J Incl Phenom Macrocycl Chem (2008) 62:311–324
DOI 10.1007/s10847-008-9473-x

ORIGINAL ARTICLE

Crystalline inclusion compounds of lower rim propyl substituted calix[4]arenes featuring different number and positions of the modifying groups

Tobias Gruber · Max Peukert · Diana Schindler · Wilhelm Seichter · Edwin Weber · Petra Bombicz

Received: 19 February 2008 / Accepted: 27 June 2008 / Published online: 15 July 2008

Abstract Three lower rim *n*-propyl substituted calix[4]-arenes (**1–3**) with varied number and position of the modifying groups have been prepared. Inclusion compounds (five species) involving different kinds of guest solvents have been isolated. Their X-ray crystal structures were determined and comparatively discussed using isostructurality calculations. Two of the inclusion compounds obtained (**1a** and **1b**) are polymorphs containing the same host and guest molecules in equal stoichiometric ratio but different Z' values caused by a phase transition around 140 K. The inclusion compounds **2a** and **2b** refer to the interesting case of a mixed solvent complex while **3a** allows studying the effect of full lower rim *n*-propyl substitution.

Keywords Calixarene hosts · Organic guests · Crystalline inclusion compounds · Polymorphism · Supramolecular interactions · X-ray crystal structures · Isostructurality calculation

Introduction

Calixarenes are a class of supramolecular receptors, prepared by phenol–formaldehyde condensation reaction to yield macrocycles composed of varying repeat phenolic units linked by methylene groups in the ortho positions [1]. The quintessential prototype of this compound family is calix[4]arene [2] of which a wide range of derivatives exist, having different substituents at the upper and lower rim of the cone-shaped framework [3]. These substituents play a decisive role in the selectivity of inclusion formation and also in the conformational control of the calixarene molecule [4]. Hence, by studying the closely connected group of alkylated calix[4]arenes **1–3** (Scheme 1), featuring *n*-propyl substitution in different number and at different positions of the lower rim, should make possible a substantial comparison in this respect.

For this purpose, preparation, X-ray crystal structures and isostructurality calculations [5–8] of five different inclusion compounds of **1–3** (Scheme 1) involving acetonitrile, dimethylformamide, methanol and tetrahydrofuran as guest solvents (**1a**, **1b**, **2a**, **2b** and **3a**) are reported, showing interesting polymorphism [9, 10] and rarely observed mixed solvent inclusion behaviour [11, 12] aside from other structure-property relationships of this selected series of *n*-propyl substituted calix[4]arenes.

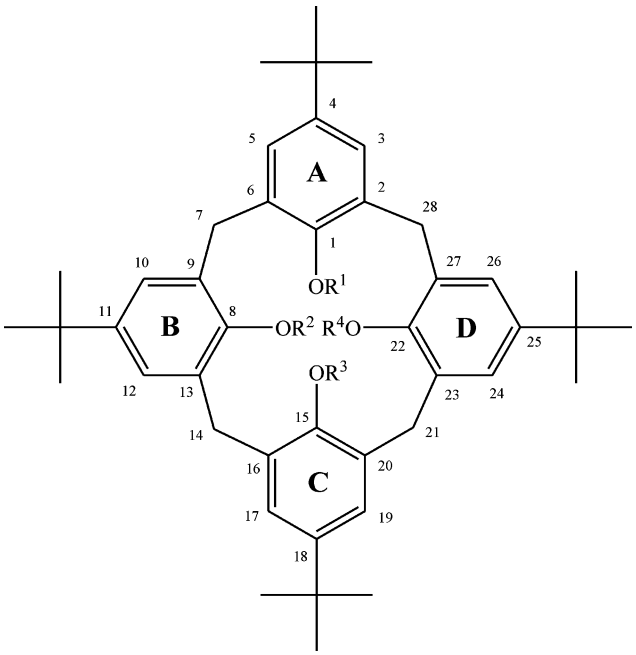
Results and discussion

Synthesis

The parent tetra-*tert*-butylcalix[4]arene [13] was used as the starting compound for the synthesis of **1–3**. Stepwise alkylation reactions following described protocols [14, 15] were performed using 1-bromo- or 1-iodopropane. The inclusion compounds **1a**, **2a**, **2b** and **3a** were obtained by recrystallization of the respective calixarene from the corresponding guest solvent or solvent mixture. Details are specified in the "Experimental" Section.

T. Gruber · M. Peukert · D. Schindler · W. Seichter · E. Weber (✉)
Institut für Organische Chemie, Technische Universität Bergakademie Freiberg, Leipziger Str. 29, 09596 Freiberg/Sachs, Germany
e-mail: edwin.weber@chemie.tu-freiberg.de

P. Bombicz
Institute of Structural Chemistry, Chemical Research Center, Hungarian Academy of Sciences, P.O. Box 17, 1525 Budapest, Hungary



1 R^1, R^2 = H; R^3, R^4 = *n*-Pr

2 R^1, R^3 = H; R^2, R^4 = *n*-Pr

3 R^1, R^2, R^3, R^4 = *n*-Pr

1a **1**·MeCN (2:3) [Polymorph 1]

1b **1**·MeCN (4:6) [Polymorph 2]

2a **2**·DMF (1:1)

2b **2**·DMF·MeOH (2:2:1)

3a **3**·THF (2:1)

Scheme 1 Compounds studied in this paper

X-ray structural study

X-ray crystal structures of the inclusion compounds **1a** [**1** · MeCN (2:3)], **1b** [**1** · MeCN (4:6)], **2a** [**2** · DMF (1:1)], **2b** [**2** · DMF · MeOH (2:2:1)] and **3a** [**3** · THF (2:1)] have been determined (Table 1). A common atom labelling diagram for the calixarene moiety is given in Scheme 1. Perspective views of the molecular structures including graphics of superimposed molecules and illustrations of the crystal packings are shown in Fig. 1–11, respectively.

In general, the conformation of the calixarene framework can be described by a set of interplanar angles which defines the inclination of the aromatic rings with respect to the mean plane given by the methylene atoms C(7), C(14), C(21) and C(28). These data are included in Tables 2 and 3. Hydrogen bond parameters are listed in Table 4. In the present crystal structures, the calixarene skeleton itself is perfectly ordered whereas the *tert*-butyl and propoxy groups show higher displacement parameters or are disordered over several positions, even at low temperatures. In the structure of **1a**, one *tert*-butyl fragment of each host molecule as well as the DMF solvent in **2b** have proven to be difficult to model as there is enough free space in the voids to have for the guest molecule effectual possibilities to move, thus have higher displacement parameters, and therefore were only refined isotropically.

Crystallization of the calixarene **1** from acetonitrile yields colourless crystals of **1a** which turned out to be a 2:3 **1** · acetonitrile inclusion compound of the triclinic space group $P-1$. The asymmetric unit of the cell contains two crystallographically independent 1:1 host-guest complex units and one uncomplexed acetonitrile molecule (Fig. 1). According to a classification of host-guest compounds [16], the present inclusion structure can be regarded as a co-existing cavitate and a clathrate. In **1a**, the calixarene molecules adopt a distorted cone conformation in which the phenolic hydrogens and one of the ether oxygens form an open intramolecular hydrogen bond system with O···O distances ranging between 2.682(2) and 2.840(2) Å. The interplanar angles between the opposite ring pairs A/C and B/D are 54.29/68.06° and 55.12/47.17°, respectively. The complexed acetonitrile molecules are arranged in such a manner that their methyl groups are located inside the aromatic cavity while their nitrogen atoms are directed exo. The distances C_{guest}···M (M = center of the aromatic ring), which are 3.586–3.671 Å (complex 1) and 3.541–3.665 Å (complex 2), suggest that weak CH_3···π host-guest interactions play an important role for complex stabilization. However, it should be mentioned that only one contact within each host-guest entity strictly follows geometric criteria for C–H···π hydrogen bonding [17], so that even weaker non-bonding interactions contribute to guest fixation within the host cavity. This may explain why the rod axes of the guest molecules are tilted with respect to the methylene plane by 65.68° and 53.32°, respectively.

In the course of our work, we found that the inclusion compound **1a** undergoes a reversible solid phase transition at approximately 140 K to turn into the polymorphous structure **1b**. Experimental verification was accomplished by determining temperature dependence of unit cell parameters using ten-degree intervals over a temperature range of 93–293 K and smaller steps around the transition point. Below the transition temperature, the unit cell (space group $P-1$) has nearly twice the volume of the high temperature modification and contains four independent calixarene molecules and six acetonitrile molecules. This means that two symmetry-equivalent calixarene molecules in **1a** become non-equivalent in the low temperature modification **1b**. A detailed conformational analysis of the

Table 1 Crystal data and selected details of the data collection and refinement calculations of compounds **1a**, **1b**, **2a**, **2b** and **3a**

Compound	**1a**	**1b**	**2a**	**2b**	**3a**
Empirical formula	2 $C_{50}H_{68}O_4 \cdot 3\ C_2H_3N$	4 $C_{50}H_{68}O_4 \cdot 6\ C_2H_3N$	$C_{50}H_{68}O_4 \cdot C_3H_7NO$	$C_{50}H_{68}O_4 \cdot C_3H_7NO \cdot 0.5\ CH_4O$	$C_{56}H_{80}O_4 \cdot 0.5\ C_4H_8O$
Formula weight	1589.25	3178.50	806.14	822.16	853.25
Crystal system	Triclinic	Triclinic	Orthorhombic	Orthorhombic	Monoclinic
Space group	$P-1$	$P-1$	$Pna2_1$	$Pna2_1$	$C2/c$
a (Å)	14.0606(2)	17.994(4)	12.6692(3)	12.6679(3)	50.7269(9)
b (Å)	18.0714(4)	21.514(4)	17.8984(4)	17.9558(5)	10.6119(2)
c (Å)	21.8151(4)	26.919(5)	21.4779(5)	21.4256(6)	20.5491(3)
α (°)	73.810(1)	92.81(3)	90.0	90.0	90.0
β (°)	76.152(1)	105.74(3)	90.0	90.0	110.275(1)
γ (°)	67.243(1)	106.19(3)	90.0	90.0	90.0
V (Å^3)	4854.47(16)	9544(4)	4870.29(19)	4873.5(2)	10376.4(3)
Z/Z'	4/2	8/4	4/1	4/1	8/1
$F(000)$	1732	3464	1760	1796	3744
D_c (Mg m^{-3})	1.087	1.106	1.099	1.120	1.092
μ (mm^{-1})	0.067	0.068	0.069	0.071	0.067
Data collection					
Temperature (K)	153(2)	93(2)	153(2)	93(2)	93(2)
No. of collected reflections	90528	225598	37073	32828	58548
Within the θ-limit (°)	1.4–26.1	0.8–27.4	1.5–30.5	1.5–28.1	2.0–27.2
Index ranges $\pm h$, $\pm k$, $\pm l$	−17/16, −22/22, −27/26	−23/23, −27/27, −34/34	−18/18, −25/11, −30/30	−16/16, −23/15, −22/28	−64/64, −13/13, −26/26
No. of unique reflections	19139	43378	7572	6061	11469
R_{int}	0.0322	0.0515	0.0398	0.0406	0.0495
Refinement calculations: full-matrix least- squares on all F^2 values					
Weighting expression w[a]	$\sigma^2(F_o^2) + (0.1101P)^2 + 1.6644P)^{-1}$	$\sigma^2(F_o^2) + (0.1031P)^2 + 0.9600P)^{-1}$	$\sigma^2(F_o^2) + (0.0855P)^2 + 0.4440P)^{-1}$	$\sigma^2(F_o^2) + (0.0939P)^2 + 2.0608P)^{-1}$	$[\sigma^2(F_o^2) + (0.1046P)^2 + 2.9861P)^{-1}$
No. of refined parameters	1116	2248	579	566	624
No. of F-values used [$I > 2\sigma(I)$]	13082	27785	6254	5036	8505
Final R-indices					
$R(=\Sigma\|\Delta F\|/\Sigma\|F_o\|)$	0.0697	0.0620	0.0485	0.0630	0.0468
wR on F^2	0.2233	0.1904	0.1398	0.1738	0.1529
S (=Goodness of fit on F^2)	1.056	1.095	1.041	1.133	0.946
Final $\Delta\rho_{max}/\Delta\rho_{min}$ (e Å^{-3})	0.54/−0.43	0.53/−0.58	0.32/−0.23	0.52/−0.54	0.38/−0.30

[a] $P = (F_o^2 + 2F_c^2)/3$

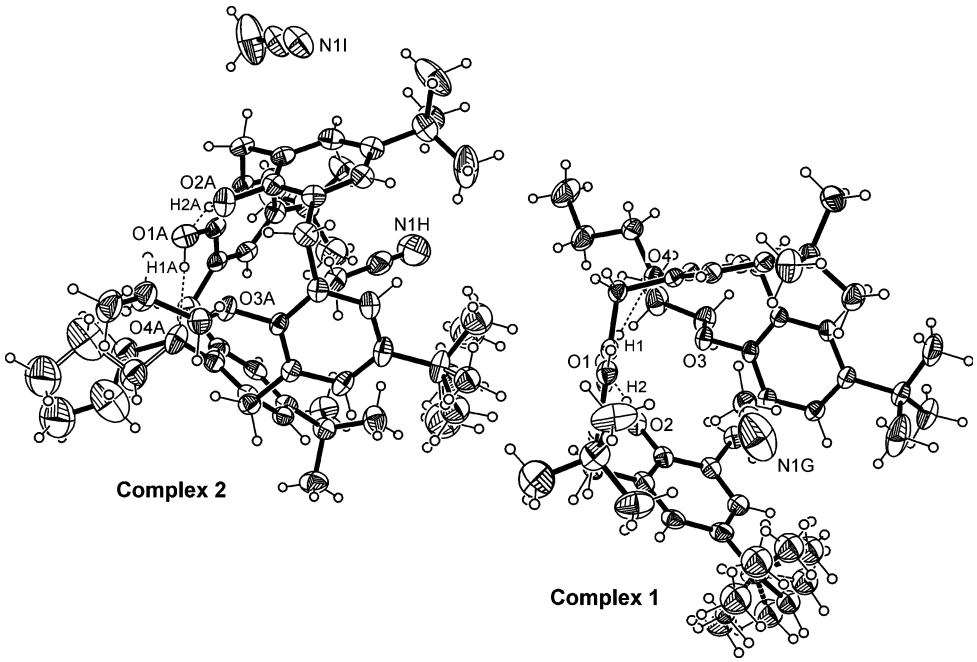


Fig. 1 Perspective view of the stoichiometric unit of the **1** · acetonitrile (2:3) inclusion compound **1a**. Displacement ellipsoids are drawn at the 40% probability level. Hydrogen bonds are indicated by dashed lines

calixarene molecules of **1b** reveals considerable differences of interplanar angles between facing aromatic rings (A/C: 46.85–58.04°; B/D: 51.24–68.97°), which indicates conformational flexibility of the calix moiety in the crystal lattice. Also the guest molecules, being located within the host cavities, are more or less tilted with regard to the methylene plane of the calixarenes [complex 1: 53.87°; complex 2: 50.12°; complex 3: 61.55°; complex 4: 62.28°).

Views of the crystal packings (Fig. 2) along the crystallographic *b* axis (**1a**) and *a* axis (**1b**) reveal layered packing structures, which, at first sight, show no fundamental differences. However, a comparative examination of the internal layer structure indicates that the phase transition is accompanied by significant changes of the calixarene conformation, which is reflected by different interplanar angles between the aromatic building blocks and the O–C–C–C torsion angles within the propoxy substituents. They are listed in Tables 2 and 3, respectively. The layer structure of **1a** is presented in Fig. 3. Although the uncomplexed guest molecules are located between molecular layers, their relative positions in the two phases are different. In the high temperature modification (**1a**),

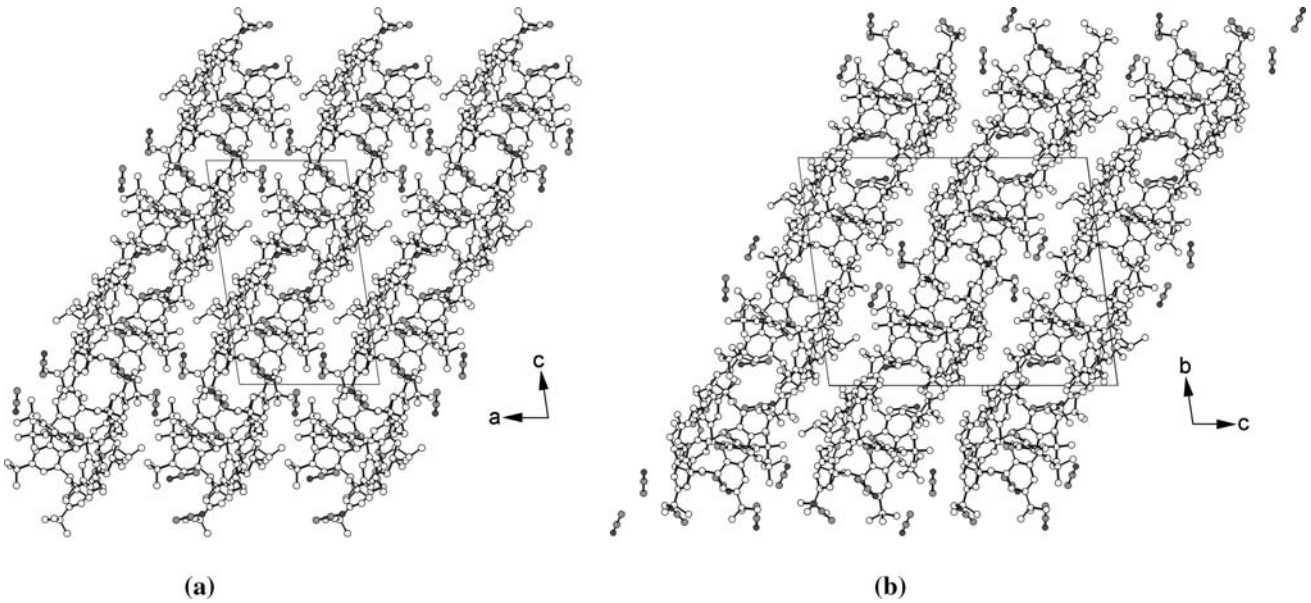


Fig. 2 (**a**) Packing structure of the **1** · acetonitrile (2:3) inclusion compound **1a** viewed down the crystallographic *b* axis and (**b**) packing structure of the **1** · acetonitrile (4:6) inclusion compound **1a** viewed down the *a* axis. Heteroatoms are shaded

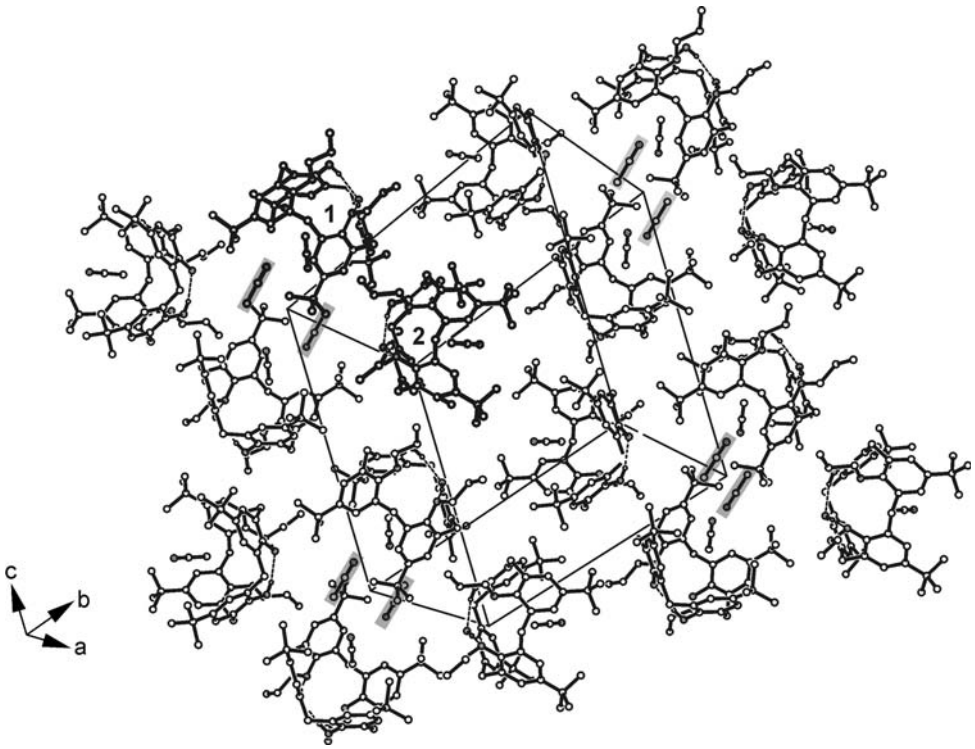


Fig. 3 View of the molecular layer of **1a**. Molecules within the asymmetric cell unit are displayed in bold type. The symmetry related pairs of interstitial acetonitrile molecules are indicated by shading

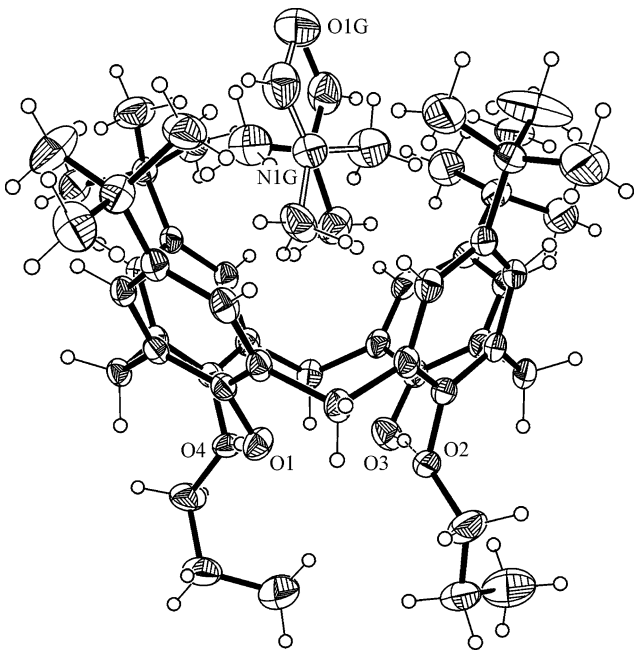


Fig. 4 Perspective view of the asymmetric unit of the **2** · DMF (1:1) inclusion compound **2a**. Displacement ellipsoids are drawn at the 50% probability level. The two disordered positions of the guest molecule are distinguished by different bond types

pairs of symmetry related guest molecules with distances of approximately 5.0 Å are accommodated in voids which are left by six calixarene molecules. A similar structure motif is also found in the low temperature modification (**1b**), however the arrangement of these guest molecules have become less symmetric, resulting in a doubling of one cell axis of structure **1b** (Fig. 2).

The calixarene **2** (constitutional isomer of **1**) yields a crystalline 1:1 complex with DMF, being defined as **2a**, which has the orthorhombic space group $Pna2_1$. According to the symmetric lower rim substitution, the calixarene geometry is primarily determined by two strong intramolecular O–H···O hydrogen bonds, which link the phenolic hydroxy groups to one of the adjacent propoxy oxygen atoms [*d*(O···O) 2.682(3), 2.732(3) Å] leading to a pinched cone conformation (Fig. 4). The torsion angles along the lower rim show that the calixarene part deviates from ideal twofold symmetry, possibly due to complex formation. The least-squares plane of the DMF molecule is inclined by 80.51(9)° with respect to the methylene plane of the calixarene. In the complex, the non-polar parts of the guest molecule occupy the aromatic cavity whereas its oxygen is directed exo, forming a weak C–H···O contact to an adjacent host molecule [C(19)–H(19)···O1G = 2.59 Å, 162.5°]. The dimethylformamide is disordered around its N···O axis with site occupation factors being 0.6 and 0.4. In each of these orientations, both methyl groups are associated with the aromatic rings of the host via weak $CH_3\cdots\pi$ (arene) interactions with $C_{guest}\cdots M$ (M = center of the aromatic ring) distances between 3.42 and 3.67 Å. The propoxy groups exhibit the favourable gauche conformation with the corresponding torsion angles 73.7(3)° [O(2)–C(37)–C(38)–C(39)] and −62.1(3)° [O(4)–C(48)–C(49)–C(50)].

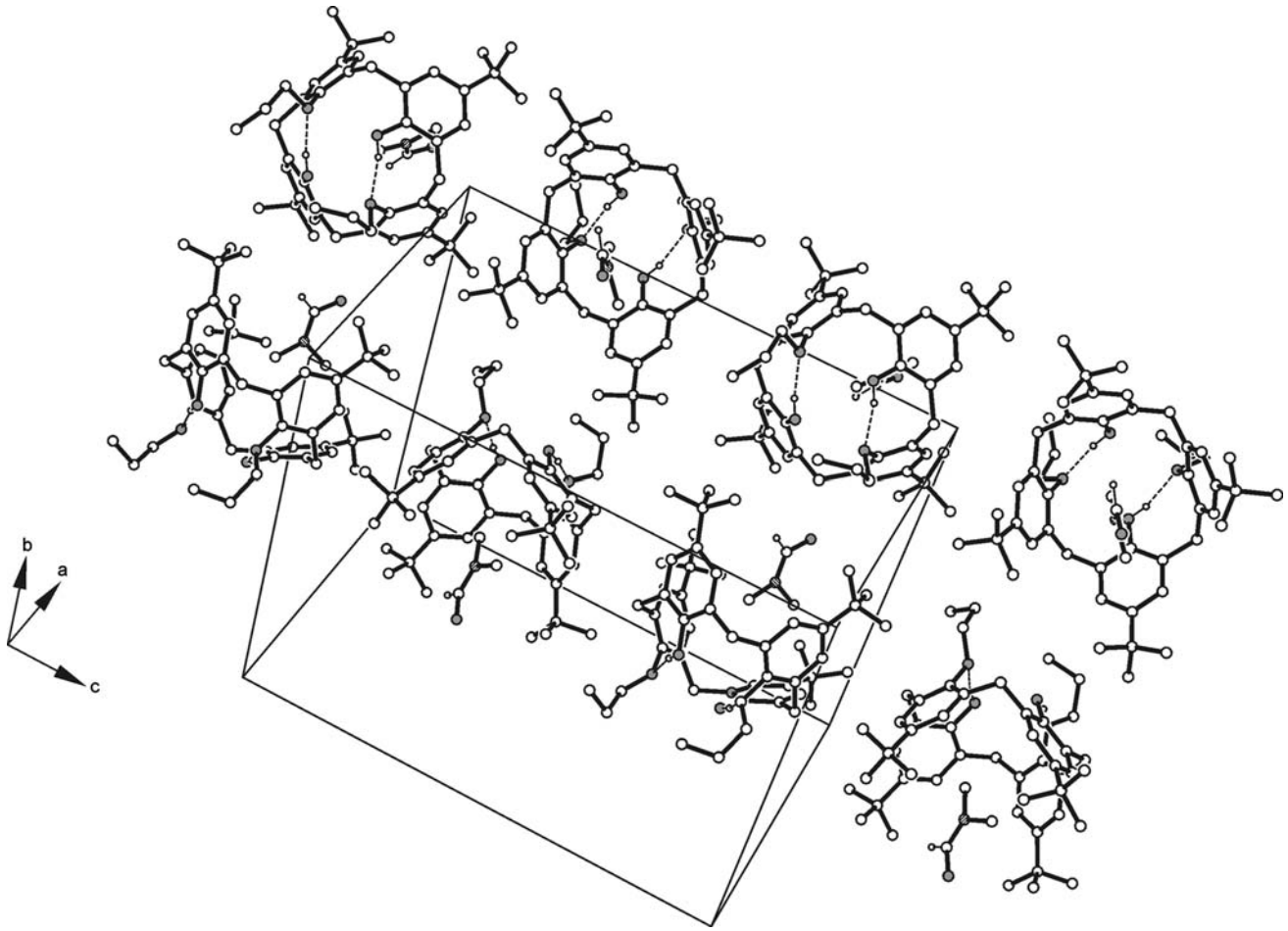


Fig. 5 Packing structure of **2a** showing the molecular ensemble within a molecular layer. Only one disordered position of the guest molecule is shown. With the exception of the formyl and coordinating hydrogens, all other hydrogen atoms are omitted for clarity

The crystal packing of **2a**, which is displayed in Fig. 5, is composed of molecular layers extending parallel to the crystallographic *ab* plane. According to the non-polar nature of the calixarene, the crystal structure is dominated by weak intermolecular interactions. Apart from the presence of a host-guest hydrogen bond, a rather complicated interplay of weak intermolecular van der Waals type forces, comprising arene···alkyl and alkyl···alkyl contacts, stabilize the crystal structure of **2a**.

Interestingly, crystallization of **2** from a mixture of dimethylformamide and methanol yields a mixed solvent 1:1:0.5 inclusion compound **2b** (Fig. 6) of the orthorhombic space group $Pna2_1$ with nearly identical crystallographic parameters to those found for **2a** (cf. Table 1). The mean difference between the complex structures **2a** and **2b** is the way the guest molecule is incorporated into the host cavity. In **2b**, the DMF molecule is disordered around the N(1G1)–C(2G1) bond, thus creating two acceptor sites (occupation factors: 0.5) which fulfil different coordination tasks. In one orientation, the oxygen is connected to the methanol molecule via a conventional hydrogen bond [O(1G2)–H(1G2)···O(1G3) 1.97 Å, 174.3°]. In its alternative orientation, the guest forms a weak aryl-H···O contact to a neighbouring host molecule [C(5)–H(5)···O(1G1) 2.53 Å, 160.7°]. A possible reason for the unusual host-guest stoichiometric ratio of **2b** can be seen in a statistical distribution of alcohol molecules in lattice voids (Fig. 7), which are also present in the more simple **2a** crystal inclusion.

The inclusion compound **3a**, which is formed by **3** with THF (2:1), crystallizes in the monoclinic space group *C*2/*c*. Because of the bulky lower rim substituents, the calixarene is fixed in the partial cone conformation (Fig. 8). The orientation of the aromatic rings is such that the two facing rings are almost parallel to each other [11.3(1)°] while the other two adopt an angle of 42.0(1)°. In this geometry, the terminal carbon atom of the propoxy substituent, being attached to the down oriented aromatic ring, is in contact to the flanking *tert*-butyl groups. The space filling model displayed in Fig. 8a reveals that the calixarene forms a nearly closed cavity which obviously prevents encapsulation of a guest molecule like THF. This finding is consistent with previous investigations showing that **3** in its

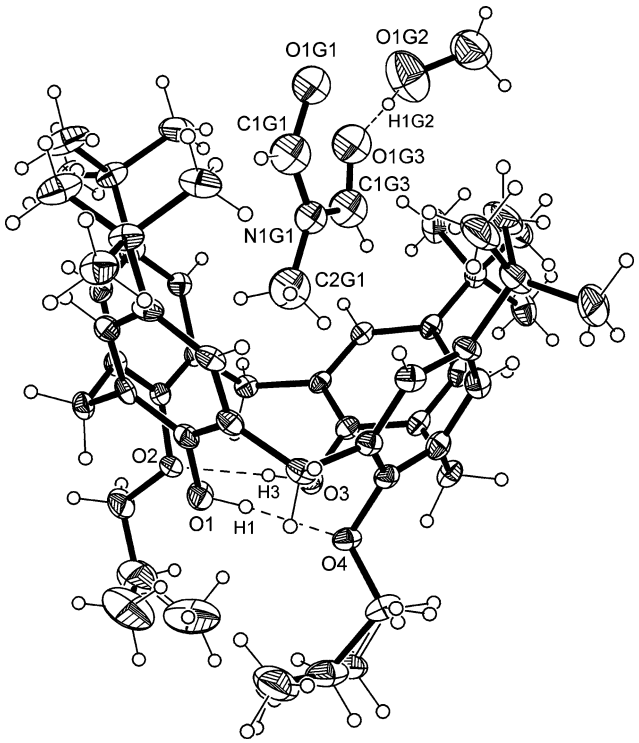


Fig. 6 Molecular structure of the **2** · DMF · MeOH (2:2:1) inclusion compound **2b**. Displacement ellipsoids are drawn at the 30% probability level. Hydrogen bonds are indicated by dashed lines

partial cone conformation allows complexation only of small guest species such as nitric oxide [18] or Ag^+ [19] .

In the crystal structure of **3a** the guest molecule is disordered around the twofold symmetry element. The most striking feature, however, is that irrespective of its distinct hydrogen bonding abilities, the guest molecule seems not to be subjected to any intermolecular interactions. As illustrated in Fig. 9, the calixarene adopts a bilayer type packing structure which is primarily stabilized by alkyl···alkyl contacts, known also from other tetraalkylcalix[4]arenes [20–22]. The guest molecules are located in lattice voids between double layers and are surrounded by the upper rim substituents of two calixarene molecules exhibiting an offset arrangement.

Isostructurality calculations

The cell similarity indices (π) as well as the molecular isometricity indices [$I(m)$] were estimated covering in addition to the present inclusion compounds (**1a**,**b**, **2a**,**b**) three further literary known inclusion species of the calixarene **2**: **2** · acetonitrile (1:1) (**2c** [23]), **2** · chloroacetonitrile (1:1) (**2d** [24]) and **2** · malonodinitrile/1,4-dioxane (1:1:2) (**2e** [24]), thus allowing of a comparison as complete as possible. The cell similarity index (π) has been calculated as $\pi = [(a + b + c)/(a' + b' + c') - 1]$, where a, b, c, and a', b', c' are the

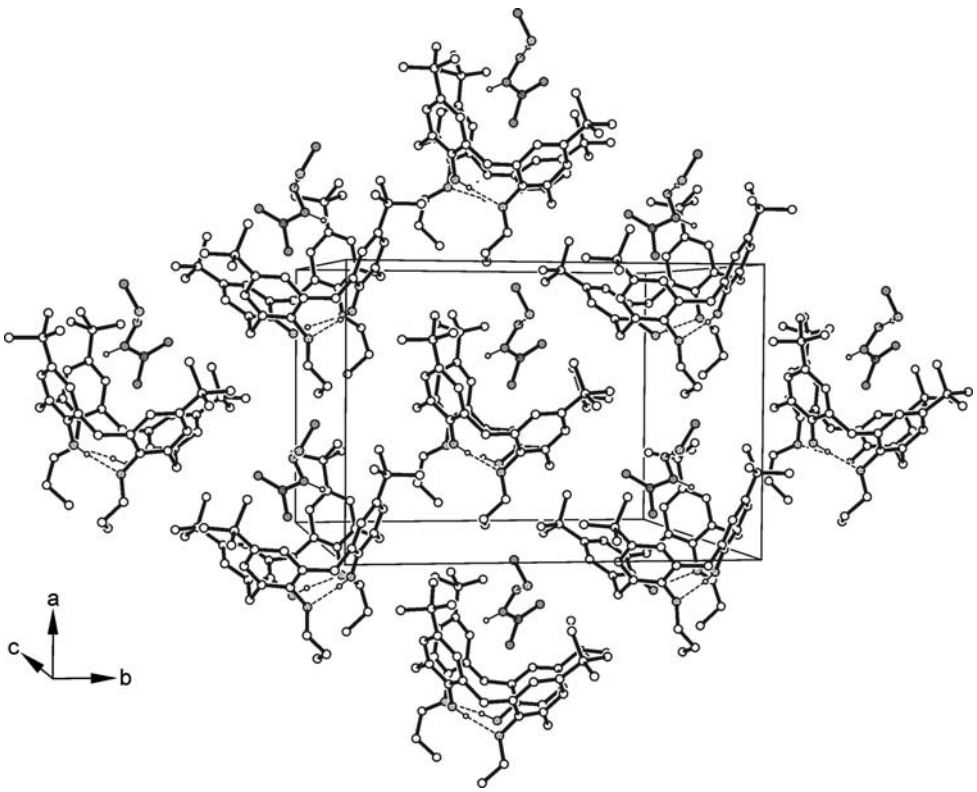


Fig. 7 Packing structure of **2b**. Hydrogen atoms (except the formyl and coordinating hydrogens) are omitted for clarity

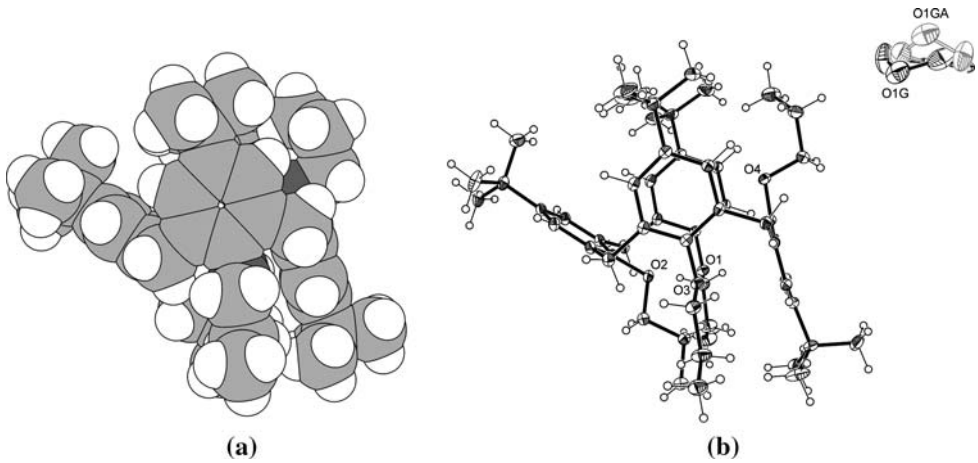


Fig. 8 (**a**) Space filling model of the calix[4]arene **3** in its 1:2 inclusion compound with THF (**3a**) and (**b**) ORTEP plot of the host-guest unit. Displacement ellipsoids are drawn at the 50% probability level

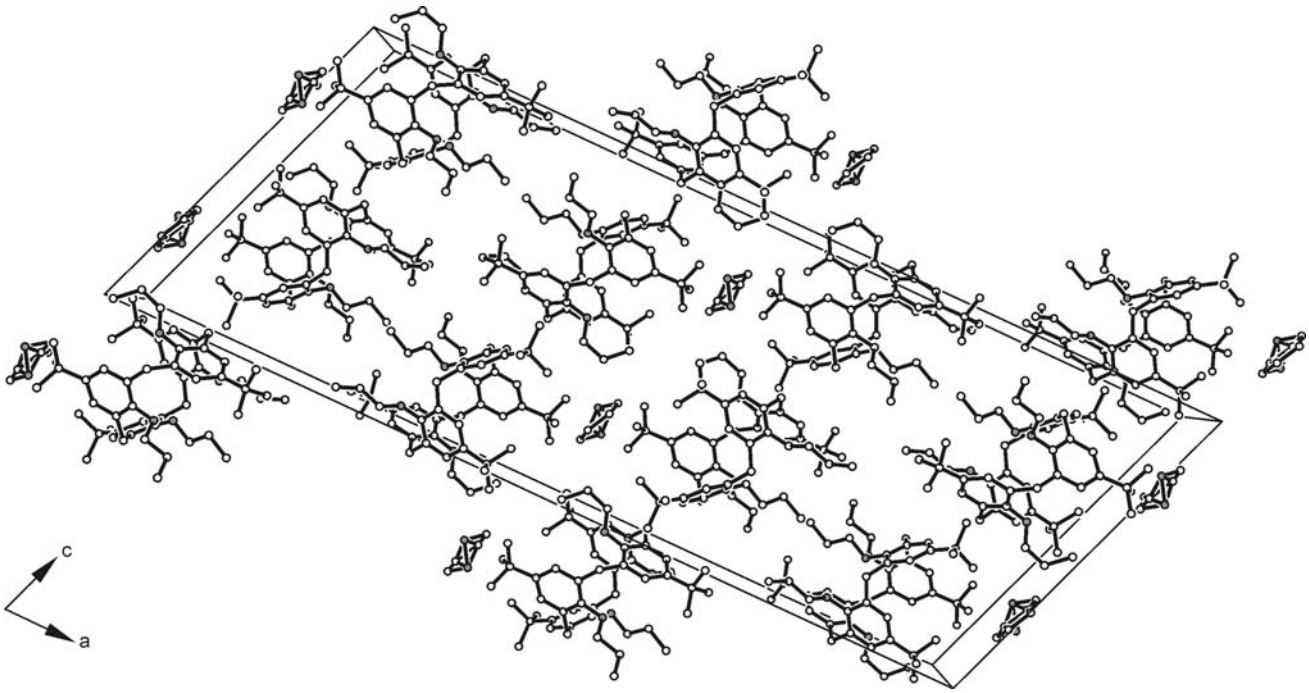


Fig. 9 Packing structure of **3a** viewed along the crystallographic *b* axis. All hydrogen atoms are omitted for clarity

orthogonalized lattice parameters of the compared crystals. In the event of great similarity of the two unit cells, the value of π is close to zero. For the calculation of the isostructurality index [$I(s)$], the distance differences between the crystal coordinates of identical non-H atoms within the same section of the related structures were used. The $I(s)$ takes into account both the differences in the geometry of the molecules and the positional differences caused by rotation and translation. The molecular isometricity calculations were carried out by least-squares fitting of the positions occupied by the identical heavy atoms of the two related molecules [5–8].

In the first place, isostructurality calculations of the calixarene frameworks were carried out for the inclusion compounds of the calixarene **2**, including with **2a**–**2e** a total of five different species. A comparison of **2a** with **2b** shows rather similar cell parameters. The placement of the two calixarene molecules with largely similar conformation in the unit cell is comparable, resulting in an isostructurality index of 38.0 %. The cell volume of **2a** does not increase significantly by the additional inclusion of the small guest molecule MeOH to yield **2b**. The MeOH molecule can be accommodated in the voids of the cell by the displacement of the relatively rigid host molecule. This explains the rather high molecular isometricity (Fig. 10a) and the low isostructurality indices between **2a** and **2b** (Tables 5, 6). Thus, the density of the **2a** crystal increases by the additional guest uptake.

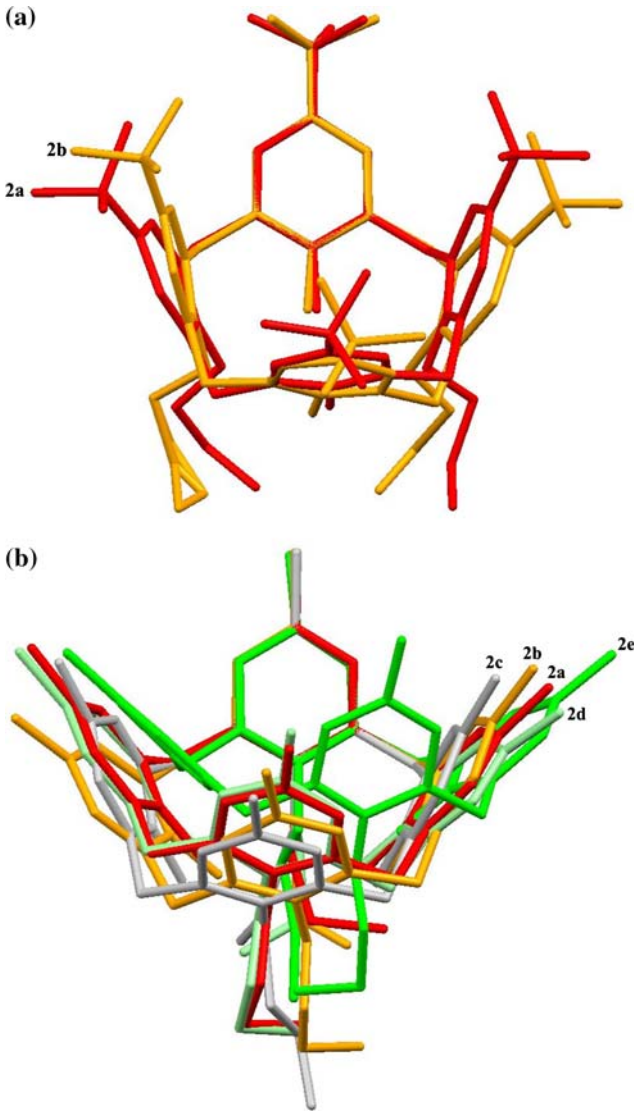


Fig. 10 Superimposed host molecules from the inclusion compounds (**a**) **2a** and **2b**, and (**b**) **2a**–**2e** calculated for the calixarene molecules in the asymmetric unit, demonstrating the differences in the molecular conformation. Hydrogens and the terminal methyl groups of the *tert*-butyl moieties are omitted for clarity. In order to enhance the differences in the molecular conformation, one of the phenyl rings of each calixarene molecule is superimposed in the figure

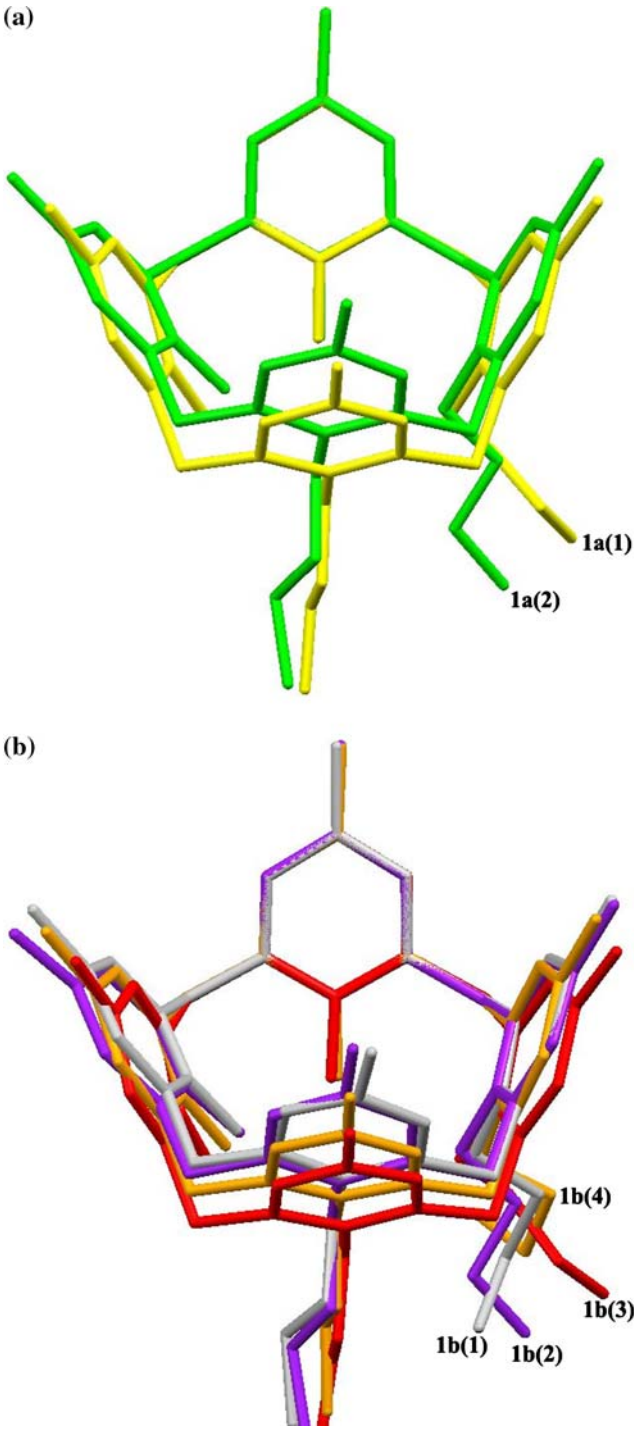


Fig. 11 Comparison of molecular conformations of the symmetrically independent calixarene molecules in the asymmetric unit of the inclusion compounds **1a** (**a**) and **1b** (**b**). Hydrogens and the terminal methyl groups of the *tert*-butyl moieties are omitted for clarity. One of the phenyl rings of each calixarene molecule is superimposed in the figure

An examination of the complexes **2c** and **2d**, with acetonitrile and chloroacetonitrile as the guest solvents, by viewing the cells from the crystallographic *a* direction illustrates that the two calixarene molecules in the two different cells are placed similar but upside-down considering the *bc* diagonal. The space groups of **2c** and **2d** ($P2_1/a$ and $P-1$, resp.) and the crystal systems as well as the packings of the molecules are different in the respective cells of **2c** and **2d**. Thus, we cannot speak of isostructurality in this case. The molecular conformations of the calixarene hosts are also rather different (Table 6). In **2e**, with malonodinitrile/1,4-dioxane (1:1:2) as the included solvents, the three guest molecules of the inclusion compound increase the cell volume and change the placement of the calixarene host in the unit cell to such a great extent

Table 2 Selected conformational parameters of the calixarene molecules in the complexes **1a**, **1b**, **2a**, **2b** and **3a**

Compound	**1a(1)**	**1a(2)**	**1b(1)**	**1b(2)**	**1b(3)**	**1b(4)**	**2a**	**2b**	**3a**
Interplanar angles (°)[a]									
mpla[b]/A	47.70(6)	57.45(7)	67.21(6)	66.44(6)	53.28(7)	61.27(6)	49.31(5)	53.65(7)	78.35(4)
mpla/B	68.37(6)	59.67(7)	49.58(6)	46.92(7)	64.62(6)	56.12(6)	69.88(5)	63.40(7)	44.91(4)
mpla/C	64.55(6)	68.26(5)	63.64(6)	66.79(5)	68.63(6)	62.46(6)	51.70(4)	47.03(9)	89.60(3)
mpla/D	64.55(5)	65.26(6)	68.30(6)	64.08(6)	64.25(5)	71.05(5)	63.81(4)	70.33(9)	86.81(3)
A/C	68.06(7)	54.29(7)	49.24(8)	46.86(8)	58.09(6)	56.37(7)	79.02(5)	79.35(9)	11.28(7)
B/D	47.17(9)	55.12(8)	62.18(7)	69.00(7)	51.25(8)	52.83(7)	46.31(6)	46.29(9)	41.94(6)

[a] Aromatic rings: ring A: C(1)…C(6); ring B: C(8)…C(13); ring C: C(15)…C(20); ring D: C(22)…C(27)

[b] Best plane through atoms C(7), C(14), C(21) and C(28)

Table 3 Torsion angles (°) of the calixarene molecule in the complexes **1a**, **1b**, **2a**, **2b** and **3a**

Compound	**1a**	**1b**	**2a**	**2b**	**3a**
C(1)–C(6)–C(7)–C(9)	81.8(3)	−100.0(2)	85.6(2)	−91.9(4)	110.0(2)
C(6)–C(7)–C(9)–C(8)	−101.0(3)	82.6(2)	−105.0(2)	100.3(4)	−78.3(2)
C(8)–C(13)–C(14)–C(16)	96.0(3)	−83.0(2)	95.9(2)	−92.1(4)	75.7(2)
C(13)–C(14)–C(16)–C(15)	−93.6(3)	93.1(2)	−80.0(2)	78.6(4)	−116.7(1)
C(15)–C(20)–C(21)–C(23)	97.9(2)	−94.8(2)	90.2(2)	−84.1(4)	65.4(2)
C(20)–C(21)–C(23)–C(22)	−96.1(2)	101.4(2)	−101.0(2)	106.7(4)	64.9(2)
C(22)–C(27)–C(28)–C(2)	94.2(3)	−97.4(2)	92.0(2)	−96.2(4)	−65.5(2)
C(27)–C(28)–C(2)–C(1)	−80.4(3)	95.0(2)	−80.0(2)	81.9(4)	−57.2(2)
C(1A)–C(6A)–C(7A)–C(9A)	89.6(3)	−99.5(2)			
C(6A)–C(7A)–C(9A)–C(8A)	−92.4(3)	81.5(2)			
C(8A)–C(13A)–C(14A)–C(16A)	89.2(3)	−79.6(2)			
C(13A)–C(14A)–C(16A)–C(15A)	−97.9(3)	96.0(2)			
C(15A)–C(20A)–C(21A)–C(23A)	99.3(3)	−97.2(2)			
C(20A)–C(21A)–C(23A)–C(22A)	−96.2(3)	96.5(2)			
C(22A)–C(27)–C(28A)–C(2A)	95.9(3)	−94.5(2)			
C(27A)–C(28A)–C(2A)–C(1A)	−87.2(3)	94.7(2)			
C(1B)–C(6B)–C(7B)–C(9B)		−84.6(2)			
C(6B)–C(7B)–C(9B)–C(8B)		96.7(2)			
C(8B)–C(13B)–C(14B)–C(16B)		−93.2(2)			
C(13B)–C(14B)–C(16B)–C(15B)		99.1(2)			
C(15B)–C(20B)–C(21B)–C(23B)		−99.1(2)			
C(20B)–C(21B)–C(23B)–C(22B)		93.8(2)			
C(22B)–C(27B)–C(28B)–C(2B)		−94.2(2)			
C(27B)–C(28B)–C(2B)–C(1B)		84.7(2)			
C(1C)–C(6C)–C(7C)–C(9C)		−94.2(2)			
C(6C)–C(7C)–C(9C)–C(8C)		87.2(2)			
C(8C)–C(13C)–C(14C)–C(16C)		−86.9(2)			
C(13C)–C(14C)–C(16C)–C(15C)		92.5(2)			
C(15C)–C(20C)–C(21C)–C(23C)		−92.8(2)			
C(20C)–C(21C)–C(23C)–C(22C)		102.4(2)			
C(22C)–C(27C)–C(28C)–C(2C)		−102.3(2)			
C(27C)–C(28C)–C(2C)–C(1C)		89.5(2)			

that isostructurality seems also out of place here. Nevertheless, the molecular isometricity can be compared since the same host molecule is present in all crystal structures of the inclusion compounds of **2**, although there are serious differences in the molecular geometry of the relatively rigid calixarene host induced by the guest molecules

Table 4 Distances and angles of possible hydrogen bond type interactions, observed for compounds **1a**, **1b**, **2a** and **2b**

Atoms involved	Symmetry	Distances (Å)		Angles (°)
		D···A	H···A	D-H···A
1a				
O(1)–H(1)···O(4)	*x*, *y*, *z*	2.682(2)	1.86	167.7
O(2)–H(2)···O(1)	*x*, *y*, *z*	2.811(2)	2.00	161.2
O(1A)–H(1A)···O(4A)	*x*, *y*, *z*	2.840(2)	2.00	173.9
O(2A)–H(2A)···O(1A)	*x*, *y*, *z*	2.748(2)	1.93	163.2
C(1G1)–H(2G1)···M(A)*	*x*, *y*, *z*	3.586(3)	2.64	168.7
C(1G2)–H(2G2)···M(C′)*	*x*, *y*, *z*	3.541(3)	2.59	169.9
1b				
O(1)–H(1)···O(2)	*x*, *y*, *z*	2.799(3)	2.00	164.4
O(2)–H(2)···O(3)	*x*, *y*, *z*	2.666(4)	1.86	1.686
O(1A)–H(1A)···O(2A)	*x*, *y*, *z*	2.771(3)	1.97	164.3
O(2A)–H(2A)···O(3A)	*x*, *y*, *z*	2.708(3)	1.91	163.5
O(1B)–H(1B)···O(4B)	*x*, *y*, *z*	2.757(3)	1.96	153.3
O(2B)–H(2B)···O(1B)	*x*, *y*, *z*	2.725(3)	1.91	171.4
O(1C)–H(1C)···O(2C)	*x*, *y*, *z*	2.681(4)	1.87	167.9
O(2C)–H(2C)···O(3C)	*x*, *y*, *z*	2.748(3)	1.95	164.4
2a				
O(1)–H(1)···O4	*x*, *y*, *z*	2.682(3)	1.86	167.9
O(3)–H(3)···O2	*x*, *y*, *z*	2.732(3)	1.90	169.7
C(19)–H(19)···O1G	0.5 + *x*, 1.5−*y*, *z*	3.511(3)	2.59	162.5
2b				
O(1)–H(1)···O4	*x*, *y*, *z*	2.758(3)	1.92	173.3
O(3)–H(3)···O2	*x*, *y*, *z*	2.681(3)	1.87	163.0
O(1G2)–H(1G2)···O(1G3)	1−*x*, 1−*y*, 0.5 + *z*	2.803(4)	1.97	174.3
C(5)–H(5)···O(1G1)	−0.5 + *x*, 1.5−*y*, *z*	3.434(4)	2.53	160.7

*M(A): ring centroid C(1)…C(6); M(B): ring centroid C(8)…C(13); M(C): ring centroid C(15)…C(20); M(D): ring centroid C(22)…C(27); M(A′): ring centroid C(1A)…C(6A); M(B′): ring centroid C(8A)…C(13A); M(C′): ring centroid C(15A)…C(20A); M(D′): ring centroid C(22A)…C(27A); M(A″): ring centroid C(1B)…C(6B); M(B″): ring centroid C(8B)…C(13B); M(C″): ring centroid C(15B)…C(20B); M(D″): ring centroid C(22B)…C(27B); M(A‴): ring centroid C(1C)…C(6C); M(B‴): ring centroid C(8C)…C(13C); M(C‴): ring centroid C(15C)…C(20C); M(D‴): ring centroid C(22C)…C(27C)

Table 5 Cell similarity indices (π) calculated for compounds **2a**–**2e**

	2a	**2b**	**2c**	**2d**	**2e**
2a	–	0.00007	0.01004	0.47143	0.07667
2b		–	0.01011	0.47154	0.07660
2c			–	0.45681	0.08585
2d				–	0.37249
2e					–
Space group	$Pna2_1$	$Pna2_1$	$P2_1/a$	$P-1$	$Pna2_1$

Table 6 Molecular isometricity indices I_m calculated for compounds **2a**–**2e**

	2a	**2b**	**2c**	**2d**	**2e**
2a	–	91.563	76.784	94.611	94.870
2b		–	83.058	96.734	96.489
2c			–	81.751	80.731
2d				–	98.775
2e					–

(Fig. 10b). Obviously, there is no relationship between π and I_m in the investigated structures, as observed with other calixarenes [25]. Thus, calixarene host molecules may have similar conformation in different unit cells trying to achieve a low energy conformation in different packing arrangements. However, calixarene molecules may adopt different conformations to a certain degree in order to accommodate guest molecules with different sizes keeping the same packing arrangement of their inclusion compounds.

In a second step, the inclusion compounds **1a**, **1b** and **2d**, all three crystallizing in the space group $P-1$, were compared (Table 7). The guest molecule is acetonitrile in **1a** and **1b**, while being chloroacetonitrile in **2d**. The calixarene host molecules of the inclusion compounds differ in the placement of the lower rim *n*-propyl substituents, i.e. **1a** and **1b** are proximal, while **2d** is distal substituted. There is a forth inclusion compound, namely **2c**, where the calixarene host corresponds to **2d** and the acetonitrile guest corresponds to **1a** and **1b**, but this particular inclusion compound crystallizes in the space group $P2_1/a$. On the other hand, in spite of the fact that **1a**, **1b** and **2d** crystals have the same $P-1$ space group and are also chemically similar, they are not isostructural. All three crystals provide different Z' values (number of crystallographically independent molecular units

Table 7 Molecular isometricity indexes (I_m) comparing the calixarene molecules in space group $P-1$ (**1a**, **1b** and **2d**) at different levels calculating with 36 and 42 heavy atoms

I_m calculation	I(m) in %	
	36 Heavy atoms	42 Heavy atoms
1a(1)–2d	89.550	–
1a(2)–2d	78.017	–
1b(1)–2d	80.417	–
1b(2)–2d	77.883	–
1b(3)–2d	93.817	–
1b(4)–2d	87.467	–
1a(1)–1a(2)	88.217	86.760
1a(1)–1b(1)	90.517	89.245
1a(1)–1b(2)	88.067	86.375
1a(1)–1b(3)	95.417	95.340
1a(1)–1b(4)	95.417	95.741
1a(2)–1b(1)	97.200	97.531
1a(2)–1b(2)	96.150	96.250
1a(2)–1b(3)	83.667	82.240
1a(2)–1b(4)	99.267	90.649
1b(1)–1b(2)	94.550	95.278
1b(1)–1b(3)	85.933	84.755
1b(1)–1b(4)	93.350	93.026
1b(2)–1b(3)	83.767	82.224
1b(2)–1b(4)	90.033	89.569
1b(3)–1b(4)	93.050	91.158

in the asymmetric unit; **1a**: $Z' = 2$, **1b**: $Z' = 4$ and **2d**: $Z' = 1$) and stoichiometries (**1a**: 2:3, **1b**: 4:6 and **2d**: 1:1) (Fig. 11a). It is highly interesting to note that **1a** and **1b** which are chemically the same inclusion compounds, crystallizing in the same space group, have to be considered as polymorphs because of the significantly different (approximately doubled) unit cell arrangements caused by phase transition around 140 K.

Molecular similarity has been examined for the calixarene frames (36 atoms) in case of the cone conformation hosts in **1a**, **1b** and **2d** (the lower rim substituents and the terminal methyl groups of the mostly rotating *tert*-butyl groups are omitted from the calculation). Furthermore, molecular similarity including the lower rim substituents has also been calculated for the calixarene molecules in the inclusion complexes **1a** and **1b** (two and four crystallographically independent molecules in the asymmetric unit, respectively). Thus, it is possible to distinguish between the influence of the placement of the lower rim substituents of the calixarene and the influence of packing arrangement to the conformation of the chalice (Table 7). Based on the molecular isometricity calculation, it is shown that the placement of the *n*-propyl substituents has a significant influence on the conformation of the calixarene frame. The distal substitution results in the most open molecular structure (Fig. 11b). In case of proximal substitution, the molecular isometricity indices vary from 83.7% to 99.3% for the calixarene frame (36 atoms) which is a bit equalized if we consider the *n*-propyl substituents in the calculation 82.2–97.5% (42 atoms). On the other hand, the data show that crystal packing has less influence on the molecular conformation than the position of the lower rim substituents.

Conclusion

The crystal structures of five inclusion compounds (**1a**,**b**, **2a**,**b**, **3a**) involving three calix[4]arenes (**1**–**3**) with varied number and position of lower rim *n*-propyl substituents and containing different guest solvents have been determined in order to explain structural relationships of this class of compounds. Incorporation of isostructurality calculations into the comparative discussion with added data of three previously known structures of inclusion compounds of **2** (**2c**–**2e**) provides the information as given in the following.

(1) From the conformational parameters it is evident that the unsymmetric functionalization of the lower rim substituents in **1** is accompanied by a loss of molecular symmetry and induces a higher degree of conformational flexibility in their solid state phases compared to the parent tetrahydroxycalix[4]arene. (2) According to crystal structures determined of the inclusion compounds of **1** and **2**, the substitution pattern at the lower rim of calix[4]arenes generally seems to have a lower effect on the conformation of the chalice and the packing arrangement than type and location of an enclosed guest molecule. (3) The present structures also suggest that the *n*-propoxy unit, frequently used as a protecting and steering group in calixarene chemistry, does not predominate but is subordinated to the inclusion behaviour of the calixarene cavity. (4) In case of the inclusion compound of the tetra-*n*-propoxycalix[4]arene **3**, the partial cone conformation seems to be preferred allowing a close packing of the molecules.

Moreover, the polymorphic phase transition found for the inclusion compounds **1a/1b** and the mixed solvent inclusion behaviour of compound **2b** are promising subjects [9–12] inviting more detailed studies of these properties in future.

Experimental

Preparation of compounds

The calix[4]arenes **1**–**3** were synthesized from 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrahydroxycalix[4]arene [13] and 1-bromo- or 1-iodopropane according to the literature procedures [14, 15]. The tetra-*n*-propyl substituted

calix[4]arene **3** was isolated as a mixture containing the immobile cone and partial cone conformations in an approx. 1:9 ratio, which is in agreement with the literature [26].

The inclusion compounds **1a**, **2a** and **3a** were obtained by recrystallization of the respective calixarene from the corresponding pure guest solvent; **2b** was crystallized from MeOH/DMF (9:1), and the polymorph **1b** is formed by phase transition of **1a** on cooling below 140 K. The crystals of **1a**, **2a**, **2b** and **3a** suitable for crystallographic data collection were obtained by slow evaporation of the respective solution.

X-ray crystallography

A Bruker APEX II diffractometer ($\lambda_{MoK\alpha} = 0.71073$ Å, graphite monochromator) was employed for data collection using the ω-2θ scan mode. Data reduction was carried out with the XCAD4 program [27]. All non-hydrogen atoms were refined anisotropically unless otherwise noted. With the exception of the lower rim hydroxy hydrogens, the positions of which could be extracted from the difference electron density map, all other hydrogens were included in the model in calculated positions and refined as constrained to bonding atoms.

All data were corrected for Lorentz and polarization effects. Preliminary structure models were derived by application of direct methods [28] and were refined by full-matrix least squares calculation based on F^2 for all reflections [28]. The crystal data and experimental parameters are summarized in Table 1. Crystallographic data for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC-676732 to CCDC-676736. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223-336033, E-mail: deposit@ccdc.cam.ac.uk).

Acknowledgments Financial support from the German Federal Ministry of Economics and Technology (BMWi) under grant No. 16IN0218 'ChemoChips' and Hungarian Research Fund (OTKA T049712) is gratefully acknowledged.

References

1. Gutsche, C.D.: Calixarenes Revisited. The Royal Society of Chemistry, Cambridge (1998)
2. Mandolini, L., Ungaro, R. (eds.): Calixarenes in Action. Imperial College Press, London (2000)
3. Vicens, J., Böhmer, V. (eds.): Calixarenes—A Versatile Class of Macrocyclic Compounds. Kluwer, Dordrecht (1991)
4. Asfari, Z., Böhmer, V., Harrowfield, J., Vicens, J. (eds.): Calixarenes 2001. Kluwer, Dordrecht (2001)
5. Kálmán, A., Párkányi, L., Argay, G.: Classification of the isostructurality of organic molecules in the crystalline state. Acta Crystallogr. B **49**, 1039–1049 (1993). doi:10.1107/S0108768193006103
6. Kálmán, A.: On the isostructurality of supramolecules packing similarities governed by molecular complementarity. In: Gans, W., Amann, A., Boeyens, J.C.A. (eds.) Fundamental Principles of Molecular Modeling, pp. 201–221. Plenum Press, New York (1996)
7. Kálmán, A., Párkányi, L.: Isostructurality of organic crystals: a tool to estimate the complementarity of homo- and heteromolecular associates. In: Hargittai, M., Hargittai, I. (eds.) Advances in Molecular Structure Research, vol. 3, pp. 189–226. JAI Press, Greenwich, Conn. (1997)
8. Kálmán, A., Fábián, L.: Structural similarities in tetraaryltins described by virtual non-crystallographic rotations or translations: Kitaigorodskii's morphotropism is revisited. Acta Crystallogr. B **63**, 411–417 (2007). doi:10.1107/S0108768107010968
9. Dale, S.H., Elsegood, M.R.J., Redshaw, C.: Polymorphism and pseudopolymorphism in calixarenes: acetonitrile clathrates of *p*-Bu^t-calix[*n*]arenes ($n = 6$ and 8). CrystEngComm **5**, 368–373 (2003). doi:10.1039/b308407h
10. Atwood, J.L., Barbour, L.J., Jerga, A.: Polymorphism of pure *p*-*tert*-butylcalix[4]arene: conclusive identification of the phase obtained by desolvation. Chem. Commun. (Camb.), 2852–2953 (2002)
11. Le Roex, T., Nassimbeni, L.R., Weber, E.: Clathrates with mixed guests. Chem. Commun. (Camb.) 1124–1126 (2007) doi:10.1039/b618782j
12. Bourne, S.A., Gifford Nash, K.L., Toda, F.: An unusual mixed-guest inclusion compound. Crystal structures of the host compound hexakis(3-hydroxy-3,3-diphenylprop-2-ynyl)benzene, and its inclusion compound with acetonitrile and benzene. J. Incl. Phenom. Mol. Recogn. Chem. **32**, 91–102 (1998). doi:10.1023/A:1007946923878
13. Gutsche, C.D., Iqbal, M., Stewart, D.: Synthesis procedures for *p*-*tert*-butylcalix[4]arene. J. Org. Chem. **51**, 742–745 (1986). doi:10.1021/jo00355a033
14. Boyko, V.I., Podoprigorina, A.A., Yakovenko, A.V., Pirozhenko, V.V., Kalchenko, V.I.: Alkylation of narrow rim calix[4]arenes in a DMSO-NaOH medium. J. Incl. Phenom. Macrocycl. Chem. **50**, 193–197 (2004). doi:10.1007/s10847-005-5240-4
15. Iwamoto, K., Araki, K., Shinkai, S.: Conformations and structures of tetra-*O*-alkyl-*p*-*tert*-butylcalix[4]arenes. How is the conformation of calix[4]arenes immobilized. J. Org. Chem. **56**, 4955–4962 (1991). doi:10.1021/jo00016a027
16. Weber, E., Josel, H.P.: A proposal for the classification and nomenclature of host-guest-type compounds. J. Incl. Phenom. **1**, 79–85 (1983). doi:10.1007/BF00658018
17. Tsuzuki, S., Honda, K., Uchimaru, T., Mikami, M., Tanabe, K.: The magnitude of the CH/π interaction between benzene and some model hydrocarbons. J. Am. Chem. Soc. **122**, 3746–3753 (2000). doi:10.1021/ja993972j
18. Rathore, R., Lindeman, S.V., Rao, K.S.S.P., Sun, D., Kochi, J.K.: Guest penetration deep within the cavity of calix[4]arene hosts: the tight binding of nitric oxide to distal (cofacial) aromatic groups. Angew. Chem. Int. Ed. **39**, 2123–2127 (2000). doi:10.1002/1521-3773(20000616)39:12≤2123::AID-ANIE2123≥3.0.CO;2-4
19. Ikeda, A., Tsuzuki, H., Shinkai, S.: NMR spectroscopic and X-ray crystallographic studies of calix[4]arene · Ag^+ complexes. Influence of bound Ag^+ on $C_{2v} - C_{2v}$ interconversion in cone-calix[4]arenes. J. Chem. Soc. Perkin Trans. **2**, 2073–2080 (1994). doi:10.1039/p29940002073
20. Stumpf, S., Goretzki, G., Gloe, K., Gloe, K., Seichter, W., Weber, E., et al.: Solution and X-ray crystal structures of the di- and tetra-allyl ether of *tert*-butylcalix[4]arene. J. Incl. Phenom. Macrocycl. Chem. **45**, 225–233 (2003). doi:10.1023/A:1024568408356

21. Gruber, T., Weber, E., Seichter, W.: Crystal structure of 25,26,27,28-tetrabenzyloxy-5,11,17,23-*tert*-butylcalix[4]arene. Z. Kristallogr. NCS **222**, 222–224 (2007)
22. Fischer, C., Gruber, T., Seichter, W., Weber, E.: 5,11,17,23-Tetra-*tert*-butyl-25,26,27,28-tetramethoxycalix[4]arene tetrahydrofuran solvate. Acta Crystallogr. Sect. E Struct. Rep. Online **63**, o4572–o4573 (2007). doi:10.1107/S1600536807053925
23. Arena, G., Contino, A., Longo, E., Spoto, G., Arduini, A., Pochini, A., et al.: An integrated approach to the study of the recognition of guests containing CH_3 and CH_2 acidic groups by differently rigidified cone *p-tert*-butylcalix[4]arene derivatives. New J. Chem. **28**, 56–61 (2004). doi:10.1039/b308996g
24. Arduini, A., Nachtigall, F.F., Pochini, A., Secchi, A., Ugozzoli, F.: Calix[4]arene cavitands: a solid state study on the interactions of their aromatic cavity with neutral organic guests characterised by acid CH_3 and CH_2 groups. Supramol. Chem. **12**, 273–291 (2000). doi:10.1080/10610270008029449
25. Gruber, T., Weber, E., Seichter, W., Bombicz, P., Csöregh, I.: Versatile inclusion behavior of a dinitrocalix[4]arene having two ester pendants—preparation and X-ray crystal structures of complexes. Supramol. Chem. **18**, 537–547 (2006). doi:10.1080/10610270600847040
26. Araki, K., Iwamoto, K., Matsuda, T.: On the conformational isomers in tetra-*O*-alkylcalix[4]arenes. Chem. Lett. **10**, 1747–1751 (1989). doi:10.1246/cl.1989.1747
27. Harms, K.: XCAD, Program for the Reduction of CAD-4 Diffractometer Data. University of Marburg, Germany (1997)
28. Sheldrick, G.M.: SHELX-97, Program for Crystal Structure Solution and Refinement. University of Göttingen, Germany (1997)