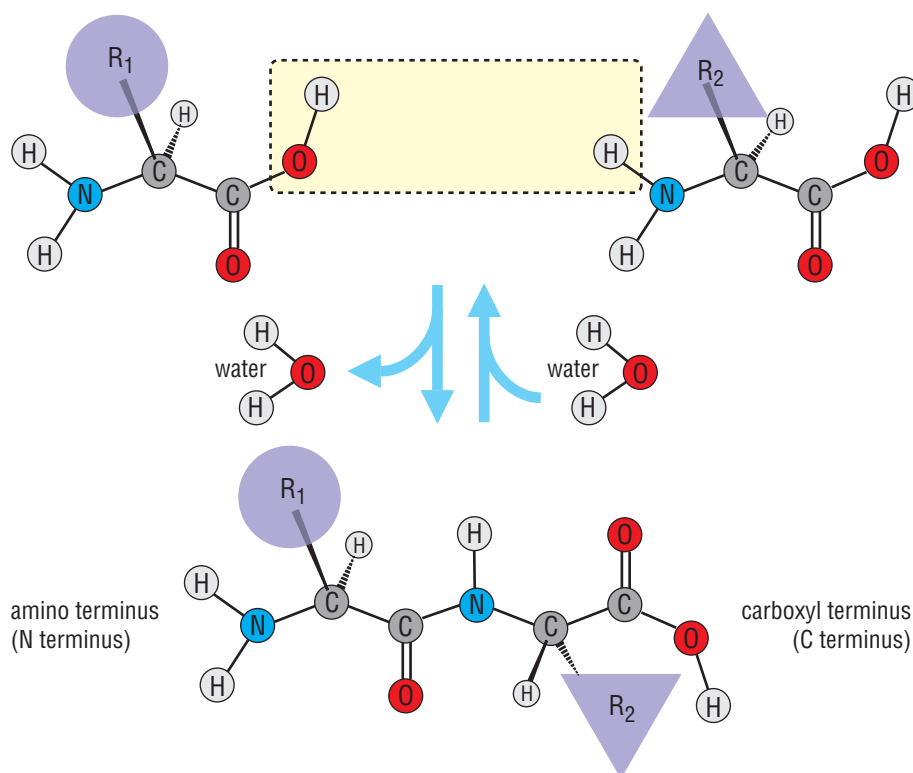


## 1-3 The Peptide Bond

### Proteins are linear polymers of amino acids connected by amide bonds

Amino acids are crucial components of living cells because they are easy to polymerize.  $\alpha$ -Amino acids are preferable to  $\beta$ -amino acids because the latter are too flexible to form spontaneously folding polymers. The amino acids of a protein chain are covalently joined by amide bonds, often called **peptide bonds**; for this reason, proteins are also known as **polypeptides**. Proteins thus have a repeating **backbone** from which 20 different possible kinds of side chains protrude (see Figure 1-8). On rare occasions, nonstandard side chains are found. In plants, a significant number of unusual amino acids have been found in proteins. In mammals, however, they are largely confined to small hormones. Sometimes, post-translational modification of a conventional amino acid may convert it into a nonstandard one. Examples are the non-enzymatic carbamylation of lysine, which can produce a metal-ion ligand, thereby activating an enzyme; and the deamidation of asparagine, which alters protein stability and turnover rate.

Chemically, the peptide bond is a covalent bond that is formed between a carboxylic acid and an amino group by the loss of a water molecule (Figure 1-7). In the cell, the synthesis of peptide bonds is an enzymatically controlled process that occurs on the ribosome and is directed by the mRNA template. Although peptide bond formation can be reversed by the addition of water (**hydrolysis**), **amide bonds** are very stable in water at neutral pH, and the hydrolysis of peptide bonds in cells is also enzymatically controlled.



**Figure 1-7 Peptide bond formation and hydrolysis** Formation (top to bottom) and hydrolysis (bottom to top) of a peptide bond requires, conceptually, loss and addition, respectively, of a molecule of water. The actual chemical synthesis and hydrolysis of peptide bonds in the cell are enzymatically controlled processes that in the case of synthesis nearly always occurs on the ribosome and is directed by an mRNA template. The end of a polypeptide with the free amino group is known as the amino terminus (N terminus), that with the free carboxyl group as the carboxyl terminus (C terminus).

#### Definitions

**amide bond:** a chemical bond formed when a carboxylic acid condenses with an amino group with the expulsion of a water molecule.

**backbone:** the repeating portion of a **polypeptide** chain, consisting of the N-H group, the alpha-carbon C-H group, and the C=O of each amino-acid residue. Residues are linked to each other by means of **peptide bonds**.

**dipole moment:** an imaginary vector between two

separated charges that may be full or partial. Molecules or functional groups having a dipole moment are said to be polar.

**hydrolysis:** breaking a covalent bond by addition of a molecule of water.

**peptide bond:** another name for **amide bond**, a chemical bond formed when a carboxylic acid condenses with an amino group with the expulsion of a water molecule. The term peptide bond is used only when both groups come from amino acids.

**phi torsion angle:** see **torsion angle**.

**polypeptide:** a polymer of amino acids joined together by **peptide bonds**.

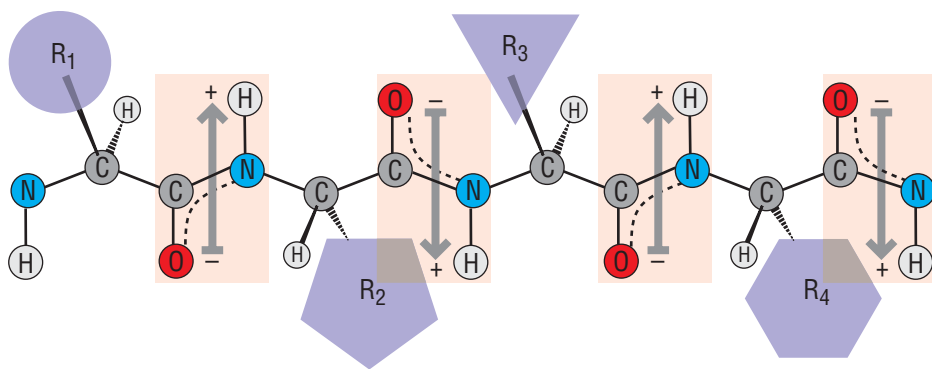
**psi torsion angle:** see **torsion angle**.

**resonance:** delocalization of bonding electrons over more than one chemical bond in a molecule. Resonance greatly increases the stability of a molecule. It can be represented, conceptually, as if the properties of the molecule were an average of several structures in which the chemical bonds differ.

### The properties of the peptide bond have important effects on the stability and flexibility of polypeptide chains in water

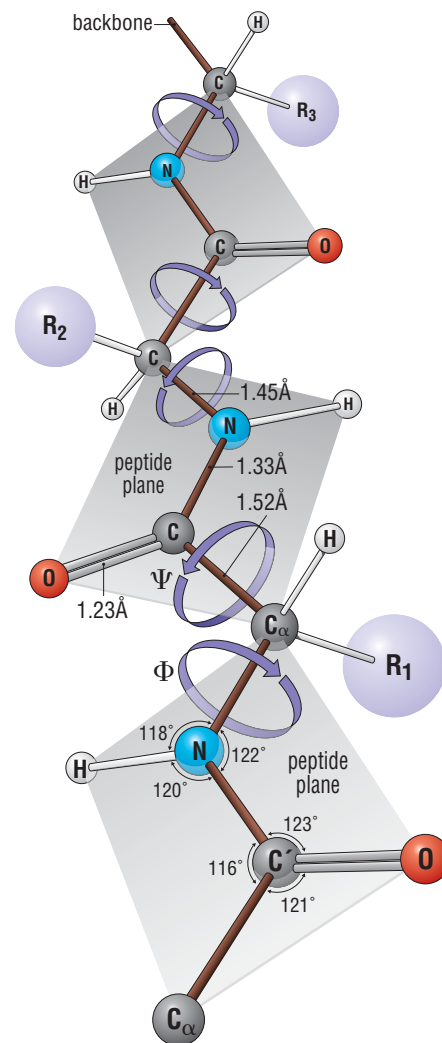
The properties of the amide bond account for several important properties of polypeptide chains in water. The stability of the peptide bond, as well as other properties important for the behavior of polypeptides, is due to **resonance**, the delocalization of electrons over several atoms. Resonance has two other important consequences. First, it increases the polarity of the peptide bond: the **dipole moment** of each peptide bond is shown in Figure 1-8. The polarity of the peptide bond can make an important contribution to the behavior of folded proteins, as discussed later in section 1-6.

Second, because of resonance, the peptide bond has partial double-bond character, which means that the three non-hydrogen atoms that make up the bond (the carbonyl oxygen O, the carbonyl carbon C and the amide nitrogen N) are coplanar, and that free rotation about the bond is limited (Figure 1-9). The other two bonds in the basic repeating unit of the polypeptide backbone, the N-C $\alpha$  and C $\alpha$ -C bonds (where C $\alpha$  is the carbon atom to which the side chain is attached), are single bonds and free rotation is permitted about them provided there is no steric interference from, for example, the side chains. The angle of the N-C $\alpha$  bond to the



**Figure 1-8** Schematic diagram of an extended polypeptide chain. The repeating backbone is shown, with schematized representations of the different side chains (R<sub>1</sub>, R<sub>2</sub> and so on). Each peptide bond is shown in a shaded box. Also shown are the individual dipole moments (arrows) associated with each bond. The dashed lines indicate the resonance of the peptide bond.

adjacent peptide bond is known as the **phi torsion angle**, and the angle of the C-C $\alpha$  bond to the adjacent peptide bond is known as the **psi torsion angle** (see Figure 1-9). Thus a protein is an unusual kind of polymer, with rotatable covalent bonds alternating with rigid planar ones. This combination greatly restricts the number of possible conformations that a polypeptide chain can adopt and makes it possible to determine from simple steric considerations the most likely backbone conformation angles for polypeptide residues other than glycine.



**Figure 1-9** Extended polypeptide chain showing the typical backbone bond lengths and angles. The planar peptide groups are indicated as shaded regions and the backbone torsion angles are indicated with circular arrows, with the phi and psi torsion angles marked. The omega torsion angle about the C-N peptide bond is usually restricted to values very close to 180° (*trans*), but can be close to 0° (*cis*) in rare cases. X-H bond lengths are all about 1 Å.

**torsion angle:** the angle between two groups on either side of a rotatable chemical bond. If the bond is the C $\alpha$ -N bond of a peptide backbone the torsion angle is called **phi**. If the bond is the C $\alpha$ -C backbone bond, the angle is called **psi**.

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