Chemistry 104: Synthesis of Aspirin

INTRODUCTION

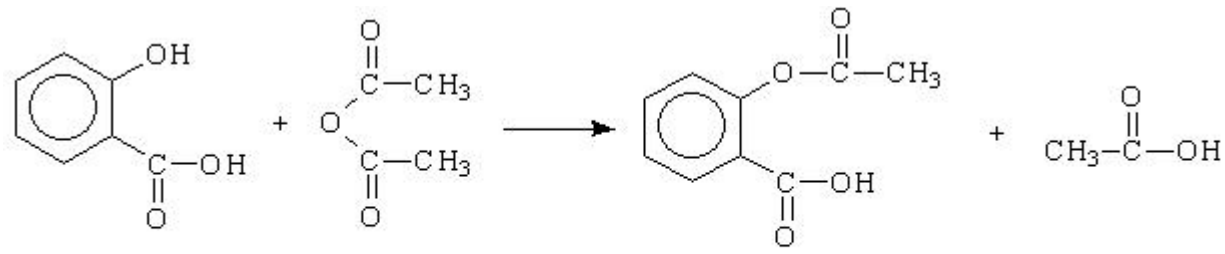
Aspirin (acetylsalicylic acid) is a synthetic organic derived from salicylic acid. Salicylic acid is a natural product found in the bark of the willow tree and was used by the ancient Greeks and Native Americans, among others, to counter fever and pain. However, salicylic acid is bitter and irritates the stomach.

A German chemist named Felix Hoffman is credited with being the first to synthesize aspirin in 1897. Hoffman's father had severe arthritis but could not tolerate salicylic acid he was taking for pain relief. The name given for Hoffman's new compound was **A-spirin**. Apparently this comes from acetylation (**A-**), together with **Spirin**, part of the name for Meadow-sweet (Spiraea ulmaria), a plant rich in salicylates.

Friedrich Bayer, the employer of Hoffman, patented the name and began marketing the product in 1899. It was a huge success and sales grew rapidly. Bayer's company set up by himself, is generally reckoned to have been the first pharmaceutical company, and the production of aspirin is generally accepted to have laid the foundation of the modern pharmaceutical industry.

In this experiment you will synthesize aspirin (acetylsalicylic acid, $C_9H_8O_4$), purify it, and determine the percent yield. The purity of the product will be confirmed by qualitative analysis and by measuring its melting point range.

The reaction that is used for the synthesis is shown below. In this reaction, an excess of acetic anhydride ($C_4H_6O_3$) is added to a measured mass of salicylic acid ($C_7H_6O_3$) in the presence of a catalyst, sulfuric acid (H_2SO_4). The mixture is heated to form the acetylsalicylic acid ($C_9H_8O_4$) and acetic acid ($C_2H_4O_2$). After the reaction takes place, water is added to destroy the excess acetic anhydride and cause the product to crystallize. The aspirin is then collected, purified by recrystallization, and its melting temperature measured.



SAFETY CONSIDERATIONS

Wear goggles throughout this experiment. This experiment uses salicylic acid, acetic anhydride and phosphoric acid. The salicylic acid and aspirin may cause irritation to your skin or eyes, but are basically not hazardous. An excess of these can be disposed of in the sink or, if packaged, in the trash. If you spill some, wipe it up with a wet paper towel and throw the towel in the trash. The acetic anhydride and sulfuric acid can cause bad burns.

Use them only in the hood and be sure the hood fan is on! Wear gloves when using these chemicals. Excess chemicals must be disposed of in the plastic tub of water. This will convert the acetic anhydride to vinegar and dilute the sulfuric acid. If you spill a lot of either of these, notify your instructor.

EXPERIMENTAL PROCEDURE FOR SYNTHESIS OF ASPIRIN

1. **PUT ON YOUR CHEMICAL SPLASH-PROOF SAFETY GOGGLES!**
2. **Adding The Starting Materials**

A. Using a **weigh boat**, weigh out 5.00 g (± 0.01 g) of salicylic acid ($C_7H_6O_3$). Transfer this to a **125 mL Erlenmeyer flask** using a **powder funnel**. Record this mass on the Data Sheet.

B. Using the **graduated cylinder** located under the hood, measure out 7.00 mL of acetic anhydride and add this to the flask. Be sure to do this in the hood and wearing your goggles. Don't let the acetic anhydride

contact your skin and don't get the vapors in your eyes.

C. Carefully add 8 drops of concentrated sulfuric acid (18 M H_2SO_4), a catalyst, to the flask.

3. **Heating The Starting Materials**

A. At your lab bench, assemble a **hot water bath** using a **600 or 800 mL beaker** and place the flask in the water bath as shown in Figure 1. Make sure that the water bath is located directly under the hood at your lab bench.

B. Place the flask in the water bath and heat. **After** the water begins to boil, heat for an additional 15 minutes. (NOTE: The hot water bath will be used again later in the procedure.)

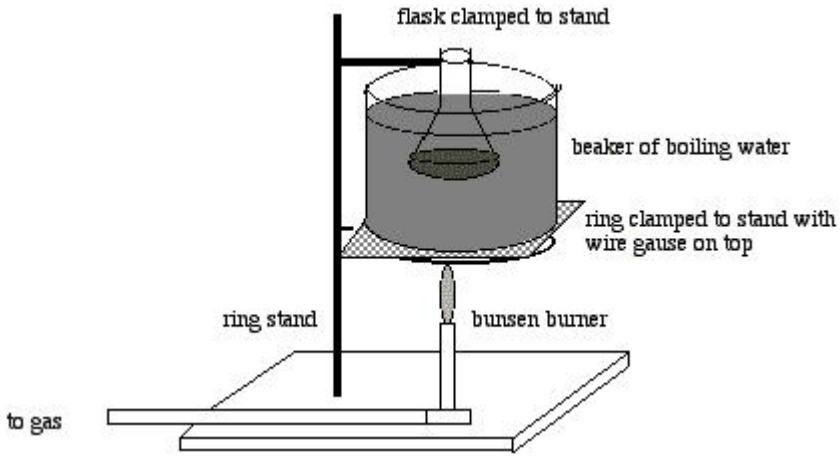


Figure 1.

4. **Cooling The Reaction Mixture**

A. After heating, turn the bunsen burner off and **CAREFULLY** remove the flask from the water bath (remember it is hot!) and allow the flask and contents to cool on the lab bench for about 3 minutes.

B. After the flask has cooled for about 3 minutes, **CAUTIOUSLY** add 15 mL of room temperature water to the flask to facilitate the decomposition of the excess acetic anhydride. Swirl the flask to mix the contents.

C. Label your flask containing the reaction mixture and place it in an **ice bath** and cool until the crystallization of the aspirin appears complete (approx. 15 min.). If crystals do not appear, you can scratch the walls of the flask with a stirring rod to induce crystallization.

5. **Isolating The Product**

A. Collect the solid aspirin using a **Buchner funnel** and filter paper as shown in Figure 2. Be sure to seat the filter paper in the filter with a small amount of water.

B. Rinse the flask twice with 3 mL of ice cold water to remove any residual crystals.

C. Discard the filtrate left in the filter flask into the waste container under the hood.

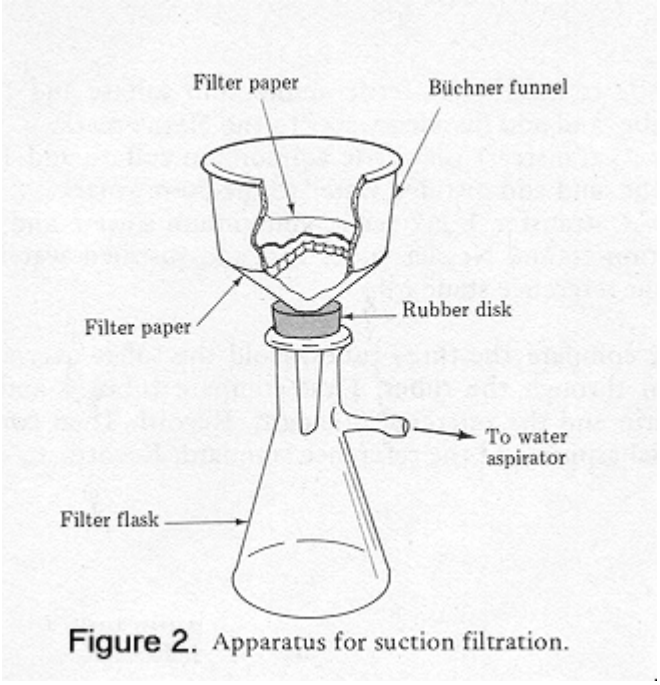


Figure 2. Apparatus for suction filtration.

6. **Recrystallizing The Aspirin**

A. Transfer as much of the solid as possible from the Buchner funnel to a clean, dry **250 mL beaker**.

B. Add 10 mL of 95% ethanol to the beaker and if necessary, warm (do not boil!) the mixture in the water bath to dissolve the crystals. If the crystals do not all dissolve, add 2 mL more of the ethanol and continue to warm the mixture to dissolve the crystals.

C. When the crystals are all dissolved, add 10 mL of deionized water, cover the beaker with a **watch glass**, and allow the solution to cool slowly on the lab bench undisturbed for about 10 minutes.

D. After the 10 minutes cooling on the lab bench, complete the crystallization by placing the beaker and contents in the ice bath. (Label your beaker!) Crystals should form. If an "oil" appears instead of a solid, reheat the beaker in the hot water bath until the oil disappears. If crystals do not appear, you can scratch the bottom of the beaker with a stirring rod to induce crystallization.

7. **Drying The Purified Aspirin**

A. Using a clean circle of filter paper, collect the purified aspirin by suction filtration as before.

B. Dry the crystals by pulling air through them for about 15 minutes. (Discard the filtrate left in the filter flask into the waste container under the hood. Rinse the filter flask with water and discard the rinse water into the waste container under the hood.)

C. Place the aspirin onto a doubled piece of paper towel and set aside to dry while performing the qualitative analysis of the aspirin. (Wash the filter funnel with water and discard the rinse water into the waste container under the hood.)

8. **Analyzing the Aspirin Quality**

A. The presence of unreacted salicylic acid in the synthesized aspirin can be detected with the **iron(III) chloride test**.

1. Add about 1 mL of deionized water to five clean 10-cm test tubes. Using a clean stirring rod, place a crystal of salicylic acid into the first test tube. In the second, place a crystal of powdered commercial aspirin, and in the third, place a crystal of your synthesized aspirin. The forth test tube is the control.

2. To each test tube add 1 drop of iron(III) chloride) solution. Shake each test tube and observe the colors produced. Record your observations and conclusions on the Data Sheet.

B. Measure the melting point range of your synthesized aspirin with the Meltemp Apparatus as demonstrated by your lab instructor and compare to the value for pure aspirin of 138-140 ^{o}C. Record the melting temperature on the Data Sheet.

9. **Calculating the Percent Yield of Aspirin**

A. Weigh the aspirin and calculate the theoretical (maximum) yield. [Note: The acetic anhydride is in excess and the salicylic acid is the limiting reagent. Use the salicylic acid to calculate the theoretical yield.]

B. Based on your percent yield, iron(III) chloride test, and the measured melting point range, draw a conclusion about the success of your synthesis.

C. Place your aspirin in the jar labeled "Student Prep Aspirin".

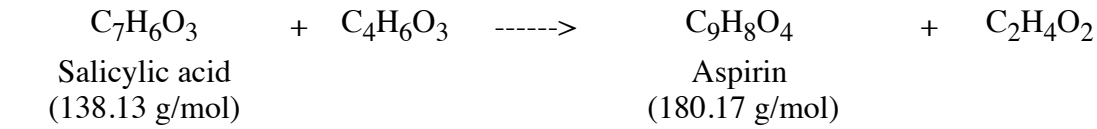
Chemistry 104: Synthesis of Aspirin

Name _____ Hood No. _____ Date _____

PUT ON YOUR CHEMICAL SPLASH-PROOF SAFETY GOGGLES!

Show all calculations.

grams of salicylic acid ($C_7H_6O_3$)	
moles of salicylic acid	
Theoretical yield of aspirin in grams ($C_9H_8O_4$)	
Actual yield of aspirin in grams ($C_9H_8O_4$)	
Percent yield aspirin ($C_9H_8O_4$)	



CALCULATIONS:

IRON (III) CHLORIDE TEST

Test Tube #	Color **BEFORE** adding iron(III) chloride	Color **AFTER** adding iron(III) chloride)
# 1 (salicylic acid)		
# 2 (commercial aspirin)		
# 3 (prepared aspirin)		
# 4 (control)		

Observed melting point of aspirin. _____ ^{o}C

CONCLUSIONS ABOUT PURITY OF ASPIRIN: