Pergamon

Tetrahedron 58 (2002) 3729–3736

TETRAHEDRON

# Macrocyclic, linear and starlike assemblies of calix[4]arenes covalently bridged by methylenes at the upper rims: simple route to novel receptors with defined polycavities☆

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Received 13 December 2001; revised 20 February 2002; accepted 21 March 2002

**Abstract**—Chloromethylation of 5,17-di-*tert*-butyl-25,27-dihydroxy-26,28-dimethoxycalix[4]arene with chloromethyl methyl ether in the presence of zinc chloride led to the formation of macrocyclic and linear oligomers containing three to five calix[4]arenes bridged via methylenes at the upper rims. Under the identical conditions, however, 5,17-di-*tert*-amyl-25,27-dihydroxy-26,28-dimethoxycalix[4]arene was converted into a mixture of linear dimer and trimer in yields of 39.5 and 34%, respectively. Only dimer was obtained as the sole product in 41% yield when 25,27-dihydroxy-26,28-diethoxycalix[4]arene was used. Efficient synthesis of linear or starlike polycalixarenes was achieved utilizing the Friedel–Crafts reaction of debutylated or partially debutylated calix[4]arenes with chloromethylated calix[4]arene promoted by anhydrous zinc chloride. © 2002 Elsevier Science Ltd. All rights reserved.

## 1. Introduction

The past thirty years have seen tremendous developments in supramolecular science.[2] One of the most noticeable aspects in this interdisciplinary area is the emergence of a wide range of intriguing molecules and supermolecules designed and created on the basis of complementarity to function as biological and abiotic receptors. Extensive studies of non-covalent interactions between synthetic receptors and simple species such as cations, anions and small and simple neutral molecules have not only led to various molecular and supramolecular devices but, more importantly, had a significant impact on the development of chemistry as well.[3] A challenging research area in this field is the design and construction of sophisticated artificial receptors with polytopicity and polyfunctionality that would be highly efficient in complexation with larger and more complicated molecules.

Calixarenes **1**, macrocyclic oligomers of phenols bridged with methylenes, are one of the most extensively studied synthetic receptors in recent years due to their unique structure and versatile complexation properties.[4] (Fig. 1)

One of the key features of calix[*n*]arenes as host molecules is the regulation of cavity and hydrophobic surface through controlled synthesis of calix[4–8]arenes and their transformations and functionalizations. Thus a large number of calixarene derivatives with defined cavity and function have been designed and synthesized allowing efficient and selective complexation with various species.[5] More importantly, calixarenes provide building blocks for more complex architectures.[6,7] Cylinder-shaped receptors have been achieved for instance by combining two calix[4]arenes via both lower rims, tail-to-tail, utilizing a variety of spacers with different rigidity and length, and some of them have been shown to exhibit interesting complexation properties with alkali metal cations.[8] The same synthetic strategy has been applied to construct covalently bonded macrocycles containing up to three to eight calix[4]arenes with large cavities.[8b,c,9] Assemblies of two calix[*n*]arenes via both upper rims, head-to-head using covalently bonded spacers such as saturated[10] and unsaturated aliphatic[11] chains, aromatic chains[12] and porphyrin[13] have led to molecular capsules with enforced cavity. More interestingly, properly functionalized calixarene derivatives have been reported to undergo self-assembly to yield non-covalently bonded dimers on the basis of hydrogen bonding.[14,15] The resulting

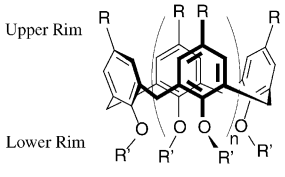


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**Figure 1.** Structure of calix[*n*]arene.

☆ See Ref. 1.

*Keywords*: calix[4]arenes; methylene bridges; receptor polycavities.

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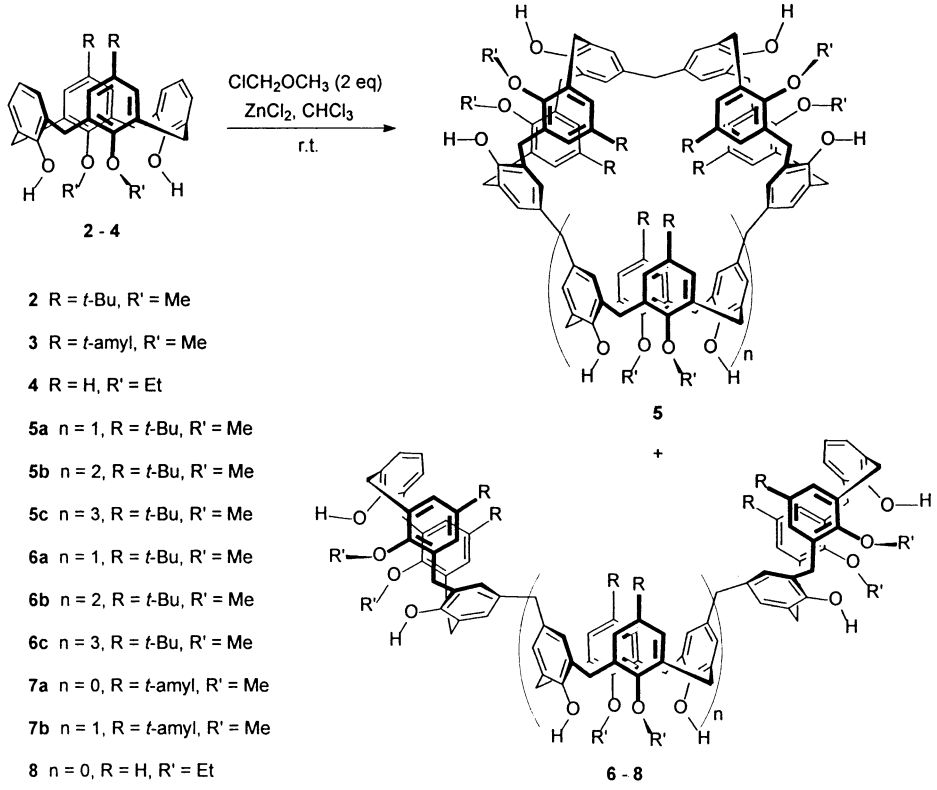
PII: S0040-4020(02)00342-3




**Scheme 1.**

molecular capsules were capable of encapsulating a number of aromatic molecules.[14]

Study of artificial receptors capable of complexing larger molecules remain largely unexplored. This is particularly true for the calixarene-based receptors. Reinhoudt and co-workers[16] designed and synthesized the first receptor molecule holand with a rigid cavity of nanosize dimension by connecting two calix[4]arenes and two resorcin[4]arenes via highly organized amido spacers. Later the same group reported[17,18] construction of more flexible linear molecules of either two calix[4]arenes and one resorcin[4]arene or of either one calix[4]arene and two resorcin[4]arenes. These U-shaped receptors having polycavities showed promising properties in selective complexation with certain corticosteroids,[17] sugar derivatives and alkaloids.[18] Recently, a cyclic trimer of calix[4]arenes connected by but-2-ene units via the upper rims has been reported by McKervey and co-workers.[11b] Based on the intrinsic cavity of calix[4]arene and its hydrophobic and CH-$\pi$[19] interactions with guest substrates we envisaged that oligomeric calix[4]arenes would provide novel and efficient receptors to complex larger and more complicated organic molecules. This led us to undertake the current investigation.[1]

## 2. Results and discussion

### 2.1. Chloromethylation of calix[4]arenes with chloromethyl methyl ether

To build up both macrocyclic and linear architectures of oligomeric calix[4]arenes, dichloromethylated calix[4]arene derivatives are promising building blocks. Ungaro, Reinhoudt and their co-workers[20] described an efficient synthesis of 11,23-bis(chloromethyl)-5,17-di-*tert*-butyl-25,27-dihydroxy-26,28-dimethoxycalix[4]arene (**9**) from selective chloromethylation of 5,17-di-*tert*-butyl-25,27-dihydroxy-26,28-dimethoxycalix[4]arene (**2**) using chloromethyl *n*-octyl ether in the presence of $SnCl_4$ at $-40^{\circ}C$. When we attempted the same synthesis varying chloromethylation reagent and Lewis acid to chloromethyl methyl ether and $ZnCl_2$ at ambient temperature, the reaction did not give the desired product. Instead, a white powder containing no chlorine resulted. Amazingly, macrocyclic **5a–c** and linear **6a–c** oligomers of calix[4]arenes bridged with methylenes at the upper rims were isolated after separation using preparative thin layer chromatography, albeit in low yield (3–12%) (Scheme 1).

The structures of products **5a–c** and **6a–c** were established on the basis of spectroscopic data and elemental analyses. Thus mass spectra showed clearly that compounds **5a–c** contained three, four and five calix[4]arenes in a cyclic array connected by three, four and five methylene units, respectively. While in **6a–c**, three, four and five calix[4]arenes were also evident but only two, three and four methylenes were confirmed, respectively, indicating the linear structures of products **6a–c**. It is interesting to note that cyclic trimer **5a**, tetramer **5b** and pentamer **5c** gave almost identical infrared spectra. Their $^1H$ NMR spectra also appeared the same and simpler than that of their parent calix[4]arene **2**. Except for the signals of hydroxy, methoxy and *tert*-butyl protons, a new singlet signal was observed at

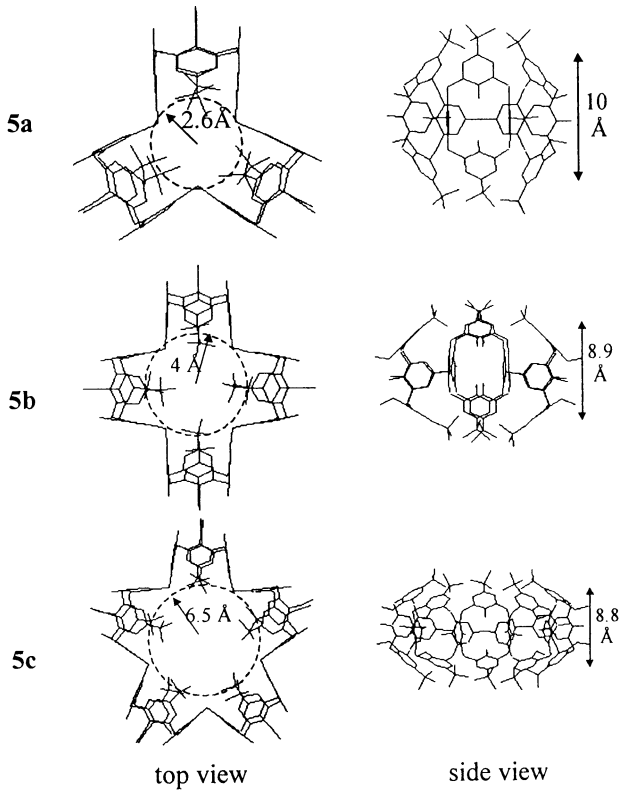



**Figure 2.** Two views of an energy-minimized **5**. All hydrogens are omitted for viewing clarity.

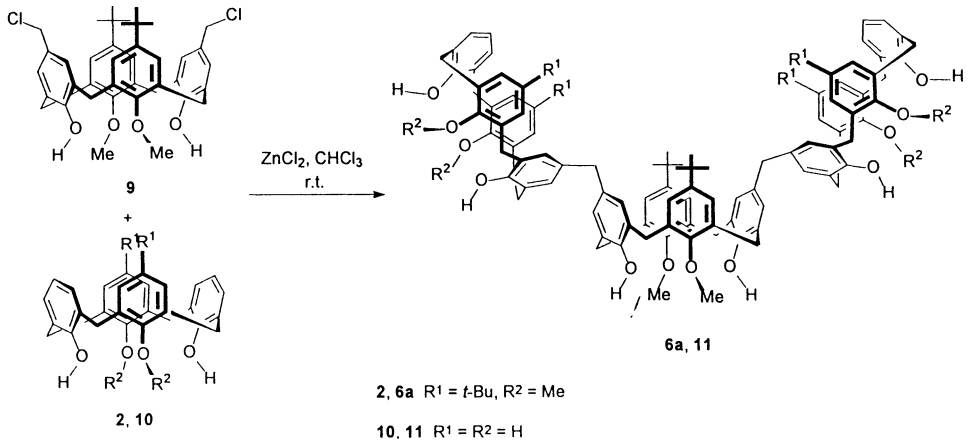
3.75 ppm. In addition, two singlet peaks were found at 6.88 and 6.78 ppm. These showed clearly that all *para* positions of phenol rings of starting calix[4]arene **2** were substituted by methylene units. In other words, calix[4]arenes in cyclic oligomers **5a–c** were linked covalently by methylenes via the upper rims. All calix[4]arenes adopted a cone conformation, which was evidenced by the AB system of the methylene protons within calix[4]arene units with a coupling constant of 13.2 Hz. In contrast to macrocycles **5a–c**, each linear oligomer **6** gave considerably different $^1$H NMR spectra. However, several common features of their $^1$H NMR spectra were noticeable. In addition to other singlet aromatic proton signals, one doublet of four protons and one triplet of two protons at 7.07 and 6.68 ppm were always observed, indicating that two phenol rings were still not substituted at their *para* positions. While all protons of methylenes linking calix[4]arenes resonated as singlet peak at 3.75 ppm, the methylene protons within calix[4]-arenes were split into two pairs of AB quartet peaks integrating proton ratios of 8:16, 8:24 and 8:32 for **6a**, **6b** and **6c**, respectively. These data were in good agreement with the linear oligomeric structures of **6a–c** since the four methylenes adjacent to two phenol rings in the terminal calix[4]arenes were different magnetically from the rest of the methylenes within calix[4]arenes. The non-equivalence of terminal calix[4]arenes with the middle one(s) was further demonstrated by the observation of two singlet singlet of *tert*-butyl groups at 0.98 and 0.99 ppm with proton raio of 36:18, 36:36 and 36:54 respectively for **6a**, **6b** and **6c**. It should be noted that the observation of only one singlet peak corresponding to all methylenes linking calix[4]arenes at the upper rims is most probably due to the flexibility of **6a–c**, in spite of three to five calix[4]arenes being connected in a linear array.

Under identical conditions, chloromethylation of 5,17-di-*tert*-amyl-25,27-dihydroxy-26,28-dimethoxycalix[4]-arene (**3**) did not give any macrocyclic product, and linear dimer **7a** and trimer **7b** were obtained in the yield of 39.5 and 34%, respectively. In the case of 26,28-diethoxycalix[4]arene **4**, only dimeric compound **8** was isolated as the sole product in moderate yield. Compound **7b** gave a $^1$H NMR spectrum very similar to that of **6a** as they have similar linear structure. Because two calix[4]arenes were linked together by one methylene spacer at the upper rims, the resulting dimers **7a** and **8** led to two pairs of well-resolved AB quartet signals integrating eight protons of each. Observations of one singlet peak of all methoxy protons and one set signals of all *tert*-amyl protons in the case of **7a** suggested a clam-shaped structure of dimeric product like those proposed by Shinkai.[21] The different outcomes of the same reaction employing differently substituted calix[4]arenes **2**, **3** and **4** demonstrated the subtle and crucial role the substituents played in determining the course of the reaction.

In order to shed light on the structure of macrocycles **5a–c**, computer modeling was performed using the $MM^+$ method implemented within the 'HyperChem' package.[22] As illustrated in Fig. 2, energetically favored macrocyclic trimer **5a**, tetramer **5b** and pentamer **5c** adopted respective triangle, cross and five-star conformations (top view). Consistent with their $^1$H NMR spectra (vide supra),**5a–c** are rigid molecules and enjoy high symmetry. Cyclic trimer **5a** and tetramer **5b** are of $D_{3h}$ and $D_{4h}$ symmetry, respectively, whereas cyclic pentamer **5c** belongs to $D_{5h}$ group. This is to the best of our knowledge one of the few organic molecules having $D_{5h}$ symmetry under normal conditions.[23] The molecules have well-defined cavities, the volume of cavity increasing from 210 Å$^3$ (trimer **5a**) to 450 Å$^3$ (tetramer **5b**) and to 1170 Å$^3$ (pentamer **5c**) (Fig. 2, side view). These compounds therefore would be potentially useful as organic zeolites to complex molecules with different sizes.

### 2.2. Synthesis of linear trimers of calix[4]arenes with methylene spacers at the upper rims

The formation of cyclic and linear oligomers **5–8** from the chloromethylation of calix[4]arenes **2–4** is apparently from the ready Friedel–Crafts reaction of **2–4** with the primarily formed chloromethylated calix[4]arenes under the reaction conditions. In order to synthesize U-shaped calix[4]arene trimers such as **6a** effectively and efficiently, a different approach was investigated. Starting with chloromethylated calix[4]arene **9** as developed by Ungaro and Reinhoudt,[20] linear trimer **6a** was prepared in moderate yield when calix[4]arene **2** was used in a large excess in the reaction. Trimer **11** with different substituents on the calix[4]arene units located in the middle and at terminus was similarly obtained in 44% yield when **10** was used. (Scheme 2) Since the cavity of debutylated calix[4]arene differs from that of *tert*-butylated one, trimer **11** represents a novel receptor molecule with polycavities derived from different calix[4]-arene units.



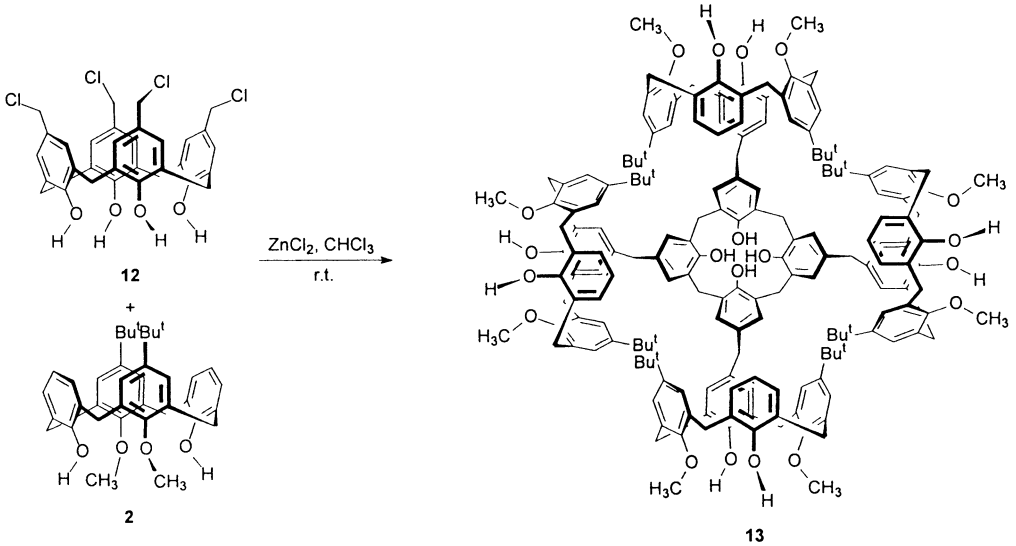

**Scheme 2.**

### 2.3. Synthesis of starlike pentamer of calix[4]arenes with methylene spacers at the upper rims

Under similar conditions, a starlike pentamer of calix[4]-arenes **13** has also been prepared starting with tetra-chloromethylated calix[4]arene **12** in a yield of 14% when calix[4]arene **2** was used. (Scheme 3) The MALDI-TOF mass spectra showed clearly $(M+Na)^+$ peak at 2752. From its $^1H$ NMR spectrum, the central calixarene adopted cone conformation, which was similar to *p-tert*-butylcalix-arene.[4d] The proton signals of methylene between limbic and central calixarenes showed a singlet at 3.69 ppm, from which it is difficult to deduce the orientation of the cavities of the limbic calixarenes. To our best knowledge, this is the first synthesis of this kind of starlike calixarene.

## 3. Conclusion

In conclusion, chloromethylation of 5,17-di-*tert*-butyl-25,27-dihydroxy-26,28-dimethoxy-calix[4]arene (**2**) with chloromethyl methyl ether in the presence of zinc chloride at room temperature led to the formation of macrocyclic and linear oligomers containing three to five calix[4]arenes bridged via methylenes at the upper rims. Molecular modeling indicated that macrocyclic trimer **5a**, tetramer **5b** and pentamer **5c** enjoy high symmetry and they belong to the point groups of $D_{3h}$, $D_{4h}$ and $D_{5h}$, respectively. The cavities formed within these rigid macrocycles **5a**, **5b** and **5c** are defined, respectively, as 210, 450 and 1170 Å$^3$. In contrast, linear trimer **6a**, tetramer **6b** and pentamer **6c** are flexible molecules containing polycavities of calix[4]arenes. Under the identical conditions, however, 5,17-di-*tert*-amyl-25,27-dihydroxy-26,28-dimethoxycalix[4]arene (**3**) was converted into a mixture of linear dimer **7a** and trimer **7b** in yields of 39.5 and 34%, respectively. Dimer **8** was obtained as the sole product in 41% yield when 25,27-dihydroxy-26,28-diethoxycalix[4]arene (**4**) was used. Efficient synthesis of linear trimers was achieved utilizing the Friedel–Crafts reaction of debutylated or the partially debutylated calix[4]arenes with chloromethylated calix[4]arene promoted by anhydrous zinc chloride. Thus trimers **11** and **6a** were prepared in moderate yield from 11,23-bis(chloromethyl)-5,17-di-*tert*-butyl-26,28-dimeth-oxycalix[4]arene (**9**) by the treatment of calix[4]arene **10** and 5,17-di-*tert*-butyl-26,28-dimethoxycalix[4]arene (**2**), respectively. The




**Scheme 3.**

dimers obtained adopted most probably a clam-shaped conformation whereas trimers were U-shaped. Under similar conditions, a starlike pentamer of calix[4]arenes **13** has also been prepared in a yield of 14% starting from all chloromethylated calix[4]arene **12** when calix[4]arene **2** was used.

## 4. Experimental

### 4.1. General

Melting points are uncorrected. $^1$H NMR spectra were recorded with a Varian Unity 200 spectrometer. IR spectra were recorded on a Perkin–Elmer 782 spectrometer using KBr discs. Field decomposition (FD) mass spectra were measured on an AEI MS-50/PS 30 instrument by Beijing Institute of Microanalytic Chemistry. MALDI-TOF mass spectra were measured on a Bruker BIFLEX III instrument with CCA as matrix by Institute of Chemistry. Elemental analyses were performed by the Analytical Laboratory of the Institute. Compounds **2**,[20] **4**,[24] **9**,[20] **10**,[25] and **12**[26] were prepared according to literature procedures. Chloroform was dried over 4 Å molecular sieve and $ZnCl_2$ was melted before use.

### 4.2. Preparations of macrocyclic and linear oligomers 5 and 6

To a stirred solution of 5,17-di-*tert*-butyl-25,27-dihydroxy-26,28-dimethoxycalix[4]arene (**2**) (2.0 g, 3.54 mmol) in chloroform (400 ml) was added chloromethyl methyl ether (0.56 g, 7.00 mmol) and anhydrous zinc chloride (1.0 g, 7.33 mmol). After the reactant disappeared (ca. 2 h), which was monitored by TLC, the reaction mixture was washed three times with water. The organic layer was separated and dried over anhydrous $MgSO_4$. After removal of solvent, a white powder (2.3 g) precipitated when methanol was added. No chlorine was found from microanalysis. (C, 80.80; H, 7.79). Careful separation of 0.2 g of the resulting white powder using preparative TLC (petroleum ether (60–90°C)/EtOAc 3:2) gave compounds **5a–c** and **6a–c**.

**4.2.1. Cyclic trimer 5a.** White power, yield 24 mg (12%), mp 290°C (dec.). $^1$H NMR ($CDCl_3$): $\delta$ 7.22 (s, 6H, OH), 6.89 (s, 12H, ArH), 6.77 (s, 12H, ArH), 4.27 (d, $J$=13.2 Hz, 12H, $ArCH_2Ar$), 3.93 (s, 18H, $OCH_3$), 3.74 (s, 6H, bridging $CH_2$), 3.30 (d, $J$=13.2 Hz, 12H, $ArCH_2Ar$), 1.00 (s, 54H, $C(CH_3)_3$). IR (KBr): $\nu$ 3480, 3380, 1480, 1460, 1430 cm$^{-1}$. FD MS: $m/z$ 1731 [$(M+2)^+$]. $C_{117}H_{132}O_{12}$: calcd C 81.21, H 7.69; found C 80.81, H 7.61.

**4.2.2. Cyclic tetramer 5b.** White power, yield 9 mg (4.5%). $^1$H NMR ($CDCl_3$): $\delta$ 7.21 (s, 8H, OH), 6.88 (s, 16H, ArH), 6.78 (s, 16H, ArH), 4.25 (d, $J$=13.2 Hz, 16H, $ArCH_2Ar$), 3.93 (s, 24H, $OCH_3$), 3.75 (s, 8H, bridging $CH_2$), 3.30 (d, $J$=13.2 Hz, 16H, $ArCH_2Ar$), 0.99 (s, 72H, $C(CH_3)_3$). IR (KBr): $\nu$ 3400, 1475, 1460, 1430 cm$^{-1}$. FD MS: $m/z$ 2307 [$(M+2)^+$]. $C_{156}H_{176}O_{16}$: calcd C 81.21, H 7.69; found C 80.31, H 7.80.[28]

**4.2.3. Cyclic pentamer 5c.** White power, yield 8 mg (4%). $^1$H NMR ($CDCl_3$): $\delta$ 7.21 (s, 10H, OH), 6.88 (s, 20H, ArH), 6.78 (s, 20H, ArH), 4.26 (d, $J$=13.2 Hz, 20H, $ArCH_2Ar$), 3.94 (s, 30H, $OCH_3$), 3.75 (s, 10H, bridging $CH_2$), 3.30 (d, $J$=13.2 Hz, 20H, $ArCH_2Ar$), 0.99 (s, 90H, $C(CH_3)_3$). IR (KBr): $\nu$ 3470, 3380, 1475, 1460, 1425 cm$^{-1}$. FD MS: $m/z$ 2882 ($M^+$). $C_{195}H_{220}O_{20}$: calcd C 81.21, H 7.69; found C 80.82, H 7.76.

**4.2.4. Linear trimer 6a.** White power, yield 6 mg (3%). $^1$H NMR ($CDCl_3$): $\delta$ 7.37 (s, 2H, OH), 7.21 (s, 2H, OH), 7.19 (s, 2H, OH), 7.06 (d, $J$=8.0 Hz, 4H, ArH), 6.90 (s, 8H, ArH), 6.78 (s, 8H, ArH), 6.77 (s, 4H, ArH), 6.68 (t, $J$=8.0 Hz, 2H, ArH), 4.30 (d, $J$=14.0 Hz, 4H, $ArCH_2Ar$), 4.26 (d, $J$=13.3 Hz, 8H, $ArCH_2Ar$), 3.94 (s, 18H, $OCH_3$), 3.76 (s, 4H, bridging $CH_2$), 3.37 (d, $J$=14.0 Hz, 4H, $ArCH_2Ar$), 3.30 (d, $J$=13.3 Hz, 8H, $ArCH_2Ar$), 0.99 (s, 18H, $C(CH_3)_3$), 0.98 (s, 36H, $C(CH_3)_3$). IR (KBr): $\nu$ 3480, 3380, 1470, 1455, 1430 cm$^{-1}$. FD MS: $m/z$ 1718 [$(M-1)^+$]. $C_{116}H_{132}O_{12}$: calcd C 81.08, H 7.74; found C 81.07, H 7.78.

**4.2.5. Linear tetramer 6b.** White power, yield 7 mg (3.5%). $^1$H NMR ($CDCl_3$): $\delta$ 7.37 (s, 2H, OH), 7.21 (s, 6H, OH), 7.07 (d, $J$=7.8 Hz, 4H, ArH), 6.90 (s, 12H, ArH), 6.78 (s, 8H, ArH), 6.77 (s, 8H, ArH), 6.68 (t, $J$=7.8 Hz, 2H, ArH), 4.30 (d, $J$=13.6 Hz, 4H, $ArCH_2Ar$), 4.25 (d, $J$=13.2 Hz, 12H, $ArCH_2Ar$), 3.95 (s, 24H, $OCH_3$), 3.75 (s, 6H, bridging $CH_2$), 3.37 (d, $J$=13.6 Hz, 4H, $ArCH_2Ar$), 3.31 (d, $J$=13.2 Hz, 12H, $ArCH_2Ar$), 1.00 (s, 36H, $C(CH_3)_3$), 0.99 (s, 36H, $C(CH_3)_3$). IR (KBr): $\nu$ 3475, 3390, 1473, 1455, 1430 cm$^{-1}$. FD MS: $m/z$ 2295 [$(M+2)^+$]. $C_{155}H_{176}O_{16}$: calcd C 81.11, H 7.73; found C 80.63, H 7.71.

**4.2.6. Linear pentamer 6c.** White power, yield 8 mg (4%). $^1$H NMR ($CDCl_3$): $\delta$ 7.37 (s, 2H, OH), 7.21 (s, 8H, OH), 7.07 (d, $J$=7.8 Hz, 4H, ArH), 6.90 (s, 16H, ArH), 6.78 (s, 20H, ArH), 6.68 (t, $J$=8.0 Hz, 2H, ArH), 4.30 (d, $J$=13.4 Hz, 4H, $ArCH_2Ar$), 4.25 (d, $J$=13.0 Hz, 16H, $ArCH_2Ar$), 3.95 (s, 30H, $OCH_3$), 3.75 (s, 8H, bridging $CH_2$), 3.37 (d, $J$=13.4 Hz, 4H, $ArCH_2Ar$), 3.30 (d, $J$=13.0 Hz, 16H, $ArCH_2Ar$), 0.99 (s, 54H, $C(CH_3)_3$), 0.98 (s, 36H, $C(CH_3)_3$). IR (KBr) $\nu$ 3470, 3390, 1475, 1463, 1430 cm$^{-1}$. FD MS: $m/z$ 2872 [$(M+2)^+$]. $C_{194}H_{220}O_{20}$: calcd C 81.13, H 7.72; found C 80.62, H 7.79.

**4.2.7. Dimer 7a and trimer 7b.** The reactant **3** was prepared according to a literature method[27] by 1,3-*distal* methylation of *p-tert*-amylcalix[4]arene followed by a selective deamylation reaction. Thus a mixture of *p-tert*-amylcalix[4]arene (1.4 g, 2 mmol), methyl tosylate (0.744 g, 4 mmol) and $K_2CO_3$ (0.276 g, 2 mmol) in acetonitrile was refluxed for 6 h. After removal of solvent, the residue was dissolved in chloroform and washed with water. The organic layer was dried over with anhydrous $MgSO_4$. After solvent was stripped off, product 5,11,17,23-*p-tert*-amyl-26,28-dimethoxycalix[4]-arene precipitated from methanol. White power, yield 1.3 g (92%), mp 218–220°C. $^1$H NMR ($CDCl_3$): $\delta$ 7.25 (s, 2H, OH), 7.00 (s, 4H, ArH), 6.70 (s, 4H, ArH), 4.28 (d, $J$=14.2 Hz, 4H, $ArCH_2Ar$), 3.95 (s, 6H, $OCH_3$), 3.33 (d, $J$=14.2 Hz, 4H, $ArCH_2Ar$), 1.60 (q, $J$=7.2 Hz, 4H, $C(CH_3)_2CH_2CH_3$), 1.30 (s, 12H, $C(CH_3)_2CH_2CH_3$), 1.17 (q, $J$=7.2 Hz, 4H, $C(CH_3)_2CH_2CH_3$), 0.90 (s, 12H, $C(CH_3)_2CH_2CH_3$), 0.55 (t,

$J$=7.2 Hz, 6H, $C(CH_3)_2CH_2CH_3$), 0.15 (t, $J$=7.2 Hz, 6H, $C(CH_3)_2CH_2CH_3$). IR (KBr): $\nu$ 3370, 1590, 1480, 1460 $cm^{-1}$. MALDI-TOF MS: $m/z$ 755.3 $[(M+Na)^+]$, 703.3 $[(M-C_2H_5)^+]$. $C_{50}H_{68}O_4$: calcd C 81.92, H 9.35; found C 81.51, H 9.48. To a mixture of 5,11,17,23-*tert*-amyl-26,28-dimethoxy-calix[4]arene (400 mg, 0.55 mmol) in chloroform (8 ml) and toluene (2 ml) was added anhydrous $AlCl_3$ (400 mg, 3 mmol). The reaction mixture was stirred for 1.5 h at room temperature and was then quenched by adding water. The organic layer was separated, washed several times with water and dried over anhydrous $MgSO_4$. After the solvent was removed under vacuum, product **3** was obtained as a precipitant from methanol. White power, yield 200 mg (60%), mp 233–234°C. $^1H$ NMR ($CDCl_3$): $\delta$ 7.40 (s, 2H, OH), 7.06 (d, $J$=7.4 Hz, 4H, ArH), 6.73 (s, 4H, ArH), 6.69 (t, $J$=7.4 Hz, 2H, ArH), 4.28 (d, $J$=14.4 Hz, 4H, $ArCH_2Ar$), 3.95 (s, 6H, $OCH_3$), 3.37 (d, $J$=14.4 Hz, 4H, $ArCH_2Ar$), 1.25 (q, $J$=7.0 Hz, 4H, $C(CH_3)_2$ $CH_2CH_3$), 0.98 (s, 12H, $C(CH_3)_2CH_2CH_3$), 0.23 (t, $J$=7.0 Hz, 6H, $C(CH_3)_2CH_2CH_3$). IR (KBr): $\nu$ 3270, 1580, 1475, 1455, 1440 $cm^{-1}$. MALDI-TOF MS: $m/z$ 615.2 $[(M+Na)^+]$, 563.2 $[(M-C_2H_5)^+]$. $C_{40}H_{48}O_4$: calcd C 81.04, H 8.16; found C 80.30, H 8.42. To a stirred solution of 5,17-di-*tert*-amyl-25,27-dihydroxy-26,28-dimethoxycalix[4]arene (**3**) (0.10 g, 0.17 mmol) in chloroform (20 ml) was added chloromethyl methyl ether (0.17 mmol) and anhydrous $ZnCl_2$ (0.05 g, 0.37 mmol). After most of **3** disappeared, which was monitored by TLC, the reaction mixture was washed three times with water. The organic layer was separated and dried over anhydrous $MgSO_4$. After removal of solvent, the residue was subjected to preparative TLC (petroleum ether (60–90°C)/EtOAc 3:2) to give **7a** and **7b**.

**4.2.8. Dimer 7a.** White power, yield 40 mg (39.5%), mp 275–277°C. $^1H$ NMR ($CDCl_3$): $\delta$ 7.35 (s, 2H, OH), 7.20 (s, 2H, OH), 7.07 (d, $J$=8.0 Hz, 4H, ArH), 6.90 (s, 4H, ArH), 6.72 (s, 8H, ArH), 6.65 (t, $J$=8.0 Hz, 2H, ArH), 4.27 (d, $J$=13.5 Hz, 4H, $ArCH_2Ar$), 4.23 (d, $J$=13.2 Hz, 4H, $ArCH_2Ar$), 3.93 (s, 12H, $OCH_3$), 3.74 (s, 2H, bridging $CH_2$), 3.36 (d, $J$=13.5 Hz, 4H, $ArCH_2Ar$), 3.30 (d, $J$=13.2 Hz, 4H, $ArCH_2Ar$), 1.25 (q, $J$=7.2 Hz, 8H, $C(CH_3)_2CH_2CH_3$), 0.94 (s, 24H, $C(CH_3)_2CH_2CH_3$), 0.24 (t, $J$=7.2 Hz, 12H, $C(CH_3)_2CH_2CH_3$). IR (KBr): $\nu$ 3460, 3350, 1470, 1450 $cm^{-1}$. FD MS: $m/z$ 1196 $[(M-1)^+]$. $C_{81}H_{96}O_8$ calcd C 81.23, H 8.08; found C 81.10, H 8.64.

**4.2.9. Trimer 7b.** White power, yield 35 mg (34%), mp 183–185°C. $^1H$ NMR ($CDCl_3$): $\delta$ 7.35 (s, 2H, OH), 7.20 (s, 2H, OH), 7.17 (s, 2H, OH), 7.07 (d, $J$=7.6 Hz, 4H, ArH), 6.89 (s, 8H, ArH), 6.71 (s, 12H, ArH), 6.65 (t, $J$=7.8 Hz, 2H, ArH), 4.27 (d, $J$=12.8 Hz, 4H, $ArCH_2Ar$), 4.24 (d, $J$=13.2 Hz, 8H, $ArCH_2Ar$), 3.95 (s, 18H, $OCH_3$), 3.75 (s, 2H, bridging $CH_2$), 3.37 (d, $J$=12.8 Hz, 4H, $ArCH_2Ar$), 3.31 (d, $J$=13.2 Hz, 8H, $ArCH_2Ar$), 1.26 (q, $J$=7.4 Hz, 12H, $C(CH_3)_2CH_2CH_3$), 0.95 (s, 36H, $C(CH_3)_2CH_2CH_3$), 0.25 (t, $J$=7.4 Hz, 18H, $C(CH_3)_2CH_2CH_3$). IR (KBr): $\nu$ 3460, 3350, 1470, 1450 $cm^{-1}$; FD MS: $m/z$ 1801 $(M^+)$. $C_{122}H_{144}O_{12}$: calcd C 81.29, H 8.05; found C 81.22, H 7.96.

**4.2.10. Dimer 8.** Followed the procedure as for the preparation of **7**, the reaction of **4** gave dimer **8**: white power, yield 41%, mp 297–298°C. $^1H$ NMR ($CDCl_3$): $\delta$ 8.28 (s, 2H, OH), 8.10 (s, 2H, OH), 6.50–7.15 (m, 22H, ArH), 4.33 (d, $J$=13.3 Hz, 4H, $ArCH_2Ar$), 4.31 (d, $J$=13.3 Hz, 4H, $ArCH_2Ar$), 4.10 (q, $J$=7.1 Hz, 8H, $OCH_2$), 3.71 (s, 2H, bridging $CH_2$), 3.40 (d, $J$=13.3 Hz, 4H, $ArCH_2Ar$), 3.32 (d, $J$=13.3 Hz, 4H, $ArCH_2Ar$), 1.65 (t, $J$=7.1 Hz, 12H, $CH_3$). IR (KBr) $\nu$ 3280, 1470, 1460, 1445, 1435 $cm^{-1}$. FD MS: $m/z$ 972 $(M^+)$. $C_{65}H_{64}O_8$: calcd C 80.21, H 6.63; found C 79.67, H 6.56.

### 4.3. Preparation of linear trimers 6a and 11

To a stirred solution of 11,23-bis(chloromethyl)-5,17-di-*tert*-butyl-25,27-dihydroxy-26,28-dimethoxycalix[4]arene (**9**) (0.16 g, 0.25 mmol) and of 5,17-di-*tert*-butyl-26,28-dihydroxy-25,27-dimethoxy-calix[4]arene (**2**) (0.75 mmol) or calix[4]arene **10** (0.75 mmol) in chloroform (20 ml) was added anhydrous $ZnCl_2$ (0.05 g, 0.36 mmol). The reaction mixture was stirred for 3 h and was then quenched by adding water. After washing with water and drying over anhydrous $MgSO_4$, the organic solvent was removed and the residue was subjected to preparative TLC (petroleum ether (60–90°C)/EtOAc 3:2) to give **6a** or **11**.

**4.3.1. Trimer 6a.** White power, yield 200 mg (46%), mp 330°C (dec.). The spectra was identical to those of **6a** isolated from chloromethylation of **2** (vide supra).

**4.3.2. Trimer 11.** White power, yield 160 mg (44%), mp 240°C (dec.). $^1H$ NMR ($CDCl_3$): $\delta$ 10.20 (s, 8H, OH), 7.30 (s, 2H, OH), 6.65–7.10 (m, 30H, ArH), 4.27 (d, $J$=13.5 Hz, 4H, $ArCH_2Ar$), 4.25 (d, $J$=13.3 Hz, 8H, $ArCH_2Ar$), 3.95 (s, 18H, $OCH_3$), 3.62 (s, 4H, bridging $CH_2$), 3.38 (d, $J$= 13.5 Hz, 4H, $ArCH_2Ar$), 3.31 (d, $J$=13.3 Hz, 8H, $ArCH_2Ar$), 1.00 (s, 18H, $C(CH_3)_3$). IR (KBr) $\nu$ 3440, 3150; 1540, 1470, 1460 $cm^{-1}$. FD MS: $m/z$ 1436 $[(M-1)^+]$. $C_{96}H_{92}O_{12}$: calcd C 80.19, H 6.45; found C 79.58, H 6.16.

### 4.4. Preparation of starlike pentamer 13

To a stirred solution of 5,11,17,23-tetra(chloromethyl)-25,26,27,28-tetra-hydroxycalix[4]arene (**12**) (0.1 g, 0.16 mmol) and of 5,17-di-*tert*-butyl-26,28-dihydroxy-25,27-dimethoxy-calix[4]-arene (**2**) (0.37 g, 0.66 mmol) in chloroform (30 ml) was added anhydrous $ZnCl_2$ (0.1 g, 0.72 mmol). The reaction mixture was stirred for 3 h and was then quenched by adding water. After washed with water and dried over anhydrous $MgSO_4$, the organic solvent was removed and the residue was subjected to preparative TLC (petroleum ether (60–90°C)/EtOAc 3:2) to give **13**. White power, yield 61 mg (14%), mp 245–246°C. $^1H$ NMR ($CDCl_3$): $\delta$ 10.21 (s, 4H, OH), 7.41 (s, 4H, OH), 7.09–6.70 (m, 48H, ArH, OH), 4.29 (d, $J$=13.1 Hz, 16H, $ArCH_2Ar$), 4.10 (d, $J$=13.0 Hz, 4H, $ArCH_2Ar$), 3.95 (s, 24H, $OCH_3$), 3.69 (s, 8H, bridging $CH_2$), 3.33–3.40 (m, 20H, $ArCH_2Ar$), 0.98 (s, 72H, $C(CH_3)_3$). $^{13}C$ NMR ($CDCl_3$): $\delta$ 152.8, 151.3, 151.0, 147.0, 146.9, 132.2, 132.2, 132.0, 129.2, 128.6, 128.5, 128.5,128.4, 128.3, 128.2, 125.6, 125.5, 119.1 (ArC), 63.3 ($OCH_3$), 34.0 ($C(CH_3)_3$), 31.5, 31.4, 31.3, 31.2 ($ArCH_2Ar$, $calixCH_2calix$), 31.1 ($C(CH_3)_3$), 14.2 IR (KBr) $\nu$ 3441, 3138, 1476, 1398 $cm^{-1}$. MALDI-TOF MS: $m/z$ 2752 $[(M+Na)^-]$. $C_{184}H_{200}O_{20}$: calcd C 80.90, H 7.38; found C 80.27, H 7.51.

## Acknowledgements

We are grateful to the National Natural Science Foundation of China, the Major State Basic Research Development Program of China (Grant No. G2000078100) and Chinese Academy of Sciences for the financial support.

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