \frac{\text{g acetylsalicylic acid}}{\text{g aspirin sample}} \times 100 \quad (29.6)$$

In Part C, the analysis for the percent acetylsalicylic acid in an aspirin sample can be performed on the aspirin prepared in Part A *or* on a commercial aspirin tablet.

EXPERIMENTAL PROCEDURE

Procedure Overview: Crystalline aspirin is quickly synthesized and then purified by the procedure of recrystallization. The melting point and the percent purity of the aspirin are measured, the latter by titration with a standardized NaOH solution.

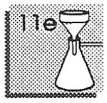
A. Preparation of Aspirin



It is safest to prepare the aspirin in a fume hood. Set up a boiling water bath in a 400-mL beaker. Prepare about 100 mL of ice water.

1. Mix the Starting Materials and Heat. Measure about 2 g (±0.01 g) of salicylic acid (**caution:** *this is a skin irritant*) in a 125-mL Erlenmeyer flask. Cover the crystals with 4–5 mL of acetic anhydride. (**Caution:** *acetic anhydride is a severe eye irritant—avoid skin and eye contact.*) Swirl the flask to wet the salicylic acid crystals. Add 5 drops of conc H_2SO_4 to the mixture and gently heat the flask in a boiling water bath (Figure 29.1) for 5–10 minutes. (**Caution:** H_2SO_4 *causes severe skin burns.*)

2. Cool to Crystallize the Aspirin. Remove the flask from the hot water bath and add 10 mL of deionized ice water to decompose any excess acetic anhydride. Chill the solution in an ice bath until crystals of aspirin no longer form, stirring occasionally to decompose residual acetic anhydride. *If* an "oil" appears instead of a solid, reheat the flask in the hot water bath until the oil disappears and again cool.



3. Separate the Solid Aspirin from the Solution. Set up a vacuum filtration apparatus and "turn it on." Seal the filter paper with water in the Büchner funnel. *Decant* the liquid onto the filter paper; minimize any transfer of the solid aspirin. Some aspirin, however, may be inadvertently transferred to the filter; that's OK.

4. Wash and Transfer the Aspirin to the Filter Paper and Wash. Add 15 mL of

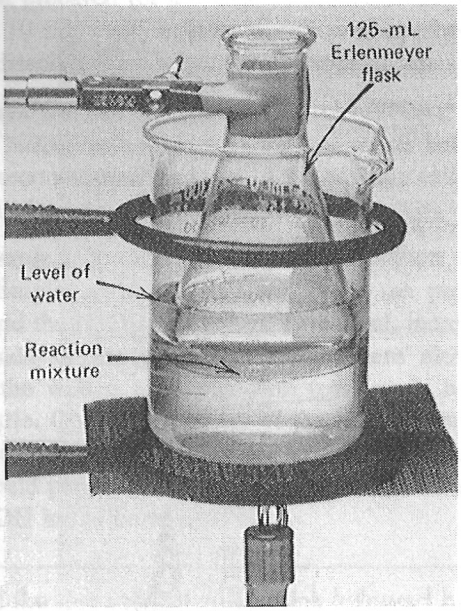
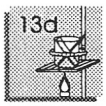


Figure 29.1 Boiling water bath for the dissolution of the acetylsalicylic acid crystals.

"cold" water to the flask, swirl, and chill again. Repeat until the transfer of the crystals to the vacuum filter is complete; maintain the vacuum to dry the crystals as best possible. Wash the aspirin crystals on the filter paper with 10 mL of ice water.

If aspirin forms in the filtrate, transfer the filtrate and aspirin to a beaker, chill in an ice bath, and vacuum filter as before, using a new piece of filter paper. Dispose of the filtrate in the sink.

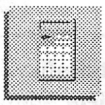


5. Recrystallize the Aspirin. Transfer the crystals from the filter paper(s) to a 100-mL beaker. Dissolve crystals in a minimum volume (≤20 mL) of ethanol. Warm the mixture in a 60°C water bath (*no flame*, use a hot plate or a hot water bath). Pour 50 mL of water at about 60°C into the solution. If a solid forms, continue warming until the solid dissolves.

Cover the beaker with a watchglass, remove it from the heat, and set it aside to cool slowly. Set the beaker in an ice bath. Beautiful needlelike crystals of acetylsalicylic acid form.

6. How Much Did You Prepare? Vacuum filter the crystals on filter paper, the mass of which has been previously measured (±0.01 g). Wash the crystals with two 10-mL volumes of ice water. Place the filter paper and aspirin sample on a watchglass and allow them to air-dry. The time for air-drying the sample may require that it be left in your lab drawer until the next laboratory period.

Determine the mass of the dry filter paper and sample. Dispose of the filtrate in the sink.



7. Correct for Residual Solubility. The solubility of acetylsalicylic acid is 0.25 g per 100 mL of water. Correcting for this inherent loss of product, calculate the percent yield.

8. What Do You Do with It? Don't use it for a headache! Place the sample in a

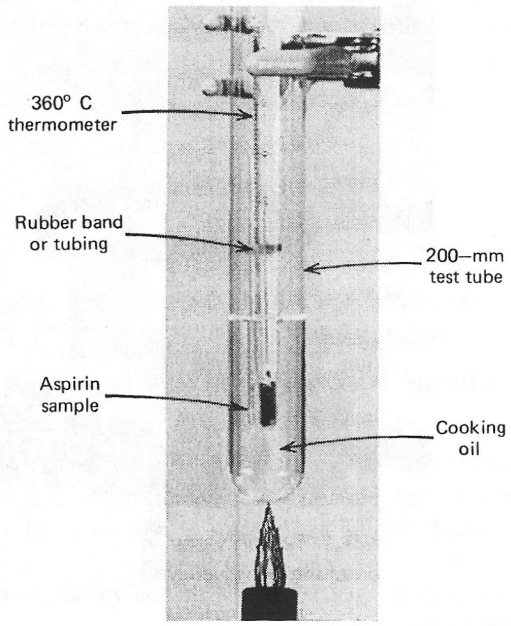


Figure 29.2 Melting point apparatus for aspirin.

properly labeled test tube, stopper, and submit it along with your Report Sheet to your laboratory instructor at the conclusion of the experiment.

B. Melting Point of the Aspirin Sample

1. Prepare the Sample. Fill a capillary melting point tube to a depth of 1 cm (see Figures 2.2 and 2.3) with the recrystallized aspirin prepared in Part A.6. Attach the tube to a 360°C thermometer with a rubber band (or band of rubber tubing). Place the sample alongside the thermometer bulb (Figure 29.2). As the melting point for aspirin is greater than 100°C, oil must be used for the heating bath.

2. Determine the Melting Point. Slowly heat the oil bath at a rate of 5°C per minute until the aspirin melts. (**Caution:** *the oil bath is at a temperature greater than 100°C—do not touch!*) Cool the bath and aspirin to just below this approximate melting point until the aspirin in the tube solidifies; at a slower 1°C per minute rate, heat again until it melts; this is the melting point of your prepared aspirin.

3. Repeat the Melting Point Measurement. Again, cool the bath and aspirin to just below the melting point until the aspirin in the tube solidifies; at a 1°C per minute rate, heat again until it melts.

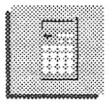
Disposal: Ask your instructor about proper disposal of the oil. Be sure the oil is cool when handling it.

C. Percent Acetylsalicylic Acid in the Aspirin Sample

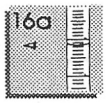
Three trials are to be completed in the analysis of the aspirin. Prepare three clean 125- or 250-mL Erlenmeyer flasks and determine the mass of all three aspirin samples while occupying the balance. Obtain a 50-mL buret from the stockroom.

1. Prepare the Aspirin Sample for Analysis. Assuming 100% purity of your aspirin

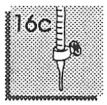
sample, calculate the mass of aspirin that requires 20 mL of 0.1 *M* NaOH to reach the stoichiometric point. On weighing paper measure the calculated mass (±0.01 g) of the aspirin you have just prepared (or a crushed commercial aspirin tablet) and transfer it to the flask. Add 10 mL of 95% ethanol, followed by about 50 mL of deionized water, and swirl to dissolve the aspirin. Add 2 drops of phenolphthalein indicator.



2. Prepare the Buret for Titration. Prepare a clean buret, rinse, and fill it with a standardized 0.1 *M* NaOH solution.[1] Be sure that no air bubbles are present in the buret tip. After 30 seconds, read and record the volume (±0.02 mL) and the actual molar concentration of the NaOH solution.



3. Titrate the Sample. Slowly add the NaOH solution from the buret to the dissolved aspirin sample, swirling the flask (with the proper hand[2]) after each addition. Initially, add the NaOH solution in 1- to 2-mL increments. As the endpoint nears, the color fade of the indicator occurs more slowly (see color plate). Occasionally rinse the wall of the flask with (previously boiled, deionized) water from your wash bottle. Continue addition of the NaOH titrant until the endpoint is reached. The endpoint in the titration should be within one-half drop of a faint pink color. The color should persist for 30 seconds. After 30 seconds, read and record the final volume of NaOH in the buret.



Disposal: Discard the test solution in the sink followed by a generous supply of water.

CLEANUP: Discard the NaOH titrant into a properly labeled bottle; rinse the buret with several 5-mL volumes of tap water, followed by two 5-mL volumes of deionized water.

[1]You may need to prepare the 0.10 *M* NaOH solution using the procedure in Experiment 9, or the stockroom personnel may have it already prepared.
[2]Check Technique 16C of the laboratory manual.

Experiment 29 *Prelaboratory Assignment*

Aspirin Synthesis and Analysis

Date _____ Lab Sec. ____ Name _____ Desk No._____

1. What is an antipyretic?

2. What is an analgesic?

3. What is the "active ingredient" in aspirin? Why is it *not* ingested directly?

4. In this experiment, 2.00 g of salicylic acid reacts with an excess amount of acetic anhydride. Calculate the theoretical yield of acetylsalicylic acid for this synthesis.

5. A 0.331-g sample of aspirin prepared in the laboratory was dissolved in 95% ethanol and titrated to a phenolphthalein endpoint with 16.7 mL of 0.107 *M* NaOH.
   a. Calculate the moles of acetylsalicylic acid in the aspirin sample.

   b. What mass (g) of acetylsalicylic acid is present in the aspirin sample?

   c. Calculate the percent purity of the aspirin sample.

Experiment 29 *Report Sheet*

Aspirin Synthesis and Analysis

Date _____ Lab Sec. _____ Name _____ Desk No._____

A. Preparation of Aspirin

1. Mass of salicylic acid (g) _____
2. Theoretical yield of aspirin (g) _____
3. Experimental yield of aspirin (g) _____
4. Experimental yield, corrected for solubility (g) _____
5. Percent yield (%) _____

B. Melting Point of the Aspirin Sample

1. Melting point measurements (°C) _____ _____ _____

C. Percent Acetylsalicylic Acid in the Aspirin Sample

Calculation for the mass of aspirin for the titrimetric analysis

	Trial 1	*Trial 2*	*Trial 3*
1. Mass of weighing paper plus aspirin sample (g)			
2. Mass of weighing paper (g)			
3. Mass of aspirin sample (g)			
4. Molar concentration of the NaOH solution (mol/L)			
5. Buret reading, *final* (mL)			

6. Buret reading, *initial* (mL) _____ _____ _____

7. Volume of NaOH used (mL) _____ _____ _____

8. Amount of NaOH added (mol) _____ _____ _____

9. Amount of acetylsalicylic acid (mol) _____ _____ _____

10. Mass of acetylsalicylic acid (g) _____ _____ _____

11. Percent acetylsalicylic acid in aspirin sample (%) _____ _____ _____

12. Average percent acetylsalicylic acid in aspirin sample (%) _____

Class Data/Group	1	2	3	4	5	6
Average percent acid in sample						

Determine the average deviation of the percent acetylsalicylic acid in aspirin from the class data. See Appendix B.

Laboratory Questions

Circle the questions that have been assigned.

1. What can you conclude if your dry aspirin sample has a lower melting point than the literature value?
2. If the yield of your dry aspirin is greater than 100%, what must you do experimentally to obtain a more reasonable yield?
3. Can a water bath be substituted for the oil bath in Part B? Explain.
4. Would the product isolated after Part A.4 have a higher or lower melting point than that isolated after Part A.6?
5. If the endpoint is surpassed in the analysis of the aspirin sample in Part C, will its percent purity be reported too high or too low? Explain.