5,17-Bis(acetamido)-25,26,27,28-tetrapropoxycalix[4]arene; the first example of two different pinched cone conformations in the solid state

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Abstract. Crystals of 5,17-bis(acetamido)-25,26,27,28-tetrapropoxycalix[4]arene · ethyl-acetate (1:1), $C_{44}H_{54}N_2O_6 \cdot C_4H_8O_2$ are triclinic, space group $P-1$, $a = 13.319(4)$, $b = 15.519(4)$, $c = 22.386(6)$ Å, $\alpha = 104.73(3)^\circ$, $\beta = 99.02(3)^\circ$, $\gamma = 95.30(3)^\circ$, $T = 100(5)$ K, $Z = 4$. The asymmetric unit contains two calix[4]arene molecules and two ethyl acetate molecules. The two calix[4]arene molecules have different pinched cone conformations. The phenyl rings show small but consistent boat-like deformations. The final R factor is 7.9%.

Introduction

Calixarenes are a very important class of compounds in supramolecular chemistry^{1–3}. Calix[4]arene, the most well-known representative, has been widely used as a molecular platform for the synthesis of selective molecular receptors for cations, anions, and neutral molecules. Calix[4]arenes can adopt four extreme conformations in solution, *viz.* cone, partial cone, 1,2-alternate, and 1,3-alternate^{1–3}. The introduction of bulky substituents ($R > \text{ethyl}$) at the lower rim prevents the interconversion among these four stereoisomers⁴. However, tetra-*O*-alkylated calix[4]arenes in the cone conformation still have some flexibility and it has been proven that the C_{4v} symmetry, usually observed in the ¹H-NMR spectra, is the result of a fast interconversion between two C_{2v} structures (Scheme 1)^{5,6}. In the C_{2v} -symmetrical structure, called the pinched cone conformation, two opposite aromatic rings are almost parallel while the other two adopt a flattened position⁷. However, crystal structures of these tetra-*O*-alkylated calix[4]arenes reveal that in the solid state most derivatives adopt a pinched-cone conformation⁸.

Recently, we reported that calix[4]arenes, substituted at the upper rim with two (thio)urea moieties or with two acetamido groups (**1**), adopt a pinched cone conformation in solution as a result of diametrical, intramolecular hydrogen bonding^{9,10}. In this paper, we show that, in the solid state,

bis(acetamido)calix[4]arene **1**¹¹ is present in two different pinched cone conformations.

Experimental

The title compound **1** was synthesized as described before¹¹. Crystals suitable for X-ray analysis were obtained from ethyl acetate. Crystal data are given in Table I. Cell constants were obtained from repeated measurements of 25 reflections in the range $\theta = 5\text{--}15^\circ$. Intensity data were obtained on an Enraf-Nonius Cad 4 diffractometer, using graphite monochromated $\text{MoK}\alpha$ radiation, with scan width (ω) $[0.70 + 0.23 \cdot \tan(\theta)]^\circ$. The structure was solved by means of direct methods¹². The unit cell contains two independent calix[4]arene and ethyl acetate molecules. The number of parameters refined was 765 [scale factor, positional parameters of the heavy atoms, thermal parameters (anisotropic for the O and N atoms, the terminal C atoms of the propyl groups and the acetamide groups, the C atoms of the ethyl acetate molecules; isotropic for the rest of the C atoms)]. The resulting atomic coordinates are collected in Table II; the structure of the molecules is depicted in Figure 1. The H atoms were put at calculated positions. The final R factors were $R = 7.9\%$ and $R_w = 8.9\%$.

The atoms of the ethyl acetate molecules show rather large thermal motion, indicating some disorder or partial occupancy. The rather high R factors are due to the mediocre quality of the small crystals available.

Results and discussion

The structure of bis(acetamido)calix[4]arene **1** in the solid state was determined by X-ray crystallography on a single

Scheme 1.

Table 1 Crystallographic data

Crystal data		Data Collection		Refinement	
Formula	$C_{44}H_{54}O_6N_2 \cdot C_4H_8O_2$	Radiation	MoK α	final R	0.079
M_r	795.02	Scan type	$\omega/2\theta$	R_w	0.089
Crystal system	triclinic	θ_{max}	20°	S	4.74
Space group	$P-1$	Refl. measured	8132	Reflections	4579
a	13.319(4) Å	Refl. obs. $I >$	4579	Parameters	765
b	15.519(4) Å	$3.0 \cdot \sigma(I)$	-12 → 12	$(\Delta/\sigma)_{max}$	0.02
c	22.386(6) Å	h range	-14 → 14	$\Delta\rho_{max}$	0.50 e·Å $^{-3}$
α	104.73(3)°	k range	0 → 21	$\Delta\rho_{min}$	-0.56 e·Å $^{-3}$
β	99.02(3)°	l range			
γ	95.30(3)°				
V	4377(5) Å 3				
Z	4				
D_x	1.206 Mg·m $^{-3}$				
μ	0.076 mm $^{-1}$				
T	100(5) K

crystal grown from ethyl acetate. The surprising feature of the crystal structure is the existence of two different pinched cone conformers of the molecule alongside one another. Half of the

molecules adopt a pinched cone in which the two acetamido groups converge, while in the other half the amido groups diverge (Figure 1).

Both conformers form part of an infinite hydrogen-bonded network which extends throughout the crystal (Figures 2 and 3)¹³. In spite of the intramolecular hydrogen bond in bis-(acetamido)calix[4]arene **1** observed in solution⁹, this hydrogen bond motif is not found in the solid state. The "divergent" conformers form infinite ribbons through hydrogen bonding of the amido NH with an amido CO of another identical molecule (Figure 3). The distance between the N atom and the O atom of the two amido groups involved is 2.87(1) Å, with a rather small N-H...O angle of 146.60° (Table III). The ribbons are interconnected by the "parallel" conformer through one normal hydrogen bond and one bifurcated hydrogen bond. The former has the shortest N...O distance [2.80(1) Å] and is virtually linear. The two hydrogen bonds involved in the bifurcated hydrogen bond are substantially longer [N...O = 2.93(1) and 3.10(1) Å], and deviate more from linearity [N-H...O angles of 160.8(6)° and 164.9(6)°].

Table IV presents the angles between the planes of the four

Figure 1. X-ray single crystal structures of the "parallel" (left) and the "divergent" (right) conformers of **1**. Hydrogen bonds depicted as thin solid lines.

Figure 2. Hydrogen-bonded array of "parallel" and "divergent" pinched cones.

Table II Final atomic coordinates and equivalent thermal parameters with e.s.d. (estimated standard deviation) values in parentheses. Atomic numbering for the first and the second calix[4]arene molecule and the two ethyl acetate molecules starts from C110, C210, C301 and C401, respectively

Atom	x	y	z	B (Å ²) ^a
O116	0.2634(5)	0.4755(4)	0.9277(3)	3.0(2)
O123	0.0169(6)	0.4581(5)	0.6491(3)	6.2(2)
O136	0.0642(5)	0.2860(4)	0.8642(3)	3.1(2)
O156	0.1227(5)	0.0774(4)	0.8244(3)	3.2(2)
O163	-0.0594(4)	0.0777(4)	0.5477(3)	2.8(2)
O176	0.3153(5)	0.2546(4)	0.8617(3)	2.8(2)
O216	0.3794(5)	0.3778(4)	0.2722(3)	2.7(2)
O223	0.7147(4)	0.7378(4)	0.4125(3)	2.6(2)
O236	0.1376(4)	0.1555(4)	0.2726(3)	2.5(2)
O256	0.3178(5)	0.1797(4)	0.2861(3)	2.7(2)
O263	0.3828(4)	-0.1597(4)	0.4063(3)	3.0(2)
O276	0.5489(4)	0.2201(4)	0.2558(3)	2.6(2)
O303	0.8284(7)	0.1520(7)	0.9454(5)	8.7(3)
O304	0.6644(7)	0.1757(6)	0.9286(4)	6.6(3)
O403	0.1436(9)	0.848(1)	0.6731(6)	22.9(7)
O404	0.1742(6)	0.7760(6)	0.5861(4)	6.6(2)
N121	0.1610(6)	0.3941(5)	0.6653(4)	3.0(2)
N161	0.0929(5)	0.1627(5)	0.5952(4)	2.3(2)
N221	0.5420(5)	0.7281(4)	0.4120(3)	2.1(2)
N261	0.2440(5)	-0.0849(5)	0.4060(4)	2.5(2)
C110	0.2359(7)	0.4570(6)	0.8614(4)	2.6(2) *
C111	0.3117(7)	0.4316(6)	0.8261(4)	2.8(2) *
C112	0.2840(7)	0.4143(6)	0.7612(4)	2.8(2) *
C113	0.1857(7)	0.4159(6)	0.7334(4)	2.5(2) *
C114	0.1095(7)	0.4368(6)	0.7686(4)	2.9(2) *
C115	0.1358(7)	0.4545(6)	0.8349(4)	2.2(2) *
C117	0.3046(9)	0.5702(7)	0.9545(5)	4.2(3)
C118	0.3290(9)	0.5868(8)	1.0253(6)	4.6(3)
C119	0.236(1)	0.5837(8)	1.0507(6)	6.3(4)
C120	0.0493(8)	0.4669(6)	0.8712(5)	3.1(2) *
C122	0.0820(8)	0.4126(7)	0.6288(5)	4.0(3)
C124	0.076(1)	0.3770(8)	0.5594(6)	5.6(3)
C130	-0.0264(7)	0.3036(6)	0.8324(4)	2.5(2) *
C131	-0.0383(7)	0.3928(6)	0.8385(4)	2.7(2) *
C132	-0.1297(8)	0.4109(7)	0.8058(5)	3.7(2) *
C133	-0.2018(8)	0.3410(7)	0.7664(5)	3.9(2) *
C134	-0.1839(8)	0.2531(7)	0.7590(5)	3.4(2) *
C135	-0.0948(7)	0.2317(6)	0.7914(4)	2.6(2) *
C137	0.0565(9)	0.2549(7)	0.9197(5)	4.1(3)
C138	0.0701(9)	0.3273(7)	0.9761(5)	4.1(3)
C139	0.063(1)	0.2874(9)	1.0329(6)	6.2(4)
C140	-0.0687(7)	0.1383(6)	0.7776(4)	2.8(2) *
C150	0.1131(7)	0.1039(6)	0.7675(4)	2.3(2) *
C151	0.0234(7)	0.1292(6)	0.7440(4)	2.4(2) *

Table II (continued)

Atom	x	y	z	B (Å ²) ^a
C152	0.0154(7)	0.1503(6)	0.6864(4)	2.5(2) *
C153	0.0985(7)	0.1469(6)	0.6564(4)	2.6(2) *
C154	0.1912(7)	0.1290(6)	0.6851(4)	2.6(2) *
C155	0.2008(7)	0.1081(6)	0.7417(4)	2.6(2) *
C157	0.0874(9)	-0.0168(6)	0.8118(5)	4.1(3)
C158	0.113(1)	-0.0437(7)	0.8718(5)	5.0(3)
C159	0.066(1)	0.0063(8)	0.9224(6)	6.0(4)
C160	0.3057(8)	0.0882(7)	0.7718(5)	3.4(2) *
C162	0.0222(7)	0.1227(6)	0.5467(4)	2.4(2)
C164	0.0378(8)	0.1385(6)	0.4842(5)	3.2(3)
C170	0.3846(7)	0.2504(6)	0.8218(4)	2.5(2) *
C171	0.3861(7)	0.1683(6)	0.7782(4)	2.7(2) *
C172	0.4557(8)	0.1653(7)	0.7373(5)	3.5(2) *
C173	0.5179(7)	0.2402(6)	0.7376(4)	2.7(2) *
C174	0.5111(8)	0.3218(6)	0.7785(5)	3.1(2) *
C175	0.4429(7)	0.3295(6)	0.8201(4)	2.5(2) *
C177	0.3617(8)	0.2629(7)	0.9263(5)	4.0(3)
C178	0.381(1)	0.1729(8)	0.9353(5)	5.3(3)
C179	0.430(1)	0.180(1)	1.0041(6)	8.4(5)
C180	0.4184(8)	0.4173(6)	0.8563(5)	3.0(2) *
C210	0.4206(7)	0.4641(6)	0.3099(4)	2.1(2) *
C211	0.5279(7)	0.4838(6)	0.3262(4)	1.9(2) *
C212	0.5702(7)	0.5707(6)	0.3617(4)	2.1(2) *
C213	0.5070(7)	0.6353(6)	0.3791(4)	1.9(2) *
C214	0.4003(7)	0.6107(6)	0.3674(4)	2.1(2) *
C215	0.3575(7)	0.5237(6)	0.3336(4)	1.9(2) *
C217	0.3304(8)	0.3787(6)	0.2084(5)	3.5(3)
C218	0.4057(9)	0.3747(7)	0.1683(5)	4.3(3)
C219	0.352(1)	0.3873(9)	0.1035(6)	6.4(4)
C220	0.2425(7)	0.4926(6)	0.3307(4)	2.6(2) *
C222	0.6389(7)	0.7728(6)	0.4261(4)	2.3(2)
C224	0.6468(7)	0.8699(6)	0.4601(5)	3.2(3)
C230	0.1829(7)	0.3350(6)	0.3359(4)	2.3(2) *
C231	0.2341(7)	0.4213(6)	0.3665(4)	2.3(2) *
C232	0.2811(7)	0.4390(6)	0.4280(4)	2.8(2) *
C233	0.2793(7)	0.3747(6)	0.4590(4)	2.9(2) *
C234	0.2308(7)	0.2881(6)	0.4271(4)	2.6(2) *
C235	0.1834(7)	0.2673(6)	0.3652(4)	2.1(2) *
C237	0.0302(7)	0.3246(6)	0.2641(5)	3.0(3)
C238	-0.0072(8)	0.3189(7)	0.1954(5)	4.4(3)
C239	-0.1231(9)	0.3183(8)	0.1810(6)	5.6(3)
C240	0.1351(7)	0.1705(6)	0.3299(4)	2.1(2) *
C250	0.3035(7)	0.1142(6)	0.3165(4)	2.2(2) *
C251	0.2117(7)	0.1047(6)	0.3381(4)	2.0(2) *
C252	0.1963(7)	0.0379(6)	0.3673(4)	2.1(2) *
C253	0.2713(7)	-0.0158(6)	0.3775(4)	1.9(2) *
C254	0.3658(7)	-0.0003(6)	0.3620(4)	2.2(2) *
C255	0.3826(7)	0.0676(6)	0.3319(4)	1.8(2) *

Figure 3. Schematic representation of the hydrogen-bonded network of the "parallel" and the "divergent" conformers of 1.

Table II (continued)

Atom	x	y	z	B (Å ²) ^a
C257	0.3170(8)	0.1485(7)	0.2207(5)	3.5(3)
C258	0.2157(8)	0.1250(7)	0.1814(5)	3.8(3)
C259	0.222(1)	0.1036(8)	0.1101(5)	5.5(3)
C260	0.4913(7)	0.0927(6)	0.3208(4)	2.5(2) *
C262	0.2959(7)	-0.1523(6)	0.4160(4)	2.7(2)
C264	0.2358(7)	-0.2220(6)	0.4366(5)	3.4(3)
C270	0.5546(7)	0.2528(6)	0.3201(4)	2.5(2) *
C271	0.5287(7)	0.1925(6)	0.3534(4)	2.1(2) *
C272	0.5333(7)	0.2250(6)	0.4169(4)	2.6(2) *
C273	0.5601(7)	0.3151(6)	0.4481(5)	3.0(2) *
C274	0.5805(8)	0.3750(6)	0.4128(5)	3.0(2) *
C275	0.5779(7)	0.3446(6)	0.3497(4)	2.1(2) *
C277	0.6446(7)	0.1960(7)	0.2385(5)	3.7(3)
C278	0.6293(9)	0.1649(8)	0.1677(6)	5.5(3)
C279	0.5537(9)	0.0801(8)	0.1396(5)	4.7(3)
C280	0.5950(7)	0.4110(6)	0.3123(4)	2.6(2) *
C301	0.724(1)	0.146(1)	1.0238(7)	9.9(5)
C302	0.749(1)	0.157(1)	0.9627(7)	7.5(4)
C305	0.673(1)	0.1854(8)	0.8649(6)	6.1(4)
C306	0.663(1)	0.0962(9)	0.8196(6)	6.0(4)
C401	0.244(1)	0.9177(9)	0.5932(8)	8.6(5)
C402	0.191(1)	0.863(1)	0.6251(7)	9.3(5)
C405	0.117(1)	0.712(1)	0.6094(8)	15.5(5)
C406	0.133(1)	0.627(1)	0.5788(9)	13.0(6)

^a Starred atoms were refined isotropically. Anisotropically refined atoms are given in the form of the isotropic equivalent displacement parameter defined as: $(4/3) \cdot [a^2 \cdot B(1,1) + b^2 \cdot B(2,2) + c^2 \cdot B(3,3) + a \cdot b \cdot \cos(\gamma) \cdot B(1,2) + a \cdot c \cdot \cos(\beta) \cdot B(1,3) + b \cdot c \cdot \cos(\alpha) \cdot B(2,3)]$

Table III Distances and angles of hydrogen bonds in the X-ray crystal structure of **1**^a

N-H...O	N...O (Å)	H...O (Å)	<N-H...O (°)
N212-H121...O223	3.10(1)	2.171(8)	164.9(6)
N161-H161...O223	2.93(1)	2.016(8)	160.8(6)
N221-H221...O263	2.87(1)	2.024(8)	146.6(6)
N261-H261...O163	2.80(1)	1.851(8)	177.7(6)

^a Hydrogen atoms put at calculated positions assuming an N-H distance of 0.95 Å.

phenyl rings and the mean plane of the bridging methylene carbons. Both conformers Phe1 and Phe3 contain the acetamido-substituted phenyl rings. The angles between the mean planes of opposing phenyl rings of the two conformers also provide interesting information. In the "parallel" conformer, the angle between the two amido-substituted rings is 26.3°, while the angle between the "flattened" rings is 103.5°. For the "divergent" conformer opposite values are found: an angle of 119.8° between the substituted rings and 26.6° between the other two rings. These values indicate that

Table IV Angles between the planes of the phenyl rings and the mean plane of the bridging methylene carbon atoms (φ) and dihedral angles between opposing planes (θ)^a

Plane	"Divergent" conformer		"parallel" conformer	
	φ (°)	θ (°)	φ (°)	θ (°)
Phe1	33.5	119.8	109.3	
Phe3	26.7		97.0	-26.3
Phe2	103.0		36.2	103.2
Phe4	103.5	-26.5	40.6	

^a Phe1 and Phe3 contain the acetamido substituent.

the degree of pinching is practically the same for both conformers.

The phenyl rings are almost planar. Closer inspection of the deviations from the mean planes shows a small but consistent deformation in a boat-like fashion of all the rings. The largest deviation (order of magnitude 0.04 Å) is found for the C atoms to which the propoxy group is connected. Similar distortions, which are characteristic for calix[4]arene molecules, have been noticed before¹⁴.

To our knowledge, this is the first example of a crystal structure of a calix[4]arene in which two different C_{2v} conformers are present. Surprisingly, in the solid state intramolecular hydrogen bonding between the acetamide moieties is not observed. This situation is different from that in apolar solvents, where intramolecular hydrogen bonds cause only one of the two pinched cones to exist. This aspect may be used to increase the degree of preorganization of a substituent connected via an amide bond to the calix[4]arene. We are currently investigating hydrogen bonding calix[4]arenes that use this feature in hydrogen bond directed aggregation both in solution and in the solid state.

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¹⁵ Previously, we reported the presence of two cone conformers with different intramolecular hydrogen bonding schemes in the crystal structure of a 1,2-disubstituted calix[4]arene. In that case, however, the

difference between the two structures was too small to speak of two conformers: L.C. Groenen, B.H.M. Ruël, A. Casnati, P. Timmerman, W. Verboom, S. Harkema, A. Pochini, R. Ungaro and D.N. Reinhoudt, *Tetrahedron Lett.* **32**, 2675 (1991).