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Calix[4]arene Anion Receptors Bearing 2,2,2-trifluoroethanol Groups at The *Upper* Rim

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Several di- and tetrafunctionalized anion receptors have been synthesized by attaching 2,2,2-trifluoroethanol binding groups at the upper rim of *cone* calix[4]arenes using two different synthetic procedures. The best results were obtained by treating calix[4]arene formyl derivatives with trifluoromethyltrimethylsilane and tetrabutylammonium fluoride in dry THF. The bis-trifluoroethanol calix[4]arene receptors are able to bind anions showing selectivity for carboxylates and dihydrogenphosphate but at a lower efficiency compared to analogous receptors bearing urea, sulfonamide or activated amide binding groups. The conformational properties of the free ligands and their acetate complexes have been investigated by Dynamic ^{1}H NMR, Molecular Modeling and in one case, by X-ray crystallography. Calix[4]arenes bearing cation coordinating groups at the lower rim and 2,2,2-trifluoroethanol moieties at the upper rim behave as ditopic receptors, since they bind simultaneously cation and anion and extracts ion pairs in organic media. In one case evidence was obtained that coordination of sodium metal ion at the lower rim enhances the binding of acetate anion at the upper rim (positive allosteric effect).

Keywords: Anion receptors; Calix[4]arenes; Ditopic receptors; Allosteric effect; X-ray structure; Molecular modeling

INTRODUCTION

Although examples of synthetic receptors able to recognize anions were reported since the early stages of Supramolecular Chemistry [1,2] anion recognition chemistry received less attention compared to cation binding. However, in the past two decades the topic has been extensively investigated and the interest is still very high as testified by several recent review articles in the literature [3–9]. To design new efficient and selective anion receptors one has to take into account several parameters, such as the large variety of anion structures and their pH dependence, the specific solvation by hydroxylic solvents etc. Most of the synthetic receptors for anions are charged or contain a metal center which directly coordinates to the anion [4,10,11]. However, it is recognized that in Nature anions (especially phosphates and carboxylates) are also complexed through hydrogen bonding [12]. This has stimulated the design and synthesis of neutral hydrogen bonding receptors [13] which mainly exploit amides [14], (thio)ureas [15,16] or a combination of the two [17]. These groups have been also attached to calixarenes, both at the upper and at the lower rim giving selective anion receptors [18]. Heteroditopic receptors [19], able to bind simultaneously the cation and the anion of an ion pair [20–26] have been also synthesized and some of these show co-operative or allosteric effects [27]. It is well-known [9] that perfluoroalcohols are very good anion solvating agents [28], and that they can affect the kinetics of chemical processes by specific anion solvation [29]. Moreover, Pirkle *et al.* used chiral fluoroalcohols as chiral solvating agents and were able to determine the enantiomeric compositions of chiral Lewis bases [30]. Surprisingly enough, so far nobody, except us [31,32], has exploited the fluoroalcoholic function as binding site in the design of more complex receptors for anions and polar organic molecules [25,26]. We report herein a general and mild strategy to introduce one, two or four trifluoroethanol functions at the upper rim of

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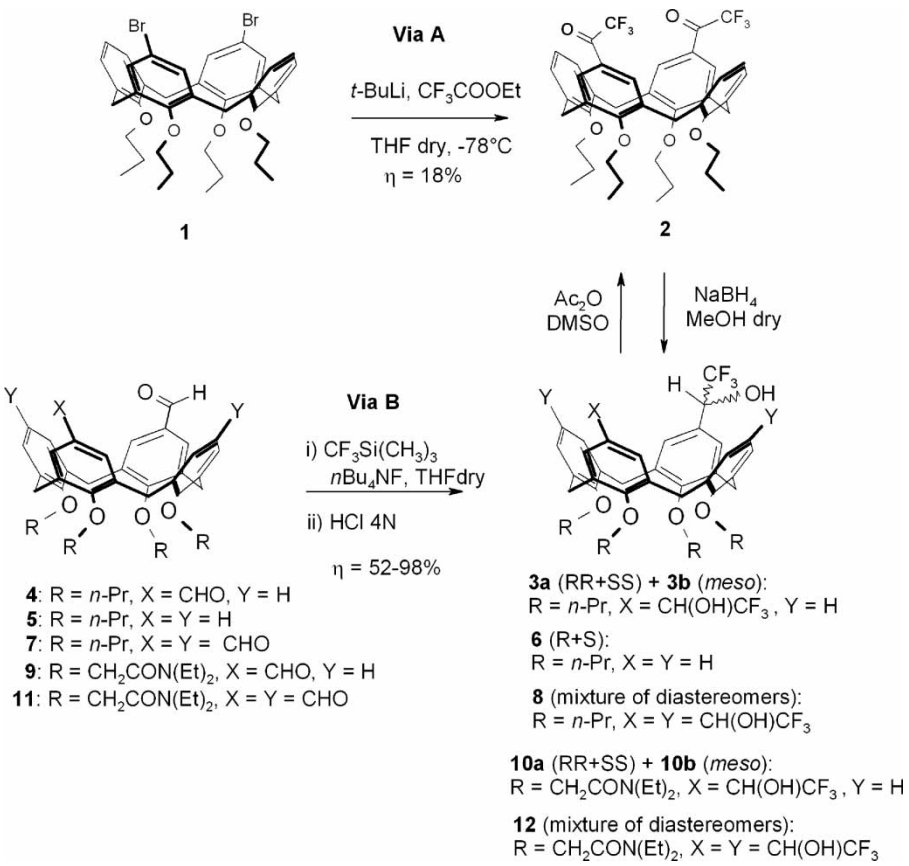


SCHEME 1 Synthesis of Triflouroethanol Tetrapropoxycalix[4]arenes.

calix[4]arene derivatives, together with their binding properties towards anions and ion pairs.

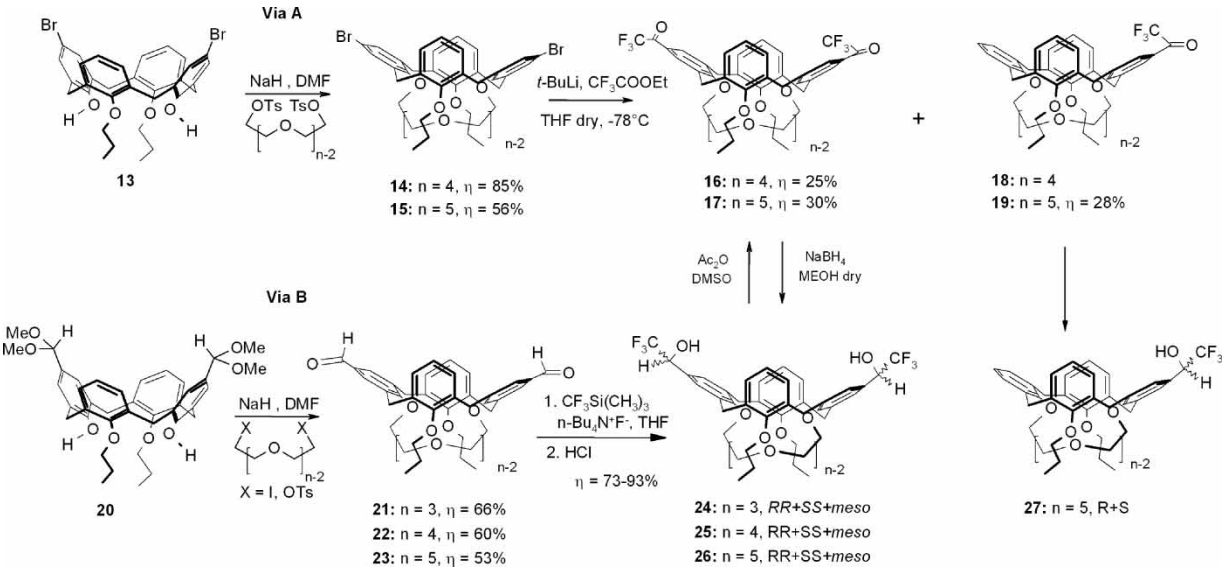
RESULTS AND DISCUSSION

Synthesis of the Ligands

We first studied the possibility of introducing two trifluoroethanol moieties at the upper rim of calix[4]arenes fixed in the *cone* conformation by the presence of four propoxy groups. Our initial strategy explored the introduction of trifluoromethylketone groups at the upper rim, followed by the reduction of the ketone to alcohol (*Via A*, Scheme 1).

Following well-established procedures on simple bromobenzenes [33,34] and starting from the easily available 1,3-dibromo-tetrapropoxycalix[4]arene **1** [16] we prepared the lithium aryl derivative [35] in dry THF at −78°C by using *t*-BuLi [36], which was subsequently reacted with ethyl trifluoroacetate. However, the bis(trifluoromethylketone) derivative **2** was isolated only in 18% yield; considerable amounts of calixarenes having one or two depleted bromine atoms were also formed. The dibromo-calix[4]arene-crown-4 and -crown-5 derivatives (**14** and **15**), which were obtained by a cyclization reaction of the dibromo-dipropoxycalix[4]arene **13** [16] with the appropriate oligoethylene glycol ditosylate, demonstrated quite similar behaviour. The reaction with *t*-BuLi and CF_3COOEt in dry THF (*Via A* in Scheme 2) yielded both the bis-ketones **16** and **17** in 25–30% yields and the monoketones **18** [37] and **19**.

All these ketone derivatives **2**, **16**, **17** and **19** were reduced to the target trifluoroethanol alcohols **3** (60%), **25** (75%), **26** (82%) and **27** (90%), respectively (Schemes 1 and 2). However, due to the low yields of ketone formation and to the difficulties encountered in their purification, we decided to explore an alternative route for the synthesis of trifluoroethanol derivatized calix[4]arenes which exploits the fluoroalkylation reaction with organosilicon reagents [38]. The reaction of trifluoromethyltrimethylsilane [39,40] (*Via B* in Scheme 1) on the diformyl-tetrapropoxycalix[4]arene **4** in dry THF in the presence of tetrabutylammonium fluoride, followed by quenching with 4N HCl, gave compound **3** in excellent yield (84%). The reaction is very efficient, clean and general for different calixarene derivatives. In fact, the trifluoromethylation of the monoformyl- (**5**), tetraformyl-tetrapropoxycalix[4]arenes (**7**) and of the diformylcalix[4]arene-crown-3 (**21**), -crown-4 (**22**) and -crown-5 (**23**) gave the trifluoroethanol derivatives **6**, **8**, **24**, **25** and **26** in 73–98% isolated yields (*Via B* in Schemes 1 and 2). *Via B* is particularly convenient in



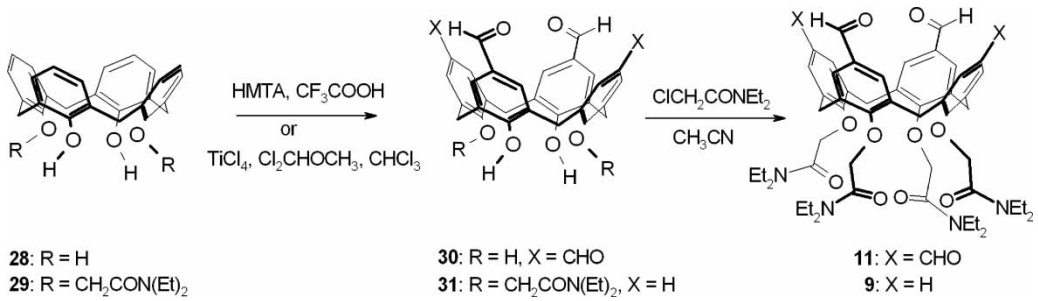
SCHEME 2 Synthesis of Trifluoroethanol Calixcrowns.

comparison to *via A* also because milder conditions are required and it is compatible with different functional groups which otherwise react with organolithium compounds. In particular, we were interested in introducing trifluoroethanol moieties at the upper rim of the tetramide of calix[4]arene, since this compound is particular efficient in the complexation of alkali metal ions [9,41].

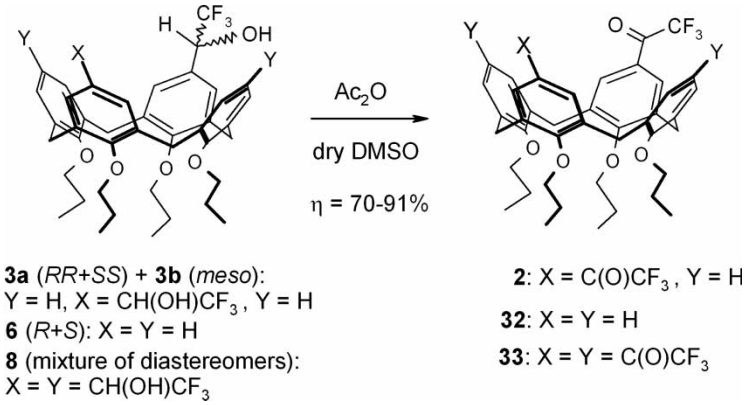
Since the direct formylation of the calix[4]arene tetramide failed to furnish either the di- (**9**) or tetra- (**11**) formyl derivatives using different formylation conditions, we carried out the alternative route depicted in Scheme 3. Tetrahydroxycalix[4]arene (**28**) was first formylated at the upper rim with hexamethylene tetramine (HMTA) in trifluoroacetic acid to afford the tetraformyl-tetrahydroxycalix[4]-arene (**30**) in 95% yield. This procedure is faster and more efficient than the two-step procedure reported by Huang *et al.* [42] and is, to our knowledge, the first example of direct formylation of a native calixarene. On the other hand, the regioselective introduction of two formyl groups in the 1,3 position at the upper rim of the calix[4]arene was obtained exploiting the so-called *indirect route* [43,44]. Calix[4]arene diamide (**29**) [45] was selectively formylated on the positions para to the phenolic hydroxy groups. The tetra- (**30**) or diformyl (**31**) derivatives were subsequently alkylated with N,N-diethyl-α-cloroacetamide to give the tetramides **11** and **9** in very good yields. Trifluoromethylation of these compounds gave the trifluoromethyl alcohols **12** and **10a,b** rather efficiently (68 and 52% yields, respectively).

Although trifluoroethanol derivatives are easily available through the trifluoromethylation reaction, the trifluoromethyl ketones are also of interest in this context since they have been shown to selectively bind oxyanions such as carbonates [46–48]. Moreover, their enantioselective reduction can give enantiomerically enriched trifluoroethanol receptors, potentially useful in chiral discrimination. These trifluoromethyl ketones can be easily obtained by oxidation of the alcohols using acetic anhydride in DMSO (Scheme 4). Trifluoromethyl ketones of tetrapropoxycalix[4]arene (**2**, **32**, **33**) and of calixcrown-4 (**16**) have been obtained in 70–91% yields from the corresponding alcohols (**3ab**, **6**, **8** and **25**).

All the synthesized trifluoroethanol derivatives show typical NMR absorptions: i) a doublet for the CF_3 group around -78 to -79 ppm ($^3J_{H-F} = 5$–6 Hz) in the ^{19}F NMR spectra ($CDCl_3$); ii) quartet for



SCHEME 3 Synthesis of Trifluoroethanol Tetramidecalix[4]arenes.



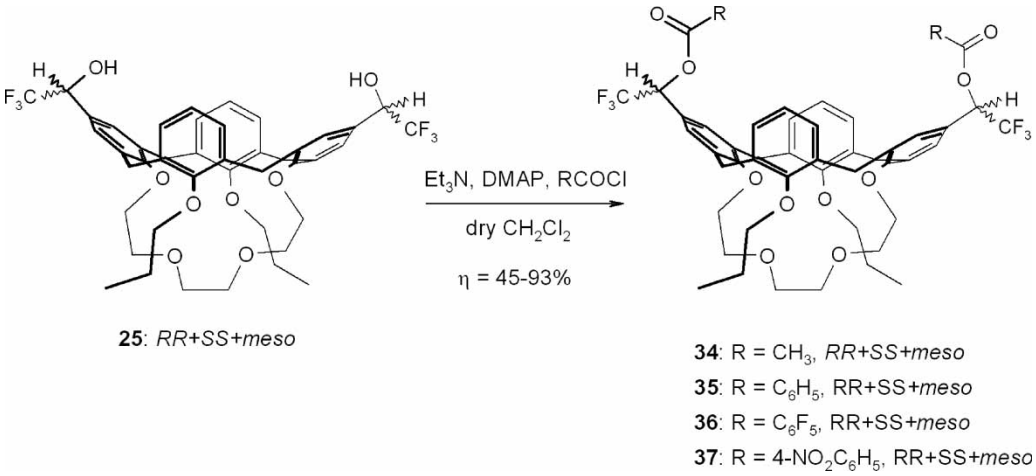
SCHEME 4 Oxidation to Trifluoromethylketones.

the $CH(OH)CF_3$ carbon at ~72 ppm ($^2J_{C-C-F}$ ~32 Hz) and a quartet for the CF_3 group at ~124 ppm ($^1J_{C-F}$ ~280 Hz) in the ^{13}C NMR spectrum; iii) a quartet between 4.4–5.0 ppm ($^3J_{H-C-C-F} = 6–7$ Hz) for the $CH(OH)CF_3$ in the ^1H NMR spectra ($CDCl_3$). The ^1H and ^{19}F NMR spectra of the tetralcohols **8** and **12** clearly show, as expected, the presence of a mixture of diastereomers which could not be separated. The dialcohols of the tetrapropoxy calix[4]arene **3ab** and of the calix-crown ether series **24**, **25** and **26** have quite different properties. The (*RR* + *SS*) (**3a**) and *meso* (**3b**) diastereomers can be easily separated by chromatography on silica gel and show clearly different signals in their ^1H and ^{19}F NMR spectra ($CDCl_3$). Their structure could be easily assigned by analysis of the protons of the unsubstituted aromatic nuclei. Thus, in the (*RR* + *SS*) mixture, where the compounds have a binary axis of symmetry, there is a singlet and two doublets of doublets, while the *meso* compound, having a symmetry plane, gives rise to two triplets and two doublets. On the other hand, dialcohols of calix-crowns **24**, **25** and **26** have ^1H NMR spectra whose symmetry indicates the presence of the *meso* compounds only. Their ^{13}C and ^{19}F NMR spectra also show only single absorptions. All the attempts to prove the presence of both the (*RR* + *SS*) and *meso* compounds by chromatography (TLC, HPLC) failed. To clarify if this effect was due to diastereoselectivity in the trifluoromethylation reaction or to an accidental superimposition of some signals, we carried out acylation reactions on **25** with different acyl chlorides (Scheme 5).

While the acetylated derivatives **34** still show a spectrum compatible with that of the *meso* compound, all the benzoyl derivatives **35**–**37** clearly show the splitting of most of the signals into two sets of absorptions (see Experimental Section) which indicates the presence of a 1:1 mixture of the (*RR* + *SS*) and *meso* compounds, thus ruling out that the trifluoromethylation reaction is diastereoselective.

CONFORMATIONAL PROPERTIES IN SOLUTION AND IN THE SOLID STATE OF TRIFLUOROETHANOL CALIX[4]ARENES

The conformational properties of the bis-trifluoroethanol receptors in solution were studied by means of ^1H NMR spectroscopy. The *mobile cone*



SCHEME 5 Acylation of Triflouroethanol Calixcrown-4(25).

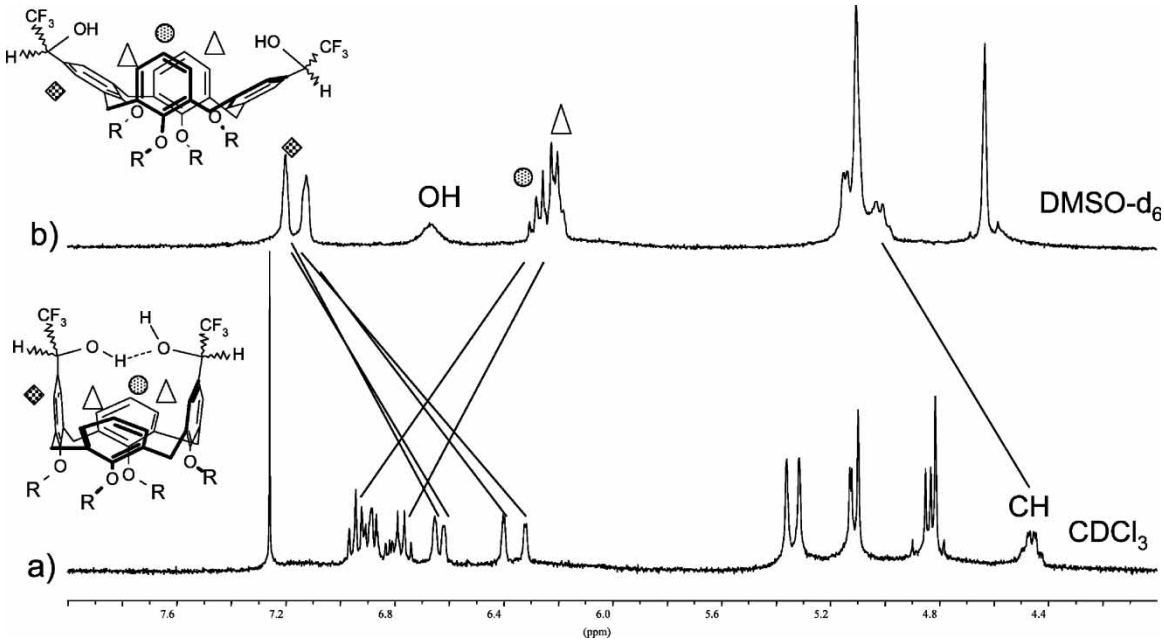


FIGURE 1 Portions of the ^{1}H NMR spectra of compound **3a** in a) $CDCl_3$ and b) DMSO-d_6.

[49] derivatives having four propoxy groups (**3a,b**) or four acetamide moieties (**10a,b**) at the lower rim, show a quite similar behaviour. For instance, the tetrapropoxy derivatives show different absorptions for the (*RR* + *SS*) (**3a**) and *meso* (**3b**) compounds, in apolar solvents like $CDCl_3$ (see Fig. 1a), which indicate that these derivatives are in a *closed flattened cone* conformation, where the substituted aromatic protons resonate at high-fields because of the shielding of the unsubstituted aromatic nuclei. This strongly suggests that the two trifluoroethanol moieties are engaged in an *intra*molecular hydrogen bond (Fig. 1).

On the other hand, in DMSO-d_6, the trifluoroethanol groups interact with the donor solvent, and the calixarene adopts an *open flattened cone* conformation where the two unsubstituted aromatic nuclei are parallel each to the others (Fig. 1b). The calix-crown series **24**, **25** and **26** having the constrain of the oligoethylene glycol chain bridging the oxygen atoms of the phenolic nuclei which bear the trifluoroethanol moiety, show an *open flattened cone conformation* both in apolar and polar solvents as evidenced by the presence of the unsubstituted aromatic protons at higher fields than the substituted aromatic ones. No *intra*molecular hydrogen bond is therefore present in these compounds in apolar solvents such as $CDCl_3$. In the case of compound **3a** we were able to determine the X-ray crystal structure of its ethanol solvate (Fig. 2). The macrocycle has twofold symmetry (only one half of molecule is symmetry-independent) and the whole molecule is generated by the action of a crystallographic C_2 axis which coincides with the molecular C_2 axis.

In this structure, the calix[4]arene is in a *flattened cone* conformation; the dihedral angles between the least-squares planes through the two symmetry-independent aromatic rings (**A** and **B**) and the reference plane **R** (the plane containing the four methylene bridging groups) calculated according to standards rules [50], are $\mathbf{R} - \mathbf{A} = 80.07(8)^\circ$ and $\mathbf{R} - \mathbf{B} = 146.10(7)^\circ$. The complete and unequivocal description of the calixarene conformation is given by the Conformational Parameters ϕ and χ reported in Table I and lead to the $C_2 + -$, $+-$ symbolic representation [51].

The most interesting feature of this structure is the organization of the calix[4]arene and ethanol molecules in the crystal lattice. The role of the ethanol molecules is pivotal in the self-assembly process: each pair of centrosymmetrically-related ethanol molecules acts as connectors between adjacent calixarene molecules exploiting multiple strong hydrogen bonds between the OH groups of the trifluoroethanol moieties on the calixarenes and of the solvent as shown in Fig. 3. The OH group of each ethanol acts both as donor and acceptor of hydrogen bonds towards the OH groups of the two nearest neighboring calixarenes (see Table II for the geometrical parameters) giving rise to four membered rings of hydrogen bonds. In this way calixarene and ethanol molecules are self-assembled in linear arrays oriented along [−1 0 1] (namely parallel to a diagonal of the **ac** plane) of the crystal lattice (see also Fig. 4).

The whole crystal lattice is thus formed of separated layers of calixarenes parallel to the **ac** plane and the macrocycles are piled-up in columns directed along [0 0 1] (namely oriented along the

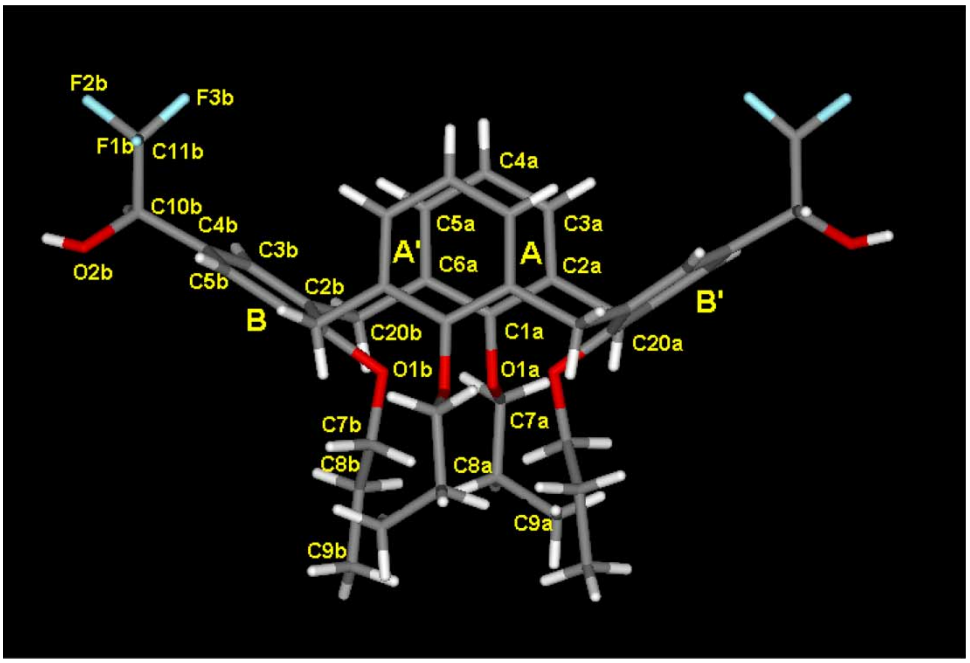


FIGURE 2 Perspective view of the molecular structure of **3a** together the atom numbering scheme in the symmetry-independent half-molecule.

TABLE I Conformational Parameters ϕ and χ (°) in the molecular structure of **3a** in the solid state.

	ϕ	χ
A–B′	55.6(4)	−110.8(3)
B′–A′	110.0(3)	−52.2(4)
A′–B	55.6(4)	−110.8(3)
B–A	110.0(3)	−52.28(4)

crystallographic **c** axis) giving rise to the nanotube-like structure illustrated in Fig. 4.

Along each column the calixarenes have all the same "orientation" (the propyl-chains of one calixarene faces on the fluorinated chains of the nearest neighboring one).

Anion Binding Properties

The complexation properties of the trifluoroethanol calix[4]arenes **3** and **25** towards spherical (Br^-), linear (CN^-), Y-shaped (CH_3COO^-, $PhCOO^-$) or tetrahedral anions ($H_2PO_4^-$, HSO_4^-) as tetra-*n*-butylammonium salts were evaluated using ^1H NMR titrations in $CDCl_3$ solution. To a solution of host (5×10^{-3} M), increasing amounts of guest (4.4×10^{-2} M) were added in order to span a host/guest ratio between 0.5 and 9. Usually, the most sensitive signals to complexation are the $CH(CF_3)$ and substituted aromatic protons (ArH_s) but the unsubstituted aromatic (ArH_u) and the $OCH_2CH_2CH_3$ protons were also used for K_{ass}

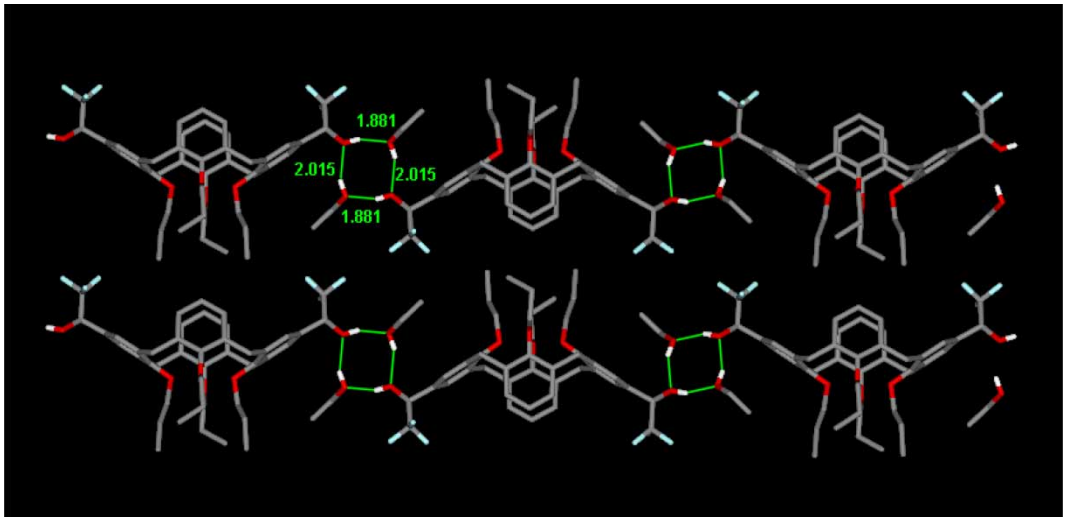


FIGURE 3 Linear arrays of calixarenes and ethanol molecules assisted by four-membered rings of hydrogen bonds. Hydrogen bonds are depicted by dotted lines. Only OH hydrogen atoms are shown.

TABLE II Geometrical parameters (Å and °) for hydrogen bonds

	Donor-H (Å)	Donor···Acceptor (Å)	H···Acceptor (Å)	Donor-H···Acceptor (°)
O_{guest}t-H···O2B$_{Host}$	0.820(4)	2.778(5)	2.015(3)	154(3)
O2B$_{Host}$···Oguest	0.820(4)	2.661(6)	1.881(5)	158.6(3)

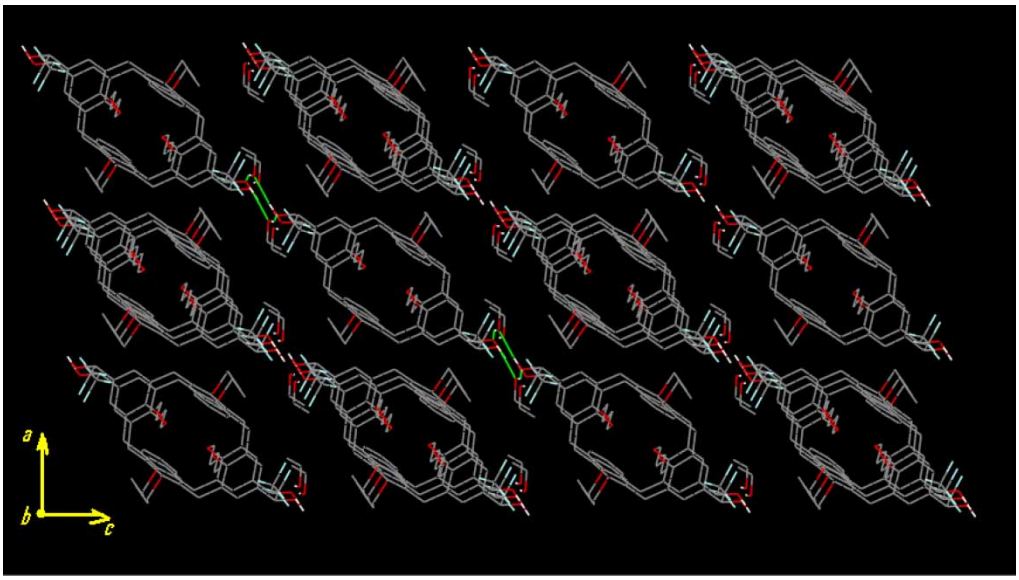


FIGURE 4 The nanotubes-like structure of **3a**. The linear arrays of hydrogen-bonded calixarenes and ethanol molecules are oriented along [−1 0 1]. Hydrogen bonds (dotted lines) have been evidenced only for one array.

calculation. In some cases the CH(CF_3) protons were superimposed by other signals and could not be used for the determination. The experimental data obtained, were fitted to a 1:1 complexation model and K_{ass} were determined using a non-linear regression analysis [52] (Table III and Fig. 5). Both difunctionalized receptors **3** and **25** show a marked preference for carboxylate and dihydrogenphosphate anions whereas spherical (Br^-), linear (CN^-) or more hydrophilic and charged dispersed (HSO_4^-) anions are not complexed to any significant extent.

In general the conformationally more mobile tetrapropoxy derivatives **3** are more efficient than the crown derivative **25**. Interestingly the (*RR* + *SS*) racemic mixture (**3a**) is more efficient in binding than the *meso* compound (**3b**) and this is especially true for sterically more demanding anions such as benzoate and phenylalaninate. If we compare the binding properties of receptor **3a** toward acetate anion with other difunctionalized calix[4]arene receptors we find that trifluoroethanol is less efficient than other anion binding groups such as urea [15,16], sulfonamide [53] or activated carboxyamides [54–56]. However, a comparison with receptors which contain simple alcoholic functions, which show no binding ability towards acetate anion [31], points out the importance of the electrowithdrawing groups CF_3 in enhancing the H bonding ability of the OH groups. The modest binding constants and the "normal" acetate > benzoate selectivity observed for ligand **3a** suggests that the apolar cavity of the calix[4]arene does not play an important role in anion binding in contrast to that observed with other receptors [16,55,57,58].

We have also investigated the complexation properties of **3b** towards the acetate anion by using molecular modeling methods. The conformational space of **3b** was initially explored to obtain the lowest energy conformers to be used in

TABLE III Association constants (K_{ass}, M^{-1}) of hosts **3a**, **3b** and **25** towards anions of tetrabutylammonium salts at T = 300 K

Ligand	CH_3COO^-	$PhCOO^-$	N-LauPheCOO$^-$ (L)	$H_2PO_4^-$	$HSO_4^-/Br^-/CN^-$
3a (*RR* + *SS*)	435	255	165	170	<5[a]
3b *meso*	200	45	40	70	<5[a]
25	90			50	
25·Na^+	420				

[a] = no significant shifts observed.

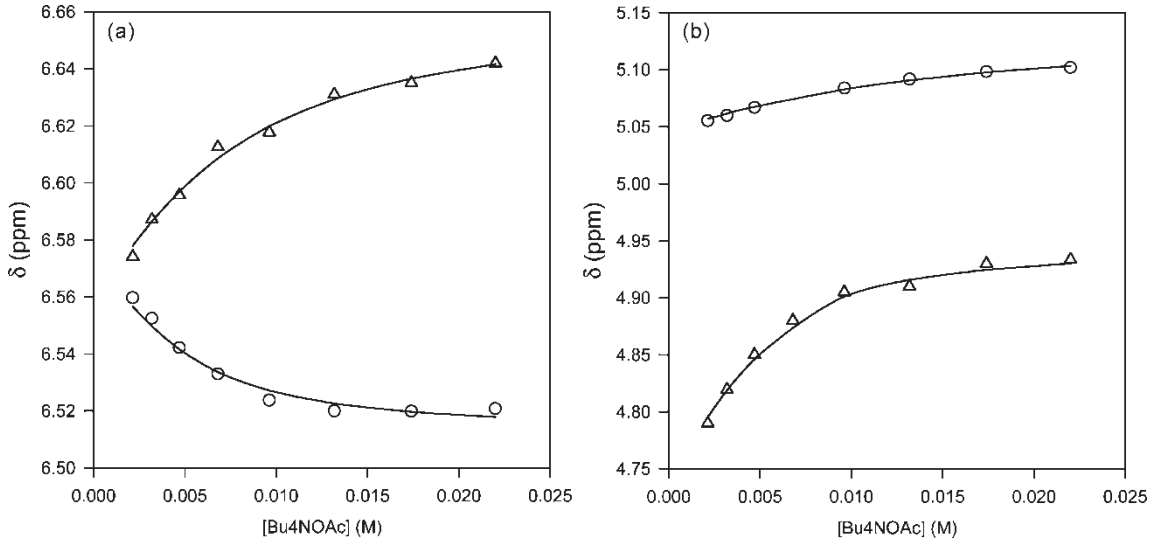


FIGURE 5 ^{1}H NMR titration plots for the complexation of tetrabutylammonium acetate (Bu_4NOAc) in $CDCl_3$. a) Selected aromatic protons of compound **3a** (△) and **3b** (○); b) C*H*(CF_3)OH signals of compound **25** (△) and **25**·Na^+(○). The solid lines are calculated according to the 1:1 complexation; points are measured values.

modeling of complexes. A conformer distribution search carried out using MMFF force field implemented in Spartan 04, gave a few stable conformers whose energies were further optimized at the HF/6-31G** level. The lowest energy conformers possess an *intra*molecular hydrogen bond OH···O between the alcohol functions at the upper rim (e.g. Fig. 6 **I**) and differ just slightly for the $O_2C_{10}C_4C_5$ dihedral angles, confirming the data obtained in $CDCl_3$ solution by NMR (*vide supra*). The *open flattened cone* conformer (Fig. 6 **II**), found in DMSO-d_6 solution, is slightly less stable (its total energy is +9 kcal/mol higher than that of **I**) and its stability is close to that of the regular cone conformer **III** ($\Delta E_{III-I} = +10.5$ kcal/mol) which has the two CF_3 groups facing each other. The less stable conformer among those studied, is however the isomer **IV** (Fig. 6) were a OH···F hydrogen bond is present and whose total energy is 70 kcal/mol higher than that of **I** ($\Delta E_{IV-I} = +70$ kcal/mol).

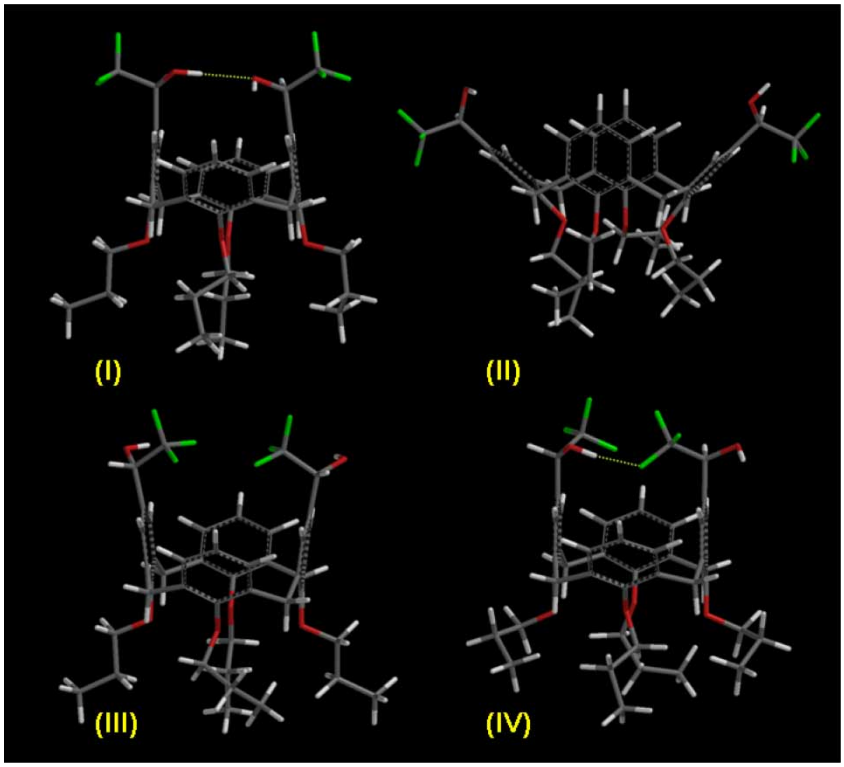


FIGURE 6 Optimized geometry of some of the most stable conformers of compound **3b**. Hydrogen bonds have been evidenced by dotted lines.

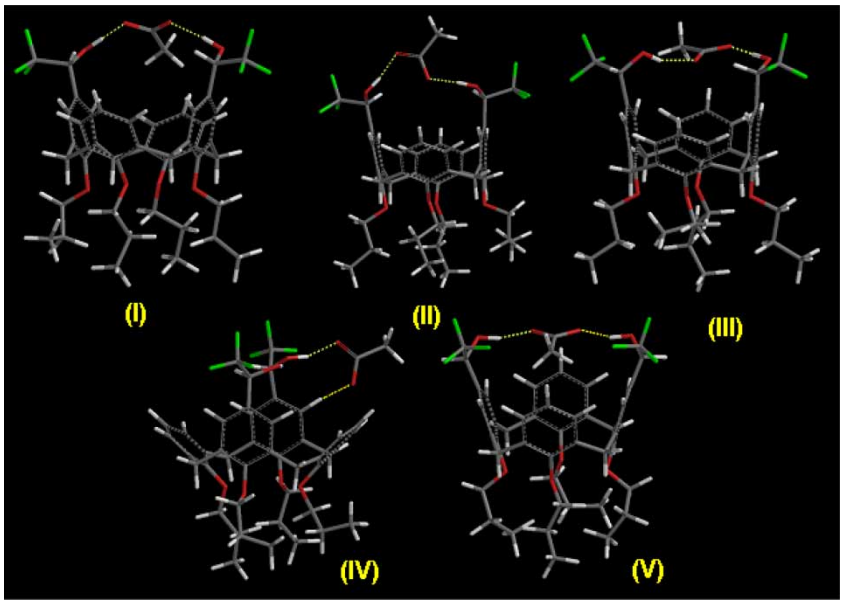


FIGURE 7 Optimized geometry of acetate complexes of **3b**. Hydrogen bonds have been evidenced by dotted lines.

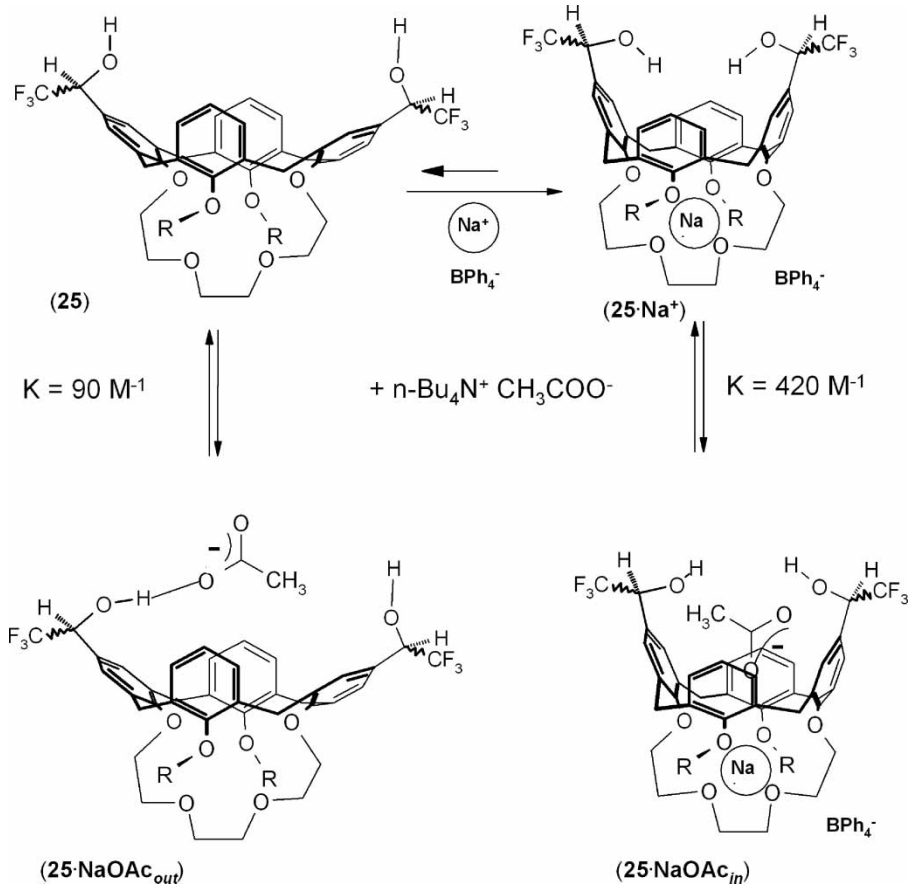
The structures of acetate complexes of **3b** are shown in Fig. 7. The binding energies of the acetate anion to the host in the five complexes are collected in Table IV. The most stable complex (**I**) and the least stable one (**V**) have C_2 symmetry. In both cases the acetate is linked to the OH groups of the host through two symmetric $O{-}H_{host}\cdots O_{Ac}$ hydrogen bonds, but in (**I**) the methyl group of the acetate points outside and in (**V**) inside the intramolecular space of the calixarene. In complexes (**II**) and (**III**) the two $O{-}H_{host}\cdots O_{Ac}$ hydrogen bonds are asymmetric and the CH_3 of the acetate is outside the host cavity.

In one case (**IV**) the complexation of the acetate involves only one OH group of the host in the $O{-}H_{host}\cdots O_{Ac}$ hydrogen bond. In such a case, however, another (weaker) hydrogen bond $O_{Ac}\cdots H{-}C_{Ph}$ occurs between an acetate oxygen and one aromatic hydrogen of the calixarene basket.

From these data it is reasonable to assume that in hosts **3** the bidentate carboxylates are simultaneously coordinated by two hydroxy groups, thus spanning the two distal trifluoroethanol moieties at the upper rim of the calixarene. This seems to be confirmed by the lower binding ability of receptor **25** for acetate anion. This calixcrown-4 derivative, in fact, is compelled to be in an *open flattened cone* conformation by the ether bridge at the lower rim and shows a lower binding constant ($90\,M^{-1}$) in comparison to **3** in the *closed flattened cone*. The acetate anion cannot span the distance of these two trifluoroethanol groups and is probably bound by only one of them (see Scheme 6). Upon addition of increasing amounts of sodium tetraphenylborate ($NaBPh_4$) to a $CDCl_3$ solution of **25** a new set of signals appears together with those of the free ligand indicating that the sodium complex (**25·Na**) is formed and is in a slow exchange regime on the ^1H NMR time-scale. When 1 equivalent of $NaBPh_4$ is added, all the signals of the free ligand disappear indicating that all ligand **25** is complexed. The signals of the sodium complex **25·Na** indicate that the calixarene is rearranging its conformation from an *open flattened cone* conformation to a more regular one. This is evident from the upfield shifts of the unsubstituted aromatic (Ar_u) protons ($\Delta\delta = +0.9/+1.0$ ppm) which are outside the shielding cone of the substituted aromatic nuclei (Ar_s) and from the downfield shifts of the $CH(CF_3)$ protons which, on the other hand, slightly enter the shielding cone of the Ar_u nuclei. The latter observation indicates that, contrary to what is observed in urea-based calix[4]arene ditopic receptors [20], coordination of the cation at the lower rim does not induce an increase in the acidity of the hydrogen bond donating groups of anion coordinating ligands. Addition of tetrabutylammonium acetate to a solution of $\mathbf{25{\cdot}Na^+}$ shows that at G/H ratios higher that 4, the acetate anion tends to decomplex the sodium cation from the ligand since signals of free **25** start to appear. However, experimental data (Fig. 5b) fit correctly with a 1:1 stoichiometry ($\mathbf{25{\cdot}Na^+/{}^-OAc}$) and an association constant K_{ass} of $420\,M^{-1}$ was determined which is nearly 5 times the association of free ligand **25** with the same acetate anion. Molecular modeling shows that, although the two alcohol functions are getting

TABLE IV Calculated binding energies (kcal/mol) in the acetate complexes of **3b**

(I)	(II)	(III)	(IV)	(V)
−35.51	−35.09	−32.18	−25.30	−23.52



SCHEME 6 Complexation of Sodium Acetate (NaOAc) By Calixcrown-4(25).

closer in the **25·Na**$^+$ complex, still the acetate anion does not span the distance and can hydrogen bond to only one of the two hydroxy groups (*see* Scheme 6, **25·NaOAc$_{out}$**). However, molecular modeling shows that the acetate ion can enter the calixarene cavity (Scheme 6, **25·NaOAc$_{in}$**) positioning one of the carboxylate oxygen atoms at 2.45 Å from the sodium ion (ligand separated ion-pair).

The tetramide-tetralcohol **12** also behaves as a ditopic receptor as shown by its ability to extract solid sodium salts (3 equiv. of NaCl, NaBr, NaI or NaOAc) into a $CDCl_3$ solution of the ligand. After filtration of the undissolved salts, ^{1}H NMR spectra were recorded and compared with that of the complex obtained upon addition of 1 equiv. of $NaBPh_4$ to a solution of **12**. In all cases, extraction percentages $>95\%$ were observed since no signals of the free ligand could be detected. The shifts observed for the sodium complexes of **12** are very similar to those of monotopic sodium complexes [59], that is upfield shifts for the equatorial $ArCH_2Ar$ protons (H_{eq}) and downfield shifts for the aromatic and OCH_2CO protons. This clearly indicates that the sodium ion is firmly included in the hydrophilic pseudo-cavity created at the lower rim of the macrocycle by the four acetamide chelating groups. Unfortunately, the hydroxy groups of the trifluoroethanol moieties are exchanging rather fast on the NMR time-scale and their position in ^{1}H NMR spectra of the free ligand **12** or of its complexes could not always be established. However, the signals of the C*H*(CF_3)OH protons, which move upfield only slightly in the presence of the non-coordinating anion of the $NaBPh_4$ complex ($\Delta\delta = -0.1/-0.2$ ppm), are strongly deshielded ($\Delta\delta = +0.3/+0.5$ ppm) in the halide and acetate complexes, indicating that the alcoholic functions are coordinating these anions [60].

CONCLUSIONS

In summary, we have developed a general synthetic procedure for the introduction of one, two or four 2,2,2-trifluoroethanol groups at the upper rim of calix[4]arenes fixed in the cone conformation. The tetrapropoxy bis-trifluoroethanol calix[4]arene anion receptors **3a** (RR + SS) and **3b** (RS) show selectivity for carboxylates and $H_2PO_4^-$ over HSO_4^-, Br^- and CN^- anions, the former being more efficient than the latter. Combined ^{1}H NMR and Molecular Modeling studies indicate that both the trifluoroethanol moieties bind acetate anion *via* hydrogen bonds. Calixarenes bearing a crown ether (**24**–**26**) or four

acetamide moieties (**10** and **12**) at the lower rim and trifluoroethanol groups at the upper rim behave as ditopic receptors which simultaneously bind the cation and the anion counterparts of ion pairs. The calixcrown-4 derivative **25** shows a 5-fold increase in the binding of acetate anion when a sodium ion is complexed in the polyether bridge.

EXPERIMENTAL SECTION

Melting points were determined with an Electrothermal apparatus in sealed capillaries under nitrogen. ^{1}H and ^{13}C NMR spectra were recorded with Bruker spectrometers AC300 (^{1}H: 300 MHz, ^{13}C: 75 MHz) or AMX400 (^{1}H: 400 MHz) with TMS as internal standard, while ^{19}F NMR spectra (^{19}F: 188.3 MHz) were obtained with a Bruker CXP 200 spectrometer using hexafluorobenzene in $CDCl_3$ as external standard ($\delta = -163$ ppm). Mass spectra were obtained in the ESI mode with Micromass 4LCZ or in the CI (CH_4) mode with Finnigan Mat SSQ710 spectrometers. TLC was performed on precoated silica gel Merck 60 F_{254}. All solvents were purified by standard procedures; dry solvents were obtained by literature methods and stored over molecular sieves. All reactions were carried out under a nitrogen atmosphere unless otherwise stated. 5,17-Dibromo-25,26,27,28-tetrapropoxycalix[4]arene (**1**) [16], 11,23-diformyl-25,26,27,28-tetrapropoxycalix[4]arene (**4**) [61], 5,11,17,23-tetraformyl-25,26,27,28-tetrapropoxycalix[4]arene (**7**) [62], 5,17-dibromo-25,27-dipropoxycalix[4]arene (**13**) [16], 11,23-bis(1,1-dimethoxymethyl)-26,28-di-*n*-propoxycalix[4]arene (**20**) [61] and 5,27-bis(N,N-diethylaminocarbonylmethoxy)calix[4]arene (**29**) [45] were prepared according to procedures reported in the literature.

5,17-Bis(trifluoroacetyl)-25,26,27,28-tetra-*n*-propoxycalix[4]arene (2)

Via A: From the Bromoaryl Derivative 1

A sample of 1,3-dibromo-tetrapropoxycalix[4]arene **1** (0.8 g, 1.1 mmol) dissolved in dry THF (10 ml) was carefully degassed by three cycles of freeze-pump-thaw, then argon was introduced in the flask and cooled to −78°C. Then 3.15 ml (5.4 mmol) of a 1.7 M solution of *t*-BuLi was added under argon atmosphere. After 1 h, this solution was poured into a flask containing a solution of ethyl trifluoroacetate (0.64 ml, 5.4 mmol) in 15 ml of dry THF previously degassed and cooled to −78°C. The cooling bath was removed and when the temperature reached 5°C, the reaction mixture was quenched by addition of 50 ml of an aqueous 1 N HCl solution (CAREFUL!). This mixture was extracted with ethyl acetate (50 ml) and the separated organic layer washed with water (2 × 50 ml) and subsequently dried over anhydrous $MgSO_4$. The product was purified by column chromatography (SiO_2: eluent hexane-ethyl acetate = 19:1). Yield: 18%.

Via B: Oxidation of the Alcohol 3

To a solution of compounds **3a,b** (0.160 g, 0.2 mmol) in dry DMSO (1.5 ml) was slowly added acetic anhydride (0.38 ml, 4 mmol). The reaction mixture was stirred at rt for 18 h and then poured into 30 ml of an aqueous NaOH solution (pH ≈ 11) cooled with an ice-bath. This solution was extracted with dichloromethane (30 ml), the organic layer washed with water and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure to give a white solid. Yield: 91%.

NMR (300 MHz; $CDCl_3$): δ 7.49 (s, 4H, ArH); 6.57–6.50 (m, 6H, ArH); 4.49 (d, 4H,ArCH_{ax}Ar, $J = 13.5$ Hz); 4.02 (t, 4H, OCH_2CH$_2$CH$_3$, $J = 7.4$ Hz); 3.83 (t, 4H, OCH_2CH$_2$CH$_3$, $J = 7.4$ Hz); 3.26 (d, 4H, ArCH_{eq}Ar, $J = 13.5$ Hz); 1.97–1.87 (m, 8H, OCH$_2$-CH_2CH$_3$); 1.03 (t, 6H, OCH$_2$CH$_2$CH_3, $J = 7.4$ Hz); 1.00 (t, 6H, OCH$_2$CH$_2$CH_3, $J = 7.4$ Hz). ^{13}C NMR (75 MHz; $CDCl_3$): δ 179.4 (q, $COCF_3$, $J_{C-C-F} =$ 34 Hz); 163.5, 155.7 (s, Ar ipso); 136.4, 133.4 (s, Ar ortho); 130.7, 128.3 (d, Ar meta); 123.8 (s, Ar para); 122.7 (d, Ar para); 116.6 (q, $COCF_3$, $J_{C-F} = 290$ Hz); 77.0, 76.8 (t, OCH$_2$CH$_2$CH$_3$); 30.8 (t, ArCH$_2$Ar); 23.2, 23.1 (t, OCH$_2$CH$_2$CH$_3$); 10.2, 10.0 (q, OCH$_2$-CH$_2$CH$_3$). IR (KBr), ν (cm^{-1}): 1710 (C=O). MS (CI) m/z: 785 $(M + H)^+$100%. $C_{44}H_{46}F_6O_6$ (784.84).

5,17-Bis(2,2,2-trifluoroethanol)-25,26,27,28-tetra-*n*-propoxycalix[4]arene (3a) (3b)

Via A: Reduction of the Ketone

To a sample of 1,3-bis(trifluoroacetyl)-tetrapropoxycalix[4]arene **2** (0.11 g, 0.14 mmol) dissolved in dry methanol (20 ml) was added $NaBH_4$ (0.10 g, 2.7 mmol). The reaction mixture was stirred at rt and under nitrogen for 10 hs and then quenched with water (30 ml). After removal of methanol under reduced pressure, the water phase was extracted in ethyl acetate (30 ml). The organic layer was dried over anhydrous $MgSO_4$, the solvent removed and the residue submitted to column chromatography (SiO_2: eluent hexane—ethyl acetate = 9:1). The racemic mixture **3a** (*RR* + *SS*) elutes slower than the meso compound 3b. Yield: 30% (each).

Via B: Trifluoromethylation

To a solution of 1,3-diformyl-tetrapropoxycalix[4] arene **4** (0.1 g, 0.15 mmol), dissolved in dry THF (15 ml), was added trifluoromethyl trimethylsilane

(0.10 ml, 1.2 mmol). After cooling to 0°C, tetra-n-butylammonium fluoride (0.05 g, 0.15 mmol) was addet to the solution (molar ratio $CHO:CF_3(CH_3)_3$-$Si:Bu_4NF = 1:4:0.5$). The yellow solution turned to brown in few minutes and after 4 hs an aqueous 4 N HCl solution (60 ml) was added and the mixture stirred for an additional 6 h period. This solution was extracted with ethyl ether and the separated organic layer washed twice with water (2 × 70 ml). The organic phase was evaporated under reduced pressure and the racemic mixture and meso compound separated by column chromatography (see above). Yield: 42% (each).

Compound 3a (*RR* + *SS*). ^{1}H NMR ($CDCl_3$): δ 6.97–6.91 (m, 4H, ArH), 6.81 (dd, 2H, ArH, $J = 7.4$ Hz); 6.58 (d, 2H, ArH, $J = 2.0$ Hz); 6.31 (d, 2H, ArH, $J = 2.0$ Hz); 4.46 (d, 2H, ArCH_{ax}Ar, $J = 13.3$ Hz); 4.45 (d, 2H, ArCH_{ax}Ar, $J = 13.3$ Hz); 4.42 (q, 2H, ArC*H*(OH)CF_3, $J = 6.6$ Hz); 3.99 (t, 4H, OC$H_2$$CH_2CH_3$, $J = 8.0$ Hz); 3.74 (t, 4H, OC$H_2$$CH_2$ CH_3, $J = 7.1$ Hz); 3.18 (d, 2H, ArCH_{eq}Ar, $J = 13.3$ Hz); 3.16 (d, 2H, ArCH_{eq}Ar, $J = 13.3$ Hz); 2.01–1.86 (m, 8H, $OCH_2CH_2CH_3$); 1.06 (t, 6H, $OCH_2CH_2CH_3$, $J = 7.5$ Hz); 0.93 (t, 6H, OCH_2CH_2 CH_3, $J = 7.4$ Hz); ^{13}C NMR ($CDCl_3$): δ 156.8, 156.7 (s, Ar ipso); 135.6, 134.4, 133.7 (s, ArH ortho); 128.7, 128.4, 128.0 (d, Ar meta); 125.1 (d, ArH para); 123.9 (q, CF_3, $J = 275$ Hz); 122.1 (s, Ar para); 76.9, 76.3 (t, OCH_2 CH_2CH_3); 72.2 (q, ArCH(OH)CF_3, $J = 30$ Hz); 30.7, 30.6 (t, $ArCH_2Ar$); 23.1, 22.7 (t, $OCH_2CH_2CH_3$); 10.3, 9.7 (q, $OCH_2CH_2CH_3$). MS (CI) *m/z*: 789 $(M)^+$90%; 771 $(M-H_2O)^+$100%; 751 $(M-2H_2O)^+$80%. $C_{44}H_{50}F_6O_6$ (788.87).

Compound 3b (*meso*). ^{1}H NMR ($CDCl_3$): δ 7.01 (d, 2H, ArH, $J = 7.2$ Hz), 6.98 (d, 2H, ArH, $J = 7.2$ Hz); 6.85 (t, 1H, ArH, $J = 7.2$ Hz); 6.84 (t, 1H, ArH, $J = 7.2$ Hz); 6.55 (d, 2H, ArH, $J = 2.0$ Hz); 6.22 (d, 2H, ArH, $J = 2.0$ Hz); 4.46 (d, 4H, ArCH_{ax}Ar, $J = 13.3$ Hz); 4.43 (q, 2H, ArC*H*(OH)CF_3, $J = 6.6$ Hz); 4.00 (t, 4H, OCH_2 CH_2CH_3, $J = 8.7$ Hz); 3.73 (t, 4H, OC$H_2CH_2CH_3$, $J = 7.0$ Hz); 3.19 (d, 2H, ArCH_{eq}Ar, $J = 13.3$ Hz); 3.15 (d, 2H, ArCH_{eq}Ar, $J = 13.3$ Hz); 2.01–1.84 (m, 8H, $OCH_2CH_2CH_3$); 1.07 (t, 6H, OCH_2CH_2 CH_3, $J = 7.3$ Hz); 0.92 (t, 6H, $OCH_2CH_2CH_3$, $J = 7.3$ Hz); ^{13}C NMR ($CDCl_3$): δ 157.2, 157.0, 156.7 (s, Ar ipso); 135.9, 134.2, 133.6 (s, ArH ortho); 128.9, 128.7, 127.6 (d, Ar meta); 125.1 (d, ArH para); 123.9 (q, CF_3, $J = 285$ Hz); 122.2, 122.1 (s, Ar para); 77.1, 76.4 (t, $OCH_2CH_2CH_3$); 72.2 (q, ArCH(OH)CF_3, $J = 33$ Hz); 30.9,30.7 (t, $ArCH_2Ar$); 23.3, 22.8 (t, $OCH_2CH_2CH_3$); 10.5, 9.8 (q, $OCH_2CH_2CH_3$). MS (CI) *m/z*: 789 $(M)^+$100%; 771 $(M-H_2O)^+$95%; 751 $(M-2H_2O)^+$65%. $C_{44}H_{50}F_6O_6$ (788.87).

Compounds 3a,b. ^{19}F NMR (188.3 MHz, $CDCl_3$): δ −78.81 (d, $J = 6.9$ Hz); −79.38 (d, $J = 6.9$ Hz). ^{19}F NMR (188.3 MHz, DMSO-d_6): δ −72.91 (d, $J = 6.4$ Hz).

5-Formyl-25,26,27,28-tetra-*n*-propoxycalix[4]arene (5)

A sample of 25,26,27,28-tetra-*n*-propoxycalix[4]arene (0.5 g, 8.4 mmol) was dissolved dry $CHCl_3$ (30 ml) and the solution cooled to −10°C. Then were added Cl_2CHOCH_3 (0.88 ml, 9.1 mmol) and $SnCl_4$ (1.15 ml, 9.8 mmol) and the reaction mixture was stirred at −10°C. After 0.5 h it was quenched with a 0.1 N HCl aqueous solution and transferred in a separatory funnel. The organic layer was separated and washed twice with water (2 × 30 ml). Pure compound **5** was obtained by column chromatography (SiO_2: eluent hexane—ethyl acetate = 85:15). Yield: 67%. Mp: 178–179°C. ^{1}H NMR (100 MHz; $CDCl_3$): δ 9.56 (s, 1 H, CHO); 6.99 (s, 6H, ArH); 6.74 (s, 2H, ArH); 6.42 (s, 3H, ArH); 4.49 (d, 2H, ArCH_{ax}Ar, $J = 13.3$ Hz); 4.45 (d, 2H, ArCH_{ax}Ar, $J = 13.2$ Hz); 3.98–3.23 (m, 8H, OC$H_2CH_2CH_3$); 3.23 (d, 2H, ArCH_{eq}Ar, $J = 13.3$ Hz); 3.16 (d, 2H, ArCH_{eq}Ar, $J = 13.4$ Hz); 2.23–1.74 (m, 8H, $OCH_2CH_2CH_3$); 1.12–0.90 (m, 12H, OCH_2 CH_2CH_3). $C_{41}H_{48}O_5$ (734.82). The other spectroscopic properties are like those reported in the literature [63].

5-(2,2,2-Trifluoroethanol)-25,26,27,28-tetra-*n*-propoxycalix[4]arene (6)

Via A

From ketone **32** using the same reduction conditions used for the preparation of compound **3**. Yield: 97%.

Via B

From aldehyde **5** using the same trifluoromethylation conditions used for the preparation of compound **3**.

Yield: 98%. ^{1}H NMR (300 MHz; $CDCl_3$): δ 6.88–6.83 (m, 4H, ArH); 6.75 (t, 2H, ArH, $J = 7.5$ Hz); 6.59 (d, 1H, ArH, $J = 1.9$ Hz); 6.51 (s, 3H, ArH); 6.40 (d, 1H, ArH, $J = 1.9$ Hz); 4.51 (d, 2H, ArCH_{ax}Ar, $J = 13.5$ Hz); 4.50 (m, 1H, ArC*H*(OH)CF_3); 4.49 (d, 2H, ArCH_{ax}Ar, $J = 13.4$ Hz); 4.01–3.92 (m, 4H, OC$H_2CH_2CH_3$); 3.85 (t, 2H, OC$H_2CH_2CH_3$, $J = 7.1$ Hz); 3.80 (t, 2H, OC$H_2CH_2CH_3$, $J = 7.1$ Hz); 3.21 (d, 2H, ArCH_{eq}Ar, $J = 13.5$ Hz); 3.19 (d, 2H, ArCH_{eq}Ar, $J = 13.4$ Hz); 2.02–1.88 (m, 8H, OCH_2 CH_2CH_3); 1.13–1.04 (m, 6H, $OCH_2CH_2CH_3$); 0.99 (t, 6H, $OCH_2CH_2CH_3$, $J = 7.4$ Hz). MS (CI) *m/z*: 690 $(M)^+$100%; 672 $(M-H_2O)^+$38%. $C_{42}H_{49}F_3O_5$ (690.84).

5,11,17,23-Tetrakis(2,2,2-trifluoroethanol)-25,26,27,28-tetra-*n*-propoxycalix[4]arene (8)

From the tetraldehyde **7** using the same trifluoromethylation conditions used for the preparation of compound **3**. Yield: 95%. Mp: 141–143°C. ^{1}H NMR (300 MHz; $CDCl_3$): δ 7.08, 6.97, 6.95, 6.91, 6.88, 6.84, 6.82, 6.76, 6.72, 6.71, 6.67, 6.61, 6.47 (s, 8H, ArH);

4.81–4.74 (m, ArC*H*(OH)CF_3); 4.64 (q, ArC*H*(OH)CF_3, $J = 6.3$ Hz); 4.56–4.48 (m, ArC*H*(OH)CF_3); 4.47 (d, 4H, ArCH_{ax}Ar, $J = 13.4$ Hz); 3.96–3.80 (m, 8H, OCH_2CH_2CH_3); 3.21 (d, 2H, ArCH_{eq}Ar, $J = 13.4$ Hz); 3.19 (d, 2H, ArCH_{eq}Ar, $J = 13.4$ Hz); 2.02–1.91 (m, 8H, OCH_2CH_2CH_3); 1.07–0.96 (m, 12H, OCH_2 CH_2CH_3); ^{19}F NMR (188.3 MHz, $CDCl_3$): δ −78.59 (d, $J = 6.7$ Hz); −78.90 (d, $J = 6.9$ Hz); −78.98 (d, $J = 6.4$ Hz); −79.02 (d, $J = 7.3$ Hz); −79.36 (d, $J = 6.4$ Hz); −79.37 (d, $J = 6.4$ Hz); −79.44 (d, $J = 6.4$ Hz); −79.66 (d, $J = 6.4$ Hz); ^{19}F NMR (188.3 MHz, DMSO-d_6): δ −72.90– − 73.15 (m). M/S (CI) m/z: 987 $(M)^+$100%; 951 $(M-2H_2O)^+$70%. $C_{48}H_{55}F_{12}O_8$ (987.94).

5,17-Diformyl-25,26,27,28-tetrakis[(N,N-diethylaminocarbonyl)methoxy]calix[4]arene (9)

A suspension of diformylated calixarene **31** (0.81 g, 1.15 mmol), Na_2CO_3 (3.41 g, 32.2 mmol), NaI (1.67 g, 11.1 mmol) and α-chloro-N,N-diethylacetamide (1.53 ml, 11.1 mmol) in dry acetonitrile (100 ml) was stirred at 90°C for 18 hs. The solvent was removed under reduced pressure and 1 N HCl solution (100 ml) and dichloromethane (100 ml) were added. The organic layer was separated, washed twice with water (2 × 150 ml) and dichloromethane removed under reduced pressure. The residue was submitted to column chromatography (SiO_2: eluent ethyl acetate 100%—ethyl acetate/methanol/triethylamine 10:1:1). The product obtained, being a mixture of free ligand and cation complex, was dissolved in dichloromethane (50 ml) and washed with 1 N HCl (75 ml) and water (3 × 70 ml). Yield: 80%. ^{1}H NMR (300 MHz; $CDCl_3$): δ 9.63 (s, 2H, ArCHO); 7.23 (s, 4H, ArH); 6.49 (s, 6H, ArH); 5.26 (d, 4H, ArCH_{ax}Ar, $J = 13.5$ Hz); 5.10 (s, 4H, OCH_2CON); 4.78 (s, 4H, OCH_2CON); 3.36–3.19 (m, 20H, ArCH_{eq}Ar, NCH_2CH_3); 1.13–1.02 (m, 24H, NCH_2CH_3); ^{13}C NMR (75 MHz; $CDCl_3$): δ 191.7 (d, Ar*C*HO); 168.2 (s, *C*ON), 162.5, 156.1 (s, Ar ipso); 136.5, 133.6 (s, Ar para and ortho); 130.5, 128.7 (d, Ar meta); 122.9 (d, Ar para); 71.7, 71.6 (t, O*C*H_2CO); 42.1, 40.0 (t, O*C*H_2 CON); 31.8 (t, ArCH_2Ar); 14.3, 13.0 (q, NCH_2*C*H_3). IR (liquid film), ν (cm^{-1}): 1698 (ArHC=O), 1660 (NC=O). MS (CI) m/z: 933.2 $(M + H)^+$100%. $C_{54}H_{68}N_4O_{10}$ (933.16).

5,17-Bis(2,2,2-trifluorethanol)-25,26,27,28-tetrakis[(N,N-diethylaminocarbonyl)methoxy]calix[4]arene (10a,b)

Compound **10** was synthesized from the dialdehyde **9** according to the trifluoromethylation conditions used for the preparation of compound **3**. It was obtained pure after crystallization from ethyl ether—hexane. Yield: 52%. Mp: 252–253°C. ^{1}H NMR (300 MHz; $CDCl_3$): δ 6.95 (d, 2H, ArH (SS,RR), $J = 7.1$ Hz), 6.93 (d, 2H, ArH (SS,RR), $J = 6.9$ Hz); 6.91–6.85 (m, 4H, ArH (SR)); 6.83–6.77 (m, 2H, ArH(SR)); 6.76 (dd, 2H, ArH (SS,RR), $J = 7.4$ Hz); 6.65 (d, 2H, ArH(SS,RR), $J = 1.9$ Hz); 6.62 (d, 2H, ArH(SR), $J = 1.9$ Hz); 6.40 (d, 2H, ArH(SS,RR), $J = 1.9$ Hz); 6.32 (d, 2H, ArH(SR), $J = 1.9$ Hz); 5.33 (d, 8H, ArCH_{ax}Ar (SS,RR, SR), $J = 13.4$ Hz); 5.12 (s, 4H, OCH_2CO); 5.10 (s, 4H, OCH_2CO); 4.87 (d, 2H, OCH_2CO (SS,RR), $J = 14.5$ Hz); 4.80 (d, 2H, OCH_2CO (SS,RR), $J = 14.5$ Hz); 4.81 (s, 4H, OCH_2CO (SR)); 4.48–4.43 (m, 4H, ArC*H*(OH)CF_3); 3.34–3.21 (m, 40H, NCH_2CH_3, ArCH_{eq}Ar); 1.16–1.03 (m, 48H, NCH_2CH_3); ^{19}F NMR (188.3 MHz, $CDCl_3$): δ −78.84 (d, $J =$ 7.3 Hz); −79.35 (d, $J = 6.9$ Hz); ^{19}F NMR (188.3 MHz, DMSO-d_6): δ −72.83 (d, $J = 7.4$ Hz); −72.84 (d, $J =$ 6.9 Hz). MS (CI) m/z: 1073 $(M + H)^+$100%. $C_{56}H_{70}F_6N_4O_{10}$ (1073.18).

5,11,17,23-Tetraformyl-25,26,27,28-tetrakis[(N,N-diethylaminocarbonyl)methoxy]calix[4]arene (11)

A suspension of tetraformyl calix[4]arene **30** (1 g, 1.8 mmol), Na_2CO_3 (7.8 g, 73.6 mmol), NaI (5.5 g, 36.8 mmol) and α-chloro-N,N-diethylacetamide (5.0 ml, 36.8 mmol) in dry acetonitrile (130 ml) was stirred at 90°C for 24 hs. The solvent was removed under reduced pressure and 50 ml of a 1 N HCl solution and dichloromethane were added. The organic layer was separated, washed twice with water (2 × 50 ml) and dichloromethane removed under reduced pressure. Pure compound **11** was obtained by column chromatography (SiO_2: eluent ethyl acetate 100%—ethyl acetate/triethylamine 10:1). Yield: 62%. Mp: 224–226°C. ^{1}H NMR (300 MHz; $CDCl_3$): δ 9.53 (s, 4H, ArCHO); 7.12 (s, 8H, ArH); 5.37 (d, 4H, ArCH_{ax}Ar, $J = 14.0$ Hz); 4.96 (s, 8H, OCH_2CON); 3.38 (d, 4H, ArCH_{eq}Ar, $J = 14.0$ Hz); 3.33–3.22 (m, 16H, NCH_2CH_3); 1.16 (t, 12H, NCH_2CH_3, $J = 7.0$ Hz); 1.04 (t, 12H, NCH_2CH_3, $J = 7.0$ Hz); ^{13}C NMR (75 MHz; $CDCl_3$): δ 191.1 (d, Ar*C* HO); 167.4 (s, *C*ON), 161.8 (s, Ar ipso); 135.3 (s, Ar ortho); 131.3 (s, Ar para); 130.4 (d, Ar meta); 71.6 (t, O*C*H_2CO); 40.6, 40.0 (t, O*C*H_2CON); 31.6 (t, ArCH_2Ar); 14.1, 12.9 (q, NCH_2*C*H_3). IR (liquid film), ν (cm^{-1}): 1696 (ArHC=O), 1659 (NC=O). MS (CI) m/z: 989 $(M + H)^+$100%. $C_{56}H_{68}N_4O_{12}$ (989.18).

5,11,17,23-Tetrakis(2,2,2-trifluorethanol)-25,26,27,28-tetrakis[(N,N-diethylaminocarbonyl)methoxy]calix[4]arene (12)

Compound **12** was synthesized from the tetraldehyde **11** according to the trifluoromethylation conditions used for the preparation of compound **3**. It was obtained pure after crystallization from ethyl ether—hexane. Yield: 68%. Mp: 272–288°C. ^{1}H NMR (300 MHz; $CDCl_3$): δ 6.97, 6.90, 6.88, 6.85, 6.84, 6.81,

6.77, 6.66, 6.63, 6.52 (s, 8H, ArH); 5.29–5.33 (m, 4H, ArCH_{ax}Ar); 5.03, 4.97, 4.92 (s, 8H, OCH_2CO); 4.69 (q, 4H, ArCH(OH)CF_3, $J = 6.8$ Hz); 4.61–4.59 (m, ArCH(OH)CF_3); 4.52 (q, 4H, ArCH(OH)CF_3, $J = 6.2$ Hz); 3.30–3.22 (m, 20H, NC$H_2$$CH_3$, ArC$H_{eq}$ Ar); 1.17–1.07 (m, 24H, NCH_2CH_3); ^{1}H NMR (400 MHz; DMSO-d_6): δ 7.08, 7.06, 7.05, 6.97, 6.89 (s, 8H, ArH); 6.55–6.40 (m, 4H, ArCH(OH)CF_3) 5.26 (d, 4H, ArCH_{ax}Ar, $J = 12.4$ Hz); 5.02, 5.01 (s, 8H, OCH_2CO); 4.77–4.72 (m, 4H, ArCH(OH)CF_3); 3.31–3.27 (m, 20H, NC$H_2$$CH_3$, ArC$H_{eq}$Ar); 1.17–1.07 (m, 24H, NCH_2CH_3); ^{19}F NMR (188.3 MHz, $CDCl_3$): δ −78.68– −78.87 (m); ^{19}F NMR (188.3 MHz, DMSO-d_6): δ −72.78– −73.05 (m); ^{19}F NMR (188.3 MHz, CD_3OD): δ −76.37– −76.55 (m). MS (CI) m/z: 1269 $(M)^+$100%; 1251 $(M-H_2O)^+$80%. $C_{60}H_{72}F_{12}N_4O_{12}$ (1269.23).

5,17-Dibromo-25,27-di-*n*-propoxycalix[4]arene-26,28-crown-4 (14)

To a suspension of NaH (0.12 g, 2.7 mmol, 55% w/w in oil), previously washed with dry toluene, in dry DMF (30 ml), were added the dibromo derivative **13** (0.5 g, 0.8 mmol) and the triethylene glycol ditosylate (0.38 g, 0.8 mmol). The solution was heated for 24 hs at 70°C and then quenched (CAUTION!) with 1 N HCl (100 ml). The precipitate formed was filtered on a buchner funnel, washed with water and triturated with methanol to give pure compound **14**. Yield: 85%. Mp: 220°C. ^{1}H NMR ($CDCl_3$): δ 7.28 (bs, 4H, ArH); 6.27 (t, 2H, ArH, $J = 7.5$ Hz); 6.14 (d, 4H, ArH, $J = 7.5$ Hz); 4.36 (d, 4H, ArCH_{ax}Ar, $J = 13.4$ Hz); 4.09 (s, 8H, ArO$CH_2CH_2OCH_2$); 3.76 (s, 4H, OCH_2CH_2O); 3.65 (t, 4H, $OCH_2CH_2CH_3$, $J = 6.9$ Hz); 3.12 (d, 4H, ArCH_{eq}Ar, $J = 13.4$ Hz); 1.95–1.88 (m, 4H, $OCH_2CH_2CH_3$); 1.11 (t, 6H, $OCH_2CH_2CH_3$, $J = 7.4$ Hz); ^{13}C NMR ($CDCl_3$): δ 157.4, 154.7 (s, Ar ipso); 138.8, 132.2 (s, Ar ortho); 131.6, 127.7 (d, Ar meta); 122.4 (d, Ar para); 114.7 (s, Ar para); 77.3 (t, OC $H_2CH_2CH_3$); 74.0, 71.9, 70.2 (t, ArOC H_2C H_2OC H_2); 30.3 (t, ArC H_2Ar); 23.6 (t, OCH_2C H_2CH_3); 10.9 (q, OCH_2CH_2C H_3). MS (CI) m/z: 782 $(M + 4)^+$70%; 780 $(M + 2)^+$100%; 778 $(M)^+$40%. $C_{40}H_{44}Br_2O_6$ (780.60).

5,17-Dibromo-25,27-di-*n*-propoxycalix[4]arene-26,28-crown-5 (15)

Compound **15** was synthesized according to the procedure used for compound **14** using tetraethylene glycol ditosylate. The product was purified by column chromatography (SiO_2: eluent hexane-ethyl acetate = 7:3). Yield: 56%. Mp: 183–185°C. ^{1}H NMR (300 MHz; $CDCl_3$): δ 7.27 (s, 4H, ArH); 6.26 (t, 2H, ArH, $J = 7.3$ Hz); 6.10 (d, 4H, ArH, $J = 7.3$ Hz); 4.33 (d, 4H, ArCH_{ax}Ar, $J = 13.6$ Hz); 4.24 (t, 4H, ArOCH_2 CH_2O, $J = 7.7$ Hz); 4.01 (t, 4H, ArOCH_2CH_2O, $J = 7.7$ Hz); 3.75 (s, 8H, OCH_2CH_2O); 3.66 (t, 4H, $OCH_2CH_2CH_3$, $J = 7.0$ Hz); 3.12 (d, 4H, ArCH_{eq}Ar, $J = 13.6$ Hz); 1.95–1.85 (m, 4H, $OCH_2CH_2CH_3$); 1.08 (t, 6H, $OCH_2CH_2CH_3$ $J = 7.3$ Hz); ^{13}C NMR (25 MHz; $CDCl_3$): δ 157.9, 155.1 (s, Ar ipso); 138.9, 132.4 (s, Ar ortho); 131.8, 127.9 (d, Ar meta); 122.8 (d, Ar para); 114.9 (s, Ar para); 77.6 (t, OC $H_2CH_2CH_3$); 73.1, 71.6, 71.1, 69.3 (t, Ar OC H_2C H_2OC H_2C H_2O); 30.9 (t, ArCH_2Ar); 23.7 (t, OCH_2C H_2CH_3); 11.1 (q, OCH_2 CH_2C H_3). MS (CI) m/z: 826 $(M + 4)^+$50%; 824 $(M + 2)^+$100%; 822 $(M)^+$45%. $C_{42}H_{48}Br_2O_7$ (824.65).

5,17-Bis(trifluoroacetyl)-25,27-di-*n*-propoxycalix[4]arene-26,28-crown-4 (16)

Via A

From the bromoaryl derivative **14** using the same conditions used for the preparation of compound **2**. Pure compound **16** was purified by preparative thin layer chromatography (SiO_2: eluent hexane-ethyl acetate 7:3). Yield: 25%.

Via B

By oxidation of alcohol **24** using the same conditions used for the preparation of compound **2**. Compound **16** was obtained by trituration from ethyl ether. Yield: >95%.

Mp: 202–204°C. ^{1}H NMR (300 MHz; $CDCl_3$): δ 7.95 (s, 4H, ArH); 6.28 (t, 2H, ArH, $J = 7.5$ Hz); 6.10 (d, 4H, ArH, $J = 7.5$ Hz); 4.51 (d, 4H, ArCH_{ax}Ar, $J = 13.5$ Hz); 4.31 (t, 4H, ArOCH_2CH_2O, $J = 6.0$ Hz); 4.13 (t, 4H, ArOCH_2CH_2O, $J = 6.0$ Hz); 3.81 (s, 4H, OCH_2CH_2O); 3.73 (t, 4H, $OCH_2CH_2CH_3$, $J = 6.5$ Hz); 3.35 (d, 4H, ArCH_2Ar eq, $J = 13.5$ Hz); 2.03–1.92 (m, 4H, $OCH_2CH_2CH_3$); 1.18 (t, 6H, $OCH_2CH_2CH_3$, $J = 7.4$ Hz); ^{13}C NMR (75 MHz; $CDCl_3$): δ 165.0, 154.7 (s, Ar ipso); 136.8, 132.3 (s, Ar ortho); 130.7, 127.7 (d, Ar meta); 129.2 (q, $COCF_3$, $J_{C-F} = 277$ Hz); 124.0 (s, Ar para); 122.3 (d, Ar para); 77.3 (t, OC H_2CH_2 CH_3); 74.0, 71.9, 70.3 (t, OC H_2C H_2OC H_2); 30.5 (t, ArC H_2Ar); 23.6 (t, OCH_2C H_2CH_3); 10.9 (q, OCH_2 CH_2C H_3). IR (liquid film), ν (cm^{-1}): 1707 (C=O). MS (CI) m/z: 814 $(M)^+$30%; 727 (M-2Pr)$^+$100%. $C_{44}H_{44}F_6O_8$ (814.82).

5,17-Bis(trifluoroacetyl)-25,27-di-*n*-propoxycalix[4]arene-26,28-crown-5 (17)

Via A

From the bromoaryl derivative **15** with the same procedure used for the synthesis of compound **2**. Compound **17** was purified by preparative thin layer chromatography (SiO_2: eluent hexane - ethyl acetate 9:2). Yield: 30%. Mp: 183°C. ^{1}H NMR (300 MHz; $CDCl_3$): δ 7.91 (s, 4H, ArH); 6.24 (t, 2H, ArH, $J = 7.4$ Hz); 6.02 (d, 4H, ArH, $J = 7.4$ Hz); 4.44 (d, 4H, ArCH_{ax}Ar, $J = 13.5$ Hz); 4.45–4.39 (m, 4H, ArOCH_2

CH_2O); 4.06–4.01 (m, 4H, $ArOCH_2CH_2O$); 3.76 (bs, 8H, OCH_2CH_2O); 3.71 (t, 4H, $OCH_2CH_2CH_3$, $J = 7.0$ Hz); 3.33 (d, 4H, $ArCH_{eq}Ar$, $J = 13.5$ Hz); 1.97–1.87 (m, 4H, $OCH_2CH_2CH_3$); 1.06 (t, 6H, $OCH_2CH_2CH_{3,J} = 7.5$ Hz); ^{13}C NMR (75 MHz; $CDCl_3$): δ 165.2, 154.9 (s, Ar ipso); 137.5, 131.8 (s, Ar ortho); 131.5, 127.8 (d, Ar meta); 124.1 (s, Ar para); 122.8 (d, Ar para); 127.6 (q, $COCF_3$, $J_{C-F} = 379$ Hz); 77.4 (t, $OCH_2CH_2CH_3$); 73.3, 71.4, 70.6, 68.9 (t, $OCH_2CH_2OCH_2CH_2O$); 30.9 (t, $ArCH_2Ar$); 23.5 (t, $OCH_2CH_2CH_3$); 10.9 (q, $OCH_2CH_2CH_3$). MS (CI) m/z: 858 $(M)^+$100%. $C_{46}H_{48}F_6O_9$ (858.87).

5-Trifluoroacetyl-25,27-di-*n*-propoxycalix[4]arene-26,28-crown-5 (19)

Compound **19** was obtained as a by-product during the preparation of compound **17**.

Yield: 28%. ^{1}H NMR (300 MHz; $CDCl_3$): δ 7.90 (s, 2H, ArH); 7.14 (d, 2H, ArH, $J = 7.4$ Hz); 6.96 (t, 1H, ArH, $J = 7.4$ Hz); 6.21 (t, 2H, ArH, $J = 7.6$ Hz); 6.07 (d, 2H, ArH, $J = 7.6$ Hz); 5.98 (d, 2H, ArH, $J = 7.6$ Hz); 4.45 (d, 2H, $ArCH_{ax}Ar$, $J = 13.6$ Hz); 4.38 (d, 2H, $ArCH_{ax}Ar$, $J = 13.6$ Hz); 4.44–4.40 (m, 2H, $ArOCH_2CH_2O$); 4.30–4.25 (m, 2H, $ArOCH_2CH_2O$); 4.07–4.01 (m, 4H, $ArOCH_2CH_2O$); 3.77 (bs, 8H, OCH_2CH_2O); 3.74–3.67 (m, 4H, $OCH_2CH_2CH_3$); 3.32 (d, 2H, $ArCH_{eq}Ar$, $J = 13.6$ Hz); 3.19 (d, 2H, $ArCH_{eq}Ar$, $J = 13.5$ Hz); 1.96–1.85 (m, 4H, $OCH_2CH_2CH_3$); 1.10 (t, 6H, $OCH_2CH_2CH_3$, $J = 7.4$ Hz); ^{13}C NMR (75 MHz; $CDCl_3$): δ 179.6 (q, $COCF_3$, $J_{C-C-F} = 34.4$ Hz); 165.4, 158.4, 154.8 (s, Ar ipso); 137.5, 136.5, 133.2, 131.4 (s, Ar ortho); 131.3, 129.2, 127.9, 127.2 (d, Ar meta); 123.7 (s, Ar para); 122.5, 122.3 (d, Ar para); 117.0 (q, $COCF_3$, $J_{C-F} = 290$ Hz); 77.3 (t, $OCH_2CH_2CH_3$); 73.0, 72.8, 71.5, 71.2, 70.53, 70.49, 69.0, 68.9 (t, $ArOCH_2CH_2OCH_2CH_2OCH_2CH_2OCH_2CH_2OAr$); 30.9, 30.8 (t, $ArCH_2Ar$); 23.4 (t, $OCH_2CH_2CH_3$); 10.9 (q, $OCH_2CH_2CH_3$). MS (CI) m/z: 763 $(M + H)^+$100%; 762 $(M)^+$90%. $C_{44}H_{49}F_3O_8$ (762.87).

5,17-Diformyl-25,27-di-*n*-propoxycalix[4]arene-26,28-crown-3 (21)

To a suspension of compound **20** (500 mg, 0.76 mmol) and NaH (66 mg, 1.52 mmol, 55% w/w in oil) in dry DMF (200 ml) was added the 2-iodoethyl ether (345 mg, 1.06 mmol) and the reaction mixture heated at 80°C for 24 h. Then an aqueous 1 N HCl solution (200 ml) (CAUTION!) and dichloromethane (400 ml) were added. After extraction, the organic layer was separated, washed twice with water (2 × 200 ml) and the solvent removed. The residue was purified by column chromatography (SiO_2: hexane/ethyl acetate 3:1) giving compound **21** as a white solid. Yield: 70%. Mp: 216–218°C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.99 (s, 2 H, CHO); 7.70 (s, 4 H, ArH); 6.20 (t, 2 H, ArH, $J = 7.8$ Hz); 5.96 (d, 4 H, ArH, $J = 7.8$ Hz); 4.42 (d, 4 H, $J = 13.5$ Hz, $ArCH_{ax}Ar$); 4.18 (m, 4 H, $ArOCH_2CH_2O$); 4.08 (m, 4 H, $ArOCH_2CH_2O$); 3.68 (t, 4 H, $J = 6.9$ Hz, $OCH_2CH_2CH_3$); 3.30 (d, 4 H, $J = 13.5$ Hz, $ArCH_{eq}Ar$); 1.92–1.80 (m, 4 H, $OCH_2CH_2CH_3$); 1.10 (t, 6 H, $J = 7.5$ Hz, $OCH_2CH_2CH_3$); ^{13}C NMR (75 MHz, $CDCl_3$): δ 191.5 (s, C=O); 164.2, 154.8 (s, Ar ipso); 138.0, 132.3 (s, Ar ortho); 131.1, 122.5 (d, Ar meta); 77.5 (t, $OCH_2CH_2CH_3$); 73.4 (t, $ArOCH_2CH_2O$); 70.5 (t, $ArOCH_2CH_2O$); 31.1 (t, $ArCH_2Ar$); 23.9 (t, $OCH_2CH_2CH_3$); 11.3 (q, $OCH_2CH_2CH_3$). MS (CI) m/z: 635 $(M + H)^+$ 100%. $C_{40}H_{42}O_7$ (634.77).

5,17-Diformyl-25,27-di-*n*-propoxycalix[4]arene-26,28-crown-4 (22)

To a suspension of NaH (0.23 g, 5.2 mmol, 55% w/w in oil), previously washed with dry toluene, in dry DMF (30 ml), were added the compound **20** (1 g, 1.5 mmol) and the triethylene glycol ditosylate (0.77 g, 1.7 mmol). The solution was heated for 14 hs at 70°C and then quenched (CAUTION!) with 1 N HCl (100 ml). The precipitate formed was filtered on a buchner funnel, washed with water and submitted to column chromatography (SiO_2: eluent hexane-ethyl acetate 3:2). Yield: 60%. Mp: 206–207°C. ^{1}H NMR (300 MHz; $CDCl_3$): δ 9.98 (s, 2H, ArCHO); 7.70 (s, 4H, ArH); 6.21 (t, 2H, ArH, $J = 7.5$ Hz); 6.06 (d, 4H, ArH, $J = 7.5$ Hz); 4.46 (d, 4H, $ArCH_{ax}Ar$, $J = 13.5$ Hz); 4.23 (t, 4H, $ArOCH_2CH_2O$, $J = 6.0$ Hz); 4.11 (t, 4H, $ArOCH_2CH_2O$, $J = 6.0$ Hz); 3.78 (s, 4H, OCH_2CH_2O); 3.70 (t, 4H, $OCH_2CH_2CH_3$, $J = 6.8$ Hz); 3.30 (d, 4H, $ArCH_{eq}Ar$, $J = 13.5$ Hz); 1.99–1.91 (m, 4H, $OCH_2CH_2CH_3$); 1.14 (t, 6H, $OCH_2CH_2CH_3$ $J = 7.4$ Hz); ^{13}C NMR (25 MHz; $CDCl_3$): δ 191.7 (d, ArCHO); 164.3, 155.1 (s, Ar ipso); 137.9, 132.3 (s, Ar ortho); 131.5 (s, Ar para); 131.2, 128.0 (d, Ar meta); 122.7 (d, Ar para); 77.6 (t, $OCH_2CH_2CH_3$); 74.5, 72.2, 70.5 (t, Ar $OCH_2CH_2OCH_2$); 30.8 (t, $ArCH_2Ar$); 23.8 (t, $OCH_2CH_2CH_3$); 11.1 (q, $OCH_2CH_2CH_3$). IR (liquid film), ν (cm^{-1}): 1688 (CO). MS (CI) m/z: 678 $(M)^+$100%, $(M\text{-}2Pr)^+$80%. $C_{42}H_{46}O_8$ (678.82).

5,17-Diformyl-25,27-di-*n*-propoxycalix[4]arene-26,28-crown-5 (23)

Compound **23** was synthesized according to the procedure used for compound **22** using tetraethylene glycol ditosylate. It was purified by column chromatography (SiO_2: eluent hexane-ethyl acetate 7:2). Yield: 53%. Mp: 221–223°C. ^{1}H NMR (300 MHz; $CDCl_3$): δ 9.98 (s, 2H, ArCHO); 7.70 (s, 4H, ArH); 6.21 (t, 2H, ArH, $J = 7.6$ Hz); 6.03 (d, 4H, ArH, $J = 7.6$ Hz); 4.43 (d, 4H, $ArCH_{ax}Ar$, $J = 13.5$ Hz); 4.40–4.36 (m, 4H, $ArOCH_2CH_2O$); 4.04 (t, 4H, $ArOCH_2CH_2O$, $J = 7.0$ Hz); 3.76 (s, 8H, OCH_2CH_2O); 3.71 (t, 4H,

$OCH_2CH_2CH_3$, $J = 6.9$ Hz); 3.31 (d, 4H, $ArCH_{eq}Ar$, $J = 13.5$ Hz); 1.95–1.88 (m, 4H, $OCH_2CH_2CH_3$); 1.11 (t, 6H, $OCH_2CH_2CH_3$ $J = 7.4$ Hz); ^{13}C NMR (25 MHz; $CDCl_3$): δ 191.7 (d, ArC HO); 164.3, 155.2 (s, Ar ipso); 137.8, 132.3 (s, Ar ortho); 131.2, 128.0 (d, Ar meta); 131.4 (d, Ar para); 122.9 (d, Ar para); 77.7 (t, OC H_2 CH_2CH_3); 73.4, 71.6, 71.1, 69.3 (t, Ar OC H_2C H_2 OC H_2C H_2O); 31.1 (t, $ArCH_2Ar$); 23.7 (t, OCH_2C H_2 CH_3); 11.1 (q, OCH_2CH_2C H_3). IR (liquid film), ν (cm^{-1}): 1685 (CO). MS (CI) *m/z*: 722 $(M)^+$100%. $C_{44}H_{50}O_9$ (722.88).

5,17-Bis(2,2,2-trifluoroethanol)-25,27-di-*n*-propoxy calix[4]arene-26,28-crown-3 (24)

Compound **24** was synthesized from the dialdehyde **21** according to the trifluoromethylation conditions used for the preparation of compound **3**. It was obtained pure after crystallization from dichloromethane—hexane.

Yield: 73%. Mp: 264–266°C. ^{1}H NMR (300 MHz; CD_3OD): δ 7.29 (s, 2H, ArH); 7.26 (s, 2H, ArH); 6.12 (t, 2H, ArH $J = 7.4$ Hz); 5.97 (dd, 4H, ArH, $J = 7.4$ Hz); 5.02 (q, 2H, $ArCH(OH)CF_3$, $J = 6.8$ Hz); 4.41 (d, 4H, $ArCH_{ax}Ar$, $J = 13.8$ Hz); 4.24–4.22 (m, 4H, $ArOCH_2CH_2O$); 4.04–4.02 (m, 4H, $ArOCH_2$ CH_2O); 3.66 (t, 4H, $OCH_2CH_2CH_3$, $J = 6.6$ Hz); 3.19 (d, 4H, $ArCH_{eq}Ar$, $J = 13.8$ Hz); 1.91–1.81 (m, 4H, $OCH_2CH_2CH_3$); 1.13 (t, 6H, $OCH_2CH_2CH_3$ $J = 7.4$ Hz); ^{13}C NMR (75 MHz; CD_3OD): δ 160.4, 156.2 (s, Ar ipso); 138.3, 138.2, 134.0 (s, Ar ortho); 130.5, 130.0, 129.5 (d, Ar meta); 128.4 (d, Ar para); 126.6 (q, CF_3, $J_{C-F} = 282$ Hz); 123.2 (s, Ar para); 78.1 (t, OC $H_2CH_2CH_3$); 74.1, 71.6, (t, Ar OC H_2C H_2O); 73.1 (d, ArC H(OH)CF_3, $J_{C-C-F} = 31$ Hz); 31.7 (t, $ArCH_2Ar$); 24.5 (t, OCH_2C H_2CH_3); 11.5 (q, OCH_2 CH_2C H_3); ^{19}F NMR (188.3 MHz; CD_3OD): δ −76.65 (d, $J = 7.4$ Hz). MS (CI) *m/z*: 775 $(M + H)^+$100. $C_{42}H_{44}F_6O_7$ (774.80).

5,17-Bis(2,2,2-trifluoroethanol)-25,27-di-*n*-propoxycalix[4]arene-26,28-crown-4 (25)

Via A

By reduction of the diketone **16** according to the procedure used for the synthesis of **3**. It was obtained pure, as mixture of diastereomers, by column chromatography (SiO_2: eluent hexane-ethyl acetate = 7:3). Yield: 75%.

Via B

From the dialdehyde **22** according to the trifluoromethylation conditions used for the preparation of compound **3**. It was obtained pure after crystallization from chloroform. Yield: 85%.

Mp: 211–212°C. ^{1}H NMR (300 MHz; $CDCl_3$): δ 7.26 (s, 2H, ArH); 7.24 (s, 2H, ArH); 6.22–6.17 (m, 2H, ArH); 6.05 (d, 2H, ArH, $J = 7.3$ Hz); 6.03 (d, 2H, ArH, $J = 7.3$ Hz); 5.01 (q, 2H, $ArCH(OH)CF_3$, $J = 6.7$ Hz); 4.42 (d, 4H, $ArCH_{ax}Ar$, $J = 13.3$ Hz); 4.16–4.11 (m, 8H, $ArOCH_2CH_2O$); 3.78 (s, 4H, OCH_2CH_2O); 3.68 (t, 4H, $OCH_2CH_2CH_3$, $J = 6.8$ Hz); 3.20 (d, 4H, $ArCH_{eq}Ar$, $J = 13.3$ Hz); 1.99–1.88 (m, 4H, $OCH_2CH_2CH_3$); 1.14 (t, 6H, $OCH_2CH_2CH_3$ $J = 7.3$ Hz); ^{1}H NMR (300 MHz; DMSO-d_6): δ 7.31 (s, 2H, ArH); 7.27 (s, 2H, ArH); 6.73 (d, 2H, OH, $J = 5.4$ Hz); 6.22–6.10 (m, 6H, ArH); 5.14–5.05 (m, 2H, $ArCH(OH)CF_3$,); 4.34 (d, 2H, $ArCH_{ax}Ar$, $J = 13.0$ Hz); 4.33 (d, 2H, $ArCH_{ax}Ar$, $J = 13.0$ Hz); 4.12 (t, 4H, $ArOCH_2CH_2O$, $J = 6.0$ Hz); 4.02 (t, 4H, $ArOCH_2CH_2O$, $J = 6.0$ Hz); 3.71 (s, 4H, OCH_2CH_2O); 3.64 (t, 4H, $OCH_2CH_2CH_3$, $J = 6.6$ Hz); 3.21 (d, 2H, $ArCH_{eq}Ar$, $J = 13.0$ Hz); 3.20 (d, 2H, $ArCH_{eq}Ar$, $J = 13.0$ Hz); 1.94–1.82 (m, 4H, $OCH_2CH_2CH_3$); 1.11 (t, 6H, $OCH_2CH_2CH_3$, $J =$ 7.3 Hz); ^{13}C NMR (75 MHz; $CDCl_3$:CD_3OD 10:3): δ 158.4, 154.5 (s, Ar ipso); 136.4, 136.3, 132.4 (s, Ar ortho); 128.5, 128.7, 127.9 127.4 (d, Ar meta); 127.2 (d, Ar para); 124.7 (q, CF_3, $J = 280$ Hz); 121.8 (s, Ar para); 77.0 (t, OC $H_2CH_2CH_3$); 73.4, 71.4, 70.1 (t, Ar OC H_2C H_2OC H_2); 71.8 (d, ArC H(OH)CF_3, $J_{C-C-F} = 31$ Hz); 30.2 (t, $ArCH_2Ar$); 23.3 (t, OCH_2C H_2CH_3); 10.6 (q, OC H_2CH_2C H_3); ^{19}F NMR (188.3 MHz; $CDCl_3$): δ −78.15 (d, $J = 5.5$ Hz); ^{19}F NMR (188.3 MHz; DMSO-d_6): δ −72.89 (d, $J = 7.3$ Hz). MS (CI) *m/z*: 818 $(M)^+$100%. $C_{44}H_{48}F_6O_8$ (818.85).

5,17-Bis(2,2,2-trifluoroethanol)-25,27-di-*n*-propoxy calix[4]arene-26,28-crown-5 (26)

Via A

By reduction of the diketone **17** according to the procedure used for the synthesis of **3**. It was obtained pure, as mixture of diastereomers, by column chromatography (SiO_2: eluent hexane-ethyl acetate = 7:3). Yield: 82%.

Via B

From the dialdehyde **23** according to the trifluoromethylation conditions used for the preparation of compound **3**. It was obtained pure after crystallization from chloroform. Yield: 93%.

Mp: 202–203 °C. ^{1}H NMR (300 MHz; $CDCl_3$): δ 7.26 (s, 2H, ArH); 7.22 (s, 2H, ArH); 6.22–6.17 (m, 2H, ArH); 6.00 (d, 2H, ArH, $J = 7.4$ Hz); 5.98 (d, 2H, ArH, $J = 7.4$ Hz); 5.03 (q, 2H, $ArCH(OH)CF_3$, $J = 6.7$ Hz); 4.40 (d, 4H, $ArCH_{ax}Ar$, $J = 13.5$ Hz); 4.33–4.28 (m, 4H, $ArOCH_2CH_2O$); 4.04 (t, 4H, $ArOCH_2CH_2O$, $J = 7.1$ Hz); 3.78–3.74 (m, 8H, OCH_2CH_2O); 3.69 (t, 4H, $OCH_2CH_2CH_3$, $J = 6.8$ Hz); 3.20 (d, 4H, $ArCH_{eq}Ar$, $J = 13.5$ Hz); 1.95–1.84 (m, 4H, OCH_2 CH_2CH_3); 1.10 (t, 6H, $OCH_2CH_2CH_3$, $J = 7.3$ Hz);

^{1}H NMR (300 MHz; DMSO-d_6): δ 7.31 (s, 2H, ArH); 7.26 (s, 2H, ArH); 6.74 (d, 2H, OH, $J = 5.4$ Hz); 6.19 (t, 2H, ArH, $J = 7.5$ Hz); 6.05 (d, 2H, ArH, $J = 7.4$ Hz); 6.03 (d, 2H, ArH, $J = 7.4$ Hz); 5.14–5.08 (m, 2H, ArC*H*(OH)CF_3,); 4.30 (d, 4H, ArCH_{ax}Ar, $J = 13.4$ Hz); 4.18–4.14 (m, 4H, ArOCH_2CH_2O); 4.01 (t, 4H, ArOCH_2CH_2O, $J = 7.6$ Hz); 3.67–3.63 (m, 12H, OCH_2CH_2O, OCH_2CH_2CH_3); 3.21 (d, 4H, ArCH_{eq}Ar, $J = 13.4$ Hz); 1.91–1.81 (m, 4H, OCH_2CH_2CH_3); 1.09 (t, 6H, OCH_2CH_2CH_3, $J = 7.3$ Hz); ^{13}C NMR (75 MHz; $CDCl_3$): δ 159.4, 154.8 (s, Ar ipso); 136.8, 136.7, 132.4 (s, Ar ortho); 128.3, 127.7, 127.4 (d, Ar meta); 127.3 (d, Ar para); 124.4 (q, CF_3, $J_{C-F} = 280$ Hz); 122.4 (s, Ar para); 77.2 (t, OCH_2 CH_2CH_3); 72.7, 71.3, 70.4, 70.0 (t, Ar OCH_2 CH_2 OCH_2CH_2O); 72.6 (d, ArC H(OH)CF_3, $J_{C-CF} = 31.7$ Hz); 30.8 (t, ArCH_2Ar); 23.4 (t, OCH_2CH_2CH_3); 10.8 (q, OCH_2CH_2CH_3). ^{19}F NMR (188.3 MHz; $CDCl_3$): δ −79.27 (d, $J = 6.4$ Hz). MS (CI) m/z: 862 (M^+) 100%. $C_{46}H_{52}F_6O_9$ (862.91).

5-(2,2,2-Trifluoroethanol)-25,27-di-n-propoxycalix[4]arene-26,28-crown-5 (27)

Compound **27** was synthesized by reduction of the monoketone **19** according to the procedure used for the synthesis of **3**. It was obtained pure, as mixture of enantiomers, by column chromatography (SiO_2: eluent hexane-ethyl acetate = 7:3). Yield: 90%. ^{1}H NMR (300 MHz; $CDCl_3$): δ 7.26 (s, 1H, ArH); 7.23 (s, 1H, ArH); 7.14 (d, 2H, ArH, $J = 7.4$ Hz); 6.95 (t, 1H, ArH, $J = 7.4$ Hz); 6.20 (t, 2H, ArH, $J = 7.5$ Hz); 6.06 (d, 2H, ArH, $J = 7.5$ Hz); 6.02–5.98 (m, 2H, ArH); 5.02 (q, 1H, ArC*H*(OH)CF_3, $J = 6.7$ Hz); 4.41 (d, 2H, ArCH_{ax}Ar, $J = 13.4$ Hz); 4.38 (d, 2H, ArCH_{ax}Ar, $J = 13.4$ Hz); 4.36–4.27 (m, 4H, ArOCH_2CH_2O); 4.06 (t, 4H, ArOCH_2CH_2O, $J = 7.5$ Hz); 3.80–3.75 (m, 8H, OCH_2CH_2O); 3.70 (t, 4H, OCH_2CH_2CH_3, $J = 7.0$ Hz); 3.21 (d, 2H, ArCH_{eq}Ar, $J = 13.4$ Hz); 3.19 (d, 2H, ArCH_{eq}Ar, $J = 13.4$ Hz); 1.98–1.85 (m, 4H, OCH_2 CH_2CH_3); 1.12 (t, 6H, OCH_2CH_2CH_3, $J = 7.4$ Hz); ^{13}C NMR (75 MHz; $CDCl_3$): δ 159.4, 158.5, 154.8 (s, Ar ipso); 136.8, 136.7, 136.5, 133.0, 132.3 (s, Ar ortho); 129.1, 127.5, 127.2, 122.3 (d, Ar meta); 128.3, 127.8 (d, Ar para); 124.4 (q, CF_3, $J_{C-F} = 283$ Hz); 122.0 (s, Ar para); 77.2 (t, OCH_2CH_2CH_3); 72.6 (d, ArC H(OH)CF_3, $J_{C-CF} = 32.0$ Hz); 72.6, 71.4, 70.5, 69.1, 69.0 (t, ArOCH_2CH_2OCH_2CH_2OCH_2CH_2OCH_2CH_2 OAr); 30.8 (t, ArCH_2Ar); 23.4 (t, OCH_2CH_2CH_3); 10.9 (q, OCH_2CH_2CH_3). MS (CI) m/z: 764 (M^+)100%. $C_{44}H_{51}F_3O_8$ (764.88).

5,11,17,23-Tetraformylcalix[4]arene (30)

A suspension of hexamethylene tetramine HMTA (12 g, 85.6 mmol) and calix[4]arene **28** (1 g, 2.4 mmol) in trifluoroacetic acid (80 ml) was heated at 110°C for 24 hs. After cooling, the reaction mixture was added to a 1 N HCl solution (200 ml) together with 150 ml of dichloromethane and stirred at rt for 5 hs. The separated organic layer was washed twice with water (2 × 150 ml) and the solvent removed under reduced pressure. The residue was triturated in dichloromethane to give pure compound **30**. Yield: 95%. Mp: >340°C (dec). ^{1}H NMR (300 MHz; DMSO-d_6): δ9.63 (s, 4H, ArCHO); 8.75 (bs, 4H, ArOH); 7.65 (s, 8H, ArH); 3.95 (bs, 8H, ArCH_2Ar); ^{13}C NMR (75 MHz; DMSO-d_6): δ 190.4 (d, ArCHO); 160.1 (s, Ar ipso); 130.5 (d, Ar meta); 129.8 (s, Ar ortho); 128.1 (s, Ar para); 31.2 (t, ArCH_2Ar). MS (CI) m/z: 537 $(M + H)^+$100%. $C_{32}H_{24}O_8$ (536.54).

5,17-Diformyl-25,27-bis[(N,N-diethylaminocarbonyl)methoxy]calix[4]arene (31)

To a solution of diamide **29** (1.0 g, 1.54 mmol) in 80 ml of dry $CHCl_3$ were added $TiCl_4$ (6.75 ml, 62 mmol) and dichloromethyl methyl ether (2.8 ml, 62 mmol). The reaction mixture was stirred for 14 hs at rt and then quenched by adding a 2 N HCl solution (100 ml). The mixture was stirred for 4 hs, transferred in a separatory funnel and the organic layer washed twice with water (2 × 80 ml). After removal of the solvent under reduced pressure, pure compound **31** was obtained by precipitation with diethyl ether. Yield: 75%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 9.69 (s, 2H, CHO); 9.53 (s, 2H, OH); 7.53 (s, 4H, ArH); 7.00 (d, 4H, $J = 7.2$ Hz, ArH); 6.80 (t, 2H, $J = 7.2$ Hz, ArH); 4.83 (s, 4H, OCH_2CO); 4.58 (d, 4H, $J = 13.0$ Hz, ArCH_{ax} Ar); 3.64–3.35 (m, 12H, NCH_2CH_3, ArCH_{eq}Ar); 1.32–1.12 (m, 12H, NCH_2CH_3). M/S (CI) m/z: 935 $(M)^+$100%. $C_{42}H_{46}N_2O_8$ (934.82).

5-(Trifluoroacetyl)-25,26,27,28-tetra-*n*-propoxycalix[4]arene (32)

Compound **32** was synthesized according to the procedure for the synthesis of compound **2**. Yield: 70%. ^{1}H NMR (300 MHz; $CDCl_3$): δ 7.16 (s, 2H, ArH); 6.88–6.84 (m, 4H, ArH); 6.78 (t, 2H, ArH, $J = 7.3$ Hz); 6.39–6.33 (m, 3H, ArH); 4.52 (d, 2H, ArCH_{ax}Ar, $J = 13.7$ Hz); 4.47 (d, 2H, ArCH_{ax}Ar, $J = 13.6$ Hz); 4.01–3.85 (m, 6H, OCH_2CH_2CH_3); 3.80 (t, 2H, OCH_2CH_2CH_3, $J = 7.1$ Hz); 3.25 (d, 2H, ArCH_{eq}Ar, $J = 13.7$ Hz); 3.19 (d, 2H, ArCH_{eq}Ar, $J = 13.6$ Hz); 1.99–1.89 (m, 8H, OCH_2CH_2CH_3); 1.12–1.05 (m, 6H, OCH_2CH_2CH_3); 0.99 (t, 6H, OCH_2CH_2CH_3, $J = 7.4$ Hz); ^{13}C NMR (75 MHz; $CDCl_3$):δ 179.4 (q, *C*OCF_3, $J_{C-C-F} = 34$ Hz); 156.9, 156.6, 156.0, (s, Ar ipso); 136.1, 135.9, 134.7, 134.3 (s, Ar ortho); 130.5, 129.2, 128.4, 127.9 (d, Ar meta); 123.8 (s, Ar para); 122.3, 121.8 (d, Ar para); 116.7 (q, CO*C*F_3 $J_{C-F} = 290$ Hz); 76.7, 76.6 (t, OCH_2CH_2CH_3); 30.9, 29.7 (t, ArCH_2Ar); 23.4, 23.3, 23.1 (t, OCH_2CH_2CH_3); 10.5, 10.4, 10.1 (q, OCH_2CH_2CH_3). IR (liquid film),

ν (cm^{-1}): 1701 (C=O). MS (CI) m/z: 688 (M^+) 100%. $C_{42}H_{47}F_3O_5$ (688.83).

5,11,17,23-Tetrakis-(trifluoroacetyl)-25,26,27,28-tetra-*n*-propoxycalix[4]arene (33)

Compound **33** was synthesized according to the procedure for the synthesis of compound **2**. Yield: 70%. Mp: 148 °C. ^{1}H NMR (100 MHz; $CDCl_3$): δ 7.41 (s, 2 H, ArH); 4.51 (d, 4H, $ArCH_{ax}Ar$, $J = 13.7$ Hz); 3.97 (t, 8H, $OCH_2CH_2CH_3$, $J = 7.0$ Hz); 3.39 (d, 4H, $ArCH_{eq}Ar$, $J = 13.8$ Hz); 2.04–1.82(m, 8H, $OCH_2CH_2CH_3$); 1.02 (t 12H, $OCH_2CH_2CH_3$, $J = 7.3$ Hz). MS (CI) m/z: 977 $(M + H)^+$. $C_{48}H_{44}F_{12}O_8$ (976.85).

5,17-Bis(1-acetyloxy-2,2,2-trifluoroethyl)-25,27-di-*n*-propoxycalix[4]arene-26,28-crown-4 (34)

To a solution of dialcohol **25** (0.14 g, 0.17 mmol) dissolved in dichloromethane (15 ml) were added triethylamine (0.096 ml, 0.69 mmol), a catalytic amount of dimethylamino pyridine (DMAP) and acetyl chloride (0.037 ml, 0.52 mmol). The solution was stirred at rt for 4 hs and then an aqueous 1 N HCl solution (15 ml) added. The organic layer was separated, washed twice with water (2 × 20 ml) and the solvent removed under reduced pressure. Pure compound **34** was obtained by column chromatography (SiO_2: eluent hexane—THF 2:1). Yield: 45%. Mp: 158–160°C. ^{1}H NMR (300 MHz; $CDCl_3$): δ 7.52 (s, 2H, ArH); 7.50 (s, 2H, ArH); 6.52–6.40 (m, 4H, ArH and $ArCH(OCOCH_3)CF_3$); 6.32 (d, 2H, ArH, $J = 7.5$ Hz); 6.23 (d, 2H, ArH, $J = 7.5$ Hz); 4.69 (d, 4H, $ArCH_{ax}Ar$, $J = 13.4$ Hz); 4.43–4.35 (m, 8H, $ArOCH_2CH_2O$); 4.04 (s, 4H, OCH_2CH_2O); 3.94 (t, 4H, $OCH_2CH_2CH_3$, $J = 6.7$ Hz); 3.46 (d, 4H, $ArCH_{eq}Ar$, $J = 13.4$ Hz); 2.54 (s, 6H, CH_3COO); 2.26–2.14 (m, 4H, $OCH_2CH_2CH_3$); 1.41 (t, 6H, $OCH_2CH_2CH_3$, $J = 7.3$ Hz); ^{13}C NMR (75 MHz; $CDCl_3$): δ 168.8 (s, C=O); 159.4, 154.7 (s, Ar ipso); 137.0, 136.9, 135.8, 132.4, 132.3, 128.7, 127.4, 127.2, 125.4, 122.4, 122.3 (Ar ortho, Ar meta, Ar para); 123.3 (q, CF_3, $J_{C\text{-}F} = 278$ Hz); 76.5 (t, $OCH_2CH_2CH_3$); 73.8, 71.8, 70.2 (t, $ArOCH_2CH_2OCH_2$); 71.7 (dq, $ArCH(OCOCH_3)CF_3$, $J_{C-C-F} = 33$ Hz); 20.7 (q, $COCH_3$); 30.4, 30.3 (t, $ArCH_2Ar$); 23.5 (t, $OCH_2CH_2CH_3$); 10.9 (q, $OCH_2CH_2CH_3$). IR (liquid film), ν (cm^{-1}): 1758 (C=O). MS (CI) m/z: 903 $(M + H)^+$100%. $C_{48}H_{52}F_6O_{10}$ (902.93).

5,17-Bis(1-benzoyloxy-2,2,2-trifluoroethyl)-25,27-di-*n*-propoxycalix[4]arene-26,28-crown-4. (35)

Compound **35** was obtained as described for **34** using benzoyl chloride as acylating agent. It was purified by preparative thin layer chromatography (SiO_2: eluent hexane - ethyl acetate 7:3). Yield: 72%. Mp: 170–174°C. ^{1}H NMR (400 MHz; $CDCl_3$): δ 8.18 (d, 8H, PhH, $J = 7.2$ Hz); 7.63 (t, 4H, PhH, $J = 7.2$ Hz); 7.51 (t, 8H, PhH, $J = 7.2$ Hz); 7.34–7.32 (m, 8H, ArH); 6.40 (q, 4H, $ArCH(OCOPh)CF_3$, $J = 6.8$ Hz); 6.23 (t, 1H, ArH, $J = 7.6$ Hz); 6.14 (t, 2H, ArH, $J = 7.6$ Hz); 6.07–6.04 (m, 5H, ArH); 5.93–5.89 (m, 4H, ArH); 4.42 (d, 4H, $ArCH_{ax}Ar$, $J = 13.4$ Hz); 4.40 (d, 4H, $ArCH_{ax}Ar$, $J = 13.4$ Hz); 4.16–4.06 (m, 16H, $ArOCH_2CH_2O$); 3.76 (s, 8H, OCH_2CH_2O); 3.66 (t, 8H, $OCH_2CH_2CH_3$, $J = 6.8$ Hz); 3.20 (d, 8H, $ArCH_{eq}Ar$, $J = 13.4$ Hz); 1.96–1.87 (m, 8H, $OCH_2CH_2CH_3$); 1.15–1.10 (m, 12H, $OCH_2CH_2CH_3$); ^{13}C NMR (75 MHz; $CDCl_3$): δ 164.5 (s, C=O); 159.4, 154.6 (s, Ar ipso); 137.1, 137.0, 133.7, 132.3, 129.9, 128.9, 128.7, 128.6, 127.4, 127.2, 124.7, 122.4, 122.3, 122.2 (Ar ortho, Ar meta, Ar para, Ph); 123.5 (q, CF_3, $J_{C-F} = 279$ Hz); 76.5 (t, $OCH_2CH_2CH_3$); 73.7, 71.8, 70.2 (3t, $ArOCH_2CH_2OCH_2$); 72.2 (dq, $ArCH(OCOPh)CF_3$, $J_{C-C-F} = 32$ Hz); 30.5, 30.4 (t, $ArCH_2Ar$); 23.5 (t, $OCH_2CH_2CH_3$); 10.9 (q, $OCH_2CH_2CH_3$). IR (liquid film), ν (cm^{-1}): 1734 (C=O). MS (CI) m/z: 1027 $(M + H)^+$100%. $C_{58}H_{56}F_6O_{10}$ (1027.07).

5,17-Bis(1-pentafluorobenzoyloxy-2,2,2-trifluoroethyl)-25,27-di-*n*-propoxycalix[4]arene-26,28-crown-4 (36)

Compound **36** was obtained as described for **34** using pentafluorobenzoyl chloride as acylating agent. Yield: 93%. ^{1}H NMR (300 MHz; $CDCl_3$): δ 7.31 (s, 4H, ArH); 6.37 (q, 2H, $ArCH(OCOC_6F_5)CF_3$, $J = 6.6$ Hz); 6.23–6.13 (m, 2H, ArH); 6.04 (d, 2H, ArH, $J = 7.6$ Hz); 5.94 (d, 2H, ArH, $J = 7.6$ Hz); 4.44 (d, 4H, $ArCH_{ax}Ar$, $J = 13.2$ Hz); 4.17 (t, 4H, $ArOCH_2CH_2O$, $J = 5.0$ Hz); 4.10 (t, 4H, $ArOCH_2CH_2O$, $J = 5.0$ Hz); 3.77 (s, 4H, OCH_2CH_2O); 3.68 (t, 4H, $OCH_2CH_2CH_3$, $J = 6.8$ Hz); 3.21 (d, 4H, $ArCH_{eq}Ar$, $J = 13.2$ Hz); 1.98–1.87 (m, 4H, $OCH_2CH_2CH_3$); 1.14 (t, 6H, $OCH_2CH_2CH_3$, $J = 7.4$ Hz). IR (liquid film), ν (cm^{-1}): 1754 (C=O). MS (CI) m/z: 1207 $(M + H)^+$100%. $C_{58}H_{46}F_{16}O_{10}$ (1206.97).

5,17-Bis[1-(4-nitrobenzoyloxy)-2,2,2-trifluoroethyl]-25,27-di-*n*-propoxycalix[4]arene-26,28-crown-4 (37)

Compound **37** was obtained as described for **34** using 4-nitrobenzoyl chloride as acylating agent. Yield: 91%. Mp: 126–129°C. ^{1}H NMR (400 MHz; $CDCl_3$): δ 8.37–8.33 (m, 16H, PhH); 7.34 (s, 4H, ArH); 7.31 (s, 4H, ArH); 6.40 (q, 4H, $ArCH(OCOPhNO_2)CF_3$, $J = 6.6$ Hz); 6.22 (t, 1H, ArH, $J = 7.6$ Hz); 6.14 (t, 2H, ArH, $J = 7.6$ Hz); 6.08–6.03 (m, 5H, ArH); 5.91–5.88 (m, 4H, ArH); 4.43 (d, 8H, $ArCH_{ax}Ar$, $J = 13.4$ Hz); 4.16–4.06 (m, 16H, $ArOCH_2CH_2O$); 3.77 (s, 8H, OCH_2CH_2O); 3.66 (t, 8H, $OCH_2CH_2CH_3$, $J = 6.7$ Hz); 3.21 (d, 8H, $ArCH_{eq}Ar$, $J = 13.4$ Hz); 1.96–1.87 (m, 8H, $OCH_2CH_2CH_3$); 1.15–1.10 (m, 12H, $OCH_2CH_2CH_3$). IR (liquid film), ν (cm^{-1}): 1743

TABLE V Crystal data and experimental details for **3a**

Formula	$C_{44}H_{50}F_3O_6{\cdot}2C_2H_5OH$
Cryst syst.	Monoclinic
Space group.	C2/c
Cell parameters at 295 K[a]	
a,Å	26.309(5)
b,Å	10.079(5)
c,Å	18.554(5)
β,°	98.59(1)
V,Å^3	4865(3)
Z	4
D_{calcd},g cm^{-3}	1.203
F(000)	1872
Mol wt	881.003
Linear abs. Coeff. for $Cu_{k\alpha}$, mm^{-1}	0.804
2θ range, °	6 to 140
Reflect. Measd.	5089($\pm h$, $+k$, $+l$)
Unique data	4539($R_{int} = 0.035$)
Parameters, restraints	322,1
Observed reflect	2768 Fo $\geq 4\sigma$(Fo)
Final R indices[b]	$R_1 = 0.086$ $wR_2 = 0.276$
Goodness of fit	1.016
Highest[b] peak, deepest hole in final difference ΔF map eÅ^{-3}	0.78, −0.29

Calix[4]arene anion receptors bearing 2,2,2-trifluoroethanol groups at the *upper* rim

Alessandro Casnati, Andrea Sartori, Laura Pirondini, Francesca Bonetti, Nicola Pelizzi, Francesco Sansone, Rocco Ungaro, Franco Ugozzoli.[a] Unit cell parameters were obtained by least-squares analysis of the setting angles of 30 reflections found in a random search on the reciprocal space. [b] $R_1 = \Sigma||Fo| - |Fc||/\Sigma|Fo|$, $wR_2 = [\Sigma w(Fo^2 - Fc^2)^2/\Sigma wFo^4]^{1/2}$. goodness − of − fit = $[\Sigma w(Fo^2 - Fc^2)^2/(n - p)]^{1/2}$, where n is the number of reflections and p the number of parameters.

(C=O). MS (CI) m/z: 1117 $(M + H)^+$100%. $C_{58}H_{54}F_6N_2O_{14}$ (1117.06).

Single Crystal X-ray Analysis

The X-ray measurements were carried out at room temperature on a Enraf Nonius CAD4 diffractometer using a graphite-monochromated $Cu_{K\alpha}$ radiation ($\lambda = 1.54178$ Å). Cell dimensions were determined from 32 $I_{hkl}(\theta,\chi,\phi)$ reflections found in a random search on the reciprocal lattice. During the systematic data collection one standard reflection, collected every 100, showed no significant fluctuations. The intensities were corrected from Lorentz and polarization but not for absorption. Crystallographic data, experimental and refinement parameters are summarized in Table V. The structure was solved by Direct Methods using SIR92 [64]. It was then completed by successive cycles of Fourier ΔF maps and refined by blocked full-matrix least-squares methods on F using SHELXL-97 [65]. Parameters refined were: the overall scale factor, the atomic coordinates and anisotropic thermal parameters for all the non-hydrogen atoms excluding the fluorine atoms for which isotropic temperature factors were used. In the symmetry-independent CF3 group the F3 group was disordered over two different orientations (site occupancy factors 0.5). In the asymmetric unit one ethanol molecule and one-half calixarene were found reaching to a 1:2 calix[4]arene: ethanol stoichiometry.

All the hydrogen atoms in the aliphatic and aromatic groups were placed at their calculated positions with the geometrical constraint C−H 0.96 Å and refined "riding" on their corresponding parent atoms. The hydroxyl hydrogen atoms were calculated by searching the best fitting of the electron density under rotations of the C−OH groups (of the calixarene and of the ethanol) along the C−O bond. The geometrical calculations were obtained by PARST97 [66]. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-272177. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax +44)1223-336-033. E-mail: deposit@ccdc.cam.ac.uk).

Molecular Modeling Calculations

The optimized structures of the complexes have been obtained by using semiempirical methods in the PM3 model [67] to have a reasonable computing time. The optimised structures of the acetate complexes were obtained starting from **3b** in its minimum energy structure and by placing the acetate anion (in its optimised structure) in selected different orientations with respect to the ligand and leaving the structure free to relax without constraints. Always all the different calculations lead to one of the five different acetate-ligand structures here reported.

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