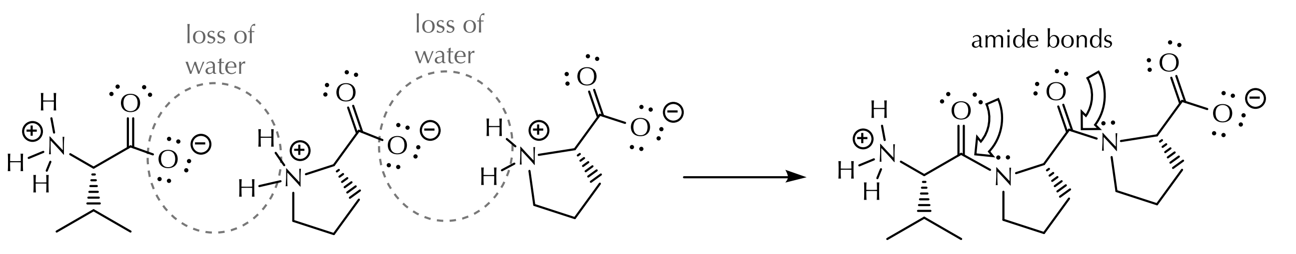
Reflections About Science: The Amide in Nature

Among all of the acid derivatives, the formation of the amide bond is high on the list of the most important ones. The stability of the amide bond is reflected in their occurrence in nature: amino acids are joined together by amide bonds (Figure 1370). Because, as the name suggests, amino acids have an acid and a base in the same molecule, the more stable zwitterionic form is shown in Figure 1370.

Figure 1370

Individual amino acids are joined through amide bonds.



valine　proline　proline

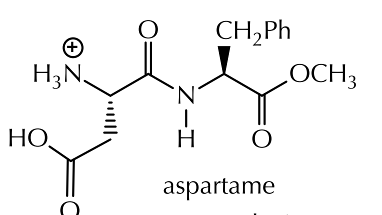
three amino acids

a tripeptide found in fermented milk containing added biologically active peptides, shows blood pressure lowering effects in animal tests

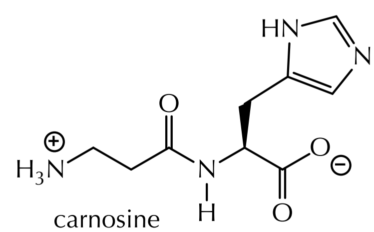
The process of connecting one amino acid to another can be repeated many times. Although the classifications are not used precisely, molecules made from connecting 2–20 amino acids together are called oligopeptides (dipeptide for 2, tripeptide for 3, etc.). Lengths in 10–30 range are simply called peptides, and combinations of these are called polypeptides or proteins. A few of these small molecules and their biological functions are shown in Figure 1371.

Figure 1371

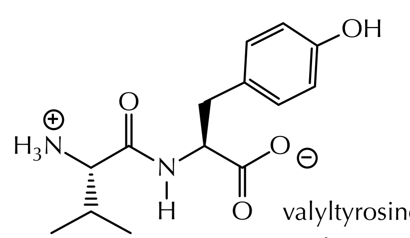
Small peptides that are biologically active.



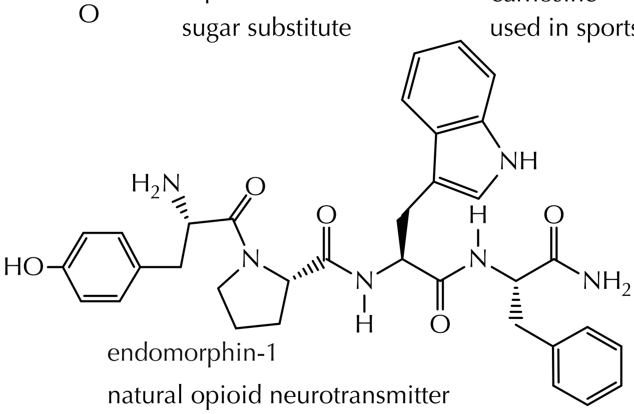
aspartame
sugar substitute



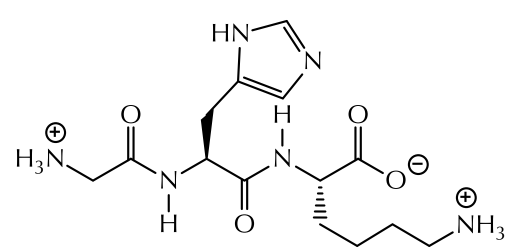
carnosine
used in sports medicines



valyltyrosine
antihypertensive



endomorphin-1
natural opioid neurotransmitter



copper peptide GHK-Cu
antiaging cosmetic

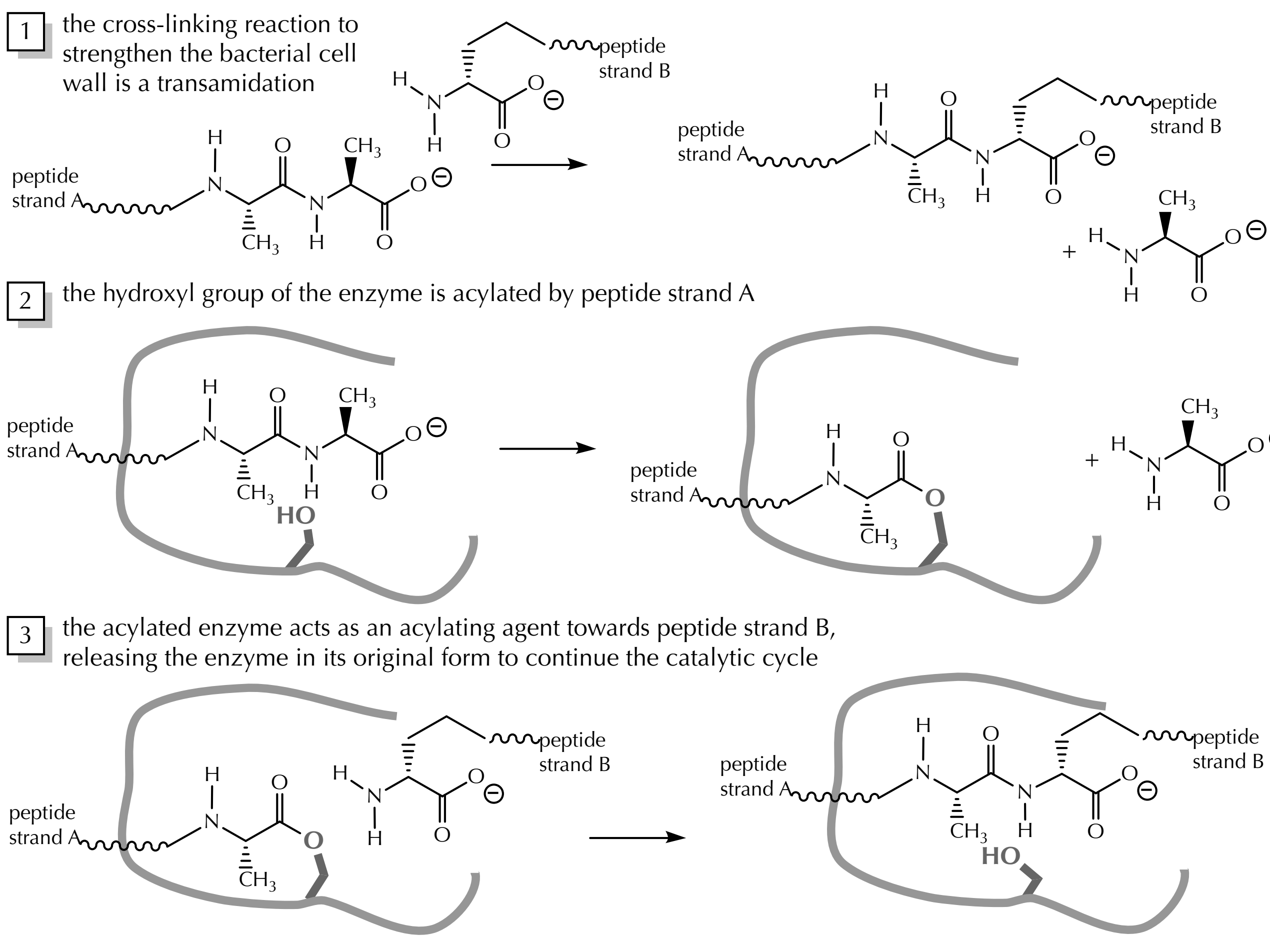
Proteins are important biomolecules that play various roles in your body, including contributing to structure of bone, skin, and nails, and serving as enzymes, which are the key chemical catalysts for the reactions in your cells. The genetic code carried by your genes provides the specific sequences for 19,000–20,000 different proteins, all of which are strands of amino acids connected to each other with amide bonds.

There are no life forms on earth that do not involve the chemistry of proteins, peptides, and the amide bond. Bacteria, which are neither plant nor animal, have cell walls that are rigid, as are the cell walls in plants. Bacterial cell walls include short strands of proteins that need to be stitched together with carbohydrate molecules, through the formation of amide bonds, to provide mechanical strength to the cell walls. The class of molecules known as penicillin antibiotics disrupts the formation of these amide bonds and cause the bacteria to mature with flaws in the construction of their cell walls. Like a water balloon with a thin spot, the flawed bacteria rupture due to their inability to handle their internal water pressure.

The amide bonds that get incorporated into a bacterial cell wall are formed by an acylation reaction. Under normal conditions, two amino acids need to be joined in an acylation reaction to give a new amide bond. This process requires an enzyme with a singularly important hydroxyl group. The carboxylic acid end of one of the amino acids in the growing bacterial cell wall forms an ester with the hydroxyl group of the enzyme (yet another acylation reaction). The acylated enzyme is the acylating agent used by the other amino acid to form the desired amide bond. The schematic process for how the amide bond forms that strengthens the bacterial cell wall is shown in Figure 1372.

Figure 1372

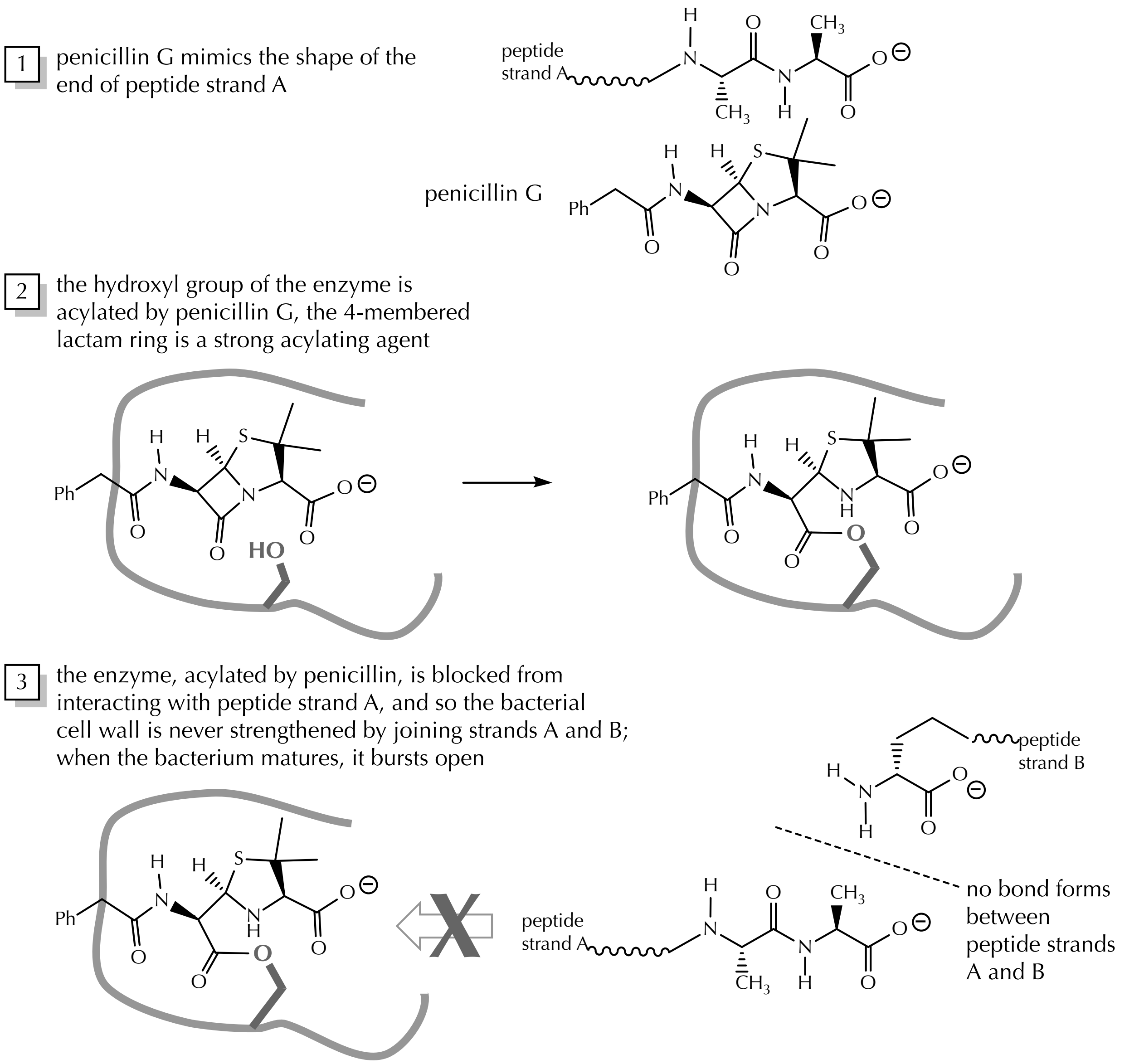
Schematic diagram for forming an amide bond in a bacterial cell wall using the hydroxyl group of an enzyme and a series of acylation reactions.



Penicillin molecules have molecular shapes that mimic a piece of the bacterial cell wall, and the enzyme will react with them in competition with the bacteria. The reactive part of a penicillin molecule is also an amide, but it is a cyclic amide (called a beta-lactam) that is highly reactive due to the strain energy of the 4-membered ring (Figure 1373). Penicillin molecules are potent acylating agents, and when the enzyme needed to strengthen the cell wall gets acylated, it no longer has the hydroxyl group it needs to help form that important amide bond. The lack of some of these amide bonds weakens the cell wall, and the bacterium ruptures and is not functional.

Figure 1373

Schematic diagram for how penicillin acylates the enzyme needed for forming an amide bond in a bacterial cell wall.



This penicillin example begins to reveal the underlying organic chemistry that can be used to help explain complex biological phenomena. The general description about weakening the cell wall during its development is something you could understand before learning organic chemistry. But, with this chapter on acylation reactions, your ability to appreciate this story is higher than it would have been prior to learning the chemistry in this chapter. Look forward to more of these examples as you move through the remaining chapters.