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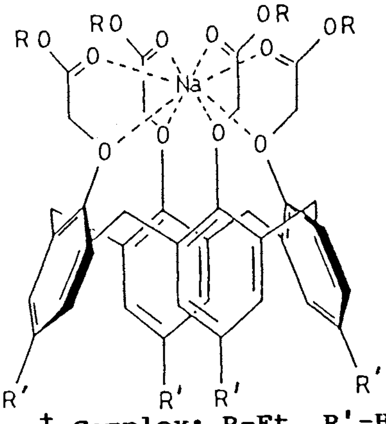
Chromogenic Calix[4]arene

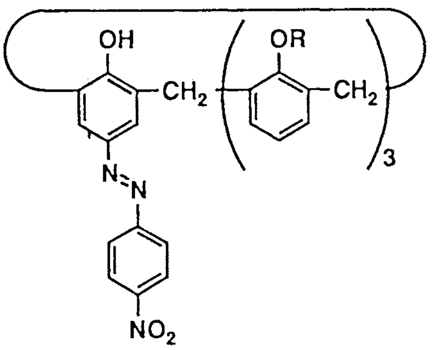
Hiroyasu SHIMIZU, Koji IWAMOTO, Kiyoshi FUJIMOTO, and Seiji SHINKAI*
Department of Organic Synthesis, Faculty of Engineering,
Kyushu University, Fukuoka 812

A chromogenic calix[4]arene which has within a molecule both the triester moiety as a metal-binding site and the azophenol moiety as a coloration site was synthesized. This calix[4]arene showed the high Li^+ selectivity.

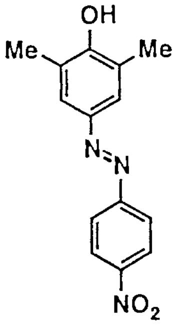
Molecular design of so-called "chromogenic crown ethers" attracts much attention. They change their absorption (or fluorescence) spectra upon the binding of metal cations or amines.[1)] The coloration process thus serves as a transducer of the chemical signal (i.e., concentrations) to the physical signal (i.e., spectral parameters). We have currently been interested in molecular design of calixarene-based ionophores.[2)] The particular interest in this field arises from the fact that calix[4]aryl tetraester (**1**) exhibits the remarkably high selectivity toward Na^+.[3-6)] This stimulated us to design a new calix[4]arene-based, chromogenic ionophore. In this paper we address molecular design of a chromogenic calix[4]arene (**2**) which has within a molecule both the calix[4]aryl triester moiety as a metal-binding site and the azophenol moiety as a coloration site. We have found that compound **2** shows the nearly "perfect" Li^+ selectivity in solid-liquid two-phase solvent extraction.



1·Na^+ Complex: R=Et, R'=H or t-Bu



2 ; R=CH_2CO_2Et



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It is known that $Ba(OH)_2$ is useful as a template base to selectively synthesize cone-shaped trialkoxycalix[4]arenes from calix[4]arene-25,26,27,28-tetrol and alkyl halides.7) In alkylation with ethyl bromoacetate, however, this base causes the hydrolytic decomposition of the ester. Instead, we used CaH_2 (7.5 mmol) for the reaction of calix[4]arene-25,26,27,28-tetrol (2.5 mmol) and ethyl bromoacetate (7.5 mmol) in DMF (25 ml) at 60 °C for 24 h, expecting that Ca^{2+} is capable of maintaining the cone conformation as does Ba^{2+}.8) The product (calix[4]aryl triester) was recrystallized from chloroform-ethanol: yield 68%, mp 134-136 °C.9) This calix[4]aryl triester was treated with p-nitrophenylbenzenediazonium tetrafluoroborate in THF at 0 °C in the presence of pyridine.10) Compound **2** was isolated by preparative TLC (chloroform-ethyl acetate (3:1 v/v), silica gel): yield 13%, mp 93-95 °C.9) The ^1H NMR spectrum established that **2** adopts a cone conformation.9)

In calix[4]arene derivatives, the δ_{OH} in ^1H NMR shifts to lower magnetic field and the ν_{OH} in IR shifts to lower frequency when the OH groups form strong intramolecular hydrogen bonds.11) The δ_{OH} ($CDCl_3$, 25 °C) and the ν_{OH} (KBr) for **2** appeared at 7.53 ppm and 3400 cm^{-1} (broad), respectively, whereas those for **3** (noncyclic analogue) appeared at 5.14 ppm and 3500 cm^{-1} (sharp), respectively. The results show that the OH group in **2** forms the intramolecular hydrogen bond with the ester groups. This is also evidenced by the acid-base neutralization (Fig. 1): when 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) was added to the 1,2-dichloroethane solution, the dissociation of **3** was completed at [DBU]/[**3**] = 10 whereas the phenol group in **2** was fully dissociated at [DBU]/[**2**] = 10^4.

The metal selectivity of **2** was estimated by solid-liquid two-phase solvent extraction. The 1,2-dichloroethane solution (4 ml) containing **2** (5.0×10^{-5} mol dm^{-3}) and imidazole (Im: 0.050 mol dm^{-3}) was mixed with powdered MCl or $MClO_4$ (M = Li^+, Na^+, K^+, Cs^+, and $NMe_4{}^+$: 0.20 mmol). Imidazole was added to facilitate the metal-induced proton-dissociation (imidazole itself could not induce the dissociation of **2**). The mixture was stirred at 25 °C for 1 h. The equilibrium was attained in 10-20 min. The extractability (Ex%) was determined from the difference between the spectrum of **2** (no dissociation) and that in the presence of excess DBU (100% dissociation). The results are summarized in Table 1.

When chloride salts were used, **2** extracted Li^+ (48%) and a trace amount of Na^+ (3%) (Fig. 2). When perchlorate salts were used, **2** extracted Li^+ (98%) and Na^+ (56%). The results show that **2** displays the very high selectivity toward Li^+. Why does **2** show the Li^+ selectivity in contrast to the Na^+ selectivity of **1** ? It is presumed that the Na^+ selec-

Table 1. Extrability (%) of alkali metal and ammonium salts (MX)

M^+	$X^- = Cl^-$	$X^- = ClO_4^-$
Li^+	48	98
Na^+	3	56
K^+	0	0
Cs^+	0	0
Me_4N^+	0	0

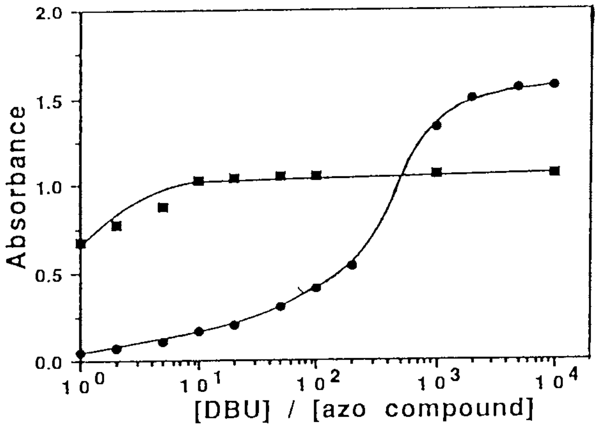

Fig. 1. Absorbance (640 nm for **2** (● : 5.00 x 10^{-5} mol dm^{-3}) and 584 nm for **3** (■ : 5.00 x 10^{-5} mol dm^{-3})) of the dissociated azophenolate unit plotted against the DBU concentration (25 °C, 1,2-dichloroethane).

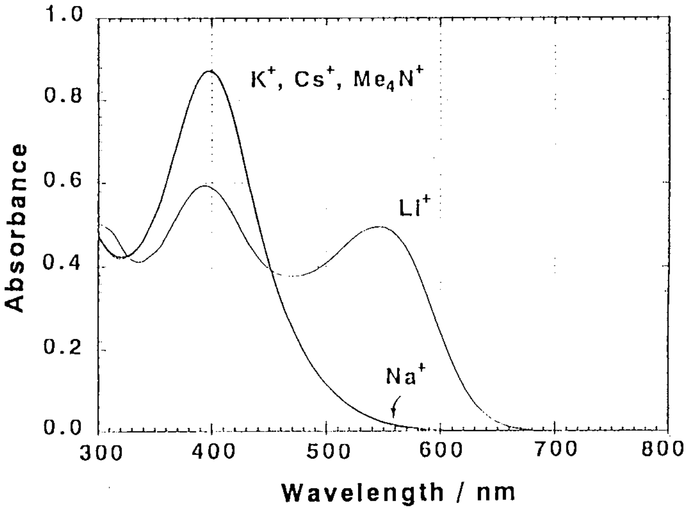

Fig. 2. Spectral change of **2** (5.00 x 10^{-5} mol dm^{-3}) in 1,2-dichloroethane in the presence of MCl (solid) at 25 °C.

tivity of **1** stems from the $Na^+ \cdots C=O$ interaction.[3-6] On the other hand, calix[4]arene itself and tetramethoxycalix[4]arene show the Li^+ selectivity, indicating that the cavity composed of four phenolic oxygens fits the size of Li^+.[12-14] We measured the ^1H NMR spectra of **2** (2.5 mmol dm^{-3}) in the presence of $LiClO_4$ or $NaClO_4$ (25 mmol dm^{-3}) (30 °C, $Cl_2CDCDCl_2$). The δ_H values for the OCH_2CO methylene protons in the presence of Na^+ (4.33 plus 4.66 (4H, d each, proximal to azophenol) and 4.46 (2H, s, distal to azophenol)) appeared at higher magnetic field than those in the absence of metal (4.52 plus 4.68 and 5.07), whereas those in the presence of

Li^+ (4.68 plus 4.85 and 4.91) appeared at lower magnetic field.15) This suggests that Li^+ is bound to **2** as a countercation of the azophenolate anion and interacts with the three phenolic oxygens.

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8)We later found that BaO is also useful as a template base: yield 63%.

9)The products were identified by IR and NMR spectral evidence and elemental analysis data. Compound **2**: mp 94-96 °C; in ^1H NMR ($CDCl_3$, 25 °C), the $ArCH_2Ar$ methylene protons appeared as two pairs of doublets (3.31 and 4.96 ppm for one pair (J = 13.4 Hz) and 3.48 and 4.44 ppm for another pair (J = 13.9 Hz)). This split pattern is in accord with a cone conformation.

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15)The OCH_2CO_2 protons appeared as three different peaks. This suggests that the rotation of the OCH_2CO_2 groups is slower than the NMR time-scale, which provides three inequivalent protons.

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