

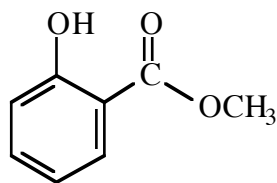
Synthesis of Salicylic Acid

Source: AEM Handout, adapted from Mohrig, J. R.; Hammond, C. N.; Morrill, T. C.; Neckers, D. C. **Experimental Organic Chemistry**. New York: Freeman, 1998. p. 32-36.

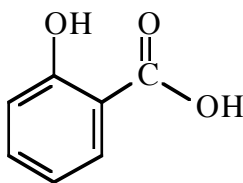
Derivatives of salicylic acid are familiar and important compounds. Among them are methyl salicylate (oil of wintergreen) and acetylsalicylic acid (aspirin). All of these structures are shown below. This experiment will serve as your introduction to the chemistry of these materials and to the art of organic synthesis. You will use the techniques of recrystallization and melting point determination, which you have recently learned.

Salicylic acid is a white crystalline compound, which can be isolated from the bark of birch trees. Since it is a valuable substance that can be isolated from nature, it is called a useful "natural product". Although it was used historically as an analgesic (pain reliever), today it is commonly used in ointments and plasters for the removal of warts from the skin. Acetylsalicylic acid (an ester derivative) is much more commonly used than salicylic acid itself for pain relief, because the parent compound can be rather irritating to your stomach linings. Acetylsalicylic acid is marketed as aspirin.

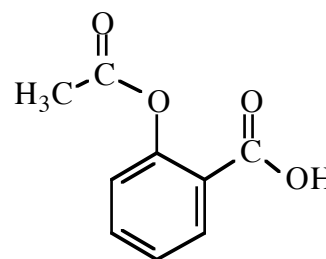
Methyl salicylate has a fragrant, minty smell that has made it a favorite flavoring in candies. It is also the major constituent of oil of wintergreen, making up over 90% of the essential oil from the wintergreen plant. However, most methyl salicylate used in foods is made synthetically, a cheaper process than its extraction from wintergreen leaves or sweet birch bark. Note that it is a different ester derivative of salicylic acid.



methyl salicylate



salicylic acid



acetyl salicylic acid

In any synthetic procedure, a chemist must use a series of techniques that can be classified as:

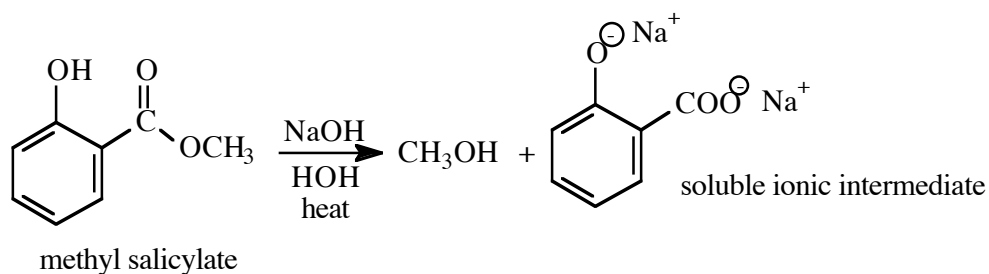
- (1) carrying out the reaction,
- (2) isolating the product (perhaps using extraction, crystallization, distillation, etc.),
- (3) purifying the product (again, perhaps using crystallization, distillation, chromatography, etc.),
- (4) and characterizing the product and estimating its purity (perhaps using melting point, spectroscopy, various types of chromatography, etc.).

Steps (2) and (3), the isolation and purification of the reaction product, are often called the "work-up" of the reaction mixture. The types of techniques that are used for each of these steps depend on the energy requirements of the reaction and on the physical and chemical properties of both the starting materials and the products.

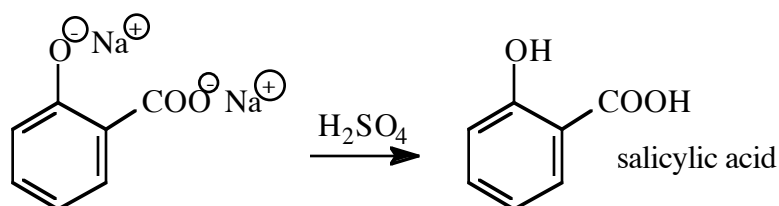
For each reaction, the chemist also computes a theoretical and % yield. To do this, you must know the stoichiometry of the reaction, and thus the mechanistic details are often useful to know. With this information, you can tell for example if a substance added to the reaction mixture is a catalyst or if it is a reagent that gets used up in the process. Of the materials that are consumed, the one that is used up 1st is called the limiting reagent. Once the ID of the limiting reagent is known, that can be used to determine the theoretical amount of the product that you hope for. With this in hand, the percent yield can be determined.

The overall reaction that you will carry out is shown here, in two steps. The process is an example of ester hydrolysis under strongly basic conditions. We will discuss the mechanistic detail in recitation.

Step 1:



Step 2:



Procedure

CAUTION! NaOH is quite caustic! Do not let this solid contact your skin!

To carry out the reaction: Clamp a 25-mL round-bottomed flask, from a blue macroscale kit, to a ring stand or vertical support. Place 1.2 g (know the exact mass!) of sodium hydroxide and 7 mL of water in the flask; swirl the mixture until the solid dissolves. Add 0.5 mL (know the exact mass of this volume!) of methyl salicylate. A white solid will quickly form. Add one or two boiling stones to the reaction mixture to prevent bumping of the solution when it is heated and place a heating mantle/sand bath under the flask. Note that neither of our heating mantle sizes is exactly right for a 25 ml roundbottom; some sand must be used with either of these heating mantles, however do try to "sink" the roundbottom $\sim 1/3$ to $1/2$ way into the sand. Attach a water-cooled reflux condenser to the round-bottomed flask. Heat the reaction mixture to its boiling point, and allow it to reflux for 15 min. The solid that formed initially will dissolve as the mixture is warmed.

After the reflux period, remove the heating mantle and let the mixture cool to room temperature. Placing a beaker of cold tap water under the flask speeds the cooling process. Carefully add 3M sulfuric acid solution in approximately 1-mL increments until a heavy white precipitate of salicylic acid forms and *remains* when the mixture is well stirred. You will need approximately 4 or 5 mL of the sulfuric acid solution.

To isolate the product: After you have added just enough 3M sulfuric acid to give a heavy white precipitate, add 0.5 mL more acid to ensure complete precipitation of the salicylic acid. Cool the mixture in an ice-water bath to $\square 5^\circ\text{C}$. Collect the precipitated crude product by vacuum filtration, using a Buchner funnel. Rinse the solid product well with ice-cold water, in the Buchner funnel, with the suction flowing.

To purify the product: Recrystallize the product from water in a 25 or 50 mL Erlenmeyer flask. Follow the usual procedures for recrystallization

To characterize the product and estimate its purity: After the recrystallized product has dried completely, measure its mass and calculate its theoretical and % yield. Measure the melting point range of the product and compare it to the literature value.

Cleanup. Neutralize any excess acid in the filtrate of the synthesis using aqueous sodium carbonate and flush it down the drain with lots of water. The recrystallization filtrate can be flushed directly down the drain with lots of water.