Experiment 26A

FV 8/7/02

SYNTHESIS AND PURIFICATION OF ESTERS

MATERIALS: Two 25 x 150 mm test tubes, 50 mL beaker, 50 mL Erlenmeyer flask, 10 mL graduated cylinder, Bunsen burner, wooden boiling sticks, salicylic acid, methanol, concentrated sulfuric acid, acetic anhydride, cyclohexane, ethyl acetate, ethanol, acetone, iron(III) chloride solution, ice, five 13 x 100 mm test tubes, weighing boat, filter paper, suction flask, Büchner funnel, plastic disposable pipets, microscope.

PURPOSE: The purpose of this experiment is to synthesize two different esters from a single starting material, salicylic acid.

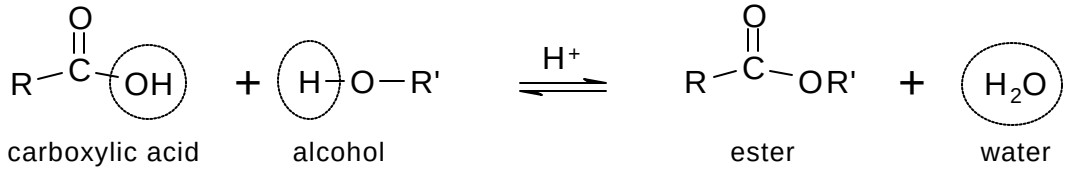
LEARNING OBJECTIVES: By the end of this experiment, the students should be able to demonstrate the following proficiencies:

1. Select the appropriate carboxylic acid and alcohol from which to synthesize an ester.
2. Purify an impure solid by recrystallization.
3. Predict the solubility of a compound in a particular solvent.
4. Test the solubility of a compound in a variety of solvents.
5. Determine percent yield for a reaction.

INTRODUCTION:

Synthesis

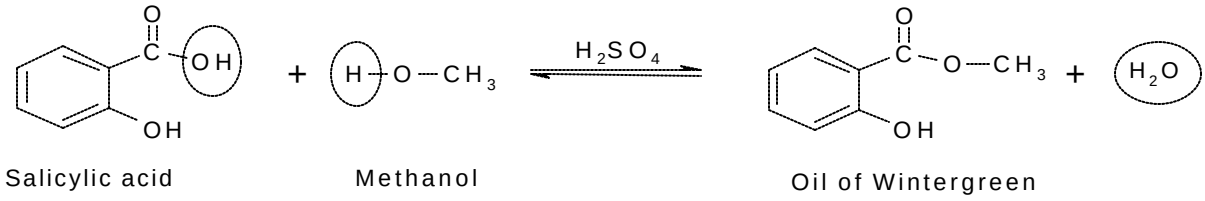
Esters are organic compounds with the general formula RCOOR', where R and R' can be an alkyl group (such as methyl (CH_3-) or ethyl (CH_3CH_2-)) or an aromatic group. Aromatic compounds are a special class of molecules that usually have six-membered carbon rings with delocalized pi electrons. The bonding in the ring is commonly shown as a series of alternating single and double bonds. This type of group is found in salicyclic acid and aspirin and can be seen in the structures below. Many esters have characteristic odors and are used as flavoring agents and in perfumes. Esters are readily synthesized by the reaction between a carboxylic acid, RCOOH, and an alcohol, R'OH, as shown in the following reaction.



(1)

This is known as a condensation reaction, where the carboxylic acid and the alcohol combine to form the ester and a molecule of water. There are many different esters and, in principle, they can all be formed by reaction (1).

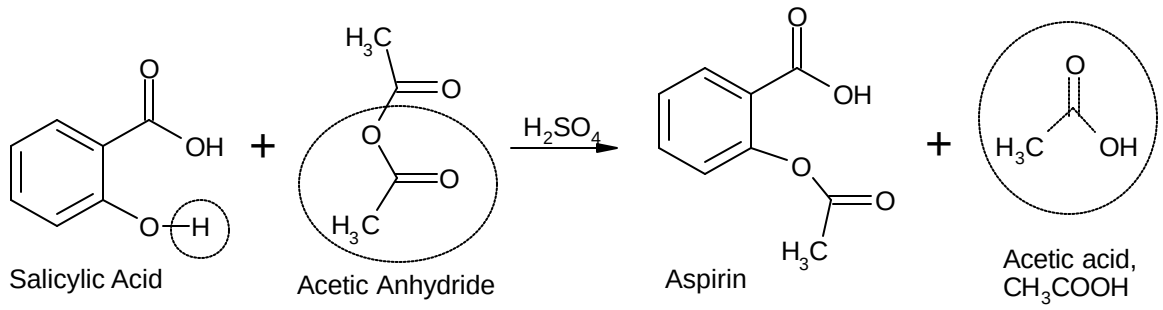
Methyl salicylate, commonly known as oil of wintergreen, is a widely used flavoring agent and is the active ingredient in topical ointments such as Ben-Gay®. This common ester can be prepared by reacting salicylic acid and methanol, using sulfuric acid as a catalyst, according to the following reaction.



(2)

Notice that salicylic acid has **both** carboxylic acid and alcohol functional groups. In this reaction, salicylic acid acts as the acid component of the condensation reaction. The hydroxyl group (-OH) of the carboxylic acid group combines with the H from the alcohol group (HO-R) and water is "split" out or formed as a product. The oil of wintergreen produced in this reaction could be purified by distillation of the product and its purity assessed by determining its boiling point. In this experiment, however, the oil of wintergreen will not be purified but its presence will be detected by its distinctive odor.

Acetylsalicylic acid, commonly known as aspirin, is also a derivative of salicylic acid. In contrast to the oil of wintergreen synthesis, in the formation of aspirin, salicylic acid acts as the alcohol in the condensation reaction. The hydroxyl group of salicylic acid reacts with acetic anhydride, again using sulfuric acid as a catalyst as shown in the following reaction. In this condensation reaction, aspirin and acetic acid, not water, are the products.



(3)

Recrystallization

Pure aspirin is a white crystalline solid. The aspirin initially produced by synthesis may be light tan, indicating the presence of impurities. Solid products are often purified by recrystallization. In recrystallization, the impure solid is dissolved in a hot solvent and the resulting solution is allowed to cool slowly. As the solution cools, crystals of the product will form and soluble impurities will remain in solution. When repeated a number of times, recrystallization is an effective purification method. Commercial aspirin is recrystallized several times to remove all of the impurities.

Recrystallization is possible because most solids are more soluble in hot solvents than in cold solvents. For example, in water, the solubility of aspirin increases as temperature increases. When aspirin is dissolved in boiling water, 1.00 g of aspirin will dissolve in each gram of water. At 35°C, the solubility is 0.03 g of aspirin per gram of water and at 15°C, the solubility is only 0.01 g of aspirin per gram of water. This means that if 1.00 g of aspirin is dissolved in 1 mL of boiling water to produce a saturated solution and that solution is cooled to 15°C, 0.99 g or 99% of the aspirin will crystallize during the cooling. One common error in recrystallization is to use too much solvent. If 1.0 g of aspirin is dissolved in 10 mL of boiling water, upon cooling to 15°C, only 0.90 g or 90% will recrystallize rather than the 99% described above.

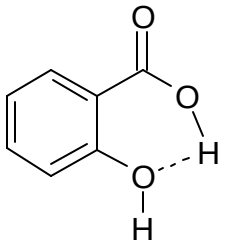
The aspirin prepared in this experiment is relatively impure, even after the recrystallization steps have been completed. One common impurity in this synthesis is unreacted salicylic acid. One way to test for the presence of unreacted salicylic acid is by treating a solution of the aspirin product with an iron(III) chloride solution, $FeCl_3$(aq). Iron(III) chloride reacts with –OH groups attached to aromatic rings, such as in salicylic acid, to form a colored complex. Esters, such as aspirin, do not react with iron(III) chloride.

Solubility

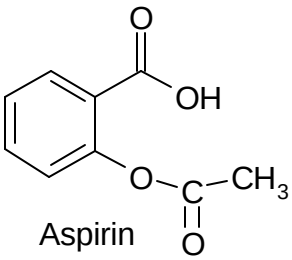
The solubility of a molecular solid is influenced by three factors: (1) the strength of the interactions between solute molecules, (2) the strength of the interactions between solvent molecules and (3) the strength of the interactions between solute molecules and the solvent molecules. While this is discussed in greater detail in the text, these interactions are due to intermolecular forces of attraction[1]. By examining the structure of the compound and the solvent, it is possible to predict solubilities. A useful generalization is that "like dissolves like," meaning that "substances with similar intermolecular attractive forces tend to be soluble in one another."[1,2] The structures of salicylic acid, aspirin, and the possible solvents are shown below. Both salicylic acid and aspirin are polar organic

[1] "Chemistry", Brown, LeMay, and Bursten, pp. 395-403.
[2] "Chemistry", Brown, LeMay, and Bursten, pp. 422-426.

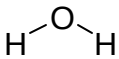
compounds and, in their pure forms, the intermolecular forces present are hydrogen bonding, dipole-dipole attractions and London dispersion forces. One difference between these two compounds is in the atoms involved in hydrogen bonding. Aspirin forms *inter*molecular hydrogen bonds and salicylic acid forms *intra*molecular hydrogen bonds, indicated with a dashed line. Intermolecular forces are attractive forces between separate molecules that make up the solid or liquid substance. Intramolecular forces are attractive forces within a single molecule.



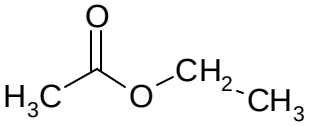
Salicylic acid



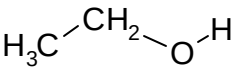
Aspirin



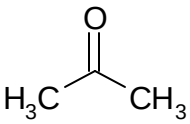
water



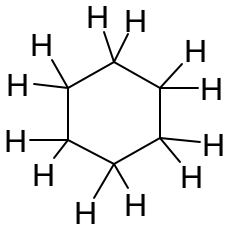
ethyl acetate



ethanol



acetone



cyclohexane

PROCEDURE:

Part A. Preparation of Oil of Wintergreen

1. Mix 1 gram of salicylic acid with 2 **drops** of concentrated sulfuric acid and 2 mL of methanol in a test tube.

2. **Gently** warm this mixture and note the odor produced. If the warm mixture is poured into 25 mL of cold water, the odor may be more noticeable.

Part B. Preparation of Aspirin

1. Place a 50 mL Erlenmeyer flask on the top-loading balance and add one gram of salicylic acid. Record the mass in Part C of the Data and Observation section.

2. Add the following reagents to the Erlenmeyer containing the salicylic acid, *in the order* given:
   a. 2 mL of acetic anhydride
   b. 2 drops of concentrated sulfuric acid

Acetic anhydride is a severe eye and skin irritant. Measure it directly into the reaction flask from the buret in the hood and use caution in handling.

3. Swirl the flask for a minute or two to mix the contents.

4. Allow the mixture to stand for at least 5 minutes, then stir well with a stirring rod and cool in an ice bath until a stiff crystalline paste is obtained. Add 20 mL of water, stir the slurry and cool well in an ice bath.

5. Collect the solid on filter paper using the Büchner funnel.

6. Wash these crystals with 5 mL of cold water and transfer them to a 50 mL beaker for recrystallization.

7. To recrystallize, place a wooden boiling stick in the beaker, add a small amount of water (approximately 3 mL) and gently bring the solution to a boil.

8. While the mixture is gently boiling, continue to add small amounts of water until the minimum amount of water has been added that will dissolve all the solid (usually no more than 5 mL).

9. Remove the boiling stick and allow the solution to cool to room temperature. Observe the formation of the crystals.

10. When the solution is at room temperature and the aspirin has crystallized, filter with the Büchner funnel and wash the solid with a small amount of cold water. Draw air through the funnel for a few minutes to help dry the crystals.

11. Transfer the aspirin to a piece of dry filter paper. As the crystals are drying on the piece of filter paper, study their shape. Looking at them through the stereomicroscope may be helpful. Describe the general shape and appearance of the crystals in the appropriate place in the Data and Observations section.

Part C. Determination of Product Yield

1. Spread the aspirin in a thin layer on a paper towel. Fold the edges of the towel over on the aspirin and press the aspirin firmly between layers of the towel to dry it. Repeat several times, using dry portions of the towel.

2. After the aspirin is dry, transfer the solid to a small weighing boat and determine the mass of aspirin obtained. Record the mass in the Data and Observations section.

Part D. Solubility Tests

1. After determining the mass of the aspirin, test its solubility at room temperature. Prepare 5 small test tubes by placing a pea-sized sample of aspirin in each.

2. To the first test tube, add 1 mL of water, stir, and observe.

3. Repeat this procedure with each of the other solvents listed on page E26A-6. Using the terms "very soluble," "soluble," "slightly soluble" or "insoluble," describe the solubility properties of aspirin in the solvents tested in the Data and Observations section.

Part E. Test for Unreacted Salicylic Acid

1. Dissolve a few crystals of salicylic acid in 5 mL of water in a small test tube. Add a drop of 1% aqueous iron(III) chloride solution. Record the color of the resulting solution in the Data and Observations section.

2. Dissolve a few crystals of your recrystallized product in 5 mL of water in a small test tube. Add a drop of 1% aqueous iron(III) chloride solution. Record the color of the resulting solution in the Data and Observations section.

Name _____ Section _____

Partner _____ Date _____

DATA AND OBSERVATIONS
Experiment 26A

Part A. Preparation of Oil of Wintergreen

Record the observations about the preparation of oil of wintergreen.

_____

_____

Part B. Preparation of Aspirin

Record the observations about the aspirin crystals.

_____

_____

Part C. Determination of Product Yield

Mass of salicylic acid used _____

Mass of aspirin _____

Part D. Solubility Tests

Solvents to be Tested		**Observations/Solubility**
i.	Water	_____
ii.	Ethyl acetate, $CH_3COOC_2H_5$	_____
iii.	Ethanol, CH_3CH_2OH	_____
iv.	Acetone, CH_3COCH_3	_____
v.	Cyclohexane, C_6H_{12}	_____

Part E. Test for Unreacted Salicylic Acid

Color of solution with salicylic acid _____

Color of solution with aspirin sample _____

QUESTIONS
Experiment 26A

1. Calculate the theoretical yield (in grams) of aspirin for this reaction. (Assume that salicylic acid is the limiting reagent.)

Theoretical Yield = _____

2. Calculate the percent yield of aspirin obtained in this experiment.

% Yield = _____

3. Rank the solubility of aspirin in the various solvents, from most soluble to least soluble.

_____ > _____ > _____ > _____ > _____
Most soluble Least soluble

4. Explain this ranking, based on intermolecular forces and the generalization "like dissolves like."

5. What impurities remain in the aqueous phase after the aspirin is recrystallized? (Be specific!)

6. Does your solid contain unreacted salicylic acid? How do you know this?

7. If the test was positive for unreacted salicylic acid, explain why your recrystallization did not remove all of the salicylic acid. In your explanation, consider the solubility tests done in Part E.