Novel Rotaxanes Based on the Inclusion Complexation of Biphenyl Guests by Cyclobis(paraquat-*p*-phenylene)

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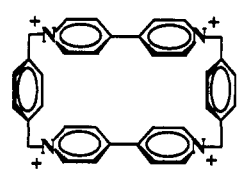
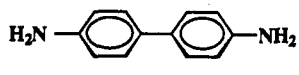
Summary: The finding that benzidine and 4,4′-biphenol form stable inclusion complexes in acetonitrile with the previously reported receptor cyclobis(paraquat-*p*-phenylene) was used to self-assemble novel redox-active rotaxanes based on the interactions that stabilize these inclusion complexes.

Recently, we have reported[1] the self-assembly of a number of rotaxanes based on the noncovalent interactions between the electron deficient receptor cyclobis(paraquat-*p*-phenylene), 1^{4+}, and electron-rich aromatic subunits, such as hydroquinol or 1,5-naphthoquinol. A particular rotaxane, which contains two identical hydroquinol donor stations in the thread of the dumbbell component and only one electron acceptor bead, was termed a *molecular shuttle*[2] because the bead moves back and forth between the two hydroquinol stations at thermally controlled rates. Desymmetrization of the thread by insertion of two different donor stations should produce rotaxanes in which the position of the electron acceptor bead could be controlled by redox means. Several such structures have been self-assembled already[3] and are currently under evaluation in our laboratories. However, these studies have made us realize that it would be desirable to increase the number of recognition subunits suitable for the self-assembly of these complicated molecular structures in order to enhance the likelihood of preparing systems having the sought-after switching functions. Therefore, we have investigated the complexation of benzidine (**2**) and 4,4′-biphenol (**3**) by host 1^{4+}. These two guests are structurally related since both are 4,4′-disubstituted biphenyl derivatives. However, their redox properties differ as **2** is much more easily oxidized than **3**. We show here that both these compounds form stable inclusion complexes with 1^{4+}. We also demonstrate that novel rotaxanes can be self-assembled around the interactions that stabilize these inclusion complexes.

Addition of **2** to a solution of $1\cdot(PF_6)_4$ in CH_3CN resulted in the immediate development of blue color. This color is a result of the formation of a charge-transfer complex between the two compounds, with an associated broad absorption at λ_{max} = 644 nm. Detailed spectroscopic analysis of this band during the titration of a 0.2 mM solution of $1\cdot(PF_6)_4$ with **2** allowed us to determine the



1^{4+}



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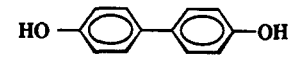

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equilibrium constant for the formation of the $2\cdot1^{4+}$ complex[4] as 1044 ± 280 M^{-1} while the molar absorptivity coefficient of the charge transfer band ($\Delta\epsilon$) was found to be 560 ± 65 M^{-1} cm^{-1}. ^1H NMR (400 MHz) spectroscopic analysis in CD_3CN revealed strong complexation-induced shifts for the aromatic protons of benzidine upon addition of 1 equiv of 1^{4+} (see Table I). Similar results were obtained with **3** as the guest. Formation of the $3\cdot1^{4+}$ charge transfer complex is characterized by the following parameters: λ_{max} = 500 nm, K = 140 ± 4 M^{-1}, and $\Delta\epsilon$ = 438 ± 30 M^{-1} cm^{-1}. The smaller complexation-induced shifts observed (see Table I) in this case for the guest's aromatic protons correlate well with the lower binding constant measured for **3** as compared to **2**.

The ^1H NMR data, as well as the ^{13}C NMR data (not shown), clearly suggest that both guests penetrate the host cavity during complexation. This proposal was further confirmed by homonuclear NOE measurements. For instance, irradiation of the NH_2 protons of **2** does not have any effect upon the host resonances, while irradiation of the benzidine's β protons results in sizable NOE's into all the aromatic protons of 1^{4+}. These facts, along with the complexation-induced downfield shift observed (see Table I) for the host's C_6H_4 protons, constitute clear evidence for the formation of an inclusion complex over other possible interaction modes, such as external docking of **2** against one of the host's bipyridinium units. The benzidine's NH_2 protons would be kept distant from the host if benzidine penetrates the cavity so that its symmetry center is very close to the center of the cavity (as shown in Scheme I). This supramolecular geometry explains the lack of through-space communication between these protons and the host protons. By contrast, irradiation of the benzidine's α protons induces NOE's into the aromatic host protons similar to those observed upon irradiation of the β protons.

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(2) Anelli, P. L.; Spencer, N.; Stoddart, J. F. *J. Am. Chem. Soc.* **1991**, *113*, 5131.
(3) (a) Ashton, P. R.; Bissell, R. A.; Spencer, N.; Stoddart, J. F.; Tolley, M. S. *Synlett* **1992**, 914. (b) Ashton, P. R.; Bissell, R. A.; Górski, R.; Philp, D.; Spencer, N.; Stoddart, J. F.; Tolley, M. S. *Synlett* **1992**, 919. (c) Ashton, P. R.; Bissell, R. A.; Spencer, N.; Stoddart, J. F.; Tolley, M. S. *Synlett* **1992**, 923.

(4) Treatment of the spectroscopic data was carried out using an improved version of our published method (Bernardo, A. R.; Stoddart, J. F.; Kaifer, A. E. *J. Am. Chem. Soc.* **1992**, *114*, 10624). Very briefly, the complexation parameters were obtained from computer fitting of the absorbance *vs* concentration data to the following two equations by regression methods

$$\Delta A/b = L_t K \Delta\epsilon [G]/(1 + K[G]) \quad (1)$$

$$G_t = ([G] + L_t K[G])/(1 + [G]) \quad (2)$$

where L_t is the total host concentration, G_t is the total guest concentration, [G] is the equilibrium guest concentration, ΔA is the charge transfer absorbance, $\Delta\epsilon$ is the molar absorptivity of the complex, b is the optical pathway, and K is the binding constant.

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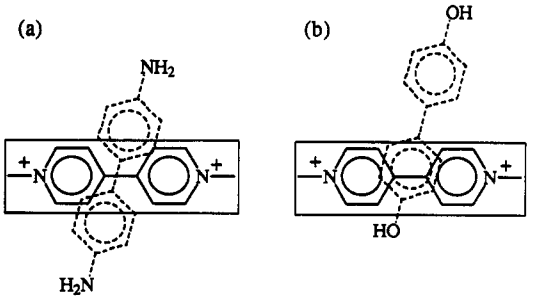
Table I. Chemical Shift Displacements ($\Delta\delta$ Data)[a] in the 400-MHz ^{1}H NMR Resonances of Biphenyl Guests upon Addition of 1 Equiv of Receptor 1^{4+}

guest	α-CH(bipy)	β-CH(bipy)	C_6H_4	CH_2	α-CH(guest)	β-CH(guest)	XH[b]
benzidine	−0.041	−0.371	0.192	−0.007	−1.375	−1.068	−0.004
4,4′-biphenol	−0.004	−0.181	0.102	0.002	−0.760	−0.291	0.058

[a] $\Delta\delta$ values were calculated as $\Delta\delta = \delta_{complex} - \delta_{free}$. [b] NH_2 protons for benzidine and OH protons for 4,4′-biphenol.

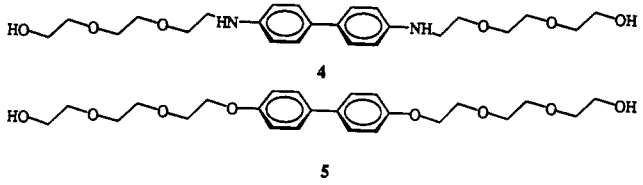
Scheme I. Postulated Averaged Superstructures for the 1^{4+} Complexes of (a) Benzidine and (b) 4,4′-Biphenol in CD_3CN Solution at 25 °C



A similar NMR spectroscopic study with guest **3** yielded different results. For instance, irradiation of the OH protons of **3** causes a strong NOE into the β and the C_6H_4 protons of the host. This observation is different from the benzidine results where irradiation of the NH_2 protons did not have any effects in the resonances of 1^{4+}. It is also in agreement with the appreciable $\Delta\delta$ value for the OH protons of **3** and the negligible value for the NH_2 protons of **2** (see Table I). Furthermore, irradiation of the β protons of 4,4′-biphenol induces NOE's in the host's β and C_6H_4 protons, while no effect was observed in the host's α protons. Irradiation of the α protons of **3** causes sizable NOE's into the β and C_6H_4 protons of 1^{4+}, but again no effect was detected on the intensities of the bipyridinium α proton signals. These results are consistent with the formation of an inclusion complex between **3** and 1^{4+} which has a different geometry from that of the $2\cdot1^{4+}$ complex. Guest **3** seems not to penetrate the cavity of the host as much as guest **2**. The proposed averaged superstructures for the complexes in CD_3CN solution are shown in Scheme I.

The complexation of **2** by 1^{4+} in CH_3CN was also verified using voltammetric techniques. The half-wave potential for the monoelectronic oxidation of benzidine ($2^{+/0}$) shifts anodically by 23 mV after addition of 15 equiv of host 1^{4+}. The half-wave potential for the monoelectronic reduction of each of the bipyridinium units of the host (the $1^{4+/2+}$ couple) shifts cathodically by 27 mV upon addition of 30 equiv of **2**. Similarly, addition of 42 equiv of **3** causes a cathodic shift of 11 mV on the $1^{4+/2+}$ half-wave potential. The smaller complexation-induced potential shift detected for guest **3** as compared to **2** is consistent with the lower thermodynamic stability of the corresponding complex.

The relatively large binding constants of these complexes, plus their inclusion character, suggested the possibility of building rotaxanes based on the molecular recognition between their components. Thus, we prepared compounds **4** and **5** which are elongated analogs of **2** and **3**, respectively. Compound **5** was prepared[5] by reaction of **3** with 2-[2-(2-chloroethoxy)ethoxy]ethanol in KOH/EtOH. Compound **4** was synthesized[6] by a similar procedure starting from benzidine. The tri(ethyleneoxy) sidearms do not seem to alter substantially the binding affinity of host 1^{4+} for these compounds. The measured equilibrium binding constants of 800 ± 87 for $4\cdot1^{4+}$ and



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104 ± 13 M^{-1} for $5\cdot1^{4+}$ which we obtained are similar to the values measured for the complexation of underivatized benzidine and 4,4′-biphenol.[7] These inclusion complexes offer primary hydroxyl groups whose reactivity and steric accessibility are optimal for *capping* reactions (attachment of bulky terminal groups), thus making the self-assembly of new rotaxane structures possible.

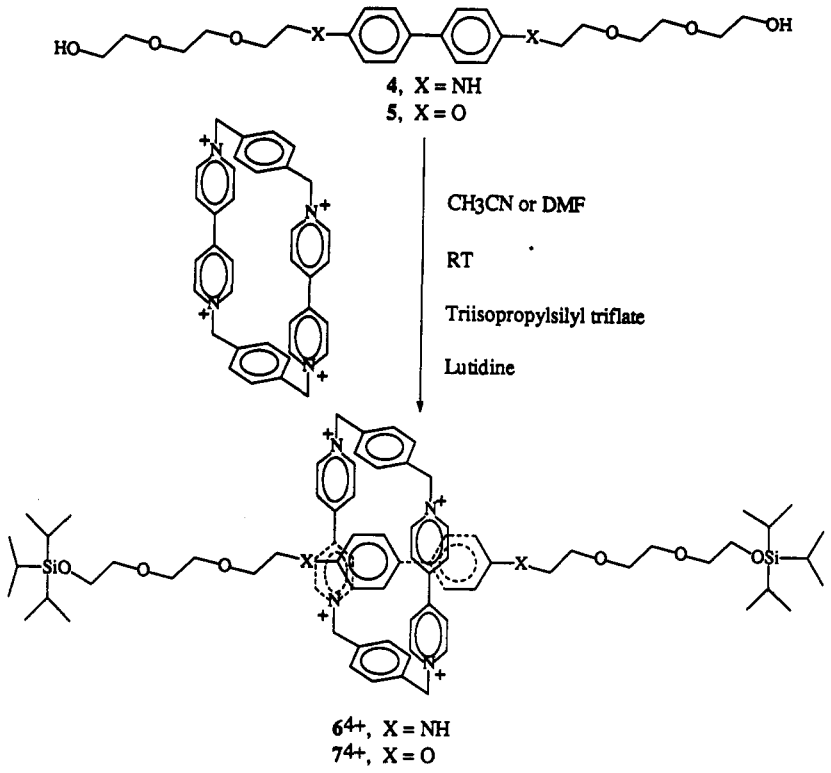
The benzidine derivative **4** was converted into the corresponding rotaxane (see Chart I) by reacting $1\cdot(PF_6)_4$ (61 mg, 0.055 mmol), **4** (74 mg, 0.165 mmol), triisopropylsilyl triflate (127 mg, 0.42 mmol), and lutidine (44 mg, 0.42 mmol) in 1.5 mL of dry CH_3CN. The reaction mixture was stirred under nitrogen at room temperature for 12 h, after which time it was suspended in CH_2Cl_2/Et_2O (1:1, v/v, 5 mL) and centrifuged. The supernatant was discarded, and this process was repeated two more times. The purple residue was dissolved in 2 mL of CH_3NO_2 before adding CH_2Cl_2 to precipitate a white solid which was separated by centrifugation. The residue was suspended in CH_3NO_2/CH_2Cl_2 (1:2, v/v, 4 mL) and centrifuged again. The combined organic extracts were reduced in vacuo, and the residue was purified by column chromatography [SiO_2, CH_3OH–CH_3NO_2–saturated NH_4PF_6 (160:35:5)]. The rotaxane-containing fractions were reduced in vacuo, and the residue was washed with water (3 × 1 mL) before being dissolved in ethyl acetate (4 mL). Et_2O was added until cloudiness was observed, at which point the solution was stored in a refrigerator for 12 h. The powdery green precipitate that formed was filtered off and washed with CH_3OH (0.5 mL). The resulting green solid (yield = 41

(5) A solution of 2-[2-(2-chloroethoxy)ethoxy]ethanol in anhydrous ethanol (10 mL) was added dropwise to a warm solution of **3** (4.3 g, 23 mmol) and KOH (2.8 g, 50 mmol) in anhydrous ethanol (30 mL). The reaction mixture was refluxed overnight under nitrogen. The mixture was taken up in $CHCl_3$ (20 mL), washed with water (3 × 20 mL), and dried ($MgSO_4$). The organic extract was evaporated in vacuo and recrystallized from EtOH (2×) to yield a white crystalline solid (9.3 g, 90%); mp 111–112 °C; FAB MS 450 (M^+); ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.52 (4H, d), 6.98 (4H, d), 4.10 (2H, t), 3.74 (4H, t), 3.59 (4H, t), 3.56 (4H, t), 3.53 (4H, t), 3.48 (4H, t), 3.42 (4H, t).

(6) Benzidine (7 g, 45.4 mmol), 2-[2-(chloroethoxy)ethoxy]ethanol (20.2 g, 136.1 mmol), and triethylamine (11.2 g, 112 mmol) were stirred in benzene (100 mL) and refluxed for 2 weeks under nitrogen. The reaction mixture was cooled, and the solvent, along with the excess of triethylamine, was removed under vacuum. The residue was dissolved in $CHCl_3$ (200 mL) and washed with water (3 × 50 mL). The organic layer was dried ($MgSO_4$) and concentrated to yield a crude oil which was purified by column chromatography [SiO_2, $CHCl_3$/acetone (2:1 v/v)]. The product was recrystallized from EtOH/Et_2O to yield a yellowish solid (7.54 g, 45%) which discolored in the presence of light or air: ^{1}H NMR (400 MHz, CD_3CN) δ 7.33 (4H, d), 6.66 (4H, d), 4.45 (2H, b), 3.64 (4H, t), 3.55–3.59 (12H, m), 3.50 (4H, t), 2.72–2.74 (4H, m); mp 90–91 °C.

(7) The effect of the sidearm ethyleneoxy units on the binding constants is very small compared to their effect when attached to hydroquinol rings (see ref 1) probably reflecting the geometric and size differences between the 1,4-disubstituted benzene rings and the 4,4′-disubstituted biphenyl residues.

Chart I



mg, 39%) was dried under vacuum and identified as the rotaxane $6\cdot(PF_6)_4$.[8]

A similar procedure using **5** as the starting material (and DMF as the solvent) yielded the corresponding biphenol-based rotaxane compound $7\cdot(PF_6)_4$ as a red solid.[9] However, the isolated yield in this case was substantially less (5%) probably as a result of the lower binding constant between **5** and 1^{4+}.

The electrochemical properties of both these rotaxanes are interesting, particularly because we propose to use parts of these structures as building blocks for redox-driven molecular shuttles. Table II shows the most relevant half-wave potentials. The oxidations correspond to the benzidine subunits while the reductions are centered on the bipyridinium residues. The oxidation of the benzidine group becomes substantially more difficult in the rotaxane 6^{4+} than in the free thread (compound **4**). This difference reveals the stabilization of the threaded benzidine subunit, as well as the difficulty of generating additional positive charges in a molecule which already has a +4 charge. A similar comparison with the biphenol-based compounds is not feasible because the electrochemistry of this subunit is not reversible. On the cathodic side, the rationalization of the half-wave potentials of the bispyridinium groups is more difficult since these potentials are affected by numerous structural and electronic factors.

Table II. Half-Wave Potentials[a] in CH_3CN (at 25 °C) for the Elongated Benzidine Derivative 4, the Rotaxanes 6^{4+} and 7^{4+}, and the Receptor 1^{4+}

	oxidation		reduction	
compd	first	second	first	second
4	0.49	0.69		
6^{4+}	0.72	1.02	−0.26	−0.75
7^{4+}			−0.24	−0.79
1^{4+}			−0.24	−0.66

[a] All potentials were measured in V against a Ag/AgCl reference electrode.

In summary, we have shown that benzidine and 4,4′-biphenol are efficient guests for inclusion complexation by the versatile host 1^{4+}. The electron-rich aromatic moieties of these compounds have subsequently been used to template the synthesis of novel rotaxanes (compounds 6^{4+} and 7^{4+}) in which 1^{4+} acts as the bead. These are the first reported rotaxanes of this class in which hydroquinol or 1,5-naphthoquinol templates are not used in the thread. Furthermore, the ease of oxidation of the benzidine subunit suggests its use as a redox-switchable donor station in controllable molecular shuttle structures. We are currently evaluating this possibility.

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(8) FAB MS: 1716 $(M - PF_6)^+$, 1571 $(M - 2PF_6)^+$, 1426 $(M - 3PF_6)^+$; ^1H NMR (400 MHz, CD_3CN) δ 8.82 (8H, d), 7.90 (8H, s), 7.60 (8H, d), 5.76 (8H, s), 5.31 (4H, d), 4.76 (4H, d), 4.30 (2H, t), 3.83 (4H, t), 3.77–3.79 (12H, m), 3.61 (4H, t), 3.09 (4H, m), 1.05–1.09 (42 H, m).

(9) FAB MS: 1718 $(M - PF_6)^+$, 1573 $(M - 2PF_6)^+$; ^1H NMR (400 MHz, CD_3CN) δ 8.83 (8H, d), 7.89 (8H, s), 7.54 (8H, d), 5.75 (8H, s), 5.66 (4H, d), 4.85 (4H, d), 4.01 (4H, t), 3.85–3.90 (8H, m), 3.77–3.79 (8H, m), 3.62 (4H, t), 1.05–1.07 (42 H, m).