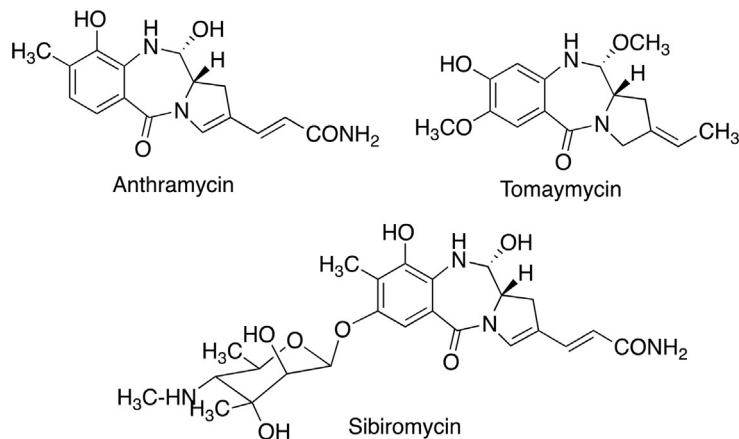


7 PYRROLO[1,4]BENZODIAZEPINES

Anthramycin, tomaymycin, and sibiromycin are natural pyrrolo[1,4]benzodiazepine antitumor antibiotics that react with the minor groove of DNA to form covalently bound complexes.¹⁰⁰ They show activity toward several tumors, but their clinical use is limited by their cardiotoxicity and tissue necrosis induction.



These compounds form a covalent bond with the 2-amino group of guanine, as shown by X-ray diffraction,¹⁰¹ through the formation of an intermediate iminium cation (Figure 6.28).

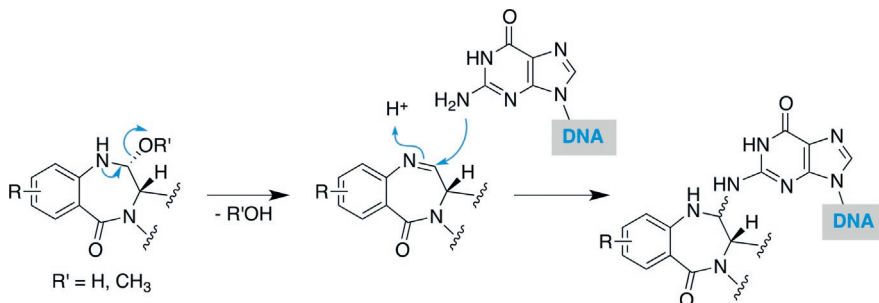


FIGURE 6.28

DNA alkylation by pyrrolo[1,4]benzodiazepines.