Amino Acids and Proteins

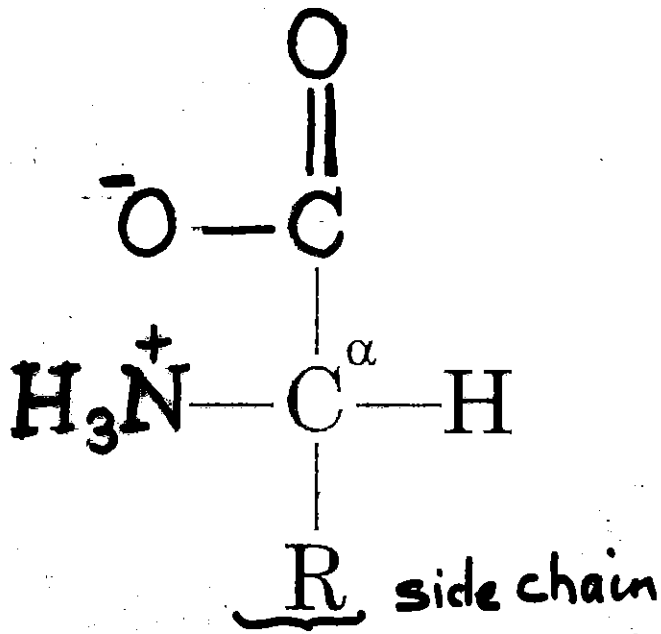
Proteins are the most abundant and functionally divers molecules in living systems. Every life process depends on this class of molecules.

Types and functions of Proteins

1. Enzymes - increase rate of reaction x 1 billion
2. Carriers - hemoglobin, transferrin
3. Receptors - hormones, cytokines
4. Transport - membrane channels
5. Structure - collagen, elastin
6. Protective - immunoglobulins
7. Contractile - muscle, cytoskeleton
8. Regulatory (Hormones)- govern metabolic pathway

- There are more than 300 a. a. found in the nature, only 20 are found in mammalian **proteins** and these are coded for by DNA
- The nature of the side chain decides the role of an amino acids in a protein
- Amino acids can be classified according to the properties of their side chains

At physiologic pH

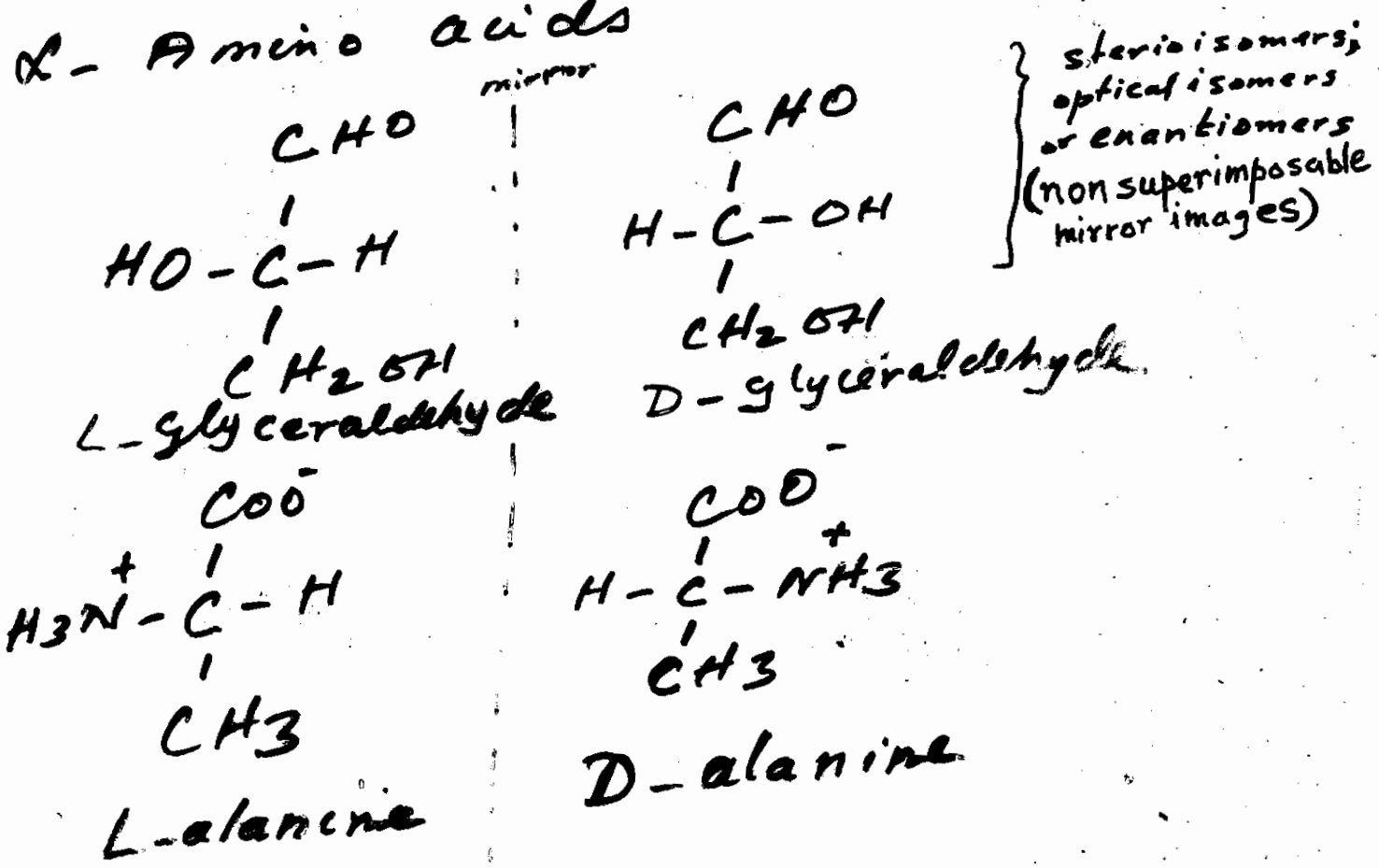


Zwitterionic form

Stereospecifity of Amino Acids

- Glycine is the only amino acid achiral - symmetrical
- Amino acids having an asymmetrical center at α-carbon exist in two forms D- + L- configuration
- All amino acids found in proteins are of the L-configuration

α- Amino acids



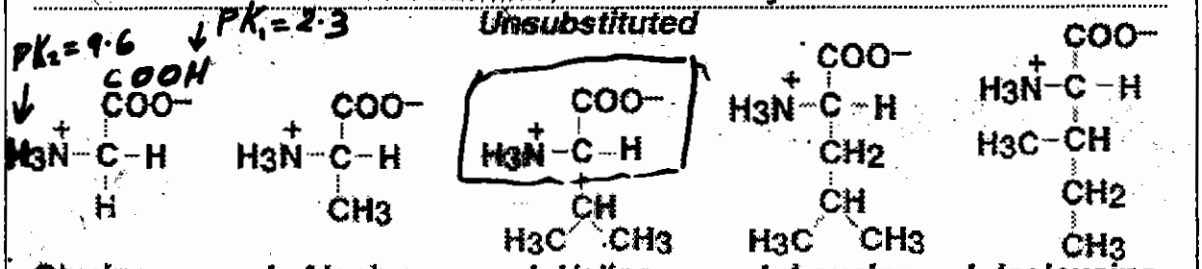
However, D-amino acids are found in few places:- some antibiotics and in bacterial (not plants) cell walls.

Structures of the Common Amino Acids

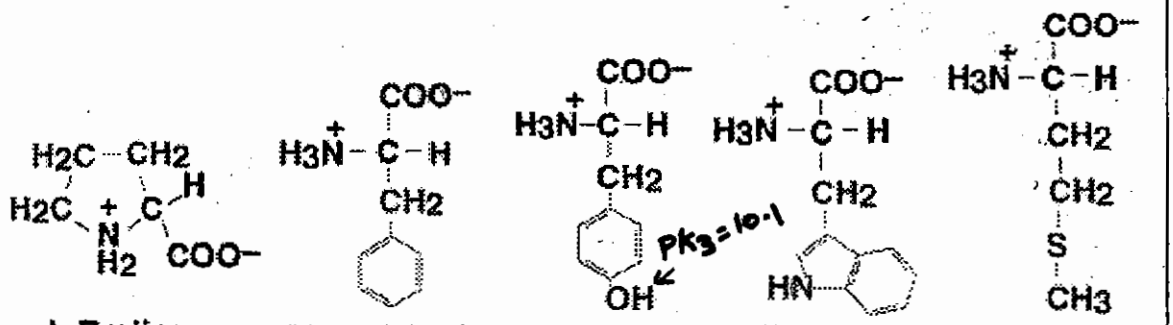
Non-Polar R

Monoamino, monocarboxylic

Unsubstituted



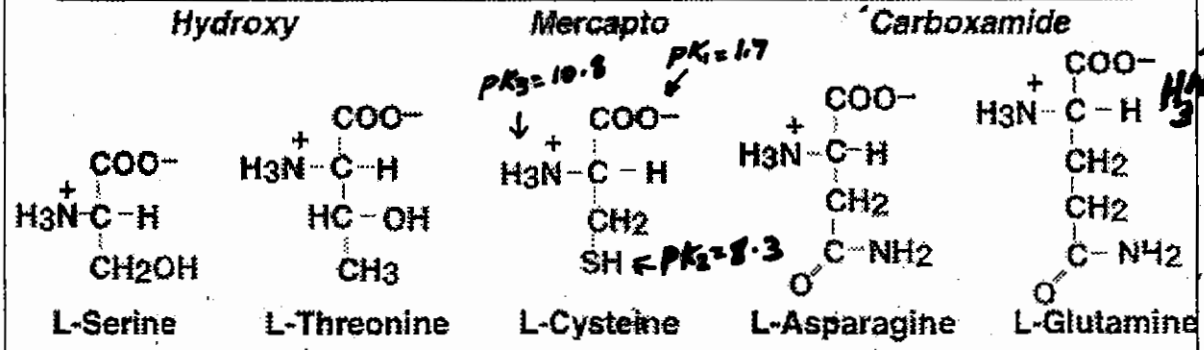
Heterocyclic *Aromatic* *Thioether*

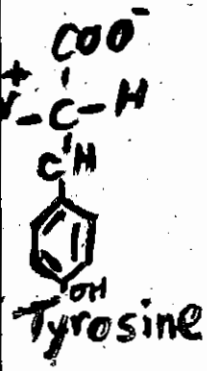


Polar

Uncharged Polar R:-

Hydroxy *Mercapto* *Carboxamide*

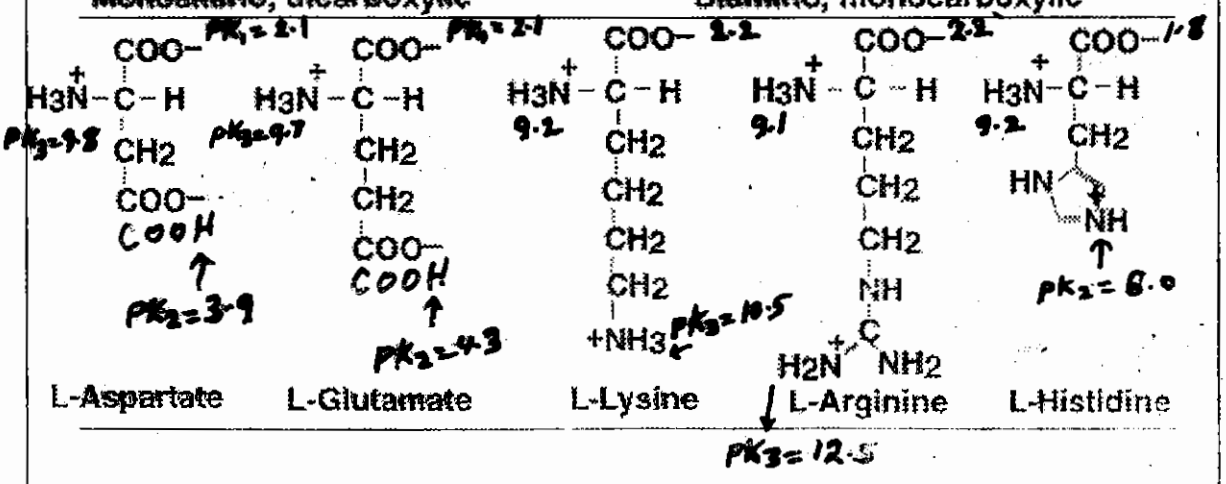




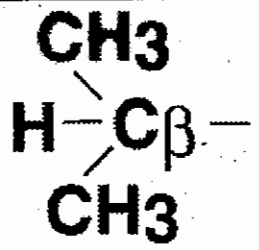
Polar-Charged:-

Acidic R **Basic R**

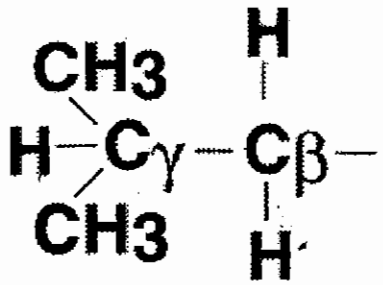
Monoamino, dicarboxylic **Diamino, monocarboxylic**



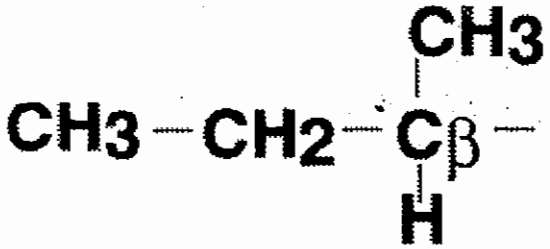
Alkyl Side chains of Branched Chain Amino Acids: Valine, Leucine + Isoleucine



Isopropyl R group of valine



Isobutyl R group of leucine



Isobutyl R group of isoleucine

Table 3.1

Table of abbreviations of the 20 amino acids found in proteins

Unique amino acids or most commonly occuring

Name	One-Letter Abbreviation	Three-Letter Abbreviation
Glycine*	G	Gly
Alanine*	A	Ala
Valine*	V	Val
Leucine*	L	Leu
Isoleucine*	I	Ile
Methionine*	M	Met
Phenylalanine	F	Phe
Proline*	P	Pro
Serine*	S	Ser
Threonine*	T	Thr
Cysteine*	C	Cys
Asparagine	N	Asn
Glutamine	Q	Gln
Tyrosine	Y	Tyr
Tryptophan	W	Trp
Aspartate	D	Asp
Glutamate	E	Glu
Histidine*	H	His
Lysine	K	Lys
Arginine	R	Arg

Table 3-1 Concepts in Biochemistry, 3/e

- Amino acids with nonpolar side chains
  1- location in the proteins
  2- Proline
     - Imino aminacid
     - contributes to fibrous structure of collage
     - interrupt the α- helical structure

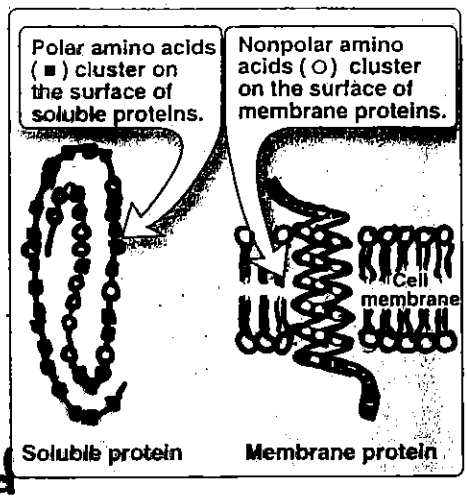


Figure 1.4
Location of nonpolar amino acids in soluble and membrane proteins.

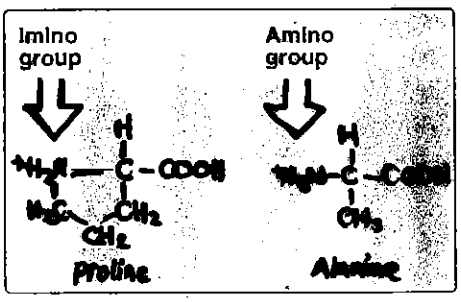


Figure 1.5
Comparison of the imino group found in proline with the α-amino group found in other amino acids, such as alanine.

- Amino acids with uncharged Polar Side chains
  Ser, thr, tyr, Asn, Gln participates in H-bondings

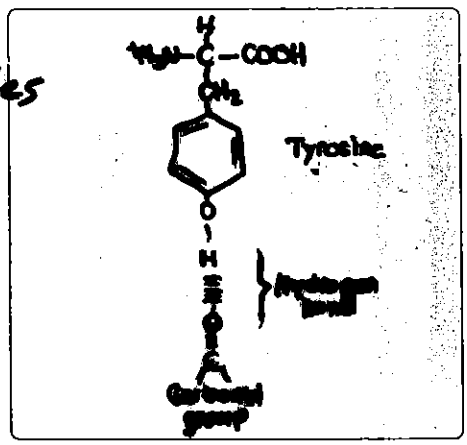


Figure 1.6
Hydrogen bond between the phenolic hydroxyl group of tyrosine and another molecule containing a carbonyl group.

- Side chains are sites of attachment for other compounds
  Ser & thr → phosphate
  Asn, ser, thr → oligosaccharides in glycoprotein

- Amino acids with acidic side chains

  Asp
  Glu → -ve charged ionized

- Amino acids with basic side chains

  Lys
  Arg → ionized +ve charged

  His → positively charged
  or
  neutral
  contribute to buffering action

- Disulfide bonds
  - Cys (-SH) is impt. component of the active site for many enzymes
  - -SH can be oxidized to form cystine

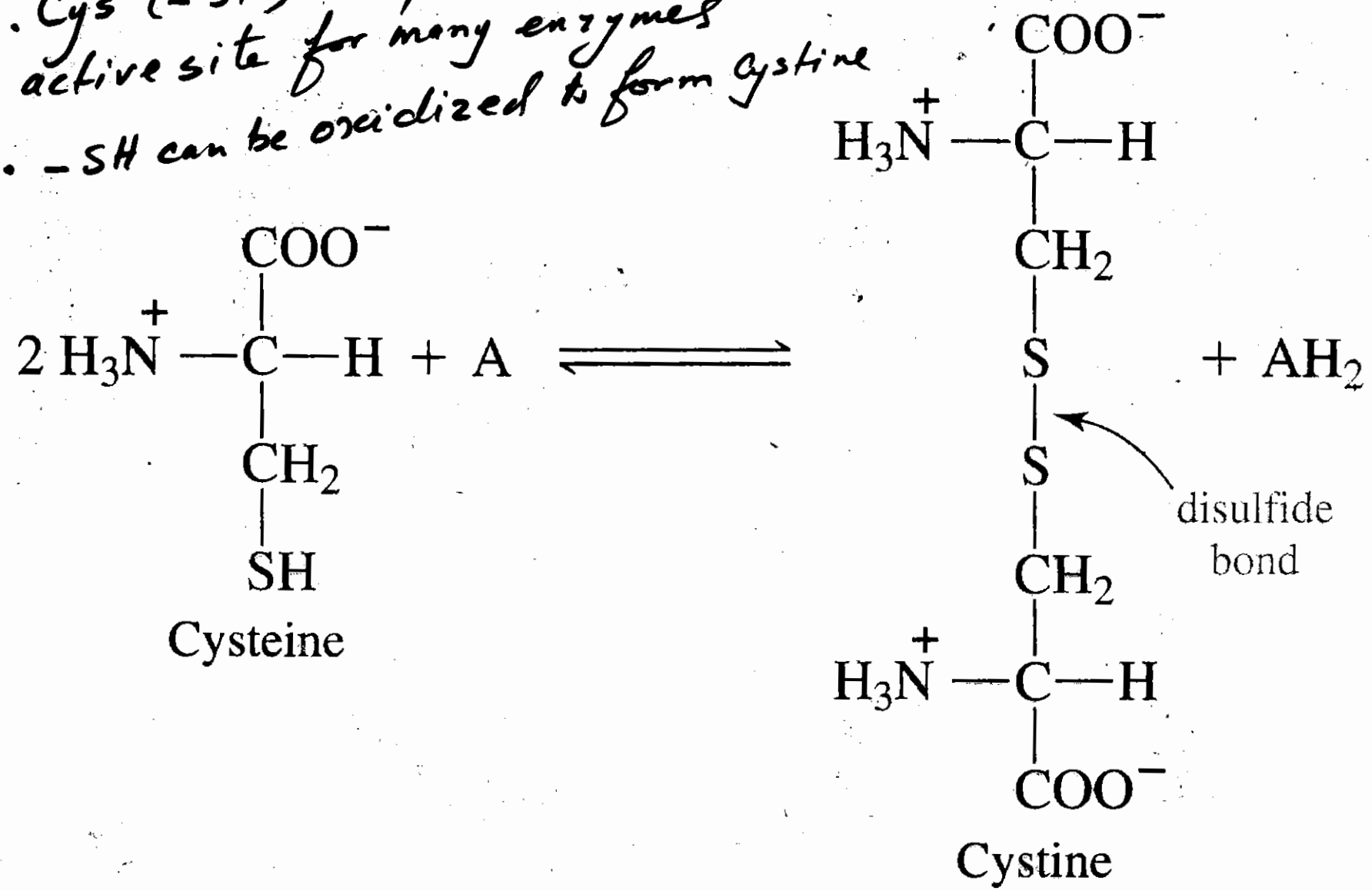


Figure 3-6 Concepts in Biochemistry, 3/e

DERIVED Amino Acids:

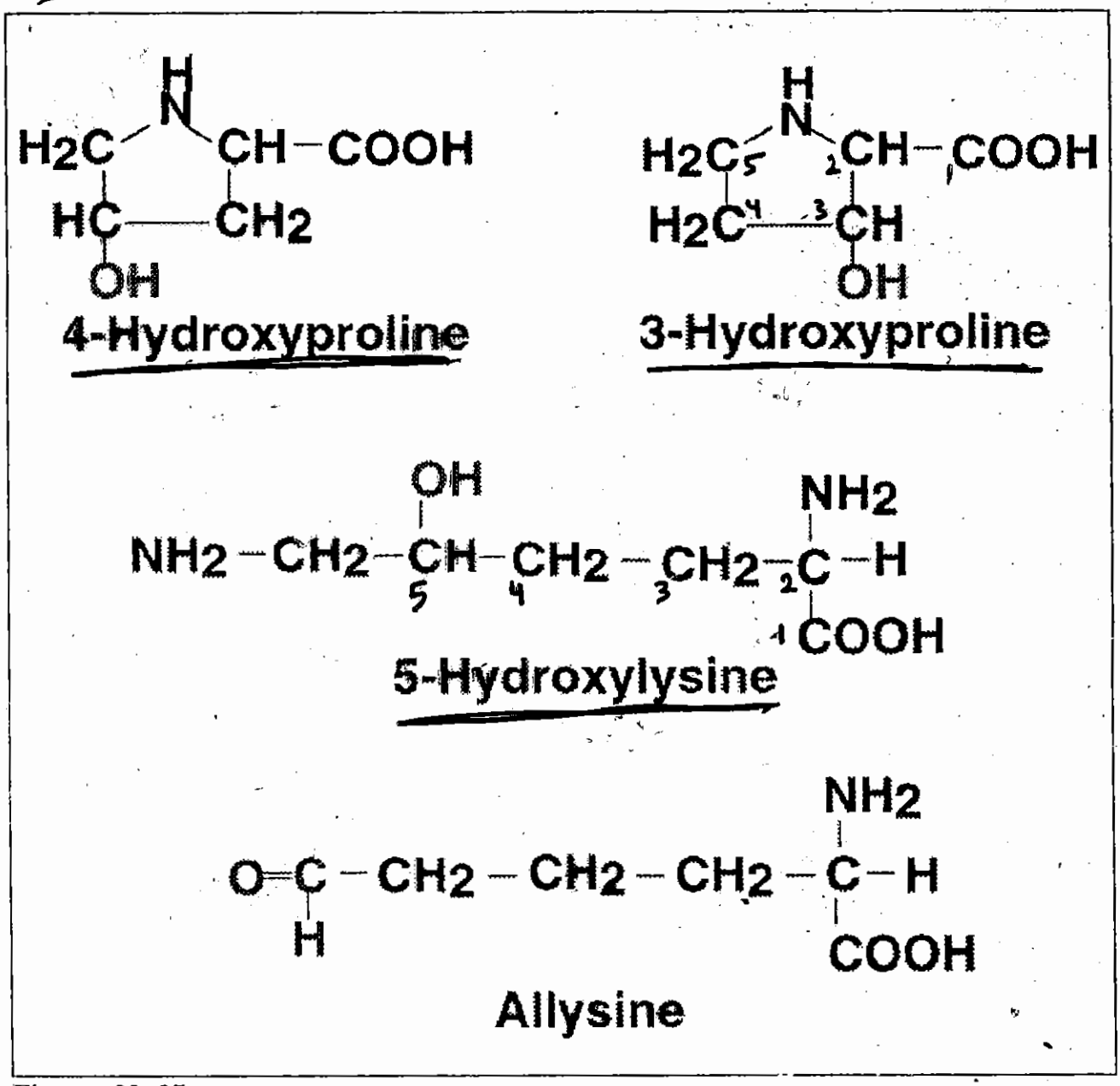
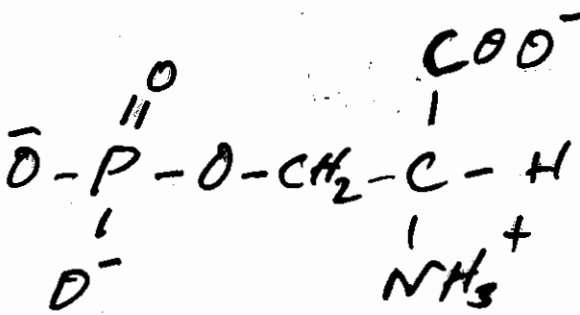
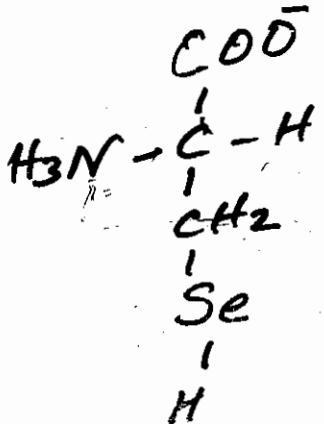


Figure: 02_37
Derived amino acids found in collagen.

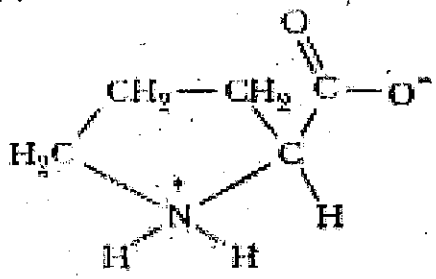


phospho serine
phosphotyrosine

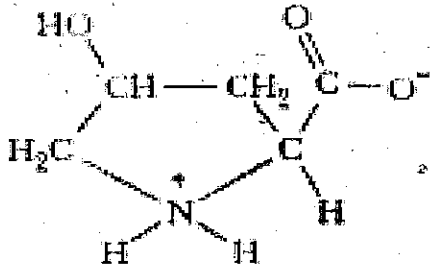


Selenocysteine

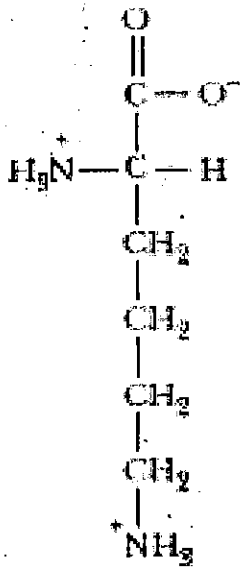
Derived Amino Acids



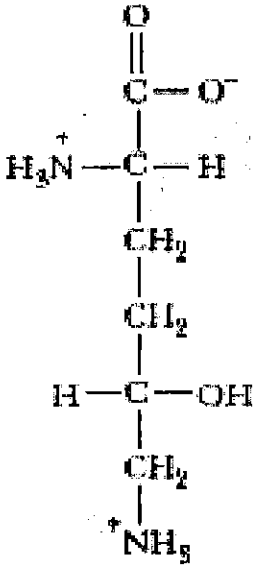
Proline



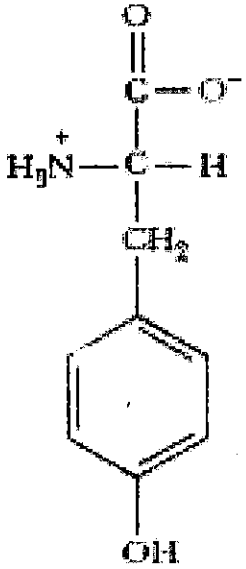
Hydroxyproline



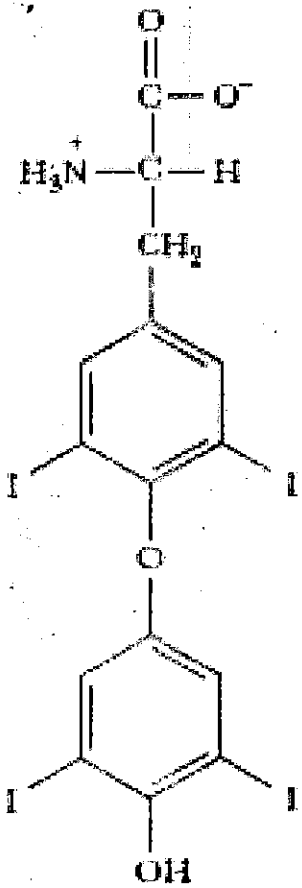
Lysine



Hydroxylysine



Tyrosine



Thyroxine

Fig 3.11

Amino Acids as Acids and Bases

- Ionization of the $-NH_3^+$ and the -COOH group
- Zwitterion has both +ve and -ve charge
- Zwitterion is neutral overall

$NH_3^+-CH_2-COOH \longrightarrow H_3\overset{+}{N}-CH_2-COO^-$

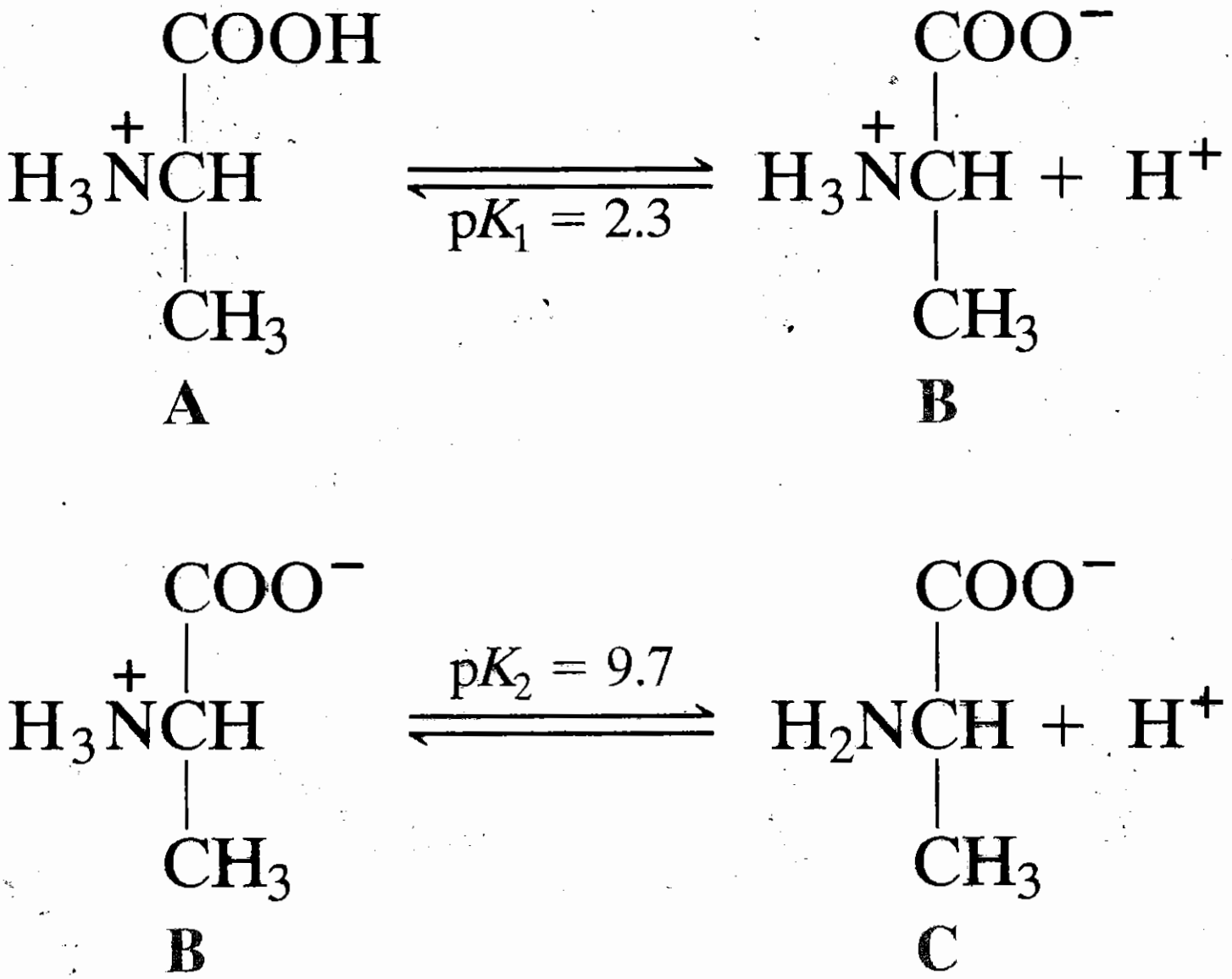
glycine — Zwitterion of glycine at neutral pH

pH and ionization of amino acids

$H_3\overset{+}{N}-CH_2-COOH \xleftarrow{H^+} H_3\overset{+}{N}-CH_2-COO^- \xrightarrow{OH^-} H_2N-CH_2-COO^-$

Positive ion	zwitterion	Negative ion
Low pH	neutral pH	High pH

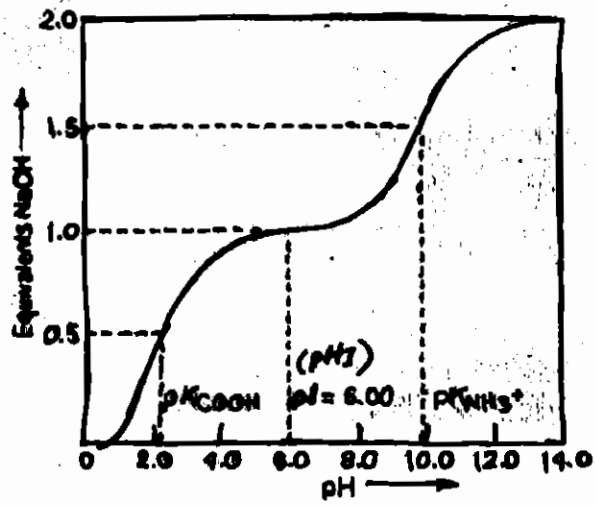
Titration for mono amino mono carboxylic acid (Alanine)



Unnumbered figure pg 66 Concepts in Biochemistry, 3/e

Titration of mono amino mono Carboxylic acid 3

Determination of PI



$$PI = \frac{pKa\ COOH + pKa\ NH_3^+}{2} = \frac{2.4+9.6}{2} = 6.0$$

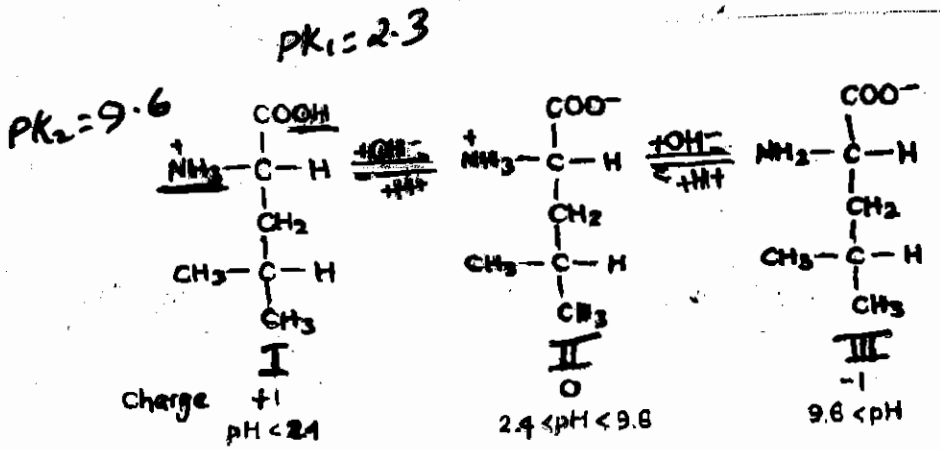
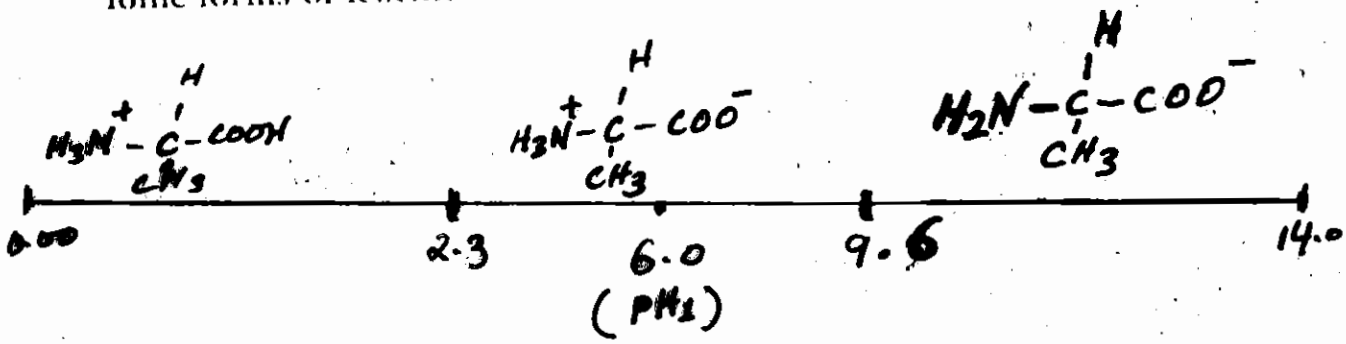
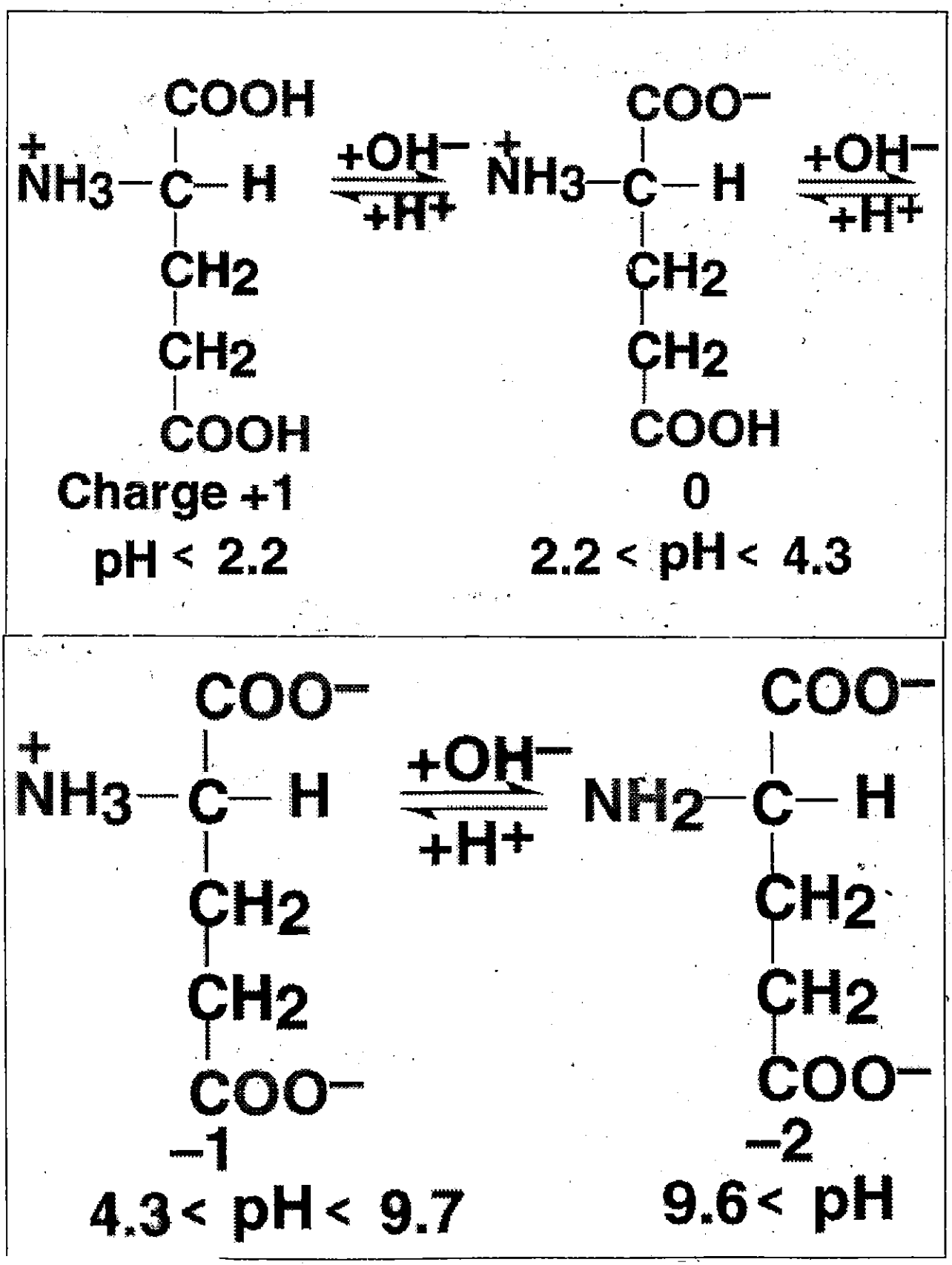


FIGURE 2.14
Ionic forms of leucine.



Ionic Forms of Glutamic Acid.



Titration Curve for Glutamic acid

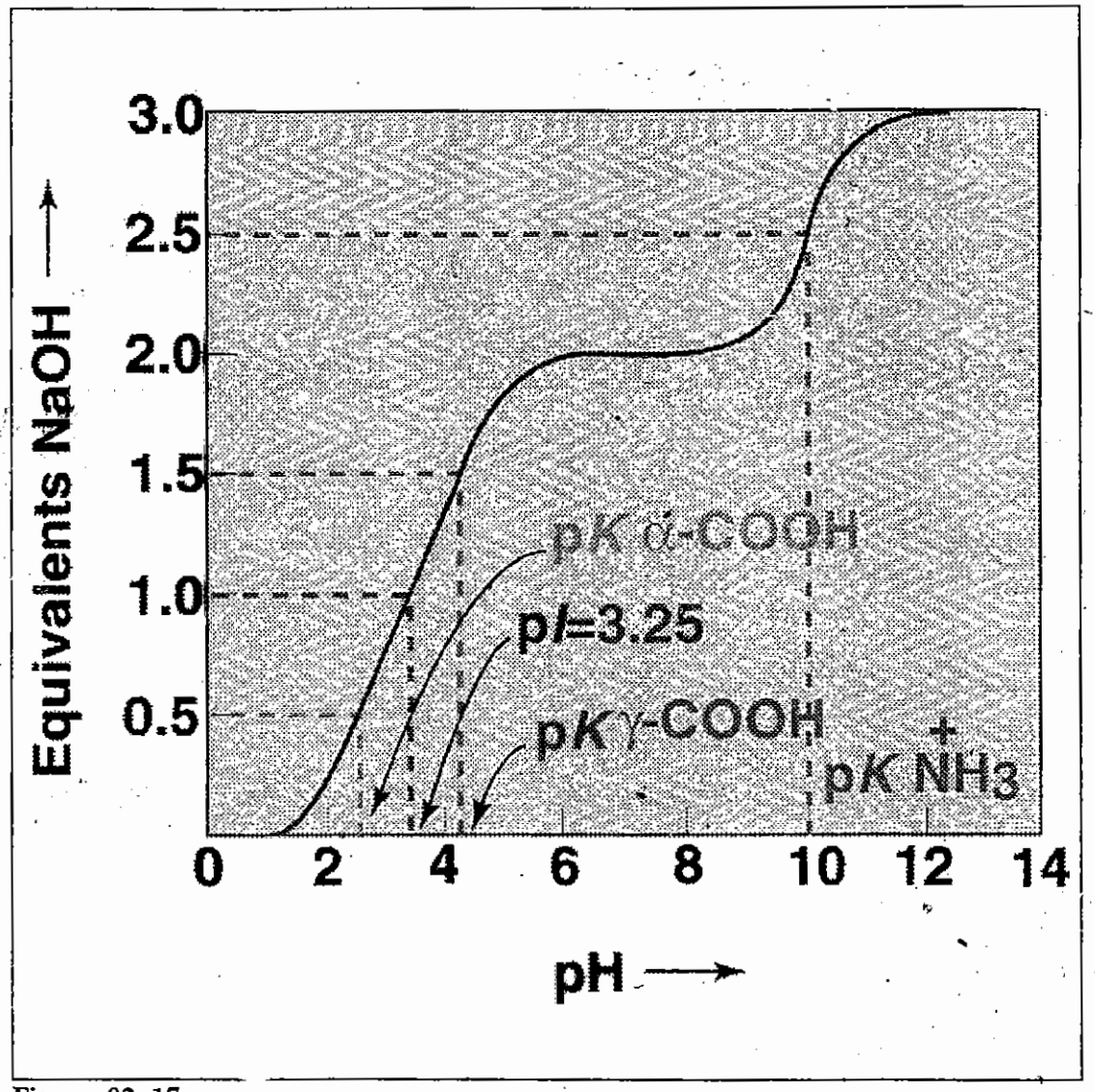
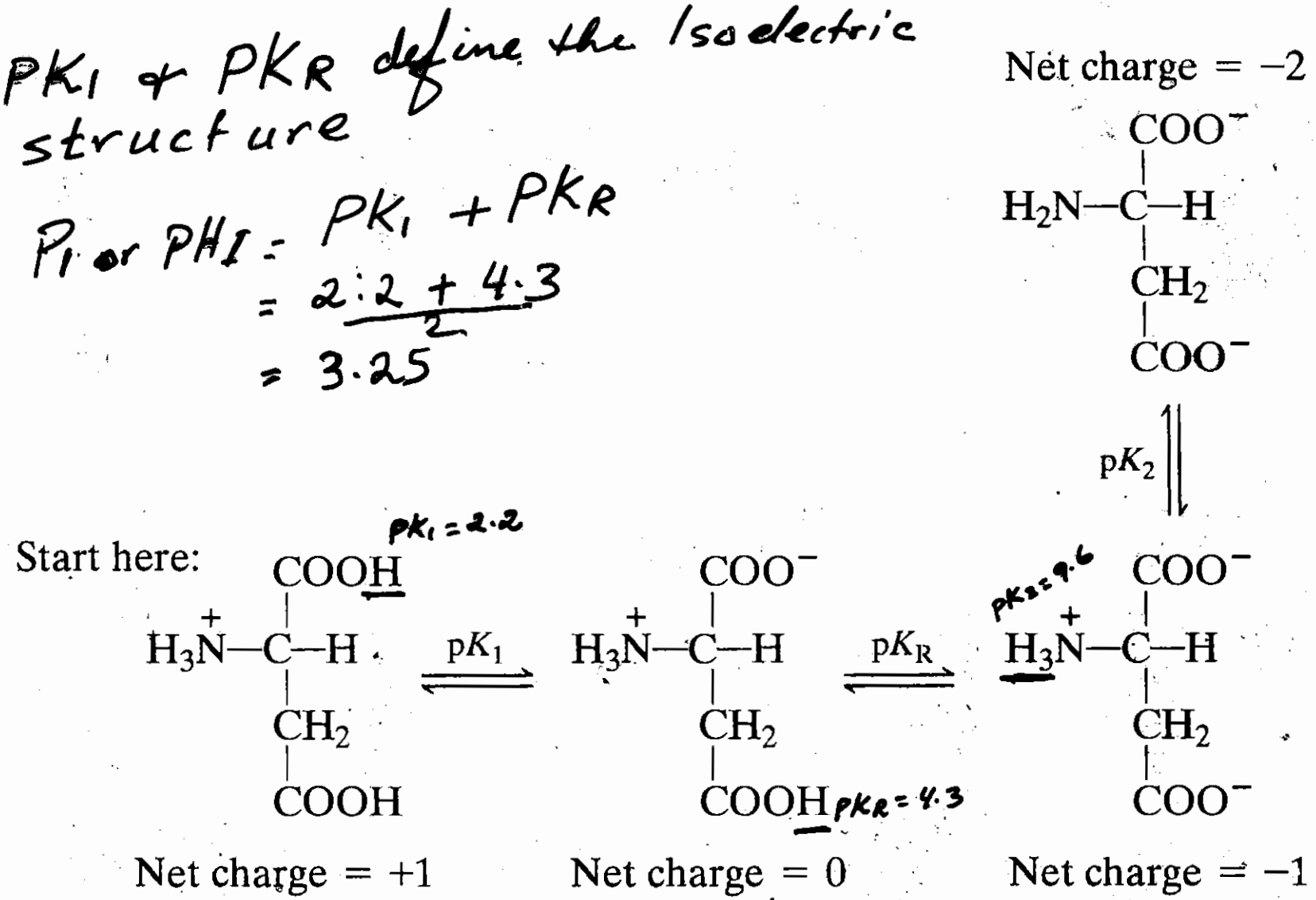


Figure: 02_17
Titration curve of glutamic acid.

$$P_I = \frac{2.2 + 4.3}{2} = 3.25$$

pK_1 & pK_R define the Isoelectric structure

$$P_I \text{ or } pH_I = \frac{pK_1 + pK_R}{2} = \frac{2.2 + 4.3}{2} = 3.25$$



Predominat species between pH 2.2 and 4.3

Titration Curve for Histidine 7

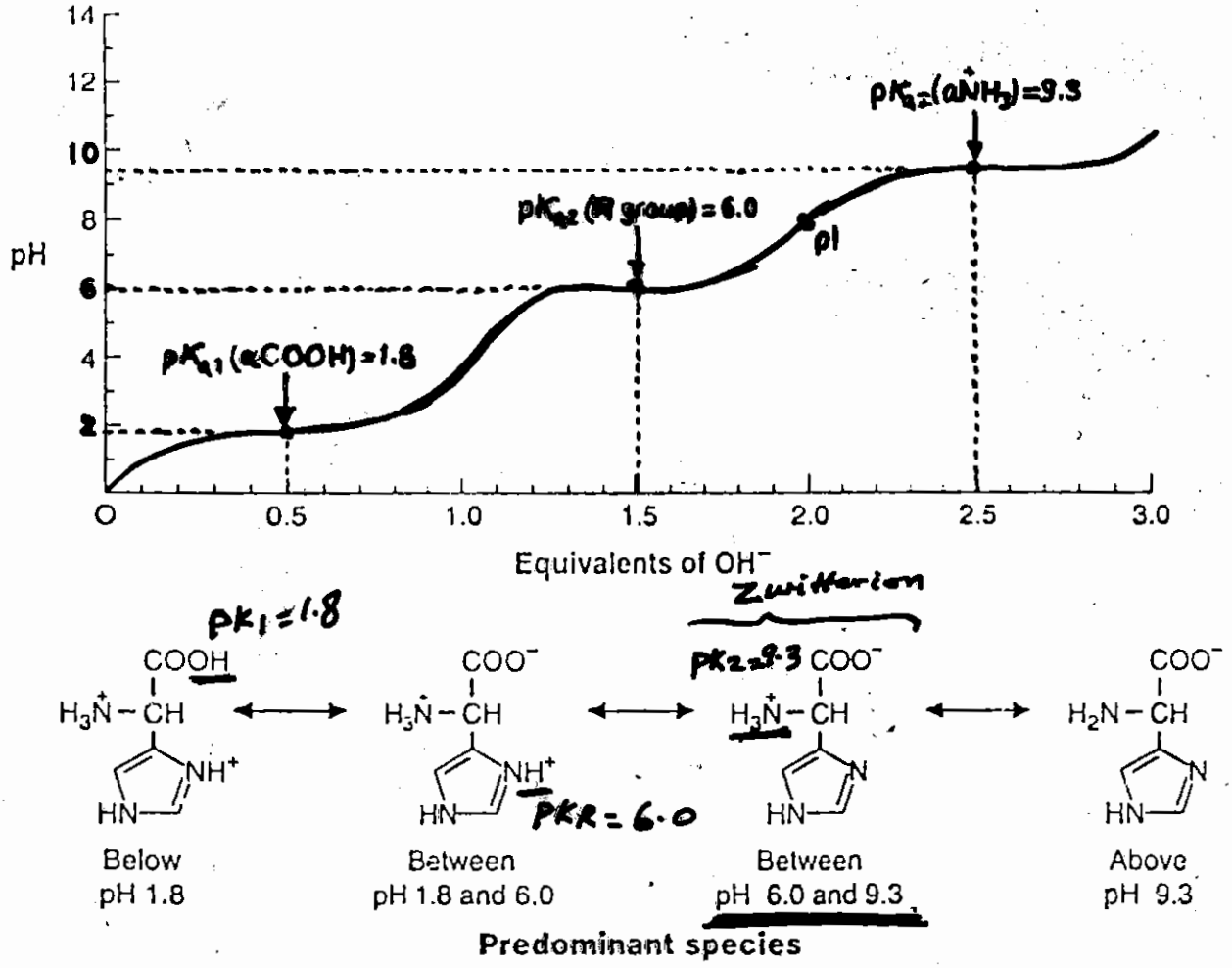


Fig. 7.17. Titration curve of histidine. The ionic species that predominates in each region is shown below the graph. pI is the isoelectric point (at which there is no net charge on the molecule).

$$P_I \; (PHI) = \frac{6.0 + 9.3}{2} = 7.65$$

Dissociation of the side-chains of Amino acids.

at pH equal to the pKa indicated

Conjugate base / Acid = 1

$$pH = pKa + \log \frac{[A^-]}{[HA]}$$

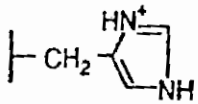
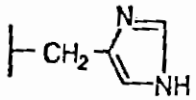
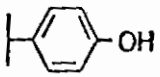
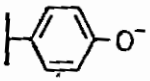
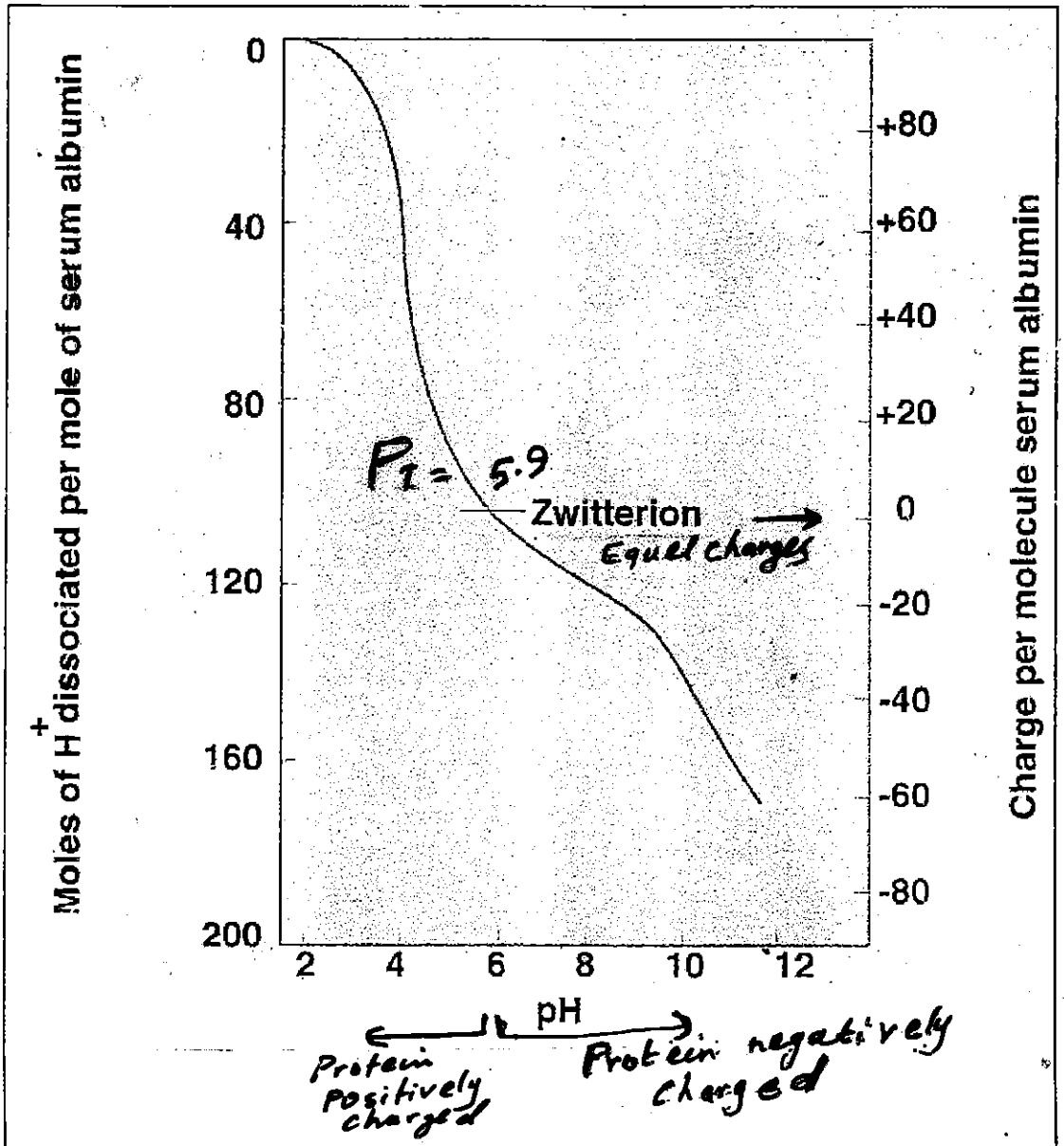
	Form that predominates below the pK_a	pK_a (Both are Equal)	Form that predominates above the pK_a
Aspartate	$-CH_2-COOH$	3.9	$-CH_2-COO^-$ + H^+
Glutamate	$-CH_2-CH_2-COOH$	4.1	$-CH_2-CH_2-COO^-$ + H^+
Histidine		6.0	 + H^+
Cysteine	$-CH_2SH$	8.4	$-CH_2S^-$ + H^+
Tyrosine		10.5	 + H^+
Lysine	$-CH_2-CH_2-CH_2-CH_2-\overset{+}{N}H_3$	10.5	$-CH_2-CH_2-CH_2-CH_2-NH_2$ + H^+
Arginine	$-CH_2-CH_2-CH_2-NH-C(=\overset{+}{N}H_2)-NH_2$	12.5	$-CH_2-CH_2-CH_2-NH-C(=NH)-NH_2$ + H^+

Fig. 7.15. Dissociation of the side chains of the amino acids. As the pH increases, the charge on the side chain goes from 0 to − or from + to 0. The pK_a is the pH at which half the molecules of an amino acid in solution have side chains that are charged. Half are uncharged.

Titration Curve of Human Serum ALBUMIN and its Relationship with charges



pH > p*I*, then protein charge negative
pH < p*I*, then protein charge positive

Protein	PI
Pepsin	~1.0
HbA	7.1
Ribonuclease	7.8
Cyt. C	10.0

Proteins Can be Separated based on their different PI values 10

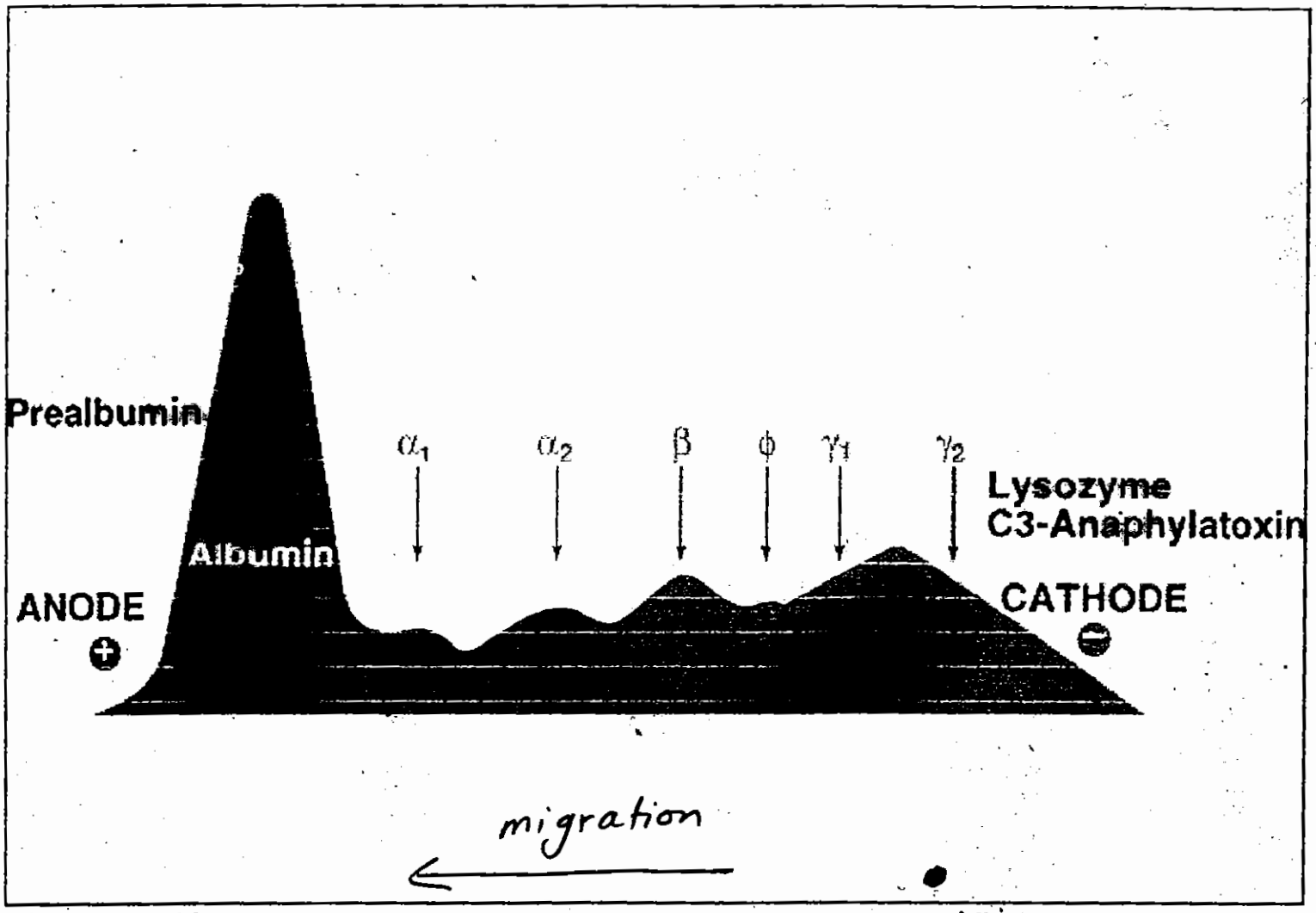


Figure: 02_20a.
Electrophoresis pattern for plasma proteins at pH 8.6.

Titration Curve for Histidine

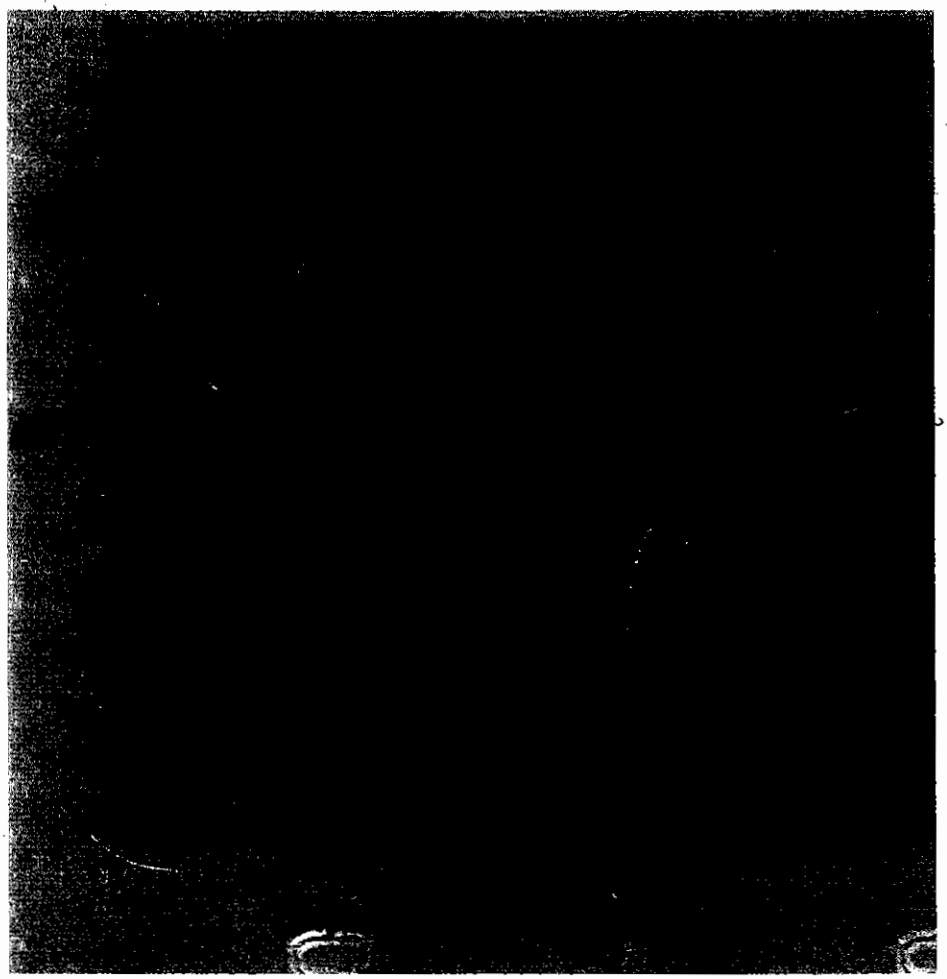


Fig 3.7 : The titration curve of Histidine .

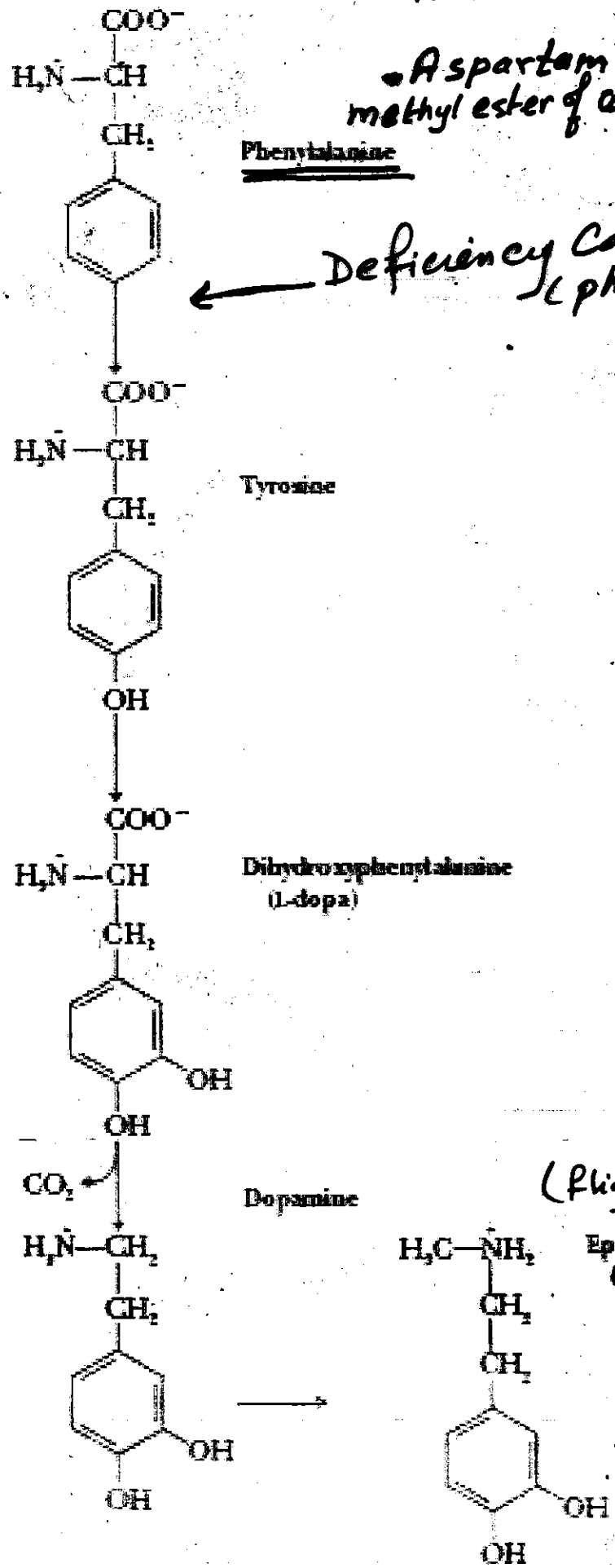
The isoelectric pH (pI) is the value at which positives and negative charges are the same. The molecule has no net charge.

$$P_I\ (pH_I) = \frac{6.0 + 9.2}{2} = 7.6$$

Some Special Products of Amino Acids

1

- Aspartam (Diet sweetner):- methyl ester of aspartyl-phenylalanine dipeptide



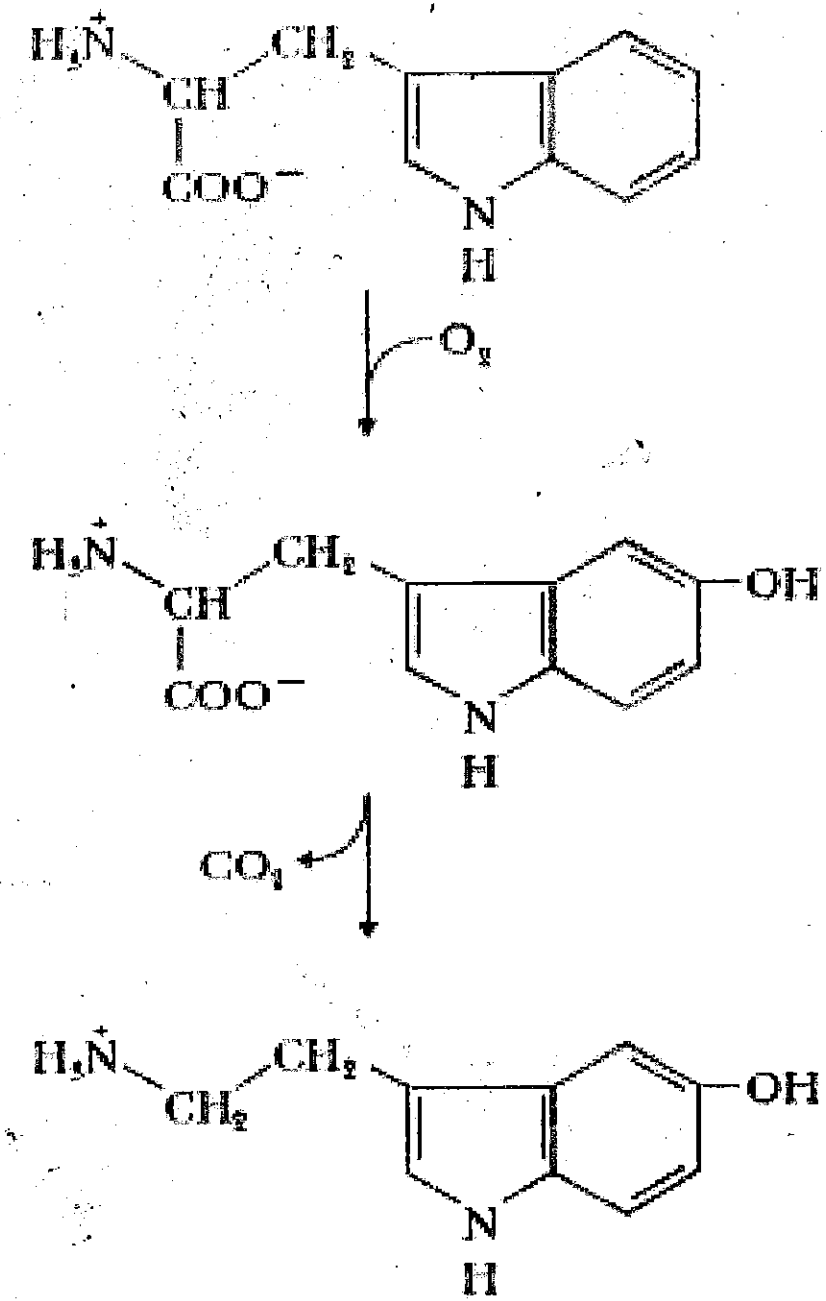
Deficiency causes PKU (phenyl ketonuria)

(flight or fight hormone)

→ Norepinephrine

Stimulatory hormones

- Release of glucose

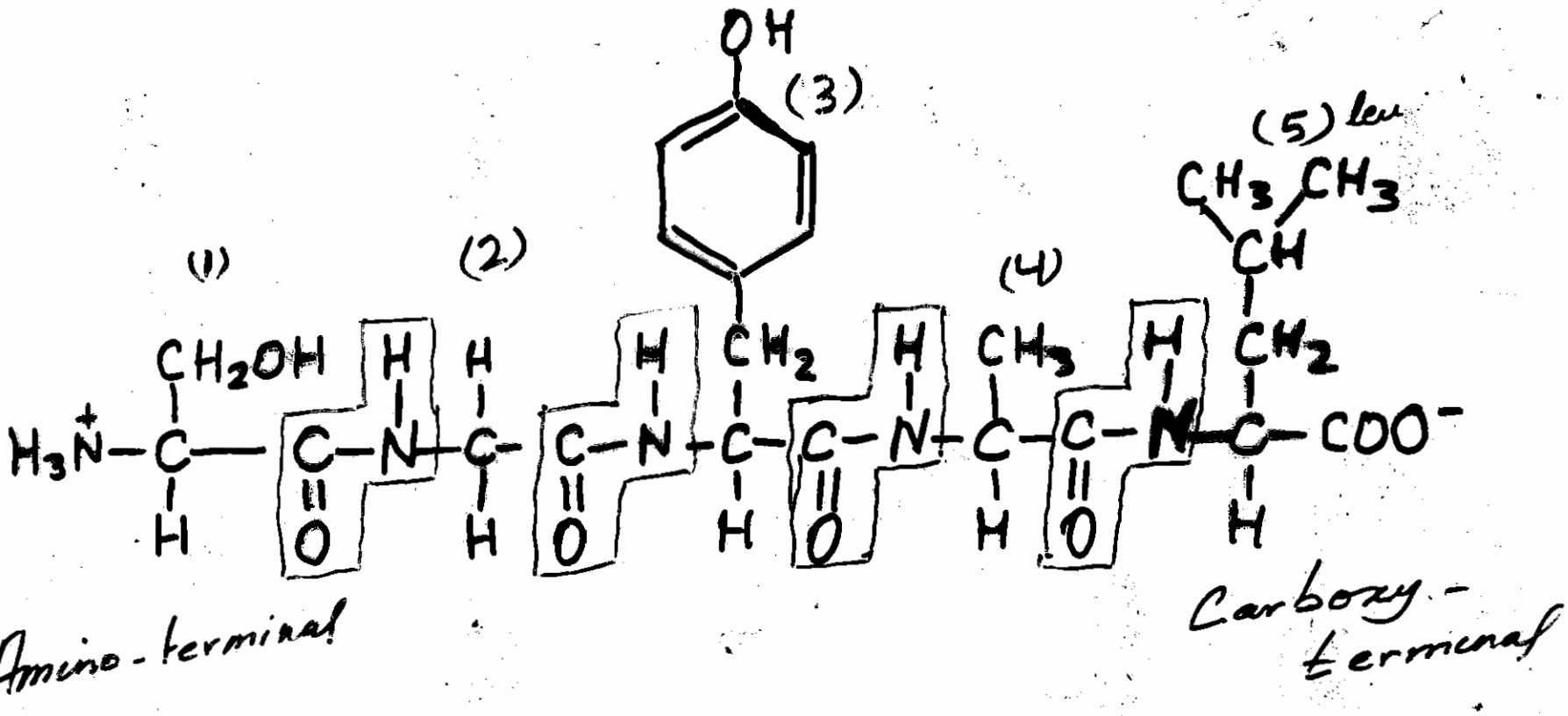


Tryptophan high in milk proteins

5-Hydroxytryptophan

Serotonin → sedative effect

. plays some role in SIDS

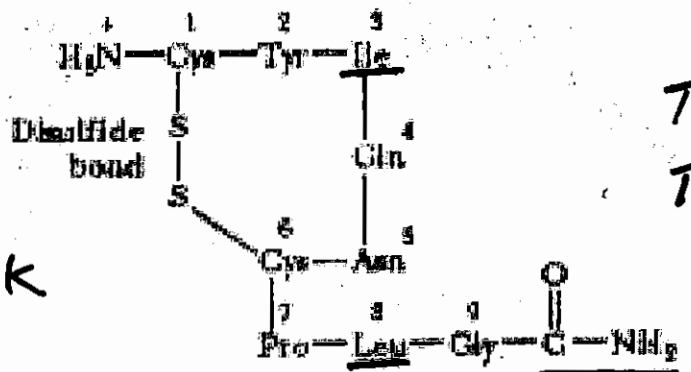

(1)
(2)
(3)
(4)
(5) leu
Amino-terminal
Carboxy-terminal

Cyclic Peptides :-

- Oxytocin

Induces contraction

- contraction of uterine muscle during Labor
- mammary glands to contract → milk

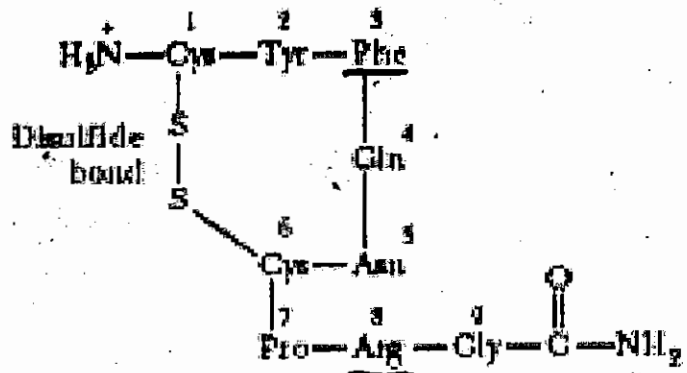


amide terminal

- Vasopressin

- secreted by the posterior hypothalamus

- Antidiuretic
- Increases blood pressure
- social behavior



amide terminal

Two Pentapeptides

Leu-enkephalin
Met-enkephalin

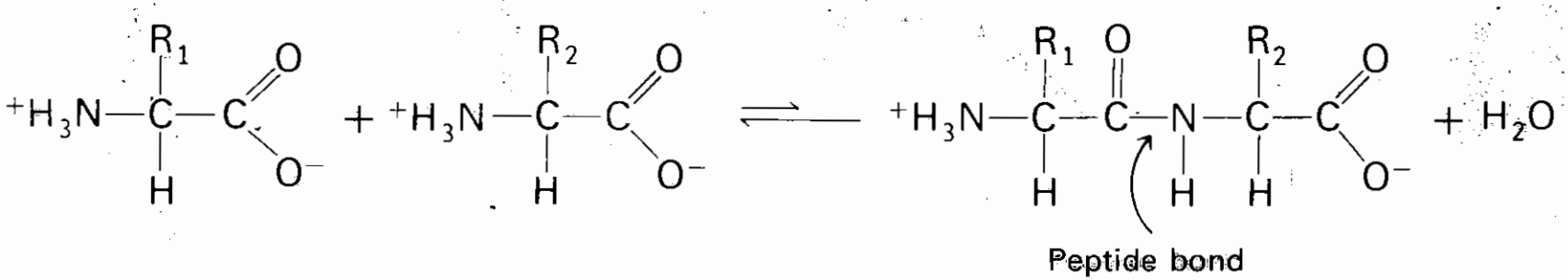
Tyr-Gly-Gly-phe-leu
Tyr-Gly-Gly-phe-Met

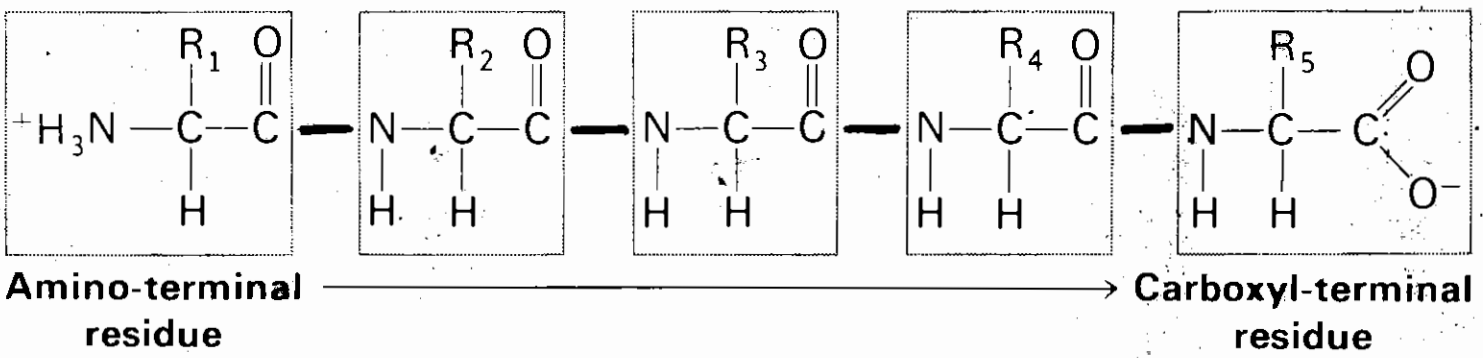
- in the brain
- Analgesics
- opiates as morphin

bind the same enkephaline receptors

Fig 3.12

Formation of the Peptide bond

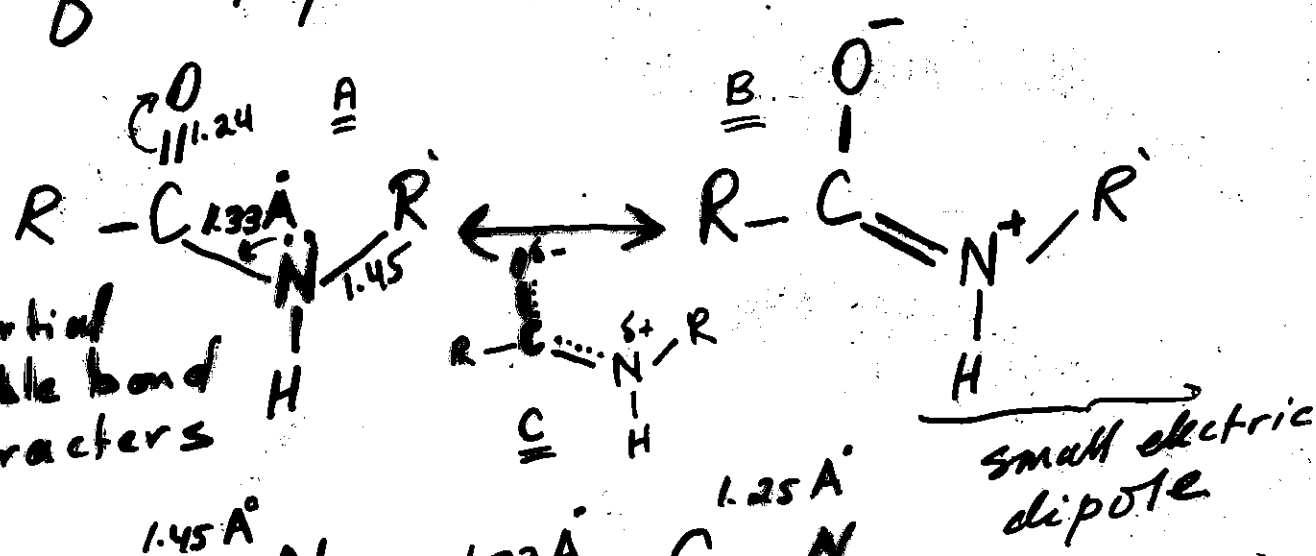




Figures 2-20 and 2-21, page 24

PEPTIDE BONDS

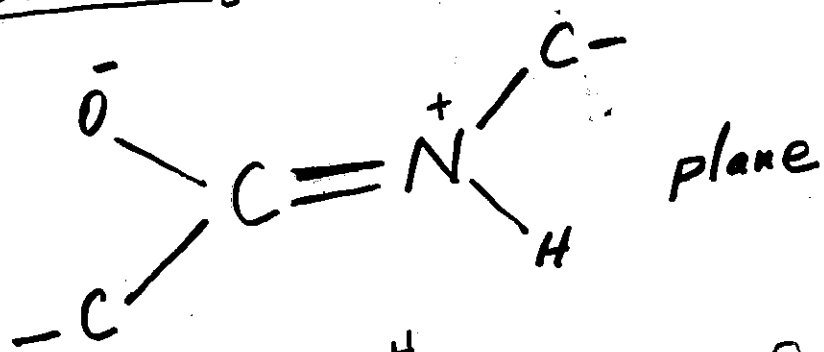
- Electronic Isomer Structures of a Peptide bond. (Resonance forms)

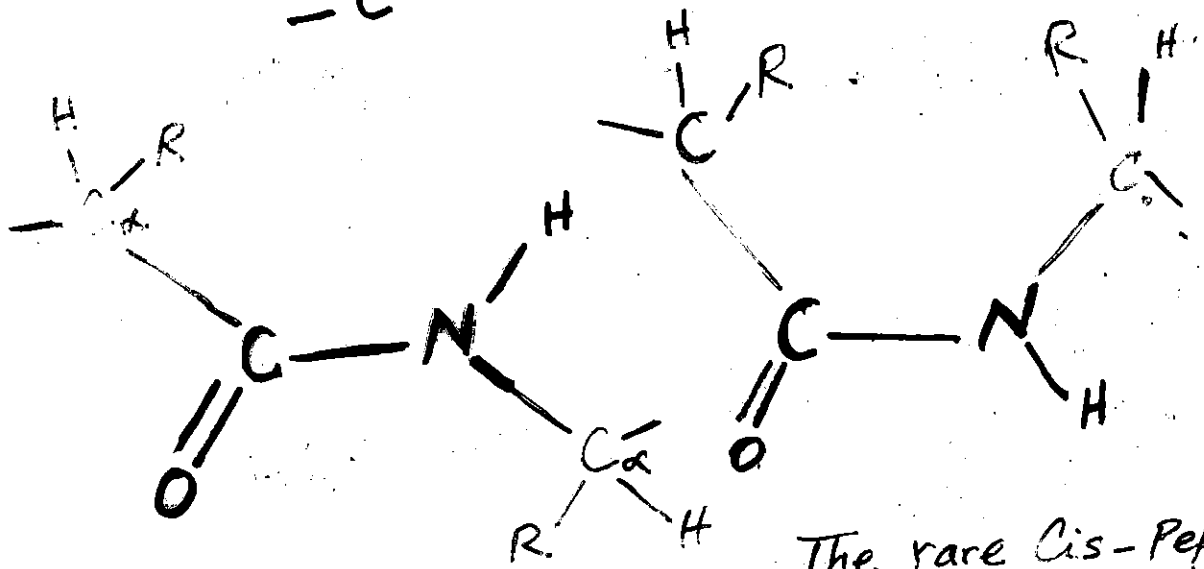


- Partial double bond characters

$C \overset{1.45Å}{—} N$ $\quad$ 1.33Å $\quad$ $C = N$ $\quad$ 1.25Å

- The Peptide Unit is Rigid and planer





- trans-peptide bond configuration in all proteins

The rare Cis-Peptide bond Configuration - steric interference of R-groups

Amino Acid Residue

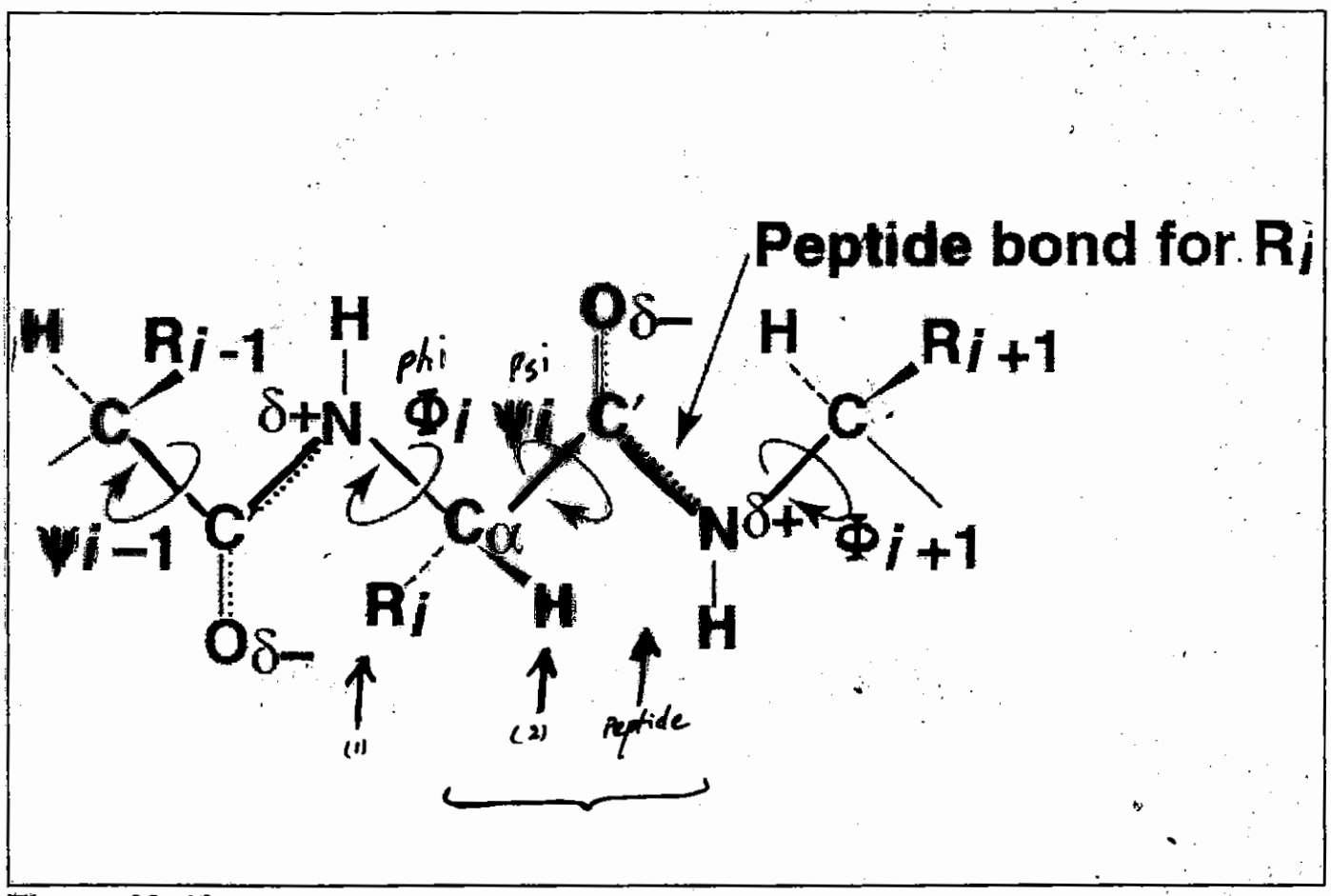
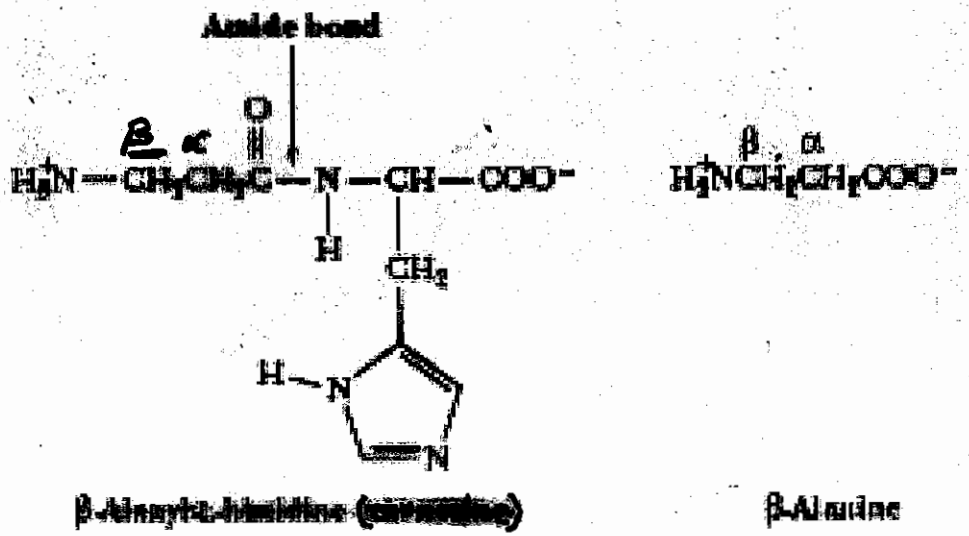


Figure: 02_10
Each amino acid residue of a polypeptide contributes two single bonds and one peptide bond to the chain.

Small peptides with Biological Functions

Carnosine : dipeptide
present plenty i muscle, activates myosin contraction



Glutamic acid
MSG – monosodium Glutamate, flavor enhancer
. may cause physiological reactions :- chills, headaches, dizziness (chinese restaurent syndrome)

Histamine : . decarboxylated histidine
. Potent vasodilator

Fig 3-11

PEPTIDES

Amino Acids Linked by Amide (Peptide) bonds

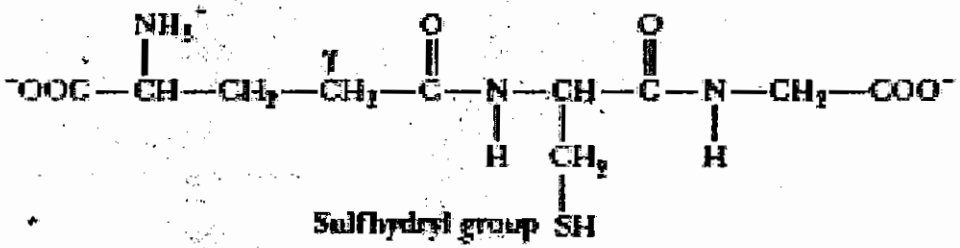
Ala — Gly — Glu — Phe — Ser — Lys

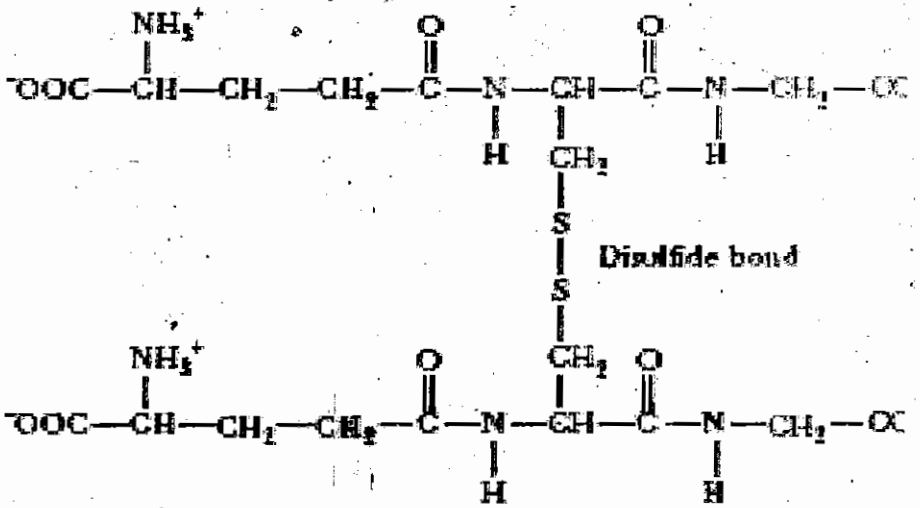
Peptide bonds

Alanyl Glycyl Glutamyl phenylalanyl seryl lysine

Oxⁿ & Redⁿ of Glutathione (GSH)

- Antioxidant Effect





Reaction of 2GSH to give GSSG

Gramicidin S and Tyrocidine A

Cyclic decapeptide (10 a.a.) containing D- & L-amino acids and ornithine (a.a. does not occur in proteins)

Fig 3.12

Vit D

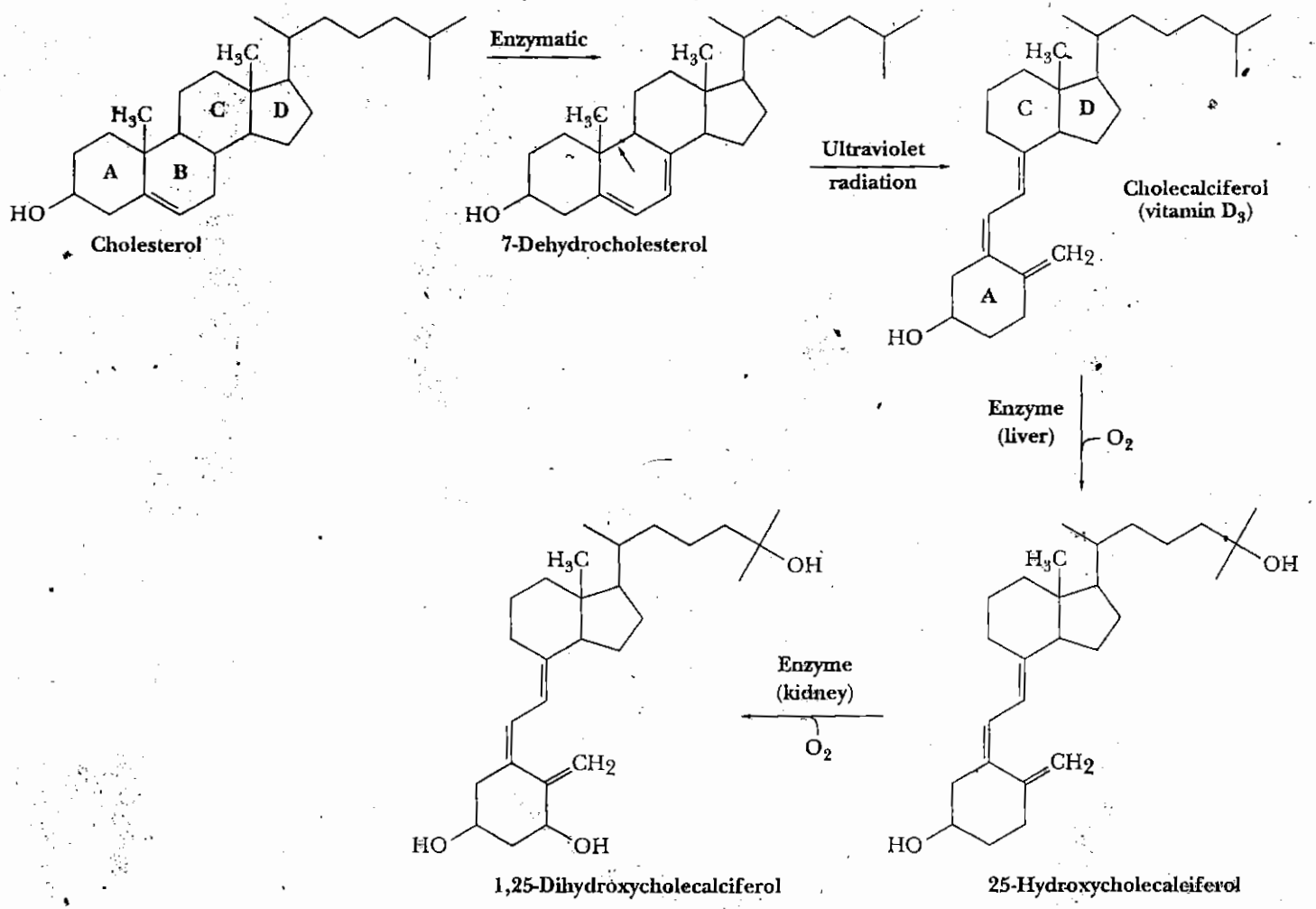
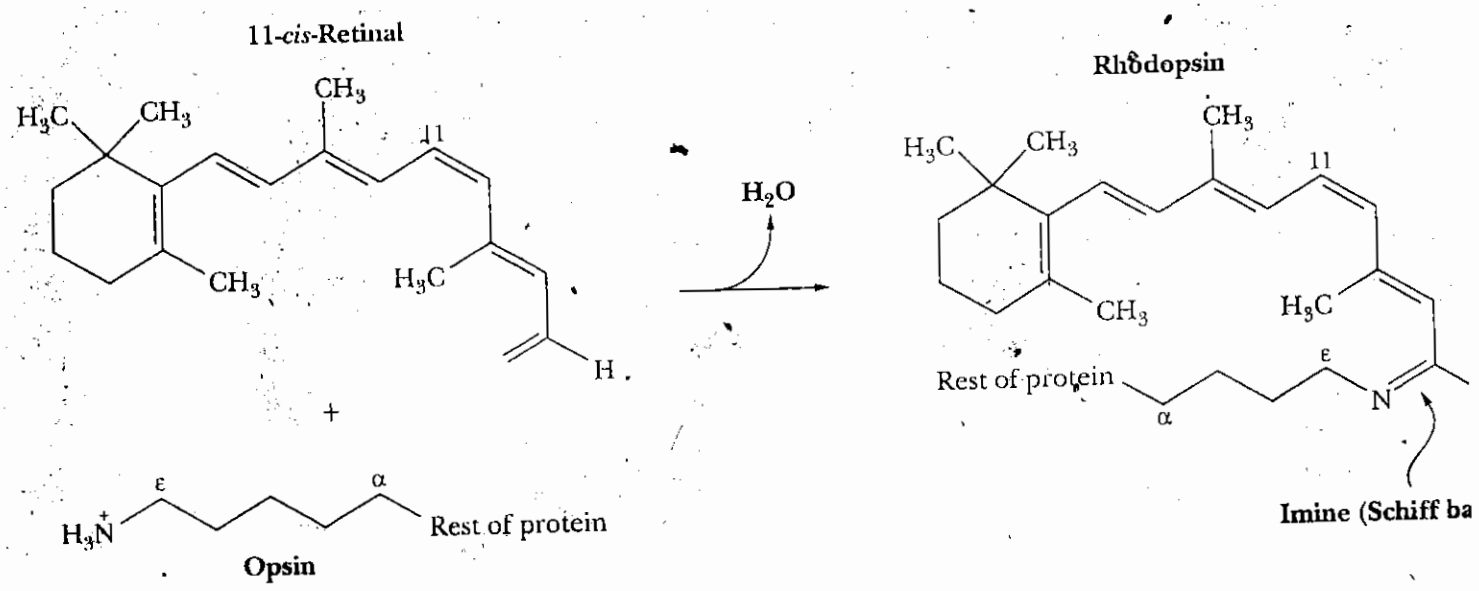


FIGURE 8.31 Reactions of vitamin D. The photochemical cleavage occurs at the bond shown by the arrow; electron rearrangements after the cleavage produce vitamin D_3. The final product, 1,25-dihydrocholecalciferol, is the form of the vitamin that is most active in stimulating the intestinal absorption of calcium and phosphate and in mobilizing calcium for bone development.



■ FIGURE 8.30 The formation of rhodopsin from 11-*cis*-retinal and opsin.

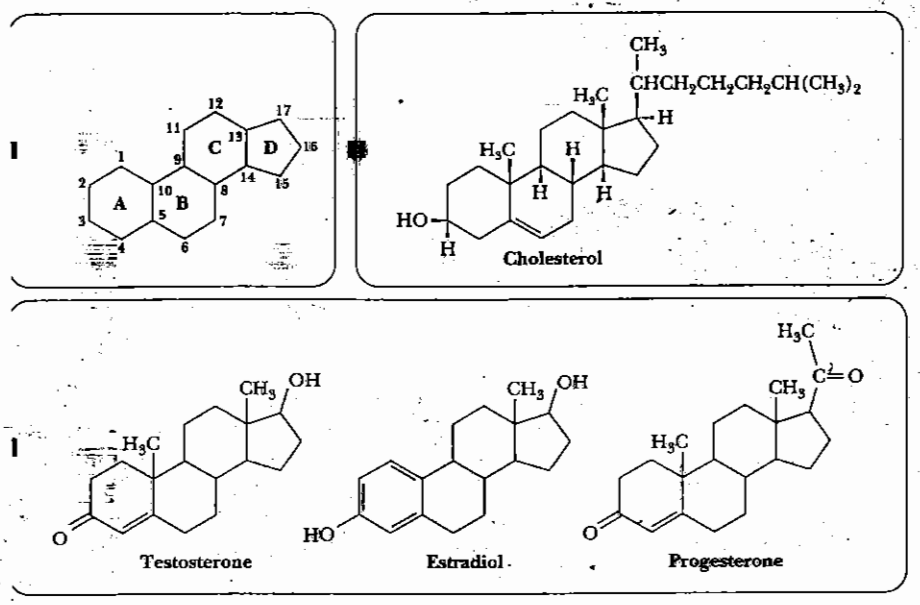
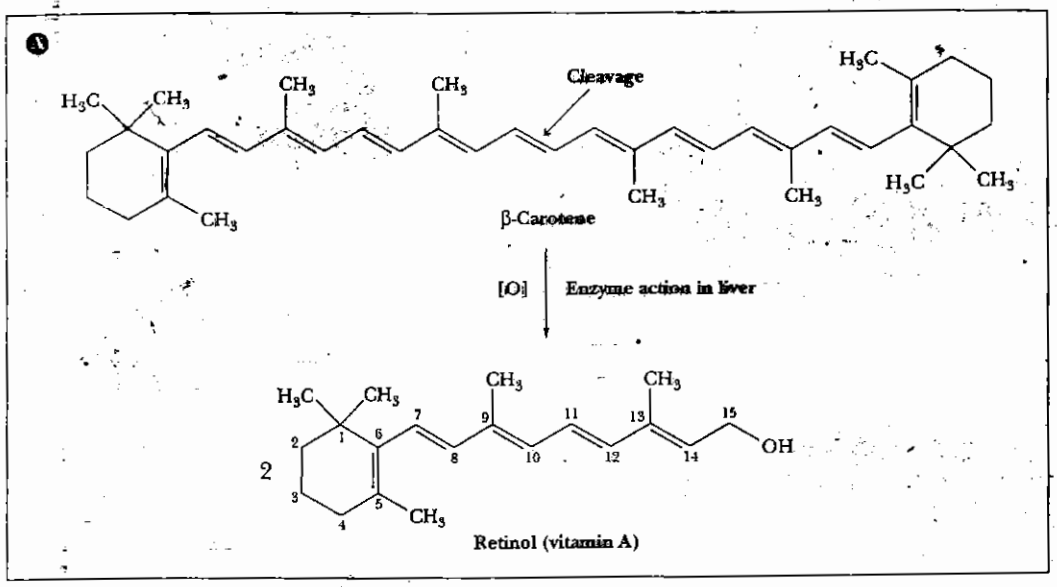
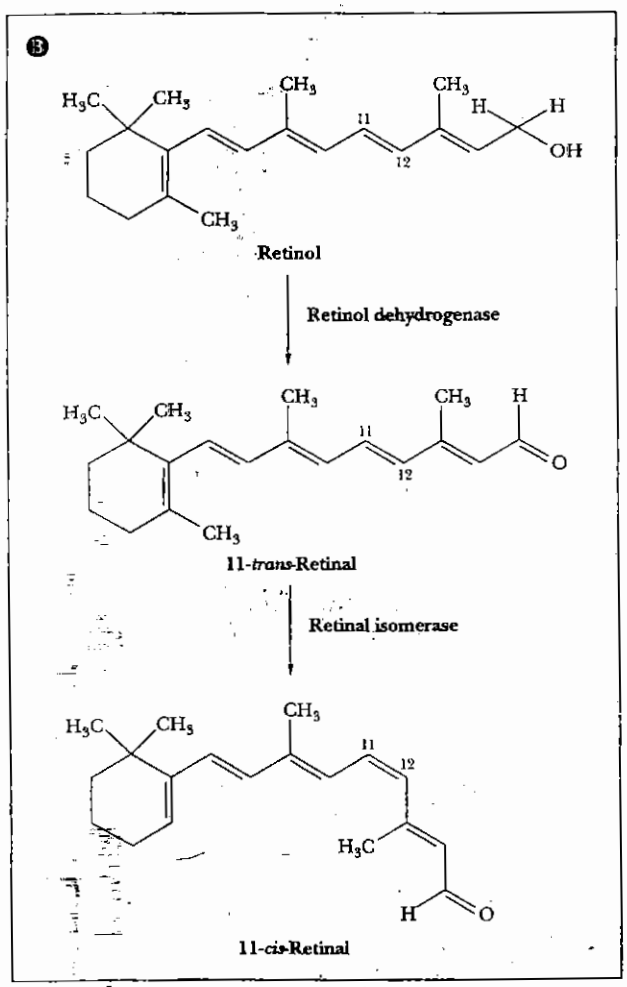


FIGURE 8.9 Structures of some steroids. (1) The fused-ring structure of steroids. (2) Cholesterol. (3) Some steroid sex hormones.

Vit A





■ **FIGURE 8.29 Reactions of vitamin A.** (a) The conversion of β-carotene to vitamin A. (b) The conversion of vitamin A to 11-*cis*-retinal.