AMINO ACIDS

↳ Amino acids are organic acids having an amino ($-NH_2$) group attached to a chain containing an acid group.

↳ **Natural α-Amino Acids**—

↳ There are 20 naturally occuring α-amino acids.

↳ These α-amino acids are obtained from hydrolysis of peptides or proteins.

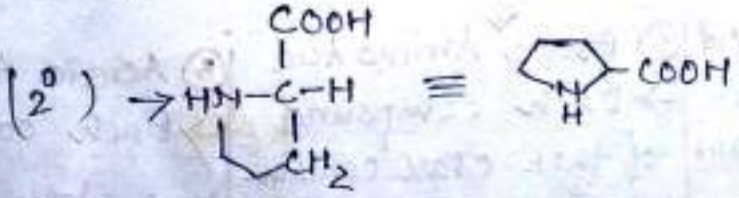
↳ All these naturally occuring amino acids are α-amino acids, where the amino ($-NH_2$) group is attached to the C-atom next to the acid group.

General formula: $R-\overset{\alpha}{C}H(NH_2)-\overset{\text{carboxyl}}{C}(=O)-OH$

α-carbon

R = aliphatic or aromatic or heterocyclic unit.

Note— Proline is α-imino acid, here $-NH$ (2^0-amine) group is present instead of $-NH_2$ (1^0-amine) group



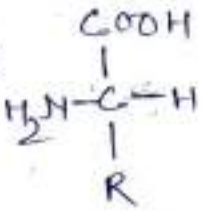
Proline

↳ All these naturally occuring amino acids are chiral (optically active) as they contain at least one chiral carbon atom (except Glycine, it is achiral & therefore optically inactive).

{ Note — Chiral carbon —
It is a carbon atom that is attached to four different types of atoms or groups of atoms. }

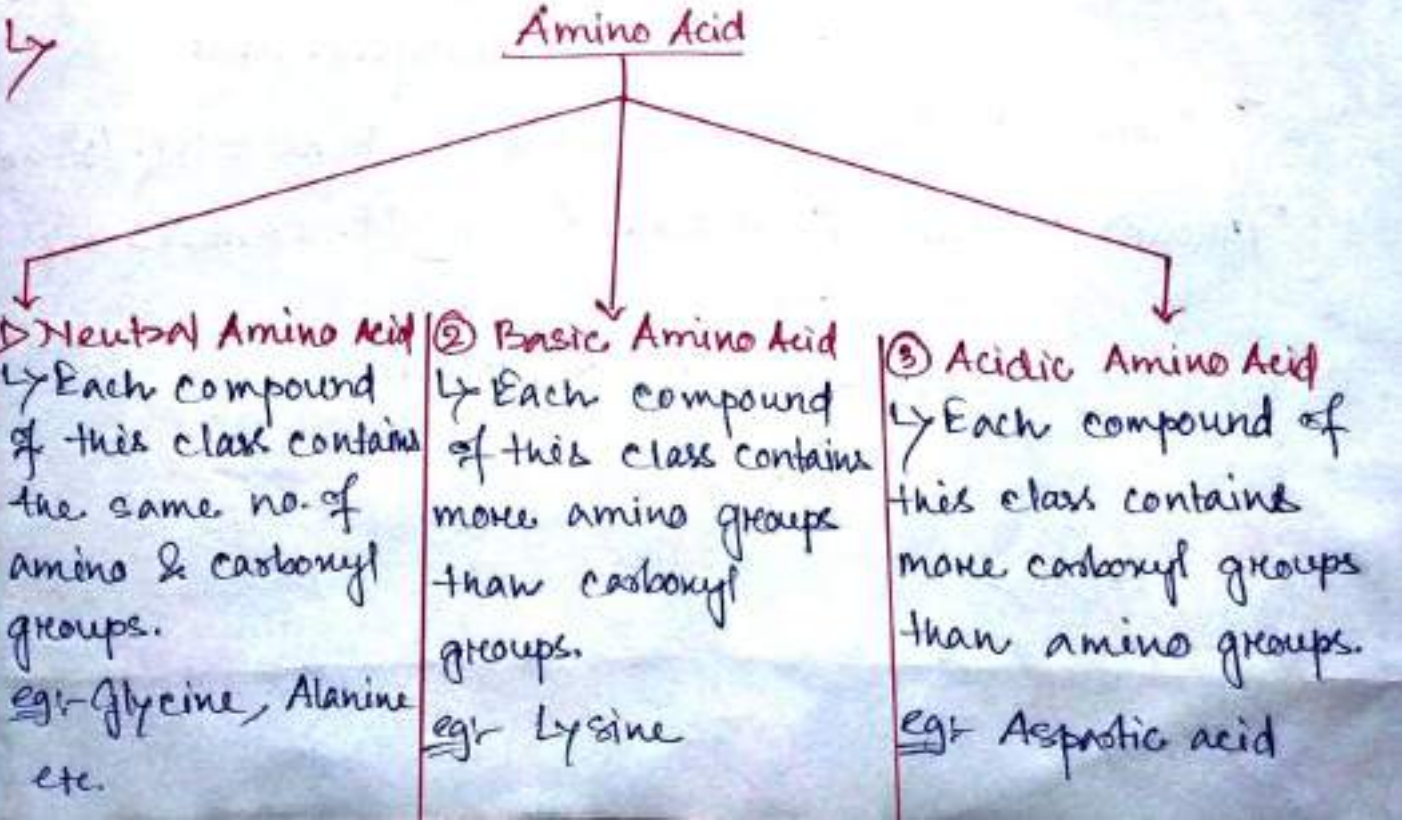
↳ α-amino acids are L-amino acids, because ($-NH_2$) group is present on the left hand side of the α-carbon atom.

General formula:



L-amino acid

↳



Essential (Indispensable) Amino Acids —

↳ Those amino acids that cannot be synthesized by the body & must be supplied in the diet are called essential amino acids.

Non-essential (Dispensable) Amino Acids —

These amino acids that can be synthesized from other compounds by the tissues of the body are called non-essential amino acids.

Essential Amino Acids	Non-essential Amino Acids.
1) Valine	1) Glycine
2) Isoleucine	2) Tyrosine
3) Tryptophane	3) Proline
4) Methionine	4) Cysteine
5) Arginine	5) Aspartic Acid
6) Leucine	6) Alanine
7) Phenyl alanine	7) Serine
8) Threonine	8) Hydroxy proline
9) Lysine	9) Cystine
10) Histidine	10) Glutamic acid

↳ These amino acids have high melting point values.

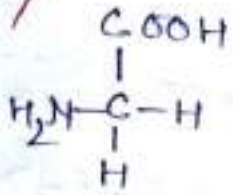
↳ All these α-amino acids are of S-configuration

except Cysteine (R- configuration.)

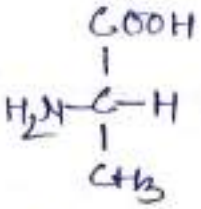
1) Neutral Amino Acids —

Aliphatic Amino Acids —

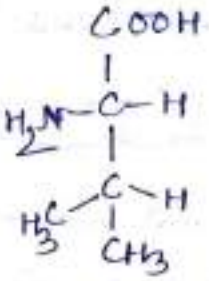
↳



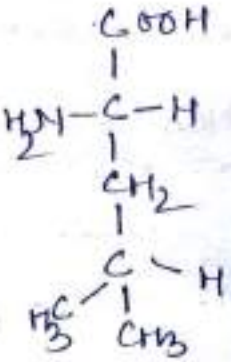
Glycine (Gly)



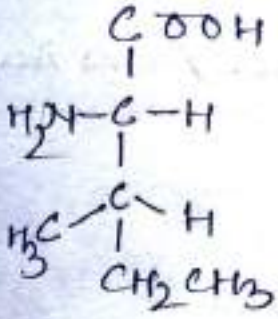
Alanine (Ala)



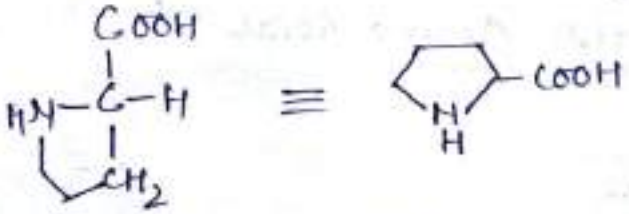
Valine (Val)



Leucine (Leu)



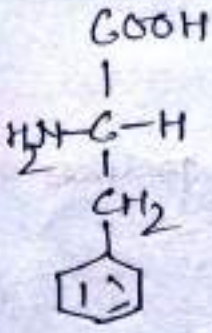
Isoleucine (Ile)



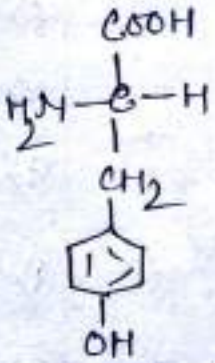
Proline (Pro)

Aromatic Amino Acids —

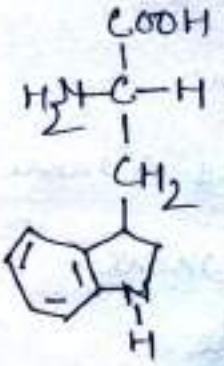
↳



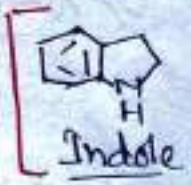
Phenylalanine (Phe)



Tyrosine (Tyr)



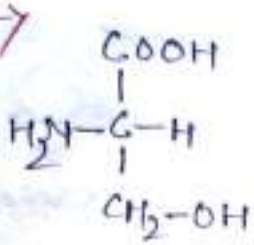
Tryptophan (Try)



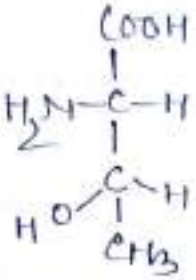
Indole

Amino Acids with –OH group —

↳



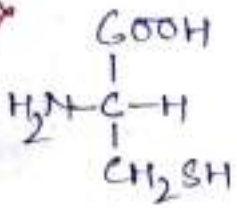
Serine (Ser)



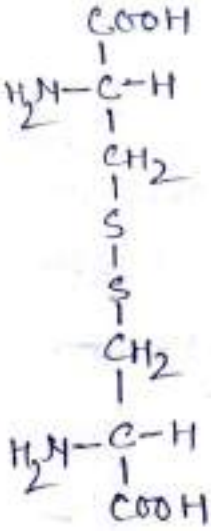
Threonine (Thr)

Amino Acids with S- group —

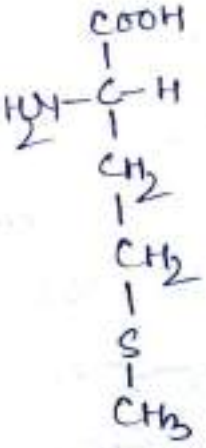
↳



Cysteine (Cys)



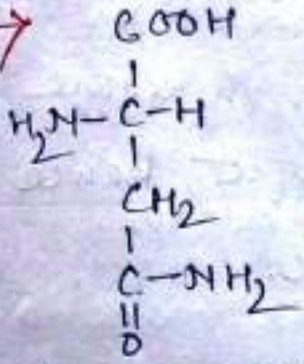
Cysteine (Cys–Scy)



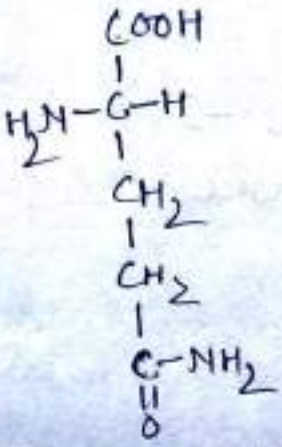
Methionine (Met)

Amino Acids containing Amide ($-\overset{O}{\overset{\|}{C}}-NH_2$) group —

↳



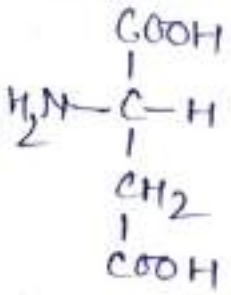
Asparagine (Asn)



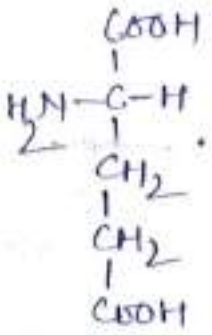
Glutamine (Gln)

2) Acidic Amino Acids —

↳



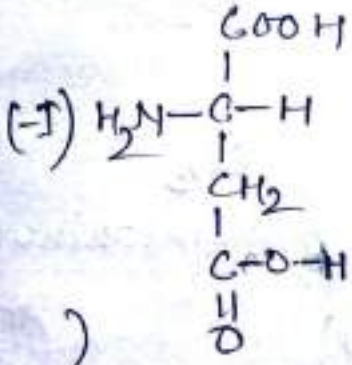
Aspartic Acid (Asp)



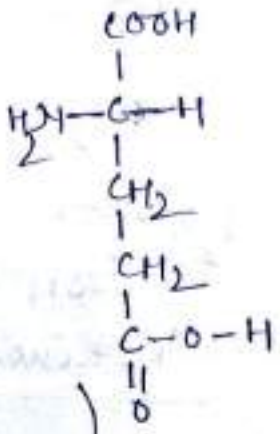
Glutamic Acid (Glu)

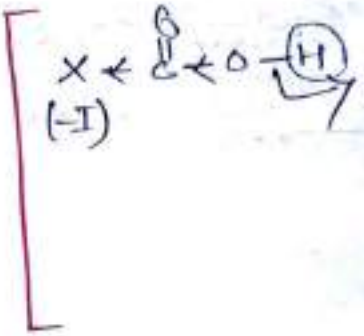
↳ Aspartic acid is more acidic than Glutamic acid.

$-NH_2$ group shows $-I$ effect and inductive (I) effect is distance dependent.



↳ Here distance is less between $-NH_2$ & $-COOH$ group, therefore, more $-I$ effect, hence more acidic

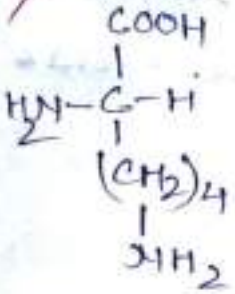




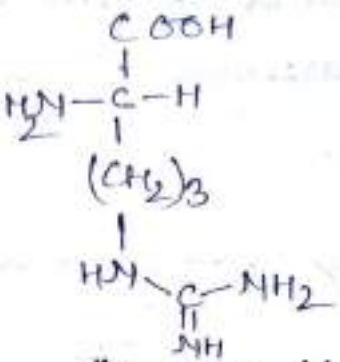
↳ Here distance between $-NH_2$ & $-COOH$ groups is more, therefore less $-I$ effect, hence less acidic.

3) Basic Amino Acids —

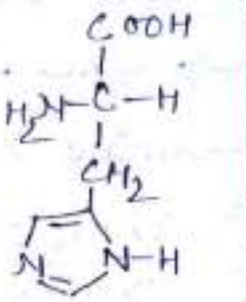
↳



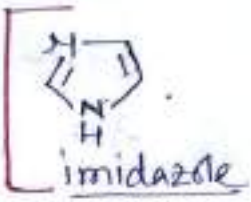
Lysine (Lys)



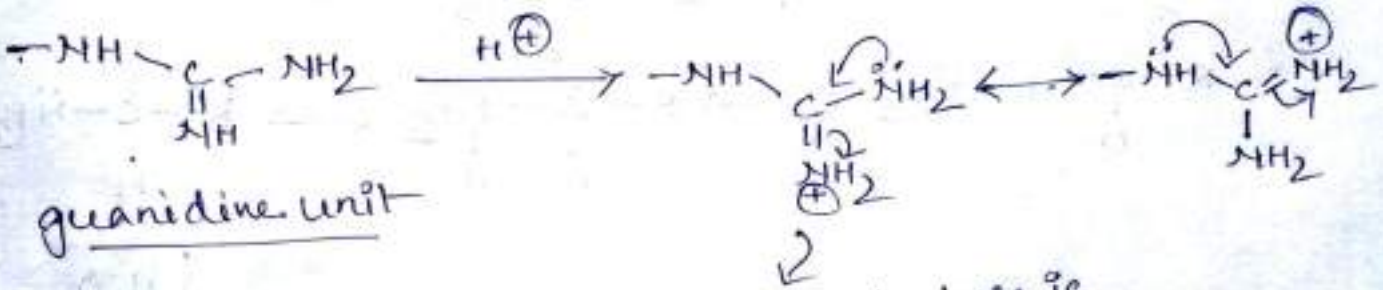
Arginine (Arg)



Histidine (His)



↳ Arginine is most basic amino acid, due to the presence of guanidine unit.



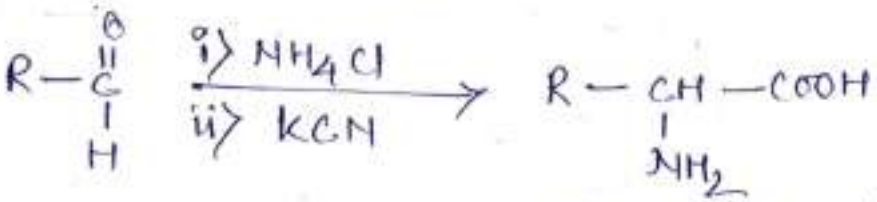
↳ Basicity order —

Arginine > Histidine > Lysine

Preparation of Amino Acids —

① Strecker Synthesis — In this method, an aldehyde is treated with ammonium cyanide ($NH_4Cl + KCN$) to form the

corresponding cyanohydrin which is made to react with ammonia to give an α-amino nitrile. The hydrolysis of the nitrile yields an α-amino acid.

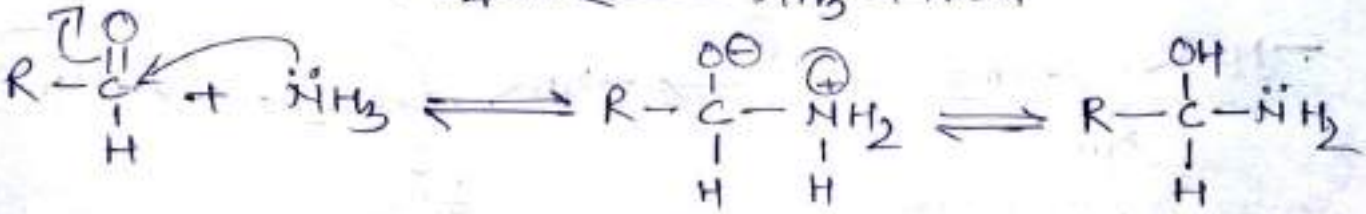


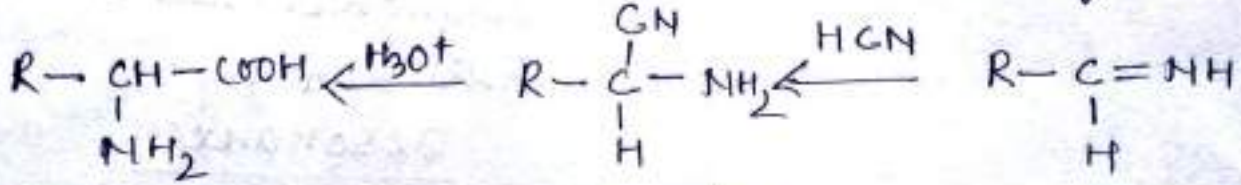
α-amino acid

Mechanism–

$$NH_4Cl + KCN \longrightarrow NH_4CN + KCl$$

$$NH_4CN \rightleftharpoons NH_3 + HCN$$





α-amino acid

α-amino nitrile

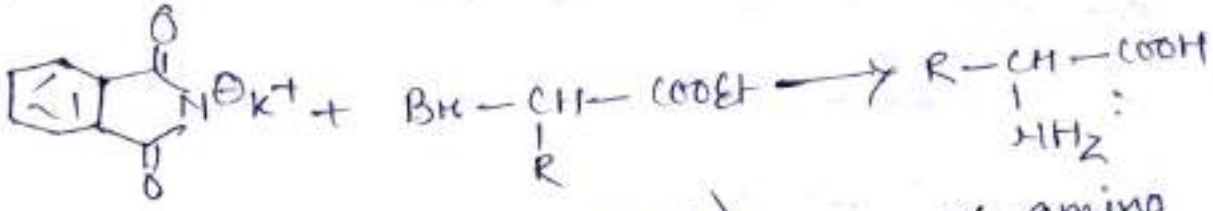
If, $R = -CH_2-C_6H_5$ gives phenylalanine

$R = -CH_3$ gives Alanine

$R = -CH_2-C_6H_4-OH$ gives Tyrosine etc.

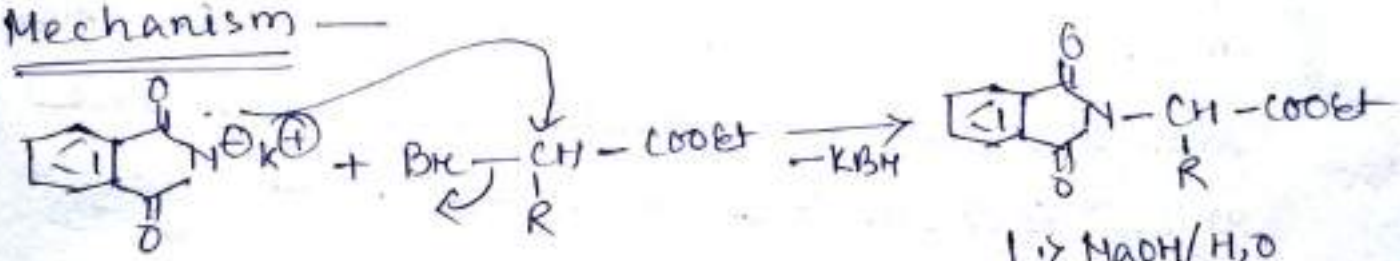
Gabriel's phthalimide Synthesis —

↳ In this method treatment of α-halo acids or haloesters with potassium phthalimide followed by hydrolysis yield an α-amino acid.

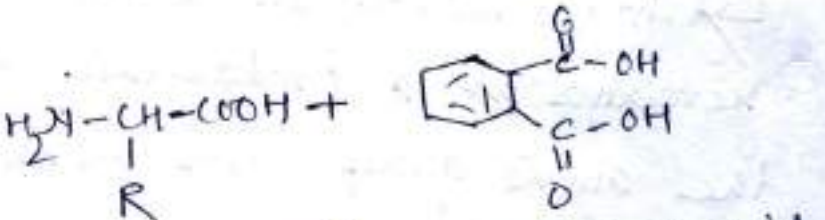


(Potassium phthalimide) (α-bromo ester) α-amino acid

Mechanism —

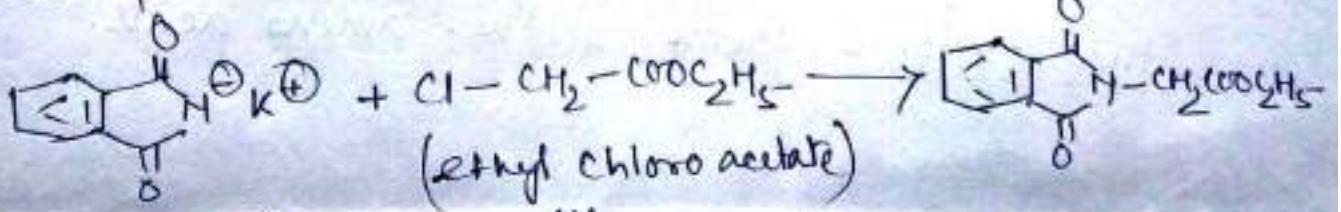


↓ 1) NaOH/H2O
2) HCl

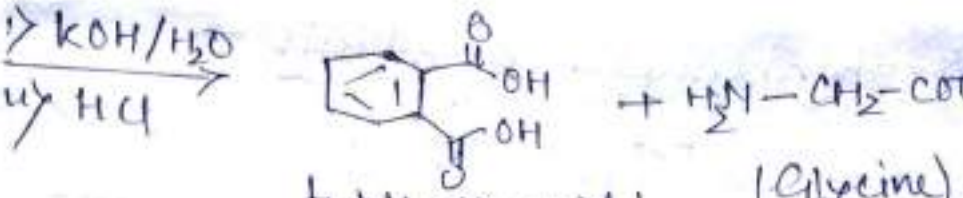


α-amino acid phthalic acid

↳ Examples —

i) 

(Potassium phthalimide) (ethyl chloro acetate or α-chloro ester)



(phthalic acid) (Glycine)

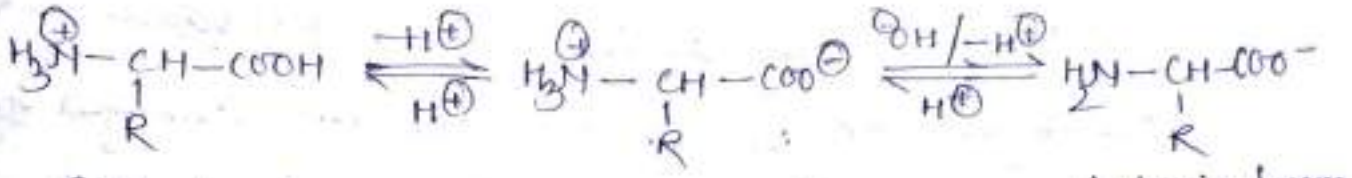
↳ By this method, we can synthesize Glycine, Alanine, Serine, Threonine, Valine, Leucine & Isoleucine.

Zwitter ions —

↳ Since amino acids contain one or more amino group ($-NH_2$) and one or more carboxyl group ($-COOH$); therefore, in dry solid state, amino acids form inner salts which are called zwitter ions or dipolar ions or ampholytes.

↳ In zwitter ion form, the carboxyl group remains as a carboxylate ($-COO^{\ominus}$) group and the amino group exists as an ammonium ($-\overset{\oplus}{N}H_3$) group.

↳ In aqueous medium, an equilibrium exists involving the zwitter ion, the anionic and the cationic forms of the amino acids.



Cationic form

↳ Conjugate acid of the zwitter ion

↳ Predominant at $pH < 2$

Zwitter ion

↳ Predominant at isoelectric point ($pH = 7$)

Anionic form

↳ Conjugate base of the zwitter ion

↳ Predominant at $pH > 11$

↳ A zwitter ion is a compound that has a negative charge on one atom and a positive charge on a non-adjacent atom.

Isoelectric point (p^I) —

↳ The isoelectric point (p^I) of an amino acid is the pH at which it has no net charge.

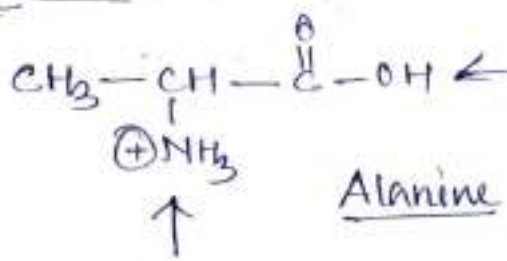
↳ In other words, it is the pH at which the amount of negative charge on an amino acid exactly balances the amount of positive charge.

↳ p^I (isoelectric point) = pH at which there is no net charge.

↳ Every amino acid has its own isoelectric point.

↳ For neutral amino acids, p^I value is the average pK_a values of positively charged or basic groups and negatively charged or acidic groups.

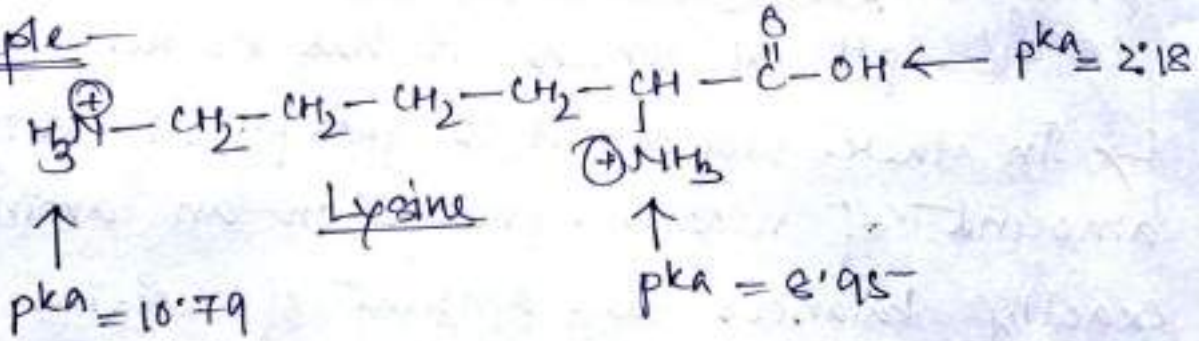
Example —



$$\therefore p^I = \frac{2.34 + 9.69}{2} = \frac{12.03}{2} = 6.02$$

↳ For basic amino acids, p^I value is the average of pK_a values of positively charged groups are basic groups.

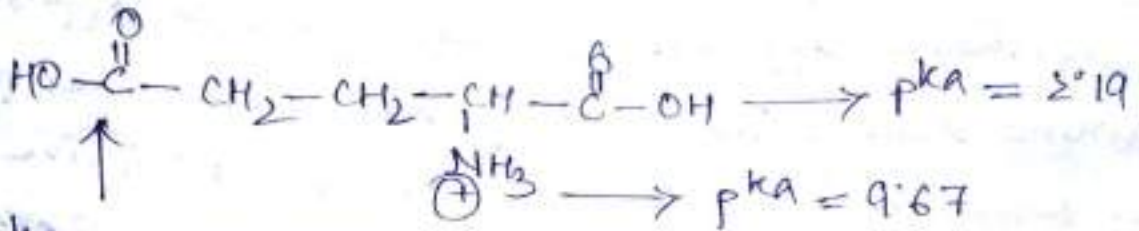
Example —



$$\therefore p^I = \frac{10.79 + 8.95}{2} = \frac{19.74}{2} = 9.87$$

↳ Similarly, for acidic amino acids, p^I value is the average of pK_a values of negatively charged groups are acidic groups.

Example —



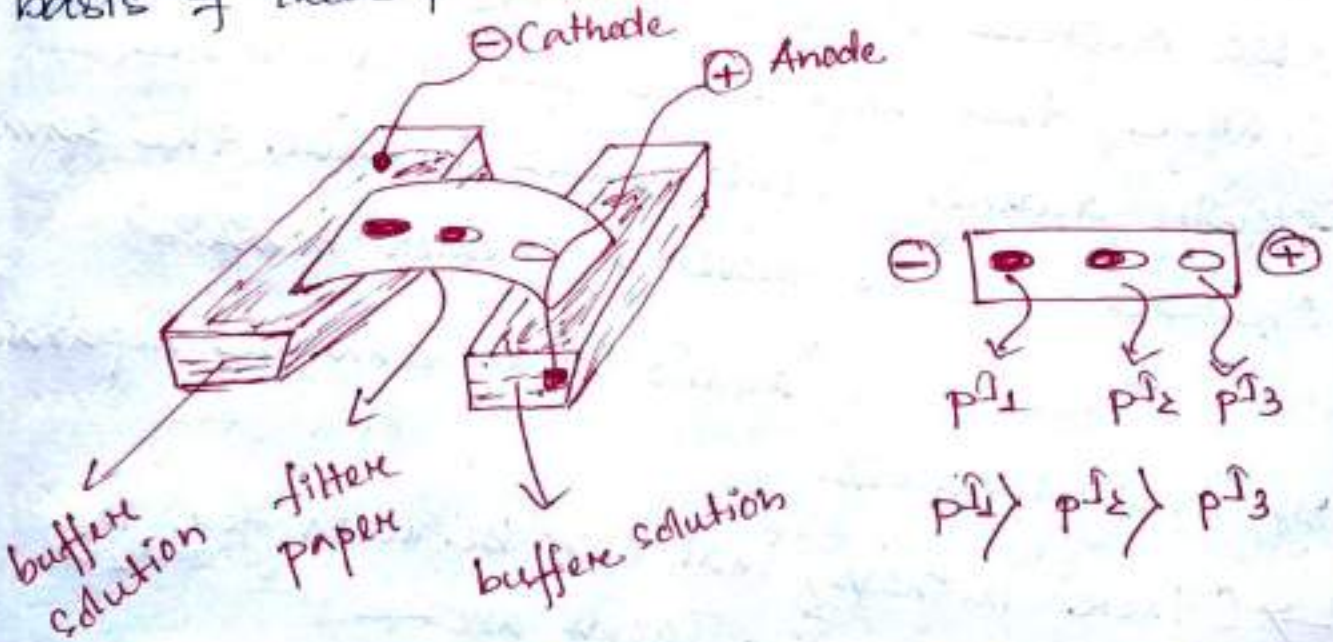
$pK_a = 4{\cdot}25$ Glutamic acid

$$\therefore pI = \frac{4{\cdot}25 + 2{\cdot}19}{2} = \frac{6{\cdot}44}{2} = \underline{3{\cdot}22}$$

Electrophoresis: — (Separation of amino acids)

↳ A mixture of amino acids can be ~~sepated~~ separated by several different techniques, electrophoresis is one of them.

↳ Electrophoresis separates amino acids on the basis of their pI values.



A few drops of a solution of amino acid mixture are applied to the middle of a piece of filter paper or to a gel. When the filter

paper (or gel) is placed in a buffered solution between two electrodes and an electric field is applied, an amino acid with a p^I greater than the p^H of the solution will have an overall positive charge and will migrate towards the cathode (the negative electrode). The farther its p^I is from the p^H of the buffer, the more positive it will be and the farther it will migrate toward the cathode in a given amount of time. An amino acid with a p^I less than the p^H of the buffer will have an overall negative charge and will migrate toward the anode (the positive electrode). If two ~~nucleus~~ molecules ~~it~~ have the same charge, the larger one will move more slowly during electrophoresis because the same charge has to move a greater mass.

This way amino acids can be separated by electrophoresis.

↳ Other methods, that can be used for the separation of amino acids are —

i) Paper chromatography

ii) Thin-layer chromatography

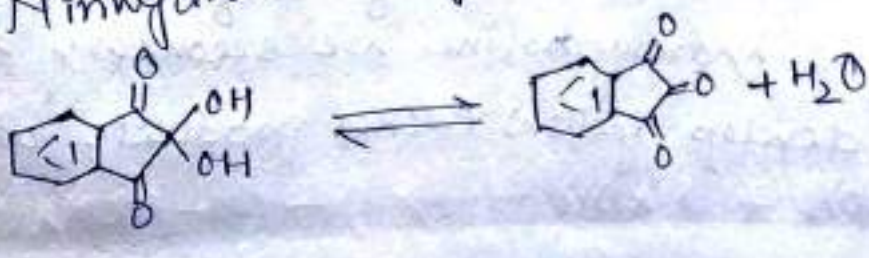
iii) Ion- exchange chromatography etc.

Ninhydrein Test—

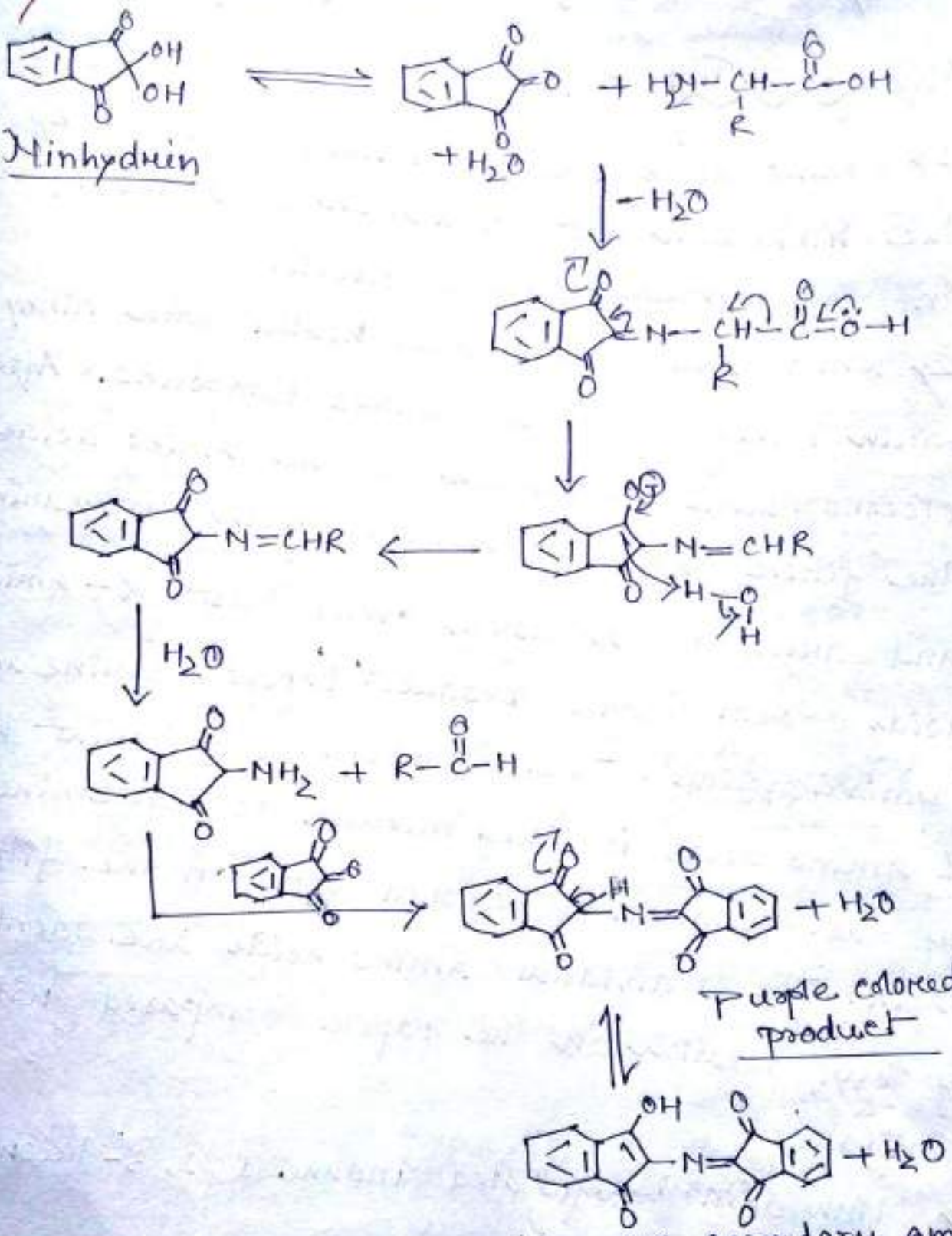
↳ Amino acids are colourless, therefore by the Ninhydrein test separation of amino acids in the mixture can be detected.

↳ When amino acids are heated with ninhydrein, they form a coloured compound. After electrophoresis separation of the amino acids, the filter paper is sprayed with ninhydrin and dried in a warm oven. Most α-amino acids form purple product (Except proline and hydroxyproline). The number of different kinds of amino acids in the mixture is determined by the number of colored spots on the filter paper. The individual amino acids are identified by their location on the paper compared with a standard.

↳ Ninhydrein is hydrated indane 1, 2, 3-trione.



↳

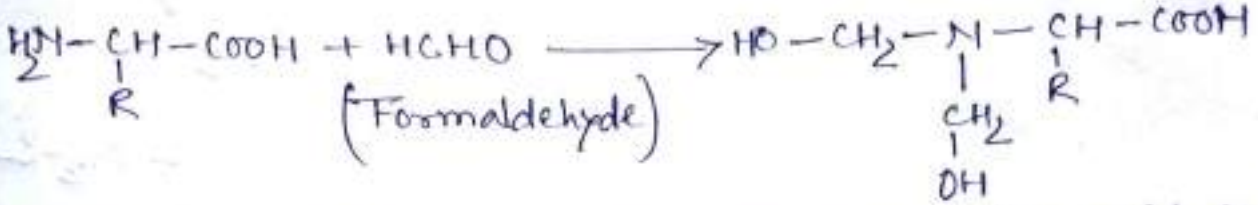


↳ Proline and hydroxyproline are secondary amino acids and develop yellow colored products with ninhydrin.

Reactions of Amino Acids —

1) Reactions involving the amino ($-NH_2$) group —

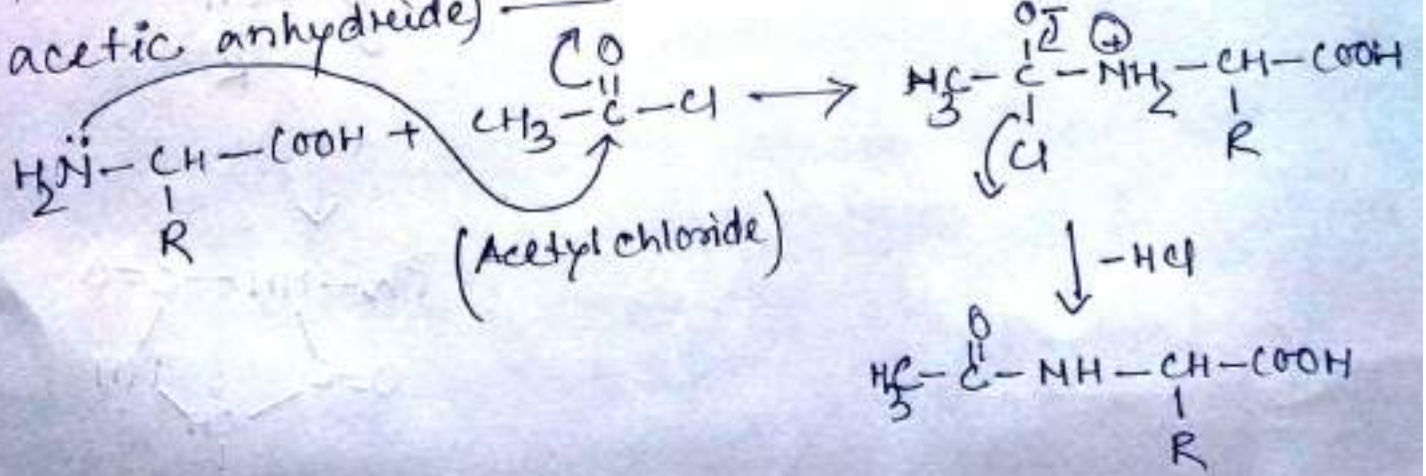
a) Reaction with formaldehyde —

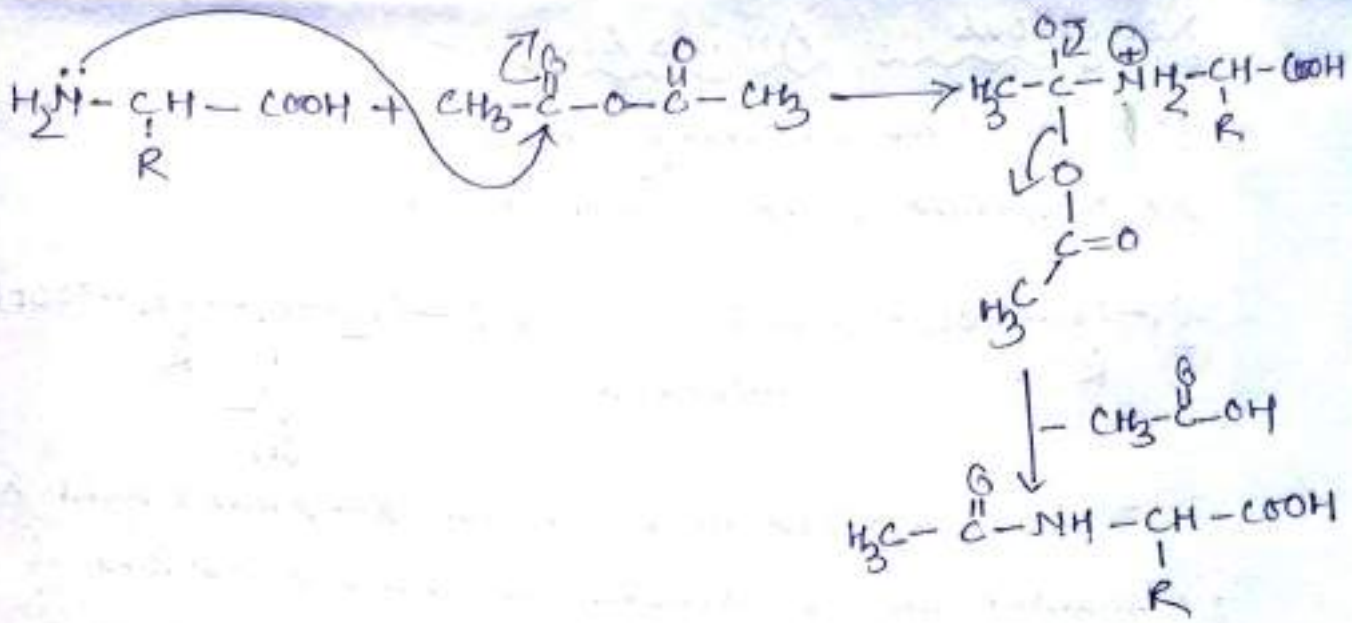


This reaction between an α-amino acid and formaldehyde is utilized in the estimation of α-amino acid. The blocked amino group by reacting with formaldehyde makes α-amino acid to act as a strong acid.

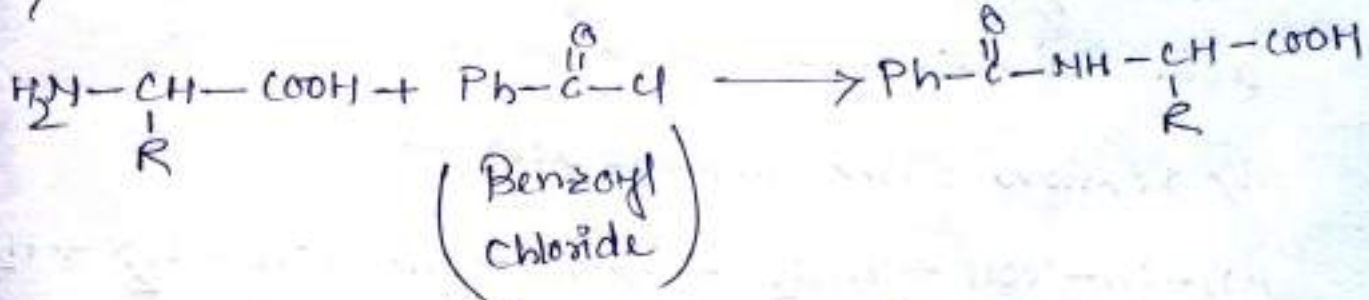
b) Reation with nitrous acid —

c) Acetylation (Reaction with acetyl chloride or acetic anhydride) —

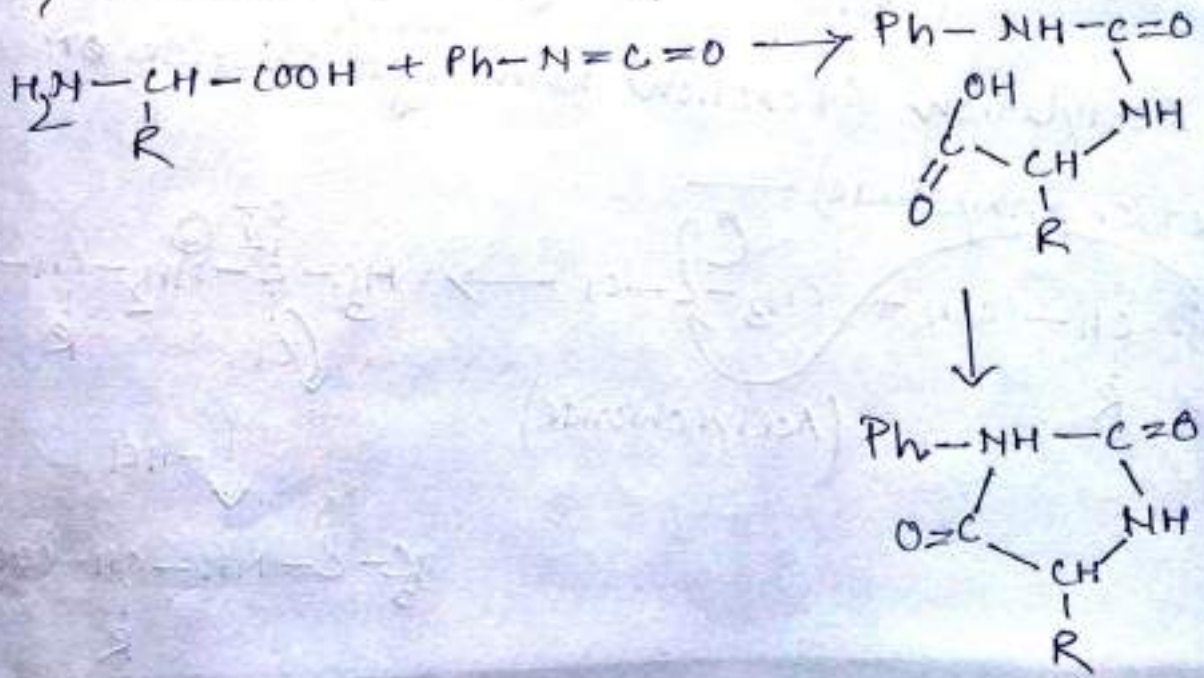




d) Benzylation ——

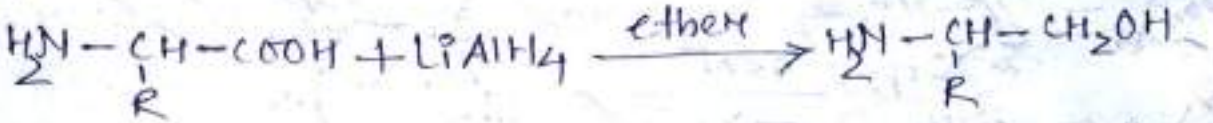


e) Reaction with phenyl isocyanate ——



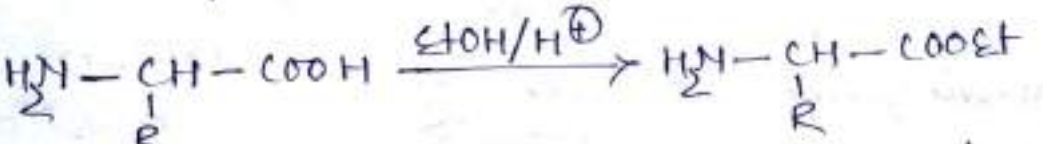
2) Reactions involving the carboxyl (-COOH) group—

a) Reduction —



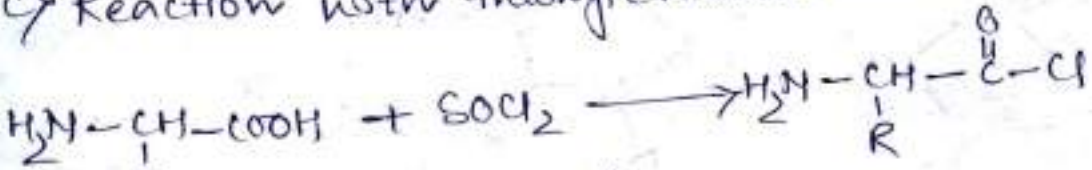
Aminoalcohol

b) Esterification —



Aminoester

c) Reaction with thionyl chloride —



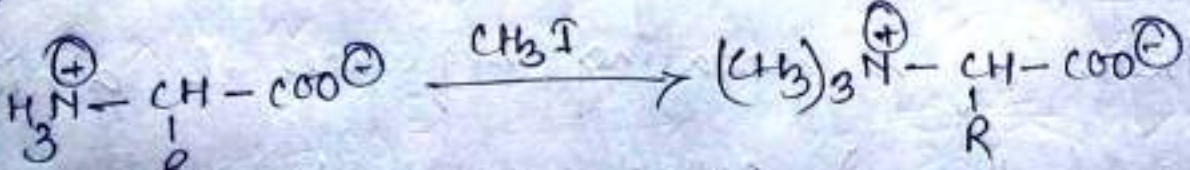
(Thionyl chloride)

d) Reaction with base —

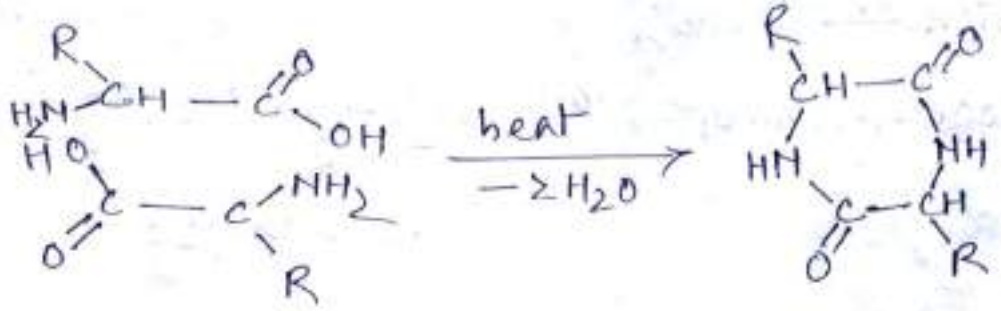
(Sod. Salt)

3) Reactions involving both $-NH_2$ and -COOH groups—

a) Reaction with methyl iodide —

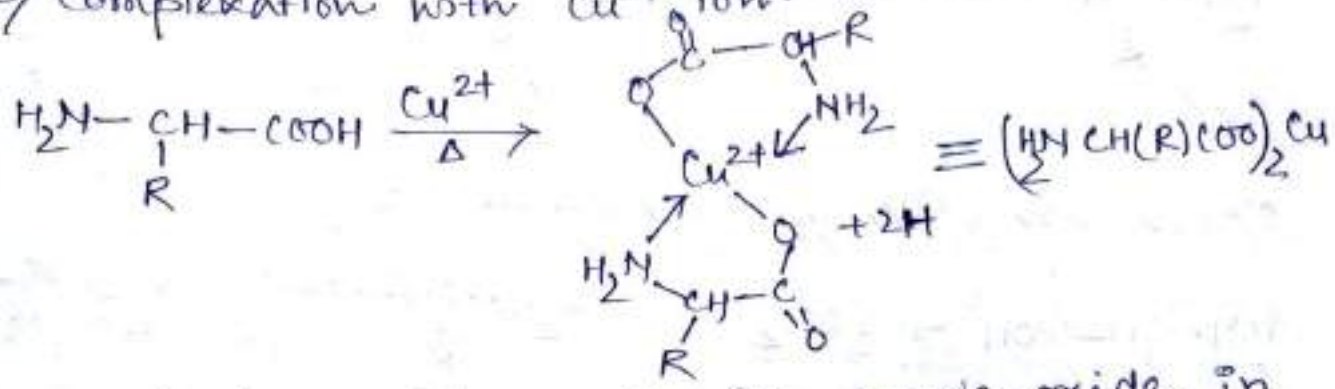


b) Action of heat —



Diketopiperazine

c) Complexation with Cu^{2+} ion —



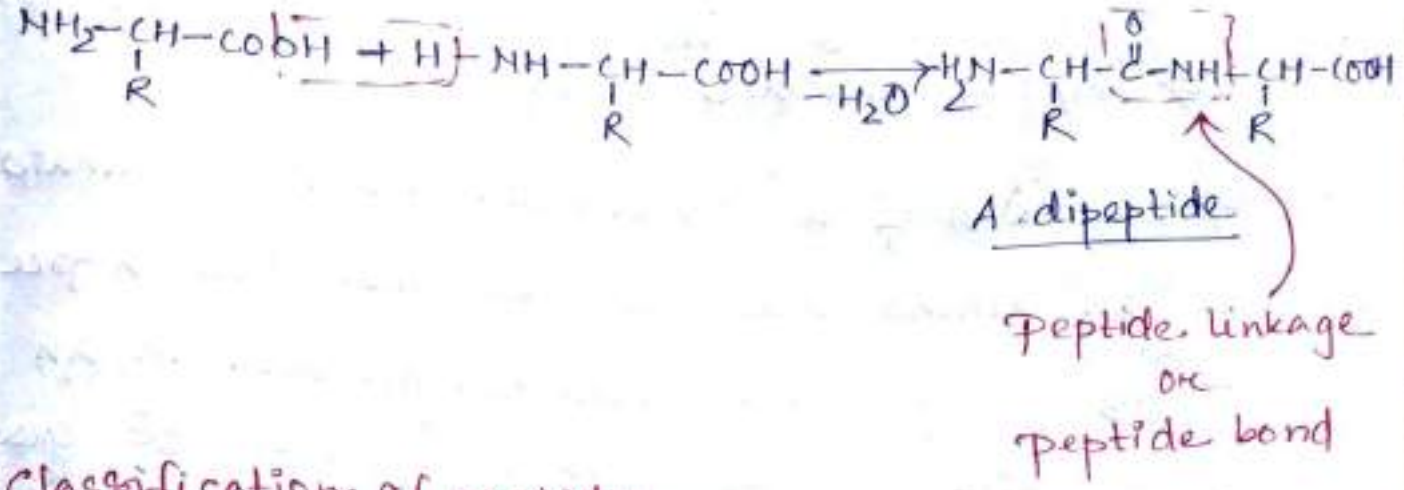
Amino acids react with cupric oxide in water to produce deep-blue complex salts.

Peptide linkage —

↳ Peptides are the polyamides formed by the condensation of amino group of one amino acid with the carboxylic group of the other.

↳ The amino acid units of peptide are bound together by a repeating sequence of amide bonds ($-\overset{O}{\overset{\|}{C}}-NH$), called peptide linkage or

peptide bond.



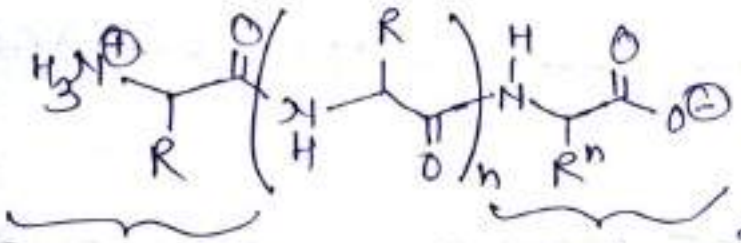
Classification of peptides —

- Depending upon the number of amino acid residues per molecule they are referred as dipeptides, tripeptides, oligopeptides and polypeptides.
- Peptides that contain 2, 3, a few (3–10) or many amino acids are called dipeptides, tripeptides, oligopeptides and polypeptides respectively.
- Each amino acid in the peptide is called an amino acid residue.
- Proteins are also polyamides.
- The compounds having molecular weight of 10,000 or less are called polypeptides while the compounds which have molecular weight

higher than 10,000 are called proteins.

↳ Polypeptides are linear polymers.

↳ One end of a polypeptide chain terminates in an amino acid residue that has a free $-\overset{\oplus}{N}H_3$ group; the other terminates in an amino acid residue with a free $-COO^{\ominus}$ group. These two groups are called the N-terminal and the C-terminal residues respectively.

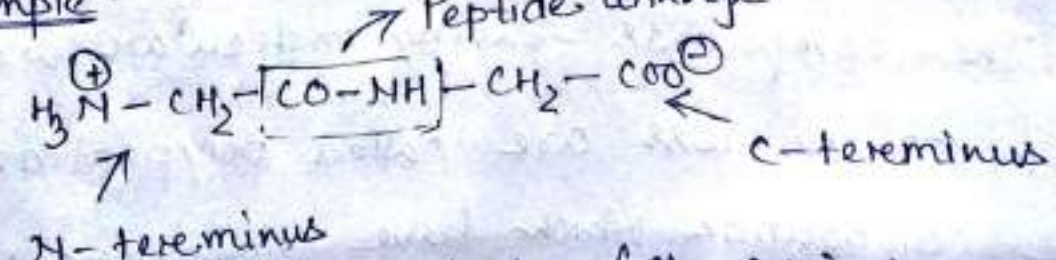


N-terminal residue

C-terminal residue

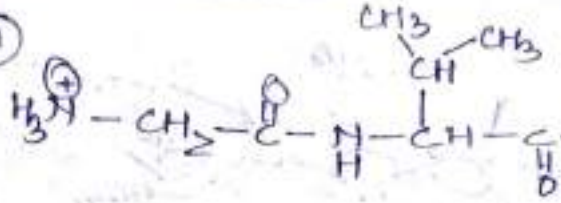
↳ By convention, we write peptide and protein structures with the N-terminal amino acid residue on the left and the C-terminal residue on the right.

↳ Example —



Glycyl glycine (Gly-Gly) (A dipeptide)

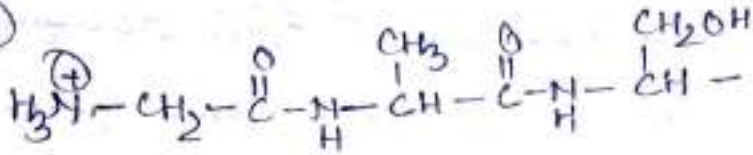
(ii)



→ A dipeptide.

Glycyl valine (Gly-Val)

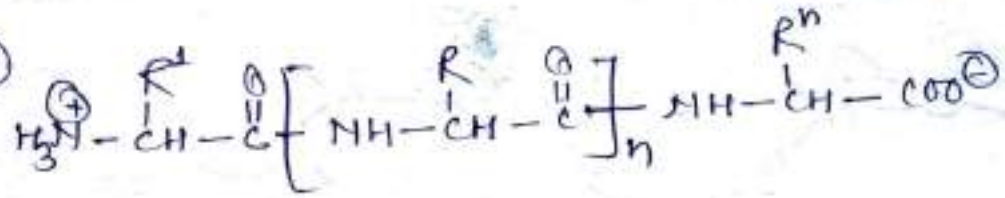
(iii)



→ A tripeptide

Glycyl alanyl serine (Gly-Ala-Ser)

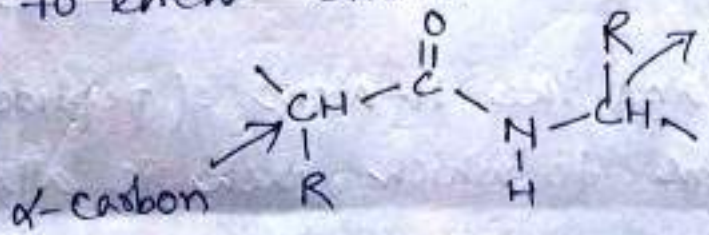
(iv)

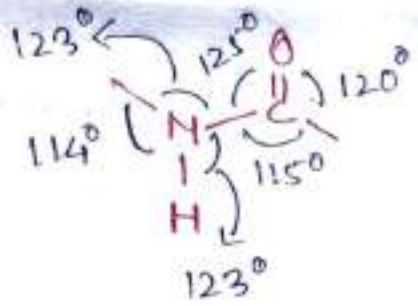


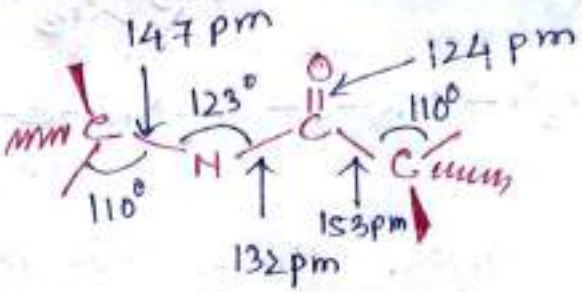
A polypeptide

Geometry of peptide linkage —

↳ The α-carbons of adjacent amino acids are trans to each other, while the carbonyl and amino groups lie in one plane having 'H' of 'NH' and 'O' of 'CO' trans with respect to each other.



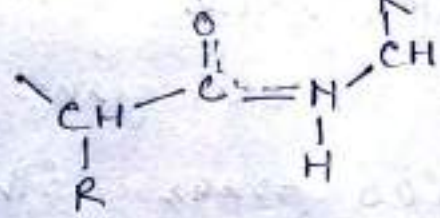




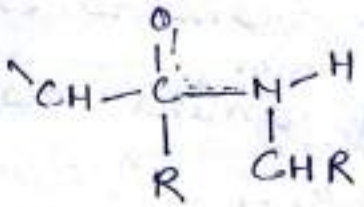
↳ A peptide bond has about 40% double bond character, therefore the lone pair on the N-atom in the peptide is delocalized over C=O group —

Resonating structure of a peptide bond.

↳ Due to double bond character in C–N bond, the rotation about C–N bond is restricted and show geometrical isomerism.



trans (more stable)



Cis (less stable)

↳ The C-atom and the N-atom of peptide bond and two atoms to which each is attached are held rigidly in a plane.

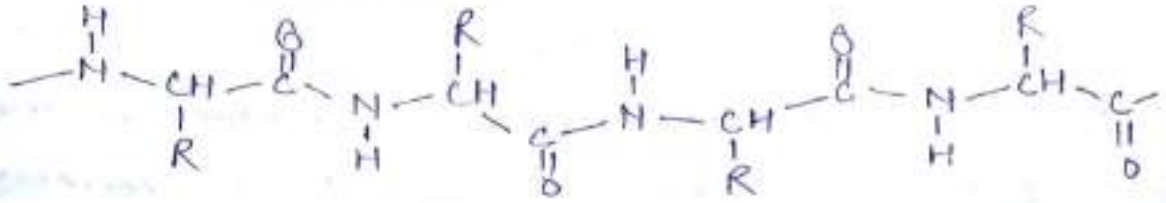
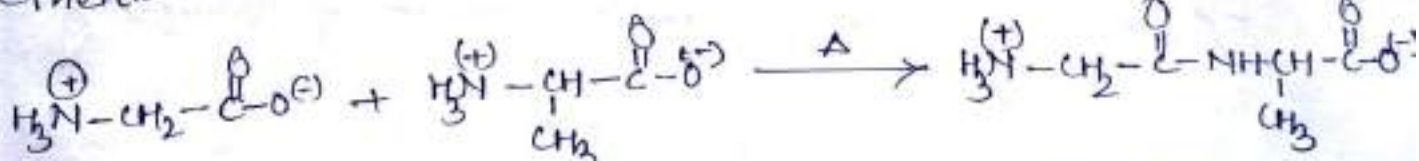


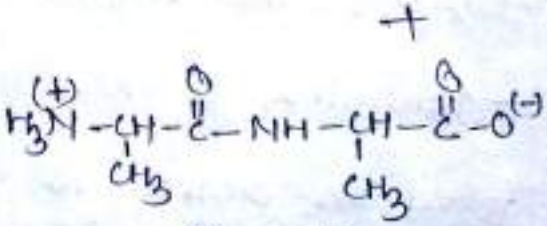
fig: A segment of a polypeptide chain. The R-groups bonded to the α-carbons are on alternate sides of the peptide backbone.

Peptide Synthesis — (N-protection and C-activation)

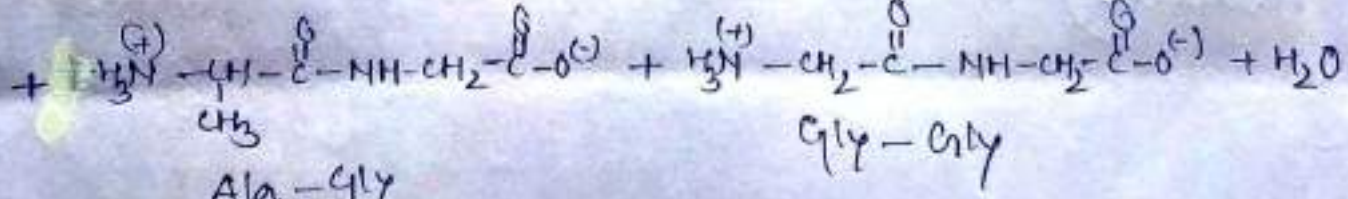
Ly Because amino acids have two functional groups, a problem arises when one attempts to make a particular peptide bond. For example— If you wanted to make the dipeptide Gly-Ala. Heating a mixture of Glycine and Alanine results in four dipeptides, the one you want and three others —



Glycine + Alanine → Gly-Ala



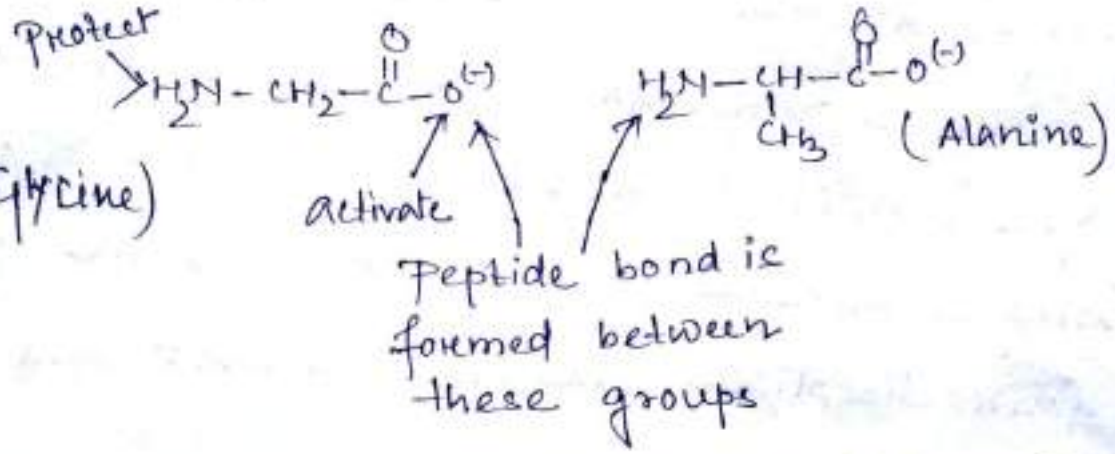
Ala-Ala



Ala-Gly + Gly-Gly + H_2O

↳ Therefore, if the amino group of the amino-acid that is to be on the N-teremínal end (in this case Glycine) is protected, it will not be available to form a peptide bond.

↳ If the amino group of the added amino acid (in this case Ala) will react with the activated carboxyl group of Glycine in preference to reacting with a non activated carbonyl group of another alanine molecule.



↳ The peptide synthesis consists of following steps ——

i) Protection of amino group (The amino group of the amino acid unit which forms the N-teremínal of the required peptide is to be blocked in order to make the amino group inactive)

$H_3\overset{(+)}{N}-CH(R)-COO^{(-)}$ + PR − X ⟶ PR−NH−CH(R)−COOH

N− terminal unit ↑ Protecting group of $-NH_2$ group

N− protected amino acid

PR = Stands for protecting group.

ii) Activation of carboxylic group (The carboxyl group of the N-terminal amino acid unit is to be activated in order to make the carboxyl group more reactive than the carboxyl group of the next amino acid unit in the peptide chain)

PR−NH−CH(R)−COOH $\xrightarrow[\text{agent of } -COOH \text{ group}]{\text{activating}}$ PR−NHCH(R)−COA

A ⟶ stands for activating group

iii) The protection of carboxyl group (The carboxyl group of the second amino acid unit of the peptide chain is to be deactivated by blocking the group)

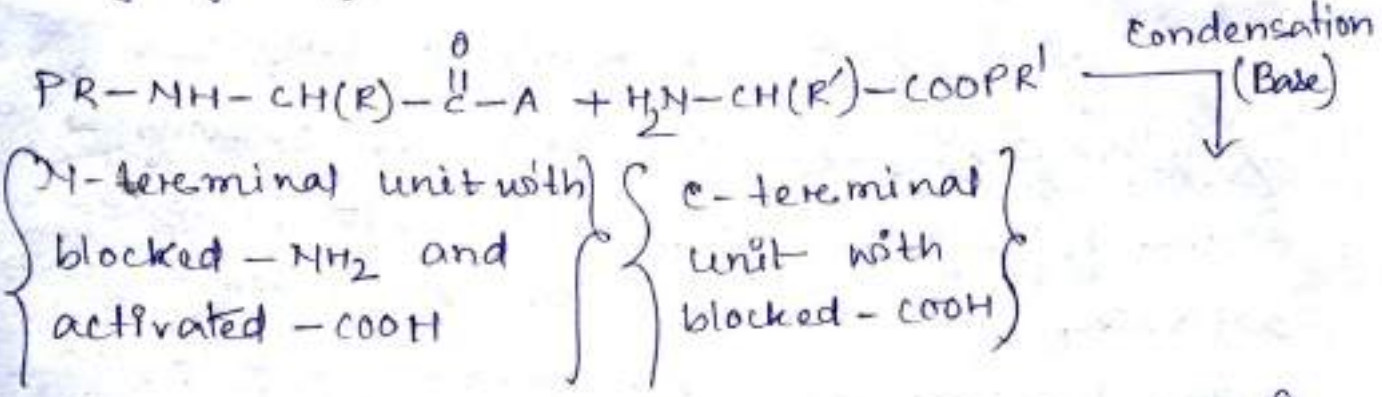
$H_3\overset{(+)}{N}-CH(R')-COO^{(-)}$ $\xrightarrow[\text{agent of } -COOH \text{ group}]{\text{blocking/Protecting}}$ $H_2N-CH(R')-COOPR'$

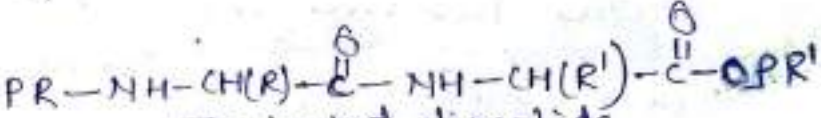
C− terminal unit

C− protected amino acid

PR' = Stands for protecting group

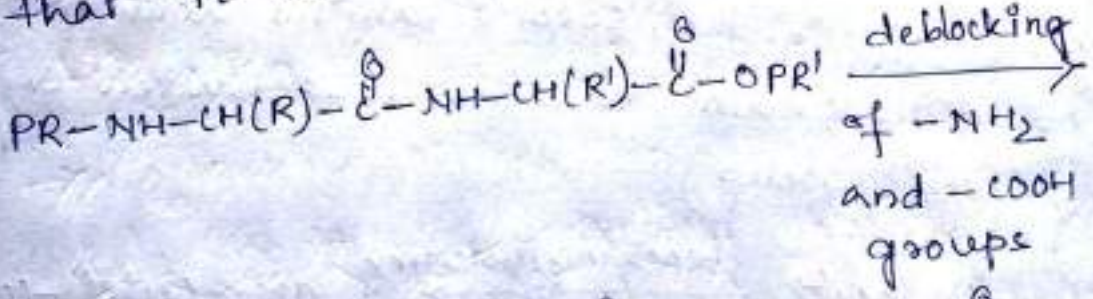
iv) Condensation (the N-teremminal amino acid unit with blocked amino group and activated carboxyl group is to be treated with the second amino acid unit with blocked carbo-xyl group).





Protected dipeptide

v) Removal of protecting group (The amino group of the N-teremminal unit and the carboxyl group of the C-teremminal unit of the peptide chain are to be deblocked under mild conditions such that it donot affect the peptide chain).



A dipeptide.

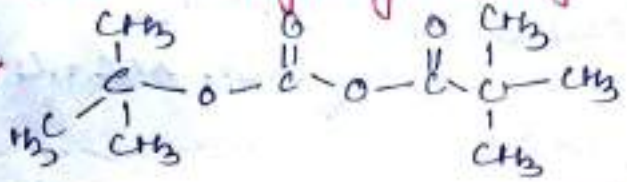
Note: It is to be noted that, the step IV is repeated several times using desired amino acids one by one till the protected polypeptide of appropriate length is obtained.

Protecting agents —

↳ A good protecting agent is that, which can react with the amino or carboxyl groups easily and can be removed at the end of the synthesis without affecting the peptide bond.

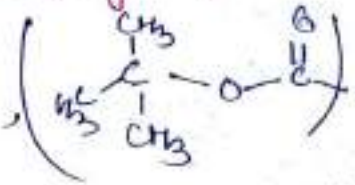
N-terminus protecting groups —

1) tert-Butyloxycarbonyl (Boc) group —

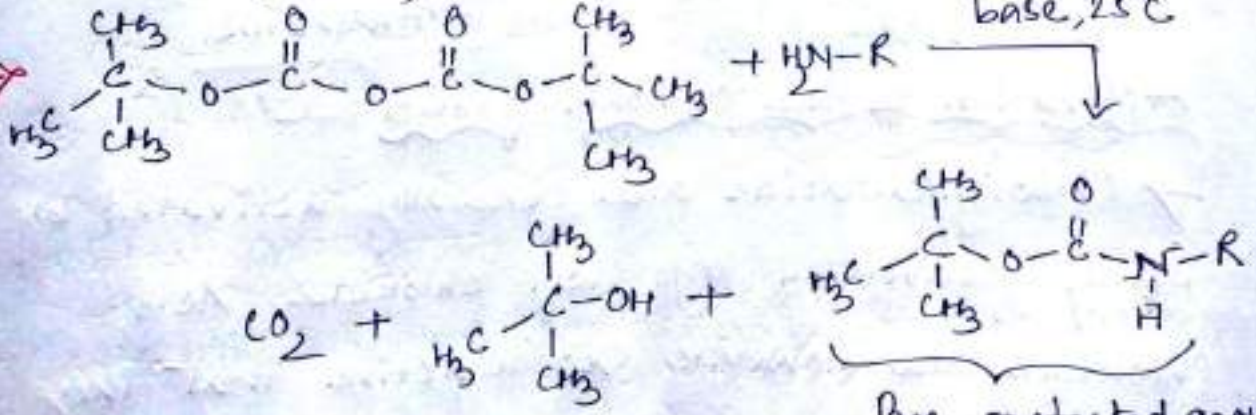
↳ 

Di tert-butyl dicarbonate

(Boc_2O)

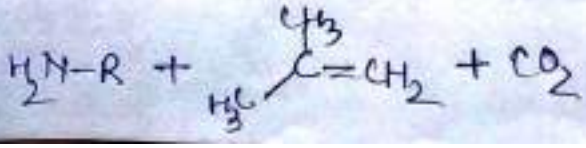


Boc group

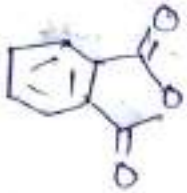
↳ 

Boc protected group

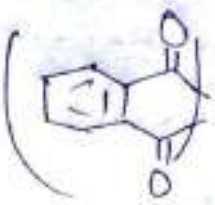
(Deprotection) | HCl in or CF_3COOH acetic acid, 25°C



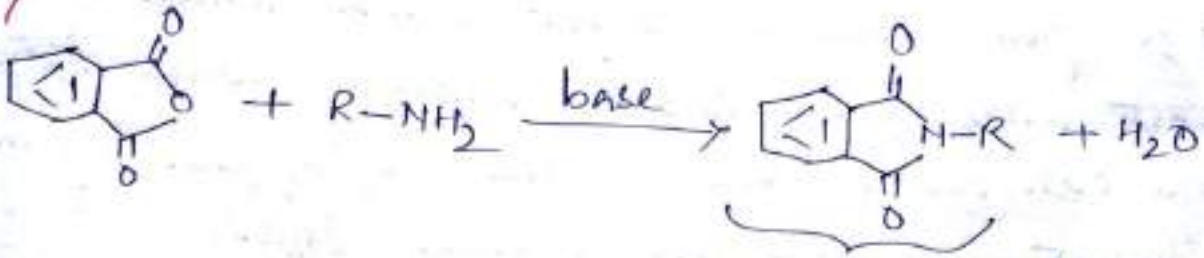
Phthaloyl group —



Phthalic anhydride

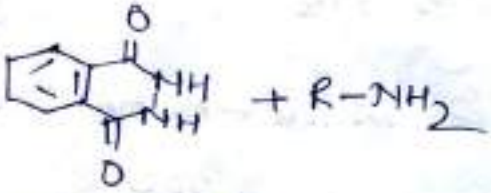


Phthaloyl group



Phthaloyl protected amine

(Deprotection) | H_2N-NH_2, EtOH and HCl



Phthalazine

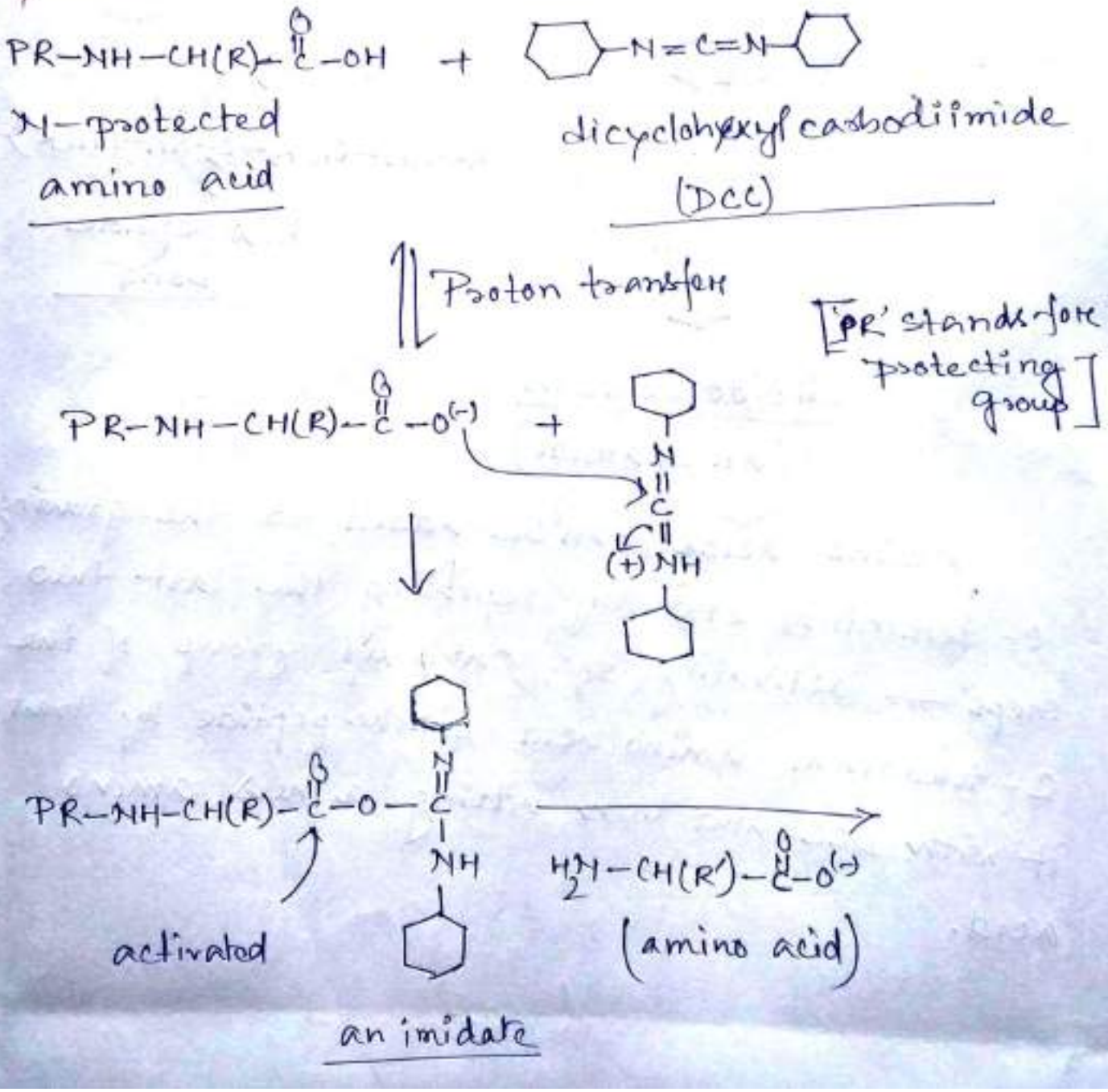
Activation of the carboxyl group —

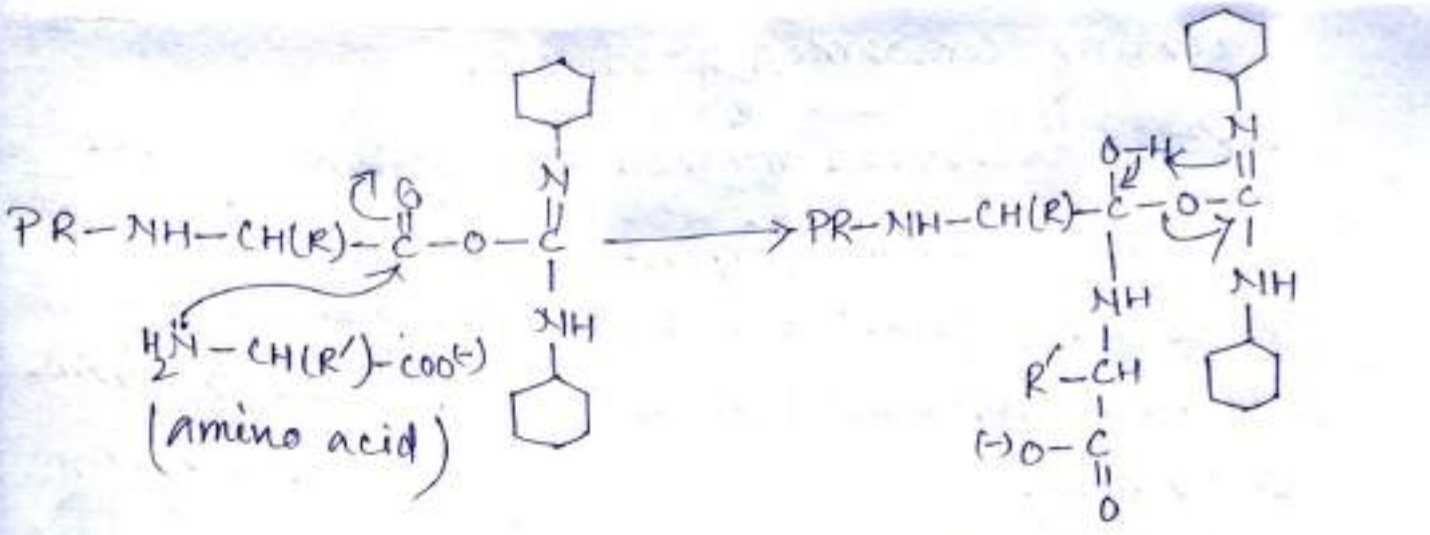
↳ Carboxylic acids are generally activated by being converted into acyl chlorides. Acyl-chlorides are however so reactive that they can readily react with the substitutents of some of the amino acids during peptide synthesis,

Creating unwanted products.

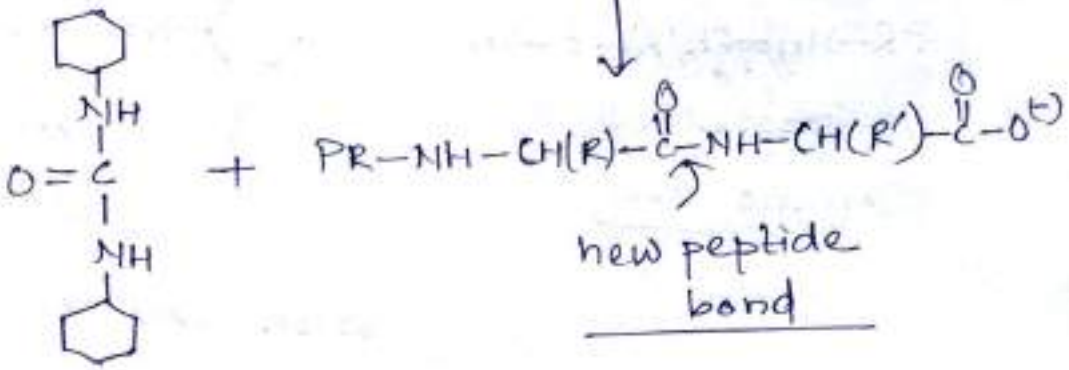
↳ The preferred method for activating the carboxyl group of an N-protected amino acid is to be convert it into an imidate using dicyclohexylcarbodiimide (DCC). DCC activates a carboxyl group by putting a good leaving group on the carboxyl carbon.

↳





tetrahedral intermediate



dicyclohexylurea (a diamide)

new peptide bond

Amino acids can be added to the growing c-terminal end by repeating the last two steps — activating the carboxyl group of the c-terminal amino acid of the peptide by treating it with DCC and then adding a new amino acid.

Automated peptide Synthesis — (Merrifield automated solid-phase synthesis)

↳ The classical methods fore polypeptide synthesis as discussed above are not only time consuming but also the yield of the polypeptides are poor since at everey step of a total synthesis requires purification and separation of intermediates.

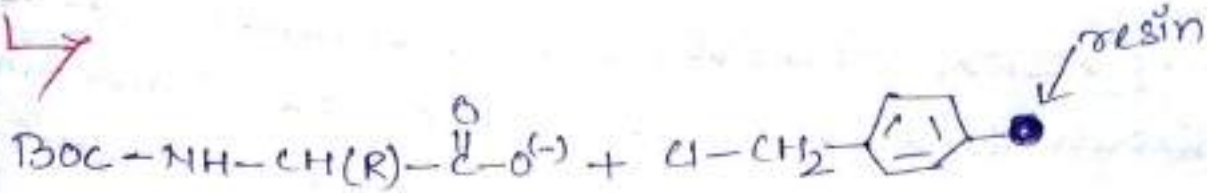
↳ R. B. Merrifield has discovered an automated method of polypeptide synthesis which doesnot involve separation of intermediates.

↳ Solid-phase peptide synthesis begins with the attachment of the first amino acid by its carboxyl group to the polymer bead of polystyrene resin by forming an estere linkage. Each N-terminal blocked amino acid is added one at a time, along with other reagents, so the protein is synthesized from the C-terminal end to the N-terminal end, (Notice that this is opposite to the way proteins are synthesized in nature, from the N-terminal end to the C-terminal end.)

↳ Because it uses a solid support and is automated, this method of protein synthesis

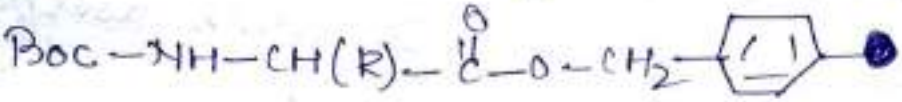
is called automated solid-phase peptide synthesis.——

↳



Step I

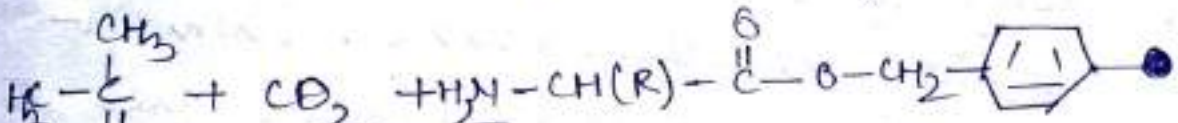
(Attaches C-terminal Boc-protected amino acid residue to the resin)



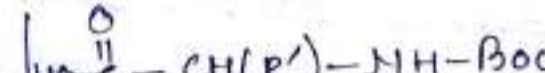
Step II

CF_3COOH and CH_2Cl_2

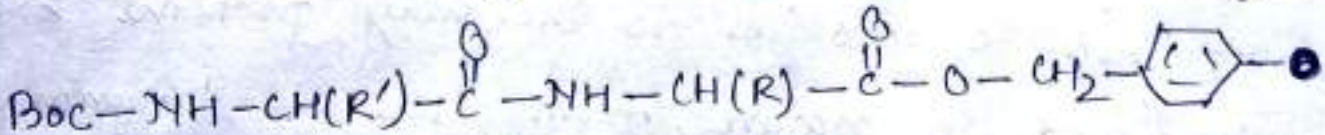
(Removes Boc-protecting group)



Step III



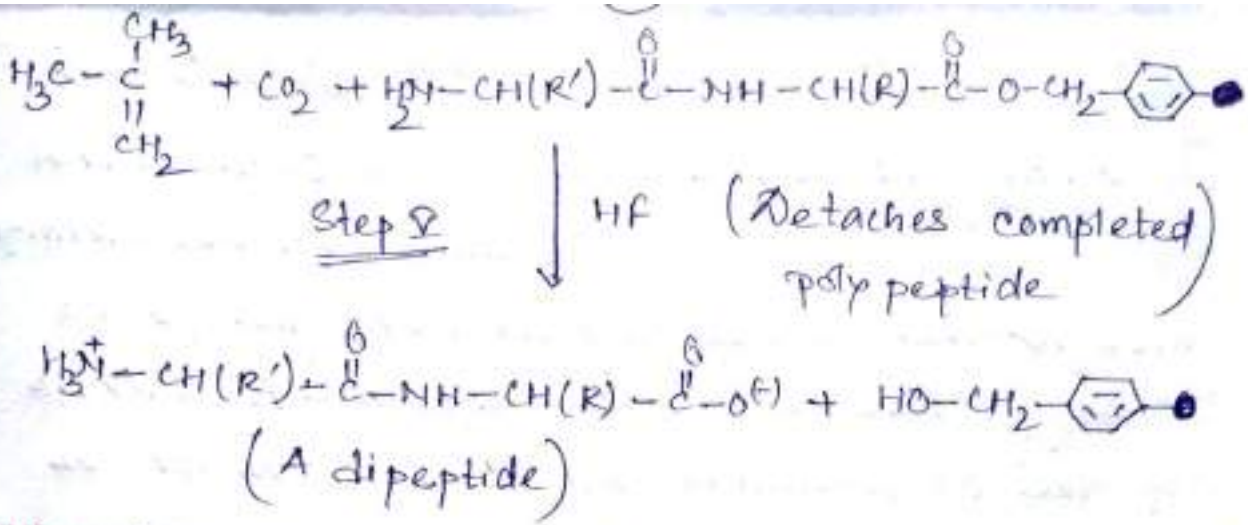
(Adds next Boc-protected amino acid residue)



Step IV

CF_3COOH and CH_2Cl_2

(Remove protecting group)



(A dipeptide)

Note:- Step III and Step IV are repeated over and over again to get the desired polypeptide.

↳ Advantages of solid-phase peptide synthesis are —

i) Purification of the peptide at each stage involves simply rinsing the beads of the solid support to wash away excess reagents, by-products and solvents.

ii) It is a rapid and efficient method, yield ≈ 99%

iii) Separation of intermediates donot required.

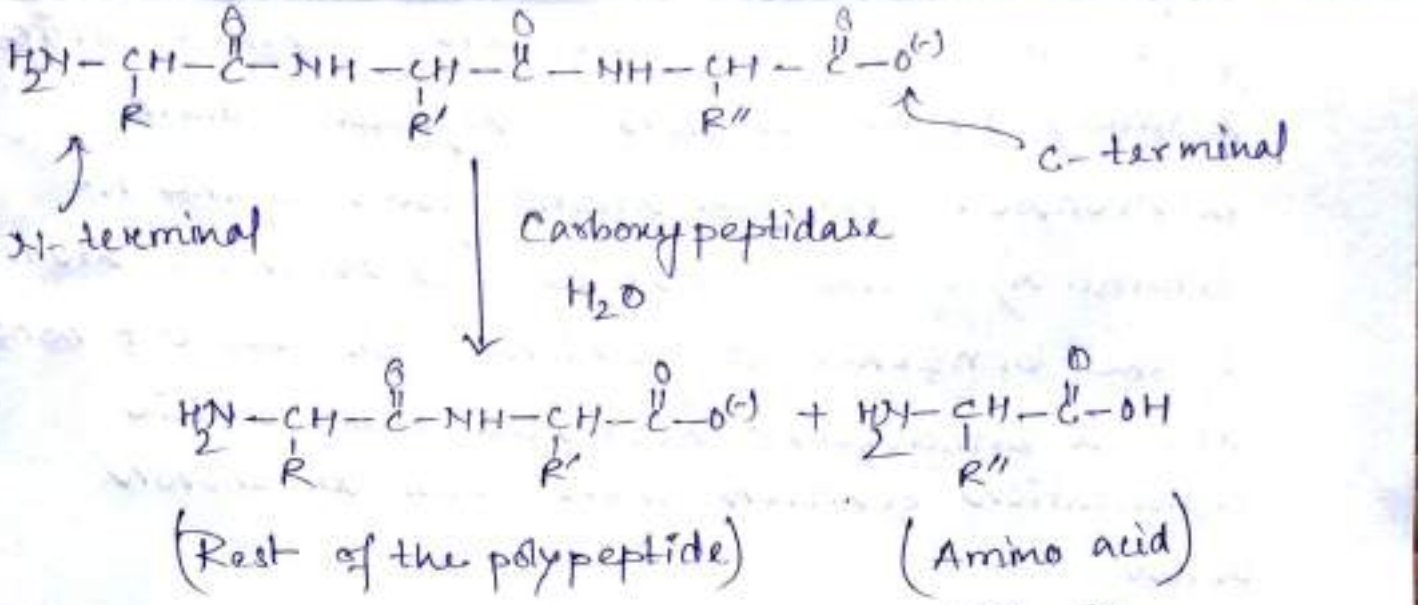
Determination of primary structure of peptides —

↳ The exact sequence of amino acids that are present in a polypeptide chain can be determined by the selective cleavage of the C-terminal and N-terminal amino acid residues of the polypeptide chain.

Determination of c-terminal amino acid unit —

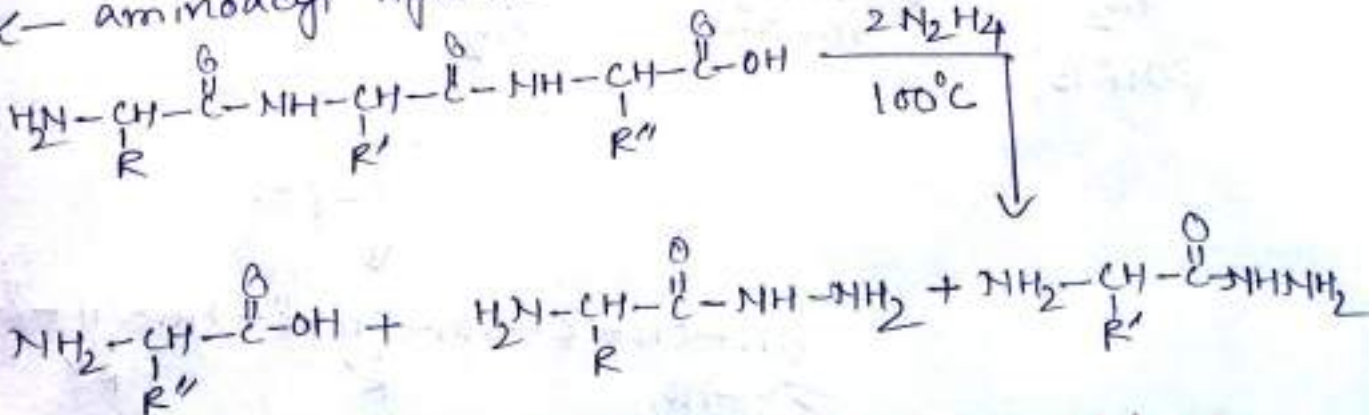
@ Carboxypeptidase methode — c-terminal residues can be identified through the use of digestive enzyme called carboxypeptidases. Carboxypeptidase A cleaves off the c-terminal amino acid as long as it is not arginine or lysine. Carboxypeptidase B, on the other hand cleaves off only if it is arginine or lysine. Carboxypeptidases are exopeptidases. An exopeptidase is an enzyme that catalyze the hydrolysis of a peptide bond at the end of a peptide chain.

The enzyme carboxypeptidase hydrolyses the peptide linkage at the c-terminal which holds an amino acid unit with a free carboxyl group. After hydrolysis, the product consits of two units, one of them is a free amino acid unit of the c-terminal of the polypeptide under analysis, and the other unit is the rest of the polypeptide having one amino acid unit less than the parent peptide.



(Rest of the polypeptide) (Amino acid)

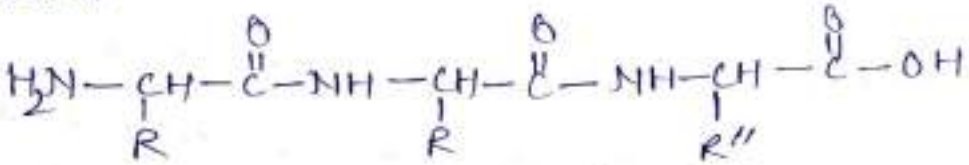
(b) **Akabori method** — When a polypeptide is heated at 100°C with anhydrous hydrazine, the C-terminal amino acid separates and these amino acids of the parent polypeptide chain form the corresponding α-aminoacyl hydrazides.



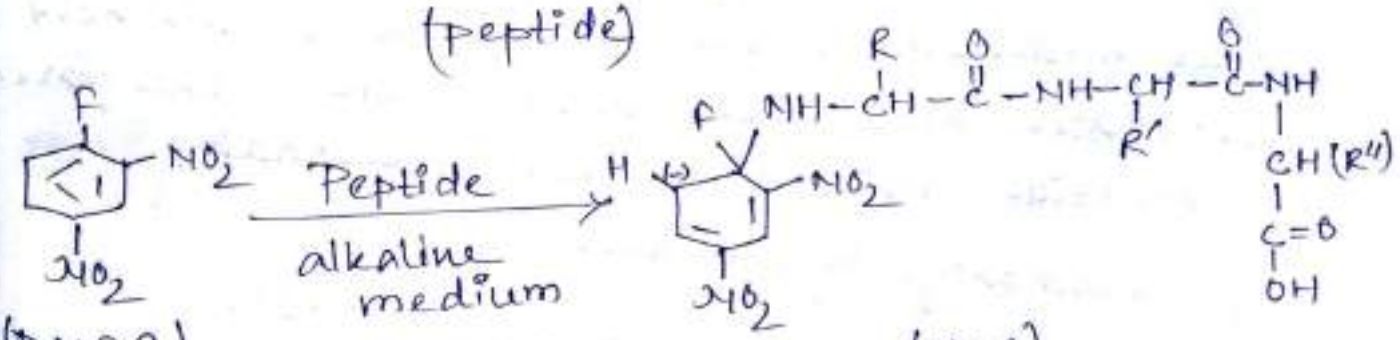
Determination of the N-terminal amino acid unit—

(a) **Sanger's method** — 2,4-Dinitrofluorobenzene (DNFB) is the reagent for the method. The reaction between DNFB and the

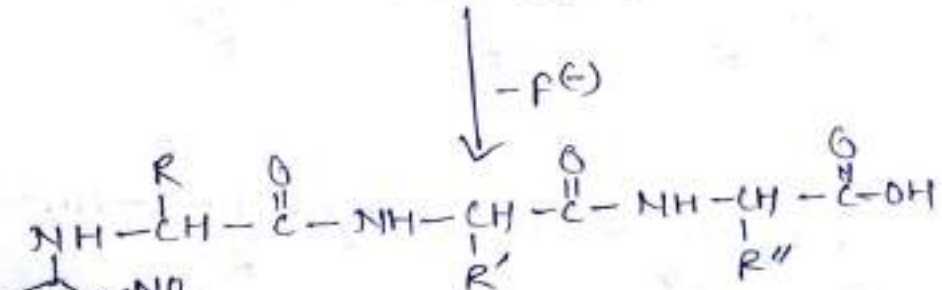
polyamide under consideration is carried out in a mildly basic solution of aqueous sodium bicarbonate. The free amino group (of the N-terminal) of the polyamide attacks the C-atom of the benzene ring which holds the C-F bond, and a bimolecular aromatic nucleophilic substitution reaction takes places as shown below ——

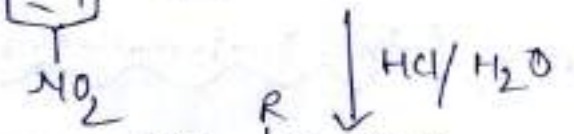


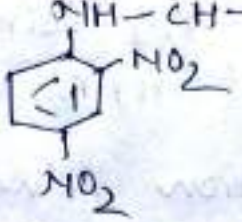
(peptide)



(DNFB) (T.S)







+ mixture of α-amino acids

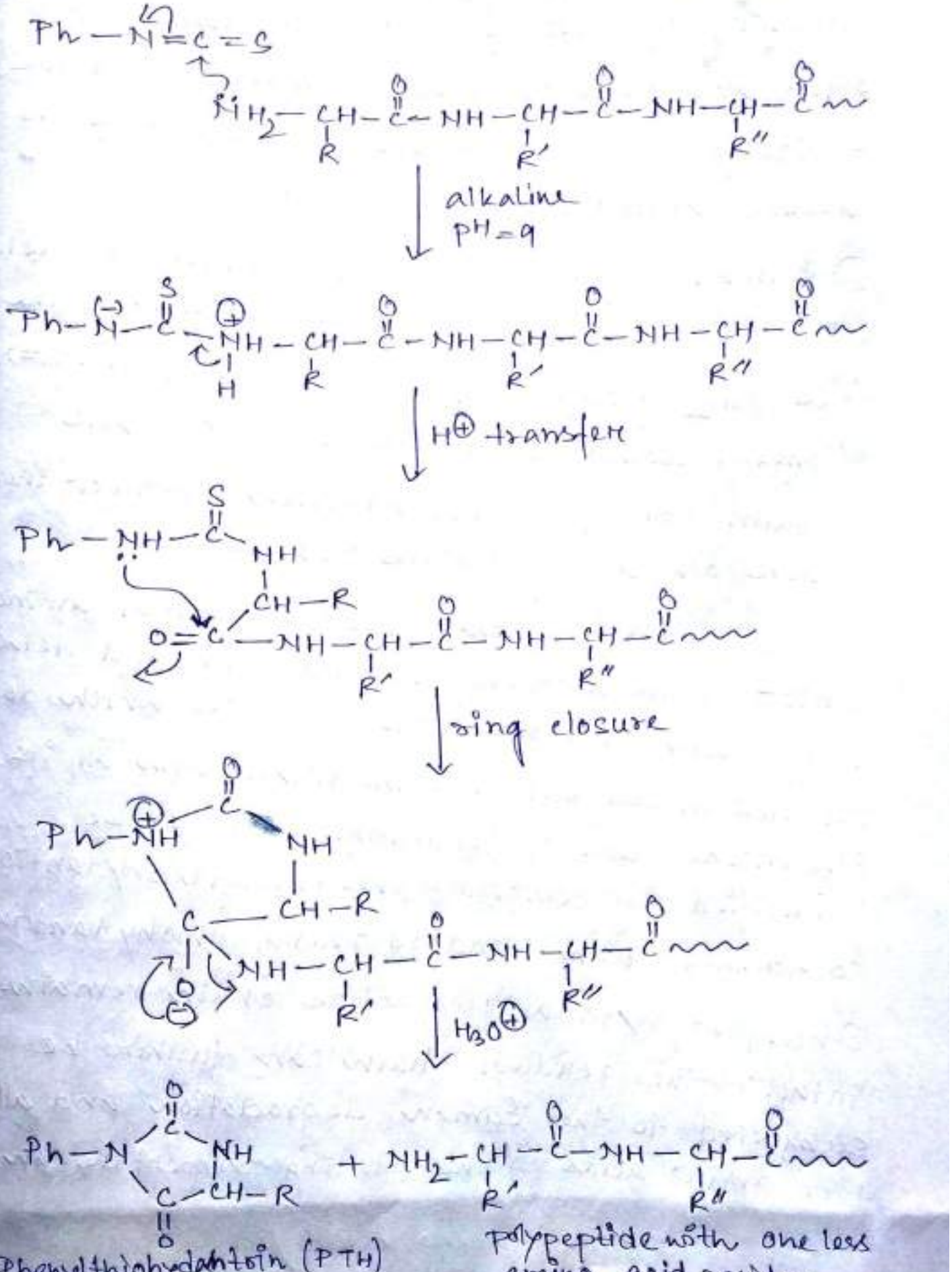
(labelled N-terminal amino acid)

The labelled N-teremina amino acid is then separated and identified. The electron-with--drawing property of two nitro groups at ostho and para-positions with respect to the F-group of DNPB makes separation of the labelled amino acid very easy.

(b) Edman degradation — This involves a nucleo--philic addition of the free NH_2 group of the polypeptide to the C=N of phenyl isothiocyanate in a mildly basic medium (pH = 9). The addition product then undergoes a ring closure reaction.

In this reaction, the N-teremina amino unit forms a phenyl thiohydantoin and detaches itself from the rest of the peptide which does not decompose but remains intact with all its sequences. The N-teremina unit can be identified by comparing the phenyl thiohydantion so formed with standard phenyl thiohydantoins. Since, the residual polypeptide chain remains intact, the residual chain can further be subjected to the Edman degradation and all the amino acids of the starting polypeptide can be

identified sequentially; here is the superiority of the Edman's method to the Sanger's method.



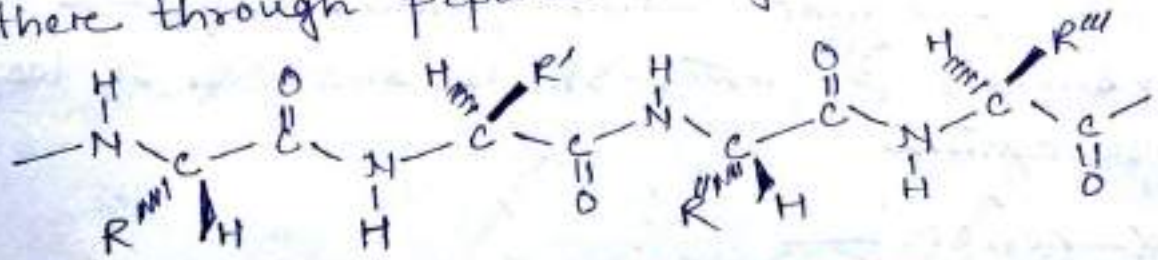
Proteins — Proteins are considered as polymers of amino acids. Their molecular weight is very high ≈ 18,000 — 10,000,000.

Structure of protein:—

↳ Structures of protein can be classified into four levels —

i) Primary,
ii) Secondary,
iii) Tertiary and
iv) Quaternary.

i) Primary structure of protein — The sequence of amino acid residues in a polypeptide or protein is called its primary structure. It is mainly the linear sequence of amino acid residues that are connected to each other through peptide linkage.



ii) Secondary structure of protein —

↳ The secondary structure of protein is defined by the local conformation of its polypeptide backbone. In order to minimize energy, a polypeptide chain tends to fold in a repeating

geometric structure.

↳ Three factors determine the choice of secondary structure —

1) Planar structure of each peptide bond minimizes the possible conformations of peptide chain

2) Maximizing the number of peptide groups that engage in hydrogen bonding. (eg:- hydrogen bonding between the carbonyl oxygen of one amino acid residue and the amide hydrogen of another). [>C=O---H-N<]

3) Adequate separation between nearby R-groups to avoid the steric hindrance and repulsion of like charges.

↳ The secondary structures are specified in terms of regular folding patterns called — α-helices, β-pleated sheets and coil or loop conformations.

a) α-helices —

↳ One type of secondary structure is the α-helix. In a α-helix, the backbone of the polypeptide coils around the long axis of the protein molecule.

↳ The helix is stabilized by hydrogen bonds — each hydrogen attached to an amide nitrogen is

hydrogen bonded to a carbonyl oxygen of an amino acid four residues away.

↳ The substituents on the α-carbons of the amino acids protrude outward from the helix, thereby minimizing steric hindrance.

↳ Because the amino acids have the L-configuration, the α-helix is a right handed helix. A right-handed helix rotates in a clockwise direction as it spirals down.

↳ Each turn of the helix contains 3.6 amino acid residues and the repeat distance of the helix is 5.4 Å.

↳

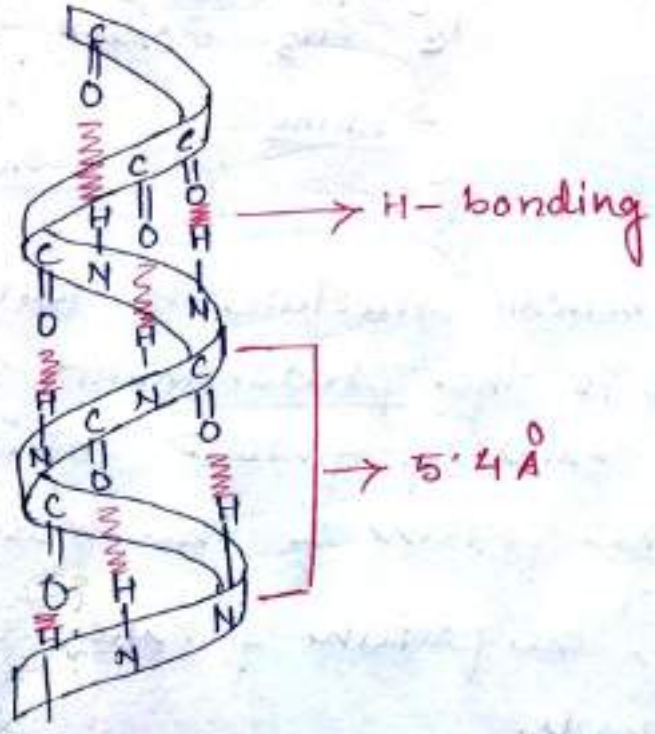
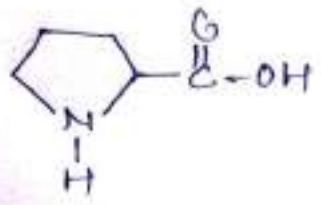


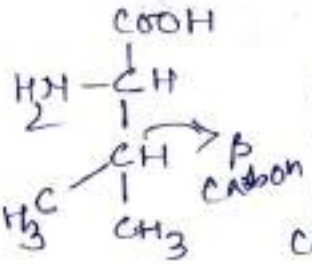
fig: A segment of a protein in an α-helix

↳ Not all amino acids are able to fit into an α-helix. A proline residue, for example, forces a bend in a helix because the bond between the proline nitrogen and the α-carbon cannot rotate to enable it to fit readily into a helix.

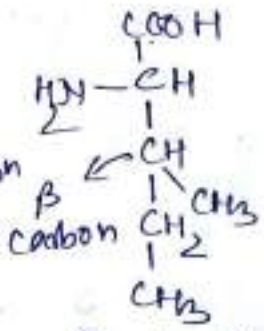
Two adjacent amino acids that have more than one substituent on a β-carbon (valine, isoleucine, or threonine) cannot fit into a helix because of ~~erst~~ steric crowding between the R-groups



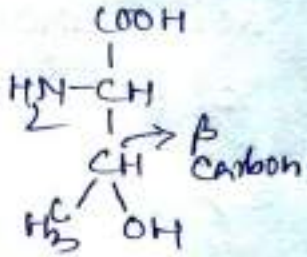
Proline



Valine



Isoleucine



Threonine

↳ The α-helical structure is found in many proteins; it is the predominant structure of the polypeptide chains of fibrous proteins such as myosin, the protein of the muscle and of α-keratin, the protein of hair, unstretched wool and nails.

b) β- pleated sheet —

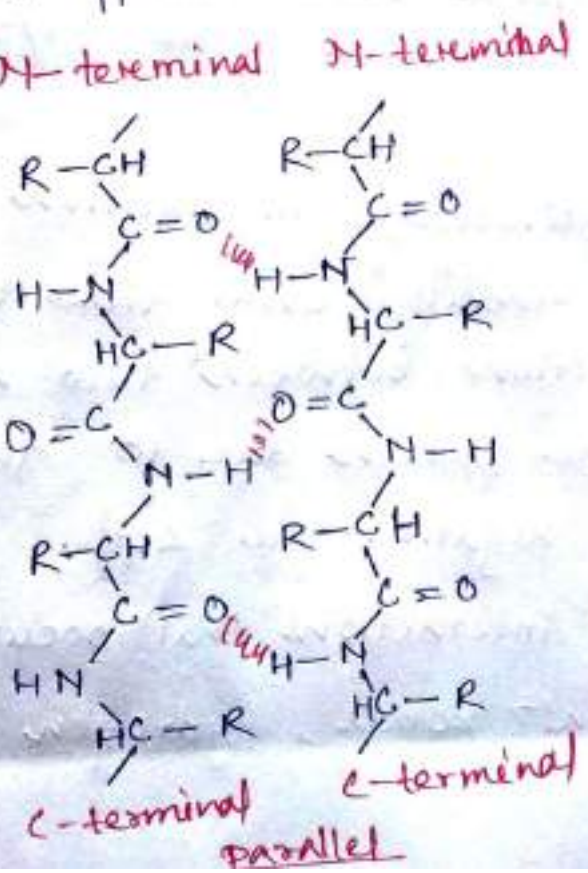
↳ In a β-pleated sheet, the polypeptide backbone is extended in a zigzag structure resembling a series of pleats.

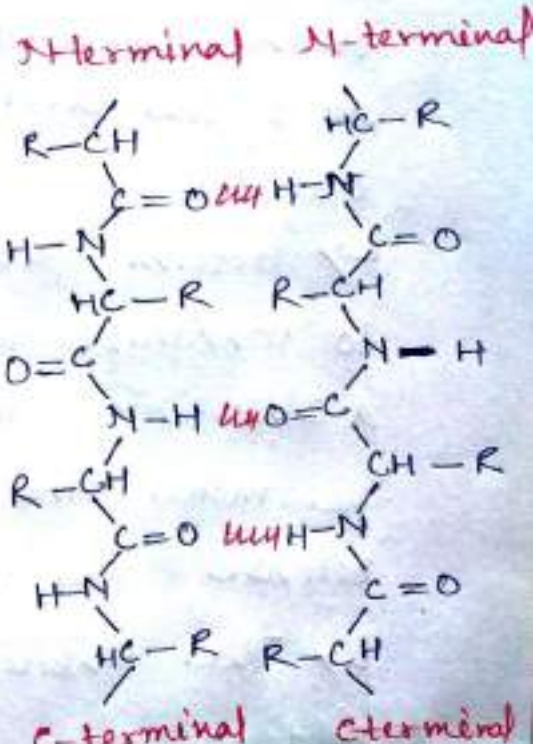
↳ A β-pleated sheet is almost fully extended — the average two residue repeat distance is 7.0 Å.

↳ The hydrogen bonding in a β-pleated sheet occurs between neighboring peptide chains. The adjacent hydrogen-bonded peptide chains can run in the same direction or in opposite directions.

↳ In a parallel β-pleated sheet, the adjacent chains run in the same direction. In an anti-parallel β-pleated sheet, the adjacent chains run in opposite directions.

↳





↳ Because the β-pleated sheet is a fully extended structure, these proteins cannot be stretched.

↳ The secondary structures of silk and spider webs are predominantly β-pleated sheets.

c) Coil conformation—

↳ Certain peptide chains assume what is called a random coil arrangement, a structure that is flexible, changing and statistically random.

↳ For example, synthetic ~~polysti~~ polylysine exists as a random coil and does not normally form an α-helix.

iii) Tertiary structure of protein—

↳ The tertiary structure of a protein is the overall three-dimensional shape that arises from all of the secondary structures of its polypeptide chain.

↳ Proteins fold spontaneously in solution in order to maximize their stability. Every time there is a stabilizing interaction between two atoms, the more stable the protein due to free energy release (the more negative the ΔG°).

↳ The stabilizing interactions that occur in folding are covalent bonds, hydrogen bonds,

electrostatic attractions and hydrophobic (van der Waals) interactions.

↳ The interactions can occur between peptide groups (atoms in the backbone of the protein), between side-chain groups (α-substituents), and between peptide and side-chain groups.

↳ Pleated sheet structure

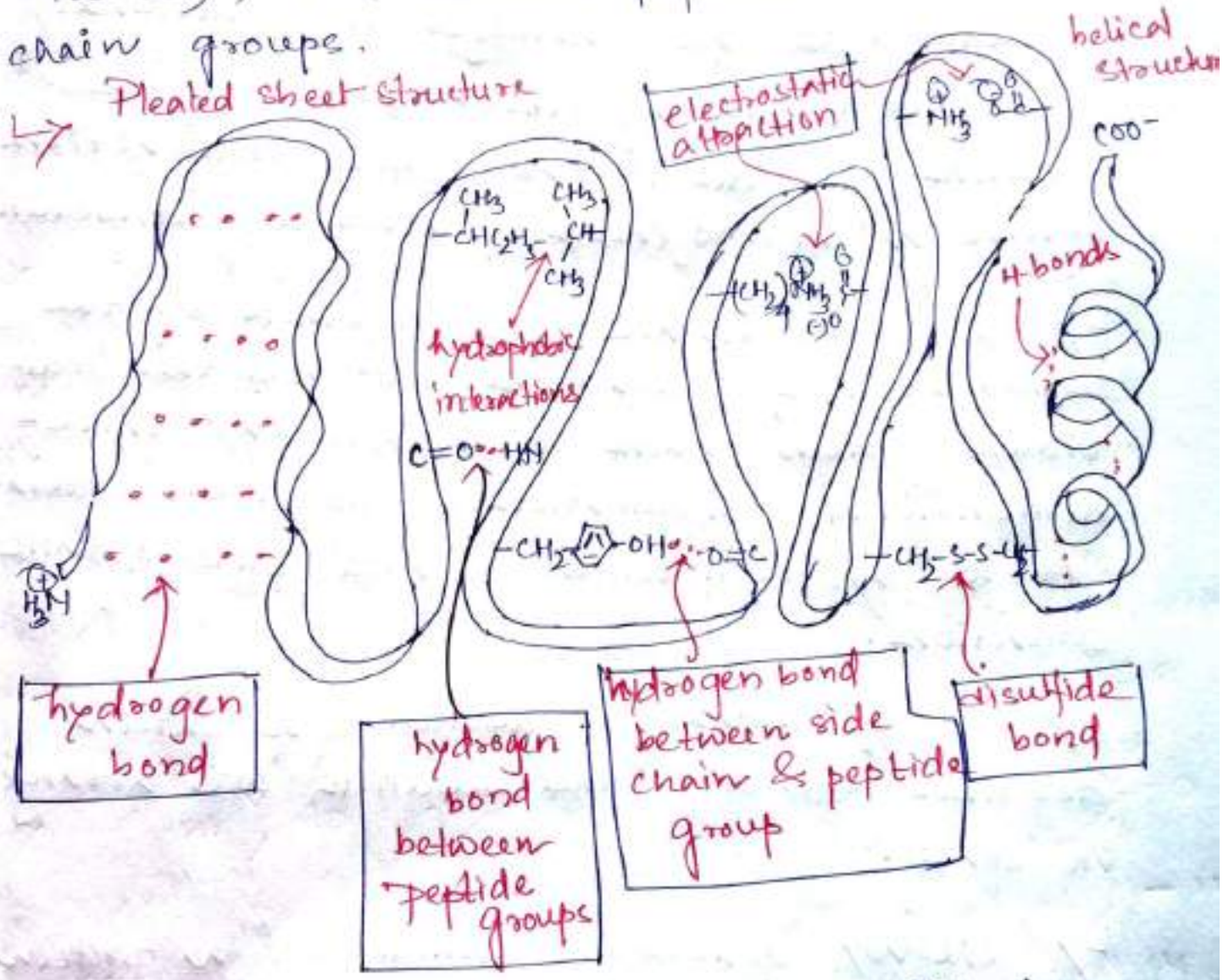


fig: Stabilizing interactions - responsible for the tertiary structure of a protein

iv) Quaternary structure of Protein—

↳ Quaternary structure results from interaction between separate polypeptide units of a protein having more than one subunit.

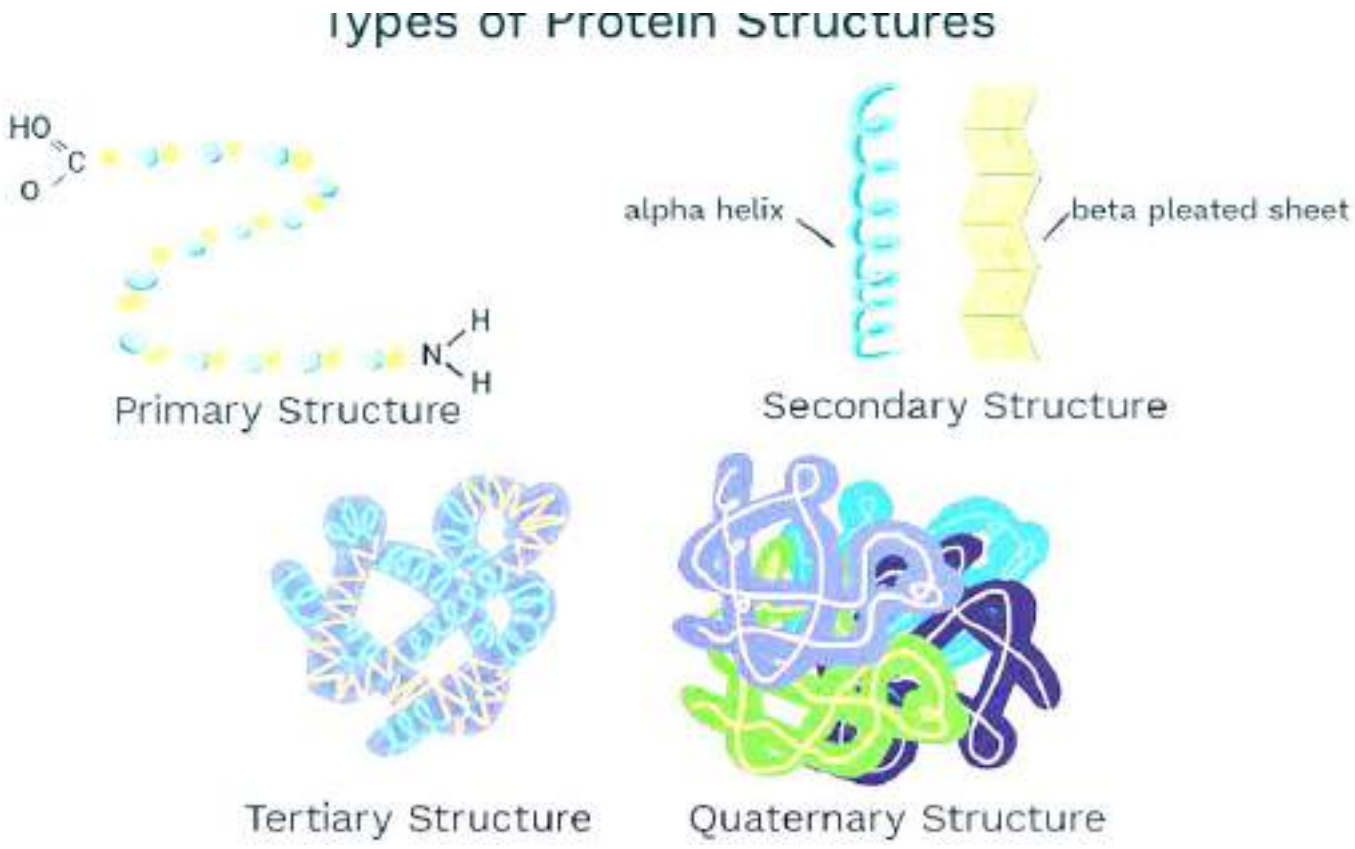
↳ When ~~two~~ such subunits are similar, the structure is called homogeneous quaternary structure. On the other hand, if the subunits are dissimilar, their interactions develop a heterogeneous quaternary structure.

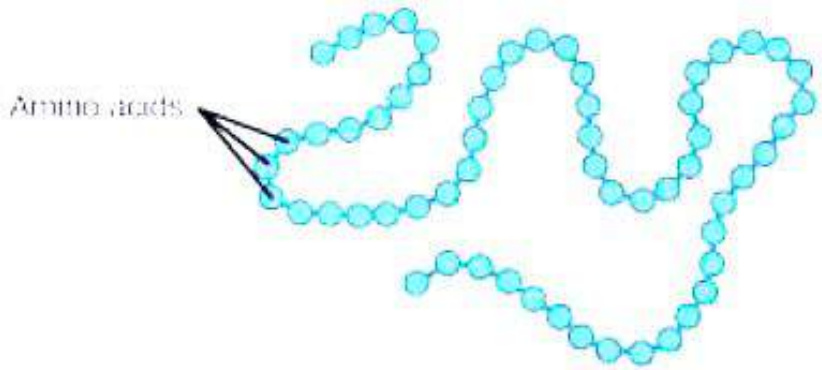
↳ The subunits are held together by the same kinds of interactions that hold the individual protein chains in a particular three-dimensional conformation — hydrophobic interactions, hydrogen bonding, and electrostatic attractions.

↳ The quaternary structure of a protein describes the way the subunits are arranged in space.

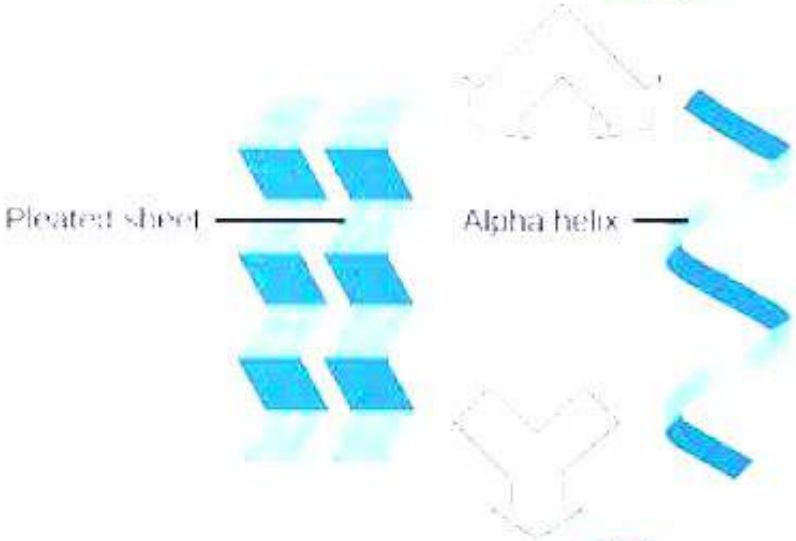
↳ Generally quaternary structure of a protein is stable and ordered non-covalent aggregates of more than one polypeptide chain.

↳ The quaternary structure of hemoglobin for example, involves four subunits.


Types of Protein Structures
HO
C
O
N
H
H
Primary Structure
alpha helix
beta pleated sheet
Secondary Structure
Tertiary Structure
Quaternary Structure

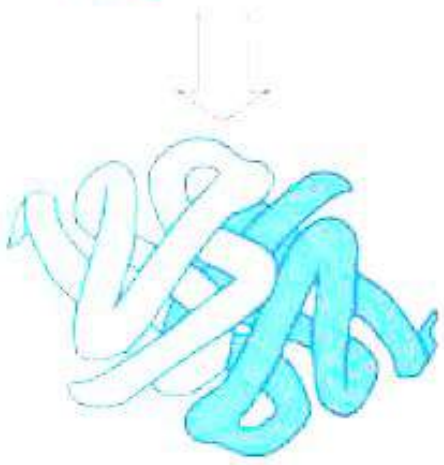


Primary protein structure
sequence of a chain of amino acids



Secondary protein structure
hydrogen bonding of the peptide backbone causes the amino acids to fold into a repeating pattern

Tertiary protein structure
three-dimensional folding pattern of a protein due to side chain interactions



Quaternary protein structure
protein consisting of more than one amino acid chain