Experiment #9

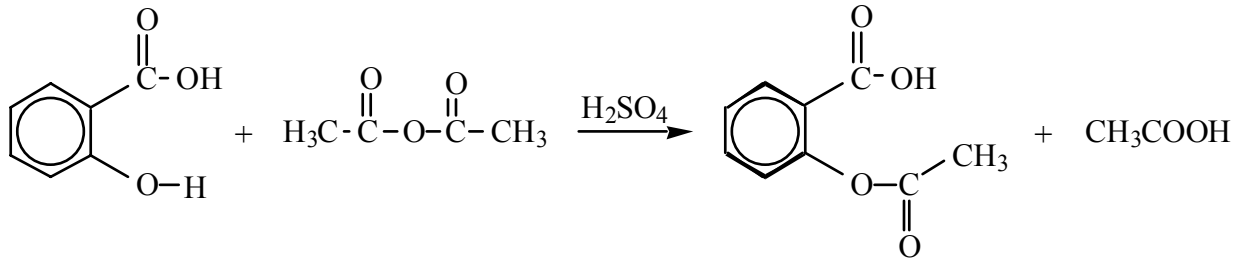
Making Aspirin

Introduction

The salicylate ion is credited with the pain relieving effect in aspirin. The ion is easily formed from salicylic acid and is a chemical relative to salicin, which is found naturally in the bark of the willow tree. Since salicylic acid is internally corrosive and the sodium salicylate has an objectionable sweet taste; aspirin was synthesized (by a German chemist working for the Baeyer firm!) and found to be non-corrosive and palatable. ion under the more basic conditions found in the intestines.

Aspirin is stable to the acidic conditions found in the stomach but is converted to the salicylate

Aspirin is usually prepared by reacting salicylic acid with acetic anhydride in the presence of a catalyst. The general class of reaction is ester formation.



Salicylic Acid **Acetic Anhydride** **Aspirin** **Acetic Acid**

The Problem

To prepare aspirin via several different routes, analyze the aspirin for purity using thin layer chromatography, and determine which synthesis is most efficient.

Procedure

CAUTION acetic anhydride is a dangerous chemical. The vapors will irritate the eyes and nose. The liquid can cause burns on the skin. Use the chemicals in your hood area and if you spill any, wash with large amounts of water. Sulfuric acid is another dangerous chemical. It likes a diet of cotton clothing but will eat other materials, including skin. If you spill any (even a drop) clean it up immediately using lots of water.

WEEK 1: Preparation of Aspirin

In each experiment roughly 1 g of salicylic acid and 2 mL of acetic anhydride will be used as the starting material. Different catalysts will be added to determine which catalyst makes this reaction work the best. As usual, record your observations after each step.

For each procedure, accurately weigh out approximately 1 g of salicylic acid and add 2 mL of acetic anhydride in a medium test tube. Record the mass of salicylic acid used. Once the acetic anhydride has been added, stir carefully with a glass rod until as much of the solid has dissolved as possible. Cautiously add two drops of catalyst (see the table below). Heat the reaction in a warm water bath (about 40 ^{o}C, it is OK if the temperature fluctuates some) for 15 minutes. Not all the solid will dissolve in some cases.

Refer to the table on the next page for the catalysts to use for procedures 1-4.

Procedure	mass of salicylic acid (g)	volume of acetic anhydride (mL)	catalyst
1	1	2	2 drops 18 M H_2SO_4
2	1	2	2 drops glacial acetic acid
3	1	2	2 drops 12 M HCl
4	1	2	No catalyst

Now begin the crystallization process. Cool for 5 minutes in an ice water bath (just a mixture of ice and water in a 400 mL beaker). Then add a mixture of about 5 g of ice and 5 mL of cold water directly to the reaction mixture, and continue cooling for 10 minutes in the ice water bath. Watch for crystal formation. You may need to swirl the test tubes and /or stir with a glass rod to cause crystals to form.

Obtain 4 pieces of filter paper and write a "#1-#2-#3-#4" on them with pencil. Record the weight of each filter paper on its own numbered watch glass.

Use a Büchner funnel and filter off the crystals. Use a rubber policeman to quantitatively transfer the crystals to the filter paper. Wash each reaction test tube with two-5 mL portions of ice cold water, pouring the liquid over the crystals on the filter paper to help wash them. Set each filter paper on its watch glass and set aside to dry until next week. You will weigh each dried product next week.

Place the labeled filter papers/watch glasses on a sheet of plain paper that has your name, partner's name, and lab section on it. Place these on the desk top at the back of the lab.

Waste Management The chemicals used in this experiment are dangerous and toxic. Save your waste in a large beaker until the end of the lab. Pour your waste from part one in a labeled bottle in the hood.

WEEK 2

Weigh the air-dried filter papers + watch glasses + product. Record the mass of each and calculate the mass of product.

Recrystallization is a process used to purify chemicals. Heat some water on a hot plate and put 5 mL of ethanol into a test tube and warm it in the hot water bath. Divide the aspirin from **PROCEDURE #1** of last week into two piles about 1/4: 3/4. Dissolve the 3/4 portion in about 2.5 mL of the warm ethanol. Warm this at the same time that you warm 5 mL of distilled water in another test tube. When the ethanol-aspirin mixture starts to boil remove it from the heat and add the warm water directly to the test tube. If a precipitate forms, heat the test tube until everything has dissolved (it may be necessary to add 2 additional mL of ethanol). Let it cool slowly to room temperature (10 minutes) and then place the test tube in an ice water bath to complete crystallization. You may need to swirl the test tube contents or stir with a glass rod to caurse crystals to form. Filter the crystals using a Buchner funnel and save them as recrystallized aspirin.

Thin layer chromatography (TLC) is an analytical procedure used to separate and identify similar chemicals. You are going to test seven samples so first you must prepare 7 spotting capillaries. The seven samples you will do TLC on are:

1) commercial aspirin (grind the aspirin tablets in mortar and pestle)
2) salicylic acid, you used this as the starting material last week
3) some of your RECRYSTALLIZED aspirin from procedure #1
4) your crude product from procedure #1
5) your crude product from procedure #2

6) your crude product from procedure #3
7) your crude product from procedure #4

Specific directions follow on the next page!

- Obtain a TLC plate and gently draw a pencil line across it 1 cm from the bottom on the grainy side
- Make 7 pencil marks spaced along the line to spot samples, stay at least 0.5 cm from the edges
- Place very small piles (match head size) of your 7 samples into separate wells of a spot plate
- Add a couple of drops of acetone to the first sample (do them one at a time) and use one of your spotting capillaries to gently mix the sample. Use the capillary to place a very small drop of the solution on your first mark on the TLC plate (Repeat this procedure with each sample in turn)
- While the spots dry, place 10 mL of TLC solvent in a 400 mL beaker and cover it with a watch glass
- Carefully place your spotted TLC plate with the sample end down in the TLC beaker and cover
- Allow the solvent to move up the plate to about 1 cm from the top edge. Remove the TLC plate from the beaker and let the solvent evaporate.
- Go to the UV black light in the hood, view your plate under the UV light, and gently outline each visible spot with a pencil. You should observe two different appearances for spots of compounds. Record that information in your lab book!
- Include your TLC plate or a sketch of it in your lab report!

Waste Management The chemical used in this experiment are dangerous and toxic. The chemical in the TLC eluting solution are toxic and should disposed of in the labeled bottle in the hood. The chemicals from part 1 and part 2 must go into separate waste bottles.

Data Analysis Questions on the Report Sheet

1. For each of the four procedures calculate the theoretical yield for aspirin using salicylic acid as the limiting reagent. Calculate the percent yield of product. Show a sample calculation.

2. In the crystallization process, why did you use ice water?

3. You know which compounds you spotted at marks 1 and 2. Compare your TLC results for 1 &2 to the results for samples 3-7 and conclude which compound(s) are present in samples 3-7? Include a sketch of your TLC plate indicating the appearance of the spots.

4. Think about **quantity** versus **quality** of product! Which procedure gave the greatest yield of product? Which procedure gave the purest aspirin?

5. What is the purpose of recrystallization? Look at your TLC results for samples 3 and 4, did your recrystallization work? What is the evidence?

6. What is a catalyst? Based on your results, do all the acids work as suitable catalysts in this synthesis? Which catalyst gave you the best aspirin?

For the lab report you need:
- Lab notebook that includes all calculations
- Completed report sheet ; attach or sketch your TLC plate results
- Make certain to include sample calculations

ASPIRIN REPORT
NAME_____

Discretionary	___/20 pts	ATTACH TLC OR DRAWING
Lab book	___/20 pts	
Theoretical yield	___/20 pts	
Percent Yield	___/30 pts	
TLC results	___/20 pts	
Data Analysis questions	___/90 pts	
# days late ___ × 10%	-___ pts	
Total points	**____/200**	

TABLE OF RESULTS

PROCEURE CATALYST	Starting Salicylic Acid (g)	Product (g)	Theoretical Yield (g)	Percent Yield (%)
1. Sulfuric Acid				
2. Acetic Acid				
3. Hydrochloric Acid				
4. No Catalyst				

DATA ANALYSIS QUESTIONS

1. Sample calculations for Theoretical Yield and Percent Yield:

2.

3.

4.

5.

6.