The First Ru^{II} Bipyridyl-Capped Cyclodextrin: Evidence of Electron-Transfer Through the Cavity

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The narrow rim of an α-cyclodextrin has been AD-capped with a photoactive ruthenium(II) tris(2,2′-bipyridyl) fragment giving a diastereomeric mixture of complexes that bind 1,4-benzoquinone in water. Steady-state and time-resolved emission studies have been used to probe electron-transfer processes occurring inside and outside the cavity.

Introduction

Supramolecular assemblies displaying *vectorial* photoinduced electron-transfer (ET) reactions have attracted much attention in recent years from the view point of designing efficient artificial photosynthetic systems and light-driven molecular machines.[1−5] In order to gain a better understanding of through-space ET processes, it is necessary to closely position the reactants in a *rigid* manner but to avoid either direct orbital contact or a connecting organic framework. Here, we describe the synthesis and photophysical properties of a water-soluble α-cyclodextrin (α-CD) host for which a photoactive ruthenium(II) centre is held, for the first time, at a *fixed* distance above the receptor. Our approach involves capping the α-CD with a difunctionalized 2,2′-pyridyl ligand before subsequent metallation. The resulting complex is expected to behave as a metallo-receptor which, upon illumination, will transfer an electron between the excited metal centre and a redox-active substrate trapped in the cavity. Photoactive Ru^{II}(bipy) centres appended to cyclodextrin receptors have been reported previously, but these systems contain *flexible* Ru−CD connectors, thus preventing full geometrical control of the ET process.[6]

Results and Discussion

The key precursor for our study is 6A,6D-diamino-6A,6D-dideoxy-hexadeca-*O*-methyl-α-CD (**2**) which allows effective capping with diacid chlorides and good solubility in organic solvents. Compound **2** was synthesised in two steps from the dimesylate **1**[7] according to Scheme 1. Macrocyclisation of **2** under high dilution with 4,4′-bis(chlorocarbonyl)-2,2′-bipyridine in the presence of triethylamine afforded the "exo"-bipy ligand **3** in ca. 50% yield which, on treatment with the solvent complex $[Ru(bipy)_2(Me_2CO)_2][BF_4]_2$, gave an equimolar mixture of the diastereomeric complexes **4a/4b**[8] which was not resolved (see Experimental Section). Unlike ligand **3**, these complexes are soluble in water as well as in organic solvents.

Both ^1H NMR and ^{13}C NMR spectroscopy revealed the diastereomeric nature of the ruthenium complexes **4a/4b**. Each individual compound retains the C_2 symmetry of the ligand. Complexes **4a/4b** undergo chemical shift changes in D_2O upon addition of varying amounts of 1,4-benzoquinone (BQ) indicative of bimolecular association (Figure 1). A titration procedure involving the measurement of chemicals shifts for aqueous solutions containing excess BQ confirmed the 1:1 stoichiometry of the resultant supramolecular assembly and indicated an association constant (K_a) of 9 ± 3 M^{-1}.[9] The CIS[10] (complexation-induced shift on 100% complexation) values obtained from these ^1H NMR spectra are listed in Table 1 for nonoverlapping probes and provide clear indication for the inclusion of BQ into the CD cavity. Amongst the most significant changes are those experienced by the H-3,3′ protons ($\Delta\delta_{max} = +0.22$, vs. +0.05 for H-5,5′ and +0.03 ppm for H-6,6′) of the 4,4′-dicarbonyl-2,2′-bipyridyl fragment, the only 2,2′-bipyridyl (bipy) protons that point towards the cavity interior. Interestingly, some of the CD MeO-3 protons[10] which also point towards the interior of the cavity are strongly upfield shifted ($\Delta\delta_{max} = -0.20$ and -0.23) whereas others are slightly downfield shifted or remain unchanged ($\Delta\delta_{max} = +0.05$ and -0.01) (Figure 1), suggesting that a particular guest orientation within the CD cavity is favoured, perhaps because of some structural distortion imposed by the bipy cap. Furthermore, the chemical shift change found for the H_{CD}-5 protons[11] ($\Delta\delta_{max} = +0.13$) is consistent with medium immersion of BQ.[10]

Luminescence from the metal complex in **4** is quenched upon addition of BQ but Stern-Volmer plots show *pronounced* positive deviations from linearity without reaching a plateau at high quinone concentrations (Figure 2). This situation arises from a combination of both diffusional and static emission quenching processes, as confirmed by time-

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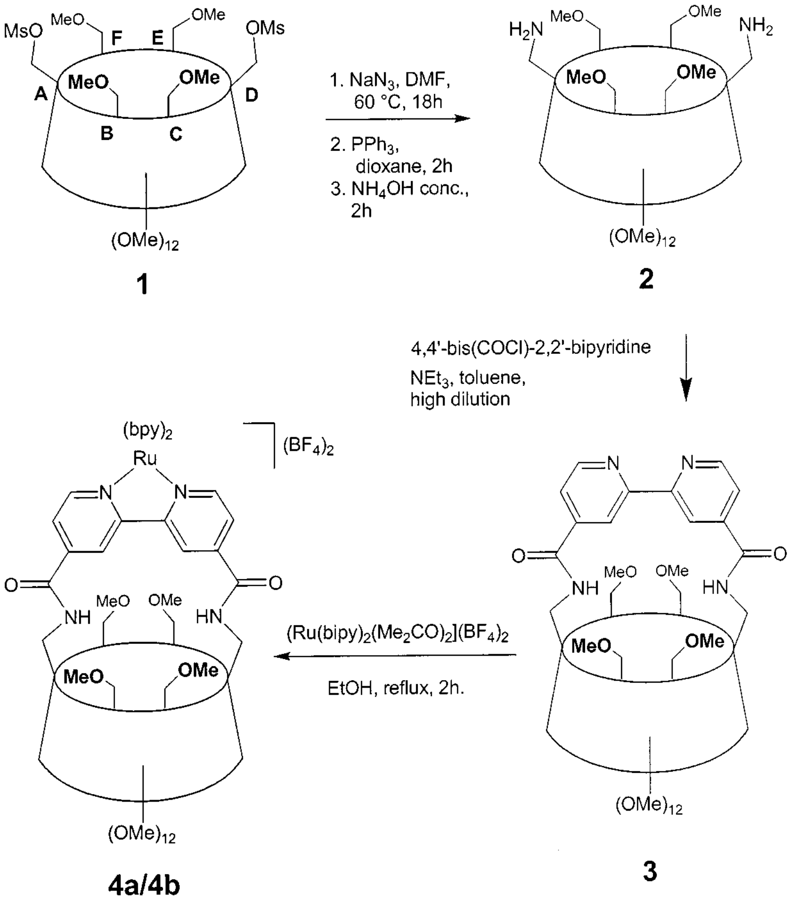

Scheme 1. Synthesis of the diastereomeric mixture **4a/4b**

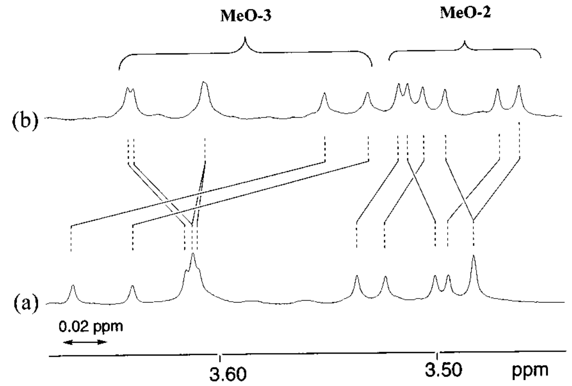

Figure 1. ^{1}H NMR (500 MHz) spectra in the MeO-2 and MeO-3 regions: (a) spectrum of **4a/4b** in the absence of 1,4-benzoquinone; (b) spectrum of **4a/4b** in the presence of 40 equiv. of 1,4-benzoquinone

resolved luminescence studies. Fitting the titration data collected over a wide variation in BQ concentration, however, requires a second diffusional process which becomes important only at high BQ concentrations. These results are readily accommodated within a model for which BQ quenches emission from **4** via a diffusional process having a bimolecular rate constant of 3×10^9 M^{-1} s^{-1} and that competes with inclusion of BQ into the cavity. The second diffusional step, which also occurs with a bimolecular rate constant of 3×10^9 M^{-1} s^{-1}, can now be assigned to quenching of residual emission from the BQ·**4** complex. The best fit to the luminescence data gives $K_a = 45$ M^{-1} and indicates that the encapsulated quinone quenches the excited state of the metal complex with a first-order rate constant of 3.0×10^7 s^{-1}. Insisting on $K_a = 10$ M^{-1}, as indicated by the NMR studies, raises this latter rate constant to 4.7×10^7 s^{-1}. Each quenching step is attributed to ET from the triplet excited metal complex to BQ, although the radical ion products could not be detected by transient absorption spectroscopy.

The NMR studies indicate that the BQ guest is located at an edge-to-edge separation distance (R) of ca. 7 Å[12] from the bipy capping unit. Since the rate of electron transfer usually decreases exponentially with increasing R according to $k = \mathrm{A}\exp(-\beta\mathrm{R})$, where the pre-exponential factor A has a value of ca. 10^{13} s^{-1}, we can approximate the attenuation factor β as being ca. 1.8 Å^{-1}. This means that the cavity exerts a serious damping effect on the rate of ET, being comparable to that of a solvent molecule. In the present study, the preferential 3D orientation of an electron-accepting guest takes place within an AD-capped α-CD and, for the first time, photoinduced ET within a Ru(bipy)−cyclodextrin receptor that guests a benzoquinone is shown to occur. Although the rigidified metalloreceptor **4** facilitates study of through-space, light-induced electron transfer in which a variety of redox-active substrates could

Table 1. ^{1}H NMR chemical shifts data ($\Delta\delta$ values)[a] for the **4a/4b** mixture; BQ in D_2O at 25 °C

Ligand of **4**	Probe[a][b]									
	H-3,3′	H-4,4′	H-5,5′	H-6,6′	H_{CD}-1	H_{CD}-2	H_{CD}-5	MeO-2	MeO-3	MeO-6
2,2′-bipyridine	< 0.01	< 0.01	< 0.01	+0.03 < 0.01	–	–	–	–	–	–
3	+0.22 +0.21	–	+0.05	+0.03	+0.05	+0.04	+0.13	+0.02	−0.20 −0.23	–
					−0.02 < 0.01	−0.07 −0.04	+0.07 +0.04	−0.04 −0.04	+0.05 < 0.01	−0.05 +0.04

[a] The $\Delta\delta$ values relate to the chemical shift changes experienced by nonoverlapping probe protons in the host on 100% 1:1 complexation (CIS values). They were obtained after treatment of the binding data by an iterative nonlinear curve fitting program. All measurements were carried out using external $Me_4Si/CDCl_3$ as reference. The H_{CD}-3, H_{CD}-4, and H_{CD}-6 protons could not be identified. – [b] H-n,n′ stands for bipy protons while H_{CD}-n corresponds to cyclodextrin signals. For some probes two distinct signals were observed either because of diastereomer distinction, or because of the presence of two nonequivalent H atoms belonging to the same diastereomer.

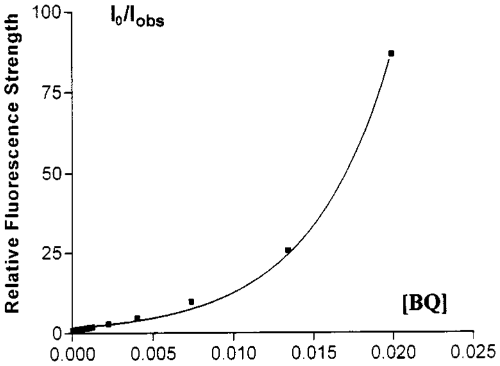

Figure 2. Stern-Volmer plot for the Ru-quinone system derived from **4a/4b**; [Ru] = 1.94 × 10^{-5} M in H_2O, at 25 °C; [Q] in mol/L

be used, it is necessary to optimise the binding process. This is most easily accomplished by enlarging the cavity and such studies are now underway.

Experimental Section

General: All manipulations were performed under dry nitrogen using purified solvents. A COSY experiment on complexes **4a/4b** allowed precise assignment of the bipy protons. The luminescence experiments were performed using a Perkin−Elmer LS 50B spectrofluorometer at room temperature. Full details for the synthesis of compounds **2** and **3** will be described elsewhere. For the atom numbering of α-cyclodextrin, see ref.[13].

Compound 2: yield 88% (starting from **1**). M.p. 184−186 °C. − ^{1}H NMR (200.13 MHz, $CDCl_3$): δ = 1.40 (br s, 4 H, NH_2), 3.38 (s, 6 H, CH_3O-6), 3.39 (s, 6 H, CH_3O-6), 3.49 (s, 18 H, CH_3O), 3.63 (s, 6 H, CH_3O), 3.64 (s, 6 H, CH_3O), 3.65 (s, 6 H, CH_3O), 2.99−3.94 (m, 36 H, H_{CD}-2, H_{CD}-3, H_{CD}-4, H_{CD}-5 and H_{CD}-6), 5.02 (d, ^3J = 3 Hz, 2 H, H_{CD}-1), 5.06 (d, ^3J = 3.5 Hz, 4 H, H_{CD}-1). − $^{13}C\{^1H\}$ NMR (50.32 MHz, $CDCl_3$): δ = 42.7 (CH_2N), 57.8 (×2) and 58.0 (CH_3O), 59.0 and 59.1 (CH_3O-6), 61.7 and 61.8 (×2) (CH_3O), 71.1, 71.2, and 72.4 (C_{CD}-5), 71.1 (×2) (C_{CD}-$6^{B,C,E,F}$), 81.3 (×3), 82.2 (×4), 82.5, 83.2 (C_{CD}-2, C_{CD}-3, and C_{CD}-4), 99.8, 100.0, and 100.3 (C_{CD}-1). − $C_{52}H_{94}N_2O_{28}$ (1195): calcd. C 52.25, H 7.93, N 2.34; found C 52.19, H 8.00, N 2.22.

Ligand 3: yield 50%. M.p. 195−197 °C. − IR (KBr): $\tilde{\nu}$ = 1655 (CO) cm^{-1}. − ^{1}H NMR (200.13 MHz, $CDCl_3$): δ = 3.02 (s, 6 H, CH_3O-6), 3.12 (s, 6 H, CH_3O-6), 3.45 (s, 6 H, CH_3O), 3.47 (s, 12 H, CH_3O), 3.60 (s, 6 H, CH_3O), 3.63 (s, 6 H, CH_3O), 3.65 (s, 6 H, CH_3O), 3.13−4.14 (m, 36 H, H_{CD}-2, H_{CD}-3, H_{CD}-4, H_{CD}-5 and H_{CD}-6), 4.94 (d, ^3J = 3 Hz, 2 H, H_{CD}-1), 5.00 (d, ^3J = 3.5 Hz, 2 H, H_{CD}-1), 5.03 (d, ^3J = 3.1 Hz, 2 H, H_{CD}-1), 7.57 (br. t, 2 H, CONH), 7.89 (d, ^3J = 5 Hz, 2 H, H_{pyr}-5,5′), 8.28 (s, 2 H, H_{pyr}-3,3′), 8.96 (d, ^3J = 5 Hz, 2 H, H_{pyr}-6,6′). − $^{13}C\{^1H\}$ NMR (50.32 MHz, $CDCl_3$): δ = 43.2 (CH_2NH), 57.8 and 58.1 (×2) (CH_3O), 58.8 and 59.1 (CH_3O-6), 61.6 and 61.7 (×2) (CH_3O), 70.7, 71.4, and 72.9 (C_{CD}-5), 70.9 and 72.3 (C_{CD}-$6^{B,C,E,F}$), 80.6, 81.3, 81.4, 81.8 (×3), 82.1 (×2), 82.3, and 85.8 (C_{CD}-2, C_{CD}-3, and C_{CD}-4), 99.5, 99.6, and 100.1 (C_{CD}-1), 118.7 (C_{pyr}-5,5′), 121.7(C_{pyr}-3,3′), 142.3 (C_{pyr}-4,4′), 151.8 (C_{pyr}-6,6′), 157.1 (C_{pyr}-2,2′), 164.5 (CONH). − $C_{64}H_{98}N_4O_{30}$ (1404): calcd. C 54.77, H 7.04, N 3.99; found C 54.70, H 7.09, N 3.84.

Complexes 4a + 4b (mixture): A mixture of *cis*-$RuCl_2(bipy)_2$ (0.074 g, 0.14 mmol) and $AgBF_4$ (0.064 g, 0.32 mmol) in acetone (20 mL) was refluxed for 2 h. After cooling, the filtered solution was added to a solution of **3** (0.200 g, 0.14 mmol) in ethanol (10 mL). Acetone was removed under reduced pressure and the ethanolic solution was stirred under reflux for 2 h. A solution of $NaBF_4$ in water (1 M, ca. 20 mL) was then added to the mixture. Extraction with CH_2Cl_2 (3 × 50 mL) and drying over $MgSO_4$ afforded **4** as a mixture of two diastereomers.[8] Yield: 0.270 g, 95%. − IR (KBr): $\tilde{\nu}$ = 1655 (CO) cm^{-1} − UV/Vis (H_2O): λ_{max} (ε) = 485 (11000), 421 (10400). − ^{1}H NMR (500.14 MHz, D_2O, ext. ref.: $SiMe_4$ in $CDCl_3$): δ = 2.60 (s, 6 H, CH_3O-6), 2.92 (s, 6 H, CH_3O-6), 3.05 (s, 6 H, CH_3O-6), 3.21 (s, 6 H, CH_3O-6), 3.23−3.37 (6dd, ^3J = 2.8 and 9.7 Hz, 12 H, H_{CD}-2), 3.48 (s, 12 H, CH_3O-2), 3.49 (s, 6 H, CH_3O-2), 3.50 (s, 6 H, CH_3O-2), 3.52 (s, 6 H, CH_3O-2), 3.54 (s, 6 H, CH_3O-2), 3.55−4.22 (m, 48 H, H_{CD}-3, H_{CD}-4, and H_{CD}-6), 3.96−4.20 (m, 6 H, H_{CD}-5), 5.11 (d, ^3J = 3.7 Hz, 2 H, H_{CD}-1), 5.12 (d, ^3J = 3.7 Hz, 2 H, H_{CD}-1), 5.16 (d, ^3J = 2.8 Hz, 2 H, H_{CD}-1), 5.20 (d, ^3J = 2.8 Hz, 2 H, H_{CD}-1), 5.27 (d, ^3J = 3.4 Hz, 2 H, H_{CD}-1), 5.29 (d, ^3J = 3.4 Hz, 2 H, H_{CD}-1), 7.35−7.43 (m, 8 H, H_{pyr}-5,5′), 7.68 (d, ^3J = 5.4 Hz, 2 H, H_{pyr}-6,6′), 7.72 (d, ^3J = 5.4 Hz, 2 H, H_{pyr}-6,6′), 7.80 (dd, ^3J = 5.5 Hz and ^4J = 1.8 Hz, 4 H, H_{pyr}-5,5′ connected to CD), 7.82 (d, ^3J = 5.4 Hz, 2 H, H_{pyr}-6,6′), 7.86 (d, ^3J = 5.4 Hz, 2 H, H_{pyr}-6,6′), 8.04−8.13 (m, 12 H, H_{pyr}-4.4′ of bipy and H_{pyr}-6,6′ connected to CD), 8.57−8.59 (m, 8 H, H_{pyr}-3,3′), 9.07 (d, ^4J = 1.8 Hz, 2 H, H_{pyr}-3,3′ connected to CD), 9.12 (d, ^4J = 1.8 Hz, 2 H, H_{pyr}-3,3′ connected to CD). − $^{13}C\{^1H\}$ NMR (50.32 MHz, $CDCl_3$): δ = 44.3 (×2) (CH_2NH), 57.4 (×2), 57.7 (×2) and 57.6 (×2) (CH_3O), 58.5 (×2), 58.7 and 58.9 (CH_3O-6), 61.5 (×2), 61.7 (×2) and 62.0 (×2) (CH_3O), 70.1(×2), 70.4 (×2), and 70.5 (×2) (C_{CD}-5), 70.7 (×2) and 71.3 (×2) (C_{CD}-$6^{B,C,E,F}$), 80.3 (×2), 81.9 (×4), 82.1 (×2), 82.3 (×4), 82.4 (×2), 82.6 (×2), and 84.2 (×2) (C_{CD}-2, C_{CD}-3, and C_{CD}-4), 99.9 (×2), 100.2 (×2), and 100.4 (×2) (C_{CD}-1), 120.1 (×2), 124.6

(×4) (C_{pyr}-3,3′), 127.7 (×2), 127.9 (×2), and 128.5 (×2) (C_{pyr}-5,5′), 138.4 (×2), 138.6 (×2), 143.3 and 143.4 (C_{pyr}-4,4′), 150.5 (×2), 151.2 (×2), 152.1 (×2) (C_{pyr}-6,6′), 156.0 (×2), 156.7 (×2), 157.3 (×2) (C_{pyr}-2,2′), 162.2 (×2) (CONH). − FAB-MS: *m/z* (%) = 1903 (15) $(M - BF_4)^+$, 1816 (100) $(M - 2BF_4)^+$. − $C_{84}H_{114}B_2F_8N_8O_{30}Ru$ (1991): calcd. C 50.69, H 5.77, N 5.63; found C 50.62, H 5.90, N 5.41.

The determination of the association constants is based on the chemical shift variation of certain nonoverlapping H-signals upon addition of an excess (3−40 equiv.) of BQ to a 2.7×10^{-3} M solution of **4** in D_2O. The data were treated by a nonlinear regression analysis program in order to extract K_a and CIS values. A similar procedure was used to evaluate the K_a value ($K_a = 8 \pm 3\ M^{-1}$) for the complex formed between [hexakis(2,3,6-tri-*O*-methyl-α-cyclodextrin] (TM-α-CD) and BQ. Comparison of the two K_a values suggests that the [Ru(bipy)$_2$(4,4′-biscarbonylbipy)] cap has little influence on the complexation process.

Emission spectra (room temperature, $\lambda_{exc} = 460$ nm) in air-saturated water were obtained for a concentration of complex **4** that was maintained constant throughout the titration (1.94×10^{-5} M). The quinone concentration ranges from 1.94×10^{-5} M to 2.00×10^{-2} M.

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[8] Molecule **4** combines an enantiomerically pure cyclodextrin fragment with the dissymetric ruthenium centre. This combination results in the formation of two diastereomers.

[9] Both diastereomers **4a/4b** were found to undergo similar chemical shift changes upon complexation with BQ and therefore identical K_a values for the 1:1 complexes were obtained. Probes giving the maximum chemical shift changes were used to evaluate the K_a values, namely H-3,3′ protons of the 4,4′-dicarbonyl-2,2′-bipyridyl moiety and one of the CD MeO-3 signals.

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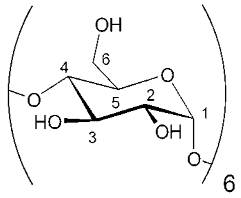
[11] Unfortunately, the H_{CD}-3 signals which are usually strongly upfield-shifted, even for a shallow complexation process, could not be identified as a result of signal overlap. However, the H_{CD}-3 signal of the (TM-α-CD)·BQ complex could be clearly seen and undergoes a significant upfield-shift on complexation (CIS = −0.42 ppm on 100% complexation). Based on this probe, an association constant of $8 \pm 3\ M^{-1}$ was determined; this value is in agreement with that obtained for BQ complexation with **4a/4b** ($9 \pm 3\ M^{-1}$).

[12] This value was estimated on the basis of the NMR CIS values found for protons located in the CD cavity together with molecular models. Clearly, the large chemical shift changes on BQ-complexation experienced by some of the MeO-3 protons indicate a shallow guest inclusion of the guest at the cavity entrance. For steric reasons the *OO*-axis of included BQ was assumed to be oriented along the CD C_2 axis. The estimated edge-to-edge separation stands for the distance between an N atom of the substituted bipy and the nearest BQ-oxygen atom.

[13] Numbering in α-CD:



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