

# High Complexation Ability of Thiocalixarene with Transition Metal Ions. The Effects of Replacing Methylene Bridges of Tetra(*p-t*-butyl)calix[4]aretetrol by Epithio Groups

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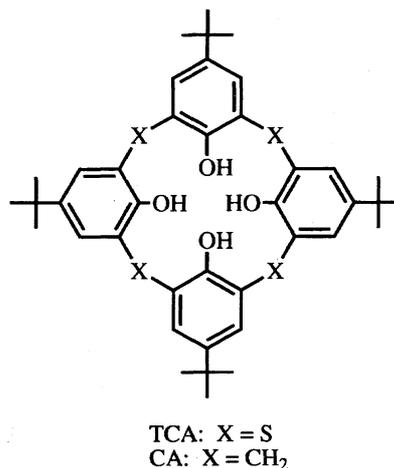
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The ability of tetra(*p-t*-butyl)tetrathiocalix[4]aretetrol (TCA, H<sub>4</sub>L), a cyclic tetramer of *p*-(*t*-butyl)phenol bridged with four epithio groups, to bind metal ions was investigated via a solvent extraction study. Although tetra(*p-t*-butyl)calix[4]aretetrol (CA) has very poor affinity for transition metal ions (M<sup>2+</sup>), TCA is an excellent extractant of these metal ions. The chemical formulae of the extracted TCA metal complexes were found by slope analysis to be neutral 1 : 1 complexes [MH<sub>2</sub>L]. The origin of the high affinity of TCA for transition metal ions is discussed, in which it is suggested that ligation of the epithio group is important as evidenced by an NMR study of the [ZnH<sub>2</sub>L] complex.

Calixarenes and their derivatives are one of the most important materials in molecular recognition chemistry. A wide variety of their functions have been developed via synthetic approaches.<sup>1)</sup> For example, in order to bind metal ions, the lower rim, the phenolic hydroxy group, has been modified by various functional groups bearing ligating atoms.<sup>2)</sup> Part of the upper rim has also been modified.<sup>3)</sup> These modified calixarenes have been applied as ligands for separation<sup>4)</sup> and sensing<sup>5)</sup> systems for metal ions.

So far, there have been only limited reports on the development of new types of calixarene analogues by replacing the bridge methylene groups with hetero atoms. Sone et al. first reported the synthesis of tetra(*p-t*-butyl)tetrathiocalix[4]aretetrol (TCA) by acid-catalyzed cyclization of a cyclic tetramer,<sup>6)</sup> and reported the results of an Scheme 1 <sup>1</sup>H NMR study.<sup>7)</sup> König et al. synthesized tetra(*p-t*-butyl)tetrasilacalix[4]aretetrol tetramethyl ether, where the linking unit is Si(CH<sub>3</sub>)<sub>2</sub>, by stepwise reaction of 1-(*t*-butyl)-4-methoxybenzene and dichloromethylsilane followed by cyclization.<sup>8)</sup> However, these studies were mainly concerned with the synthesis of the hetero calixarenes themselves, and only little is known about the properties and applications of such cyclic entities.

Recently, one of us reported a convenient and easy synthesis of TCA in a satisfactory yield by simply heating *p*-(*t*-butyl)phenol with elemental sulfur in the presence of a base.<sup>9)</sup> Now, with substantial quantities of TCA in hand, we have started a project to discover the properties of TCA and to exploit the latent functions of it as high-performance material. As the first successful example in this line, here we report a high complexation ability of TCA for transition metal ions, which was unexpected from the low complexation ability of tetra(*p-t*-butyl)calix[4]aretetrol (CA, Scheme 1). We also discuss how the replacement of methylene bridges in



Scheme 1. The structure and abbreviations for tetra(*p-t*-butyl)tetrathiocalix[4]aretetrol (TCA) and tetra(*p-t*-butyl)calix[4]aretetrol (CA).

CA by epithio groups affects the complexation ability, via a quantitative solvent extraction study.

## Results and Discussion

**Extractability of Metal Ions by TCA.** We first studied the solvent extraction of various metal ions by TCA from an aqueous phase to a chloroform phase. The concentration of the metal ion extracted into organic phase, [Metal]<sub>org</sub>, as TCA complex is calculated by Eq. 1,

$$[\text{Metal}]_{\text{org}} = [\text{Metal}]_{\text{aq,init}} - [\text{Metal}]_{\text{aq}}, \quad (1)$$

where [Metal]<sub>aq,init</sub> and [Metal]<sub>aq</sub> are the initial and final concentration of the metal ion in the aqueous phase. The percent extraction, *E*%, was calculated by Eq. 2.

$$E\% = [\text{Metal}]_{\text{org}} / [\text{Metal}]_{\text{aq, init}} \times 100\%. \quad (2)$$

Table 1 shows the  $E\%$  at time  $t = 24$  h for alkali and alkaline earth metal ions.<sup>10</sup> It can be seen that TCA could hardly extract alkali metal ions under acidic to alkaline conditions at  $[\text{TCA}]_{\text{Total}}/[\text{Metal}]_{\text{Total}} = 5$ ; the pH dependence on the extractability is not clearly explained at present. Alkaline earth metal ions were substantially not extracted either by TCA.

By contrast, TCA behaved quite differently in the extraction of transition metal ions (Table 2). The extractabilities were distinctly dependent on pH. Thus at lower pH, almost no extraction was observed. On the other hand, at higher pH, the numerical values of the  $E\%$  were very high. It can be seen that TCA extracted  $\text{Co}^{2+}$ ,  $\text{Ni}^{2+}$ , and  $\text{Zn}^{2+}$  ions quantitatively at pH 8.0, while  $\text{Cu}^{2+}$  ion was extracted more effectively ( $E\% = 98.9\%$ ) at pH 7.0. These values of extractability were further verified by back extraction of the metal ions from the chloroform phase into 0.1–6 M HCl solution (1 M = 1 mol dm<sup>-3</sup>). Recovery of the metal ions was almost quantitative, and then loss of the ions by reactions such as formation of metal hydroxide and/or adsorption onto the vial wall seemed negligible during the extraction process.

To the best of our knowledge, the extraction of transition metal ions with unmodified *p*-alkylcalixarenes has not been reported except for that of  $\text{Cu}^{2+}$  and  $\text{UO}_2^{2+}$  by a hexa(*p*-*t*-butyl)calix[6]arenehexol.<sup>11,12</sup> In fact at our hands, tetra(*p*-*t*-butyl)calix[4]arenetetrol (CA) could scarcely extract metal

ions at pH 8.0 (Table 2), showing the high extraction ability of TCA to be rather exceptional. Table 2 also contains the data showing that addition of 100-fold of pyridine against the metal ions slightly improved the  $E\%$  data, which will be discussed later. All the conventional strategies to design extraction reagents by use of calix[4]arenetetrols relied on modification of the upper<sup>2)</sup> or lower<sup>3)</sup> rim by introducing suitable functional groups, which have high affinity for metal ions. Therefore our approach is unique in changing the basic skeleton of a calix[*n*]arene via replacing the CH<sub>2</sub> bridges by epithio groups.

**Acceleration Effect.** Although the extractability of TCA for transition metal ions is high at higher pH, the extraction was rather slow, especially at lower pH. These prevented studies on the extraction mechanism by equilibrium measurements. TCA seems to have strong intramolecular hydrogen bonding and has flip-flop inversion<sup>7,9</sup> as conventional calix[4]arenetetrols do.<sup>13,14</sup> These may prevent rapid complexation of metal ions by TCA and thus limit the extraction rate.

It has been reported that formation of metal complexes is sometimes greatly accelerated by use of a catalyst. As an example, aromatic-containing amino acids<sup>15</sup> or heterocyclic aromatic compounds<sup>16</sup> accelerate the formation of metal porphyrin complexes, in which  $\pi$ - $\pi$  interaction between the aromatic nuclei of the porphyrin and the catalyst has been supposed to be important. Therefore, expecting a similar  $\pi$ - $\pi$  stacking effect, we first used pyridine as the acceleration agent for TCA extraction. Figure 1A shows the time profile of  $E\%$  for  $\text{Co}^{2+}$  ion at pH 6.5, without or with adding 10 or 100-fold pyridine against  $\text{Co}^{2+}$ . The dependence of  $E\%$  on time was fitted by non-linear least squares using the first order kinetics expressed by Eq. 3,

$$E\% = E\%_{\text{eq}} \left[ 1 - \exp\left(-\frac{t}{\tau}\right) \right], \quad (3)$$

where  $E\%_{\text{eq}}$  and  $\tau$  are  $E\%$  at  $t$  infinite and the time constant. As shown, the rate of extraction increased as the pyridine concentration increased. In this study, it is assumed that equilibrium state is practically reached when  $t = 3\tau$ , where  $E\%/E\%_{\text{eq}}$  is 0.95. About 5 h ( $3\tau$ ) is enough to reach equilibrium when 100-fold pyridine was used (curve (c) in Fig. 1A). On the contrary, equilibration time ( $3\tau$ ) without pyridine is estimated to be more than 40 h (curve (a) in Fig. 1A), which is not practical for an equilibrium study.

In the extraction process, pyridine seems first to coordinate to metal ion, and then to associate with the TCA molecule through a  $\pi$ - $\pi$  stacking effect.<sup>17</sup> This may increase the chance for one of the phenolic hydroxy groups to coordinate to the metal ion. In this context, it should be noted that tryptophan had a slightly better acceleration effect than pyridine, probably due to an indole moiety bearing a larger  $\pi$  electron system than the pyridine ring. (For example,  $\tau = 4.0$  and 1.9 h at pH 6.5<sub>2</sub> when  $5 \times 10^{-4}$  and  $5 \times 10^{-3}$  M of tryptophan were added, respectively. For raw data, refer to supplementary materials deposited as Document No. 71034 at the Office of the Editor of Bull. Chem. Soc. Jpn.)

Table 1. Percent Extraction ( $E\%$ ) of Alkali and Alkaline Earth Metal Ions by TCA at Various pH

pH	Li <sup>+</sup>	Na <sup>+</sup>	K <sup>+</sup>	Rb <sup>+</sup>	Cs <sup>+</sup>	Mg <sup>2+</sup>	Ca <sup>2+</sup>	Ba <sup>2+</sup>
2.2	18	12	4	8	6	4	0	0
5.5	15	9	32	18		7	0	0
8.0	14		25	0		6	0	0

Aqueous phase:  $1.0 \times 10^{-4}$  M of metal chloride, 0.05 M of pH buffer ( $\text{H}_3\text{PO}_4$ - $\text{NH}_3$  for pH = 2.2, succinic acid- $\text{NH}_3$  for pH = 5.5, or Tris-HCl for pH = 8.0), and 0.1 M tetramethylammonium chloride to adjust ionic strength ( $I = 0.1$ ). Organic phase: chloroform containing  $5.0 \times 10^{-4}$  M TCA. Both phases are shaken together for 24 h at room temperature (ca. 20 °C).

Table 2. Percent Extraction ( $E\%$ ) of Transition Metal Ions by TCA and CA

Ligand	pH	Accelerator	Mn <sup>2+</sup>	Co <sup>2+</sup>	Ni <sup>2+</sup>	Cu <sup>2+</sup>	Zn <sup>2+</sup>
TCA	2.2	None		0	0	3	
	5.5	None		0	2	50	
	8.0	None	35	99	97	69	99
Ca	8.0	None		5	1	1	6
	8.0	0.01 M pyridine		10	4	6	23

Aqueous phase:  $1.0 \times 10^{-4}$  M of metal chloride, 0.05 M of pH buffer ( $\text{H}_3\text{PO}_4$ - $\text{NH}_3$  for pH = 2.2, succinic acid- $\text{NH}_3$  for pH = 5.5, or Tris-HCl for pH = 8.0), and 0.1 M tetramethylammonium chloride to adjust ionic strength ( $I = 0.1$ ). Organic phase: chloroform containing  $5.0 \times 10^{-4}$  M TCA. Pyridine was added to the aqueous phase as an accelerator only for CA at pH 8.0 system. Both phases are shaken together for 24 h at room temperature (ca. 20 °C).

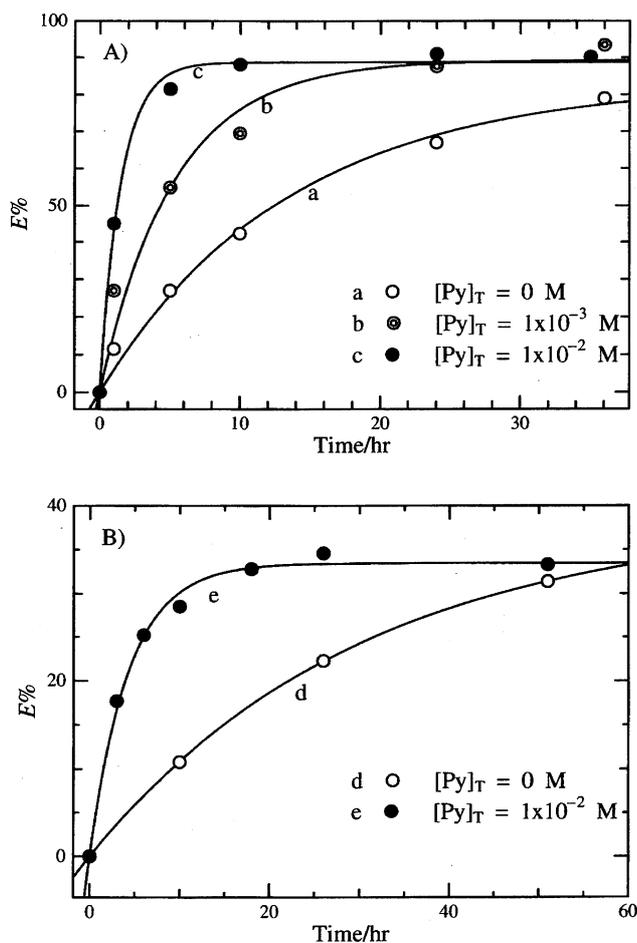


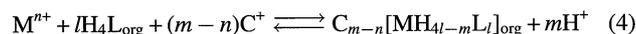
Fig. 1. Acceleration effect of pyridine on the extraction of  $\text{Co}^{2+}$  ion. A) Aq:  $1.0 \times 10^{-4}$  M  $\text{CoCl}_2$ , 0.05 M PIPES- $\text{NH}_3$  at pH 6.54, accelerator: 0,  $1.0 \times 10^{-3}$ , or  $1.0 \times 10^{-2}$  M pyridine. Org.:  $4 \times 10^{-4}$  M TCA, B) Aq:  $1.0 \times 10^{-4}$  M  $\text{CoCl}_2$ , 0.05 M succinic acid- $\text{NH}_3$  at pH 5.67, accelerator: 0 or  $1.0 \times 10^{-2}$  M pyridine. Org.:  $2.0 \times 10^{-3}$  M TCA. The data were fitted by Eq. 3 to give  $\tau$  and  $E\%_{\text{eq}}$  as; a) 13.6 h, 83.2%; b) 5.3 h, 89.3%; c) 1.5 h, 88.7%; d) 30.2 h, 38.5%; and e) 4.3 h, 33.4%, respectively.

Even at lower pH ( $= 5.6$ ), pyridine showed acceleration effect for  $\text{Co}^{2+}$  extraction (Fig. 1B). Hence it had been confirmed that  $\text{Cu}^{2+}$  and  $\text{Zn}^{2+}$  had faster extraction than  $\text{Co}^{2+}$ , the equilibration time of 13 h ( $3\tau$  for 100-fold pyridine against  $\text{Co}^{2+}$ ) is enough for all these three metal ions. In the following study, extraction was continued for 24 h to ensure equilibration. We did not attempt to obtain equilibrium data for  $\text{Ni}^{2+}$ , which showed much slower extraction than  $\text{Co}^{2+}$  even if an accelerator was used.

It is known that neutral ligands often accelerate the extraction via the formation of an adduct complex in synergistic extraction.<sup>18)</sup> We, however, exclude the possibility of synergistic extraction mechanism in the following discussion, because pyridine in a wide range of concentrations (0–0.01 M) did not affect the  $E\%_{\text{eq}}$  value in Fig. 1.

**Extraction Mechanism.** To discover the composition of the extracted metal species, we used slope analysis. The general extraction reaction of metal ion by TCA is described

as Eq. 4 under the assumption of no formation of dimer or polymer of the metal complexes;



where  $\text{M}^{n+}$ ,  $\text{H}_4\text{L}$ ,  $\text{C}^+$ ,  $[\text{MH}_{4l-m}\text{L}_l]^{-(m-n)}$ ,  $\text{C}_{m-n}[\text{MH}_{4l-m}\text{L}_l]$  are metal ion, free TCA, counter cation, TCA metal complex, and its ion associate, respectively, while  $l$ ,  $m$ , and  $n$  are the number of ligands reacted with one metal ion, number of protons released, and the valence of metal ion. Subscript org means species in organic phase. Hence the ionic strength depends on buffer components and pH, which varies at each datum point, all the terms should be based on activity. (For details, see Experimental section). The thermodynamic extraction constant,  $K_{\text{ex}}$  is given by Eq. 5,

$$K_{\text{ex}} = \frac{a_{\text{C}_{m-n}[\text{MH}_{4l-m}\text{L}_l]_{\text{org}}} \cdot a_{\text{H}^+}^m}{a_{\text{M}^{n+}} \cdot a_{\text{H}_4\text{L}_{\text{org}}}^l \cdot a_{\text{C}^+}^{m-n}}, \quad (5)$$

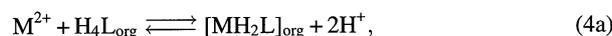
where  $a_{\text{C}_{m-n}[\text{MH}_{4l-m}\text{L}_l]_{\text{org}}}$ ,  $a_{\text{H}^+}$ ,  $a_{\text{M}^{n+}}$ ,  $a_{\text{C}^+}$ , and  $a_{\text{H}_4\text{L}}$  are the activities. To see the degree of distribution of  $\text{C}_{m-n}[\text{MH}_{4l-m}\text{L}_l]$  in organic phase against  $\text{M}^{n+}$  in aqueous phase, Eq. 5 was converted into Eq. 6.

$$\begin{aligned} \log a_{\text{C}_{m-n}[\text{MH}_{4l-m}\text{L}_l]_{\text{org}}} - \log a_{\text{M}^{n+}} \\ = \log K_{\text{ex}} + l \log a_{\text{H}_4\text{L}_{\text{org}}} + m\text{pH} + (m-n) \log a_{\text{C}^+}. \end{aligned} \quad (6)$$

The left term ( $\log a_{\text{C}_{m-n}[\text{MH}_{4l-m}\text{L}_l]_{\text{org}}} - \log a_{\text{M}^{n+}}$ ) corresponds to the distribution ratio of metal species. The dependence of ( $\log a_{\text{C}_{m-n}[\text{MH}_{4l-m}\text{L}_l]_{\text{org}}} - \log a_{\text{M}^{n+}}$ ) on  $\log a_{\text{H}_4\text{L}_{\text{org}}}$  and pH gives  $l$  and  $m$  in the chemical formula of extracted species  $\text{C}_{m-n}[\text{MH}_{4l-m}\text{L}_l]_{\text{org}}$  when other terms are kept constant. We calculated the left term ( $\log a_{\text{C}_{m-n}[\text{MH}_{4l-m}\text{L}_l]_{\text{org}}} - \log a_{\text{M}^{n+}}$ ) from raw data as shown in experimental section.

First, the ( $\log a_{\text{C}_{m-n}[\text{MH}_{4l-m}\text{L}_l]_{\text{org}}} - \log a_{\text{M}^{n+}}$ ) versus  $\log a_{\text{H}_4\text{L}_{\text{org}}}$  plots are shown in Fig. 2. The slopes,  $l$ , for  $\text{Cu}^{2+}$  and  $\text{Zn}^{2+}$  ions equal to 1, which confirms TCA binds to each metal ion in 1:1 manner. While  $\text{Co}^{2+}$  ion had a somewhat high  $l$  value, that implies partial formation of self-adduct or 1:2 complex. Second, the pH dependence of ( $\log a_{\text{C}_{m-n}[\text{MH}_{4l-m}\text{L}_l]_{\text{org}}} - \log a_{\text{M}^{n+}}$ ) was studied (Fig. 3). The plot for  $\text{Co}^{2+}$  and  $\text{Cu}^{2+}$  ions showed that the slopes  $m$  are equal to 2, which shows that 2 protons were released upon complexation. There is no contribution of  $\text{C}^+$  such as  $\text{NH}_4^+$  or pyridinium ion. On the other hand, the  $m$  for  $\text{Zn}^{2+}$  ion slightly deviated from 2. This may suggest that some fraction of TCA released three protons rather than two upon the reaction with  $\text{Zn}^{2+}$  ion.

Since the valence of those transition metal ions equals 2,<sup>19)</sup> we can summarize the above extraction system as  $l = 1$ ,  $m = 2$ , and  $n = 2$ . Therefore Eqs. 4, 5, and 6 are rewritten by Eqs. 4a, 5a, and 6a.



$$K_{\text{ex}} = \frac{a_{[\text{MH}_2\text{L}]_{\text{org}}} \cdot a_{\text{H}^+}^2}{a_{\text{M}^{2+}} \cdot a_{\text{H}_4\text{L}_{\text{org}}}}, \quad (5a)$$

$$\log a_{[\text{MH}_2\text{L}]_{\text{org}}} - \log a_{\text{M}^{2+}} = \log K_{\text{ex}} + \log a_{\text{H}_4\text{L}_{\text{org}}} + 2\text{pH}. \quad (6a)$$

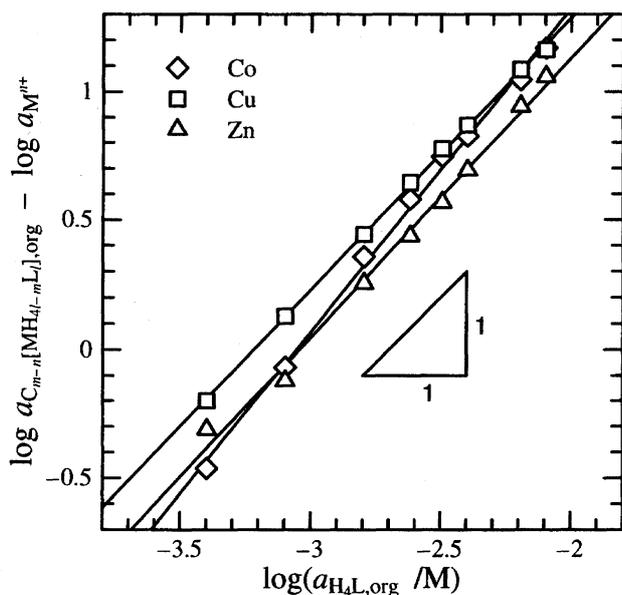


Fig. 2. ( $\log a_{C_{m-n}[MH_{4l-m}L_l]_{org}} - \log a_{M^{n+}}$ ) versus  $\log a_{H_4L_{org}}$  plot. Aq:  $1.0 \times 10^{-4}$  M Metal Chloride, 0.01 M pyridine, 0.05 M buffer (succinic acid– $NH_3$  of pH 5.87 for  $Co^{2+}$ , succinic acid– $NH_3$  of pH 5.20 for  $Cu^{2+}$ , PIPES– $NH_3$  of pH 5.97 for  $Zn^{2+}$ ), Org.:  $0.4\text{--}8.0 \times 10^{-3}$  M TCA. The slopes ( $l$ ) obtained were  $1.26 \pm 0.03$  ( $Co^{2+}$ ),  $1.06 \pm 0.03$  ( $Cu^{2+}$ ), and  $1.08 \pm 0.03$  ( $Zn^{2+}$ ).

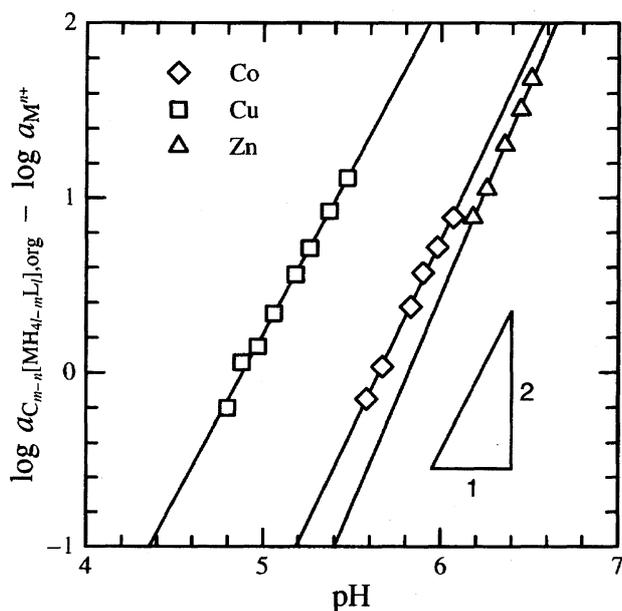


Fig. 3. ( $\log a_{C_{m-n}[MH_{4l-m}L_l]_{org}} - \log a_{M^{n+}}$ ) versus pH plot. Aq:  $1.0 \times 10^{-4}$  M Metal Chloride, 0.01 M pyridine, 0.05 M buffer (succinic acid– $NH_3$  for  $Co^{2+}$  and  $Cu^{2+}$ , PIPES– $NH_3$  for  $Zn^{2+}$ ). For  $Co^{2+}$  extraction, L-ascorbic acid was added to avoid oxidation of  $Co^{2+}$ . Org.:  $2.0 \times 10^{-3}$  M TCA. The slope ( $m$ ) obtained were  $2.16 \pm 0.06$  ( $Co^{2+}$ ),  $1.90 \pm 0.04$  ( $Cu^{2+}$ ), and  $2.40 \pm 0.10$  ( $Zn^{2+}$ ).

It may be concluded that the metal ions were extracted via the formation of neutral TCA chelate,  $[MH_2L]$ .

We fit Eq. 6a to the raw data in Figs. 2 and 3 to obtain  $K_{ex}$

Table 3. The thermodynamic Extraction Constant of Metal Ions by TCA Obtained by Slope Analysis

Variable	Data source	$\log(K_{ex}/M)$		
		$Co^{2+}$	$Cu^{2+}$	$Zn^{2+}$
$\log a_{H_4L_{org}}$	Fig. 2	$-8.58 \pm 0.03$	$-7.15 \pm 0.03$	$-8.86 \pm 0.03$
pH	Fig. 3	$-8.57 \pm 0.02$	$-7.09 \pm 0.02$	$-8.72 \pm 0.02$

$\log(K_{ex}/M)$  was obtained by fitting Eq. 6a where  $l$ ,  $m$ , and  $n$  are fixed as  $l = 1$ ,  $m = 2$ , and  $n = 2$ . The error is the standard deviation of the difference between original data and the fitting function.

values (Eq. 5a) for the  $[MH_2L]$ , which are listed in Table 3. These two  $K_{ex}$  values obtained by different experiments for each metal ion agreed quite well within experimental error. The values for  $Co^{2+}$  and  $Zn^{2+}$  are very close while  $K_{ex}$  for  $Cu^{2+}$  is one and half orders larger. As a consequence of the regular solution theory<sup>20,21</sup> the difference in the stability of complexes causes the difference in  $K_{ex}$ .<sup>22</sup> In this context, TCA may be an ionophore that can bind  $Cu^{2+}$  ion selectively in matrices containing  $Co^{2+}$  and  $Zn^{2+}$  ions.

**NMR Study.** The formula  $[MH_2L]$  suggests that TCA binds of metal ion in the central cavity of the cone conformation in a similar manner to reported metal–CA complexes.<sup>23</sup> To identify the structure of the TCA complexes,  $^1H$  and  $^{13}C$  NMR studies were done for  $Zn^{2+}$  complex, the only one that is diamagnetic among the transition metal complexes prepared. The aromatic region of the  $^1H$  NMR spectrum of TCA– $Zn^{2+}$  complex is shown in Fig. 4. The absence of a free TCA peak ( $\delta_H = 7.64$  ppm from  $(CH_3)_4Si$  in  $CDCl_3$ ) confirms that TCA forms the  $Zn^{2+}$  complex quantitatively. Most importantly, all the major aromatic protons had a meta coupling pattern ( $J_{H-H,meta} = 2.40\text{--}2.64$  Hz). The four pairs of coupled protons belonging to the same aromatic ring were assigned by COSY, which showed that all the aromatic rings are nonequivalent. This was also supported by  $^{13}C$  NMR spectra. For instance, methyl groups in  $Bu'$  groups ( $(CH_3)_3C-$ ) gave four discrete resonances at  $\delta_C = 31.26, 31.33, 31.38,$  and  $31.44$  ppm (from  $(CH_3)_4Si$  in  $CDCl_3$ ). The aromatic carbon for the *ipso* position to epithio group had eight resonance lines.<sup>24</sup> These cannot be explained by the cone structure proposed for the conventional metal-calix[4]arenetetrol complexes, which should have a symmetrical structure.<sup>23</sup> The only structure that can accommodate the 4 nonequivalent phenyl groups is that TCA in partial-cone form binds to  $Zn^{2+}$  ion via phenolic  $O^-$ , sulfide S, and phenolic  $O^-$  groups to form two five-membered chelated rings.

In conclusion, the manner of bonding of TCA to metal ions is quite different from that of CA, which seems to provide TCA much higher affinity to metal ions than CA. In addition, the flexibility of the epithio linkage may allow TCA to optimize its conformation to coordinate to transition metal ions  $M^{2+}$ .

## Conclusion

Although the structures of TCA and CA are apparently not very different from each other, they are quite different in the ability to recognize transition metal ions (see Table 2),

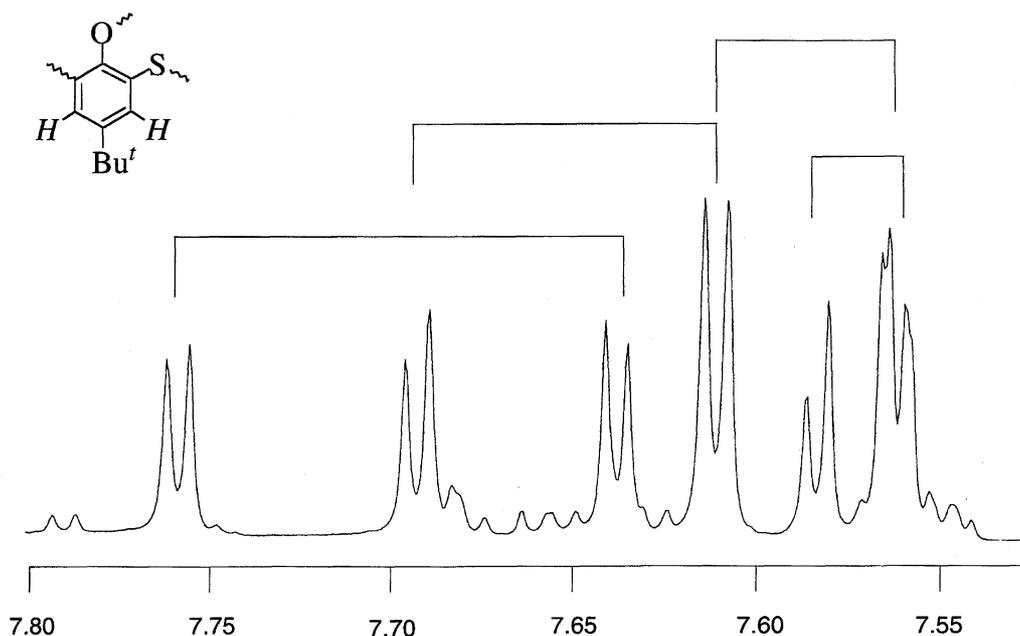


Fig. 4.  $^1\text{H}$ NMR spectra of  $\text{Zn}^{2+}$ -TCA complex. Sample:  $5.0 \times 10^{-2}$  M  $[\text{ZnH}_2\text{L}]$  in  $\text{CDCl}_3$ . COSY spectrum was measured in order to assign the aromatic protons coupled together. Minor peaks are possibly from  $\text{Zn}^{2+}$ -TCA complexes of other conformations.

the reason of which was considered here from the effect of addition of pyridine on the rate of the formation of the metal complexes. As stated above, the extraction rate by use of TCA was greatly accelerated by addition of pyridine (Fig. 1), while the data in Table 2 shows that it exerted a measurable but only slight effect on the extraction rate of the relevant metal ions by CA. This may suggest that the low  $E\%$  values provided by CA are mainly ascribed to thermodynamic reasons rather than kinetic ones. It should be noted that the reported metal-CA complexes have usually been synthesized under anhydrous conditions.<sup>23)</sup> In other words, it seems that CA is too weak a ligand to expel the ligating water molecules from the  $\text{M}^{n+}$  ions in aqueous solutions to form the metal-CA complexes. It may be said that the higher stability of the TCA complexes are provided by virtue of the epithio groups, one of which could join to form tridentately coordinated complexes with the aid of two phenolate oxygens, as suggested by the NMR study.

It should be noted here again that no accelerator was needed to accumulate the  $E\%$  data by use of TCA in Table 2, as it formed complexes rather promptly. This implies that TCA is greatly favored over CA not only from thermodynamic reasons but also from kinetic reasons to coordinate to the metal ions. The latter reasons may largely owe to the flexibility of the TCA skeleton linked by epithio bridges, as suggested by Sone et al.<sup>7)</sup>

In conclusion, we have shown here that tetra(*p-t*-butyl)-tetrathiocalix[4]arenetetrol has high ability to form  $[\text{MH}_2\text{L}]$ -type transition metal complexes, providing a new strategy to design metal-binding host molecules by placing a hetero atom in the methylene bridge of the parent calixarenes. The unique structure of the  $[\text{MH}_2\text{L}]$  complexes as indicated by NMR study asks for further structural analysis including X-

ray crystal analysis, which is now underway.

## Experimental

**Materials.** A sample of TCA was generously supplied by Cosmo Research Institute.<sup>9)</sup> Standard solutions (0.01 M) of transition and alkaline earth metal ions were prepared by dissolving the chlorides into 0.01 M HCl solution. The accurate concentration were checked with accepted chelatometry.<sup>25)</sup> Stock solution of alkali metal ions were prepared from their chlorides, which were dissolved in distilled water. Succinic acid, tris(hydroxymethyl)aminomethane (Tris), and 1,4-piperazinediethanesulfonic acid (PIPES) were used as pH buffers. All the reagents purchased were of guaranteed reagent grade.

**Solvent Extraction. Procedure.** A typical procedure for the extraction study is as follows. To a 30  $\text{cm}^3$  vial tube were pipetted an aqueous solution (10  $\text{cm}^3$ ) containing metal ion as well as pH buffer and a solution of TCA in chloroform (10  $\text{cm}^3$ ), and then this was shaken at 300 strokes/min for 24 h. For the detailed initial compositions of both phases, see the caption of tables and figures. The total concentration of metal species remaining in aqueous phase,  $[\text{Metal}]_{\text{aq}}$ , was measured by Varian SpectraAA 600 flame or Zeeman atomic absorption spectrometers. For pH measurement of aqueous phase, a Horiba D-14 pH meter with S8720 electrode was used.

**NMR Measurement.** An aqueous phase (10  $\text{cm}^3$ ) containing  $7.5 \times 10^{-2}$  M  $\text{Zn}^{2+}$  and 0.5 M Tris buffer (pH = 8.0) and chloroform solution of  $5.0 \times 10^{-2}$  M TCA are shaken for 24 h. A sample of the organic phase was filtered through Omnipore JH Filter (0.5  $\mu\text{m}$ , Millipore), evaporated to dryness, and dissolved into the same volume of  $\text{CDCl}_3$ .  $^1\text{H}$  and  $^{13}\text{C}$ NMR was measured with Bruker DPX-400 spectrometer operated at 400 and 100 MHz, respectively.

**Estimation of Activities.** In the usual slope analysis study, excess salt is added to the aqueous phase in order to keep  $I$ , ionic strength, constant. Because the concentration of buffer component (0.05 M) as well as pyridinium ion (ca. 0.01 M level) was already quite high, additional excessive salt might form complex with TCA

(see Table 1) or ion associate with such as  $[\text{MH}_{4-m}\text{L}]^{-(m-n)}$ . For this reason, excess salt was not added to aqueous phase. Therefore  $I$  was not kept constant. All the calculation was accomplished by using a concentration-based equilibrium constant that was finally converted from the thermodynamic equilibrium constant by an activity coefficient at each datum point. In this study, the activity coefficient,  $\gamma_i$ , of charged species,  $i$ , is calculated by Davies equation (Eq. 7),<sup>26)</sup>

$$\log \gamma_i = z_i^2 \left( 0.15I - \frac{0.51\sqrt{I}}{1 + \sqrt{I}} \right) \quad (7)$$

under the condition  $0.05 < I < 0.2$  where  $z_i$  is the charge of species  $i$ . In order to use this equation to calculate  $\gamma_i$ ,  $I$  must be estimated first. Therefore we first estimate  $I$  as well as the concentrations of major species such as  $[\text{NH}_3]$  and  $[\text{py}]$  by successive approximation procedure.<sup>27)</sup>

After  $I$ ,  $[\text{NH}_3]$  and  $[\text{py}]$  were estimated,  $[\text{Metal}]_{\text{aq}}$  was converted into  $[\text{M}^{n+}]_{\text{aq}}$  by considering the reaction of  $\text{M}^{n+}$  with  $\text{NH}_3$  and  $\text{py}$ .<sup>28)</sup> Finally  $a_{\text{M}^{n+}}$  was obtained by Eq. 8 via  $\gamma_{\text{M}^{n+}}$  value.

$$a_{\text{M}^{n+}} = \gamma_{\text{M}^{n+}} [\text{M}^{n+}]_{\text{aq}} \quad (8)$$

The activity for any neutral species was assumed to be equal to the concentration, hence  $z_i=0$  and then  $\gamma_i=1$  in Eq. 7. Therefore,

$$a_{\text{C}_{m-n}[\text{MH}_{4-m}\text{L}]_{\text{org}}} = [\text{Metal}]_{\text{org}} \quad (9)$$

where  $[\text{Metal}]_{\text{org}}$  is given by using Eq. 2. For the activity of TCA in organic phase,

$$a_{\text{H}_4\text{L}_{\text{org}}} = [\text{H}_4\text{L}]_{\text{org}} \quad (10)$$

where  $[\text{H}_4\text{L}]_{\text{org}}$  is the initial concentration of TCA because the amount of TCA in the organic phase is excess to metal ion. Activity of the proton,  $a_{\text{H}^+}$  was directly converted from the pH reading by Eq. 11

$$\text{pH} = -\log a_{\text{H}^+} \quad (11)$$

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27) Under certain pH,  $I$  was first let to be zero as an initial value. Then  $[\text{H}^+]$  was converted from  $\alpha_{\text{H}^+}$  (via Eq. 11) and  $\gamma_{\text{H}^+}$  (via Eq. 7). The concentration of buffer components and accelerator were calculated by mass balance, charge balance, and equation

of equilibrium constants. Then the new ionic strength ( $I_{\text{new}}$ ) was calculated. If  $I_{\text{new}}$  was greatly different from the initial  $I$ ,  $[\text{H}^+]$  as well as other concentrations at  $I=I_{\text{new}}$  was estimated. This was repeated until  $I_{\text{new}}$  converged. For the routine in detail, the equations, and constants used, refer to supplementary materials (Deposited Document No. 71034).

28) Because,  $[\text{Metal}]_{\text{aq}}$  obtained by atomic absorption spectrometry contains the concentration of not only  $\text{M}^{n+}$  but also the metal species such as ammine or pyridine complexes. For the equations and constants used, refer to supplementary materials (Deposited Document No. 71034).

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