Pergamon

Tetrahedron Vol. 51, No. 2, pp. 591-598, 1995
Elsevier Science Ltd
Printed in Great Britain
0040-4020/95 $9.50+0.00

0040-4020(94)00918-X

Bridged Calix[6]arenes in the Cone Conformation: New Receptors for Quaternary Ammonium Cations

Alessandro Casnati,[a] Paola Jacopozzi,[a] Andrea Pochini,[a] Franco Ugozzoli,[b] Roberta Cacciapaglia,[c] Luigi Mandolini,[c] Rocco Ungaro.[a*]

[a] Dipartimento di Chimica Organica e Industriale, [b] Dipartimento di Chimica Generale ed Inorganica, Chimica Analitica, Chimica Fisica e Centro di Studio per la Strutturistica Diffrattometrica del CNR, Università degli Studi di Parma, Viale delle Scienze 78, I-43100 Parma, Italy; [c] Centro CNR di Studio sui Meccanismi di Reazione Dipartimento di Chimica, Università La Sapienza, I-00185 Roma, Italy.

Abstract: The synthesis of calix[6]arene crown ethers **3** and **4** has been accomplished for the first time by selective bridging of the parent macrocycles. The alkylation of **3** with α-chloro-N,N-diethyl acetamide produces a compound **6** whose conformational flexibility is strongly reduced and which assumes a cone conformation both in solution and in the solid state. Compound **6** represents a new type of ditopic receptor which binds tetramethylammonium cation in the polar region at the lower rim, showing an association constant K_a=750 M^{-1} in $CDCl_3$.

The suggestion, based on model studies[1] and on crystallographic evidence,[2] that the quaternary ammonium ion of acetylcholine can be bound to Acetylcholine Esterase (AChE) through the interaction with some of the 14 aromatic residues present in a narrow gorge of the enzyme, has influenced the synthetic strategies for quaternary ammonium cation receptors.

Previously, macrocyclic polyethers bearing anionic functional groups have been used to bind tetraalkylammonium salts in water solution[3] and, more recently, attention has been devoted to charged aromatic cavities[4] where attractive charge-charge interactions mainly determine the binding.

Dougherty and coworkers in an illuminating series of papers have shown that positively charged alkylammonium salts can interact with the aromatic π systems of certain cyclophanes both in water and chloroform solution, giving strong binding, essentially through an ion-dipole effect.[5] This interaction, together with other effects, is also operating in the complexes between cryptophanes and tetramethylammonium salts studied by Collet.[6] Very recently also calixarenes have been used as hosts for quaternary ammonium cations.[7-11] In particular, Harrowfield has reported on tetraalkylammonium cation binding by calixarene anions in solution and in the solid state,[9] Masci has synthesized doubly bridged tetrahomodioxacalix[4]arenes which bind tetraalkylammonium salts in $CDCl_3$ ($\Delta G° = 2.3\text{-}4.5$ kcal·mol^{-1}),[10] whereas Shinkai and coworkers have found evidence of the inclusion of these cations in several calixarenes.[11] In their more systematic work the Japanese authors concluded that calix[6]arenes could provide the best cavity size for alkyl trimethyl ammonium cations and that preorganization of the macrocycle in the cone conformation should provide the best opportunity for cation/π interaction to occur.[11]

Whereas the fixation of calix[4]arenes in the cone conformation has been accomplished easily by functionalization of the lower rim,[12] the same objective failed so far for calix[6]arenes in spite of several attempts.[13-16] This is due to the higher flexibility of these macrocycles and to the fact that topomerization occurs not only *via* the oxygen through the annulus but also *via* the p-alkyl through the annulus pathway.[15,16]

We partially succeded in reducing the conformational flexibility of p-*tert*-butylcalix[6]arene **1** through selective 1,3,5-methylation followed by introduction of bulky substituents on the remaining OH groups.[14,15] The partial freezing of the calix conformation in the flattened cone is due to the "self inclusion" of methoxy groups inside the apolar cavity (CH_3-π interactions).[15]

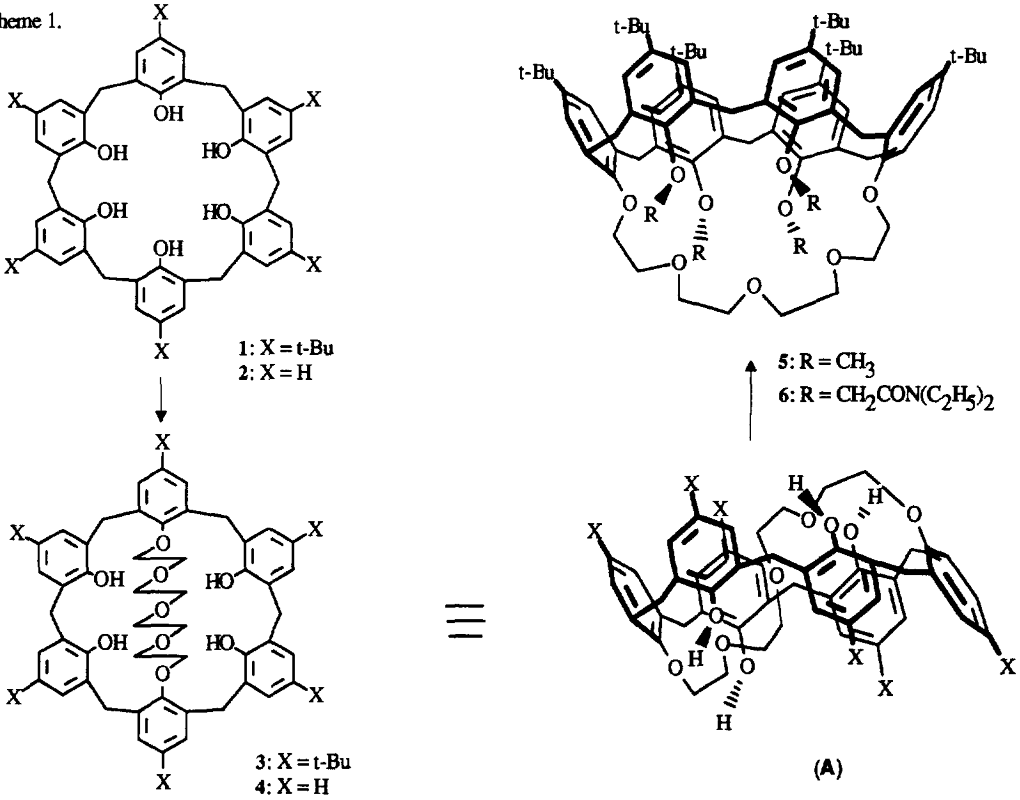
In this paper we report the results of a complementary approach aimed at reducing the conformational flexibility of calix[6]arene *via* selective bridging followed by alkylation with bulky groups. We report also the X-ray crystal structure of the first example of a calix[6]arene derivative in the cone conformation together with preliminary evidence for its interaction in solution with tetramethylammonium cation.

RESULTS AND DISCUSSION

Synthesis and Conformational Properties of the Ligands

The selective 1,4-bridging of calix[6]arenes with rigid groups has been accomplished by Gutsche et al.,[13] but no report is available for flexible polyether chains, which instead have been used to bridge calix[4]arenes[17] and p-*tert*-butylcalix[5]arene[18] at the lower rim.

Scheme 1.



Upon treatment of calix[6]arenes **1** and **2** with tetraethylene glycol di-p-toluenesulfonate in the presence of potassium *tert*-butoxide in dry benzene under high dilution conditions, the corresponding crown ethers **3** and **4** were obtained in 36% and 42% yield respectively. Analysis of the ^{1}H NMR spectra ($CDCl_3$) of compounds **3** and **4** reveals some common features, which suggest essentially a similar structure. Compound **3** shows two singlets for the *tert*-butyl groups at 1.13 and 1.23 ppm in the ratio 1:2, two doublets and a singlet for the $ArCH_2Ar$ protons (ratio 1:1:1), a singlet and two doublets (meta coupling) for the aromatic protons. This pattern can be explained only by assuming a 1,2,3-alternate (**u**, u, d, d, d, u)[13] structure (**A** in Scheme 1) or a semi-flexible one where only the four phenolic nuclei pass through the annulus and the two bridged aromatic nuclei remain fixed anti to each other. This is also supported by a through-space correlation in the NOESY spectrum between the methylene protons of the polyether bridge and the aromatic protons around 7 ppm in compound **4**.

Methylation of compound **3** gives the tetramethoxy derivative **5** in quantitative yield, whereas alkylation with α-chloro-N,N-diethylacetamide affords the tetramide **6** in 36% yield. The ^{1}H NMR spectrum (400 MHz, $CDCl_3$) of **6** is very sharp and symmetrical and with the aid of COSY and NOESY experiments all signals have been completely assigned. Some extra peaks, present expecially in the *tert*-butyl region, are probably due to a second conformer present in much lower quantity (<5%). The multiplicity and the number of signals indicate that the major isomer is in a cone conformation. Two sets of doublets at 5.02, 3.41 ppm and at 4.69 and 3.42 ppm (ratio 1:2) for the $ArCH_2Ar$; an AB system at 4.80 and 4.73 ppm for the diastereotopic protons of the OCH_2CO; an AB system at 6.94 and 6.79 ppm and a singlet at 6.89 ppm are only compatible with a cone (**u**, u, u, u, u, u)[13] conformation where all aromatic nuclei are syn oriented. Another indication of the presence of this conformation comes from the NOESY spectrum which evidences cross-peaks between the high field doublet of the equatorial $ArCH_2Ar$ protons and the neighbouring aromatic protons. The X-ray crystal structure of compound **6** (Figure 1), shows that all *tert*-butyl groups are oriented in the same direction with respect to an ideal plane containing the bridging methylenes ($ArCH_2Ar$) as required for a cone conformation.

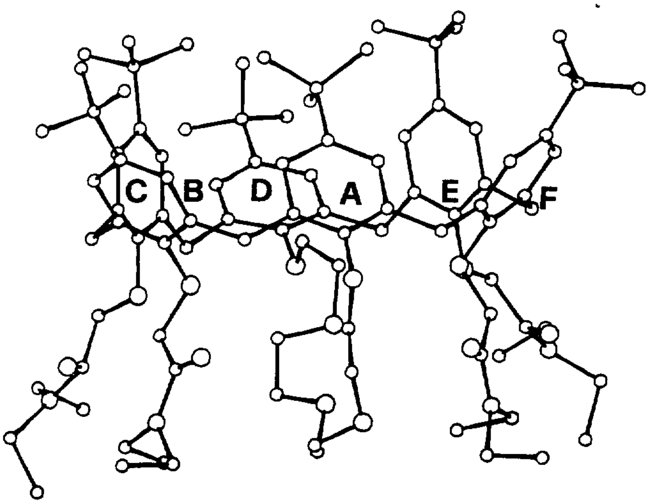


Figure 1. X-ray crystal structure of compound **6**.

An overall and unequivocal description of the macroring conformation is given by the conformational parameters reported in Table 1[19] which indicate the molecular conformation as C_1 +-, +-, +-, +-, +-, corresponding to the (**u**, u, u, u, u, uo).[13] The largest deviations of these parameters among themselves (for a symmetric cone conformation $\varphi = -\chi$ is expected) are observed when the two phenolic units A or D bearing the crown bridge are involved. The calculation of the dihedral angles (δ) between the phenolic rings and the reference plane (R) through the six methylene bridging carbon atoms[20] (see Table 1) shows also that the phenolic rings A and D are almost parallel to each other and tilted in such a way that their oxygens and the attached bridge are oriented toward the observer.

Table 1. Conformational Parameters φ and χ (°)[19] and Dihedral Angles δ (°)[20] between the Least Squares Plane (R) of the Methylene Carbon Bridges and the Least Squares Planes through the Phenolic Rings for compound **6**.

Conformational Parameters (°)	A-B	B-C	C-D	D-E	E-F	F-A
φ	19(1)	95(1)	25(1)	92.3(9)	60(1)	93.6(9)
χ	-93(1)	-60(1)	-82(1)	-37(1)	-98.1(9)	-14(1)
Dihedral Angles (°)	A-R	B-R	C-R	D-R	E-R	F-R
δ	59.3(2)	127.4(2)	93.1(2)	140.4(2)	94.3(2)	131.1(2)

Complexation Studies

The X-ray crystal structure suggests that compound **6** is a potential ditopic receptor for complexation of several salts and ion pairs. It was therefore attractive to investigate its binding ability toward tetramethylammonium cation in comparison with its conformationally more mobile precursors **3**. It was also of interest to see whether the ammonium salt interacts preferentially with the aromatic nuclei of the calix or the polar region created by the polyether bridge and by the four amide groups.

Addition of increasing amount of host **3** to a 0.8 mM solution of tetramethylammonium acetate at 30°C causes very small but regular and reproducible upfield shifts of the methyl groups of the $(CH_3)_4N^+$ cation, ($\Delta\delta$=0.024 ppm at [**3**]=0.02M). A plot of chemical shifts against [**3**] is strictly linear within experimental errors, with no detectable curvature. This experiment indicates that, although the binding constant is too small to measure, an interaction of $(CH_3)_4N^+$ with aromatic nuclei of the host takes place,[10,11] and that exchange between complexed and uncomplexed guest is fast on the NMR time scale (300 MHz). Solid-liquid extractions of $(C_4H_9)_4N^+Cl^-$ and $(CH_3)_4N^+Cl^-$ by ligand **6** in $CDCl_3$ followed by ^1H NMR analysis of the solution show that only the tetramethylammonium salt is solubilized in the organic phase. From the integrated intensities a 1:1 stoichiometry between ligand and cation was established. Titration experiments in homogeneous solution using $(CH_3)_4N^+CH_3COO^-$ in $CDCl_3$ show that exchange of the ligand is slow on the NMR timescale (400 MHz), so that separate signals of the complexed and free host are present. By integration of these signals at different host/guest ratios and at constant concentration of tetramethylammonium acetate ($1.5\cdot10^{-3}$ M) an association constant $K_a = 750\ M^{-1}$ ($\Delta G°$= -3.9 kcal/mol) at 28°C was calculated. Because the signal of the complexed cation is buried under the signals of the host, no indication of the possible interaction of the former with the π system of the aromatic nuclei of the latter could be obtained. However, the large shifts experienced by the methylene groups of the polyether bridge as well as by methylene groups α

to carbonyls (see Experimental Section) provide a strong indication that tetramethylammonium cation is interacting more strongly with the polar region of the lower rim of the calix than with the aromatic nuclei.

We are currently investigating other bridged calix[6]arenes derived from **3** and **4** to verify if the observed binding mode of tetramethylammonium salt is due to the presence of *tert*-butyl groups at the upper rim of **6**[11] or to the unfavourable competition between the aromatic π base and the harder oxygen donor groups of the polar region.

EXPERIMENTAL SECTION

Melting points were determined on an Electrothermal apparatus in a sealed capillary tubes and are uncorrected . Mass spectra were performed on a Finngan MAT SSQ710 spectrometer. ^1H NMR and ^{13}C NMR spectra were recorded on Bruker AMX400, AC300 and AC100 spectrometers of the Centro Interdipartimentale di Misure (C.I.M.) of the University of Parma. Chemical shifts (δ) are expressed in ppm from $(CH_3)_4Si$. IR spectra were performed on a spectrophotometer Perkin-Elmer 298. Elemental analyses were carried out at the Istituto di Chimica Farmaceutica of the University of Parma. All solvents were purified by standard procedures. Analytical TLC were performed on precoated silica gel plates (SiO_2, Merck, 60 F_{254}), while silica gel 60 (Merck, particle size 0.040-0.063 mm, 230-240 mesh) was used for preparative column chromatography. p-*tert*-Butylcalix[6]arene **1** and calix[6]arene **2** were prepared as described in literature.[21]

37,38,40,41-Tetrahydroxy-39,42-(crown-5)-5,11,17,23,29,35-hexakis(1,1-dimethylethyl)calix[6]arene (3).
To a solution of compound **1** (4 g, 4.1 mmol) in 350 ml of dry benzene, KOtBu (0.92 g, 8.2 mmol) was added. The reaction mixture was then refluxed under nitrogen atmosphere and a solution of $TsO(CH_2CH_2O)_4Ts$ (2.06 g, 4.1 mmol) in 150 ml of dry benzene was slowly dropped in three hours. After 18h of reflux 0.40 g (4.1 mmol) of KOtBu were added and the reaction was quenched after 24 hours of reflux with 300 ml of HCl 1N. The organic phase was washed with water (2x300 ml) and benzene removed under reduced pressure. This crude solid was added of 50 ml of CH_2Cl_2. After cooling the solution, most of the unreacted p-tert-butilcalix[6]arene (**1**) was removed by filtration. Then 50 ml of methanol were added to the dichloromethane solution and upon slow evaporation pure compound (**3**) was collected (36% yield): m.p.=184-185°C ; IR(KBr) υ_{max} 3400(bs) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.13 (s, 18H, $C(C\underline{H}_3)_3$), 1.23 (s, 36H, $C(C\underline{H}_3)_3$), 3.57 (d, 4H, $ArCH_2Ar$, J=14.8Hz), 3.76 (s, 4H, $ArCH_2Ar$), 3.86 (s, 12H, OCH_2CH_2), 4.09 (m, 4H, OCH_2CH_2), 4.38 (d, 4H, $ArCH_2Ar$, J=14.8Hz), 6.98 (s, 4H, ArH), 7.01 (d, 4H, ArH, J= 2.1Hz), 7.07 (d, 4H, ArH, J=2.1Hz), 7.64 (s, 4H, ArOH); ^{13}C NMR ($CDCl_3$) δ 31.3 (q, $C(\underline{C}H_3)_3$), 31.5 (t, $ArCH_2Ar$), 31.6 (q, $C(\underline{C}H_3)_3$), 32.2 (t, $ArCH_2Ar$), 34.0, and 34.3 (s, $\underline{C}(CH_3)_3$), 70.1, 71.3, 72.3 and 74.7 (t, OCH_2CH_2), 125.4, 125.7 and 126.2 (d, Ar meta), 126.5, 126.7 and 132.6 (s, Ar ortho), 142.6 and 147.5 (s, Ar para), 149.5 and 150.3 (s, Ar ipso); mass spectrum (CI), 1131 (M^+ calcd 1130.78). Anal. calcd for $C_{74}H_{98}O_9$: C, 78.55, H; 8.72. Found: C, 78.66; H, 8.65.

37,38,40,41-Tetrahydroxy-39,42-(crown-5)-calix[6]arene (4).
A sample of compound **2** (2 g, 3.1 mmol) was treated following the procedure described above for compound **1**. The crude solid was first purified on a silica gel column (eluent: hexane/ethyl acetate = 1:2) and then

triturated with methanol (42% yield): m.p.=180-182°C; IR(KBr) υ_{max} 3380 (bs) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.56 (d, 4H, $ArCH_2Ar$, J=14.4Hz), 3.67 (d, 2H, $ArCH_2Ar$, J=14.6Hz), 3.75 (m, 4H, OCH_2CH_2), 3.78 (m, 4H, OCH_2CH_2), 3.81 (d, 2H, $ArCH_2Ar$, J=14.6Hz), 3.99 (m, 4H, OCH_2CH_2), 4.15 (m, 4H, OCH_2CH_2), 4.43 (d, 4H, $ArCH_2Ar$, J=14.4Hz), 6.77 (t, 4H, ArH, J=7.9Hz), 6.90-6.98 (m, 6H, ArH), 7.01-7.04 (m, 8H, ArH), 7.38 (s, 4H, ArOH); ^{13}C NMR ($CDCl_3$) δ 31.3 and 31.5 (t, $ArCH_2Ar$), 70.2, 71.5 and 75.3 (t, OCH_2CH_2), 120.2 and 125.6 (d, Ar para), 127.3 (s, Ar ortho), 128.7, 128.9 and 129.1 (d, Ar meta), 133.3 (s, Ar ortho), 151.8 and 152.6 (s, Ar ipso); mass spectrum (CI), 794.6 (M^+, calcd 794.4). Anal. calcd for $C_{50}H_{50}O_9$: C, 75.55; H, 6.33. Found: C, 75.63; H, 6.28.

37,38,40,41-Tetramethoxy-39,42-(crown-5)-5,11,17,23,29,35-hexakis(1,1-dimethylethyl)calix[6]arene (5).
A sample of compound 3 (1.5 g, 1.3 mmol) was suspended in 60 ml of dry THF and 6 ml of dry DMF under nitrogen atmosphere; then NaH (1.5 g, 62.5 mmol, 80% in oil) and CH_3I (3.4 g, 24.1 mmol) were added and the reaction mixture was refluxed for 18h. After evaporation of THF under reduced pressure, the reaction was quenched with 30 ml of HCl 1N. A portion of 30 ml of CH_2Cl_2 was added and the organic phase washed with water (2x30 ml) and dried over $MgSO_4$. The solvent was evaporated and the crude solid was purified by recrystallization from CH_2Cl_2/CH_3OH (yield >95%): m.p.=230-231°C; IR(KBr) υ_{max} 1200(s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.09 (s, 36H, $C(C\underline{H}_3)_3$), 1.15 (s, 18H, $C(C\underline{H}_3)_3$), 3.00 (s, 12H, $OC\underline{H}_3$), 3.45 (d, 4H, $ArCH_2Ar$, J=15.4Hz), 3.54 (d, 2H, $ArCH_2Ar$, J=14.9Hz), 3.74 (bs, 12H, OCH_2CH_2), 3.80 (m, 4H, OCH_2CH_2) 4.38 (d, 2H, $ArCH_2Ar$, J=14.9Hz), 4.53 (d, 4H, $ArCH_2Ar$, J=15.4Hz), 6.92 (d, 4H, ArH, J=2.2Hz), 6.95 (d, 4H, ArH, J=2.2Hz), 7.02 (s, 4H, ArH); ^{13}C NMR ($CDCl_3$) δ 29.7 and 30.1 (t, $ArCH_2Ar$), 31.0 and 31.4 (q, $C(\underline{C}H_3)_3$), 34.0 and 34.2 (s, $\underline{C}(CH_3)_3$), 60.2 (q, $O\underline{C}H_3$), 70.6, 71.3 and 72.2 (t, OCH_2CH_2), 125.6 and 125.8 (d, Ar meta), 132.9, 133.5 and 134.0 (s, Ar ortho), 145.4 and 145.7 (s, Ar para), 152.4 and 154.2 (s, Ar ipso); mass spectrum (CI), 1187.4 (M^+ calcd 1186.8). Anal. calcd for $C_{78}H_{106}O_9$: C, 78.89; H, 8.99. Found: C, 79.08; H, 8.85.

37,38,40,41-Tetrakis[(N,N-diethylaminocarbonyl)methoxy]-39,42-(crown-5)-5,11,17,23,29,35-hexakis(1,1-dimethylethyl)calix[6]arene (6).
To a solution of compound 3 (0.5 g, 0.44 mmol) in 150 ml of dry DMF, NaH (0.21 g, 7.00 mmol, 80% in oil), NaI (0.1 g, 0.66 mmol) and α-chloro-N,N-diethylacetamide (1.05 g, 6.98 mmol) were added. The reaction mixture was refluxed under nitrogen atmosphere for 18h and then quenched with 150 ml of HCl 1N. The organic material was extracted with 100 ml of CH_2Cl_2, washed with distilled water (2x100 ml) and dried over $MgSO_4$. The solvent was evaporated and the residue treated with CH_2Cl_2/MeOH to afford compound **6** (36% yield): m.p.=296-297°C; IR(KBr) υ_{max} 1670(s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.99 (s, 36H, $C(C\underline{H}_3)_3$), 1.12 (s, 18H, $C(C\underline{H}_3)_3$), 1.13 (t, 12H, $NHCH_2C\underline{H}_3$, J=7.4Hz), 1.21 (t, 12H, $NCH_2C\underline{H}_3$, J=7.4Hz), 3.16 (t, 4H, OCH_2, J=5.2Hz), 3.23 (t, 4H, OCH_2, J=5.2Hz), 3.33-3.52 (m, 22H, Heq, $NC\underline{H}_2CH_3$), 3.61 (t, 4H, OCH_2, J=5.2Hz), 3.71 (t, 4H, OCH_2, J=5.2Hz), 4.69 (d, 4H, Hax, J=14.8Hz), 4.73 (d, 4H, $OC\underline{H}_2CO$, J=13.6Hz), 4.80 (d, 4H, $OC\underline{H}_2CO$, J=13.6Hz), 5.02 (d, 2H, Hax, J=14.1Hz), 6.79 (d, 4H, ArH, J=2.1Hz), 6.89 (s, 4H, ArH), 6.94 (d, 4H, ArH, J=2.1Hz); ^{13}C NMR ($CDCl_3$) δ 13.0 and 14.5 (q, $NCH_2\underline{C}H_3$), 29.7 and 30.1 (t, $ArCH_2Ar$), 31.3 and 31.6 (q, $C(\underline{C}H_3)_3$), 34.0 and 34.1 (s, $\underline{C}(CH_3)_3$), 39.9 and 41.3 (t, $N\underline{C}H_2CH_3$), 69.4, 70.1 and 70.5 (t, OCH_2CH_2), 72.0 (t, $O\underline{C}H_2CO$), 125.1, 125.7 and 126.2 (d, Ar meta), 132.6 and 132.7 (s, Ar ortho), 145.0 and 145.3 (s, Ar para), 153.2 and 153.6 (s, Ar ipso), 168.0 (s, C=O);

mass spectrum (CI), 1584.3 (M^+, calcd 1583.2). Anal. calcd for $C_{98}H_{142}N_4O_{13}$: C, 74.31; H, 9.03; N, 3.54. Found: C, 74.48; H, 8.96; N, 3.69.

6·$(CH_3)_4N^+$ Complex: ^1H NMR Spectrum.

Tetramethylammonium acetate was added to a 0.01 M solution of host **6** in $CDCl_3$ until the ^1H NMR spectrum showed no change, indicating complete saturation of the host: ^1H NMR ($CDCl_3$) δ 0.98 (s, 36H, $C(C\underline{H}_3)_3$), 1.11 (t, 12H, $NHCH_2C\underline{H}_3$, J=7.2Hz), 1.17 (t, 12H, $NCH_2C\underline{H}_3$, J=7.2Hz), 1.34 (s, 18H, $C(C\underline{H}_3)_3$), 1.96 (s, CH_3CO), 3.26-3.45 (m, $NC\underline{H}_2CH_3$, $^+NCH_3$, $ArCH_2Ar$), 3.51 (d, 4H, Heq, J=14.8Hz), 3.72, 3.77, 3.89, 4.11 (m, 4H each, OCH_2), 4.51 (d, 4H, $OC\underline{H}_2CO$, J=13.6Hz), 4.87 (d, 4H, Hax, J=14.8Hz), 4.88 (d, 4H, $OC\underline{H}_2CO$, J=13.6Hz), 4.98 (d, 4H, Hax, J=14.0Hz), 6.71 (d, 4H, ArH, J=2.0Hz), 7.24 (d, 4H, ArH, J=2.0), 7.30 (s, 4H, ArH).

*X-ray crystallography of **6**.*

Crystal data: $C_{98}H_{142}N_4O_{13}$, molecular weight 1584.219; monoclinic a = 13.673(4), b = 30.007(8), c = 23.869(6) Å; $\beta = 103.83(2)°$; V = 9510(4) $Å^3$; space group $P2_1/n$; Z = 4; $D_{calc} = 1.106$ $g{\cdot}cm^{-3}$; $\mu_{Cu\text{-}K\alpha} = 5.7$ cm^{-1}. X-ray diffraction measurements were performed at room temperature on a Siemens A.E.D. diffractometer using graphite monocromatized Cu-Kα radiation ($\lambda = 1.54178$ Å). The cell parameters were determined by least squares fit of 37 $(\vartheta, \chi, \phi)_{hkl}$ reflections found in a systematic search on the reciprocal lattice. The intensities were determined by profile analysis according to literature.[22] All the ±h, ±k, ±l reflections in the range $3° \leq \vartheta \leq 65°$ were measured by the step scanning method with scan width from $[\vartheta - 0.65]°$ to $[\theta + 0.65 + \Delta\lambda \cdot \lambda^{-1} \cdot tg\theta]°$. A total of 16397 reflections were measured. The 4662 observed reflections ($I \geq 2\sigma(I)$) were used in the refinement. The structure was solved by SIR92[23] and refined with SHELX76.[24] The H atoms were calculated with the geometrical constraint C-H = 0.96 Å. The refinement was stopped to R = 0.067 (unit weights). All the calculations were carried out on the GOUL ENCORE91 of the Centro di Studio per la Strutturistica Diffrattometrica del C.N.R. (Parma). Geometrical calculations were obtained by PARST.[25] The complete lists of final atomic coordinates, for non hydrogen atoms, anisotropic thermal parameters, atomic coordinates of H atoms, bond distances and angles, observed and calculated structure factors and a full list of the experimental data for X-ray diffraction studies have been deposited as supplementary materials with the Cambridge Crystallographic Data Centre, 12 Union Road, GB-Cambridge CB21EZ, UK (CCDC).

ACKNOWLEDGEMENTS

This work was partially supported by M.U.R.S.T. (Ministero dell'Università e della Ricerca Scientifica e Tecnologica), by C.N.R. (Consiglio Nazionale delle Ricerche) and by the EC Project "Management and Storage of Radioactive Waste" (Contract n. F12W-CT90-0062 (TSTS)).

REFERENCES

1. Dougherty, D.A.; Stauffer, D.A. *Science* **1990**, *250*, 1558-1560.
2. Sussman, J. L.; Harel, M.; Frolow, F.; Oefner, C.; Goldman, A.; Toker, L.; Silman, I. *Science* **1991**, *253*, 872-879.

3. a) Lehn, J.-M.; Vierling, P.; Hayward, R.C. *J. Chem. Soc., Chem. Commun.* **1979**, 296-298. b) Dhaenens, M.; Lacombe, L.; Lehn, J.-M.; Vigneron, J.-P. *J. Chem. Soc., Chem. Commun.* **1984**, 1097-1099. c) Behr, J.-P.; Lehn, J.-M.; Vierling, P. *Helv. Chim. Acta* **1982**, *65*, 1853-1867.
4. Diederich, F. *Cyclophanes*; Stoddart J. F. Ed.; Royal Society of Chemistry: Cambridge, 1991; chp. 4.
5. Kearney, P. C.; Mizoue, L. S.; Kumpf, R. A.; Forman, J. F.; McCurdy, A.; Dougherty, D.A. *J. Am. Chem. Soc.* **1993**, *115*, 9907-9919 and references therein.
6. Collet, A.; Dutasta, J.-P.; Lozach, B.; Canceill, J. *Top. in Curr. Chem.* **1993**, *165*, 103-129. Garel, L.; Lozach, B.; Dutasta, J.-P.; Collet, A. *J. Am. Chem. Soc.* **1993**, *115*, 11652-11653.
7. Arduini, A.; Casnati, A.; Fabbi, M.; Minari, P.; Pochini, A.; Sicuri, A. R.; Ungaro, R. in *Supramolecular Chemistry*; Balzani, V.; De Cola, L. Eds.; Kluwer Academic Publishers: Dordrecht, 1992; pp. 31-50.
8. Kobayashi, K.; Asakawa, Y.; Aoyama, Y. *Supramol. Chem.* **1993**, *2*, 133-135.
9. a) Harrowfield, J. M.; Ogden, M. I.; Richmond, W. R.; Skelton, B. W.; White, A. H. *J. Chem. Soc., Perkin Trans. 2* **1993**, 2183-2190. b) Harrowfield, J. M.; Richmond, W. R.; Sobolev, A. N.; White, A.H. *J. Chem. Soc., Perkin Trans. 2* **1994**, 5-9.
10. De Iasi, G.; Masci, B. *Tetrahedron Lett.* **1993**, *34*, 6635-6638.
11. a) Shinkai, S. *Tetrahedron* **1993**, *49*, 8933-8968. b) Araki, K.; Shimizu, H.; Shinkai, S. *Chem. Lett.* **1993**, 205-208.
12. a) Gutsche, C.D. *Calixarenes*; Stoddard, J. F. Ed.; The Royal Society of Chemistry: Cambridge, 1989. b) Vicens, J.; Böhmer, V., Eds., *Calixarenes: a Versatile Class of Macrocyclic Compounds*; Kluwer Academic Publishers: Dordrecht, 1990.
13. Kanamathareddy, S.; Gutsche, C. D. *J. Am. Chem. Soc.* **1993**, *115*, 6572-6579.
14. Casnati, A.; Minari, P.; Pochini, A.; Ungaro, R. *J. Chem. Soc., Chem. Commun.* **1991**, 1413-1414. Casnati, A.; Minari, P.; Pochini, A.; Ungaro, R.; Nijenhuis, W.F.; de Jong, F.; Reinhoudt, D.N. *Isr. J. Chem.* **1992**, *32*, 79-87.
15. van Duyhoven, J. P. M.; Janssen, R. G.; Verboom, W.; Franken, S. M.; Casnati, A.; Pochini, A.; Ungaro, R.; de Mendoza, J.; Nieto, P. M.; Prados, P.; Reinhoudt, D.N. *J. Am. Chem. Soc.* **1994**, submitted.
16. Otsuka, H.; Araki, K.; Sakaki, T.; Nakashima, K.; Shinkai, S. *Tetrahedron Lett.* **1993**, *34*, 7272-7278.
17. Alfieri, C.; Dradi, E.; Pochini, A.; Ungaro, R.; Andreetti, G. D. *J. Chem. Soc., Chem. Commun.* **1983**, 1075-1077. Ghidini, E.; Ugozzoli, F.; Ungaro, R.; Harkema, S.; El-Fadl, A. A.; Reinhoudt, D. N. *J. Am. Chem. Soc.*, **1990**, *112*, 6979-6985. Ungaro, R.; Casnati, A.; Ugozzoli, F.; Pochini, A.; Dozol, J.-F.; Hill, C; Rouquette, H. *Angew. Chem. Int. Ed. Eng.*, submitted.
18. Kraft. D.; Arnecke, R.; Böhmer, V.; Vogt, W. *Tetrahedron* **1993**, *49*, 6019-6024.
19. Ugozzoli, F.; Andreetti, G. D. *J. Incl. Phenom. Mol. Recogn. Chem.* **1992**, *13*, 337-348.
20. Perrin, H.; Oehler, D. in ref. 12b, pp. 65-85.
21. a) Gutsche C. D. *Org. Syntheses* **1989**, *68*, White, J. D. Ed., 234-246. b) Gutsche, C.D.; Lin, L.-G. *Tetrahedron* **1986**, *42*, 1633-1640.
22. Lehman, M.S.; Larsen, F.K. *Acta Cryst. Sect. A* **1974**, *30*, 580-584.
23. SIR92; Altomare, A.; Burla, M. C.; Camalli, M.; Cascarano, G.; Giacovazzo, C.; Guagliardi, A.; Polidori, G. *J. Appl. Cryst.* **1994**, in press.
24. Sheldrick, G. M.; SHELX76, *Program for Crystal Structure Determination*, Univ. of Cambridge, 1976.
25. Nardelli, M. *Comput. Chem.* **1983**, *3*, 95-98.

(*Received* 4 *April* 1994)