

Conformations and Structures of Two Novel Upper Rim Disubstituted Derivatives of Tetra-*O*-alkylcalix[4]arene: The Effect of Substituents

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Abstract

Two new calix[4]arene derivatives, 5,17-dinitro-26,28-dimethoxy-25,27-dipropoxycalix[4]arene (**4**) and 5,17-diamino-26,28-dimethoxy-25,27-dipropoxycalix[4]arene (**5**), have been synthesized and fully characterized. The ¹H NMR spectra measured in different solvents and temperatures indicated that the dominant conformer is partial cone for **4** and cone for **5**, though there are some variations in relative ratio of partial cone to cone conformers. The structures of partial cone **4** and cone **5** are determined by X-ray crystallography. The different conformational behavior in compounds **4** and **5** is governed by the two substituents at the upper rim. The repulsion of the dipole due to the *p*-nitro substituents and weak interaction between methoxy group and the inverted anisole ring in the **4** may be responsible for stabilizing the partial cone conformation.

Introduction

As new generation of macrocyclic compounds after crown ether and cyclodextrin, calixarenes have attracted more and more attention [1–4], since they are readily available from cheap starting materials and can be easily functionalized at both lower and upper rims. They have been widely used as the platform for molecular construction for molecular recognition and for forming host-guest complexes as well as for bio-mimics [5–11]. Although both calix[4]arene and cyclodextrin have a cavity-shaped construction, there is a crucial difference. The cyclodextrin cavity is conformationally stiff, but the conformation of the calixarene cavity still remains flexible. A control of conformation for calix[4]arene is very important for the design of functional calixarene derivatives [12]. Calix[4]arene and its upper and lower rims-modified derivatives may adopt four different extreme conformations: cone, partial cone, 1,2-alternate, and 1,3-alternate (Chart 1). Unmodified calix[4]arene usually adopts a cone conformation because of strong intramolecular hydrogen-bonding interactions among the OH groups. The substituents at upper and lower rims of calix[4]arene affect distribution of the conformers. There were some investigations reported regarding the relationship between substituent effect and conformer distribution [13, 14].

It is known that the ‘lower rim through the annulus’ pathway is available for the interconversion of calix[4]arene conformers [1]. Calix[4]arenes bearing small substituents such as methoxy or ethoxy groups at lower rim are conformationally mobile, since small groups can rotate through the calixarene annulus. The conformation distribution of these calix[4]arene derivatives is controlled by the relative stabilities of their conformers. Some researches revealed that the relative stability of the four conformers for tetramethoxycalix[4]arene derivatives is strongly influenced by upper rim substituents. For example, in CDCl₃ solution at 243 K, the ratio of the four conformers are 5.5% cone, 85.6% partial cone, 6.1% 1,2-alternate, and 2.8% 1,3-alternate respectively for 5,11,17,23-tetra-*t*-butyl-25,26,27,28-tetramethoxycalix[4]arene, however, 27% cone and 73% partial cone for 25,26,27,28-tetramethoxycalix[4]arene [15], and 22% cone and 78% partial cone for 5,11,17,23-tetrabromo-25,26,27,28-tetramethoxycalix[4]arene [16] at room temperature. This is due to the influence of the stereo-electronic effects of the upper rim substituents [16]. The *n*-propoxy group is bulky enough to inhibit the oxygen-through-the-annulus rotation and therefore tetra-*O*-propylations result in conformationally immobile calix[4]arenes [13]. The conformation distribution of those calix[4]arene derivatives bearing larger substituents than ethoxy group at lower rim is controlled by the condition of modified reaction of the parent calix[4]arene [17, 18].

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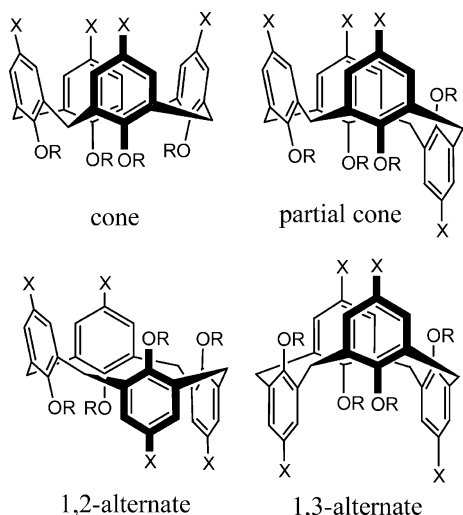


Chart 1.

In a research project aimed at the synthesis of calix[4]arene-based bio-mimics, we have synthesized two new compounds, 5,17-dinitro-26,28-dimethoxy-25,27-dipropoxycalix[4]arene and 5,17-diamino-26,28-dimethoxy-25,27-dipropoxycalix[4]arene. The phenyl rings bearing methoxy group can rotate through the calixarene annulus, but the phenyl rings bearing propoxy group in these two compounds are unable to rotate. In this paper, we report their X-ray structures and ^1H NMR spectra to show how the upper rim substituents affect the conformations of calix[4]arene derivatives.

Experimental

Analytical procedures

Elemental analysis was performed on Perkin–Elmer 240C instrument. Molecular mass was determined by electrospray mass spectrometer (LCQ, Finnigan) in positive mode. ^1H NMR spectra were recorded with an AM 500 MHz nuclear magnetic resonance spectrometer, ^{13}C NMR, ^1H – ^1H Cosy, and HSQC spectra were conducted on a Bruker AV 300 MHz nuclear magnetic resonance spectrometer. Typically, samples were dissolved in deuterated solvent and chemical shifts were recorded using TMS as internal reference. X-ray crystallographic data for the **4** and **5** compounds were collected on a Bruker Smart Apex CCD diffractometer. The melting point is uncorrected.

Synthesis

All materials and solvents were of analytical grade and used without further purification. *p*-*tert*-butylcalix[4]arene [19], 25,26,27,28-tetrahydroxycalix[4]arene (**1**) [20], 25,27-dihydroxy-26,28-dipropoxycalix[4]arene (**2**) [21], 5,17-dinitro-26,28-dihydroxy-25,27-dipropoxycalix[4]arene (**3**) [22] and diazomethane [23] were prepared

according to procedures previously described in the literatures.

5,17-dinitro-26,28-dimethoxy-25,27-dipropoxycalix[4]arene (**4**) was synthesized as follows. A 0.467 g (0.78 mmol) of **3** was dissolved in 30 ml of CH_2Cl_2 , and the solution obtained was cooled at $0\text{ }^\circ\text{C}$, and then a solution of diazomethane in ether (*Caution!*) was added to the solution dropwise. After adding completely, the reaction mixture was then kept stirring at room temperature for ≈ 4 h until the **3** disappeared, monitored by TLC. The reaction solution was treated with acetic acid, washed twice with water, and then dried with anhydrous sodium sulfate. The organic solvent was removed under reduced pressure, yielding a crude product. The crude product was purified by column chromatography, with eluant of petroleum ether/ethyl acetate in volume ratio 20/1, and then recrystallized from a mixed solvent of petroleum ether and ethyl acetate to give 0.37 g of **4** as yellow crystals (76% yield). The molecular mass calculated for $\text{C}_{36}\text{H}_{38}\text{N}_2\text{O}_8$ is 626.3; the observed value by positive charge of ESI-MS is 649.3 ($\text{M} + \text{Na}^+$) and 1274.9 ($2\text{M} + \text{Na}^+$). ^1H NMR (δ in CDCl_3): 8.25 (s), 8.10 (s) and 8.02 (s) (4H, ArH); 6.93 (d, $J_{\text{H-H}} = 7.1$ Hz), 6.53 (t, $J_{\text{H-H}} = 7.5$ Hz), 6.36–6.33 (m) and 6.28 (d, $J_{\text{H-H}} = 7.4$ Hz) (6H, ArH); 4.40 (d, $J_{\text{H-H}} = 13.4$ Hz), 4.08 (d, $J_{\text{H-H}} = 13.8$ Hz), 3.83–3.67 (m), 3.33 (d, $J_{\text{H-H}} = 13.4$ Hz) and 3.23 (d, $J_{\text{H-H}} = 13.8$ Hz) (8H, ArCH_2Ar); 4.03 (s), 3.80 (s), 3.14 (s) (6H, OCH_3); 3.88–3.67 (m), 3.61–3.58 (m) (4H, OCH_2); 1.96–1.92 (m, 4H, CH_2); 1.17–1.08 (m, 6H, CH_3). ^{13}C NMR (δ in CDCl_3): 164.6, 163.9, 156.1, 155.7, 142.9, 142.8, 142.0, 138.2, 138.0, 135.0, 132.3, 131.8, 130.9, 129.3, 128.6, 127.8, 126.2, 124.4, 124.2, 122.7, 122.3, 77.3, 76.2, 61.2, 60.3, 59.7, 25.7, 30.6, 23.8, 10.9, 10.8. *Anal. Calcd.* for $\text{C}_{36}\text{H}_{38}\text{N}_2\text{O}_8$: C, 68.99; H, 6.11; N, 4.47. *Found*: C, 68.88; H, 6.08; N, 4.64. Melting point: 221–222 $^\circ\text{C}$.

5,17-diamino-26,28-dimethoxy-25,27-dipropoxycalix[4]arene (**5**) was synthesized as follows. A 0.2 g of Raney nickel was added to a solution of 0.3 g (0.48 mmol) of **4** in 10 ml of $\text{CH}_3\text{COOC}_2\text{H}_5$, and 7 ml of CH_3OH was added, followed by 5 ml of $\text{NH}_2\text{NH}_2 \cdot \text{H}_2\text{O}$ in portions at room temperature with occasional stirring. Another 5 ml of $\text{NH}_2\text{NH}_2 \cdot \text{H}_2\text{O}$ was added 5 h after the reaction mixture was refluxed, and the reaction mixture was continued to reflux for 6 h and then filtered. The residue was washed with CH_2Cl_2 and CH_3COCH_3 . The combined filtrate was concentrated under reduced pressure, and then poured dropwise over ice-cold water with stirring to give a white precipitate (turned to light brown on exposure to air). The crude product was recrystallized from a mixed solvent of ethyl acetate and petroleum ether to give 0.24 g of **5** as buff crystals (89% yield). The molecular mass calculated for $\text{C}_{36}\text{H}_{42}\text{N}_2\text{O}_4$ is 566.3; the observed value by positive charge of ESI-MS is 567.3 ($\text{M} + \text{H}^+$) and 589.3 ($\text{M} + \text{Na}^+$). ^1H NMR (δ in CDCl_3): 6.90 (s), 6.72 (s), 6.51–6.30 (m) (10H, ArH); 4.31 (d, $J_{\text{H-H}} = 13.1$ Hz, ArCH_2Ar), 4.04 (br), 3.83 (s, OCH_3), 3.69 (t, $J_{\text{H-H}} = 6.3$ Hz, OCH_2), 3.58 (s), 3.13 (br), 3.06 (d, $J_{\text{H-H}} = 13.1$ Hz, ArCH_2Ar), 3.01 (br) (18H); 1.88 (m, 4H,

CH_2); 1.10 (t, 6H, $J_{\text{H-H}} = 6.6$ Hz, CH_3). ^{13}C NMR (δ in CDCl_3): 155.8, 151.9, 140.4, 137.5, 133.2, 127.2, 122.0, 115.8, 75.6, 60.9, 30.8, 23.8, and 11.0. *Anal. Calcd.* for $\text{C}_{36}\text{H}_{42}\text{N}_2\text{O}_4$: C, 76.29; H, 7.47; N, 4.94. *Found*: C, 76.24; H, 7.46; N, 5.02. Melting point: 277–278 °C.

X-ray data collection, structure determination and refinement

The single crystals of the **4** and **5** suitable to X-ray crystallographic analysis were obtained by recrystallization from a mixed solvent of ethyl acetate and petroleum ether. The intensity data for the two compounds were collected on a Bruker Smart Apex CCD diffractometer with graphite-monochromated MoK_α radiation (0.71073 Å) at room temperature. SAINT program and SADABS program carried out the data integration and the empirical absorption corrections [24]. The structure was solved by direct method and refined on F^2 using SHELXTL suite of program [24]. All non-hydrogen atoms were anisotropically refined by full-matrix least-squares methods. All hydrogen atoms were geometrically generated and isotropically refined using a riding model. The crystallographic data for the two structures have been deposited in the Cambridge Crystallographic Data Centre with CCDC Nos. 231000 for **4** and 231001 for **5**.

Results and discussion

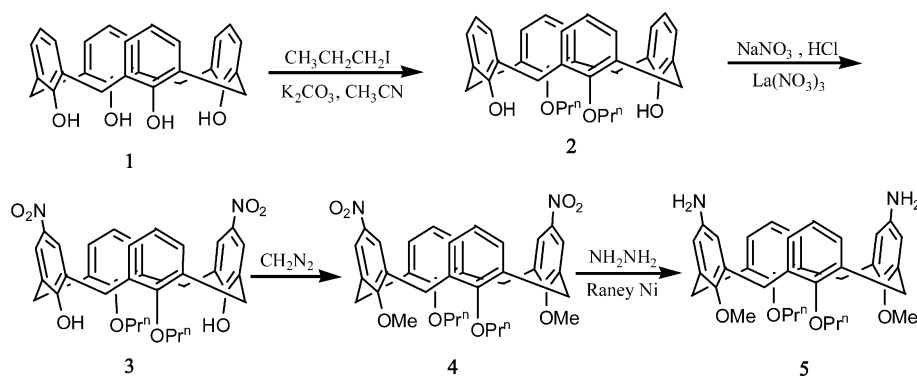
Synthesis

The partial nitration of calix[4]arene tetraether is very complicate [25]. As shown in Scheme 1, we obtained 5,17-dinitro-26,28-dimethoxy-25,27-dipropoxycalix[4]arene (**4**) in good yield (76%) by the reaction of diazomethane with 5,17-dinitro-26,28-dihydroxy-25,27-dipropoxycalix[4]arene (**3**), which was synthesized by the selective propylation of 25,26,27,28-tetrahydroxycalix[4]arene (**1**) at lower rim, and then by selective nitration at upper rim according to the literatures [21, 22]. The 5,17-dinitro-26,28-dimethoxy-25,27-dipropoxycalix[4]arene (**4**) was reduced by hydrazine hydrate

in the presence of Raney nickel to form 5,17-diamino-26,28-dimethoxy-25,27-dipropoxycalix[4]arene (**5**) in high yield (89%) [26].

NMR study in solution

The ^1H NMR spectra of **4** and **5** compounds were recorded in CDCl_3 at 293 K. These spectra are basically similar to those reported previously [27]. Assignment of the ArCH_2Ar methylene protons is a characteristic for each conformer: one pair of doublets for “cone”, two pairs of doublets or one pair of doublets and one singlet for “partial cone”, one singlet and one pair of doublets for “1,2-alternate”, one singlet for “1,3-alternate”. The 1,2-alternate conformer is absent in the equilibrium mixture of **4** or **5**, since the two phenyl rings bearing propoxy group are unable to rotate through the calixarene annulus. In the ^1H NMR spectrum of **4**, a doublet of doublet signal at 4.40 and 3.33 ppm ($J_{\text{H-H}} = 13.4$ Hz) was assigned to the ArCH_2Ar methylene protons of the cone conformer. The partial cone conformer has two pairs of doublets for the ArCH_2Ar methylene protons. One pair showed a large difference in the chemical shifts (4.08 and 3.23 ppm, $J = 13.8$ Hz), which were assigned to H_{exo} and H_{endo} in the ArCH_2Ar protons flanked by two syn phenol units. The other pair, which was assigned to the ArCH_2Ar protons flanked by two anti phenol units, showed a relatively small difference in the chemical shifts in the range of 3.83–3.67 ppm. This pair signal was confirmed by 2D NMR spectra (COSY and HSQC), though overlapped with the signals of OCH_2 and OCH_3 , as shown in Figure 1. It is evident that the **4** exists in partial cone and cone conformations. The ratio of partial cone to cone, obtained from the integration of the Ar-H -signals of the phenyl rings bearing nitro group and the ArCH_2Ar methylene protons, is about 75%:25% in CDCl_3 solvent at 293 K. In the ^1H NMR spectrum of **5**, a doublet of doublet signal at 4.31 and 3.06 ppm ($J_{\text{H-H}} = 13.1$ Hz) was assigned the ArCH_2Ar methylene protons of the cone conformer. One pair of doublets for partial cone was found in the ^1H - ^1H COSY spectra as shown in Figure 6(d) and further confirmed by the ^1H NMR spectra at lower temperature as shown in Figure 2(b). From integration of the ArCH_2Ar



Scheme 1.

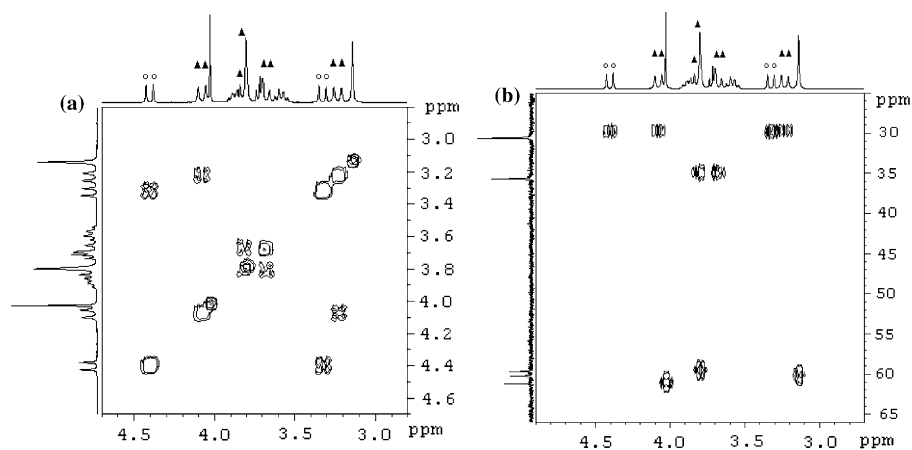


Figure 1. Partial 2D NMR spectra (300 MHz, 298 K) of **4** in CDCl_3 : (a) COSY; (b) HSQC. \circ and \blacktriangle in the ^1H NMR spectra are assigned as cone and partial cone conformers respectively.

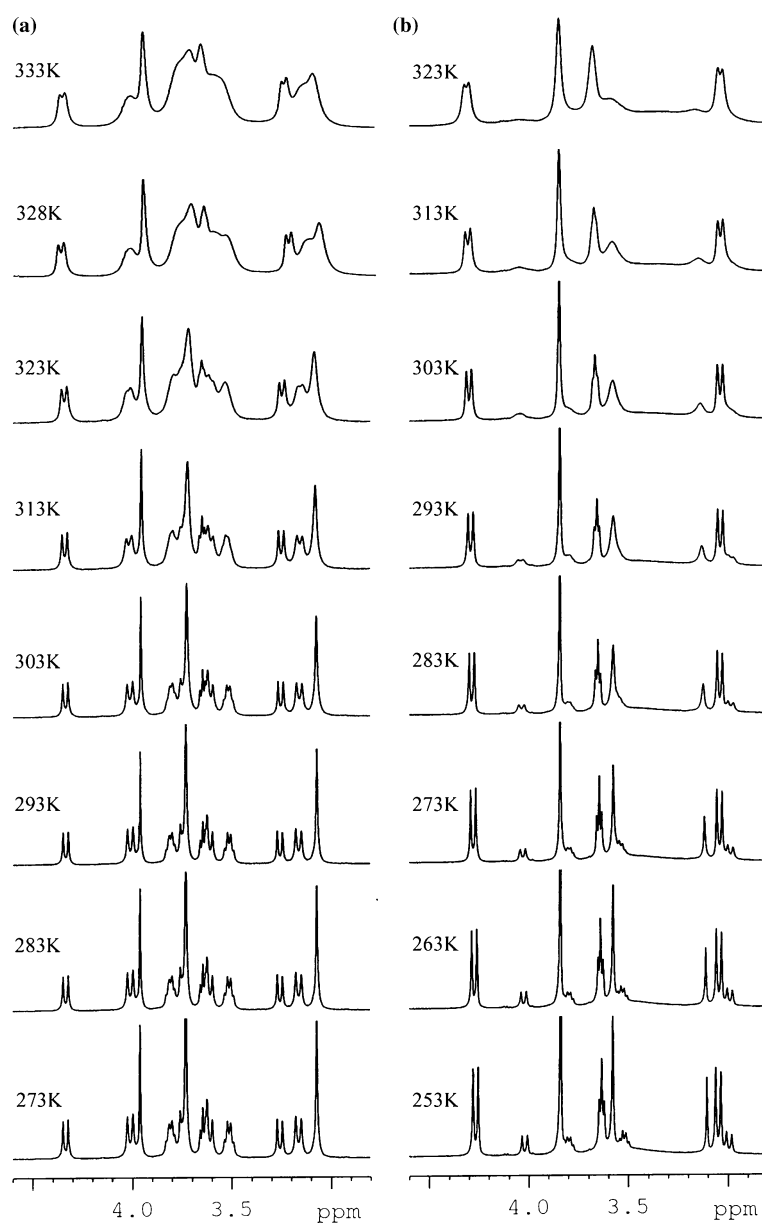


Figure 2. Temperature dependent ^1H NMR spectra for **4**, (a) and **5**, (b) (500 MHz, CDCl_3).

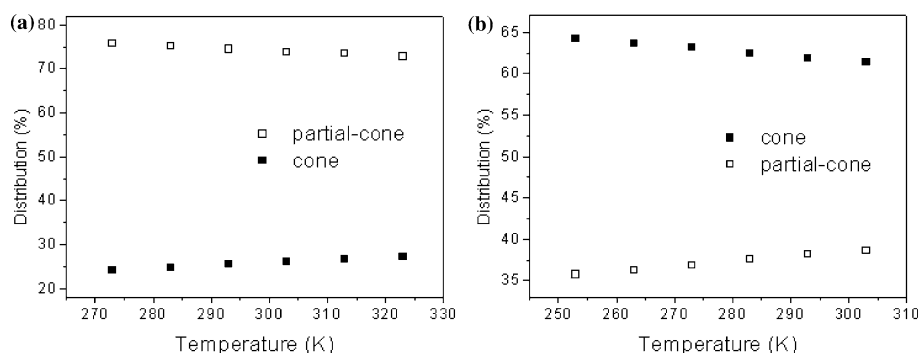


Figure 3. Temperature dependence of the conformer distribution in **4**, (a) and **5**, (b).

protons signals, a composition containing 62% cone and 38% partial cone conformers was deduced in CDCl_3 solvent at 293 K.

Figure 2 shows the temperature dependent ^1H NMR spectra for **4** and **5** compounds. The spectra of partial cone **4** and partial cone **5** conformers broadened apparently at 323 and 293 K. For cone **4** and cone **5** conformers, the broad spectra appeared at higher temperature, 333 and 323 K, respectively.

As shown in Figure 3, the conformer distribution changes smoothly with increasing temperatures. In the range of temperature measured, the percentage of the cone **4** and partial cone **5** conformers raised from 24.2% and 35.7% to 27.2% and 38.6%, while the percentage of the partial cone **4** and cone **5** conformers decreased from 75.8% and 64.3% to 72.8% and 61.4%. These numbers indicated that the partial cone **4** and cone **5** conformers as dominant ones in the equilibrium mixture were kept in the temperature range used. The van't Hoff plots of these temperature dependences are given in Figure 4. The thermodynamic parameters for the isomerization between partial cone and cone conformations are estimated from the plots and listed in Table 1.

It has been known that the calix[4]arene derivatives could form solvate in solution or in solid [28–32]. The complexation effect or polarity of solvent may affect the conformer distribution in solution [33]. For the compounds **4** and **5**, the difference is only in the upper rim substituents. The phenyl rings bearing methoxy group can rotate through the calixarene annulus in both

compounds, however, the dominant conformer is partial cone for **4** but cone for **5** in CDCl_3 solvent. In order to understand the effect of solvents on the conformer distribution, ^1H NMR spectra of the **4** and **5** were measured in three solvents with different polarities. The solvent dependent ^1H NMR and ^1H - ^1H COSY spectra for the **4** and **5** are shown in Figures 5 and 6 respectively. Similar to the results obtained in CDCl_3 , only the partial cone and cone conformers can be assigned in C_6D_6 and DMF-d_7 solvents. Table 2 summarized the effect of solvents on the ^1H NMR chemical shift of ArCH_2Ar methylene protons and the conformer distribution for the **4** and **5** compounds. Compared to the ^1H NMR spectra in CDCl_3 , C_6D_6 makes the ^1H NMR chemical shifts more separate, due to its magnetic anisotropy. As shown in Table 2, the solvents only affect the relative amount of the conformer distributions in the **4** and **5** in some extent, and the dominant conformers were still remained upon the solvents changed.

X-ray crystallographic analysis

To gain further insight into the structures of conformational isomers, we carried out X-ray crystallographic analysis for the **4** and **5**. The crystal parameters are given in Table 3. The geometry parameters of the **4** and **5** are well accessible via web directly from Cambridge database.

The X-ray structure of the **4** is illustrated in Figure 7. It crystallizes in a monoclinic system, space group $\text{P}2_1/\text{c}$.

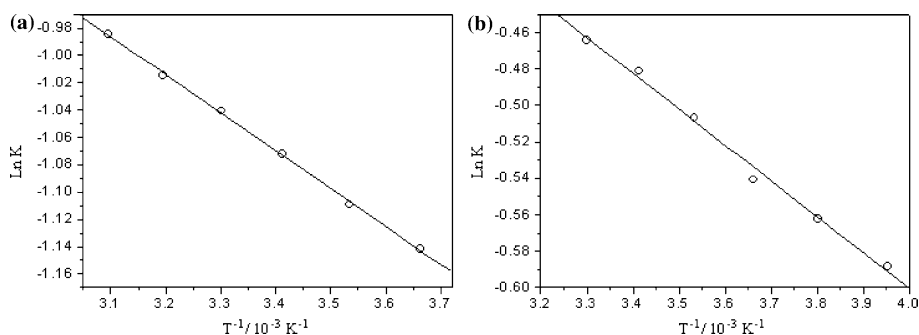
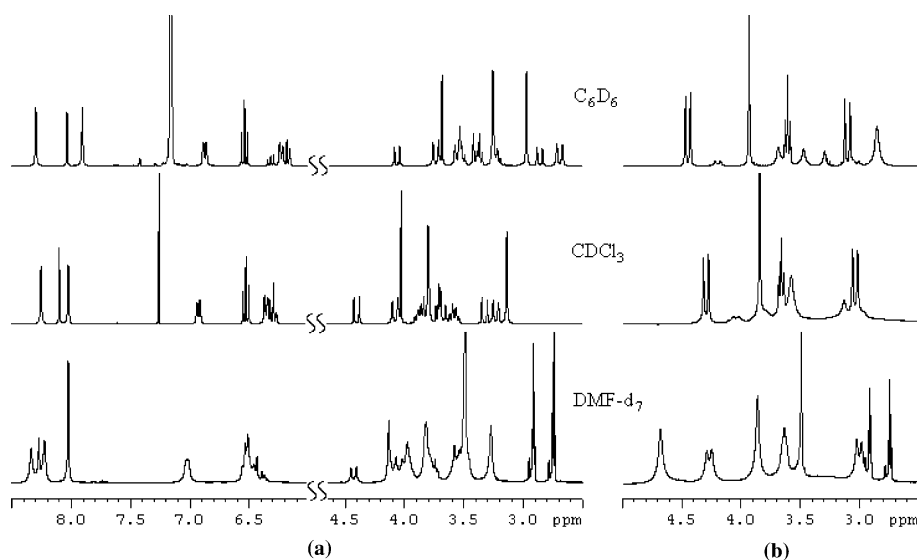
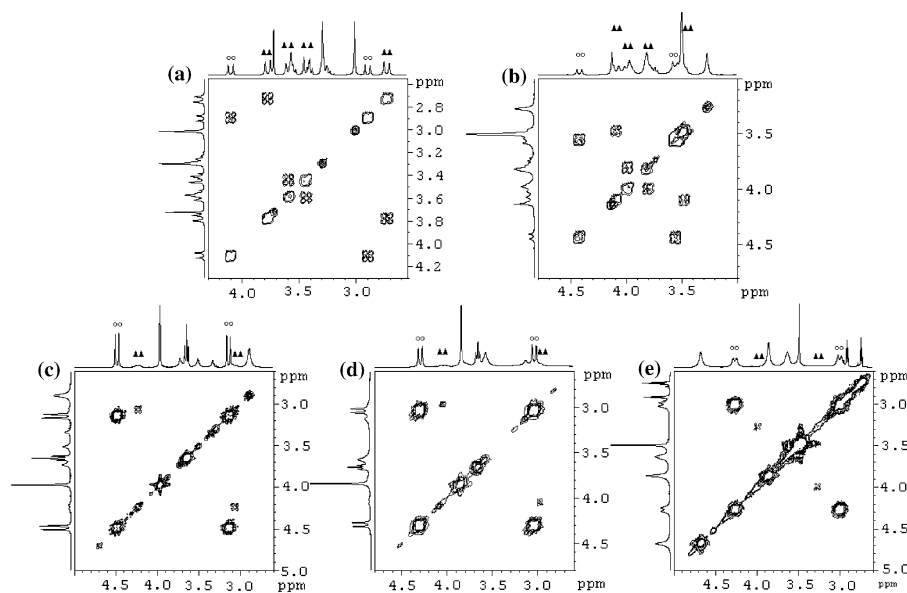


Figure 4. van't Hoff plot for: (a) a partial cone-**4** \rightleftharpoons cone-**4** equilibrium (where $K = [\text{cone-4}]/[\text{partial cone-4}]$, $\gamma = 0.999$; and (b) a cone-**5** \rightleftharpoons partial cone-**5** equilibrium (where $K = [\text{partial cone-5}]/[\text{cone-5}]$, $\gamma = 0.997$).

Table 1. Thermodynamic parameters for the isomerization of conformations for compounds **4** and **5**

Compound	Isomerization	$\Delta H/\text{kJ mol}^{-1}$	$\Delta S/\text{J mol}^{-1} \text{K}^{-1}$	$\Delta G/\text{kJ mol}^{-1} (T = 298 \text{ K})$
4	Partial cone \rightleftharpoons cone	2.31 ± 0.04	1.05 ± 0.12	2.00 ± 0.08
5	Cone \rightleftharpoons partial cone	1.64 ± 0.07	-1.56 ± 0.24	2.10 ± 0.14

Figure 5. Partial ^1H NMR spectra **4**, (a); **5**, (b) in different solvents (300 MHz, 298 K).Figure 6. Partial 2D NMR spectra (^1H - ^1H COSY, 300 MHz, 298 K). (a) **4** in C_6D_6 ; (b) **4** in DMF-d_7 ; (c) **5** in C_6D_6 ; (d) **5** in CDCl_3 ; (e) **5** in DMF-d_7 .

The compound adopts a partial cone conformation. The dihedral angles between the four phenyl rings and the mean plane of the methylene groups are (starting from the inversed phenolic rings) -83.0° , 82.6° , 26.4° , and 85.0° , respectively. The so-called flattened phenyl unit (distal to the inversed phenyl unit) is flattened. The two

opposite phenyl rings bearing propoxy groups are almost parallel; the dihedral angle between these two planes is 12.4° . One methoxy group lies almost directly above the plane of the inverted anisole ring. The distance of this methoxy carbon (C37) to the centroid of the inverted anisole ring is $3.842(2) \text{ \AA}$. This distance is

Table 2. The effect of solvents on the ^1H NMR signals of the ArCH_2Ar methylene protons and the conformer distribution for **4** and **5**

Solvent	δ/ppm (^1H NMR signal of the ArCH_2Ar methylene protons) ^a				Conformer distribution			
	Compound 4		Compound 5		Compound 4		Compound 5	
	Cone	Partial cone	Cone	Partial cone	Cone %	Partial cone (%)	Cone (%)	Partial cone (%)
C_6D_6	4.10 (d), 2.90 (d) ($J = 13.3$ Hz)	3.77 (d), 2.73 (d) ($J = 13.7$ Hz); 3.59 (d), 3.44 (d) ($J = 13.2$ Hz)	4.49 (d), 3.14 (d) ($J = 12.9$ Hz)	4.24 (d), 3.07 (d) ($J = 13.2$ Hz); 3.73 (s)	22	78	71	29
CDCl_3	4.40 (d), 3.33 (d) ($J = 13.4$ Hz)	4.08 (d), 3.23 (d), ($J = 13.8$ Hz); 3.86 (d), 3.68 (d) ($J = 13.1$ Hz)	4.31 (d), 3.06 (d) ($J = 13.1$ Hz)	4.06 (d), 3.01 (d), ($J = 12.9$ Hz); 3.60 (s)	25	75	62	38
DMF-d_7	4.45 (d), 3.56 (d) ($J = 13.2$ Hz)	4.10 (d), 3.49 (d) ($J = 13.6$ Hz); 4.00 (d), 3.80 (d) ($J = 13.2$ Hz)	4.27 (d), 3.00 (d) ($J = 12.3$ Hz)	4.00 (d), 3.27 (d), ($J = 12.7$ Hz); 3.63 (s)	19	81	83	17

^aSome signals overlapped with the signals of OCH_2 and OCH_3 were assigned by 2D NMR spectra.

Table 3. Crystallographic data and parameters of refinement for **4** and **5**

Compound	4	5
Empirical formula	$\text{C}_{36}\text{H}_{38}\text{N}_2\text{O}_8$	$\text{C}_{36}\text{H}_{42}\text{N}_2\text{O}_4$
Formula weight	626.68	566.72
Temperature/K	293(2)	293(2)
Wavelength/ \AA	$\text{MoK}_{\alpha}/0.71073$	$\text{MoK}_{\alpha}/0.71073$
Crystal system	Monoclinic	Monoclinic
Space group (No.)	$\text{P}2_1/\text{c}$ (No.14)	$\text{P}2_1/\text{n}$ (No. 14)
$a/\text{\AA}$	13.645(1)	15.657(2)
$b/\text{\AA}$	12.435(1)	14.243(2)
$c/\text{\AA}$	20.201(1)	28.688(4)
α/deg	90	90
β/deg	108.66(1)	90.43(1)
γ/deg	90	90
$V/\text{\AA}^3$	3247.5(4)	6397.3(15)
Z	4	8
$D_c/\text{g cm}^{-3}$	1.282	1.177
μ/mm^{-1}	0.091	0.076
$F(0\ 0\ 0)$	1328	2432
Crystal size/mm	$0.20 \times 0.20 \times 0.30$	$0.20 \times 0.20 \times 0.30$
Crystal color	Buff	Yellow
θ range for data collection/deg	2.0–26.0	1.9–26.0
Limiting indices	$-16 \leq h \leq 11$ $-15 \leq k \leq 15$ $-22 \leq l \leq 24$	$-19 \leq h \leq 18$ $-9 \leq k \leq 17$ $-34 \leq l \leq 35$
No. of reflections collected	17,084	33,584
No. of unique reflections	6356	12,553
R_{int}	0.024	0.022
No. of parameters refined	419	765
wR_2^a	0.130	0.147
R_1	0.057	0.054
S (Goodness-of-fit on F^2)	1.07	1.04
Largest diff. Peak and hole/ $e \text{\AA}^{-3}$	+0.36, -0.53	+0.62, -0.73

^a In the refinement calculations (using SHELXL) F^2 values have been used as input for compounds **4** and **5**. The weights of the F^2 values were calculated as $w = 1/[s^2(F_0^2) + (c_1 \cdot P)^2 + c_2 \cdot P]$ where $P = (F_0^2 + 2F_c^2)/3$, and the constants, c_1 and c_2 had the values 0.060 and 1.990 for **4**, 0.040 and 1.760 for **5**.

in the range of weak interaction [34]. As mentioned above, temperatures and solvents with different polarities do not affect the dominant partial cone conformer of the **4** in solution. Therefore, the partial cone conformer may be stabilized by a weak interaction between the methoxy group protons and the inverted anisole ring as well as the repulsion of dipoles due to the p -nitro substituents. In order to estimate the weak interaction between the methoxy group and inverted anisole ring, we carried out theoretical investigations with aid of Bader's atoms in molecules (AIM) theory [35]. AIM essentially deals with molecular electron density, and it can provide invaluable information in terms of bonding interactions, both intermolecular and intramolecular ones. It has been pointed out [36] that the existence of bond critical point (BCP) on the bond path linking two interacting atoms could be regarded as a universal indicator of bonding between the atoms. Crystallographic geometry was directly used to obtain B3LYP/6-31g* electron density with Gaussian 98 program suite [37]. Topological analysis was performed by means of AIMPAC program package [38]. A BCP was identified between one hydrogen atom of the methoxy group (H37B) and C11, a carbon atom of the inverted anisole ring. The electron density and its Laplacian characterizing the BCP are 0.0053 a.u. and 0.0183 a.u., respectively. Small value of electron density at BCP indicates its nature of a weak interaction (covalent bonds normally have values two orders of magnitude larger). Positive value of the Laplacian indicates a depletion of the electron density, which is common in closed-shell interactions [35]. This bonding, albeit weak, may be considered to be one of factors in stabilizing the partial cone conformer.

The structure of the **5** is given in Figure 8. It crystallizes in a monoclinic system, space group $\text{P}2_1/\text{n}$, with two independent molecules in an asymmetric unit. Both independent molecules are in cone conformation.

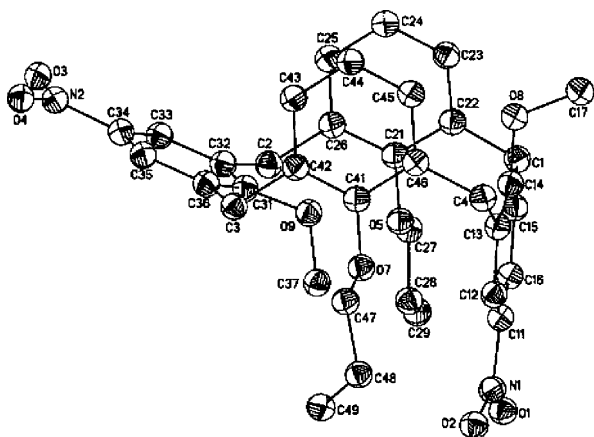


Figure 7. Structure of **4** with numbering scheme. All hydrogen atoms are omitted for clarity.

There is a slight difference between the two independent molecules as shown by dihedral angles between the phenolic rings with respect to average plane of four methylene carbon atoms. They are (starting from the phenolic ring bearing propoxy group) 85.9° (89.8°), 36.0° (38.2°), 84.2° (84.7°), and 38.1° (38.2°) (values for the second molecule are in parentheses). The two phenyl rings bearing methoxy group are more flattened. The two opposite phenyl rings bearing propoxy group are almost parallel; the dihedral angle between these two planes is 10.1° (5.3°) (values for the second molecule are in parentheses).

In comparison of **4** with **5**, the substituents at lower rims are identical and same procedures were used for recrystallization. Only difference is the substituents at upper rim, two nitro groups in **4**, and two amino groups in **5**. As a result, only the partial cone **4** and cone **5** conformers were obtained in solid state. These results are consistent well with that observed in solution.

Conclusion

The partial cone conformer is the most stable one for both 5,11,17,23-tetranitro-25,26,27,28-tetramethoxycal-

ix[4]arene [39] and 5,11,17,23-tetraamino-25,26,27,28-tetramethoxycalix[4]arene [16]. However, in the two new calix[4]arene derivatives of **4** and **5**, the different conformational behavior was found both in solution and in solid state. The temperatures and solvents merely affect the relative ratio of partial cone to cone conformers in some extent, but the dominant conformations in the **4** and **5** were reserved under the experimental conditions used. The dominant conformer in the **4** adopts partial cone and the **5** prefers cone conformation. The partial cone conformation in the **4** may be stabilized by repulsion of the dipoles of *p*-nitro substituents and weak interaction between the methoxy group and inverted anisole ring. The conformation controlled upon altering two substituents at the upper rim could be useful for further studies in the field of supramolecular calix[4]arene chemistry and for design of functional calixarene derivatives with required conformations.

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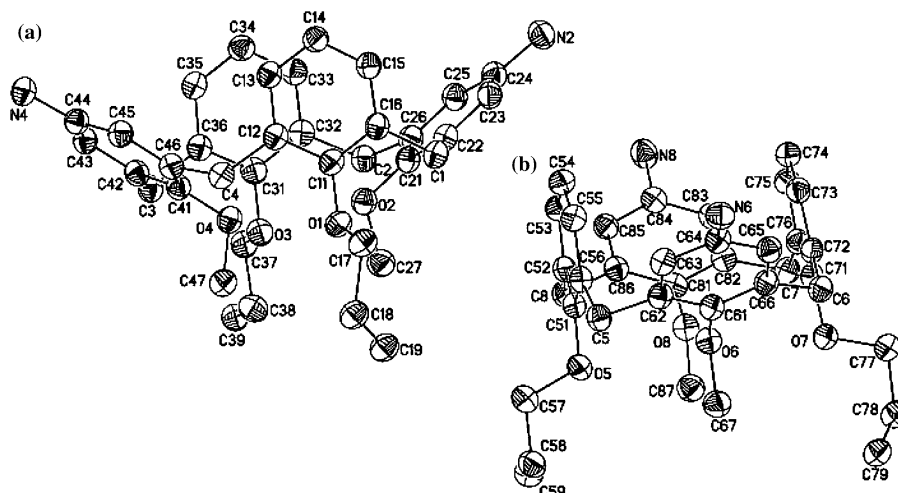


Figure 8. Structure of **5** with numbering scheme. All hydrogen atoms are omitted for clarity.

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