Session-2018-19

Organic Chemistry IV

Presented by:

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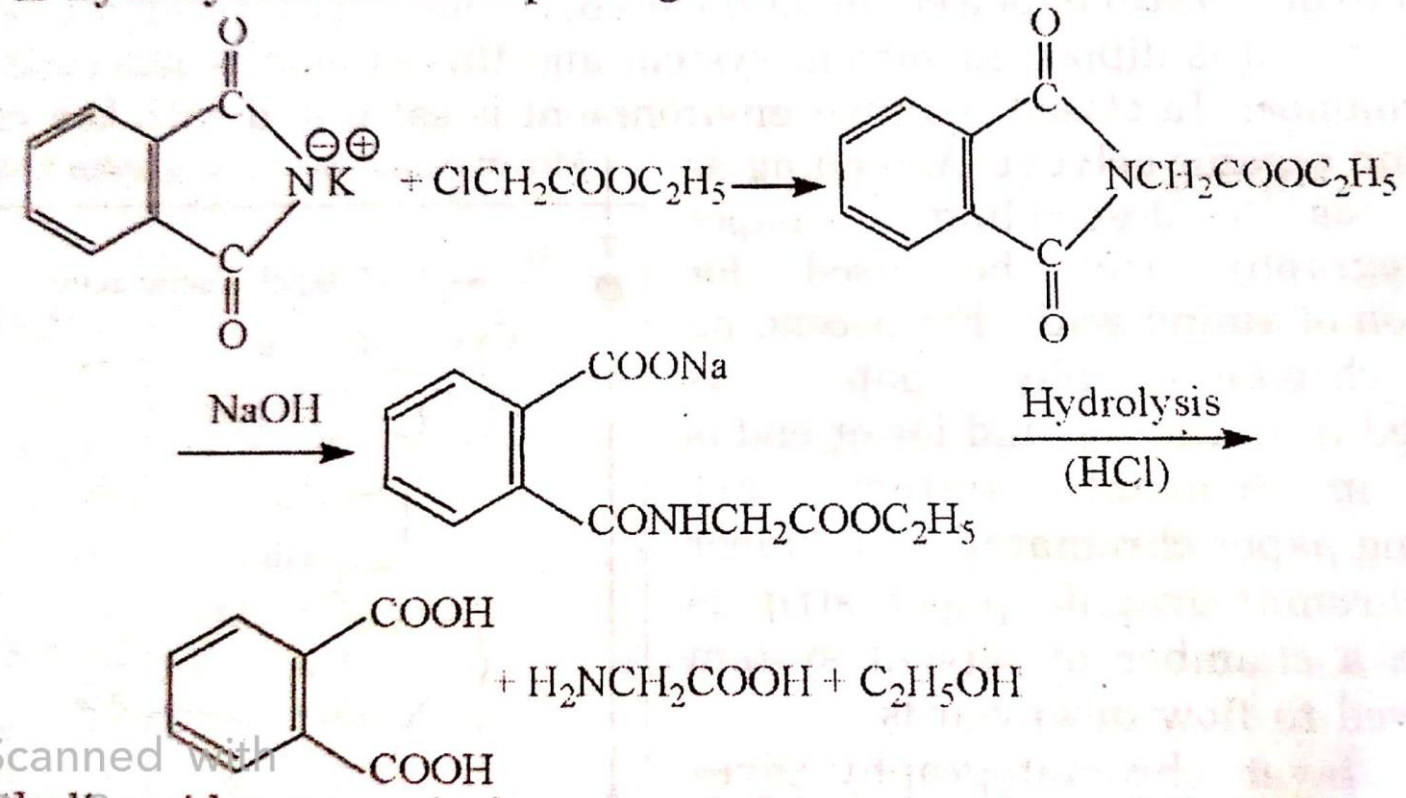
Synthesis of Amino Acids

Few important methods of synthesis of ...

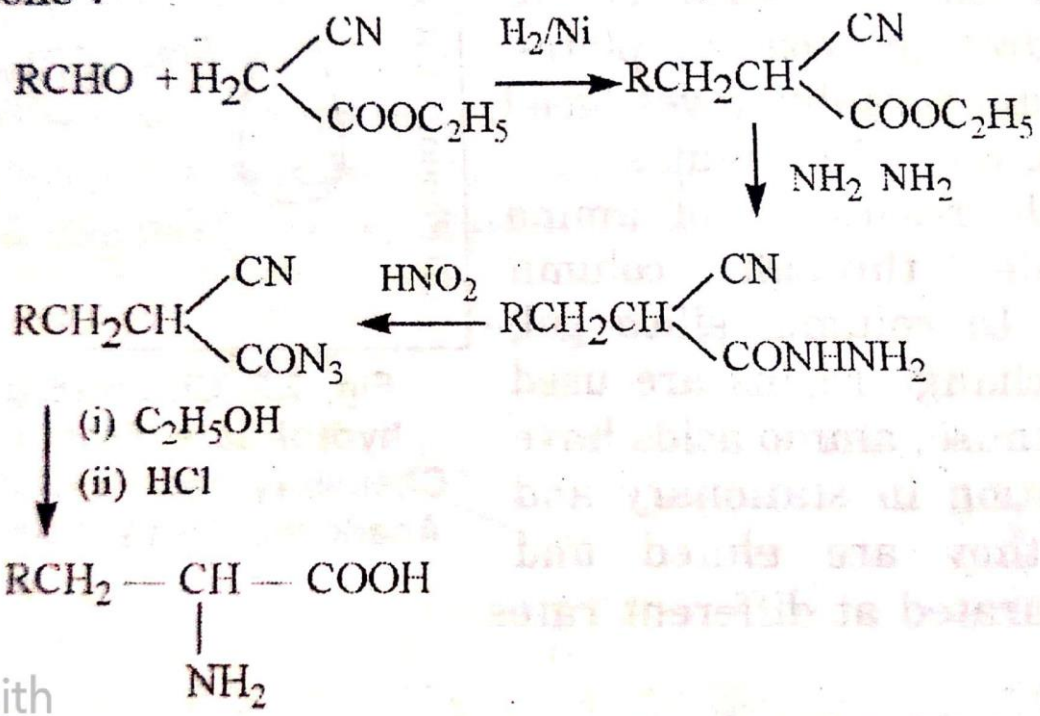
(1) Gabriel phthalimide synthesis : Good yields of α-amino acids are obtained when α-halogen acids are reacted with potassium phthalimide and the product is hydrolysed. An example is given below :



Phthalic acid may again be converted to potassium phthalimide.

Synthesis of Amino Acids

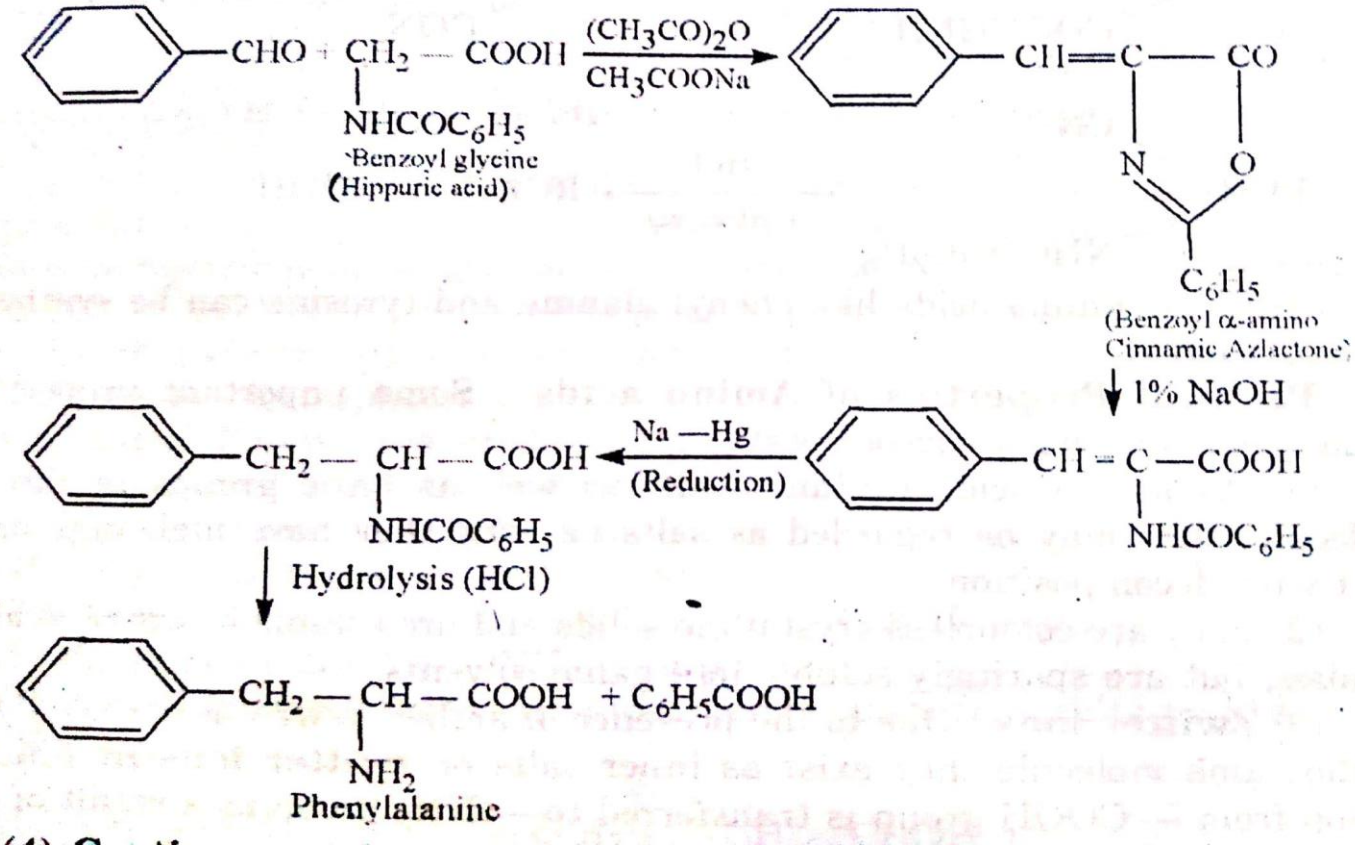
(2) Darapsky synthesis : Condensation of an aldehyde with alkyl cyanoacetic ester and their simultaneous reduction gives α-amino acids after following operations :



Synthesis of Amino Acids

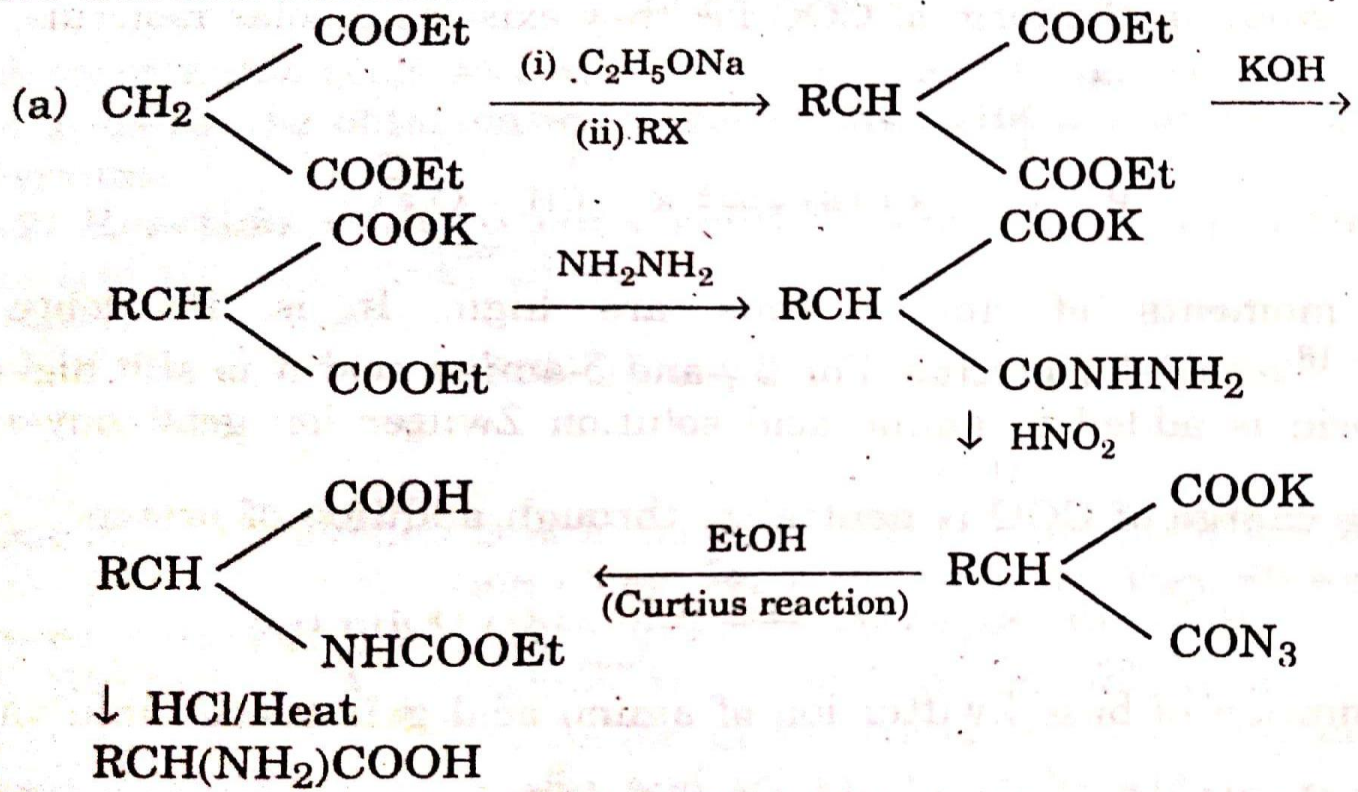
This synthesis is known as Bargasky synthesis.

(3) Erlenmeyer azlactone synthesis : Hippuric acid (benzoyl glycine) upon heating with aromatic aldehyde in presence of acetic anhydride and sodium acetate yields azlactone. Azlactone upon hydrolysis with 1% NaOH followed by reduction with sodium-amalgam and subsequent hydrolysis under acidic condition gives α-aminoacids. This method was introduced by **Erlenmeyer** for the synthesis of aromatic amino acids.



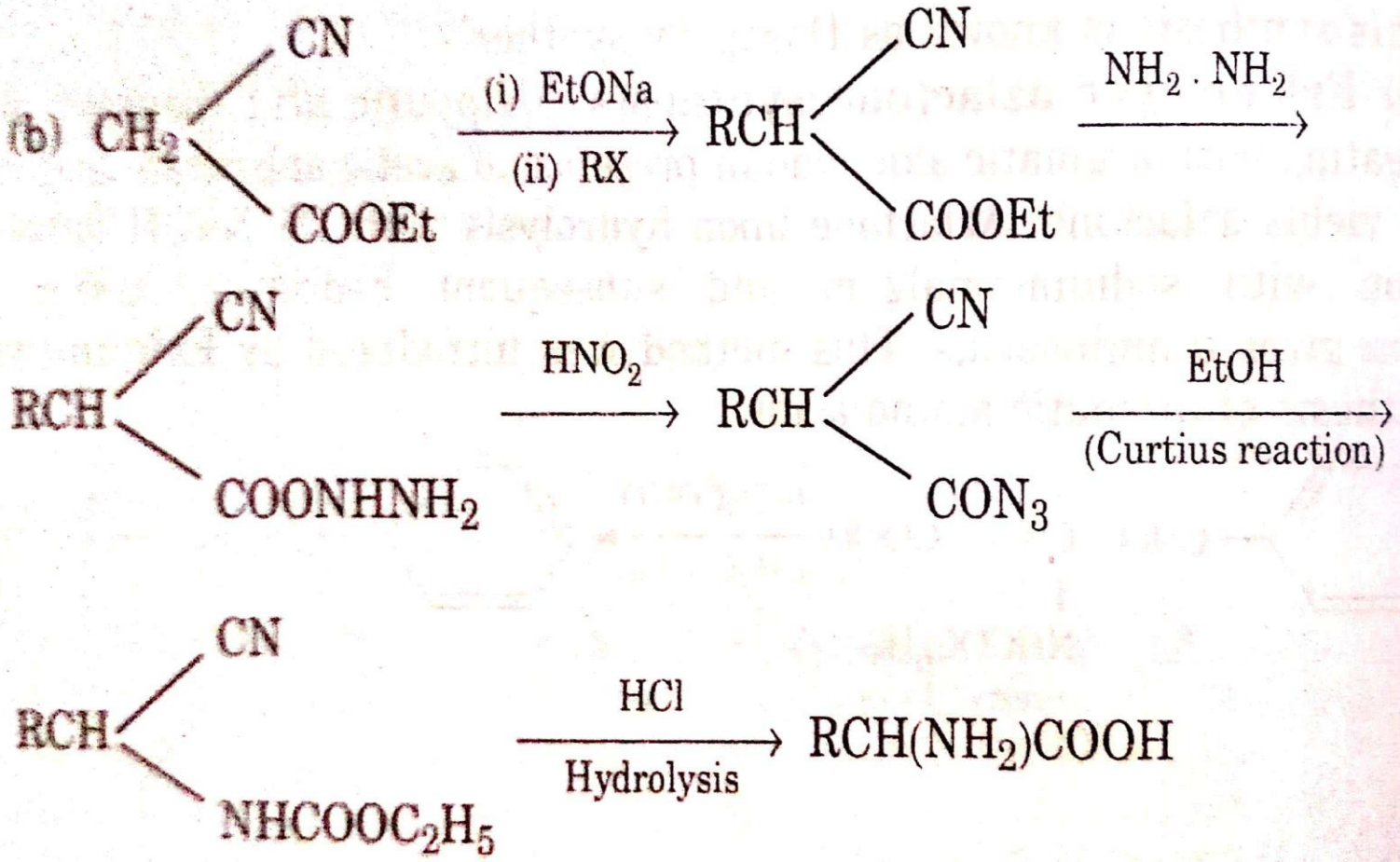
Synthesis of Amino Acids

(4) Curtius reaction Method : Malonic ester and cyanoacetic ester give amino acids according to reaction sequences discussed ahead. Both the sequences involve **Curtius reaction.**



Glycine, alanine, phenylalanine and valine can be synthesised by this method.

Synthesis of Amino Acids



Aromatic amino acids like phenyl alanine and tyrosine can be synthesised by this method.

Physical Properties of Amino Acids

- Amino acids are colorless, crystalline solid.

- All amino acids have a high melting point greater than 200^{o}

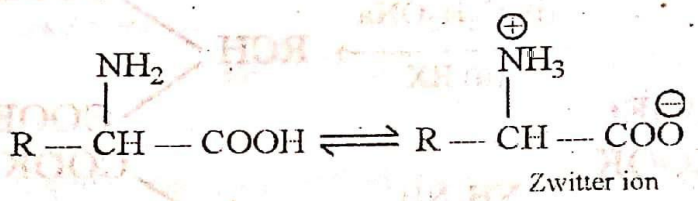
- **Solubility**: They are soluble in water, slightly soluble in alcohol and dissolve with difficulty in methanol, ethanol, and propanol.

- On heating to high temperatures, they decompose.

Physical Properties of Amino Acids

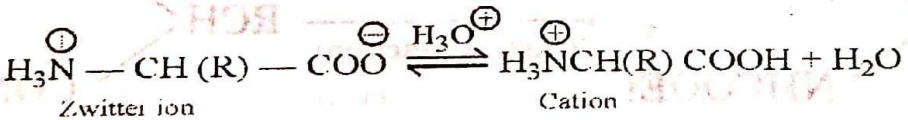
alkanes, but are sparingly

(3) **Zwitter ions** : Due to the presence of amino as well as carboxyl groups in the same molecule they exist as inner salts or **zwitter ions in** which one proton from — COOH group is transferred to — NH_2 group as a result of which positive charge develops on — NH_2 group in the form of $\overset{\oplus}{N}H_3$ and negative charge on — COOH group in the form of $\overset{\ominus}{C}OO$ *i.e.* they exist as dipolar molecule.

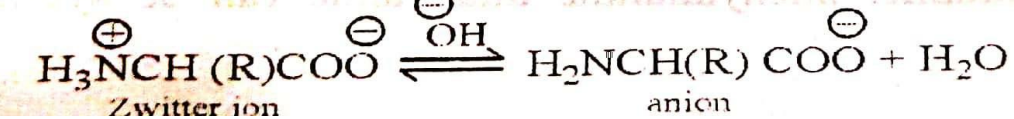


Dipole moments of amino acids are high. It is 15 debye unit ($1D = 1 \times 10^{-18}$ e.s.u.) for glycine. For β-γ-and δ-amino acid it is still higher.

When acid is added to amino acid solution Zwitter ion gets converted to cation as – ve charge of $\overset{\ominus}{C}OO$ is neutralize through addition of proton



Upon addition of base Zwitter ion of amino acid gets turned into an anion as $\overset{\ominus}{O}H$ ion of NaOH takes away one proton for $\overset{\oplus}{N}H_3$ group



Physical Properties of Amino Acids

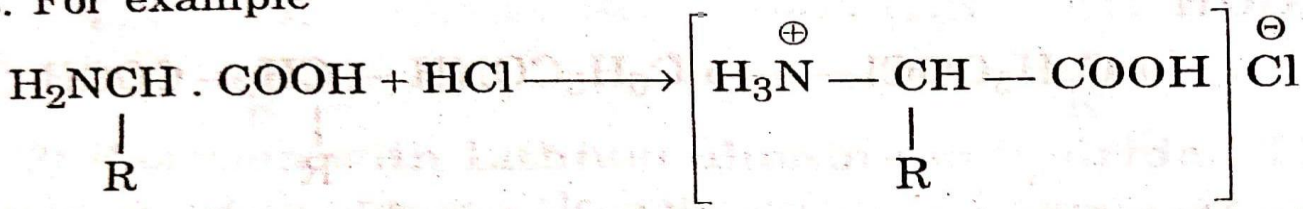
(4) **Isoelectric point** : At a particular pH the concentration of cation of amino acid is exactly equal to concentration of anion; at this pH there is no migration of amino acid in an electric field. It is worth mentioning that in strongly acidic medium amino acids migrate towards cathode, but in strongly basic medium amino acids migrate towards anode. **The pH at which an amino acid does not migrate under the influence of electric field is known as "isoelectric point" (pI) of that particular amino acid.** The equilibrium between cation, Zwitter ion and anion is illustrated below :

Isoelectric point of an aminoacid depends upon basicity of amino group and acidity of the carboxyl group; which depend upon nature of-R in amino acid. For

Chemical Properties of Amino Acids

Properties due to -NH_2 Group

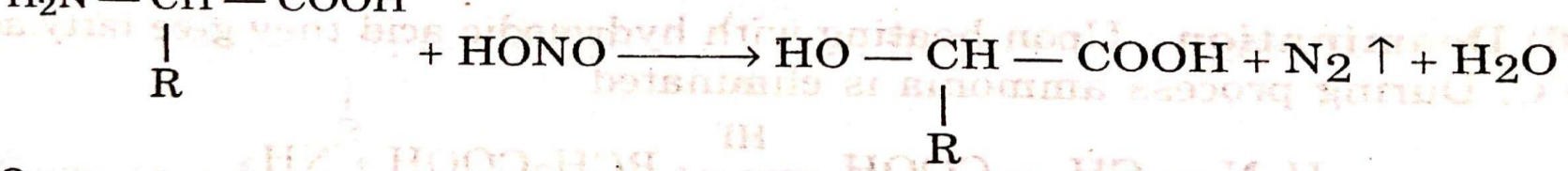
(1) Reactions with mineral acids : Amino acids form salts with inorganic acids. For example



Hydrochloride of α-amino acid

Salts of amino acids with mineral acids are sparingly soluble in water. Free amino acids can be obtained from these salts by means of strong organic base like pyridine.

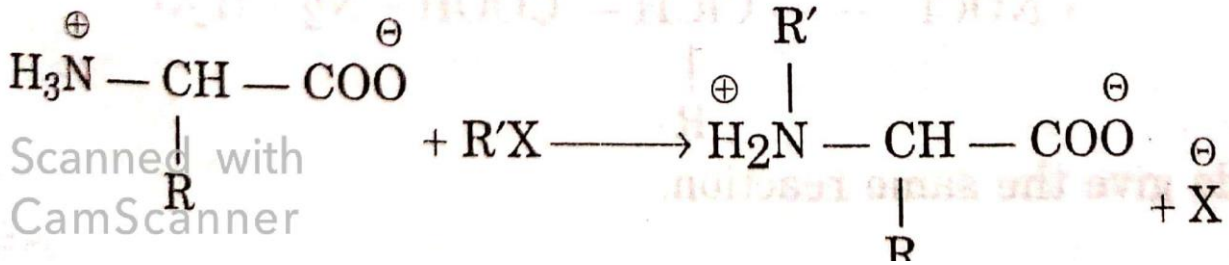
(2) Reaction with Nitrous acid : α-Amino acids upon treatment with nitrous acid give α-hydroxy acids



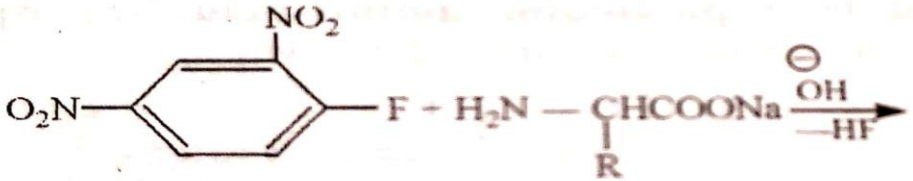
One mole of nitrogen is eliminated in this reaction for each primary amino group (— NH_2). This reaction constitutes the basis for **Van Slyke method** for the determination of free — NH_2 group in proteins.

Chemical Properties of Amino Acids

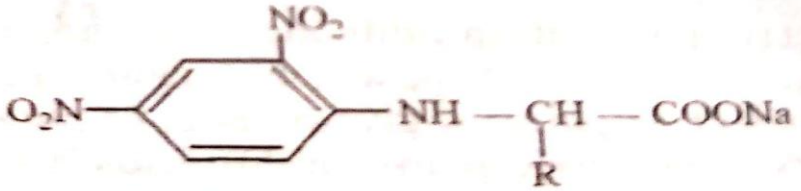
3. Alkylation : Alkylation of amino acids in alkaline medium gives N-alkyl amino acids. Excess of alkyl halide gives quaternary ammonium salts. These salts have Zwitterionic character and are known as **betaines**.



With 2, 4-dinitrofluorobenzene (Sanger's reagent) dinitrophenyl derivatives are formed which are crystalline compounds. This reaction is used in detecting which amino acid of protein or polypeptide has free — NH_2 group.



2, 4-Dinitrofluoro benzene (2, 4-DNF)



2, 4-Dintrophenyl derivative of amino acid