The Template-directed Synthesis of Porphyrin-stoppered [2]Rotaxanes

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Two [2]rotaxanes, composed of (*i*) a polyether chain intercepted by (*a*) one centrally-located and (*b*) two symmetrically-located π-electron-rich hydroquinol rings and terminated by free-base and metallated (Zn) tetraarylporphyrin groups respectively and (*ii*) a tetracationic cyclophane constructed of two π-electron-deficient bipyridinium units linked by paraphenylenedimethyl residues, have been self-assembled by a clipping procedure.

As our interest[1–3] in templating the synthesis of [2]rotaxanes, employing aromatic π–π stacking interactions as the major source of molecular recognition, has been developing,[4,5] there have been several reports[6–11] in the literature[12] of [2]rotaxanes and polyrotaxanes, self-assembled as a result of employing other kinds of non-covalent and coordinative bonding interactions. Aside from illustrating the potential of self-assembly in synthesis,[3,13,14] the mechanical properties of rotaxanes suggest[5] them as prototypes for the construction of molecular devices. The concept of a molecular shuttle,[15] which may be addressed photochemically, is an objective that currently appeals to us. This goal has led us to identify tetraarylporphyrins[16] as groups which could serve the dual purpose of stoppers and of photochemically-active functions in a [2]rotaxane with molecular switching possibilities. Here, we report on the self-assembly† of [2]rotaxanes **11**·4PF_6 and **12**·4PF_6 (Scheme 1), whose dumbbell components contain one and two molecular recognition sites, respectively. In both [2]rotaxanes,

† *Spectral data* for **7**: m.p. 195–197 °C; *m/z* (positive-ion FABMS) 1897 for $[M + H)^+$; ^{1}H NMR: ($CDCl_3$, 300 MHz) δ 8.97 (4 H, d, *J* 4.5 Hz), 8.94 (4H, d, *J* 4.5 Hz), 8.89 (2H, d, *J* 5.5 Hz), 8.81 (4H, d, *J* 5.5 Hz), 8.10–8.15 (12H, m), 7.82 (4H, d, *J* 8.0 Hz), 7.54–7.58 (12H, m), 6.19 (4H, d, *J* 8.0 Hz), 6.10 (4H, s), 3.22–3.26 (4H, m), 2.73 (6H, s), 2.69 (12H, s), 2.61–2.68 (8H, m), 2.38–2.47 (12H, m), 2.20–2.25 (4H, m), 2.12–2.17 (4H, m), ^{13}C NMR: ($CDCl_3$, 75 MHz) δ 156.9, 152.3, 150.5, 150.3, 150.0, 150.0, 140.8, 140.6, 137.0, 136.7, 135.7, 135.6, 134.8, 134.5, 132.0, 131.6, 131.5, 127.3, 120.5, 120.4, 115.5, 114.8, 111.6, 68.8, 68.6, 68.3, 67.9, 66.1, 65.9, 22.6, 21.5; for **11**·4PF_6: m.p. 247–249 °C; *m/z* (positive-ion FABMS) 2872 for $[M + H]^+$, 2727 for

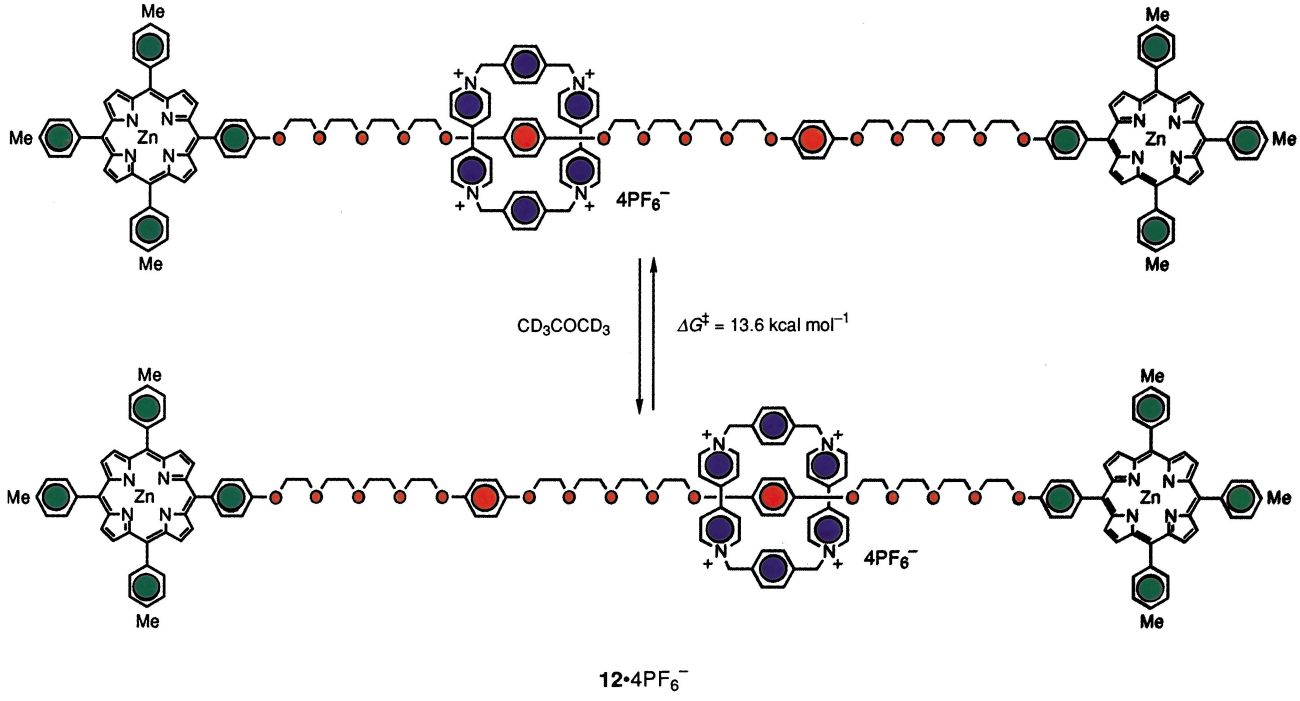


Fig. 1 The degenerate shuttling process in **12**·PF_6

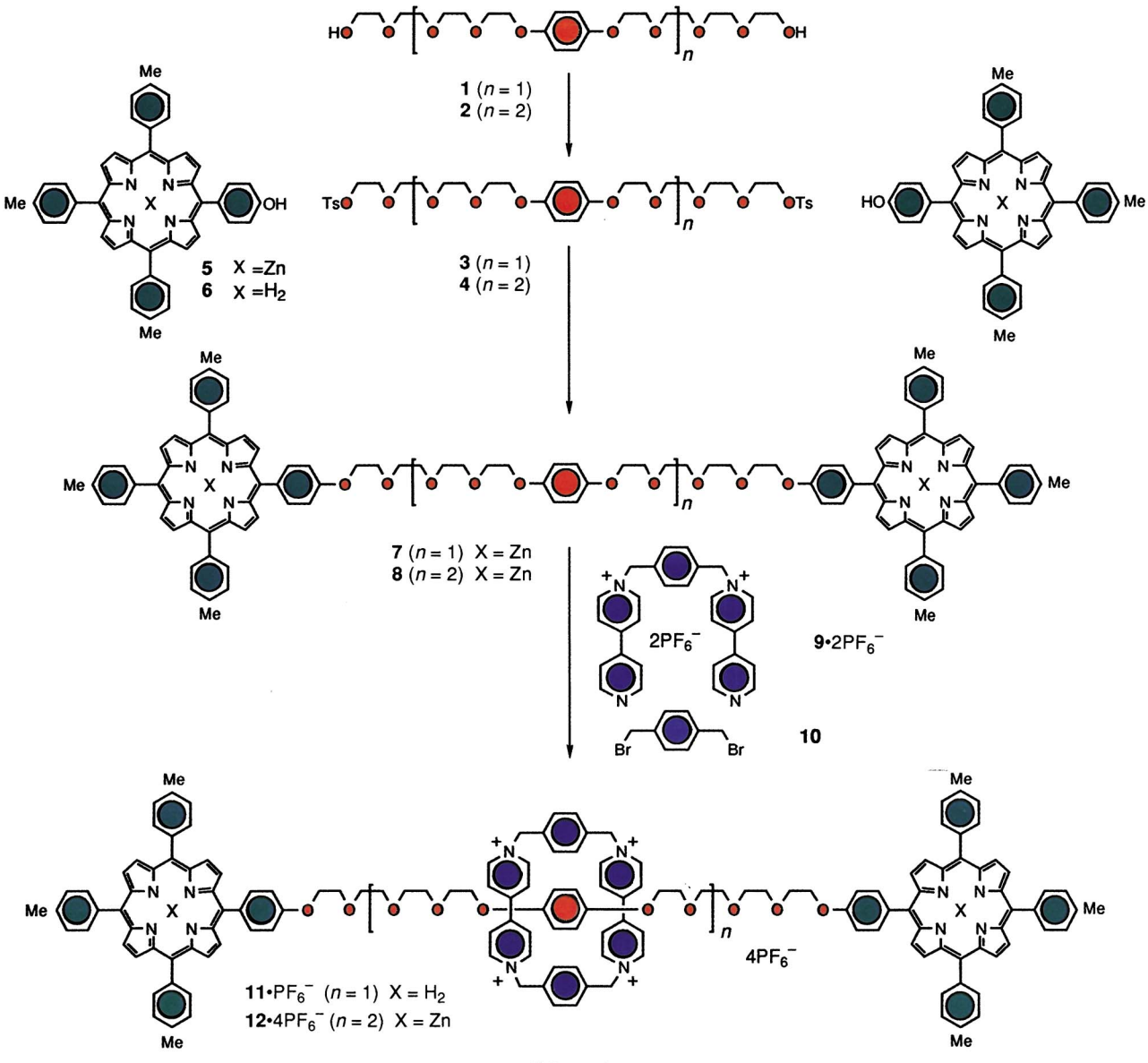
tetraarylporphyrin groups act as the stoppers and hydroquinol rings act as the molecular recognition sites.

Reaction (K_2CO_3, Me_2CO, reflux, 24 h) of the zinc porphyrin **5**—isolated after metallation[17] of the free-base porphyrin **6**[18] with $Zn(OAc)_2{\cdot}2H_2O$ in $CHCl_3$–MeOH—with the ditosylate **2**, obtained on tosylation (TsCl, Et_3N, CH_2Cl_2, room temp., 20 h) of the diol **1**,[5] yielded the metallated bisporphyrin derivative **7** as a crystalline compound (m.p. 195–197 °C) in 47% yield. The [2]rotaxane **11**·4PF_6, with m.p. 247–249 °C was self-assembled by a clipping procedure[5] from **7**, **9**·2PF_6 and **10** and work-up [involving precipitation (Et_2O), washing (CH_2Cl_2), redissolving (MeOH, $MeNO_2$), counterion exchange (NH_4PF_6/H_2O), silica gel chromatography (eluting with CH_2Cl_2–EtOAc, 4:1 and then with MeOH, $MeNO_2$, 2 mol dm^{-3} NH_4Cl, 4:4:1), and further counterion exchange (NH_4PF_6,H_2O)], which resulted in demetallation of its two porphyrin rings by, we suspect, the ethyl acetate employed as an eluent component during the chromatography. Characterisation of the [2]rotaxane **11**·4PF_6 was based upon a positive-ion FABMS,‡ which revealed an $[M]^+$ 'fragmentation' peak for the demetallated dumbbell component **7** at *m/z* 1772, as well as peaks for $[M + H]^+$, $[M\text{-}PF_6]^+$, $[M\text{-}2PF_6]^+$ and $[M\text{-}3PF_6]^+$ at *m/z* 2872, 2727, 2582 and 2436, respectively. The ^1H NMR spectra recorded in CD_3COCD_3 demonstrate substantial shielding ($\Delta\delta = -2.9$ ppm) of the hydroquinol ring protons in **11**·4PF_6, indicating[4,5] the encirclement of the π-electron rich aromatic ring in the dumbbell component by the π-electron rich bipyridinium units present in the tetracationic bead component.

Safe in the knowledge that the [2]rotaxane **11**·4PF_6 had been synthesised and characterised, we turned our attention to the making of **12**·4PF_6, a [2]rotaxane which is expected to possess molecular shuttling properties.[15] Alkylation (K_2CO_3, MeCN, reflux, 48 h) of 1,11-bis(4-hydroxyphenoxy)-3,6,9-trioxaundecane[5] with {2-[2-(2-chloroethoxy)ethoxy]ethoxy} ethanol afforded the diol **2** (m.p. 54–55 °C) which was converted (TsCl, Et_3N, CH_2Cl_2, DMAP, 4 °C, 4 d) (DMAP = 4-dimethylaminopyridine) into its ditosylate **4**. Reaction

$[M\text{-}PF_6]^+$, 2582 for $[M\text{-}2PF_6]^+$; ^1H NMR: (CD_3COCD_3, 400 MHz) δ 9.39 (8H, d, *J* 7.0 Hz), 8.69–8.82 (16H, m), 8.32 (8H, d, *J* 7.0 Hz), 8.06 (8H, s), 8.01 (12H, d, *J* 8.0 Hz), 7.79 (4H, d, *J* 8.5 Hz), 7.51 (12H, d, *J* 7.5 Hz), 6.80 (4H, d, *J*, 8.5 Hz), 6.05 (8H, s), 3.88–3.92 (8H, m), 3.87 (4H, s), 3.75–3.77 (4H, m), 3.67–3.70 (4H, m), 3.64–3.66 (4H, m), 3.50–3.53 (4H, m), 3.38–3.41 (8H, m), 2.61 (18H, s), −2.75 (4H, s), ^{13}C NMR: (CD_3COCD_3, 100 MHz) δ 159.3, 151.2, 151.0, 150.9, 147.7, 146.0, 139.9, 139.8, 138.4, 137.9, 137.8, 136.2, 135.1, 132.4, 132.0, 128.4, 128.0, 126.9, 121.4, 121.1, 121.0, 120.5, 114.1, 113.6, 113.3, 71.7, 71.4, 71.2, 70.9, 70.5, 70.0, 68.2, 67.6, 65.8, 21.4; for **2**: m.p. 54–55 °C; *m/z* (positive-ion FABMS) 730 for M^+; ^1H NMR: ($CDCl_3$, 300 MHz) δ 6.83 (8H, s), 4.05–4.09 (8H, m), 3.81–3.84 (8H, m), 3.67–3.74 (28H, m), 3.59–3.62 (4H, m), 2.41 (2H, s); for **4**: *m/z* (positive-ion FABMS) 1038 for $[M]^+$; ^1H NMR: ($CDCl_3$, 300 MHz) δ 7.79 (4H, d, *J* 8.5 Hz), 7.33 (4H, d, *J* 8.5 Hz), 6.83 (8H, s), 4.15 (4H, t, *J* 4.5 Hz), 4.04–4.09 (8H, m), 3.80–3.84 (8H, m), 3.62–3.74 (20H, m), 3.59 (8H, m), 2.43 (6H, s); for **8**: m.p. 113–115 °C; *m/z* (positive-ion FABMS) 2167 for $[M + H]^+$; ^1H NMR: ($CDCl_3$, 300 MHz) δ 8.84–8.91 (16H, m), 8.02–8.06 (12H, m) 7.92 (4H, d, *J* 8.0 Hz), 7.48—7.52 (12H, m), 6.99 (4H, d, *J* 8.0 Hz), 6.52 (4H, d, *J* 8.5 Hz), 6.37 (4H, d, *J* 8.5 Hz), 3.99–4.02 (4H, m), 3.71–3.74 (4H, m), 3.57–3.61 (4H, m), 3.47–3.52 (4H, m), 3.35–3.41 (4H, m), 3.02–3.05 (4H, m), 2.68 (6H, s), 2.66 (12H, s), 2.63–2.68 (8H, m), 2.37–2.42 (4H, m), 2.32–2.35 (4H, m); ^{13}C NMR: ($CDCl_3$, 75 MHz) δ 158.3, 152.9, 152.7, 150.4, 150.2, 140.1, 137.0, 135.5, 135.4, 134.4, 131.8, 127.3, 120.9, 120.6, 115.4, 112.6; for free-base of **8**: m.p. 99–101 °C; *m/z* (positive-ion FABMS) 2040 for $[M + H]^+$; ^1H NMR: ($CDCl_3$, 270 MHz) δ 8.85 (16H, s), 8.06–8.10 (16H, m), 7.53 (12H, d, *J* 7.5 Hz), 7.24 (4H, d, *J* 8.0 Hz), 6.68–6.89 (8H, m), 4.34–4.37 (4H, m), 3.98–4.07 (8H, m), 3.87–3.91 (4H, m), 3.81–3.85 (8H, m), 3.73–3.78 (8H, m), 3.61–3.66 (8H, m), 3.49–3.55 (8H, m), 2.68 (18H, s); ^{13}C NMR: ($CDCl_3$, 75 MHz) δ 159.1, 153.1, 139.3, 137.3, 135.5, 135.0, 134.5, 127,4, 120.1, 119.8, 115.6, 112.9, 71.0, 70.8, 70.7, 70.5, 69.9, 69.7, 68.1, 68.0, 67.7, 21.5; for **12**·4PF_6: m.p. 224–226 °C, *m/z* (positive-ion FABMS) 2978 for $[M\text{-}2PF_6]^+$; ^1H NMR: (CD_3SOCD_3, 400 MHz, +100 °C) δ 9.24 (8H, d, *J* 7.0 Hz), 8.78 (16H, s), 8.19 (8H, d, *J* 7.0 Hz), 8.03—8.07 (16H, m), 7.90 (8H, s), 7.56–7.60 (12H, m), 7.29 (4H, d, *J* 8.0 Hz), 5.87 (8H, s), 5.22 (4H, d, *J* 7.5 Hz), 5.15 (4H, d, *J* 7.5 Hz), 4.37 (4H, t, *J* 4.5 Hz), 3.95 (4H, t, *J* 5.0 Hz), 3.69–3.83 (40H, m), 2.68 (18H, s).

‡ FABMS was carried out on a Kratos MS80RF mass spectrometer (accelerating voltage, 3 keV; resolution 1500) coupled to a DS90 data system. The atom gun was an adapted saddle field source (Ion Tech Ltd.) operated at *ca.* 7 keV with a tube current of *ca.* 2 mA. Krypton was used to provide a primary beam of atoms. The sample was dissolved in a small volume of 3-nitrobenzylalcohol, 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 30 s per decade.



Scheme 1

(K_2CO_3, DMF, 80 °C, 48 h) (DMF = *N*,*N*′-dimethylformamide) of **4** with the free-base porphyrin **6** gave (38%) a bisporphyrin derivative, which was subsequently metallated with $Zn(OAc)_2.2H_2O$ in $CHCl_3$–MeOH, affording **8** as a crystalline compound (m.p. 113–115 °C) in 67% yield. On this occasion, the metallated [2]rotaxane **12**·4PF_6 (m.p. 224–226 °C) was isolated in 9% yield following its self-assembly from **8**, **9**·2PF_6 and **10** by the same clipping procedure[5] as described previously for the template-directed synthesis of **11**·4PF_6, except that pure **12**·4PF_6 was eluted directly from a silica gel chromatography column using CH_2Cl_2–MeOH, 95 : 5 as the eluent, *i.e.* the demetallation observed in the case of the crude **11**·4PF_6 by the ethyl acetate present in the eluent was avoided. A positive-ion FABMS, carried out on the supposed [2]rotaxane, revealed two high mass peaks, one at *m/z* 2978 corresponding to the loss of two PF_6^- counterions from **12**·4PF_6 and the other at *m/z* 2167 for the dumbbell component **8**. The ^{1}H NMR spectrum (400 MHz) of **12**·4PF_6 in CD_3COCD_3 is temperature dependent. At + 20 °C, the signals (δ 3.3–4.2) for the *O*-methylene protons are broad while those for the hydroquinol ring protons are so broad they cannot be detected. When the sample is cooled down to −30 °C, an AA′BB′ system (δ 6.08–6.33) can be identified for the free hydroquinol ring protons with the corresponding AA′BB′ system for the bound hydroquinol protons masked by signals for the *O*-methylene protons.§ Other expected signal changes, on the basis of the degenerate shuttling process illustrated in Fig. 1, occur, *e.g.* the methylene protons in the tetracationic bead which resonate as a singlet (δ 5.90) at +20 °C separate out into an AB system (δ_A 5.88, δ_B 5.94) at −30 °C while the doublet (δ 9.23) for the α-protons on the bipyridinium rings re-emerge following extensive line-broadening as two doublets (δ 9.22 and 9.26). An iterative computer line shape analysis[19] of this (broad) signal at −10 °C gave a rate constant of 25 s^{-1} for the site-exchange process. This corresponds to a free-energy barrier of 13.6 kcal mol^{-1} (1 cal = 4.184 J) for the degenerate shuttling process in keeping with expectations based on an analogous system.[15]

§ When a sample of **12**·4PF_6 is warmed up to +100 °C in CD_3SOCD_3, an AA′BB′ system emerges in the range δ 5.13–5.24 for the hydroquinol ring protons, which are undergoing fast site-exchange on the ^{1}H NMR timescale.

The fact that [2]rotaxanes[20] with both free-base and metallated porphyrins¶ as stoppers can be self-assembled augurs well for the development of molecular devices that can be addressed photochemically.

We thank the SERC for financial support and the Laporte Group for the award of a Centenary Fellowship to M. R. J.

Received, 13th May 1992; Com. 2/02476D

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¶ While this research was in progress, we learnt of the synthesis of a [2]rotaxane with two rigidly held porphyrins as stoppers by a copper(I)-based strategy in Strasbourg (ref. 20).