The Synthesis and   
Analysis of Aspirin

Acetylsalicylic acid is the chemical name for aspirin, the ubiquitous pain reliever. One of the compounds used in the synthesis of aspirin is salicylic acid, which is itself a pain reliever that was known to many ancient cultures, including the Native Americans who extracted it from willow tree bark. Salicylic acid is extremely bitter tasting, and frequent use can cause severe stomach irritation. The search for a milder form of this pain reliever led to the successful synthesis of acetylsalicylic acid by the German chemist Felix Hoffmann in 1893.

Your two primary objectives in this experiment will be to synthesize and analyze aspirin. There is more than one way to synthesize aspirin; in this experiment, you will react acetic anhydride with salicylic acid in the presence of phosphoric acid (which acts as a catalyst). The reaction equation is shown below.

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|  |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Salicylic acid | Acetic anhydride |  | Acetylsalicylic acid | Acetic  acid |

You will conduct two tests of your synthesis to verify that you did indeed make aspirin and to determine its relative purity. First, you will measure the melting temperature of a sample of your product, using a melt station. Second, you will use a spectrophotometer to test the absorbance of salicylic acid impurity in your aspirin sample after it has been complexed with Fe3+ from iron (III) nitrate solution.

OBJECTIVES

* Synthesize a sample of acetylsalicylic acid (aspirin).
* Calculate the percent yield of your synthesis.
* Measure the melting temperature of your aspirin sample.
* Conduct a spectrophotometric analysis of your aspirin sample.

MATERIALS

Part I  Synthesize Aspirin

50 mL Erlenmeyer flask

two 10 mL graduated cylinders

25 mL graduated cylinder

250 mL beaker

vacuum filtration apparatus

spoon, spatula, or rubber policeman

watch glass

Wide-Range Temperature Probe or thermometer[[1]](#footnote-1)

solid salicylic acid

85% phosphoric acid solution, H3PO4

liquid acetic anhydride

distilled water

cold distilled water

balance

ice bath

hot plate

plastic Beral pipet or eyedropper

Part II  Melting Temperature

Chromebook, computer, or mobile device

Graphical Analysis app

Melt Station[[2]](#footnote-2)

glass capillary tubes, one end closed

aspirin crystals (from Part I)

tissues (preferably lint-free)

mortar and pestle (optional)

Part III  Spectrophotometric Absorbance

Chromebook, computer, or mobile device

Vernier Spectral Analysis app

UV-VIS Spectrophotometer[[3]](#footnote-3) cuvette(s)

50 mL graduated cylinder

250 mL beaker

100 mL beaker

250 mL volumetric flask

100 mL volumetric flask

salicylic acid

ethanol, denatured

aspirin crystals (from Part I)

distilled water

PROCEDURE

Part I  Synthesize Aspirin

1. Obtain and wear goggles. Protect your arms and hands by wearing a long-sleeve lab coat and gloves. Conduct this reaction in a fume hood.
2. Measure out 2.0 g of salicylic acid into a 50 mL Erlenmeyer flask.
3. Add 5.0 mL of acetic anhydride and 5 drops of 85% phosphoric acid solution. Swirl the mixture. If necessary, use a sparingly small amount of distilled water to rinse down any bits of solid that may be on the inner walls of the flask. DANGER: Phosphoric acid solution, H3PO4: Do not eat or drink when using this product—harmful if swallowed. Causes severe skin burns and eye damage. Fatal if inhaled. WARNING: Acetic acid, CH3COOH: Causes skin and eye irritation. Avoid breathing mist, vapors, or spray.
4. You are now ready to begin the synthesis of aspirin.
   1. Prepare a 70–80°C hot-water bath using a 250 mL beaker on a hot plate. Monitor the water temperature using a Temperature Probe or thermometer.
   2. Hold and partially submerge the 50 mL flask and contents in the water bath.
   3. Heat the mixture in the hot-water bath for 15 minutes, or until the mixture ceases releasing vapors. Stir the mixture occasionally during heating. Add 2 mL of distilled water about 10 minutes into the heating.
5. Crystallize the aspirin.
   1. When you are confident that the reaction has reached completion (no vapors appearing), carefully remove the flask from the hot plate and add 20 mL of distilled water.
   2. Allow the mixture to cool to near room temperature. Transfer the flask to an ice bath for about 5 minutes. As the mixture cools, crystals of aspirin should form in the flask.
6. Wash the synthesized aspirin.
   1. Set up a vacuum filtration. Be sure to weigh and record the mass of the filter paper to the nearest 0.001 g before filtering the solid.
   2. Filter the mixture with vacuum suction.
   3. When most of the liquid has been drawn through the funnel, turn off the suction and wash the crystals with 5 mL of cold, distilled water.
   4. After about 15 seconds, turn the suction back on. Wash the crystals with cold, distilled water twice more in this manner.
   5. Gently transfer the filter paper with your product onto the watch glass to air dry. As directed by your instructor, either direct a gentle stream of air (low flow) to help dry the solid, or let them air dry until the next lab period.
   6. Weigh the dried recrystallized product on the filter paper and record the mass to 0.001 g.
7. Determine the mass of your dry aspirin sample and record in the data table.

Part II  Test the Melting Temperature of an Aspirin Sample

1. Obtain a small amount of your synthesized aspirin from Part I. The solid should be in a powdered form. If it is not, use a mortar and pestle to carefully grind the solid to a powder. Pack the capillary tube.
2. Check the control dial on the melt station to confirm that it is in the cooling fan position. Connect the melt station power supply to a powered electrical outlet.
3. Launch Graphical Analysis. Connect the melt station to your Chromebook, computer, or mobile device. Use an interface if necessary.
4. Carefully insert the capillary tube of solid into one of the sample holders of the melt station.
5. Begin collecting melting temperature data. In the first trial, you will want to observe the melting process and make a rough estimate of the melting temperature of your unknown sample.
6. When you have determined the approximate melting temperature range for the sample, stop data collection and turn the dial to the cooling fan position. Record the melting temperature range in your data table.
7. Now that you have a rough idea of the melting temperature, a more accurate determination of the melting temperature can be made. Prepare a sample in a capillary tube and determine the melting temperature of the sample.
8. When finished, stop data collection and turn the dial to the cooling fan position. Record the melting temperature range in your data table.
9. At the end of the experiment turn the control dial on the melt station to Off. Dispose of the capillary tubes as directed by your instructor.
10. Complete the Data Analysis section before exiting the data-collection program. Print a copy of your graph and/or save your data, as directed by your instructor.

Part III  Test the Spectrophotometric Absorbance of an Aspirin Sample

Your synthesis converted most, but not all, of the salicylic acid into acetylsalicylic acid. You will spectrophotometrically analyze several samples to determine the amount of salicylic acid impurity in your synthesized aspirin. You can use this information to calculate the purity of your aspirin sample. Follow Steps 18–25 to prepare a set of salicylic acid standard solutions and conduct testing to develop your own Beer's law plot of the standards.

1. Quantitatively prepare 250 mL of a 5.79 × 10–3 mol/L stock salicylic acid solution. Record the mass of salicylic acid to the nearest 0.001 g. Note: Dissolve the salicylic acid in 10 mL of ethanol first then add distilled water. DANGER: Solid salicylic acid, C6H4(OH)CO2H: Do not eat or drink when using this product—toxic if swallowed. Causes skin and serious eye irritation.
2. Prepare serial dilutions of the salicylic acid stock solutions with distilled water in the following concentrations: 2.31 × 10–4 mol/L, 1.85 × 10–4 mol/L, 1.48 × 10–4 mol/L, and 1.18 × 10–4 mol/L.
3. Disconnect the melt station and close Graphical Analysis. Launch Spectral Analysis. Connect the spectrophotometer to your computer or Chromebook, and then click or tap Absorbance vs. Concentration. **Note**: If using a Go Direct spectrophotometer, you can also connect to a mobile device.
4. Prepare a blank by filling a cuvette 3/4 full with distilled water. Calibrate the spectrophotometer.
5. Remove the cuvette from the spectrophotometer, empty and rinse the cuvette, and fill the cuvette with the first standard solution. Insert the cuvette into the spectrophotometer. Determine the optimal wavelength for analysis following the instructions in the Choose a Wavelength screen. Record the λ max. Select Done when you are ready to continue.
6. Collect data for the standard solutions. Record the absorbance and concentration values in the data table.
   1. With the cuvette containing the salicylic acid solution still in the device, click or tap Collect to start data collection. When the value displayed on the screen has stabilized, click or tap Keep and enter the molar concentration. Click or tap Keep Point. The absorbance and concentration values have now been saved for the first solution.
   2. Discard the cuvette contents as directed by your instructor. Using the solution in the second 100 mL volumetric flask, rinse the cuvette twice with ~1 mL amounts, and then fill it 3/4 full. Wipe the outside, place it in the device, and close the lid. After closing the lid, wait for the absorbance to stabilize and click or tap Keep. Enter the molar concentration, and click or tap Keep Point.
   3. Repeat the procedure for the remaining salicylic acid solutions that you prepared.
   4. Click or tap Stop to stop data collection and view a graph of absorbance vs. concentration.
   5. To examine the data pairs on the displayed graph, click or tap any data point. As you click or tap each data point, the absorbance and concentration values of each data set are displayed. Record the absorbance and concentration values in your data table. Note: You can also adjust the Examine line by dragging the line.
7. Perform a linear regression analysis. After the preparation and testing of your aspirin sample in the following steps, you will be instructed to interpolate along this plot to determine the concentration of salicylic acid impurity in your aspirin sample.
   1. Click or tap Graph Tools, , and choose Apply Curve Fit.
   2. Select Linear as the curve fit. Click or tap Apply. Leave the curve fit displayed and continue with Step 25.
8. Prepare the synthesized aspirin sample for testing. Complete this step quickly and be ready to proceed directly to Step 26.
   1. Measure out about 0.4 g of aspirin and transfer it to the 250 mL beaker. Record the mass of aspirin that you use to the nearest 0.001 g.
   2. Add 10 mL of ethanol to the beaker of aspirin sample. Swirl the mixture to dissolve the solid.
   3. Add 150 mL of distilled water to the beaker. Mix the solution.
   4. Quantitatively transfer the solution from the beaker to a 250 mL volumetric flask. Thoroughly rinse the beaker with several portions of distilled water, and transfer the rinse water to the volumetric flask. Add distilled water, as needed, to fill the flask to the 250 mL mark. Mix the solution thoroughly.
   5. Transfer 5 mL of the aspirin solution from the 250 mL volumetric flask to a clean and dry 100 mL volumetric flask. If using a UV-VIS spectrophotometer, add distilled water to the flask to make precisely 100.0 mL. Mix the solution thoroughly.
9. Measure and record the absorbance value of the aspirin sample. This must be done within 10 minutes of completing Step 25.
   1. Rinse and fill the cuvette 3/4 full with the sample. Cap the cuvette and place it in the spectrophotometer.
   2. Monitor the absorbance readouts. If the absorbance value falls within the range of the salicylic acid standard solutions, record it in your data table. Note: If the absorbance value does not fall within the range of the salicylic acid standard solutions in your data table, you can repeat Step 25e using a more dilute or more concentrated solution.
10. To determine the concentration of the salicylic acid impurity in the treated aspirin sample, interpolate along the regression line to convert the absorbance value of the unknown to concentration.
    1. Click or tap Graph Tools, , and turn on Interpolate.
    2. Click or tap any point along the regression curve to find the absorbance value that is closest to the absorbance reading you obtained in Step 26. The corresponding salicylic acid concentration, in mol/L, will be displayed.
    3. Record the concentration of salicylic acid in your data table.
11. Discard all solutions as directed.

DATA TABLE

Part I  Synthesis of Aspirin

|  |  |
| --- | --- |
| Mass of salicylic acid used (g) |  |
| Volume of acetic anhydride used (mL) |  |
| Mass of acetic anhydride (1.08 g/mL) used (g) |  |
| Mass of aspirin and filter paper (g) |  |
| Mass of filter paper (g) |  |
| Mass of aspirin synthesized (g) |  |

Part II  Melting Temperature Data

|  |  |
| --- | --- |
| Melting temperature range (°C) |  |

Part III  Salicylic Acid Standard Stock Solution

|  |  |
| --- | --- |
| Initial mass of salicylic acid (g) |  |
| Moles of salicylic acid (mol) |  |
| Initial molarity of salicylic acid (mol/L) |  |

Part III  Beer's Law Data for Salicylic Acid Standard Solutions

λmax (nm): \_\_\_\_\_\_\_\_\_\_\_\_\_\_

| Trial | Concentration  (mol/L) | Absorbance |
| --- | --- | --- |
| 1 |  |  |
| 2 |  |  |
| 3 |  |  |
| 4 |  |  |
| 5 |  |  |

Part III  Test of the Purity of the Synthesized Aspirin

|  |  |
| --- | --- |
| Initial mass of aspirin sample (g) |  |
| λmax (nm) |  |
| Absorbance of aspirin sample |  |
| Concentration of salicylic acid (mol/L) |  |
| Moles of salicylic acid in aspirin sample (mol) |  |
| Mass of salicylic acid in aspirin sample (g) |  |
| Mass of aspirin in sample (g) |  |
| Percent aspirin in sample (%) |  |

DATA ANALYSIS

1. What is the theoretical yield of aspirin in your synthesis? The mole ratio is 1:1 between salicylic acid and acetic anhydride in this reaction.
2. Using a literature source or the internet, find the accepted melting temperature value of pure acetylsalicylic acid. How does the melting temperature test of your aspirin compare to the accepted value?
3. Based on the results of the absorbance testing with the spectrophotometer, what is the percent purity of your sample of aspirin? Does this percent purity compare well with the results of the melting temperature test? Explain.
4. Use your percent purity calculations to determine the percent yield of your synthesis of aspirin.

1. Use Graphical Analysis app to collect data if using a temperature probe. A data-collection interface is required if using a Wide‑Range Temperature Probe (order code: WRT‑BTA); no interface required if using a Go Direct Wide‑Range Temperature Probe (GDX‑WRT). [↑](#footnote-ref-1)
2. If using a Melt Station (order code MLT‑BTA), an interface such as LabQuest Mini is also required. If using a Go Direct Melt Station (GDX‑MLT), an interface is not needed. [↑](#footnote-ref-2)
3. The procedure is written for UV-VIS spectrophotometers from Vernier including the Go Direct UV-VIS Spectrophotometer (order code: GDX-SPEC-UV) and the Vernier UV-VIS Spectrophotometer (VSP-UV). [↑](#footnote-ref-3)