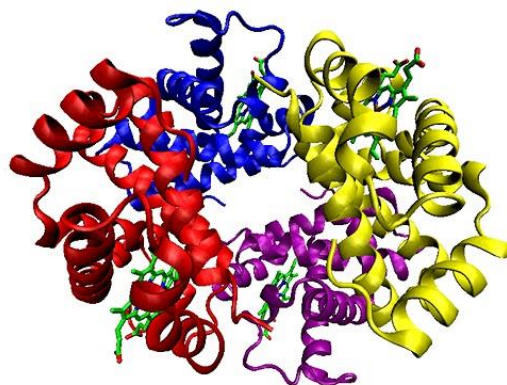


2302272 – Org Chem II – Part IV

Lecture 2

Protein-2



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Recommended Textbook:

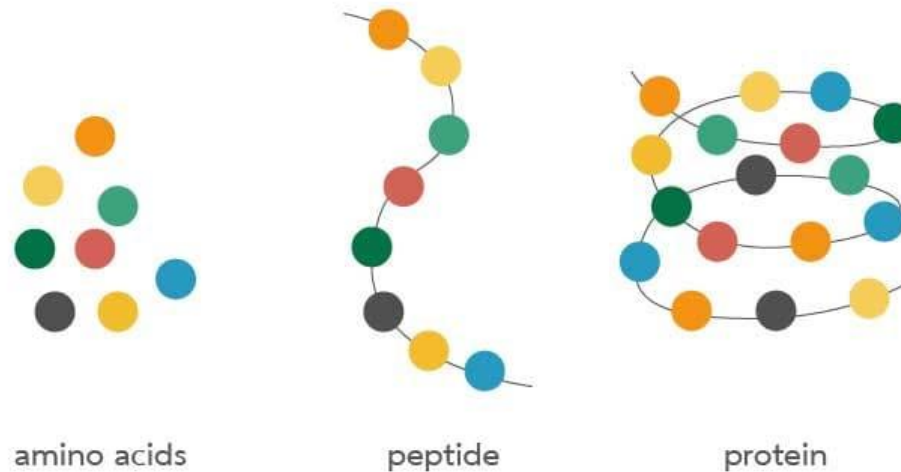
Chapter 24 in *Organic Chemistry*, 8th Edition, L. G. Wade, Jr., **2010**,
Prentice Hall (Pearson Education)

Key concepts:

- 1) Peptide คืออะไร? เกี่ยวข้องอย่างไรกับกรดอะมิโน?
- 2) พันธะ peptide คืออะไร? มีโครงสร้างและมีสมบัติอย่างไร?

Peptide bond / Amide bond

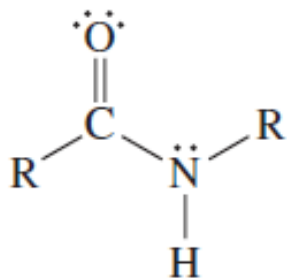
- The most important reaction of amino acids is the formation of **peptide bonds**



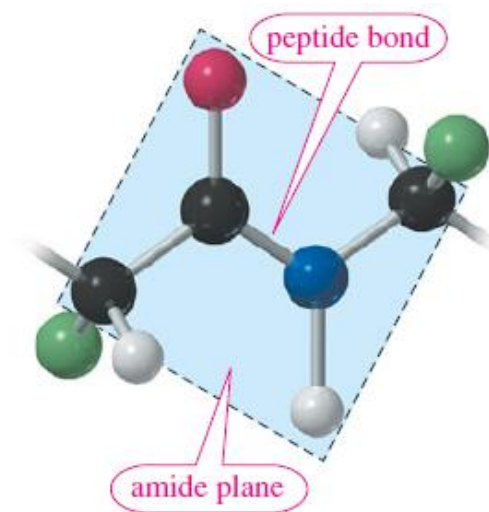
- Amines** and **acids** can condense, with the loss of water, to form **amides**

Peptide bond / Amide bond

- Amides are the **most stable** acid derivatives. This stability is partly due to the strong **resonance interaction** between the nonbonding electrons on nitrogen and the carbonyl group

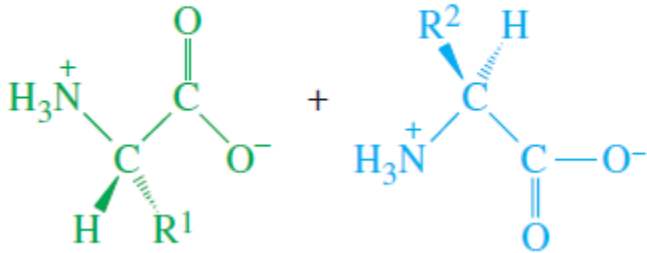


- The amide bond has **restricted rotation** because of its **partial double-bond character**; resulting in six atoms being held rather **rigidly in a plane**



Peptides

- A **peptide** is a compound containing two or more amino acids linked by amide bonds
- Under the proper conditions, the amino group of one amino acid condenses with the carboxyl group of another
- The product is an amide called a **dipeptide** because it consists of two amino acids



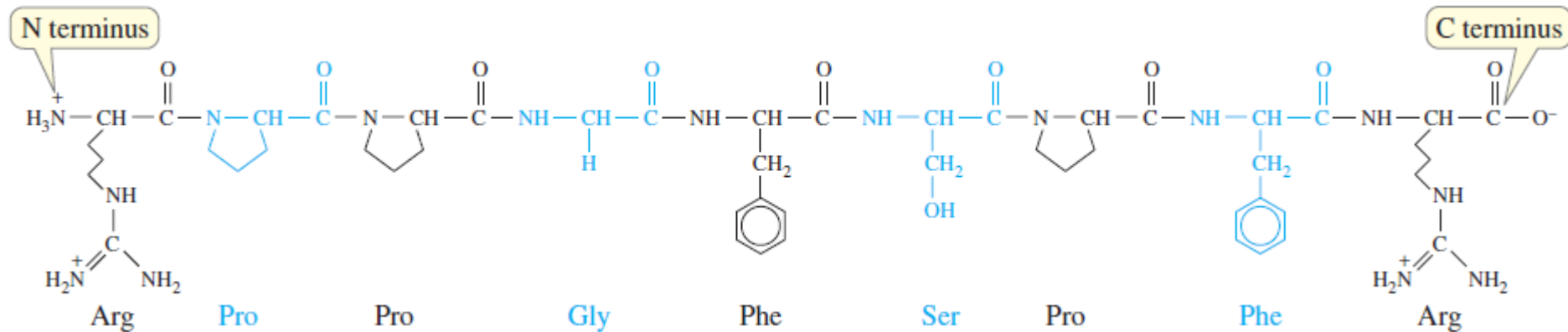
- Each amino acid unit in the peptide is called a **residue**
- A **polypeptide** is a peptide containing many amino acid residues but usually having a molecular weight of less than about **5000**
- **Proteins** contain more amino acid units, with molecular weights ranging from about **5000** to about **40,000,000**

Key concepts:

3) เราสามารถเรียกชื่อ peptide แต่ละชนิดได้อย่างไร?

Peptides

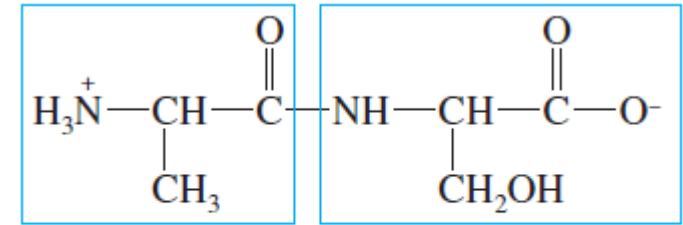
- Nonapeptide **bradykinin**, a human hormone that helps to control blood pressure



- The end of the peptide with the free amino group ($-\text{NH}_3^+$) is called the **N terminus**
- The end with the free carboxyl group ($-\text{CO}_2^-$) is called the **C terminus**
- Peptide structures are generally drawn with the **N terminus at the left** and the **C terminus at the right**

Peptides – Nomenclature

- The names of peptides reflect the names of the **amino acid residues** involved in the amide linkages, **beginning at the N terminus**; All **except the last** are given the **-yl suffix** of acyl groups

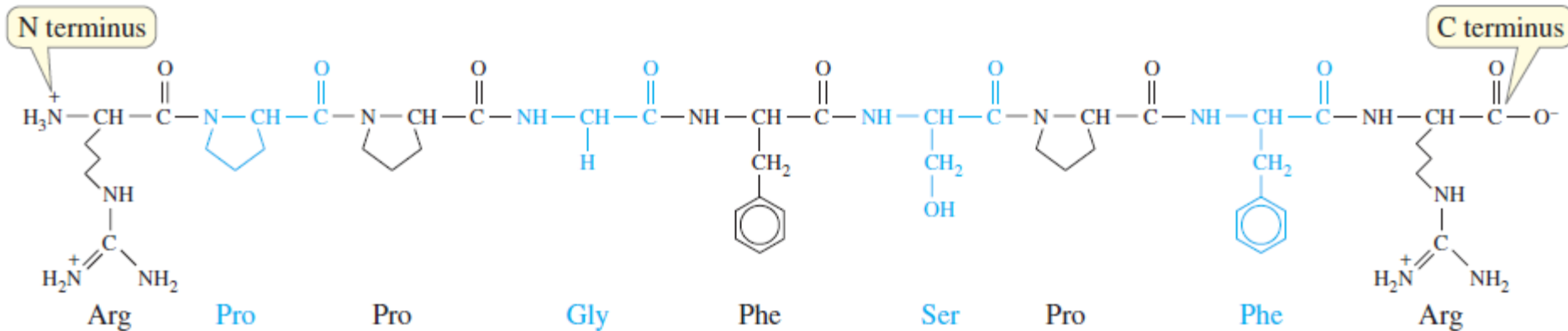


alanyl

serine

Ala-Ser

alanylserine



arginyl prolyl prolyl glycyll phenylalanyl seryl prolyl phenylalanyl arginine

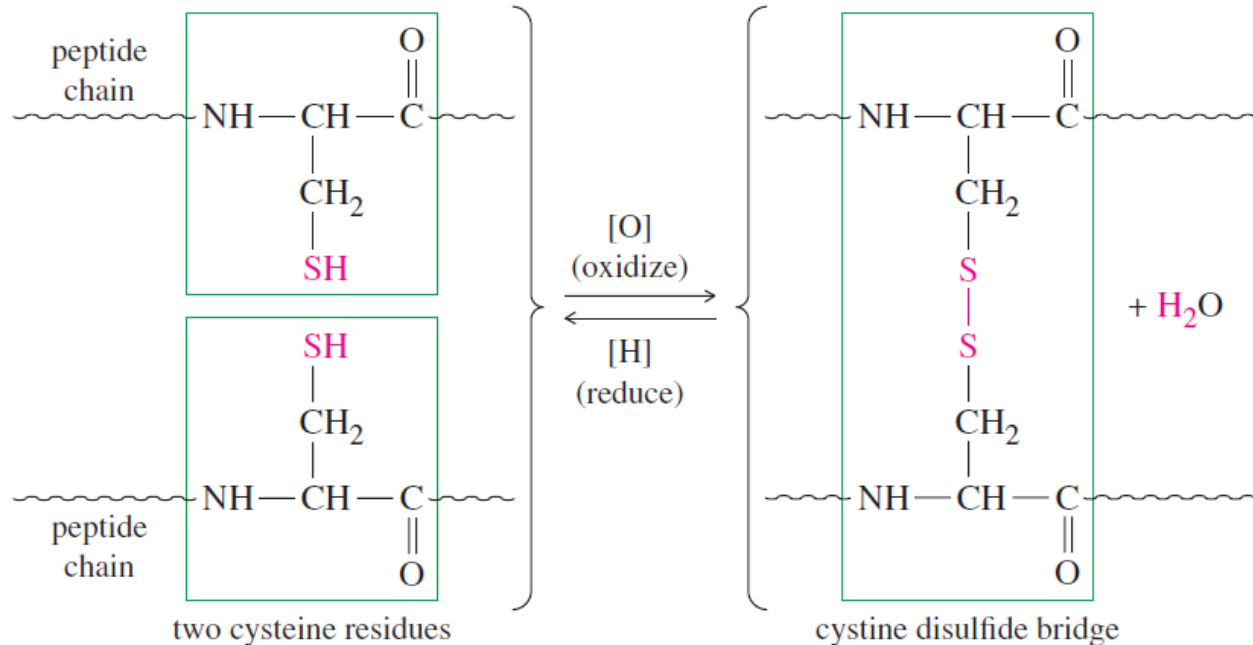
- A **shorthand system** is more convenient, representing each amino acid by its three-letter abbreviation : **Arg-Pro-Pro-Gly-Phe-Ser-Pro-Phe-Arg**
- Single-letter symbols** are becoming widely used as well : **RPPGFSPFR**

Key concepts:

4) นอกเหนือจากพันธะ peptide แล้ว ยังมีพันธะ disulfide ด้วย

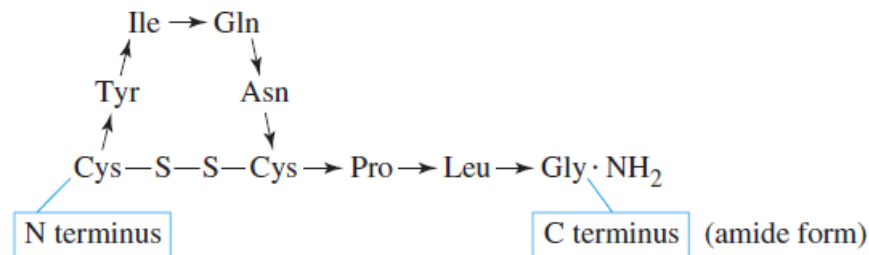
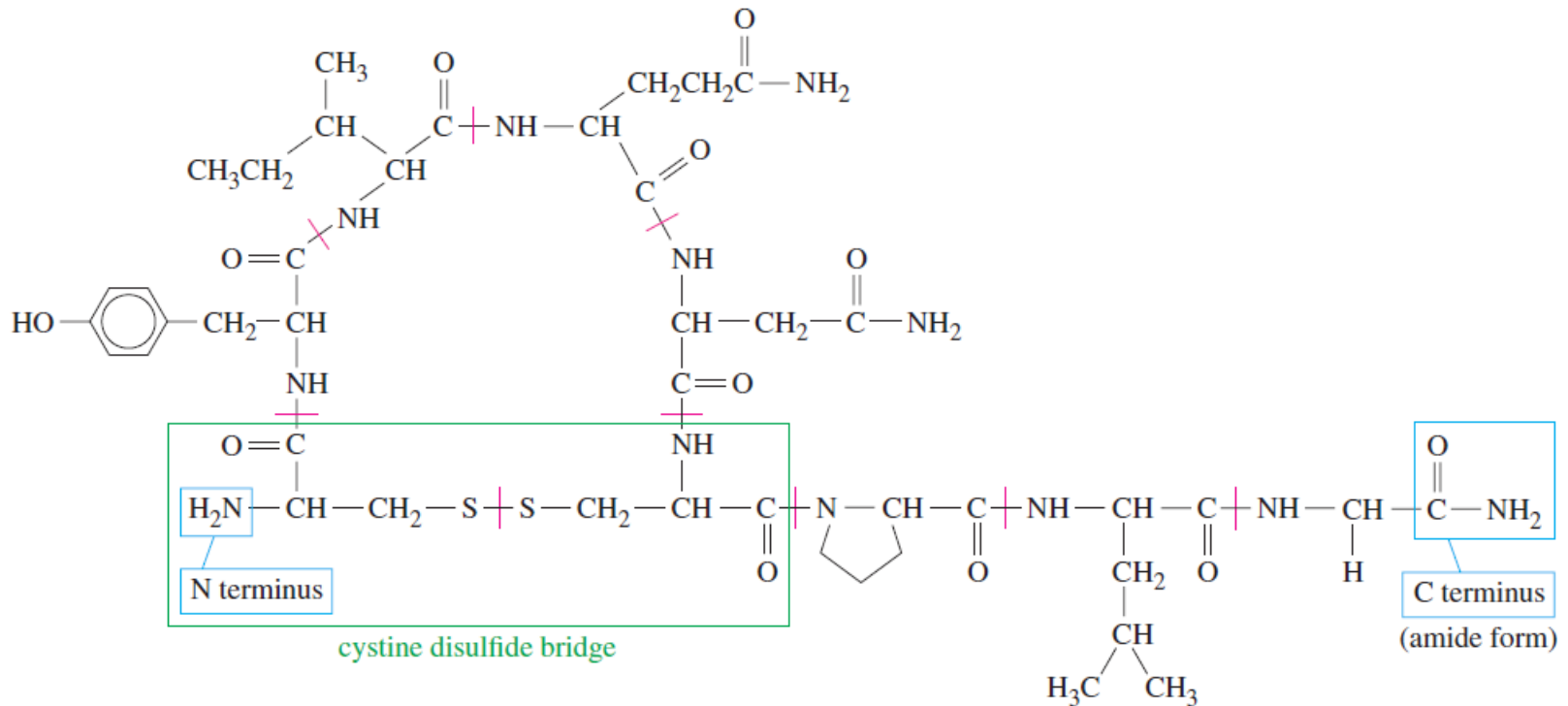
Disulfide bond

- Amide linkages (peptide bonds) form the backbone of peptides and proteins.
- A second kind of covalent bond is possible between any **cysteine** residues present. Cysteine residues can form disulfide linkages.
- **Mild oxidation** joins two molecules of a thiol into a disulfide, forming a disulfide linkage between the two thiol molecules. This reaction is reversible, and a **mild reduction** cleaves the disulfide.



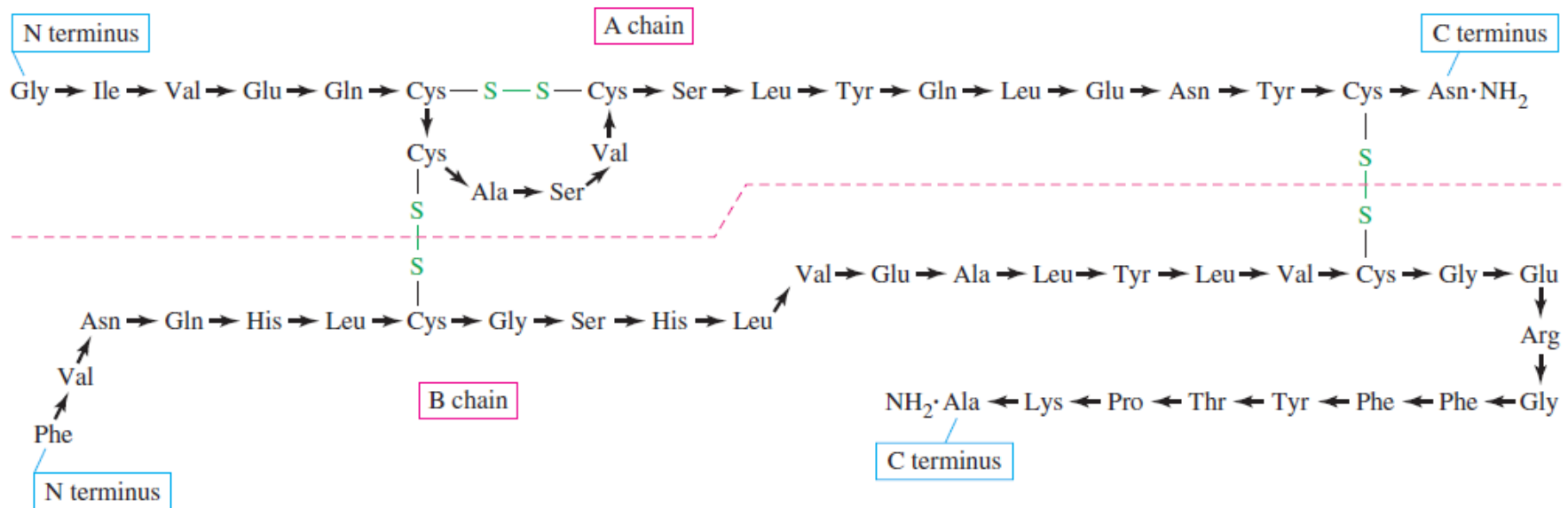
Disulfide bond

- Oxytocin (Oxt)** is a **peptide hormone** and neuropeptide that plays a role in social bonding, reproduction, childbirth, and the period after childbirth.



Disulfide bond

- Insulin** is a more complex peptide hormone that regulates glucose metabolism



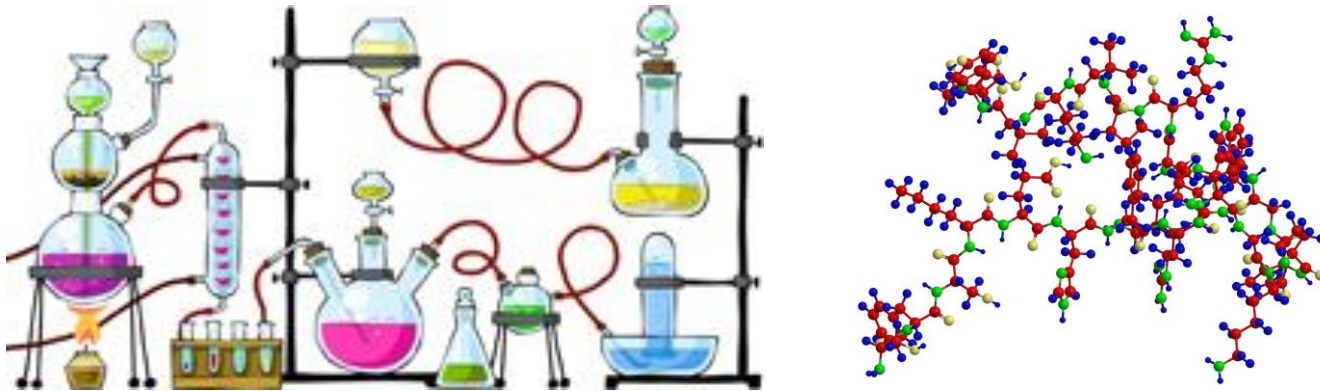
- Insulin is composed of two separate peptide chains, the **A chain**, containing **21 amino acid residues**, and the **B chain**, containing **30**.
- The A and B chains are joined at **two positions by disulfide bridges**, and the A chain has an **additional disulfide bond** that holds six amino acid residues in a ring.

Key concepts:

5) หากต้องการสังเคราะห์ peptide ขึ้นมาเอง จะทำได้อย่างไร?

Peptide Synthesis

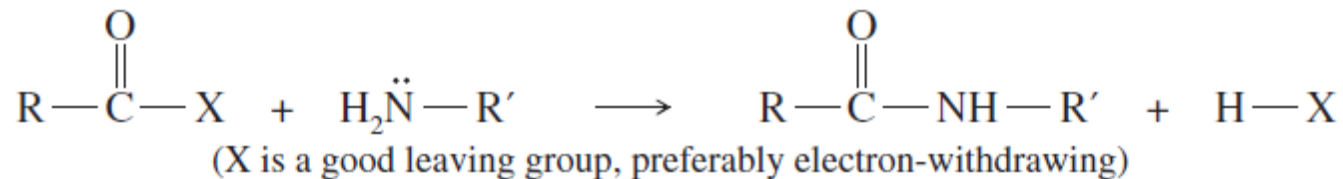
- Total synthesis of peptides is **rarely an economical method** for their commercial production.
- Important peptides are usually **derived from biological sources**.



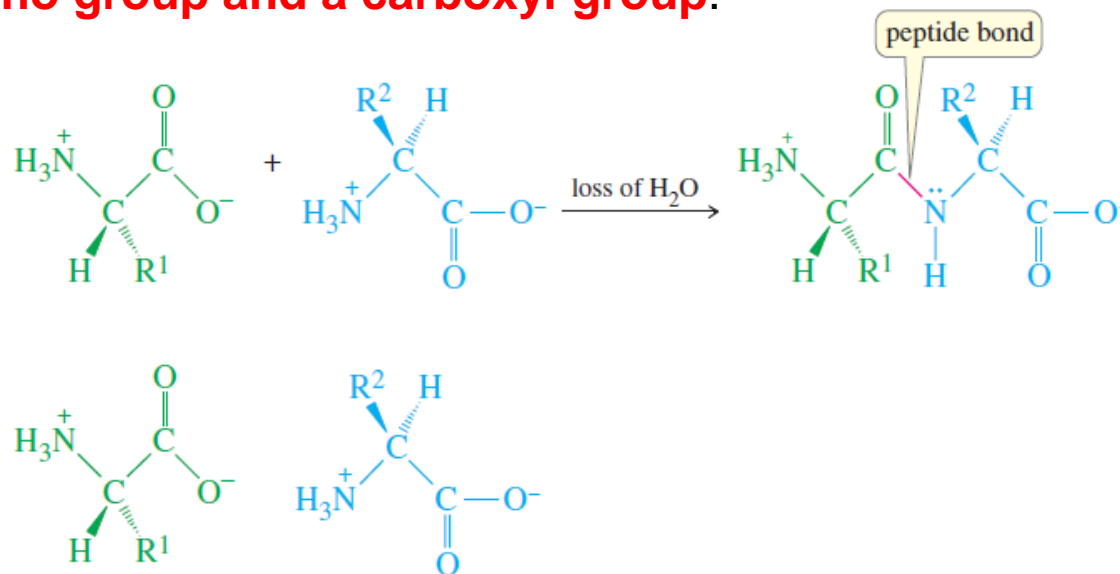
- Laboratory peptide synthesis is still an important area of chemistry, however, for two reasons:
 - If the synthetic peptide is the same as the natural peptide, it **proves the structure** is correct; and the synthesis provides a **larger amount** of the material for further biological testing.
 - Also, synthetic peptides can be made with **altered amino acid sequences** to compare their biological activity with the natural peptides.

Peptide Synthesis

- Peptide synthesis requires the formation of **amide bonds** between the **proper amino acids** in the **proper sequence**.
- With simple acids and amines, we would form an amide bond simply by converting the acid to an **activated derivative** (such as an acyl halide or anhydride) and adding the **amine**.

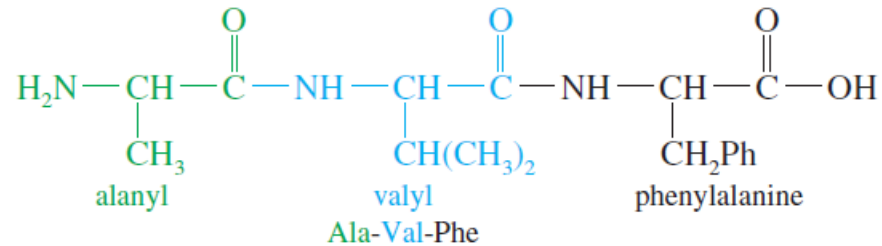


- Amide formation is not so easy with amino acids, however. **Each amino acid has both an amino group and a carboxyl group**.



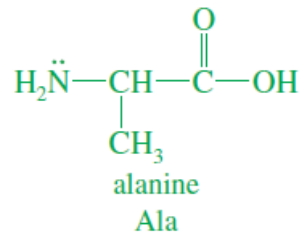
Peptide Synthesis – Solution-Phase Method

- Synthesis begins at the N terminus and ends at the C terminus,



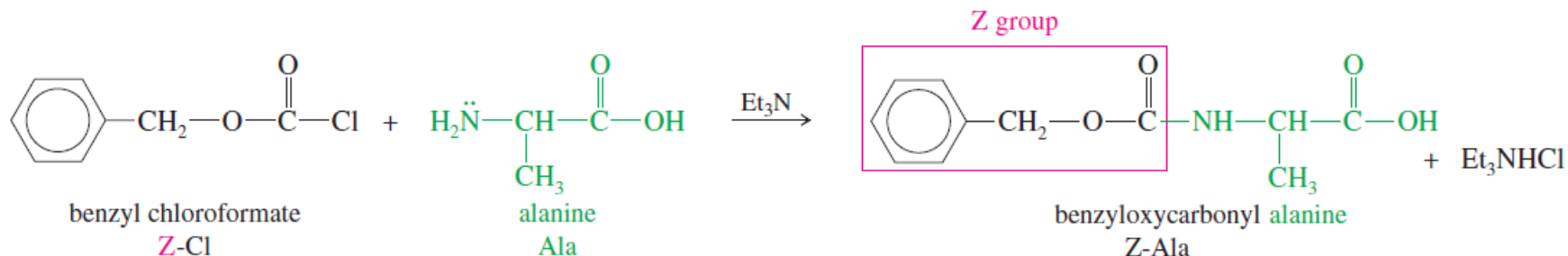
Step #1 Couple the carboxyl group of alanine to the amino group of valine

Step #1.1 Activate the carboxyl group of alanine

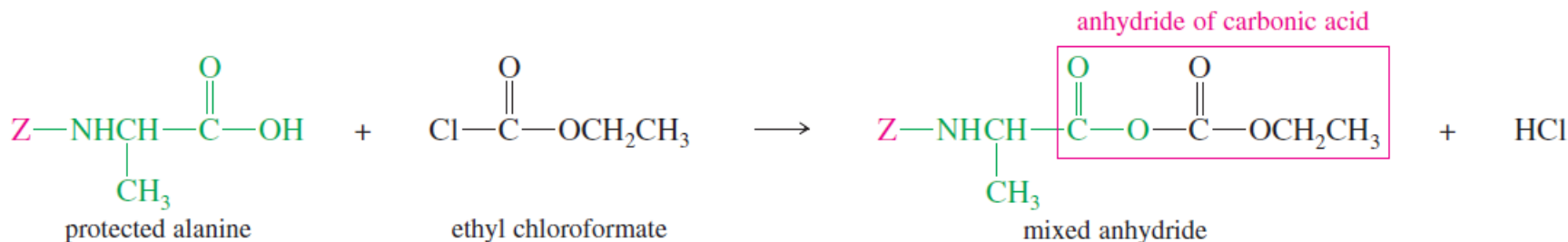


Peptide Synthesis – Solution-Phase Method

#Prestep: Protect the amino group to make it nonnucleophilic

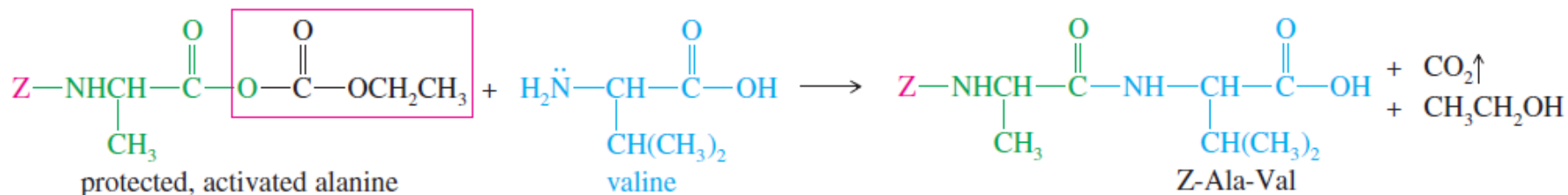


Step #1.1 Activate the carboxyl group

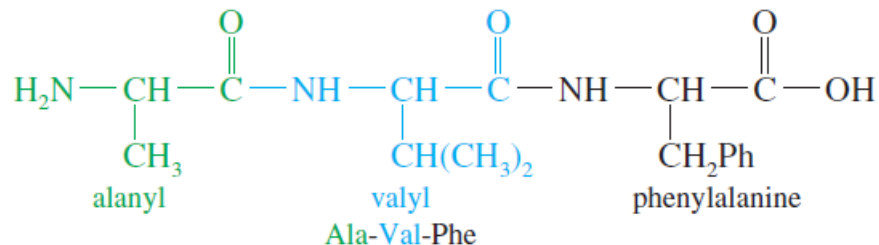


Peptide Synthesis – Solution-Phase Method

Step #1.2 Form an amide bond to couple the next amino acid



Step #1 Couple the carboxyl group of alanine to the amino group of valine

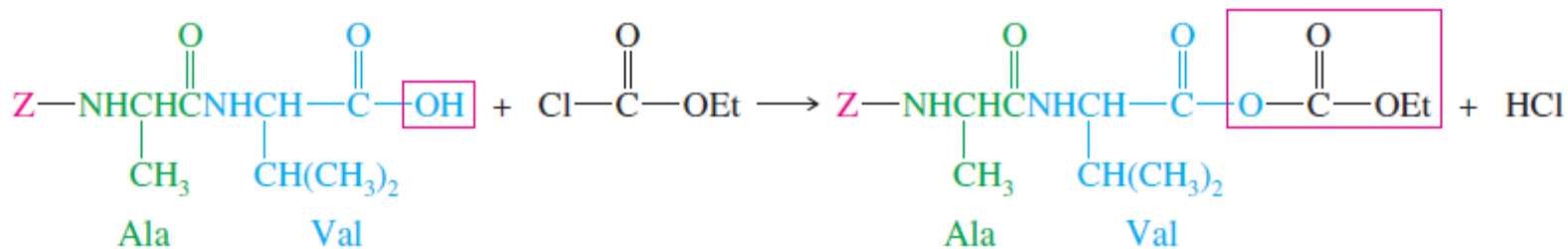


Step #2 Couple the carboxyl group of AlaVal to the amino group of Phe

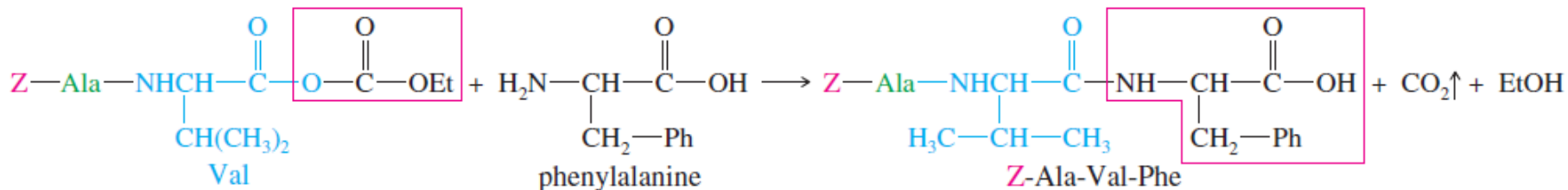
Peptide Synthesis – Solution-Phase Method

Step #2 Couple the carboxyl group of AlaVal to the amino group of Phe

Step #2.1 Activate the carboxyl group



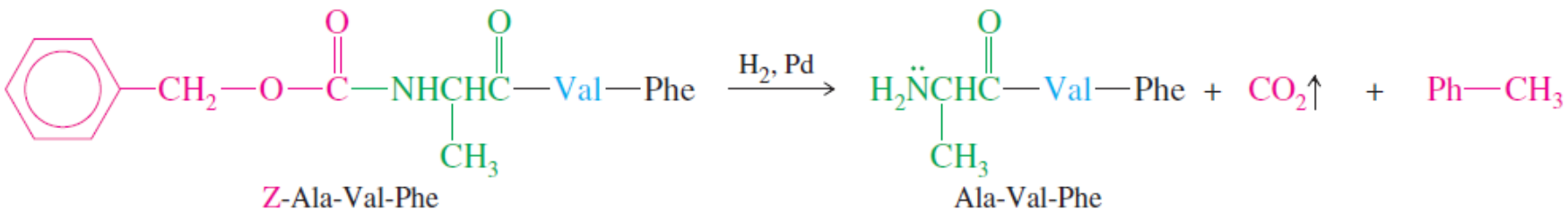
Step #2.2 Form an amide bond to couple the next amino acid



* To make a larger peptide, repeat these two steps for the addition of each amino acid residue.

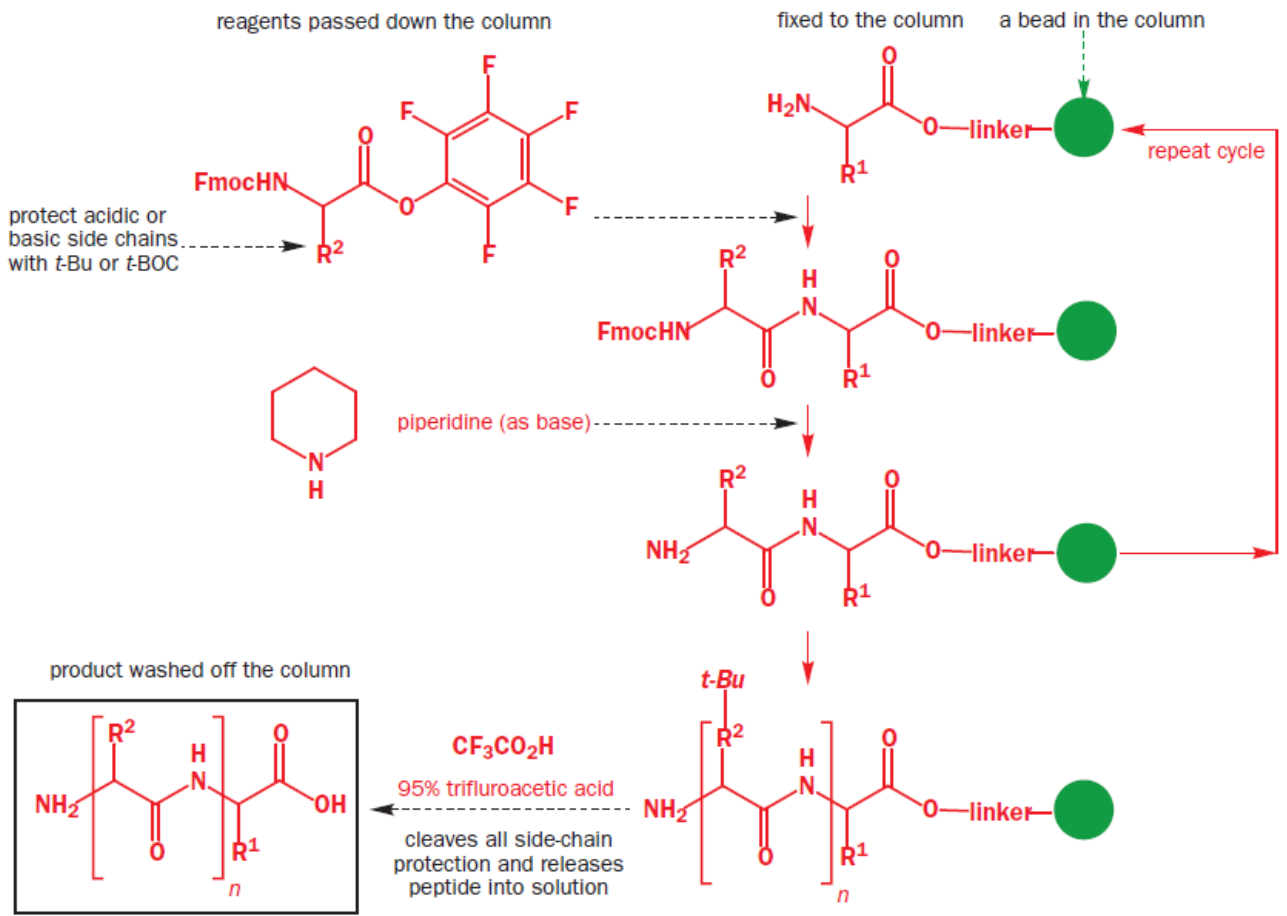
Peptide Synthesis – Solution-Phase Method

#Poststep: Remove the protecting group



Peptide Synthesis – Solid-Phase Method

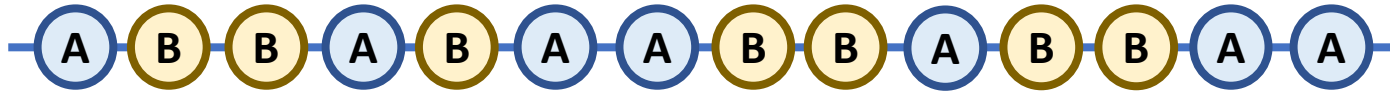
(concept)



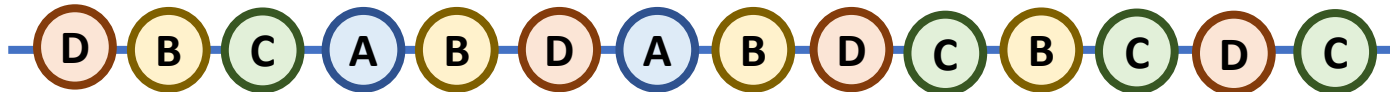
Protein structure – Primary structure

- The primary structure is the **covalently bonded structure** of the molecule. This definition includes the **sequence of amino acids**, together with any **disulfide bridges**.

#1



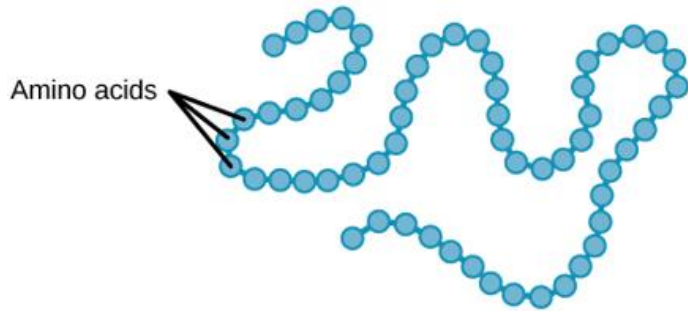
#2



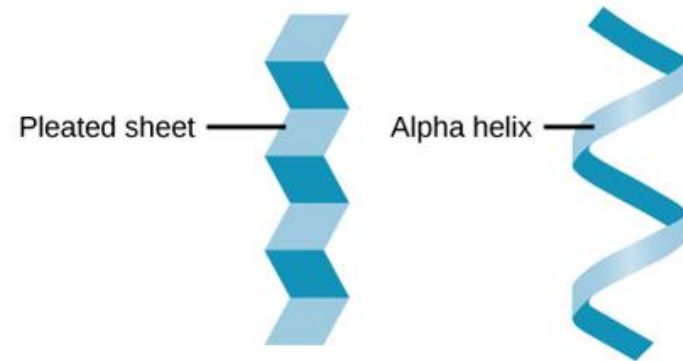
Protein structure

Level of Protein Structure:

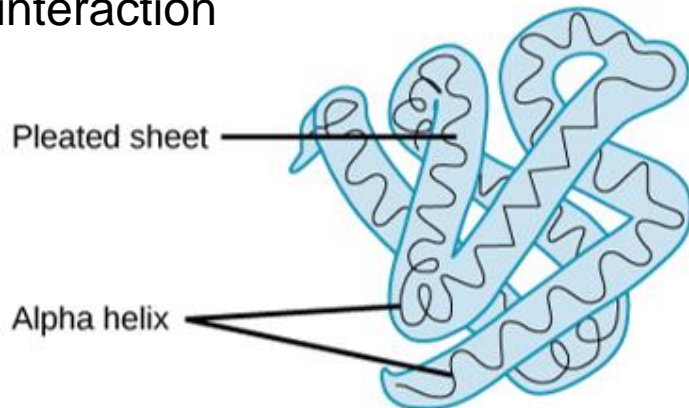
1) Primary: sequence of a chain of amino acids



2) Secondary: folding of peptide into a repeating pattern due to H-bonding of peptide backbone



3) Tertiary: three dimensional folding pattern due to side chain interaction



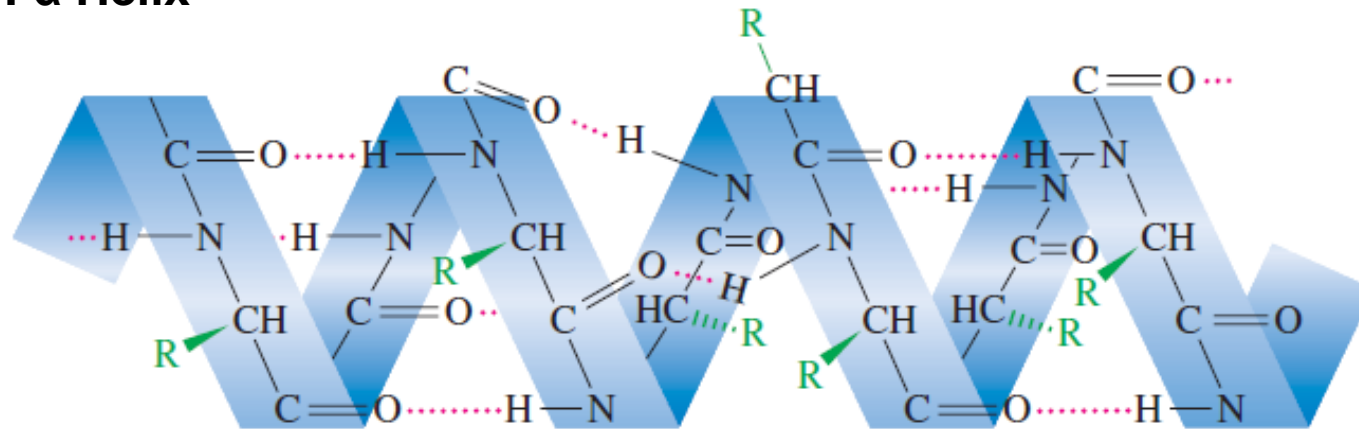
4) Quaternary: protein that consists of more than one peptide chain



Protein structure – Secondary structure

- Peptide chains in **not a linear structure**, they tend to form **orderly hydrogen-bonded arrangements**
- **Two** of the most found secondary structures:

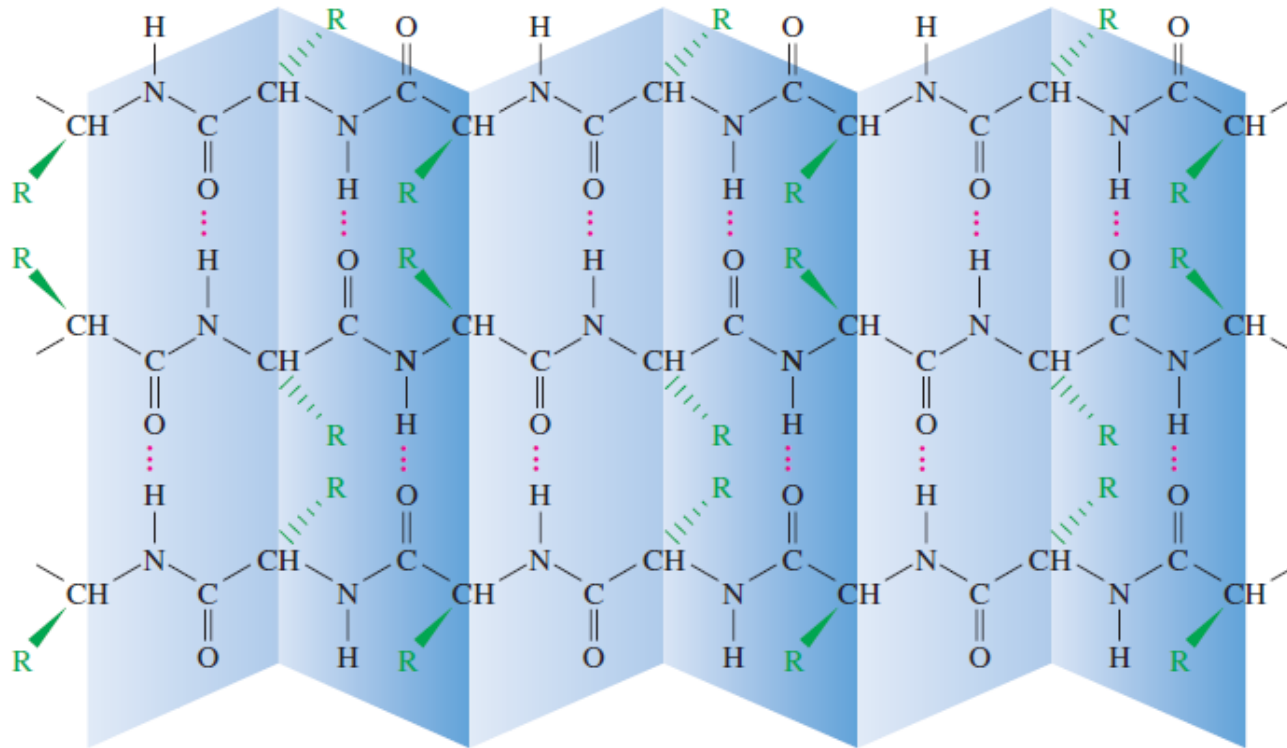
#1: α Helix



- Each **carbonyl oxygen** can **hydrogen-bond** with an **N-H hydrogen** on the next turn of the coil.
- Many proteins wind into an α helix (a helix that looks like the thread on a right-handed screw) with the **side chains positioned on the outside** of the helix.

Protein structure – Secondary structure

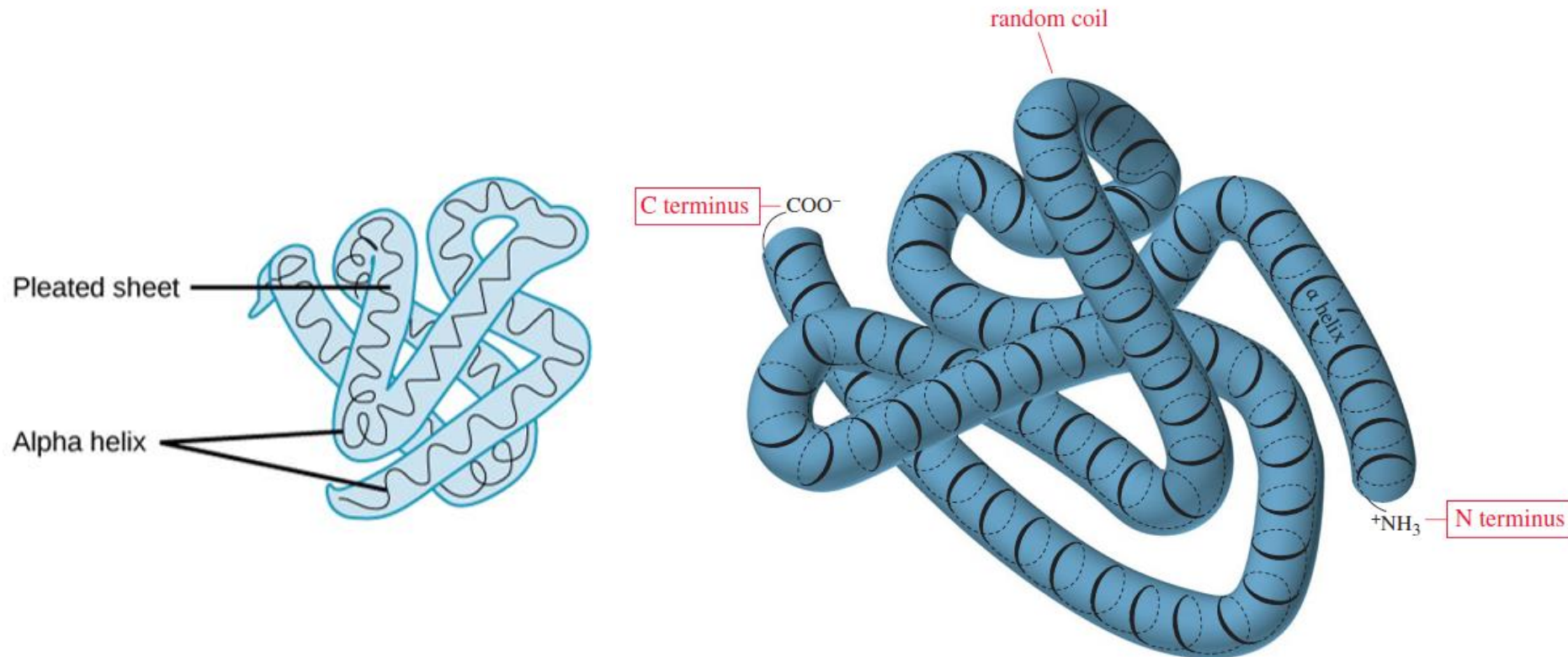
#2: β sheet (pleated-sheet)



- Each **carbonyl group on one chain** forms a **hydrogen bond** with an **N-H hydrogen** on an adjacent chain.
- This arrangement may involve many peptide molecules lined up side-by-side, resulting in a **two-dimensional sheet**.

Protein structure – Tertiary structure

- **Secondary structure** is only a **spatial pattern** in a local region of the molecule.
- The **tertiary structure** includes all the secondary structure and all the kinks and folds in between. = **complete three-dimensional conformation**.

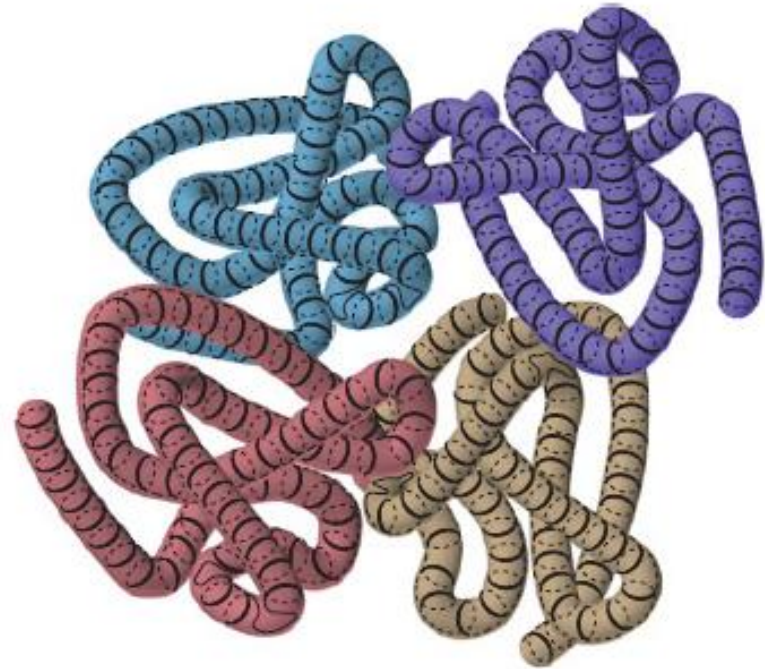


Protein structure – Quaternary structure

- Quaternary structure refers to the **association of two or more peptide chains in the complete protein.**
- **Not all proteins have quaternary structure.** The ones that do are those that **associate together in their active form.**
- For example, hemoglobin, the oxygen carrier in mammalian blood, consists of four peptide chains fitted together to form a globular protein.



tertiary structure



quaternary structure

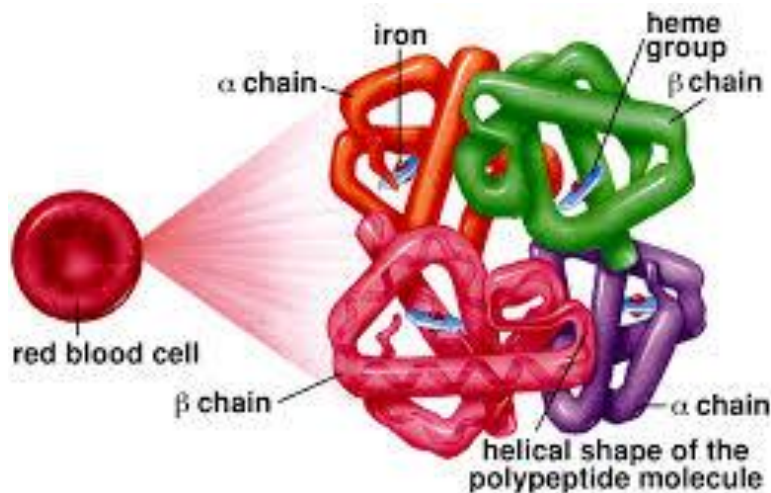
Key concepts:

7) โพรตีนมีประเภทไหนบ้าง? แต่ละประเภททำหน้าที่อะไร?

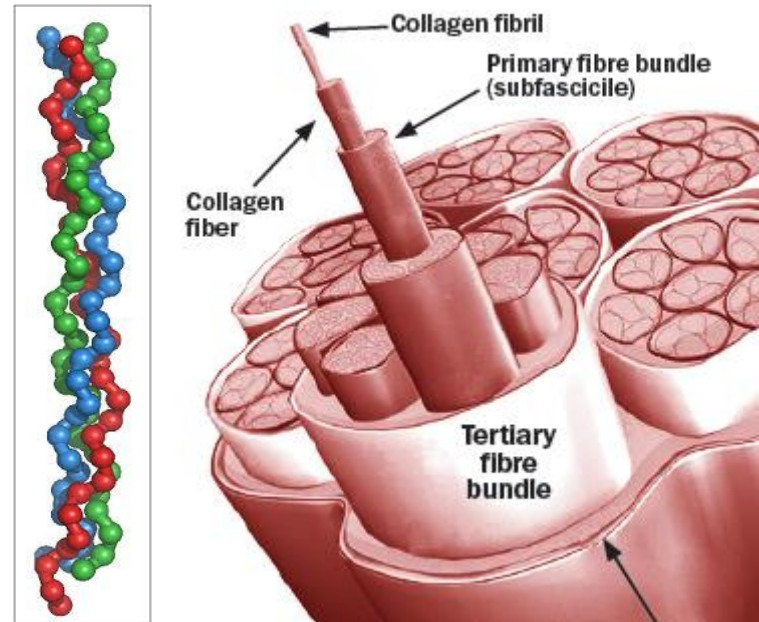
Classification of Proteins – by structure

Proteins

- **Globular proteins:** are folded into roughly spherical shapes. They usually function as **enzymes, hormones, or transport proteins**



- **Fibrous proteins:** stringy, tough, and usually insoluble in water. They function primarily as **structural** parts of the organism



Classification of Proteins – by composition



- **Simple proteins**: those that hydrolyse to give **only amino acids**

- **Conjugated proteins**: bonded to a nonprotein **prosthetic group** such as a sugar, a nucleic acid, a lipid, or some other group

TABLE 24-3

Classes of Conjugated Proteins

Class	Prosthetic Group	Examples
glycoproteins	carbohydrates	γ -globulin, interferon
nucleoproteins	nucleic acids	ribosomes, viruses
lipoproteins	fats, cholesterol	high-density lipoprotein
metalloproteins	a complexed metal	hemoglobin, cytochromes