

## Conversion of 1,3-Alternate to Partial Cone Conformation of tetra-Substituted Calix[4]arene

Sung Ok Kang and Kye Chun Nam\*

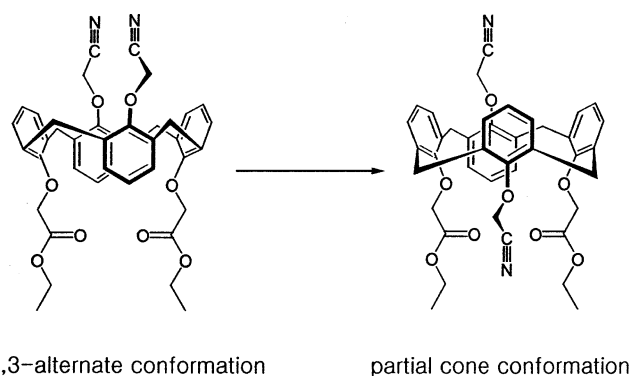
Department of Chemistry and Institute of Basic Science, Chonnam National University, Kwangju 500-757, Korea

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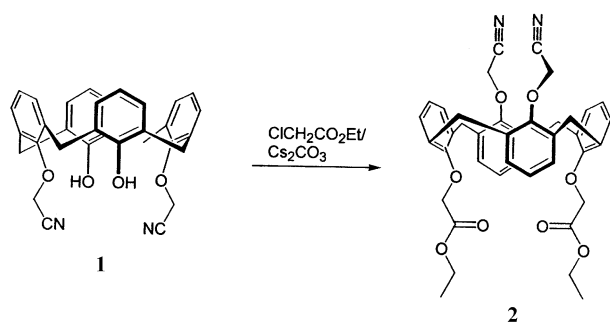
Due to the nonplanar structure, calix[4]arenes can exist in one of the four conformations, and has been designated<sup>1</sup> as cone, partial cone, 1,2-alternate, and 1,3-alternate. By placing substituents at OH groups larger than methyl, conformation can be locked. Very often cone and partial cone conformers were synthesized by the alkylation<sup>2</sup> and acylation<sup>3</sup> reaction at the lower rim of calix[4]arene. But, 1,3-alternate<sup>4</sup> and 1,2-alternate<sup>5</sup> conformers also were observed under the certain reaction conditions. Rapid interconversion of conformation was observed with parent calix[4]arene, but tetra-substituted calix[4]arenes particularly were found to be locked in one conformation. The stability sequence for the parent calix[4]arene was predicted by calculation<sup>6</sup> to be cone > partial cone > 1,2-alternate > 1,3-alternate, but the stability sequence of tetrasubstituted calix[4]arene was not calculated generally yet. Only recently cone to partial cone conversion of calix[4]crown was reported in the presence of potassium ion.<sup>7</sup>

During the synthesis of bifunctional receptor we synthesized a tetrasubstituted calix[4]arene **2** and observed a conversion of 1,3-alternate to partial cone conformation at room temperature. In our best knowledge it is believed that this is the first example of conformational conversion of tetrasubstituted calix[4]arene at room temperature in the absence of metal ion.

The tetrasubstituted calix[4]arene **2**<sup>8</sup> was obtained by treating **1** with ethyl chloroacetate in the presence of Cs<sub>2</sub>CO<sub>3</sub> in Scheme 1. It was reported<sup>9</sup> that 1,3-alternate conformation product was obtained in the presence of Cs<sub>2</sub>CO<sub>3</sub> with alkyl halides. As expected the <sup>1</sup>H NMR spectrum of **2** shows the characteristics<sup>10</sup> of 1,3-alternate conformation such as a narrow range chemical shift of aromatic protons at  $\delta$  6.8-7.2 and methylene protons at  $\delta$  3.6-4.2 as shown at spectrum (a) in Figure 1. Peak multiplicities are consistent with the expected 1,3-alternate conformer, three singlets at 3.6-4.1 for the



16 methylene protons and a broad doublet and two triplets at 6.8-7.2 for the 12 aromatic protons. It was observed accidentally that the 1,3-alternate conformer was transformed into partial cone slowly in CDCl<sub>3</sub> solution and after 2 days the mixture of 1,3-alternate and partial cone conformers were found. Conversion was completed after 10 days at room temperature in CDCl<sub>3</sub> and only pure partial cone conformer was observed as shown at spectrum (c) in Figure 1. Spectrum (c) shows a typical characteristics of partial cone conformation, wide range peaks of aromatic protons at  $\delta$  6.5-7.5



Scheme 1

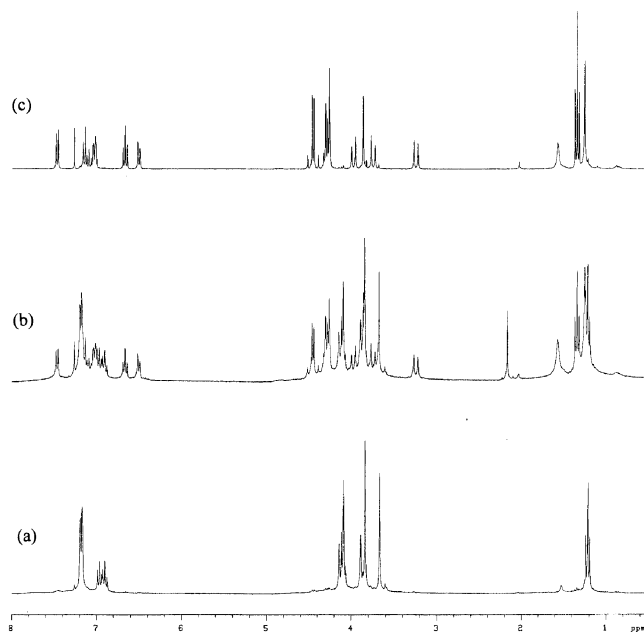
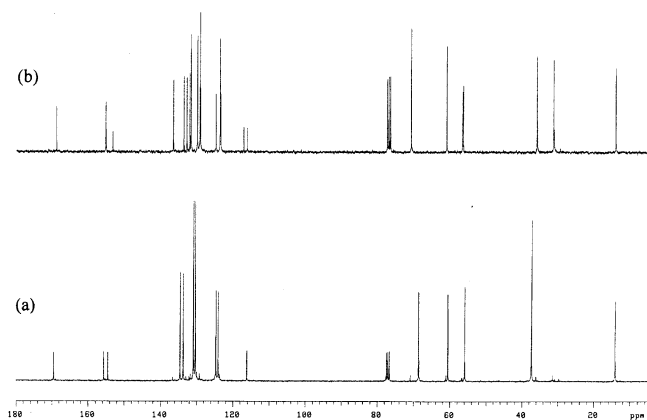


Figure 1. <sup>1</sup>H NMR spectrum of **2** in CDCl<sub>3</sub> (a) within 1 hr (1,3-alternate conformation) (b) after 2 days (a mixture of 1,3-alternate and partial cone conformations) (c) after 10 days (partial cone conformation).



**Figure 2.**  $^{13}\text{C}$  NMR spectrum of **2** in  $\text{CDCl}_3$  (a) within 1 hr (1,3-alternate conformation) (b) after 10 days (partial cone conformation).

and methylene protons at  $\delta$  3.2–4.5. Peak multiplicities were consistent as expected in partial cone conformation such as two pairs of doublets of eight bridge methylene protons at  $\delta$  3.3–4.4 and four methylene protons of two  $-\text{CH}_2\text{CO}_2^-$  groups as a pair of doublets at  $\delta$  4.5 due to diastereomeric relationship. One triplet at  $\delta$  1.3 in spectrum (c) for the two methyl group indicates that one cyanomethyl group is rotated from up to down position, presumably due to the small size of the cyanomethyl group.

The  $^{13}\text{C}$  NMR spectrum confirmed the conformation conversion as shown in Figure 2. Spectrum (a) shows a characteristic of 1,3-alternate conformation such as one peak at  $\delta$  37.3 for the bridge carbons consistent with *anti*-oriented<sup>11</sup> phenolic ring of 1,3-alternate conformation. On the other hand spectrum (b) shows a characteristic of partial cone conformation, which can be seen from two peaks at  $\delta$  36.1 and 31.4 for the bridge carbons arising from *syn*- and *anti*-oriented phenolic rings of partial cone conformation. Aromatic carbon peaks are also consistent with the expected results from each conformation such as eight aromatic carbon peaks for the 1,3-alternate and fourteen aromatic peaks for the partial cone conformer.

The stability sequence for the parent calix[4]arene was predicted by calculation<sup>6</sup> to be cone > partial cone > 1,2-alternate > 1,3-alternate and the improved program appear to predict the stability sequence of tetramethylcalix[4]arene in good agreement<sup>12</sup> with experiment. Although we did not have the stability sequence of **2**, 1,3-alternate to partial cone conversion of **2** at room temperature in  $\text{CDCl}_3$  clearly suggests that partial cone conformation of **2** is more stable than 1,3-alternate and cyanomethyl group is small enough to

rotate. Currently we are investigating the size effect for the conformational conversion.

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