Cyclometallated platinum(II) complexes as luminescent switches for calf-thymus DNA

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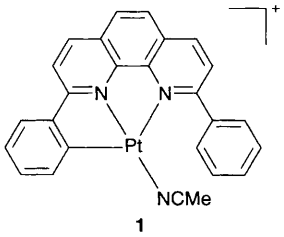
Intercalation of $[Pt^{II}(dpp\text{-}C,N,N')(MeCN)]^+$ 1 (dpp-*C*,*N*,*N*′ = C-deprotonated 2,9-diphenyl-1,10-phenanthroline) and $[Pt^{II}_2(pby\text{-}C,N,N')_2(\mu\text{-}dppm)]^{2+}$ 2 (pby-*C*,*N*,*N*′ C-deprotonated 6-phenyl-2,2′-bipyridine, dppm = diphenylphosphinomethane) into calf-thymus DNA leads to a dramatic enhancement of the photoluminescence of the platinum(II) complexes (I/I_0 = 271 1, 117 2); a much weaker DNA binding affinity of 2 [$K = (4.2 \pm 0.3) \times 10^4$ dm^3 mol^{-1}] than of 1 [$K = (1.0 \pm 0.1) \times 10^6$ dm^3 mol^{-1}] is observed.

The design of new coordinative unsaturated metallointercalators with emissive excited states for DNA binding studies is an area of growing interest.[1–4] Recently we reported that the photoluminescence of the platinum(II) complex, $[Pt^{II}(5,5'\text{-}Me_2bpy)(4\text{-}ampy)_2]^{2+}$ (5,5′-Me_2bpy = 5,5′-dimethylbipyridine, 4-ampy = 4-aminopyridine), is enhanced upon intercalation into calf-thymus DNA (ct DNA).[1] We rationalize the findings to the emission of $[Pt^{II}(5,5'\text{-}Me_2bpy)(4\text{-}ampy)_2]^{2+}$ to have metal-to-ligand [Pt → π*(5,5′-Me_2bpy)] charge-transfer character. Because MLCT excited states of Pt^{II} have a coordinative unsaturated metal centre, presumably Pt^{III}, they would undergo rapid substrate binding reactions. Consequently, the emissions from these states are anticipated to be sensitive to environmental changes.[4,5] In this context cyclometallated platinum(II) complexes have received our attention. Extensive studies[3,6,7] have established that this class of complexes have emissive MLCT excited states in solution, and both their MLCT absorption and emission are known to undergo solvatochromism. Herein is described an investigation of the interaction of complexes **1** and **2** with nucleic acids. The findings highlight the important applications of cyclometallated platinum(II) complexes as new luminescent switches for DNA.

Complexes **1** $[CF_3SO_3]$[3] and **2** $[CF_3SO_3]_2$[7] were prepared by literature methods. Calf-thymus DNA (Sigma Chemical Co.) was purified to remove protein according to the literature.[8]



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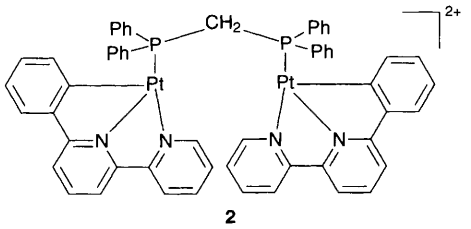

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Poly(dG-dG)$_2$ and poly(dA-dT)$_2$ (Sigma Chemical Co.) were used as received. All experiments were carried out in mixed MeOH–tris buffer solutions (0.050 mol dm^{-3} NaCl–0.005 mol dm^{-3} tris, pH 7.2).

The absorption spectra of **1** in the presence of ct DNA reveal interesting results. At [DNA]:[complex] ratios of < 1.6, the UV–VIS spectral changes show hypochromism at the absorption maximum (330 nm) (hypochromicity = 19%) with a small red shift ($\Delta\lambda$ = 4 nm). When the ratio is greater than 1.6, hyperchromism at 334 nm appears. These results are indicative of two different binding modes for the interaction with ct DNA, as is the case of proflavin.[9] Presumably, intercalation is the preferred binding mode at high [DNA]: [complex] ratios and surface (or minor groove) binding becomes appreciable when all possible sites of intercalation are occupied.[10] Since we are interested in the intercalation binding mode, all the studies were conducted at [DNA]: [complex] ratios > 1.6. The spectral changes for the interaction of **2** with DNA show an isosbestic point at 289 nm and with hypochromism (15%) and a small red shift ($\Delta\lambda$ = 1 nm) at the absorption maximum of 341 nm. Sequence specificity of the bindings has been studied. The interaction of **1** with poly(dG-dC)$_2$ displays a red shift of absorption maximum ($\Delta\lambda$ = 4 nm) and a hypochromicity (15%), similar to that observed with ct DNA. Unfortunately, an emulsion was formed upon reacting **1** with poly(dA-dT)$_2$, thus the interaction could not be determined. However, this finding indicates that **1** binds to DNA preferentially at the GC site, since the reaction of **1** with ct DNA does not produce an emulsion. For the binding of **2** with poly(dG-dC)$_2$ and poly(dA-dT)$_2$, the respective hypochromicity are 15 and 13% and $\Delta\lambda$ = 2 and 1 nm respectively. The corresponding values for ct DNA (hypochromicity = 15% and $\Delta\lambda$ = 1 nm) are similar to the values for both poly(dG-dC)$_2$ and poly(dA-dT)$_2$, meaning that there appears to be nonspecificity of the base pairs. With the absorption data, the intrinsic binding constants, K, are estimated to be $(1.0 \pm 0.1) \times 10^6$ for **1** and $(4.4 \pm 0.3) \times 10^4$ dm^3 mol^{-1} for **2**. That the K value for **1** is twenty-four times larger than that for **2** indicates much stronger binding of **1** to ct DNA. This is not unreasonable since the stretch force produced as the two Pt(CNN) moieties intercalate in between the base pairs would make the intercalation of **2** with ct DNA weaker.

In the absence of ct DNA, complexes **1** and **2** show relatively weak photoluminescence with emission maxima at 549, 593 and 632(sh) nm for **1** and 647 nm for **2** in tris buffer. As shown in Figs. 1 and 2, addition of ct DNA leads to a dramatic change of the emissions with the emission maxima red shifted to 556, 599 and 635 nm for **1** and blue shifted to 630 nm for **2**. The emission of **1** is metal-to-ligand (Pt → π*) charge transfer in nature.[3] Complex **2**, however, has two Pt(CNN) planes held at a separation of 3.35 Å by the dppm ligand.[7] The substantial red shift of the emission energy from **1** to **2** has been attributed to the weak metal–metal and ligand–ligand interactions and the emitting state of **2** was previously assigned to be $^3[(d_{\sigma^*})\sigma(\pi^*)]$. The similarity in the emission spectra of **2** in the presence and absence of ct DNA suggests that the emitting states in the two cases are of the same electronic origin. If only one of the Pt(CNN) moieties intercalates in between the base pairs while

the other is suspended out of the ct DNA molecule, the metal–metal and ligand–ligand interactions will be disrupted and hence no $^3[(d_{\sigma*})\sigma(\pi^*)]$ excited state is expected. Should this be the case, one would expect to observe ^{3}MLCT emission from the mononuclear Pt(CNN) unit, as in **1**. Thus the emission data is indicative of the intercalation of a binuclear $[Pt_2(CNN)_2(\mu\text{-dppm})]^{2+}$ unit into DNA. Interestingly, a 271-fold enhancement in emission intensity is seen at [DNA] : [complex] ≈ 13 for **1** and 117-fold at [DNA] : [complex] ≈ 32 for **2**. Similar increases in the emission lifetimes have also been found {$\tau_0/\mu s$: 0.23 for **1** and 0.82 for **2**, $\tau_{max}/\mu s$ at ([DNA] : [complex] ratio) = 20(13) for **1**, 2.3 (32) for **2**}. It should be noted that both the emissions of **1** and **2** follow a single exponential decay at high [DNA] : [complex] ratio (> 1.6), indicative of only a single binding mode. In the literature, the dramatic enhancement of the photoluminescence of transition-metal complexes upon intercalation into DNA has only been observed with ruthenium(II) complexes bearing extended π-aromatic organic ligands.[11,12] In this context, the cyclometallated platinum(II) complexes, like planar aromatic organic ligands, behave as molecular 'light switches'. A Scatchard analysis of the emission titration data, using the McGhee–von Hippel equation,[13] yields the binding constant with ct DNA as $(1.1 \pm 0.2) \times 10^6$ for **1** and $(4.2 \pm 0.3) \times 10^4$ dm^3 mol^{-1} for **2**. These values agree well with the values of $(1.0 \pm 0.1) \times 10^6$ for **1** and $(4.4 \pm 0.3) \times 10^4$ dm^3 mol^{-1} for **2** obtained from UV data. The site size for **1** was estimated to 4.4 ± 0.4, which compares well with the reported value of 4 for $[Ru(bpy)_2(phi)]^{2+}$ (phi = 9,10-phenanthrenequinonediimine).[11]

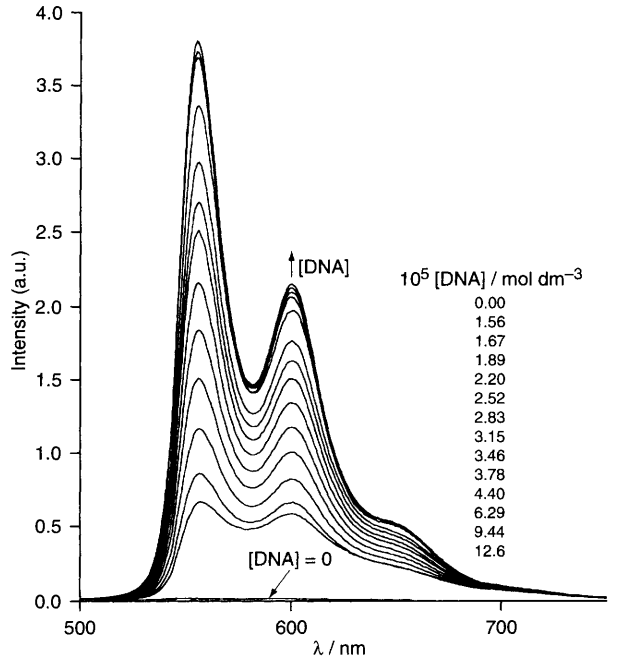

Fig. 1 Emission titration spectra of **1**$[CF_3SO_3]$ with addition of ct DNA in 3% MeOH–tris buffer; [**1**] ≈ 1.0×10^{-5} mol dm^{-3}

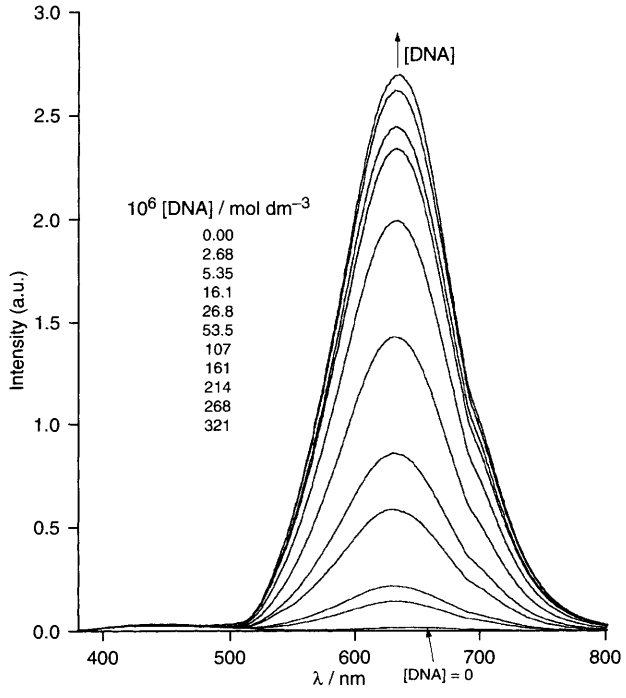

Fig. 2 Emission titration spectra of **2**$[CF_3SO_3]_2$ with addition of ct DNA in 3% MeOH–tris buffer; [**2**] ≈ 1.2×10^{-5} mol dm^{-3}

We attribute the dramatic enhancement of the emissions to the intercalation of **1** and **2** into ct DNA. This would prohibit the solvent-induced quenching process which usually occurs at a metal centre with vacant coordination sites.[4,5] In this context, quenching of the emission of **1** by $[Fe(CN)_6]^{4-}$ becomes less effective upon addition of ct DNA. The intercalated complex located between the base pairs of the helix is less accessible to the anionic $[Fe(CN)_6]^{4-}$ in solution, accounting for the decrease in quenching rate constants (determined from the Stern–Volmer plots) from 8.0×10^9 in 3% MeOH–tris to 2.0×10^9 dm^3 mol^{-1} s^{-1} in 3% MeOH–tris in the presence of ct DNA.

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