Bifunctional compounds having an acidic carboxylic acid group & basic amino groups are known as amino acid.

$$\underset{\alpha\text{-amino acid}}{\underset{|\;CO_2H}{R-CH-NH_2}} \rightleftharpoons \underset{\text{zwitterion}}{\underset{|\;CO_2^-}{RCH-\overset{+}{N}H_3}}$$

The acidic group is actually $-\overset{+}{N}H_3$ & basic group is actually $-CO_2^-$. Most of the amino acid (α) has 1°amine but it can have 2°amine group.

There are 20 naturally occuring α amino acids are present which are monomeric unit of biopolymer called protein. Chemically proteins are high polymers. A single protein molecule contains hundreds or even thousands of amino acid joined by amide linkage. So proteins are polyamide (found in living cells).

Classification of Amino Acids:

I. Based on chemical nature:

⇒ If it has same number of NH_2 & $-CO_2H$ groups then they are called neutral amino acids.

e.g $\underset{|\;CO_2H}{R-CH-NH_2}$ $R=CH_3$ ⇒ Alanine.

⇒ If it has more number of CO_2H groups with respect to number of $-NH_2$ groups, then they are called acidic amino acids.

e.g $\underset{|\;CO_2H}{R-CH-NH_2}$ $R \Rightarrow -CH_2-CO_2H$ ⇒ Aspartic Acid

⇒ If it has more ... groups, then they are called basic amino acids.

e.g $R-\underset{NH_2}{CH}-CO_2H$ $R \Rightarrow -(CH_2)_4-NH_2$ ⇒ Lysine.

II. Based on Requirement:

⇒ If amino acids are itself synthesised in body, then they are known as nonessential amino acids.

e.g $R-\underset{NH_2}{CH}-CO_2H$ $R \Rightarrow -H$ ⇒ glycine.

Out of 20 amino acids, 10 are non essential amino acids

⇒ If amino acids can not be synthesised in human body so intake is required through diet, then they are known as essential amino acids.

e.g $R-\underset{NH_2}{CH}-CO_2H$ $R \Rightarrow$ Isopr $-\underset{CH_3}{CH}-CH_3$ ⇒ Valine.

Out of 20 amino acids, 10 are essential amino acids.

III Based on Occurance:

All 20 amino acids given (next page) are example of naturally occuring amino acid & man made amino acids are example of synthetic amino acids.

⇒ Points to be remembered. (supporting zwitterion str).

i) Amino acids are crystalline solid, high m.point.

ii) They are water soluble, insoluble in organic solvent

iii) They are amphoteric in nature.

iv) They has low Ka (acid dissociation constant) & Kb (base dissociation constant)

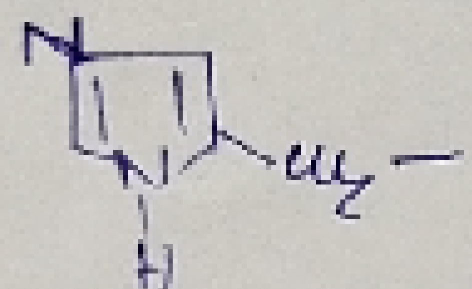
v) Except glycine; all α-amino acids are chiral.

Table of Natural Amino Acids. (3)

Name. R. abbreviated form.

1. Glycine. $-H$. Gly. (nonessential) G
2. Alanine $-RH_3$ Ala. (nonessential) A
3. Valine $-CH(CH_3)_2$ Val. (essential) V
4. Leucine $-CH_2-CH-CH_3$ (CH_3) Leu. (essential) L
5. Isoleucine $-CH-CH_2-CH_3$ (CH_3) Ile. (essential) I
6. Phenyl Alanine $-CH_2-Ph$ Phe. (essential) P.

⟵ All are neutral amino acids ⟶

7. Lysine. $-(CH_2)_4-NH_2$ Lys (essential) L
8. Arginine $-(CH_2)_3-NH-C(=NH)-NH_2$ Arg (essential) A
9.  Histidine. His (essential) H

⟵ All are basic amino acids ⟶

10. Glutamic Acid $-(CH_2)_2-CO_2H$ Glu (nonessential) G
11. Aspartic Acid $-CH_2-CO_2H$ Asp. (nonessential) A

⟵ All are acidic amino acid ⟶

12. Glutamine $-(CH_2)_2-CONH_2$ Gln (nonessential) G
13. Asparagine $-CH_2-CONH_2$ Asn. (non ,,) A.
14. Threonine. $-CH(OH)-CH_3$ Thr (essential)
15. Serine. $-CH_2-OH$ Ser. (nonessential)
16. Tyrosine. $HO-C_6H_4-CH_2-$ Tyr (nonessential)

⟵ Neutral amino acids — all are ⟶

14, 15, 16 ⇒ Amino acids having alcoholic $-OH$ & Phenolic $-OH$ (Threatening seriously, try na kore)

Name R abbreviated form.

17. Methionine $-CH_2CH_2-S-CH_3$ Met (essential)

18) a) Cysteine $-CH_2-SH$. Cys. (nonessential)

b) Cystine. $-CH_2-S-S-CH_2$ (—) (—)

← All are amino acids sulphur containing →

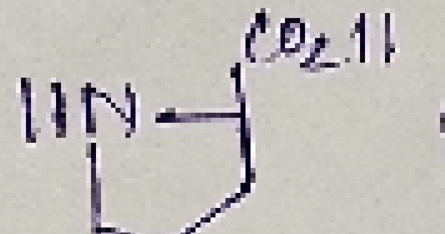
[E = mc²; to make it remembered [☺]]

Structure of cystine ⇒ $HO_2C-\underset{}{\overset{NH_2}{CH}}-CH_2-S-S-CH_2-\overset{NH_2}{CH}-CO_2H$

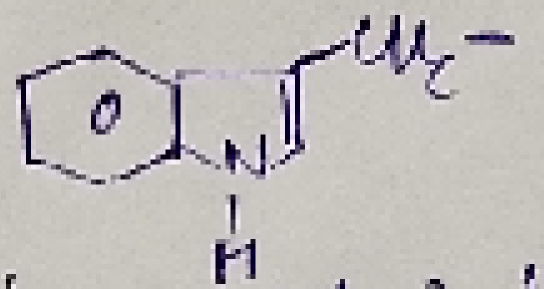
⇅

Cysteine ⇒ $HO_2C-\underset{NH_2}{CH}-CH_2-SH$

Structure of amino acids.

19. Proline.  Pro Amino acids having 2° amine group.

(Nonessential amino acids) [Heterocyclic ring present]

20. Tryptophan: R ⇒  Trp.

(Essential amino acids), it has heterocyclic ring present.

⇒ Threonine is amino acids with 2 chiral centre

⇒ Lysine is the most basic amino acids.

⇒ Serine is the amino acids with 1° alcoholic $-OH$ group but Threonine is the amino acids with 2° alcoholic $-OH$ group.

⇒ Tyrosine is the amino acid with Phenolic $-OH$.

⇒ Lysine is the amino acid which gives the carbyl amine test.

⇒ Isoleucine is the amino acids with 2 chiral centre.

: Preparation of Amino acids:

A. HVZ:

$$CH_3-\underset{O}{\overset{\|}{C}}-OH \xrightarrow[+Br_2]{red\ P} \underset{Br}{CH_2}-\underset{O}{\overset{\|}{C}}-OH \xrightarrow{NH_3} \underset{\overset{+}{N}H_3}{CH_2}-CO_2^-$$ (glycine)

B. Koop Synthesis:

$$CH_3-\underset{O}{\overset{\|}{C}}-CO_2H \xrightarrow{NH_3} CH_3-\underset{NH}{\overset{}{\underset{\|}{C}}}-CO_2H \xrightarrow{H_2/Ni} CH_3-\underset{\overset{+}{N}H_3}{CH}-CO_2^-$$

Pyruvic acid (Alanine)

C. Strecker Synthesis:

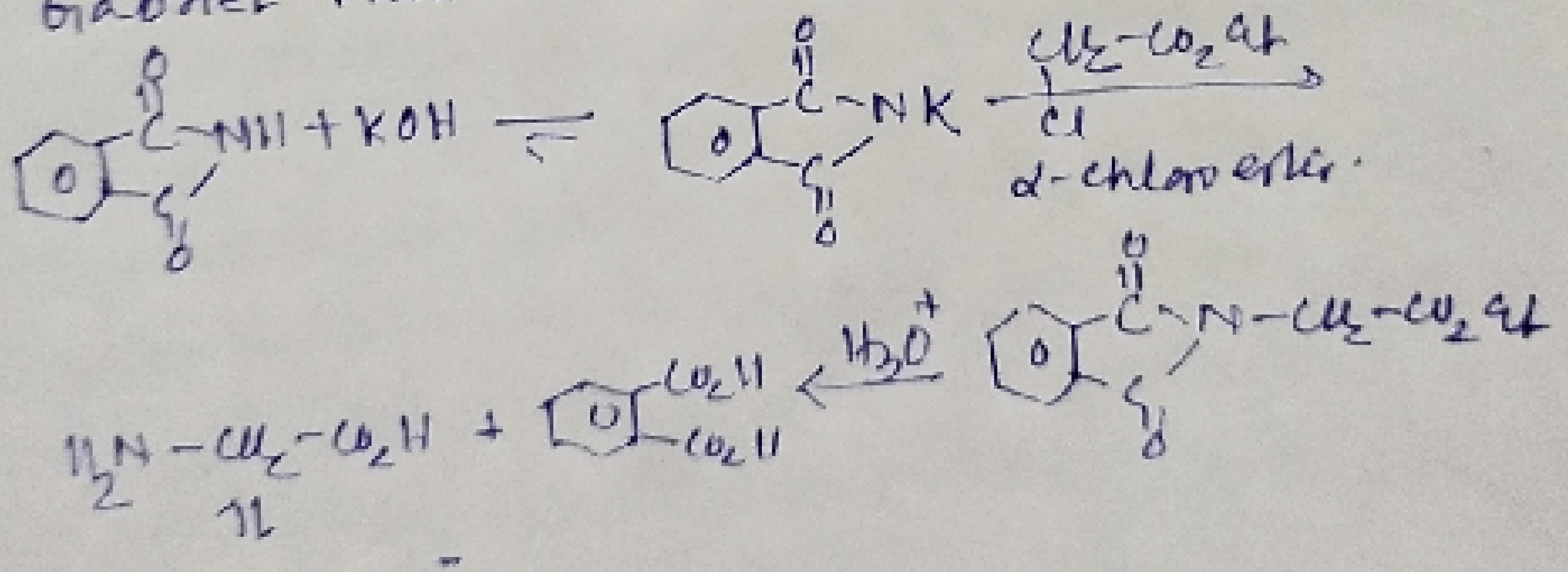
$$RCH=O \xrightarrow{i)\ NH_3} RCH=NH \xrightarrow[/Base]{HCN} RCH\begin{matrix}-NH_2\\-CN\end{matrix}$$

$$\uparrow\downarrow H_3O^+$$

[α amino acid] $RCH\begin{matrix}-\overset{+}{N}H_3\\-CO_2^-\end{matrix} \rightleftharpoons RCH\begin{matrix}-NH_2\\-CO_2H\end{matrix}$

glycine can not be synthesised by streeker Synthesis. [R=H, $HCH=O \xrightarrow{NH_3}$ Urotropine is fored].

D. Gabriel Phthalimide Synthesis:

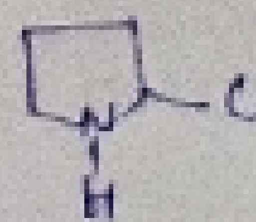


E:

$$HO_2C-(CH_2)_4-CO_2H \xrightarrow[NH_3]{SOCl_2(1eq)} HO-\underset{O}{\overset{\|}{C}}-(CH_2)_4-\overset{O}{\overset{\|}{C}}-NH_2$$

$$\downarrow Br_2+KOH$$

$$HO_2C-\overset{Br}{CH}-CH_2-CH_2 \xleftarrow[/Br_2]{red\ P} HO-\underset{O}{\overset{\|}{C}}-(CH_2)_4-NH_2$$

$$H_2N-H_2C-CH_2 \longrightarrow$$  CO_2H (Proline)

Chemical reactions of amino acids.

A. Reaction of $-CO_2H$ group.

$$R\underset{\overset{|}{\overset{+}{N}H_3}}{CH}-CO_2^- \xrightarrow{H^+} R\underset{\overset{|}{\overset{+}{N}H_3}}{CH}-CO_2H$$

$\xrightarrow{SOCl_2} R\underset{|}{\overset{NH_3}{CH}}-COCl$

$\xrightarrow{NaHCO_3} RCH_2-\overset{+}{N}H_3 + CO_2\uparrow$

$\xrightarrow{LAH} R\underset{\overset{+}{NH_3}}{CH}-CH_2OH$

$\xrightarrow{NH_3} R\underset{\overset{+}{NH_3}}{CH}-CONH_2$

$\xrightarrow{NaOH + CaO/\Delta} RCH_2-\overset{+}{N}H_3$

$\xrightarrow{EtOH} R\underset{\overset{+}{NH_3}}{CH}-CO_2Et$

$\xrightarrow{NaOH/Na} R\underset{\overset{+}{NH_3}}{CH}-CO_2^-\overset{+}{Na} + H_2O/H_2\uparrow$

Esterification of amino acids take place in acidic medium.

B. Reactions of $-NH_2$ group.

$$R\underset{\overset{+}{NH_3}}{CH}-CO_2^- \xrightarrow{\bar{O}H} R\underset{NH_2}{CH}-CO_2^-$$

$\xrightarrow{MeCOCl} R\underset{NH-\underset{O}{\overset{\|}{C}}-CH_3}{CH}-CO_2^-$ (1)

$\xrightarrow{Ph\underset{O}{\overset{\|}{C}}-Cl} R\underset{NH-\underset{O}{\overset{\|}{C}}-Ph}{CH}-CO_2^-$ (2)

$\xrightarrow{NaNO_2 + HCl} R\underset{OH}{CH}-CO_2^- + N_2\uparrow$

$\xrightarrow{NOCl} R\underset{Cl}{CH}-CO_2^-$

$\xrightarrow{HCHO/\Delta} R\underset{\overset{|}{N}=CH_2}{CH}-CO_2^-$

(1) ⇒ acylation of amino acid take place in basic medium, m. weight is increased by 42 unit.

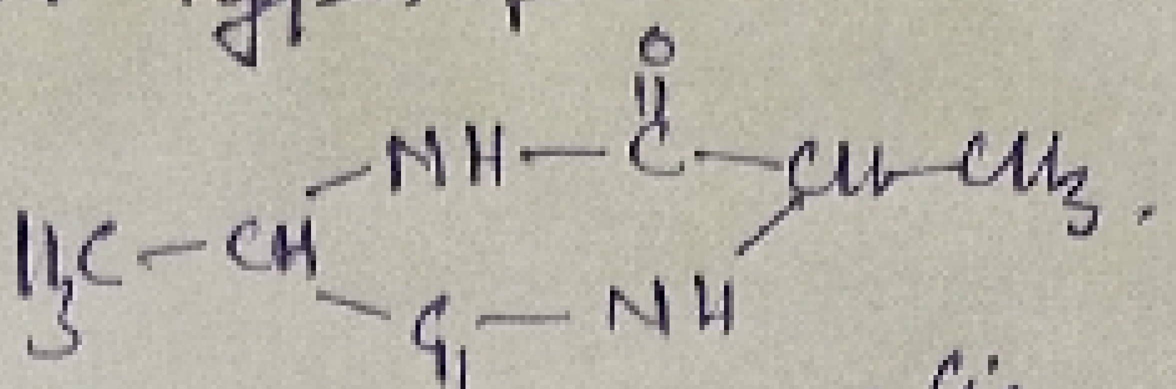
(2) ⇒ benzoylation of amino acid take place in basic medium, m. weight is increased by 114 unit.

⇒ Proline does not give N_2 gas when it reacts with $NaNO_2 + HCl$.

⇒ 1 mole Lysine gives 2 mole N_2 gas when it reacts with $NaNO_2 + HCl$.

⇒

Heating of different types of amino acids.

1. $H_3C-CH(NH_2)-CO_2H \xrightarrow{\Delta}$ 

(Alanine)

3 products → cis (Rs one) → 2 pdts. optically active.

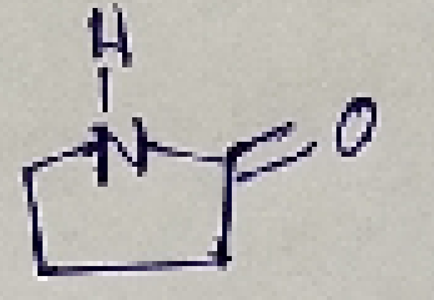
→ Trans → 1 pdt (isomers) [Centre of symmetry] present. optically inactive

⇒ glycine on heating gives 1 product (optically inactive)

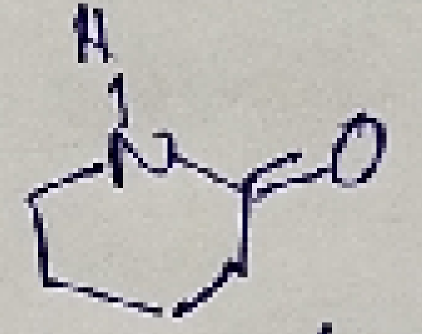
⇒

2. $\overset{\beta}{C}H_2(NH_2)-CH_2-C(=O)-OH \xrightarrow{\Delta} CH_2=CH-C(=O)-OH$

β-amino acids. α-β unsaturated acid.

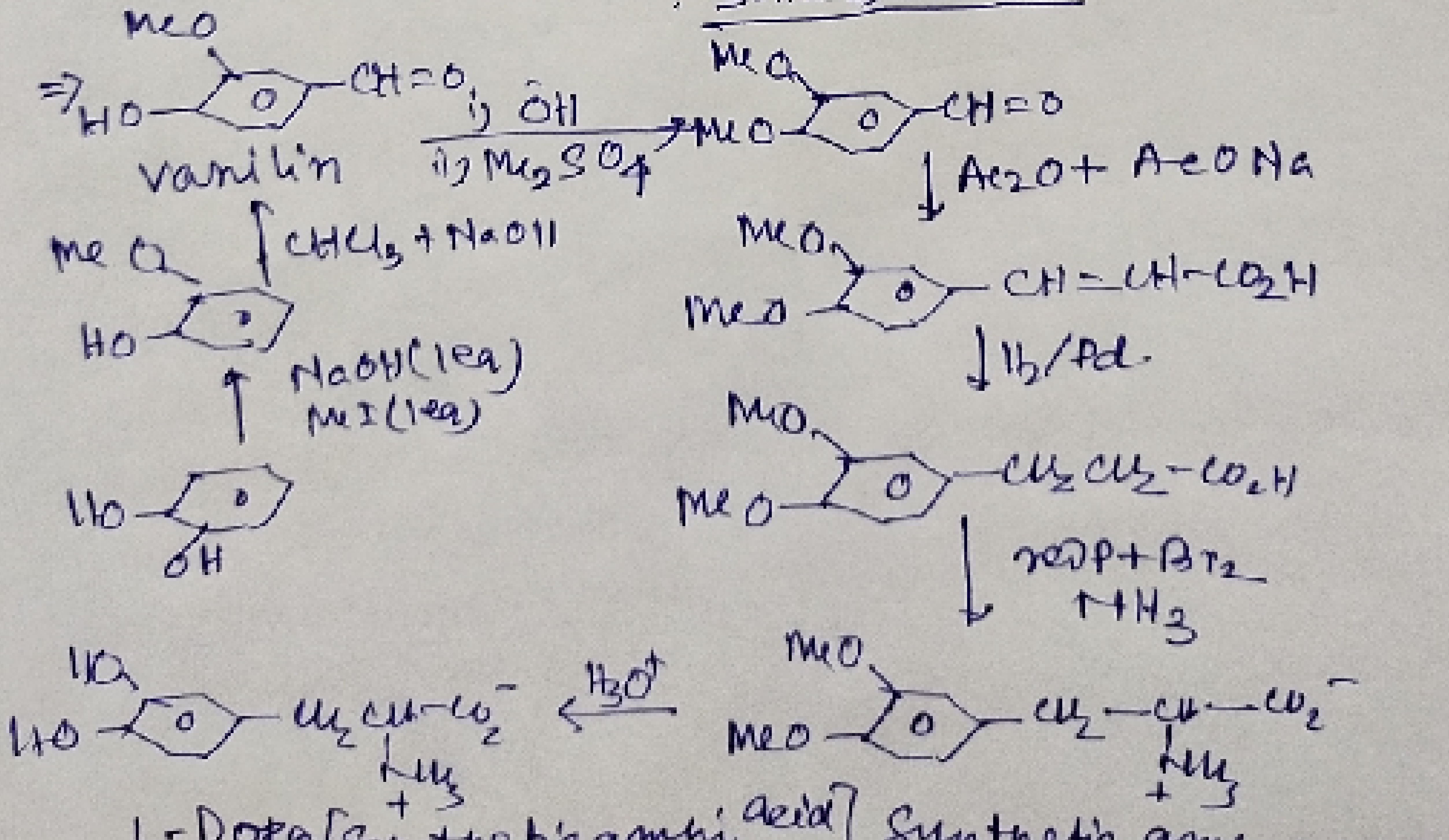
3. $\overset{\gamma}{C}H_2(NH_2)-\overset{\beta}{C}H_2-\overset{\alpha}{C}H_2-C(=O)-OH \xrightarrow{\Delta}$ 

γ-amino acids. γ-Lactum.

4. $CH_2(NH_2)-CH_2CH_2CH_2-C(=O)-OH \xrightarrow{\Delta}$ 

δ-amino acids. δ-Lactum.

! Some Questions:



L-Dopa [Synthetic amino acid]. Synthetic amino acids

Isoelectric point of amino acids:

There is equilibrium exits between different structures of an amino acids when it is placed in either acidic or basic medium.

$$\underset{\overset{+}{N}H_3}{RCH-CO_2H} \underset{K_1}{\rightleftharpoons} \underset{\overset{+}{N}H_3}{RCH-CO_2^-} + H^+ \underset{K_2}{\rightleftharpoons} \underset{NH_2}{RCH-CO_2^-} + H^+$$

conjugate acid [C.A] — neutral (Amino acid) zwitterion/[D.I] — conjugate base [C.B].

⇒ conjugate acid of amino acids is characterised by 2 pKa value. [pK_1 & pK_2].

⇒ $$K_1 = \frac{[D.I][H^+]}{[C.A]} \quad \text{——— (1)}$$

$$K_2 = \frac{[C.B][H^+]}{[D.I]} \quad \text{——— (2)}$$

$$K_1 K_2 = [H^+]^2 \cdot \frac{[C.B]}{[C.A]} \quad \text{——— (3)}$$

⇒ Every neutral amino acid has 1 pK value.

⇒ In highly acidic medium, [C.A]/cation exits in large amount, Under this condition if electric current is passed through electrode, then amino acids migrates to cathode [cationic form].

⇒ In highly basic medium, [C.B]/anion exits in large amount. Under this condition, if electric current is passed through electrode, then amino acids migrate to anion [anionic form].

At a certain pH, there is no net migration of amino acids. This point is called isoelectric point. At this point, the concn of dipolar/zwitterion is maximum.

At isoelectric point [C.B] = [C.A]

$$[H^+]^2 = K_1 K_2$$

$$[H^+] = \sqrt{K_1 K_2} \qquad pH = \frac{1}{2}[pK_1 + pK_2]$$

e.g. conjugate acid of glycine : $pK_1 = 2.3$ $pK_2 = 9.7$

$$[pH]_{I.P} = \frac{1}{2}[2.3 + 9.7] = 6.$$

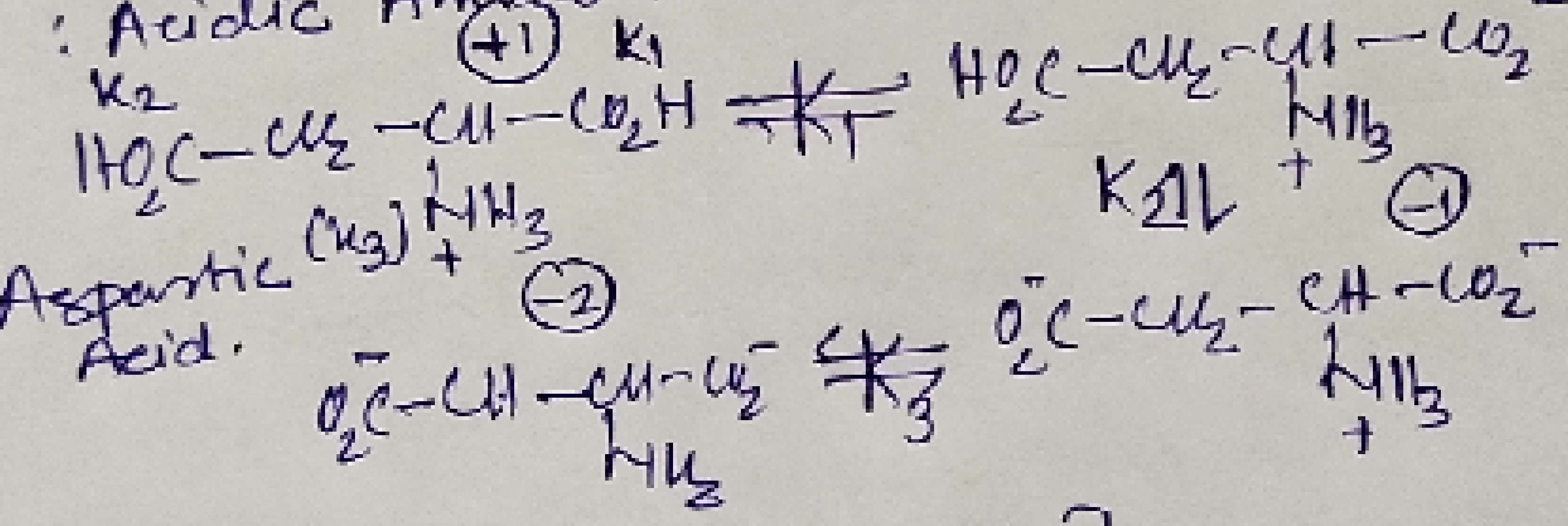
At pH = 6, neutral amino acid exists as zwitterion.

At pH = 0, amino acid exists as conjugate acid (cationic form (C.A)), it migrates to cathode.

At pH = 14, amino acid exists as conjugate base (anionic form (C.B)), it migrates to anode

All neutral amino acids have $[pH]_{I.P} \approx$ (5-6)

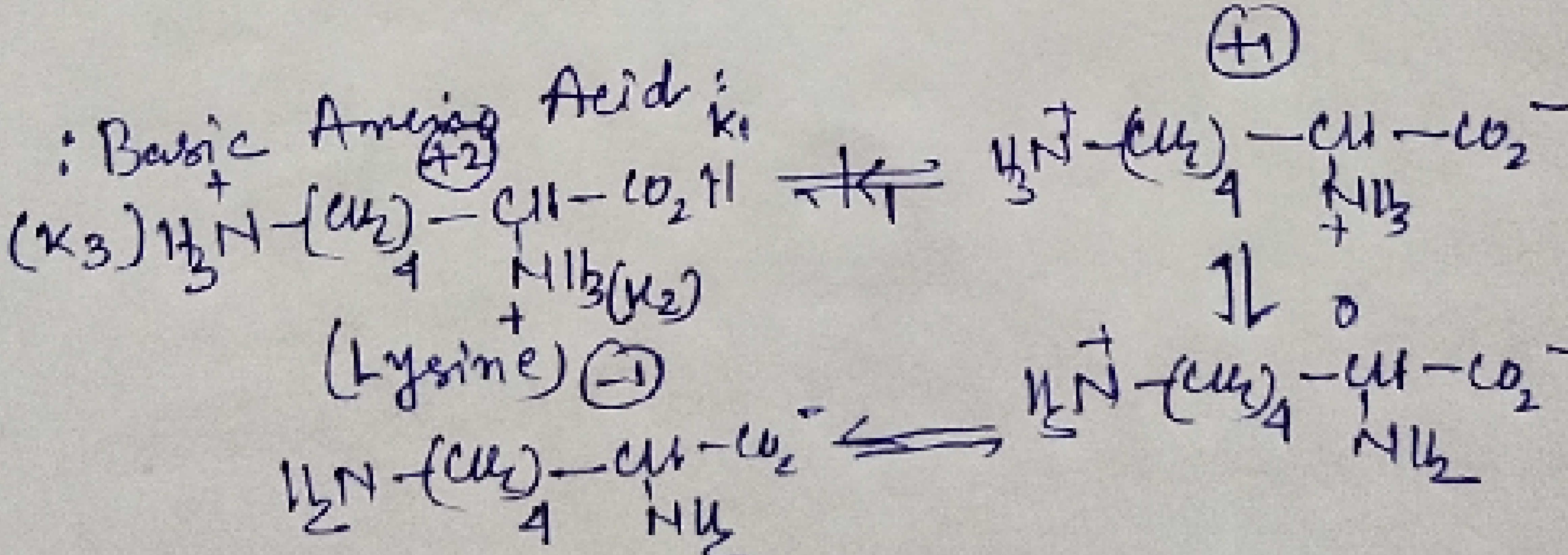
: Acidic Amino Acid:



Aspartic Acid.

$$[pH]_{I.P} = \frac{1}{2}[pK_1 + pK_2].$$

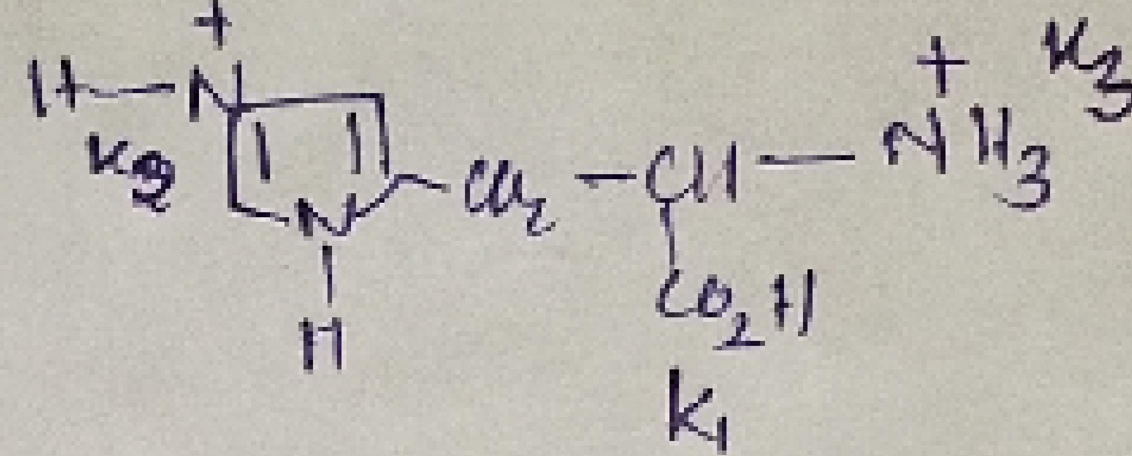
: Basic Amino Acid :



(Lysine)

$$[pH]_{I.P} = \frac{1}{2}[pK_2 + pK_3].$$

Isoelectric point of Histidine.



$pK_1 = 1.82,\ pK_2 = 6.04$
$pK_3 = 9.17.$

$$[pH]_{I.P} = \frac{1}{2}\left[pK_2 + pK_3\right] = \frac{1}{2}\left[6.04 + 9.17\right] = 7.605$$

Q. What is the correct dipolar ion structure of
i) Lysine (ii) Aspartic Acids iii) Isoleucine?

i) $H_2N-(CH_2)_4-\underset{NH_2}{CH}-CO_2H \rightleftharpoons H_3\overset{+}{N}-(CH_2)_4-\underset{NH_2}{CH}-CO_2^-$

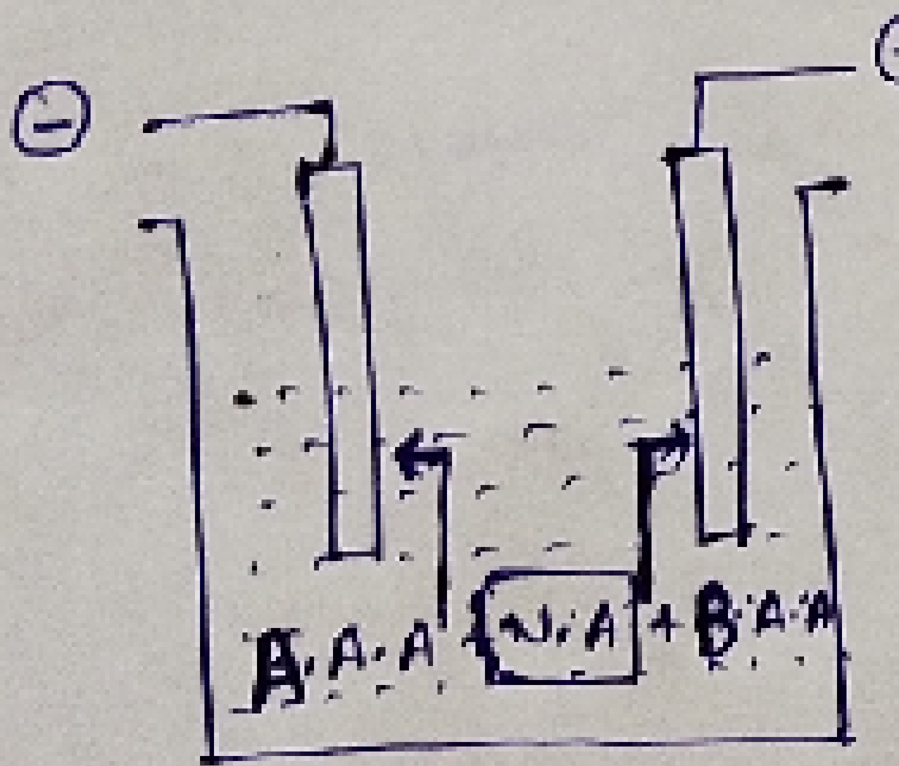
Lysine. (Correct dipolar str of Lysine)

ii) $HO_2C-(CH_2)-\underset{NH_2}{CH}-CO_2H \rightleftharpoons HO_2C-CH_2-\underset{\overset{+}{N}H_3}{CH}-CO_2^-$

Aspartic Acid (correct dipolar str of Aspartic Acid)

iii) (Iso) Leucine $H_3\overset{+}{N}-\underset{CO_2^-}{CH}-CH_2-\underset{CH_3}{CH}-CH_3$

(Correct dipolar str. of Isoleucine)



B.A.A => Basic amino acid (Arginine)
N.A => Neutral amino acid (Alanine)
A.A.A => Acidic amino acid (Glutamic acid)

At pH = 5 to 6, If 3 amino acids are dissolved in electric field, then N.A does not migrate.

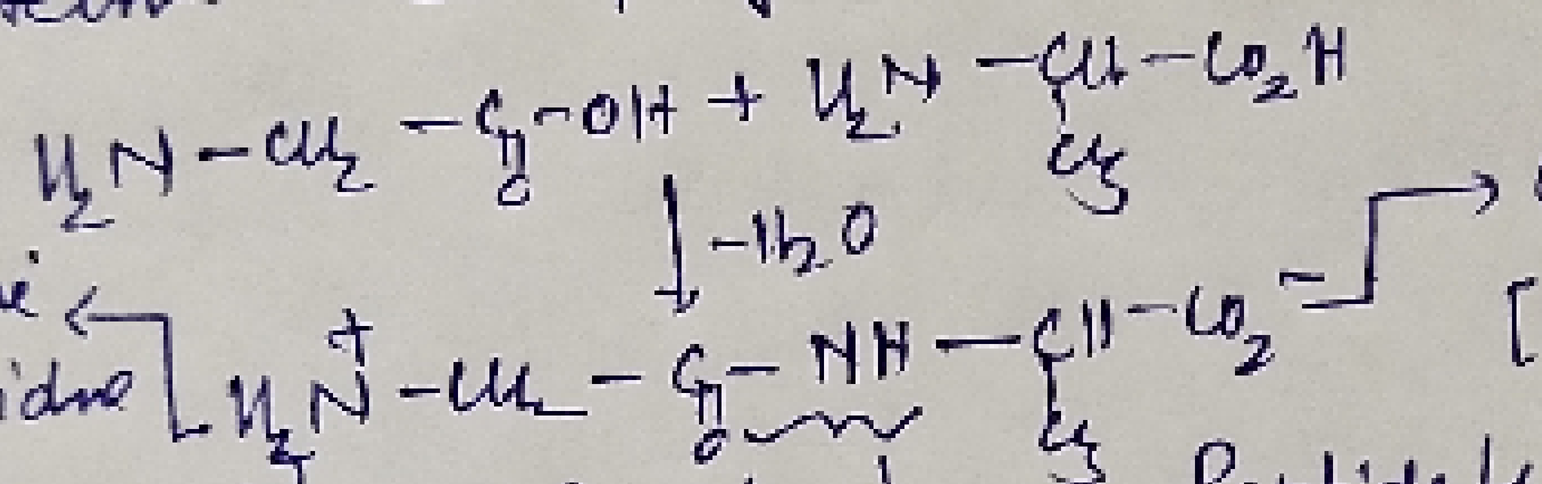
A.A.A exists as anion & it goes to anode
B.A.A exists as cation & it goes to cathode.
So all types of amino acids are separated. This phenomenon is called Electrophoresis.

: Peptide:

When α-amino acids are connected to each other a kind of amide linkage is formed by intermolecular reaction of amino group of one amino acid & the carboxyl group of a another amino acid. A a bio-polymer resulted which is called protein [

i) Dipeptide are made from two amino acids.
ii) Tripeptide are made from three amino acids & so on, tetra, penta.., hexa. If number of amino acids is more than 10, the the products formed are called polypeptides. A polypeptide with more than 100 amino acids residue (M.Wt >10000) is called protein.

: Example of Dipeptide: [formation].

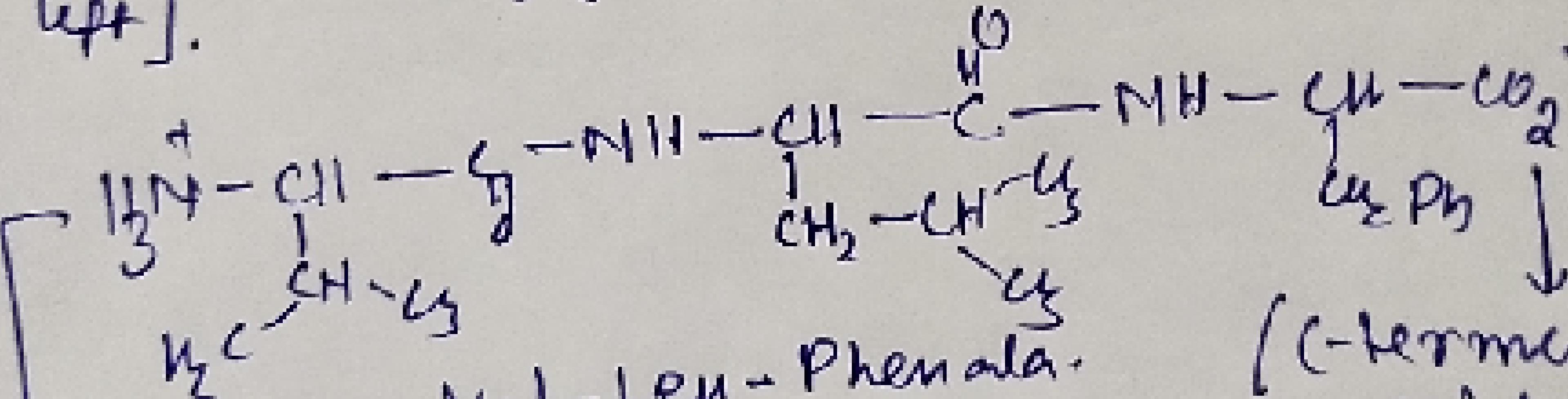


N-terminal residue [extreme left].

C-terminal residue [extreme right]

gly-ala.

Peptide linkage



Val-Leu-Phen ala.

N-terminal residue.

(C-terminal residue)

: Tripeptide:

⇒ for n-peptide, no. of peptide linkage (n-1) (amide)

⇒ It consumes (n-1) H_2O molecules, for n^{th} peptide

⇒ for Decapeptide, no. of water molecules consumed = 9.

⇒ No. of $-\overset{O}{\overset{\|}{C}}-$ linkage present, (Val-Leu-Phen Ala) = 3]

- Features of Peptide Linkage:

=> In peptide linkage amino acids has L-configuration

=> C-N bond in peptide linkage show geometrical isomerism & it exists in trans form. (mainly)

=> C-N bond in peptide linkage has some double bond character [because it shows resonance]

$(C-N)_{CH_3-NH_2} > (C-N)_{\text{peptide linkage}} > (C-N)_{CH_2=NH}$.

[Bond length order].

=> Glycine can form 1 dipeptide or 1 tripeptide.

=> Glycine & Alanine can form 4 dipeptides.

=> Glycine, Alanine & phenyl Alanine can form 9 no. of dipeptides.

=> Gly. Ala can form 8 no. of Tripeptides.

=> Peptide linkage reacts with very dilute solution of $CuSO_4$ & violet colour appeared. This is called biuret test. This test is applicable for individual amino acid, but for protein, urea which has $-\underset{O}{C}-NH-$.

=> Questions:

Q. A decapeptide (M.Wt = 796) on complete hydrolysis gives glycine (M.Wt = 75) alanine & phenylalanine. Glycine contributes 47% to the total weight of the hydrolysis products. Find out no of glycine units of decapeptide.

Ans: Total water needed = 9 mole, = 9 × 18 = 162 gm.

Net mass of decapeptide = 796 + 162 = 958.

% mass of glycine = $958 \times \frac{47}{100}$ = 450 gm.

No. of glycine unit present = $\frac{450}{75} = 6$.

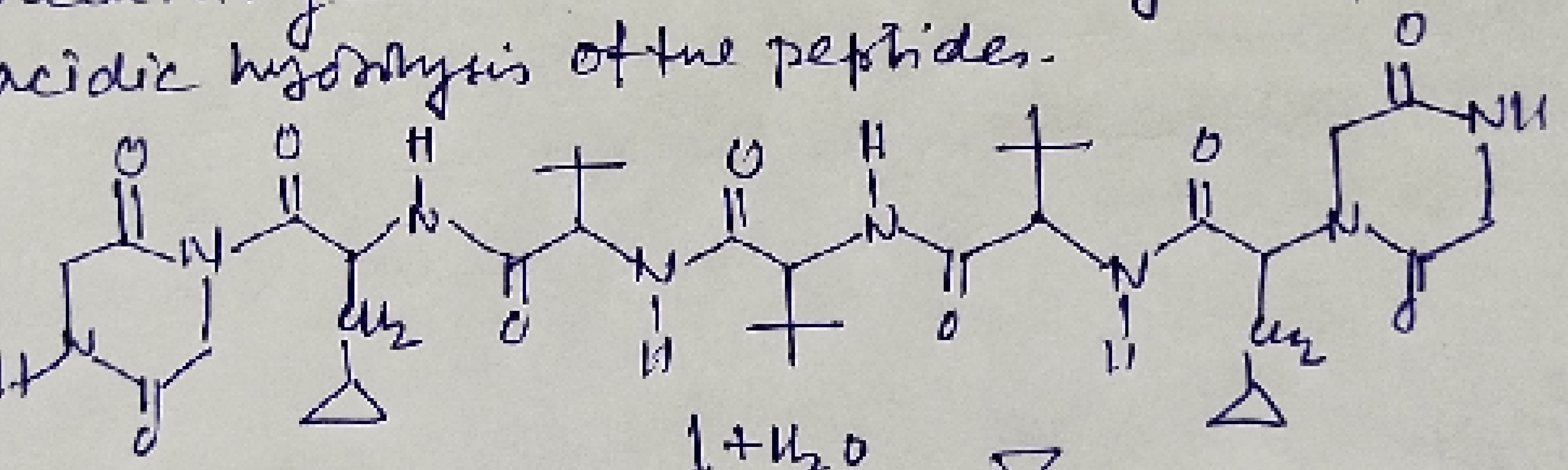
Q2. A tetrapeptide has $-CO_2H$ group on alanine. This produces gly, val, Phen. & Ala on complete hydrolysis. Find out the number of possible sequences (Primary amine str.) with $-NH_2$ group attached to a chiral centre is:

Ans: Glycine can't be with $-NH_2$ group, so it can't be extreme left side. So Possible primary strs.

i) Val. gly. ~~ala~~. phen. ala ala.
ii) val phen ala gly. ala.
iii) Phen ala. val. gly. ala
iv) Phen ala gly val. ala.

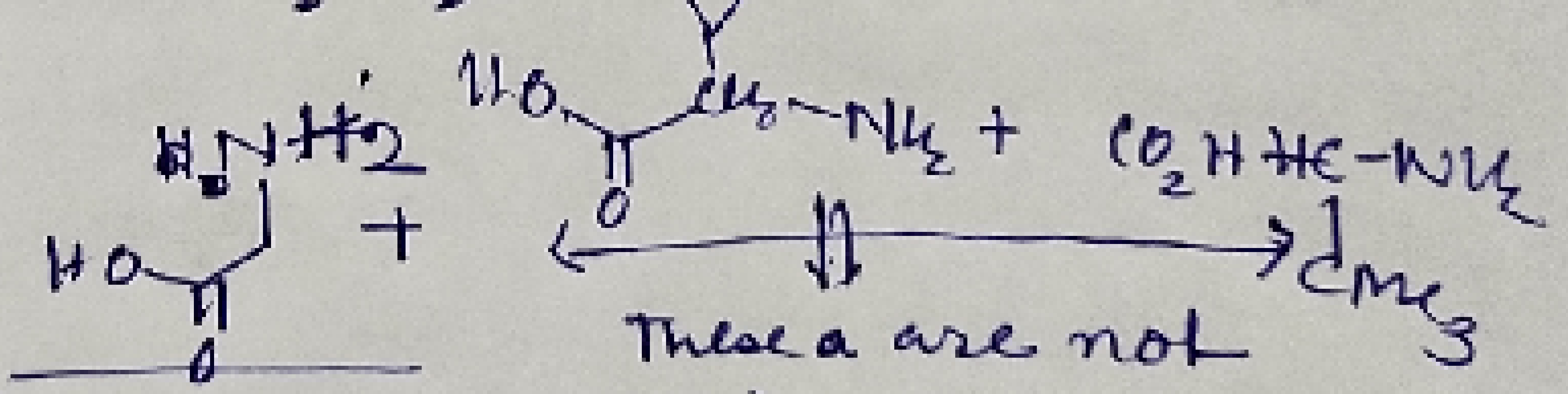
4 possible primary structures. (It is just possible arrangements).

Q3. Find out the total number of distinct naturally occurring amino acids obtained by complete acidic hydrolysis of the peptides.



1 + H_2O

Ans: On hydrolysis
1 →



$H_2N-CH_2-CO_2H$ +

It is naturally occurring amino acid.

These are not naturally occurring amino acid.

Q4. What is the net charge of mono sodium glutamate (MSG) a commonly used food additive.

Ans: 0: str. $Na^+ [CO_2^- - CH_2CH_2CH(NH_3^+)CO_2^-]$.

Q5. A pentapeptide on complete hydrolysis gives 2 units of glycine, 1 unit of valine, leucine & phenylalanine each. Find out possible number of sequences (primary structure) if its $-CO_2H$ & $-NH_2$ group both will be attached to achiral centre.

Ans: 6
a) gly. val. phe. Leu. gly.
b) gly. val. Leu. phen. gly
c) gly phenl. val. Leu gly.
d) gly phe Leu val gly.
e) gly Leu val phen. gly
f) gly. Leu phen. val. gly.

Q6. A tetrapeptide on complete hydrolysis give glycine, alanine, valine, phenylalanine. It has $-CO_2H$ group on alanine. Find out possible no of primary structure

Ans: 6

Q7. Aspartame, an artificial sweetener, is a peptide has following structures

$$H_2N-\underset{CH_2CO_2H}{CH}-CONH-\underset{CH_2-C_6H_5}{CH}-CO_2CH_3.$$

a) Identify functional groups. b) Write zwitterion str.
c) Write the strs. of amino acids obtained from hydrolysis of aspartame.
d) Which of the two amino acids is more hydrophobic?

Ans: i) 4 F.G. are present ($-NH_2$, CO_2H, $-CONH_2$, $-CO_2CH_3$).

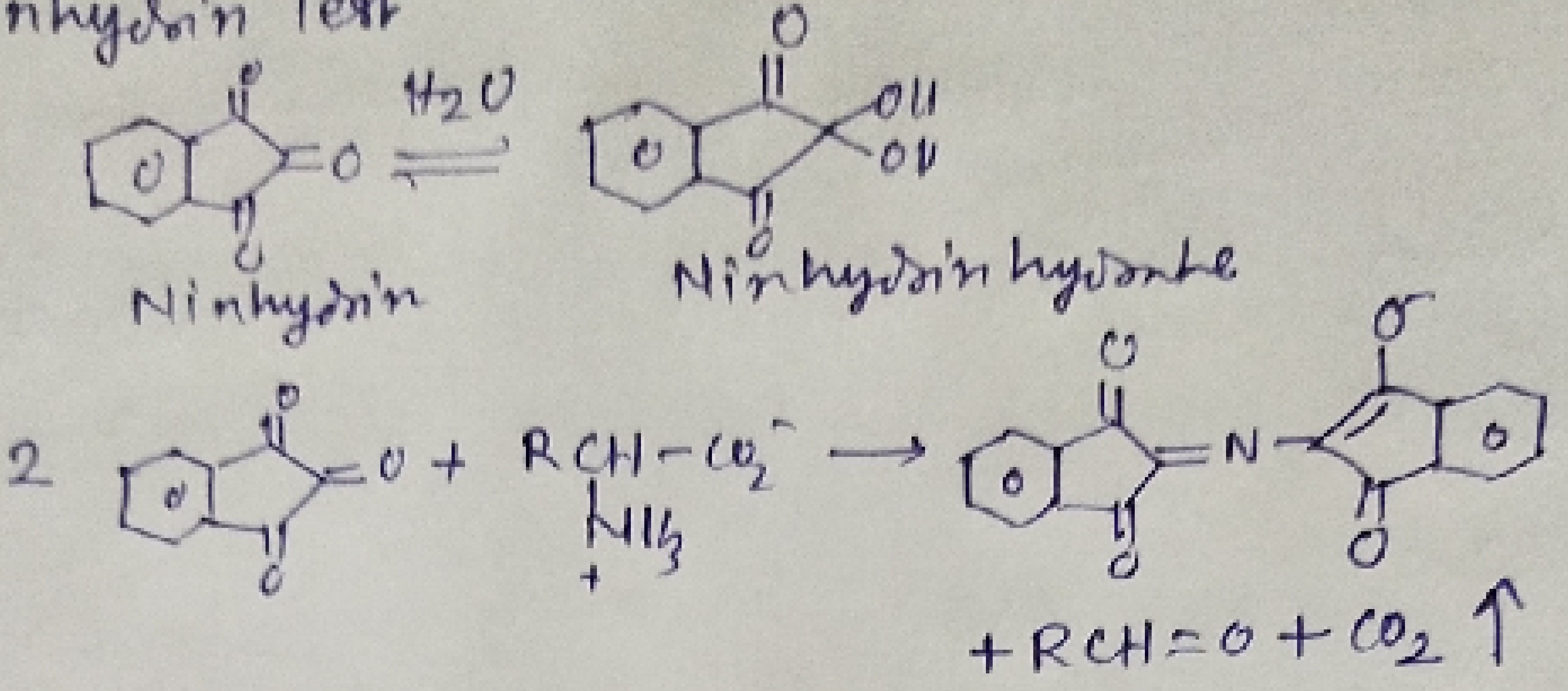
ii) $$H_3\overset{+}{N}-\underset{CH_2-CO_2^-}{CH}-CONH-\underset{CH_2Ph}{CH}-CO_2CH_3$$

iii) $$H_2N-\underset{CH_2CO_2H}{CH}-CO_2H + H_2N-\underset{CH_2Ph}{CH}-CO_2H + MeOH$$

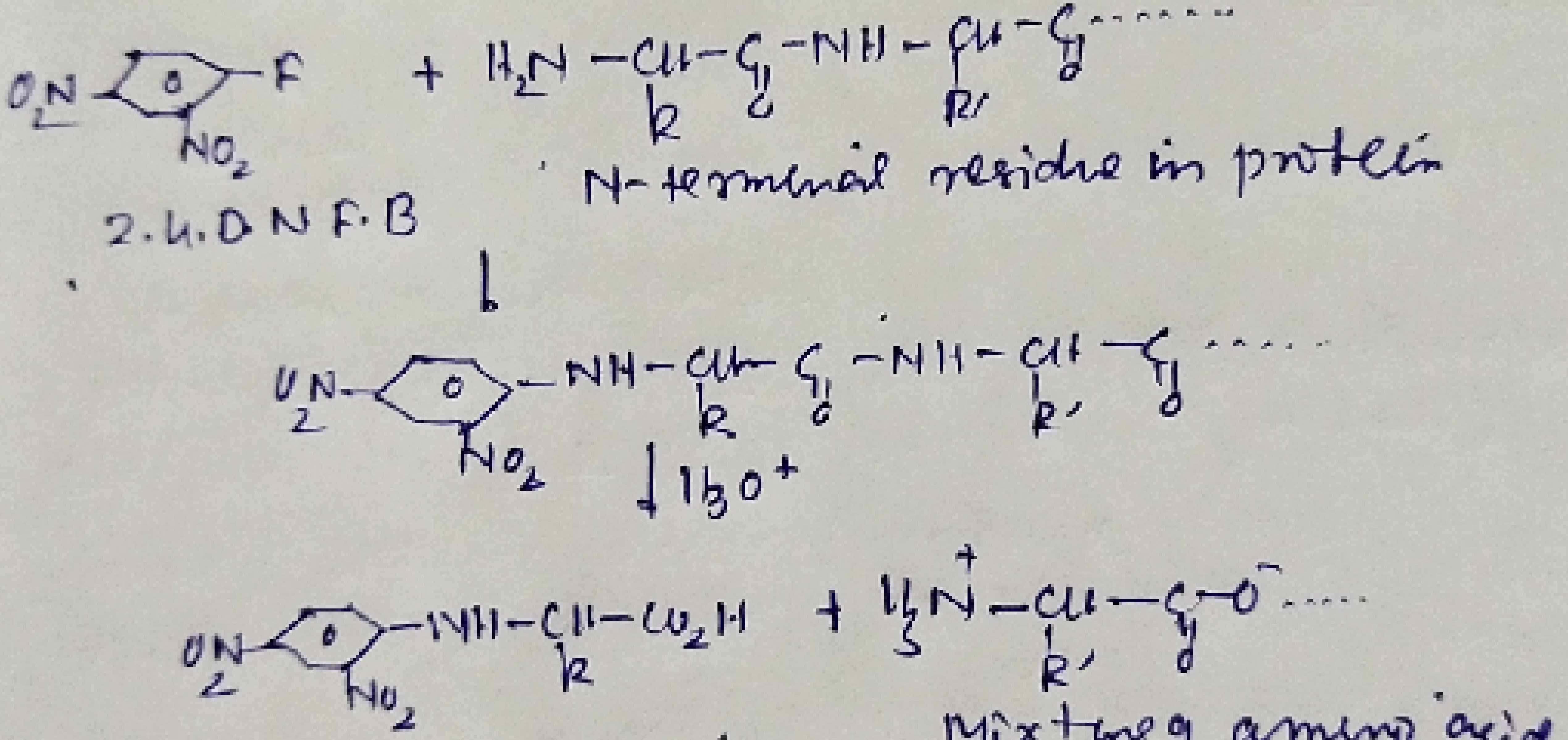
(Aspartic acid) Phenyl alanine (more hydrophobic)

Amino Acid detection:

Ninhydrin Test



Detection of N-terminal Residue



Labeled N-terminal residue (amino acid) ∴ separate & identify it

Polypeptides with fewer amino acids are likely to be called proteins if they ordinarily have a well defined conformation of a protein such as insulin which contain 51 amino acid.