Octa(*p*-hydroxy)octakis(propyloxy)calix[8]arene: The First Crystal Structure of a *p*-Hydroxy Calixarene

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Abstract. Octa(*p*-hydroxy)octakis(propyloxy)calix[8]arene.9(pyridine).2(H_2O) crystallises in the triclinic space group P -1, $a = 14.083(2)$, $b = 14.478(2)$, $c = 15.652(2)$ Å, $\alpha = 70.109(4)$, $\beta = 74.146(3)$, $\gamma = 75.572(4)°$, V = 2843(1) Å^3, Z = 1. Refinement led to a final R_1 value of 0.0757 for 4693 reflections. The calixarene sits around a crystallographic centre of inversion and is in the 'chair-like' conformation. All *p*-hydroxyl groups form hydrogen bonds with either pyridine or water molecules leading the extended structure to be composed of infinite ribbons parallel to the [1 0 −1] direction.

Key words: calixarene, hydroquinone derivative, crystal structure, hydrogen bonding

1. Introduction

The study of the various properties and possible functionalizations of calixarenes has been the subject of intense research work over the last two decades and occupy a well-established place in today's supramolecular chemistry [1–4]. An interesting class of these macrocyclic molecules is that of quinone and hydroquinone derivatives because of their binding and redox properties and for their possible further chemical modifications, especially at the *meta* position [5–14]. Recently the group of Ungaro published a convenient synthesis of such calix[8]arene derivatives [15]. Herein we present the crystal structure of octa(*p*-hydroxy)octakis(propyloxy)calix[8]arene.9(pyridine).2(H_2O) (**1**), the first of a *p*-hydroxy calixarene.

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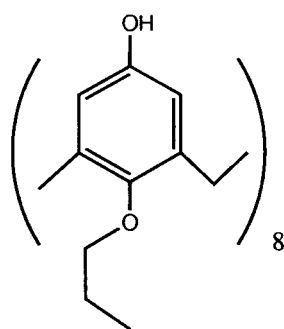
2. Experimental

2.1. SYNTHESIS

Octa(*p*-hydroxy)octakis(propyloxy)calix[8]arene was prepared by a method derived from the one of reference 15. The main chemical differences consisted in the use of KO^{t}Bu instead of NaOH in the first cyclization step and of NaH instead of CsCO$_3$ in the alkylation reaction. These differences led to an improved overall yield of 45%.

2.1.1. *Octa(p-benzyloxy)calix[8]arene (A)*

Paraformaldehyde (12 g, 0.4 mol) and KO^{t}Bu (1 g) were added to a xylene (400 mL) solution of (*p*-benzyloxy)phenol (40 g, 0.2 mol) in a flask equipped with a dean-stark water collector and a condenser. The resulting suspension was degassed and refluxed for 4 h under a nitrogen atmosphere. The suspension was then left at ambient temperature for three days before being filtered. The solid A obtained was washed with acetone and petroleum ether and then dried under vacuum (28.7 g, 0.017 mol, 66%).

2.1.2. *Octa(p-benzyloxy)octakis(n-propyloxy)calix[8]arene (B)*

NaH (0.4 g, 60% dispersion in mineral oil) was carefully added to a suspension of A (3 g, 1.77 mmol) in a DMF/THF (60/15) solution (50 mL) under a nitrogen atmosphere. The resulting yellow solution was refluxed for 30 min and *n*-PrI (1 mL) was added. After 30 min of refluxing the solution was cooled to ambient temperature and this sequence was repeated 4 times. The resulting light brown solution was filtered, washed with water before being concentrated and chromatographed (SiO$_2$/CH$_2$Cl$_2$). B was obtained as a white solid after drying of the solution (3 g, 1.42 mmol, 80%).

2.1.3. *Octa(p-hydroxy)octakis(n-propyloxy)calix[8]arene*

B (2.4 g, 1.18 mmol) was submitted to hydrogenolysis on Pd/C (10% Pd) in THF for 3 h. The resulting solution was filtered on celite. Solvents were removed under reduced pressure affording octa(*p*-hydroxy)octakis(*n*-propyloxy)calix[8]arene as a white solid (1.33 g, 1 mmol, 85%). Recrystallisation from a mixture of pyridine and xylene afforded beautiful colourless single crystals of (**1**) suitable for X-ray analysis. m/z: 1312.9(M$^+$) (MALDI), NMR (Bruker AC-200) (D$_6$-acetone/CCl$_4$: 80/20) 0.94 (*t*, C*H*$_3$, 24H), 1.7 (*sextuplet*, CH$_2$C*H*$_2$CH$_3$, 16H), 3.6 (*t*, OC*H*$_2$CH$_2$, 16H), 3.89 (*s*, ArC*H*$_2$Ar, 16H), 6.37 (*s*, Ar*H*, 16H), 7.68 (*s*, O*H*, 8H).

2.2. CRYSTAL STRUCTURE ANALYSIS

Crystal Data: Octa(*p*-hydroxy)octakis(propyloxy)calix[8]arene.9(pyridine). 2(H$_2$O) (**1**), C$_{125}$ H$_{145}$ N$_9$ O$_{18}$, formula weight 2061.50, triclinic, Space group *P*-1, *a* = 14.083(2), *b* = 14.478(2), *c* = 15.652(2) Å, α = 70.109(4), β = 74.146(3), γ = 75.572(4)°, V = 2843(1) Å^3, Z = 1, ρ_{calc} = 1.204 g cm^{-3}, μ = 0.081 mm^{-1}, F(000) = 1102.

Data Collection: A crystal of (**1**) (0.25 × 0.25 × 0.15 mm) was fixed with paratone [16] in a glass capillary and placed on a Nonius Kappa-CCD diffractometer. Data were collected at 123 K to a 2θ limit of 58.38° using graphite-monochromatised Mo-Kα radiation. After positioning the detector at a 28 mm distance from the crystal, the data collection was performed by recording 90 images while applying a 180° scan on Phi (2° steps). Data were 94% complete to a 2θ value of 42.72°. Unit cell parameters were determined with the 10 initial frames and then refined using all independent reflections.

Structure Analysis: The structure was solved by direct methods [17] and then re-fined on F^2 using SHELXTL [18]. Out of the 37460 reflections measured, 6306 were found independent (R$_{int}$ = 0.155), 4693 of which were considered as observed (I > 2σI) and used in the refinement of the 580 parameters, leading to a final R$_1$ of 0.0757 and R$_{all}$ of 0.1118. Individual weights were applied in the refinement according to the scheme w = [σ^2(Fo^2) + (0.0207P)^2 + 8.5027P]$^{-1}$ where P = (Fo^2 + 2Fc^2)/3. wR$_{obs}$ and wR$_2$ were respectively equal to 0.1483 and 0.1987. The goodness-of-fit parameter S was 1.105 and the maximum residual density 0.370 eÅ^{-3}.

All atoms were considered anisotropic except the carbons of the calixarene core which were kept isotropic in order to keep a reasonable data/parameters ratio. For the same reason, the aromatic six member rings of pyridine molecules and of the calixarene were constrained to regular hexagons. One of the pyridine molecules lies around a crystallographic inversion centre. As it was impossible to determine the exact position of the nitrogen atom in the ring from either the values of U or from hydrogen bonding in the lattice, all atoms of this group were considered to be

Table I. Selected geometric parameters (Å,°) with ESD in parentheses (symmetry code: $'' = 1 - x, -y, -1 - z$)

O(12)–H(12) 0.820	H(12)–N(1) 1.920(7)	O(12)–N(1) 2.768(9)
O(22)–H(22) 0.820	H(12)–O(1w) 1.843(7)	O(22)–O(1w) 2.658(9)
O(32)–H(32) 0.820	H(32)–N(3) 1.955(7)	O(32)–N(3) 2.762(9)
O(42)–H(42) 0.820	H(42)–N(4) 1.939(7)	O(42)–N(4) 2.749(9)
O(1w)–H(wa) 1.108(6)	H(wa)–N(2) 1.695(7)	O(1w)–N(2) 2.774(9)
O(1w)–H(wb) 1.015(6)	H(wb)–O(11'') 1.781(7)	O(1w)–O(11'') 2.784(9)
O(12)–H(12)–N(1) 168.2(8)	O(22)–O(1w)–O(11'') 139.4(7)	
O(22)–H(22)–O(1w) 171.8(8)	O(22)–O(1w)–N(2) 107.3(7)	
O(32)–H(32)–N(3) 167.8(8)	N(2)–O(1w)–O(11'') 111.9(7)	
O(42)–H(42)–N(4) 169.4(8)		
O(1w)–H(wa)–N(2) 163.2(8)		
O(1w)–H(wb)–O(11'') 169.1(8)		

carbon. All hydrogen atoms – except those of the oxygen atoms – were included in the calculation as riding on calculated positions (U = 1.2 times the one of the corresponding atom). The four hydrogen atoms of the phenolic groups were refined as rigid groups with fixed O—H distance (0.82 Å) and C—O—H angle (109.5°). Those of the water molecule were introduced from positions located in the last Fourier map and not refined. Selected geometric parameters are given in Table 1.

3. Results and Discussion

In the solid state, (**1**) (Figure 1) sits on a centre of symmetry like four [19, 20, 22, 23] of the five other uncomplexed calix[8]arenes structurally characterised to date [19–23]. Crystal structures of calix[8]arenes used as ligands in coordination chemistry are more numerous, but can hardly be compared here as their geometry is mostly imposed by metal complexation [24–30]. The centroids of the phenolic faces are comprised in a plane defined at ±0.07 Å, making the global shape that of a flat ellipse. The calixarene core (Figure 2) can best be described as being arranged in the 'chair' or 'stairway' conformation [23], reminiscent of the 'pinched' conformation suggested in the eighties [31]. The phenolic ring bearing O(21) defines a plane which includes the crystallographic centre of inversion (± 0.04 Å) and is therefore coplanar to its symmetry equivalent bearing O(21′). This plane is also almost parallel to the one defined by the ring bearing O(41) with an angle between the two planes of only 8.0(3)°.

Another general aspect of the conformation is that six of the ether substituted oxygen atoms are oriented towards the inside of the molecule while two are on the outside (O(41) and O(41′)). This geometry is also found in the solid state for the
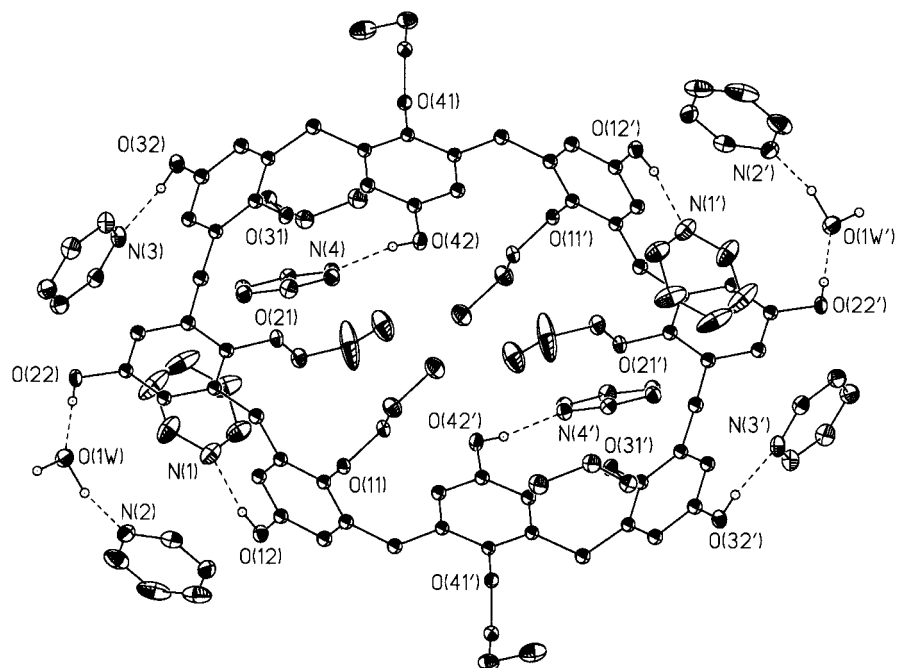
Figure 1. View of the title compound with partial atom labelling (symmetry code: $' = -x, -y, -z$). Displacement ellipsoids are drawn at the 20% probability level except for the H atoms which are represented as sphere of arbitrary radii. H atoms not forming hydrogen bonds as well as the disordered pyridine molecule on the inversion centre have been omitted for clarity.
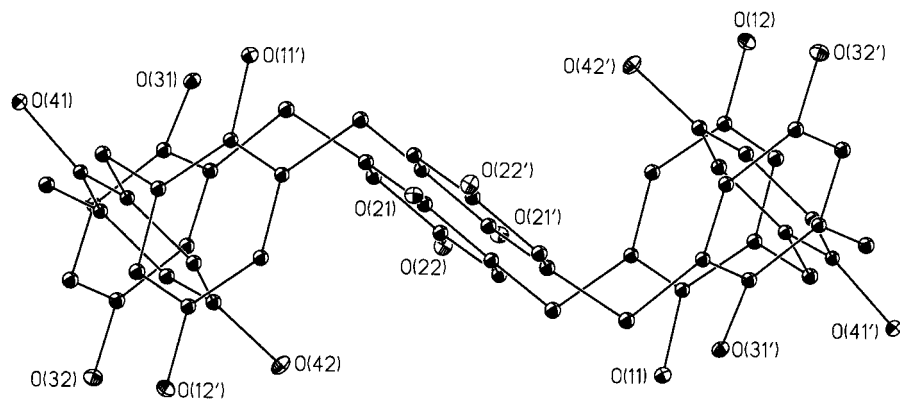

Figure 2. View of the calixarene core with an orientation emphasising its conformation. Solvent molecules, H atoms and propyl groups have been omitted.
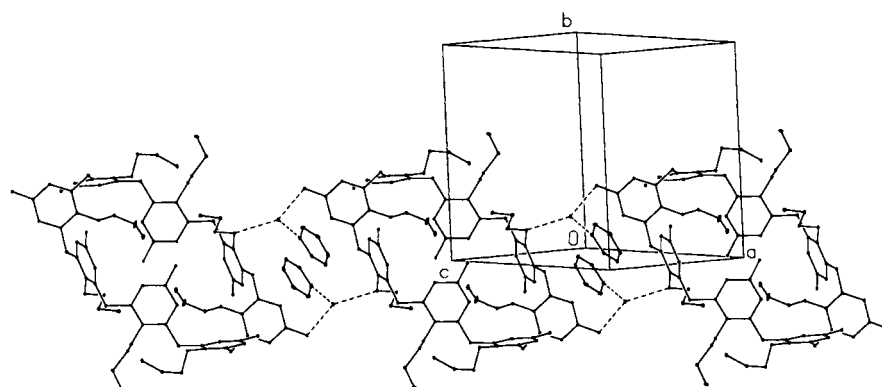
Figure 3. View of the H bonding in the extended structure. The pyridine molecules not participating in the packing and all the H atoms have been omitted. Hydrogen bonds are indicated by dashed lines.

acetate of p-^{t}butyl-calix[8]arene [19], the methyl ether of calix[8]arene [22] and for the pyridine clathrate of p-^{t}butyl-calix[8]arene [23] but differs from the usually accepted all-in pleated-loop geometry [21]. An interesting feature of this structure is the self inclusion of two of the propyl groups inside the cavity of the macrocycle (carried by O(21) and O(21′)), leaving no space for solvent molecules [1–4] or chemical groups of adjacent molecules [32–36]. This topology helps to minimise the molecular volume and to maximise the crystal density [20].

All p-hydroxy substituents form hydrogen bonds with either pyridine (O(12), O(32) and O(42)) or water molecules (O(22)) (Table I). The mean O–N distance is equal to 2.758(8) Å which is slightly longer than the O–N distances found for the H-bonds of p-^{t}butyl- calix[8]arene.8(pyridine) [23] (2.708(6) Å), p-benzyl-calix[5]arene.3(pyridine) (2.677(7) and 2.628(5) Å) [34] and p-^{t}butyl-calix[7]arene.3(pyridine) (2.632(8) Å) [35]. This is in agreement with the fact that protons of phenolic groups are more acidic than those of hydroquinone derivatives. The water molecule accepting the hydrogen bond from O(22) is itself donating hydrogen bonds to a pyridine molecule and to the oxygen atom (O(11″), symmetry code: $'' = 1 - x, -y, -1 - z$) of the propoxyl group of an adjacent calixarene in the lattice. In the packing, this arrangement results in the formation of ribbons of macrocycles that extend parallel to the [1 0 −1] direction (Figure 3). This unusual pyridine-water-calixarene contact which plays a prominent role in governing the packing, is a new example of the possible interaction between calixarene and pyridine (both polar and possessing π electron systems, both donating or accepting hydrogen bonds). The variety of those interactions could be at the origin of the well known efficiency of this solvent for the crystallisation of calixarenes.

Noteworthy is the fact that unlike phenolic calixarenes [21, 23], this p-hydroxy calix[8]arene (that might be considered as a hydroquinone derivative), does not form intramolecular hydrogen bonds. Although probably flexible enough to ac-

commodate such a phenomenon, the macrocycle prefers to bind to solvent molecules. This fundamental difference between the calixarene bearing the hydroxyl group at the lower rim and the one at the upper rim, probably implies an even more labile geometry in the solution and will probably be the cause of intrinsic chemical properties.

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