

Structural Study of the 1 : 1 Clathrate of an Asymmetric Calix[4]arene and Acetone

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Abstract. The crystal and molecular structure of the 1 : 1 clathrate of the asymmetric calix[4]arene, **1**, and acetone has been determined by X-ray analysis. The crystal data are: tetragonal, space group $P4/n$, $a = b = 12.574(6)$, $c = 12.572(6)$ Å, $V = 1988(2)$ Å³, $Z = 2$, $D_x = 1.111$ g cm⁻³, $D_m = 1.108$ g cm⁻³. Least-squares refinement based on 1131 observed reflections with $F_0 > 3\sigma(F_0)$ and anisotropic temperature factors led to $R = 0.096$. In spite of the molecular asymmetric calixarene **1** the crystal structure has high symmetry, because a part of the host and guest molecules are in disordered states.

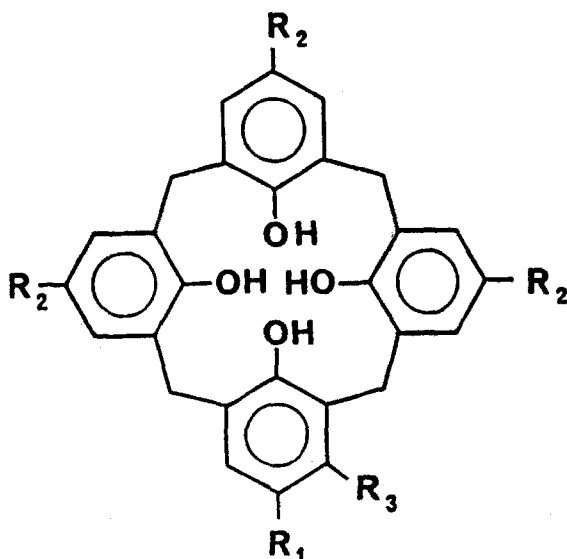
Key words: Molecular asymmetry, calixarene, acetone, clathrate, crystal structure.

1. Introduction

Calix[4]arenes are macrocycles made up from four phenolic units *meta*-linked by methylene bridges at the *ortho*-position of the hydroxyl groups [1, 2]. They are bowl-shaped molecules which are capable of including either neutral or cationic guests [1, 2]. Because they are not planar, Böhmer *et al.* [3] synthesized calix[4]arenes consisting of four different *p*-substituted phenol rings which are chiral. Subsequently, calix[4]arenes consisting of three phenolic units in the order *AABC* having no symmetry planes were prepared by the same authors [4]. More recently, the same group produced dissymmetric calix[4]arenes with C_2 and C_4 symmetry obtained by clockwise *meta*-substitution with methyl groups in a symmetric calix[4]arene [5].

Earlier, in 1987, Casabianca *et al.* [6] described the synthesis of calix[4]arenes having no symmetry plane in which one *meta*-position is substituted by a methyl group, by cyclocondensation of linear phenolic trimers with appropriate 2,6-bis-(bromomethyl)phenols. The absence of a symmetry plane in calix[4]arene **1** was

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	R ₁	R ₂	R ₃
1	<i>i</i> -Pr	<i>i</i> -Pr	Me
2	<i>i</i> -Pr	<i>i</i> -Pr	H
3	<i>i</i> -Pr	<i>t</i> -Bu	Me

Scheme. Molecular structures of compounds **1**, **2**, and **3**.

deduced from the presence of 23 peaks in the aromatic region of its ^{13}C -NMR spectrum compared to the *p*-isopropylcalix[4]arene analog **2** (without a *meta*-methyl group) which exhibited only four peaks because of the high symmetry of the molecule [6]. Two years later, 300 MHz temperature-dependent ^1H -NMR spectra of **1** in CDCl_3 showed that the methylene protons $\text{Ar-CH}_2\text{-Ar}$ appear as two pairs of doublets *AB* and *A'B'* (ratio 3/1) below room temperature [7]. This pair of doublets was attributed to a rigidification of **1** in the cone conformation and MMP2 calculations showed that the cone conformation is adopted because of circular hydrogen bonds within the OH groups; the activation energy was calculated as 58.5 kJ mol^{-1} , leading to a rate of interconversion of 100 s^{-1} [7], as usually found for symmetric calix[4]arenes [8]. These findings were recently confirmed [9] by the nuclear Overhauser effect and simulated spectra on the calix[4]arene **3**, related to **1**. At the same time **3** was prevented from ring inversion by introducing *n*-propyl substituents on the OH groups and the tetra-*O*-propylated derivative in the cone conformation was successfully optically resolved for the first time [9].

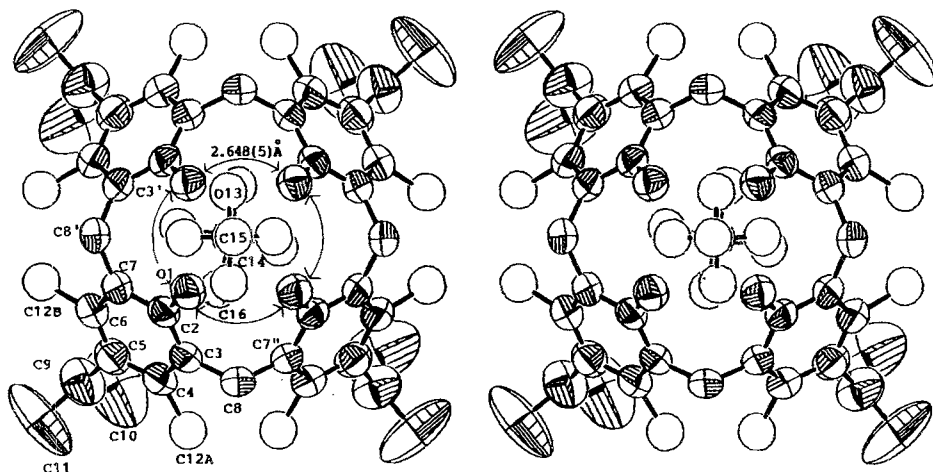


Fig. 1. Stereoscopic view of the host and guest molecules of the calix[4]arene **1**-acetone (1 : 1) clathrate with atom numbering; the thermal ellipsoids are given at 50% probability.

In this communication we present the X-ray determination of the structure of crystalline **1**. This work was performed to reveal evidence of the stable cone conformation of **1** in the crystalline state and to gain information on the chemical modifications added to molecular asymmetry in calix[4]arenes by the presence of the *meta*-methyl group. In addition, no inclusion complexes of molecular asymmetric calix[4]arenes have been reported to date.

2. Experimental

Pentacyclo[19.3.1.1^{3,7}.1^{9,13}.1^{15,19}]octacos-1(25),3,5,7(28),9,11,13(27),17,19(26),21,23-dodecaene-4-methyl-5,11,17,23-tetrakis(1-methylethyl)-25,26,27,28-tetraol **1** was prepared according to reference [6]. The clathrate crystals were prepared by recrystallizing **1** from acetone for four weeks at room temperature.

A single crystal used for data collection was selected with dimensions $0.70 \times 0.70 \times 0.50 \text{ mm}^3$ and sealed in a thin-walled capillary to avoid decomposition during the X-ray experiment. X-ray diffraction data were measured at 22°C on a Rigaku automatic four-circle diffractometer (AFC-R) using graphite monochromated $\text{CuK}\alpha$ ($\lambda = 1.5418^\circ \text{ \AA}$) radiation. The lattice constants were calculated from 20 reflections in the range of $56^\circ < 2\Theta < 61^\circ$. The systematic data collection, in the range of $2\Theta < 125^\circ$, was performed with the $\omega - 2\Theta$ scan technique at a constant $4^\circ/\text{min}$ rate, with scan range ($\omega = 1.2 + 0.17 \tan \Theta$) $^\circ$. The intensity data were corrected for Lorentz and polarization effects. The crystal structure was solved by a direct method (SIR88) [10]. The refinement of the structure was car-

TABLE I. Final atomic coordinates and equivalent isotropic thermal parameters (\AA^2) of **1** and their e.s.d.'s in parentheses for non-hydrogen atoms. $B_{\text{eq}} = (4/3) \sum_i \sum_j B_{ij} a_i \cdot a_j$.

	o c c.	<i>x</i>	<i>y</i>	<i>z</i>	B_{eq}
O(1)		0.3187(3)	0.3821(3)	1.0414(3)	6.42(3)
C(2)		0.3477(4)	0.4344(4)	0.9482(4)	5.67(5)
C(3)		0.2764(4)	0.5065(4)	0.9044(4)	5.94(6)
C(4)		0.3082(4)	0.5626(4)	0.8137(5)	6.68(6)
C(5)		0.4083(4)	0.5473(4)	0.7684(5)	7.16(6)
C(6)		0.4765(4)	0.4730(4)	0.8141(4)	6.56(6)
C(7)		0.4475(4)	0.4152(4)	0.9044(4)	5.85(5)
C(8)		0.1667(4)	0.5230(4)	0.9519(4)	6.45(6)
C(9)		0.4446(6)	0.6122(6)	0.6704(5)	10.14(9)
C(10)		0.3743(11)	0.6025(11)	0.5820(7)	21.06(24)
C(11)		0.5039(10)	0.7084(8)	0.7021(7)	19.47(24)
C(12A)	0.11	0.223 (5)	0.641 (5)	0.770 (5)	9.1
C(12B)	0.14	0.586 (4)	0.448 (4)	0.762 (4)	9.0
O(13)	0.25	0.278 (5)	0.166 (2)	0.565 (2)	21.3
C(14)	0.25	0.250 (0)	0.250 (0)	0.611 (2)	15.5
C(15)	0.25	0.250 (0)	0.250 (0)	0.730 (2)	19.6
C(16)	0.25	0.238 (9)	0.351 (4)	0.554 (4)	27.0

ried out by block-diagonal least-squares, including the positional and anisotropic thermal parameters of all atoms except the disordered non-hydrogen atoms and hydrogen atoms. Occupancies of the disordered atoms were also refined by full-matrix least-squares. The guest acetone molecule was refined with constraint of the bond distances and angles. The hydrogen atoms were located on a difference Fourier map by geometric calculations. Atomic scattering factor for neutral atoms, f' and f'' were used from the *International Tables for X-ray Crystallography* [11]. The final difference Fourier maps revealed no indication of incorrectly placed or missing atoms. All computations were carried out with the IBM-3081 GX3 computer at the Information Processing Center, Shimane University.

3. Results and Discussion

The crystal structure of the 1 : 1 1-acetone clathrate $\text{C}_{41}\text{H}_{50}\text{O}_4 : \text{C}_3\text{H}_6\text{O}$ was found to be of space group $P4/n$ with $a = b = 12.574(6)$, $c = 12.572(6)$ \AA , $V = 1988(2)$ \AA^3 , $Z = 2$, $D_x = 1.111$ g cm^{-3} , $D_m = 1.108$ g cm^{-3} and linear absorption parameter $\mu = 5.24$ cm^{-1} .

Table I reports the fractional atomic coordinates. Bond distances and angles are shown in Tables II and III, respectively. Lists of atomic coordinates for hydrogens, thermal parameters, and structure factors have been deposited.

TABLE II. Bond distances (Å) of **1** with e.s.d.'s in parentheses.

O(1)-C(2)	1.392(6)	C(4)-C(12A)	1.56 (6)	C(9)-C(11)	1.476(15)
C(2)-C(3)	1.389(7)	C(5)-C(6)	1.392(8)	C(13)-C(14)	1.23 (6)
C(2)-C(7)	1.391(7)	C(5)-C(9)	1.547(9)	C(14)-C(15)	1.50 (3)
C(3)-C(4)	1.399(8)	C(6)-C(7)	1.396(8)	C(14)-C(16)	1.47 (11)
C(3)-C(8)	1.517(8)	C(6)-C(12B)	1.56 (5)	C(8)-C(7)*	1.523(8)
C(4)-C(5)	1.395(8)	C(9)-C(10)	1.425(16)		

* Symmetry ($1/2 - y, x, z$).TABLE III. Bond angles (°) of **1** with e.s.d.'s in parentheses.

O(1)-C(2)-C(3)	118.2(3)	C(5)-C(4)-C(12A)	124 (2)	C(5)-C(9)-C(10)	113.1(6)
O(1)-C(2)-C(7)	119.2(3)	C(4)-C(5)-C(6)	118.7(4)	C(5)-C(9)-C(11)	111.5(7)
C(3)-C(2)-C(7)	122.6(5)	C(4)-C(5)-C(9)	121 (5)	C(10)-C(9)-C(11)	126.4(8)
C(2)-C(3)-C(4)	117.9(4)	C(6)-C(5)-C(9)	120.1(4)	O(13)-C(14)-C(15)	117 (3)
C(2)-C(3)-C(8)	121.3(5)	C(5)-C(6)-C(7)	121.6(5)	O(13)-C(14)-C(16)	122 (5)
C(4)-C(3)-C(8)	120.8(4)	C(5)-C(6)-C(12B)	120 (2)	C(15)-C(14)-C(16)	119 (4)
C(3)-C(4)-C(5)	121.4(5)	C(7)-C(6)-C(12B)	118 (2)	C(3)-C(8)-C(7)*	112.0(4)
C(3)-C(4)-C(12A)	114 (2)	C(2)-C(7)-C(6)	117.8(4)	C(2)-C(7)-C(8)**	121.6(5)
				C(6)-C(7)-C(8)**	120.5(4)

* Symmetry ($1/2 - y, x, z$).** Symmetry ($y, 1/2 - x, z$).

Figure 1 shows the structure of the host and guest molecules [12]. The hydroxyl groups of the host molecule are linked by four-fold cyclic hydrogen bonds, $O(1)(x, y, z)-O(1)(y, 1/2 - x, z) = 2.648(5)$ Å. The cone conformation is supported by this strong intramolecular hydrogen bonding system between each hydroxyl group. Only the methyl *meta*-substituted phenol is expected to make a difference in the dihedral angle between the plane determined by the four hydroxyl groups and the phenol ring. But the four phenol rings are in an equivalent structure related by crystallographic symmetry. That is, 1 : 1 (*R*) and (*S*) enantiomers of **1** are packed and disordered in the crystal. Thus, the crystal structure is an averaged structure in an asymmetric unit. This crystal has a crystallographic four-fold axis through the C-C bond of the guest molecule, acetone, which is included in the cavity of the host molecule. The methyl group of the host molecule is disordered at eight points related by a four-fold axis and its enantiomer occupies the same position caused by the molecular asymmetry. The guest molecule is also disordered at four positions related by a crystallographic four-fold axis. In this clathrate, the above observations mean that better recognition of the guest molecule is impossible at

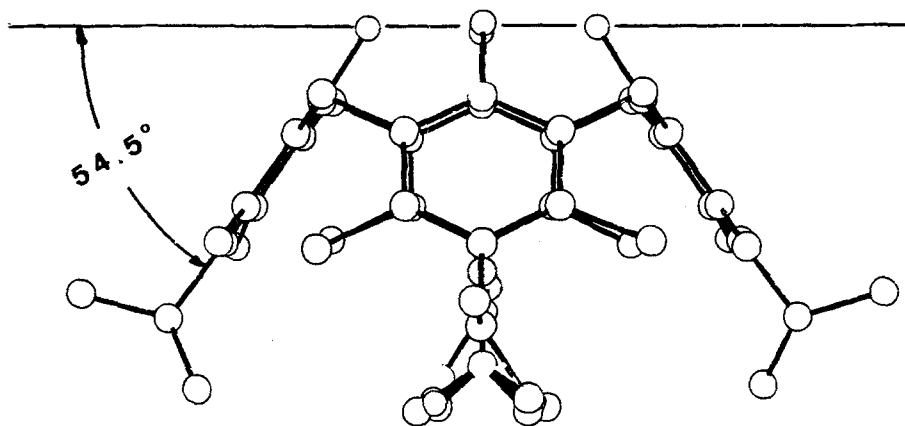


Fig. 2. The orientation of the phenol ring from a best plane constituted of the four hydroxyl groups in the calix[4]arene **1**-acetone (1 : 1) clathrate.

the hydrophobic cavity by the introduced methyl group. The guest molecules are packed in the host molecule, directing its methyl group toward the cavity of the host molecule because that methyl group is used for molecular recognition of host and guest molecules by each other in the hydrophobic cavity.

The dihedral angle is 54.5° between the weighted least squares plane through the four hydroxyl groups in the host molecule and the phenol ring plane through C(3) to C(8) (Figure 2 [13]).

The shape of the average hydrophobic cavity in the crystal is shown in Figure 3 [14]. The volume is about 49 \AA^3 . The cavity seems to rotate a little, because it shaves the methyl moiety of the isopropyl group of the host molecule. CH_3 - π interactions seem to exist between the methyl of the acetone and the aromatic moieties of the host molecule (the shortest contact is at C(15)-C(2) of $3.80(3) \text{ \AA}$), but absence of the atomic coordinates of the hydrogen atoms of the methyl group prevents any further consideration. The crystal packing is shown in Figure 4 [13]. Comparison of cell parameters of the present complex with the *p*-*tert*-butylcalix[4]arene-toluene (1 : 1) clathrate [15], the *p*-*iso*-propylcalix[4]arene-toluene (1 : 1) clathrate [16] and the *p*-*iso*-propylcalix[4]arene-*o*, *m*, and *p*-xylenes (1 : 1) clathrates [17] shows a difference in the length of the *c*-axis probably due to the size of the guest molecule.

4. Conclusion

To conclude, we have for the first time revealed the crystal structure of an asymmetric calixarene. According to previous conclusions based on $^1\text{H-NMR}$ observations, calixarene **1** was shown to adopt the cone conformation in the crystalline

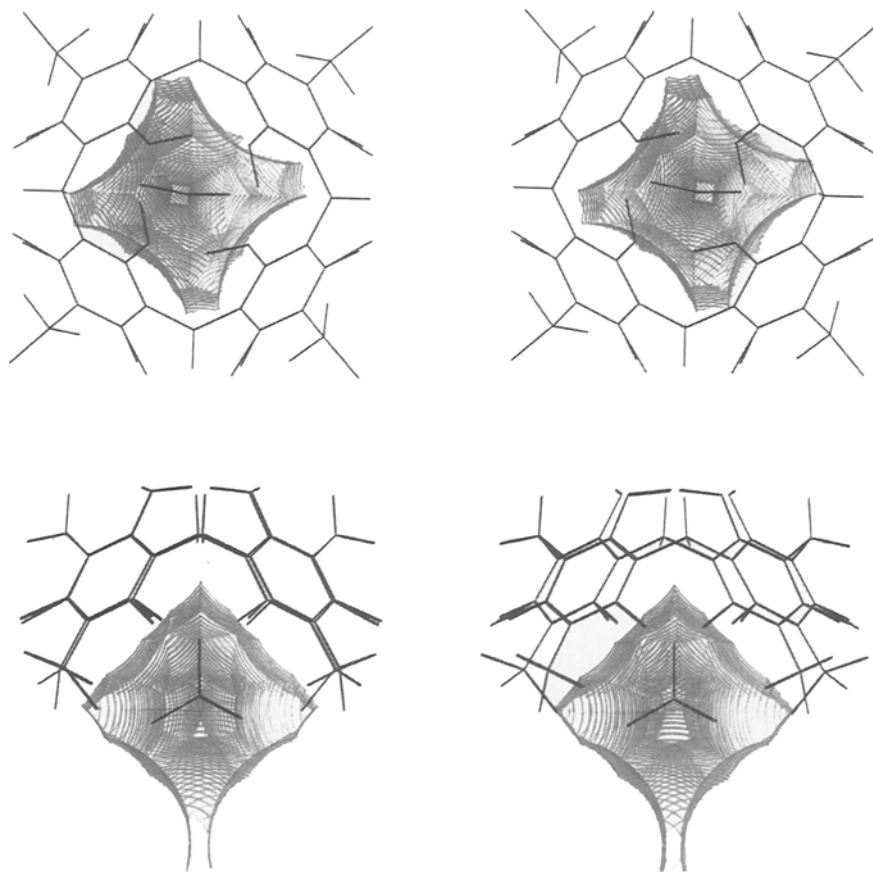


Fig. 3. Stereoscopic views of the cavity including the guest molecule for the calix[4]arene 1-acetone (1 : 1) clathrate. Above: the view along the four fold axis; below: the side view.

state. This conformation is imposed by the presence of circular hydrogen bonds within the phenolic OH groups. In this conformation calixarene **1** is able to include one acetone molecule. However, the presence of a supplementary methyl group at a *meta*-position does not affect the symmetry of the hydrophobic cavity which is not capable of molecular recognition. In addition the observation of eight positions for the additional methyl group allows one to conclude that no spontaneous resolution has occurred during the crystallization of (*R*) and (*S*) enantiomers of **1**.

Acknowledgements

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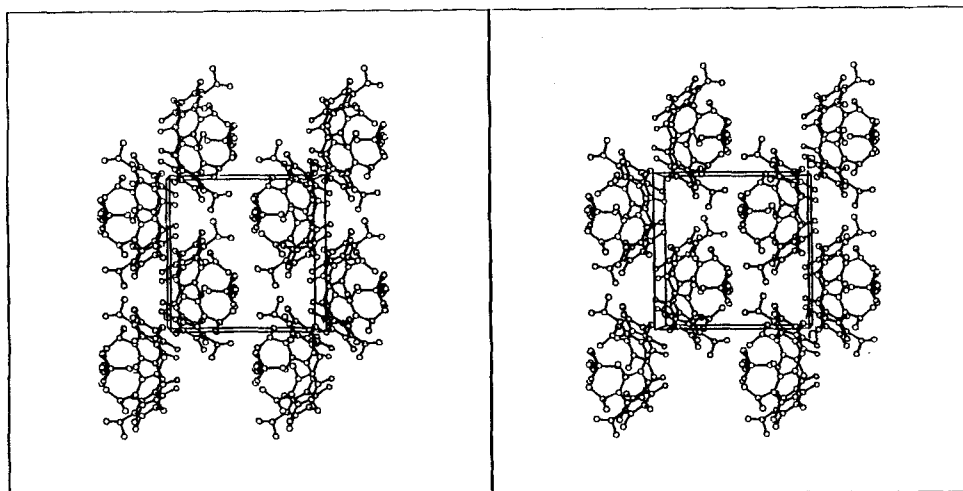


Fig. 4. Stereoscopic view of the crystal structure of the title clathrate along the a -axis.

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