

FIGURE 11.12 • Rotation around the glycosidic bond is sterically hindered; syn versus anti conformations in nucleosides are shown.

Nucleoside Conformation

In nucleosides, rotation of the base about the glycosidic bond is sterically hindered, principally by the hydrogen atom on the C-2' carbon of the furanose. (This hindrance is most easily seen and appreciated by manipulating accurate molecular models of these structures.) Consequently, nucleosides and nucleotides (see next section) exist in either of two conformations, designated *syn* and *anti* (Figure 11.12). For pyrimidines in the *syn* conformation, the oxygen substituent at position C-2 lies immediately above the furanose ring; in the *anti* conformation, this steric interference is avoided. Consequently, pyrimidine nucleosides favor the *anti* conformation. Purine nucleosides can adopt either the *syn* or *anti* conformation. In either conformation, the roughly planar furanose and base rings are not coplanar but lie at approximately right angles to one another.

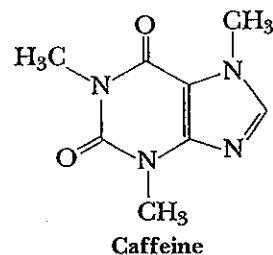
HUMAN BIOCHEMISTRY

Adenosine: A Nucleoside with Physiological Activity

For the most part, nucleosides have no biological role other than to serve as component parts of nucleotides. Adenosine is an exception. In mammals, adenosine functions as an **autocoid**, or "local hormone." This nucleoside circulates in the bloodstream, acting locally on specific cells to influence such diverse physiological phenomena as blood vessel dilation, smooth muscle contraction, neuronal discharge, neurotransmitter release, and metabolism of fat. For example, when muscles work hard, they release adenosine, causing the surrounding blood vessels to dilate, which in turn increases the flow of blood and its delivery of O₂ and nutrients to the muscles. In a different autocoid role, adenosine acts in regulating heartbeat. The natural rhythm of the heart is controlled by a pacemaker, the sinoatrial node, that cyclically sends a wave of electrical excitation to the heart muscles. By blocking the flow of electrical current, adenosine slows the heart rate. *Supraventricular tachycardia* is a heart condition characterized by a rapid heartbeat. Intravenous injection of adenosine causes a momentary interruption of the rapid cycle of contraction and

restores a normal heart rate. Adenosine is licensed and marketed as *Adenocard*TM to treat supraventricular tachycardia.

In addition, adenosine is implicated in sleep regulation. During periods of extended wakefulness, extracellular adenosine levels rise as a result of metabolic activity in the brain, and this increase promotes sleepiness. During sleep, adenosine levels fall. Caffeine promotes wakefulness by blocking the interaction of extracellular adenosine with its neuronal receptors.*



*Porrka-Heiskanen, T., et al., 1997. Adenosine: A mediator of the sleep-inducing effects of prolonged wakefulness. *Science* 276:1265-1268.