CHEMISTRY LETTERS, pp. 835-838, 1990.

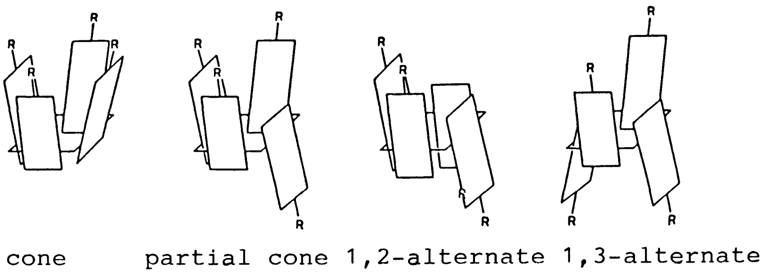
Metal Selectivity of Conformational Isomers Derived from p-t-Butylcalix[4]arene

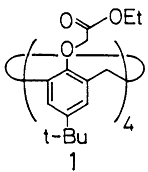
Seiji SHINKAI,* Toshio OTSUKA, Kiyosi FUJIMOTO, and Tsutomu MATSUDA
Department of Organic Synthesis, Faculty of Engineering,
Kyushu University, Fukuoka 812

"Cone" and "partial cone" isomers of 25,27-bis(2-pyridylmethoxy)-26,28-bis(ethoxycarbonylmethoxy)-p-t-butylcalix[4]arene (**3**) were isolated by a TLC method and the structures were identified by ^{1}H NMR. From two-phase solvent extraction of alkali picrates, the size of the ionophoric cavities was estimated to be in the order, partial-cone-**3** > tetrakis(ethoxycarbonylmethoxy)-p-t-butylcalix[4]arene (cone) > cone-**3**. This is the first quantitative estimation of the ionophoricity of conformationally-isomeric calix[4]arenes.

Calix[4]arenes have the smallest void among calix[n]arenes. In unmodified calix[4]arenes a conformational change through the oxygen-through-the-annulus rotation is still allowed, whereas in tetra-O-alkylcalix[4]arenes having alkyl groups greater than Et the rotation is sterically inhibited and four conformational isomers result: they are "cone", "partial cone", "1,2-alternate", and "1,3-alternate".[1-3)] It is known that tetra-O-alkylation with simple alkyl halogens such as PrBr and BuBr affords a mixture of "cone" and "partial cone",[2,3)] whereas the reaction with $BrCH_2COOEt$ affords only "cone".[4-6)] The difference suggests the view that in the reaction with $BrCH_2COOEt$ alkali metal cations (Na^+ or K^+ used as NaH or K_2CO_3) act as a template metal, because the product (tetrakis(ethoxycarbonylmethoxy)-p-t-butylcalix[4]arene: cone-**1**) shows the strong ionophoricity for these metal cations.[4-6)]

Cone-**1** shows a high selectivity toward Na^+.[4-6)] We considered that if one could synthesize **1** with the different conformation, then it would exhibit the different metal selectivity. The attempt to synthesize **1** with the conformation other than "cone" failed. Instead, when we synthesized a new ionophoric calix[4]arene, 25,27-bis(2-pyridylmethoxy)-26,28-bis(ethoxycarbonylmethoxy)-p-t-butylcalix[4]arene (**3**) from 25,27-bis(pyridylmethoxy)-p-t-butylcalix[4]arene (**2**), we unexpectedly found that the product is a mixture of cone-**3** and partial-cone-**3** and they can be isolated by a TLC method. In this communication we report the structure assignment and the metal selectivity of these conformationally-isomeric, ionophoric calix[4]arenes.





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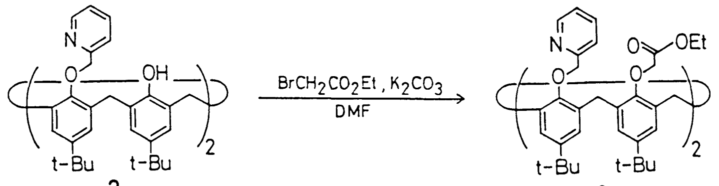
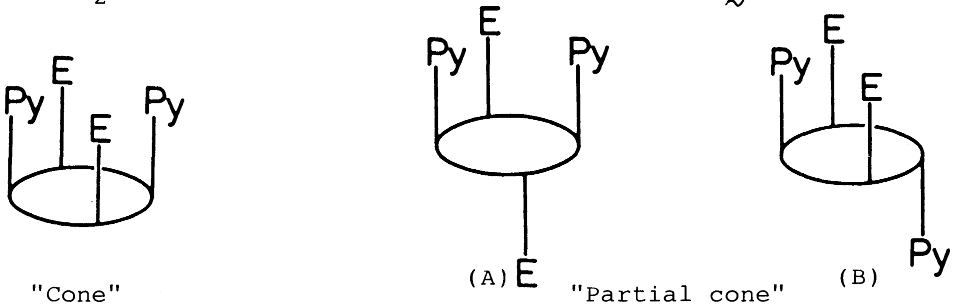


2 3

Preparation of 2 was described previously.[7] 2 (1.50 g, 1.8 mmol) was treated with $BrCH_2COOEt$ (3.00 g, 18 mmol) and K_2CO_3 (11 g) in N,N-dimethylformamide (60 ml) at 70-80 °C for 17 h. After cooling, the solution was diluted with water and the precipitate was collected by filtration. The product was dissolved in chloroform and the solution was washed with water. The chloroform layer was dried with $MgSO_4$ and concentrated in vacuo. The residue was subjected to TLC separation (silica gel, hexane:ethyl acetate = 3:2 v/v): cone-3, R_f = 0.15, mp 144-145 °C, yield 32%; partial-cone-3, R_f = 0.60, mp 211-213 °C, yield 7.7%.[8]

The structures of these two isomers were assigned from the split pattern of the $ArCH_2Ar$ protons in ^1H NMR (Fig. 1). Cone-3 gave a pair of doublets at 3.16 and 4.68 ppm, which is commensurate with the "cone" conformation.[1-3] Partial-cone-3 gave two pairs of doublets, which are commensurate with the "partial cone" conformation.[1-3] Two possible partial cone isomers ((A) and (B)) exist, however. The $PyCH_2$ methylene protons gave a pair of doublets at 4.76 and 4.89 ppm (because of geminal coupling). On the other hand, all protons in the $EtOCOCH_2$ groups appeared in duplicate: 1.05 and 1.33 ppm for CH_3, 3.83 and 4.24 for $(CH_3)CH_2$, and 4.27 and 4.33 ppm for OCH_2. The result establishes that one of two $EtOCOCH_2$ groups is inversed (i.e., partial-cone-3 has the structure (A)).



"Cone" "Partial cone"

Py:2-Pyridylmethoxy, E:Ethoxycarbonylmethoxy

Table 1. Solvent extraction of alkali picrates (M^+Pic^-) at 25 °C[a)]

Calixarene	Extractability/%			
	M^+=Li^+	Na^+	K^+	Cs^+
Cone-3	59.1	93.4	57.7	13.8
Partial-cone-3	1.7	12.6	27.0	23.6
Cone-1[b)]	15.0	94.6	49.1	48.9

a) Aqueous phase (5 ml):[M^+Pic^-] = 2.50×10^{-4} M, [MOH] = 0.10 M, [MCl] = 0.50 M. Organic phase (dichloromethane 5 ml):[3] = 2.5×10^{-3} M. The two-phase mixture was shaken for 30 min.

b) Cited from, M. A. McKervey, E. M. Seward, G. Ferguson, B. Ruhl, and S. J. Harris, J. Chem. Soc., Chem. Commun., 1985, 388: aqueous phase 2.5×10^{-4} M picric acid and 0.1 M MOH; organic phase (dichloromethane) 2.5×10^{-4} M cone-1.

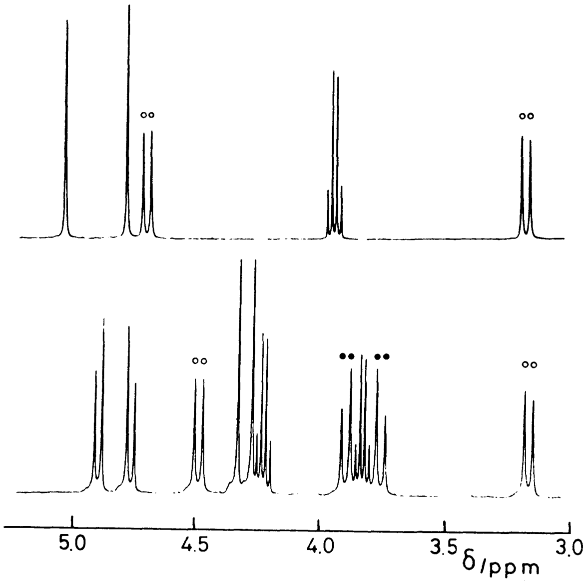


Fig. 1. Partial ^1H NMR (400 MHz) for the $ArCH_2Ar$ methylene protons in 3 ($CDCl_3$, 25 °C): cone-3 (upper) features a pair of doublets (open circles); partial-cone-3 (lower) features two pairs of doublets (open and filled circles).

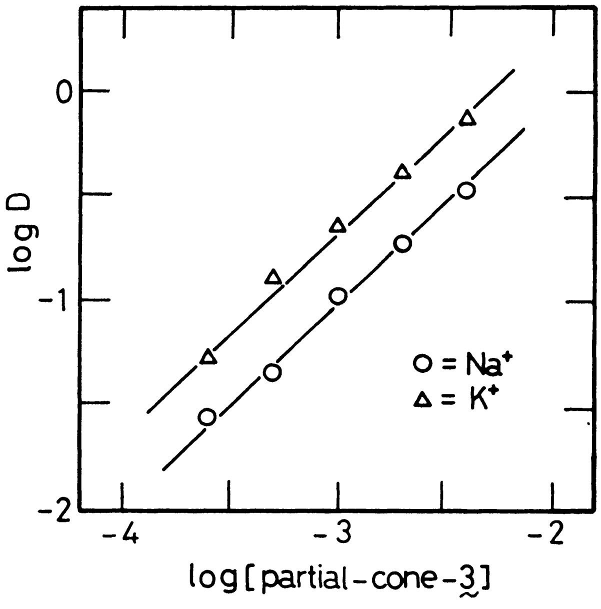


Fig.2. Plots of log [partial-cone-3] vs. log D. The extraction conditions are similar to those recorded in a footnote to Table 1.

Here, we performed two-phase solvent extraction of alkali picrates for understanding a possible relation between the metal selectivity and the cavity shape in 3. The results are summarized in Table 1. It is already known that cone-1 shows the high selectivity toward Na^+ and forms mostly a 1:1 complex because metals are encapsulated deeply in the ionophoric cavity.[4-6] Cone-3 also showed the Na^+ selectivity but bound a considerable amount of Li^+. The result suggests that the cavity formed by two pyridines and two $EtOCOCH_2$ groups is somewhat smaller than that of cone-1 formed by four $EtOCOCH_2$ groups. Interestingly, partial-cone-3 showed the K^+ selectivity and bound a considerable amount of Cs^+. As illustrated in Fig. 2, we determined the distribution ratios (D) as a function of [partial-cone-3]. The slopes are all equal to unity. This indicates the formation of 1:1 complexes with these metal cations: that is, the formation of a 1:2 metal/partial-cone-3 sandwich complex is not the case. Based on these findings, one can conclude that the ionophoric cavity in partial-cone-3 binds only one metal cation and is somewhat greater than those in cone-1 and cone-3.

The foregoing results establish that the ionophoric cavity formed on the lower rim of calix[4]arene is controllable not only by substituents but also by its conformation. We believe that the skillful combination of these two factors would enable "fine tuning" of the ionophoric cavity size, which would eventually lead to precise recognition of metal cations.

This work was supported by the Grant-in-Aid from the Ministry of Education, Science and Culture of Japan.

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8) In addition to cone-3 and partial-cone-3, the third, relatively small spot appeared at $R_f = 0.90$. The structure of this fraction is not yet specified.

(Received February 24, 1990)