Monatshefte für Chemie 128, 863–879 (1997)

Monatshefte für Chemie
Chemical Monthly

Head-to-Tail Connected Double Calix[4]arenes

W. Wąsikiewicz[1], G. Rokicki[1,*], J. Kiełkiewicz[1], E. F. Paulus[2], and V. Böhmer[3]

[1] Faculty of Chemistry, Warsaw University of Technology, PL-00664 Warsaw, Poland
[2] Hoechst AG, D-65926 Frankfurt/Main, Germany
[3] Institut für Organische Chemie, Johannes Gutenberg Universität, D-55099 Mainz, Germany

Summary. New macrotricyclic compounds consisting of two calix[4]arene substructures connected by aliphatic chains of various length (three to five carbon atoms) between two opposite *p*-positions and two distal phenolic oxygens have been synthesized. Starting with *p-tert*-butyl-calix[4]arene, two O-protected phenolic units are attached *via* ether links in 1,3-position by reaction with the corresponding tosylates. After deprotection, the new calix[4]arene is formed by fragment condensation with 2,6-*bis*bromomethylated 4-alkylphenols. The structure of one example (**8c**) has been confirmed by single crystal X-ray analysis. Both calixarene parts assume the cone conformation, a molecule of acetonitrile being included in both cavities.

Keywords. Calix[4]arenes; Macrocycles; Double calixarenes; X-Ray analysis.

Doppelte Calix[4]arene in Kopf-Schwanz-Verknüpfung

Zusammenfassung. Neue makrotricyclische Verbindungen, in denen zwei Calix[4]aren-Einheiten durch aliphatische Ketten unterschiedlicher Länge (drei bis fünf C-Atome) zwischen zwei gegenüberliegenden *p*-Positionen und zwei gegenüberliegenden Phenolsauerstoffen verknüpft sind, wurden hergestellt. Ausgehend von *p-tert*-Butyl-calix[4]aren werden zunächst zwei O-geschützte Phenolbausteine in 1,3-Stellung durch Umsetzung mit den entsprechenden Tosylaten etherartig gebunden. Nach Abspaltung der Benzylether-Schutzgruppe wird durch Fragmentkondensation mit 2,6-*bis*brommethylierten 4-Alkylphenolen das neue Calix[4]aren gebildet. Für **8c** wurde die Struktur durch Einkristallröntgenstrukturanalyse bestätigt. Beide Calixarenteile nehmen die *cone*-Konformation ein, wobei in die beiden Hohlräume je ein Molekül Acetonitril eingeschlossen wird.

Introduction

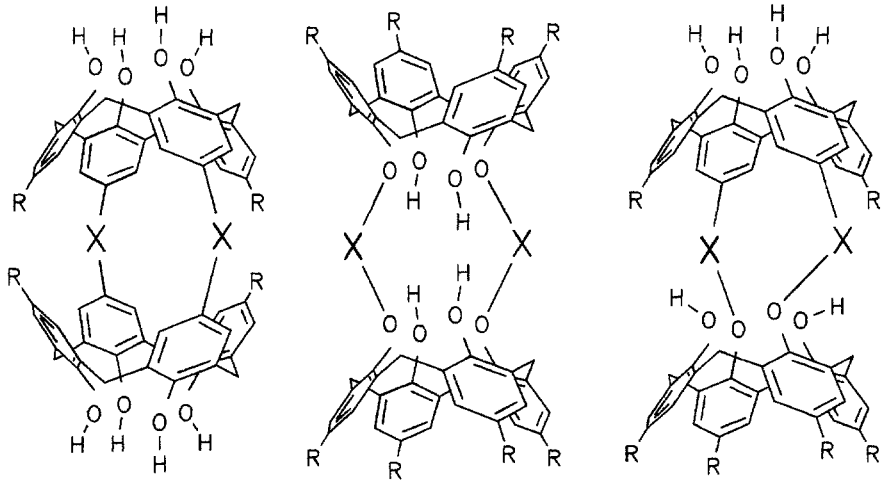
Calixarenes are readily available macrocyclic molecules [1] which can be selectively functionalized to serve as building blocks for the construction of larger molecular assemblies. These may be held together by covalent links or, following the present trend of self organization, by weaker forces like hydrogen bonds [2–4]. Probably the most intensely studied examples of covalently linked compounds are *Cram*'s carcerands and hemicarcerands [5] in which two resorcarene based cavitands are connected *via* their wide rims[1] by suitable

[1] The terms "wide rim" (= tail) and "narrow rim" (= head) are suggested instead of the expressions "upper rim" and "lower rim" which are especially inappropriate in the case of 'double calixarenes'

bridges, thus permanently including smaller molecules. An especially attractive variation in which a resorcarene derived cavitand and a calix[4]arene are combined was introduced by *Reinhoudt et al.* [6]. Its desymmetrized structure (no symmetry plane perpendicular to the molecular axis) allows to distinguish two orientations of the imprisoned molecule with respect to the surrounding container molecule. Similar effects have recently been observed for carcerands composed of two different resorcarenes [7].

The analogous connection of two calix[4]arenes *via* four bridges between their wide rims is less easily achieved [8], although a first example, obtained in very low yield, has already been described in 1989 [9]. One reason for this is probably the fact that the distorted or flattened cone conformation which is assumed by a tetraether (or tetraester) of a calix[4] arene fixed in the cone conformation is less favorable for a fourfold covalent connection than the C_4-symmetrical cavitands derived from resorcarenes.

In contrast to resorcarenes, calix[4]arenes are easily derivatized not only at their wide rim, but also at their narrow rim, and procedures for selective (partial) derivatization are also available. Consequently, various examples are known for larger molecules consisting of two (or even more) calix[4]arene substructures which are connected by one or more bridges [10–12]. The calix[4]arenes may exist not only in the cone, but also in the 1,3-alternate conformation [13]. Considering doubly-bridged double calix[4]arenes in the cone conformation, three possibilities exist if opposite phenolic units are connected (Scheme 1). These arrangements may be called head-to-head (**II**) [14], tail-to-tail (**I**) [15], head-to-tail (**III**) [16–17]. We report here on the synthesis of some new examples of type **III**.

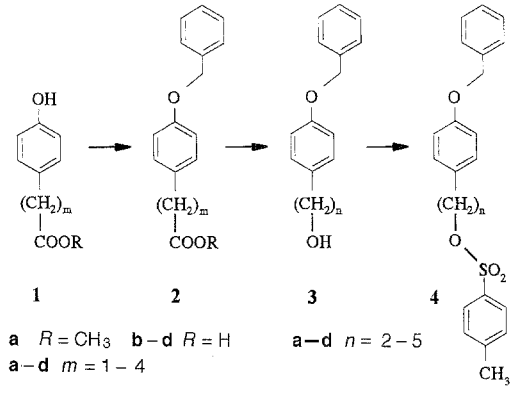


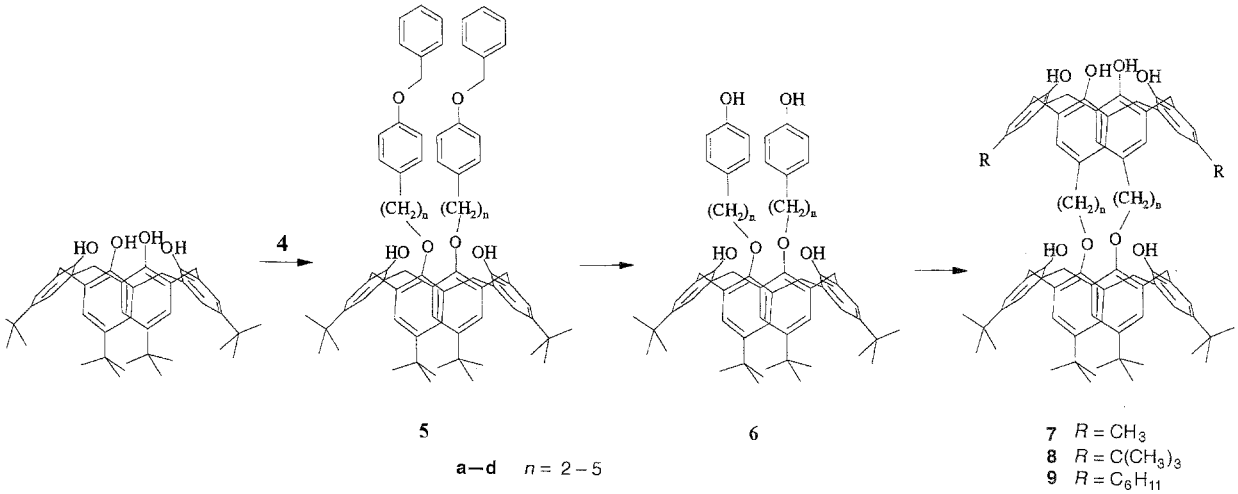
Scheme 1

Results and Discussion

All double calix[4]arenes (**7–9**) were obtained as outlined in Scheme 2. The tosylates **4** were prepared from the known (or even commercially available) 4-hydroxyphenyl carboxylic acids **1** in three steps (O-benzylation, 71–82%; reduction with $LiAlH_4$, 90–93%; reaction with tosyl chloride, 78–93%) using standard procedures.

O-Alkylation of *p-tert*-butyl-calix[4]arene by reaction with the stoichiometric amount of (4-benzyloxyphenyl)alkyl tosylate **4** in boiling acetonitrile in the presence of K_2CO_3 gave the 1,3-diethers **5** with *syn*-arrangement of the ether groups in yields of 65–90% after simple recrystallization. The benzyl ether groups were easily cleaved by hydrogenation using Pd/C as catalyst, and the diethers **6** were thus obtained from **5** in yields of 78–93%. Surprisingly, the tendency to crystallize was less pronounced for **6** than for **5**, and purification of **6** by chromatography was often more successful.





Scheme 2

The diethers **6** can be considered as diphenols with free *o*-positions, and their cyclization with *bis*-bromomethylated phenols to the double calixarenes **7–9** is formally analogous to the synthesis of *p*-bridged calix[4]arenes from α,ω-(4-hydroxyphenyl) alkanes [18]. Unfortunately, the optimum conditions for this synthesis, namely $TiCl_4$ in dioxane, which most probably take advantage of the prearrangement of three phenolic units by a Ti template [19], were not successful in the present case. The undesired interaction of Ti with the phenolic functions of the original calix[4]arene, leading eventually even to ether cleavage, is a likely explanation.

The cyclization proceeded smoothly under dilution conditions in boiling acetic acid in the presence of $Zn(OOCCH_3)_2$. Most probably, Zn^{2+} acts as *Lewis* acid (and *Friedel-Crafts* catalyst), whereas the acetate, as the strongest *Brönstedt* base possible in this solvent, neutralizes the HBr formed during the reaction.

Optimization of the reaction conditions performed for the synthesis of **8b** led to a concentration of 0.0055 *M* for **6b**. Accordingly, nearly all further reactions were conducted under similar conditions using a ratio of **6**: *bis*(bromomethyl)phenol: $Zn(CH_3COO)_2$ = 1:2:2. The reaction time (in the range of 30–40 h) was adjusted according to an intermediate analysis of the reaction mixture by TLC.

The pure products could easily be isolated by flash chromatography in yields of 3–10% for the double calix[4]arenes **7b–d**, **8b–d**, and **9b–d** (n = 3–5), which is reasonable considering the sophisticated structure. The lower yield of **9b** (1.6%) might not yet be significant, but the yield drops to 0.6–0.9% for **7–9a**, obviously caused by the short chains connecting the two calixarene moieties.

There is no clear indication that the yield of double calix[4]arene would depend on the kind of the alkyl residue *R* in the *bis*bromomethylated phenol. All attempts to obtain double calixarenes using 3,5-*bis*(bromomethyl)-4-hydroxybenzoic acid or its ethyl ester *R* = COOH or $COOC_2H_5$) failed, however.

Spectra

Due to their macrotricyclic structure all double calix[4]arenes **7–9** show very simple mass spectra. The molecular ion is found with a relative abundance of 100% in all cases, and little fragmentation is observed.

For a chain length of n = 3–5 the ^{1}H NMR spectra of compounds **7–9** are not only in agreement with the structure of double calixarene but also with the cone conformation of both calix[4]arene parts (although by the type of connection only the 1,2-alternate conformation is excluded). They show two singlets for the *t*-butyl groups of the original calix[4]arene (**I**) and, in the case of **7** and **8**, one singlet for the *p*-substituents of the unbridged phenolic units in the newly formed calix[4]arene (**II**). The aromatic protons appear as four singlets of equal intensity and the OH-protons as two singlets with a ratio of 2:1. Chemical shifts above 10 ppm for the stronger OH singlet (for 4 protons) indicate an undisturbed cyclic array of intramolecular hydrogen bonds in **II** for **c** and **d**, whereas for **b** (n = 3) a weakening of the OH···OH bonds due to a distortion of the 'perfect' cone conformation can be deduced from chemical shift arguments around (*ca.* 9.3 ppm). The singlet for the two 'isolated' OH groups of **I** appearing between 6.1 and 7.4 ppm (8.1 ppm for **9b** in benzene) is a result of weaker hydrogen bonding to the adjacent ether oxygens and shielding by the phenolic units of **II**.

The most interesting region in the ^{1}H NMR spectra of double calixarenes is that of the benzylic methylene protons of the two calix[4]arene systems. All

compounds with chains containing three and more carbon atoms (**7b–d**, **8b–d**, **9b–d**) show two pairs of doublets in the ^{1}H NMR spectra which are assigned to the calix[4]arene systems **I** and **II** (compare Fig. 1). In all cases, there are evident differences in the coupling constants ($\Delta J \approx 1$ Hz). To obtain a more detailed insight into the conformation of the double calixarene **8b** ($R = C(CH_3)_3$, $n = 3$), we performed nuclear *Overhauser* effect (NOE) experiments. Fig. 1 shows the NOE peak intensities measured with respect to the hydroxy protons of the newly formed calix[4]arene **II** and of the original calix[4]arene **I**. On that basis it is possible to assume that the coupling constants for the protons of methylene bridges are greater for calix[4]arene **II** than for calix[4]arene **I**; this may be explained by a greater deformation of the original calixarene due to the missing complete cyclic array of hydrogen bonds. As shown by *Sternhel* [20], an increasing angle between C–H bonds and π orbitals of aromatic rings leads to a decrease of the coupling constant of vicinal protons.

In contrast to **7b–d**, **8b–d**, and **9b–d**, the ^{1}H NMR spectra of compounds **7–9a** are not consistent with an effective C_{2v} symmetry of the molecule but rather with a C_s symmetrical conformation. This follows for instance from two signals for the OH groups of calixarene **I** and, in the case of **9a**, from three *t*-butyl signals in the ratio of 1:2:2.

Although the exact conformation of the double calixarenes **7–9a** cannot be deduced from their rather complicated NMR spectra, it can be stated that for the short bridge ($n = 2$) a distortion of both calix[4]arene parts takes place. The

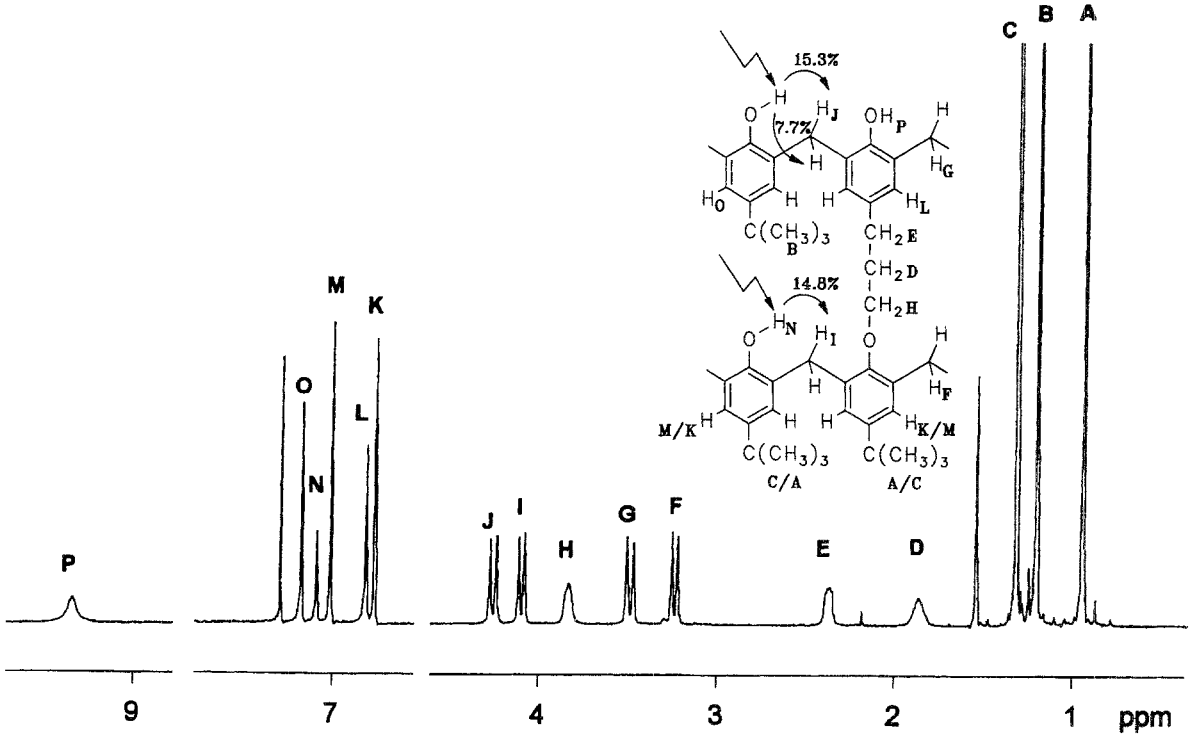


Fig. 1. ^{1}H NMR spectrum (200 MHz, $CDCl_3$) of **8b**, showing peak assignments and NOEs

tendency to form a cyclic array of intramolecular hydrogen bonds in **II** probably makes this new calixarene stiff enough to induce a 'flattened partial cone' conformation in **I**, similar to calix-spherands where two opposite oxygens are bridged by the rigid terphenyl unit [21]. In this conformation, one of the phenolic units of **I** is bent with its OH group into and with its *t*-butyl group out of the cavity. Furthermore, one of the two calixarenes may be inclined relative to the other (compare the X-ray structure of **8c**), thus avoiding an eclipsed conformation for the two CH_2 groups of the bridges.

Single Crystal X-Ray Analysis

The molecular conformation of **8c** is shown in Fig. 2, indicating also the numbering scheme (numbering of the phenolic units corresponds to the number of their oxygen atoms). Both calix[4]arene substructures of the molecule assume a cone conformation in agreement with the ^{1}H NMR data in solution. These cones are tilted towards each other. The angle between their mean planes, defined by the four bridging methylene carbon atoms, is 41.4°. The shape of the cone or calix may be described by the inclination of the phenyl rings with respect to these mean planes. The corresponding dihedral angles are 123.3, 134.3, 115.3, and 127.4° (from 1 to 4) in the newly formed calixarene (calix **II**) as compared to values of 123–126° found in calix[4]arenes with a fourfold axis [22]. This means that the

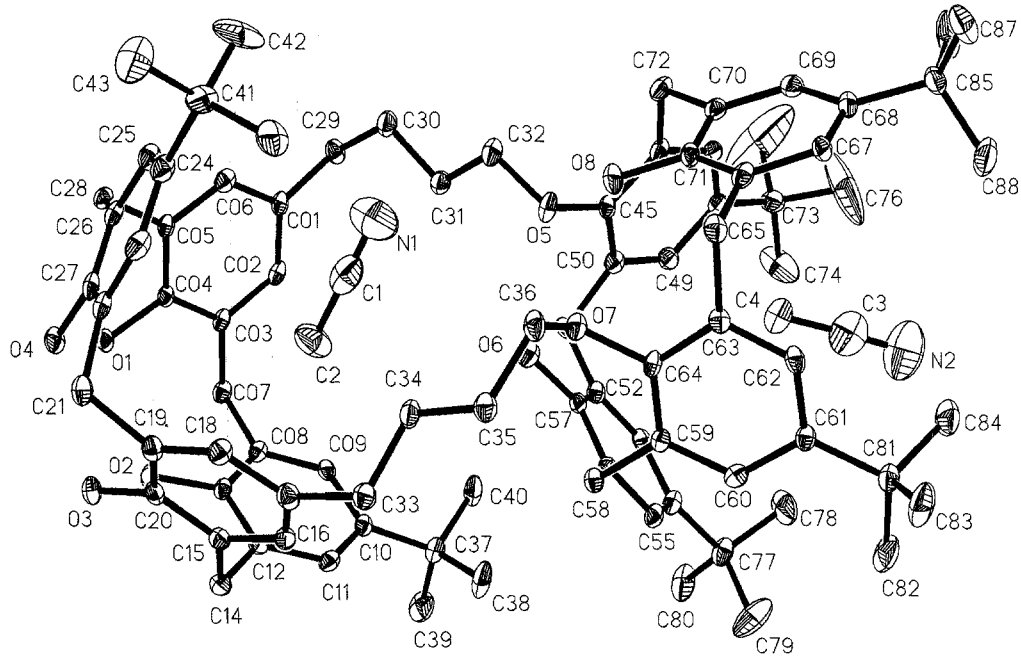


Fig. 2. Molecular conformation of **8c** and indication of the numbering scheme; thermal ellipsoids: 20% probability level; intramolecular O-O-distances (Å): O1-O2 = 2.64, O2-O3 = 2.65, O3-O4 = 2.68, O4-O1 = 2.67; selected torsion angles (°): C01-C29-C30-C31 = 71.5(7), C29-C30-C31-C32 = −177.9(5), C30-C31-C32-O5 = −178.0(5), C17-C33-C34-C35 = 173.6 (5), C33-C34-C35-C36 = 177.0(5), C34-C35-C36-O7 = −72.0(6)

'unconnected' phenolic units 2 and 4 are slightly bent outwards in comparison to rings 1 and 3 which are connected *via* their *p*-position to the 'original' calixarene; these deformations, however, are not stronger than found also sometimes for single calix[4]arenes.

In the original calix (calix **I**), the dihedral angles (from 5 to 8) are 118.2, 120.7, 109.4, and 126.7° with the phenol ether units 5 and 7 being slightly bent towards the cavity, but again these deformations are less than those often found in 1,3-diether derivatives of calix[4]arenes where the ether units tend to be nearly parallel and perpendicular to the mean plane [22]. The average of these dihedral angles, 125.1° *vs* 118.8°, shows that calix **II** is slightly wider or "more open" than calix **I**.

Both cavities are ready, however, to host an acetonitrile molecule with the methyl group pointing into the cavity as found in other cases [23]. This inclusion of acetonitrile, which favors a fourfold symmetry if possible [23], may at the other hand be the reason for the comparatively small distortion of calix **I**. The orientation of the included acetonitrile is nearly parallel (3.6°) to the main axis (perpendicular to the main plane) of calix **I**, whereas it assumes an angle of 43.6° in the cavity of calix **II**, reflecting again the fact that this cavity is larger.

The O···O distances of oxygens O1 to O4 (2.64–2.67 Å) are in agreement with strong intramolecular hydrogen bonds in calix **II**. These distances are longer (2.81–3.06 Å) for oxygens O5 to O8 in calix **I** where only weaker hydrogen bonds between OH groups and the adjacent ether oxygens are possible. The torsion angles around the C–C bonds of the chains connecting the two calixarenes reveal a relaxed arrangement with two *anti* conformations per chain (Fig. 2).

In the crystal lattice the molecules of **8c** are arranged around inversion centers between the planes of the hydroxyl groups O1 to O4 as shown in Fig. 3. This leads to short intermolecular O···O distances like O1···O1A = 2.92 Å which would be compatible with weak intermolecular O–H···O hydrogen bonds. The linear arrangement of the respective oxygen and carbon atoms (*e.g.* O1–O1a–C04 = 176.4°) shows, however, that there cannot be any intermolecular hydrogen bonding. Voids in the crystal lattice are occupied by chloroform molecules. It should be noted that chloroform is exclusively found between the molecules, whereas acetonitrile is exclusively found in both cavities. This is in agreement with the fact that crystal structures of calix[4]arene derivatives with included chloroform are rare [22].

Experimental

^{1}H NMR spectra were recorded on a Bruker AC 200 (200 MHz) or AC 400 (400 MHz) spectrometer using $2 \cdot 10^{-3} M$ solutions in $CDCl_3$. Chemical shifts are reported as δ values in ppm relative to $(CH_3)_4Si$ as internal standard. EI (70 eV) and FD mass spectra were recorded on a CH 7A Varian MAT instrument.

Melting points reported are uncorrected. Values higher than 200°C were determined in sealed capillary tubes under argon. All compounds were checked for purity by thinlayer chromatography on silica gel plates of 0.25 mm thickness (E. Merck, 70–230 mesh ASTM). Silica gel (E. Merck Silica Gel 60, 40–63 mm) was used for column chromatography. All solvents were purified by standard procedures. All solutions were dried over Na_2SO_4.

Most starting materials were purchased from Merck; methyl (4-hydroxyphenyl)acetate (**1a**) was obtained from Acros Chimica, and 3-(4-hydroxyphenyl)-propionic acid (**1b**) from Fluka.

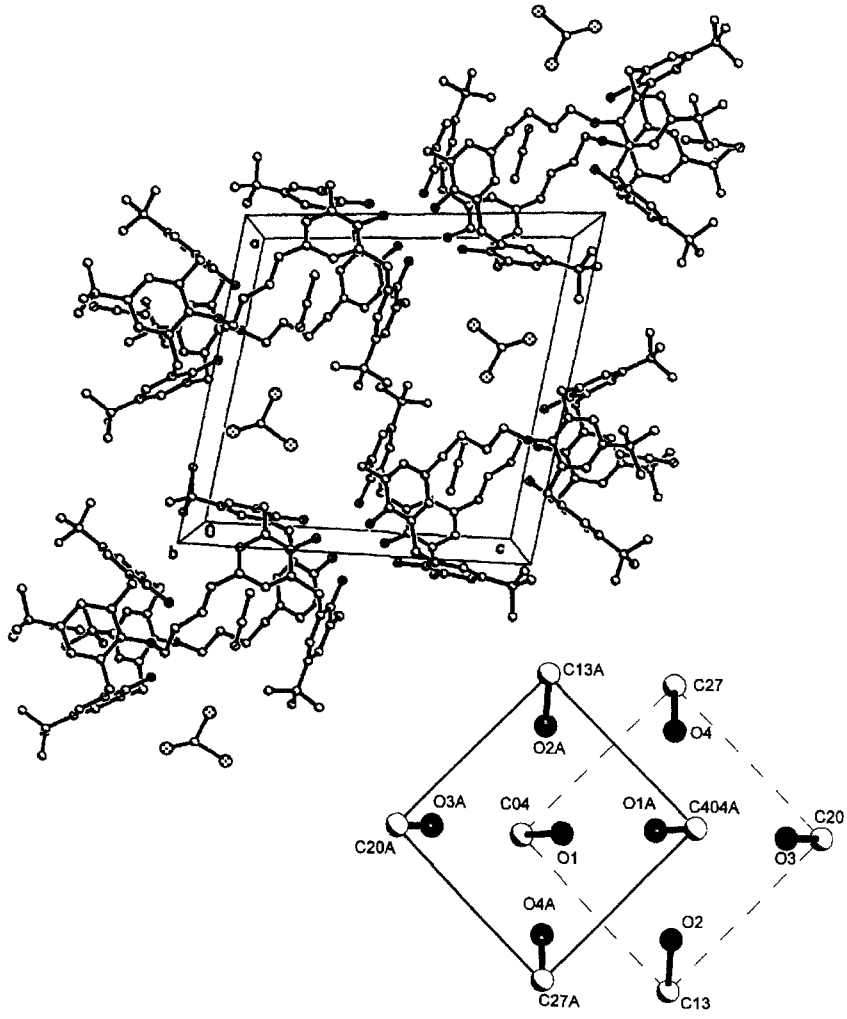


Fig. 3. Crystal packing of **8c** showing the inclusion of $CHCl_3$; the insert describes the arrangement around the inversion center seen perpendicular to the plane of four oxygens; intermolecular O-O-distances (Å): O1-O1A = 2.92, O1-O2A = 3.16, O1-O4A = 3.09; "intermolecular" angles (°): O1A-O1-C04 = 176, O2A-O1-C04 = 131, C13A-O2A-O1 = 171

4-(4-Methoxyphenyl)-4-oxobutanoic acid and 5-(4-methoxyphenyl)-5-oxo-pentanoic acid were prepared by *Friedel-Crafts* acylation of anisole with succinic or glutaric anhydrides, respectively [24]. Subsequent *Clemmensen* reduction using the modification described by *Martin* [25] and cleavage of the methoxy groups [26] led to 4-(4-hydroxyphenyl)butanoic acid (**1c**) and 5-(4-hydroxyphenyl)pentanoic acid (**1d**), respectively. *p-tert*-Butylcalix[4]arene was synthesized according to a literature procedure [27].

Methyl (4-benzyloxyphenyl)acetate (**2a**)

A mixture of **1a** (4.47 g, 26.9 mmol), K_2CO_3 (3.71 g, 26.9 mmol), benzyl bromide (3.19 g, 26.9 mmol), and 50 ml of dry acetone was refluxed under argon for 17 h. After evaporation of the solvent, the residue was taken up in 20 ml of $CHCl_3$, washed twice with water and subsequently with brine, dried,

and evaporated. Hexane (5 ml) was added to the remaining oil, and the mixture was left in a refrigerator for crystallization. The crude product was finally purified by recrystallization from $CHCl_3$/hexane to give 4.9 g (71%) of pure **2a**.

M.p.: 61–62 °C; ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 3.55$ (s, 2H, $ArCH_2CO$), 3.67 (s, 3H, $COCH_3$), 5.03 (s, 2H, OCH_2Ar), 6.89–7.39 (m, 9H, ArH) ppm; MS: $m/z = 256.3$ (M^+); $C_{16}H_{16}O_3$ (256.3); calcd.: C 74.98, H 6.29; found: C 74.37, H 6.10.

3-(4-Benzyloxyphenyl)propionic acid (**2b**)

A solution of benzyl bromide (14.2 ml, 0.12 mol) in 30 ml of ethanol was added dropwise to a mixture of **1b** (20.0 g, 0.12 mmol), 360 ml of ethanol (96%), and 240 ml of 1*M* NaOH. The reaction mixture was stirred for 30 min and then left overnight. The resulting solution was dropped into 600 g of ice water, and the *pH* value was adjusted to 2 by addition of conc. HCl. The white precipitate was filtered, washed three times with 100 ml portions of cold water, dried, and recrystallized from benzene/petroleum ether to give 23.8 g (77%) of **2b** as white crystals.

M.p.: 118–119 °C (Ref. [28]: 118–120 °C); ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 2.42$ (t, $J = 7.8$ Hz, 2H, $ArCH_2$), 2.65 (t, $J = 6.2$ Hz, 2H, CH_2COOH), 5.00 (s, 2H, OCH_2Ar), 6.90–7.15 (m, 4H, Ar), 7.28–7.44 (m, 6H, ArH and COOH) ppm; MS: $m/z = 257.4$ (M^+); $C_{16}H_{16}O_3$ (256.3); calcd.: C 74.98, H 6.29; found: C 74.65, H 6.62.

4-(4-Benzyloxyphenyl)butanoic acid (**2c**)

2c was prepared as described for **2b**. Starting with 19.9 g (0.11 mol) of **1c**, 21.4 g (72%) of **3c** were obtained after recrystallization from toluene/petroleum ether as white crystals.

M.p.: 106–107 °C; ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 1.89$–2.00 (m, 2H, CH_2), 2.37 (t, $J = 7.4$ Hz, 2H, $ArCH_2$), 2.61 (t, $J = 7.8$ Hz, 2H, CH_2COOH), 5.04 (s, 2H, OCH_2Ar), 6.86–7.11 (m, 4H, ArH), 7.28–7.46 (m, 6H, ArH and COOH) ppm; MS: $m/z = 270.5$ (M^+); $C_{17}H_{18}O_3$ (270.3); calcd.: C 75.53, H 6.71; found: C, 75.80, H, 6.83.

5-(4-Benzyloxyphenyl)pentanoic acid (**2d**)

2d was prepared as described for **2b**. Starting with 5.0 g (25.8 mmol) of **1d**, 6.32 g (86%) of **2d** were obtained after recrystallization from toluene/petroleum ether as white crystals.

M.p.: 102–103 °C; ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 1.55$–1.75 (m, 4H, $CH_2(CH_2)_2CH_2$), 230–2.37 (m, 2H, $ArCH_2$), 2.53–2.63 (m, 2H, CH_2CO), 5.03 (s, 2H, OCH_2Ar), 6.95–7.90 (m, 9H, ArH) ppm; MS: $m/z = 284.3$ (M^+); $C_{18}H_{20}O_3$ (284.4); calcd.: C 76.03, H 7.09; found: C 76.10, H 7.15.

2-(4-Benzyloxyphenyl)ethanol (**3a**)

A solution of **2a** (14.1 g, 54.6 mmol) in 320 ml of ether was added dropwise during 30 min to a suspension of $LiAlH_4$ (5.18 g, 0.136 mol) in 150 ml of dry ether and refluxed for 4 h. After cooling, the excess of $LiAlH_4$ was decomposed by water and the resulting $Al(OH)_3$ dissolved in diluted sulfuric acid. The organic layer was separated, and the aqueous phase was extracted with ether (3 times 30 ml). The combined organic phases were washed with brine, dried, and the solvent was evaporated. The residue was purified by recrystallization from ethanol/water to give 11.6 g (93%) of **3a** as white crystals.

M.p.: 87.5–88 °C; ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 1.38$ (t, $J = 5.8$ Hz, 1H, OH), 2.80 (t, $J = 6.5$ Hz, 2H, CH_2Ar), 3.77–3.87 (m, 2H, CH_2OH), 5.05 (s, 2H, OCH_2Ar), 6.93, 7.16 (2 × d, $J = 8.6$ Hz each, ArH), 7.33–7.45 (m, 5H, ArH) ppm; MS: $m/z = 228.2$ (M^+); $C_{15}H_{16}O_2$ (228.3); calcd.: C 78.92, H 7.06; found: C 78.85, H 7.11.

3-(4-Benzyloxyphenyl)propanol (**3b**)

3b was prepared in a manner similar to that described for **3a**. From 10.0 g (0.039 mol) of **2b** and 4.0 g (0.105 mol) of $LiAlH_4$, 8.6 g (90%) of **36** were obtained as white crystals after recrystallization from ethanol/water.

M.p.: 62–63°C; ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 1.33$ (s, 1H, OH), 1.79–1.93 (m, 2H, $CH_2CH_2CH_2$), 2.65 (t, $J = 7.8$ Hz, 2H, CH_2Ar), 3.66 (t, $J = 6.3$ Hz, 2H, CH_2OH), 5.04 (s, 2H, OCH_2Ar), 6.87–7.14 (m, 4H, ArH), 7.31–7.46 (m, 5H, ArH) ppm; MS: $m/z = 242.4$ (M^+); $C_{16}H_{18}O_2$ (242.3); calcd.: C 79.31, H 7.49; found: C 79.37, H 7.57.

4-(4-Benzyloxyphenyl)butanol (**3c**)

3c was prepared in a manner similar to that described for **3a**. From 10.8 g (40 mmol) of **2c** and 4.1 g (0.108 mol) of $LiAlH_4$, 9.5 g (93%) of **3c** were obtained as white crystals after recrystallization from ethanol/water.

M.p.: 57–58°C; ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 1.41$ (br, 1H, OH), 1.56–1.74 (m, 4H, $CH_2(CH_2)_2CH_2$), 2.59 (t, $J = 7.8$ Hz, 2H, CH_2OH), 3.65 (t, $J = 6.2$ Hz, 2H, CH_2Ar), 5.04 (s, 2H, OCH_2Ar), 6.88–7.12 (m, 4H, ArH), 7.28–7.45 (m, 5H, ArH) ppm; MS: $m/z = 256.4$ (M^+); $C_{17}H_{20}O_2$ (256.3); calcd.: C 79.65, H 7.80; found: C 79.80, H 7.91.

5-(4-Benzyloxyphenyl)pentanol (**3d**)

3d was prepared in a manner similar to that described for **3a**. From 10.1 g (35.2 mmol) of **3d** and 3.6 g (94.5 mmol) of $LiAlH_4$, 9.5 g (93%) of **3d** were obtained as white crystals after recrystallization from ethanol/water.

M.p.: 67–68°C; ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 1.24$ (br, 1H, OH), 1.32–1.70 (m, 6H, $CH_2(CH_2)_3CH_2$), 2.55 (t, $J = 7.8$ Hz, 2H, $ArCH_2$), 3.62 (t, $J = 6.6$ Hz, 2H, CH_2CH_2O), 5.03 (s, 2H, OCH_2Ar), 6.87–7.44 (m, 9H, ArH) ppm; MS: $m/z = 270.3$ (M^+); $C_{18}H_{22}O_2$ (270.4); calcd.: C 79.96, H 8.20; found: C 79.79, H 8.20.

2-(4-Benzyloxyphenyl)ethyl tosylate (**4a**)

12.2 g (52.6 mmol) of **3a** and 10.1 g (52.6 mmol) of tosyl chloride were dissolved in 25 ml of dry chloroform, and dry pyridine (8.6 ml, 58.8 mmol) was added dropwise at 0 ± 3°C. The reaction mixture was stirred at this temperature for 3 h and kept at 0°C overnight. Finally, the resulting mixture was slowly dropped into ice (20 g) / aqueous HCl (9 ml of conc. HCl). The organic layer was separated, washed with water (3 times 25 ml), dried, and concentrated to give a yellow oil which crystallized on cooling. The crude product was recrystallized from $CHCl_3$/hexane to yield 18.1 g (90%) of **4a** as white crystals.

M.p.: 90–91°C; ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 2.41$ (s, 3H, CH_3), 2.85 (t, $J = 7.2$ Hz, 2H, CH_2CH_2Ar), 4.14 (t, $J = 7.2$ Hz, 2H, CH_2CH_2O), 5.02 (s, 2H, OCH_2Ar), 6.82–7.69 (m, 13H, ArH) ppm; MS: $m/z = 382.2$ (M^+); $C_{22}H_{22}O_4S$ (382.5); calcd.: C 69.09, H 5.80, S 8.38; found: C 68.93, H 5.84, S 8.64.

3-(4-Benzyloxyphenyl)propyl tosylate (**4b**)

4b was prepared as described for **4a**. From 8.56 g (35.3 mmol) of **3b** and 6.74 g (35.3 mmol) of tosyl chloride, 9.1 g (78%) of **4b** were obtained as white crystals after recrystallization from $CHCl_3$/ petroleum ether.

M.p.: 61–62°C; ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 1.84$–1.95 (m, 2H, $CH_2CH_2CH_2$), 2.45 (s, 3H, CH_3), 2.57 (t, $J = 7.8$ Hz, 2H, CH_2CH_2Ar), 4.01 (t, $J = 6.2$ Hz, 2H, CH_2CH_2O), 5.02 (s, 2H,

OCH_2Ar), 6.82–6.99 (m, 4H, ArH), 7.31–7.8 (m, 9H, ArH) ppm; MS: $m/z = 396.1$ (M^+); $C_{23}H_{24}O_4S$ (396.5); calcd.: C 69.67, H 6.10, S 8.09; found: C 69.69, H 6.11, S 8.05.

4-(4-Benzyloxyphenyl)butyl tosylate (**4c**)

4c was prepared as described for **4a**. From 9.12 g (35.6 mmol) of **3c** and 6.79 g (35.6 mmol) of tosyl chloride, 13.5 g (93%) of **4c** were obtained as white crystals after recrystallization from $CHCl_3$/petroleum ether.

M.p.: 45.5–46.5°C; ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 1.56$–1.64 (m, 4H, $CH_2(CH_2)_2CH_2$) 2.43 (s, 3H, CH_3), 2.48 (t, $J = 7.8$ Hz, 2H, CH_2CH_2Ar), 4.02 (t, $J = 6.2$ Hz, 2H, CH_2CH_2O), 5.03 (s, 2H, OCH_2Ar), 6.85–7.03 (m, 4H, ArH), 7.31–7.79 (m, 9H, ArH) ppm; MS: $m/z = 410.9$ (M^+); $C_{24}H_{26}O_4S$ (410.5); calcd.: C 70.22, H 6.38, S 7.81; found: C 70.90, H 6.64, S 7.79.

5-(4-Benzyloxyphenyl)pentyl tosylate (**4d**)

4d was prepared as described for **4a**. From 12.0 g (52.6 mmol) of **3d** and 10.1 g (52.6 mmol) of tosyl chloride, 18.1 g (90%) of **4d** were obtained as white crystals after recrystallization from $CHCl_3$/petroleum ether.

M.p.: 69–70°C; ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 1.27$–1.69 (m, 6H, $CH_2(CH_2)_3CH_2$), 2.43 (s, 3H, CH_3), 2.49 (t, $J = 7.3$ Hz, 2H, CH_2CH_2O), 4.00 (t, $J = 6.4$ Hz, 2H, CH_2CH_2Ar), 5.03 (s, 2H, OCH_2Ar), 6.85–7.79 (m, 13H, ArH) ppm; MS: $m/z = 424.3$ (M^+); $C_{25}H_{28}O_4S$ (424.6); calcd.: C 70.73, H 6.65, S 7.55; found: C 70.69, H 6.67, S 7.59.

25,27-Bis(2-(4-benzyloxyphenyl)ethoxy)-26,28-dihydroxy-p-tert-butylcalix[4]arene (**5a**)

A mixture of 13.0 g (17.6 mmol) of the *p-tert*-butylcalix[4]arene-toluene complex, 13.8 g (36.0 mmol) of **4a**, 2.76 g (19.3 mmol) of K_2CO_3, and 550 ml of dry CH_3CN was refluxed with stirring under argon. After 40 h, the solvent was evaporated. CH_2Cl_2 (100 ml) was added to the residue, and the resulting suspension was washed with water (60 ml), diluted HCl (twice 30 ml), brine (60 ml), dried, and concentrated to dryness. The brown product was purified using a short chromatographic column (diameter: 30 mm, height: 10 cm, eluent: $CHCl_3$). The crude white product was recrystallized from acetone/methanol to yield 12.17 g (65%) of **5a** as white crystals.

M.p.: 98.5–100°C; ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 0.94$, 1.29 (2× s, 18H each, $C(CH_3)_3$), 3.30 (t, $J = 7.5$ Hz, 4H, $ArCH_2$), 3.32, 4.25 (2× d, $J = 13.0$ Hz, 4H each, $ArCH_2Ar$), 4.16 (t, $J = 6.1$ Hz, 4H, OCH_2CH_2), 4.99 (s, 4H, OCH_2Ar), 6.77–7.41 (m, 28H, ArH, OH) ppm; MS: $m/z = 1069.8$ (M^+); $C_{74}H_{84}O_6$ (1069.5); calcd.: C 83.11, H 7.92; found: C 82.81, H 7.91.

25,27-Bis(3-(4-benzyloxyphenyl)propoxy)-26,28-dihydroxy-p-tert-butylcalix[4]arene (**5b**)

5b was prepared as described for **5a**. 4.0 g (5.4 mmol) of the *p-tert*-butylcalix[4]arene-toluene complex, 4.8 g (12.1 mmol) of **4b**, 0.82 g (5.92 mmol) of K_2CO_3, and 180 ml of dry CH_3CN were refluxed for 40 h with stirring under argon. After recrystallization from acetone, **5b** (5.27 g, 89%) was obtained as white crystals.

M.p.: 194–197°C; ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 0.99$, 1.28 (2 × s, 18H each, $C(CH_3)_3$), 2.25–2.32 (m, 4H, $CH_2CH_2CH_2$), 2.94 (t, $J = 7.1$ Hz, 4H, $ArCH_2CH_2$), 3.30, 4.29 (2 × d, $J = 12.9$ Hz, 4H each, $ArCH_2Ar$), 3.97 (t, $J = 6.1$ Hz, 4H, OCH_2CH_2), 4.99 (s, 4H, OCH_2Ar), 6.84–7.43 (m, 26H, ArH), 7.90 (s, 2H, OH) ppm; MS: $m/z = 1099.3$ (M^+); $C_{76}H_{88}O_6$ (1097.5); calcd.: C 83.17, H 8.08; found: C 82.78, H 8.04.

25,27-Bis(4-(4-benzyloxyphenyl)butoxy)-26,28-dihydroxy-p-tert-butylcalix[4]arene (**5c**)

5c was prepared as described for **5a**. 7.0 g (9.45 mmol) of the *p-tert*-butyl-calix[4]arene-toluene complex, 8.7 g (21.2 mmol) of **4c**, 1.43 g (10.4 mmol) of K_2CO_3, and 210 ml of dry CH_3CN were refluxed for 110 h. After recrystallization from acetone, white crystals of **5c** (7.83 g, 70%) were obtained.

M.p.: 90–91°C; ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 0.99$, 1.29 (2 × s, 18H each, $C(CH_3)_3$), 1.97–1.98 (m, 8H, $CH_2(CH_2)_2CH_2$), 2.65 (t, $J = 7.1$ Hz, 4H, $ArCH_2CH_2$), 3.30, 4.30 (2 × d, $J = 12.9$, 4H each, $ArCH_2Ar$), 3.95 (t, $J = 6.2$ Hz, 4H, OCH_2CH_2), 5.01 (s, 4H, OCH_2Ar), 6.84–7.45 (m, 26H, ArH), 7.77 (s, 2H, OH) ppm; MS: $m/z = 1125.5$ (M^+); $C_{78}H_{92}O_6$ (1125.6); calcd.: C 83.23, H 8.24; found: C 83.06, H 7.97.

25,27-Bis(5-(4-benzyloxyphenyl)pentoxy)-28,28-dihydroxy-p-tert-butylcalix[4]arene (**5d**)

5d was prepared as described for **5a**. 15.0 g (20.3 mmol) of the *p-tert*-butyl-calix[4]-arene-toluene complex, 17.8 g (41.5 mmol) of **4d**, 3.08 g (22.3 mmol) of K_2CO_3, and 400 ml of dry CH_3CN were refluxed for 42 h. After recrystallization from acetone/methanol, **5d** (16.1 g, 89%) was obtained as white crystals.

M.p.: 145–147°C; ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 0.99$, 1.27 (2 × s, 18H each, $C(CH_3)_3$), 1.64–1.75 (m, 8H, $CH_2(CH_2)_2CH_2$), 1.95–2.10 (br, 4H, $ArCH_2CH_2$), 2.57 (t, $J = 6.6$ Hz, 4H $ArCH_2CH_2$), 3.20, 3.77 (2 × d, $J = 12.9$ Hz, 4H each, $ArCH_2Ar$), 3.92 (t, $J = 6.5$ Hz, 4H, OCH_2CH_2), 5.0 (s, 4H, OCH_2Ar), 6.75–7.45 (m, 26H, ArH), 7.75 (s, 2H, OH) ppm; MS: $m/z = 1152.6$ (M^+); $C_{80}H_{96}O_6$ (1153.6); calcd.: C 83.29, H 8.39; found: C 83.30, H 8.37.

25,27-Bis[2-(4-hydroxyphenyl)ethoxy]-26,28-dihydroxy-p-tert-butylcalix[4]arene (**6a**)

A suspension of 8.3 g of Pd/C (5%) and 8.32 g (9.36 mmol) of **5a** in 200 ml of acetic acid was vigorously stirred under hydrogen at normal pressure. When the hydrogen up-take was complete (about 7 h), the catalyst was filtered off and washed with 20 ml of acetic acid. The combined solvent were evaporated, and the crude product was purified by recrystallization from acetic acid to give 7.82 g (94%) of pure **6a** as a white powder.

M.p.: 90–91°C; ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 0.92$, 1.27 (2 × s, 18H each, $C(CH_3)_3$), 3.20–3.52 (m, 4H, $ArCH_2$ and 4H $ArCH_2Ar$), 4.12 (t, $J = 7.4$ Hz, 4H, OCH_2), 4.30 (d, $J = 13.0$ Hz, 4H, $ArCH_2Ar$), 6.73–7.31 (m, 20H, ArH, OH) ppm; MS: $m/z = 887.5$ (M^+); $C_{60}H_{72}O_6$ (889.2); calcd.: C 81.04, H 8.16; found: C 80.78, H 8.20.

25,27-Bis(3-(4-hydroxyphenyl)propoxy)-26,28-dihydroxy-p-tert-butylcalix[4]arene (**6b**)

5d was prepared as described for **6a**, but after evaporation of the acetic acid the residue was dissolved in CH_2Cl_2 (50 ml), washed with aqueous $NaHCO_3$ (twice 10 ml), brine (10 ml), and dried. After evaporation, the crude product was purified using a chromatographic column diameter: 50 mm, height: 7 cm, eluent: $CHCl_3$/diethyl ether (50:1). Thus, from 2.6 g (2.37 mmol) of **5b**, 1.99 g (92%) of **6b** were obtained as amorphous product.

M.p.: 111–120°C; ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 0.98$, 1.28 (2 × s, 18H each, $C(CH_3)_3$), 2.23–2.28 (m, 4H, $CH_2CH_2CH_2$), 2.83 (t, $J = 8.3$ Hz, 4H, $ArCH_2$), 3.30, 4.30 (2 × d, $J = 13.0$ Hz, 4H each, $ArCH_2Ar$), 3.96 (t, $J = 6.3$ Hz, 4H, OCH_2), 5.5 (br, 2H, OH), 6.68–7.07 (m, 16H, ArH), 7.86 (s, 2H, OH) ppm; MS: $m/z = 917.3$ (M^+); $C_xH_yO_z$ $C_{62}H_{76}O_6$ (917.18).

25,27-Bis(4-(4-hydroxyphenyl)butoxy)-26,28-dihydroxy-p-tert-butylcalix[4]arene (**6c**)

6c was prepared described for **6b**. From 5.11 g (4.54 mmol) of **5c**, 3.64 g (86%) of **6c** were obtained after chromatographic purification.

M.p.: 97–105°C; ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 0.98$, 1.28 (2 × s, 18H each, $C(CH_3)_3$), 1.89–1.94 (m, 8H, $CH_2(CH_2)_2CH_2$), 2.59 (t, $J = 6.7$ Hz, 4H, $ArCH_2$), 3.30, 4.27 (2 × d, $J = 12.9$ Hz, 4H each, $ArCH_2Ar$), 3.93 (t, $J = 5.9$ Hz, 4H, OCH_2), 4.83 (s, 2H, OH) 6.71–7.09 (m, 16H, ArH), 7.70 (s, 2H, OH) ppm; MS: $m/z = 945.5$ (M^+); $C_xH_yO_z$ $C_{64}H_{80}O_6$ (945.23).

25,27-Bis(5-(4-hydroxyphenyl)pentoxy)-26,28-dihydroxy-p-tert-butylcalix[4]arene (**6d**)

6d was prepared as described for **6b**. From 7.0 g (6.07 mmol) of **5d**, 5.0 g (85%) of **6d** were obtained after chromatographic purification as a colorless, amorphous product.

M.p.: 77–85°C; ^{1}H NMR ($CDCl_3$, 200 MHz): $\delta = 0.98$, 1.27 (2 × s, 18H each, $C(CH_3)_3$), 1.60–1.70 (br, 8H, $CH_2(CH_2)_2CH_2$), 1.91–2.25 (br, 4H, CH_2CH_2O), 2.49–2.60 (br, 4H, $ArCH_2$), 3.30, 4.25 (2×d, $J = 12.9$ Hz, 4H each, $ArCH_2Ar$), 3.94 (t, $J = 6.4$ Hz, 4H, OCH_2), 4.78 (s, 2H, OH), 6.67–7.03 (m, 16H, ArH), 7.75 (s, 2H, OH) ppm; MS: $m/z = 972.4$ (M^+); $C_xH_yO_z$ $C_{66}H_{84}O_6$ (972.65).

General procedure for the preparation of double calix[4]arenes

Solutions of 1.64 mmol of 1,3-diether **6a–d** in 25 ml of glacial acetic acid and 3.28 mmol of *p*-substituted 2,6-*bis*(bromomethyl)phenol in 25 ml of glacial acetic acid were added simultaneously to a boiling solution of 0.6 g (3.28 mmol) of $Zn(CH_3COO)_2$ in 200 ml of acetic acid over a period of 12–15 h. The reaction mixture was additionally refluxed for 24 h. After the reaction was complete (the disappearance of the 2,6-*bis*(bromomethyl)phenol was monitored by TLC), the solvent was evaporated, and the dark-green or brown residue was dissolved in 100 ml of $CHCl_3$, washed with aqueous $NaHCO_3$, brine, and dried. The crude product thus obtained was separated and purified by flash chromatography with $CHCl_3$, hexane/CH_2Cl_2 (2/3), and in some cases additionally with hexane/diethyl ether (10/1). All double calixarenes were obtained after evaporation as white crystalline solids which did not melt until 400°C.

Double calix[4]arene **7a** *from* **6a** *and 2,6-bis(bromomethyl)-4-methylphenol*

Yield: 14 mg (0.7%); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 0.84$, 1.31, 1.32 (3 × s, 18H, 9H, 9H, $C(CH_3)_3$), 2.14 (s, 6H, CH_3), 2.63–2.68 (dd or 2×d, 2H, $(CH_2)_2$), 3.25, 3.32 (2 × d, $J = 13.3$ Hz, 2H each, $ArCH_2Ar$), 3.40 (d, $J = 13.8$ Hz, 3H, $ArCH_2Ar$), 3.4 (m, 2H, $(CH_2)_2$), 3.69 (d, $J = 13.6$ Hz, 1H, $ArCH_2Ar$), 4.03, 4.16 (2 × m, 2H, $(CH_2)_2$), 4.03, 4.18 (2 × d, $J = 13.6/14.3$ Hz, 1 H each, $ArCH_2Ar$), 4.21, 4.25, 4.42 (3 × d, $J = 13–14.1$ Hz, 2H each, $ArCH_2Ar$), 6.17 (s, 1H, OH), 6.64, 6.68 (2 × d, $J = 2.3$ Hz, 2H each, ArH), 6.77 (s, 1H, OH), 6.82 (s, 6H, ArH), 7.07, 7.09, 8.40 (3 × s, 2H each, ArH), 10.04 (s, 4H, OH) ppm; MS: $m/z = 1152.5$ [M+]; $C_{78}H_{88}O_8$ (1152.68).

Double calix[4]arene **8a** *from* **6a** *and 2,6-bis(bromomethyl)-4-tert-butylphenol*

Yield: 19 mg (0.9%); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 0.84$, 1.20, 1.31, 1.32 (4 × s, 18 H, 18H, 9H, 9H each, $C(CH_3)_3$), 2.64–2.70 (dd or 2 × d, 2H, $(CH_2)_2$), 3.25, 3.31, 3.45 (3 × d, $J = 13.3–13.8$ Hz, 2H each, $ArCH_2Ar$), 3.4 (m, 2H, $(CH_2)_2$), 3.47, 3.71 (2 × d, $j = 13.8/14.2$ Hz, 1H each, $ArCH_2Ar$), 4.0, 4.2 (2 × m, 2H each, $(CH_2)_2$), 4.05, 4.2, 4.24, 4.42 (4 × d, $J = 13.0–13.7$, 1H, 1H, 4H, 2H, $ArCH_2Ar$), 6.14 (s, 1H, OH), 6.65, 6.68 (2 × d, $J = 2.2$ Hz, 2H each, ArH) 6.75 (s, 1H, OH), 6.84 (br s, 2H, ArH), 7.00, 7.056 (2 × d, $J = 2.2$ Hz, 2H each, ArH), 7.08, 7.09, 8.43 (3 × s, 2H each, ArH), 10.12 (s, 4H, OH) ppm; MS: $m/z = 1236.9$ [M+]; $C_{84}H_{100}O_8$ (1236.77).

Double calix[4]arene **9a** *from* **6a** *and 2,6-bis(bromomethyl)-4-cyclohexylphenol*

Yield: 10 mg (0.6%); ^{1}H NMR (C_6D_6, 400 MHz); $\delta = 0.905$ (s, 18H, $C(CH_3)_3$), 1.12–1.3 (m, 12H, cyc-hex), 1.415, 1.464 (2 × s, 9H each, $C(CH_3)_3$), 1.55–1.73 (m, 8H, cyc-hex), 2.14–2.30 (m, 2H,

cyc-hex), 2.82–2.92 (m, 2H, $(CH_2)_2$), 3.32, 3.34, 3.38, 3.42 (4 × d, J = 13.5–14.1, 2H, 2H, 3H, 1H, $ArCH_2Ar$), 3.78–4.0 (m, 4H, $(CH_2)_2$, 2H, $ArCH_2Ar$), 4.10, 4.35, 4.43 (3 × d, J = 13.0–13.6 Hz, 1H, 2H, 1H, $ArCH_2Ar$), 4.35 (m, 2H, $(CH_2)_2$), 4.74 (d, J = 13.0 Hz, 2H, $ArCH_2Ar$), 6.51 (s, 2H, ArH), 6.81, 6.88, 6.92, 6.97 (4 × d, J = 2.0–2.3 Hz, 2H each, ArH), 7.20, 7.27 (2 × s, 2H each, ArH), 7.39, 7.75 (2 × br s, 1H each, OH), 8.58 (s, 2H, ArH), 10.2 (br s, 4H, OH) ppm; MS: m/z = 1288.5 (M^+); $C_{88}H_{104}O_8$ (1288.80).

Double calix[4]arene **7b** *from* **6b** *and 2,6-bis(bromomethyl)-4-methylphenol* [29]

Yield: 75 mg (3.9%); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.93, 1.26 (2 × s, 18H each, $C(CH_3)_3$), 1.88–1.93 (m, 4H, $CH_2CH_2CH_2$), 2.21 (s, 6H, CH_3), 2.35 (t, J = 9.0 Hz, 4H, $ArCH_2$), 3.24, 4.11 (2 × d, J = 13.0 Hz, 4H each, $ArCH_2Ar$), 3.40, 4.20 (2 × d, J = 14.1 Hz, 4H each, $ArCH_2Ar$), 3.79 (t, J = 8.4 Hz, 4H, OCH_2), 6.75, 6.77, 6.96, 6.99 (4 × s, 4H each, ArH), 7.22, 9.35 (2 × s, 2H, 4H, OH) ppm; MS: m/z = 1181.9 (M^+); $C_{80}H_{92}O_8$ (1180.71).

Double calix[4]arene **8a** *from* **6b** *and 2,6-bis(bromomethyl)-4-tert-butylphenol*

Yield: 203 mg (10%); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.89, 1.15, 1.26 (3 × s, 18H each, $C(CH_3)_3$), 1.85–1.90 (br, 4H, $CH_2CH_2CH_2$), 2.4–2.45 (br, 4H, $ArCH_2$), 3.19, 4.05 (2 × d, 4H each, J = 12.9 Hz, $ArCH_2Ar$), 3.44, 4.21 (2 × d, 4H each, J = 13.9 Hz, $ArCH_2Ar$), 3.75–3.82 (br, 4H, CH_2O), 6.72, 6.78, 6.96 (3 × s, 4H each, ArH), 7.04 (s, 2H, OH), 7.12 (s, 4H, ArH), 9.28 (s, 4H, OH); MS: m/z = 1264.5 (M^+); $C_{86}H_{104}O_8$ (1264.80).

Double calix[4]arene **9b** *from* **6b** *and 2,6-bis(bromomethyl)-4-cyclohexylphenol*

Yield: 31 mg (1.6%); ^{1}H NMR (C_6D_6, 400 MHz): δ = 0.78 (s, 18H, $C(CH_3)_3$), 1.33–1.36 (m, 4H, $CH_2CH_2CH_2$), 1.48 (s, 18H, $C(CH_3)_3$), 1.55–1.58 (m, 10H, cyc-hex), 1.78–1.85 (m, 10H, cyc-hex), 2.15–2.18 (br t, 4H, $ArCH_2$), 2.25–2.31 (m, 2H, cyc-hex), 3.32, 4.32 (2 × d, J = 13.7 Hz, 4H each, $ArCH_2Ar$), 3.38, 4.30 (2 × d, J = 12.5 Hz, 4H each, $ArCH_2Ar$), 3.59 (t, J = 7.4 Hz, 4H, CH_2O), 6.69, 6.85, 6.91, 7.23 (4 × s, 4H each, ArH), 8.11, 9.65 (2 × s, 2H, 4H, OH) ppm; MS: m/z = 1316.8 (M^+); $C_{90}H_{108}O_8$ (1316.84).

Double calix[4]arene **7c** *from* **6c** *and 2,6-bis(bromomethyl)-4-methylphenol*

Yield: 88 mg (4.5%); ^{1} H NMR ($CDCl_3$, 400 MHz): δ = 0.81, 1.29 (2 × s, 18H, $C(CH_3)_3$), 1.63–1.68, 1.79–1.85 (2 × m, 4H each, $CH_2(CH_2)_2CH_2$), 1.9 (s, 6H, CH_3), 2.60 (t, J = 6.2 Hz, 4H, $ArCH_2$), 3.20, 4.11 (2 × d, J = 13.1 Hz, 4H each, $ArCH_2Ar$), 3.42, 4.21 (2 × d, J = 13.8 Hz, 4H each, $ArCH_2Ar$), 3.85 (t, J = 7.5 Hz, 4H, CH_2O), 6.14 (s, 2H, OH), 6.57, 6.83, 6.90, 7.01 (4 × s, 4H each, ArH), 10.18 (s, 4H, OH) ppm; MS: m/z = 1209.9 (M^+); $C_{82}H_{92}O_8$ (1208.44).

Double calix[4]arene **8c** *from* **6c** *and 2,6-bis(bromomethyl)-4-tert-butylphenol*

Yield: 84 mg (3.9%); ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.80, 1.04, 1.30 (3 × s, 18H each, $C(CH_3)_3$), 1.62–1.67, 1.77–1.81 (2 × m, 4H each, $CH_2(CH_2)_2CH_2$, 2.55 (t, J = 6.5 Hz, 4H, $ArCH_2$), 3.16, 4.09 (2 × d, 4H each, J = 13.2 Hz, $ArCH_2Ar$), 3.47, 4.25 (2 × d, 4H each, J = 13.9 Hz, $ArCH_2Ar$), 3.85 (t, J = 7.0 Hz, 4H, CH_2O), 6.06 (s, 2H, OH), 6.55, 6.91, 6.98, 7.04 (4 × s, 4H each, ArH), 10.36 (s, 4H, OH); MS: m/z = 1292.5 (M^+); $C_{88}H_{108}O_8$ (1292.84).

Double calix[4]arene **9c** *from* **6c** *and 2,6-bis(bromomethyl)-4-cyclohexylphenol*

Yield: 72 mg (3.3%); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 0.93$, 1.26 (2 × s, 18H each, $C(CH_3)_3$), 1.26–1.37 (m, 4H, $CH_2(CH_2)_2CH_2$ and 10H, cyc-hex), 1.48–1.55 (br, 4H, $CH_2CH_2CH_2O$), 1.78–1.80 (m, 10H, cyc-hex), 2.31–2.39 (m, 2H, cyc-hex), 2.51 (t, $J = 6.5$ Hz, 4H, $ArCH_2$), 3.21, 4.19 (2 × d, $J = 12.9$ Hz, 4H each, $ArCH_2Ar$), 3.44, 4.20 (2 × d, $J = 13.9$ Hz, 4H each, $ArCH_2Ar$), 3.88 (t, $J = 7.0$ Hz, 4H, CH_2O), 6.75, 6.83, 6.90, 6.98 (4 × s, 4H each, ArH), 7.31, 10.05 (2 × s, 2H, 4H, OH) ppm; MS: $m/z = 1344.7$ (M^+); $C_{92}H_{112}O_8$ (1344.87).

Double calix[4]arene **7d** *from* **6d** *and 2,6-bis(bromomethyl)-4-methylphenol*

Yield: 82 mg (4.5%); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 0.94$, 1.25 (2 × s, 18H each, $C(CH_3)_3$), 1.26–1.32, 1.49–1.53, 1.82–1.89 (3 × m, 4H each, $CH_2(CH_2)_3CH_2$), 2.17 (s, 6H, CH_3), 2.47 (t, $J = 7.2$ Hz, 4H, $ArCH_2$), 3.22, 4.22 (2 × d, $J = 13.0$ Hz, 4H each, $ArCH_2Ar$), 3.42, 4.19 (2 × d, $J = 13.9$ Hz, 4H each, $ArCH_2Ar$), 3.91 (t, $J = 7.9$ Hz, 4H, CH_2O), 6.76, 6.84, 6.85, 6.98 (4 × s, 4H, ArH), 7.37, 10.18 (2 × s, 2H, 4H, OH); MS: $m/z = 1236.6$ (M^+); $C_{84}H_{100}O_8$ (1236.77).

Double-calix[4]arene **8d** *from* **6d** *and 2,6-bis(bromomethyl)-4-tert-butylphenol*

Yield: 123 mg (5.5%); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 0.95$, 1.23, 1.25 (3 × s, 18H, $C(CH_3)_3$), 1.23–1.28, 1.47–1.52, 1.77–1.81 (3 × m, 4H each, $CH_2(CH_2)_3CH_2$), 2.46 (t, $J = 7.1$ Hz, 4H, $ArCH_2$), 3.21, 4.18 (2 × d, $J = 12.9$ Hz, 4H each, $ArCH_2Ar$), 3.46, 4.24 (2 × d, $J = 13.9$ Hz, 4H each, $ArCH_2Ar$), 3.87 (t, $J = 7.6$ Hz, 4H, CH_2O), 6.77, 6.83, 6.98, 7.06 (4 × s, 4H each, ArH), 7.42, 10.14 (2 × s, 2H, 4H, OH); MS: $m/z = 1320.5$ (M^+); $C_{90}H_{112}O_8$ (1320.87).

Double calix[4]arene **9d** *from* **6d** *and 2,6-bis(bromomethyl)-4-cyclohexylphenol*

Yield: 96 mg (4.3%); ^{1}H NMR ($CDCl_3$, 400 MHz): $\delta = 0.80$ (s, 18H, $C(CH_3)_3$), 1.07–1.11 (m, 10H, cyc-hex), 1.24–1.28 (m, 4H, $CH_2CH_2CH_2CH_2CH_2$), 1.29 (s, 18H, $C(CH_3)_3$), 1.57–1.59 (br, 4H, $ArCH_2CH_2$), 1.70–1.74 (m, 10H, cyc-hex), 1.79–1.83 (m, 4H, OCH_2CH_2), 1.23–1.25 (m, 2H, cyc-hex), 2.57 (t, $J = 6.2$ Hz, 4H, $ArCH_2$), 3.15, 4.12 (2 × d, $J = 13.1$ Hz, 4H each, $ArCH_2Ar$), 3.46, 4.23 (2 × d, $J = 13.9$ Hz, 4H each, $ArCH_2Ar$), 3.80 (t, $J = 6.8$ Hz, 4H, CH_2O), 6.16 (s, 2H, OH), 6.54, 6.89, 6.91, 6.99 (4 × s, 4H each, ArH), 10.33 (s, 4H, OH); MS: $m/z = 1372.7$ (M^+); $C_{94}H_{116}O_8$ (1372.9).

X-Ray Analysis

Single crystals of **8c** were obtained by slow evaporation of a solution in acetonitrile/chloroform. Their X-ray analysis gave the following data: empirical formula: $C_{88}H_{108}O_8 \cdot 2CH_3CN \cdot 0.6CHCl_3$, $M_r = 1495.22$, triclinic, $P\bar{1}$, $a = 15.857(2)$ Å, $b = 17.143(3)$ Å, $c = 17.529(4)$ Å, $\alpha = 64.22(2)°$, $\beta = 80.424(5)°$, $\gamma = 88.92(2)°$, $V = 4223.3(13)$ Å^3, $Z = 2$, $D_c = 1.176$ Mg·m^{-3}.

A crystal of the dimensions $0.4 \cdot 0.3 \cdot 0.2$ mm^3 was sealed in a *Lindemann* glass capillary. 25 reflections were used to determine the cell parameters on a four circle computer controlled R3m/V SIEMENS apparatus which was also used for the measurements. $2\Theta/\Theta$-scan, Cu-K_α radiation, 8642 reflections ($\Theta_{min} = 1.83, \Theta_{max} = 50.08; -15 < h < 0, -17 < k < 16, -17 < 1 < 16$), 8477 of which were unique and were all used for the structure analysis. The phase problem was solved by direct methods [29], refinement of the structure parameters was performed by least-squares methods (minimization of $(F_o^2 - F_c^2)^2$ [30]; weighting scheme: $w = 1/(\sigma^2(F_o^2) + (0.1682 \cdot P)^2)$, $P = (\mathrm{Max}(F_o^2, 0) + 2 \cdot F_c^2)/3$, where σ is, according to the counting statistics, 971 parameters), the coordinates of the H atoms were calculated, $S = 1.012, R = 0.1128$ ($R = 0.0783$ for $Fo > 4\sigma$, 5516

reflections), $R_w = 0.2401$, minimum and maximum peak in the different map: -0.570 and 0.825 electrons/A^3. All calculations were done by a μ VAXII with the SHELXS-86 [31], the SHELXTL-PLUS [32], and the SHELXL-93 [30] programs.[2]

Acknowledgments

This work was financially supported by the *Polish State Committee for Scientific Research* within the research grant No. 2/0635/91/01 (PB0616/P3/92/02) and in part by the *Deutsche Forschungsgemeinschaft.*

References

[1] Böhmer V (1995) Angew Chem **107**: 785; (1995) Angew Chem Int Ed Engl **34**: 713
[2] Koh K, Araki K, Shinkai S (1994) Tetrahedron Lett **35**: 8255
[3] (a) Shimizu KD, Rebek Jr J (1995) J Proc Nat Acad Sci **92**: 12403; (b) Mogck O, Böhmer V, Vogt W (1996) Tetrahedron **52**: 8489; (c) Hamann BC, Shimizu KD, Rebek Jr J (1996) Angew Chem **108**: 1425 (1996) Angew Chem Int Ed Engl **35**: 1326; (d) Mogck O, Paulus EF, Böhmer V, Thondors I, Vogt W (1996) Chem Commun 2533
[4] Chapman RG, Sherman J C (1995) J Am Chem Soc **117**: 9081
[5] (a) Byun Y-S, Vadhat O, Blanda MT, Knobler CB, Cram DJ (1995) J Chem Soc Chem Commun 1825; (b) Byun Y-S, Robbins TA, Knobler CB, Cram DJ (1995) ibid 1947; (c) Eid Jr CN, Knobler CB, Gronbeck DA, Cram DJ (1994) J Am Chem Soc **116**: 8506; (d) Robbins TA, Knobler CB, Bellew DR, Cram DJ (1994) ibid **116**: 111
[6] Timmerman P, Verboom W, van Veggel FCJM, van Duynhoven JPM, Reinhoudt DN (1994) Angew Chem **106**: 2437; (1994) Angew Chem Int Ed Engl **33**: 2345
[7] Fraser JR, Borecka B, Trotter J, Sherman JC (1995) J Org Chem **60**: 1207
[8] (a) Blanda MT, Griswold KE (1994) J Org Chem **59**: 4313; (b) Araki K, Sisido K, Hisaichi K, Shinkai S (1993) Tetrahedron Lett **34**: 8297
[9] Böhmer V, Goldmann H, Vogt W, Vicens J, Asfari Z (1989) Tetrahedron Lett **30**: 1391
[10] Hajek F, Graf E, Hosseini MW (1966) Tetrahedron Lett **37**: 1409
[11] (a) Kraft D, van Loon J-D, Owens M, Verboom W, Vogt W, McKervey MA, Böhmer V, Reinhoudt DN (1990) Tetrahedron Lett **31**: 4941; (b) Beer PD, Keefe AD, Slawin AMZ, Williams DJ (1990) J Chem Soc Dalton Trans 3675
[12] (a) Lhotak P, Shinkai S (1995) Tetrahedron **51**: 7861; (b) Mogck O, Böhmer V, Vogt W (unpublished results)
[13] (a) Ikeda A, Shinkai S (1994) J Chem Soc Chem Commun 2375; (b) Rérez-Adelmar J-A, Abraham H, Sánchez C, Rissanen K, Prados P, de Mendoza J (1996) Angew Chem **108**: 1088; (1996) Angew Chem Int Ed Engl **35**: 1009
[14] (a) Ross H, Lüning U (1995) Angew Chem **107**: 2723; (1995) Angew Chem Int Ed Engl **34**: 2555; (b) Zhong ZL, Chen Y-Y, Lu XR (1995) Tetrahedron Lett **36**: 6735; (c) Ohseto F, Shinkai S (1995) J Chem Soc Perkin Trans 2, 1103
[15] (a) Arduini A, Fanni S, Manfredi G, Pochini A, Ungaro R, Sicuri AR, Ugozzoli F (1995) J Org Chem **60**: 1448; (b) Fujimoto K, Shinkai S (1994) Tetrahedron Lett **35**: 2915; (c) Arduini A, Pochini A, Sicuri AR, Secchi A, Ungaro R (1994) Gazz Chim Ital **124**: 129

[2] Additional material to the structure determination may be ordered from Fachinformationszentrum Karlsruhe, Gesellschaft für wissenschaftlich-technische Information mbH, D-76344 Eggenstein-Leopoldshafen, Federal Republic of Germany, referring to the deposition number CSD-406997 and the full citation of the present paper

[16] Wasikiewicz W, Rokicki G, Kiełkiewicz J, Böhmer V (1994) Angew Chem **106**: 230; (1994) Angew Chem Int Ed Engl **33**: 214
[17] Beer PD, Gale PA, Hesek D (1995) Tetrahedron Lett **36**: 767
[18] Goldmann H, Vogt W, Paulus E, Böhmer V (1988) J Am Chem Soc **110**: 6811
[19] (a) Olmstead MM, Sigel G, Hope H, Xu X, Power PP (1985) J Am Chem Soc **107**: 8087; (b) Bott SG, Coleman AW, Atwood JL (1986) J Chem Soc Chem Commun 610; (c) Andreetti GD, Calestani G, Ugozzoli F, Arduini A, Ghidini E, Pochini A, Ungaro R (1987) J Incl Phenom **5**: 123
[20] Sternhel S (1969) Quart Rev **23**: 236
[21] Groenen LC, Brunink J AJ, Bakker WI, Harkema S, Wijmenga SS, Reinhoudt DN (1992) J Chem Soc Perkin Trans 2, 1899
[22] (a) Perrin M, Oehler D (1990) In: Vicens J, Böhmer V (eds) Calixarenes, a Versatile Class of Macrocyclic Compounds. Kluwer, Dordrecht, pp 65–85; (b) Andreetti GD, Ugozzoli F (1990) In: ibid, pp 87–123
[23] (a) McKervey MA, Seward EM, Ferguson G, Ruhl BL (1986) J Org Chem **51**: 3581; (b) Xu W, Puddephatt RJ, Manojlovic-Muir L, Muir KW, Frampton CS (1994) J Incl Phenom Mol Recogn **19**: 277; (c) Böhmer V, Dörrenbächer R, Frings M, Heydenreich M, de Paoli D, Vogt W, Ferguson G, Thondorf I (1996) J Org Chem **61**: 549
[24] Hanley-Smith P, Whiting A D (1980) J Chem Soc Perkin Trans 1, 614
[25] Martin EL (1936) J Am Chem Soc **58**: 1438
[26] Kharasch N, Kalfayan SH (1956) J Org Chem **21**: 929
[27] Gutsche CD, Iqbal M, Stewart D (1986) J Org Chem **51**: 742
[28] Doherty DG (1955) J Am Chem Soc **77**: 4887
[29] Sheldrick GM (1990) Acta Cryst **A46**: 467
[30] Sheldrick GM (1993) SHELXL-93 program for crystal structure refinement. University of Göttingen, Germany
[31] Sheldrick GM (1986) SHELXS-86 program for the solution of crystal structures. University of Göttingen, Germany
[32] Sheldrick GM (1991) SHELXTL-PLUS, an integrated system for solving, refining and displaying crystal structures from diffracting data. Siemens Analytical X-Ray Instruments Inc, Madison, Wisconsin, USA

Received March 10, 1997. Accepted March 20, 1997