The Controlled Self-assembly of a [3]Rotaxane Incorporating Three Constitutionally Different Components

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The self-assembly, by means of a slippage procedure, of a [3]rotaxane comprised of three constitutionally different sub-units—a dumbbell-shaped component, incorporating two 4,4′-bipyridinium units encircled by one bisparaphenylene-34-crown-10 macrocycle and one 1,5-dinaphtho-38-crown-10 macrocycle—is described.

Rotaxanes[1–7] are molecular compounds composed of one or more macrocycles, trapped on the thread-like portion of a dumbbell component by large blocking groups or stoppers at its two ends. By exploiting noncovalent bonding interactions, such as π–π aromatic stacking and hydrogen bonding, we have been able to devise three different approaches to self-assembling[8–10] rotaxanes, namely clipping,[11–13] threading[14–17] and slipping.[18,19] In the case of clipping, a complete dumbbell-shaped component is preformed and the macrocycle is then clipped around it. In the case of threading, the complexation between a preformed macrocycle and a thread-like molecule is followed by the covalent bonding of two stoppers which prevent the unthreading of the macrocycle from the dumbbell component. In the case of slipping, the macrocycle and the dumbbell component are preformed separately and then encouraged to associate one with the other under the influence of just the right amount of thermal energy. We have employed[18,19] successfully the threading and the slipping procedures for the construction of rotaxanes formed by π-electron deficient dumbbell components, incorporating one or two bipyridinium units, encircled by one or two bisparaphenylene-34-crown-10 (**BPP34C10**) macrocycles. In this previous research,[18] in order to establish the credentials of the slipping approach as a synthetic route to rotaxanes, we have prepared a range (**1a**·2PF_6–**1d**·2PF_6) of dumbbells (Fig. 1), incorporating just one bipyridinium unit, wherein the size of the stoppers was varied systematically. After heating **1a**·2PF_6–**1c**·2PF_6 with an excess of **BPP34C10** in acetonitrile at 55 °C for 10 d, we were able[18] to isolate the corresponding [2]rotaxanes in 52, 45 and 47% yield, respectively. By contrast, no rotaxane was isolated, under otherwise identical conditions, starting from the dumbbell **1d**·2PF_6, containing 4-isopropylphenyl-bis(4-*tert*-butylphenyl)methyl groups as the stoppers. Thus, in practice, the barrier for the slipping of the **BPP34C10** macrocycle only begins to be surmountable on going from R = Pr^i to R = Et.

Since the size complementarity between the macrocycle and the stoppers is the major consideration in the regulation of the slipping process, the opportunity of changing the size of the macrocycle instead of that of the stoppers had to be explored. The macrocyclic crown ether 1,5-dinaphtho-38-crown-10 (**1/5DN38C10**)[20,21] has a cavity size just slightly larger than that of **BPP34C10**. Furthermore, the presence of two π-electron rich dioxynaphthalene rings enhances the binding of paraquat-like moieties as a result of stronger π–π stacking interactions. When the dumbbell compound **1d**·2PF_6 (2 equiv.) was heated for 24 h at 55 °C in MeCN in the presence of **1/5DN38C10** (1 equiv.) (Scheme 1) the purple [2]rotaxane **2**·2PF_6† was isolated, after column chromatography, in a 57% yield. Therefore, although the isopropyl-substituted stoppers (R = Pr^i) are bulky enough to prevent the slipping on of **BPP34C10**, they permit threading of the larger **1/5DN38C10** when just the right amount of thermal energy is supplied. Also, we observed that the slipping process of **1/5DN38C10** over the isopropyl-substituted stoppers (R = Pr^i) requires only 1 d for completion, while the slipping of **BPP34C10** over size complementary stoppers (R = H, Me, Et) requires 10 days for completion. Furthermore, in the case of the slipping of **1/5DN38C10**, the yield of the resulting [2]rotaxane is 57%, while in the case of **BPP34C10** the yields are 52, 45 and 47%, respectively.

These results suggest the possibility of constructing more complicated molecular assemblies by choosing (i) appropriate components for and (ii) approaches to their self-assembly. The fact that the isopropyl-containing stoppers (R = Pr^i) are too bulky to permit the slipping of **BPP34C10** means that they can be used for the synthesis of rotaxanes *via* the threading approach, where the actual threading on of the macrocycle to the linear portion precedes the covalent attachment of the second stopper. Indeed, when **3**·2PF_6 was reacted (Scheme 2) in the presence of **BPP34C10** (1.1 equiv.) with an excess of **4** in DMF at 30 °C under ultra high pressure for 36 h, the corresponding

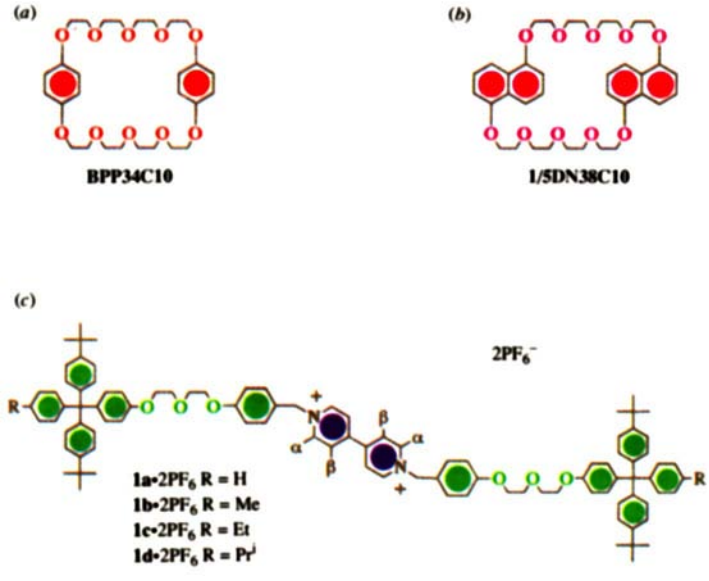
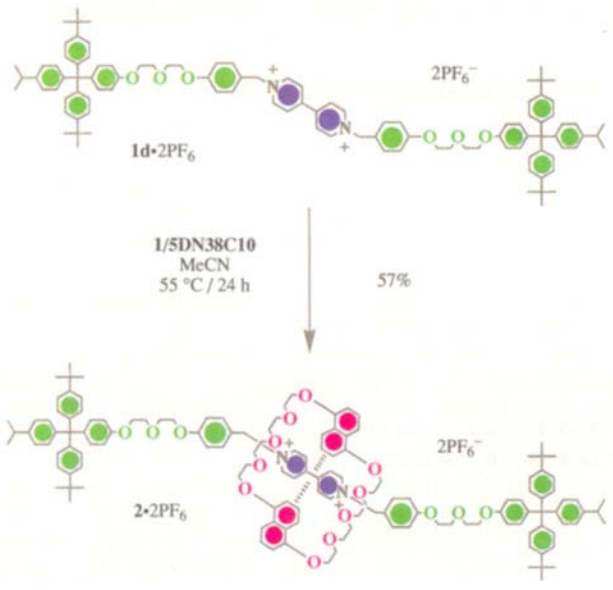


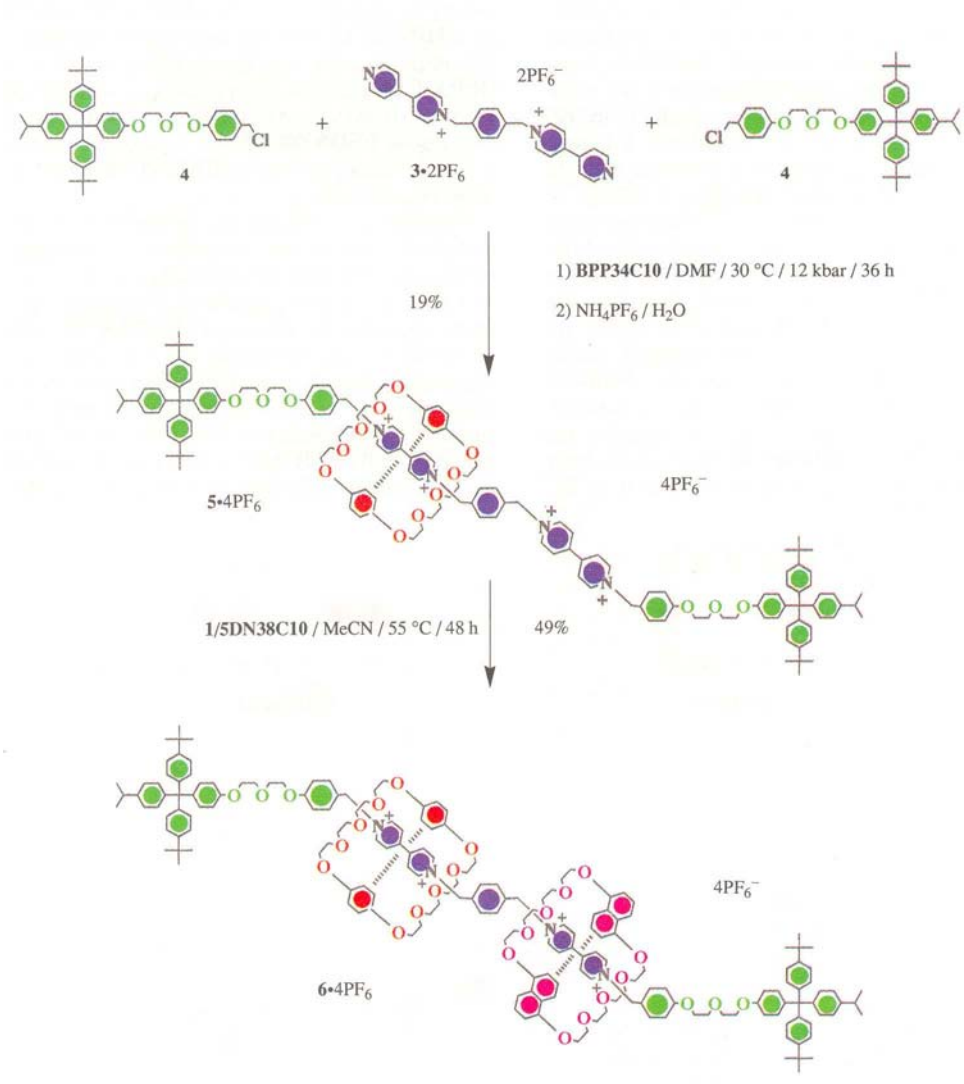
Fig. 1 (*a*) The macrocyclic crown ether **BPP34C10**. (*b*) The macrocyclic crown ether **1/5DN38C10**. (*c*) The dumbbell-shaped compounds **1a**·2PF_6–**1d**·2PF_6 bearing different substituents on the blocking groups.



Scheme 1 Synthesis of a [2]rotaxane by the slipping of **1/5DN38C10** over the isopropyl-substituted stoppers of a preformed dumbbell-shaped component. The dashed lines indicate the dispersive interactions occurring between the bipyridinium unit and the 1,5-dioxynaphthalene rings.

[2]rotaxane **5**·4PF_6† was obtained in a yield of 19%. The [2]rotaxane **5**·4PF_6 has within its dumbbell component two bipyridinium recognition sites, but only one macrocycle. The presence of a free recognition site in **5**·4PF_6, along with the size of the stoppers, suggests the possibility of self-assembling a [3]rotaxane by the slipping on of one **1/5DN38C10** macrocycle. In fact, by heating **5**·4PF_6 in MeCN at 55 °C for 48 h in the presence of **1/5DN38C10** (3 equiv.), the [3]rotaxane **6**·4PF_6† was obtained (Scheme 2) in a yield of 49% after column chromatography.

The rotaxanes **2**·2PF_6, **5**·4PF_6 and **6**·4PF_6 were fully characterised by FAB mass spectrometry, and ^1H and ^{13}C NMR spectroscopies. The FAB mass spectra (Table 1) revealed peaks corresponding to the loss of one and two counterions, giving rise, respectively, to signals with *m/z* values for $(M - PF_6)^+$ and $(M - 2PF_6)^+$ for all three rotaxanes. The evidence for the formation of the rotaxanes was confirmed by the ^1H NMR spectra recorded in CD_3COCD_3 at room temperature. The chemical shifts of the protons α and β to the nitrogen atoms in the bipyridinium units, incorporated within the dumbbell components of the rotaxanes **2**·2PF_6, **5**·4PF_6 and **6**·4PF_6, are listed in Table 2. The ^1H NMR spectrum of the dumbbell-shaped compound **1d**·2PF_6 shows one doublet at δ 9.46 for the α protons and one doublet at δ 8.79 for the β protons. After the slipping on of **1/5DN38C10** to afford the [2]rotaxane **2**·2PF_6, the resonance of the α protons appears at δ 9.02, while the



Scheme 2 Synthesis of a [3]rotaxane by the slipping of **1/5DN38C10** over the isopropyl-substituted stoppers of a preformed [2]rotaxane having a free recognition site in its dumbbell-shaped component. The dashed lines indicate the dispersive interactions occurring between the bipyridinium units and the π-electron rich aromatic rings.

Table 1 FABMS data[a] for the rotaxanes **2**·2PF_6, **5**·4PF_6 and **6**·4PF_6

Compound	M[b]	$(M - PF_6)^+$	$(M - 2PF_6)^+$
2·2PF_6	(2417)	2272	2128
5·4PF_6	(2867)	2721	2576
6·4PF_6	(3503)	3360	3215

[a] FABMS were recorded on a Kratos MS80RF mass spectrometer (accelerating voltage, 3 kV; resolution, 1000) coupled to a DS90 data system. The atom gun was an adapted saddle field source (Ion Tech Limited) operating *ca.* 7 keV with a tube current of *ca.* 2 mA. Krypton was used to provide a primary beam of atoms and samples of the rotaxanes were dissolved in a small volume of 3-nitrobenzyl alcohol, which had previously been coated on to a stainless steel probe tip. Spectra were recorded in the positive-ion mode at a scan speed of 10 s per decade. [b] The peaks corresponding to the molecular ions were not observed. The molecular weights (M) are listed in parentheses. The measured masses correspond to the centroids of the unresolved isotopic distributions for each species.

Table 2 Chemical shifts[a] for the protons α and β to nitrogen in the bipyridinium units incorporated within the dumbbell components of the compounds **1d**·2PF_6, **2**·2PF_6, **5**·4PF_6 and **6**·4PF_6

Compound	α (δ)	β (δ)
1d·2PF_6	9.46	8.79
2·2PF_6	9.02	7.38
5·4PF_6[b]	9.32, 9.27	8.47, 8.44
6·4PF_6[c]	9.16, 9.09, 9.05, 9.00	8.14–8.07, 7.39, 7.33

[a] The ^{1}H NMR spectra were recorded at room temperature in CD_3COCD_3 on a Bruker AC300 (300 MHz) spectrometer. [b] The ^{1}H NMR spectrum of **5**·4PF_6 shows two pairs of doublets for the α and β protons. [c] The ^{1}H NMR spectrum of **6**·4PF_6 shows four doublets for the α protons and one multiplet and two doublets for the β protons.

signal for the β protons resonates at δ 7.38. The anticipated up-field shifts of both doublets, caused by the shielding effect exerted by the two naphthalene rings, demonstrates the inclusion of the bipyridinium moiety within the cavity of the macrocycle **1/5DN38C10**. The ^{1}H NMR spectrum at room temperature of the [2]rotaxane **5**·4PF_6 shows only two pairs of doublets (δ 9.32, 9.27 and δ 8.47, 8.44) for the diastereotopic α and β protons. The simplicity of the spectrum is a result of the fast shuttling‡ motion on the NMR timescale of the **BPP34C10** back and forth from one bipyridinium unit to the other. After the slipping on of **1/5DN38C10** to afford the [3]rotaxane **6**·4PF_6, the averaged end-to-end constitutional symmetry of the system is lost and the spectrum shows four doublets (δ 9.16, 9.09, 9.05 and 9.00) for the α protons and one multiplet and two doublets (δ 8.14–8.07 and δ 7.39 and 7.33) for the β protons. The expected up-field shift of the resonances for both the α and the β hydrogen atoms, which confirms that the slipping of **1/5DN38C10** has taken place, is a consequence of the shielding effect exerted by the two naphthalene rings incorporated within the macrocycle.

The [3]rotaxane **6**·4PF_6 is composed of three different components. To the best of our knowledge, it is the first example to be reported in the literature of a rotaxane comprised of two constitutionally different macrocycles located on the same linear dumbbell component. By choosing the appropriate sub-units and by carefully selecting the approaches to self-assemble them, we have demonstrated how it is possible to build relatively large and complex molecular assemblies from very simple molecular components. Furthermore, we have shown that the slipping approach to rotaxanes can be extended to a range of different building blocks, simply by matching the two major requirements of the procedure—namely, size complementarity and molecular recognition between the components.

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Footnotes

† *Spectroscopic data* for **2**·2PF_6: mp 146 °C (decomp.); FABMS 2272 $(M - PF_6)^+$, 2128 $(M - 2PF_6)^+$; ^{1}H NMR (CD_3COCD_3) δ 9.02 (4H, d, *J* = 7 Hz), 7.88 (4H, d, *J* = 9 Hz), 7.38 (4H, d, *J* = 7 Hz), 7.30–7.19 (12H, m), 7.14–7.04 (16H, m), 7.01 (4H, d, *J* = 9 Hz), 6.72 (4H, d, *J* = 9 Hz), 6.70–6.55 (8H, m), 6.45 (4H, d, *J* = 7 Hz), 6.02 (4H, s), 4.23–4.18 (4H, m), 4.04–3.91 (32H, m), 3.87–3.75 (12H, m), 2.90–2.81 (2H, m), 1.28 (36H, s), 1.20 (12H, d, *J* = 7 Hz); ^{13}C NMR (CD_3CN) δ 161.31, 157.45, 154.01, 149.32, 147.09, 145.77, 145.39, 144.46, 140.54, 132.52, 132.24, 131.37, 131.11, 126.56, 126.37, 126.24, 126.00, 125.28, 124.92, 116.50, 114.12, 114.01, 106.64, 106.06, 71.85, 71.72, 71.36, 70.79, 70.31, 70.05, 68.86, 68.17, 65.33, 63.94, 34.83, 34.11, 31.50, 24.14.

For **5**·4PF_6: mp 220 °C (decomp.); FABMS 2721 $(M - PF_6)^+$, 2576 $(M - 2PF_6)^+$; ^{1}H NMR (CD_3COCD_3) δ 9.32 (4H, d, *J* = 7 Hz), 9.24 (4H, d, *J* = 7 Hz), 8.47 (4H, d, *J* = 7 Hz), 8.44 (4H, d, *J* = 7 Hz), 7.91 (4H, s), 7.68 (4H, d, *J* = 9 Hz), 7.30 (8H, d, *J* = 9 Hz), 7.18–7.05 (24H, m), 6.82 (4H, d, *J* = 9 Hz), 6.19 (4H, s), 6.05 (12H, s), 4.21 (4H, t, *J* = 5 Hz), 4.12 (4H, t, *J* = 5 Hz), 3.92–3.85 (8H, m), 3.81–3.70 (24H, m), 3.64–3.61 (8H, m), 2.93–2.80 (2H, m), 1.29 (36H, s), 1.22 (12H, d, *J* = 7 Hz); ^{13}C NMR (CD_3CN) δ 161.33, 157.79, 153.15, 149.61, 149.04, 147.38, 146.73, 146.35, 146.01, 145.64, 140.86, 135.75, 132.84, 132.56, 131.62, 131.36, 127.49, 127.29, 126.62, 125.74, 125.53, 116.55, 115.79, 114.45, 71.51, 71.28, 70.76, 70.59, 70.38, 68.87, 68.64, 68.47, 65.33, 65.04, 64.20, 35.05, 34.32, 31.69, 24.33.

For **6**·4PF_6: mp 134 °C (decomp.); FABMS 3360 $(M - PF_6)^+$, 3215 $(M - 2PF_6)^+$; ^{1}H NMR (CD_3COCD_3) δ 9.16 (2H, d, *J* = 7 Hz), 9.09 (2H, d, *J* = 7 Hz), 9.05 (2H, d, *J* = 7 Hz), 9.00 (2H, d, *J* = 7 Hz), 8.28–8.15 (4H, m), 8.14–8.07 (4H, m), 7.91 (2H, d, *J* = 9 Hz), 7.70 (2H, d, *J* = 9 Hz), 7.39 (2H, d, *J* = 7 Hz), 7.35–7.22 (12H, m), 7.19–7.03 (22H, m), 6.87–6.76 (4H, m), 6.72–6.63 (4H, m), 6.60–6.48 (8H, m), 6.22 (2H, s), 6.18 (2H, s), 6.09 (2H, s), 6.02–5.96 (10H, m), 4.24–4.17 (4H, m), 4.14–3.54 (76H, m), 2.93–2.79 (2H, m), 1.29 (18H, s), 1.28 (18H, s), 1.22 (6H, d, *J* = 7 Hz), 1.21 (6H, d, *J* = 7 Hz); ^{13}C NMR (CD_3CN) δ 154.13, 152.94, 149.53, 147.30, 146.43, 145.54, 145.01, 140.78, 136.14, 132.75, 132.59, 132.46, 132.17, 132.00, 131.53, 131.27, 126.80, 126.53, 126.07, 125.44, 125.18, 124.96, 118.29, 116.59, 116.39, 115.60, 114.35, 114.04, 106.31, 71.96, 71.82, 71.34, 71.18, 70.92, 70.66, 70.49, 70.29, 69.03, 68.78, 68.51, 68.38, 64.10, 34.97, 34.24, 31.60, 24.25.

‡ In previous investigations,[17,18] a free energy of activation ($\Delta G^{\ddagger}$) of *ca.* 10 kcal mol^{-1} (1 cal = 4.184 J) for the degenerate site-exchange process occurring within [2]rotaxanes, incorporating either tris(4-*tert*-butylphenyl) methyl groups (R = Bu^t) or trisphenylmethyl groups (R = H) as the stoppers, was derived by the coalescence method.[22] This $\Delta G^{\ddagger}$ value corresponds to the **BPP34C10** ring moving from one dicationic binding site to the other at a rate of *ca.* 300000 s^{-1} at 298 K.

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