Cavitands containing Cleft- and Collar-shaped Voids

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Macrocyclic oligomers (cavitands) composed of four or six ethyl-substituted dibenzofuran units are reported which contain enforced concave inner surfaces large enough to embrace a variety of organic compounds.

Cavitands are synthetic organic compounds that contain enforced cavities large enough to embrace simple molecules or ions. Their concave inner surfaces can be designed to have a variety of shapes, with either integrated or appended binding sites so that they can act as hosts to complex guests with complementary shapes and binding sites.[1] Examples of cavitands are $[O^n]$*meta*-cyclophanes[2] (benzene-lined cavities, n = 5—10), spherands[3] (cavities lined with electron pairs), calixarenes[4] (tolyl-lined cavities), and certain multi-bridged *ortho*-cyclophanes[5] or *meta*-cyclophanes (aryl-, methylene-, and oxygen-lined cavities).[1]

We report here the syntheses of new cavitands based on the dibenzofuran unit. This unit is rigid, possesses two large flat surfaces, and is very suitable in that it undergoes metallation in its 4- or 6-positions, but undergoes electrophilic substitution in its 2- and 8-positions. Corey–Pauling–Koltun (CPK) molecular models of the macrocycles (**1**), (**2**), and (**3**) indicate that they contain enforced cavities of substantial size and with interesting shapes.

In an attempted synthesis of (**1**), dibenzofuran was metallated with BuLi in tetrahydrofuran (THF), and the resulting organometallic compound was oxidatively coupled with $Fe(acac)_3$ (Hacac = acetylacetone) in benzene[6] to give (**4**)[7] (70%). Similar dimetallation of (**4**), and bromination of the product, gave (**5**)† (43%, m.p. 301—305 °C). This material was dilithiated with s-butyl-lithium in THF at −78 °C, and the resulting solution was cannulated into a refluxing solution of $Fe(acac)_3$ in C_6H_6. The toluene- and chloroform-insoluble product was sublimed at 450 °C and 10^{-5} Torr to give a white powder whose mass spectrum indicated the presence of (**1**) and a hexameric oligomer. The extremely low solubilities of these compounds prevented their purification. Accordingly, syntheses were designed for (**2**) and (**3**), whose ethyl groups both extend their cavities and enhance their solubilities.

Acetylation of dibenzofuran gave 2,8-diacetyldibenzofuran (52%, m.p. 161—162 °C)[7] reduction of which with KOH–NH_2NH_2–$(HOCH_2CH_2)_2O$ under reflux for 4 h gave 2,8-

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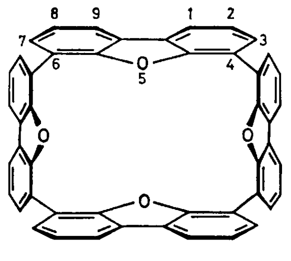
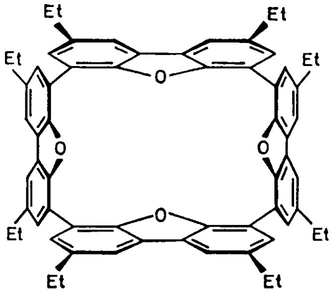
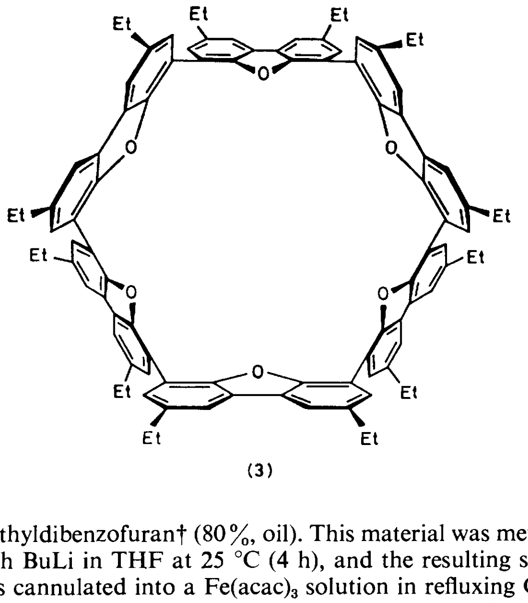
† Carbon and hydrogen analyses were within 0.3% of theory, mass spectra gave M^+ ions, and the ^1H n.m.r. spectra were consistent with assigned structures.



(1)

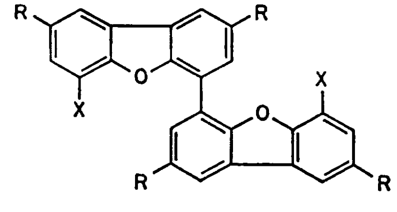


(2)

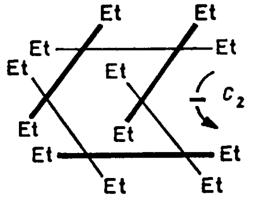


(3)

diethyldibenzofuran† (80%, oil). This material was metallated with BuLi in THF at 25 °C (4 h), and the resulting solution was cannulated into a Fe(acac)$_3$ solution in refluxing C_6H_6 to give (6)† (90%, oil). This compound was dimetallated with BuLi in THF at 25 °C (8 h), and the resulting solution was cannulated into a refluxing C_6H_6 solution of Fe(acac)$_3$. Cavitands (2)† (11%, m.p. > 360 °C) and (3)† (1.6%, m.p. > 360 °C) were isolated by chromatographic and crystallisation techniques. Their structures are established by mass and ^{1}H n.m.r. spectroscopy, their methods of syntheses, and elemental analyses.‡



(4), R = X = H
(5), R = H, X = Br
(6), R = Et, X = H



(7)

Cavitand (2) belongs to the D_{2d} point group. Molecular model (CPK) examination indicates that (2) is free of strain, and that it contains two cleft-shaped cavities approximately 12 Å long, 3.4 Å deep, and 4.3 Å wide. Synchronised rotation seems possible for the aryl groups through a maximum angle *ca.* 35° about the four Ar–Ar bonds in either of two directions, and at its limits narrows the cavity to about 3 Å. This rotation is resisted by deformations of the aryl–aryl bond angles, and ultimately by contacts between two pairs of oxygens. CPK models show that each cleft is large enough to embrace on at least three sides, one molecule of *p,p'*-dimethylbiphenyl or one of nonane in its extended form. The four oxygens occupy the same plane. They line a hole connecting the two cavities which is just large enough in models to embrace a model of CH_4, NH_4^+, or Cs^+.

Macrocycle (3) in the conformation drawn possesses D_{3d} symmetry. Its ^{1}H n.m.r. spectrum at 300 K in $CDCl_3$ is consistent with a compound of this symmetry. The signals are sharp, and move or broaden very little when the temperature is changed from 300 to 191 K in $CDCl_3$–CS_2 as solvent. A molecular model of (3) with this conformation appears free of strain, and contains a large cavity of dimension *ca.* 11 × 7 × 7 Å. Cross-sections of the model that are perpendicular to its C_3 axis are hexagonal. The six oxygens lie in one plane, neatly embracing a model of a benzene ring in the same plane and dividing the cavity into halves, each of which can accommodate three additional benzene models stacked in planes perpendicular to the benzene in the oxygens' plane. The twelve ethyl-groups nearly close the gaps on the surfaces of the collar-shaped cavity. Synchronised rotations of the aryl-groups about their aryl–aryl bonds are possible in the model, but result in aryl–aryl bond deformations. At the limits of rotation, further resistance is created by contacts between pairs of ethyl-groups, and between the oxygens and the hydrogens in the 3- and 7-positions of the aromatic rings. The resulting minimum cavity has irregular hexagonal cross-sections, and dimensions of 11 × 9 × 3.5 Å. It is still large enough to accommodate four suitably stacked molecular models of benzene rings.

Molecular models of six folded conformations of C_2 symmetry represented by (7) can also be constructed for compound (3). In structure (7), the model is viewed from a position perpendicular to the most central point on the C_2 axis. In (7) the aryl–aryl bond angles are somewhat deformed, and two

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‡ 1.5 M BuLi in hexane (25 ml) was added to a solution of (6) (6.4 g) in THF (300 ml) under N_2. The mixture was stirred for 8 h (25 °C), cooled to −78 °C, and cannulated (10 min) into a refluxing solution of Fe(acac)$_3$ (18 g) in C_6H_6 (2 l). After refluxing for 2 h, the suspension was cooled to 25 °C, stirred for 10 h, diluted with 2M HCl (600 ml) and stirred for a further 4 h. Solvent (800 ml) was removed, H_2O (500 ml) was added, and the mixture was left for 10 h at 25 °C, and the resultant brown precipitate was collected and dried (7 g). This material was triturated with boiling Et_2O (150 ml) for 30 minutes, cooled to 25 °C (30 min), filtered, washed with Et_2O (30 ml) and dried at 25 °C (0.1 mmHg). The solid (0.75 g) was then dissolved in hot C_6H_6 (150 ml) and chromatographed on MCB alumina (150 g) in C_6H_6. The cyclotetramer (2) was eluted with C_6H_6 (3 l) and crystallised as a white solid, 0.70 g (11%), m.p. > 360 °C, M^+ 888;† ^{1}H n.m.r. (200 MHz, $CDCl_3$), δ 1.17 (t, CH_3, 24 H), 2.69 (q, CH_2, 16 H), 7.09 (s, ArH, 8 H), and 7.60 (s, ArH, 8 H). The Et_2O filtrate from the trituration, when kept in a stoppered flask, deposited a white solid (0.12 g) after 7 days at 25 °C. This material was dissolved in C_6H_6 (100 ml) and chromatographed on MCB alumina (100 g) in C_6H_6. Product (3) was eluted with C_6H_6 (3 l), and recrystallised from *p*-xylene to give white crystals (0.1 g, 1.6%), m.p. > 360 °C, M^+ 1332;† ^{1}H n.m.r. (200 MHz, $CDCl_3$) δ 1.15 (t, CH_3, 36 H), 2.69 (q, CH_2, 24 H), 7.47 (d, *J* 1.6 Hz, ArH, 12 H), and 7.59 (d, *J* 1.6 Hz, ArH, 12 H). Irradiation of the CH_3 protons gave a singlet for the CH_2 at 191 K in CS_2–$CDCl_3$ (1.5 : 1.0).

ethyl-groups are turned inward to face the walls of the trans-annularly-located aryl-groups. The ^1H n.m.r. spectrum of (3) is inconsistent with a single C_2 structure, since the ethyl and aryl proton signals of each oligomeric unit give the same chemical shift.‡ However, the spectrum is consistent with either the D_{3d} structure or with six C_2 structures rapidly equilibrating on the ^1H n.m.r. time scale. The degenerate structure (C_2) is improbable, since the chemical shifts of the CH_2 and CH_3 protons in (**2**) are almost the same as they are in (3). Models of (7) suggest the CH_3CH_2 protons should move upfield because two of these groups are located in the shielding cone of transannular aryl-groups. These protons in models of (2) and the D_{3d} form of (3) are distant from the shielding cone of transannular aryl-groups. Furthermore, the indifference of the ^1H n.m.r. spectrum of (3) to temperature changes suggests the compound has only the D_{3d} structure.

Unlike the other cavitands studied,[1] (2) and (3) are more soluble in benzene, toluene, or the xylenes than in $CHCl_3$ or CH_2Cl_2. This fact correlates with the better fit of molecular models of aromatic solvents into the cavities of models of (2) and (3) than into those of the other cavitands so far examined. When crystallized from benzene, (3) forms heavily solvated crystals that release benzene too readily for crystal-structure determination.

The dissolution and separation of (2) and (3) were made possible by the presence of ethyl groups in the 2- and 8-positions of their dibenzofuran units. These positions are located on the peripheries of the cavities, and are ideal for the placement of functional groups in the design of hosts. Functional groups in these positions can be used to control solubility properties, to provide binding sites for guests, or to act co-operatively in catalysing the reactions of bound guests. For example, in (**1**), a carboxylate group in one 2-position and an ammonium ion group in a second, but near 2-position, cannot reach one another. However, in molecular models, they can be connected through a carbonyl group of a guest or by a water molecule.

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