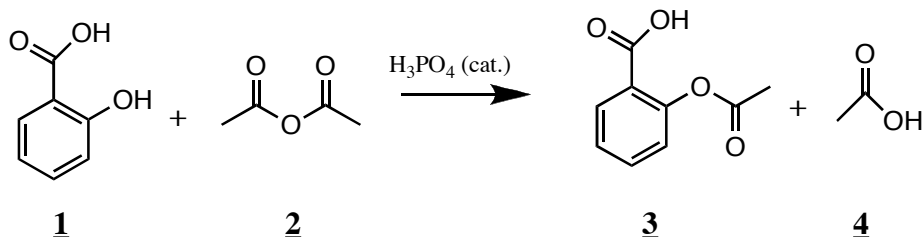


Preparation, Purification and Analysis of Aspirin (acetylsalicylic acid)

Synthesis:

We will prepare aspirin by reacting salicylic acid **1** with an excess of acetic anhydride **2** to produce aspirin **3** and acetic acid **4** :



The solid aspirin product will be separated from the reaction mixture by suction filtration and further purified by recrystallization. A variety of techniques will then be used to assess the purity of the product.

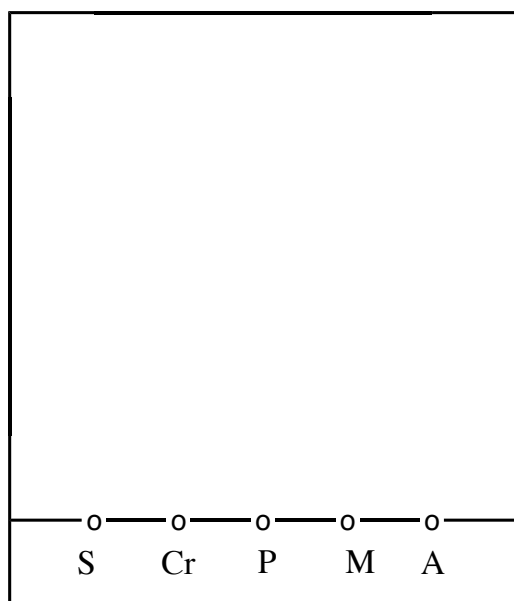
- 1) Start by creating a warm water bath: Fill a 250-mL Beaker with approximately 50-mL of water, heat it on a Heater/Stirrer to 70-80 °C.
- 2) Weigh 2.0 g of salicylic acid into a 50-mL Erlenmeyer flask, then using a 10-mL graduated cylinder measure out 4-mL acetic anhydride. Add the anhydride drop wise to the flask containing acid using a Pasteur pipette. Dissolve the solid acid by gently swirling the mixture, then add 10 drops of concentrated (85%) phosphoric acid (H_3PO_4) to the solution.
- 3) Place the Erlenmeyer flask containing the solution in the warm water bath and heat your mixture for 10 min. at 70-80 °C; be careful that the flask does not tip over into the water bath. The solution should be agitated when heating by gently swirling the flask or by using a glass stir rod. Add 20 drops of dd water to the Erlenmeyer flask and heat for another 5 min.
- 4) Cool the mixture on an ice/water bath. Filter off the crystals that form by suction filtration, then wash the collected solid with 2-3-mL portions of ice-cold water. Leave the crystals on the suction apparatus to aid in drying them. Meanwhile, place a small amount of your crystals (the tip of a spatula, ca. 50-mg) in a 3" test tube and add a few drops of the iron chloride solution (FeCl_3). If your solution turns purple it indicates starting material salicylic acid remains in your product and it needs to be further purified by recrystallization. Proceed to the step #5 below. If the FeCl_3 remains yellow, even after stirring and waiting a few minutes skip step #5 and go on to the Analysis section.
- 5) Remove your crystals from the Buchner funnel/filter paper (after turning of your suction filtration) by scraping them into a 50-mL beaker using a spatula. Dissolve the crystals in a minimum amount of warm ethanol, add the ethanol drop wise, using a Pasteur pipette, while heating on the hotplate, about 10 drops of ethanol should be

sufficient. Then add warm water drop wise (approximately 10-mL), until your solution turns cloudy. Again add just enough warm ethanol drop wise until the solution turns clear. Cool the solution on an ice/water bath prepared in a 250-mL beaker. Once sufficient amount of crystals have formed collect them by suction filtration as you originally did in Step 4

Analyses of Aspirin Product:

1) Thin Layer chromatography (TLC).

Place a spatula tip of your purified aspirin in a 2-mL glass vial (GC/MS vial) and dissolve it in 1-mL of ethanol. With a separate spotter for each compound, spot a TLC plate with each solution as outlined in the diagram below. The places to apply the spots can be lightly sketched with a pencil prior to spotting.



Where S = salicylic acid
A = aspirin
Cr = crude product
P = purified product
M = mixture of S + A
(co-spot both)

Using tweezers, carefully place the spotted plate into a developing chamber containing the eluting solution and cap the chamber. Allow the solution to rise up the plate until it nearly reaches the top. Remove the plate from the chamber and mark the top of the solvent front with a pencil. Place it on a clean paper towel in a fume hood and allow it to dry for several minutes. Visualize the eluted compounds on the plate using UV light, circle any spots observed with your pencil and note the colors and intensities of each spot. Measure the distance from the origin to the center of each spot and also the distance from the origin to the top of the solvent front. Use these values to calculate the R_f values for each spot: distance traveled by spot

$$R_f = \frac{\text{distance traveled by spot}}{\text{distance traveled by solvent front}}$$

Caution: wear goggles and never look directly into the UV lamp

2) Melting Point Analysis

Place a spatula tip of your purified aspirin into the well of a spot plate. Use the bottom of a test tube to grind into a fine powder. Prepare a sample for melting point analysis by inserting a small amount of your crystals into closed end capillary tubes (your instructor will demonstrate packing the tubes) and place this in the melting point apparatus. Your instructor will explain the operation of the melting point apparatus. Record your melting *range* of each sample. Compare the values you obtain with the literature melting point of pure aspirin.

3) GC/MS

screw a cap on the GC/MS vial filled with your Aspirin/Ethanol and close tightly. Place this in an envelope and print your name on it. Your sample will be run overnight and data will be available to you by next week.