## 1 DNA INTERCALATION AND ITS CONSEQUENCES

In general, intercalation can be defined as the reversible inclusion of a molecule into a compound with a layered structure. In biochemistry, intercalation refers to a mode of interaction of small organic molecules with DNA.

Many anticancer drugs in clinical use interact with DNA through intercalation, which can be defined as the process by which compounds containing planar aromatic or heteroaromatic ring systems are inserted between adjacent base pairs perpendicularly to the axis of the helix and without disturbing the overall stacking pattern due to Watson–Crick hydrogen bonding. Because many typical intercalating agents contain three or four fused rings that absorb light in the ultraviolet (UV)-visible region of the electromagnetic spectrum, they are usually known as chromophores. In addition to the chromophore, other substituents in the intercalator molecule may highly influence the binding mechanism, the geometry of the ligand–DNA complex, and the sequence selectivity, if any.

The intercalation process[1,2] starts with the transfer of the intercalating molecule from an aqueous environment to the hydrophobic space between two adjacent DNA base pairs. This process is thermodynamically favored because of the positive entropy contribution associated with disruption of the organized shell of water molecules around the ligand (hydrophobic effect). To accommodate the ligand, DNA must undergo a conformational change involving an increase in the vertical separation between the base pairs to create a cavity for the incoming chromophore. The double helix is thereby partially unwound,[3] which leads to distortions of the sugar–phosphate backbone and changes in the twist angle between successive base pairs (Figure 7.1). Once the drug has been sandwiched between the DNA base

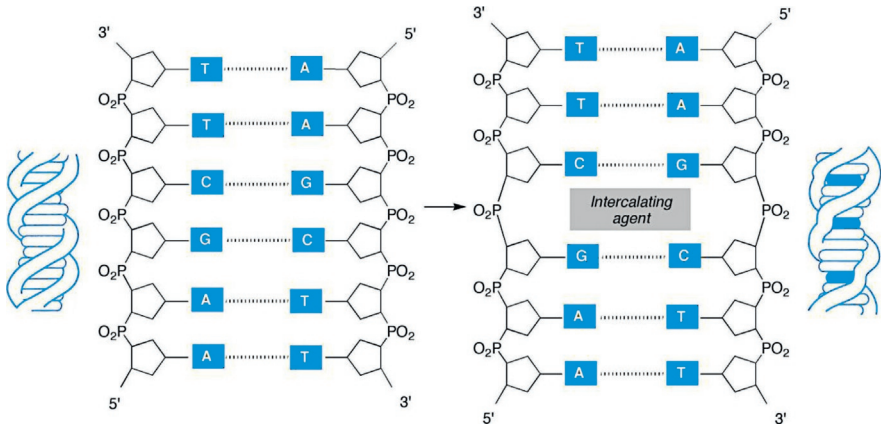


**FIGURE 7.1**

Deformation of DNA by intercalating agents.