

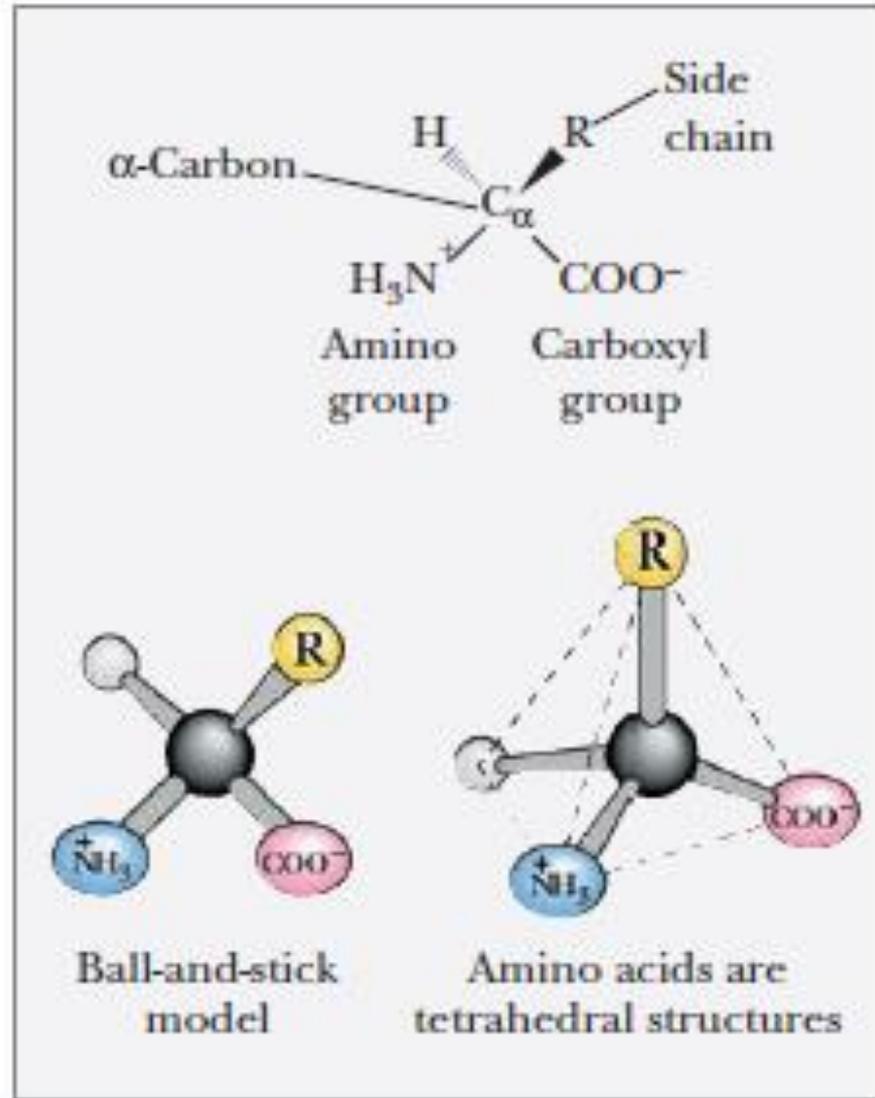


Amino acids and peptides

Dr. Diala Abu-Hassan, DDS, PhD

Dr.abuhassand@gmail.com

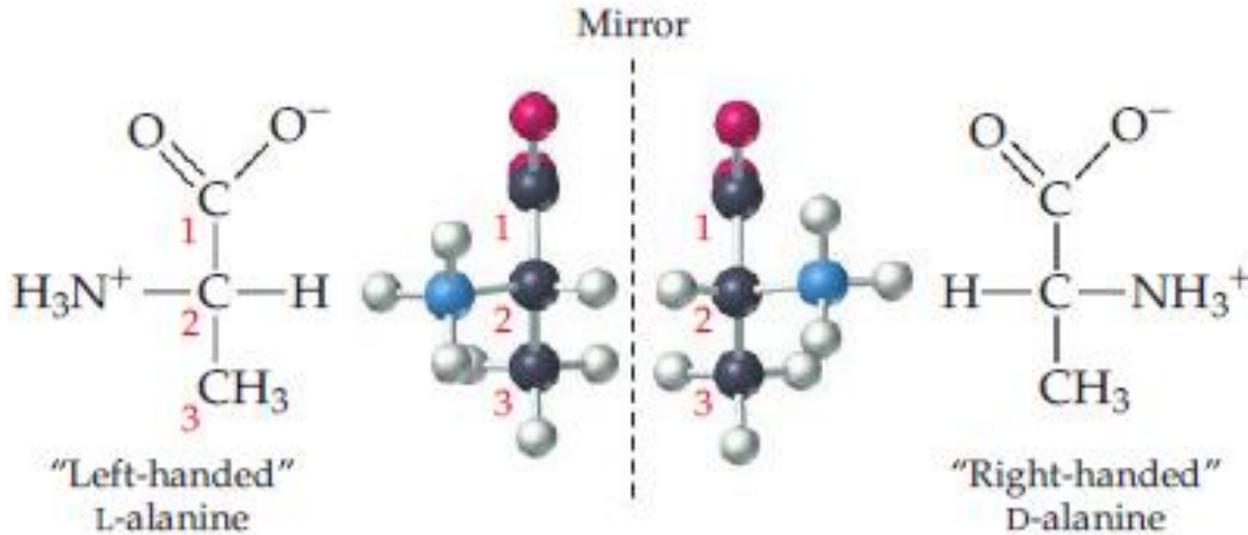
Amino Acid Structure



Only 20 are usually found in proteins

Amino acid stereoisomers or optical isomers

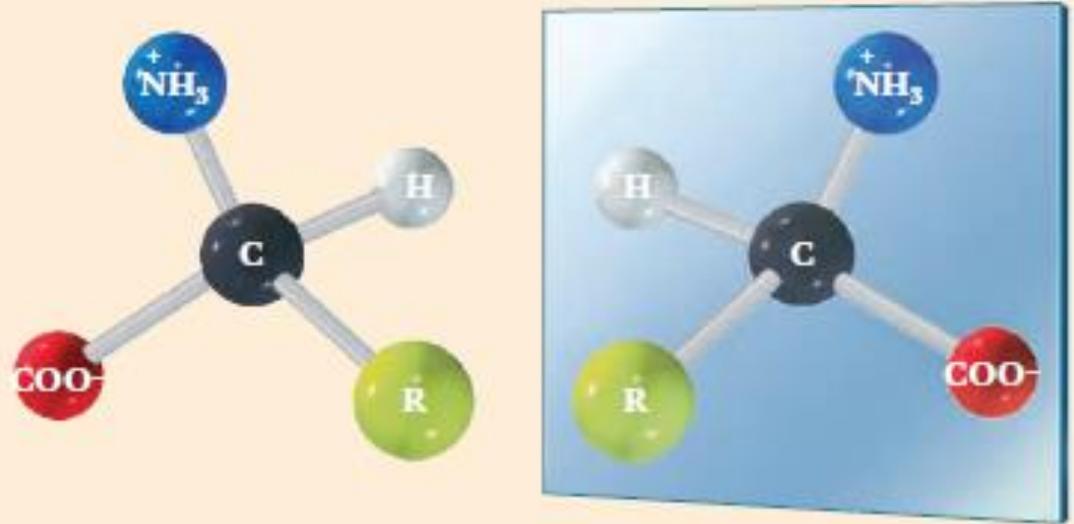
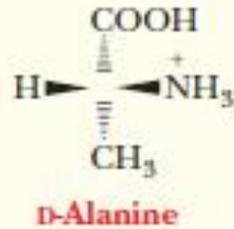
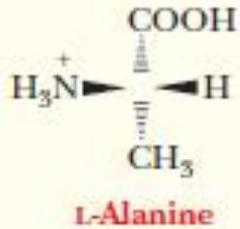
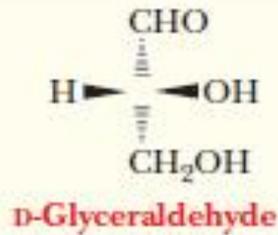
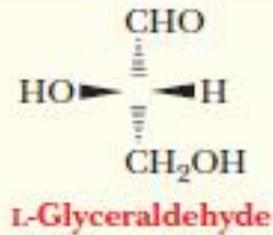
Alanine, a chiral molecule



The amino acids in proteins are not superimposable on their mirror images (with the exception of glycine).

Latin *laevus* and *dexter*, meaning “left” and “right,” respectively, (the ability to rotate polarized light to the left or the right).

Amino acid stereoisomers



D-amino acids occur in nature, in bacterial cell walls and in some antibiotics, but not in proteins.

Amino acid classification

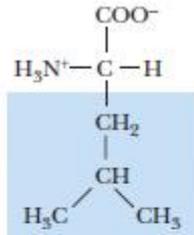
Polarity of the
side chain

Acid/base
properties of the
side chain

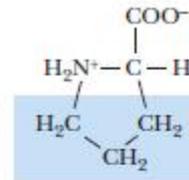
Functional group
presence and
nature in the side
chain

Non-polar (hydrophobic) Amino acids

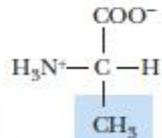
A Non-polar (hydrophobic)



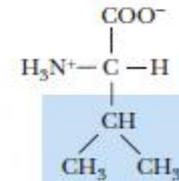
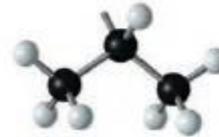
Leucine (Leu, L)



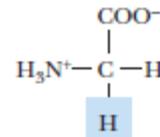
Proline (Pro, P)



Alanine (Ala, A)



Valine (Val, V)



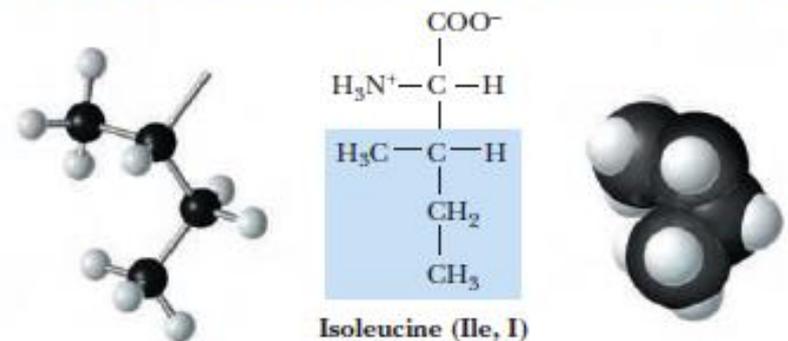
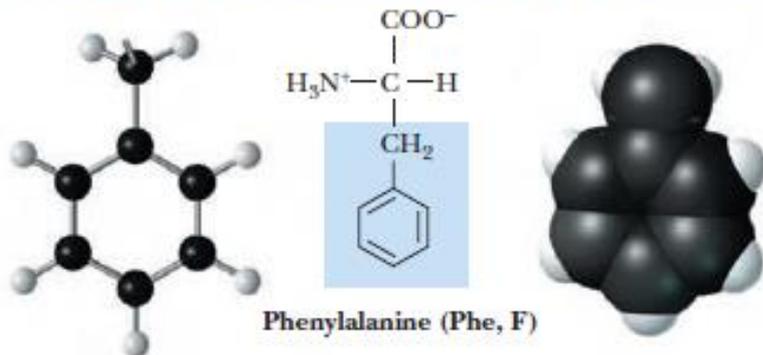
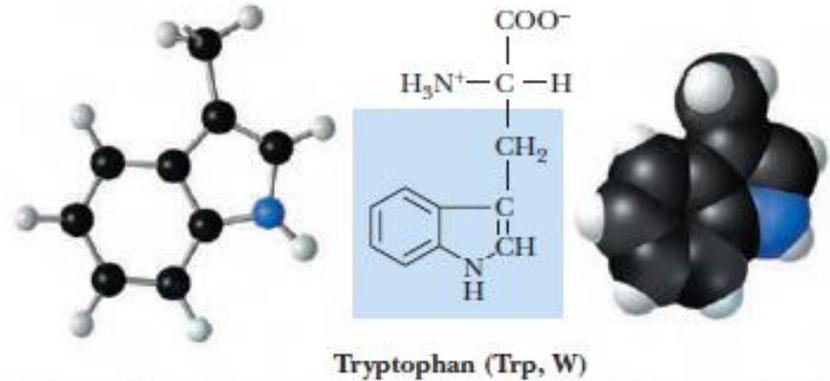
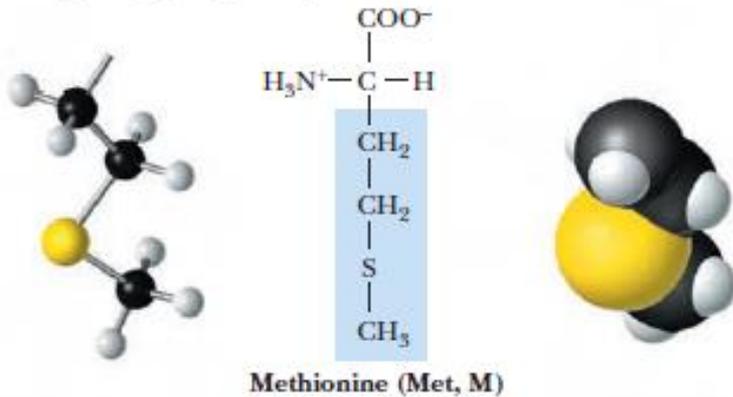
Glycine (Gly, G)

Aliphatic: no benzene ring

All amino acids are primary amines except Pro, a secondary amine

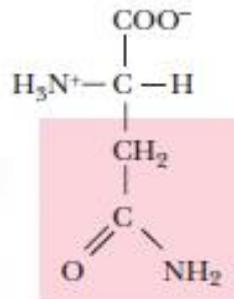
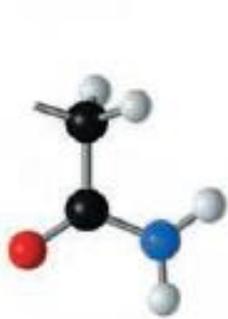
Non-polar Hydrophobic Amino acids

A Non-polar (hydrophobic)

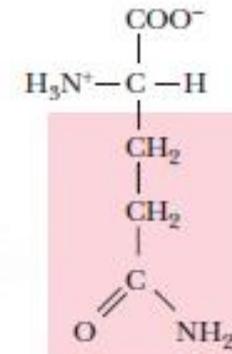


Polar Uncharged Amino acids

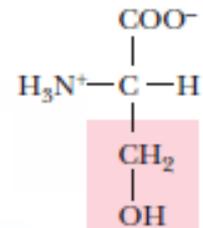
B Polar, uncharged



Asparagine (Asn, N)



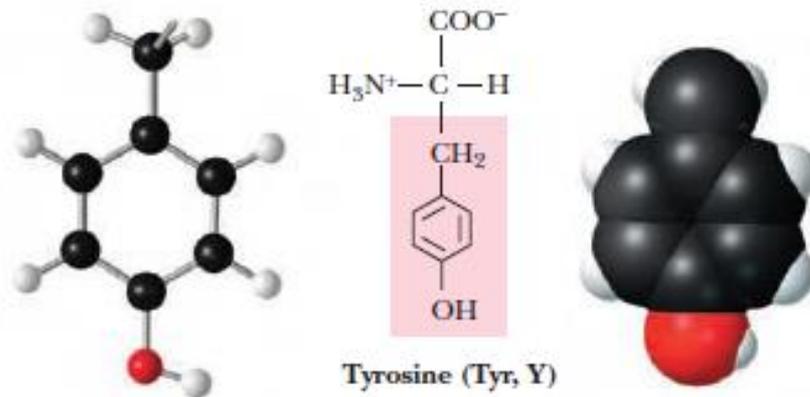
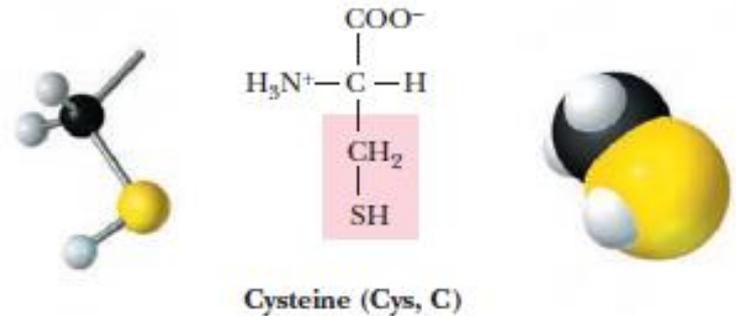
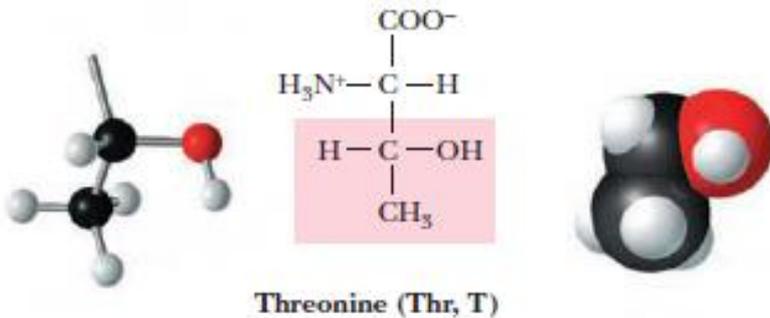
Glutamine (Gln, Q)



Serine (Ser, S)

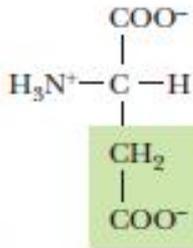
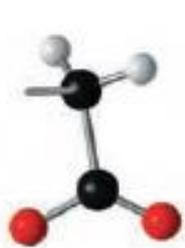
Polar Uncharged Amino acids

B Polar, uncharged

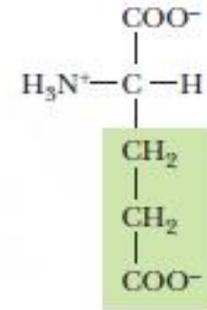
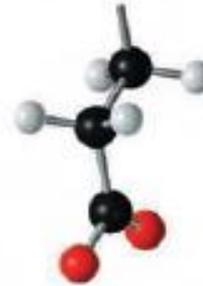


Acidic Amino acids

Acidic



Aspartic acid (Asp, D)

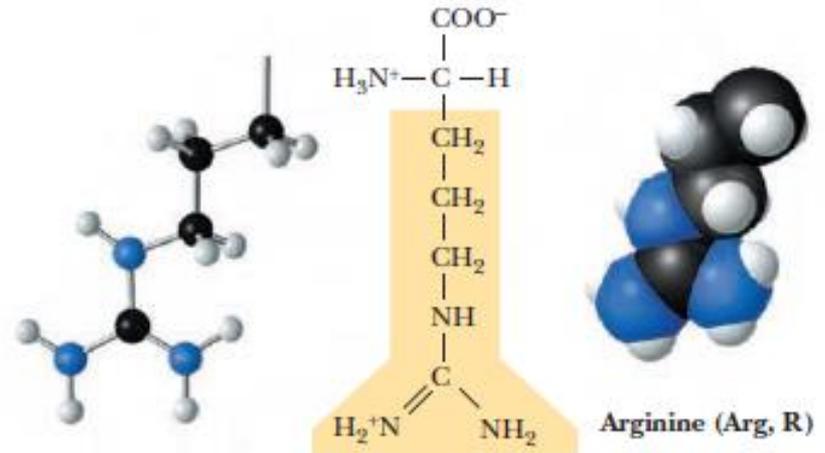
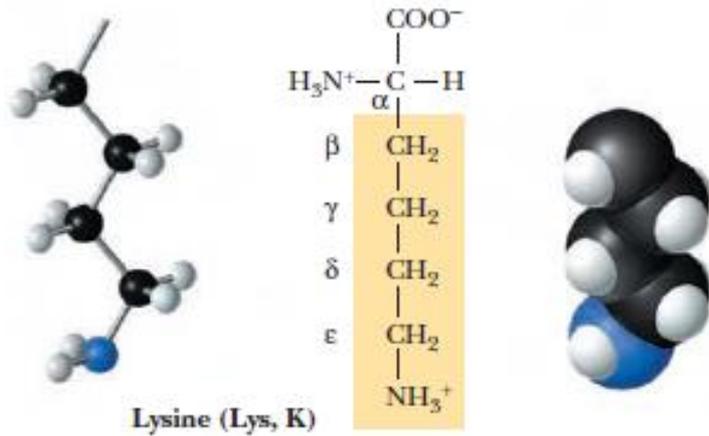


Glutamic acid (Glu, E)

Carboxylate anions
Negatively charged at neutral pH

Basic Amino acids

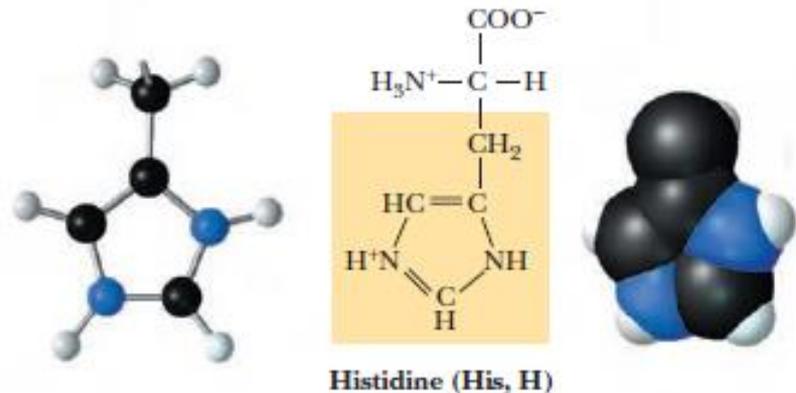
D Basic



The side chain is positively charged at or near neutral pH.

His can be found in the protonated or unprotonated forms in proteins

The properties of many proteins depend on whether each His residue is charged or not.



Imidazole group

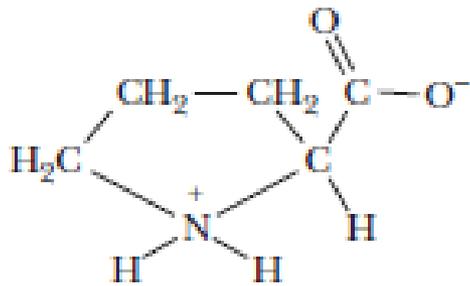
QUIZ

What is specific about proline?

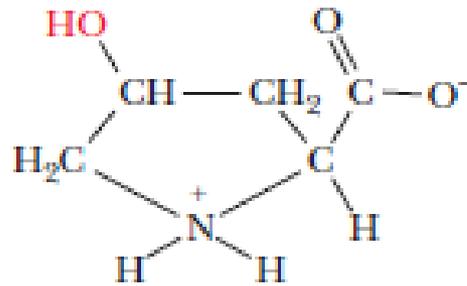
An acidic amino acid is _____ charged at physiological conditions

Name 2 amino acids that share a functional group in their side chain

Uncommon Amino acids



Proline

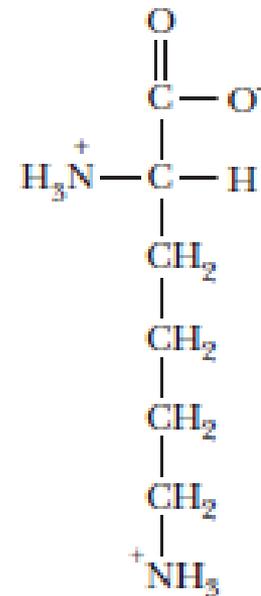


Hydroxyproline

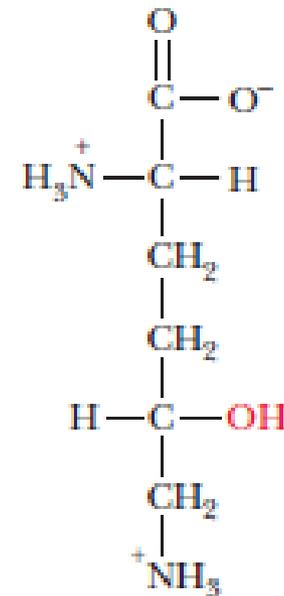
Collagen

Derived from the common amino acids.

Produced by modification of the parent amino acid **after** protein synthesis, posttranslational modification.



Lysine



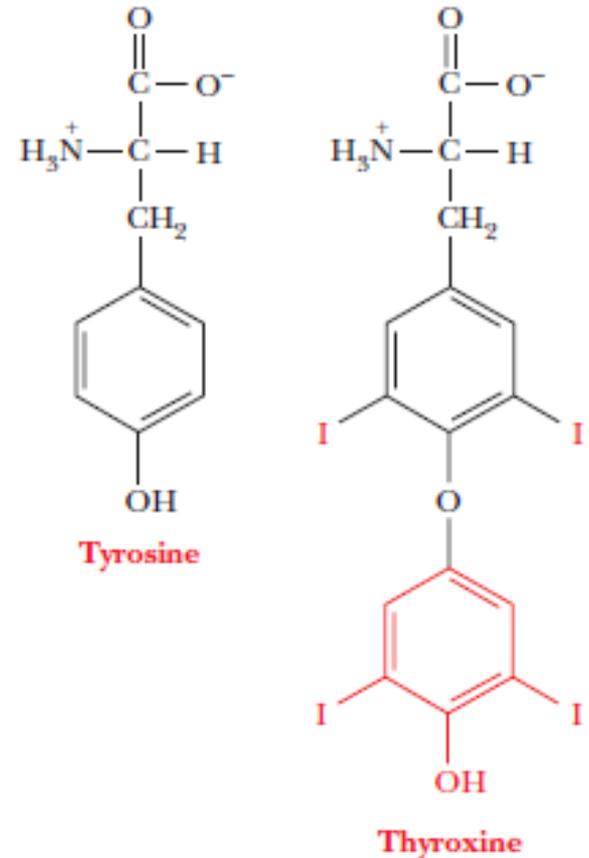
Hydroxylysine

Collagen

Uncommon Amino acids

Thyroxine is formed by posttranslational modification of tyrosine residues in the protein thyroglobulin.

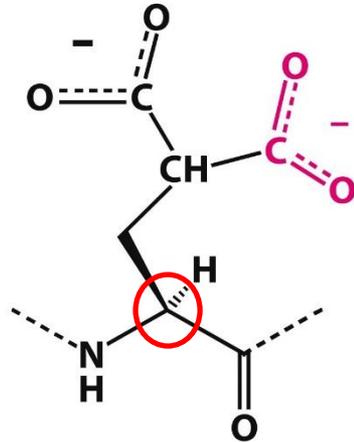
Thyroxine is then released as a hormone by proteolysis of thyroglobulin



Thyroxine

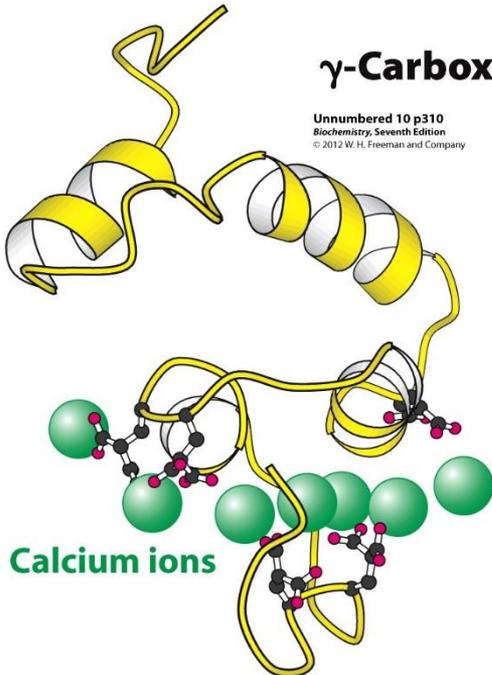
Uncommon Amino acids

γ -carboxyglutamic acid (or γ -carboxyglutamate)



γ -Carboxyglutamate residue

Unnumbered 10 p310
Biochemistry, Seventh Edition
© 2012 W. H. Freeman and Company



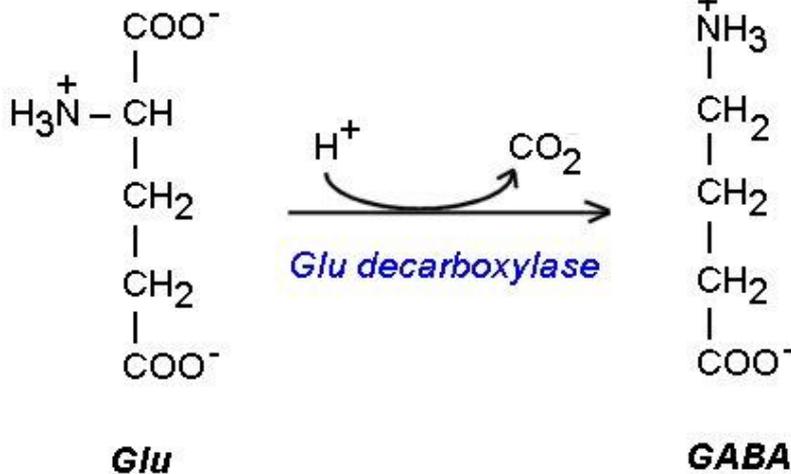
Is a post-translational carboxylation of glutamic acid residues.

Found in clotting factors and other proteins of the coagulation cascade to introduce an affinity for calcium ions.

Vitamin K is required to introduce γ -carboxylation of clotting factors II, VII, IX, X

Uncommon Amino acids

γ -aminobutyric acid (GABA)

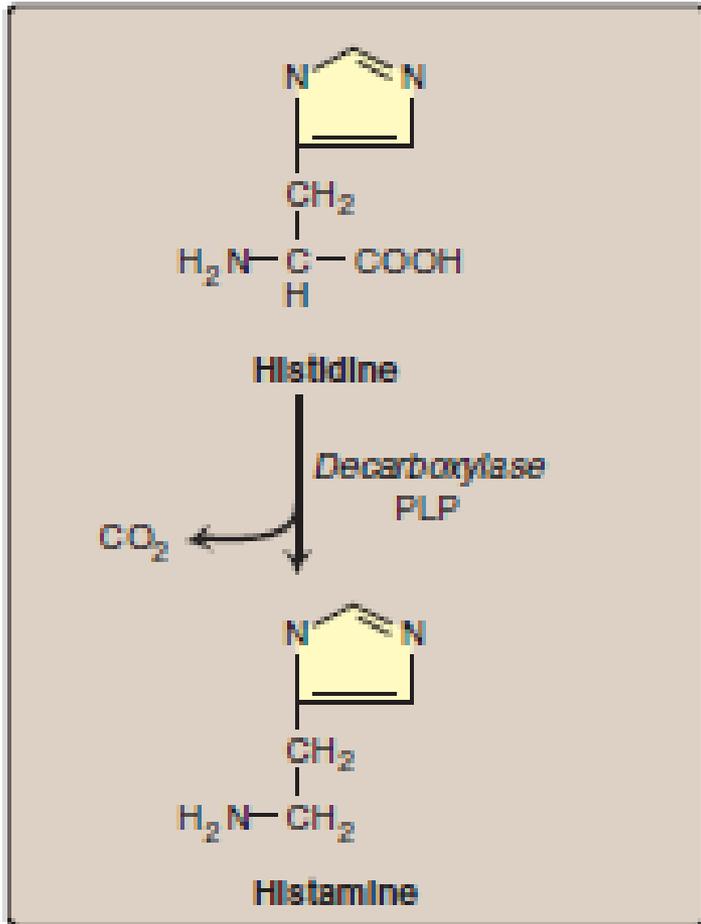


Is an essential inhibitory neurotransmitter in the CNS by reducing neuronal excitability.

GABA is synthesized in brain because it does not cross the BBB.

GABA have relaxing, anti-anxiety, and anti-convulsive effects.

Amino acids and the synthesis of other nitrogen containing compounds



Histamine

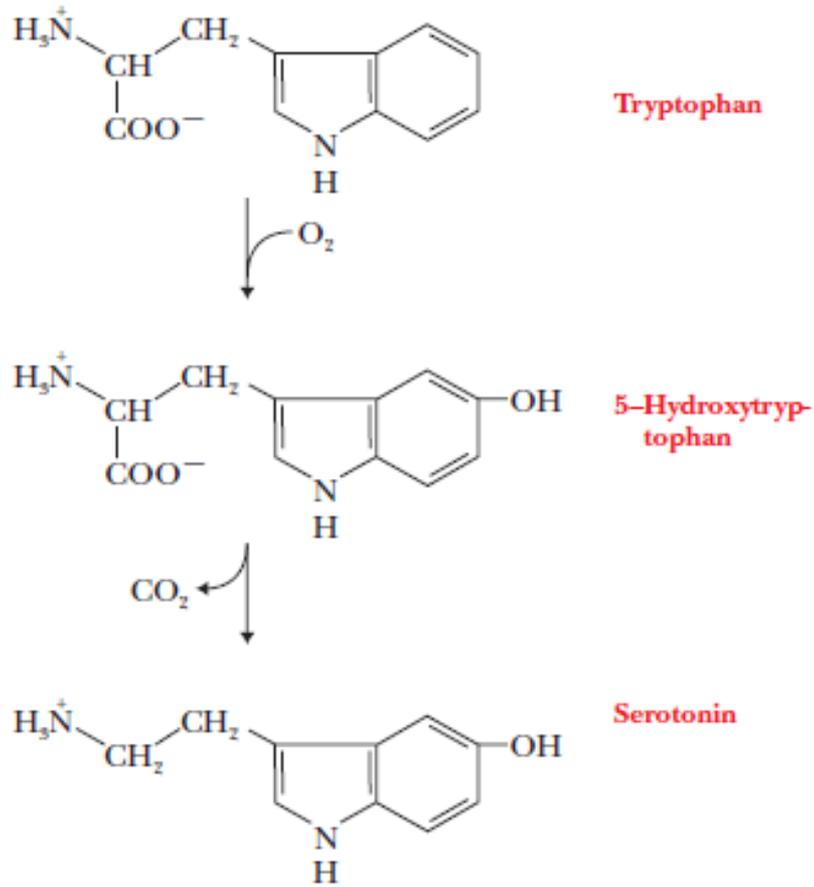
Is a potent vasodilator

Is released as part of the immune response, increases the localized blood volume for white blood cells resulting in swelling and stuffiness associated with a cold.

Most cold medications contain antihistamines to overcome stuffiness.

Amino acids and the synthesis of other nitrogen containing compounds

Serotonin



Serotonin has a sedative effect, giving a pleasant feeling.

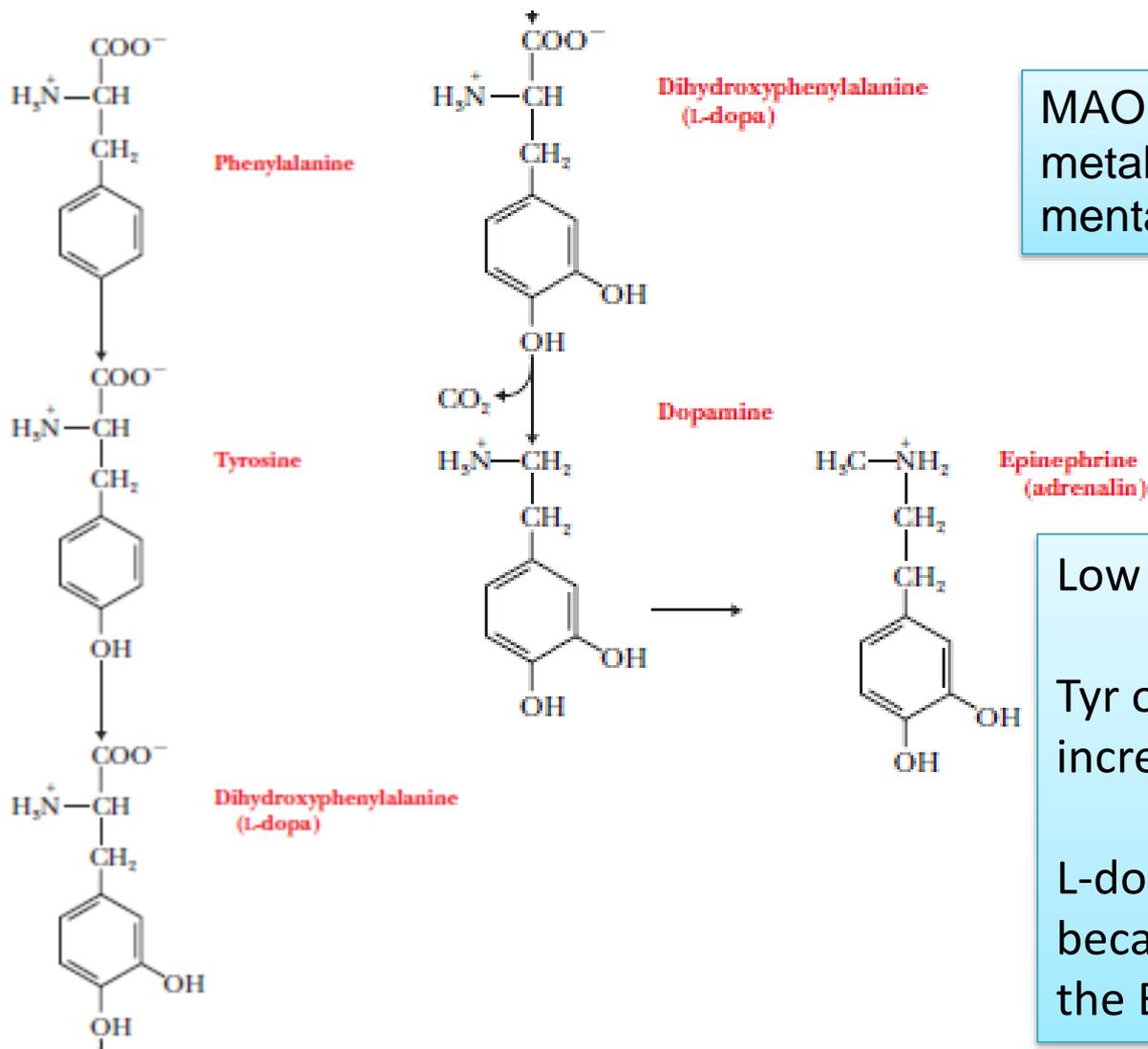
Low serotonin, depression

High serotonin levels, a manic state.

Bipolar disorder (manicdepressive illness) can be managed by controlling the levels of serotonin and its further metabolites.

Amino acids and the synthesis of other nitrogen containing compounds

Catecholamines



MAO inhibitors inhibit epinephrine metabolism and results in a high mental state

Low L-dopa, Parkinson's disease.

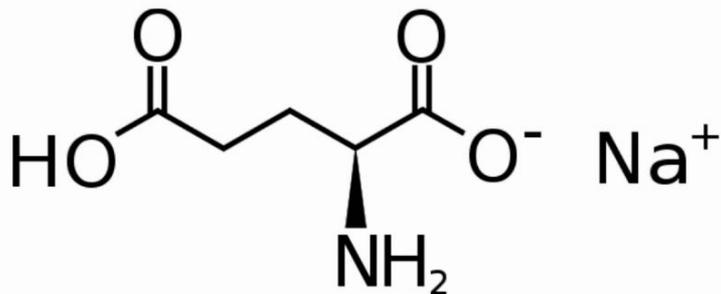
Tyr or Phe supplements might increase the levels of dopamine

L-dopa is usually prescribed because it passes quickly through the BBB

Biochemical applications: Monosodium glutamate (MSG)



MONOSODIUM GLUTAMATE



SODIUM SALT OF GLUTAMIC ACID

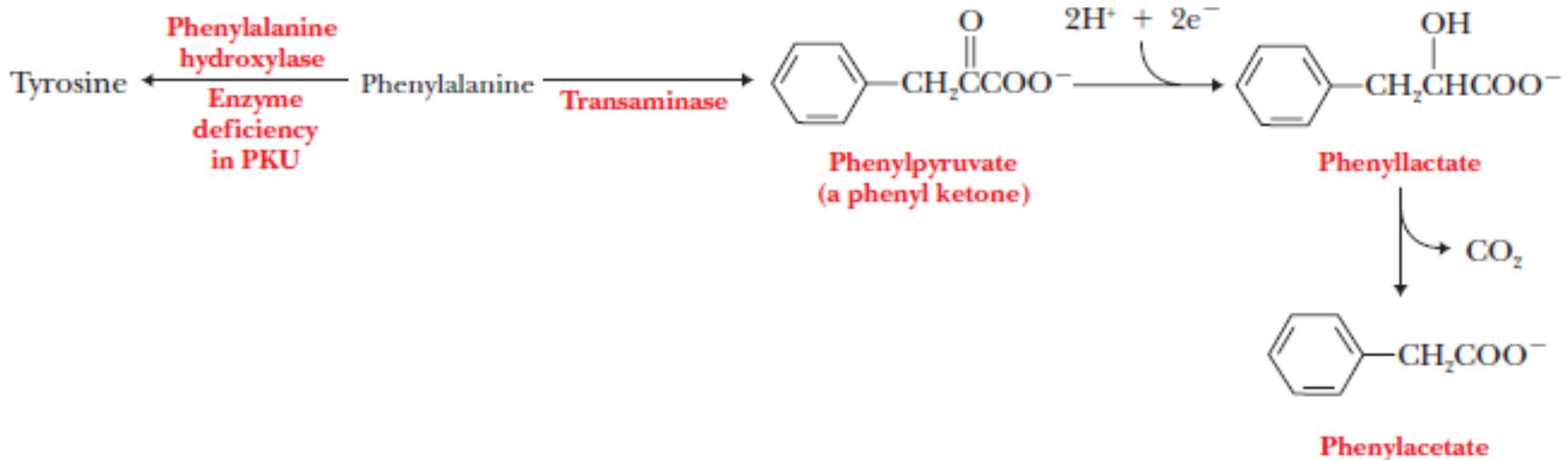
Glutamic acid derivative

Flavor enhancer, Asian food.

MSG causes a physiological reaction in some people (chills, headaches, and dizziness)

Chinese restaurant syndrome.

Clinical hint: Phenylketonuria (PKU)

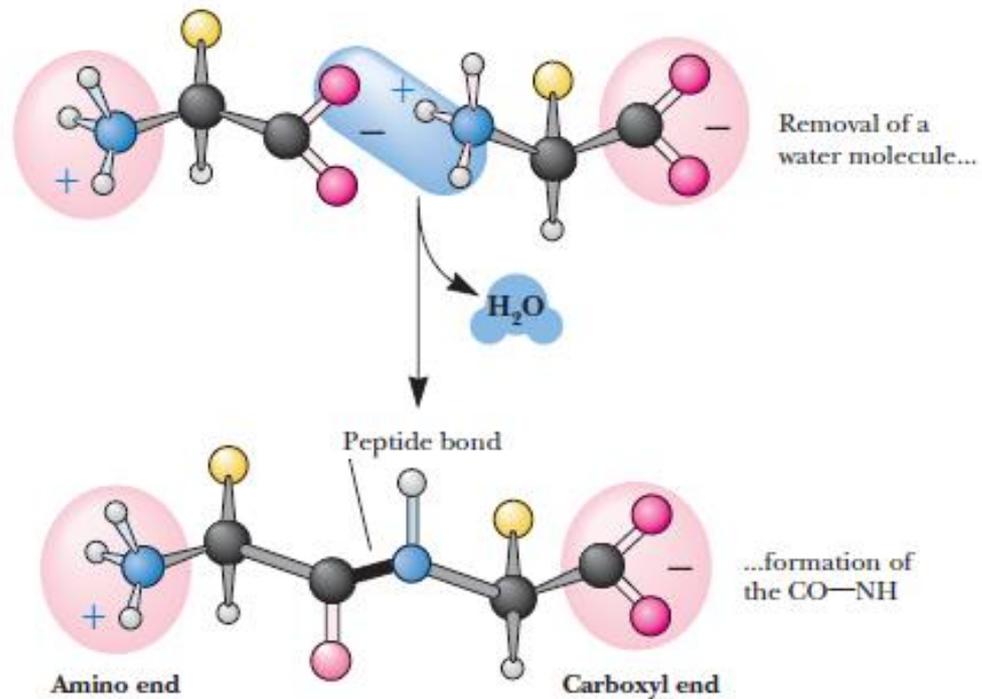
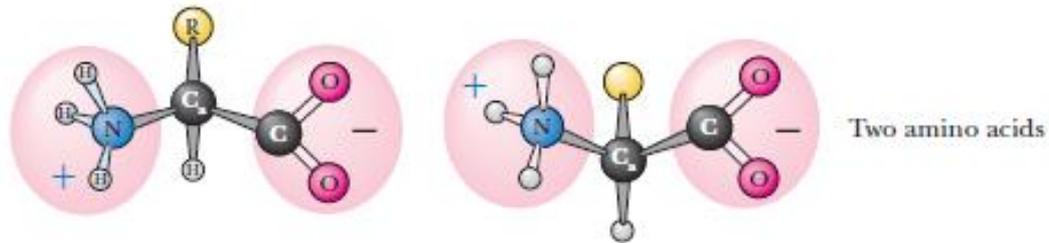


- Reactions involved in the development of phenylketonuria (PKU). A deficiency in the enzyme that catalyzes the conversion of phenylalanine to tyrosine leads to the accumulation of phenylpyruvate, a phenyl ketone.

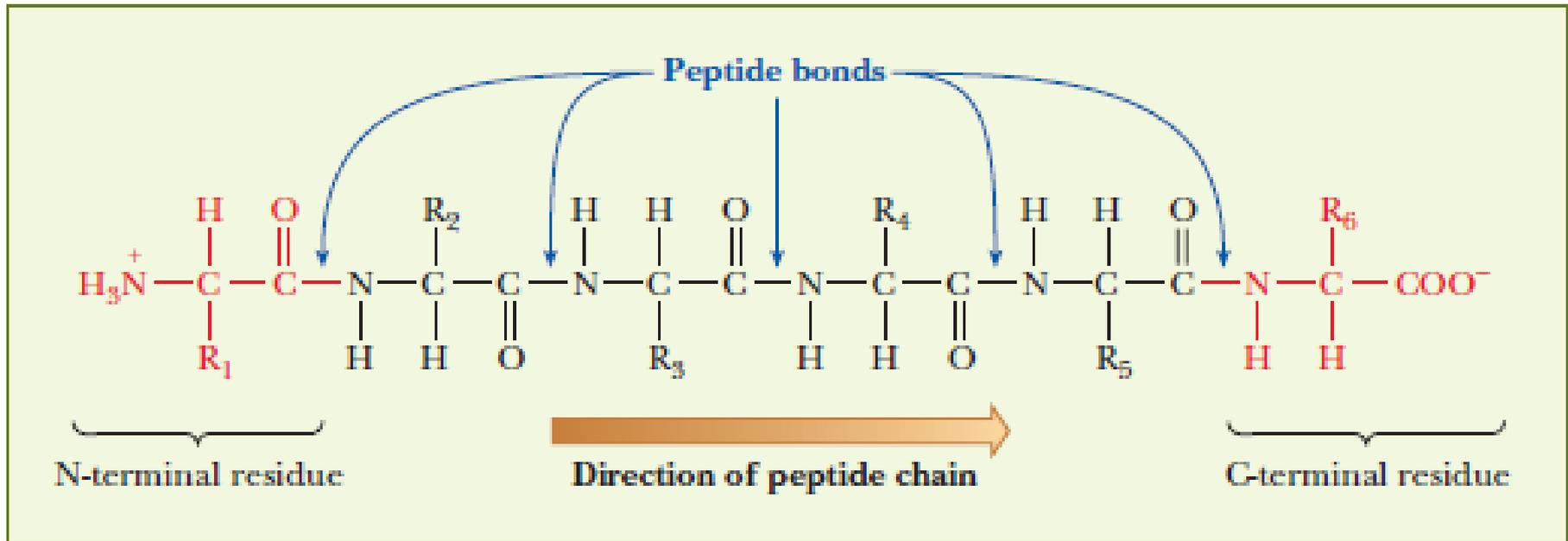
Amino acid and protein molecular weight

- The average molecular weight of an amino acid residue is about 110
 - The molecular weights of most proteins are between 5500 and 220,000 (*calculate how many amino acids*)
- We refer to the mass of a polypeptide in units of Daltons
 - A 10,000-MW protein has a mass of 10,000 Daltons (Da) or 10 kilodaltons (kDa)

The peptide bond



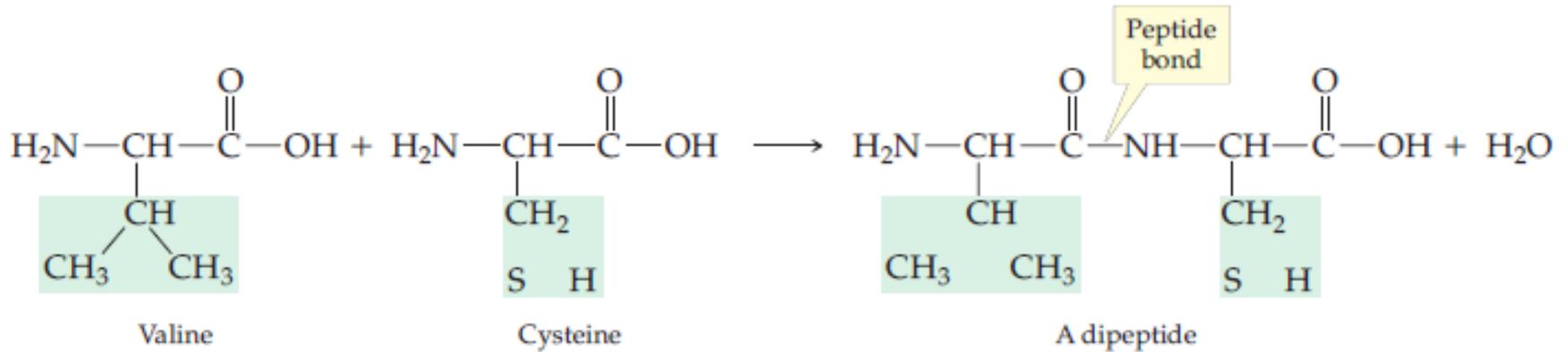
Peptide and polypeptide chains



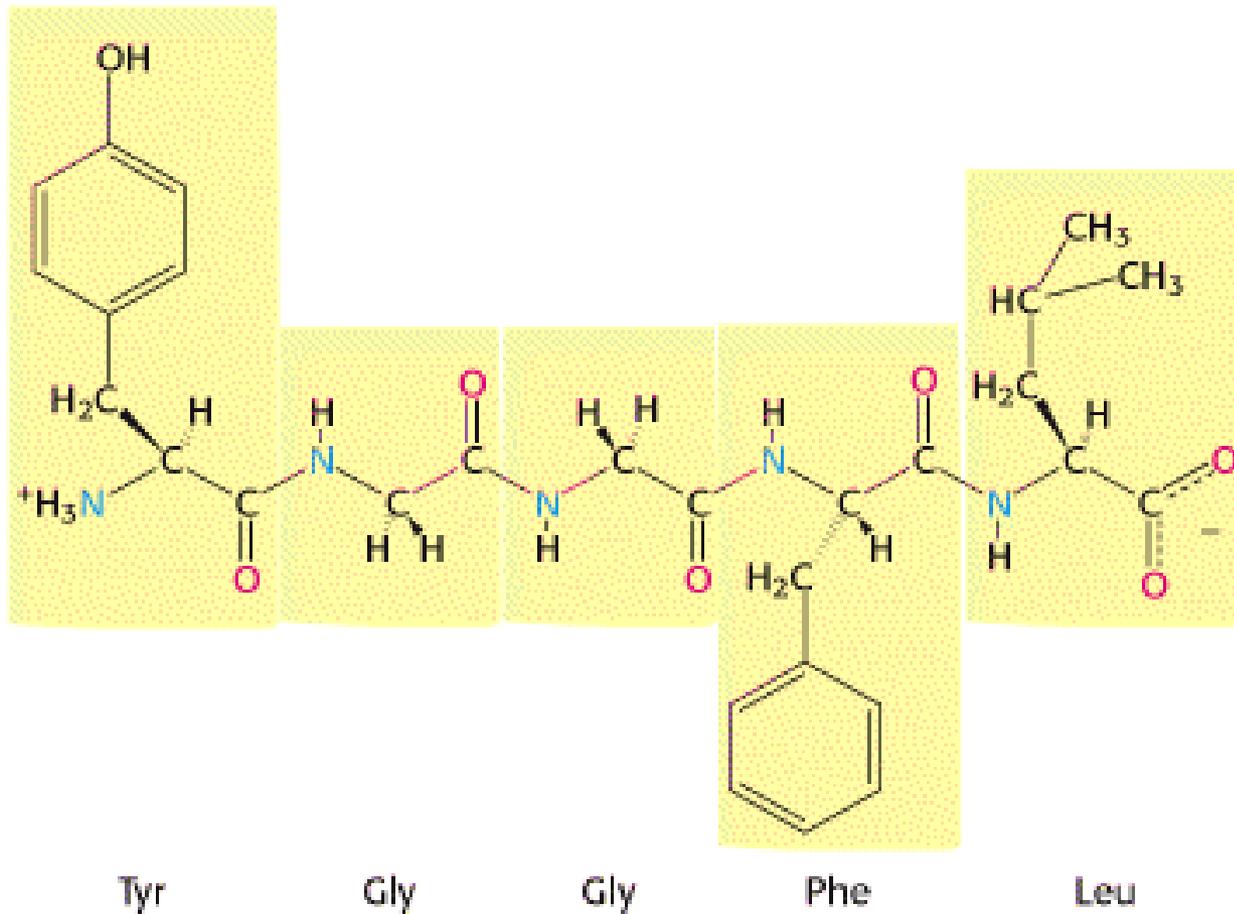
Peptides: two to several dozens AA.

Polypeptide chain: many amino acids (usually more than a hundred)

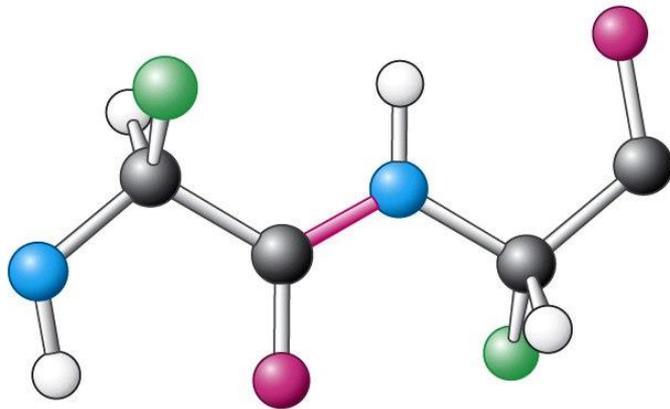
Proteins are polymers of amino acids



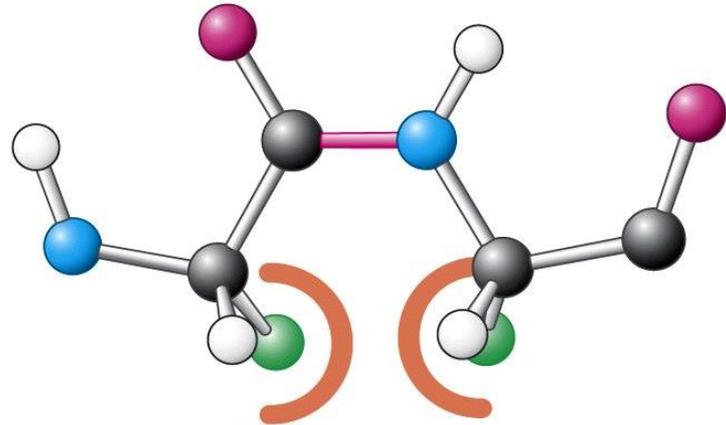
Cis vs. trans configurations



Why is it all trans?



Trans

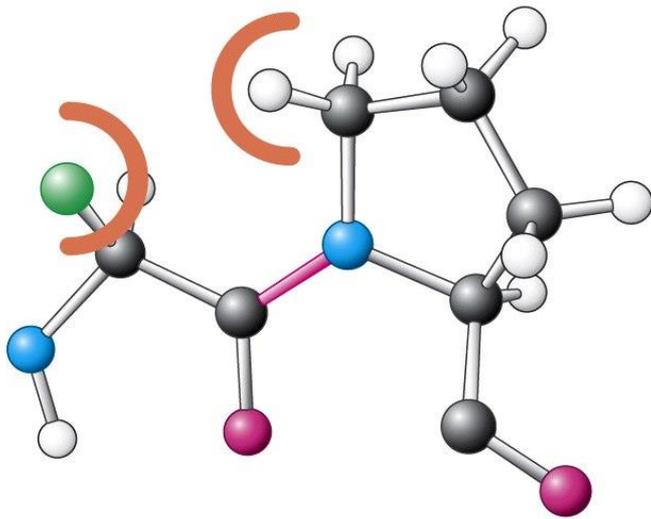


Cis

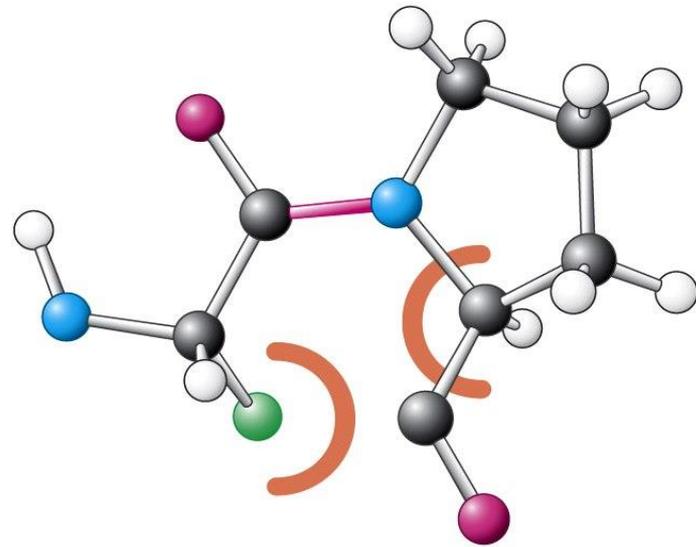
Figure 2-25
Biochemistry, Sixth Edition
© 2007 W. H. Freeman and Company

Except for proline

- In proline, both *cis* and *trans* conformations have about equivalent energies
- Proline is thus found in the *cis* configuration more frequently than other amino acid residues

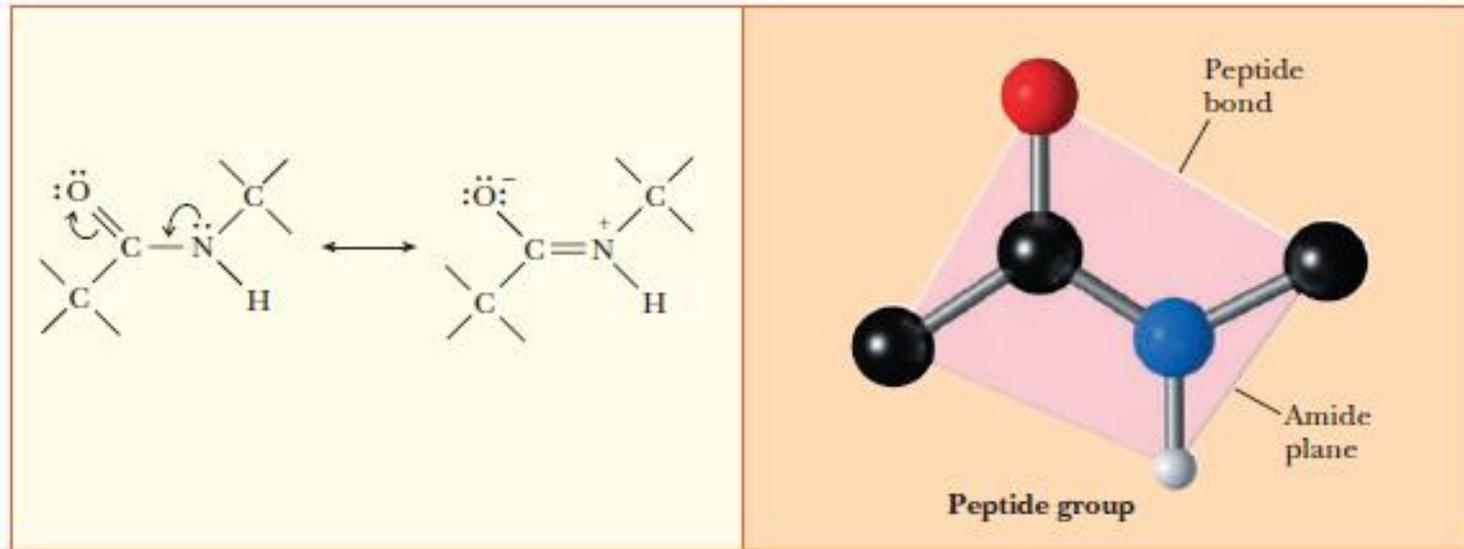


Trans



Cis

Resonance structures



A Resonance structures of the peptide group.

B The planar peptide group.

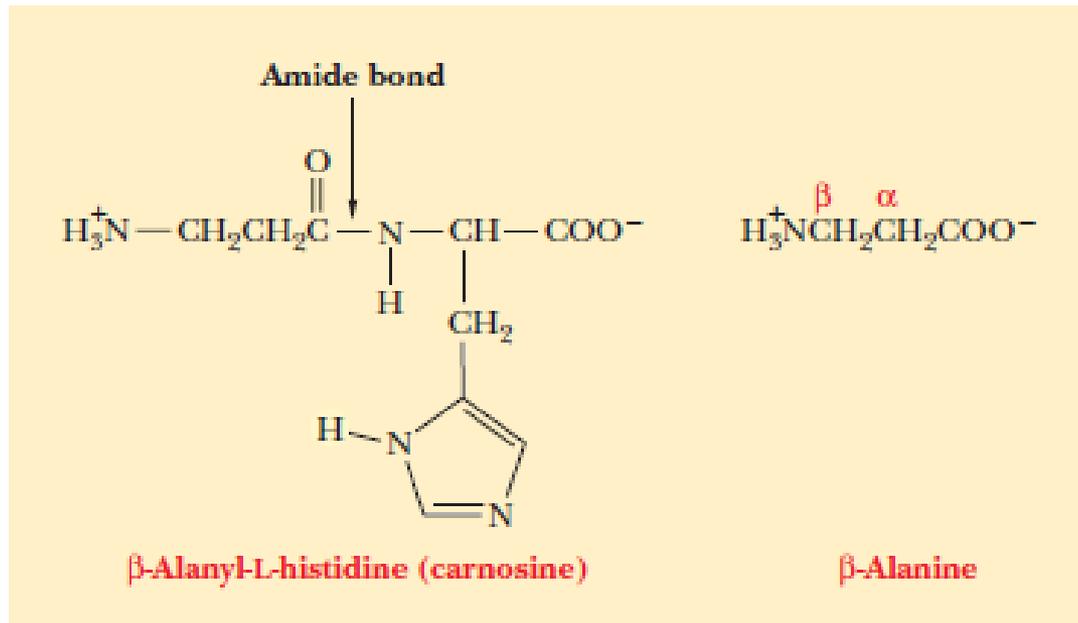
The peptide bond group is planar because it has partial double bond character.

The peptide bond is stronger than an ordinary single bond because of the resonance stabilization.

No significant rotation around the peptide bond acts as a stereochemical constraint that affects protein folding.

Small peptides with physiological functions

Carnosine



■ **FIGURE 3.11** Structures of carnosine and its component amino acid β -alanine.

- A naturally occurring dipeptide
- It is highly concentrated in muscle and brain tissues
 - Protection of cells from ROS (radical oxygen species) and peroxides
 - Muscle contraction

Small peptides with physiological functions

Enkephalins

Tyr—Gly—Gly—Phe—Leu (three-letter abbreviations)

Y—G—G—F—L (one-letter abbreviations)

Leucine enkephalin

Tyr—Gly—Gly—Phe—Met

Y—G—G—F—M

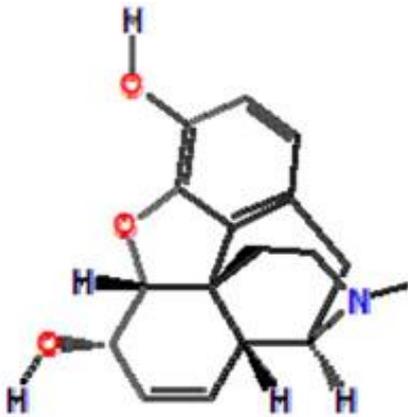
Methionine enkephalin

Two pentapeptides found in the brain

Naturally occurring analgesics (pain relievers).

The aromatic side chains of Tyr and Phe in these peptides play a role in their activities.

Morphine and enkephalins



Morphine



Enkephalins

3D structures of opiates, such as morphine, and enkephalins are similar, hence, opiates bind to enkephalin receptors in the brain to produce their physiological activities.

Small peptides with physiological functions

Oxytocin and vasopressin

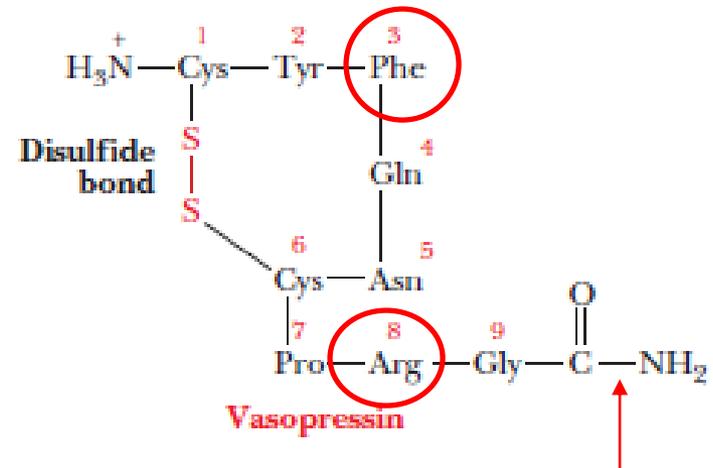
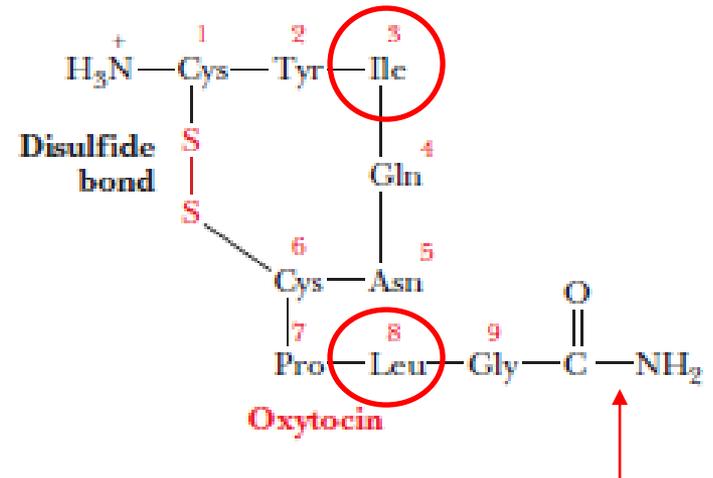
Cyclic structures due to an —S—S— bond

Each contains nine amino acid residues

Each has an amide group (rather than a free carboxyl group) at the C-terminal end

Each has a disulfide link between Cys residues at positions 1 and 6.

Both are hormones



■ FIGURE 3.13 Structures of oxytocin and vasopressin.

Peptide hormones: oxytocin and vasopressin

Oxytocin induces labor in pregnant women by controlling contraction of uterine muscle and stimulates the flow of milk in a nursing mother

During pregnancy, the number of receptors for oxytocin in the uterine wall increases.

As the cervix stretches, sending nerve impulses to the hypothalamus as a positive feedback to release more oxytocin by the posterior pituitary gland.

Vasopressin controls of blood pressure by regulating smooth muscle contraction.

Vasopressin is released by the action of the hypothalamus on the posterior pituitary.

Vasopressin stimulates water reabsorption by the kidney (an antidiuretic effect) resulting in water retention and blood pressure increase.

Textbook

Campbell and Farrell's Biochemistry,
Chapters 3 (pp.72-78) and 4