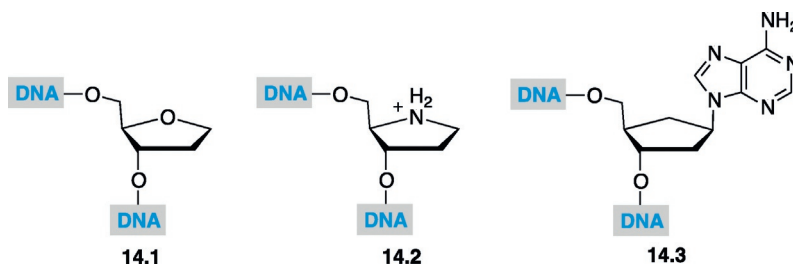


FIGURE 14.21

DNA strand scission by bifunctional glycosylases.



4.2.2 Inhibitors of APE-1 and Compounds Targeting the AP Site at DNA

APE-1 is a multifunctional protein of approximately 35.5 kDa that possesses several nuclease activities, including the cleaving of the phosphodiester bonds at the 5' end of the AP sites. In one of the proposed mechanisms for the APE-1 catalyzed reaction,¹²⁷ His-309 acts as a base and abstracts a proton from a water molecule to generate the active site nucleophile, while Asp-283 helps to stabilize the generated positive charge by forming a hydrogen bond with the His-NH group. The metal ion bound by