Journal of Inclusion Phenomena **6** (1988), 119–134.

p-t-Butylcalix[4]arene Tetra-acetamide: a New Strong Receptor for Alkali Cations [1]

ARTURO ARDUINI, ELEONORA GHIDINI, ANDREA POCHINI, and ROCCO UNGARO*
Istituto di Chimica Organica Organica dell'Università di Parma, Viale delle Scienze, 43100 Parma, Italy

GIOVANNI DARIO ANDREETTI, GIANLUCA CALESTANI, and FRANCO UGOZZOLI*
Istituto di Strutturistica Chimica dell'Università di Parma, Centro di Studio per la Strutturistica Diffrattometrica del C.N.R., Viale delle Scienze, 43100 Parma, Italy

(Received: 6 February 1987; in final form: 8 September 1987)

Abstract. From the reaction of *p-t*-butylcalix[4]arene with α-chloro-*N,N*-diethyl acetamide a new lipophilic ether-amide ligand (**2**) has been obtained in high yield. Solution studies show (**2**) to be a very strong cation receptor for alkali cations, especially sodium and potassium. The X-ray crystal structure determination of the free ligand (**2**) and two potassium complexes (KI and KSCN) shows the calix[4]arene in a fixed 'cone' structure and the cation completely encapsulated in a polar cavity of eight oxygen atoms.

Key words. *p-t*-butylcalix[4]arene; cation receptor; X-ray crystal structure analysis; potassium complex.

Supplementary Data relating to this article are deposited with the British Library as supplementary publication No. SUP 82059 (57 pages).

1. Introduction

The preorganization of binding sites prior to complexation is an important principle which has been used by Cram *et al.* to synthesize highly structured cation receptors, the spherands, which possess an enforced cavity and form strong complexes with alkali cations (especially lithium and sodium) [2]. We have recently found [3] that it is possible to introduce on *p-t*-butylcalix[4]arene (**1**) four ester groups locking the parent macrocycle in a fixed 'cone' structure where the binding units are convergent, all *cis* with respect to an ideal plane containing the bridging methylenes of the macrocycle.

Similar results have been obtained by other authors [4] and all the calix[4]arene ether–ester ligands have shown a remarkable extraction ability towards alkali metal cations [4, 5].

With the aim of further improving the cation binding efficiency of calix[4]arene ligands and to isolate crystalline complexes with alkali salts suitable for X-ray analysis, we have synthesized a new calix[4]arene derivative (**2**) which has four amide binding groups [6].

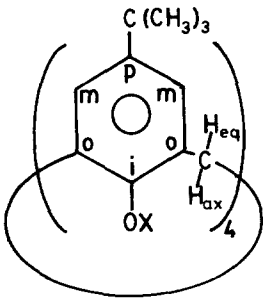
2. Experimental

For instrumentation, chemicals and experimental procedures for cation picrate extraction, ^{1}H NMR complexation experiments and optical spectra see [5]. A sample of ligand (**2**) was dried *in vacuo* for 48 h at 100°C before submission for elemental analysis.

Presented at the Fourth International Symposium on Inclusion Phenomena and the Third International Symposium on Cyclodextrins, Lancaster, U.K., 20–25 July 1986.
* Authors for correspondence.

2.1. SYNTHESIS

5,11,17,23-tetra-*t*-Butyl-25,26,27,28-tetrakis(*N*,*N*-diaethylaminocarbonyl)methoxycalix-[4]arene [7] (LBC-Tetramide) (**2**).



$X = CH_2CON(CH_2CH_3)_2$ (**2**)

In a three-necked round bottomed flask under a dry nitrogen atmosphere *p*-*t*-butylcalix[4]arene (**1**) (1 g, 1.5 mmol) was suspended in anhydrous THF (40 mL) and dry DMF (8 mL), then gently warmed under stirring until most of the solid was dissolved. After cooling, 0.6 g of NaH (60% in oil) was added followed by 1.8 g (12 mmol) of α-chloro-*N*,*N*-diaethylacetamide [8] and the reaction mixture refluxed under N_2 for 3 h. Most of the solvent was removed *in vacuo* and the oily residue treated with water, then acidified and extracted with CH_2Cl_2.

The combined organic solutions were washed with water and the solvent removed *in vacuo*. The pale yellow oily residue on treatment with diethyl ether gave 1.56 g (95% yield) of white needles which were pure compound (**2**). Samples for analysis were obtained by recrystallization from methanol. M.p. 228–229°C. IR (KBr) 1665, 1640, 1200, 1160 cm^{-1}, ^1H NMR ($CDCl_3$) δ 1.08 [s, 36H, $C(CH_3)_3$], 1.05–1.24 (m, 24H, CH_2CH_3), 3.19 (d, 4H, Heq), 3.33 (m, 16H, NCH_2CH_3), 5.02 (s, 8H, CH_2CO), 5.30 (d, 4H, Hax, $J_{AB} = 12.8$ Hz), 6.77 (s, 8H, Arom). ^{13}C NMR ($CDCl_3$), 12.5, 14.3 (NCH_2CH_3), 31.4 [$C(CH_3)_3$], 32.3 (*C*HaxHeq), 33.6 [$C(CH_3)_3$]; 40.0, 40.9 (NCH_2CH_3), 71.7 (OCH_2CO), 125.1 (Cm), 133.4 (Co), 144.2 (Cp), 153.8 (Ci), 169.1 (C=O); $C_{68}H_{100}N_4O_8$ (1101.6). Calc. C 74.12 H 9.16 N 5.08. Found C 73.88 H 9.16 N 4.90.

LBC-Tetramide KSCN complex (**3**)

After slow evaporation of the solvent from samples of ^1H NMR titration experiments [5] containing 1 : 1 LBC tetramide (**2**)/KSCN molar ratio in $CDCl_3/CD_3OD$, colourless needles separated which were collected and dried *in vacuo* (room temperature, 0.1 mm Hg). ^1H HMR ($CDCl_3$) δ 1.19 [s, 36H, $C(CH_3)_3$], 1.07–1.23 (m, 24H, NCH_2CH_3), 3.35 (d, 4H, Heq), 3.36–3.50 (m, 16H, NCH_2CH_3), 4.61 (s, 4H, Hax), 4.65 (s, 8H, CH_2CO), 7.16 (s, 8H, Arom). ^{13}C NMR ($CDCl_3$), 13.1, 14.2 (NCH_2CH_3), 29.5 (*C*HaxHeq), 31.3 [$C(CH_3)_3$], 34.15 [$C(CH_3)_3$], 40.7, 41.1 (NCH_2CH_3), 73.5 (OCH_2CO), 125.7 (Cm), 134.5 (Co), 147.2 (Cp), 151.2 (Ci), 167.9 (C=O).

Almost identical NMR data were shown by the corresponding KI complex (**4**).

LBC-Tetramide NaSCN complex (**5**)

By an analogous procedure to the potassium complex a NaSCN 1 : 1 complex was isolated which showed the following ^1H NMR spectrum ($CDCl_3$) δ 1.19 [s, 36H, $C(CH_3)_3$],

1.07–1.23 (m, 24H, NCH_2CH_3), 3.33 (d, 4H, Heq), 3.36–3.50 (m, 16H, NCH_2CH_3), 4.45 (d, 4H, Hax), 4.53 (s, 8H, CH_2CO), 7.16 (s, 8H, Arom).

2.2. X-RAY STRUCTURAL ANALYSIS

Colourless transparent single crystals suitable for X-ray diffraction were obtained by slow evaporation from methanolic solutions of the free ligand (**2**) and of the two complexes (**3**) and (**4**).

The crystals of the complexes were stable only in the presence of the crystallization solvent. If they dried, a sharp increase of the lattice defects which led in a short time to the collapse of the crystal lattice was observed. This phenomenon is characteristic of compounds for which the solvent, although not influencing the molecular structure, is fundamental for the retainment of the crystal lattice. For this reason the intensity data were collected from crystals sealed in a quartz capillary in the presence of the crystallization solvent. In spite of this, a small but significant decrease (1%) of the unit cell volume due to the shortening of the *c* axis was observed during the data collection. This was attributed to the continuous evaporation of the solvent retained in the intermolecular cavities of the crystal.

The intensities I_{hkl} were collected in the θ–2θ step scanning mode in the range $3° \leqslant \theta \leqslant 60°$ analyzing the reflection profile with a modified version of the Lehmann and Larsen procedure [9, 10]. One standard reflection was measured every 50 collected reflections to monitor specimen decomposition and instrumental stability.

The intensity data were corrected for Lorentz and polarization effects. Absorption corrections (see Table I) based on a semiempirical method (Absorb) [11], were applied in the final stage of isotropic structure refinement. Table I summarizes the crystal data, the number of collected, observed and symmetry independent reflections together with the statistical criteria adopted.

The structure of the free ligand (**2**) was solved, after many trials, by direct methods and refined by least squares techniques using anisotropic thermal parameters for C, N, O atoms except for the disordered *t*-butyl groups and the guest methanol molecule that were refined with isotropic temperature factors. H atoms were calculated with the geometrical constraint (C—H = 1.08 Å) and their contribution to the observed structure factors were taken into account in the last cycle of refinement. Two opposite *t*-butyl groups (A and C) are disordered presenting two possible conformations with occupancies of 0.43 and 0.57 respectively. Methanol molecules, distributed in a disordered way around a center of symmetry were located in the Fourier ΔF map in the intermolecular cavities and refined using the scattering factor of C for all atoms because of their disorder.

In the structure determination of the KSCN complex (**3**) $F_{hkl} = F_{khl}$ (within the e.s.d.s), gave Laue Group D_{4h} and the space group $I4/mmm$ was initially assumed. The structure was solved by direct methods that revealed at first, only the phenolic rings. Starting from the macrocycle atomic coordinates, two possible conformations of the amide chains were found by successive steps of refinement and Fourier maps. The two chain conformations are related, each to the other, by a mirror plane, and the refinement of the occupancy led to comparable values (0.5) for both conformations. An attempt to solve the chain disorder with lower symmetry space groups $I422$, $I4/m$, and $I4$ showed an identical structural arrangement with a regular calixarene unit and two possible chain conformations statistically distributed. It was therefore preferable to refine the structure in the space group $I4/mmm$ which describes the 'averaged' structure with the minor number of parameters. The

Table I. Crystal data for the free ligand (**2**) and the complexes (**3**) and (**4**)

Compound	(**2**)	(**3**)	(**4**)
Chemical formula M (a.m.u.)	$(C_{17}H_{25}O_2N)_4 \cdot CH_3OH$ 1133.61	$(C_{17}H_{25}O_2N)_4 \cdot KSCN \cdot CH_3OH$ 1230.79	$(C_{17}H_{25}O_2N)_4 \cdot KI \cdot CH_3OH$ 1299.60
Crystal system and lattice parameters [Å]	Orthorhombic $a = 28.828(3)$ $b = 19.120(8)$ $c = 26.236(3)$	Tetragonal $a = b = 15.192(4)$ $c = 37.040(6)$	Tetragonal $a = b = 15.208(9)$ $c = 37.753(6)$
Space group	*Pbca* (no. 61)	*I4/mmm* (no. 139)	*I4/m* (no. 87)
Z	8	4	4
D_c $[g \cdot cm^{-3}]$	1.04	0.956	0.989
$F(000)$	4944	2560	2760
$\mu(CuK\alpha)$ $[cm^{-1}]$	5.08	10.5	36.78
Collected reflections	$+h+k+l$ 8165 $3° \leqslant \theta \leqslant 70°$	$+h+k+l$ 3966 $3° \leqslant \theta \leqslant 65°$	$+h+k+l$ 3604 $3° \leqslant \theta \leqslant 60°$
Observed reflections	4944 $I \geqslant 3\sigma(I)$	1938 $I \geqslant 3\sigma(I)$	1832 $I \geqslant 2\sigma(I)$
Symmetry independent refl.	3171	1121	1633
Absorption correction	No	No	Yes

structure was refined assigning anisotropic thermal parameters to the non-hydrogen atoms with the exception of the C atoms in the *tert*-butyl and ethyl groups which were refined with isotropic temperature factors together with the counterion and the guest molecule.

The counterion is distributed disorderly around the center of an intermolecular cavity. The disorder was fitted by four SCN groups (two by two symmetry related by the center of symmetry) refined with the following occupancies: 0.065(3) for S, C and N and 0.060(3) for S′, C′ and N′. The final R was 0.113.

In the structure determination of the KI complex (**4**) $F_{hkl} \neq F_{khl}$ (within the e.s.d.s) gave Laue Group C_{4h} and the space group $I4/m$ was initially assumed.

The structure was partially solved by Patterson and direct methods giving the atomic coordinates of I and K, as well as of the phenolic ring with the ether oxygen atom. Successive cycles of refinements and Fourier maps led to the determination of the amide chains which are disordered showing two possible chain conformations.

Nevertheless, in contrast to the situation observed for the KSCN complex (**3**), the two chain conformations are not related by a mirror plane differing from each other by the orientation of the terminal ethyl groups. This is responsible for the decrease of the symmetry from the space group *I4/mmm* observed in the KSCN complex (**3**) to the actual one *I4/m* which furnishes the best 'averaged' description of the structure. The structure was

refined using anisotropic thermal parameters for the non-hydrogen atoms except for the N and C atoms of the terminal ethyl groups of the disordered chains which were refined using isotropic temperature factors.

As observed in the KSCN complex (**3**) the *t*-butyl groups are affected by a severe disorder that was solved in two *t*-butyl groups each of them refined as a rigid group. H atoms were calculated with the geometrical constraints (C—H = 1.08 Å). The iodide ion is situated in the same intermolecular cavity which was seen to house the SCN ion in the complex (**3**). The final R value was $R = 0.158$ and the highest peak in the final electron density map was 0.75 e $Å^{-3}$ at 1.16 Å from I^-.

In both structures of the complexes (**3**) and (**4**) the difference Fourier maps showed, in a large intermolecular cavity, several electron density peaks suggesting the presence of disordered methanol molecules. The presence of a non negligible quantity of solvent in these intermolecular cavities could explain the surprisingly low density calculated without taking into account their contribution.

Attempts to refine these peaks using the scattering factors of the C atom failed because of the strong correlation between partial occupancies and high thermal motion. In both structures it was possible to refine only one methanol molecule, which was found to reside inside the intramolecular apolar cavity.

All structures were solved using the SHELX 76 system of crystallographic computer programs [12] and the calculations were performed on the GOULD 32/77 of Centro di Strutturistica Diffrattometrica C.N.R. Parma.

2.3. OPTICAL SPECTRA

Complex formation constants for the ion-pair separation process of sodium and potassium picrates in THF were measured by evaluating the fraction of tight ion pairs Pi^-, Na^+ (λ_{max} 351 nm), Pi^-, K^+ (λ_{max} 356 nm) and of the ligand separated ion-pairs Pi^-, L, M^+ (λ_{max} 380 nm for both cations) spectrophotometrically. Molar absorbitivities ε (M^{-1} cm^{-1}) necessary for the calculations [13] were the following. Sodium picrate: $\varepsilon_{351} = 16\,500$, $\varepsilon_{380} = 8900$ for Na^+, Pi^- and $\varepsilon_{380} = 21\,000$, $\varepsilon_{351}10\,000$ for Na^+, L, Pi^-. Potassium picrate: $\varepsilon_{356} = 16\,800$, $\varepsilon_{380} = 10\,600$ for K^+, Pi^- and $\varepsilon_{380} = 21\,000$, $\varepsilon_{356} = 12\,600$ for K^+, L, Pi^-.

3. Results and Discussion

3.1. SYNTHESIS AND X-RAY STRUCTURE

Compound (**2**) has been obtained via the following reaction scheme:

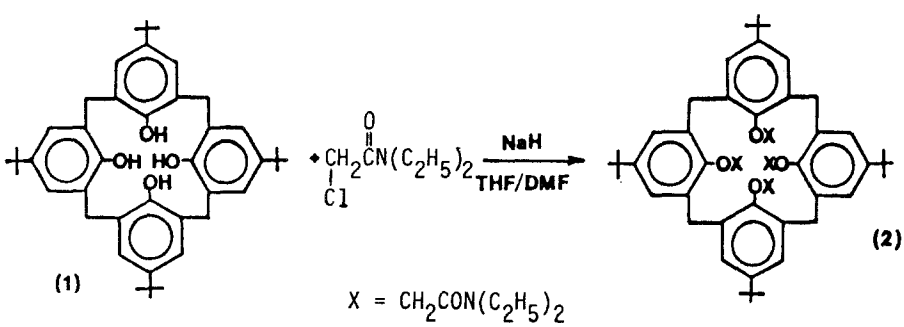


Table II reports bond distances, bond angles and selected torsion angles for the free ligand and the two potassium complexes (KSCN and KI). The numbering scheme adopted for the fundamental unit in LBC tetramide (2), (3) and (4) is shown in the Appendix.

Figure 1 shows the X-ray crystal structure of the free ligand (**2**). The reciprocal orientation of the four aromatic rings, which lie below the reference plane passing through the four CH_2 bridging groups, determine the well known distorted cone conformation of the molecule which has been observed in the tetrabutyl ester [5].

TABLE II(a). Fractional atomic coordinates ($\times 10^4$) of the nonhydrogen atoms for the LBC tetramide(**2**)

Atom	x/a	y/b	z/c	Atom	x/a	y/b	z/c
C(1a)	3845(4)	1862(6)	4127(5)	C(3c)	3100(4)	123(6)	2449(5)
C(2a)	3366(4)	1812(6)	4123(4)	C(4c)	3344(5)	−276(6)	2802(5)
C(3a)	3118(4)	2223(6)	3790(5)	C(5c)	3825(4)	−272(6)	2782(5)
C(4a)	3336(4)	2636(6)	3417(5)	C(6c)	4063(4)	123(7)	2453(6)
C(5a)	3820(4)	2665(6)	3421(5)	O(7c)	2615(2)	122(3)	2450(3)
C(6a)	4071(4)	2287(7)	3785(5)	C(8c)	2403(5)	−520(6)	2278(5)
O(7a)	2630(3)	2189(4)	3789(3)	C(9c)	2303(5)	−386(7)	1716(7)
C(8a)	2408(5)	2822(6)	3980(4)	O(10c)	2073(4)	129(5)	1565(4)
C(9a)	2349(5)	2683(7)	4541(6)	N(11c)	2406(4)	−855(6)	1358(4)
O(10a)	2137(4)	2192(5)	4726(4)	C(12c)	2647(5)	−1523(5)	1490(6)
N(11a)	2555(4)	3121(6)	4867(4)	C(13c)	3175(5)	−1461(10)	1423(8)
C(12a)	2813(6)	3774(6)	4728(6)	C(14c)	2279(5)	−775(8)	808(5)
C(13a)	3340(6)	3681(11)	4798(11)	C(15c)	2668(7)	−420(10)	503(5)
C(14a)	2580(6)	2987(8)	5430(4)	C(16c)	4593(3)	94(7)	2435(6)
C(15a)	2166(7)	3320(11)	5710(5)	C(17c)	4761(9)	−658(7)	2335(10)
C(16a)	4613(3)	2406(6)	3823(5)	C(18c)	4751(11)	319(13)	2972(6)
C(17a)	4853(8)	1753(8)	4042(8)	C(19c)	4812(9)	588(10)	2039(8)
C(18a)	4826(7)	2579(10)	3300(5)	C(20c)	4854(9)	−301(11)	2856(9)
C(19a)	4687(8)	3027(9)	4186(7)	C(21c)	4619(12)	−328(13)	1935(8)
C(20a)	4777(14)	1847(14)	3441(11)	C(22c)	4820(8)	814(7)	2353(9)
C(21a)	4811(11)	2237(16)	4354(7)	C(30c)	3080(4)	1029(6)	1744(4)
C(22a)	4790(11)	3128(10)	3652(11)	C(1d)	3536(4)	3083(6)	2177(5)
C(30a)	3133(4)	1313(6)	4491(4)	C(2d)	3197(4)	2736(6)	2486(5)
C(1b)	3573(4)	−745(6)	4042(5)	C(3d)	3018(4)	2105(6)	2305(5)
C(2b)	3238(4)	−410(6)	3751(5)	C(4d)	3186(4)	1781(6)	1874(5)
C(3b)	3062(4)	230(6)	3930(5)	C(5d)	3512(4)	2150(6)	1577(5)
C(4b)	3238(4)	567(6)	4350(5)	C(6d)	3680(4)	2814(7)	1727(5)
C(5b)	3577(4)	193(6)	4635(5)	O(7d)	2698(3)	1777(3)	2620(3)
C(6b)	3740(4)	−451(7)	4482(5)	C(8d)	2252(4)	1602(6)	2417(6)
O(7b)	2736(3)	575(3)	3613(3)	C(9d)	1916(4)	2187(7)	2528(5)
C(8b)	2293(4)	750(6)	3834(6)	O(10d)	2026(3)	2761(4)	2682(4)
C(9b)	1947(5)	173(7)	3687(6)	N(11d)	1466(3)	2056(5)	2413(4)
O(10b)	2063(3)	−417(5)	3555(4)	C(12d)	1107(4)	2616(6)	2478(5)
N(11b)	1507(4)	345(6)	3765(5)	C(13d)	880(6)	2581(10)	3007(7)
C(12b)	1146(5)	−207(7)	3678(6)	C(14d)	1295(5)	1352(5)	2247(6)
C(13b)	1014(6)	−257(10)	3111(7)	C(15d)	1175(7)	1342(9)	1677(6)
C(14b)	1333(6)	1061(6)	3897(8)	C(16d)	4055(4)	3179(6)	1379(4)
C(15b)	1241(9)	1131(12)	4472(9)	C(17d)	3958(5)	3086(8)	807(4)
C(16b)	4125(4)	−828(6)	4796(5)	C(18d)	4071(6)	3966(6)	1504(6)
C(17b)	4585(6)	−692(9)	4516(6)	C(19d)	4528(4)	2850(8)	1508(7)
C(18b)	4161(6)	−549(8)	5345(5)	C(30d)	3072(4)	3020(5)	3000(4)
C(19b)	4030(6)	−1618(7)	4811(6)	C(1me)	4464(13)	298(19)	523(16)
C(30b)	3091(4)	−682(5)	3226(5)	C(2me)	4822(19)	49(29)	209(22)
C(1c)	3821(5)	541(7)	2109(5)	C(3me)	4616(23)	994(21)	545(26)
C(2c)	3334(5)	539(6)	2104(5)				

Table II(b). Fractional atomic coordinates ($\times 10^4$) of the non-hydrogen atoms for the LBC tetramide·KSCN complex (**3**)

Atom	*x/a*	*y/b*	*z/c*
K	1/2	1/2	1324(1)
C(1)	2669(4)	4217(5)	2566(2)
C(2)	3031(4)	4202(4)	2221(2)
C(3)	3173(6)	1/2	2053(2)
C(6)	2457(6)	1/2	2745(3)
O(7)	3453(4)	1/2	1687(2)
C(8)	2715(7)	1/2	1447(3)
C(9)	2922(13)	5481(12)	1112(4)
O(10)	3570(8)	5932(9)	1086(3)
N(11)	2302(11)	5412(9)	0849(3)
C(12)	1406(12)	1/2	0881(5)
C(13)	1537(20)	4009(12)	0759(9)
C(14)	2360(24)	5967(17)	0514(6)
C(15)	2036(25)	6916(14)	0583(8)
C(16)	2022(8)	1/2	3113(3)
C(17)	2580(20)	4425(20)	3376(6)
C(18)	1894(24)	5903(12)	3272(7)
C(19)	1111(14)	4528(22)	3076(8)
C(20)	1037(20)	1/2	3011(19)
C(21)	2219(24)	4173(19)	3340(9)
C(22)	1455(20)	4201(17)	3204(8)
C(23)	2839(27)	1/2	3361(17)
C(30)	3326(4)	3326(4)	2047(3)
O(me)	1/2	1/2	2848(11)
C(me)	1/2	1/2	3222(11)
C	1/2	0	0
N	4252(19)	0	0
S	5984(14)	0	0
S′	1/2	0	0
C′	5984(14)	0	0
N′	6787(24)	0	0

Table II(c). Fractional atomic coordinates ($\times 10^4$) and occupancies of the non-hydrogen atoms for the LBC tetramide·KI complex (**4**)

Atom	*x/a*	*y/b*	*z/c*	s.o.f.
K	1/2	1/2	1343(2)	0.250
I	1/2	1/2	0	0.250
C(1)	2669(9)	4241(9)	2559(5)	1.000
C(2)	3023(8)	4185(9)	2224(4)	1.000
C(3)	3185(8)	4992(8)	2047(4)	1.000
C(4)	3024(9)	5801(9)	2233(4)	1.000
C(5)	2666(8)	5782(9)	2561(4)	1.000
C(6)	2451(9)	5009(11)	2731(4)	1.000
O(7)	3456(6)	4999(6)	1697(3)	1.000
C(8)	2738(11)	4999(12)	1463(4)	1.000
C(9)	2932(19)	5430(26)	1166(9)	0.550
O(10)	3615(19)	5954(22)	1112(7)	0.550
N(11)	2285(24)	5389(23)	0855(9)	0.550
C(12)	1417(14)	5002(22)	0900(7)	1.000
C(13)	1417(41)	3996(23)	0844(18)	0.550
C(14)	2623(26)	5691(34)	0498(9)	0.550
C(15)	3405(39)	5107(50)	0362(15)	0.550
C(16)	1992(10)	5006(10)	3088(4)	1.000
C(17)	0990(13)	4963(46)	3026(11)	0.517
C(18)	2209(40)	5861(20)	3289(8)	0.517
C(19)	2277(39)	4213(20)	3313(9)	0.517
C(20)	2700(27)	5052(69)	3379(11)	0.483
C(21)	1454(46)	4153(28)	3137(19)	0.483
C(22)	1366(43)	5800(29)	3128(19)	0.483
C(30)	3311(9)	3311(9)	2055(4)	1.000
C(9′)	2943(18)	4540(28)	1146(10)	0.450
O(10′)	3530(17)	4059(23)	1091(8)	0.450
N(11′)	2373(26)	4671(26)	0849(8)	0.450
C(13′)	1401(43)	5989(27)	0805(28)	0.450
C(14′)	2532(34)	4189(43)	0495(9)	0.450
C(15′)	1940(63)	3333(39)	0496(23)	0.450
O(1me)	0	0	2118(15)	0.250
C(1me)	0	0	1713(37)	0.250

Table II(d). Bond distances (Å) and angles (°) involving K atoms. a and b refer to opposite and adjacent chains respectively. In compound (**4**) 010 and 010′ atoms are the amide oxygens of the disordered chains.

LBC tetramide·KSCN complex (**3**)		LBC tetramide·KI complex (**4**)	
K—O(7)	2.708(7)	K—O(7)	2.702(11)
K—O(10)	2.739(13)	K—O(10)	2.702(30)
		K—O(10a′)	2.820(29)
O(10)—K—O(10a)	142.5(3)	O(10) —K—O(10a)	142.3(8)
O(10)—K—O(10b)	84.1(4)	O(10) —K—O(10b)	84.0(9)
O(7b)—K—O(10)	127.5(3)	O(7b) —K—O(10)	128.8(7)
O(7) —K—O(10b)	73.2(3)	O(7) —K—O(10b)	72.1(7)
O(7) —K—O(10a)	148.0(3)	O(7) —K—O(10a)	146.8(7)
O(7) —K—O(10)	58.1(3)	O(7) —K—O(10)	58.8(7)
O(7) —K—O(7b)	75.7(2)	O(7) —K—O(7b)	75.8(3)
O(7) —K—O(7a)	120.5(2)	O(7) —K—O(7a)	120.7(3)
		O(10′)—K—O(10′a)	140.6(9)
		O(10′)—K—O(10′b)	83.5(9)
		O(7b) —K—O(10′)	74.1(7)
		O(7) —K—O(10′b)	127.4(7)
		O(7) —K—O(10′a)	148.9(7)
		O(7) —K—O(10′)	58.5(6)

Table II(e). Selected torsion angles (°).

LBC tetramide		LBC Tetramide·KSCN complex	
C(8a) —O(7a) —C(3a)—C(2a)	111.1(1.2)	C(2)—C(3) —O(7) —C(8)	89.1(.8)
C(8a) —O(7a) —C(3a)—C(4a)	−74.3(1.3)	C(3)—O(7) —C(8) —C(9)	148.0(.9)
C(3a) —O(7a) —C(8a)—C(9a)	−91.5(1.1)	O(7)—C(8) —C(9) —O(10)	−12.2(2.0)
O(7a) —C(8a) —C(9a)—O(10a)	−57.8(1.7)	O(7)—C(8) —C(9) —N(11)	171.5(1.2)
O(7a) —C(8a) —C(9a)—N(11a)	120.3(1.3)	C(8)—C(9) —N(11)—C(12)	7.9(2.3)
C(12a)—N(11a)—C(9a)—C(8a)	4.8(2.0)	C(8)—C(9) —N(11)—C(14)	171.3(1.7)
C(14a)—N(11a)—C(9a)—C(8a)	−171.2(1.2)		
C(8b) —O(7b) —C(3b)—C(2b)	124.5(1.1)	LBC tetramide·KI complex	
C(8b) —O(7b) —C(3b)—C(4b)	−64.4(1.4)		
C(3b) —O(7b) —C(8b)—C(9b)	−96.9(1.2)	C(2)—C(3) —O(7) —C(8)	88.1(1.5)
O(7b) —C(8b) —C(9b)—O(10b)	21.1(1.8)	C(4)—C(3) —O(7) —C(8)	−89.0(1.5)
O(7b) —C(8b) —C(9b)—N(11b)	−165.4(1.1)	C(3)—O(7) —C(8) —C(9)	148.7(1.9)
C(12b)—N(11b)—C(9b)—C(8b)	−174.6(1.1)	C(3)—O(7) —C(8) —C(9′)	147.7(1.9)
C(14b)—N(11b)—C(9b)—C(8b)	10.2(2.0)	O(7)—C(8) —C(9) —O(10)	−13.6(4.2)
C(8c) —O(7c) —C(3c)—C(2c)	111.1(1.2)	O(7)—C(8) —C(9′) —O(10′)	15.2(4.7)
C(8c) —O(7c) —C(3c)—C(4c)	−70.8(1.4)	O(7)—C(8) —C(9) —N(11)	171.1(2.4)
C(3c) —O(7c) —C(8c)—C(9c)	−95.6(1.1)	O(7)—C(8) —C(9′) —N(11′)	−164.4(2.6)
O(7c) —C(8c) —C(9c)—O(10c)	133.9(1.3)	C(8)—C(9) —N(11) —C(12)	9.3(4.7)
O(7c) —C(8c) —C(9c)—N(11c)	−54.5(1.7)	C(8)—C(9) —N(11) —C(14)	−165.4(3.0)
C(12c)—N(11c)—C(9c)—C(8c)	−3.1(2.0)	C(8)—C(9′)—N(11′)—C(12)	−21.8(4.8)
C(14c)—N(11c)—C(9c)—C(8c)	174.6(1.2)	C(8)—C(9′)—N(11′)—C(14′)	−178.9(3.3)
C(8d) —O(7d) —C(3d)—C(4d)	124.9(1.5)		
C(8d) —O(7d) —C(3d)—C(4d)	−62.6(1.5)		
C(3d) —O(7d) —C(8d)—C(9d)	−93.3(1.2)		
O(7d) —C(8d) —C(9d)—O(10d)	12.0(1.7)		
O(7d) —C(8d) —C(9d)—N(11d)	−172.2(1.0)		
C(12d)—N(11d)—C(9d)—C(8d)	−176.3(1.0)		
C(14d)—N(11d)—C(9d)—C(8d)	7.3(1.7)		

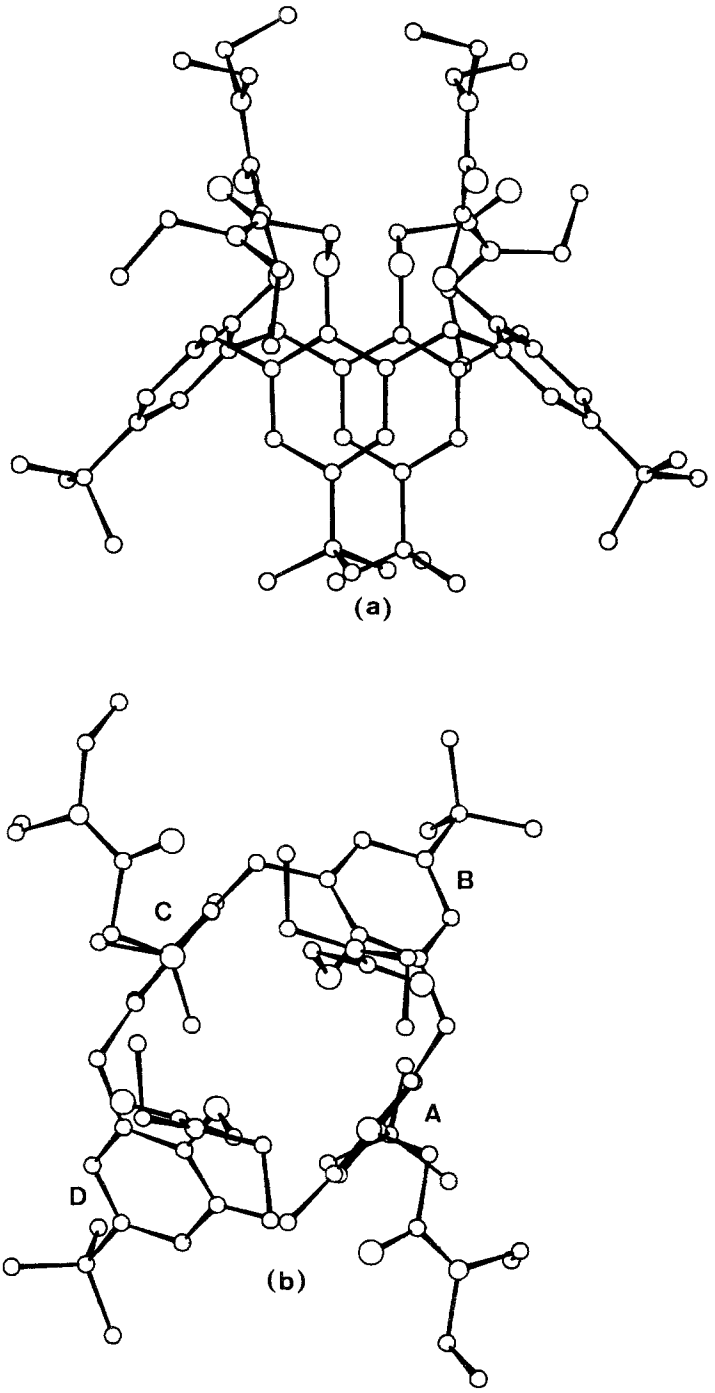


Fig. 1. Molecular structure of *p-t*-butylcalix[4]arene-amide (**2**). (a) Perspective view; (b) view perpendicular to the reference plane.

Above the reference plane a top hydrophilic cavity is created by the four ether oxygen atoms and by the four amide groups.

The cone structure can be described by the dihedral angles which the four aromatic rings (A–D) make with the reference plane: A (87.4(3)°), B (136.5(2)°), C (89.5(4)°) and D (135.9(3)°). Two opposite aromatic rings ($A\hat{C} = 2.2(4)°$) are almost parallel while the other two ($B\hat{D} = 92.4(3)°$) are almost perpendicular.

Significant differences in the conformation of the chelating chains are observed in the tetramide (**2**) if compared with the correspondent tetraester [5]. In the tetraester, two chains are in *cis* conformation and the other two are *trans* with respect to the O—CH_2 bond, but in the tetramide (**2**) the torsion angles C(6)—O(7)—C(8)—C(9) are all near to 90° with a mean value of 94.15°.

This conformation of the chains, which orients the four carbonyl groups towards the interior of the macrocycle, makes the ligand (**2**) more preorganized prior to complexation compared with the tetraester ligand (X = CH_2COOBu-*t*) [5]. In fact the complexes can be obtained by a simple rotation of the amide groups of the free ligand (**2**) around the Ar—O—CH_2 bonds, which brings all carbonyl groups into the interior and the CH_2 groups towards the exterior of the hydrophilic cavity.

Although solved and refined in different space groups as explained above, the crystal and molecular structure of the *p*-*t*-butylcalix[4]arene amide KI and KSCN complexes are quite similar (see Figure 2) showing that the nature of the counterion seems to play a negligible influence in the general features of the structures. In fact the lattice parameter *a*, which depends mainly on the steric interactions between macrocycles, does not change significantly in the two structures; while the length of the *c* axis, which depends mainly on the size of the solvated counterion housed in the intermolecular cavity, shows a small but significant increase of 2% on passing from the KSCN complex (**3**) to the KI complex (**4**).

The conformations of the complexes (**3**) and (**4**) are more symmetrical if compared to the free ligand (**2**); in fact, both molecules possess a fourfold axis passing through the K atom, which is encapsulated in a nice polar environment of eight oxygen atoms in the form of an antiprism. The ether and amide oxygen atoms lie on two distinct parallel planes. The projections of the K···O bonds on the *xy* plane appear tilted by almost 32°.

The distances between two opposite ether oxygen atoms are 4.700(6) and 4.696(9) Å for complexes (**3**) and (**4**) respectively, while that between the two opposite amide oxygens are 5.186(14) and 5.11(3) Å in (**3**) and (**4**) respectively.

Bond distances and angles involving K atoms are summarized in Table II, showing no significant differences for both complexes.

By passing from the free ligand (**2**) to the two complexes (**3**) and (**4**) a strong rearrangement in the distribution of the four aromatic rings around the fourfold axis is observed. The dihedral angle formed by each aromatic ring with respect to the reference plane containing the four bridging CH_2 groups is 66.7(4)°. With this rearrangement of the aromatic rings the hydrophobic pocket of the macrocycle in both compounds is able to accommodate a methanol molecule for which no strong interaction with the host molecule has been evidenced.

For both complexes (**3**) and (**4**) the crystal packing consists of layers of calixarene units disposed parallel to the *a*–*b* plane as shown in Figures 3 and 4. This packing leaves in the lattice large intermolecular cavities lying on the planes at $z = 0$ and $z = 1/2$ which are packed in a 'body centered' way. Each cavity (roughly of spherical shape with a diameter of about 9 Å) lies on a fourfold axis and is bounded in the [001] direction by the H atoms of the *t*-butyl groups of two calixarene units related by a mirror plane perpendicular to the

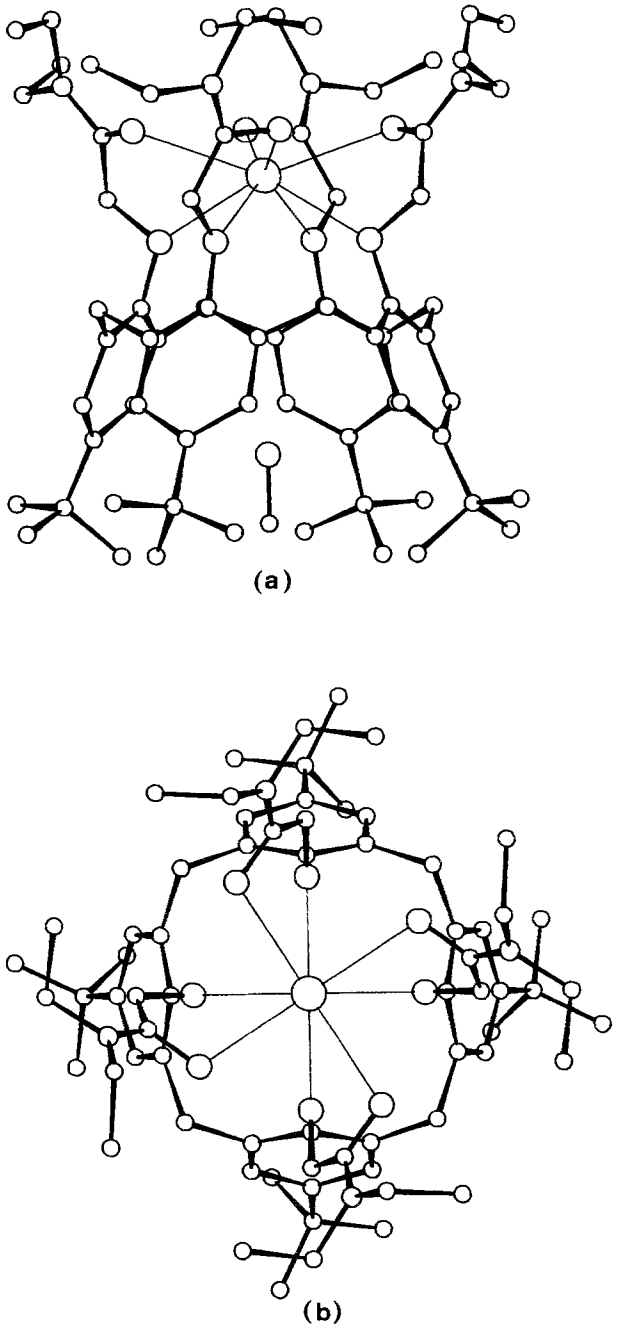


Fig. 2. Molecular structure of *p-t*-butylcalix[4]arene amide 1 : 1 KSCN (**3**) and 1 : 1 KI (**4**) complexes. (a) Perspective view; (b) view perpendicular to the reference plane.

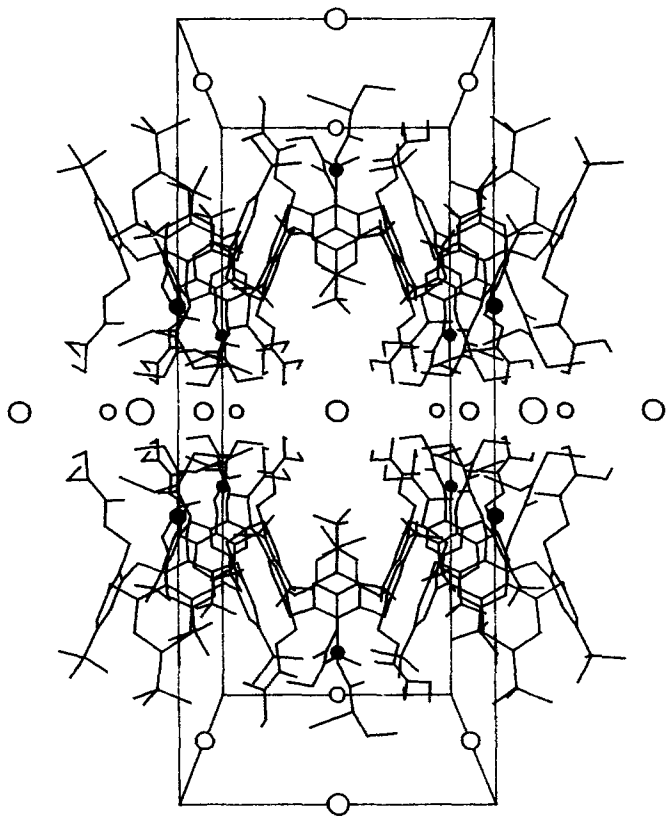


Fig. 3. Molecular packing of complexes (**3**) and (**4**). Perspective view along [100]. Cations and anions are represented by black and white balls respectively.

z axis. Normal to the fourfold axis the cavity is surrounded by eight calixarene units; four lying above and four below the mirror plane (see Figures 3 and 4). The large cavities lying on the same plane are interconnected by smaller cavities elongated in the *z* direction, which act as channels and accommodate the counterions, SCN^- and I^- which are blocked by interactions with the terminal ethyl groups of the host. The residual electron density in the large spherical intramolecular cavities could be assigned to disordered solvent which seems to play a crucial role in stabilizing the lattice; this explains the macroscopic behaviour of the crystals which tend to collapse in the absence of the mother liquor.

The rigid 'cone' structure of the free ligand (**2**) is also present in solution since the ^1H and ^{13}C NMR spectra show a very simple and symmetrical pattern (see experimental and [5]).

3.2. COMPLEXATION STUDIES IN SOLUTION

The cation binding ability of ligand (**2**) towards alkali cations in solution has been assessed through extraction, NMR (^1H and ^{13}C) and UV-vis. experiments [5].

Table III reports the mean value of the extraction equilibrium constant K_e [5] for the heterogeneous equilibrium,

$$M^+_{aq} + Pi^-_{aq} + L_{org} \overset{K_e}{\rightleftharpoons} LM^+, Pi^-_{org}$$

where the organic phase is chloroform.

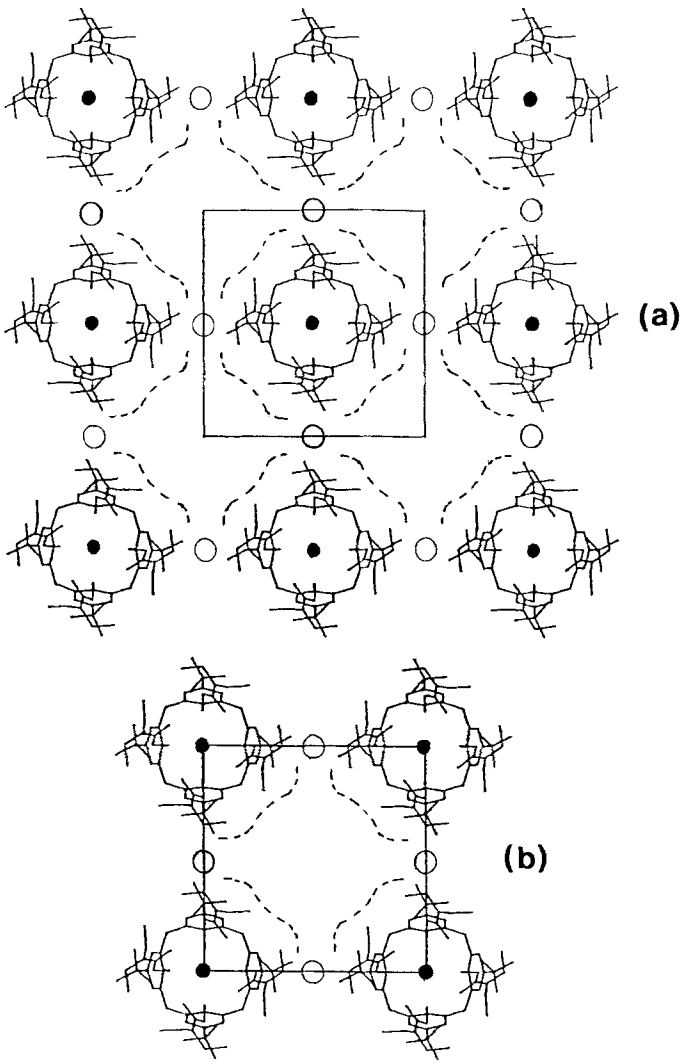


Fig. 4. Complexes (**3**) and (**4**): layers of the crystal packing along [001] showing the large cavities (dashed lines) distribution: (a) view on the plane xy at $z = 0$; (b) view on the plane xy at $z = \frac{1}{2}$. Black and white balls indicate cations and anions respectively.

Table III. Extraction equilibrium constant $K_e(H_2O \rightarrow CHCl_3)$ of alkali metal picrates in the presence of tetramide (**2**) at 20°C[a]

Metal ion M^+	K_e ($\times 10^{-6} M^{-2}$)	Selectivity factor $K_e(Na^+)/K_e(M^+)$
Li^+	13	146
Na^+	1900	1
K^+	28	68
Cs^+	17	111

[a] $[Picrate]_{H_2O} = 5 \times 10^{-4}$–$10^{-3}$M $[L_{org}] = 10^{-3}$M

The K_e value observed for sodium ($1.9 \times 10^9 M^{-2}$) is among the highest reported for neutral ligands under the same conditions [14].

By comparing these data with those obtained with the analogous *p-t*-butylcalix[4]arene tetraester [5] it can be seen that the tetramide ligand (**2**) is more efficient but less selective in the extraction of alkali metal picrates.

This is in agreement with the higher donicity of the tertiary amide group compared with the ester [15] and explains the fact that crystalline 1 : 1 adducts of ligand (**2**) with both sodium and potassium salts have been isolated, although only the structure of the latter has been solved by X-ray.

By adding variable amounts of NaSCN and KSCN in CD_3OD to a $CDCl_3$ solution of the ligand (**2**) the ^1H HMR spectrum of the latter greatly changes in all signals (no change is observed when, in a blank experiment, a comparable amount of salt free CD_3OD is added) and remains unchanged after the [Ligand]/[salt] molar ratio has reached the unity value.

For higher values of this ratio, the signals of the complexed and the uncomplexed host are both present in the spectrum indicating that, at room temperature, the exchange rate between the two species is slow on the NMR time scale and that both cations are tightly encapsulated in the hydrophilic cavity of the ligand.

That the solution structure of the two complexes is similar to the one shown in the solid state (Figure 2) is indicated by the fact that, upon complexation, the methylene protons of the acetamide groups (CH_2CON) moves 0.37 ppm (K^+) and 0.49 ppm (Na^+) upfield. These shifts can be explained by assuming that in the complexes the amide binding groups are all in the *trans* conformation which brings the CO group towards the cation located in the interior of the hydrophilic cavity and the CH_2 groups above the aromatic rings, where they experience a shielding effect.

The presence of two alkyl groups on each nitrogen of the ligand (**2**) efficiently reduces the interaction of the encapsulated cation with its counteranion leading to ion-pair separation, a phenomenon already observed and discussed in the case of the *p-t*-butylcalix[4]arene tetraester [5]. This explains the absorption maxima of the picrate anion (380 nm) in the two complexes (Na^+ and K^+) with ligand (**2**).

From the overlapping spectra it has been possible to evaluate a complex formation constant K_f

$$M^+, Pi^- + L \overset{K_f}{\rightleftharpoons} M, L, Pi$$

of ligand (**2**) with sodium ($K_f = 1.18 \times 10^4 M^{-1}$) and potassium ($K_f = 0.90 \times 10^4 M^{-1}$) picrate ion pairs at 20°C in THF.

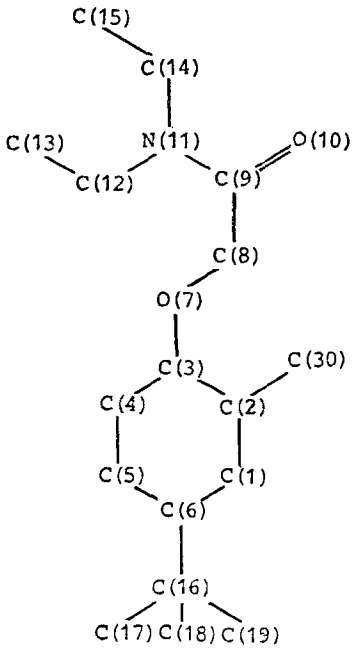
The selectivity order ($Na^+ > K^+$) based on K_f values agrees with that based on extraction data (Table III) and also the higher efficiency in complexation of ligand (**2**) compared with the reported tetrabutyl ester [5] is confirmed [16].

3.3. CONCLUSIONS

The X-ray crystal structure determination of two potassium complexes of *p-t*-butylcalix[4]arene tetra-acetamide (**2**) indicates that the cation is completely 'encapsulated' inside a polar cavity of eight oxygen atoms, which form an antiprism.

It represents the first solid state evidence of a complex formation by a new class of strong cation receptors [4, 5], whose binding properties are closer to cryptands and spherands than to classical crown ethers.

Appendix



Numbering scheme of the fundamental unit in LBC tetramide (**2**), (**3**), (**4**).

The high efficiency of these ligands is clearly linked to the convergence of the ester or amide binding groups, ensured by the rigid 'cone' structure of *p-t*-butylcalix[4]arene. The results obtained show the important role played by 'preorganization' in determining the complexing abilities of synthetic host molecules [2].

References and Notes

1. Part 15 in Molecular Inclusion in Functionalized Macrocycles. For part 14 see Ref. 6.
2. D. J. Cram: *Angew. Chem. Int. Ed. Engl.* **25**, 1039 (1986) and references therein.
3. A. Arduini, A. Pochini, S. Reverberi, and R. Ungaro: *J. Chem. Soc. Chem. Commun.* 981 (1984).
4. M. A. McKervey, E. M. Seward, G. Ferguson, B. Ruhl, and S. J. Harris: *J. Chem. Soc. Chem. Commun.* 388 (1985); S. K. Chang and I. Cho, *J. Chem. Soc. Perkin Trans.* 1, 211 (1986).
5. A. Arduini, A. Pochini, S. Reverberi, R. Ungaro, G. D. Andreetti, and F. Ugozzoli: *Tetrahedron*, **42**, 2089, (1986).
6. Preliminary communication: G. Calestani, F. Ugozzoli, A. Arduini, E. Ghidini, and R. Ungaro: *J. Chem. Soc. Chem. Commun.* 344 (1987).
7. For the nomenclature of calixarenes and their derivatives, see G. D. Gutsche: *Top. Curr. Chem.* **123,** 1 (1984).
8. N. L. Drake, C. H. Eaker, and W. Shenk: *J. Chem. Soc.* **70,** 677 (1948).
9. D. Belletti, F. Ugozzoli, A. Cantoni, and G. Pasquinelli: Centro di Studio per la Strutturistica Diffrattometrica del CNR, Parma, Italy, Internal Reports 1/79, 2/79, 3/79 (1979).
10. M. S. Lehman and F. K. Larsen: *Acta Crystallogr.* **A30**, 80 (1974).

11. F. Ugozzoli: *Computers & Chemistry* **11**, 109 (1987).
12. G. M. Sheldrick: SHELX76. *Program for Crystal Structure Determination.* Univ. of Cambridge, England (1976).
13. Cf. U. Takaki, T. E. Hogen-Esh, and J. Smid: *J. Am. Chem. Soc.* **93,** 6760 (1971).
14. J. Smid and R. Sinta: *Top. Curr. Chem.* **121**, 105 (1984).
15. V. Gutmann: *Coordination Chemistry Review* **18**, 225 (1976).
16. We thank a referee for suggesting that the presence in ligand (**2**) of ether-amide binding groups could enhance its complexing ability toward alkaline-earth cations, by analogy with calcium-selective ether-amide podands (cf. W. E. Morf *et al.*: *Progress in Macrocyclic Chemistry* (R. M. Izatt and J. J. Christensen, Eds.) Wiley-Interscience 1979, p. 1).

^{1}H titration experiments, similar to that described in this paper, show that ligand (**2**) is indeed able to complex $Ca(SCN)_2$ in $CDCl_3$ with a 1 : 1 stoichiometry. However, since we do not have the overall picture of the association constants, we cannot discuss the problem of monovalent/divalent cation selectivity of our ligand (**2**).