Host–Guest Chemistry

Lithium-Templated Synthesis of a Donor–Acceptor Pseudorotaxane and Catenane**

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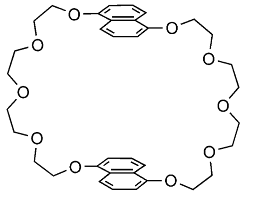
In memory of Norma Stoddart

One of the key goals of supramolecular chemistry is to assemble structural building blocks into arrays with new properties that emerge only in supramolecular architectures. These new properties may improve our understanding of noncovalent interactions, or they may endow useful functionality. Catalysts, sensors, and molecular machines or computers are all possible applications. However, to achieve this aim we need powerful methods for the synthesis of supramolecular systems, and while there has been dramatic progress in the past 30 years, we still have much to learn. We report herein an efficient cation-templated approach to donor–acceptor pseudorotaxanes and catenanes developed from an accidental observation.

Rotaxanes and catenanes have for some time been the subject of intense study[1–7] both because of their fascinating architectures,[8–18] and because they may have useful properties as molecular-level switches and sensors.[5,19–25] Our approach has been to bring together neutral electron-rich components such as crown ether **1** (the "donor") and electron-poor components such as pyromellitic diimide **2** (the "acceptor") to create highly colored donor–acceptor systems that are neutral, chemically robust, and capable of postsynthetic modification.[3] Catenanes **4** and **5** are formed from **2** and **3b** by alkene metathesis, but we have used a range of other bond-forming reactions with related building blocks.[3] Weak C–H···O hydrogen bonds and donor–-acceptor (DA) interactions are both important driving forces for complex formation,[26–28] but the charge-transfer (CT) band resulting from DA interactions provides the key diagnostic color test that led to the unexpected discovery discussed below.

When **1** and **2** are mixed (each 5.5 mM concentration) in chloroform solution they give a pale yellow solution due to a very weak CT band at 440 nm; the NMR spectrum of such a solution is essentially the sum of the two components, that is, there is insufficient complexation to be detected by NMR. We found that the addition of solid LiI gave a brightly colored orange solution (Figure 1) with a CT band at 498 nm, and a ^{1}H NMR spectrum with broadened and shifted peaks that could not be readily interpreted.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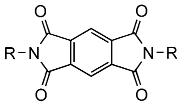
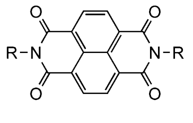
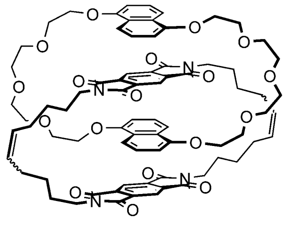

2: R = $(CH_2)_4CH{=}CH_2$


3a: R = Hexyl
3b: R = $(CH_2)_4CH{=}CH_2$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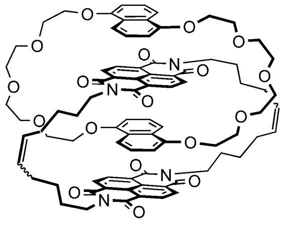
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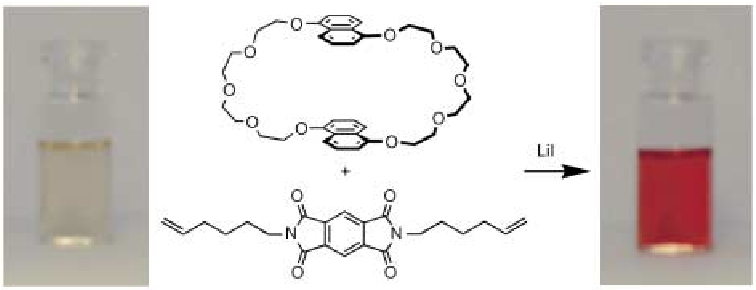

Figure 1. Observed color change after the addition of lithium iodide to a $CHCl_3$ solution of **1** and **2** (5.5 mM in each component).

Further investigation revealed that 98:2 chloroform–methanol was the best solvent mixture for spectroscopic and crystallographic study, and all results below are reported for that system. A 1:1 mixture of **1** and **2** allows two equivalents of LiI to become soluble over a period of hours, thus giving intense orange coloration to the solution in close proximity to the solid salt. This implies, but does not prove, formation of a 1:1:2 complex of **1**:**2**:LiI. Sonication greatly increases the rate of solubilization to give a clear orange solution. On heating, the complex dissociates and color is lost; cooling restores color as expected.

^{1}H NMR spectra of a solution of **1** and **2** following the addition of 1 and 2 equivalents of LiI are shown in Figure 2. The most striking observation (Figure 2B) is that after the

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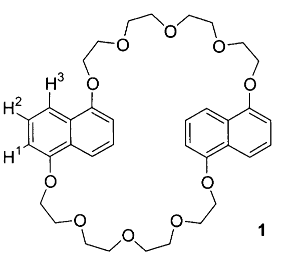
[**] We thank EPSRC, BBSRC, Astra-Zeneca, and the Cambridge European Trust for financial support.

Supporting information for this article is available on the WWW under http://www.angewandte.org or from the author.

DOI: 10.1002/ange.200353075



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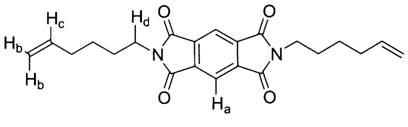

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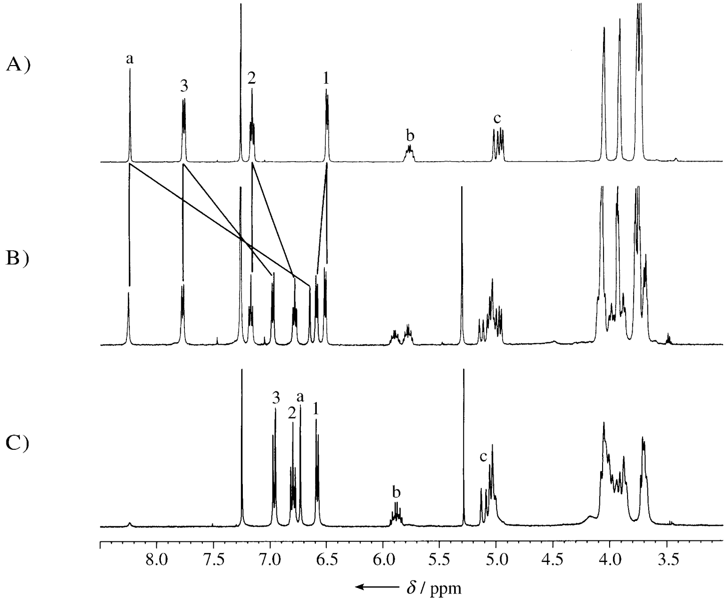

Figure 2. Room temperature ^{1}H NMR spectra (500 MHz) of a 98:2 $CDCl_3$:MeOH solution of **1** and **2** (5.5 mM each) following the addition of A) 0, B) 1, and C) 2 equivalents of LiI.

addition of 1 equivalent of LiI, 50% of the organic material remains unchanged, while 50% is present in a new species in slow exchange on the chemical shift timescale. This is unambiguous confirmation of the 1:1:2 stoichiometry, and implies a dramatic cooperativity between binding of the first and second cations. In the spectrum of the solution that contains 2 equivalents of LiI, the pyromellitic diimide signal from H_a is shifted upfield by 1.6 ppm, which implies close proximity to the naphthalene aromatic ring current. Smaller upfield shifts are observed for H^3 and H^2 of the naphthalene unit. Complexation does not alter the symmetry of this unit, whereas the methylene protons of the ethylene glycol chains show splitting owing to a loss of effective local symmetry: an HMQC spectrum confirms that each pair of CH_2 protons is diastereotopic, but the effective number of carbon-atom environments is unchanged. A NOESY spectrum shows pyromellitic diimide–glycol and naphthalene–hexenyl interactions consistent with the same relative pyromellitic diimide–naphthalene diimide geometry observed in the crystal structure of **4**.[29]

These results are consistent with the formation in solution of a highly symmetrical pseudorotaxane that consist of one crown and one pyromellitic diimide held together by two Li ions, presumably through the coordination of oxygen atoms of both organic components. Isolation of orange crystals from a concentrated chloroform/methanol 98:2 solution of a 1:1 mixture of crown ether **1** and pyromellitic diimide **2** with an excess of LiI confirmed the following conclusions (Figure 3):[30]

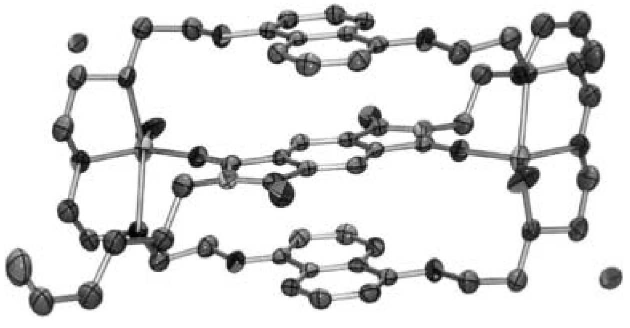

Figure 3. Crystal structure of $[Li_2\cdot\mathbf{1}\cdot\mathbf{2}]^{2+}$. Ortep representation (thermal ellipsoids set at the 50% level of probability), hydrogen atoms have been omitted for clarity.

a) The interplanar separation between the effectively coplanar donor and acceptor rings is 3.2 Å, which is consistent with related catenanes.
b) The lithium cations are five-coordinate, in a distorted trigonal bipyramidal arrangement. Three glycol oxygen atoms and one pyromellitic diimide carbonyl are bound to each cation, the fifth coordination site is taken by a water molecule. The preference for water over methanol to fill the fifth coordination site is remarkable considering the large excess of methanol in solution. The iodide anions are not coordinated to the lithium cations.
c) The unit cell structure does not involve any significant stacking of the pseudorotaxanes, that is, no π–π stacking or hydrogen bonding between different complexes has been observed. The unit cell contains chloroform molecules but no further water or methanol molecules.

We have studied the binding of **1** to **2** in the absence and presence of LiI by using isothermal titration calorimetry (ITC). ITC is a powerful technique, which in two automated experiments[31] gives the enthalpy (ΔH°), the equilibrium constant (hence, ΔG°), and the stoichiometry of binding. From the enthalpy and free-energy changes, the entropy of binding can also be obtained. The results are shown in Table 1.[32] The equilibrium constant for binding of **1** to **2** is modest in the absence of LiI, but increases tenfold in the presence of 10 equivalents of LiI. In both cases binding is completely enthalpy-driven with an almost negligible contribution of entropy.

Table 1: Equilibrium constants and thermodynamics of binding of **1** to **2** in the absence and presence of LiI.

	K [M^{-1}]	ΔG° [kJ mol^{-1}]	ΔH° [kJ mol^{-1}]	$T\Delta S^\circ$ [kJ mol^{-1}]
0 equiv LiI	21	−7.6	−7.5	0.1
10 equiv LiI	2.1×10^2	−13	−12	1

One successful example of a lithium templated synthesis of [2]-catenanes by using metathesis has been reported previously.[33] We have explored the influence of Li-templated complexation on catenane formation in our system: as previously reported, catenanes **4** and **5** could be synthesized by using the reversible-alkene-metathesis reaction.[34] The yield obtained was in accordance with the strength of the donor–acceptor interactions giving a 20 % yield of **4** and 60 % yield for **5**. We found that the metathesis was successful in a dichloromethane/methanol 98:2 solution that contained LiBr and by using the second-generation Grubbs' catalyst.[35] While there was almost no template effect on the synthesis of the naphthyl diimide catenane **5**, a major improvement was observed for the formation of pyromellitic diimide catenane **4** (60 % yield compared to 20 % without lithium).

The pseudorotaxane formation of naphthyl diimide **3a** was also investigated in presence of lithium. Surprisingly, no color change was observed after the addition of lithium bromide. Further NMR experiments also showed no lithium effect, which could explain why the same yield of the naphthyl diimide catenane **5** is obtained with and without lithium. Taking advantage of this observation, we investigated the switchable nature of the pseudorotaxane system. The starting point was a pale yellow solution of the pyromellitic diimide **2** with the crown ether **1**. The ^{1}H NMR signals are not shifted because of the weakness of the donor–acceptor complex. After the addition of the naphthalene diimide **3a**, the solution changed color from pale yellow to light purple (Figure 4). The corresponding ^{1}H NMR spectrum displays the characteristic shifts and broadening of the naphthalene diimide complex, thus showing that naphthalene diimide unit is bound selectively by the macrocycle. When lithium bromide was added, this situation was reversed. The solution changed to bright orange, which suggests that the pyromellitic diimide **2** replaces the naphthalene diimide **3a**. This assumption was confirmed by the corresponding ^{1}H NMR spectrum, which displays the characteristic signal pattern for the lithium-templated pseudorotaxane. The aromatic signal of the pyromellitic diimide **2** shifted to $\delta = 6.72$ ppm, whereas the aromatic signal of the naphthalene diimide **3a** shifted downfield to the unbound position at $\delta = 8.73$ ppm. This experiment confirms that switching between the naphthalene diimide and the pyromellitic diimide pseudorotaxane can be induced by lithium cations.

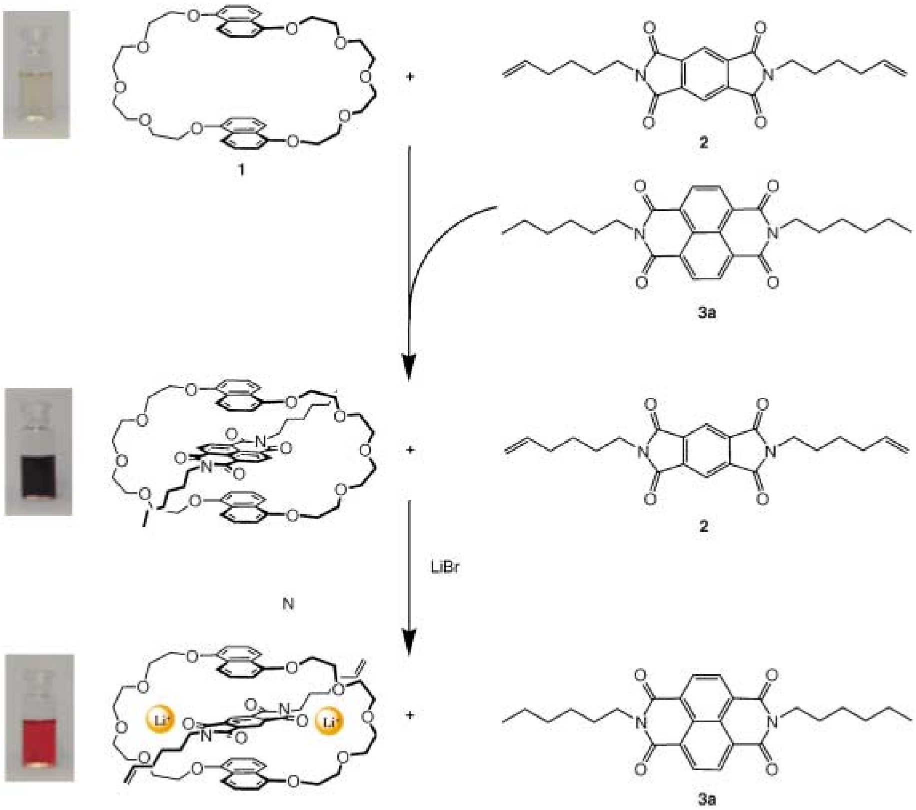

Figure 4. Switching experiment.

In conclusion we have shown that simultaneous coordination of an aromatic electron donor and acceptor to metal cations can lead to the formation of highly stable colored pseudorotaxane complexes. In at least one favorable case described here, the pseudorotaxane is an effective precursor to a [2]-catenane. Elsewhere we will describe the application of this donor–acceptor template to the synthesis of switchable covalent rotaxanes and additional catenanes.

Received: October 13, 2003
Revised: January 7, 2003 [Z53075]

Keywords: catenanes · host–guest chemistry · molecular devices · rotaxanes · supramolecular chemistry · template synthesis

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[30] Crystal data for $[\mathbf{1}\cdot\mathbf{2}\cdot(\mathrm{Li})_2]^+(\mathrm{I}^-)_2$. $\mathrm{C}_{64}\mathrm{H}_{72}\mathrm{N}_2\mathrm{O}_{16}\mathrm{Li}_2\mathrm{I}_2\cdot 2\,\mathrm{CHCl}_3$, $M_r = 2037.06$, crystal size $0.51 \times 0.25 \times 0.21$, $Z = 2$, monoclinic, space group $P2_1/c$, $a = 15.9797(2)$, $b = 10.5420(2)$, $c = 26.2623(5)$ Å, $\alpha = 90$, $\beta = 95.5990(10)$, $\gamma = 90°$, $U = 4402.99(13)$ Å^3, $\rho_{\mathrm{calc}} = 1.537\,\mathrm{mg\,m^{-3}}$, $T = 180(2)$ K, $\theta_{\min} = 1.02$, $\theta_{\max} = 27.48$, $\lambda = 0.71073$. Radiation type $\mathrm{Mo}_{\mathrm{K}\alpha}$, measurement method thin slice ω and φ scans, multiscan absorption corrections applied, $\mu(\mathrm{Mo}_{\mathrm{K}\alpha}) = 1.318\,\mathrm{mm^{-1}}$, $T_{\min} = 0.680$, $T_{\max} = 0.758$. Data collected on a Nonius KappaCCD diffractometer. Of 34046 reflections measured, 10014 were independent ($R_{\mathrm{int}} = 0.0490$). The structure was solved by direct methods (SIR92) and refined by full-matrix least-squares on F^2 (SHEXLTL v.6.12). Final $R1 = 0.0488$ (7121 reflections with $I > 2(I)$) and $wR2(F^2) = 0.1319$ (all data). Residual electron density $\rho_{\max} = 1.396\,\mathrm{e\,Å^{-3}}$, $\rho_{\min} = -0.958\,\mathrm{e\,Å^{-3}}$.

[31] Heat effects resulting from the titration of a concentrated solution of **2** into **1** are a sum of the enthalpy change upon complexation of **1** to **2** and the heat of dilution of **2**. The complexation enthalpy can be calculated by subtracting the heat of dilution of **2**, which is obtained in an independent titration of **2** into solvent.

[32] The equilibrium constants refer to the following processes: $\mathbf{1} + \mathbf{2} \rightleftharpoons \mathbf{1}\cdot\mathbf{2}$ and $\mathbf{1}\cdot(\mathrm{Li})_2 + \mathbf{2} \rightleftharpoons \mathbf{1}\cdot\mathbf{2}\cdot(\mathrm{Li})_2$ assuming complete binding of **1** to Li^+.

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