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Synthesis of acetylsalicylic acid (Aspirin)	عنوان المحاضرة باللغة الانجليزية
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3	رقم المحاضرة
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محتوى المحاضرة

Synthesis of acetylsalicylic acid (Aspirin)

1-Introduction

Aspirin, an acetyl derivative of salicylic acid

It is considered one of the most popular and widely used pharmaceutical drugs worldwide.

It was first prepared in the late 19th century by the German company Bayer.

It is used as a nonsteroidal anti-inflammatory drug (NSAID), pain reliever, and fever reducer.

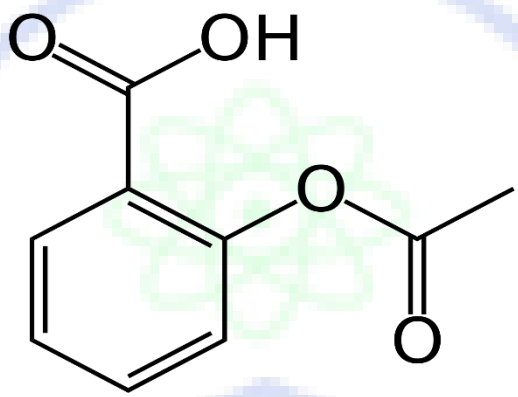
2-Chemical Structure

Aspirin contains three groups:

•Carboxylic acid functional group (R-COOH)

•Ester functional group (R-O-CO-R')

•Aromatic group (benzene ring)



3-Physical Properties

- **Aspirin occurs as white crystals or as a white crystalline powder.**
- **weakly acidic, with a melting point of 136°C, molar mass 180.15 g/mol**
- **It is slightly soluble in water (1:300), soluble in alcohol (1 :5), chloroform (1:17) & ether (1:15). It dissolves easily in glycerin.**
- **Practically all salts of aspirin (soluble in aqueous media), except those of aluminum and calcium (insoluble in aqueous media), are unstable for , pharmaceutical use.**
- **Aspirin gives no color with FeCl3 solution.**

4-Chemical Properties (Reactions)

Aspirin decomposes rapidly in solutions of ammonium acetate, acetate, carbonate, citrate, or alkali metal hydroxides. Aspirin remains stable in dry air but gradually hydrolyzes upon contact with moisture to acetic and salicylic acids. Hydrolysis proceeds rapidly in solution with alkalis, and clear solutions may consist entirely of acetate and salicylate.

5- Chemical Reactions

- **With bases (NaOH): Decomposes to give sodium salicylate.**
- **With bicarbonates: Froths (releases CO_2).**
- **Unstable in strong basic media.**

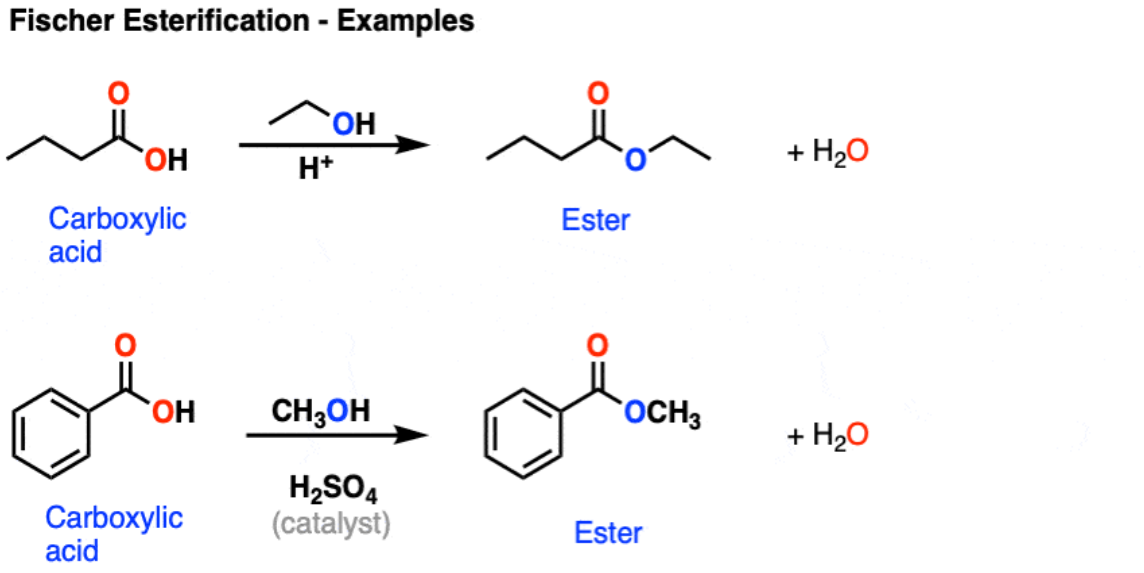
6-Preparation of Esters

Esters can be prepared in several ways:

1- Direct esterification:

The reaction of a carboxylic acid with an alcohol in the presence of an acidic catalyst (usually H_2SO_4).

The reaction is slow and reversible, requiring the removal of water to drive the reaction forward.



2- Using acyl chlorides:

They react quickly with alcohols to produce esters.

Disadvantage: They release HCl gas (irritating, dangerous, and corrosive).

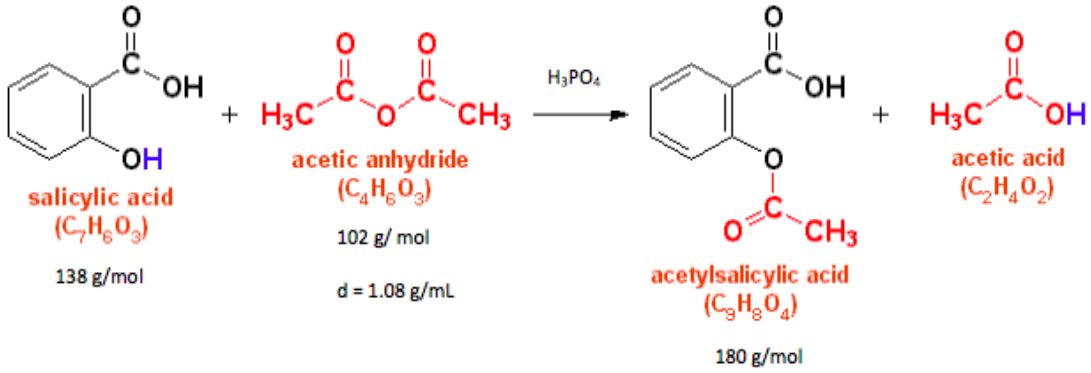
3- Using acid anhydrides:

A safer and less hazardous method.

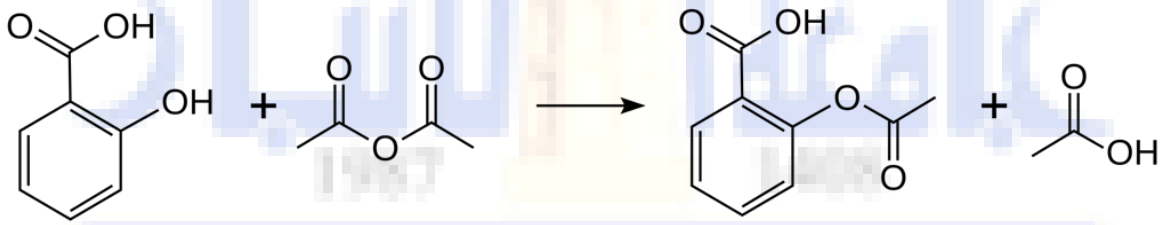
It yields good yields without producing HCl.

The anhydride sometimes acts as both a solvent and a reactant.

Example: Acetylation of salicylic acid (preparation of aspirin)



Aspirin is prepared by reacting salicylic acid with acetic anhydride. Salicylic acid is treated with acetic anhydride, an acid derivative, resulting in a chemical reaction that converts the salicylic acid hydroxyl group into an ester group. This process produces aspirin and acetic acid, which are byproducts of this reaction. Small amounts of sulfuric acid (and sometimes phosphoric acid) are used as a catalyst. This method is commonly used in laboratories.



7-Reaction Mechanism

1- Initiation of the reaction:

The –OH group in salicylic acid acts as a nucleophile.

2- Nucleophilic attack:

Salicylate anion attacks the carbonyl carbon atom in acetic anhydride.

3- Formation of an intermediate complex:

A tetrahedral addition occurs.

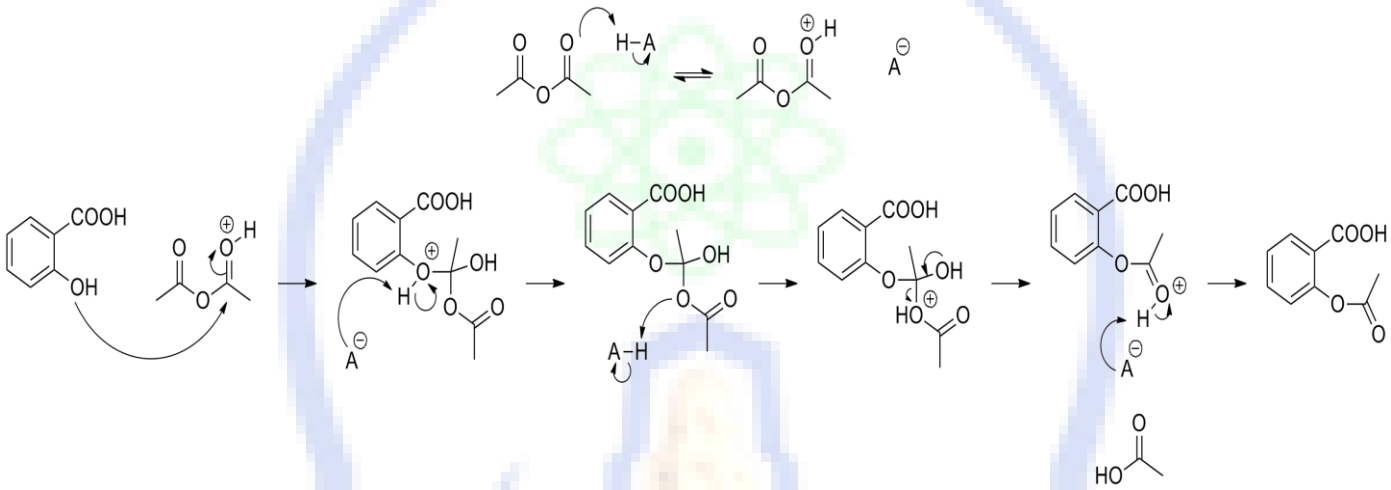
4- Removal of a leaving group:

The –OCOCH₃ group (acetic acid) is released.

5- Final product:

Acetylsalicylic acid (aspirin) is formed as the primary product.

Acetic acid (CH_3COOH) is formed as a secondary product.



8-Pharmaceutical uses

- **Analgesic.**
- **Antipyretic.**
- **Anti-inflammatory.**
- **In small doses, it acts as an antiplatelet → prevents blood clots.**

9- Procedure (Preparation of Aspirin)

1 -Add 2 gm salicylic acid with 15 ml acetic acid, then add 4 drops of sulfuric acid

2 -Place the mixture in a water bath at 60°C (10-15 minutes)

3 -Add 20-25 ml of cold distilled water

4- Filter and wash with cold water to obtain aspirin

5- Recrystallization of the product to obtain a pure substance.

10-Tests and Verification

- **Measure the melting point to compare purity with reference values.**
- **Using $FeCl_3$: Salicylic acid gives a purple color, while aspirin does not react → evidence of complete reaction.**