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Synthesis and Conformational Evaluation of *p-tert*-Butylthiacalix[4]arene-crowns

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Bridging of *p-tert*-butylthiacalix[4]arene afforded 1,3-dihydroxythiacalix[4]arene-monocrown-5 (**3b**), 1,2-alternate thiacalix[4]arene-biscrown-4 and -5 (**4a**,**b**), and 1,3-alternate thiacalix[4]arene-biscrown-5 and -6 (**5a**,**b**), depending on the metal carbonates and oligoethylene glycol ditosylates used. Starting from 1,3-dialkylated thiacalix[4]arenes, the corresponding bridging reaction gave 1,3-alternate, partial-cone, and cone conformers **10**−**19**, depending on the substituents present. Temperature-dependent studies revealed that the conformationally flexible 1,3-dimethoxythiacalix-[4]arene-crowns **10a**−**c** exclusively occupy the 1,3-alternate conformation. Demethylation exclusively gave the cone 1,3-dihydroxythiacalix[4]arene-crowns (**3a**,**c**), which could not be obtained by direct bridging of thiacalix[4]arene. The different structures were assigned on the basis of several X-ray crystal structures and extensive 2-D ^{1}H NMR studies.

Introduction

The structural differences between thiacalix[4]arene and calix[4]arene are the bridging sulfur atoms instead of methylene units. The thiacalix[4]arenes are being used more and more in supramolecular chemistry due to the additional features induced by the sulfur atoms.[1−5] In the past, we have found that calix[4]arene-crowns are highly selective ionophores for potassium and cesium cations.[6,7] Therefore, one of the obvious classes of ionophores suitable for selective complexation of alkaline metal cations would be the thiacalix[4]arene-crowns. A number of thiacalix[4]arene-crowns have already been reported by several groups viz. 1,3-alternate thiacalix[4]arene-biscrowns,[8,9] diametrically bridged 1,3-alternate thiacalix-[4]arene-monocrowns,[10,11] and proximally bridged thiacalix-[4]arene-monocrowns.[12] Thiacalix[4]arenes can adopt four different conformations viz. 1,2-alternate, 1,3-alternate, partial cone, and cone.[4,13] Whereas the structures of calix-[4]arenes can be assigned on the basis of the positions of the bridging methylene groups in the ^{1}H and ^{13}C NMR spectra,[13,14] in the spectra of thiacalix[4]arenes these characteristic protons are not present. However, the conformation can often be established using ^{1}H NMR spectroscopy in combination with X-ray crystal structures.[15−17] In some cases, additional proof was obtained by 2D ^{1}H NMR spectroscopy.[18−21] Except for the X-ray crystal structures of the 1,3-alternate thiacalix[4]arene-biscrown-5 and -6,[8] there is little structural information on thiacalix[4]arene-crown conformers.

In this paper, we report our results of a systematic study on the formation and conformations of *p-tert*-butylthiacalix[4]arene-(bis)crowns-4, -5, and -6.[22]

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SCHEME 1

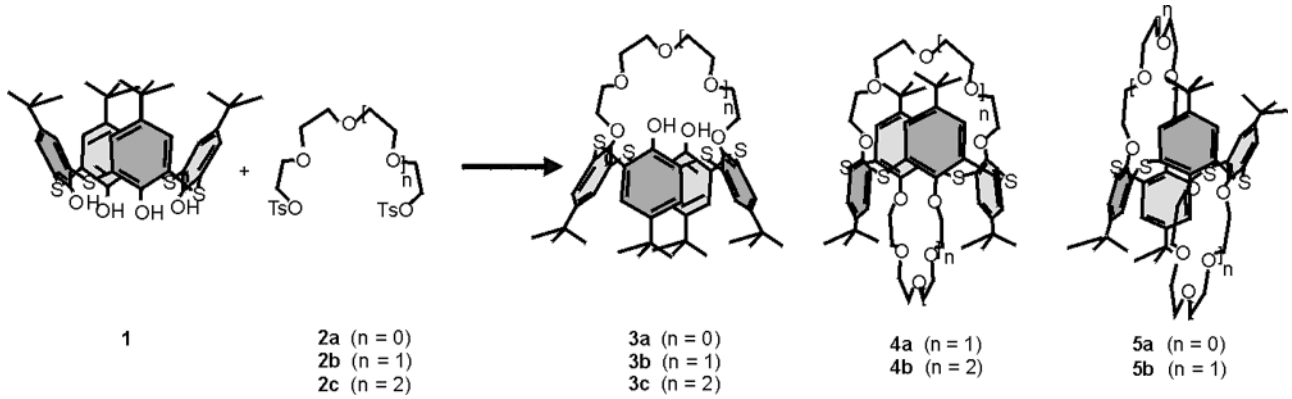

TABLE 1. Direct Functionalization of Thiacalix[4]arene 1

entry	crown	base (equiv)	reaction time	conv of **1**[a] (%)	products formed[a] (ratio)
1	**2a** (crown-4)	Na_2CO_3 (12)	15 d	50	**3a**
2		K_2CO_3 (4)	2 d	40	**5a**
3		Cs_2CO_3 (4)	6 h	100	**5a**
4	**2b** (crown-5)	Na_2CO_3 (12)	11 d	50	**3b**
5		K_2CO_3 (4)	12 h	100	**4a**
6		Cs_2CO_3 (4)	12 h	100	**5b**/**4a** (1:1)
7	**2c** (crown-6)	Na_2CO_3 (1.2)	15 d	40	**3c**
8		K_2CO_3 (4)	7 d	100	**4b**/**3c** (1:4)
9		Cs_2CO_3 (4)	6 h	70	**4b**

[a] Determined from the ^{1}H NMR spectra of the crude reaction mixtures.

Results and Discussion

Direct Bridging of Thiacalix[4]arene. The reactions of thiacalix[4]arene **1** with tri-, tetra-, and pentaethylene glycol ditosylates **2a**−**c** in acetonitrile were systematically studied by varying the base, reaction time, etc. The results are summarized in Table 1.

The reactions between **1** and **2** (1 equiv) with Na_2CO_3 as a base gave diametrically bridged thiacalix[4]arene-crowns **3** (Scheme 1). The template effect induced by the sodium cation appears favorable for the formation of monocrown derivatives in the cone conformation. However, only thiacalix[4]arene-crown-5 (**3b**) could be isolated in low yield (Table 1, entry 4). Reaction times of 11−15 days together with conversions of only 40−50% indicate that Na_2CO_3 is not the optimal base for the direct bridging of thiacalix[4]arene.

Reactions of **1** with **2** (1.8 equiv), using K_2CO_3, gave thiacalix[4]arene-monocrowns (**3**), 1,3-alternate thiacalix[4]arene-biscrowns (**4**), and 1,2-alternate thiacalix[4]arene-biscrowns (**5**). The shorter reaction times and the formation of biscrowns show that K_2CO_3 is a more efficient base. Reaction of **2a** with **1** gave slow conversion to 1,2-alternate thiacalix[4]arene-biscrown-4 (**5a**) (Table 1, entry 2). The reaction of **1** and **2b** exclusively yielded the 1,3-alternate thiacalix[4]arene-biscrown-5 (**4a**)[9] (Table 1, entry 5), while **1** and **2c** afforded a mixture of **4b**[9] and **3c** (Table 1, entry 8).

The reaction between **1** and **2** (1.8 equiv), with Cs_2CO_3 as base, only yielded thiacalix[4]arene-biscrowns **4** and **5**. The reaction of **1** with **2a** exclusively afforded the 1,2-alternate thiacalix[4]arene-biscrown-4 (**5a**) (Table 1, entry 3). With **2b** as a bridging agent for **1**, a mixture of the 1,2-alternate thiacalix[4]arene-biscrown-5 (**5b**) (27%) and the corresponding 1,3-alternate conformer **4a** (15%) was obtained (Table 1, entry 6). Bridging **1** using **2c** gave conversion to only **4b**[9] (Table 1, entry 9).

Not only the metal carbonate but also the number of ethylene glycol units in the bridging agent (**2**) influences the product formation. The smallest of the crown-ether bridges **2a** only forms diametrically bridged monocrown and proximally bridged 1,2-alternate biscrowns. For steric reasons, formation of diametrically bridged 1,3-alternate biscrown-4 products is unfavorable. However, tetraethylene glycol ditosylate **2b** gave all three products **3b**, **4a**, and **5b**. The largest of the ethylene glycol ditosylates used (**2c**) only gave rise to diametrically bridging.

Diametrically Substituted Thiacalix[4]arene-monocrowns. In addition to the direct bridging of thiacalix[4]arene **1**, various diametrically substituted thiacalix[4]arene derivatives (**6**−**9**) were reacted with **2** (Scheme 2).

The known 1,3-dialkoxythiacalix[4]arenes **6**−**9**[2,10,21,23] were reacted with 1 equiv of oligoethylene glycol ditosylates **2a**−**c** in the presence of 4 equiv of K_2CO_3 in acetonitrile to give the thiacalix[4]arene-monocrowns **10**−**19**. K_2CO_3 turned out to be the most efficient base,[24] allowing the formation of all three conformers: 1,3-alternate, partial cone, and cone. The results are summarized in Table 2.

Reaction of 1,3-dimethoxythiacalix[4]arene **6** with **2a**−**c** exclusively gave the 1,3-alternate products **10a**−**c** (Table 2, entries 1−3).[10,25] Crystallization of **10c** gave full conversion to crystals of the partial-cone conformer **14a**, underlining the conformational flexibility of this compound (vide infra).

The reaction of 1,3-dipropoxythiacalix[4]arene **7** with **2a** (Table 2, entry 4) mainly gave the 1,3-alternate

(22) Part of the work has been published in a preliminary communication: van Leeuwen, F. W. B.; Beijleveld, H.; Kooijman, H.; Spek, A. L.; Verboom, W.; Reinhoudt, D. N. *Tetrahedron Lett.* **2002**, *43*, 9675−9678.

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(24) An attempt to synthesize a cone derivative using **9** and **2b** with NaH (4 equiv) gave poor conversion after 5 days and was therefore abandoned.

(25) The ^{1}H NMR spectrum of the crude reaction mixture shows the presence of an additional conformer. Due to the behavior observed for the crystals of **14a**, we can exclude the partial cone conformation.

SCHEME 2

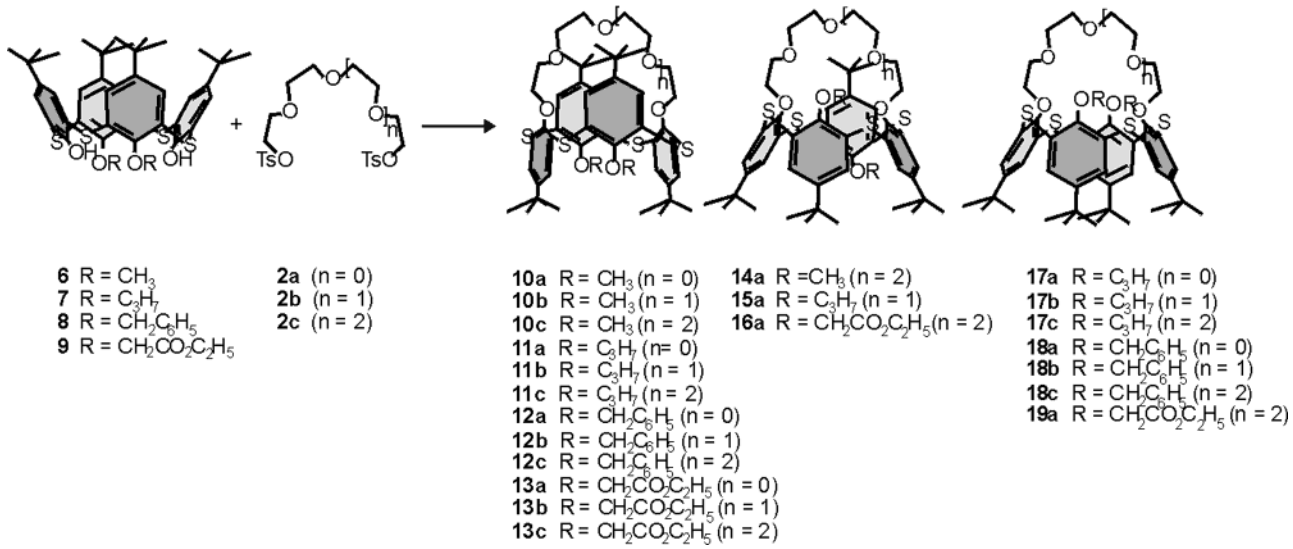

TABLE 2. Diametrically Substituted Thiacalix[4]arene-crowns

entry	starting compound	bridging agent	reaction time	conformer ratio[a] 1,3-alt/pc/cone
1	dimethoxythiacalix[4]arene **6**	**2a**	5 d	**10a**/−/− (1:0:0)
2		**2b**	5 d	**10b**/−/− (1:0:0)
3		**2c**	5 d	**10c**/−/− (1:0:0)
4	dipropoxythiacalix[4]arene **7**	**2a**	5 d	**11a**/−/**17a**[b] (20:0:1)
5		**2b**	5 d	**11b**/**15a**/**17b** (15:1:1)
6		**2c**	5 d	**11c**/−/**17c**[b] (20:0:1)
7	bis(benzyloxy)thiacalix[4]arene **8**	**2a**	5 d	**12a**/−/**18a**[b] (2:0:1)
8		**2b**	5 d	**12b**/−/**18b** (1:0:1)
9		**2c**	5 d	**12c**/−/**18c** (1:0:1)
10	thiacalix[4]arene diethyl ester **9**	**2a**	12 h	**13a**/−/− (1:0:0)
11		**2b**	12 h	**13b**/−/− (1:0:0)
12		**2c**	12 h	**13c**/**16a**[b]/**19a**[b] (7:10:4)

[a] Ratio obtained from ^{1}H NMR spectra of the crude reaction mixtures. [b] Formation deducted from ^{1}H NMR spectra of the crude reaction mixtures but not supported by analytical data of the isolated compounds.

conformer **11a**. Reacting **7** and **2b** yielded all possible conformers (Table 2, entry 5): 1,3-alternate (**11b**;[10] 59%), partial cone (**15a**; 2%), and cone (**17b**; 8%). Isolation of the partial cone conformer **15a** proves the ability of rotation by the propoxy groups through the annulus before rigidification by the crown-ether bridge. The largest ethylene glycol unit **2c** (Table 2, entry 6), as bridging agent, gave the 1,3-alternate conformer **11c**[10] (57%).

Bridging of 1,3-bis(benzyloxy)thiacalix[4]arene **8** gave in all cases a mixture of 1,3-alternate **12a**−**c** and cone conformers **18a**−**c** (Table 2, entries 7−9). The formation of only cone and 1,3-alternate products can be ascribed to the size of the benzyloxy groups, preventing them from rotation through the annulus.

Bridging of 1,3-thiacalix[4]arene diethyl ester **9** with crown-ether bridges **2a**−**c** proceeded much faster than with **6**−**8**, namely 12 h instead of 5 days. The ethyl ester functionalities may bind the potassium cations,[16] hence influencing product formation. Bridging with **2a**,**b** afforded the respective 1,3-alternate products **13a**[26] and **13b** (Table 2, entries 10 and 11). Reacting **9** and **2c**, however, afforded a mixture of 1,3-alternate **13c**, partial cone **16a**, and cone conformer **19a** (Table 2, entry 12), of which only **13c** could be isolated (16%). The formation of **16a** suggests that the ethyl ester groups are able to rotate through the annulus, which is very surprising as they were considered to be bulky enough to prevent rotation.[19]

Indirect Synthesis of Dihydroxythiacalix[4]arene-crowns. Of the diametrically bridged thiacalix[4]arene-crowns **3a**−**c**, only the crown-5 derivative **3b** could be obtained in pure form upon bridging of thiacalix[4]arene **1** using Na_2CO_3 as base. Therefore, an alternative synthetic approach to synthesize diametrically bridged dihydroxythiacalix[4]arene-crowns was developed by deprotection of the diametrically substituted dimethoxythiacalix[4]arene-crowns **10a**−**c**.[7,27]

Attempts to remove the benzyl group in 1,3-bis(benzyloxy)thiacalix[4]arene-crown-5 **18b** using acetic acid or trimethylsilyl iodide, as is common practice for the corresponding calix[4]arene-crowns,[28] were unsuccessful. Starting from 1,3-dimethoxythiacalix[4]arene-crown-5 **10a**, trimethylsilyl iodide also gave partial cleavage of the crown-ether bridge, which does not occur in the case of the corresponding 1,3-calix[4]arene-crowns,[7]

(26) Yields are low due to loss of product during column chromatography.

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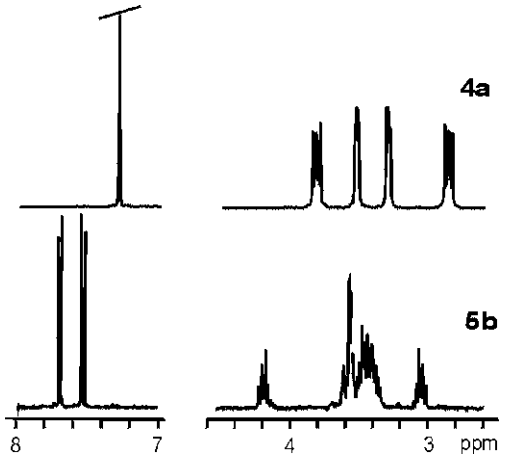

FIGURE 1. ^{1}H NMR data of the ArH (left) and crown-ether bridge protons (right) of 1,3-alternate thiacalix[4]arene-biscrown-5 **4a** (top) and 1,2-alternate thiacalix[4]arene-biscrown-5 **5b** (bottom; $CHCl_3$ peak at 7.26 ppm has been removed).

while the demethylation agent lithium diphenylphosphide[29] gave no conversion. Reacting 1,3-dimethoxythiacalix[4]arene-crowns **10a**−**c** with 5 equiv of sodium ethanethiolate in DMF, however, gave the corresponding 1,3-dihydroxythiacalix[4]arene-crowns **3a** (18%), **3b** (25%), and **3c** (16%) in the cone conformation.[26]

Assignment of the Conformation. The structures of the different conformers of the thiacalix[4]arene-crowns were determined by a combination of ^{1}H NMR spectroscopy and X-ray crystallography. Since the crown-5 derivatives were available in all the conformers, they were used for the conformational analysis. These conformers exhibit distinct differences in their ^{1}H NMR spectra. Using the knowledge obtained with the crown-5 derivatives, extrapolations toward the crown-4 and -6 derivatives were made.

Thiacalix[4]arene-biscrowns. MS and ^{1}H NMR peak intensities can be used to distinguish monocrown from biscrown products, after which the different conformers can be assigned. Of the biscrowns only the 1,3-alternate (diametrical) and 1,2-alternate (proximal) conformers were obtained. For both the 1,2-alternate (**4**) and 1,3-alternate (**5**) thiacalix[4]arene-biscrown-5 derivatives, X-ray crystal structures[22] were obtained. The 1,3-alternate thiacalix[4]biscrown-5 **4a** is a highly symmetrical molecule (C_2, $2\sigma_h$); consequently, both the aromatic and *tert*-butyl hydrogen atoms are present as only one signal in the ^{1}H NMR spectrum. Furthermore, the crown-ether bridge protons of **4a** give a highly symmetrical set of peaks (1:1:1:1; Figure 1). Compared to **4a**, the 1,2-alternate thiacalix[4]arene-biscrown-5 (**5b**) has a plane of symmetry less and an inversion point in the thiacalix[4]arene annulus more (I, C_2, and σ_v).This results in two doublets for the ArH's (7.72 and 7.56 ppm), whereas the *tert*-butyl groups appear as one peak (1.37 ppm) because they are equivalent (Figure 1). The crown-ether bridge protons of **5b** show an asymmetrical pattern (1:6:1; Figure 1). HCOSY correlations revealed that the outer two peaks in the crown-ether bridge region both belong to the methylene groups that are attached to the phenolic oxygens. Consequently, these methylene groups are diastereotopic; the rest of the methylene groups all appear as one broad multiplet (Figure 1). The observed differences in crown-ether bridge peak order result in a second diagnostic tool in the ^{1}H NMR spectra to distinguish the 1,3-alternate conformer **4a** and 1,2-alternate conformer **5b**.

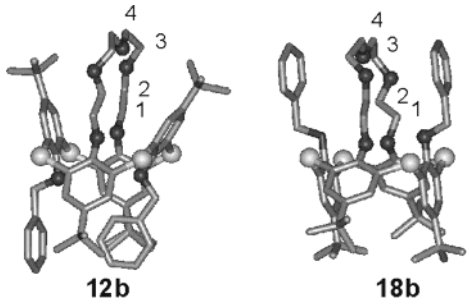

FIGURE 2. X-ray structures of 1,3-bis(benzyloxy)thiacalix-[4]arene-crown-5 1,3-alternate **12b** (left) and cone **18b** (right).

Thiacalix[4]arene-biscrown-6 (**4b**)[9] shows a single peak for the ArH's and *tert*-butyl hydrogen atoms (at 7.38 and 1.34 ppm, respectively) in the ^{1}H NMR spectrum indicating a 1,3-alternate conformation. In addition, a symmetrical pattern of the crown-ether bridge protons was observed, also pointing to the 1,3-alternate conformation. Thiacalix[4]arene-biscrown-4 (**5a**) exhibits two doublets for the ArH protons (7.77 and 7.52 ppm) and one for the *tert*-butyl groups (1.37 ppm) in the ^{1}H NMR spectrum. This ^{1}H NMR pattern shows a high degree of similarity to that of **5b**, indicating a 1,2-alternate conformation.

Rigid Thiacalix[4]arene-monocrowns. Of the diametrically bridged 1,3-thiacalix[4]arene-monocrowns, three different conformers can be obtained, namely 1,3-alternate, partial cone, and cone. Both the 1,3-alternate and the cone conformers, having the same symmetry elements (C_2, $2\sigma_h$), afford similar peak patterns of the protons of the thiacalix[4]arene platform. The pattern of the crown-ether bridge protons, however, is different. In the case of the partial cone conformation the C_2 rotational symmetry axis is lost, resulting in a distinctly different splitting pattern for the protons of the thiacalix[4]arene skeleton.

X-ray crystal structures were obtained for both 1,3-bis(benzyloxy)thiacalix[4]arene-crown-5 conformers **12b** and **18b** (Figure 2). The benzyloxy groups are too large for rotation through the annulus; therefore, the conformation is identical both in the solid state and in solution.

The chemical environment of the crown-ether bridge of **12b** is very similar to that of the 1,3-alternate thiacalix[4]arene-biscrown-5 (**4a**) (Figures 1 and 2).[22] The benzyloxy groups are positioned perpendicular; one benzyloxy group fills the cavity between the two aromatic units of the thiacalix[4]arene. In the X-ray crystal structure of the cone conformer **18b** (Figure 2), the benzyloxy groups are parallel and the crown-ether bridge fills the space between them. Furthermore, the aromatic rings of the thiacalix[4]arene to which the benzyloxy groups are attached are also parallel, resulting in a pinched cone conformation.[30]

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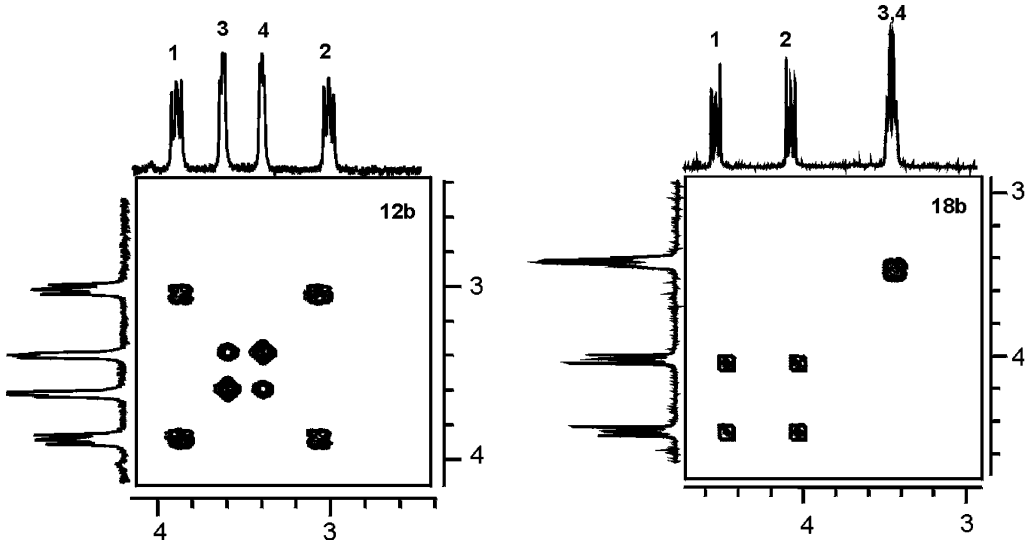

FIGURE 3. 2D COSY ^{1}H NMR spectra and methylene bridge peak order of 1,3-bis(benzyloxy)thiacalix[4]arene-crown-5, 1,3-alternate **12b** (1−3−4−2, left) and cone **18b** (1−2−3,4, right).

Differences between the ^{1}H NMR spectra of **12b** and **18b** are solely caused by the chemical environment of the different crown-ether bridges. Hence, the most obvious difference lies in the pattern of the crown-ether bridge protons between 3 and 5 ppm (Figure 3). The 1,3-alternate conformer **12b** gives four highly symmetrically spaced peaks (1:1:1:1; Figure 3), resembling the ^{1}H NMR spectrum of **4a**. Since the benzyl substituents are at the other site of the molecule, they hardly have any influence on the chemical shifts of the crown-ether bridge. Additional HCOSY experiments revealed coupling between the outer peaks of the crown-ether bridge protons. Therefore, these peaks are those of the first two methylene groups of the crown-ether bridge (1 and 2; Figure 3). The inner two peaks also show correlation with each other, indicating they correspond to the second set of methylene groups (3 and 4; Figure 3). The large upfield shift of methylene group 2 is caused by the anisotropy effect, induced by the aromatic groups of the thiacalix[4]arene platform in the 1,3-alternate conformation. Since both **4a** and **12b** have the same peak order for the crown-ether bridge protons (Figures 1 and 3), this can be used to determine the conformation. Additional proof was obtained from the NOE interactions between the ArH groups and both the benzyloxy groups and outer two peaks of the crown-ether bridge protons (1 and 2), and between the *tert*-butyl groups and the inner two peaks (3 and 4) of the crown-ether bridge. All these interactions are only possible in the 1,3-alternate conformation.

The cone conformer **18b** exhibits in its ^{1}H NMR spectrum three unsymmetrical peaks for the crown-ether bridge protons (1:1:2; Figure 3). HCOSY coupling between the two downfield shifted peaks reveals them as the first two methylene groups of the crown-ether bridge (1 and 2). Using HCOSY correlations, it is possible to differentiate between the 1,3-alternate and cone conformer based on the difference in peak order of the crown-ether bridge protons 1−3−4−2 and 1−2−3,4,[31] respectively (for numbers, see Figures 2 and 3). ROE experiments of the cone conformer **18b** show interactions between the ArH protons of the chemically different, aromatic groups of the thiacalix[4]arene platform. In addition, the methylene group of the benzyl substituents and the crown-ether bridge show interactions. Interactions can only occur in the cone conformation, they can act as additional proof for this conformation. On the basis of the X-ray crystal structure, interactions were expected between the benzyloxy groups and the crown-ether bridge, but none were observed. Apparently, in solution the benzyloxy groups point outward.

The ^{1}H NMR spectrum of the 1,3-thiacalix[4]arene-crown-5 diethyl ester **13b** shows two ArH and *tert*-butyl peaks. The crown-ether bridge peak order of 1−3−4−2 was similar to that of **12b** (Figure 3), indicating a 1,3-alternate conformation, which was confirmed by its X-ray crystal structure (Supporting Information).

1,3-Dipropoxythiacalix[4]arene-crown-5 shows up in all three conformers, viz. 1,3-alternate, partial cone, and cone. The 1,3-alternate (**11b**) and cone (**17b**) derivatives, both having two ArH (Figure 4) and *tert*-butyl signals in their ^{1}H NMR spectra, could be distinguished using the pattern and peak order of the crown-ether bridge protons. Due to the absence of a C_2-symmetry axis, the partial cone conformation **15a** can be distinguished by the four ArH signals (1:1:1:1; Figure 4) and the three *tert*-butyl signals (1:2:1). In addition, the upfield shift, present due to the anisotropic effect, of the signal belonging to the propoxy group of the rotated aryl ring is a strong indication for the partial cone conformation.

Bridging **8** with pentaethylene glycol ditosylate (**2c**) gave rise to a different conformational outcome, compared to that obtained with **2b** (Table 2). As with the crown-5 derivatives, two distinctly different ^{1}H NMR spectra were observed for the crown-ether bridges of the 1,3-alternate and cone conformers. 1,3-Bis(benzyloxy)thiacalix[4]arene-crown-6 could only be obtained in the 1,3-alternate (**12c**) and the cone (**18c**) conformation, probably because of the substituent size. HCOSY experiments revealed that the outer peaks of the crown-ether bridge region, in the 1,3-

(31) Methylene groups are numbered from the thiacalix[4]arene platform, and the "peak order" refers to the sequence in which resonances are found in the spectrum when moving from low to high field.

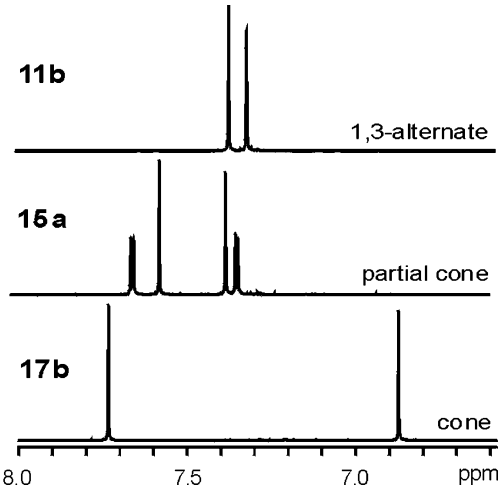

FIGURE 4. ^{1}H NMR region of the ArH peaks of the 1,3-dipropoxythiacalix[4]arene-crown-5, 1,3-alternate **11b** (top), partial cone **15a** (middle), and cone **17b** (bottom; $CHCl_3$ peak at 7.26 ppm has been removed).

alternate conformation, correspond to the first and second methylene protons of the crown-ether bridge, respectively, giving a 1−5−3,4−2[31] peak order. In the cone conformation, the two downfield shifted peaks correspond to the first two methylene protons of the crown-ether bridge (1−2−5−3−4). Since both conformers behave in a similar manner as their crown-5 analogues, the crown-ether bridge peak order can be applied to differentiate between the cone and 1,3-alternate crown-6 conformers. 1,3-Thiacalix[4]arene-crown-6 diethyl ester can have three conformers: 1,3-alternate (**13c**), partial cone (**16a**), and cone (**19a**). The 1,3-alternate and cone conformers could be distinguished by their double ArH and *tert*-butyl peaks and their crown-ether bridge peak order and the partial cone conformer from its distinct splitting pattern (1:1:1:1) of the ArH protons. In analogy, 1,3-dipropoxythiacalix[4]arene-crown-6 products, having two ArH and *tert*-butyl signals, were the 1,3-alternate (**11c**)[10] and cone (**17c**) conformers.

The 1,3-thiacalix[4]arene-crown-4 derivatives **11a**, **12a**, and **13a** have two peaks corresponding to the ArH and *tert*-butyl protons, indicating either a cone or 1,3-alternate conformation. Furthermore, the hydrogens of the bridging crown-ether units exhibit almost the same chemical shifts [3.7−4.1 (m, 4H), 3.4−3.6 (m, 4H), 2.5 (s, 4H) ppm], suggesting they all have a conformation in which there is no influence of the substituents. HCOSY NMR spectra of the crown-4 derivatives exhibit peak orders similar to those of the cone crown-5 conformers (1−2−3[31]).[32] However, in this case NOE interactions between the crown-ether bridge and the ArH protons of the thiacalix[4]arene platform were observed. These interactions are only possible in the 1,3-alternate conformation (see the discussion of **12b**). The ^{1}H NMR spectra of the crude reaction mixtures of 1,3-bis(benzyloxy)- and 1,3-dipropoxythiacalix[4]arene-crown-4 exhibit an additional set of signals, of which the ArH peaks have similarities to those of the cone crown-5 isomer **17b** (approximately at 7.7 and 6.9 ppm; Figure 5). Therefore, we believe that the signals correspond to the cone conformer.

Conformationally Flexible Dihydroxy- and Dimethoxythiacalix[4]arene-monocrowns. 1,3-Dihydroxythiacalix[4]arene-crowns can be considered as borderline, between rigid and flexible, thiacalix[4]arene-crowns. Although the size of the hydroxyl groups allows rotation through the annulus, hydrogen-bonding[21] can stabilize the cone conformation. HCOSY couplings found for 1,3-dihydroxythiacalix[4]arene-crown-5 and -6 (**3b**,**c**) show that they have the crown-ether bridge peak order corresponding to that of a cone conformation. The X-ray crystal structure of **3c** showed a pinched cone conformation with stabilizing hydrogen bonds between phenolic hydrogens and one of the oxygens of the crown-ether bridge (Figure 5). Unlike the other crown-4 derivatives (**11a**, **12a**, and **13a**), the peaks of the dihydroxythiacalix[4]arene-crown-4 conformer, peak order (1,2,3), lie downfield [4.76 (t, 4 H), 4.25 (t, 4 H), 3.91 (s, 4 H) ppm]. NOE interactions, ArH/ArH and OH/crown-ether bridge, again confirmed a cone conformation (**3a**).

Temperature-dependent ^{1}H NMR studies were performed in order to study the possible conformational flexibility of the 1,3-dihydroxythiacalix[4]arene-crowns **3a**−**c**. Samples of **3a**−**c** measured in $CDCl_3$ (steps of 10°; temperature range 223−323 K) showed no conformational changes. In CD_2Cl_2 (223−313 K), we observed changes in the ^{1}H NMR spectrum of **3a**. The ArH, *tert*-butyl, Ar−O−CH_2, and OH peaks shift downfield upon increasing the temperature; at lower temperature the two ArH peaks are closer (Figure 6). The temperature-dependent, linear shifts may indicate a fast exchange between a non-hydrogen-bonded cone and a hydrogen-bonded pinched cone conformation. The reason that only

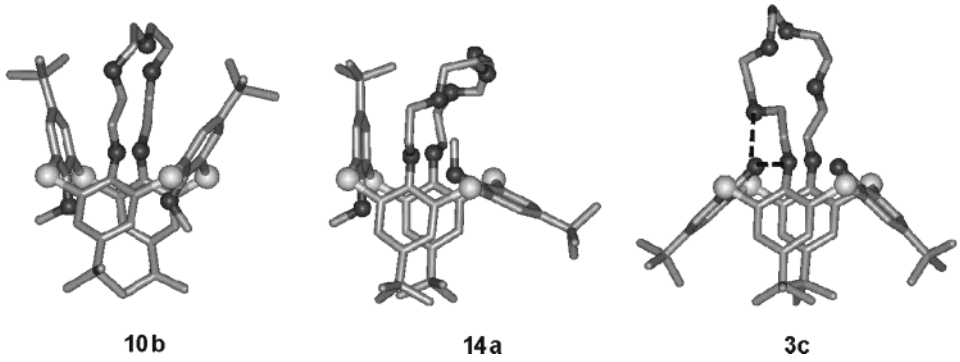

FIGURE 5. X-ray crystal structures of flexible thiacalix[4]arene-crown: 1,3-alternate 1,3-dimethoxythiacalix[4]arene-crown-5 **10b** (left), partial cone 1,3-dimethoxythiacalix[4]arene-crown-6 **14a** (middle), and cone 1,3-dihydroxythiacalix[4]arene-crown-6 **3c** (dotted lines depict H-bonds observed for the hydroxy group; right).

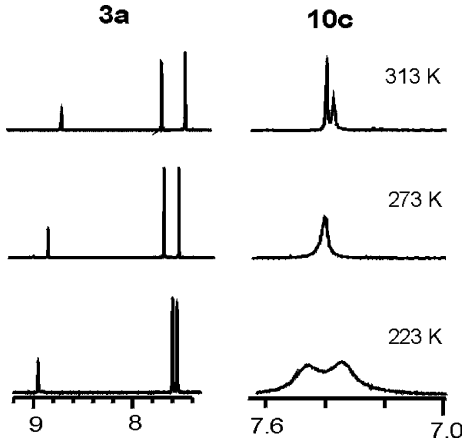

FIGURE 6. Temperature-dependent ^{1}H NMR studies: (left) OH and ArH peaks of cone 1,3-dihydroxythiacalix[4]arene-crown-4 **3a** (top to bottom: 313, 273, and 223 K) in CD_2Cl_2; (right) ArH peaks of 1,3-alternate 1,3-dimethoxythiacalix[4]-arene-crown-6 **10c** (top to bottom: 283, 253, and 223 K; $CHCl_3$ peak at 7.26 ppm has been removed).

3a and not **3b**,**c** exhibits this behavior may be caused by the smaller crown-size of **3a**. Smaller crown-sizes favor a pinched cone conformation, due to the formation of stabilizing hydrogen bonds.

The ^{1}H NMR spectrum of the rotationally flexible[21] 1,3-dimethoxythiacalix[4]arene-crown-5, in $CDCl_3$ at 298 K, shows only two peaks for the ArH, the *tert*-butyl, and the crown-ether bridge hydrogens (1:3). HCOSY correlations revealed an intermediate peak order (1−2,3,4).[31] In CD_2Cl_2, the resolution of the crown-ether bridge area is better, showing a similar peak order (1−3−4−2) as **12b**, which suggests a 1,3-alternate conformation. Both an X-ray crystal structure and NOE interactions verify the 1,3-alternate conformation (**10b**; Figure 5). (The crystal structure of the related compound **13b** also shows a 1,3-alternate conformation. Plots of this compound are included in the Supporting Information). The 1,3-dimethoxythiacalix[4]arene-crown-6 conformer obtained gives an order of the crown-ether bridge protons (1−2−3,4,5) similar to that of cone compound **18c**. NOE interactions, however, reveal that it has a 1,3-alternate conformation (**10c**). Surprisingly, crystallization of **10c** from CH_2Cl_2/hexane exclusively gave single crystals of **14a**, the X-ray crystal structure of which clearly proved the partial cone conformation (Figure 5). Furthermore, redissolving the crystals of **14a** in $CDCl_3$ gave a ^{1}H NMR spectrum identical to that of 1,3-alternate conformer **10c**. Since the anisole units are mobile,[21] this gives rise to a different conformation in the solid state and in solution. 1,3-Dimethoxythiacalix[4]arene-crown-4 has a ^{1}H NMR spectrum similar to those of **11a**, **12a**, and **13a**, suggesting a 1,3-alternate conformation (**10a**), which was confirmed with ROESY NMR.

Temperature-dependent ^{1}H NMR studies of 1,3-dimethoxythiacalix[4]arene-crowns **10a**−**c**, in the range 223−323 K, in $CDCl_3$ only revealed shifts for **10c** (Figure 6). Although no conformational interconversion was observed, even upon heating for 24 h at 407 K, the shifts are probably the result of the presence of two 1,3-alternate conformers. This was confirmed by observed NOE interactions and relates to the pinched-cone pinched-cone transitions observed by Čajan et al.[33] for tetrapropoxythiacalix[4]arenes.

Lang et al. have reported that propoxy groups are small enough to rotate through the thiacalix[4]arene annulus at elevated temperatures.[19] Therefore, solutions of 1,3-alternate conformers **11a**−**c** in $CDCl_2CDCl_2$ were heated at 407 K for 24 h.[34] Surprisingly, this did not give rise to any change in their conformation, indicating a high stability for the 1,3-alternate conformers.

Conclusions

This study describes the first synthesis of several thiacalix[4]arene-(bis)crown conformers, viz. the 1,2-alternate thiacalix[4]arene-biscrowns **5**, the partial cone **14**−**16**, and cone conformers of thiacalix[4]arene-monocrowns **3** and **17**−**19**. Both the cation and the length of the oligoethylene glycol used have a distinct influence on the outcome of the bridging reaction of thiacalix[4]-arene. The structural assignment of the different thiacalix-[4]arene-crown conformers was mainly based on X-ray crystal structures, supported by different ^{1}H NMR techniques. The order of the peaks of the crown-ether bridge, determined with COSY NMR, is very characteristic for a particular conformation. The ^{1}H NMR spectra of the conformationally flexible 1,3-dihydroxy- (**3**), 1,3-dimethoxy- (**10**), and 1,3-dipropoxythiacalix[4]arene-crowns (**11**) showed no conformational changes between 223 and 323 K (**3**, **10**) and after heating for 24 h at 407 K (**3**, **10**, **11**). The ArH peaks and the crown-ether bridge peak order provide conformational "signatures" of the different conformers that can act as a practical tool in the assignment of conformations of thiacalix[4]arene-crowns.

Experimental Section

General Methods. All solvents were purified by standard laboratory procedures. All other chemicals were analytically pure and used without further purification, except for pentaethylene glycol di-*p*-toluenesulfonate, which was prepared from pentaethylene glycol and tosyl chloride obtained from a commercial supplier. Acetonitrile, acetone, and dimethylformamide were dried on molecular sieves. *tert*-Butylthiacalix[4]-arene (**1**) was prepared according to the procedure described in the literature.[2] All reactions were carried out under an inert argon atmosphere.

The 2D DQF−COSY spectra (300 MHz) consisted of 1024 data points in t_2 and 256 increments in t_1. The ROESY spectra (400 MHz) were acquired with a mixing time of 400 ms, 1024 data points in t_2 and 128 increments in t_1, or 2984 data points in t_2 and 256 increments in t_1.

Thin-layer chromatography was performed on aluminum sheets precoated with silica gel 60 F254; spots were visualized by UV-Absorbency. Chromatographic separations were performed on silica gel 60 (0.040−0.063 mm, 230−240 mesh). Melting points are uncorrected.

General Procedure for the Formation of 25,27-Difunctionalized 5,11,17,23-Tetra-*tert*-butyl-2,8,14,20-tetrathiacalix[4]arenes Monocrown-*n* (*n* = 4, 5, or 6). To a suspension of 1,3-dialkoxythiacalix[4]arenes (**6**−**9**) in acetonitrile were added 4 equiv of K_2CO_3 and 1 equiv of tetra-, penta-, or hexaethylene glycol di-*p*-toluenesulfonate (**2a**−**c**). The mixture was refluxed for 5 d (12 h in case of **9**). Acetonitrile was

(32) Without two distinctly different spectra of two pure conformers, or an X-ray crystal structure, it was not possible to use the crown-ether bridge peak order to assign the conformations.

(33) Čajan, M.; Lhoták, P.; Lang, J.; Dvorráková, H.; Stibor, I.; Koca, J. *J. Chem. Soc., Perkin Trans. 2* **2002**, 1922−1929.

removed and the residue extracted with $CH_2Cl_2/CHCl_3$. The solution was washed twice with 10% HCl and water and dried on $MgSO_4$. Solvents were removed under reduced pressure and the residue was triturated with MeOH to remove unreacted glycol di-*p*-toluenesulfonates, yielding after drying white solids.

5,11,17,23-Tetra-*tert*-butyl-25,27-dimethoxy-2,8,14,20-tetrathiacalix[4]arene-monocrown-4, 1,3-Alternate (10a). A suspension of **6** (1.50 g, 2.0 mmol) in acetonitrile (100 mL) was reacted with **2a** (0.92 g, 2.0 mmol). After trituration with MeOH, the residue was triturated with CH_2Cl_2 to give **10a** (1.50 g, 87%): mp > 250 °C; ^{1}H NMR δ 7.49 (s, 4H), 7.30 (s, 4H), 4.10 (t, 4H, J = 4.0 Hz), 3.54 (t, 4H, J = 4.0 Hz), 3.32 (s, 6H), 2.51 (s, 4H), 1.33 (s, 18H), 1.30 (s, 18H); ^{13}C NMR δ 157.6, 156.3, 146.3, 145.9, 130.0, 129.3, 127.2, 126.1, 71.0, 70.3, 69.0, 55.7, 34.4, 34.2, 31.4, 31.2; MALDI-TOF *m*/*z* 863.9 $[M + H]^+$, 885.8 $[M + Na]^+$, 901.8 $[M + K]^+$, calcd 863.3 $[M + H]^+$. Anal. Calcd for $C_{48}H_{62}O_6S_4$: C, 66.78; H, 7.24. Found: C, 66.94; H, 6.95.

5,11,17,23-Tetra-*tert*-butyl-25,27-dimethoxy-2,8,14,20-tetrathiacalix[4]arene-monocrown-5, 1,3-Alternate (10b).[10] A suspension of **6** (1.50 g, 2.0 mmol) in acetonitrile (100 mL) was reacted with **2b** (1.05 g, 2.0 mmol) to give **10b** (1.68 g, 93%): mp > 250 °C (lit.[10] mp 266−268 °C). The spectral data are identical to those reported.[10]

5,11,17,23-Tetra-*tert*-butyl-25,27-dimethoxy-2,8,14,20-tetrathiacalix[4]arene-monocrown-6, 1,3-Alternate (10c).[10] A suspension of **6** (1.75 g, 2.3 mmol) in acetonitrile (100 mL) was reacted with **2c** (1.26 g, 2.3 mmol). After trituration with MeOH, column chromatography (SiO_2, 2% acetone in CH_2Cl_2) was performed to give **10c** (1.23 g, 59%): mp > 250 °C (lit.[10] mp 272−274 °C). The spectral data are identical to those reported.[10]

5,11,17,23-Tetra-*tert*-butyl-25,27-dipropoxy-2,8,14,20-tetrathiacalix[4]arene-monocrown-4, 1,3-Alternate (11a). A suspension of **7** (0.50 g, 0.6 mmol) in acetonitrile (50 mL) was reacted with **2a** (0.28 g, 0.6 mmol). After trituration with MeOH, column chromatography (SiO_2, EtOAc/hexane 0.5/9.5) was performed to give **11a** (0.33 g, 58%): mp > 250 °C; ^{1}H NMR δ 7.37 (s, 4H), 7.31 (s, 4H), 4.00−4.03 (m, 4H), 3.70−3.76 (m, 4H), 3.52 (t, 4H, J = 4.0 Hz), 2.48 (s, 4H), 1.31 (s, 18H), 1.26 (s, 18H), 0.80−0.92 (m, 4H), 0.65 (t, 6H, J = 7.3 Hz); ^{13}C NMR δ 158.0, 156.0, 145.9, 145.7, 128.6, 127.8, 126.8, 71.1, 70.0, 69.5, 68.6, 34.4, 34.2, 31.4, 31.2, 30.2, 29.7, 21.3, 9.7; MALDI-TOF *m*/*z* 919.6 $[M + H]^+$, 941.6 $[M + Na]^+$, 957.5 $[M + K]^+$, calcd 919.4 $[M + H]^+$. Anal. Calcd for $C_{52}H_{70}O_6S_4 \cdot 0.3H_2O$: C, 67.52; H, 7.62. Found: C, 67.50; H, 7.46.

5,11,17,23-Tetra-*tert*-butyl-25,27-dipropoxy-2,8,14,20-tetrathiacalix[4]arene-monocrown-5, 1,3-Alternate (11b),[10] Partial Cone (15a), and Cone (17b). A suspension of **7** (0.50 g, 0.6 mmol) in acetonitrile (50 mL) was reacted with **2b** (0.30 g, 0.6 mmol). After trituration with MeOH, column chromatography (SiO_2, EtOAc/hexane 0.5/9.5) was performed to give **11b**[10] (0.35 g, 59%), **15a** (9 mg, 2%), and **17b** (50 mg, 8%). **11b**: mp > 250 °C (lit.[10] mp 262−264 °C). The spectral data are identical to those reported.[10] **15a**: mp > 250 °C; ^{1}H NMR δ 7.63 (d, 2H, J = 2.2 Hz), 7.55 (s, 2H), 7.35 (s, 2H), 7.32 (d, 2H, J = 2.2 Hz), 4.00−4.06 (m, 8H), 3.74−3.76 (m, 4H), 3.51−3.59 (m, 6H), 3.09 (t, 2H, J = 6.2 Hz), 1.85−1.97 (m, 2H), 1.42 (s, 9H), 1.28 (s, 18H), 1.06 (s, 9H), 1.03 (t, 3H, J = 7.5 Hz), 0.38−0.49 (m, 2H), 0.02 (t, 3H, J = 7.3 Hz); ^{13}C NMR 158.1, 157.7, 146.4, 146.0, 145.9, 134.0, 131.1, 129.9, 129.4, 128.9, 128.0, 127.7, 79.2, 73.6, 71.2, 71.0, 70.6, 70.3, 34.3, 34.1, 31.4, 31.3, 31.0, 29.7, 23.1, 22.2, 10.6, 10.0; MALDI-TOF *m*/*z* 963.4 $[M + H]^+$, 985.4 $[M + Na]^+$, 1001.4 $[M + K]^+$, calcd 963.4 $[M + H]^+$. Anal. Calcd for $C_{54}H_{74}O_7S_4$: C, 67.32; H, 7.74. Found: C, 67.24; H, 7.69. **17b**: mp > 250 °C; ^{1}H NMR δ 7.70 (s, 4H), 6.84 (s, 4H), 4.55−4.61 (m, 4H), 4.25−4.31 (m, 4H), 3.90 (t, 4H, J = 7.0 Hz), 3.82 (s, 8H), 1.89−2.01 (m, 4H), 1.34 (s, 18H), 1.10 (t, 6H, J = 7.5 Hz), 0.82 (s, 18H); ^{13}C NMR δ 160.8, 157.9, 146.1, 145.8, 135.3, 132.5, 131.0, 128.7, 79.3, 72.9, 71.5, 71.0, 69.6, 34.4, 33.8, 31.5, 31.3, 30.9, 23.4, 10.8; MALDI-TOF *m*/*z* 963.6 $[M + H]^+$, 985.6 $[M + Na]^+$, 1001.6 $[M + K]^+$, calcd 963.4 $[M + H]^+$. Anal. Calcd for $C_{54}H_{74}O_7S_4$: C, 67.32; H, 7.74. Found: C, 67.47; H, 7.99.

5,11,17,23-Tetra-*tert*-butyl-25,27-dipropoxy-2,8,14,20-tetrathiacalix[4]arene-monocrown-6, 1,3-Alternate (11c).[10] A suspension of **7** (0.36 g, 0.4 mmol) in acetonitrile (50 mL) was reacted with **2c** (0.22 g, 0.4 mmol). After trituration with MeOH, column chromatography (SiO_2, 2% acetone in CH_2Cl_2) was performed to give **11c** (0.25 g, 57%): mp > 250 °C (lit.[10] mp 280−282 °C). The spectral data are identical to those reported.[10]

25,27-Bis(benzyloxy)-5,11,17,23-tetra-*tert*-butyl-2,8,14,-20-tetrathiacalix[4]arene-monocrown-4,1,3-Alternate (12a). A suspension of **8** (0.40 g, 0.4 mmol) in acetonitrile (50 mL) was reacted with **2a** (0.18 g, 0.4 mmol). After trituration with MeOH, column chromatography (SiO_2, CH_2Cl_2/hexane 1/1) was performed to give **12a** (0.15 g, 33%): mp > 250 °C; ^{1}H NMR δ 7.39 (s, 4H), 7.07−7.18 (m, 6H), 7.11 (s, 4H) 6.85−6.88 (m, 4H), 5.09 (s, 4H), 4.02−4.05 (m, 4H), 3.52−3.60 (m, 4H), 2.58 (s, 4H), 1.36 (s, 18H), 0.85 (s, 18H); ^{13}C NMR δ 157.7, 155.5, 146.2, 146.2, 137.3, 129.3, 128.8, 127.9, 127.8, 127.7, 127.3, 126.9, 71.2, 70.0, 69.9, 68.6, 34.4, 33.8, 31.4, 30.7; MALDI-TOF *m*/*z* 1015.9 $[M + H]^+$, 1037.9 $[M + Na]^+$, calcd 1015.4 $[M + H]^+$. Anal. Calcd for $C_{60}H_{70}O_6S_4$: C, 70.97; H, 6.95. Found: C, 70.82; H, 6.74.

25,27-Bis(benzyloxy)-5,11,17,23-tetra-*tert*-butyl-2,8,14,-20-tetrathiacalix[4]arene-monocrown-5,1,3-Alternate (12b) and Cone (18b). A suspension of **8** (0.50 g, 0.6 mmol) in acetonitrile (50 mL) was reacted with **2b** (0.30 g, 0.6 mmol). After trituration with MeOH, column chromatography (SiO_2, CH_2Cl_2/hexane 1/1) was performed to give **12b** (0.21 g, 33%); eluent change to 5% acetone in CH_2Cl_2 gave **18b** (0.12 g, 20%). **12b**: mp > 250 °C; ^{1}H NMR δ 7.41 (s, 4H), 7.09 (t, 2H, J = 7.4 Hz), 7.03 (s, 4H), 6.98 (t, 4H, J = 7.5 Hz), 6.84 (d, 4H, J = 7.6 Hz), 5.03 (s, 4H), 3.94 (t, 4H, J = 8.1 Hz,), 3.60−3.67 (m, 4H), 3.36−3.44 (m, 4H), 3.05 (t, 4H, J = 8.2 Hz), 1.38 (s, 18H), 0.85 (s, 18H); ^{13}C NMR δ 156.1, 155.9, 146.2, 146.1, 137.4, 128.5, 127.8, 127.5, 127.4, 127.2, 127.0, 126.8, 73.6, 71.4, 70.4, 70.1, 65.4, 34.4, 33.8, 31.5, 30.8; MALDI-TOF *m*/*z* 1059.5 $[M + H]^+$, 1081.4 $[M + Na]^+$, 1097.4 $[M + K]^+$, calcd 1059.4 $[M + H]^+$. Anal. Calcd for $C_{62}H_{74}O_7S_4$: C, 70.29; H, 7.04. Found: C, 69.99; H, 7.26. **18b**: mp 248−252 °C; ^{1}H NMR δ 7.69 (s, 4H), 7.60 (d, 4H, J = 6.2 Hz), 7.28−7.39 (m, 6H), 6.86 (s, 4H), 4.99 (s, 4H), 4.45−4.51 (m, 4H), 3.99−4.05 (m, 4H), 3.41−3.44 (m, 8H), 1.33 (s, 18H), 0.84 (s, 18H); ^{13}C NMR δ 160.6, 157.1, 146.1, 137.1, 135.2, 132.6, 130.9, 129.6, 129.0, 128.3, 128.0, 79.0, 73.0, 71.1, 70.6, 69.3, 34.3, 33.9, 31.4, 30.9; MALDI-TOF *m*/*z* 1059.7 $[M + H]^+$, 1081.6 $[M + Na]^+$, 1097.6 $[M + K]^+$, calcd 1059.4 $[M + H]^+$. Anal. Calcd for $C_{62}H_{74}O_7S_4$: C, 70.29; H, 7.04. Found: C, 70.06; H, 7.27.

25,27-Bis(benzyloxy)-5,11,17,23-tetra-*tert*-butyl-2,8,14,-20-tetrathiacalix[4]arene-monocrown-6,1,3-Alternate (12c) and Cone (18c). A suspension of **8** (1.0 g, 1.1 mmol) in acetonitrile (75 mL) was reacted with **2c** (0.60 g, 1.1 mmol). After trituration with MeOH, column chromatography (SiO_2, CH_2Cl_2/hexane 1/1) was performed to give **12c** (0.29 g, 24%); eluent change to 10% acetone in CH_2Cl_2 gave **18c** (0.25 g, 20%). **12c**: mp 227−230 °C; ^{1}H NMR δ 7.43 (s, 4H), 7.12 (d, 2H, J = 7.3 Hz), 7.07 (s, 4H), 7.03 (t, 4H, J = 7.3 Hz), 6.88 (d, 4H, J = 7.0 Hz), 5.06 (s, 4H), 3.96 (t, 4H, J = 7.3 Hz), 3.59 (s, 4H), 3.52 (s, 8H), 3.06 (t, 4H, J = 7.5 Hz), 1.38 (s, 18H), 0.87 (s, 18H); ^{13}C NMR δ 156.4, 156.1, 146.4, 146.1, 137.4, 128.7, 127.8, 127.6, 127.2, 126.8, 71.5, 71.4, 70.8, 70.2, 69.5, 66.8, 34.4, 33.8, 31.4, 30.7; MALDI-TOF *m*/*z* 1103.7 $[M + H]^+$, 1125.6 $[M + Na]^+$, 1141.6 $[M + K]^+$, calcd 1103.5 $[M + H]^+$. Anal. Calcd for $C_{64}H_{78}O_8S_4$: C, 69.66; H, 7.12. Found: C, 69.56; H, 7.10. **18c**: mp 229−234 °C; ^{1}H NMR δ 7.67 (s, 4H), 7.58−7.61 (m, 4H), 7.31−7.41 (m, 6H), 6.87 (s, 4H), 5.01 (s, 4H), 4.43−4.48 (m, 4H), 3.95−4.00 (m, 4H), 3.56 (s, 8H), 3.52−3.55 (m, 4H), 3.37−3.41 (m, 4H), 1.32 (s, 18H), 0.84 (s, 18H); ^{13}C NMR δ 160.5, 157.2, 146.2, 137.1, 135.2, 132.7, 131.0, 129.5, 129.1, 128.3, 128.1, 79.0, 72.8, 70.9, 70.5, 69.6, 34.4, 33.9, 31.4, 30.9; MALDI-TOF *m*/*z* 1103.5 $[M + H]^+$, 1125.5 $[M + Na]^+$, 1141.4

$[M + K]^+$, calcd 1103.5 $[M + H]^+$. Anal. Calcd for $C_{64}H_{78}O_8S_4$: C, 69.66; H, 7.12. Found: C, 69.75; H, 7.23.

5,11,17,23-Tetra-*tert*-butyl-25,27-bis[(ethoxycarbonyl)-methoxy]-2,8,14,20-tetrathiacalix[4]arene-monocrown-4, 1,3-Alternate (13a). A suspension of **9** (0.30 g, 0.3 mmol) in acetonitrile (30 mL) was reacted with **2a** (0.14 g, 0.3 mmol). After trituration with MeOH, column chromatography (SiO_2, 10% acetone in CH_2Cl_2) was performed to give **13a** (98 mg, 29%): mp 213-217 °C; ^{1}H NMR δ 7.35 (s, 4H), 7.32 (s, 4H), 4.41 (s, 4H), 4.08 (q, 4H, $J = 7.1$ Hz), 4.01−4.04 (m, 4H), 3.47−3.50 (m, 4H), 2.57 (s, 4H), 1.32 (s, 18H), 1.24 (s, 18H), 1.78 (t, 6H, $J = 7.3$ Hz); ^{13}C NMR δ 167.7, 157.7, 154.2, 146.4, 146.1, 129.8, 128.4, 127.3, 127.2, 71.2, 70.1, 68.9, 64.8, 60.1, 34.4, 34.1, 31.4, 31.0, 14.0; MALDI-TOF *m*/*z* 1007.9 $[M + H]^+$, 1029.9 $[M + Na]^+$, 1045.9 $[M + K]^+$, calcd 1007.4 $[M + H]^+$. Anal. Calcd for $C_{54}H_{70}O_{10}S_4$: C, 64.38; H, 7.00. Found: C, 64.20; H, 6.82.

5,11,17,23-Tetra-*tert*-butyl-25,27-bis[(ethoxycarbonyl)-methoxy]-2,8,14,20-tetrathiacalix[4]arene-monocrown-5, 1,3-Alternate (13b). A suspension of **9** (0.50 g, 0.5 mmol) in acetonitrile (50 mL) was reacted with **2b** (0.25 g, 0.5 mmol) to give **13b** (0.42 g, 71%): mp > 250 °C; ^{1}H NMR δ 7.36 (s, 4H), 7.34 (s, 4H), 4.36 (s, 4H), 4.06 (q, 4H, $J = 7.2$ Hz), 3.75−3.80 (m, 4H), 3.53−3.56 (m, 4H), 3.39−3.41 (m, 4H), 3.12−3.16 (m, 4H), 1.35 (s, 18H), 1.23 (s, 18H), 1.16 (t, 6H, $J = 7.1$ Hz); ^{13}C NMR δ 167.9, 156.9, 154.3, 146.2, 129.5, 128.3, 127.4, 127.0, 72.8, 70.9, 70.5, 67.6, 65.2, 60.1, 34.3, 34.1, 31.4, 31.0, 29.7, 23.7, 14.1; MALDI-TOF *m*/*z* 1051.8 $[M + H]^+$, 1068.8 $[M + Na]^+$, 1089.7 $[M + H]^+$, calcd 1051.4 $[M + H]^+$. Anal. Calcd for $C_{56}H_{74}O_{11}S_4 \cdot 0.5\ H_2O$: C, 63.43; H, 7.13. Found: C, 63.43; H, 7.36.

5,11,17,23-Tetra-*tert*-butyl-25,27-bis[(ethoxycarbonyl)-methoxy]-2,8,14,20-tetrathiacalix[4]arene-monocrown-6, 1,3-Alternate (13c). A suspension of **9** (0.30 g, 0.3 mmol) in acetonitrile (30 mL) was reacted with **2c** (0.16 g, 0.3 mmol). After trituration with MeOH, column chromatography (SiO_2, EtOAc/hexane 1/9) was performed to give **13c** (60 mg, 16%): mp > 250 °C; ^{1}H NMR δ 7.39 (s, 4H), 7.37 (s, 4H), 4.39 (s, 4H), 4.09 (q, 4H, $J = 7.1$ Hz), 3.74 (t, 4H, $J = 6.6$ Hz), 3.55 (s, 4H), 3.48−3.51 (m, 4H), 3.42−3.45 (m, 4H), 3.21 (t, 4H, $J = 6.8$ Hz), 1.33 (s, 18H), 1.24 (s, 18H), 1.18 (t, 6H, $J = 7.1$ Hz); ^{13}C NMR δ 167.6, 157.0, 154.3, 145.8, 130.2, 128.2, 127.4, 127.0, 70.9, 70.7, 70.6, 69.5, 68.8, 65.2, 59.9, 33.9, 33.7, 30.9, 30.6, 29.3, 13.6; MALDI-TOF *m*/*z* 1095.8 $[M + H]^+$, 1117.8 $[M + Na]^+$, 1133.8 $[M + K]^+$, calcd 1095.4 $[M + H]^+$. Anal. Calcd for $C_{58}H_{78}O_{12}S_4$: C, 63.59; H, 7.18. Found: C, 63.70; H, 7.18.

General Procedure for the Formation of 5,11,17,23-Tetra-*tert*-butyl-25,27-dihydroxy-2,8,14,20-tetrathiacalix-[4]arene-monocrown-*n* (*n* = 4, 5, or 6). A suspension of 1,3-dimethoxy-*p*-*tert*-butylthiacalix[4]arene-monocrown-*n* (**10a**−**c**) and 5.5 equiv of CH_3SNa or C_2H_5SNa in DMF was heated at 80 °C for 5 d. DMF was removed under reduced pressure, and the residue was redissolved in CH_2Cl_2/$CHCl_3$. The organic layer was washed with 1 N HCl (2 × 20 mL) and dried on $MgSO_4$. The solvents were removed, and the residue was purified by column chromatography and/or precipitation from MeOH, yielding white solids.

5,11,17,23-Tetra-*tert*-butyl-25,27-dihydroxy-2,8,14,20-tetrathiacalix[4]arene-monocrown-4, Cone (3a).[27] A suspension of **10a** (0.50 g, 0.6 mmol) in DMF (50 mL) was reacted with C_2H_5SNa (0.28 g, 3.3 mmol). Column chromatography (SiO_2, EtOAc/hexane 1/9) was performed to give **3a** (87 mg, 18%): mp > 250 °C (lit.[27] mp 272−273 °C). The spectral data are identical to those reported.[27]

5,11,17,23-Tetra-*tert*-butyl-26,28-dihydroxy-2,8,14,20-tetrathiacalix[4]arene-monocrown-5, Cone (3b).[22] A suspension of **10b** (0.50 g, 0.55 mmol) in DMF (25 mL) was reacted with CH_3SNa (0.21 g, 3.0 mmol). Column chromatography (SiO_2, EtOAc/hexane 1/9), followed by precipitation from MeOH, gave **3b** (0.12 g, 25%): mp 233−234 °C (lit.[27] mp 240−243 °C). The spectral data are identical to those reported.[22]

5,11,17,23-Tetra-*tert*-butyl-26,28-dihydroxy-2,8,14,20-tetrathiacalix[4]arene-monocrown-6, Cone (3c). A suspension of **10c** (0.30 g, 0.26 mmol) in DMF (30 mL) was reacted with C_2H_5SNa (0.12 g, 1.4 mmol) to give **3c** (39 mg, 16%): mp 175−185 °C; ^{1}H NMR δ 8.04 (s, 2H), 7.66 (s, 4H), 6.92 (s, 4H), 4.75 (t, 4H, $J = 4.4$ Hz), 4.13 (t, 4H, $J = 4.6$ Hz), 3.85−3.88 (m, 4H), 3.79−3.82 (m, 4H), 3.74 (s, 4H), 1.33 (s, 18H), 0.77 (s, 18H); ^{13}C NMR δ 156.0, 147.9, 142.5, 134.6, 132.6, 129.1, 122.2, 73.8, 71.0, 70.9, 70.8, 34.2, 34.0, 31.5, 30.7; MALDI-TOF *m*/*z* 923.3 $[M + H]^+$, 945.3 $[M + Na]^+$, calcd 923.4 $[M + H]^+$. Anal. Calcd for $C_{50}H_{66}O_8S_4$: C, 65.04; H, 7.20; S, 13.89. Found: C, 64.97; H, 7.13; S, 13.83.

X-ray Crystallographic Data. Crystal Data for 3c, 10b, 12b, 14a, and 18b. Diffraction data were collected at 150 K on a Nonius KappaCCD diffractometer on rotating anode ($\lambda_{MoK\alpha} = 0.710\ 73$ Å). All structures were solved using direct methods (SHELXS86[35]) and refined on F^2 (SHELXL-97[36]). The structures contained a number of disordered moieties that could be satisfactorily described with two-site disorder models: *tert*-butyl groups in **3c**, **12b**, **14a**, and **18b**; crown ether moieties in **10b** and **14a**; and benzyloxy groups in **18b**. Severely disordered solvent molecules in structures **10b**, **12b**, and **18b** were treated with corrections based on numerical Fourier transformations of the solvent area (SQUEEZE[37]). Ordered non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were included on calculated positions riding on their carrier. Full details of the structure determinations are given in the Supporting Information.

Compound **3c**: $C_{50}H_{66}O_8S_4$, $M_r = 923.31$, triclinic, $P\bar{1}$ (No. 2) with $a = 13.7693(10)$ Å, $b = 18.219(2)$ Å, $c = 20.773(2)$ Å, $\alpha = 77.239(15)°$, $\beta = 88.394(12)°$, $\gamma = 86.938(12)°$, $V = 5074.5(8)$ Å^3, $Z = 4$, R1[14423$I > 2\sigma(I)$] = 0.0650, wR2 (23162 refl) = 0.1903.

Compound **10b**: $C_{50}H_{66}O_7S_4$, $M_r = 907.31$, orthorhombic, *Pnma* (No. 62) with $a = 28.704(2)$ Å, $b = 12.6928(10)$ Å, $c = 14.2236(10)$ Å, $V = 5182.1(7)$ Å^3, $Z = 4$, R1[4732$I > 2\sigma(I)$] = 0.0613, wR2 (6218 refl) = 0.1646.

Compound **12b**: $C_{62}H_{74}O_7S_4$, $M_r = 1059.49$, monoclinic, $P2_1/c$ (No. 14) with $a = 15.327(2)$ Å, $b = 15.272(2)$ Å, $c = 27.561(4)$ Å, $\beta = 96.322(12)°$, $V = 6412.1(15)$ Å^3, $Z = 4$, R1-[7483$I > 2\sigma(I)$] = 0.0766, wR2 (11606 refl) = 0.1796.

Compound **14a**: $C_{52}H_{70}O_8S_4$, $M_r = 951.36$, monoclinic, $P2_1/c$ (no. 14) with $a = 15.2781(10)$ Å, $b = 12.2052(15)$ Å, $c = 28.622(2)$ Å, $\beta = 103.12(2)°$, $V = 5197.9(8)$ Å^3, $Z = 4$, R1[7745$I > 2\sigma(I)$] = 0.0645, wR2 (11884 refl) = 0.1882.

Compound **18b**: $C_{62}H_{74}O_7S_4$, $M_r = 1059.49$, triclinic, $P\bar{1}$ (No. 2) with $a = 13.986(2)$ Å, $b = 14.416(2)$ Å, $c = 33.061(6)$ Å, $\alpha = 92.229(16)°$, $\beta = 91.131(14)°$, $\gamma = 99.872(10)°$, $V = 6559.8(18)$ Å^3, $Z = 4$, R1[7675$I > 2\sigma(I)$] =0.1007, wR2(15964 refl) = 0.3031.

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Supporting Information Available: X-ray crystallographic data in CIF format, displacement ellipsoid plots for **3c**, **10b**, **12b**, **13b**, **14a**, and **18a**, and the X-ray crystallographic data of **13b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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