"The meeting of two personalities is like the contact of two chemical substances; if there is any reaction, both are transformed."

—Carl Gustav Jung
Psychiatrist and Philosopher

One of the more important functions of organic chemistry is the synthesis of useful organic chemicals. Thousands of laboratories in industry and academia the world over are responsible for the vast array of materials available to us today. Perhaps the most important application of synthetic organic chemistry is the manufacture of medications. Pharmaceutical companies employ large numbers of organic chemists to develop new drugs and to seek out better ways to make existing drugs.

No study of chemistry would be complete without an investigation of chemical synthesis. In this experiment you will make the most common pain reliever in use today: aspirin. In the process you will be introduced to the basic components of the synthesis process.

**Educational Objectives:** A student who has successfully completed this experiment will be able to

- perform an organic synthesis,
- isolate a reaction product,
- purify a product using recrystallization,

**Experimental Objectives:** A student who performs this experiment is asked to

- synthesize acetylsalicylic acid from salicylic acid and acetic anhydride,
- isolate the product using filtration,
- purify the product using recrystallization, and

**Background**

The synthetic chemical industry is only about 150 years old. It began when scientists understood enough about the atomic nature of matter to be able to routinely make specific molecules. One of the first applications of chemical synthesis was the search for more effective medications and dyes. And one of the most dramatic successes was the discovery of aspirin.

For thousands of years it has been known that a tea made from the bark of the willow tree is effective for relieving certain kinds of pain. By the middle of the nineteenth century, chemists had determined that salicylic acid was the chemical responsible. Although effective medicinally, its acidic properties caused irritation of mucous membranes. As the 19th century came to a close, chemists working for the Bayer company in Germany had discovered that acetylsalicylic acid possessed all of the beneficial properties of salicylic acid, without the unpleasant side effects. They produced and marketed their new wonder drug under the trademark name “aspirin,” and the rest is history.
Since then, the search for new and better medications has continued at an ever-expanding rate. While the techniques used today are substantially more complicated (and more expensive) than those used to make aspirin, the process is pretty much the same.

Chemical synthesis is discussed in chapter 12 of your technique book. You need to review this material before continuing.

This guide covers the first week of the experiment: the synthesis and isolation of aspirin. The characterization techniques will be performed in the second week and are covered in the next guide.

**Overview**

In this experiment, you will react salicylic acid with acetic anhydride in the presence of an acid catalyst to make acetylsalicylic acid (aspirin) and acetic acid. This reaction is represented in equation 1. Because the reaction is destroyed by water, you will need to take to keep water out of the reaction flask.

Since aspirin is insoluble in water it will precipitate from solution in the reaction flask. You will use vacuum filtration to separate your product from the solution. You will then employ the technique known as recrystallization to purify your aspirin. This will involve dissolving your crude reaction product in a small amount of hot ethanol, cooling the ethanol and collecting the crystals of aspirin that form in the cold solvent. Recrystallization is discussed in section 5-4 of the lab book.

![Equation 1](image)

\[\text{Salicylic Acid} + \text{Acetic Anhydride} \xrightarrow{\text{Acid Catalyst}} \text{Acetylsalicylic Acid} + \text{Acetic Acid}\] (1)

**Procedure**

Use the *Summary of Steps* at the end of section 12-1 as your guide when preparing your procedures. The following information should be useful.

**Chemicals**

The following are provided for your use.

**Salicylic acid** - a white, crystalline solid in a jar on the reagent bench. Take only what you need.

**Acetic anhydride** - a strongly acidic liquid producing caustic vapor that is destroyed by water in the air. Contained in a bottle fitted with a dispenser especially designed to prevent spills, contain the vapor and prevent water vapor from entering the bottle. This is pictured to the right (figure 1). The bottle is located in a hood.

**Concentrated sulfuric acid** - a strongly acidic liquid located in the acid storage hood.

![Figure 1. Acetic anhydride dispenser.](image)
Equipment
The following are provided for your use and are pictured in figure 2.

- 250mL Filter Flask
- Buchner Funnel
- Vacuum Hose
- 50mL Erlenmeyer Flask
- Stir Bar
- Stainless Steel “Freddie” bowl
- Spatula

In addition, you will have the use of an alcohol thermometer.

Pointers
You will need to consider the following when preparing your procedures.

- The reaction is best performed in an Erlenmeyer flask suspended in a hot water bath. A cotton plug will keep water vapor out of the flask. Figure 3 illustrates a suitable arrangement.

- Recommended amounts of chemicals. 2 grams of salicylic acid, 5 mL of acetic anhydride and five drops of concentrated sulfuric acid. An excess of acetic anhydride is used because this chemical is also the solvent for the reaction.

- Order of addition. Put the salicylic acid in a flask and add the acetic anhydride. Swirl to mix before adding the sulfuric acid. Add the sulfuric acid slowly.

- The reaction mixture must be protected from water in the air. Cotton plugs are provided.

- The reaction mixture must be heated for 10 to 15 minutes. The temperature will be decided by your group and will be somewhere between 50 and 100 °C. At the end of this time raise the reaction flask out of the water bath.

NOTE
Any water present on your glassware will destroy the acetic anhydride. Make sure your glassware is dry!
When complete the reaction mixture must be reacted with water to destroy the unreacted acetic anhydride. This is a potentially dangerous operation due to the large amount of heat generated by the destruction of the acetic anhydride. It is best to allow the reaction flask to cool for a few minutes before adding the water. Remove the cotton plug and, using a transfer pipet, add 3 mL of water dropwise while swirling the flask.

**CAUTIONS**
Both the acetic anhydride and sulfuric acid used in this procedure are concentrated acids that can cause immediate destruction of tissue. Acetic anhydride has also been known to cause allergic reactions in rare cases. You must take the following precautions.
- Avoid breathing the fumes.
- Should you get any on your skin, immediately begin irrigation with water and notify your instructor.
- Make sure any spills are covered with bicarbonate to neutralize the acid.
- To protect yourself from inadvertent contact with these chemicals you are required to wear gloves while performing the experiment.

**Obtaining product**
Once you have destroyed the acetic anhydride your aspirin will be dissolved in the reaction mixture. The following procedure should get your aspirin to crystallize from this solution.
- Put the reaction flask into an ice bath to cool. The best ice bath consists of a slurry of ice, a little water and rock salt.
- After a while, crystals of aspirin should begin to form. While you are waiting for the aspirin to crystallize, set up the vacuum filtration apparatus (chapter 5-2). If you observe oil forming in the bottom of the reaction flask instead of crystals, reheat the flask for about five minutes in the boiling water bath then rapidly transfer it to the ice bath. Crystals should now form.
- When crystallization appears to be complete, filter the mixture using the vacuum filtration apparatus. Use your spatula to transfer as much of the solid material as possible into the Büchner funnel. Rinse the flask with a small amount of chilled water. Allow the crystals to sit in the funnel with the vacuum drawing air through them for at least ten min. (this will aid in drying the crystals and make them easier to transfer). While waiting you can clean any glassware that is not being used.
- When the crystals appear to be dry determine the mass.
**Recrystallization**  Recrystallization is discussed in section 5-4 of the lab book. *Ethanol* is provided for you to use as the recrystallization solvent. It is a volatile liquid that also readily absorbs water. If the ethanol becomes wet with water it will be much less effective. Therefore you will need to avoid allowing any water to get into your ethanol. Because it is volatile you will also need to be careful heating it. You can easily boil it all away!