

DNA mediated energy transfer in dinuclear heterometallic dipyridophenazine complexes

M. Towrie and A. W. Parker

Central Laser Facility, CCLRC Rutherford Appleton Laboratory, Chilton, Didcot, Oxon., OX11 0QX, UK

S. P. Foxon and J. A. Thomas

Department of Chemistry, University of Sheffield, Sheffield, S3 7HF, UK

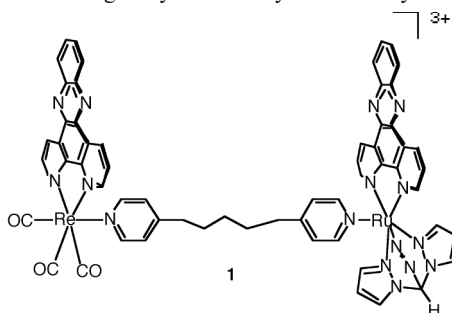
Main contact email address james.thomas@sheffield.ac.uk

Introduction

Polypyridyl-based transition metal cations that interact with DNA are excellent probes for physical properties of DNA.^[1] The majority of such complexes are known to possess low-lying MLCT excited states, thus allowing the metal complexes to be efficient reporters of their immediate surroundings. In this context, the “DNA light-switch”, $[\text{Ru}(\text{phen})_2(\text{dppz})]^{2+}$, (dppz = dipyrido-[3,2-a:2',3'-c]-phenazine, phen = 1,10-phenanthroline), has attracted particular attention, as it displays a huge luminescence enhancement on intercalation into DNA. It is established that intercalation of the dppz ligand into the DNA base stack forms the physical basis of this effect.^[2] The photophysical properties of these complexes are highly dependent on the nature of the metal. For example, although *indirect* flash-quench experiments on $[\text{Ru}(\text{phen})_2(\text{dppz})]^{2+}$, involving ground state oxidants result in DNA cleavage,^[3] the $\text{Ru}^{\text{II}} \rightarrow \text{dppz}^3\text{MLCT}$ state of this complex *cannot* cleave DNA. This contrasts with the complex $[\text{Re}(\text{CO})_3(\text{py})(\text{dppz})]^+$ which displays a much less intense light-switch effect due to an intraligand $\pi\pi^*$ excited state centred on the dppz moiety but is capable of *direct* DNA cleavage.^[4]

Although related complexes have been used to probe DNA-mediated electron transfer,^[5] much less work on analogous energy transfer processes has been carried out. Using modified oligonucleotides, Tor and colleagues have investigated quenching processes between non-intercalating Ru^{II} and Os^{II} -centres covalently appended to nucleosides.^[6] While, Barton, *et al.* carried out related experiments involving oligonucleotides similarly tethered with Ru^{II} and Os^{II} metallo-intercalating units based on dppz.^[7]

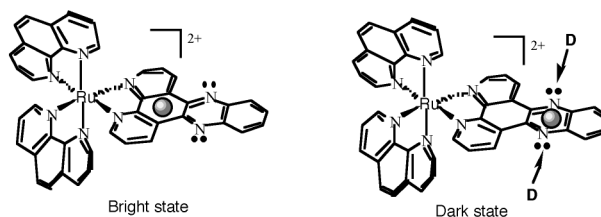
In related work, bimetallic systems based on the $[\text{Ru}(\text{dppz})]$ unit have recently been reported. For example, Nordén *et al.* have synthesised chiral bimetallic complexes connected via dppz moieties, which slowly intercalate via a threading mechanism, resulting in high affinity DNA binding.^[8] However, the construction of such enantiopure architectures from coordinatively saturated monomer units is synthetically demanding and, although subtle differences in binding geometries and photophysics between diastereomers have been observed, the overall binding constants of these systems are not greatly affected by the chirality.



In an attempt to create a more facile synthetic methodology for the synthesis of oligomeric metallo-intercalators, we have been exploring the chemistry and photophysical properties of achiral, coordinatively unsaturated $[\text{Ru}(\text{tpm})(\text{L})(\text{dppz})]^{2+}$ architectures, (tpm = tris-(1-pyrazolyl)methane, L = N-donor ligands). We recently reported^[9] that such systems have binding parameters that compare favourably to $[\text{Ru}(\text{phen})_2(\text{dppz})]^{2+}$. Using these units – and previously reported Re^{I} complexes – as building blocks we have developed a potentially generalised methodology for the construction of bimetallic architectures.^[10] This new approach is attractive in that it is modular and thus a wide variety of complexes can be readily constructed. Using this method, we have synthesised the first heterobimetallic Ru/Re dppz system, complex **1**. This system is unusual as it incorporates both a light-switch and a photo-cleavage unit in one system.

Results and Discussion

The steady-state absorption and emission spectra of **1** are consistent with the properties of other ligand-bridged, dinuclear d^6 -metal complexes displaying electronic interaction, suggesting energy transfer from the Re^{I} to Ru^{II} metal centre. However, the excited state properties of this complex are potentially very complex: it has been established that the light-switch effect for $[\text{Ru}(\text{phen})_2(\text{dppz})]^{2+}$ and related complexes involves a bright and dark $^3\text{MLCT}$ state. The bright state is non-hydrogen bonded and localised on the bpy moiety of dppz, while the dark state is hydrogen bonded and localised on the phenazine moiety – Scheme 1.^[11]



Scheme 1. $^3\text{MLCT}$ states involved in the $[\text{Ru}(\text{phen})_2(\text{dppz})]^{2+}$ light switch. Dark circle represents the electron involved in charge transfer, D represents a hydrogen-bond donor group.

Excitation of $[\text{Re}(\text{CO})_3(\text{L})(\text{dppz})]^+$ systems also involves two states, but in this case they are the intraligand dppz $\pi\pi^*$ and $\text{Re}^{\text{I}} \rightarrow \text{dppz}^3\text{MLCT}$ state respectively.^[12] Therefore excitation of **1** could involve any combination of four different kinds of excited states.

While luminescence spectroscopy is a convenient probe for the Ru^{II} -centre of **1**, the carbonyl ligands of *fac*- $(\text{CO})_3\text{Re}(\text{dppz})^+$ facilitate IR spectroscopic studies on the excited state of the second metal centre of this complex.

Therefore, preliminary studies on $[1][(\text{PF}_6)_3]$ in CH_3CN using nanosecond time-resolved infrared (ns-TRIR) were performed to probe the development of Re-based excited states populated by near-UV excitation and also to investigate any electronic interaction between the Re^{I} and Ru^{II} centres.

The ground state FTIR spectrum of $[1][(\text{PF}_6)_3]$ in CH_3CN displays two bands in the $\nu(\text{CO})$ stretching region at 2036 and 1932 cm^{-1} . Both bands occur at almost identical frequencies to those reported for $[\text{fac}-(\text{CO})_3\text{Re}(\text{dppz})(\text{py})]^+$.^[12] TRIR studies on **1** show the bleaching of these bands and the appearance of transient absorptions centered at 2028 and 1920 cm^{-1} . These features are consistent with analogous studies on $[\text{fac}-(\text{CO})_3\text{Re}(\text{dppz})(\text{py})]^+$ and indicate the formation of a dppz centred $\pi \rightarrow \pi^*$ ^3IL state. For the mononuclear complex, this state shows a slow bi-exponential decay ($\tau = 500$ ns and 3.5 μs).^[12] In contrast, the lifetime of **1** is significantly shorter ($\tau_{\text{IL}} = 108$ ns and 968 ns). In water decay of the $\pi \rightarrow \pi^*$ ^3IL state is around two orders of magnitude more rapid than in MeCN Figure 1, with $\tau_{\text{IL}} = 4$ ns and 23 ns. Schanze, *et al.* have suggested that the non-luminescence of $[\text{fac}-(\text{CO})_3\text{Re}(\text{dppz})(\text{Mepy})]^+$ (MePy = 4-methylpyridine) in water is due to deactivation of the IL state via the close-lying and (in water) short-lived $\text{Re}(\text{d}\pi) \rightarrow \text{dppz}(\pi^*)$ MLCT manifold.^[11a] This latter state has been observed in TRIR studies on $[\text{fac}-(\text{CO})_3\text{Re}(\text{dppz})(\text{py})]^+$ in MeCN.^[11b] Contrastingly, our TRIR studies in water offer no evidence for the formation of such a state, with only ^3IL decay observed. Again, the facts that **1** is non-luminescent in water, and no $\text{Re}(\text{d}\pi) \rightarrow \text{dppz}(\pi^*)$ $^3\text{MLCT}$ manifold is observed are consistent with energy transfer.

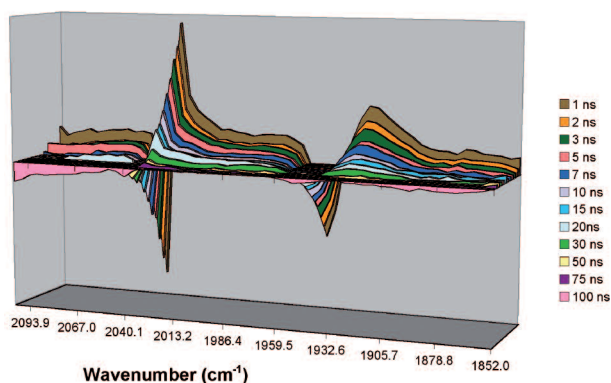


Figure 1. ns-TRIR spectra obtained between **1** and 100 ns following excitation of an aqueous solution of $[1][(\text{Cl})_3]$.

It seems likely that in both MeCN and water, the dppz centred $\pi \rightarrow \pi^*$ ^3IL state of the Re unit is being deactivated via the $\text{Ru}(\text{d}\pi) \rightarrow \text{dppz}(\pi^*)$ $^3\text{MLCT}$ state, which is extremely short lived in water.^[1] We then investigated the interaction of **1** with calf thymus DNA (CT-DNA) in aqueous buffer (25 mM NaCl, 5 mM Tris, pH 7.0).

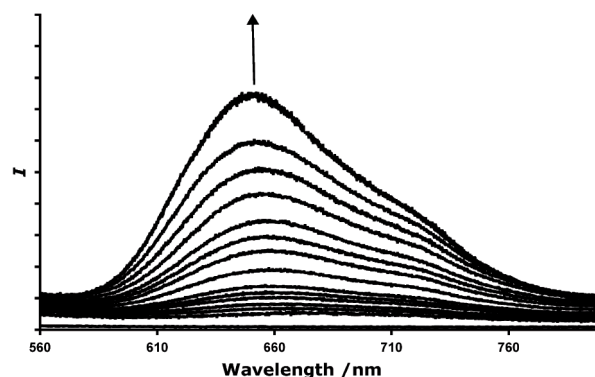


Figure 2. Changes in luminescence of $[1][(\text{Cl})_3]$ in aqueous buffer on addition of CT-DNA. Inset: luminescent decay of excited state.

As expected, **1** is non-luminescent in aqueous solution. On addition of DNA, $\text{Ru}(\text{d}\pi) \rightarrow \text{dppz}(\pi^*)$ $^3\text{MLCT}$ based luminescence of **1** is restored – Figure 2. This observation is consistent with the intercalation of the $[\text{Ru}^{\text{II}}(\text{dppz})]$ unit, as is the observed bi-exponential decay of this excited state. ns-TRIR studies reveal that addition of CT-DNA to aqueous buffer solutions extends the lifetime of the ^3IL state of the Re unit by an order of magnitude, indicating that this moiety is also interacting with DNA.

Comparison with data for $[\text{fac}-(\text{CO})_3\text{Re}(\text{dppz})(\text{Mepy})]^+$ is revealing. Bound to DNA the monomer also displays biexponential decay, but $\tau_{\text{IL}} = 170$ ns and 13.5 ms.^[11] The rapid deactivation of the ^3IL state of **1** relative to the Re monomer is again consistent with energy transfer from $[\text{Re}^{\text{I}}(\text{CO})_3(\text{dppz})]$ to $[\text{Ru}^{\text{II}}(\text{dppz})]$. However, in contrast to $[\text{fac}-(\text{CO})_3\text{Re}(\text{dppz})(\text{Mepy})]^+$, the lifetime of the ^3IL state in DNA is still significantly shorter than in MeCN. These results suggest that energy transfer is facilitated by base-pairs between intercalated moieties, a phenomenon that has been observed in oligonucleotides covalently appended with metal complexes.

Conclusions

In summary, the first hetero-dinuclear dppz complex is reported. Using spectroscopy, the excited state of both metal centres can be independently monitored. In water and DNA, it appears that the $[\text{Re}^{\text{I}}(\text{CO})_3(\text{dppz})]$ -based ^3IL state is deactivated through energy transfer to the $[\text{Ru}^{\text{II}}(\text{dppz})]$ unit and this process may be mediated by DNA. Detailed studies, involving other nucleotide sequences and related complexes, designed to investigate this hypothesis further will form the basis of future reports.

References

1. (a) K. E. Erkkila D. T. Odom, J. K. Barton, *Chem. Rev.* **99** 2777, (1999) (b) C. Metcalfe, J. A. Thomas, *Chem. Soc. Rev.* **32** 215, (2003)
2. (a) A. E. Friedman, J.-C. Chambron, J.-P. Sauvage, N. J Turro, J. K. Barton, *J. Am. Chem. Soc.* **112** 4960, (1990) (b) C. Hiort, P. Lincoln, B. Nordén, *J. Am. Chem. Soc.* **115** 3448, (1993)
3. E. D. A. Stemp, M. R. Arkin, J. K. Barton, *J. Am. Chem. Soc.* **119** 2921, (1997)
4. V. W.-W. Yam, K. K.-W. Lo, K.-K. Cheung, R. Y.-C. Kong, *J. Chem. Soc., Dalton Trans.* 2067, (1997)
5. D. B. Hall, R. E. Holmlin, J. K. Barton, *Nature* **382** 731, (1996)
6. D. J. Hurley, Y. Tor, *J. Am. Chem. Soc.* **124** 13231, (2002) and reference therein.
7. R. E. Holmlin, R. T. Tong, J. K. Barton, *J. Am. Chem. Soc.* **120** 9724, (1998)
8. (a) B. Önfelt, P. Lincoln, B. Nordén, *J. Am. Chem. Soc.* **121** 10846, (1999) (b) L. M. Wilhelmsson, F. Westerlund, P. Lincoln, B. Nordén, *J. Am. Chem. Soc.* **124** 12092; (2002)
9. C. Metcalfe, H. Adams, I. Haq, J. A. Thomas, *Chem. Commun.* 1152, (2003)
10. C. Metcalfe, I. Haq, J. A. Thomas, *Inorg. Chem.* **43** 317, (2004)
11. J. Olofsson, L. M. Wilhelmsson, P. Lincoln, *J. Am. Chem. Soc.* **126** 15458 (2004) and references therein.
12. (a) H. D. Stoeffler, N. B. Thornton, S. L. Temkin, K. S. Schanze, *J. Am. Chem. Soc.* **117** 7119, (1995) (b) J. Dyer, W. J. Blau, C. G. Coates, C. M. Creely, J. D. Gavey, M. W. George, D. C. Grills, S. Hudson, J. M. Kelly, P. Matousek, J. J. McGarvey, J. McMaster, A. W. Parker, M. Towrie, J. A. Weinstein, *Photochem. Photobiol. Sci.* **2** 542, (2003)

Acknowledgments

We are grateful to BBSRC for financial support.