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Synthesis of "Macrocycle of Macrocycles" Containing 3~8 Calix[4]arene Units. Unexpected Generation of Large Super-macrocycles

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Abstract: A new class of calixarene-based macrocycles consisting of three to eight calix[4]arene subunits has been prepared from starting 5,11,17,23-tetra-*tert*-butyl-25,27-dihydroxy-26,28-dipropoxycalix[4]-arene. The macrocyclization has been achieved either by direct alkylation with 1,6-dibromohexane in DMF in the presence of NaH or via appropriate intermediates. Thus, the starting compound was transformed into bis-calix[4]arenes bearing two bromoalkyl substituents or two hydroxyl groups in positions suitable for further cyclization. By the mutual reactions of the above noticed compounds super-macrocycles containing 3, 4, 6, and 8 calix[4]arene subunits connected by hexamethylene chains have been prepared and characterized. This is a novel strategy to design a "macrocycle of macrocycles".

INTRODUCTION

Calix[n]arenes are macrocyclic oligophenols readily accessible by condensation of p-substituted phenols with formaldehyde under basic catalysis.[1] It has been shown that because of their unique molecular architecture, easy derivatization, and well-preorganized cavity, appropriately modified calix[n]arenes are capable of acting as receptors for cations, anions, and even neutral guest molecules.[2] The versatility of calix[4]arenes as host molecules in host-guest chemistry suggests that they can serve as potential starting blocks for designing more elaborated structures consisting of multiple calix[4]arenes.[3] Since each calix[4]arene can act as one recognition site, such multiple-calix[4]arene assemblies can lead to a novel receptor system with multi-point recognition sites possessing new binding properties unknown in simple calix[4]arene monomers.

As an initial system to test the feasibility of this idea we planned to synthesize a macrocyclic array based on calix[4]arenes where simple aliphatic chains are used as a linkage. While there are several examples of cyclic bis-calix[4]arene derivatives in literatures,[3,4] to the best of our knowledge only two cyclic tris-calix[4]arene macrocycles have been synthesized so far.[5] However, rigid spacers based on aromatic sulfonyl or carboxyl chlorides have been used to avoid unimolecular cyclization arising from

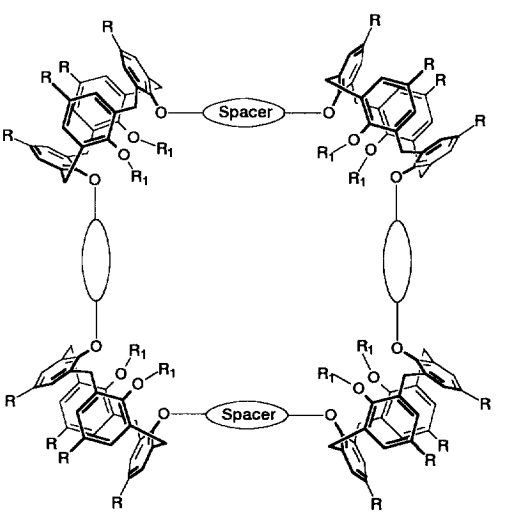


Figure 1: Structure of "macrocycle of macrocycles".

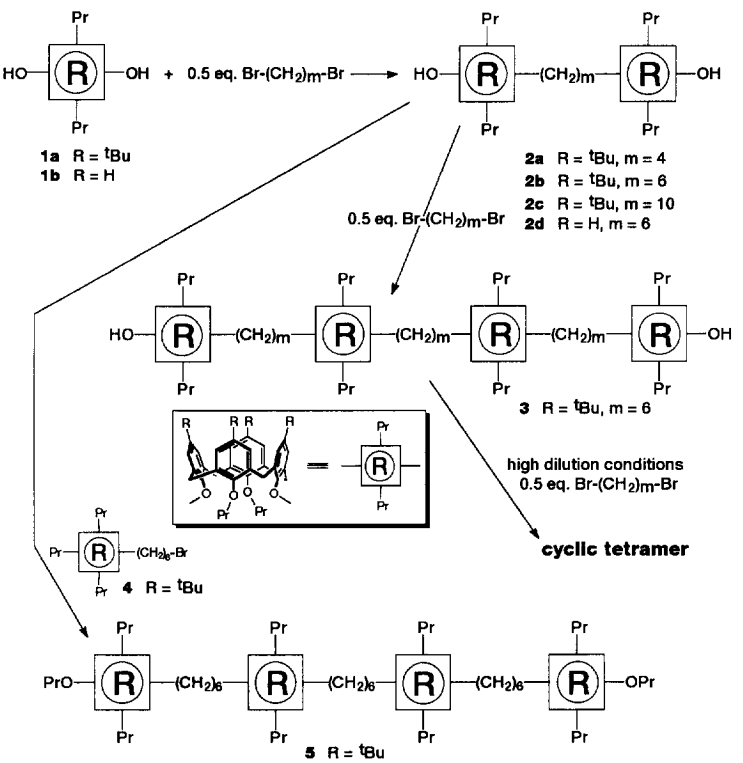
intramolecular bridging of starting *p-tert*-butylcalix[4]arene.

Recently, we have developed novel synthetic methods for linear and dendritic oligo-calix[4]arenes utilizing the Williamson type reaction between starting partially alkylated calix[4]arene derivatives and α,ω-dibromoalkanes.[6] During this study, we unexpectedly came across an indication that a significant amount of calix[4]arene-containing macrocycles is formed as by-products. Such a type of compounds can be called a "macrocycle of macrocycles" because of the presence of a cyclic array made of cyclic subunits. We found that after optimization of the reaction conditions macrocycles containing 3, 4, 6, and 8 calix[4]arenes can be isolated in reasonable yields. The presence of such large calix[4]arene-based macrocycles has never been expected and in fact, they have never been synthesized. We believe, therefore, that the results are very noteworthy in the field of calix[n]arene chemistry. Here, we report on the syntheses and spectroscopic properties of these new compounds.

RESULTS AND DISCUSSION

SYNTHESES:

Our first attempt toward the preparation of large calix[4]arene-based macrocycles is depicted in Scheme 1. The method represents "step-by-step" synthesis via linear precursors. We have realized that if we can prepare compounds of type **2**, they will act as very useful building blocks for the construction of macrocycles.

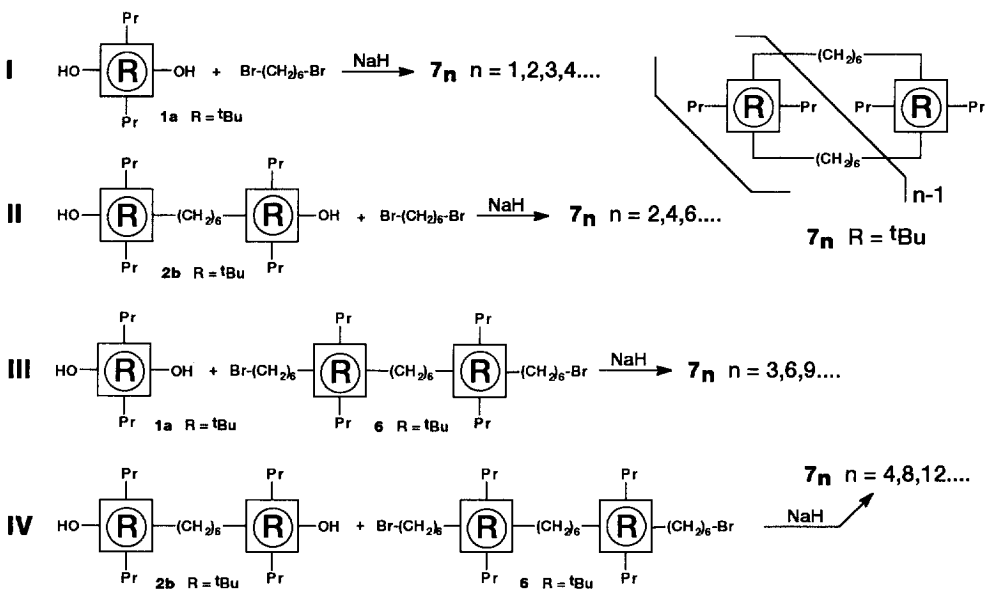


Scheme 1: Step-by-step preparation of calix[4]arene-based macrocycles via linear precursors.

The starting compounds **1a** and **1b** were alkylated with α, ω-dibromoalkanes Br-$(CH_2)_m$-Br (m = 4, 6, and 10) to find the most suitable spacer length and reaction conditions. The best results were achieved using 0.55

equivalent of alkylation agent for 1 mol of calix[4]arene **1a** or **1b** in DMF solution at room temperature and in the presence of NaH (2.5 eq.). Under these conditions derivative **2b** was isolated in 61% yield by simple crystallization of the crude product, and the corresponding derivative **2d** was obtained in 28% yield after repeating preparative TLC separation. Bis-calix[4]arenes **2a** and **2c** containing C_4 or C_{10} spacers were prepared in lower yields (20% and 15%, respectively) again after time-consuming preparative TLC separation. When dipropyl derivative **1b** was treated with C_4 or C_{10} dibromides, the reaction mixtures were so complex that we were unable to isolate proposed bis-calix[4]arene of type **2** at all. The structure of compound **2b** has been confirmed by ^{1}H NMR spectroscopy. It is known that the propyl group is bulky enough to suppress the oxygen-through-the-annulus rotation in calix[4]arenes and the conformation of resultant O-propylation products is immobilized.[7,8] Since NaH as base and DMF as solvent are typical reaction conditions to produce cone conformers,[7-9] the phenyl units linked to the $(CH_2)_6$ spacer would be immobilized into the same direction as two proximal O-propylated phenyl units. The splitting pattern of the Ar-CH_2-Ar methylene bridges (two pairs of dublets) together with three singlets of the *tert*-butyl groups (0.82 ppm, 1.33 ppm, and 1.34 ppm in 2:1:1 ratio) clearly shows that both calix[4]arene subunits are symmetrically fixed in a cone conformation. The signal in the mass spectrum at m/e 1547 (positive SIMS) is another evidence for the proposed structure.

Since the m=6 spacer gave the best results for the preparation of linear bis-calix[4]arenes **2**, we decided to use Br-$(CH_2)_6$-Br hereafter for the cyclization. Employing the same alkylation procedure, derivative **2b** was then treated with 0.5 eq. of Br-$(CH_2)_6$-Br to yield linear tetramer **3** as a precursor for macrocyclic array



Scheme 2: Direct preparation of calix[4]arene-based macrocycles.

(Scheme 1). Unfortunately, unlike the first alkylation procedure, this repeated reaction did not give the satisfactory yield and compound **3** was obtained only in 15% yield after an intricate isolation. We have noticed during the isolation procedure, however, that the essential part of the reaction mixture consists of macrocyclic compounds. We came to this conclusion using ^{1}H NMR spectra that exhibit a very simple splitting pattern (see later). The absence of free hydroxyl groups in the IR spectra also commensurates with the proposed macrocyclic structures. Therefore, we have focused our interest on the direct preparation of macrocyclic calix[4]arene derivatives 7_n.

To make the synthetic procedure and the spectroscopic analysis as simple as possible we used conformationally-immobilized calix[4]arene derivatives bearing propyl groups as O-substituents and an alkylation procedure (NaH, DMF or THF-DMF) that is known to yield cone-conformers as major products.[7-9] First possible approach was based on the direct condensation of starting dipropoxy derivative **1a** with 1,6-dibromohexane (1:1 molar ratio) under the same reaction conditions as has been already mentioned for **2** (Scheme 2, Equation I). From the very complicated reaction mixture we were able to isolate four main cyclic derivatives. Originally, we assumed that the main cyclic products of this reaction should be intramolecularly bridged monocalix[4]arene 7_1 together with bis-calix[4]arene derivative 7_2 and probably tris-calix[4]arene derivative 7_3. To our surprise, however, mass spectrometry established that none of the isolated compound seems to be either 7_1 or 7_2, and isolated products are assigned (see later) to 7_3 (7%), 7_4 (4%), 7_6 (2%), and 7_8 (1%).

In order to obtain a less complicated reaction mixture we have carried out a macrocyclization step according to Scheme 2 (Equation II), where only compounds exhibiting the even number of calix[4]arene subunits can be derived. It was proved that three first fractions obtained by the preparative TLC on *silica-gel* are identical with those compounds already isolated from the previous reaction. Their structures have been assigned using the combination of gel permeation chromatography (GPC), mass spectrometry, and ^{1}H NMR spectrometry to 7_4 (12%), 7_6 (6%), and 7_8 (4%). Another simplification of the reaction mixture is possible according to Equations III and IV, where one should obtain only selected derivatives 7_n (n=3,6,9...), and 7_n (n=4,8,12...), respectively. Bis-calix[4]arene dibromo derivative **6** was prepared in 72% yield by alkylation of **2b** with an excess amount of 1,6-hexanedibromide in the presence of NaH. Using this dibromide as an alkylation agent and **1a** as a starting compound, the reaction was carried out according to Equation III, and macrocycles 7_3 and 7_6 were thus obtained as the sole isolable products in 20% and 5% yields, respectively. Similarly, alkylation of **2b** with **6** (Equation IV) yielded macrocyclic tetrakis-calixarene 7_4 (32%) and octakis-derivative 7_8 (4%). In all cases the isolation of products was achieved by the preparative TLC method (see

Table 1: Isolated yields and GPC yields of 7_n

Preparation method	Yield determination	Yield (%)			
		7_3	7_4	7_6	7_8
I	Isolated	7	4	2	1
I	GPC	16	7	5	4
II	Isolated	0	12	6	4
II	GPC	0	23	8	10
III	Isolated	20	0	5	0
III	GPC	22	0	8	0
IV	Isolated	0	32	0	4
IV	GPC	0	39	0	9

Experimental). The crude fraction containing only cyclic derivatives and possessing much higher R_f than the rest of reaction products (linear oligomers and polymers) was first separated and then carefully re-

chromatographed using the mixture of $CHCl_3$ and hexane as an eluent. From the above-mentioned results it has become obvious that the more highly are the starting compounds preorganized (the higher is the number of already connected calix[4]arene subunits), the higher are the yields of corresponding cyclic derivatives. Very surprising is the fact that cyclic bis-derivative 7_2 is absent in the reaction products from Equations I and II. Probably, because of the sterical reasons these molecules tend to create higher products to minimize interannular interactions between the calixarene subunits.

To obtain a quantitative insight into the product distribution, we determined the yields of each macrocyclic compounds before isolation directly from the GPC chart. 5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetrapropoxycalix[4]arene (cone) was used as an internal standard and we assumed that the extinction coefficient of the phenyl unit at 254 nm is the same for all compounds. The results are summarized in Table 1, together with the corresponding isolated yields. Examination of Table 1 reveals that the highest GPC yield is 39% observed for 7_4 prepared by Equation IV. In general, the isolated yields for 7_8 are less than half of the GPC yields whereas the isolated yields for 7_3 and 7_4 are relatively good and particularly so when the yields are high. In Equations I and II the present distribution is rather broad. In Equations III and IV, on the other hand, the yields of the 1:1 reaction products (i.e., 7_3 in III and 7_4 in IV) are much higher than those of the 2:2 reaction products. This tendency implies that as mentioned above, the higher preorganization makes the product distribution more selective.

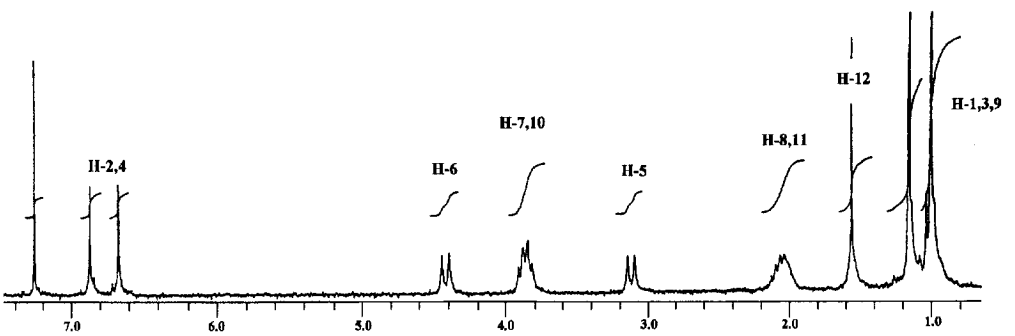


Figure 2: ^1H NMR spectrum of 7_4 (250 MHz, $CDCl_3$, 5 mmol, 300 K). For numbering see Figure 3.

CHARACTERIZATION:

All new cyclic derivatives 7_n possess very similar ^1H NMR spectra ($CDCl_3$, 300 K) with an identical splitting pattern (Figure 2). In the aliphatic part one can see two singlets of *tert*-butyl groups H-1 and H-3, together with a triplet of methyl H-9 from propoxy substituent that is coincidently hidden by one of *tert*-butyl signals (for general numbering accepted in this work for 7_n derivatives, see Figure 3). Two doublets of Ar-CH_2-Ar groups are situated in normal region (~3.15 ppm for equatorial H-5, and ~4.40 ppm for axial H-6 protons) proving the fixed cone conformation of all calix[4]arene subunits. The presence of two singlets H-2 and H-4 in the aromatic part of these spectra again confirms the highly symmetrical structure of these compounds. Chemical shifts of both aromatic and

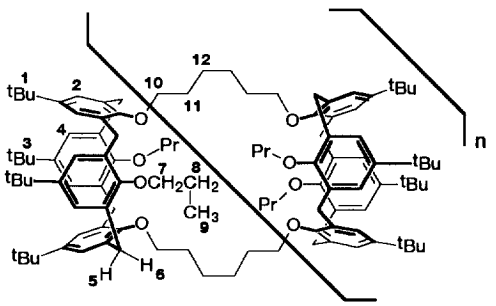


Figure 3: Numbering system of 7_n.

aliphatic singlets are characteristic of appropriate macrocycles and can be used for easy characterization and discrimination of individual derivatives. Moreover, we have found that there is very interesting dependence between the size of macrocycles and chemical shifts of the above noticed singlets. As can be seen from Figure 4, the plot of chemical shifts versus the number of calix[4]arene subunits exhibits nearly an ideal linearity. This phenomenon likely reflects the subtle change in the interannular angle α as indicated in Figure 5. While

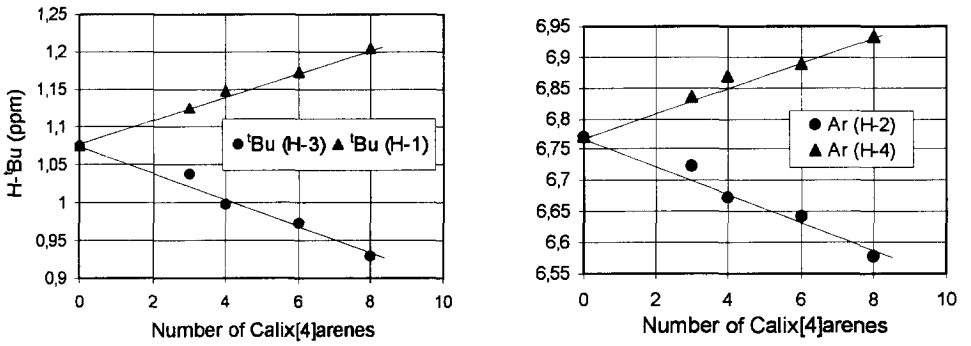


Figure 4: Dependence between the chemical shifts of selected protons and the size of macrocycle 7_n. Point x=0 is the chemical shift of 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrapropoxycalix[4]arene for the comparison.

in small macrocycles, α is apparently similar to that in the "parent" 25,26,27,28-tetrapropoxycalix[4]arene derivative, in larger macrocycles the value of α is higher due to the effort of the molecule to minimize the sterical hindrance between calix[4]arene subunits. The mutual interactions are minimized by the "straightening" of phenyl units bearing C_6 spacers on their lower rims. The larger is the macrocycle, the more are lower rims pushed from each other, which results in a linear dependence mentioned in Figure 4.

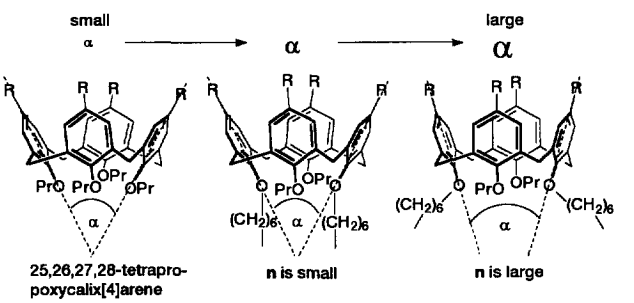


Figure 5: Comparison of interannular angle α in macrocycles 7_n.

DETERMINATION OF THE MOLECULAR WEIGHTS:

The molecular weights of 7_n were primarily determined by mass spectrometry. For 7_3 its parent peak was detectable at m/z 2444 by positive SIMS mode; in the presence of $LiClO_4$ its metal complex peak ($[M+Li]^+$) appeared at 2451. The parent peak of 7_4 could not be detected, but the $[M+Li]^+$ and $[M+K]^+$ peaks were detectable at m/z 3266 and 3295, respectively, in the presence of $LiClO_4$ and KCl. For 7_6 and 7_8, on the other hand, neither their parent peaks nor their metal complex ($[M+Li]^+$ or $[M+K]^+$) peaks could be detected because the maximum range of our mass spectrometry apparatus (vide supra) is ca. 4000. Instead, we could observe their half mass peaks for dicationic species $[M+2Li]^{2+}$ at m/z 2452 for 7_6 and 3265 for 7_8.

To obtain the complementary results to mass spectrometry we estimated the molecular weights of 7_6 and 7_8 by GPC (vide supra). As shown in Figure 6, a calibration curve was prepared from 7_3, 7_4, and three

linear oligocalix[4]arenes (tetramer **5**, and corresponding dimer, and trimer: for their preparation see Reference 6). Separately, the validity of this calibration curve up to MW 7000 has been confirmed by using monodispersed polystyrene samples. As expected, the peaks for 7_6 and 7_8 appeared at the reasonable retention times required for their molecular weights (although the peak for 7_6 exhibits some deviation).

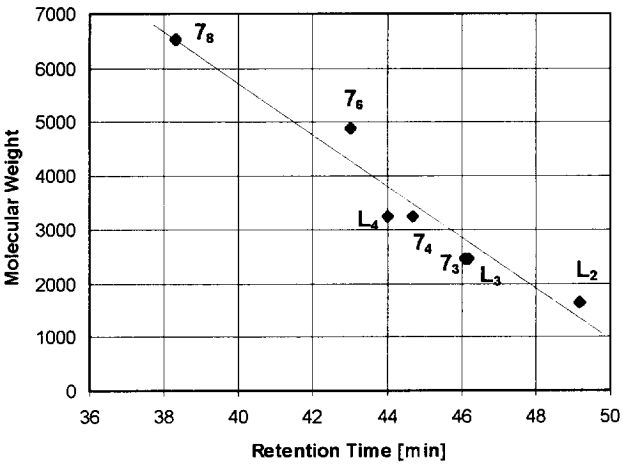


Figure 6: Plot of retention time and molecular weight in GPC: for the measurement conditions see Miscellaneous. L_2, L_3, and L_4 denote dimeric, trimeric, and tetrameric linear oligocalix[4]arenes (for their structures see Reference 6).

CONCLUSIONS:

We have demonstrated the possibility of the preparation of large macrocycles consisting of calix[4]arene subunits. By the choise of appropriate starting compounds and using simple alkylation procedures we could prepare derivatives containing 3 to 8 calixarenes in a cyclic array, the structure of which was proved by the combination of NMR, MS, and GPC. All new compounds could be interesting as multi-recognition host molecules in the field of supramolecular chemistry.

EXPERIMENTAL

Miscellaneous: Melting points were determined on a Micro Melting Point Apparatus Yanaco MP-500D and are uncorrected. ^{1}H NMR spectra were measured on a Bruker AC-250P and JEOL-GSX 400 spectrometers in $CDCl_3$ at 300 K with TMS as an internal standard. Mass spectra were recorded with a Hitachi M-2500 spectrometer using the positive SIMS method with *m*-nitrobenzyl alcohol as a matrix. IR spectra were obtained with a Jasco A-100 spectrophotometer. GPS analyses were performed with the help of LC-908 chromatograph (JAI) using a JAIGEL 2H column with a UV detector at 254 nm and $CHCl_3$ as an eluent. Preparative thin layer chromatography was performed on glass plates (20 x 20 cm) coated by *Silica gel* GF_{254} (Merck). All reactions were carried out under a nitrogen atmosphere.

Compounds **1a**, **1b**, and **4** were prepared according to the known procedures.[6,7]

Preparation of bis-calix[4]arenes 2a-d: To a solution of derivative **1a** or **1b** (0.41 mmol) in 10 ml of dry DMF was added 1.23 mmol of NaH (60% oil susp., 0.050 g, 1.23 mmol) at room temperature. The reaction mixture was stirred for 30 min, after which 0.45 mmol of appropriate dibromide was added. The reaction was continued under stirring for 2 days, and the resultant mixture was poured into 1 M HCl. The precipitate was collected by filtration. The product was isolated by preparative TLC using a hexane:AcOEt (20:1) mixture as an eluent.

2a: Yield 15%, m.p. 336-338 °C ($CHCl_3$-MeOH). ^{1}H NMR spectrum (250 MHz, $CDCl_3$): δ 0.84 (s, 36H, $C(CH_3)_3$); 1.10 (t, 12H, J=7.4 Hz, O-$CH_2CH_2\underline{CH_3}$); 1.32 (s, 18H, $C(CH_3)_3$); 1.33 (s, 18H, $C(CH_3)_3$); 2.00 (m, 8H, O-$CH_2\underline{CH_2}CH_3$); 2.40 (brs, 4H, -$CH_2\underline{CH_2}\underline{CH_2}CH_2$-); 3.18 (d, 4H, J=12.1 Hz, Ar-CH_2-Ar, eq); 3.23 (d, 4H, J=12.6 Hz, Ar-CH_2-Ar, eq); 3.79 (m, 8H, O-$\underline{CH_2}CH_2CH_3$); 4.03 (brs, 4H, -$\underline{CH_2}CH_2CH_2\underline{CH_2}$-); 4.33 (d, 4H, J=12.8 Hz, Ar-CH_2-Ar, ax); 4.38 (d, 4H, J=12.6 Hz, Ar-CH_2-Ar, ax); 5.95 (s, 2H, OH); 6.53 (s, 4H, H-arom); 6.55 (s, 4H, H-arom); 7.06 (s, 4H, H-arom); 7.14 (s, 4H, H-arom). EA calculated for $C_{104}H_{142}O_8$: C, 82.17; H, 9.41%. Found: C, 82.08, H, 9.33%.

2b: Yield 61%, isolated by simple crystallization from an AcOEt-MeOH mixture, m.p. 275-278 °C. ^{1}H NMR spectrum (400 MHz, $CDCl_3$): δ 0.82 (s, 36H, $C(CH_3)_3$); 1.12 (t, 12H, J=7.3 Hz, O-$CH_2CH_2\underline{CH_3}$); 1.33 (s, 18H, $C(CH_3)_3$); 1.34 (s, 18H, $C(CH_3)_3$); 1.48 (brs, 4H, O-$CH_2CH_2\underline{CH_2}$); 1.94 (m, 8H, O-$CH_2\underline{CH_2}CH_3$); 2.37 (m, 4H, O-$CH_2\underline{CH_2}CH_2$); 3.18 (d, 4H, J=12.8 Hz, Ar-CH_2-Ar, eq); 3.23 (d, 4H, J=13.1 Hz, Ar-CH_2-Ar, eq); 3.76 (m, 8H, O-$\underline{CH_2}CH_2CH_3$); 3.94 (t, 4H, J=8.2 Hz, O-$\underline{CH_2}(CH_2)_4\underline{CH_2}$-O); 4.35 (d, 4H, J=13.1 Hz, Ar-CH_2-Ar, ax); 4.39 (d, 4H, J=12.5 Hz, Ar-CH_2-Ar, ax); 5.70 (s, 2H, OH); 6.51 (s, 4H, H-arom); 6.52 (s, 4H, H-arom); 7.04 (s, 4H, H-arom); 7.14 (s, 4H, H-arom). EA calculated for $C_{106}H_{146}O_8$: C, 82.23; H, 9.50%. Found: C, 82.19, H, 9.48%. Mass spectrum (possitive SIMS): m/e 1547 (M^+).

2c: Yield 15%, oil. ^{1}H NMR spectrum (250 MHz, $CDCl_3$): δ 0.82 (s, 36H, $C(CH_3)_3$); 1.10 (t, 12H, J=7.5 Hz, O-$CH_2CH_2\underline{CH_3}$); 1.32 (s, 18H, $C(CH_3)_3$); 1.33 (s, 18H, $C(CH_3)_3$); 1.42 (brs, 4H, O-$CH_2CH_2(\underline{CH_2})_6CH_2CH_2$; 1.94 (m, 8H, O-$CH_2\underline{CH_2}CH_3$); 2.35 (m, 4H, O-$CH_2\underline{CH_2}(CH_2)_6\underline{CH_2}CH_2$); 3.16 (d, 4H, J=13.1 Hz, Ar-CH_2-Ar, eq); 3.22 (d, 4H, J=13.1 Hz, Ar-CH_2-Ar, eq); 3.76 (m, 8H, O-$\underline{CH_2}CH_2CH_3$); 3.94 (t, 4H, J=7.6 Hz, -$\underline{CH_2}(CH_2)_8\underline{CH_2}$-); 4.33 (d, 4H, J=13.3 Hz, Ar-CH_2-Ar, ax); 4.38 (d, 4H, J=13.2 Hz, Ar-CH_2-Ar, ax); 5.74 (s, 2H, OH); 6.51 (s, 4H, H-arom); 6.52 (s, 4H, H-arom); 7.04 (s, 4H, H-arom); 7.12 (s, 4H, H-arom). EA calculated for $C_{110}H_{154}O_8$: C, 82.35; H, 9.67%. Found: C, 82.23, H, 9.59%.

2d: Yield 28%, m.p. 277-279 °C (AcOEt-$CHCl_3$). ^{1}H NMR spectrum (250 MHz, $CDCl_3$): δ 1.11 (t, 12H, J=7.4 Hz, O-$CH_2CH_2\underline{CH_3}$); 1.45 (brs, 4H, O-$CH_2CH_2\underline{CH_2}$); 1.88 (m, 8H, O-$CH_2\underline{CH_2}CH_3$); 2.38 (brs, 4H, -$CH_2\underline{CH_2}CH_2$); 3.21 (d, 4H, J= 13.4 Hz, Ar-CH_2-Ar, eq); 3.29 (d, 4H, J= 13.8 Hz, Ar-CH_2-Ar, eq); 3.73 (t, 8H, J= 6.7 Hz, O-$\underline{CH_2}CH_2CH_3$); 3.92 (t, 4H, J= 6.7 Hz, -$\underline{CH_2}CH_2CH_2$); 4.38 (d, 4H, J=13.4 Hz, Ar-CH_2-Ar, ax); 4.38 (d, 4H, J=13.3 Hz, Ar-CH_2-Ar, ax); 4.76 (s, 2H, OH); 6.38 (m, 12H, H-arom); 6.77 (t, 2H, J= 7.3 Hz, H-para); 7.97 (t, 2H, J= 7.3 Hz, H-para); 7.09 (d, 4H, J= 7.4 Hz, H-meta); 7.18 (d, 4H, J= 7.5 Hz, H-meta). EA calculated for $C_{74}H_{82}O_8$: C, 80.83; H, 7.53%. Found: C, 80.76, H, 7.49%.

Preparation of linear derivative 3: Prepared in a fashion similar to **2** using **2b** as a starting compound and a THF:DMF (1:1) mixture as a solvent. The reaction was continued for 4 days under stirring. The product was isolated by repeated preparative TLC separation using hexane:AcOEt and hexane:$CHCl_3$ mixtures as an eluent. Yield 15%, oil. ^{1}H NMR spectrum (400 MHz, $CDCl_3$): δ 0.82 (s, 36H, $C(CH_3)_3$); 0.97 (m, 48H, 2 x 18H $C(CH_3)_3$ + 12H O-$CH_2CH_2\underline{CH_3}$); 1.08 (t, 12H, J=7.3 Hz, O-$CH_2CH_2\underline{CH_3}$); 1.18 (s, 36H, $C(CH_3)_3$); 1.32 (s, 18H, $C(CH_3)_3$); 1.34 (s, 18H, $C(CH_3)_3$); 1.45 (m, 4H, O-$CH_2CH_2\underline{CH_2}$); 1.54 (m, 8H, O-$CH_2CH_2\underline{CH_2}$); 1.85-2.10 (m, 24H, O-$CH_2\underline{CH_2}CH_3$ + O-$CH_2\underline{CH_2}CH_2$); 2.34 (m, 4H, O-$CH_2\underline{CH_2}CH_2$); 3.08-3.23 (m, 16H, Ar-CH_2-Ar, eq); 3.70-3.95 (m, 28H, O-$\underline{CH_2}CH_2CH_3$ + O-$\underline{CH_2}CH_2CH_2$); 4.31-4.45 (m, 16H, Ar-CH_2-Ar, ax); 5.69 (s, 2H, OH); 6.49 (s, 4H, H-arom); 6.51 (s, 4H, H-arom); 6.63 (s, 4H, H-arom); 6.91 (s, 8H, H-arom); 7.04 (s, 4H, H-arom); 7.11 (s, 4H, H-arom). EA calculated for $C_{106}H_{146}O_8$: C, 82.23; H, 9.50%. Found: C, 82.19, H, 9.48%.

Preparation of linear tetramer 5: Dihydroxy derivative **2b** (0.100 g, $6.46x10^{-5}$ mol) was treated with 4 eqs. of NaH in a THF-DMF (1:1) mixture; after addition of 4 eq. of bromide **4**[6] (0.24 g, $2.58x10^{-4}$ mol), the reaction mixture was stirred for 5 days at room temperature. The mixture was poured into dilute HCl, and the precipitate was collected by suction. The crude product was purified by preparative TLC on *silica gel* using hexane:AcOEt=17:3 as an eluent to yield 120 mg of white solid (57%): m.p.: 256-259 °C (AcOEt). ^{1}H NMR spectrum (400 MHz, $CDCl_3$, 25 °C): δ 0.95 (s, 18H, $C(CH_3)_3$), 0.96 (s, 18H, $C(CH_3)_3$); 0.97 (m, 30H, O-$CH_2CH_2\underline{CH_3}$); 1.05 (s, 18H, $C(CH_3)_3$); 1.06 (s, 18H, $C(CH_3)_3$); 1.08 (s, 36H, $C(CH_3)_3$); 1.19 (s, 36H, $C(CH_3)_3$); 1.52 (m, 12H, O-$CH_2\underline{CH_2}CH_2$); 1.98-2.05 (m, 32H, O-$CH_2\underline{CH_2}CH_3$); 3.05-3.14 (m, 16H, Ar-CH_2-Ar, eq); 3.76-3.91 (m, 32H, O-$\underline{CH_2}CH_2CH_3$ + O-$\underline{CH_2}CH_2CH_2$); 4.37-4.45 (m, 16H, Ar-CH_2-Ar, ax); 6.62 (s, 4H, H-arom); 6.63 (s, 4H, H-arom); 6.74 (s, 4H, H-arom); 6.75 (s, 4H, H-arom); 6.78 (s, 8H, H-arom); 6.98 (s, 8H, H-arom). EA calcd. for $C_{224}H_{314}O_{16}$: C, 82.46; H, 9.70%. Found: C, 82.17; H, 9.62%. MS (positive SIMS): m/z 3262 $(M+H)^+$.

Preparation of dibromide 6: Dihydroxy derivative **2b** (0.30 g, $1.9x10^{-4}$ mol) was dissolved in 15 ml of a DMF-THF (1:2) mixture, and to this solution were added 4 eqs. of NaH at room temperature. The contents were stirred for 30 min, and 20 eqs. of 1,6-dibromohexane (600 μl, $38.8x10^{-4}$ mol) were added. The reaction mixture was then stirred for 2 days at the same temperature. The reaction mixture was acidified with dilute HCl, and the product was extracted into $CHCl_3$, and dried over $MgSO_4$. After evaporation of the solvent the residue was reprecipitated from $CHCl_3$-ethanol to yield 0.26 g of **6** (72%) as a white powder: m.p.: 165.5-168 °C. ^{1}H NMR spectrum (250 MHz, $CDCl_3$): δ 1.04 (m, 48H, $C(CH_3)_3$ + O-$CH_2CH_2\underline{CH_3}$); 1.11 (s, 36H, $C(CH_3)_3$); 1.60 (brs, 4H, O-$CH_2CH_2\underline{CH_2}$); 2.02 (m, 16H, O-$CH_2\underline{CH_2}CH_3$ + O-$CH_2\underline{CH_2}CH_2$); 3.11 (d, 8H, J=Ar-CH_2-Ar, eq); 3.41 (t, 4H, $CH_2CH_2\underline{CH_2}Br$); 3.84 (m, 16H, O-$\underline{CH_2}CH_2CH_3$ + O-$\underline{CH_2}CH_2CH_2$); 4.40 (m, 8H, Ar-CH_2-Ar, ax); 6.73 (s, 8H, H-arom); 6.81 (s, 8H, H-arom). EA calculated for $C_{118}H_{168}O_8Br_2$: C, 75.61; H, 9.03%. Found: C, 76.01, H, 9.18%.

Preparation of cyclic derivatives 7_n: To a solution of diol **1** or **2b** (0.1 mmol) in 10 ml of a DMF-THF (1:1) mixture were added 10 eqs. of NaH (60% oil dispersion) at room temperature and the mixture was stirred for 30 min. Then, 0.1 mmol of corresponding dibromide (**6** or 1,6-dibromohexane) was added and the reaction was continued for 5 days at room temperature. The reaction mixture was then poured onto crushed ice, acidified with 1 M HCl and the product was extracted into $CHCl_3$. Chloroform extracts were combined and washed twice with water and brine, and dried over $MgSO_4$. After evaporation of solvent the residue was chromatographed on preparative TLC (*silica gel*) using hexane-$CHCl_3$ (6:1 to 2:1) mixtures as an eluent.

1+1,6-dibromohexane *(Equation I)*: 7_3, (7% yield), m.p. >350 °C (AcOEt). ^{1}H NMR spectrum (250 MHz, $CDCl_3$): δ 1.03 (s, 48H, H-1 or H-3 + H-9); 1.12 (s, 36H, H-3 or H-1); 1.60 (brs, 8H, H-12); 2.06 (m, 16H, H-8 + H-11); 3.13 (d, 8H, J=13.1 Hz, H-5); 3.87 (m, 16H, H-7 +H-10); 4.43 (d, 8H, J=12.9 Hz, H-6); 6.72 (s, 8H, H-2 or H-4); 6.83 (s, 8H, H-4 or H-2). EA calculated for $C_{168}H_{234}O_{12}$: C, 82.51; H, 9.64%. Found: C, 82.23, H, 9.50%. MS (positive SIMS): m/z 2444 (M^+); (positive SIMS+$LiClO_4$): m/z 2451 $(M+Li)^+$.

7_4, (4% yield), m.p. >355-360 °C decomp. (AcOEt). ^{1}H NMR spectrum (250 MHz, $CDCl_3$): δ 1.00 (s, 96H, H-1 or H-3 + H-9); 1.15 (s, 72H, H-3 or H-1); 1.55 (brs, 16H, H-12); 2.04 (m, 32H, H-8 + H-11); 3.11 (d, 16H, J=13.1 Hz, H-5); 3.85 (m, 32H, H-7 + H-10); 4.42 (d, 16H, J=12.8 Hz, H-6); 6.67 (s, 16H, H-2 or H-4); 6.87 (s, 16H, H-4 or H-2). EA calculated for $C_{224}H_{312}O_{16}$: C, 82.51; H, 9.64%. Found: C, 82.23, H, 9.50%. MS (positive SIMS+$LiClO_4$): m/z 3266 $(M+Li)^+$, 1636 $(M+2Li)^{2+}$; (positive SIMS+KCl): m/z 3295 $(M+K)^+$.

7_6, (2% yield), m.p. 200-215 °C (AcOEt-acetone).[10] ^{1}H NMR spectrum (250 MHz, $CDCl_3$): δ 0.97 (s, 144H, H-1 or H-3 + H-9); 1.20 (s, 108H, H-3 or H-1); 1.55 (brs, 24H, H-12); 2.02 (m, 48H, H-8 + H-11); 3.10 (d, 24H, J=12.7 Hz, H-5); 3.85 (m, 48H, H-7 + H-10); 4.40 (d, 24H, J=12.6 Hz, H-6); 6.64 (s, 24H, H-2

or H-4); 6.89 (s, 24H, H-4 or H-2). EA calculated for $C_{336}H_{468}O_{24}$: C, 82.51; H, 9.64%. Found: C, 82.23, H, 9.50%. MS (positive SIMS+$LiClO_4$): m/z 2452 $(M+2Li)^{2+}$.

7_8, (1% yield), m.p. 185-200 °C (AcOEt-acetone).[10] ^1H NMR spectrum (250 MHz, $CDCl_3$): δ 0.93 (s, 192H, H-1 or H-3 + H-9); 1.25 (s, 144H, H-3 or H-1); 1.57 (brs, 32H, H-12); 2.05 (m, 64H, H-8 + H-11); 3.08 (d, 32H, J=12.5 Hz, H-5); 3.87 (m, 64H, H-7 + H-10); 4.40 (d, 32H, J=12.8 Hz, H-6); 6.58 (s, 32H, H-2 or H-4); 6.94 (s, 32H, H-4 or H-2). EA calculated for $C_{448}H_{624}O_{32}$: C, 82.51; H, 9.64%. Found: C, 82.13, H, 9.50%. MS (positive SIMS+$LiClO_4$): m/z 3265 $(M+2Li)^{2+}$.

2b+1,6-dibromohexane *(Equation II)*: Similar procedure as described for the above cyclization reaction. All compounds are identical with those assigned above: 7_4 (12%), 7_6 (6%), and 7_8 (4%).

1a+6 *(Equation III)*: These compounds are identical with those assigned above: 7_3 (20%) and 7_6 (5%).

2b+6 *(Equation IV)*: These compounds are identical with those assigned above: 7_4 (32%) and 7_8 (4%).

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10. Compounds 7_6 and 7_8 are amorphous mass without the accurate melting point.

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