Synthesis of Aspirin and Oil of Wintergreen

Cautions

Acetic Anhydride – corrosive and a lachrymator – all transfers should be done in the vented fume hood

Methanol, *Ethanol* – flammable and highly toxic

Salicylic Acid – toxic and irritant

Sulfuric Acid, *Phosphoric Acid* – highly toxic, corrosive, and an oxidant

Purpose

To synthesize acetylsalicylic acid (aspirin) and methyl salicylate (oil of wintergreen) to review the concepts of theoretical and percent yields.

Introduction

Organic chemistry plays a vital part in the chemical industry as it is used in making petroleum products, polymers/plastics, pharmaceuticals, and health and beauty aids. Many everyday products are primarily comprised of organic molecules.

Organic molecules are classified by how different atoms are arranged in their structures. For examples, all alcohols contain a carbon atom bound to an OH group; for example, methyl alcohol is CH_3OH. Aspirin and oil of wintergreen are esters. An ester is an organic compound that contains the molecular connectivity shown in **Figure 1**. Esters tend to be volatile and have pleasant odors. This class of organic molecules is responsible for the inviting aromas and fragrances of fruits and flowers. The cosmetic industry has exploited the use of esters in the production of cosmetics and perfumes. The food and pharmaceutical industry also use esters in the form of flavoring agents in solid and liquid products.

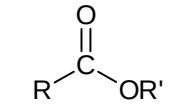
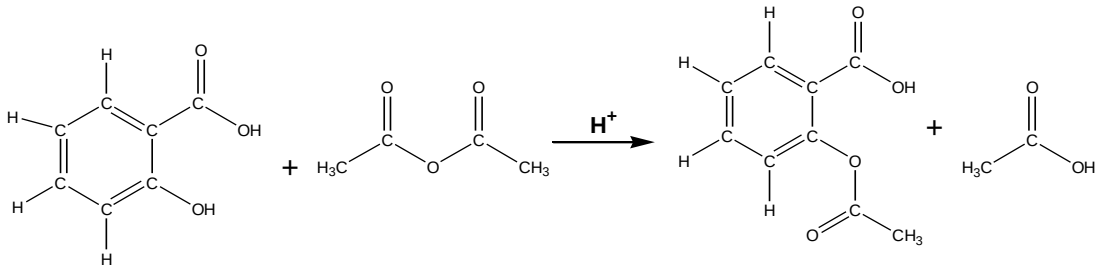


Figure 1: *The general structure of an ester*

Aspirin is the most widely used medical compound in the world. Aspirin, known chemically as acetylsalicylic acid, is a white solid that has a very low solubility in water (0.25 g in 100 ml of water). A regular strength aspirin tablet contains 325 mg of acetylsalicylic acid held together with an inert binder such as starch. Aspirin is derived from salicylic acid which occurs naturally in the bark of willow trees. This reaction is shown in **Reaction 1**. Both aspirin and salicylic acid are important due to their analgesic (pain reliever) and antipyretic (fever reducer) properties. Aspirin is less acidic than salicylic acid which helps in the reducing the number of stomach, mouth, and mucus membrane irritations. Therefore, it is used instead of salicylic acid. However, some people find that aspirin is still too acidic and may opt for some of the less acidic alternatives such as Tylenol (acetaminophen) or Advil (ibuprofen). It is believed that all of these compounds act within the human body to inhibit the production of prostaglandins, which are used in the perception of pain.

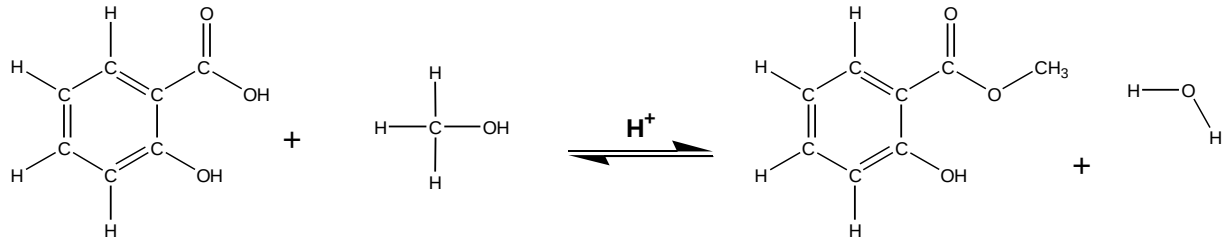


Salicylic Acid **Acetic Anhydride** **Acetylsalicylic Acid** **Acetic Acid**

Reaction 1: *The reaction between salicylic acid and acetic anhydride to form aspirin.*

Synthesis of Aspirin and Oil of Wintergreen

Methyl salicylate is the active ingredient in Oil of Wintergreen; its synthesis reaction is shown in **Reaction 2**. It has a very distinct minty odor. As a derivative of salicylic acid, it is used commonly in ointments for the relief of muscle pain and cramping because it can penetrate the skin. Oil of wintergreen is also used as a flavoring agent in commercial food products.



Reaction 2*: The reaction between salicylic acid and methanol to form methyl salicylate*

During this experiment, two organic esters, acetylsalicylic acid (aspirin) and methyl salicylate (oil of wintergreen) will be synthesized. The percent yield of the aspirin will then be calculated using the equation below.

$$\text{percent yield} = \frac{\text{experimental yield (g)}}{\text{theoretical yield (g)}} \times 100$$

Synthesis of Aspirin and Oil of Wintergreen

Procedure

Synthesis of Aspirin

1. Prepare a hot water bath by placing 250 mL of tap water in a 400 or 600 mL beaker on a ring stand and heating to 70-85 °C using a Bunsen burner flame. Continue on to steps 2 - 4 while heating.
2. Place 75 mL of DI water into a small Erlenmeyer flask; and place this flask into a large beaker of ice water. This will be used in steps 7 and 8. Continue on to steps 3 - 6 while the water is being chilled.
3. Weigh 2.5 ± 0.25 grams of salicylic acid into a 125-mL Erlenmeyer flask. Record the weight of the salicylic acid on the data sheet.
4. Carefully add 5.0 mL of acetic anhydride to the flask along with 7 drops of phosphoric acid ***in the hood***. Swirl the flask carefully to ensure mixing of the reagents.
5. Place the flask in the hot water bath and secure the flask to the ring stand using a utility clamp (see **Figure 2**). Heat the solution for 20 minutes, stirring occasionally using a glass stirring rod.
6. After heating, remove the flask carefully and immediately add 2.0 mL of DI water to the flask ***in the hood***. The addition of the water will react with any excess acetic anhydride to convert it to acetic acid. Avoid inhaling the acetic acid vapors.
7. Add 30.0 mL of the cold DI water from step 2 to the flask. Then place the flask in an ice bath to complete the aspirin crystallization process for at least 10 minutes.

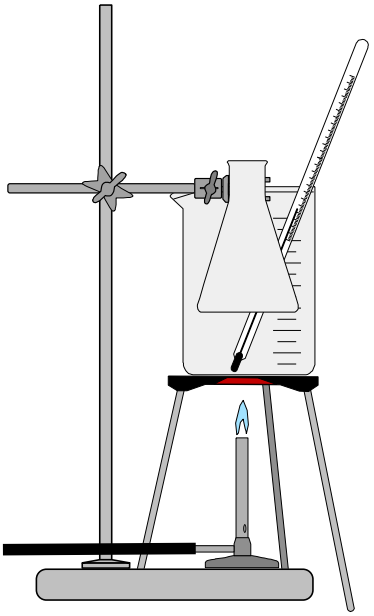


Figure 2: *The experimental setup for the aspirin reaction.*

8. Collect the crystals by vacuum filtration using a Büchner funnel. See **Figure 3** for the Buchner funnel setup. Use the heavy black tubing to connect the flask to the house vacuum line. Before pouring any of the crystallized aspirin through the funnel, dampen the filter paper with a spray of DI water. Rinse all product from the sides of the Erlenmeyer flask using small amounts of DI water. After all solid has been transferred to the funnel, wash the crystals with a small amount of the cold DI water remaining from step 2. Let the crystals dry on the filter paper with the vacuum for at least 10 minutes or until the crystals are dry.
9. Weigh and record the actual yield of aspirin.
10. Calculate the theoretical yield and percent yield of aspirin.

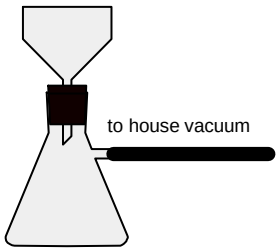


Figure 3: *Buchner funnel setup.*

Synthesis of Aspirin and Oil of Wintergreen

Synthesis of Oil of Wintergreen

1. Weigh 0.25 grams of salicylic acid into a 10-15-cm test tube. *This weight does not need to be recorded.*
2. Add 2.0 mL of methanol to the test tube and swirl until the solid dissolves.
3. Slowly add 10 drops of sulfuric acid.
4. Place the test tube in a hot water bath and secure by using a utility clamp and heat for 15 minutes.
5. Cool the test tube in running water.
6. Smell the contents by wafting (wave a hand over the top of the test tube to direct any fumes) and record any observations.

Disposal

Place all waste and compounds in the appropriate labeled waste bottles in the laboratory.

Clean-Up

Wash all glassware with soap then rinse 3 times with tap water, and once with deionized water.

Synthesis of Aspirin and Oil of Wintergreen

Data Sheet

Name: _____ **Lab Partner**_____

Show all calculations on a separate sheet of paper and attach to the lab.

Synthesis of Aspirin:

	DATA
Mass of Salicylic Acid (g)	
Moles of Salicylic Acid (mol)	
Volume of Acetic Anhydride (mL)	
Moles of Acetic Anhydride (mol) **(Density = 1.081 g/mL)**	
Mass of Aspirin collected (g)	
Moles of aspirin collected (mol)	
Theoretical Yield (label with units!)	
Percent Yield	
Observations:	

Synthesis of the Oil of Wintergreen:

	Observations
Color	
Smell	
Other Characteristics	

Synthesis of Aspirin and Oil of Wintergreen

Post-Lab Questions

Name: _____

1. A student obtains a yield of 79% from his salicylic acid. How many grams of salicylic acid will the student need to produce 135 g of aspirin?

2. Based on the percent yield obtained in this experiment, how much salicylic acid would be needed as starting material to produce 35.00 g of aspirin?

3. What steps could have been taken to improve the percent yield of aspirin?

Synthesis of Aspirin and Oil of Wintergreen

Pre-lab Assignment

Name: _____

1. Briefly define the following terms:

    a. Analgesic

    b. Antipyretic

2. A student begins with 2.22 g of salicylic acid (MW = 138 g/mol) and 4.04 mL of acetic anhydride (MW = 102 g/mol density = 1.081 g/mL) in the preparation of aspirin. Show any calculations in the space below.

    a. How many moles of salicylic acid were used? _____

    b. How many moles of acetic anhydride were used? _____

    c. Which compound is the limiting reagent in the preparation of aspirin? _____

    d. Calculate the theoretical yield for the reaction in **moles** and in **grams** of aspirin.