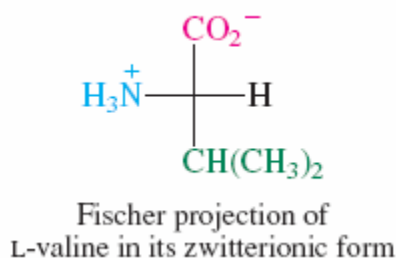


# AMINO ACIDS, PEPTIDES, AND PROTEINS

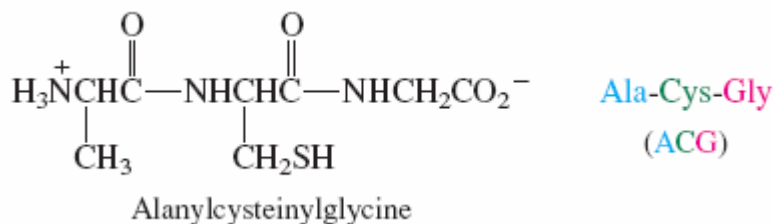
## SUMMARY

This chapter revolves around **proteins**. The first half describes the building blocks of proteins, progressing through **amino acids** and **peptides**. The second half deals with proteins themselves.

- Section 27.1 The 20 amino acids listed in Table 27.1 are the building blocks of proteins. All are  $\alpha$ -amino acids.
- Section 27.2 Except for glycine, which is achiral, all of the  $\alpha$ -amino acids in Table 27.1 are chiral and have the L configuration at the  $\alpha$  carbon.
- Section 27.3 The most stable structure of a neutral amino acid is a **zwitterion**. The pH of an aqueous solution at which the concentration of the zwitterion is a maximum is called the isoelectric point (pI).

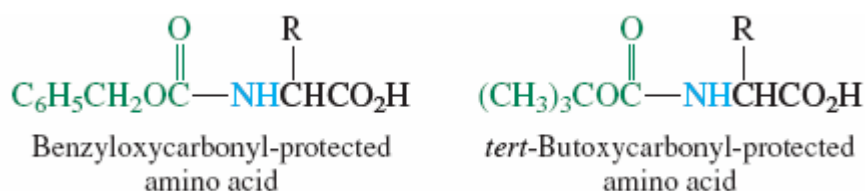


- Section 27.4 Amino acids are synthesized in the laboratory from
1.  $\alpha$ -Halo acids by reaction with ammonia
  2. Aldehydes by reaction with ammonia and cyanide ion (the Strecker synthesis)
  3. Alkyl halides by reaction with the enolate anion derived from diethyl acetamidomalonate
- Section 27.5 Amino acids undergo reactions characteristic of the amino group (e.g., amide formation) and the carboxyl group (e.g., esterification). Amino acid side chains undergo reactions characteristic of the functional groups they contain.
- Section 27.6 Among the biochemical reactions of  $\alpha$ -amino acids, several use pyridoxal 5'-phosphate as a coenzyme. These reactions involve bonds to the  $\alpha$  carbon and include transamination, decarboxylation, and racemization.
- Section 27.7 An amide linkage between two  $\alpha$ -amino acids is called a **peptide bond**. By convention, peptides are named and written beginning at the N terminus.



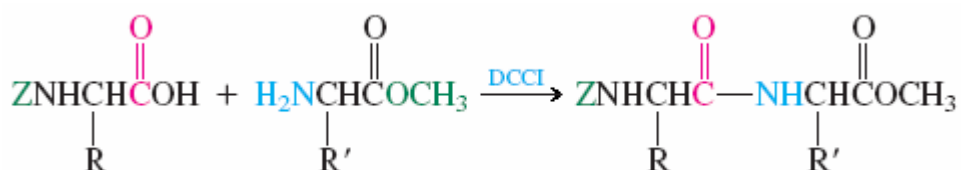
- Section 27.8 The **primary structure** of a peptide is its amino acid sequence plus any disulfide bonds between two cysteine residues. The primary structure is determined by a systematic approach in which the protein is cleaved to smaller fragments, even individual amino acids. The smaller fragments are sequenced and the main sequence deduced by finding regions of overlap among the smaller peptides.

- Section 27.9 Complete hydrolysis of a peptide gives a mixture of amino acids. An **amino acid analyzer** identifies the individual amino acids and determines their molar ratios.
- Section 27.10 Selective hydrolysis can be accomplished by using enzymes to catalyze cleavage at specific peptide bonds.
- Section 27.11 Carboxypeptidase-catalyzed hydrolysis can be used to identify the C-terminal amino acid. The N terminus is determined by chemical means. One reagent used for this purpose is Sanger's reagent, 1-fluoro-2,4-dinitrobenzene (see Figure 27.8).
- Section 27.12 The procedure described in Sections 27.8–27.11 was used to determine the amino acid sequence of insulin.
- Section 27.13 Modern methods of peptide sequencing follow a strategy similar to that used to sequence insulin, but are automated and can be carried out on a small scale. A key feature is repetitive N-terminal identification using the **Edman degradation**.
- Section 27.14 Synthesis of a peptide of prescribed sequence requires the use of protecting groups to minimize the number of possible reactions.
- Section 27.15 Amino-protecting groups include *benzyloxycarbonyl* (Z), *tert-butoxycarbonyl* (Boc), and *9-fluorenylmethoxycarbonyl* (Fmoc).



Hydrogen bromide may be used to remove either the benzyloxycarbonyl or *tert*-butoxycarbonyl protecting group. The benzyloxycarbonyl protecting group may also be removed by catalytic hydrogenolysis. Fmoc is removed in base.

- Section 27.16 Carboxyl groups are normally protected as benzyl, methyl, or ethyl esters. Hydrolysis in dilute base is normally used to deprotect methyl and ethyl esters. Benzyl protecting groups are removed by hydrogenolysis.
- Section 27.17 Peptide bond formation between a protected amino acid having a free carboxyl group and a protected amino acid having a free amino group can be accomplished with the aid of *N,N*-dicyclohexylcarbodiimide (DCCI).



- Section 27.18 In the Merrifield method the carboxyl group of an amino acid is anchored to a solid support and the chain extended one amino acid at a time. When all the amino acid residues have been added, the polypeptide is removed from the solid support.
- Section 27.19 Two **secondary structures** of proteins are particularly prominent. The *pleated sheet* is stabilized by hydrogen bonds between NOH and C=O groups of adjacent chains. The *α helix* is stabilized by hydrogen bonds within a single polypeptide chain.
- Section 27.20 The folding of a peptide chain is its **tertiary structure**. The tertiary structure has a tremendous influence on the properties of the peptide and the biological role it plays. The tertiary structure is normally determined by X-ray crystallography.

Many globular proteins are enzymes. They accelerate the rates of chemical reactions in biological systems, but the kinds of reactions that take place are the fundamental reactions of organic chemistry. One

way in which enzymes accelerate these reactions is by bringing reactive functions together in the presence of catalytically active functions of the protein.

Section 27.21 Often the catalytically active functions of an enzyme are nothing more than proton donors and proton acceptors. In many cases a protein acts in cooperation with a **coenzyme**, a small molecule having the proper functionality to carry out a chemical change not otherwise available to the protein itself.

Section 27.22 Many proteins consist of two or more chains, and the way in which the various units are assembled in the native state of the protein is called its **quaternary structure**.