Experiment # 13
PREPARATION OF ASPIRIN

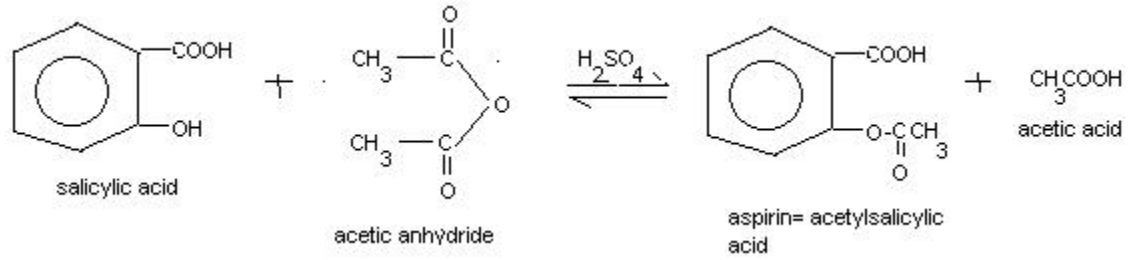
Objective

In this experiment you will synthesize acetyl salicylic acid (aspirin), determine the limiting reagent, and then determine the theoretical and percent yields of the reaction.

Introduction

The antipyretic (fever reducing), anti-inflammatory (reducing swelling) and analgesic (pain relieving) properties of the extracts isolated from the bark of willow and birch trees have been known for some time. In 1763 an English clergyman, Edward Stone, presented a paper to the Royal Society of London entitled, "An Account of the Success of the Bark of the Willow in the Cure of Agues (malaria)". By the late 1800's the active ingredient in willow bark had been isolated and named salicylic acid (from *salix*, the Latin name for the willow tree). By the end of the 17th century, mass production of salicylic acid had begun. However, because of its acidity, salicylic acid has undesirable side effects including hemorrhaging and ulceration of the mouth, throat, and stomach lining. A breakthrough came when Felix Hofmann, a chemist working for the German firm, Bayer, introduced a new derivative, acetylsalicylic acid or aspirin, which exhibited all the same medical benefits as salicylic acid with fewer side-effects.

Chemically, aspirin is an ester. Esters are typically formed by reacting an alcohol (the OH group on salicylic acid in the structure below) with a carboxylic acid or even better, with an acid anhydride. Aspirin, acetyl salicylic acid, is the product of the acid catalyzed reaction between the hydroxyl group (OH) of salicylic acid and the anhydride group (COC) of acetic anhydride (Equation 1).



Equation 1

From Equation 1 it is seen that one mole of salicylic acid (MM =138 g/mol) reacts with 1 mole of acetic anhydride (MM=102 g/mol; d=1.08g/mL) to produce 1 mole of aspirin (MM=180 g/mol). Sulfuric acid plays the role of a catalyst, therefore only a very small amount is necessary. As indicated in Equation 1, the reaction is reversible. Thus it is useful to shift the equilibrium to the product side by using an excess of one of the reactants. Often when a solid product is expected and one of the reactants is a liquid and the other is a solid, it is easier to achieve a good separation of the excess reactant from product if the liquid rather than the solid reactant is used in excess. In this reaction, salicylic acid and aspirin are both solids and acetic anhydride is a liquid so acetic anhydride is used in excess.

At elevated temperatures in the presence of even trace amounts of water, Equation one may be reversed in a process called hydrolysis, which results in production of

salicylic acid and acetic acid (a reversal of the esterification process). Therefore, care must be taken to use dry glassware and measuring devices.

The reaction takes place in an anhydrous environment, at a temperature of about 100 ^{o}C. After the reaction is complete, the excess acetic anhydride is decomposed by slow addition of water and the product is allowed to crystallize on ice at 0 ^{o}C. The solid aspirin is separated from the reaction mixture by filtration then dried and weighed. The theoretical and percent yields for the reaction are then determined.

Procedure

Reaction

1. Set up a hot water bath in the fume hood. Start with a ring stand, set a hot plate on the stand's base. Secure a two-prong clamp and a large ring (below the clamp) to the stand, then place a 400 mL beaker 2/3-filled with tap water into the ring and on the plate. Start heating the water in the beaker.

2. Using a tared weighing dish, weigh 1.00 g of salicylic acid (to 0.01g). Carefully transfer the solid to a clean, dry 125-mL Erlenmeyer flask.

3. Using the Brinkman dispenser provided, add 2.0 mL of acetic anhydride and 3 drops of concentrated H_2SO_4 to the flask. Cover the flask with a watchglass before transporting it to another hood.

4. Use the clamp above the hot water bath to secure the flask in such a way that the entire volume of the reaction mixture is immersed in the bath. Boil the water in the bath and keep the reaction mixture immersed in the boiling water bath for 15 minutes.

5. While the reaction takes place, prepare an ice bath (use roughly 1:1 ice and water). Pour about 30 mL of distilled water into a 50-mL beaker and place it in the ice-bath to cool.

6. After 15 minutes of heating, remove the reaction mixture from the hot-water bath. Use the clamp as a holder.

7. While still in the hood, add 0.5 mL of ice-cold water repeat 9 more times (10, 0.5 mL portions total). Do this slowly, swirling thoroughly after each addition. Adding water too fast will contribute to hydrolysis of the product.

Crystallization

8. Take the flask out of the hood and place it in the ice bath next to the beaker with water.

9. Let the product crystallize for 10-15 minutes. If no crystals are formed after 5 minutes, scratch the inside wall of the flask with a glass stirring rod. If oil droplets form, you may need to reheat and then slowly cool your reaction mixture.

Separating aspirin
10. While the product is crystallizing, prepare the vacuum filtration set up. See the procedure at the end of the lab.

Rinse the solid in the following way:
11. Break the vacuum and, using a medicine dropper, pour about 2 mL of chilled distilled water all over the solid. Stir the solid with water using the stirring rod (be careful not to tear the filter paper). Apply vacuum and let the liquid drain.

12. Repeat step 11.

13. Let the solid dry on vacuum for at least 10 minutes.

Yield Determination
14. Weigh a clean, dry watchglass.

15. Once the aspirin is dry, break the vacuum and turn it off. Remove the Buchner funnel and using a spatula, scrape the solid onto the pre-weighed watchglass.

16. Weigh the watchglass with aspirin.

Report
Use the data sheet provided to record your results and calculations. In your report describe the physical appearance of your product, state the actual, theoretical and percent yields, and outline any sources of error in your experiment.

DATA SHEET

Mass of salicylic acid	
Volume of acetic anhydride	
Mass of watchglass	
Mass of watchglass with aspirin	

RESULT SHEET

	Formula and calculation	**Result**
Mass of acetic anhydride	V X d	
Moles of acetic anhydride	m / MM	
Moles of salicylic acid	m / MM	
Theoretical yield in grams	mol S.A. X MM_{Asp}	
actual yield of aspirin	experimental	
% yield	(actual yield/theoretical yield)X 100%	

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1. Sketch a proposed set up for the hot bath. Make sure that all of the listed equipment is included in the sketch (the drawing does not have to be of professional quality, of course.)

2. Calculate the theoretical yield of aspirin if 1.05 g of salicylic acid is combined with 2.0 mL of acetic anhydride. Follow your Result Sheet if you need help.

3. What is an ester?

4. Why is sulfuric acid added to the esterification reaction?

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Explain all answers

1. How would the % yield be changed if the aspirin was not completely dried after filtration? Be specific.

2. What is the limiting reagent if 2.00 g of acetyl salicylic acid were reacted with 1.50 g of acetic anhydride? What is the theoretical yield?

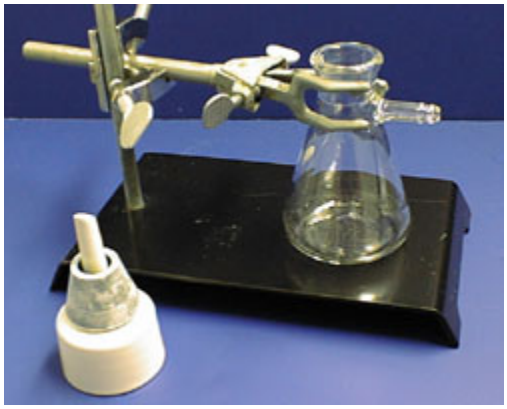
3. Explain the theory behind the fact that ice was used to help crystallize the product from the reaction mixture. In other words: why did you use ice?

4. How would the % yield of aspirin be changed if the final rinse of the solid product on the filter paper was done with warm water instead of ice-cold water?

Procedure for vacuum filtration

1) Assemble the apparatus

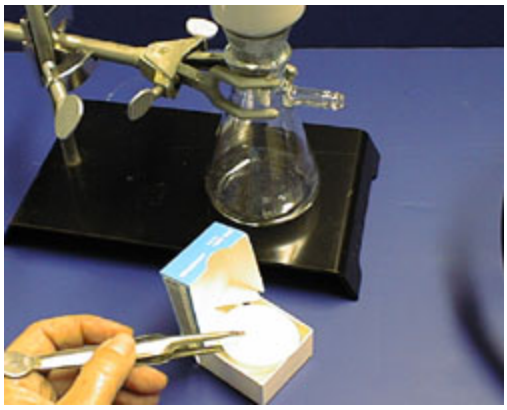
Check the side arm flask (filtering flask or vacuum flask) carefully for cracks, since cracks could cause the flask to break when vacuum is applied. Then, clamp the flask securely to a ring stand. Add an adaptor and a Buchner funnel. Place a piece of filter paper in the funnel that is small enough to remain flat but large enough to cover all of the holes in the filter.



clamp a side arm flask securely to a ring stand

place the rubber adaptor in the side arm flask

place the Buchner funn adaptor



get a piece of filter paper . . .

. . . and put it in the Buchner funnel

connect the side arm vacuum source - alway walled tubing, since Ty will collapse under redu

Note on Vacuum Sources: U
mechanical vacuum systems
possible. See the vacuum sys
for a discussion of these syste
water aspirators.

If you use a water aspirator, r

The photo to the left shows th
vacuum filtration glassware c
to a "water-trap". The black t
the water-trap would be conn
water aspirator.

Whenever you use a water as
you run the risk of sucking w
the aspirator into your vacuu
filtration unit. The water-trap
in-line will catch any such wa
you do NOT need the filtrate,
need the solid matter collecte
Buchner funnel, this presents
problem. Most of the time thi
case, and usually students do
a water-trap.

If you do need one, they are l
under the main hood or on th
shelves of each lab room.

You never need a water-trap
using the mechanical vacuum

2) Wet the paper with a small amount of the solvent to be used in the filtration. Turn on the vacuum source.

Wet the paper - this causes the paper to adhere to the plate and keeps materials from passing under the paper during filtration.

Make sure that the paper is secure on the filter, that air is being drawn through the paper, and that all of your apparatus is securely clamped. If you are using a Neoprene

filter adaptor, you might need to press on the funnel to engage the seal and thus the vacuum.

Now you are ready to begin filtration.

3) Filter the solution

Pour the mixture to be filtered onto the filter paper. The vacuum should rapidly pull the liquid through the funnel. Watch that particulates do not creep under the edges of the paper. If this happens, start over and carefully pour portions of the solution onto the very center of the paper.

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Notice that the vacuum has pulled the solvent through the filter and into the filter flask.

4) Rinse the solids.

Rinse the cake with a small amount of fresh, cold solvent to help remove impurities that were dissolved in the filtrate. Disconnect the rubber tubing before turning off the water aspirator. Remove the filter paper and the collected solid that is on it. Usually you will set it on a watch glass and let it air dry for a while.

Rinse the flask with a little fresh solvent and pour it into the filter funnel.

Disconnect the vacuum AT THE FLASK and before turning off the water aspirator. This prevents water from being sucked into the vacuum flask.

Carefully remove the filter paper and solid from the Buchner funnel.

Set the filter cake onto a watch glass to air dry.