

The Crystal Structure of the *Syn-proximal*-5,11,17,23-tetra-*tert*-butyl-25,26-bis[(2-pyridylmethyl)oxy]-27,28-dihydroxy-calix[4]arene Ethanol 1 : 1 Inclusion Complex

GEORGE FERGUSON* and JOHN F. GALLAGHER

Department of Chemistry and Biochemistry, University of Guelph, Guelph, Ontario, Canada, N1G 2W1.

SEBASTIANO PAPPALARDO*

Dipartimento di Scienze Chimiche, Università di Catania, Viale A. Doria 8, 95125 Catania, Italy.

(Received 27 July 1992; in final form: 16 November 1992)

Abstract. The crystal structure of the title compound ($1 \cdot C_2H_5OH$) has been determined by single-crystal X-ray analysis and refined to an R -value of 0.074 for 2732 observed reflections [$I > 2.0\sigma(I)$]. Crystals are triclinic, space group $P\bar{1}$, with $a = 13.6150(18)$, $b = 13.7195(11)$, $c = 16.5497(16)$ Å, $\alpha = 73.132(7)$, $\beta = 66.165(9)$, $\gamma = 65.580(8)^\circ$ and $Z = 2$. Calix[4]arene (**1**) adopts a relatively open distorted cone conformation in the solid state, with two pendant *syn-proximal* O-CH₂-Py groups. The major conformation determining features in ($1 \cdot C_2H_5OH$) are the presence of (a) an intramolecular O—H \cdots O hydrogen bond between adjacent proximal phenolic oxygens, O \cdots O 2.719(7) Å, and (b) an intramolecular O—H \cdots N hydrogen bond between a phenolic oxygen and a proximal pyridinyl nitrogen, O \cdots N 2.810(8) Å. The intramolecular hydrogen bonding and the interplanar angles of 65.1(3) and 50.7(3)° between opposite aromatic rings facilitate the inclusion of an ethanol molecule within the calixarene cup.

Key words. 1,2-Dialkylated calix[4]arene, crystal structure, ethanol inclusion complex, intramolecular hydrogen bonding patterns.

Supplementary Data relating to this article are deposited with the British Library as Supplementary Publication No. SUP 82141 (26 pages).

1. Introduction

The ability of calix[4]arenes to form inclusion complexes with neutral organic molecules in the solid state is well known [1, 2]. It has been noticed that inclusion of aromatic guests *only* occurs when the calix[4]arene is in the cone conformation and carries inflexible alkyl groups (*t*-butyl, isopropyl) at the upper rim [3], so as to provide a deep cavity and favourable CH₃ \cdots π interactions between the methyl groups and the π system of the guest molecule [4]. Complexation of small nonaromatic guests (CH₃CN, CH₃OH) inside the cavity of the calix[4]arenes is less common, and known complexes all possess fourfold symmetry, the included guest lying along the crystallographic fourfold axis [3, 5, 6].

We have recently described the regioselective synthesis of *syn-proximal* di-[(2-pyridylmethyl)oxy]calix[4]arene (**1**) [7, 8], which has been shown to be a useful intermediate for the production of atropisomeric inherently chiral calix[4]arenes

*Authors for correspondence.

[9, 10]. In order to gain insight into the molecular architecture of this pivotal achiral precursor, as well as elucidating the geometry of the voids available for guest accommodation, single-crystal X-ray analysis of the ethanol inclusion complex of (1) was undertaken.

2. Experimental Section

Compound (1) was synthesized as described in Ref. 8. Colourless crystals suitable for the X-ray analysis were obtained by slow evaporation of an ethanol solution of (1) at room temperature. Crystal data for (1 · C₂H₅OH) are summarized in Table I along with details of data acquisition and structure solution and refinement.

The structure was solved by direct methods which initially revealed most of the non-hydrogen atoms. Refinement was by block-matrix least-squares refinement calculations on *F*, initially with isotropic and finally with anisotropic thermal parameters. Peaks corresponding to included ethanol were also found within the calix cavity; the distinction between the methyl and hydroxyl atoms of the ethanol molecule was made after considering electron density peak heights and bond lengths. The hydroxyl H atom appears to be disordered in the crystal about the C—O bond, and we were unable to define its coordinates unambiguously. The terminal C atoms of the *t*-butyl group attached to C(4A) are disordered over two orientations with site occupancy factors of 75% and 25%, respectively (from difference map peak heights). The decision as to which was a nitrogen atom and which was a carbon in the pyridine rings was unequivocally made in each case from difference maps by the unambiguous location of all pyridine H atoms. Hydrogen atoms bonded to carbon were positioned on geometric grounds (C—H 0.95 Å) and included as riding atoms in the structure factor calculations. The hydroxyl hydrogen atoms (HOC and HOD) were also visible in difference maps and were included at the difference map coordinates (but not refined) in the last cycles of refinement.

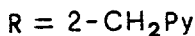
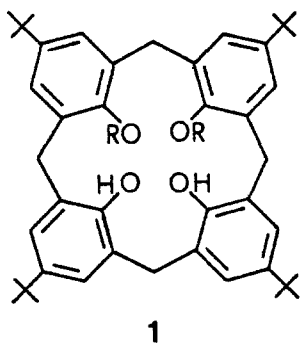


Table I. Summary of data collection, structure solution and refinement details

(a) Crystal Data	1
empirical formula	C ₅₈ H ₇₂ O ₅ N ₂
chemical formula	C ₅₆ H ₆₆ O ₄ N ₂ · C ₂ H ₅ OH
fw	877.22
color, habit	colorless, block
crystal size, mm	0.25 × 0.35 × 0.40
cryst syst	Triclinic
a, Å	13.6150(18)
b, Å	13.7195(11)
c, Å	16.5497(16)
α, °	73.132(7)
β, °	66.165(9)
γ, °	67.580(8)
V, Å ³	2579.9(5)
space group	P $\bar{1}$
Z	2
molecular symmetry	none
F(000)	948
d _{calc} , g cm ⁻³	1.128
μ, mm ⁻¹	0.07
(b) Data acquisition^a	
temp, °C	21
unit-cell reflens (2θ-range°)	25 (18–39)
max. 2θ (°) for reflens	43.8
hkl range of reflens	0 14, -14 14, -16 17
variation in 3 standard reflens	<3%
reflens measured	6289
unique reflens	6289
reflens with I > nσ(I), n	2732, 2.0
(c) Structure Solution and Refinement^b	
solution method	Direct methods
refinement type	block-matrix
H-atom treatment	riding for C–H, see text for O–H
no. of variables in LS	614
k in w = 1/(σ ² F _o + kF _o ²)	0.0012
R, R _w , g _{of}	0.074, 0.079, 1.44
density range in	
final Δ-map, e Å ⁻³	-0.27, 0.26
final shift/error ratio	0.030
secondary extinction correction	0.97(13)

^aData collection on an Enraf–Nonius CAD4 diffractometer with graphite monochromatised Mo-K_α radiation (λ 0.7093 Å)

^bAll calculations were done on a Silicon Graphics 4D-35TG computer system with the NRCVAX system of programs (E. J. Gabe, Y. Le Page, J-P. Charland, F. L. Lee and P. S. White: *J. Appl. Crystallogr.* **22**, 384–389 (1989)).

Scattering factor data were taken from *International Tables for X-ray Crystallography* (1974) [11]. All calculations were performed on a Silicon Graphics SG35-TG workstation using the NRCVAX suite of programs. Atomic coordinates and a summary of the bond lengths are given in Tables II and III, respectively. Figures 1 and 2 are views of the molecule prepared by using ORTEP II [12] and PLUTON [13].

Table II. Positional parameters and their e.s.d.s.

Atom	x	y	z
O(1A)	0.4686(4)	0.3550(4)	0.2990(3)
C(1A)	0.5000(6)	0.2672(6)	0.2585(5)
C(2A)	0.5211(5)	0.2829(6)	0.1651(5)
C(3A)	0.5563(6)	0.1907(6)	0.1282(5)
C(4A)	0.5746(6)	0.0890(6)	0.1748(5)
C(5A)	0.5523(6)	0.0793(6)	0.2665(5)
C(6A)	0.5164(5)	0.1663(6)	0.3096(5)
C(7A)	0.5154(6)	0.3900(6)	0.1055(5)
C(8A)	0.6175(7)	-0.0090(6)	0.1310(6)
C(9A)	0.6454(13)	-0.1155(10)	0.1926(10)
C(10A)	0.7307(12)	-0.0082(11)	0.0580(12)
C(11A)	0.5301(14)	-0.0125(14)	0.0992(15)
C(9A)*	0.5438(39)	-0.0665(43)	0.1650(56)
C(10A)*	0.7302(35)	-0.0682(31)	0.1195(35)
C(11A)*	0.6169(32)	0.0314(29)	0.0301(26)
C(12A)	0.3576(7)	0.4249(7)	0.3125(5)
C(13A)	0.2926(6)	0.4413(6)	0.4085(5)
N(14A)	0.3483(5)	0.3968(5)	0.4669(4)
C(15A)	0.2900(8)	0.4129(7)	0.5520(5)
C(16A)	0.1806(8)	0.4683(7)	0.5824(6)
C(17A)	0.1256(7)	0.5145(8)	0.5205(6)
C(18A)	0.1824(7)	0.5004(7)	0.4333(6)
O(1B)	0.5796(4)	0.5254(3)	0.1667(3)
C(1B)	0.6628(6)	0.4644(6)	0.1028(4)
C(2B)	0.7737(6)	0.4628(5)	0.0768(4)
C(3B)	0.8522(6)	0.4088(5)	0.0064(4)
C(4B)	0.8242(6)	0.3567(5)	-0.0376(4)
C(5B)	0.7134(6)	0.3547(6)	-0.0044(5)
C(6B)	0.6307(6)	0.4066(5)	0.0659(4)
C(7B)	0.8114(6)	0.5134(6)	0.1247(4)
C(8B)	0.9079(6)	0.3039(6)	-0.1189(5)
C(9B)	0.9130(9)	0.1888(8)	-0.1014(7)
C(10B)	1.0253(8)	0.3101(9)	-0.1441(7)
C(11B)	0.8697(9)	0.3600(9)	-0.1993(6)
C(12B)	0.5285(7)	0.6290(6)	0.1269(5)
C(13B)	0.4460(6)	0.6942(6)	0.1996(5)
N(14B)	0.3635(5)	0.7736(5)	0.1753(5)
C(15B)	0.2911(7)	0.8363(7)	0.2379(7)
C(16B)	0.3010(8)	0.8236(8)	0.3206(7)
C(17B)	0.3853(8)	0.7425(8)	0.3406(6)
C(18B)	0.4607(7)	0.6758(7)	0.2812(5)
O(1C)	0.6982(4)	0.4465(4)	0.3013(3)
C(1C)	0.8108(6)	0.3964(5)	0.2735(4)
C(2C)	0.8647(6)	0.3163(6)	0.3291(4)
C(3C)	0.9799(6)	0.2732(6)	0.2948(5)
C(4C)	1.0451(6)	0.3046(6)	0.2098(4)
C(5C)	0.9879(6)	0.3855(5)	0.1554(4)
C(6C)	0.8707(6)	0.4307(5)	0.1868(4)
C(7C)	0.7989(6)	0.2767(6)	0.4238(4)
C(8C)	1.1729(6)	0.2563(6)	0.1761(5)
C(9C)	1.2193(8)	0.2543(11)	0.0785(7)
C(10C)	1.2108(9)	0.1465(10)	0.2189(8)

Table II. (Continued).

Atom	x	y	z
C(11C)	1.2237(9)	0.3224(13)	0.1945(14)
O(1D)	0.5831(4)	0.3142(4)	0.4261(3)
C(1D)	0.6484(6)	0.2085(5)	0.4255(4)
C(2D)	0.6142(6)	0.1304(6)	0.4199(4)
C(3D)	0.6850(6)	0.0257(6)	0.4235(5)
C(4D)	0.7922(6)	-0.0009(6)	0.4301(4)
C(5D)	0.8246(6)	0.0822(6)	0.4316(5)
C(6D)	0.7564(6)	0.1864(6)	0.4281(4)
C(7D)	0.5027(6)	0.1483(6)	0.4074(5)
C(8D)	0.8677(7)	-0.1176(6)	0.4375(5)
C(9D)	0.9882(10)	-0.1260(9)	0.4102(14)
C(10D)	0.8557(11)	-0.1770(9)	0.3821(9)
C(11D)	0.8284(13)	-0.1728(10)	0.5292(8)
O(S1)	0.9994(10)	0.0676(9)	0.1907(9)
C(S1)	0.9480(18)	0.1177(17)	0.1357(14)
C(S2)	0.8308(9)	0.1503(11)	0.1767(7)

The site occupancy is 1.0 except for the terminal methyl carbons of the *t*-butyl group attached to C(4A); these atoms (C(9A) to C(11A*)) were disordered over two orientations with occupancies of 0.75 and 0.25 for each of the two orientations (from difference Fourier syntheses through the plane of the relevant six carbon atom sites).

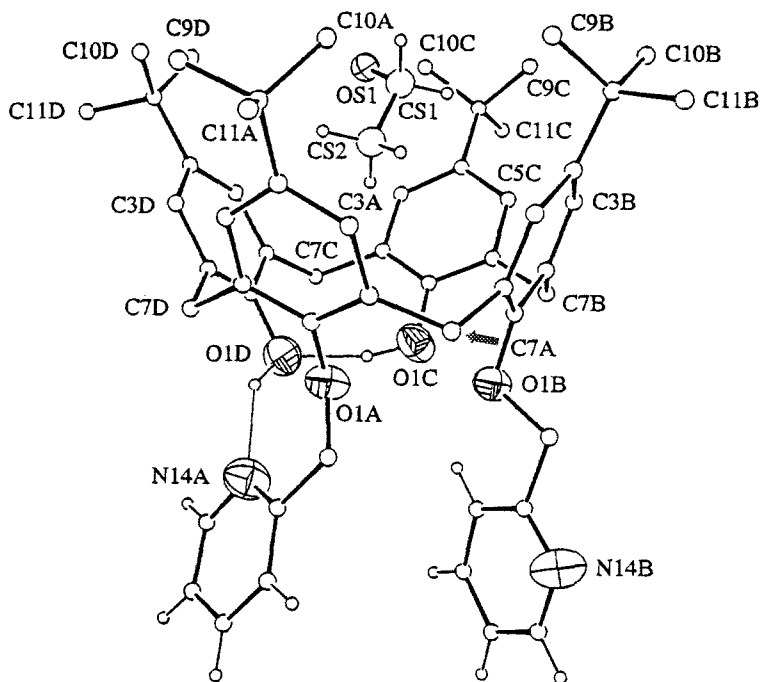


Fig. 1. A general view of the molecule (1) with its distorted cone conformation and the numbering scheme. For clarity, H atoms are only included on the ethanol and pyridinyl carbon atoms, C atoms are shown as small spheres of an arbitrary size and the N and O atoms are shown as thermal ellipsoids drawn at the 50% probability level.

Table III. Summary of bond lengths (Å) for (1 · C₂H₅OH)

Bond	Range	Mean
C(ar)—O(ether)	1.388(8)–1.389(8)	1.389(8)
C(ar)—O(phen)	1.358(8)–1.382(8)	1.370(8)
C(sp ³)—O(ether)	1.414(9)–1.418(8)	1.416(9)
C(sp ³)—C(py)	1.510(10)–1.510(10)	1.510(10)
C(py)—N(py)	1.333(10)–1.352(10)	1.342(10)
C(py)—C(py)	1.335(15)–1.384(15)	1.363(13)
C(ar)—C(ar)	1.360(10)–1.420(10)	1.389(10)
C(ar)—C(sp ³)	1.507(10)–1.539(10)	1.520(10)
C(sp ³)—C(<i>t</i> -Bu methyl) #	1.456(13)–1.530(16)	1.495(13)

The minor site of the disordered *t*-butyl group attached to C(4A) was not included.

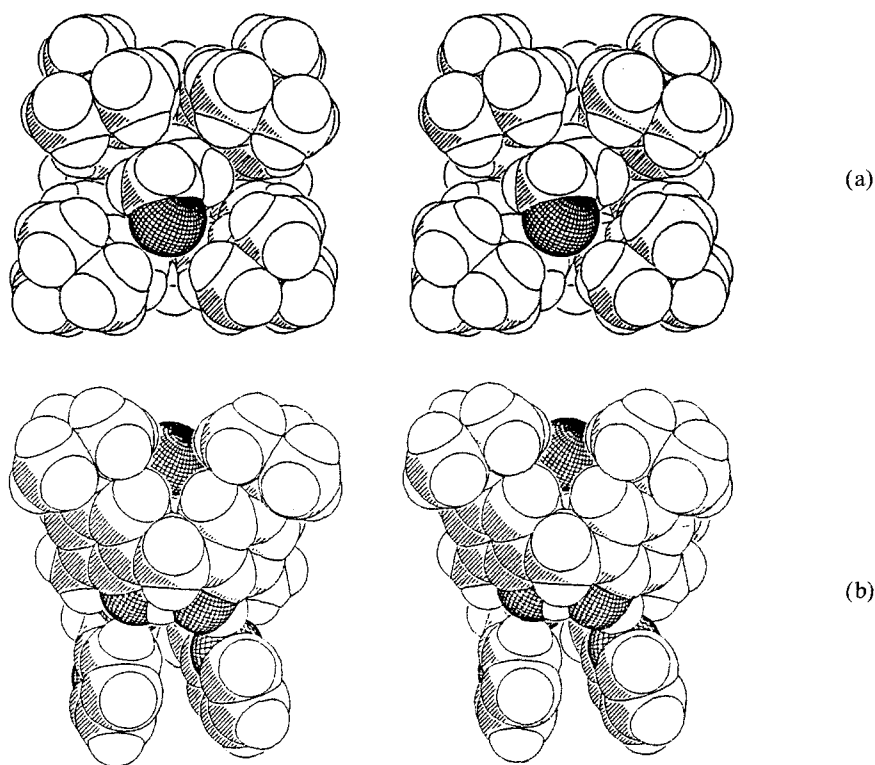


Fig. 2. Two stereoviews of the molecule (1) with the atoms drawn as their van der Waals spheres (a) looking down at the calixarene cavity and (b) a sideview looking at the intramolecular hydrogen bonding. The ethanol hydroxyl hydrogen is disordered and is not shown.

3. Results and Discussion

The *syn-proximal t*-butyl-di-[(2-pyridylmethyl)oxy]calix[4]arene (1) adopts a relatively open cone conformation in the solid state (Figures 1 and 2). Molecular dimensions, summarized in Table III, are as anticipated for such calixarenes.

The major conformation determining features in this molecule are the presence of (a) an intramolecular O—H \cdots O hydrogen bond between adjacent phenolic oxygens, [O(1C) \cdots O(1D) 2.719(7) Å, HOC \cdots O(1D) 1.74 Å, O(1C)—HOC \cdots O(1D) 161°], and (b) an intramolecular O—H \cdots N hydrogen bond between the phenolic oxygen O(1D) and the proximal pyridinyl nitrogen N(14A) [O(1D) \cdots N(14A) 2.810(8) Å, HOD \cdots N(14A) 1.97 Å, O(1D)—HOD \cdots N(14A) 146°]. The other pyridinyl nitrogen [N(14B)] is not involved in hydrogen bonding. The calix conformation is defined by the angles that the aromatic rings make with the plane of the four CH₂ moieties which link them, *viz.* 118.1(2)° (A), 111.1(2)° (B), 127.0(2)° (C) and 119.5(2)° (D) (interplanar angles > 90° indicate that the ring system is tilted so that its *t*-butyl group is directed *away* from the ring cavity). One pair of aromatic rings, (A and C), is tilted at an interplanar angle of 65.1(3)° to one another, while the corresponding angle for rings B and D is 50.7(3)°. This open calix conformation leads to O \cdots O separations of 3.802(7) Å between OA and OC and 4.434(6) Å between OB and OD; the O \cdots O distances between adjacent oxygen atoms in the calixarene are in the range 2.719(7) to 3.097(7) Å. The conformation adopted by (1) creates a cavity which is large enough to accommodate a solvent molecule, and an ethanol molecule is included in the calixarene cavity (as shown in Figures 1 and 2) with the hydroxyl end of the molecule directed out of the calix cavity.

The structure of a related dihydroxy calix[4]arene devoid of *t*-butyl groups, a *syn*-1,2-bis(ethoxyethyl)ether derivative is also known [14, 15]; in this structure there are two independent molecules and two different modes of intramolecular O—H \cdots O hydrogen bonding. In one molecule both hydrogen bonds are between the calix[4]arene phenolic oxygens; in the second molecule, one of the hydrogen bonds is to a side-chain oxygen. The first molecule has a relatively open cone conformation, whereas the second is more closed (interplanar angles corresponding to those quoted above are 104.4, 133.9, 119.8, 128.5° for molecule 1, and 92.6, 144.9, 101.2, 139.2° for molecule 2). In neither case is there any included solvent.

The calix conformation found here is similar to that reported previously for the open calixarene conformation in tetraethyl-*p-t*-butylcalix[4]arene tetracarboxylate, which has a molecule of acetonitrile included within the calix cavity [5]. The crystal structures of some hemicarcerands and hemicarceplexes readily demonstrate the encapsulation of small molecules, (CH₃CN or CH₂Cl₂), inside the host cavity [16], with solvent molecules also present in the lattice.

Additional material available from the Cambridge Crystallographic Data Centre comprises atom coordinates, a full listing of bond lengths and angles, thermal parameters, hydrogen coordinates, torsion angles, mean plane data and structure factor listings for the compound.

Acknowledgement

G. F. thanks NSERC Canada for Grants in Aid of Research. S. P. thanks M.U.R.S.T. for partial support of this work.

References

1. C. D. Gutsche: *Calixarenes*. Monographs in Supramolecular Chemistry, Vol. 1; Ed. J. F. Stoddart; The Royal Society of Chemistry: Cambridge, 1989.

2. J. Vicens and V. Böhmer (Eds.): *Calixarenes: A Versatile Class of Macrocyclic Compounds*, Kluwer Academic Publishers: Dordrecht, 1990.
3. G. D. Andreetti and F. Ugozzoli: *Inclusion Properties and Host–Guest Interactions of Calixarenes in the Solid State*, in Ref. 2, pp. 173–198.
4. J. Uzawa, S. Zuchi, Y. Komada, Y. Fukuda, K. Nichihata, K. Umemura, M. Nishio, and M. Hirota: *Bull. Chem. Soc. Jpn.* **53**, 3623 (1980).
5. M. A. McKervey, E. M. Seward, G. Ferguson, and B. L. Ruhl: *J. Org. Chem.* **51**, 3581 (1986).
6. A. Arduini, E. Ghidini, A. Pochini, R. Ungaro, G. D. Andreetti, G. Calestani, and F. Ugozzoli: *J. Incl. Phenom.* **6**, 119 (1988).
7. F. Bottino, L. Giunta, and S. Pappalardo: *J. Org. Chem.* **54**, 5407 (1989).
8. S. Pappalardo, L. Giunta, M. Foti, G. Ferguson, J. F. Gallagher, and B. Kaitner: *J. Org. Chem.* **57**, 2611 (1992).
9. S. Pappalardo, S. Caccamese, and L. Giunta: *Tetrahedron Lett.* **32**, 7747 (1991).
10. S. Pappalardo, L. Giunta, and M. Parici: manuscript in preparation.
11. *International Tables for X-ray Crystallography*, Vol. IV; Kynoch Press: Birmingham, England, 1974. Distr. Kluwer Academic Publishers, Dordrecht, The Netherlands.
12. C. K. Johnson: *ORTEPII*, Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, U.S.A. (1976).
13. A. L. Spek: *PLUTON* Molecular Graphics Program, University of Utrecht, The Netherlands (1991).
14. L. C. Groenen, B. H. M. Ruël, A. Casnati, P. Timmerman, W. Verboom, S. Harkema, A. Pochini, R. Ungaro, and D. N. Reinhoudt: *Tetrahedron Lett.* **32**, 2675 (1991).
15. L. C. Groenen: Ph.D. Thesis, University of Twente, Enschede, The Netherlands, 1992.
16. M. E. Tanner, C. B. Knobler, and D. J. Cram: *J. Org. Chem.* **57**, 41 (1992).