Inclusion chemistry of cyclotetracatechylene

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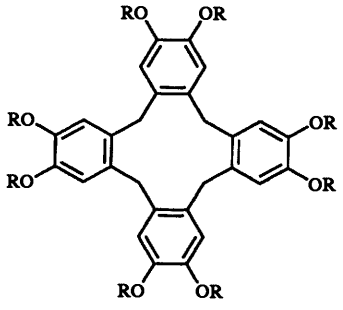
The synthesis and X-ray crystal structures of the first inclusion complexes of cyclotetracatechylene (CTTC, **1**) are reported. Crystals grown from a dimethylformamide (DMF) solution of **1** contain a total of six DMF molecules per CTTC unit (**1**·6DMF, **5**) whilst crystals obtained from methanol in the presence of pyridine vapour form as a 1:2:2 complex (**1**·2pyridine·2methanol, **6**). Hydrogen-bonded interactions between host and guest(s) play an important role in the molecular structure and, in the case of **6**, a terminated eleven-atom hydrogen bonded chain is observed.

Introduction

The extensively studied condensation reaction of the veratryl cation has been shown to give rise to two primary products.[1] The major component, cyclotriveratrylene (CTV, **2**), is a cyclic oligomer containing three *o*-dimethoxybenzene units linked by methylenic spacer groups. In solution and the solid state **2**



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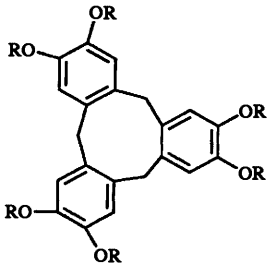
3 R = Me



2 R = Me
4 R = H

adopts a characteristic crown conformation[2] resulting in the formation of a bowl-shaped molecular cavity. A cyclic tetramer, cyclotetraveratrylene (CTTV, **3**) is also formed in relatively low yield depending on reaction conditions and has been shown by our own recent structural investigation to adopt a chair conformation[3] (analogous to the 'partial-cone' description in calixarene nomenclature[4]).

Compounds **2** and **3** form a wide range of solid-state inclusion complexes resulting both from their irregular shapes (which preclude close packing) and hydrogen bond acceptor sites which encourage interactions with H-bond donor solvents.[3,5] These types of host–guest interaction have generated extensive interest[6] and we have recently shown their extreme importance and usefulness by developing a route to the separation of fullerenes based on the formation of fullerene inclusion complexes with **2** and calixarenes.[7]

Demethylation of **2** by reaction with BBr_3 yields the related hexaol cyclotricatechylene (CTC, **4**)[8] which demonstrates a marked propensity to form inclusion compounds exhibiting novel channel and clathrate packing modes with extensive hydrogen-bonded networks.[5a,9] Accordingly we have examined the inclusion chemistry of the related demethylation product of **3**, cyclotetracatechylene (CTTC, **1**) in the expectation of discovering extensive host–guest chemistry (*cf.*, the vast range of inclusion compounds formed by tri-*o*-thymotide which also possesses a flexible, twelve-membered macroring[10]) and possibly altering the conformation of the chair-shaped tetrameric unit (*e.g.*, to produce a shallow cone) by the formation of intramolecular hydrogen bonds.

Experimental

Cyclotetraveratrylene 3

Compound **3** was synthesized according to the method of White and Gesner.[11] In a typical preparation veratryl alcohol (80 cm^3) was warmed with glacial acetic acid (200 cm^3) and sulfuric acid (0.2 cm^3) at 90 °C for 15 min resulting in the formation of a mixture of trimer **2** and tetramer **3**. Pure **3** was obtained (as its chloroform solvate) by fractional crystallisation from a 1:1 mixture of chloroform and benzene.

Cyclotetracatechylene 1

BBr_3 (1.5 cm^3, 6.0 mmol) was added to a solution of **3** (0.68 g, 1.1 mmol) in dry toluene (40 cm^3) and the mixture stirred under reflux in a dynamic dry nitrogen atmosphere for 2 h. Water (20 cm^3) was slowly added to the resulting suspension to yield a white gum which was isolated by filtration, washed with cold water and recrystallised from ethanol–water (1:1). Yield 0.35 g, 0.72 mmol, 65%, δ_H[200 MHz; $(CD_3)_2SO$; 20 °C] 8.52 (s, br, 8 H, Ar), 6.41 (s, br, 8 H, $-CH_2-$), 3.22 (s, br, 8 H, OH).

Crystal structure determination of 5 and 6

Sample preparation and data collection. Single crystals of **5** were grown by slow diffusion of diethyl ether into a solution of **1** in DMF while those of **6** were similarly grown by diffusion of pyridine into a solution of **1** in methanol. A suitable crystal of each compound was sealed with mother liquor in a Lindemann glass capillary and mounted on an Enraf-Nonius CAD4 diffractometer. Intensity data were collected at 293 K using graphite monochromated radiation (Mo-Kα, λ = 0.7107 Å for **5** and Cu-Kα, λ = 1.5406 Å for **6**). Accurate cell parameters were obtained by least-squares analysis of the setting angles of 25 reflections and the ω–2θ scan mode was used. Intensities were corrected for Lorentz and polarisation effects and for

Table 1 Crystal data, data collection and final refinement parameters

	5	6
Crystal data		
Guest(s)	Dimethylformamide	Methanol, pyridine
Empirical formula	$C_{28}H_{24}O_8$·6(C_3H_7ON)	$C_{28}H_{24}O_8$·2(CH_4O)·2(C_5H_5N)
Formula weight	927.05	710.76
λ/Å	0.710 69	1.540 60
Space group	$P\bar{1}$	$P\bar{1}$
Z	1	1
a/Å	7.088(1)	8.7998(9)
b/Å	13.245(5)	9.191(2)
c/Å	14.065(3)	11.7029(9)
α/°	108.58(2)	87.59(1)
β/°	97.27(2)	74.956(8)
γ/°	101.20(2)	89.72(1)
V/Å^3	1202.3(4)	913.3(2)
D_c/g cm^{-3}	1.280	1.292
μ/mm^{-1}	0.095	0.768
F(000)	496	376
Data collection parameters		
Crystal dimensions/mm	0.8 × 0.6 × 0.4	0.4 × 0.5 × 0.4
θ range scanned/°	2–25	2–60
Range of indices h, k, l	6, ±15, ±16	±9, 10, ±13
Overall intensity variation (%)	−57	−3
No. of unique reflections	3369	2685
No. of reflections with $I_{rel} > 2\sigma I_{rel}$	2997	2338
Final refinement parameters		
Number of variables	325	250
R_1, wR_2 (all data)	0.0843, 0.2170	0.0760, 0.1962
R_1, wR_2 ($I_{rel} > 2\sigma I_{rel}$)	0.0770, 0.2123	0.0681, 0.1912
a, b in $w = [\sigma^2(F_o^2) + (aP)^2 + bP]^{-1}$ where $P = [\max(F_o^2,0) + 2F_c^2]/3$	0.1211, 0.62	0.1123, 0.29
Goodness of fit on F^2	1.134	1.232
Max. shift/esd	0.075	0.225
Max., min. heights in diff. Fourier (e Å^{-3})	0.663, −0.320	0.448, −0.561

crystal decay in the case of **5**. Empirical absorption corrections were considered unnecessary.

Structure solution and refinement. The structures were solved by direct methods using SHELXS-86[12] and refined by the full-matrix least-squares method on F^2 using SHELXL-93.[13] Refinement of both structures proceeded in a similar fashion. All non-hydrogen atoms were treated anisotropically and aromatic, methylenic and formyl hydrogen atoms were placed in calculated positions and were assigned common isotropic temperature factors according to the type of parent atom. Hydroxy and methyl hydrogen atoms were placed by modelling the moieties as rigid groups with idealised geometry, maximising the sum of the electron density at the calculated hydrogen positions.

Results and discussion

Although the synthesis of **1** has been briefly reported[14] in connection with the synthesis of stacked liquid crystal polymers, no experimental details were given. The ^{1}H NMR spectrum of **1** indicates that, like **3**, the molecule is fluxional in $(CD_3)_2SO$ solution. This results in the averaging of all four aromatic rings and suggests a dynamic process involving inversion of the flexible cyclododecatetraene macroring.

Recrystallisation of **1** from ethanol resulted in the formation of a crystalline inclusion complex which readily lost solvent upon exposure to the atmosphere. However, the use of less volatile solvents resulted in significantly more stable inclusion species. Slow diffusion of diethyl ether vapour into a solution of **1** in DMF readily yielded large, colourless, columnar crystals of the inclusion complex **5** which contains six DMF molecules per CTTC unit. Similar results were obtained for dimethyl sulfoxide (host:guest ratio 1:4, evaluated by ^{1}H NMR spectral integration) and acetonitrile (1:2). Interestingly, a similar attempt at growing crystals by diffusion of diethyl ether vapour into a solution of **1** in methanol resulted in the formation of the 1:2:2 (**1**·methanol·pyridine) inclusion complex **6**. The surprising presence of pyridine was traced to diffusion of small amounts of pyridine vapour from a separate container within the apparatus used for batch crystal growth experiments. The incorporation of pyridine, even though it was present in relatively small quantities, is attributed to its excellent H-bond acceptor properties relative to the hydroxy functionalities of either **1** or methanol. It is also interesting to note that diffusion of diethyl ether vapour into a solution of **1** in pyridine resulted in the formation of an amorphous powder, suggesting that properties such as steric bulk as well as hydrogen bonding donor/acceptor ability play a role.

X-Ray diffraction analysis

Details of data collection and structure refinement of **5** and **6** are given in Table 1. Final fractional coordinates, anisotropic thermal parameters and bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre.† Details of all the hydrogen bonds are given in Table 2 and the atomic labelling system used for the host molecule is shown in Fig. 1.

Molecular structure

The molecular structure and crystal packing of **5** are shown in Figs. 2 and 3, respectively. Contrary to expectation the solid-

† For details of the CCDC deposition scheme, see 'Instructions for Authors (1995)', *J. Chem. Soc., Perkin Trans. 2*, 1995, issue 1.

Table 2 Hydrogen-bond details

Compound	(D)onor	(A)cceptor	D–H (Å)[a]	D···A (Å)	H···A (Å)	D–H···A (°)
5	O(1)	O(1B)	0.820	2.707	1.888	176.6
	O(2)	O(1C)	0.820	2.701	1.919	159.2
	O(3)	O(1A)	0.820	2.581	1.762	176.0
	O(4)[b]	O(3)	0.820	2.837	2.115	146.9
6	O(1)	O(2)[c]	0.820	2.848	2.103	144.2
	O(1G2)	O(1)	0.820	2.832	2.021	170.4
	O(2)	N(1G1)	0.820	2.699	1.881	177.9
	O(4)[d]	O(3)	0.820	2.790	2.104	143.4
	O(3)	O(1G2)[e]	0.820	2.613	1.805	171.2

[a] These lengths were constrained during refinement. [b] Transformed by $(-x, -y, -z)$. [c] Transformed by $(1-x, -y, -z)$. [d] Transformed by $(-1-x, -y, 1-z)$. [e] Transformed by $(x-1, y, z+1)$.

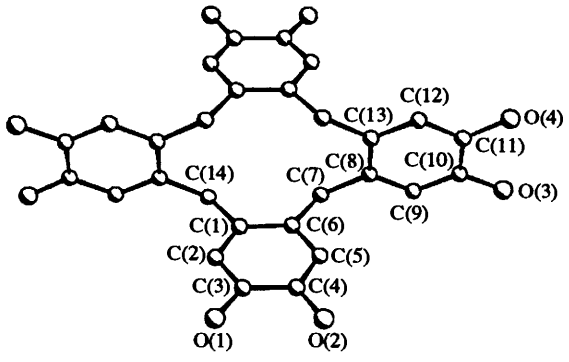


Fig. 1 Perspective view of the host molecule showing the atomic labelling scheme adopted

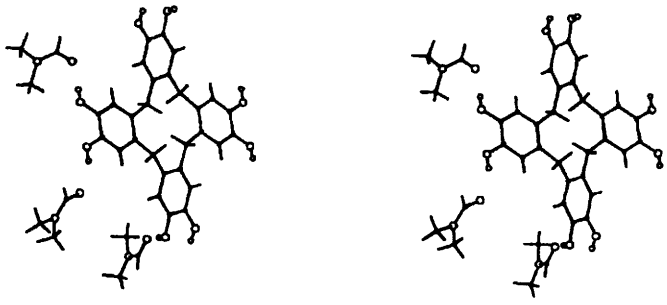


Fig. 2 Stereoview of the molecular structure of **5**

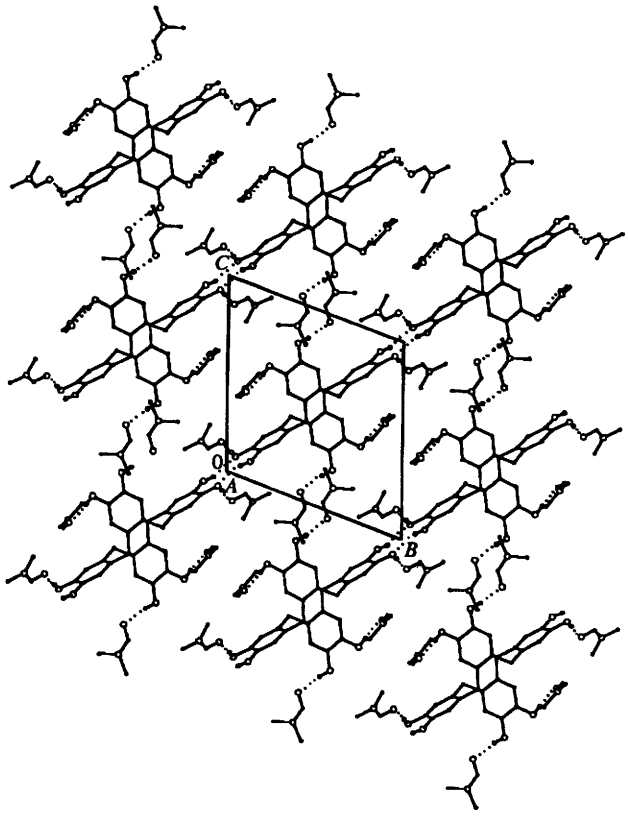


Fig. 3 Packing diagram of **5** viewed along [100]—hydrogen bonds are shown as dotted lines and non-hydroxy hydrogen atoms have been omitted for clarity

state structure is dominated by three strong, crystallographically unique *intermolecular* hydrogen bonds from the CTTC hydroxy moieties to the DMF carbonyl oxygen atoms. Hence the CTTC molecule adopts the chair conformation seen for **3**, with half the molecule related to the other half by a crystallographic inversion operation. This is in contrast with the shallow bowl which might result from the formation of intramolecular hydrogen bonds between the hydroxy moieties of adjacent rings (*cf.*, the bowlic calix[4]resorcinarenes).[15] The two axial hydroxy functionalities O(1) and O(2) form hydrogen bonds to DMF carbonyl oxygen atoms O(1B) and O(1C), respectively (2.707 and 2.701 Å) whilst only one of the more sterically hindered equatorial oxygen atoms interacts with a third solvent molecule which lies partially within the fold of the CTTC unit: O(3)···O(1A), 2.581 Å. The fourth crystallographically unique hydroxy functionality O(4) acts as the donor of a further intermolecular hydrogen bond to the equatorial plane of an adjacent CTTC molecule, O(4)····O(3′) 2.837 Å. This gives rise to infinite chains of CTTC units separated above and below by DMF molecules which form an extensive channel network extending along both the *b* and *c* crystallographic axes and along the *b*–*c* diagonal.

The CTTC molecule in **6** also adopts the chair conformation and is situated about a crystallographic centre of inversion in the unit cell. The molecular structure is shown in Fig. 4. It is immediately noteworthy that the voids above and below the equatorial plane of the molecule are comfortably filled by the hydrophobic residues of the guest species. More interestingly, Fig. 5 demonstrates the fascinating linear, eleven-atom hydrogen bonded array which stabilises the structure. This chain begins with the host oxygen O(4), proceeding *via* H(4) to O(3) (O···O = 2.790 Å) to the methanol oxygen O(1G2) (2.613 Å) which then forms an intermolecular bridge to O(1) of a second host molecule (2.832 Å), hence to O(2) (2.848 Å) with the chain finally terminating in a hydrogen bond to the pyridine guest (2.699 Å). In contrast with the structure of **5**, the only appreciable intermolecular host–host interaction is *via* the bridging methanol guest. It is suggested that the bridging network of hydrogen bonds is essential to the stabilisation of the structure. In the structure containing only pyridine there would be no such long-range hydrogen-bonded network to stabilise the crystal, and hence no such complex is formed. On the other

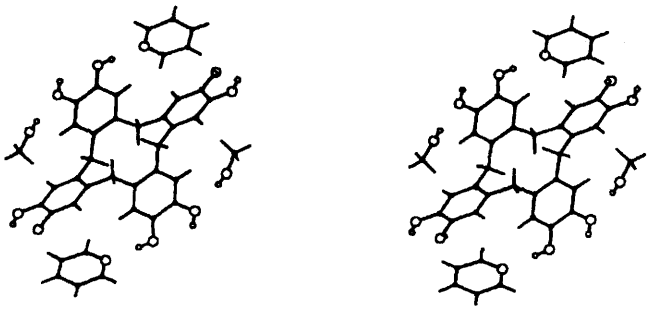


Fig. 4 Stereoview of the molecular structure of **6**

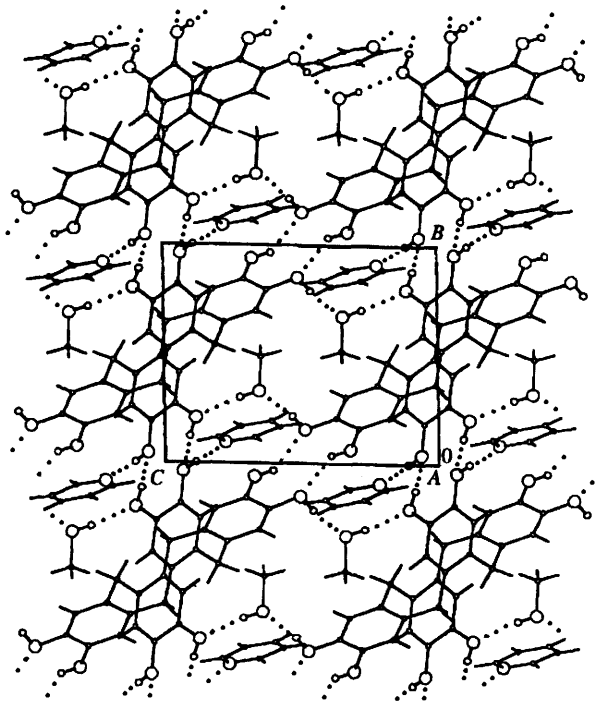


Fig. 5 Packing diagram of **6** viewed along [100]—hydrogen bonds are shown as dotted lines

hand, an inclusion complex formed solely with small guests such as methanol or ethanol may not fill the vacant areas of the crystal adequately resulting in facile loss of the solvent molecules as noted by us for crystals of CTTC grown from ethanol. Indeed, this may be evidenced by the failure of attempts to form an inclusion complex of **4** with ethanol.[9]

Within the CTTC molecule itself, bond lengths and angles are as expected with the only exception being the opening up of the angles at the methylenic carbon atoms C(7) and C(14) from the ideal 109.5° to 115.3° (average) as a result of strain in the macroring as frequently observed in structures of complexes of **2**–**4**.[5] The parameter which best describes the conformation of the CTTC molecule is the dihedral angle between the least-squares planes two unique aryl moieties. This angle is 88.4° and 95.8° for **5** and **6**, respectively and it is suggested that this difference reflects the difference in bulk between the DMF and pyridine guest molecules.

Conclusions

Whilst failing to observe a modified conformation from the parent CTTV in the solid-state structure of CTTC, it is clear that the demethylated host is capable of forming a much wider range of inclusion complexes, even of high guest : host ratio, in comparison with methylated compounds such as CTV and CTTV (the latter forms well characterised solvates only with chlorinated methane solvents[3]). This study therefore serves to support the observations of Hyatt *et al.* for CTC[9] that a rich host–guest chemistry exists for polycatechylenes, although the formation of stable inclusion species is clearly dependent upon the complimentarity of steric bulk and hydrogen-bonding properties of the host–guest system.

Acknowledgements

We are grateful to the National Science Foundation for support of this work and to SERC/NATO for the award of a research fellowship (to J. W. S.).

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Paper 4/05536E
Received 12*th September* 1994
Accepted 23*rd December* 1994