

# Acid/Base-controlled supramolecular switch

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A rotaxane-like complex incorporating a hydroquinone-intercepted acyclic polyether chain terminated by *tert*-butylaniline rings and encircled by cyclobis(paraquat-*p*-phenylene) self-assembles spontaneously in acetonitrile solution from which it can be crystallized. Protonation of the nitrogen atoms of the guest is accompanied by the complete dissociation of the supramolecular complex into its free components. Addition of a base restores the original equilibrium affording back the rotaxane-like complex.

The incorporation of appropriate chemically-, electrochemically-, and/or photochemically-responsive units into either the host or guest components of supramolecular complexes creates conditions under which the application of suitable external stimuli can effect<sup>1</sup> decomplexation/complexation processes. Hence, we were interested to establish if the introduction of positively charged sites near to the termini of a hydroquinone-based thread could influence (Fig. 1) its complexation within the cyclobis(paraquat-*p*-phenylene)<sup>2,3</sup> tetracation **1**<sup>4+</sup>. To this end, we have synthesized the thread **2** which contains two distal amino functions and report here (i) the X-ray crystal structure of the 1:1 complex formed between **1**<sup>4+</sup> and **2** and (ii) the UV and <sup>1</sup>H-NMR spectroscopic evidence for the acid/base controlled decomplexation/complexation of this host–guest system.

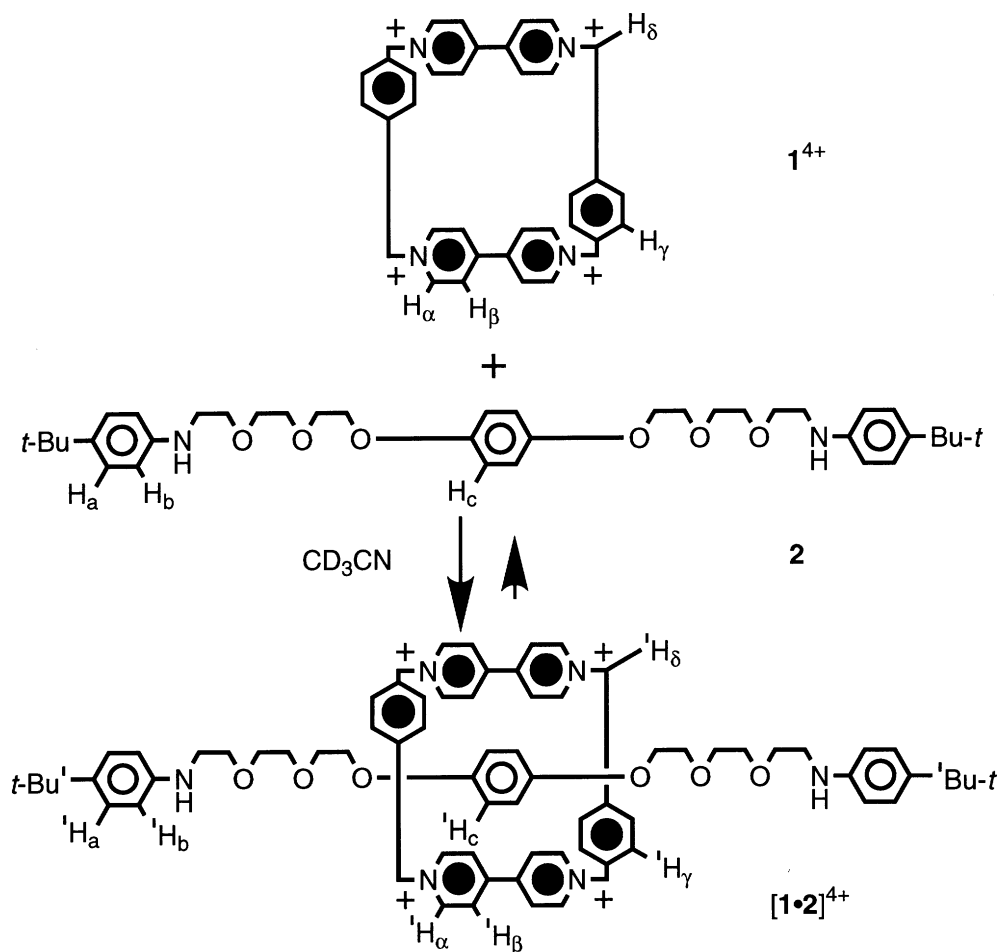
Reaction (MeCN–K<sub>2</sub>CO<sub>3</sub>) of 4-*tert*-butylaniline with 1,4-bis [2 - [2 - [2 - (4 - methylphenylsulfonyloxy) ethoxy] ethoxy] - ethoxy]benzene<sup>4</sup> gave the thread **2**.<sup>5</sup> On mixing it with an equimolar amount of **1**<sup>4+</sup> in MeCN at 25 °C, a charge transfer band ( $\lambda_{\text{max}}$  = 490 nm), indicative of complex formation, developed during *ca.* 5 min.<sup>6</sup> Vapor diffusion of *i*-Pr<sub>2</sub>O into this solution afforded orange-brown rhombs of the 1:1 complex [**1**·**2**]<sup>4+</sup>·4PF<sub>6</sub><sup>−</sup> suitable for X-ray crystallography.<sup>7</sup> The solid-state structure shows (Fig. 2) the thread **2** to be inserted symmetrically through the center of the tetracationic cyclophane **1**<sup>4+</sup> with its  $\pi$ -electron rich hydroquinone ring system sandwiched between the two  $\pi$ -electron deficient bipyridinium units of the cyclophane. Complex stabilization is achieved by a combination of face-to-face  $\pi$ -stacking (i) between the hydroquinone and bipyridinium ring systems and (ii) between the *tert*-butylaniline groups of the thread and their proximal pyridinium rings within the tetracation, supplemented by (iii) edge-to-face [C–H... $\pi$ ] interactions between diametrically-opposite pairs of *ortho* hydrogen atoms on the hydroquinone ring and the *para*-xylylene spacers of the cyclophane.<sup>8</sup> It is notable that there is an absence of the customary [C–H...O] interactions we normally associate with complexes of this type. This could be due to the influence of the second of the aforementioned  $\pi$ -stacking interactions which force the polyether chain away from the  $\alpha$ -pyridinium and the methylene/methine hydrogen atoms of the cyclophane.<sup>9</sup> It is interesting

that there is a close approach (3.26 Å) between the amino nitrogen atoms of the guest and their proximal pyridinium nitrogen atoms on the host. Further evidence for an interaction between these centers is a noticeable pyramidalization at the amino centers and a directing of the associated nitrogen lone pairs toward the pyridinium nitrogen atoms.

The <sup>1</sup>H-NMR spectrum of an equimolar solution of the tetrakis(hexafluorophosphate) salt of **1**<sup>4+</sup> and **2** in CD<sub>3</sub>CN at 25 °C shows [Fig. 3(a)] separate signals for complexed and uncomplexed species, *i.e.*, the 1:1 complex and the free host and guest are in slow exchange on the <sup>1</sup>H-NMR timescale under these conditions. The resonances associated with the complex are shifted upfield with respect to those of **1**<sup>4+</sup> and **2**. In particular, the signal associated with the hydroquinone ring protons shifts by  $\Delta\delta$  −3.80 on complexation and appears as a broad resonance centered on  $\delta$  3.03. This dramatic chemical shift change is a result of shielding effects exerted by the sandwiching bipyridinium units in the complex. By measuring the relative intensities of the resonances associated with the complexed and uncomplexed species, an association constant ( $K_a$  value) of  $3100 \pm 600 \text{ M}^{-1}$  ( $\Delta G^\circ = -4.9 \pm 0.1 \text{ kcal mol}^{-1}$ ) was determined at 25 °C for the 1:1 complex.<sup>6,10</sup> Upon titration of an equilibrated equimolar CD<sub>3</sub>CN solution of the tetrakis(hexafluorophosphate) salt of **1**<sup>4+</sup> and **2** with CF<sub>3</sub>CO<sub>2</sub>H at 25 °C, the <sup>1</sup>H-NMR spectra show<sup>6</sup> (i) the gradual disappearance of the resonances associated with [**1**·**2**]<sup>4+</sup>, (ii) a corresponding gradual increase of the intensity of the resonances of **1**<sup>4+</sup>, and (iii) significant changes<sup>11</sup> of the chemical shift values of the resonances associated with **2**. After the addition of 10 mol equivalents of CF<sub>3</sub>CO<sub>2</sub>H, only the resonances of **1**<sup>4+</sup> and of the protonated form(s) of **2** are observed [Fig. 3(b)]: no signals for the complex can be detected. However, after the addition of 10 mol equivalents of *i*-Pr<sub>2</sub>NEt, deprotonation occurs and the original equilibrium between **1**<sup>4+</sup>, **2**, and [**1**·**2**]<sup>4+</sup> is restored. Similar behavior was observed<sup>6</sup> by absorption UV-VIS spectroscopy: the *A* value associated with the charge-transfer band of [**1**·**2**]<sup>4+</sup> decreases (Fig. 4) upon titration of an equilibrated equimolar MeCN solution of the tetrakis(hexafluorophosphate) salt of **1**<sup>4+</sup> and **2** with CF<sub>3</sub>CO<sub>2</sub>H at 25 °C. After the addition of 20 mol equiv. of CF<sub>3</sub>CO<sub>2</sub>H, no charge-transfer band can be detected. On neutralization of the solution with *i*-Pr<sub>2</sub>NEt, the *A* value increases gradually to reach the original value after the addition of 20 mol equiv. of base. The change of the *A* value, associated with the charge-transfer band, is reflected in the color of the solution. On addition of CF<sub>3</sub>CO<sub>2</sub>H the initial red color fades affording, after the addition of a total of 20 mol

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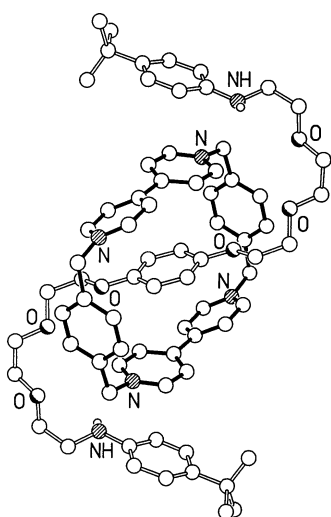


**Fig. 1** Spontaneous formation of the rotaxane-like complex  $[1 \cdot 2]^{4+}$  from an equimolar mixture of the hexafluorophosphate salt of  $1^{4+}$  and the thread **2**

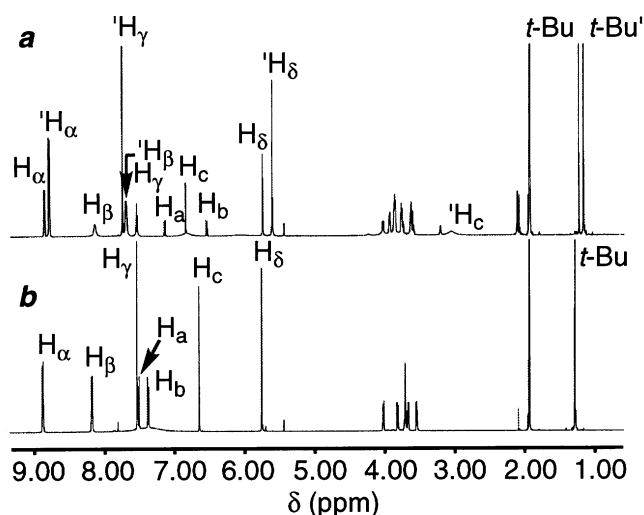
equiv. of acid, a colorless solution. By contrast, the neutralization of the solution with *i*-Pr<sub>2</sub>NEt is accompanied by the reappearance of the red color.

The changes observed in the <sup>1</sup>H-NMR and UV-VIS spectra can be explained by considering the multiple equilibria illustrated in Scheme 1. Before the addition of CF<sub>3</sub>CO<sub>2</sub>H, the only

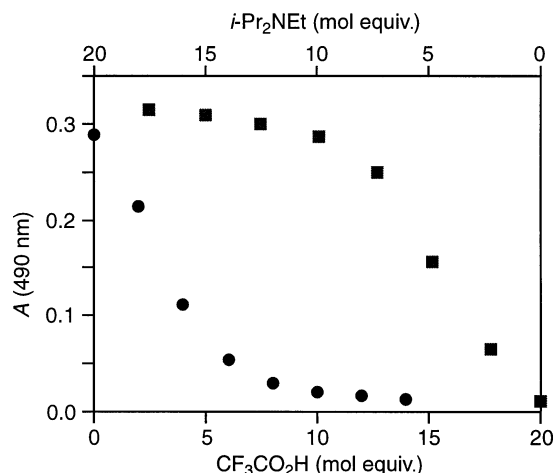
species present in solution are  $1^{4+}$ , **2**, and  $[1 \cdot 2]^{4+}$  whose concentrations are determined by the *K<sub>a</sub>* value—i.e., the 1 : 1 complex is the most abundant species in solution. On addition of CF<sub>3</sub>CO<sub>2</sub>H, the nitrogen atoms of the aniline rings of **2** and, presumably, also of  $[1 \cdot 2]^{4+}$  become protonated.<sup>12</sup> As the concentration of **2** decreases, the equilibrium I is shifted to the



**Fig. 2** Ball-and-stick representation of  $[1 \cdot 2]^{4+}$  in the solid state



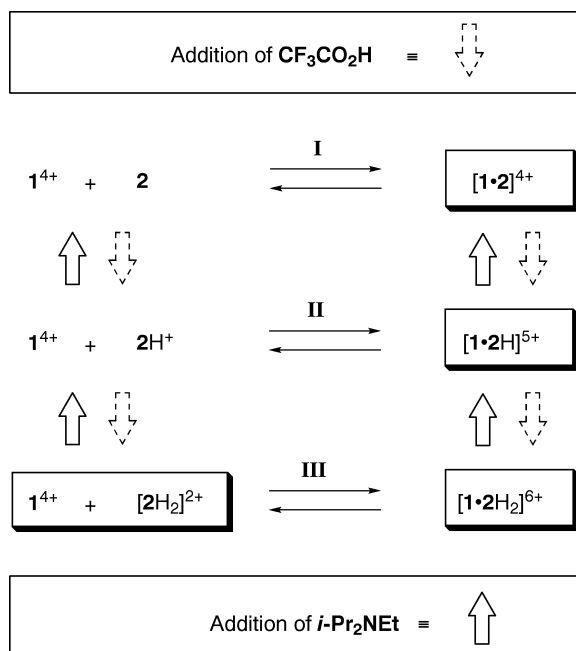
**Fig. 3** <sup>1</sup>H-NMR spectra (400 MHz, CD<sub>3</sub>CN, 25 °C) of an equimolar mixture of the hexafluorophosphate salt of  $1^{4+}$  and the thread **2** (a) before and (b) after the addition of 10 mol equivalents of CF<sub>3</sub>CO<sub>2</sub>H



**Fig. 4** Plot of the absorbance ( $A$ ) associated with the charge-transfer band ( $\lambda_{\text{max}} = 490 \text{ nm}$ ) of  $[1 \cdot 2]^{4+}$  against the number of molar equivalents of  $\text{CF}_3\text{CO}_2\text{H}$  (●) or  $i\text{-Pr}_2\text{NEt}$  (■)

left and  $[1 \cdot 2]^{4+}$  dissociates into its free host and guest components. Presumably, the concentration of  $[1 \cdot 2]^{4+}$  decreases also as a result of its protonation<sup>12</sup> to afford  $[1 \cdot 2\text{H}]^{5+}$  and  $[1 \cdot 2\text{H}_2]^{6+}$  which dissociate (equilibria II and III) into their host and guest components, as a result of electrostatic repulsions between the tetracationic host and the mono- and dicationic guests, respectively. Thus, on acidification, the overall process (from top right to bottom left in the cycle shown in Scheme 1) corresponds to the conversion of  $[1 \cdot 2]^{4+}$  totally into  $1^{4+}$  and  $[2\text{H}_2]^{2+}$ . On addition of  $i\text{-Pr}_2\text{NEt}$ ,  $[2\text{H}_2]^{2+}$  is converted back into **2** which is bound by  $1^{4+}$ , affording the 1 : 1 complex. Thus, on neutralization, the overall process (from bottom left to top right in the cycle shown in Scheme 1) corresponds to the conversion of  $1^{4+}$  and  $[2\text{H}_2]^{2+}$  into mainly  $[1 \cdot 2]^{4+}$ .

A simple acid/base controlled supramolecular switch<sup>13,14</sup> in the form of a rotaxane-like complex<sup>15</sup> has been demonstrated. The decomplexation/complexation cycle is completely reversible and, in principle, can be repeated indefinitely without risk of degrading its components. The simplicity of the design logic and the ease by which the switching mechanism can be realized in such a simple system means that this



**Scheme 1** Acid/base-controlled decomplexation/complexation cycle. Hexafluorophosphate anions were employed as counter ions

approach to the design of molecular machines<sup>1,16</sup> holds great promise for the generation of more complex molecular and supramolecular devices able to perform gating operations at the molecular level.

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- A mixture of 4-*tert*-butylaniline (0.7 g, 4 mmol), 1,4-bis[2-[2-(4-methylphenylsulfonyloxy)ethoxy]ethoxy]benzene (1.0 g, 1.5 mmol) and  $\text{K}_2\text{CO}_3$  (0.7 g, 5 mmol) in MeCN (10 mL) was heated under reflux for 2 d. After cooling down to room temperature, the solvent was evaporated under reduced pressure and the residue was partitioned between  $\text{CH}_2\text{Cl}_2$  and  $\text{H}_2\text{O}$ . The organic layer was washed with an aqueous solution of  $\text{NaHCO}_3$  (1 M), with  $\text{H}_2\text{O}$ , dried ( $\text{MgSO}_4$ ), and concentrated under reduced pressure. The residue was purified by column chromatography ( $\text{SiO}_2$ ,  $\text{Me}_2\text{CO}-\text{MeCO}_2\text{Et}$ -hexane, 2 : 3 : 20) to afford **2** (0.3 g, 10%). M.p. = 67–69 °C; LSIMS:  $m/z$  = 637 [ $\text{M} + \text{H}$ ]<sup>+</sup>; HRMS (LSI) calcd. for [ $\text{M} + \text{H}$ ]<sup>+</sup> ( $\text{C}_{38}\text{H}_{57}\text{N}_2\text{O}_6$ ):  $m/z$  = 637.4217, found:  $m/z$  = 637.4226;  $^1\text{H-NMR}$  (300 MHz,  $\text{CD}_3\text{CN}$ ):  $\delta$  7.15–7.12 (m, 4H); 6.83 (s, 4H), 6.55–6.52 (m, 4H), 4.28 (br s, 2H), 4.03–4.00 (m, 4H), 3.75–3.72 (m, 4H), 3.62–3.57 (m, 12H), 3.21–3.18 (t, 4H,  $J$  = 5.5 Hz), 1.22 (s, 18H);  $^{13}\text{C-NMR}$  (75 MHz,  $\text{CD}_3\text{CN}$ ):  $\delta$  153.9, 147.3, 140.2, 126.6, 116.2, 113.2, 71.2, 70.8, 70.3, 70.1, 68.7, 44.2, 34.2, 31.7.
- In the case of the related hydroquinone-based acyclic polyether guest, incorporating terminal OH rather than  $\text{HNC}_6\text{H}_4\text{Bu-}t$  groups, complexation with  $1 \cdot 4\text{PF}_6$  in MeCN at 25 °C reaches equilibrium almost instantaneously: the association constant ( $K_a$ ) for the 1 : 1 complex is  $2200 \pm 250 \text{ M}^{-1}$  ( $\Delta G^\circ = -4.6 \pm 0.1 \text{ kcal mol}^{-1}$ ). On acidification of a corresponding  $\text{CD}_3\text{CN}$  solution, no significant change is observed in either the  $^1\text{H-NMR}$  or UV-VIS spectra.
- Crystal data:  $\text{C}_{74}\text{H}_{88}\text{N}_6\text{O}_6 \cdot 4\text{PF}_6 \cdot 4\text{MeCN}$ ,  $M$  = 1901.6, triclinic,  $P\bar{1}$  (no. 2),  $a$  = 13.079(2),  $b$  = 14.046(2),  $c$  = 14.166(2) Å,  $\alpha$  = 81.68(1),  $\beta$  = 75.25(1),  $\gamma$  = 79.34(1)°,  $U$  = 2460.2(7) Å<sup>3</sup>,  $Z$  = 1 (the molecule has crystallographic  $C_i$  symmetry),  $D_c$  = 1.283 g cm<sup>-3</sup>,  $\mu(\text{Mo-K}\alpha)$  = 1.74 cm<sup>-1</sup>,  $F(000)$  = 986,  $T$  = 203 K. An orange-brown rhomb of dimensions 1.00 × 0.83 × 0.83 mm was used. 7690 Independent reflections were measured on a Siemens P4/PC diffractometer with Mo-K $\alpha$  radiation using  $\omega$  scans. The structure was solved by direct methods and all of the major occupancy non-hydrogen atoms (there is disorder in the terminal *tert*-butyl groups and in the included MeCN molecules) were refined anisotropically using full-matrix least-squares based on  $F^2$  to give  $R_1$  = 0.084,  $wR_2$  = 0.228 for 4826 independent observed reflections [ $|F_o| > 4\sigma(|F_o|)$ ,  $2\theta \leq 48^\circ$ ] and 593 parameters. CCDC reference number 101 425.
- The mean interplanar separation between the hydroquinone ring and the bipyridinium units is 3.55 Å and that between the *tert*-butylaniline rings and their adjacent pyridium ring systems is 3.29 Å, with a centroid-centroid separation of 3.72 Å and inter-ring tilt angle of 10°. The [ $\text{H} \cdots \pi$ ] distances and [ $\text{C}-\text{H} \cdots \pi$ ] angles associated with the hydroquinone-*para*-xylylene edge-to-face interaction are 2.87 Å and 158°, respectively. The  $-\text{OC}_6\text{H}_4\text{O}-$  axis of the hydroquinone ring is inclined by 45° to the mean plane of the cyclophane.
- There are no inter-complex  $\pi$ - $\pi$  stacking interactions, approach to the non-interacting faces of the  $\pi$ -systems being hindered by the bulky *tert*-butyl groups.
- A continuous variation experiment carried out using absorption UV-VIS spectroscopy, confirmed the 1 : 1 stoichiometry of the complex.

- 11 Addition of  $\text{CF}_3\text{CO}_2\text{H}$  to a  $\text{CD}_3\text{CN}$  solution of **2** at  $25^\circ\text{C}$  causes the formation of its mono- ( $2\text{H}^+$ ) and di-protonated ( $[2\text{H}_2]^{2+}$ ) forms. These species (**2**,  $2\text{H}^+$  and  $[2\text{H}_2]^{2+}$ ) are in fast exchange on the  $^1\text{H}$ -NMR timescale and averaged signals, whose chemical shifts are correlated to the number of equivalents of  $\text{CF}_3\text{CO}_2\text{H}$ , can be observed in the  $^1\text{H}$ -NMR spectrum. Thus, the chemical shift changes observed during the titration of an equimolar  $\text{CD}_3\text{CN}$  solution of the tetrakis(hexafluorophosphate) salt of **1** $^{4+}$  and **2** with  $\text{CF}_3\text{CO}_2\text{H}$  at  $25^\circ\text{C}$  are a result of the interconversion of **2** into  $2\text{H}^+$  and  $[2\text{H}_2]^{2+}$ .
- 12 We cannot establish if the species  $[\mathbf{1} \cdot 2\text{H}]^{5+}$  and  $[\mathbf{1} \cdot 2\text{H}_2]^{6+}$  are formed in solution. If they are formed, however, they dissociate completely into their constituent host and guest components, as the  $^1\text{H}$ -NMR spectrum shown in Fig. 3(b) does not reveal the characteristic resonances of complexed species.
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