

# Reductive and Oxidative DNA Damage by Photoactive Platinum(II) Intercalators

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## Abstract:

Several photoactive platinum  $\pi$ -diimine intercalators have been prepared to develop new probes of DNA oxidation and reduction chemistry. Five water-soluble bis(mes')Pt(II) complexes (mes' = *N,N,N',3,5*-pentamethylaniline) with various aromatic  $\pi$ -diimine ligands (dppz = dipyridophenazine, np = naphtha[2,3-*f*][1, $\pi$ ]phenanthroline, CN-np = naphtho[2,3-*f*][1,10]phenanthroline-9-carbonitrile, CN<sub>2</sub>-np = naphtho[2,3-*f*][1,10]phenanthroline-9,14-dicarbonitrile, and bp = benzo-*f*[1,10]phenanthroline) were synthesized. The complex [(np)Pt(mes')<sub>2</sub>]Cl<sub>2</sub> was also characterized by X-ray crystallography, and the crystal structure shows that the *ortho*-methyl groups of the mes' ligands conveniently block substitution at the vacant sites of platinum without overlapping with the intercalating  $\pi$ -diimine ligand. The Pt(II) complexes were found to have excited-state oxidation and reduction potentials of -0.6 to -1.0 and 1.0 to 1.5 V versus NHE, respectively, making them potent photoreductants as well as photooxidants. Many of the complexes are found to promote the photooxidation of *N*<sup>2</sup>-cyclopropyldeoxyguanosine (d<sup>Cp</sup>G). Photoexcited [(dppz)Pt(mes')<sub>2</sub>]<sup>2+</sup> is found to be most efficient in this photooxidation, as well as in the photoreduction of *N*<sup>4</sup>-cyclopropylcytidine (<sup>Cp</sup>C); these modified nucleosides rapidly decompose in a ring-opening reaction upon oxidation or reduction. Photoexcited [(dppz)Pt(mes')<sub>2</sub>]Cl<sub>2</sub>, upon intercalation into the DNA  $\pi$ stack, is found, in addition, to promote reductive and oxidative damage within the DNA duplex, as is also probed using the kinetically fast electron and hole traps, <sup>Cp</sup>C and <sup>Cp</sup>G. These Pt complexes may therefore offer useful reactive tools to compare and contrast directly reductive and oxidative chemistry in double helical DNA.