Singly Bridged Calix[8]crowns

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Received February 14, 2000

Crowned calix[8]arenes are obtained by direct alkylation of *p-tert*-butylcalix[8]arene (**1**) with poly(ethylene glycol) ditosylates in the presence of various bases. K_2CO_3 promotes the preferential formation of 1,3-calix[8]crowns. Cs_2CO_3 mainly gives the 1,5-isomers, which are selectively obtained in high yields when shorter chains are used (1,5-crown-2, 88%; 1,5-crown-3, 78%). NaH affords the 1,4-isomers in yields up to 46%, often as the sole crown derivative, besides unreacted **1**. 1,2-Calix[8]crowns are also obtained in appreciable amount in some instances. The observed regioselectivity is rationalized in terms of preferential formation of specific anions in dependence of the base strength. Dynamic NMR and modeling studies prove that the polyether chain, depending on its bridging mode, may significantly reduce the available space for the *through the annulus* passages leading to derivatives conformationally blocked (on the NMR time scale).

Introduction

In the past decade particular attention has been paid to the combination of calixarene[1] frameworks with crown-ether[2] moieties, which affords a class of compounds collectively named calixcrowns.[3] By changing calixarene size and number and length of the polyether chains, a large variety of macropolycycles with different physicochemical properties are obtained.[3] Of prominent interest is their complexing ability toward cations, often displayed with very remarkable and unparalleled selectivity. For instance, high Cs^+/Na^+ and K^+/Na^+ selectivities have been observed for 1,3-alternate calix[4]crowns-6 ionophores[4] and the corresponding crowns-5,[5] respectively, while crowns-4, in the partial-cone conformation, possess a reverted Na^+/K^+ preference.[6]

These successes have sparked a general interest in calixcrowns, leading to all the possible regio- and atropisomers of single- and double-crowned calix[4]arenes[3−7] and to the synthesis of a few examples of calix[5]crowns[8] and calix[6]crowns.[9] As concerns calix[8]crowns, the majority of the work has been carried out in our laboratory[10] and unexpectedly led to cesium-selective ionophores.[11] All of these results have been reported in preliminary communications,[11−13] and we give here full experimental data on the synthesis and characterization of singly bridged calix[8]crowns (calix[8]mono-crowns), while calix[8]bis-crowns and their complexing properties will be reported in forthcoming papers.

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10.1021/jo0002036 CCC: $19.00
Published on Web 07/21/2000

Chart 1

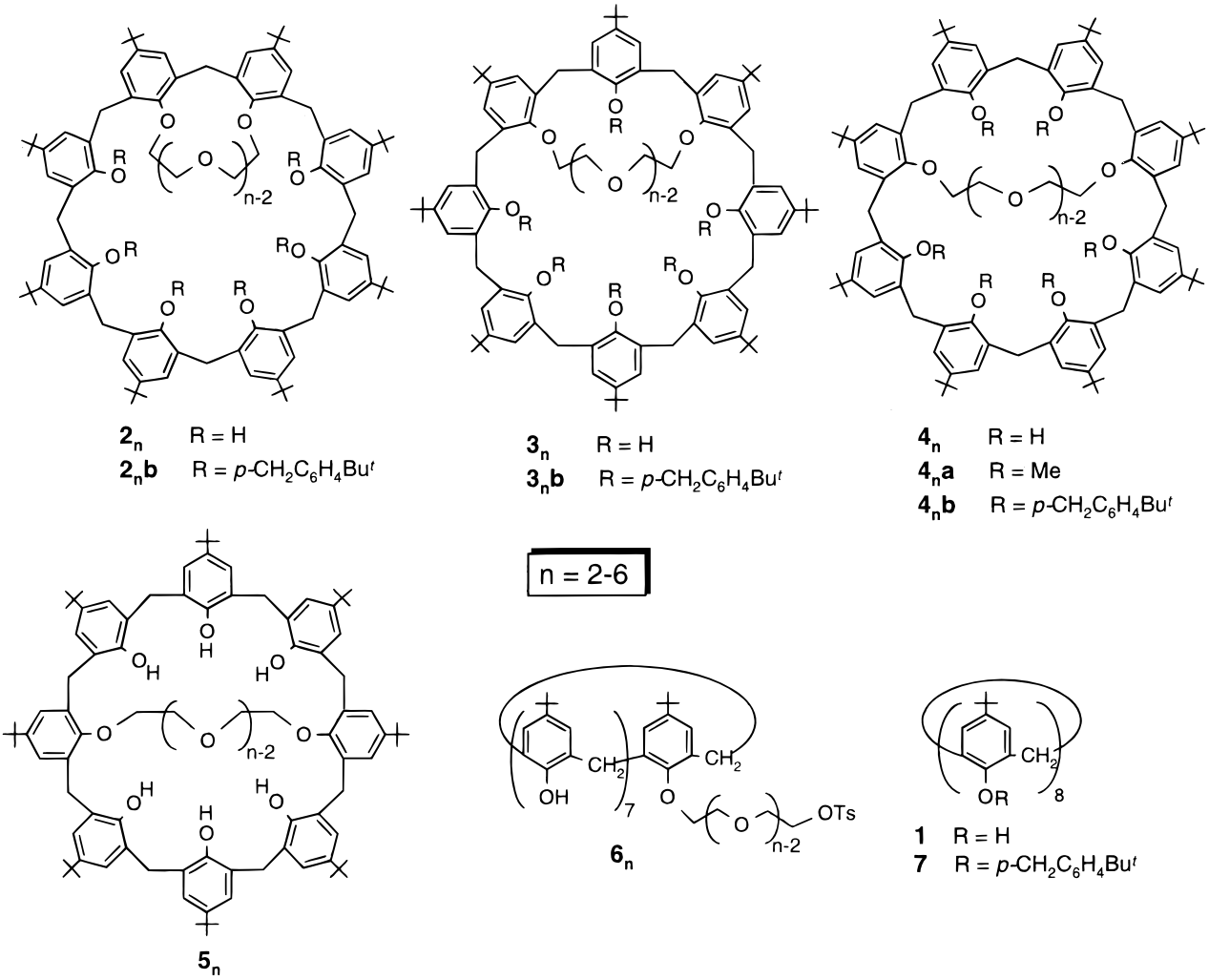


Table 1. Yield of Calix[8]crown-*n* in Direct Alkylation of 1 with $TsO(CH_2CH_2O)_mTs$ (1 equiv)[a] in the Presence of Various Bases (8 equiv)

entry	m	base	solvent (temp)	time (h)	compound (yield %)
1	3	K_2CO_3	Me_2CO (refl)	47	$\mathbf{2_4}$ (5), $\mathbf{3_4}$ (12), $\mathbf{6_4}$ (6)
2	3	Cs_2CO_3	Me_2CO (refl)	22	$\mathbf{2_4}$ (7), $\mathbf{4_4}$ (8), $\mathbf{5_4}$ (10)
3	1	Cs_2CO_3	DMF (60 °C)	12	$\mathbf{5_2}$ (88)
4	2	Cs_2CO_3	DMF (60 °C)	7	$\mathbf{5_3}$ (78)
5	3	KH	THF/DMF 10:1 (refl)	17	$\mathbf{2_4}$ (8), $\mathbf{4_4}$ (28)
6	3	NaH	THF/DMF 10:1 (refl)	3	$\mathbf{4_4}$ (35)
7	3	NaH	THF/DMF 10:1 (refl)	17	$\mathbf{4_4}$ (46)
8	4	NaH	THF/DMF 10:1 (refl)	3	$\mathbf{4_5}$ (31)
9	5	NaH	THF/DMF 10:1 (refl)	3	$\mathbf{4_6}$ (25)

[a] In the case of entries 3 and 4, 2 equiv of alkylating agent was used.

Results and Discussion

The synthesis of calix[8]crowns was carried out by direct alkylation of *p-tert*-butylcalix[8]arene **1** with an oligo(ethylene glycol) ditosylate in the presence of a base.[13] In this reaction four different singly bridged regioisomers can form, which we refer to as 1,2- ($\mathbf{2}_n$), 1,3- ($\mathbf{3}_n$), 1,4- ($\mathbf{4}_n$), or 1,5-calix[8]crown-*n* ($\mathbf{5}_n$), where *n* represents the number of oxygen atoms in the bridge (Chart 1). Since the experiments (Table 1) showed the crucial role of the base in the regiochemical outcome,[13] the results will be discussed in accordance with the base used.

Alkylation of *p-tert*-Butylcalix[8]arene in the Presence of Akali Carbonates. As summarized in Table 1, reactions in the presence of cesium, potassium, and sodium carbonates were performed in refluxing acetone using a stoichiometric amount of tri(ethylene glycol) ditosylate. Under these conditions sodium carbonate was unable to promote calix[8]crown formation even when present in large excess and with protracted reaction time (72 h).

K_2CO_3 was moderately efficient, and after 4 h monotosylpolyether $\mathbf{6_4}$ was obtained. Extending the reaction time to 47 h, 1,2-calix[8]crown-4 $\mathbf{2_4}$ and 1,3-calix[8]crown-4 $\mathbf{3_4}$ were also obtained in 5% and 12% yield, respectively (Table 1, entry 1).

The use of Cs_2CO_3 increased the yield of 1,2-calix[8]-crown-4 $\mathbf{2_4}$ (7%), and in addition two new compounds were obtained, 1,4-calix[8]crown-4 $\mathbf{4_4}$ (8%) and 1,5-calix-[8]crown-4 $\mathbf{5_4}$ (10%) (Table 1, entry 2). Thus, using two different bases it was possible to obtain all the four possible calix[8]crown-4 regioisomers, although in poor yields.

An impressive increase in calix[8]crowns yield was observed when shorter chain ditosylates were used, with Cs_2CO_3 as the base in DMF at 60 °C. Under these conditions 1,5-calix[8]crown-3 $\mathbf{5_3}$[11] and the corresponding 1,5-crown-2 $\mathbf{5_2}$ were formed in 78 and 88% yield, respectively (Table 1, entries 3 and 4). It is worth noting that under identical conditions the longer chain derivatives

are still formed in rather lower yields ($\mathbf{5_4}$, 15%), indicating that the chain shortness is mainly accountable for the higher yield of $\mathbf{5_3}$ and $\mathbf{5_2}$.

Alkylation of *p-tert*-Butylcalix[8]arene in the Presence of Alkali Hydrides. Alkylation of **1** with tri(ethylene glycol) ditosylate was extended to the stronger bases NaH and KH, in refluxing anhydrous THF/DMF (10:1). KH showed much better efficiency and selectivity than alkaline carbonates, and after 17 h compounds $\mathbf{2_4}$ and $\mathbf{4_4}$ were formed in 8% and 28% yield, respectively (Table 1, entry 5). Further improvement was obtained with NaH, which gave $\mathbf{4_4}$ as the sole crown derivative in 35% yield in 3 h (Table 1, entry 6), besides unreacted **1**. The yield reached 46% after 17 h (Table 1, entry 7).[14]

Considering the high efficiency and selectivity obtained for crown-4, the same conditions were applied to tetra- and penta(ethylene glycol) ditosylate. 1,4-crown-5 $\mathbf{4_5}$ and 1,4-crown-6 $\mathbf{4_6}$ were thus obtained in 31% and 25% yield, respectively (Table 1, entries 8 and 9). The preparative value of the NaH-promoted reactions was increased by suspending the crude reaction mixture in acetonitrile and filtering off the unreacted calix[8]arene. Almost pure 1,4-crown-n $\mathbf{4_n}$ derivatives could be thus obtained in preparative scale without resorting to chromatographic methods.

Structure Assignment. The structures of calix[8]-crowns were determined by NMR analysis (^{1}H, ^{13}C, and 2D NMR), once the molecular weight had been confirmed by FAB(+) measurements. The elementary analyses are in accordance with the molecular formula of the compounds. Discrimination among the four bridging modes (1,2, 1,3, 1,4, and 1,5) was mainly based on molecular symmetry as evidenced by the NMR signal patterns expected for conformationally mobile derivatives (see below).[15]

1,3-Calix[8]crown-*n* ($\mathbf{3_n}$). Among the four regioisomers, 1,3-crowns are characterized by a single binary symmetry element bisecting opposite aromatic rings (Ar−Ar symmetry).[15] This should be reflected by the appearance of a typical five-signal pattern (1:2:2:2:1) for the *tert*-butyl groups of the five types of aromatic rings. Indeed, in the ^{1}H NMR spectrum of compound $\mathbf{3_4}$ the expected five singlets were seen at δ 1.18, 1.23, 1.24, 1.26, and 1.27 (1:2:1:2:2). In addition, the symmetry was confirmed by the presence of 10 resonances in the 140−155 ppm region of the ^{13}C NMR spectrum (see Experimental Section) due to the quaternary aromatic carbons bearing oxygen atoms or *tert*-butyl groups.

1,5-Calix[8]crown-*n* ($\mathbf{5_n}$). 1,5-Crown derivatives possess the highest symmetry (double Ar−Ar) producing simple NMR spectra, characterized by a three-resonance pattern (1:2:1) for *tert*-butyls in the ^{1}H NMR spectra and six signals in the low field region of the ^{13}C NMR spectra. These features were both observed in the three 1,5-crowns ($\mathbf{5_2}$, $\mathbf{5_3}$, and $\mathbf{5_4}$) isolated in the present work. For instance, in the ^{1}H NMR spectrum of compound $\mathbf{5_3}$, acquired at 330 K, the three *tert*-butyl singlets were clearly seen at δ 1.12, 1.28, and 1.31 (1:2:1).

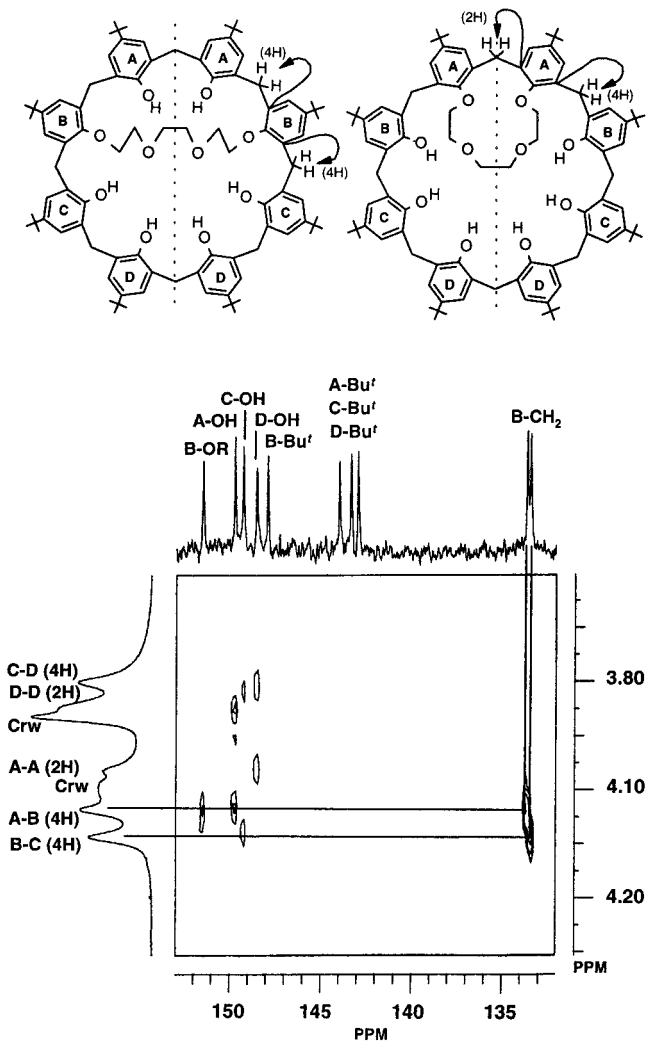


Figure 1. Portion of the ^{1}H−^{13}C long-range HETCOR NMR spectrum of 1,4-crown-4 $\mathbf{4_4}$. The structurally relevant correlations between bridgehead aromatic carbons (B−CH_2) and ArCH_2Ar protons (A−B, B−C) are indicated. For comparison, the expected correlations for 1,2 or 1,4 isomer are also indicated in the structure drawings.

1,4-Calix[8]crown-*n* ($\mathbf{4_n}$). 1,4- and 1,2-intrabridging are both characterized by a 2-fold symmetry element bisecting opposite ArCH_2Ar groups (CH_2−CH_2 symmetry). Consequently, their NMR spectra should display a four-singlet pattern (1:1:1:1) for *t*-Bu groups and eight signals for *C*-O and *C*-Bu quaternary carbons. Therefore, discrimination between these two bridging modes required additional information.

As an example, the CH_2−CH_2 symmetry of $\mathbf{4_4}$ was evidenced by four ^{1}H NMR signals at δ 1.17, 1.97, 1.22, and 1.25 (1:1:1:1) related to *tert*-butyl groups and eight ^{13}C NMR peaks for quaternary carbons in the low field region of the spectrum. Discrimination between 1,2- and 1,4-bridging patterns was achieved by a combination of 2D HETCOR and 2D Long-Range HETCOR NMR experiments, performed in C_6D_6 at 310 K in order to sufficiently resolve the methylene signals. Using the correlations observed in these spectra in conjunction with chemical shift arguments all the low-field ^{13}C NMR signals were assigned. In particular the bridgehead aromatic carbons of the alkylated rings (rings B in Figure 1) were clearly identified at 133.4 and 133.6 ppm, because of the downfield displacement produced by the *O*-alky-

(14) (a) Under similar conditions NaH promoted the 1,4-bridging of *p-tert*-butylcalix[8]arene with some bis(bromomethyl)arene derivatives: Ikeda, A.; Akao, K.; Harada, T.; Shinkai, S. *Tetrahedron Lett.* **1996**, *37*, 1621. (b) The 1,4-bridging with an acridone-based linker was also reported: Tsantrizos, Y. S.; Chew, W.; Colebrook, L. D.; Sauriol, F. *Tetrahedron Lett.* **1997**, *38*, 5411.

(15) The general principle of this approach has been detailed in ref 10 and in: Neri, P.; Consoli, G. M. L.; Cunsolo, F.; Geraci, C.; Piattelli, M. *New J. Chem.* **1996**, *20*, 443.

lation.[16] The presence of cross-peaks between these two carbons and two $ArCH_2Ar$ singlets of 4 H intensity (δ 4.04 and 4.08) revealed the 1,4-bridging (Figure 1), since the alternative 1,2-crown-4 structure requires these cross-peaks between two singlets of 4 and 2 H intensity, respectively.

Structure assignment of 1,4-calix[8]crown-5 **4$_5$** was based on analogous 2D NMR studies.

1,2-Calix[8]crown-4 (2$_4$). From NMR analysis it was evident that **2$_4$** possesses the same CH_2-CH_2 symmetry as the 1,4-regioisomer, since the typical four 18 H singlets for *t*-Bu groups were seen at δ 1.20, 1.23, 1.237, and 1.24, as well as the eight signals for quaternary aromatic carbons in the 140−155 ppm region of the ^{13}C NMR spectrum. At this point, since 1,4-crown-4 had been already identified, the 1,2-crown-4 structure was immediately assigned to **2$_4$** by exclusion.

1,4-Calix[8]crown-6 (4$_6$). OH Chemical Shifts. In the case of 1,4-calix[8]crown-6 **4$_6$**, the additional information to discriminate between 1,2- or 1,4-bridging was derived from ^1H NMR chemical shifts of the phenolic hydroxyls.[17] In fact, it is now well documented that in calixarene family the strength of intramolecular hydrogen bonds increases with increasing the number of consecutive hydroxyls, to reach a maximum in the closed, "circular H-bond" of the parent calixarenes.[18] This is reflected in the concomitant increase of OH groups chemical shift, reaching values up to more than 10 ppm for the closed systems.[18] Generalization of these observations leads to the following conclusions: "isolated" OH groups usually resonate at $\delta < 7.7$; "singly bonded" hydroxyls give signals at $7.7 < \delta < 8.7$; "doubly bonded" OH groups resonate at $\delta > 8.7$.[16,19] These limits move to lower field if stronger cooperativity occurs.[16]

Consideration of hydroxyl chemical shifts for calix[8]-crowns with unambiguously assessed structures (Figure 2) showed that the above empirical rules hold also for them. For instance, 1,3-crown-4 displays four distinct OH signals attributable to the isolated (δ 7.65, 1 H), singly bonded (δ 8.66, 2 H), and doubly bonded (δ 9.01 and 9.24, 2 and 1 H) hydroxyls.

Therefore, we confidently used the chemical shifts of OH groups as an aid in the structure determination of **4$_4$** and **4$_5$,** in which a fair distinction was possible within the singly bonded OH groups on the basis of the downfield shift produced by the cooperativity effect of the "semicircular" H-bond.[16] For both compounds the singly bonded hydroxyls involved in the "semicircular" H-bond (phenolic rings at positions 5 and 8 of the macrocycle)

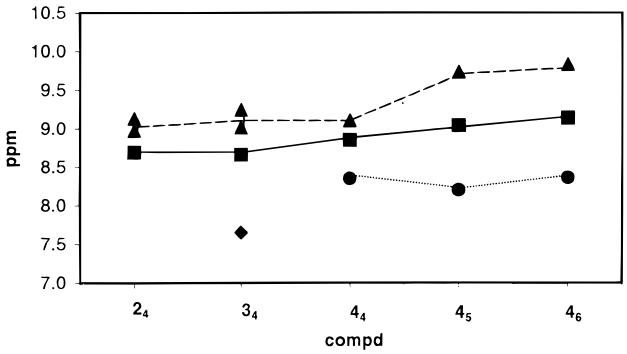


Figure 2. ^1H NMR chemical shift (see Experimental Section) of OH groups of selected calix[8]crowns. The different types of hydroxyls are indicated as follows: ♦ = isolated, ● = singly bonded, ■ = singly bonded involved in "semicircular" H-bond, ▲ = doubly bonded.

are seen at distinctly lower field (8.85 and 9.04 ppm) with respect to those at positions 2 and 3 (8.35 and 8.20 ppm), singly bonded only to each other. An examination of Table 1 shows that this cooperativity effect is present in all compounds having at least three consecutive hydroxyls and leads to a chemical shift not lower than 8.66 ppm. On this basis, the occurrence of a resonance at 8.36 ppm for **4$_6$** was considered diagnostic of the relegated singly bonded hydroxyls characteristic of 1,4-bridging.

On the Regiochemical Outcome in the Synthesis of Calix[8]mono-crowns. The regiochemical preferences in the reaction that leads to singly bridged calix-[8]crowns can be explained mainly in terms of strength of the base. A first deprotonation of **1** followed by nucleophilic attack to the oligo(ethylene glycol) ditosylate initially affords the open-chain monotosyl derivative **6$_n$** (Scheme 1). This can then give rise, after deprotonation, to a ring closure reaction at one of the four different phenolic rings, originating the four calix[8]crowns regioisomers. Obviously, the second deprotonation is crucial in determining the regiochemical outcome.[13]

In the presence of excess strong base, such as NaH or KH, a multiple deprotonation of open-chain derivative **6$_n$** has to be expected.[20] Very likely, a 2,4,6,8-tetraanion of type **8** (Scheme 1) is formed wherein the repulsive charge interaction is minimized and the hydrogen-bond stabilization maximized.[21] The subsequent closure step would lead to 1,4-bridged calix[8]crowns **4$_n$**. In the case of the KH-promoted reaction, the concurrent 1,2-bridging is likely due to metal template effect exerted by the potassium cation.[22]

In the case of the weaker base K_2CO_3 a preferential mono-deprotonation at position 3 of **6$_n$** should occur to give anion **9** (Scheme 1). In fact, previous studies had shown that alkylation of **1** proceeds through the *alternate pathway*,[23] with the intermediate formation of monoanions stabilized by proximal hydrogen bonds. Consequently, in this instance 1,3-crowns **3$_n$** are preferentially

(16) The validity of this "downfield displacement" rule and the comparison of OH chemical shift in a series of partial methoxycalix-[8]arenes have been discussed in: Cunsolo, F.; Consoli, G. M. L.; Piattelli, M.; Neri, P. *J. Org. Chem.* **1998**, *63*, 6852.

(17) For other examples of the use of OH chemical shift as a structural probe, see refs 8a, 16, and: Neri, P.; Battocolo, E.; Cunsolo, F.; Geraci, C.; Piattelli, M. *J. Org. Chem.* **1994**, *59*, 3880.

(18) Gutsche, C. D. *Acc. Chem. Res.* **1983**, *16*, 161. Keller, S. W.; Schuster, G. M.; Tobiason, F. L. *Polym. Mater. Sci. Eng.* **1987**, *57*, 906. The OH chemical shift in "large" calix[*n*]arenes ($n = 9-20$) has been comparatively discussed in: Stewart, D. R.; Gutsche, C. D. *J. Am. Chem. Soc.* **1999**, *121*, 4136.

(19) For a discussion on the OH chemical shift in partial alkoxycalix-[4]arenes, see: Araki, K.; Iwamoto, K.; Shinkai, S.; Matsuda, T. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 3480. Groenen, L.; Steinwender, E.; Lutz, B.; van der Maas, J.; Reinhoudt, D. N. *J. Chem. Soc., Perkin Trans. 2* **1992**, 1893. Similarly, for the partial alkoxycalix[6]arene series, see: Otsuka, H.; Araki, K.; Shinkai, S. *J. Org. Chem.* **1994**, *59*, 1542. Janssen, R. G.; Verboom, W.; Lutz, B. G.; van der Maas, J. H.; Maczka, M.; van Duynhoven, J. P. M.; Reinhoudt, D. N. *J. Chem. Soc., Perkin Trans. 2* **1996**, 1869.

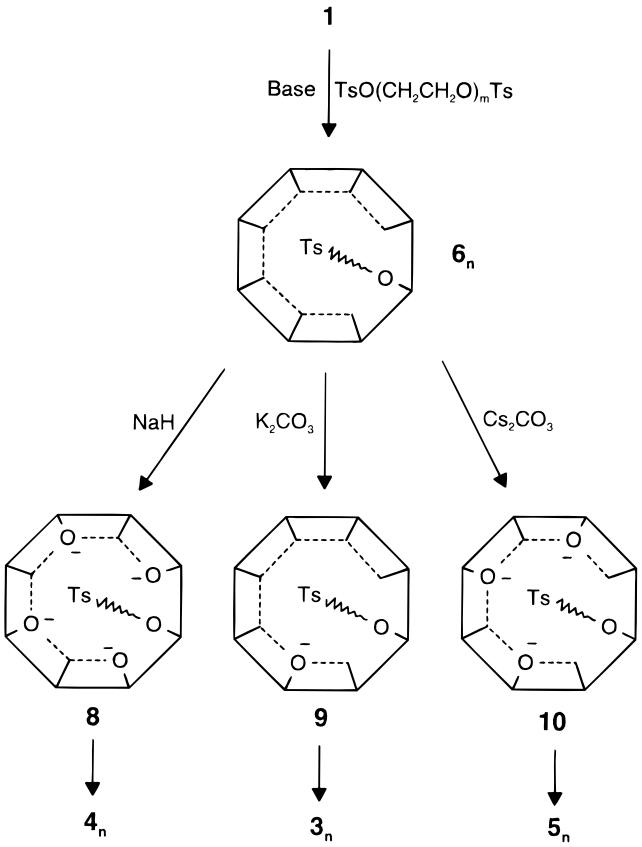
(20) Rogers, J. S.; Gutsche, C. D. *J. Org. Chem.* **1992**, *57*, 3152. Kanamathareddy, S.; Gutsche, C. D. *J. Org. Chem.* **1992**, *57*, 3160.

(21) For a discussion on the behavior of a preformed calix[8]arene trianion, see: Neri, P.; Consoli, G. M. L.; Cunsolo, F.; Rocco, C.; Piattelli, M. *J. Org. Chem.* **1997**, *62*, 4236.

(22) This template effect has also been invoked to explain the formation of 1,2-calix[4]crown: Yamamoto, H.; Sakaki, T.; Shinkai, S. *Chem. Lett.* **1994**, 469.

(23) Neri, P.; Geraci, C.; Piattelli, M. *J. Org. Chem.* **1995**, *60*, 4126. Consoli, G. M. L.; Cunsolo, F., Neri, P. *Gazz. Chim. Ital.* **1996**, *126*, 791.

Scheme 1



formed in the closure step. Again, the presence of potassium template effect could explain the concomitant formation of 1,2-crowns.[22]

In the reaction promoted by Cs_2CO_3, formation of a di- or trianion has to be anticipated, since this base in organic solvent has intermediate strength between K_2CO_3 and NaH.[24] In the case of triple deprotonation a 3,5,7-trianion like **10** should be formed (Scheme 1), more stabilized by hydrogen bonding with respect to other trianions. As a result of the high mobility of the calix[8]arene macrocycle, the 3,5,7-trianion can adopt a conformation characterized by the spatial proximity of diametrical 1 and 5 positions, such as the *pinched*[25] and the *chairlike*[26] ones recently characterized by X-ray crystallography, which explain the preferential 1,5-bridging. This consideration is supported by the finding that under identical conditions shorter chains give 1,5-bridged derivative $\mathbf{5_3}$ and $\mathbf{5_2}$ with yields (78% and 88%, respectively) remarkably higher than the longer ones (e.g., $\mathbf{5_4}$, 15%). Notably, this explains the apparent contradiction with the intuitive concept that farther positions requires longer bridges.[27]

Conformational Features. As mentioned in the structure assignment section, singly bridged calix[8]-crowns are conformationally mobile derivatives, as indicated by the presence in their room temperature ^{1}H NMR spectrum of broad signals for $ArCH_2Ar$ groups which sharpen at higher temperatures (Figures 3a,b and 4a,b). This mobility is even higher than that of calix[8]arene **1**, because the polyether chain breaks the stabilizing circular hydrogen bond in the parent compound.[18] However, the remaining H-bonds still contribute to reduce mobility.[28] Their suppression following methylation of the free OH groups leads to the corresponding hexamethoxy derivative $\mathbf{4_4a}$, highly mobile on the NMR time scale, as evidenced by the appearance of sharp singlets for $ArCH_2Ar$ groups (Figure 3c).

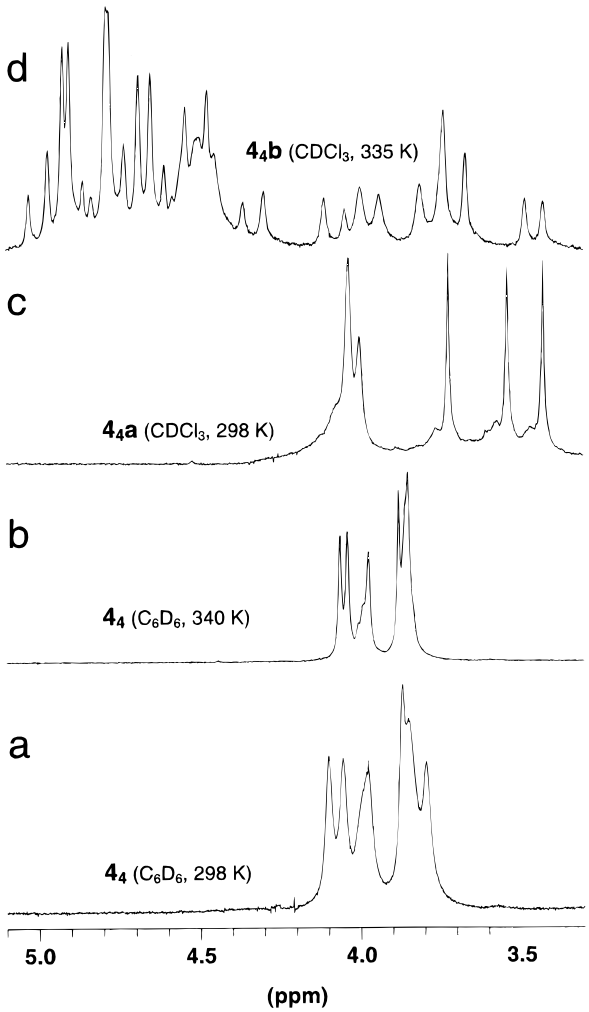


Figure 3. Comparison of the methylene region of ^{1}H NMR spectra of 1,4-calix[8]crown-4 derivatives at pertinent temperatures.

An additional effect of the presence of the polyether chain is the reduction of available space for the ring inversion process, which may occur either by the *oxygen* or *tert-butyl through the annulus* pathway (Figure 5). This finding suggests that the appendage of sufficiently bulky groups at the lower rim should inhibit the *oxygen through the annulus* route while the alternative *tert-butyl through the annulus* passage, although quite encumbered, in principle could not be excluded.[29] Consequently,

(24) Dijkstra, G.; Hruizinga, W. H.; Kellogg, R. M. *J. Org. Chem.* **1987**, *52*, 4230. Iwamoto, K.; Araki, K.; Shinkai, S. *Tetrahedron* **1991**, *47*, 4325. Shinkai, S. *Tetrahedron* **1993**, *49*, 8933 and references therein.

(25) Clague, N. P.; Clegg, W.; Coles, S. J.; Crane, J. D.; Moreton, D. J.; Sinn, E.; Teat S. J.; Young, N. A. *Chem. Commun.* **1999**, 379. This conformation was first suggested by Gutsche: Gutsche, C. D.; Bauer, L. J. *Tetrahedron Lett.* **1981**, *22*, 4763.

(26) Czugler, M.; Tisza, S.; Speier, G. *J. Incl. Phenom. Mol. Recognit. Chem.* **1991**, *11*, 323.

(27) Shinkai and co-workers similarly observed a preference for 1,4-bridging with longer and 1,5-bridging with shorter spacer in the alkylation of **1** with bis(bromomethyl)arenes.[14a]

(28) For a discussion on the conformational restriction by the residual hydrogen bonding in mono-*O*-substituted calix[6]arenes, see: Magrans, J. O.; Rincon, A. M.; Cuevas, F.; Lopez-Prados, J.; Nieto, P. M.; Pons, M.; Prados, P.; de Mendoza, J. *J. Org. Chem.* **1998**, *63*, 1079.

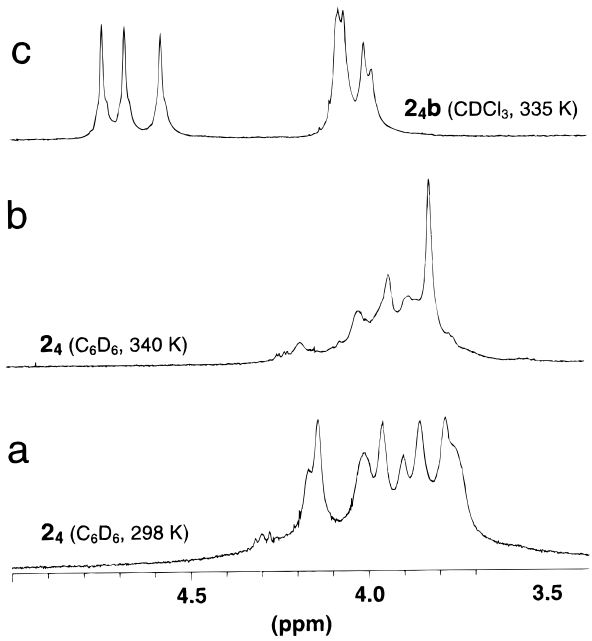


Figure 4. Comparison of the methylene region of ^{1}H NMR spectra of 1,2-calix[8]crown-4 derivatives at pertinent temperatures.

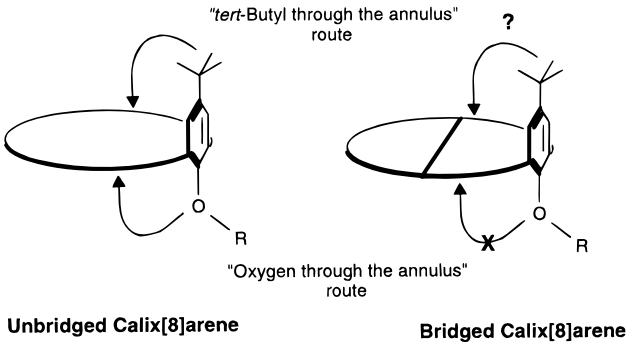


Figure 5. Pathways for conformational interconversion in *p-tert*-butylcalix[8]arenes and in their mono-crown derivatives.

any eventual conformational conversion could proceed only by the second mechanism, whose occurrence should be strongly dependent on the regioisomeric position of the bridging chain.

To verify these considerations we prepared the hexasubstituted *tert*-butylbenzyl derivatives of calix[8]crowns by exhaustive alkylation in the presence of Cs_2CO_3 (see Experimental Section), and their conformational mobility was investigated by dynamic NMR. Interestingly, the methylene region of the ^{1}H NMR spectrum of hexakis(*p-tert*-butylbenzyl)-1,4-crown-4 **4₄b** displays three AX and two AB systems for $ArCH_2Ar$ groups, which do not give any hint of coalescence by heating to 350 K (Figure 3d). This demonstrates that in **4₄b** conformational interconversions are prevented, at least on the NMR time scale. This finding can be understood on the basis of CPK computer models[30] of **4₄b**, which show that indeed *p-tert*-butylbenzyl groups quite effectively inhibit the *oxygen through the annulus* inversion and probably also the passage of the calixarene *tert*-butyls through the annulus. Obviously, this conformational behavior is entirely ascribable to the presence of the polyether chain, since unbridged octakis(*p-tert*-butylbenzyl)-calix[8]arene **7** is completely mobile at room temperature. Similar conclusions can be drawn from the CPK computer models of hexakis(*p-tert*-butylbenzyl)-1,3-crown-4 **3₄b,** which also contains temperature-independent AX systems for $ArCH_2$-Ar groups.[31]

On moving to hexakis(*p-tert*-butylbenzyl)-1,2-crown-4 **2₄b** a different situation is observed, since its ^{1}H NMR spectrum shows five singlets for $ArCH_2Ar$ groups indicating a high conformational mobility (Figure 4c). Again, this can be understood using computer models which show that upon 1,2-bridging a large portion of the calix[8]arene annulus remains available for conformational conversion (Figure 6), which may take place as easily as in the related octabenzylcalix[8]arene **7**.

Complexation Tests. In analogy to calix[4]crowns,[3−7] the presence of a polyether chain in calix[8]mono-crowns above-described suggests a potential complexing ability toward alkali cations. To test this potentiality two-phase picrate extraction[32] and ^{1}H NMR experiments were performed. In both cases, none of compounds **2$_n$**−**5$_n$**, **4₄a**, and **2₄b**−**4₄b** showed complexing properties worthy of note for Li^+, Na^+, K^+, Rb^+, or Cs^+. This could be explained in terms of poor preorganization of any ionophoric cavity probably because of the residual mobility of both calix[8]arene macrocycle and polyether chain. More effectively preorganized calix[8]bis-crown-3 derivatives show quite interesting size-dependent complexing properties.[11]

Conclusions

Intramolecular bridging is considered of central relevance for the preparation of calix[8]arene-based new preorganized hosts. In this respect, the results reported in this paper constitute the groundwork for the use of polyether chains as bridging elements. It is here demonstrated that direct alkylation of *p-tert*-butylcalix[8]arene with oligo(ethylene glycol) ditosylate gives the four possible calix[8]mono-crown regioisomers in yields and selectivity sometime quite surprising. The observed regioselectivity is amenable to rationalization in terms of preferential formation of specific anions, dependent on the base strength, shedding new light on the intricacies of calix[8]arene chemistry.

From the conformational viewpoint, the introduction of a single polyether chain does not significantly affect the intrinsic mobility of calix[8]arene macrocycle. However, its presence may significantly reduce the available space for the *through the annulus* passages leading to conformationally blocked (at least on the NMR time scale) derivatives when sufficiently bulky groups are attached

(29) It is worth to recall here that the *tert-butyl through the annulus* passage in unbridged *p-tert*-butylcalix[8]arenes is always operating as demonstrated by the fact that it occurs even in the smaller *p-tert*-butylcalix[6]arenes: Otsuka, H.; Araki, K.; Sakaki, T.; Nakashima, K.; Shinkai, S. *Tetrahedron Lett.* **1993**, *34*, 7275. van Duynhoven, J. P. M.; Janssen, R. G.; Verboom, W.; Franken, S. M.; Casnati, A.; Pochini, A.; Ungaro, R.; de Mendoza, J.; Nieto, P. M.; Prados, P.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1994**, *116*, 5814. Kanamathareddy, S.; Gutsche, C. D. *J. Org. Chem.* **1994**, *59*, 3871.

(30) Molecular modeling was performed with the *MacroModel V4.5* computer program: Mohamadi, F.; Richards, N. G. J.; Guida, W. C.; Liskamp, R.; Lipton, M.; Caufield, C.; Chang, G.; Hendrickson, T.; Still, W. C. *J. Comput. Chem.* **1990**, *11*, 440.

(31) On the basis of computer models this conclusions should also be applicable to the corresponding 1,5-crown-4 derivative. However, in this case the difficulty encountered in obtaining a sufficiently pure compound impeded the experimental NMR confirmation.

(32) Arduini, A.; Pochini, A.; Reverberi, S.; Ungaro, R.; Andreetti, G. D.; Ugozzoli, F. *Tetrahedron* **1986**, *42*, 2089.

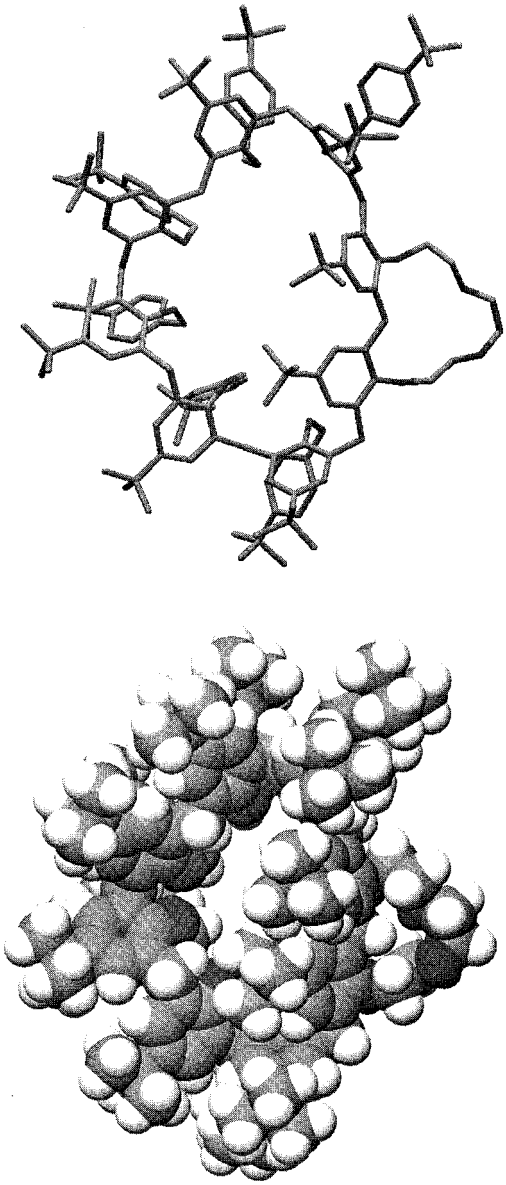


Figure 6. Polytube (top) and CPK (bottom) computer model of **2_4b** showing that the polyether chain does not inhibit the *tert-butyl through the annulus* passage.

at the lower rim. Of course, this influence can be altered by controlling the bridging mode and the length of the polyether chain.

As demonstrated in preliminary studies, the introduction of additional bridges in calix[8]mono-crowns leads to truly preorganized derivatives able to host suitable guests.[11] In these instances, intriguing stereochemical problems could be associated,[12b,c,33] and sophisticated topological implications could also be evidenced.

Experimental Section

General Comments. Melting points are uncorrected. NMR spectra were taken at 250.13 (^{1}H) and 62.9 (^{13}C) MHz, using Me_4Si as internal standard. FAB MS measurements were performed at the I.C.T.M.P.-C.N.R. (Catania) using 3-nitrobenzyl alcohol as matrix. Elemental analyses were obtained from the Department of Pharmaceutical Sciences, University of Catania. Column chromatography was performed using silica gel (Kieselgel 60, 63−200 μm, Merck). All chemicals were reagent grade and were used without further purification. Anhydrous THF and DMF were purchased from Aldrich. *p-tert*-Butylcalix[8]arene (**1**) was prepared as reported.[34]

General Procedures for the Synthesis of Calix[8]-crowns. A. A solution of **1** (0.5 g, 0.385 mmol) in Me_2CO (30 mL) was stirred in the presence of Cs_2CO_3 (1.0 g, 3.08 mmol) or K_2CO_3 (0.425 g, 3.08 mmol) for 30 min at reflux. Tri(ethylene glycol) ditosylate (0.176 g, 0.385 mmol) dissolved in Me_2CO (1 mL) was then slowly added, and the mixture stirred under reflux for 22−47 h according to the base used. After concentration under vacuum the residue was triturated with 100 mL of HCl, collected by filtration, washed with MeOH, and dried. The crude product was suspended in acetonitrile, and the insoluble starting material removed by filtration. The filtrate containing the calix[8]crowns was taken to dryness, and the residue purified by chromatography on silica gel.

B. To a solution of **1** (0.5 g, 0.385 mmol) in THF/DMF (30/3 mL) was added NaH (or KH) (3.08 mmol) under stirring. The mixture was refluxed for 30 min, and then the oligo(ethylene glycol) ditosylate (0.385 mmol) in THF (2 mL) was added dropwise. The reaction was refluxed under stirring for 3−17 h (Table 1). Workup of the reaction mixture followed procedure A.

C. Cs_2CO_3 (1.0 g, 3.08 mmol) was added under stirring to a solution of **1** (0.5 g, 0.385 mmol) in DMF (70 mL). The mixture was kept at 60−70 °C for 20 min, and then a solution of mono- or di(ethylene glycol) ditosylate (0.77 mmol) in DMF (4 mL) was added dropwise. The reaction was stirred at 60−70 °C for 7 or 12 h for compounds **5_3** and **5_2**, respectively. After concentration under vacuum the residue was triturated with 100 mL of HCl, collected by filtration, washed with MeOH, and dried. The crude product was purified by chromatography on silica gel.

Open-chain monotosylcalix[8]crown-4 6_4: procedure A, entry 1, Table 1, purification by column chromatography (SiO_2, gradient AcOEt/cyclohexane) white powder (6%), mp 178−182 °C; ^{1}H NMR ($CDCl_3$, 295 K) δ 1.26, 1.27, 1.29, 1.30 (s, 36 H, 18 H, 9 H, 9 H), 2.23 (s, 3 H), 3.30, 3.53 (br t, 2 H each), 3.60−4.23 (overlapped, 24 H), 6.96−7.36 (overlapped, 18 H), 7.68 (d, 2H, J = 8.0 Hz), 8.96, 9.22, 9.42 (br s, 2 H, 2 H, 3 H); ^{13}C NMR ($CDCl_3$, 295 K) δ 30.4, 31.6, 32.2, 32.6 (t), 31.5, 34.0 (q), 34.0, 34.3 (s), 68.5, 69.0, 70.2, 70.6, 70.7, 74.7 (t), 125.2, 125.4, 125.6, 125.7, 125.8, 126.6, 127.6, 127.8, 129.6 (d), 125.9, 126.9, 127.4, 127.7, 127.9, 133.1, 133.5, 143.1, 144.3, 144.5, 144.6, 146.6, 147.0, 147.1, 147.9, 148.4, 150.3 (s); FAB(+) MS m/z 1583 $(MH)^+$. Anal. Calcd for $C_{101}H_{130}O_{13}S$: C, 76.48; H, 8.26; S, 2.02. Found: C, 76.51; H, 8.28; S, 2.00.

1,2-Calix[8]crown-4 2_4: procedure B, entry 5, Table 1, purification by column chromatography (SiO_2, gradient AcOEt/cyclohexane) white powder (8%), mp 196−198 °C; ^{1}H NMR ($CDCl_3$, 295 K) δ 1.24, 1.25, 1.26 (s, 36 H, 18 H, 18 H), 3.70−4.35 (overlapped, 28 H), 7.00−7.27 (overlapped, 16 H), 8.69, 8.97, 9.13 (br s, 2 H each). ^{1}H NMR ($(CD_3)_2CO$), 324 K) δ 1.20, 1.23, 1.237, 1.24 (s, 18 H each); ^{13}C NMR ($CDCl_3$, 295 K) δ 28.0, 29.7, 31.3, 32.1, 32.3 (t), 31.5 (q), 34.0, 34.3 (s) 70.1, 71.5, 74.8 (t), 125.4, 125.7, 126.4 (d), 127.0, 127.6, 127.9, 132.9, 143.3, 143.7, 143.9, 147.2, 147.4, 147.6, 148.3, 150.5 (s); FAB-(+) MS m/z 1411 $(MH)^+$. Anal. Calcd for $C_{94}H_{122}O_{10}$: C, 79.96; H, 8.71. Found: C, 79.91; H, 8.68.

1,3-Calix[8]crown-4 3_4: procedure A, entry 1, Table 1, purification by column chromatography (SiO_2, gradient AcOEt/cyclohexane) white powder (12%), mp 199−202 °C; ^{1}H NMR ($CDCl_3$, 295 K) δ 1.18, 1.23, 1.24, 1.26, 1.27 (s, 9 H, 18 H, 9 H, 18 H, 18 H), 3.65−4.35 (overlapped, 28 H), 7.01, 7.14−7.18 (overlapped, 16 H), 7.65, 8.66, 9.01, 9.24 (br s, 1 H, 2 H, 2 H, 1 H); ^{13}C NMR ($CDCl_3$, 295 K) δ 30.4, 31.2, 32.2, 32.3 (t), 31.5 (q), 34.0, 34.3 (s), 69.5, 70.8, 74.1 (t), 124.7, 125.1, 125,5, 125.6, 125.8, 126.2, 127.0 (d), 127.4, 127.5, 127.6, 128.1, 132.7, 133.5, 142.6, 143.4, 143.8, 144.0, 147.4, 147.6, 147.7, 148.2, 148.8, 150.9 (s); FAB(+) MS m/z 1411 $(MH)^+$. Anal. Calcd for $C_{94}H_{122}O_{10}$: C, 79.96; H, 8.71. Found: C, 79.85; H 8.78.

(33) Ikeda, A.; Suzuki, Y.; Shinkai, S. *Tetrahedron: Asymmetry* **1998**, *9*, 97. Geraci, C.; Bottino, A.; Piattelli, M.; Gavuzzo, E.; Neri, P. *J. Chem. Soc., Perkin Trans. 2* **2000**, 185.

(34) Munch, J. H.; Gutsche, C. D. *Org. Synth.* **1989**, *68*, 243.

1,5-Calix[8]crown-4 5_4: procedure A, entry 2, Table 1, purification by column chromatography (SiO_2, gradient AcOEt/cyclohexane) white powder (10%), mp 230−233 °C; ^{1}H NMR ($CDCl_3$, 295 K) δ 1.24, 1.32, 1.35 (s, 36 H, 18 H, 18 H), 3.65−4.35 (overlapped, 28H), 7.12 (d, 8 H, J = 1.5 Hz), 7.22, 7.29 (s, 4 H each), 8.99, 9.65 (br s, 4 H, 2 H); ^{13}C NMR ($CDCl_3$, 295 K) δ 26.8, 32.9 (t), 31.4, 31.5, 31.6 (q), 34.0, 34.3 (s), 70.4, 71.9, 75.1 (t), 125.0, 125.5, 126.2, 126.6 (d), 127.1, 127.2, 127.3, 133.1, 143.0, 143.5, 147.9, 148.3, 148.6, 150.1 (s); FAB(+) MS m/z 1411 $(MH)^+$. Anal. Calcd for $C_{94}H_{122}O_{10}$: C, 79.96; H, 8.71. Found: C, 79.80; H, 8.68.

1,5-Calix[8]crown-2 5_2: procedure C, entry 3, Table 1, white powder (88%), purification by column chromatography (SiO_2, gradient AcOEt/petroleum ether), mp > 280 °C (dec); ^{1}H NMR ($CDCl_3$, 330 K) δ 1.11, 1.25, 1.33, (s, 18, 18, 36 H), 3.81, 3.89 (br s, 8 H each), 5.20 (br s, 4 H), 6.96, 7.12 (s, 4 H each), 7.17 and 7.19 (AB system, 8 H, J = 1.5 Hz), 8.62, 8.99 (s, 4 H, 2 H); ^{13}C NMR ($CDCl_3$, 330 K) δ 31.1, 31.5, 31.7 (q), 32.3 (t), 34.0, (s), 70.9 (t), 125.7, 126.5, (d), 127.3, 128.2, 133.0, 143.4, 149.0, 151.6, 152.6 (s); FAB(+) MS m/z 1345 $(MNa)^+$. Anal. Calcd for $C_{90}H_{114}O_8$: C, 81.71; H, 8.68. Found: C, 81.35; H, 8.72.

1,5-Calix[8]crown-3 5_3: procedure C, entry 4, Table 1, white powder (78%), purification by column chromatography (SiO_2, gradient AcOEt/cyclohexane), mp > 280 °C (dec); ^{1}H NMR ($CDCl_3$, 330 K) δ 1.12, 1.29, 1.31, (s, 18, 36, 18 H), 3.83 (br s, 8 H), 3.95, 4.27 (br t, 4 H each), 4.67 (br s, 8 H), 7.00 (s, 4 H), 7.09, 7.17 (AB system, 4 H each, J = 2.2 Hz) 7.21 (s, 4 H), 7.17 and 7.19 (AB system, 8 H, J = 1.5 Hz), 8.57, 8.65 (s, 2 H, 4 H); ^{13}C NMR ($CDCl_3$, 295 K) δ 31.2, 32.4 (t), 31.5 (q), 33.9, 34.2 (s), 69.7, 74.7 (t), 125.3, 125.4, 125.9, 127.0 (d), 143.1, 143.8, 147.7, 148.1, 148.1, 148.9, 149.4 (s); FAB(+) MS m/z 1367 $(MH)^+$. Anal. Calcd for $C_{92}H_{118}O_9$: C, 80.78; H, 8.69. Found: C, 80.55; H, 8.62.

1,4-Calix[8]crown-4 4_4: procedure B, entry 7, Table 1, purification by column chromatography (SiO_2, gradient AcOEt/cyclohexane) white powder (46%), mp 229−232 °C; ^{1}H NMR $(CD_3)_2CO$, 295 K) δ 1.17, 1.97, 1.22, 1.25 (s, 18 H each), 3.70−4.10 (overlapped, 28 H), 7.06 (d, 2 H, J = 2,2 Hz), 7.12 (d, 2 H, J = 2.2 Hz), 7.16 (d, 2 H, J = 2.4 Hz), 7.18 (d, 2 H, J = 2.3 Hz), 7.28 (d, 2 H, J = 2.0 Hz), 7.30 (d, 2 H, J = 2.5 Hz), 7.34 (d, 2 H, J = 2.3 Hz), 8.35, 8.85, 9.05 (br s, 2 H each); ^{1}H NMR (C_6D_6, 307 K) δ 1.20, 1.25 (s, 18 H each), 1.26, (s, 36 H), 3.82, 3.85, 3.87 (br s, 4 H, 2 H, 6 H), 3.97, 4.04, 4.08 (br s, 8 H, 4 H, 4 H), 7.10−7.30 (overlapped, 16 H); ^{13}C NMR (C_6D_6, 307 K) δ 30.5, 31.2, 32.4, 32.6, 32.8 (t), 31.5, 31.8 (q), 34.1, 34.4 (s), 70.5, 71.5, 75.1 (t), 125.1, 125.7, 126.0, 126.3, 126.6, 127.0, 128.3 (d), 129.1, 133.4, 133.6, 143.0, 143.4, 144.0, 147.9, 148.5, 149.3, 149.7, 151.5 (s); FAB(+) MS 1411 $(MH)^+$. Anal. Calcd for $C_{94}H_{122}O_{10}$: C, 79.96; H; 8.71. Found: C, 79.89, H, 8.62.

1,4-Calix[8]crown-5 4_5: procedure B, entry 8, Table 1, purification by column chromatography (SiO_2, gradient AcOEt/cyclohexane), white powder (31%), mp 197−199 °C; ^{1}H NMR ($CDCl_3$, 306 K) δ 1.24, 1.28, 1.32, 1.34 (s, 18 H each), 3.84 (br s, 8 H), 3.91, 3.94 (s, 2 H each), 3.95, 4.01, 4.11 (s, 4 H each), 4.13, 4.36 (br t, 4 H each), 7.06 (d, 2 H, J = 2.2 Hz), 7.14 (d, 2 H, J = 2.3 Hz), 7.17 (d, 4 H, J = 2.1 Hz), 7.20 (d, 4 H, J = 2.3 Hz), 7.21 (d, 2 H, J = 2.4 Hz), 7.23 (d, 2 H, J = 2.4 Hz), 8.20, 9.04, 9.73 (br s, 2 H each); ^{13}C NMR ($CDCl_3$, 306 K) δ 30.6, 30.9, 31.7, 31.9, 32.8 (t), 31.3, 31.6 (q), 34.0, 34.3 (s) 70.1, 71.0, 71.5, 74.9 (t), 125.3, 125.7, 125.9, 126.2, 126.3, 126.4 (d), 126.5, 126.9, 127.1, 127.4, 127.7, 132.4, 132.9, 142.9, 143.0, 143.7, 147.9, 148.0, 148.8, 150.2 (s); FAB(+) MS m/z 1455 $(MH)^+$. Anal. Calcd for $C_{96}H_{126}O_{11}$: C, 79.18; H, 8.72. Found: C, 79.30, H, 8.73.

1,4-Calix[8]crown-6 4_6: procedure B, entry 9, Table 1, purification by column chromatography (SiO_2, gradient AcOEt/cyclohexane), white powder (25%); ^{1}H NMR ($CDCl_3$, 293 K) δ 1.18, 1.23, 1.27, 1.28 (s, 18 H each), 3.69 (br s, 4 H), 3.77, 3.83 (m, 4 H each), 3.86, 3.90, 4.00, 4.10 (br s, 4 H each), 4.11, 4.26 (m, 4 H each), 7.00 (d, 2 H, J = 1.9 Hz), 7.08 (d, 2 H, J = 2.5 Hz), 7.14−7.23 (overlapped, 12 H), 8.36, 9.14, 9.83 (br s, 2 H each); ^{13}C NMR ($CDCl_3$, 306 K) δ 30.7, 31.2, 32.7 (t), 31.3, 31.5 (q), 34.0, 34.3 (s), 70.7, 70.8, 71.8, 75,0 (t), 125.2, 125.6, 125.7, 125.9, 126.2, 126.4 (d), 126.6, 126.9, 127.1, 127.3, 127.6, 128.7, 132.3, 132.7, 142.8, 143.1, 143.7, 147.6, 147.6, 147.9, 148.9, 150.5 (s); FAB(+) MS m/z 1499 $(MH)^+$. Anal. Calcd for $C_{98}H_{130}O_{12}$: C, 78.47; H, 8.73. Found: C 78.55; H, 8.78.

Hexamethoxy-1,4-calix[8]crown-4 4_4a. A mixture of 1,4-calix[8]crown-4 (70 mg, 0.050 mmol) and NaH (38 mg, 1.6 mmol) in anhydrous THF (30 mL) was refluxed under stirring for 30 min. CH_3I (0.1 mL, 1.6 mmol) was then added, and the reaction mixture was refluxed for 30 h. Evaporation under vacuum left a residue that was suspended in 1 N HCl, collected by filtration, dried, and purified by column chromatography (SiO_2, increasing concentrations of AcOEt in cyclohexane as the eluting system) to give **4_4a** (40 mg, 53%): white powder, mp 142−144 °C; ^{1}H NMR ($CDCl_3$, 295 K) δ 1.06, 1.07, 1.11, 1.32 (s, 18 H each), 2.76 (br s, 4 H), 2.80, 2.95 (br t, 4 H each), 3.43, 3.54, 3.72 (s, 6 H each), 4.00, 4.03 (br s, 4 H, 12 H), 6.69 (d, 2 H, J = 2.2 Hz), 6.82 (d, 2 H, J = 2.2 Hz), 6.87 (d, 2 H, J = 2.3 Hz), 6.98 (d, 2 H, J = 2.2 Hz), 7.04 (d, 2 H, J = 2.3 Hz), 7.09 (d, 2 H, J = 2.3 Hz), 7.12 (d, 2 H, J = 2.4 Hz), 7.22 (d, 2 H, J = 2.4 Hz); FAB(+) MS m/z 1495 $(MH)^+$. Anal. Calcd for $C_{100}H_{134}O_{10}$: C, 80.28, H, 9.03. Found: C, 80.06; H 9.00.

General Procedure for Benzylation of Calix[8]crowns. Cs_2CO_3 (400 mg, 1.23 mmol) was added to a suspension of the calix[8]crown-4 of choice (50 mg, 0.035 mmol) in Me_2CO (30 mL), and the mixture was stirred under reflux for 20 min. Then, a solution of 4-(*tert*-butyl)benzyl bromide (0.052 mL, 0.283 mmol) in Me_2CO (2 mL) was added, and stirring was maintained under reflux for 22 h. The solvent was evaporated under vacuum, and the residue was suspended in 1 N HCl (50 mL), collected by filtration, dried, and purified by preparative TLC (silica gel plates Kieselgel 60 F_{254}, 1 mm, Merck, CH_2Cl_2/petroleum ether 7:13).

Hexakis(*p-tert*-butylbenzyl)-1,2-calix[8]crown-4 2_4b: white powder (42%), mp 158−162 °C; ^{1}H NMR ($CDCl_3$, 325 K) δ 0.90, 0.97, 1.06, 1.15, 1.25, 1.29, 1.31 (s, 18 H each), 2.76 (br s, 8 H), 3.15 (br t, 4 H), 4.01, 4.06, 4.12, 4.13, 4.14 (s, 2 H, 2 H, 4 H, 4 H, 4 H), 4.64, 4.76, 4.82 (s, 4 H each), 6.7−7.6 (overlapped, 40 H); ^{13}C NMR ($CDCl_3$, 295 K) δ 28.2, 29.1, 29.7, 30.7 (t), 31.4 (q), 34.1, 34.4 (s), 69.3, 70.4, 72.3, 74.5, 74.8, 77.2 (t), 125.2, 125.7, 126.3, 127.1, 127.3, 128.1(d), 132.3, 133.1, 133.3, 133.4, 133.42, 133.6, 133.7, 134.7, 145.1, 145.9, 146.3, 150.5, 150.6, 152.5, 152.7, 152.8, 153.3 (s); FAB(+) MS m/z 2287 $(MH)^+$. Anal. Calcd for $C_{160}H_{206}O_{10}$: C, 83.94; H, 9.07. Found: C, 83.70; H 9.10.

Hexakis(*p-tert*-butylbenzyl)-1,3-calix[8]crown-4 3_4b: white powder (72%), mp > 280 °C (dec); ^{1}H NMR ($CDCl_3$, 320 K) δ 0.70, 0.86, 1.00, 1.19, 1.26, 1.31, 1.32, 1.35, 1.37 (s, 9 H, 9 H, 18 H, 18 H, 18 H, 9 H, 9 H, 18 H, 18 H), 2.40, 2.61, 2.65, 2.77 (m, 12 H), 3.67 and 4.64 (AX system, 4 H, J = 16.6 Hz), 3.68 and 4.67 (AX system, 4 H, J = 16.6 Hz), 3.78 and 4.74 (AX system, 4 H, J = 15.1 Hz), 4.00 and 4.40 (AB system, 4 H, J = 16.1), 4.98, 5.03 (s, 12 H), 6.59 (s, 2 H), 6.66 (s, 2 H), 6.80 and 7.07 (AX system, 4 H, J = 2.0 Hz), 7.04 (d, 2 H, J = 2.2 Hz), 7.10−7.60 (overlapped, 30 H); ^{13}C NMR ($CDCl_3$, 295 K) δ 29.2, 29.9, 30.1 (t), 31.4, 31.5 (q), 34.0, 34.3, 34.5, 34.6 (s), 68.8, 72.9, 73.2, 74.0, 74.7 (t), 122.7, 123.6, 123.8, 124.6, 125.2, 125.3, 127.1, 127.5, 127.6, 127.8, 128.0, 128.2, 128.8 (d), 131.5, 132.5, 132.7, 133.0, 133.5, 134.0, 134.1, 134.3, 134.7, 135.3, 145.3, 145.5, 146.0, 146.1, 146.2, 150.7, 150.8, 151.9, 152.7, 152.8, 153.0, 154.3 (s); FAB(+) MS m/z 2287 $(MH)^+$. Anal. Calcd for $C_{160}H_{206}O_{10}$: C, 83.94; H, 9.07. Found: C 83.81, H 9.01.

Hexakis(*p-tert*-butylbenzyl)-1,4-calix[8]crown-4 4_4b: white powder (43%), mp 164−168 °C; ^{1}H NMR ($CDCl_3$, 324 K) δ 0.97, 1.06, 1.09, 1.26, 1.32, 1.33, 1.36 (s, 18 H each), 2.05, 2.24, 2.28, 2.36 (m, 2 H each), 2.73 (br t, 4 H), 3.42 and 4.96 (AX system, 2 H, J = 14.4 Hz), 3.67 and 4.47 (AX system, 4 H J = 17.1 Hz), 3.75 and 4.45 (AX system, 4 H, J = 16.5 Hz), 3.93 and 4.30 (AB system, 2 H, J = 15.4 Hz), 4.60 and 4.68 (AB system, 4 H, J = 11.2 Hz), 4.87, 4.89, 4.76 (s, 4 H each), 6.5−7.5 (overlapped, 40 H); ^{13}C NMR ($CDCl_3$, 295 K) δ 27.6, 29.1, 30.3 (t), 31.4, 31.6 (q), 34.06, 34.1, 34.2, 34.4, 34.5 (s), 69.1, 72.3, 74.5, 74.3 (t), 123.8, 125.0, 125.2, 125.3, 125.6, 125.9, 127.8, 128.1, 128.2 (d), 132.0, 132.1, 132.6, 133.1, 133.6, 134.0, 134.4, 134.5, 134.8, 145.3, 145.9, 150.1, 150.5, 150.7, 152.2,

152.5, 152.7, 154.0 (s); FAB(+) MS 2287 $(MH)^+$. Anal. Calcd for $C_{160}H_{206}O_{10}$: C, 83.94; H, 9.07. Found: C, 83.89; H 9.10.

Acknowledgment. Financial support from the italian MURST (Supramolecular Devices Project) is gratefully acknowledged. Thanks are due to Mr. R. Rapisardi (I.C.T.M.P., C.N.R., Catania) for FAB MS measurements and to Mrs. C. Rocco (I.S.S.N., C.N.R., Valverde) for NMR spectra acquisition.

JO0002036