Oxidative Damage by Ruthenium Complexes Containing the Dipyridophenazine Ligand or Its Derivatives: A Focus on Intercalation

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Abstract:

Interactions with DNA by a family of ruthenium(II) complexes bearing the dppz (dppz = dipyridophenazine) ligand or its derivatives have been examined. The complexes include $Ru(bpy)_2(dppx)^{2+}$ (dppx = 7,8-dimethyldipyridophenazine), $Ru(bpy)_2(dpq)^{2+}$ (dpq = dipyridoquinoxaline), and $Ru(bpy)_2(dpqC)^{2+}$ (dpqC = dipyrido-6,7,8,9-tetrahydrophenazine). Their ground and excited state oxidation/reduction potentials have been determined using cyclic voltammetry and fluorescence spectroscopy. An intercalative binding mode has been established on the basis of luminescence enhancements in the presence of DNA, excited state quenching, fluorescence polarization values, and enantioselectivity. Oxidative damage to DNA by these complexes using the flash/quench method has been examined. A direct correlation between the amount of guanine oxidation obtained via DNA charge transport and the strength of intercalative binding was observed. Oxidative damage to DNA through DNA-mediated charge transport was also compared directly for two DNA-tethered ruthenium complexes. One contains the dppz ligand that binds avidly by intercalation, and the other contains only bpy ligands, that, while bound covalently, can only associate with the base pairs through groove binding. Long range oxidative damage was observed only with the tethered, intercalating complex. These results, taken together, all support the importance of close association and intercalation for DNA-mediated charge transport. Electronic access to the DNA base pairs, provided by intercalation of the oxidant, is a prerequisite for efficient charge transport through the DNA π-stack.

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