Ionophoric Properties of a Doubly-Bridged Calix[8]arene Bearing a Eight-Oxygens Converging Cavity

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A novel globular molecule was synthesized by doubly-bridging calix[8]arene at 1,5- and 3,7-phenol units. The structure is very unique because of its high molecular symmetry and eight oxygens convergently integrated in a cavity. Extraction and ^{1}H NMR spectroscopic studies established that this cavity shows the high Cs$^+$ affinity as well as the high Cs$^+$ / Na$^+$ selectivity.

It has been demonstrated that calix[n]arenes act versatile platforms for designing supramolecular systems showing high ion selectivity, energy-transfer luminescence, molecular inclusion, *etc.*[1] Among them, however, calix[8]arenes have been left less exploited because of its flexibility inherent to the large ring system,[1,2] complexity in stoichiometry in molecular inclusion,[1,3] and difficulty in regioselective modification of eight OH groups.[1,4-6] Neri *et al.*[4] reported that the reactions of *p-t*-butylcalix[8]arene with bis(bromomethyl) reagents, which are useful as a protecting group for calix[6]arenes,[7] afford only polymeric materials even under high-dilution conditions. In contrast, we recently found that when *o*-bis (bromomethyl) benzene is used as a bridging reagent, a 1,5-singly-bridged calix[8]arene **1a** and a 1,5-3,7-doubly-bridged calix[8]arene **2a** are produced as major products.[6] The structure of compound **2a** is very intriguing: it has D_{2d} symmetry and eight phenolic oxygens are converged into the cavity, four of them (1,3,5,7-bridged oxygens) adopting a tetrahedral arrangement and residual 2,4,6,8-oxygens (unmodified OH's) adopting a square planar arrangement (Figure 1). We were thus prompted to apply this novel globular molecule as a metal cation receptor.

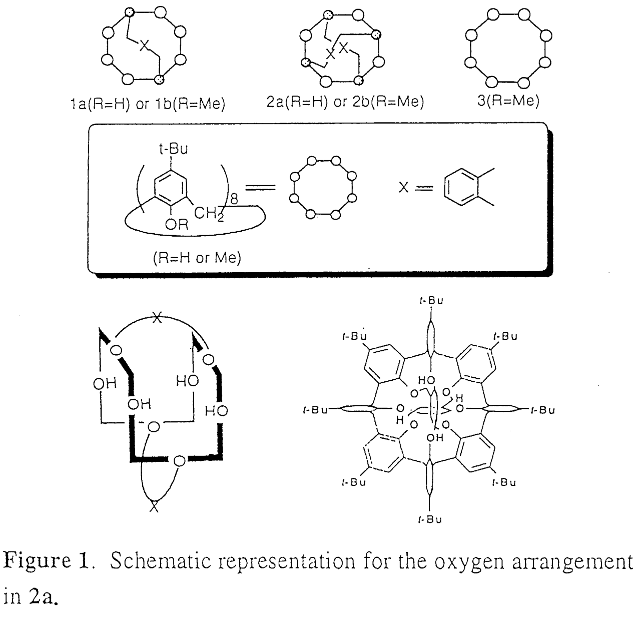

Figure 1. Schematic representation for the oxygen arrangement in 2a.

Compounds **1b** (mp 198 ℃) and **2b** (mp (dec) > 310 ℃) were synthesized from **1a** and **2a**,[6] respectively, by the reaction with MeI in acetone in the presence of Cs_2CO_3 and identified by IR and ^{1}H NMR spectral evidence and elemental analyses. Compounds **1b** and **3**[8] were used as reference compounds for **2b**.

Table 1. Extraction of alkali picrates[a]

Calix[8]arene	Ex % M$^+$ = Na$^+$	K$^+$	Rb$^+$	Cs$^+$
1b	< 1	< 1	< 1	< 1
2b	< 1	2	7	22
3	< 1	< 1	< 1	< 1

[a] 25 °C, organic phase (5.0 ml) : [1b, 2b, or 3] = 5.00 × 10^{-4} mol dm^{-3}, aqueous phase (5.0 ml) : [alkali picrate] = 1.00 × 10^{-4} mol dm^{-3}, [MOH] = 1.00 × 10^{-4} mol dm^{-3}. The mixture was shaked for 12 h.

To obtain a qualitative insight into the metal selectivity of **2b** we carried out two-phase solvent-extraction of alkali picrates between water and dichloromethane. The results (Table 1) indicate that **2b** possesses the highest affinity toward Cs$^+$ and next toward Rb$^+$. On the other hand, extraction of Na$^+$ could not be detected (Ex % < 1). The inner cavity size of **2b** is estimated to be *ca.* 3 Å and the molecular structure is considerably rigidified by double bridging. These steric factors are the origin of high Cs$^+$ selectivity. In contrast, neither **2a** nor **3** gave the measurable Ex % value. The difference clearly shows that "preorganization" of eight phenolic oxygens is indispensable to construct an effective ionophoric cavity.

More quantitative data were obtained from ^{1}H NMR spectroscopy. In THF-d_8 : $CDCl_3$ = 5 : 1 v/v at 30 ℃ signals for the **2b**·M$^+$ complexes (M$^+$ = K$^+$, Rb$^+$, and Cs$^+$: added as their tetraphenylborate salts) appeared separately from those of free **2b** (Figure 2). The association constants (K_{ass}) were determined directly by comparing the integral intensities of these peaks : K_{ass} (dm^3 mol^{-1}) = 150 for K$^+$, 720 for Rb$^+$, and 5200 for Cs$^+$. On the other hand, the ^{1}H NMR spectrum of **2b** was scarcely affected by Na$^+$. Similarly, the ^{1}H NMR spectrum of the **2b**·Cs$^+$ was not affected by an excess (100-fold) amount of other alkali metal cations (Na$^+$, K$^+$, and Rb$^+$), indicating that these metal cations are incapable of substituting Cs$^+$ bound to the **2b** cavity. These results, together with the extraction data, establish the high Cs$^+$ affinity and the high Cs$^+$ / Na$^+$ selectivity of **2b**.

Careful examination of ^{1}H NMR spectra of **2b** and its metal cation complexes disclosed several intriguing dynamics of this molecule. At 30 ℃, the methylene protons of the xylenyl cap in free **2b** appeared as a singlet resonance (5.44 ppm) but those of the **2b**·Cs$^+$ became a pair of doublets (5.27 and 5.17 ppm). Accordingly, a pair of doublets for the $ArCH_2Ar$ methylene protons (3.23 and 4.48 ppm) changed into two pairs of doublets (3.17, 3.65, 3.96, and 4.44 ppm; the peak at 3.65 ppm was found by 2D ^{1}H NMR) in the presence of Cs$^+$. Energy-minimization of **2b** with MM3 (92) predicated that the

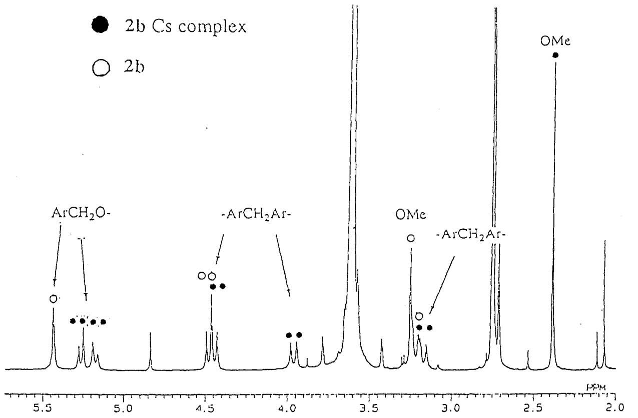

Figure 2. Partial ^{1}H NMR spectrum of 2b (1.00×10^{-3} mol dm^{-3}) in the presence of $Ph_4B^-Cs^+$ (1.00×10^{-3} mol dm^{-3}) : THF-d_8 : $CDCl_3$ = 5 : 1 v/v, 30 °C.

xylenyl unit adopts a zigzag structure composed of (OCH_2)-phenyl-(CH_2O), which results in inequivalency between two methylene protons.[6] This bridge can enjoy a twisting motion: in free **2b** this motion should be faster than the NMR time-scale whereas bound Cs^+ should suppress this motion below the NMR time-scale. The **2b**$\cdot Rb^+$ also gave a AB pattern for the xylenyl CH_2 protons, but in the **2b**$\cdot K^+$ complex it became a singlet resonance. The results are explained as such that the stronger the interaction with the cavity, the slower the twisting motion becomes.

We considered that the rate of the metal association-dissociation equilibria might be estimated from the coalescence temperature between free **2b** and **2b**$\cdot M^+$ complexes. However, such a peak coalescence for $M^+ = K^+$, Rb^+, and Cs^+ did not take place even at 130 ℃. The results indicate that the metal exchange with the capsule-like, rigid cavity is extermely slow.

We also determined the K_{ass} for ammonium cations (added as their tetraphenylborate salts) from the ^{1}H NMR spectra in THF-d_8 : $CDCl_3$ = 5 : 1 v/v (or CD_2Cl_2) at 30 ℃. The K_{ass} values obtained from the ^{1}H NMR spectra were 1200 (or 15000) dm^3 mol^{-1} for NH_4^+ and *ca.* 10 (or 150) dm^3 mol^{-1} for $MeNH_3^+$.[9] It may be strange that NH_4^+ the ion size of which is usually comparable with that of K^+, is strongly bound to the **2b** cavity. Conceivably, the complex is stabilized by some specific hydrogen bonding interactions with the cavity oxygens. In contrast, the spectral change was not induced by the addition of $EtNH_3^+$. The results indicate that this cavity shows the strict size selectivity for the alkyl substituent.

In conclusion, the present paper indicated that **2b** has the high Cs^+ affinity as well as the high Cs^+ / Na^+ selectivity. Recently, the exploitation of Cs^+-selective ionophores has become an active area of endeavor in relation to the treatment of nuclear wastes. In fact, an European group has developed an excellent Cs^+-selective ionophore from calix[4]arene.[10] We believe that **2b** has the latent abilities comparable with their compounds. Further studies are currently continued in this laboratory.

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9 Since the ionophoric cavity is located in the center of this globular molecule, the K_{ass} values are largely affected by the ammonium guest structure.

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