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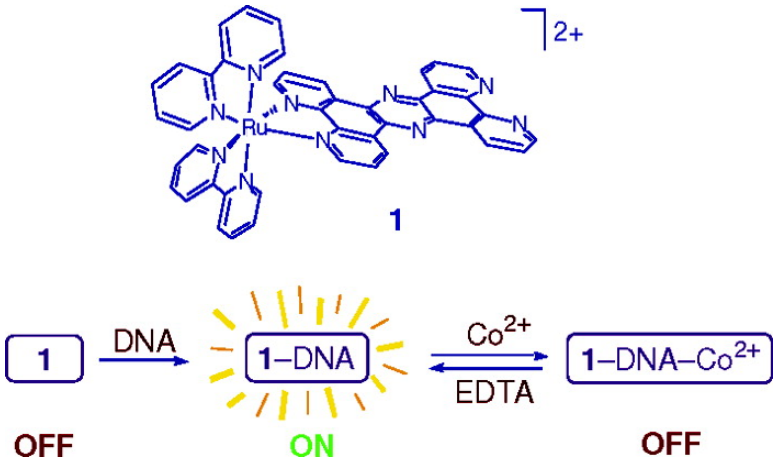

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Chemical Control of the DNA Light Switch: Cycling the Switch ON and OFF

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Since the initial report of long-range charge transfer through DNA,[1] a body of research has been amassed that supports the conclusion that duplex DNA is able to transport charge over long distances.[2] Various applications of the long distance charge transport by DNA have been explored, including electrochemical sensors of selected DNA sequences, hybridization, and base pair mismatches.[3] In addition, DNA may have potential applications as a template or as an element in DNA-based nanocircuits and molecular electronics,[4] including photoelectronics.[5] A requirement for the latter is a means to switch the photoactive molecule on and off, otherwise irradiation always results in charge transport.[5]

The emission of $[Ru(L)_2(dppz)]^{2+}$ (L = bpy (2,2′-bipyridine), phen (1,10-phenanthroline); dppz = dipyrido[3,2-*a*:2′,3′-*c*]phenazine) is enhanced ("turned on") upon DNA intercalation. These and related systems, commonly known as "DNA light-switch" complexes,[6] may prove to be useful in applications such as molecular-scale logic gates, DNA sensing, detection of mismatches, and in the signaling of DNA−protein binding.[7] Although other DNA light-switch complexes have appeared in the literature,[8] the steady-state photophysical properties and DNA binding of $[Ru(L)_2(dppz)]^{2+}$ (L = bpy, phen) remain the most widely investigated.[6,9] It was proposed that two or three Ru → dppz low-energy ^{3}MLCT excited states give rise to the DNA light-switch effect in these systems, one of which is nonemissive.[10] Calculations on these and related complexes support the presence of multiple low-lying triplet states.[11]

The emission properties of Ru(II) complexes possessing ligands with a phenazine unit provide a means to turn their luminescence on and off.[12] In the present work, we report two DNA light-switch complexes, one of which can be repeatedly cycled on and off through the addition of external agents. The molecular structures of $[Ru(bpy)_2(tpphz)]^{2+}$ (**1**) and $[Ru(bpy)_2(taptp)]^{2+}$ (**2**) are shown in Figure 1 (tpphz = tetrapyrido[3,2-*a*:2′,3′-*c*:3″,2″-*h*:2‴,3‴-*j*]phenazine, taptp = 4,5,9,18-tetraazaphenanthreno[9,10-*b*] triphenylene).

The absorption spectra of **1** and **2** exhibit ligand-centered $^1\pi\pi^*$ transitions at ∼285 nm (bpy) and in the 350−400 nm region (tpphz or taptp), as well as Ru → bpy and Ru → L (L = tpphz, taptp) MLCT transitions in the visible region. These assignments are supported by time-dependent density functional theory (TDDFT) calculations (Supporting Information). A 59-fold decrease in emission quantum yield, Φ_{em}, was measured for **1** in H_2O ($\Phi_{em} = 1.7 \times 10^{-4}$) relative to CH_3CN ($\Phi_{em} = 0.010$).[11,12] Similarly, for **2**, Φ_{em} increases from 5.9×10^{-4} in H_2O to 9.0×10^{-3} in CH_3CN.

For **1** (5 mM Tris, pH = 7.5, 50 mM NaCl), addition of calf-thymus DNA, ct-DNA, results in 38% hypochromicity of the $\pi\pi^*$ absorption at 380 nm, together with a shift to 387 nm. Less pronounced changes were observed for solutions of **2** in the presence of ct-DNA. As a consequence of π-stacking aggregation of **1** and **2** in aqueous media,[13] fitting of the absorption changes of each complex as a function of DNA concentration to obtain binding constants was not possible. An increase in the relative viscosity of herring sperm DNA solutions similar to that measured for the intercalator ethidium bromide was observed upon addition of each metal complex (Supporting Information), consistent with their DNA intercalation.[14]

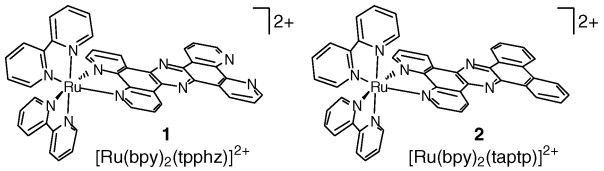

Figure 1. Molecular structures of **1** and **2**.

The 50- and 4-fold increases in the emission intensities of **1** and **2** in the presence of ct-DNA (5 mM Tris, pH = 7.5, 50 mM NaCl), respectively, also point at the intercalation of the complexes.[6−9] A shift in the emission maxima of 8.2 μM **1** from 634 nm ($\tau \approx 10$ ns) to 628 nm ($\tau = 640$ ns) is observed upon addition of up to 80 μM ct-DNA. In addition, the luminescence of 10.5 μM **2** ($\lambda_{em} = 623$ nm, $\tau = 178$ ns) shifts to 609 nm in the presence of 80 μM ct-DNA, with the appearance of a biexponential decay with $\tau_1 = 31$ ns (40%) and $\tau_2 = 569$ ns (60%), similar to results reported for related Ru(II) dppz complexes.[6,9] Fits of the changes in the emission intensity as a function of ct-DNA concentration for **1** and **2** result in $K_b = 8.8 \times 10^6$ M^{-1} ($s = 2.22$) and $K_b = 3.6 \times 10^5$ M^{-1} ($s = 0.69$), respectively.[15] Equilibrium dialysis of **1** and **2** with ct-DNA, results in $K_b = 3.5 \times 10^5$ M^{-1} and $K_b = 4.2 \times 10^5$ M^{-1}, respectively, which are typical for intercalators.[16]

The emission of DNA−intercalated **1** (switch on) can be statically quenched by various transition metal ions, thus turning the light switch off. The addition of an equimolar concentration of Co^{2+} to 9 μM **1** bound to 90 μM DNA (5 mM Tris, pH = 7.5, 50 mM NaCl) results in the static quenching of 95% of the luminescence (Supporting Information). Relative viscosity measurements of 50, 100, and 200 μM **1** bound to 1 mM herring sperm DNA (5 mM Tris, pH = 7.5, 50 mM NaCl) in the presence of 1:2, 1:1, and 2:1 [**1**]:[Co^{2+}] indicate that **1** remains intercalated in the presence of the ion (Supporting Information). No quenching of DNA−intercalated **2** by Co^{2+} is observed under similar experimental conditions. Static quenching of intercalated **1** was also observed upon addition of Zn^{2+}, Ni^{2+}, and Cu^{2+} ions.[12c,d]

The $^1\pi\pi^*$ transition of the tpphz ligand in intercalated **1** shifts from 387 to 383 nm in the presence of Co^{2+}, which provides additional evidence for the coordination of the ion to the tpphz ligand. Many intercalating octahedral Ru(II) and Rh(III) complexes have been shown to intercalate from the major groove of DNA.[17] If **1** intercalates from the major groove, then the transition metal

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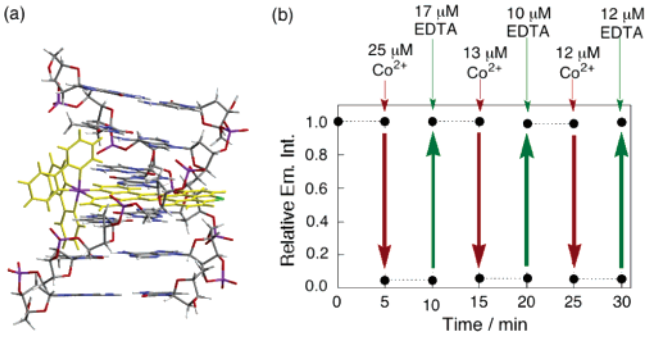

Figure 2. (a) Molecular docking model of Λ-**1** intercalated from the major groove between the central base pairs of a 5′-GTCGAC-3′ palindromic duplex with Co^{2+} coordinated to the tpphz ligand. (b) Relative emission intensity of a solution containing 12 μM **1** and 120 μM DNA (5 mM Tris, pH = 7.5, 50 mM NaCl) upon successive additions of Co^{2+} and EDTA (λ_{exc} = 450 nm, λ_{em} = 628 nm).

ion quenchers must bind to the tpphz ligand from the minor groove, as depicted in the model shown in Figure 2a.

The metal-centered oxidation potentials of **1** and **2** observed at +1.58 and +1.57 V vs NHE and bpy-centered reductions at −1.17 and −1.14 V vs NHE in CH_3CN, respectively, are typical for Ru(II) complexes with polypyridyl ligands.[18] The reduction waves at −0.73 and −0.85 V vs NHE are consistent with the reduction of the tpphz and taptp ligands in **1** and **2**, respectively.[12] Upon binding of Co^{2+} and Zn^{2+}, the tpphz ligand is easier to reduce by ∼0.13 V in **1**, and no shift of the reduction potential of the taptp ligand is observed in **2**. Owing to the high oxidation potential of Co^{2+} and Zn^{2+} ($E_{1/2}(M^{3+/2+})$ > 1.7 V vs NHE (M = Co, Zn) in 1:1 M^{2+}:**1** in CH_3CN), reductive quenching of the excited states of **1** ($E_{1/2}(Ru^{2+*/+})$ ≈ +1.5 V vs NHE) by these ions is unfavorable. The coordination of transition metal ions to the distal nitrogen atoms of the tpphz ligand in **1** results in changes to the electronic structure of the complex and affects the electronic transitions and reduction potential of the tpphz ligand. The quenching of the emission by the d^{10} Zn^{2+} ion indicates that the coordination of transition metals to the tpphz nitrogen atoms of **1** affects the relative energies of the emissive and nonemissive ^{3}MLCT excited states. It is likely that, in the case of the Co^{2+} ion, both energy transfer and electronic changes to the tpphz ligand result in the decrease in luminescence.

If one begins with 12 μM **1** and 25 μM Co^{2+} in the presence of 120 μM DNA (5 mM Tris, pH = 7.5, 50 mM NaCl), which represents conditions wherein the DNA light switch is off, the emission can be recovered completely (turned back on), by addition of 17 μM EDTA. It should be noted that the concentrations of Co^{2+} ions and EDTA required to turn the emission off and on are not equimolar due to the different binding constants of Co^{2+} for tpphz and EDTA.[19] Figure 2b shows the changes in the relative emission intensity of **1** bound to DNA as Co^{2+} and EDTA are added successively, thus flipping the DNA light switch on and off over a series of cycles. In this system the emission quenching and recovery is observed immediately following the addition of Co^{2+} or EDTA, respectively. Similar behavior was also observed for the Zn^{2+} ions, but in the case of Ni^{2+}, complete recovery of the emission following the addition of EDTA required several hours, consistent with the greater affinity of Ni^{2+} for the tpphz ligand in **1** relative to Co^{2+} and Zn^{2+}.[19]

In summary, cycling of the DNA light switch off and on has been accomplished for **1** through the successive introduction of Co^{2+} ions and EDTA, respectively. To our knowledge, this work presents the first example of a reversible DNA light switch.

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Supporting Information Available: Synthesis and characterization, relative viscosity measurements, quenching, electronic structure calculations. This material is available free of charge via the Internet at http://pubs.acs.org.

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