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Enlarging the size of calix[4]arene-crowns-6 to improve Cs^+/K^+ selectivity: a theoretical and experimental study☆

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Abstract—Ab initio calculations in the gas-phase indicate that the substitution of an ethylene with a propylene moiety in the polyether bridge of 1,3-di-*iso*-propoxycalix[4]arene-crowns-6 could result in an enhanced Cs^+/K^+ selectivity which is of particular interest in nuclear waste treatment. We therefore synthesised two novel calix[4]arene-crown-6 compounds (**1** and **2**) having a propylene moiety in their structure and for this named calix[4]arene-propylene-crown-6. The structures of compounds **1** and **2** were elucidated by NMR in solution and for **1** also by X-ray diffraction studies in the solid state. Association constants (K_a) in $CHCl_3$ of the two novel calix-crowns were measured and pointed out a plateau selectivity towards alkali metal ions which was not predicted by molecular modelling calculations. These results indicate the important role played by the solvent molecules and counter-anions in binding for this class of ionophores.

1. Introduction

Calix[4]arene-crown ethers or calix[4]crowns are among the most widely studied class of synthetic ionophores.[1,2] They show binding properties for alkali metal ions strongly dependent on the number of oxygen atoms in the ether bridge and on the conformation of the calixarene skeleton. In the last 20 years, we synthesised a large number of these macrobicyclic ionophores and showed that cation binding involves not only ether oxygen atoms but also the calixarene aromatic nuclei providing experimental evidence for the operation of cation/π interactions.[3] As expected from the size complementarity, 1,3-calix[4]crowns-4 are selective for sodium ion,[4] 1,3-calix[4]crowns-5[5,6] for potassium and the 1,3-calix[4]crowns-6 for cesium.[7] Usually, the conformationally mobile derivatives are much less efficient and selective than the more preorganized receptors fixed in the 1,3-alternate conformation. The high Cs^+/Na^+ selectivity exhibited by the 1,3-dialkoxy-calix[4]crowns-6 in the 1,3-alternate conformation (**I**) prompted us[8,9] to use this class of compound for the selective extraction of cesium from acidic radioactive waste where sodium is present at high concentration (5–7 M) while cesium is only present in trace amounts (10^{-4}–10^{-6} M). Other authors[10–12] have slightly modified the calix-crown-6 structure in order to enhance the cesium selectivity. Compound **Ia** is still one of the ionophores having the highest Cs^+/Na^+ selectivity ($\alpha_{Cs/Na}$=28,500) in extraction and its application in the removal of cesium from radioactive fuel reprocessing waste is currently under study.[9] The substitution of ethylene moieties Y or X with benzo units allowed us also to develop the calix[4]-monobenzo- (**Ib**) and dibenzo- (**Ic**) crown-6[13–15] compounds where the Cs^+/Na^+ selectivity is even slightly increased ($\alpha_{Cs/Na}$=34,000 and 31,000, respectively). However, all these compounds suffer from an $\alpha_{Cs/K}$ at least two orders of magnitude lower than the $\alpha_{Cs/Na}$ selectivity, which might be a drawback in the case of some basic radioactive waste where K^+ concentration can reach values around 1 M. Ring-enlarged crown-ethers, (3*m*+*n*)-crown-*m*, also known as crown ethers of low symmetry,[16] usually show decreased cation binding ability in comparison to the corresponding symmetric crown ethers, but sometimes enhanced selectivity.[17] For example, the potassium selectivity of 18-crown-6 is shifted to rubidium and cesium for less symmetric 20-crown-6 and 22-crown-6, respectively. Therefore, in the present work, we modified the structure of calix[4]crown-6 (**Ia**) and calix[4]dibenzocrown-6 (**Ic**) enlarging the crown ether

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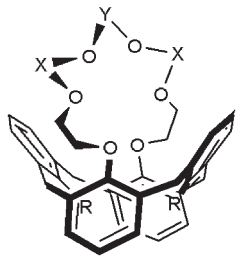
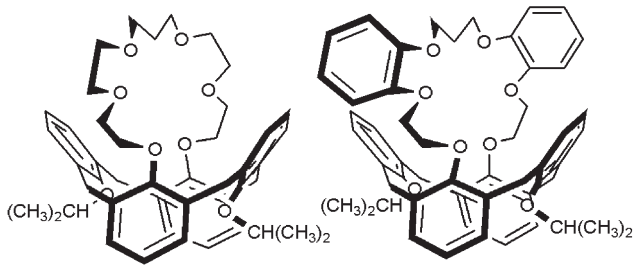
bridge by the introduction of a propylene unit in the Y position and thus obtaining compounds **1** and **2**.



Ia: X = Y = CH_2CH_2; R = O-*i*Pr
Ib: X = CH_2CH_2; Y = 4-*t*-Oct-1,2-C_6H_4; R = O-*n*Oct
Ic: X = 1,2-C_6H_4; Y = CH_2CH_2; R = O-*n*Oct



1 2

2. Results and discussion

2.1. Modeling studies

We first investigated the structural and electronic factors which influence the binding properties of ligand **1** by using ab initio calculations in the gas-phase. In order to find the equilibrium geometries of the **1**·K^+ and **1**·Cs^+ cationic complexes we also preliminarily modelled the structure of the ligand **1** in the gas-phase which was obtained in two steps: (i) the structure of the minimum energy conformer was calculated with semiempirical methods at the PM3 level; (ii) the geometry of the minimum energy conformer was further minimized at the HF/3-21G level. The final equilibrium geometry of the isolated molecule **1** is shown in Figure 1. In the gas-phase the calix[4]arene moiety shows a pseudo C_{2v} symmetry where all the aromatic rings are almost orthogonal to the reference plane R (the weighted

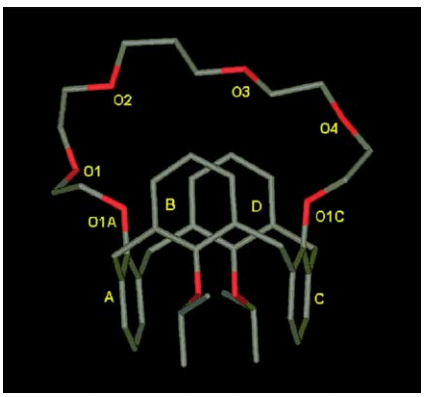


Figure 1. Optimised geometry of the ligand **1** at the HF/3-21G level in the gas-phase.

Table 1. Dihedral angles τ (°) between the reference plane (R) and the planes through the phenolic rings in the calculated structures of **1**, **1**·K^+ and **1**·Cs^+ in the gas-phase and in the solid state structure of **Ia**·Cs^+[7]

	τ			
	1(gas)	**1**·K^+	**1**·Cs^+	**Ia**·Cs^+
R–A	86.99	99.99	101.26	103.3(3)
R–B	257.07	262.3	258.74	257.5(2)
R–C	87.27	101.83	103.02	105.9(2)
R–D	271.44	255.65	248.87	246.3(2)

Table 2. Dihedral angles θ (°) between opposite phenolic rings

	θ			
	1(gas)	**1**·K^+	**1**·Cs^+	**Ia**·Cs^+
A–C	5.81	22.06	24.28	29.2(3)
B–D	3.71	21.82	38.81	36.2(2)

least-squares plane between the four CH_2 bridging groups according to standard rules for calixarenes)[18] and the opposite rings are almost parallel (Tables 1 and 2). This conformation of the calix forces the crown to adopt an elliptical shape with the major axis orthogonal to the pseudo C_2 axis (see Fig. 1). In a second step of calculations, the geometries of **1**·K^+ and **1**·Cs^+ (Fig. 2(a) and (b), respectively) have been obtained by geometry optimisation at the HF/3-21G level. As an initial guess for geometry optimisation the structure of each complex was built-up from that of **1** (optimised in the gas-phase) by placing the metal cation in the barycentre of the six oxygen atoms of the crown. The final structures of **1**·K^+ and **1**·Cs^+, optimised without geometrical constraints, are shown in Figure 2.

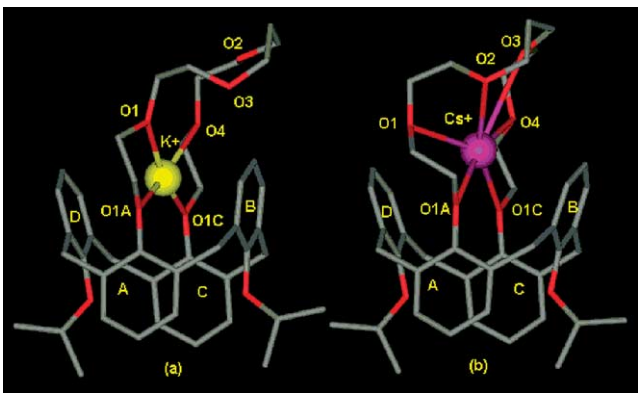


Figure 2. Optimised geometries of the cationic complexes in the gas-phase. (a) **1**·K^+, (b) **1**·Cs^+.

The calix[4]arene basket undergoes a significant conformational reorganization upon complexation. The strong variations of the dihedral angles τ and θ reported in Tables 1 and 2 indicate that the opposite phenolic units are forced to rotate towards the exterior of the macrocycle to favour the binding of the metal ion and that the rotations increase as the size of the cation increases.

The analysis of the interatomic M^+-O distances, summarized in Table 3, shows that the K^+ ion is tetracoordinated to

Table 3. $M^+\cdots O$ interatomic distances (Å) in the **1**·K^+ and **1**·Cs^+ complexes calculated in the gas-phase and in the solid state structure of **Ia**·Cs^+

	1·K^+	**1**·Cs^+	**Ia**·Cs^+
$M^+\cdots$O1A	2.64	3.15	3.189(5)
$M^+\cdots$O1C	2.65	3.00	3.188(5)
$M^+\cdots$O1	2.89	3.09	3.245(6)
$M^+\cdots$O2	4.44	3.43	3.475(7)
$M^+\cdots$O3	4.55	3.13	3.276(9)
$M^+\cdots$O4	2.71	3.23	3.100(5)

O1A, O1C, O1 and O4, whereas the two oxygen atoms O2 and O3 with $K^+-O>4.4$ Å are excluded from the cooordination sphere of the potassium ion.

The K^+-O bond distances range from 2.64 to 2.89 Å (av. 2.72 Å) and are shorter than those found in the X-ray structure of the partial cone di-*iso*propoxy-*p*-*tert*-butylcalix[4]arene-crown-5·KPic (Pic=picrate),[19] (from 2.748(8) to 3.015(10) Å av. 2.872 (9) Å) and in the cone di-ethoxy-*p*-*tert*-butylcalix[4]arene-crown-5·KPic[19] (from 2.76(1) to 2.87(1) Å av. 2.81(1) Å). On the contrary in **1**·Cs^+ the cesium ion is hexacoordinated: the Cs^+-O bond distances range from 3.0 to 3.43 Å (av. 3.172 Å) and are slightly shorter than those in the X-ray structure of the 1,3-alternate di-*iso*-propoxycalix[4]arene-crown-6·CsPic **Ia**·Cs^+ previously reported by us[7] (from 3.100(5) to 3.475(7) Å av. 3.245(7) Å). It is also of some interest to compare the optimised molecular geometry of **1**·Cs^+ with the X-ray structure[6] of the **Ia**·Cs^+ to highlight how the substitution of the ethylene moiety with a propylene unit influences the binding ability of the ligand. In the two structures, shown in Figure 3, the calix[4]arene conformation is quite similar with small differences in the dihedral angles τ (see Table 1). The crown conformation is almost identical at least from O1A to O1 and from O1C to O4. Then, along the chain from O1 to O4 the conformational differences are more relevant, as expected. It is however surprising that the increase in size of the crown length in **1**·Cs^+ does not increase the Cs^+-O bond distances but, on the contrary, a small but not negligible shortening of them (av. 3.172 vs. 3.245(8) Å) is observed.

Therefore these data, which show a relevant difference in the coordination numbers of the two metal ions suggesting a high Cs^+/K^+ selectivity, which prompted us to synthesise

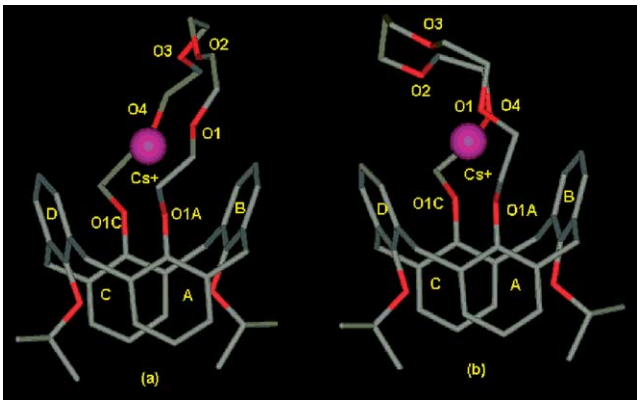
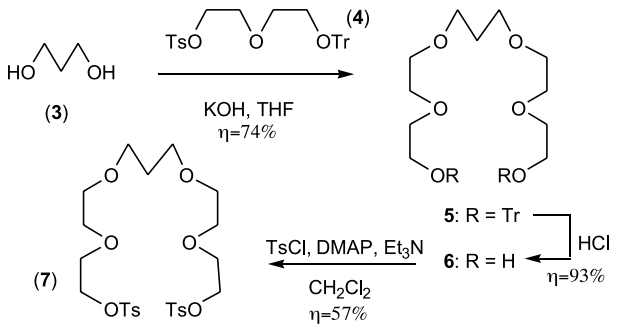


Figure 3. Molecular structure of the cationic complexes (a) **Ia**·Cs^+ (solid state), (b) **1**·Cs^+ (gas-phase).

the two calix[4]arene-propylene-crown-6 compounds **1** and **2** in order to experimentally determine their binding properties.

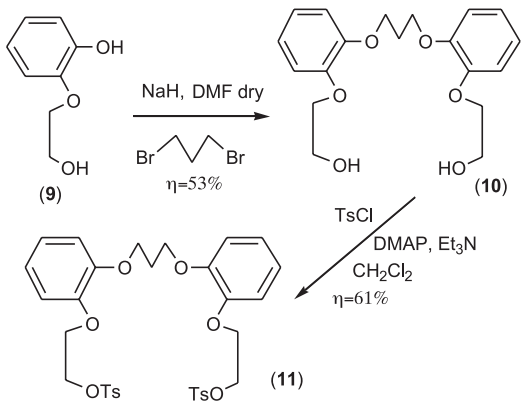
2.2. Synthesis and structure of the ligands

Ditosylate **7** was prepared starting from propylene glycol **3** and diethylene glycol monotrityloxy monotosylate **4**,[20] in 40% overall yield through a protection–deprotection strategy (Scheme 1).



Scheme 1.

After coupling of the glycol **3** with 2.2 equiv. of the diethylene glycol monotosylate **4**, the resulting trityloxy derivative **5** was deprotected with HCl to give the diol **6**. The latter was reacted with tosyl chloride (TsCl) and triethylamine in dichloromethane using a catalytic amount of dimethylamino pyridine (DMAP). Ditosylate **11** was obtained by reaction (Scheme 2) of 1,3-dibromopropane with 2 equiv. of 2-(2-hydroxyethoxy)phenol (**9**)[15] with NaH in DMF. Under these conditions alkylation of the catechol free hydroxy group was mainly obtained and compound **10** could be isolated in 53% yield. Subsequent reaction of **10** with tosyl chloride (TsCl) and triethylamine in dichloromethane gave **11** in 61% yield.



Scheme 2.

For the final cyclization reaction we followed the classical conditions reported for calix[4]crown-6 and reacted 1,3-di-*i*-propoxycalix[4]arene (**8**) with a slight excess (1.2 equiv.) of the appropriate ditosylate **7** or **11** and an excess of Cs_2CO_3 in dry acetonitrile. After quenching, extraction and purification by column chromatography, calix[4]arene-propylene-crown-6 compounds **1** and **2** were obtained in 54 and 59% yield, respectively. The identity of the two calix[4]crowns were characterised using NMR and mass

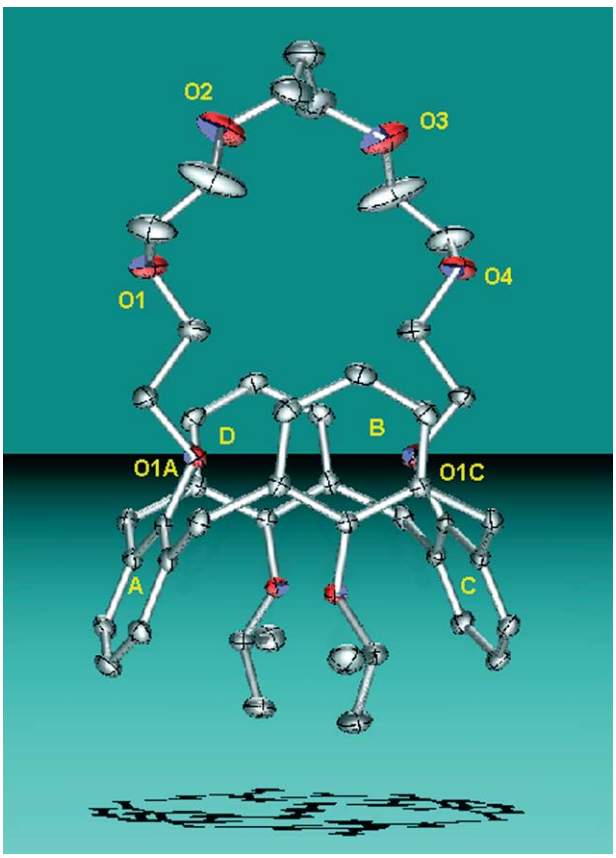


Figure 4. ORTEP view of the molecular structure of the ligand **1**. Thermal ellipsoids at 20% probability. Hydrogen atoms have been omitted for clarity.

spectrometry. In particular the 1,3-alternate structure was confirmed by the presence of an AB system for the methylene bridge at δ_H=3.75–3.82 and a triplet at δ_C=38.5 in the NMR spectra. Isolation of a single crystal of compound **1** allowed us to solve its X-ray diffraction structure. The molecular geometry of **1** in the solid state is shown in Figure 4.

Table 4. Conformational parameters ϕ, χ (°) and dihedral angles τ (°) between the least-squares reference plane (R) and the least-squares planes through the phenolic rings in the solid state structure of **1**

Conformational parameters (°)			Dihedral angles (°)	
	ϕ	χ		τ
A–B	128.5(3)	130.6(3)	R–A	111.18(6)
B–C	−129.5(3)	−130.7(3)	R–B	252.24(6)
C–D	130.4(3)	127.6(3)	R–C	110.87(6)
D–A	−129.2(3)	−131.4(3)	R–D	252.71(7)

The calix[4]arene is blocked in the 1,3-alternate conformation in a pseudo C_{2v} symmetry. The polyether crown moiety shows an elliptical shape with its minor axis orthogonal to the pseudo C_2 axis. The dihedral angles τ between opposite phenolic rings are: A–C 42.06(8)° and B–D 35.05(8)°. The whole conformation of the calix[4]-arene basket is unequivocally described by the dihedral angles τ and by the conformational parameters[21] reported in Table 4 leading to the symbolic representation C_1 ++,−−,++,−−.

The values of the pairs ϕ and χ, together with the τ values clearly indicate that the distortion of the 1,3-alternate structure from an ideal C_{2v} symmetry is very small. Probably due to packing forces, this solid state structure slightly differs from the calculated one (Fig. 1) both in the shape of the calixarene basket and in the conformation of the crown. In the gas-phase, in fact, the calix[4]arene moiety shows also a pseudo C_{2v} symmetry but the phenolic rings are almost orthogonal to the reference plane R and the opposite rings are almost parallel in pairs (Tables 1 and 2). This conformation of the calix forces the crown to adopt an elliptical shape with the major axis orthogonal to the pseudo C_2 axis (see Fig. 1).

2.3. Complexation studies

In order to evaluate the binding properties of ligands **1**-**2** in comparison with calix[4]arene-crown-6 **Ia** and -dibenzo-crown-6 **Ic** we determined the association constants (log K_a) with alkali picrates in chloroform, using Cram's method[22,23] (Table 5 and Fig. 5).

The data show, in general, a strong decrease in cation binding properties of propylene-crown-6 (**1** and **2**) in comparison with calix[4]crown-6 (**Ia** and **Ic**). This effect is more significant for larger cations ($Cs^+ > Rb^+ > K^+$) and

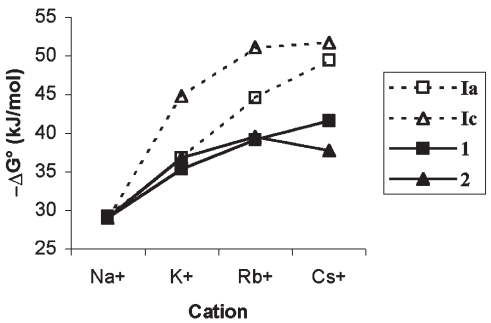


Figure 5. Binding free energies (−ΔG°, kJ/mol) of complexes of calixcrowns-6 with alkali metal picrates in $CHCl_3$ saturated with water at 22 °C.

Table 5. Association constants (K_a)[a] and binding free energies (−ΔG°, kJ/mol) of complexes of calixcrowns-6 with alkali metal picrates in $CHCl_3$ saturated with water at 22 °C

Ligand	log K_a				−ΔG° (kJ/mol)				$\alpha_{Cs/K}$
	Na^+	K^+	Rb^+	Cs^+	Na^+	K^+	Rb^+	Cs^+	(ΔΔG°)
Ia[7]	5.2	6.4	7.9	8.8	29.2	36.8	44.6	49.4	12.6
Ic[15]	<5	7.8	8.9	9.0	<29.0	44.8	51.1	51.7	6.9
1	<5	6.1	6.8	7.2	<29.0	35.3	39.1	41.6	6.3
2	<5	6.4	6.9	6.6	<29.0	36.8	39.5	37.7	1.2

[a] Errors <10%.

in the dibenzo-crown-6 derivative **2**. The stability of the cesium complex drops by 14.0 kJ/mol with the introduction of the propylene moiety in the dibenzo-crown-6 series, while it decreases only by 7.8 kJ/mol when no benzo units are present in the crown bridge. This causes a plateau selectivity of calix-dibenzo-propylene-crown-6 (**2**) which indeed shows only a very weak preference for Rb^+. Moreover, while in calixcrowns-6 (**I**) the stabilities of the complexes remarkably rise with the introduction of two benzo units, in propylene-crown-6 there are only minor differences between propylene-dibenzo-crown-6 (**2**) and -propylene-crown-6 (**1**). In conclusion, the substitution of an ethylene with a propylene moiety in the bridge of calix-crown-6 compounds decreases both the efficiency and selectivity of cesium complexation in contrast to what was predicted by ab initio calculations. The origin of such a discrepancy should be ascribed to the fact that, in the modeling, effects due to solvation and interaction with the counter-anion are not taken into account.

3. Experimental

3.1. Synthesis

Materials and methods. Most of the solvents and all reagents were obtained from commercial supplies and used without further purification. DMF was freshly distilled and stored over 4 Å molecular sieves while acetonitrile for synthesis was dried over 3 Å molecular sieves. Proton and carbon nuclear magnetic resonance spectra (^{1}H NMR and ^{13}C NMR) were recorded on a Bruker AC300 and Bruker 300 Avance spectrometers of the Centro Interdipartimentale of the Parma University. Chemical shifts are reported as δ values in ppm from TMS (δ 0.0) as internal standard. Analytical thin-layer chromatography was carried out on silica gel plates (SiO_2, Merk 60 F_{254}). Mass spectra were performed with FINNIGAN MAT SSQ 710 (CI, CH_4). Melting points were obtained in a nitrogen-sealed capillary on an Electrothermal Apparatus. Diethylene glycol monotrityloxy monotosylate (**4**),[20] 2-(2-hydroxyethoxy)phenol (**9**)[15] and 25,27-di-*iso*-propoxycalix[4]arene (**8**)[7] were synthesised according to the literature.

3.1.1. 2-(2-{3-[2-(2-Trityloxy-ethoxy)-ethoxy]-propoxy}-ethoxy)-ethanol (5). A sample of propylene glycol **3** (0.46 g, 6.0 mmol) in dry THF (20 mL) was added to a suspension of KOH (1.30 g, 23 mmol) in dry THF (30 mL) at reflux under nitrogen atmosphere; the mixture was stirred for 1 h. Then compound **4** (6.7 g, 13.3 mmol) in dry THF (20 mL) was added and the reaction mixture stirred for 2 days. After cooling, the solvent was distilled off and the residue extracted with 50 mL of CH_2Cl_2 and 50 mL of water; the organic solvent was removed under reduced pressure. The pure product **5** was obtained by column chromatography (SiO_2 CH_2Cl_2/hexane/ethyl acetate 3:8:1) as an oil (3.30 g, 74%); ^{1}H NMR ($CDCl_3$): δ 7.44–7.41 (m, 12H, ArH *meta*), 7.32–7.22 (m, 18H, ArH *ortho* and *para*), 3.69–3.55 (m, 16H, OCH_2CH_2O), 3.16 (t, J=6.2 Hz, 4H, $OCH_2CH_2CH_2O$), 1.90 (quin, J=6.2 Hz, 2H, $OCH_2CH_2CH_2O$); ^{13}C NMR ($CDCl_3$): δ 144.1 (Ar), 128.7, 127.6, 126.8 (ArH), 86.5 ($C(C_6H_5)_3$), 70.7, 70.6, 70.2, 68.3, 63.3 (OCH_2), 30.0 ($CH_2CH_2CH_2$); MS *m/z*: 660 ($M-C_6H_5$), 493 ($M-C_{19}H_{15}$). Anal Calcd for $C_{49}H_{52}O_6$: C, 79.86; H, 7.11. Found: C, 80.02; H, 7.19.

3.1.2. 2-(2-{3-[2-(2-Hydroxy-ethoxy)-ethoxy]-propoxy}-ethoxy)-ethanol (6). A sample of compound **5** (3.3 g, 4.5 mmol) was dissolved at room temperature in 100 mL of a 1:1 mixture of CH_2Cl_2 and CH_3OH and then 0.5 mL of a 12 M HCl solution were added. After 3 h the reaction was cooled to 0 °C, 50 mL of a 5% $NaHCO_3$ solution were slowly added (CAUTION!) and the solution was stirred for 30 min. Then the solvent was distilled off under reduced pressure and the residue extracted with 100 mL of CH_2Cl_2 and 100 mL of 1 M HCl. Water was removed under vacuum from the aqueous layer and the solid residue extracted twice with MeOH (2×30 mL). After removal of methanol pure product **6** was isolated as an oil (1.05 g, 93%). ^{1}H NMR (CD_3OD): δ 3.70–3.50 (m, 20H, OCH_2), 1.85 (quin, J=6.3 Hz, 2H, $CH_2CH_2CH_2$); ^{13}C NMR (CD_3OD): δ 72.5, 70.24, 70.16, 68.2 ($CH_2CH_2CH_2$), 61.1 (CH_2OH), 29.8 ($CH_2CH_2CH_2$); MS *m/z*: 253.0 (M+1). Anal Calcd for $C_{11}H_{24}O_6$: C, 52.36; H, 9.59. Found: C, 52.41; H, 9.63.

3.1.3. 2-(2-{3-[2-(2-Tosyloxy-ethoxy)-ethoxy]-propoxy}-ethoxy)-ethanol (7). Compound **6** (1.0 g, 4.0 mmol) was dissolved in dry CH_2Cl_2 (50 mL) at room temperature and under nitrogen atmosphere. The stirred solution was cooled at 0 °C and tosyl chloride (1.86 g, 9.8 mmol), dry triethylamine (1.8 mL), and a catalytic amount of dimethylaminopyridine (DMAP) were slowly added. After 20 h the solvent was removed under reduced pressure and the residue was extracted with 100 mL of CH_2Cl_2 and 100 mL of 1 M HCl. The organic layer was washed twice with water (2×100 mL) and the solvent distilled off to give compound **7** (57%) as oil; ^{1}H NMR ($CDCl_3$): δ 7.79 (d, J=8.4 Hz, 4H, TsH), 7.34 (d, J=8.4 Hz, 4H, TsH), 4.15 (t, J=4.8 Hz, 4H, CH_2OTs), 3.68 (t, J=4.8 Hz, 4H, OCH_2CH_2OTs), 3.59–3.55 (m, 4H, $OCH_2CH_2OCH_2CH_2OTs$), 3.52–3.48 (m, 8H, $CH_2OCH_2CH_2CH_2OCH_2$), 2.44 (s, 6H, $TsCH_3$), 1.82 (quin, J=6.5 Hz, 2H, $CH_2CH_2CH_2$; ^{13}C NMR ($CDCl_3$): δ 144.7, 133.0 (Ar), 129.7, 127.9 (ArH), 70.6, 70.0, 69.1, 68.6, 68.1 (OCH_2), 29.8 ($CH_2CH_2CH_2$), 21.5 (CH_3); MS *m/z*: 561 (M+1). Anal Calcd for $C_{25}H_{36}O_{10}S_2$: C, 53.55; H, 6.47. Found: C, 53.60; H, 6.45.

3.1.4. Glycol 10. A mixture of compound **9** (5.3 g, 34.4 mmol) and NaH (0.83 g, 34.4 mmol) in dry DMF (100 mL) was stirred at room temperature for 30 min. Then a solution of 1,3-dibromopropane (**9**) (3.5 g, 17.2 mmol) dissolved in dry DMF (50 mL) was added dropwise and the mixture stirred at room temperature for 24 h. After removal of DMF under vaccum, the residue was dissolved in dichloromethane and washed with water (CAUTION!). The organic layer was dried over sodium sulfate and the solvent evaporated under reduced pressure. The pure product **10** (3.2 g, 53%) was obtained by crystallization from ethanol/water (1:1); mp 87–88 °C; ^{1}H NMR ($CDCl_3$): δ 7.00–6.89 (m, 8H, ArH), 4.30 (t, J=5.7 Hz, 4H, $OCH_2CH_2CH_2O$), 4.08 (t, J=4.2 Hz, 4H, $ArOCH_2CH_2OH$), 3.90 (t, J=4.2 Hz, 4H, $ArOCH_2CH_2OH$), 2.23 (quin, J=5.7 Hz, 2H, $OCH_2CH_2CH_2O$); ^{13}C NMR ($CDCl_3$): δ 149.3, 148.4 (Ar), 122.2, 121.6, 115.7, 114.4 (ArH), 71.1, 66.5 ($ArOCH_2$), 61.2 (CH_2OH), 29.0 ($CH_2CH_2CH_2$); MS *m/z*:

348.15 (M^+). Anal. Calcd for $C_{19}H_{24}O_6$: C, 65.50; H, 6.94. Found: C, 65.45; H, 6.85.

3.1.5. Ditosylate 11. A mixture of compound **10** (2.5 g, 7.2 mmol) and triethylammine (3 mL, 21 mmol) in dichloromethane (50 mL) was stirred at room temperature. To this solution were added tosyl chloride (3.2 g, 16.8 mmol) and a catalytic amount of 4-dimethylaminopyridine DMAP. After heating at reflux for 24 h the mixture was cooled at room temperature and extracted with 60 mL of 1 M HCl. The organic layer was dried over sodium sulfate and the solvent evaporated under vacuum. The residue was purified by column chromatography (SiO_2 Et_2O/hexane 7:3) to afford compound **11** as white solid (2.9 g, 61%); mp 79–83 °C; ^{1}H NMR ($CDCl_3$): δ 7.78 (d, J=8.3 Hz, 4H, TsH), 7.29 (d, J=8.3 Hz, 4H, TsH), 6.94–6.91 (m, 4H, ArH), 6.87–6.79 (m, 4H, ArH), 4.31 (t, J=4.2 Hz, 4H, TsOCH_2CH$_2$O), 4.19–4.15 (m, 8H, CH_2OArOCH_2), 2.41 (s, 6H, TsCH_3), 2.25 (quin, J=6.2 Hz, 2H, CH$_2$CH_2CH$_2$); ^{13}C NMR ($CDCl_3$): δ 149.4, 147.9, 144.8, 132.9 (Ar), 129.8, 127.9, 122.7, 121.2, 116.1, 114.4 (ArH), 68.2, 67.3, 65.7 (OCH_2), 29.3 (CH$_2$$CH_2CH_2$), 21.5 (CH$_3$). MS m/z: 656.6 (M^+). Anal. Calcd for $C_{33}H_{36}O_{10}S_2$: C, 60.35; H, 5.52. Found: C, 60.44; H, 5.46.

3.2. General procedure for the synthesis of calix-crown-6 (1 and 2)

25,27-Di-*iso*-propoxycalix[4]arene **8** (2 mmol) was dissolved in CH_3CN (300 mL) and an excess of Cs_2CO_3 (2.60 g, 8 mmol) and of the appropriate glycol di-*p*-toluenesulfonate (2.5 mmol) added under a nitrogen atmosphere. The reaction mixture was refluxed for 24 h. Then CH_3CN was removed under reduced pressure and the residue extracted with 70 mL of CH_2Cl_2 and 70 mL of 10% HCl. The organic phase was separated, washed twice with water (2×100 mL) and the solvent distilled off. The pure compounds were isolated as described below.

3.2.1. Calix[4]arene-propylene-crown-6 (1). Calix-crown-6 **1** was obtained after purification on a silica gel column using ethyl acetate/hexane (2:3) as eluent; yield=54%; mp 216–218 °C; ^{1}H NMR ($CDCl_3$): δ 7.07 (d, J=7.4 Hz, 4H, ArH *meta*), 7.01 (d, J=7.4 Hz, 4H, ArH *meta*), 6.79 (t, J=7.4 Hz, 2H, ArH *para*), 6.78 (t, J=7.4 Hz, 2H, ArH *para*), 4.22 (ept, J=6.1 Hz, 2H, CH(CH$_3$)$_2$), 3.81 (d, J=15.6 Hz, 4H, ArCH_2Ar), 3.74 (d, J=15.6 Hz, 4H, ArCH_2Ar), 3.67 (t, J=5.8 Hz, 4H, OCH_2CH$_2$CH_2O), 3.63 (t, J=4.8 Hz, 4H, ArOCH$_2$CH$_2$OCH$_2$CH_2O), 3.54–3.49 (m, 8H, ArOCH$_2$CH_2 and ArOCH$_2$CH$_2$OCH_2CH$_2$O), 3.31 (t, J=5.8 Hz, 4H, ArOCH_2CH$_2$), 1.86 (quin, J=5.8 Hz, 2H, OCH$_2$CH_2CH$_2$O), 0.92 (d, J=6.1 Hz, 12H, CH(CH_3)$_2$); ^{13}C NMR ($CDCl_3$): δ 156.6, 154.7 (Ar *ipso*), 134.4, 133.4 (Ar *ortho*), 130.0, 129.6 (ArH *meta*), 121.8, 121.4 (ArH *para*), 70.7 (*C*H(CH$_3$)$_2$), 70.4, 70.2, 69.8, 69.2, 66.9 (OCH$_2$), 38.5 (Ar*C*H$_2$Ar), 30.1 (CH$_2$*C*H$_2$CH$_2$), 21.8 (CH(*C*H$_3$)$_2$). MS m/z: 724.5 (M^+). Anal Calcd for $C_{45}H_{56}O_8$: C, 74.56; H, 7.79. Found: C, 74.63; H, 7.71.

3.2.2. Calix[4]arene-propylene-dibenzocrown-6 (2). Calix-benzocrown-6 **2** was obtained after column chromatography on silica gel using first CH_2Cl_2/hexane (1:1) and then ethyl acetate/methanol (95:5) as eluent and crystallisation from methanol; yield=59%; mp 83–85 °C; ^{1}H NMR ($CDCl_3$): δ 7.04–6.93 (m, 12H, ArH), 6.86 (d, J=7.4 Hz, 4H, ArH *meta*), 6.81 (t, J=7.4 Hz, 2H, ArH *para*), 6.65 (t, J=7.4 Hz, 2H, ArH *para*), 4.28 (t, J=6.2 Hz, 4H, CH_2CH$_2$CH_2), 4.20 (ept, J=6.0 Hz, 2H, CH(CH$_3$)$_2$), 3.82 (d, J=15.9 Hz, 4H, ArCH_2Ar), 3.74 (d, J=15.9 Hz, 4H, ArCH_2Ar), 3.67 (t, J=6.4 Hz, 4H, ArOCH_2CH$_2$OArOCH$_2$), 3.44 (t, J=6.4 Hz, 4H, ArOCH$_2$CH_2OArOCH$_2$), 2.32 (quin, J=6.2 Hz, 2H, CH$_2$CH_2CH$_2$), 0.88 (d, J=6.0 Hz, 12H, CH(CH_3)$_2$). ^{13}C NMR ($CDCl_3$): δ 156.2, 154.8 (Ar *ipso*), 150.5, 149.7 (Bn), 134.5, 133.7 (Ar *ortho*), 130.2, 129.5 (Ar *meta*), 123.0, 121.98, 121.97, 121.92 (ArH *para* and BnH), 119.9, 117.0 (BnH), 70.5, 69.9, 68.0, 67.1 (OCH_2), 38.9 (Ar*C*H$_2$Ar), 30.1 (CH$_2$*C*H$_2$CH$_2$), 21.7 (*C*H$_3$); MS m/z: 820.1 (M^+). Anal. Calcd for $C_{53}H_{56}O_8$: C, 77.53; H, 6.87. Found: C, 77.58; H, 6.93.

3.3. X-ray crystallographic studies of 1

Crystal data and the most significant parameters for the structure refinement of **1** are reported in Table 6. A single transparent crystal was mounted on a glass fibre and protected from air by a thin film of perfluoric oil.

Table 6. Crystallographic data and experimental details for **1**[a]

Crystal data	
Empirical formula	$C_{45}H_{56}O_8$
Formula weight	724.933
Crystal size [mm]	0.4×0.3×0.4
Crystal system	Triclinic
Space group	*P*-1
a (Å)	10.962(5)
b (Å)	17.945(5)
c (Å)	11.009(5)
α (°)	104.06(2)
β (°)	91.34(2)
γ (°)	76.09(2)
V (Å^3)	2038(2)
Z	2
ρ (Calcd) (g/cm^3)	1.182
F(000)	780
Data collection	
T (K)	295
Index range	$-12\le h\le 12, -20\le k\le 19, 0\le l\le 19$
Reflections collected	6757
Independent reflections	6374(R_{int}=0.016)
Observed reflections	4262 [$F_0\ge 4\sigma(F_0)$]
Structure refinement	
Data/restraints/parameters	6374/0/488
Goodness-of-fit on F^2[a]	1.161
Final R indices (obs. data)[a]	R_1=0.056, wR_2=0.178
R indices (all data)	R_1=0.0832, wR_2=0.164
Largest diff. peak and hole (e/Å^3)	0.53, −0.43

[a] $R_1=\sum||F_0|-|F_c||/\sum|F_0|$, $wR_2=[\sum w(F_0^2-F_c^2)^2/\sum wF_0^4]^{1/2}$. Goodness-of-fit=$[\sum w(F_0^2-F_c^2)^2/(n-p)]^{1/2}$, where n is the number of reflections and p the number of parameters.

The X-ray measurements were performed at room temperature on a Philips PW1100 diffractometer using graphite monochromated Mo K_α radiation (λ=0.71073 Å). The cell parameters were obtained from a least-squares fitting on 25 $I_{\theta,\chi,\phi}$ reflections found in a random search on the reciprocal lattice in the range $16\le\theta\le20°$. One standard reflection, collected every 100 to monitor crystal decay and instrumental linearity, showed a linear decay of almost 10%. The intensities were corrected for Lorentz and polarization but not for absorption. The structure was solved by Direct

Methods using SIR92[24] and refined by full-matrix least-squares methods on F^2 using SHELXL-97.[25] All non-hydrogen atoms were refined with anisotropic atomic displacement parameters. The hydrogen atoms were placed at their calculated positions with the geometrical constraint C–H 0.96 Å and refined 'riding' on their parent carbon atoms. The structure has also been tested in the monoclinic system (a=15.716, b=15.353, c=17.945 Å, β=109.03°), space group $C2/c$, however the refinement was unsuccesful. Geometrical calculations were obtained by PARST97.[26] Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre: CCDC deposition number 232991.

3.4. Computational methods

All the calculations were executed on a Pentium IV PC (2.5 MHz). The semiempirical calculations at the PM3 level were performed with SPARTAN 02.[27] The ab initio calculations at the HF level were carried out using GAUSSIAN03 in the G03W suite.[28] Molecular symmetry was disabled in all calculations. The basis set for cesium was taken from literature.[29]

4. Supplementary data available

Cartesian coordinates of HF/3-21G** optimized structures of all compounds reported in this work and the .cif file of the X-ray crystal structure of ligand **1** are available on-line as Supplementary Data.

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