Molecular Inclusion in Functionalized Macrocycles. Part 6.† The Crystal and Molecular Structures of the Calix[4]arene from *p*-(1,1,3,3-Tetramethylbutyl)phenol and its 1 : 1 Complex with Toluene ‡

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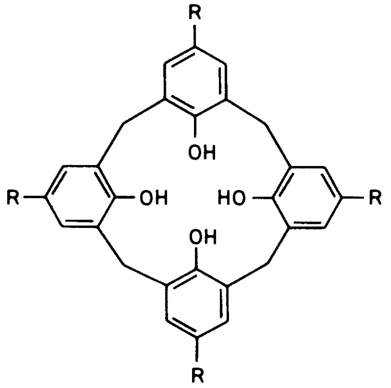
The cyclic tetramer (1a) isolated from the reaction mixture of the base-catalysed reaction of *p*-(1,1,3,3-tetramethylbutyl)phenol and formaldehyde crystallizes from acetone without including the solvent whereas in the presence of toluene a 1 : 1 complex between (1a) and toluene is formed. Crystals of the empty phase are monoclinic, space group $P2_1/a$, a = 12.753(8), b = 38.778(16), c = 11.370(7) Å, β = 101.98(9)°, Z = 4, final R value 0.092; the toluene complex is orthorhombic, space group $Fmm2$, a = 21.227(16), b = 21.227(17), c = 14.522(14) Å, Z = 4, final R value 0.069. The macrocycle exists in the cone conformation both in the empty form and in the complex, where the guest molecule occupies intermolecular cavities of channel type in the host lattice.

Calixarenes[1] are a class of synthetic macrocycles having phenolic residues in a cyclic array linked by methylene groups at positions *ortho* of the hydroxy groups. Some of them are able to form inclusion complexes with several organic guest molecules; their structures have been elucidated by us by *X*-ray diffraction methods.[2-5] We have preferred *X*-ray analysis for the study of the inclusion behaviour of these macrocycles since it allows the unequivocal establishment of the structure of the complex, showing in particular whether a guest can occupy the intramolecular cavities. This is of fundamental importance when studying the ' neutral molecule ' complexes[6] of natural hosts such as cyclodextrins[7] or synthetic ones such as phanes,[6,8] cavitands,[9] and speleands[10] since all these systems have been considered as potential enzyme models.

The calix[4]arene (1b) derived from *p*-t-butylphenol has been shown to form 1 : 1 inclusion complexes with aromatic guest molecules which always occupy intramolecular cavities, whereas the intermolecular cavities of the host lattice remain empty.[2,11] However, our previous studies have also shown that this is not always the case and the inclusion behaviour of these compounds depends on several factors such as the size of the macro-ring,[3,5] the nature of the substituents in the *para*-position of the starting phenol,[11] and the conformational rigidity of the macrocycle.[4]

As a part of our systematic work on the inclusion properties of calixarenes, we report in this paper the crystal and molecular structure of the empty form of calix[4]arene (1a) derived from *p*-(1,1,3,3-tetramethylbutyl)phenol (*p*-octylphenol) and its 1 : 1 complex with toluene. The isolation of this macrocycle in a pure form from the reaction mixture of the base-catalysed condensation of *p*-octylphenol and formaldehyde and its characterization has been reported elsewhere.[12]

This paper also gives definitive proof of our structural assignment of a compound for which some confusion exists in the literature.[13,14] Compound (1a) corresponds to the low melting material (LOC) isolated by Cornforth *et al.*[13] whereas the high melting product (HOC) of these authors has been shown to be the cyclic octamer[15] and corresponds to the compound studied by Munch.[14]



(1) a; R = 1,1,3,3-tetramethylbutyl (LOC)
b; R = Bu^t (LBC)
c; R = H

X-*Ray Structure Analysis*.—*LOC* (1a) *empty form*. The crystals were prepared by dissolving the unsolvated host[12] in acetone and are colourless, rough prisms elongated on [001]. Lattice parameters were refined by least-squares by use of $29(\theta,\chi,\varphi)_{hkl}$ measurements taken on a Siemens AED single-crystal diffractometer on line to a General Automation Jumbo 220 minicomputer.[16] A crystal specimen of 0.6 × 0.2 × 0.8 mm was used for data collection.

Crystal data. $C_{60}H_{88}O_4$, M = 873.4. Monoclinic, a = 12.753(8), b = 38.778(16), c = 11.370(7) Å, β = 101.98(9)°, U = 5 500(5) Å^3, Z = 4, D_c = 1.055 g cm^{-3}, $F(000)$ = 1 920, Cu-K_α radiation, λ = 1.541 78 Å, μ(Cu-K_α) = 4.6 cm^{-1}. Absent spectra: $h0l$ $h \neq 2n$, $0k0$ $k \neq 2n$ define space group $P2_1/a$ (C_{2h}^5, No. 14, non-standard setting; apply matrix $||001/010/100||$ to transform in the standard setting $P2_1/c$).

Intensity data were collected up to θ 70° by using the ω–2θ step-scanning mode with nickel-filtered Cu-K_α radiation. The method described in ref. 17 was used to analyse the reflection profiles. One standard reflection recorded every hour showed no significant fluctuation in intensity. 4 707 significant reflections with $I > 3\sigma(I)$ [$\sigma(I)$ based on counting statistics] have been retained out of a total of 10 495 measured reflections. No corrections were made for absorption.

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† Part 5, ref. 5.

‡ Presented in part at the 1st International Symposium on Clathrate Compounds and Molecular Inclusion Phenomena, Yakranka (Warsaw), 1980.

Table 1. LOC. Fractional atomic co-ordinates (× 10^4)

	x/a	y/b	z/c		x/a	y/b	z/c
O(1)	840(2)	1 350(1)	5 887(3)	O(1″)	1 263(2)	2 149(1)	7 964(3)
C(1)	1 408(3)	1 048(1)	6 230(4)	C(1″)	2 018(4)	2 141(1)	9 050(4)
C(2)	2 385(3)	998(1)	5 918(4)	C(2″)	1 627(4)	2 035(1)	10 085(5)
C(3)	2 919(3)	695(1)	6 237(4)	C(3″)	2 364(4)	2 032(1)	11 159(5)
C(4)	2 530(4)	437(1)	6 877(4)	C(4″)	3 437(4)	2 128(1)	11 257(5)
C(5)	1 551(3)	498(1)	7 188(4)	C(5″)	3 764(4)	2 223(1)	10 214(5)
C(6)	988(3)	800(1)	6 870(4)	C(6″)	3 050(4)	2 230(1)	9 087(4)
C(7)	3 194(4)	107(1)	7 271(4)	C(7″)	4 292(5)	2 097(2)	12 500(5)
C(8)	4 280(4)	228(2)	8 052(6)	C(8″)	3 791(7)	1 904(3)	13 417(7)
C(9)	2 635(5)	−139(1)	8 044(5)	C(9″)	5 266(9)	1 895(4)	12 279(9)
C(10)	3 511(4)	−81(1)	6 173(5)	C(10″)	4 603(13)	2 450(4)	12 980(12)
C(11)	2 648(5)	−293(1)	5 293(5)	C(11″)	4 130(8)	2 725(2)	13 591(9)
C(12)	1 557(5)	−95(2)	4 903(5)	C(12″)	5 115(7)	2 972(3)	13 662(7)
C(13)	2 464(5)	−660(1)	5 780(5)	C(13″)	3 772(10)	2 696(3)	14 772(7)
C(14)	3 212(7)	−348(2)	4 176(6)	C(14″)	3 274(7)	2 822(2)	12 518(9)
C(15)	2 896(4)	1 276(1)	5 272(4)	C(15″)	502(3)	1 908(1)	10 031(5)
O(1′)	2 156(2)	1 887(1)	6 250(3)	O(1‴)	3(2)	1 598(1)	7 687(3)
C(1′)	3 231(3)	1 805(1)	6 625(4)	C(1‴)	163(3)	1 377(1)	8 692(5)
C(2′)	3 894(3)	2 018(1)	7 408(4)	C(2‴)	93(3)	1 036(1)	8 505(4)
C(3′)	4 976(3)	1 937(1)	7 713(4)	C(3‴)	266(3)	818(1)	9 540(4)
C(4′)	5 405(3)	1 653(1)	7 240(4)	C(4‴)	520(3)	958(1)	10 725(4)
C(5′)	4 704(3)	1 448(1)	6 456(4)	C(5‴)	563(3)	1 307(1)	10 815(4)
C(6′)	3 626(3)	1 515(1)	6 124(4)	C(6‴)	388(3)	1 524(1)	9 841(5)
C(7′)	6 627(3)	1 579(1)	7 572(5)	C(7‴)	790(4)	718(1)	11 826(4)
C(8′)	7 254(5)	1 862(2)	8 410(12)	C(8‴)	440(5)	335(1)	11 513(5)
C(9′)	7 061(6)	1 624(4)	6 436(8)	C(9‴)	169(4)	854(2)	12 795(5)
C(10′)	6 930(5)	1 224(2)	7 990(10)	C(10‴)	2 003(3)	758(1)	12 438(4)
C(11′)	6 715(5)	1 121(3)	9 393(7)	C(11‴)	2 900(4)	691(2)	11 717(5)
C(12′)	7 427(6)	1 244(3)	10 541(7)	C(12‴)	2 856(5)	320(2)	11 173(6)
C(13′)	5 490(4)	1 153(2)	9 420(6)	C(13‴)	2 947(4)	971(2)	10 735(5)
C(14′)	7 073(7)	725(3)	9 286(8)	C(14‴)	3 960(4)	721(2)	12 711(5)
C(15′)	3 482(3)	2 323(1)	7 977(4)	C(15‴)	−80(3)	861(1)	7 302(4)

Structure analysis and refinement. The structure was solved at the first trial by direct methods using the SHELX system of computer programs.[18] The E map computed with the most consistent set of signs revealed the positions of all non-hydrogen atoms. The approximate atomic parameters were adjusted by several cycles of full-matrix least-squares calculations first with isotropic and then with anisotropic temperature factors. The final R value was 0.092 (unit weights). No attempts have been made to locate or to refine the hydrogen atoms because of limitations of the core of the computer. The final difference electron-density map showed the highest residual peaks of *ca.* 0.9 e Å^{-3} mainly located where the hydrogen positions were expected so no clathrated, ordered molecules are present in the crystal at least at the level of significance of X-ray analysis. Plots of $|\Delta F|$ as a function of scattering angle, magnitude of $|F_o|$, and Miller indices revealed a linear trend. The largest $|\Delta F|$ are at low scattering angles as usually found when, for low absorbing organic materials, the hydrogen atoms are omitted.

Calculations were carried out on the CDC Cyber 76 computer of CINECA, Casalecchio, Bologna. Scattering factors were taken from ref. 19. Atomic fractional co-ordinates are listed in Table 1 and various parameters connected with the molecular geometry are listed in Table 2.

LOC (1a)*-Toluene* 1 : 1 *Complex.*—Crystals were obtained after dissolving the unsolvated host in acetone containing 10% toluene and are colourless bipyramids elongated on [001]. A crystal specimen of 0.3 × 0.3 × 0.5 mm was sealed in a Lindeman capillary in the presence of some toluene. Lattice parameters were refined by least-squares by use of $26(\theta,\chi,\varphi)_{hkl}$ measurements taken on the same diffractometer.

Crystal data. $C_{60}H_{88}O_4{\cdot}C_7H_8$, $M = 965.4$. Orthorhombic, $a = 21.227(16)$, $b = 21.227(17)$, $c = 14.522\ (14)$ Å, $U = 6\,543(9)$ Å^3, $Z = 4$, $D_c = 0.98$ g cm^{-3}, $F(000) = 2\,112$. Cu-K_α radiation, $\lambda = 1.54\,178$ Å, $\mu(\text{Cu-}K_\alpha) = 4.2$ cm^{-1}. Absent spectra: $hkl\ h + k \neq 2n, k + l \neq 2n, l + h \neq 2n$ define space groups $Fmmm$ or $Fmm2$ (D_{2h}^{23}, No. 69 or C_{2v}^{18}, No. 42) and the latter was confirmed by the analysis.

Intensity data were collected up to θ 70° by use of the ω–2θ step-scanning mode. 5 132 $\pm h,k,l$ reflections have been measured of which 2 926 have been considered significant having $I > 3\sigma(I)$ [$\sigma(I)$ based on counting statistics]. After merging equivalent reflections, with an internal consistency of 2%, a set of 1 072 unique reflections was retained and used for the structure analysis.

Structure analysis and refinement. Several attempts have been made to solve the structure by direct methods but all were unsuccessful. At the end it was solved by trial and error assuming for the molecule a C_{2v} symmetry, with the planes passing through the bridging methylene group or through the phenolic rings and using the geometry found in the empty phase. The correct structure gave the lowest R factor. The refinement was carried out by full-matrix least-squares methods with anisotropic thermal parameters. The hydrogen atoms were included in the refinement in their geometrically constructed positions with C–H 1.08 Å and with variable isotropic thermal parameters. The final R value was 0.069 (unit weights). The final difference electron-density map did not show residual peaks >0.4 e Å^{-3} and plots of $|\Delta F|$ as a function of scattering angle, magnitude of $|F_o|$, and Miller indices revealed a linear trend.

Scattering factors were taken from ref. 19. Atomic fractional co-ordinates are listed in Table 3 and bond distances, bond angles, and selected torsional angles are listed in Table 4.

Observed and calculated structure factors and anisotropic

Table 2. LOC. Bond distances (Å), bond angles (°), and selected torsion angles (°)

	Distances			
		′	″	‴
O(1)–C(1)	1.390(5)	1.386(5)	1.399(5)	1.409(6)
C(1)–C(2)	1.378(6)	1.370(5)	1.430(8)	1.340(6)
C(1)–C(6)	1.380(6)	1.400(6)	1.352(7)	1.399(8)
C(2)–C(3)	1.369(5)	1.387(5)	1.378(7)	1.428(6)
C(2)–C(15)	1.524(6)	1.495(6)	1.506(7)	1.501(6)
C(3)–C(4)	1.388(6)	1.387(6)	1.400(7)	1.426(6)
C(4)–C(5)	1.387(7)	1.377(5)	1.386(8)	1.357(6)
C(4)–C(7)	1.549(6)	1.552(5)	1.599(7)	1.540(7)
C(5)–C(6)	1.382(5)	1.373(5)	1.410(7)	1.372(7)
C(7)–C(8)	1.554(7)	1.561(10)	1.527(12)	1.570(6)
C(7)–C(9)	1.566(8)	1.517(11)	1.533(15)	1.575(8)
C(7)–C(10)	1.569(7)	1.481(9)	1.496(17)	1.567(6)
C(10)–C(11)	1.559(7)	1.721(14)	1.469(14)	1.561(8)
C(11)–C(12)	1.570(9)	1.505(11)	1.568(15)	1.562(11)
C(11)–C(13)	1.562(6)	1.573(9)	1.509(15)	1.567(10)
C(11)–C(14)	1.598(11)	1.613(16)	1.506(13)	1.576(7)
C(15)–C(6′)	1.513(6)	1.521(7)	1.507(6)	1.559(6)

	Angles			
		′	″	‴
O(1)–C(1)–C(6)	119.9(4)	118.4(4)	120.6(4)	118.5(4)
O(1)–C(1)–C(2)	119.5(4)	120.0(4)	116.0(4)	118.6(5)
C(2)–C(1)–C(6)	120.6(4)	121.5(4)	123.4(5)	123.0(4)
C(1)–C(2)–C(15)	121.6(4)	122.2(4)	123.5(5)	125.7(4)
C(1)–C(2)–C(3)	118.6(4)	118.3(4)	116.2(5)	117.4(4)
C(3)–C(2)–C(15)	119.7(4)	119.5(4)	120.2(5)	116.8(4)
C(2)–C(3)–C(4)	123.1(4)	122.3(4)	122.9(5)	121.3(4)
C(3)–C(4)–C(7)	120.9(4)	120.6(4)	121.7(5)	120.4(4)
C(3)–C(4)–C(5)	116.7(4)	117.0(4)	117.7(5)	116.6(4)
C(5)–C(4)–C(7)	122.3(4)	122.4(4)	120.3(6)	122.8(4)
C(4)–C(5)–C(6)	121.6(4)	123.2(4)	122.0(5)	123.6(4)
C(1)–C(6)–C(5)	119.4(4)	117.7(4)	117.7(5)	118.1(4)
C(15)–C(6′)–C(5′)	120.5(4)	118.8(5)	119.7(4)	119.2(4)
C(15)–C(6′)–C(1′)	121.8(4)	123.5(4)	122.1(4)	121.4(4)
C(4)–C(7)–C(10)	111.7(4)	115.6(4)	109.5(7)	109.6(4)
C(4)–C(7)–C(9)	112.4(4)	107.3(5)	108.7(6)	107.8(4)
C(4)–C(7)–C(8)	106.5(4)	112.3(4)	109.6(6)	112.5(4)
C(9)–C(7)–C(10)	112.7(3)	105.3(7)	111.4(9)	104.5(4)
C(8)–C(7)–C(10)	104.4(4)	113.0(6)	108.4(8)	113.7(4)
C(8)–C(7)–C(9)	108.6(4)	102.0(6)	109.3(8)	108.3(4)
C(7)–C(10)–C(11)	119.4(5)	115.6(6)	108.9(9)	120.9(4)
C(10)–C(11)–C(14)	101.9(5)	92.8(7)	95.6(8)	102.9(4)
C(10)–C(11)–C(13)	113.0(5)	110.5(6)	126.6(11)	113.5(5)
C(10)–C(11)–C(12)	112.9(4)	123.2(7)	93.7(10)	113.0(5)
C(13)–C(11)–C(14)	106.6(4)	112.0(6)	115.9(9)	107.8(5)
C(12)–C(11)–C(14)	111.1(5)	103.8(7)	109.1(7)	107.9(6)
C(12)–C(11)–C(13)	110.9(5)	112.4(6)	112.7(7)	111.1(5)
C(2)–C(15)–C(6′)	113.1(4)	113.1(3)	113.1(4)	112.5(4)

	Torsion angles			
		′	″	‴
C(1)–C(2)–C(15)–C(6′)	90.9(5)	83.1(5)	89.2(6)	85.6(6)
C(3)–C(2)–C(15)–C(6′)	−86.8(5)	−94.2(5)	−86.4(6)	−90.1(5)
C(1)–C(6)–C(15′)–C(2′)	−87.6(6)	−89.7(6)	−87.9(6)	−88.0(6)
C(5)–C(6)–C(15′)–C(2′)	89.2(5)	87.9(5)	88.5(6)	87.9(6)
C(5)–C(4)–C(7)–C(10)	127.6(5)	−52.0(7)	75.5(9)	−65.0(6)
C(3)–C(4)–C(7)–C(10)	−55.5(6)	129.3(7)	−110.2(8)	111.5(5)
C(4)–C(7)–C(10)–C(11)	−75.5(6)	−71.1(8)	76.2(18)	−57.6(6)

thermal parameters are listed for both structures in Supplementary Publication No. SUP 23707 (40 pp.).*

Molecular Geometry.—In Figure 1 are given the projections of the molecules on the plane of the four phenolic oxygen atoms. The conformation of the macrocycle is very similar in the two crystal structures and mainly determined by intramolecular hydrogen bonds [in LOC: O(1)···O(1′) =

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* For details of Supplementary Publications see Instructions for Authors, *J. Chem. Soc., Perkin Trans. 2*, 1983, Issue 1.

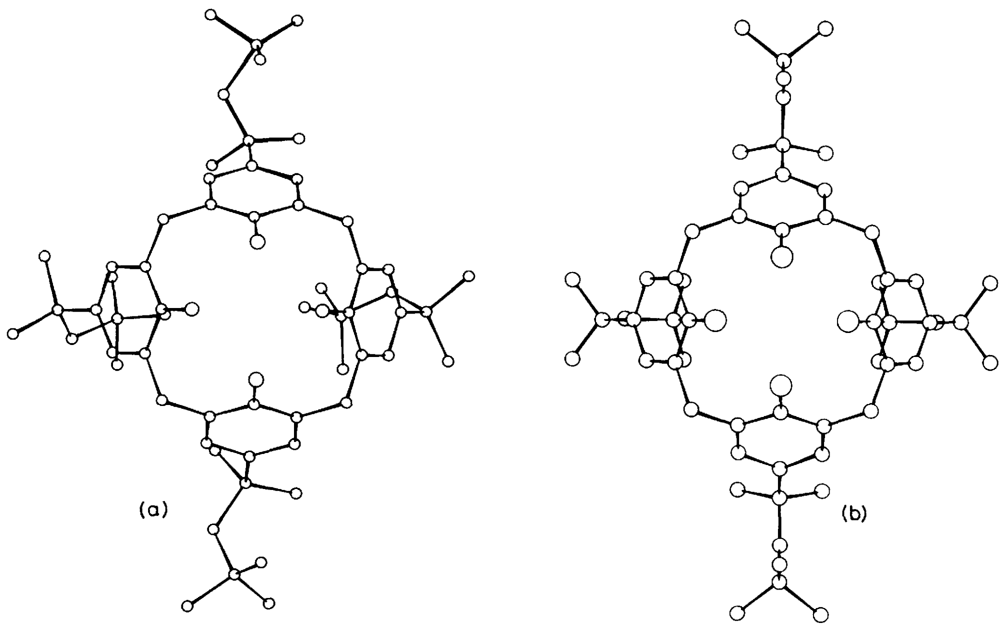

Figure 1. Projection of the molecules on the plane of phenolic oxygen atoms: a, LOC; b, LOC–toluene complex

Table 3. LOC–toluene complex. Fractional atomic co-ordinates

	x/a	y/b	z/c
O(1)	890(3)	0	25(7)
C(1)	1 238(4)	0	−778(8)
C(2)	1 418(3)	573(3)	−1 178(7)
C(3)	1 798(3)	553(3)	−1 968(7)
C(4)	1 985(5)	0	−2 367(9)
C(7)	2 400(7)	0	−3 247(10)
C(8)	2 797(10)	−535(8)	−3 330(16)
C(10)	2 082(12)	0	−4 085(16)
C(11)	1 444(14)	0	−4 498(17)
C(12)	1 307(13)	533(9)	−5 092(17)
C(13)	863(13)	0	−3 806(23)
C(15)	1 202(3)	1 201(3)	−787(8)
O(1′)	0	870(3)	0
C(1′)	0	1 230(4)	−818(8)
C(2′)	578(3)	1 408(3)	−1 194(7)
C(3′)	560(4)	1 779(3)	−1 979(7)
C(4′)	0	1 983(5)	−2 384(9)
C(7′)	0	2 382(5)	−3 264(9)
C(8′)	−567(8)	2 278(9)	−3 831(11)
C(10′)	−320(8)	3 021(7)	−3 065(12)
C(11′)	0	3 517(6)	−2 401(10)
C(12′)	−556(7)	3 954(8)	−2 570(13)
C(13′)	0	3 282(7)	−1 391(10)
C(1t)	2 500	2 500	2 778(33)
C(2t)	2 090(12)	2 098(11)	3 418(33)
C(3t)	2 243(15)	2 211(17)	4 436(31)
C(4t)	2 500	2 500	5 400(69)
C(5t)	2 500	2 500	1 889(70)

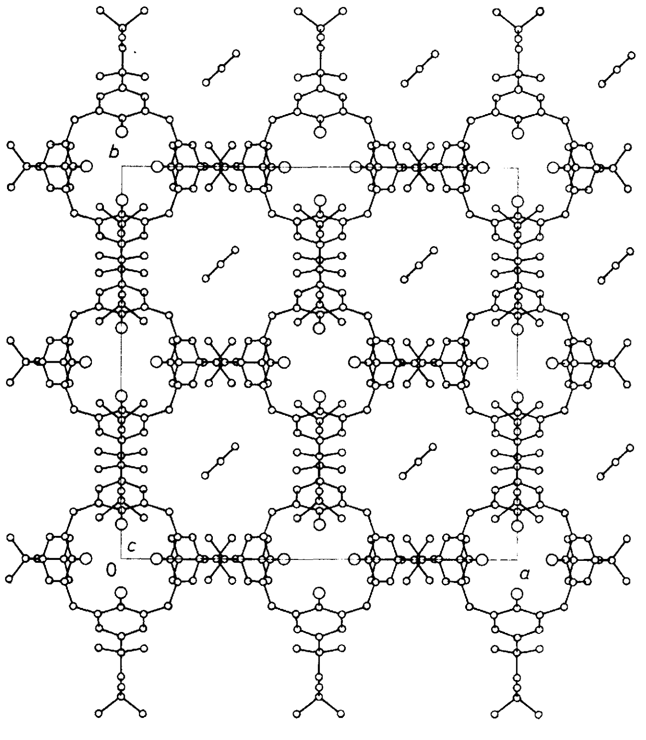

Figure 2. Molecular packing diagram along [001] of LOC–toluene complex

2.653(8), O(1′)···O(1″) = 2.655(9), O(1″)···O(1‴) = 2.653(8), O(1‴)···O(1) = 2.676(9) Å; in LOC–toluene complex: O(1)···O(1′) = 2.640(10), O(1)···O(1″) = 2.630(10) Å]. The inclination of the phenyl rings with respect to the normal of the four oxygens plane are 121.4(3), 128.6(4), 121.4(3), 122.9(3)° in LOC and 124.7(3), 125.0(4)° in LOC–toluene complex, to be compared with 123(1)° observed in the *p*-t-butylcalix[4]arene [2] (1b). So the intramolecular hydrogen bonds are mainly responsible of the conformation of the macrocycle while steric effects due to *para*-substitution to phenyl rings seem to play a limited role.

Apart from small but significant differences the orientation of the octyl chains are similar in the two structures. Two of them, *trans* to each other, point inside (see Figure 1) and the other two extend outside the intramolecular cavity [in the structure of LOC–toluene complex the methylene carbon atom of the alkyl chain, C(11′), lies in a special position but it is disordered and it should have a conformation as observed in LOC with an average position on the plane of symmetry]. So the cavity is partly filled by the alkyl chain and, at least in the solid state, it is not possible to have inclusion compounds with the guest

Table 4. LOC–toluene complex. Bond distances (Å), bond angles (°), and selected torsion angles (°)

	Distances	
O(1)–C(1)	1.380(14)	1.413(11)
C(1)–C(2)	1.401(9)	1.395(9)
C(2)–C(3)	1.403(12)	1.386(13)
C(3)–C(4)	1.368(9)	1.395(11)
C(4)–C(7)	1.552(19)	1.533(17)
C(7)–C(8)	1.420(20)	1.475(18)
C(7)–C(10)	1.392(30)	1.544(18)
C(10)–C(11)	1.481(38)	1.581(20)
C(11)–C(12)	1.452(30)	1.522(18)
C(11)–C(13)	1.591(40)	1.549(20)
C(15)–C(2′)		1.516(10)
C(1t)–C(2t)	1.53(5)	
C(1t)–C(5t)	1.30(11)	
C(2t)–C(3t)	1.53(6)	
C(3t)–C(4t)	1.62(9)	

	Angles	′
O(1)–C(1)–C(2)	119.8(3)	118.4(7)
C(2)–C(1)–C(6)	120.5(5)	120.9(7)
C(1)–C(2)–C(3)	118.0(5)	116.8(7)
C(1)–C(2)–C(15)	121.6(6)	122.5(7)
C(3)–C(2)–C(15)	120.4(6)	120.6(6)
C(2)–C(3)–C(4)	122.6(6)	123.1(7)
C(3)–C(4)–C(5)	118.2(5)	118.6(4)
C(3)–C(4)–C(7)	120.9(3)	121.5(4)
C(4)–C(7)–C(8)	114.0(8)	112.5(10)
C(4)–C(7)–C(10)	116.4(15)	109.2(9)
C(7)–C(10)–C(11)	142.9(3)	120.7(1)
C(10)–C(11)–C(12)	102.7(3)	89(1)
C(10)–C(11)–C(13)	116.9(3)	111
C(12)–C(11)–C(13)	102.7(9)	110

Torsion angles	
C(5)–C(6)–C(15′)–C(2′)	90(1)
C(1)–C(6)–C(15′)–C(2′)	−89(1)
C(5)–C(4)–C(7)–C(8)	151(2)
C(5)–C(4)–C(7)–C(10)	−90(2)
C(4)–C(7)–C(10)–C(11)	0
C(7)–C(10)–C(11)–C(12)	121(3)
C(7)–C(10)–C(11)–C(13)	0
C(3′)–C(2′)–C(15)–C(6)	−91(1)
C(1′)–C(2)–C(15)–C(6)	88(1)
C(5′)–C(4′)–C(7′)–C(8′)	150(1)
C(5′)–C(4′)–C(7′)–C(10′)	−120(1)
C(4′)–C(7′)–C(10′)–C(11′)	68(2)
C(7′)–C(10′)–C(11′)–C(12′)	180(2)
C(7′)–C(10′)–C(11′)–C(13′)	−69(2)

interacting inside a host cavity as observed for the first time in the crystal structure of *p*-t-butylcalix[4]arene.[2]

Figure 2 shows the [001] molecular packing diagram of the LOC–toluene complex and Figures 3 and 4 show the packing of empty LOC along [100] and along the normal to the plane of the four oxygens of the macrocycle, respectively (Figure 4 shows the difference of packing of guest molecules with respect to that of the toluene complex of Figure 2). In the toluene complex the guest molecules interact with the channels mainly by van der Waals contacts with the aliphatic chains. By using computing procedures for the molecular packing analysis [20] with the potentials given in ref. 21 the motion of the host molecules in the channels has been analysed. Figure 5 shows the equipotential lines with 0.1 kcal mol^{-1} contours. The minimum at 0 Å and 0° corresponds to the actual position of the host molecule and a quite small energy loss allows rotation of the molecule around the two-fold axis by *ca.* ±30° or a translation along the channel which goes like a screw with a 90° rotation for a *c*/2 translation. This could explain the lack of selectivity shown by crystallization experiments from mixtures of aromatic solvents.[11]

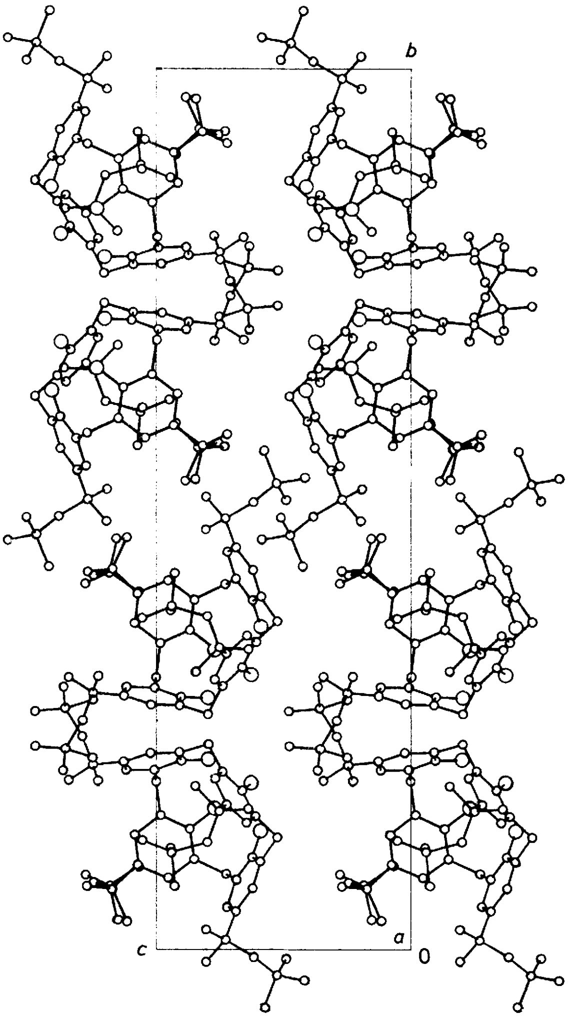

Figure 3. Molecular packing diagram along [100] of LOC

Discussion

The results obtained show first of all that the macrocycle exists, both in the empty form and in the toluene complex in the ' cone ' conformation which is determined by the strong intramolecular hydrogen bonds of the phenolic OH, while steric effects of the *para*-alkyl substituents on the phenyl ring are quite negligible in this respect. However the *para*-substituents are rather important in determining the inclusion behaviour of the macrocycle (1a). In spite of the cone conformation the calix[4]arene (1a) is not able to include the aromatic guest molecule inside the intramolecular cavity as does the calix[4] arene (1b).[2,11] The reason is that two of the four terminal t-butyl groups of the octyl chains in (1a) are pointing into the cavity (Figure 1) partly occupying it and preventing the guest molecule from penetrating. At the same time intermolecular cavities suitable for accommodating the aromatic guest (Figure 2) are formed in the crystals along the [001]

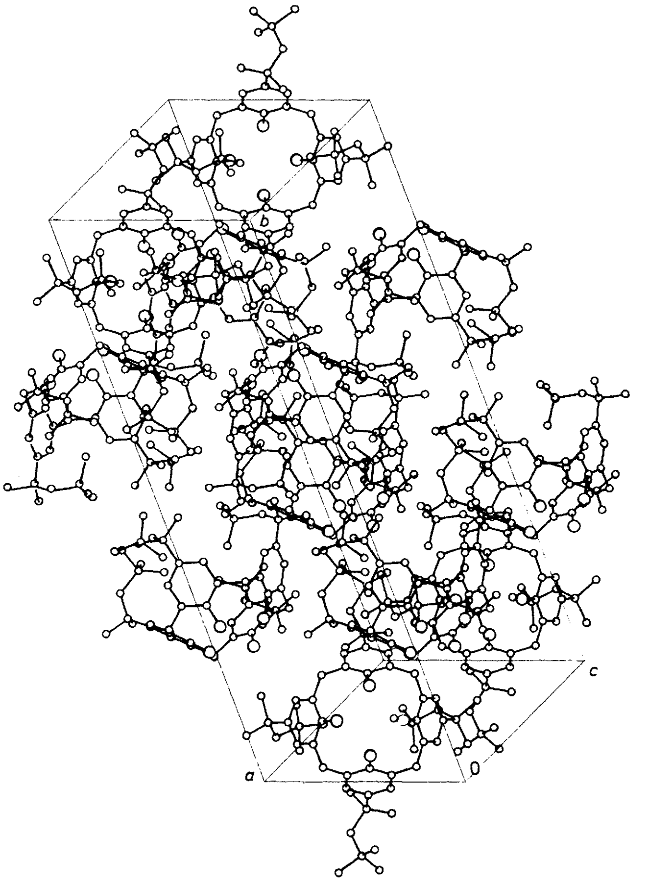

Figure 4. Molecular packing diagram along the calix axis of LOC

axis by the alkyl chains which extend outside the macro-ring. So it is the presence of the aromatic molecules in solution which stabilizes the growth of the observed crystal structure of the complex. Therefore, the transformation of the empty phase (Figure 4) into the clathrate phase does not seem to be a solid-state process. The clathrate is of the channel type [22] and the channels are formed by piles of macrocyclic molecules with the same orientation and with van der Waals contacts between the phenolic oxygen ring and the inside octyl chains of the subsequent molecule. Four such piles with the molecules at x,y,z; $\frac{1}{2} + x,y,\frac{1}{2} + z$; $x,\frac{1}{2} + y,\frac{1}{2} + z$; $\frac{1}{2} + x,\frac{1}{2} + y,z$ define at $\frac{1}{4},\frac{1}{4},z$ the cavity occupied by the toluene molecules. The benzene complex of (1a) is isostructural with the toluene one showing the same cell parameters.[23]

The results of this study confirm our previous observations that, although calixarenes (and particularly the calix[4]arenes) are able to include organic molecules, the complexes do not always have intramolecular host–guest character. They also show that the presence of a ' cone ' conformation [24] in the host macrocycle is not sufficient to ensure the intramolecularity of inclusion since other factors could become predominant. In calix[4]arenes a very special role in stabilizing intramolecular complexes with aromatic molecules seems to be played by the t-butyl groups present at the phenyl nuclei [*e.g.* (1b)]. The size of these substituents is not too large to occlude the cavity, and moreover attractive CH_3–π interactions [25] between the methyl groups and the aromatic moiety of the guest molecules help to enhance the stability of the intramolecular complexes.

If we remove the t-butyl groups from the macrocycle (1a) to obtain the calix[4] arene (1c) the ability to form inclusion complexes with aromatic guest molecules drops dramatically and no such complex has been isolated so far with (1c).

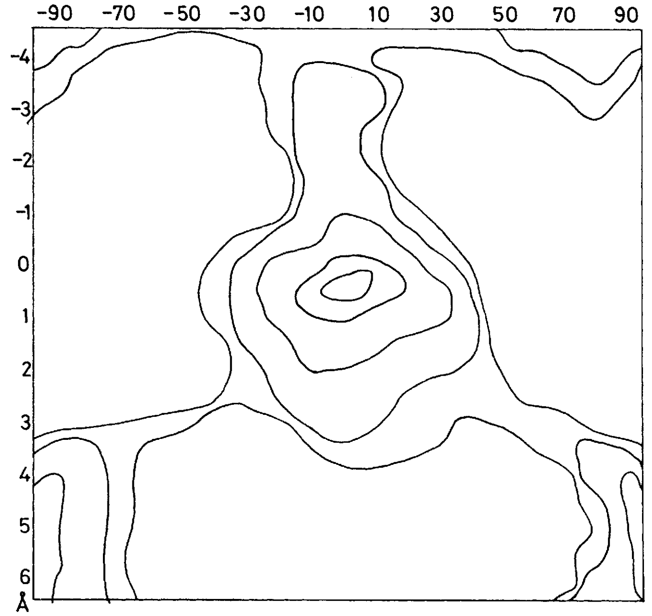

Figure 5. Equipotential lines (0.1 kcal mol^{-1} contours) for rotation and translation along the channel

We can therefore conclude, quoting Hilgenfeld and Saenger,[8] that often ' subtle changes of molecular structure may result in severe changes of inclusion behaviour of a potential host molecule due to the complicated interplay of weak intermolecular forces that govern host–guest complex formation.' The differences in inclusion behaviour can, on the other hand, dramatically influence the guest-selectivity properties of the host molecules as has been also observed with calix[4]-arenes in crystallization experiments from equimolar mixtures of aromatic solvents.[11]

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