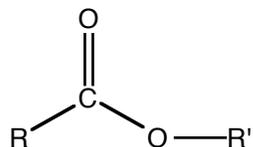


## Experiment 18: Esters

Esters are derivatives of the carboxylic acids and contain the following functional group:



A pleasant, often fruity, odor is characteristic of some of the simpler esters. Ethyl butyrate smells similar to pineapples, the odor of *n*-propyl acetate is reminiscent of pears and isopentyl acetate has a strong banana fragrance.

The synthesis of an ester can be accomplished in one of several ways. An esterification occurs when an alcohol and a carboxylic acid are reacted in the presence of a mineral acid catalyst, such as sulfuric acid. Because these reactions result in an equilibrium mixture of both products and reactants, the reaction conditions must be manipulated in order to produce a reasonable yield. A large excess of one of the reactants can be used in the starting mixture or alternatively, one of the products can be removed as the reaction proceeds (as by a distillation), to shift the equilibrium to the right.

Other synthetic pathways to esters also exist. Acid chlorides react with alcohols to yield an ester and hydrochloric acid. A small amount of pyridine is usually added to the reaction mixture to neutralize the resulting acid. Acid anhydrides can also react with alcohols to produce esters. Unlike the reactions between carboxylic acids and alcohols, neither of these two methods for preparing esters results in an equilibrium mixture.

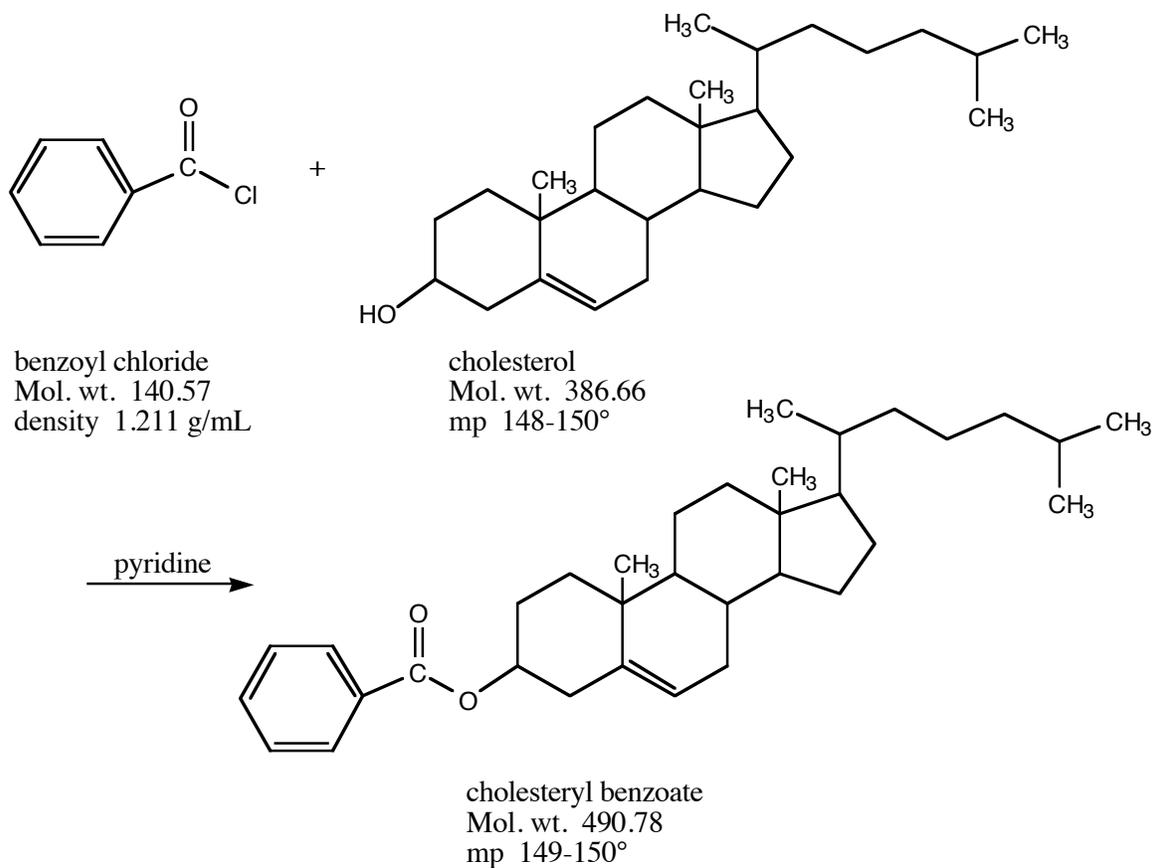
### *Cholesteryl Benzoate, a Liquid Crystal*

Liquid crystals differ from the usual liquid phase in that the molecules in a liquid crystal are still ordered to a certain extent. The first observation of this phenomenon occurred in 1888 when an Austrian botanist prepared cholesteryl benzoate, a compound you will synthesize in today's experiment. Due to their chirality, cholesteryl benzoate molecules lie with their long axes parallel to each other in layers that are stacked in a spiral arrangement. Although the solid crystals are colorless, as the solid melts and enters the liquid phase, the spiral organization of the molecules causes light to selectively scatter into different colors.

In this experiment, cholesteryl benzoate is prepared by reacting cholesterol with an acid chloride in a pyridine solution (see reaction scheme on the top of the next page).

### *Acetylsalicylic Acid, Aspirin*

Acetylsalicylic acid, or aspirin, is one of the most widely used and versatile drugs known today. It was first synthesized by Charles von Gerhardt in 1853 and was later patented by a German dye chemist named Friedrich Bayer in 1893 who recognized its potential as an analgesic (pain reliever). Salicylic acid, a component of willow and poplar bark, had been used as a pain killer for centuries, but its highly acidic property caused irritation of the mucous membranes of the mouth and throat and also resulted in uncomfortable gastric pain. By transforming the acidic phenol functionality into an ester group, the compound retained its analgesic properties but lost some of its irritating side-

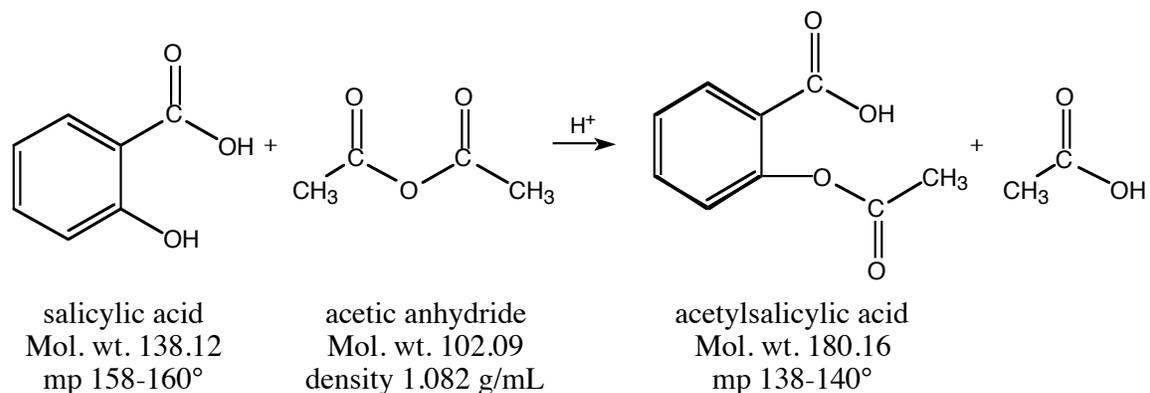


### Reaction scheme for the preparation of cholesteryl benzoate

effects. In addition to relieving pain, aspirin is also an antipyretic (fever reducer) and an anti-inflammatory agent (used for arthritis).

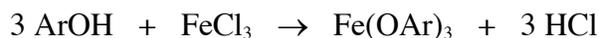
Like all drugs, aspirin also has some undesirable side-effects which should be noted. When taken in large quantities (several grams per day), gastric problems can result. Its use has been implicated in Reyes syndrome, a brain disorder that can affect people under the age of 18. Some people are highly allergic to aspirin. Finally, aspirin interferes with platelets and affects normal blood clotting which can lead to hemorrhaging in extreme cases. However, its anticoagulant properties can also be used to advantage in preventing blood clots from forming in the arteries. Recent studies have shown that the consumption of one-half of an aspirin tablet per day can help to prevent heart attacks and strokes.

Aspirin can be synthesized by the esterification of salicylic acid via reaction with acetic anhydride. A few drops of phosphoric acid are added to serve as a catalyst for the reaction. The use of acetic anhydride as a reactant, instead of acetic acid, results in a rapid and irreversible conversion of salicylic acid to acetylsalicylic acid.



### Testing for phenols

A solution of ferric chloride can provide a reliable test for phenols, since it reacts according to the following equation:



You will perform the ferric chloride test on solutions of your aspirin product as well as on the salicylic acid starting material.

**Outline** the steps of the following procedures:

### Synthesis of cholesteryl benzoate

**Caution: Pyridine is an irritating and toxic liquid. Use only in the fume hood and avoid contact with skin.**

Weigh 1.0 g of cholesterol into a *dry* 50 mL Erlenmeyer flask. Add 3 mL of pyridine to the flask and swirl to dissolve the cholesterol.

**Caution: Benzoyl chloride is a lachrymator (tear gas) and is moisture sensitive. Work with this liquid in a fume hood!**

Use the syringe plus Pasteur pipet measuring device to measure 0.4 mL of benzoyl chloride and add this liquid to the flask. Heat the mixture on a steam bath for 10 minutes.

Cool the flask by swirling it in a beaker of cold water, then dilute the mixture with 15 mL of methanol and collect the solid cholesteryl benzoate by vacuum filtration. Use methanol to rinse out the flask and wash the crystals.

Recrystallize the cholesteryl benzoate by heating it on a steam bath with 20 mL of ethyl acetate until all the solid has dissolved. If some solid material is present which will not dissolve, you will need to filter the hot solution by gravity. Place a small amount of ethyl acetate in the receiving flask and place the flask on a steam bath. Line a stemless funnel with fluted filter paper, and allow the ethyl acetate vapors to warm the funnel before filtering the hot solution. Only perform this gravity filtration if solid material is present.

Allow the ethyl acetate solution of the product to cool to room temperature and then on ice. Collect the crystals by vacuum filtration, washing them with **cold** ethyl acetate. Leave the vacuum on for awhile to allow the crystals to dry. Weigh the dried crystals. Mix equal amounts (a few crystals each) of the recrystallized product and cholesterol. Obtain melting points of both the purified product and this mixture.

Obtain a lamp and bring it to your fume hood.

Place 0.1 g of the cholesteryl benzoate on one end of a glass microscope slide. Rest this end of the slide on a hot plate and turn on the hot plate to a high setting. As the solid melts, it will first turn to a cloudy liquid and then to a clear liquid. After the clear liquid appears, use your test tube holder to grasp the end of the slide which has no material on it, and lift the slide off the hot plate. Shine the lamp at the slide from the side as the sample cools and record your observations. You can repeat the heating and cooling many times with the sample.

### *Synthesis of acetylsalicylic acid*

Heat a 400 mL beaker containing about 150 mL of water to the boiling point on a hot plate. Weigh out 2 g of salicylic acid and place in a 125 mL Erlenmeyer flask. Dispense 5 mL of acetic anhydride from the dispensing buret into the flask. **Caution! Acetic anhydride is corrosive. Avoid contact with skin.** Add 5 drops of 85% phosphoric acid,  $\text{H}_3\text{PO}_4$  (**corrosive!**). Swirl the flask to mix the reactants and then clamp it in the boiling water bath. Heat for about 8 minutes. Carefully remove the flask from the hot water bath and turn off the hot plate. **Cautiously**, add 2 mL of deionized water to the flask. The water will react (possibly vigorously!) with any unreacted acetic anhydride that remains.

Once the reaction between acetic anhydride and water has subsided, add 40 mL of water to the flask. Allow the contents to cool at room temperature for 10 minutes then place the flask in ice. Stir the contents of the flask with a glass rod periodically during this cooling period. Collect the solid product by vacuum filtration and wash it with ice-cold water. Set aside a small portion (spatula-tip full, 20-30 mg) of this crude acetylsalicylic acid.

To recrystallize the acetylsalicylic acid, transfer it to a 125 mL Erlenmeyer flask and add 6 mL of 95% ethanol. Slowly heat the flask on a hot plate just until the aspirin completely dissolves. *As soon as all of the solid has dissolved*, remove the flask from the hot plate. Add water to the solution in 5 mL portions, swirling after each addition, until a total of 25 mL of water has been added.

Place the flask in an ice bath for 10 minutes to complete the crystallization. Collect the purified aspirin by vacuum filtration. Wash the crystals in the funnel with ice-cold water. Leave the vacuum on for a few minutes to air dry the purified aspirin, then press the crystals between two pieces of filter paper to thoroughly dry them.

Test the solubility of your purified acetylsalicylic acid in toluene and in hot water. Observe what happens when the aqueous solution is cooled and when it is then rubbed against the tube with a stirring rod. Test the solubility of your purified product in 1.5 M sodium hydroxide solution, and then add an equal amount of 1.5 M hydrochloric acid. Record your observations. Test the solubility of an aspirin tablet in toluene and in hot water and compare the results with your product. Obtain the melting point of a bit of the tablet. Observe carefully what happens to the commercial aspirin in the melting point capillary and compare it with your observations when your product is melted.

Prepare 5 clean, small test tubes (they do not have to be dry). Place a spatula-tip amount of the following in the test tubes:

Test tube 1: salicylic acid

Test tube 2: your crude product

Test tubes 3 and 4: your purified product

Test tube 5: empty (control)

Add 5-10 drops of water to test tubes 1-3 and 5. Add 5-10 drops of 0.1 M HCl solution to test tube 4 and heat it in a beaker of boiling water for 5 minutes. Then add 1-2 drops of 1% ferric chloride solution to each of the five test tubes. Record your observations.

Save your remaining purified aspirin product in your drawer. Obtain the mass and melting point next week.

Name \_\_\_\_\_ Date \_\_\_\_\_

T. A. \_\_\_\_\_ Lab period \_\_\_\_\_

**Results and Calculations** (to be handed in, with the discussion, two days after the next lab period)

Calculate the percent yield of cholesteryl benzoate.

Melting range for cholesteryl benzoate \_\_\_\_\_

Melting range for (cholesteryl benzoate + cholesterol) mixture \_\_\_\_\_

Calculate the percent yield of acetylsalicylic acid.

Melting range for acetylsalicylic acid \_\_\_\_\_

Melting range for commercial aspirin \_\_\_\_\_