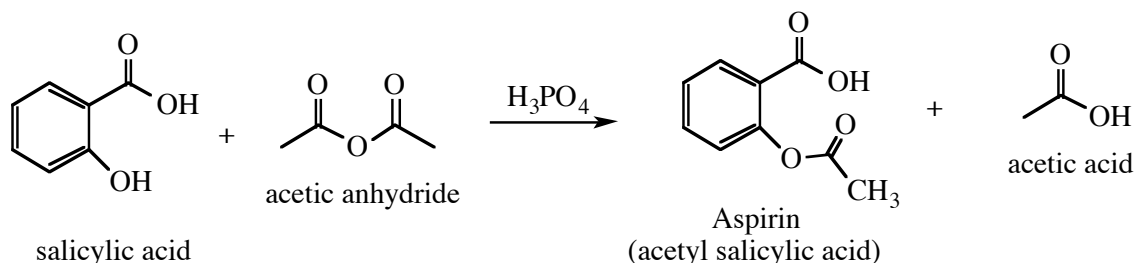


Esterification: Preparation of Aspirin (acetylsalicylic acid)

One of the most well studied reactions is the conversion of alcohols to esters by using a carboxylic acid. Phenols, unlike the alcohols, cannot be esterified by direct interaction of the phenol with an organic acid. The esterification of a phenol is usually carried out by treating it with a much more reactive reagent, such as an acid anhydride or an acyl chloride. In this experiment, salicylic acid is converted into the acetate ester, aspirin, by treatment with acetic anhydride. The reaction is shown below.



A. Preparation of Aspirin

Place 2.00 g of salicylic acid in a 50 mL Erlenmeyer flask, add 5.0 mL of acetic anhydride, and 5 drops of 85% phosphoric acid. (*Caution: Phosphoric acid is a very corrosive liquid that causes serious acid burns. Spills should be washed immediately with large amounts of water.*) Stir the mixture well. Heat the flask on a sand bath for 5 minutes (keep the sand temperature below 150 °C), remove the flask from the bath, and while still hot, carefully add 2 mL of water in one portion. (*Caution: The solution may boil from the heat of decomposition of the excess acetic anhydride: handle the flask carefully.*) After a few minutes, add the reaction mixture to 40 mL of water in a 125 mL Erlenmeyer flask and stir the solution until crystals begin to form. Cool the mixture in an ice bath for 20 minutes to complete the crystallization. Collect the product by suction filtration. Wash the crystals with cold water and pull air through the filter until most of the water is gone. Recrystallize the product from a minimum amount of a hot ethanol-water (1:3) mixture. Start with about 10 mL of the hot ethanol-water mixture and add 2 mL aliquots (portions) until the product completely dissolves. Remember to keep the mixture hot while adding the aliquots. After the product completely dissolves, allow the solution to slowly cool to room temperature, and then place the flask in an ice-water bath for 20 minutes to complete the recrystallization. Filter off the recrystallized product, wash the crystals with cold water, and dry the crystals. Determine the melting point of your product and calculate the % yield of the reaction.

B. Test for the Phenolic Hydroxyl Group

Dissolve a few crystals of aspirin in 1 mL of methanol in a test tube and add one drop of 1% ferric chloride solution. Record your observation. Repeat the test with salicylic acid and record your results. What can you conclude about your results?

1. Shown below is a normal esterification of an alcohol. Pay attention to the rate determining step of the mechanism to explain why a phenol requires the much more reactive anhydride or acid chloride.

