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THE PREPARATION AND PROPERTIES OF A NEW LIPOPHILIC SODIUM SELECTIVE ETHER ESTER LIGAND DERIVED FROM p-t-BUTYLCALIX[4]ARENE [1]

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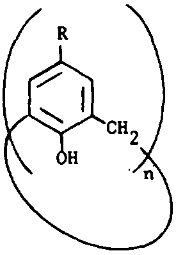
Abstract - A new lipophilic cation ligand (2), which shows selectivity for sodium in extraction experiments, has been obtained by the reaction of p-t-butylcalix[4]arene and t-butyl bromoacetate. The X-ray crystal structure determination and ^{1}H and ^{13}C NMR studies show compound (2) in a fixed "cone" structure both in the solid state and in solution. Compound (2) in apolar media strongly encapsulates sodium cation with a 1:1 stoichiometry and is able to separate the tight sodium picrate ion pair in THF.

Although many examples of synthetic receptors showing unique complexing abilities toward metal cations are known,[2] the research in this field is still very active with the aim of obtaining complexones showing new properties or improved selectivities. In the last few years we have been engaged in several aspects of the chemistry of calixarenes (I), which are phenol-formaldehyde cyclic oligomers.[3] Beside the inclusion abilities of these synthetic macrocycles toward neutral organic molecules which has been reported,[4] a second aspect of calixarenes attracted us, once their structures were firmly established. It was their lipophilic nature and the presence of several hydroxy groups ordered in cyclic arrays of different sizes, which could be functionalized with suitable cation binding units to build up new lipophilic ligands .



(I)

In previous papers we have reported several examples of cation ligands built on calixarenes some of them bearing neutral binding sites,[5] some other ionizable groups[6,7] capable to form with cations neutral ion-pairs, which eventually were transferred into organic media.

In preliminary communications[7] we have reported on the synthesis and X-ray crystal structure of a tetra-butyl ester of p.t-butylcalix[4]arene which shows remarkable complexing properties toward alkali metal cations and in particular sodium. This paper is a full account of the results obtained with this new ligand.

RESULTS AND DISCUSSION

Synthesis and structure of the ligand (2)

The compound has been obtained in 70% yield by heating p.t-butylcalix[4]arene (1) with t-butyl bromoacetate and sodium hydride in THF/DMF (Scheme 1).

Scheme 1

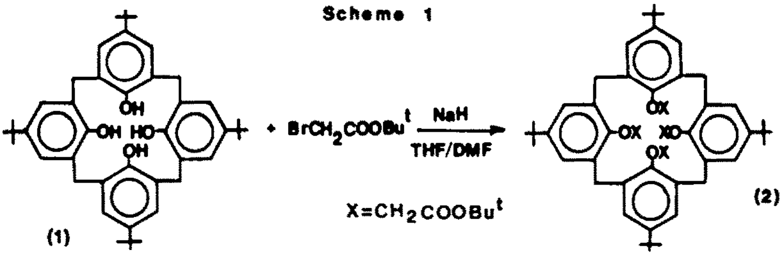


Fig. 1 shows the X-ray crystal structure of the ligand (2) carried out as described in the experimental section on a prismatic crystal obtained from hexane.

The molecule shows clearly a "cone" structure, although slightly distorted, with two distinct regions. With respect to an ideal plane containing the bridging methylene groups we can distinguish a top hydrophilic region (cavity?) created by the ether oxygens and that of the four ester groups which are all on the same side (cis), and a second hydrophobic cavity on the bottom created by the aromatic and t-butyl groups.

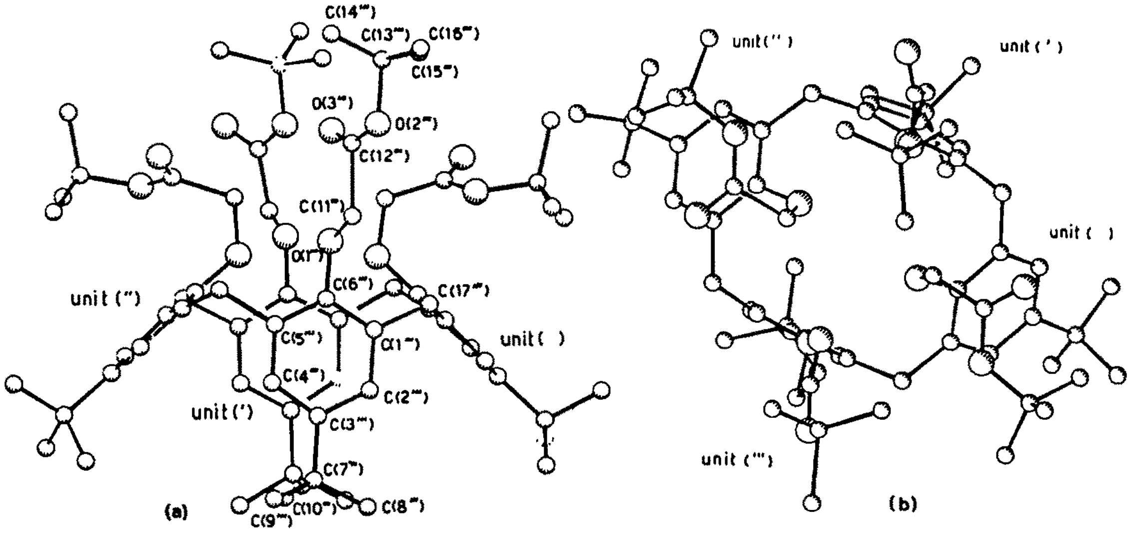


Fig. 1. Structure of ligand (2): (a) view along the mean molecular plane and atom numbering; (b) view perpendicular to the molecular plane.

Molecular geometry can be referred to this mean molecular plane where the CH$_2$ bridges show out of plane distances of 0.151(8), -0.151(8), 0.150(8), -0.151(8) Å for the units ( ) to (''') respectively. So the conformation of the macrocycle may be defined by the dihedral angles the aromatic rings of the four units ( )-(''') make with the mean molecular plane: 135.9(2)°, 96.1(2)°, 135.8(1)°, 93.3(2)°.

The relative dihedral angles between two adjacent rings are : ( )-(')=$88.2(3)^{o}$, (')-('')=$79.4(3)^{o}$, ('')-(''')=$86.6(3)^{o}$ and (''')-( )=$81.8(2)^{o}$ whereas that between two opposite rings are: (')-(''')=9.4^{o} and ( )-('')=91.7^{o}.

The conformation of the ester chains may be conveniently described by the torsion angles C(6)-O(1)-C(11)-C(12) which are $-23.3(10)^{o}$ and $-26.8(11)^{o}$ for the chains ( ) and ('') and indicates a <u>cis</u> conformation whereas the corresponding values for the chains belonging to the (') and (''') units are $180.0(6)^{o}$ and $178.9(6)^{o}$ giving a <u>trans</u> conformation.

Therefore the ester chains attached to the aromatic rings (') and ('''), which are almost parallel each other and perpendicular to the molecular plane, show the hydrogens of the methylene groups pointing outside and the alkyl part of the ester moieties inside the hydrophilic cavity, whereas the other two ester chains of the units ( ) and ('') show the CH_2 inside and the $COOBu^{t}$ groups directed toward the exterior of the macrocycle.

Bond angles involving the bridging methylenes are $108.3(6)^{o}$, $111.1(6)^{o}$, $108.1(6)^{o}$, $111.3(6)^{o}$ for units ( )-(''') respectively, which slightly deviates from the theoretical value of 109.5^{o}. This shows that the macrocycle conformation, in the absence of any intramolecular hydrogen bonds, is mainly determined by steric interactions between the ester chains.

This is also confirmed by the torsion angles involving the bridging methylene carbon atoms which deviates significantly from the value of $\pm 90^{o}$ observed in other cyclic oligomers investigated by us[4,8] where the cone structure was essentially determined by strong intramolecular hydrogen bonds.

The four ether oxygen basis of the hydrophilic cavity has roughly an elliptical shape since the distances between two opposite oxygen atoms are O(3)-O(3'') =8.019(9) Å and O(3')-O(3''') =7.149(16) Å.

A symmetrical and rather rigid "cone" structure is also present in solution as inferred from the ^{1}H and ^{13}C NMR spectra which show a very simple pattern, independent on temperature.

In particular the ^{1}H NMR spectrum (Fig. 2) shows only singlets for both t-butyl groups, and aromatic protons whereas the bridging methylene show an AB system with two 4H doublets.

On the basis of Nuclear Overhauser Effect experiments on compound (2) and other simple calix [4]arene derivatives[9] the high field doublet at 3.18 δ has been assigned to the equatorial proton H_B whereas the low field signal at 4.89 δ to the axial one H_A.

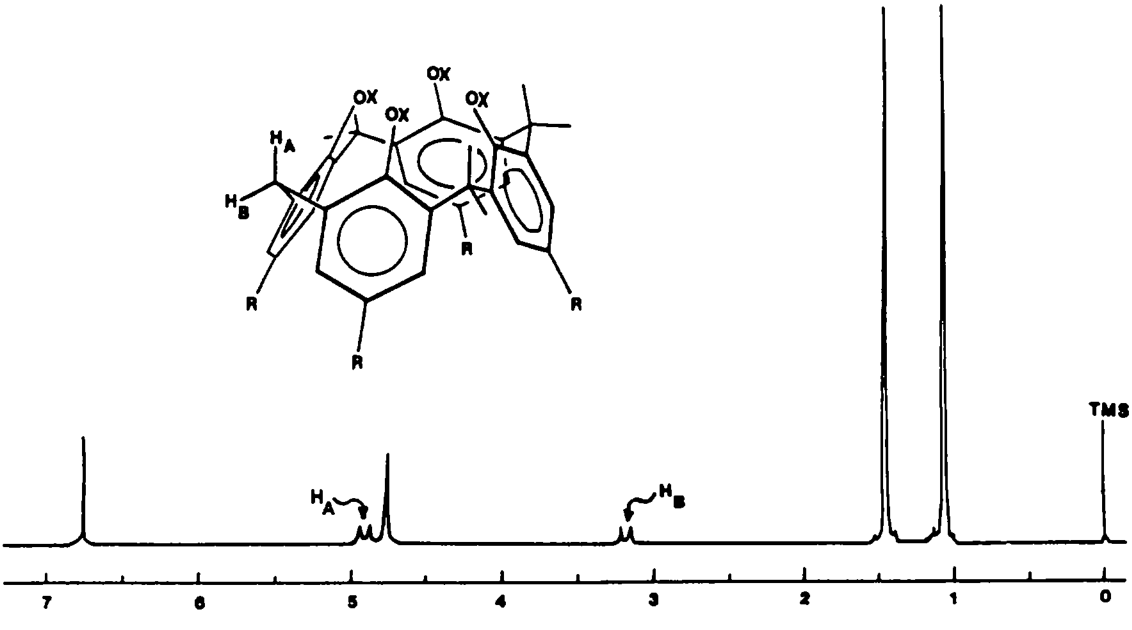


Fig. 2 . ^{1}H NMR spectrum (200 MHz , δ from TMS) of compound (2) which shows the fixed "cone" conformation. X = CH_2COOBu^{t}.

Alkali metal picrate extraction from water to chloroform

In order to establish, in a quantitative way, the complexing and phase transfer abilities of this new ligand toward cations, the extraction of alkali picrates from water to chloroform was chosen. Many water/solvent systems have been used for this purpose[10,11] and recently Smid and Sinta have critically reviewed the effect of solvent and salt concentration on the extraction equilibrium constant Ke.[11] These authors point out that the system water/chloroform give usually more reliable data, since at complex concentration $\geq 5\times10^{-5}$M the ionic species in the organic phase are usually present in the form of ion pairs and dissociation into free ions is negligible.

In this case the overall extraction equilibrium can be expressed by

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

where M^+_{aq} and Pi^-_{aq} represent the alkali cation and picrate anion in aqueous phase and L_{org} and LM^+,Pi^-_{org} are, respectively, the ligand and ligand-metal picrate complex in chloroform. The extraction equilibrium constant Ke is given by the following expression

$$Ke = \frac{\left[LM^+,Pi_{org}\right]}{\gamma_{\pm}^{2}\left[M^+_{aq}\right]\left[Pi^-_{aq}\right]\left\{\left[L_{org}\right]_0 - \left[LM^+,Pi^-_{org}\right]\right\}}$$

where $\gamma_{\pm}$ is the mean activity coefficient of the picrate in water, $\left[L_{org}\right]_0$ is the initial ligand concentration in chloroform and $\left[LM^+,Pi^-_{org}\right]$ is the ligand picrate complex concentration in chloroform, which can be measured either directly by UV-Visible spectroscopy or by difference from the decrease of the picrate in water solution. For these reasons and from the fact that preliminary extraction experiments in the more frequently used H_2O/CH_2Cl_2 system showed too high extraction (almost saturation) for our ligand, we chose chloroform as the organic solvent. The results of extraction experiments are reported in table 1.

Table 1. Extraction equilibrium constants of alkali metal picrates in the presence of ligand (2) for the system $H_2O \longrightarrow CHCl_3$ at 20°C.+

Metal ion M^+	$[\text{Picrate}]_0$ ($\times10^3$M)	$\frac{[\text{Ligand}]_{comp}}{[\text{Ligand}]_0}$	Ke ($\times10^{-6}M^{-2}$)	$\overline{Ke}$ ($\times10^{-6}M^{-2}$)	Selectivity factor $\overline{Ke}(Na^+)/\overline{Ke}(M^+)$
Li^+	4.4	0.12	0.0080	0.0056	202
	8.0	0.17	0.0033		
Na^+	0.26	0.06	1.73	1.13	1
	0.51	0.14	1.16		
	0.74	0.21	0.97		
	0.97	0.25	0.66		
K^+	5.1	0.19	0.011	0.010	113
	8.4	0.32	0.009		
Cs^+	3.5	0.13	0.014	0.011	103
	4.9	0.14	0.008		

+ $\left[L_{org}\right] = 10^{-3}$ M; λ_{max} for all complexes in $CHCl_3$ = 378 nm

The data refer to experiments performed in such a way that the concentration of the extracted complexes is always higher than 10^{-4} M and the fraction of complexed ligand ranges between 0.06 and 0.32. This ensures that most of the complex is in the form of an ion pair and that saturation of the ligand is avoided. However a trend is observed in which Ke increases by decreasing the concentration of the extracted complexes and become considerable higher (even 10 times) for all cations at concentrations lower than 10^{-4}M, which can be possibly due to dissociation of the complexed ion pair in these conditions.[12]

The extraction ability of the macrocycle is rather high and the selectivity is toward sodium.[13] This result sharply contrasts the behaviour of other ligands derived from calix[6]- and calix[8]arenes, which show selectivity toward the large and less hydrated cations such as cesium, guanidinium and potassium.[5,13,14]

A comparison between the observed values of $\overline{Ke}$ for sodium cation with reported values,[15] in the same $H_2O/CHCl_3$ system, shows that our ligand is 305 times more efficient than methyl-mono-benzo-15-crown-5 and 491 times than methyl-monobenzo-18-crown-6. Unfortunately no comparison is possible with cryptands[16] and other more lipophilic complexing agents which show selectivity for sodium[17,18] due to the different systems used to establish their complexing ability. However the $\overline{Ke}$ value found for ligand (2) is one of the highest observed for the system $CHCl_3/H_2O$ and the selectivity factor, as measured by the $\overline{Ke}$ $(Na^+)/\overline{Ke}(M^+)$ ratio, ranges between 103 $(M^+=Cs^+)$ and 202 $(M^+=Li^+)$.

Complexation in aprotic solvents (NMR studies)

Complexation studies in aprotic solvents have been performed by ^1H, ^{13}C NMR and UV-VIS spectroscopy.

In fig. 3 is shown the ^1H NMR spectrum of the free ligand and of its sodium thiocyanate complex.

By adding variable amounts of NaSCN in CD_3OD to a $CDCl_3$ solution of the ligand the ^1H NMR spectrum of the latter greatly changes in all signals.

The largest variation in chemical shifts is experienced by the axial protons H_A which moves 0.73 ppm upfield and by the aromatic protons which moves 0.38 ppm downfield. Also the methylene protons of the acetate moieties move 0.37 ppm upfield whereas all ether signals shift downfield upon complexation with sodium ion.

This behaviour is due to the contribution of the complexed cation, which induces downfield shifts on protons adjacent to the binding sites, and also to conformational changes. So the upfield shift experienced by the methylene protons of the acetate groups can be explained by assuming that upon complexation all these groups adopt a trans conformation, which brings the methylene protons out from the hydrophilic oxygen region and above the aromatic ring where they experience a shielding effect. More difficult is to the explain the high upfield shift (0.7 ppm) of the axial protons H_A which seems to be very sensitive to small variations in the polar environment of the ether and ester oxygens, which are in close proximity.

The ^1H NMR titration experiment (Fig. 3) clearly indicates a 1:1 stoichiometry for the NaSCN complex with ligand (2), since all signals remain unchanged after the salt/ligand ratio has reached the unity value (c) .

For lower values of this ratio (b) both signals of the complexed and uncomplexed host are present in the spectrum, indicating that, at room temperature, the exchange rate between the two species is slow on the NMR time scale.

This behaviour contrasts with that of KSCN which induces, in the same conditions, a large broadening of all signals of host (2) (exchange rates comparable with the NMR time scale) until the $[K^+]/[\text{ligand}]$ ratio reaches the value of 1 when all signals become sharp showing resonance values close to that of the sodium complex (see experimental). The data obtained with NaSCN indicate that sodium cation is tightly "encapsulated" in the hydrophilic cavity and exchanges more slowly than potassium and, presumably, other cations with larger ionic radii.

Ligand (2) behaves toward sodium cation similarly as do other powerful complexing agents such as cryptands[16,19] and spherands,[20] which have low exchange rates and high complexation constants toward alkali cations. This is noteworthy since the binding sites of ligand (2) are aromatic ether and ester groups, which are not the best donor groups toward alkali cations.[21]

As pointed out by Cram and coll. in explaining the complexing ability of spherands[20] the proper organization of the oxygens can usually more then compensate for negative electronic effects. This seems to be the most important factor also in the case of ligand (2), where the preorganization of binding sites in a structure with little conformational freedom results in remarkable binding properties.

The involvment of the phenolic oxygens in complexation is indicated by the high downfield shift experience by the aromatic protons in the ^{1}H NMR spectrum of the sodium complex and by the ^{13}C chemical shifts of the aromatic carbon atoms which follow the same pattern observed with benzocrown ether complexes.[22]

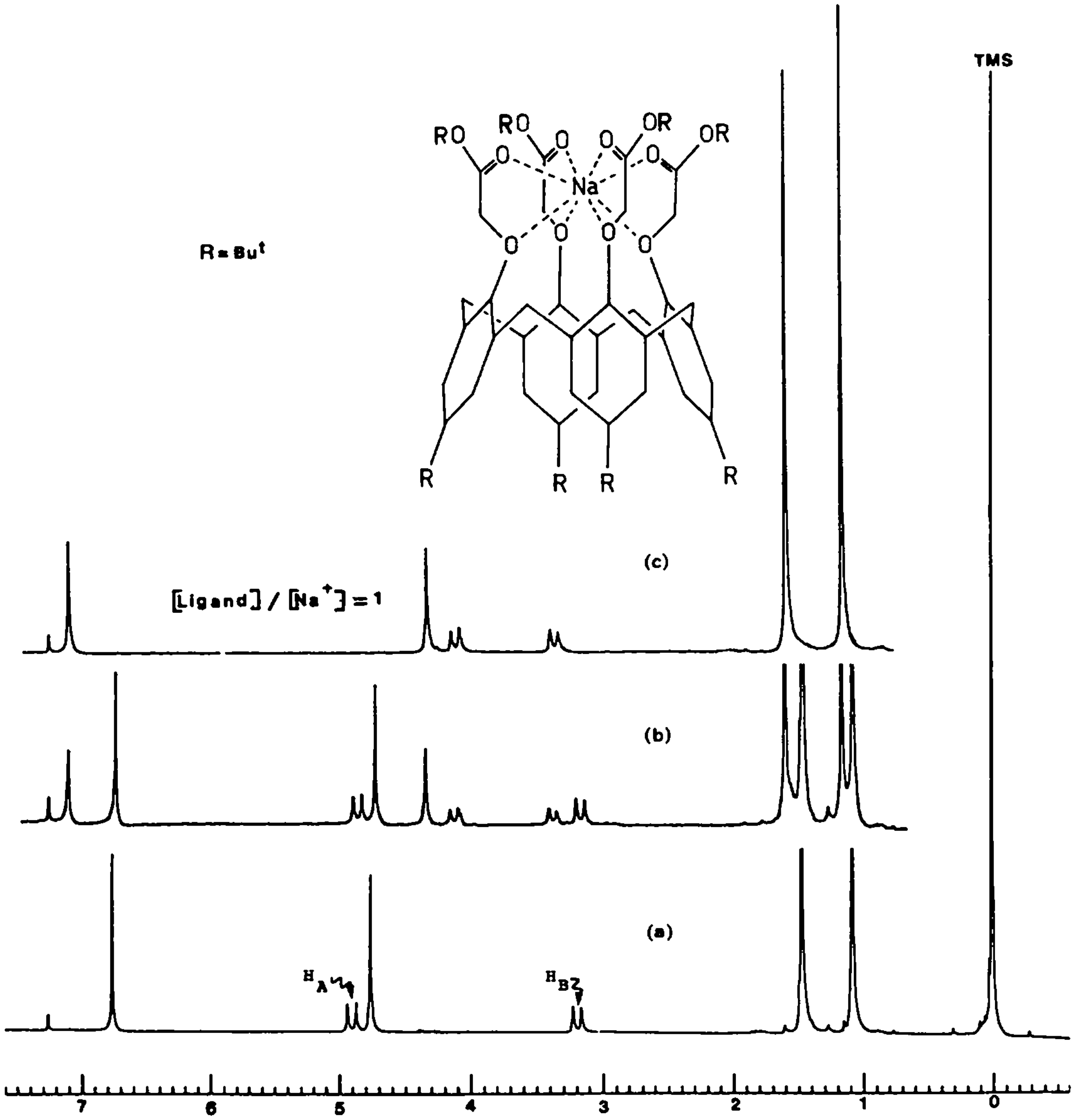


Fig. 3. Encapsulation of NaSCN by ligand (2). ^{1}H NMR spectra (200 MHz) in $CDCl_3$ at 25 °C: (a) = free ligand; (b)= 40 % complex ; (c)= 100 % complex ; $[Ligand]_{CDCl_3}$ = 5x 10^{-2} M

Although less clearly indicated, because masked by other conformational effects, the four ester moieties seem to participate on complexation via the carbonyl groups, as expected.[23] This is shown by the low downfield shift ($\Delta\delta = 1.2$ ppm) experienced by the C=O carbon in ^{13}C NMR of the sodium thiocyanate complex and by the formation of a single carbonyl stretching absorption band at 1740 cm^{-1} in the IR spectrum of the same complex, whereas the free ligand shows two strong bands at 1750 and 1720 cm^{-1}.

Ion pair separation by ligand (2) (Optical Spectra)

Another interesting property of ligand (2) is its ability to separate ion pairs in low polarity media.

This fact, which was already indicated (Table 1) by the observed absorption maxima of the complexed picrate salts extracted in $CHCl_3$, is more clearly shown in Fig. 4. Addition of variable amounts of (2) to a 10^{-3} M THF solution of NaPi in THF, causes a bathochromic shift of the obsorbtion maximum from 351 to 380 nm (isosbestic point at 361 nm), which indicates the transformation from a tight ion pair to a ligand separated one, having a larger interionic distance between sodium and picrate anion.[24]

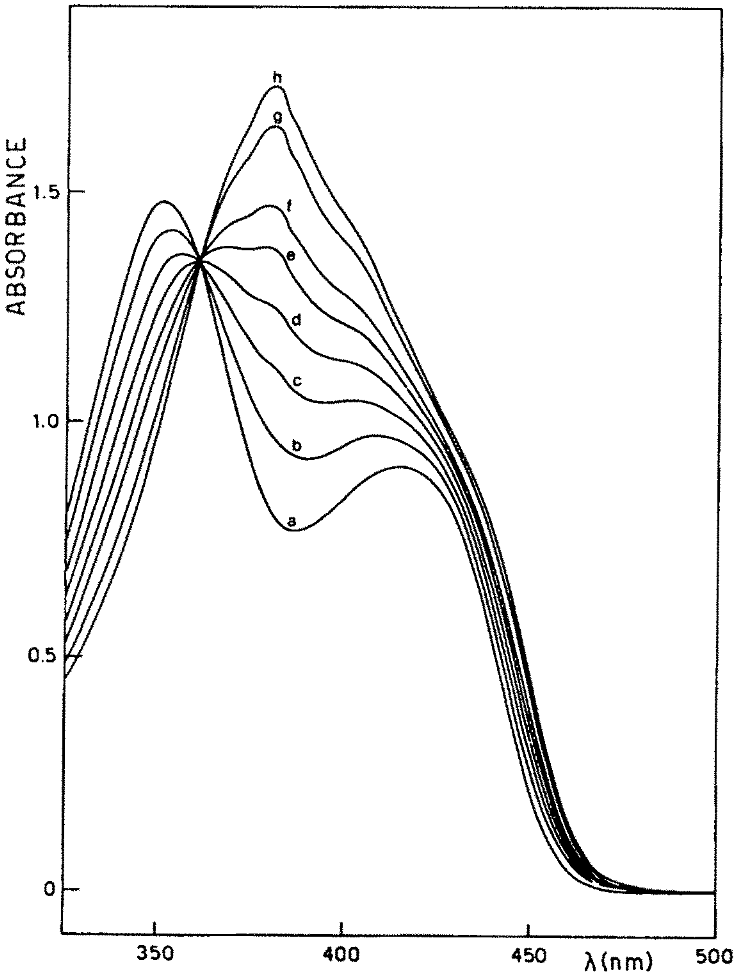


Fig.4 . Optical spectra of a 0.89×10^{-3} M THF solution of sodium picrate in the presence of different amounts of LBC-Tetraester (2) at 25° C . Molar ratio of ligand to picrate salt : (a)=0; (b)= 0.22 ;(c)=0.45;(d)= 0.89 ; (e)=1.12; (f)=1.68; (g)=2.24 ; (h)=5.62

This contrasts with the behaviour of benzo-18-crown-6 and benzo-15-crown-5 which form under the same conditions 1:1 complexes with sodium picrate having absorption maxima at 362 and 356 nm respectively, which are typical of ion pairs externally coordinated by crown ethers.[15] The same behaviour is shown by other crown ethers in apolar solvents.[25] Even bis-benzo-12-crown-4, which forms an intramolecular sandwich type complex with sodium ion and belongs to a family of powerful sodium selective complexing agents,[18] is not able to separate the tight sodium picrate ion pair, under the same conditions.[26] Knowing the molar absorptivity of the two species Na^+,Pi^- and Na^+,L,Pi^- at 357 and 380 nm it has been possible to calculate the complex formation constant Kf

$$Na^+,Pi^- + L \xrightleftharpoons{Kf} Na^+,L,Pi^-$$

of ligand (**2**) with the sodium picrate ion pair in THF. Its value is $5.6 \times 10^3\ M^{-1}$. This value is not very high because refers to the complexation of a tight ion pair involving an oxy-anion (the picrate) strongly associated with sodium cation.

It is comparable with some values reported by Smid and coll.[27] for the complexation of sodium picrate in THF by crown ether containing network polymers. However these refer to the formation of externally complexed tight ion pairs (Pi^-,Na^+,L), whereas complexation by ligand (**2**) leads to ion pair separation. The situation is similar to the behaviour of macrobicyclic polyethers (bis-15-crown-5) which are more effective complexing agents for K^+,Pi^- ion pair, leading to its separation in THF, compared with monomeric benzo-15-crown-5 although the numerical value for the 1:1 complex formation constant is similar in the two cases.[24]

CONCLUSIONS

Compound (**2**) belongs to a new type of powerful cation binding ligand whose properties are much closer to spherands and cryptands than to classical crown ethers.

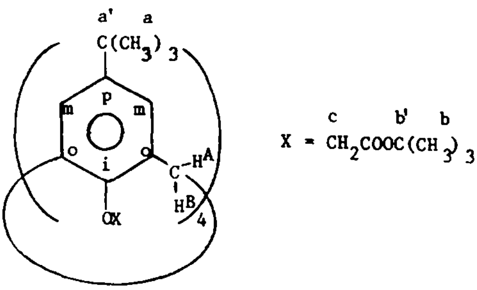
Studies are in progress to determine formation constants in different solvents and complexation and decomplexation rate constants for compound (**2**) toward alkali cations to compare with that observed with other known neutral ligands and to establish which factors are important in determining the selectivity order observed.

A key factor for the high efficiency and selectivity of ligand (**2**) is the preorganization of the binding groups in a rigid framework such as that offered by the p-t-butylcalix[4]arene in the fixed "cone" structure. Therefore it should be possible, as earlier anticipated,[5] to synthesize a wide variety of powerful and selective new complexing agents using calixarenes as "building blocks" and changing the nature of the binding units.

EXPERIMENTAL

^1H and ^{13}C NMR spectra were recorded at 200 MHz using a BRUKER CXP-200 instrument in $CDCl_3$ with TMS as internal standard. Chemical shifts (δ) are expressed in ppm. M.P. was taken on a Electrothermal^R apparatus in a capillary sealed in vacuo and has not been corrected. IR spectra have been registered on a Perkin Elmer 298 Instrument and only the most relevant absorption peaks are reported. UV-Vis spectra were registered on a JASCO UVIDEC-505 Spectrophotometer and microanalyses were carried out by Istituto di Chimica Farmaceutica - Universita' di Parma.

Chemicals.
p.t-butylcalix[4]arene (1) was available from previous work.[5] t-Butyl Bromoacetate and sodium hydride (60% on oil) were used as purchased (Fluka), THF was distilled over $LiAlH_4$ and stored over Na pellets, whereas DMF was kept over Linde Molecular Sieves 4 Å before use. Flash chromatography was performed using Merck Silica gel 230-400 mesh. Thin layer chromatography analyses were performed on Carlo Erba Stratochrom SIF_{254} silica gel plates (0.2 mm thicknes). Sodium and potassium thiocyanate were reagent grade from VENTRON (Alpha) and were dried in vacuo at 50°C for 24 h before use. Picrate salts were obtained by neutralizing picric acid with the appropriate base in aqueous ethanol recrystallizing twice from the same solvent and dried in vacuo at ambient temperature for several days. The solid picrates and their water solutions were stored in the dark. Acetonitrile was distilled from Linde Molecular Sives 3 Å and stored on the same sieves.



$X = CH_2COOC(CH_3)_3$

5,11,17,23-tetra-t-Butyl-25,26,27,28-tetra(t-butoxycarbonyl)-methoxy-calix[4]arene[28] (LBC-tetraester) (2).

In a three necked round bottomed flask under a dry nitrogen atomosphere p.t-butylcalix[4]arene (1) (1.62, 2.5 mmol) was suspended in anhydrous THF (80 ml) and dry DMF (15 ml), then gentle warmed with magnetic stirring until most of the solid was dissolved. After cooling 1.6 g of NaH was added followed by an excess of t-butyl bromoacetate (33 ml, ca. 0.2 mol) and the reaction mixture refluxed under N_2 for 3 h. Most of the solvent and the excess bromoacetate was removed in vacuo, then the residue treated with water and extracted with CH_2Cl_2. The combined organic extracts were washed with water and the solvent removed in vacuo. Addition of n-hexane to the oily residue often caused the separation of a solid which consists of almost pure (2). To recover all the product the oily residue was purified by flash-cromatography by eluting first with ethyl acetate, which removes the oily impurities, followed by THF which is able to detach and elute all the compound, strongly absorbed on silica gel. Solvent evaporation from the combined chromatographic fractions (controlled on TLC, Ethyl acetate as eluent) gave 1.92 g (70% yield) of a white solid which is pure compound (2). Recrystallization from n-hexane gave transparent prysmatic crystals, m.p. 258-261°C. IR (KBr) 1750, 1720, 1220, 1200, 1160, 1120, 1065, cm^{-1}; ^1H NMR ($CDCl_3$)δ 1.07 (s, 36H, $CH_3{}^a$), 1.45 (s, 36H, $CH_3{}^b$), 3.18 (d,4H,H^Beq), 4.75 (s, 8H $CH_2{}^c$), 4.89 (d, 4H, H^Aax), J_{AB} = 13 Hz, 6.76 (s, 8H, H^m). ^{13}C NMR($CDCl_3$), 28.1 ($CH_3{}^b$), 31.3 ($CH_3{}^a$), 32.1 (CH^AH^B), 33.7 ($C^{a'}$), 71.9 ($CH_2{}^c$), 80.4 ($C^{b'}$), 125.0 (C^m), 133.3 (C^o), 144.5 (C^p), 153.1 (C^i), 169.5 (C=O). $C_{68}H_{96}O_{12}$ (1105.5) calc. C 73.88 H 8.75; found C 73.97 H 8.76.

LBC-Tetraester (2). NaSCN complex

After slow evaporation of the solvent from samples of ^1H NMR complexation experiments containing a 1:1 LBC-Tetraester (2)/NaSCN molar ratio in $CDCl_3/CD_3OD$ white needels formed, which were collected and dried in vacuo (room temperature, 0.1 mm Hg). IR (KBr) 2050, 1740, 1250, 1160, 1130, 1070 cm^{-1}, ^1H NMR ($CDCl_3$) δ 1.16 (s, 36H $CH_3{}^a$), 1.60 (s, 36H, $CH_3{}^b$), 3.40 (d, 4H, H^Beq), 4.16 (d, 4H, H^Aax, J_{AB} = 12 Hz, 4.38,(s, 8H, $CH_2{}^c$), 7.14 (s, 8H, H^m). ^{13}C NMR($CDCl_3$) 28.5 ($CH_3{}^b$), 30.6 (CH^AH^B) 31.4 ($CH_3{}^a$), 34.4 ($C^{a'}$), 74.0 ($CH_2{}^c$), 83.5 ($C^{b'}$), 126.2 (C^m), 134.6 (C^o), 148.7 (C^p),150.3 (C^i), 170.7 (C=O).

LBC-Tetraester (2).KSNC complex

By an analogous procedure to the sodium complex a (2). KSCN 1:1 complex has been isolated which shows the following ^1H NMR spectrum ($CDCl_3$) δ 1.16 (s, 36H, $CH_3{}^a$), 1.60 (s, 36H, $CH_3{}^b$), 3.39 (d, 4H, H^B_{eq}), 4.31 (d, 4H, H^A_{ax}), J_{AB} = 12 Hz, 4.39 (s, 8H, $CH_2{}^c$), 7.15 (s, 8H, H^m).

^1H NMR complexation experiments

From stock solutions (1.2-1.5 M) of the salt in CD_3OD, aliquots were withdrawn with a 10 µl siringe and added to a $CDCl_3$ solution ($\sim 10^{-2}$M) of the ligand directly in the NMR tube. The spectra were registered after each addition and the temperature of the NMR probe kept constant at 25°C.

Cation picrate extraction

Solution of metal picrates were made in demineralized water, whereas the ligand was dissolved in $CHCl_3$ purified by washing it several time with H_2O followed by fractional distillation. The two solvents were saturated with each other before use to prevent volume changes during the extraction. Equal volumes (5 ml) of chloroform solution of ligand (2) and aqueous alkali metal picrates were repeatedly shaken in a stoppered flask at 20°C. After phase separation the concentration of the complexed picrate salt in the $CHCl_3$layer was determined spectrophotometrically by diluting the sample (2 ml) with an equal volume of acetonitrile and using $\varepsilon = 18000\ M^{-1}\ cm^{-1}$ at 378 nm. For an internal check also the decrease in concentration of the picrate salts in water solution (λmax 354 nm $\varepsilon = 14500\ M^{-1}\ cm^{-1}$) was measured and found in agreement with that of the chloroform layer. Each Ke value reported in Table 1 is the mean of three independent measurements. Calculated values[15] of $Y_\pm$ = 0.79 for 10^{-2}M, 0.88 for $5x10^{-3}$ M and 0.95 for 10^{-3} M aqueous solutions of metal picrates were used.

Optical spectra

Complex formation constant for the ion-pair separation process of sodium picrate and ligand (2) in THF was measured by evaluating the fraction of tight ion pair Na^+, Pi^- (λ_{max} 351 nm) and of ligand separated ion pair Na^+,L,Pi^- (λ_{max} 380 nm) spectrophotometrically. Molar absorbitivities necessary for calculations[29] were: ε_{351} = 16500 M^{-1} cm^{-1}, ε_{380} = 8900 M^{-1} cm^{-1} for the tight ion pair and ε_{380} = 20000 M^{-1} cm^{-1}, ε_{351} = 11600 M^{-1} cm^{-1} for the solvent separated species.

X-ray structure analysis of compound (2)

Crystal data: $C_{68}H_{96}O_{12}$, Formula weight. 1105.5 Monoclininc; a = 15.475(3), b = 27.002(2), c = 16.339(3) Å, β = 92.24(3), U= 6822.1(1.3) $Å^3$, Z = 4, D_c = 1.076 g cm^{-3}, space group (from systematic absences) $P2_1/n$, Cu-Kα radiation $\bar{\lambda}$ = 1.5418 Å, μ (Cu-Kα) = 5.4 cm^{-1}.

Measurements. A single colourless transparent crystal of 0.6 x 0.5 x 0.4 mm (from hexane), suitable for the X-ray analysis was used for the intensities measurements. Lattice parameters were calculated from 30 $(\theta,\chi,\phi)_{h\,k\,l}$ measurements taken on a Siemens AED single crystal diffractometer on line to a General Automation Jumbo 220 microcomputer[30].

A total of 10500 reflections were collected at room temperature with θ – 2θ step scanning mode in the range $3^\circ \le \theta \ge 60^\circ$ using Nickel filtered Cu-Kα radiation. The intensities $I_{h\,k\,l}$ were determined analyzing the reflection profiles with the Lehman Larsen procedure[30,31] and only the 5139 reflections with $I \ge 2\sigma(I)$ ($\sigma(I)$ based on statistic count) were retained as observed. One standard reflection was recorded almost every hour to account for instrumental linearity. No correction was made for absorption effect.

Structure Analysis

The structure was solved and refined using the SHELX[32] package of crystallographic computer programs. From direct methods, after many trials, the analysis of the E-map computed with the most consistent set of signs, lead to the approximated positions of 70% of all non hydrogen atoms. Successive fourier maps have made possible to complete the structure.

Afterwards, with cicles of full matrix least squares (blocked to 181 variables), the atomic parameters were refined at first with isotropic and then with anisotropic thermal parameters.

The position of the 96 hydrogen atoms were calculated with C-H = 1.08 Å, and their contribution was substracted to the Fo's because of the upper limit of 80 anisotropic atoms in SHELX program.

The refinement process was stopped at R = 0.12. The final difference electron density map showed the highest residual peak of 0.86 e $Å^{-3}$. Scattering factors were taken from ref. 33 and the calculations were performed on the GOULD 32/77 of Centro di Studio per la Strutturistica Diffrattometrica del CNR (PARMA). Bond distances, bond angles and relevant torsion angles are reported in Tab.2 .

Atomic coordinates, thermal parameters and a list of observed and calculated structure factors have been deposited at the Cambridge Crystallographic Data Centre[34].

Table 2

Bond distances (Å)

	( )	(')	(")	(''')
C(1)-C(2)	1.408(10)	1.356(11)	1.354(10)	1.418(11)
C(1)-C(6)	1.385(10)	1.414(11)	1.365(10)	1.372(9)
C(1)-C(17)	1.538(10)	1.500(11)	1.534(8)	1.524(10)
C(2)-C(3)	1.354(10)	1.410(12)	1.447(11)	1.444(12)
C(3)-C(4)	1.396(11)	1.385(12)	1.343(11)	1.324(11)
C(3)-C(7)	1.542(14)	1.525(12)	1.536(11)	1.507(11)
C(4)-C(5)	1.367(11)	1.396(11)	1.381(11)	1.388(11)
C(5)-C(6)	1.412(12)	1.367(11)	1.418(11)	1.386(9)
C(6)-O(1)	1.368(9)	1.417(10)	1.382(9)	1.407(7)
C(7)-C(8)	1.402(16)	1.471(16)	1.583(14)	1.469(17)
C(7)-C(9)	1.490(20)	1.510(18)	1.539(14)	1.484(18)
C(7)-C(10)	1.438(22)	1.429(20)	1.488(14)	1.410(18)
O(1)-C(11)	1.406(10)	1.419(8)	1.420(10)	1.364(10)
C(11)-C(12)	1.489(13)	1.508(12)	1.514(15)	1.668(14)
C(12)-O(2)	1.338(10)	1.284(10)	1.293(12)	1.175(14)
C(12)-O(3)	1.218(12)	1.196(11)	1.220(14)	1.184(14)
O(2)-C(13)	1.442(10)	1.472(10)	1.460(12)	1.499(14)
C(13)-C(14)	1.507(15)	1.458(17)	1.487(16)	1.435(21)
C(13)-C(15)	1.508(15)	1.510(15)	1.540(16)	1.503(22)
C(13)-C(16)	1.514(14)	1.502(17)	1.495(17)	1.538(24)
C(17)-C(5')	1.527(10)	1.543(11)	1.523(10)	1.534(10)

Bond angles (°)

	( )	(')	(")	(''')
C(6)-C(1)-C(17)	121.1(6)	121.6(7)	121.5(6)	124.5(7)
C(2)-C(1)-C(17)	118.9(7)	121.1(7)	119.3(6)	117.2(7)
C(2)-C(1)-C(6)	119.6(6)	117.4(7)	118.7(6)	118.2(7)
C(1)-C(2)-C(3)	120.7(7)	122.7(7)	122.0(7)	119.6(7)
C(2)-C(3)-C(7)	122.3(8)	122.3(7)	119.4(7)	118.0(7)
C(2)-C(3)-C(4)	119.7(8)	117.7(8)	117.1(7)	117.8(8)
C(4)-C(3)-C(7)	118.0(8)	119.9(7)	123.4(7)	124.1(8)
C(3)-C(4)-C(5)	120.9(7)	121.2(7)	122.7(7)	124.4(7)
C(4)-C(5)-C(6)	119.7(7)	118.6(7)	118.1(7)	117.5(7)
C(1)-C(6)-C(5)	119.2(6)	122.1(8)	121.3(7)	122.3(6)
C(5)-C(6)-O(1)	117.6(6)	119.1(7)	115.4(7)	119.8(6)
C(1)-C(6)-O(1)	123.1(6)	118.8(7)	123.2(6)	117.9(6)
C(3)-C(7)-C(10)	111.6(11)	115.0(9)	112.6(8)	108.3(8)
C(3)-C(7)-C(9)	107.6(10)	112.2(8)	109.6(7)	110.1(8)
C(3)-C(7)-C(8)	117.5(10)	109.9(8)	111.7(7)	115.3(8)
C(9)-C(7)-C(10)	105.8(13)	101.7(10)	108.7(8)	110.1(10)
C(8)-C(7)-C(10)	106.9(14)	111.8(10)	107.8(8)	113.4(10)
C(8)-C(7)-C(9)	106.7(11)	105.7(10)	106.2(8)	99.3(10)
C(6)-O(1)-C(11)	119.7(6)	111.3(5)	118.9(6)	117.4(6)
O(1)-C(11)-C(12)	115.6(7)	110.9(6)	116.0(7)	106.5(7)
C(11)-C(12)-O(3)	123.6(7)	118.6(7)	119.3(10)	116.1(9)
C(11)-C(12)-O(2)	113.8(7)	114.7(7)	114.0(9)	106.4(9)
O(2)-C(12)-O(3)	122.7(9)	126.5(8)	126.5(10)	137.3(11)
C(12)-O(2)-C(13)	123.8(7)	121.6(7)	121.6(7)	112.7(10)
O(2)-C(13)-C(16)	110.4(7)	103.1(7)	110.6(8)	99.5(10)
O(2)-C(13)-C(15)	103.8(7)	110.4(7)	101.0(8)	108.9(10)
O(2)-C(13)-C(14)	110.3(7)	110.7(8)	110.7(8)	112.3(11)
C(15)-C(13)-C(16)	112.4(8)	108.6(9)	109.7(9)	108.4(14)
C(14)-C(13)-C(16)	108.4(8)	111.7(10)	114.2(9)	109.6(13)
C(14)-C(13)-C(15)	111.5(8)	112.1(10)	109.8(9)	116.7(13)
C(1)-C(17')-C(5')	108.3(6)	111.1(6)	108.1(6)	111.3(6)
C(17)-C(5')-C(4')	118.1(6)	122.6(7)	120.0(6)	122.7(7)
C(17)-C(5')-C(6')	123.2(7)	119.3(7)	122.2(7)	117.6(6)

Torsion angles (°) concerning the ester groups

	( )	(')	('')	(''')
C(6)-O(1)-C(11)-C(12)	-23.3(10)	180.0(6)	-26.8(11)	178.9(6)
O(1)-C(11)-C(12)-O(2)	-56.4(10)	26.2(9)	-50.9(12)	-167.3(8)
O(1)-C(11)-C(12)-O(3)	122.7(10)	-154.7(8)	123.1(10)	8.8(12)
C(11)-C(12)-O(2)-C(13)	173.1(7)	177.6(7)	171.7(8)	179.3(9)

Torsion angles (°) concerning the methylene bridges

	( )	(')	('')	(''')
C(6)-C(1)-C(17)-C(5')	-73.8(9)	-113.1(8)	-73.8(8)	-111.9(8)
C(1)-C(17)-C(5')-C(6')	114.2(8)	76.6(9)	114.7(7)	76.1(8)
C(2)-C(1)-C(17)-C(5')	98.8(8)	65.2(9)	98.1(8)	63.8(9)
C(1)-C(17)-C(5')-C(4')	-62.0(8)	-101.1(9)	-59.4(8)	-105.1(8)

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