Self-Assembly of a Chiral Bis[2]catenane

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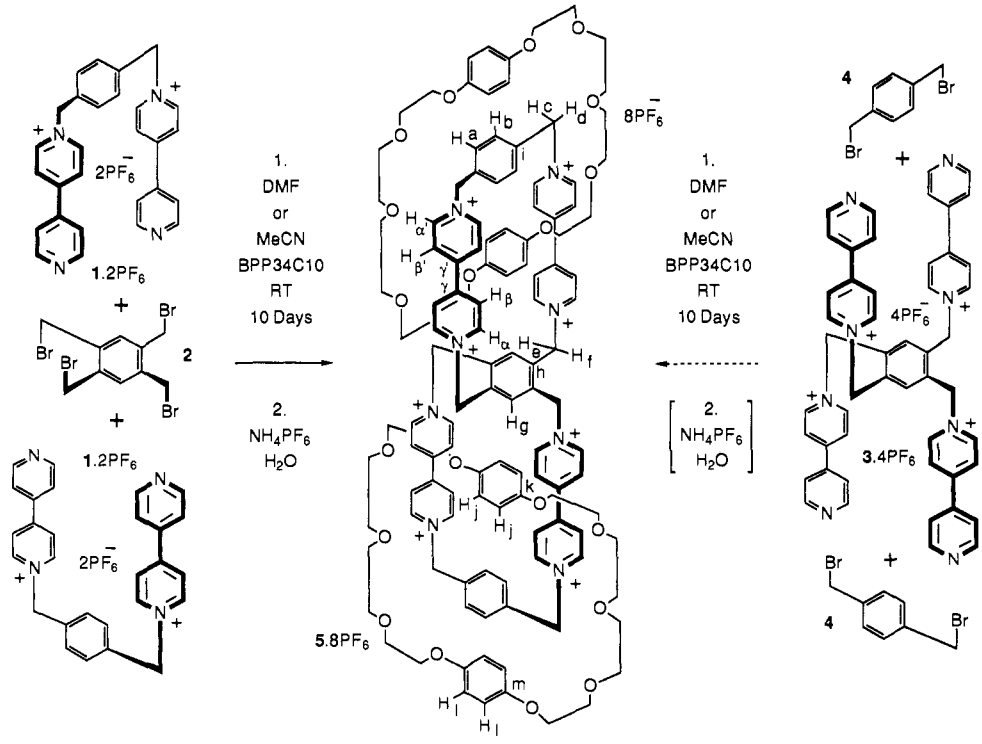
Since we reported[1] the efficient self-assembly[2] of a [2]catenane composed of a neutral macrocyclic polyether, bisparaphenylene-34-crown-10 (BPP34C10),[3] and an interlocking tetracationic cyclophane [cyclobis(paraquat-*p*-phenylene)],[4] a large number of catenanes and rotaxanes have been synthesized[5] using these components or higher homologs and/or structural analogs of them. In the search for novel building blocks to incorporate into new types of molecular assemblies, we have been attracted to 1,2,4,5-tetrakis(bromomethyl)benzene with its four reactive benzylic centers. Not only is it capable of introducing a common benzene unit in between two macrocycles,[6] but, provided the macrocycles utilize the benzene unit in the *para/para* mode of tetrasubstitution, it is also able[7] to support planar chirality.

Here, we describe the self-assembly (Scheme I) of a bis[2]catenane (**5**·8PF_6) with averaged D_2 symmetry that incorporates two fused cyclobis(paraquat-*p*-phenylene) rings, each catenated with BPP34C10, from reaction of **1**·2PF_6[1,8] (2 molar equiv) and **2** (1 molar equiv) in either dry MeCN or dry *N,N*-dimethylformamide (DMF) during 10 days at room temperature in the presence of an excess (3 molar equiv) of BPP34C10. After column chromatography [SiO_2/2 N aqueous NH_4Cl–MeOH–DMF (5:4:2)] and counterion exchange with aqueous NH_4PF_6, **5**·8PF_6 was isolated in 13% yield as a deep red-colored solid which formed single crystals, suitable for the collection[9] of X-ray diffraction data, when it was dissolved in MeCN and subjected to vapor diffusion with $^iPr_2O$. Positive-ion FABMS revealed three groups of three peaks at *m/z* 3051/2905/2759, 2514/2369/2224, and 1976/1832/1687 corresponding to the loss within each group progressively of one, two, and three PF_6^- counterions from the "molecular" ion M, M-BPP34C10, and M-2BPP34C10, respectively. Subsequent attempts to self-assemble **5**·8PF_6 by reacting (Scheme I) **3**·4PF_6[10] (1 molar equiv) with **4** (2 molar equiv) in the presence of an excess (3 molar equiv) of BPP34C10 under the same conditions that produced the bis[2]catenane previously were unsuccessful.[11]

The incorporation of the common tetrasubstituted benzene ring between the fused tetracationic cyclophane units in a *para/para* manner, rather than in either a *meta/meta* or an *ortho/ortho* manner, follows[12] unambiguously from the catenating of two BPP34C10 rings and the presence of a highly diagnostic AB system (δ_A 6.40, δ_B 6.80, J_{AB} = 9 Hz) for the four homotopic groups of diastereotopic benzylic methylene protons (H-e/H-f) in the ^1H NMR spectrum[13] of **5**·8PF_6 under conditions (51 °C in CD_3COCD_3) where the two translational isomers I and II (Scheme II) are undergoing rapid equilibration. The observation of *single* doublets at δ 8.18, 8.30, 9.29, and 9.39 for all the protons—H-β', H-β, H-α, and H-α', respectively—on the bipyridinium units suggests that rotation about the N–N axes of these units is also a rapid process on the ^1H NMR time scale. Nonetheless, under the same conditions, two sets of eight protons for "inside" and "alongside" hydroquinol rings are evident as broad signals resonating at δ 3.93 (H-j) and 6.33 (H-l), respectively. It was possible to observe the coalescence of the corresponding signals for these hydroquinol ring protons resonating at δ 3.62 and 6.24 in CD_3CN solution when it was warmed up to 85 °C. The free energy of activation ($\Delta G_c^{\ddagger}$) for the circumrotation of the BPP34C10 rings through the tetracationic macrocycles was calculated[14] to be ca. 16.0 kcal mol^{-1}, in good agreement with similar exchange processes in simpler systems.[1,5] When the sample of **5**·8PF_6 in CD_3COCD_3 solution was cooled down to −70 °C, a total of 8 H-α, 8 H-β, 8 H-α', and 8 H-β'

Scheme I. Selection in Operation as Expressed in the Successful and Unsuccessful Self-Assembly of **5**·8PF_6[a]



[a] Note that the structure of the bis[2]catenane is represented formalistically as an averaged one with respect to rapid interconversion between the translational isomers I and II (shown in Scheme II) and other rapid degenerate changes involving the relative positions of the two BPP34C10 rings on the bipyridinium units of the octacationic framework of **5**·8PF_6 at room temperature in solution.

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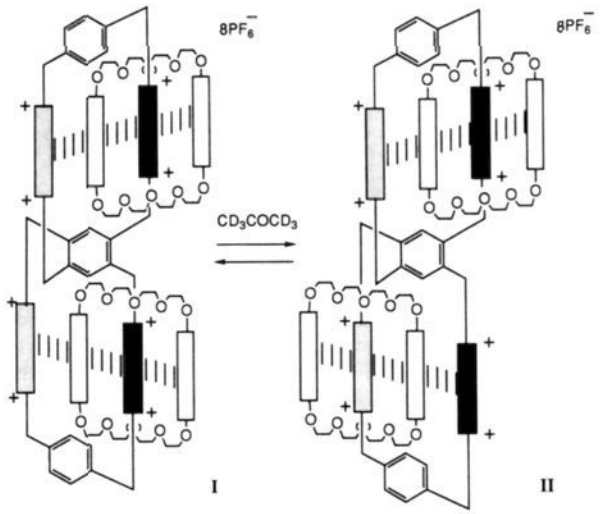
Scheme II. Equilibration of the Translational Isomers I and II of **5**·8PF_6 in CD_3COCD_3[a]



[a] The unshaded rectangles are hydroquinol rings, and the shaded (solid and hatched) rectangles are bipyridinium units. Note that a pair of solid rectangles and a pair of hatched rectangles selected from the *separate* fused tetracationic macrocycle have an ortho relationship with reference to the central benzenoid ring, whereas this cross-relationship between solid and hatched rectangles is always meta. The translational isomers I and II are interconverted when the BPP34C10 rings pirouette around the tetracationic macrocycles by a process which involves rotation about the axes of the C–O bonds of the "inside" hydroquinol rings so that the "alongside" hydroquinol rings reorganize themselves such as to encircle two ortho-related bipyridinium units (isomer I) or two meta-related bipyridinium units (isomer II).

signals, all of equal intensitites, were identified. This outcome represents a situation where the two translational isomers (Scheme II) are populated to equal extents, with the movements of the BPP34C10 rings with respect to the pairs of bipyridinium units expressing themselves slowly on the ^1H NMR time scale.

The highly selective construction of **5**·8PF_6 from *five* molecular components in *one* step demonstrates the power of self-assembly as a synthetic paradigm. In view of its constitution, topology, and chirality, this bis[2]catenane represents an important new molecular assembly comprised of *three* interlocked components: a pair of fused tetracationic macrocycles with BPP34C10 rings passing through each of its *two* loops. This topologically interesting molecule[15,16] contains a fascinating ditopic receptor in the shape of the layered octacationic cyclophane. Its bifunctionality could find numerous applications in the macromolecular and supramolecular fields of chemistry.

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(6) For two recent examples, see: (a) Lee, W. Y.; Sim, W.; Park, O. S. *Synlett* **1992**, 157–159. (b) Loeb, S. J.; Shimizu, G. K. H. *Synlett*, **1992**, 823–824.

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(9) Crystal data for **5**·8PF_6: monoclinic, space group $P2_1/n$, $a = 14.054(5)$, $b = 28.359(25)$, and $c = 45.840(23)$ Å; $\beta = 91.53(4)°$; $V = 18\,264$ Å^3. Despite encapsulation of the crystals, they decomposed before sufficient observed data for the solution of the structure had been obtained.

(10) Treatment of **2** with 4,4′-bipyridine (8 molar equiv) in refluxing dry MeCN for 10 h afforded **3**·4PF_6 in 37% yield following column chromatography [SiO_2/2 N aqueous NH_4Cl–MeOH–DMF (5:4:2)] and counterion exchange with aqueous NH_4PF_6. Positive-ion FABMS reveal three peaks at m/z 1189, 1044, and 899 corresponding to the loss of one, two, and three PF_6^- counterions, respectively, from **3**·4PF_6. ^1H NMR (300.2 MHz, CD_3CN) for **3**·4PF_6: δ 5.88 (s, 8 H, CH_2), 6.94 (s, 2 H, ArH), 7.75 (d, $J = 7$ Hz, 8 H, H-β'), 8.34 (d, $J = 7$ Hz, 8 H, H-β), 8.69 (d, $J = 7$ Hz, 8 H, H-α'), 8.82 (d, $J = 7$ Hz, 8 H, H-α).

(11) Initially, we found this result to be rather a surprising one. However, it might be telling us something about the detailed mechanism of catenane formation. In both reactions illustrated in Scheme I, the first step in the production of the tetracationic macrocyclic units must be the formation of tricationic species. Let us assume that a BPP34C10 ring will complex with the so-formed bipyridinium units and then, during the final macrocyclization step, endeavor to move within the tricationic species in order to bind to the second developing bipyridinium unit. It is obvious that these relocations, involving the BPP34C10 rings and the incipient tetracationic macrocycles, are *not* possible during the attempted formation of **5**·8PF_6 starting from **3**·4PF_6 *without decomplexation*—and hence catenation *not* occurring—whereas they are possible starting from **1**·2PF_6 during the actual self-assembly of **5**·8PF_6. It should be added that all attempts to isolate the octacationic component of **5**·8PF_6 by itself have thus far failed. It appears that it is only formed under the conditions of the reaction when BPP34C10 is present, *i.e., it is easier to make the self-assembled molecular structure than it is one of the components.*

(12) Molecular modeling reveals that the four equivalent pairs of benzylic methylene protons associated with the common tetrasubstituted benzene ring are homotopic and hence would give rise in ^1H NMR spectra to *one* singlet in each case—*i.e.*, for either the *ortho–ortho* or *meta–meta* isomers—always assuming they were capable of catenating spontaneously two BPP34C10 rings.

(13) ^1H NMR spectroscopic data for **5**·8PF_6 (proton and carbon assignments as indicated in Scheme I) (400 MHz, CD_3COCD_3, 51 °C): δ 3.50–4.25 (m, 64 H, OCH_2), 3.93 (br s, 8 H, H-j), 6.02–6.09 (AB system, $J_{AB} = 9$ Hz, 8 H, H-c/d), 6.33 (br s, 8 H, H-l), 6.40 and 6.80 (AB system, $J_{AB} = 9$ Hz, 8 H, H-e and H-f), 8.06 (br s, 8 H, H-a/b), 8.18 (d, $J = 6$ Hz, 8 H, H-β'), 8.30 (d, $J = 6$ Hz, 8 H, H-β), 8.81 (s, 2 H, H-g), 9.29 (d, $J = 6$ Hz, 8 H, H-α), 9.39 (d, $J = 6$ Hz, 8 H, H-α'). These proton assignments were made by a combination of double irradiation techniques including decoupling difference, NOE, saturation transfer, and a COSY45 carried out between 40 and 55 °C. The following pairwise assignments for the 32 signals observed for the H-α1/β1···H-α8/β8 and H-α'1/β'1···H-α'8/β'8 protons in the ^1H NMR spectrum recorded in CD_3COCD_3 at −70 °C were achieved by means of a COSY45 experiment: δ 8.82/7.63, 9.05/8.39, 9.07/8.34, 9.16/7.90, 9.21/8.27, 9.25/8.21, 9.32/8.12, 9.37/8.51, 9.44/8.58, 9.51/8.47, 9.54/8.29, 9.60/8.66, 9.64/8.76, 9.71/8.53, 9.71/8.61, 9.77/8.70. A ^{13}C NMR spectrum was recorded at 75.1 MHz using the DEPT135 sequence in CD_3COCD_3 at room temperature and assigned with the aid of 2D CH correlation: δ 61.2 (C-e/f), 65.5 (C-c/d), 67.1, 68.3, 69.3, 69.9, 70.2, 70.6, 70.8 and 71.0 (8 × OCH_2), 114.5 (C-j), 115.9 (C-l), 126.5 (C-β'), 127.2 (C-β), 131.6 (C-a/b), 137.3 (C-g), 145.3 (C-α), 145.9 (C-α'). The quaternary carbons were observed by conventional proton-decoupled ^{13}C NMR spectroscopy at 51 °C: δ 137.9 and 138.2 (C-h/C-i), 146.7 and 148.5 (C-γ/C-γ'), 151.6 (C-k), 153 (C-m).

(14) The free energy barrier ($\Delta G_c^{\ddagger} = 16.0$ kcal mol^{-1}) for this exchange process between "inside" and "alongside" hydroquinol rings was calculated using the information that $\Delta\nu = 1048$ Hz, $k_c = 2329$ s^{-1}, and $T_c = 85$ °C. Values for k_c were obtained (Sutherland, I. O. *Annu. Rep. NMR Spectrosc.* **1971**, *4*, 71–235) by using the approximate expression $k_c = \pi(\Delta\nu)/(2)^{1/2}$, and the Eyring equation was used to calculate the $\Delta G_c^{\ddagger}$ value at T_c.

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