Bis(*meta*-phenylene)-32-crown-10-based cryptand/diquat inclusion [2]complexes

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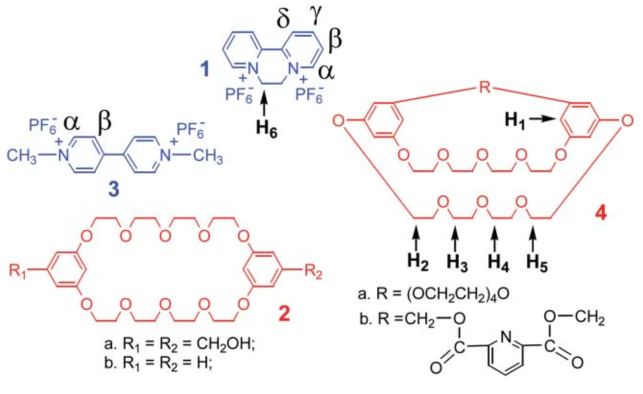
Bis(*meta*-phenylene)-32-crown-10-based cryptands have been proved to complex diquat much more strongly than bis(*meta*-phenylene)-32-crown-10 itself; in fact, one containing a pyridyl moiety has one of the highest K_a values yet reported.

Inclusion complexes have been widely studied for different purposes.[1] Diquat (**1**) is an effective herbicide that presents toxicity challenges to fish, mammals, *etc.* and thus needs to be carefully monitored in the environment.[2] Partially, for this reason, it has been studied as the guest in numerous inclusion complexes.[3] Inspired by the formation of a taco complex in the solid state from bis(*meta*-phenylene)-32-crown-10 (BMP32C10) derivative **2a** and paraquat (**3**),[4] with the aim of preparing large supramolecular systems, we designed and prepared a series of crown ether-based cryptands which can complex paraquat derivatives, such as **3**, much more strongly than the corresponding simple crown ethers.[4,5] Since BMP32C10 and diquat also form a complex,[3e] we reasoned that BMP32C10-based cryptands should also be able to complex diquat much more strongly than BMP32C10 itself. Here we demonstrate that this is true by studying the complexation between two cryptands (**4a**[4] and **4b**[5d]) and diquat **1**.



Solutions of **4** and **1** have a yellow color due to charge transfer between the electron-poor pyridinium rings of guest **1** and the electron-rich aromatic rings of hosts **4**. Partial proton NMR spectra of **4a**, **1**, and a mixture of **4a** and **1** are shown in Fig. 1; only one set of peaks was found for the solution of **4a** and **1**, indicating fast-exchange complexation. Significant upfield shifts of aromatic protons H_1 and α-ethyleneoxy H_2 on **4a** and *N*-methylene protons H_6 of **1**, and a downfield shift of ethyleneoxy protons H_3 on **4a** are observed. The stoichiometries of the complexes between cryptand hosts **4** and diquat guest **1** were both determined to be 1 : 1 in solution by Job plots[6] using proton NMR data; the Job plot for the complex between **4a** and **1** is shown in Fig. 2.

The association constant (K_a) of **4a·1**, calculated based on the proton NMR data, was 2.0 (±0.2) × 10^4 M^{-1} in acetone-d_6,[7] which is a little lower than the K_a of **4a·3**, 6.1 × 10^4 M^{-1} in

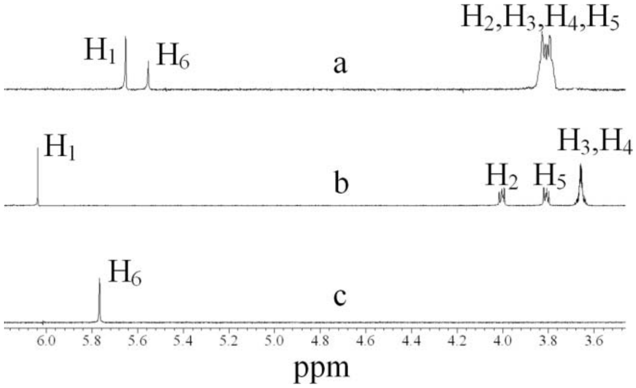


Fig. 1 Partial proton NMR spectra (400 MHz, acetone-d_6, 22 °C) of diquat **1** (c, bottom), cryptand **4a** (b, middle), and 1.00 mM **1** and 1.00 mM **4a** (a, top).

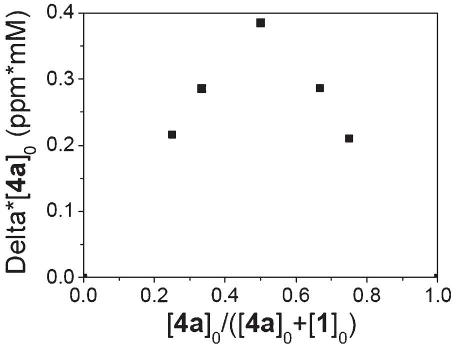


Fig. 2 Job plot showing the 1 : 1 stoichiometry of the complex between **4a** and **1** in CD_3COCD_3 solution using data for H_1 of **1**. $[\mathbf{4a}]_0$ and $[\mathbf{1}]_0$ are the initial concentrations of **4a** and **1**. $[\mathbf{4a}]_0 + [\mathbf{1}]_0$ = 2.00 mM.

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acetone-d_6,[4] but about 50 times higher than the K_a of **2b·1**, 390 M^{-1} in acetone-d_6.[3e]

The K_a of **4b·1**, determined using a competitive method developed by the Smith group,[9] was 3.30 ($\pm$0.66) × 10^5 M^{-1} in acetone-d_6,[10] which is lower than the K_a of **4b·3**, 5.0 ($\pm$2.0) × 10^6 M^{-1} in acetone-d_6,[5d] but about 840 times higher than the K_a of **2b·1**. Thus it was demonstrated that BMP32C10-based cryptands **4** are much better hosts for diquat **1** than the corresponding simple crown ether, BMP32C10.

In comparison, a porphyrin-linked bis(*meta*-phenylene)-32-crown-10-based cryptand bound **1** with a K_a = 1.2 × 10^5 M^{-1} (CD_3COCD_3 : $CDCl_3$, 86 : 14).[3k] Dibenzo-30-crown-10 is reported to bind diquat **1** with a K_a = 1.75 × 10^4 M^{-1} (CD_3COCD_3),[3a] while a dibenzo-30-crown-10-based cryptand exhibited a K_a = 2.6 × 10^5 M^{-1} (CD_3COCD_3).[3d]

Solutions of **4** and **1** in 4 : 1 acetonitrile : chloroform were characterized by electrospray ionization mass spectrometry (Fig. 3). Two relevant peaks were found for **4a·1**: *m*/*z* 1055.43 (6.9%) [**4a·1** − PF_6]$^+$ and 455.25 (100%) [**4a·1** − 2PF_6]$^{2+}$. Interestingly, two peaks at *m*/*z* 818.55 (6.5%) and 500.33 (8.4%) appear to be due to the [3]complex **4a$_2$·1**: [**4a$_2$·1** − 2PF_6]$^{2+}$ and [**4a$_2$·1** − $CH_2CH(OCH_2CH_2)_3O$ − 2PF_6 + K]$^{3+}$; this is noteworthy because the analogous **4a$_2$·3** has been isolated and characterized by X-ray crystallography.[5b] For **4b·1**, two relevant peaks were also found: *m*/*z* 1056.41 (13.0%) [**4b·1** − PF_6]$^+$ and 455.74 (100%) [**4b·1** − 2PF_6]$^{2+}$. However, no peaks were found for **4b$_2$·1**.

The formation of the inclusion complex **4a·1** was confirmed by X-ray analysis (Fig. 4).‡ X-Ray quality, yellow, single crystals of **4a·1** were grown by vapor diffusion of pentane into an acetone solution of **1** with excess **4a**. The 1 : 1 complex **4a·1** is stabilized by hydrogen bonding and face-to-face π-stacking interactions in the solid state. Three *N*-methylene hydrogens (**A**, **B** and **E** in Fig. 4), one α-pyridinium hydrogen (**C** and **D** in Fig. 4) and one β-pyridinium hydrogen (**I** in Fig. 4) are directly hydrogen bonded to ethyleneoxy oxygen atoms of the host. One δ-pyridinium hydrogen is indirectly connected to an ethyleneoxy chain of host **4a** by a hydrogen bonding water bridge (**F**, **G** and **H** in Fig. 4). This is interesting, since the two β-pyridinium hydrogens of **3** are also connected to an ethyleneoxy chain of host **4a** by a hydrogen bonding water bridge in the 1 : 1 complex **4a·3**.[4] Furthermore, neither of the δ-pyridinium hydrogens are involved in interactions between the host and guest in the 1 : 1 complex **2b·1**.[3e] Neither of the γ-pyridinium hydrogens of **1** are involved in hydrogen bonding to the host in **4a·1**, but one γ-pyridinium carbon has a short contact with an ethyleneoxy oxygen atom of **2b** in **2b·1**, the 1 : 1 complex based on the simple crown ether.[3e]

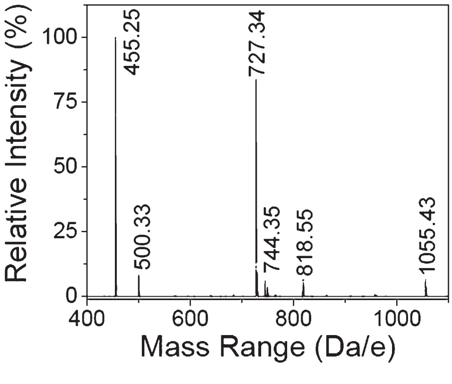

Fig. 3 Electrospray mass spectrum of a solution of **4a** and **1** in a mixture of acetonitrile and chloroform (4 : 1). Assignments of the main peaks: *m*/*z* 1055.43 [**4a·1** − PF_6]$^+$, 818.55 [**4a$_2$·1** − 2PF_6]$^{2+}$, 744.35 [**4a** + H_2O]$^+$, 727.34 [**4a** + H]$^+$, 500.33 [**4a$_2$·1** − $CH_2CH_2(OCH_2CH_2)_3O$ − 2PF_6 + K]$^{3+}$ and 455.25 [**4a·1** − 2PF_6]$^{2+}$.

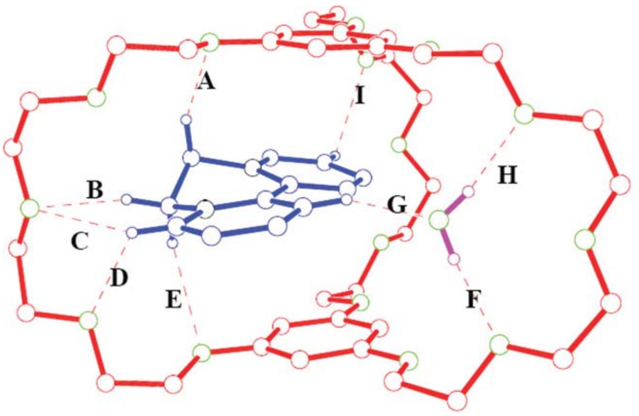

Fig. 4 A ball-and-stick view of the X-ray structure of **4a·1**. **4a** is red, **1** is blue, the water molecule is magenta, oxygens are green and nitrogens are black. The two PF_6^- counterions, other solvent molecules and hydrogens, except the ones involved in hydrogen bonding between **4a** and **1**, are omitted for clarity. Hydrogen bond parameters: H···O distances (Å), C(O)–H···O angles (°), C(O)···O distances (Å) **A**: 2.47, 153, 3.38; **B**: 2.29, 162, 3.25; **C**: 2.60, 146, 3.43; **D**: 2.65, 119, 3.21; **E**: 2.65, 134, 3.42; **F**: 1.99, 173, 2.85; **G**: 2.27, 137, 3.04; **H**: 1.98, 170, 2.84; **I**: 2.77, 124, 3.40. Face-to-face π-stacking parameters: centroid–centroid distances (Å) 3.72, 4.09, 4.05 and 4.68; ring plane–ring plane inclinations (°): 7.4, 1.6, 14.0 and 8.4. The centroid–centroid distance (Å) and dihedral angle (°) between the two phenylene rings of **4a**: 6.79 and 6.8. The centroid–centroid distance (Å) and dihedral angle (°) between the pyridinium rings of **1**: 4.23 and 15.5.

The values of the dihedral angle between the two pyridinium rings of **1** in uncomplexed **1**, **2b·1** and **4a·1** are 18.5°,[11] 20°[3e] and 15.5° (Fig. 4), respectively. The two aromatic rings of the host in **4a·1** are almost parallel (6.8°) with a centroid–centroid distance of 6.79 Å, a value smaller than the corresponding values 6.94 Å in **4a·3**[4] and 7.0 Å, in **2b·1**, whose crystals are yellow.[3e] These rotational changes take place presumably in order to maximize face-to-face π-stacking and charge transfer interactions between the two electron-rich phenylene rings of the cryptand host and the two electron-poor pyridinium rings of the diquat guest, leading to the bright yellow color of crystals of **4a·1**.

Overall, the inclusion complexation of diquat (**1**) by crown ethers and cryptands involves the enclosure of the guest in such a way that charge transfer interactions are allowed, augmenting host–guest hydrogen bonding. This involves folding into "taco-complexes" for smaller crown ethers,[3a,3b] while for the larger crown ethers **2b**[3e] and its *para*-analog,[3f] folding is not necessary for π-stacking, nor is it observed. The structures of cryptands **4** and a dibenzo-30-crown-10-based analog[3c] are pre-organized in taco-like conformations that facilitate π-stacking.

In summary, we have demonstrated that bis(*meta*-phenylene)-32-crown-10-based cryptands can complex diquat much more strongly than bis(*meta*-phenylene)-32-crown-10 itself. In fact, cryptand **4b** has one of the highest association constants for diquat reported to date. These complexes have a 1 : 1

stoichiometry in solution. This efficient recognition motif will be used in the preparation of other supramolecular systems.

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Notes and references

‡ Crystal data of **4a·1**: rods, yellow, 0.270 × 0.154 × 0.078 mm, $C_{54}H_{80}F_{12}N_2O_{18}P_2$, M = 1335.14, orthorhombic, space group $Pna2_1$, a = 24.869(2), b = 22.922(2), c = 10.8407(13) Å; $\alpha = \beta = \gamma = 90°$; V = 6179.7(11) $Å^3$, Z = 4, D_c = 1.435 g cm^{-3}, T = 100 K, μ = 1.77 cm^{-1}, 38121 measured reflections, 11848 independent reflections (R_{int} = 0.0587), 805 parameters, $F(000)$ = 2800, R_1 = 0.0531, wR_2 = 0.0919 [$I > 2\sigma(I)$], maximum residual density 0.351 e·$Å^{-3}$, and GoF(F^2) = 1.046. CCDC 294375. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b600227g

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7 ^{1}H NMR characterizations were done on solutions with a constant $[\mathbf{4a}]_0$ and varied $[\mathbf{1}]_0$. Based on these NMR data, Δ_0, the difference in δ values for H_1 of **4a** in the uncomplexed and fully complexed species, was determined as the y-intercept of a plot of $\Delta = \delta - \delta_u$ *vs.* $1/[\mathbf{1}]_0$ in the high initial concentration range of **1**; Δ_0 = 0.448 ppm. Then $p = \Delta/\Delta_0$; Δ = observed chemical shift change relative to the uncomplexed species. K_a values were calculated from $K_a = p/\{(1 - p)([\mathbf{1}]_0 - p[\mathbf{4a}]_0)\}$. The average value given in the text resulted from 8 data points ranging from p = 0.313 to 0.993; the error bar is the standard deviation from the mean. It was found that for this system that K_a does not have the concentration dependence we found in two other systems.[8] The concentration dependence of the K_a calculated in this manner results because the complexes are not ion paired, although the guest salts are ion paired. In such cases, more extensive studies are required to determine the dissociation constant for the ion pair and the binding constant for the cationic guest with the host[8].

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