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Conformational properties of cyanomethoxy calix[4]arenes†

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Received 2nd June 2005, Accepted 2nd August 2005
First published as an Advance Article on the web 5th September 2005

O-Alkylation of the dinitro calix[4]arene **2**, easily available by selective *ipso*-nitration of the di-cyanomethyl ether **1**, with allylbromide (DMF/Cs_2CO_3) gave tetraethers **3** and **4** with *anti*- and *syn*-orientations of the two allyl ether residues. The two possible stereoisomers of **3** in the *partial cone* and 1,2-*alternate* conformation exist as an equilibrium mixture which could be quantitatively analysed by ^1H NMR spectroscopy. The temperature dependence of this equilibrium leads to $\Delta H_0 = -7.6$ to -9.7 kJ mol^{-1} in different solvents (tetrachloroethane, benzene, dimethylsulfoxide). Since **3**(**1,2-*alt***) could be obtained in pure form, its isomerisation to the equilibrium mixture with **3**(***paco***) could be followed also kinetically. An activation energy of $E_a = 110.5$ kJ mol^{-1} was found for this reaction in DMSO-d_6. The results were confirmed by similar studies with tetraethers **5** and **6** obtained by *O*-allylation of **1**, although exact thermodynamic and kinetic studies were not possible in this case, since the NMR signals of the respective isomers were strongly overlapping. Single crystal X-ray structures were obtained for **2**, **3**(**1,2-*alt***), **4**(***paco***) and **5**(**1,2-*alt***).

Introduction

Calixarenes, bearing aminoalkoxy groups at the narrow rim (aminoalkyl ethers), are versatile platforms to attach various further residues, *e.g. via* amide,[1] urea[2] or azomethine[3] links. They may be prepared by *O*-alkylation with *N*-(ω-bromoalkyl) phthalimides[4] or ω-bromonitriles,[5] followed by hydrazinolysis or reduction. To obtain aminoethyl ethers the alkylation is restricted to bromoacetonitrile, since elimination (followed by further reactions) occurs with bromoethyl phthalimide under alkaline conditions.[6,7] For the synthesis of calix[4]arenes fixed in the 1,3-*alternate* conformation and bearing four amino groups at one side of the molecule we recently developed a strategy[8] which involves the selective *ipso*-nitration of the phenolic units of a 1,3-diether formed in a first *O*-alkylation step from *tert*-butylcalix[4]arene. To fix a tetraether in the 1,3-*alternate* conformation, caesium carbonate Cs_2CO_3 is usually recommended as base. While the Cs cations shift the conformation towards 1,3-*alternate* due to favorable cation–π interactions the carbonate as a weak base requires in turn a reactive *O*-alkylating agent, due to the lower nucleophilicity of the *p*-nitrophenol units. This was found in allylbromide, and the allyl ether groups thus introduced could be easily (and simultaneously) converted to propyl ether groups during the hydrogenation of the nitro groups. Applying this reaction sequence to the *syn* 1,3-di(cyanomethyl)ether **1** as starting material,[9] we were surprised by the fact that the resulting tetraethers are conformationally unstable. In contrast to early reports in the literature,[10] the cyanomethoxy group obviously can pass the annulus of the calix[4]arene skeleton. In the following we report details for this conformational interconversion.

Synthesis

Pure **1** was obtained in 55% from *tert*-butylcalix[4]arene by reaction with excess (4 mole) chloroacetonitrile in refluxing acetone in the presence of K_2CO_3–KI. Tri-*O*-alkylated products were identified as main side products by MS-FAB. *ipso*-Nitration led in 37% (not optimized) to the desired dinitro derivative **2**. Its ^1H NMR spectrum clearly proves the *cone* conformation of the *syn* isomer for this compound, *e.g.* by the presence of two singlets for aromatic protons, one singlet for O–CH_2–CN groups and a single pair of doublets for the Ar–CH_2–Ar bridges. A single crystal X-ray structure obtained for **2** adds further evidence, although it is not a proof for the conformation in solution. The subsequent *O*-alkylation with allylbromide in DMF using Cs_2CO_3 as base led to a mixture of at least three compounds according to TLC. Slow crystallization from $CHCl_3$–methanol led to single crystals of an isomer **3** in the 1,2-*alternate* conformation with an *anti*-orientation of the allyl ether residues (like in the *partial cone* isomer usually formed as a side product during the synthesis of 1,3-*alternate* tetraethers). After several days 34% of **3**(**1,2-*alt***) could be collected by filtration. Further single crystals formed afterwards in the filtrate which were identified as the isomer **4** with a *partial cone* conformation (**4**(***paco***)). Here the newly introduced allyl ether residues have the *syn*-orientation relative to each other, the orientation required for the requested 1,3-*alternate* conformer. This means that in both compounds the cyanomethyl ether residues have changed from *syn* to *anti*. Since cleavage and reformation of ether groups seems unlikely as an explanation, one of these cyanomethyl ether residues must have passed through the annulus during the synthesis or the subsequent work up. Larger amounts of pure **4**(***paco***) could not be obtained. 18% of crystalline material isolated after several days consisted of a mixture with **4** in the cone conformation (**4**(**cone**)), while the desired 1,3-*alternate* conformer of **4** was not obtained. Repeated *O*-alkylations of **2** led to analogous results, although the amounts of isolated fractions differed. Evaporation of the mother liquor after the isolation of 12% **3**(**1,2-*alt***) gave a residue of about 75–80% of a mixture, which according to the ^1H NMR spectrum in $CDCl_3$ contained about 9% **3**(**1,2-*alt***), 44% **3**(***paco***), 20% **4**(***cone***), and 20% **4**(***paco***). Some remaining signals might be interpreted as **4**(**1,3-*alt***), which means that overall the 1,3-*alternate* isomer is formed as 5% or less.

These synthetic results are summarized in Scheme 1. When the *O*-alkylation with allylbromide was carried out with **1** under the same conditions a similar result was obtained. 11% of the

† In memory of our colleague and friend Libor Mikulášek.

DOI: 10.1039/b507780j

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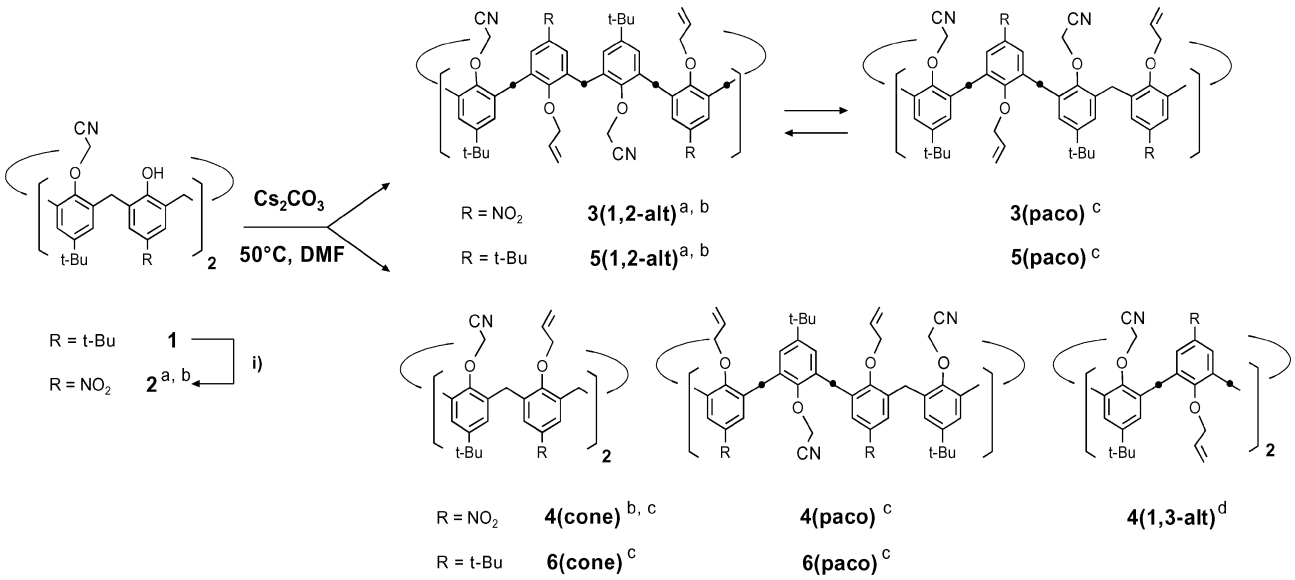

Scheme 1 Synthesis of tetra-*O*-alkylated derivatives **3** and **5** (*anti*-orientation of the allyl ether groups) and **4** and **6** (*syn*-orientation of the allyl ether groups): [a] isolated as pure compounds; [b] single crystals; [c] isolated as binary mixture only; [d] deduced from NMR signals in a complex mixture.

1,2-*alternate* isomer **5(1,2-*alt*)** could be isolated in pure form by recrystallization, while the mother liquor contained 68% of the *partial cone* and *cone* isomers **6(*paco*)** and **6(*cone*)** in this case. The absence of the nitro groups led to a stronger overlap of signals in this case, and hence to a lower accuracy in the determination of concentration ratios.

Conformational studies

The ^{1}H NMR spectra of **3(1,2-*alt*)** in different solvents (C_6D_6, TCE-d_2, DMSO-d_6) are entirely in agreement with the 1,2-*alternate* conformation found in the crystalline state (see Fig. 1, in C_6D_6, for instance). Especially characteristic are two pairs of doublets with geminal coupling for the methylene protons, which appear as an AX system ($\delta = 2.99/4.01$) for the Ar–CH_2–Ar bridges between *syn*-oriented aromatic units and as an AB system ($\delta = 3.38/3.45$) for those between *anti*-oriented units. Also the aromatic protons appear as *m*-coupled doublets ($\delta = 6.89/7.08$ and $7.78/7.95$ respectively) for the *tert*-butyl- and nitrophenyl rings, respectively (Fig. 1a). After short time already a second set of signals appears, increasing with the time until an equilibrium is reached (Fig. 1b). These signals can be attributed to the *partial cone* isomer **3(*paco*)** obtained by rotation of the cyanomethyl group through the annulus. Most characteristic are here the aromatic protons, two singlets for the nitrophenyl units ($\delta = 7.78/8.04$) and two *m*-coupled doublets for the *tert*-butyl phenol units ($\delta = 6.75/6.89$). The signals for the two conformational isomers are partly overlapped, but the spectra allow us to determine the ratio of the two isomers, the equilibrium constant K, by simple integration.

$$\mathbf{3(1,2\text{-}alt)} \underset{k_{II}}{\overset{k_I}{\rightleftharpoons}} \mathbf{3(paco)} \quad K = \frac{c(paco)}{c(1,2\text{-}alt)} \qquad (1)$$

This has been done for three different solvents as a function of the temperature.[11] The results are graphically shown in Fig. 2, according to eqn (2).

$$\ln K = -\Delta G_0/RT = -\Delta H_0/RT + \Delta S_0/R \qquad (2)$$

From the slope and the intercept the standard enthalpy ΔH_0 and entropy ΔS_0 for the isomerization (1) can be derived. These values are collected in Table 1. The formation of the *partial cone* conformer from the 1,2-*alternate* conformer is exothermic, but entropically disfavored.

Since the 1,2-*alternate* conformer **3(1,2-*alt*)** could be isolated in a pure crystalline form, its isomerization could be followed

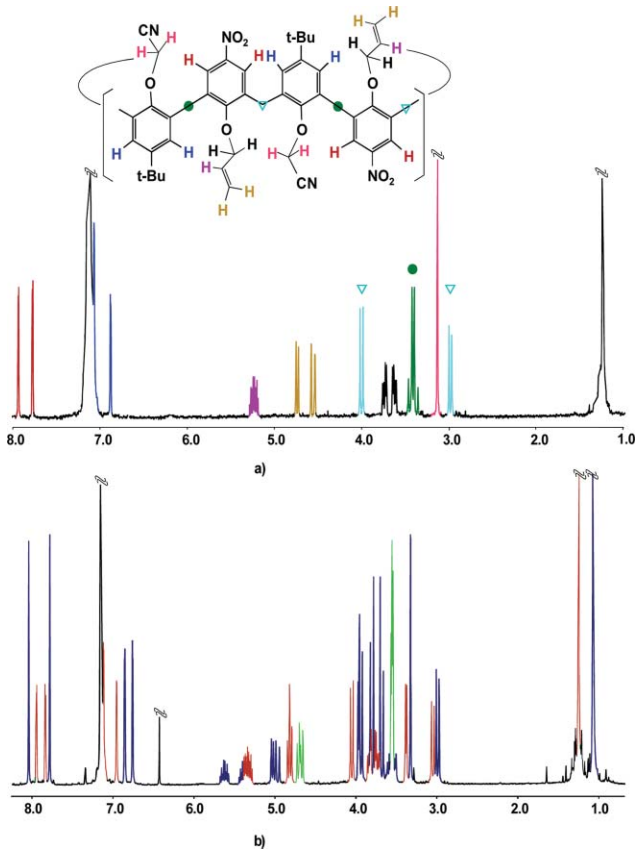

Fig. 1 ^{1}H-NMR spectrum of **3(1,2-*alt*)** in C_6D_6 at rt, immediately after dissolution (a); ^{1}H-NMR spectrum of the equilibrium mixture of **3(1,2-*alt*)** [red signals] and **3(*paco*)** [blue signals] in C_6D_6 at 75 °C; overlapping signals in green (b).

Table 1 The values of the standard enthalpy ΔH_0 and entropy ΔS_0 for the isomerization (1)

Solvent	ΔH_0/kJ mol^{-1}	ΔS_0/J K^{-1} mol^{-1}
TCE-d_2	−7.60	18.61
C_6D_6	−9.7	25.76
DMSO-d_6	−8.47	18.11

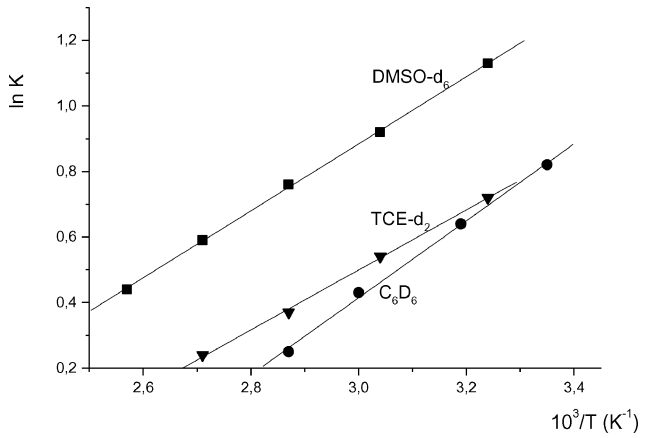

Fig. 2 Plot of ln K *vs.* $1/T$ for the equilibrium **3(1,2-*alt*)** ⇌ **3(*paco*)** in different solvents.

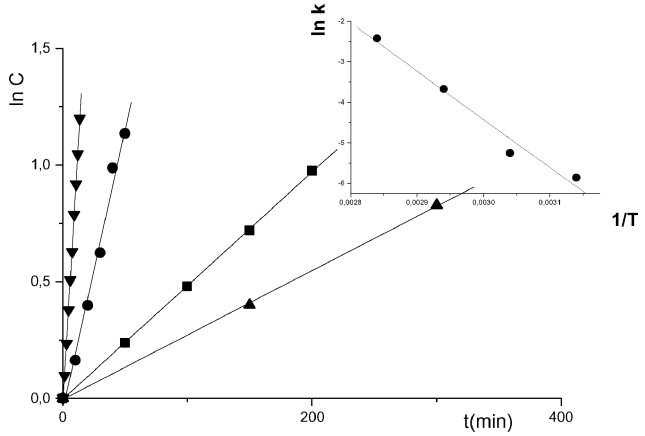

Fig. 3 First order plots for the conversion of **3(1,2-*alt*)** to the equilibrium mixture at different temperatures (▲ 45 °C, ■ 55 °C, ● 65 °C, ▼ 75 °C) and Arrhenius plot (insert) for k_1.

also kinetically by ^{1}H NMR spectroscopy. Fig. 3 shows first order plots for different temperatures.

From the apparent first order rate constant $k_{(1)} = k_I + k_{II}$ and the equilibrium constant $K = k_I/k_{II}$ the rate constant k_I for the conversion of **3(1,2-*alt*)** into **3(*paco*)** can be calculated. Fig. 3 (insert) shows an Arrhenius plot for k_1, which leads to an activation energy of $E_a = 110.5$ kJ mol^{-1}.

While the cyanomethoxy group was considered initially to be too large to pass the annulus of a calix[4]arene, conformational conversions involving this "passage" were reported more recently.[12,13] To the best of our knowledge, the present study is the first to give a quantitative thermodynamic description of such an equilibrium involving two conformers with *syn*- and *anti*-orientation of a cyanomethoxy group (and *anti*-orientation of the remaining ether groups, that is the allyl ether groups.) Kinetic studies for such a conversion were also not yet reported.

Two further questions we tried to address in this connection:

a) The first one is related to the conformational isomers with a *syn*-orientation of the allyl ether residues. Three isomers are possible here (*cone*, *partial cone*, 1,3-*alternate*), but as mentioned above, the presence of **4(1,3-*alt*)** was not unambiguously detected in the mixture. For the equilibrium **4(*cone*)** ⇌ **4(*paco*)** an equilibrium constant of $K = 2$ is found in C_6D_6. No significant change in K is detected between $T = 298$ K and $T = 323$ K. This means that ΔH_0 is close to zero in this case, if the unlikely assumption is excluded that the energy barrier E_a is too high in this case to shift the equilibrium in reasonable times.

b) As mentioned above, we were able to obtain also the 1,2-*alternate* isomer **5(1,2-*alt*)** in pure form. The equilibrium **5(1,2-*alt*)** ⇌ **5(*paco*)** cannot be studied as exactly/easily as in the case of **3**, where the presence of nitro groups leads to a stronger splitting of the (aromatic) signals in the ^{1}H NMR spectra. In $C_2D_2Cl_4$ (TCE-d_2) an equilibrium constant of $K = 1.24$ was determined at 115 °C, which corresponds to the value found for **3**. The replacement of *tert*-butyl by nitro groups obviously has no significant influence on the relative stability of these conformers.

X-Ray structures

Four compounds were further characterized by single crystal X-ray analysis. Essential geometrical parameters are collected in Table 2.

The dicyanomethoxy compound **2** (two crystallographically independent molecules) is found in the typical pinched *cone* conformation (Fig. 4a), which is stabilized by intramolecular –OH · · · O– hydrogen bonds. This is in agreement with the NMR data in solution, where no other conformers could be detected, although in principle all oxygen functions can pass the annulus, and these hydrogen bonds would be possible also for a 1,2-*alternate* conformer. As usual, the angle with the reference plane (defined by the carbon atoms of the methylene bridges) is larger for the phenolic units than for the phenol ether units (one of which is even perpendicular in one of the two molecules).

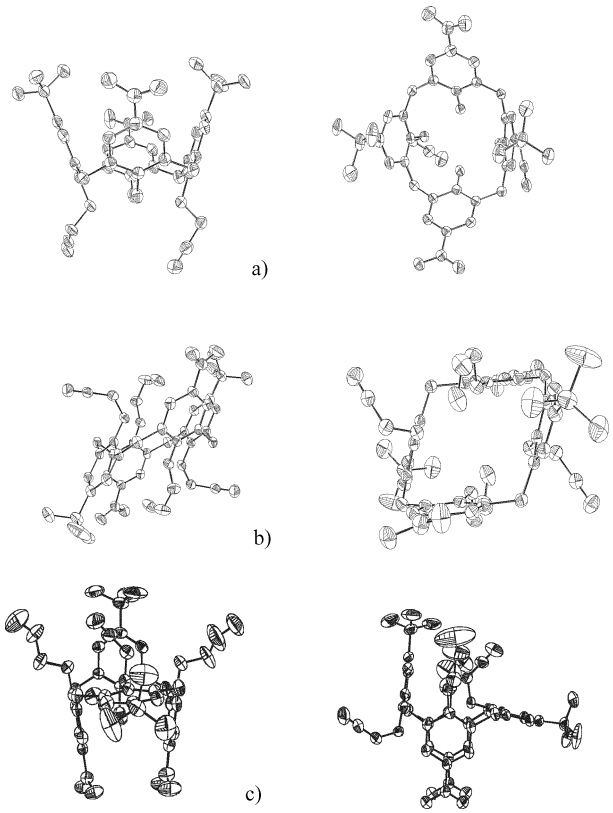

Fig. 4 Molecular conformation of: a) **2**, two independent molecules seen from different directions; b) **3(1,2-*alt*)**, seen from different directions; c) **4(*paco*)**, seen from different directions.

The regular packing of the 1,2-*alternate* conformers consisting of columns (or of perpendicular layers, respectively) in all three directions, is shown for **5(1,2-*alt*)** in Fig. 5. It may explain their preferred crystallization from the equilibrium mixture with the *partial cone* conformer, although the latter is present in excess.

For **4(*paco*)** a remarkable distortion of the *partial cone* conformation is observed. While the two nitrophenyl residues are bent inwards ($\delta < 90°$), one cyanomethoxy-*tert*-butyl ring lies nearly in the reference plane ($\delta = 169°$). The opposite "inverted" phenolic unit is nearly perpendicular to the reference plane ($\delta = 100°$, or 260° to express the inversion). The reference plane itself forms a regular square, as mentioned above.

Table 2 Selected crystallographic data: **I**) torsion angles (°) around the Ar–CH_2 bonds; **II**) distances within the reference plane, the best plane through the carbon atoms of the methylene bridges; **III**) Inclination δ (°) of the aromatic units with respect to the reference plane

	3(1,2-*alt*)	**5(1,2-*alt*)**	**4(*paco*)**	**2**[a]	**2**[a]
I. Torsion angles					
C12–C11–C1–C43	45.20	104.70	70.79	75.38	−75.12
C11–C1–C43–C42	41.62	−95.14	65.55	−96.78	118.72
C22–C21–C2–C13	−99.64	38.32	46.09	106.52	−97.99
C21–C2–C13–C12	99.22	51.98	−114.90	−85.21	92.57
C32–C31–C3–C23	−45.20	−104.70	118.21	74.93	−79.65
C31–C3–C23–C22	−41.62	95.14	−47.37	−95.86	107.11
C42–C41–C4–C33	99.64	−38.32	−68.90	107.02	−108.76
C41–C4–C33–C32	−99.22	−51.98	−70.02	−81.65	68.76
II. Reference planes C1–C4					
rmsd/Å	0	0	0.00825	0.0982	0.1223
Distance C1–C2/Å	5.093	5.128	5.060	5.099	5.083
Distance C2–C3/Å	5.127	5.101	5.079	5.089	5.089
Distance C3–C4/Å	5.093	5.128	5.060	5.105	5.080
Distance C1–C4/Å	5.127	5.101	5.028	5.095	5.102
Distance C1–C3/Å	7.764	6.681	7.162	7.408	7.038
Distance C2–C4/Å	6.647	7.746	7.133	6.992	7.335
III. Inclination of the aromatic units (δ)					
C11–C16[b]	118.8	−112.7	81.5	134.2	139.2
C21–C26[c]	−118.8	119.8	169.1	110.8	109.2
C31–C36[b]	118.8	−112.7	100.1	137.8	139.3
C41–C46[c]	−118.8	119.8	95.1	110.6	89.2

[a] Two crystallographically different/independent molecules. [b] Allyloxy or hydroxy and nitro or *tert*-butyl. [c] Cyanomethoxy and *tert*-butyl.

Experimental

5,17-Di-*tert*-butyl-11,23-dinitro-25,27-bis-cyanomethoxy-26,28-dihydroxy-calix[4]arene 2

Nitric acid (65%, 13 ml) was added with stirring to a cold (0 °C) solution of **1** (3.2 g, 4.3 mmol) in dry CH_2Cl_2 (130 ml). After 10 min the color changed from black–indigo to yellow and the reaction was complete. Water was added (100 ml) and the mixture was stirred for 30 min. After phase separation the organic phase was washed with water (3 × 100 ml) until a neutral pH was reached, dried ($MgSO_4$) and the solvent was evaporated. The residue was dissolved in chloroform (20 ml) and the pure product was obtained after twofold recrystallization from methanol (30 ml) as yellow powder (1.2 g, 37%). Mp 326–327 °C

^{1}H-NMR (300 MHz, $CDCl_3$) δ 0.93 (s, 18H, *t*-Bu), 3.61, 4.23 (2d, 8H, ^2J = 14.0 Hz, Ar–CH_2–Ar), 4.85 (s, 4H, –CH_2–CN), 6.82 (s, 4H, ArH), 7.01 (s, 2H, OH), 8.11 (s, 4H, ArH).

^{13}C-NMR (400 MHz, $CDCl_3$) $_\delta$ 30.93 (*t*-Bu, $C_{prim.}$), 31.45 (Ar–CH_2–Ar), 34.23 (*t*-Bu, $C_{quat.}$), 60.47 (O–CH_2–), 114.47 (*C*N–), 124.51, 126.82 (aromatic *C*H), 128.26, 130.38, 140.29, 148.74, 150.29, 158.33 (aromatic $C_{quat.}$).

5,17-Di-*tert*-butyl-11,23-dinitro-25,27-bis-cyanomethoxy-26,28-diallyloxy-calix[4]arene 3

A stirred suspension of dinitro calixarene **2** (0.56 g, 0.8 mmol) and Cs_2CO_3 (2.6 g, 8 mmol) in dry DMF (20 ml) was heated to 50 °C under nitrogen. After 1 h allylbromide (0.7 ml, 8 mmol) was added and the reaction mixture was kept under these conditions for 7 days. The DMF was removed under reduced pressure and the residue was treated with chloroform (15 ml) and water (50 ml). The organic phase was washed twice with water (2 × 50 ml), dried ($MgSO_4$) and the solvent was evaporated. TLC analysis of the residue showed the presence of three isomers (1,2-*alt*, *cone* and *paco*). Recrystallization from chloroform–methanol (10 ml, 1 : 4) gave single crystals of **3(1,2-*alt*)** and a white powder (0.21 g, 34%). From the mother liquor a mixture of **4(*cone*)** and **4(*paco*)** was isolated as yellow powder (0.1 g, 18%).

3(1,2-*alt*). Mp 236 °C; ^{1}H-NMR (400 MHz, C_6D_6) δ 1.24 (s, 18H, *t*-Bu), 3.05 (d, 2H, ^2J = 13.3 Hz, Ar–CH_2–Ar), 3.14 (s, 4H, –CH_2–CN), 3.39, 3.47 (2d, 4H, ^2J = 16.8 Hz, Ar–CH_2–Ar), 3.61–3.77 (m, 4H, –CH_2–CH=CH_2), 4.01 (d, 2H, ^2J = 13.2 Hz, Ar–CH_2–Ar), 4.55–4.77 (m, 4H, CH=CH_2), 5.20–5.30 (m, 2H, –*C*H=CH_2), 6.89, 7.08 (2d, 4H, ^4J = 2.3 Hz, Ar*H*), 7.78, 7.95 (2d, 4H, ^4J = 2.7 Hz, Ar*H*).

^{1}H-NMR (400 MHz, TCE-d_2) δ 1.30 (s, 18H, *t*-Bu), 3.05 (d, 2H, ^2J = 13.2 Hz, Ar–CH_2–Ar), 3.90, 3.94 (2d, 4H, ^2J = 16.2 Hz, Ar–CH_2–Ar), 4.01, 4.02 (2s, 4H, –CH_2–CN), 4.09 (m, 4H, –CH_2–CH=CH_2), 4.16 (d, 2H, ^2J = 13.2 Hz, Ar–CH_2–Ar), 4.77–4.90 (m, 4H, CH=CH_2), 5.47 (m, 2H, –*C*H=CH_2), 7.13, 7.21 (2s, 4H, Ar*H*), 8.05 (s, 4H, Ar*H*).

^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.29 (s, 18H, *t*-Bu), 3.40 (d, 2H, ^2J = 13.2 Hz, Ar–CH_2–Ar), 3.88–4.01 (m, 12H, –CH_2–CH=CH_2, –CH_2–CN, Ar–CH_2–Ar), 4.21 (d, 2H, ^2J = 13.2 Hz, Ar–CH_2–Ar), 4.77–4.90 (m, 4H, CH=CH_2), 5.48 (m, 2H, –*C*H=CH_2), 7.12, 7.22 (2d, 4H, ^4J = 2.2 Hz, Ar*H*), 8.05 (s, 4H, Ar*H*).

^{13}C-NMR (400 MHz, $CDCl_3$) after dissolution δ 30.13, 37.82 (Ar–CH_2–Ar), 31.36 (*t*-Bu, $C_{prim.}$), 34.38 (*t*-Bu, $C_{quat.}$), 57.20, 74.13 (O–CH_2–), 115.40 (*C*N–), 117.23 (CH_2=), 124.47, 126.50 126.66, 127.72, (aromatic *C*H), 130.71, 132.81, 134.14, 136.40, 143.09, 148.04, 151.17, 161.13 (aromatic $C_{quat.}$), 132.64 (*C*H=).

Although **3(*paco*)** was not isolated as a pure compound we can derive most of the proton signals in the ^{1}H-NMR spectrum shown by the equilibrium mixture of the *partial cone* and 1,2-*alternate* isomers of **3**.

3(*paco*). ^{1}H-NMR (400 MHz, C_6D_6) δ 1.07 (s, 18H, *t*-Bu), 2.99 (d, 2H, ^2J = 13.2 Hz, Ar–CH_2–Ar), 3.32, 3.325 (2s, 4H, –CH_2–CN), 3.67, 3.79 (2d, 4H, ^2J = 15.6 Hz, Ar–CH_2–Ar), 3.94 (d, 2H, ^2J = 13.2 Hz, Ar–CH_2–Ar), 4.94–5.05 (m, 4H, CH=CH_2), 5.41, 5.65 (2m, 2H, –*C*H=CH_2), 6.75, 6.89 (2d, 4H, ^4J = 2.2 Hz, Ar*H*), 7.78, 8.04 (2s, 4H, Ar*H*).

^{1}H-NMR (400 MHz, TCE-d_2) δ 1.02 (s, 18H, *t*-Bu), 3.27 (d, 2H, ^2J = 13.3 Hz, Ar–CH_2–Ar), 4.46, 4.47 (2d, 4H, ^2J = 15.6 Hz, Ar–CH_2–Ar), 5.48–5.58 (2m, 2H, –*C*H=CH_2), 6.72, 6.91 (2d, 4H, ^4J = 2.2 Hz, Ar*H*), 7.86, 8.13 (2s, 4H, Ar*H*).

^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.13 (s, 18H, *t*-Bu), 3.37 (d, 2H, ^2J = 12.9 Hz, Ar–CH_2–Ar), 4.45, 4.54 (2d, 4H, ^2J = 15.6 Hz, Ar–CH_2–Ar), 5.54–5.71 (2m, 2H, –*C*H=CH_2), 6.86, 7.01 (2d, 4H, ^4J = 2.2 Hz, Ar*H*), 7.92, 8.21 (2s, 4H, Ar*H*).

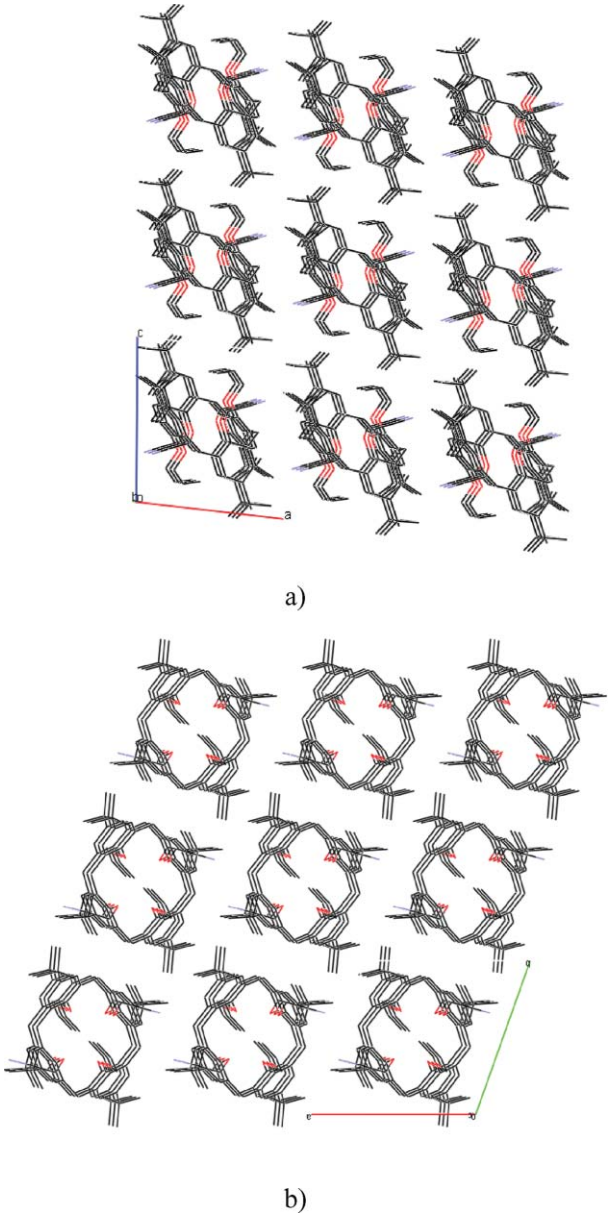

Fig. 5 Packing of **5**(**1,2-*alt***), seen along the *b*-axis (a) and along the *c*-axis (b).

For **4**(***cone***) and **4**(***paco***) only those peaks are listed which are essential and which can be unambiguously distinguished.

4(***cone***). ^{1}H-NMR (400 MHz, CD_2Cl_2) δ 1.41 (s, 18H, *t*-Bu), 3.37, 4.70 (2d, 8H, ^2J = 14.1, 13.7 Hz, Ar–CH_2–Ar), 6.29 (m, 2H, –CH=CH_2), 7.06, 7.32 (2s, 8H, ArH).

4(***paco***). ^{1}H-NMR (400 MHz, CD_2Cl_2) δ 1.36, 1.38 (2s, 18H, *t*-Bu), 3.31, 4.22 (2d, 4H, ^2J = 14.5 Hz, Ar–CH_2–Ar), 3.83, 3.86 (2d, 4H, ^2J = 13.7, 14.1 Hz, Ar–CH_2–Ar), 6.26 (m, 2H, –CH=CH_2), 7.21, 7.83 (2d, 4H, ^4J = 2.3 Hz, ArH), 7.23, 7.36 (2s, 4H, ArH).

5,11,17,23-Tetra-*tert*-butyl-25,27-bis-cyanomethoxy-26,28-diallyloxy-calix[4]arene 5

The reaction was carried out under the same conditions described above starting from 1,3-di-*O*-alkylated compound **1** (2 g, 2.75 mmol) in dry DMF (75 ml) and Cs_2CO_3 (9 g, 27.5 mmol). Recrystallization from chloroform–methanol gave single crystals of **5**(**1,2-*alt***) and a total of 0.23 g (11%). A white powder (1.5 g, 68%) consisting of a mixture of **6**(***cone***) and **6**(***paco***) was obtained from the mother liquor after slow evaporation of the solvent.

5 (1,2-*alt*). Mp 243–245 °C; ^{1}H-NMR (400 MHz, TCE-d_2) δ 1.30, 1.34 (2s, 36H, *t*-Bu), 3.30 (d, 2H, ^2J = 12.9 Hz, Ar–CH_2–Ar), 3.70, 3.91 (2d, 4H, ^2J = 16.0 Hz, Ar–CH_2–Ar), 3.93 (s, 2H, –CH_2–CN), 4.03 (m, 4H, –CH_2–CH=CH_2), 4.11 (d, 2H, ^2J = 12.5 Hz, Ar–CH_2–Ar), 4.72–4.86 (m, 4H, CH=CH_2), 5.49 (m, 2H, –CH=CH_2), 7.05, 7.12 (2d, 4H, ^4J = 2.3 Hz, ArH), 7.22, 7.24 (2d, 4H, ^4J = 2.3 Hz, ArH).

^{13}C-NMR (400 MHz, $CDCl_3$) after dissolution δ 30.04, 38.46 (Ar–CH$_2$–Ar), 31.40, 31.51 (*t*-Bu, $C_{prim.}$) 34.11 (*t*-Bu, $C_{quat.}$), 56.67, 73.45 (O–CH$_2$–), 115.51 (CH$_2$=), 116.47 (CN–), 125.63, 126.08, 126.18, 126.68 (aromatic CH), 132.18, 132.43, 134.10, 134.24, 145.63, 146.56, 151.36, 152.95 (aromatic $C_{quat.}$), 134.24 (CH=).

Although **5**(***paco***) was not isolated as a pure compound we can derive the most representative signals in the ^{1}H-NMR spectrum shown by the equilibrium mixture of the *partial cone* and 1,2-*alternate* isomers of **5** at 135 °C.

5(***paco***). ^{1}H-NMR (400 MHz, TCE-d_2) δ 3.32, 4.29 (2d, 4H, ^2J = 12.5 Hz, Ar–CH_2–Ar), 4.42, 4.58 (2d, 4H, ^2J = 15.6 Hz, Ar–CH_2–Ar), 5.43, 6.11 (2m, 2H, –CH=CH_2)

For **6**(***cone***) and **6**(***paco***) only those peaks are listed which are essential and which we can be unambiguously distinguished.

6(***cone***). ^{1}H-NMR (400 MHz, CD_2Cl_2) δ 3.29, 4.38 (2d, 8H, ^2J = 13.3, 12.9 Hz, Ar–CH_2–Ar), 6.48, 7.19 (2s, 8H, ArH).

Table 3 Summary of crystal data

	3(**1,2-*alt***)	**5**(**1,2-*alt***)	**4**(***paco***)	**2**(***cone***)
Formula	$C_{46}H_{48}N_4O_8$	$C_{54}H_{66}N_2O_4$	$C_{46}H_{48}N_4O_8$	$C_{41}H_{43}ClN_4O_{8,5}$
M_W	784.88	807.09	784.88	763.24
Crystal system	triclinic	triclinic	triclinic	triclinic
Space group	$P\bar{1}$	$P\bar{1}$	$P\bar{1}$	$P\bar{1}$
T/K	173	173	293	100
a/Å	9.7073(14)	10.4041(19)	10.3157(11)	11.4637(8)
b/Å	10.5690(14)	10.6679(19)	12.4728(12)	18.3534(12)
c/Å	10.9986(15)	11.557(2)	17.753(2)	19.8397(14)
α/°	92.126(11)	105.672(14)	99.611(8)	74.256(5)
β/°	109.791(10)	91.147 (15)	103.810(8)	85.809(6)
γ/°	101.734(11)	108.061(14)	99.245(8)	83.824(5)
V/Å^3	1032.7(2)	1166.6(4)	2138.5(4)	3990.1(5)
Z	1	1	2	4
μ/mm^{-1}	0.087	0.071	0.084	0.153
Reflns. Measured	11250	14867	27339	32778
Unique reflns [$I > 2\sigma(I)$]	2611	3565	5324	10482
$wR(F^2)$ [$I > 2\sigma(I)$]	0.1031	0.3160	0.1962	0.2126

6(*paco*). ^{1}H-NMR (400 MHz, CD_2Cl_2) δ 3.19, 3.65, 3.86, 4.30 (4d, 8H, ^2J = 13.3, 14.1, 14.1, 12.9 Hz, Ar–CH_2–Ar), 6.57, 6.96 (2d, 4H, ^4J = 2.0 Hz, Ar*H*), 7.14, 7.31 (2s, 4H, Ar*H*).

Crystallographic data

Data were collected on a STOE-IPDS-II two-circle diffractometer employing graphite-monochromated MoKα radiation (0.71073 Å). Data reduction was performed with the X-Area software.[14] For **2** an empirical absorption correction was performed using the MULABS[15] option in PLATON.[16] Structures were solved by direct methods with SHELXS-90[17] and refined by full-matrix least-squares techniques with SHELXL-97.[18] All non-H atoms were refined with anisotropic displacement parameters. Hydrogens were included at calculated positions and again allowed to ride on their parent atoms. One *tert*-butyl groups of **2** is disordered over two positions with a ratio of the site occupation factors of 0.552(8)/0.448(8). The data set for **4(*paco*)** had to be collected at room temperature because the crystals were decomposing upon cooling. One ether group of **4(*paco*)** is disordered over two positions with a ratio of the site occupation factors of 0.51(1)/0.49(1). The crystal of **5(1,2-*alt*)** was twinned. The two twin components were related by the twin law (−1 0 0/0 −1 0/0.256 0.665 1) and the ratio of the two components refined to 0.500(4)/0.500(4). Table 3 lists the most important parameters of the X-ray analyses. CCDC reference numbers 272778–272781. See http://dx.doi.org/10.1039/b507780j for crystallographic data in CIF or other electronic format.

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