Bioorganic chemistry provides a link between the work of the organic chemist and biochemist, and this chapter is intended to serve as a link between organic chemistry, biochemistry, and protein and medicinal chemistry or pharmacology. The emphasis is chemical and one is continually reminded to compare and contrast biochemical reactions with mechanistic and synthetic counterparts. The organic chemistry of the peptide bond and the phosphate ester linkage (see Chapter 3) are presented “side by side”; this way, a surprising number of similarities are readily seen.

The last decade has witnessed an important breakthrough in the field of asymmetric synthesis of amino acids. We can now tailor make all kinds of α-amino acids with a high control of chirality. Now we have ways to minimize a problem always present before: the danger of racemization. We also have access to asymmetric synthesis in the presence of polyfunctional groups. In pharmaceutical industries this is particularly useful for the synthesis of enantiomerically pure peptides for direct therapeutic use.

Although this chapter is devoted to the chemistry of amino acids and molecules appertained to amino acids, a small introduction to the chemistry of the living cells seems appropriate at the beginning of a book oriented toward the understanding of biological processes at the chemical level. A better understanding of enzyme action and biological transformations in general often relies on a profound knowledge of simpler processes in the cells such as sugar metabolism and energy storage. Therefore, this
exercise will serve to bridge comprehension of activation processes in biochemistry with reactivity in organic chemistry.

2.1 Chemistry of the Living Cells

Historically, the metabolism of glucose goes back to the seminal work of A. Szent-Györgyi and H. Krebs, between 1935 to 1937. For the sake of simplicity the presentation will be limited to the combustion of sugar molecules in foods. In the context of bioorganic chemistry, where models of enzymes are developed, it is important to have a general understanding of the chemistry within the biological cell. An appreciation of these processes at a molecular and a supramolecular level is of prime importance since the network connecting these metabolic cycles is an integral part of the “unifying theme” of bioorganic chemistry (16).

When food such as carbohydrate is eaten and digested, a large number of enzymes are called upon to cleave the sugar molecules to smaller fragments that will eventually be further oxidized by mitochondrial enzymes. Because of the exothermic nature of these processes, a good fraction (up to 46%) of the energy liberated will be stored as energy-rich phosphodiester bonds in the form of ATP molecules (see Chapter 3). At the far end of the chain, molecular oxygen is ultimately reduced to water molecules. This is the essence of breathing. Respiration is basically the result of a series of oxidation of carbon molecules to produce water.

The metabolism of a sugar molecule such as glucose is much more complex than this general presentation seems to indicate. In fact, two distinct processes are involved. First, the six carbon molecules of glucose are cleaved and converted into two molecules of pyruvic acid (a three-carbon molecule) by a series of up to ten different enzymatic reactions. This linear sequence of events is known as glycolysis. On the other hand, acetyl-CoA (acetylated coenzyme A) is completely burned to CO$_2$ molecules via the universally accepted tricarboxylic acid (TCA) or Krebs cycle. Interestingly, the bridge between pyruvate ion, the end product of the glycolysis, and the starting material of the TCA cycle is not a direct process but involves a pathway where the coenzyme thiamine pyrophosphate (TPP) and lipoic acid (LA) are both implicated (see