Calix[4]arene Having a Convergent Carboxylic Acid Function: Synthesis and Ion Binding Properties of a New Cs^+-selective Ionophore

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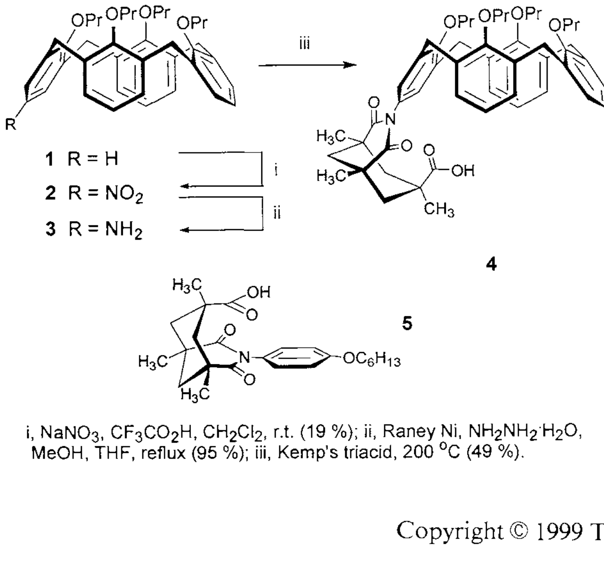
Calix[4]arene bearing a convergent carboxylic acid function employing the Kemp's triacid motif exhibited a pronounced selective ionophoric behavior toward Cs^+ over other alkali metal ions. The selectivities of calix[4]arene-acid for Cs^+ over Rb^+, K^+, and Na^+ ions assessed by competitive transport experiments were 7.9, 26, and 121, respectively.

The developments of cesium-specific ionophores are very important due to the potential applications for the nuclear waste treatment. Although a myriad of intriguing ionophores for the recognition of alkali metal cations have been developed during last decades, relatively little attentions have been paid for the cesium-selective ionophores.[1] Among many building blocks that have been studied for the synthesis of Cs^+-selective ionophores, calixarenes are particularly useful, and considerable interest has been focused into the use of calixarenes as a versatile platform for the construction of Cs^+-specific supramolecular systems.[2,3]

Recently, ingeniously designed supramolecular systems employing cation-π interaction have been widely investigated.[4] Calixarenes are again one of the most ideal motifs for the construction of such system due to their unique structural characteristics of electron rich cavities comprising of cyclic arrays of aromatic rings.[5,6] In this paper, we have prepared a new type of host system by combining the two well-known motifs of calix[4]arene and Kemp's triacid moieties which could provide handles for the molecular recognition of many interesting guest ions by enjoying both electrostatic and cation-π interactions.

Nitro derivative of calix[4]arene **2**[7] was prepared from the tetrapropyl ether **1** in cone conformation by the reaction with $NaNO_3/CF_3CO_2H$ (Scheme 1).[8] The reduction of **2** with Raney Ni and $NH_2NH_2{\cdot}H_2O$ smoothly afforded the amino derivative **3** in good yield.[9] The condensation of amine **3** with Kemp's triacid without solvent gave the desired calix[4]arene-acid **4** having a carboxylic acid function on the upper rim which can point toward the cavity of the calix[4]arene. The acid **5** was prepared as a reference compound for **4** from the 4-hexyloxyaniline.[10]

Scheme 1.



i, $NaNO_3$, CF_3CO_2H, CH_2Cl_2, r.t. (19 %); ii, Raney Ni, $NH_2NH_2{\cdot}H_2O$, MeOH, THF, reflux (95 %); iii, Kemp's triacid, 200 °C (49 %).

Table 1. Ionophoric properties as assessed by FAB-MS[a]

	Relative peak intensity of $[\text{ionophore} + \text{metal}]^+/[\text{ionophore} + H]^+$				
	Li^+	Na^+	K^+	Rb^+	Cs^+
1	0.31	0.09	0.29	0.71	1.44
4	4.17	0.32	0.79	4.39	32.0
5	22.9	0.55	0.17	0.22	1.64

[a] Under the competitive conditions with two equiv. each of metal chlorides in *m*-NBA.

The preliminary ion binding affinities of the ionophores toward alkali metal cations were assessed by the FAB mass spectrometry. Ionophores **1**, **4**, and **5** were treated with a mixture of alkali metal chlorides solution (each in 2 equiv. of ionophore) and the mass spectrum was obtained in *m*-nitrobenzyl alcohol (*m*-NBA) matrix. The calix[4]arene-acid **4** exhibited a high selectivity toward Cs^+ ion and a prominent peak of $[4 + Cs]^+$ at *m/z* of 962 was observed. Other peaks owing to the complex formation with the rest of alkali metal cations are also observed, however, with much reduced intensity at their respective *m/z* values for the complexes of $[4 + \text{metal}]^+$ (Table 1). The selectivity toward Cs^+ over Na^+, which is important for the development of Cs^+-selective ionophores, estimated from the relative binding affinities represented in Table 1 as the peak ratio of $[4 + \text{metal}]^+/[4 + H]^+$, was found to be 100.

As is already reported,[6] the propyl ether **1** itself exhibited a moderate selectivity toward Cs^+ under the present measurement conditions. One thing to note is that the acid **4** exhibited more intense peaks of $[4 + \text{metal}]^+$, while the propyl ether **1** showed a relatively intense peak at $[1 + H]^+$ ion instead of the $[1 + \text{metal}]^+$ peaks. The intensity of peak at $[1 + H]^+$ was at least 30 times larger than $[4 + H]^+$, which might suggest much stronger complex formation properties of **4** compared with the propyl ether **1**. Meanwhile, the reference compound **5** exhibited relatively high affinity toward Li^+ over other alkali metal cations. That is, all the other alkali metal ions except for Li^+ ion exhibited very weak peaks, which might be due to the strong electrostatic interaction between the Li^+ and the carboxylic acid moiety. The results suggest that the structural characteristics of **4** clearly enhanced selectivity and efficiency for the recognition of Cs^+ ions compared with **1** and **5** by ensuring the efficient interaction with the guest as postulated in Scheme 2.

The ionophoric properties of the resulting carboxylic acid

Table 2. Transport of alkali metal cations[a]

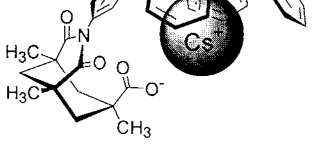
	Transport rate (x 10^{-6} mol h^{-1})					Selectivity (Cs^+/M^+)[b]		
	Li^+	Na^+	K^+	Rb^+	Cs^+	Na^+	K^+	Rb^+
1	~0	~0	~0	~0	~0	-[c]	-[c]	-[c]
4	4.1	1.3	6.0	19.9	157	121	26	7.9
5	13.4	1.9	5.3	10.7	35.0	18	6.6	3.3

[a] Source phase: mixture of alkali metal chlorides each in 0.1 M (5.0 mL, pH 9.0, Tris-HCl buffer). Membrane phase: 5.0 mM of ionophore in $CHCl_3$ (15 mL). Receiving phase: 0.1 M HCl (5 mL). [b]Ratio of transport rate values. [c]Can not be estimated.

derivative were further investigated by the competitive transport experiments. The transport through a chloroform liquid membrane using a standard U-tube apparatus (i.d. = 1.5 cm) from basic source phase (Tris-HCl buffer, pH 9.0) into acidic receiving phase (HCl, pH 1.0) was performed for 48 h at 25 °C. The transport rate was determined by measuring the ion concentrations in the receiving phase by means of the ion chromatography (Table 2). The transport results manifest that acid **4** exhibited a prominent selective ionophoric properties toward Cs^+ ion among the alkali metal cations, and the selectivity pattern decreases in sequence as follows: $Cs^+ > Rb^+ > K^+ > Li^+ > Na^+$. The selectivity of **4** for the discrimination of Cs^+ over Rb^+, K^+, and Na^+ ions are 7.9, 26, and 121, respectively. The parent propyl ether derivative **1** was also tested, but found to exhibit almost no transport efficiency toward any metal ions tested. On the other hand, the reference compound **5** showed moderate efficiency and selectivity pattern to **4**, however, the Cs^+-flux of **5** is much smaller than **4**. One more thing to note is that the selectivity in transport is greatly enhanced on going from reference compound **5** to acid **4**. For example, the selectivity of **4** in transport of Cs^+ over Na^+, among others, is enhanced about 7-fold compared with **5**. The experimental conditions for the transport, in fact, is not so appropriate for the accurate visualization of the cation-π interaction, because the strong electrostatic interaction of the Kemp's acid moiety is dominating the possible cation-π interaction in the present system. However, the results obtained imply that the selective Cs^+ binding and transport is definitely realized by the cooperation of the calix[4]arene cavity and the convergent carboxylic acid moiety in **4** both serving as efficient anchoring handles.

The structural characteristics of the ionophore **4** seem to be suitable for the recognition of Cs^+ ions. The molecular modeling studies examined by the Corey-Pauling-Koltun space filling model and HyperChem[11] package suggest that the carboxylic acid function of **4** in *endo* conformation can be positioned just above the calix[4]arene cavity as shown in Scheme 2. Upon complexation with calix[4]arene-acid, the Cs^+ or other guests having π-accepting ability can be situated in the very vicinity of the upper rim part of the calix[4]arene cavity in somewhat nesting mode, and possibly can enjoy the extra stabilization by interacting with maximum four-fold benzene rings.

Scheme 2.



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9 Selected data for **4**: mp 275-276 ℃; yield 49%; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 7.01 (d, 2H, J = 7.5 Hz), 6.85 (t, 1H, J = 7.4 Hz), 6.75 (br s, 2H), 6.32 (t, 2H, J = 7.5 Hz), 6.26 (d, 2H, J = 7.6 Hz), 6.19 (d, 2H, J = 7.5 Hz), 4.44 (d, 2H, J = 13.5 Hz), 4.42 (d, 2H, J = 13.2 Hz), 3.95 (t, 4H, J = 7.8 Hz), 3.72-3.66 (m, 4H), 3.14 (d, 2H, J = 13.5 Hz), 3.11 (d, 2H, J = 13.2 Hz), 2.83 (d, 2H, J = 14.1 Hz), 2.15 (d, 1H, J = 12.0 Hz), 1.99-1.81 (m, 8H), 1.47 (d, 1H, J = 13.2 Hz), 1.36 (s, 6H), 1.33 (s, 3H), 1.27 (d, 2H, J = 14.1 Hz), 1.07 (t, 6H, J = 7.4 Hz), 0.92–0.85 (m, 6H); FAB-MS (*m*-NBA) *m/z* $[M+H]^+$ = 830; Anal. Calcd for $C_{52}H_{63}NO_8{\cdot}H_2O$: C, 73.64; H, 7.73; N, 1.65. Found: C, 73.50; H, 7.42; N, 1.82. For **5**: mp 208-210 ℃; yield 84%; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 6.98 (br d, 2H, J = 9.0 Hz), 6.87 (d, 2H, J = 9.3 Hz), 3.92 (t, 2H, J = 6.6 Hz), 2.80 (d, 2H, J = 13.8 Hz), 2.11 (d, 1H, J = 13.2 Hz), 1.76 (m, 2H, J = 6.3 Hz), 1.48-1.28 (m, 6H), 1.47 (d, 1H, J = 13.5 Hz), 1.33 (s, 6H), 1.31 (s, 3H), 1.26 (d, 2H, J = 14.7 Hz), 0.90 (t, 3H, J = 6.9 Hz); FAB-MS (*m*-NBA) *m/z* $[M+H]^+$ = 416; Anal. Calcd for $C_{24}H_{33}NO_5$: C, 69.37; H, 8.00; N, 3.37. Found: C, 69.66; H, 8.13; N, 3.34.

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