Amino Acids

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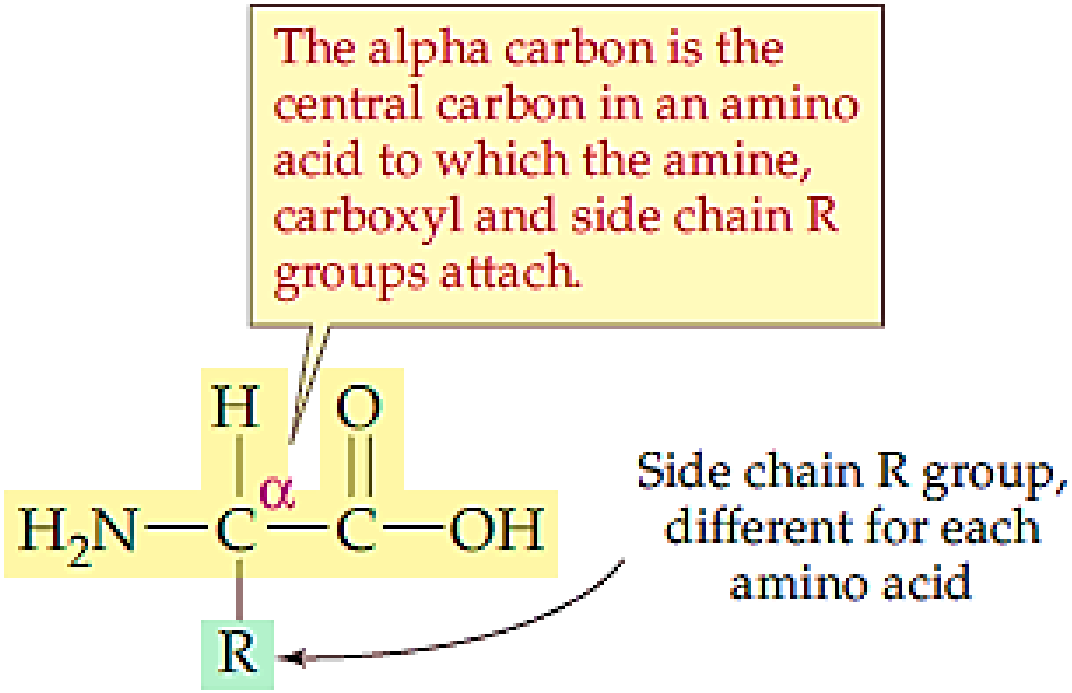
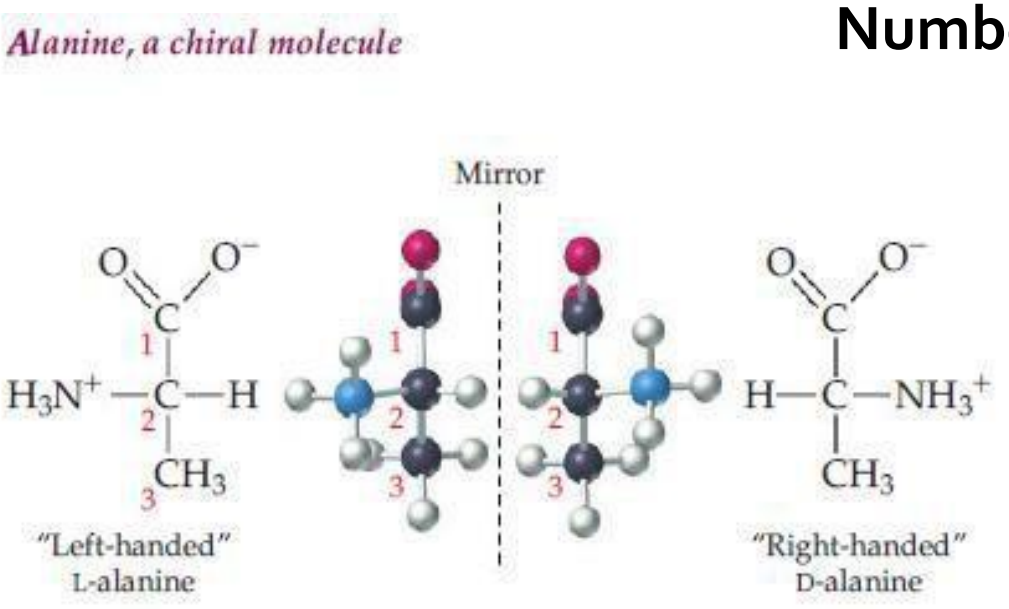
Protein structure and function

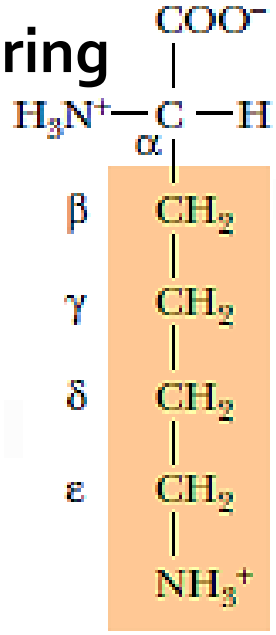
- Greek: proteios, primary (importance)
- 50 % of body's dry weight is protein
- Free vs. attached (**residue**), **D vs. L**

TYPE	FUNCTION	EXAMPLE
Enzymes	Catalysts	*Amylase*—begins digestion of carbohydrates by hydrolysis
Hormones	Regulate body functions by carrying messages to receptors	*Insulin*—facilitates use of glucose for energy generation
Storage proteins	Make essential substances available when needed	*Myoglobin*—stores oxygen in muscles
Transport proteins	Carry substances through body fluids	*Serum albumin*—carries fatty acids in blood
Structural proteins	Provide mechanical shape and support	*Collagen*—provides structure to tendons and cartilage
Protective proteins	Defend the body against foreign matter	*Immunoglobulin*—aids in destruction of invading bacteria
Contractile proteins	Do mechanical work	*Myosin and actin*—govern muscle movement





Carbon Numbering



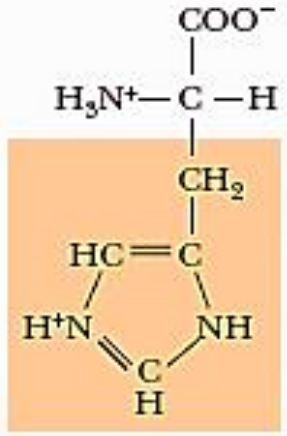
Names and codes

Amino Acid	3-letter code	1-letter code	Amino Acid	3-letter code	1-letter code
Alanine	Ala	A	Leucine	Leu	L
Arginine	Arg	R	Lysine	Lys	K
Asparagine	Asn	N	Methionine	Met	M
Aspartic acid	Asp	D	Phenylalanine	Phe	F
Cysteine	Cys	C	Proline	Pro	P
Glutamic acid	Glu	E	Serine	Ser	S
Glutamine	Gln	Q	Threonine	Thr	T
Glycine	Gly	G	Tryptophan	Trp	W
Histidine	His	H	Tyrosine	Tyr	Y
Isoleucine	Ile	I	Valine	Val	V

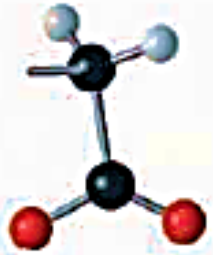
Classification (according to the polarity of R group)

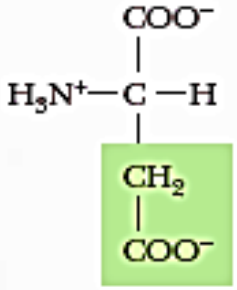
Non-polar	Polar	Charged (positive)	Charged (negative)
Alanine	Serine	Lysine	Glutamate
Valine	Threoeine	Arginine	Aspartate
Leucine	Glutamine	Histidine	
Isoleucine	Asparagine		
Methionine	Cysteine		
Tryptophan	Tyrosine		
Phenylalanine			
Proline			
Glycine			

Polar, Charged

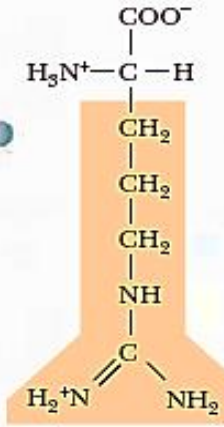


Histidine (His, H)

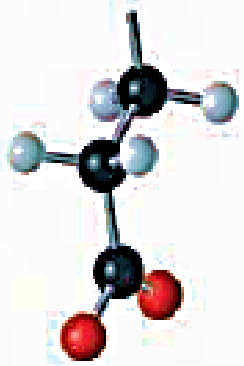


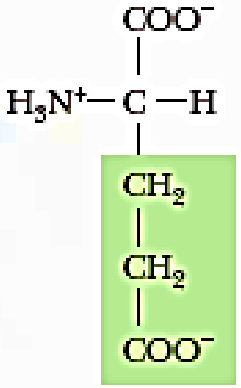


Aspartic acid (Asp, D)

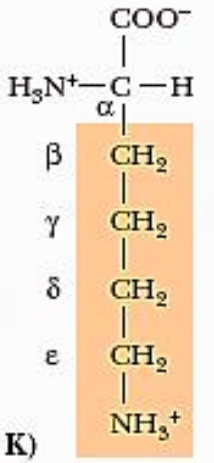


Arginine (Arg, R)



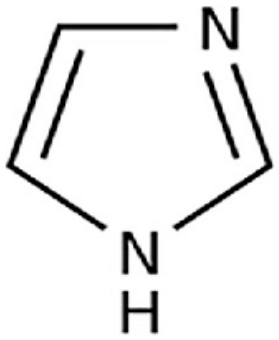


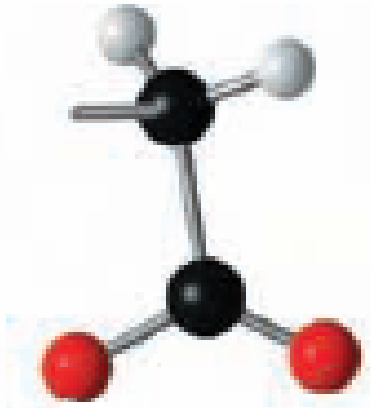
Glutamic acid (Glu, E)

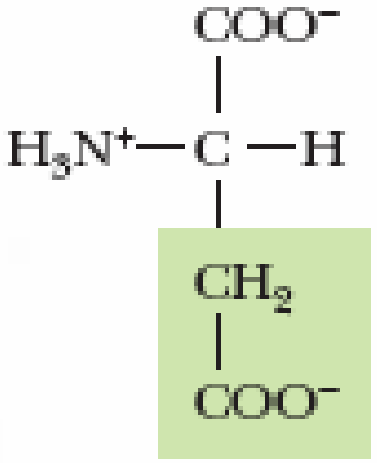


Lysine (Lys, K)

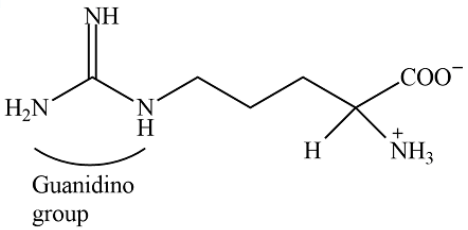
Polar, Charged





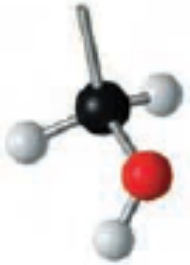


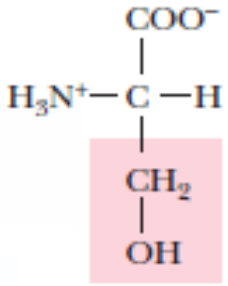
Aspartic acid (Asp, D)



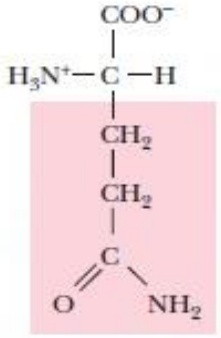
Arginine

Polar, Uncharged

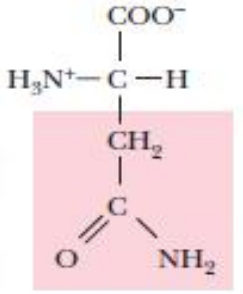




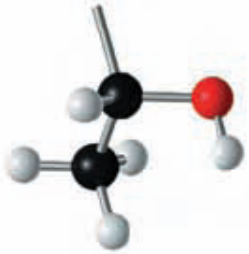
Serine (Ser, S)

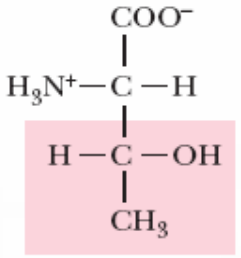


Glutamine (Gln, Q)

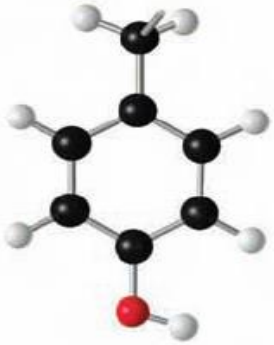


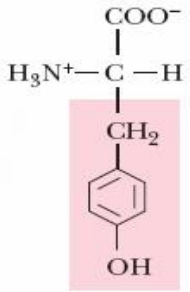
Asparagine (Asn, N)



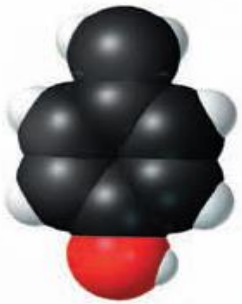


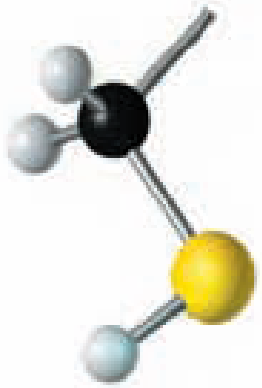
Threonine (Thr, T)



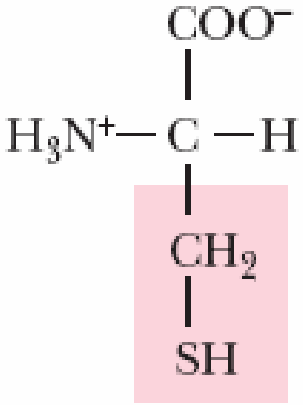


Tyrosine (Tyr, Y)



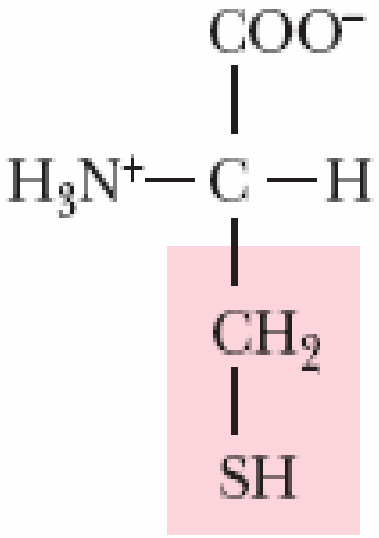


(—S—S—)



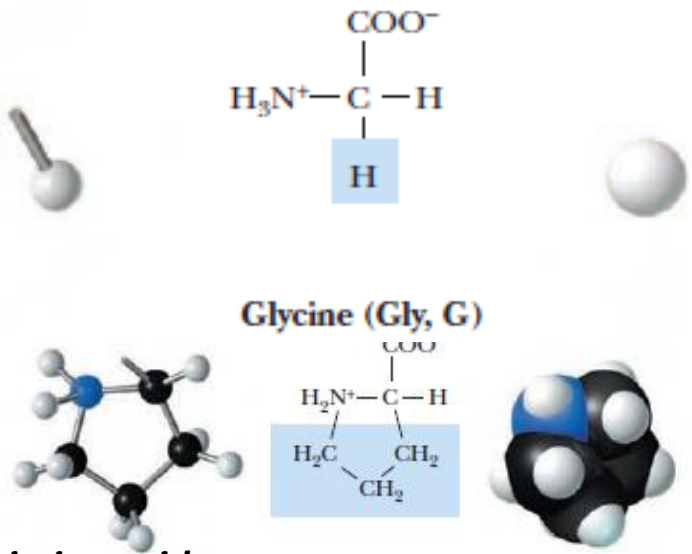
Cysteine (Cys, C)

Polar, Uncharged

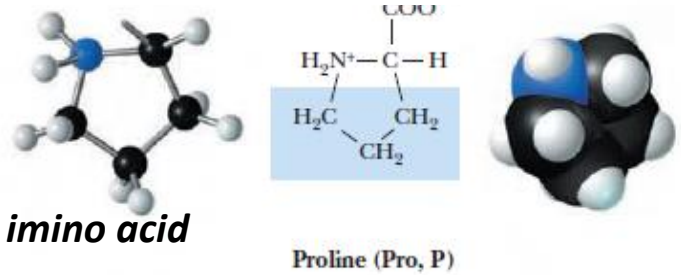


Cysteine (Cys, C) **(—S—S—)**

Non-polar, Uncharged

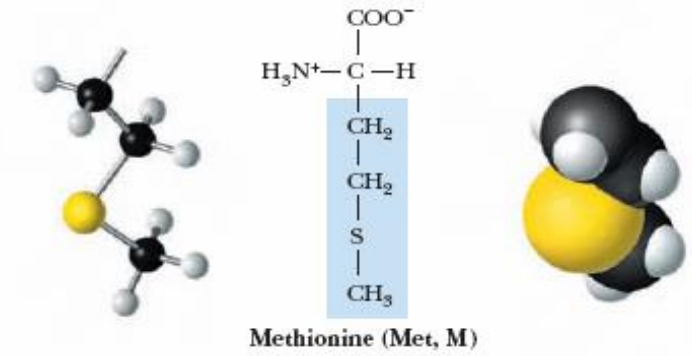


Glycine (Gly, G)

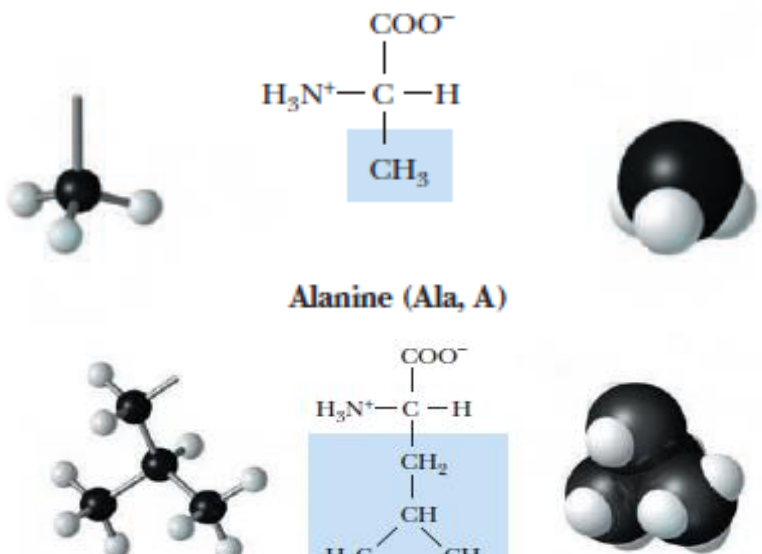


imino acid

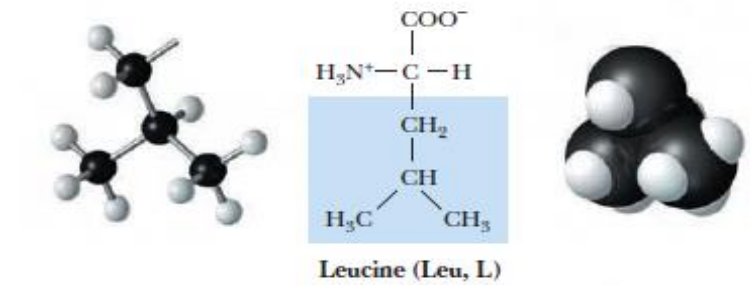
Proline (Pro, P)



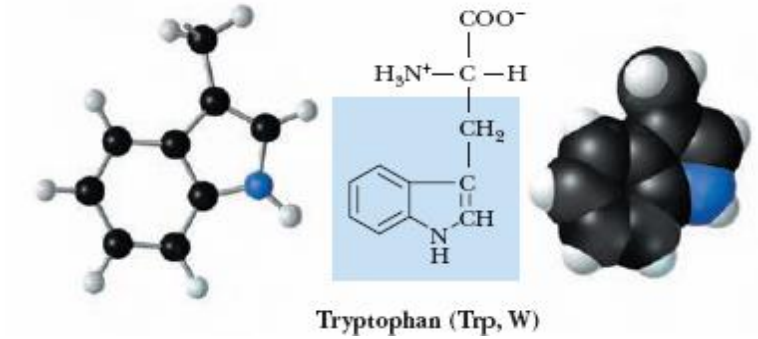
Methionine (Met, M)



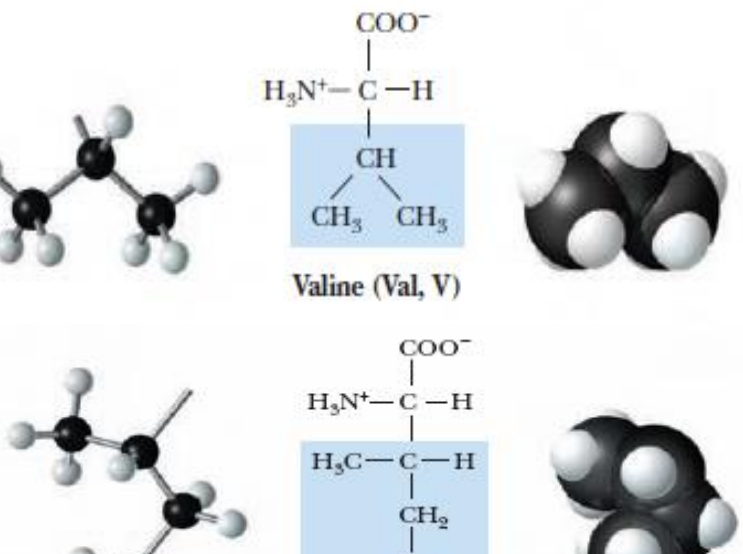
Alanine (Ala, A)



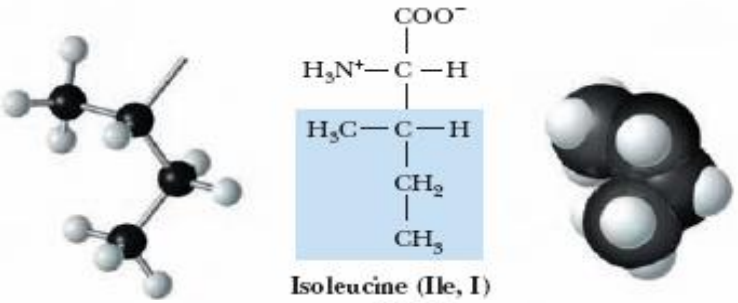
Leucine (Leu, L)



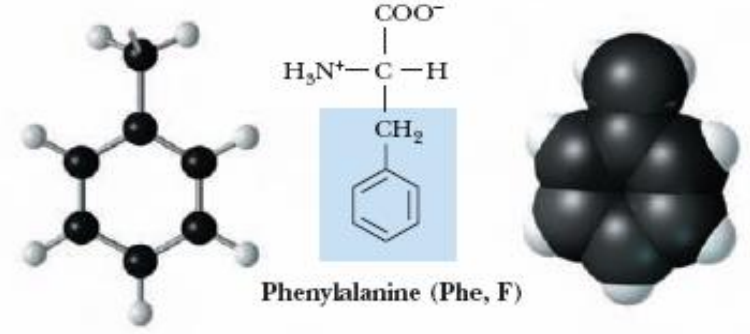
Tryptophan (Trp, W)



Valine (Val, V)

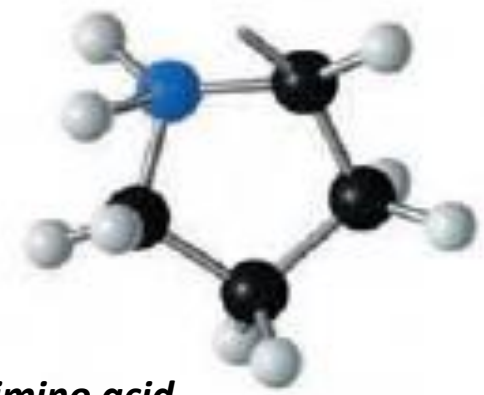


Isoleucine (Ile, I)

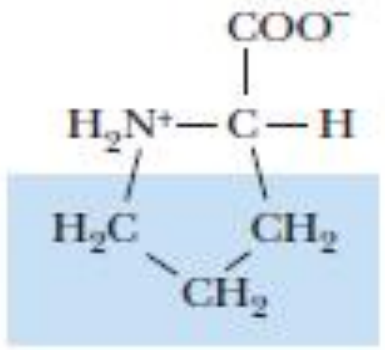


Phenylalanine (Phe, F)

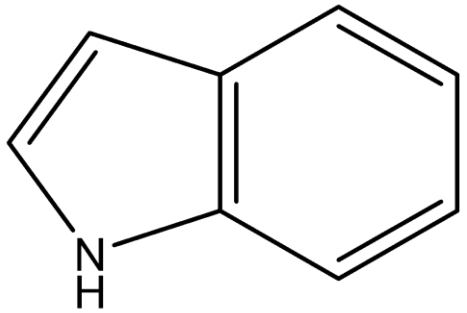
Non-polar, Uncharged



imino acid

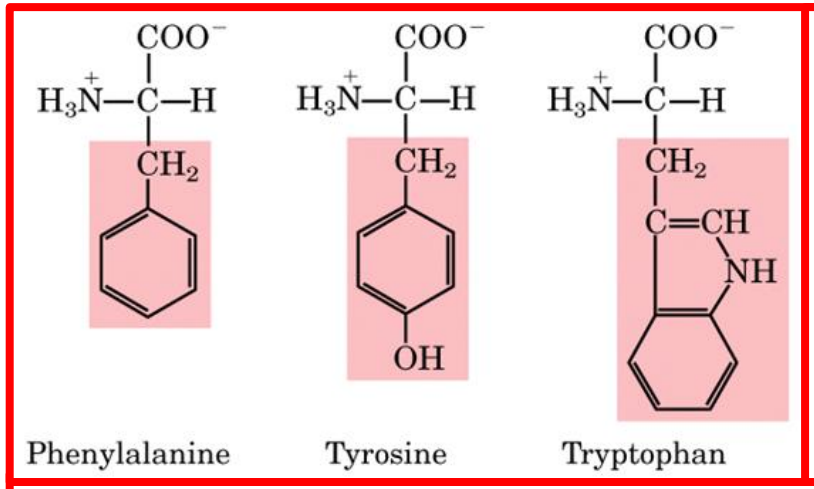


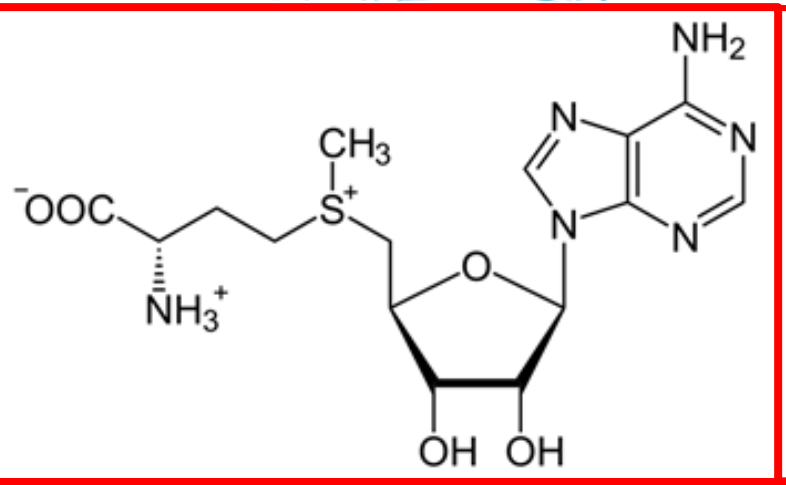
Proline (Pro, P)

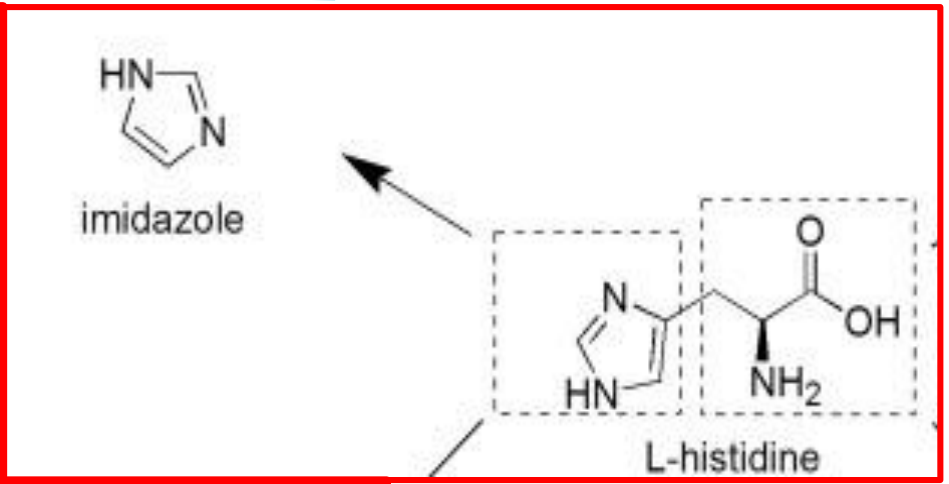


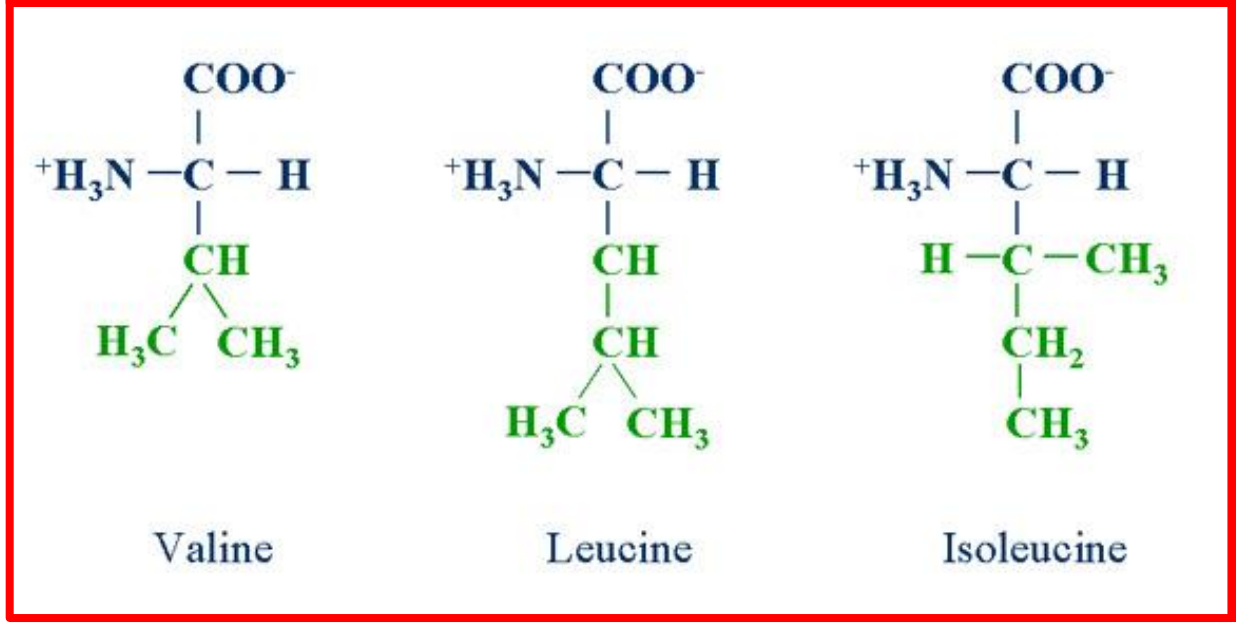
Indole

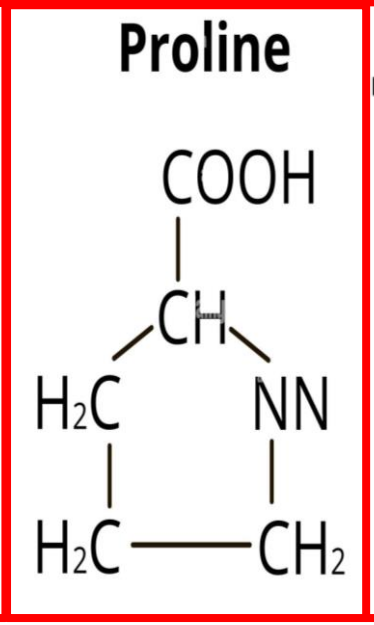
Important notes

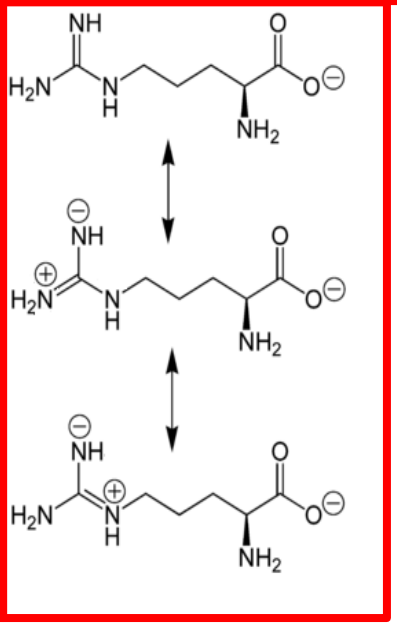




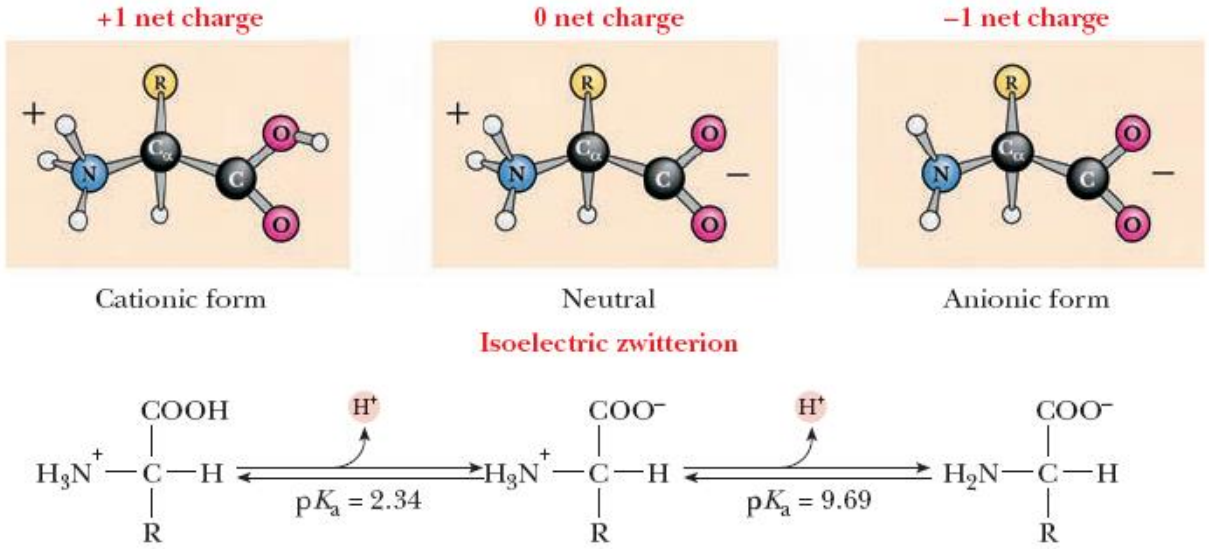






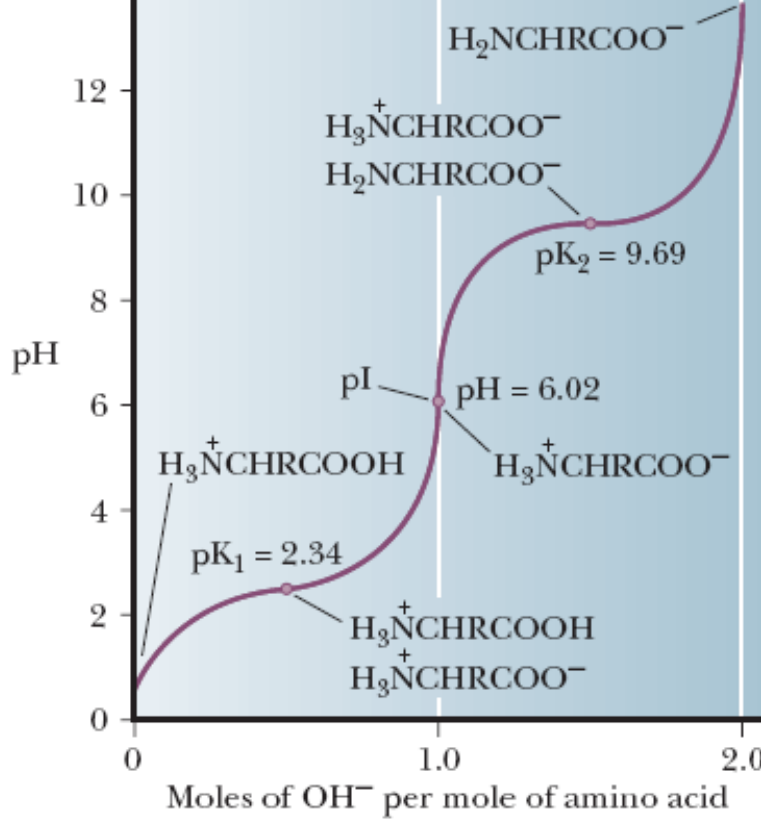


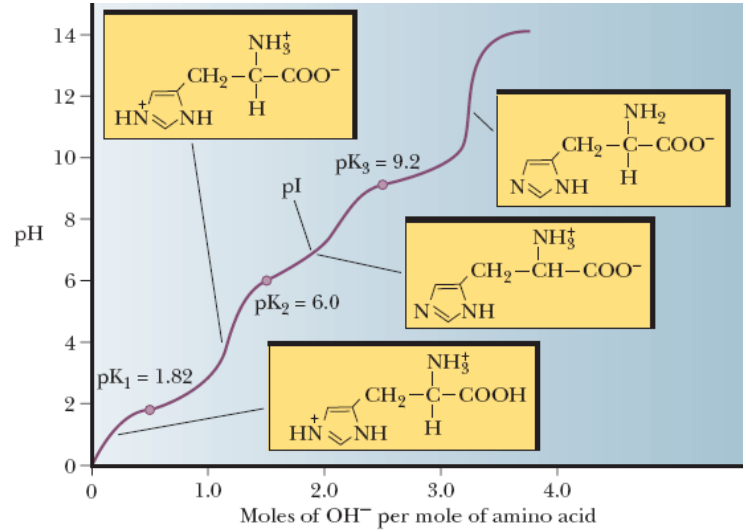
Titration of amino acids: what is an isoelecrtic point (pI)?

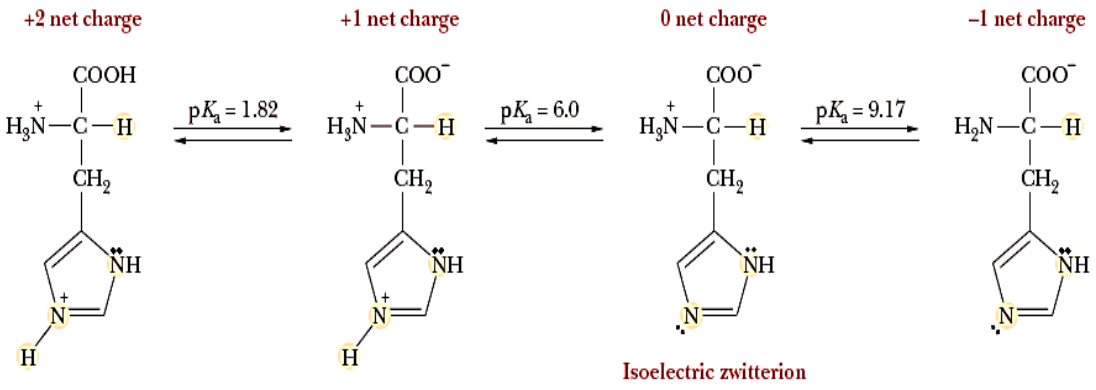


Zwitterion form

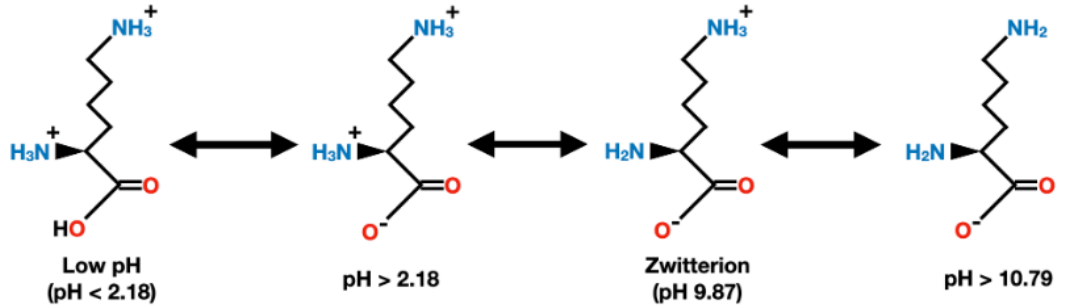
$$\mathrm{pI} = \frac{\mathrm{p}K_{a1} + \mathrm{p}K_{a2}}{2}$$



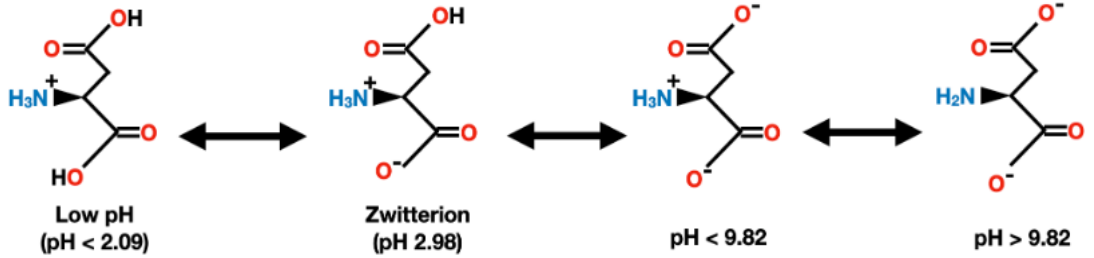




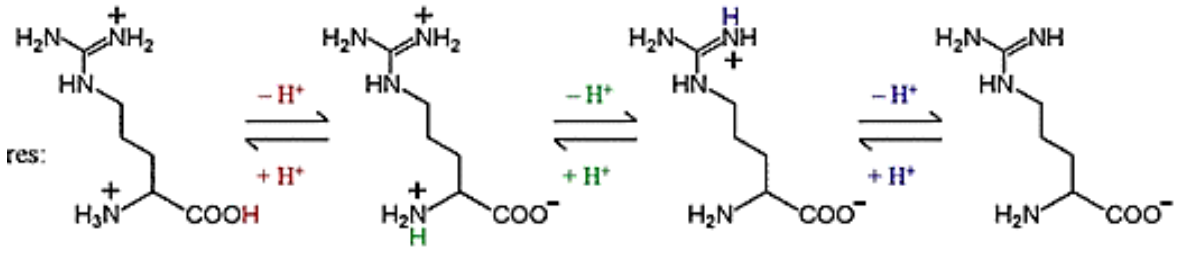
Lysine as a Zwitterion



Aspartic Acid as a Zwitterion



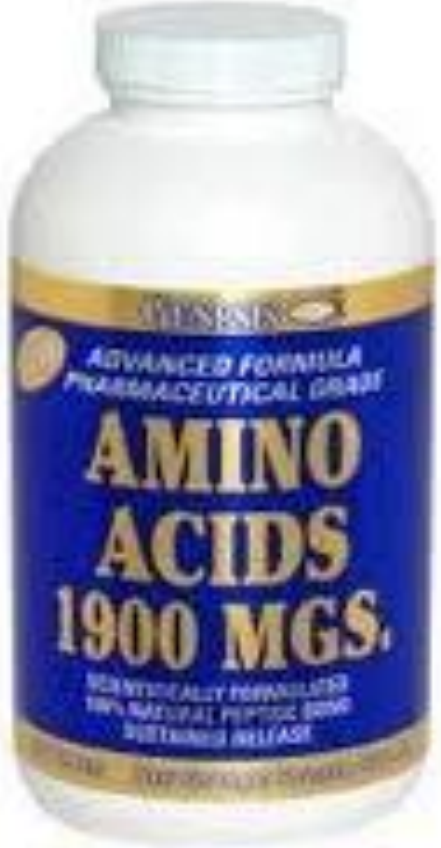
Amino Acid	Abbreviation		pK_1	pK_2	pK_R	pI
	3-Letters	1-Letter	-COOH	$-NH_3^+$	R group	
Alanine	Ala	A	2.34	9.69	-	6.00
Arginine	Arg	R	2.17	9.04	12.48	10.76
Asparagine	Asn	N	2.02	8.80	-	5.41
Aspartic Acid	Asp	D	1.88	9.60	3.65	2.77
Cysteine	Cys	C	1.96	10.128	8.18	5.07
Glutamic Acid	Glu	E	2.19	9.67	4.25	3.22
Glutamine	Gln	Q	2.17	9.13	-	5.65
Glycine	Gly	G	2.34	9.60	-	5.97
Histidine	His	H	1.82	9.17	6.00	7.59
Isoleucine	Ile	I	2.36	9.60	-	6.02
Leucine	Leu	L	2.36	9.60	-	5.98
Lysine	Lys	K	2.18	8.95	10.53	9.74
Methionine	Met	M	2.28	9.21	-	5.74
Phenylalanine	Phe	F	1.83	9.13	-	5.48
Proline	Pro	P	1.99	10.60	-	6.30
Serine	Ser	S	2.21	9.15	-	5.58
Threonine	Thr	T	2.09	9.10	-	5.60
Tryptophan	Trp	W	2.83	9.39	-	5.89
Tyrosine	Tyr	Y	2.20	9.11	10.07	5.66
Valine	Val	V	2.32	9.62	-	5.96



Is it the same in proteins?

Dissociating Group	pK_a Range
α-Carboxyl	3.5-4.0
Non-α COOH of Asp or Glu	4.0-4.8
Imidazole of His	6.5-7.4
SH of Cys	8.5-9.0
OH of Tyr	9.5-10.5
α-Amino	8.0-9.0
e-Amino of Lys	9.8-10.4
Guanidinium of Arg	~12.0

Amino Acids & life

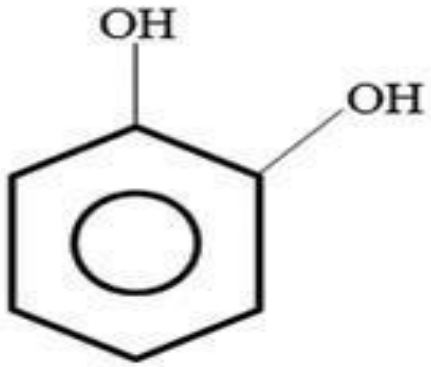


Posttranslational modification of Amino Acids

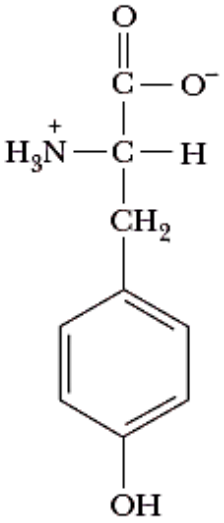
- Hydroxylation (-OH)
- Carboxylation (-COOH)
- Methylation ($-CH_3$)
- Formylation (-CH=O)
- Acetylation (CH_3CO)
- Phosphorylation ($-PO_3^{2-}$)

- These modifications significantly extend the biologic diversity of proteins by altering their solubility, stability, catalytic activity, and interaction with other proteins

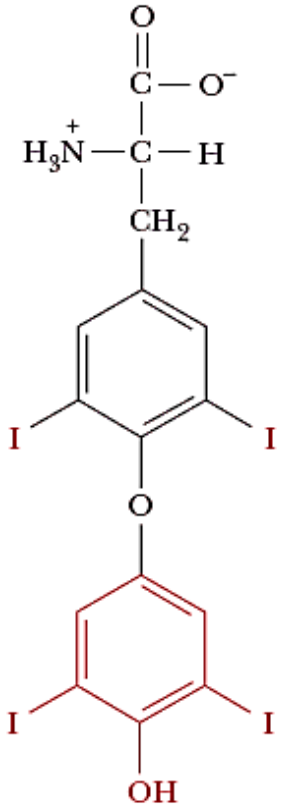
Tyrosine



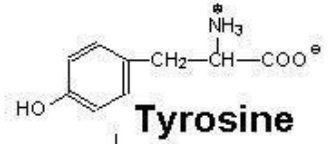
catechol



Tyrosine



Thyroxine

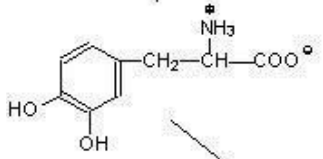


Tyrosine

tyrosine hydroxylase

tetrahydrobiopterin + O_2

dihydrobiopterin + H_2O



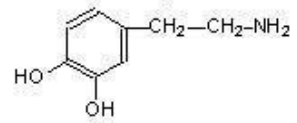
DOPA

DOPA decarboxylase

CO_2

Tyrosine (Tyr, Y)

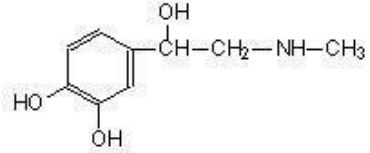
dopamine β- hydroxylase



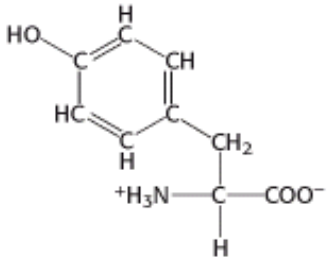
Dopamine

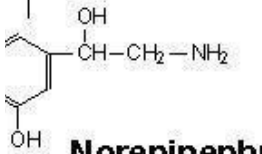
S-adenosylhomocysteine

phenylethanolamine N-methyltransferase

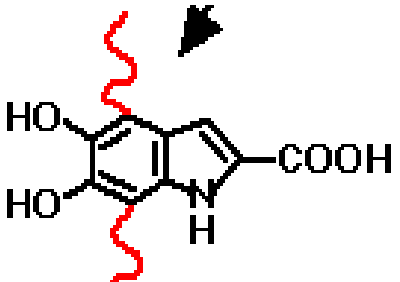


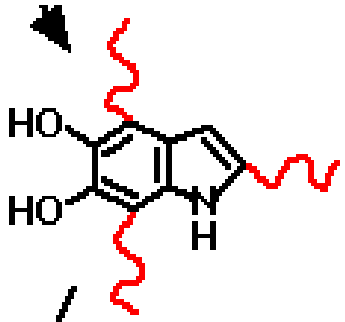
Epinephrine



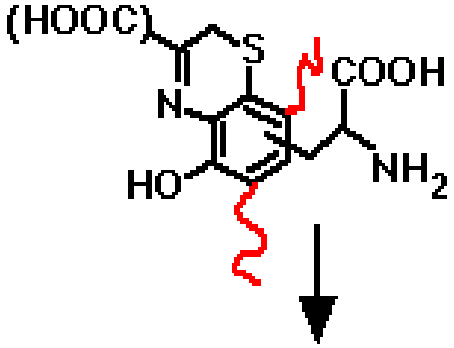


Norepinephrine

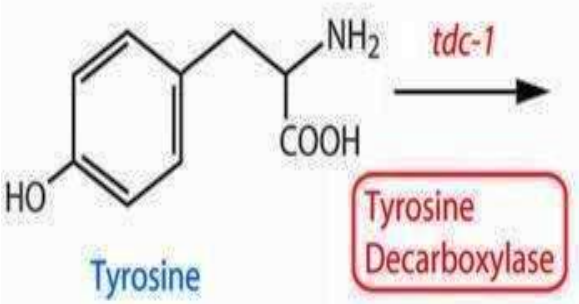




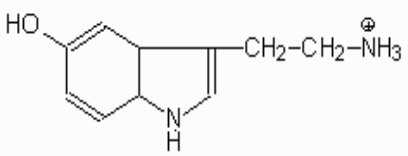
EUMELANINS



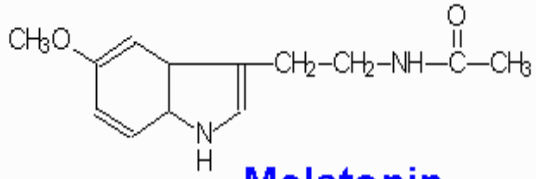
PHEOMELANINS



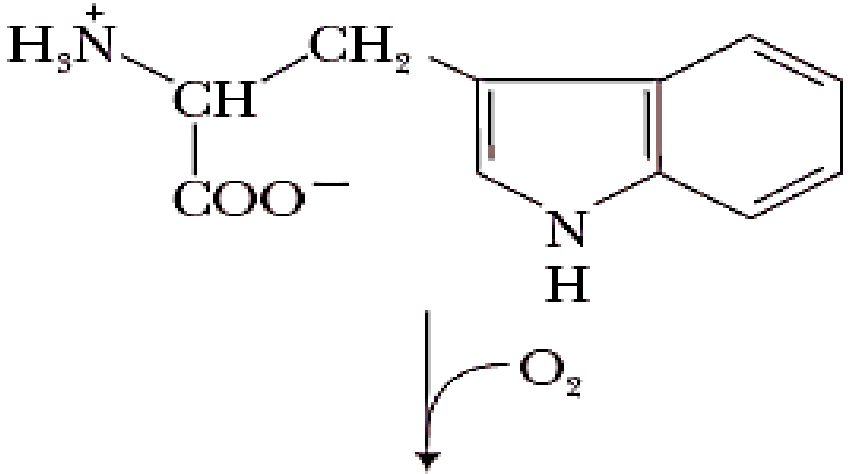
Tryptophan



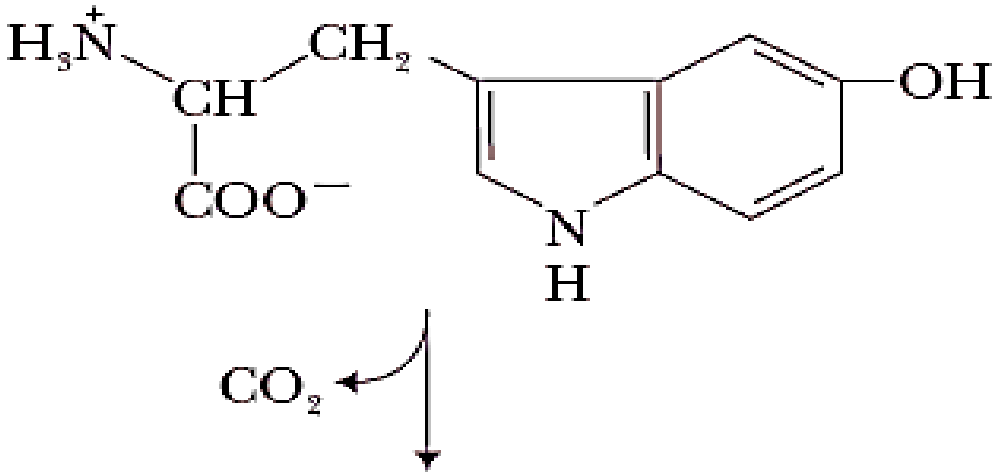
Serotonin
(5-hydroxytryptamine)



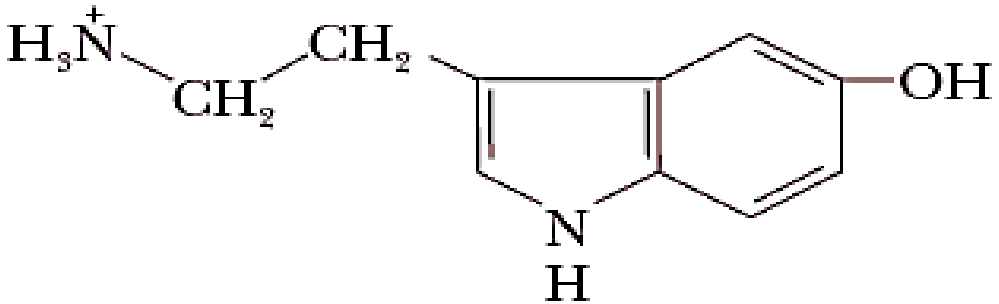
Melatonin



Tryptophan



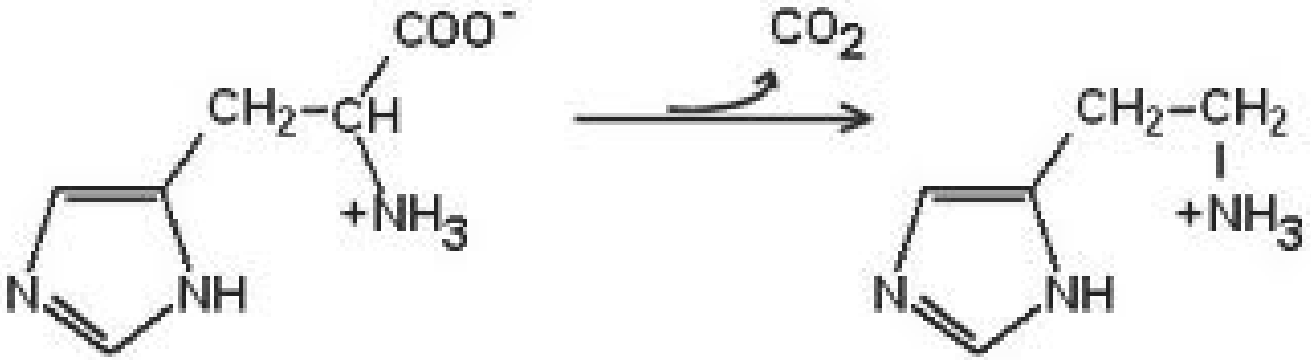
5–Hydroxytryp-tophan



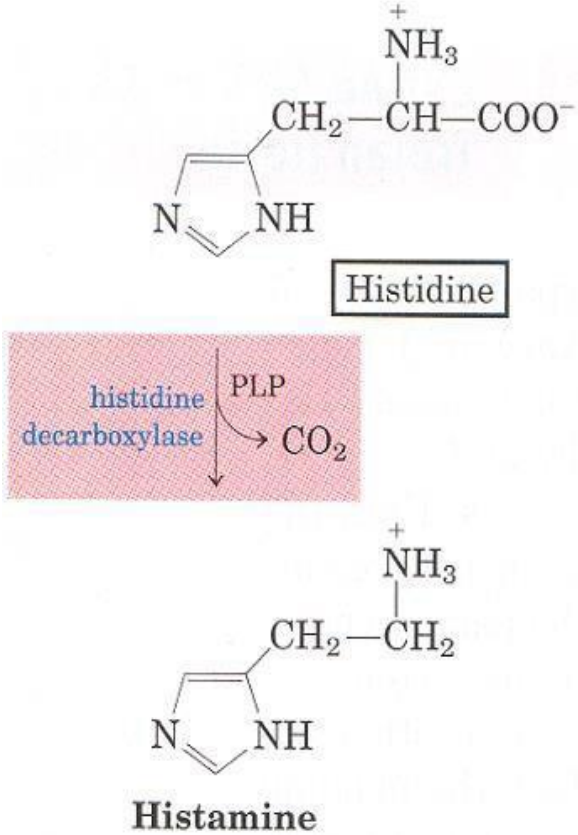
Serotonin

Histidine

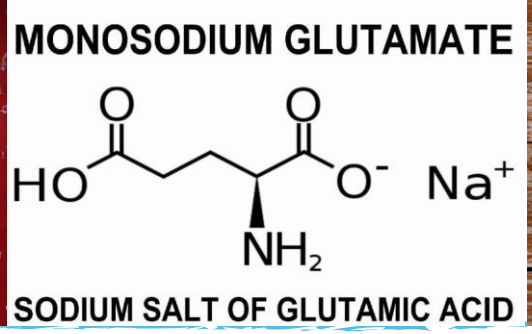
- A potent vasodilator
- Part of the immune response
- Results in swelling and stuffiness
- Most cold medications contain antihistamines



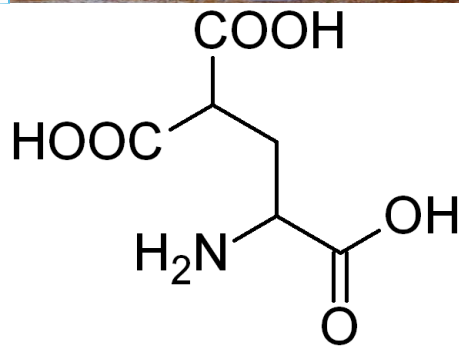
Histidine *Histamine*

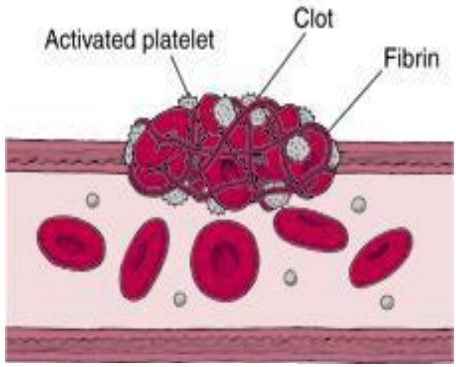


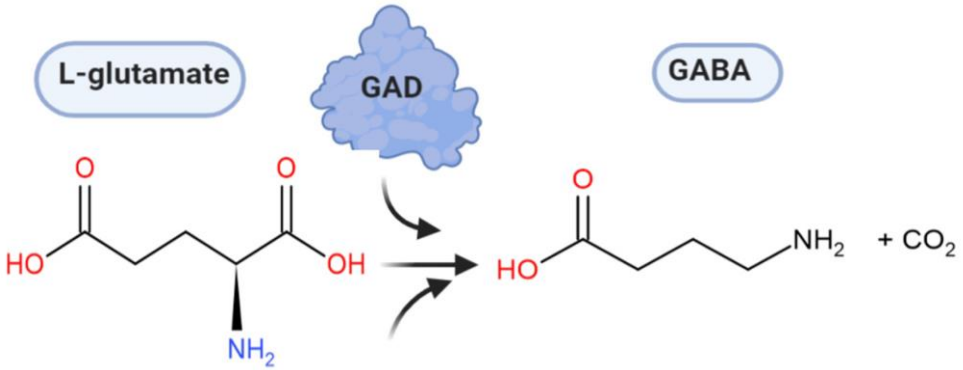
Glutamic Acid

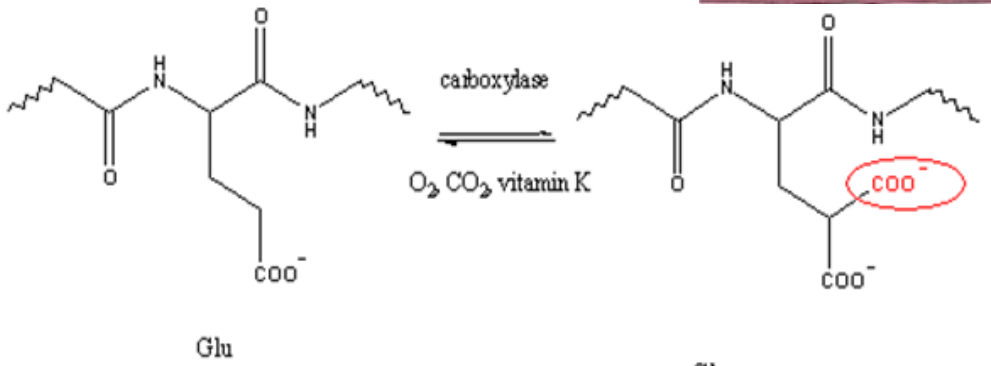


- MSG: a flavor enhancer, causes a physiological reaction in some people (*Chinese restaurant syndrome) or* MSG symptom complex: chills, headaches, and dizziness
- GABA: Inhibitory neurotransmitter (CNS), reduces neuronal excitability. Synthesized in brain because it does not cross the BBB. Have relaxing, anti-anxiety, and anti-convulsive effects
- γ- carboxyglutamate (Gla): Vitamin K is essential for the process



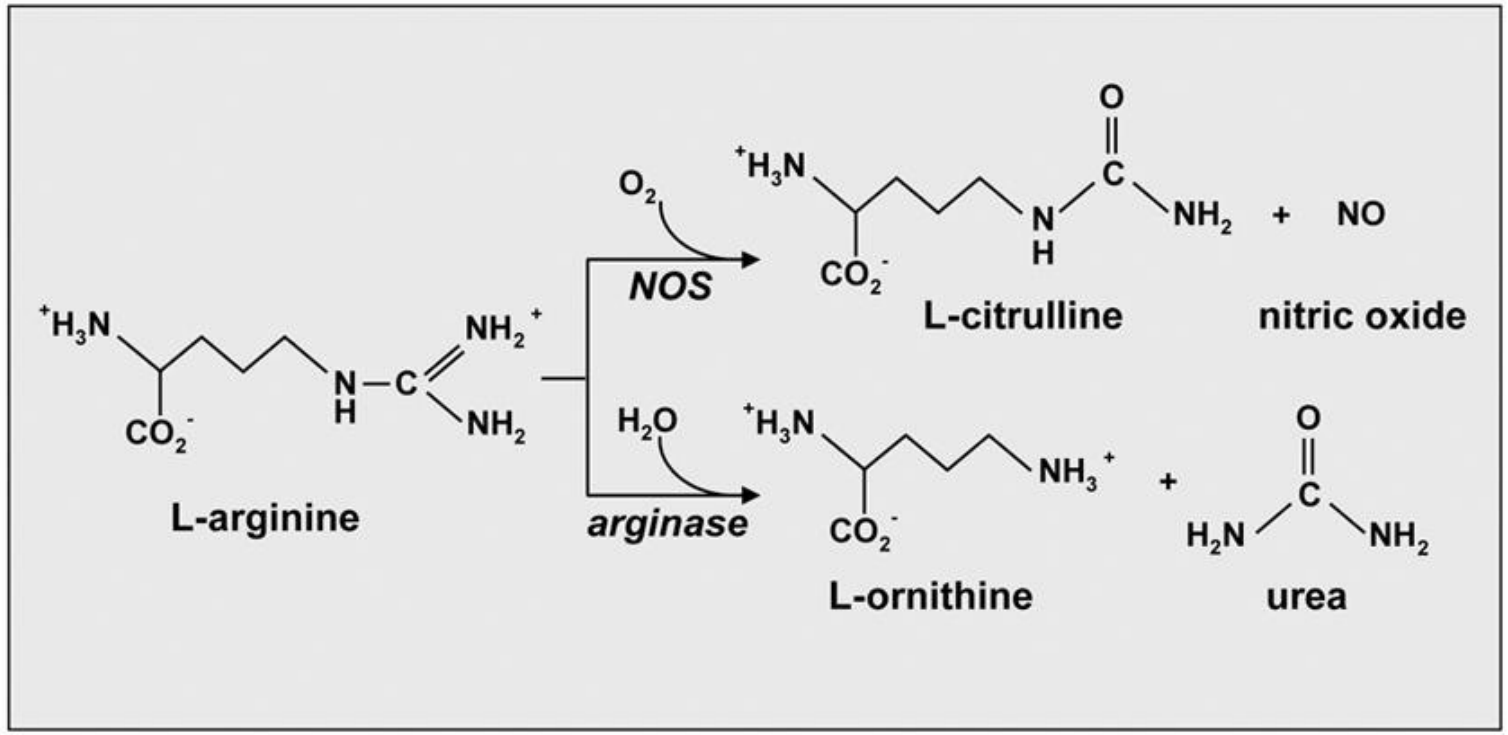






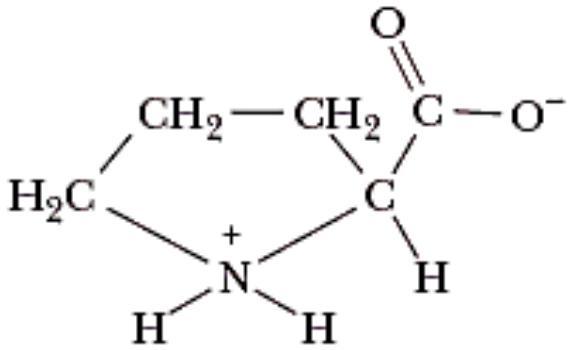
Arginine

- Precursor of nitric oxide (NO) and Urea
- NO functions: Vasodilation, inhibition of platelet adhesion, anti-oxidant, anti-inflammatory

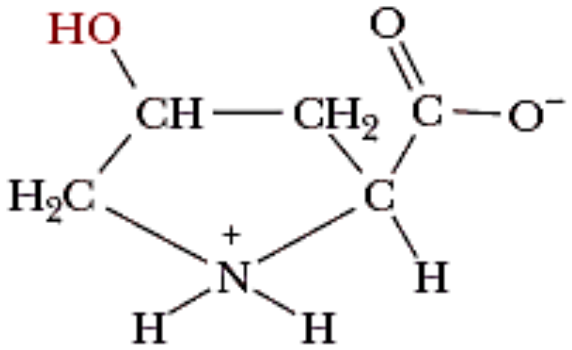


Lysine and proline

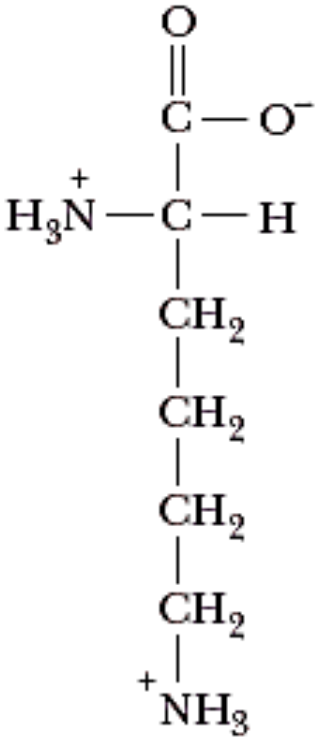
- Part of collagen structure
- Modified as residues (post-translational modification)
- Vitamin C relation and scurvy



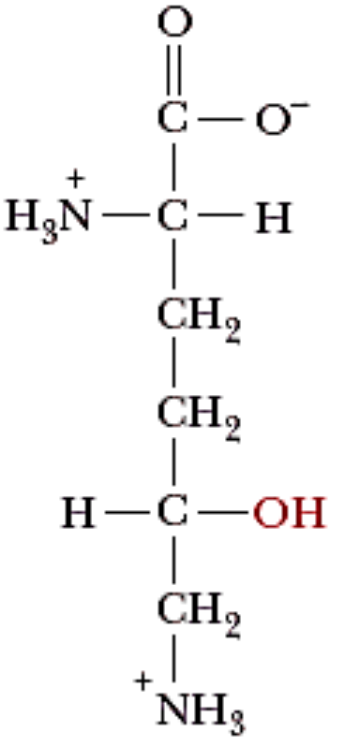
Proline



Hydroxyproline



Lysine

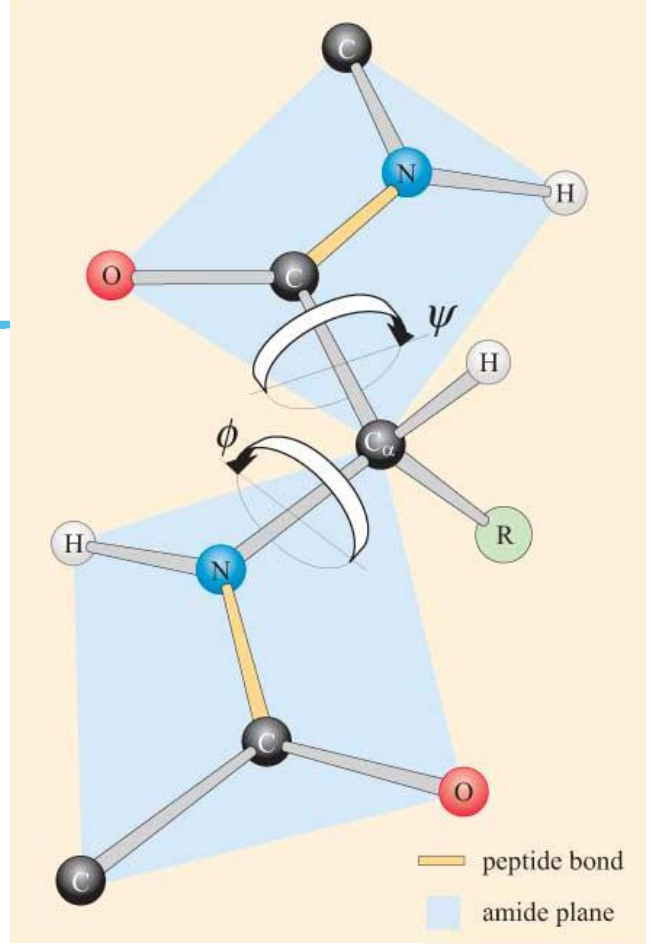


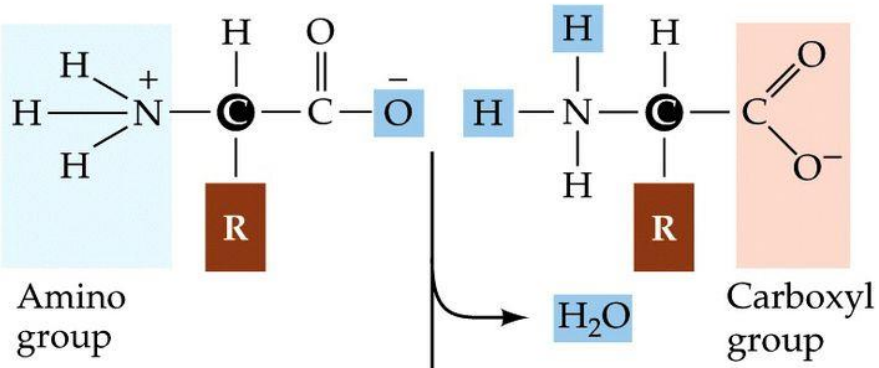
Hydroxylysine

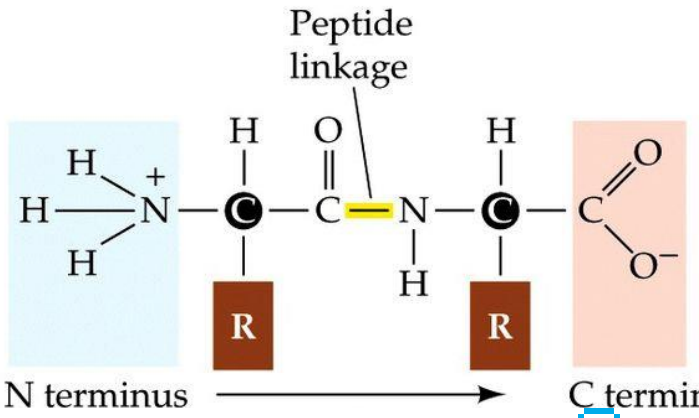
Peptides

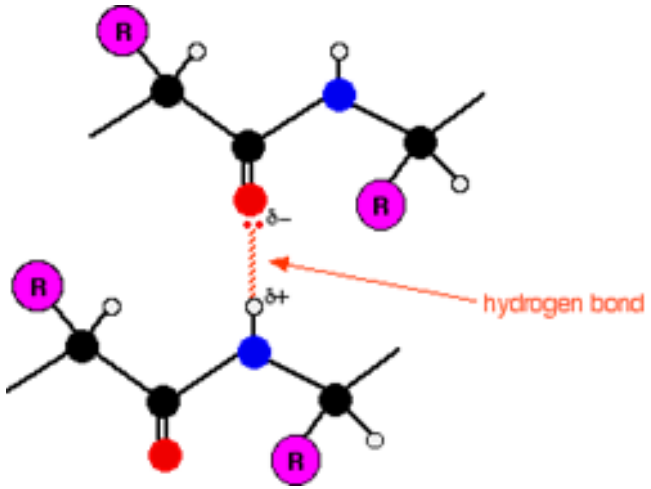
Peptide bond

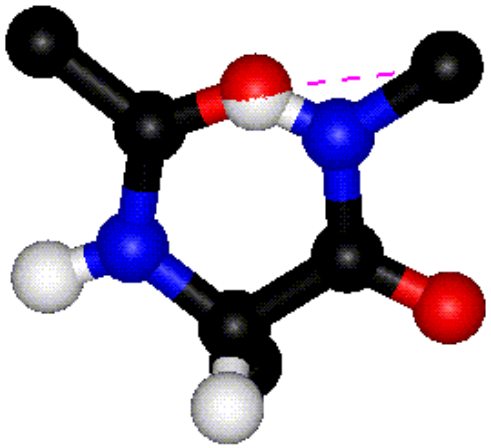
- Amide bond
- Resonance, Double bond
  - Planar, charged, Rigid, Un-rotatable
- Hydrogen bonding; Except proline

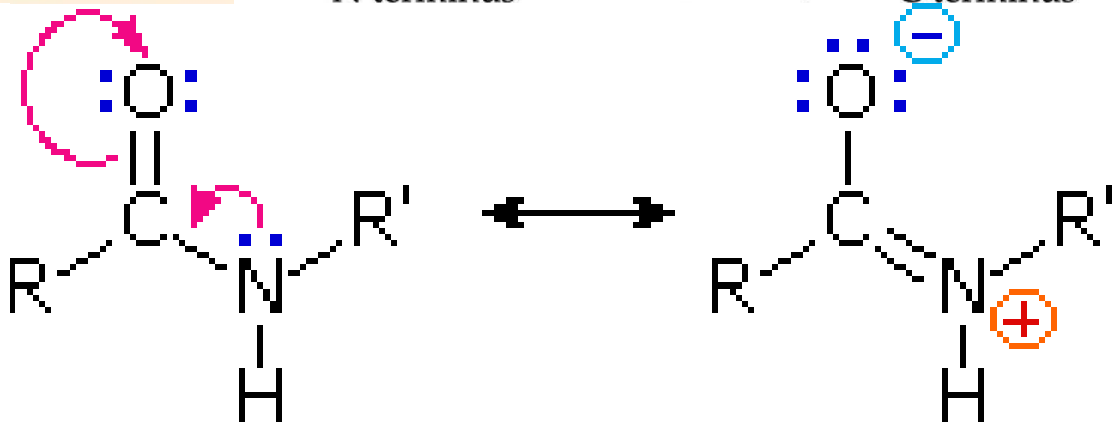




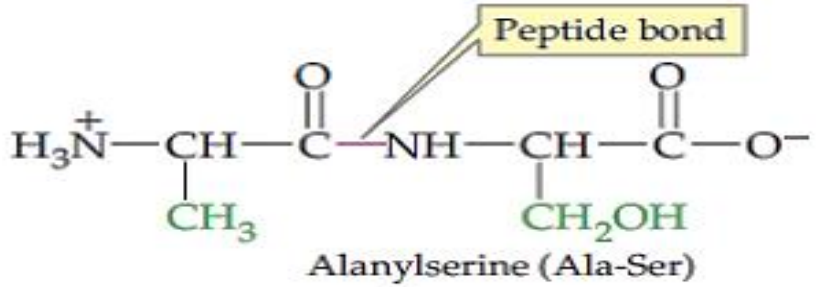


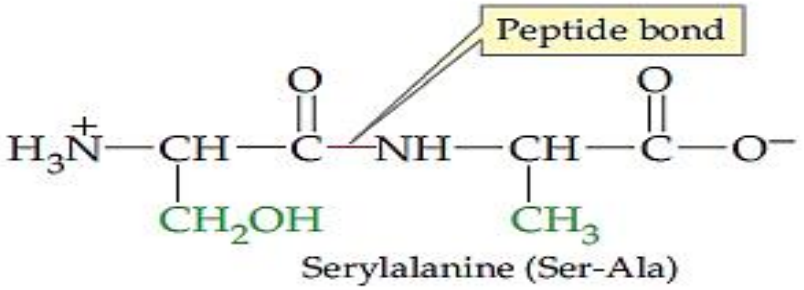


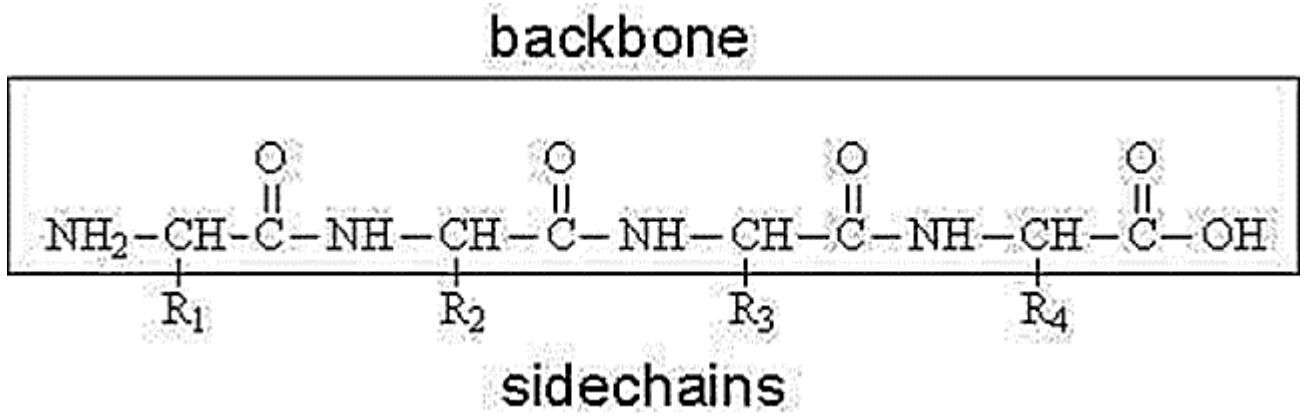




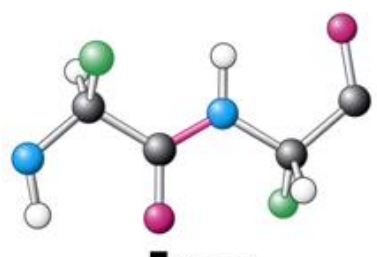
Backbone, orientation and directionality

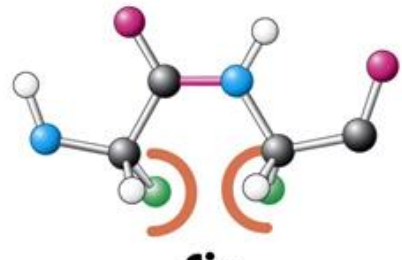


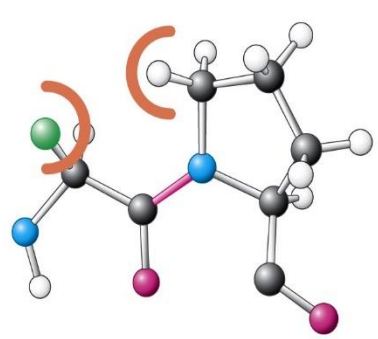




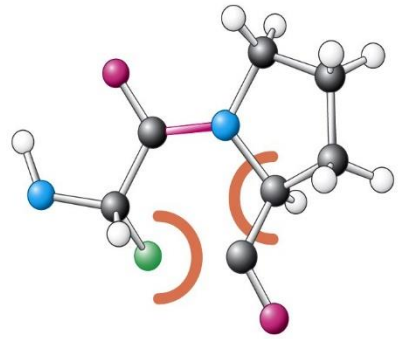
All other amino acids

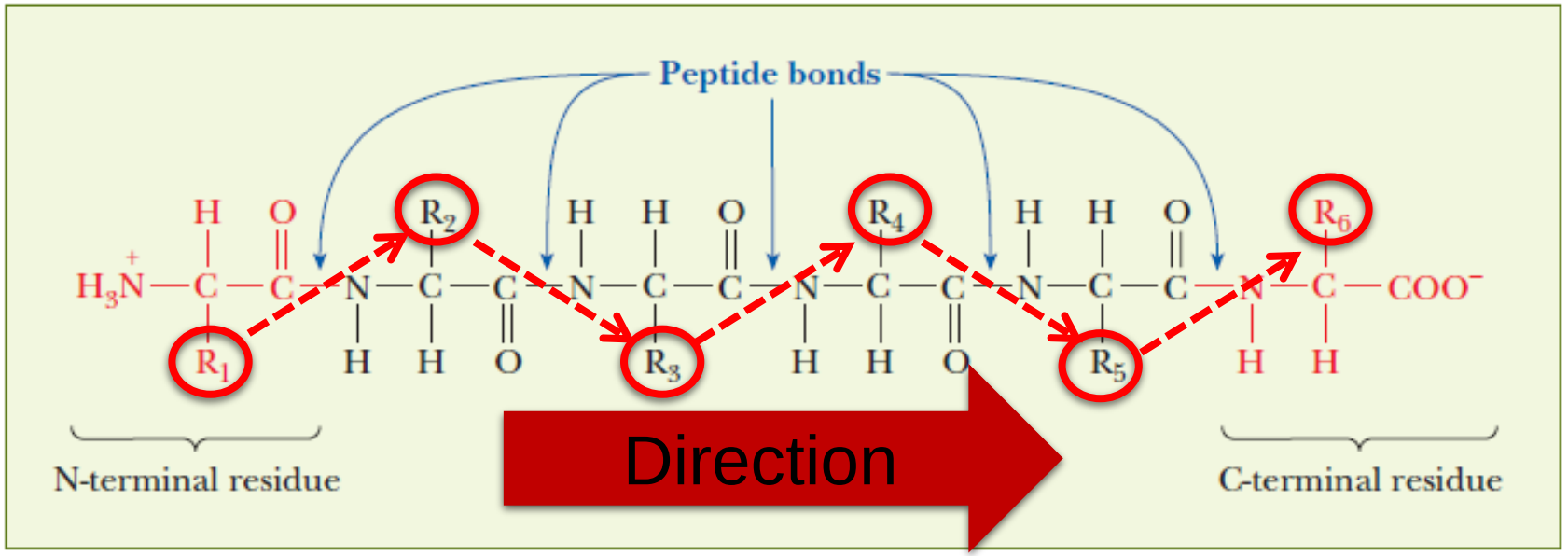






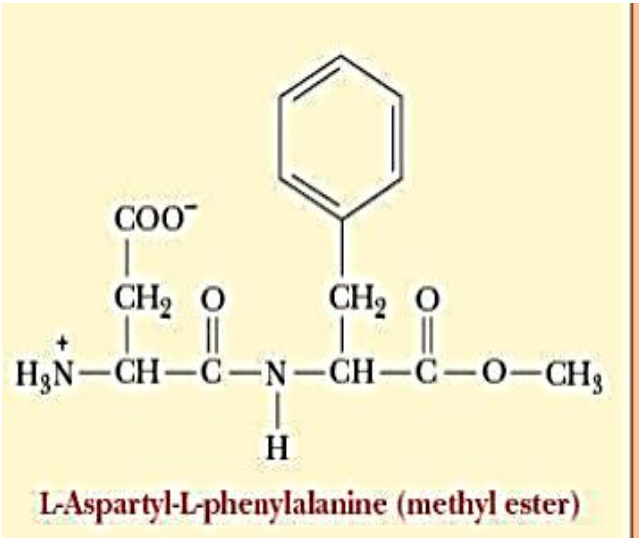
Proline





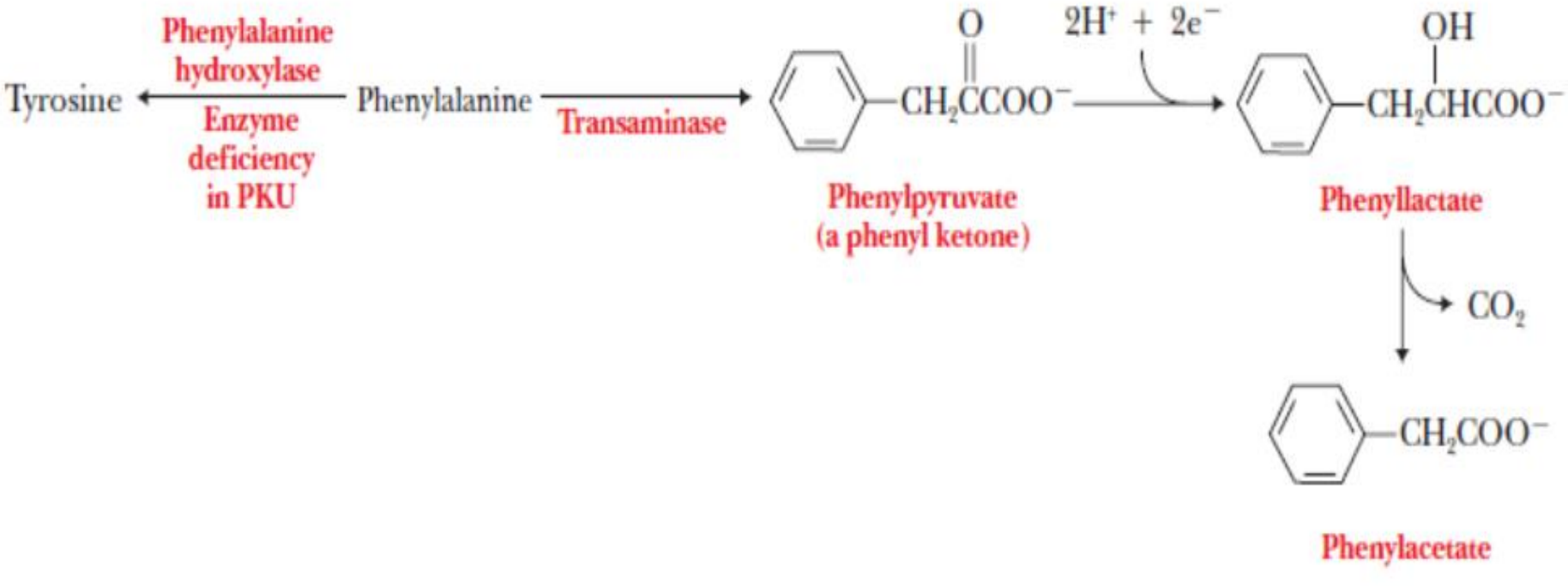
Aspartame, the Sweet Peptide

- L-aspartyl-L-phenylalanine
- Commercial importance
- The methyl ester derivative is called aspartame
- 200 times sweeter than sugar



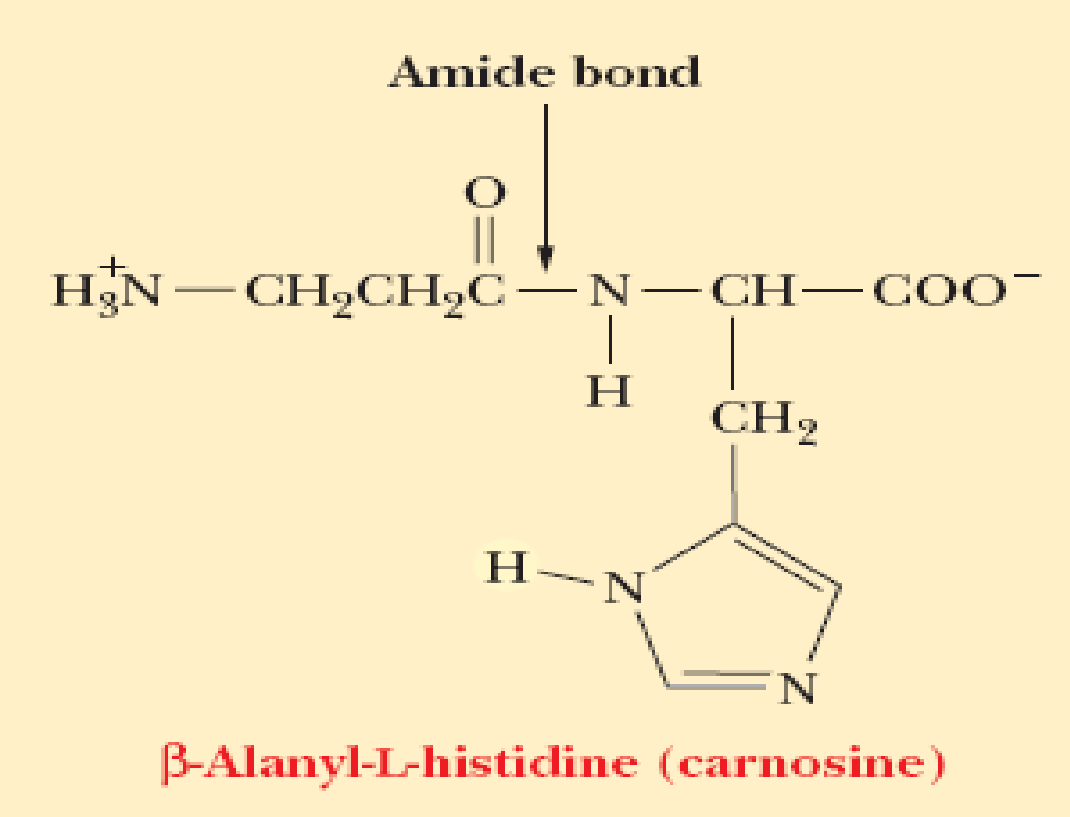
Phenylketonuria

- Inborn errors of metabolism; errors in enzymes of amino acids metabolism
- PKU can be easily detected and managed in newborns
- Aspartame carry a warning, Alatame (Ala instead of Phe) is a substituent

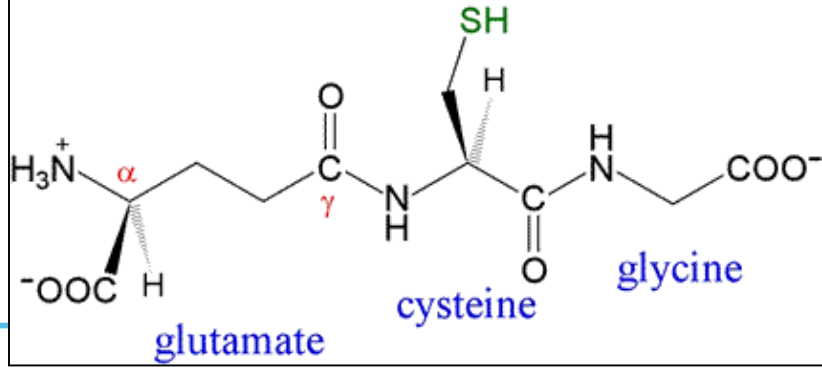


Carnosine

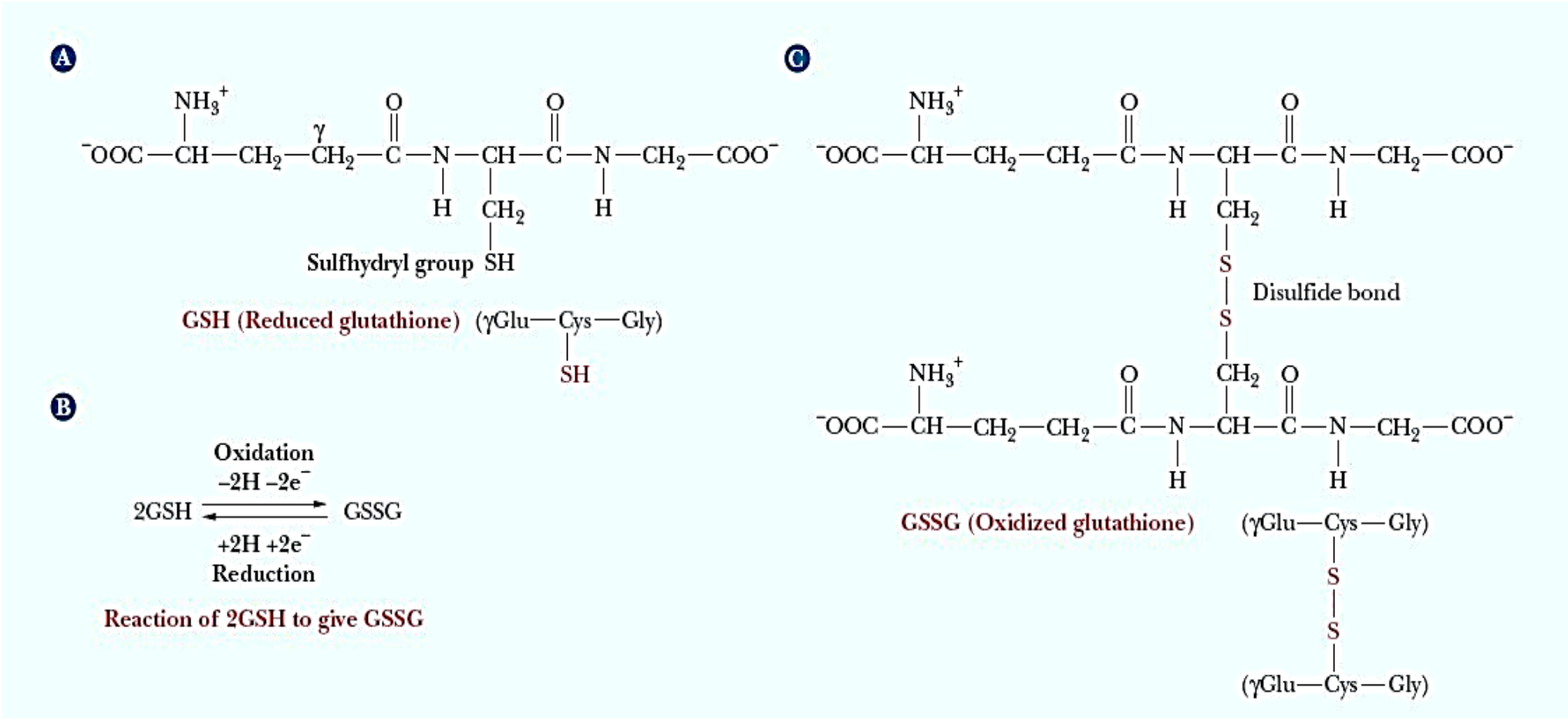
- Dipeptide: found in muscle tissue, (β-alanyl-L-histidine), anti-oxidant, chelation of heavy metals



Glutathione

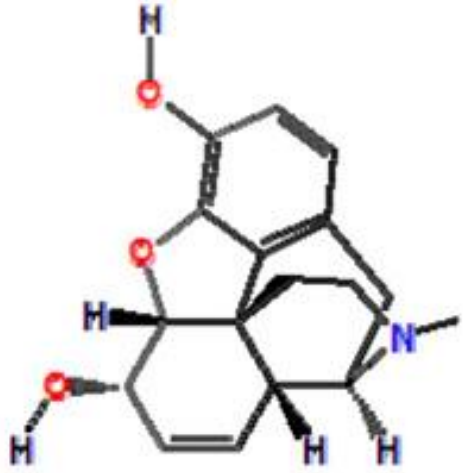


- Tripeptide: (γ-glutamyl-L-cysteinylglycine); a scavenger for oxidizing agents



Enkephalins

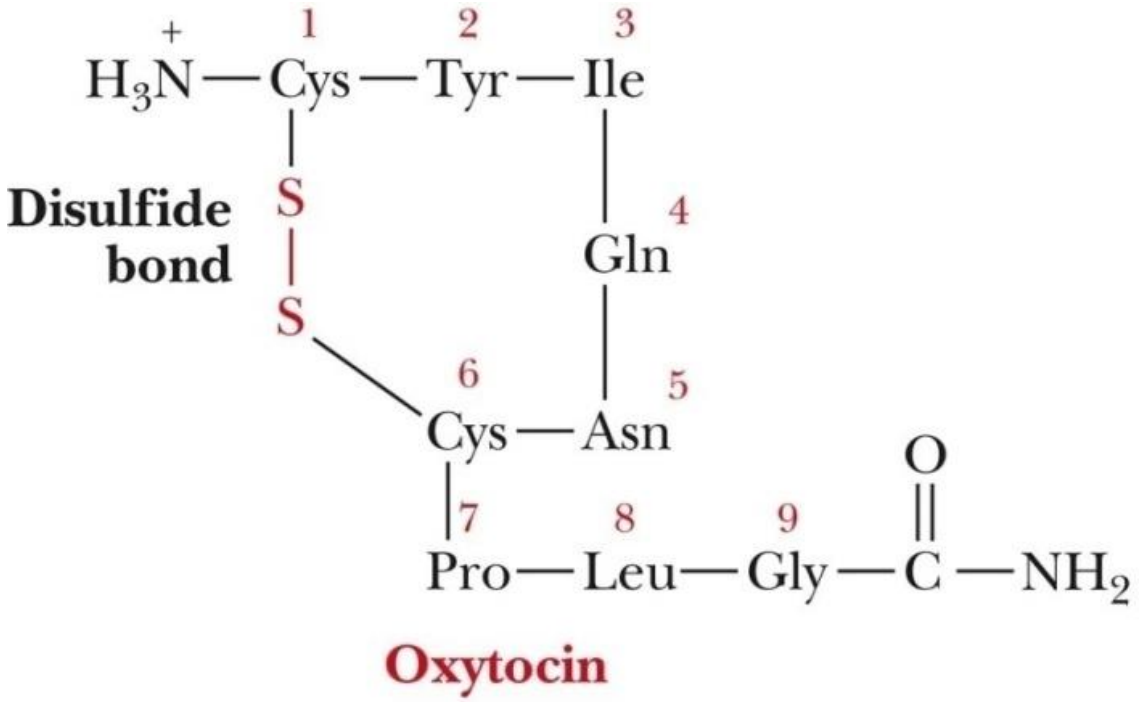
- Pentapeptides: naturally occurring analgesics
  - Tyr—Gly—Gly—Phe—Leu (Leucine enkephalin)
  - Tyr—Gly—Gly—Phe—Met (Methionine enkephalin)
- Similarities of three-dimensional structures to opiates (e.x, morphine)



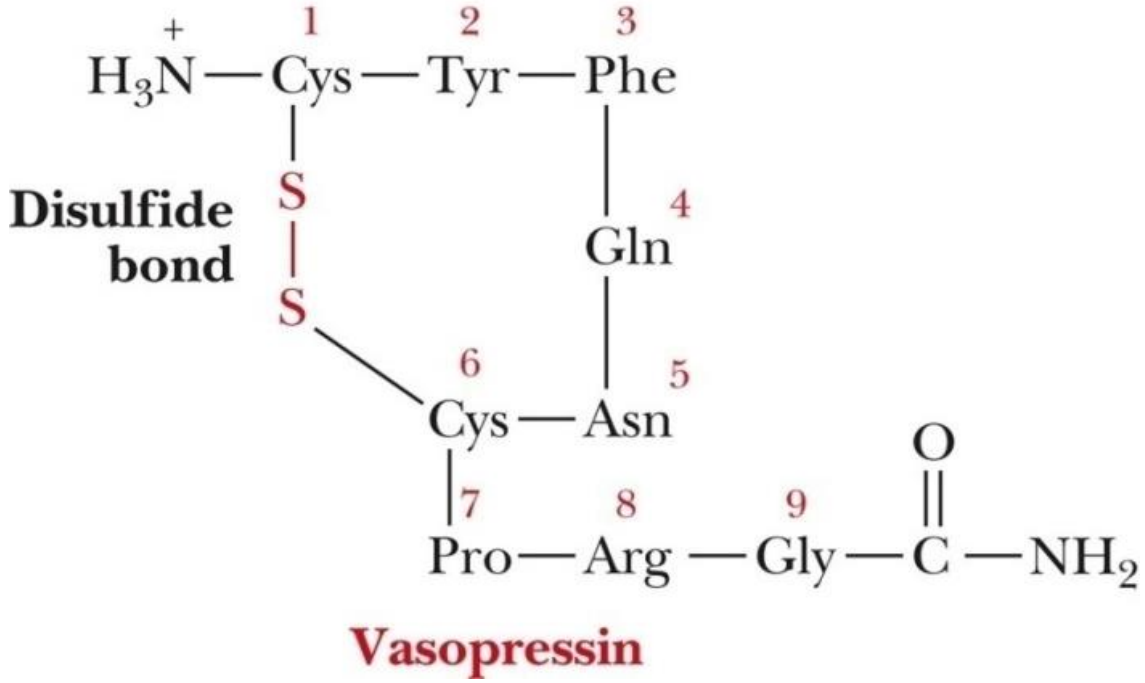
Morphine

Enkephalins

Cyclic structures



Oxytocin



Vasopressin