# AMINO ACIDS AND PROTEINS

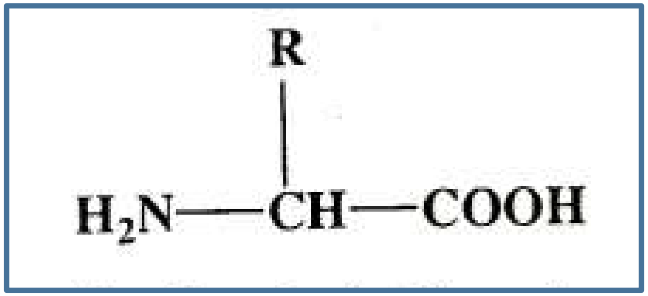
# Biological roles:

- 1. Amino acids can be metabolized to produce energy. This is especially important during fasting, when the breakdown of muscle protein is a major source of energy and biosynthetic precursors.
- 2. Some amino acids act as neurotransmitters, and some act as starting materials for the biosynthesis of neurotransmitters, hormones, and a wide variety of other important biochemical compounds.
- 3. Amino acids are the primary building blocks for proteins.

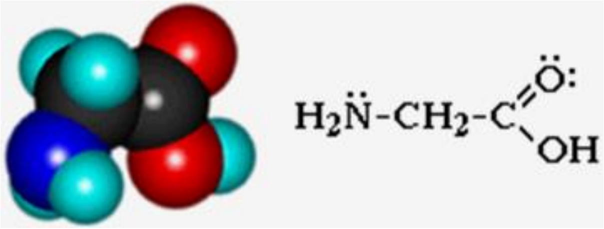
# Structure and classification

- **Amino acids** or amino carboxylic acids are derivatives of carboxylic acids, in which at least one hydrogen atom is replaced by an amine group.
- **Amino acid** molecules are Heterofunctional compounds that have two functional groups, an amine group, $-NH_2$, and a carboxyl group, $-COOH$.

# The general formula for a 2-amino(α-amino) acid is:



$$H_2N-\overset{\overset{R}{|}}{C}H-COOH$$



Glycine

The biologically important amino acids have the amino group attached to the carbon atom next door to the -COOH group.

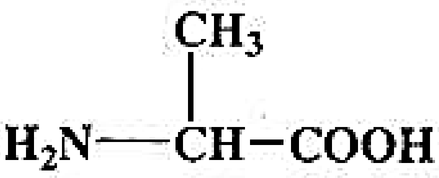
They are known as ***2-amino acids***. They are also known as ***α-amino acids***.

# "R" is called a side chain

- The nature of amino acid side chain R varies considerably.
- Its structure defines the chemical properties of individual α-amino acids

# Naming proteinogenic α-amino acids

- The commonly used terms for designating proteinogenic α-amino acids are their trivial and semi-trivial names

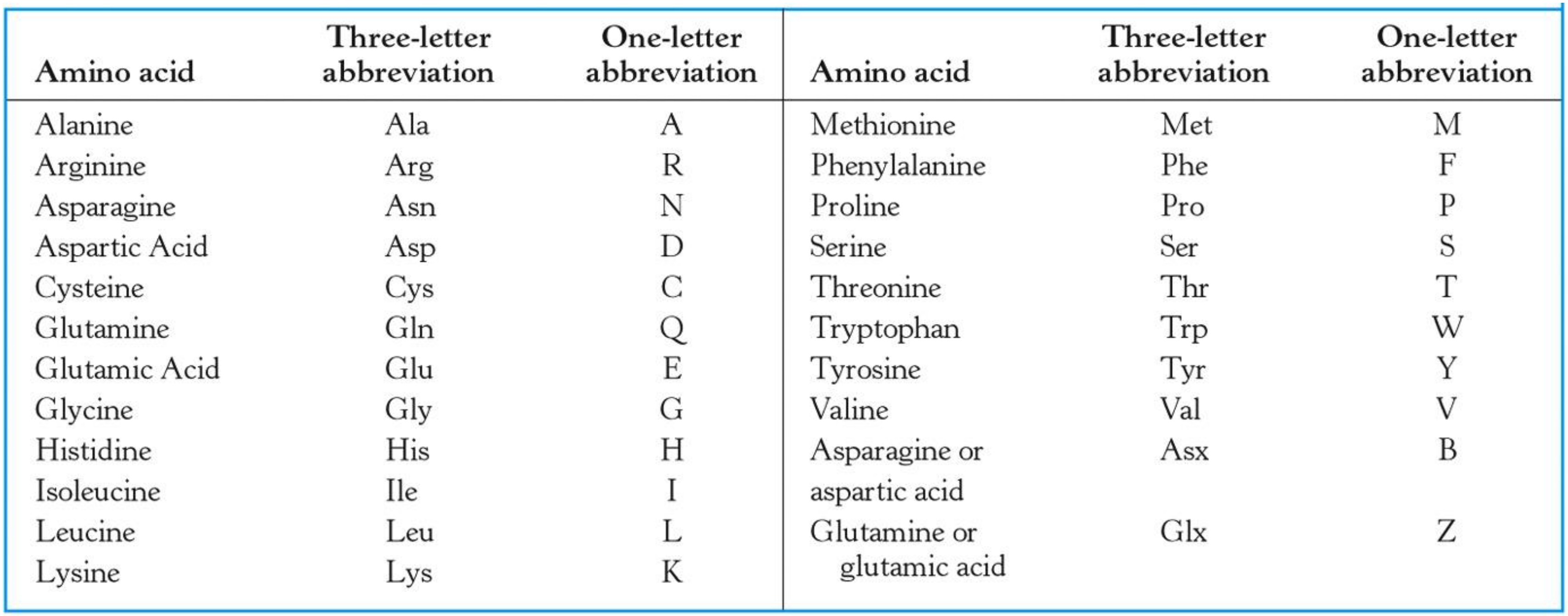


$$H_2N-\overset{\displaystyle CH_3}{\overset{|}{C}}H-COOH$$

*Alanine* (trivial name)

*2-Aminopropanoic acid* (IUPAC name)

# Abbreviations of the standard amino acids



| Amino acid | Three-letter abbreviation | One-letter abbreviation |
|---|---|---|
| Alanine | Ala | A |
| Arginine | Arg | R |
| Asparagine | Asn | N |
| Aspartic Acid | Asp | D |
| Cysteine | Cys | C |
| Glutamine | Gln | Q |
| Glutamic Acid | Glu | E |
| Glycine | Gly | G |
| Histidine | His | H |
| Isoleucine | Ile | I |
| Leucine | Leu | L |
| Lysine | Lys | K |
| Methionine | Met | M |
| Phenylalanine | Phe | F |
| Proline | Pro | P |
| Serine | Ser | S |
| Threonine | Thr | T |
| Tryptophan | Trp | W |
| Tyrosine | Tyr | Y |
| Valine | Val | V |
| Asparagine or aspartic acid | Asx | B |
| Glutamine or glutamic acid | Glx | Z |

# CLASSIFICATION OF AMINO ACID

- A. Based on structure – AA with aliphatic side chains,
  AA with hydroxyl group
  AA with sulphur group
  Acidic amino acid
  Basic amino acid
  Aromatic amino acid
  Imino acid
- B. Based on polarity – Non polar amino acid
  Polar amino acid with no charge on R
  Polar amino acid with positive R charge
  Polar amino acid with negative R charge

- C. Based on nutrition – Essential amino acid
  Non essential amino acid
- D. Based on metabolic fate – Glycogenic Amino acid
  Ketogenic amino acid

# AMINO ACIDS

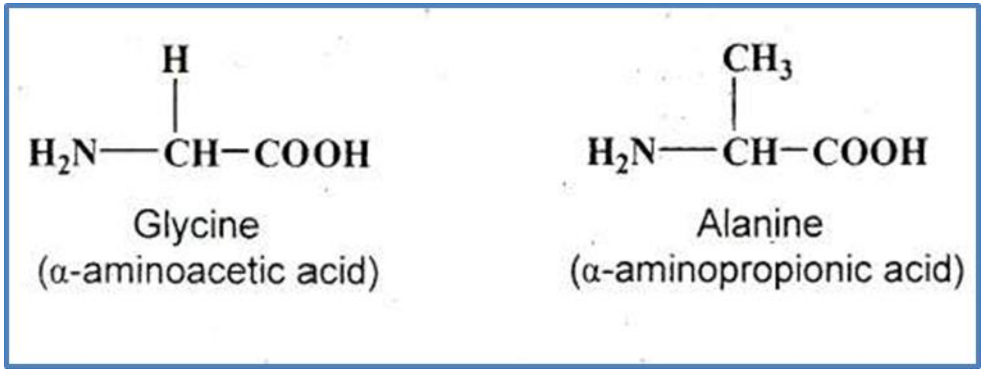
- Hydrophobic amino acids
  non-polar
  - R = alkyl
    - Glycine
    - Alanine
    - Valine
    - Leucine
    - Isoleucine
    - Methionine
    - Proline
  - R = aromatic group
    - Phenylalanine
    - Tryptophan
- Hydrophilic amino acids
  polar
  - Neutral
    - Tyrosine
    - Serine
    - Threonine
    - Cysteine
    - Glutamine
    - Asparagine
  - Acidic
    - Glutamic acid
    - Aspartic acid
  - Basic
    - Lysine
    - Histidine
    - Argenine

# *Structural classification of a-amino acids*

# ALIPHATIC SIDE CHAINE

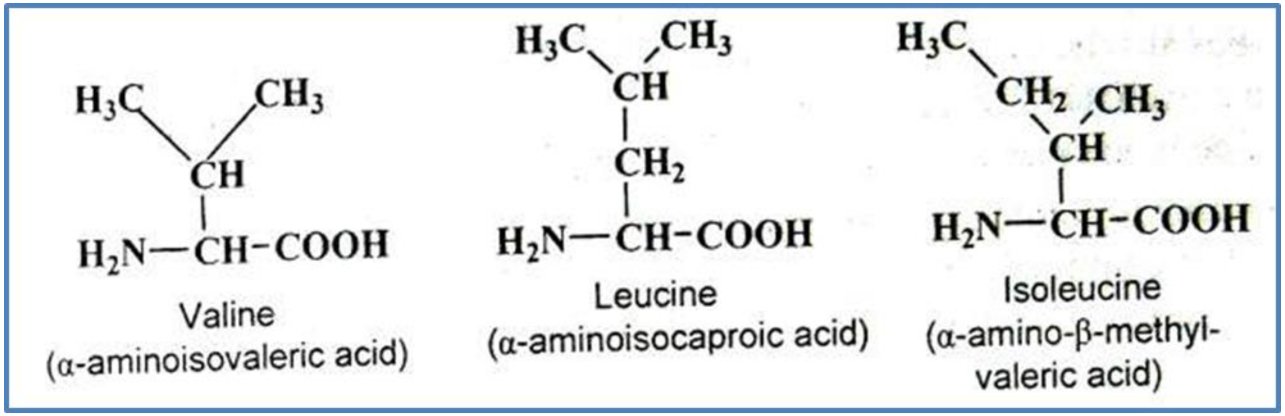
- ***neutral***

The hydrocarbon R group in this class of amino acids is nonpolar and hydrophobic. Glycine has the simplest amino acid structure. The bulky side chain of valine, isoleucine and leucine are important in promoting hydrophobic interactions within protein structures.



Glycine
(α-aminoacetic acid)

Alanine
(α-aminopropionic acid)



Valine
(α-aminoisovaleric acid)

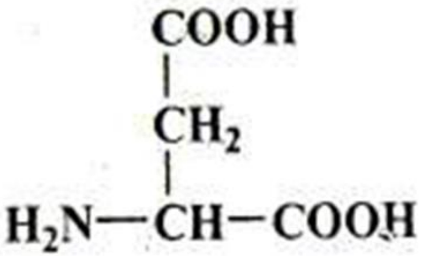
Leucine
(α-aminoisocaproic acid)

Isoleucine
(α-amino-β-methyl-valeric acid)

# Polar Amino acids

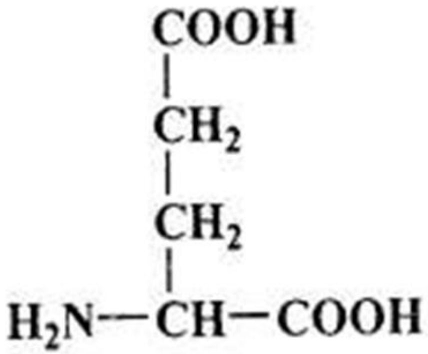
The R group of these amino acids is more soluble in water, or hydrophilic than those of non polar amino acids, because they contain functional groups that form hydrogen bond with water

***acidic***



$\mathrm{H_2N{-}CH(CH_2{-}COOH){-}COOH}$

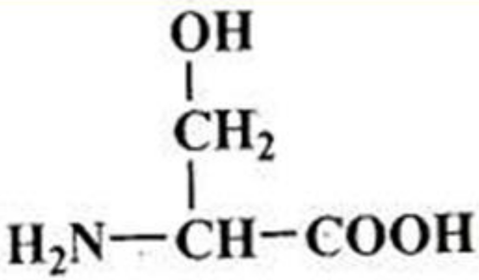
Aspartic acid (aspartate; aminosuccinic acid)



$\mathrm{H_2N{-}CH(CH_2{-}CH_2{-}COOH){-}COOH}$

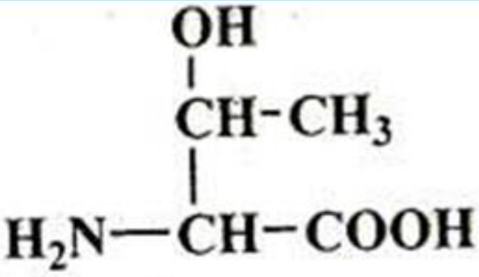
Glutamic acid (glutamate; α-aminoglutaric acid)

- Hydroxyaminoacids



$$H_2N-\overset{OH}{\overset{|}{\overset{CH_2}{\overset{|}{CH}}}}-COOH$$

Serine
(α-amino-β-hydroxy-
propionic acid)

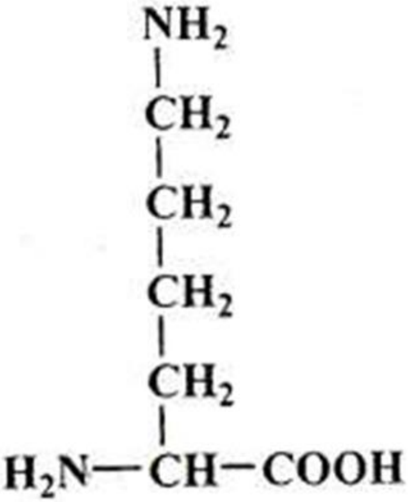


$$H_2N-\overset{OH}{\overset{|}{\overset{CH-CH_3}{\overset{|}{CH}}}}-COOH$$

Threonine
(α-amino-β-hydroxy-
butyric acid)

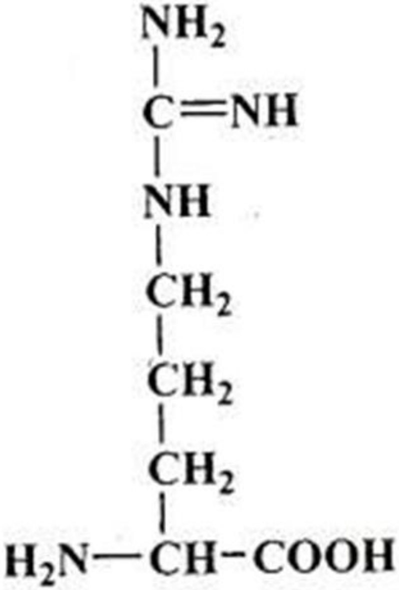
# This amino acids have a net positive charge at pH 7.0

- ***basic***



$H_2N-CH(CH_2-CH_2-CH_2-CH_2-NH_2)-COOH$

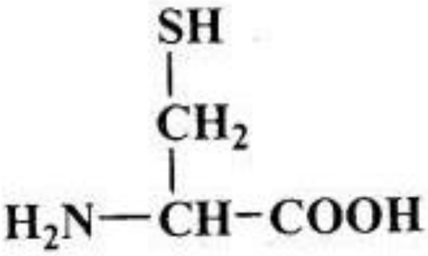
Lysine
(α,ε-diaminocaproic acid)



$H_2N-CH(CH_2-CH_2-CH_2-NH-C(=NH)-NH_2)-COOH$

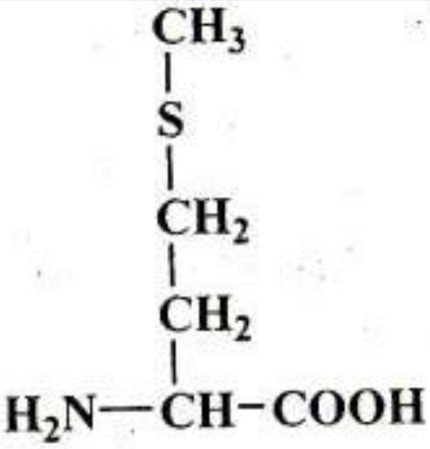
Arginine (α-amino-
δ-guanidinovaleric acid)

# *with Sulphur containing side chains:*



$$H_2N-\overset{\overset{\displaystyle SH}{|}}{\underset{}{\overset{\displaystyle CH_2}{\overset{|}{CH}}}}-COOH$$

Cysteine
(α-amino-β-thiopropionic acid)

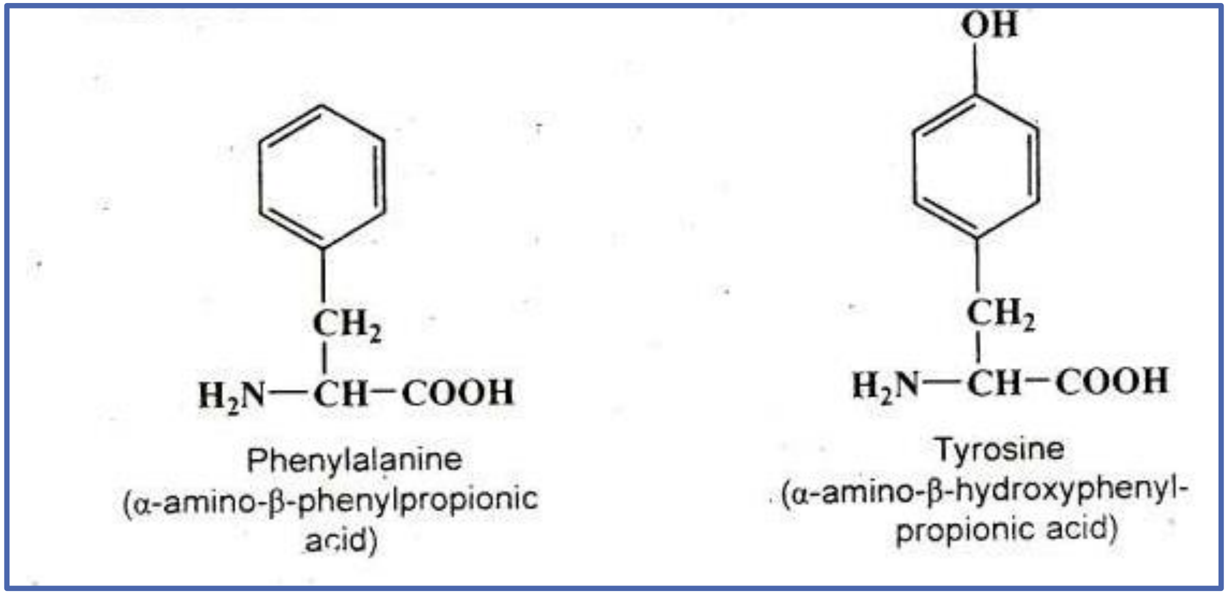


$$H_2N-\overset{\overset{\displaystyle CH_3}{|}}{\overset{\displaystyle S}{\overset{|}{\overset{\displaystyle CH_2}{\overset{|}{\overset{\displaystyle CH_2}{\overset{|}{CH}}}}}}}-COOH$$

Methionine
(β-amino-γ-methylthio-butyric acid)

# Cyclic amino acids

- *Aromatic amino acids.*



Phenylalanine
(α-amino-β-phenylpropionic acid)

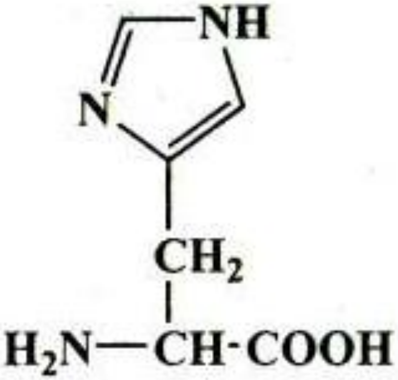
Tyrosine
(α-amino-β-hydroxyphenyl-propionic acid)

Their aromatic side chains are relatively nonpolar. All can participate in hydrophobic interactions. The OH group of tyrosine can form hydrogen bond and can act as an important functional group in the activity of some enzymes.

# Cyclic amino acids

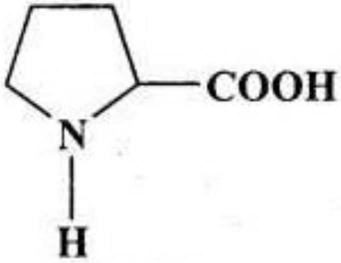
- ***Heterocyclic amino acids:***

Tryptophan
(α-amino-β-indolyl-
propionic acid)

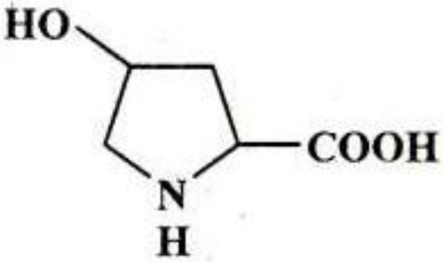


Histidine
(α-amino-β-imidazolyl-
propionic acid)

# Imino acids



Proline
(pyrrolidine-α-carboxylic acid)



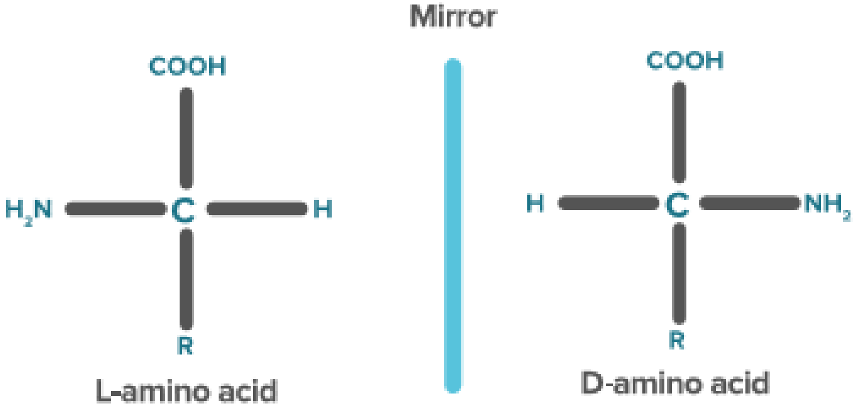
4-Hydroxyproline

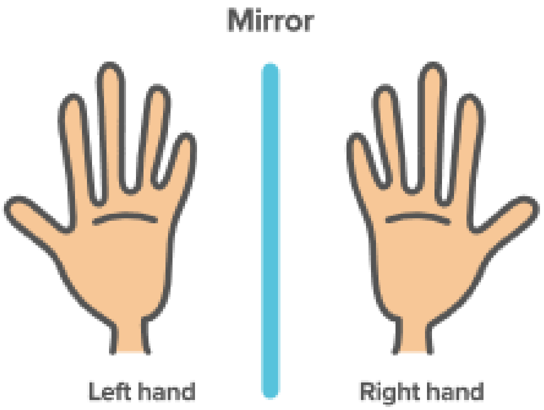
# Nutritional classification

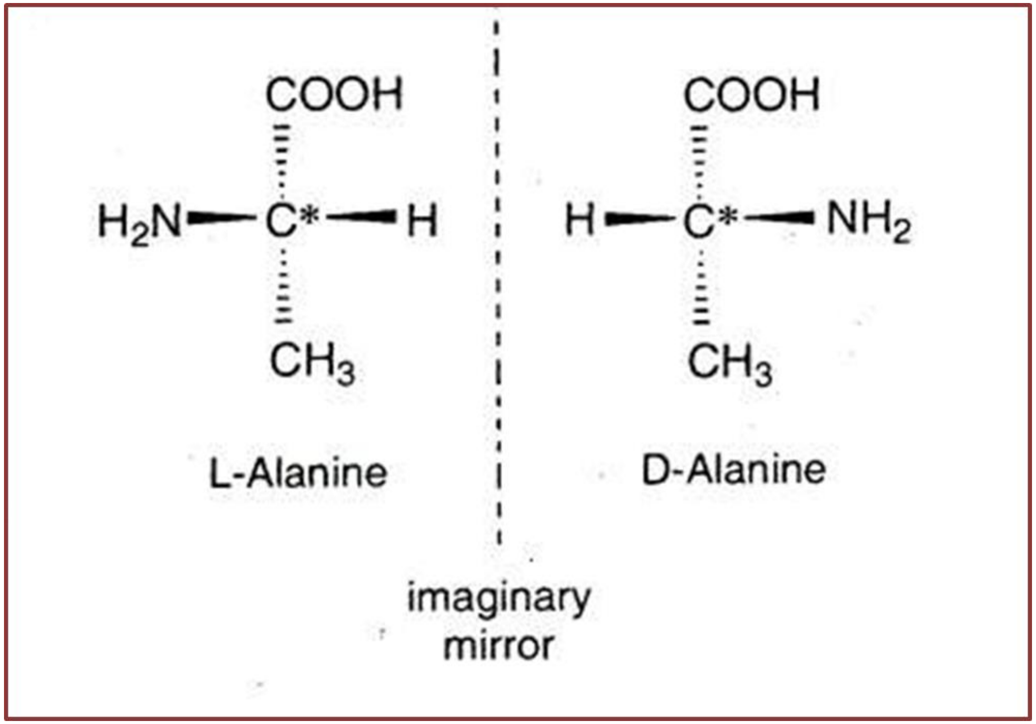
- **Essential amino acids**
- - the human body cannot synthesize them from other compounds at the level needed for normal growth, so they must be obtained from food.
- They include **valine, leucine, isoleucine, phenylalanine, threonine, tryptophan, methionine and lysine.**
- *Cysteine*, *tyrosine*, histidine and arginine are semi essential amino acids in children, because the metabolic pathways that synthesize these amino acids are not fully developed (they are not synthesized in sufficient quantity during growth).
- ***Non-essential amino acids***
- These can be synthesized by the body and may not be the requisite component of the diet.

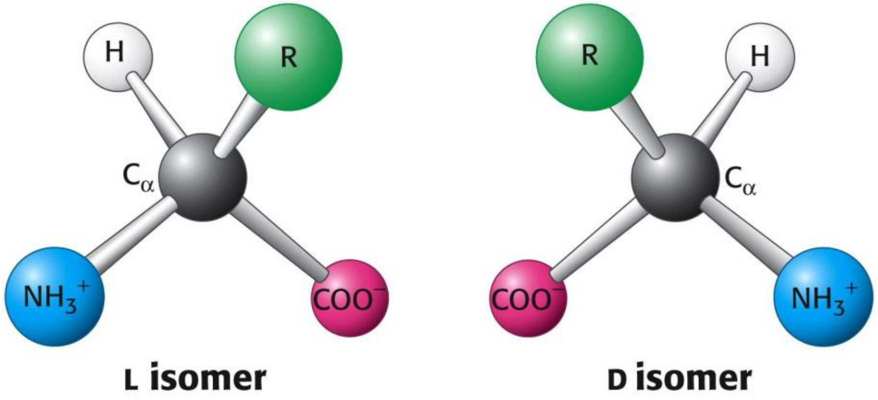
# Stereoisomerism and optical activity of a-amino acids

- the carbon atom, which is bonded to four different groups, is called *asymmetric* carbon or ***chiral*** carbon.
- In the proteinogenic amino acids, with the exception of glycine, the α-carbon atom is an asymmetric carbon. So, **the amino acids are chiral molecules.**


Mirror
COOH
$H_2N$
C
H
R
L-amino acid
COOH
H
C
$NH_2$
R
D-amino acid


Mirror
Left hand
Right hand

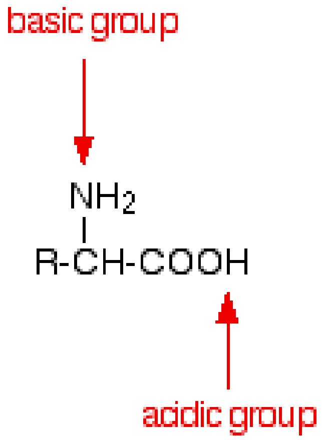

COOH
$H_2N$
C*
H
$CH_3$
L-Alanine
COOH
H
C*
$NH_2$
$CH_3$
D-Alanine
imaginary
mirror



- **The amino acids that are incorporated into natural peptides and proteins are of the L-configuration.**
- Only L-amino acids are intermediates in metabolic reactions in animal and human tissues, which is due to the chirality of biological catalysts *enzymes*

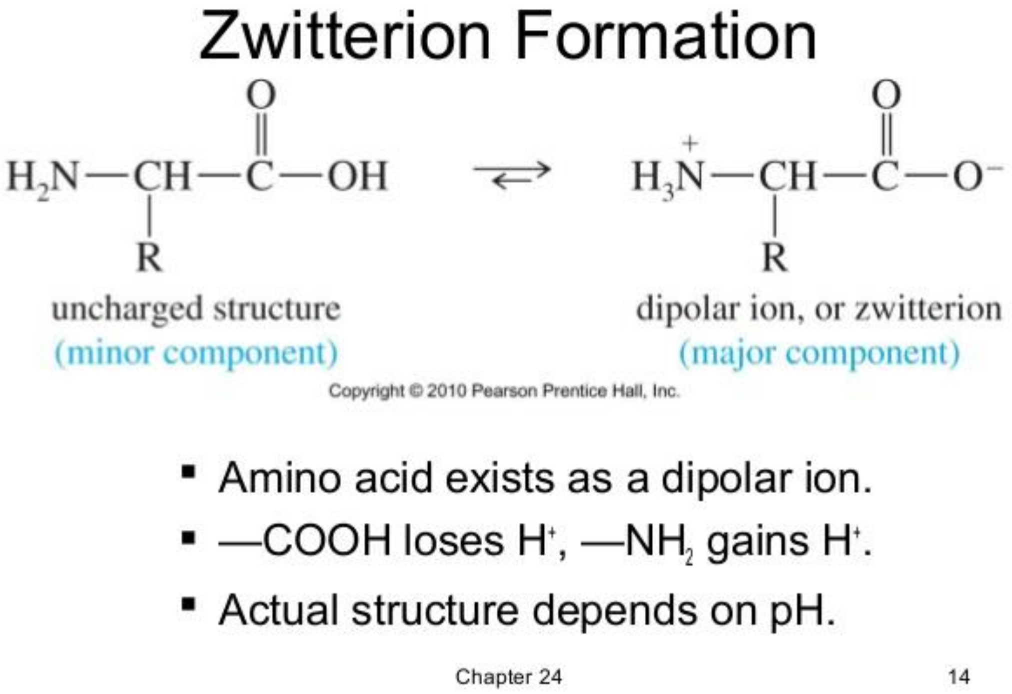
# The acid-base characteristics of amino acids

- Amino acids are heterofunctional compounds. They have two different functional groups: an amine group (—$NH_2$) and a carboxyl group (-COOH).
- In water solutions the basic amine group and the acidic carboxylic acid group can react with each other.



$R-CH(NH_2)-COOH$

# Formation of ionic and dipolar (zwitterions) forms of amino acid



## Zwitterion Formation

uncharged structure
(minor component)

dipolar ion, or zwitterion
(major component)

- Amino acid exists as a dipolar ion.
- —COOH loses $H^+$, —$NH_2$ gains $H^+$.
- Actual structure depends on pH.

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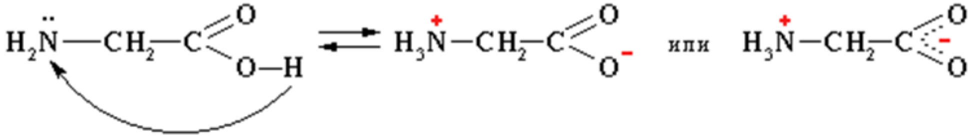
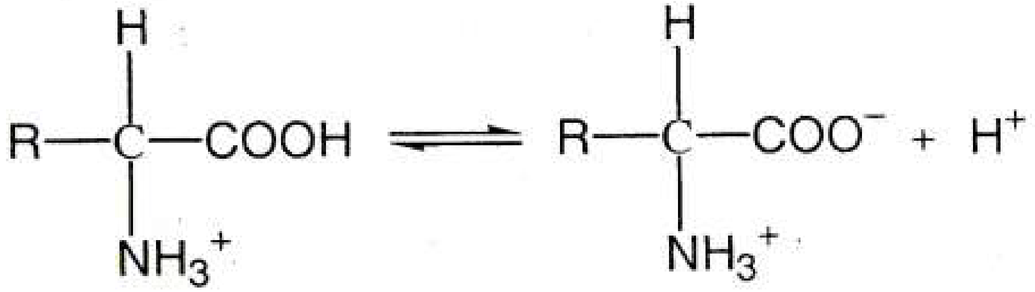
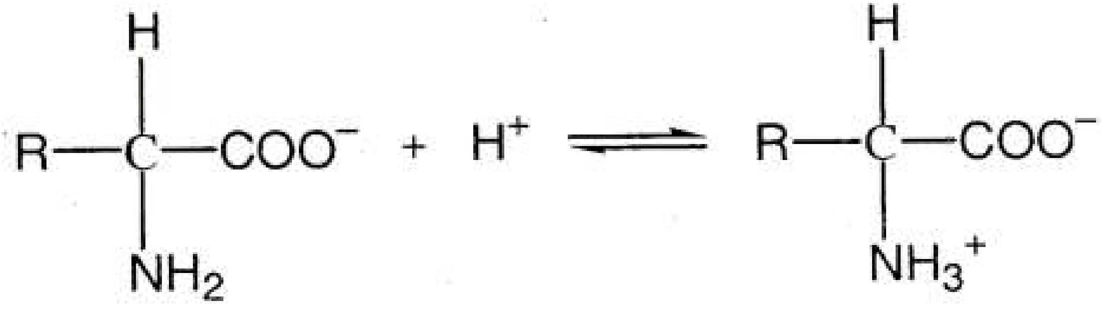


- According to Brensted-Lowry definition, the substances which donate proton are acids, and those accepting proton are bases. Thus, in water solutions, amino acids can behave, chemically, as acids (protons donors):



$$R-\underset{\underset{NH_3^+}{|}}{\overset{\overset{H}{|}}{C}}-COOH \rightleftharpoons R-\underset{\underset{NH_3^+}{|}}{\overset{\overset{H}{|}}{C}}-COO^- + H^+$$

or bases (protons acceptors):



$$R-\underset{\underset{NH_2}{|}}{\overset{\overset{H}{|}}{C}}-COO^- + H^+ \rightleftharpoons R-\underset{\underset{NH_3^+}{|}}{\overset{\overset{H}{|}}{C}}-COO^-$$

- the substances, which are capable of exhibiting both acidic and basic properties, reacting with both bases and acids, are named ***amphoteric electrolytes*** or ***ampholytes.***
- ***amino acids*** which contain separate acidic and basic groups within one molecule, ***are the ampholytes*** too
- at low pH the carboxyl group accepts a proton and becomes uncharged, so that the overall charge on the molecule is positive ***(cationic form*** of amino acid) and the amino acid behaves as *an acid.*
- At high pH, the amine group loses its proton and becomes uncharged; thus the overall charge on the molecule is negative ***(anionic form*** of amino acid) and the amino acid becomes *a base.*

# *Isoelectric point of amino acids (pI)*

- Is defined as the pH of a solution, at which amino acid exist as the zwitterion

# Biochemical reactions of proteinogenic L-amino acids

These biochemical reactions take place under the action of the special catalysts of a protein nature named ***enzymes***.

## The general ways of amino acids degradation:

- **Deamination**
- **Transamination**
- **Decarboxilation**

**The major site of amino acid degradation** - the liver.

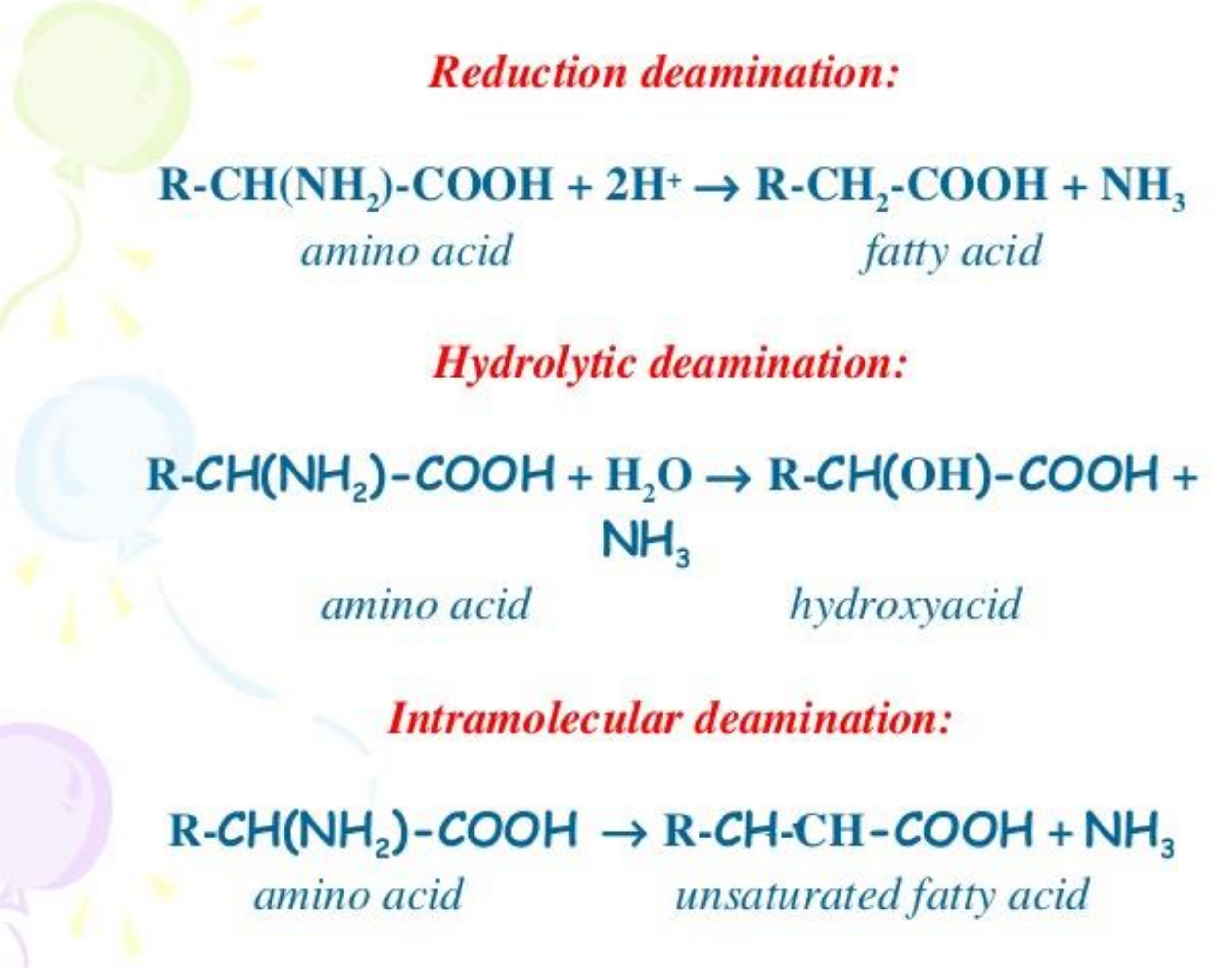
## Deamination of amino acids

**Deamination** - ***elimination of amino group from amino acid with ammonia formation*****.**

**Four types of deamination:**

- ***oxidative*** (the most important for higher animals),
- ***reduction,***
- ***hydrolytic, and***
- ***intramolecular***

# Deamination of aminoacids



**Reduction deamination:**

$R\text{-}CH(NH_2)\text{-}COOH + 2H^+ \rightarrow R\text{-}CH_2\text{-}COOH + NH_3$

*amino acid* *fatty acid*

**Hydrolytic deamination:**

$R\text{-}CH(NH_2)\text{-}COOH + H_2O \rightarrow R\text{-}CH(OH)\text{-}COOH + NH_3$

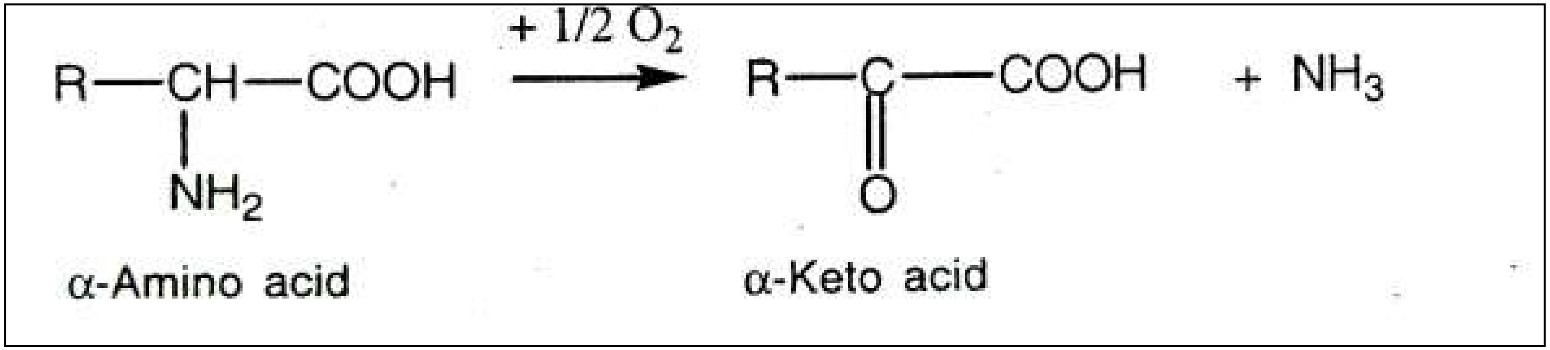
*amino acid* *hydroxyacid*

**Intramolecular deamination:**

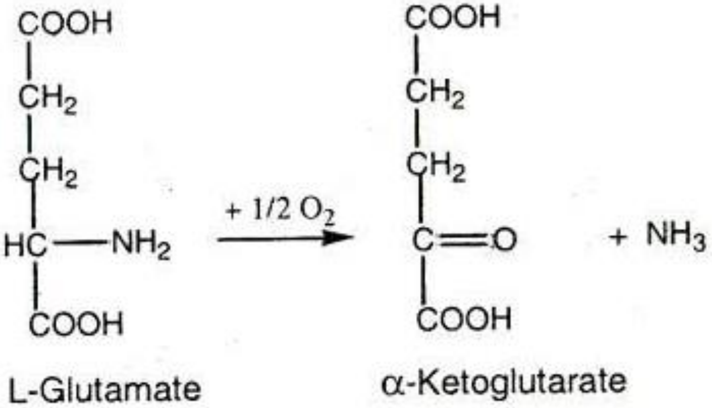
$R\text{-}CH(NH_2)\text{-}COOH \rightarrow R\text{-}CH\text{-}CH\text{-}COOH + NH_3$

*amino acid* *unsaturated fatty acid*

# oxidative deamination:



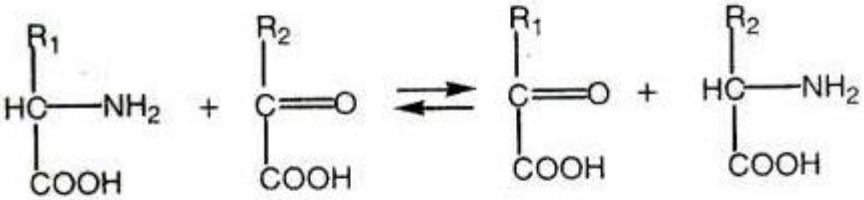
This is the kind of amino acids transformation which is prevalent in human tissues. In accordance with this scheme of reaction *L-glutamic acid (L-gluiamate)* is converted to *a-ketoglutaric acid {a-ketoglutarate):*



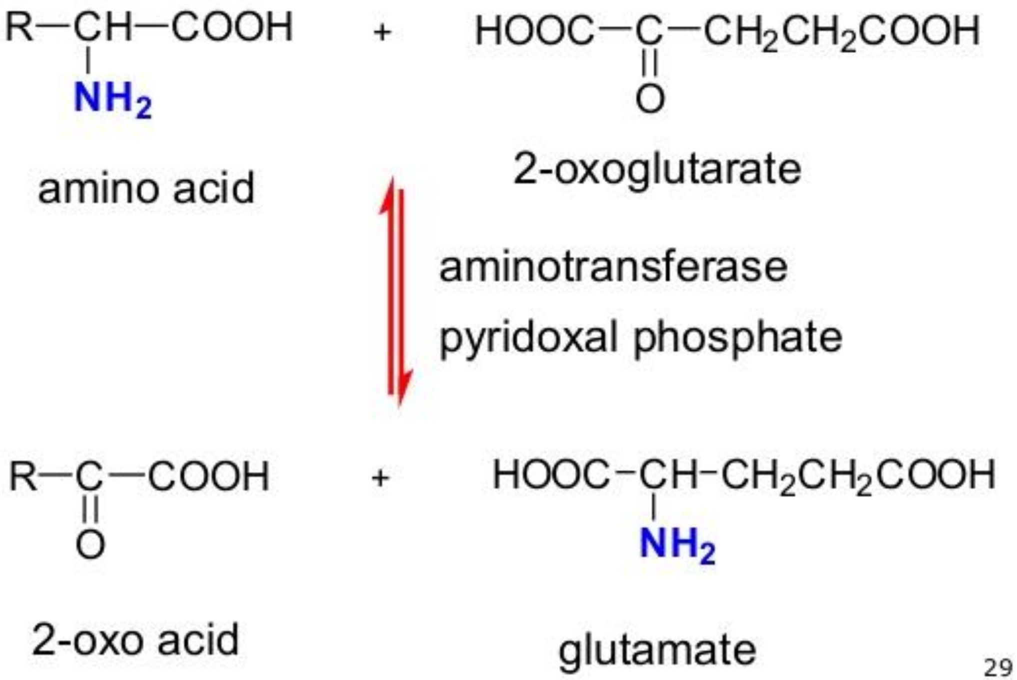
# Transamination of amino acids

**Transamination** - *transfer of an amino group from an α-amino acid to an α-keto acid (usually to α-ketoglutarate)*

**Enzymes:** *aminotransferases (transaminases).*



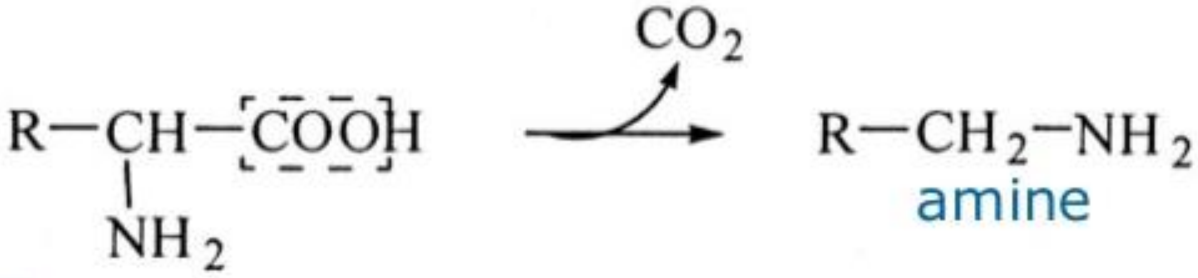
# General scheme of oxydative transamination



$$R-\underset{NH_2}{CH}-COOH + HOOC-\underset{O}{\overset{}{C}}{=}\!\!-CH_2CH_2COOH \xrightleftharpoons[\text{pyridoxal phosphate}]{\text{aminotransferase}} R-\underset{\|O}{C}-COOH + HOOC-\underset{NH_2}{CH}-CH_2CH_2COOH$$

# Decarboxylation of amino acids

**Decarboxylation – removal of *carbon dioxide* from amino acid with formation of *amines*.**



$$R-\underset{NH_2}{\underset{|}{CH}}-\boxed{COO}H \xrightarrow{CO_2} R-CH_2-NH_2$$

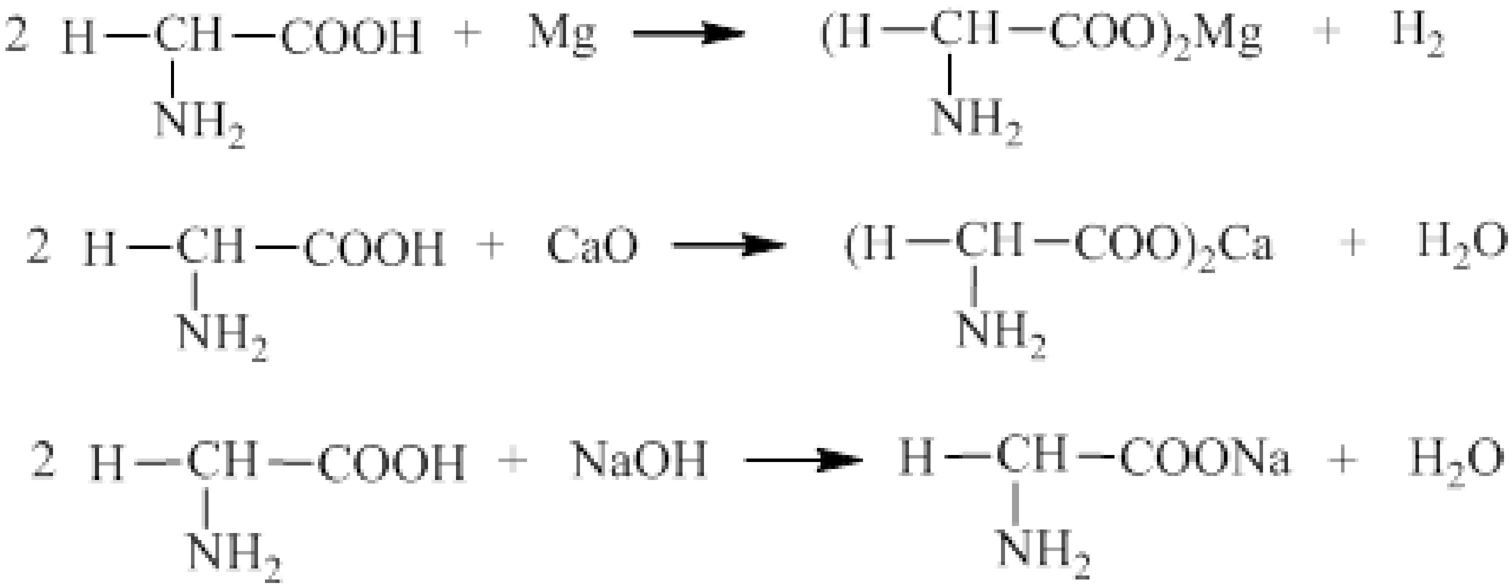
amine

Usually amines have high physiological activity (hormones, neurotransmitters etc).

Enzyme: ***decarboxylases***
Coenzyme – **pyrydoxalphosphate**

# REACTION OF ***–COOH*** GROUP

# Salt formation



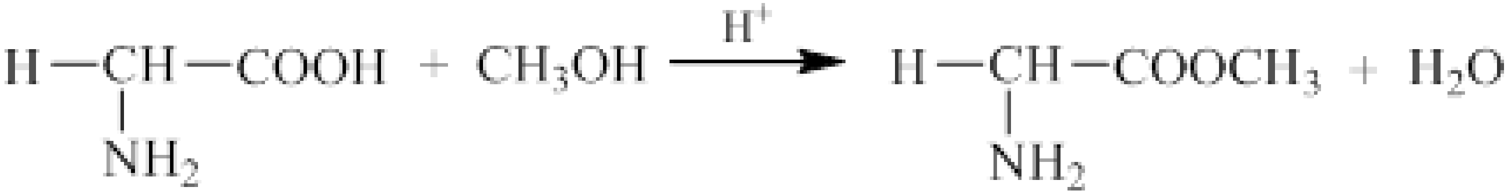
$$2\ \mathrm{H}-\underset{\substack{|\\ \mathrm{NH_2}}}{\mathrm{CH}}-\mathrm{COOH} + \mathrm{Mg} \longrightarrow (\mathrm{H}-\underset{\substack{|\\ \mathrm{NH_2}}}{\mathrm{CH}}-\mathrm{COO})_2\mathrm{Mg} + \mathrm{H_2}$$

$$2\ \mathrm{H}-\underset{\substack{|\\ \mathrm{NH_2}}}{\mathrm{CH}}-\mathrm{COOH} + \mathrm{CaO} \longrightarrow (\mathrm{H}-\underset{\substack{|\\ \mathrm{NH_2}}}{\mathrm{CH}}-\mathrm{COO})_2\mathrm{Ca} + \mathrm{H_2O}$$

$$2\ \mathrm{H}-\underset{\substack{|\\ \mathrm{NH_2}}}{\mathrm{CH}}-\mathrm{COOH} + \mathrm{NaOH} \longrightarrow \mathrm{H}-\underset{\substack{|\\ \mathrm{NH_2}}}{\mathrm{CH}}-\mathrm{COONa} + \mathrm{H_2O}$$

$$\mathrm{H_2N{-}CH_2{-}COOH + NH_3 \longrightarrow H_2N{-}CH_2{-}COONH_4}$$

# Esterification

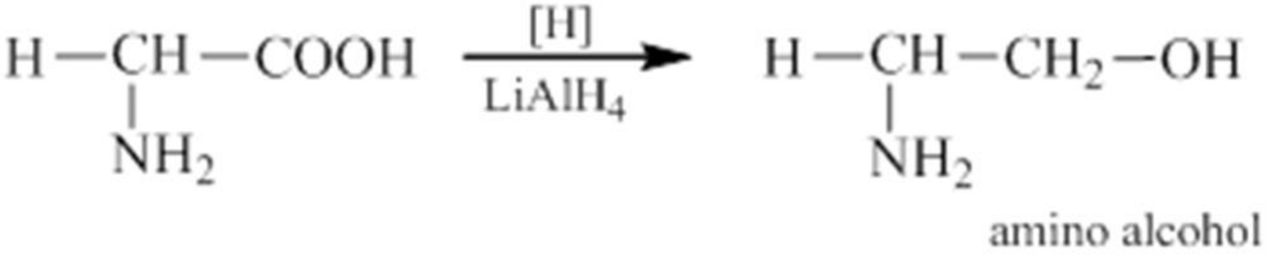


$$H-\underset{\displaystyle NH_2}{\underset{|}{CH}}-COOH + CH_3OH \xrightarrow{H^+} H-\underset{\displaystyle NH_2}{\underset{|}{CH}}-COOCH_3 + H_2O$$

# Decarboxylation

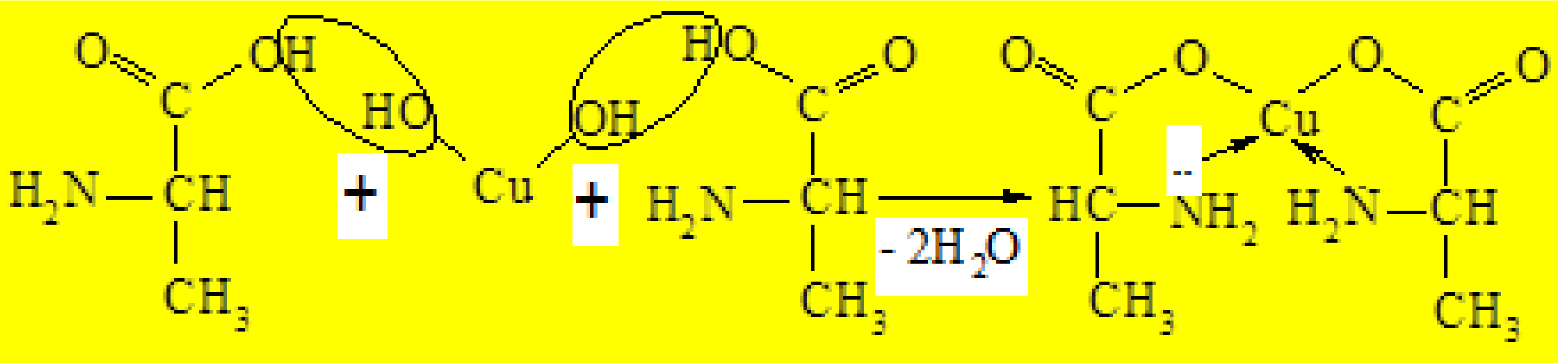
- *in vitro* $H_2N–CH_2–COOH \xrightarrow{Ba(OH)_2, t} H_2N–CH_3 + BaCO_3\downarrow + H_2O$

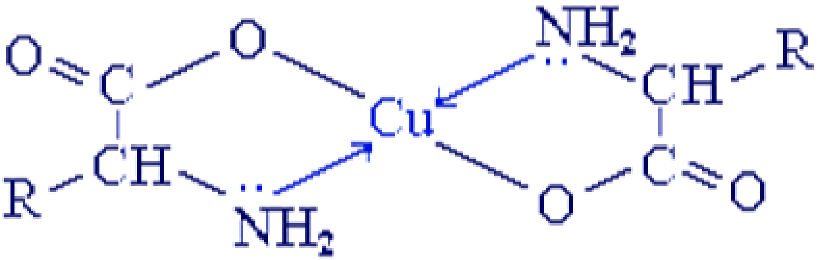
# Reduction to amino alcohol *(in vitro):*



$$H-\underset{\displaystyle NH_2}{\underset{|}{CH}}-COOH \xrightarrow[LiAlH_4]{[H]} H-\underset{\displaystyle NH_2}{\underset{|}{CH}}-CH_2-OH$$

# Reactions with hard metals ions

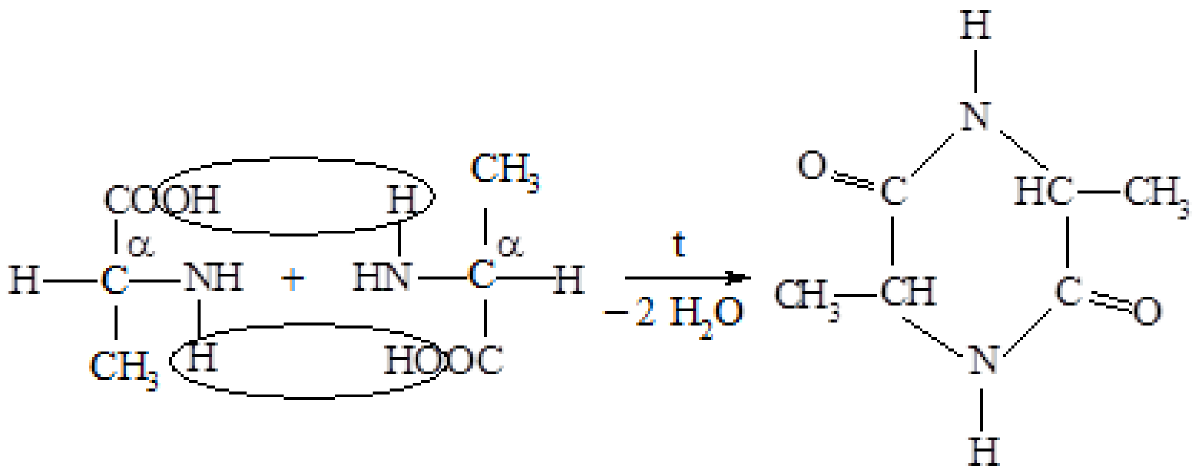




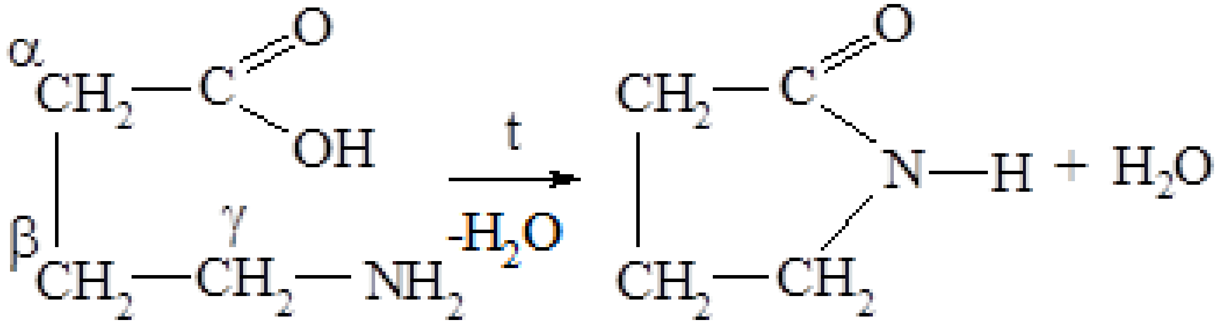
Complexes of copper (II) have a dark blue color
are used to determination of α-amino acids.

# Dehydration

- When two molecules of water are removed from two molecules of α-amino acids, cyclic compounds are formed :

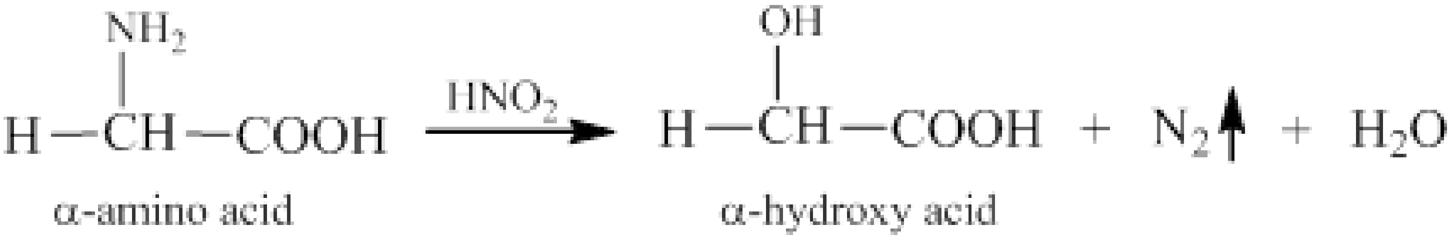


- Under the heating of γ-amino acids lactam is formed:



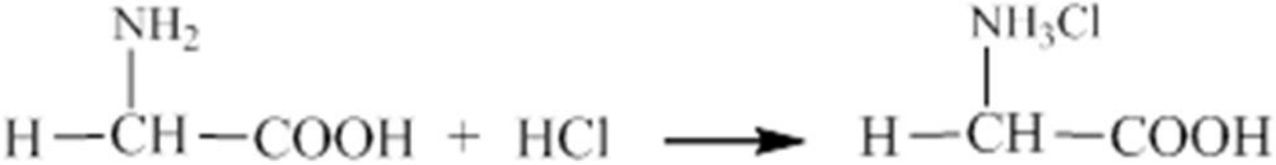
# REACTION OF NH2- GROUP

# Reaction with $HNO_2$ (nitrous acid)



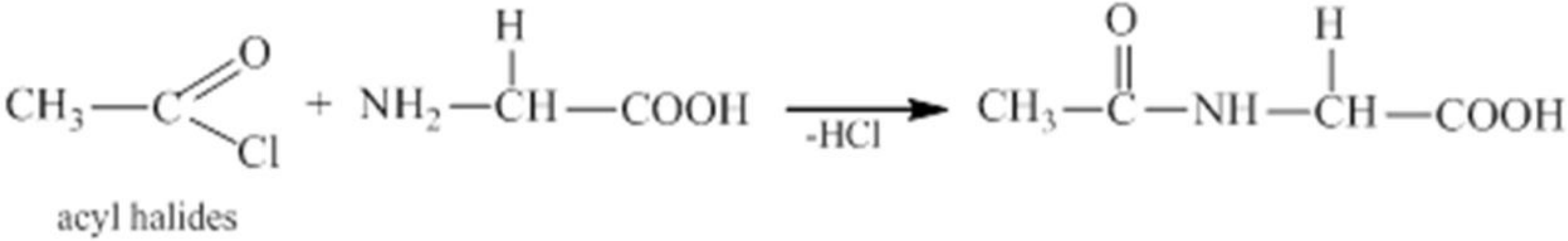
$$H-\overset{NH_2}{\overset{|}{C}H}-COOH \xrightarrow{HNO_2} H-\overset{OH}{\overset{|}{C}H}-COOH + N_2\uparrow + H_2O$$

# Salt formation with acids:

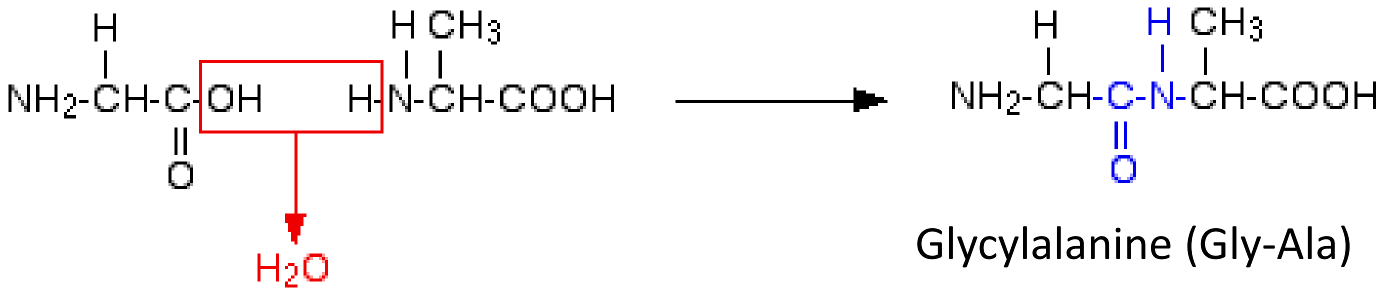


$$H-\overset{NH_2}{\overset{|}{C}H}-COOH + HCl \longrightarrow H-\overset{NH_3Cl}{\overset{|}{C}H}-COOH$$

# Acylation



# Peptide bond formation

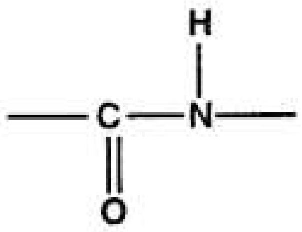


$$NH_2\text{-}\overset{\overset{\displaystyle H}{|}}{C}H\text{-}\underset{\underset{\displaystyle O}{\|}}{C}\text{-}\boxed{OH\quad}H\text{-}\overset{\overset{\displaystyle H}{|}}{N}\text{-}\overset{\overset{\displaystyle CH_3}{|}}{C}H\text{-}COOH \longrightarrow NH_2\text{-}\overset{\overset{\displaystyle H}{|}}{C}H\text{-}\underset{\underset{\displaystyle O}{\|}}{C}\text{-}\overset{\overset{\displaystyle H}{|}}{N}\text{-}\overset{\overset{\displaystyle CH_3}{|}}{C}H\text{-}COOH$$

$H_2O$

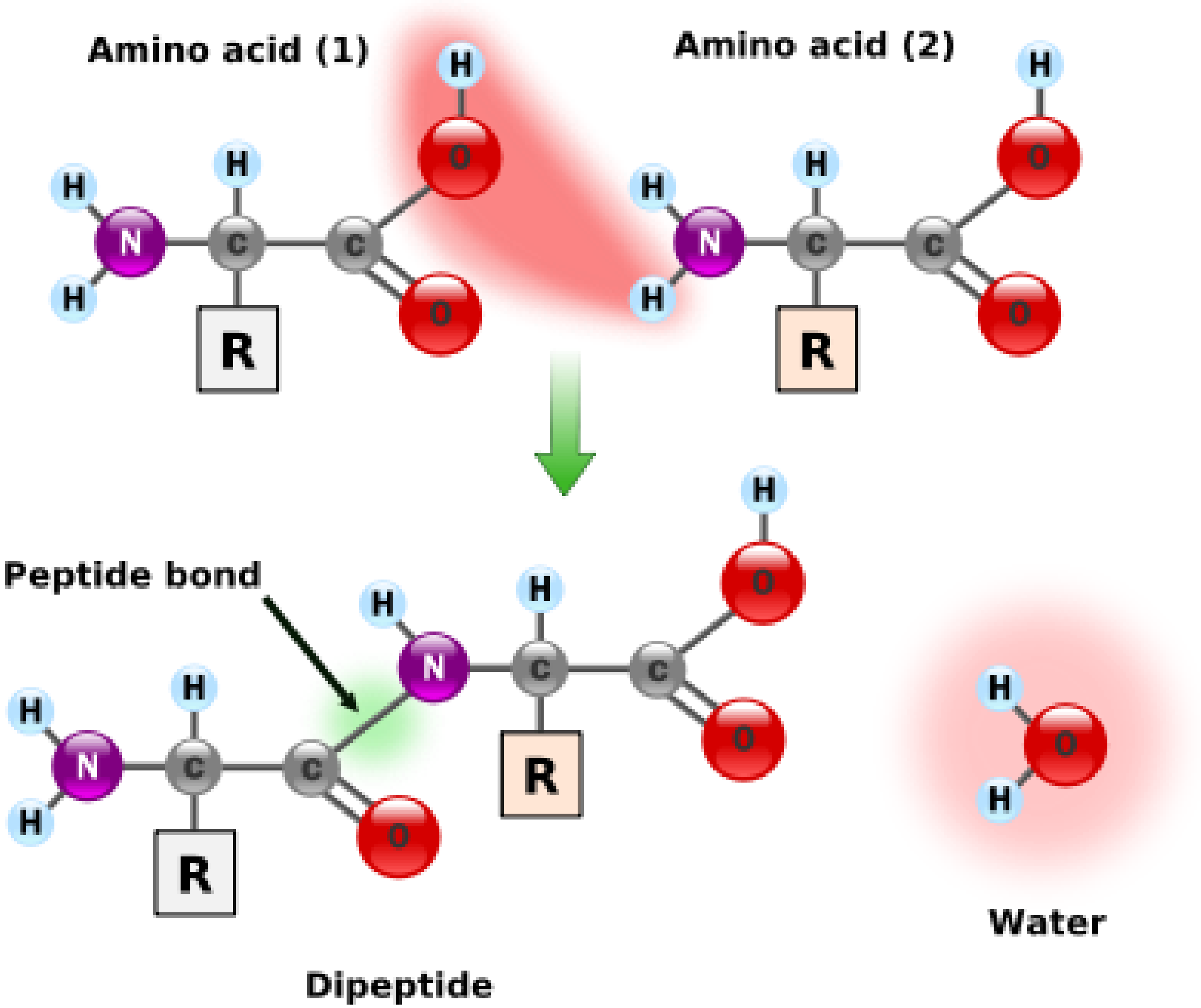
Glycylalanine (Gly-Ala)

The **peptide bond** (—**CO**—**NH**—) is the bond formed between the a-carboxyl group of one amino acid and the a-amino group of another.

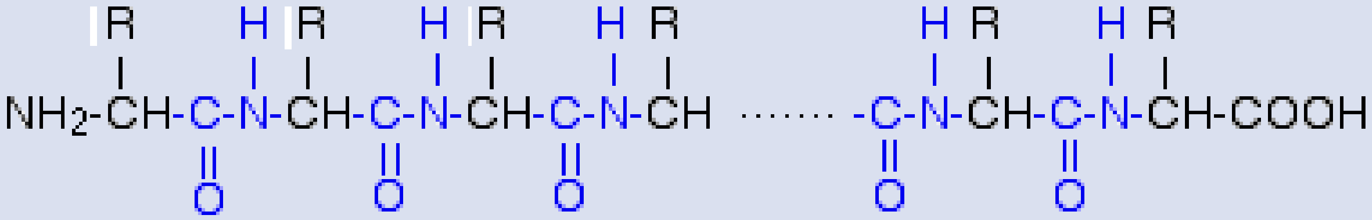


$$—\underset{\underset{\displaystyle O}{\|}}{C}—\overset{\overset{\displaystyle H}{|}}{N}—$$

Peptide group

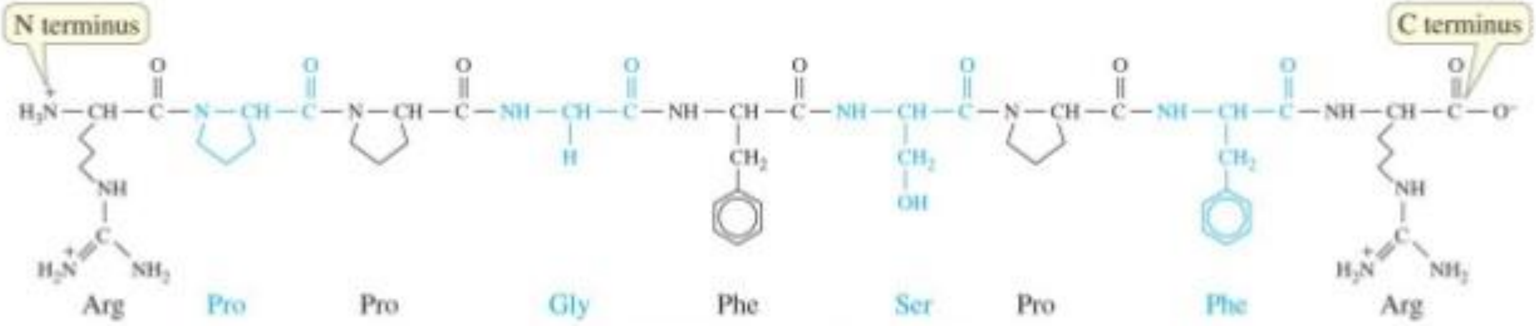

Amino acid (1)
Amino acid (2)
Peptide bond
Dipeptide
Water

- When  joined three amino acids together,  would get a tripeptide.
- When  joined lots and lots together (as in a protein chain), get a ***polypeptide***.
- The end of the peptide chain with the -$NH_2$ group is known as the ***N-terminal***, and the end with the -COOH group is the ***C-terminal***.



$$\mathrm{NH_2\text{-}CH\text{-}C\text{-}N\text{-}CH\text{-}C\text{-}N\text{-}CH\text{-}C\text{-}N\text{-}CH} \cdots\cdots\cdot \mathrm{\text{-}C\text{-}N\text{-}CH\text{-}C\text{-}N\text{-}CH\text{-}COOH}$$

# Human Hormone Bradykinin



- An oligopeptide is made out of four to ten amino acids.
- Peptide structures are drawn with the N-terminal end at the left.
- Peptides are named from left to right: arginylprolylprolyl……arginine.

# Proteins

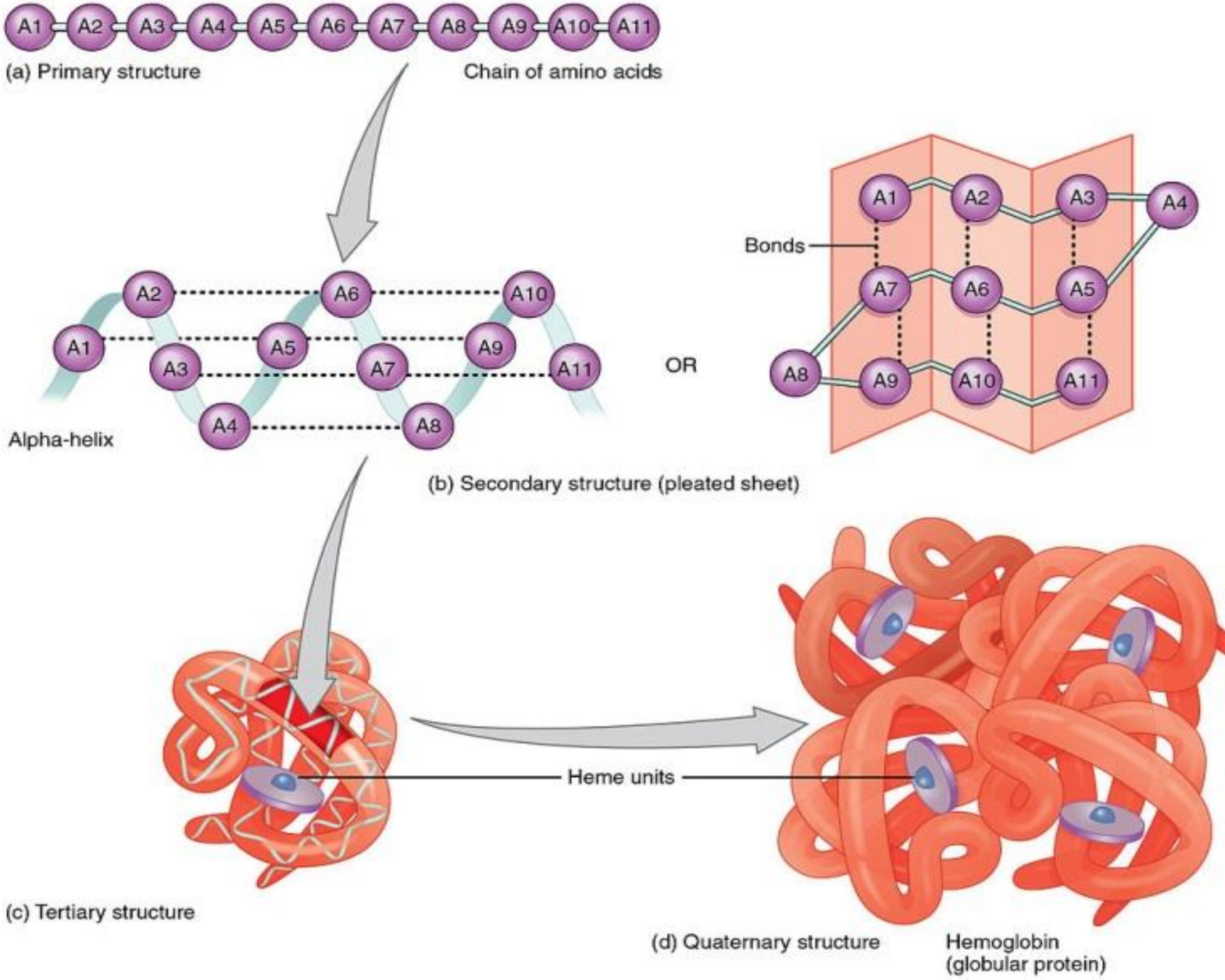
## Levels of proteins structure

# Proteins

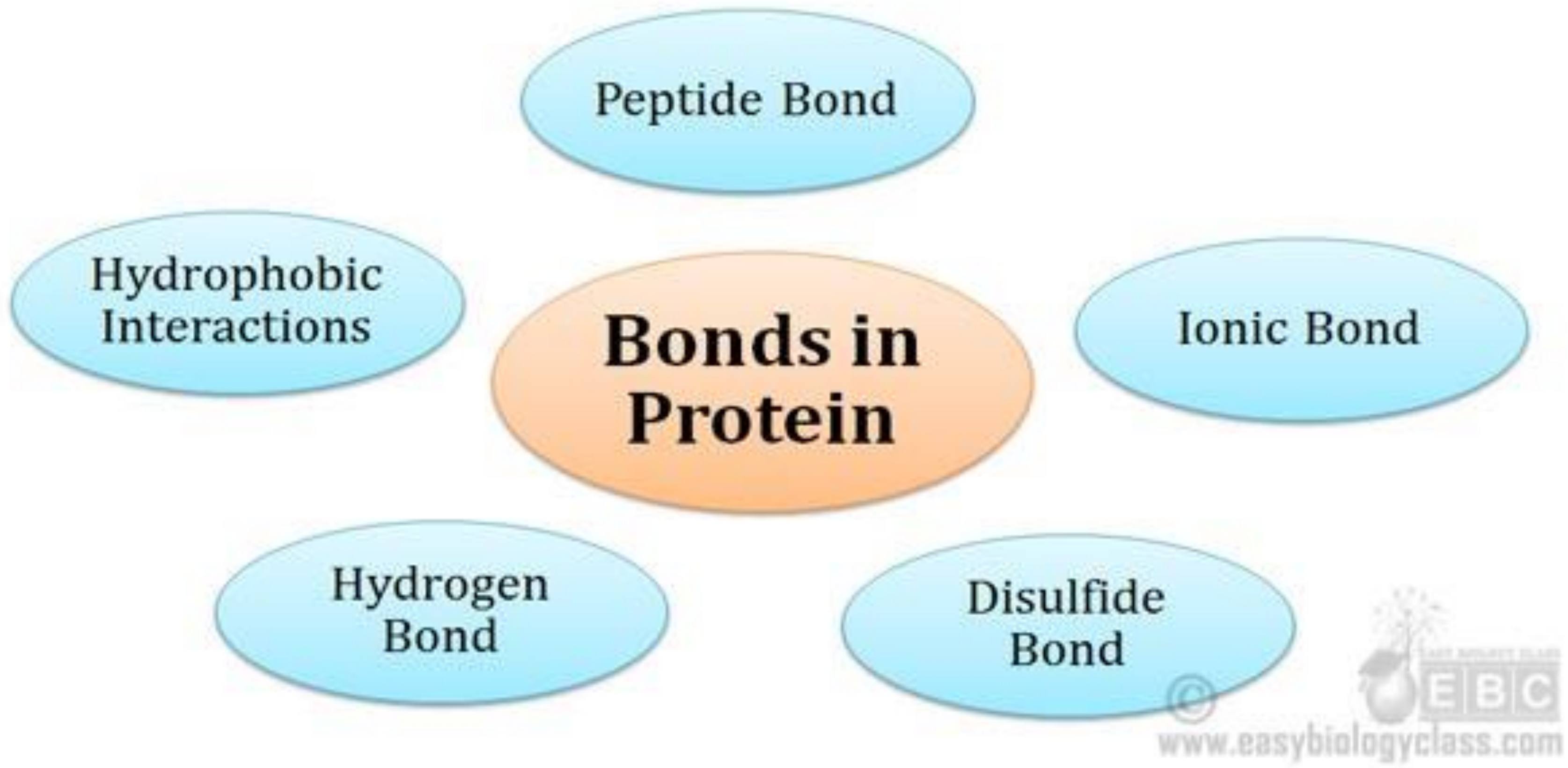
- Biopolymers of $\alpha$-amino acids.
- Amino acids are joined by peptide bond.
- They serve a variety of functions:
  - Structure
  - Enzymes
  - Transport
  - Protection
  - Hormones

- ***Primary structure*** is the amino acid sequence in polypeptide chain that forms a protein
- ***Secondary structure*** refers to the spatial arrangement of amino acid residues that constitute polypeptide linear sequence.
- ***Tertiary structure*** refers to the spatial arrangement of amino acids residues that are far apart in the linear sequence.
- **Quaternary structure** of a protein refers to the spatial arrangement of individual subunits and the nature of their contact.

Pauling and Corey proposed two secondary structures in proteins many years before they were actually proven: *alpha – helix beta - sheet*

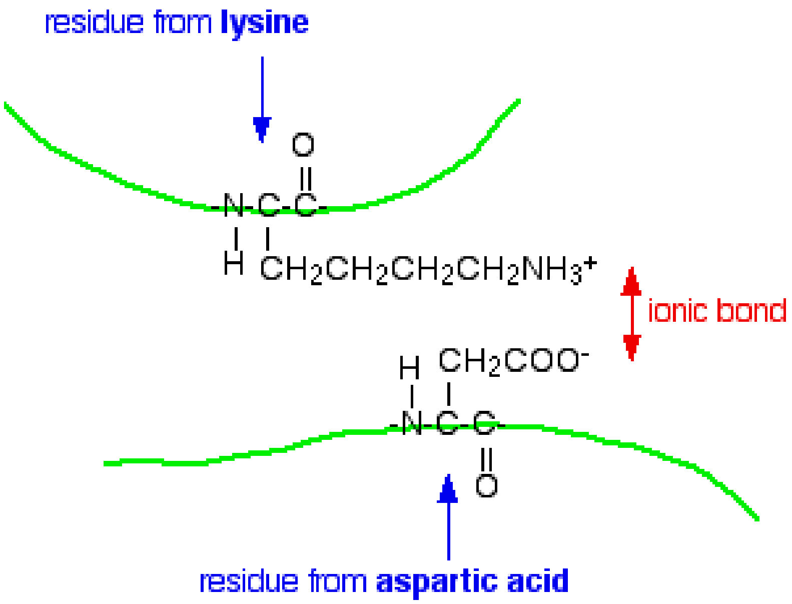


# TYPES OF BONDING IN PROTEINS



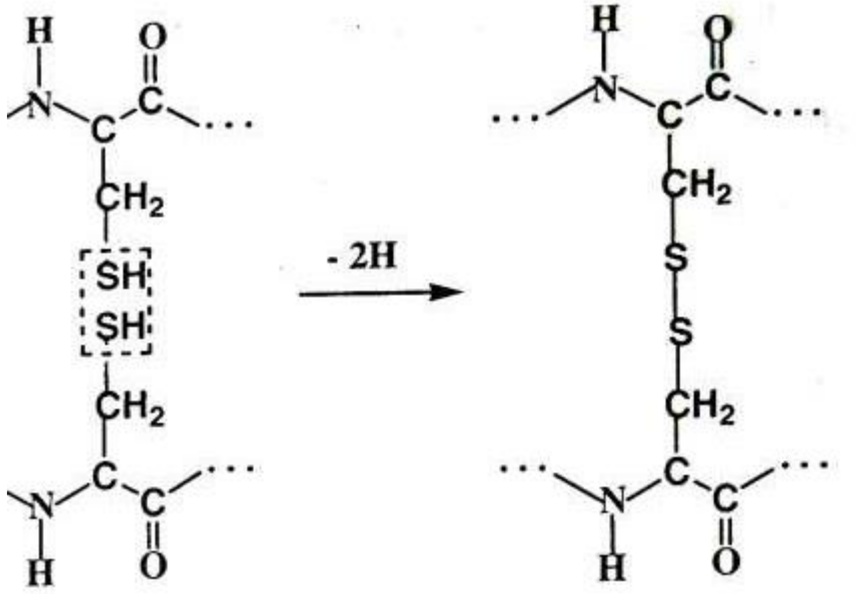
# Ionic Bonding

- This can occur between acidic R groups and basic R groups, causing the polypeptide chain to fold or bend. This bond can be broken by changes in pH, heat, radiation, heavy metals and high concentration of salts.



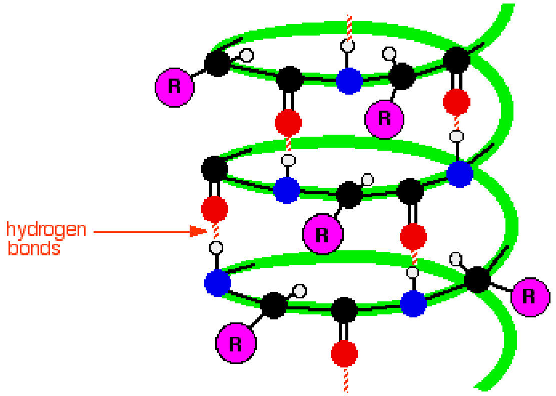
# Disulfide Bridges

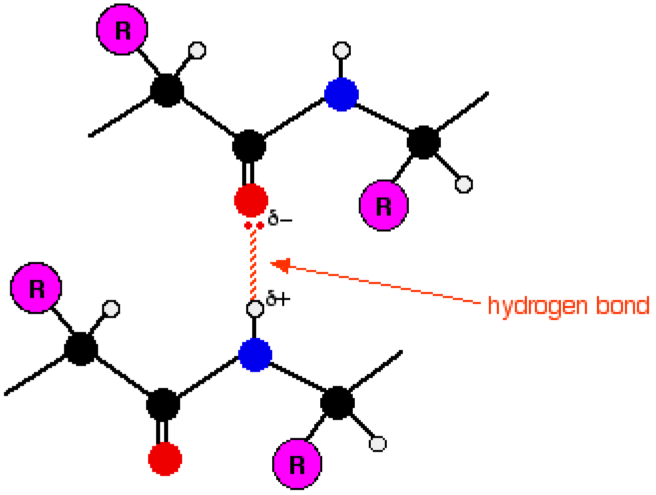
- This occurs between the sulfhydryl groups, SH of the R groups of two cysteine amino acids on the polypeptide chain. Hydrogen is removed and the disulfide bond is formed. This bond is a covalent bond and very strong. It can be broken by reducing agents.



# Hydrogen Bonding

- Hydrogen bonds can occur between CO and NH groups of neighboring amino acid residues or between amino acids which are located far from each other on the polypeptide chain. In this case, it is the R groups that will be involved. These are weak bonds and can be broken by high temperature, changes in pH, radiation, organic solvents and detergents.

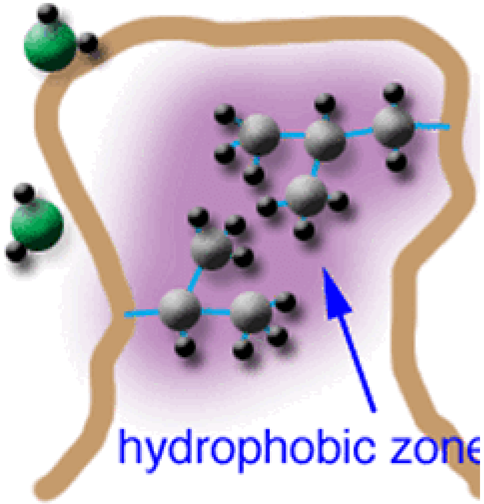


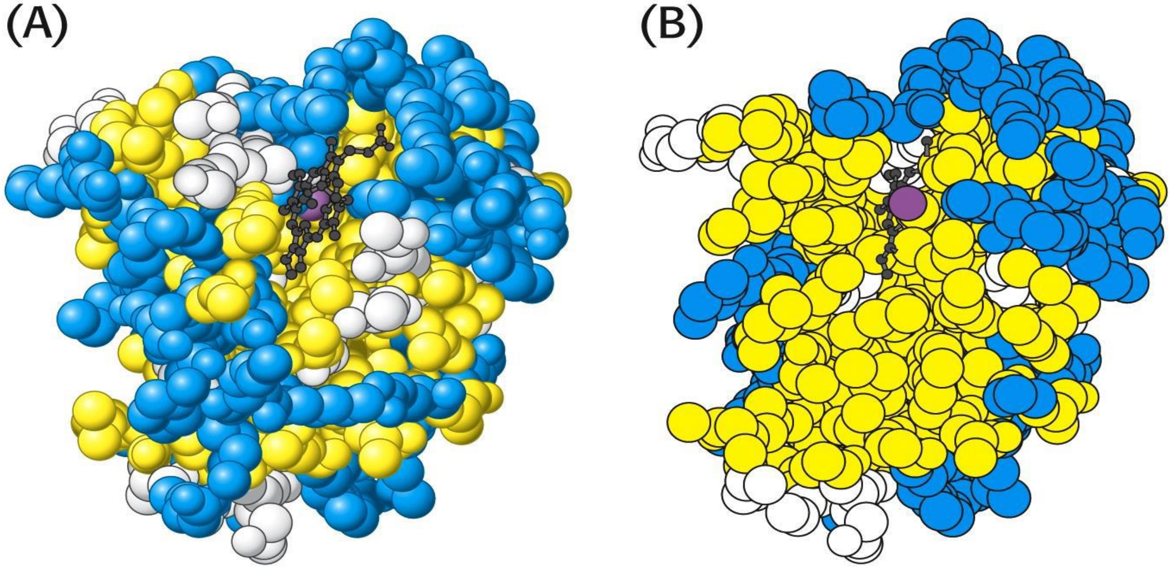


# Hydrophobic Interactions

- These can occur between hydrophobic R groups found on the polypeptide chain. It can be broken by organic solvents and detergents.

In the case of myoglobin and many other proteins, the majority of hydrophobic amino acids (yellow) are found inside in structure:



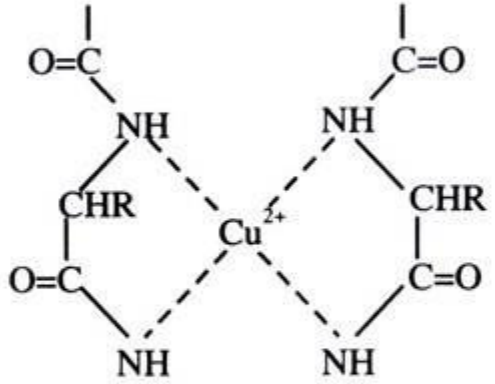


# Qualitative Tests for Amino Acids and Proteins

- There are six tests for the detection of functional groups in amino acids and proteins. The six tests are: (1) Ninhydrin Test (2) Biuret Test (3) Xanthoproteic Test (4) Millon’s Test (5) Hopkins-Cole Test and (6) Nitroprusside Test.

# Biuret Test:

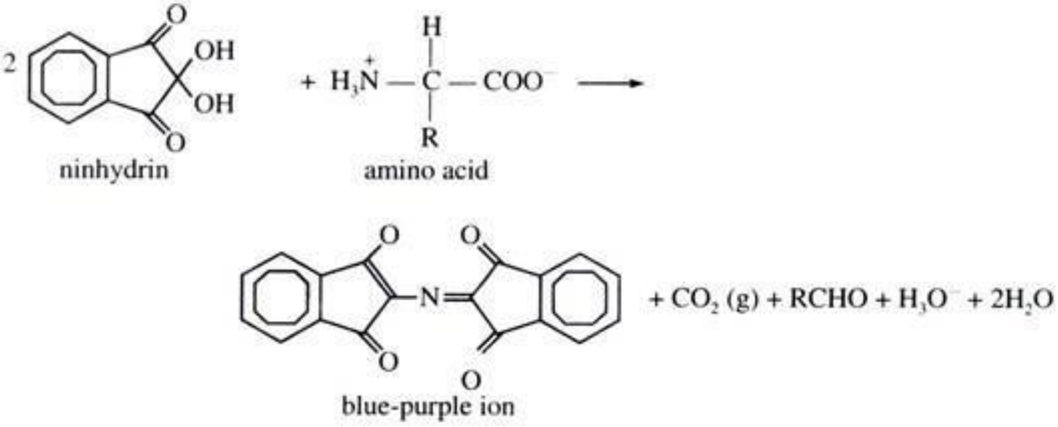
- The biuret test for proteins positively identifies the presence of proteins in solution with a deep violet color. Biuret, $H_2NCONHCONH_2$, reacts with copper (II) ions in a basic solution to form a deep violet complex.



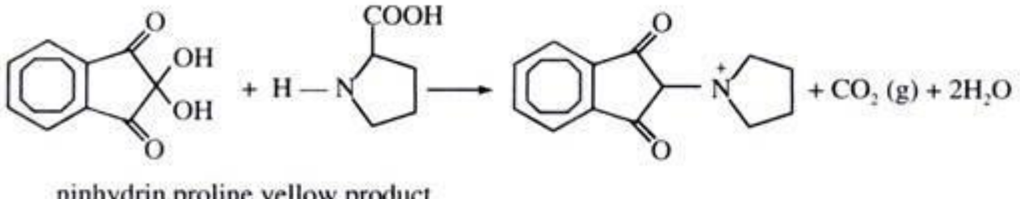
Protein-copper(II) ion complex, also called the biuret complex

# Ninhydrin Test:

- Amino acids contain a free amino group and a free carboxylic acid group that react together with ninhydrin to produce a coloured product. When an amino group is attached to the first, or alpha, carbon on the amino acid’s carbon chain, the amino group’s nitrogen atom is part of a blue-purple product, as shown in Equation (2) . Proteins also contain free amino groups on the alpha carbon and can react with ninhydrin to produce a blue-purple product.



(Eq. 2)



(Eq. 3

# Xanthoproteic Test:

- Some amino acids contain aromatic groups that are derivatives of benzene. These aromatic groups can undergo reactions that are characteristic of benzene and benzene derivatives. One such reaction is the nitration of a benzene ring with nitric acid. The amino acids tyrosine and tryptophan contain activated benzene rings and readily undergo nitration.
- Xanthoproteic comes from the Greek word xanthos, which means yellow. The intensity of the yellow colour deepens when the reaction occurs in basic solution. This reaction is one of the reactions that occur if you spill a concentrated solution of nitric acid onto your skin. The proteins in skin contain tyrosine and tryptophan, which become nitrated and turn yellow.

Protein denaturation changes the solubility of individual protein molecules, entrapping solvent water into a semisolid gel structure.

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