Biochemistry and
Microbial Physiology
2024-2025

University of Basrah
College of Veterinary Medicine
Department of Microbiology

Amino Acids, Polypeptides

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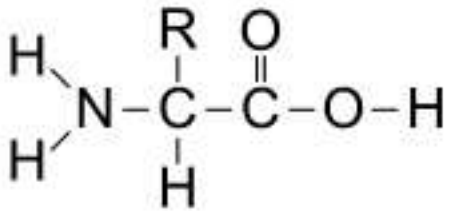
Amino Acids

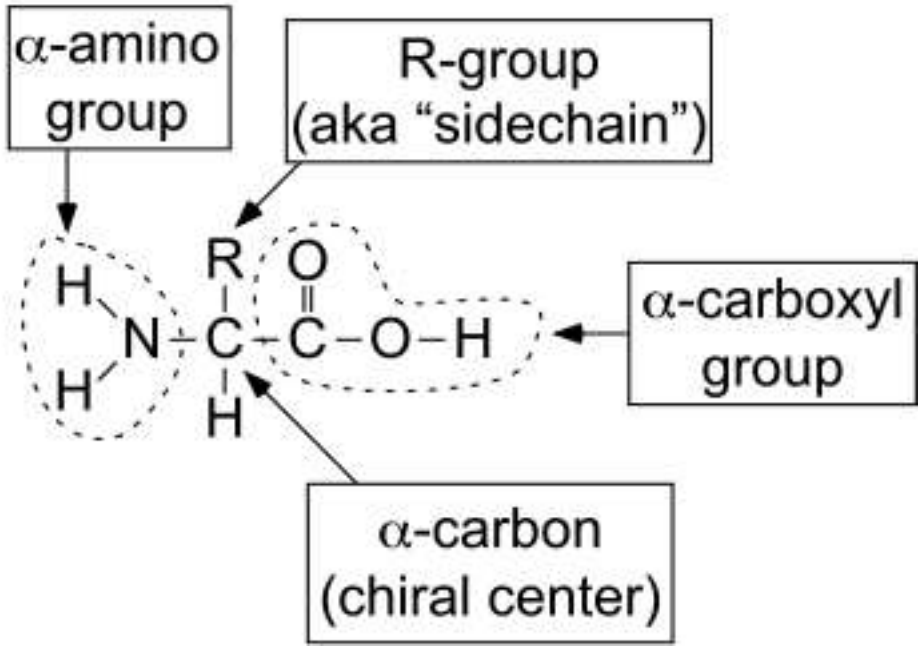
- An amino acid is a molecule that contains a carboxyl (–COOH) and an amino group (–NH2) attached to the same carbon atom, the α-carbon.
- The identity of the amino acid is determined by its side chain or side residue, often called the R-group.
- The simplest amino acid is glycine, where the residue is a single hydrogen atom. Other amino acids carry more complex side chains.
- The side chain determines the chemical properties of the amino acid. For example, it may attract or repel water (hydrophilic or hydrophobic), carry a negative charge (acidic), or form hydrogen bonds (polar).

Anatomy of an amino acid

General amino acid structure

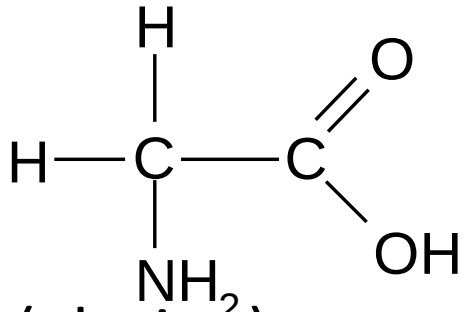


Chemical anatomy of an amino acid

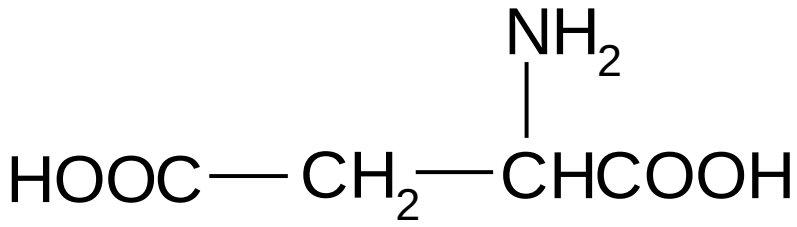


α-Amino acids

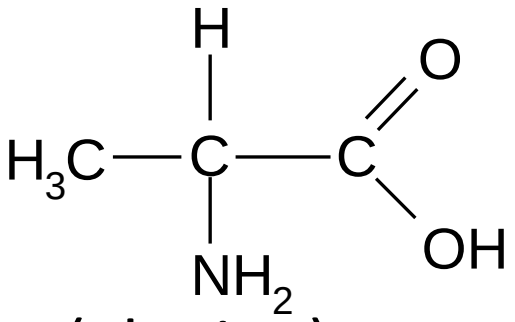
A.Example



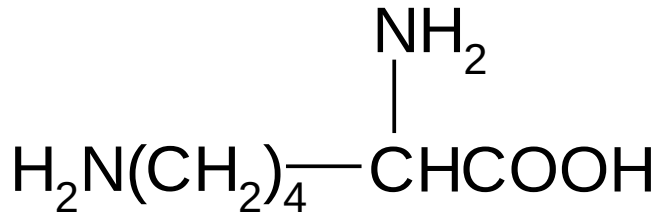
(glycine)



(aspartic acid)



(alanine)

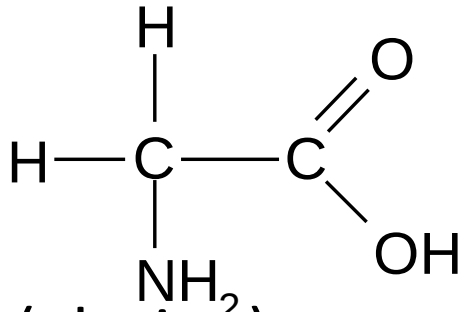


(lysine)

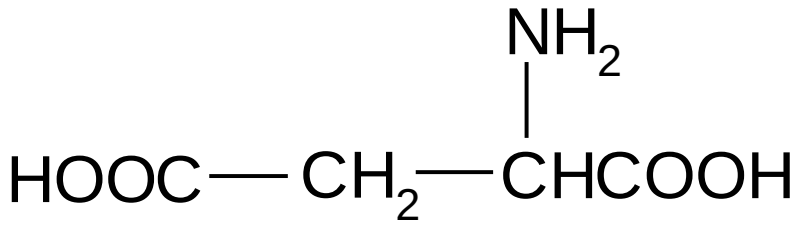
All known amino acids, 20 are used to create proteins in eukaryotes (the genetic code encodes only 20 of these).
Amino acids are abbreviated using a three letter (e.g., Gly, Val, Pro) or one letter code (e.g., G, V, P).
The linear chain of amino acid residues forms the backbone of the protein. The free amino group at one end is called the N-terminus, while the free carboxyl group on the other end constitutes the C-terminus.
The chemical properties of the side chains heavily determine the final structure of the protein as they interact with each other and with polar water molecules.

α-Amino acids

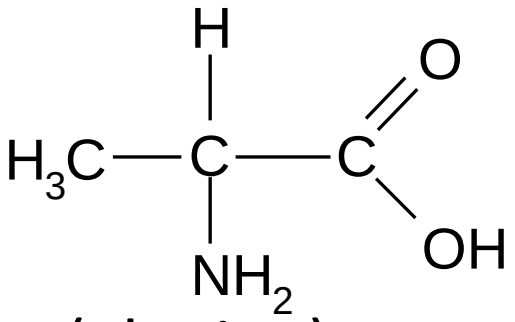
A.Example



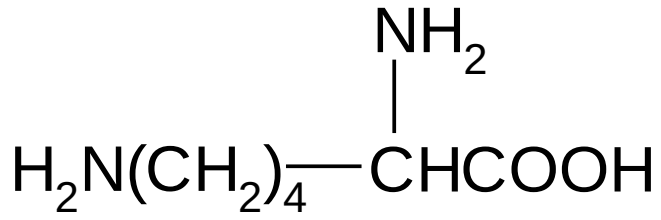
(glycine)



(aspartic acid)



(alanine)

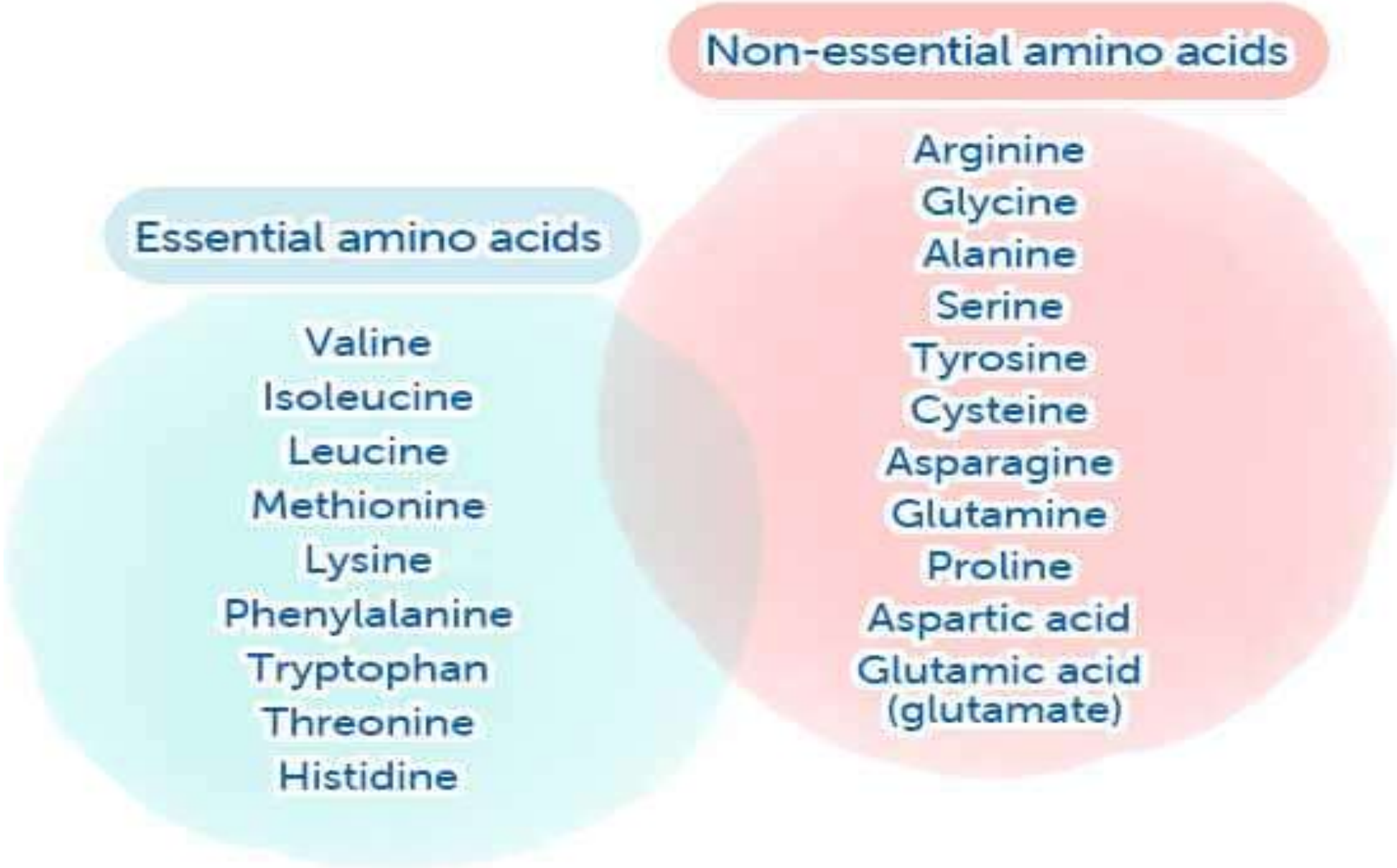


(lysine)

- Amino acids have both a basic and an acidic group. They can, therefore, act as a base (hydrogen ion recipient) or as an acid (hydrogen ion donor).
- The chemical property depends on the pH of the surrounding medium. At low pH (e.g., pH2) both the carboxyl and amino groups are protonated (–NH_3, –COOH), so the amino acid acts as a base.
- At an alkaline pH (e.g., pH13), both the carboxyl and amino groups are deprotonated (–NH_2, –COO^-) and the amino acid will act as an acid.

At a neutral pH (i.e., most physiological environments, ~pH7.4), the amino group is protonated (–NH3) and the carboxyl group is deprotonated (–COO-), giving rise to a zwitterion, a molecule with both a positive and negative charge.

These chemical properties at physiological pH are essential to creating hydrogen bonds, which in turn contribute to the formation of more complex protein structures.


Non-essential amino acids
Arginine
Glycine
Alanine
Serine
Tyrosine
Cysteine
Asparagine
Glutamine
Proline
Aspartic acid
Glutamic acid
(glutamate)
Essential amino acids
Valine
Isoleucine
Leucine
Methionine
Lysine
Phenylalanine
Tryptophan
Threonine
Histidine

Amino acids help:

- Break down food.
- Grow and repair body tissue.
- Make hormones and brain chemicals (neurotransmitters).
- Provide an energy source.
- Maintain healthy skin, hair and nails.
- Build muscle.
- Boost your immune system.
- Sustain a normal digestive system.

TWENTY-ONE PROTEINOGENIC α-AMINO ACIDS

Side chain charge at physiological pH 7.4

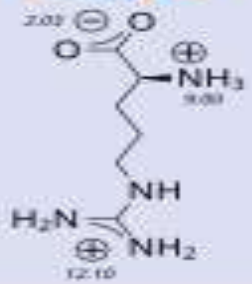
pK_a values shown italicized

⊕ Positive
⊖ Negative

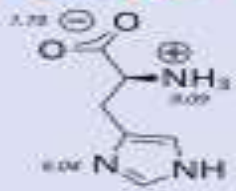
A. Amino Acids with Electrically Charged Side Chains

Positive

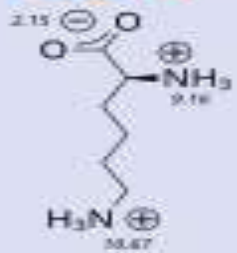
Arginine Arg R



Histidine His H

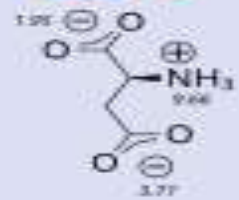


Lysine Lys K

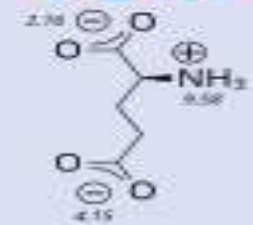


Negative

Aspartic Acid Asp D

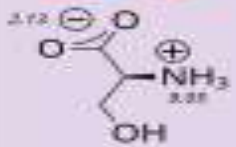


Glutamic Acid Glu E

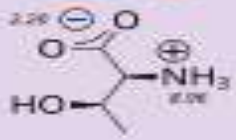


B. Amino Acids with Polar Uncharged Side Chains

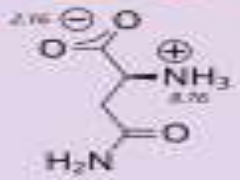
Serine Ser S



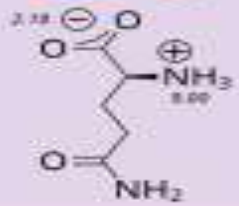
Threonine Thr T



Asparagine Asn N

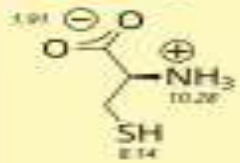


Glutamine Gln Q

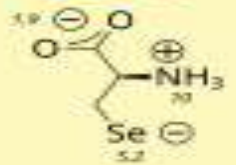


C. Special Cases

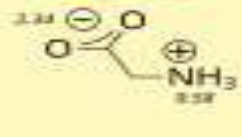
Cysteine Cys C



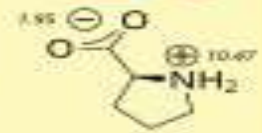
Selenocysteine Sec U



Glycine Gly G

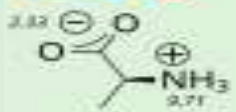


Proline Pro P

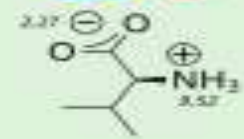


D. Amino Acids with Hydrophobic Side Chains

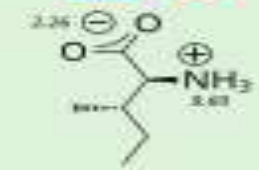
Alanine Ala A



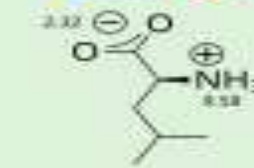
Valine Val V



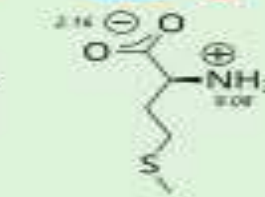
Isoleucine Ile I



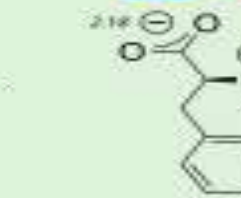
Leucine Leu L



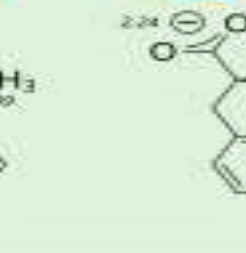
Methionine Met M



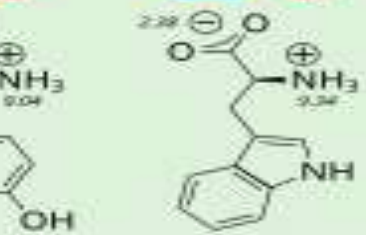
Phenylalanine Phe F



Tyrosine Tyr Y



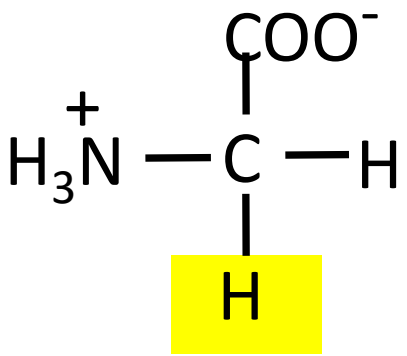
Tryptophan Trp W



Amino acids

- **Polar, uncharged amino acids**
  - Contain R-groups that can form hydrogen bonds with water
  - Includes amino acids with alcohols in R-groups (Ser, Thr, Tyr)
  - Amide groups: Asn and Gln
  - Usually more soluble in water
    - Exception is Tyr (most insoluble at 0.453 g/L at 25 °C)
  - Sulfhydryl group: Cys
    - Cys can form a disulfide bond (2 cys*teines* can make one cys*tine*)

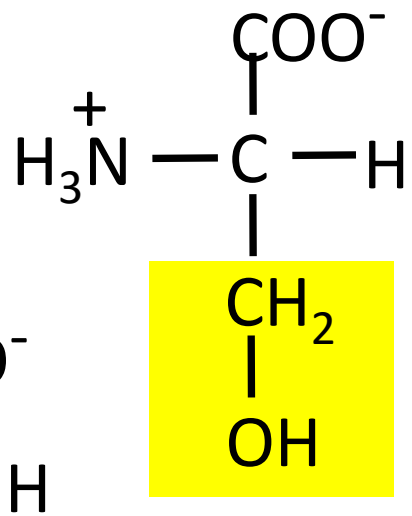
Uncharged polar side chains



Glycine

Gly

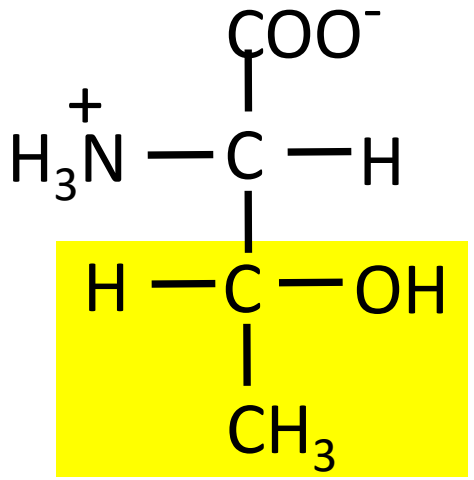
G



Serine

Ser

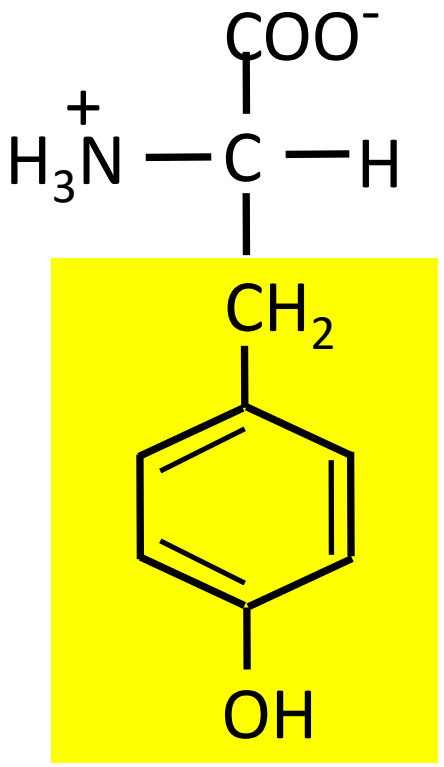
S



Threonine

Thr

T



Tyrosine

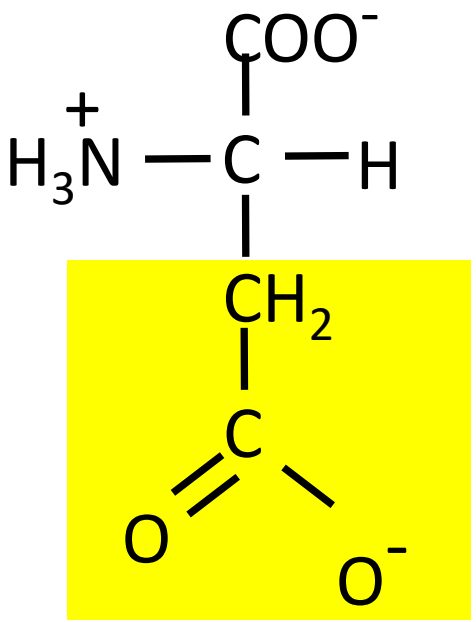
Tyr

Y

Amino acids

- **Acidic amino acids**
  - Amino acids in which R-group contains a carboxyl group
  - Asp and Glu
  - Have a net negative charge at pH 7 (negatively charged pH > 3)
  - Negative charges play important roles
    - **Metal-binding sites**
    - **Carboxyl groups may act as nucleophiles in enzymatic interactions**
    - **Electrostatic bonding interactions**

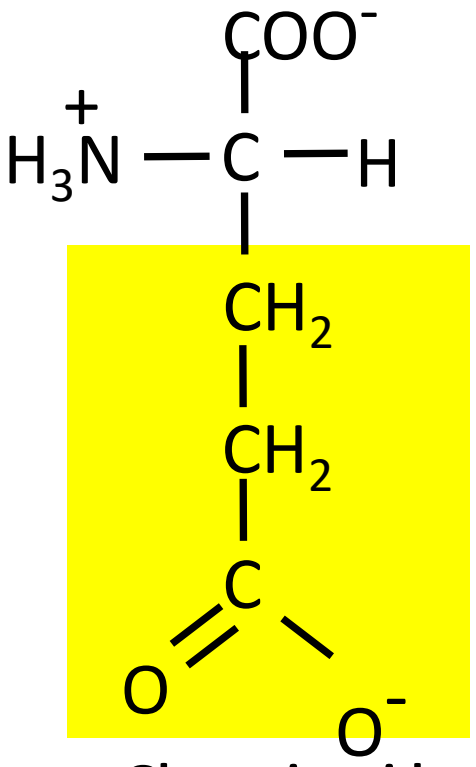
Charged polar (acidic) side chains



Aspartic acid

Asp

D



Glutamic acid

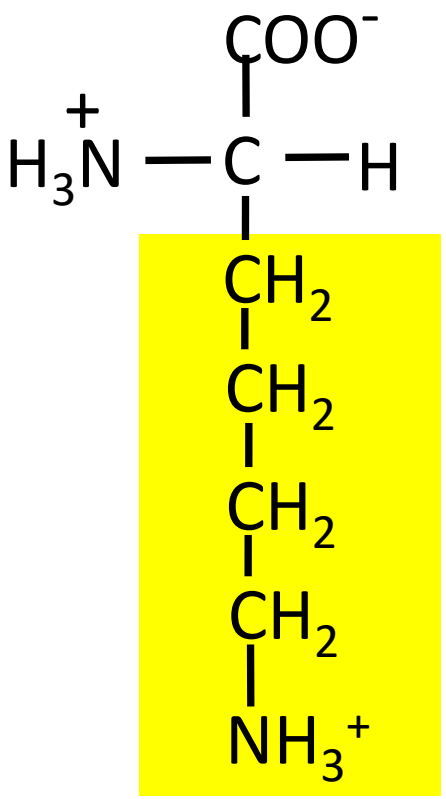
Glu

E

Amino acids

- **Basic amino acids**
  - Amino acids in which R-group have net positive charges at pH 7
  - His, Lys, and Arg
  - Lys and Arg are fully protonated at pH 7
    - Participate in electrostatic interactions
  - His has a side chain pK_a of 6.0 and is only 10% protonated at pH 7
  - Because His has a pK_a near neutral, it plays important roles as a proton donor or acceptor in many enzymes.
  - His containing peptides are important biological buffers

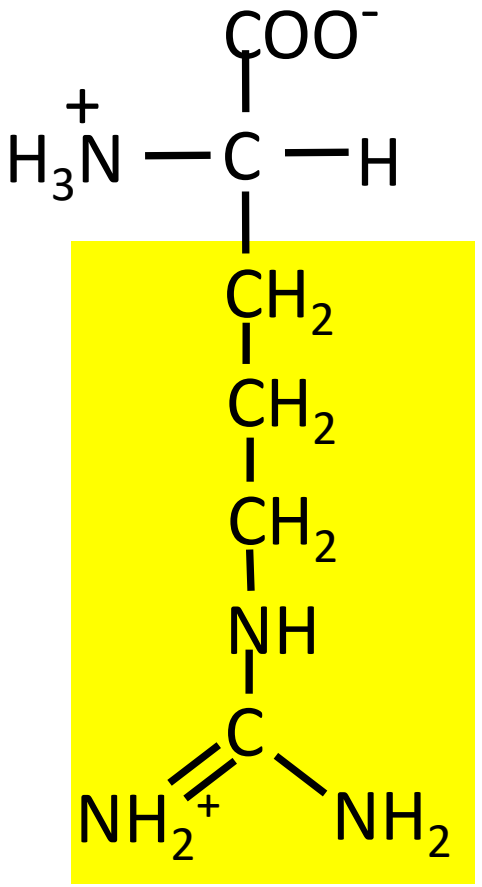
Charged polar (basic) side chains



Lysine

Lys

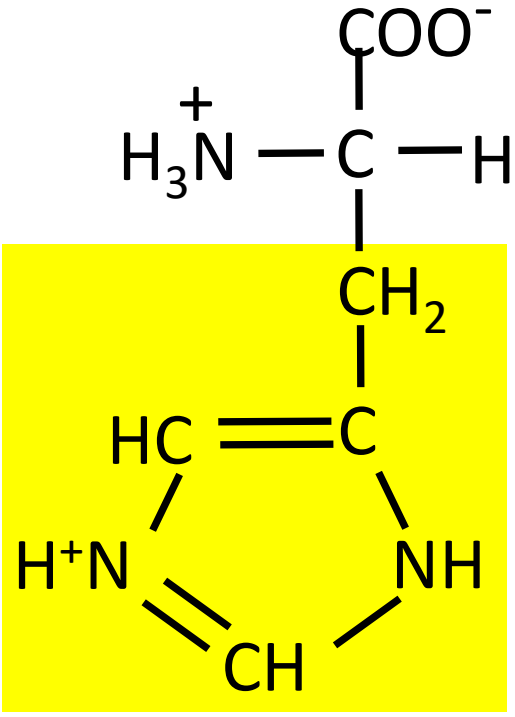
K



Arginine

Arg

R

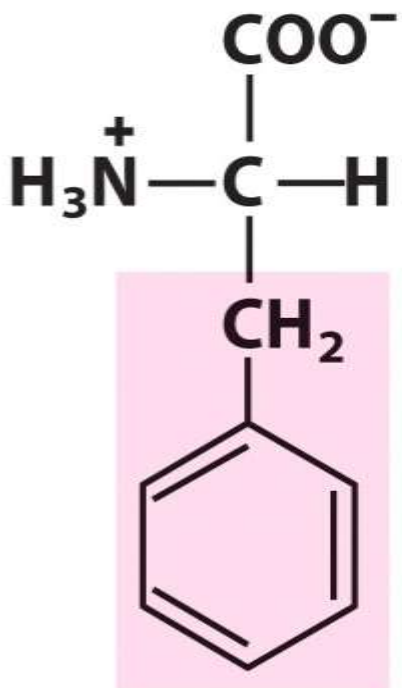


Histidine

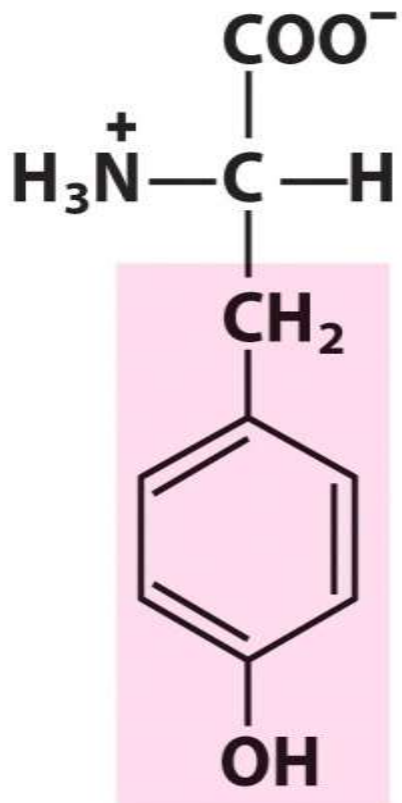
His

H

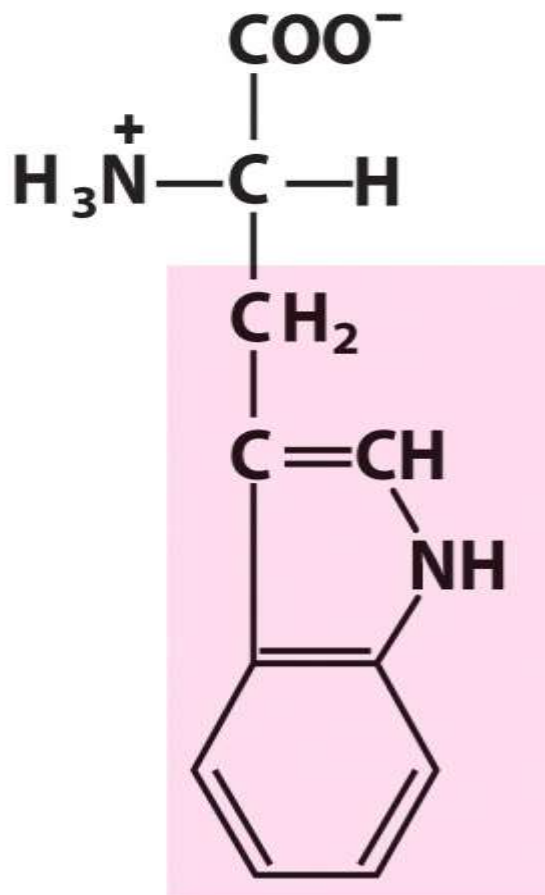
Aromatic R groups



Phenylalanine

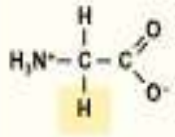


Tyrosine

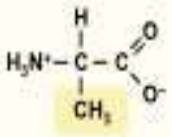


Tryptophan

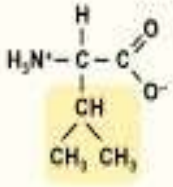
NON-POLAR



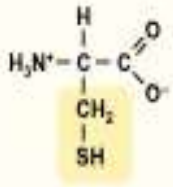
Glycine
(Gly / G)



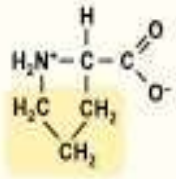
Alanine
(Ala / A)



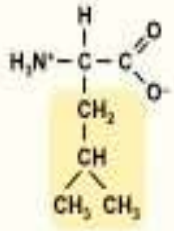
Valine
(Val / V)



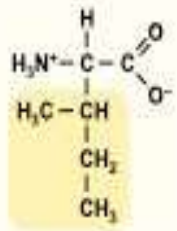
Cysteine
(Cys / C)



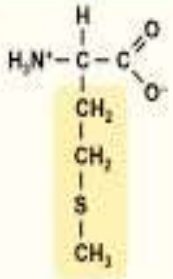
Proline
(Pro / P)



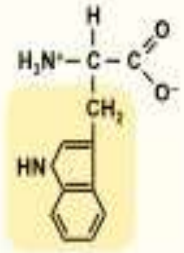
Leucine
(Leu / L)



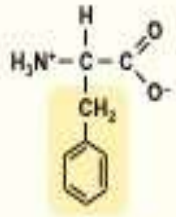
Isoleucine
(Ile / I)



Methionine
(Met / M)

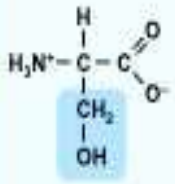


Tryptophan
(Trp / W)

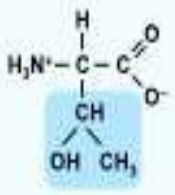


Phenylalanine
(Phe / F)

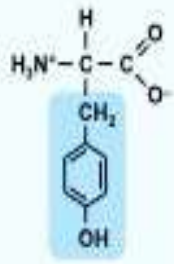
POLAR



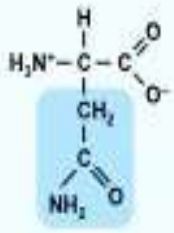
Serine
(Ser / S)



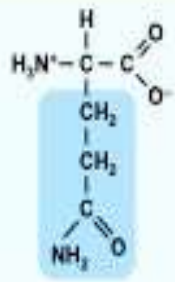
Threonine
(Thr / T)



Tyrosine
(Tyr / Y)

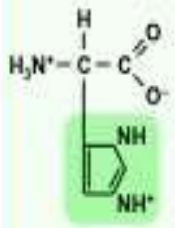


Asparagine
(Asn / N)

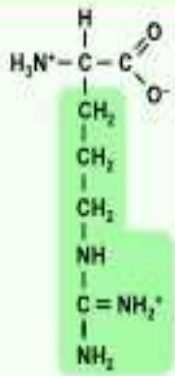


Glutamine
(Gln / Q)

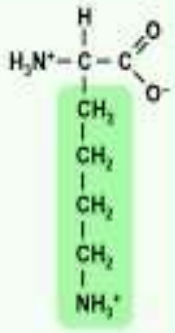
POSITIVE



Histidine
(His / H)

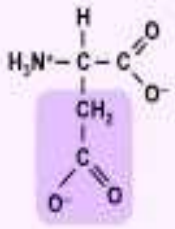


Arginine
(Arg / R)

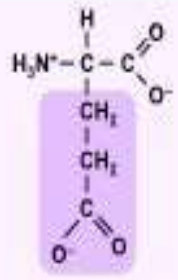


Lysine
(Lys / K)

NEGATIVE



Aspartic Acid
(Asp / D)

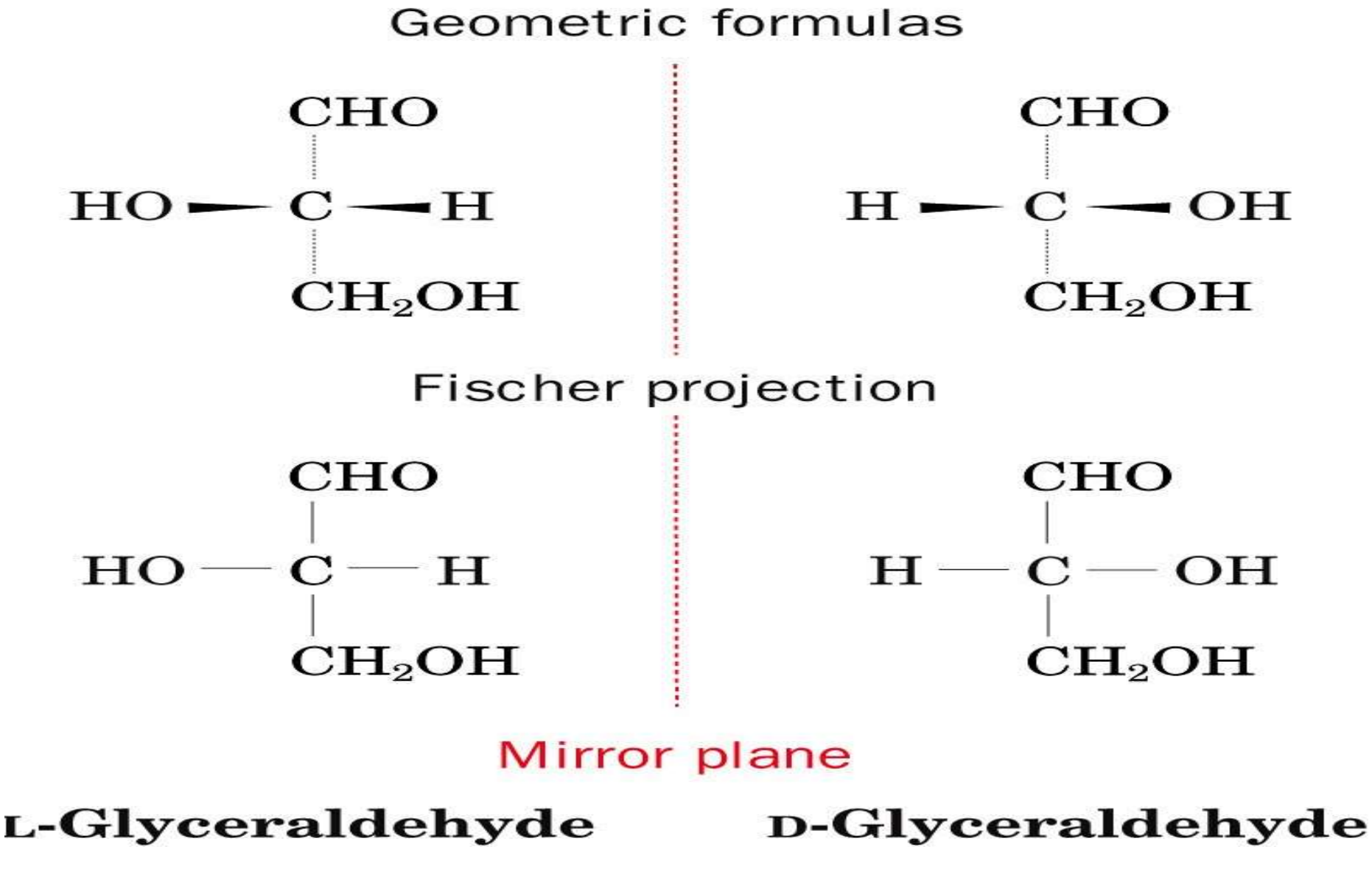


Glutamic Acid
(Glu / E)

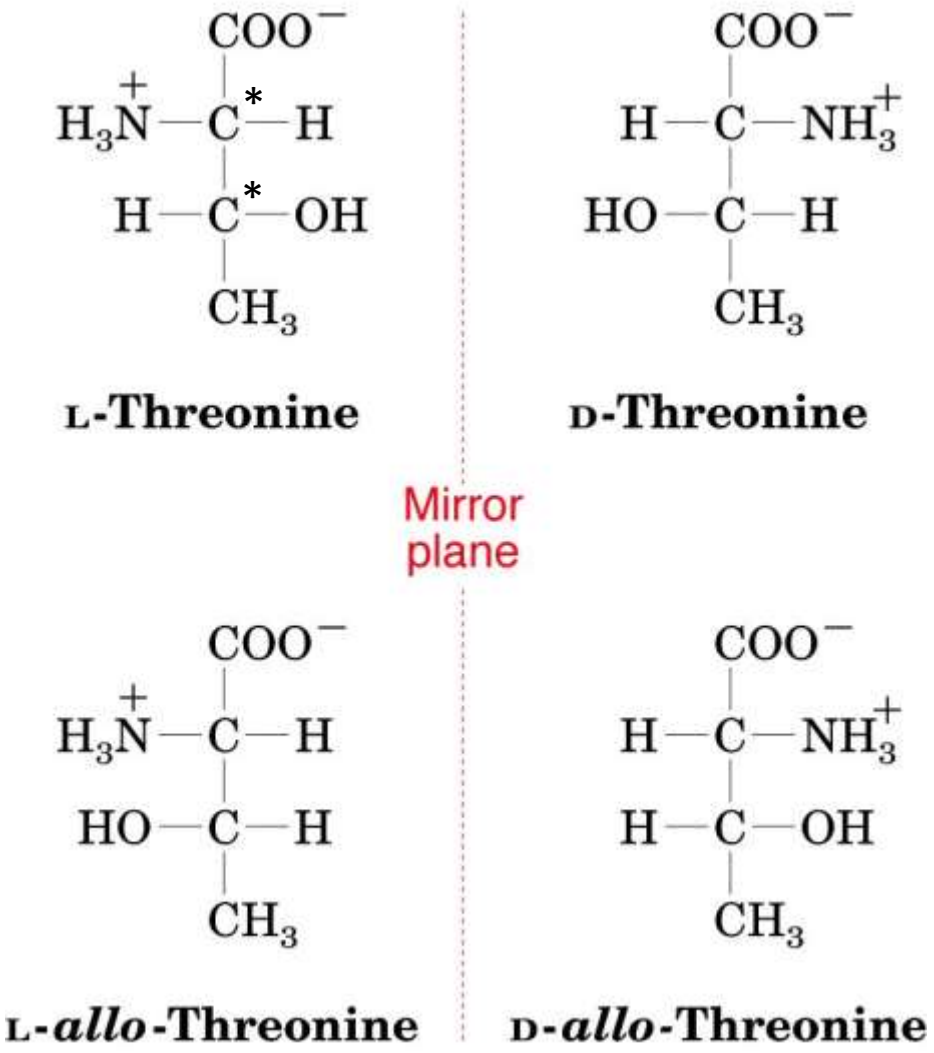
Nonstandard amino acids

- **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, etc.
- Nonstandard amino acids are usually the result of modification of a standard amino acid after a polypeptide has been synthesized.

Asymmetry


Geometric formulas
CHO
HO
C
H
CH2OH
CHO
H
C
OH
CH2OH
Fischer projection
CHO
HO
C
H
CH2OH
CHO
H
C
OH
CH2OH
Mirror plane
L-Glyceraldehyde
D-Glyceraldehyde

Diastereomers

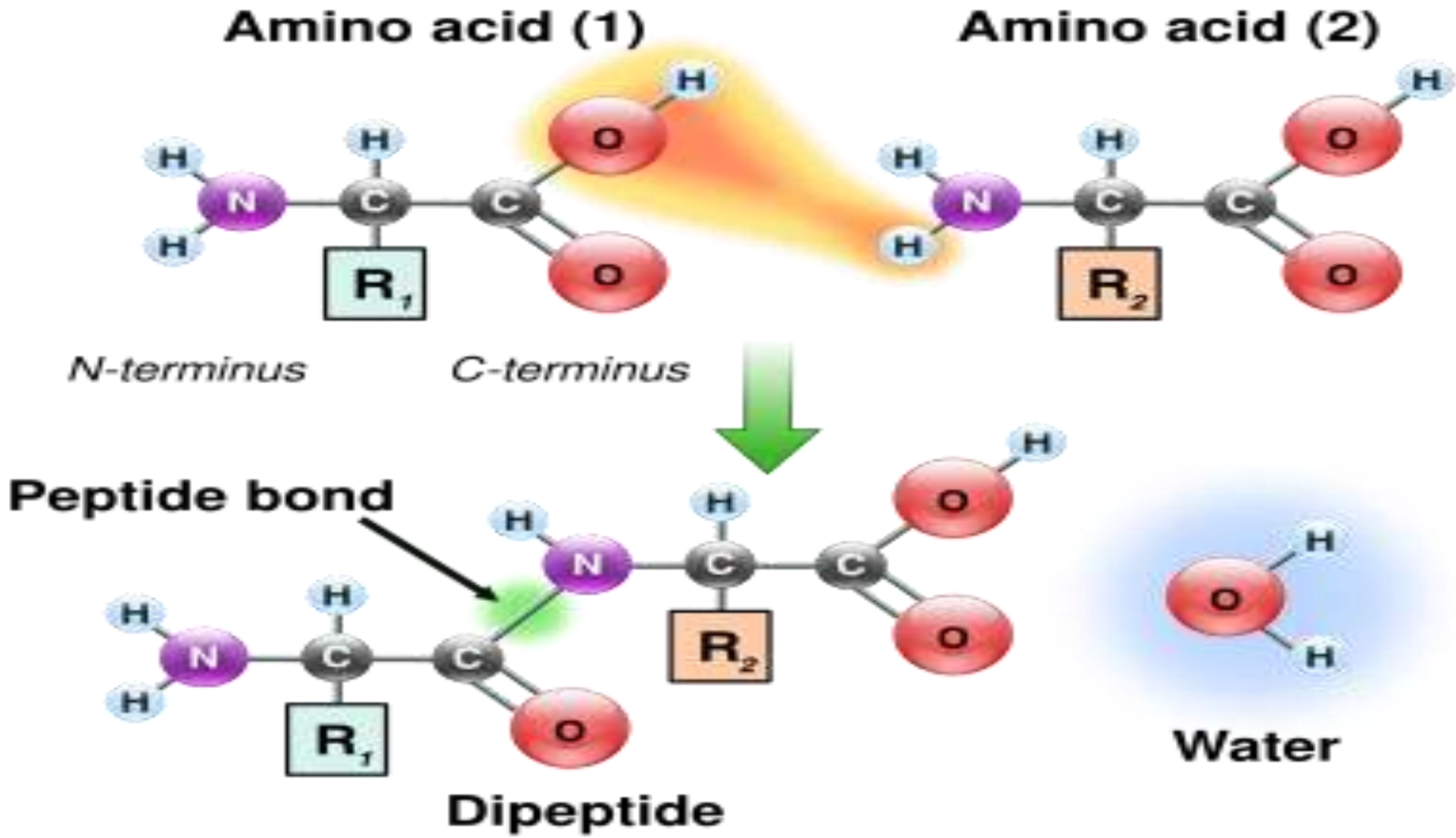


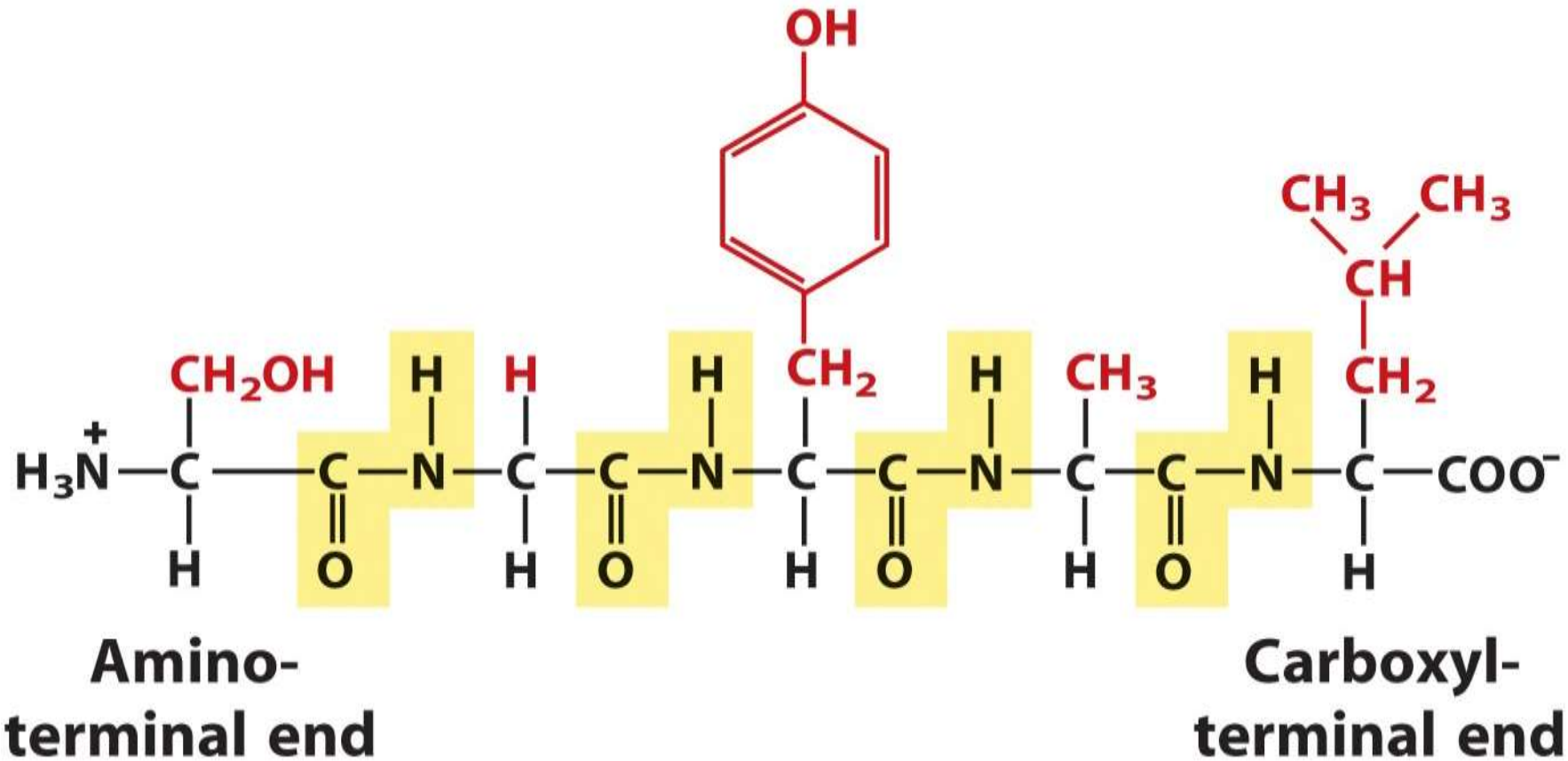
Amino Acids Are Joined By Peptide Bonds In Peptides

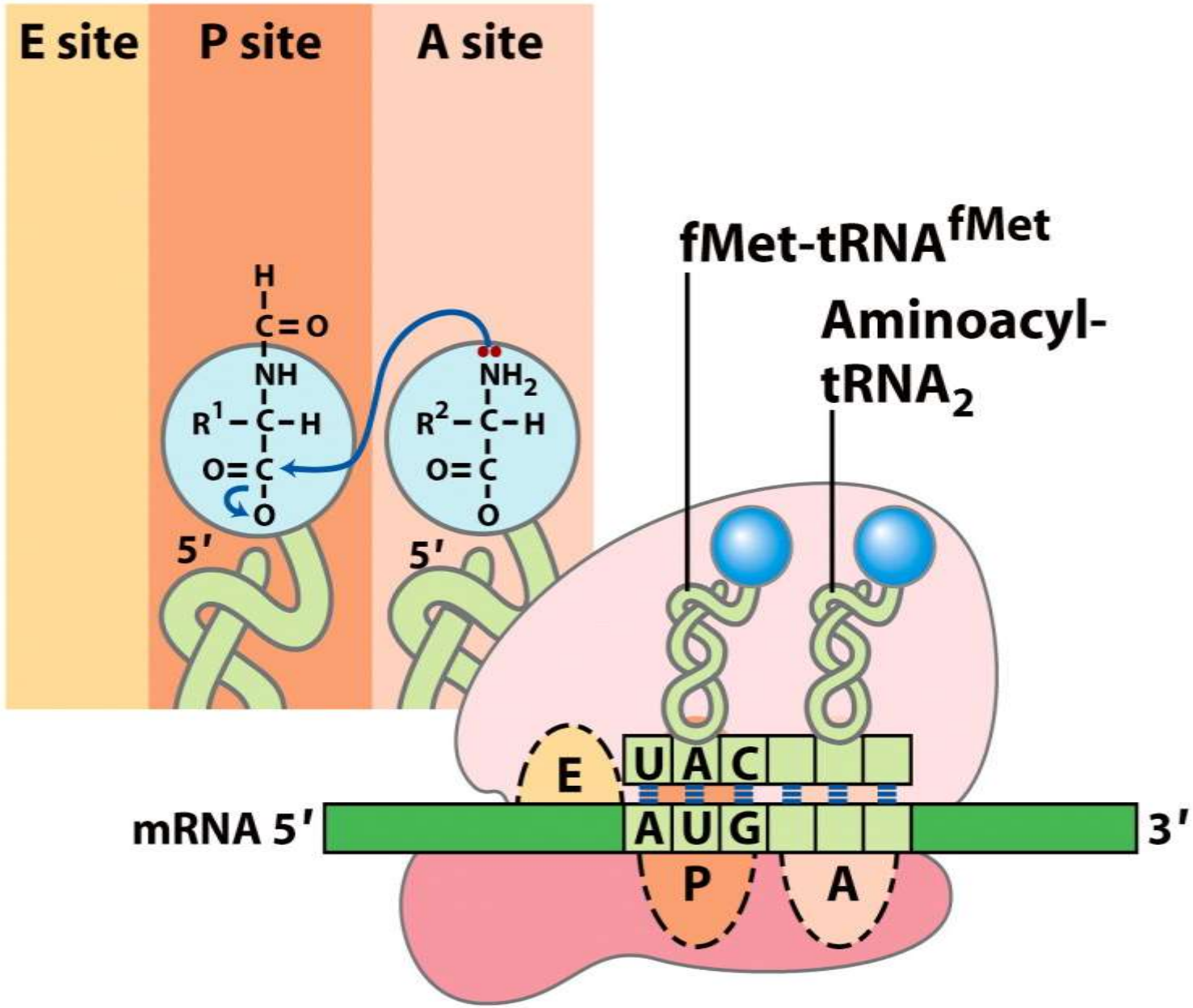
- α-carboxyl of one amino acid is joined to α-amino of a second amino acid (with removal of water)
- only α-carboxyl and α-amino groups are used, not R-group carboxyl or amino groups

Peptides

Peptides are short chains of amino acids that have been linked by amide (or peptide), bonds. While the term “peptide” generally refers to a compound made up of two or more amino acids, peptides can be further classified as either oligopeptides or polypeptides. Oligo-, meaning “few”, describes peptides that contain generally fewer than 20 amino acids. Poly- , meaning “many” peptides, on the other hand, are composed of between 20 and 50 amino acids. Peptides are defined by their amino acid sequence, which is simply the order in which the different building blocks occur in the peptide, starting from the first (N-terminal) amino acid, to the last (C-terminal) amino acid.


Amino acid (1)
Amino acid (2)
N-terminus
C-terminus
Peptide bond
Dipeptide
Water


OH
CH3 CH3
CH
CH2OH
H
H
H
CH2
H
CH3
H
CH2
H3N+
C
C
N
C
C
N
C
C
N
C
C
N
C
COO-
H
O
H
O
H
O
H
O
H
Amino-
terminal end
Carboxyl-
terminal end


E site
P site
A site
fMet-tRNA fMet
Aminoacyl-
tRNA2
H
C=O
NH
R1–C–H
O=C
O
NH2
R2–C–H
O=C
O
5′
5′
E
U A C
A U G
mRNA 5′
3′
P
A

Hydrolysis of polypeptides & amino acid analysis

- Polypeptides can be hydrolyzed to constituent amino acids.
- This is typically done by *boiling* the polypeptide in 6 M HCl for 24 hours.

$^{+}H_3N\text{-}CHR\text{-}CONH\text{-}CHR\text{-}CONH\text{-}CHR\text{-}CO_2^{-}$

$+ 2\ H_2O \rightarrow 3\ {}^{+}H_3N\text{-}CHR\text{-}CO_2^{-}$

Disulfide bonds

2 cysteine $\rightarrow$ cystine

2 R-SH $\rightarrow$ R-S-S-R (Note: This is an **oxidation**)

- Intracellular conditions are maintained sufficiently reducing to inhibit formation of most disulfide bonds.
- Extracellular conditions (as well as those found in some organelles) are more oxidizing, favoring disulfide formation.
- Thus, extracellular proteins containing cysteine often have disulfides, while intracellular (cytosolic) proteins rarely have disulfides.

Reactions with amino acids:

I. Amino group

1. Acylation $\rightarrow$ R-(C=O)-NH-R'
2. Ninhydrin reaction

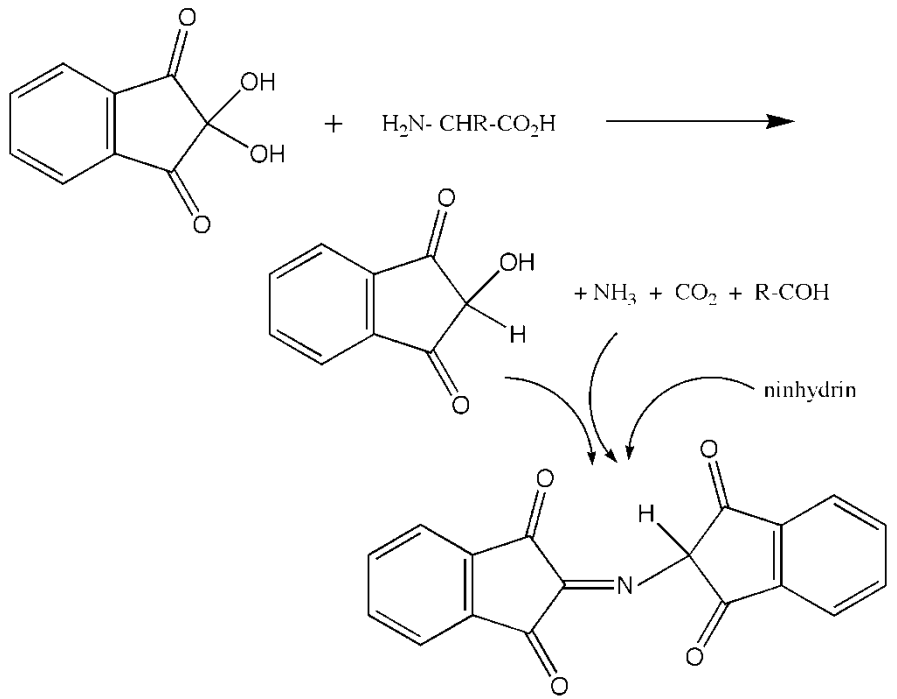
   Causes oxidative decarboxylation of α-amino acids, and release of ammonia, which reacts with a second molecule of ninhydrin to form a purple product.

   (You don't need to know details – just know that it reacts with any free amino group and the final product is purple.)

Reactions with amino acids:

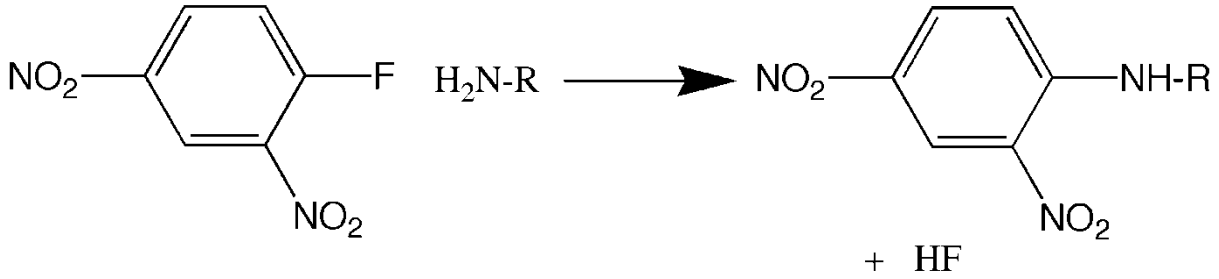
I. Amino group

Ninhydrin reaction

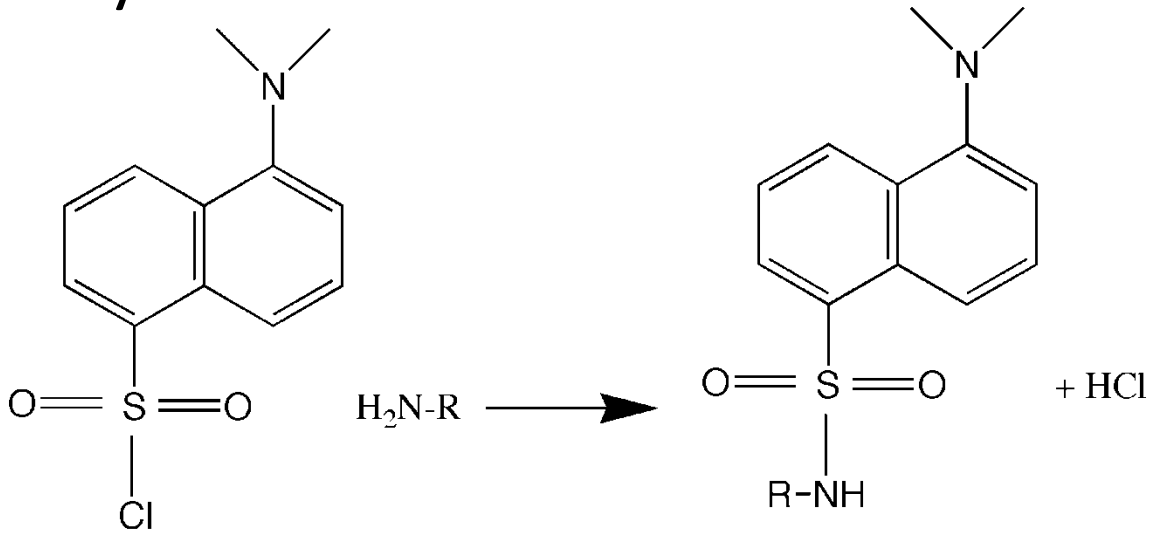


Reactions with amino acids:

3. Fluorodinitrobenzene reaction



4. Dansyl chloride reaction



Reactions with amino acids:

II Carboxyl group

1. Amide formation
2. Ester formation
3. Acyl halide formation
4. Reduction to alcohol (via aldehyde)