



Short Communication

## Crystal Structures and Solvate Formation of Two Conformationally Frozen Isomers of a Bridged Calix[6]arene

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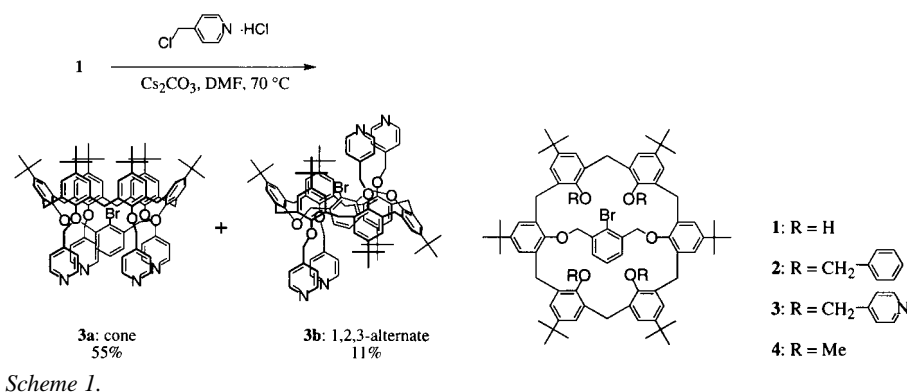
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Whereas the conformation of calix[4]arenes can be easily immobilized by functionalization at the lower rim to form four conformational isomers [1], it has been very difficult to freeze the conformation of calix[6]arenes despite a large demand for their structurally well-defined derivatives [2]. Recently, some examples have been reported of calix[6]arenes fixed in one conformation [3], but there has been no example of crystallographic analysis of the plural conformational isomers of a calix[6]arene. We have recently reported the isolation of two conformationally frozen isomers (cone and 1,2,3-alternate) of the bridged calix[6]arene **2** obtained by exhaustive benzylation of the lower rim of the tetrahydroxyl compound **1** [4]. The structure of the 1,2,3-alternate isomer of **2**, however, was determined based only on its spectral data although that of the cone isomer was unambiguously established by X-ray analysis. In this communication, we report the crystallographic analysis of both isomers of the bridged calix[6]arene **3** bearing 4-pyridylmethyl groups at the lower rim. The formation of a 1 : 5 solvate between the cone isomer of **3** and 1,1,2,2-tetrachloroethane only by crystal packing force is also delineated.

Compound **3** was designed as the 4-pyridylmethyl analog of the benzylated compound **2**. Its conformational isomers bearing the pyridyl groups in the arrangements different from each other are expected to serve as ligands for transition metals. The cone isomer **3a** and the 1,2,3-alternate isomer **3b** were synthesized in 55 and 11% yields, respectively, according to Scheme 1. Both isomers **3a** and **3b** showed the spectral features essentially the same as those of the corresponding isomers of **2**, indicating that they are conformationally immobilized in solution similar to **2**.<sup>1</sup>

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<sup>1</sup> **3a**. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 1.04 (s, 36H), 1.45 (s, 18H), 3.27 (d, *J* = 15.0 Hz, 2H), 3.38 (d, *J* = 15.2 Hz, 4H), 3.93 (s, 4H), 4.25 (d, *J* = 15.0 Hz, 2H), 4.45 (d, *J* = 13.3 Hz, 4H), 4.47 (d, *J*



Scheme 1.

Single crystals of the cone isomer **3a** suitable for X-ray analysis were obtained from the 1,1,2,2-tetrachloroethane solution, one of which was mounted in a glass capillary containing the mother liquor to avoid efflorescence. Recrystallization of the 1,2,3-alternate isomer **3b** from methanol/chloroform afforded the single crystals which were stable without the mother liquor. The crystal structures of both isomers are shown in Figure 1 and their crystallographic data are summarized in Table I.<sup>2</sup>

The figure shows that the ellipse made up of six benzene rings of the cone isomer **3a** is somewhat larger than that of the 1,2,3-alternate isomer **3b**, where two

= 15.2 Hz, 4H), 4.48 (d,  $J = 13.3$  Hz, 4H), 6.84 (d,  $J = 1.6$  Hz, 4H), 6.89 (d,  $J = 5.8$  Hz, 8H), 7.08 (t,  $J = 7.5$  Hz, 1H), 7.21 (d,  $J = 1.6$  Hz, 4H), 7.34 (s, 4H), 7.34 (d,  $J = 7.5$  Hz, 2H), 8.38 (d,  $J = 5.8$  Hz, 8H). **3b**. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  1.017 (s, 18H), 1.020 (s, 18H), 1.28 (s, 9H), 1.31 (s, 9H), 3.27 (d,  $J = 15.7$  Hz, 2H), 3.35 (d,  $J = 15.7$  Hz, 2H), 3.69 (dd,  $J = 7.6, 1.8$  Hz, 1H), 3.72 (d,  $J = 12.8$  Hz, 2H), 3.77 (d,  $J = 12.8$  Hz, 2H), 4.01 (s, 2H), 4.04 (d,  $J = 15.7$  Hz, 2H), 4.20 (s, 2H), 4.46 (d,  $J = 15.7$  Hz, 2H), 4.85 (d,  $J = 12.7$  Hz, 2H), 4.88 (d,  $J = 12.7$  Hz, 2H), 4.91 (s, 4H), 6.22 (t,  $J = 7.6$  Hz, 1H), 6.62 (br, 2H), 6.76 (brd,  $J = 2.4$  Hz, 2H), 6.92 (dd,  $J = 7.6, 1.8$  Hz, 1H), 6.97 (d,  $J = 2.4$  Hz, 2H), 7.08 (d,  $J = 2.4$  Hz, 2H), 7.10 (s, 2H), 7.11 (s, 2H), 7.49 (d,  $J = 5.6$  Hz, 4H), 7.57 (d,  $J = 5.8$  Hz, 4H), 8.69 (d,  $J = 5.6$  Hz, 4H), 8.70 (d,  $J = 5.8$  Hz, 4H).

<sup>2</sup> Crystallographic data for **3a**·5C<sub>2</sub>H<sub>2</sub>Cl<sub>4</sub>: C<sub>108</sub>H<sub>119</sub>BrCl<sub>20</sub>N<sub>4</sub>O<sub>6</sub>,  $M = 2358.12$ , monoclinic,  $Cc$ ,  $a = 12.2440(2)$  Å,  $b = 36.038(2)$  Å,  $c = 26.1300(9)$  Å,  $\beta = 100.220(2)^\circ$ ,  $V = 11346.9(6)$  Å<sup>3</sup>,  $Z = 4$ ,  $\rho_{\text{calcd}} = 1.380$  g cm<sup>-3</sup>. The intensity data were collected at 150 K on a MAC Science DIP-2030 imaging plate area detector with MoK $\alpha$  radiation ( $\lambda = 0.71069$  Å). Of the 44438 reflections which were collected, 9888 were independent. The non-hydrogen atoms were refined anisotropically except for two carbon atoms of a solvent molecule involving disorder. Hydrogen atoms were included but not refined. The final cycle of full-matrix least-squares refinement on  $F$  was based on 8323 observed reflections [ $I > 3.00 \sigma(I)$ ].  $R = 0.059$ ,  $R_w = 0.059$  for 1266 parameters. Crystallographic data for **3b**·2CHCl<sub>3</sub>: C<sub>100</sub>H<sub>111</sub>BrCl<sub>6</sub>N<sub>4</sub>O<sub>6</sub>,  $M = 1757.62$ , triclinic,  $P-1$ ,  $a = 13.488(3)$  Å,  $b = 15.124(4)$  Å,  $c = 12.699(2)$  Å,  $\alpha = 103.37(2)^\circ$ ,  $\beta = 95.76(2)^\circ$ ,  $\gamma = 111.97(2)^\circ$ ,  $V = 2286.6(2)$  Å<sup>3</sup>,  $Z = 1$ ,  $D_{\text{calcd}} = 1.276$  g cm<sup>-3</sup>. The intensity data were collected at 296 K on a Rigaku AFC5R diffractometer with MoK $\alpha$  radiation ( $\lambda = 0.71069$  Å). Of the 10964 reflections which were collected, 10517 were independent. The non-hydrogen atoms were refined anisotropically except for those in disordered central bridging unit. Hydrogen atoms were included but not refined. The final cycle of full-matrix least-squares refinement was based on 3857 observed reflections [ $I > 3.00 \sigma(I)$ ].  $R = 0.080$ ,  $R_w = 0.079$  for 512 parameters.

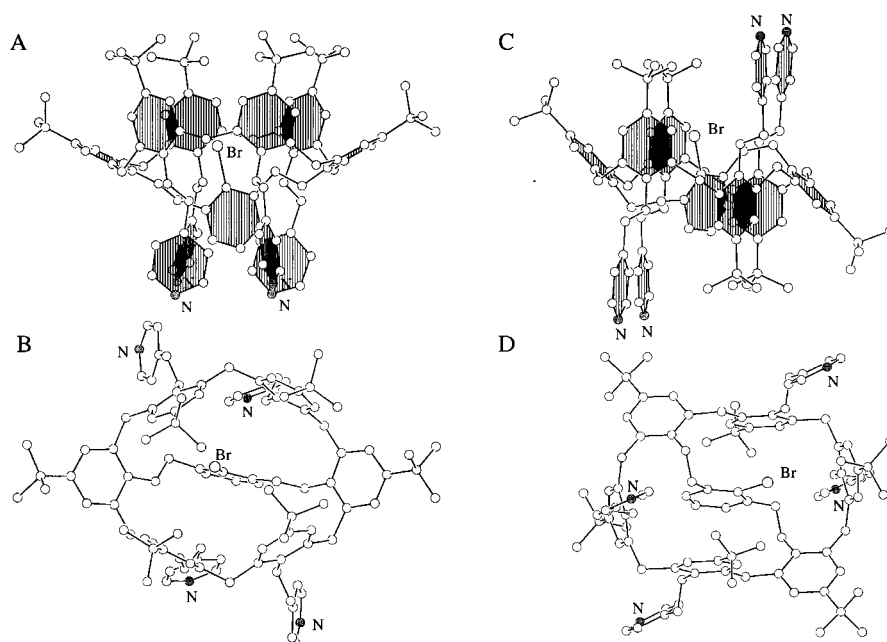


Figure 1. X-ray structures of the cone isomer **3a** (A: side view; B: top view) and the 1,2,3-alternate isomer **3b** (C: side view; D: top view). Disordered atoms and hydrogen atoms are omitted for clarity.

non-bridged aromatic rings and the central xylenyl ring are almost parallel with a distance of about 3.5 Å. Such stacking of benzene rings was also found in the crystal structure of the tetramethyl derivative **4** [5]. While the four pyridine rings of **3a** are oriented to almost the same direction, two pairs of two pyridine rings of **3b** are fixed in opposite directions. The molecular mechanics calculations of **3a** and **3b** were carried out using the molecular modeling system MacroModel V.6.5 with the MM3\* force field [6]. The lowest energy structures of both isomers were found to be essentially the same as their crystal structures in regard to the conformation of the calix[6]arene macrocycle and the bridging unit although there are small differences in the orientation of the 4-pyridylmethyl moieties. It was also found that the cone and the 1,2,3-alternate isomers have similar thermodynamic stability (337.33 vs. 335.23 kJ mol<sup>-1</sup>), indicating that the predominant formation of the cone isomer in the pyridylmethylation reaction of **1** is due to kinetic reasons.

There is also a characteristic difference in the solvent inclusion between the two isomers. While the 1,2,3-alternate isomer **3b** is solvated by two chloroform molecules, the cone isomer **3a** forms a 1:5 (host:guest) solvate with 1,1,2,2-tetrachloroethane. Figure 2 shows the crystal packing views of **3a**·5Cl<sub>2</sub>CHCl<sub>2</sub> and **3b**·2CHCl<sub>3</sub>. In either case, no solvent molecule is located in the cavity of a calixarene. Recently, quasi completely solvated calixresorcarenes in the crystalline state have been attracting much attention [7]. Molecules of **3a** are not completely

Table I. Crystallographic data and experimental details

	<b>3a</b> ·5Cl <sub>2</sub> CHCHCl <sub>2</sub>	<b>3b</b> ·2CHCl <sub>3</sub>
Formula	C <sub>108</sub> H <sub>119</sub> BrCl <sub>20</sub> N <sub>4</sub> O <sub>6</sub>	C <sub>108</sub> H <sub>111</sub> BrCl <sub>6</sub> N <sub>4</sub> O <sub>6</sub>
Molecular weight	2358.12	1757.62
Crystal system	Monoclinic	Triclinic
Lattice parameters	$a = 12.2440(2) \text{ \AA}$ $b = 36.038(2) \text{ \AA}$ $c = 26.1300(9) \text{ \AA}$ $\alpha = 90^\circ$ $\beta = 100.220(2)^\circ$ $\gamma = 90^\circ$ $V = 11346.9(6) \text{ \AA}^3$	$a = 13.488(3) \text{ \AA}$ $b = 15.124(4) \text{ \AA}$ $c = 12.699(2) \text{ \AA}$ $\alpha = 103.37(2)^\circ$ $\beta = 95.76(2)^\circ$ $\gamma = 111.97(2)^\circ$ $V = 2286.6(10) \text{ \AA}^3$
Space group	<i>Cc</i>	<i>P</i> -1
<i>Z</i>	4	1
$D_{\text{calcd}}$	1.380 g cm <sup>-3</sup>	1.276 g cm <sup>-3</sup>
$\mu(\text{MoK}\alpha)$	8.87 cm <sup>-1</sup>	6.82 cm <sup>-1</sup>
Diffractometer	MAC Science DIP-2030	Rigaku AFC5R
Radiation	MoK $\alpha$ ( $\lambda = 0.71069 \text{ \AA}$ )	MoK $\alpha$ ( $\lambda = 0.71069 \text{ \AA}$ )
$2\theta_{\text{max}}$	51.2°	55.0°
Temperature	150 K	295 K
Independent reflections	9888	10517
Observed ( $I > 3.00\sigma(I)$ )	8323	3857
Variables	1266	512
$R, R_w$	0.059, 0.059	0.080, 0.079
Goodness-of-fit on $F$	3.71	2.73
Largest diff. peak and hole	0.85, -1.12 e <sup>-</sup> /Å <sup>3</sup>	0.70, -0.49 e <sup>-</sup> /Å <sup>3</sup>

solvated; the calixarene molecules are stacked along the crystallographic *a* axis without solvent molecules among them. It is noteworthy, however, that **3a** forms a 1 : 5 solvate in spite of the absence of any particular interaction such as hydrogen bonding between them. Crystalline hosts which contains more than five solvent molecules are quite rare except for the systems including hydrogen bonding [8]. We previously reported that the cone isomer of the tetrabenzyl compound **2** forms a 2 : 1 (host : guest) solvate with *p*-xylene [4]. In the present case, where 1,1,2,2-tetrachloroethane with a greater steric demand is used as a solvent, it is likely that the solvation by only one molecule leaves a large void between the adjacent molecules of **3a** with the rigid cone-shaped structure, which requires four more solvent molecules to be filled up.

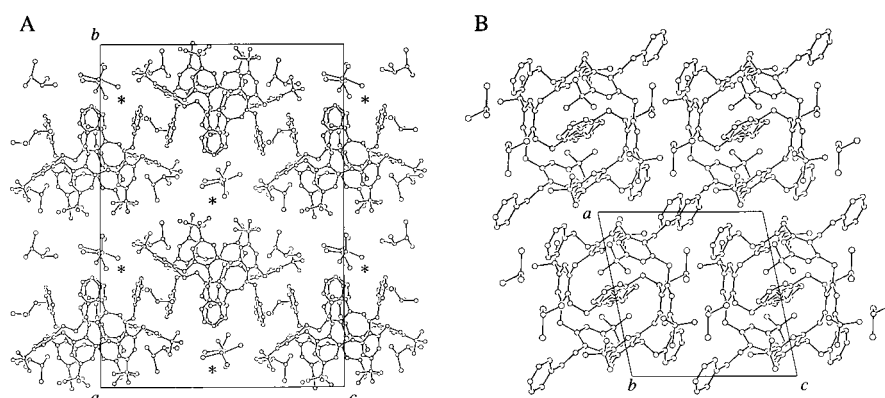


Figure 2. (A) Crystal packing view of the cone isomer **3a** along the crystallographic *a* axis. In the positions marked by asterisks two crystallographically independent solvent molecules are overlaid along the *a* axis, one of which is disordered in the ratio of 0.64 : 0.36 (The minor component is omitted for clarity). (B) Crystal packing view of the 1,2,3-alternate isomer **3b** along the crystallographic *b* axis. The central bridging unit of the calixarene part of **3b** is disordered into two positions to form the crystallographic center of symmetry.

In **3a** and **3b**, the pyridine moieties are suspended from the rigid calix[6]arene platforms in different ways. Further investigations on their use as ligands for transition metals are currently in progress.

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