Promotion of host folding during the formation of a taco complex†

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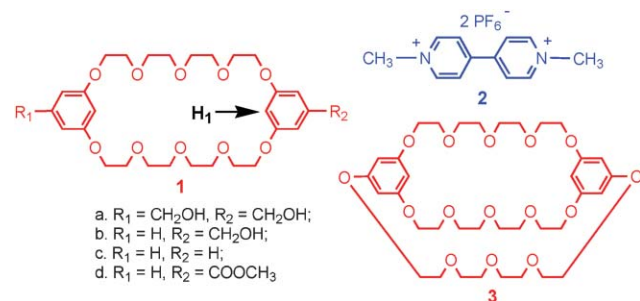Host folding for the formation of taco complexes can be promoted by introduction of additional interactions between the host and guest as shown by enhanced associations and X-ray crystal structures.

Paraquat derivatives (N,N′-dialkyl-4,4′-biyridinium salts) have been widely used as guests in supramolecular chemistry to construct numerous host–guest complexes.[1] We reported the first solid-state paraquat-based taco complex from a bis(m-phenylene)-32-crown-10 (BMP32C10) derivative (diol **1a**) and paraquat (**2**).[2] In this crystal structure, **1a** and **2** formed a folded, *exo* type complex instead of the expected threaded structure. Later we successfully prepared the first solid state supramolecular poly(taco complex).[3] Based on the crystal structure of the paraquat-based taco complex, we designed and prepared the first crown ether-based cryptand host **3**,[2] a series of bis(m-phenylene)-26-crown-8- and bis(m-phenylene)-32-crown-10-based cryptand hosts,[4] and a trifluoroacetate anion chelated supramolecular cryptand for paraquat derivatives[5a] and also water and trifluoroacetate chelated supramolecular cryptands for a bisparaquat derivative.[5b] It was found that cryptands and supramolecular cryptands are much better hosts than the simple crown ethers for paraquat derivatives[2,4,5a] and the bisparaquat derivative.[5b] We demonstrated that the main reason for this improvement is the entropy change difference during the complexation processes resulting from preorganization of the cryptands in the folded state.[4c] Herein, we prove that folding is an addressable step for the formation of taco complexes and can be promoted by proper introduction of substituents that provide additional attractive host–guest interactions.

When crown ether host **1b**[6] was mixed with an equivalent of paraquat guest **2** in CD₃COCD₃, a yellow color was observed immediately due to charge transfer interactions between the electron-rich aromatic rings of **1b** and the electron-poor pyridinium rings of paraquat **2**. A Job plot[7] (Fig. 1) based on proton NMR data of H_1 demonstrated that the complex between **1b** and **2** was of 1 : 1 stoichiometry in solution. The association constant (K_a) of **1b·2** calculated based on the proton NMR data was 8.2 ($\pm$0.8) $\times 10^2$ M^{-1} in acetone.[8] This K_a value is higher than that, 5.5 ($\pm$0.5) $\times 10^2$ M^{-1}, for **1c·2**,[4a] but lower than that, 1.23 ($\pm$0.07) $\times 10^3$ M^{-1}, for **1a·2**.[9] These results indicated that the introduction of the benzylic alcohol group affects the complexation between the BMP32C10 derivative and the paraquat guest **2**. That is to say, the benzylic alcohol group can provide additional stabilizing interactions between the host and guest.

A solution of **1b** and **2** in 4 : 1 acetonitrile : chloroform was characterized by electrospray ionization mass spectrometry (Fig. 2). Two relevant peaks were found for **1b·2**: m/z 897.37 (60%) [**1b·2** − PF₆]⁺ and 376.29 (100%) [**1b·2** − 2PF₆]²⁺. Interestingly two peaks at m/z 1463.95 (5%) and 659.51 (26%) appear to be due to the [3]complex **1b₂·2**: [**1b₂·2** − PF₆]⁺ and [**1b₂·2** − 2PF₆]²⁺; this is noteworthy because in several cases analogous (cryptand)₂·paraquat complexes[4a] have been isolated and characterized.

Single crystals of **1b**‖ (Fig. 3a) were grown by vapor diffusion of pentane into its acetone solution, while single crystals of the complex **1b·2**‖ (Fig. 3d) were grown from an acetone solution of **1b** and **2** (molar ratio: 3 : 1) by the same method. The crystal structure of **2** (Fig. 3b) was reported before.[4c] The 1 : 1 stoichiometry for the complex between **1b** and **2** was confirmed by X-ray analysis (Fig. 3d). Just like the taco complex **1a·2**,[2] **1b·2** is also stabilized by C–H···O hydrogen bonding and face-to-face

a. R_1 = CH₂OH, R_2 = CH₂OH;
b. R_1 = H, R_2 = CH₂OH;
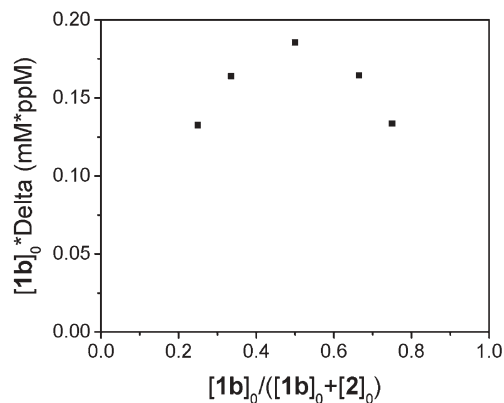c. R_1 = H, R_2 = H;
d. R_1 = H, R_2 = COOCH₃

Fig. 1 Job plot: the stoichiometry of the complex between **1b** and **2** in CD₃COCD₃ solution using data for H_1 of **1b**. [**1b**]₀ and [**2**]₀ are initial concentrations of **1b** and **2**. [**1b**]₀ + [**2**]₀ = 2.00 mM.
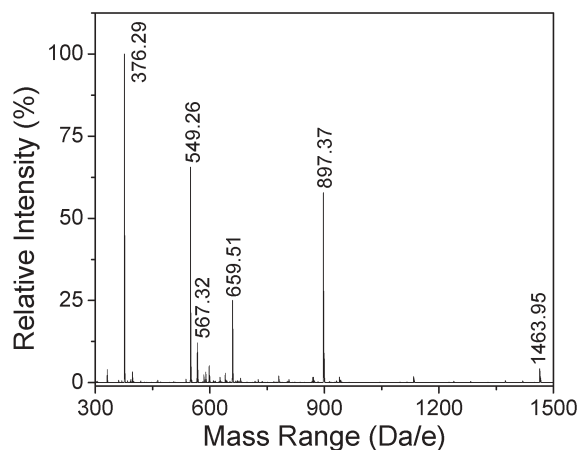
Fig. 2 Electrospray mass spectrum of a solution of **1b** and **2** in a mixture of acetonitrile and chloroform (4 : 1). Assignments of main peaks: m/z 1463.95 [**1b₂·2** − PF₆]⁺, 897.37 [**1b·2** − PF₆]⁺, 659.51 [**1b₂·2** − 2PF₆]²⁺, 567.32 [**1b** + H]⁺, 549.26 [**1b** − OH]⁺, and 376.29 [**1b·2** − 2PF₆]²⁺.

π-stacking interactions between the phenylene rings of the host and the pyridinium rings of the guest.

However, there are some obvious differences. First, **1a·2** is stabilized by three hydrogen bonds between the guest and host based on two α-pyridinium hydrogens of **2**,[2] while **1b·2** has five hydrogen bonds between the guest and host based on one α-pyridinium hydrogen (**B** in Fig. 3d), two β-pyridinium hydrogens (**C** and **D** in Fig. 3d), and two *N*-methyl hydrogens of **2** (**A** and **E** in Fig. 3d). *N*-methyl hydrogens of paraquat **2** usually are not involved in hydrogen bonding with the host in paraquat-based complexes. Two examples reported up to now are a pseudorotaxane-like [2]complex[10] based on bis(*p*-phenylene)-34-crown-10 and **2** and a [3]pseudorotaxane[11] between a bis(*m*-phenylene)-32-crown-10-based bis(crown ether) host and **2**. Second, in **1a·2**, two β-pyridinium hydrogens are hydrogen bonded to a fluorine atom of a PF₆ counterion, but in **1b·2** here two β-pyridinium hydrogens are hydrogen bonded to the oxygen atom of the OH moiety of the host! These two hydrogen bonds demonstrate that the benzylic alcohol group does provide additional stabilizing interactions between the host and guest. These additional interactions between the host and guest account for the increase in K_a from **1c·2** to **1b·2** because CH₂OH has a Hammett σ value of zero[12] and thus is not expected to influence the complexation of **1b** with **2** electronically. It is likely that in solution the two CH₂OH groups of **1a** are involved in hydrogen-bonding to β-pyridinium hydrogens in **1a·2** though these were not observed in the solid state structure of **1a·2**.[2] This is probably why there is doubling of K_a from **1c·2** to **1a·2**.

Third, face-to-face π-stacking interactions are different in **1a·2** and **1b·2**; the dihedral angle and the centroid–centroid distance between the two crown aromatic rings change from 6.9° and 7.39 Å to 13.5° and 6.86 Å, respectively. This latter distance is very short. Even in a pseudorotaxane-like [2]complex based on cryptand host **3** and paraquat guest **2**, the corresponding value is 6.94 Å.[2] This demonstrated that the folding of crown ether host was promoted by the introduction of the benzylic alcohol group, which provided two hydrogen bonds between the host and guest. Strong charge transfer between **1b** and **2** gave the bright yellow color of the crystals of **1b·2**.
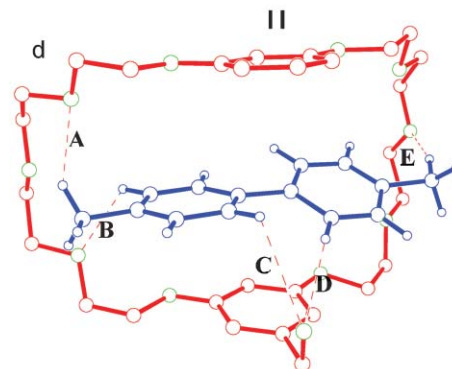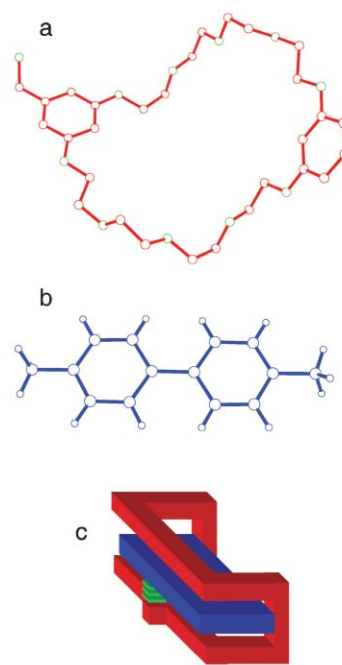

Fig. 3 X-ray crystal structures of **1b** (a), **2** (b), and **1b·2** (d), and a cartoon representation of **1b·2** (c). The crown ether host (**1b**) is red, the paraquat guest (**2**) is blue, and oxygens are green. In **1b**, hydrogens have been omitted for clarity. In **2**, two PF₆⁻ ions have been omitted for clarity. In **1b·2**, two PF₆⁻ ions, two acetone molecules, and hydrogens except the ones on **2** have been omitted for clarity. Hydrogen-bond parameters are as follows: C···O distances (Å), H···O distances (Å), C–H···O angles (deg) **A**, 3.25, 2.39, 145; **B**, 3.19, 2.52, 124; **C**, 3.46, 2.46, 177; **D**, 3.34, 2.50, 142; **E**, 3.26, 2.29, 162. Face-to-face π-stacking parameters: centroid–centroid distances (Å) 3.98, 4.39; ring plane/ring plane inclinations (deg): 13.1, 5.0. The centroid–centroid distance (Å) and dihedral angle (deg) between the phenylene rings of **1b**: 6.86 and 13.5. The centroid–centroid distance (Å) and dihedral angle (deg) between the pyridinium rings of paraquat guest **2**: 4.29 and 22.0.

Alcohol **1b** was prepared from ester **1d**.[6] It is clear that both uncomplexed **1b** (Fig. 3a) and **1d**‖ (Fig. 4) are not folded as shown by their X-ray crystal structures. By comparing the crystal structures of **1b** (Fig. 3a) and **1b·2** (Fig. 3d), it can be seen that the conformations of **1b** are very different. In order to form taco complex **1b·2**, **1b** has to be folded. This is entropically unfavorable. However, folding is not necessary during the formation of the cryptand-based complexes, *e.g.*, **3·2**, because the host is preorganized.[2] Also the conformation of **2** is changed during the complexation; the dihedral angle between the pyridinium rings
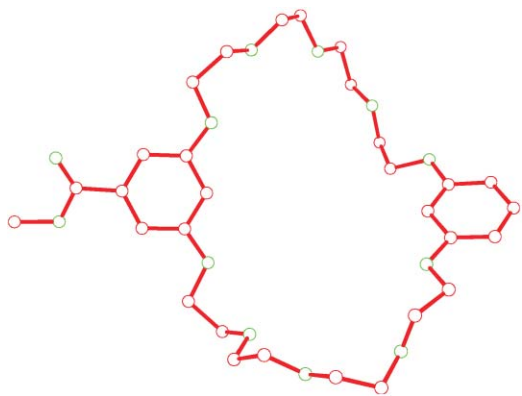
Fig. 4 X-ray crystal structure of ester **1d**. Hydrogens have been omitted for clarity and oxygens are green.

of **2** changes from $0°$ to $22°$ in order to allow the attractive interactions (Figs. 3b and 3d).

In summary, we have proved that host folding during the formation of taco complexes is addressable and can be promoted by incorporation of suitably situated substituents. This leads to improvement of complexation from taco complexes based on simple crown ethers (*e.g.*, **1c**) to taco complexes based on crown ethers with substituents that engage the guest (*e.g.*, **1a** and **1b**).

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Notes and references

‖ Crystal data of **1b**: prism, colorless, $0.21 \times 0.40 \times 0.58$ mm^3, $C_{29}H_{39}O_{11}$, $FW = 563.62$, Triclinic, space group P-1, $a = 10.3115(19)$, $b = 11.0844(17)$, $c = 13.8563(19)$ Å, $\alpha = 76.203(14)°$, $\beta = 70.914(14)°$, $\gamma = 83.447(14)°$, $V = 1452.4(4)$ Å^3, $Z = 2$, $D_c = 1.497$ g cm^{-3}, $T = 100(2)$ K, $\mu = 0.99$ cm^{-1}, 18237 measured reflections, 9130 independent reflections, 371 parameters, $F(000) = 602$, $R_1 = 0.0799$, $wR_2 = 0.0920$ (all data), $R_1 = 0.0474$, $wR_2 = 0.0704$ [$I > 3\sigma(I)$], max. residual density 0.49 e·Å^{-3}, and goodness-of-fit (F^2) = 0.8278. CCDC 262642. Crystal data of **1b·2**: prism, yellow, $0.10 \times 0.25 \times 0.30$ mm^3, $C_{47}H_{62}F_{12}N_2O_{13}P_2$, $FW = 1157.98$, Triclinic, space group P-1, $a = 11.6764(12)$, $b = 15.9293(19)$, $c = 16.8706(18)$ Å, $\alpha = 62.902(11)°$, $\beta = 83.880(9)°$, $\gamma = 73.69(1)°$, $V = 2680.1(6)$ Å^3, $Z = 2$, $D_c = 1.435$ g cm^{-3}, $T = 100(2)$ K, $\mu = 1.85$ cm^{-1}, 25101 measured reflections, 10960 independent reflections, 685 parameters, $F(000) = 1210$, $R_1 = 0.1991$, $wR_2 = 0.1882$ (all data), $R_1 = 0.1570$, $wR_2 = 0.1808$ [$I > 0.5\sigma(I)$], max. residual density 0.63 e·Å^{-3}, and goodness-of-fit (F^2) = 0.8671. CCDC 262643. Crystal data of **1d**: prism, colorless, $C_{30}H_{42}O_{12}$, $FW = 594.64$, Monoclinic, space group $P2_1/n$, $a = 10.9525(3)$, $b = 11.2070(2)$, $c = 25.0146(4)$ Å, $\beta = 97.6555(4)°$, $V = 3043.06(16)$ Å^3, $Z = 4$, $T = 173(2)$ K, 379 parameters, $R_1 = 0.0853$, $wR_2 = 0.1708$ (all data), $R_1 = 0.0618$, $wR_2 = 0.1551$ [$I > 2\sigma(I)$], 5107 reflections were used in refinements by full-matrix least-squares on F^2, max. residual density 0.264 e·Å^{-3}, and goodness-of-fit (F^2) = 1.680. CCDC 262641. See http://www.rsc.org/suppdata/cc/b5/b503092g/index.sht for crystallographic data in CIF or other electronic format.

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8 ^{1}H NMR characterizations were done on solutions with constant [**1b**]$_0$ and varied [**2**]$_0$. Based on these NMR data, $\Delta_{0,1b}$, the difference in δ values for H$_1$ of **1b** in the uncomplexed and fully complexed species, was determined as the y-intercept of a plot of $\Delta = \delta - \delta_u$ *vs.* 1/[**2**]$_0$ in the high initial concentration range of **2** to be 0.531 ppm. Then $K_{a,1b·2}$ values at different [**1b**]$_0$ and [**2**]$_0$ were calculated from $K_{a,1b·2} = (\Delta_{1b}/\Delta_{0,1b})/\{1 - (\Delta_{1b}/\Delta_{0,1b})\}\{[\mathbf{2}]_0 - (\Delta_{1b}/\Delta_{0,1b})[\mathbf{1b}]_0\}$. The values and errors of $K_{a,1b·2}$ are the means and standard deviations from seven or nine data points with different [**1b**]$_0$ and [**2**]$_0$ and $0.1 < \Delta_{1b}/\Delta_{0,1b} < 0.9$.
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