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# Two structural types of *1,3-alternate* tetrapropoxycalix[4]arene derivatives in the solid state

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The solid state structures of seven tetrapropoxycalix[4]arene derivatives immobilised in a *1,3-alternate* conformation were determined using single-crystal X-ray crystallography. The cavity shapes of investigated derivatives (upper rim unsubstituted, distally di-substituted and tetra-substituted) and the nature of intermolecular interactions in molecular packing were compared. The results indicate that there are only two structural types adopted by basic tetrapropoxycalix[4]arene derivatives in the *1,3-alternate* conformation.

## Introduction

Calixarenes represent a versatile class of macrocyclic compounds.[1–4] Some of them are readily available from cheap starting materials and can easily be used as building blocks for the design of more sophisticated supramolecular systems with specific properties. Among them, calix[4]arenes have received the most attention due to their accessibility and controllable molecular architecture as well as diverse complexation abilities.[5]

Generally, calix[4]arenes are compounds created by four phenolic units connected by methylene bridges in 2,6-positions, thus forming a small cavity. They can adopt four conformers depending on the mutual orientation of the aromatic rings around the cavity. Depending on this orientation, these are *cone*, *partial cone*, *1,2-alternate* and *1,3-alternate* conformers.

The *1,3-alternate* derivatives of calix[4]arene offer several unique properties.[6] They are relatively rigid molecules possessing high symmetry. A distal pair of aromatic units is well preorganized for the complexation of soft cations *via* cation–π interactions.[7] A feasible derivatisation of a *1,3-alternate* skeleton enables the construction of "both-sides" ditopic receptors for cations [8,9] and anions.[10] The *1,3-alternate* calix[4]arenes could be used as a "core" in dendrimers[11] and oligomacrocycles.[12] Their tubular shape also invokes the idea of forming the channels in the solid state based on non-covalent interactions.[7,13,14]

All these extremely interesting characteristics are definitely associated with the conformation of these semi-rigid molecules. In this paper, we report on the results of the solid-state conformational analysis of several *1,3-alternate* calix[4]arene derivatives.

We were concerned with *1,3-alternate* derivatives substituted on the phenolic part (lower rim) by four propoxy groups. It is known that this group is sufficient for stabilizing the system in the desired conformation. Furthermore, we considered symmetrically substituted calix[4]arenes on the aromatic part (upper rim) as the most convenient molecules for conformational analysis. We intended to compare the cavity size, cavity shape and intermolecular interactions in the molecular packing of these derivatives. Di-*tert*-butyl-**7**, dibromo-**8**, diphenyl-**9** as representatives of distally di-substituted tetrapropoxycalix[4]arene and tetra-*tert*-butyl-**10**, unsubstituted tetrapropoxycalix[4]arene **11**, tetrabromo-**12** and tetraphenyl-**13** derivatives as representatives of symmetrical tetrapropoxycalix[4]arenes were synthesised for this purpose (Scheme 1). Suitable single crystals were grown and proven by X-ray crystallography.†

Further tetrapropoxy derivatives were searched for in the Cambridge Structure Database (CSD version 5.26, February 2005 release). Among more than 600 structures of calix[4]arene derivatives, we found 61 derivatives with propoxy groups, but only four of them in the *1,3-alternate* conformation. Unfortunately these structures could not be included in the conformational study because they didn't represent structures of free calix[4]arene but rather complexes or solvates. As the complexed molecules or ions are affecting the final shape of the calixarene cavity we left these structures out of consideration.

## Results and discussion

### Conformation analysis

The basic skeleton of every determined structure was numbered according to the rules of calix[4]arene nomenclature (Fig. 1). Furthermore, the propoxy groups were numbered (C33–C44) while the substituents on the aromatic part were numbered as the last. Every quarter of the calix[4]arene derivative was labeled with a lower case letter to distinguish individual substituents for the purpose of intermolecular interaction comparison; Pr(b) means the propoxy group on the aromatic ring b (C3–C7, C28).

Conformational analysis consisted of (i) comparison of the distance between distal aromatic rings (C23–C11 and C5–C17), (ii) calculation of the dihedral angle between the plane defined by the aromatic ring and the plane defined by four methylene bridges (C2–C8–C14–C20), and (iii) calculation of the torsion angle of these groups.

We can find two basic types of cavity shape among the *1,3-alternate* derivatives studied. More than half of the studied calix[4]arenes (**8**, **9**, **11**, **12**) adopt the first, *closed* cavity type (Table 1). The cavity of these derivatives is nearly closed on both sides and propoxy groups are turned into the space making

† CCDC reference numbers 178413–178416, 267155–267157. See http://www.rsc.org/suppdata/ob/b5/b505454k/ for crystallographic data in CIF or other electronic format.

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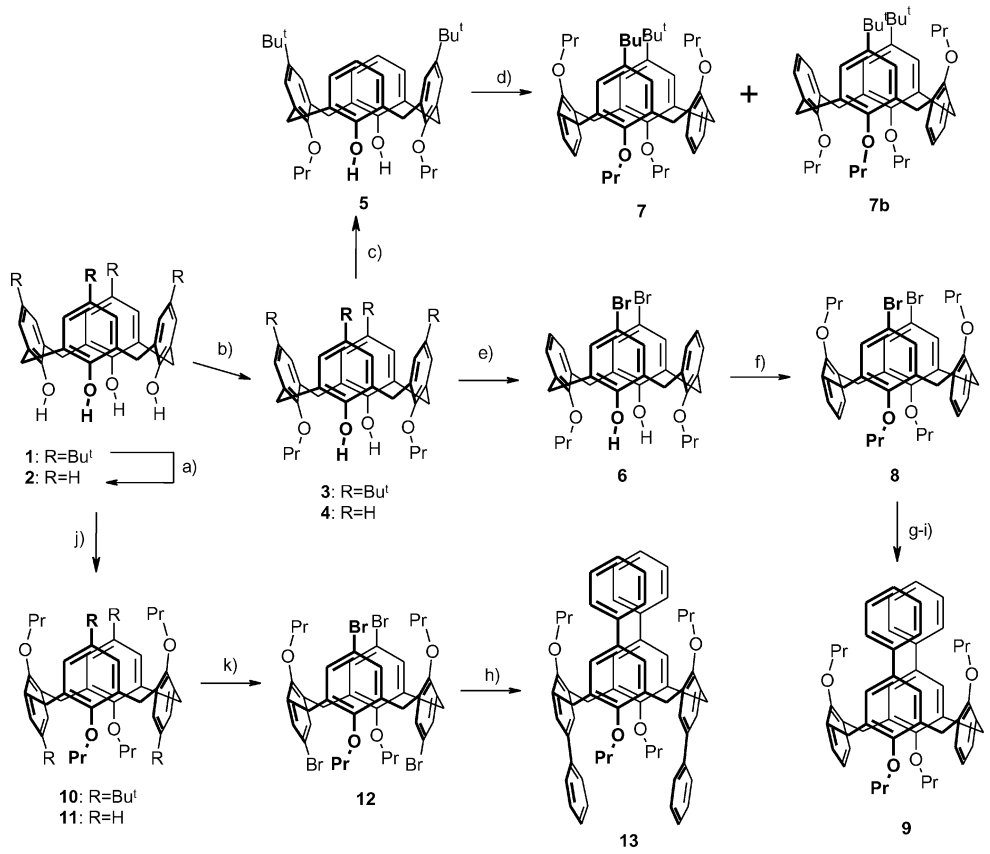

**Scheme 1** (a) Phenol, $AlCl_3$, toluene, rt, (b) propyl iodide, 1.1 eq. $K_2CO_3$, acetone, reflux, (c) from **3**, $AlCl_3$, dichloromethane, toluene, rt, (d) propyl iodide, $Cs_2CO_3$, acetone, reflux, (e) from **4**, 2.2 eq. $Br_2$, chloroform, rt, (f) propyl iodide, $(CH_3)_3SiOK$, THF, rt, (g) phenylmagnesium iodide, $[Ni(dppe)]Cl_2$, ether, reflux, (h) 1. $Bu^t$–Li, THF, −78 °C, 2. zinc chloride, THF, –78 °C, 3. phenyl iodide, THF, $Pd(PPh_3)_4$, rt, (i) phenylboronic acid, $Pd(PPh_3)_4$, toluene–methanol, 100 °C, (j) propyl iodide, $Cs_2CO_3$, acetone, reflux, (k) from **11**, NBS, butan-2-one, rt.

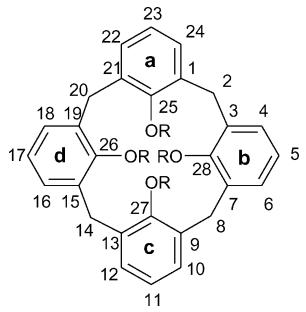

**Fig. 1** Schematic overview of basic skeleton numbering.

**Table 1** Torsion angles and distances at the aromatic part

| | Torsion angle/°[a] | Distance/Å[a] | |
|---|---|---|---|
| Structure no. | C2–C8–C14–C20 | C5–C17 | C11–C23 |
| **7**(1) | 5.4 | 7.19 | 7.45 |
| **7**(2) | 7.0 | 7.27 | 7.58 |
| **7**(3) | 5.2 | 5.53 | 6.06 |
| **8** | 0.8 | 4.60 | 4.49 |
| **9** | 3.1 | 4.54 | 4.35 |
| **10** | 6.5 | 7.22 | 7.22 |
| **11** | 0.4 | 4.33 | 4.31 |
| **12** | 0 | 4.75 | 4.69 |
| **13** | 12.0 | 7.19 | 7.32 |

[a] Distances and angles calculated with ORTEPIII.

the top of the cavity more accessible for the next calixarene unit.

The second type, the *wide open* cavity, is adopted by the rest of the molecules (**7**, **10**, **13**). The stability of the *open* cavity is provided by intramolecular CH–π interactions between propoxy groups and neighbouring aromatic rings (Fig. 2). The structure of **7** represents such an intermediate state. Two of the three molecules creating an independent part of the unit cell adopt the *wide open* type of structure but the shape of the last molecule is much more similar to the *closed* type. The differences between both types are clearly demonstrated in Fig. 3.

The torsion angle of the methylene bridges acquires higher values in *open* conformers. Compound **13** represents the most distorted structure with a torsion angle equal to 12° (Table 1). Values of dihedral angles in the *closed* conformers vary only slightly, within the range of 2.5° for each structure. These varieties are significantly higher for *open* conformers (Table 2).

Furthermore, the investigated crystal structures were compared with the shape of the ideal *1,3-alternate* conformer that adopts an S4 symmetry; it has a four-fold inversion axis passing through the cavity center, its methylene bridges are lying in the plane creating a square and all aromatic units are tilted by the same angle.

**Table 2** Dihedral angles of aromatic rings and plane C2–C8–C14–C20

| | Dihedral angle/°[a] | | | |
|---|---|---|---|---|
| Structure no. | a | b | c | d |
| **7**(1) | 118.9 | 119.3 | 111.2 | 106.3 |
| **7**(2) | 124.7 | 109.8 | 109.0 | 117.2 |
| **7**(3) | 96.7 | 91.4 | 95.8 | 93.6 |
| **8** | 80.7 | 79.4 | 79.7 | 79.5 |
| **9** | 79.8 | 77.8 | — | — |
| **10** | 113.9 | 107.8 | 109.3 | 118.5 |
| **11** | 77.5 | 77.4 | — | — |
| **12** | 83.8 | 82.2 | 81.5 | 82.3 |
| **13** | 111.1 | 113.5 | 112.7 | 112.2 |

[a] Calculated with PARST97.

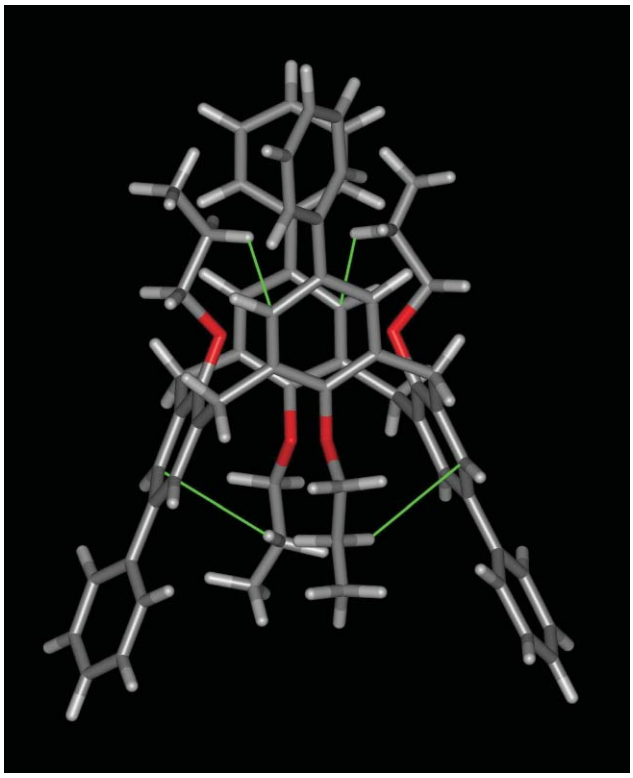

**Fig. 2** Detail of intramolecular CH–π interactions in structure **13** adopting the *open* cavity shape.

At first sight, both types seem to be closed to the ideal S4 shape. In detail, it's obvious that the individual inner symmetry is much lower. Thus, compounds **7**, **8**, **10**, **13** possess C1 symmetry, derivative **12** has $C_v$ symmetry, while calixarenes **9** and **11** exhibit C2 symmetry.

### Intermolecular interactions

It is generally known that classical calix[4]arenes and thiacalix[4]arenes (the phenols are connected *via* four sulfur atoms instead of $CH_2$ groups) in the *1*,*3-alternate* conformation are inclined to form infinite channels in the solid state.[15] This property is in fact predetermined by the shape of these molecules. Indeed, there are only two exceptions among studied derivatives, compounds **7** and **13**; both adopt the open type of structure.

As it is evident, *e.g.* from the molecular packing of **11** (Fig. 4), molecules in the *1*,*3-alternate* conformation simply interlock like a box of bricks in the solid state. Hydrogens in *para* positions are attracted into the cavity of the next calixarene unit. The shortest distance CH $\cdots$ C(arom) is less than 3.15 Å. The other derivatives behave similarly depending on the substitution. Generally, if the substituent is attracted towards the next calix[4]arene cavity, the molecules will likely adopt the *closed* cavity shape and form infinite channels (compare Fig. 4). Otherwise, the CH–π interactions of propoxy groups or methylene bridges become the most important interactions in the molecular packing (Table 3) and the molecules adopt the more distorted *open* cavity shape. The CH–π interactions were considered only when a hydrogen atom was localised directly above the aromatic ring at a distance shorter than 3.2 Å.[16] It has been proved that the CH–π interactions play a crucial role in the molecular packing of both structural types adopted by *1*,*3-alternate* tetrapropoxycalix[4]arene. The significant CH–π contacts are summarized in Table 3.

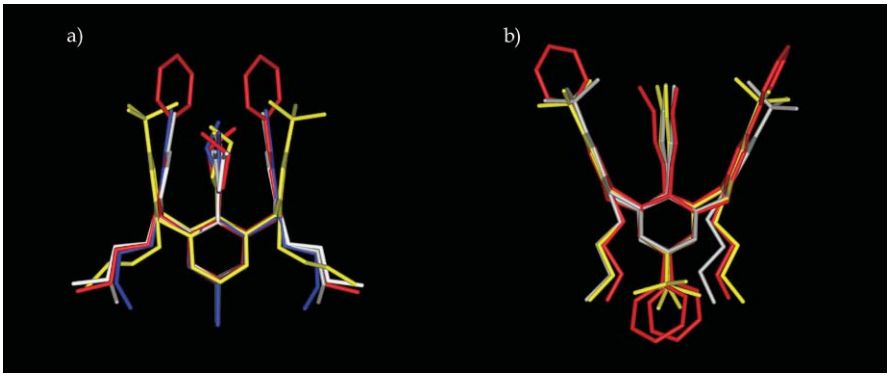


**Fig. 3** (a) Structures adopting the closed cavity type (white-**8**, red-**9**, grey-**11**, blue-**12**) and molecule **7(3)** (yellow) representing such an intermediate state, (b) the *open* cavity shape (grey-**7**, yellow-**10**, red-**13**).

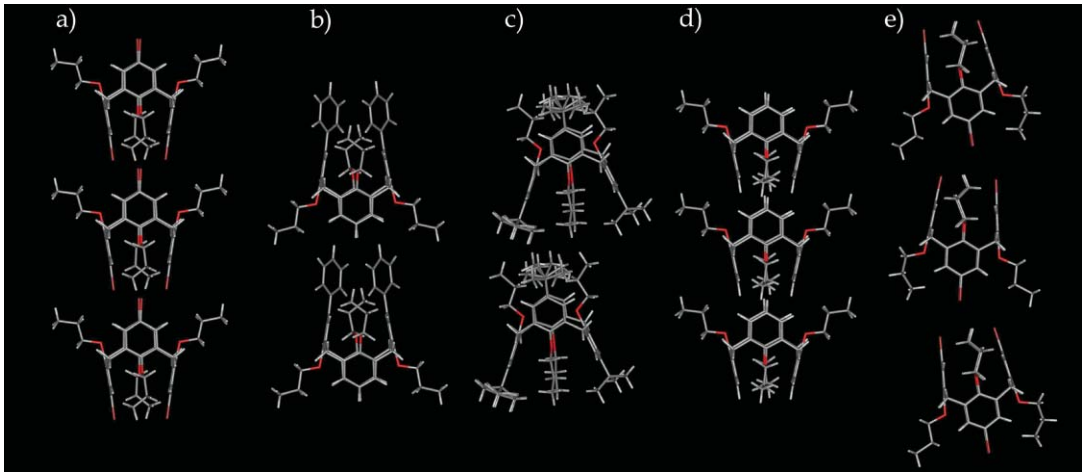


**Fig. 4** The various infinity channel types created by *1*,*3-alternate* tetrapropoxycalix[4]arene derivatives (a) **8**, (b) **9**, (c) **10**, (d) **11**, (e) **12**.

**Table 3** CH–π contacts in the crystal structures of *1,3-alternate* tetrapropoxycalix[4]arene derivatives

| Structure | | | | | | | |
|---|---|---|---|---|---|---|---|
| CH–π interaction | Distance/Å[c] | Ar—aromatic ring, Bu$^t$—*tert*-butyl group, Mb—methylene bridge, Pr—propoxy group, Ph—phenyl group | | | | | |
| **7** | | **8** | | **10** | | **13** | |
| Bu$^t$(1**c**)–Ar(3**d**) | 2.79 | Pr(**a**)–Ar(**b**) | 3.09 | Bu$^t$(**b**)–Ar(**a**) | 2.91 | Ar(**d**)–Ar(**b**) | 3.11 |
| Bu$^t$(2**c**)–Ar(3**b**) | 2.80 | Pr(**c**)–Ar(**d**) | 2.94 | Bu$^t$(**c**)–Ar(**d**) | 3.07 | Mb(**a**)–Ph(**c**) | 2.99 |
| Mb(2**c**)–Ar(1**b**) | 2.84 | | | Pr(**a**)–Ar(**d**) [a] | 3.05 | Mb(**b**)–Ar(**a**) | 3.03 |
| Mb(3**b**)–Ar(2**c**) | 2.80 | **9** | | Pr(**d**)–Ar(**a**)[a] | 2.82 | Ph(**a**)–Ph(**d**) | 3.04 |
| Mb(3**d**)–Ar(1**c**) | 2.88 | Mb(**c**)–Ph(**a**) | 2.83 | Pr(**d**)–Ar(**c**)[a] | 2.89 | Ph(**b**)–Ph(**a**) | 3.10 |
| Pr(1**a**)–Ar(1**d**) [a] | 2.80 | Mb(**a**)[b]–Ph(**c**) | 2.83 | | | Ph(**c**)–Ar(**c**) | 3.09 |
| Pr(1**b**)–Ar(1**c**)[a] | 2.98 | | | **12** | | Ph(**d**)–Ph(**b**) | 3.00 |
| Pr(1**d**)–Ar(2**b**) | 2.94 | | | Pr(**c**)–Ar(**b**) | 2.88 | Ph(**d**)–Ph(**b**) | 3.09 |
| Pr(2**a**)–Ar(2**b**)[a] | 2.78 | | | Pr(**c**)–Ar(**b**)[b] | 2.88 | Pr(**a**)–Ar(**d**)[a] | 2.99 |
| Pr(2**a**)–Ar(2**d**)[a] | 2.89 | | | | | Pr(**b**)–Ar(**a**)[a] | 2.94 |
| Pr(2**b**)–Ar(1**d**) | 2.87 | | | | | Pr(**c**)–Ar(**b**)[a] | 2.80 |
| Pr(2**d**)–Ar(2**a**)[a] | 2.90 | | | | | Pr(**d**)–Ar(**c**)[a] | 2.78 |

[a] Intramolecular interaction. [b] Generated by the symmetry. [c] Calculated in PARST97.

## Conclusion

Some general conformational rules for *1,3-alternate* tetrapropoxycalix[4]arene derivatives in the solid state can be derived from the comparison of studied crystal structures. Irrespective of the substituent on the aromatic part of the *1,3-alternate* tetrapropoxycalix[4]arene, only two different cavity shapes were found in the crystal structures studied. The cavity of the *1,3-alternates* (unsubstituted, distally di-substituted and tetra-substituted tetrapropoxycalix[4]arene derivatives) is either open or closed, both in a narrow range of dihedral angle between the plane defined by the aromatic ring and the plane defined by four methylene bridges.

The internal cavity parameters differ only slightly among the representatives of each group. The *open* type is more distorted but both types are closed to S4 symmetry. The *closed* type is preferred in structures creating infinite channels in the solid state. Both groups then apply different intermolecular interactions in molecular packing.

The results of our conformational analysis can be used for the rational design of novel *1,3-alternate* calix[4]arenes possessing interesting properties in the solid state, *e.g.* crystal engineering.

## Experimental

### Synthesis

Compounds prepared according to published methods: 5,11,17,23-tetra-*tert*-butylcalix[4]arene-25,26,27,28-tetraol **1**,[17] calix[4]arene-25,26,27,28-tetraol **2**,[18,19] 5,11,17,23-tetra-*tert*-butyl-6,28-dipro-poxycalix[4]arene-25,27-diol **3**,[20] 26,28-dipropoxycalix[4]arene-25,27-diol **4**,[21,22] 11,23-dibromo-26,28-dipropoxycalix[4]arene-25,27-diol **6**,[23] 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrapropoxycalix[4]arene (*1,3-alternate*) **10**,[24] 25,26,27,28-tetrapropoxycalix[4]arene (*1,3-alternate*) **11**.[25]

**5,17-Di-*tert*-butyl-26,28-dipropoxycalix[4]arene-25,27-diol 5**[26]**.** Aluminium chloride (0.6 g, 3.3 mmol) was stirred in 4 ml of dry dichloromethane for 15 minutes. Then, the solution of derivative **3** (0.5 g, 1.36 mmol) in 12 ml of dry toluene was added. The mixture was stirred vigorously and the course of the reaction was monitored by TLC (petroleum ether–ethyl acetate 15 : 1). After 25 minutes, the mixture was dissolved in 15 ml of 1 M HCl, stirred for 10 minutes and then extracted with 3 × 10 ml of ethyl acetate. The extracts were combined, washed with brine and water, dried over magnesium sulfate and evaporated to dryness. The preparative TLC (petroleum ether–ethyl acetate 15 : 1, $R_F = 0.75$) yielded 115 mg (28%) of title compound **5** as a white solid, mp 204–207 °C (ethyl acetate), found: C, 81.0; H, 8.5. $C_{42}H_{52}O_4$ requires: C, 81.25; H 8.4%). $\delta_H$(300 MHz; $CDCl_3$; $Me_4Si$) 8.05 (2H, s, OH), 7.03 (4H, d, *J* 7.2, Ar–H), 6.86 (4H, s, Ar–H), 6.62 (2H, t, *J* 7.2, Ar–H), 4.31 (4H, d, *J* 12.6, Ar–$CH_2$–Ar ax), 3.95 (4H, t, *J* 6.6, 2 × $OCH_2$), 3.34 (4H, d, *J* 12.6, Ar–$CH_2$–Ar eq), 2.08–2.02 (4H, m, 2 × $OCH_2CH_2$), 1.26 (6H, t, *J* 7.2, 2 × $CH_3$), 1.03 (18H, s, 2 × *tert*-Bu).

**5,17-Di-*tert*-butyl-25,26,27,28-tetrapropoxycalix[4]arene (*1,3-alternate*) 7 and 5,17-di-*tert*-butyl-25,26,27,28-tetrapropoxycalix[4]arene (*partial cone*) 7b**[25]**.** A mixture of derivative **5** (115 mg, 0.19 mmol), caesium carbonate (240 mg, 0.75 mmol) and of propyl iodide (0.11 ml, 1.14 mmol) was refluxed in 20 ml of dry acetone. The reaction was monitored by TLC. After 48 hours, the mixture was cooled, evaporated to dryness, and dissolved in a mixture of 20 ml of chloroform and 15 ml of 1 M HCl. The organic layer was separated and the aqueous layer was extracted twice with 15 ml of chloroform. The chloroform layers were combined, washed with water and dried over magnesium sulfate. After filtration, the mixture was evaporated to dryness and separated by preparative TLC (petroleum ether–ethyl acetate 15 : 1) to yield 34 mg (26%) of *1,3-alternate* **7** ($R_F = 0.7$), mp 204–206 °C (ethyl acetate), found: C, 81.2; H, 9.1; $M^+$, 704.6. $C_{48}H_{64}O_4$ requires C 81.8; H 9.15%; M, 704.5). $\delta_H$(300 MHz; $CDCl_3$; $Me_4Si$) 6.99 (4H, d, *J* 7.2, Ar–H), 6.97 (4H, s, Ar–H), 6.75 (2H, t, *J* 7.7, Ar–H), 3.76 (8H, s, Ar–$CH_2$–Ar), 3.36 (4H, t, *J* 7.7, 2 × $OCH_2$), 3.35 (4H, t, *J* 7.7, 2 × $OCH_2$), 1.27–1.16 (8H, m, 4 × $OCH_2CH_2$), 1.25 (18H, s, 2 × *tert*-Bu), 0.71 (6H, t, *J* 7.7, 2 × $CH_3$), 0.69 (6H, t, *J* 7.7, 2 × $CH_3$), and 24 mg (18%) of *partial cone* isomer **7b** ($R_F = 0.85$), mp 180–182 °C (ethyl acetate), found: C, 81.5; H, 9.1. $C_{48}H_{64}O_4$ requires C 81.8; H 9.15%). $\delta_H$(300 MHz; $CDCl_3$; $Me_4Si$) 7.23 (2H, d, *J* 7.2, Ar–H), 7.08 (2H, d, *J* 7.2, Ar–H), 6.89 (2H, t, *J* 7.2, Ar–H), 6.86 (2H, d, *J* 2.2, Ar–H), 6.51 (2H, d, *J* 2.7, Ar–H), 4.05 (2H, d, *J* 12.7, Ar–$CH_2$–Ar), 3.80–3.72 (2H, m, $OCH_2$), 3.74–3.60 (4H, m, Ar–$CH_2$–Ar), 3.62 (2H, t, *J* 7.7, $OCH_2$), 3.51–3.43 (2H, m, $OCH_2$), 3.39–3.33 (2H, m, $OCH_2$), 3.04 (2H, d, *J* 12.6, Ar–$CH_2$–Ar), 1.90–1.78 (6H, m, 3 × $OCH_2CH_2$), 1.52–1.43 (2H, m, $OCH_2CH_2$), 1.01 (18H, s, 2 × *tert*-Bu), 1.03 (6H, t, *J* 7.7, 2 × $CH_3$), 0.95 (3H, t, *J* 7.2, $CH_3$), 0.71 (3H, t, *J* 7.7, $CH_3$).

**5,17-Dibromo-25,26,27,28-tetrapropoxycalix[4]arene (*1,3-alternate*) 8.** Derivative **6** (8.0 g, 12 mmol) and 7.7 g (60 mmol, 5 equivalents) of potassium trimethylsilanolate were dissolved in 150 ml of dry tetrahydrofuran. After cooling to −5 °C, 5.8 ml (60 mmol) of propyl iodide were added dropwise over a period of 20 minutes. The mixture was stirred at room temperature for 5 days. Then, 150 ml of 1 M HCl were added and the mixture was extracted with 4 × 50 ml of chloroform. The organic layers were combined, dried over magnesium sulfate, filtered and evaporated to dryness. Crude product was precipitated from

chloroform–methanol to give 6.66 g (74%) of derivative **8**, mp 248–251 °C (THF), found: C, 63.7; H, 6.2; Br 21.0; $M^+$ 747.3. $C_{40}H_{46}O_4Br_2$ requires C 64.0; H 6.2; Br 21.3%; M, 748.18). $\delta_H$(300 MHz; $CDCl_3$; $Me_4Si$) 7.17 (4H, s, Ar–H), 6.98 (4H, d, *J* 7.2, Ar–H), 6.69 (2H, t, *J* 7.2, Ar–H), 3.61 (4H, t, *J* 6.6, 2 × $OCH_2$), 3.58 (8H, s, Ar–$CH_2$–Ar), 3.46 (4H, t, *J* 6.6, 2 × $OCH_2$), 1.72–1.65 (4H, d m, 2 × $OCH_2CH_2$), 1.62–1.52 (4H, d m, 2 × $OCH_2CH_2$), 1.01 (6H, t, *J* 7.2, 2 × $CH_3$), 0.87 (6H, t, *J* 7.2, 2 × $CH_3$).

**5,17-Diphenyl-25,26,27,28-tetrapropoxycalix[4]arene (*1,3-alternate*) 9.**

*Method A*[27]. A mixture of derivative **8** (100 mg, 0.13 mmol) and 10 mg (0.02 mmol) of [Ni(dppe)]$Cl_2$ was dissolved in 50 ml of dry diethyl ether. The reaction flask was evacuated 4 times and filled with argon. A solution of phenylmagnesium bromide (0.4 ml of 3 M, 1.2 mmol) in diethyl ether was injected *via* a septum and the mixture was refluxed for 48 hours. The ether was evaporated and the mixture was dissolved in 50 ml of dichloromethane and washed with 30 ml of 1 M HCl. The organic layer was separated, neutralized by 30 ml of 2 M $Na_2CO_3$, washed with 2 × 20 ml of water and dried over magnesium sulfate. The mixture was filtered and evaporated to dryness to give 126 mg of crude product, which was purified by preparative TLC (petroleum ether–chloroform 3 : 1) to remove the diphenyl ($R_F = 1.0$). The second fraction yielded 34 mg (34%) of derivative **9** ($R_F = 0.45$), mp 228–231 °C (ethyl acetate), found: C, 83.2; H, 7.6; $M^+$ 744.7. $C_{52}H_{56}O_4$ requires C 83.8; H 7.6%; M, 744.42). $\delta_H$(300 MHz; $CDCl_3$; $Me_4Si$) 7.33 (4H, m, Ar–H), 7.21 (4H, s, Ar–H), 7.17 (6H, m, Ar–H), 7.05 (4H, d, *J* 7.2, Ar–H), 6.73 (2H, t, *J* 7.2, Ar–H), 3.71 (8H, s, Ar–$CH_2$–Ar), 3.59 (4H, t, *J* 6.8, 2 × $OCH_2$), 3.57 (4H, t, *J* 6.8, 2 × $OCH_2$), 1.65–1.54 (8H, m, 4 × $OCH_2CH_2$), 0.92 (6H, t, *J* 7.6, 2 × $CH_3$), 0.79 (6H, t, *J* 7.6, 4 × $CH_3$).

*Method B*[28]. To a solution of derivative **8** (0.5 g, 0.67 mmol) in 10 ml of dry THF cooled to −78 °C, 2.3 ml of 1.7 M *tert*-butyllithium in pentane (4.0 mmol, 6 equiv.) were injected and the resulting yellow solution was stirred at −78 °C for 1 hour. During this period, a solution of 0.82 g (6.0 mmol, 9 equiv.) of freshly fused $ZnCl_2$ in 5 ml of dry THF was prepared, which was then cannulated into the reaction mixture. After the addition was complete, the cooling bath was removed and the colourless solution was stirred at room temperature for 30 minutes. The resulting organozinc salt solution was then cannulated into a flask containing 0.67 ml of phenyl iodide (6.0 mmol) and 10 mg (0.01 mmol) of $Pd(PPh_3)_4$ in 10 ml of dry THF. The mixture was stirred at room temperature for 12 hours in the dark, then dissolved in 50 ml of 4 M HCl and extracted with 3 × 20 ml of chloroform. The combined organic layers were successively washed with 20 ml of brine, 20 ml of a 10% solution of $Na_2SO_3$ and water, dried over magnesium sulfate and then evaporated to dryness. The crude product (0.7 g) was purified by column chromatography using petroleum ether to remove the excess of phenyl iodide and then by using a mixture of petroleum ether–chloroform 3 : 1 to yield 0.24 g (49%) of title compound **9**.

*Method C*[29]. A mixture of derivative **8** (0.4 g, 0.54 mmol), $Pd(PPh_3)_4$ (250 mg, 0.23 mmol) and phenylboronic acid (153 mg, 1.26 mmol) was dissolved under an atmosphere of argon in 10 ml of dry toluene and 1 ml of dry methanol and the reaction mixture was heated at 100 °C. After 15 minutes, 2 ml of a 2 M solution of $Na_2CO_3$ were added and heating was continued for 40 hours. After cooling, the mixture was dissolved in 100 ml of 1 M HCl and extracted with 3 × 20 ml of chloroform. The combined organic layers were washed successively with water, 20 ml of brine, and again with water and dried over magnesium sulfate. After evaporation, the residue was purified using column chromatography on silica gel (petroleum ether–chloroform 4 : 1) to yield 0.14 g (36%) of derivative **9**.

**5,11,17,23-Tetrabromo-25,26,27,28-tetrapropoxycalix[4]arene (*1,3-alternate*) 12**[30]**.** A mixture of derivative **11** (2.0 g, 3.37 mmol) and *N*-bromosuccinimide (6.0 g, 33.7 mmol, 10 equiv.) in 100 ml of butan-2-one was stirred at room temperature for 5 days. The precipitate formed was filtered off to give 2.68 g (88%) of derivative **12**, mp 354–356 °C (from THF), found: C, 52.8; H, 4.9; Br 34.3. $C_{40}H_{44}O_4Br_4$ requires C 52.9; H 4.9; Br 35.2%). $\delta_H$(300 MHz; $CDCl_3$; $Me_4Si$) 7.15 (8H, s, Ar–H), 3.56 (8H, t, *J* 6.6, 4 × $OCH_2$), 3.54 (8H, s, Ar–$CH_2$–Ar), 1.66 (8H, m, 4 × $OCH_2CH_2$), 0.99 (12H, t, *J* 7.7, 4 × $CH_3$).

**5,11,17,23-Tetraphenyl-25,26,27,28-tetrapropoxycalix[4]arene (*1,3-alternate*) 13**[28]**.** To a solution of 0.5 g (0.55 mmol) of derivative **12** in 10 ml of dry THF cooled to −78 °C were injected 3.2 ml of 1.7 M *tert*-butyllithium in pentane (5.5 mmol, 10 equiv.) and the yellow solution was stirred at −78 °C for 1 hour. During this period, a solution of freshly fused $ZnCl_2$ (1.02 g, 7.5 mmol, 14 equiv.) in 5 ml of dry THF was prepared, and then cannulated into the reaction mixture. After the addition, the cooling bath was removed and the colorless solution was stirred at room temperature for 30 minutes. The organozinc salt solution was then cannulated into a flask containing phenyl iodide (0.85 ml, 7.5 mmol) and $Pd(PPh_3)_4$ (15 mg, 0.014 mmol) in 10 ml of dry THF. The reaction mixture was stirred in the dark at room temperature for 12 hours and then poured into 50 ml of 4 M HCl and extracted with 3 × 20 ml of chloroform. The combined organic layers were washed successively with 20 ml of brine, 20 ml of a 10% solution of $Na_2SO_3$ and water, dried over magnesium sulfate and then evaporated to dryness. The residue (0.9 g) was separated by column chromatography on silica gel. The excess of phenyl iodide was removed using petroleum ether as an eluent. The second fraction, obtained using a petroleum ether–chloroform 3 : 1 mixture, contained 0.25 g of crude product. The pure title compound **13** (0.15 g, 31%) was isolated by subsequent preparative TLC (petroleum ether–chloroform 1 : 1, $R_F = 0.45$–0.55). Mp 278–280 °C (from ethyl acetate), found: C, 85.2; H, 7.1%; $M^+$ 896.8. $C_{64}H_{64}O_4$ requires C 85.7; H 7.2%; M, 896.48). $\delta_H$(400 MHz; $CDCl_3$; $Me_4Si$) 7.37 (8H, m, Ar–H), 7.23 (8H, s, Ar–H), 7.17 (12H, m, Ar–H), 3.77 (8H, s, Ar–$CH_2$–Ar), 3.61 (8H, t, *J* 7.2, 4 × $OCH_2$), 1.58–1.51 (8H, m, 4 × $OCH_2CH_2$), 0.78 (12H, t, *J* 7.2, 4 × $CH_3$).

## Crystal structure determination

The single crystals of **7**, **9**, **10**, **11** and **12** were measured on a Nonius Kappa CCD diffractometer with graphite monochromated Mo–Kα radiation. Single crystals of **8** and **13** were measured on an Enraf-Nonius CAD4 with graphite monochromated Cu–Kα radiation. The structures were solved by direct methods[31] and were refined by full matrix least-squares on *F* values.[32]

**X-Ray data for 7.** $C_{48}H_{64}O_4$, $M = 705.04$ g mol$^{-1}$, monoclinic system, space group $P21/c$, $a = 13.9231(1)$, $b = 35.1563(2)$, $c = 25.7578(2)$ Å, $\beta = 94.5875(3)$, $Z = 12$, $V = 12567.7(1)$ Å$^3$, $D_c = 1.12$ g cm$^{-3}$, $\mu$(Mo–Kα) = 0.7 mm$^{-1}$, crystal dimensions of 0.3 × 0.3 × 0.2 mm, $T = 150(2)$ K. All heavy atoms were refined anisotropically. Hydrogen atoms were placed from expected geometry and were not refined. This model converged to final $R = 0.0765$ and $R_w = 0.0799$ using 17406 independent reflections ($\theta_{max} = 25.4°$). CCDC reference number 267155.†

**X-Ray data for 8.** $C_{40}H_{46}O_4Br_2$, $M = 750.61$ g mol$^{-1}$, triclinic system, space group $P\bar{1}$, $a = 10.055(2)$, $b = 13.297(2)$, $c = 15.802(3)$ Å, $\alpha = 75.12(1)$, $\beta = 74.15(2)$, $\gamma = 69.45(1)$, $Z = 2$, $V = 1872.5(6)$ Å$^3$, $D_c = 1.33$ g cm$^{-3}$, $\mu$(Cu–Kα) = 30.4 mm$^{-1}$, crystal dimensions of 0.1 × 0.1 × 0.1 mm, $T = 293$ K. All heavy atoms were refined anisotropically. Hydrogen atoms were placed from expected geometry and were not refined. Disorder of bromine atoms was modeled. The refinement converged to final $R = 0.0736$ and $R_w = 0.0701$ using 2567 independent reflections ($\theta_{max} = 60°$). CCDC reference number 178413.†

**X-Ray data for 9.** $C_{52}H_{56}O_4$, $M = 745.02$ g mol$^{-1}$, monoclinic system, space group $C2/c$, $a = 24.088(1)$, $b = 12.665(1)$, $c = 17.274(1)$ Å, $\beta = 126.477(1)$, $Z = 4$, $V = 4237.5(1)$ Å$^3$, $D_c = 1.17$ g cm$^{-3}$, $\mu$(Mo–K$\alpha$) = 0.7 mm$^{-1}$, crystal dimensions of 0.2 × 0.1 × 0.1 mm, $T = 150(2)$ K. The independent part of the unit cell is created by one half of the molecule. All heavy atoms were refined anisotropically. Hydrogen atoms were located from Fourier maps and refined isotropically. This model converged to final $R = 0.0493$ and $R_w = 0.0183$ using 3902 independent reflections ($\theta_{max} = 27°$). CCDC reference number 178414.†

**X-Ray data for 10.** $C_{56}H_{80}O_4$, $M = 817.25$ g mol$^{-1}$, triclinic system, space group $P\bar{1}$, $a = 10.3974(2)$, $b = 13.0709(3)$, $c = 19.4131(3)$ Å, $\alpha = 107.941(1)$, $\beta = 93.567(1)$, $\gamma = 97.093(1)$, $Z = 2$, $V = 2476.7(1)$ Å$^3$, $D_c = 1.10$ g cm$^{-3}$, $\mu$(Mo–K$\alpha$) = 0.7 mm$^{-1}$, crystal dimensions of 0.2 × 0.2 × 0.2 mm, $T = 150(2)$ K. All heavy atoms were refined anisotropically. Hydrogen atoms were placed from expected geometry and were not refined. Disorder of two *tert*-butyl groups was modeled. This model converged to final $R = 0.0520$ and $R_w = 0.0313$ using 7878 independent reflections ($\theta_{max} = 27.5°$). CCDC reference number 267157.†

**X-Ray data for 11.** $C_{40}H_{48}O_4$, $M = 592.83$ g mol$^{-1}$, monoclinic system, space group $C2/c$, $a = 25.714(1)$, $b = 8.002(1)$, $c = 19.113(1)$ Å, $\beta = 121.01(1)$, $Z = 4$, $V = 3370.7(1)$ Å$^3$, $D_c = 1.16$ g cm$^{-3}$, $\mu$(Mo–K$\alpha$) = 0.73 mm$^{-1}$, crystal dimensions of 0.2 × 0.2 × 0.3 mm, $T = 150(2)$ K. The independent part of the unit cell is created by one half of the molecule. All heavy atoms were refined anisotropically. Hydrogen atoms were placed from expected geometry and were refined isotropically. Disorder of one propoxy group was modeled. The refinement converged to final $R = 0.0558$ and $R_w = 0.0600$ using 3160 independent reflections ($\theta_{max} = 27.5°$). CCDC reference number 267156.†

**X-Ray data for 12.** $C_{40}H_{44}O_4Br_4$, $M = 908.40$ g mol$^{-1}$, orthorhombic system, space group $Pnma$, $a = 23.851(1)$, $b = 12.333(1)$, $c = 13.079(1)$ Å, $Z = 4$, $V = 3845.6(1)$ Å$^3$, $D_c = 1.57$ g cm$^{-3}$, $\mu$(Mo–K$\alpha$) = 4.22 mm$^{-1}$, crystal dimensions of 0.3 × 0.3 × 0.2 mm, $T = 200(2)$ K. The independent part of the unit cell is created by one half of the molecule. All heavy atoms were refined anisotropically. Disorder of one propoxy group was modeled. Hydrogen atoms were located from Fourier maps and expected geometry. Only hydrogens with full occupancies were refined isotropically. This model converged to final $R = 0.0327$ and $R_w = 0.0337$ using 2353 independent reflections ($\theta_{max} = 27°$). CCDC reference number 178416.†

**X-Ray data for 13.** $C_{64}H_{64}O_4$, $M = 897.21$ g mol$^{-1}$, monoclinic system, space group $P21/c$, $a = 14.921(1)$, $b = 18.436(2)$, $c = 19.880(2)$ Å, $\beta = 108.21(1)$, $Z = 4$, $V = 5194.5(8)$ Å$^3$, $D_c = 1.15$ g cm$^{-3}$, $\mu$(Cu–K$\alpha$) = 5.4 mm$^{-1}$, crystal dimensions of 0.5 × 0.5 × 0.3 mm, $T = 293$ K. All heavy atoms were refined anisotropically. Hydrogen atoms were placed from expected geometry and were not refined. This model converged to final $R = 0.1015$ and $R_w = 0.0829$ using 5801 independent reflections ($\theta_{max} = 68°$). CCDC reference number 178415.†

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