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Protein Biochemistry (BCH 303)

Chapter 2

Peptides

PEPTIDES

Peptides Are Chains of Amino Acids:

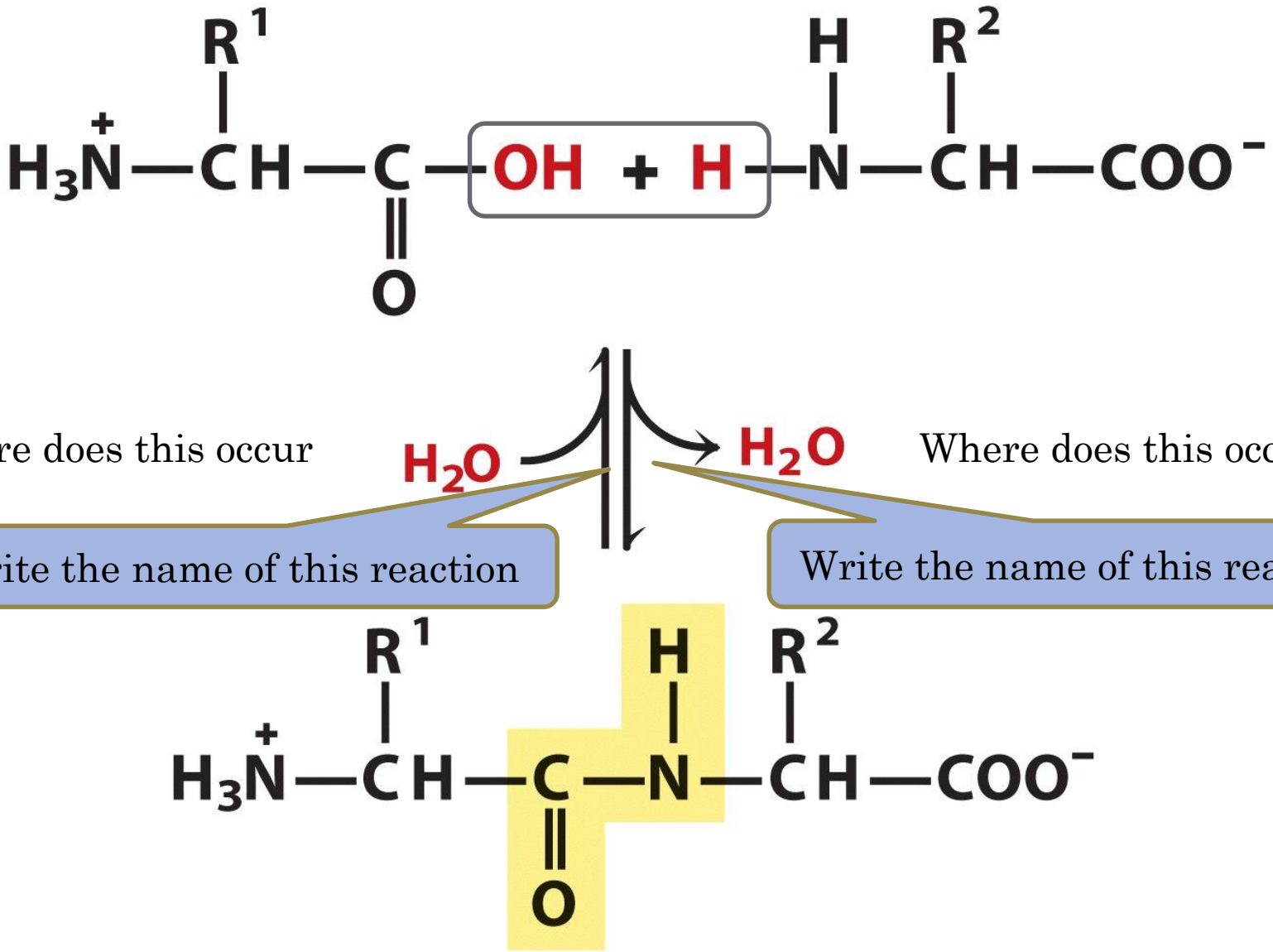
Two amino acid molecules can be covalently joined through a substituted amide linkage, termed a **peptide bond**, to yield a dipeptide.

Such a linkage is formed by removal of the elements of water (dehydration) from the -carboxyl group of one amino acid and the –amino group of another.

Biologically occurring polypeptides range in size from small to very large number of amino acid residues.

Do you remember the meaning of residue?

Peptide Bond Formation



- Three amino acids can be joined by two peptide bonds to form a tripeptide.
- Similarly we have tetrapeptides and pentapeptides.
- The number of peptide bonds is n-1 the number of amino acids.
- When there are many amino acids joined in the same way the structure is called a polypeptide.

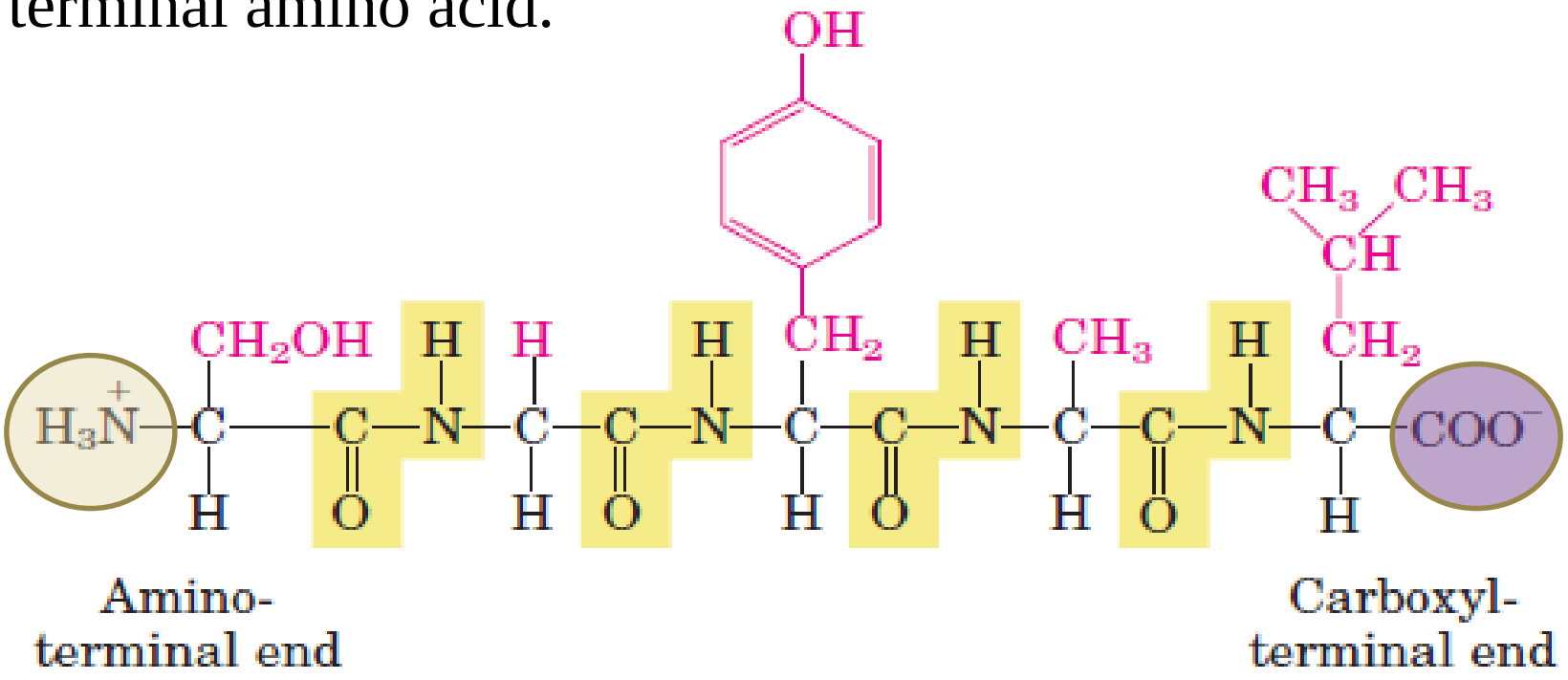
- Each peptide or protein have two terminals.
- It starts from the left and designated the amino terminal (N-terminal) and terminates in the right and designated carboxy terminal (C-terminal).

- Peptides contain only one free α-amino group and one free α-carboxyl group at their terminal residues. So, it is unbranched.

Naming peptides: start at the N-terminus

- **Using full amino acid names**
  - **Serylglycyltyrosylalanylleucine**
- **Using the three-letter code abbreviation**
  - **Ser-Gly-Tyr-Ala-Leu**
- **For longer peptides (like proteins) the one-letter code can be used**
  - **SGYAL**

- Peptides are named from the sequence of their constituent amino acids beginning from the N-terminal residue.
- In a polypeptide, all amino acid residues have their suffixes (-ine, -an, -ic, or -ate) changed to -yl, with the exception of the C-terminal amino acid.



So, the pentapeptide shown above is called serylglycyltyrosylalanylleucine, or Ser–Gly–Tyr–Ala–Leu. The peptide bonds are shaded in yellow; the R groups are in red.

The rule of thumb

Each amino acid has its characteristic molecular weight because the differences in the size of the R group.
The highest molecular weight is of tryptophan and the smallest is of glycine.

The average molecular weight is 130 Da but when we calculate the molecular weight of peptide we consider each amino acid molecular weight to be 110 Da.
Do you know why?
Because of the each peptide bond is formed by elimination H_2O (Mwt 18)

Amino acid	Mr
L	131.17
A	89.09
G	75.07
V	117.15
E	147.13
S	105.09
I	131.17
K	146.19
R	174.20
D	133.10
T	119.12
P	115.13
N	132.12
Q	146.15
F	165.19
Y	181.19
M	149.21

14. A rule of thumb for amino acid content of proteins

The simple average molecular weight of the 20 common amino acids is 138, but most biochemists use 110 when estimating the number of amino acids in a protein of known molecular weight. Why do you suppose this is? (Hint: there are two contributing factors to the answer. One of them will be apparent from a brief consideration of amino acid compositions of common proteins. See for example Figure 5.16 of this text.)

Answer: The first thing to realize is that a protein is composed of amino acid residues, not complete amino acids. When a peptide bond is formed between a carboxyl group and an amino group through a condensation reaction a water molecule is lost. Thus, the average molecular weight must be corrected for water loss (138 - 18 =) to 120. Figure 5.16 shows the frequency of amino acids in the SWISS-PROT protein knowledgebase. This information can be found at http://ca.expasy.org/sprot/relnotes/relstat.html for the 2011 release. It is clear from the data that the frequencies of finding amino acids in proteins are not all equal. Leucine, alanine, and serine are the most frequently-found amino acids whereas histidine, cysteine and tryptophan are found least frequently. Leucine is approximately 9 times more abundant in the data base than is tryptophan.

QUIZ

1-The formation of a protein or polypeptide relies on linking amino acids by way of .....

A-dehydration bonding B- hydrolysis C- hydration D- non-polar covalent

2-The type of bond that forms between amino acids in order to eventually form a protein is called a....

A-glycosidic linkage B- hydrogen bond C- ionic bond D- peptide bond

3-The peptide bond in protein is formed between .....

A-R-groups of two amino acids B- Two carboxylic group protein

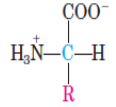
C-Two amino group D- One amino and one carboxyl group

4-The bonding of two amino acid molecules to form a larger molecule requires .....

A-the addition of a water molecule. B- the release of a water molecule.

C-the addition of a nitrogen atom D- the release of a carbon dioxide molecule.

5-In the typical amino acid shown in the figure, "R" represents.....



A- One atom of any element B-Another amino group or carboxyl group, depending on the amino acid

C-A variable group, different in each of the 20 amino acids D-none of the above.

Properties of peptides:

- Acid – base properties:

The total acid-base behavior of a peptide can be predicted from ⟹ - its single free α-amino group at the end of the chain.

- its single free α-carboxyl group at the end of the chain.

- the nature and number of its ionizing R-groups.

- Peptides have a characteristic isoelectric point (pI).

- Peptides have characteristic titration curves.

- Complex mixtures of peptides can be separated from each other by ion exchange chromatography and electrophoresis.

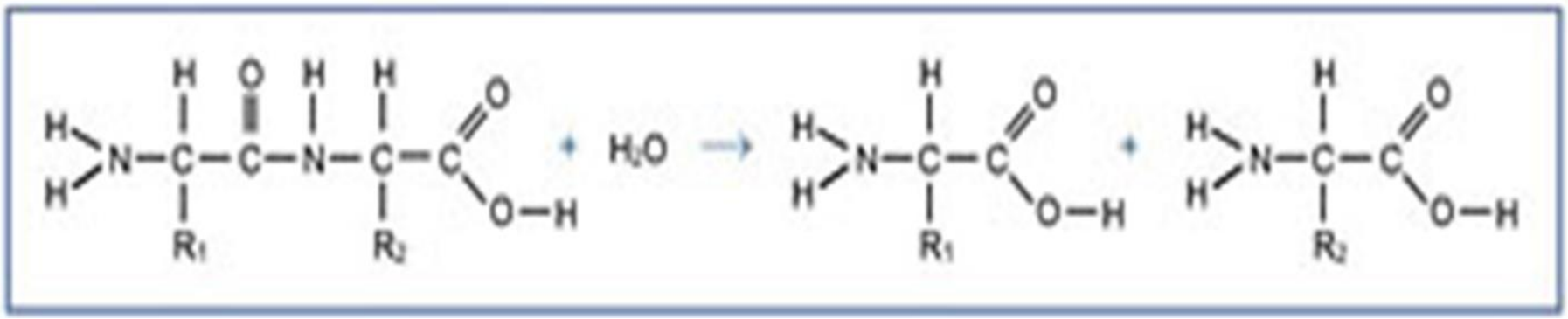
Characteristic chemical reactions of peptides

These reactions are characteristic for functional groups (free α-amino group, free α-carboxyl group, R-groups).

1- Hydrolysis

a- chemical hydrolysis

The peptide bonds can be hydrolyzed by boiling with either strong acid or base to yield the constituent amino acids in free form.

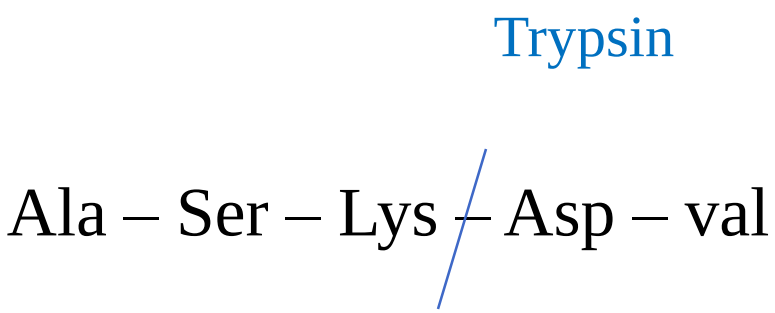


b- Enzyme hydrolysis

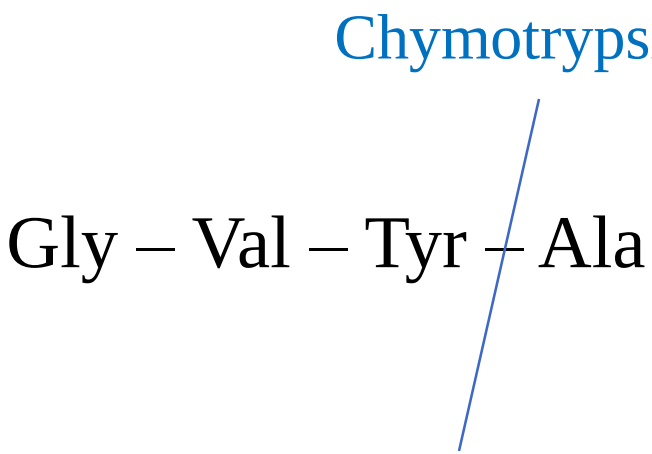
Peptide bonds can also be hydrolyzed by proteolytic enzymes secreted into the intestine for protein digestion (pepsin, trypsin and chymotrypsin).

Pepsin: is most efficient in cleaving peptide bonds between hydrophobic and preferably aromatic amino acids such as phenylalanine, tryptophan, and tyrosine.

Trypsin: cleaves the peptide bond on the carbonyl side of Arg and Lys except when either is followed by proline.



Chymotrypsin: cleaves the peptide bond on the carbonyl side of Phe, Trp, Tyr.



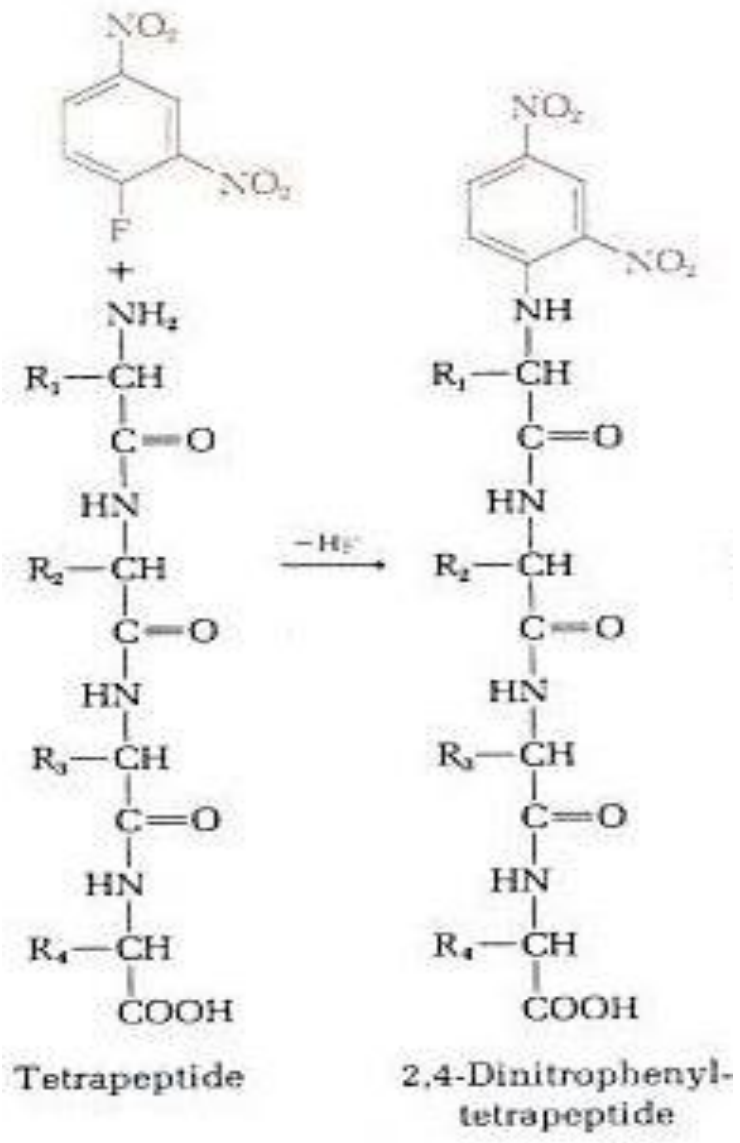
Notice; pepsin and chymotrypsin cleave the peptide bond after Phe, Trp or Tyr. What is the difference?????

Search

2- Reaction with 1-fluoro – 2,4 dinitrobenzene:

This reagent reacts with α-amino group of a free amino acid to yield a 2,4 dinitrophenyl amino acid.

- It also reacts with the α-amino group of the amino terminal residue of peptide.



Biological functions of peptides

Certain peptides have variety of biological functions:

Examples:

- **Hormones and pheromones**
  - insulin (think sugar) (2 linked polypeptides chains, resposinble for controlling blood glucose level, secreted from pancreas.
  - Oxytocin (think childbirth) (9 amino acid residues). It is secreted by the posterior pituitary and stimulates uterine contractions.
  - Calcitonin. Responsible for control of blood calcium. Secreted from thyroid gland.
  - Thyrotropin releasing factor (3 amino acid residues). It is formed in the hypothalamus and stimulates the release of another hormone, thyrotropin, from the anterior pituitary gland.
- Bradykinin (9 amino acid residues). Inhibits inflammation of tissues.

Search about more peptide hormones and pheromones

Glutathione

- add

Peptides: A Variety of Functions

- **Hormones and pheromones**
  - insulin (think sugar metabolism)
  - oxytocin (think childbirth)
  - sex-peptide (think fruit fly mating)
- **Neuropeptides**
  - substance P (pain mediator)
- **Antibiotics**
  - polymyxin B (for Gram – bacteria)
  - bacitracin (for Gram + bacteria)
- **Protection, e.g., toxins**
  - amanitin (mushrooms)
  - conotoxin (cone snails)
  - chlorotoxin (scorpions)