BT351

Amino acids

Amino Acids

Organic compounds containing an amino group and an acidic group (usually, but not always, a carboxylic acid)

Amino Acid Biology

Biological roles:

1. Amino acids can be metabolized to **produce energy**.

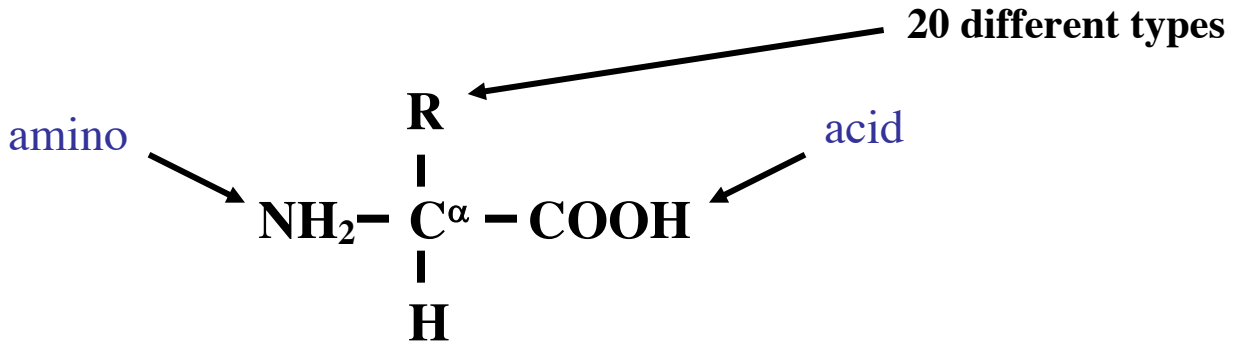
2. Some amino acids act as **neurotransmitters**, and some act as starting materials for the **biosynthesis** of neurotransmitters, hormones, and a wide variety of other important biochemical compounds.

3. The primary building blocks for **proteins**.

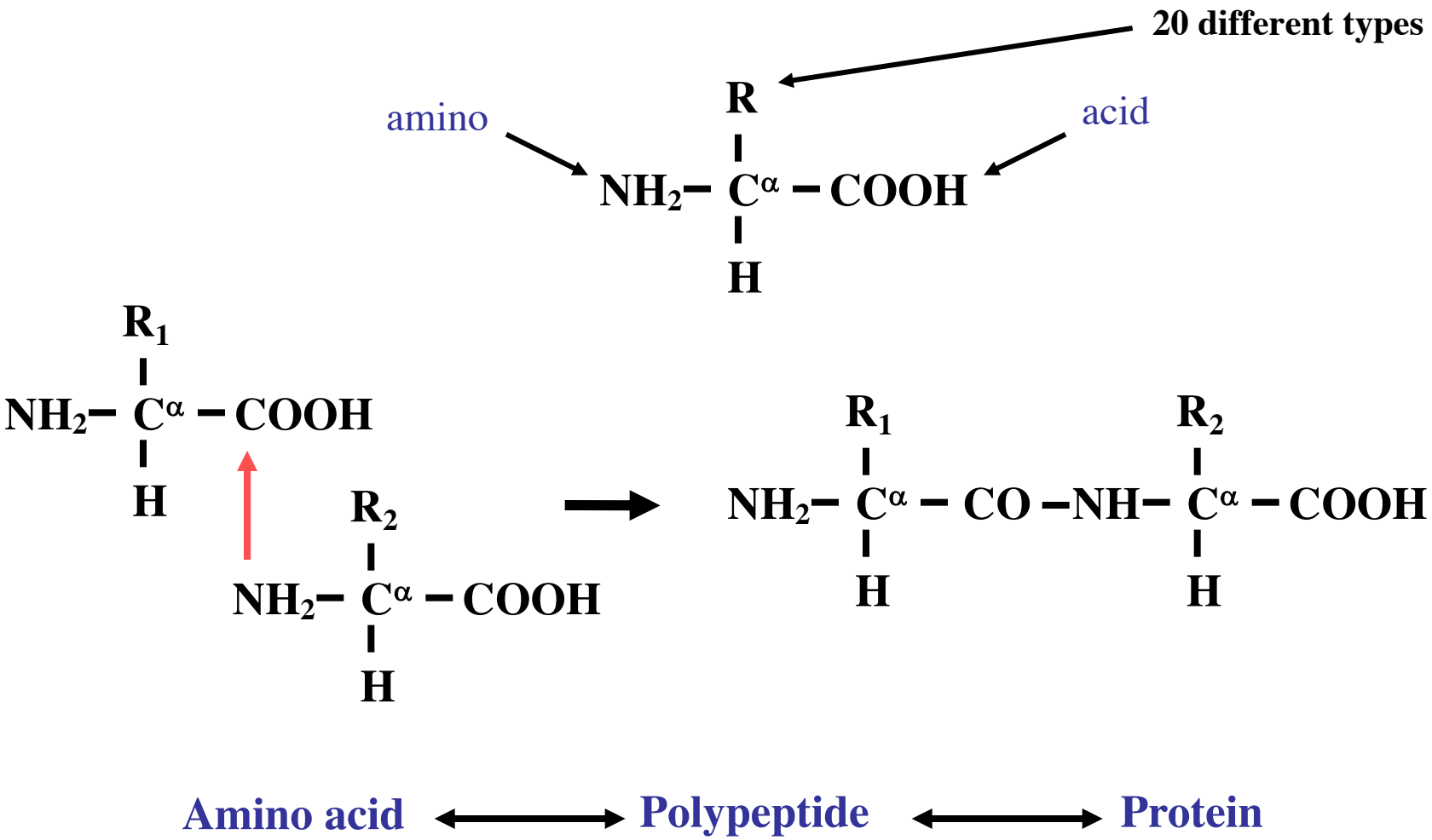
Nonstandard (uncommon) amino acids

- 20 common amino acids programmed by genetic code
- Nature often needs more variation
- Nonstandard amino acids play a variety of roles:
  - Structural
  - Antibiotics
  - Signals
  - Hormones
  - Neurotransmitters
  - intermediates in metabolic cycles
- Nonstandard amino acids are usually the result of modification of a standard amino acid after a polypeptide has been synthesized.
- **> 700 non standard amino acids have been detected in living organisms**

Amino Acid Chemistry

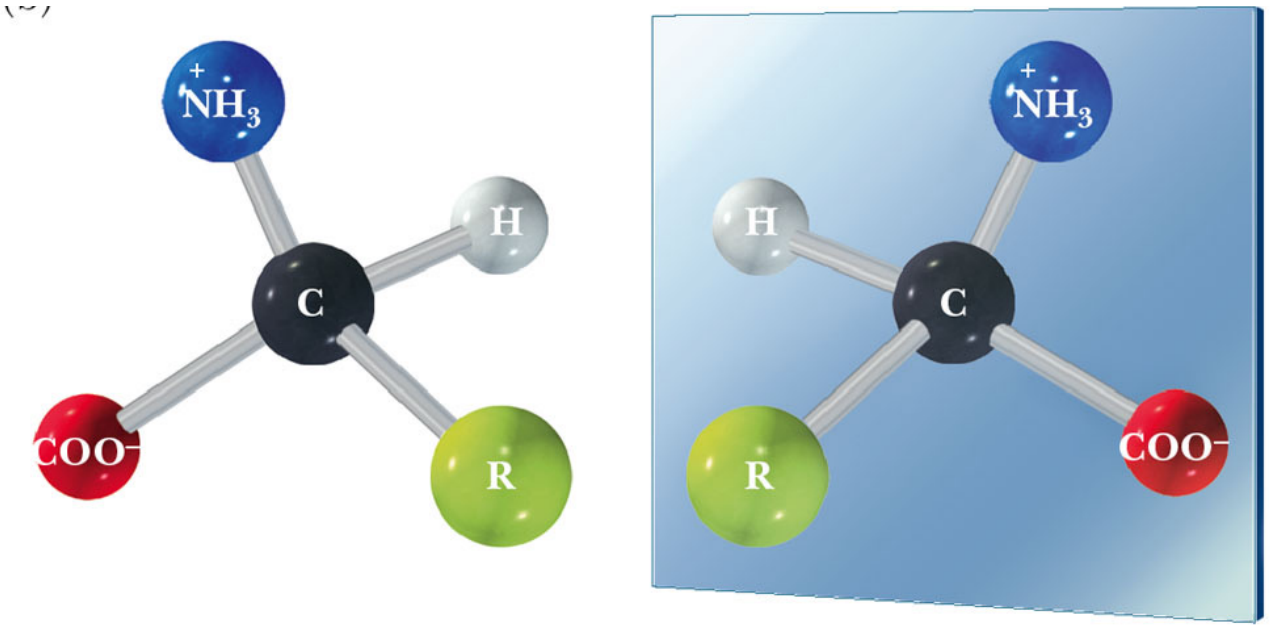


Amino Acid Chemistry



Steriochemistry

- Steriochemistry: is the three-dimensional shape of a molecule
- Object that is Not superimposable on its mirror image is ***chiral***



Amino Acid Stereochemistry

Optical activity: The ability to rotate plane polarized light

- Asymmetric carbon atom
- Chirality - Not superimposable
- Mirror image - enantiomers
- (+) Dextrorotatory - right - clockwise
- (-) Levorotatory - left counterclockwise

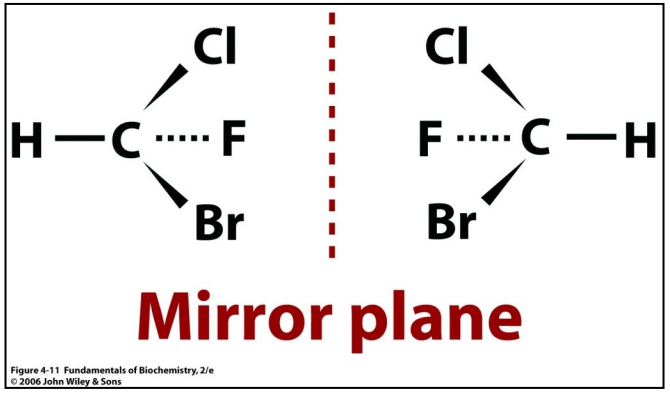
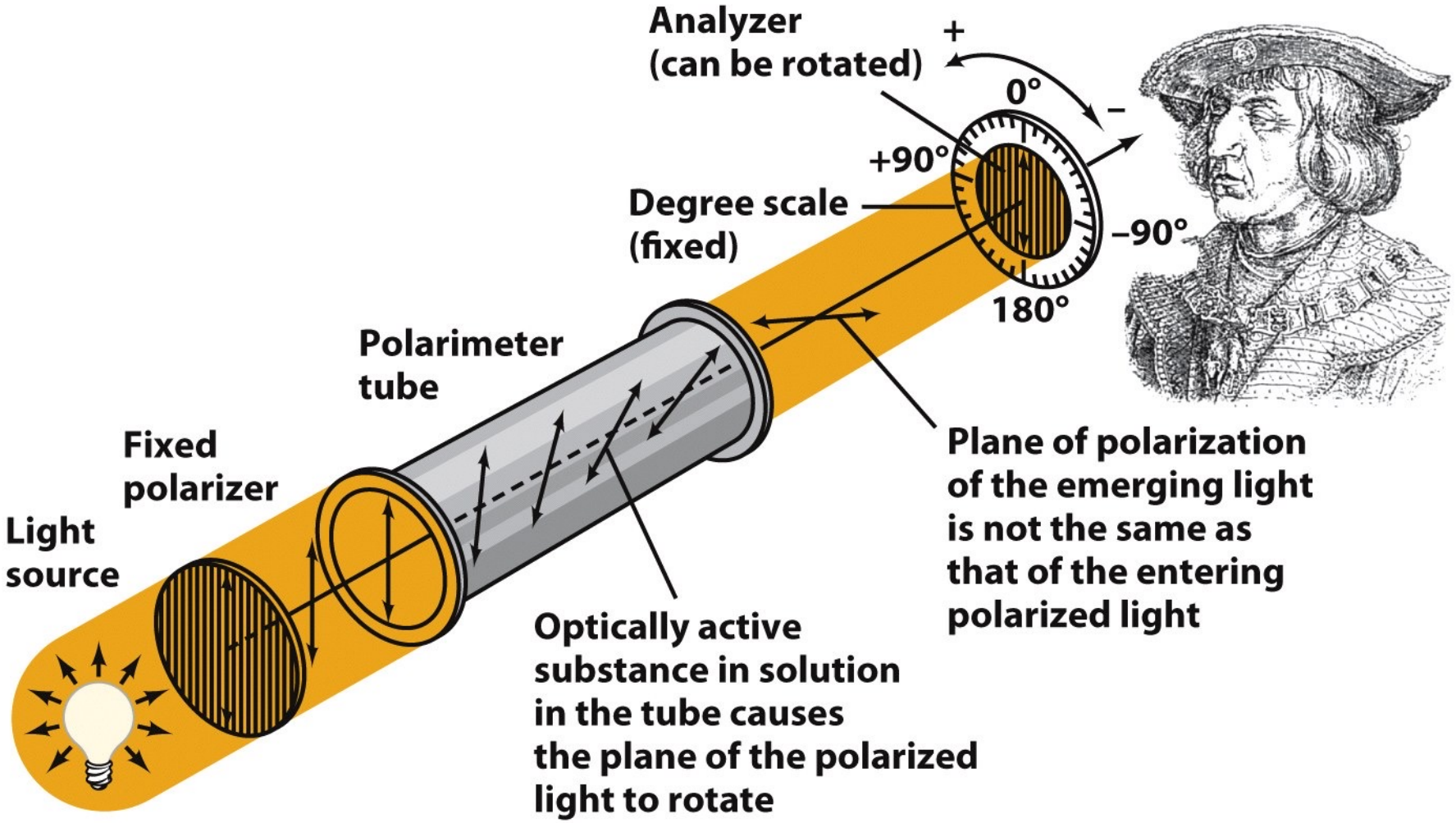
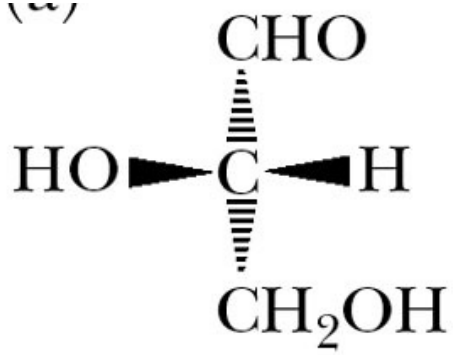


Figure 4-11 Fundamentals of Biochemistry, 2/e

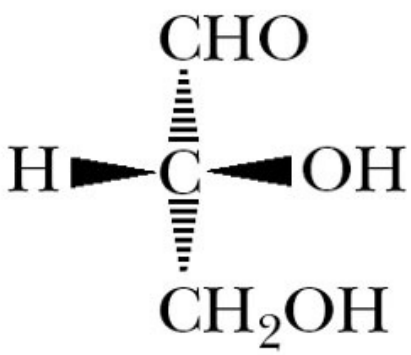
Optical Activity



Amino Acid Stereochemistry

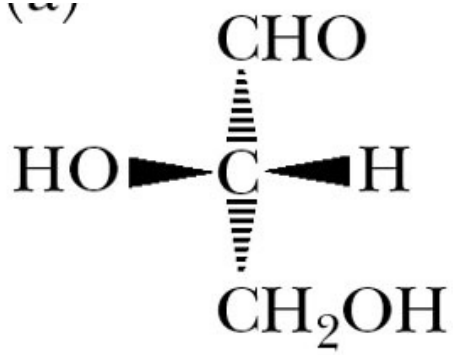


L-Glyceraldehyde

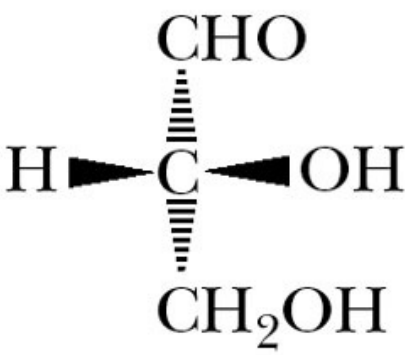


D-Glyceraldehyde

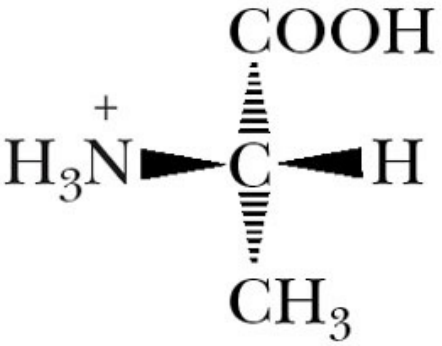
Amino Acid Chemistry



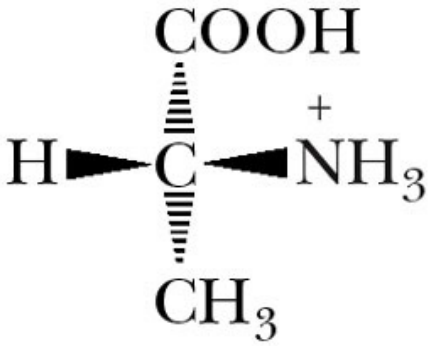
L-Glyceraldehyde



D-Glyceraldehyde



L-Alanine



D-Alanine

Criteria of R-group and amino acids classification

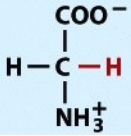
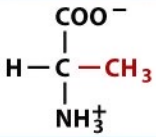
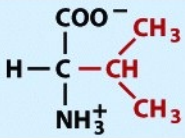
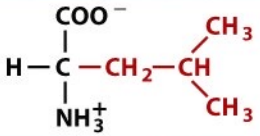
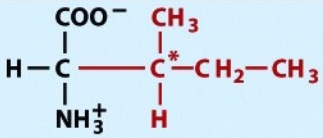
- Polar and non Polar nature of the side chain
- Presence of acidic or basic group in the side chain
- Presence of other functional groups
- Side chain carbon atoms are designated with letters of
- Greek alphabet counting from α-carbon: β, γ, δ, ε
- Amino acids can be abbreviated by one or three letters

Table 3.1

Names and Abbreviations of the Common 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
Glutamic acid	Glu	E
Glutamine	Gln	Q
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

Table 4-1 Covalent Structures and Abbreviations of the "Standard" Amino Acids of Proteins, Their Occurrence, and the pK Values of Their Ionizable Groups

Name, Three-letter Symbol, and One-letter Symbol	Structural Formula[a]	Residue Mass (D)[b]	Average Occurrence in Proteins (%)[c]	pK_1 α-COOH[d]	pK_2 α-NH_3^+[d]	pK_R Side Chain[d]
Amino acids with nonpolar side chains						
Glycine Gly G		57.0	7.2	2.35	9.78	
Alanine Ala A		71.1	7.8	2.35	9.87	
Valine Val V		99.1	6.6	2.29	9.74	
Leucine Leu L		113.2	9.1	2.33	9.74	
Isoleucine Ile I		113.2	5.3	2.32	9.76	

flexible

small hydrophobic

hydrophobic

hydrophobic

hydrophobic rigid

[a]The ionic forms shown are those predominating at pH 7.0 (except for that of histidine[f]) although residue mass is given for the neutral compound. The C_α atoms, as well as those atoms marked with an asterisk, are chiral centers with configurations as indicated according to Fischer projection formulas (Section 4-2). The standard organic numbering system is provided for heterocycles.

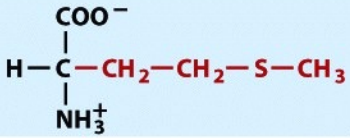
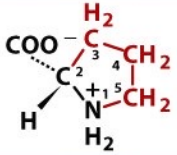
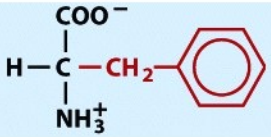
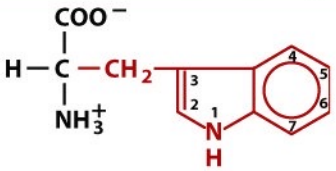
[b]The residue masses are given for the neutral residues. For the molecular masses of the parent amino acids, add 18.0 D, the molecular mass of H_2O, to the residue masses. For side chain masses, subtract 56.0 D, the formula mass of a peptide group, from the residue masses.

[c]Calculated from a database of nonredundant proteins containing 300,688 residues as compiled by Doolittle, R.F., *in* Fasman, G.D. (Ed.), *Predictions of Protein Structure and the Principles of Protein Conformation*, Plenum Press (1989).

[d]Data from Dawson, R.M.C., Elliott, D.C., Elliott, W.H., and Jones, K.M., *Data for Biochemical Research* (3rd ed.), pp. 1–31, Oxford Science Publications (1986).

Table 4-1 part 1

Table 4-1 Covalent Structures and Abbreviations of the "Standard" Amino Acids of Proteins, Their Occurrence, and the pK Values of Their Ionizable Groups

Name, Three-letter Symbol, and One-letter Symbol	Structural Formula[a]	Residue Mass (D)[b]	Average Occurrence in Proteins (%)[c]	pK_1 α-COOH[d]	pK_2 α-NH_3^+[d]	pK_R Side Chain[d]	
Amino acids with nonpolar side chains							
Methionine Met M		131.2	2.2	2.13	9.28		hydrophobic metal binder
Proline Pro P		97.1	5.2	1.95	10.64		hydrophobic no NH
Phenylalanine Phe F		147.2	3.9	2.20	9.31		hydrophobic aromatic
Tryptophan Trp W		186.2	1.4	2.46	9.41		hydrophobic aromatic

[a]The ionic forms shown are those predominating at pH 7.0 (except for that of histidine[f]) although residue mass is given for the neutral compound. The C_α atoms, as well as those atoms marked with an asterisk, are chiral centers with configurations as indicated according to Fischer projection formulas (Section 4-2). The standard organic numbering system is provided for heterocycles.

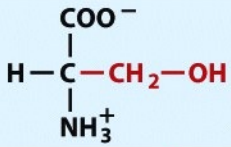
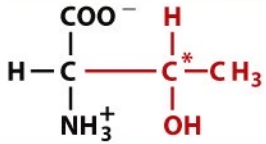
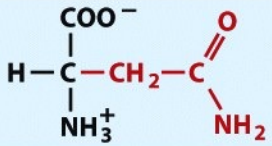
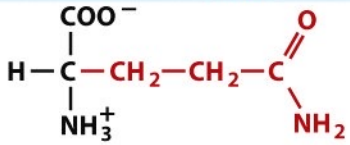
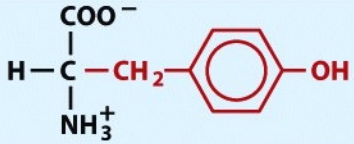
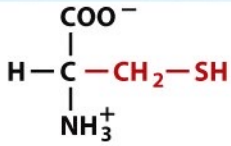
[b]The residue masses are given for the neutral residues. For the molecular masses of the parent amino acids, add 18.0 D, the molecular mass of H_2O, to the residue masses. For side chain masses, subtract 56.0 D, the formula mass of a peptide group, from the residue masses.

[c]Calculated from a database of nonredundant proteins containing 300,688 residues as compiled by Doolittle, R.F., *in* Fasman, G.D. (Ed.), *Predictions of Protein Structure and the Principles of Protein Conformation*, Plenum Press (1989).

[d]Data from Dawson, R.M.C., Elliott, D.C., Elliott, W.H., and Jones, K.M., *Data for Biochemical Research* (3rd ed.), pp. 1–31, Oxford Science Publications (1986).

Table 4-1 part 2

Table 4-1 (continued)

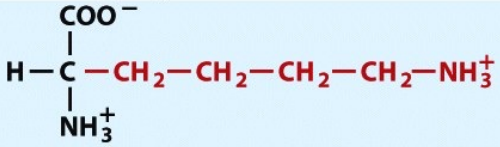
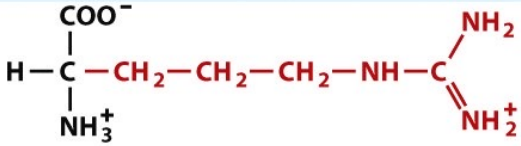
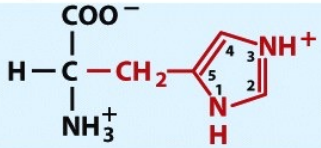
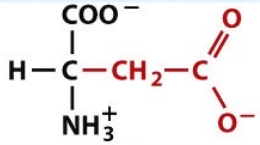
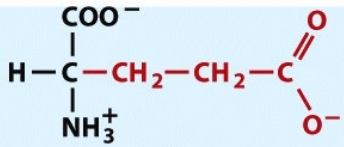
Name, Three-letter Symbol, and One-letter Symbol	Structural Formula[a]	Residue Mass (D)[b]	Average Occurrence in Proteins (%)[c]	pK_1 α-COOH[d]	pK_2 α-NH_3^+[d]	pK_R Side Chain[d]	
Amino acids with uncharged polar side chains							
Serine Ser S		87.1	6.8	2.19	9.21		hydroxyl
Threonine Thr T		101.1	5.9	2.09	9.10		hydroxyl
Asparagine[e] Asn N		114.1	4.3	2.14	8.72		amide
Glutamine[e] Gln Q		128.1	4.3	2.17	9.13		amide
Tyrosine Tyr Y		163.2	3.2	2.20	9.21	10.46 (phenol)	aromatic hydroxyl
Cysteine Cys C		103.1	1.9	1.92	10.70	8.37 (sulfhydryl)	thiol redox, metal

[e]The three- and one-letter symbols for asparagine or aspartic acid are Asx and B, whereas for glutamine or glutamic acid they are Glx and Z. The one-letter symbol for an undetermined or "nonstandard" amino acid is X.

[f]Both neutral and protonated forms of histidine are present at pH 7.0, since its pK_R is close to 7.0.

Table 4-1 part 3

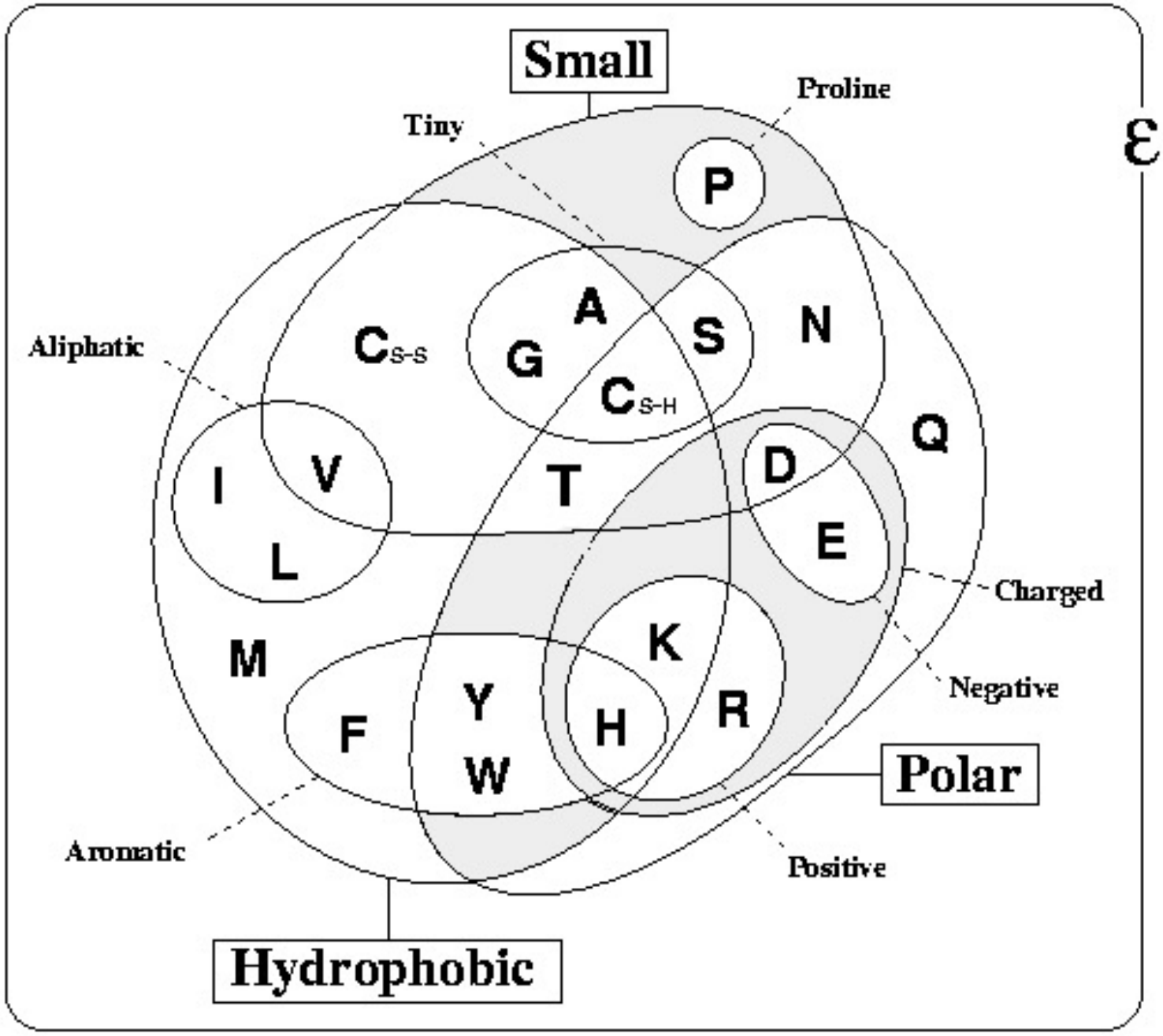
Table 4-1 (continued)

Name, Three-letter Symbol, and One-letter Symbol	Structural Formula[a]	Residue Mass (D)[b]	Average Occurrence in Proteins (%)[c]	pK_1 α-COOH[d]	pK_2 α-NH_3^+[d]	pK_R Side Chain[d]	
Amino acids with charged polar side chains							
Lysine Lys K		128.2	5.9	2.16	9.06	10.54 (ε-NH_3^+)	base
Arginine Arg R		156.2	5.1	1.82	8.99	12.48 (guanidino)	base
Histidine[f] His H		137.1	2.3	1.80	9.33	6.04 (imidazole)	acid/base
Aspartic acid[e] Asp D		115.1	5.3	1.99	9.90	3.90 (β-COOH)	acid
Glutamic acid[e] Glu E		129.1	6.3	2.10	9.47	4.07 (γ-COOH)	acid

[e]The three- and one-letter symbols for asparagine or aspartic acid are Asx and B, whereas for glutamine or glutamic acid they are Glx and Z. The one-letter symbol for an undetermined or "nonstandard" amino acid is X.

[f]Both neutral and protonated forms of histidine are present at pH 7.0, since its pK_R is close to 7.0.

Table 4-1 part 4



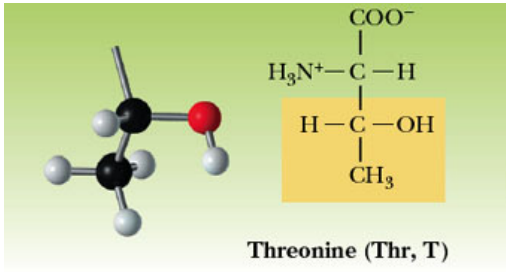
http://www.russell.embl-heidelberg.de/aas/

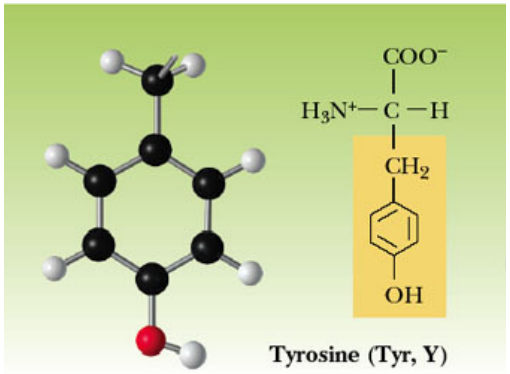
Hydrophilicity/Hydrophobicity

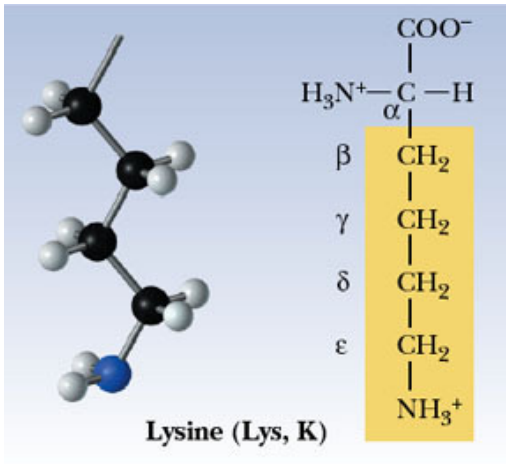
- Most amino acids' R-groups have both hydrophobic and hydrophilic character - they are **amphiphilic**

- Can we categorize an amino acid side chain as hydrophilic or hydrophobic? No.

- Instead, the issue is typically addressed by assessing the relative solubilities of the amino acid in water and some non-polar solvent, like octanol or cyclohexane







Side chain surface polarity

Amino Acid	Total Surf. Area of sidechain ($Å^2$)	Polar Surf. Area in the Sidechain ($Å^2$)	$\Delta G_{transfer}$ of sidechain (kcal/mol)
Alanine	113	-	-0.87
Arginine	241	107	15.93
Asparagine	158	69	5.22
Aspartate	151	58	9.71
Cysteine	140	69	-0.34
Glutamine	189	91	6.51
Glutamate	183	77	7.78
Glycine	85	-	0
Histidine	194	49	5.63
Isoleucine	182	-	-4.00
Leucine	180	-	-4.00
Lysine	211	48	6.52
Methionine	204	43	-1.42
Phenylalanine	218	-	-2.05

- $\Delta G_{transfer}$ refers to the free energy of transfer from water to cylcohexane.
- The greater the polar surface area of the sidechain, the more positive the free energy of transfer.

Amino acid Charge dependence on pH

I. **Zwitterions** : no net charge on a.a

II. **Isoelectric pH (pI)**: the pH at which the amino acid has no net charge

III. **Electrophoresis**: common method of seperating molecule in an electrical field

Amino acids are Ampholytes

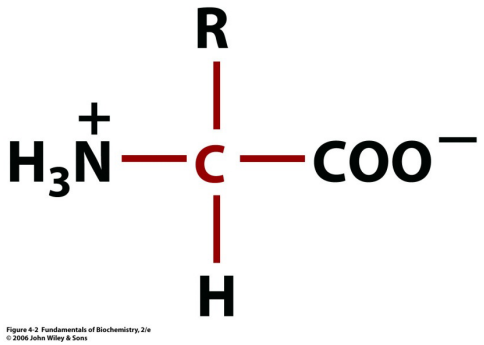


Figure 4-2 Fundamentals of Biochemistry, 2/e
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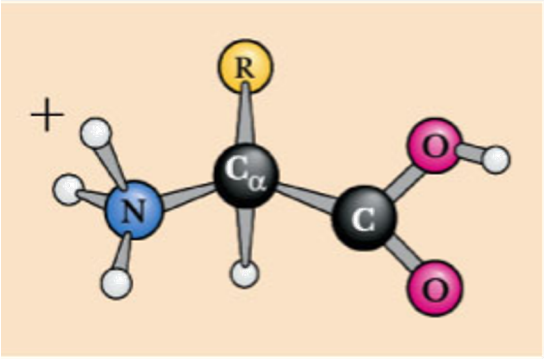
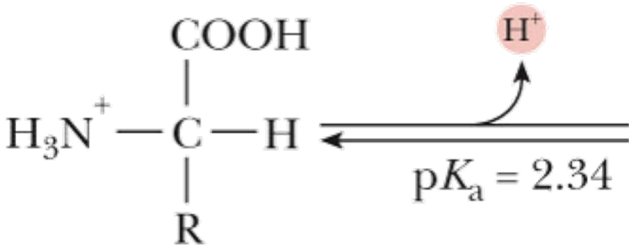
- $pK_1 \approx 2.2$ while $pK_2 \approx 9.4$, pK_R for R group pK's
- In the physiological pH range, both NH_2 and COOH are completely ionized
- They can act as either an acid or a base
- They are Zwitterions, molecules having charged groups of opposite polarity
- Because of their ionic nature they have extremely high melting temperatures

Ionization of Amino Acids

+1 net charge

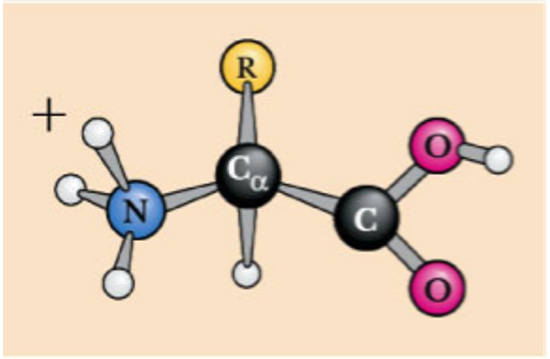


Cationic form



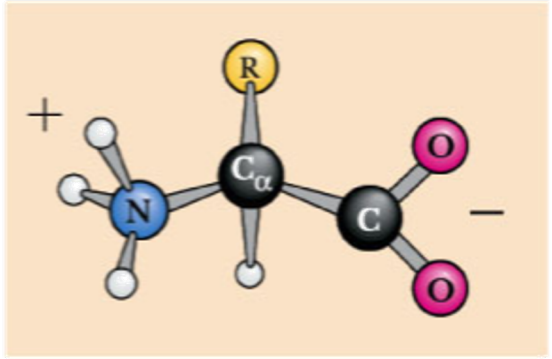
Ionization of Amino Acids

+1 net charge



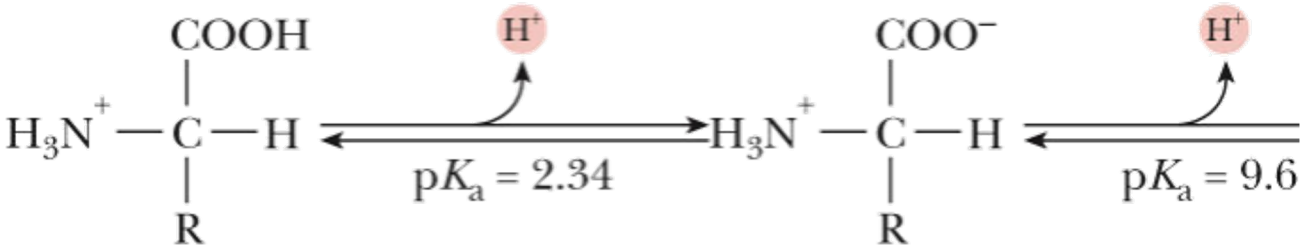
Cationic form

0 net charge



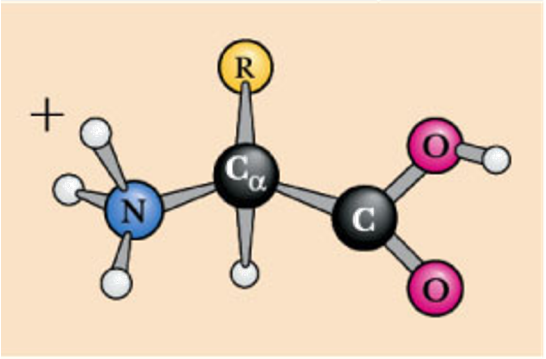
Neutral

Isoelectric zwitterion



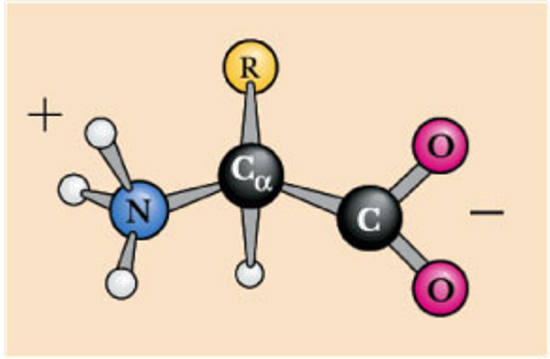
Ionization of Amino Acids

+1 net charge



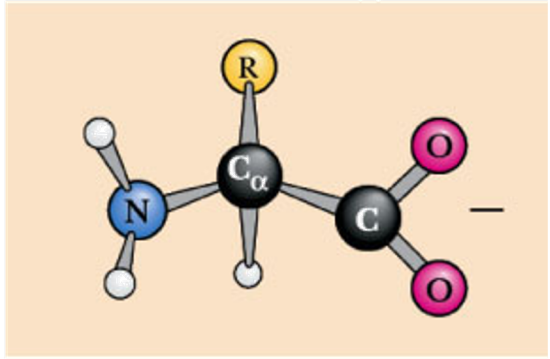
Cationic form

0 net charge



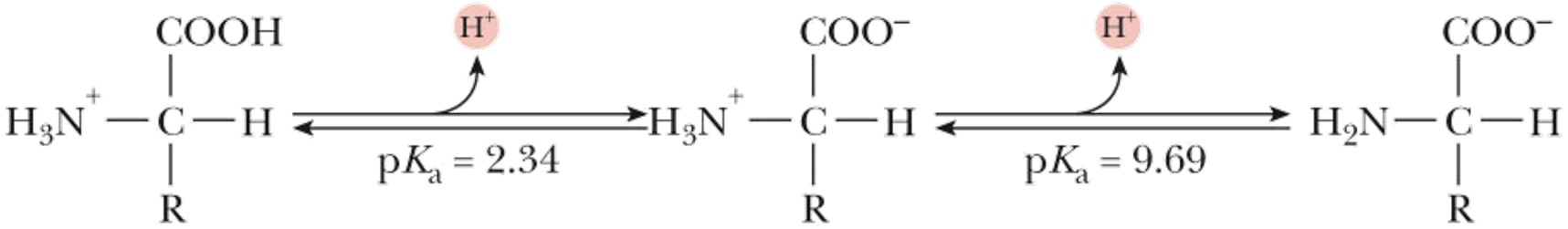
Neutral

–1 net charge

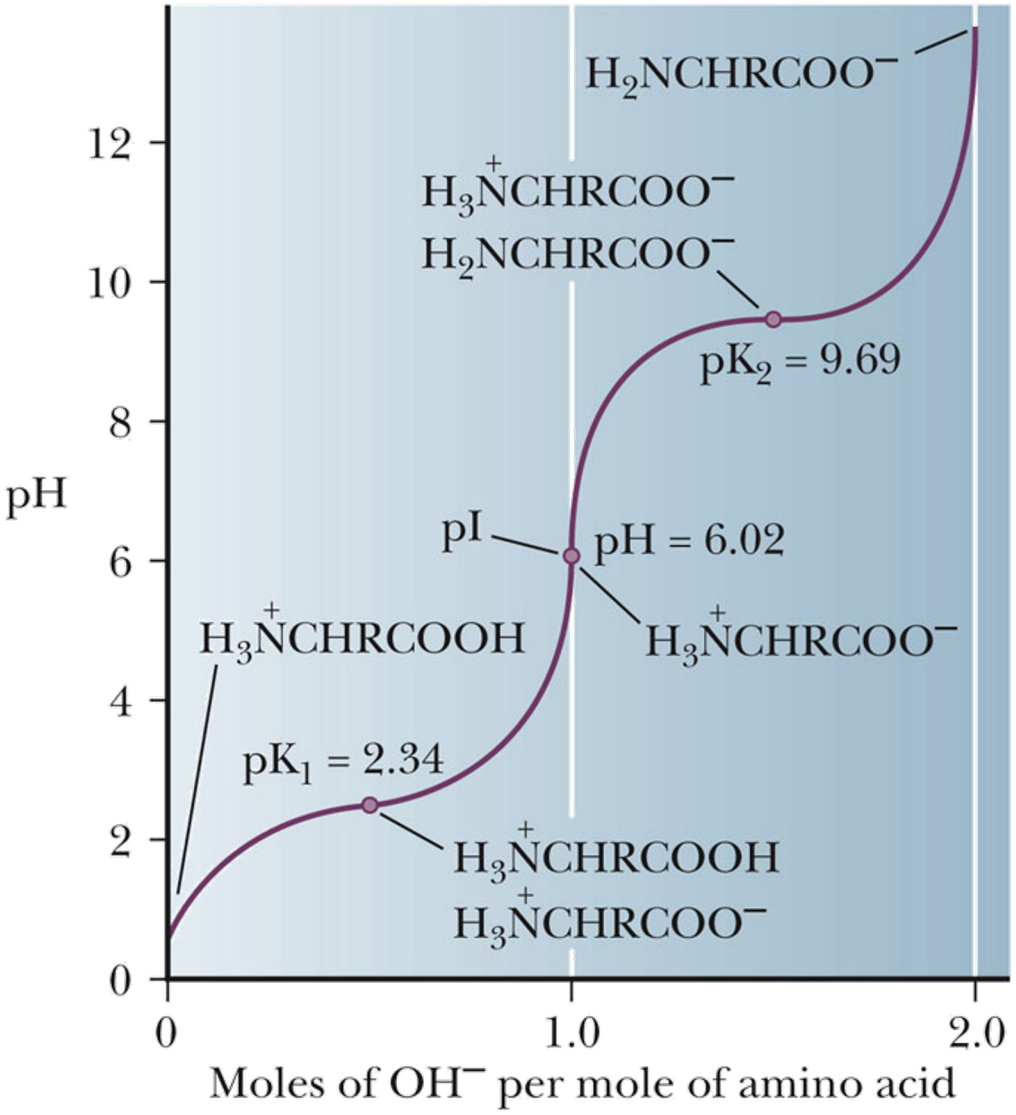


Anionic form

Isoelectric zwitterion

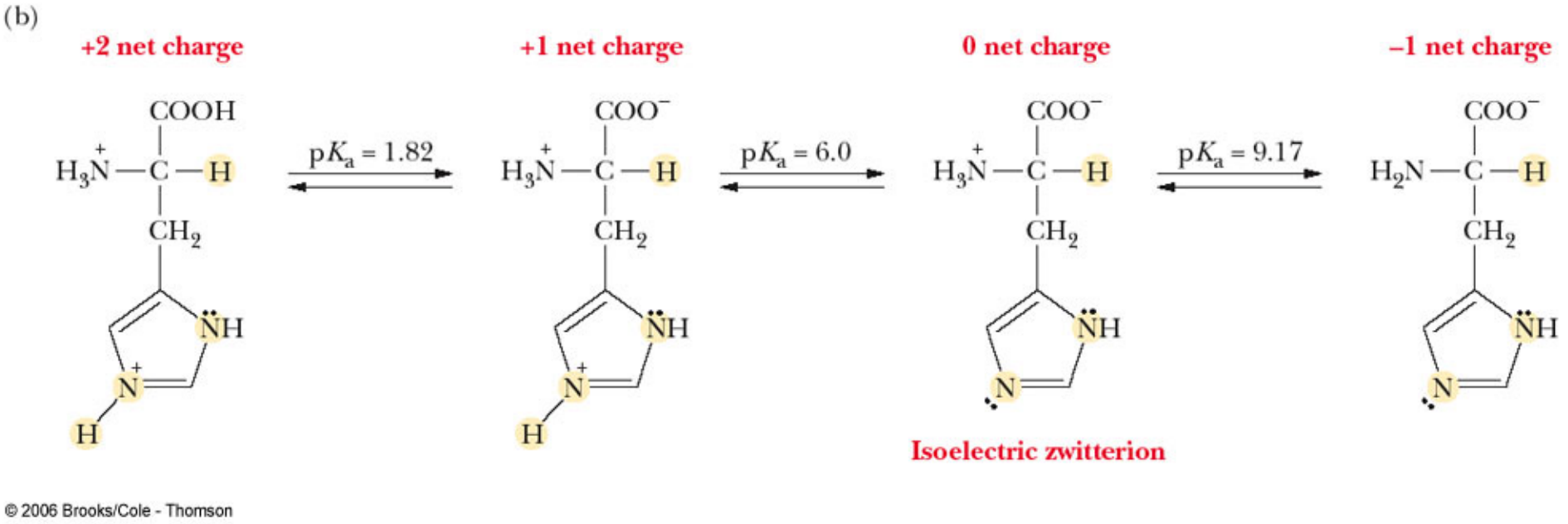


Titration of Amino Acids

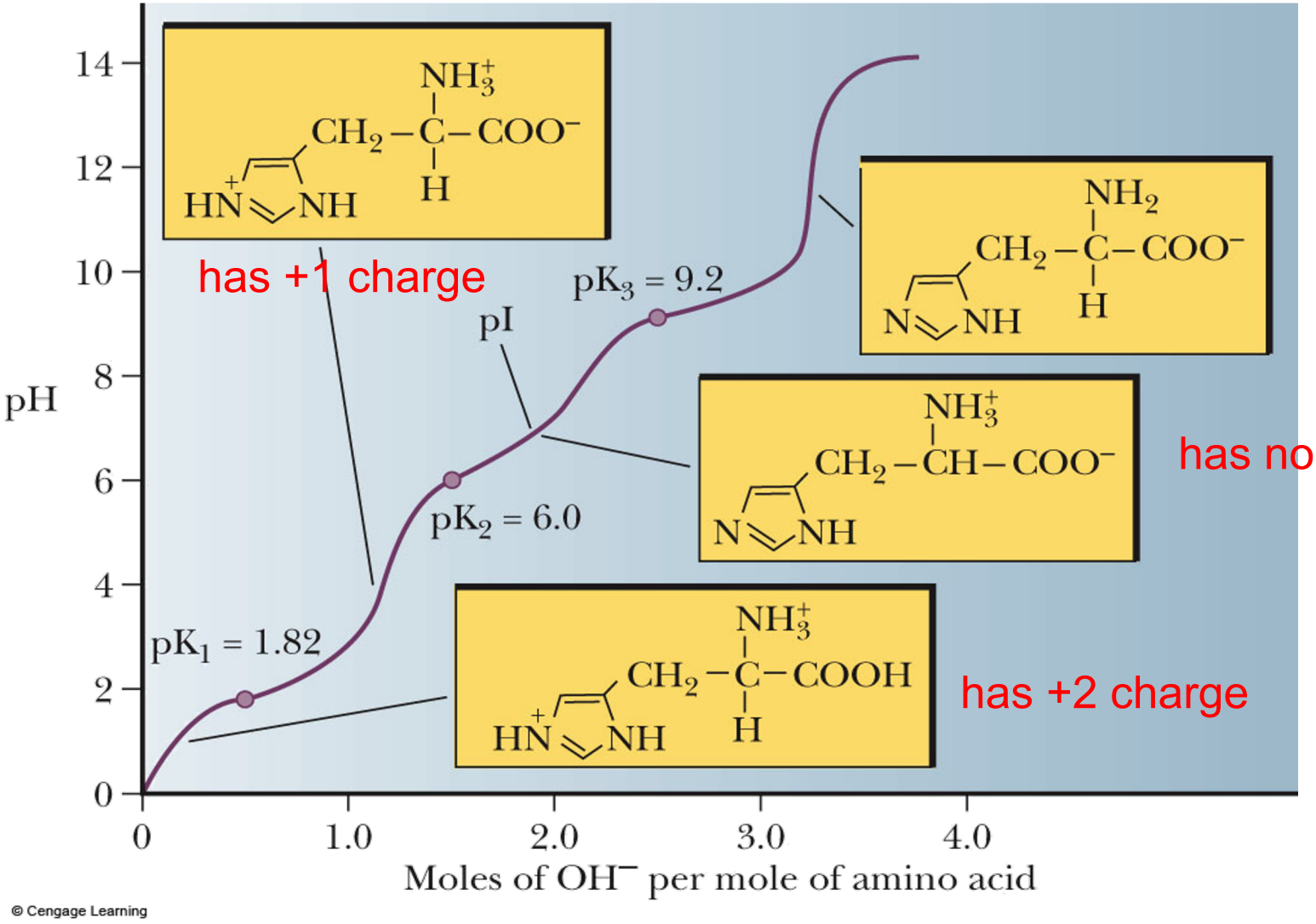


$$pI = \frac{pK_{a1} + pK_{a2}}{2}$$

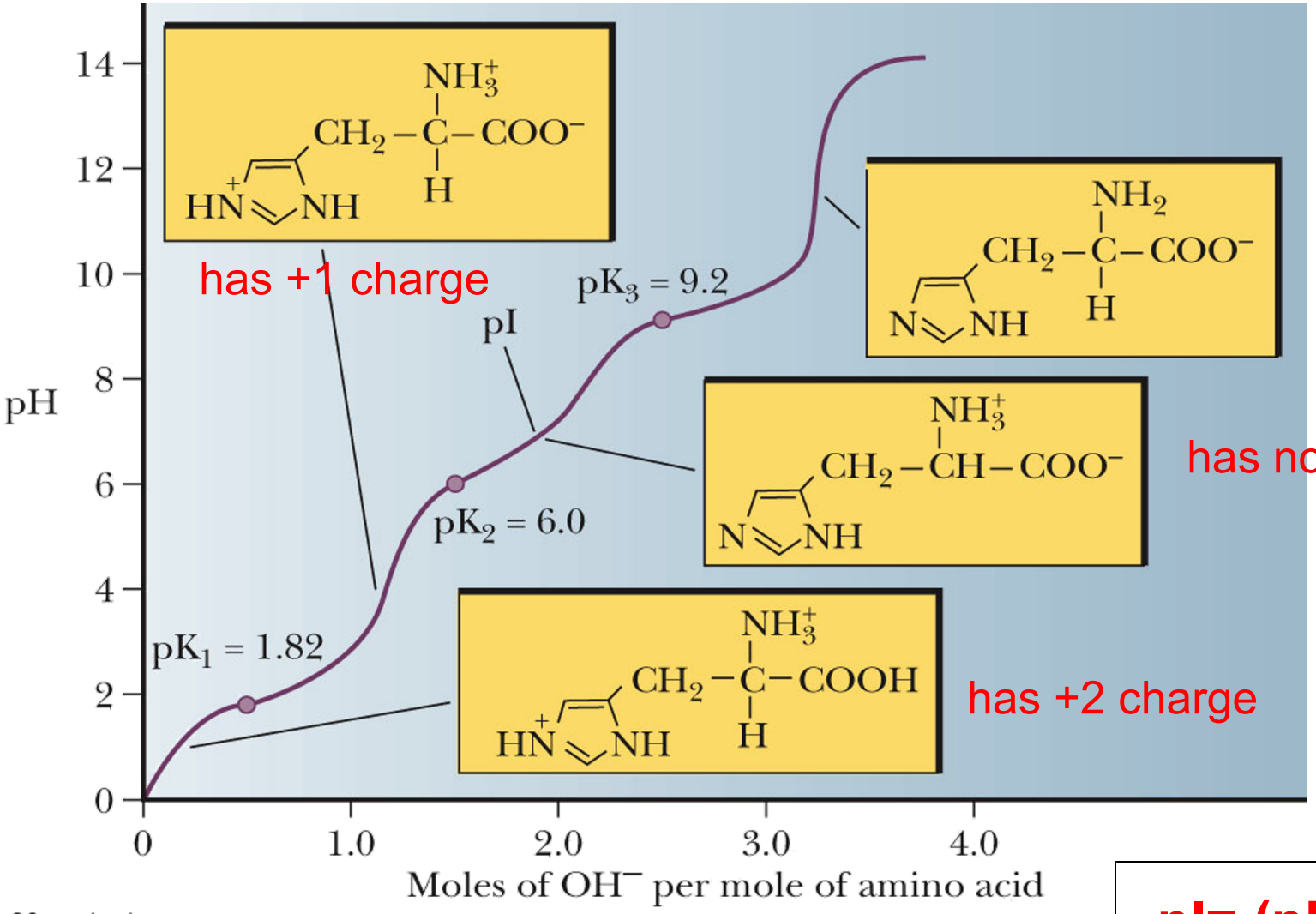
Ionization of histidine



Titration of histidine with NaOH



Titration of histidine with NaOH



$$pI = (pK_2 + pK_3)/2$$

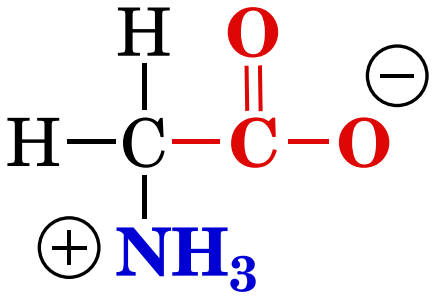
The local environment alters the pK_a values for ionizable groups

The pK_a of acetic acid in various solvents.

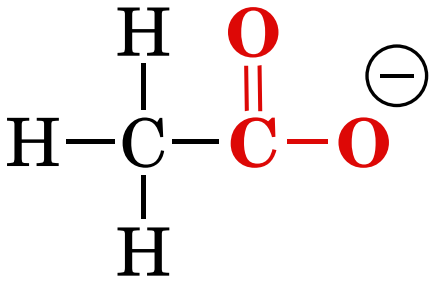
Solvent	**pK_a**
Water	4.7
Methanol	9.6
Dimethylsulfoxide	12.6

- The pKa of a given functional group is not an absolute.
- It varies substantially with its immediate chemical environment.

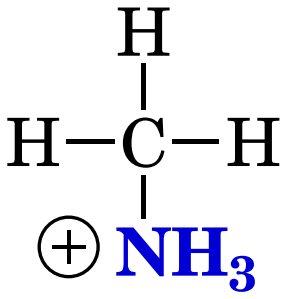
The local environment alters the pK_a values for ionizable groups



Glycine



Acetate



Methylamine

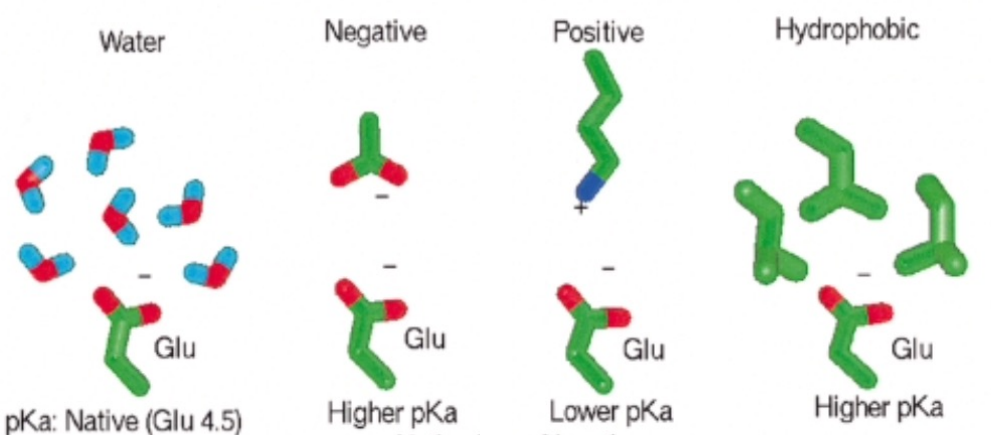
$pKa_{COOH} = 2.34$

$pKa_{COOH} = 4.76$

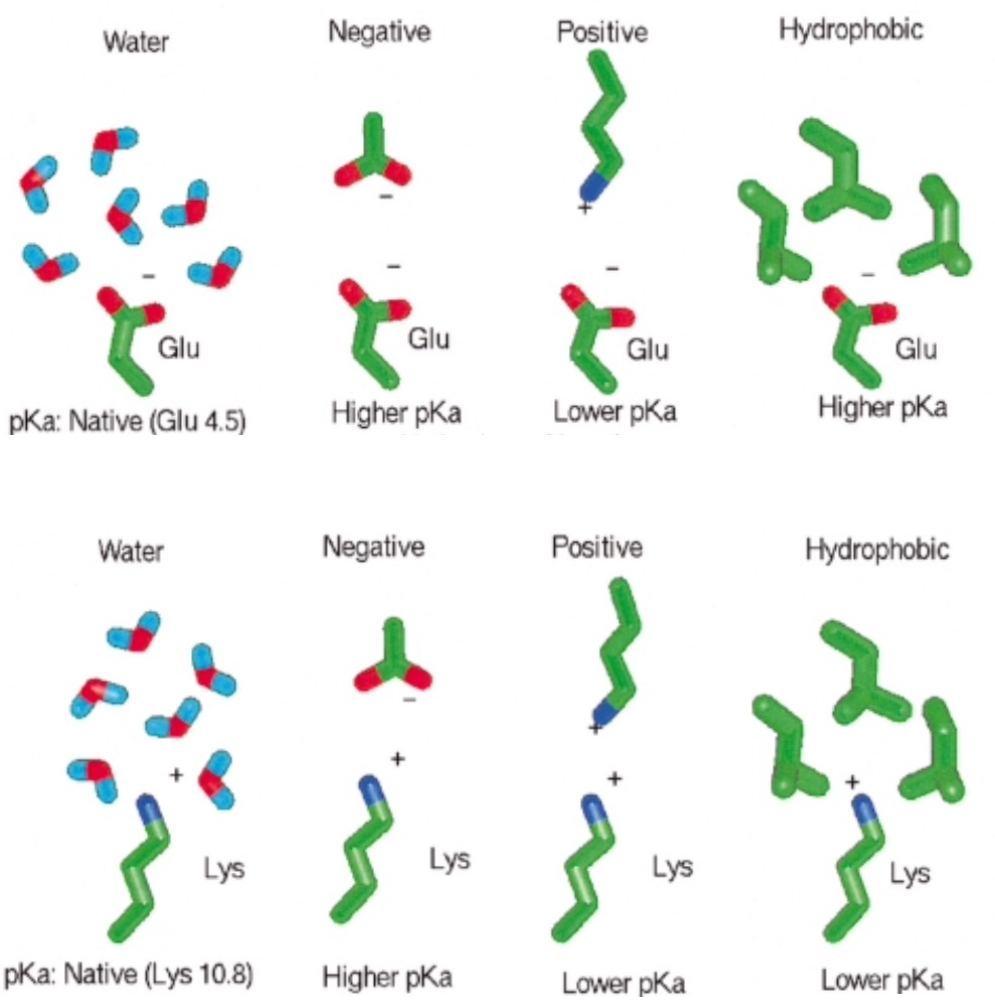
$pKa_{NH3} = 9.6$

$pKa_{NH3} = 10.6$

The local environment alters the pK_a values for ionizable groups



The local environment alters the pK_a values for ionizable groups



Oxidation and Reduction of Cysteine

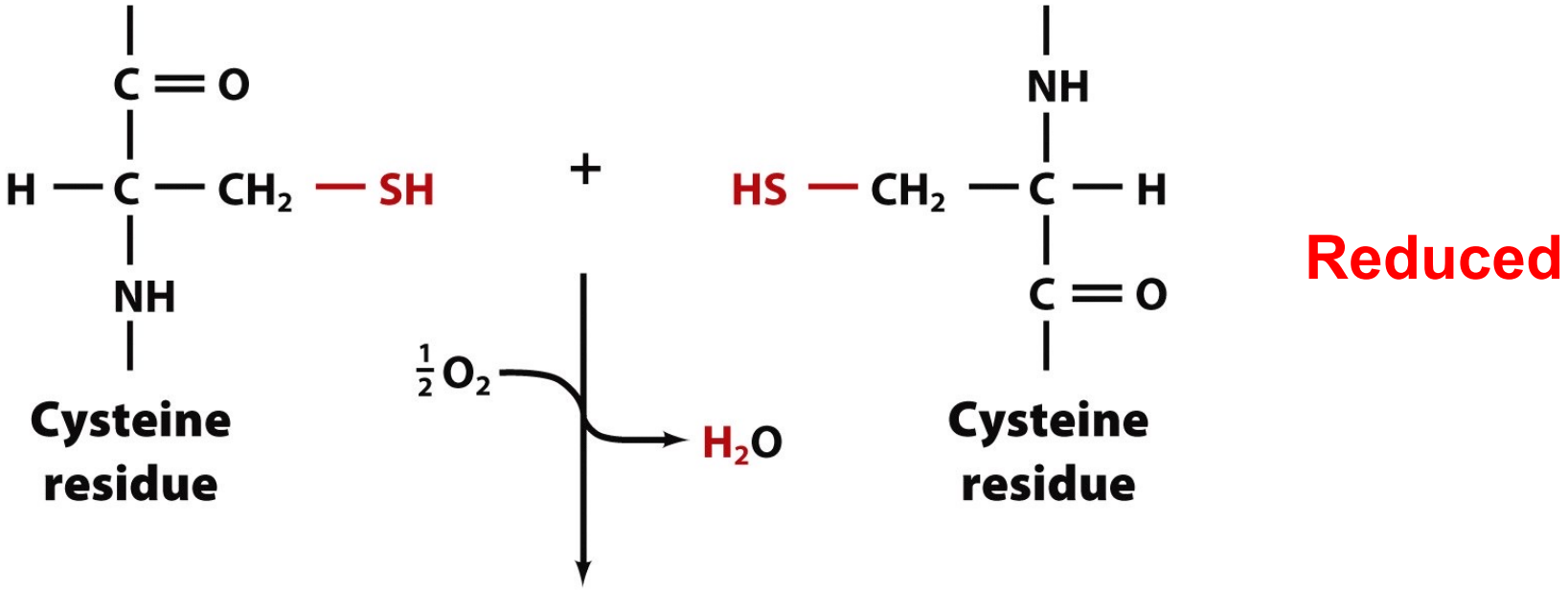


Figure 4-6

Oxidation and Reduction of Cysteine

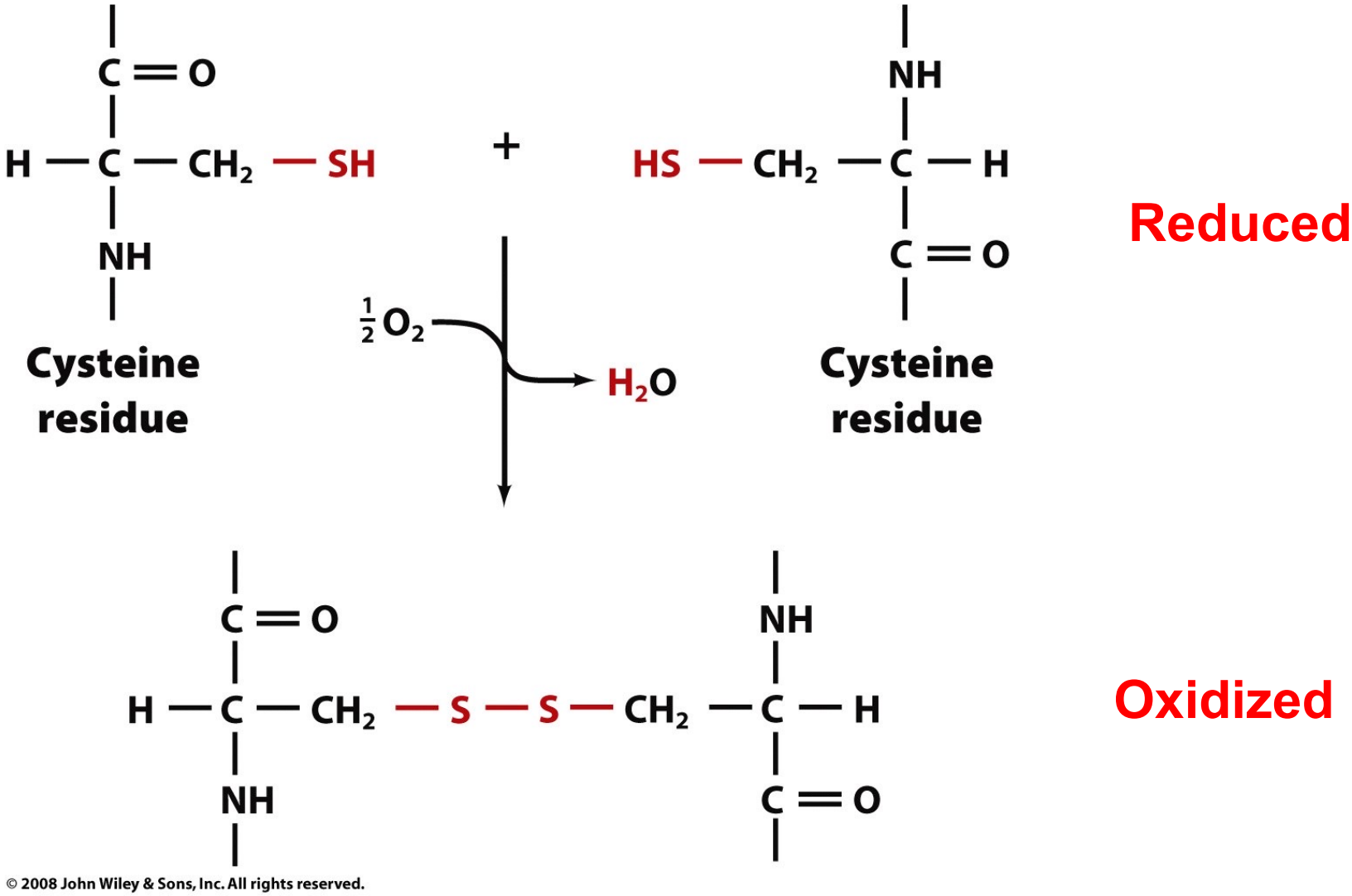


Figure 4-6

Modified amino acids

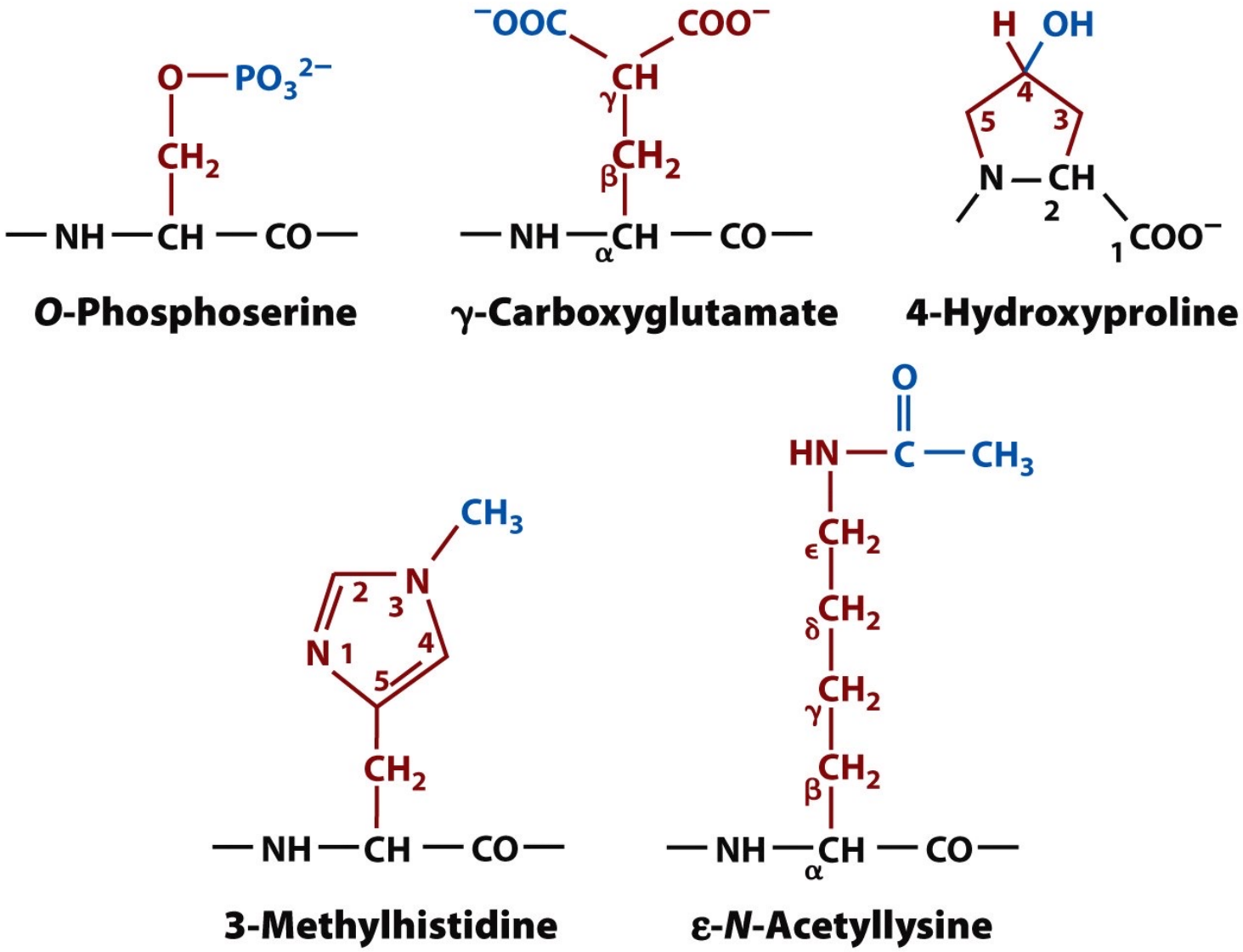
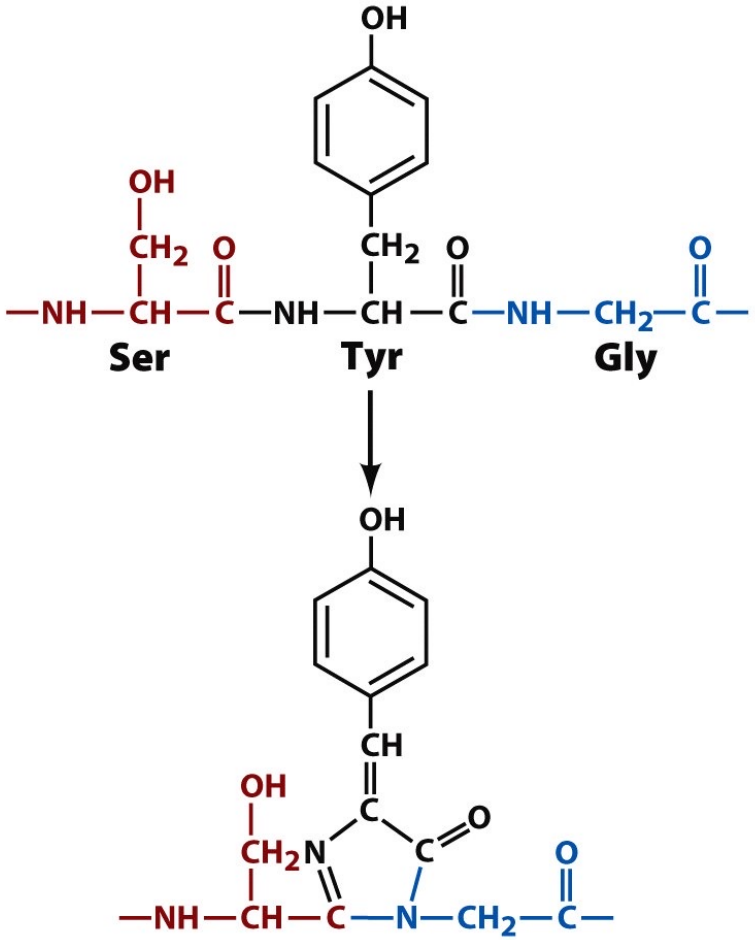
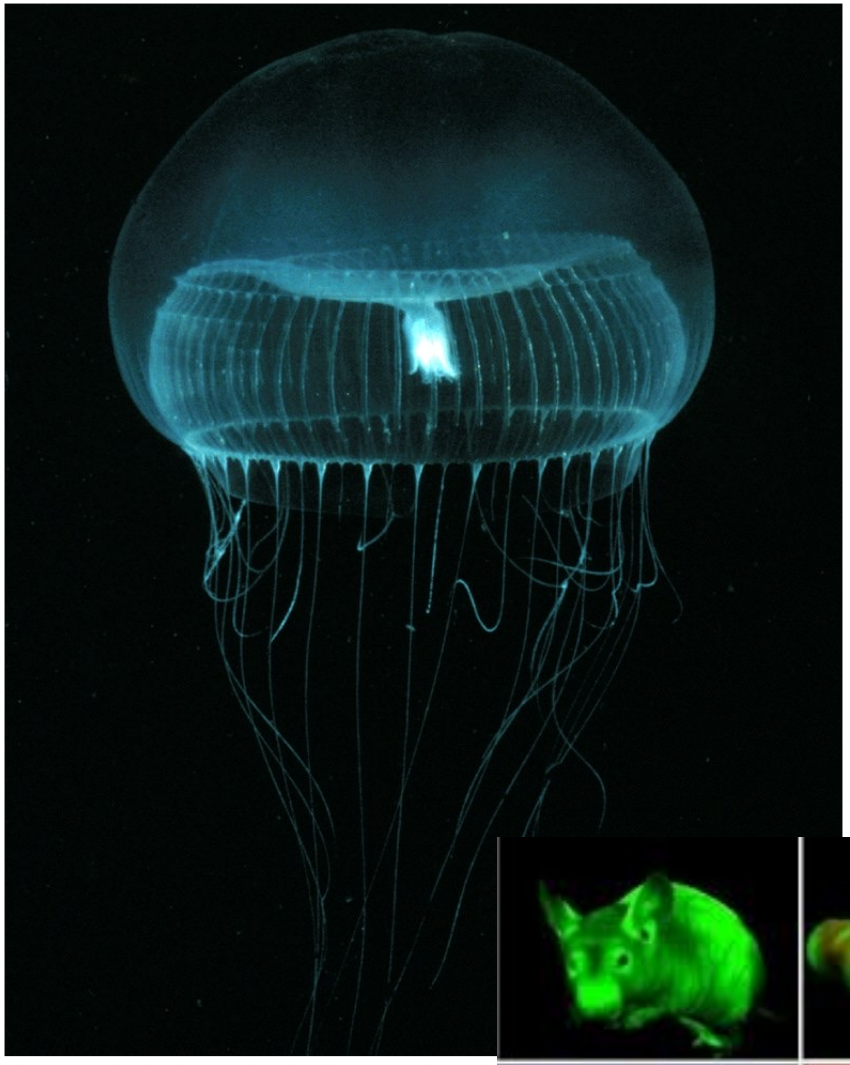
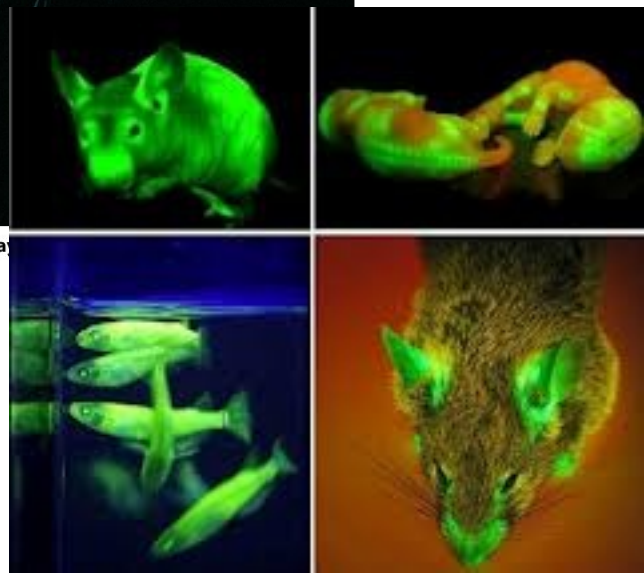


Figure 4-14

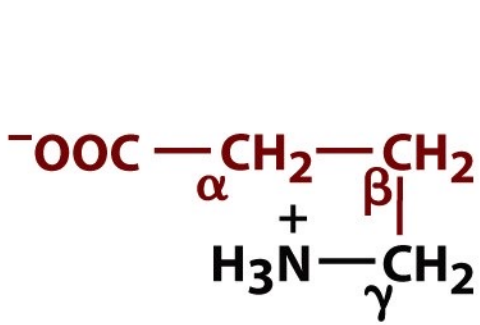


Fluorophore of green fluorescent protein

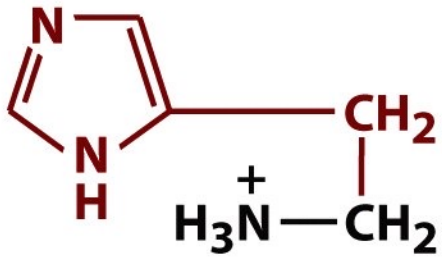




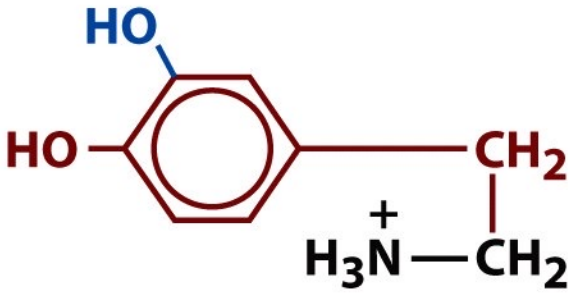
Biologically active amino acids



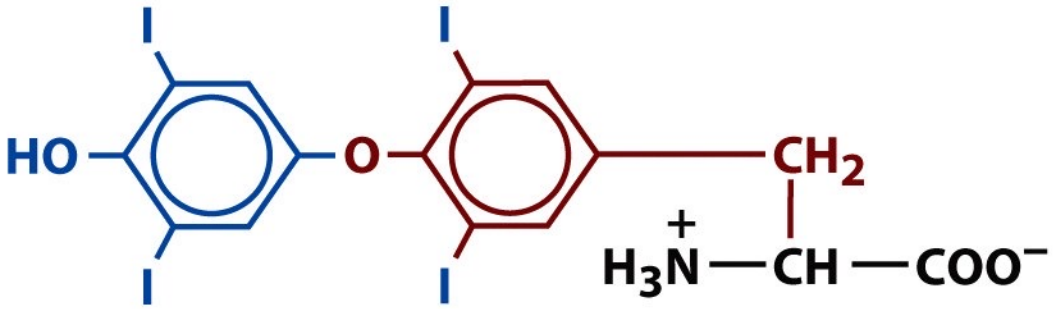
γ-Aminobutyric acid (GABA)



Histamine



Dopamine



Thyroxine

Figure 4-15

Peptide bond formation

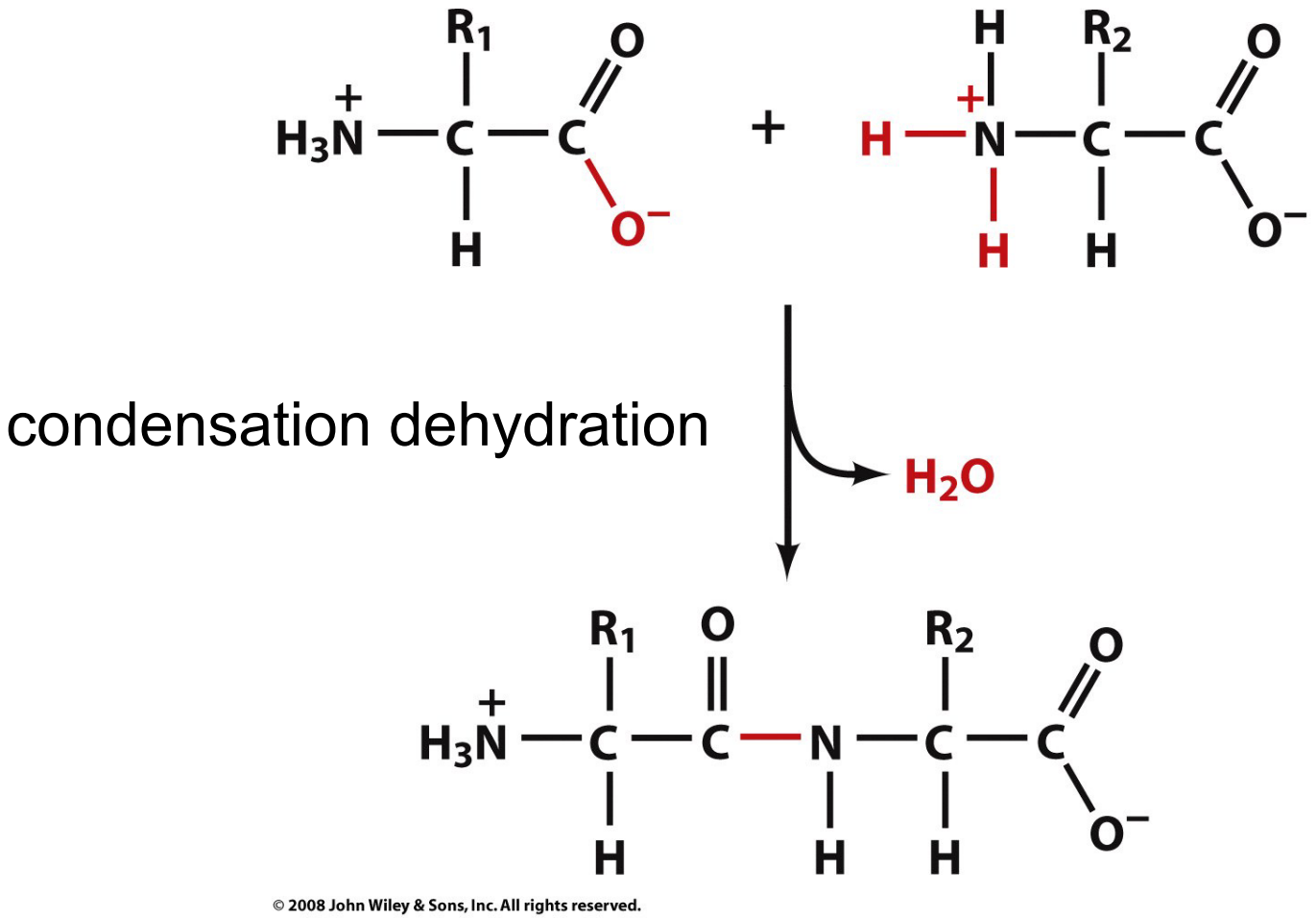
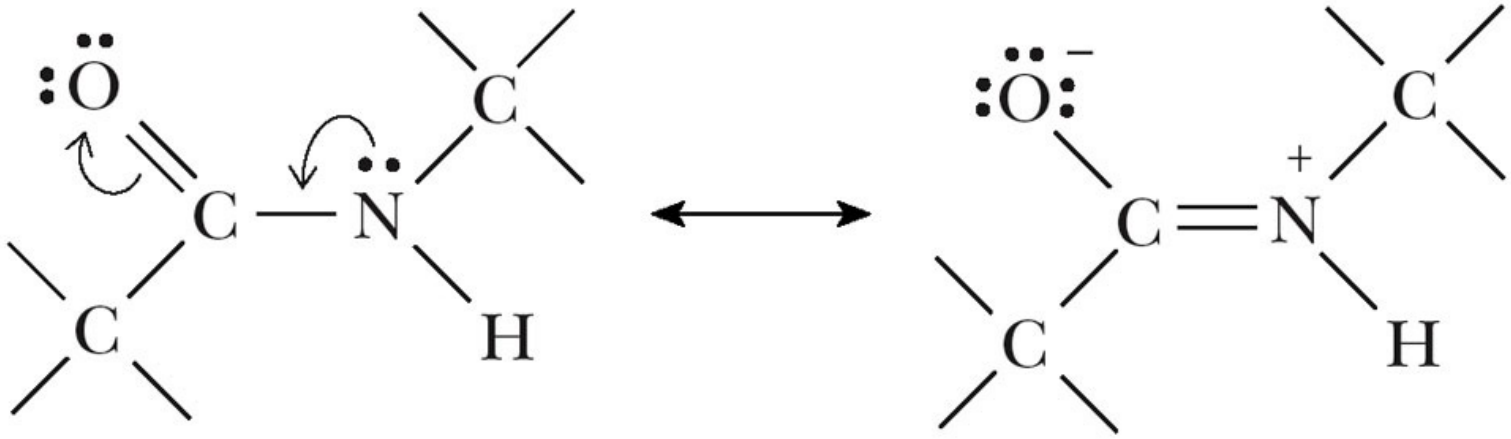
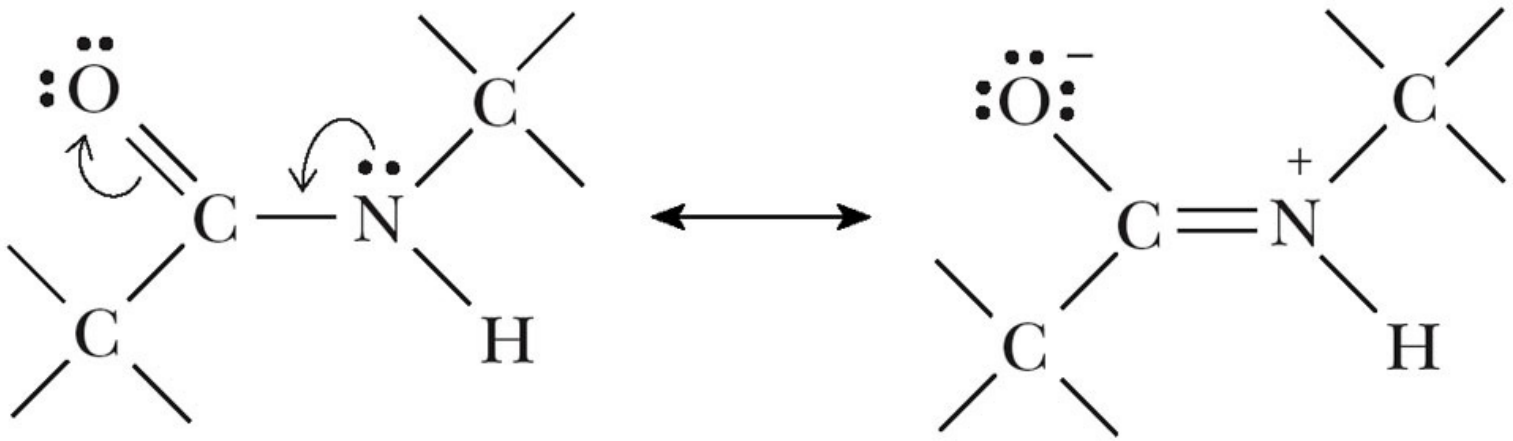


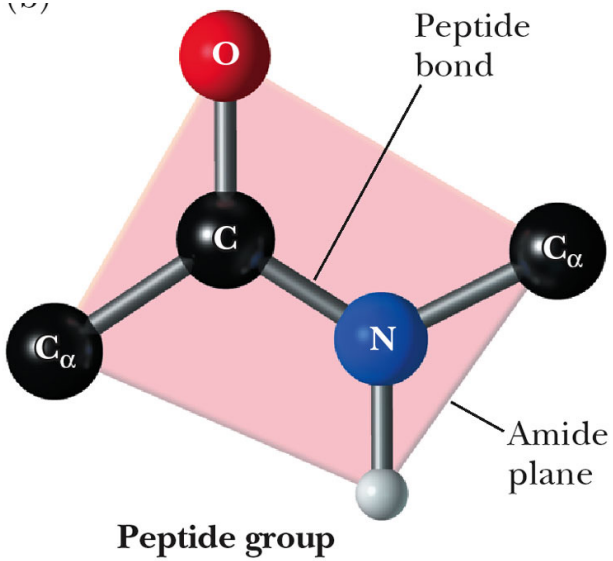
Figure 4-3

Geometry of Peptide Bond



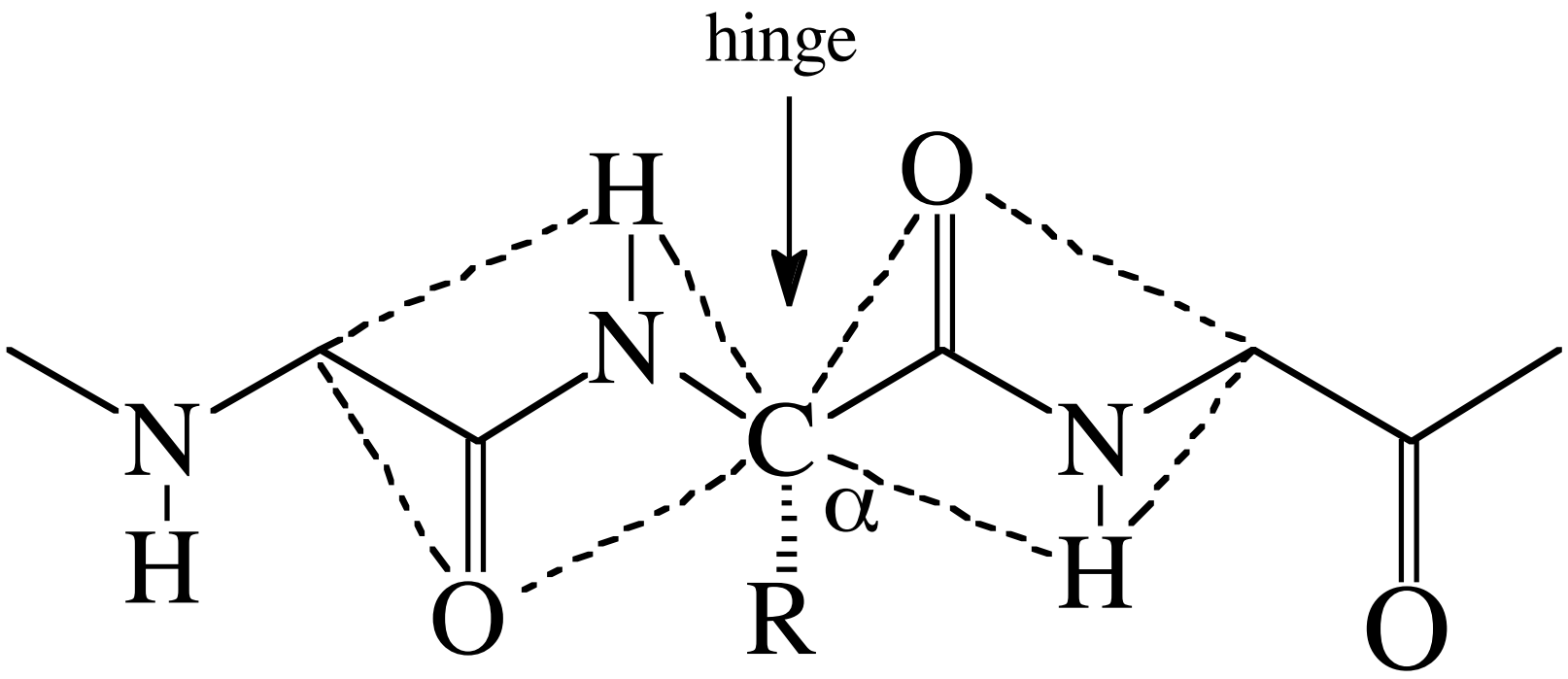
Geometry of Peptide Bond

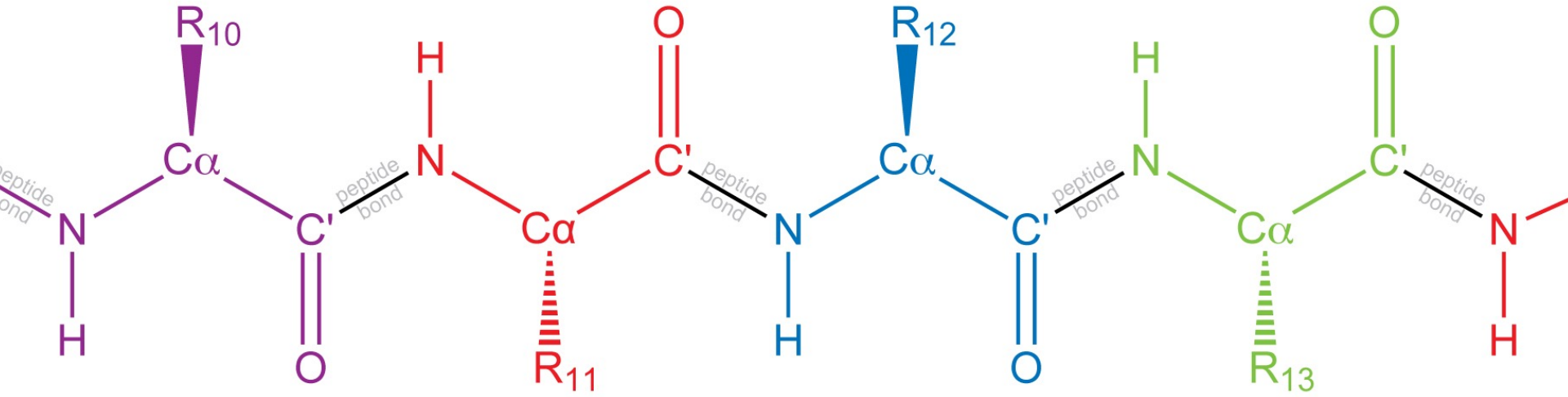




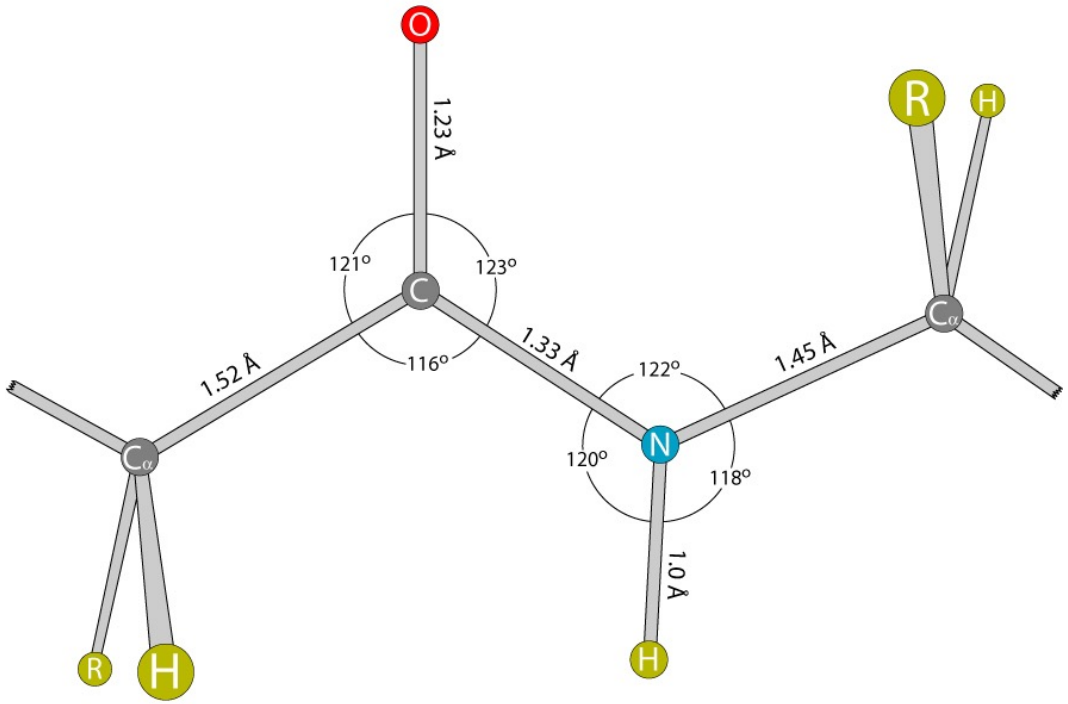
Peptide group

Geometry of Peptide Bond





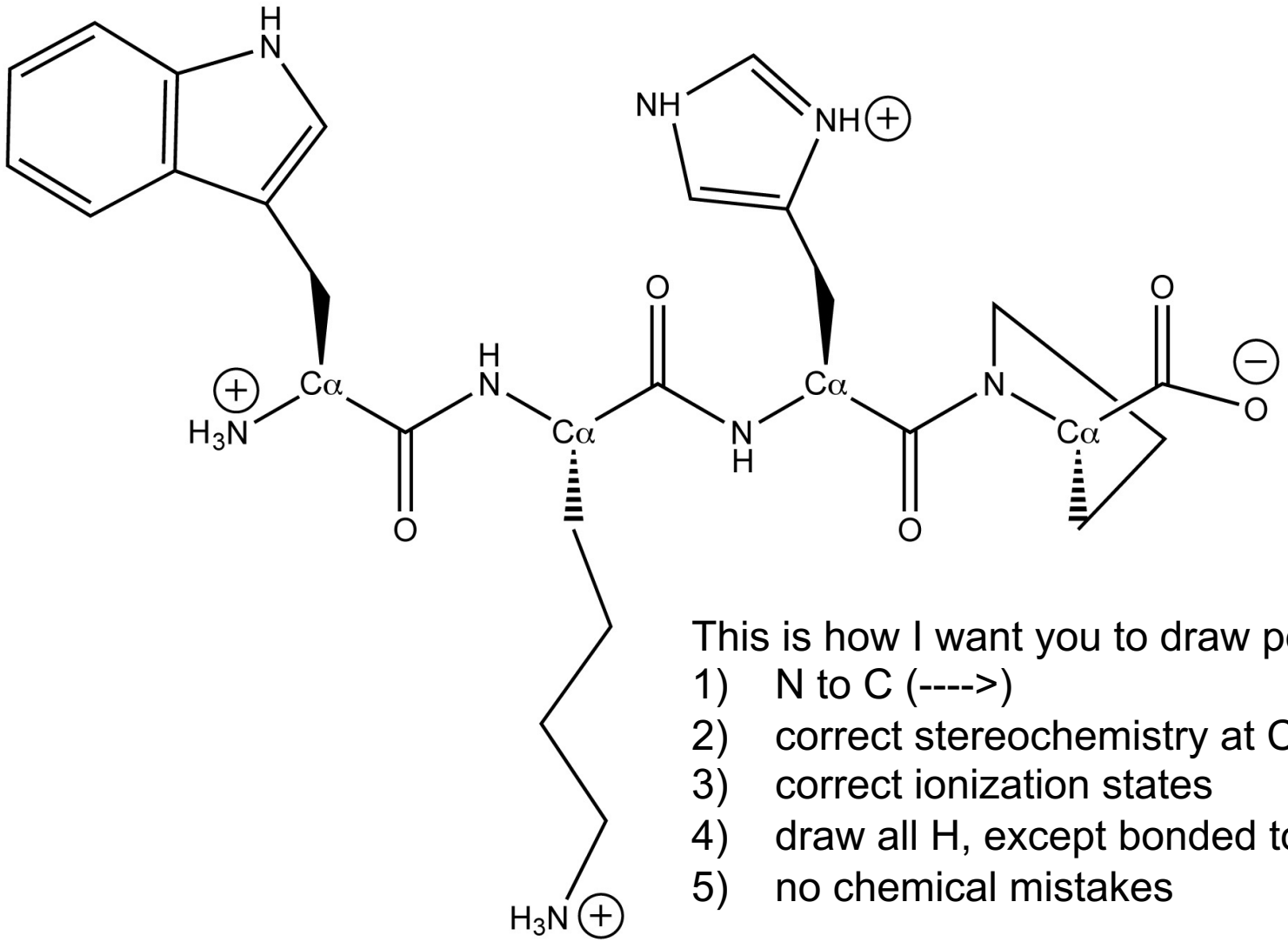
Loren William



Loren Williams, Georgia Tech

Draw the predominant form of WKHP at pH 5.5

Draw the predominant form of WKHP at pH 5.5



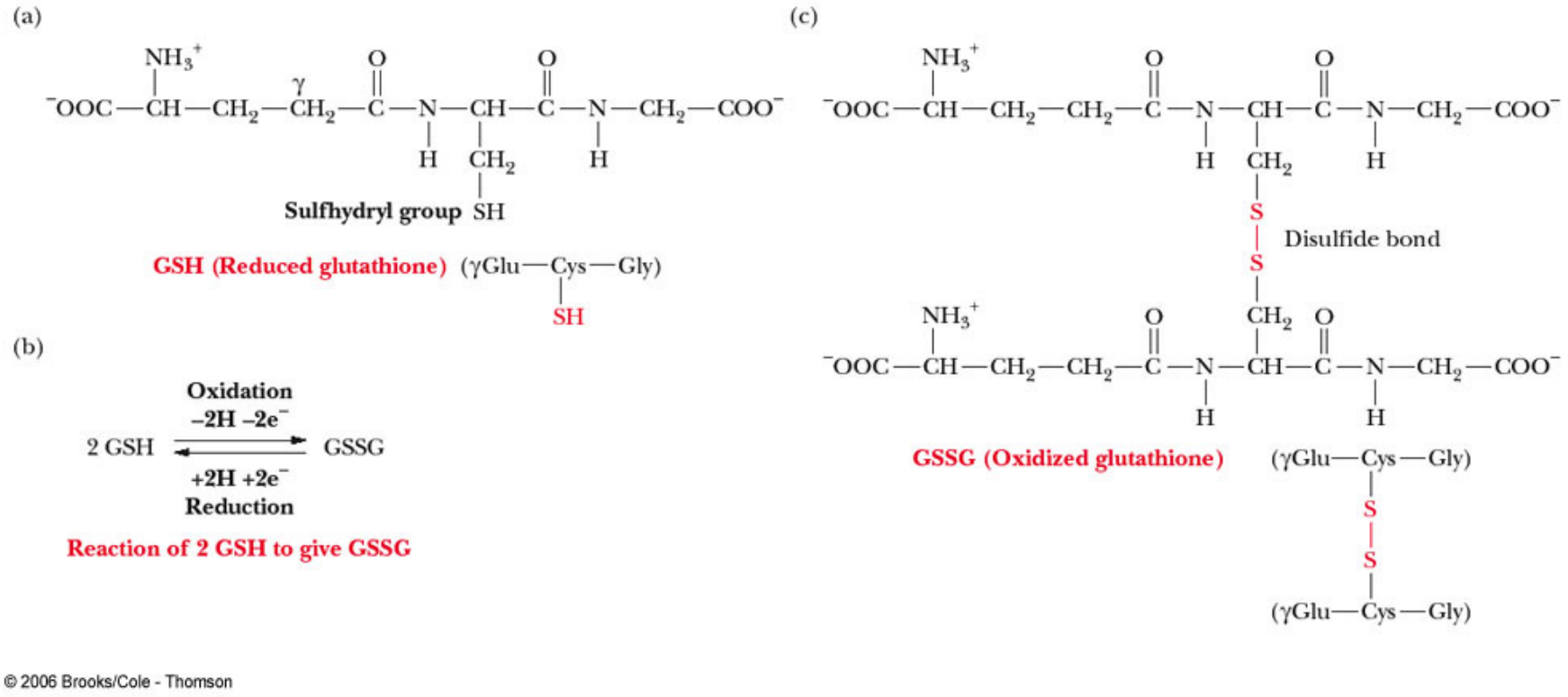
This is how I want you to draw peptides

1) N to C (---->)
2) correct stereochemistry at Cα
3) correct ionization states
4) draw all H, except bonded to C
5) no chemical mistakes

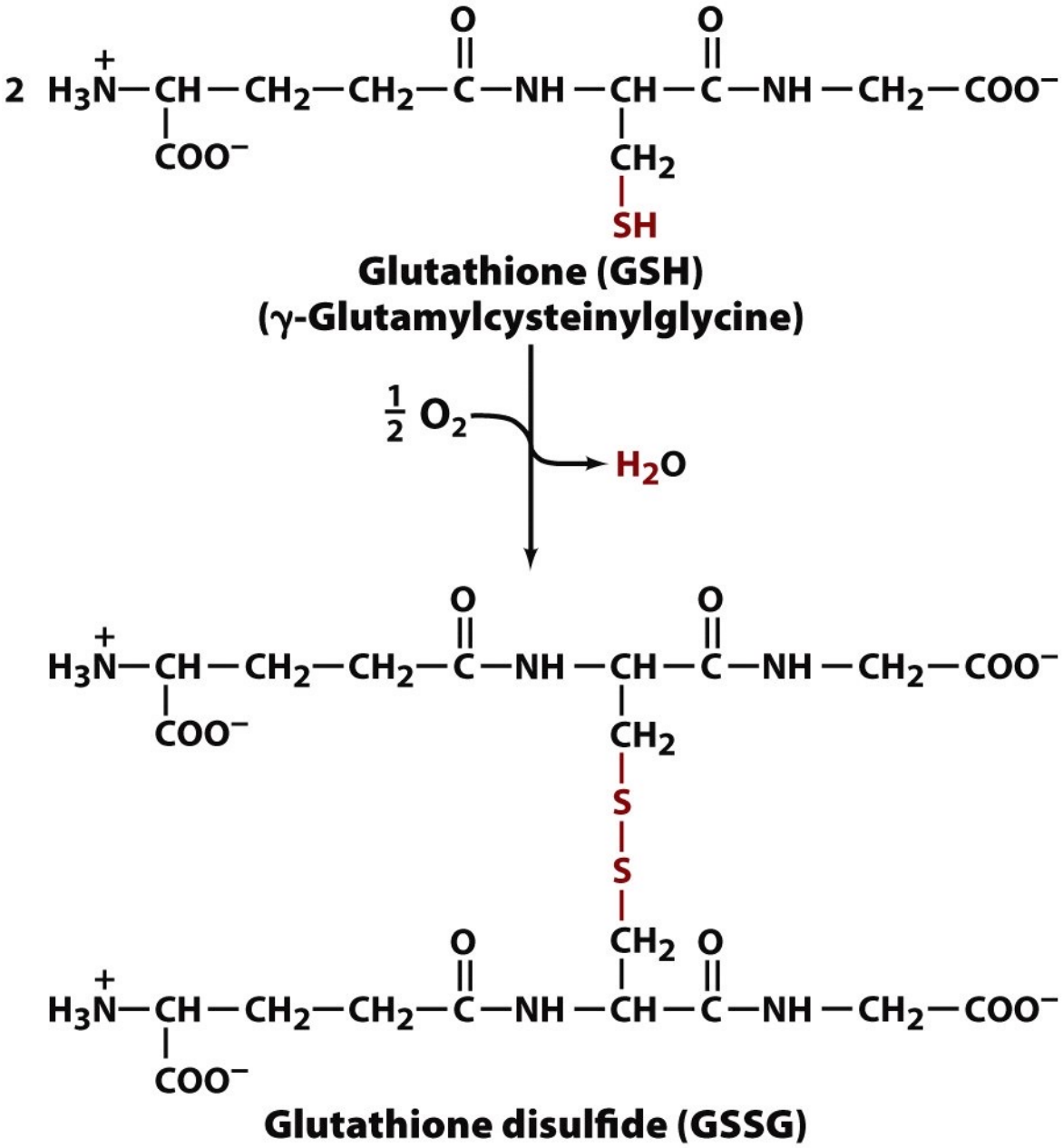
Peptides

- Peptide: the name given to a short polymer of amino acids joined by peptide bonds; they are classified by the number of amino acids in the chain
- Dipeptide: a molecule containing two amino acids joined by a peptide bond
- Tripeptide: a molecule containing three amino acids joined by peptide bonds
- Oligopeptides 20 or so amino acids joined by peptide bonds
- Polypeptide: a macromolecule containing many amino acids joined by peptide bonds (more than hundred)
- Protein: a biological macromolecule consisting of one or more polypeptide chains

Glutathione (Tripeptide)



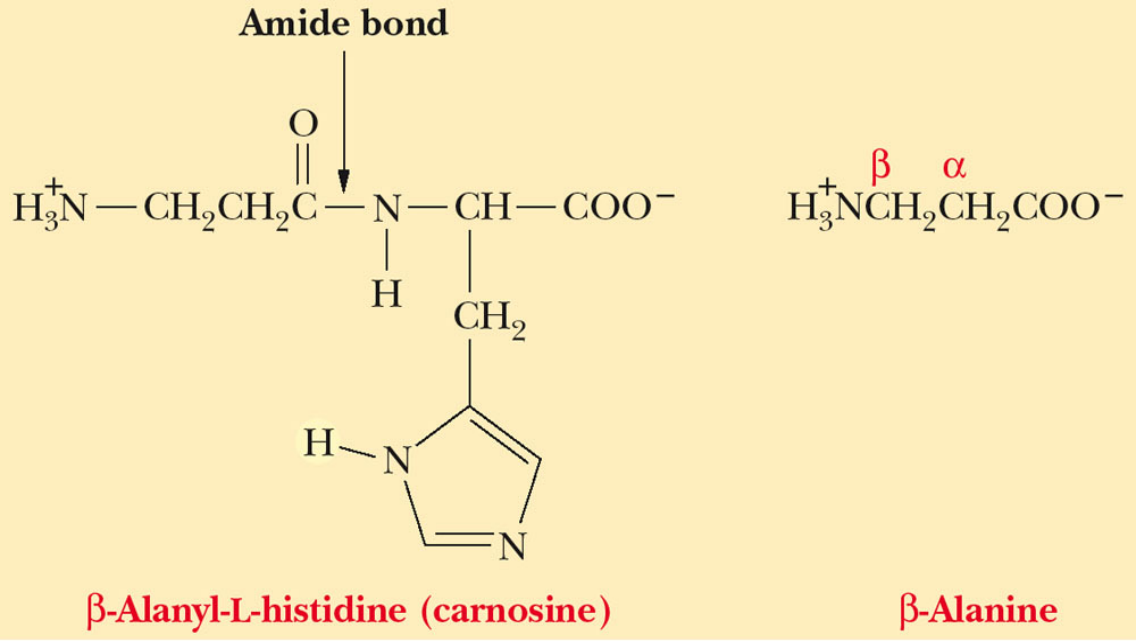
Glutathione is a scavenger for oxidizing agents



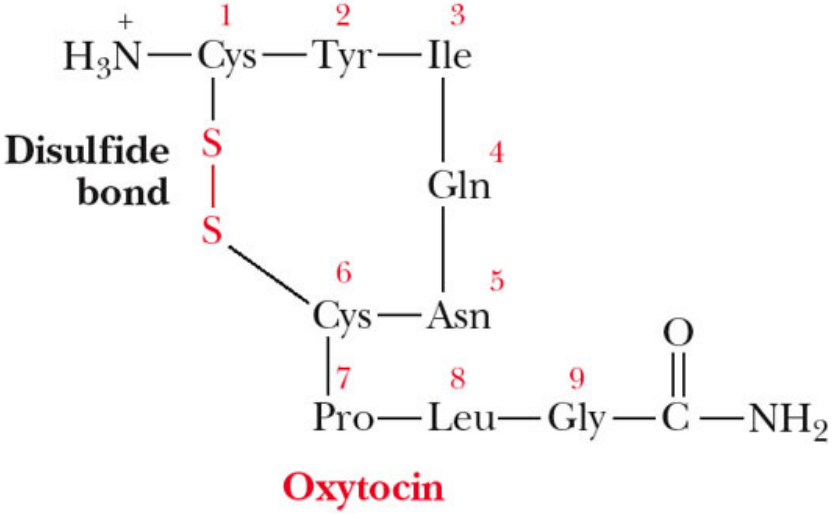
Small Peptides with Physiological Activity

- Small peptides, containing two to several dozen amino acid residues, can have marked physiological effects in organisms.

- **Carnosine** is naturally occurring dipeptides (β-alanine and Histidine) in muscle tissue.

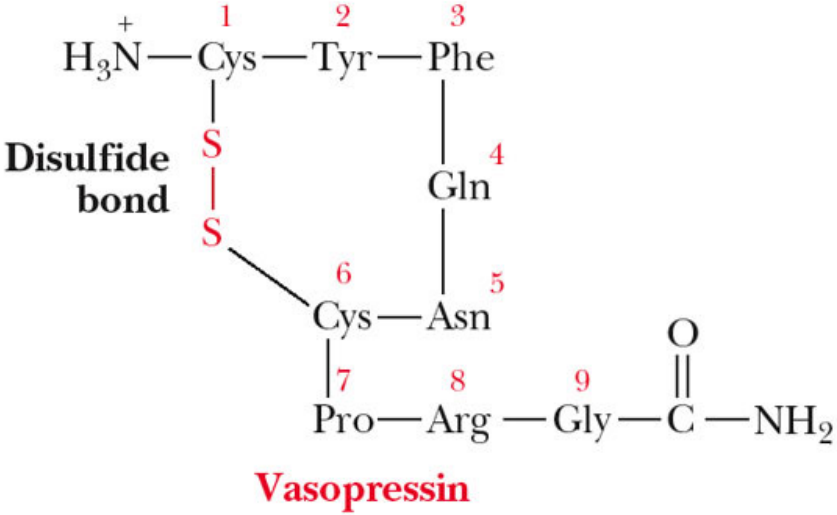


- **Oxytocin** has an isoleucine at position 3 and a leucine at position 8; it stimulates smooth muscle contraction in the uterus during labor and in the mammary glands during lactation.



Oxytocin

- **Vasopressin** has a phenylalanine at position 3 and an arginine at position 8; it stimulates resorption of water by the kidneys, thus raising blood pressure.



Vasopressin