Self-assembled [2]Catenanes exhibiting Highly Selective Translational Isomerism

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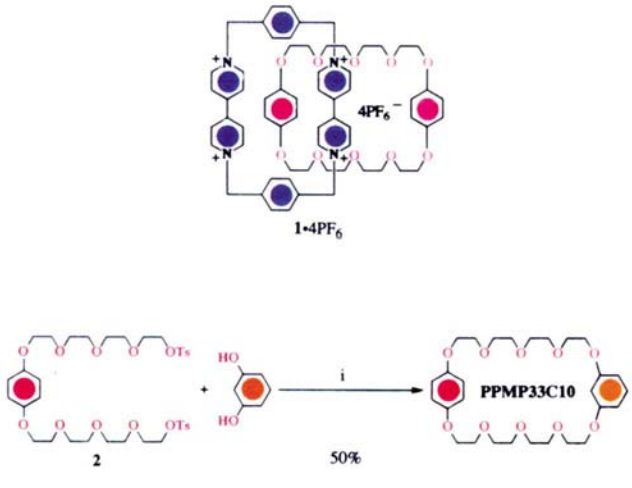
Template-directed synthesis is used to construct two isomeric [2]catenanes incorporating the macrocyclic polyether, (paraphenylene-metaphenylene)-33-crown-10, and either (*i*) cyclobis(paraquat-*p*-phenylene) or (*ii*) cyclo(paraquat-*p*-phenylene)(paraquat-*m*-phenylene) as their tetrakis(hexafluorophosphates); these isomeric [2]catenanes are found to have a remarkable preference to exist as one translational isomer, both in the solid (by X-ray crystallography) and solution (by variable-temperature ^{1}H NMR spectroscopy) states—the one in which a hydroquinone, rather than a resorcinol, ring is located inside the cavities of the isomeric tetracationic cyclophanes.

The self-assembly[1] of catenanes and rotaxanes from ring and dumbbell-like components incorporating π-electron deficient paraquat dications and π-electron rich units, *e.g.* hydroquinone, can be an extremely efficient synthetic process.[2] The [2]catenane **1**·4PF$_6$ comprised of bis(paraphenylene)-34-crown-10 (**BPP34C10**)[3] and cyclobis(paraquat-*p*-phenylene) can be self-assembled[4] in 70% yield. Changing the constitution of either the macrocyclic polyether[5,6] or the tetracationic cyclophane component[7,8] not only affects the efficiency of the self-assembly process, but it also alters the nature of the static and the dynamic properties between the interlocked rings. Here, we report the effects of constitutional change in the macrocyclic polyether component upon the efficiency of formation and properties of [2]catenanes incorporating either cyclobis(paraquat-*p*-phenylene) or cyclo(paraquat-*p*-phenylene)(paraquat-*m*-phenylene). We describe (*i*) the synthesis of the macrocyclic polyether (paraphenylene)(metaphenylene)-33-crown-10 (**PPMP33C10**), (*ii*) its binding with the paraquat dication, (*iii*) the self-assembly of two new [2]catenanes using **PPMP33C10** as the ring template, (*iv*) their preference to exist predominantly as one translational isomer in solution, and (*v*) the X-ray crystal structure of the [2]catenane incorporating **PPMP33C10** and cyclobis(paraquat-*p*-phenylene).†

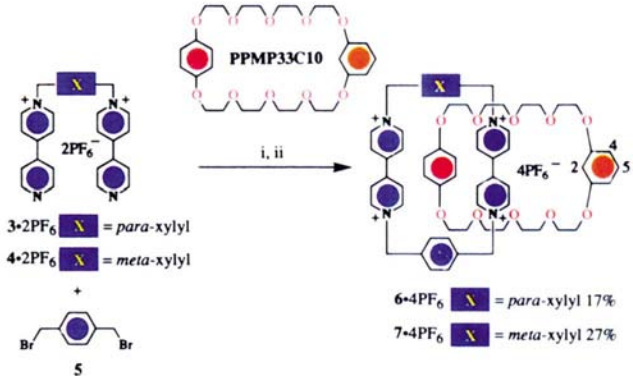
The macrocyclic polyether‡ **PPMP33C10** was synthesised in 50% yield from the bistosylate[9] **2** and resorcinol, employing pseudo-high dilution conditions in dimethylformamide (DMF) using caesium carbonate as a base in the presence of caesium tosylate and a phase transfer catalyst, Bu$_4$NI (Scheme 1). Mixing equimolar proportions of **PPMP33C10** and paraquat bis(hexafluorophosphate) in either acetone or acetonitrile produced a golden-yellow solution as a result of the charge transfer interaction in the complex which has an absorption band centred on 410 nm. Comparison of the ^{1}H NMR spectra (300 MHz, room temp., CD_3COCD_3) of the 1 : 1 complex with the individual components reveals significant upfield shifts for the hydroquinone and resorcinol proton resonances in **PPMP33C10** upon complexation. The hydroquinone and H-2 resorcinol proton resonances are shifted upfield by 0.38 and 0.69 ppm, respectively. A ^{1}H NMR spectroscopic titration (CD_3COCD_3) at 298 K, employing the hydroquinone proton resonance as the probe, yielded a K_a value of 3333 dm^3 mol^{-1} for the 1 : 1 complex§ formed between **PPMP33C10** and paraquat bis(hexafluorophosphate). This value corresponds to a free energy of complexation of 4.80 kcal mol^{-1} (1 cal = 4.184 J).



Scheme 1 Synthesis of the macrocyclic polyether **PPMP33C10**. *Reagents and conditions*: i, Cs_2CO_3, CsOTs, Bu$_4$NI, DMF, 110 °C.

The [2]catenanes were prepared under identical conditions by reaction of either **3**·2PF$_6$ or **4**·2PF$_6$ with 1,4-bis(bromomethyl)benzene **5** in the presence of excess **PPMP33C10** in DMF at room temp. (Scheme 2). After 10 days, the reaction mixtures were subjected to column chromatography on silica gel, affording the [2]catenanes **6**·4PF$_6$ and **7**·4PF$_6$ as red solids in 17 and 27% yields, respectively, after counterion exchange. They were subsequently characterised,¶‖ by ^{1}H and ^{13}C NMR spectroscopies and by FAB-MS. The yields of these [2]catenanes are intermediate between those reported[7,10] for the self-assembly of isomeric [2]catenanes incorporating **BPP34C10** and bis(metaphenylene)-32-crown-10 (**BMP32C10**).

Both **6**·4PF$_6$ and **7**·4PF$_6$ exhibit temperature dependent behaviour in their ^{1}H NMR spectra. This is a direct result of the equilibration (Scheme 3) between the translational isomers of the [2]catenanes and a degenerate process experienced by each of these isomers. Translational isomers **A** and **B** may be interconverted by the circumrotation of the π-electron rich macrocyclic polyether through the cavity of the tetracationic cyclophane (Process I, shown in Scheme 3). Thus, each π-electron rich aromatic residue of the macrocyclic polyether can be located either 'alongside' or 'inside' the tetracationic cyclophane. Another dynamic process in these systems involves the pirouetting[5] of the tetracationic cyclophane about the O–O axis of the 'inside' π-electron rich aromatic unit. This



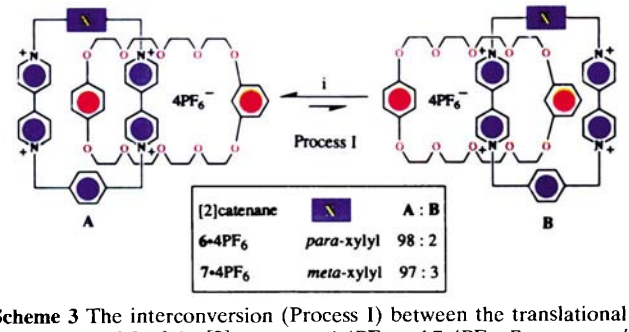
Scheme 2 Self-assembly of the two new [2]catenanes **6**·4PF$_6$ and **7**·4PF$_6$. *Reagents and conditions*: i, DMF, room temp., 10 d; ii, NH_4PF_6, H_2O.

process results in a change of the environments of the 4,4′-bipyridinium residues in the tetracationic cyclophane between 'alongside' and 'inside' positions with respect to the macrocyclic polyether. The ^{1}H NMR spectra (400 MHz, room temp.) of both **6**·4PF$_6$ and **7**·4PF$_6$ in CD_3COCD_3 solution display slightly broadened resorcinol proton resonances centred on approximately δ 5.54 (H-2), 6.28 (H-4) and 7.10 (H-5), corresponding to the resorcinol ring occupying the 'alongside' position with respect to the tetracationic cyclophane. Thus, at room temperature, process I is slow on the ^{1}H NMR timescale for these [2]catenanes. However, no resonances were in evidence for the two [2]catenanes with 'alongside' hydroquinone protons in either of their spectra at this temperature.

In order to establish the presence of the translational isomer **B** in **7**·4PF$_6$, a saturation transfer experiment[7] was carried out at 273 K on the small, relatively well-resolved singlet at δ 6.38, which appears in the region of the ^{1}H NMR spectrum expected for protons of an 'alongside' hydroquinone residue.** Saturation of this low intensity resonance gave transfer to broad resonances centred at δ 3.67 and 4.41, which correspond to the 'inside' hydroquinone protons positioned at the different 'ends' of the tetracationic cyclophane. Resonances corresponding to protons associated with 'inside' resorcinol units were not observed directly during the variable-temperature ^{1}H NMR spectroscopic study. However, saturation of the resonance for the protons on the 'inside' hydroquinone ring at δ 4.41 resulted in transfer not only to the small intensity signal for the 'alongside' hydroquinone signal at δ 6.38, but also to the resonance at δ 6.26 for the H-4 and H-6 protons on the 'alongside' resorcinol ring. This experiment demonstrates that the 'inside' resorcinol unit gives rise to resonances for these protons which are hidden beneath the 'inside' hydroquinone resonance at δ 4.41. Integration of the 'alongside' hydroquinone and resorcinol H-5 proton resonances indicate that the isomer ratio **A**:**B** is approximately 97:3 for **7**·4PF$_6$ in CD_3COCD_3 solution at 273 K. Cooling the CD_3COCD_3 solution of **7**·4PF$_6$ down to 193 K resulted in a ^{1}H NMR spectrum in which four resonances are observed at δ 1.86, 3.13, 5.46 and 5.57 for the 'inside' hydroquinone ring protons. The appearance of four signals for the 'inside' hydroquinone ring suggests that the π-electron ring is 'rocking' very slowly within the tetracationic cyclophane's cavity and that any 'flipping' of the *m*-xylyl spacer in the tetracationic cyclophane has also been 'frozen out' on the ^{1}H NMR timescale.[7] The signal at highest field corresponds to a proton directed into the π-face of the *p*-xylyl spacer of the tetracationic cyclophane, whilst the resonance at δ 3.13 arises from the proton pointing directly towards the *m*-xylyl spacer. These interactions amount to edge-to-face ones between aromatic rings, and the assignments of the signals follow from analogy with the isomeric [2]catenanes in which **BPP34C10** is the macrocyclic polyether component.[7,11]

Determination of the translational isomer ratio in a CD_3COCD_3 solution of **6**·4PF$_6$ was achieved by integration of the broad resonance centred on δ 6.41 at 273 K. It arises from the 'alongside' hydroquinone protons, as established by saturation transfer to the 'inside' hydroquinone proton resonances centred on δ 3.78. The ratio of **A**:**B** for **6**·4PF$_6$ was found to be approximately 98:2. Cooling the CD_3COCD_3 solution of **6**·4PF$_6$ resulted initially in separation of the tetracationic cyclophane's methylene signals into two resonances. Coalescence at 228 K and a limiting chemical shift difference of Δν of 47 Hz allowed an estimation of the rate constant (k_c) of 105 s^{-1} and hence of a free energy barrier ($\Delta G^{\ddagger}_c$) to pirouetting of the tetracationic cyclophane about the O–O axis of the included hydroquinone ring of 11.1 kcal mol^{-1}, a value which compares with one of 12.2 kcal mol^{-1} for the isomeric [2]catenane[11]†† incorporating **BPP34C10**. The lower energy barrier in **6**·4PF$_6$ could reflect the poorer 'alongside' interaction of the resorcinol unit with the outer π-electron deficient face of the bipyridinium units in the tetracationic cyclophane, a hypothesis borne out by the X-ray crystal structure of **6**·4PF$_6$.

The catenane structure of **6**·4PF$_6$ has been confirmed by X-ray crystallography. The crystal structure (Fig. 1) reveals features that are in common with **1**·4PF$_6$, but with significant conformational differences in the crown ether component as a result of its dissymmetric nature. The hydroquinone ring of the **PPMP33C10** component is located within the cavity of the tetracationic cyclophane such that it is sandwiched between the two π-electron deficient bipyridinium units, and oriented with its OC_6H_4O axis inclined by 46° to the mean plane of the cyclophane, whilst the resorcinol ring is positioned alongside one of the bipyridinium units. Whereas the inside hydroquinone ring achieves optimum intramolecular π–π overlap with respect to the two bipyridinium units of the cyclophane, the alongside resorcinol ring, though parallel with the inside bipyridinium unit, is offset laterally and, as a consequence, its intramolecular π–π overlap is somewhat reduced. The interplanar separations, however, between both the hydroquinone and resorcinol rings and their associated bipyridinium units, are both 3.5 Å (consistent with those observed in crystals of **1**·4PF$_6$). In addition to the intramolecular π–π stacking interactions, there are other stabilising interactions evident within the [2]catenane **6**·4PF$_6$. Electrostatic edge-to-face interactions between the inside hydroquinone ring protons and the *p*-xylyl spacers of the cyclophane (H···ring centroid distance 2.84 Å; *cf.* 2.85 Å in **1**·4PF$_6$) and [CH···O] hydrogen bonding between the α-protons of the inside bipyridinium unit and the oxygen atoms of the crown ether component. Both



Scheme 3 The interconversion (Process I) between the translational isomers **A** and **B** of the [2]catenanes **6**·4PF$_6$ and **7**·4PF$_6$. *Reagents and conditions*. i, CD_3COCD_3, 273 K.

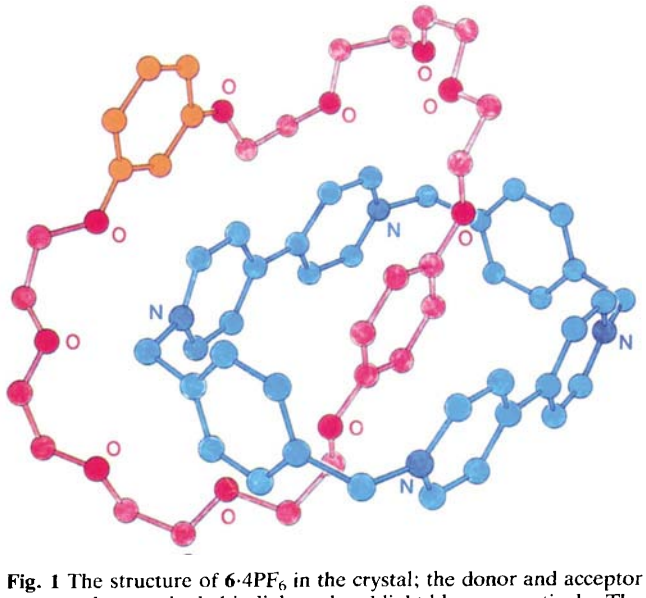


Fig. 1 The structure of **6**·4PF$_6$ in the crystal; the donor and acceptor macrocycles are shaded in light red and light blue, respectively. The resorcinol ring is highlighted in orange. O atoms are dark red and N atoms are dark blue.

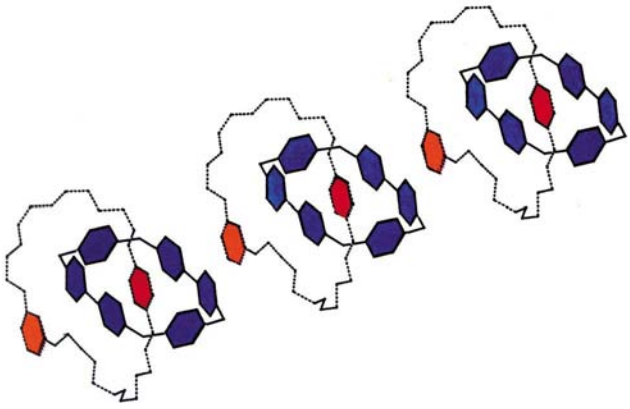


Fig. 2 Part of a polar stack of the [2]catenane **6**·4PF_6 in the crystal illustrating the alternating sequence of π-electron deficient and π-electron rich aromatic moieties

1·4PF_6 and **6**·4PF_6 form centrosymmetrically related polar stacked arrays, comprised of alternating π-electron deficient and π-electron rich moieties. The polar stacks of **6**·4PF_6 extend along the crystallographic *a* axis (Fig. 2). The loss of optimal *intramolecular* π–π overlap between the resorcinol rings and bipyridinium units is compensated for by an increase in the *intermolecular* π–π overlap between the resorcinol ring of one [2]catenane and the alongside bipyridinium unit of an immediately adjacent [2]catenane within the stacked array. The intermolecular resorcinol–bipyridinium interplanar separation within the stacked array is 3.4 Å, *cf.* 3.5 Å in **1**·4PF_6.

The solution-state host–guest[12] complex formed between **PPMP33C10** and paraquat bis(hexafluorophosphate) laid the foundations for the self-assembly of the two new [2]catenanes described in this communication. These results emphasise the dramatic difference that isomeric components involved in self-assembly processes of interlocked structures can have, both on the efficiencies of the template-directed syntheses and upon the translational[13] isomerism exhibited by the resulting [2]catenanes. Particularly remarkable is the marked preference for the inclusion of hydroquinone residues within tetracationic cyclophanes both in the solid and solution state, compared with resorcinol residues in **6**·4PF_6 and **7**·4PF_6. The remarkably high selectivity exhibited in the translational isomerism of these two new [2]catenanes bodes well for the self-assembly of controllable molecular and supramolecular devices.[14–19]

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Footnotes

† *Crystal data* for **6**·4PF_6: $C_{64}H_{72}N_4O_{10}$·4PF_6·7.25MeCN·0.25H_2O, *M* = 1915.9. triclinic, *a* = 14.28(1), *b* = 17.74(2), *c* = 20.26(2) Å, α = 77.66(9), β = 74.61(7), γ = 69.22(8)°, *U* = 4586 Å^3, space group $P\bar{1}$, *Z* = 2, D_c = 1.39 g cm^{-3}, μ = 17.3 cm^{-1}, *F*(000) = 1958.5. 11 348 independent reflections (2θ < 110°) were measured on a Siemens P4 rotating anode diffractometer with Cu-Kα radiation (graphite monochromator) using ω-scans. 4919 had $|F_o| > 4\sigma(|F_o|)$ and were considered to be observed. The structure was solved by direct methods. There is severe disorder in the PF_6^- counterions. This disorder was resolved into two partial occupancy orientations for one of the counterions, but could not be resolved for the remaining three, which consequently have high anisotropic thermal parameters. There is also disorder in the part of the macrocyclic polyether which lies outside the cavity of the tetracationic cyclophane, this component was thus refined subject to conventional polyether distance and angle geometry constraints. The position and orientation of the resorcinol ring is definitive. There is also disorder in the included MeCN molecules. Refinement was by full-matrix least-squares analysis. Because of the shortage of observed data, only the major occupancy counterions and the major occupancy atoms of the polyether chain were refined anisotropically. The remaining atoms were refined isotropically. The tetracationic cyclophane is comparatively rigid and does not usually display appreciable anisotropy. The final *R* values are consequently somewhat high with $R = 0.151$, $R_w = 0.157$ [$w^{-1} = \sigma^2(F) + 0.0005F^2$]. Computations were carried out on a Silicon Graphics Iris Indigo using the SHELXTL-IRIS program system. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Information for Authors, Issue No. 1.

‡ *Spectroscopic data* for **PPMP33C10**: FAB-MS: *m/z* 559 and 536, corresponding to $[M + Na]^+$ and $[M]^+$, respectively; ^{1}H NMR (CD_3COCD_3, 300 MHz) δ 3.58–3.65 (16H, m), 3.75–3.81 (8H, m), 4.01–4.06 (8H, m), 6.46–6.52 (3H, m), 6.81 (4H, s), 7.13 (1H, t); ^{13}C NMR (CD_3COCD_3, 75 MHz) δ 67.5, 68.3, 68.3, 69.7, 69.8, 70.8, 70.9, 79.6, 101.6, 107.1, 115.8, 129.8, 153.1, 160.1.

§ The ^{1}H NMR spectroscopic data was analysed by an iterative non-linear curve fitting program run on an Apple Macintosh Classic II microcomputer. The requirements for 1 : 1 complexation between host and guest as defined in the programme were satisfied by the ^{1}H NMR spectroscopic data obtained for **PPMP33C10** and paraquat bis(hexafluorophosphate) in CD_3COCD_3 solution. An analogous ^{1}H NMR spectroscopic titration was carried out on **PPMP33C10** and paraquat bis(hexafluorophosphate) in CD_3CN using the same probe. A lower binding constant of 580 dm^3 mol^{-1} was obtained corresponding to a free energy of complexation of 3.80 kcal mol^{-1}.

¶ *Spectroscopic data* for **6**·4PF_6: FAB-MS: *m/z* 1636, 1491, 1346 and 1201, corresponding to $[M]^+$, $[M - PF_6]^+$, $[M - 2PF_6]^+$ and $[M - 3PF_6]^+$, respectively; ^{1}H NMR (CD_3COCD_3, 300 MHz) δ 3.35–3.45 (4H, m), 3.57 (4H, br s), 3.70–3.86 (12H, m), 3.89–4.09 (16H, m), 5.52 (1H, br s), 6.03 (8H, s), 6.29 (2H, br d), 7.01–7.15 (1H, br t), 8.03 (8H, s), 8.14 (8H, d), 9.33 (8H, d); ^{13}C NMR (CD_3COCD_3, 101 MHz) δ 65.6, 67.7, 68.5, 70.6, 70.7, 70.9, 71.2, 71.5, 71.8, 101.7, 108.4, 114.0, 126.5, 131.4, 131.9, 137.9, 145.9, 147.2, 151.2, 160.7.

‖ *Spectroscopic data* for **7**·4PF_6: FAB-MS: *m/z* 1491, 1346 and 1201, corresponding to $[M - PF_6]^+$, $[M - 2PF_6]^+$ and $[M - 3PF_6]^+$, respectively; ^{1}H NMR (CD_3COCD_3, 300 MHz) δ 3.35–3.42 (4H, m), 3.57 (4H, br s), 3.76–4.05 (28H, m), 5.56 (1H, s), 6.04 (4H, s), 6.11 (4H, s), 6.29 (2H, d), 7.08 (1H, t), 7.89 (1H, t), 8.04 (5H, s), 8.11–8.26 (10H, m), 9.23 (4H, d), 9.33 (4H, d); ^{13}C NMR (CD_3COCD_3, 101 MHz) δ 64.1, 64.5, 66.2, 67.3, 69.5, 69.6, 69.8, 70.1, 70.2, 70.5, 100.4, 107.3, 113.3, 125.0, 125.3, 130.4, 130.9, 132.2, 133.7, 134.0, 136.7, 144.7, 145.5, 146.0, 150.2, 159.6.

** Such a well-resolved signal for the protons associated with the hydroquinone 'alongside' ring was not observed for **6**·4PF_6 at 273 K.

†† Values of k_c were obtained (I. O. Sutherland, *Annu. Rep. NMR Spectrosc.*, 1971, **4**, 71) by using the approximate expression $k_c = \pi(\Delta\nu)/(2)^{1/2}$ and the Eyring equation was then employed to calculate the $\Delta G_c^{\ddagger}$ value at T_c.

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