Calix[4]arene dimers; self-assembly *via* hydrogen bonding at the upper rim

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The X-ray structure determination of calix[4]arenedicarboxylic acid unequivocally proves the self-assembled dimeric structure in the solid state. Also in apolar solvents two calix[4]arene molecules are connected *via* carboxylic acid moieties at the upper rim. NMR studies show that in polar solvents the calix[4]arenedicarboxylic acid is present as a monomer with a pinched cone conformation that differs from the dimeric structure in apolar solvents.

Introduction

The design of noncovalently bonded, structurally well-defined capsules, boxes and aggregates based on calix[4]arene[1] building blocks is of increasing interest in the field of supramolecular chemistry.[2–6] Very recently, Rebek *et al.* reported the reversible encapsulation of aromatic guest molecules in a hydrogen bonded, self-assembled calix[4]arene dimer.[3] Four urea functions at the upper rim of one calix[4]arene unit result in the formation of 16 H-bonds in the dimer.[3,4] Regen *et al.* suggested for a calix[4]arenetetracarboxylic acid a monomeric structure with one intramolecular hydrogen bond between two diametrical carboxylic acid groups at the upper rim.[7] However, based on VPO measurements in CHCl₃ solution, Arduini *et al.* recently reported that a related calix[4]arenedicarboxylic acid forms instead of one intra- four inter-molecular hydrogen bonds in a dimer.[5]

We have studied the dimerization *via* hydrogen bonding of appropriately functionalized calix[4]arenes in more detail. In this paper, we present the first single crystal X-ray structure of a calix[4]arene dimer (**5·5**) self-assembled by H-bonds at the upper rim. In solution, this calix[4]arenedicarboxylic acid **5** adopts two different and temperature-independent pinched cone conformations: in chlorinated solvents by intermolecular hydrogen bonding in a dimer and in the hydrogen bond breaking solvent (CD₂)₂SO (solvent induced stabilization) as a monomer with a different pinched cone conformation.

Results and discussion

Synthesis of calix[4]arenecarboxylic acids

Gross formylation of 1,3-dinitrocalix[4]arene **1**[8] with titanium tetrachloride and α,α-dichloromethyl methyl ether in CH₂Cl₂ at −10 °C at either the 2-, or both 2- and 4-positions of the upper rim, afforded the corresponding monoaldehyde **2** and dialdehyde derivative **3** in 84 and 96% yield, respectively.[9,10] Subsequent oxidation of the aldehyde moieties with sodium chlorite and sulfamic acid in a chloroform–acetone mixture gave the corresponding calix[4]arene(di)carboxylic acids **4** and **5** in almost quantitative yield.[11]

The FAB mass spectra of the calix[4]arenecarboxylic acids **4** (*m/z* 1451.6) and **5** (*m/z* 1538.9) using *o*-nitrophenyl octyl ether (ONPOE) as an apolar matrix already indicate the presence of the respective dimers. However, using *m*-nitrobenzyl alcohol (NBA) as a polar matrix no dimer was observed for diacid **5** (see Experimental).

X-Ray structure determination

Single crystals suitable for X-ray structure determination could only be obtained by very slow evaporation of a CHCl₃–CH₂Cl₂ solution mixture (*ca.* 1 : 2) of calix[4]arenedicarboxylic acid **5** at room temperature. Details of the X-ray analysis are given in the Experimental section. Selected bond lengths and angles are listed in Table 1.

The centrosymmetric assembly **5·5** in the solid state with non-crystallographic, idealized D_{2h} symmetry is depicted in Fig. 1. The dimerization results in two hydrogen bonds per calix[4]arene unit;[5] Regen *et al.* reported one intramolecular hydrogen bond in a calix[4]arenetetracarboxylic acid.[7]

The hydrogen-bonded dimer **5·5** adopts the pinched cone conformation in which the aromatic units bearing the carboxylic acid groups are oriented face-to-face whereas the other two aromatics are 'flattened'. The intermolecular O···O distances of the hydrogen-bonded carboxylic acid groups are O(2)···O(8′) 2.644(10) and O(1)···O(7′) 2.621(10) Å. The carboxylic acid groups of the **5·5** are oriented in the plane with respect to the aromatic units. To the best of our knowledge
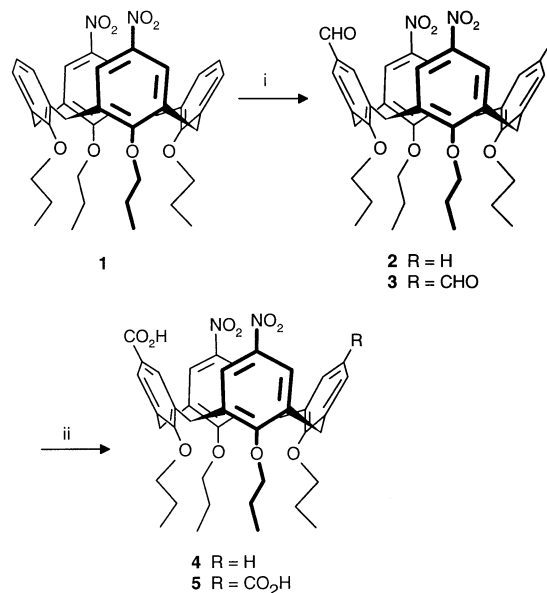
Scheme 1 *Reagents and conditions*: i, TiCl₄, Cl₂CHOCH₃, CH₂Cl₂, −10 °C; ii, H₂NSO₃H, NaClO₂, CHCl₃–acetone, room temp.

this represents the first X-ray crystal structure of a calix[4]arene dimer hydrogen-bonded *via* the upper rim.[12] The hydrogen-bonded dimers stack in layers parallel with the *ab*-plane, cemented by layers of $CHCl_3$ and CH_2Cl_2 solvent molecules.

Conformational behaviour in solution

The different distances between the equatorial calix[4]arene bridging methylene hydrogens (H_{eq}) and the two different adjacent aromatic hydrogens (H_1 and H_2, Table 2) indicate that calix[4]arenedicarboxylic acid **5** also adopts a pinched cone conformation in $C_2D_2Cl_4$ solution.[6]

The respective distances (Table 2) were determined by NOESY spectroscopy using the initial rate approximation in which the distance of 1.79 Å between the equatorial and axial bridging methylene hydrogen atoms was used as a reference.† The distances determined in solution are in good agreement with the distances from the X-ray structure analysis. Generally, the respective distances for symmetrically tetrasubstitued calix[4]arene derivatives in $CDCl_3$ solution are equal (time-averaged C_{4v} cone conformation).[6]

Calix[4]arenes in the 'cone' conformation still possess flexibility of the skeleton. The C_{4v} symmetrical cone conformation usually observed by ^{1}H NMR spectroscopy is in fact the result of fast interconversion between the two C_{2v} symmetrical pinched cone conformers (time-averaged structure, Scheme 2).
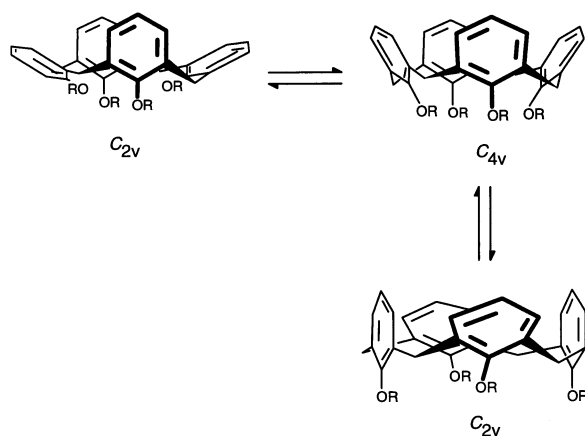
Scheme 2 C_{2v}–C_{2v} pinched cone interversion of calix[4]arenes

In CD_2Cl_2 the ^{1}H NMR spectrum of the calix[4]arenedicarboxylic acid **5** shows two different singlets for the aromatic hydrogens. The aromatic hydrogens of the CO_2H-substituted aromatic rings absorb at unusual high field (δ_H 6.75), whereas the aromatic hydrogens of the NO_2-phenyl rings are shifted to low field (δ_H 8.14, Fig. 2).‡

These characteristic shifts correspond to a pinched cone conformation of **5**, which is a consequence of the hydrogen-bonded dimeric assembly of the calix[4]arenedicarboxylic acid **5**.§ The two opposite aromatic rings substituted with the carboxylic acid groups are fixed in close proximity ('parallel') which results in shielding of these aromatic hydrogens. The 'flattened' aromatics bearing the NO_2 groups are not affected by shielding effects. These results fit nicely with what is observed in the solid state (*vide supra*). The characteristic shielding effects of the aromatic protons of calix[4]arenes are a sensitive probe for con-

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† For further details see ref. 6 and references cited therein. In Chart 2 and Table 2 of ref. 6 H_1 has to be interchanged with H_2.

‡ Recently, we have covalently rigidified the pinched cone conformation *via* a diametrical CH_2-bridge at the upper rim.[10] This gives a molecule which is related to compound **5**. In the ^{1}H NMR spectrum of this calix[4]arene in $CDCl_3$ the hydrogens of the 'flattened' aromatic units bearing the NO_2 groups absorb at δ_H 8.10.

§ No reliable osmometric molecular mass determination, which would prove the dimeric structure in solution, could be performed due to the insufficient solubility of calix[4]arene **5** in $CHCl_3$ ($\leqslant 10^{-2}$ M).
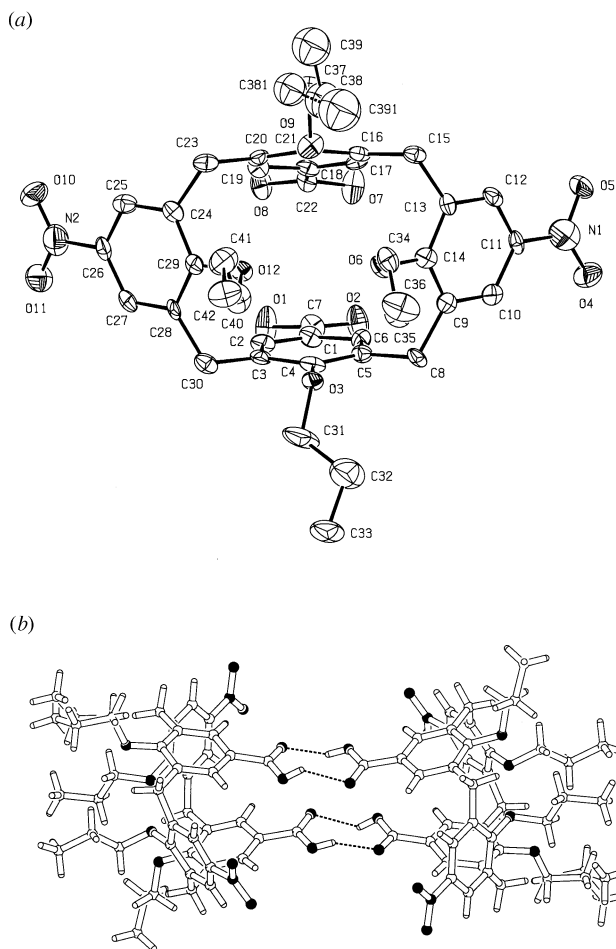
(a)

(b)

Fig. 1 (*a*) Thermal ellipsoid plot (50% probability) of calix[4]arene dicarboxylic acid **5** with the adopted atom-labelling. Hydrogen atoms and the co-crystallized solvent molecules are left out for clarity (top). (*b*) X-Ray structure of the hydrogen bonded calix[4]arene dimer **5·5**. The co-crystallized solvent molecules are omitted for clarity (bottom).
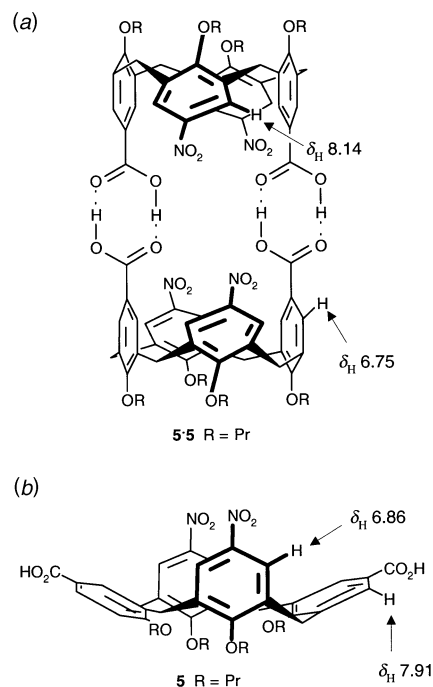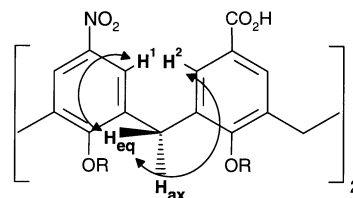
(a)

5·5 R = Pr

(b)

5 R = Pr

Fig. 2 Pinched cone conformation of the dimer **5·5** with selected chemical shifts δ_H in CD_2Cl_2 (top), and the different pinched cone conformer of **5** in [$(CD_3)_2SO$] (bottom)

Table 1 Selected bond lengths (Å) and bond angles (°) for calix-[4]arenedicarboxylic acid **5**

Bond lengths

O(1)–C(7)	1.272(12)	C(9)–C(10)	1.386(14)
O(2)–C(7)	1.234(13)	C(9)–C(14)	1.392(15)
C(10)–C(11)	1.398(14)	C(11)–C(12)	1.398(14)
O(4)–N(1)	1.233(12)	C(12)–C(13)	1.357(13)
O(5)–N(1)	1.243(12)	C(13)–C(14)	1.418(14)
C(13)–C(15)	1.520(13)	C(15)–C(16)	1.514(11)
O(7)–C(22)	1.256(11)	C(16)–C(17)	1.407(13)
O(8)–C(22)	1.245(10)	C(16)–C(21)	1.368(13)
C(17)–C(18)	1.372(13)	C(18)–C(19)	1.387(13)
O(10)–N(2)	1.228(12)	C(18)–C(22)	1.495(13)
O(11)–N(2)	1.220(12)	C(19)–C(20)	1.405(13)
C(20)–C(21)	1.407(12)	C(20)–C(23)	1.503(13)
N(1)–C(11)	1.441(13)	C(23)–C(24)	1.513(13)
N(2)–C(26)	1.456(11)	C(24)–C(25)	1.410(12)
C(1)–C(2)	1.344(13)	C(24)–C(29)	1.379(13)
C(1)–C(6)	1.401(11)	C(25)–C(26)	1.364(13)
C(1)–C(7)	1.511(14)	C(26)–C(27)	1.405(13)
C(2)–C(3)	1.376(13)	C(27)–C(28)	1.362(11)
C(3)–C(4)	1.414(11)	C(28)–C(29)	1.421(13)
C(3)–C(30)	1.517(13)	C(28)–C(30)	1.515(13)
C(4)–C(5)	1.375(14)	C(5)–C(6)	1.371(13)
C(5)–C(8)	1.540(11)	C(8)–C(9)	1.514(13)

Bond angles

O(4)–N(1)–O(5)	120.9(9)	O(4)–N(1)–C(11)	120.4(9)
O(5)–N(1)–C(11)	118.7(9)	O(10)–N(2)–O(11)	122.7(8)
O(10)–N(2)–C(26)	118.1(8)	O(11)–N(2)–C(26)	119.2(8)
C(2)–C(1)–C(6)	120.1(8)	C(2)–C(1)–C(7)	122.2(8)
C(6)–C(1)–C(7)	117.7(8)	C(1)–C(2)–C(3)	122.5(8)
C(2)–C(3)–C(4)	116.1(8)	C(2)–C(3)–C(30)	121.2(7)
C(4)–C(3)–C(30)	122.7(8)	O(3)–C(4)–C(3)	118.2(8)
O(3)–C(4)–C(5)	119.2(7)	C(3)–C(4)–C(5)	122.6(9)
C(4)–C(5)–C(6)	118.3(8)	C(4)–C(5)–C(8)	121.6(8)
C(6)–C(5)–C(8)	120.1(8)	C(1)–C(6)–C(5)	120.0(9)
O(1)–C(7)–O(2)	124.6(10)	O(1)–C(7)–C(1)	115.4(9)
O(2)–C(7)–C(1)	119.9(8)	C(5)–C(8)–C(9)	110.8(7)
C(8)–C(9)–C(10)	121.9(8)	C(8)–C(9)–C(14)	119.8(9)
C(10)–C(9)–C(14)	118.1(9)	C(9)–C(10)–C(11)	120.5(9)
N(1)–C(11)–C(10)	119.7(9)	N(1)–C(11)–C(12)	119.7(9)
C(10)–C(11)–C(12)	120.6(9)	C(11)–C(12)–C(13)	119.7(9)
C(12)–C(13)–C(14)	119.7(9)	C(12)–C(13)–C(15)	120.9(9)
C(14)–C(13)–C(15)	118.5(8)	O(6)–C(14)–C(9)	117.2(9)
O(6)–C(14)–C(13)	121.4(9)	C(9)–C(14)–C(13)	121.1(9)
C(13)–C(15)–C(16)	108.5(7)	C(15)–C(16)–C(17)	119.4(8)
C(15)–C(16)–C(21)	122.6(8)	C(17)–C(16)–C(21)	117.8(8)
C(16)–C(17)–C(18)	121.3(9)	C(17)–C(18)–C(19)	120.0(8)
C(17)–C(18)–C(22)	119.9(8)	C(19)–C(18)–C(22)	120.0(7)
C(18)–C(19)–C(20)	120.6(8)	C(19)–C(20)–C(21)	117.4(8)
C(19)–C(20)–C(23)	120.3(8)	C(21)–C(20)–C(23)	122.0(8)
C(16)–C(21)–C(20)	122.7(8)	O(7)–C(22)–O(8)	125.1(9)
O(7)–C(22)–C(18)	116.7(7)	O(8)–C(22)–C(18)	118.2(8)
C(20)–C(23)–C(24)	108.1(8)	C(23)–C(24)–C(25)	121.6(8)
C(23)–C(24)–C(29)	119.1(7)	C(25)–C(24)–C(29)	118.8(8)
C(24)–C(25)–C(26)	118.4(9)	N(2)–C(26)–C(25)	118.3(8)
N(2)–C(26)–C(27)	118.8(8)	C(25)–C(26)–C(27)	122.7(8)
C(26)–C(27)–C(28)	119.5(9)	C(27)–C(28)–C(29)	118.1(8)
C(27)–C(28)–C(30)	122.3(8)	C(29)–C(28)–C(30)	119.4(7)
C(24)–C(29)–C(28)	122.0(7)	C(3)–C(30)–C(28)	111.4(8)

Table 2 Distances (Å) between the H_{eq}[a] and the adjacent aromatic hydrogens $H_{1,2}$ in **5** calculated from NMR data[b] and X-ray analysis[c]

H^1–H_{eq}	2.3[b]	2.4[c]
H^2–H_{eq}	2.7[b]	2.7[c]

[a] H_{eq} are the equatorial calix[4]arene bridging methylene hydrogens.
[b] Determined by NOESY spectroscopy in $C_2D_2Cl_4$ at 243 K, ±0.2 Å.
[c] Calculated, averaged distances from the X-ray structure analysis.

due to a cooperative effect. For comparison, the dimerization constant for benzoic acid in $CHCl_3$ is 400 dm³ mol⁻¹.[13] The cooperative effect may be due to a large positive entropic contribution as we recently discussed for the self-association of diuracil containing calix[4]arenes.[14] Concentration dependent FTIR studies clearly demonstrated the presence of the dimeric structure of **5**. Both at 2.0×10^{-3} and 2.0×10^{-4} M in $CHCl_3$ a characteristic absorption at 1700 cm⁻¹ (C=O) was present pointing to dimer formation;[13] no signal of the monomer (expected at *ca.* 1725 cm⁻¹)[13] could be observed.

The ¹H NMR spectrum of the corresponding monocarboxylic acid reference derivative **4** shows conformational mobility in $CDCl_3$ (time-averaged structure). The aromatic hydrogens of the NO_2- and the CO_2H-substituted rings are almost at the same position (δ_H 7.49 and 7.41, respectively). For the mono-acid **4**, a conformational restriction (pinched cone conformation) is not a prerequisite for dimerization.

In $(CD_3)_2SO$ as a hydrogen bond breaking solvent (consequently no dimer formation is possible) the calix[4]arenedicarboxylic acid **5** shows a different pinched cone conformation (Fig. 2).¶ The ¹H NMR spectrum of calix[4]arenedicarboxylic acid **5** in $(CD_3)_2SO$ at room temperature exhibits the signal for the aromatic hydrogens of the carboxylic acid phenyl rings downfield shifted to δ_H 7.91 (*cf.* 6.75 in CD_2Cl_2), while the aromatic protons of the nitro phenyl rings are positioned at δ_H 6.86 (*cf.* 8.14 in CD_2Cl_2).‖** The OCH_2 hydrogen resonances are 0.28 ppm apart. Variable temperature ¹H NMR experiments with **5** in $(CD_3)_2SO$ show no pinched cone interconversion in a range of +20 to +115 °C ($\Delta\Delta\delta_H \cong 0.1$).

We explain the presence of this different pinched cone conformation of monomeric calix[4]arenedicarboxylic acid **5** (solvent induced stabilization) to a combination of two effects: (*i*) a more favourable solvation (hydrogen bonding) of the carboxylic acid groups by the Me_2SO molecules when the respective aromatic units are oriented in a 'flattened' position, and (*ii*) a preferred 'parallel' orientation of the NO_2-aromatic units in Me_2SO as a solvent.

The ¹H NMR spectrum of monocarboxylic acid **4** in $(CD_3)_2$-SO indicates that the aromatic unit bearing the carboxylic acid group prefers a 'flattened' orientation due to the low-field shift (δ_H 7.72, *cf.* δ_H 7.49 in $CDCl_3$) like calix[4]arenedicarboxylic acid **5**, but less pronounced.

formational studies.[5,6] Also the chemical shifts of the OCH_2 hydrogens, which are 0.44 ppm apart, are in agreement with the pinching in CD_2Cl_2.[6]

Variable temperature ¹H NMR experiments with **5** in a range of +20 to +115 °C in $C_2D_2Cl_4$ show no chemical shifts, implying that the pinched cone conformation and consequently the dimeric structure of **5** is stable up to at least 115 °C in solution. Corresponding behaviour of the pinched cone conformation has been observed for 5,17-bis[*N'*-(*R*)-ureido]25,26,27,28-tetrakis[(ethoxycarbonyl)methoxy]calix[4]arenes which proved to be stable in $C_2D_2Cl_4$ up to at least 120 °C.[6] Also dilution experiments of the calix[4]arenedicarboxylic acid **5** in CD_2Cl_2 (from 0.6×10^{-2} to 1.2×10^{-4} M) show no shifts in the ¹H NMR spectra which is in agreement with a high dimerization constant

¶ Arduini *et al.* reported that a related dicarboxylic acid is conformationally mobile in CD_3OD as a hydrogen bond breaking solvent.[5]
‖ The chemical shifts of the aromatic protons of reference compound 2,6-dimethyl-4-nitro-1-propoxybenzene in $CDCl_3$ or $(CD_3)_2SO$ as a solvent differ only very little ($\Delta\delta_H \leqslant 0.03$) in the ¹H NMR spectra. The difference in chemical shifts of the same aromatic protons in the carboxylic acids **4** and in **5** are the result of the shielding effects of the opposite aromatic rings in a pinched cone conformation.
** Also in the ¹H NMR spectrum of 1,3-dinitrocalix[4]arene **1** in $(CD_3)_2SO$, the respective high-field shift indicates that the NO_2-aromatic rings (δ_H 6.99) are in close proximity, more than in $CDCl_3$ solution (δ_H 7.42, time-averaged structure in $CDCl_3$).

Conclusions

For the first time, the solid state structure of a calix[4]arene dimer **5·5** hydrogen bonded *via* the upper rim could be confirmed by X-ray structure determination. The calix[4]arene units of the self-assembled dimer adopt a pinched cone conformation in the solid state.

Further, we have demonstrated that in chlorinated hydrocarbons the calix[4]arenedicarboxylic acid **5** is present as a dimer. Calix[4]arenedicarboxylic acid **5** adopts the same pinched cone conformation, as was determined by X-ray structure analysis, due to intermolecular hydrogen bonding between the carboxylic acid functions. The conformation is stable up to at least 115 °C in C$_2$D$_2$Cl$_4$.

In (CD$_3$)$_2$SO as a solvent the 'reversed' pinched cone conformation for the monomeric calix[4]arenedicarboxylic acid **5** was observed (solvent induced stabilization). Also this conformation showed no interconversion in a range of +20 to +115 °C in solution.

Experimental

General

Melting points were determined using an electrothermal apparatus and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker spectrometers at 250 and 400 MHz with SiMe$_4$ as an internal standard. Chemical shifts are reported in ppm (δ). J_H values are given in Hz. The assignments of the respective aromatic hydrogens of **5** in CD$_2$Cl$_2$ or (CD$_3$)$_2$SO as a solvent were performed by HMQC and HMBC NMR experiments. NOESY, HMQC, HMBC and temperature-dependent ^{1}H NMR spectra were recorded on the 400 MHz spectrometer. FAB mass spectra were recorded with a Finnigan MAT90 using *m*-nitrobenzyl alcohol (NBA) or *o*-nitrophenyl octyl ether (ONPOE) as a matrix. FTIR spectra were recorded with a BIO-RAD FTS-60 spectrophotometer. CHCl$_3$ was obtained from Merck (Uvasol). Commercial CH$_2$Cl$_2$ was distilled over CaCl$_2$ and then stored for at least 3 h over molecular sieves (3 Å). All other solvents and chemicals were used without purification. Analytical TLC were performed on precoated silica plates (SiO$_2$, Merck, 60F$_{254}$). Silica gel (particle size 0.040–0.063 mm, 230–240 mesh) was obtained from Merck. All reactions were carried out under an argon atmosphere. For convenience the name calix[4]arene is used instead of the more systematic name pentacyclo[19.3.1.1^{3,7}.1^{9,13}.1^{15,19}]octacosa-1(25),3,5,7(28),9,11, 13(27),15,17,19(26),21,23-dodecaene. Before the elemental analysis the samples were dried overnight over P$_2$O$_5$ at 80 °C *in vacuo*.

5,17-Dinitro-25,26,27,28-tetrapropoxycalix[4]arene 1

5,17-Dinitro-25,26,27,28-tetrapropoxycalix[4]arene was prepared from tetrapropoxycalix[4]arene as described in ref. 8. δ_H-(250 MHz; CDCl$_3$) 7.42 (4 H, s, ArH-NO$_2$), 6.73 (6 H, s, ArH), 4.47 (4 H, d, *J* 13.7, ArCH$_2$Ar), 3.91 and 3.86 (8 H, 2t, *J* 7.2 and 7.9, OCH$_2$), 3.24 (4 H, d, *J* 13.7, ArCH$_2$Ar), 1.96–1.85 (8 H, m, OCH$_2$C*H*$_2$CH$_3$), 1.03 and 0.97 (12 H, 2t, *J* 7.5 and 7.2, OCH$_2$-CH$_2$C*H*$_3$); δ_H[250 MHz; (CD$_3$)$_2$SO], 7.20 (4 H, d, *J* 7.3, ArH), 7.02–6.99 (2 H, m, ArH), 6.99 (4 H, s, ArH-NO$_2$), 4.38 (4 H, d, *J* 13.5, ArCH$_2$Ar), 3.95 and 3.81 (8 H, 2t, *J* 7.6 and 6.4, OCH$_2$), 3.39 (4 H, d, *J* 14.2, ArCH$_2$Ar), 1.89–1.83 (8 H, m, OCH$_2$-C*H*$_2$CH$_3$), 1.09 and 0.91 (12 H, 2t, *J* 7.2 and 7.1, OCH$_2$CH$_2$-C*H*$_3$).

Formylation of calix[4]arenes

A solution of dinitrocalix[4]arene **1** (0.68 g, 1.0 mmol) in CH$_2$Cl$_2$ (25 cm^3) was rapidly added to a mixture of α,α-dichloromethyl methyl ether (1.15 cm^3, 13 mmol) and freshly distilled TiCl$_4$ (0.53 cm^3, 4.8 mmol) in CH$_2$Cl$_2$ (25 cm^3) at -10 °C, and was stirred for 30 min at this temperature. The reaction was quenched by addition of a mixture of 2 M HCl (30 cm^3) and MeOH (30 cm^3). The organic layer was separated,

washed with water to neutrality, dried over Na$_2$SO$_4$, and evaporated to dryness.

5,17-Dinitro-25,26,27,28-tetrapropoxycalix[4]arene-11-carbaldehyde 2

The crude product was purified by flash column chromatography (SiO$_2$; CH$_2$Cl$_2$–ethyl acetate, 99.5 : 0.5) to give calix[4]arene **2** as a light-yellow powder (0.59 g, 84%), mp 215–216 °C (from CH$_2$Cl$_2$)(Found: C, 69.48; H, 6.61; N, 4.26. Calc. for C$_{41}$H$_{46}$N$_2$O$_9$: C, 69.28; H, 6.52; N, 3.94%); δ_H(250 MHz; CDCl$_3$) 9.65 (1 H, s, CHO), 7.57 (4 H, 2d, *J* 4.7, ArH-NO$_2$), 7.11 (2 H, s, Ar*H*-CHO), 6.55 (3 H, s, ArH), 4.51 and 4.46 (4 H, 2d, *J* 13.7 and 13.5, ArCH$_2$Ar), 4.01–3.78 (8 H, m, OCH$_2$), 3.34 and 3.27 (4 H, 2d, *J* 14.0 and 13.8, ArCH$_2$Ar), 1.97–1.82 (8 H, m, OCH$_2$C*H*$_2$CH$_3$), 1.04–0.97 (m, 12 H, OCH$_2$CH$_2$C*H*$_3$); δ_C-(62.5 MHz; CDCl$_3$) 191.0 (CHO), 162.2, 161.6 and 156.1 (ArC-O), 142.5 (ArC-NO$_2$), 136.8, 135.8, 135.0, 133.7, 131.5, 130.3, 128.7, 124.1, 123.5 and 123.0 (ArC and ArCH), 77.4 and 77.3 (ArOCH$_2$), 31.0 (ArCH$_2$Ar), 23.3 and 23.2 (OCH$_2$-C*H*$_2$CH$_3$), 10.3 and 10.2 (OCH$_2$CH$_2$C*H*$_3$); *m*/*z* (FAB, NBA) 711.8 [(M + H)$^+$, 100%].

5,17-Dinitro-25,26,27,28-tetrapropoxycalix[4]arene-11,23-dicarbaldehyde 3

5,17-Dinitro-25,26,27,28-tetrapropoxycalix[4]arene-11,23-dicarbaldehyde was prepared as described for compound **2** starting from calix[4]arene **1** (0.68 g, 1.0 mmol) using TiCl$_4$ (1.36 cm^3, 12.4 mmol) and α,α-dichloromethyl methyl ether (2.30 cm^3, 26 mmol). The crude product was purified by flash column chromatography (SiO$_2$; CH$_2$Cl$_2$–ethyl acetate, 99.5 : 0.5) to give dialdehyde **3** as a light-yellow powder (0.71 g, 96%); mp 299–301 °C (decomp.) (Found: C, 68.56; H, 6.47; N, 3.82. Calc. for C$_{42}$H$_{46}$N$_2$O$_{10}$: C, 68.28; H, 6.28; N, 3.79%); δ_H(250 MHz; CDCl$_3$) 9.55 (2 H, s, CHO), 7.61 (4 H, s, ArH-NO$_2$), 7.10 (4 H, s, Ar*H*-CHO), 4.50 (4 H, d, *J* 13.9, ArCH$_2$Ar), 3.97 and 3.90 (8 H, 2t, *J* 7.5 and 7.4, OCH$_2$), 3.36 (4 H, d, *J* 14.0, ArCH$_2$Ar), 2.04–1.83 (8 H, m, OCH$_2$C*H*$_2$CH$_3$), 1.01 and 1.00 (12 H, 2t, *J* 7.5 and 7.4, OCH$_2$CH$_2$C*H*$_3$); δ_C(62.5 MHz; CDCl$_3$) 191.0 (CHO), 161.5 and 162.1 (ArC-O), 142.7 (ArC-NO$_2$), 136.0, 134.9, 131.7, 130.2 and 124.0 (ArC and ArCH), 77.4 and 77.0 (ArOCH$_2$), 31.0 (ArCH$_2$Ar), 23.3 (OCH$_2$C*H*$_2$CH$_2$), 10.2 and 10.1 (OCH$_2$CH$_2$C*H*$_3$); *m*/*z* (FAB, NBA) 739.6 [(M + H)$^+$, 100%].

5,17-Dinitro-25,26,27,28-tetrapropoxycalix[4]arene-11-carboxylic acid 4

To a solution of calix[4]arene **2** (178 mg, 0.25 mmol) in a mixture of chloroform (20 cm^3) and acetone (20 cm^3) was added a solution of sulfamic acid (100 mg, 1.02 mmol) and NaClO$_2$ (80 mg, 0.87 mmol) in water (1 cm^3). The mixture was vigorously stirred at room temp. for 6 h. The solvents were completely evaporated, the residue was taken up with HCl (10%, 10 cm^3), filtered, and dried *in vacuo* to give monocarboxylic acid **4** as a light-yellow powder (176 mg, 97%); mp >320 °C (Found: C, 67.11; H, 6.43; N, 3.84. Calc. for C$_{41}$H$_{46}$N$_2$O$_{10}$·0.25H$_2$O: C, 67.34; H, 6.41; N, 3.83%); δ_H(400 MHz; CDCl$_3$) 7.49 (4 H, s, ArH-NO$_2$), 7.41 (2 H, s, Ar*H*-CO$_2$H), 6.64 (3 H, s, ArH), 4.50 and 4.47 (4 H, 2d, *J* 13.9 and 14.4, ArCH$_2$Ar), 3.96–3.87 (6 H, m, OCH$_2$), 3.83 (2 H, t, *J* 7.4, OCH$_2$) 3.31 and 3.24 (4 H, 2d, *J* 14.0 and 13.8, ArCH$_2$Ar), 1.94–1.85 (8 H, m, OCH$_2$C*H*$_2$CH$_3$), 1.02–0.96 (12 H, m, OCH$_2$CH$_2$C*H*$_3$); δ_H[250 MHz; (CD$_3$)$_2$SO] 12.75 (1 H, s, CO$_2$H), 7.72 (2 H, s, Ar*H*-CO$_2$H), 7.10–7.08 (6 H, m, ArH-NO$_2$ and ArH), 6.91 (1 H, t, *J* 7.2, ArH), 4.38 (4 H, d, *J* 13.7, ArCH$_2$Ar), 4.01 (2 H, t, *J* 7.2, OCH$_2$), 3.95–3.81 (6 H, m, OCH$_2$), 3.54 and 3.41 (4 H, 2d, *J* 13.8 and 14.2, ArCH$_2$Ar), 1.92–1.83 (8 H, m, OCH$_2$C*H*$_2$CH$_3$), 1.07 and 0.92 (12 H, 2t, *J* 7.3, OCH$_2$CH$_2$C*H*$_3$); δ_C(62.5 MHz; CDCl$_3$) 171.3 (CO$_2$H), 162.0, 161.2 and 156.2 (ArC-O), 142.5 (ArC-NO$_2$), 136.6, 135.7, 134.6 and 133.9 (ArC), 131.0, 128.9 and 123.9 (ArCH), 123.8 (ArC), 123.4 and 123.1 (ArCH), 77.4 (ArOCH$_2$), 31.1

(ArCH$_2$Ar), 23.3 and 23.2 (OCH$_2$CH$_2$CH$_3$), 10.2 (OCH$_2$-CH$_2$CH$_3$); m/z (FAB, ONPOE, negative) 725.5 [(M − H)$^-$, 100%], 1451.6 [(2M − H)$^-$, 5%].

5,17-Dinitro-25,26,27,28-tetrapropoxycalix[4]arene-11,23-dicarboxylic acid 5

5,17-Dinitro-25,26,27,28-tetrapropoxycalix[4]arene-11,23-dicarboxylic acid was prepared as described for compound **4** starting from calix[4]arene **3** (185 mg, 0.25 mmol). The procedure was performed twice to afford dicarboxylic acid **5** as a light-yellow powder (183 mg, 95%); mp >320 °C (Found: C, 65.15; H, 6.06; N, 3.74. Calc. for C$_{42}$H$_{46}$N$_2$O$_{12}$: C, 65.44; H, 6.02; N, 3.63%); δ_H(400 MHz; CD$_2$Cl$_2$) 12.65 (2 H, s, CO$_2$H), 8.14 (4 H, s, ArH-NO$_2$), 6.75 (4 H, s, ArH-CO$_2$H), 4.47 (4 H, d, J 13.9, ArCH$_2$Ar), 4.14 and 3.70 (8 H, 2t, J 8.1 and 6.7, OCH$_2$), 3.34 (4 H, d, J 14.0, ArCH$_2$Ar), 1.92–1.85 (8 H, m, OCH$_2$-CH_2CH$_3$), 1.09 and 0.87 (12 H, 2t, J 7.3 and 7.4, OCH$_2$-CH$_2$CH_3); δ_H(400 MHz; (CD$_3$)$_2$SO) 12.45 (2 H, s, CO$_2$H), 7.91 (4 H, s, ArH-CO$_2$H), 6.86 (4 H, s, ArH-NO$_2$), 4.36 (4 H, d, J 14.0, ArCH$_2$Ar), 4.04 and 3.76 (8 H, 2t, J 8.0 and 6.8, OCH$_2$), 3.52 (4 H, d, J 14.0, ArCH$_2$Ar), 1.92–1.82 (8 H, m, OCH$_2$-CH_2CH$_3$), 1.08 and 0.87 (12 H, 2t, J 7.2, OCH$_2$CH$_2$CH_3); δ_C-(62.5 MHz; CD$_2$Cl$_2$) 171.7 (CO$_2$H), 164.1 and 160.5 (ArC-O), 142.9 (ArC-NO$_2$), 137.9 and 133.2 (ArC), 130.2 and 125.1 (ArCH), 123.9 (ArC), 77.9 and 77.8 (ArOCH$_2$), 31.3 (ArCH$_2$Ar), 23.9 and 23.6 (OCH$_2$CH$_2$CH$_3$), 11.0 and 9.9 (OCH$_2$CH$_2$CH$_3$); m/z (FAB, ONPOE, positive) 753.2 [(M − OH)$^+$, 100%], 1538.9 [2M + H)$^+$, 4%]; m/z (FAB, NBA, positive) 793.7 [(M + Na)$^+$, 100%].

X-Ray crystallography

Crystal data for 5. C$_{42}$H$_{46}$N$_2$O$_{12}$·3CHCl$_3$·CH$_2$Cl$_2$. M = 1213.90. Triclinic, space group $P\bar{1}$, a = 13.166(3), b = 13.296(3), c = 17.221(2) Å, α = 69.40(1), β = 76.13(2), γ = 77.41(2)°, V = 2710(1) Å^3 found by least-squares treatment (SET4) of 25 centred reflections with 10.17° < θ < 13.79°, λ = 0.710 73 Å; Z = 2, D_c = 1.488 g cm^{-3}. Colourless plate shaped (twinned) crystal, crystal decomposition by contact with air due to the loss of the cocrystallized solvent molecules. Crystal dimensions: 0.18 × 0.65 × 0.65 mm, μ(Mo-Kα) = 6.2 cm^{-1}.

Data collection and processing. X-Ray data were collected for an inert-oil-covered fresh crystal taken from the mother liquor and transferred directly into the cold nitrogen stream of a CAD4T diffractometer with rotating anode, ω-scan mode with ω = (0.97 + 0.35 tan θ)°, graphite-monochromated Mo-Kα radiation; 9278 reflections (T = 150 K, 1.28 < θ < 25.35°; h 0 to 15; k −14 to 15; l −20 to 19) were collected for one of the twin-lattices and were corrected for a linear decay (18% during 27 h of the X-ray exposure time) of the intensity control reflections and for absorption (DIFABS)[15] and merged into a dataset of 8852 unique reflections.

Structure analysis and refinement. Structure solved with direct methods (SIR-96).[16] Full-matrix least-squares refinement on F^2 with all 8852 unique reflections and 652 parameters with all non-hydrogen and non-disordered atoms anisotropic. Atoms C(38) and C(39) were found to be disordered in a 0.56(3):0.44(3) ratio; in view of the limited quality of the data, these atoms were refined with isotropic thermal parameters. H-atoms were included on calculated positions and refined in riding mode with thermal parameters related to the U_{eq} of their carrier atoms. The slight non-linearity in the carboxy bridge is probably a refinement artefact. Final R_1 [$\Sigma(|F_o| − |F_c|)/\Sigma|F_o|$] for 4257, F_o > 4σ(F_o) = 0.1241, wR_2 {$\Sigma[w-(F_o{}^2 − F_c{}^2)^2]/\Sigma[w(F_o{}^2)^2]$}$^{0.5}$ for the 8852 refined reflections = 0.3685 and S {$\Sigma[w(F_o{}^2 − F_c{}^2)^2]/(n − p)$}$^{0.5}$ = 1.128; weighting scheme: w = 1/[$\sigma^2(F_o{}^2)$ + (0.2 P)^2] with P = [$F_o{}^2$ + 2$F_c{}^2$]/3; F_o from counting statistics. Neutral-atom scattering factors and anomalous dispersion factors were taken from ref. 17. All calculations were performed with SHELXL-96[18] and the PLATON[19] package (geometrical calculations and illustrations) on a DEC-5000 cluster.††

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