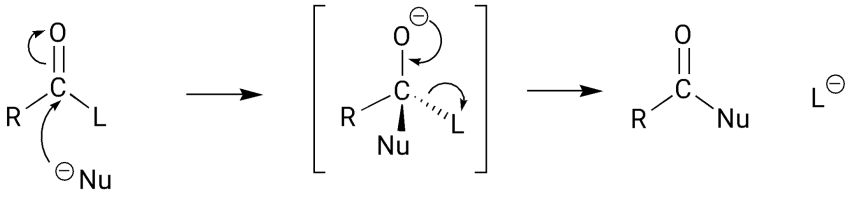
Synthesis of Aspirin:
Nucleophilic Acyl Substitution

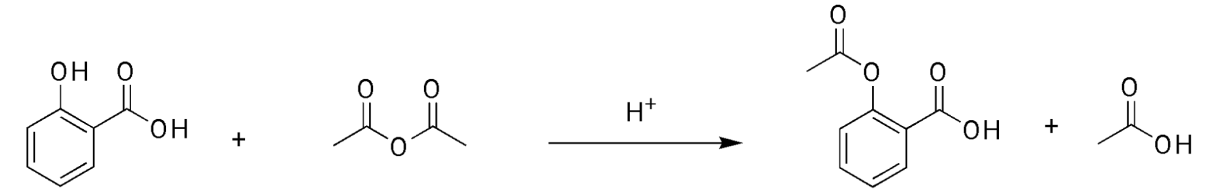
Background

Nucleophilic acyl substitution is a useful way to convert between different types of carboxylic acid derivatives. These derivatives include acid chlorides, acid anhydrides, esters and amides. Like carboxylic acids, they each have an electronegative atom bonded to a carbonyl that can be turned into a leaving group.

The first step in acyl substitution is the attack of a nucleophile at the carbonyl carbon to form a tetrahedral (sp^3) intermediate. Next, the electrons on the oxygen reform the carbonyl, kicking out the leaving group in the process.



In this lab you will synthesize aspirin from salicylic acid using nucleophilic acyl substitution. Phosphoric acid is used as a catalyst to make the carbonyl group more electrophilic and thus more reactive towards nucleophiles.



salicylic acid | acetic anhydride | aspirin (acetylsalicylic acid) | acetic acid

Procedure

Reaction Setup

Add 3.0 g of salicylic acid to a 250 mL Erlenmeyer flask. Next, add 6.0 mL of acetic anhydride to the flask. **Carefully** add 5 to 10 drops of 85% phosphoric acid to the reaction mixture and swirl to mix everything thoroughly. Heat the mixture for about 10 minutes in a beaker of warm water (about 70-80°C).

Workup

After heating, cautiously add 20 drops of deionized water after which you may quickly add an additional 20 mL of deionized water. Cool the flask in an ice bath. If crystals do not appear after 5 minutes, scratch the walls of the flask with a glass stirring rod at the air solvent interface to induce crystallization.Isolate the solid product by vacuum filtration and wash the crystals with up to 10 mL of chilled water. Continue to pull air through the solid and filter paper for several minutes. Allow the solid to dry in an envelope for at least two days.

Characterization

Characterize by melting point and percent yield.

Chemicals: salicylic acid, acetic anhydride, 85% phosphoric acid

Prelab – Synthesis of Aspirin

Name_____

1. Draw a mechanism for the formation of aspirin and identify the nucleophile and the electrophile.
(In the presence of acid, protonation of the acyl group is the first step and the leaving group is protonated before it leaves)

2. Which type of carboxylic acid derivative is aspirin an example of?

3. Aspirin will slowly breakdown in the presence of moisture through a process known as hydrolysis. Write a balanced equation for the hydrolysis of aspirin. What smell would indicate that a bottle of aspirin has gone bad because of hydrolysis?

4. Why must you wait several days before weighing your product?

5. Stomach irritation is a common side effect of aspirin. Explain this effect based on aspirin's structure.