e-Content Developed By	Dr. Manjulla Gupta Assistant Professor in Chemistry, Govt. Degree College Samba (JK-UT)
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Syllabus	Preparation of Amino Acids: Strecker Synthesis, using Gabriel phthalimide Synthesis; Zwitter ion, Isoelectric Point and Electrophoresis; Reactions of Amino Acids

E-Content for AMINO ACIDS

(Preparation of Amino Acids: Strecker Synthesis, using Gabriel phthalimide Synthesis; Zwitter ion, Isoelectric Point and Electrophoresis; Reactions of Amino Acids)

Dr. Manjulla Gupta, Assistant Professor

AMINO ACIDS

OBJECTIVES OF THE STUDY

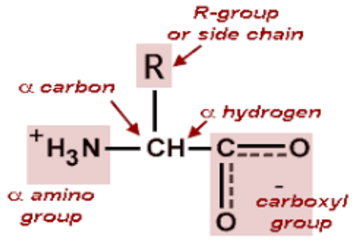
A
- Introduction to Amino Acids

B
- Zwitter Ions
- Isoelectric Point
- Electrophoresis

C
- Preparation of Amino Acids
- Reactions of Amino Acids

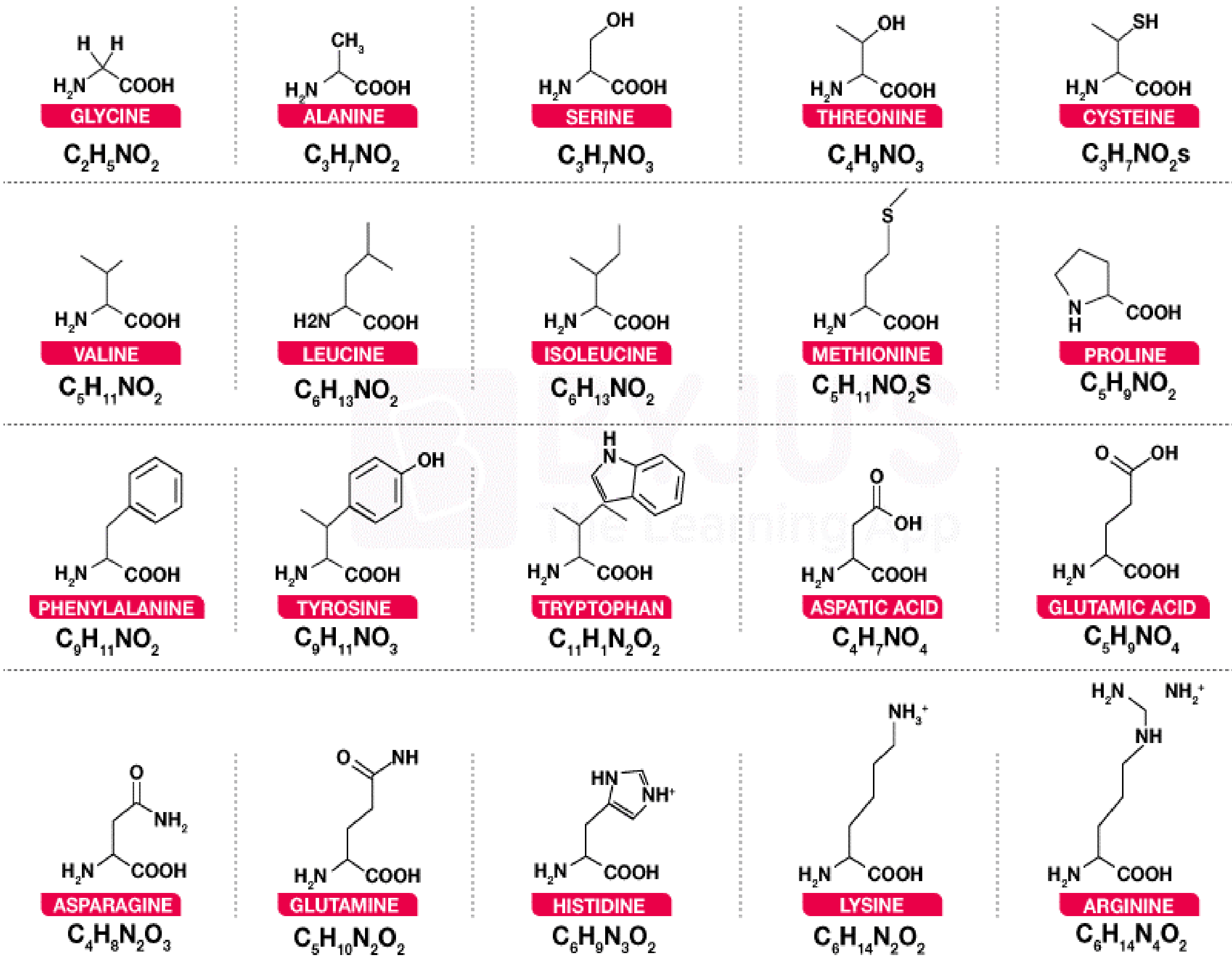
What are Amino Acids?

Amino acids are organic compounds that contain amine (-NH2) and carboxyl (-COOH) functional groups, along with a side chain (R group) specific to each amino acid.



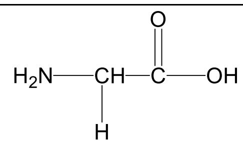
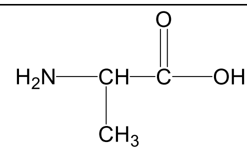
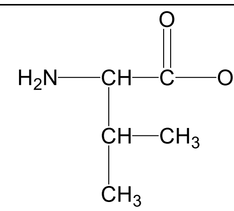
Twenty-six α- amino acids have been isolated by the hydrolysis of various proteins. Out of these, **20 amino acids** occur in almost all proteins and remaining six are found in special tissues.

Structure of twenty Amino Acids is attached herewith



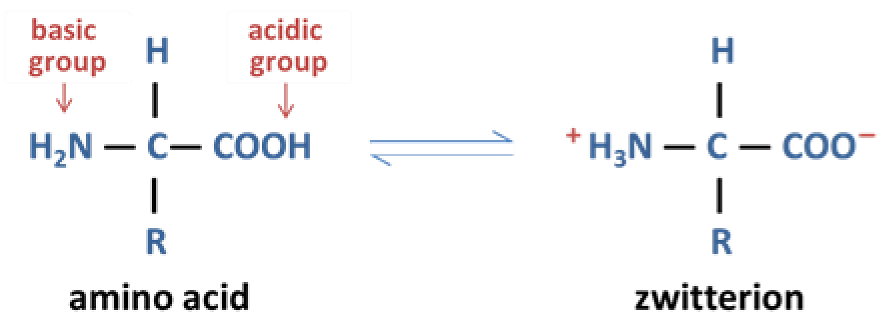
NOMENCLATURE OF AMINO ACIDS

Although amino acids can be named by IUPAC system, but they are most likely to be known by their common names. Their common names end with suffix ‘ine’. Each amino acid has been given a standard abbreviation or a code that consists of first three letters of the common name.

Structure			
IUPAC Name	2-Aminoethanoic acid	2-Aminopropanoic acid	2-Amino-3-methylbutanoic acid
Common Name	**Glycine**	**Alanine**	**Valine**
Abbreviation	**Gly**	**Ala**	**Val**

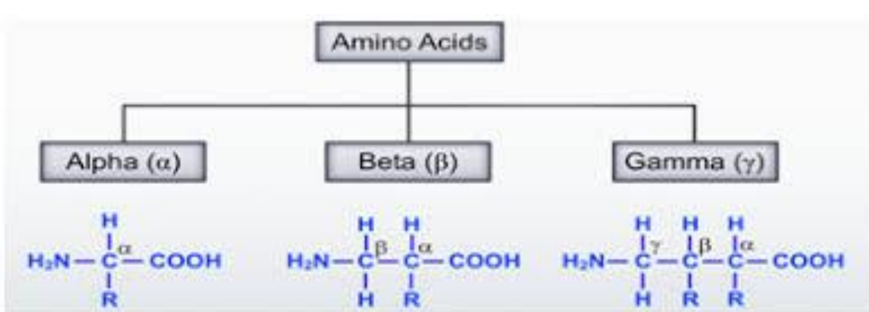
STRUCTURE OF AMINO ACIDS

Amino acids contain an amine group (basic) and a carboxylic group (acidic). The $-NH_2$ group is the stronger base, and so it picks up H^+ from the -COOH group to leave a zwitterion (i.e. the amine group de-protonates the carboxylic acid):[1]



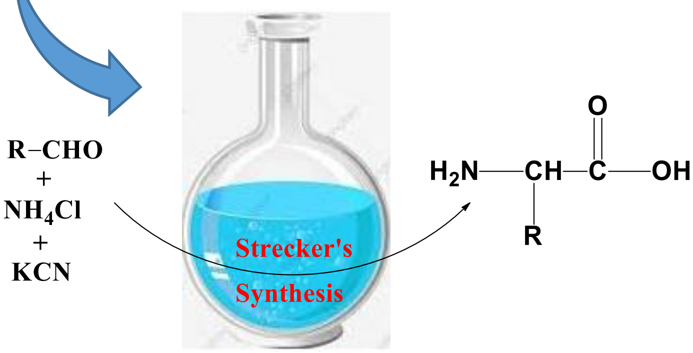
CLASSIFICATION OF AMINO ACIDS

Depending upon the position of amino group, i.e., α-, β-, γ- etc. on the carbon chain w.r.t. the carboxyl group they are classified as α-, β-, γ- etc. amino acids respectively. Out of these, α- amino acids are the most important because they are constituents of proteins which are very important biomolecules.

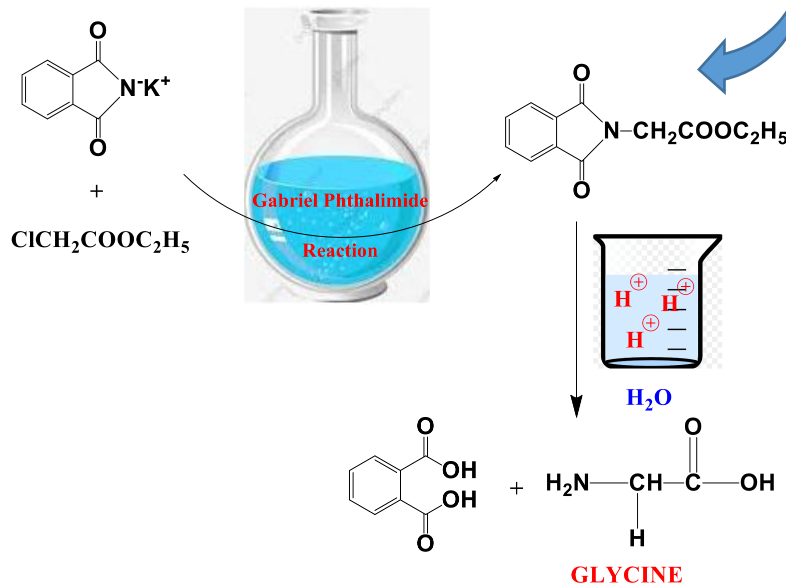


PREPARATION OF AMINO ACIDS

STRECKER'S SYNTHESIS



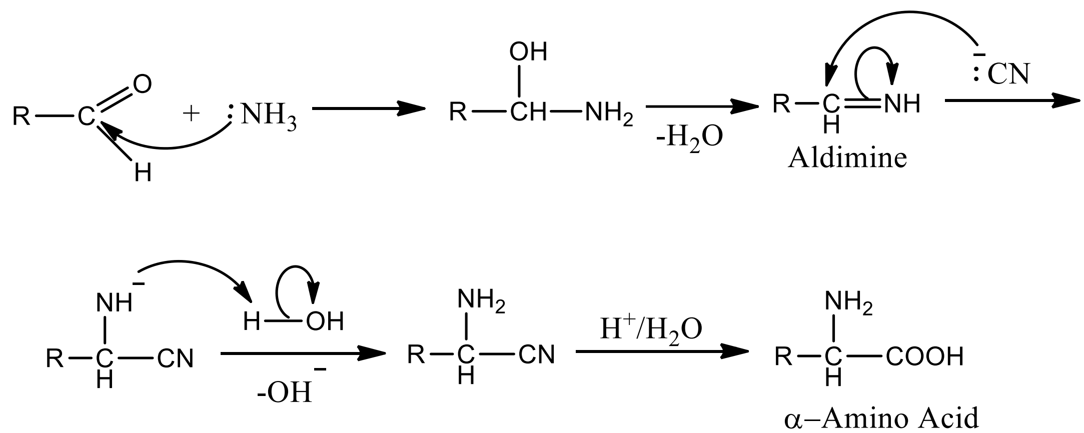
GABRIEL PHTHALIMIDE REACTION



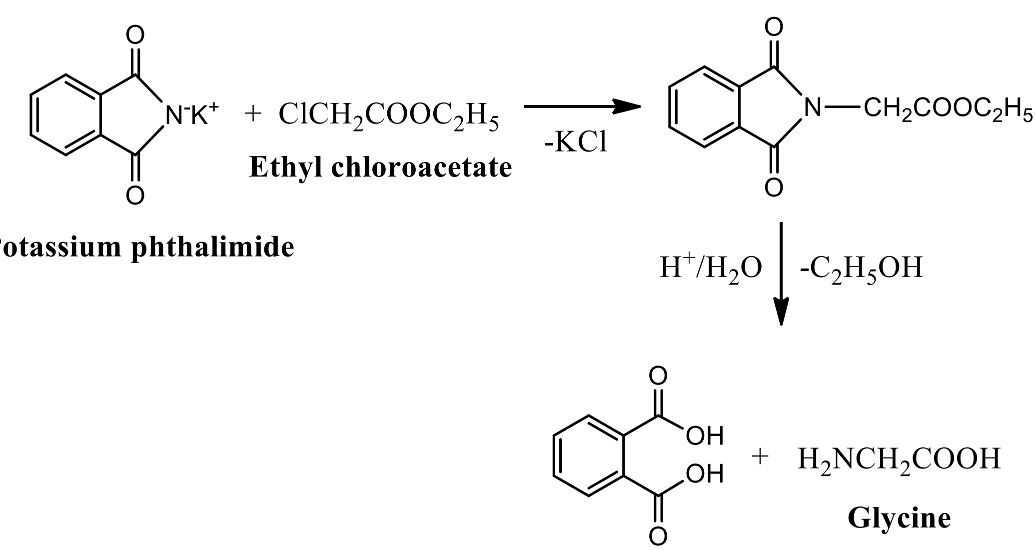
Detailed discussion on Preparation of Amino Acids

1. **Strecker's Synthesis:** It is one of the convenient methods for the synthesis of α-amino acids. It involves the reaction between an aldehyde, ammonium chloride and potassium cyanide. The aminonitrile thus formed on hydrolysis gives the corresponding α-amino acid.

$$NH_4Cl + KCN \rightleftharpoons NH_3 + HCN + KCl$$

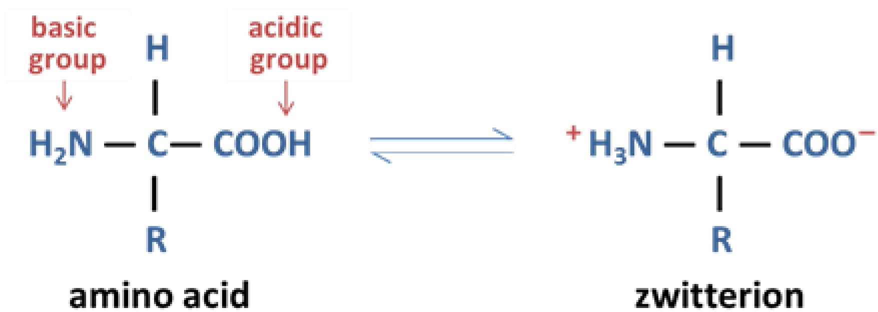


2. **Gabriel Phthalimide Reaction:** Potassium phthalimide on treatment with α-halo acids or their esters give the corresponding N-substituted phthalimides. These upon hydrolysis yield the corresponding α-amino acids.



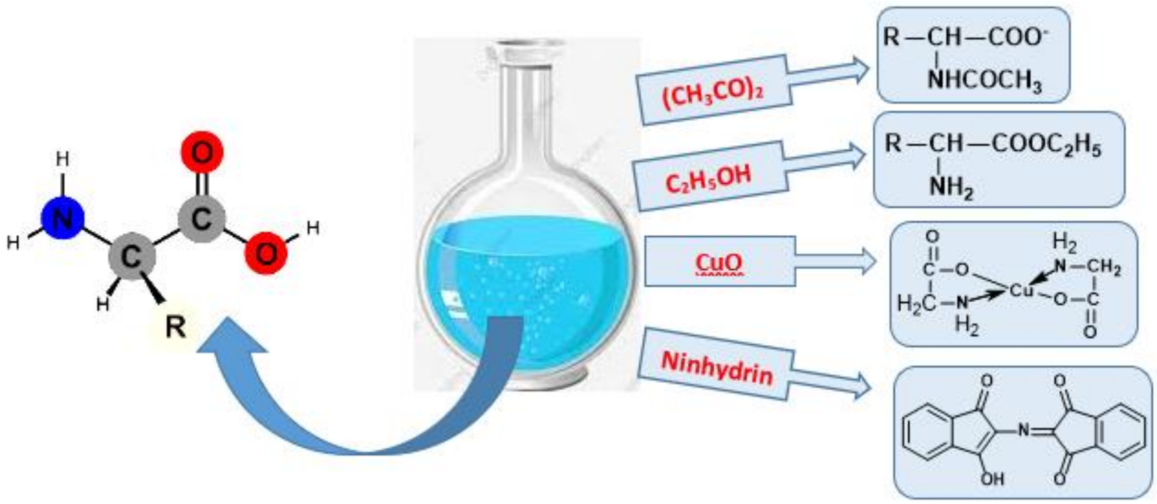
Zwitter Ion

A zwitterion is a molecule that has at least two functional groups: one having a positive charge and the other having a negative charge, with an overall charge of zero. The name comes from the German word “zwitter”, meaning hybrid. Amino acids are the most well-known zwitterions. They have an amino group (NH_3^+) which is positive and a carboxyl group (COO^-) which is negative. There is an internal transfer of a hydrogen ion from the -COOH group to the $-NH_2$ group to leave an ion with both a negative charge and a positive charge. This is called a zwitter ion or dipolar ions. This is the form that amino acids exist in even in the solid state.



For example, the amino acid glycine has the formula $H_2N.CH_2.COOH$. However, under neutral conditions, it exists in the different form of the zwitterion $^+H_3N.CH_2.COO^-$, which can be regarded as having been produced by an internal neutralization reaction (transfer of a proton from the carboxyl group to the amino group).

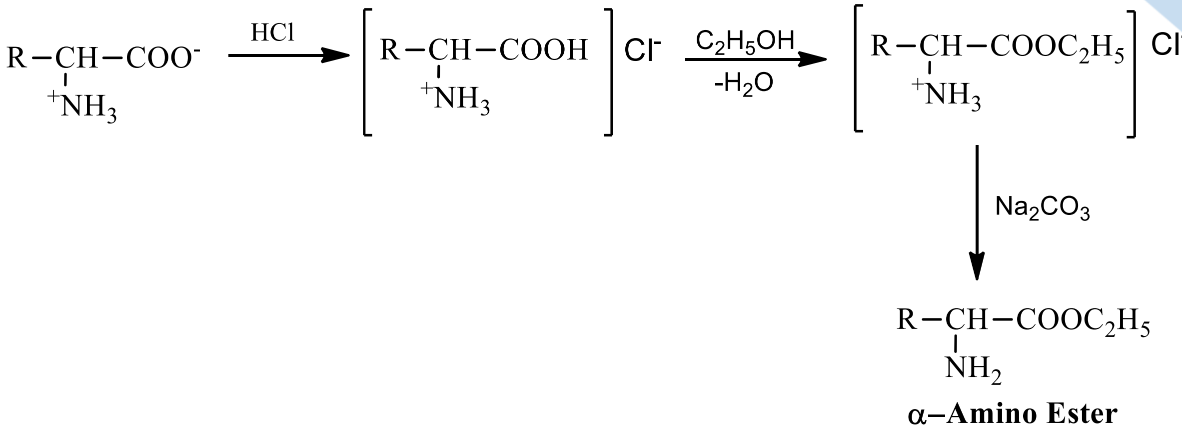
REACTIONS OF AMINO ACIDS



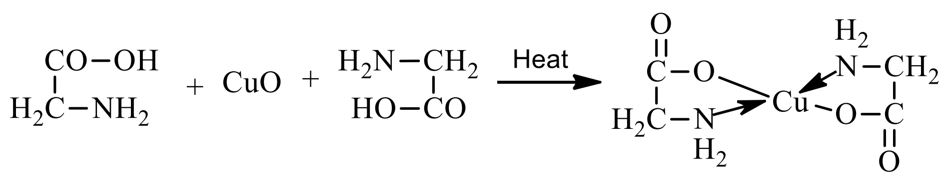
1. **Acylation:** The amino group of amino acid can undergo acylation with acid chlorides or anhydrides in the basic medium.

$$\underset{\displaystyle NH_2}{R-\overset{}{CH}}-COO^- + (CH_3CO)_2O \xrightarrow{\text{pyridine}} \underset{\displaystyle NHCOCH_3}{R-CH}-COO^- + CH_3COOH$$

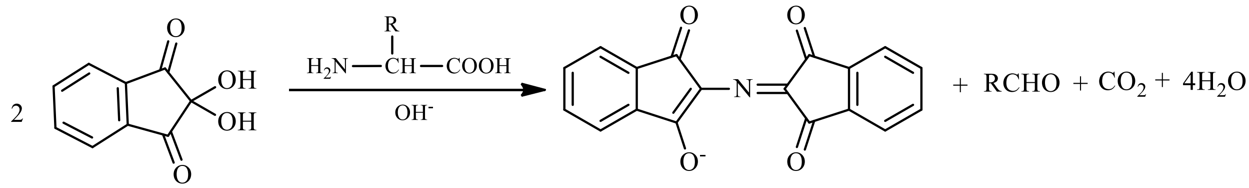
2. **Esterification:** When heated with an alcohol in presence of dry hydrogen gas, amino acid undergoes esterification to form the corresponding amino ester hydrochloride. This on treatment with an aqueous solution of Na_2CO_3 or moist silver oxide gives the corresponding free acid.



3. **Reaction with heavy metals- Formation of chelates:** Amino acids reacts with heavy metals in aqueous solutions to form chelate complexes.



4. **Ninhydrin Test:** α-Amino Acid react with an alcoholic solution of ninhydrin to give deep blue or violet coloured complexes.

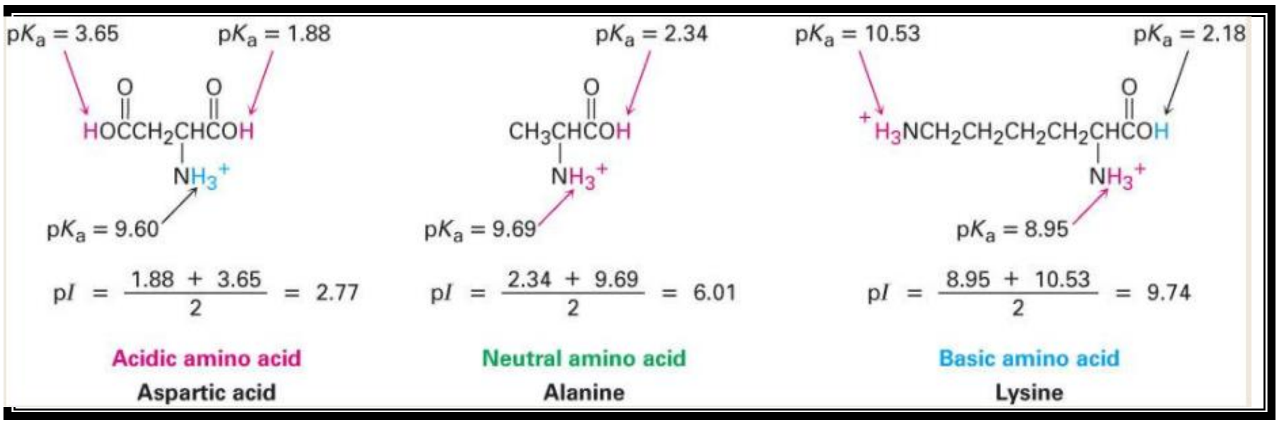


ISO ELECTRIC POINT OF α-AMINO ACIDS: ELECTROPHORESIS

- The **isoelectronic point** or **isoionic point** is the pH at which the amino acid does not migrate in an electric field.
- This means it is the pH at which the amino acid is neutral, *i.e.* the zwitterion form is dominant.
- The standard nomenclature to represent the isoelectric point is pH(I). However, pI is also used.
- The isoelectric point of an amino acid depends upon its structure and hence amino acid has a characteristic isoelectric point.
- The pI of an amino acid can be calculated by the following equation:

$$pI = \frac{pK_{a1} + pK_{a2}}{2}$$

- The 4 amino acids with either a strongly or weakly acidic chain, pI is the average of the two lowest pKa values
- The 13 amino acids with a neutral side chain, pI is the average of pKa1 and pKa2
- The 3 amino acids with a basic side chain, pI is the average of the two highest pKa values



DESCRIPTION

The exact structure of an amino acid depends upon the pH of the medium in which the amino acid is dissolved.

When the solution of an amino acid is made acidic, the dipolar ion (I) gets converted into cation (II).

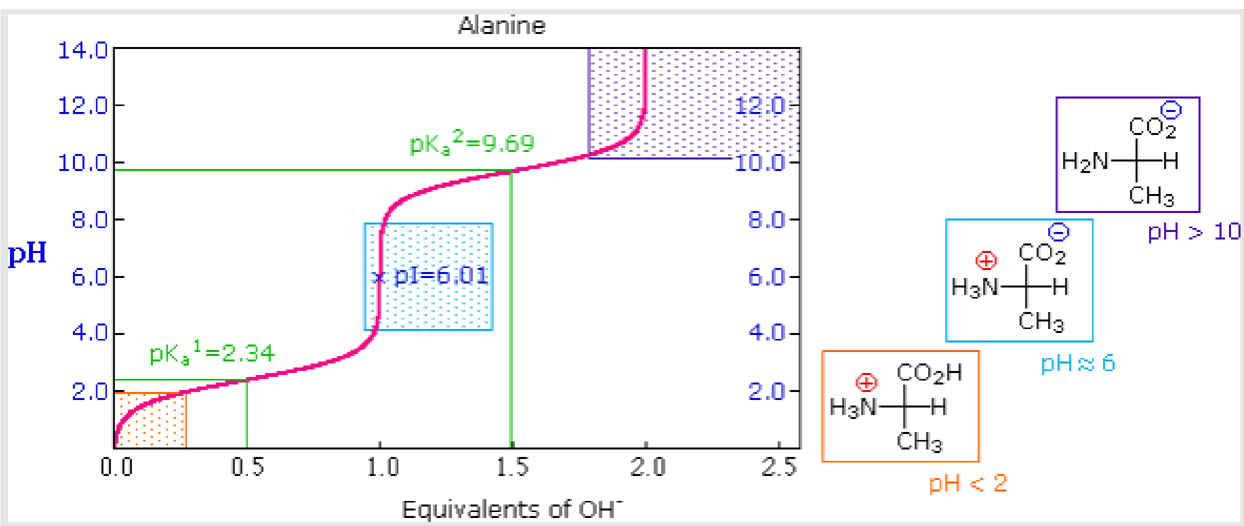
However, if the solution of an amino acid is made alkaline, the dipolar (I) gets converted into anion (III).

At any pH value which lies between these extreme values of pH, the zwitterion (I) is in equilibrium with varying amounts of ions (II) and (III).

When an electric current is passed through the aqueous solution of an amino acid, its behavior depends upon the pH of the solution. If the solution is strongly acidic (i.e. low pH), the amino acid exists predominantly in the cationic form (II) and thus migrates towards the cathode in the electric field. In strongly basic conditions, it predominantly exists in the anionic form (III) and thus migrates towards anode in the electric filed. Therefore, at some intermediate value of pH, the concentration of cationic form (II) and anionic form (III) are minimum and equal to each other. In other words, at this pH, the concentration of dipolar ionic form is the maximum and amino acid primarily exists as neutral dipolar ion (I). At this pH, there will be no net migration of the amino acid in the electric field. This pH at which there is no net migration of the amino acid under the influence of the applied electric field is called the **isoelectric point (pI).**

- At pH lower than pI, there will be net migration of the amino acid towards cathode because the amino acid exists predominantly in the cationic form (II).
- At pH higher than pI, there will be net migration of the amino acid towards anode because the amino acid exists predominantly in the anionic form (II).

For example: ALANINE
At a pH lower than 2, both the carboxylate and amine functions are protonated, so the alanine molecule has a net positive charge. At a pH greater than 10, the amine exists as a neutral base and the carboxyl as its conjugate base, so the alanine molecule has a net negative charge. At intermediate pH's the zwitterion concentration increases, and at a characteristic pH, called the isoelectric point (pI), the negatively and positively charged molecular species are present in equal concentration. This behavior is general for simple (difunctional) amino acids.



Electrophoresis is a technique of separation and purification of compounds on the basis of differential movement of charged particles in an electric field.

The mobility of ions in an electric field depends on:

(a) charge

- **Positively charged ions moved towards the negatively charged electrode.** (All amino acids contain at least one amino and one carboxyl group. In acid solutions, the amino groups are positively charged while the carboxyls are not ionized. Therefore, in strong acid solutions, amino acids are positively charged and migrate in an electric field to the negative electrode.)
- **Negatively charged ions moved towards the positively charged electrode** (In basic or alkaline solutions, the carboxyls are negatively charged while amino groups are not ionized. It follows then that in strong alkaline solutions, amino acids are negatively charged, and migrate to the positive electrode during electrophoresis)
- Neutral particles will remain stationary.

(b) mass

Ions with the least mass will move further than ions with greater mass.

In this process, a strip of paper/a suitable plastic/cellulose acetate is used as the solid support. In paper electrophoresis, mixture of amino acids to be separated is placed in the form of a spot in the centre of the strip of paper. The strip is soaked with an aqueous buffer of a particular pH. The pH of the buffer depends upon the isolectric points of the amino acids to be separated. The two ends of the filter paper are dipped into the buffer solution containing electrodes. When an electric field is applied, the following changes occur:

1. The amino acids whose isoelectric point is below the pH of the buffer start moving towards the anode because they exist mainly in the anionic form.
2. The amino acids whose isoelectric point is above the pH of the buffer start moving towards the cathode because they exist mainly in the cationic form.
3. The amino acids whose isoelectric point corresponds to the pH of the buffer do not migrate from the origin because they have no net charge.