5. B) COMMON ORGANIC REACTIONS IN DRUG SYNTHESIS

Hydrolysis

- Hydrolysis is a chemical reaction that led to the breaking of a complex compound into a simple molecule on reaction with water.
- The word Hydrolysis is composed of "hydro" and "lysis" which means water and breaking down. Hence, the meaning of hydrolysis is the breaking of a compound with the help of water via a chemical reaction.
- In these reactions, water is the key reagent that cleaves the bond and thus breaks the compound. Several examples of hydrolysis are hydrolysis of glucose, hydrolysis of ester and ether etc.
- Hydrolysis is a chemical reaction in which a compound reacts with water which ultimately leads breakage of bonds within that compound. This reaction creates two or more compounds which are simple ions.
- In hydrolysis, water splits into hydrogen ions (H^+) and hydroxide ions (OH^-) which then participate in the breaking of bonds within the compound itself.

$$\text{A-B} + H_2O \longrightarrow \text{A-H} + \text{B-OH}$$

Hydrolysis Reaction

- Hydrolysis is a chemical process by which a chemical compound interacts with water molecules, which causes the splitting of bonds between atoms within the molecule and new bond formation.
- This reaction partially affects the scission of a molecule during the addition of a water molecule.
- Here's a generalized equation for a hydrolysis reaction:

Compound + Water → Product 1 + Product 2

✓ In this environment, water is regarded as a reagent; it can be added to the molecule in several ways, or the product can depend on the compound structure and reaction conditions.

An example of the acid-catalyzed hydrolysis reaction of an ester:
Let's use methyl acetate (CH_3COOCH_3) reacting with water (H_2O) in the presence of acid (H^+), forming acetic acid (CH_3COOH) and methanol (CH_3OH).

$$CH_3COOCH_3 + H_2O \xrightarrow{H^+} CH_3COOH + CH_3OH$$

Hydrolysis Mechanism

Water decomposition is a process employed by water molecules to break bonds between a compound's atoms. Here's a brief overview:

✓ **Nucleophilic Attack:** Under acidic conditions, the carbonyl oxygen of methyl acetate is protonated, increasing the electrophilicity of the carbonyl carbon.

Water (H_2O) now acts as a nucleophile, attacking the carbonyl carbon and forming a tetrahedral intermediate.

$$CH_3C(OH)^+(OCH_3)(OH_2) \rightarrow \text{Tetrahedral intermediate}$$

- ✓ **Bond Cleavage:** The tetrahedral intermediate rearranges. The C–O bond between the carbonyl carbon and the methoxy group ($-OCH_3$) is cleaved. Methanol (CH_3OH) begins to form as the leaving group.
- ✓ **Ionization:**
  Proton transfers occur:
  The leaving methoxy group gains a proton (H^+) → becomes CH_3OH. The remaining intermediate may also donate a proton to stabilize and regenerate the acid catalyst.

$$\text{Intermediate} \rightarrow CH_3COOH + CH_3OH$$

- ✓ **Formation of Products:** Acetic acid (CH_3COOH) gets the –OH part from water. Methanol (CH_3OH) gets the H^+ from water. This satisfies your criteria: one product receives –OH, the other receives H^+ from water decomposition.

Fundamentally, hydrolysis reactions are the reaction between water molecules to transform complex chemical compounds into simpler products through the breakdown of the molecules.

Types of Hydrolysis

Hydrolysis reactions are classified into types determined by the catalyst and the substances undergoing hydrolysis. The main types of hydrolysis include:

- ✓ **Acid Hydrolysis-**
  A reaction in which water, assisted by an acid catalyst (H^+), breaks chemical bonds (commonly in esters, amides, or glycosidic bonds).
  Example:
  Hydrolysis of an ester (ethyl acetate) in acidic medium:

$$CH_3COOCH_2CH_3 + H_2O \xrightarrow{H^+} CH_3COOH + CH_3CH_2OH$$

  Catalyst: H^+ (acid)
  Products: Acetic acid and ethanol

- ✓ **Base Hydrolysis-**
  Hydrolysis of a compound using a base (OH^-), which breaks bonds - often used for esters and amides.
  Example:
  Hydrolysis of ethyl acetate with sodium hydroxide:

$$CH_3COOCH_2CH_3 + NaOH \rightarrow CH_3COONa + CH_3CH_2OH$$

  Hydroxide ions from a base to react with a compound resulting into cleavage of bonds.
  Catalyst: NaOH (base)
  Products: Sodium acetate and ethanol

- ✓ **Enzymatic Hydrolysis-** process of using biological catalysts which are enzymes to promote hydrolysis of specific bonds in organic molecules. Enzymes act as biological catalysts to hydrolyze specific bonds (e.g., in carbohydrates, proteins, fats).
  Example:
  Hydrolysis of lactose by the enzyme lactase:

$$\text{Lactose} + H_2O \xrightarrow{\text{lactase}} \text{Glucose} + \text{Galactose}$$

  Enzyme: Lactase
  Products: Two monosaccharides (glucose and galactose)
- ✓ **Salt Hydrolysis**- reaction between water and the ions of a salt which gives a resulting solution that is either acidic or basic. This type of hydrolysis happens when either the cation or the anion of the salt goes through hydrolysis to produce hydrogen ions (H+) or hydroxide ions (OH–).
  Example:
  Hydrolysis of ammonium chloride (NH_4Cl):

$$NH_4^+ + H_2O \rightarrow NH_3 + H_3O^+$$

  Salt: NH_4Cl (from weak base NH_3 and strong acid HCl)
  Result: Acidic solution due to production of hydronium (H_3O^+)

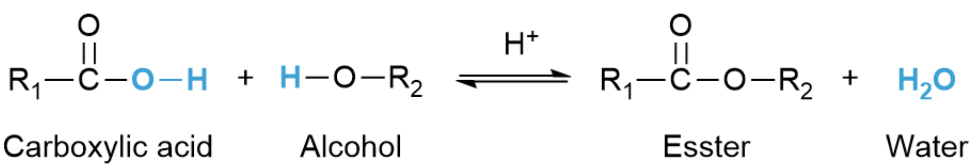
Application of Hydrolysis

Chemical Synthesis: The method of hydrolysis is commonly used in laboratory settings in synthesizing smaller molecule to a more convenient sized part. This is a process in which these fragments are used as building blocks that can be used to synthesize these different compounds.

Esterification

- ✓ Esterification is a type of condensation reaction as water is a by-product.
- ✓ Esterification is a chemical reaction in which an alcohol reacts with a carboxylic acid, acyl chloride, or acid anhydride to form an ester and a by-product, typically water or hydrogen chloride.
- ✓ This process often requires an acid catalyst and is commonly used in organic synthesis to produce esters, which are important compounds in fragrances, flavours, and industrial applications.
- ✓ Esters are characterised by their pleasant aromas and are commonly found in natural substances, such as fruits and flowers, as well as in many synthetic compounds used in food flavouring and fragrances.

General reaction of esterification reactions



Mechanism of Fischer esterification reactions