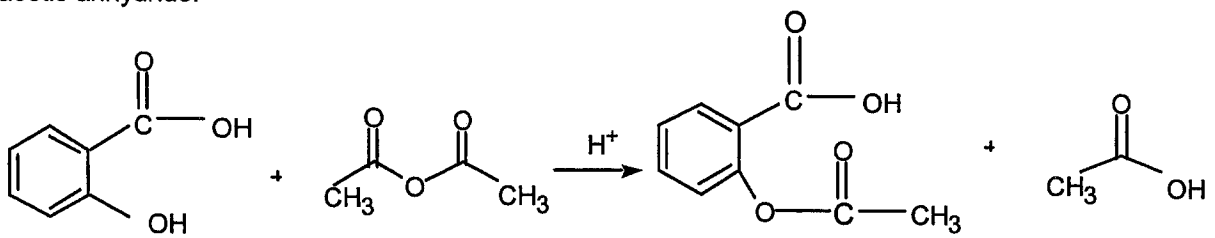
Microscale Preparation of Aspirin (My achey, breaky head!)

Pre-lab: Read about aspirin in your text book.

Salicylic acid has been used to relieve pain for almost 2500 years. The early Greeks extracted it from willow bark. Unfortunately, consumption of salicylic acid resulted in upset stomachs. To alleviate this side effect the Bayer Laboratories in Germany synthesized an ester of the salicylic acid and called it ASPIRIN. In 1915 the first aspirin tablet was sold as nonprescription drug by the Bayer company. Today, close to 50 million tablets of aspirin are consumed daily in the United States.

In the experiment, aspirin (acetylsalicylic acid) will be prepared by the reaction of salicylic acid with acetic anhydride:



Salicylic Acid o-hydroxy benzoic acid	Acetic anhydride	Acetylsalicylic acid (ASPIRIN)	Acetic acid
Carboxylic acid ***phenol***	*anhydride*	*carboxylic acid* *and an* ***ester***	*carboxylic acid* *and a*

Melting point: 135-136 ^{o}C

1 mole	reacts with	**1 mole**	to produce	**1 mole**	and	**1 mole**
138 g/mole		102 g/mole		180 g/mole		60 g/mole

density = 1.08 g/mL

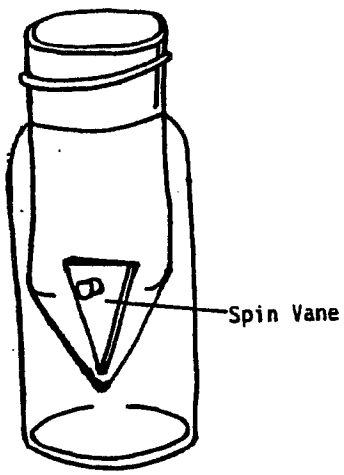
A **benzene** ring with an attached hydroxyl (**-OH**) group is called a phenol. This hydroxyl group reacts with the acetic anhydride to form the **ester** functional group. The reaction is called an **esterification.** An acid (phosphoric acid, H_3PO_4) is used as a catalyst in the reaction. Notice the appearance of the H^+ above the yield sign. Using the formulas written above, circle the **hydroxyl** functional group on the salicylic acid and the **ester** functional group on the aspirin.

As with many organic chemical reactions, the aspirin product will be contaminated with some unreacted reactants, the catalyst, and the other product (acetic acid). Fortunately, all of these unwanted chemicals are soluble in water near or below room temperature and aspirin is not. As a result, the aspirin will form crystals in cold water. The unwanted materials will remain dissolved in the cold water and can be filtered off the crystals of aspirin.

PROCEDURE:

Complete the Pasteur Pipette Technique (Part A) before beginning this experiment.

1. During the course of this reaction, it is necessary to stir the reacting chemicals. This is somewhat tricky and should be practiced with an empty vial before beginning the experiment. Drop a spin vane into the empty vial.

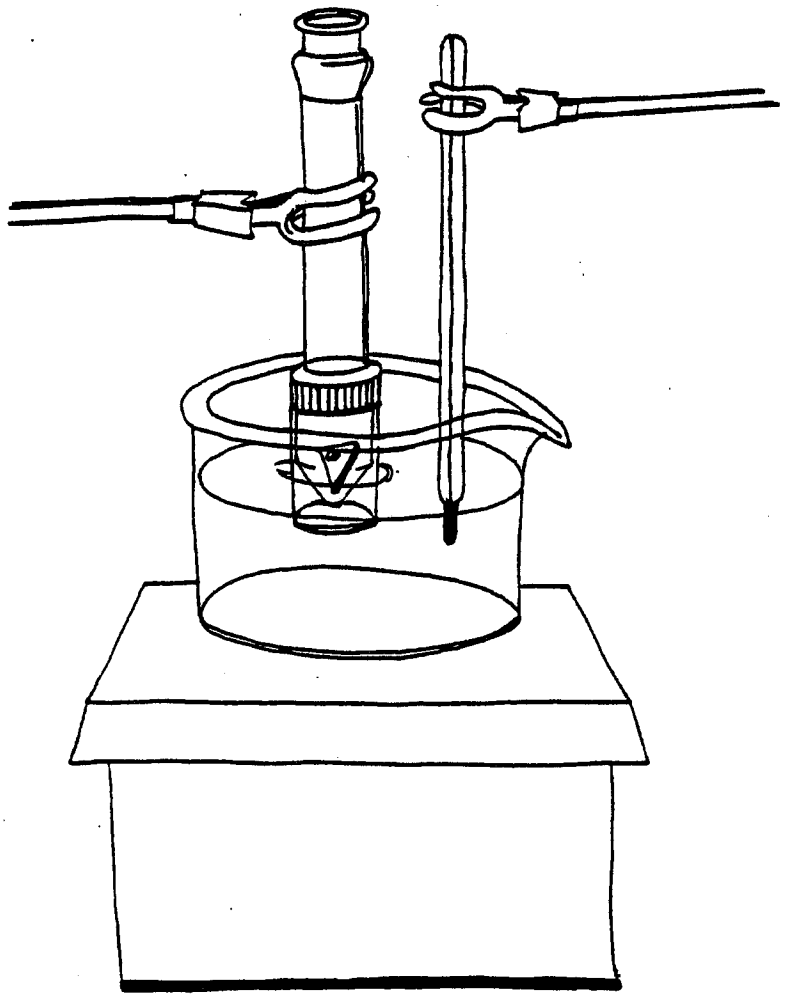


Turn on the magnetic stirrer. Place the vial on the stirrer/hot plate and move it around to find the position where the spin vane twirls around steadily and smoothly. (Try near the center and play with the speed adjustment. A slow speed works best.) The spin vane is quite small and easily misplaced. Please return it to its storage vial when it is not being used.

2. Prepare a hot water bath by adding approximately 100 mL of water to a 250 mL beaker. Suspend a thermometer in the water. Turn on the hot plate and try to maintain the water temperature at 50 ^{o}C.

3. Place **approximately** 0.20 g of salicylic acid into a tared empty 5.0 mL vial. **Record** the actual weight of salicylic acid used. Go to the hood and, using a calibrated pipet, add **approximately** 0.5 mL of acetic anhydride. (This reactant is in excess and need not be measured out exactly.) Add **EXACTLY** one drop of phosphoric acid. (CAUTION: PHOSPHORIC ACID IS HIGHLY CORROSIVE. HANDLE IT WITH GREAT CARE)

4. Assemble the apparatus which will be used in the experiment (don't forget the spin vane). Your instructor will have a sample apparatus already set up and will give you additional instructions. The O-ring ensures a tight joint. As a result, **microscale ground glass joints are <u>not</u> greased. Even a small amount of grease can become a significant contaminant.**



5. Clamp the assembly so that the vial is partially submerged in the hot water bath (50°C) as illustrated by your instructor.

6. Stir the reaction mixture until the salicylic acid dissolves. Continue to heat for an additional 3 to 4 minutes <u>after</u> the solid has dissolved. If your spin vane stalls, adjust the speed of the stirrer and/or the position of the apparatus. Try to agitate the mixture during the course of the reaction.

7. Remove the apparatus from the water bath, put it into a beaker (notice how easily tipped over this apparatus is), and allow it to cool to room temperature. After it has cooled down enough to handle, the air condenser can be carefully detached and the spin vane can be removed using clean forceps. Place the vial into a beaker and cool down to room temperature. During this time, the aspirin may begin crystallizing. If not, scratch the walls of the vial with an UNPOLISHED glass rod. Begin cooling the vial in a ice-water bath.

8. When the vials appears "full" of crystals, add approximately 3.0 mL of ice-cold distilled water(use a graduated cylinder).

9. Filter using vacuum filtration. This technique will be demonstrated by your instructor.
   a) Weigh a clean piece of dry filter paper and record its weight. Moisten the filter paper with a few drops of water.
   b) Turn on the aspirator full blast.
   c) Transfer the mixture in the conical vial to the funnel.
   d) When you have removed as much product as possible, add approximately 1.0 mL of ice-cold distilled water to the vial using a calibrated Pasteur pipet. Transfer the mixture in the conical vial to the funnel. Repeat this procedure with several 0.5 mL portions of ice-cold distilled water.
   e) Continue to draw air through the filter to dry the crystals.
   f) When your aspirin appears dry, turn off the aspirator.

10. Remove the paper from the funnel and store the product until the next laboratory period. By that time, the aspirin will be dry and it can be weighed and tested for purity.

During the next week, calculate the moles of each reactant used, confirm that salicylic acid is the limiting reactant, and calculate the theoretical yield of aspirin (in moles and grams) using the limiting reactant.

Laboratory Period 2

1. Weigh the aspirin on the filter paper. Subtract the weight of the paper to find the mass of aspirin produced in your experiment. Calculate the percent yield:

$$\text{Percent Yield} = \frac{\text{Your mass of aspirin}}{\text{Theoretical yield}} \times 100\ \%$$

2. If you were to market your aspirin product, you would recrystallized your product to insure complete removal of all the remaining unwanted chemicals. To test for these likely impurities, you can:

a) Find the melting point of your product. (Recall the effect of impurities on melting points).

b) Test your product with a reagent which will react with phenols. If phenols are present in your product, the aspirin is contaminated with salicylic acid. (What would that do to your consumer's stomach?) The reagent we will use is a iron(III)chloride (ferric chloride) solution. The Fe^{+3} ion reacts with phenols to give a definite color ranging from red to violet. If phenols are absent, the distinctive color will be absent.

To perform this test:

1. Obtain 3 small test tubes.
2. Use your calibrated Pasteur pipet to add 0.5 mL of distilled water to each tube.
3. Dissolve a small amount of salicylic acid in the first test tube.
4. Dissolve about the same amount of your aspirin in the second test tube.
5. The last test tube will be a control and will contain only water.
6. Add one drop of a 1% iron(III)chloride solution to each test tube. Shake gently and record the color of the solutions in each of the test tubes.

Name_____Section_____

Mass of Salicylic acid used _____grams

Molar mass of Salicylic acid = 138 g/mole

Moles of Salicylic acid used _____moles

Volume of acetic anhydride used _____mL

Density of acetic anhydride = 1.08 g/mL
Molar mass of acetic anhydride = 102 g/mole

Moles of acetic anhydride used _____moles

The limiting reactant is _____
The reactant in excess is _____

Moles of aspirin which could theoretically be produced _____moles

Molar mass of aspirin = 180 g/mole

Mass of aspirin which could theoretically be produced _____grams

Mass of dry filter paper _____grams

Mass of dry filter paper and aspirin _____grams

Mass of aspirin produced _____grams

Percent Yield of aspirin _____%

Melting point of the aspirin sample _____^{o}C

Literature value = 135 -136 ^{o}C

Reactions with iron(III)chloride

Color of solution in test tube	Before adding Fe^{+3}	After adding Fe^{+3}
water + salicylic acid	_____	_____
water + aspirin sample	_____	_____
water	_____	_____

What does the melting point data and the reaction of your aspirin with the iron(III)chloride tell you about the purity of your sample?