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Silver Ion Shuttling in the Trimer-Mimic Thiacalix[4]crown Tube

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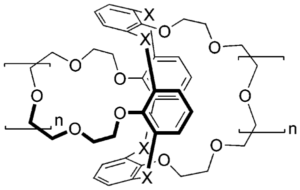
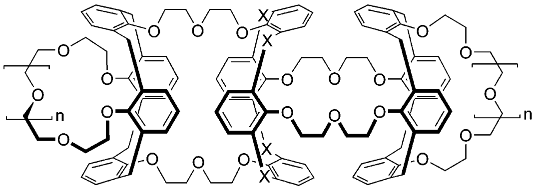
Received October 22, 2003

Abstract: Novel 1,3-alternate calix-thiacalix[4]crown trimers bearing crown-5 and crown-6 were prepared. As proven by X-ray diffraction, in a 1:2 mole ratio of ligand to metal ion, the Cs^+ and K^+ ions prefer to be encapsulated in the trimeric thiacalix[4]crown-6 and crown-5, respectively. On the contrary, the Ag^+ ion was found to be entrapped in the central thiacalix spacer as a 1:1 complex confirmed by ^1H NMR spectrosocpy. Variable-temperature ^1H NMR studies for the trimeric thiacalix[4]crown-6 encapsulating the silver ion revealed that the Ag^+ ion oscillates through the central thiacalix spacer with the aid of cation−π interactions.

Among macrocyclic compounds used as metal-ion extractants, calixarenes have been of particular interest because they have two reactive sites: (1) phenolic OHs (lower rim) and (2) para positions (upper rim) to the hydroxy groups, which can be readily functionalized by various cation-ligating groups such as carboxylic acid, crown ether, and azacrown ether.[1,2] In particular, calixcrown ethers in which the proper-sized crown rings are incorporated into the calixarene framework have attracted intense interest as a selective extractant for specific metal ions.[3] In addition, thiacalixarenes, which have sulfur atoms in place of methylene bridges between each calix-aromatic group, have also been investigated as alternatives to the conventional calixarenes. These sulfur atoms are known to provide additional coordination sites for transition metal ions as well as to undergo oxidation to sulfinyl or sulfonyl groups in which the oxygen atoms are able to act as additional binding sites.[4−6]



	n	X
1	1	CH_2
2	2	CH_2
3	1	S
4	2	S



	n	X
5	1	CH_2
6	2	CH_2
7	1	S
8	2	S

1,3-Alternate calix-bis-crowns (**1** and **2**)[7] and thiacalix-bis-crowns (**3** and **4**)[6,8,9] showed a high selectivity toward specific metal ions; for instance, compounds **1** and **3** possessing crown-5 rings showed a selectivity for K^+ and Rb^+ ions, whereas compounds **2** and **4** with crown-6 rings exhibited a Cs^+-ion selectivity. In such a molecular topology, the metal ions are entrapped not only by the crown ethereal oxygen atoms but also by the cation−π interactions between two rotated benzene rings and the metal cation.[7] Furthermore, the 1,3-alternate calix[4]-crowns allow a cation to shuttle through the π-basic calix-tube. For example, Koh et al.[10] and Kim et al.[9,11] independently reported that metal ions encapsulated by calix[4]biscrown-5 (**1** and **2**), calix[4]bisazacrown, and thiacalix[4]biscrowns (**3** and **4**) oscillate through the calix-tube. By variable-temperature ^1H NMR experiments, metal-ion shuttling rates were also compared in terms of two coalescence temperatures corresponding to both

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(1) (a) Gutsche, C. D. *Calixarenes*; Royal Society of Chemistry: Cambridge, 1989. (b) Gutsche, C. D. In *Synthesis of Macrocycles: Design of Selective Complexing Agents*; Izatt, R. M., Christensen, J. J., Eds.; Wiley: New York, 1987; p 93. (c) *Calixarenes: A Versatile Class of Macrocyclic Compounds*; Vicens, J., Böhmer, V., Eds.; Kluwer: Dordrecht, 1991. (d) Böhmer, V.; McKervey, M. A. *Chemie Unserer Zeit* **1991**, 195. (e) Gutsche, C. D. C*alixarenes, Monographs in Supramolecular Chemistry*; Stoddart, J. F., Ed.; Royal Society of Chemistry: Cambridge, U.K., 1989; Vol. 1 (f) Gutsche, C. D. In *Inclusion Compounds*; Atwood, J. L., Davies, J. E. D., MacNicol, D. D., Eds.; Oxford University Press: New York, 1991; Vol. 4, pp 27−63. (g) Van Loon, J.-D.; Verboom, W.; Reinhoudt, D. N. *Org. Prep. Proced. Int.* **1992**, *24*, 437−462. (h) Ungaro. R.; Pochini, A. In *Frontiers in Supramolecular Organic Chemistry and Photochemistry*; Schneider, H.-J., Eds.; VCH: Weinheim, Germany, 1991; pp 57−81.

(2) Andreetti, G. D.; Ugozzoli, F.; Ungaro, R.; Pochini, A. In *Inclusion Compounds*; Atwood, J. L., Davies, J. E. D., MacNicol, D. D., Eds.; Oxford University Press: New York, 1991; Vol. 4, pp 64−125.

(3) Casnati, A.; Pochini, A.; Ungaro, R.; Ugozzoli, F.; Arnaud-Neu, F.; Fanni, S.; Schwing, M.-J.; Egberink, R. J. M.; de Jong, F.; Reinhoudt, D. N. *J. Am. Chem. Soc.* **1995**, *117*, 2767.

(4) Kumagai, H.; Hasegawa, M.; Miyanari, S.; Sugawa, Y.; Sato, Y.; Hori, T.; Ueda, S.; Kamiyama, H.; Miyano, S. *Tetrahedron Lett.* **1997**, *38*, 3972.

(5) (a) Casnati, A.; Ungaro, R.; Asfari, Z.; Vicens, J. In *Calixarenes 2001*; Asfari, Z., Böhmer, V., Harrowfield, J., Vicens, J., Eds.; Kluwer Academic Publishers: Dordrecht, Holland, 2001; pp 365−384. (b) Iki, N.; Morohashi, N.; Narumi, F.; Miyano, S. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 1597. (c) Iki, N.; Kumakai, H.; Morohashi, N.; Ejima, K.; Hasegawa, M.; Miyanari, S.; Miyano, S. *Tetrahedron Lett.* **1998**, *39*, 7559. (d) Hosseini, W. In *Calixarenes 2001*; Asfari, Z., Böhmer, V., Harrowfield, J., Vicens, J., Eds.; Kluwer Academic Publishers: Dordrecht, Holland, 2001.

(6) Lamare, V.; Dozol, J.-F.; Thuéry, P.; Nierlich, M.; Asfari, Z.; Vicens, J. *J. Chem. Soc., Perkin Trans. 2* **2001**, 1920.

(7) (a) Kim, J. S.; Lee, W. K.; Kim, J. G.; Suh, I. H.; Yoon, J. Y.; Lee, J. H. *J. Org. Chem.* **2000**, *65*, 7215. (b) Thuéry, P.; Nierlich, M.; Lamare, V.; Dozol, J.-F. Asfari, Z.; Vicens, J. *J. Inclusion Phenom. Macrocyclic Chem.* **2000**, *36*, 375. (c) Kim, J. S.; Suh, I. H.; Kim, J. K.; Cho, M. H. *J. Chem. Soc., Perkin Trans. 1* **1998**, 2307.

(8) Grün, A.; Csokai, V.; Parlagh, G.; Bitter, I. *Tetrahedron Lett.* **2002**, *43*, 4153.

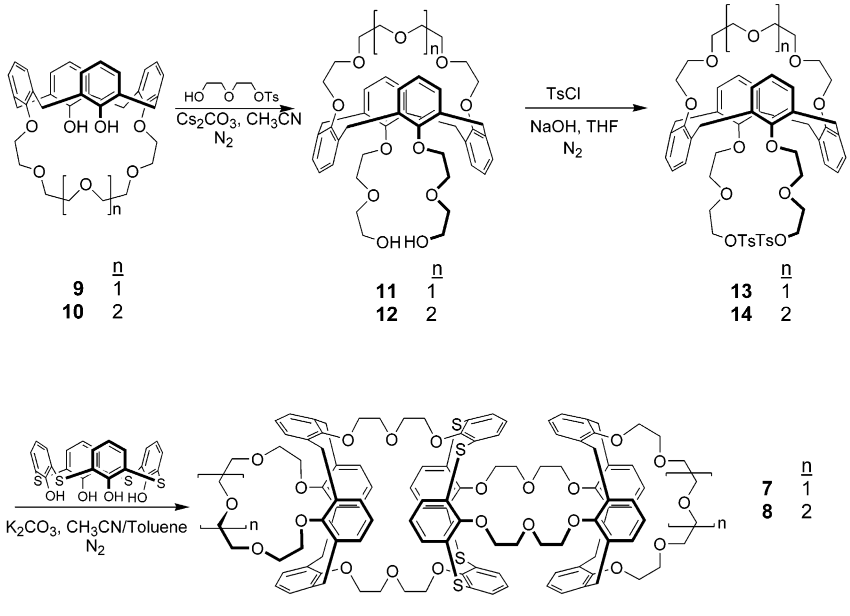
(9) Lee, J. K.; Kim, S. K.; Bartsch, R. A.; Vicens, J.; Miyano, S.; Kim, J. S. *J. Org. Chem.* **2003**, *68*, 6720.

(10) Koh, K. N.; Araki, K.; Shinkai, S.; Asfari, Z.; Vicens, J. *Tetrahedron Lett.* **1995**, *36*, 6095.

(11) Kim, J. S.; Yang, S. H.; Rim, J. A.; Vicens, J.; Shinkai, S. *Tetrahedron Lett.* **2001**, *42*, 8047.

10.1021/jo035567n CCC: $27.50

SCHEME 1. Synthetic Scheme for Calix-Thiacalix[4]crown Capsules 7 and 8



inter- and *intra*molecular metal−ligand exchange. These observations led chemists to prepare “polymeric calixarene *nano*-tubes” inside of which a metal ion shuttles feasibly.[12−14] Accordingly, we recently reported syntheses of crown ether-capped multimeric calix[4]tube consisting of two, three, four, or five conventional calix[4]crown repeating units and their metal-ion complexation behaviors to investigate the possibility of a metal-containing calix-*nano*wire.[15,16] In the case of tri-, tetra-, and pentameric calix[4]tubes, we could not observe the metal-ion shuttling because the calix linkers (spacers) between calix[4]crown-5 or between calix[4]crown-6 stoppers did not contribute to the cation complexation, suggesting that end-calixcrown stoppers are the only site to bind cations.[15,16]

With this aspect in mind, we have tried to synthesize a trimeric calix[4]crown system in which the thiacalix[4]arene unit independently recognizing metal ions was connected to two calix[4]crowns. Now we report the synthetic methods of **7** and **8** and silver-ion shuttling through the trimeric thiacalixcrown-6 tube.

Scheme 1 shows the synthetic route to trimeric calixthiacalix[4]crowns **7** and **8**. Calix[4]*mono*crown-5 (**9**)[17] and -6 (**10**)[17] were prepared by the reaction of calix[4]arene and poly(ethylene glycol) ditosylates in the presence of 1 equiv of K_2CO_3.[17] Attachment of the bisdiethyleneglycol unit onto the calix[4]*mono*crown with diethylene glycol monotosylate followed by tosylation gave **13**[15] and **14**[15] in quantitative yields. Subsequently, cyclization of thiacalix[4]arene with 2 equiv of calix ditosylates **13** and **14** in refluxing acetonitrile/toluene (1/1) with 3 equiv of Cs_2CO_3 as a base produced **7** and **8** in 34% and 33% yield, respectively. All calix[4]crown units in **7** and **8** were found to be in the 1,3-alternate conformation judging from NMR spectra: (1) a singlet at about δ 3.90 for methylenic protons of the ArCH_2Ar bridge in the ^{1}H NMR spectra and (2) a single at 38 ppm for the Ar*C*H_2Ar bridge carbons in the ^{13}C ^{1}H NMR spectra.

TABLE 1. Extractability of Cation Picrates by Ligands 5−8

	extractibility (%)								
ligand	Na^+	K^+	Rb^+	Cs^+	Ag^+	Sr^{2+}	Ba^{2+}	Pb^{2+}	NH_4^+
5	9.4	**157.7**	**143.8**	38.7	19.7	16.1	15.2	11.7	**109.7**
6	1.9	15	46.5	90.0	56.4	6.6	0.7	2.9	18.6
7	25.2	**150.7**	**143.5**	63.2	62.3	25.9	23.9	23.1	**104.5**
8	4.0	18.7	66.2	**107.9**	83.4	4.4	4.9	5.8	23.9

[a] Conditions: ligand, 0.1 mM/$ClCH_2CH_2Cl$; metal picrate, 0.2 mM/water. The intensities of the extracted picrates (λ_{max} = 373 nm) from the water into the organic layer were measured.

Extractabilities of a series of **5**−**8** for tested cations are summarized in Table 1. Compounds **5** and **7** preferentially form complexes with K^+, Rb^+, and NH_4^+ ions obviously because they have crown-5 loops suitable for those cations, as known for 1,3-alternate calix[4]crown-5 (**1**).[5] Similarly, compounds **6** and **8** both having crown-6 rings show a cesium-ion selectivity, which is also known for 1,3-alternate calix[4]crown-6 toward the Cs^+ ion.[5] In the case greater than 100% extractability, we speculate that dinuclear 1:2 (ligand/metal) complexes tend to form as indicated in Figure S1 (Supporting Information). Taking the size-agreement of the ligands with metal cations into account, extractabilities of **7** and **8** with the same central thiacalix are comparable to those of **5** and **6**, respectively. For the Ag^+ ion, however, **7** and **8** exhibit superior extractability to **5** and **6**, implying that the central thiacalix unit takes part in the Ag^+ ion complexation, which was evidenced by ^{1}H NMR spectra as well

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(12) Ikeda, A.; Shinkai, S. *J. Chem. Soc., Chem. Commun.* **1994**, 2375.

(13) Kanamathareddy, S.; Gutsche, C. D. *J. Org. Chem.* **1995**, *60*, 6070.

(14) Perez-Aldemar, J.-A.; Abraham, H.; Sanchez, C.; Rinassen, K.; Prados, P.; de Mendoza, J. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1009.

(15) Kim, S. K.; Sim, W.; Vicens, J.; Kim, J. S. *Tetrahedron Lett.* **2003**, *44*, 805.

(16) Kim, S. K.; Vicens, J.: Park, K. M.; Lee, S. S.; Kim, J. S. *Tetrahedron Lett.* **2003**, *44*, 993.

(17) Kim, J. S.; Lee, W. K.; Sim, W.; Ko, J. W.; Cho, M. H.; Ra, D. Y.; Kim, J. W. *J. Inclusion Phenom. Macrocyclic Chem.* **2000**, *37*, 359.

(see Figure S1). For divalent cations such as Pb^{2+}, Sr^{2+}, and Ba^{2+}, they were relatively seldom extracted.

Previously, we have reported that trimers **5**[15,16] and **6**[15,16] form mononuclear 1:1 and dinuclear 1:2 (ligand/metal) complexes with K^+ and Cs^+, respectively, but not 1:3 complexes. This is because the internal calix-polyether spacer cannot involve in metal ion complexation.[16] In a similar manner, trimeric calix-thiacalix[4]crown **8** is also observed to form a 1:2 complex with the Cs^+ ion as shown in Figure S1 (Supporting Information), demonstrating chemical shift changes of free **8** (Figure S1, A) in $CDCl_3$ upon addition of an excess amount of Cs^+pic^- (Figure S1, B), Ag^+pic^- (Figure S1, C), or both Cs^+pic^- and Ag^+pic^- (Figure S1, D).

Upon addition of excess Cs^+pic^-, most hydrogen peaks on the two end-crown-6 loops shift downfield and the doublet peaks corresponding to *meta*-H_b ($\Delta\delta = 0.07$) and *meta*-H_d ($\Delta\delta = 0.06$) shift downfield as well. For *meta*-H_e in the thiacalix spacer, however, the chemical shift change is hardly observed. In particular, the triplet peak of H_h on the calixcrown-6 stopper shifts downfield by $\Delta\delta = 0.27$, which is larger than that of H_k ($\Delta\delta = 0.13$) toward the central thiacalix unit, indicating that Cs^+ ions are encapsulated by the end-calixcrown-6 rings, but not by the central thiacalix spacer, which is supported by the solid-state structure of **8** prepared from the reaction with excess of $CsClO_4$ in dichloromethane (Figure S2, Supporting Information). On addition of excess Ag^+pic^-, however, the chemical shifts of *meta*-H_f and *para*-H_e on the thiacalix[4]arene unit shift markedly downfield compared to those of hydrogen atoms on calix units. In addition, the peaks of H_h and H_k on diethylene glycolic spacers broaden without splitting into two triplets. This indicates that the Ag^+ ion oscillates fast through the central thiacalix tube **8** even at room temperature (explained in more detail in Figure S3, Supporting Information).

To investigate if there is a metal-ion exchange or a 1:3 complex formation, ^1H NMR of a mixture of the metal complex has been run. Upon the addition of the Ag^+ ion to a solution of $\mathbf{8}\cdot 2Cs^+$, we observed the spectral pattern identical to those for $\mathbf{8}\cdot 2Cs^+$, implying that after the entrapping of the two Cs^+ ions by two crown-6 loops, the added Ag^+ ion cannot enter the central thiacalix[4]crown unit, presumably not only due to Cs^+-Ag^+ ion repulsion but also due to an allosteric effect. The reverse process (addition of the cesium ion to the solution of $\mathbf{8}\cdot Ag^+$, metal ion exchange) exhibits the same NMR pattern, leading us to conclude that the binding ability of crown-6 for the cesium ion is higher than that of the thiacalix spacer for the silver ion, which is consistent with the results of the two-phase extraction as mentioned above.

Figure S2 (Supporting Information) shows the X-ray crystal structure of the dinuclear complex $\mathbf{8}\cdot 2CsClO_4$ prepared by slow evaporation of methanol/dichloromethane solutions. $\mathbf{8}\cdot 2CsClO_4$ was crystallized in the monoclinic space group *C*2/*c* (Table S1, Supporting Information) and possesses an inversion center at the center of the compound. So an asymmetric unit consists of a half of the compound. As shown in Figure S2 (Supporting Information), two Cs^+ ions are encapsulated in each end-calix[4]crown-6 cavity of **8**. Each Cs^+ is coordinated to six oxygen atoms in the loop. The Cs^+-oxygen bond lengths range from 3.11 Å to 3.44 Å. Cation$-\pi$ interactions [$Cs^+\cdots C$ (*meta*) = 3.59 and 3.71 Å; $Cs^+\cdots C$ (*para*) = 3.54 Å] might give rise to an extra stabilization of the complex. The distance between two Cs^+ ions is 25.132 Å, indicating no direct interaction between the two Cs^+ ions. So, each calix[4]crown-6 cavity can independently play a role in binding with Cs^+ ions without being influenced by another Cs^+ ion encapsulated in the other calix[4]crown-6 cavity to form 1:2 (ligand/metal) complex.

Figure S3 (Supporting Information) shows variable-temperature ^1H NMR spectra of **8** in $CDCl_3$ upon addition of excess Ag^+pic^-. At 250 K, the *meta*-protons (H_f and H_f') of the thiacalix unit in the 1:1 complex shift downfield along with splitting from 7.51 to 7.59 (H_f) and 7.55 ppm (H_f'). It is probably noteworthy to mention that *meta*-H_d of the calix unit considerably shifts downfield by $\Delta\delta = 0.16$, which is larger than for H_f, meaning that the inverted benzene rings of the calix unit as well as those of the central thiacalix unit are involved in cation$-\pi$ interaction. As the temperature increases up to 300 K, two doublets for H_f and H_f' begin to coalesce and eventually become one sharp doublet. *meta*-Hydrogen atom peaks (H_d and H_d') of the calix unit also coalesce at 300 K. This coalescence temperature remains constant regardless of the metal ion concentrations (0.5, 0.75, and 1.0 equiv and the excess Ag^+ ion), which apparently indicates *intramolecular* metal-ion shuttling through the central thiacalix tube.[18] In the case of $\mathbf{8}\cdot 2Cs^+$ complex, however, we did not observe any peak-coalescence even at 330 K, indicating that Cs^+ is more tightly encapsulated by trimer **8** than is the Ag^+ ion. From these results, we can deduce that the silver ion oscillates much faster through the thiacalix-spacer than does the cesium ion through the calixcrown unit. To investigate an *intermolecular* silver-ion exchange mode, we took temperature-dependent ^1H NMR spectra of **8** with only 0.5 equiv of Ag^+ ion. However, no free-ligand peak is observed even at 230 K, which is unusual, but presumably the *intermolecular* exchange takes place below 230 K. This observation, in fact, appears to indicate differently: in metal ion exchange processes, the intramolecular process is known to be considerably more facile than the intermolecular one.[10]

In conclusion, novel calix-thiacalix[4]crown trimers possessing crown-5 and crown-6 were prepared. Their conformations and complexation behavior, characterized by X-ray diffraction and ^1H NMR spectroscopy, revealed that the Cs^+ ion is encapsulated in the end-crown rings by the 1:2 complexation ratio and the Ag^+ ion in the central thiacalix unit by the 1:1 ratio. Extractabilities of the calix-thiacalix[4]crown trimers **7** and **8** for Ag^+ are higher than those of conventional calix[4]crowns trimers **5** and **6**. Judging from the variable-temperature ^1H NMR spectra of the trimers $\mathbf{8}\cdot Ag^+$ complex, we could reach a conclusion that the silver ion oscillates through the central thiacalix spacer. With a further modification of the thiacalix[4]crowns, synthesis of function-enhanced polymeric calix-thiacalix[4]crown *nano-tube* inside of which silver ions can freely shuttle would be possible and is now in progress.

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[18] Ikeda, A.; Shinkai, S. *J. Am. Chem. Soc.* **1994**, *116*, 3102.

Experimental Section

Syntheses. Synthetic procedures and analytical data for compounds **7** (Data S1) and **8** (Data S2) are given in Supporting Information.

Two-Phase Extraction. Metal picrates were prepared by the reaction of picric acid with the appropriate metal carbonate.[19] To determine the extractability of the ligand for a metal picrate, an aqueous solution (2.0 mL) containing 0.20 mM metal picrate and a $ClCH_2CH_2Cl$ solution (2.0 mL) of the extractant (0.10 mM) were shaken for 30 min at 25 °C. The concentration of the picrate anion extracted from the aqueous phase into the organic layer was determined by UV spectrophotometry (λ_{max} = 373 nm). Three independent experiments were carried out for each combination of ligand and metal picrate. The extractability values listed in Table 1 are averages.

Acknowledgment. This research was supported by a grant from Dankook University (2003).

Supporting Information Available: Preparative procedures and analytical data (data S1−S2) for compounds **7** and **8** and additional figures (Figures S1−S3) and tables (Tables S1−S6) for **8**·$2CsClO_4$. This material is available free of charge via the Internet at http://pubs.acs.org.

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[19] Bartsch, R. A.; Yang, I. W.; Jeon, E. G.; Walkowiak, W.; Charewicz, W. A. *J. Coord. Chem*. **1992**, *27*, 75.