New Cyclophane Hosts: A Hexaoxacyclophane

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The *X*-ray crystal structure of the hexaoxacyclophane (**1**), which can be synthesized from 1,3-bis-(bromomethyl)benzene and bis(4-hydroxyphenyl) ether in one step, reveals that in the solid state the macrocyclic ring forms a large molecular void potentially capable of binding aromatic guest molecules: the *X*-ray crystal structure of the 1:1 molecular complex formed between (**1**) and benzene exposes intermolecular and intercomplex aromatic ring interactions of an edge-to-face type.

The wish to create bireceptors[1] that might potentially form inclusion complexes with alkali metal phenoxides led us to a molecular design principle (Figure 1) in which a [2.2.1.2.2.1](mp$_2$)$_2$cyclophane[2] containing six phenylene rings is bridged diagonally by a polyether ribbon. Such bireceptors can be looked upon as wholly synthetic analogues of the cyclodextrins[3] which have proved to be so successful as water-soluble receptors for directing weak electrophiles (*e.g.* HCHO, CCl_2, $\overset{+}{C}Cl_3$), bound within their hydrophobic cavities, to attack regioselectively (*ca.* 100%) the *para* positions of included phenoxide substrates.[4] In this communication, we report on (i) the synthesis of a hexaoxacyclophane (**1**) incorporating two *m*-xylylene and two bis(4-hydroxyphenyl) ether units and (ii) its characterisation by *X*-ray crystallography in the solid state, both free and as 1:1 molecular complex with benzene.

Reaction [Bu^{t}OK/Bu^{t}OH–THF–C_6H_6 (9:9:1)/reflux/24 h] of bis(4-hydroxyphenyl) ether[5] with 1,3-bis(bromomethyl)benzene afforded (**1**) [7%, m.p. 195—199 °C, *M*, 608 (f.a.b.m.s.), δ($CDCl_3$) 5.10 (8 H, s), 6.73 and 6.78 (16 H, A_2B_2), 7.23—7.36 (8 H, m)] after chromatography [SiO_2/light petroleum–EtOAc (6:1, v/v)]. Single crystals suitable for *X*-ray crystallography were grown from toluene.

The *X*-ray crystal structure† of (**1**) reveals (Figure 2) a centrosymmetric macrocyclic geometry with a large free pathway through the macro ring centre. This partially preorganised receptor cavity is reminiscent of those adopted by the conformationally more flexible bispolyether(1,4)cyclophanes[6,7] with the ability to bind[6] the bipyridinium dications, Diquat and Paraquat, and the conformationally more rigid tetracationic bisparaquat(1,4)cyclophane[8] which complexes[9] with diphenol ethers. The distance between the mean planes of the parallelly-aligned hydroquinol rings A and D, is 8.3 Å, and the diagonal distances between the C(19) and C(19′) hydrogens, and the C(22) and C(22′) hydrogens are 8.8 and 6.3 Å, respectively. In the symmetry-related diphenyl ether units (A/B and D/E) the two aromatic rings approach (Figure 3) an orthogonal attitude (75°) with respect to each other. It is noteworthy that there are two non-zero torsional components (10 and 65°) combining to produce this geometry. The methyleneoxy carbon atoms [C(1)/C(1′) and C(13)/C(13′)] are almost coplanar[10] with the aromatic rings D/A and E/B, respectively.

Adjacent molecules of (**1**) pack in the crystal (Figure 4) so as to maximise the packing density, the central void within one macrocycle being partially filled by a hydroquinol unit (A/A′) of the next and *vice versa*. This mode of packing gives rise to three approximately parallel aromatic-aromatic geometries,[11] the most notable being between B and B′ which are inclined by only 6° to each other with a centroid-centroid separation of 3.8 Å.

When 1 molar equivalent of sodium *p*-nitrophenolate was added to a $CDCl_3$ solution (*ca.* 6 mM) of (**1**), as expected, insignificantly small displacements (*ca.* 0.01 p.p.m.) in the chemical shifts of the protons on the anion relative to those for the same protons in the free sodium *p*-nitrophenolate in $CDCl_3$

† *Crystal data for compound* (**1**). $C_{40}H_{32}O_6$, *M* = 608.7, monoclinic, *a* = 18.100(5), *b* = 17.027(7), *c* = 11.336(5) Å, β = 118.10(3)°, *U* = 3 082 Å^3, space group *C*2/*c*, *Z* = 4 (the molecule is disposed about a centre of symmetry), D_c = 1.31 g cm^{-3}, μ(Cu-K_α) = 7 cm^{-1}. The structure was solved by direct methods and refined anisotropically to give *R* = 0.043, R_w = 0.052 for 1 907 independent observed reflections [$|F_o| \geqslant 3\sigma(|F_o|)$, $\theta \leqslant 58°$].

Crystal data for compound (**1**). C_6H_6:$C_{40}H_{32}O_6$.C_6H_6, *M* = 686.8, monoclinic, *a* = 20.933(4), *b* = 6.634(1), *c* = 28.758(7) Å, β = 110.97(2)°, *U* = 3 577 Å^3, space group *C*2/*c*, *Z* = 4 (the molecule is disposed about a centre of symmetry), D_c = 1.28 g cm^{-3}, μ(Cu-K_α) = 6 cm^{-1}. The structure was solved by direct methods and refined anisotropically to give *R* = 0.072, R_w = 0.075 for 1 974 independent observed reflections [$|F_o| \geqslant 3\sigma(|F_o|)$, $\theta \leqslant 58°$].

In both cases, data were measured on a Nicolet R3m diffractometer with Cu-K_α radiation (graphite monochromator) using ω-scans. Atomic co-ordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See 'Instructions for Authors (1989),' *J. Chem. Soc., Perkin Trans. 1*, 1989, Issue 1.

were observed. Significantly, when ^1H n.m.r. spectra of the hexaoxacyclophane (**1**) were recorded in C_6H_6 and $C_6D_5CD_3$, dramatic upfield displacements (−0.04 to −0.37 p.p.m.) of the chemical shifts of the singlet for the benzylic methylene protons and of the A_2B_2 system for the hydroquinol ring protons, relative to those obtained in $CDCl_3$, were observed: $\delta(C_6D_6)$ 4.75 (s), 6.65 and 6.74 (A_2B_2) and $\delta(C_6D_5CD_3)$ 4.73 (s), 6.59 and 6.69 (A_2B_2). Slow evaporation of a benzene solution of (**1**) has afforded crystals of a 1:1 inclusion complex suitable for *X*-ray crystallography.* On formation of a 1:1 molecular complex with benzene, the hexaoxacyclophane (**1**) undergoes (Figures 5 and 6) only minor conformational changes to enable entrapment of the guest molecule at the cyclophane centre. This encapsulation is achieved principally by rotations of rings B and E so as to enlarge the macro ring cavity. These rotations, together with changes in the torsional angles in the –O– and $–CH_2O–$ bridges, result in a significant increase in the A to D ring centroid-centroid distance from 8.4 to 10.5 Å. The C to F distance is also increased slightly from 12.8 to 13.2 Å and there is an accompanying small reduction in the B to E separation from 10.6 to 10.1 Å. The benzene molecule G is held within the macrocycle by edge-to-face electrostatic interactions to rings A, B, D, and E. The centroid-centroid distances are A to G, 5.25 Å and B to G, 5.03 Å—and similarly to E and D from G′ because of the crystallographic centre of symmetry. The C to G distance is 6.58 Å. The cyclophane molecules stack (Figure 7) in the crystallographic *b* direction creating continuous channels in the structure. The B and C rings in adjacent stacks interact in an edge-to-face manner with a B to C′ (and C to B′) centroid-centroid separation of 4.92 Å.

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* See footnote on p. 21.

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