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PAPER

Bridge-substituted calix[4]arenes: syntheses, conformations and application†

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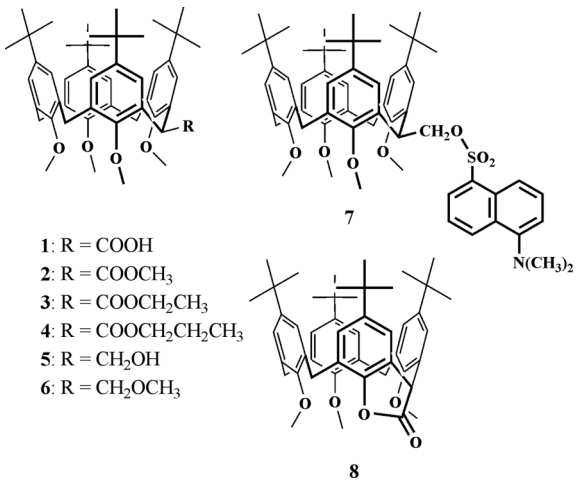
The bridge-substituted calix[4]arene carboxylic acid, 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetramethoxy-calix[4]arene-2-carboxylic acid (**1**), can be readily converted to various esters **2–4** and reduced to the alcohol **5**, which reacts with methyl iodide to give the ether **6**. The alcohol can be dansylated to give **7**, the fluorescence of which is selectively quenched by Cu(II) in acetonitrile. An attempt to convert the acid **1** to an amide resulted unexpectedly in the formation of a lactone **8**. The conformational characteristics of **1–8** have been studied in solution and, in the cases of **2** and **4**, in the solid state by determination of their single-crystal X-ray structures. With the exception of **8**, in all these compounds the bridge substituent adopts an equatorial (lateral) orientation.

Introduction

Despite the intense interest in calixarene chemistry over the past few decades, very little of this work has been focussed on derivatives formed by substitution of the methylene bridges linking the aromatic units (leaving aside, of course, the extensive studies of resorcinarenes).[1] The case of monosubstitution at these sites is of significance[2–4] because in the *cone* conformation, for example, the initial methylene protons are inequivalent[5] and thus the possibility arises of (at least partial) locking of the conformation of the substituted calixarene due to energy differences between equatorial and axial orientations of the substituent. In the simplest instance of monosubstitution on one of the four bridges of the calix[4]arene, an equatorial disposition of the lateral substituent appears to be strongly preferred, though this does not necessarily inhibit conformational changes associated with, for example, rotation of phenolic units through the annulus. The range of such substituents is rather limited,[2,3] nonetheless, and our present objective was to expand this range, in view not only of obtaining a better understanding of conformational influences but also of providing both new means of anchoring functionalised calixarenes to supports and new receptor types. Thus, we describe herein the synthesis of seven derivatives of the readily obtained bridge-monocarboxylated calix[4]arene **1** (Scheme 1) including a fluorescent derivative **7** which displays selective sensing properties for Cu(II).



Scheme 1 Compounds studied in this paper.

Results and discussion

Synthesis

The tetramethoxy-tetra-*t*-butylcalix[4]arene monocarboxylic acid **1**, in which the carboxyl group adopts a lateral disposition, displays the typical properties of a carboxylic acid in that it readily undergoes acid-catalysed reaction in the appropriate alcohol to give the methyl, ethyl and *n*-propyl esters, **2**, **3** and **4**, and is also reduced by $LiAlH_4$ to the corresponding alcohol **5**. This alcohol can be methylated with CH_3I to give the ether **6** and dansylated using dansyl chloride to give the fluorescent sulfonate ester **7**. In all these compounds, the lateral disposition of the substituent appears to be retained. In attempting to convert the acid to an amide, however, the product formed was the lactone

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† Electronic supplementary information (ESI) available: Additional NMR spectra (S1–S5), crystallographic data for compounds **2** and **4** including hydrogen bond type interactions and packing motifs (S6–S9); MM calculation results (S10–S14); fluorescence spectra of compound **7** (S15); experimental details (S16–S17). CCDC reference numbers 806418 and 806419. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c1ob00028d

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Table 1 Distribution of conformers of calixarenes **1–8** in solution of $CDCl_3$ at 294 K (mol%)

Conformation	1	2	3	4	5	6	7	8
paco1	39[a]	—	—	—	—	—	—	—
paco2	53	86	86	88	86	87	79	54
cone								46
1,2-alt	7	14	14	12	14	13	21	—

[a] Due to intramolecular hydrogen bonding between the COOH function and a neighbouring methoxy group, for compound **1** a special *paco1* conformation is observed in high amount.[2b]

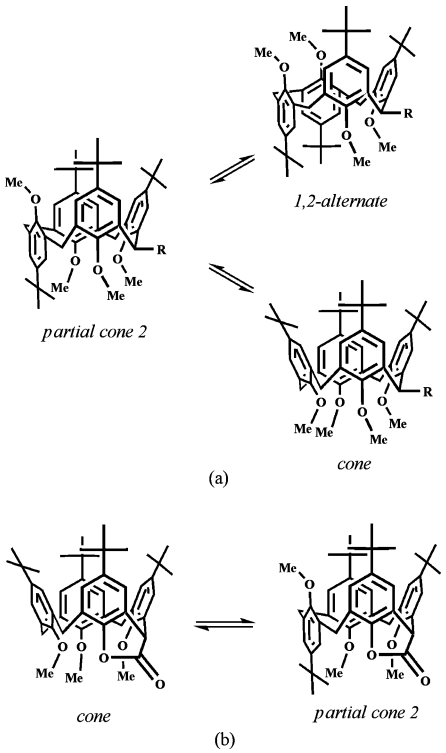
8 in which the substituent is necessarily axial, as clearly shown by the strong downfield shift of the ^{1}H NMR signal for the lateral methine proton (6.64 ppm). Thus, despite the preference for a lateral positioning of the substituent in the reactant, it is obviously possible to invert the configuration of the bridge atom. Interestingly, the lactone **8** seems to be insensitive to the presence of ammonia (even if largely protonated), in contrast to closely related lactones produced through a different pathway[6,7] which undergo ring-opening reactions with dialkylamines.

Conformations in solution

As for the unsubstituted tetramethoxy-tetra-*t*-butylcalix[4]arene,[8] all the present compounds **1–8** display complex ^{1}H NMR solution spectra indicative of the presence of mixtures of conformers. In none, however, is there an indication of the presence of species differing in configuration at the substituted bridge carbon, so that the spectra were interpretable in terms of just the conformers shown in Scheme 2. COSY, HSQC, HMBC and NOESY measurements (Fig. S1–S4†) were used to identify the different isomers present, although for compounds **2–7** overlap of the methine signals for the *partial cone* and *cone* isomers was such that they could not be separately integrated (Table 1). Introduction of the relatively large dansyl group results in a slight favouring of the *1,2-alternate* conformation but the restrictions introduced by formation of the lactone ring in **8** seem to completely exclude this conformer. Following the positive ROE-correlations between the lateral methine proton and neighbouring methoxy groups in compound **8**, two conformations were assigned (*cone* and *paco2*), the latter with a methoxy group pointing outwards from the cavity. (Scheme 2b).

Conformations in the solid state

Reports on the conformational behaviour of laterally monosubstituted tetramethoxycalix[4]arenes in the solid state are still rather rare.[9,2a,2b,2c,10] The single-crystal X-ray structure determinations on the esters **2** and **4** provide evidence of the conformational lability of these compounds in that **2** is found to adopt a *partial cone* conformation whereas **4** crystallises in the *cone* form. In crystalline **2**, while the *paco* conformation is similar to that seen in **1**,[2a] the inverted ring is tilted further, in such a way as to minimise contact of the methoxy group with the cavity formed by the other three phenyl rings (Fig. 1a). Of these three rings, the distal pair is almost parallel and the intervening ring lies at a dihedral angle of 54.1(1)° with reference to the inverted ring (Table S6†). As a consequence of the more constricted cavity in comparison with **1**, the plane



Scheme 2 Conformational interconversion of calixarenes **2–7** (a) and the lactone derivative **8** (b) in solution.

of the methoxycarbonyl group in compound **2** is arranged nearly perpendicular [81.4(1)°] with reference to the mean central plane (Table S6†).

Due to the hydrophobic nature and missing hydrogen donor groups, the intermolecular interactions of the calixarene **2** are limited to van der Waals forces and a weak C–H···O hydrogen bond[11] involving the ester oxygen and a methoxy group of a neighbouring calixarene molecule [C(43)–H(43C)···O(5) 2.53 Å, 169°, S7]. Additionally, a weak C–H···π contact[12] between a *tert*-butyl group and the aromatic ring B is observed (Table S7†). The packing motif consists of two complementary arranged centrosymmetric ester dimers stabilized by weak aryl–alkyl-interactions (Table S7†). Corresponding opposite ester functions are arranged slightly staggered along the crystallographic (0, 1, –1) plane [Fig. 2(a), Fig. S8†]. Hence, the compact structure of cumulated calixarene dimers is reflected by a marginally higher packing index[13] of 64.1 compared to the acid **1** (Table S7†).

Crystallization of **4** from acetonitrile–dichloromethane (2 : 1) yields colourless crystals of the monoclinic space group $P2_1/n$, where the calixarene molecule adopts a *cone* conformation [Fig. 1(b)]. In contrast to the fundamental work on laterally attached alkyl–aryl hybrids done by Fantini and co-workers,[2c] in the present case, no solvent molecule is occupying the upper cavity. In other words, no guest molecule stabilises the *cone* conformation, as usually demonstrated in the literature.[14]

On closer examination, the crystal structure of **4** reveals a *pinched cone* conformation with a coplanar arrangement of the opposing arene units *A*/*C* [0.6(1)°] and a nearly orthogonal arrangement of the rings *B*/*D* [75.7(1)°, Table S6†]. Unlike the methyl ester **2** and the acid **1**, the ester carbonyl group in compound **4** is orientated downwards offering free space for the

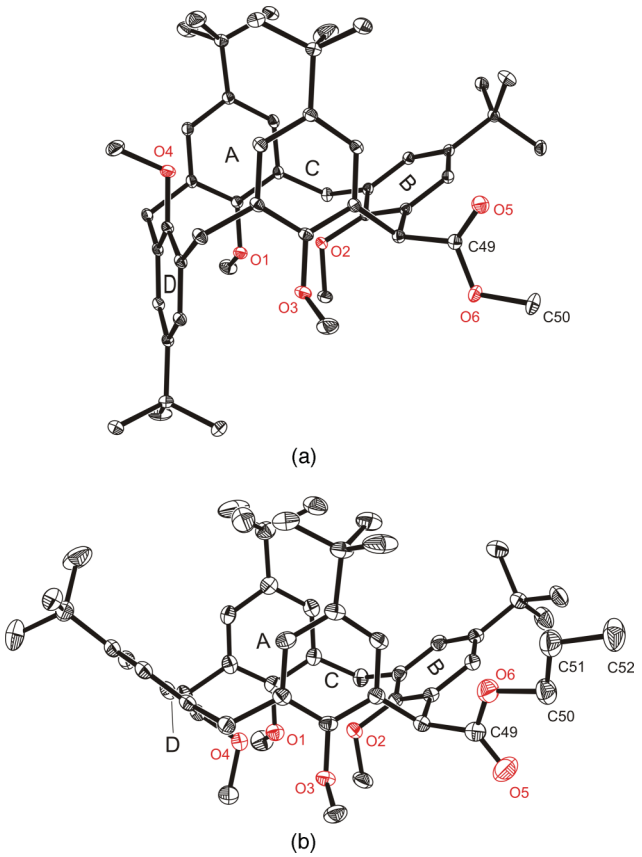


Fig. 1 Molecular structures of calixarenes **2** (a) and **4** (b), including the numbering of relevant atoms and aromatic rings.

longer propyl chain which is located in the upper hemisphere of the chalice.

In the packing of **4**, the calixarene molecules are stacked parallel to the crystallographic (1, 0, –1) plane in such a manner that two neighbouring calixarene molecules with opposite orientations of the cavities, form a kind of dimer by complementary arrangement of their lateral propoxycarbonyl substituents [Fig. 2(a), Fig. S9†]. Thus, the lateral substituents in the crystal structure of calixarene **4** have a more space filling character than in structure **2**. Moreover, the cantilevered lateral ester group stabilizes the structure by

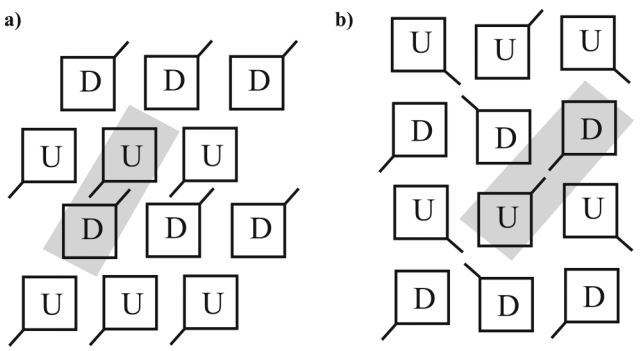


Fig. 2 Cartoon illustrating the packing motifs (highlighted in grey) of compound **2** (a) and the propoxycarbonyl compound **4** (b) running parallel to the designated planes. The different orientations of the entire calixarene cores are assigned with U (up) and D (down).

Table 2 Calculated populations (MMFF94) for possible conformers of calixarenes **2–7** in %

Conformer[a]	**1**	**2**	**3**	**4**	**5**	**7**
cone A	—	—	—	—	—	—
cone B	44.7	44.5	44.8	53.3	44.7	48.3
paco A	—	—	—	—	—	—
paco B	2.0	2.0	2.1	1.5	3.0	3.2
paco C	2.9	2.9	3.0	2.1	2.7	4.1
paco D	46.3	46.5	45.9	38.9	47.4	40.1
alt2 A	—	—	—	—	—	—
alt2 B	—	0.1	—	—	—	—
alt2 C	0.1	0.1	0.1	—	0.1	0.1
alt3	4.0	3.9	4.1	4.2	2.1	4.2

[a] *A*, *B*, *C* and *D* indicate the different possible orientations of the arene units in the conformers around the lateral substituent as illustrated in Fig. S10.

a weak C–H···π contact involving a neighbouring aryl unit (Table S7†).

Molecular mechanistic calculations

The gas phase energies of all possible conformers (Fig. S10, Table S11†) of the calixarenes **2–7** were estimated by molecular mechanics calculations (MacroModel 9.7, Schrödinger Inc. 2007, MMFF94 force field), the results obtained are given in Table 2. They indicate, consistent with the experimental data for solutions given above, that the *cone* and *paco* conformations should be dominant. In accordance with the literature,[3c] the isolated molecules **2–7** show a clear preference for those conformations bearing the lateral substituent in an equatorial position between *syn*-oriented arene units (*e.g. cone B*, *paco D*).

Following this series of calculations, one can conclude that longer ester residues in lateral position result in a manifestation of the *cone* conformation. Interestingly, the result of the MM calculations for the calixarene esters **2** and **4** is in coherence with the X-ray analysis, delivering *cone* for the propyl ester and *partial cone* for the shorter methyl ester. Also, the observed different orientation of the C═O group in both esters is in accordance with the crystallographic findings (Table S12, Fig. S14†). The determined energy deviation between the calculated lowest energy conformer structures (MMFF94) and the real crystal structures is less than 2%, thus showing the good quality of the MM calculations (Table S13†).

Fluorescence analysis with the dansyl derivative 7

Various dansylated calixarenes[15–18] are known to be fluorescent sensors for metal ions, Cu(II)[19] and Hg(II)[20] in particular being known to produce marked quenching effects. For the dansyl derivative **7**, its fluorescence in acetonitrile is especially sensitive to Cu(II), with much weaker quenching being evident with a variety of other metal ions (Fig. 3). It seems likely that the fluorescence quenching upon addition of Cu(II) results from an energy transfer involving oxidative quenching, whereas the observed smaller quenching upon addition of Hg^{2+} and Pb^{2+} is attributable to the "heavy atom effect".[21] A fluorescence titration of **7** with Cu(II) in acetonitrile gave results (Fig. 4) consistent with a 1 : 1 binding equilibrium and a stability constant at 298 K with a value of

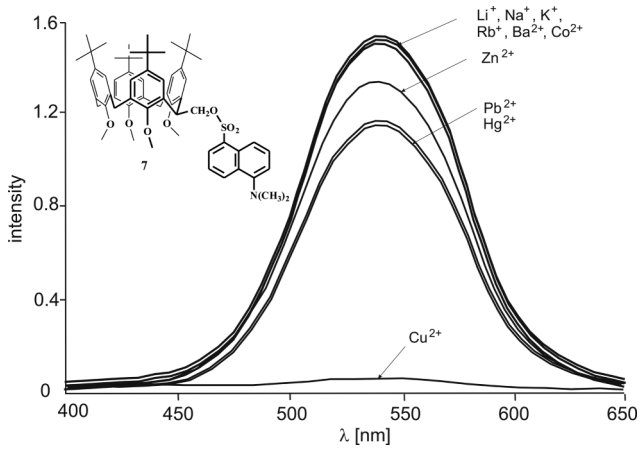


Fig. 3 Fluorescence emission spectra of **7** (35 μmol l^{-1} in acetonitrile in the presence of different metal salts).

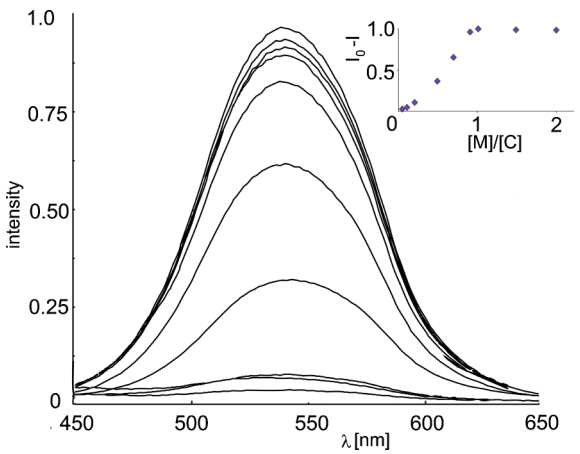


Fig. 4 Fluorescence titration of **7** in CH_3CN with increasing concentrations of Cu^{2+}. Inset: ratiometric calibration curve.

log$K$ = 3.19 ± 0.03. The detection limit[22] for Cu(II) in acetonitrile by this method is estimated as 5×10^{-6} M.

The selectivity of the complexation is demonstrated by the examination of binary mixtures composed of Cu(II) and different other metal salts as background ions (Fig. 5). As obvious from the diagram, none of the additional metal ions cause an appreciable

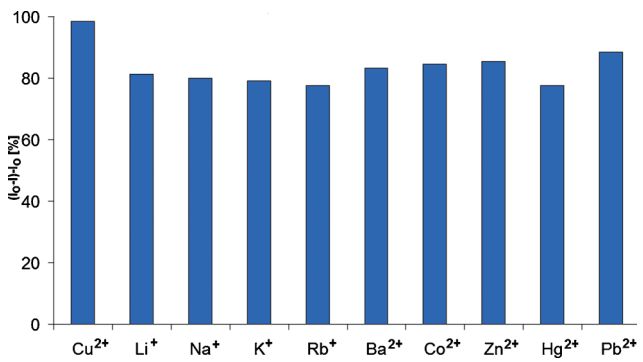


Fig. 5 Quenching ratio $[(I_0 - I/I_0)]$ of the fluorescence intensity of **7** upon addition of 1 equiv. of Cu^{2+} in the absence (first column on the left side) and presence of 4 equiv. of background metal ions in CH_3CN.

cross-sensitivity which is a favourable condition for potential use in metal ion sensing.

Although the reference compound dansyl phenolate[17] shows a moderate quenching on the addition of Cu(II), this effect is nearly 75% less than those observed for compound **7**, thus indicating a significant influence of the calixarene framework offering a preorganized complexation side.

Conclusions

From the chemical preparative point of view, it is shown that the bridge-substituted calix[4]arene carboxylic acid **1** can readily be converted to various esters and reduced to the corresponding alcohol, which reacted with dansyl chloride to give a fluorescent dansylate, while the intended conversion of **1** to an amide unexpectedly resulted in the formation of a lactone.

The conformational behaviour of the new compounds in $CDCl_3$ solution is only slightly affected by the lateral substituent. In the solid state, however, a conformational switch from *partial cone* to *cone* conformation from the shorter methyl ester to the longer propyl ester, also understandable from calculations on ground state energies of possible conformers, indicates a stronger conformational influence of the length of the lateral ester substituents than those of linear alkyl substituents tethered at a single methylene bridge.

Fluorescence measurements in acetonitrile prove the laterally dansylated calixarene **7** to be sensitive to Cu(II) ions. The complex stability as well as the sufficiently low detection limit promotes **7** to an appropriate sensor material for the detection of copper.

Experimental

Details on instrumentation and starting compounds are recorded in the ESI†, part S16 and S17.

Preparation of lateral calix[4]arene ester homologues 2–4: general procedure

1.15 g (1.5 mmol) calix[4]arene-2-carboxylic acid (**1**) was dissolved in the respective dry alcohol (20 ml), followed by the addition of 100 ml $CHCl_3$ and conc. sulfuric acid (3 ml). After 14 h heating under reflux, the mixture was cooled to room temperature and washed with water (50 ml), aqueous $KHCO_3$ solution (50 ml) and water (50 ml). The solvent was evaporated and unreacted starting compound **1** was removed by eluting the crude product through a short silica column (eluent: $CHCl_3$). Recrystallization from *n*-hexane afforded white powders.

Methyl-5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetramethoxy-calix[4]arene-2-carboxylate (2)

Methanol was used to yield 700 mg, 59% of **2**. Mp 200–202 °C; ^{1}H NMR ($CDCl_3$) δ 1.05–1.42 (C(CH_3)$_3$), 2.42–4.36 (CH_3O, CH_2 and CH_3), 5.30, 5.64, 5.86 (s, 1H, CHCOOCH$_3$), 6.84–7.49 (ArH); ^{13}C NMR ($CDCl_3$) δ 31.0–31.5 (C(CH_3)$_3$, 33.9–34.0 (CH_2), 37.1 (C(CH$_3$)$_3$), 42.7 (CHCOOCH$_3$), 51.9 (CH_3), 59.9–61.2 (CH_3O), 123.2–127.5 (ArC), 131.7–135.0 (ArC), 144.4–145.1 (ArC), 154.6–155.0 (ArC), 173.9 (COOCH$_3$); m/z (APCI) 785.43 (763.06 calcd for $C_{50}H_{66}O_6$) (MNa$^+$). Anal. calcd for $C_{50}H_{66}O_6$: C, 78.70; H, 8.72; Found: C, 78.51; H, 8.52%.

Ethyl-5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetramethoxycalix[4]arene-2-carboxylate (3)

Ethanol was used to yield 800 mg, 68% of **3**. Mp 195–197 °C; ^{1}H NMR ($CDCl_3$) δ 1.38–0.98 (C(CH_3)$_3$, 1.31 (CHCOOCH$_2$CH_3), 2.42–4.36 (CH_3O and CH_2), 4.02 (CHCOOCH_2CH$_3$), 5.29, 5.64, 5.85 (s, 1H, C*H*COOCH$_3$), 6.84–7.50 (Ar*H*); ^{13}C NMR ($CDCl_3$) δ 14.3 (CHCOOCH$_2$*C*H$_3$), 31.0–31.5 (C(*C*H$_3$)$_3$, 33.8–34.0 (*C*H$_2$), 37.0 (*C*(CH$_3$)$_3$), 43.2 (*C*HCOOCH$_3$), 59.9–61.2 (*C*H$_3$O), 64.9 (CHCOO*C*H$_2$CH$_3$), 123.4–127.5 (Ar*C*), 131.7–135.0 (Ar*C*), 144.4–145.0 (Ar*C*), 154.0–155.0 (Ar*C*), 173.5 (*C*OOCH$_3$); *m/z* (APCI) 799.42 (776.50 calcd for $C_{51}H_{68}O_6$) (MNa^+). Anal. calcd for $C_{51}H_{68}O_6$: C, 78.83; H, 8.82; Found: C, 78.60; H, 8.78%.

***n*-Propyl-5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetramethoxycalix[4]arene-2-carboxylate (4)**

n-Propanol was used to give 500 mg, 42% of **4**. Mp 174–176 °C; ^{1}H NMR ($CDCl_3$) δ 0.94 (CH$_2$CH$_2$CH_3), 1.01–1.36 (C(CH_3)$_3$), 1.68 (CH$_2$CH_2CH$_3$), 2.45–4.36 (CH_3O, CH_2, CH_2CH$_2$CH$_3$), 5.27, 5.59 5.81 (s, 1H, C*H*COOCH$_2$CH$_2$CH$_3$), 6.85–7.48 (Ar*H*); ^{13}C NMR ($CDCl_3$) δ 10.1 (COOCH$_2$CH$_2$*C*H$_3$), 22.1 (COOCH$_2$*C*H$_2$CH$_3$), 31.0–31.5 (C(*C*H$_3$)$_3$), 33.4–34.4 (*C*H$_2$), 37.1–39.4 (*C*(CH$_3$))$_3$, 43.1 (*C*HCOOCH$_2$CH$_2$CH$_3$), 59.9–61.1 (*C*H$_3$O), 66.3 (COO*C*H$_2$CH$_2$CH$_3$), 123.4–127.4 (Ar*C*), 131.8–135.0 (Ar*C*), 144.3–144.9 (Ar*C*), 153.8–155.0 (Ar*C*), 173.4, 173.6 (*C*OOCH$_2$CH$_2$CH$_3$); *m/z* (APCI) 813.51 (791.11 calcd for $C_{52}H_{70}O_6$) (MNa^+). Anal. calcd for $C_{52}H_{70}O_6$: C, 78.95; H, 8.92; Found: C, 78.88; H, 8.82%.

2-(Hydroxymethyl)-5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetramethoxycalix[4]arene (5)

A suspension of 3.36 g (4.5 mmol) calix[4]arene-2-carboxylic acid (**1**) in 90 ml dry diethyl ether was dropped to a refluxing solution of 2.3 g (60.6 mmol) $LiAlH_4$ in 100 ml dry diethyl ether. After 5 h heating under reflux, the solution was poured carefully in small portions into crushed ice. Hereafter, sulfuric acid (10%) was added until the formed precipitate was completely dissolved. The organic layer was separated and washed with water (3 × 100 ml), dried over $MgSO_4$ and evaporated to give a white foam of **5**. Recrystallization from diethyl ether yielded a white powder. (2.8 g, 85%). Mp 110–112 °C; ^{1}H NMR ($CDCl_3$) δ 1.14–1.38 (C(CH_3)$_3$), 2.17 (s, O*H*), 2.91–4.21 (CH_3O und CH_2), 4.30 (s, CH_2OH), 4.70, 4.84, 5.01 (t, 1H, C*H*CH$_2$OH), 6.80–7.70 (Ar*H*); ^{13}C NMR ($CDCl_3$) δ 29.7–31.4 (C(*C*H$_3$)$_3$, 33.9–34.0 (*C*H$_2$), 37.2–39.0 (*C*(CH$_3$)$_3$), 58.2–61.0 (*C*H$_3$O), 72.0 (*C*H$_2$OH), 120.9–121.9(Ar*C*), 125.1–127.1 (Ar*C*), 132.5–135.0 (Ar*C*), 143.3–145.1 (Ar*C*), 154.8–155.7 (Ar*C*); *m/z* (APCI) 757.42 (735.05 calcd for $C_{49}H_{66}O_5$) (MNa^+). Anal. calcd for $C_{49}H_{66}O_5$: C, 80.07; H, 9.05; Found: C, 79.67; H, 9.02%.

2-(Methoxymethyl)-5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetramethoxycalix[4]arene (6)

To a stirred solution of the calixarene alcohol **5** (1.4 g, 1.9 mmol) in dry THF (50 ml) under argon, sodium hydride (60% in paraffin, 1.0 g, 25 mmol) was carefully added. The mixture was heated under reflux for 1.5 h. After cooling to room temperature methyl iodide (1.0 ml, 16 mmol) was dropped in *via* a syringe and heating was continued for 3 h. The solvent was removed under reduced pressure and the residue was treated with water (50 ml) resulting in a light yellow precipitate of **6** which was collected and recrystallized from dichloromethane–methanol (1 : 1) to yield a white powder (1.2 g, 85%). Mp 242–244 °C, ^{1}H NMR δ 1.13–1.36 (C(CH_3)$_3$), 3.39–3.41 (CH_3O and CH_2), 4.00–4.26 (CH_2 and C*H*CH$_2$OCH$_3$), 4.71, 4.85, 4.98 (t, 1H, C*H*CH$_2$OCH$_3$), 7.05–7.15 (Ar*H*), 7.47 (Ar*H*); ^{13}C NMR δ 29.5–30.7 (C(*C*H$_3$)$_3$), 33.5–33.7 (*C*H$_2$), 35.8 (*C*(CH$_3$)$_3$, 58.7 (CH$_2$O*C*H$_3$), 63.8(*C*H$_3$O), 74.5 (*C*H$_2$OCH$_3$), 121.6 (Ar*C*), 125.2–126.5 (Ar*C*), 132.2–134.7 (Ar*C*), 146.9 (Ar*C*), 150.4 (Ar*C*); *m/z* (APCI) 771.50 (749.07 calcd for $C_{50}H_{68}O_5$) (MNa^+). Anal. calcd for $C_{49}H_{66}O_5 \cdot 2\ CH_3I$: C, 60.46; H, 7.22; Found: C, 60.24; H, 7.19%.

2-[5-(Dimethylamino)naphthyl-1-sulfonyloxy]-5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetramethoxycalix[4]arene (7)

To a stirred suspension of sodium hydride (60% paraffin, 1.0 g, 25 mmol) in dry THF (30 ml) calixarene alcohol **5** (0.5 g, 0.7 mmol) was added carefully. The mixture was heated to reflux, and, subsequently, dansyl chloride (0.2 g, 0.75 mmol) dissolved in dry THF (20 ml) was dropped in, that way the colour of the dansyl chloride faded smoothly to pale green. After 4 h of refluxing, the solvent was removed under reduced pressure and the resulting residue was taken up in dichloromethane (30 ml). Unreacted sodium hydride was carefully quenched with water (30 ml). The organic layer was washed with 2 N hydrochloric acid followed by water. Evaporation of the solvent under reduced pressure yielded a yellow-greenish crude product which was column chromatographed on SiO_2 (eluent: chloroform with increasing gradient of ethanol up to a ratio of 1 : 1, $R_f = 0.45$) to give a bright yellow solid (100 mg, 45%). Mp 121–123 °C; ^{1}H NMR ($CDCl_3$) δ 1.03–1.38 (m, 36 H, C(CH_3)$_3$), 2.80 (s, 6H, N(CH_3)$_2$), 2.54–4.10 (m, 18H, OCH_3 and CH_2), 4.10, 4.57 (m, 2 H, CHCH_2OSO$_2$), 4.31, 4.46, 4.69 (t, 1H, C*H*CH$_2$OSO$_2$), 7.09–8.56 (m, 6H, dansyl-Ar*H*); 6.58–7.07 (m, 8H, Ar*H*); ^{13}C NMR ($CDCl_3$) δ 29.7–31.3 (C(*C*H$_3$)$_3$), 33.9–37.6 (*C*(CH$_3$)$_3$ und *C*H$_2$), 45.4 (N(*C*H$_3$)$_2$), 60.2–60.7 (*C*H$_3$O), 60.7 (CH*C*H$_2$OSO$_2$), 115.5, 119.6, 123.0, 125.1–133.8, 145.0, 151.7–155.0 (Ar*C*); *m/z* (ESI) 985.5 (968.33 calcd for $C_{61}H_{77}NO_7S$) (MNH_4^+). Anal. calcd for $C_{61}H_{77}NO_7S \cdot CH_2Cl_2$: C, 70.70; H, 7.56; N, 1.33; Found: C, 70.92; H, 7.72; N, 1.22%.

5,11,17,23-Tetra-*tert*-butyl-26,27,28-trimethoxy[2:25]calix[4]aren-γ-lactone (8)

A mixture of calixarene carboxylic acid **1** (1.12 g, 1.5 mmol) and thionyl chloride (25 ml, 344.6 mmol) was heated under reflux for 3 h under argon. Subsequently, the unreacted excess of thionyl chloride was removed under reduced pressure. The resulting pale brown solid was dissolved in acetone (30 ml) followed by the addition of freshly dried ammonium acetate (2.00 g, 2.3 mmol). After stirring this solution for 12 h at room temperature, the white precipitate formed was filtered and washed with water. The resulting crude product was purified by recrystallization from methanol–chloroform (1 : 1) to yield the lactone **8** (320 mg, 30%). Mp 268–271 °C; ^{1}H NMR ($CDCl_3$) δ 0.72–1.43 (C(CH_3)$_3$); 3.23–4.47 (OCH_3, ArCH_2Ar); 6.64 (C*H*COOR); 6.29–7.31 (Ar*H*); ^{13}C NMR ($CDCl_3$) δ 30.96, 31.09, 31.20, 31.39, 31.42, 31.56, 31.59, 31.69, 31.72, 31.87, 33.47, 33.53, 33.75, 33.96, 34.04, 34.20, 34.25,

36.17, 36.88 (C(CH_3)$_3$, C(CH$_3$)$_3$), ArCH_2Ar); 48.01 (CHCOO); 58.05, 59.68, 60.45, 60.77, 60.84, 62.50 (OCH_3); 116.90, 117.17, 122.67, 123.04, 124.25, 124.74, 124.99, 125.45, 125.66, 125.74, 126.08, 126.30, 126.70, 126.95, 127.20, 127.34, 127.50, 127.55, 127.73, 128.29, 128.62, 130.87, 131.28, 131.59, 131.67, 132.02, 132.13, 133.15, 134.97, 135.77, 135.88, 136.33, 144.09, 144.16, 144.50, 144.58, 145.35, 145.86, 146.25, 149.26, 150.02, 154.16, 154.55, 154.92, 155.75, 155.81 (ArC); 176.90, 177.35 (C=O). m/z (CI) 716.5 (717.0 calcd for $C_{48}H_{65}O_5$) (M^+). Anal. calcd for $C_{48}H_{65}O_5 \cdot \frac{1}{2}$ H_2O: C, 79.41; H: 8.47. Found: C, 79.50; H, 8.38%.

X-Ray diffraction

Crystals of the inclusion compound **2**, suitable for structure analysis, were obtained by slow cooling of a hot solution of **2** in methanol–chloroform (2 : 1). Single crystals of **4** were grown in similar manner from acetonitrile–dichloromethane (2 : 1).

The intensity data were collected on a Bruker APEX II diffractometer with MoK$_\alpha$ radiation ($\lambda = 0.71073$ A) using ω- and φ-scans. Reflections were corrected for background and Lorentz polarization effects. Preliminary structure models were derived by application of direct methods[23] and were refined by full-matrix least squares calculation based on F^2 for all reflections. All hydrogen atoms were included in the models in calculated positions and were refined as constrained to bonding atoms. The crystal data and experimental parameters are summarized in the ESI.†

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