On the Origin of High Ionophoricity of 1,3-Alternate Calix[4]arenes: π-Donor Participation in Complexation of Cations and Evidence for Metal-Tunneling through the Calix[4]arene Cavity

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Abstract: Nine conformationally-immobilized calix[4]arenes (including two doubly-bridged 1,3-alternate calix[4]arenes) and several reference calix[4]arenes with other conformations were synthesized. Two-phase solvent-extraction of and determination of association constants by ^{1}H NMR spectroscopy for alkali metal cations established that, surprisingly, 1,3-alternate and partial-cone conformers show an ion affinity higher than the corresponding cone conformers. Detailed examination with ^{1}H NMR spectroscopy presented unambiguous evidence that in the 1,3-alternate conformers the metal cation is bound asymmetrically to one of two metal-binding sites composed of two phenolic oxygens and two benzene rings, whereas in the partial-cone conformers the metal cation is bound to the upper rim composed of a phenolic oxygen in the inverted phenyl unit and two benzene rings in the proximal phenyl units. These metal-binding modes were rationalized in terms of the "cation–π interaction". The contribution of the cation–π interaction was further confirmed by the finding that these conformers all show high Ag^{+} affinity without exception. The X-ray crystallographic study of the partial-cone-2·Ag^{+} complex established that Ag^{+} is bound to a phenolic oxygen in the inverted phenyl unit and two benzene rings in the proximal phenyl units. Dynamic ^{1}H NMR spectroscopy at the low-temperature region showed that Ag^{+} alternates intramolecularly between the two binding sites through a π-basic hole of 1,3-alternate calix[4]arenes. To the best of our knowledge, this is the first example for Ag^{+}-tunneling across an aromatic cavity and has important implications with regard to the metal cation–π interaction expected for metal transport through ion channels, metal inclusion in fullerenes, intercalation of metal cations into graphites, etc.

Introduction

Selective recognition of alkali metal cations is one of the central research interests in biological systems. This is now possible by the use of either naturally-occurring ionophores or synthetic, polyether-type receptors, e.g., crown ethers.[1–4] Over the last decade, it has been demonstrated that ionophoric cavities constructed from calix[4]arenes show Na^{+} selectivity much higher than that observed for crown ethers.[5–10] The high Na^{+} selectivity is ascribed to the size of the ionophoric cavity fit to Na^{+} and to the rigid calix[4]arene skeleton serving as a platform. Also, it became possible to freeze the rotation of phenyl units by introducing bulky substituents into OH groups[11a,12–18] or by cross-

linking two phenyl units.[19–22] These advances have enabled us to selectively synthesize and isolate four possible calix[4]arene conformers: cone, partial-cone, 1,2-alternate, and 1,3-alternate.[11] By using these synthetic methods, one can design new ionophoric conformers of calix[4]arene other than a cone. For example, certain rigidified calix[4]arenes such as calixcrowns and calix-spherands can form kinetically stable complexes with alkali metal cations.[19b] It is also known for conformationally-immobilized 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrakis((ethoxycarbonyl)-methoxy)calix[4]arenes that one can realize Na^{+} selectivity with the cone conformer, and conversely K^{+} selectivity with the partial-cone and the 1,3-alternate conformer.[14] These results demonstrate that conformationally-rigidified calix[4]arenes are exceptionally
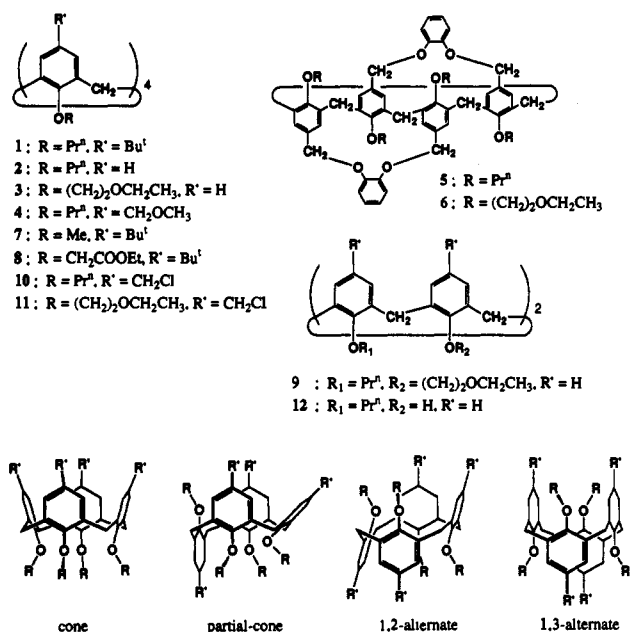
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High Ionophoricity of 1,3-Alternate Calix[4]arenes

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useful in the design of ionophoric cavities with the desired size and preorganization of ligand groups.

Among four possible conformers, the cone conformer has been extensively studied in the design of such ionophoric cavities because one can arrange ligand groups on the same side of the calix[4]-arene platform.[5-11] We noticed, however, that the 1,3-alternate conformer possesses several interesting structural characteristics which the other three conformers do not possess: for example, (i) two independent ionophoric sites exist at both edges of the calix[4]arene cavity,[14] (ii) each ionophoric site is composed of two phenolic oxygens and two benzene rings, and (iii) the two ionophoric sites are connected by a "hole" surrounded by benzene rings.[23-27] Careful examination of X-ray crystallographic pictures of 1,3-alternate conformers reveals that the size of the ionophoric sites is comparable with the size of K+ (2.7 Å).[18,23-25] This suggests that K+ complexes with 1,3-alternate conformers may be stabilized not only by the interaction with two phenolic oxygens but also by π-donor participation of two benzene rings.[28] With these things in mind, we synthesized nine different 1,3-alternate conformers plus several other conformers as reference compounds. We have found that these 1,3-alternate conformers show an unusually high affinity for K+ and Ag+, which supports the π-donor participation in the metal-binding.[29]

1 : R = Prⁿ, R' = Buᵗ
2 : R = Prⁿ, R' = H
3 : R = (CH₂)₂OCH₂CH₃, R' = H
4 : R = Prⁿ, R' = CH₂OCH₃
7 : R = Me, R' = Buᵗ
8 : R = CH₂COOEt, R' = Buᵗ
10 : R = Prⁿ, R' = CH₂Cl
11 : R = (CH₂)₂OCH₂CH₃, R' = CH₂Cl

5 : R = Prⁿ
6 : R = (CH₂)₂OCH₂CH₃

9 : R₁ = Prⁿ, R₂ = (CH₂)₂OCH₂CH₃, R' = H
12 : R₁ = Prⁿ, R₂ = H, R' = H

cone   partial-cone   1,2-alternate   1,3-alternate

Results and Discussion

Two-Phase Solvent Extraction. It has been established that neutral ligands derived from calix[4]arenes show affinity with alkali metal cations, and in particular, calix[4]aryl acetates and acetamides with a cone conformation show remarkably high Na+

Table 1. Percent Extraction of Alkali Metal Picrates (MPic) at 25 °C[a]

calix[4]arene	Ex%				
	M+ = Li+	Na+	K+	Cs+	Ag+
cone-1	0.7	0.8 (0.0)	1.9 (0.0)	5.2	−(5.8)
partial-cone-1	0.0	0.8 (0.0)	12.1 (0.0)	11.4	−(22.4)
1,2-alternate-1	0.0	2.6 (0.0)	0.4 (1.6)	1.2	−(23.0)
1,3-alternate-1	4.3	1.6 (0.2)	16.2 (1.0)	11.8	−(23.0)
cone-2	1.6	3.9 (0.0)	3.9 (1.1)	7.7	−(7.6)
1,3-alternate-2	5.3	8.8 (0.0)	56.8 (4.3)	44.7	−(34.8)
cone-3	0.0	9.0 (0.0)	3.5 (0.9)	0.0	−(4.0)
1,3-alternate-3	4.8	0.0 (0.0)	38.6 (16.6)	41.1	−(66.7)
1,3-alternate-4	1.1	0.0 (0.0)	88.8 (10.2)	95.7	−(31.9)
1,3-alternate-5	1.9	1.7 (0.0)	100.0 (21.3)	27.1	−(61.7)
1,3-alternate-6	3.0	4.5 (0.0)	100.0 (30.2)	41.5	−(89.6)

[a] Method A: Organic phase (5 mL of CH_2Cl_2) contains calix[4]arene (2.50 mM); aqueous phase (5 mL) contains MPic (0.25 mM), MOH (0.10 M), and MCl (0.50 M). The values in the parentheses (method B) are set for Ag+ extraction: aqueous phase (5 mL) contains picric acid (0.238 mM) and MNO_3 (0.01 M) at pH 4.7. The two-phase mixture was shaken for 12 h at 25 °C, and Ex% values were determined spectrophotometrically.

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selectivity.[5-11] Although the metal selectivity of ionophoric calix-[4]arenes can be changed by the conformation,[13,14] the Na+ affinity observed for cone conformers is always the highest amongst all four possible conformers.[5-11,13,14] This has been rationalized in terms of a steric characteristic of cone conformers that four ligand groups are preorganized in the same side of the calix[4]arene cavity so that they can encapsulate Na+. We also believed for a long period that the three other conformers would be useless as ionophores with high selectivity for alkali metal cations. We found quite accidentally, however, that 1,3-alternate conformers show unusually high affinity with K+.

Solvent extraction of alkali metal cations with picrate ion into dichloromethane was performed at 25 °C (method A: see a footnote to Table 1). The results are summarized in Table 1. Contrary to our expectation,[30] cone-1 and cone-2 scarcely extracted Na+ (Ex% 0.8–3.9%). Cone-3, which has an ionophoric cavity composed of four $EtOCH_2CH_2O$ groups, showed significant Na+ affinity, but the Ex% (9.0%) was relatively low. On the other hand, 1,3-alternate-1 and 1,3-alternate-2 showed moderately high Ex% for K+ and Cs+ (11.8–56.8%). Since Ex% values for 1,3-alternate-2 are higher than those for 1,3-alternate-1, *t*-Bu groups at the para position suppress the metal-binding ability of 1,3-alternate conformers. Partial-cone-1 showed the intermediary extraction ability between cone-1 and 1,3-alternate-1: it has a low but significant affinity with K+ and Cs+ (12.1% and 11.4%, respectively). On the other hand, 1,2-alternate-1 did not show any significant Ex% for alkali metal cations.

To improve the extraction ability of 1,3-alternate conformers, we synthesized 1,3-alternate-5 and 1,3-alternate-6 in which two pairs of distal phenyl units are cross-linked with catechol.[31] As recorded in Table 1, 1,3-alternate-4 (a non-cross-linked reference compound for 5 and 6) showed the metal affinity for both K+ and Cs+, whereas 1,3-alternate-5 and 1,3-alternate-6 showed very high Ex% and selectivity only for K+. The difference is attributed to rigidification of the ionophoric cavity by the cross-link.

One can easily image how cone calix[4]arenes interact with alkali metal cations: the four (or eight in the case of calix[4]aryl acetates and acetamides) oxygens arranged in the same side of the cavity encapsulate a metal cation.[5-11,32] In fact, this idea is supported by NMR spectral studies and X-ray crystallographic studies.[5-11,32] Then, how do 1,3-alternate calix[4]arenes interact

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with metal cations such as K^+ and Cs^+? Previously, X-ray crystallographic studies[23–25] and computational studies[26,27] have established that the four phenyl units in 1,3-alternate calix[4]-arenes are more or less parallel to each other. In this structure, four oxygens in 1,3-alternate calix[4]arenes cannot interact with one metal cation but rather provide two metal-binding sites, each of which consists of two distal, phenolic oxygens. It then becomes difficult to explain why two-oxygen binding sites in 1,3-alternate calix[4]arenes show an Ex% higher than a four-oxygen binding site in cone calix[4]arenes. We considered that this contradiction could be solved by taking the participation of the "cation–π interaction"[28,29] into account. The past investigations established that π-base receptors which feature the cation–π interactions always display a high affinity for Ag^+.[28,29] We thus estimated the extraction ability of calix[4]arene conformers for Ag^+. For extraction of alkali metal cations we used an aqueous phase containing alkali picrate (0.25 mM), MOH (0.10 M), and MCl (0.50 M) (method A). However, these extraction conditions were not applicable to Ag^+ extraction because the metal concentration is too high (Ex% values higher than 90% are always obtained when such a high Ag^+ concentration is used) and Ag^+ precipitates in the presence of Cl^-. We thus used an aqueous solution containing $AgNO_3$ (0.01 M) and picric acid (0.238 mM), which gave moderate Ex% values (method B). To compare extraction properties of Ag^+ with those of alkali metal cations under the same conditions, we repeated extraction of Na^+ and K^+ by method B. The results are shown in parentheses in Table 1. The cone conformers (including cone-3, which showed an affinity for Na^+) scarcely extracted Ag^+ (4.0–7.6%), indicating that the oxygenic cavity is inefficient for Ag^+-binding. In contrast, the 1,3-alternate conformers extracted Ag^+ to a level of 23.0–89.6%, and in particular, 1,3-alternate-3, 1,3-alternate-5, and 1,3-alternate-6 gave high Ex% values. Also, it is important to mention that not only the 1,3-alternate conformers but also partial-cone-1 and 1,2-alternate-1 can extract Ag^+, their Ex% values (22.4% and 23.0%, respectively) being comparable with that of 1,3-alternate-1 (23.0%).

The foregoing extraction data consistently support the view that the cation–π interaction participates in the binding of K^+, Cs^+, and Ag^+ in partial-cone, 1,2-alternate, and 1,3-alternate conformers.[33]

Association Constants. As described later, we measured ^{1}H NMR spectra of several metal complexes to specify the metal-binding site. When signals for metal complexes appear separately from those for free calix[4]arenes, one can directly estimate the association constants (K_{ass}). It is expected that such a peak separation occurs at low temperature. The measurement temperature was thus set at –50 °C. The K_{ass} values for 1:1 complexes determined from the peak-separated ^{1}H NMR are summarized in Table 2.

It is seen from Table 2 that, in contrast to the significant Li^+ and Na^+ affinity of 7, cone-2 does not show any perceptible affinity toward these metal cations. It is known that the conformation of 7 is not immobilized but changes to cone when it binds Li^+ and Na^+.[30] We consider, therefore, that the disappearance of the metal affinity in cone-2 is attributed to the enhanced steric crowding of propyl groups and the increased lipophilicity around the metal-binding site which should be unfavorable to the metal-binding. On the other hand, 1,3-alternate-2, -3, and -5 possess log K_{ass} = 4.3–5.5 for K^+ and 3.7–6.0 for Ag^+. These values compare favorably with those for crown ethers and cryptands,[1–4] indicating that the cation–π interaction plays an important role in enhancing the K_{ass} values. Also, we could determine the K_{ass} for the partial-cone-2-Ag^+ system. The value (log K_{ass} = 3.7) is smaller than that for the 1,3-alternate-2-Ag^+ system. This

(33) In the 18th International Symposium on Macrocyclic Chemistry (Twente, 1993, June–July) R. Ungaro also proposed the participation of the cation–π interaction in the Cs^+-binding to calixcrowns.

Table 2. Association Constants (K_{ass}) of Alkali and Silver Metal Cations[a]

calix[4]arene	log K_{ass}			
	$M^+ = Li^+$	Na^+	K^+	Ag^+
cone-2	<1[b]	<1[b]	<1[b]	c
partial-cone-2	<1[b]	<1[b]	c	3.7
1,2-alternate-2	<1[b]	<1[b]	<1[b]	c
1,3-alternate-2	<1[b]	<1[b]	4.7	4.3
1,3-alternate-3	<1[b]	<1[b]	5.5	6.0
1,3-alternate-5	<1[b]	<1[b]	4.3	3.7
7[d]	2.2	3.0	2.6	

[a] –50 °C, $CDCl_3:CD_3OD$ = 4:1 v/v, [calix[4]arene] = [MX] = 1.00 × 10⁻³ M, where X^- = ClO_4^- for Li^+ and Na^+, Pic^- for K^+, and $CF_3SO_3^-$ for Ag^+. These counteranions were chosen to enhance the solubility. [b] The chemical shift scarcely changed. Judging from the sensitivity of ^{1}H NMR spectroscopy, the K_{ass} is expected to be log K_{ass} < 1. [c] The association constant could not be determined because of the line broadening. [d] Cited from the following: Iwamoto, K.; Ikeda, A.; Araki, K.; Shinkai, S. *Tetrahedron* **1993**, *49*, 9937.

implies that 1,3-alternate conformers provide the most well-preorganized cavity for Ag^+-binding.

Specification of the Binding Site by NMR Spectroscopy. To specify the metal-binding site, we measured the ^{1}H NMR spectra (400 MHz) of 2-metal complexes for which significant Ex% values were observed. The temperature was set at –50 °C to avoid peak broadening arising from the complexation–decomplexation reaction, and 20 vol % of CD_3OD was mixed with $CDCl_3$ to dissolve the metal salts. The results are summarized in Figure 1.

In cone-2 the chemical shift was not affected by the addition of alkali metal cations. On the other hand, the three other conformers showed interesting changes in the chemical shift which reflect the structural characteristics of each conformer. Examination of Figure 1 reveals that a particularly large downfield shift is observed for 1,3-alternate-2 complexes with K^+ and Ag^+. In the 1,3-alternate-2-K^+ system the signals for free 1,3-alternate-2 and those for the complex appeared separately, indicating that the rate of the complexation–decomplexation reaction is slower than the NMR time scale at –50 °C. In the illustration of 1,3-alternate-2 (Figure 1) K^+ should be bound to the upper side because the $\Delta\delta_H$ for the OCH_2 protons (+0.27 ppm) on the upper side are much greater than that for the OCH_2 protons (+0.19 ppm) on the lower side. Thus, one can consider that the downfield shift of the aromatic meta and para protons in the lower side (+0.11 and +0.15 ppm, respectively) is due to the inductive effect arising from the $O\cdots K^+$ interaction. Then, why does the chemical shift for the propyl and aromatic protons in the inverted phenyl units (see Figure 1) move to lower magnetic field? The oxygen atoms in these phenyl units do not interact with K^+. The result is explicable only by the "interaction" of K^+ with the benzene rings: that is, K^+ is trapped in a cavity composed of two phenolic oxygens and two π-basic benzene rings, by both metal–oxygen electrostatic interactions and cation–π interactions. On the basis of these results we propose that K^+ is bound to 1,3-alternate-2 as in Figure 2A through the interaction with two phenolic oxygens and two benzene rings.

In the 1,3-alternate-2-Ag^+ system the signals for free 1,3-alternate-2 and those for the complex appeared separately, but the signals for the propyl and aromatic protons in the upper side and in the lower side did not appear separately. It is therefore difficult to specify the Ag^+-binding site from the ^{1}H NMR spectra at –50 °C. It is seen from Figure 1, however, that the large downfield shift (+0.42 to +0.47 ppm for OCH_2CH_2 and +0.15 to +0.16 ppm for ArH) is induced by Ag^+-binding. The results indicate that Ag^+ is strongly bound to the cavity composed of two phenolic oxygens and two π-basic benzenes. In the cyclophane·Ag^+ complexes (e.g., π-prismands and deltaphanes) it is known that Ag^+ is not bound onto the center of the benzene ring but onto the edge of the π-basic cavity, suggesting an interaction with specific C=C double bonds.[28d,e,f] In the 1,3-alternate-2·Ag^+
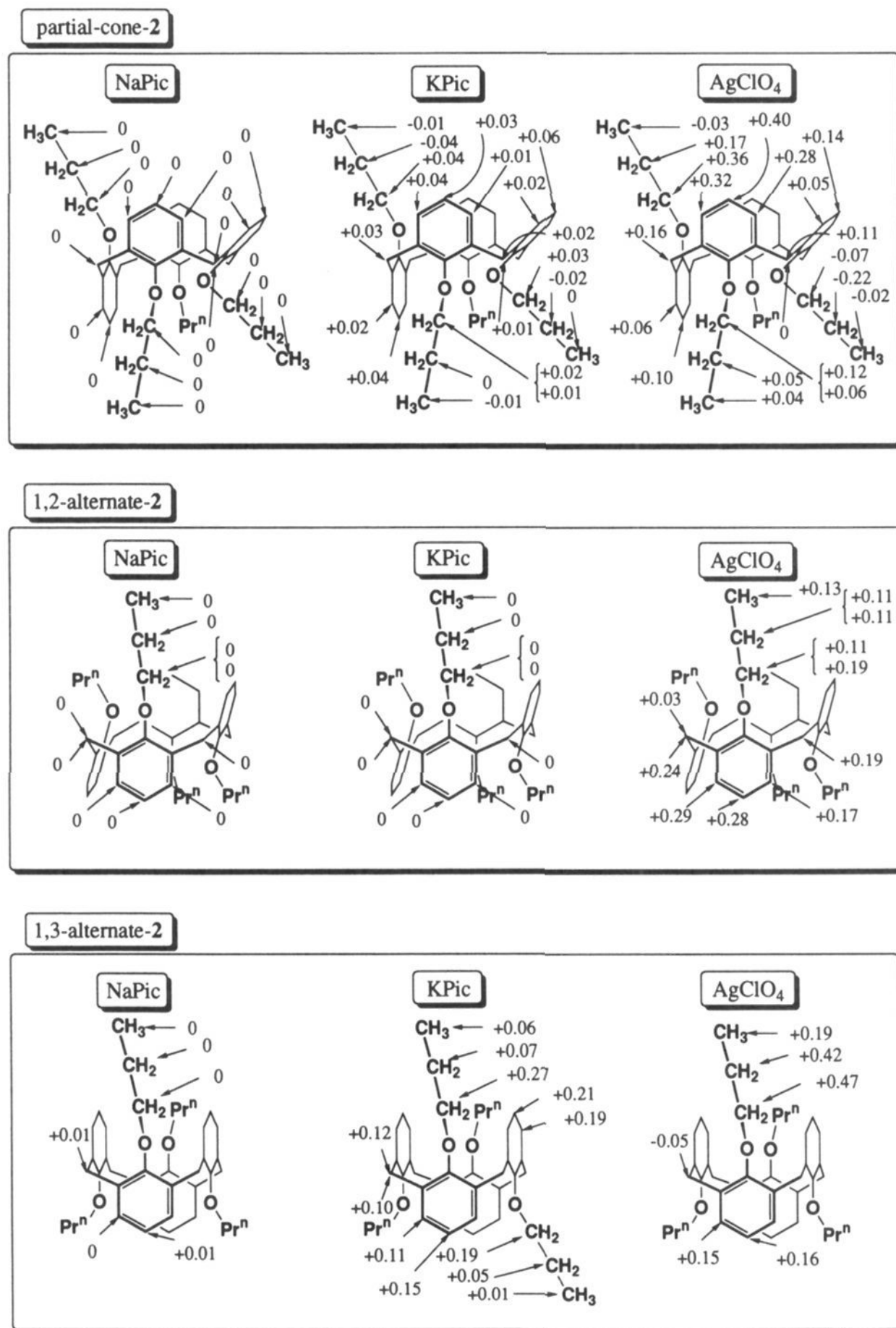
Figure 1. Changes in the ¹H NMR chemical shift induced by added metal cations: –50 °C, CDCl₃:CD₃OD = 4:1 v/v, [calix[4]arene] = [MPic] = 5.0 × 10⁻⁴ M, [AgClO₄] = 5.0 × 10⁻³ M. A plus sign (+) denotes a shift to lower magnetic field, whereas a minus sign (–) denotes a shift to higher magnetic field.
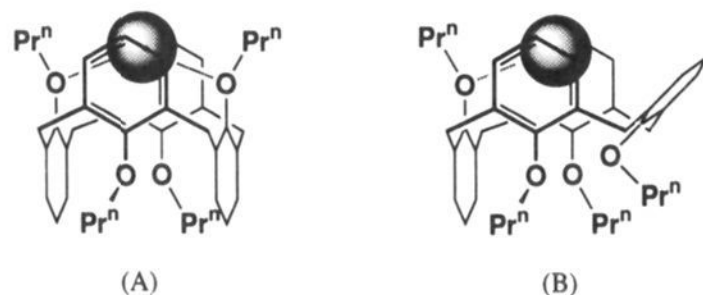
Figure 2. Binding modes of 1,3-alternate-2 and K⁺ (A) and partial-cone-2 and Ag⁺ (B).

complex the candidate C=C double bonds are the meta–para C=C double bonds.

In the partial-cone-2–Ag⁺ system the signals for free partial-cone-2 appeared separately from those for the complex. Examination of the chemical shift change suggests that Ag⁺ should

be bound to the upper rim of the cavity, which is composed of one phenolic oxygen and three benzene rings, because the large downfield shift was observed only for protons present around this cavity (Figure 1). The magnitude of the shift indicates that a phenolic oxygen in an inverted phenyl unit and two benzene rings proximal to the inverted phenyl unit mainly contribute to the Ag⁺-binding (as in Figure 2B). These spectral data suggest that the cation–π interaction is also operative in the partial-cone-2·Ag⁺ complex. On the other hand, the chemical shift change induced by addition of K⁺ was relatively small and the signals for the K⁺ complex did not separate from those for free partial-cone-2. Thus, we could not specify the K⁺-binding site. In 1,2-alternate-2 a significant downfield shift was observed only for the Ag⁺ complex. However, the signals for the propyl and aromatic protons on the upper side and the lower side did not
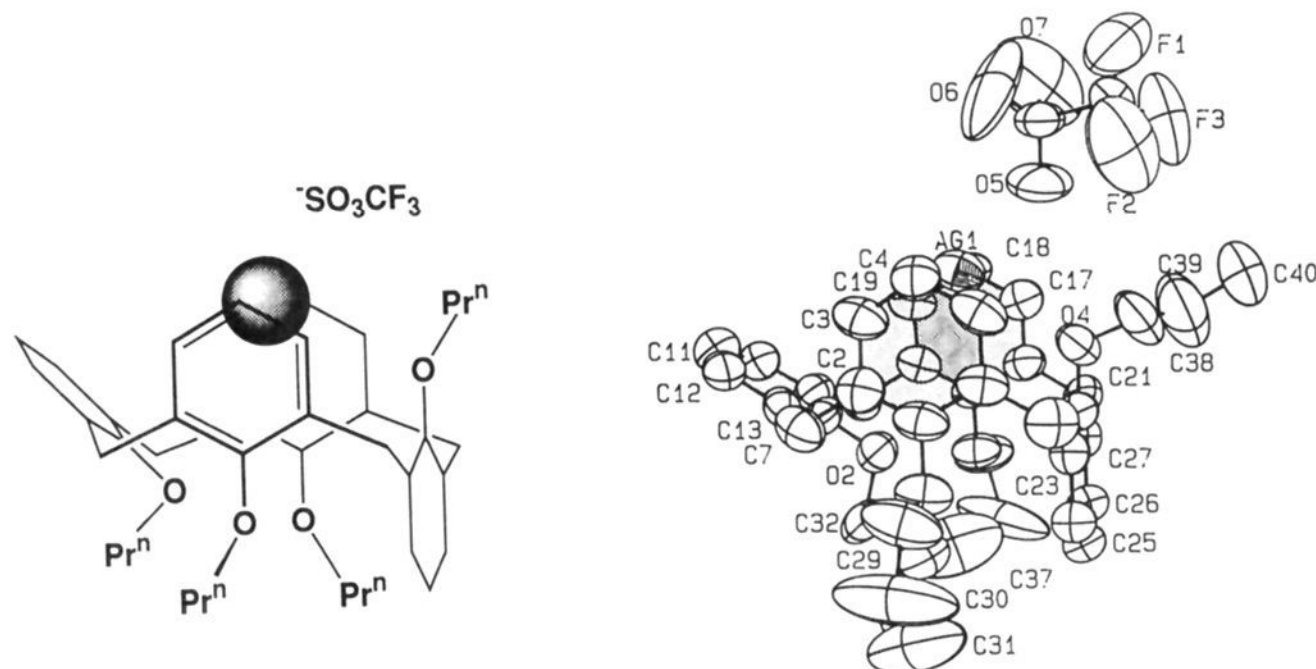
Figure 3. X-ray structure of the partial-cone-2·AgCF₃SO₃ complex.

appear separately. The large downfield shift observed for meta and para protons (+0.17 to +0.29 ppm) suggests that Ag⁺ is trapped in a cavity composed of two proximal phenolic oxygens and two proximal benzene rings.

X-ray Crystallographic Studies. In certain Ag⁺ complexes with π-prismands and deltaphanes unequivocal evidence for the π-donor participation was obtained from the X-ray crystallographic studies.[28d,e,f] The distance from Ag⁺ to the nearest carbon atom was estimated to be 2.4–2.7 Å.[28d,e,f] These values are shorter than the sum of the ion radius of Ag⁺ plus the half thickness of the π-electron cloud of the benzene ring (2.86 Å). The findings clearly substantiate the participation of the Ag⁺–π interaction in these systems.

In a calix[*n*]arene system the study of the cation–π interaction has been very limited. Harrowfield et al.[34] reported that in the crystal of mono cesium salt of 5,11,17,23-tetra-*tert*-butylcalix-[4]arene-25,26,27,28-tetrol Cs⁺ is included within the cup formed by four benzene rings, but this system is rather complicated because the calix[4]arene is a mono-OH-dissociated anionic form for which not only the cation–π interaction but also the electrostatic interaction is expected as a driving-force for inclusion. It was also reported that trimethylammonium ions are included in the cavities provided by calix[*n*]arenes, but among the calix-[4]arene conformers only cone conformers are capable of binding these trimethylammonium ions.[33,35–38] To the best of our knowledge, unequivocal X-ray evidence for the Ag⁺–π interaction in calix[*n*]arene complexes has never been reported. We attempted recrystallization of the 1,3-alternate-2·K⁺ and 1,3-alternate-2·Ag⁺ complexes, but a suitable single crystal for X-ray analysis could not be isolated. Instead, we succeeded in the crystallization of the partial-cone-2·AgCF₃SO₃ complex from acetone (for the crystal data see the Experimental Section). The X-ray structure is illustrated in Figure 3. As predicted from the ¹H NMR spectral data, Ag⁺ is trapped in the upper rim of partial-cone-2 and interacts with C=C double bonds around the para carbons. The distances from Ag⁺ to the para carbons in the two phenyl units proximal to the inverted phenyl unit are 2.40 and 2.41 Å. These values compare well with those observed for the

Ag⁺ complexes with π-prismands and deltaphanes.[28d,e,f] On the other hand, the distance from Ag⁺ to the para carbon in the phenyl unit distal to the inverted phenyl unit is 5.63 Å. This value is too large for the π-donor participation. The distance from Ag⁺ to the phenolic oxygen in the inverted phenyl unit is 2.94 Å. This value is comparable with the sum of the ion radius of Ag⁺ and O (2.78 Å). However, the distances to the other oxygens (4.24–5.15 Å) are all too long to be important in electrostatic interaction. These X-ray data clearly establish that Ag⁺ is trapped in an upper rim of partial-cone-2 through a cation–π interaction with two benzene rings and an electrostatic interaction with one phenolic oxygen.[39] Although the single crystal has not yet been isolated for the 1,3-alternate-metal complex, we believe that the metal cation is bound to the edge of the 1,3-alternate cavity through interactions with two distal benzene rings and two distal phenolic oxygens.

Evidence for Metal-Tunneling by Dynamic ¹H NMR Spectroscopy. In the ¹H NMR spectra of 1,3-alternate-2 in the presence of Ag⁺ the signals for the complex and those for free 1,3-alternate-2 appeared separately at –50 °C and coalesced at 0 °C. This corresponds to the coalescence temperature for the *intermolecular* metal exchange ($T_{c,inter}$). At 0 to –50 °C the 1,3-alternate-2·Ag⁺ complex gave symmetrical peaks and did not give any inequivalent proton signals for the Ag⁺-complexed site and the Ag⁺-uncomplexed site. This result can be interpreted in two different ways: (i) Ag⁺ occupies the central position in the calix[4]arene cavity, so that four propyl groups and benzene rings become equivalent or (ii) Ag⁺ is bound to one of the two binding sites composed of two benzene rings and two phenolic oxygens, and the two binding sites are actually inequivalent (as in Figure 2A), but they appear equivalent due to rapid Ag⁺ exchange. If explanation i is correct, this is in conflict with the general concept of cyclophane·Ag⁺ complexes that Ag⁺ resides on the edge of the π-basic cavity.[28d,e,f] If explanation ii is correct, an unsymmetrical signal pattern should appear at lower temperatures. The presence of rapid Ag⁺-hopping between two binding sites has been expected for cyclophane·Ag⁺ complexes and has become a central interest in cation–π interactions.[28] In spite of many investigations using NMR spectroscopy, the Ag⁺-hopping has not yet been established by firm experimental evidence. The ¹H NMR spectra below –50 °C are shown in Figure 4A. Very interestingly, the signals arising from the 1,3-alternate-2·Ag⁺ complex are gradually broadened and eventually separate into pairs. The finding presents unequivocal evidence for hopping of Ag⁺ between the two binding sites in 1,3-alternate-2. The coalescence temperature for this metal exchange process is estimated to be –70 °C.

(34) Harrowfield, J. M.; Ogden, M. I.; Richmond, W. R.; White, A. H. *J. Chem. Soc., Chem. Commun.* **1991**, 1159.

(35) Shinkai, S.; Araki, K.; Matsuda, T.; Nishiyama, N.; Ikeda, H.; Takasu, I.; Iwamoto, M. *J. Am. Chem. Soc.* **1990**, *112*, 9053.

(36) Araki, K.; Shimizu, H.; Shinkai, S. *Chem. Lett.* **1993**, 205.

(37) In the 2nd Workshop on Calixarenes and Related Compounds (Kurume, 1993, June) J. de Mendoza also reported the inclusion of trimethylammonium ions in the calixarene cavity.

(38) Atwood et al. reported the importance of the H–π interaction in inclusion of guests into calixarenes, which is considered to be similar to the cation–π interaction; see: Atwood, J. L.; Hamada, F.; Robinson, K. D.; Orr, G. W.; Vincent, R. L. *Nature* **1991**, *349*, 683. Atwood, J. L.; Bott, S. G.; Jones, C.; Raston, C. L. *J. Chem. Soc., Chem. Commun.* **1992**, 1349.

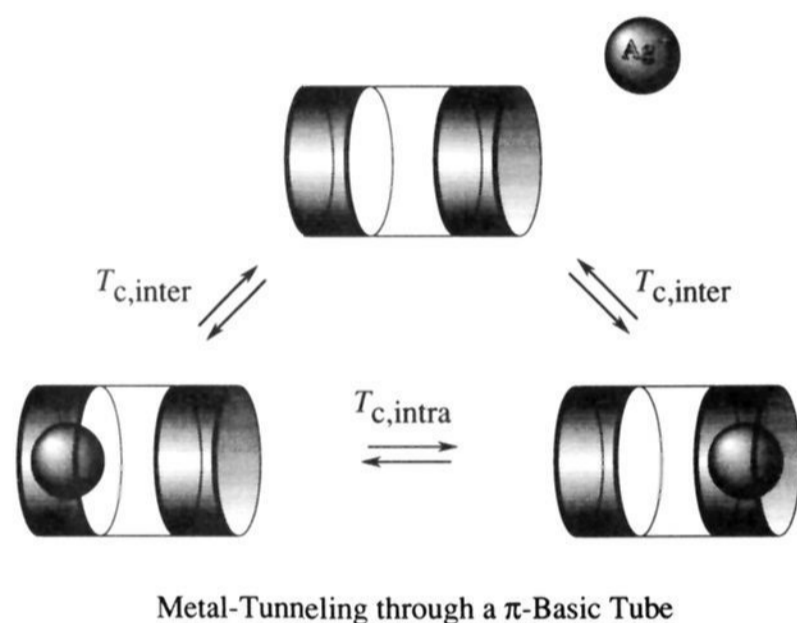(39) The details of bond lengths, bond angles, etc., will be reported elsewhere.
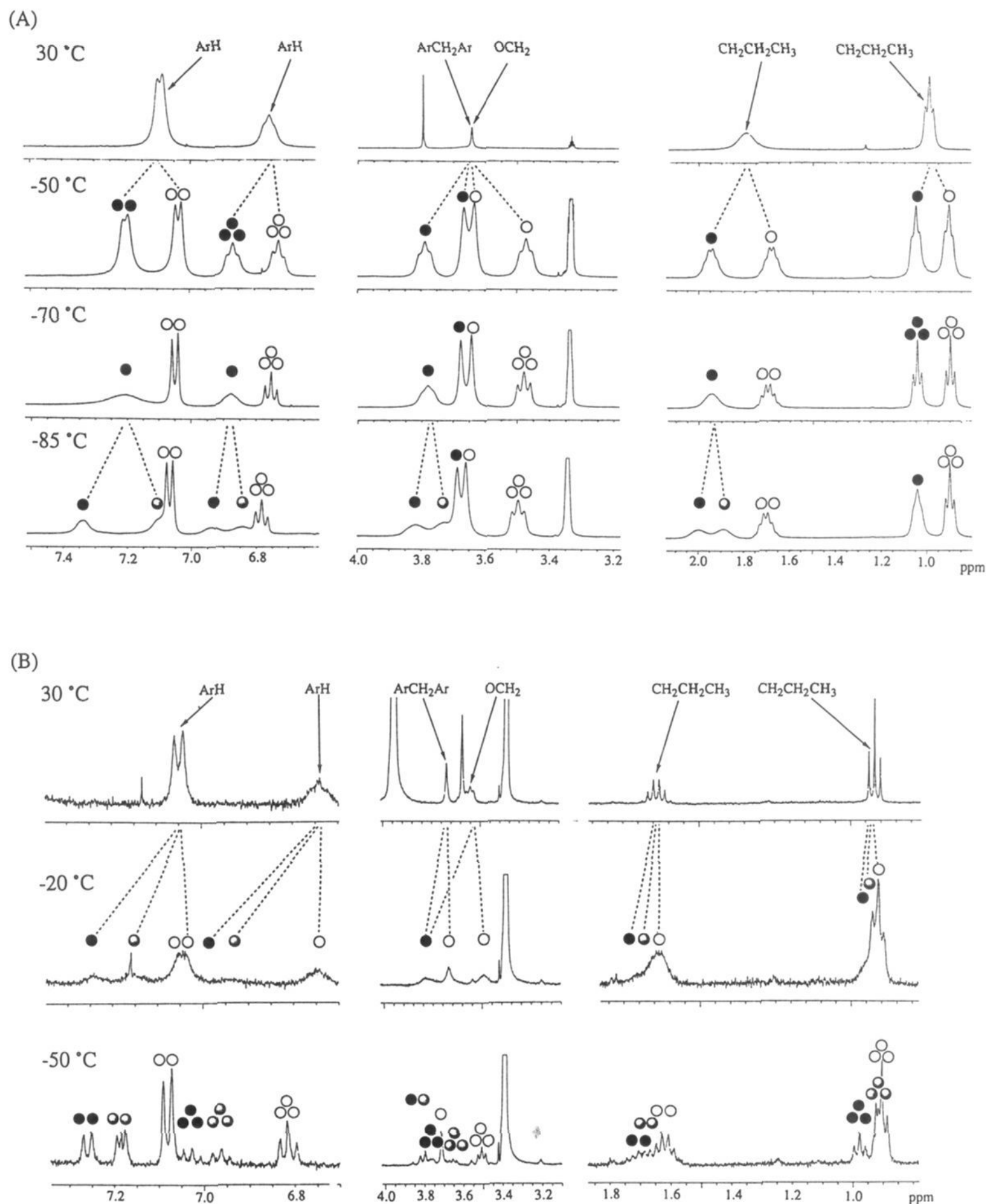
Figure 4. Partial ^{1}H NMR spectra of a 1,3-alternate-**2**·Ag$^+$ system (A) and a 1,3-alternate-**2**·K$^+$ system (B): for A, CD$_2$Cl$_2$:CD$_3$OD = 4:1 v/v, [1,3-alternate-**2**] = 1.00 × 10^{-2} M and [AgCF$_3$SO$_3$] = 5.00 × 10^{-3} M; for B CDCl$_3$:CD$_3$OD = 4:1 v/v, [1,3-alternate-**2**] = 5.00 × 10^{-4} M and [KPic] = 2.50 × 10^{-4} M. Open and solid (or shaded) circles denote the signals for free 1,3-alternate-**2** and those for the 1,3-alternate-**2**·metal complex.

Here again, the above finding can be explained in two different ways: (i) Ag$^+$ hops between two binding sites via an intermolecular metal exchange process or (ii) Ag$^+$ intramolecularly alternates between the two binding sites through a π-basic calix[4]arene hole. To discriminate between these two possibilities, we examined the influence of the metal concentration on the two coalescence temperatures (Figure 5). A plot of $\Delta\delta$ (=$\delta_{Ag^+\text{-complex}}$ - δ_{free}) versus Ag$^+$ concentration gave a break point at [AgCF$_3$SO$_3$]/[1,3-alternate-**2**] = 1.0 (CD$_2$Cl$_2$:CD$_3$OD = 4:1 v/v, 25 °C) and was saturated at higher Ag$^+$ concentrations (up to [AgCF$_3$SO$_3$]/[1,3-alternate-**2**] = 5.0, indicating that only a 1:1 1,3-alternate-**2**/AgCF$_3$SO$_3$ complex is formed. The instability of the 1:2 complex relative to the 1:1 complex is accounted for by electrostatic repulsion between two Ag$^+$ ions because the two binding sites in

1,3-alternate conformers are very close to each other (ca. 3 Å from O to O and 5 Å from edge to edge).^{14} As shown in Figure 5, the $T_{c,inter}$ dropped with increasing metal concentration, whereas the second coalescence temperature was scarcely affected by the change in the metal concentration. Above [AgCF$_3$SO$_3$]/[1,3-alternate-**2**] = 3, $T_{c,inter}$ and the second coalescence temperature coalesced. The difference in the concentration dependence clearly shows that the $T_{c,inter}$ reflects a concentration-dependent, intermolecular event, whereas the second coalescence temperature ($T_{c,intra}$) reflects a concentration-independent, intramolecular event. In a summary we can now represent the metal exchange process as in Figure 6. *Ag$^+$ is bound to one of two binding sites in 1,3-alternate-**2**, and the intermolecular complexation–decomplexation process gives the $T_{c,inter}$. Bound Ag$^+$ tunnels*
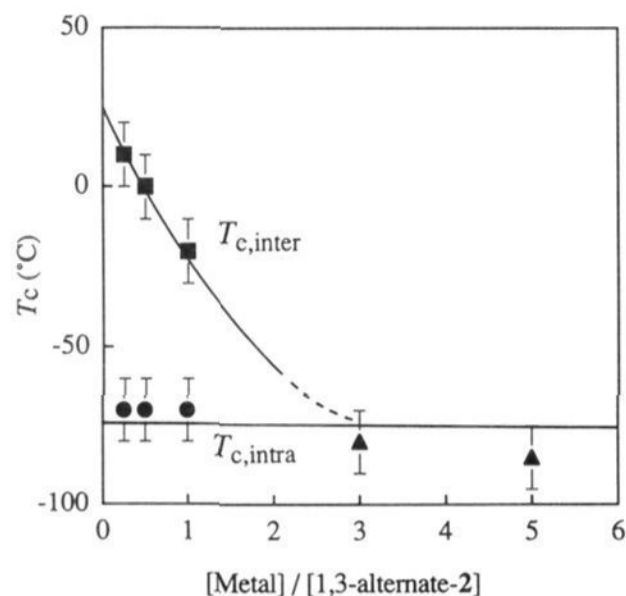
Figure 5. Concentration dependence of $T_{c,inter}$ and $T_{c,intra}$: -50 °C, CD$_2$-Cl$_2$:CD$_3$OD = 4:1 v/v. The concentration of 1,3-alternate-**2** (1.00 × 10^{-2} M) was maintained constant while the concentration of AgCF$_3$SO$_3$ was varied.

Metal-Tunneling through a π-Basic Tube

Figure 6. Schematic representation of the metal exchange in 1,3-alternate conformers.

Table 3. Intermolecular and Intramolecular Coalescence Temperatures ($T_{c,inter}$ and $T_{c,intra}$, Respectively) for the Metal Exhange[a]

run	metal salt	1,3-alternate calix[4]arene	$T_{c,inter}$ (°C)	$T_{c,intra}$ (°C)
1	AgCF$_3$SO$_3$	1	>30[e]	<−85[f]
2	AgCF$_3$SO$_3$	2	0	−70
3	AgClO$_4$	2	0	−70
4	AgCF$_3$SO$_3$	3	>30[e]	−20
5	AgCF$_3$SO$_3$	5	>30[e]	−70
6	AgCF$_3$SO$_3$	6	30	−60
7	AgCF$_3$SO$_3$[b]	8	>50[e]	20
8	AgCF$_3$SO$_3$	9	>30[e]	−50
9	KPic[c]	3	>30[e]	−10
10	NaClO$_4$[b]	8	50	30
11	KPic[d]	8	>50[e]	>50[g]

[a] 400 MHz, CD$_2$Cl$_2$:CD$_3$OD = 4:1 (v/v), [calix[4]arene] = 1.00 × 10^{-2} M, [AgCF$_3$SO$_3$ or AgClO$_4$] = 5.00 × 10^{-3} M. [b] CDCl$_3$:CD$_3$OD = 4:1 (v/v), [calix[4]arene] = 5.00 × 10^{-3} M, [AgCF$_3$SO$_3$ or NaClO$_4$] = 2.50 × 10^{-3} M. [c] CD$_2$Cl$_2$:CD$_3$OD = 4:1 (v/v), [calix[4]arene] = 5.00 × 10^{-4} M, [KPic] = 2.50 × 10^{-4} M. [d] CDCl$_3$:CD$_3$OD = 4:1 (v/v), [calix[4]arene] = 5.00 × 10^{-4} M, [KPic] = 2.50 × 10^{-4} M. [e] The proton signals for free calix[4]arene and the complex appeared separately at 30 and 50 °C. [f] The complex gave a single set of proton signals. [g] The proton signals for the complex appeared separately at 50 °C.
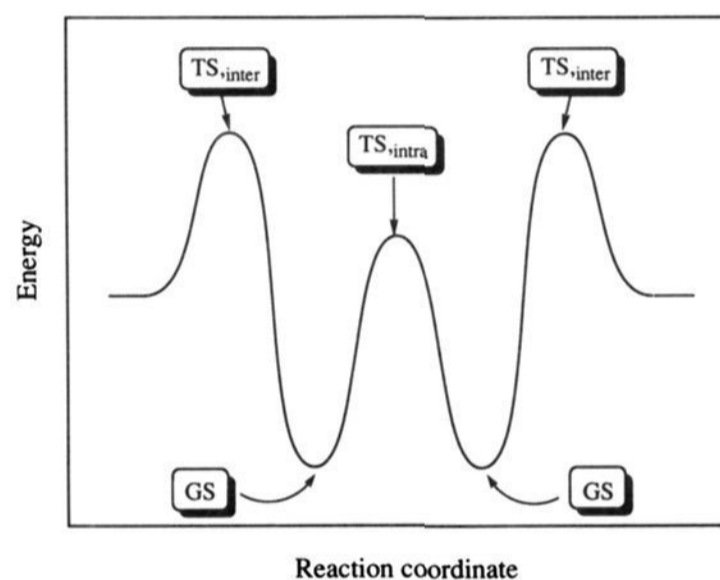
Figure 7. Energy diagram for intermolecular and intramolecular metal exchange mechanisms: GS and TS denote the ground state and the transition state, respectively.

through the π-basic tube to another binding site, the rate of the Ag$^+$ exchange being reflected by the $T_{c,intra}$.[40] The exchange rates are not affected by the difference in the counteranion (see runs 2 and 3 in Table 3). This is the first example for Ag$^+$-tunneling through a π-basic tube.

The Ag$^+$-tunneling phenomenon is also expected for 1,3-alternate-**1** with *t*-Bu groups. The temperature-dependent ^{1}H NMR spectra showed that the signals for free 1,3-alternate-**1** and those for the complex appear separately even at 30 °C, whereas the signals for the complex do not split even at −85 °C (run 1 in Table 3). This result implies that the intermolecular Ag$^+$ exchange is slower than that for 1,3-alternate-**2**, whereas the intramolecular Ag$^+$ exchange is faster than that for 1,3-alternate-**2**. The change in the exchange rates can be reasonably explained by using an energy diagram as in Figure 7. As previously demonstrated, the Ex% of 1,3-alternate-**1** is inferior to that of 1,3-alternate-**2** (Table 1); *t*-Bu groups at the para positions destabilize the 1,3-alternate-**1**·Ag$^+$ complex. This means that the ground states for the complex (GS in Figure 7) are raised. The transition state for the complexation–decomplexation process (TS$_{inter}$) should be further raised because the ^{1}H NMR spectral data indicated that the exchange rate is slower than that for 1,3-alternate-**2**. Probably, *t*-Bu groups immobilized on the cavity edges interfere with inclusion and exclusion of Ag$^+$. On the other

hand, the transition state for the intramolecular Ag$^+$ exchange (TS$_{intra}$) would not be affected by the *t*-Bu groups. The rate is thus accelerated because of the elevation of the GSs.

In 1,3-alternate-**3** both $T_{c,inter}$ and $T_{c,intra}$ are raised, indicating that both exchange rates are suppressed (run 4). Since each binding site in 1,3-alternate-**3** is composed of two EtOCH$_2$CH$_2$O groups (more ionophoric than PrO groups) and two benzene rings, the GSs should be more stabilized than those in 1,3-alternate-**2**. This proposal is supported by the high Ex% of 1,3-alternate-**3** for Ag$^+$ (Table 1). This effect increases the activation energies from GS to TS$_{inter}$ and to TS$_{intra}$, and thus both exchange rates are apparently suppressed. In catechol-bridged 1,3-alternate-**5** and 1,3-alternate-**6** the $T_{c,inter}$ values are enhanced up to 30 °C, while the $T_{c,intra}$ values are not or only slightly enhanced (runs 5 and 6). This change is attributable to rigidification of the 1,3-alternate architecture, which selectively retards the intermolecular Ag$^+$ exchange.

Runs 7 and 8 are very unique systems. 1,3-Alternate-**8** has very strong binding sites, each of which is composed of two EtOC(=O)CH$_2$O groups and two benzene rings.[14] Therefore, the GSs should be extremely stabilized. This feature of 1,3-alternate-**8** is reflected by $T_{c,intra}$ = 20 °C, an exceptionally high $T_{c,intra}$ among those observed for Ag$^+$ complexes. 1,3-Alternate-**9** also has two binding sites, but the binding abilities are different between the two sites. The ^{1}H NMR spectrum of the 1,3-alternate-**9**·Ag$^+$ complex at −85 °C showed that 8.1% of Ag$^+$ resides in the cavity

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(40) The metal "hopping" between two binding sites was reported for bis-(crown ether)s and biscalix[4]arenes: see Lehn, J.-M.; Stubbs, M. E. *J. Am. Chem. Soc.* **1974**, *96*, 4011. Ohseto, F.; Sakaki, T.; Araki, K.; Shinkai, S. *Tetrahedron Lett.* **1993**, *34*, 2149. To the best of our knowledge, however, this is the first example for the metal "tunneling" across a π-basic tube.

Table 4. Spectral Parameters, Coalescence Temperatures, Exchange Rates, and Free Energies of Activation for Intramolecular Cation Exchanges in 1,3-Alternate-3·M⁺ and 1,3-Alternate-8·M⁺ Complexes[a]

run	compound	^{1}H signal	$\Delta\nu$, Hz (temp, C°)	J, Hz	$T_{c,intra}$, ±5 °C	$k_{c,intra}$, s⁻¹	$\Delta G^{\ddagger}_{c,intra}$, kcal/mol
4	1,3-alternate-3·Ag⁺ [b]	ArH(p)	119 (−85)	7.32	−20	267	12.0
7	1,3-alternate-8·Ag⁺ [b]	ArH	58 (−50)		20	130	14.4
9	1,3-alternate-3·K⁺ [b]	ArH(p)	22 (−85)	7.63	−10	65	13.2
10	1,3-alternate-8·Na⁺ [b]	ArH	73 (−50)		30	163	14.7
11	1,3-alternate-8·K⁺ [b]	ArH	105 (30)		>50	<233	>15.4

[a] $\Delta\nu$, separation of the ^{1}H signals at the temperature indicated; J, spin–spin coupling constant; $T_{c,intra}$, coalescence temperature; $k_{c,intra}$, exchange rate at coalescence; $\Delta G^{\ddagger}_{c,intra}$, free energy of activation at coalescence calculated from $T_{c,intra}$ and $k_{c,intra}$ using the following equation. $\Delta G^{\ddagger}_{c,intra} = RT$ $\ln(6.62 \times 10^{12}/k_{c,intra})$. [b] The conditions and counteranions are similar to those described in Table 3.

composed of two Pr groups and two benzene rings and 91.9% of Ag⁺ resides in the cavity composed of two EtOCH₂CH₂O groups and two benzene rings. This implies that the latter cavity possesses an ionophoricity 10 times stronger than the former cavity.

1,2-Alternate conformers also have two binding sites at the edges of the calix[4]arene cavity, and thus metal-tunneling may be observable. Temperature-dependent ^{1}H NMR spectroscopy of 1,2-alternate-2 in the presence of Ag⁺ (the measurement conditions are similar to those for 1,3-alternate-2) resulted in a $T_{c,inter}$ at −50 °C, but the intramolecular split was not detected even at −85 °C. The spectrum for the 1,2-alternate-2·Ag⁺ complex showed a symmetrical pattern, suggesting that Ag⁺-tunneling is operating. It is known that in 1,2-alternate conformers four phenyl units are significantly flattened.[26,27] This structural feature makes the binding sites open to the bulk phase and the distance between the two binding sites shorter. Hence, the intermolecular metal exchange (as shown by $T_{c,inter}$ = −50 °C) is faster than that for 1,3-alternate-2 and the intramolecular metal exchange is very fast.

We measured the temperature-dependent ^{1}H NMR spectra of 1,3-alternate-2 in the presence of potassium picrate (KPic). Thus, we attempted to find evidence for K⁺-tunneling using other 1,3-alternate conformers. 1,3-Alternate-3 with EtOCH₂CH₂O groups and its KPic complex are more soluble in organic solvents. Separate signals for free 1,3-alternate-3 and the K⁺ complex were observed at room temperature. In the low-temperature region the signals for the complex split into pairs and the $T_{c,intra}$ appeared at −10 °C (run 9: [1,3-alternate-3] = 0.50 mM, [KPic] = 0.25 mM). The $T_{c,intra}$ was not affected by the change in the 1,3-alternate-3 (0.3–2.0 mM) and KPic (0.25–1.0 mM) concentrations. The findings support the view that K⁺ can also tunnel the π-basic tube of 1,3-alternate-3. When 1,3-alternate-8 with EtOC(=O)CH₂O groups was used, $T_{c,inter}$ and $T_{c,intra}$ were observed at 50 and 30 °C, respectively (run 10). The $T_{c,intra}$ was not affected by the change in the 1,3-alternate-8 (0.5–5.0 mM) and NaClO₄ (0.25–2.5 mM) concentrations, whereas the $T_{c,inter}$ was significantly affected. The findings indicate that even Na⁺ can permeate intramolecularly through the cavity, although the exchange rate (as shown by $T_{c,intra}$ = 30 °C) is much slower than those of the other systems.

When the splitting pattern for the intramolecular metal exchange appears clearly, one can estimate the exchange rate at the coalescence temperature.[41] The results are summarized in Table 4. It is seen from Table 4 that the exchange rate for Ag⁺ is much faster than that for K⁺ (compare run 4 and run 9). This suggests that the affinity of Ag⁺ with the π-basic calix[4]arene tube facilitates the metal-tunneling from one site to another site.

Conclusions

The investigations reported in this article were initiated by an accidental finding that among conformationally-immobilized calix[4]arenes 1,3-alternate conformers show a cation affinity higher than cone conformers. The spectral examination established that the cation is bound to one of two ionophoric binding

sites composed of two oxygenic ligands and two benzene rings with the aid of both electrostatic interaction and "cation–π interaction" and that the metal cation alternates between the two binding sites in the NMR time scale. The importance of the cation–π interaction has been pointed out by several groups by the fact that certain cyclophanes are capable of binding Ag⁺. They expected that Ag⁺ might jump from one site to another site through the cyclophane cavity.[28] To the best of our knowledge, however, concrete experimental evidence for the intramolecular Ag⁺-tunneling through the π-basic cyclophane cavity has not been obtained to date. In the present study unequivocal evidence is given for intramolecular Ag⁺ alternation between the two binding sites in 1,3-alternate conformers, and similar behavior was observed even for Na⁺ and K⁺. We believe that the novel findings reported herein are particularly important in understanding metal transport across ion channels, metal inclusion in π-base cavities (particularly, in fullerenes), intercalation of metal cations into graphites, etc. These possibilities suggest that the cation–π interaction may be a ubiquitous phenomenon operating not only in vitro but also more generally in nature.

Experimental Section

Materials. Preparations of the following compounds have been described: cone-1,[12] partial-cone-1,[12] 1,2-alternate-1,[12] 1,3-alternate-1,[12] cone-2,[42] partial-cone-2,[43] 1,2-alternate-2,[43] 1,3-alternate-2,[18,42] 5,-11,17,23-tetra-*tert*-butyl-25,26,27,28-tetramethoxycalix[4]arene (7),[44] 5,11,17,23-tetra-*tert*-butyl-25,26,27,28-tetrakis((ethoxycarbonyl)methoxy)-calix[4]arene (8),[5] and 25,27-dihydroxy-26,28-dipropoxycalix[4]arene (12).[18]

25,26,27,28-Tetrakis(ethoxyethoxy)calix[4]arene (1,3-Alternate-3). Calix[4]arene-25,26,27,28-tetrol (1.00 g, 2.36 mmol) was treated with 2-bromoethyl ethyl ether (8.01 g, 47.1 mmol) in acetone (70 mL) in the presence of Cs₂CO₃ (12.28 g, 37.7 mmol). The reaction mixture was stirred at reflux temperature for 24 h. After cooling, the mixture was diluted with ice–water and extracted with chloroform. The organic layer was washed twice with water and dried over MgSO₄. After filtration, the filtrate was concentrated to dryness. The residue was recrystallized from chloroform/methanol: yield 37%, mp 176–177 °C; ^{1}H NMR (CDCl₃, 25 °C) δ 1.30 (CH₃, t, 3H), 3.45–3.68 (OCH₂ and ArCH₂Ar, m, 6H), 3.72–3.88 (ArOCH₂, m, 2H), 6.65 and 7.10 (ArH, t and d, respectively, 1H and 2H, respectively). Anal. Calcd for C₄₄H₅₆O₈: C, 74.13; H, 7.92. Found: C, 73.67; H, 7.44.

5,11,17,23-Tetrakis(chloromethyl)-25,26,27,28-tetrapropoxycalix[4]-arene (1,3-Alternate-10). Compound 1,3-alternate-2 (1.00 g, 1.69 mmol) and paraformaldehyde (0.81 g) were suspended in dioxane (75 mL). After addition of acetic acid (4.05 g, 67.5 mmol), phosphoric acid (13.2 g, 135 mmol), and concentrated HCl (11.3 mL, 135 mmol), the reaction mixture was heated at 80 °C for 36 h. After cooling, the mixture was diluted with ice–water and extracted with chloroform. The organic layer was washed twice with water and dried over MgSO₄. The solution was evaporated to dryness, and the residue was recrystallized from chloroform/hexane: yield 82%, mp 283–285 °C; ^{1}H NMR (CDCl₃, 25 °C) δ 1.02 (CH₃, t, 3H), 1.07–1.87 (CH₂(CH₃), m, 2H), 3.54 (ArCH₂-Ar, s, 2H), 3.63 (OCH₂, t, 2H), 4.43 (ArCH₂Cl, s, 2H), 7.00 (ArH, s,

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2H). Anal. Calcd for $C_{44}H_{52}O_4Cl_4$: C, 67.18; H, 6.66. Found: C, 67.20; H, 6.59.

5,11,17,23-Tetrakis(chloromethyl)-25,26,27,28-tetrakis(ethoxyethoxy)-calix[4]arene (1,3-Alternate-11). This compound was synthesized from 1,3-alternate-3 (1.20 g, 1.69 mmol), paraformaldehyde (0.81 g), acetic acid (4.05 g, 67.5 mmol), phosphoric acid (13.2 g, 135 mmol), and concentrated HCl (11.3 mL, 135 mmol) in dioxane (75 mL). The workup was similar to that described for 1,3-alternate-10: yield 86%, mp 200–201 °C; ^{1}H NMR (CDCl$_3$, 25 °C) δ 1.37 (CH$_3$, t, 3H), 3.52 (ArCH$_2$Ar, s, 2H), 3.69 (OCH$_2$(CH$_3$), q, 2H), 3.78 and 3.91 (OCH$_2$(CH$_2$), t each, 2H each), 4.44 (ArCH$_2$Cl, s, 2H), 7.14 (ArH, s, 2H). Anal. Calcd for $C_{48}H_{60}O_8Cl_4$: C, 63.51; H, 6.67. Found: C, 63.58; H, 6.67.

5,11,17,23-Tetrakis(methoxymethyl)-25,26,27,28-tetrapropoxycalix-[4]arene (1,3-Alternate-4). Methanol (25 mL) and THF (25 mL) were treated with oil-dispersed NaH (0.81 g, 20.3 mmol) at 0 °C under a nitrogen stream. After 1 h 1,3-alternate-10 (1.00 g, 1.27 mmol) was added. The reaction mixture was stirred at reflux temperature for 6 h. After cooling, the reaction was stopped by the addition of an aqueous 1 M HCl solution and the product was extracted with chloroform. The organic layer was washed twice with water and dried over MgSO$_4$. After filtration, the filtrate was concentrated to dryness. The residue was recrystallized from chloroform/methanol: yield 76%, mp 174–176 °C; ^{1}H NMR (CDCl$_3$, 25 °C) δ 0.98 ((CH$_2$)CH$_3$, t, 3H), 1.68–1.85 (CH$_2$(CH$_3$), m, 2H), 3.26 (OCH$_3$, s, 3H), 3.50–3.70 (ArCH$_2$Ar and ArOCH$_2$, m, 4H), 4.24 (ArCH$_2$O, s, 2H), 6.95 (ArH, s, 2H). Anal. Calcd for $C_{48}H_{64}O_8$: C, 74.97; H, 8.39. Found: C, 74.95; H, 8.38.

1,3-Alternate-5. Compound 1,3-alternate-10 (1.00 g, 1.27 mmol) was dissolved in acetone (300 mL) and treated with K$_2$CO$_3$ (35.1 g, 254 mmol). The reaction mixture was stirred at reflux temperature for 1 h, and a catechol solution (1.12 mg, 10.2 mmol) in 70 mL of acetone was added from a dropping funnel for 3 h. The mixture was stirred at reflux temperature for 36 h. After cooling, the mixture was diluted with ice-water and extracted with chloroform. The organic layer was washed twice with water and dried over MgSO$_4$. After filtration, the filtrate was concentrated to dryness. The residue was recrystallized from chloroform/methanol: yield 81%, mp >310 °C; ^{1}H NMR (CDCl$_3$, 25 °C) δ 1.04 (CH$_3$, t, 3H), 1.86–1.97 (CH$_2$(CH$_3$), m, 2H), 3.50 (ArCH$_2$-Ar, s, 2H), 3.73 (ArOCH$_2$, t, 2H), 4.81 (ArCH$_2$O, s, 2H), 6.99–7.04, 7.08, and 7.10–7.16 (ArH, m, s, and m, respectively, 1H, 2H, and 1H, respectively). Anal. Calcd for $C_{56}H_{60}O_8$: C, 78.11; H, 7.02. Found: C, 78.02; H, 6.72.

1,3-Alternate-6. This compound was synthesized from 1,3-alternate-11 (1.25 g, 1.27 mmol), catechol (1.12 g, 10.2 mmol), and Cs$_2$CO$_3$ (35.14 g, 254 mmol) in acetone at reflux temperature for 24 h. The workup was similar to that described for **5**: yield 86%, mp 210–212 °C; ^{1}H NMR (CDCl$_3$, 25 °C) δ 1.17 (CH$_3$, t, 3H), 3.41 (OCH$_2$(CH$_3$), q, 2H), 3.56 (ArCH$_2$Ar, s, 2H), 3.74–3.79 ((CH$_2$)CH$_2$O, m, 2H), 3.92–3.96 (ArOCH$_2$, m, 2H), 4.83 (ArCH$_2$O, s, 2H), 6.98–7.04, 7.10–7.15, and 7.20 (ArH, m, m, and s, respectively, 1H, 1H, and 2H, respectively). Anal. Calcd for $C_{60}H_{68}O_{12}$·0.06CHCl$_3$: C, 72.99; H, 6.94. Found: C, 72.98; H, 6.91.

25,27-Bis(ethoxyethoxy)-26,28-dipropoxycalix[4]arene (1,3-Alternate-9). Compound 12 (0.25 g, 0.43 mmol) was treated with 2-bromoethyl ethyl ether (0.84 g, 4.91 mmol) in acetone (100 mL) in the presence of Cs$_2$CO$_3$ (2.77 g, 7.86 mmol). The reaction mixture was stirred at reflux temperature for 24 h. After cooling, the mixture was diluted with ice-

water and extracted with chloroform. The organic layer was washed twice with water and dried over MgSO$_4$. After filtration, the filtrate was concentrated to dryness. The residue was recrystallized from chloroform/methanol: yield 72%, mp 182–183 °C; ^{1}H NMR (CDCl$_3$, 25 °C) δ 0.95 (CH$_3$[(CH$_2$)$_2$], t, 3H), 1.29 (CH$_3$(CH$_2$O), t, 3H), 1.62–1.78 ((CH$_2$)CH$_2$(CH$_3$), m, 2H), 3.45–3.41 (ArCH$_2$Ar, ArOCH$_2$(C$_2$H$_5$), and OCH$_2$, m, 10H), 3.80 (ArOCH$_2$(CH$_2$O), t, 2H), 6.66, 6.67, 7.00, and 7.08 (ArH, t, t, d, and d, respectively, 1H, 1H, 2H, and 2H, respectively). Anal. Calcd for $C_{42}H_{52}O_6$: C, 77.27; H, 8.03. Found: C, 77.16; H, 7.99.

Solvent Extraction. Method A. Two-phase solvent extraction was carried out between water (5 mL, [alkali picrate] = 2.50 × 10^{-4} M, [MOH] = 0.10 M, [MCl] = 0.50 M) and dichloromethane (5 mL, [calix-[4]arene] = 2.50 × 10^{-3} M). The two-phase mixture was shaken for 12 h at 25 °C. The extractability was determined spectrophotometrically from the decrease in the absorbance of the picrate ion in the aqueous phase. **Method B.** The workup was similar to that described for method A but was carried out between water (5 mL, [picrate acid] = 2.38 × 10^{-4} M, [MNO$_3$] = 0.01 M, pH 4.7) and dichloromethane (5 mL, [calix-[4]arene] = 2.50 × 10^{-3} M).

Spectroscopic Measurements. The apparatus used for the measurement of ^{1}H NMR spectra was a JEOL GX-400 (400 MHz).

X-ray Crystal Structure Determination of Partial-Cone-2-AgCF$_3$SO$_3$ Complex. Colorless crystals were obtained by recrystallization from acetone. The crystal structure of partial-cone-2-Ag$^+$ complex was determined by X-ray diffraction. Crystal data: $C_{41}H_{48}O_7F_3SAg$, monoclinic, space group $P2_1/n$; a = 17.902(2) Å, b = 13.485(1) Å, c = 16.592(2) Å, β = 99.942(8)°; V = 3945.8(7) Å^3; Z = 4; d_{calc} = 1.43 g cm^{-3}, μ = 51.7 cm^{-1}. Reflections were measured at 298 K in the ω-2θ scan mode [2° < θ < 65°], using Cu Kα radiation (λ = 1.54184 Å). The structure was solved by the direct method[45] and refined with full-matrix least-squares methods. A total of 4408 reflections with $I_o^2 > 3\sigma(I_o)$ was used in the refinement. The R factors were R = 9.3% and R_w = 12.7%. All calculations were performed with MolEN.[46]

Supplementary Material Available: Four tables containing bond lengths, bond angles, positional parameters, and thermal parameters for the X-ray structure of partial-cone-2-AgCF$_3$SO$_3$ (16 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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