Experiment: Synthesis of Aspirin

Background

"Aspirin, which ranks as the most widely used drug in the United States, is one of a series of salicylic acid esters that has been known since antiquity to have therapeutic effects. In fact, many cultures have used plants containing significant amounts of these compounds in medications to relieve pain (analgesic), reduce fever (antipyretic), and decrease inflammation and swelling.

Until the turn of the century the compounds were extracted from the leaves and barks of plants. However, in the late 1900's in Germany, the Bayer Co. began chemical production of the acetyl ester of salicylic acid, which they trademarked as "aspirin". The generic form of this drug is commonly called acetylsalicylic acid (ASA). Another ester of salicylic acid, the methyl salicylate, commonly known as oil of wintergreen, is absorbed through the skin; it constitutes the active ingredient in many liniments and analgesic creams.

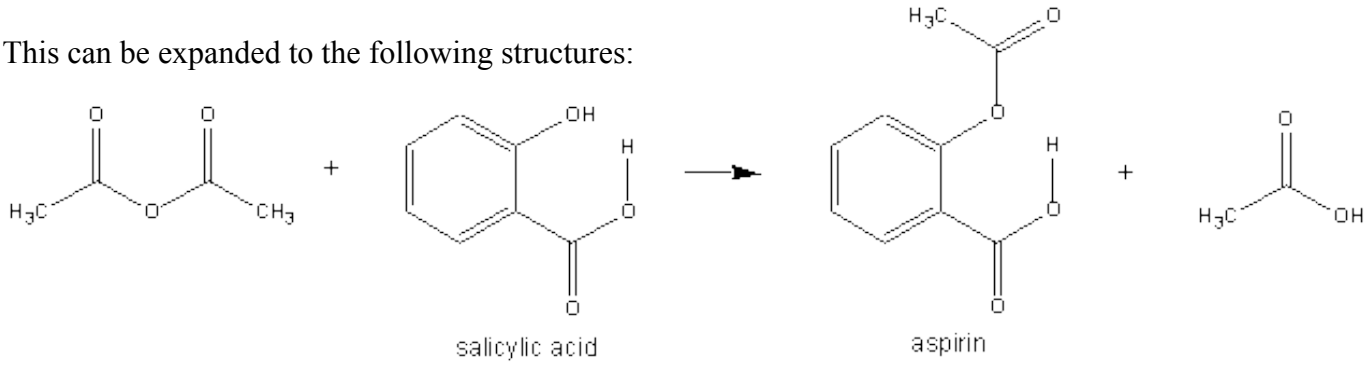
In addition to the three main uses for aspirin, recently it has been found to have other beneficial uses. Low daily doses (one tablet) can lessen the chance of heart attack in patients with certain heart problems and this dosage appears to reduce the occurrence of stroke in some men. The acidic nature of the compound, however, is known to irritate the stomach and/or cause ulcers in many people. As a precaution, many people routinely take a buffered form of aspirin to neutralize the acid as the tablet dissolves. Other side effects are also known. Reports have suggested that the use of aspirin in children and teenagers with fever due to a viral infection (especially flu or chicken pox) may cause Reye's syndrome, a serious brain illness. Aspirin is also not advised as a medication within two weeks before surgery, childbirth, or dental extractions as it may cause serious bleeding problems."[1]

Purpose

In this experiment you will synthesize aspirin from acetic anhydride and salicylic acid using phosphoric acid as a catalyst to speed up the reaction (it is not a reactant or product in the overall equation). The reaction for the synthesis is given below.

$$\underset{\text{Acetic Anhydride}}{\mathbf{C_4H_6O_3}} + \underset{\text{Salicylic Acid}}{\mathbf{C_7H_6O_3}} \xrightarrow{H_3PO_4} \underset{\text{Aspirin}}{\mathbf{C_9H_8O_4}} + \underset{\text{Acetic Acid}}{\mathbf{HC_2H_3O_2}}$$

This can be expanded to the following structures:



Note: Carbons (and hydrogens) are implied where lines (bonds) meet.

[1] Taken from Synthesis and Analysis of Aspirin, UCLA Chemistry Department

Warning: The aspirin you are making is relatively impure and should not be taken internally.
Safety Hazards: Both acetic anhydride and phosphoric acid can cause bad burns if you get them on your skin. Handle these chemicals with care.

Experimental Procedure

1) Measure out 2.0 g of salicylic acid (SA) and place the SA in to a 50-mL Erlenmeyer flask.

2) Measure out 5.0 mL of acetic anhydride (d = 1.08 g/mL) in a graduated cylinder and then pour it into the flask in such a way as to wash any crystals of SA on the walls down to the bottom.

3) Add 5 drops of 85% phosphoric acid to serve as a catalyst.

4) Clamp the flask in place in a beaker of water supported on wire gauze on a ring stand. Using a thermometer clamp, suspend a thermometer in the water bath. Heat the water with a Bunsen burner to about 75^0C, stirring the liquid in the flask occasionally with a glass stirring rod. **DO NOT OVERHEAT THE FLASK!!!!!** Maintain this temperature for 15 minutes. **Draw a picture of your assembled apparatus setup in your lab notebook.**

5) Cautiously add 2 mL of distilled water to the flask to decompose any excess acetic anhydride. There will be some hot acetic acid vapors evolved so be careful. Wait 2 minutes, then remove the flask from the water bath and add 20 mL of distilled water.

6) Let the flask cool in the air for a few minutes. You should start to see aspirin crystals start to form. Put the flask in an ice bath to hasten crystallization. If the crystals are slow to appear scratch the inside of the flask with the glass stirring rod. This will give the crystals a surface to grow on. Leave the flask in the ice bath AT LEAST 4 to 6 minutes. In the next step, you will be collecting the aspirin crystals by filtration. Secure a filtration flask (Erlenmeyer flask with a side port) to a ring stand using a large clamp. Attach the side port of the filtration flask to the vacuum line using a thick-walled rubber hose. Obtain a 7.5-cm diameter circular filter paper and write your name on it using a pencil. **Record the mass of the filter paper.**

7) Place your filter paper in a Büchner funnel. Place a rubber gasket on top of the filtration flask. Insert the Büchner funnel. Pour some distilled water onto the filter paper to make the filter paper lay flat on the bottom of the Büchner funnel. **Sketch the setup with labels in your notebook.** Open the vacuum valve and adjust to obtain light suction. Pour all of the aspirin mixture into the center of the funnel. Use distilled water as necessary for the transfer and also to rinse the solid aspirin. Turn off the suction and add about 5 mL of **ice-cold distilled** water to the crystals. After 15 seconds turn the suction back on. Repeat the washing process with another portion of **ice-cold distilled** water. Let the suction run for a couple minutes. **Record the mass of a petri dish** and label this with your name. Use forceps to carefully transfer the filter paper with aspirin to the petri dish. Place your aspirin in the tray to dry till next week.

8) **Record the total mass (mass of the petri dish + filter paper + dried aspirin) next week.** Calculate the mass of aspirin and determine the percent yield.

Data: Record data in your lab notebook. Include the mass of salicylic acid, volume of acetic anhydride, density of acetic anhydride (see above for value), mass of filter paper, mass of petri dish, mass of petri dish + filter paper + aspirin, mass of aspirin obtained. Include observations.

REPORT SHEETS: SYNTHESIS OF ASPIRIN

Show your work. Keep one to two extra digits in your calculation steps. Round calculated values to the proper number of significant figures for each value you are asked to report.

1) Determine the limiting reactant.

   a) What is the mass of salicylic acid used? _____ g SA

   b) How many moles of salicylic acid was used? _____ moles SA

   c) What is the mass of acetic anhydride used? _____ g AA

   d) How many moles of acetic anhydride was used? _____ moles AA

   e) Write the chemical equation for the reaction of salicylic acid with acetic anhydride to form aspirin and acetic acid.

   f) What is the mole ratio of salicylic acid to acetic anhydride in the equation? ____ : ____

   g) Based on parts a-e above, which is the limiting reactant? _____

2) Using the information above, determine the theoretical yield of aspirin:

   a) How many moles of limiting reactant were consumed if it reacted completely?

   _____ moles

b) How many moles of aspirin should have been produced if there was 100% yield? _____ moles aspirin

c) How many grams of aspirin should have been produced if there was 100% yield? _____ grams aspirin (Theoretical Yield)

d) How many grams of aspirin were you able to isolate in your experiment?

_____ grams aspirin (Actual Yield)

e) What is the percent yield of aspirin you obtained in this experiment?

$$\% \text{ yield} = \frac{\text{actual yield}}{\text{theoretical yield}} \times 100$$

_____ % yield

Follow-up Questions

Suppose your percentage yield was less than 100%. Provide **two** possible reasons why this may have occurred.

Suppose your percentage yield was greater than 100%. Provide at least **one** possible reason why this may have occurred.

SYNTHESIS OF ASPIRIN
Pre-Lab Assignment

Study the sections related to stoichiometry and limiting reactant in your textbook. If you need guidance, follow the steps in the Report Sheets.

1) A student prepared aspirin using 2.019 g of salicylic acid and 5.2 mL of acetic anhydride (d = 1.08 g/mL).

   a. Which reactant is limiting, salicylic acid or acetic anhydride?

   b. What is the theoretical yield of aspirin?

   c. If the student obtained 1.789 g of aspirin, what is his percent yield?

   d. How many grams of excess reactant are used in the reaction?

   e. How many grams of excess reactant are left over at the end of the reaction?

   f. At the end of reaction, how many grams of each reactant and product will be theoretically (ideally) present in the reaction mixture?

Salicyclic acid _____ g	Aspirin _____ g
Acetic anhydride _____ g	Acetic acid _____ g (optional!)