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(2-Pyridylmethoxy)calixarenes: New Versatile Ionophores for Metal Extraction

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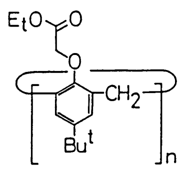
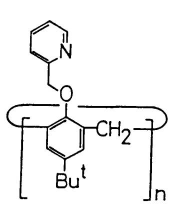
Synopsis. (2-Pyridylmethoxy)calix[*n*]arenes (n=6,8) were newly synthesized. It was shown in two-phase solvent extraction that they can extract not only alkali metal cations but Cu^{2+}, Ag^+, and UO_2^{2+} and are stable even at high pH. The results indicate that disadvantages of calixarene esters, which were previously developed as calixarene-based ionophores, can be improved by using the pyridyl group.

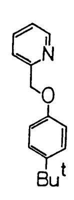
"Calixarenes" are cyclic oligomers made up of benzene units.[1,2] It has been expected, therefore, that introduction of appropriate ionophoric groups would append, like that of crown ethers, a new function as ionophores to calixarenes. Several groups have reported on the ionophoric properties of calixarenes which were obtained by introducing ester, ether, and amide groups into the edge of the cylindrical architecture.[3–9] Among them ester derivatives (**1*n***) have been studied most extensively.[3–7] We noticed through our work,[7,10] however, that there exist two inevitable disadvantages about **1*n***: (i) cannot be used at high pH region because of basic hydrolysis of the ester groups and (ii) **1*n*** can extract only "hard" metal cations because of the "hard" ionophoric nature. We considered that the defects might be removed by introducing nitrogen base (instead of oxygen base) through the ether linkage (instead of the ester linkage). In order to use them at neutral pH region, aromatic amines with low pK_a values are recommended rather than aliphatic amines with high pK_a values. We thus designed new ionophores **2*n*** in which 2-pyridylmethyl groups are appended to the calixarene cavity. We have found that **2*n*** can extract not only alkali metal cations but other heavy metal cations and are stable even at high pH.



1n



2n



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Experimental

37,38,39,40,41,42-Hexakis(2-pyridylmethoxy)-*p*-*t*-butylcalix[6]arene (2₆). *p*-*t*-Butyl calix[6]arene (1.0 g; 1.0 mmol), 2-chloromethylpyridine hydrochloride (2.1 g; 13 mmol), and powdered K_2CO_3 (7.0 g) were mixed in 70 mL of anhydrous *N,N*-dimethylformamide (DMF), and the mixture was heated at 60—70 °C for 14 h under a nitrogen stream. The solution was diluted with water, the precipitate being collected by filtration. This was dissolved in 100 mL of chloroform and washed with water. The chloroform solution was concentrated in vacuo and the residual oil was crystallized from methanol. Finally, the product (**2₆**) was recrystallized from chloroform-methanol; mp (decomp) 268 °C, yield 45%; IR (Nujol) no ν_{OH}, $\nu_{C=N}$ 1565 cm^{-1}. ^1H NMR ($CDCl_3$): δ=1.05 (9H, s, *t*-Bu), 3.9 (2H, broad s, $ArCH_2Ar$), 4.84 (2H, s, OCH_2), 7.0, 7.3, 8.3 (6H, broad, benzene and pyridine protons). Found: C, 79.87; H, 7.47; N, 5.43%. Calcd for $(C_{17}H_{19}NO)_6$: C, 80.60; H, 7.56; N, 5.53%.

49,50,51,52,53,54,55,56-Octakis(2-pyridylmethoxy)-*p*-*t*-butylcalix[8]arene (2₈). This compound was synthesized from *p*-*t*-butylcalix[8]arene in a manner similar to that described for **2₆**; mp 151—152 °C, yield 24%; IR (Nujol) no ν_{OH}, $\nu_{C=N}$ 1565 cm^{-1}. ^1H NMR ($CDCl_3$): δ=1.03 (9H, s, *t*-Bu), 4.05 (2H, s, $ArCH_2Ar$), 4.74 (2H, s, OCH_2), 6.99 (2H, s, benzene protons), 6.81, 7.00, 7.11, 8.28 (1H each, q, d, q, and d, respectively, pyridine protons). Found: C, 79.90; H, 7.55; N, 5.34%. Calcd for $(C_{17}H_{19}NO)_8$: C, 80.60; H, 7.56; N, 5.53%. The reaction of *p*-*t*-butylcalix[4]arene and 2-chloromethylpyridine under the same reaction conditions afforded di-substituted *p*-*t*-butylcalix[4]arene and no tetrasubstituted product. This is attributed to steric crowning in a small calix[4]arene ring. Thus, subsequent extraction experiments were carried out about **2₆** and **2₈**.

The methods of two-phase solvent extraction were described previously.[3–5,11] The detailed extraction conditions were recorded in footnotes to Table 1. In some cases we determined both the concentration of extracted metal cations (by atomic absorption spectroscopy) and that of extracted picrate anion (by absorption spectroscopy). At acidic to neutral pH region the concentration of picrate anion was always higher than those of metal cations. This shows that picrate anion is extracted, in part, as a counteranion of pyridinium cation. In contrast, these two values showed a good agreement (error less than 4%) in extraction from 0.1 M MOH aqueous solution.

The stability of **1₆** and **2₆** against basic hydrolysis was evaluated as follows. A CH_2Cl_2 solution containing **1₆** or **2₆** (2.5×10^{-4} M†) was shaked at 25 °C for one day with a same amount of an aqueous 0.1 M NaOH solution. The CH_2Cl_2 solution containing **2₆** separated clearly from the aqueous phase. We could recover **2₆** (>99%) from the CH_2Cl_2 solution. On the other hand, a considerable amount of white precipitates was formed at the interface between water and **1₆**-containing CH_2Cl_2. They were collected by filtration, acidified by 0.1 M HCl , and extracted with $CHCl_3$. This compound turned out to be 37,38,39,40,41,42-hexakis(carboxymethoxy)-*p*-*t*-butylcalix[6]arene[11] (yield 5%). From the CH_2Cl_2 phase we recovered **1₆** (90%).

Results and Discussion

We first compared the stability of **2*n*** and **1*n*** in solvent extraction from a strongly basic aqueous phase. It was shown that **2₆** is totally stable against basic hydrolysis whereas **1₆** is hydrolyzed to the carboxylate derivative. Thus, calixarene esters **1*n*** are recommended only for the short-period extraction. Interestingly, we could not recover any partly-hydrolyzed carboxylate derivatives from **1₆**. This implies that once the hydrolysis takes place at one

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† 1 M=1 mol dm^{-3}.

ester unit, subsequent hydrolysis in the same calixarene ring occurs acceleratively. Presumably, partly-hydrolyzed carboxylate derivatives, which are less soluble in CH_2Cl_2, are adsorbed at the water-CH_2Cl_2 interface and subsequent hydrolysis occurs rapidly thereabout.

In order to estimate the "basicity" of **2**$_n$ and **3** (*p*-(2-pyridylmethoxy)-*t*-butylbenzene: used as a reference compound) at a water-CH_2Cl_2 interface, we carried out picrate extraction as a function of pH. Since sodium picrate was not extracted by **2**$_n$ under the conditions employed (see a caption to Fig. 1), the concentration of extracted picrate anions should be equal to that of protonated pyridine (i.e., pyridinio) units. As shown in Fig. 1, pH-Ex% curves for **2**$_n$ shift to higher pH region than that for **3** (4.1 pH unit for **2**$_6$ and 2.5 pH unit for **2**$_8$) Thus, the "basicity" of **2**$_n$ is considerably strengthened because of the cyclic architecture. This suggests that calixarenes **2**$_n$, in which basic pyridine groups are arranged on the lower rim of the calixarene cavity, have a character of proton cryptates.

Results of two-phase solvent extraction of alkali picrates are summarized in Table 1. Under the present extraction conditions (0.1 M MOH in the aqueous phase) the concentration of extracted picrates was equal to that of M^+ ions, which was confirmed by the separate determinations of [picrate] by absorption spectroscopy and [M^+] by atomic absorption spectroscopy. The previous extraction study with **1**$_n$ established that (i) **1**$_6$ has the extraction ability greater than **1**$_8$ for alkali metal cations and (ii) the order of the ion selectivity is $Cs^+>K^+>Na^+$ for **1**$_6$ and $Cs^+\approx K^+>Na^+$ for large, flexible **1**$_8$.[3,5] Examination of Table 1 reveals that both **2**$_6$ and **2**$_8$ are Cs^+-selective and **2**$_6$ gives the greater Ex% than **2**$_8$ Thus, the size effect operating in **2**$_n$ is basically comparable with that operating in **1**$_n$. As expected, calixarenes **2**$_n$ are capable of extracting heavy metal cations such as Ag^+ and Cu^{2+}. In particular, extraction of Cu^{2+} is ascribed to the affinity of Cu^{2+} with pyridine nitrogens.

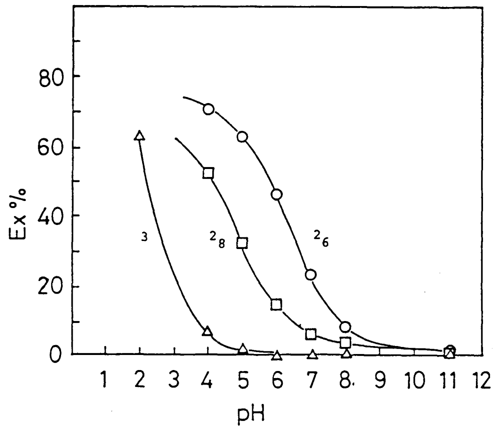

Fig. 1. Extraction of picrate anion by **2**$_n$ and **3** at 25 °C: 2.5×10^{-4} M **2**$_n$ or 2.0×10^{-3} M **3** (=8·[**2**$_n$]) in CH_2Cl_2, 2.5×10^{-4} M picric acid and $[Na^+]$=0.02 M in water. pH of the aqueous phase was adjusted by 0.02 M acetate buffer for pH 4—5, 0.02 M phosphate buffer for pH 6—8, and NaOH for pH 11. Under the conditions Na^+ was not extracted into the CH_2Cl_2 phase (confirmed by the analysis of the CH_2Cl_2 phase by atomic absorption spectroscopy).

Table 1. Extraction (%) of Metal Picrates in CH_2Cl_2 at 25 °C[a)]

Metal	Calixarene	
	2$_6$	**2**$_8$
Na^+[b)]	12.7	9.3
K^+[b)]	26.7	7.5
Cs^+[b)]	51.0	18.2
Ag^+[c)]	21.2	24.0
Cu^{2+}[c)]	3.3	1.8
UO_2^{2+}[d)]	0	5.4
UO_2^{2+}[d)] (at 100 °C)	82.1	76.8

a) 2.5×10^{-3} M calixarene in CH_2Cl_2. Extraction time 30 min. b) 2.5×10^{-4} M picric acid in aqueous 0.1 M MOH and 0.5 M MCl. Extractability denotes the percentage of picrate anion extracted by **2**$_n$. c) 2.5×10^{-3} M picric acid in aqueous 5×10^{-4} M metal nitrates at pH 11 (with 1.00×10^{-2} M NH_3) for Ag^+ and at pH 8.0 (with 1.00×10^{-2} M Bis-Tris) for Cu^{2+}. Extractability denotes the percentage of metal cations extracted by **2**$_n$ (determined by atomic absorption spectroscopy). d) 1.0×10^{-4} M calixarene in *o*-dichlorobenzene. 2.0×10^{-5} M $UO_2(CH_3COO)_2$ in aqueous buffer solution (pH 8.0 with 0.01 M *N*-tris(hydroxymethyl)methyl-3-amino-1-propanesulfonate). Extractability denotes the percentage of UO_2^{2+} extracted by **2**$_n$ (calculated by the analysis of UO_2^{2+} remaining in the aqueous phase with Arsenazo III): for details of the extraction method see Ref. 11.

We previously found that among calix[*n*]arenes (*n*=4, 5, and 6) calix[5]arene and calix[6]arene derivatives complex UO_2^{2+} selectively.[11,12] The finding is quite complementary with the X-ray crystallographic data that UO_2^{2+} complexes adopt either a pseudo-planar pentacoordinate or hexacoordinate structure.[11,12] This implies that the structure of these calixarenes is well pre-organized for selective complexation of UO_2^{2+}. We applied **2**$_n$ to solvent extraction of UO_2^{2+}. The rate of UO_2^{2+} extraction was slow at 25 °C. In particular, **2**$_6$ scarcely extracted UO_2^{2+} (see Table 1). On the other hand, efficient UO_2^{2+} extraction took place at 100 °C. It is known that the association of cyclic ligands with large, rod-like UO_2^{2+} ion occurs very slowly because of steric hindrance.[13—15] In the present system the ring structure of **2**$_6$ is expected to be rigid because of six pyridyl groups incorporated into the narrow lower rim of calix[6]arene. This view is supported not only by Corey-Pauling-Koltun molecular models but also by the broadened ^1H NMR spectrum (see Experimental). This suggests that the extraction speed with **2**$_6$ would be fairly slow at room temperature. On the other hand, **2**$_6$ and **2**$_8$ served as excellent neutral uranophiles at high temperature. This is related to the increase in the thermal molecular motion of these calixarenes. The high extractability observed for **2**$_6$ is rationalized in terms of the pre-organized structure suitable for the binding of hexacoordinate UO_2^{2+}. Although **2**$_8$ does not possess such a pre-organized structure, the ring is flexible enough to employ either a pentacoordinate or a hexacoordinate structure. Presumably, the UO_2^{2+} affinity observed for $\mathbf{2}_8$ is accounted for by "induced-fit" complexation with the large calixarene ring. In fact, the ^1H NMR peaks for $\mathbf{2}_8$ are mostly sharp (see Experimental) supporting the flexible nature of the $\mathbf{2}_8$ ring. Under the identical extraction conditions $\mathbf{1}_n$ (n=4, 6, and 8) could not extract even a trace amount of UO_2^{2+}.

In conclusion, it has been established that new calixarene-based ionophores $\mathbf{2}_n$ display versatile affinity not only for alkali metal cations but also for Ag^+, Cu^{2+}, and UO_2^{2+} and are recommended for solvent extraction from strongly basic aqueous solutions.

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