



Organic Pharmaceutical Chemistry II

4th Stage 1st Semester

Lab No: 4



Synthesis of Acetanilide

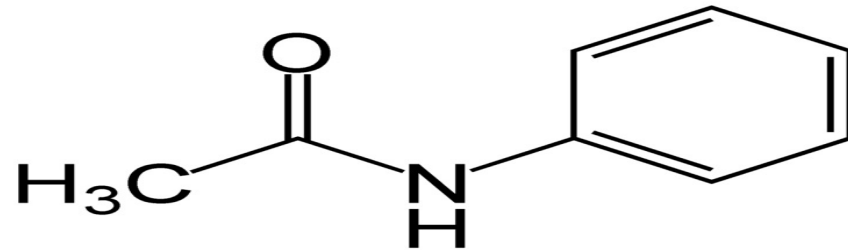
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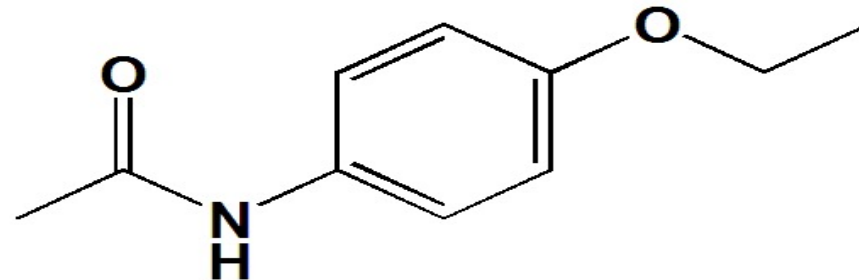
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Introduction:

- Acetanilide is an aniline derivatives that was found to have both **analgesic** and **antipyretic** properties. It was introduced in 1886.



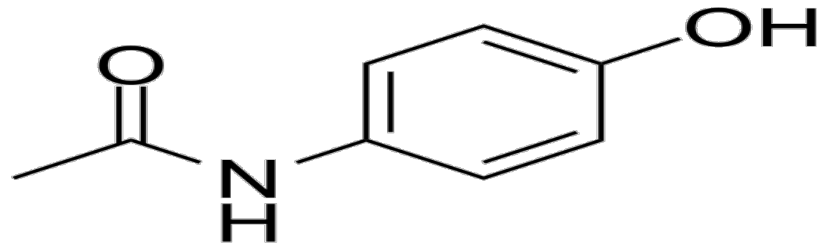
- However, the toxic evident of this substance promote the need of searching of less toxic derivatives of aniline like phenacetin in 1887.



phenacetin

Introduction:

- Phenacetin was withdrawn in 1983 owing to its carcinogenic effect.
- in 1948, it was discovered that acetanilide metabolizes into **acetyl-para-amino-phenol (paracetamol)**, and this metabolite has the analgesic and antipyretic properties.



- As a result, acetanilide was slowly replaced by its metabolite paracetamol, which is still quite well known in the pharmaceutical field.

Properties of Acetanilide:

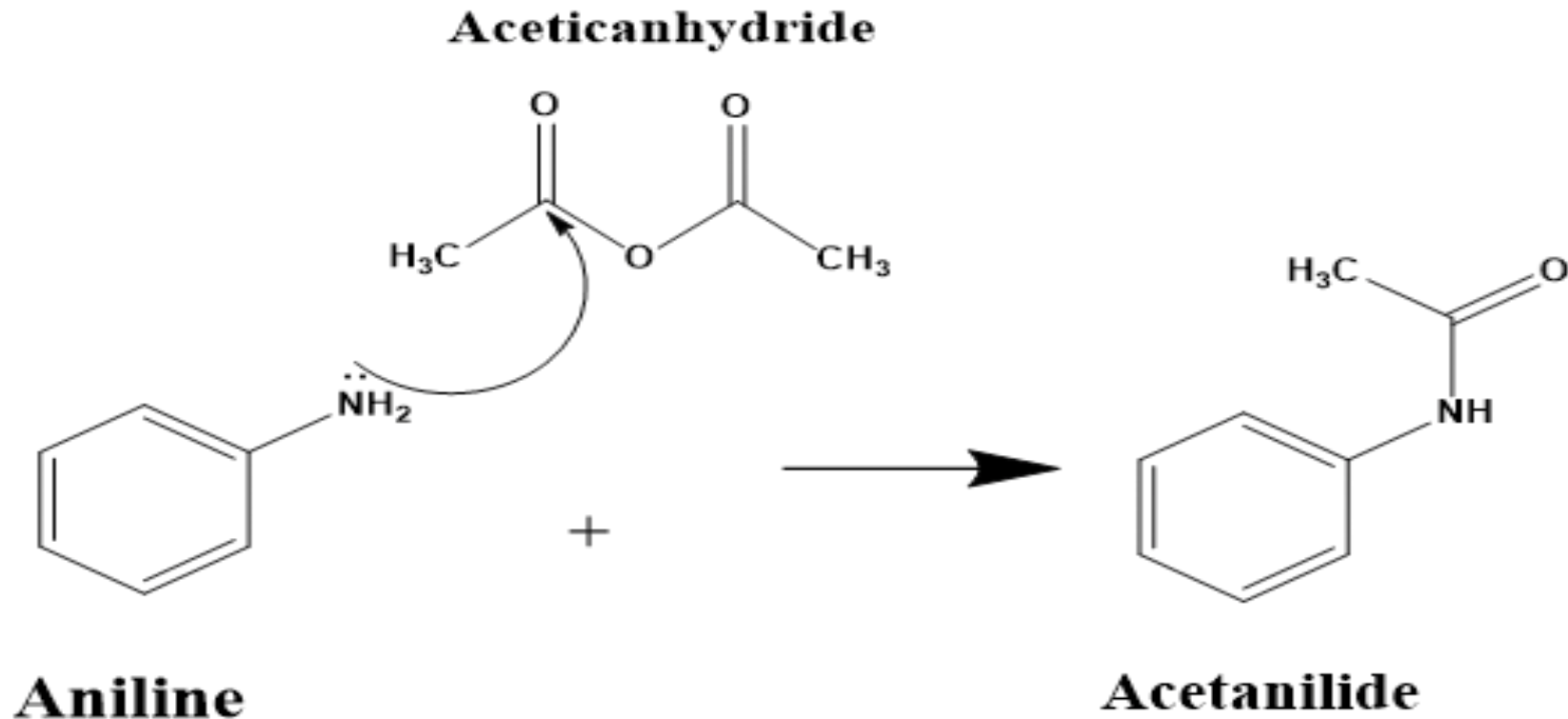
➤ Here are some of the basic properties of this organic compound:

- **Appearance:** It is a white solid with a flaky appearance.
- **Odor:** This is an odorless compound.
- **Solubility:** Acetanilide is a little soluble in water. It is also soluble in diethyl ether, ethanol, benzene and acetone.
- **Molecular Weight:** Its molecular weight is 135.17 g/mol.
- **Melting Point:** It has a melting point of 114.3 °C.
- **Density:** The density of Acetanilide is 1.219 g/ cm³



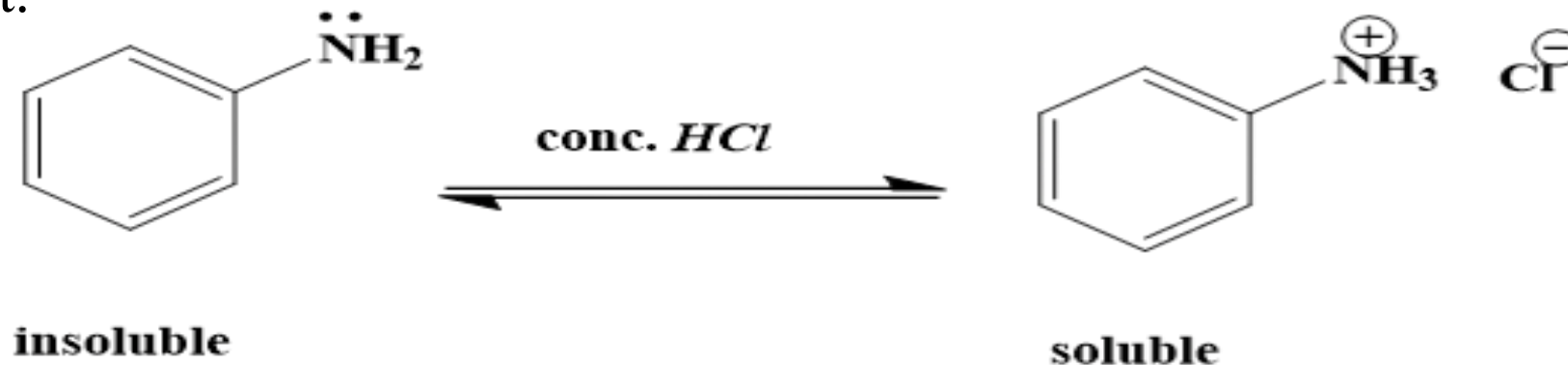
Synthesis of Acetanilide:

- In this experiment, *acetanilide* would be prepared from *aniline* by acetylating it with *acetic anhydride* in the presence of **concentrated HCl** and *anhydrous Sodium acetate*.



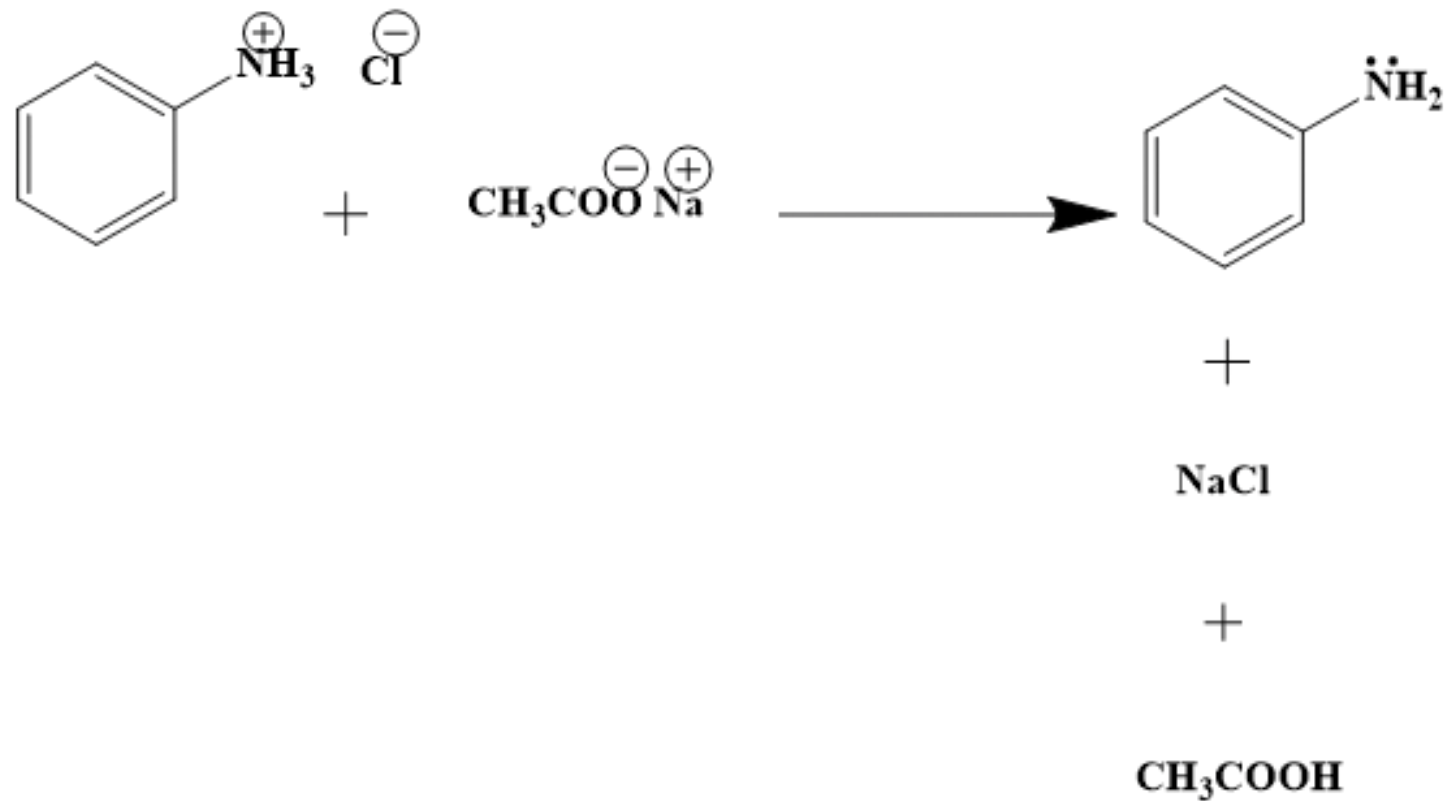
Principle:

- Both *aniline* & *acetic anhydride* are somewhat viscous liquids, so simply mixing them together does not result in the efficient formation of acetanilide.
- Therefore, a solvent is used (water) to dissolve and evenly disperse the reactants in it.
- *Aniline* is not soluble in water, so concentrated *HCl* is added in order to dissolve it.

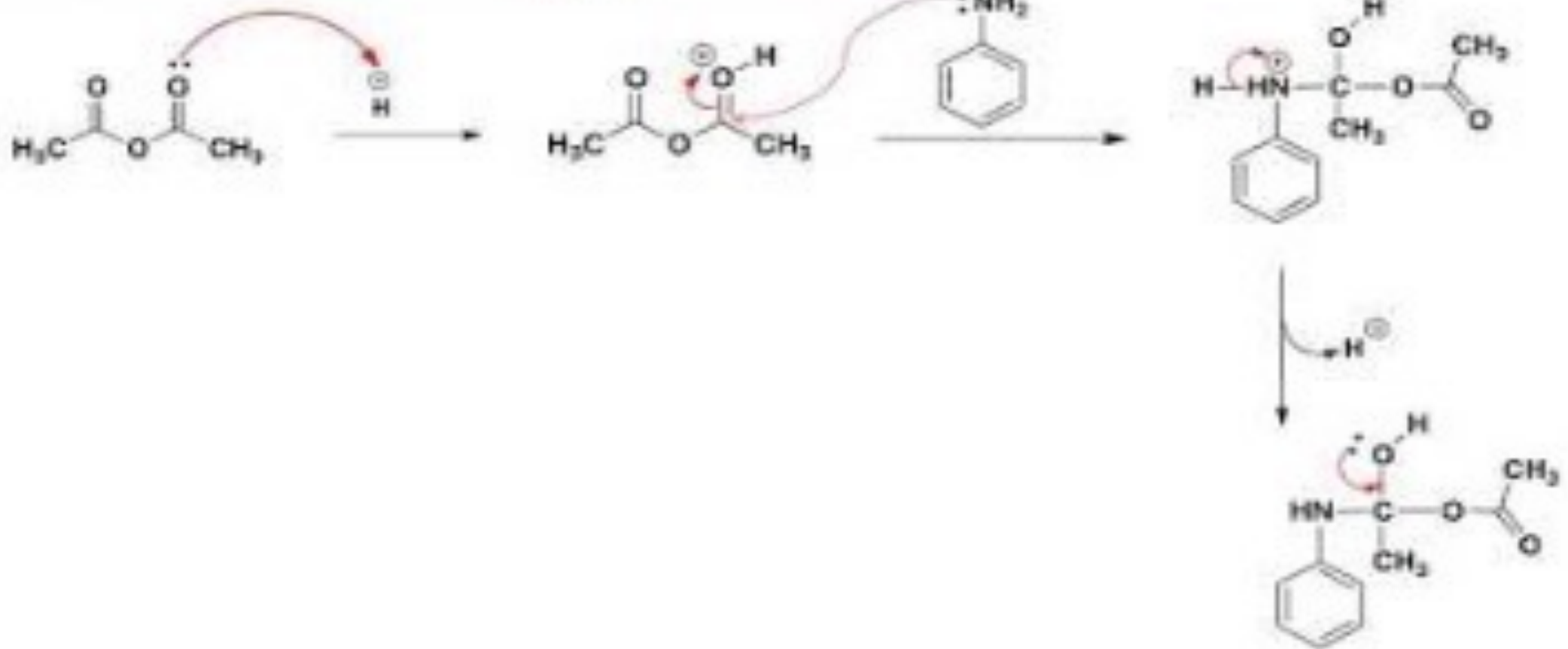


Principle:

- Only the free *aniline* can act as *nucleophile*, why?
- Therefore, *Sodium acetate* will be used in order to shift the reaction below to the left.



Mechanism of Acetanilide Reaction:



Procedure 1:

1- Conical flask **A**:

- Mix (2ml) of aniline with (4ml) of distilled water & drop wise of concentrated HCl.

2- Conical flask **B** :

- Dissolve (2.4gm) of anhydrous sodium acetate in (10ml) of distilled water, then add (6ml) of acetic anhydride.

3- Immediately Transfer the content of conical flask **B** to the content of conical flask **A** with shaking.

Procedure 1:

- 4- Cool the mixture (fridge) or add crushed ice until white crystals start to precipitate.
- 5- Filter the product and wash it with water.
- 6- Recrystallizes the acetanilide with minimum volume of hot distilled water, and then filters it.
- 7- Allow the product to dry at room temperature.
- 8- Calculate the percent of yield.

OR:

Procedure 2: that was adopt in our lab.

- 1- Mix(2ml) of aniline with (4ml) of water in conical flask.
- 2- Stirring the mixture by using magnetic stirrer apparatus.
- 3- Measure (2.5ml) acetic anhydride and add (1drop) of concentrated HCL to it.
- 4- Add the acetic anhydride to aniline mixture very slowly (drop by drop) with continuous stirring, the crystals of acetanilide will form at the end of addition.

Procedure 2: that was adopt in our lab.

5- Recrystallizes the acetanilide with minimum volume of hot distilled water, and then filters it.

6- Allow the product to dry at room temperature.

7- Calculate the percent of yield.

Calculations:

- Moles (Aniline) = Moles (Acetanilide)
- $Wt / M.Wt \text{ (Aniline)} = Wt / M.Wt \text{ (Acetanilide)}$
- Density of aniline = 1.02 g/cm^3
- $Wt = V * D$
- $Wt = 2\text{ml} * 1.02 = 2.04\text{g}$
- $2.04 \text{ g} / 93.13 \text{ g mol}^{-1} = \text{Theoretical Wt} / 135.17 \text{ mol}^{-1}$
- **% yield** = Practical Wt / Theoretical Wt

Thank You For Listening