Strikingly Selective Ionophoric Properties of Rigid Cyclophanes Having a Small Number of Ligating Sites

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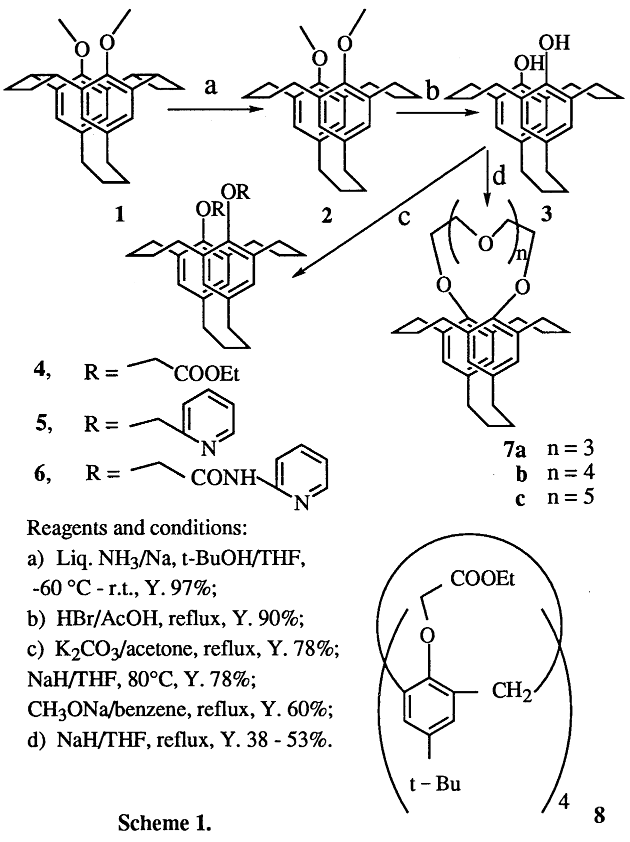
Ionophores **4** and **5** having two acetate groups and two pyridyl groups, respectively, on the aromatic rings as well as oligo(oxyethylene) linked compounds **7a-c** were prepared by Williamson ether synthesis between the corresponding halides or ditosylates and dihydroxycyclophane, which was prepared by Birch reduction of the three-bridged dimethoxycyclophane, followed by cleavage of the methoxyl groups. On the liquid-liquid extraction, **4** and **5** showed high affinities toward K⁺ ion and Ag⁺ ion, respectively. Compounds **7b** and **c** effectively extracted large alkali metal cations.

There are a number of compounds exhibiting some specific cation complexation. For the alkali metal cation complexation, both HSAB theory and size fitting between a host molecule and a cation are recognized to be significant factors. In addition to these two factors, some appropriate arrangement and the number of donor atoms of the host molecule have been found to play important roles in a heavy metal cation complexation. The rigidification of the host molecule makes the complexation selective and does the complex stable as demonstrated in spherands,[1] though their complexation is kinetically unfavorable. Hemispherands, which have half of spherand moieties and polyether or diazacrown likages,[2,3] overcame this disadvantage. We have already prepared some hybrid type of crown compounds having both relatively rigid cyclophane and flexible polyether moieties, which have named "crownophanes."[4] These crownophanes and their derivatives show kinetically and thermodynamically favorable complexation.[5] In the course of our studies on multi-bridged cyclophanes or "paddlanes,"[6] we noticed that the bridged cyclophane **3** has a suitable structure for a kind of ligand because it possesses high reactive hydroxyl groups facing to the same direction due to the rigid backbone. Hence, we designed the compounds **4-7** and investigated their extractabilities of metal cations. In this short communication, we report the results in detail.



Reagents and conditions:
a) Liq. NH_3/Na, t-BuOH/THF, -60 °C - r.t., Y. 97%;
b) HBr/AcOH, reflux, Y. 90%;
c) K_2CO_3/acetone, reflux, Y. 78%; NaH/THF, 80°C, Y. 78%; CH_3ONa/benzene, reflux, Y. 60%;
d) NaH/THF, reflux, Y. 38 - 53%.

Scheme 1.

Table 1. Extraction (%) of alkali metal picrates by ionophores to CH_2Cl_2[a]

Ionophore	Li^+	Na^+	K^+	Rb^+	Cs^+
3	0	1	0	1	1
4	0	5	52	12	3
5	1	2	2	0	1
6	0	1	1	2	4
7a	1	1	2	1	2
7b	3	9	78	92	93
7c	0	9	23	46	74
9[b]	0	11	90	80	65

[a] Extraction conditions: Aq. phase, [picric acid] = 5×10^{-5} mol dm^{-3} in 0.1 mol dm^{-3} of MOH, 5 ml; Org. phase, CH_2Cl_2, [ionophore] $=1\times10^{-3}$ mol dm^{-3}, 5 ml; 22°C, shaken for 1 h.
[b] Dibenzo-18-crown-6.

As shown in Scheme 1, dihydroxycyclophane **3** was prepared from **1**[7] by Birch reduction, followed by the ether cleavage reaction with HBr-AcOH. Cyclophane **3** was converted into **4**, **5**, and **7** by the conventional displacement method. Compound **6** was also readily derived from **5**. Analytical data of new materials prepared are given.[8]

Cation binding properties of the ionophores obtained were examined and compared with those of the reference compounds for alkali and heavy metal cations in H_2O-CH_2Cl_2 extraction systems.

Although cyclophanes **3**, **5**, and **6**, having two ligating sites, did not extract any alkali metal cation significantly, ethoxycarbonylmethyl derivative **4** efficiently extracted K⁺ ion with high selectivity as summarized in Table 1. The function of ethoxycarbonylmethyl group has been widely perceived; *i.e.*, their cooperative act with a crown ring in BiBLEs was reported by Gokel.[9]

Cone-formed *tert*-butylcalix[4]arene derivative **8**[10] exhibits high affinity toward Na⁺ ion. Compared with this example, which have four ethoxycarbonylmethyl ligating sites in the molecule, cyclophane **4** has only two ligating sites in the molecule. Despite of the minimum number of sites, it showed relatively high extractability and extremely high selectivity toward K⁺ cation. This is because of the rigid paddlane skeleton and, as the results, the enforced arrangement of the two groups. Polyether linked ionophores **7b** and **c** showed quite high selectivity toward larger cations due to their cavity size. In regard to the crown compounds with six ethereal oxygens, **7b** extracted Rb⁺ and Cs⁺ ion more than Li⁺, Na⁺, and K⁺ ion, in contrast to K⁺ ion for dibenzo-18-crown-6 **9**. This difference on the cation

Table 2. Extraction of Metal Nitrates with Ligands

Ligand	Extractability (%)[a]				
	Ag^+	Cu^{2+}	Pb^{2+}	Ni^{2+}	Zn^{2+}
3	1(7.2)	0(4.6)	0(4.7)	0(4.1)	0(5.0)
4	6(6.7)	0(4.4)	0(4.6)	0(3.6)	0(5.2)
5	88(7.4)	2(4.9)	0(4.4)	0(3.8)	0(5.0)
6	10(7.3)	1(4.4)	0(4.5)	0(4.3)	0(6.1)
7a	0(7.4)	2(4.4)	0(4.6)	1(3.5)	0(6.0)
7b	4(7.8)	0(4.5)	0(4.3)	0(4.4)	0(5.9)
7c	1(7.5)	0(4.4)	1(4.8)	0(4.4)	0(6.2)
9[b]	2(7.1)	0(4.0)	2(4.6)	0(4.6)	0(5.0)

[a] Extraction conditions: Aq. phase, [metal nitrate] = 1×10^{-1}mol dm^{-3}, 5ml; Org. phase, CH_2Cl_2, [Ligand] = 1×10^{-4}ml dm^{-3}, 5ml. Values in parentheses were equilibrium pH of aqueous phase. [b] Dibenzo-18-crown-6.

affinity is considered to be due to the expanded polyether ring of **7b** caused by largely apart aromatic nuclei. Similarly, larger one **7c** showed high affinity toward Cs^+ ion due to the cavity size and the expanded ring shape.

Pyridyl ligating sites introduced into the crown compounds play an important role in the complexation with some heavy and transition metal cations,[11] especially Ag^+ ion.[12,13] Stimulated by the effect of the pyridine moieties, we prepared cyclophane derivatives **5** and **6**. Compound **5** efficiently extracted Ag^+ ion almost exclusively despite of the lack of crown moieties in the molecule. Cyclophane **6** showed lower affinity to Ag^+ ion than that of **5**. This is caused by relatively remote ligating parts from the aromatic nuclei even if the phane skeleton is considerably rigid.

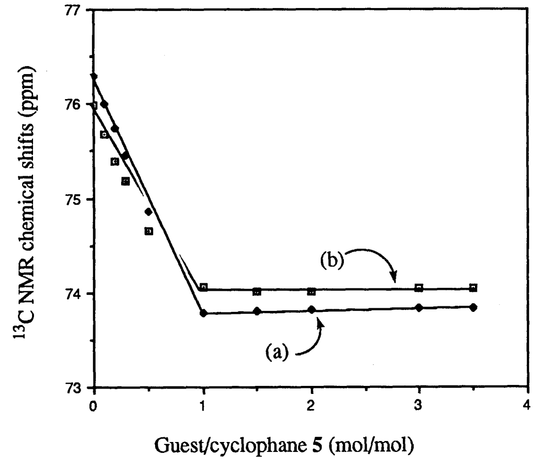


Figure 1. Ag^+-Induced changes in ^{13}C NMR chemical shifts of cyclophane **5**; The α–methylene carbon to pyridine ring was employed. (a) **5** in CD_3COCD_3; (b) **5** in CD_3COCD_3/ CD_3OD = 1 : 1.

Complexing behavior of **5** to Ag^+ ion was examined by ^{13}C NMR titration method using $AgClO_4$ in acetone-d_6. As illustrated in Figure 1a, addition of the salt to the solution caused remarkable changes at the 1 : 1 complexation. The arrangement of the ligating groups on the rigid cyclophane skeleton is considered to be favor for Ag^+ ion, which is believed to form a linear two-coordinate complex.

Since Tsukube *et al.* have reported that an N-pivot lariat ether does not completely encapsulate alkali metal cations in a polar solvent like methanol,[14] we examined the Ag^+-complexing behavior of **5** in methanol-d_4/acetone-d_6 (1:1).[15] It resulted in a quite different one from Tukube's; *i.e.*, **5** was found to function even in such a polar solvent effectively (Figure 1b).

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8 Melting points and ^1H NMR spectroscopic data ($CDCl_3$, 500 MHz): **3**; mp 231- 232 °C; δ 6.39 (4H, s), 4.27 (2H, s), 2.64 (4H, m), 2.23 (4H, m), 2.08 (4H,m), 1.69 (8H, m), 1.59 (4H, m). **4**; mp 77.5 - 78.5 °C; δ 6.43 (4H, s), 4.25 (4H, s), 4.21 (4H, q, *J* = 7.3), 2.76 (4H, m), 2.25 (4H, m), 1.99 (4H, m), 1.61 (8H, m), 1.54 (4H, m), 1.29 (6H, t, *J* = 7.3). **5**; mp 200 - 201°C; δ 8.58 (2H, d, *J* = 4.3), 7.87 (2H, d, *J* = 7.8), 7.67 (2H, *J* = 7.7 & 1.7), 7.24 (2H, m), 6.51 (4H, s), 4.86 (4H, s), 2.64 (4H, m), 2.30 (4H, m), 2.05 (4H, m), 1.85 (4H, m), 1.60 (8H, m). **6**; mp 211.5 - 212.5 °C; δ 9.21 (2H, s), 8.02 (2H, d, *J* = 8.2), 7.91 (2H, dd, *J* = 4.0 &1.0), 7.47 (2H, tt, *J* = 7.9 &1.8), 6.77 (2H, m), 6.51 (4H, s), 4.38 (4H, s), 2.67 (4H, m), 2.30 (4H, m), 2.12 (4H, m), 1.88 (4H, m), 1.75 (4H, m), 1.62 (4H, m). **7a**; mp 157 - 158 °C; δ 6.43 (4H, s), 3.87- 3.71 (16H, m), 2.66 (4H, m), 2.25 (4H, m), 1.98 (4H, m), 1.73 (4H, m), 1.55 (8H, m).

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15 Because of its low solubility in methanol, we used the mixed solvent.