

# Stereochemistry of capped calix[4]arenes in liquid and solid phase by NMR spectroscopy

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The stereochemistry of calix[4]arenes capped by diamide bridges in the 1,3-position on the lower rim was established by <sup>1</sup>H and <sup>13</sup>C solution and solid state NMR. The <sup>13</sup>C chemical shifts of ArCH<sub>2</sub>Ar were found to be diagnostic of the cone, partial cone and 1,3-alternate conformations also in the solid state. Two sets of signals appearing in the CP/MAS spectra of 1,3-alternate and partial cone compounds indicate that these molecules occupy inequivalent sites in the elemental cell.

## Introduction

The synthesis and study of functionalized calixarenes, such as calixarenes bridged with different rings, are an attractive topic. We have described a series of calix[4]arenes capped by diamide bridges in the 1,3-positions,<sup>1</sup> and our NMR studies in CDCl<sub>3</sub> solution revealed that, depending on the size of bridge and the character of the OR (R: H, alkyl) substituent, these compounds exist in a cone or flattened cone conformation (Fig. 1). Introducing indophenol subunits into the calix[4]arene skeleton of calix(aza)crowns resulted in chromogenic calixarenes exhibiting different tautomer forms in various solvents.<sup>2</sup> Also in this case, the preferred conformations were the cone and the flattened cone. Alkylation of calix[4]arenes capped by diamide bridges in the presence of Cs<sub>2</sub>CO<sub>3</sub> base gave derivatives in the 1,3-alternate conformation, which were converted to the corresponding doubly-capped alternate calix(aza)crowns.<sup>3</sup> Several studies of calix[4]arenes<sup>4–7</sup> reported conformational equilibria in solution, while the solid state structures, as determined by X-ray crystallography, showed single homogeneous conformers. We note that the preferred conformation and even the tautomers (in derivatives where they appear) in solution may differ from those in the crystalline form. In order to examine this phenomenon, we have used liquid and solid state NMR for the structural evaluation of calix(aza)crown derivatives 1–9, synthesized in our laboratory.<sup>1,3</sup>

## Results and discussion

### Calix[4]arenes capped by diamide bridges in the 1,3-position on the lower rim (1–7)

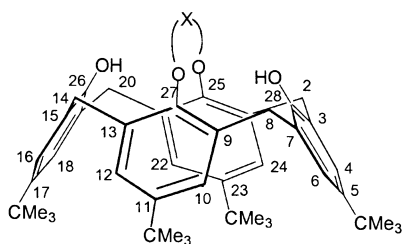
A characteristic feature of the <sup>13</sup>C NMR spectra of calix[4]arenes with the cone or flattened cone conformation is the appearance of the  $\delta_{\text{ArCH}_2\text{Ar}}$  signal at  $\delta = 30\text{--}32$ ,<sup>8</sup> while in the <sup>1</sup>H NMR spectrum a pair of AB-type doublets is observed for the diastereotopic methylene protons. The chemical shift differences between these methylene protons are in the 0.6–1.1 ppm range. We have reported that the chemical shift differences

of the  $\delta_{5\text{-CMe}_3}/\delta_{11\text{-CMe}_3}$  and  $\delta_{\text{H-4,6}}/\delta_{\text{H-10,12}}$  signals in the <sup>1</sup>H NMR spectra can be used to monitor the extent of distortion from the four-fold symmetrical cone conformation.<sup>1</sup> Starting from H-2' protons of the bridge, the signals were readily assigned along the H-2'/C-27, C-27/H-10,12, H-10,12/11-CMe<sub>3</sub> and 11-CMe<sub>3</sub>/(CH<sub>3</sub>)<sub>3</sub> HMBC cross-peaks. The results for compounds 1–7 are summarized in Fig. 1.

In compounds 1–3 with non-derivatised OH groups, the chemical shifts of protons 4,6-H and 10,12-H and *tert*-butyl groups are very close, indicating an almost symmetrical cone conformation stabilized by strong intramolecular hydrogen bonds. By increasing the chain length (compounds 4–5) we observed a pronounced diamagnetic shift of the aromatic proton (H-10,12) and *tert*-butyl (11-CMe<sub>3</sub>) signals for the phenols bonded by the bridge, accompanied by a significant decrease of  $\delta_{\text{OH}}$  values. For steric reasons, the bridged aromatic rings are now arranged in parallel, while the phenolic units are flattened. In this arrangement, strong hydrogen bonding of the hydroxy groups is not possible. We conclude that specific conformational distortions are caused by the increasing length of the bridge. Replacement of OH by the bulky O*t*Bu group (compounds 6–7) resulted in a smaller chemical shift for protons H-4,6 and 5-CMe<sub>3</sub>, indicating that the alkoxy-substituted rings are now arranged in parallel.

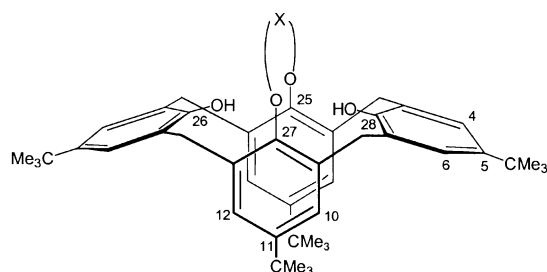
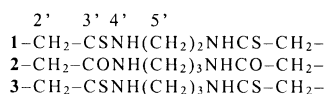
The <sup>13</sup>C chemical shifts of compounds 2, 4 and 7 in the liquid and solid phases are given in Table 1. The peaks were assigned with the help of dipolar-dephasing spectra and the general similarity between the solution and the solid state <sup>13</sup>C NMR chemical shift.<sup>9</sup>

Cross-polarization (CP) MAS is used in solid state NMR to enhance the sensitivity of rare nuclei.<sup>9</sup> The experiment is based on the transfer of polarization from an abundant spin (typically <sup>1</sup>H) to a dilute spin (typically <sup>13</sup>C). We have examined the dynamics of the polarization transfer *via* the dependence of the intensity of the peaks on the contact time for the samples 2, 4 and 7. The intensity increases with the contact time *t*, but a decay is observed for longer *t* due to the *T*<sub>1ρ</sub> relaxation of <sup>1</sup>H and <sup>13</sup>C in the rotating frame. For <sup>1</sup>H and <sup>13</sup>C, the intensity of the polarized peak is described by eqn. (1)



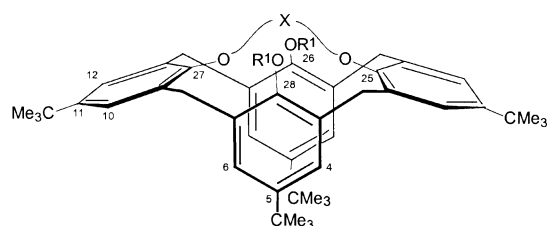
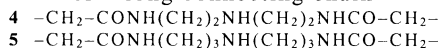
**cone conformation**

X = short connecting chain



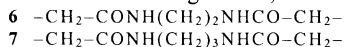
**distorted cone conformation I.**

X = long connecting chain



**distorted cone conformation II.**

X = short connecting chain, R<sup>1</sup> = nBu



<sup>1</sup> H (ppm)	cone conformation			distorted cone conformation			
	1	2	3	I. 4	I. 5	II. 6	II. 7
4,6	7.08	7.09	7.09	7.13	7.13	6.75	6.62
10,12	7.07	7.05	7.05	6.71	6.69	7.19	7.17
5-CMe <sub>3</sub>	1.26	1.26	1.27	1.33	1.34	0.89	0.86
11-CMe <sub>3</sub>	1.16	1.14	1.14	0.88	0.88	1.32	1.34
OH	8.23	8.37	8.26	6.35	6.13		

**Fig. 1** Conformations and characteristic <sup>1</sup>H chemical shifts of compounds 1–7.

$$I(t) = I_0 \left( 1 + T_{CP}/T_{1pC} - T_{CP}/T_{1pH} \right)^{-1} \left\{ \exp(-t/T_{1pH}) - \exp[-t(1/T_{CP} + 1/T_{1pC})] \right\} \quad (1)$$

where  $I_0$  is the maximum intensity,  $T_{CP}$  is the cross-polarization time and  $T_{1pH}$  and  $T_{1pC}$  are the relaxation times in the rotating frame for <sup>1</sup>H and <sup>13</sup>C, respectively. The cross-polarization rate,  $1/T_{CP}$ , depends on the square of the dipolar interaction, and thus on  $r^6$ , where  $r$  is the average distance between the <sup>1</sup>H and <sup>13</sup>C nuclei, while the relaxation time in the rotating frame provides important information on the mobility. The results for samples 2, 4 and 7 are given in Table 2.

The spectrum of 2 is well resolved and the peaks are sharp, suggesting a very mobile structure. The  $T_{CP}$  for the aromatic carbon atoms decreases in the sequence: C-5,11 (ca. 2 ms) > C-25,26 (ca. 1.5 ms) > C-3,7 (ca. 1 ms) > C-4,10 (ca. 0.2 ms). The aromatic hydrogens are the main source of polarization for C-4,10, C-3,7 and C-25,26, and the increase of the  $T_{CP}$  value reflects the increased distance. 5,11-CMe<sub>3</sub> show very long  $T_{CP}$  (5.52 ms) even if they are directly bonded to hydrogens, because the molecular rotation about the methyl symmetry axis is sufficiently fast to average out most of the <sup>13</sup>C–<sup>1</sup>H dipolar interactions. The chemical shifts are usually very close to those found in solution.

The large linewidths of the solid state <sup>13</sup>C NMR spectrum of 4 indicate a disordered structure. An important difference between the solid state and the solution NMR spectra of this sample (Table 1) is the splitting of some signals into two or more components. In particular, C-3', C-3,7, C-9,13 and C-25,26 resonate at three and two different frequencies, respectively. We see that all these carbon atoms are located in the lower rim of the calixarene bowl. The presence of the three chemical shifts for the C-3' can be attributed to the appearance of different conformers of the diamide bridge, while in compound 2 the strong hydrogen bonds fix only one preferred conformation.<sup>1</sup> The splitting could also be attributed to the coupling of C=O with the directly bonded N nucleus. However, this explanation is unlikely to be correct, given that a similar effect does not appear in the other compounds studied.

The <sup>13</sup>C solid state NMR spectrum of 7 is poorly resolved, indicating that this calixarene is disordered. As the chemical shifts are very similar to those measured in solution, the conformation should also be a flattened cone. The peak assigned to C-3' ( $\delta = 167.8$ ) has a shoulder at  $\delta = 166.2$ .  $T_{1p}$  values are only slightly shorter than those found for 4, suggesting a similar mobility. The values of  $T_{CP}$  are within a narrow range (0.06–1.23 s, see Table 2) for most of the peaks, suggesting that the dipolar field is homogeneous for the whole molecule.

The general appearance of the solution and solid state spectra is very similar. Since the chemical shift of C-2 is a useful probe for the conformation of the calixarenes,<sup>8</sup> and the values of  $\delta_{C-2}$  in the solid and in solution are almost identical, we conclude that in the case of compounds 2, 4 and 7 both phases have the cone conformation. Note that the  $\delta_{C-2}$  shifts do not reflect the possible deformation of the cone.

### 1,3-Alternate and partial cone calix[4]arenes 8 and 9

An important characteristic of the 1,3-alternate calixarene skeleton is that the two geminal protons of the methylene bridge become enantiotopic, affording a singlet in the <sup>1</sup>H NMR spectrum, while the ArCH<sub>2</sub>Ar methylene carbons are deshielded ( $\delta_{CH_2} = 36–39$ ).<sup>4</sup> This highly symmetric arrangement generally appears in double-capped calixarenes (e.g. compound 9), with the exception of compounds where the sizes of the upper and lower bridges are markedly different.<sup>3</sup>

Repeating the synthesis of 1,3-alternate 8<sup>1</sup> (Fig. 2) we recognized the paco conformer as a minor impurity. By modifying the alkylation procedure we succeeded in preparing paco 8 in an acceptable yield (see Experimental). Since it is known that conformational interconversion of calix[4]arenes takes place by the oxygen through the annulus rotation if the substituents are smaller than the propyl group, the 1,3-alternate and paco conformations of 8 can be considered to be fixed. These compounds serve as models for our solid state NMR study aimed at finding characteristic NMR features for the differentiation of conformers.

Structural elucidation was performed in CDCl<sub>3</sub> using gs-HMQC, gs-HMBC and ROESY measurements. The <sup>1</sup>H signal assignments, HMBC H,C connectivities and ROESY responses are summarised in Table 3, whereas the <sup>13</sup>C chemical shifts obtained in solution and in the solid state are compiled in Table 4.

**Table 1**  $^{13}\text{C}$  chemical shifts of compounds **2**, **4** and **7**

	<b>2</b>		<b>4</b>		<b>7</b>	
	$\text{CDCl}_3$	Solid state	$\text{CDCl}_3$	Solid state	$\text{CDCl}_3$	Solid state
2,8	32.3	32.5	31.5	32.3	31.1	30.3
3,7	127.0	127.8	128.1	129.4	132.6	134.3
		128.6		127.8		
4,6	126.2	125.4	125.6	125.0	125.6	126.0
5	143.5	144.5	143.2	141.8	145.5	146.9
				141.0		
5C	34.1	33.3	34.1	34.1	34.1	34.5
5CMe <sub>3</sub>	31.8	30.3	31.8	31.3	31.5	31.7
9,13	132.7	133.5	131.7	133.6	134.7	134.3
		132.8		132.2		
10,12	126.5	126.2	126.0	126.5	126.4	126.0
11	149.0	146.8	148.2	147.2	146.7	149.2
				146.5		
11C	34.5	33.3	34.1	34.1	34.5	34.5
11CMe <sub>3</sub>	31.3	30.3	31.0	30.4	32.0	31.7
25	147.7	149.1	149.1	150.3	153.4	153.4
				149.5		
26	149.8	149.9	150.0	151.9	151.1	150.9
				151.1		
2'	74.7	74.6	75.0	75.3	74.7	74.2
				76.0		
3'	168.5	166.2	168.7	170.2	170.2	167.8
				168.4		166.2
				167.4		
5'	36.2	34.9	40.2	40.3	38.2	36.7
				38.7		
6'	23.4	23.6	49.1	51.2	24.9	25.9
				49.6		
OBu					<sup>a</sup>	<sup>a</sup>

<sup>a</sup>  $\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ : 77.3/77.4; 31.6/31.7; 19.4/19.5; 14.4/14.6.

**Table 2**  $T_{1\rho\text{H}}$ ,  $T_{1\rho\text{C}}$  and  $T_{\text{CP}}$  for samples **2**, **4** and **7**.  $T_{1\rho\text{H}}$  and  $T_{1\rho\text{C}}$  are measured in independent experiments, while  $T_{\text{CP}}$  is calculated with equation (1). The error is generally within 5%. All the values are reported in ms

	<b>2</b>			<b>4</b>			<b>7</b>		
	$T_{1\rho\text{H}}$	$T_{1\rho\text{C}}$	$T_{\text{CP}}$	$T_{1\rho\text{H}}$	$T_{1\rho\text{C}}$	$T_{\text{CP}}$	$T_{1\rho\text{H}}$	$T_{1\rho\text{C}}$	$T_{\text{CP}}$
2,8	108	166	1.42 <sup>a</sup>	59	264	2.5 <sup>a</sup>	56	104	1.83 <sup>a</sup>
3,7	108 <sup>a</sup>	380 <sup>a</sup>	1.03 <sup>a</sup>	47 <sup>a</sup>	506 <sup>a</sup>	0.39 <sup>a</sup>	39	133	0.86
4,6	83	231	0.28	62	359	0.03	48	124	0.08
5	127	338	3.13	29	84	1.01	26	101	0.76
5,11C	141	377	2.72	54	145	6.4	48	130	1.84
5,11CMe <sub>3</sub>	409	655	5.52	61	133	3.8	56	297	1.05
9,13	104 <sup>a</sup>	disp <sup>a</sup>	1.1 <sup>a</sup>	59 <sup>a</sup>	419 <sup>a</sup>	0.67 <sup>a</sup>	39	133	0.86
10,12	90	179	0.23	51	196	0.09	48	124	0.08
11	143	572	1.95	53	66	0.81	21	115	1.08
25	121	disp	1.53	44	256	0.89	27	88	0.67
26	165	disp	1.47	45	256	0.88	30	144	0.82
2'	60	75	0.09	51	201	0.07	66	65	0.07
3'	133	234	1.11	45 <sup>a</sup>	154 <sup>a</sup>	1.2	34	92	1.23
5'	153	disp	0.07	80	23	0.05	60	66	0.07
6'	134	disp	0.07	51	50	0.05	48	72	0.06
OCH <sub>2</sub>							40	44	0.09
CH <sub>2</sub>							56 <sup>a</sup>	297 <sup>a</sup>	1.05 <sup>a</sup>
CH <sub>2</sub>							94	79	0.34
CH <sub>3</sub>							128	disp	1.49

<sup>a</sup> These values are biased by the partial overlapping of the relevant peak with other peaks or spinning sidebands; "disp" indicates that no decay was detected.

In the case of 1,3-alternate **8**, the signals of these  $\text{ArCH}_2\text{Ar}$  protons measured in  $\text{CDCl}_3$  show a pair of doublets [ $\delta = 3.89$  (d), 3.80 (d),  $J_{\text{AB}} = 16.4$  Hz], indicating a conformational distortion of the skeleton. In this case, neighbouring aromatic rings are twisted in opposite directions. This can be rationalised given the flexibility of the single-capped system. The spectra of the partial cone conformer **8** contain many more peaks, in good agreement with the lower symmetry. As expected, we observed two different pairs of  $\text{ArCH}_2\text{Ar}$  methylene signals. One pair corresponds to the conic arrangement [ $\delta_{\text{H-14,20}} = 3.38$  and 4.28,

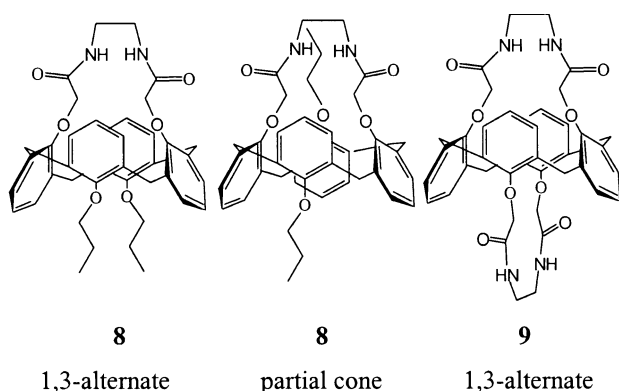
$^2J = 12.3$  Hz], while the other fits to the alternate layout [ $\delta_{\text{H-2,8}} = 3.87$  and 3.94,  $^2J = 16.4$  Hz].<sup>3,5,8</sup> The considerable difference between the geminal  $^2J$  couplings is due to the different arrangement of these protons relative to the aromatic rings.<sup>10</sup> The respective  $\delta_{\text{CH}_2}$  chemical shifts are 29.7 and 38.2 (Fig. 3).

There are some characteristic differences in the  $^1\text{H}$  chemical shifts for the OPr groups. The strong shielding of the OPr group designated by "a" indicates that the group is located in the cavity of the partial cone conformer and is exposed to the anisotropic effects from the three neighbouring aromatic rings.

**Table 3**  $^1\text{H}$  chemical shifts and ROESY responses of compounds **8** (1,3-alt; paco) in  $\text{CDCl}_3$ 

	$^1\text{H}$ 1,3-alt	$J/\text{Hz}$	$^{13}\text{C}$	HMBC connectivities	Characteristic ROESY proximities	$^1\text{H}$ paco	$J/\text{Hz}$	$^{13}\text{C}$	HMBC connectivities	Characteristic ROESY proximities
2,8c	3.89d	16.4	38.1	1,9; 3,7; 4,6; 26,28	$\text{OCH}_2$	3.94d	16.3	38.2	1,9; 3,7; 4,6; 10,24; 25,27; 26	$\text{OCH}_2^a$
2,8t	3.80d	16.4	38.1	1,9; 3,7; 10,24; 25,27	$\text{OCH}_2$ ; 2'	3.87d	16.3	38.2	1,9; 3,7; 4,6; 10,24; 25,27; 26	$\text{OCH}_2^a$ ; 2'
14,20c						4.28d	12.3	29.7	12,22; 13,21; 15,19; 16,18; 25,27; 28	$\text{CH}_2^b$ ; $\text{OCH}_2^b$
14,20t						3.38d	12.3	29.7	12,22; 13,21; 15,19; 16,18; 25,27; 28	$\text{CH}_2^b$ ; $\text{OCH}_2^b$ ; 2'
4,6	7.04d		129.5	2,8; 26,28	2'; 5'; NH	7.22d		130.4	2,8; 26	2'
5	6.80t		122.3	3,7	5'; NH	6.93t		122.5	3,7	5'
10,24	7.09d		130.0	2,8; 25,27	$\text{CH}_3^a$ ; $\text{CH}_2^a$ ; $\text{OCH}_2^a$	7.03d		129.7	2,8; 12,22; 25,27	$\text{OCH}_2^a$ ; $\text{CH}_2^a$
11	6.93t		124.0	9,13		6.91t		125.0	9,13	
12,22						7.26d		129.2	10,24; 14,20; 25,27	16,18
16,18						7.12d		128.9	14,20; 28	12,22
17						6.79t		124.4	15,19	
2'	4.14s		68.2	3'	2,8t; 4,6	4.13d	14.0	71.7	3'	2,8t
4' NH	5.33t				4,6; 5	4.37d	14.0	71.7	3'	2,8t; 4,6
5'	3.16m		37.1		4,6; 5	3.45m		38.1	5'	5; $\text{CH}_3^b$ ; $\text{CH}_2^b$ ; $\text{OCH}_2^b$
$\text{OCH}_2^a$	3.40t		71.8	$\text{CH}_3^a$ ; $\text{CH}_2^a$	2,8c; 2,8t; 10,24	3.56m		38.1	5'	5; $\text{CH}_3^b$ ; $\text{CH}_2^b$ ; $\text{OCH}_2^b$
$\text{CH}_2^a$	1.20m		22.7	$\text{CH}_3^a$ ; $\text{OCH}_2^a$	10,24	1.75t		72.4	$\text{CH}_3^a$ ; $\text{CH}_2^a$	2,8c; 2,8t; 10,24
$\text{CH}_3^a$	0.67t		10.1	$\text{CH}_2^a$ ; $\text{OCH}_2^a$	10,24	0.63t		22.6	$\text{CH}_3^a$ ; $\text{OCH}_2^a$	10,24
$\text{OCH}_2^b$						-0.16t		9.2	$\text{CH}_2^a$ ; $\text{OCH}_2^a$	
$\text{CH}_2^b$						3.75t		79.1	$\text{CH}_3^b$ ; $\text{CH}_2^b$	14,20c; 14,20t; 5'
$\text{CH}_3^b$						1.58m		22.1	$\text{CH}_3^b$ ; $\text{OCH}_2^b$	14,20c; 14,20t; 5'
1,9			133.8			0.75t		9.8	$\text{CH}_2^b$ ; $\text{OCH}_2^b$	5'
3,7			134.6					134.6		
13,21								135.4		
15,19								134.6		
25,27								135.8		
26			153.7					153.4		
28			157.0					156.7		
			157.0					154.2		

<sup>a</sup> Group located in the cavity. <sup>b</sup> Group oriented towards the diamide bridge.

**Fig. 2** Compounds **8** (1,3-alternate and partial cone conformers) and **9**.

The OPr group designated by “b” is oriented towards the diamide bridge. The different position of the propoxy groups is confirmed by the ROESY responses (Table 3 and Fig. 3). We note that, due to sterical repulsion between the two OPr groups, they are oriented outwards in the 1,3-alternate conformer. An unambiguous assignment of signals in the differently substituted aromatic moieties was made using the HMBC spectra. The quaternary carbon atoms 25,27 and 26,28 could be distinguished due to the correlation of the  $\text{OCH}_2$  methylene protons of the propoxy group and C-26 and C-28. The cross-peaks between C-28/H-4,6 and C-27/H-10,12 made the reliable assignment of the aromatic protons possible.  $^3J(\text{C},\text{H})$  couplings of the aromatic  $\text{H}_{para}$ -5 and  $\text{H}_{para}$ -11 mark out the C-3,7 and C-9,13 signals, respectively.

The rigid **9** may serve as a source of  $^{13}\text{C}$  reference data for the 1,3-alternate conformer. A comparison of  $^{13}\text{C}$  CP/MAS NMR spectra of **9** measured in both phases indicates that **9** appears in

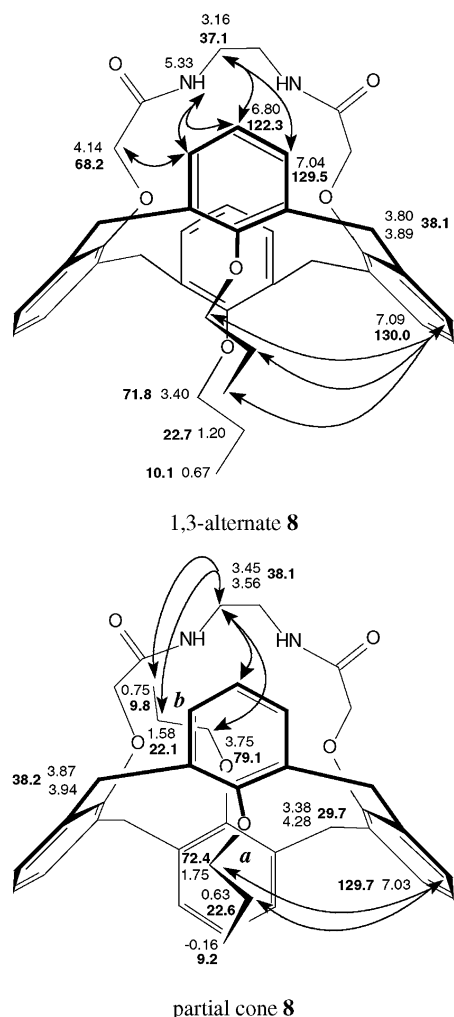
the solid as the 1,3-alternate conformer. The good agreement of the  $\delta\text{ArCH}_2\text{Ar}$  chemical shifts obtained in solution (38.7) and in the solid state (37.1) shows that the chemical shift is in accord with the “Jaime rule”,<sup>8</sup> which is therefore applicable to the solid state. All the peaks are relatively broad, especially those attributed to the three  $\text{CH}_2$  groups (2', 5' and 2), suggesting some associated disorders.

The most discriminating carbon resonances for the determination of conformations are C-2,8 and C-14,20. The  $\text{Ar-CH}_2\text{Ar}$  methylene signal of the 1,3-alternate **8** was found at 36.9 ppm in the well resolved CP/MAS spectrum, in good agreement with the result obtained in  $\text{CDCl}_3$ . No signals appeared in the 29–33 ppm range (Fig. 4).

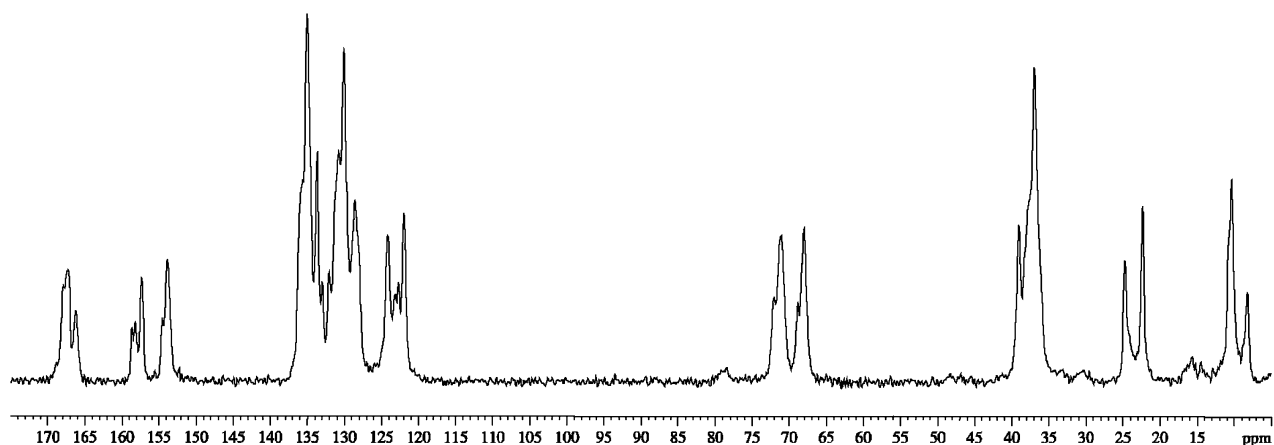
We observed two sets of signals with a *ca.* 2 : 1 intensity ratio (see Table 4, minor signals marked with “c”). This doubling of signals may be due to an asymmetric packing arrangement of adjacent molecules in a low-symmetry space group. Furthermore, we found small but significant additional signal splittings for some signals *e.g.* C-2', C-25,27 and C-26,28, proving that these atoms are no longer in symmetrical positions in the solid state. Inspection of a Dreiding stereomodel indicates that the diamide bridge connecting C-25 and C-27 may occur in two conformations and that their fast interconversion in solution results in  $C_{2v}$  symmetry. In the solid state this conformational motion is blocked, leading to the structure which does not possess symmetry planes ( $C_2$ ) and thus should be chiral. Chirality of the calix[4]arenes may originate in the chiral character of the bridge.<sup>2</sup> The diamide bridge in solution also proved to be flexible in the corresponding cone **8** compound.<sup>1</sup> For the analogous dihydroxy compound Böhmer *et al.* observed a hindered motion of the bridging atoms if the  $\text{HN-CH}_2\text{CH}_2\text{-NH}$  moiety was replaced by the *N*-methylated chain.<sup>7</sup> This molecule has a two-fold symmetry and is chiral even in solution, resulting in separated signals for the atoms in diastereotopic positions.

## Conclusions

As a result of “tuning” the structure of compounds 1–7 by altering the length of the 1,3-diamide bridge, as well as by the replacement of OH by bulky OR groups, differently distorted flattened cone conformations (I and II) were established in solution by characteristic  $^1\text{H}$  NMR chemical shifts. The  $^{13}\text{C}$  NMR chemical shifts of  $\text{ArCH}_2\text{Ar}$  (compounds 2, 4, 7–9) are diagnostic of the cone, partial cone and 1,3-alternate conformations in both phases. The appearance of two sets of signals in the CP/MAS spectra (8, 9) indicates that the mole-



**Fig. 3** Stereostructures of 1,3-alternate **8** and partial cone **8**. Double arrows indicate steric proximities observed by ROESY experiment.



**Fig. 4** CP/MAS spectrum of 1,3-alternate **8**.

cules occupied inequivalent sites in the elemental cell. The hindered motion of the diamide bridge results in chiral structure in the solid state.

## Experimental

### Solution NMR

NMR spectra were recorded in  $\text{CDCl}_3$  on a Bruker Avance DRX-500 spectrometer operating at 500 MHz for  $^1\text{H}$  at 300 K. Chemical shifts are given on the  $\delta$  scale. Pulse sequences were taken from the Bruker software library. HMBC measurements were optimized for long-range 7 Hz couplings. ROESY spectra were run with  $\tau_{\text{mixing}} = 0.5, 0.75$  and 1 s, respectively.

### Solid state NMR

$^1\text{H}$ - $^{13}\text{C}$  CP/MAS spectra were measured using Chemagnetics CMX-400 and Bruker Avance 400 WB spectrometers operating at 400 MHz for  $^1\text{H}$ , and MAS probehead and zirconia rotors 4 mm in diameter. The spinning rates were 8–12 kHz, and the  $^1\text{H}$   $\pi/2$  pulse length 3.70  $\mu\text{s}$ . The centerband Hartmann–Hahn condition was set with hexamethylbenzene. Dipolar dephasing spectra were acquired with 50  $\mu\text{s}$  of dephasing delay. The  $T_{1\rho\text{H}}$  and  $T_{1\rho\text{C}}$  relaxation times were measured using a CP pulse sequence modified by adding a delay either before or after the polarization transfer.<sup>11,12</sup> The Total Suppression of Spinning Sidebands (TOSS) pulse sequence<sup>13,14</sup> was used to remove the spinning sidebands whenever they hindered the interpretation of the spectra.

### Synthesis of 1,3-alternate **8** and partial cone **8**

A mixture of 25,27-[ethylenebis(aminocarbonylmethoxy)]calix-[4]arene (0.56 g, 1 mmol), PrBr (0.62 g, 5 mmol) and tetrabutylammonium bromide (0.05 g) in toluene (10 ml) was agitated with 50% aqueous KOH (2 ml) at 100  $^\circ\text{C}$  for 5 h. Then 10 ml water were added and the organic phase was separated, washed with dilute acid and dried ( $\text{Na}_2\text{SO}_4$ ). After the removal of the solvent, the residue was thoroughly washed with methanol affording 0.36 g (50%) white solid insoluble in methanol (1,3-alternate **8**, mp 352–356  $^\circ\text{C}$ , lit. mp 353–355  $^\circ\text{C}$ ).

The filtrate was evaporated to dryness and 0.18 g (25%) paco **8** was obtained in essentially pure form. Mp 301–303  $^\circ\text{C}$ , anal. calc. for  $\text{C}_{40}\text{H}_{44}\text{N}_2\text{O}_6$ , C 74.05, H 6.84, N 4.32; found C 73.85, H 6.80, N 4.28%.

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**Table 4**  $^{13}\text{C}$  chemical shifts of compounds **8** and **9**

	<b>8</b>				<b>9</b>	
	paco solution	paco solid state	1,3-alt solution	1,3-alt solid state	1,3-alt solution	1,3-alt solid state
2,8	38.0	39.4	38.1	36.9	38.7	37.1
14,20	29.5	~30	38.1	36.9	38.7	37.1
4,6	130.1	129.4	129.5	128.6–132.1	131.9	131.7 132.5 <sup>c</sup>
5	122.3	123.9	122.3	122.0 122.7 <sup>c</sup>	126.9	124.4
10,24	129.5	129.4	130.0	128.6–132.1	131.9	131.7 132.5 <sup>c</sup>
11	124.8	123.9	124.0	124.2 123.2 <sup>c</sup>	126.9	124.4
12,22	129.0	129.4	130.0	128.6–132.1	131.9	131.7 132.5 <sup>c</sup>
16,18	128.6	129.4	129.5	128.6–132.1	131.9	131.7 132.5 <sup>c</sup>
17	124.1	123.9	122.3	122.0 122.7	126.9	124.4
2'	71.5	72.6 75.4 <sup>c</sup>	68.2	68.0 68.8 <sup>c</sup>	68.8	68.7
5'	37.9	35.3 34.2	37.1	36.9 39.1	39.7	41.5
OCH <sub>2</sub> <sup>a</sup>	72.1	71.3 ~69 <sup>c</sup>	71.8	71.1 72.1 <sup>c</sup>		
CH <sub>2</sub> <sup>a</sup>	22.3	24.5	22.7	22.4 24.7 <sup>c</sup>		
CH <sub>3</sub> <sup>a</sup>	8.9	8.8 7.6 <sup>c</sup>	10.2	10.3 8.2 <sup>c</sup>		
OCH <sub>2</sub> <sup>b</sup>	78.9	~78				
CH <sub>2</sub> <sup>b</sup>	21.9	22.4				
CH <sub>3</sub> <sup>b</sup>	9.6	10.0 11.8 <sup>c</sup>				
1,9	135.1	134.7	134.7	133.0–135.6	136.8	135.0 137.7 <sup>c</sup>
3,7	134.4	134.7	134.3	133.0–135.6	136.8	135.0 137.7 <sup>c</sup>
13,21	135.6	134.7	134.7	133.0–135.6	136.8	135.0 137.7 <sup>c</sup>
15,19	134.4	134.7	134.3	133.0–135.6	136.8	135.0 137.7 <sup>c</sup>
25,27	153.2	153.5 154.1 <sup>c</sup>	153.5	153.9 154.5 <sup>c</sup>	155.4	154.3 152.9 <sup>c</sup>
26	156.4	157.2 158.8 <sup>c</sup>	156.3	157.3 158.2 <sup>c</sup>	155.4	154.3 152.9 <sup>c</sup>
28	154.0	156.0 155.3 <sup>c</sup>	156.3	157.3 158.7 <sup>c</sup>	155.4	154.3 152.9 <sup>c</sup>
3'	168.1	168.0 166.6 <sup>c</sup>	167.7	167.3 167.7 167.9 166.2	173.7	169.1 167.8 <sup>c</sup>

<sup>a</sup> OPr group located in the cavity. <sup>b</sup> OPr group oriented towards the diamide bridge. <sup>c</sup> Signals with half intensities.

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