Chapter 3
Bioorganic Chemistry of the Phosphate Groups and Polynucleotides

“La chimie crée son objet...”
M. Berthelot
1860

Too often a detailed description of the synthesis and properties of peptides is given without consideration of the analogous, but equally important, synthesis and properties of phosphodiesters, and vice versa. Indeed many of the problems and strategies (i.e., use of DCC, common protecting groups, polymeric synthesis, etc.) are similar, if not the same, yet they are never presented “side by side.” It is with this purpose in mind that this chapter is written.

3.1 Basic Considerations

In order to maintain the life process, it is necessary to pass on specific information from one generation of organisms to the next. Such information is vital, for it allows the continuation of those traits or properties of the organism that insure survival. This information must be stored, to be used at an appropriate time, much as data may be stored and played on a tape recorder. As such, the job of information storage and processing must have a molecular basis. Indeed, it is not difficult to imagine some of the properties that are requisite for a molecular biological “tape.”

Considering that a great deal of information must be stored on this molecule (i.e., the type of organism, physical characteristics, chemical pathways, etc.), it is expected that it must be a biopolymer. Perhaps a
protein could function as a storage molecule? Probably not, since proteins already play an important structural and functional (enzyme catalyst) role in the cell. Such an important job as data storage must require a unique macromolecular structure that cannot possibly be confused with routine cellular processes. This special biopolymer is expected to be rather homogenous in structure, for it must fulfill one crucial role. It is not expected to be as diverse as enzyme structures for the latter are capable of participating in a wide variety of chemical reactions. On the other hand, it must have a heterogenous component in order to carry the different information necessary to the cell. This biopolymer is expected to be of a rigid or defined shape, because it must be able to interact with the cellular apparatus when it becomes necessary to transmit the stored information.

The molecules that function as the monomeric units for genetic information storage are nitrogen heterocycles: derivatives of purine and pyrimidine. The polymeric molecule that functions to both store and pass on genetic information is deoxyribonucleic acid (DNA). The related polymer ribonucleic acid (RNA) helps in the passage of this genetic information. It acts as the messenger that converts a specific genetic message to a specific amino acid sequence. The common purine bases of DNA and RNA are adenine and guanine. The common pyrimidine bases of DNA are cytosine and thymine (5-methyluracil), while for RNA they are cytosine and uracil. The purines and pyrimidines occur in combination with the sugar ribose (in RNA) or deoxyribose (in DNA) via the anomeric carbon of the latter. The glycosidic linkage occurs through the ring nitrogen of the base: either nitrogen-9 of the purines or nitrogen-1 of the pyrimidines. This chemical combination of a sugar and base (with elimination of water) is referred to as a nucleoside.

Other bases are also present in the DNA and RNA polymers, but to a much lesser extent. Examples include 5-methyl cytosine (present in the DNA of some plants and bacteria), 5-hydroxymethyl cytosine (present in the DNA of T-even phages; bacterial viruses) and 4-thiouracil (present in some bacterial tRNA).

It is possible to esterify a sugar hydroxyl with either phosphoric acid, pyrophosphoric acid, or triphosphoric acid to give the nucleoside mono-, di-, or triphosphates, respectively. The example of adenosine triphosphate (ATP) has already been encountered. The combination of a base, sugar, and phosphate is referred to as a nucleotide. Just as the amino acid is the monomeric unit of the protein polymer, the nucleotide (nucleoside monophosphate) is the monomeric unit of the DNA and RNA polymers. Further, just as the monomeric amino acids are linked via an amide (peptide) linkage, the monomeric nucleotides are linked via a phosphoester linkage.

It is important to realize that it is the purine or pyrimidine base that carries the genetic information, just as the side chain of an amino acid