Molecular Inclusion in Functionalized Macrocycles. Part 9.[1] The Crystal and Molecular Structure of *p*-t-Butylcalix[4]arene–Anisole (2:1) Complex: a New Type of Cage Inclusion Compound

Rocco Ungaro * and Andrea Pochini
Istituto di Chimica Organica dell'Università di Parma, Via Massimo D'Azeglio 85, 43100 Parma, Italy
Giovanni Dario Andreetti * and Paolo Domiano
Istituto di Strutturistica Chimica dell'Università di Parma, Via Massimo D'Azeglio 85, 43100 Parma, Italy.

p-t-Butylcalix[4]arene (**1a**), the cyclic tetramer obtained by the condensation of *p*-t-butylphenol and formaldehyde, crystallizes from anisole forming a new type of cage inclusion compound with the solvent. Crystals having a 2:1 host–guest stoicheiometry are tetragonal, space group *P*4/*n*, $a = b = 12.823(6)$; $c = 25.618(8)$ Å, $Z = 2$, final *R* values 0.073. Two molecules of the macrocycle, in the cone conformation, face the methyl groups of the *para*-substituents creating a closed cavity which encapsulates one molecule of anisole. The guest is disordered in the cavity in at least eight equivalent orientations.

Calixarenes[2] (**1**), a class of synthetic macrocycles having phenolic residues in a cyclic array linked by methylene groups all *ortho* to the hydroxy groups, are able to form inclusion compounds with several organic neutral guest molecules. The nature of the three dimensional arrangement of these compounds has been elucidated by us by *X*-ray diffraction studies of some crystalline members of the series.[3–7] So far three main types of three dimensional arrangements of the inclusion compounds have been found.

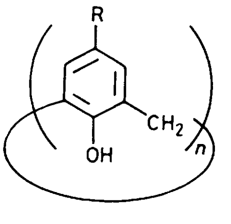
The first type has been shown by *p*-t-butylcalix[4]arene (**1a**) and aromatic molecules such as benzene and toluene;[3] the interactions observed in the crystals have an intramolecular host-guest character and the guest is held inside a molecular cavity. The stabilizing interactions are provided by the methyls of the t-butyl groups with the aromatic nuclei of the guest. These have been the first examples reported of totally synthetic uncharged host–uncharged guest inclusion compounds showing an enclosed cage structure which, from their topology in the solid state[3] could be classified as *criptato-cavitate* clathrato-complexes according to the classification and nomenclature recently proposed by Weber and Josel.[8] However, if we give a co-ordination significance to the CH_3–π interactions, which act co-operatively to stabilize the guest inside the host cavity, we probably have to consider these inclusion compounds as true molecular complexes rather than clathrates.

A second type of inclusion compounds, which can be classified as *tubulato*-clathrates, has been observed in the case of *p*-'octyl'calix[4]arene (**1b**) and toluene or benzene as guests[7] (1:1 stoicheiometry) and with calix[4]arene (**1c**) and acetone or tetrachloroethylene (3:1 host:guest stoicheiometry).[1]

Finally the last type, which can be conveniently indicated as *intercalato*-clathrate, has been observed only in the orthorhombic phase of the 1:1 inclusion compound between calix[4]arene (**1c**) and acetone.[1]

As a part of our systematic work on the inclusion properties of calixarenes we report now the crystal and molecular structure of a new type of *criptato-cavitate* inclusion compound formed by *p*-t-butylcalix[4]arene (**1a**) with anisole, which show 2:1 host–guest stoicheiometry. Crystals were obtained by slow evaporation of a solution of the macrocycle in anisole.

X-Ray Structure Analysis.—Crystals are transparent colourless tetragonal uniaxial plates. 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 microcomputer.[9] A crystal specimen of $0.4 \times 0.4 \times 0.1$ mm was used for data collection.



(**1**) R = H, Bu^t, octyl, n = 4–8
(**1a**) R = Bu^t, n = 4
(**1b**) R = 1,1,3,3,-tetramethylbutyl [octyl], n = 4
(**1c**) R = H, n = 4

Crystal data. $2C_{44}H_{56}O_4 \cdot C_7H_8O$, $M = 1\,406.0$. Tetragonal, $a = b = 12.823(6)$, $c = 25.618(8)$ Å, $U = 4\,212(4)$ Å^3, $Z = 2$, $D_c = 1.11$ g cm^{-3}, $F(000) = 1\,524$, Cu-K_α radiation, $\lambda = 1.541\,78$ Å, μ(Cu-K_α) = 5.08 cm^{-1}. Absent spectra: $hk0$ $h+k \neq 2n$ define space group $P4/n$ ($C_{4h}{}^3$, No. 85).

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. 10 was used to analyse the reflection diffraction profiles. One standard reflection recorded every hour showed no significant fluctuation in intensity. 2 088 significant reflections with $I > 3\sigma(I)$ [$\sigma(I)$ based on counting statistics] have been retained out of a total of 3 123 measured reflections. No corrections were made for absorption.

Structure analysis and refinement. Several attempts to solve the structure by direct methods were unsuccessful. Several *E* maps computed with the most consistent sets of signs gave always strong peaks along the line at 0,0,*z*. As the *a* and *b* cell parameters are quite similar to those observed for the toluene clathrate[3] and the *c* axis almost double, it was decided to use the atomic parameters obtained for that compound as starting values for a trial structure with the degrees of freedom of a rotation and a translation around and along the *c* axis. A set of structure factor computations gave a rough estimate of the position of one molecule and the signs of the structure factors determined in this way were extended by standard procedures based on tangent formula techniques. The computed *E* map revealed the position of all non-hydrogen atoms of the macrocycles. 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 *R* value at this stage was 0.15. Some of the hydrogen atoms have been located in a ΔF map and those of the methyl groups have been constructed geometrically with C–H

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

Atom	*x*	*y*	*z*	Atom	*x*	*y*	*z*
O(1)	1 191(2)	3 152(2)	−253(1)	H(4)	453(33)	5 393(37)	1 011(18)
C(1)	677(3)	3 419(3)	206(2)	H(6)	−1 046(36)	2 430(35)	1 060(19)
C(2)	845(3)	4 394(3)	424(2)	H(71)	1 629(30)	5 106(31)	−137(17)
C(3)	267(3)	4 662(3)	860(2)	H(72)	1 314(33)	5 901(36)	350(17)
C(4)	−452(3)	3 989(4)	1 087(2)	H(91)	−2 476(5)	3 411(7)	1 288(4)
C(5)	−565(3)	3 012(3)	862(2)	H(92)	−2 715(5)	4 727(7)	1 127(4)
C(6)	−14(3)	2 710(3)	427(2)	H(93)	−2 520(5)	4 364(7)	1 784(4)
C(7)	1 619(3)	5 160(4)	203(2)	H(101)	−119(8)	5 421(6)	1 795(4)
C(8)	−1 113(4)	4 292(4)	1 557(2)	H(102)	−1 362(8)	5 666(6)	2 063(4)
C(9)	−2 294(5)	4 210(7)	1 385(4)	H(103)	−1 125(8)	5 913(6)	1 396(4)
C(10)	−947(8)	5 405(6)	1 720(4)	H(111)	−1 263(9)	3 473(7)	2 383(3)
C(11)	−969(8)	3 511(7)	1 989(3)	H(112)	−169(8)	3 774(7)	1 994(3)
O(1′)	3 810(3)	3 152(2)	5 254(1)	H(113)	−1 009(8)	2 747(7)	1 813(3)
C(1′)	4 318(3)	3 420(4)	4 794(2)	H(4′)	4 616(36)	5 395(38)	4 000(19)
C(2′)	4 157(3)	4 390(3)	4 574(2)	H(6′)	6 142(38)	2 488(36)	3 988(19)
C(3′)	4 737(4)	4 660(4)	4 138(2)	H(71′)	3 367(35)	5 133(35)	5 172(19)
C(4′)	5 451(4)	3 989(4)	3 913(2)	H(72′)	3 663(40)	5 845(42)	4 719(20)
C(5′)	5 564(4)	3 011(4)	4 139(2)	H(91′)	7 360(5)	4 841(7)	3 889(4)
C(6′)	5 014(3)	2 710(3)	4 577(2)	H(92′)	7 727(5)	4 410(7)	3 261(4)
C(7′)	3 375(4)	5 158(4)	4 800(2)	H(93′)	7 609(5)	3 507(7)	3 777(4)
C(8′)	6 124(5)	4 297(5)	3 446(2)	H(101′)	5 159(8)	5 426(6)	3 146(4)
C(9′)	7 295(5)	4 213(7)	3 610(4)	H(102′)	6 460(8)	5 682(6)	2 961(4)
C(10′)	5 963(8)	5 403(6)	3 271(4)	H(103′)	6 059(8)	5 893(6)	3 611(4)
C(11′)	5 967(8)	3 539(8)	3 009(3)	H(111′)	5 148(8)	3 643(8)	2 926(3)
O(1)an	2 310(19)	3 455(14)	2 042(8)	H(112′)	6 114(8)	2 733(8)	3 105(3)
C(1)an	2 617(43)	3 017(30)	3 433(8)	H(113′)	6 420(8)	3 754(8)	2 670(3)
C(2)an	2 957(26)	3 475(13)	2 939(9)				
C(3)an	2 708(31)	2 932(13)	2 482(8)				
C(4)an	2 250(76)	2 887(32)	1 569(9)				

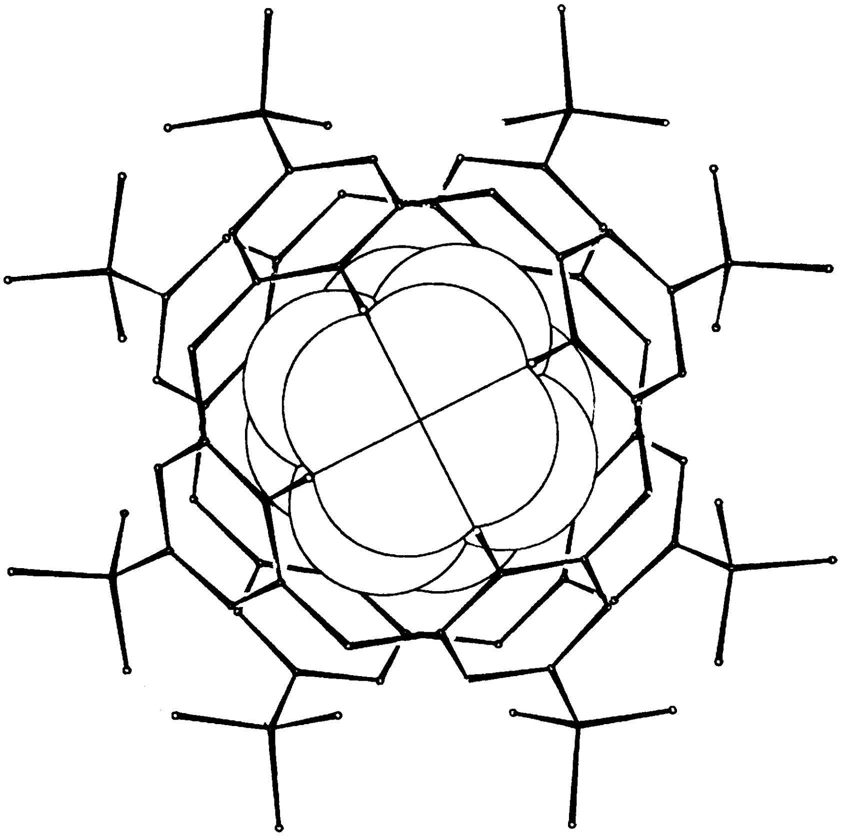
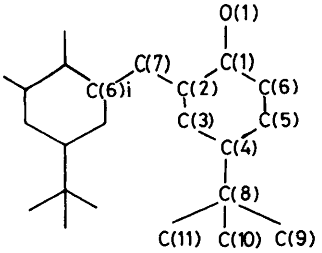


Figure 1. Perspective view of the molecular cavity along the four-fold axis. The anisole atoms have been represented by their van der Waals spheres

Table 2. Bond distances (Å), bond angles (°) and selected torsion angles (°) (atomic numbering. Labels C(J′) refer to atoms belonging to the second independent molecule)



O(1)–C(1)	1.391(6)	O(1′)–C(1′)	1.390(6)
C(1)–C(2)	1.386(6)	C(1′)–C(2′)	1.381(7)
C(1)–C(6)	1.390(6)	C(1′)–C(6′)	1.391(6)
C(2)–C(3)	1.384(6)	C(2′)–C(3′)	1.386(7)
C(2)–C(7)	1.507(6)	C(2′)–C(7′)	1.520(7)
C(3)–C(4)	1.390(6)	C(3′)–C(4′)	1.382(7)
C(4)–C(5)	1.387(7)	C(4′)–C(5′)	1.390(7)
C(4)–C(8)	1.523(7)	C(4′)–C(8′)	1.527(8)
C(5)–C(6)	1.375(7)	C(5′)–C(6′)	1.380(7)
C(7)–C(6)i	1.524(6)	C(7′)–C(6′)i	1.515(7)
C(8)–C(9)	1.581(9)	C(8′)–C(9′)	1.563(9)
C(8)–C(10)	1.502(10)	C(8′)–C(10′)	1.502(10)
C(8)–C(11)	1.504(11)	C(8′)–C(11′)	1.496(11)
O(1)an–C(3)an	1.407(31)		
O(1)an–C(4)an	1.416(36)		
C(1)an–C(2)an	1.462(37)		
C(2)an–C(3)an	1.399(31)		

O(1)–C(1)–C(6)	119.0(4)	O(1′)–C(1′)–C(6′)	118.6(4)
O(1)–C(1)–C(2)	119.3(4)	O(1′)–C(1′)–C(2′)	119.9(4)
C(2)–C(1)–C(6)	121.7(4)	C(2′)–C(1′)–C(6′)	121.5(5)
C(1)–C(2)–C(7)	122.6(4)	C(1′)–C(2′)–C(7′)	121.8(4)
C(1)–C(2)–C(3)	117.8(4)	C(1′)–C(2′)–C(3′)	118.3(4)
C(3)–C(2)–C(7)	122.6(4)	C(3′)–C(2′)–C(7′)	119.9(4)
C(2)–C(3)–C(4)	122.8(4)	C(2′)–C(3′)–C(4′)	122.4(5)
C(3)–C(4)–C(8)	117.1(4)	C(3′)–C(4′)–C(8′)	122.7(5)
C(3)–C(4)–C(5)	120.1(4)	C(3′)–C(4′)–C(5′)	117.2(5)
C(5)–C(4)–C(8)	120.1(4)	C(5′)–C(4′)–C(8′)	120.1(5)
C(4)–C(5)–C(6)	122.5(4)	C(4′)–C(5′)–C(6′)	122.6(5)
C(1)–C(6)–C(5)	118.3(4)	C(1′)–C(6′)–C(5′)	118.0(4)
C(2)–C(7)–C(6)i	112.5(4)	C(2′)–C(7′)–C(6′)i	112.5(4)
C(4)–C(8)–C(11)	110.1(5)	C(4′)–C(8′)–C(11′)	110.0(6)
C(4)–C(8)–C(10)	112.5(5)	C(4′)–C(8′)–C(10′)	113.6(5)
C(4)–C(8)–C(9)	107.2(5)	C(4′)–C(8′)–C(9′)	108.3(5)
C(10)–C(8)–C(11)	114.3(6)	C(10′)–C(8′)–C(11′)	111.8(6)
C(9)–C(8)–C(11)	106.2(6)	C(9′)–C(8′)–C(11′)	106.6(7)
C(9)–C(8)–C(10)	106.1(6)	C(9′)–C(8′)–C(10′)	106.1(6)
C(3)an–O(1)an–C(4)an	117(2)		
C(1)an–C(2)an–C(3)an	117(2)		
O(1)an–C(3)an–C(2)an	121(2)		

C(1)–C(2)–C(7)–C(6)i	−88.3(5)	C(1′)–C(2′)–C(7′)–C(6′)i	−88.5(6)
C(3)–C(2)–C(7)–C(6)i	92.1(5)	C(3′)–C(2′)–C(7′)–C(6′)i	92.0(6)
C(3)–C(4)–C(8)–C(9)	119.9(6)	C(3′)–C(4′)–C(8′)–C(9′)	119.8(6)
C(3)–C(4)–C(8)–C(10)	3.6(8)	C(3′)–C(4′)–C(8′)–C(10′)	2.2(8)
C(3)–C(4)–C(8)–C(11)	−125.1(6)	C(3′)–C(4′)–C(8′)–C(11′)	−124.0(7)

1.08 Å and with a rotation parameter to be adjusted in the refinement. Some more cycles of refinement lowered the *R* factor to 0.11. A ΔF map was then computed and several peaks of *ca.* 0.6(1) e Å^{-3} were found around the centre of the cavity formed by a couple of molecules. Several models have been tested to fit the distribution of the observed peaks and a refinement was tried of the included anisole molecule as a rigid group constructed geometrically on the basis of theoretical bond distances and angles. The refinement converged at *R* 0.073 and the highest residual peak near the anisole position was 0.1 e Å^{-3}. The thermal parameters of the included molecule were kept isotropic and in the refinement converged to a value comparable with that of the macrocycle molecules. Plots of $|\Delta F|$ as a function of scattering angle, magnitude of $|F_0|$, and Miller indices revealed a linear trend.

Atomic fractional co-ordinates are listed in Table 1 and various parameters related to the molecular geometry are listed in Table 2. Thermal parameters are in Supplementary Publication No. SUP 56097 (4 pp.).*

---

* For details of Supplementary Publications see Instructions for Authors in *J. Chem. Soc., Perkin Trans. 2*, 1985, Issue 1.

Discussion

The two independent molecules of the macrocycle possess a four-fold symmetry and the conformation is quite similar to that observed in the *p*-t-butylcalix[4]arene–toluene (1:1) inclusion compound.[3]

The intramolecular hydrogen bonding [O(1)···O(1) i = 2.652(4), O(1′)···O(1′)i = 2.654(5) Å] and the inclination of the phenyl rings with respect to the normal of the plane of the four oxygens [125.8(2), 125.8(3)°] are comparable in the two compounds. The geometry of the macrocycle is practically not influenced by the different packing interactions which act in two crystalline modifications. In Figures 1 and 2 are shown views of the intramolecular cage along the macrocycle four-fold axis and along a direction perpendicular to it respectively, whereas in Figure 3 the crystal packing projected along [001] is represented. The cavity is bimolecular, and is formed by two independent molecules of the macrocycle which face the *p*-t-butyl groups. The macrocycles are rotated about each other by 43.0(2)° to get as close as possible.

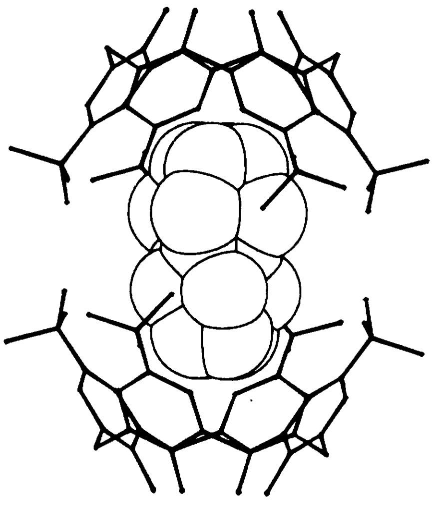


Figure 2. View of the cavity perpendicular to the four-fold axis

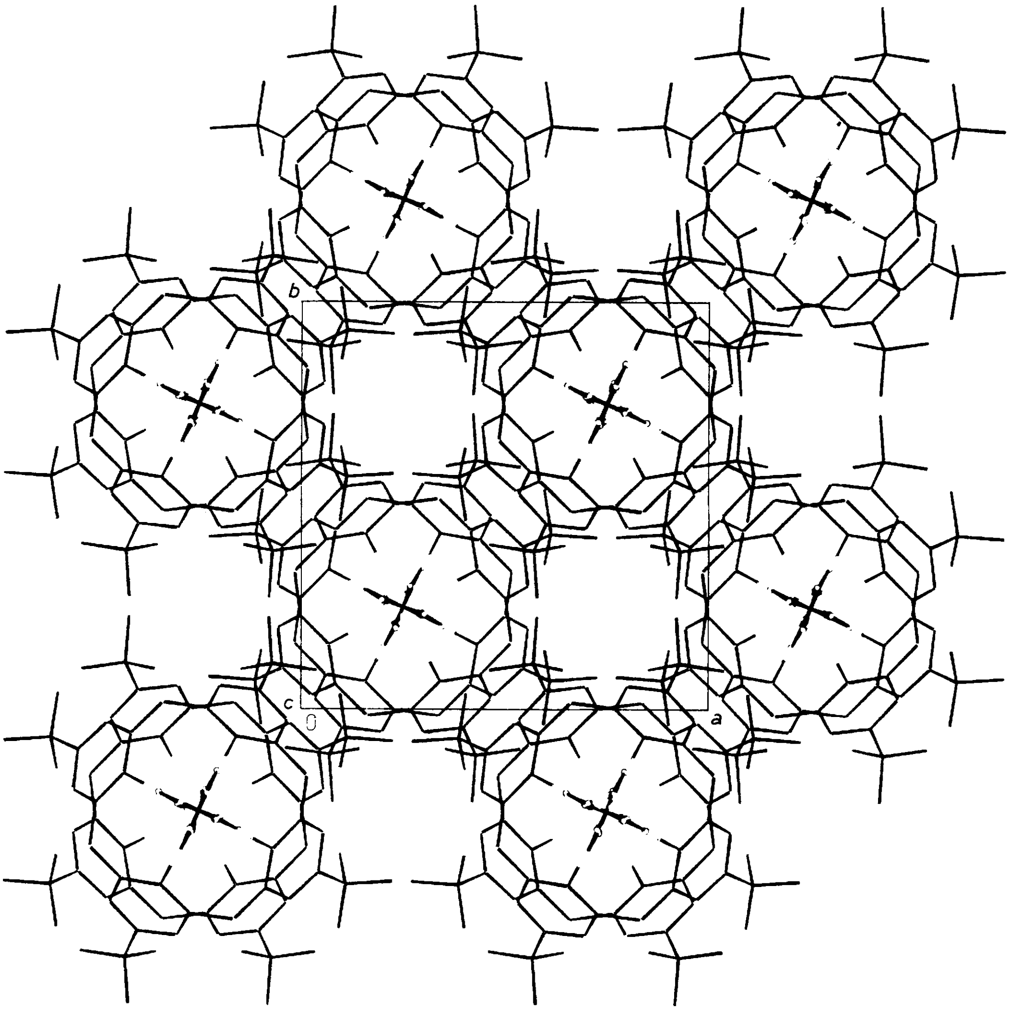


Figure 3. Molecular packing projected along [001]

The intramolecular contacts, H(93)···H(101′) = 2.76(1), H(101)···H(101′) = 2.66(1), H(111)···H(111′) = 2.48(2) Å, involving the methyl groups of the two molecules defining the cage are comparable in length with the intramolecular $CH_3 \cdots CH_3$ contacts. The interactions with the included anisole are mainly due to the methyl C(11) and C(11′) atoms which point inside the cavity with contacts H(111)···O(1)an = 2.89(2), H(111′)···O(1)an = 3.37(2), H(111′)···C(1)an = 3.42(2), H(111′)···C(2)an = 2.97(2), H(111′)···C(3)an = 3.52(2) Å.

The observed topology of this *p*-t-butylcalix[4]arene inclusion compound is a new and, to the best of our knowledge, has not been observed previously with calixarene hosts or in other neutral molecule complexes.[11] It resembles 'sandwich type' complexes of crown ethers with cations of a size larger than the polyether cavity[12] although in our case the uncharged guest is totally encapsulated (criptate) in a closed cage created by two molecules of the macrocycle, whose t-butyl groups interact with the aromatic nucleus of anisole.

Here we have another piece of experimental evidence for attractive interactions between the CH_3 groups of the host and the π-electrons of the guest which, as previously suggested,[7] determine the stability of these inclusion compounds and their intramolecular character. Although there is no conclusive theoretical interpretation of the nature of these attractive non-bonded interactions, several other experimental facts seem to indicate their general occurrence in organic and structural chemistry.[13]

Unfortunately the disorder of the guest molecule inside the cavity does not allow us to define with great accuracy the geometric and energetic requirements for this type of $CH_3 \cdots \pi$ interaction. In fact anisole is disordered in at least eight equivalent orientations, four of them generated by the four-fold axis with the anisole OCH_3 pointing into one macrocycle of the cage and four obtained with this group pointing into the other half of the cage. The superposition of the refined model with the disordered system is quite good. Although the stabilizing interactions seem to be of the same nature in the two cases, this solid state topology is quite different from that observed in the 1:1 cage complex of *p*-t-butylcalix[4]arene and toluene.[3] In the latter case one molecule of the host macrocycle includes the toluene which is entering the calix from the side of its methyl group. The full intermolecular cage in the crystal is completed by methyl groups belonging to two macrocyclic molecules and external with respect to the calix, whereas in the new (2:1) complex another calixarene half-cage defines the space in which anisole is encapsulated. The inclusion aggregates of the (2:1) phase are packed as the half-cages of the (1:1) phase, since both crystals belong to the same space group. The contacts which determine the molecular packing shown in Figure 3 are mainly due to the methyl groups pointing outside the cavity. In this way there are significant channels running at 1/4, 3/4, *z* which in our case are not occupied. The density of the (2:1) phase is 1.109 g cm^{-3} to be compared with 1.096 g cm^{-3} in the (1:1) phase. So a gain in stability is expected for the new phase. The gain is quite small and small changes in the nature of the included molecules could switch crystallization from one phase to the other. Further work is in progress in our laboratories to find new experimental evidence to clarify the nature of the stabilizing interactions in this type of inclusion compound.

References

1 Part 8, R. Ungaro, A. Pochini, G. D. Andreetti, and V. Sangermano, *J. Chem. Soc., Perkin Trans. 2*, 1984, 1979.

2 For the nomenclature of these compounds see C. D. Gutsche, B. Dhawam, K. Hyun No, and A. Muthukrishnan, *J. Am. Chem. Soc.*, 1981, **103**, 3782.

3 G. D. Andreetti, R. Ungaro, and A. Pochini, *J. Chem. Soc., Chem. Commun.*, 1979, 1006.

4 G. D. Andreetti, R. Ungaro, and A. Pochini, *J. Chem. Soc., Chem. Commun.*, 1981, 1006.

5 C. Rizzoli, G. D. Andreetti, R. Ungaro, and A. Pochini, *J. Mol. Struct.*, 1982, **82**, 133.

6 M. Coruzzi, G. D. Andreetti, V. Bocchi, A. Pochini, and R. Ungaro, *J. Chem. Soc., Perkin Trans. 2*, 1982, 1138.

7 G. D. Andreetti, A. Pochini, and R. Ungaro, *J. Chem. Soc., Perkin Trans. 2*, 1983, 1773.

8 E. Weber and H.-P. Josel, *J. Inclusion Phenomena*, 1983, **1**, 79.

9 D. Belletti, F. Ugozzoli, A. Cantoni, and G. Pasquinelli, Centro di Studio per la Strutturistica Diffrattometrica del C. N. R., Parma, Internal Reports 1/79, 2/79, 3/79, 1979.

10 R. H. Blessing, P. Coppens, and P. Becker, *J. Appl. Crystallogr.*, 1974, **7**, 488.

11 F. Vögtle, M. Sieger, and W. M. Müller, *Top. Curr. Chem.*, 1981, **98**, 107.

12 I. Goldberg, 'The Chemistry of Ethers, Crown Ethers, Hydroxyl Groups and their Sulphur Analogues,' ed. S. Patai, Wiley, New York, 1980, Supplement E, ch. 4.

13 M. Hirota *et al.*, *Tetrahedron*, 1983, **39**, 3091.

Received 9th *March* 1984; *Paper* 4/386