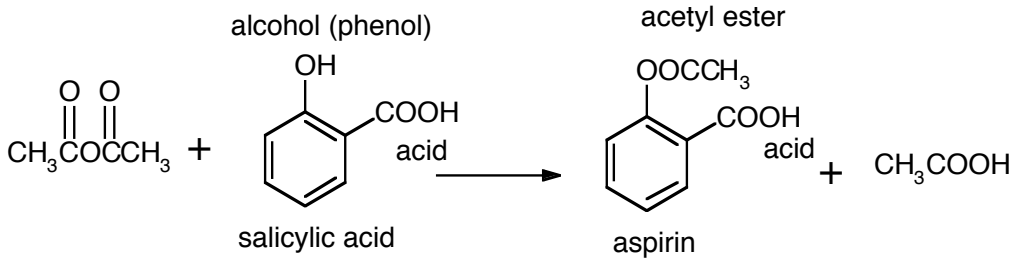
Introduction to Organic Synthesis and Structural Analysis
Esterification; Infrared / NMR Spectroscopy

[Objectives] *1) Synthesize two esters, 2) Analyze the structures of organic compounds using infrared and nuclear magnetic resonance spectroscopy*

Esters are derivatives of carboxylic acids and usually have pleasant smells. They can generally be prepared by the reaction of carboxylic acids or acid chlorides or acid anhydrides with alcohols. The reaction is termed *esterification*. A number of esters are naturally occuring compounds that are responsible for the flavors and fragrances of many fruits and flowers. For example, benzyl acetate has been found to be a principal of peach. Some common esters and their odors are: octyl acetate, oranges; n-pentyl acetate, bananas; and butyl butyrate, pineapples.

In this experiment you will prepare two aromatic esters of o-hydroxybenzoic acid, which is also known as salicylic acid. One of the esters will be acetylsalicylic acid, aspirin. It will be prepared in Part I by heating salicylic acid and acetic acid anyhydride.



Aspirin, 2-(acetyloxy)benzoic acid or salicylic acid acetate has over 20 different chemical or commercial names. It is one of the oldest, most useful and most widely consumed drugs ever discovered. It reduces fever (antipyretic), helps control swelling (anti-inflammatory), diminishes aches and pains (analgesic) and thins the blood (anti-coagulant). The compound has been used for over a century. For a centenary account see:

http://chemconnections.org/general/chem121/aspirin-econ-8-9-97.html

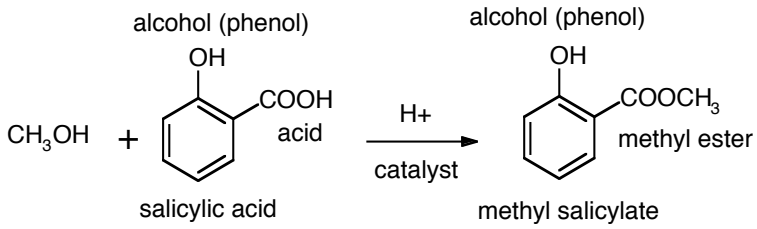
Aspirin was first synthesized commercially by the multinational company, Bayer, which is headquartered in Germany. Aspirin is prepared by esterifying salicyclic acid, which acts as the alcohol in the reaction. Salicylic acid occurs as a natural product in several plants. In California, the Miwok tribe used willow bark which contains salicylic acid as a medicinal/therapeutic agent. The leaves and bark of a large number of plant species have been used by native cultures for their medicinal properties. Many drugs have either come directly from plant natural products or are synthetic modifications of the chemically isolated, naturally occuring compounds. The scientific study of native plant use is refered to as ethnobotany. It has led to many dramatic discoveries including curare, digitalis and rotenone.

MATERIALS:

~20 mmoles salicylic acid
5 ml acetic anhydride
5 ml methyl alcohol
l% $FeCl_3$ solution
concentrated H_2SO_4
ice

Kem Kit
Hot Plate
10-ml graduated cylinder
large test tube
ring stand
clamp

The second ester that you will prepare is methyl salicylate which is a compound found in the wintergreen plant, which is in the mint family. It is used extensively as a flavoring agent and in emolients and liniments for sore muscles. It is synthesized by esterification of the carboxylic acid group ($-CO_2H$) of salicylic acid with methyl alcohol. The reaction follows.



(Conduct the synthetic procedures with caution in a fume hood. Methyl alcohol is toxic, acetic anhydride is an irritant, and sulfuric acid is highly corrosive.)

Part I: Synthesis of aspirin

Place about 20 mmoles of salicylic acid (record the exact weight of salicylic acid to 2 decimal places) in a round bottom flask. Cautiously add 5 ml of acetic anhydride and then 5 drops of concentrated sulfuric acid. Mix the reagents, equip the round bottom flask with a condenser and then heat the flask in a beaker of water, warmed to 80-90 ºC, for 10-20 minutes. The mixture does not need to boil, which would be referred to as refluxing.

Remove the water bath and allow the flask to cool to room temperature. Add 40 ml of water and cool the mixture in an ice bath to complete the crystallization. Filter and wash the crystals on the filter with a small volume of ice water. Allow the product to dry on a watch glass. Weigh the product and determine its melting point. Compare the melting point to pure aspirin, which can be found in the *Merck Index* or the *CRC Handbook* (both are available from the stockroom) or using *Wikipedia.org* online.

> *Phenols* are a class of compounds in which the -OH alcohol group is attached to an aromatic ring. Note that this group is present in both salicylic acid and methyl salicylate. Many phenols, but not all, form colored complexes with ferric chloride. The colors range from green through blue and red through violet. Hence, the use of a 1% $FeCl_3$ solution is employed as a test for the presence of phenols. In this case for unreacted salicylic acid.

Add a few crystals of crude aspirin to about 5 mL of water in one test tube and a few crystals of salicylic acid plus 5 ml of water in a second test tube. Add 1 drop of 1% $FeCl_3$ solution to each and record your observation.

Part II: Synthesis of methyl salicylate

Mix about 0.2 grams of salicylic acid with a few milliliters of methanol in a test tube or small beaker and cautiously add 5 drops of concentrated sulfuric acid. Warm the mixture in a water bath for 10 minutes, allow too cool and cautiously smell the mixture. After carefully smelling the mixture add 1 drop of 1% $FeCl_3$ solution to the test tube. Record your observations.

Carefully smell your product.