$[Ru(bpy)_2(L)]Cl_2$: Luminescent Metal Complexes That Bind DNA Base Mismatches

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Abstract:

Here we report the synthesis of luminescent ruthenium complexes that bind DNA base pair mismatches. $[Ru(bpy)_2(tpqp)]Cl_2$ (tpqp = 7,8,13,14-tetrahydro-6-phenylquino[8,7-*k*][1,8]phenanthroline), $[Ru(bpy)_2(pqp)]Cl_2$ (pqp = 6-phenylquino[8,7-*k*][1,8]phenanthroline), and $[Ru(bpy)_2(tactp)]Cl_2$ [tactp = 4,5,9,18-tetraazachryseno[9,10-*b*]triphenylene] have been synthesized, and their spectroscopic properties in the absence and presence of DNA have been examined. While $[Ru(bpy)_2(pqp)]^{2+}$ shows no detectable luminescence, $[Ru(bpy)_2(tpqp)]^{2+}$ is luminescent in the absence and presence of DNA with an excited-state lifetime of 10 ns and a quantum yield of 0.002. Although no increase in emission intensity is associated with binding to mismatch-containing DNA, luminescence quenching experiments and measurements of steady-state fluorescence polarization provide evidence for preferential binding to oligonucleotides containing a CC mismatch. Furthermore, by marking the site of binding through singlet oxygen sensitized damage, the complex has been shown to target a CC mismatch site directly with a specific binding affinity, $K_b = 4 \times 10^6\ M^{-1}$. $[Ru(bpy)_2(tactp)]^{2+}$, an analogue of $[Ru(bpy)_2(dppz)]^{2+}$ containing a bulky intercalating ligand, is luminescent in aqueous solution at micromolar concentrations and exhibits a 12-fold enhancement in luminescence in the presence of DNA. The complex, however, tends to aggregate in aqueous solution; we find a dimerization constant of $9.8 \times 10^5\ M^{-1}$. Again, by singlet oxygen sensitization it is apparent that $[Ru(bpy)_2(tactp)]^{2+}$ binds preferentially to a CC mismatch; using a DNase I footprinting assay, a binding constant to a CC mismatch of $8 \times 10^5\ M^{-1}$ is found. Hence results with these novel luminescent complexes support the concept of using a structurally demanding ligand to obtain selectivity in targeting single base mismatches in DNA. The challenge is coupling the differential binding we can obtain to differential luminescence.

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