Synthesis and Hg^{2+}-Selective Ionophoric Properties of *p-tert*-Butylcalix[4]arene-aza-crown Ethers

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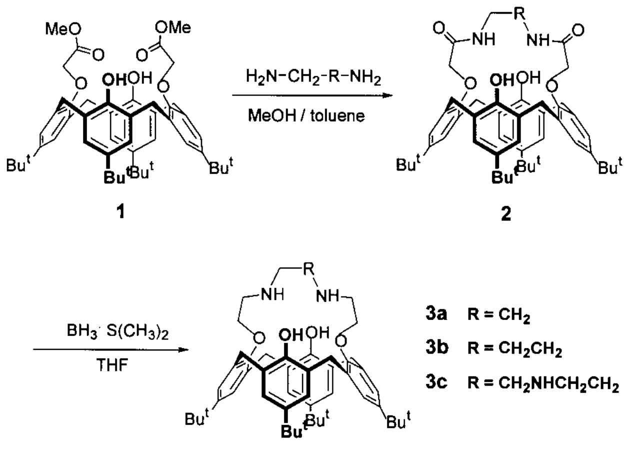
A series of new *p-tert*-butylcalix[4]arene aza-crown ethers has been prepared. They showed pronounced selective ionophoric properties in transport experiments toward Hg^{2+} ions among the heavy metal ions and Cu^{2+} ions among the transition metal ions surveyed. The calix[4]arene diaza-crown ethers are found to be relatively well optimized for the transport of Hg^{2+} ions.

The design of selective ionophores exploiting calixarene framework has been one of the most active research areas in supramolecular chemistry.[1] The ionophoric properties of specifically designed calixarene derivatives toward alkali and alkaline earth metal cations as well as some organic ionic substrates have been relatively well characterized.[2,3] However, their binding abilities toward transition metal and heavy metal ions are less well investigated.[4] To recognize these target ions, soft binding sites having large affinity for the guest ions must be employed. One possible candidate to this end is the introduction of nitrogen atoms into the ionophoric structure, which has been well verified by the classical examples of aza-crown ether systems. In fact, various attempts to introduce the aza binding sites into the calixarene framework by bridging with linkages containing nitrogen ligands have been made.[5–8] However, no systematic studies have been performed for the aza-analogues of the relatively well-studied calix-crown ether systems, in spite of the interesting structural properties of the resulting derivatives for the recognition of heavy metal or transition metal ions. We report here the synthesis and ionophoric properties of a series of new calix[4]arene-aza-crown ethers toward some heavy and transition metal ions.



1

2

3a R = CH_2
3b R = CH_2CH_2
3c R = $CH_2NHCH_2CH_2$

Scheme 1.

p-tert-Butylcalix[4]arene-aza-crown ethers for the binding of heavy metal ions have prepared following the procedure depicted in Scheme 1. Cyclic amides **2** were prepared by the reaction of dimethyl ester **1** with appropriate amines in toluene/MeOH mixture following the reported procedure.[9] Reduction of the amides **2** with $BH_3{\cdot}S(CH_3)_2$ in THF afforded the desired aza-crown ethers **3** in moderate yields.[10] To assess the optimized structures for the recognition of target metal ions, the skeleton of the aza-crown ether bridge was varied systematically by introducing two or three nitrogen atoms by the reaction with ethylenediamine, propylenediamine, or diethylenetriamine, respectively.

The ionophoric properties of the calix-aza-crown ethers **3** were investigated by the competitive transport experiments. Aqueous phase (HOAc/NaOAc buffer at pH 6) containing a mixture of representative heavy metal, transition metal, and alkaline earth metal acetates (Cd^{2+}, Hg^{2+}, Pb^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Mg^{2+}, Ca^{2+}, Sr^{2+}, and Ba^{2+}) was transported through chloroform liquid membrane by using a U-tube apparatus at 25 °C. After transport for 2 days, the amount of transported metal ions in the receiving phase was determined by means of the ICP-AES and the results are summarized in Table 1. The preliminary transport experiments of **3a** using distilled water as receiving phase revealed that the ionophores showed selective transport behavior toward Hg^{2+} ions. However, the transport efficiencies are not so satisfactory for the calix[4]arene-aza-crown ethers to act as an efficient carrier for the target metal ions. To increase the transport efficiency, receiving phase was modified with 0.2 M EDTA,[11] that is believed to assist the metal ion release at the interface between liquid membrane and receiving phase.

With EDTA solution as receiving phase, the calix[4]arene-aza-crown ethers **3** showed a pronouncedly enhanced and selective transport efficiency toward Hg^{2+} ion over other tested metal ions. Generally, the transport efficiency decreased in the sequence of $Hg^{2+} >> Pb^{2+} > Cd^{2+}$ among the heavy metal ions and $Cu^{2+} > Zn^{2+} > Ni^{2+} \approx Co^{2+}$ among the transition metal ions, with much higher preference for Hg^{2+} over Cu^{2+} ion. Diaza-crown ethers **3a** and **3b** showed much higher selectivity toward Hg^{2+} over Pb^{2+} and Cd^{2+} compared with **3c**. On the other hand, the expansion of the diaza-bridging unit by substitution of the central ethylene group of **3a** with propylene group of **3b** enhances somewhat the transport efficiency for the Hg^{2+} and Pb^{2+} ions without significantly affecting the efficiency for the rest of other metal ions. That enhances moderately the transport selectivity of **3b** toward Hg^{2+} ions. Interesting thing to note for triaza-crown ether **3c** is the increases in transport efficiency for the most of the transition metal ions compared with diaza-crown ethers **3a** and **3b**. That results in reduction of transport selectivity toward Hg^{2+} over other metal ions, which might be due to the presence of one extra nitrogen ligating atom in triaza-crown ether **3c**.

Table 1. Competitive transport of metal ions by *p-tert*-butylcalix[4]arene-aza-crown ethers[a]

Carrier	Metal ions transported /%											Receiving phase
	Hg^{2+}	Cd^{2+}	Pb^{2+}	Co^{2+}	Ni^{2+}	Cu^{2+}	Zn^{2+}	Mg^{2+}	Ca^{2+}	Sr^{2+}	Ba^{2+}	
3a	71.8	-[b]	0.25	-[b]	-[b]	3.00	-[b]	-[b]	0.41	-[b]	-[b]	0.2 M EDTA
3b	88.0	-[b]	2.48	-[b]	-[b]	3.50	-[b]	-[b]	0.23	-[b]	-[b]	0.2 M EDTA
3c	50.7	2.69	14.5	4.19	7.17	14.6	8.29	-[b]	0.47	-[b]	-[b]	0.2 M EDTA
3a	18.9	-[b]	-[b]	-[b]	-[b]	2.83	-[b]	-[b]	-[b]	-[b]	-[b]	H_2O

[a] Transport conditions. Source phase: 5 mmol of metal acetates in 5.0 mL of NaOAc/HOAc buffer (pH 6). Membrane phase: 0.05 mmol of carrier (15 mL of $CHCl_3$). Receiving phase: 5.0 mL of H_2O or 0.2 M EDTA. After transport experiments, the changes in pH of the receiving phase were found to be less than 0.5 pH unit. [b] Less than 0.2%.

To have a further insight for the ionophoric properties of the calix-aza-crown-ethers, ^1H NMR titration of the ligands **3** with $Hg(ClO_4)_2$ was performed in $CD_3OD/CDCl_3$ (1:1, v/v). Upon addition of Hg^{2+} ions, the resonances of ligands **3** are somewhat broadened and significantly shifted. In general, the most significant shifts are observed for the methylene protons bearing nitrogen atoms, that manifests the fact that the binding sites are preferentially comprised of the aza-crown moiety of the ionophores.[12] For **3b**, the most prominent changes are observed for the central part methylene protons of the aza-crown ethers ($\Delta\delta = 0.49$ and 0.43, respectively for the $NC\mathit{H}_2CH_2C\mathit{H}_2N$ and $NC\mathit{H}_2CH_2O$), while the methylene protons adjacent to the calix[4]arene phenol ether shifted less significantly ($\Delta\delta = 0.20$). The pronounced affinity of calix[4]arene-aza-crown ethers toward Hg^{2+} and Cu^{2+} ions is further confirmed by the FAB-MS measurements. The mass spectrum of ionophore **3b** under competitive condition with a mixture of $Hg(ClO_4)_2$ and $Cu(ClO_4)_2$ in *m*-nitrobenzyl alcohol (*m*-NBA) revealed prominent peaks at $m/z = 975.7$ and 836.5 corresponding to the complexes of $[\mathbf{3b}\text{-H+Hg}]^+$ and $[\mathbf{3b}\text{-H+Cu}]^+$, respectively. The relative strength of the complex semi-quantitatively estimated from the ratio of $[\mathbf{3b}\text{-H+Hg}]^+/[\mathbf{3b}\text{-H+Cu}]^+$ is assessed to be larger than 4.6 in preference for Hg^{2+} ion over Cu^{2+}, that is parallel to the transport behaviors.

In summary, the calix[4]arene-aza-crown ethers having two aza-ligating sites showed prominent ionophoric properties toward Hg^{2+} ions in competitive transport experiments and the ionophores **3a** and **3b** are found to be relatively well optimized for the transport of Hg^{2+} ions. The investigated calix[4]arene-aza-crown ethers might have potential uses as a carrier for the effective removal of the toxic Hg^{2+} ions from the waste streams to protect the environment.

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References and Notes

1 C. D. Gutsche, "Calixarenes Revisited," Royal Society of Chemistry, Cambridge (1998).

2 V. Böhmer, *Angew. Chem., Int. Ed. Engl.*, **34**, 713 (1995).

3 A. Ikeda and S. Shinkai, *Chem. Rev.*, **97**, 1713 (1997).

4 S. Blanchard, L. L. Clainche, M.-N. Rager, B. Chansou, J.-P. Tuchagues, A. F. Duprat, Y. L. Mest, and O. Reinaud, *Angew., Chem. Int. Ed.*, **37**, 2732 (1998).

5 B. Pulpoka, Z. Asfari, and J. Vicens, *Tetrahedron Lett.*, **37**, 8747 (1996).

6 T. Tuntulani, V. Ruangpornvisuti, N. Tantikunwatthana, O. Ngampaiboonsombut, R. Seangprasertkij-Magee, Z. Asfari, and J. Vicens, *Tetrahedron Lett.*, **38**, 3985 (1997).

7 A. Ikeda, T. Tsudera, and S. Shinkai, *J. Org. Chem.*, **62**, 3568 (1997).

8 V. Böhmer, G. Ferguson, J. F. Gallagher, A. J. Lough, M. A. McKervey, E. Madigan, M. B. Moran, J. Phillips, and G. Williams, *J. Chem. Soc., Perkin Trans. 1*, **1993**, 1521.

9 R. Ostaszewski, T. W. Stevens, W. Verboom, D. N. Reinhoudt, and F. M. Kaspersen, *Recl. Trav. Chim. Pays-Bas*, **110**, 294 (1991).

10 Selected data for **3a**: yield 43%; mp 268 °C; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.075 (s, 4H), 7.021 (s, 4H), 4.278 (d, J = 12.9 Hz, 4H), 4.233 (br t, J = 3.9 Hz, 4H), 3.404 (d, J = 12.9 Hz, 4H), 3.329 (br t, J = 3.9 Hz, 4H), 3.169 (s, 4H), 1.218 (s, 18H), 1.182 (s, 18H); MS (FAB, *m*-NBA): Found: *m/z* 761.5. Calcd for $C_{50}H_{69}N_2O_4$: $(M+H)^+$, 761.5. For **3b**: yield 40%; mp > 257 °C; ^1H NMR ($CDCl_3$, 300 MHz) δ 8.010 (br s, 2H), 7.059 (s, 4H), 6.912 (s, 4H), 4.330 (d, J = 12.9 Hz, 4H), 4.194 (t, J = 4.2 Hz, 4H), 3.359 (d, J = 12.9 Hz, 4H), 3.242 (t, J = 4.2 Hz, 4H), 3.041 (t, J = 6 Hz, 4H), 1.92 (m, 2H), 1.268 (s, 18H), 1.035 (s, 18H); MS (FAB, *m*-NBA): Found: *m/z* 775.5. Calcd for $C_{51}H_{71}N_2O_4$: $(M+H)^+$, 775.5. For **3c**: yield 39%; mp 273 °C; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.087 (s, 4H), 6.764 (s, 4H), 4.336 (d, J = 13.2 Hz, 4H), 4.128 (br t, 4H), 3.326 (d, J = 13.2 Hz, 4H), 3.169 (br t, 4H), 2.910 (br m, 8H), 1.308 (s, 18H), 0.913 (s, 18H); MS (FAB, *m*-NBA): Found: *m/z* 804.5. Calcd for $C_{52}H_{74}N_3O_4$: $(M+H)^+$, 804.6.

11 T. Hayashita, in "Chemical Separations with Liquid Membranes," ed. by R. A. Bartsch and J. D. Way, ACS Symposium Series 642, ACS, Washington, D.C. (1996), p. 303.

12 Although the phenolic OH groups of calix[4]arene play an important role in the complex formation, the exact nature of participation of **3** is not clear at the moment. We think that the phenolic units mainly remained in OH form in the complex at the present condition of pH 6. However, the observation of new band around 320 nm in the UV titration of **3b** with 5 equiv of $Hg(OAc)_2$ in $CHCl_3/MeOH$ (1:1, v/v) mixture suggests that a part of the phenolic OH groups is deprotonated upon interaction with Hg^{2+} ions. (J. W. Cornforth, E. D. Morgan, K. T. Potts, and R. J. W. Rees, *Tetrahedron*, **29**, 1659 (1973)).