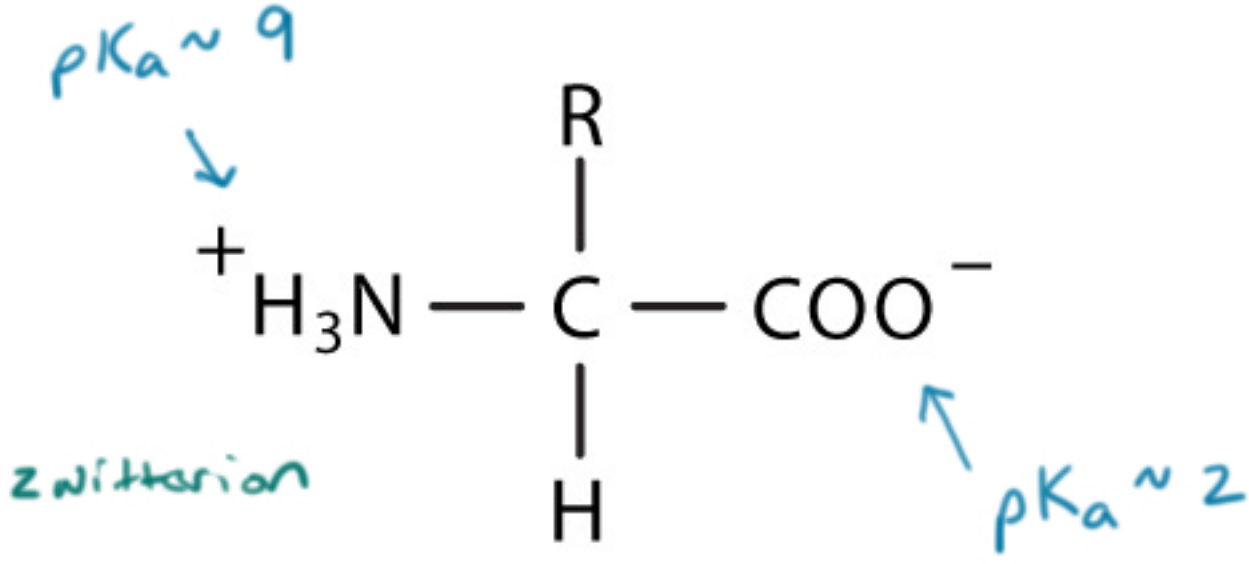
Amino Acids

Session Slides with Notes

amino acids



L amino acid

$$pH = pK_a + \log\left(\frac{[A^-]}{[HA]}\right)$$

7 2 + log(100,000/1)

Twenty-One Amino Acids

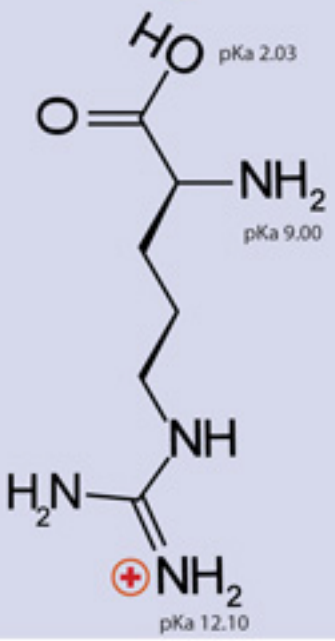
⊕ Positive ⊖ Negative

• Side chain charge at physiological **pH 7.4**

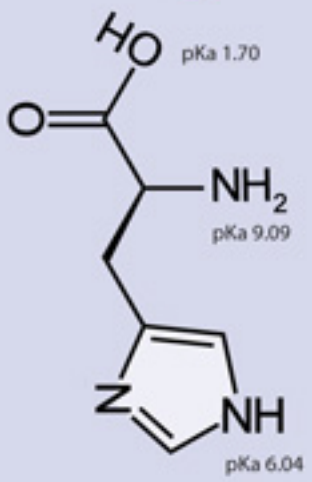
A. *Amino Acids with Electricaly Charged Side Chains*

Positive

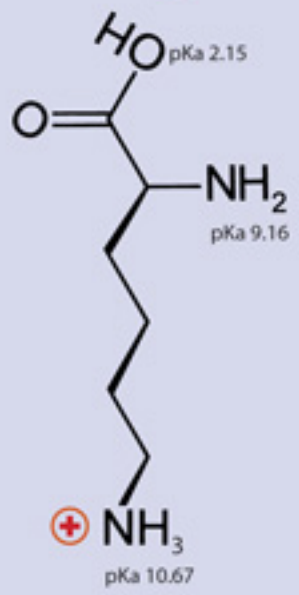
Arginine (Arg) **R**



Histidine (His) **H**

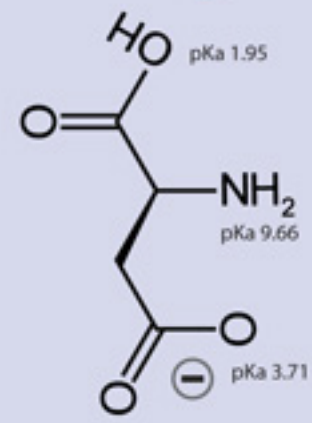


Lysine (Lys) **K**

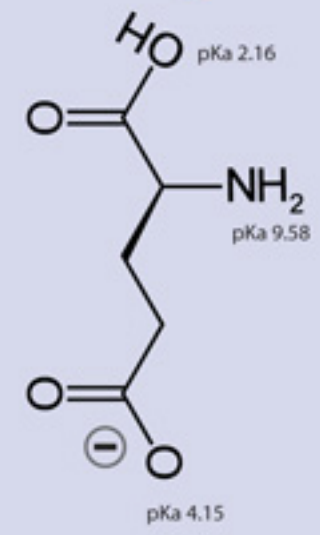


Negative

Aspartic Acid (Asp) **D**

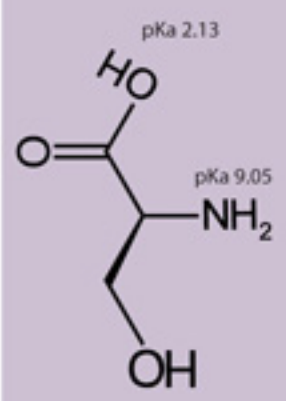


Glutamic Acid (Glu) **E**

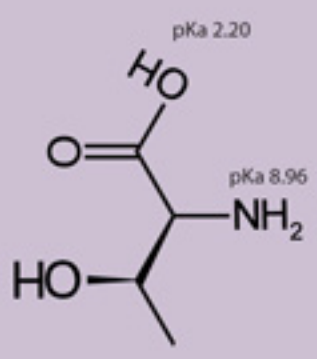


B. *Amino Acids with Polar Uncharged Side Chains*

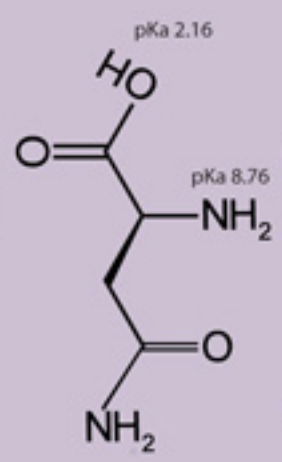
Serine (Ser) **S**



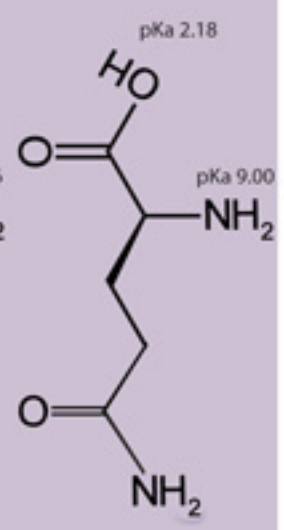
Threonine (Thr) **T**



Asparagine (Asn) **N**

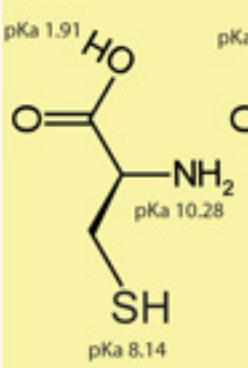


Glutamine (Gln) **Q**

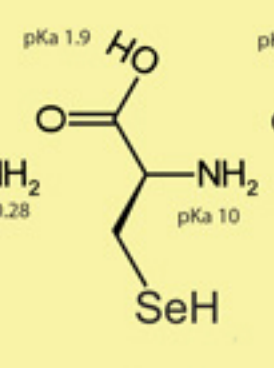


C. *Special Cases*

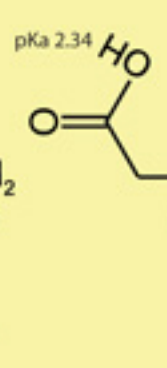
Cysteine (Cys) **C**



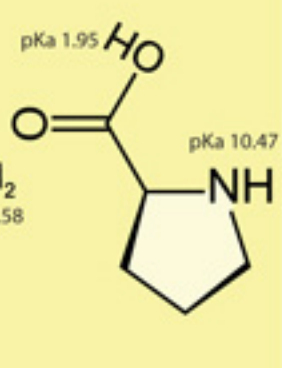
Selenocysteine (Sec) **U**



Glycine (Gly) **G**

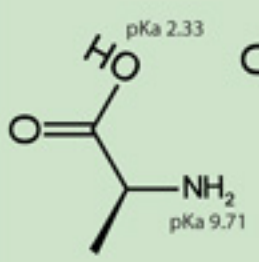


Proline (Pro) **P**

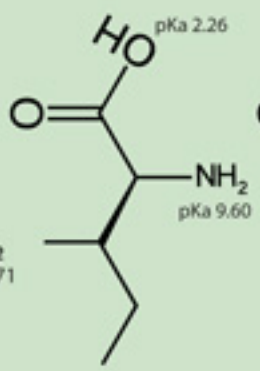


D. *Amino Acids with Hydrophobic Side Chain*

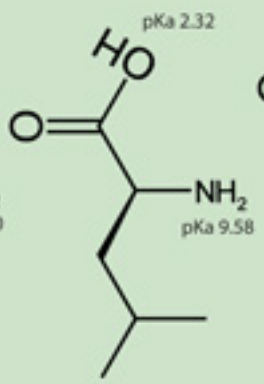
Alanine (Ala) **A**



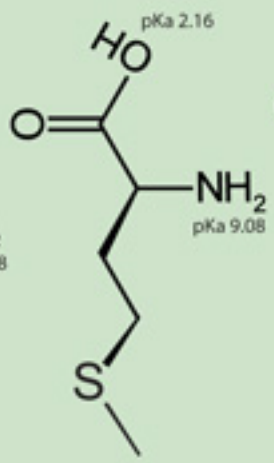
Isoleucine (Ile) **I**



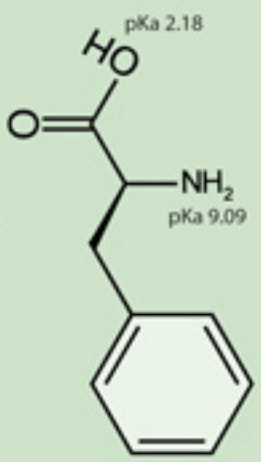
Leucine (Leu) **L**



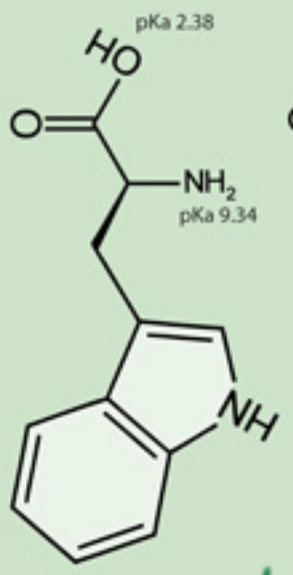
Methionine (Met) **M**



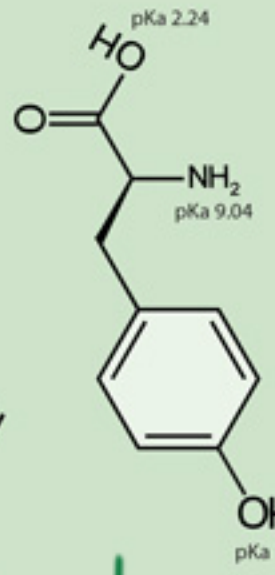
Phenylalanine (Phe) **F**



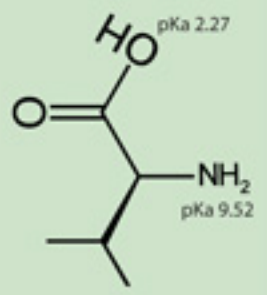
Tryptophan (Trp) **W**



Tyrosine (Tyr) **Y**



Valine (Val) **V**

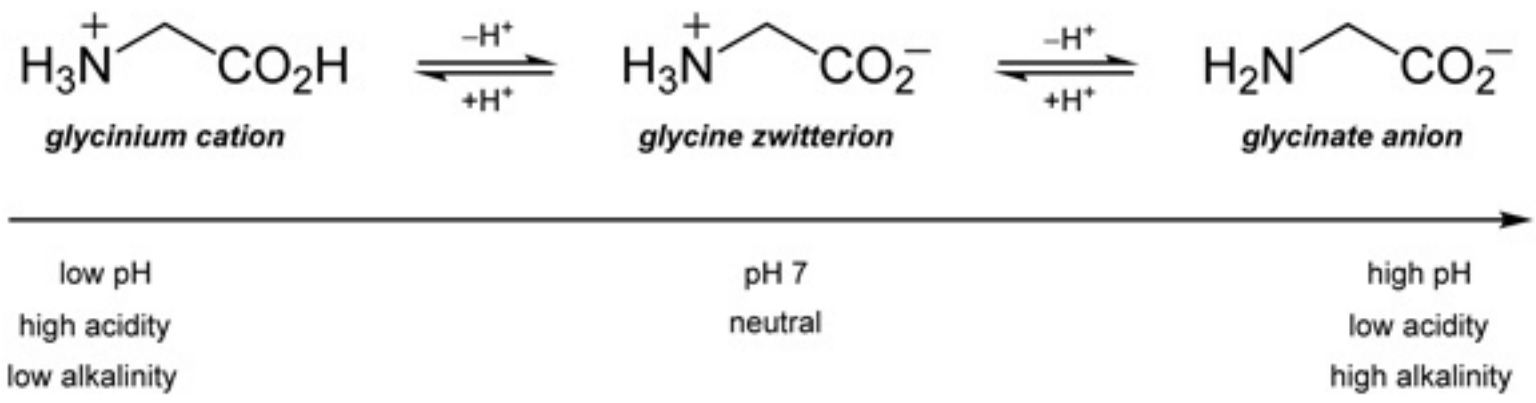


phenol type

pKa ≈ 10

pKa Data: **CRC Handbook of Chemistry, v.** 2010

pH < 2.3 2.3 < pH < 9.6 pH > 9.6

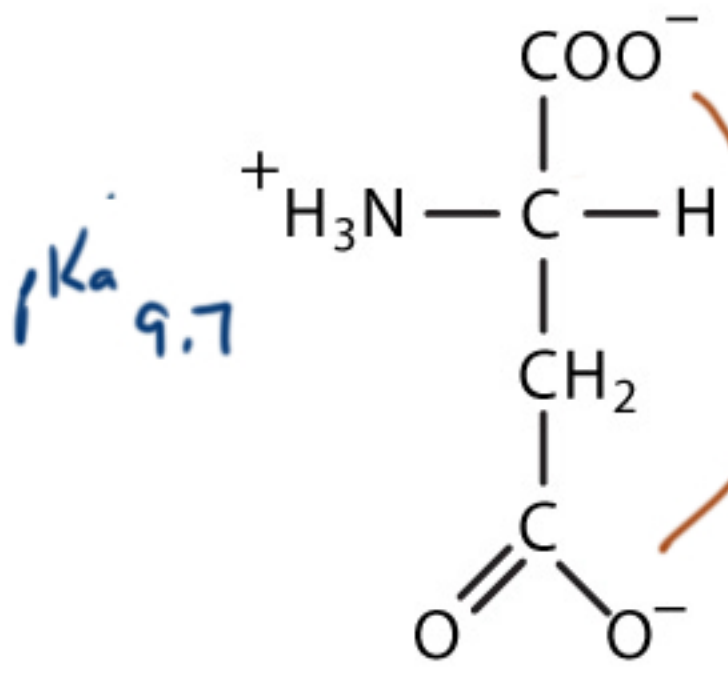


Isoelectric Point

$$\frac{2.3 + 9.6}{2} = 6.2$$

$$pH = pK_a + \log\left(\frac{[A^-]}{[HA]}\right)$$

Aspartate



pKa 2.0

pKa 9.7

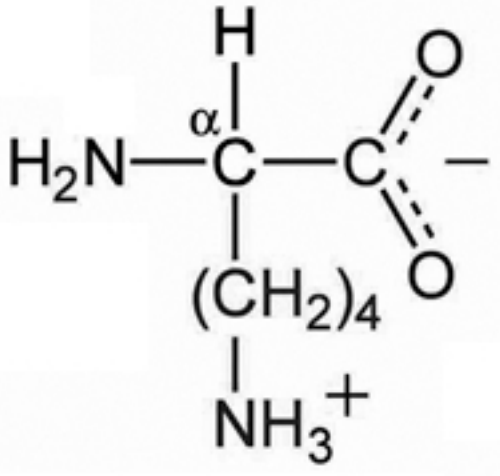
pKa 3.7

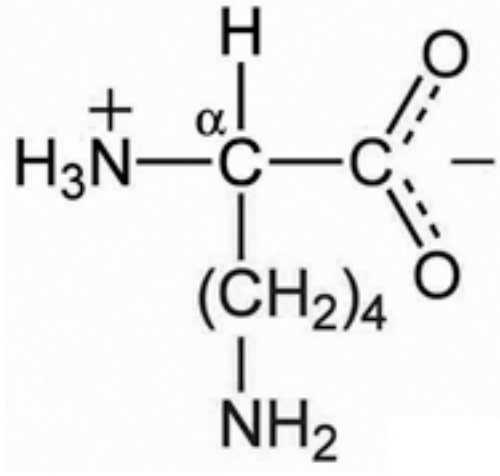
What is pI?

average the like groups

$$\frac{2.0 + 3.7}{2} = 2.9$$

Amino Acid	pKa
Asp (D)	3.9
Glu (E)	4.3
Arg (R)	12.0
Lys (K)	10.5
His (H)	6.08
Cys (C)	8.28 (-SH)
Tyr (Y)	10.1


H
α
O
H_2N
C
C
−
O
$(CH_2)_4$
NH_3^+


H
α
O
+
H_3N
C
C
−
O
$(CH_2)_4$
NH_2

hydrophobic

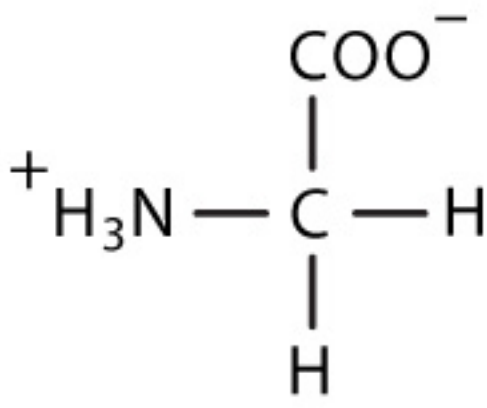
hydrophilic

Kyte and Doolittle (1)	Rose, et al (2)	Wolfenden, et al (3)	Janin (1979) (4)
Ile	Cys	Gly,Leu,Ile	Cys
Val		Val,ala	Ile
	Phe,Ile		Val
Leu	Val	Phe	Leu,Phe
	Leu,Met,Trp	Cys	Met
Phe		Met	Ala,Gly,Trp
Cys			
Met,Ala	His	Thr,Ser	
	Tyr	Trp,Tyr	His,Ser
Gly	Ala		Thr
Thr,Ser	Gly		Pro
Trp,Tyr	Thr		Tyr
Pro			Asn
		Asp,Lys,Gln	Asp
His	Ser	Glu,His	Gln,Glu
Asn,Gln	Pro,Arg	Asp	
Asp,Glu	Asn		
Lys	Gln,Asp,Glu		
			Arg
Arg	Lys	Arg	Lys

Glycine

G

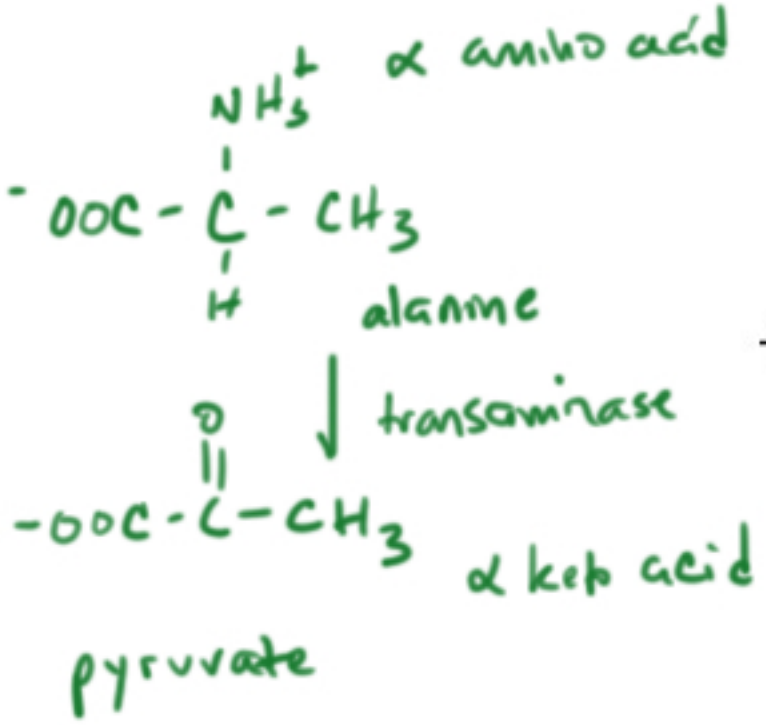
- like a missing tooth
  - oxianion hole in serine protease
  - 30% of collagen - interior of triple helix
  - backbone H bonding



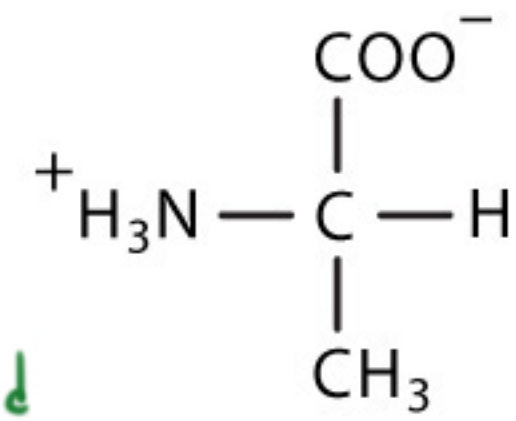
- achiral
- important precursor such as with porphyrin
  - ↑ organic component of heme

Alanine

A



Hence alaine is glucogenic



- prototype boring amino acid in proteins
- K293A

Lysine at 293 replaced with alanine

↑

is'nt a confound

- AAAAAAHHHHHH

↗

alanine spacers

↑

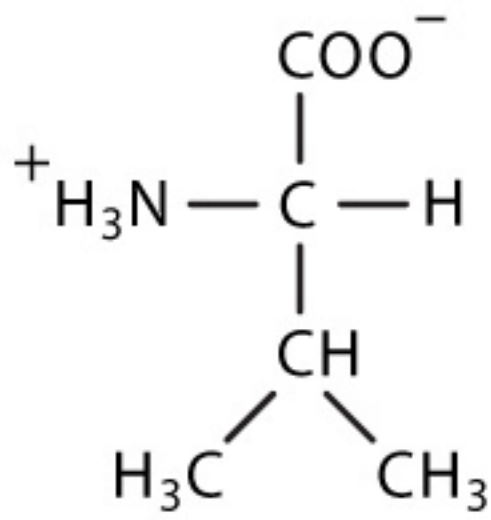
polyhistidine for affinity chromatography with nickel column

Valine

V

example don't memorize!

- hydrophobic



- breaks down to succinyl CoA

↓

succinate

↓

fumarate

↓

malate

↓

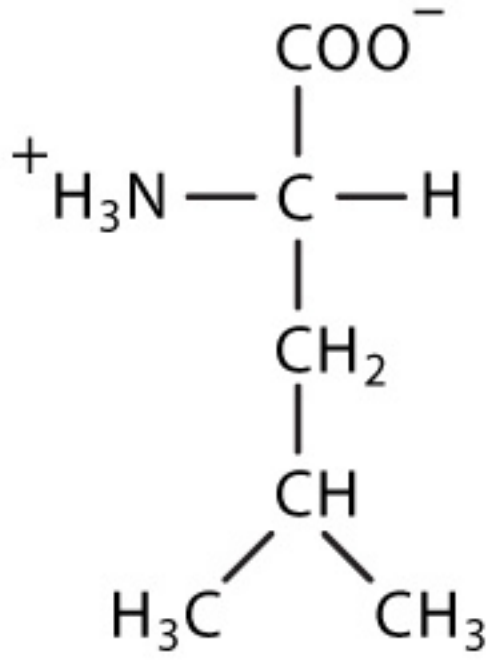
oxaloacetate

It is glucogenic.

Leucine

L

- example of an essential amino acid (don't synthesize)



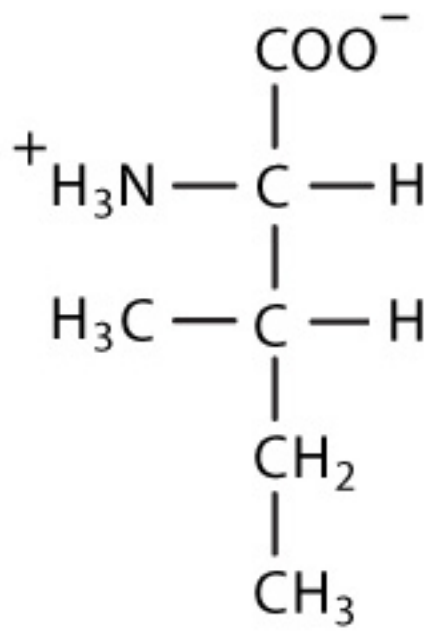
- breaks down to acetyl CoA ad acetoacetate

There's no path from acetyl CoA to glucose.

Leucine is ketogenic.

Isoleucine

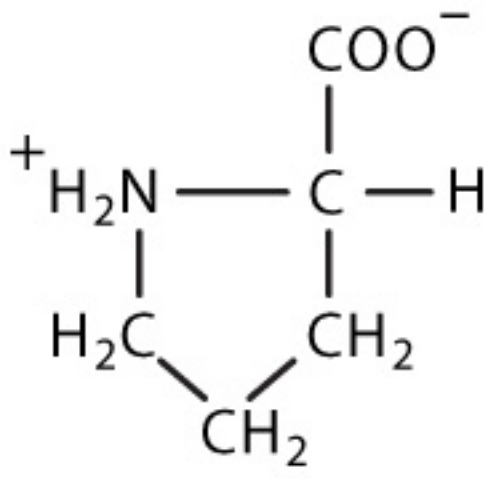
I



2 chiral centers (like threonine)

Proline

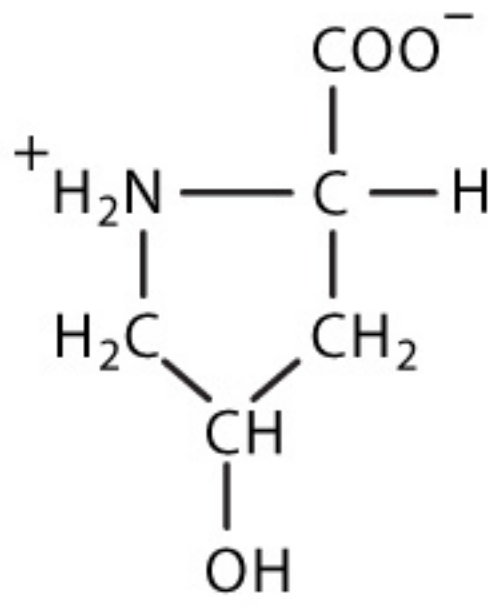
P



- Plays a big role in protein structure
- locks ϕ at 60° in polypeptide
  - reduces configurational entropy
- α helix disruptor and β turns

(essential prolines bound α helix)

Hydroxyproline



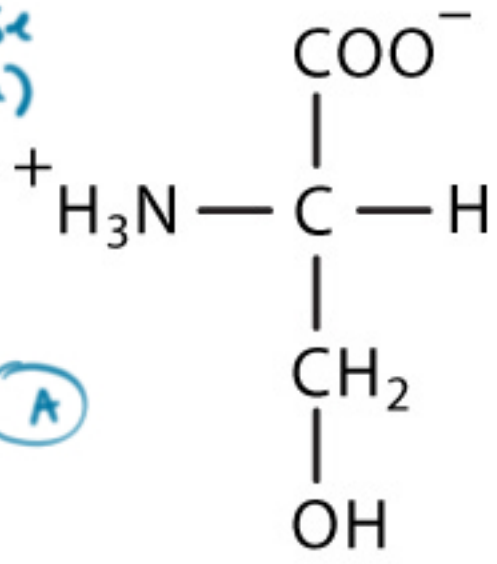
- hydroxyproline in collagen
- prolyl hydroxylase requires ascorbate (vitamin C)

P Serine

- often the target of phosphorylation by kinase (also threonine & tyrosine)

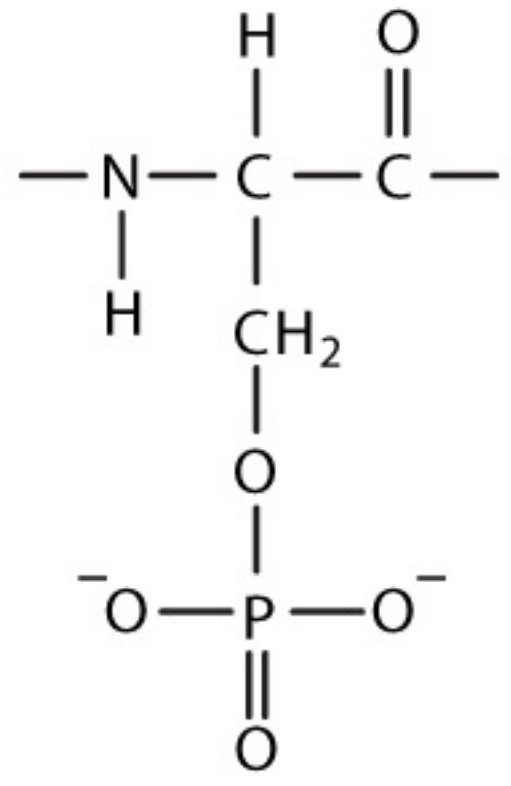
Kinase

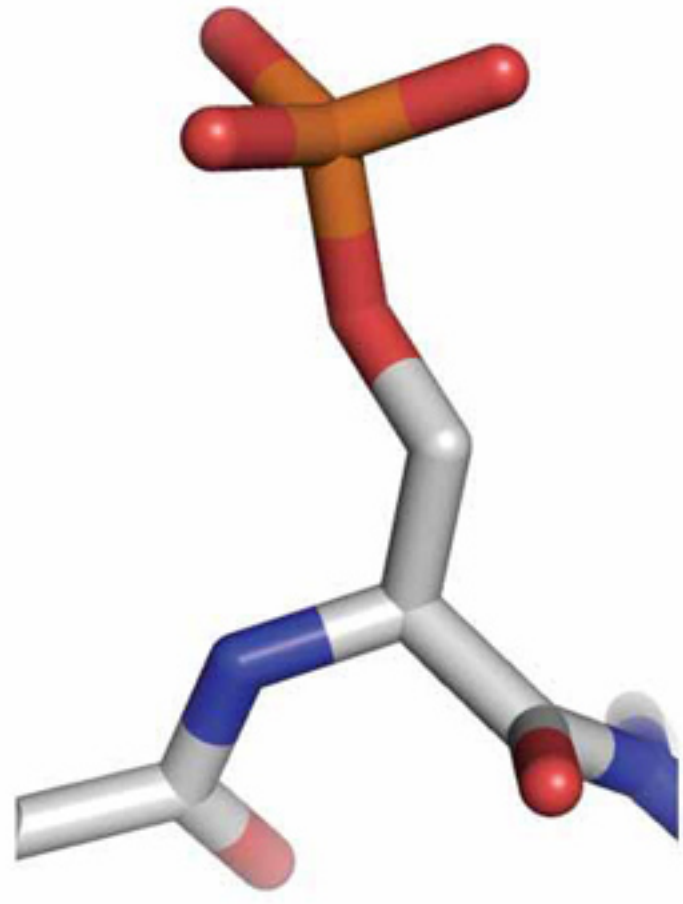
like SN2 across the phosphorus

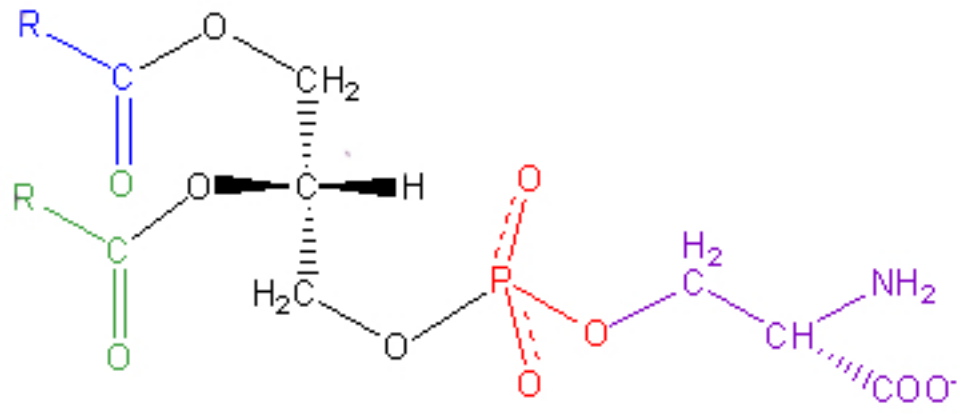


- also target of O-linked glycosylation
- precursor - part of phosphatidyl serine also sphingosine
- nucleophile in serine protease

Phosphorylated Serine

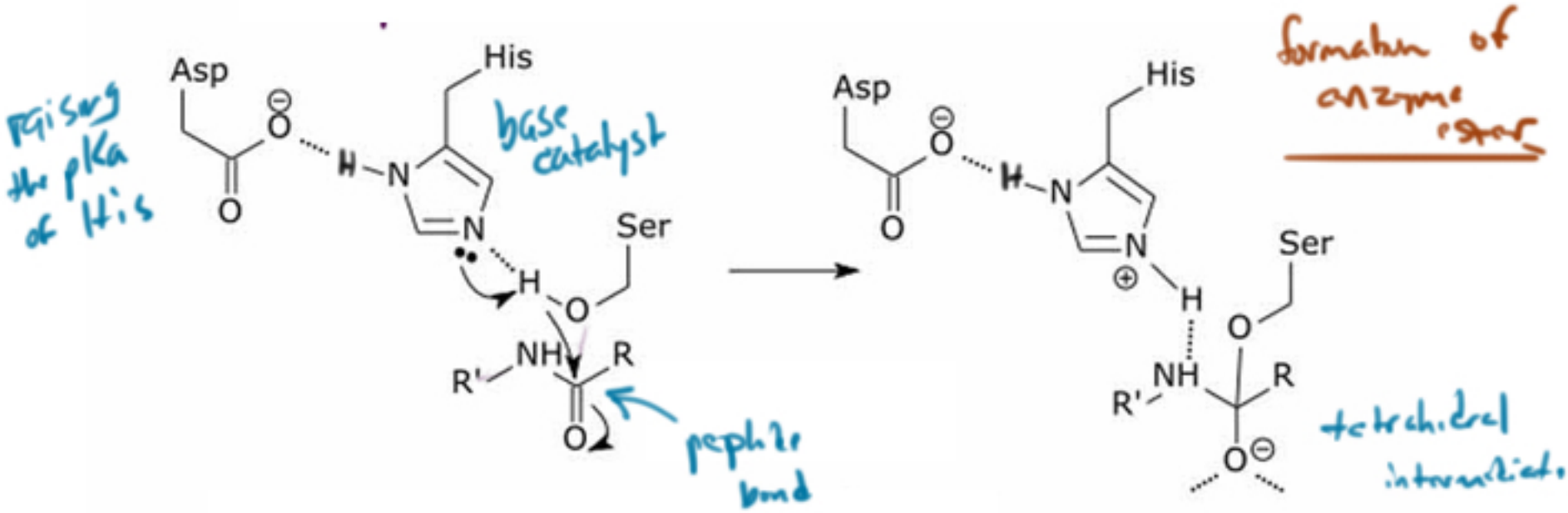


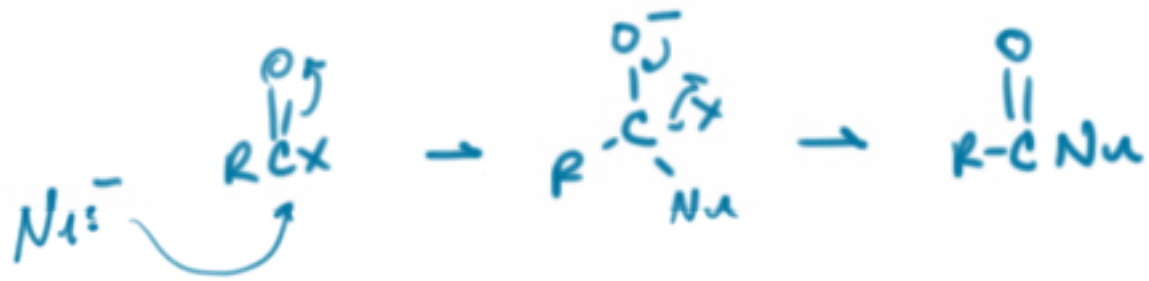


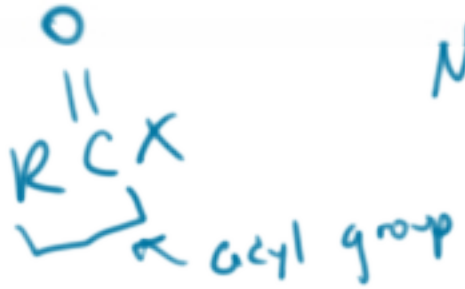


1 phosphatidate 1 serine 1

Serine protease such as chymotrypsin





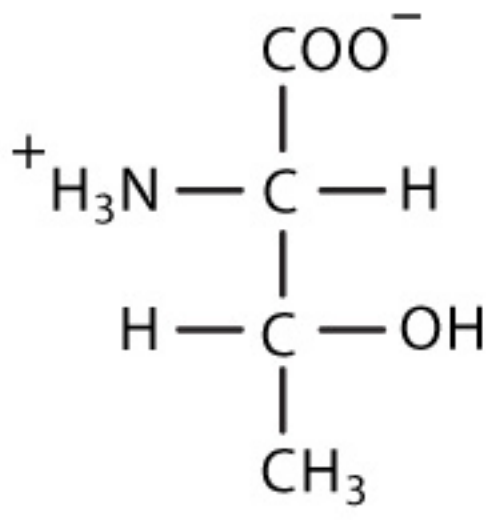


Nucleophilic Acyl Substitution

Threonine

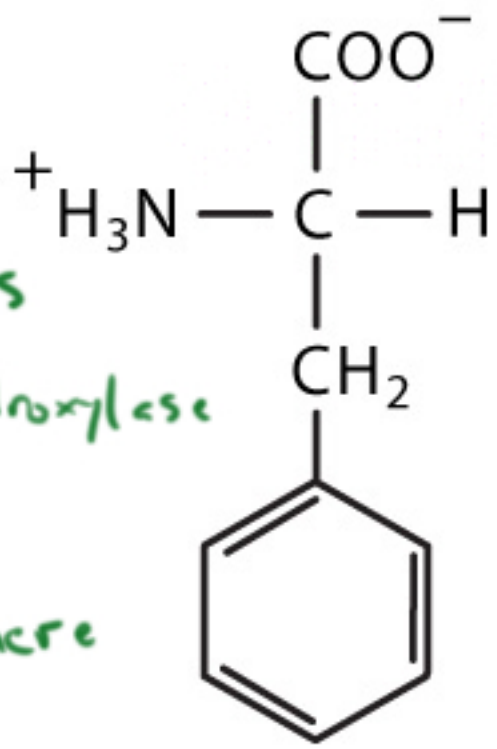
T

- Target of kinase
- Target of O-linked glycosylation



Phenylalanine

F



- Phenylalanine degradation - a few notable enzymes
  - phenylalanine hydroxylase
    F → Y
    genetic lesion here
    - homozygous - phenylketonuria
  - homogentisate oxidase
    - lesion leads to alcaptonuria
    - Archibald Garrod - one gene one enzyme

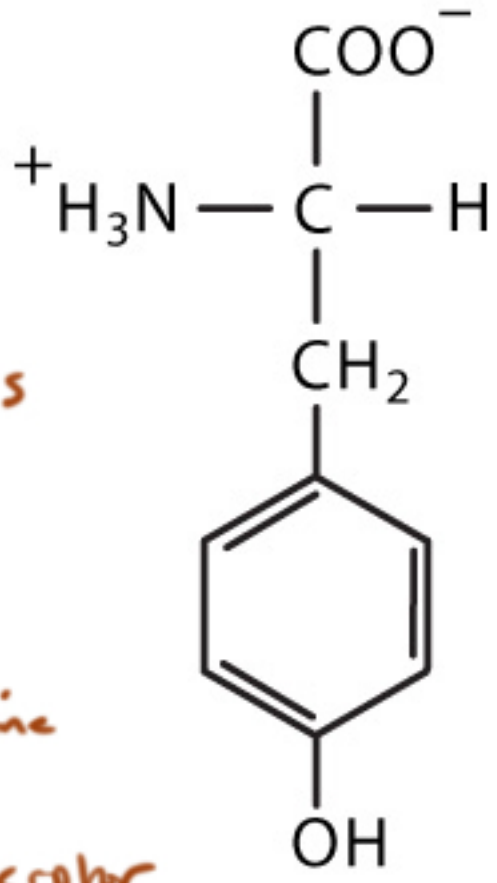
- Hydrophobic
- Membrane anchor

Phenylalanine
Hydroxylase

Tyrosine

Y

- Target of kinase
  - tyrosine kinase
  - catalytic receptors
    - growth factor receptors
      - intrinsic receptor tyrosine kinase
    - cytokine receptors
      - nonreceptor tyrosine kinase



- Hydrophobic (a bit of a gray area)
- Precursor of catecholamines epinephrine, norepinephrine dopamine

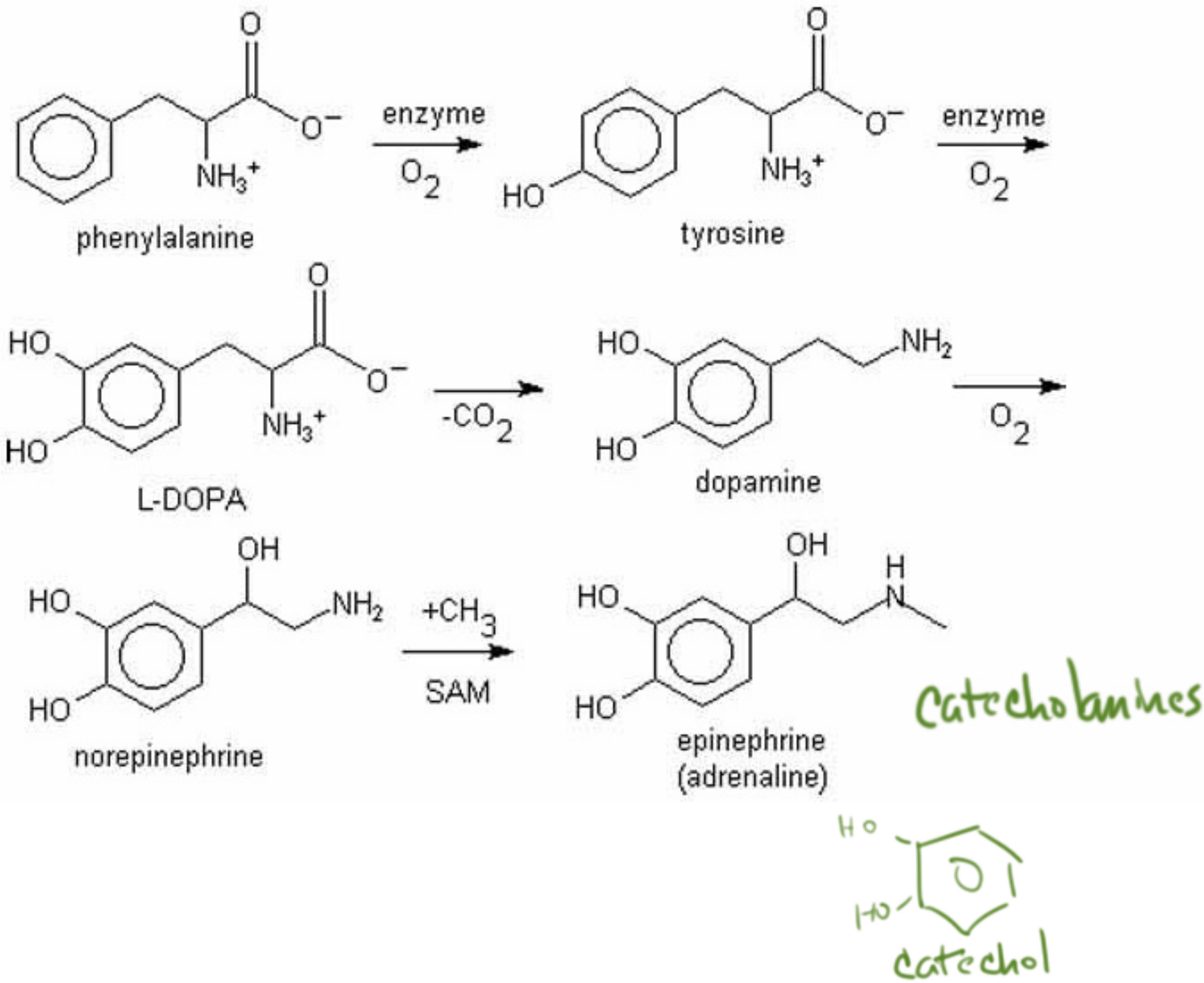
pKa ~10

GFR

1) ligand binding leads to receptor dimerization

transautophosphorylation

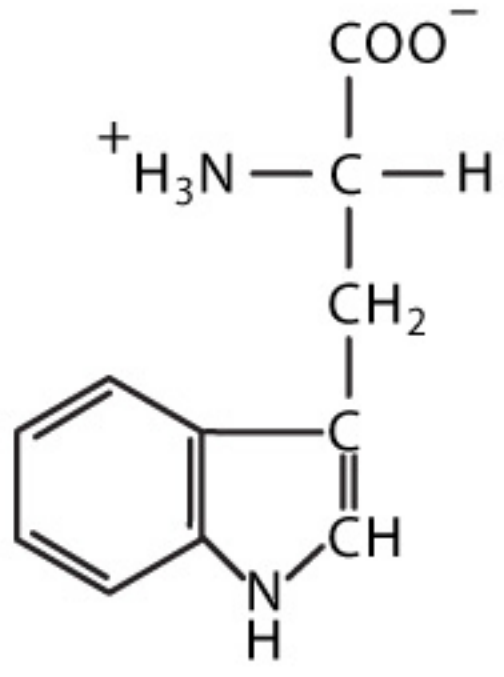
- Phosphorylated tyrosines serve as docking sites for signaling proteins activating them.


phenylalanine
enzyme
O_2
tyrosine
enzyme
O_2
L-DOPA
$-CO_2$
dopamine
O_2
norepinephrine
$+CH_3$
SAM
epinephrine
(adrenaline)
catecholamines
catechol

Tryptophan

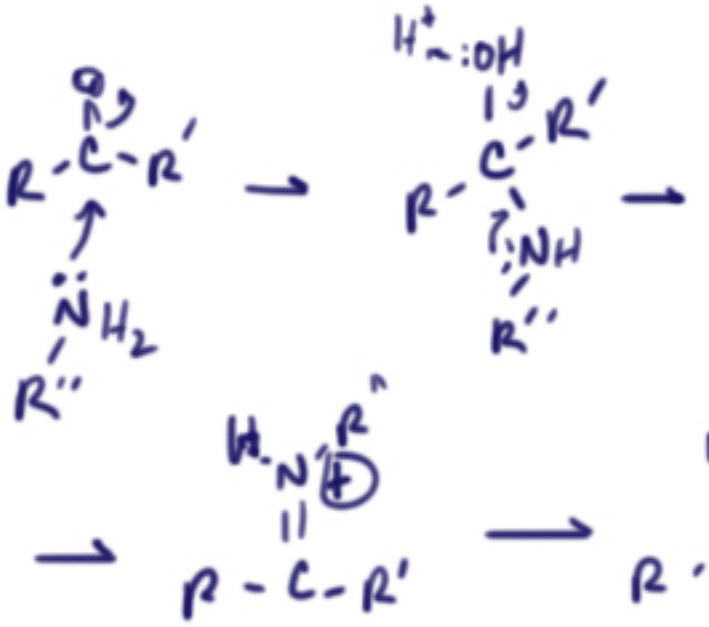
W

- Precursor of serotonin, melatonin



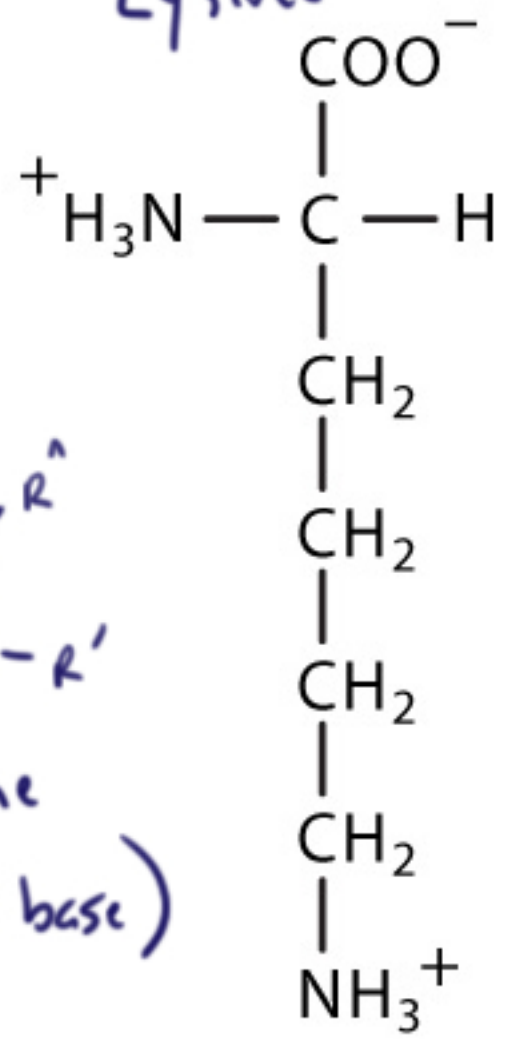
- Hydrophobic
- Membrane Anchor

Imine Formation



Lysine

K



pKa ~ 10.5

- Reliable ⊕
- often seen forming Schiff base with substrate
- can also form amide linkages

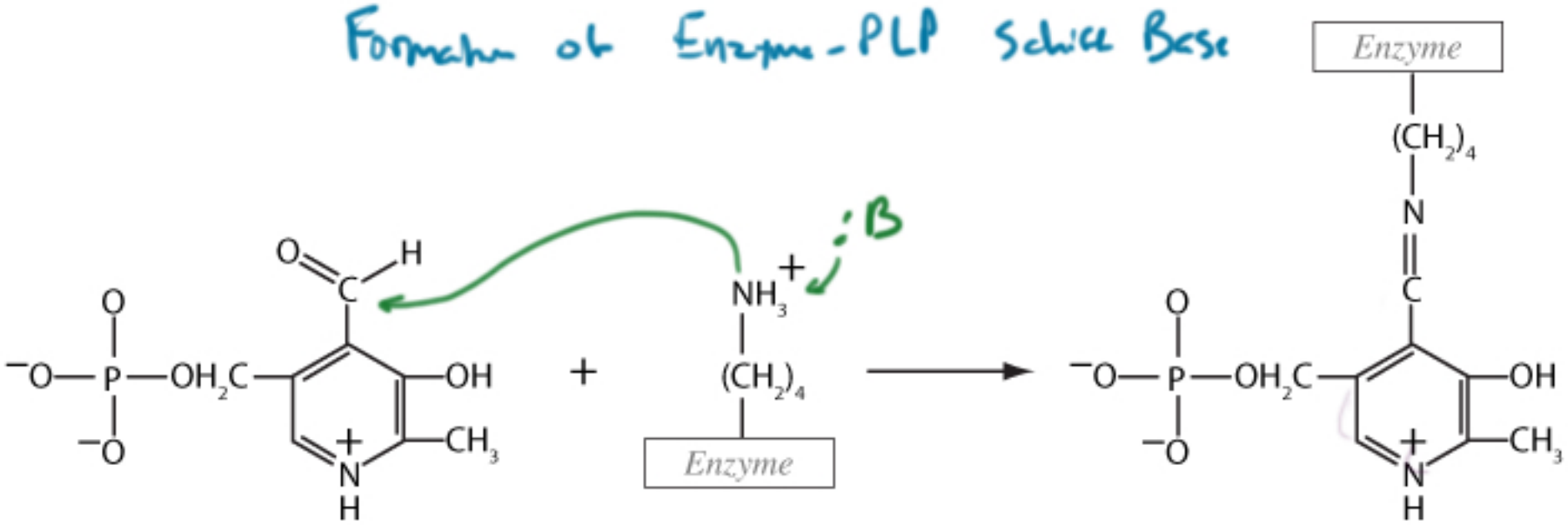
} lys - N(H) - C(=O) - gln {

- amide linkage in a hard clot

$$pH = pK_a + \log\left(\frac{[A^-]}{[HA]}\right)$$

7.4 10.5 + log (1/1000)

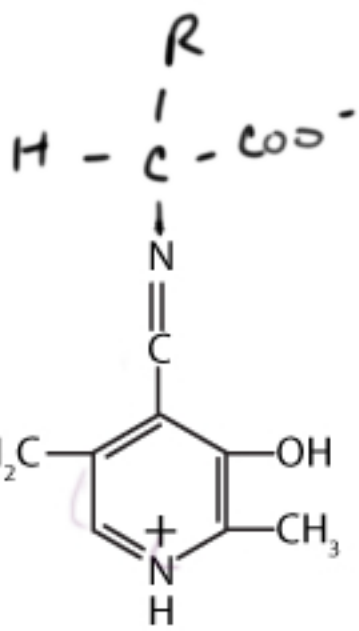
Formation of Enzyme-PLP Schiff Base



PLP (vitamin B6)

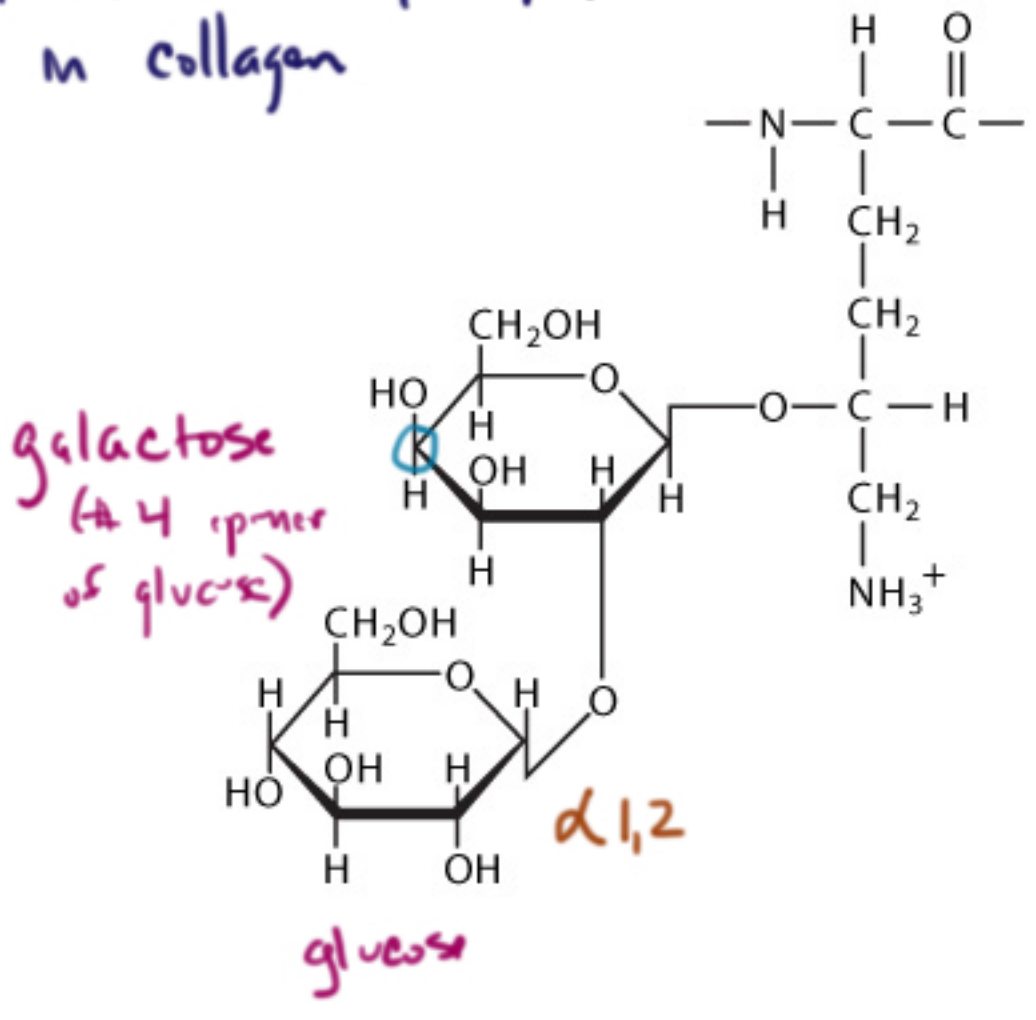
pyridoxyl phosphate

"the amino acid chemistry coenzyme"



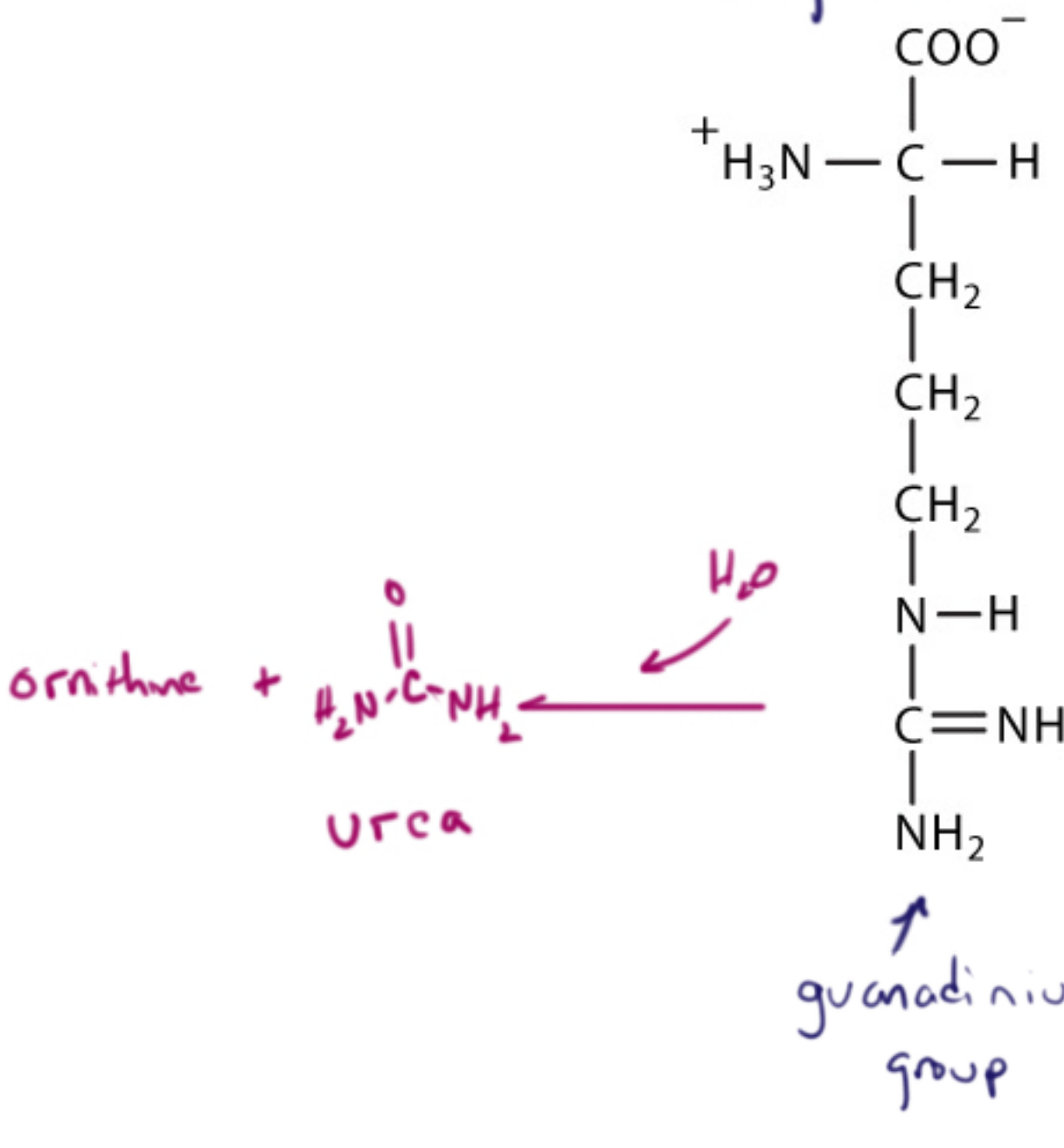
PLP-amino acid Schiff base

Glycosylated Hydroxylysine in collagen

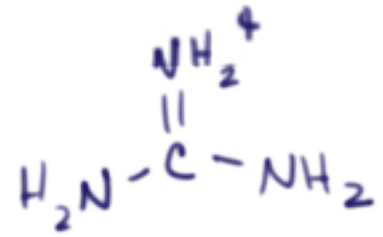


Arginine

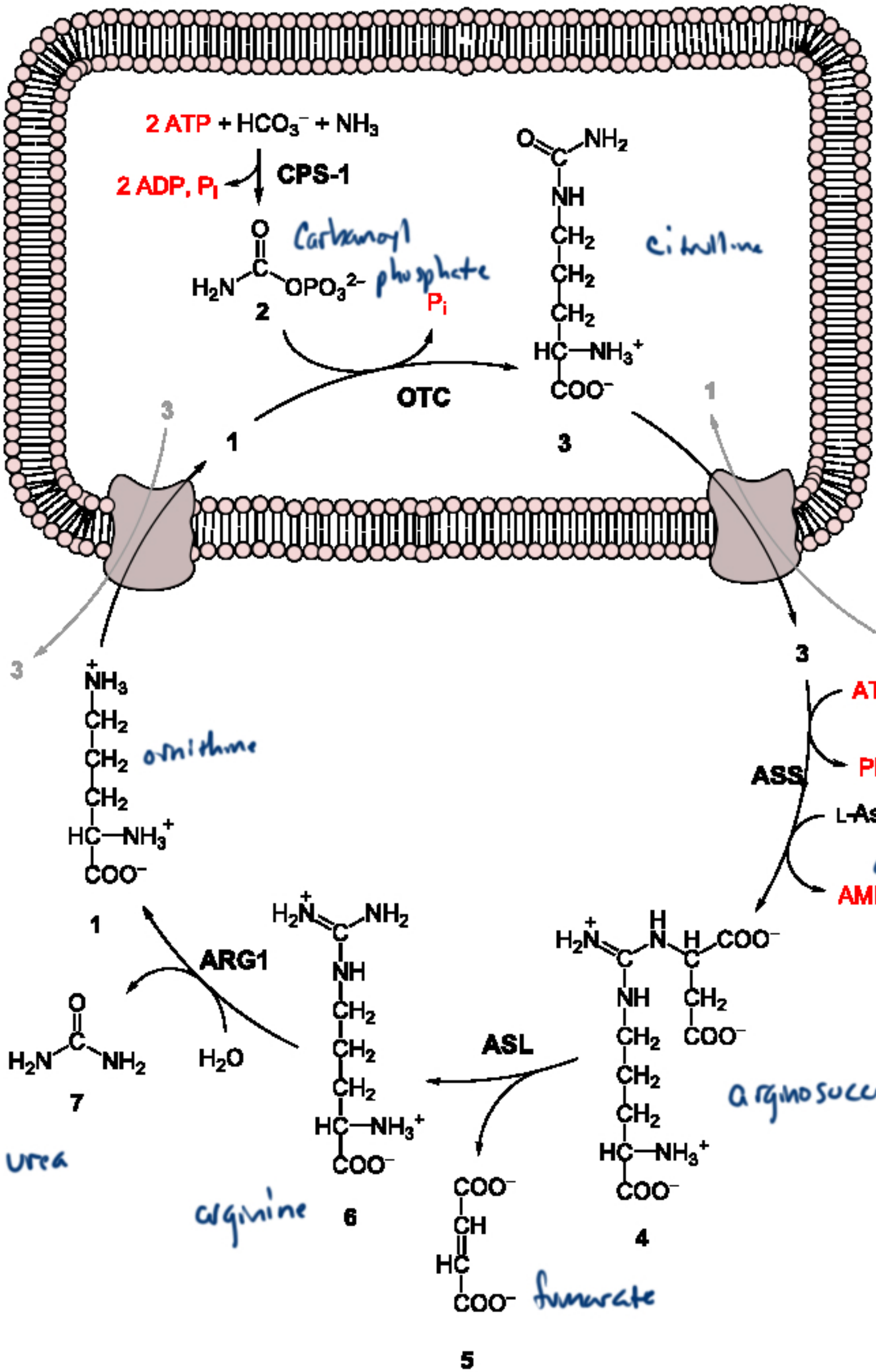
R



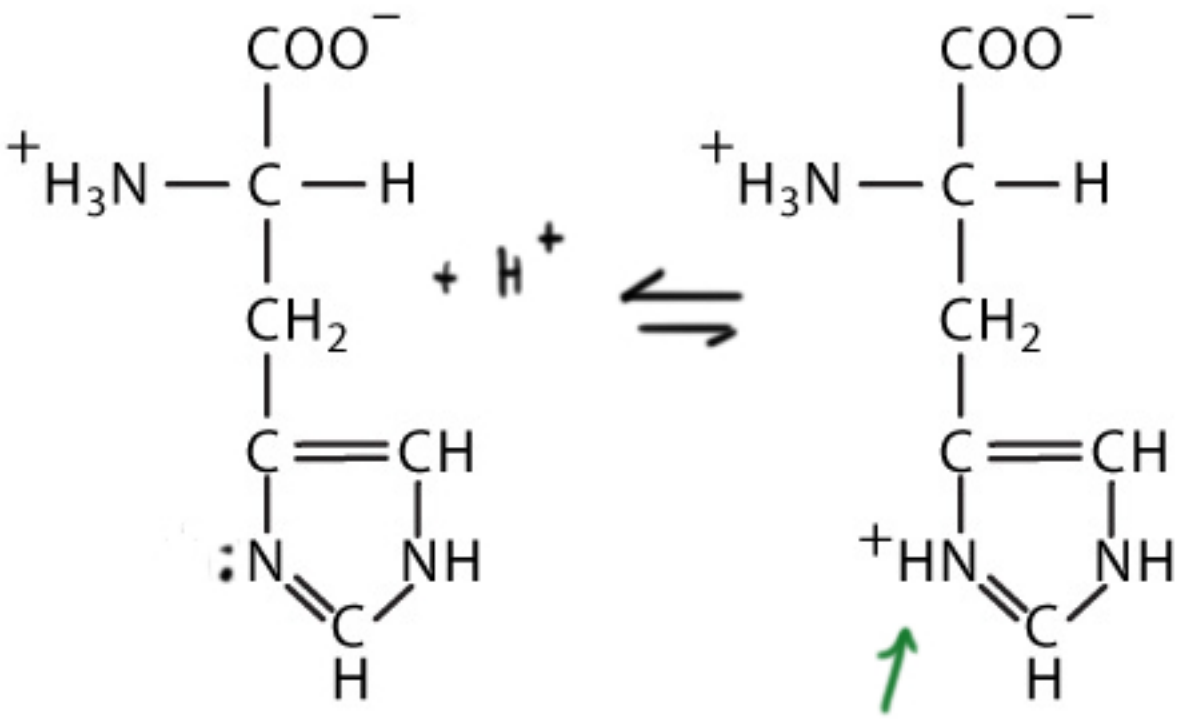
- reliable ⊕
- salt bridges and substrate binding



Urea cycle


2 ATP + HCO_3^- + NH_3
2 ADP, P_i
CPS-1
Carbamoyl phosphate
P_i
OTC
citrulline
1
2
3
4
5
6
7
ornithine
ATP
PP_i
ASS
L-Asp
aspartate
AMP
ARG1
H_2O
ASL
arginosuccinate
urea
arginine
fumarate

Histidine



- at physiological pH about one in twenty five are protonated

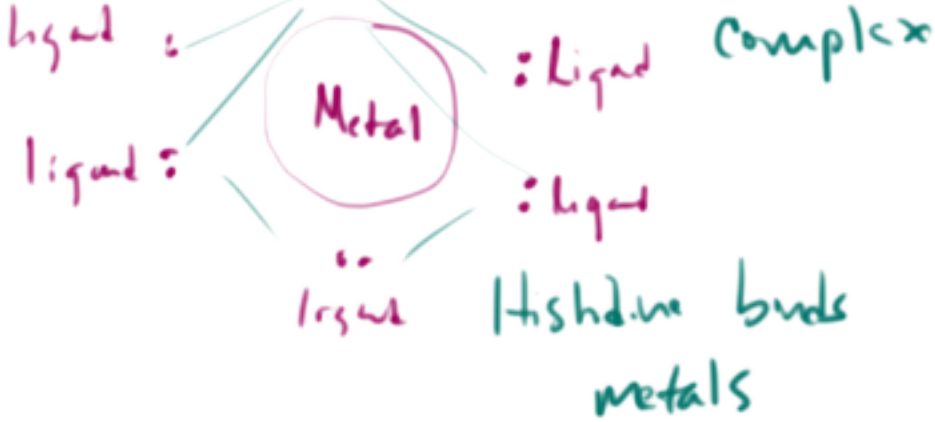
asp is raising the pKa of His

- important acid-base catalyst

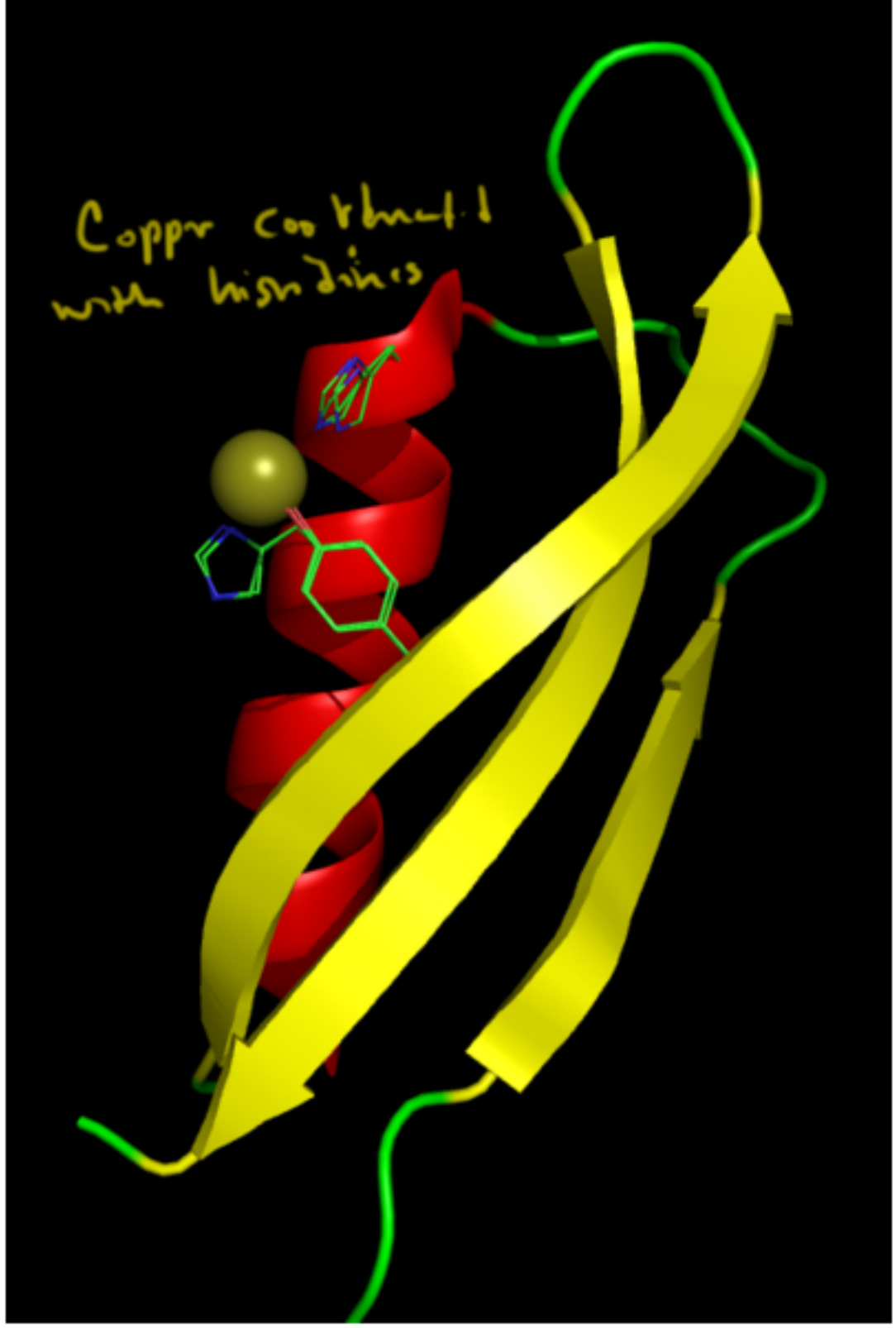
$pKa \sim 6.0$

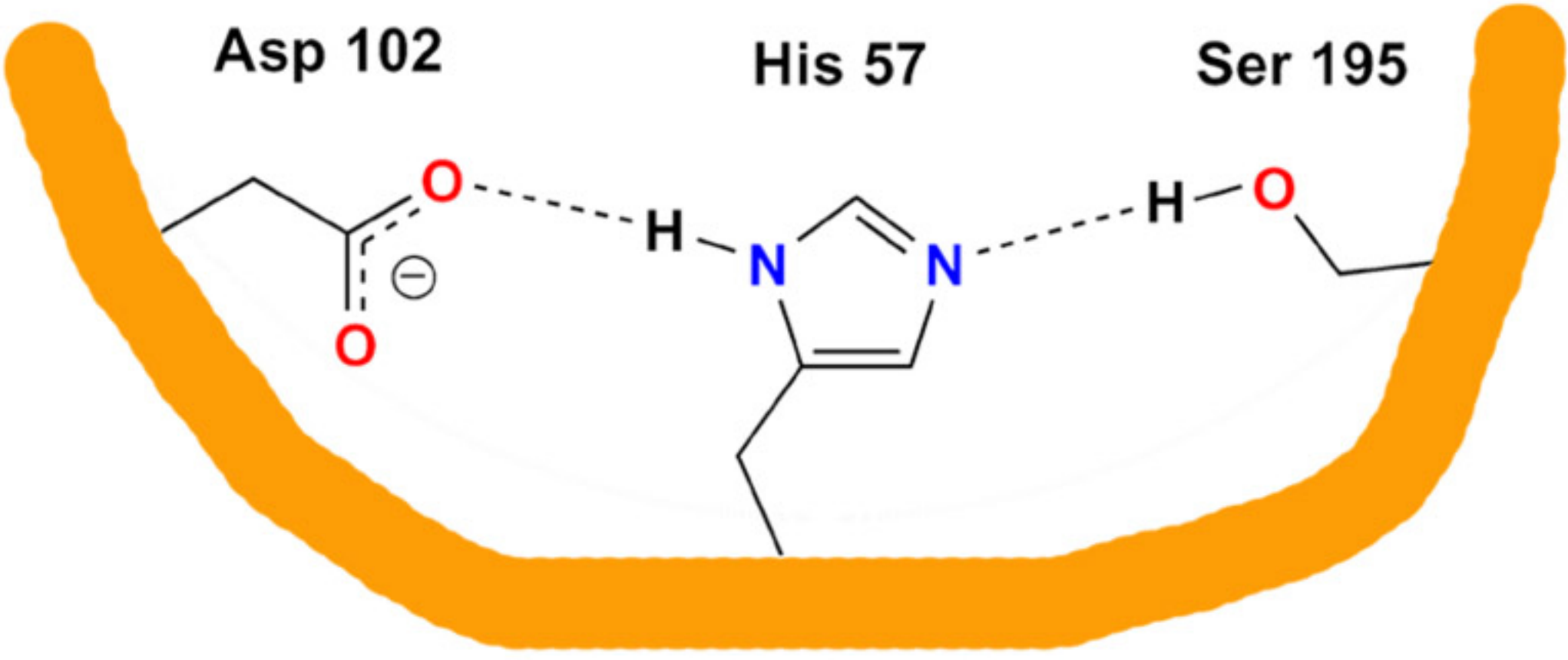
$$pH = pK_a + \log\left(\frac{[A^-]}{[HA]}\right)$$

$$7.4 = 6.0 + \log\left(\frac{25}{1}\right)$$



Histidine binds metals

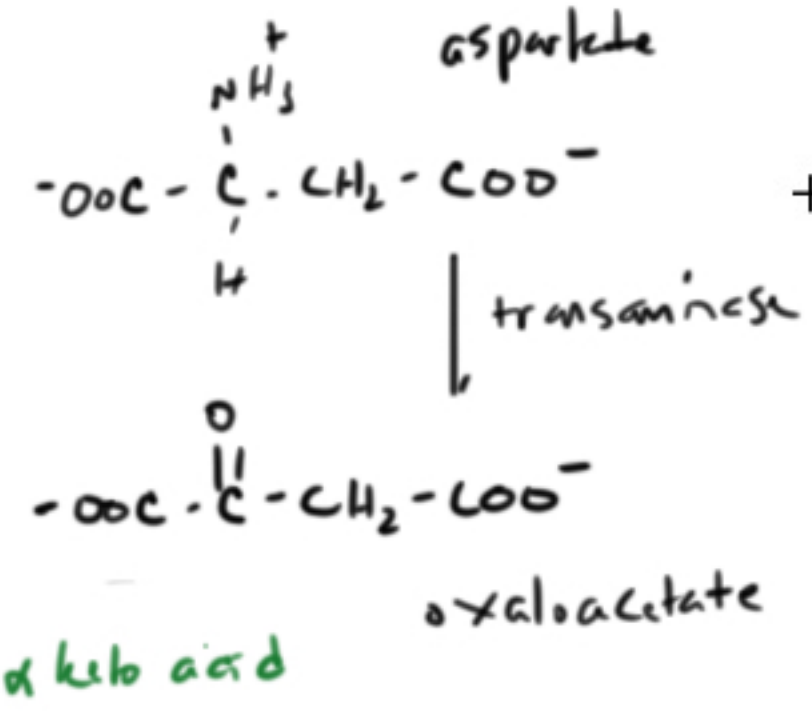

Copper coordinated
with histidines


Asp 102
His 57
Ser 195
O
O
H
N
N
H
O

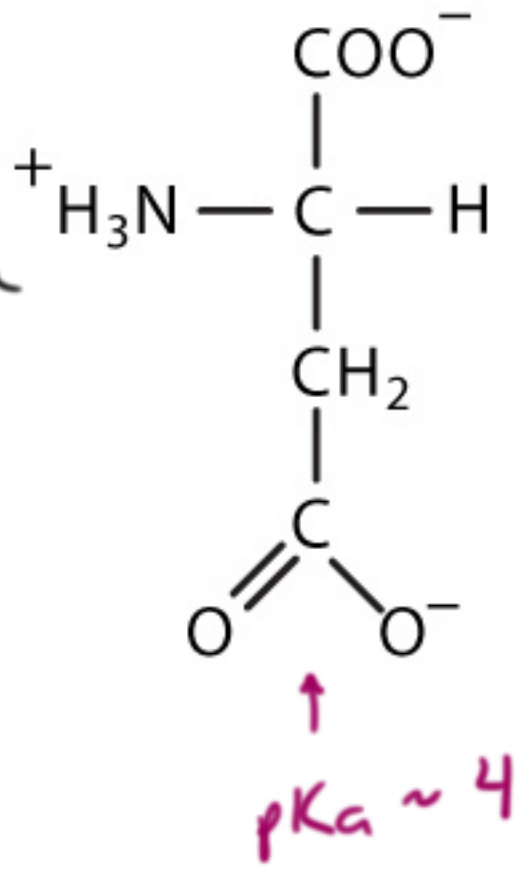
Aspartate

D

α amino acid



α keto acid

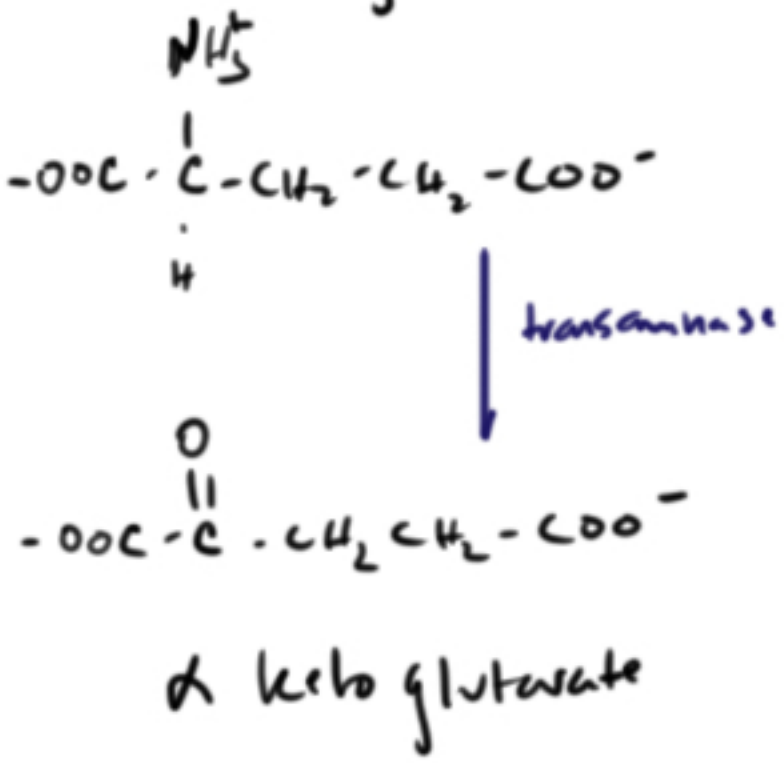


- reliable ⊖
- acid base catalyst
- carboxylate nucleophile
- salt bridges

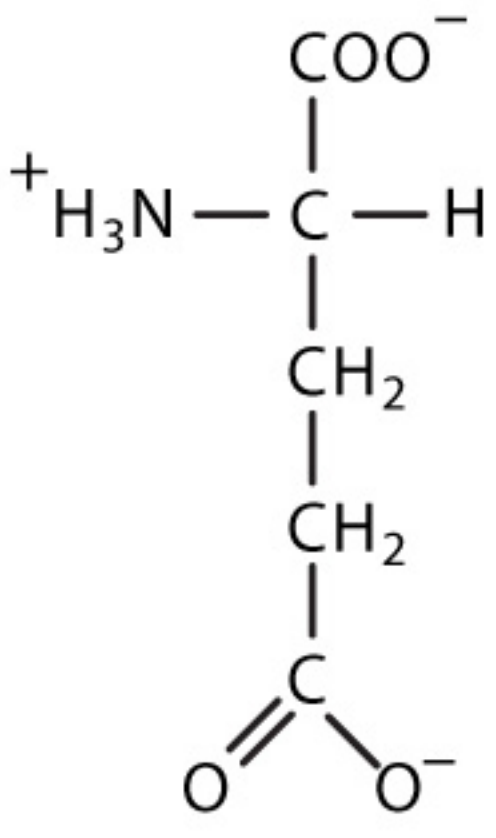
E

Glutamate

glutamate



α keto glutarate



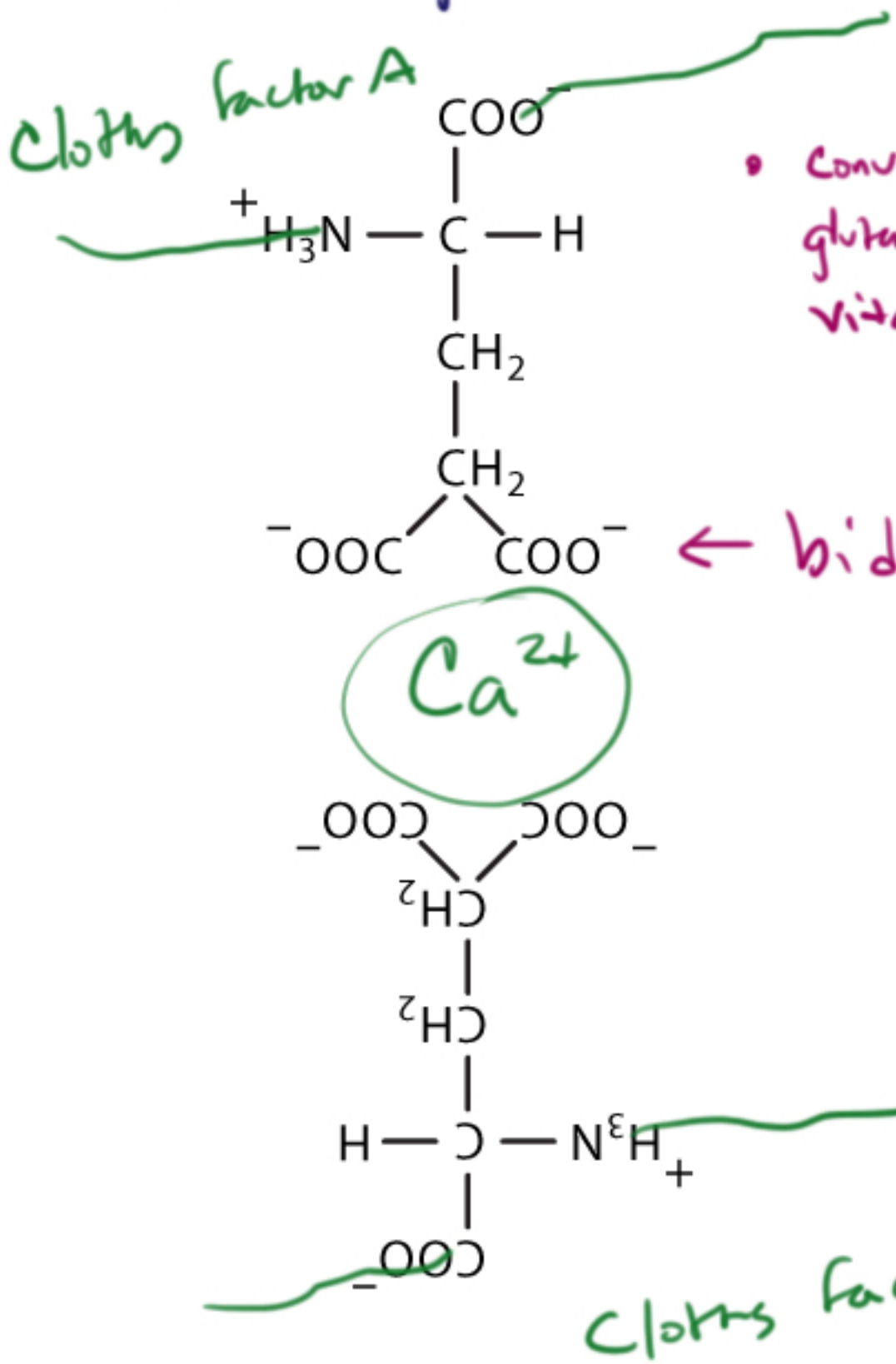
• reliable ⊖

↑ pKa ~ 4

L amino acid$_a$ ⟶ α keto acid$_a$

α keto acid$_b$ — α amino acid$_b$

γ carboxyglutamate

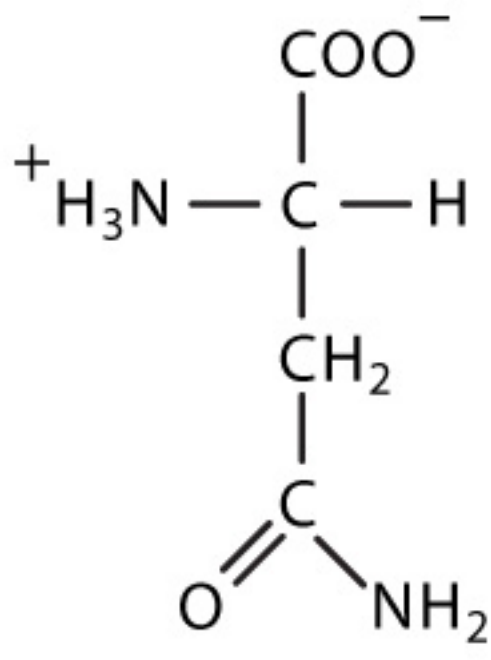


• Conversion from glutamate requires vitamin K

← bidentate ligad

Asparagine

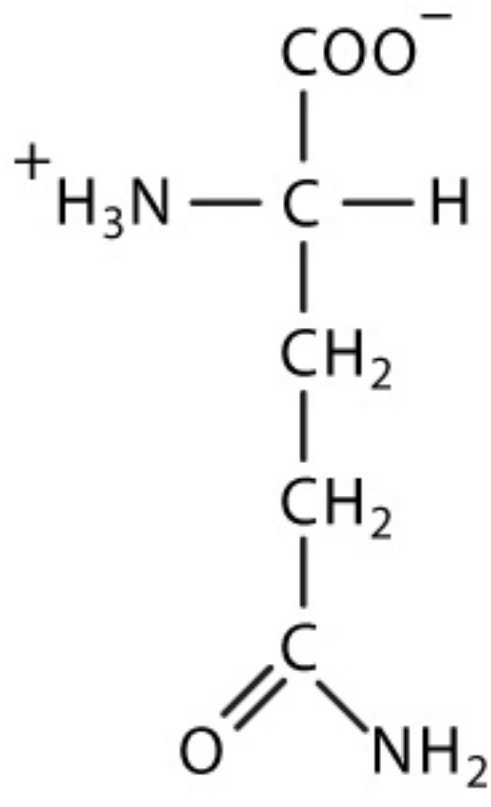
N



- H bonding - often to backbone is important for protein structure

Glutamine

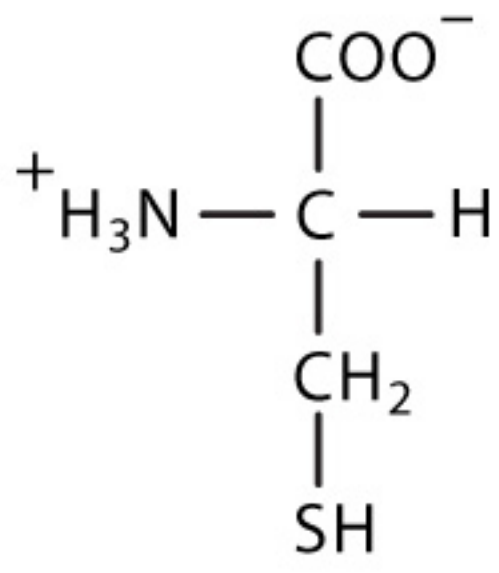
Q



- H bonding
- N source in biosynthesis

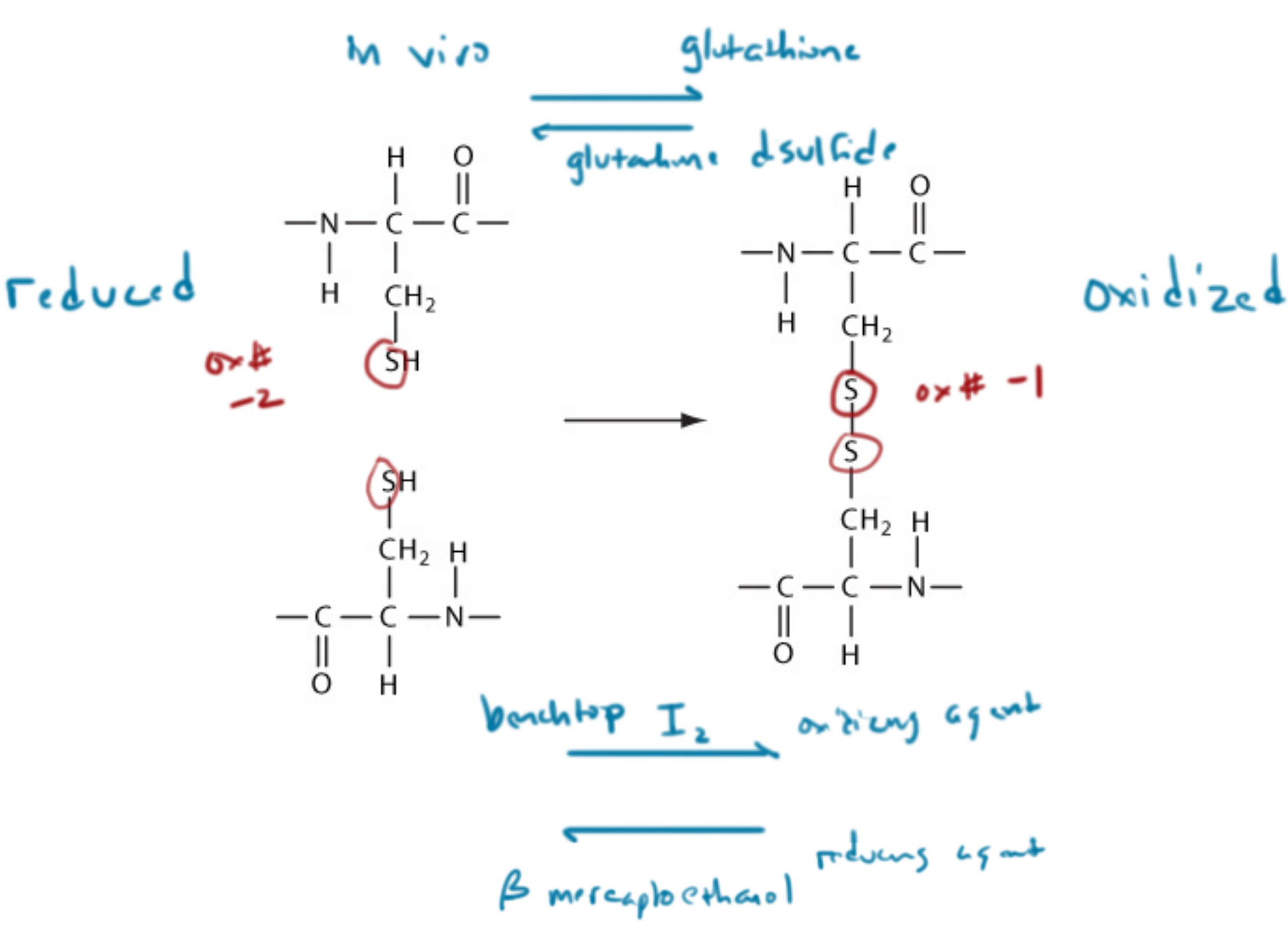
Cysteine

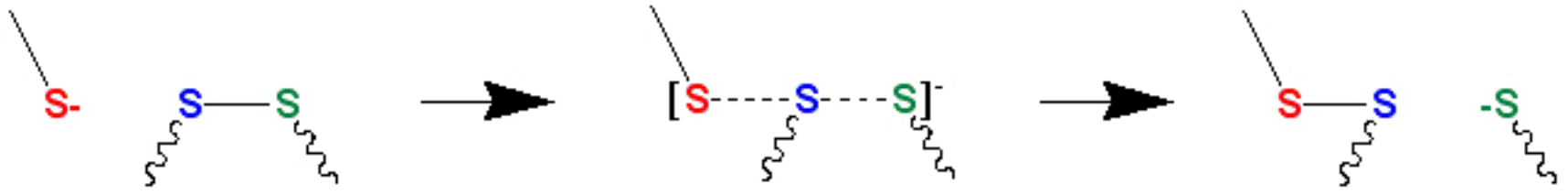
C



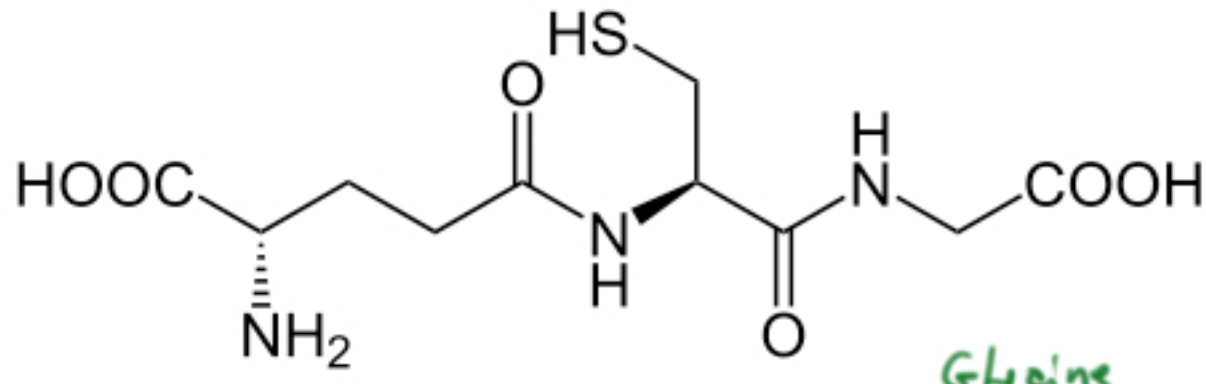
- Forms disulfide bridges (covalent)
- Nucleophile
- Ligand in coordination complexes

pKa ~ 8.1


M vio
glutathione
glutathione disulfide
Reduced
Oxidized
ox#
-2
ox# -1
benchtop I_2
oxidizing agent
reducing agent
B mercaptoethanol


S-
S
S
[S
S
S]-
S
S
-S

Glutathione

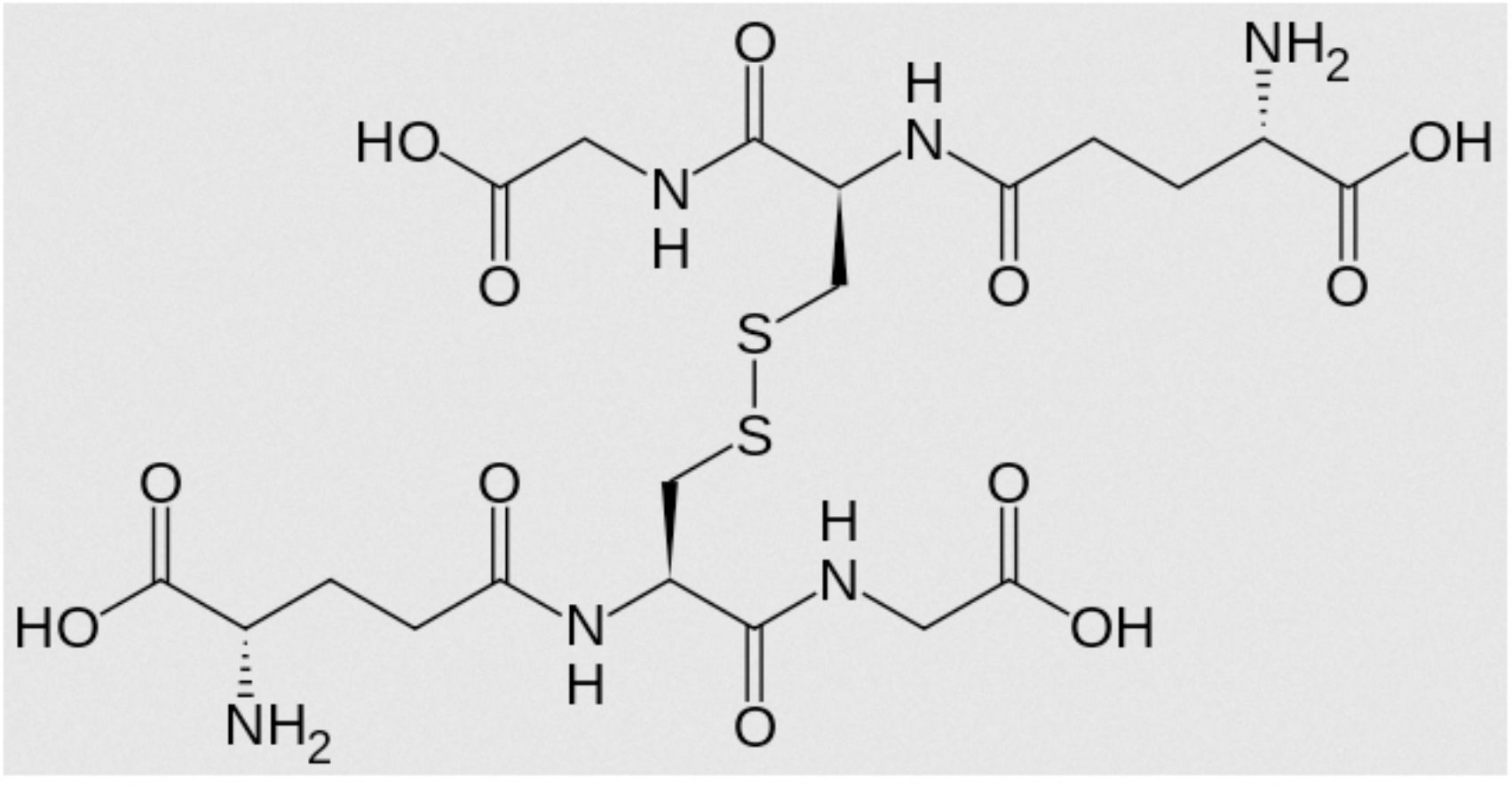


γ glutamate cystine Glycine

(Reduced)

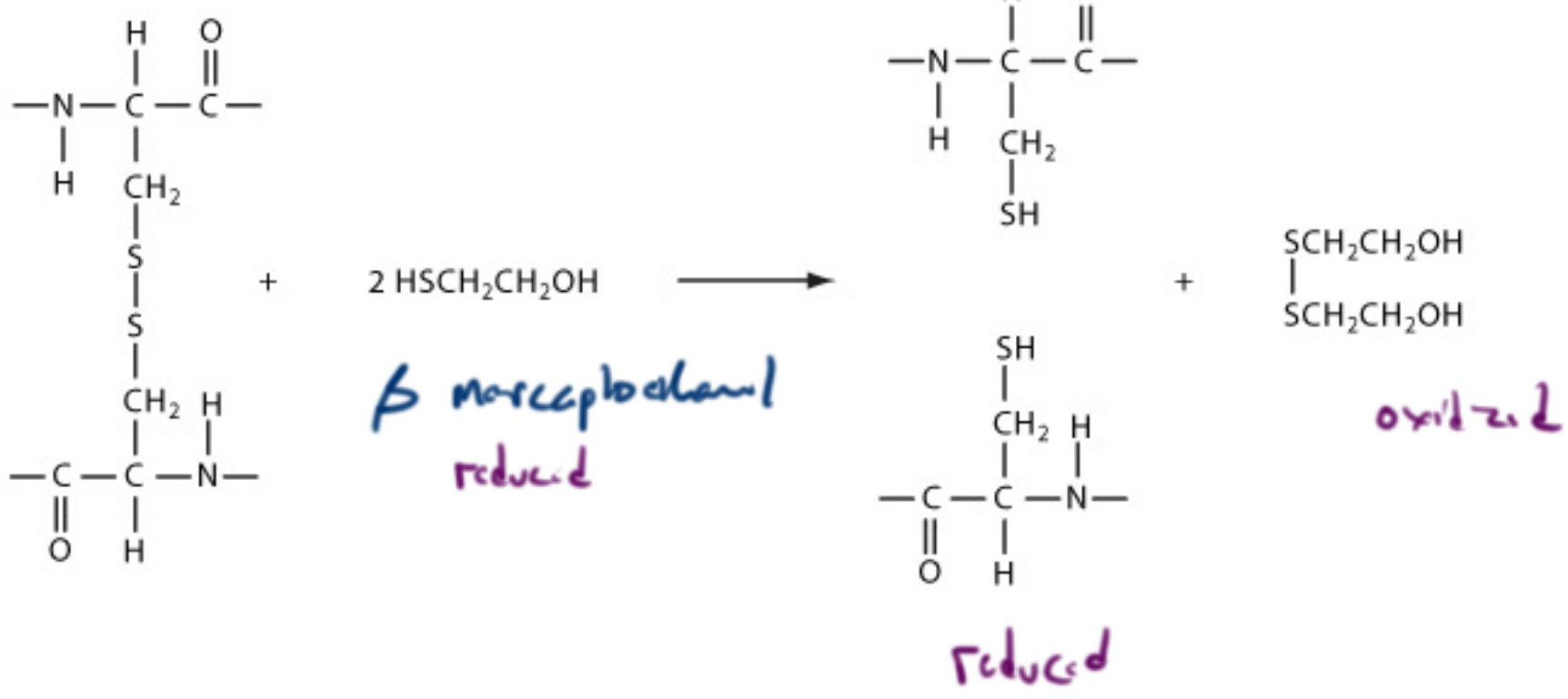
- the most important redox buffer in the blood.

Glutathione Disulfide



(oxidized)

oxidized

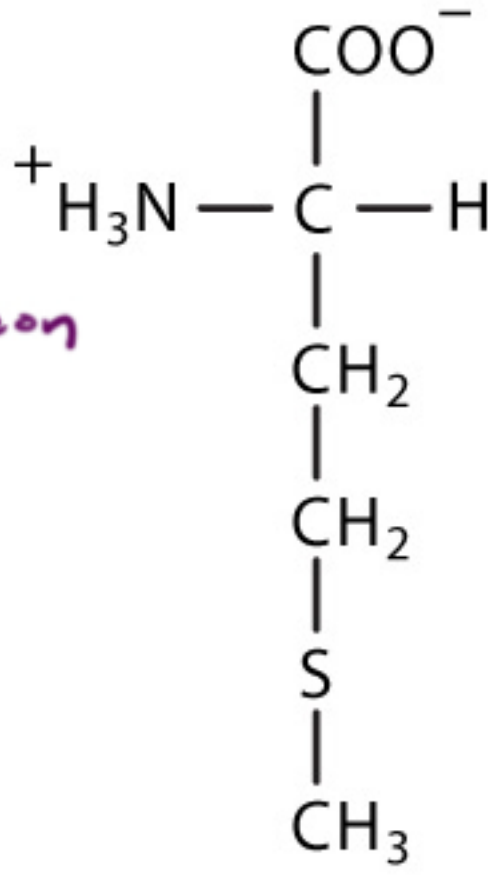


Methionine

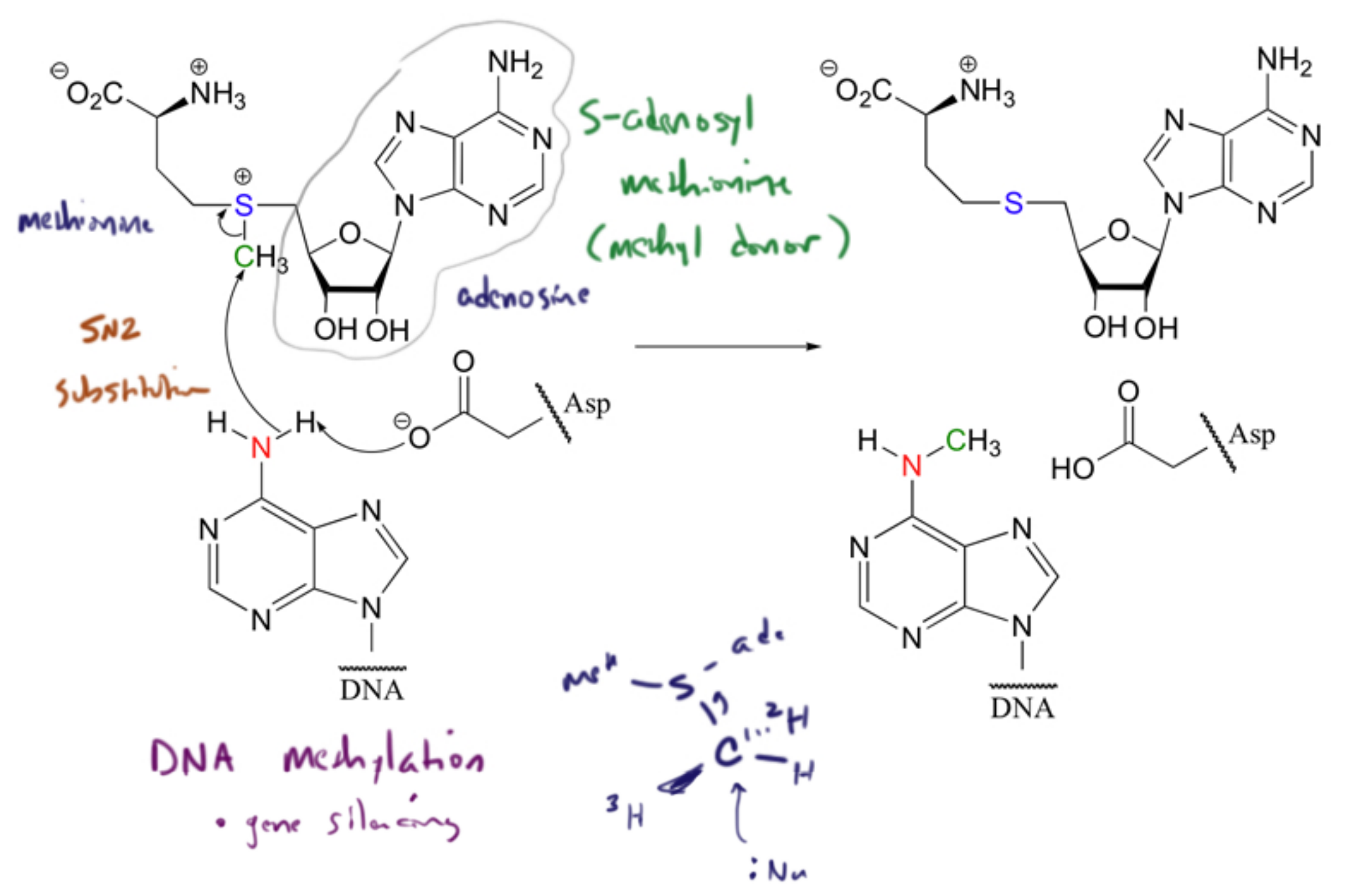
M

- AUG

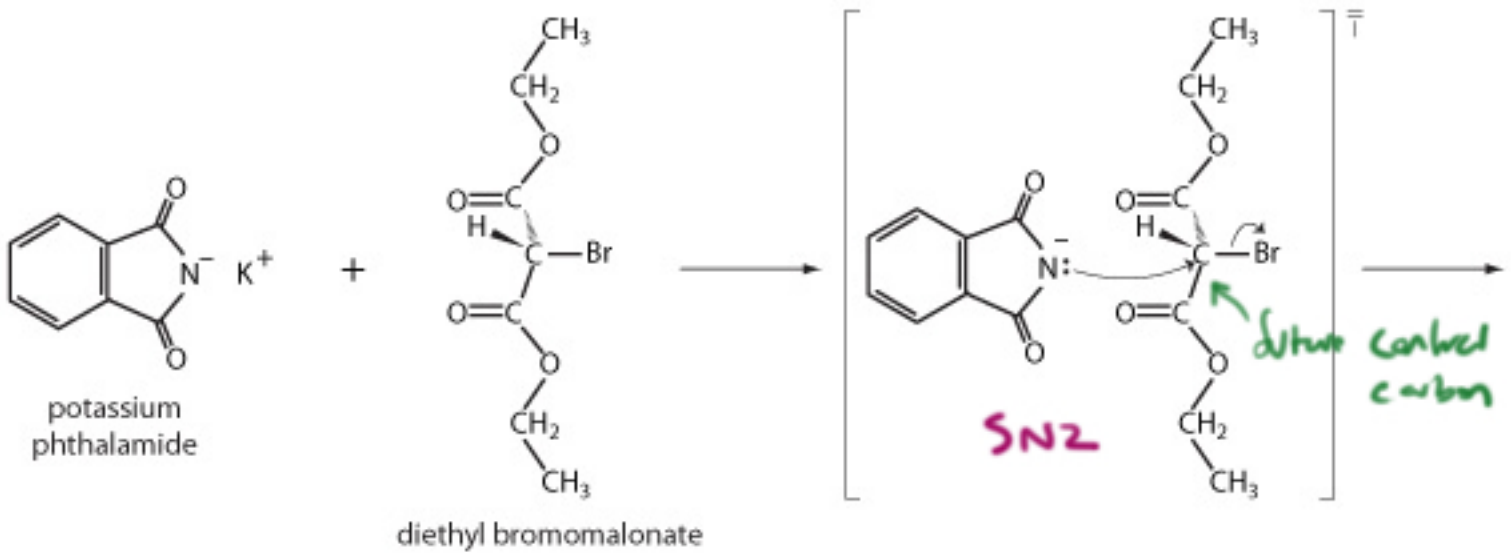
↑
start codon
is the methionine codon



- nonpolar
- hydrophobic

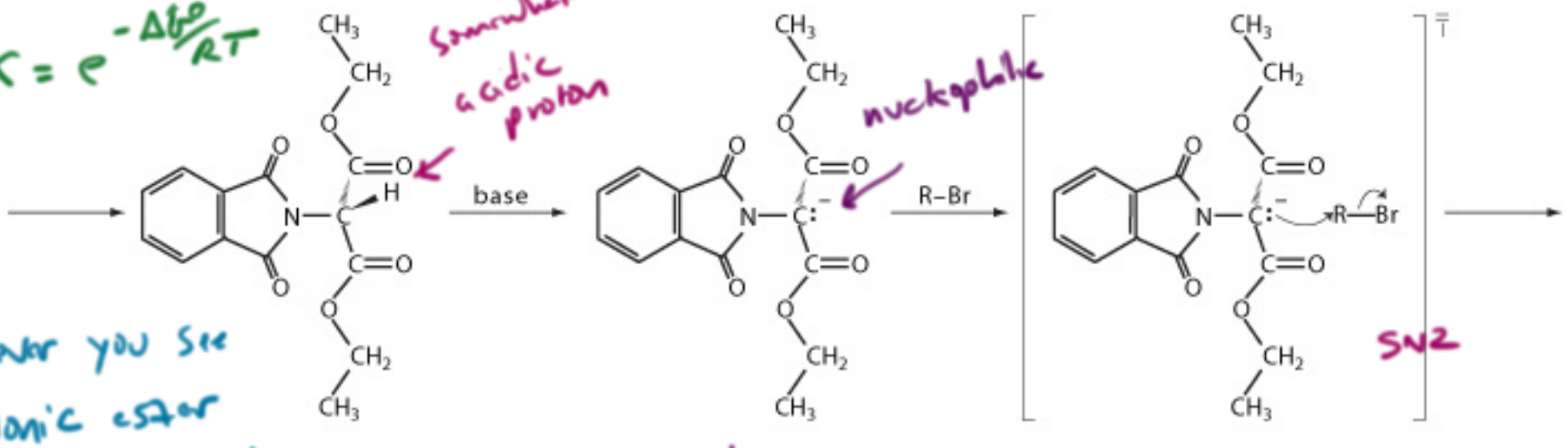

S-adenosyl methionine (methyl donor)
methionine
adenosine
SN2 substitution
Asp
DNA
DNA methylation
• gene silencing

Gabriel Synthesis - benchtop amino acid synthesis



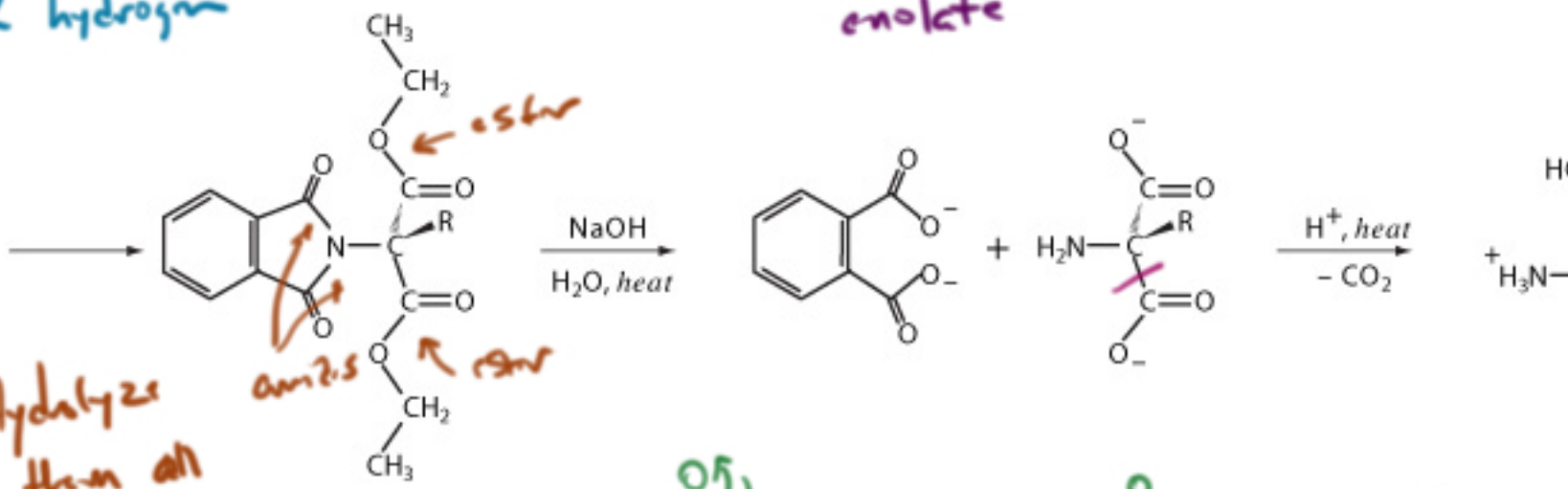
$HA \rightleftharpoons A^- + H^+$

$K = e^{-\Delta G^\circ / RT}$



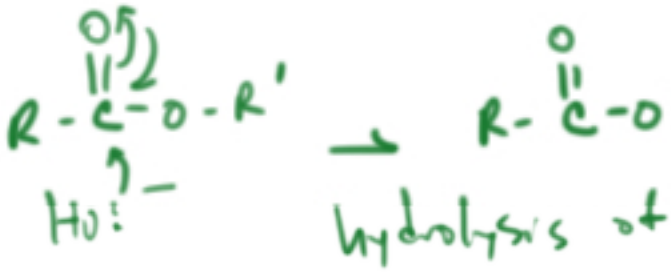
whenever you see malonic ester you have a great α hydrogen

malonic ester enolate



racemic

Hydrolyze them all



hydrolysis of ester

nucleophilic acyl substitution

Strecker Synthesis