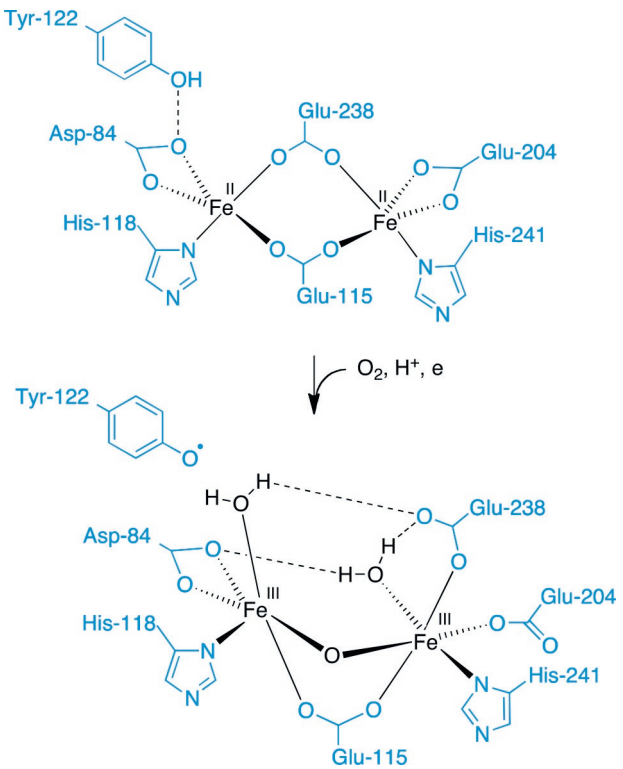
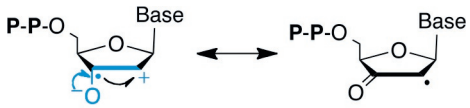


FIGURE 2.6

Generation of a tyrosyl radical in the active site of ribonucleotide reductase.



2.2

3.2 GALLIUM SALTS AND COMPLEXES

Gallium ions can inhibit DNA synthesis through substitution of Ga^{3+} for Fe^{3+} in the M_2 subunit of ribonucleotide reductase. Furthermore, their synergy with hydroxyurea has been demonstrated.[5] Ga^{3+} is usually administered as its nitrate salt or as gallium maltolate, a complex formed by a Ga^{3+} cation coordinated and three maltolate ligands, derived from 2-methyl-3-hydroxy-4-pyrone (maltol). Clinical studies have shown gallium nitrate to have significant antitumor activity against non-Hodgkin's lymphoma and bladder cancer,[6] but only 60% of patients show a positive response due to resistance problems associated with decreased Ga uptake and other mechanisms. It shows renal toxicity because it tends to