1,3-Calix[4]arene Crown Ether Conformers with a 3-Thienyl Pendant Functionality at the Lower Rim

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Synthetic protocols to novel thienyl-calix[4]crown building blocks are reported. The selective distal introduction of a 2-(3-thienyl)ethoxy functionality into mono-*O*-alkylated calix[4]arenes **1** (R = Me, Bn), followed by cyclization of the mixed di-*O*-alkylated intermediates **2** with tetra- and pentaethylene glycol ditosylate and base, produced mixtures of 1,3-alternate and cone 1,3-calix[4]arene crown ether conformers **3** and **4**, respectively. On the other hand, the selective debenzylation (Me_3SiCl) of 1-benzyloxy-3-propoxycalix[4]arene crown-5 (cone conformer **4c**) led to cone monohydroxyderivative **5**, which upon alkylation with 2-(3-thienyl)ethanol tosylate and Cs_2CO_3 afforded the rigid partial cone calix[4]arene crown-5 **6**, having the heterocyclic pendant functionality anti to the polyether ring. The ^1H NMR resonances of ^{t}Bu substituents at the upper rim of conformationally rigid mixed 1,3-dialkoxycalix[4]arene crown ethers provide a diagnostic tool for establishing the mutual inclinations of the opposing pairs of aromatic rings. The structures of 5,11,17,23-tetrakis-(1,1-dimethylethyl)-25-methoxy-27-{[2-(3-thienyl)ethoxy]}$^{\beta}$-26,28-(crown-6)$^{\alpha}$-calix[4]arene (anti-**3aa**) and 5,11,17,23-tetrakis(1,1-dimethylethyl)-25-methoxy-27-{[2-(3-thienyl)ethoxy]}$^{\alpha}$-26,28-(crown-6)$^{\alpha}$-calix[4]arene (syn-**4aa**) conformers were determined by single-crystal X-ray analyses. Methoxy-containing calix[4]arene crown ethers possess fluxional properties, and the conformational equilibria in solution are strongly affected by alkali-metal complexation.

Introduction

Conducting polythiophenes with ion receptor sites (e.g., crown ethers) covalently anchored to the polymer backbone constitute a class of hybrid materials that are receiving considerable attention for the development of advanced sensing devices.[1] Calixarene-based ion receptors are far more size-selective than crown ethers, because the calixarene platform provides a highly preorganized architecture for the assembling of converging binding sites.[2] To date, 1,3-bridged calix[4]arene crown ethers probably represent the most potent synthetic complexing agents for alkali-metal ions,[3] with efficiencies and selectivities in some instances even higher than the naturally occurring ionophore valinomycin.[4] Calixarene-based receptors are now being used as selective sensing agents in the microconstruction of ion sensory devices.[5]

Recently, we became involved in a long-term project aimed at grafting 1,3-bridged calix[4]arene crown ether units to the *β*-position of polythiophenes, in order to create new classes of molecular sensors able to recognize and electrochemically respond to alkali-metal ions.[6] The electro-oxidative polymerization of appropriately substituted (oligo)thiophene monomers was shown to provide a useful strategy for the preparation of functionalized polythiophenes.[7] A similar strategy could be applied to the synthesis of calix[4]arene-crown-ether/polythiophene conjugates, by exploiting suitably designed calixarene crown ether building blocks, bearing an electropolymerizable (oligo)thiophene pendant functionality at the lower

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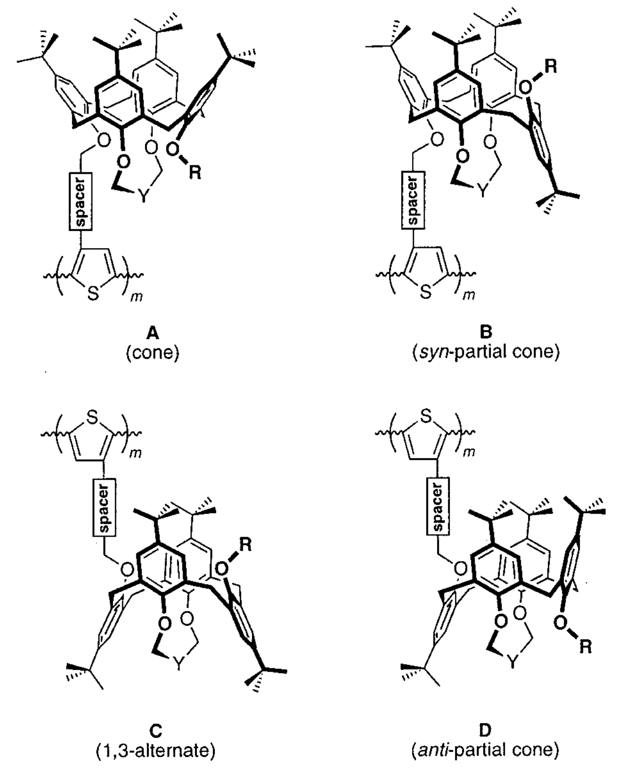


A (cone)

B (*syn*-partial cone)

C (1,3-alternate)

D (*anti*-partial cone)

Y = $(CH_2OCH_2)_n$

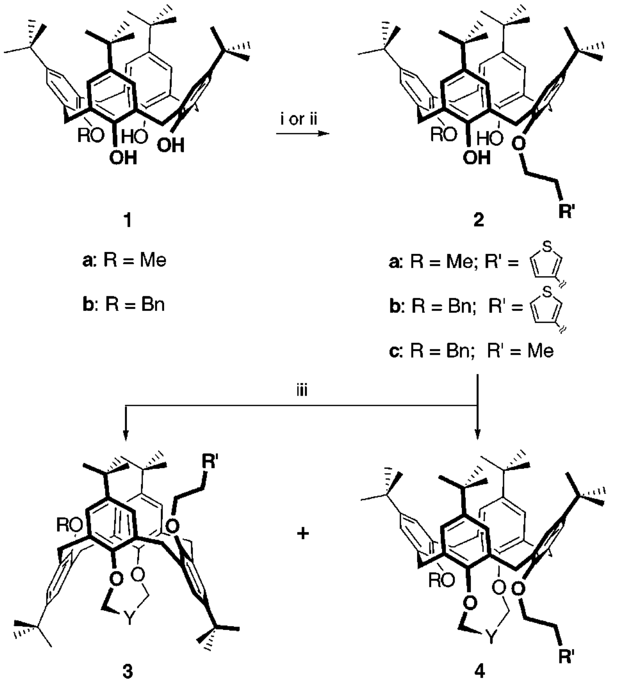
Figure 1. Structures of target conducting polymers derivable from the four possible atropisomeric calix[4]crown monomers. The sensing agents ((A) cone; (B) *syn*-partial cone; (C) 1,3-alternate; (D) *anti*-partial cone) are covalently linked to the β-position of the polythiophene backbone through a connecting spacer at the lower rim.

rim. Because calix[4]crowns with mixed functionalities at the lower rim may give rise to four atropisomers (cone, syn-partial cone, 1,3-alternate, and anti-partial cone), conducting polymers **A**–**D** with a different topology of the ionophoric moiety (see Figure 1) can be derived. It follows that the ion sensing properties of such polymers could be modulated, at least in principle, by varying the conformation of the calixarene platform, the size of the crown ether ring, and the length of the connecting spacer. To this end, the first mandatory steps are the search for efficient synthetic protocols for the stereocontrolled introduction of a 3-(oligo)thienyl pendant functionality onto the calixcrown framework, and the investigation of the ionophoric properties of the resulting calixarene building blocks. In this paper we report our initial studies on the synthesis, structural characterization, and coordinating behavior of the first 1,3-calix[4]arene crown ether conformers endowed with 2-(3-thienyl)ethoxy pendant functionality at the lower rim.[8]

Results and Discussion

Synthesis. For the synthesis of thienyl-containing *p*-*tert*-butylcalix[4]arene crown ether conformers we used two synthetic approaches: (i) the selective distal alkylation[9] of mono-*O*-alkylated *p*-*tert*-butylcalix[4]arenes **1** with 2-(3-thienyl)ethanol tosylate, followed by intrabridging of the mixed dialkylated intermediates **2** with oligoethylene glycol ditosylate and base, gave 1,3-alternate and/or cone calixcrown monomers **3** and **4** (Scheme 1); (ii) the selective debenzylation[10,11] of 1-benzyloxy-3-alkoxycalix[4]arene crown ethers (e.g., **4c**), followed by stereo-controlled introduction of the thienyl functionality afforded conformationally locked partial cone conformers (e.g., **6**, Scheme 2).

Scheme 1. Reagents and Conditions: i, 2-(3-Thienyl)ethanol Tosylate, K_2CO_3, MeCN, Reflux; ii, *n*-PrI, $KHCO_3$, MeCN, Reflux; iii, $TsOCH_2YCH_2OTs$, Cs_2CO_3, MeCN, Reflux.

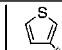
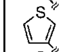
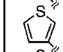
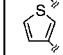


1

2

3

4

3,4	R	R'	Y
a	Me		$(CH_2OCH_2)_3$
aa	Me		$(CH_2OCH_2)_4$
b	Bn		$(CH_2OCH_2)_3$
bb	Bn		$(CH_2OCH_2)_4$
c	Bn	Me	$(CH_2OCH_2)_3$

Following the first strategy, treatment of mono-*O*-alkylated calix[4]arenes **1a**,**b** with 2-(3-thienyl)ethanol tosylate or 1-iodopropane and K_2CO_3 (molar ratio 1:1:1) in anhydrous MeCN at reflux afforded the pivotal syn-distal mixed di-*O*-alkylated derivatives **2a**–**c** in good yield (Scheme 1). The ^1H and ^{13}C NMR spectra of **2a**–**c** are consistent with a cone conformation, which is corroborated by the two AX systems of equal intensity for $ArCH_2Ar$ protons and the two resonances for the relevant carbons around 31 ppm.[2a,12] Subsequent reaction of intermediates **2a**,**b** with the appropriate oligoethylene glycol ditosylate and base produced a mixture of the

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[8] Very recently, calix[4]arenes bearing two or four 2-methylthiophene functionalities at the lower rim were reported: Danil de Namor, A. F.; Hutcherson, R. G.; Sueros Velarde, F. J.; Alvarez-Larena, A.; Briansó, J. L. *J. Chem. Soc., Perkin Trans. 1* **1998**, 2933.

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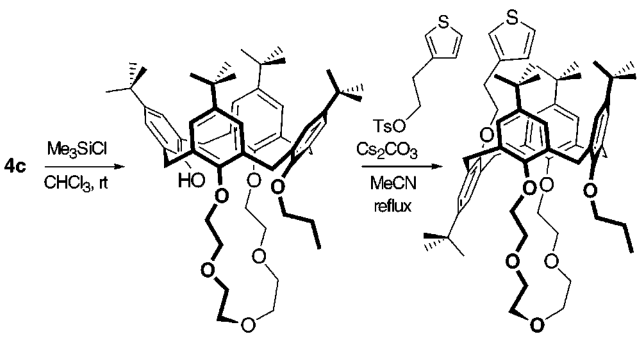
Scheme 2



5 **6**

Table 1. Product Composition in the Reaction of 2a,b with Oligoethylene Glycol Ditosylate and Cs_2CO_3 in Refluxing MeCN[a]

substrate	ditosylate	**3** (anti) %	**4** (syn) %
2a	TGD	**3a** 55 (47)	**4a** 45 (31)
2a	PGD	**3aa** 57 (41)	**4aa** 43 (24)
2b	TGD	**3b** 79 (53)	**4b** 21 (18)
2b	PGD	**3bb** 65 (55)	**4bb** 35 (25)

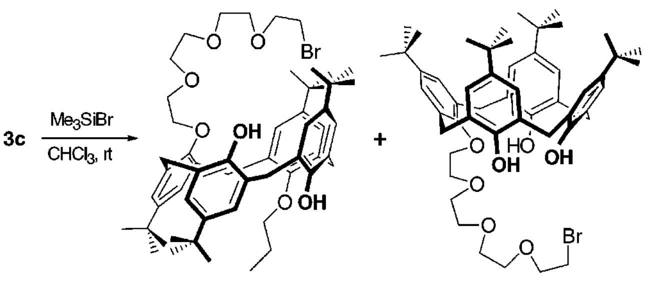
[a] Determined by ^{1}H NMR analysis of the crude product. Numbers in parentheses refer to isolated yields.

desired 1,3-calix[4]arene crown ether conformers **3** and **4** endowed with a 3-thienyl pendant functionality at the lower rim (Scheme 1), which were easily separated by column chromatography.

The stereochemical outcome of these reactions can be driven by the template effect of the cation present in the base used.[3d,e,4c] Accordingly, a preliminary reaction of **2b** with tetraethylene glycol ditosylate (TGD) and NaH in anhydrous tetrahydrofuran (THF) afforded cone crown-5 derivative **4b** as the sole product, whereas with Cs_2CO_3/MeCN a mixture of 1,3-alternate and cone conformers **3b** and **4b** (ratio 4:1, respectively) was produced. Because 1,3-alternate calix[4]arene crown ethers were shown to be more efficient and selective ionophores than their cone analogues,[4] the Cs_2CO_3/MeCN system was chosen for further reactions.

The conformer distribution in the reaction of **2a**,**b** with oligoethylene glycol ditosylates and Cs_2CO_3 in anhydrous MeCN is shown in Table 1. The reactions of **2a** with TGD and pentaethylene glycol ditosylate (PGD) surprisingly afford almost comparable yields of the two conformers. These results can be explained by taking into account the fluxional properties of methoxy derivatives, owing to the easy passage of the methoxy substituent through the annulus (vide infra).[13] Given that the *p*-*tert*-butylanisyl moiety can assume two extreme "up" or "down" orientations, henceforth the structure of each pair of isolated conformational isomers of calix[4]arene crown ethers with methoxy substituents will be designated as syn and anti, according to whether the heterocyclic pendant group is on the same side or the opposite side with respect to the polyether chain. Obviously, these notations are independent of the overall conformation(s) adopted by the molecule.

Scheme 3



7 **8**

The intrabridging of distal hydroxyl groups in **2b**,**c** with a polyether chain affords atropisomeric 1,3-alternate and/or cone crown ether derivatives. Because conformationally rigid partial cone calix[4]arene crown ethers are precluded by this procedure, a sequence involving the debenzylation of the 1,3-alternate conformer **3b** with Me_3SiBr in $CHCl_3$ followed by the stereocontrolled alkylation of the resulting mono-hydroxy intermediate was envisioned. Unfortunately, the reaction was rather unselective and produced intractable mixtures, from which no pure components could be isolated. Thus, to circumvent this problem, we applied the debenzylation procedure to the mixed benzyloxy-propoxy derivative **4c**, postponing the introduction of the thienyl functionality to the last step. Indeed, treatment of **4c** with Me_3SiCl (20 equiv) in anhydrous $CHCl_3$ at room temperature smoothly afforded mono-hydroxy calixcrown **5** (75%), which was converted into anti-partial cone **6** (54%) by alkylation with 2-(3-thienyl)ethanol tosylate and Cs_2CO_3 in refluxing MeCN (Scheme 2). This second route paves the way to the synthesis of thieno-calix[4]arene crown ethers in a fixed anti-partial cone conformation.

Attempts to extend the debenzylation procedure to the 1,3-alternate isomer **3c** were unsuccessful. The reaction with Me_3SiCl gave unreacted **3c**, while the more reactive Me_3SiBr produced a mixture of **7** (75% yield, product of further opening of the polyether ring) and **8** (8% yield, product of further cleavage of the propoxy group) (see Scheme 3). Structures **7** and **8** were assigned by NMR spectroscopy. The ^{1}H NMR spectrum of the inherently chiral **7** is very complex, and was analyzed with the aid of a 2D correlation spectroscopy (COSY) experiment. The diagnostically important $ArCH_2Ar$ protons of **7** give rise to two AX systems, a pseudo singlet and an AB system of relative intensity 1:1:1:1, and the relevant carbons show four resonances at δ 32.5, 32.9, 37.2, and 39.2 ppm. Although these patterns are compatible with a partial cone or 1,2-alternate structure, the former was ruled out on the basis of the remarkable upfield shifts experienced by both propoxy and oxyethylene protons, which only in the 1,2-alternate conformation are respectively exposed to the diamagnetic shielding effect from two pairs of adjoining aryl rings (one hemicavity above the main plane containing the four methylene groups and one below). On the other hand, the NMR spectral characteristics of **8** support a cone conformation.

The different behavior of **3c** compared to **4c** upon exposure to trimethylsilyl halides is likely ascribed to steric factors which are due to the inaccessibility in the former of the nucleophilic center (O−Bn oxygen, see Figure 2), which is shielded by the adjoining aryl rings. In agreement with this interpretation, the crystal struc-

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(12) (a) Gutsche, C. D.; Dhawan, B.; Levine, J. A.; No, K. H.; Bauer, L. J. *Tetrahedron* **1983**, *39*, 409. (b) Jaime, C.; de Mendoza, J.; Prados, P.; Nieto, P. M.; Sánchez, C. *J. Org. Chem.* **1991**, *56*, 3372.

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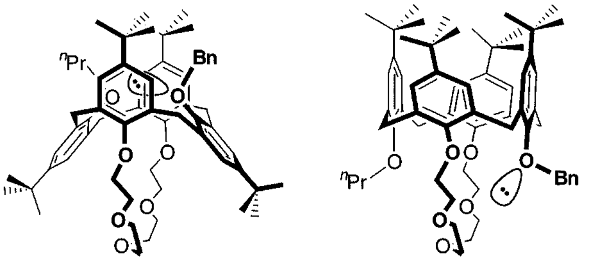


3c **4c**

Figure 2. A representation of the different orientation of the benzylic oxygen lone pair in the two conformers **3c** and **4c**. The nucleophilic attack on the bulky trimethylsilyl halide is prevented in **3c** by the steric encumbrance of the two rotated aryl rings.

ture of the diethoxy analogue of **3c** (1,3-alternate 1,3-diethoxy-*p*-*tert*-butylcalix[4]arene crown-5) showed that the oxygen lone pairs of the appended substituents point inside the cavity.[3d] Therefore, the isolation of **7** and **8** from the reaction of **3c** and Me_3SiBr implies that the less reactive but more accessible $C_\alpha-O$ bond of the polyether ring is cleaved first (relieving the steric overcrowding by conformational reorganization of the molecule), followed then by the scission of the O−Bn and eventually O−^{n}Pr linkages in that order.

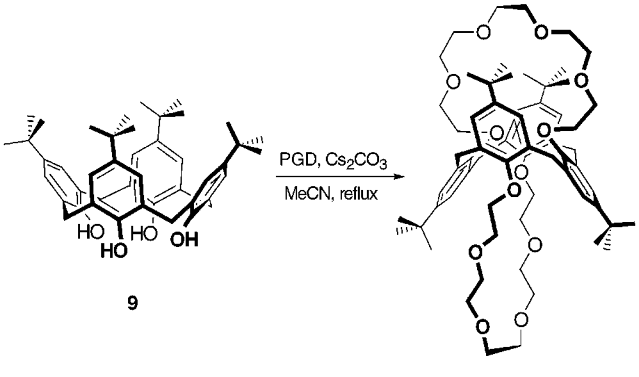
NMR Characterization of Conformationally Fixed Calix[4]arene Crown Ethers. Structural assignments of rigid calix[4]arene crown ethers **3**, **4**, and **6** were firmly established by ^{1}H and ^{13}C NMR spectroscopy, on the basis of distinctive spectral patterns of the bridging methylene protons and the position of the resonances of pertinent carbons.[12]

The spectra of each set of conformers are uniform, and as an example we here discuss the spectral characteristics of crown-6 conformers **3bb** and **4bb**. Both compounds show a C_s symmetry (plane passing through the two distal substituents as the only symmetry element), which is reflected in the NMR patterns of the calixarene skeleton. Accordingly, **3bb** and **4bb** show three singlets for ^{t}Bu groups, and an AB system and two singlets for the aromatic protons (relative intensity 2:1:1). However, they can be easily differentiated by the diagnostic spectral patterns of $ArCH_2Ar$ protons: the cone conformer **4bb** shows two AX systems (ratio 1:1), with a $\Delta\delta$ separation > 1 ppm between geminal protons, whereas the 1,3-alternate conformer **3bb** exhibits an AB system and a pseudo-singlet (ratio 1:1) in the region 3.75−3.95 ppm. The cone and 1,3-alternate structures are further corroborated by their ^{13}C NMR spectra, which show two resonances for the Ar*C*H_2Ar groups close to 31 or 39 ppm, respectively, in agreement with the de Mendoza rule for the determination of calix[4]arene conformations.[12b]

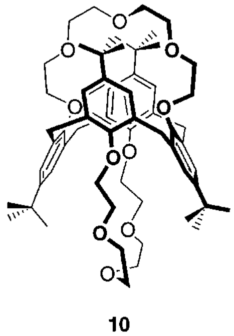
Table 2. Chemical Shifts (300 MHz, $CDCl_3$) of ^{t}Bu Groups in Conformationally Rigid 1,3-Calix[4]arene Crown Ethers 3 and 4, bis-Crown Ethers 10 and 11, and *p*-*tert*-butyl-calix[4]arene (9)

compound		δ_{tBu}, ppm	
3b	0.94 (18 H)	1.40 (9 H)	1.41 (9 H)
3bb	0.95 (18 H)	1.38 (9 H)	1.40 (9 H)
3c	1.01 (18 H)	1.38 (9 H)	1.40 (9 H)
4b	0.80 (9 H)	0.82 (9 H)	1.34 (18 H)
4bb	0.82 (9 H)	0.83 (9 H)	1.33 (18 H)
4c	0.80 (9 H)	0.82 (9 H)	1.34 (18 H)
9		1.15 (36 H)	
10		1.15 (36 H)	
11		1.36 (36 H)	

Scheme 4



9 **11**



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The chemical shifts of the ^{t}Bu groups in these molecules deserve further comment. In the parent *p*-*tert*-butylcalix[4]arene (**9**), which adopts a regular C_{4v} cone conformation by virtue of a cyclic array of H bonds,[14] the ^{t}Bu groups resonate at δ 1.15 ppm. On the other hand, in the usual C_{2v} cone conformation of 1,3-dialkoxy-*p*-*tert*-butylcalix[4]arene crown ethers, the ^{t}Bu groups of the two converging aryl rings experience an upfield shift, while concomitantly those of the two diverging aryl rings undergo a downfield shift. The extent of these upfield and downfield shifts reaches a maximum ($\Delta\delta$ ca. 0.30−0.35 ppm) when two opposing aryl rings lie in parallel planes and the other two are essentially normal to one another. The low symmetry of our mixed di-*O*-alkylated crown ethers allows us to distinguish and easily assign the ^{t}Bu resonances of the aryl rings holding the polyether chain by integration of the signals. The chemical shifts of the ^{t}Bu groups of conformationally fixed calix[4]arene crown ethers **3** and **4** are gathered in Table 2. For comparison purposes, the ^{t}Bu resonances of **9**, 1,3−2,4-*p*-*tert*-butylcalix[4]arene bis-crown-5 (**10**)[3b] and 1,3−2,4-*p*-*tert*-butylcalix[4]arene bis-crown-6 (**11**), the latter obtained in 32% yield by reaction of **9** with PGD and Cs_2CO_3 in refluxing MeCN (Scheme 4), are also reported. It is easily deduced that the aryl rings supporting the polyether chain are converging ($\delta_{t_{\text{Bu}}} < 1.15$ ppm) in 1,3-alternate conformers **3** and diverging ($\delta_{t_{\text{Bu}}} > 1.15$ ppm) in the cone conformers **4**. The isocrony of ^{t}Bu resonances in **9** and **10** ($\delta_{t_{\text{Bu}}} = 1.15$ ppm) suggests the same inclination of aryl residues with respect to the reference plane, whereas those in **11** ($\delta_{t_{\text{Bu}}} = 1.36$ ppm) assume a more flattened shape.[15] Therefore, the ^{t}Bu resonances of mixed 1,3-dialkoxycalix[4]arene

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(14) Andreetti, G. D.; Ungaro, R.; Pochini, A. *J. Chem. Soc. Chem. Commun.* **1979**, 1005.

crown ether conformers provide a diagnostic tool for establishing the mutual inclination of opposing pairs of aryl rings with respect to the methylene carbon plane.

The NMR spectra of conformer **6**, synthesized via the protection−deprotection method, are consistent with a partial cone conformation, because its methylene protons show up as an AX system and a pseudo-singlet (relative intensity 1:1) with resonances for the respective carbons close to 31 and 39 ppm. The protons of the pendant heterocyclic moiety attached to the inverted phenol ring are particularly shielded, because of their tendency to fill the hydrophobic cavity generated by the three remaining phenol rings.[16]

Fluxional Properties of Calix[4]arene Crown Ethers with a Methoxy Substituent at the Lower Rim. Structural assignments of methoxy-containing calix[4]arene crown ethers (**3a**, **4a**, **3aa**, and **4aa**) were complicated by their fluxional behavior, so that dynamic NMR studies (from −50 to +120 °C) were deemed essential to establish their conformation in solution. The room temperature ^{1}H NMR spectrum ($CDCl_3$, 300 MHz) of anti-**3a** shows broad signals, especially for the diagnostically important bridging methylene protons, compatible with a slow interconversion between conformers on the NMR time scale (Figure 3, trace c). The presence of a triplet in the high field region (ca. 2 ppm), assigned to the β-oxymethylene protons of the ethylene spacer connecting the 3-thienyl ring to the calixarene, is suggestive of an anti orientation of the heterocyclic ring relative to the polyether chain. Upon heating, a simplification of the various spectral regions is observed. At 100 °C in deuterated 1,1,2,2-tetrachloroethane (TCE), the spectrum shows an AX system (δ 3.47 and 4.22 ppm, J_{AX} = 13.9 Hz) and a pseudo-singlet at δ 3.89 ppm of equal intensity for the $ArCH_2Ar$ groups, indicative of a preferential partial cone conformation (Figure 3, trace e). The aromatic region shows, as expected, an AB system and two singlets for the aromatic protons of the calixarene skeleton, and a well-resolved 12-line pattern (AMX system) for the 3-thienyl residue. On the other hand, upon lowering the temperature to 0 °C, broadening of every region is observed (T_c) (Figure 3, trace b). Below −20 °C doubling of most signals occurs, indicating a slow equilibrium between partial cone and 1,3-alternate conformers. At −50 °C the ^{t}Bu region shows two distinct sets of signals (δ 0.84, 1.36, and 1.46 ppm; δ 1.20, 1.37, and 1.38 ppm; relative intensities 2:1:1) in the ratio 3:2, which were assigned to partial cone and 1,3-alternate conformers, respectively, by correlation of their relative intensities with those of the AX system ($ArCH_2Ar$, δ 3.18 and 4.29, J_{AX} = 12.4 Hz) diagnostic for the partial cone conformer, and of the multiplet centered at δ 2.99 ppm (α-oxymethylenes of the polyether bridge), peculiar to the 1,3-alternate conformer (Figure 3, trace a). The latter protons are typically shifted upfield by the ring current diamagnetic shielding effect of the two rotated aryl rings.

The ^{1}H NMR spectrum (TCE) of conformer syn-**4a** at +100 °C is consistent with an “up” orientation of the *p-tert*-butylanisyl residue (cone conformation), as evidenced by the presence of two AX systems of equal intensity for $ArCH_2Ar$ groups (δ 3.19 and 4.45, J_{AX} = 12.6 Hz; δ 3.38 and 4.26, J_{AX} = 12.2 Hz). The former remains sharp in the temperature range investigated (−50 to +120 °C), while the latter is broad and disappears below +70 °C to reappear again at temperatures below 0 °C. However, even at −50 °C the up−down interconversion of the *p-tert*-butylanisyl moiety is fast enough to prevent the freezing of cone and partial cone conformers.

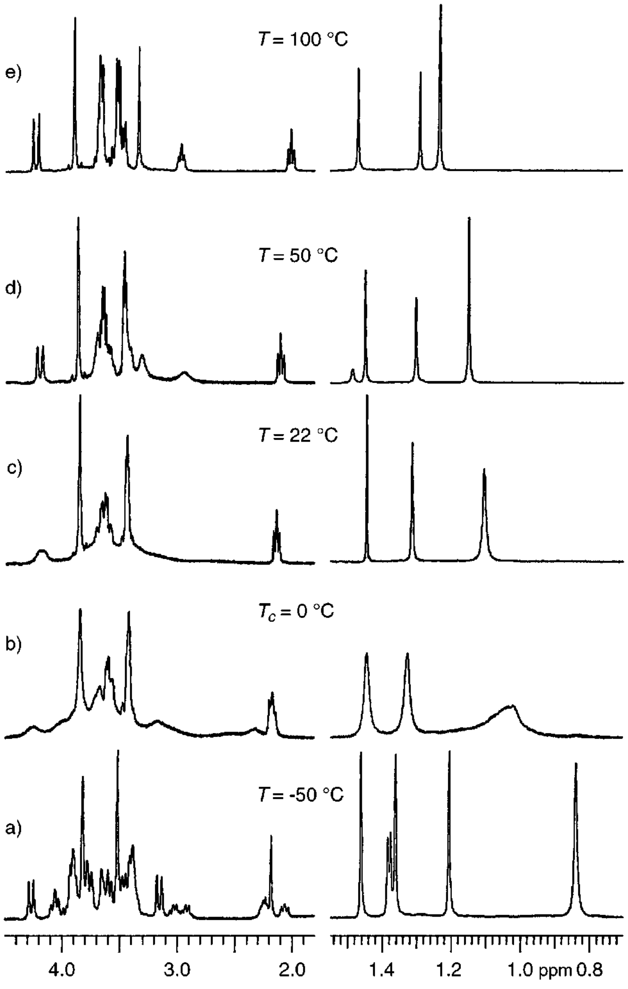

Figure 3. Variable-temperature ^{1}H NMR spectra (300 MHz) of anti-**3a**. Traces (a)−(d) in $CDCl_3$ and trace (e) in TCE. Spectral regions are plotted on different horizontal and vertical scales.

From a comparison of the fluxional properties of anti-**3a** and syn-**4a**, it emerges that the flipping motion of the *p-tert*-butylanisyl group is considerably slowed in anti-**3a** by the self-inclusion of the heterocyclic functionality attached to the inverted phenol ring inside the cavity,[16] which makes the up−down movement of the methoxy substituent more difficult. This conclusion is supported by the fact that at −50 °C in anti-**3a** the partial cone conformer prevails over cone.

Not unexpectedly, anti-**3aa** and syn-**4aa** are more mobile than their crown-5 counterparts, because of the increased size of the polyether chain. Their ^{1}H NMR spectra show sharp resonances in a wide temperature range (−30 to +120 °C), suggestive of a conformational preference for partial cone (anti-**3aa**) or cone (syn-**4aa**). Broadening of signals occurs at temperatures below −50 °C (CD_2Cl_2), but even at −90 °C it was not possible to freeze the two extreme conformations and establish their

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[15] Single-crystal X-ray analysis of **10** has shown an unusually regular 1,3-alternate conformation: Asfari, Z.; Harrowfield, J. M.; Sobolev, A. N.; Vicens, J. *Aust. J. Chem.* **1994**, *47*, 757.

[16] Pappalardo, S. *New J. Chem.* **1996**, *20*, 465.

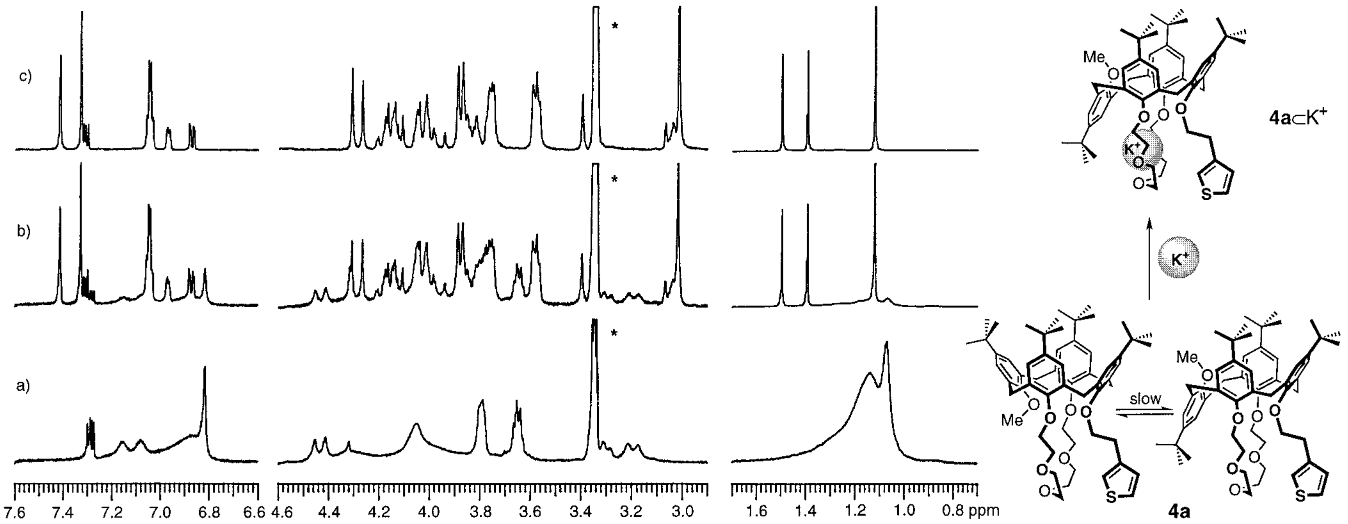

Figure 4. ^{1}H NMR spectrum (300 MHz, $CDCl_3-CD_3OD$, 1:1, v/v, 22 °C) of syn-**4a** (slow cone ⇌ partial cone equilibrium) (a), and spectral changes upon addition of 0.5 (b) and 1.0 equiv. (c) of KSCN. Spectral regions are plotted on different horizontal and vertical scales and asterisk indicates residual solvent peak.

relative populations. Structure assignments for anti-**3aa** and syn-**4aa**, deduced by dynamic NMR studies, were further proven by single-crystal X-ray analyses (see below).

The conformational equilibria of methoxy-containing calix[4]arene crown ethers are strongly affected by the presence of alkali-metal ions.[3d,4a] Previous studies in this laboratory showed that the various conformers (cone, partial cone, and 1,3-alternate) of 1,3-*p*-*tert*-butylcalix[4]arene crown-5 with picolyl pendant groups at the lower rim display a remarkable affinity for K^+.[4c] The sequence of the stability constants of K^+ complexes follows the order partial cone > 1,3-alternate > cone. This trend is qualitatively confirmed by preliminary ^{1}H NMR titration experiments ($CDCl_3-CD_3OD$ 1:1, v/v) of syn-**4a** with KSCN (up to 2 equiv.), shown in Figure 4. A sharpening of the signals is observed from the addition of the first aliquot of salt, and after 1 equiv of KSCN has been added a *single complexed species* is present, which is not further modified by the addition of an excess of salt. A close scrutiny of the spectrum of the complex indicates that the K^+ ion is best accommodated by the partial cone conformer. This is supported by a distinctive pattern for the $ArCH_2Ar$ groups (one AX and one AB system of equal intensity), and by the high field resonance of the methoxy group (ca. 3.0 ppm), shielded by the two flanking aryl rings (Figure 4, trace c).

On the other hand, the titration experiments of anti-**3a** with KSCN (not shown) indicate the formation of both partial cone and 1,3-alternate K^+ complexes in the ratio 5:1, respectively. These results parallel the stability order previously observed for the K^+ complexes of the various conformers of calix[4]arene crown-5 with picolyl pendant groups.[4c]

Titration experiments of crown-6 derivatives anti-**3aa** and syn-**4aa** with cesium picrate evidenced a higher affinity of the former for Cs^+, because it is the only isomer able to assume the 1,3-alternate conformation, which better stabilizes the Cs^+ complex through additional cation/π-electron interactions.[3d,17]

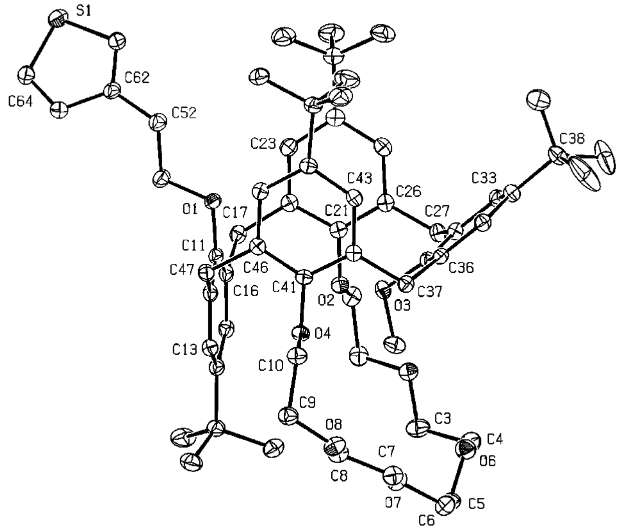

Figure 5. A view of anti-**3aa** with our numbering scheme made with PLATON.[18] Displacement ellipsoids are drawn at the 30% probability level, H atoms are omitted and only one orientation of the methyl groups at C38 is shown.

X-ray Analysis of anti-3aa and syn-4aa Conformers. Suitable crystals of the two conformers were obtained by slow evaporation of MeCN solutions. Views of the solid state conformation of anti-**3aa** and syn-**4aa** are shown in Figures 5 and 6, respectively. Molecular dimensions for both compounds are normal. In anti-**3aa** the aromatic ring C11−C16, bearing the thienyl pendant group, is on the opposite side of the plane of the bridging methylene groups (C17, C27, C37, C47) from the remaining three aromatic rings, with its ring plane essentially normal to the methylene carbon plane (dihedral angle 89.8(1)°). The two aromatic rings linked by the polyether chain (C21−C26, C41−C46) are almost parallel to one another (interplanar angles of 85.6(1) and 86.8(1)° with the reference plane), whereas ring C31−C36 containing the methoxy substituent is tilted back and makes a dihedral angle of 39.3(1)° with the methylene carbon plane. Molecule syn-**4aa** adopts a conformation commonly found in calix[4]arenes in the cone conformation, with

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[17] Lamare, V.; Dozol, J. F.; Ugozzoli, F.; Casnati, A.; Ungaro, R. *Eur. J. Org. Chem.* **1998**, *1559*, 9.

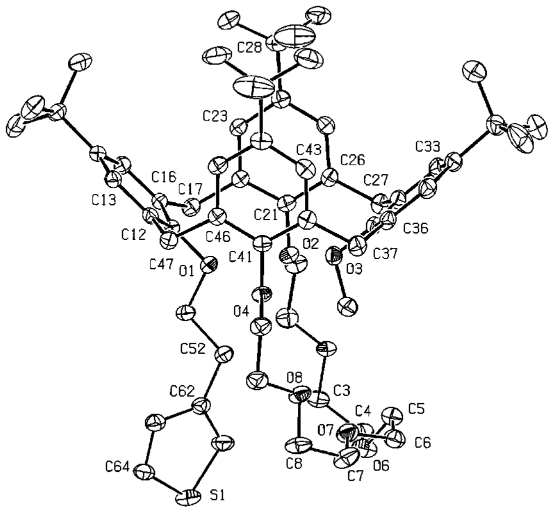

Figure 6. A view of syn-**4aa** with our numbering scheme. For clarity, displacement ellipsoids are drawn at the 30% probability level, H atoms are omitted and only one orientation of the disordered moieties (methyl groups at C28, polyether chain, and thienyl ring) is shown.

two opposite aromatic rings almost parallel and the remaining two almost normal to each other. Thus, the two rings C21−C26 and C41−C46 linked by the polyether chain are almost parallel to one another (interplanar angles of 89.5(1) and 86.5(1)°, respectively, with the reference plane, C17, C27, C37, C47). Ring C11−C16 with the thienyl substituent is inclined at 45.0(1)° to the reference plane, whereas the corresponding angle for ring C31−C36 is 38.2°.

Not surprisingly, the polyether chains in the partial cone and cone stereoisomers adopt significantly different conformations. In partial cone anti-**3aa** the unsigned values of 8 of the 10 C−O−C−C angles are in the range 169.3(2) to 179.4(2)° with the two values (C5−O6−C4−C3 86.4(2) and C8−O8−C9−C10 −89.4(2)°) being significantly different; the unsigned values of 4 of the 5 O−C−C−O angles are in the range 73.3(2) to 78.8(2)° with one value (O7−C7−C8−O8, −177.6(2)°) significantly different. By contrast, in the cone syn-**4aa** structure (in which the polyether chain is disordered over two unequal conformations) in the major (90%) conformation the unsigned values of the O−C−C−O torsion angles are all in the range 62.8(3) to 77.3(3)° and in the C−O−C−C torsion angles, only 1 of the 10 angles (C5−O6−C4−C3 −90.6(4)°) is markedly different from the others (unsigned values of remaining C−O−C−C angles in the range 166.9(2) to 179.9(2)°). In the minor conformation two O−C−C−O conformations are gauche (−65(2) and 71(3)°) with the third value −119(2)°; four C−O−C−C torsion angles are close to a fully trans conformation with one value close to gauche (−73°). Inter-calixarene contacts in both compounds are of the van der Waals variety and there are no solvent accessible voids in the crystal lattice.[18]

Conclusions

We developed straightforward synthetic procedures for the attainment of the first 1,3-calix[4]arene crown ether conformers endowed with a 3-thienyl pendant functionality at the lower rim. ^{1}H NMR complexation studies, presently confined to mobile methoxy derivatives, clearly demonstrated that the presence of the heterocyclic moiety in these systems is not prejudicial to their recognition properties for alkali-metal ions, the trend observed being consistent with previous findings on related ionophores devoid of this group.[4] The search for alternative synthetic routes leading to rigid syn-partial cone congeners, the extension of these protocols to the synthesis of analogous systems bearing an (oligo)thiophene functionality at the lower rim, and the use of these preorganized building blocks for the electrochemical synthesis of target calix[4]arene-crown-ether/poly(thiophene) conjugates are under current investigation.

Experimental Section

General. All chemicals were reagent grade and were used without further purification. Anhydrous solvents and 2-(3-thienyl)ethanol were obtained commercially. Melting points were determined on an electrothermal melting point apparatus and are uncorrected. Unless otherwise stated, ^{1}H and ^{13}C NMR spectra were recorded in CDCl$_3$ at 300 and 75 MHz, respectively, with tetramethylsilane (TMS) as the internal standard. The multiplicity of the ^{13}C signals was determined with the attached proton test (APT) technique. For fast atom bombardment (FAB) (+) mass spectra, 3-nitrobenzyl alcohol was used as the matrix. *p-tert*-Butylcalix[4]arene (**9**),[19] monoalkylated calix[4]arenes **1a**,[20] **1b**,[11b] tetra- and pentaethylene glycol ditosylates,[21] and 2-(3-thienyl)ethanol tosylate[22] were prepared according to reported procedures or slight modifications thereof. All reactions were carried out under nitrogen atmosphere.

Mixed *Syn-distal* Di-*O*-alkylated Calix[4]arenes 2. General Procedure. A stirred mixture of **1** (0.4 mmol), the appropriate electrophile (0.42 mmol), and K$_2$CO$_3$ (0.055 g, 0.4 mmol) in anhydrous MeCN (20 mL) was refluxed for 36−48 h. The reaction was monitored by thin-layer chromatography (TLC) (petroleum ether−Et$_2$O, 11:1). After the mixture was cooled, the solvent was evaporated, and the residue was partitioned between 1 N HCl and CH$_2$Cl$_2$. The organic extract was washed with water, dried over MgSO$_4$, and concentrated. The crude product was purified by column chromatography (SiO$_2$, petroleum ether−Et$_2$O 20:1 to 9:1), followed by recrystallization from an appropriate solvent.

5,11,17,23-Tetrakis(1,1-dimethylethyl)-25-methoxy-27-[2-(3-thienyl)ethoxy]-26,28-dihydroxy-calix[4]arene (2a): obtained in 67% yield from **1a** and 2-(3-thienyl)ethanol tosylate; mp 133−135 °C (MeOH); ^{1}H NMR δ 0.93, 0.95, 1.29 (s, ratio 1:1:2, 36 H), 3.29 (d, J = 13.0 Hz, 4 H), 3.35 (t, J = 7.4 Hz, 2 H), 3.96 (s, 3 H), 4.19 (t, J = 7.4 Hz, 2 H), 4.25, 4.28 (d, J = 13.0 Hz, 2H each), 6.76, 6.79 (s, 2 H each), 7.06 (pseudo-s, 4 H), 7.11 (dd, J = 4.8, 1.4 Hz, 1 H), 7.13 (br s, 1 H), 7.25 (br s, 3 H), and 7.28 (dd, J = 4.8, 2.9 Hz, 1 H); ^{13}C NMR δ 30.9, 31.4, 31.66 (t, ArCH$_2$Ar and OCH$_2$$CH_2$Th), 30.98, 31.00, 31.7 (q, C(CH$_3$)$_3$), 33.82, 33.87, 33.90 (s, C(CH$_3$)$_3$), 63.4 (q, OCH$_3$), 76.4 (t, OCH$_2$CH$_2$Th), 121.9 (d, Th), 125.02, 125.04, 125.41, 125.46, 125.52 (d, Ar and Th), 127.8, 128.0 (s, bridgehead-C), 128.5 (d, Th), 132.3, 132.4 (s, bridgehead-C), 138.1 (s, 3-Th) 141.4, 146.7, 146.9 (s, C_{sp2}−^{t}Bu), 150.1, 150.5, and 151.0 (s, C_{sp2}−O); FAB (+) MS, m/z 773 (MH$^+$). Anal. Calcd for C$_{51}$H$_{64}$O$_4$S: C, 79.23; H, 8.35; S, 4.14. Found: C, 79.45; H, 8.52; S, 4.08.

5,11,17,23-Tetrakis(1,1-dimethylethyl)-25-benzyloxy-27-[2-(3-thienyl)ethoxy]-26,28-dihydroxy-calix[4]arene (2b): obtained in 72% yield from **1b** and 2-(3-thienyl)ethanol

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[18] Spek, A. L. PLATON Molecular Geometry and Graphics Program, November, 1998 version. University of Utrecht, Utrecht, Holland.

[19] Gutsche, C. D.; Iqbal, M. *Org. Synth.* **1989**, *68*, 234.

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[21] Ouchi, M.; Inoue, Y.; Kanzaki, T.; Hakushi T. *J. Org. Chem.* **1984**, *49*, 1408.

[22] Noyce, D. S.; Castenson, R. L. *J. Am. Chem. Soc.* **1973**, *95*, 1247.

tosylate; mp 116−117 °C (MeCN); ^{1}H NMR δ 0.97, 0.99, 1.27 (s, ratio 1:1:2, 36 H), 3.26 and 4.34 (AX, J = 12.8 Hz, 4 H), 3.29 (t, J = 7.0 Hz, 2 H), 3.31 and 4.19 (AX, J = 13.1 Hz, 4 H), 4.13 (t, J = 7.0 Hz, 2 H), 5.04 (s, 2 H), 6.80, 6.85 (s, 2 H each), 7.03 (ABq, J = 2.4 Hz, 4 H), 7.12 (dd, J = 4.6, 1.5 Hz, 1 H), 7.19−7.22 (m, 2 H), 7.32−7.43 (m, 3 H), 7.46 (s, 2 H), 7.72 (d, J = 7.2 Hz, 2 H); ^{13}C NMR δ 30.8, 31.7, and 31.8 (t, ArCH$_2$Ar and OCH$_2$$CH_2$Th), 31.03, 31.05, 31.6 (q, C(CH$_3$)$_3$), 33.8, 33.96, 34.0 (s, C(CH$_3$)$_3$), 76.4 (t, OCH$_2$CH$_2$Th), 78.3 (t, OCH$_2$Ph), 122.0, 125.00, 125.04, 125.5, 125.6 (d, Ar and Ph), 127.7 (s, bridgehead-C), 128.0, 128.1, 128.52, 128.56 (d, Ar, Ph, and Th), 132.7, 132.9 (s, bridgehead-C), 136.8 (s, Ph), 138.2 (s, 3-Th), 141.5, 147.1, 147.3 (s, $C_{sp2}-{}^t$Bu), 149.7, 149.8, and 150.5 (s, $C_{sp2}-$O); FAB (+) MS, m/z 849 (MH$^+$). Anal. Calcd for $C_{57}H_{68}O_4S$: C, 80.61; H, 8.08; S, 3.77. Found: C, 80.46; H, 8.17; S, 3.82.

5,11,17,23-Tetrakis(1,1-dimethylethyl)-25-propoxy-27-benzyloxy-26,28-dihydroxy-calix[4]arene (2c): obtained in 68% yield from **1b** and propyl iodide; mp 237−238 °C (MeOH); ^{1}H NMR δ 1.00, (s, 18 H), 1.20 (t, J = 7.4 Hz, 3 H), 1.27 (s, 18 H), 1.99 (m, 2 H), 3.29 (d, J = 13.0 Hz, 4 H), 3. 92 (t, J = 6.3 Hz, 2 H), 4.26, 4.32 (d, J = 13.0 Hz, 2 H each), 5.05 (s, 2 H), 6.84, 6.85 (s, 2 H each), 7.03 (pseudo-s, 4 H), 7.36−7.45 (m, 3 H), and 7.71−7.74 (m, 4 H); ^{13}C NMR δ 10.9 (q, OCH$_2$CH$_2$$CH_3$), 23.4 (t, OCH$_2$$CH_2CH_3$), 31.05, 31.06, 31.7 (q, C(CH$_3$)$_3$), 31.8 (t, ArCH$_2$Ar), 33.8, 33.9, 34.0 (s, C(CH$_3$)$_3$), 77.9, 78.0 (t, OCH$_2$-CH$_2$CH$_3$ and OCH$_2$Ph), 125.0, 125.4, 125.6, 127.5, 127.8, 128.4 (d, Ar and Ph), 127.6, 127.7, 132.7, 132.8 (s, bridgehead-C), 137.1 (s, Ph), 141.2, 146.7, 146.9 (s, $C_{sp2}-{}^t$Bu), 149.77, 149.81, and 150.8 (s, $C_{sp2}-$O); FAB (+) MS, m/z 781 (MH$^+$). Anal. Calcd for $C_{54}H_{68}O_4$: C, 83.02; H, 8.78. Found: C, 82.75; H, 8.64.

Synthesis of 1,3-Bridged Calix[4]arene Crown Ethers 3 and 4. General Procedure. A mixture of **2** (1.0 mmol) and Cs_2CO_3 (3.26 g, 10 mmol) in anhydrous MeCN (80 mL) was refluxed for 1 h. Then a solution of the appropriate oligoethylene glycol ditosylate (1.1 equiv.) in anhydrous MeCN (20 mL) was added dropwise over 2 h under rapid stirring. The mixture was refluxed for an additional 36−48 h. Progress of the reaction was monitored by TLC, following the disappearance of the ditosylate. After evaporation of the solvent, the residue was partitioned between 1 N HCl and CH_2Cl_2. The organic extract was washed with water, dried over $MgSO_4$, and concentrated. The crude product was separated into the pure components by column chromatography (SiO$_2$, CH$_2$Cl$_2$−AcOEt 7:1; petroleum ether−AcOEt 10:1 for **3c** and **4c**) to afford conformers **3** (fastest moving products) and **4**. For **3a** and **4a**, the elution order was inverted.

5,11,17,23-Tetrakis(1,1-dimethylethyl)-25-methoxy-27-[2-(3-thienyl)ethoxy]$^\beta$-26,28-crown-5$^\alpha$-calix[4]arene,[23] anti Conformer (3a): 47% yield, mp 261−263 °C (MeCN); ^{1}H NMR (TCE, +100 °C) δ 1.22, 1.28, 1.46 (s, ratio 2:1:1, 36 H), 2.00, 2.96 (t, J = 7.2 Hz, 2 H each), 3.33 (s, 3 H), 3.44−3.68 (m, 18 H), 3.89 (pseudo-s, 4 H), 4.22 (d, J = 13.9 Hz, 2 H), 6.57 (dd, J = 3.0, 1.2 Hz, 1 H), 6.68 (dd, J = 4.9, 1.2 Hz, 1 H), 6.98 and 7.05 (ABq, J = 2.5 Hz, 4 H), 7.03 (s, 2 H), 7.14 (dd, J = 4.9, 3.0 Hz, 1 H), and 7.16 (s, 2 H); ^{13}C NMR (TCE, +85 °C) δ 30.0 (t, OCH$_2$$CH_2$Th), 31.2 (×2), 31.4, 31.6 (q, C(CH$_3$)$_3$), 33.5, 33.6, 33.7 (s, C(CH$_3$)$_3$), 33.8 (t, ArCH$_2$Ar), 60.8 (q, OCH$_3$), 69.4 (t, OCH$_2$CH$_2$Th), 70.4, 70.5, 70.6, 72.2 (t, OCH$_2$$CH_2$O), 119.7, 124.2, 125.0, 125.5, 125.8, 126.4, 128.1 (d, Ar and Th), 132.7, 133.2, 133.6, 134.1 (s, bridgehead-C), 139.1 (s, 3-Th), 144.0, 144.3, 144.4 (s, $C_{sp2}-{}^t$Bu), 154.1, 154.2, and 154.8 (s, $C_{sp2}-$O); FAB (+) MS, m/z 931 (MH$^+$). Anal. Calcd for $C_{59}H_{78}O_7S$: C, 76.09; H, 8.44; S, 3.44. Found: C, 76.27; H, 8.58; S, 3.35.

5,11,17,23-Tetrakis(1,1-dimethylethyl)-25-methoxy-27-[2-(3-thienyl)ethoxy]$^\alpha$-26,28-crown-5$^\alpha$-calix[4]arene,[23] syn Conformer (4a): 31% yield; mp 168−169 °C (MeCN); ^{1}H NMR (TCE, +100 °C) 1.03, 1.18, 1.24 (s, ratio 1:1:2, 36 H), 3.17 (br s, 3 H), 3.19 and 4.45 (AX, J = 12.6 Hz, 4 H), 3.30 (t, J = 7.9 Hz, 2 H), 3.38 and 4.25 (AX, J = 12.2 Hz, 4 H), 3.67−3.81 (m, 8 H), 4.00−4.13 (m, 8 H), 4.26 (t, J = 7.9 Hz, 2 H), 6.72, 6.86 (s, 2 H each), 6.93 and 7.01 (ABq, J = 2.5 Hz, 4 H), 7.05 (dd, J = 4.9, 1.2 Hz, 1 H), 7.10 (dd, J = 3.0, 1.2 Hz, 1 H), and 7.28 (dd, J = 4.9, 3.0 Hz, 1 H); ^{13}C NMR (TCE, +85 °C) δ 30.6, 30.9 (t, OCH$_2$$CH_2$Th and Ar$CH_2$Ar), 31.1, 31.2, 31.3 (×2) (q, C(CH$_3$)$_3$), 33.4, 33.5, 33.6 (×2) (s, C(CH$_3$)$_3$), 60.7 (q, OCH$_3$), 70.4, 70.9, 71.9, 72.3, 74.4 (t, OCH$_2$$CH_2$O and O$CH_2CH_2$Th), 120.8, 124.8 124.85, 124.91, 125.0, 125.1, 128.4 (d, Ar and Th), 132.7, 133.2, 133.7, 134.3 (s, bridgehead-C), 139.1 (s, 3-Th), 144.1, 144.8 (s, $C_{sp2}-{}^t$Bu), 152.2, 153.9, and 154.6 (s, $C_{sp2}-$O); FAB (+) MS, m/z 931 (MH$^+$). Anal. Calcd for $C_{59}H_{78}O_7S$: C, 76.09; H, 8.44; S, 3.44. Found: C, 75.82; H, 8.55; S, 3.51.

5,11,17,23-Tetrakis(1,1-dimethylethyl)-25-methoxy-27-[2-(3-thienyl)ethoxy]$^\beta$-26,28-crown-6$^\alpha$-calix[4]arene,[23] anti Conformer (3aa): 41% yield; mp 311−312 °C (MeCN−CH$_2$Cl$_2$); ^{1}H NMR (CDCl$_3$, +22 °C) δ 1.04, 1.35, 1.46 (s, ratio 2:1:1, 36 H), 3.05 and 4.29 (AX, J = 12.8 Hz, 4 H), 3.10 (br t, J = 9.0 Hz, 2 H), 3.33 (s, 3 H), 3.44−3.68 (m, 14 H), 3.70 (br s, 4 H), 3.80 (br t, J = 8.6 Hz, 4 H), 3.95 (br d, J = 9.3 Hz, 2 H), 3.94 (br t, J = 9.0 Hz, 2 H), 6.57 and 6.90 (ABq, J = 2.5 Hz, 4 H), 6.83 (dd, J = 2.9, 1.2 Hz, 1 H), 6.94 (dd, J = 4.9, 1.2 Hz, 1 H), 7.06 (s, 2 H), 7.26 (dd, J = 4.9, 2.9 Hz, 1 H), and 7.27 (s, 2 H); ^{1}H NMR (TCE, +120 °C) δ 1.12, 1.40, 1.52 (s, ratio 2:1:1, 36 H), 3.04 (br t, J = 8.3 Hz, 2 H), 3.12 and 4.35 (AX, J = 13.1 Hz, 4 H), 3.41 (s, 3 H), 3.53 (s, 4 H), 3.60−3.82 (m, 16 H), 3.86 (br t, J = 8.3 Hz, 2 H), 3.96−4.08 (m, 4 H), 6.68 and 6.94 (ABq, J = 2.5 Hz, 4 H), 6.92−6.96 (m, 2 H), 7.09, (s, 2 H), and 7.26−7.28 (m, 3 H); ^{13}C NMR (CDCl$_3$, +22 °C) δ 31.3 (t, OCH$_2$$CH_2$Th), 31.4, 31.7 (q, C($CH_3$)$_3$), 31.8 (t, Ar$CH_2$Ar), 32.0 (q, C($CH_3$)$_3$), 33.7, 34.1 (s, C(CH$_3$)$_3$), 39.1 (t, ArCH$_2$Ar), 61.1 (q, OCH$_3$), 70.6, 70.7, 71.2, 71.5, 71.7, 73.1 (t, OCH$_2$$CH_2$O and O$CH_2CH_2$Th), 120.8, 125.0, 125.4, 125.45, 125.47, 125.50, 128.2 (d, Th and Ar), 131.4, 132.8, 133.1, 135.9 (s, bridgehead-C), 138.3 (s, Th), 143.1, 143.8, 144.6 (s, $C_{sp2}-{}^t$Bu), 154.2, 154.8, and 156.0 (s, $C_{sp2}-$O); FAB (+) MS, m/z 975 (MH$^+$). Anal. Calcd for $C_{61}H_{82}O_8S$: C, 75.11; H, 8.48; S, 3.28. Found: C, 75.44; H, 8.31; S, 3.15.

5,11,17,23-Tetrakis(1,1-dimethylethyl)-25-methoxy-27-[2-(3-thienyl)ethoxy]$^\alpha$-26,28-crown-6$^\alpha$-calix[4]arene,[23] syn Conformer (4aa): 24% yield; mp 256−257 °C (MeOH−CH$_2$Cl$_2$); ^{1}H NMR (CDCl$_3$, −30 °C) δ 0.82, 1.35, 1.37 (s, ratio 2:1:1, 36 H), 3.16, 3.18 (d, J = 12.2 Hz, 2 H each), 3.51−3.78 (m, 18 H), 4.00 (t, J = 9.1 Hz, 4 H), 4.18 (s, 3 H), 4.38−4.42 (m, 2 H), 4.41, 4.49 (d, J = 12.2 Hz, 2 H each), 6.46 and 6.50 (ABq, J = 2.4 Hz, 4 H), 7.15, 7.19 (s, 2 H each), 7.27 (dd, J = 4.9, 1.2 Hz, 1 H), 7.31 (dd, J = 4.9, 2.8 Hz, 1 H), and 7.38 (dd, J = 2.8, 1.2 Hz, 1 H); ^{1}H NMR (TCE, +120 °C) 1.04, 1.26, 1.30 (s, ratio 2:1:1, 36 H), 3.20 and 4.49 (AX, J = 12.4 Hz, 4 H), 3.22 and 4.48 (AX, J = 13.1 Hz, 4 H), 3.50 (t, J = 8.2 Hz, 2 H), 3.65 (s, 4 H), 3.68−3.78 (m, 8 H), 3.84−4.06 (m, 11 H), 4.39 (t, J = 8.2 Hz, 2 H), 6.68 and 6.73 (ABq, J = 2.5 Hz, 4 H), 6.98, 7.01 (s, 2 H each), 7.14 (dd, J = 5.0, 1.2 Hz, 1 H), 7.21 (dd, J = 3.0, 1.2 Hz, 1 H), and 7.29 (dd, J = 5.0, 3.0 Hz, 1 H); ^{13}C NMR (CDCl$_3$, +22 °C) δ 31.2 (q, C(CH$_3$)$_3$), 31.46, 31.50 (t, OCH$_2$$CH_2$-Th and Ar$CH_2$Ar), 31.7 (q, C($CH_3$)$_3$), 33.6, 34.07, 34.08 (s, C(CH$_3$)$_3$), 61.9 (q, OCH$_3$), 70.9, 71.0, 71.4, 74.4, 74.7 (t, OCH$_2$$CH_2$O and O$CH_2CH_2$Th), 121.6, 124.3, 124.6, 124.7, 125.0, 125.4, 129.3 (d, Th and Ar), 131.8, 132.9, 135.5, 135.9 (s, bridgehead-C), 139.3 (s, Th), 144.3, 144.6, 144.8 (s, $C_{sp2}-{}^t$Bu), 153.0, 154.6, and 156.5 (s, $C_{sp2}-$O); FAB (+) MS, m/z 975 (MH$^+$). Anal. Calcd for $C_{61}H_{82}O_8S$: C, 75.11; H, 8.48; S, 3.28. Found: C, 75.27; H, 8.32; S, 3.23.

5,11,17,23-Tetrakis(1,1-dimethylethyl)-25-benzyloxy-27-[2-(3-thienyl)ethoxy]-26,28-crown-5-calix[4]arene, 1,3-Alternate Conformer (3b): 53% yield; mp 252−254 °C (MeCN); ^{1}H NMR δ 0.94, 1.40, 1.41 (s, ratio 2:1:1, 36 H), 2.44 (dd, J = 9.3, 7.8 Hz, 2 H), 2.96−3.04 (m, 4 H), 3.37−3.69 (m, 14 H), 3.80 and 3.87 (ABq, J = 16.7 Hz, 4 H), 3.91 (pseudo-s, 4 H), 4.59 (s, 2 H), 6.68−6.71 (m, 4 H), 6.84 (m, 1 H), 6.86 (dd, J = 4.9, 1.3 Hz, 1 H), 6.94 (d, J = 2.6 Hz, 2 H), 7.03−7.05 (m, 3 H), 7.06, 7.10 (s, 2 H each), and 7.24 (dd, J = 4.9, 2.9 Hz, 1 H); ^{13}C NMR δ 30.3 (t, OCH$_2$$CH_2$Th), 31.3, 31.9 (q, C($CH_3$)$_3$), 33.6, 34.04, 34.06 (s, C(CH$_3$)$_3$), 39.2, 39.5 (t, ArCH$_2$Ar), 67.1, 70.3, 70.5, 70.9, 71.1, 73.5 (t, OCH$_2$$CH_2O, OCH_2CH_2$Th, and O$CH_2$Ph), 120.1, 125.1, 125.2, 125.4, 125.5, 125.6, 126.0, 126.2, 127.7, 128.1 (d, Th, Ar, and Ph), 132.97, 132.99 133.05, 133.4

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[23] Notations α and β were introduced by Shinkai[11] to define the stereochemistry of calix[4]arene atropisomers having mixed substituents at the lower rim.

(s, bridgehead-C), 138.4, 138.6 (s, 3-Th and Ph), 144.4, 144.5, 144.8 (s, *C*$_{sp2}$−^{t}Bu), 153.8, 154.4, and 154.8 (s, *C*$_{sp2}$−O); FAB (+) MS, *m/z* 1007 (MH$^+$). Anal. Calcd for $C_{65}H_{82}O_7S$: C, 77.50; H, 8.20; S, 3.18. Found: C, 77.18; H, 8.31; S, 3.15.

5,11,17,23-Tetrakis(1,1-dimethylethyl)-25-benzyloxy-27-[2-(3-thienyl)ethoxy]-26,28-crown-5-calix[4]arene, Cone Conformer (4b): 12% yield; mp 254−255 °C (MeOH−CH$_2$Cl$_2$); ^{1}H NMR δ 0.80, 0.82, 1.34 (s, ratio 1:1:2, 36 H), 3.08 and 4.36 (AX, *J* = 12.4 Hz, 4 H), 3.11 and 4.31 (AX, *J* = 12.5 Hz, 4 H), 3.26 (t, *J* = 7.9 Hz, 2 H), 3.53−3.74 (m, 8 H), 3.99 (t, *J* = 7.9 Hz, 2 H), 4.04−4.20 (m, 8 H), 4.74 (s, 2 H), 6.43, 6.44 (s, 2 H each), 6.98 (dd, *J* = 4.9, 1.3 Hz, 1 H), 7.06 (dd, *J* = 2.9, 1.3 Hz, 1 H), 7.10 (pseudo-s, 4 H), 7.25 (dd, *J* = 4.9, 2.9 Hz, 1 H), and 7.35−7.53 (m, 5 H); ^{13}C NMR δ 31.0 (×2) (t, OCH$_2$*C*H$_2$-Th and Ar*C*H$_2$Ar), 31.1, 31.7 (q, C(*C*H$_3$)$_3$), 33.56, 33.59, 34.1 (s, *C*(CH$_3$)$_3$), 70.0, 71.0, 71.9, 72.5 (t, O*C*H$_2$*C*H$_2$O), 75.4 (t, O*C*H$_2$CH$_2$Th), 78.2 (t, O*C*H$_2$Ph), 121.2, 124.46, 124.52, 125.4, 125.49, 125.52 127.9, 128.3, 128.5, 129.8 (d, Ph, Th, and Ar), 131.7, 131.8, 135.3 (×2) (s, bridgehead-C), 137.7, 138.6 (s, 3-Th and Ph), 144.2, 144.4, 145.0 (s, *C*$_{sp2}$−^{t}Bu), 151.9, 152.0, and 154.9 (s, *C*$_{sp2}$−O); FAB (+) MS, *m/z* 1007 (MH$^+$). Anal. Calcd for $C_{65}H_{82}O_7S$: C, 77.50; H, 8.20; S, 3.18. Found: C, 77.40; H, 8.11; S, 3.12.

5,11,17,23-Tetrakis(1,1-dimethylethyl)-25-benzyloxy-27-[2-(3-thienyl)ethoxy]-26,28-crown-6-calix[4]arene, 1,3-Alternate Conformer (3bb): 59% yield; mp 247−249 °C (MeCN); ^{1}H NMR δ 0.95, 1.37, 1.38 (s, ratio 2:1:1, 36 H), 2.52 (dd, *J* = 9.7, 7.7 Hz, 2 H), 2.92−2.99 (m, 4 H), 3.26 (t, *J* = 7.5 Hz, 4 H), 3.51−3.59 (m, 12 H), 3.70 (dd, *J* = 9.7, 7.7 Hz, 2 H), 3.78 and 3.86 (ABq, *J* = 16.3 Hz, 4 H), 3.90 (pseudo-s, 4 H), 4.61 (s, OC*H*$_2$Ph, 2 H), 6.69−6.72 (m, 4 H), 6.86−6.89 (m, 2 H), 6.97 (d, *J* = 2.4 Hz, 2 H), 7.05−7.10 (m, 7 H), and 7.25 (dd, *J* = 4.9, 2.9 Hz, 1 H); ^{13}C NMR δ 30.3 (t, OCH$_2$*C*H$_2$Th), 31.2, 31.8 (q, C(*C*H$_3$)$_3$), 33.6, 34.05, 34.07 (s, *C*(CH$_3$)$_3$), 39.1, 39.4 (t, Ar*C*H$_2$Ar), 68.0, 70.2, 70.4, 71.0, 71.1, 71.3, 71.4 (t, O*C*H$_2$*C*H$_2$O, O*C*H$_2$CH$_2$Th, and O*C*H$_2$Ph), 120.2, 125.2, 125.8, 125.9, 126.09, 126.11, 126.3, 127.8, 128.1 (d, Ar, Th and Ph), 133.0, 133.1, 133.3, 133.7 (s, bridgehead-C), 138.4, 138.6 (s, 3-Th and Ph), 144.3, 144.6, 144.9 (s, *C*$_{sp2}$−^{t}Bu), 153.9, 154.6, and 155.0 (s, *C*$_{sp2}$−O); FAB (+) MS, *m/z* 1051 (MH$^+$). Anal. Calcd for $C_{67}H_{86}O_8S$: C, 76.53; H, 8.25; S, 3.04. Found: C, 76.30; H, 8.37; S, 3.15.

5,11,17,23-Tetrakis(1,1-dimethylethyl)-25-benzyloxy-27-[2-(3-thienyl)ethoxy]-26,28-crown-6-calix[4]arene, Cone Conformer (4bb): 26% yield; mp 207−208 °C (MeOH−CH$_2$Cl$_2$); ^{1}H NMR δ 0.82, 0.83, 1.33 (s, 1:1:2, 36 H), 3.07 and 4.36 (AX, *J* = 12.4 Hz, 4 H), 3.10 and 4.31 (AX, *J* = 12.5 Hz, 4 H), 3.25 (t, *J* = 7.9 Hz, 2 H), 3.56−3.70 (m, 12 H), 4.01 (t, *J* = 7.9 Hz, 2 H), 3.94−4.19 (m, 8 H), 4.77 (s, 2 H), 6.45, 6.46 (s, 2 H each), 6.99 (dd, *J* = 4.9, 1.3 Hz, 1 H), 7.07 (dd, *J* = 2.9, 1.3 Hz, 1 H), 7.08 (pseudo-s, 4 H), 7.25 (dd, *J* = 4.9, 2.9 Hz, 1 H), and 7.35−7.52 (m, 5 H); ^{13}C NMR δ 30.99, 31.02, 31.05 (t, OCH$_2$*C*H$_2$Th and Ar*C*H$_2$Ar), 31.1, 31.7 (q, C(*C*H$_3$)$_3$), 33.58, 33.61, 34.1 (s, *C*(CH$_3$)$_3$), 69.7, 70.5, 70.8, 71.1, 72.2 (t, O*C*H$_2$*C*H$_2$O), 75.4 (t, O*C*H$_2$CH$_2$Th), 78.0 (t, O*C*H$_2$Ph), 121.3, 124.5, 125.36, 125.43, 125.5, 128.0, 128.3, 128.4, 129.8 (d, Ar, Th and Ph), 131.9, 132.0, 135.33, 135.35 (s, bridgehead-C), 137.7, 138.6 (s, 3-Th and Ph), 144.2, 144.4, 145.1 (s, *C*$_{sp2}$−^{t}Bu), 151.9, 152.1, and 154.5 (s, *C*$_{sp2}$−O); FAB (+) MS, *m/z* 1051 (MH$^+$). Anal. Calcd for $C_{67}H_{86}O_8S$: C, 76.53; H, 8.25; S, 3.04. Found: C, 76.33; H, 8.46; S, 3.14.

5,11,17,23-Tetrakis(1,1-dimethylethyl)-25-propoxy-27-benzyloxy-26,28-crown-5-calix[4]arene, 1,3-Alternate Conformer (3c): 58% yield; mp 234−235 °C (MeCN−CH$_2$Cl$_2$); ^{1}H NMR δ 0.62 (t, *J* = 7.6 Hz, 3 H), 0.84−0.96 (m, 2 H), 1.01, 1.38, 1.40 (s, ratio 2:1:1, 36 H), 2.90−3.07 (m, 4 H), 3.21−3.27 (m, 2 H), 3.31−3.48 (m, 8 H), 3.60−3.65 (m, 4 H), 3.77 and 3.85 (ABq, *J* = 16.4 Hz, 4 H), 3.88 (pseudo-s, 4 H), 4.57 (s, 2 H), 6.69 and 6.91 (ABq, *J* = 2.5 Hz, 4 H), 6.75 (m, 2 H), 7.02, 7.09 (s, 2 H each), and 7.03−7.10 (m, 3 H); ^{13}C NMR δ 9.7 (q, OCH$_2$CH$_2$*C*H$_3$), 22.1 (t, OCH$_2$*C*H$_2$CH$_3$), 31.3, 31.9 (q, C(*C*H$_3$)$_3$), 33.6, 34.00, 34.04 (s, *C*(CH$_3$)$_3$), 39.2, 39.4 (t, ArCH$_2$Ar), 67.1, 70.5, 70.9, 71.6, 72.2, 73.4 (t, O*C*H$_2$CH$_2$CH$_3$, O*C*H$_2$CH$_2$O, and O*C*H$_2$Ph), 125.0, 125.5, 125.6, 126.4, 126.5, 127.7 (d, Ar and Ph), 132.89 (×2), 132.93, 133.4 (s, bridgehead-C), 138.4 (s, Ph), 144.2 (×3), 144.7 (s, *C*$_{sp2}$−^{t}Bu), 153.9, 154.5, and 154.8 (s, *C*$_{sp2}$−O); FAB (+) MS, *m/z* 939 (MH$^+$). Anal. Calcd for $C_{62}H_{82}O_7$: C, 79.28; H, 8.80. Found: C, 79.05; H, 8.66.

5,11,17,23-Tetrakis(1,1-dimethylethyl)-25-propoxy-27-benzyloxy-26,28-crown-5-calix[4]arene, Cone Conformer (4c): 24% yield; mp 252−253 °C (MeCN−CH$_2$Cl$_2$); ^{1}H NMR δ 0.80, 0.82, 1.34 (s, ratio 1:1:2, 36 H), 1.01 (t, *J* = 7.4 Hz, 3 H), 1.82−1.96 (m, 2 H), 3.07 and 4.35 (AX, *J* = 12.5 Hz, 4 H), 3.12 and 4.33 (AX, *J* = 12.8 Hz, 4 H), 3.50−3.72 (m, 10 H), 4.02−4.22 (m, 8 H), 4.73 (s, 2 H), 6.41, 6.44 (s, 2 H each), 7.10 (pseudo-s, 4 H), and 7.32−7.51 (m, 5 H); ^{13}C NMR δ 10.7 (q, OCH$_2$CH$_2$*C*H$_3$), 23.4 (t, OCH$_2$*C*H$_2$CH$_3$), 31.0 (t, Ar*C*H$_2$Ar), 31.1, 31.7 (q, C(*C*H$_3$)$_3$), 33.5, 33.6, 34.1 (s, *C*(CH$_3$)$_3$), 69.9, 71.1, 71.7, 72.5 (t, O*C*H$_2$*C*H$_2$O), 77.7 (t, O*C*H$_2$CH$_2$CH$_3$), 78.2 (t, O*C*H$_2$-Ph), 124.4, 124.5, 125.4, 125.6, 127.9, 128.5, 128.8 (d, Ar and Ph), 131.7, 131.8, 135.3, 135.4 (s, bridgehead-C), 137.7 (s, Ph), 143.9, 144.3, 144.9 (s, *C*$_{sp2}$−^{t}Bu), 152.0, 152.4, and 155.0 (s, *C*$_{sp2}$−O); FAB (+) MS, *m/z* 939 (MH$^+$). Anal. Calcd for $C_{62}H_{82}O_7$: C, 79.28; H, 8.80. Found: C, 79.35; H, 8.71.

Compound **4c** was prepared more conveniently by treatment of **2c** with tetraethylene glycol ditosylate and NaH in anhydrous THF at reflux for 24 h. The reaction produced exclusively the cone conformer **4c**, which was isolated in 70% yield by direct crystallization of the crude product.

5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,27-crown-5−26-propoxy-28-hydroxy-calix[4]arene, Cone Conformer (5): A solution of Me$_3$SiCl (0.65 g, 6 mmol) in anhydrous CHCl$_3$ (2 mL) was added dropwise to a stirred solution of **4c** (0.28 g, 0.3 mmol) in anhydrous CHCl$_3$ (8 mL) at room temperature. After 5 h, the reaction was quenched with water (3 mL). The organic layer was separated, and dried over MgSO$_4$. After evaporation of the solvent, the residue was purified by column chromatography (SiO$_2$, petroleum ether−AcOEt 4:1) to give **5** in 75% yield; mp 221−222 °C (MeOH); ^{1}H NMR δ 0.91, 1.22, 1.26 (s, ratio 2:1:1, 36 H), 0.97 (t, *J* = 7.5 Hz, 3 H), 2.06−2.09 (m, 2 H), 3.18 and 4.43 (AX, *J* = 12.5 Hz, 4 H), 3.20 and 4.54 (AX, *J* = 13.0 Hz, 4 H), 3.70−4.17 (m, 18 H), 6.67 and 6.68 (ABq, *J* = 2.5 Hz, 4 H), 6.89 (br s, 1 H), 6.98 and 7.00 (s, 2 H each); ^{13}C NMR δ 10.1 (q, OCH$_2$CH$_2$*C*H$_3$), 22.9 (t, OCH$_2$*C*H$_2$-CH$_3$), 31.1 (×2) (q, C(*C*H$_3$)$_3$), 31.3 (t, ArCH$_2$Ar), 31.6, 31.7 (q, C(*C*H$_3$)$_3$), 33.7 (×3), 34.0 (s, *C*(CH$_3$)$_3$), 70.7, 70.87, 70.95, 75.6 (t, O*C*H$_2$*C*H$_2$O), 76.0 (t, O*C*H$_2$CH$_2$CH$_3$), 124.6, 124.8, 125.2, 125.3 (d, Ar), 128.4, 132.7, 133.1, 135.1 (s, bridgehead-C), 140.6 (s, *C*$_{sp2}$−^{t}Bu, unalkylated ring), 145.0, 145.5 (×2) (s, *C*$_{sp2}$−^{t}Bu, alkylated rings), 150.6, 151.4 (×2), and 153.4 (s, *C*$_{sp2}$−O); FAB (+) MS, *m/z* 849 (MH$^+$). Anal. Calcd for $C_{55}H_{76}O_7$: C, 77.79; H, 9.02. Found: C, 77.47; H, 8.95.

5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,27-crown-5$^\alpha$-26-propoxy$^\alpha$-28-[2-(3-thienyl)ethoxy]$^\beta$-calix[4]arene,[23] Partial Cone Conformer (6): A stirred mixture of **5** (0.17 g, 0.2 mmol), 2-(3-thienyl)ethanol tosylate (0.12 g, 0.4 mmol), and Cs$_2$CO$_3$ (0.32 g, 1 mmol) in anhydrous MeCN was refluxed for 40 h. Usual workup followed by chromatography (SiO$_2$ column, CH$_2$Cl$_2$−AcOEt 10:1) gave **6** in 54% yield; mp 265−267 °C (MeOH−CH$_2$Cl$_2$); ^{1}H NMR δ 0.96 (t, *J* = 7.5 Hz, 3 H), 1.00, 1.28, 1.42 (s, ratio 1:2:1, 36 H), 1.03, 1.81 (t, *J* = 5.5 Hz, 2 H each), 1.85−1.95 (m, 2 H), 3.24 and 4.38 (AX, *J* = 12.0 Hz, 4 H), 3.52−3.95 (m, 22 H), 6.42 (dd, *J* = 4.9, 1.2 Hz, 1 H), 6.47 (dd, *J* = 2.9, 1.2 Hz, 1 H), 6.85 (s, 2 H), 6.97 and 7.23 (ABq, *J* = 2.5 Hz, 4 H), 7.00 (dd, *J* = 4.9, 2.9 Hz, 1 H), and 7.17 (s, 2 H); ^{13}C NMR δ 10.2 (q, OCH$_2$CH$_2$*C*H$_3$), 23.2 (t, OCH$_2$*C*H$_2$CH$_3$), 30.2, 30.5 (t, OCH$_2$*C*H$_2$Th and Ar*C*H$_2$Ar), 31.3, 31.6, 31.9 (q, C(*C*H$_3$)$_3$), 33.9, 34.05, 34.09 (s, *C*(CH$_3$)$_3$), 38.6 (t, Ar*C*H$_2$Ar), 69.1 (t, O*C*H$_2$CH$_2$Th), 70.3, 71.2, 71.6, 73.7 (t, O*C*H$_2$*C*H$_2$O), 77.8 (t, O*C*H$_2$CH$_2$CH$_3$), 119.8, 123.8, 124.9, 125.6, 125.9, 126.2, 128.5 (d, Ar and Th), 132.5, 133.42, 133.45, 136.4 (s, bridgehead-C), 140.6 (s, Th), 144.0, 144.2, 145.4 (s, *C*$_{sp2}$−^{t}Bu), 152.5, 154.27, and 154.30 (s, *C*$_{sp2}$−O); FAB (+) MS, *m/z* 959 (MH$^+$). Anal. Calcd for $C_{61}H_{82}O_7S$: C, 76.36; H, 8.62; S, 3.34. Found: C, 76.54; H, 8.77; S, 3.31.

Debenzylation of 3c with Me$_3$SiBr. Reaction of **3c** with Me$_3$SiBr (20 equiv.) in CHCl$_3$ was conducted as described above for the debenzylation of **4c**. TLC analysis of the crude product showed the presence of two components (**7** and **8**), which were separated in a pure form by column chromatography (SiO$_2$, petroleum ether−AcOEt 4:1).

Anti-proximal **5,11,17,23-Tetrakis(1,1-dimethylethyl)-25-propoxy-26-(11-bromo-3,6,9-trioxa-1-undecenyloxy)-27,28-dihydroxy-calix[4]arene (7) (fraction A):** 75% yield; mp 142−143 °C; ^{1}H NMR δ −0.34 (t, *J* = 7.4 Hz, OCH$_2$CH$_2$C*H*$_3$, 3 H), 0.53−0.65 (m, OCH$_2$C*H*$_2$CH$_3$, 2 H), 1.219, 1.222, 1.26, 1.35 (s, ^{t}Bu, 9 H each), 2.38 (dt, *J* = 8.8, 6.0 Hz, OC*H*$_a$H$_b$CH$_2$CH$_3$, 1 H), 2.50 (dt, *J* = 8.8, 6.0 Hz, OCH$_a$*H*$_b$CH$_2$CH$_3$, 1 H), 2.92 (ddd, *J* = 10.5, 9.0, 3.0 Hz, OCH$_2$CH$_2$O, 1 H), 3.25−3.36 (m, OCH$_2$CH$_2$O, 3 H), 3.40 (t, *J* = 6.3 Hz, OCH$_2$C*H*$_2$Br, 2 H), 3.46−3.63 (m, OCH$_2$CH$_2$O, 6 H), 3.49 and 4.12 (AX, *J* = 13.8 Hz, ArCH$_2$Ar, 2 H), 3.54 and 4.00 (AX, *J* = 13.8 Hz, ArCH$_2$Ar, 2 H), 3.72 (t, *J* = 6.3 Hz, OC*H*$_2$CH$_2$Br, 2 H), 3.71−3.77 (m, OCH$_2$CH$_2$O, 1 H), 3.85−3.91 (m, OCH$_2$CH$_2$O, 1 H), 3.88 (pseudo-s, ArCH$_2$Ar, 2 H), 3.90 and 4.03 (ABq, *J* = 17.3 Hz, ArCH$_2$Ar, 2 H), 6.97, 7.01, 7.02, 7.03, 7.04, 7.05, 7.19, 7.27 (d, *J* = 2.4 Hz, ArH, 1 H each), 7.66 and 8.02 (s, OH, 1 H each); ^{13}C NMR δ 8.6 (q, OCH$_2$CH$_2$*C*H$_3$), 21.7 (t, OCH$_2$*C*H$_2$CH$_3$), 31.3, 31.5 (×2), 31.6 (q, C(*C*H$_3$)$_3$), 32.5, 32.9 (t, ArCH$_2$Ar), 33.80, 33.82, 34.07, 34.12 (s, *C*(CH$_3$)$_3$), 37.2, 39.2 (t, ArCH$_2$Ar), 60.4 (t, OCH$_2$*C*H$_2$Br), 69.5, 70.32, 70.35, 70.5, 70.7, 71.1, 71.8, 72.5 (t, O*C*H$_2$*C*H$_2$O and O*C*H$_2$CH$_2$CH$_3$), 124.6, 124.8 (×2), 125.1, 125.4, 125.8, 126.2, 127.6 (d, Ar), 126.6, 128.7, 128.8, 129.0, 132.1, 132.8, 134.1, 134.9 (s, bridgehead-C), 142.4, 142.9 (s, *C*$_{sp2}$−^{t}Bu, unalkylated ring), 145.2, 147.1 (s, *C*$_{sp2}$−^{t}Bu, alkylated rings), 148.1, 150.0 (s, *C*$_{sp2}$−O, unalkylated rings), 151.0, and 153.1 (s, *C*$_{sp2}$−O, alkylated rings); FAB (+) MS, *m*/*z* 929/931 (MH$^+$). Anal. Calcd for $C_{55}H_{77}BrO_7$: C, 71.02; H, 8.34. Found: C, 70.77; H, 8.55.

5,11,17,23-Tetrakis(1,1-dimethylethyl)-25-[(11-bromo-3,6,9-trioxa-1-undecenyl)oxy]-26,27,28-trihydroxy-calix[4]arene (8) (fraction B): 8% yield; ^{1}H NMR δ 1.19, 1.20, 1.22 (s, ratio 1:2:1, 36 H), 3.39 and 4.46 (AX, *J* = 12.9 Hz, 4 H), 3.42 (t, *J* = 6.4 Hz, 2 H), 3.43 and 4.26 (AX, *J* = 13.0 Hz, 4 H), 3.60−3.71 (m, 4 H), 3.76 (t, *J* = 6.4 Hz, 2 H), 3.79−3.88 (m, 4 H), 4.08−4.16 (m, 2 H), 4.31−4.33 (m, 2 H), 6.97 and 7.06 (ABq, *J* = 2.4 Hz, 4 H), 7.05, 7.08 (s, 2 H each), 9.41 and 10.29 (s, ratio 2:1, 3 H); ^{13}C NMR δ 30.3 (t, ArCH$_2$Ar), 31.2, 31.5 (×3) (q, C(*C*H$_3$)$_3$), 32.1 (t, ArCH$_2$Ar), 33.9, 34.0, 34.2 (s, *C*(CH$_3$)$_3$), 60.4 (t, OCH$_2$*C*H$_2$Br), 70.0, 70.5, 70.7, 70.8, 70.9, 71.2, 75.1 (t, OCH$_2$), 125.62, 125.66, 125.73, 126.4 (d, Ar), 127.6, 128.2, 128.3, 133.7 (s, bridgehead-C), 143.0, 143.5, 147.96 (s, *C*$_{sp2}$−^{t}Bu), 148.05, 148.3, 149.3 (s, *C*$_{sp2}$−O); FAB (+) MS, *m*/*z* 887/889 (MH$^+$). Anal. Calcd for $C_{52}H_{71}BrO_7$: C, 70.33; H, 8.06. Found: C, 70.56; H, 8.17.

5,11,17,23-Tetrakis(1,1-dimethylethyl)-25,27;26,28-bis-crown-6-calix[4]arene (11). A slurry of **9** (toluene 1:1 complex, 0.37 g, 0.5 mmol) PGD (0.60 g, 1.1 mmol) and Cs$_2$CO$_3$ (0.65 g, 2 mmol) in anhydrous MeCN (25 mL) was refluxed for 24 h. A second portion of Cs$_2$CO$_3$ (0.65 g, 2 mmol) was then added, and heating was continued for an additional 48 h. After the mixture was cooled, the solvent was evaporated and the residue was partitioned between CH$_2$Cl$_2$ and 1 N HCl. The organic layer was dried over anhydrous Na$_2$SO$_4$ and concentrated. The crude product was purified by column chromatography (SiO$_2$, 1% MeOH in CH$_2$Cl$_2$) to afford bis-crown **11** (32%) as white crystals; mp > 280 °C (dec) (MeOH−CH$_2$Cl$_2$); ^{1}H NMR δ 1.36 (s, 36 H), 2.84, 3.39 (t, *J* = 7.6 Hz, 8 H each), 3.51, 3.58, 3.91 (s, ratio 2:1:1, 32 H), and 7.04 (s, 8 H); ^{13}C NMR δ 31.7 (q, C(*C*H$_3$)$_3$), 34.0 (s, *C*(CH$_3$)$_3$), 39.2 (t, Ar*C*H$_2$Ar), 68.0, 69.5, 70.4, 71.0, 71.4 (t, O*C*H$_2$), 125.6 (d, Ar), 132.8 (s, bridgehead-C), 144.7 (s, *C*$_{sp2}$−^{t}Bu), and 154.5 (s, *C*$_{sp2}$−O); FAB (+) MS, *m*/*z* 1053 (MH$^+$). Anal. Calcd for $C_{64}H_{92}O_{12}$: C, 72.96; H, 8.81. Found: C, 72.81; H, 8.97.

Structure Analysis of anti-3aa and syn-4aa. Details of the X-ray analysis in Crystallographic Information File (CIF) format are available in the Supporting Information. Data collection was performed at 150 K. The structures were solved using SHELXS-97.[24] In anti-**3aa** there is disorder (0.53:0.47) of the ^{t}Bu methyl carbons at C38 over two sites. In syn-**4aa** there is much more disorder; the ^{t}Bu methyl carbons at C28 are disordered over two sites (0.55:0.45), the polyether chain has two conformations (0.81:0.19) and the thienyl ring is disordered over two orientations (0.90:0.10). Refinement was done by full-matrix least-squares calculations using SHELXL-97[25] using 11262 measured data for anti-**3aa** and 11687 measured data for syn-**4aa**. Final R_{obs} values are 0.0476 (for 8299 reflections with $I > 2\sigma I$) and 0.0591 (for 6969 reflections with $I > 2\sigma I$) for anti-**3aa** and syn-**4aa**, respectively.

Supporting Information Available: Details of the X-ray analysis in Crystallographic Information File (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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