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Synthesis and Complexation Studies of Various Precursors Based on Calix[4]arene-crown-5 and -6 for the Immunoanalysis of Potassium and Caesium Ions

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In an attempt to generate antibodies for the development of an immunoanalysis method for potassium and caesium ions, new 1,3-alternate calix[4]arenes-crown-5 and -6 bearing either carboxylic or hydroxyl functions were synthesized in good yields. Their complexation properties towards potassium and caesium ions were investigated using ^{1}H NMR spectroscopy and the usual properties proved to be preserved in the presence of the anchoring arms.

Keywords: Calix[4]arenecrowns; Alkali metal complexation; Anchoring arms; Crystal structure

INTRODUCTION

There is a need for low-cost, *in situ* sensors for monitoring metal contamination in the environment and in body fluids. Metal-specific antibodies provide an interesting basis for immunoassays that can rapidly assess metal contamination in the environment. Antibodies directed towards metal chelates, such as EDTA or DTPA, have already been reported by Blake *et al.* [1–8]. However, most of these studies demonstrate that the use of such chelating agents does not allow differentiation between the various bound metals. The use of more selective ligands should permit circumvention of these selectivity limitations.

Calixarenes are known to be good candidates in metallic cation recognition [9]. Selectivity can be tuned by functionally modifying the preorganized platform defined by the phenolic moieties with a wide range of substituents.

We chose to investigate the potential of calix[4]arenes-crown-5 and -6 in the development of immunoanalysis kits for K^+ and Cs^+ determination. Calix[4]arenes-crown-5 are highly selective for K^+ complexation [10–12] and calix[4]arenes-crown-6 for Cs^+ complexation [12–14]. Their use as haptens in such methods requires chemical modification of these macrocycles to provide one or more reactive sites for coupling to a protein. Therefore, advantage should be taken of their rigid conformation that should enable the integrity of the complexation site to be preserved when anchoring a protein carrier for the immunization step.

In this study, we report the synthesis of new calix[4]arenes-crown-5 and -6 bearing NH_2-reactive groups on one side. With the prospect of using these macrocycles as haptens for the immunoanalysis of alkali metals, the complexation properties of such modified ligands towards K^+ and Cs^+ were also investigated.

RESULTS AND DISCUSSION

The aim of this work was to use the potential of calix[4]crowns-5 and -6 for alkali metal ion complexation and to modify these ligands so that they provide a carboxylic or a hydroxyl moiety able to react with the NH_2 group of a carrier-protein and far enough away from the complexation site. As it is established that the 1,3-alternate conformation

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of calixarenes seems to be the most favorable for metal complexation [11,13,15], the synthesis was oriented to obtain the new calixarenes in such a preferential conformation.

Synthesis of the Calix[4]arene-based Precursors

The synthetic pathway of calix[4]arenes-crown-5 and -6 bearing either one or two NH_2-reactive functional groups is represented in Fig. 1.

Calixarenes **14**–**17** were obtained by a three-step synthesis. The synthesis of these 1,3-dialkoxycalix[4]arene-crown ethers in a 1,3-alternate conformation was realized according to the synthetic route proposed by Casnati *et al.* [11,13]. Calix[4]arene was first selectively *O*-alkylated in the presence of K_2CO_3 with 2 equivalents of ethyl-5-oxavalerate to obtain the diester **1** or with 2 equivalents of 4-bromobutylacetate to obtain the diester **2**. The cone conformation of these two compounds was revealed by the presence in the ^{1}H NMR spectra of an AB system at 4.33 and 3.42 ppm for derivative **1** and 4.28 and 3.38 ppm for derivative **2** ($J = 13$ Hz), attributed to the methylenic protons ArCH_2Ar.

Intramolecular bridging on the lower rim was achieved by reaction with 1 equivalent of tetraethyleneglycol ditosylate (or pentaethyleneglycol ditosylate) to obtain calixarenes **6** and **8** (or **7** and **9**, respectively). The 1,3-alternate conformation was confirmed by the presence in the ^{1}H NMR spectra of a singlet for the methylenic protons ArCH_2Ar at 3.70 and 3.77 ppm for compounds **6** and **7** and 3.84 and 3.79 ppm for compounds **8** and **9**, respectively.

Finally, hydrolysis of these compounds was performed in the presence of 5 equivalents of KOH to obtain the calixarene derivatives **14**–**17**. The 1,3-alternate conformation was proved to be maintained by ^{1}H NMR spectra which revealed a singlet attributed to the methylenic protons ArCH_2Ar at 3.65, 3.80, 3.84 and 3.81 ppm for compounds **14**, **15**, **16** and **17**, respectively.

As calixarenes possessing a unique anchoring arm are likely to be more convenient, for example with regard to the formation of aggregates when coupling to a carrier protein, the synthesis of calixarenes bearing one carboxylic or one hydroxyl function was performed. Calixarenes **18**–**21** were obtained via a four-step synthesis.

Calix[4]arene was first *O*-alkylated in the presence of K_2CO_3 with 1 equivalent of methoxyethoxy-*p*-toluenesulfonate to obtain the monoalkoxycalix[4]-arene **3**. The cone conformation can be deduced from the presence in the ^{1}H NMR spectrum of two AB systems at 4.47 and 3.46 ppm and 4.31 and 3.44 ppm $J = 13$ Hz, typical for the methylenic protons ArCH_2 Ar. The calixarene derivative **3** was then functionalized by reacting 1 equivalent of ethyl-5-oxavalerate or 4-bromobutylacetate to obtain compounds **4** and **5**, respectively.

The next steps in the synthesis (intramolecular bridging and hydrolysis) were performed as for dialkoxycalix[4]arene-crowns. The 1,3-alternate conformation of the final compounds was confirmed by ^{1}H NMR where a singlet corresponding to the methylenic protons ArCH_2Ar was observed at 3.58 and 3.73 ppm for the calix[4]arene-crown-5 derivatives **18** and **20** and at 3.71 ppm for the calix[4]arene-crown-6 derivatives **19** and **21**, respectively.

Preliminary ^{1}H NMR Study of Alkali Metal Recognition by Calixarenes 14–21

NMR spectroscopy is widely used to investigate metal–ligand interactions. In this study, ^{1}H NMR spectra of the new calixarenes were recorded both in the absence and in the presence of alkali metal ions.

Metal complexes were formed by addition of an excess of either potassium or caesium picrate salt to a solution of calixarene in $CDCl_3$. The reaction mixture was then maintained under agitation at room temperature for 1 hour in the case of the potassium complexes of calixarenes-crown-5 and 72 hours for calixarenes-crown-6. The formation of caesium complexes required 24 hours agitation for calixarenes-crown-5 and 1 hour for calixarenes-crown-6.

Changes in proton chemical shifts upon addition of an excess of alkali metal are provided as supplementary data (Tables I and II). The formation of alkali metal complexes is evidenced by the appearance of a singlet attributed to picrate protons at 8.87 ppm (average value) and by modifications of the chemical shifts ($\Delta\delta$) of the overall spectra. A slight shift of the singlets attributed to methylenic protons ArCH_2Ar ($\Delta\delta = \pm 0.05$ on average was observed as well as a more important shift in the glycolic chain region ($\Delta\delta = 0.12$ on average).

Crystal Structures

Three compounds among those described above (**4**, **9** and **16**) have been obtained in single crystal form and their crystal structures determined, in addition to that of the complex of compound **6** with K^+.

The calixarene platform in compound **4** is in the cone conformation (Fig. 2), with two intramolecular hydrogen bonds between the phenolic protons and the neighboring substituted phenolic oxygen atoms [O4···O1 2.774(3), O4–H4 1.02, H4···O1 1.80 Å, O4–H4···O1 160°; O7···O5 2.701(4), O7–H7 0.99, H7···O5 1.75 Å, O7–H7···O5 159°]. The dihedral angles between the mean plane defined by the four methylenic carbon atoms [largest deviation 0.125(2) Å] and the four aromatic rings are 75.68(9), 40.84(10), 72.14(10) and 35.13(15)°, the two chain-bearing rings being further from the mean plane than

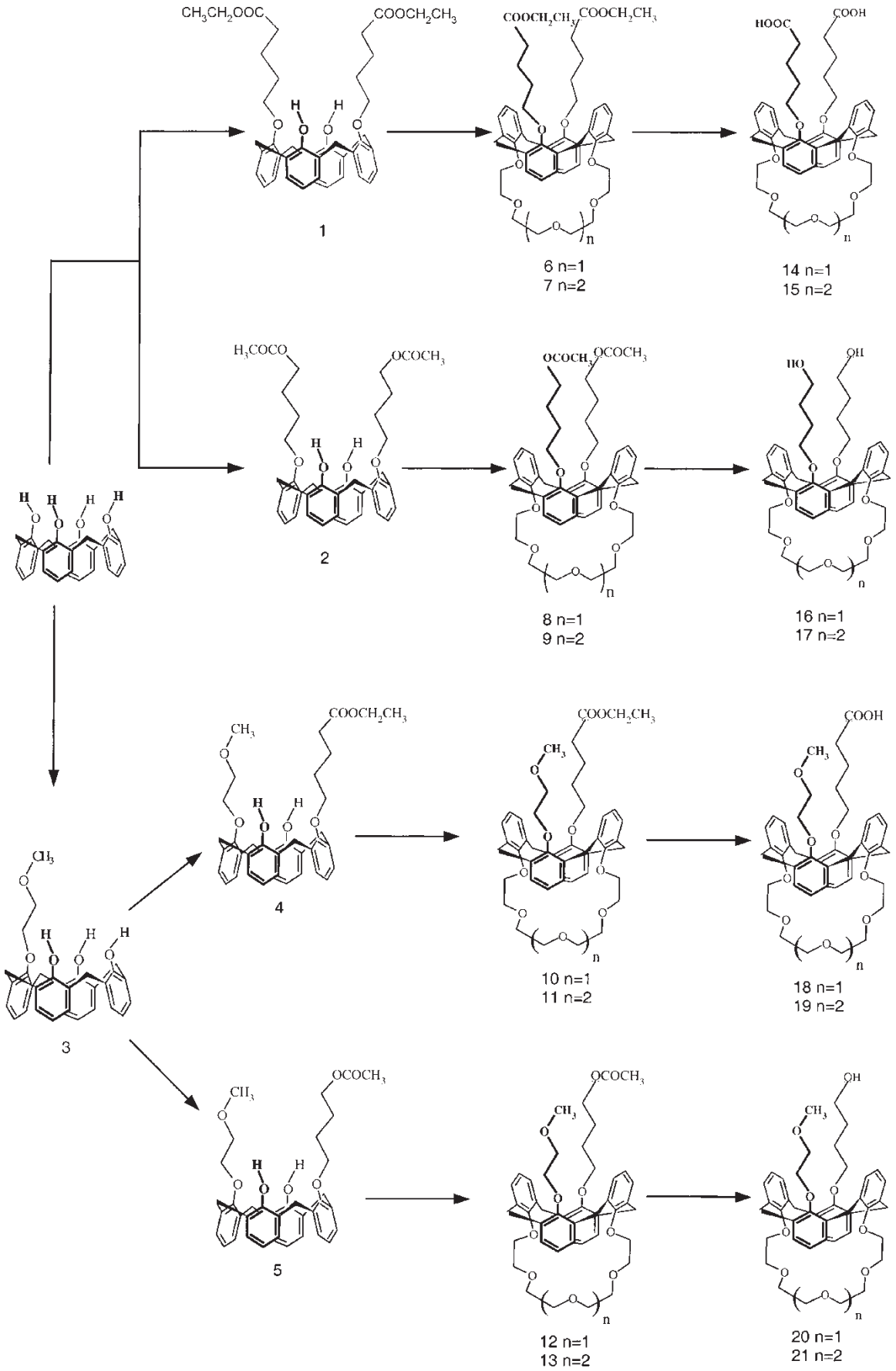

FIGURE 1 Synthetic pathway of calix[4]arenes-crown-5 and -6 bearing either one or two NH_2-reactive functions.

TABLE I Selected proton chemical shifts of calix[4]arenes-crown-5 in the absence or presence of alkali metal ions

	δ (H of picrate anion)	δ (OCH_2 of crown ether)	δ ($ArCH_2Ar$)
14	–	3.96–3.54	3.65
14 K^+	8.89	4.07–3.51	3.68
14 Cs^+	8.89	4.08–3.49	3.69
16	–	3.63–3.40	3.84
16 K^+	8.89	3.76–3.37	3.70
16 Cs^+	8.90	3.77–3.47	3.71
18	–	3.85–3.34	3.58
18 K^+	8.88	3.95–3.55	3.62
18 Cs^+	8.87	3.97–3.65	3.60
20	–	4.04–3.59	3.73
20 K^+	8.88	4.06–3.62	3.69
20 Cs^+	8.87	4.07–3.64	3.68

TABLE II Selected proton chemical shifts of calix[4]arenes-crown-6 in the absence or presence of alkali metal ions

	δ (H of picrate anion)	δ (OCH_2CH_2 of crown ether)	δ ($ArCH_2Ar$)
15	–	3.72–3.36	3.80
15 K^+	8.88	3.91–3.34	3.77
15 Cs^+	8.87	3.90–3.33	3.78
17	–	3.71–3.49	3.81
17 K^+	8.87	3.87–3.43	3.76
17 Cs^+	8.88	3.86–3.41	3.75
19	–	3.79–3.12	3.71
19 K^+	8.86	3.94–3.24	3.73
19.Cs^+	8.85	3.96–3.22	3.66
21	–	3.81–3.32	3.71
21 K^+	8.86	3.89–3.38	3.69
21 Cs^+	8.86	3.91–3.39	3.68

the others, probably as a result of steric effects associated with the chains.

Compound **9**, which comprises a crown-6 moiety and two ester-bearing chains, is in the 1,3-alternate conformation (Fig. 3). The crown ether part, which is

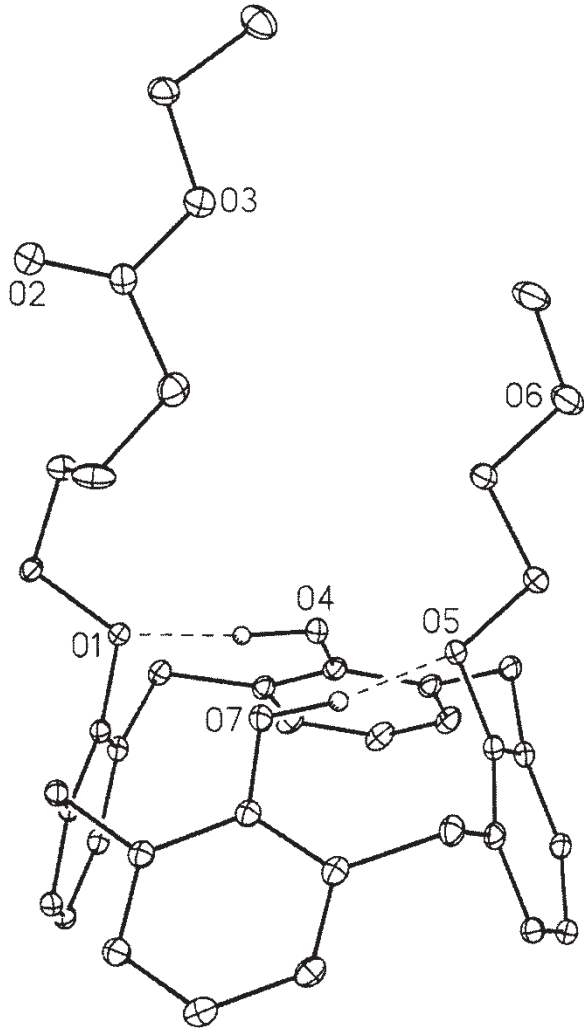

FIGURE 2 View of the molecular structure of compound **4**. Hydrogen atoms are omitted, except the phenolic ones. Hydrogen bonds are represented as dashed lines. Displacement ellipsoids are drawn at the 10% probability level.

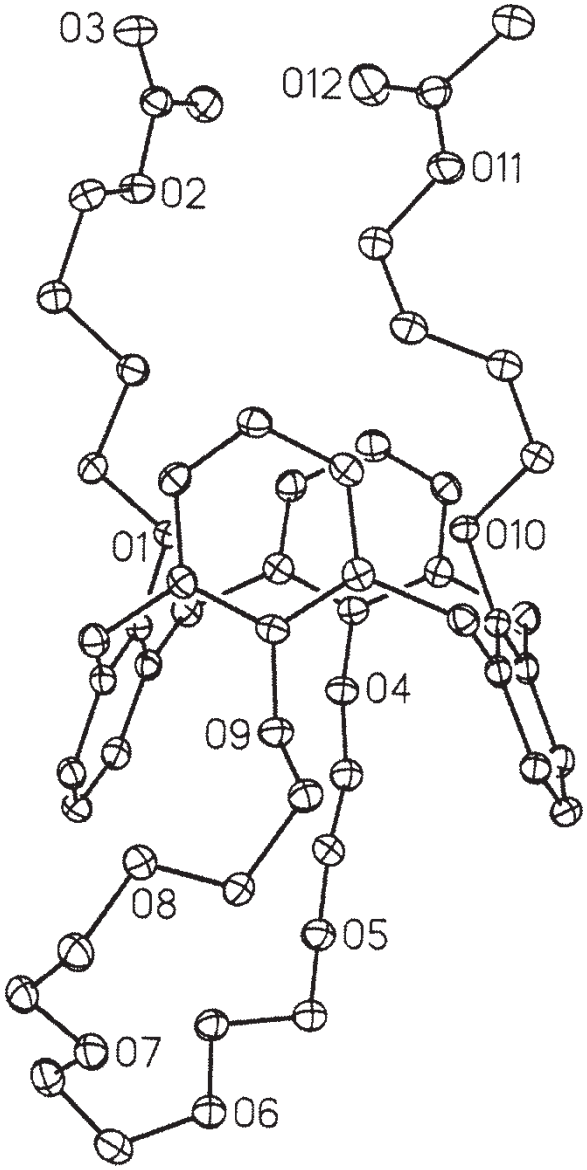

FIGURE 3 View of the molecular structure of compound **9**. Hydrogen atoms are omitted. Displacement ellipsoids are drawn at the 40% probability level.

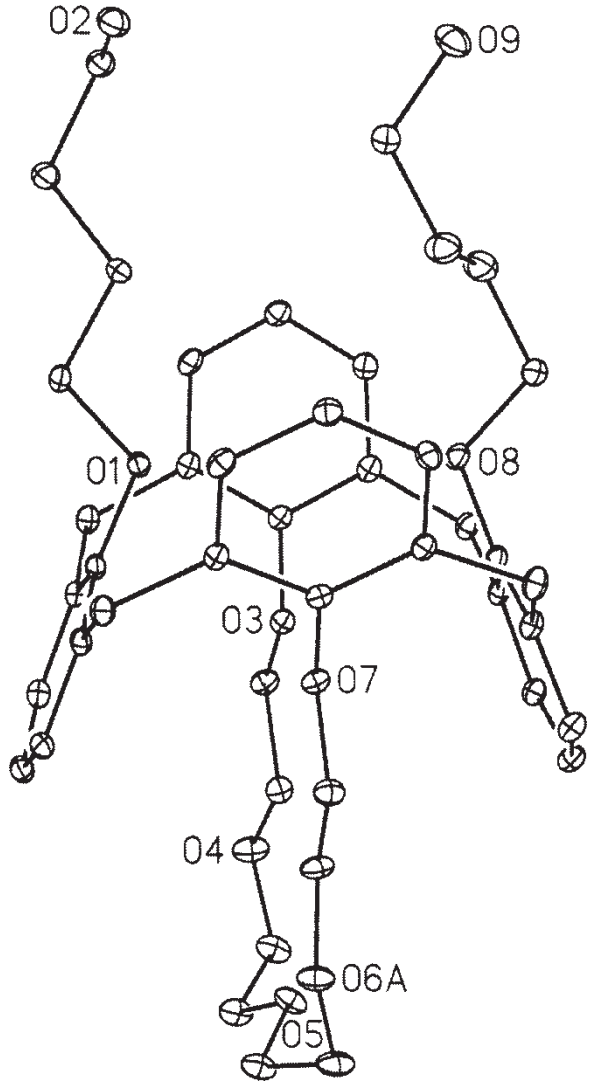

FIGURE 4 View of the molecular structure of compound **16**. Hydrogen atoms are omitted. Only one of the two positions of atom O6 is represented. Displacement ellipsoids are drawn at the 10% probability level.

not rigidified by cation or solvent complexation [16], displays a very distorted geometry in which some of the ether oxygen lone pairs are not directed toward the center of the cavity. The O–C–C–O torsion angles define an $aag^{-}g^{+}g^{-}$ sequence (where *a* and *g* are *anti* and *gauche* angles, respectively), which has never been observed in related compounds [17]. The dihedral angles between the mean plane defined by the four methylenic carbon atoms [largest deviation 0.099(1) Å] and the four aromatic rings are 68.24(5), 61.44(6), 70.74(5) and 82.90(5)°.

Compound **16**, with a crown-6 moiety and two hydroxyl-bearing chains, is also in the 1,3-alternate conformation (Fig. 4). As in the calix[4]arene-bis(crown-5), which has been structurally characterized [16], the crown ether adopts a somewhat planar geometry approximately perpendicular to the mean plane defined by the four methylenic carbon atoms: the five ether oxygen atoms define a mean plane with a maximum deviation of 0.107(2) Å, which makes a dihedral angle of 87.90(8)° with the mean plane defined by the four methylenic carbon atoms [largest deviation 0.101(2) Å]. As in compound **9**, all the ether oxygen atom lone pairs are not directed toward the crown center. The O–C–C–O torsion angles define an $ag^{-}g^{+}a$ sequence. The dihedral angles between the mean plane and the four aromatic rings are 69.33(9), 71.25(10), 69.65(10) and 59.51(10)°. The protons bound to the hydroxylic oxygen atoms O2 and O9 have not been located, but some interatomic contacts indicate the existence of hydrogen bonds between O2 and both O2′ and O9′ pertaining to a neighboring molecule [O2···O2′ 2.742(7), O2···O9′ 2.838(5) Å, $' = 0.5 - x, -0.5 - y, -z$], which gives rise to dimers bound by the extremities of the two chains. Another hydrogen bond between O9 and the ether oxygen atom O6A″ further links neighboring dimers [09···06A″ 2.670(13) Å, $'' = x, -y, -z - 0.5$].

The structure of the complex K**6**OTs·5H_2O, where OTs is the tosylate anion $CH_3(C_6H_4)SO_3$, is represented in Fig. 5. The ligand, with a crown-5 moiety and two ester-bearing chains, is in the 1,3-alternate conformation. The potassium ion is located in the crown ether cavity and is bound to the five ether oxygen atoms with K–O bond lengths in the range 2.762(3)–2.836(3) [mean value 2.81(3)] Å, in agreement with the values in other potassium complexes of calix[4]arene-crown-5 [18]. Larger bond lengths are observed in potassium complexes of calix[4]arene-bis(crown-6) [3.068(9)–3.672(8) Å] [19] and calix[4]arene-[bis(benzo)]crown-6 [2.91(1)–3.15(1) Å] [20], which confirms that these calix[4]arene-crown-6 ligands are not as well adapted to potassium complexation as the calix[4]arene-crown-5 species. The five oxygen atoms of the crown moiety define a mean plane with a maximum deviation of 0.207(2) Å, the potassium ion being at 0.063(1) Å from this plane and the dihedral angle between the latter and the mean plane defined by the four methylenic carbon atoms [largest deviation 0.008(2) Å] being 86.98(6)°, close to the value in compound **16**. The O–C–C–O torsion angles define a regular sequence $g^{-}g^{+}g^{-}g^{+}$ with all C–O–C–C torsion angles of the *anti* type, all the ether oxygen lone pairs being necessarily directed toward the crown center. As in the other complexes of K^+ and Cs^+ with calix[4]arene-crowns in the 1,3-alternate conformation, the shortest K···C contacts involving the aromatic carbon atoms closest to the cation are about 3.1 Å, which indicates the presence of cation–π interactions [16,18–20]. The dihedral angles between the mean plane defined by the four methylenic carbon atoms and the four aromatic rings are 74.06(10), 80.97(11), 82.85(9) and 81.84(10)°, the aromatic rings thus being further from the mean

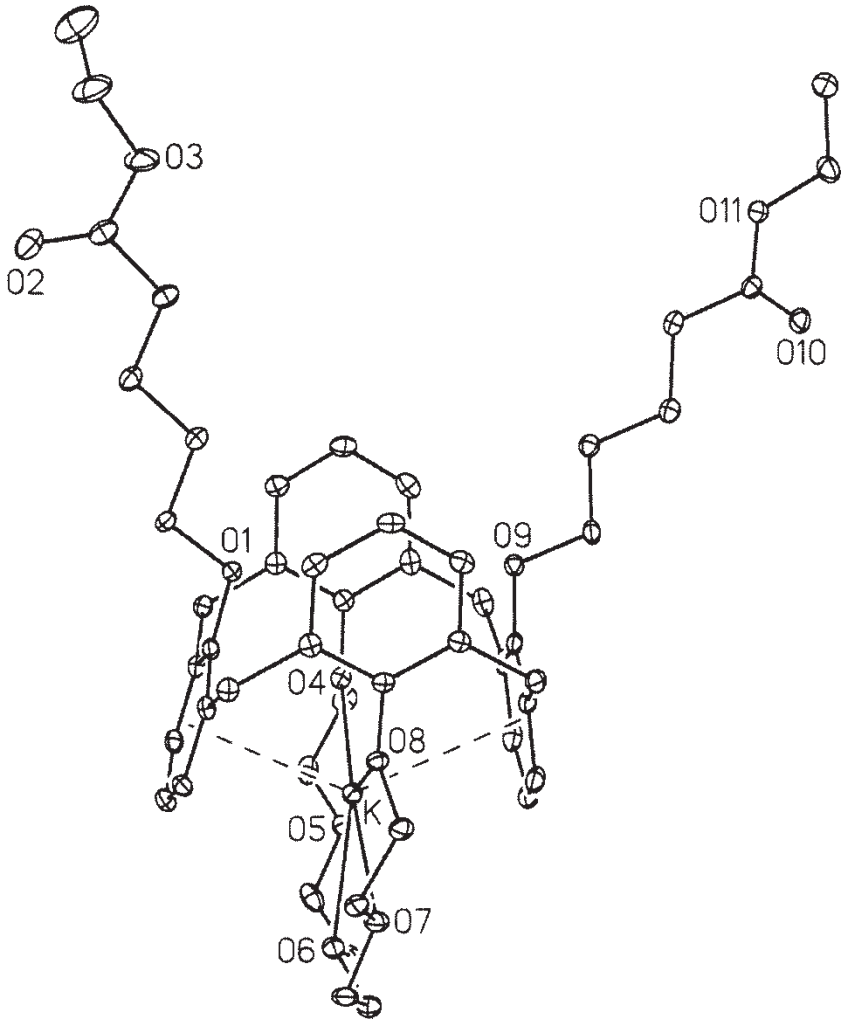

FIGURE 5 View of the complex K**6**OTs·5H_2O. The counter-ion, solvent molecules and hydrogen atoms are omitted. Cation-π interactions are represented as dashed lines. Displacement ellipsoids are drawn at the 20% probability level.

plane than in compound **16**. In contrast with the somewhat irregular conformation of the chains in the previous compounds, the two ester chains in the present case are directed along two divergent lines. The repeat unit also comprises one OTs anion and five water molecules that are interconnected by a network of 10 hydrogen bonds.

CONCLUSION

The synthesis of eight calix[4]arenes in 1,3-alternate conformation, bearing a crown ether on one side and NH_2-reactive functions on the other side, was achieved. As expected, complexation of potassium and caesium ions by these calix[4]-crowns is observed using ^{1}H NMR spectroscopy. The new calix[4]arenes-crown-5 proved to kinetically favour potassium complexation whereas the calix[4]arenes-crown-6 complex caesium more rapidly. With the aim of generating antibodies directed towards these metallic complexes, the next step in this study is to couple these non-immunogenic compounds to a carrier-protein to stimulate an immune response.

EXPERIMENTAL

Synthesis

All reagents and solvents were commercial and used without further purification. Calix[4]arene was prepared according to the literature [21]. The melting points were obtained on a Büchi 500 apparatus in capillaries sealed under nitrogen. Chromatography used SiO_2 columns with Kieselgel Merck (art. 11567). ^{1}H NMR spectra were recorded in $CDCl_3$ on a Bruker SY200 spectrometer δ in ppm, J in Hz). FAB mass spectra were obtained on a VG-Analytical ZAB HF instrument. Elemental analysis was performed at

the Service de Microanalyse of the Institut de Chimie de Strasbourg.

1,3-(Diethyl-5-oxavalerate)-calix[4]arene (1)

Calix[4]arene (4.24 g, 10.0 mmol) and K_2CO_3 (1.45 g, 10.5 mmol) were mixed in acetonitrile (150 mL) for 1 hour at room temperature under a N_2 atmosphere. Ethyl-5-oxavalerate (4.18 g, 20.0 mmol) was then added and the reaction mixture was refluxed for 4 days. After cooling to room temperature, the solvent was removed under reduced pressure. The residue was dissolved in CH_2Cl_2 and acidified with 1 N HCl. The organic phase was dried over Na_2SO_4, filtered and concentrated. Compound **1** was then purified by column chromatography (SiO_2, eluent: CH_2Cl_2) and obtained as a white solid. Yield: 3.05 g (45%); mp = 109–110°C, ^{1}H NMR (200 MHz, $CDCl_3$): 8.11 (s, 2H, ArO*H*), 7.10 (d, 4H, *J* = 7.5 Hz, Ar*H*), 6.91 (d, 4H, *J* = 7.5 Hz, Ar*H*), 6.93–6.66 (m, 4H, Ar*H*), 4.33 (d, 4H, *J* = 13.0 Hz, ArcH_2Ar), 4.19 (q, 4H, *J* = 7.0 Hz, COOCH_2CH$_3$),4.05 (t, 4H, *J* = 6.5 Hz, OCH_2CH$_2$), 3.42 (d, 4H, *J* = 13.0 Hz, ArCH_2Ar), 2.55 (t, 4H, *J* = 6.5 Hz, CH$_2$COOCH$_2$CH$_3$), 2.14–2.12 (m, 8H, OCH$_2$CH_2 CH_2), 1.29 (t, 6H, *J* = 7.0 Hz, COOCH$_2$CH_3); Elemental analysis calc. for $C_{42}H_{48}O_8$: C, 74.09; H, 7.11; found: C, 74.28; H, 7.28; Mass spectrum (FAB + , NAB): $m/z = 681.3$ [MH$^+$].

1,3-(Di-4-oxabutylacetate)-calix[4]arene (2)

Calix[4]arene (8.49 g, 20.0 mmol) and K_2CO_3 (2.90 g, 21.0 mmol) were mixed in acetonitrile (700 mL) for 1 hour at room temperature under a N_2 atmosphere. 4-Bromobutylacetate (7.80 g, 40.0 mmol) was then added and the reaction mixture was refluxed for 5 days. After cooling to room temperature, the solvent was removed under reduced pressure. The residue was dissolved in CH_2Cl_2 and acidified with 1 N HCl. The organic phase was dried over Na_2SO_4, filtered and concentrated. Compound **2** was then purified by column chromatography (SiO_2, eluent: CH_2Cl_2) and obtained as a white solid. Yield: 5.50 g (42%); mp = 121–122°C; ^{1}H NMR (200 MHz, $CDCl_3$): 8.02 (s, 2H, ArO*H*), 7.07 (d, 4H, *J* = 7.5 Hz, Ar*H*), 6.91 (d, 4H, *J* = 7.5 Hz, Ar*H*), 6.78–6.62 (m, 4H, Ar*H*), 4.28 (d, 4H, *J* = 13.0 Hz, ArCH_2 Ar), 4.25 (s br., 4H, CH_2OCOCH$_3$), 4.04 (s br., 4H, OCH_2CH$_2$), 3.38 (d, 4H, *J* = 13.0 Hz, ArCH_2Ar), 2.11–2.09 (m, 8H, OCH$_2$CH_2CH_2), 2.09 (s, 6H, OCOCH_3); Elemental analysis calc. for $C_{40}H_{44}O_8$: C, 73.60; H, 6.79; found: C, 73.57; H, 6.86; Mass spectrum (FAB + , NAB): $m/z = 653.3$ [MH$^+$].

Methoxyethoxycalix[4]arene (3)

Calix[4]arene (8.49 g, 20.0 mmol) and methoxy-ethoxy-*p*-toluenesulfonate (4.60 g, 20.0 mmol) were refluxed in acetonitrile (350 mL) in the presence of K_2CO_3 (1.44 g, 10.4 mmol) for 4 days under a N_2 atmosphere. After cooling to room temperature, the solvent was removed under reduced pressure. The residue was dissolved in CH_2Cl_2 and acidified with 1 N HCl. The organic phase was dried over Na_2SO_4 and concentrated. Methoxyethoxycalix[4]arene **3** was then purified by column chromatography (SiO_2, eluent: CH_2Cl_2) and obtained as a white solid. Yield: 4.67 g (49%); mp = 211–212°C; ^{1}H NMR (200 MHz, $CDCl_3$): 9.89 (s, 1H, ArO*H*), 9.25 (s, 2H, ArO*H*), 7.12–6.98 (m, 8H, Ar*H*), 6.91–6.84 (m, 1H, Ar*H*), 6.72–6.62 (m, 3H, Ar*H*), 4.47 (d, 2H, *J* = 13.0 Hz, ArCH_2Ar), 4.34–4.27 (m, 2H, OCH_2), 4.31 (d, 2H, *J* = 13.0 Hz, ArCH_2Ar), 4.03–3.99 (m, 2H, OCH$_2$CH_2), 3.61 (s, 3H, OCH_3), 3.46 (d, 2H, *J* = 13.0 Hz, ArCH_2Ar), 3.44 (d, 2H, *J* = 13.0 Hz, ArCH_2Ar); Elemental analysis calc. for $C_{31}H_{30}O_5$: C, 77.14; H, 6.27; found: C, 77.39; H, 6.40; Mass spectrum (FAB + , NAB): $m/z = 483.2$ [MH$^+$].

1-(Ethyl-5-oxavalerate)-3-methoxyethoxycalix[4]arene (4)

Calix[4]arene derivative **3** (3.86 g, 8.0 mmol) and K_2CO_3 (0.57 g, 4.2 mmol) were mixed in acetonitrile (200 mL) for 1 hour at room temperature under a N_2 atmosphere. Ethyl-5-oxavalerate (1.67 g, 8.0 mmol) was then added and the reaction mixture was refluxed for 4 days. After cooling to room temperature, the solvent was removed under reduced pressure. The residue was dissolved in CH_2Cl_2 and acidified with 1 N HCl. The organic phase was dried over Na_2SO_4, filtered and concentrated. Compound **4** was then purified by column chromatography (SiO_2, eluent: CH_2Cl_2/acetone 98/2) and obtained as a white solid. Yield: 3.80 g (76%); mp = 139–140°C; ^{1}H NMR (200 MHz, $CDCl_3$): 7.96 (s, 2H, ArO*H*), 7.06 (d, 4H, *J* = 7.5 Hz, Ar*H*), 6.90 (d, 4H, *J* = 7.5 Hz, Ar*H*), 6.77–6.61 (m, 4H, Ar*H*), 4.41 (d, 2H, *J* = 13.0 Hz, ArCH_2Ar), 4.29 (d, 2H, *J* = 13.0 Hz, ArCH_2Ar), 4.22–4.11 (m, 4H, COOCH_2CH$_3$ and ArOCH_2CH$_2$OCH$_3$), 4.02 (s br., 2H, OCH_2CH$_2$), 3.94–3.84 (m, 2H, OCH$_2$CH_2OCH$_3$), 3.55 (s, 3H, CH$_2$CH$_2$OCH_3), 3.38 (d, 2H, *J* = 13.0 Hz, ArCH_2Ar), 3.37 (d, 2H, *J* = 13.0 Hz, ArCH_2Ar) 2.51 (s br., 2H, CH_2COOCH$_2$ CH$_3$), 2.09 (s br., 4H, OCH$_2$CH_2CH_2), 1.27 (t, 3H, *J* = 7.0 Hz, COOCH$_2$CH_3); Elemental analysis calc. for $C_{38}H_{42}O_7$: C, 74.73; H, 6.93; found: C, 74.34; H, 6.67; Mass spectrum (FAB + , NAB): $m/z = 611.2$ [MH$^+$].

1-(4-Oxabutyl-5-acetate)-3-methoxyethoxycalix[4]arene (5)

Calix[4]arene derivative **3** (3.86 g, 8.0 mmol) and K_2CO_3 (0.57 g, 4.2 mmol) were mixed in acetonitrile (200 mL) for 1 h at room temperature under a N_2

atmosphere. 4-Bromobutylacetate (1.60 g, 8.0 mmol) was then added and the reaction mixture was refluxed for 4 days. After cooling to room temperature, the solvent was removed under reduced pressure. The residue was dissolved in CH_2Cl_2 and acidified with 1 N HCl. The organic phase was dried over Na_2SO_4, filtered and concentrated. Compound **5** was then purified by column chromatography (SiO_2, eluent: CH_2Cl_2/acetone 98/2) and obtained as a white solid. Yield: 3.24 g (68%); mp = 147–148°C; ^{1}H NMR (200 MHz, $CDCl_3$): 7.94 (s, 2H, ArO*H*), 7.06 (d, 4H, *J* = 7.5 Hz, Ar*H*), 6.90 (d, 4H, *J* = 7.5 Hz, Ar*H*), 6.77–6.61 (m, 4H, Ar*H*), 4.41 (d, 2H, *J* = 13.0 Hz, ArCH_2Ar), 4.32–4.26 (m, 4H, CH_2 OCOCH$_3$ and ArCH_2Ar), 4.19–4.14 (m, 2H, CH$_2$ CH_2OCH$_3$), 4.03 (s br., 2H, OCH_2), 3.93–3.88 (m, 2H, OCH_2CH$_2$OCH$_3$), 3.54 (s, 3H, CH$_2$CH$_2$OCH_3), 3.38 (d, 2H, *J* = 13.0 Hz, ArCH_2Ar), 3.37 (d, 2H, *J* = 13.0 Hz, ArCH_2Ar), 2.15–2.05 (m, 7H, OCH$_2$CH_2 CH_2CH$_2$ and OCOCH_3); Elemental analysis calc. for $C_{37}H_{40}O_7$: C, 74.47; H, 6.76; found: C, 74.34; H, 6.67; Mass spectrum (FAB +, NAB): *m*/*z* = 597.3 [MH$^+$].

Calixcrowns 6–13

The calix[4]arene derivative and K_2CO_3 (5.52 g, 40.0 mmol) were mixed in acetonitrile for 1 hour at room temperature under a N_2 atmosphere. Polyethyleneglycol ditosylate was then added and the reaction mixture was refluxed for 10 days. After cooling to room temperature, acetonitrile was removed under reduced pressure. The residue was dissolved in CH_2Cl_2 and acidified with 1 N HCl. The organic phase was separated, dried over Na_2SO_4, filtered and concentrated. The calixcrown was then recovered after purification by column chromatography (SiO_2, eluent: CH_2Cl_2/acetone 90/10).

1,3-(Diethyl-5-oxavalerate)-calix[4]arene-crown-5 (6)

Calix[4]arene derivative **1**: 2.72 g, 4.0 mmol, K_2CO_3: 5.52 g, 40.0 mmol, tetraethyleneglycol ditosylate: 2.01 g, 4.0 mmol, acetonitrile: 700 mL. White solid, yield: 1.51 g (45%); mp = 94–95°C; ^{1}H NMR (200 MHz, $CDCl_3$): 7.21 (d, 4H, *J* = 7.5 Hz, Ar*H*), 7.04 (d, 4H, *J* = 7.5 Hz, Ar*H*), 6.88 (t, 2H, *J* = 7.5 Hz, Ar*H*), 6.82 (t, 2H, *J* = 7.5 Hz, Ar*H*), 4.15 (q, 4H, *J* = 7.0 Hz, COOCH_2CH$_3$), 3.95–3.89 (m, 4H, OCH_2CH$_2$), 3.78–3.67 (m, 4H, OCH_2CH$_2$), 3.70 (s, 8H, ArCH_2Ar), 3.64–3.58 (m, 12H, OCH_2CH$_2$), 2.26 (t, 4H, *J* = 6.5 Hz, CH_2COOCH$_2$CH$_3$), 1.51 (s br., 8H, OCH$_2$CH_2CH_2), 1.27 (t, 6H, *J* = 7.0 Hz, COOCH$_2$CH_3); Elemental analysis calc. for $C_{50}H_{62}O_{11}$: C, 71.58; H, 7.45; found: C, 71.62; H, 7.37; Mass spectrum (FAB +, NAB): *m*/*z* = 877.4 [MK$^+$].

1,3-(Diethyl-5-oxavalerate)-calix[4]arene-crown-6 (7)

Calix[4]arene derivative **1**: 2.72 g, 4.0 mmol, K_2CO_3: 5.53 g, 40.0 mmol, pentaethyleneglycol ditosylate: 2.01 g, 4.0 mmol, acetonitrile: 700 mL. Brown paste, yield: 2.00 g (57%); mp = 39–40°C; ^{1}H NMR (200 MHz, $CDCl_3$): 7.08 (d, 4H, *J* = 7.5 Hz, Ar*H*), 7.04 (d, 4H, *J* = 7.5 Hz, Ar*H*), 6.83 (t, 2H, *J* = 7.5 Hz, Ar*H*), 6.77 (t, 2H, *J* = 7.5 Hz, Ar*H*), 4.16 (q, 4H, *J* = 7.0 Hz, COOCH_2CH$_3$), 3.77 (s, 8H, ArCH_2Ar), 3.70 (s, 4H, OCH_2CH$_2$), 3.66–3.55 (m, 8H, OCH_2CH$_2$), 3.49–3.31 (m, 12H, OCH_2CH$_2$), 2.27 (t, 4H, *J* = 6.5 Hz, CH_2COOCH$_2$CH$_3$), 1.54–1.39 (m, 4H, OCH$_2$CH_2CH$_2$), 1.32–1.17 (m, 4H, OCH$_2$CH$_2$ CH_2CH$_2$COOCH$_2$CH$_3$), 1.29 (t, 6H, *J* = 7.0 Hz, COOCH$_2$CH_3); Elemental analysis calc. for $C_{52}H_{66}O_{12}$: C, 70.71; H, 7.54; found: C, 70.61; H, 7.71; Mass spectrum (FAB +, NAB): *m*/*z* = 884.4 [MH$^+$].

1,3-(Di-4-oxabutylacetate)-calix[4]arene-crown-5 (8)

Calix[4]arene derivative **2**: 2.61 g, 4.0 mmol, K_2CO_3: 5.53 g, 40.0 mmol, tetraethyleneglycol ditosylate: 2.01 g, 4.0 mmol, acetonitrile: 700 mL. White solid, yield: 1.45 g (45%); mp = 96–97°C; ^{1}H NMR (200 MHz, $CDCl_3$): 7.09 (d, 4H, *J* = 7.5 Hz, Ar*H*), 7.01 (d, 4H, *J* = 7.5 Hz, Ar*H*), 6.91–6.77 (m, 4H, Ar*H*), 3.93 (t, 4H, *J* = 7.0 Hz, CH_2OCOCH$_3$), 3.84 (s, 8H, ArCH_2Ar), 3.62–3.54 (m, 8H, OCH_2CH$_2$), 3.46–3.37 (m, 8H, OCH_2CH$_2$), 3.10 (t, 4H, *J* = 7.0 Hz, OCH_2CH$_2$), 2.08 (s, 6H, OCOCH_3), 1.41–1.11 (m, 8H, OCH$_2$CH_2CH_2); Elemental analysis calc. for $C_{48}H_{58}O_{11}$: C, 71.09; H, 7.21; found: C, 70.87; H, 7.26; Mass spectrum (FAB +, NAB): *m*/*z* = 810.5 [MH$^+$], *m*/*z* = 849.4 [MK$^+$], 100%.

1,3-(Di-4-oxabutylacetate)-calix[4]arene-crown-6 (9)

Calix[4]arene derivative **2**: 1.30 g, 2.0 mmol, K_2CO_3: 2.76 g, 20.0 mmol, pentaethyleneglycol ditosylate: 1.15 g, 2.0 mmol, acetonitrile: 400 mL. Transparent viscous liquid, yield: 0.99 g (58%); ^{1}H NMR (200 MHz, $CDCl_3$): 7.09 (d, 4H, *J* = 7.5 Hz, Ar*H*), 7.02 (d, 4H, *J* = 7.5 Hz, Ar*H*), 6.89–6.75 (m, 4H, Ar*H*), 3.99 (t, 4H, *J* = 7.0 Hz, CH_2OCOCH$_3$), 3.79 (s, 8H, ArCH_2Ar), 3.71 (s, 4H, OCH_2CH$_2$O), 3.68–3.56 (m, 8H, OCH_2CH$_2$), 3.51–3.41 (m, 8H, OCH_2CH$_2$), 3.34 (t, 4H, *J* = 6.5 Hz, OCH_2CH$_2$), 2.09 (s, 6H, OCOCH_3), 1.59–1.25 (m, 8H, OCH$_2$ CH_2CH_2CH$_2$); Elemental analysis calc. for $C_{50}H_{62}O_{12}$: C, 70.45; H, 7.12; found: C, 70.22; H, 7.31; Mass spectrum (FAB +, NAB): *m*/*z* = 855.4 [MH$^+$].

1-(Ethyl-5-oxavalerate)-3-methoxyethoxycalix[4]arene-crown-5 (10)

Calix[4]arene derivative **4**: 3.05 g, 5.0 mmol, K_2CO_3: 6.90 g, 50.0 mmol, tetraethyleneglycol ditosylate: 2.54 g, 5.0 mmol, acetonitrile: 300 mL. Transparent liquid, yield: 2.26 g (59%); ^{1}H NMR (200 MHz, $CDCl_3$): 7.22–7.08 (m, 8H, Ar*H*), 6.92–6.83 (m, 4H, Ar*H*), 4.16 (q, 2H, $J = 7.0$ Hz, $COOCH_2CH_3$), 3.97–3.94 (m, 4H, OCH_2CH_2), 3.88–3.75 (m, 16H, OCH_2CH_2), 3.65 (s, 8H, $ArCH_2Ar$), 3.41 (t, 2H, $J = 6.5$ Hz, OCH_2CH_2), 3.26 (s, 3H, CH_2OCH_3), 2.31 (s br., 2H, $OCH_2CH_2CH_2CH_2COOCH_2CH_3$), 1.54 (s br., 4H, $OCH_2CH_2CH_2CH_2COOCH_2CH_3$), 1.28 (t, 3H, $J = 7.0$ Hz, $COOCH_2CH_3$); Elemental analysis calc. for $C_{46}H_{56}O_{10}$: C, 71.85; H, 7.34; found: C, 71.78; H, 7.62; Mass spectrum (FAB +, NAB): $m/z = 807.6$ [MK^+].

1-(Ethyl-5-oxavalerate)-3-methoxyethoxycalix[4]arene-crown-6 (11)

Calix[4]arene derivative **4**: 1.22 g, 2.0 mmol, K_2CO_3: 2.76 g, 20.0 mmol, pentaethyleneglycol ditosylate: 1.15 g, 2.0 mmol, acetonitrile: 300 mL. Transparent viscous liquid, yield: 0.76 g (48%); ^{1}H NMR (200 MHz, $CDCl_3$): 7.11–7.00 (m, 8H, Ar*H*), 6.88–6.76 (m, 4H, Ar*H*), 4.17 (q, 2H, $J = 7.0$ Hz, $COOCH_2CH_3$), 3.79–3.77 (m, 4H, OCH_2CH_2), 3.70 (s, 8H, $ArCH_2Ar$), 3.77–3.25 (m, 20H, OCH_2CH_2), 3.23 (s, 3H, CH_2OCH_3), 3.09 (t, 2H, $J = 7.0$ Hz, OCH_2CH_2), 2.26 (t, 2H, $J = 7.0$ Hz, $CH_2CH_2COOCH_2CH_3$), 1.53–1.23 (m, 4H, $OCH_2CH_2CH_2CH_2COOCH_2CH_3$), 1.29 (t, 3H, $J = 7.0$ Hz, $COOCH_2CH_3$); Elemental analysis calc. for $C_{48}H_{60}O_{11}$: C, 70.90; H, 7.44; found: C, 70.76; H, 7.57; Mass spectrum (FAB +, NAB): $m/z = 813.4$ [MH^+].

1-(4-Oxabutyl-5-acetate), 3-methoxyethoxycalix[4]arene-crown-5 (12)

Calix[4]arene derivative **5**: 1.19 g, 2.0 mmol, K_2CO_3: 2.76 g, 20.0 mmol, tetraethyleneglycol ditosylate: 1.00 g, 2.0 mmol, acetonitrile: 300 mL. Transparent liquid, yield: 0.61 g (40%); ^{1}H NMR (200 MHz, $CDCl_3$): 7.23 (d, 4H, $J = 7.5$ Hz, Ar*H*), 7.05 (d, 4H, $J = 7.5$ Hz, Ar*H*), 6.94–6.80 (m, 4H, Ar*H*), 4.04 (t, 2H, $J = 7.0$ Hz, CH_2OCOCH_3), 3.95–3.92 (m, 4H, OCH_2CH_2), 3.84–3.57 (m, 16H, OCH_2CH_2), 3.72 (s, 8H, $ArCH_2Ar$), 3.37 (t, 2H, $J = 7.0$ Hz, OCH_2CH_2), 3.28 (s, 3H, CH_2OCH_3), 2.09 (s, 3H, $OCOCH_3$), 1.56–1.53 (m, 4H, $OCH_2CH_2CH_2$); Elemental analysis calc. for $C_{45}H_{54}O_{10}$: C, 71.60; H, 7.21; found: C, 71.87; H, 7.26; Mass spectrum (FAB +, NAB): $m/z = 754.4$ [MH^+], 40%, $m/z = 777.4$ [MNa^+], 92%, $m/z = 793.4$ [MK^+], 59%.

1-(4-Oxabutyl-5-acetate)-3-methoxyethoxycalix[4]arene-crown-6 (13)

Calix[4]arene derivative **5**: 1.19 g, 2.0 mmol, K_2CO_3: 2.76 g, 20.0 mmol, tetraethyleneglycol ditosylate: 1.15 g, 2.0 mmol, acetonitrile: 300 mL. Transparent liquid, yield: 0.74 g (46%); ^{1}H NMR (200 MHz, $CDCl_3$): 7.05–7.00 (m, 8H, Ar*H*), 6.89–6.79 (m, 4H, Ar*H*), 4.00 (t, 2H, $J = 7.0$ Hz, CH_2OCOCH_3), 3.80–3.34 (m, 24H, OCH_2CH_2), 3.71 (s, 8H, $ArCH_2Ar$), 3.24 (s, 3H, CH_2OCH_3), 3.12 (t, 2H, $J = 7.0$ Hz, OCH_2CH_2), 2.10 (s, 3H, $OCOCH_3$), 1.50–1.25 (m, 4H, $OCH_2CH_2CH_2$); Elemental analysis calc. for $C_{47}H_{58}O_{11}$: C, 70.66; H, 7.32; found: C, 70.87; H, 7.26; Mass spectrum (FAB +, NAB): $m/z = 799.4$ [MH^+].

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The calix[4]arene derivative and KOH were refluxed in a 50/50 ethanol/water mixture for 3 hours. After cooling to room temperature, the solvents were removed under reduced pressure. The residue was dissolved in CH_2Cl_2 and acidified with 1 N HCl. The organic phase was separated, dried over Na_2SO_4, filtered and concentrated.

1,3-(Diethyl-5-oxavaleric Acid)-calix[4]arene-crown-5 (14)

Calix[4]arene derivative **6**: 1.09 g, 1.3 mmol, KOH: 0.29 g, 5.2 mmol, ethanol/water: 200 mL. Yellow solid, yield: 0.95 g (94%); mp = 261–262°C; ^{1}H NMR (200 MHz, $CDCl_3$): 7.20 (d, 4H, $J = 7.5$ Hz, Ar*H*), 7.09 (d, 4H, $J = 7.5$ Hz, Ar*H*), 6.95–6.83 (m, 4H, Ar*H*), 3.96–3.92 (m, 4H, OCH_2CH_2), 3.81–3.54 (m, 16H, OCH_2CH_2), 3.65 (s, 8H, $ArCH_2Ar$), 2.92 (s br., 2H, COO*H*), 2.35 (s br., 4H, CH_2COOH), 1.50 (s br., 8H, $OCH_2CH_2CH_2$); Elemental analysis calc. for $C_{46}H_{54}O_{11}$: C, 70.57; H, 6.95; found: C, 70.38; H, 6.88; Mass spectrum (FAB +, NAB): $m/z = 821.2$ [MK^+].

1,3-(Diethyl-5-oxavaleric Acid)-calix[4]arene-crown-6 (15)

Calix[4]arene derivative **7**: 1.14 g, 1.3 mmol, KOH: 0.29 g, 5.2 mmol, ethanol/water: 200 mL. Yellow solid, yield: 0.96 g (94%); mp = 70–71°C; ^{1}H NMR (200 MHz, $CDCl_3$): 8.19 (s br., 2H, COO*H*), 7.10 (d, 4H, $J = 7.5$ Hz, Ar*H*), 7.03 (d, 4H, $J = 7.5$ Hz, Ar*H*), 6.90–6.76 (m, 4H, Ar*H*), 3.80 (s, 8H, $ArCH_2Ar$), 3.72 (s, 4H, OCH_2CH_2), 3.68–3.56 (m, 12H, OCH_2CH_2), 3.47–3.36 (m, 8H, OCH_2CH_2), 2.32 (t, 4H, $J = 7.0$ Hz, CH_2COOH), 1.54–1.45 (m, 4H, $OCH_2CH_2CH_2CH_2COOH$), 1.34–1.25 (m, 4H, $OCH_2CH_2CH_2$); Elemental analysis calc. for $C_{48}H_{58}O_{12}$: C, 69.70; H, 7.07; found: C, 69.65; H, 7.12; Mass spectrum (FAB +, NAB): $m/z = 826.6$ [MH^+].

1,3-(Di-4-oxabutanol)-calix[4]arene-crown-5 (16)

Calix[4]arene derivative **8**: 1.50 g, 1.9 mmol, KOH: 0.56 g, 10.0 mmol, ethanol/water: 260 mL. White solid, yield: 1.30 g (97%); mp = 117–118°C; ^{1}H NMR

(200 MHz, $CDCl_3$): 7.11 (d, 4H, $J = 7.5$ Hz, Ar*H*), 7.05 (d, 4H, $J = 7.5$ Hz, Ar*H*), 6.92–6.82 (m, 4H, Ar*H*), 3.84 (s, 8H, ArCH_2Ar), 3.63–3.57 (m, 8H, OCH_2CH_2O), 3.50–3.40 (m, 12H, OCH_2CH_2), 3.14 (t, 4H, $J = 6.5$ Hz, CH_2OH), 2.62 (s br., 2H, O*H*), 1.36 (s br., 8H,CH_2CH_2 CH_2OH); Elemental analysis calc. for $C_{44}H_{54}O_9$: C, 72.70; H, 7.49; found: C, 72.81; H, 7.39; Mass spectrum (FAB + , NAB): $m/z = 727.2$ [MH^+], 765.2 [MK^+].

1,3-(Di-4-oxabutanol)-calix[4]arene-crown-6 (17)

Calix[4]arene derivative **9**: 1.18 g, 1.4 mmol, KOH: 0.78 g, 14.0 mmol, ethanol/water: 200 mL. Yellow solid, yield: 1.00 g (94%); mp = 74–75°C; ^{1}H NMR (200 MHz, $CDCl_3$): 7.11–7.05 (m, 8H, Ar*H*), 6.90–6.83 (m, 4H, Ar*H*), 3.81 (s, 8H, ArCH_2Ar), 3.71 (s, 4H, OCH_2CH_2), 3.67–3.49 (m, 20H, OCH_2CH_2O), 3.32 (t, 4H, $J = 6.5$ Hz, CH_2OH), 2.18 (s br., 2H, O*H*), 1.39 (s br., 8H, OCH$_2$CH_2CH_2); Elemental analysis calc. for $C_{46}H_{58}O_{10}$: C, 71.66; H, 7.58; found: C, 71.81; H, 7.85; Mass spectrum (FAB + , NAB): $m/z = 771.6$ [MH^+].

1-(Ethyl-5-oxavaleric Acid)-3-methoxyethoxycalix[4]arene-crown-5 (18)

Calix[4]arene derivative **10**: 0.77 g, 1.0 mmol, KOH: 0.23 g, 4.1 mmol, ethanol/water: 50 mL. White solid, yield: 0.70 g (95%); mp = 157–158°C; ^{1}H NMR (200 MHz, $CDCl_3$): 7.16 (d, 4H, $J = 7.5$ Hz, Ar*H*), 7.03 (d, 4H, $J = 7.5$ Hz, Ar*H*), 6.88–6.78 (m, 4H, Ar*H*), 5.41 (s br., 1H, COO*H*), 3.85–3.53 (m, 20H, OCH_2CH_2O and OCH_2CH_2OCH$_3$), 3.58 (s, 8H, ArCH_2Ar), 3.34 (t, 2H, $J = 6.5$ Hz, OCH_2CH$_2$), 3.23 (s, 3H, CH$_2$OCH_3), 1.91 (s br., 2H, CH_2COOH), 1.47 (s br., 4H, OCH$_2$CH_2 CH_2); Elemental analysis calc. for $C_{44}H_{52}O_{10}$: C, 71.33; H, 6.45; found: C, 71.45; H, 6.48; Mass spectrum (FAB + , NAB): $m/z = 779.3$ [MK^+], 98%.

1-(Ethyl-5-oxavaleric Acid)-3-methoxyethoxycalix[4]arene-crown-6 (19)

Calix[4]arene derivative **11**: 1.09 g, 1.3 mmol, KOH: 0.29 g, 5.2 mmol, ethanol/water: 200 mL. White paste, yield: 0.298 g (96%); mp = 43–44°C; ^{1}H NMR (200 MHz, $CDCl_3$): 7.11–7.01 (m, 8H, Ar*H*), 6.89–6.78 (m, 4H, Ar*H*), 3.79–3.77 (m, 4H, OCH_2CH$_2$), 3.71 (s, 8H, ArCH_2Ar), 3.67–3.31 (m, 20H, OCH_2CH$_2$), 3.25 (s, 3H, CH$_2$OCH_3), 3.15 (t, 2H, $J = 7.0$ Hz, OCH_2CH$_2$), 2.30 (t, 2H, $J = 7.0$ Hz, CH_2COOH), 1.52–1.21 (m, 4H, OCH$_2$CH_2CH_2); Elemental analysis calc. for $C_{46}H_{56}O_{11}$: C, 70.57; H, 6.95; found: C, 70.75; H, 7.05; Mass spectrum (FAB + , NAB): $m/z = 785.2$ [MH^+].

1-(4-Oxabutyl-5-acetate)-3-methoxyethoxycalix[4]arene-crown-5 (20)

Calix[4]arene derivative **12**: 0.30 g, 0.4 mmol, KOH: 0.12 g, 2.0 mmol, ethanol/water: 50 mL. White solid, yield: 0.28 g (97%); mp = 175–176°C; ^{1}H NMR (200 MHz, $CDCl_3$): 7.26–7.24 (m, 4H, Ar*H*), 7.18–7.12 (m, 4H, Ar*H*), 6.93–6.86 (m, 4H, Ar*H*), 4.04–3.97 (m, 4H, OCH_2CH$_2$), 3.85–3.59 (m, 18H, OCH_2CH$_2$), 3.73 (s, 8H, ArCH_2Ar), 3.41 (t, 2H, $J = 6.5$ Hz, CH_2OH), 3.32 (s, 3H, CH$_2$OCH_3), 1.91 (s br., 1H, O*H*), 1.67–1.48 (m, 4H, OCH$_2$CH_2CH_2); Elemental analysis calc. for $C_{43}H_{52}O_9$: C, 72.45; H, 7.35; found: C, 72.36; H, 7.68; Mass spectrum (FAB + , NAB): $m/z = 751.3$ [MK^+].

1-(4-Oxabutyl-5-acetate), 3-methoxyethoxycalix[4]arene-crown-6 (21)

Calix[4]arene derivative **13**: 0.32 g, 0.4 mmol, KOH: 0.12 g, 2.0 mmol, ethanol/water: 50 mL. White solid, yield: 0.295 g (97%); mp = 143–144°C; ^{1}H NMR (200 MHz, $CDCl_3$): 7.12–7.03 (m, 8H, Ar*H*), 6.89–6.79 (m, 4H, Ar*H*), 3.81–3.32 (m, 26H, OCH_2CH$_2$), 3.71 (s, 8H, ArCH_2Ar), 3.28 (s, 3H, CH$_2$OCH_3), 3.17 (t, 2H, $J = 7.0$ Hz, CH_2OH), 1.90 (s br., 1H, O*H*), 1.36 (s br., 4H, CH_2CH_2CH$_2$OH); Elemental analysis calc. for $C_{45}H_{56}O_{10}$: C, 71.41; H, 7.46; found: C, 71.36; H, 7.35; Mass spectrum (FAB + , NAB): $m/z = 757.5$ [MH^+].

Crystallography

The data were collected at 100(2) K on a Nonius Kappa-CCD area detector diffractometer [22] using graphite-monochromated Mo–Kα radiation (0.71073 Å). The crystals were introduced in Lindemann glass capillaries with a protecting 'Paratone' oil (Exxon Chemical Ltd) coating. The unit cell parameters were determined from the reflections collected on 10 frames and were then refined on all data. The data were processed with DENZO-SMN [23]. The structures were solved by direct methods with SHELXS-97 [24] and subsequent Fourier-difference synthesis and refined by full-matrix least-squares on F^2 with SHELXL-97 [24]. Absorption effects in the compound K**6**OTs·5H_2O were corrected empirically with the program DELABS from PLATON [25]. All non-hydrogen atoms were refined with anisotropic displacement parameters. One of the ether oxygen atoms in compound **16** is disordered over two positions that have been refined with occupancy factors constrained to sum to unity. The hydrogen atoms bound to the phenolic oxygen atoms in **4** and those of the water molecules in K**6**OTs·5H_2O were found on Fourier-difference maps and all the others in all compounds (except the hydroxyl protons in **16**) were introduced at calculated positions. All hydrogen atoms were treated as riding atoms with an isotropic displacement parameter equal to 1.2 (OH, CH, CH_2) or 1.5 (CH_3) times that of the parent atom. The molecular plots were drawn with SHELXTL [26]. All calculations were performed on a Silicon Graphics R5000

TABLE III Crystal data and structure refinement details

	4	**9**	**16**	K**6**OTs·5H_2O
Empirical formula	$C_{38}H_{42}O_7$	$C_{50}H_{62}O_{12}$	$C_{44}H_{54}O_9$	$C_{57}H_{79}KO_{19}S$
Mol. wt.	610.72	855.00	726.87	1139.36
Crystal system	Triclinic	Triclinic	Monoclinic	Triclinic
Space group	$P\bar{1}$	$P\bar{1}$	*C*2/*c*	$P\bar{1}$
a, Å	10.0974(11)	9.8997(7)	35.8417(18)	10.4907(7)
b, Å	11.8462(11)	10.6410(8)	11.4543(7)	14.0022(10)
c, Å	14.7527(17)	23.1043(11)	19.7183(10)	20.8948(16)
α, deg	81.110(6)	92.122(4)	90	103.593(3)
?β, deg	72.622(5)	97.799(4)	108.812(4)	103.093(4)
γ, deg	71.103(6)	110.764(3)	90	93.042(4)
V, Å^3	1590.1(3)	2245.2(3)	7662.7(7)	2887.4(4)
Z	2	2	8	2
μ, mm^{-1}	0.087	0.089	0.087	0.201
F(000)	652	916	3120	1216
Reflections collected	12012	17204	28917	20017
Independent reflections	5461	7855	7214	10134
Observed reflections [$I > 2\sigma(I)$]	3747	5555	3853	5820
R_{int}	0.065	0.051	0.093	0.083
Parameters refined	408	561	489	706
R_1	0.091	0.049	0.082	0.064
wR_2	0.230	0.117	0.181	0.145
S	0.980	1.004	1.012	1.030
$\Delta\rho_{min}$, eÅ^{-3}	−0.33	−0.32	−0.35	−0.47
$\Delta\rho_{max}$, eÅ^{-3}	1.12	0.39	0.60	0.74

workstation. Crystal data and structure refinement details are given in Table III.

Crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre, CCDC nos 222427-222430. Copies of the information may be obtained free of charge from the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223-336-033; E-mail: deposit@ccdc.cam.ac.uk; or http://www.ccdc.cam.ac.uk).

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