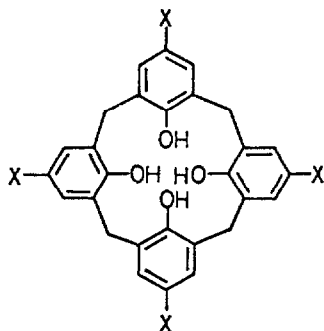


"TEMPLATE EFFECTS" ON CALIXARENE CONFORMATIONS
THROUGH HOST-GUEST-TYPE INTERACTIONS

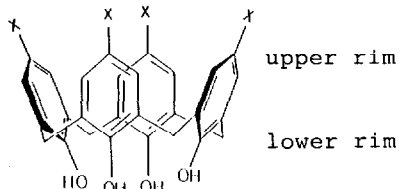
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Abstract: The conformational change in p-sulfonatocalix[4]arene in water is subject to the "template effect" of cations, especially to that of organic ammonium cations.

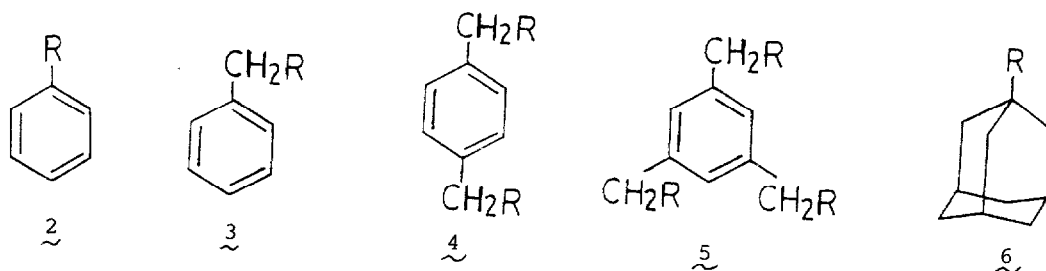
Calixarenes, when in the "cone" conformation, are cavity-shaped macrocyclic compounds but are conformationally flexible in solution.¹⁻³⁾ It is known that the "cone" conformer is more stabilized in aprotic solvents than the "alternate" one because of intramolecular hydrogen-bonding interactions among OH groups.^{1,2)} This implies that the hydrogen-bonding interactions are capable of freezing up the conformational freedom in calixarenes. The similar effect may be expected for guest molecules if they are bound to the appropriate position of the calixarene cavity. However, the study of the guest template effect has been very limited: the difficulty is related to the absence of the calixarenes suitably functionalized for this study. We recently synthesized water-soluble p-sulfonatocalix[4]arene (1), the host-guest interactions of which have been well characterized.^{4,5)} Thus, this system is undoubtedly suitable to examination of the guest template effect. In this communication we wish to report a new finding that cationic guests (in particular, organic ammonium cations) can efficiently stabilize the "cone" conformation.



1 (X=SO₃Na)



"Cone" structure of 1



Guest molecules ($R = \text{NMe}_3^+ \text{Cl}^-$)

It is known that the calix[4]arene conformation is conveniently monitored by the temperature-dependent $^1\text{H-NMR}$ spectrum for the ArCH_2Ar protons: they display a singlet peak at high temperature and a pair of doublets at low temperature.⁶⁾ Thus, the coalescence temperature (T_c) serves as an indication of the "cone" stability: the higher the T_c , the more stable the "cone" conformation. $\underline{2}$ in D_2O gave a singlet peak for the ArCH_2Ar protons at 3.93 ppm at high temperature and split peaks at low temperature (JEOL GX-400 NMR apparatus). As summarized in Table 1, T_c values increase with increasing alkali metal concentrations. The large metal cations (e.g., Cs^+) are more effective at low concentration whereas the small metal cations (e.g., Li^+) are more effective at high concentration. The highest T_c (26 $^\circ\text{C}$) was attained in the presence of 4.60 M Li^+ , which was higher by 17 $^\circ\text{C}$ than that in the absence of alkali metal cations. It has been established that the lower rim of the calixarene cavity, consisting of appended OH groups, can bind alkali metal cations strongly.^{6,7)} The T_c rise is thus attributed to the "template effect" of metal cations which are entrapped by the oxy-anionic groups on the calixarene lower rim.⁸⁾ The finding supports the view that in an aqueous system the electrostatic metal-oxy anion interaction plays a crucial role for the stabilization of the "cone" conformation.

Interestingly, T_c was further enhanced in the presence of organic cations (Table 2). In particular, dicationic $\underline{4}$, tricationic $\underline{5}$, and hydrophobic cation $\underline{6}$ are very effective, the T_c values being enhanced up to 50-65 $^\circ\text{C}$. The CPK model building and the X-ray crystallographic studies suggest that the "cone" conformation provides a cavity-shaped stoma suitable to guest inclusion.^{1-3,9)} The recent circular dichroism studies also support this: the conformation of water-soluble calixarenes is fixed to "cone" upon inclusion of guest molecules.¹⁰⁾ Thus, both of the electrostatic and the hydrophobic interaction are responsible for the efficient template effect.

Table 1. Influence of Bound Alkali Metal Cations on T_c^a

Guest (conc. /M)	T_c ($^{\circ}\text{C}$)
None ^b	9
LiCl (0.17)	9
LiCl (4.60)	26
NaCl (0.25)	9
NaCl (2.20)	17
NaCl (4.70)	25
KCl (0.17)	11
KCl (2.30)	20
CsCl (0.17)	17
CsCl (3.80)	17

^a pD 8.9 with 0.5 M borate buffer, $[1] = 1.10 \times 10^{-2}$ M.

^b The sample solution contains Na^+ (0.077 M) as counterions and buffer species.

Then, how are these ammonium cations bound to 1 ? The association geometry can be presumed from the shift width of their $^1\text{H-NMR}$ peaks. In the presence of excess 1 ($[1] = 2.0 \times 10^{-2}$ M, $[\text{guest}] = 2.0 \times 10^{-3}$ M)¹¹) the $^1\text{H-NMR}$ peaks were all shifted to higher magnetic field (Fig. 1). In particular, $\text{N}^+\text{-CH}_3$ and para-H in 2 and $\text{N}^+\text{-CH}_3$ and CH_2 in 3 give the largest up-field shifts by 1.2 - 1.7 ppm. This supports the view that monocationic 2 and 3 are bound deeply in the aromatic calixarene cavity. In contrast, dicationic 4 and tricationic 5 cause the relatively small up-field shifts. The difference is reasonably understood by such that these guests rather "perch" on the

Table 2. Influence of Bound Ammonium Cations on T_c^a

Guest (conc. /M)	T_c ($^{\circ}\text{C}$)
2 (0.005)	20
2 (0.010)	43
2 (0.020)	50
2 (2.00)	65
3 (0.010)	30
3 (2.00)	65
4 (0.010)	50
5 (0.010)	50
6 (0.005)	25
6 (0.010)	50
6 (0.020)	57

^a pD 8.9 with 0.5 M borate buffer, $[1] = 1.10 \times 10^{-2}$ M.

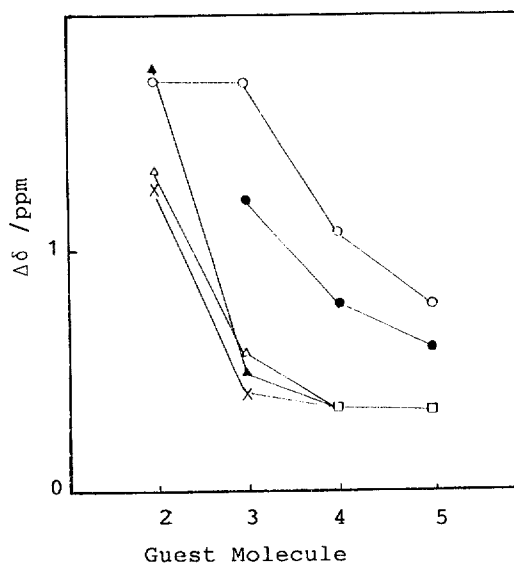


Fig. 1. Up-field shifts of $^1\text{H-NMR}$ peaks of guest molecules in the presence of excess 1 ($=10[\text{guest}]$): pD 7.3, 25°C , (○) $\text{N}^+\text{-CH}_3$, (●) CH_2 , (Δ) o-H, (×) m-H, (▲) p-H.

edge of the calixarene cavity.

In conclusion, this paper demonstrated for the first time the presence of guest template effects on the calixarene conformation. This suggests that host-guest interactions in calixarenes occur in an induced-fit manner. Molecular recognition in calixarenes has still been a matter of some controversy because of the remaining conformational freedom.^{1,2,4,5)} Thus, the present conclusion is of great significance in the design of functionalized calixarenes with the guest recognition ability.

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