CHEMISTRY LETTERS, pp. 1263-1266, 1990.

"Cone"-"Partial Cone" Isomerism in Tetramethoxy-p-t-butylcalix[4]arene. Novel Solvent Effects and Metal Template Effects

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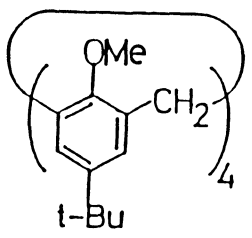
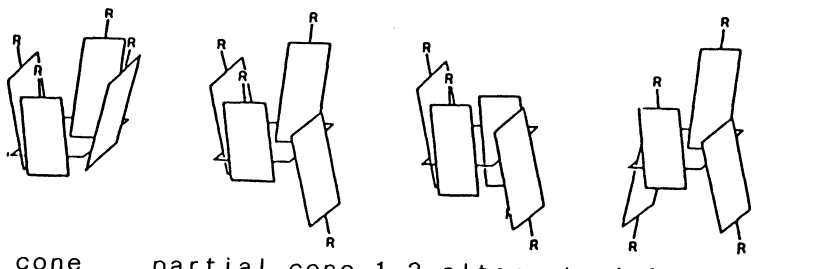
The solvent effects on the "cone"-"partial cone" equilibrium in tetramethoxy-p-t-butylcalix[4]arene were studied for the first time. It was found that the concentration of the "cone" isomer is increased with increasing solvent polarity. The shift in the equilibrium was accounted for by the differece in the dipole moment between "cone" and "partial cone" isomers.

Calixarenes are cyclic oligomers made up of phenol units. Although each phenol unit can rotate according to the oxygen-through-the-annulus rotation mechanism, they favorably adopt a "cone" coformation because of the stabilization by intramolecular hydrogen-bonding interactions among OH groups.[1-3] In tetra-O-alkyl derivatives, on the other hand, the "cone" conformation is not necessarily stabilized because of the absence of such intramolecular hydrogen-bonding interactions.[4,5] Thus, one must take the presence of four different conformational isomers into account.[1-6] In the past, only the "partial cone" isomer was detected by ^{1}H NMR.[4] It has so far been believed, therefore, that other isomers are much less stable than the "partial cone" isomer. In the course of our studies on the conformational isomerism in 1-Me, we unexpectedly detected the "cone" isomer in polar solvents and the concentration increased with increasing solvent polarity. In this communication, we discuss why "cone" 1-Me can exist in poler solvents.



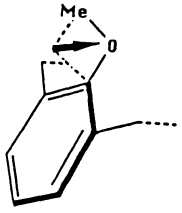
1-Me



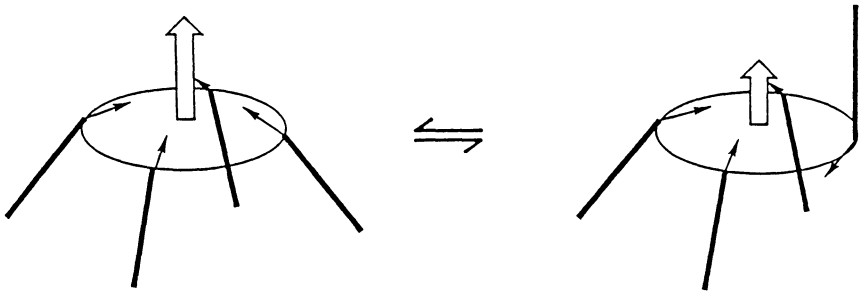
cone partial cone 1,2-alternate 1,3-alternate

The concentration of each isomer can be easily evaluated by a ^{1}H NMR method because they give different split patterns for the $ArCH_2Ar$ protons: a pair of doublets for "cone", two pairs of doublets for "partial cone", a single peak and a pair of doublets for "1,2-alternate", and a single peak for "1,3-alternate".[1-5] The ^{1}H NMR spectrum (400 MHz) of 1-Me measured in $CDCl_3$ at -20 °C gave only two pairs of doublets (3.79 and 3.85 ppm for one pair and 3.18 and 4.19 ppm for another pair) for the $ArCH_2Ar$ protons. This established that in $CDCl_3$, 1-Me totally exists as a "partial cone" isomer and other three isomers are unstable. When CD_3CN was mixed with $CDCl_3$, the intensity of these peaks was weakened and a pair of doublets newly appeared at around 3.25 and 4.32 ppm. The intensity of the new peaks was more and more strengthened with increasing CD_3CN concentration. This indicates that CD_3CN solvent is capable of stabilizing a "cone" conformation.[7] An increase in the "cone" isomer was also observed when $(CD_3)_2NCDO$ was mixed with $CDCl_3$. The equilibrium constants K (= [cone]/[partial cone]) were estimated by a ^{1}H NMR method at -50~10 °C. The van't Hoff plots are shown in Fig. 2. From least-squares computation of these plots ($r > 0.99$), we determined the slopes ($-\Delta H^\circ/R$) and the intercepts ($\Delta S^\circ/R$): thus, ΔH° =-0.99 kcal mol^{-1} and ΔS° =-5.9 e.u. for $CDCl_3$:CD_3CN = 1:1 v/v and ΔH° =-2.54 kcal mol^{-1} and ΔS° =-12.9 e.u. for $CDCl_3$:$(CD_3)_2NCDO$ = 1:4 v/v.

Why is the "cone"-"partial cone" equilibrium in 1-Me solvent-dependent? The p-t-butylanisole unit has a dipole arising from the ether linkage.[8] In the "cone" conformation, four dipoles orientate into the same direction. This means that the "cone" isomer behaves as a polar molecule. In the "partial cone" conformation, on the other hand, one dipole is reversed. Thus, the "partial cone" isomer behaves as a less polar molecule. This is why the "cone" conformation is more stabilized in polar solvents.



dipole monent inherent to the ether linkage



polar "cone" ⇌ less polar "partial cone"

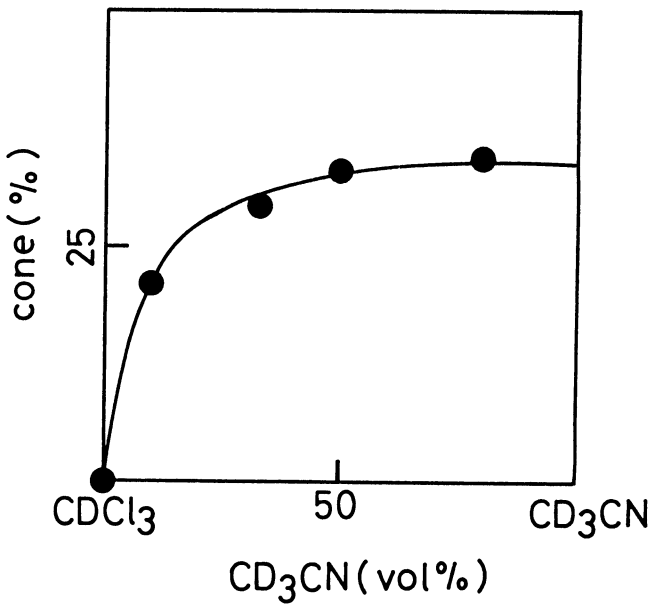


Fig. 1. Concentration of a "cone" isomer at -20 °C plotted against $E_T(30)$ in a $CDCl_3$-CD_3CN mixed system.

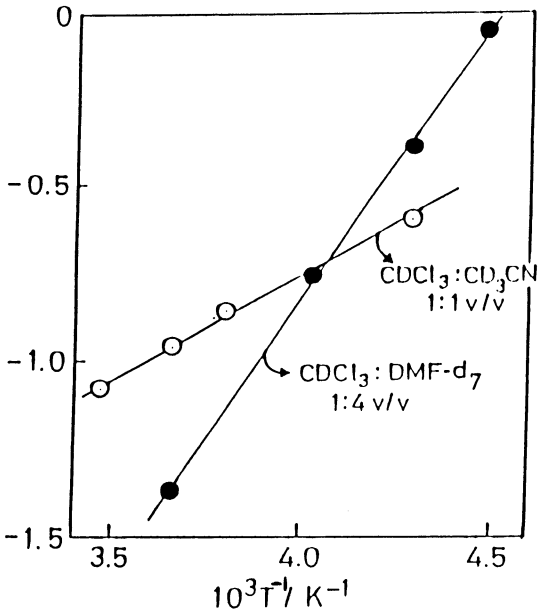


Fig. 2. van't Hoff plots for a "cone"-"partial cone" equilibrium in (○) $CDCl_3$-CD_3CN (1:1 v/v) and (●) $CDCl_3$-$(CD_3)_2NCDO$ (1:4 v/v).

Table 1. Final steric energies (E_s) and dipole moments for conformational isomers of 1-Me [a)]

Conformation	E_s /kcal mol^{-1}	Dipole moment /D
Cone	6.76	0.834
Partial cone	5.64	0.538
1,2-Alternate	11.33	0.021
1,3-Alternate	3.92	0.002

a) The four methyl groups are placed outside the ring. Except "1,2-alternate", the E_s values are increased when one of them is placed inside the ring. In "1,2-alternate", the conformation with two "inside" methyls gave the smallest E_s(=9.96 kcal mol^{-1}). Dipole moment for p-t-butylanisole estimated by MM2PP[9)] is 1.559 D.

We estimated final steric energies and dipole moments of four conformational isomers by molecular mechanics (MM2PP).[9] The results are summarized is Table 1. From the steric energy, "1,3-alternate" is most stable and "partial cone" is the next. From the dipole moment, "cone" is more polar than "partial cone" and "1,3-alternate" is nonpolar. These results suggest that although "cone" and "partial cone" are sterically less stable than "1,3-alternate", the solvation by polar solvents can compensate the steric disadvantage. "Cone" with the relatively high dipole moment is particularly stabilized in such polar solvents.

Furthermore, we found that the concentration of the "cone" isomer increases on the addition of $LiClO_4$ and $NaClO_4$. For example, when $LiClO_4$ was added to a $CDCl_3$-CD_3CN (1:1 v/v) solution, an additional pair of doublets appeared at 3.49 and 4.19 ppm, which can be assigned to a Li^+·1-Me(cone) complex. Thus, this equilibrium shift is attributed to an interaction of alkali metal cations with four methoxy oxygens, a typical template effect on ionophoric 1-Me.

We are grateful to Professor Eiji Osawa for helpful discussions.

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7)The mole percentage of the "cone" isomer is linearly correlated with $E_T(30)$ (r=0.99): "cone" (mol %)= $5.1 \cdot E_T(30)-197$.
8)Dipole moment of anisole =1.35 D: "Kagaku Binran (Chemistry Date Table)," ed by Chemical Society of Japan, Maruzen, Tokyo, 1966, 1227.
9)Toray Computer Aided Molecular Engineering System(MM2PP). The estimation of hydrogen-bonding interactions by molecular mechanics, which have a crucial effect on the calixarene conformation,[1-3] is quite difficult. This is why the application of molecular mechanics to "unmodified" calixarenes has been very limited. In the present tetra-O-alkylated 1-Me, one can disregard such hydrogen-bonding interactions.

(Received April 27, 1990)