ASPIRIN SYNTHESIS*

Lab Overview

The natural precursor to aspirin is an organic compound named salicylic acid. Salicylic acids and its esters are found in several plants, including willow tree. The entire willow plant contains pain-killing components (called analgesics), but the highest concentrations are found in the inner bark. Although willow bark and leaves have been used for centuries as natural treatments to relieve pain and fever, it wasn't until the 1800's that salicin, the active component from willow, was isolated. The aspirin precursor, salicylic acid, is derived from salicin. However, salicylic acid is not used as extracted (due to its irritating effects on the stomach lining) and instead it undergoes a chemical transformation in order to form the aspirin (acetylsalicylic acid).

Synthesis of aspirin: the chemical transformation from salicylic acid to aspirin is an esterification reaction. Esters are formed by acid-catalyzed reactions between an alcohol and a carboxylic acid (an organic acid). To form the acetylsalicylic acid (aspirin) in this experiment, salicyclic acid is reacting as an alcohol and the acetic anhydride is reacting as if it were a carboxylic acid (the chemical equation will be provided and explained by your TA).

Materials:

- 125-mL Erlenmeyer flask, 400-mL beaker, heat source, dispensing pipet, crystallization dish, glass rod, 10-mL and 100-mL graduated cylinders, Büchner funnel, filter flask, test tubes

Reagents:

- Salicylic acid, acetic anhydride, conc. sulfuric acid, 4% phenol solution, 2.5% iron (III) chloride (aka ferric chloride) solution. ***CAUTION: Concentrated sulfuric acid is highly corrosive; it must be handled with extreme care. Acetic anhydride must be handled with extreme care.***

Experimental Procedure: Part I. Synthesis of aspirin

1) Using your 400-mL beaker, set up a water bath and begin heating the water with a heat source. Water should be hot (reach a temperature above 60-70 °C) but the actual temperature is not critical hence no thermometer is needed.

2) While your water bath is heating, weigh 2.0 g (0.015 mole) of salicylic acid crystals and place them in a 125-mL Erlenmeyer flask. Add, 5 mL (0.05 mole) of acetic anhydride, followed by 5 drops of concentrated sulfuric acid (in exactly this order!). Gently swirl the flask until the salicylic acid dissolves.

3) Heat the Erlenmeyer flask gently by partially immersing it in the water bath for 10-15 min.

* Reference: D. Guinn and R. Brewer, Essentials of General, Organic, and Biochemistry. A Lab Manual

4) Remove the flask from the water bath and allow it to cool down to room temperature on the bench. Upon cooling down, the acetylsalicylic acid should begin to crystallize from the reaction mixture (if crystals do not appear, scratch the inside walls of the flask with a glass rod; scratches on the inside of your flask will create a rough surface that will promote crystal formation).

5) Cool the mixture slightly in an ice bath until complete crystallization has occurred. If crystallization has completely failed to occur (even after scratching and cooling on ice), you may use a seed crystal from your TA to create a nucleation site, from which your crystals can grow.

6) After crystallization is complete, add 50 mL of water to your crystals and cool the mixture again in an ice bath. Your product will usually appear as a solid mass when crystallization is complete.

7) Collect the product by vacuum filtration using a Büchner funnel. You might need to rinse your Erlenmeyer flask to transfer all crystals on the filter; you can use the filtrate for this purpose. Rinse the collected crystals (in the filter) with small portions of cold water (3-4 times). After rinsing, allow crystals to dry under vacuum (by continuing to draw air through the filter).

8) Weigh your product (called crude product). Note that the crude product may contain unreacted salicylic acid.

<u>Part II: Purity Testing</u>

- To test the purity of your product, set up three test tubes:

1. Test tube 1 with 5 mL water and 10 drops 4% phenol
2. Test tube 2 with 5 mL water and a few crystals of salicylic acid
3. Test tube 3 with 5 mL water and a few crystals of your product

- Next, add 10 drops of a 2.5% iron(III) chloride solution to each tube and note the color. Salicylate and salicylic acid do not absorb visible light, creating an experimental challenge for their identification. However, upon reaction with iron (III) ions, salicylic acid forms a deeply colored species. Thus the addition of excess iron(III) to a solution of salicylate generates a deep purple solution, indicating the formation of an iron(III)-phenol complex. The presence of the purple species in test tube 3 is thus an indication of an impurity (unreacted material).

Name_____

Lab Data Sheet and Post-lab: ***Submit this page to bblearn***

Part I: Synthesis of aspirin

1. Record the mass of salicylic acid used and the mass of your product:

Mass salicylic acid: _____ Mass aspirin (product): _____

2. Calculate the theoretical yield of acetylsalicylic acid (aspirin). This is the maximum amount of product that can be formed form your reagents. It is based on the amount of reactants and the stoichiometry of the balanced reaction. _____grams

a. Calculate moles of salicylic acid (aspirin)_____

You started with 0.05 moles of acetic anhydride in this experiment. Which reactant is the limiting reagent, salicylic acid or acetic anhydride? (Note: The limiting reagent is the reactant that is completely consumed in a reaction).

c. Determine the actual yield_____%

Part II: Testing the purity of product

Results of the iron(III) chloride test:

Test tube # 1 color_____ Test tube # 2 color_____ Test tube # 3 color_____

Considering the results of colorimetric test with the iron(III) chloride, what can you say about the purity of your product?

Part III. Post Lab Questions

1. Why was sulfuric acid added to the reaction mixture?

2. Your actual yield will likely be different than 100% (can be smaller than or even greater than 100%). Give a potential reason to explain your actual yield.