The template-directed synthesis of cyclobis(paraquat-4,4′-biphenylene)

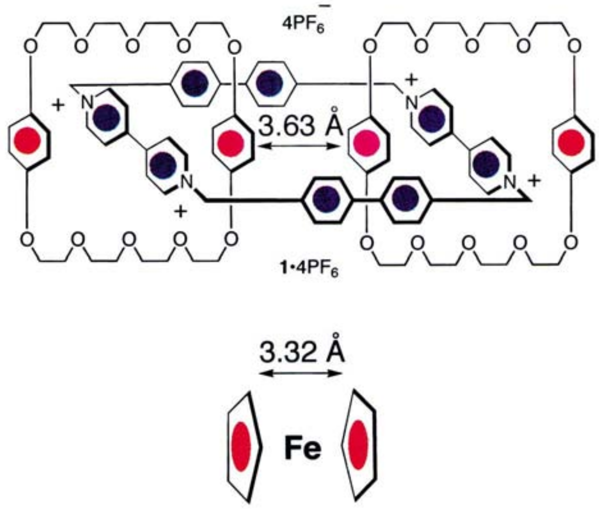
Peter R. Ashton,[a] Stephan Menzer,[b] Françisco M. Raymo,[a] George K. H. Shimizu,[a] J. Fraser Stoddart*[a] and David J. Williams[b]

[a] *School of Chemistry, University of Birmingham, Edgbaston, Birmingham, UK B15 2TT*
[b] *Department of Chemistry, Imperial College, South Kensington, London, UK SW7 2AY*

The self-assembly of a π-electron deficient bipyridinium-based cyclophane around a π-electron rich ferrocene-based polyether as template provides a relatively simple method of self-assembling, in preparative yields, an organic molecular square—namely, cyclobis(paraquat-4,4′-biphenylene)—that is able to recognise and bind π-electron rich guests.

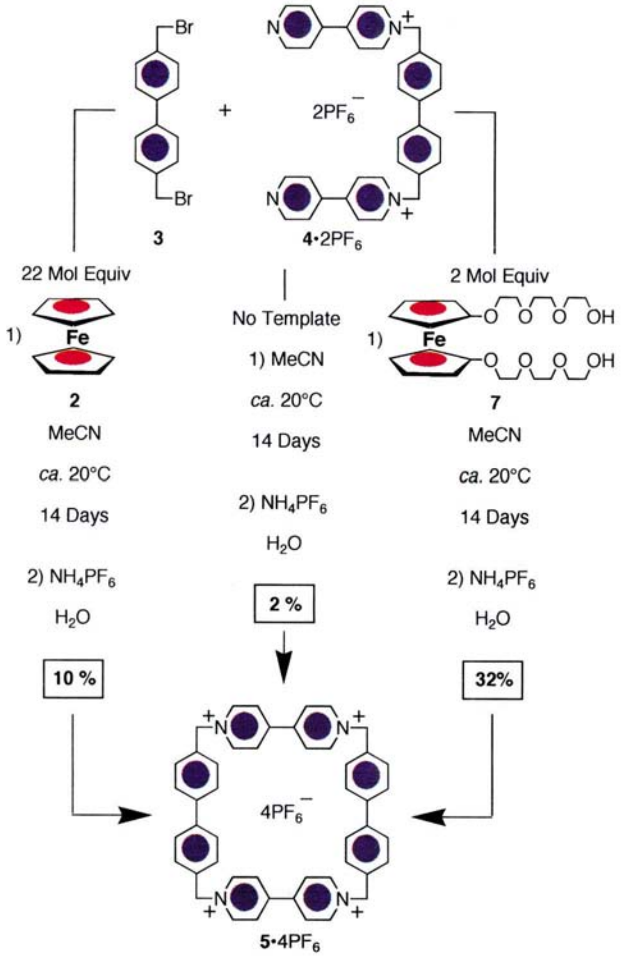
In the last few years, a wide variety of abiotic self-assembling systems have been described in the chemical literature.[1] Recently, we have developed an efficient and simple approach[2] to the construction of molecular assemblies, such as catenanes[3] and rotaxanes,[3,4] and supramolecular arrays, such as pseudorotaxanes[5] and double helices.[6] The methodology relies upon the stereoelectronic complementarity that exists between π-electron rich aromatic rings (*e.g.* hydroquinone) and π-electron deficient aromatic units (*e.g.* bipyridinium), which are located strategically within these structures and superstructures. These self-assembly processes are driven mainly by π–π stacking interactions[7] between the hydroquinone rings and the bipyridinium units, augmented by hydrogen bonding[8] and edge-to-face T-type interactions[9] between orthogonally-disposed aromatic ring systems. By employing these noncovalent bonding interactions in template-directed syntheses,[10] we have been able to self-assemble numerous catenanes, rotaxanes, and pseudorotaxanes containing from two to five mechanically-interlocked components.[3]

The [3]catenane $\mathbf{1}{\cdot}4PF_6$, depicted in Fig. 1, has been self-assembled[3,11] in a yield of 25% by treating the dibromide **3** with the dicationic salt $\mathbf{4}{\cdot}2PF_6$ in the presence of bis-*para*-phenylene-34-crown-10 (**BPP34C10**) in MeCN at room temperature over 10 d. By contrast, the tetracationic cyclophane $\mathbf{5}{\cdot}4PF_6$ incorporated within the [3]catenane $\mathbf{1}{\cdot}4PF_6$ can only be obtained[3] (Scheme 1) in very low yield (2%) in the absence of templating agents such as **BPP34C10**. Indeed, the self-assembly of the [3]catenane $\mathbf{1}{\cdot}4PF_6$ is much easier than is the synthesis of its tetracationic cyclophane component! Intrigued by the possibility of producing quantities of $\mathbf{5}{\cdot}4PF_6$—a molecular square[12] able to incorporate simultaneously within its cavity two π-electron rich aromatic units—we went out in search of a suitable template for $\mathbf{5}{\cdot}4PF_6$ in order to improve its meagre yield. The X-ray crystal structure of the [3]catenane $\mathbf{1}{\cdot}4PF_6$ reveals[3,11] the essential stereoelectronic features which a suitable template has to possess. The interplanar separation between the two hydroquinone rings (Fig. 1) included in the cavity of the π-electron deficient cyclophane is 3.63 Å. Contrast this separation with the fact that the cyclopentadienyl rings in ferrocene **2** are separated[13] by 3.32 Å. Furthermore, many examples of charge transfer complexes between ferrocene-



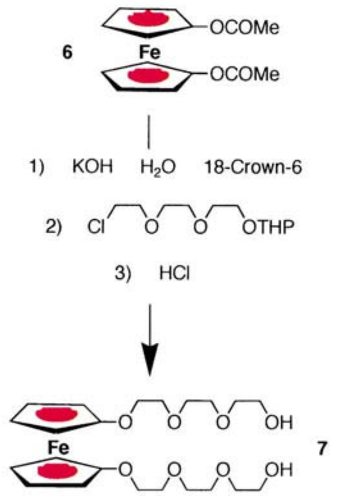
1·4PF6

Fig. 1 The interplanar separation between the two hydroquinone rings residing inside the cavity of the tetracationic cyclophane within the [3]catenane $\mathbf{1}{\cdot}4PF_6$ and interplanar separation between the two cyclopentadienyl rings of ferrocene **2**

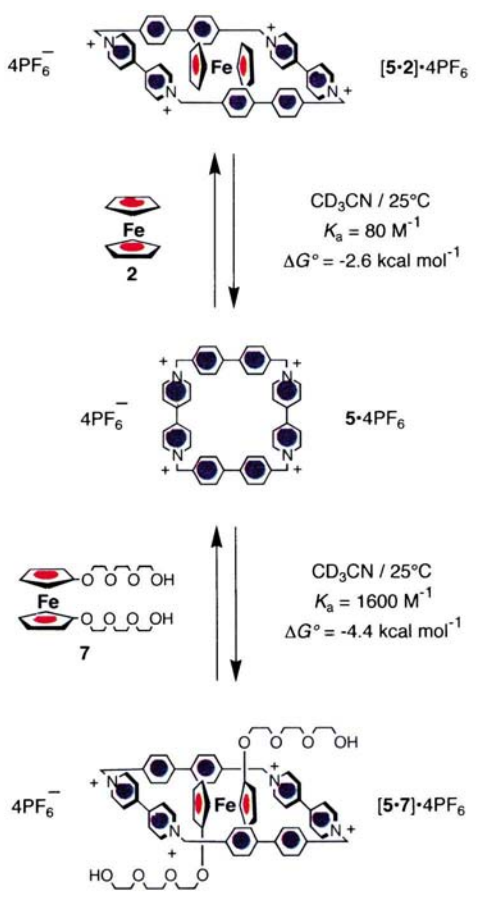


Scheme 1 The self-assembly of $\mathbf{5}{\cdot}4PF_6$ templated by ferrocene **2** and the 1,1′-disubstituted ferrocene derivative **7**

based derivatives and π-electron deficient compounds have been reported in the literature.[14] Therefore, we reasoned that, by acting as second sphere coordinators,[15] ferrocene-based derivatives should be able to promote the self-assembly of the tetracationic cyclophane $\mathbf{5}\cdot 4PF_6$. Indeed, reaction of the dibromide **3** with the dication $\mathbf{4}\cdot 2PF_6$ in the presence of 22 equiv. of **2**, under otherwise identical conditions, afforded† $\mathbf{5}\cdot 4PF_6$ in an improved yield of 10%. In order to improve yet further upon this yield, we synthesised (Scheme 2) the 1,1′-disubstituted ferrocene derivative† **7** containing two polyether chains, both capable of sustaining hydrogen bonding interactions with the CH-acidic protons on the bipyridinium units of $\mathbf{5}\cdot 4PF_6$. Gratifyingly, reaction of the dibromide **3** with the dication $\mathbf{4}\cdot 2PF_6$ in the presence of only 2 equiv. of **7** in MeCN at room temperature during 14 d afforded cyclobis(paraquat-4,4′-biphenylene) ($\mathbf{5}\cdot 4PF_6$) in the acceptable yield of 32%. Here we report (i) the X-ray crystal structure of $\mathbf{5}\cdot 4PF_6$, assess (ii) the complexing ability of $\mathbf{5}\cdot 4PF_6$ towards both **2** and **7** by ^1H NMR spectroscopy in solution (Scheme 3) as well as establish (iii) the formation of the pseudorotaxane $[\mathbf{5}\cdot\mathbf{7}]\cdot 4PF_6$ by FABMS.



Scheme 2 The synthesis of the 1,1′-disubstituted ferrocene derivative **7**



Scheme 3 The formation of the 1 : 1 adducts between $\mathbf{5}\cdot 4PF_6$ and ferrocene **2** and between $\mathbf{5}\cdot 4PF_6$ and the 1,1′-disubstituted ferrocene derivative **7**

The X-ray analysis‡ of $\mathbf{5}\cdot 4PF_6$ shows (Fig. 2) the tetracationic component to have an open box geometry very similar to that observed[3b,11] in the [3]catenane $\mathbf{1}\cdot 4PF_6$. Differences are observed in the twist angles between the aromatic rings of the bipyridinium and the biphenylene units as well as in the out-of-plane bending existing within these units. The most noticeable change is in the twist angles between the pyridinium rings within the two bipyridinium units, which correspond to 27 and 24°, *cf.* 18° in $\mathbf{1}\cdot 4PF_6$. The angles about the bond linking the two phenylene rings of the biphenylene residues are only slightly increased, 31 and 34°, *cf.* 29° in $\mathbf{1}\cdot 4PF_6$. The angles subtended between the N–CH_2 bonds emanating from the bipyridinium units are 20 and 21°, *cf.* 17° in $\mathbf{1}\cdot 4PF_6$, and those between C–CH_2 bonds of the biphenylene units are 19 and 21°, *cf.* 25° in $\mathbf{1}\cdot 4PF_6$. The overall internal dimensions of the free tetracationic macrocycle $\mathbf{5}\cdot 4PF_6$, as defined by the distances between the centroids of the bonds linking the pyridinium rings in one instance, and the centroids of the bonds linking the phenylene rings in the other, are 10.87 and 10.96 Å, respectively. These compare with the distances of 10.75 and 11.24 Å, respectively, in $\mathbf{1}\cdot 4PF_6$, reflecting the ability of the cyclophane to 'breathe' in order to facilitate the inclusion of guest species. The molecules pack to form (Fig. 3) a sheet mosaic, with, in one direction, the bipyridinium units of adjacent molecules in register and separated by *ca.* 3.7 Å. In the other direction, the biphenylene units are offset such that only one of the two phenylene rings in each unit is overlapped with its centrosymmetrically related counterpart in the adjacent molecule. As a result of the absence of a crystallographic centre of symmetry within each molecule, two types of phenylene–phenylene π–π stacking interactions are observed within each sheet. The parallel inter-ring plane separations are effectively the same at 3.35 and 3.36 Å, but the phenylene centroid–centroid separations differ at 3.56 and 3.69 Å, respectively, as a result of the different degrees of stagger within each sheet. Adjacent sheets are separated by 7.8 Å and are offset such that one of the methylene carbon atoms of each cyclophane within one sheet is positioned approximately over the centre of a macrocycle in the next.

The ^1H NMR spectrum recorded at room temperature in CD_3CN of the 1 : 1 adduct $[\mathbf{5}\cdot\mathbf{2}]\cdot 4PF_6$ reveals (Table 1) rather small changes in chemical shifts relative to **2** and $\mathbf{5}\cdot 4PF_6$– presumably as a result of the relatively weak binding of

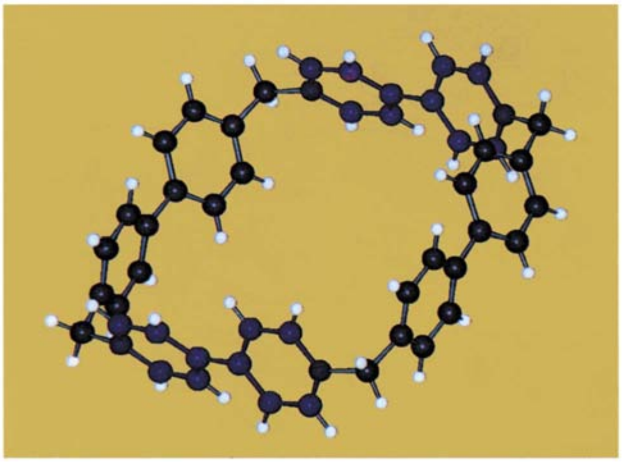


Fig. 2 Ball-and-stick representation of the molecular structure of the tetracationic cyclophane 5^+ in the crystal. The bipyridinium units are depicted in blue.

ferrocene by the tetracationic cyclophane. However, when **7** is mixed in equimolar amounts with **5**·4PF$_6$, not only does a green colour develop immediately as a result of the charge transfer interaction between the cyclopentadienyl rings of **7** and the bipyridinium rings of **5**·4PF$_6$, but the resonances corresponding to the cyclopentadienyl protons in the ^{1}H NMR spectrum of [**5**·**7**]·4PF$_6$ recorded at room temperature in CD$_3$CN are shifted upfield by *ca.* 1.5 ppm, consistent with a pseudorotaxane-like geometry for the 1 : 1 adduct. Association constants of 80 and 1600 dm^{-3} mol^{-1}, corresponding to binding energies of −2.6 and −4.4 kcal mol^{-1} (1 cal = 4.184 J), were obtained for [**5**·**2**]·4PF$_6$ and [**5**·**7**]·4PF$_6$, respectively, in CD$_3$CN at 25 °C using a ^{1}H NMR titration procedure. The FAB mass spectrum§ of [**5**·**7**]·4PF$_6$ revealed a peak at *m*/*z* 1735 corresponding to the 'molecular weight' of the pseudorotaxane, together with additional peaks at *m*/*z* 1589, 1443 and 1298, originating from the loss of one, two and three hexafluorophosphate counterions respectively, from the 1 : 1 adduct.

The self-assembly of cyclobis(paraquat-4,4′-biphenylene) (**5**·4PF$_6$) around ferrocene-based templates opens up the opportunity to complex two π-electron donating substrates simultaneously within the cavity of this rigid preorganised receptor containing π-acceptor and hydrogen bond donor recognition sites. These particular features raise the prospect of self-assembling doubly interlocked molecular compounds as well as constructing electrochemically controllable rotaxanes and catenanes[16] with redox-active ferrocene-containing components.[17]

This research was supported in the UK by the European Community Human Capital and Mobility Programme and by the Natural Sciences and Engineering Research Council of Canada, as well as by the Engineering and Physical Sciences Research Council and the Biotechnology and Biological Sciences Research Council.

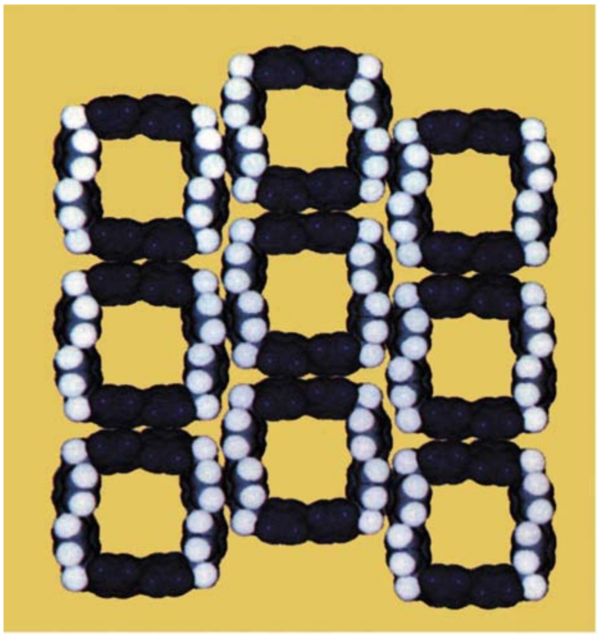


Fig. 3 Space-filling representation of part of one of the mosaic layers of the cyclophane **5**·4PF$_6$, showing the two different types of phenylene–phenylene stacking interactions

Table 1 ^{1}H NMR Spectroscopic data for the 1 : 1 adducts [**5**·**2**]·4PF$_6$ and [**5**·**7**]·4PF$_6$ and the reference compounds **2**, **5**·4PF$_6$, and **7** recorded in CD$_3$CN at room temperature

	Tetracationic component		Neutral component
Compound	α-Bipy-H[a] δ (Δδ)	β-Bipy-H[b] δ (Δδ)	C$_5$H$_5$[c] δ (Δδ)
2			4.16
5·4PF$_6$	8.94	8.25	
[**5**·**2**]·4PF$_6$	8.89 (−0.05)	8.12 (−0.13)	4.08 (−0.08)
7[d]			4.12, 3.94
[**5**·**7**]·4PF$_6$[d]	8.95 (−0.01)	8.09 (−0.03)	2.63 (−1.49), 2.41 (−1.53)

[a] Protons attached to the bipyridinium units in the α position with respect to the nitrogen atoms. [b] Protons attached to the bipyridinium units in the β position with respect to the nitrogen atoms. [c] Protons attached to the cyclopentadienyl rings. [d] The 1,1′-disubstituted ferrocene derivative **7** comprises two pairs of constitutionally heterotopic protons for the two equivalent cyclopentadienyl rings. These protons give rise in the ^{1}H NMR spectrum at room temperature to two broad resonances each centred upon the δ values reported in the Table.

Footnotes

† *Spectroscopic data* for **5**·4PF$_6$: mp 194 °C (decomp.); FABMS 1107 (M − PF$_6$)$^+$, 962 (M − 2PF$_6$)$^+$ and 817 (M − 3PF$_6$)$^+$; ^{1}H NMR (CD$_3$CN) δ 8.95 (8 H, d, *J* 7 Hz), 8.25 (8 H, d, *J* 7 Hz), 7.66 (8 H, d, *J* 8 Hz), 7.54 (8 H, d, *J* 8 Hz) and 5.82 (8 H, s); ^{13}C NMR (CD$_3$CN) δ 150.8, 146.3, 141.6, 134.8, 130.8, 128.9, 128.5 and 65.8. For **7**: EIMS 482 (M)$^+$; ^{1}H NMR (CD$_3$COCD$_3$) δ 4.22 (4 H, br s), 3.88–4.05 (8 H, m) and 3.49–3.78 (22 H, m); ^{13}C NMR (CD$_3$COCD$_3$) δ 73.5, 71.3, 71.1, 70.6, 70.5, 63.1, 61.9, 61.8 and 56.5.

‡ *Crystal data* for **5**·4PF$_6$·4MeCN: Single crystals, suitable for X-ray crystallography, were grown by vapour diffusion of Pr$^i_2$O into a MeCN solution of **5**·4PF$_6$. Triclinic, a = 12.778(3), b = 14.548(3), c = 16.667(3) Å, α = 89.80(3), β = 98.47(3), γ = 91.79(3)°, V = 3063 Å^3, T = 213 K, space group = $P\bar{1}$, Z = 2, D_c = 1.54 g cm^{-3}, μ(Cu-Kα) = 22.2 cm^{-1}, 7700 independent measured reflections, 5832 with [$|F_o| > 4\sigma(|F_o|)$, $2\theta \leqslant 100°$] refined to R_1 = 0.083, wR_2 = 0.208. Siemens P4/RA diffractometer, ω scans, Cu-Kα radiation (graphite monochromator). The structure was solved by direct methods and refined anisotropically. Three of the PF$_6^-$ anions are in general positions, whilst two are positioned on independent symmetry centres. In a structure which contains disordered solvent molecules and where the X-ray scattering is dominated by the PF$_6^-$ anions, which are also subjected to disorder even at the reduced temperature of this study, it is difficult to distinguish with confidence nitrogen from carbon atoms. The assignment was based on comparing the crystallographic R values obtained from refinements of the bipyridinium units as biphenylenes and *vice versa*. The arrangement illustrated corresponds to the one that gave the lower residual. The apparently unfavourable proximal relationship between the bipyridinium units within each sheet mosaic is a result of a unit lattice translation. It should be noted, however, that the separation between these units is significantly greater than the more favourable π–π stacking arrangement observed between phenylene rings in adjacent molecules. The possibility of randomised orientations throughout the crystal cannot be totally discounted in view of the overall isotropic shape of the cyclophane. Hydrogen atoms positions are determined from Δ*F* maps and optimised. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Informations for Authors, Issue No. 1.

§ FABMS was carried out on a Kratos MS80RF mass spectrometer (accelerating voltage 3 kV, resolution 1000) coupled to a DS90 data system and off-line Sun Workstation for processing the raw data experiments. The atom gun was an adapted saddlefield source (Ion Tech Limited) that operated at *ca.* 8 keV and with a tube current of *ca.* 2 mA. Krypton was used to provide a primary beam of atoms and the samples 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 30 s per decade.

References

1 (*a*) J. S. Lindsey, *New J. Chem.*, 1991, **15**, 153; (*b*) G. M. Whitesides, J. P. Mathias and C. T. Seto, *Science*, 1991, **254**, 1312; (*c*) J. F. Stoddart, in *Host–Guest Molecular Interactions: From Chemistry to Biology*, CIBA Foundation Symposium 158, Wiley, Chichester, 1991, pp. 5–22.

2 (*a*) D. Philp and J. F. Stoddart, *Synlett*, 1991, 445; (*b*) D. B. Amabilino and J. F. Stoddart, *Pure Appl. Chem.*, 1993, **65**, 2351; (*c*) D. B. Amabilino and J. F. Stoddart, *New Scientist*, 19 February, 1994, No. 1913, 25–29.

3 D. B. Amabilino, P. R. Ashton, C. L. Brown, E. Córdova, L. A. Godínez, T. T. Goodnow, A. E. Kaifer, S. P. Newton, M. Pietraszkiewicz, D.

Philp, F. M. Raymo, A. S. Reder, M. T. Rutland, A. M. Z. Slawin, N. Spencer, J. F. Stoddart and D. J. Williams, *J. Am. Chem. Soc.*, 1995, **117**, 1271.

4 (*a*) P. L. Anelli, N. Spencer and J. F. Stoddart, *J. Am. Chem. Soc.*, 1991, **113**, 5131; (*b*) E. Córdova, R. A. Bissell and A. E. Kaifer, *J. Org. Chem.*, 1995, **60**, 1033.

5 (*a*) P. R. Ashton, D. Philp, N. Spencer, J. F. Stoddart and D. J. Williams, *J. Chem. Soc., Chem. Commun.*, 1994, 181.

6 P. R. Ashton, D. Philp, N. Spencer and J. F. Stoddart, *Makromol. Chem., Macromol. Symp.*, 1992, **54/55**, 441.

7 (*a*) C. A. Hunter and J. K. M. Sanders, *J. Am. Chem. Soc.*, 1990, **112**, 5525; (*b*) C. A. Hunter, *Angew. Chem., Int. Ed. Engl.*, 1993, **32**, 1584; (*c*) C. A. Hunter, *Chem. Soc. Rev.*, 1994, **23**, 101.

8 (*a*) M. C. Etter, *Acc. Chem. Res.*, 1990, **23**, 120; (*b*) A. D. Hamilton, *J. Chem. Ed.*, 1990, **67**, 821; (*c*) G. R. Desiraju, *Acc. Chem. Res.*, 1991, **24**, 290; (*d*) C. B. Aekeröy and K. R. Seddon, *Chem. Soc. Rev.*, 1993, **22**, 397.

9 (*a*) R. O. Gould, A. M. Gray, P. Taylor and M. D. Walkinshaw, *J. Am. Chem. Soc.*, 1985, **107**, 5921; (*b*) S. K. Burley and G. A. Petsko, *J. Am. Chem. Soc.*, 1986, **108**, 7995; (*c*) W. L. Jorgensen and D. L. Severance, *J. Am. Chem. Soc.*, 1990, **112**, 4786; (*d*) M. J. Zaworotko, *Chem. Soc. Rev.*, 1994, **23**, 283.

10 (*a*) D. H. Busch, *J. Incl. Phenom.*, 1992, **12**, 389; (*b*) S. Anderson, H. L. Anderson and J. K. M. Sanders, *Acc. Chem. Res.*, 1993, **26**, 389; (*c*) R. Hoss and F. Vögtle, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 375.

11 P. R. Ashton, C. L. Brown, E. J. T. Chrystal, T. T. Goodnow, A. E. Kaifer, K. P. Parry, A. M. Z. Slawin, N. Spencer, J. F. Stoddart and D. J. Williams, *Angew. Chem., Int. Ed. Engl.*, 1991, **30**, 1039.

12 For examples of other large molecules with square geometries, see: (*a*) M. Fujita, S. Yazak and K. Ogura, *J. Am. Chem. Soc.*, 1990, **112**, 5645; (*b*) M. Fujita, S. Nagao, K. Ilida, K. Ogara and K. Ogura, *J. Am. Chem. Soc.*, 1993, **115**, 1574; (*c*) P. J. Stang and V. V. Zhdankin, *J. Am. Chem. Soc.*, 1993, **115**, 9808; (*d*) H. Rauter, E. C. Hillgeris, A. Erxleben and B. Lippert, *J. Am. Chem. Soc.*, 1994, **116**, 616; (*e*) M. Fujita, Y. J. Kwon, S. Washizu and K. Ogura, *J. Am. Chem. Soc.*, 1994, **116**, 1151; (*f*) P. J. Stang and D.H. Cao, *J. Am. Chem. Soc.*, 1994, **116**, 4981; (*g*) C. L. Drain and J. M. Lehn, *J. Chem. Soc., Chem. Commun.*, 1994, 2313; (*h*) P. J. Stang and J. A. Whiteford, *Organometallics*, 1994, **13**, 3776; (*j*) P. J. Stang and K. Chen, *J. Am. Chem. Soc.*, 1995, **117**, 1667; (*k*) P. J. Stang, D. H. Cao, S. Saito and A. M. Arif, *J. Am. Chem. Soc.*, 1995, **117**, 6273; The self-assembly of molecular-sized boxes has recently been the subject of a 'highlight'. See C. A. Hunter, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 1079.

13 J. D. Dunitz, L. E. Orgel and A. Rich, *Acta Crystallogr.*, 1956, **9**, 373.

14 (*a*) G. A. Candela, L. J. Swartzendruber, J. S. Miller and M. J. Rice, *J. Am. Chem. Soc.*, 1979, **101**, 2755. (*b*) A. H. Reis Jr., L. D. Preston, J. M. Williams, S. W. Peterson, G. A. Candela, L. J. Swartzendruber and J. S. Miller, *J. Am. Chem. Soc.*, 1979, **101**, 2755; (*c*) J. S. Miller, A. J. Epstaein and W. M. Reiff, *Chem. Rev.*, 1988, **88**, 201; (*d*) J. S. Miller, J. C. Calabrese, R. L. Harlow, D. A. Dixon, J. H. Zhang, W.M. Reiff, S. Chittipeddi, M. A. Selover and A.J. Epstein, *J. Am. Chem. Soc.*, 1990, **112**, 5946; (*e*) R. Lehmann and J. K. Kochi, *J. Am. Chem. Soc.*, 1979, **101**, 2755; (*f*) D. Stein, H. Sitzmann and R. Boese, *J. Organomet. Chem.*, 1991, **421**, 275; (*g*) K. M. Chi, J. C. Calabrese, W. M. Reiff and J. S. Miller, *Organometallics*, 1991, **10**, 688; (*h*) A. Togni, M. Hobi, G. Rihs, G. Rist, A. Albinati, P. Zanello, D. Zech and H. Keller, *Organometallics*, 1994, **13**, 1224.

15 (*a*) J. F. Stoddart and R. Zarzycki, in *Cation Binding by Macrocycles*, ed. Y. Inoue and G. W. Gokel, Dekker, New York, 1990, pp. 631–699; (*b*) I. Ando, H. Fujimoto, K. Nakayama, K. Ujimoto and H. Kurihara, *Polyhedron*, 1991, **10**, 1139; (*c*) I. Ando, D. Ishimura, M. Mitsumi, K. Ujimoto and H. Kurihara, *Polyhedron*, 1992, **11**, 2335; (*d*) M. D. Todd, Y. H. Dong, J. Horney, D. I. Yoon and J. T. Hupp, *Inorg. Chem.*, 1993, **32**, 2001; (*e*) J. E. Kicham and S. J. Loeb, *Inorg. Chem.*, 1994, **33**, 4351.

16 (*a*) A. Livoreil, C. O. Dietrich-Buchecker and J. P. Sauvage, *J. Am. Chem. Soc.*, 1994, **116**, 9399; (*b*) R. A. Bissell, E. Córdova, A. E. Kaifer and J. F. Stoddart, *Nature*, 1994, **369**, 133.

17 (*a*) P. D. Beer, *Adv. Inorg. Chem.*, 1992, **39**, 79; (*b*) P. D. Beer, *Advan. Mater.*, 1994, **6**, 607; (*c*) A. C. Benniston and A. Harriman, *Angew. Chem., Int. Ed. Engl.*, 1993, **32**, 1459; (*d*) P. R. Ashton, C. G. Claessens, W. Hayes, S. Menzer, J. F. Stoddart, A. J. P. White and D. J. Williams, *Angew. Chem., Int. Ed. Engl.*, 1995, **34**, 1862.

Received, 20th October 1995; Com. 5/06929G