

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

Sung Ok Kang and Kye Chun Nam*

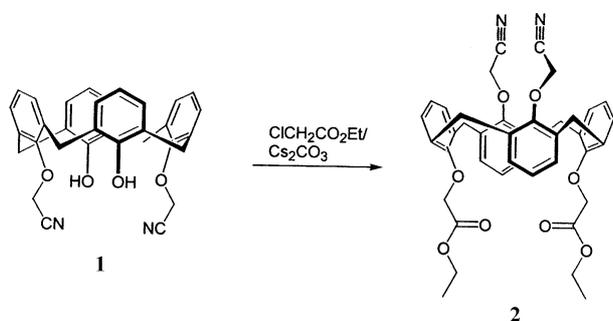
Department of Chemistry and Institute of Basic Science, Chonnam National University, Kwangju 500-757, Korea

Received December 21, 1999

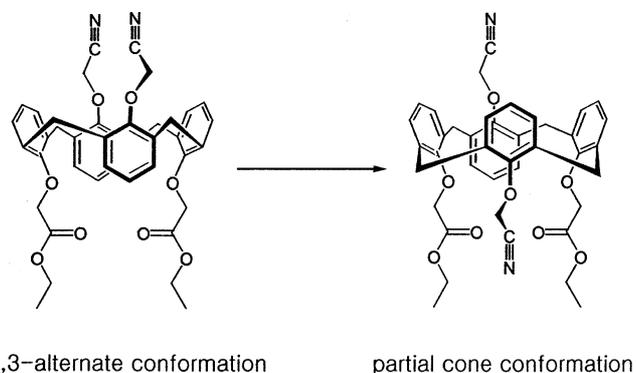
Due to the nonplanar structure, calix[4]arenes can exist in one of the four conformations, and has been designated¹ as cone, partial cone, 1,2-alternate, and 1,3-alternate. By placing substituents at OH groups larger than methyl, conformation can be locked. Very often cone and partial cone conformers were synthesized by the alkylation² and acylation³ reaction at the lower rim of calix[4]arene. But, 1,3-alternate⁴ and 1,2-alternate⁵ 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 calculation⁶ 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.⁷

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**⁸ was obtained by treating **1** with ethyl chloroacetate in the presence of Cs₂CO₃ in Scheme 1. It was reported⁹ that 1,3-alternate conformation product was obtained in the presence of Cs₂CO₃ with alkyl halides. As expected the ¹H NMR spectrum of **2** shows the characteristics¹⁰ of 1,3-alternate conformation such as a narrow range chemical shift of aromatic protons at δ 6.8-7.2 and methylene protons at δ 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



Scheme 1



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 CDCl₃ 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 CDCl₃ 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 δ 6.5-7.5

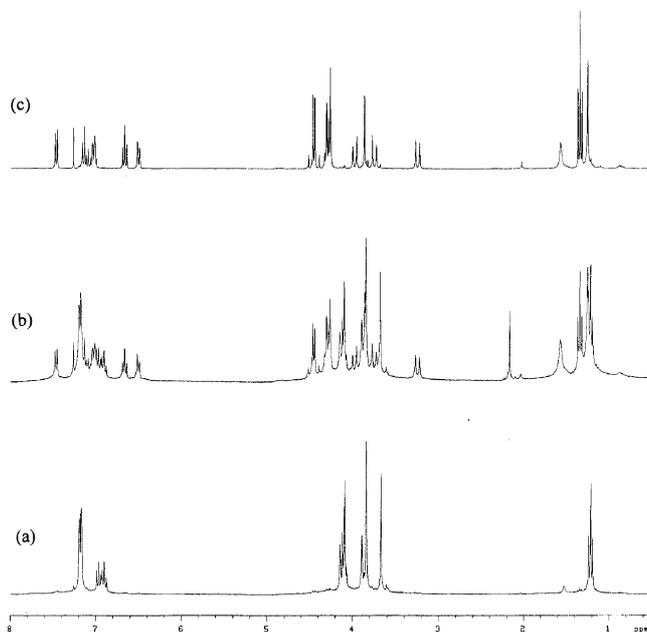


Figure 1. ¹H NMR spectrum of **2** in CDCl₃ (a) within 1 hr (1,3-alternate conformation) (b) after 2 days (a mixture of 1,3-alternate and partial cone conformations) (c) after 10 days (partial cone conformation).

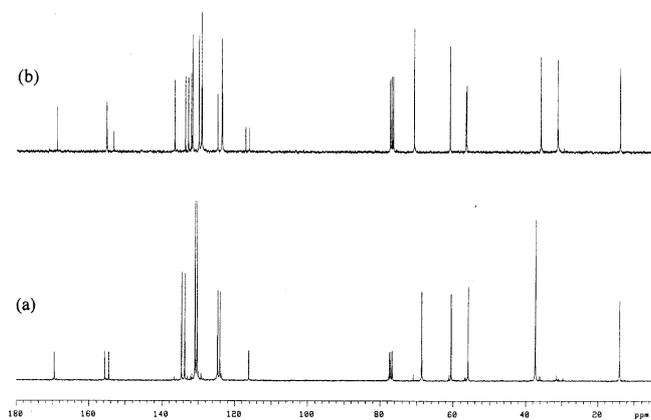


Figure 2. ^{13}C NMR spectrum of **2** in CDCl_3 (a) within 1 hr (1,3-alternate conformation) (b) after 10 days (partial cone conformation).

and methylene protons at δ 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 δ 3.3–4.4 and four methylene protons of two $-\text{CH}_2\text{CO}_2-$ groups as a pair of doublets at δ 4.5 due to diastereomeric relationship. One triplet at δ 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}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 δ 37.3 for the bridge carbons consistent with *anti*-oriented¹¹ 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 δ 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 calculation⁶ 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 agreement¹² 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 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.

Acknowledgment. We are indebted to the Basic Science Research Institute Program, Ministry of Education of Korea (BSRI 98-3429) for generous support of this work.

References

- Gutsche, C. D.; Dhawan, B.; Levine, J. A.; No, K. H.; Bauer, L. J. *Tetrahedron* **1983**, *39*, 409.
- (a) Collins, E. M.; McKervey, M. A.; Madigan, E.; Moran, M. B.; Owens, M.; Ferguson, G.; Harris, S. J. *J. Chem. Soc., Perkin Trans. 1* **1991**, 3137. (b) Iwamoto, K.; Araki, K.; Shinkai, S. *Tetrahedron* **1991**, *47*, 4325. (c) Pappalardo, S.; Giunta, L.; Foti, M.; Ferguson, G.; Gallagher, J. F.; Kaitner, B. *J. Org. Chem.* **1992**, *57*, 2611.
- (a) Gutsche, C. D.; Lin, L. G. *Tetrahedron* **1986**, *42*, 1633. (b) Gutsche, L. D.; See, K. A. *J. Org. Chem.* **1992**, *57*, 4527. (c) See, K. A.; Fronczek, F. R.; Watson, W. H.; Kashyap, R. P.; Gutsche, C. D. *J. Org. Chem.* **1991**, *56*, 7256.
- (a) Ikeda, A.; Shinkai, S. *Tetrahedron Lett.* **1992**, *33*, 7385. (b) Aeungmaitrepirom, W.; Asfari, Z.; Vicens, J. *Tetrahedron Lett.* **1997**, *38*, 1907. (c) Rudkevich, D. M.; Mercer-Chalmers, J. D.; Verboom, W.; Ungaro, R.; Jang, F.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1995**, *117*, 6124.
- (a) Pappalardo, S.; Petringe, A.; Parisi, M. F.; Ferguson, G. *Tetrahedron Lett.* **1996**, *37*, 3907. (b) Arduini, A.; Domiano, L.; Pochini, A.; Secchi, A.; Ungaro, R.; Ugozzoli, F.; Struck, O.; Verboom, W.; Reinhoudt, D. N. *Tetrahedron* **1997**, *53*, 3767. (c) Ferguson, G.; Lough, A. J.; Notti, A.; Pappalardo, S.; Parisi, M.; Petringe, A. *J. Org. Chem.* **1998**, *63*, 9703.
- Grootenhuys, P. D. J.; Kollman, P. A.; Groenen, L. C.; Reinhoudt, D. N.; van Hummel, G. J.; Ugozzoli, F.; Andreetti, G. D. *J. Am. Chem. Soc.* **1990**, *112*, 4165.
- Ferguson, G.; Gallagher, J. F.; Lough, A. J.; Notti, A.; Pappalardo, S.; Parisi, M. F. *J. Org. Chem.* **1999**, *64*, 5876.
- Mixtures of 1,3-alternate and cone conformers (6 : 4 ratio) were obtained by the reaction and the 1,3-alternate conformer was separated from column chromatography.
- Verboom, W.; Datta, S.; Asfari, Z.; Harkema, S.; Reinhoudt, D. N. *J. Org. Chem.* **1992**, *57*, 5394.
- Igbal, M.; Mangiafico, T.; Gutsche, C. D. *Tetrahedron* **1987**, *43*, 4917.
- Casnati, A.; Arduini, A.; Ghidini, E.; Pochini, A.; Ungaro, R. *Tetrahedron* **1991**, *47*, 2221.
- Fisher, S.; Grootenhuys, P. D. J.; Groenen, L. C.; van Hoorn, W. P.; van Veggel, F. C. J. M.; Reinhoudt, D. N.; Karplus, M. *J. Am. Chem. Soc.* **1995**, *117*, 1611.