Synthesis of α-amino acids

I Strecker Synthesis

In strecker synthesis, α-aminonitriles obtained by the treatment of aldehydes with ammonia & HCN are hydrolysed to α-amino acids

$$R-CHO + NH_3 + HCN \rightarrow R-\underset{\underset{NH_2}{|}}{CH}-CN \xrightarrow{H_3O^+} R-\underset{\underset{NH_2}{|}}{CH}-COO^-$$

The mechanism of formation of the α-aminonitrile probably involves the addn of HCN to imine, which is formed by the condensation of aldehyde & ammonia.

$$R-\overset{\overset{O}{\curvearrowright}}{\underset{\underset{H}{|}}{C}}-H + \ddot{N}H_3 \rightleftharpoons R-\underset{\underset{H}{|}}{\overset{O}{\overset{|}{C}}}-\overset{+}{N}H_3 \rightleftharpoons R-\underset{\underset{H}{|}}{\overset{OH}{\overset{|}{C}}}-NH_2$$

$$\rightleftharpoons R-\underset{\underset{CN}{|}}{CH}-\overset{\ominus}{N}H \xrightleftharpoons{CN^-} R-CH=NH \quad (-H_2O)$$

$$R-\underset{\underset{CN}{|}}{CH}-NH_2$$

II Gabriel phthalimide Synthesis

The halogen in the α-halo ester is replaced by a phthalimide group, the intermediate ester yields the desired amino acid by hydrolysis in two steps (base & then acidic)

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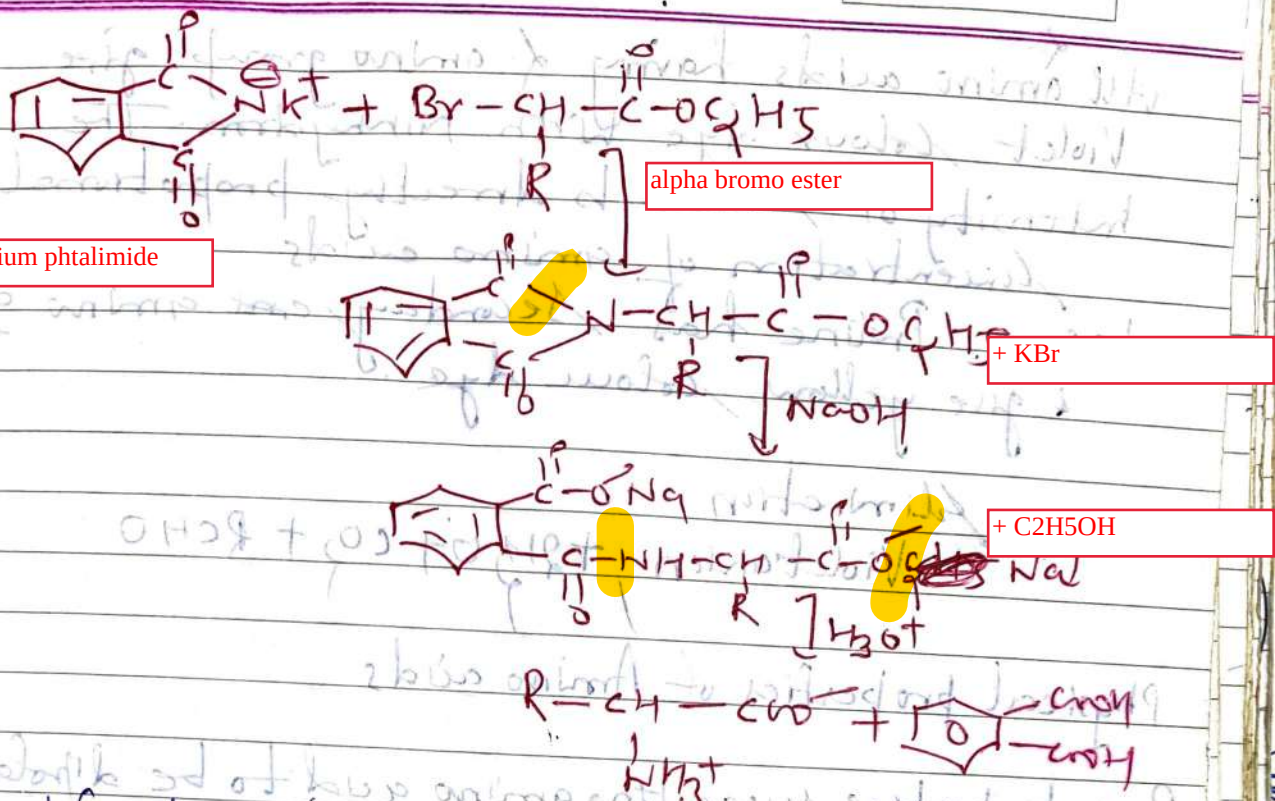
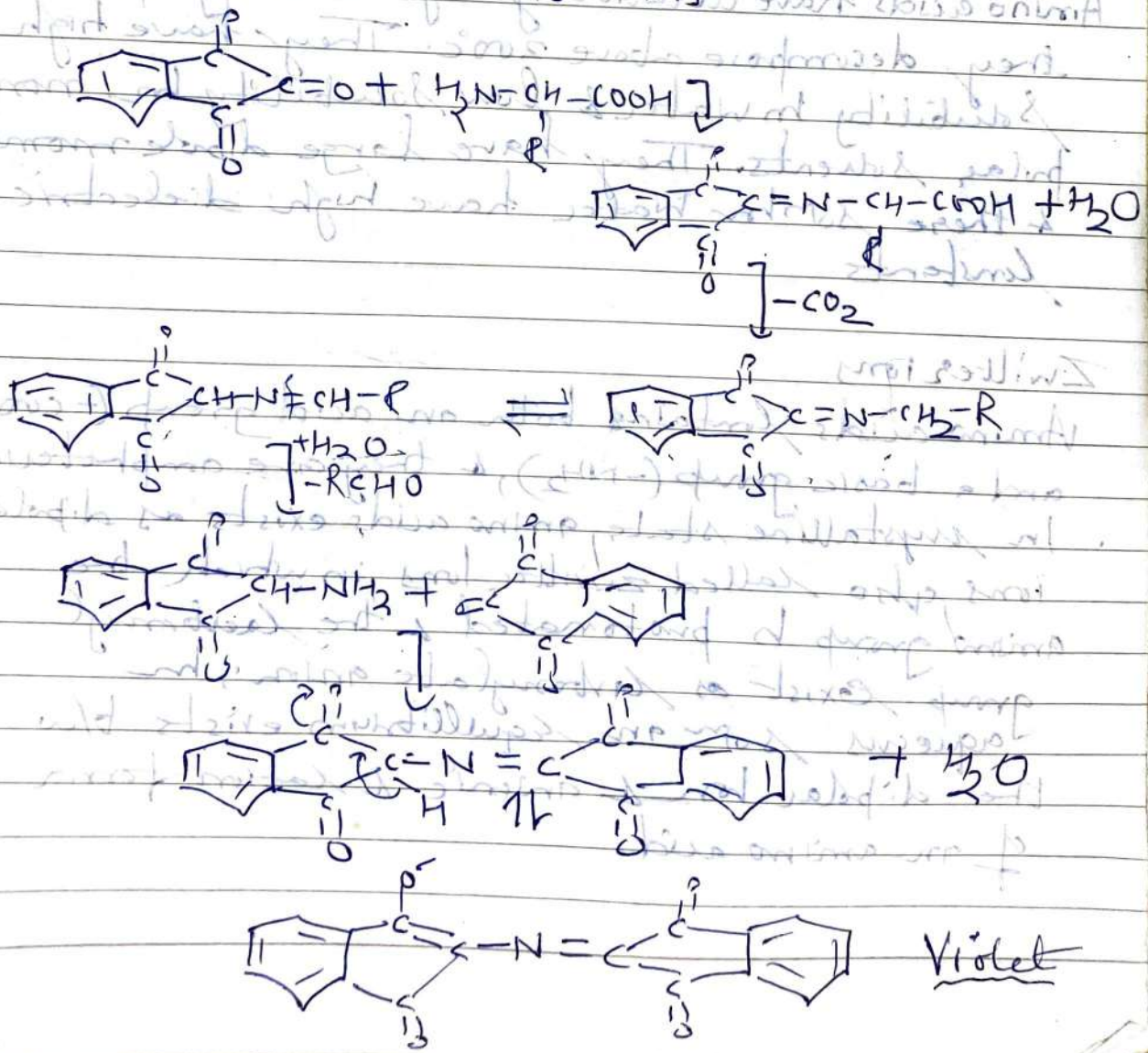
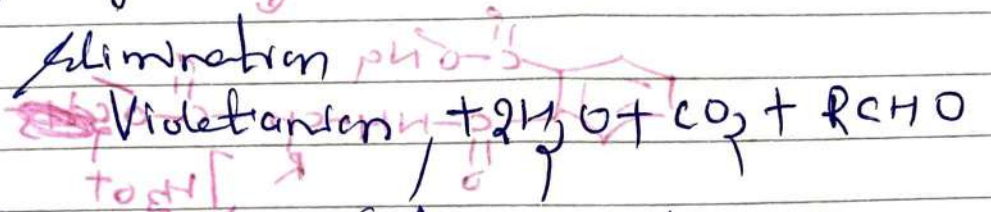


Identification of α-amino acids



All amino acids having α-amino group give Violet colour dye with Ninhydrin. The intensity of colour is directly proportional to concentration of amino acids

Note: Proline has secondary amino gp & give yellow colour dye.

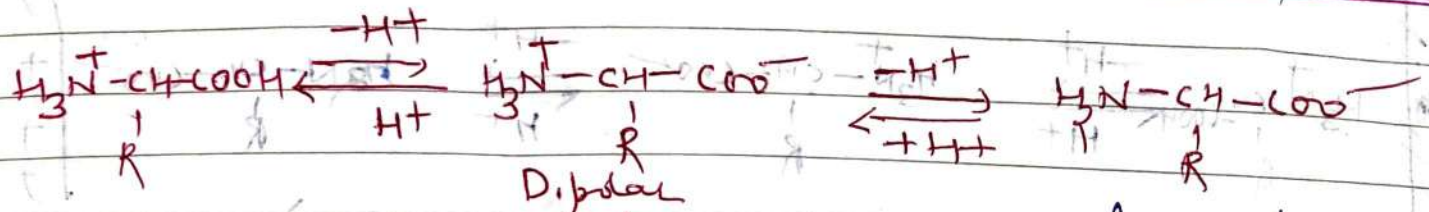


Physical properties of Amino acids

Basic properties suggesting amino acid to be dipolar.
Amino acids have relatively high melting point & they decompose above 200°C. They have high solubility in water & low solubility in non polar solvents. They have large dipole moment & these solution in water have high dielectric constants.

Zwitter ions

Amino acids contains both an acid group (-COOH) and a basic group ($-NH_2$), & they are amphoteric. In crystalline state, amino acids exists as dipolar ions also called zwitter ions, in which the amino group is protonated & the carboxyl group exist as carboxylate anion; in aqueous solution an equilibrium exists b/w the dipolar ion & anionic & cationic form of an amino acid.



Cationic form (Predominant in strongly acidic soln) [acid]

Dipolar ion

Anionic form (Anionic form predominant in strongly basic soln)

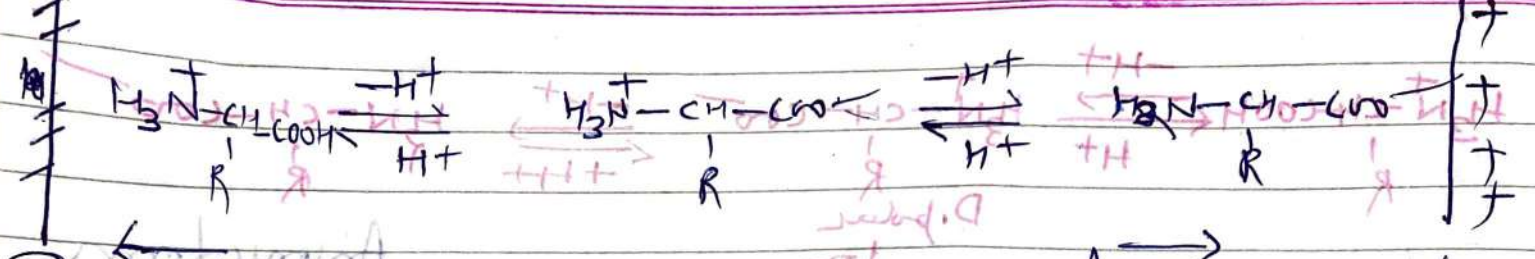
Note:- The predominant form of the amino acid present in a solution depends on the pH of the soln. In strongly acidic soln, all amino acids are present as cations & in strongly basic solutions, they are present as anions.

Isoelectric Point

During the course of titration of an amino acid with NaOH a point is reached at which all structures in solution exist as zwitterions. The pH of the soln at this stage is known as the isoelectric point. At isoelectric point particular amino acid is does not migrate towards either the cathode or anode under the influence of electric field.

However, generally when a soln of amino acids is placed in an electric field, the migration towards Anode or cathode depends on the acidity or basicity of soln.

In alkaline soln there is net migration of the amino acids towards the anode & in the acidic soln, there is net migration of amino acids towards cathode.



Cathodic migration, lower pH

Newton

Anionic migration High pH.

For the cationic form of ~~any~~ amino acid, we have two ionisable gps $-COOH$ & $-NH_3^+$, therefore at least two pH values for some (not for acidic & basic amino acids)

$$pI = \frac{pK_{a_1} + pK_{a_2}}{2}$$

pI ← Isoelectric point pH

Isoelectric point

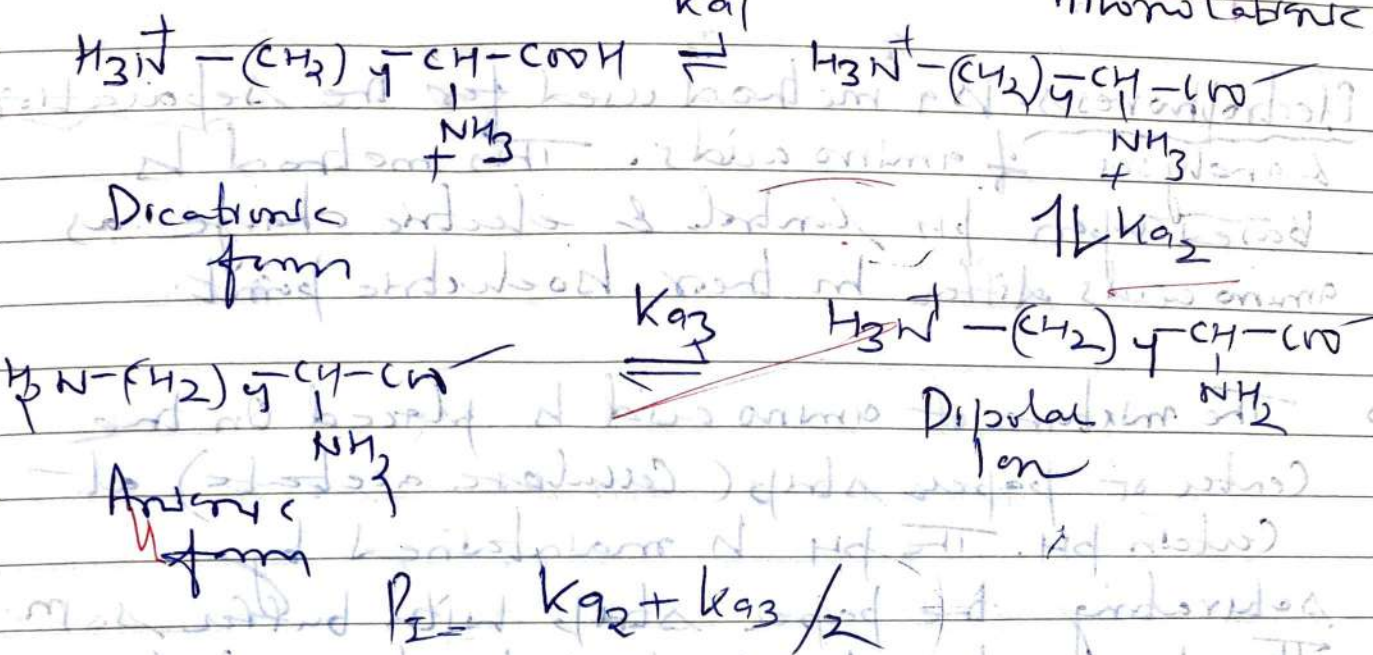
Isoelectric point pH Value of some amino acids

		PI
Glycine	→	6.1
Alanine	→	6.1
Valine	→	6.0

(for neutral amino acids PI. 5.5-6.5)

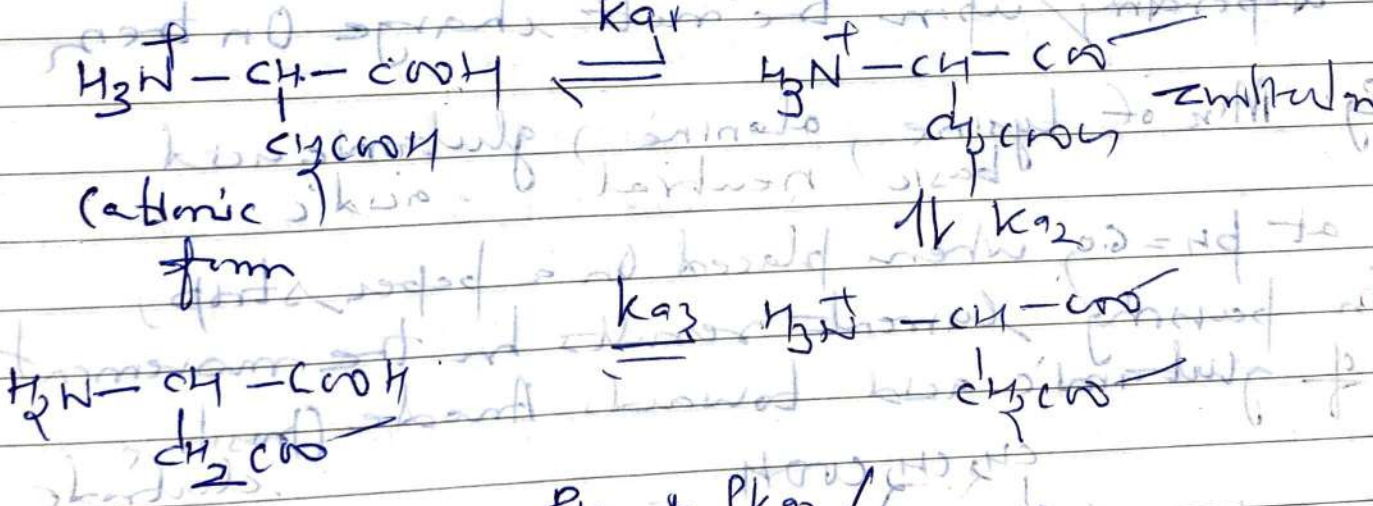
Aspartic acid	→	3.0
Glutamic acid	→	3.2
Lysine	→	9.7
Arginine	→	10.8

For basic amino acids



$$pI = \frac{pK_{a2} + pK_{a3}}{2}$$

For acidic amino acids



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