

Investigation of Metal Ion Complexation of π -Coordinate Calixarene Derivatives by Electrospray-Ionization Mass Spectrometry

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Abstract

Complexation of π -coordinate calix[4]arene derivatives toward soft metal ions, silver and thallium (I) ions, has been studied by electrospray-ionization mass spectrometry. Competitive metal-ion complexation of three calix[4]arene derivatives demonstrates a significant effect of olefinic substituents and its location on the silver ion complexation, but there was no effect of them on the thallium ion complexation. The stability constants for the metal ion complexes of the calixarene derivatives in methanol have been successfully determined by a mass-spectrometric method using 18-crown-6 as the reference ligand.

Introduction

Calixarene derivatives are well-known host compounds for small organic molecules or ionic species, depending on their chemical modification. Since calixarene derivatives consist of aromatic rings, they are also promising candidates of π -coordinate ligands for metal ions, especially for soft metal ions such as Ag^+ and Tl^+ [1, 2]. Cation- π interaction, which is seen frequently in biological systems [3, 4], is a weak interaction as compared with conventional coordination bonding, but the π -coordination by aromatic rings and olefinic moieties is quite selective for soft metal ions. Therefore, we have already tested several π -coordinate calix[4]arene derivatives for their usefulness as neutral carriers of ion-selective electrodes for Ag^+ and Tl^+ [5, 6], which requires a weak but ion-selective interaction with the metal ions to realize fast response and high sensitivity in the ion sensors.

Due to the course of the studies concerning the soft metal ion-selective electrodes based on calix[4]arene derivatives, comparisons of stability constants for the metal ion complexes are important for evaluation of the ion selectivities of the resulting electrodes. The stability constants for calixarene complexes with soft metal ions may be determined by using $^1\text{H-NMR}$ spectroscopy [7], but they may not be very easy to determine by the conventional methods. Recently, a determination method using electrospray-ionization mass spectrometry

(ESI-MS) had been applied for the determination of stability constants of crown ether-metal ion complexes by Kempen and Brodbelt [8]. This method is simple and requires only short time and small sample sizes to measure. Taking the use of the ESI-MS method, we had already succeeded in the determination of stability constants for the metal ion complexes of crowned bis(spirobenzopyran)s under dark [9] and photoirradiation [10] conditions.

Here, we report the ESI-MS study and the evaluation of the metal-ion complex stability constants for Ag^+ and Tl^+ complexes of π -coordinate calix[4]arene derivatives **1–3** (Figure 1). This is the first example for stability constant determination of the metal ion complexes of π -coordinate calix[4]arene derivatives by an ESI-MS method, to the best of our knowledge.

Experimental

Materials

The π -coordinate calixarene derivatives, *t*-butylcalix[4]arene allyl ether (**1**), *t*-butylcalix[4]arene propyl ether (**2**), and *t*-butylcalix[4]arene octenyl ether (**3**), were prepared according to the procedure reported previously [5]. The reference compound, 18-crown-6, was purified by distillation under vacuum. The Ag^+ and Tl^+ salts were their corresponding nitrates of analytical grade. Methanol for ESI-MS measurements was of analytical grade and was used without further purification.

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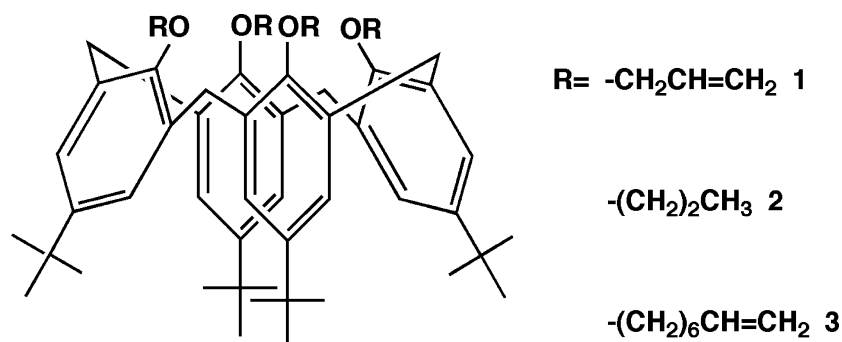


Figure 1. π -Coordinate calix[4]arene derivatives used in this study.

ESI-MS Measurements

Competitive metal-ion complexation for the qualitative evaluation of the metal-ion complexing ability of calixarene derivative was studied with an ESI-MS spectrometer (Finnigan LCQTM DECA) using a methanol solution containing 2×10^{-5} M calixarene and a metal nitrate mixture (2×10^{-5} M each). ESI-MS was performed at a capillary temperature of 70–120 °C and a capillary voltage of 5–100 V with a sample flow rate of 12.5–15 $\mu\text{l min}^{-1}$. The ionization efficiencies for the mass spectrometry of Ag^+ complexes were estimated in the presence of equal amounts of the three calixarene derivatives and 200-fold amount of the metal ion, under which condition almost all of calixarene molecules are complexed by a given metal ion. The normalized values

for the ionization efficiencies are 0.06, 1, 0.07, for the metal ion complexes **1**, **2**, and **3**, respectively. Similarly, the efficiencies for the mass spectrometry of Tl^+ complexes were 0.35, 1, and 0.74 for the complexes of **1**, **2**, and **3**, respectively.

Determination of stability constant

The determination of stability constants was carried out by ESI-MS using a methanol solution containing a calixarene derivative, a metal nitrate, and 18-crown-6 (the reference ligand), with a modification of a procedure in the literature [8]. The concentrations for the metal ion were in the range from 5×10^{-6} to 2.5×10^{-5} M and that for the calixarene derivative was 2.5×10^{-5} M. The capillary temperature and voltage

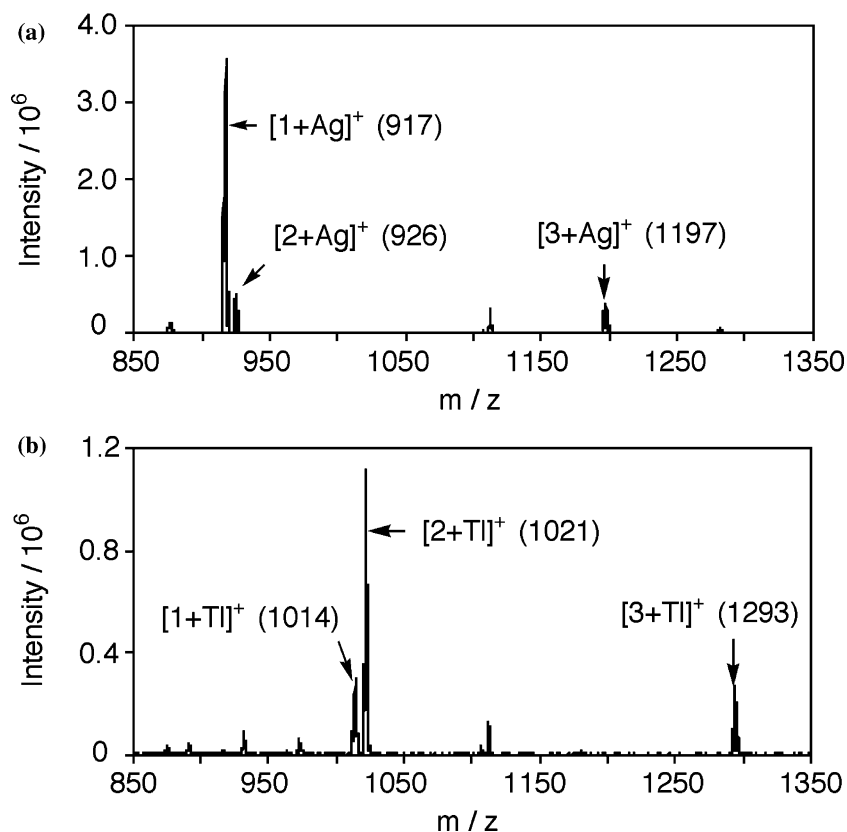


Figure 2. ESI-MS spectra for competitive complexation of Ag^+ (a) or Tl^+ (b) among π -coordinate calix[4]arene derivatives **1–3**. [calixarene] = 2×10^{-5} M, $[\text{MNO}_3] = 2 \times 10^{-5}$ M in methanol.

were 30–120 °C and 10–100 V, respectively. The flow rate of the sample solution was 10–12.5 $\mu\text{l min}^{-1}$. A calibration graph of a reference complex, of which the stability constant is known, was obtained at first. When a new ligand (a calixarene derivative) was added to the solution containing a reference (18-crown-6) complex, each of the stability constants (K) for the corresponding 1:1 metal ion/ligand complexes is defined as follows; $K_R = [\text{L}_R + \text{M}^{n+}]/[\text{L}_R]_F[\text{M}^{n+}]_F$ and $K_N = [\text{L}_N + \text{M}^{n+}]/[\text{L}_N]_F[\text{M}^{n+}]_F$. Here, the abbreviations L and M stand for the ligand (a calixarene derivative and 18-crown-6) and metal ion, respectively. The subscripts R, N, and F represent the reference and new ligands, and the free (uncomplexed) ligand, respectively. The concentration of reference complex $[\text{C}_R + \text{M}^{n+}]$ was obtained from the calibration plots, and then the concentration of free reference ligand $[\text{L}_R]_F$ was calculated as the difference between the total concentrations of reference ligand and the concentration of reference complex, $[\text{L}_R]_T$ and $[\text{L}_R + \text{M}^{n+}]$. Since K_R is known, $[\text{M}^{n+}]_F$ can be calculated. As $[\text{M}^{n+}]_F$ is a difference between $[\text{M}^{n+}]_T$ and $[\text{L}_R + \text{M}^{n+}] + [\text{L}_N + \text{M}^{n+}]$, $[\text{L}_N + \text{M}^{n+}]$ can be obtained. The concentration of the free new ligand is also available from the difference between $[\text{L}_N]_T$ and $[\text{L}_N + \text{M}^{n+}]$. The value K_N can be thus calculated from the stability constant definition.

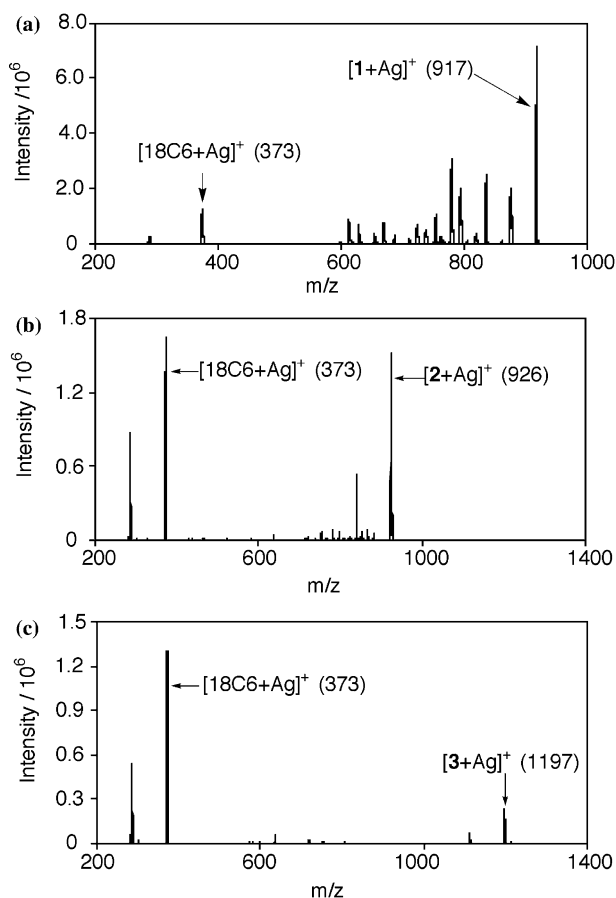


Figure 3. ESI-MS spectra for competitive Ag^+ complexation between a calix[4]arene derivative and 18-crown-6. (a): **1**, (b): **2**, (c): **3**. [calixarene] = [18-crown-6] = 3×10^{-5} M, $[\text{AgNO}_3] = 3 \times 10^{-5}$ M in methanol.

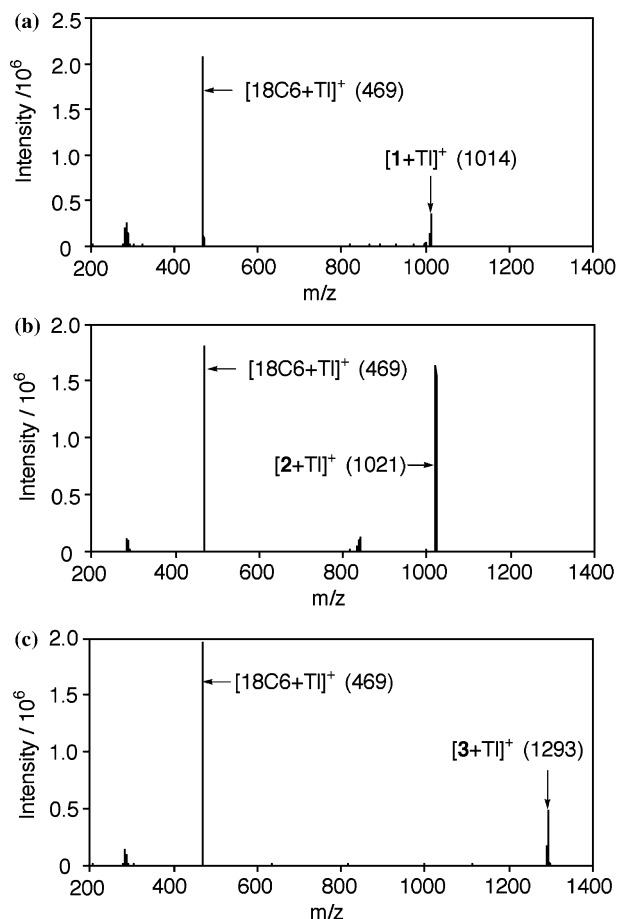


Figure 4. ESI-MS spectra for competitive TI^+ complexation between a calix[4]arene derivative and 18-crown-6. (a): **1**, (b): **2**, (c): **3**. [calixarene] = [18-crown-6] = 3×10^{-5} M, $[\text{TINO}_3] = 3 \times 10^{-5}$ M in methanol.

Results and discussion

Competitive metal–ion complexation among calixarene derivatives

Since three of the π -coordinate calix[4]arenes, **1–3**, were applied to neutral carriers for ion-selective electrodes of soft metal ions, Ag^+ and TI^+ [5, 6], the complexing properties of the calixarene derivatives towards Ag^+ and TI^+ in methanol were elucidated by ESI-MS. Figure 2 shows typical ESI-MS spectra for the competitive complexation of Ag^+ or TI^+ among the calix[4]arene derivatives. In the Ag^+ complexation (Figure 2a), the MS peak intensity for the 1:1 complex of Ag^+ and the calix[4]arene carrying allyl groups as a special π -coordinate substituent, **1**, is greater than those of the other calix[4]arene derivatives, **2** and **3**. The data in Figure 2a indicates that the 1:1 complex of Ag^+ and **1** is definitely more stable than those of **2** and **3**, even taking account of the relative ionization efficiencies for the three Ag^+ complexes of the calixarene derivatives in ESI-MS (See Experimental). In the TI^+ complexation, on the other hand, the calix[4]arene carrying propyl groups at the lower rim, **2**, exhibited a higher affinity to the metal ion

than **1** and **3**. The results for the competitive metal ion complexation among the three calix[4]arene derivatives imply that the difference in the metal ion affinity is related to that in the participation of the olefinic group in the π -coordination to the respective metal ions, as discussed later.

Competitive metal-ion complexation between calixarene derivative and 18-crown-6

It is of much interest to compare the metal-ion complexing abilities of the π -coordinate calix[4]arene derivatives with 18-crown-6, a typical crown ether, which is

known to form stable complexes with Ag^+ and Tl^+ [11, 12]. Figure 3 demonstrates the competitive Ag^+ complexation between one of the π -coordinate calix[4]arene derivatives and 18-crown-6. Calix[4]arene carrying allyl groups **1** is greater than, calix[4]arene carrying propyl groups **2** is comparable to, and calix[4]arene carrying octenyl groups **3** is smaller than 18-crown-6 in the MS peak intensity of the 1:1 Ag^+ /ligand complexes. For the competitive Tl^+ complexation between a calix[4]arene derivative and 18-crown-6 (Figure 4), the calixarene derivatives were comparable to or smaller than 18-crown-6 in the MS peak intensity of the 1:1 Tl^+ /ligand complex. These results imply that the π -coordinate

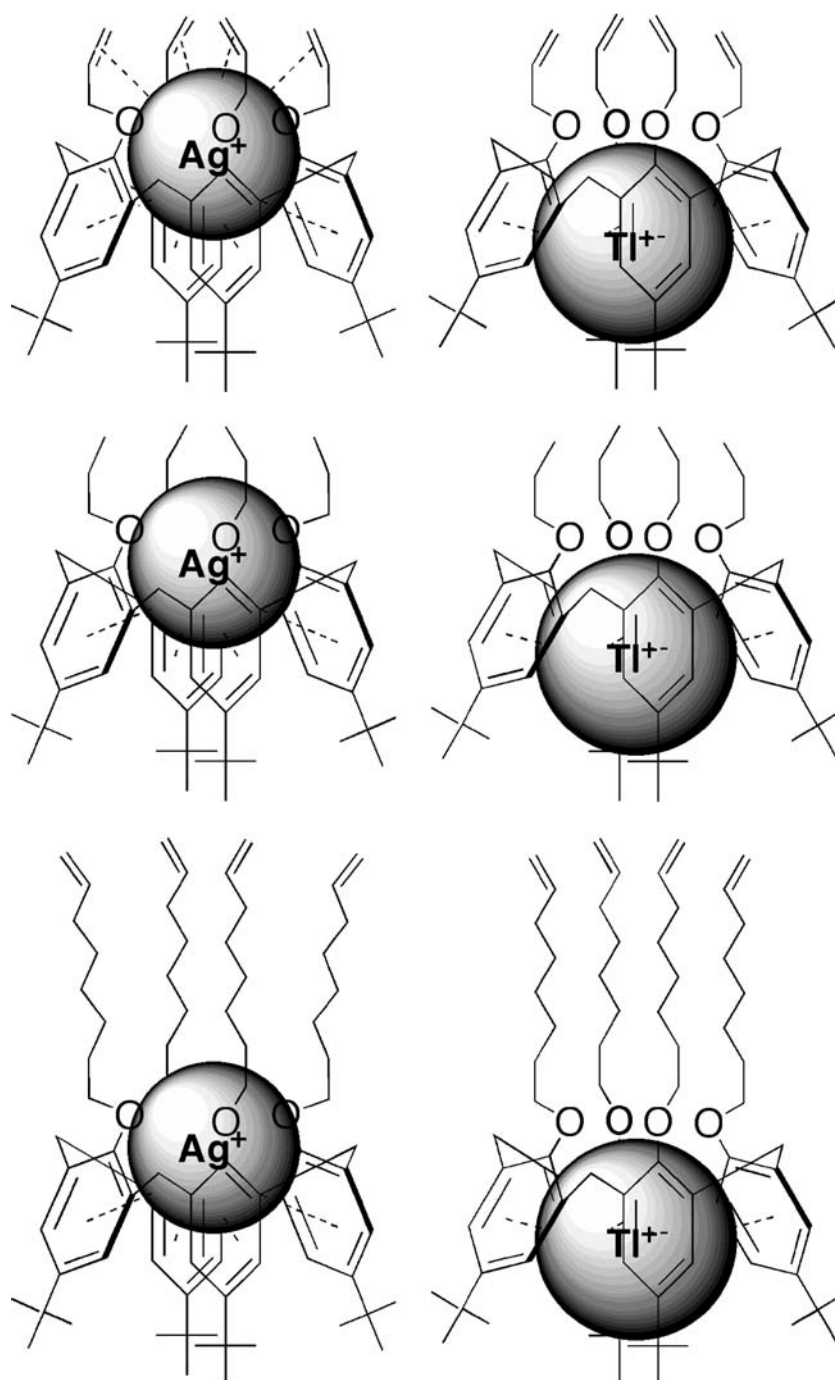


Figure 5. Plausible structures for Ag^+ and Tl^+ complexes of π -coordinate calix[4]arene derivatives **1**–**3**.

Table 1. Data of linear calibration graphs for peak intensities *versus* concentration of metal–ligand complexes for stability constant determination by ESI-MS

Metal complex for stability constant determination	Reference metal complex	Concentration range of reference metal complex (mol dm ⁻³)	Slope (mol ⁻¹ dm ³)	Intercept	Square of correlation coefficient (<i>R</i> ²)
1–Ag ⁺	18-crown-6–Ag ⁺	2.4 × 10 ⁻⁶ –9.3 × 10 ⁻⁶ ^a	4.3 × 10 ¹¹	-1.9 × 10 ⁶	0.999
2–Ag ⁺	18-crown-6–Ag ⁺	2.4 × 10 ⁻⁶ –9.3 × 10 ⁻⁶ ^a	3.1 × 10 ¹¹	-9.3 × 10 ⁵	0.998
3–Ag ⁺	18-crown-6–Ag ⁺	2.4 × 10 ⁻⁶ –9.3 × 10 ⁻⁶ ^a	3.1 × 10 ¹¹	-9.3 × 10 ⁵	0.998
1–Tl ⁺	18-crown-6–Tl ⁺	4.1 × 10 ⁻⁶ –1.6 × 10 ⁻⁵ ^b	1.6 × 10 ¹¹	-3.3 × 10 ⁵	0.997
2–Tl ⁺	18-crown-6–Tl ⁺	4.1 × 10 ⁻⁶ –1.6 × 10 ⁻⁵ ^b	1.6 × 10 ¹¹	-3.3 × 10 ⁵	0.997
3–Tl ⁺	18-crown-6–Tl ⁺	4.1 × 10 ⁻⁶ –1.6 × 10 ⁻⁵ ^b	1.6 × 10 ¹¹	-3.3 × 10 ⁵	0.997

^a Stability constant (log *K*) used for calculation of 18-crown-6–Ag⁺ complex is 4.58 [11].

^b Stability constant (log *K*) used for calculation of 18-crown-6–Tl⁺ complex is 5.34 [12].

calix[4]arene derivatives possess a higher and lower affinity to Ag⁺ and Tl⁺, respectively, than 18-crown-6 does.

Determination of stability constants for metal ion complexes of π -coordinate calixarene derivatives

We attempted to determine the stability constants for the Ag⁺ and Tl⁺ complexes of π -coordinate calix[4]arene derivatives, **1**, **2**, and **3**, in methanol by using ESI-MS. The ESI-MS procedure employed is based on the measurement of peak intensity for a reference complex with a known stability constant, and can afford reasonable stability constants in crown ether complexes of alkali and alkaline-earth metal ions [8–10], and the validity for the stability constant determination of various crown ether/metal ion complexes with ESI-MS had been already verified. As the reference complexes were adapted the Ag⁺ and Tl⁺ complexes of 18-crown-6, whose stability constants (log *K*) in methanol had been already determined by conventional methods [11, 12]. In order to verify the linearity in the calibration plots for each of the metal ion/ligand systems, the slope and intercept for the straight lines, their correlation coefficients, and the concentration range for the corresponding reference complex are summarized in Table 1.

Table 2 summarizes the stability constants of Ag⁺ and Tl⁺ complexes of calixarene derivatives **1**, **2**, and

Table 2. Stability constants (log *K*) for metal–ion complexes of π -coordinate calix[4]arene derivatives **1–3** determined by ESI-MS

	Ag ⁺	Tl ⁺
1	5.42 ± 0.09 ^a	4.25 ± 0.07 ^b
2	4.86 ± 0.11 ^a	5.34 ± 0.05 ^b
3	4.60 ± 0.08 ^a	4.50 ± 0.16 ^b
18-crown-6	4.58 ^c	5.34 ^d

The values for the standard deviation were determined by repeating the measurement 4–10 times.

The log *K* values were determined by using ^a 18-crown-6–Ag⁺ complex, ^b 18-crown-6–Tl⁺ complex as the reference complex.

^c Ref. [11].

^d Ref. [12].

3, together with those of 18-crown-6 for comparison. As anticipated from the peak intensity comparison in the competitive complexation mentioned above, the Ag⁺ complex of calix[4]arene possessing allyl groups as the special π -coordinate substituent **1** is significantly more stable than those of the two other calix[4]arene derivatives **2** and **3**. Interestingly, the stability constant for the Tl⁺ complex of calix[4]arene possessing propyl groups **2** is higher than those of **1** and **3**. Also, the Ag⁺ and Tl⁺ complexes of the three calixarene derivatives are more and less stable than the corresponding metal ion complexes of 18-crown-6, respectively.

We had already found by ¹H NMR experiments in our previous work [5] that, in the Ag⁺/1 complex, the metal ion interacts with both the allyl groups and aromatic skeleton of the calixarene, as shown schematically in Figure 5. In the Ag⁺ complexes of **2** and **3**, on the other hand, the metal ion interacts mainly with the aromatic skeleton. Presumably, the cooperative action of the aromatic skeleton and allyl groups in the Ag⁺ complexation of **1** resulted in the higher stability constant for the metal ion complex than those for the two other calixarene derivatives. The NMR data was not indicative of any significant interaction between the Ag⁺ and olefinic moiety of the octenyl groups of **3**, probably because the olefinic moieties are too far from the aromatic skeleton to bind the metal ion cooperatively with the latter π -coordinate moiety. To the contrary, the NMR spectra of the Tl⁺ complexes showed that the metal ion interacts only with the aromatic skeleton in any of the complexes of the calix[4]arene derivatives, both of the olefinic groups of **1** and **3** not participating in the Tl⁺ complexation. It is not understood yet why the stability for the Tl⁺ complex of the calix[4]arene carrying propyl groups, which cannot π -coordinate to the central metal ion, is higher than those for the two other calixarenes.

Thus, the stability constants for Ag⁺ and Tl⁺ complexes of calix[4]arene derivatives **1–3** have been successfully determined by using ESI-MS and their complex stabilities have been able to compare quantitatively to each another.

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