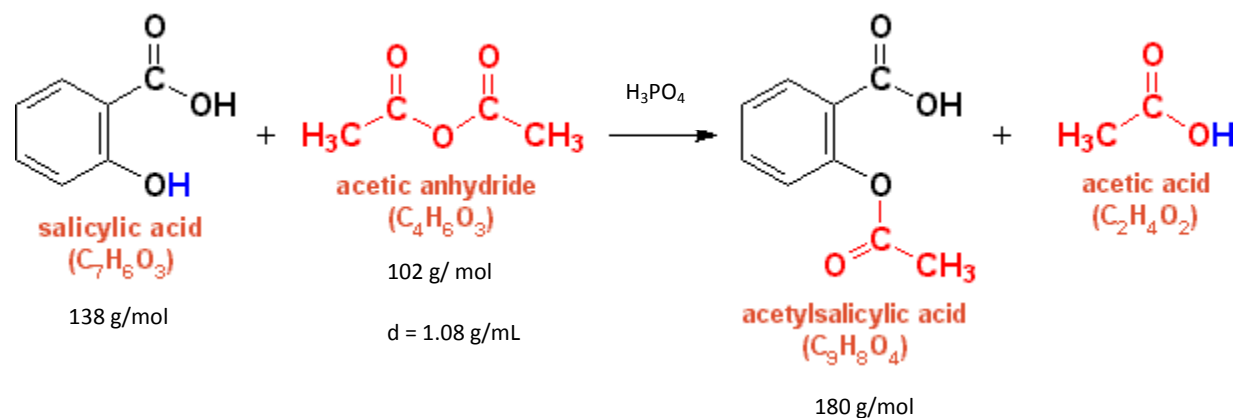


Experiment 5 - Synthesis of Aspirin

Aspirin is the common name for the compound acetylsalicylic acid, widely used as a fever reducer and as a pain killer. Salicylic acid, whose name comes from *Salix*, the willow family of plants, was derived from willow bark extracts. In folk medicine, willow bark teas were used as headache remedies and other tonics. Nowadays, salicylic acid is administered in the form of aspirin which is less irritating to the stomach than salicylic acid. To prepare aspirin, salicylic acid is reacted with an excess of acetic anhydride. A small amount of a strong acid is used as a catalyst which speeds up the reaction. In this experiment, phosphoric acid will be used as the catalyst. The excess acetic acid will be quenched with the addition of water. The aspirin product is not very soluble in water so the aspirin product will precipitate when water is added. The synthesis reaction of aspirin is shown below:



Since acetic acid is very soluble in water, it is easily separated from the aspirin product. The aspirin isolated in this step is the “crude product”. A “purified product” can be obtained through recrystallization of the crude product in hot ethanol. In this experiment, the crude product will be the desired product. The percent yield of the crude product will be determined for this reaction. The purity of the product will also be analyzed. The product will be analyzed by three different methods: melting point, titration, and spectroscopic assay.

The melting point range of pure aspirin is 138-140 °C and the melting point range of the salicylic acid starting material is 158-161 °C. If impurities are present in your crude sample, the melting point range for your product will be lower than the range of pure aspirin. Also, your melting point range may be greater than 2 degrees.

From the titration of your sample, the moles of acetylsalicylic acid present can be determined assuming that there is not a large percentage of an acid impurity present in your crude sample.

The spectroscopic analysis of aspirin will involve the complexing of iron(III) to the deprotonated form of salicylic acid (salicylate ion) to give a purple solution. Only the salicylate ion complexes to iron(III). Your aspirin product as well as a commercial aspirin tablet will be compared to a standard 0.15% ferric-salicylate solution. In the presence of moisture, aspirin may decompose (hydrolysis) into salicylic acid

and acetic acid. This reaction is the reverse of the synthesis reaction. The maximum allowable amount of free salicylic acid in an aspirin sample is 0.15% salicylic acid.

Equipment and Reagents

First Period

Salicylic acid	buret clamp	burner
Acetic anhydride	stand with iron ring	distilled water
85% phosphoric acid	wire gauze	ice bath
50 mL flask	beaker of tap water	filter paper
Büchner funnel	aspirator	

Second Period

Shell Vial	melting point apparatus	capillary tubes
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Third Period

125 mL Flask	phenolphthalein indicator	buret
0.1 M NaOH	mortar and pestle	aspirin tablets

Forth Period

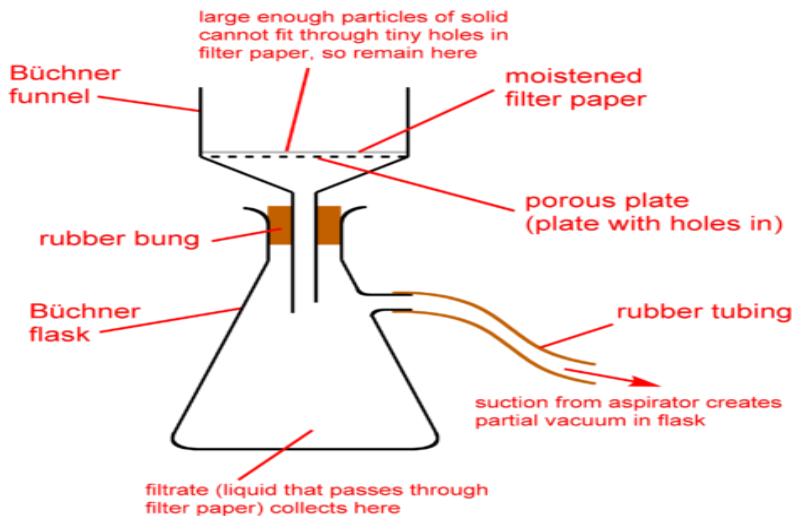
3 x 50 mL test tubes	ferric chloride	dropper
2 x 50 mL beakers	ethanol	hot plate
Mortar and pestle	aspirin tablets	50 mL graduated cylinder
Parafilm	spec 20	cuvettes
Distilled water	centigram balance	shell vial
Filter funnel	filter paper	stand with iron ring

Procedure

Day 1 – Synthesis

1. Use a centigram balance to weigh a 50 mL Erlenmeyer flask. Place about 2 g of salicylic acid in the flask and weigh again. In the fume hood, the instructor will transfer 5.0 mL of acetic anhydride from a buret into the flask. Add 5 drops of 85% phosphoric acid (catalyst) to the flask.
2. Clamp the flask in a beaker of tap water supported on a ring stand over a burner flame. Stir if needed to dissolve the salicylic acid. Heat the water to boiling, and shut off the flame. Keep the flask in the hot water bath for 10 more minutes.
3. While the flask is still in the water bath, slowly add 2 mL of distilled water to the flask to decompose any excess acetic anhydride.
4. After a minute, remove the flask from the water bath and add 20 mL of distilled water. Let the flask cool to room temperature. As the solution cools, crystals of aspirin will appear. Cool the solution further by placing the reaction flask in an ice bath. Chill 5-10 mL of distilled water in a separate container.

5. Weigh a watch glass and filter paper on the centigram balance.
6. Set up a Büchner funnel on a vacuum flask connected to a water aspirator. Place the filter paper in the funnel and moisten with distilled water from a squirt bottle. Turn on the aspirator and transfer the aspirin slurry into the funnel. Wash the crystals with 5 mL of the cold DI water.



7. Transfer the filter paper and aspirin to a pre-weighed watch glass and allow to air dry in your locker until the next lab period.
8. It is safe to discard of the filtrate down the sink with water.

Day 2 – Analysis/Melting Point

1. Weigh the dry product to obtain the yield of the reaction. Calculate the theoretical yield and percent yield of the reaction.
2. Pack a few crystals of your aspirin product in a melting point capillary tube. *Your instructor will demonstrate how to use the melting point apparatus.* Allow the temperature of the melting point apparatus to increase 1 °C per minute starting from 120 °C. Measure the melting point range of the aspirin product. The melting point range is the temperature when you first notice the aspirin crystals melting up until the temperature when no crystals remain.

Day 3 – Titration Analysis

1. Accurately weigh between 0.10-0.15 g of the aspirin product into a 125 mL Erlenmeyer flask. Add 15 mL of 95 % ethanol and swirl to dissolve. Add 2 drops of phenolphthalein indicator to the flask.
2. Record the exact concentration of the standard 0.1 M NaOH solution. Fill a buret with the standard NaOH solution and record the initial volume. Titrate the sample until a faint pink end point is reached. The pink color should last for at least 30 seconds after swirling.
3. Repeat the titration with 0.10-0.15 g of a crushed aspirin tablet. You may need to use a mortar and pestle to crush the tablet.

Day 4 – Spectroscopic Analysis

1. Obtain three 50 mL test tubes. Mark them A, B, C with labeling tape.
2. With a clean dropper, add 20 drops of a ferric chloride solution to each tube.
3. Reagent A – Weigh 1.00 g of the aspirin product into a 50 mL beaker. Add 10 mL of ethanol and gently warm the mixture on a hot plate to dissolve. Do not use a Bunsen burner because ethanol is flammable. Transfer 20 drops of this aspirin-ethanol solution into tube A.
4. Reagent B – Weigh 1.00 g of the crushed aspirin tablet into a 50 mL beaker. Add 10 mL of ethanol and gently warm the mixture on a hot plate to dissolve. The solution may appear cloudy due to additives in the commercial aspirin. Filter this solution into a shell vial and transfer 20 drops of this aspirin-ethanol solution into tube B.
5. Reagent C - Transfer 20 drops of the standard 0.15% salicylic acid solution into tube C.
6. Transfer 48 mL of DI water into each tube and seal the top with parafilm. Invert the tube several times to mix the solution.
7. *Your instructor will show you how to operate the spectrometer.* Allow the spectrometer to warm up for 10 minutes. Fill a cuvette 2/3 full with the ferric chloride blank solution. Set the spec 20 to a wavelength of 530 nm and zero the spectrometer (zero absorbance) with a ferric chloride blank solution. Fill a clean cuvette 2/3 with solution A and measure the absorbance reading. Repeat the process for solutions B and C. Clean and return the cuvettes once you are done with the readings so others can take readings.

Report

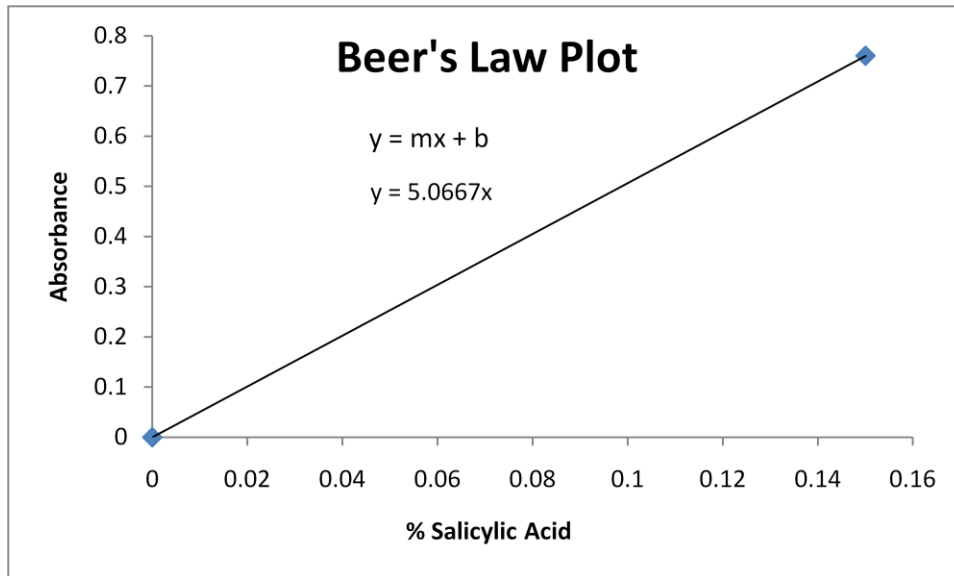
Report the theoretical yield and the percent yield of the aspirin product.

Compare the melting point of your aspirin product to the theoretical melting point (138-140 °C). Is the crude product above or below this mark? Explain why this is the case.

Determine the moles of aspirin from the titration and calculate the percent purity of the crude aspirin product from the titration analysis.

$$\% \text{ Purity} = \frac{\text{actual moles of acid}}{\text{theoretical moles of aspirin}} \times 100$$

Plot a Beer's Law graph of the standard 0.15% salicylic acid solution (C) on excel with Absorbance (y-axis) vs % salicylic acid (x-axis). To make a Beer's Law plot, enter % Salicylic Acid into one column on the excel spread sheet (0 and 0.15) and absorbance into the next column (0 and the absorbance reading). Highlight the data and select insert, and scatter (w/ only markers). Right click a data point and select add trend line. Now set the y-intercept to 0 and check the display equation box. To add titles to the plot, select layout, axis titles, and then chart titles.



The % concentration for samples A and B can be determined by plugging in the absorbance readings for those samples into the linear equation and solving for x. Clearly state if the samples are below the maximum allowable limit for percent salicylic acid (0.15 %).