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Cooperative Host/Guest Interactions via Counterion Assisted Chelation: Pseudorotaxanes from Supramolecular Cryptands

Jason W. Jones,[†] Lev N. Zakharov,[‡] Arnold L. Rheingold,[‡] and Harry W. Gibson*,[†]

Department of Chemistry, Virginia Polytechnic Institute and State University, Blacksburg, Virginia 24061-0212, and Department of Chemistry, University of Delaware, Newark, Delaware 19716

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In the late 1980s, Stoddart et al. reported on the formation of pseudorotaxanes from paraquats (e.g., dimethyl viologen, **1**-2PF$_6$) and bisarylene crown ethers bearing 32−34 core atoms.[1] More recently, Gibson et al. showed that one of the complexes formed between bis(5-hydroxymethyl-1,3-phenylene)-32-crown-10[2] (**2**) and **1**-2PF$_6$ was not a pseudorotaxane, but an exo- or taco-complex (see Figure 1),[3] which suggested the favorable effect of confining the flexible host molecule to the folded shape. When a covalent linker was used to do so in forming bicyclic host **3**, a 100-fold increase in apparent association constant (K_a) resulted![3]

Encouraged by these exciting results, we have since explored other methods to drive pseudorotaxane formation. In studying the influence of counteranions on complexation, we serendipitously discovered a ready and facile method of increasing K_a in the complexation of paraquats by host **2**.

As a control experiment, an acetone-d_6 solution of **2** and 2 equiv of **4**-PF$_6$ was studied. Neither ^{1}H nor ^{19}F NMR signals shifted for either of the two components, indicating that **4**-PF$_6$ does not complex with **2**. Under similar conditions, ^{1}H and ^{19}F NMR indicated that no interaction occurs between paraquat diol **5**-2PF$_6$[4] and **4**-PF$_6$.

In a second control experiment designed to study the effect of added salt on complexation, we titrated **4**-PF$_6$ into an acetone-d_6 solution of **2** and **5**-2PF$_6$. As discussed elsewhere,[1,5] upon mixing the host and guest components, a bright orange solution resulted. Notably, in the presence of **4**-PF$_6$ the ^{1}H NMR resonances of the crown signals all shift toward their uncomplexed positions, signaling a *decrease* in association (see Figure 2). For confirmation, the spectra were analyzed to estimate K_a; Δ_0, the difference in δ values for the uncomplexed and fully complexed species, was taken from earlier studies[6] to be 0.472 ppm for H$_b$. On the basis of this value, we calculated $K_a = 830 \pm 130\ \mathrm{M}^{-1}$ for **2**/**5**-2PF$_6$ alone and $K_a = 520 \pm 80\ \mathrm{M}^{-1}$ for **2**/**5**-2PF$_6$ in the presence of **4**-PF$_6$, representing a 40% reduction in apparent K_a.[7] Because the added **4**-PF$_6$ does not interact directly with host **2**, we believe this reduction to be the result of increased ionic strength. Indeed, in related experiments,[8] we observed a continuous reduction in K_a with increasing salt concentration.

We then observed the influence of a ditopic H-bond accepting counteranion. When mixed with **2**, **6**-TFA demonstrated *no* interaction with either component as prescribed by ^{1}H and ^{19}F NMRS. However, in opposition to the studies described above for **4**-PF$_6$, the ^{1}H NMR resonances of the crown signals all shifted toward their fully complexed positions upon addition of 1.18 equiv of **6**-TFA to **2**/**5**-2PF$_6$, signaling an increase in association (see Figure 3b). Indeed, using Δ_0 from above, we determine a *6.8-fold increase* in K_a ($830 \pm 130\ \mathrm{M}^{-1}$ to $5.63 \times 10^3 \pm 1.53 \times 10^3\ \mathrm{M}^{-1}$).[9] Doubling [**6**-TFA] to 4.70 mM results in a doubling of K_a to $1.20 \times 10^4 \pm 4.62 \times 10^3\ \mathrm{M}^{-1}$ (Figure 3c).[10]

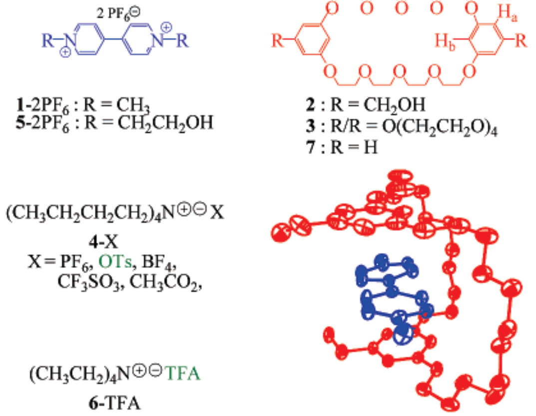

Figure 1. Compounds used in this study, and an ORTEP diagram[3] of the taco-complex **2**/**1**-2PF$_6$.

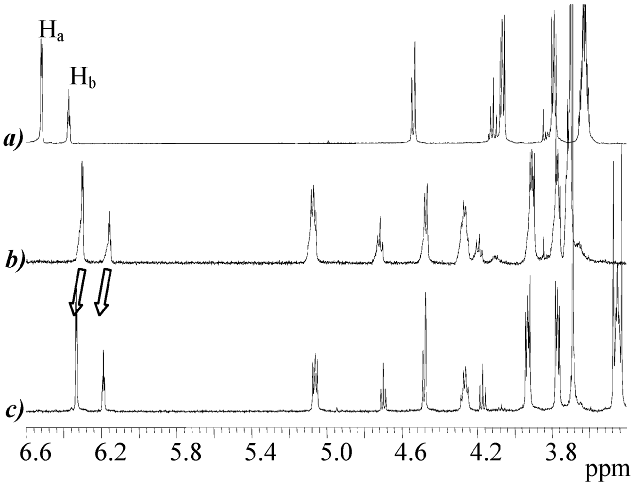

Figure 2. ^{1}H NMR spectra (400 MHz, acetone-d_6, 23 °C) of (a) **2**; (b) 2.00 mM **2** + 2.00 mM **5**-2PF$_6$; and (c) 2.00 mM **2** + 2.00 mM **5**-2PF$_6$ + 4.63 mM **4**-PF$_6$.

To be certain that the hydroxyl functionality of guest **5**-2PF$_6$ was not influencing association, a solution of **1**-2PF$_6$ and **2** was subjected to similar treatment. H$_a$ and H$_b$ shifted upfield in the presence of **6**-TFA, indicating that the OH groups of guest **5**-2PF$_6$ are not essential for the cooperative effect of **6**-TFA. Further confirmation of the key role of host **2**'s OH moieties was obtained by use of unsubstituted crown **7**: addition of **6**-TFA to solutions

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* To whom correspondence should be addressed. E-mail: hwgibson@vt.edu.
[†] Virginia Polytechnic Institute and State University.
[‡] University of Delaware.

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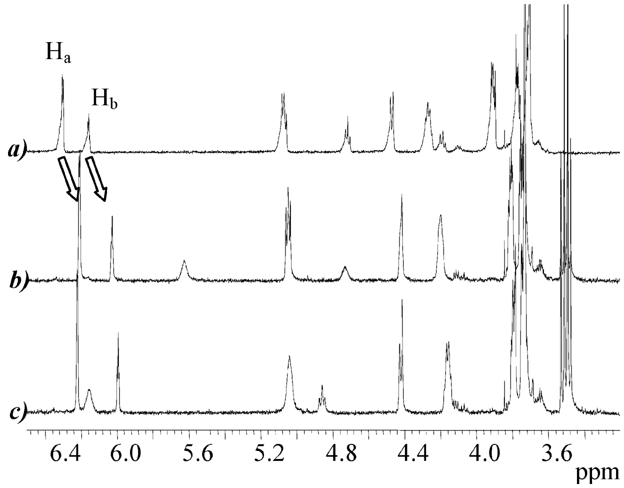
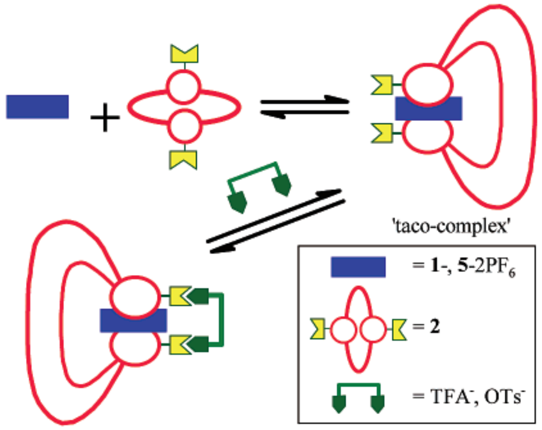


Figure 3. ^{1}H NMR spectra (400 MHz, acetone-d_6, 23 °C) of (a) 2.00 mM **2** + 2.00 mM **5**-2PF$_6$; (b) 2.00 mM **2** + 2.00 mM **5**-2PF$_6$ + 2.35 mM **6**-TFA; and (c) 2.00 mM **2** + 2.00 mM **5**-2PF$_6$ + 4.70 mM **6**-TFA.

Scheme 1. Cartoon Representation of a Cooperative Host/Guest Interaction via a Chelation Event



of **1**-2PF$_6$/**7** and **5**-2PF$_6$/**7** resulted in reduced apparent K_a's because of the increase in ionic strength.

We reasoned that the cooperativity arises because folding of **2** by **5**-2PF$_6$ into the exo- or taco-complex[10] is assisted by H-bonding of the ditopic TFA ion with the crown diol functionalities, as outlined in Scheme 1. This hypothesis was confirmed by X-ray diffraction analysis of crystals of **2**/**5**-PF$_6$/TFA (Figure 4). Such a counteranion interaction effectively forms a supramolecular cryptand, thereby stabilizing the three-component complex.[11] In agreement with this observation, the interatomic distances between atoms C2 and C18 decrease in the order **2**/**1**-2PF$_6$ (7.67 Å)[3] > **2**/**1**-PF$_6$/TFA (7.65 Å) > **3**/**1**-2PF$_6$ (7.09 Å).[3]

The influences of **4**-BF$_4$ and **4**-OTs on the complexation of **2** with **5**-2PF$_6$ were consistent with those described above: tridentate OTs$^-$ increased $K_a \approx$1.5-fold (920 ± 140 M^{-1}, [**2**] = 1.99 mM, [**5**-2PF$_6$] = 2.00 mM, [**4**-OTs] = 2.01 mM), while the nonchelating BF$_4^-$ reduced association. Addition of **4**-CF$_3$SO$_3$ also diminished K_a values, a result of the reduced basicity of triflate relative to TFA. At the other extreme, addition of the more basic acetate anion via **4**-CH$_3$CO$_2$ to **2**/**5**-2PF$_6$ resulted in electron-transfer reactions,[12] which destroyed the guest ligand.

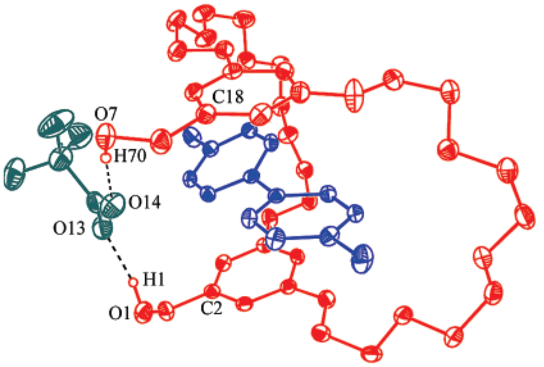


Figure 4. ORTEP diagram of **2**/**1**-PF$_6$/TFA with 50% probability ellipsoids. Hydrogens and spectator PF$_6^-$ have been omitted for clarity. Selected interatomic distances and angles: O1···O13 2.73(3) Å, O1−H1 0.94(4) Å, O13···H1 1.80(4) Å, O1−H1···O13 170(4)°; O7···O13 2.821(3) Å, O7−H70 0.83(4) Å, O14···H70 1.99(4) Å, O7−H70···O14 170(4)°; C2···C18 7.649(4) Å.

While paraquat binding is more pronounced with covalent bicyclic host **3**[3] than the current supramolecular cryptands, the simplicity of this cooperative system combined with the ready availability of starting materials is very exciting and suggests a number of extensions and elaborations, which are currently being pursued.

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Supporting Information Available: Experimental details (PDF) and an X-ray crystallographic file (CIF) for **1**/**2**-PF$_6$/TFA. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) Allwood, B. L.; Spencer, N.; Sharhriari-Zavareh, H.; Stoddart, J. F.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1987**, (a) 1058−1061; (b) 1064−1066.

(2) Gibson, H. W.; Nagvekar, D. S. *Can. J. Chem.* **1997**, *75*, 1375−1384.

(3) Bryant, W. S.; Jones, J. W.; Mason, P. E.; Guzei, I. A.; Rheingold, A. L.; Nagvekar, D. S.; Gibson, H. W. *Org. Lett.* **1999**, *1*, 1001−1004.

(4) Shen, Y. X.; Engen, P. T.; Berg, M. A. G.; Merola, J. S.; Gibson, H. W. *Macromolecules* **1992**, *25*, 2786−2787. **5**-PF$_6$ is generally more soluble than **1**-PF$_6$, and hence we have preferred its use in such studies.

(5) Gillard, R. E.; Raymo, F. M.; Stoddart, J. F. *Chem.-Eur. J.* **1997**, *3*, 1933−1940.

(6) Gong, C.; Balanda, P. B.; Gibson, H. W. *Macromolecules* **1998**, *31*, 5278−5289. Δ_0 is defined as the average value calculated by Benesi−Hildebrand, Scatchard, and Creswell−Allred treatments.

(7) Errors are reported by assuming a 5% variation in Δ/Δ_0 values.

(8) We have found that the apparent K_a for pseudorotaxane formation is highly concentration dependent. Therefore, it is imperative to specify initial concentrations in these systems.

(9) In the absence of **2**, counterion exchange under experimental conditions between **1**- or **5**-2PF$_6$ and **6**-TFA results in the precipitation of **1**- or **5**-2TFA, as characterized by X-ray analyses.

(10) NMRS studies on solutions of **2**/**6**-TFA do not reveal interaction, suggesting that templation of **2** by **1**- or **5**-2PF$_6$ is necessary for anion chelation.

(11) Ion-paired binding by neutral hosts to form pseudorotaxane complexes has also been shown by (a) Deetz, M. J.; Shukla, R.; Smith, B. D. *Tetrahedron* **2002**, *58*, 799−805 and references therein, as well as (b) Wisner, J. A.; Beer, P. D.; Drew, M. G. B. *Angew. Chem., Int. Ed.* **2001**, *40*, 3606−3609.

(12) Naik, D. B.; Moorthy, P. N. *J. Chem. Soc., Perkin Trans. 2* **1990**, *5*, 705−709.

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