# Selective Extraction of Silver Ion with Proton-Switchable Calix[4]arene

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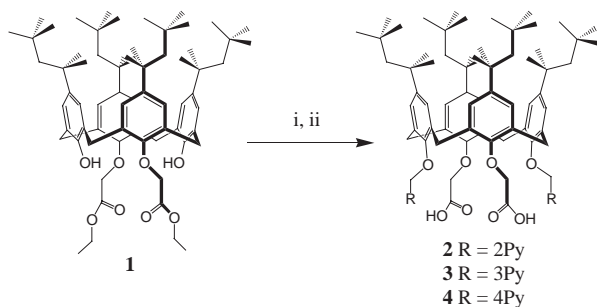[†]*Institut für Anorganiche Chemie, der Technischen Universität Dresden, Mommsenstrasse 13, D-01062, Dresden, Germany*

New pyridine-functionalized proton-switchable calix[4]-arenes were synthesized to investigate extraction properties, and performed good extractability toward silver ion in acidic solution.

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Calix[*n*]arenes are synthetic phenolic cyclic compounds obtained by the condensation of phenol and formaldehyde. Calix[4]arene has a cavity with small size and is capable of taking four conformational isomers; "cone," "partial cone," "1,2-alternate", and "1,3-alternate."[1] Since calix[4]arenes provide a preorganized coordination site for guest molecule or ion, chemically modified calix[4]arenes have been prepared and used as molecular recognition reagents in the fields of analytical and separation chemistry.[2] Calix[4]arene carboxylates are ion-exchangeable compounds and one of well-studied calix[4]-arenes.[3–6] Calix[4]arene tetracarboxylate binds metal ion more strongly than dicarboxylate,[4,5] monocarboxylate[5] and corresponding monomer[6] because of the preorganized coordination site and strong binding property of the carboxyl groups. When neutral nonionizable functional groups are additionally introduced into residual phenolic oxygens,[7] carboxyl groups act as anionic functioinal groups to neutralizing the metal charge, although calix[4]arene dicarboxylate itself only weakly binds metal ion. High affinity to silver ion of 2-pyridinocalix[4]arene had been reported.[8] Therefore calix[4]arene with the combination of two carboxylic acids and two 2-pyridyl groups is expected to show high silver ion affinity. Now we report the synthesis and silver extraction with pyridine-based proton-switchable calix[4]-arenes.

The *p-tert*-octylcalix[4]arene was prepared according to a manner similar to that described by Gutsche et al.[9] Calix[4]-arenes **2**, **3**, and **4** were synthesized from 1,3-diester calix[4]-arene **1**[10] shown in Figure 1. The splitting pattern of the ArCH_2-Ar protons in $^1$H NMR spec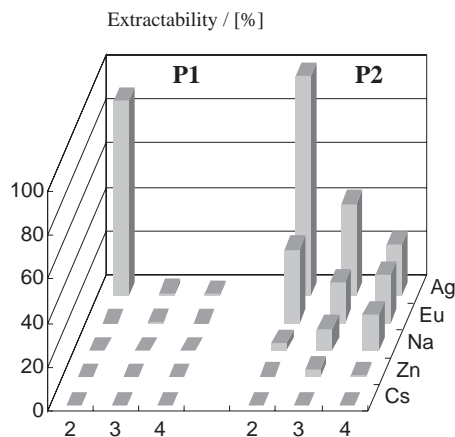troscopy for calix[4]arenes **2**, **3**, and **4** shows a pair of doublet which means these compounds are in cone conformation. Since compounds **2**, **3**, and **4** possess two soft pyridine moieties and two hard carboxylic acid groups at each distal position, the extraction of both soft and hard metal ions is expected. The pyridine moieties act as a coordination site for soft metal like $Ag^+$ and carboxylic acid groups release $H^+$ to keep the neutrality. In general, extraction of metal ions with pyridine-containing extractants is influenced with the change of pH, mostly around pH = 5 where the deprotonation of the pyridine nitrogen takes place ($pK_a$(pyridine) = 5.25).[11]

The extraction studies were performed at $25 \pm 1\,^\circ$C in $2\,cm^3$ microreaction vials by means of mechanical shaking. The phase ratio $V$(org):$V$(w) was 1:1 ($0.5\,cm^3$ each); the shaking time was 30 min. The extraction equilibrium was attained within a few minutes. The determination of the metal concentration in both phases was carried out radiometrically with the $\gamma$ radiation measurement of $^{22}$Na, $^{65}$Zn, $^{110m}$Ag, $^{137}$Cs, and $^{152}$Eu in a NaI(Tl) scintillation counter (CobraII, Canberra-Packard) and the distribution ratios ($D = [Ag^+]_{org.} / [Ag^+]_{aq}$) were calculated. The radioisotopes were supplied by Medgenix Diagnostics GmbH, Ratingen.
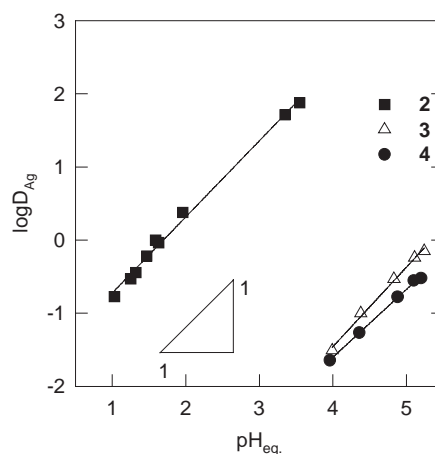


**Figure 2.** Extraction of silver ion with **2**, **3**, and **4** as a function of pH. $[AgNO_3] = 0.1\,mmol\,dm^{-3}$, [calixarene] = $1\,mmol\,dm^{-3}$ in chloroform, pH adjusted by $HNO_3$ and HEPES.

Figure 2 shows the influence of pH on $Ag^+$ extraction with **2**, **3**, and **4**. The slopes of the log $D$–pH diagrams are neary 1 which mean that the extraction takes place as ion-exchange mechanism. 2-Pyridyl derivative **2** showed high extractability in lower pH region, while **3** and **4** showed relatively lower extractability under the studied condition. The difference in extraction behavior is based on both of the nitrogen position in pyridine moiety and a structural effect of calix[4]arene. Owing to the strong interaction between 2-pyridine and $Ag^+$, **2** extracts



**Figure 1.** Synthetic routes and chemical structures of extractants i) *n*-Chloromethyl pyridine (*n* = 2, 3, 4), NaH, DMF; ii) H$^+$.

**2** R = 2Py
**3** R = 3Py
**4** R = 4Py

Extractability / [%]



**Figure 3.** Extractability of different metal ions with **2**, **3**, and **4**. [M] = 0.1 mmol dm$^{-3}$, [calixarene] = 1 mmol dm$^{-3}$ in chloroform, **P1**: 5 mmol dm$^{-3}$ HClO$_4$ (pH = 2.3). **P2**: 0.1 mol dm$^{-3}$ HEPES (pH = 5.3).

Ag$^+$ strongly as a result. On the other hand, the pyridine groups in 3-pyridyl derivative **3** and 4-pyridyl derivative **4**, were very weakly interacted with Ag$^+$ in comparison with **2**. The structural effect of calixarene is not effective for **3** and **4**, because pyridine nitrogens are positioned outer of calixarene cavity.

Compounds **2**, **3**, and **4** bear two carboxylic acids which interact with metal ions, extraction of monovalent (Na$^+$, Cs$^+$), divalent (Zn$^{2+}$) and trivalent (Eu$^{3+}$) metal ions were carried out at two selected points; P1 and P2. These metals are selected from the reasons of size differences (Na$^+$, Cs$^+$) and charge differences (Zn$^{2+}$, Eu$^{3+}$). As shown in Figure 3, higher extractabilities for all studied metals are observed at P2 than P1. This result means that the extraction of metal ions with **2**, **3**, and **4** takes place on the basis of ion-exchange mechanism. For compound **2**, high selectivity is observed for Ag$^+$ over Cs$^+$, Zn$^{2+}$, Na$^+$, and Eu$^{3+}$ in both conditions, particularly at P1. Because of the weak participation of 3-positional-pyridine nitrogens in complexation, weak selectivity to Ag$^+$ is observed for compound **3**. 4-Positional-pyridine nitrogens are not effective for selective complexation at all. And the residual carboxylic acids participate in complexation with metal ions. A reverse order of extractability was observed on Na$^+$ extraction at P2. According to the HSAB theory, sodium ion is classified as hard acid and pyridine nitrogen is as soft base. Since pyridine nitrogens in **2** suppress the complexation with sodium ion, lower extractability was observed.

In conclusion, 2-pyridine-based proton-switchable calix[4]-arene extracts silver ion selectively. The extraction of metal ions takes place via ion-exchange mechanism was found for all calixarene studied. The origin of the high selectivity toward silver ion is a structural effect of 2-pyridine-based calix[4]arene. Further investigation of the extraction properties with this class of calix[4]arenes is in progress.

**References and Notes**

1    "Calixarenes 2001," ed. by Z. Asfari, V. Boehmer, J. M. Harrowfield, and J. Vicens, Kluwer Academic Publishers, the Netherlands (2001).

2    a) A. Ikeda and S. Shinkai, *Chem. Rev.*, **97**, 1713 (1997). b) R. Ludwig, *Fresenius' J. Anal. Chem.*, **367**, 103 (2000).

3    a) R. M. Izatt, J. D. Lamb, R. T. Hawkins, P. R. Brown, S. R. Izatt, and J. J. Christensen, *J. Am. Chem. Soc.*, **105**, 1782 (1983). b) S. R. Izatt, R. T. Hawkins, J. J. Christensen, and R. M. Izatt, *J. Am. Chem. Soc.*, **107**, 63 (1985). c) G. Montavon, G. Duplatre, N. Barakat, M. Burgard, Z. Asfari, and J. Vicens, *J. Inclusion Phenom. Mol. Recognit. Chem.*, **27**, 155 (1997). d) N. Barakat, M. Burgard, Z. Asfari, J. Vicens, G. Montavon, and G. Duplatre, *Polyhedron*, **17**, 3649 (1998).

4    N. T. K. Dung and R. Ludwig, *New J. Chem.*, **23**, 603 (1999).

5    F. Arnaud-Neu, G. Barrett, S. J. Harris, M. Owens, M. A. McKervey, M. J. Schwing-Weill, and P. Schwinte, *Inorg. Chem.*, **32**, 2644 (1993).

6    a) K. Ohto, M. Yano, K. Inoue, T. Yamamoto, M. Goto, F. Nakashio, S. Shinkai, and T. Nagasaki, *Anal. Sci.*, **11**, 893 (1995). b) K. Ohto, M. Yano, K. Inoue, T. Nagasaki, M. Goto, F. Nakashio, and S. Shinkai, *Polyhedron*, **16**, 1655 (1997). c) K. Ohto, K. Fujimoto, and K. Inoue, *Anal. Chim. Acta*, **387**, 61 (1999).

7    M. Ogata, K. Fujimoto, and S. Shinkai, *J. Am. Chem. Soc.*, **116**, 4505 (1994).

8    a) A. F. Danil de Namor, O. E. Piro, L. E. Pulcha Salazar, A. F. Aguilar Cornejo, N. Al Rawi, E. E. Castellano, and F. J. Sueros Velarde, *J. Chem. Soc., Faraday Trans.*, **94**, 3097 (1998). b) K. Ohto, H. Higuchi, and K. Inoue, *Solvent Extr. Res. Dev., Jpn.*, **8**, 37 (2001). c) H. Higuchi, T. Shinohara, T. Oshima, K. Ohto, and K. Inoue, *Ars Separatoria Acta*, **1**, 99 (2002). d) K. Shimojo and M. Goto, *Chem. Lett.*, **33**, 320 (2004).

9    C. D. Gutsche and M. Iqbal, *Org. Synth.*, **68**, 234 (1989).

10   General experimental procedure: Under a N$_2$ stream, compound **1** (5.00 g, 4.78 mmol) and NaH (62.7% in oil, 1.50 g, 40.9 mmol) were mixed in DMF cooled in an ice bath. The mixture was stirred for 1 h at room temperature and the DMF solution of 2-chloromethylpyridine (38.4 mmol) was added dropwise with cooling in an ice bath. The reaction mixture was stirred at room temperature for 23 h. After the mixture was cooled, excess NaH was decomposed with ethanol. The reaction mixture was concentrated under reduced pressure. This was dissolved in chloroform and washed with 1 M HCl and water. The chloroform phase was dried over anhydrous MgSO$_4$. The chloroform was removed by evaporation, residue being recrystallized from hexane: **2**, yield 57.8%, $^1$H NMR (CDCl$_3$, 298 K) $\delta$ 0.53 and 0.74 (C(CH$_3$), s each, 18H each), 0.93 and 1.29 (C(CH$_3$)$_2$, s each, 12H each), 1.41 and 1.65 (C–CH$_2$–C, s each, 4H each), 3.05 and 4.20 (ArCH$_2$Ar, d each (J = 12.9 Hz), each, 4H each), 4.54 (OCH$_2$CO, s, 4H), 5.01 (OCH$_2$Py, s, 4H), 6.63 and 7.00 (ArH, s each, 4H each), 7.29, 7.30, 7.68, and 8.59 (PyH, d, t, t, d, respectively, 2H each). Anal. Found: C, 77.86; H, 8.87; N, 2.67%. Calcd for C$_{76}$H$_{102}$N$_2$O$_8$:C, 77.91; H, 8.77; N, 2.39%. **3**, Recrystallized from ethanol: yield 56.0%, $^1$H NMR (CDCl$_3$, 298 K) $\delta$ 0.55 and 0.74 (C(CH$_3$), s each, 18H each), 0.85 and 1.32 (C(CH$_3$)$_2$, s each, 12H each), 1.39 and 1.67 (C–CH$_2$–C, s each, 4H each), 2.89 and 3.92 (ArCH$_2$Ar, d each (J = 12.9 Hz), 4H each), 4.57 (OCH$_2$CO, s, 4H), 5.02 (OCH$_2$Py, s, 4H), 6.58 and 7.02 (ArH, s each, 4H each), 7.25, 7.57, 8.31, and 8.62 (PyH, t, d, s, d, respectively, 2H each). Anal. Found: C, 76.31; H, 8.57; N, 2.61%. Calcd for C$_{76}$H$_{102}$N$_2$O$_8$:C, 77.91; H, 8.77; N, 2.39%. **4**, Recrystallized from ethanol: yield 75.4%, $^1$H NMR (CDCl$_3$, 298 K) $\delta$ 0.55 and 0.74 (C(CH$_3$), s each, 18H each), 0.87 and 1.32 (C(CH$_3$)$_2$, s each, 12H each), 1.40 and 1.67 (C–CH$_2$–C, s each, 4H each), 2.94 and 4.04 (ArCH$_2$Ar, d each (J = 12.9 Hz), 4H each), 4.59 (OCH$_2$CO, s, 4H), 4.96 (OCH$_2$Py, s, 4H), 6.60 and 7.02 (ArH, s each, 4H each), 7.16, and 8.56 (PyH, d, d, respectively, 4H each). Anal. Found: C, 76.18; H, 8.86; N, 2.19%. Calcd for C$_{76}$H$_{102}$N$_2$O$_8$:C, 77.91; H, 8.77; N, 2.39%.

11   H. Stephan, T. Krueger-Rambusch, K. Gloe, W. Hesse, B. Ahlers, K. Cammann, K. Rissanen, G. Brodesser, and F. Voegtle, *Chem.—Eur. J.*, **4**, 434 (1998).