Organic Chemistry

Introductory of Amino Acid

by
Nurlin Abu Samah, Dr. Md. Shaheen & Dr. Nadeem Akhtar
Faculty of Industrial Sciences & Technology
nurlin@ump.edu.my

Chapter Description

- Aims
  - The students should **understand** the fundamental of organic chemistry in terms of amino acids
  - The students should be able to **explain** the fundamental of organic chemistry in terms of amino acids

- Expected Outcomes
  - Explain the basic knowledge in amino acids
  - Describe the chemical reactions and conditions for amino acids reactions
  - Describe the peptides synthesis

- References

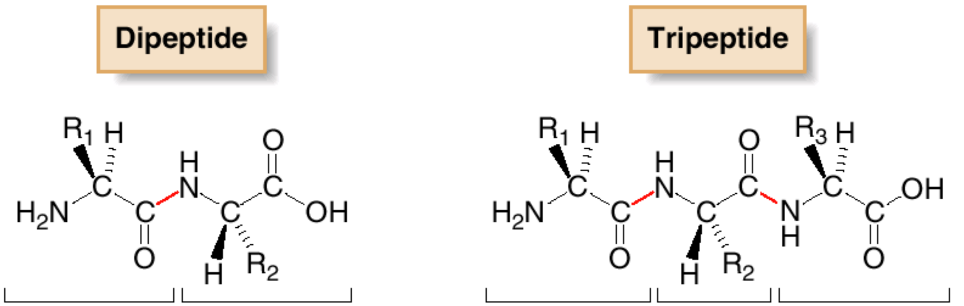
  - Janice Gorzynski Smith (2008), Organic chemistry,Mc Graw-Hill
  - T. W. Graham Solomons. (2008). Organic chemistry, 9th ed, Mc Graw-Hill
  - K. Peter C. Vollhardt, Neil E. Schore, (2009). Organic chemistry, Fourth Edition: Structure and Function, Pub Chem

Peptides and Proteins

Peptides

- When amino acids are joined together by amide bonds, they form larger molecules called peptides and proteins.

> - A *dipeptide* has two amino acids joined together by *one* amide bond.
> - A *tripeptide* has three amino acids joined together by *two* amide bonds.



Two amino acids joined together. Three amino acids joined together.

[Amide bonds are drawn in red.]

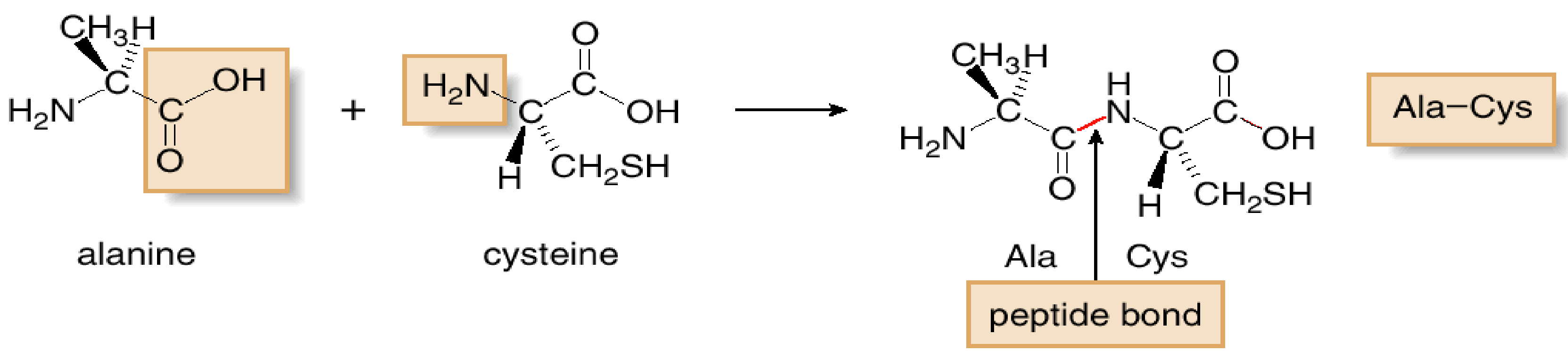
- The term protein is usually reserved for polymers of more than 40 amino acids.

> - The amide bonds in peptides and proteins are called *peptide bonds.*
> - The individual amino acids are called *amino acid residues.*

Peptides

- To form a dipeptide, the amino group of one amino acid forms an amide bond with the carboxy group of another amino acid. Since each amino acid has both an amino group and a carboxy group, two different peptides can be formed.

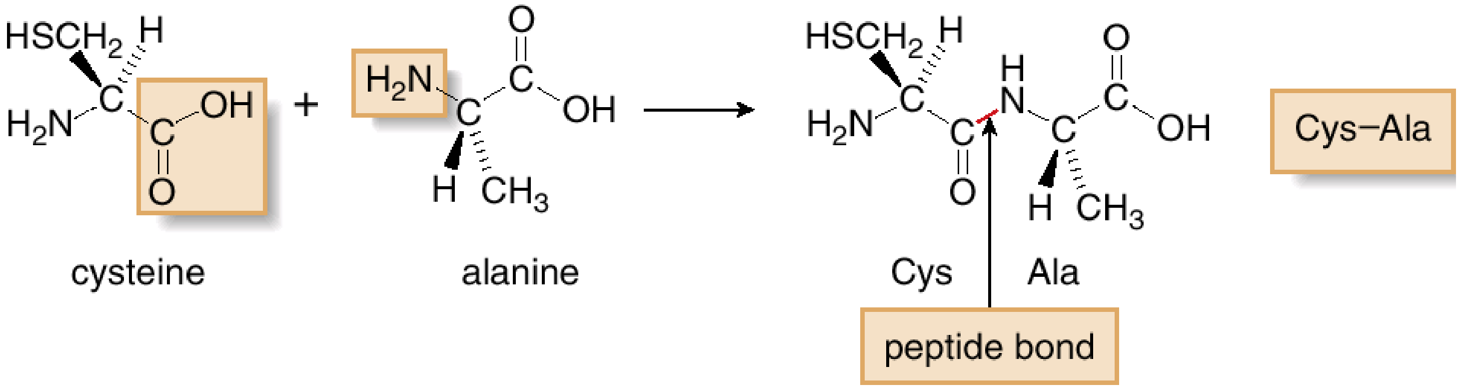
The COOH group of alanine can combine with the NH_2 group of cysteine.



Peptides and Proteins

Peptides

The COOH group of cysteine can combine with the NH_2 group of alanine.



- The amino acid with the free amino group is called the *N-terminal amino acid.*
- The amino acid with the free carboxy group is called the *C-terminal amino acid.*

- Note that, by convention, the N-terminal amino acid is always written at the left end of the chain and the C-terminal amino acid at the right.
- The peptide can be abbreviated by writing the one- or three-letter symbols for the amino acids in the chain from the N-terminal to the C-terminal end.

Peptides and Proteins

Peptides

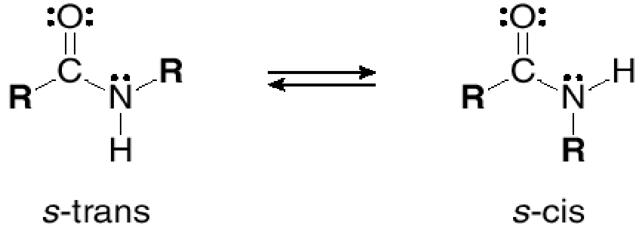
The carbonyl carbon of an amide is *sp*^{2} hybridized and has trigonal planar geometry. Amides are more resonance stabilized than other acyl compounds, so the resonance structure having the C=N makes a significant contribution to the hybrid.

two resonance structures for the peptide bond

Peptides

Resonance stabilization has important consequences. Rotation about the C—N bond is restricted because it has partial double bond character. As a result, there are two possible conformations.

Two conformations of the peptide bond

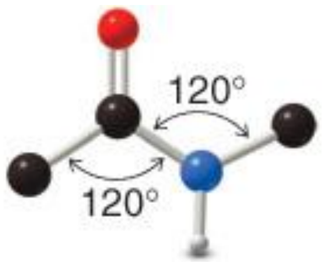


- The *s*-trans conformation has the two R groups oriented on *opposite* sides of the C–N bond.
- The *s*-cis conformation has the two R groups oriented on the *same* side of the C–N bond.
- The *s*-trans conformation of a peptide bond is typically more stable than the *s*-cis, because the *s*-trans has the two bulky R groups located farther from each other.

Peptides and Proteins

Peptides

- A second consequence of resonance stabilization is that all six atoms involved in the peptide bond lie in the same plane.
- All bond angles are ~120° and the C=O and N—H bonds are oriented 180° from each other.



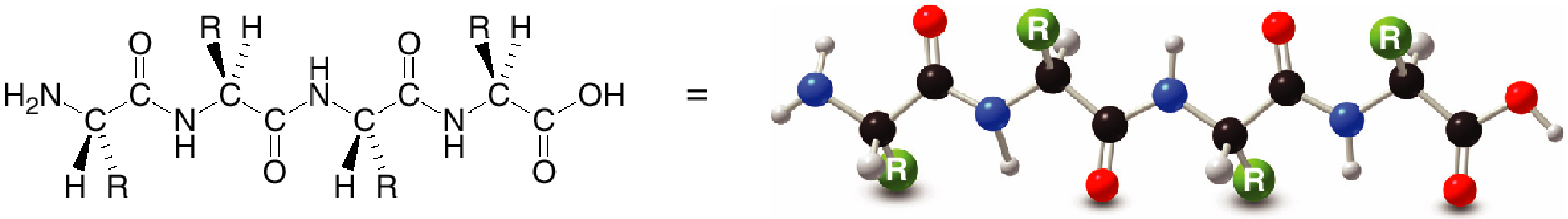
These six atoms lie in a plane.

Peptides

- The structure of a tetrapeptide illustrates the results of these effects in a long peptide chain.

> - The *s*-trans arrangement makes a long chain with a zigzag arrangement.
> - In each peptide bond, the N–H and C=O bonds lie parallel and at 180° with respect to each other.

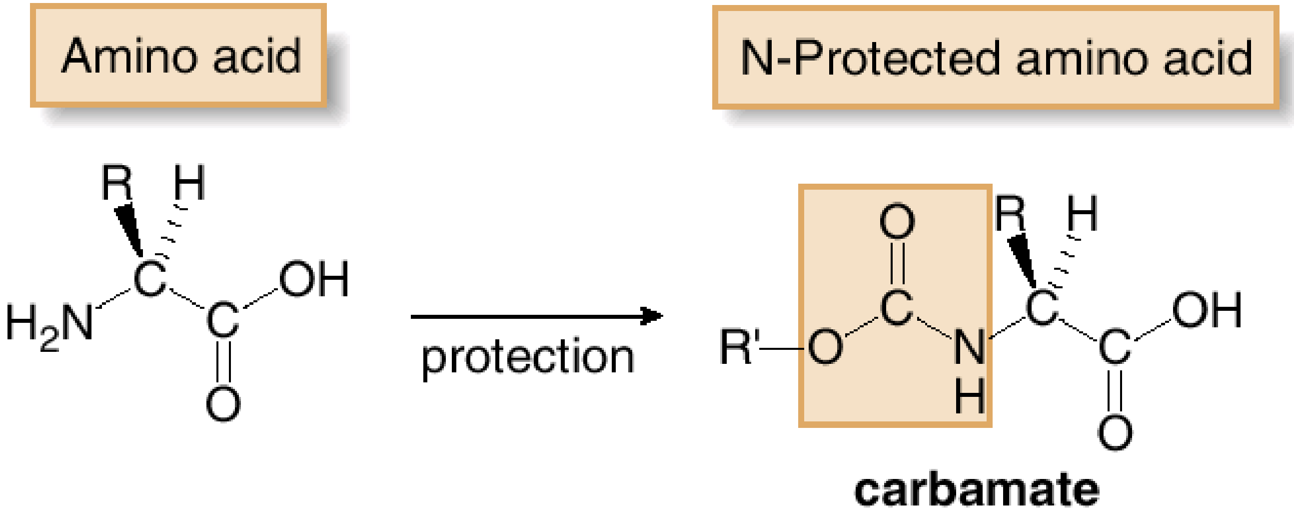
A tetrapeptide



Peptides and Proteins

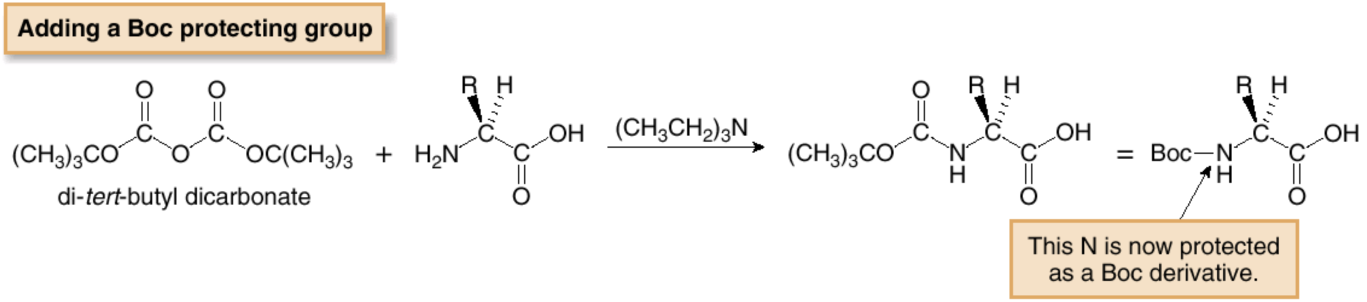
Peptide Synthesis

- Two widely used amino protecting groups convert an amine into a carbamate, a functional group having a carbonyl bonded to both an oxygen and a nitrogen atom.
- Since the N atom of the carbamate is bonded to a carbonyl group, the protected amino group is no longer nucleophilic. Why?

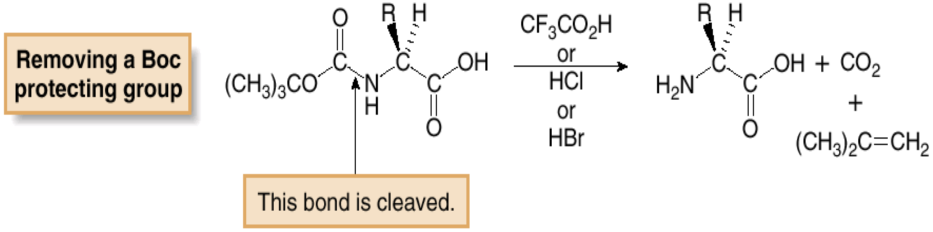


Peptide Synthesis

Example: the *tert*-butoxycarbonyl protecting group, abbreviated Boc, is formed by reacting the amino acid with di-*tert*-butyl dicarbonate in a nucleophilic acyl substitution reaction.



- To be a useful protecting group, the Boc group must be removed under reaction conditions that do not affect the other functional groups in the molecule. It can be removed by acids such as trifluoroacetic acid, HCl or HBr.



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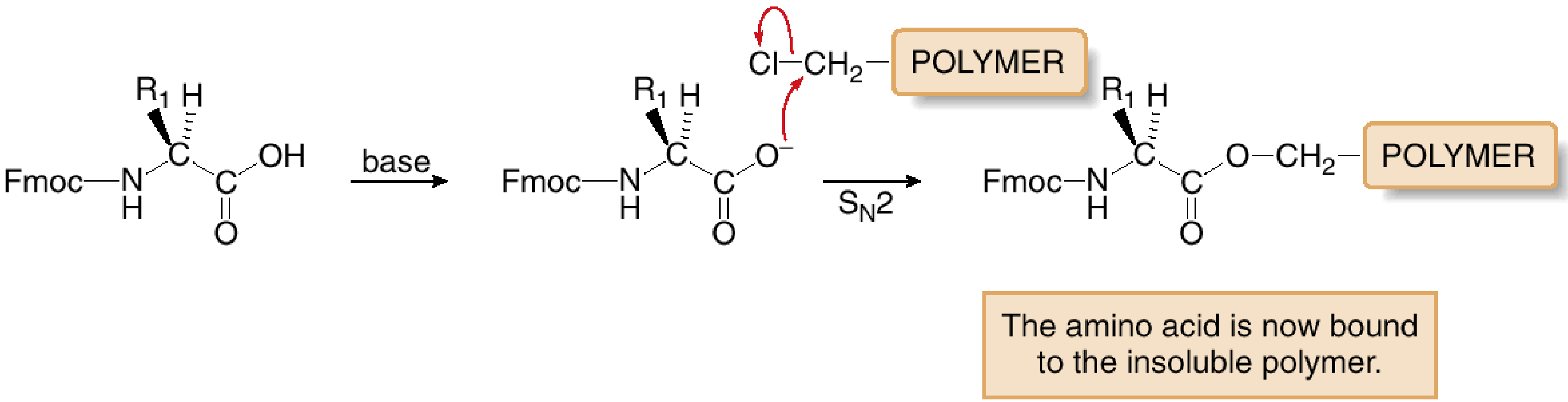
Automated Peptide Synthesis

- An Fmoc-protected amino acid is attached to the polymer at its carboxy group by an S_N2 reaction.



- Once the first amino acid is bound to the polymer, additional amino acids can be added sequentially. In the last step, HF cleaves the polypeptide chain from the polymer.

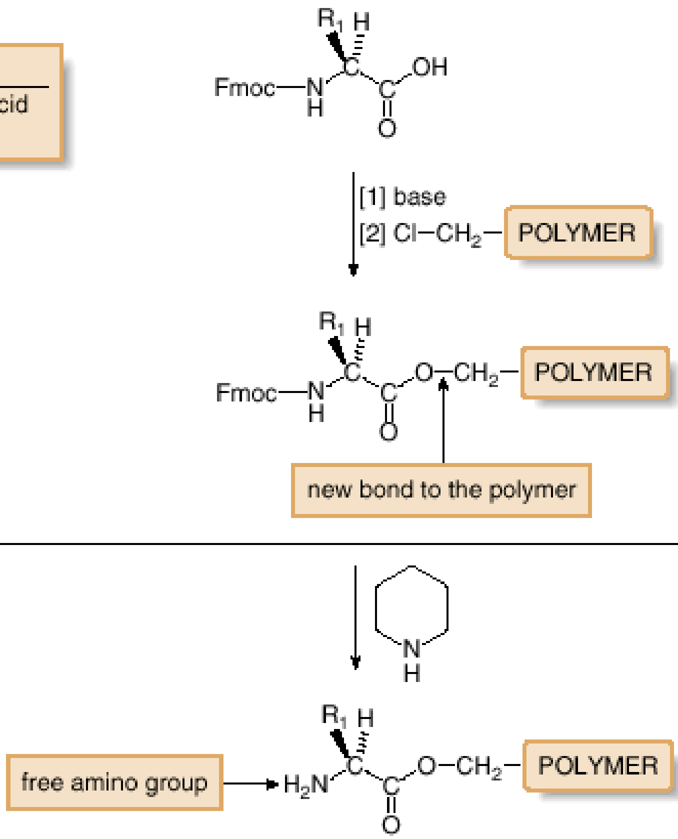
Peptides and Proteins

Automated Peptide Synthesis

How To Synthesize a Peptide Using the Merrifield Solid Phase Technique

Step [1]
Attach an Fmoc-protected amino acid to the polymer.

Step [2]
Remove the protecting group.



Introductory of Amino Acids
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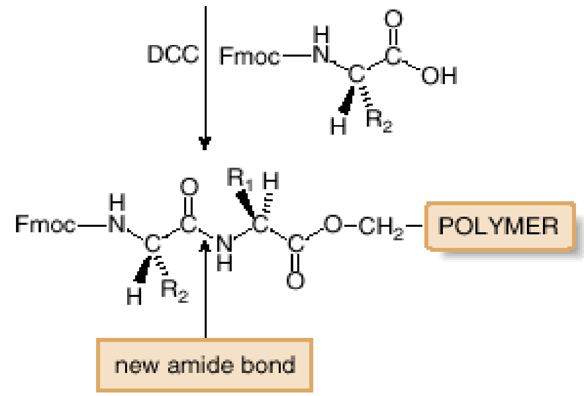
Peptides and Proteins

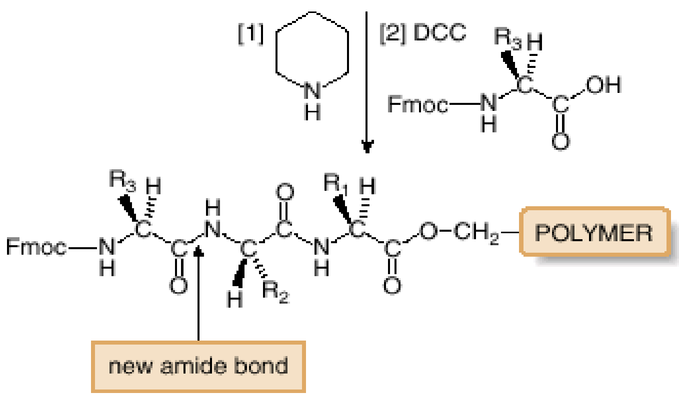
Automated Peptide Synthesis

How To, continued . . .

Step [3]
Form the amide bond with DCC.



Step [4]
Repeat Steps 2 and 3.

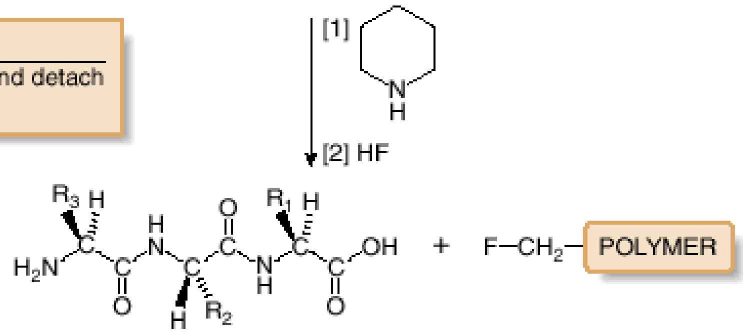


Peptides and Proteins

Automated Peptide Synthesis

How To, continued . . .

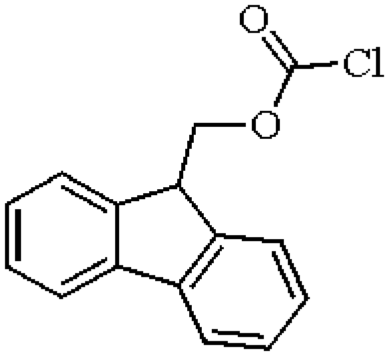
Step [5]
Remove the protecting group and detach the peptide from the polymer.



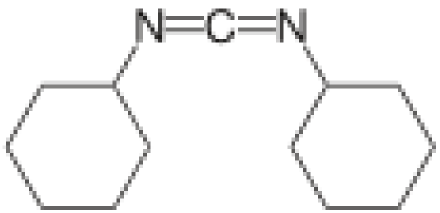
tripeptide

- The Merrifield method has now been completely automated.

9-Fluorenylmethyl Chloroformate Fmoc



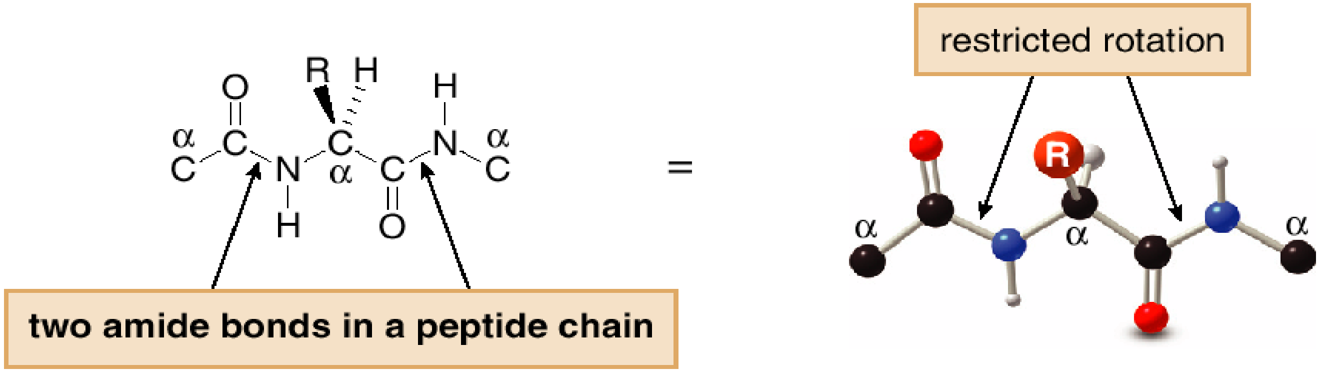
N,N'-Dicyclohexylcarbodiimide



1. Proteins—Primary Structure

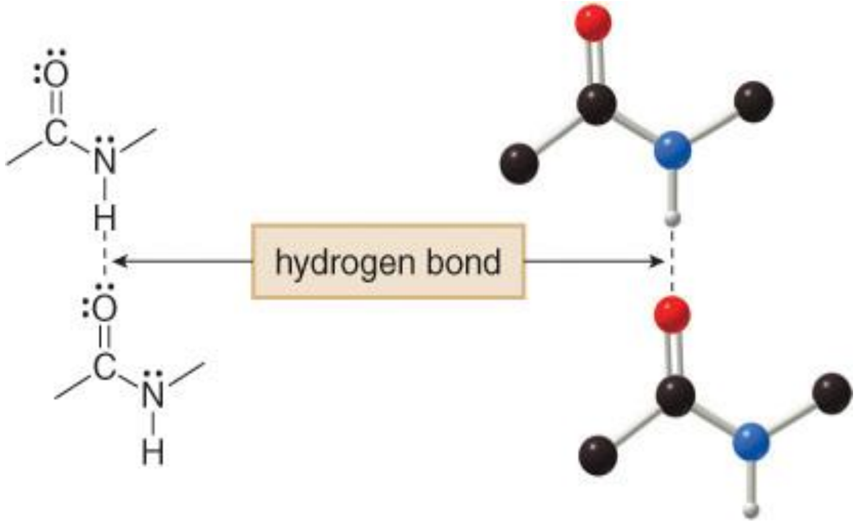
- The primary structure of proteins is the particular sequence of amino acids that is joined together by peptide bonds. The most important element of primary structure is the amide bond.

- Rotation around the amide C–N bond is *restricted* because of electron delocalization, and the *s*-trans conformation is the more stable arrangement.
- In each peptide bond, the N–H and C=O bonds are directed 180° from each other.



2. Proteins—Secondary Structure

- The three-dimensional conformations of localized regions of a protein are called its secondary structure. These regions arise due to hydrogen bonding between the N—H proton of one amide and the C=O oxygen of another.
- Two arrangements are particularly stable—the α-helix and the β-pleated sheet.



Conclusion of The Chapter

- Conclusion #1
  - The introductory of amino acids with its nomenclature were understandable.
- Conclusion #2
  - The fundamental of amino acids included its reactions involves were practically explained.
- Conclusion #3
  - The peptides synthesis was practically explained.

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Co-author Information

Nurlin Abu Samah is an analytical chemistry lecturer since 2010 and currently she further her PhD study in Universitat Autonoma de Barcelona, Spain. She was graduated from Universiti Kebangsaan Malaysia for her Master of Science in Chemistry. During her undergraduate, she was studied in Universiti Sains Malaysia, Penang.

nurlin@ump.edu.my