

Selective Ion Clefts Based on a Three-Bridged [4₃]Cyclophane

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Abstract. A variety of new three-bridged cyclophanes, clefts **4–14**, have been conveniently prepared, and their cation-binding properties have been examined. Compounds **4–6** have a special affinity for alkali metal cations. Ethyl ester **5** and methyl ester **4** selectively formed 2 : 1 complexes with K⁺ and Na⁺ ions, respectively. Clefts **11–13**, which possess pyridyl groups, bind Ag⁺ cation exclusively. ¹H NMR titration studies confirmed that **11** or **12**, having 2- or 3-pyridyl groups, form a 1 : 1 complex with Ag⁺ cation, while **13**, with 4-pyridyl ligating groups, forms a 2 : 1 complex. Cleft **10**, with aminimide groups, also shows an affinity for Ag⁺ cation in a 2 : 1 ratio in a polar solvent, while it forms a 1 : 1 complex in a nonpolar solvent. The same solvent effect was observed for clefts **13** and **15c**, which is discussed qualitatively.

Key words: Ion cleft, three-bridged cyclophane, crownophane, extraction, metal cation, ester, pyridyl group, aminimide.

1. Introduction

Molecular clefts are compounds possessing two or more functional groups as ligating or binding sites for multi-functional organic guests [1]. They are usually designed to have relevant, preorganized spaces, constructed by their binding sites, so that particular guests can be bound [2, 3]. When the cleft concept is applied to the construction of ion clefts, one needs only to consider a rigid framework and two ligating sites on it. As a result, their construction generally becomes simple, if a suitable rigid parent framework is available.

Among cyclophanes synthesized by our group, some paddlane-like compounds **1** [4] suggested to us a likely possibility for the basic framework of ion clefts such as those mentioned above. Attaching some appropriate functional or ligating groups to them, which possess strong ion–dipole association, would allow us to obtain some selective ionophore-type clefts.

In fact, we have recently succeeded in modifying the phenoxy groups of **3**, which was obtained by the reductive opening of the cyclobutane rings of **1**, followed by the cleavage of the methoxy groups, with several kinds of functional groups to make ion clefts. We have actually used the clefts as ionophores for alkali metal and heavy metal cations, compared their extractability with those of catechol-based

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agent **16**, calix[4]arenes **17a,b,c**, and conventional dibenzo-18-crown-6 **18**, and finally determined the stoichiometries of their complexes in homogeneous and binary media in order to examine their fundamental properties. The preliminary study of their metal cation extractability has been reported as a short communication [5].

In this paper we would like to report the results in detail, including those obtained during the further work.

2. Experimental

2.1. APPARATUS AND MATERIALS

^1H NMR spectra were recorded on a Varian Gemini-200 FT NMR spectrometer. Metal cations were analyzed using a Hitachi 170-50 atomic spectrophotometer. Melting points were determined on a Yanaco MP-S3 micro melting point apparatus and are not corrected.

Unless specified otherwise, highest grade reagents and solvents were used as received from chemical suppliers. Picrates were prepared by the reported method [6]. Isopropyl alcohol, *tert*-butyl alcohol, benzene, and acetone were purified by distillation, and acetone was stored over anhydrous K_2CO_3 . Tetrahydrofuran was distilled over sodium before use, and *N,N*-dimethylformamide was dried over molecular sieves (4A). Aqueous solutions were prepared in distilled deionized water.

2.2. PREPARATION OF COMPOUNDS 4–15

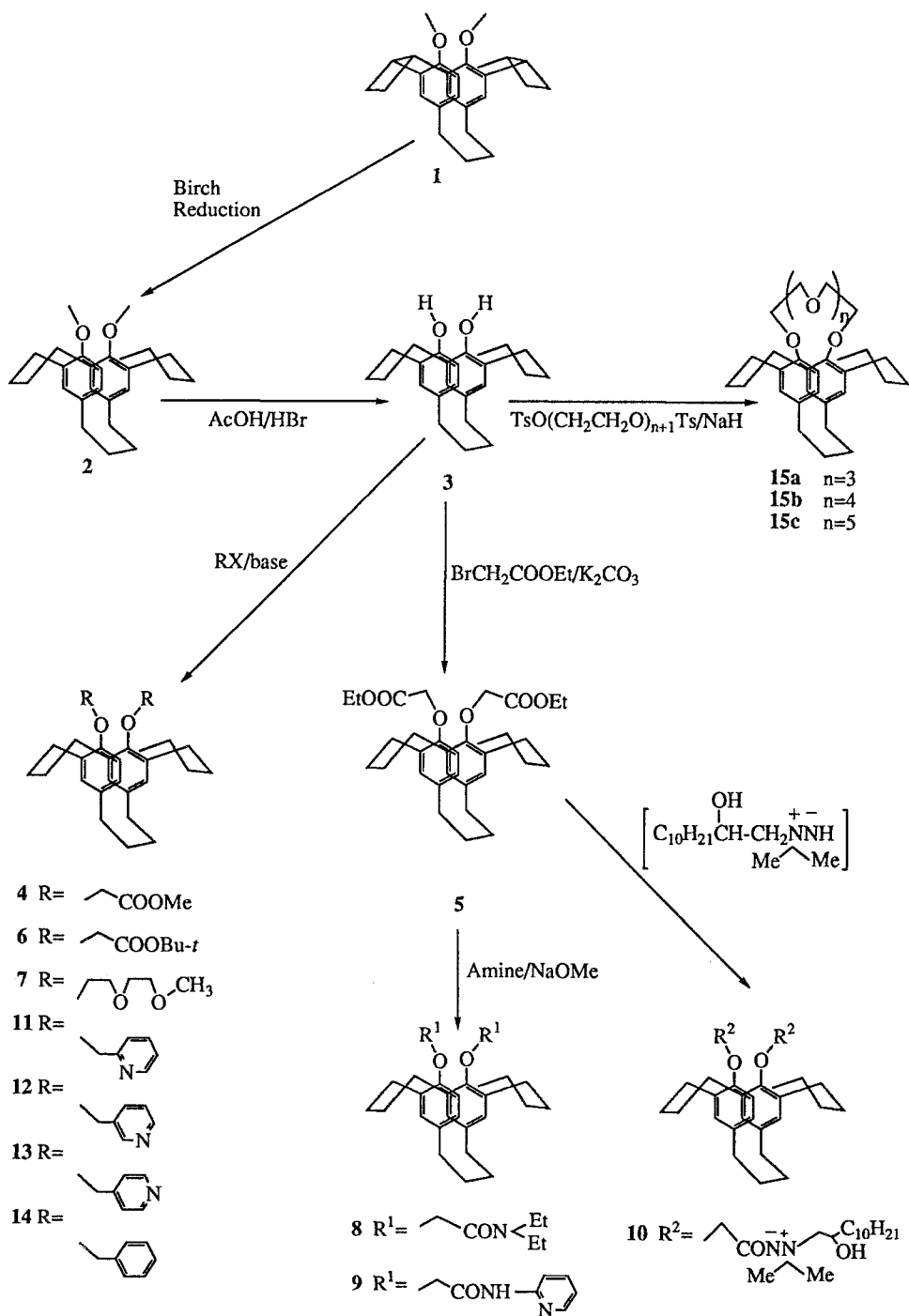
The synthetic methods for **5**, **9**, **11**, and **15** were reported in the previous communication [5].

2.2.1. Preparation of **4** and **6**

Compound **3** (0.18 g, 0.52 mmol) was dissolved in dry acetone (10 mL) containing anhydrous K_2CO_3 (0.21 g, 1.5 mmol) and methyl (0.31 g, 2.0 mmol) or *tert*-butyl bromoacetate (0.39 g, 2.0 mmol). The mixture was refluxed for 8 h. The cooled mixture was filtered, and the solvent was distilled off from the filtrate. The residue was purified by column chromatography on silica gel using benzene–acetone (1 : 10–10 : 1) as an eluent to give product **4** or **6** as crystals.

Compound 4. Yield; 86%. Mp. 117.0–118.0 °C. ^1H NMR (CDCl_3); δ 6.44 (4H, s), 4.26 (4H, s), 3.77 (6H, s), 2.74 (4H, m), 2.26 (4H, m), 2.00 (4H, m), 1.61 (12H, m). *Anal. Calcd.* for $\text{C}_{30}\text{H}_{38}\text{O}_6$: C, 72.85; H, 7.74. *Found:* C, 72.62; H, 8.03.

Compound 6. Yield; 73%. Mp. 98.0–99.0 °C. ^1H NMR (CDCl_3); δ 6.43 (4H, s), 4.14 (4H, s), 2.78 (4H, m), 2.24 (4H, m), 1.96 (4H, m), 1.61 (8H, m), 1.54 (4H,



Scheme 1.

m), 1.49 (18H, s). *Anal. Calcd.* for $C_{36}H_{50}O_6$: C, 74.71; H, 8.71. *Found*: C, 74.58; H, 8.74.

Preparation of 7. Into a sodium hydride (0.03 g, 1.25 mmol) suspension in tetrahydrofuran (20 mL) was added **3** (0.15 g, 0.43 mmol) dropwise, which was dissolved in tetrahydrofuran (10 mL) in a period of 15 min at r.t. Into the reaction mixture so prepared, 3,6-dioxahheptyl tosylate (0.47 g, 1.71 mmol) in tetrahydrofuran (20 mL) was added dropwise over a period of 2 h at 40 °C. After the mixture was stirred under reflux for 20 h, the precipitate was filtered and washed repeatedly with benzene, and the solvents of the combined filtrate and washings were distilled off. The residue was purified by column chromatography on silica gel using benzene–acetone (1 : 10–10 : 1) as an eluent to give product **7** as a colorless viscous liquid. Yield; 26%. $^1\text{H NMR}$ (CDCl_3); δ 6.42 (4H, s), 3.79–3.57 (16H, m), 3.42 (6H, s), 2.66 (4H, m), 2.24 (4H, m), 1.97 (4H, m), 1.60 (12H, m). *Anal. Calcd.* for $C_{34}H_{50}O_6$: C, 73.61; H, 9.08. *Found*: C, 73.49; H, 9.29.

Preparation of 8. The solvent of a sodium methoxide–methanol solution (28%, 0.73 g, 3.8 mmol) was completely distilled off under reduced pressure, and then **5** (0.20 g, 0.38 mmol), diethylamine (2.80 g, 38.3 mmol), and benzene (7 mL) were added at r.t. The reaction mixture was allowed to react at 50 °C for 15 h. The solvent was distilled, and the residue was purified by column chromatography on silica gel using benzene–acetone (1 : 10–10 : 1) as an eluent to give product **8** as a yellow crystal. Mp 89.5–91.0 °C. Yield; 36%. $^1\text{H NMR}$ (CDCl_3); δ 6.43 (4H, s), 4.21 (4H, s), 3.42 (8H, q, 7.1), 2.65 (4H, m), 2.24 (4H, m), 2.00 (4H, m), 1.6 (12H, m), 1.2 (12H, t, 7.0). *Anal. Calcd.* for $C_{36}H_{52}O_4N_2$: C, 74.96; H, 9.09; N, 4.86. *Found*: C, 74.52, H, 9.38, N, 5.03.

Preparation of 10. 1,2-Dodecene oxide (0.30 g, 1.63 mmol) and 1,1-dimethylhydrazine (0.10 g, 1.66 mmol) were dissolved in isopropyl alcohol (5 mL), and the mixture was sealed and kept in the dark at r.t. for 24 h. Compound **5** (0.35 g, 0.67 mmol) was added to the mixture and stored in the dark at r.t. for 48 h. The solvent was removed under reduced pressure, and the residue was purified by column chromatography on silica gel using ethanol as an eluent to give product **10** as a colorless viscous liquid. Yield, 40%. IR (characteristic absorption of aminimide), 1580 cm^{-1} . $^1\text{H NMR}$ (CDCl_3); δ 6.42 (4H, s), 4.21 (2H, s), 3.61 (4H, m), 3.51 (12H, s), 3.49 (4H, m), 3.25 (2H, m), 2.80 (4H, m), 2.24 (4H, m), 1.95 (4H, m), 1.60 (12H, m), 1.27–1.20 (42H, m). *Anal. Calcd.* for $C_{56}H_{94}O_6N_4$: C, 73.16; H, 10.31; N, 6.09. *Found*: C, 73.01; H, 10.52; N, 6.21.

Preparation of 12, 13, and 14. Into a sodium hydride (0.06 g, 2.50 mmol) suspension in tetrahydrofuran (10 mL) was added **3** (0.12 g, 0.34 mmol) dropwise in *N,N*-dimethylformamide (10 mL) over a period of 10 min at r.t. Chloromethyl pyridine hydrochloride (0.21 g, 1.29 mmol) or benzyl bromide (0.22 g, 1.29 mmol)

in *N,N*-dimethylformamide (10 mL) was added dropwise into the reaction mixture obtained above over a period of 20 min, and the reaction mixture was stirred at 80 °C for 18 h. The cooled mixture was filtered off. The residue was purified by column chromatography on silica gel using benzene–acetone (1 : 10–10 : 1) as an eluent to give product **12**, **13**, or **14** as crystals.

Compound 12. Yield; 72%. Yellow crystals. Mp 245.0–246.5 °C. ¹H NMR (CDCl₃); δ 8.62 (2H, d, 5), 8.58 (2H, d, 5), 7.79 (2H, d, 10), 7.30 (2H, dd, 10&5), 6.48 (4H, s), 4.72 (4H, s), 2.57 (4H, m), 2.28 (4H, m), 2.01 (4H, m), 1.75 (4H, m), 1.64 (4H, m), 1.51 (4H, m). *Anal. Calcd.* for C₃₆H₄₀O₂N₂: C, 81.17; H, 7.57; N, 5.26. *Found:* C, 81.35; H, 7.61; N, 5.05.

Compound 13. Yield; 94%. Brown crystals. Mp 190.0–191.5 °C. ¹H NMR (CDCl₃); δ 8.62 (4H, d, 6.1), 7.41 (4H, d, 5.2), 6.50 (4H, s), 4.74 (4H, s), 2.57 (4H, m), 2.29 (4H, m), 2.03 (4H, m), 1.81 (4H, m), 1.61 (4H, m) 1.55 (4H, m). *Anal. Calcd.* for C₃₆H₄₀O₂N₂: C, 81.17; H, 7.57; N, 5.26. *Found:* C, 81.09; H, 7.46; N, 5.11.

Compound 14. Yield; 78%. Brown crystals. Mp 160.5–161.5 °C. ¹H NMR (CDCl₃); δ 7.46 (4H, m), 7.34 (4H, m), 7.30 (2H, m), 6.48 (4H, s), 4.74 (4H, s), 2.64 (4H, m), 2.28 (4H, m), 2.00 (4H, m), 1.80 (4H, m), 1.63 (8H, m). *Anal. Calcd.* for C₃₈H₄₂O₂: C, 85.99; H, 7.98. *Found:* C, 85.79; H, 8.12.

2.3. SOLVENT EXTRACTION OF METAL CATIONS

2.3.1. Solvent extraction of heavy metal cation

The metal picrate (5.0×10^{-5} M) was prepared in situ by dissolving the metal hydroxide (0.1 mol) in picric acid (5.0×10^{-5} M). A solution (1.0×10^{-3} M) of the subjected ion cleft was prepared in CH₂Cl₂. Equal volumes (5.0 mL) of two solutions were shaken vigorously for 60 min in a 20-mL test tube with a ground glass stopper at ambient temperature. After the two phases were separated, the concentration of the metal picrate in the aqueous phase was determined by UV spectroscopy.

2.3.2. Solvent extraction of heavy metal cation

A CH₂Cl₂ solution of the subjected ion cleft (1.0×10^{-4} M, 5.0 mL) and an aqueous metal nitrate solution (0.1 M, 5.0 mL), whose pH was adjusted as high as hydroxide precipitation did not take place, was shaken in a 20-mL test tube with a ground-glass stopper at ambient temperature (ca. 20 °C) for 1 h. The two liquid phases were separated, and the equilibrium pH of the aqueous phase was measured. An aliquot (2.0 mL) of the organic phase was evaporated under reduced pressure,

and then aqueous HNO₃ (0.1 M, 2.0 mL) was added to the residue. Finally, the concentration of the extracted cation was analyzed by atomic absorption analysis.

3. Results and Discussion

3.1. SYNTHESIS OF ION CLEFTS BASED ON A THREE-BRIDGED CYCLOPHANE

Although three-bridged cyclophanes can be prepared from α,ω -bis(3,5-divinylphenyl)alkanes by our efficient intramolecular photocycloaddition method as mentioned in the introduction, they are usually mixtures of three possible isomers [7], because each vinyl group contained in α,ω -bis(3,5-divinylphenyl)alkanes can take every possible conformation with respect to the other vinyl group on the benzene nucleus. In order to fix their conformation to one direction and to introduce a functional group for further modifications, a methoxy group was introduced at the position between the two vinyl groups on the benzene nucleus, namely at the C4 position [4]. This attempt turned out to be effective and gave eventually only one isomer, namely paddlane **1**, in surprisingly high yield. We chose this product as the starting material to make the basic rigid framework of the ion clefts in the present study.

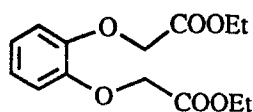
First we tried to cleave the methoxy groups on paddlane **1**. The starting material was, however, quantitatively recovered from the reaction mixture, whenever we tried to cleave its methoxy groups by an acid, such as HBr/AcOH, BBr₃, or HCl/CHCl₃/MeOH. Examination of the framework using CPK molecular models revealed that the framework has a fixed conformation, directing the methyl group to the outside and the oxygen lone pairs to the inside of the molecule. Since the acid-promoted cleavage reactions of an alkoxyphenyl group first occur by an electrophilic attack of a proton on the lone pairs, paddlane **1** could actually not react in this way, because its reaction site – the lone pair – is buried deeply in its skeleton. Hence, we decided to widen its O–O distance further, in order to avoid the steric hindrance, and to open the cyclobutane rings to tetramethylene units.

Actually the desired dihydroxy[4₃]cyclophane **3** was obtained by the Birch reduction of **1** to cyclobutane ring-opened **2**, followed by the ether cleavage reaction with HBr–AcOH. The Birch reduction of **1** gave compound **2** in 66% yield. The ether cleavage of **2** afforded **3** in 81% yield. Clefts **4–15** were prepared from **3** by the reported methods [8–10].

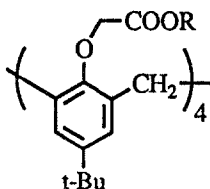
3.2. BINDING PROPERTIES OF THE ION CLEFTS WITH METAL CATIONS

3.2.1. Extraction of alkali metal picrate

The extraction profile of diesters **4–6** should be compared with that of *tert*-butylcalix[4]arene tetraesters **17a,b,c** [11]. Almost all calixarene esters examined efficiently extracted Na⁺ cation, and the selectivity increased in the order of *tert*-butyl ester < ethyl ester < methyl ester. Interestingly, as shown in Table I, diesters **4–6**



16



17a R=Me
 17b R=Et
 17c R=*t*-Bu

Formula.

altered the selectivity; methyl ester **4** showed selective extractability for Na⁺ cation and ethyl ester **5** for K⁺ cation, whereas *tert*-butyl ester **6** showed no extractability at all under the same conditions. Thus it was revealed that the extraction selectivity of diesters **4** and **5** was quite different from that of the calixarene tetraesters, and was greatly affected by the structure of the ester residue [11]. The large effect is considered to be due to the rigidity of the paddlane skeleton, as mentioned below.

As shown in Table II, esters **4** and **5** formed 2 : 1 complexes with Na⁺ and K⁺ cations in CH₂Cl₂ and MeCN, respectively. These 2 : 1 sandwich-type complexes should have the structure depicted in Figure 1, because no other type could be possible. In the cavity formed by two molecules of **4** after the complexation, rather small steric interference is expected between the methoxy groups and the linkages, but in the cavity made by two molecules of **5**, the interference is considered to be much larger than the one above. Therefore, the relatively small cavity made by **4** matches the Na⁺ cation, while that made by **5** is suitable for the larger K⁺ cation. Reference compound **16**, which possesses ethyl ester groups, also formed a 2 : 1 complex and extracted Na⁺ cation selectively. In this complexation, the steric interference between closely adjacent molecules **16** is again expected to be small. Finally, molecule **6**, with large *tert*-butyl groups, is considered not to form any cavity by its self-assembly to accommodate any alkali metal ion.

Compound **7**, having ether moieties as the ligating sites, showed almost no extractability. This is attributed to the fact that the ether oxygens in **7** have less electron-donating property than the carbonyl oxygens of ion clefts **4** and **5**, and moreover, its rather flexible ligating sites might not be well preorganized to bind the metal ions.

The extractability and ion selectivity of **8–10**, having amide or aminimide groups, were generally low. Their low extractability can be attributed to steric factors, such as bulkiness of the arms, which prevents the formation of the complexes with alkali metals. In particular, compound **9** showed only a low extractability. This result is considered to be due to the competition between the chelation of the carbonyl oxygens to a metal cation and their hydrogen bond formation with the amide NH hydrogens. The low selectivity shown by **8** and **10** is attributed to

Table I. Extraction (%) of alkali metal picrates by ion clefts to CH₂Cl₂.^a

Cleft	Li ⁺	Na ⁺	K ⁺	Rb ⁺	Cs ⁺
4	1	16	0	0	0
5	0	5	52	12	3
6	1	1	2	3	2
7	0	0	1	2	0
8	8	23	8	9	13
9	0	1	1	2	4
10	10	13	17	16	14
11	1	2	2	0	1
12	1	0	0	0	1
13	0	1	0	1	0
14	1	2	1	0	1
15a	1	1	2	1	1
15b	3	9	78	92	93
15c	0	9	23	46	74
16	1	23	1	0	0
17a^b	7	86	22	10	26
17b^b	15	95	49	24	49
17c^b	28	94	76	53	82
18^c	0	11	90	80	65

^a Extraction conditions: Aq. phase (5 mL), [picric acid] = 5.0×10^{-5} M, [MOH] = 0.1 M; Org. phase, CH₂Cl₂ (5 mL), [cleft] = 1.0×10^{-3} M; ca. 20 °C, shaken for 1 h. The values were based on the concentration of picrates.

^b Data taken from Ref. 11. Extraction conditions: Aq. phase (5 mL), [picric acid] = 2.5×10^{-4} M, [MOH] = 0.01 M; Org. phase, CH₂Cl₂ (5 mL), [calixarene] = 2.5×10^{-4} ; shaken for 1 min.

^c Dibenzo-18-crown-6.

their electron-donating nitrogens, which can work to bind all cations without any selectivity. The same tendency on the selectivity has been pointed out in the case of *tert*-butylcalix[4]arene tetraamide [12].

Generally speaking, pyridine moieties as lariats can intramolecularly cooperate with cyclic polyethers in the binding of alkali metal cations [13]. However, clefts **11**, **12**, and **13**, which have pyridine moieties but no cyclic ligating part, did not work as alkali metal ionophores.

As is well known, size-complementarity is generally recognized for the complexation of alkali metal cations with crown compounds; 12-crown-4 for lithium ion, 15-crown-5 for sodium ion, and 18-crown-6 for potassium ion. We then pre-

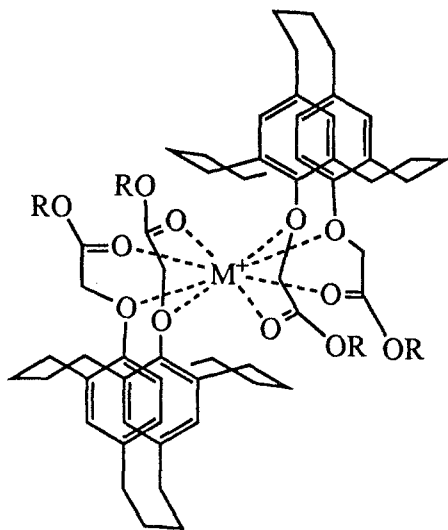
Table II. Stoichiometry of ion cleft-metal complexes.^a

Complex	Stoichiometry	Complex	Stoichiometry
4 -Na ⁺	2:1	15b -K ⁺	1:1
5 -K ⁺	2:1	15b -Rb ⁺	1:1
10 -Ag ⁺ ^b	2:1 (1:1) ^c	15b -Cs ⁺	1:1
11 -Ag ⁺ ^b	1:1	15c -K ⁺	2:1 (1:1) ^c
12 -Ag ⁺ ^b	1:1	15c -Rb ⁺	2:1 (1:1) ^c
13 -Ag ⁺ ^b	2:1 (1:1) ^c	15c -Cs ⁺	2:1 (1:1) ^c
		16 -Na ⁺	2:1

^a Molar ratio plot of [Host]/([Host] + [metal picrate]) by UV spectroscopic titration method; [metal picrate] = 1.0×10^{-4} M; [Host] = $0-2.0 \times 10^{-3}$ M in CH₃CN.

^b Molar ratio plot of [Host]/([Host] + [AgClO₄]) by ¹H NMR titration method; [Host] = 4.9×10^{-3} M; [AgClO₄] = $0-1.96 \times 10^{-2}$ M in acetone-*d*₆.

^c Job plots of [M⁺ picrate]/([M⁺ picrate] + [cleft]): Aq. phase, [M⁺ picrate] = 1.0×10^{-3} mol dm⁻³; Org. phase, CH₂Cl₂, [cleft] = 1.0×10^{-3} mol dm⁻³.



4 R=Me with M=Na
5 R=Et with M=K

Figure 1. Sandwich-type complex of paddlane ester with metal cation.

pared three crown ether-type clefts **15**, which are called crownopaddlanes, a kind of crownophanes [5]. Crownopaddlane **15a**, which has five ethereal oxygen atoms, however, did not extract any alkali metal cation, while **15b** and **15c**, having six and seven oxygen atoms, respectively, did extract selectively larger cations efficiently. Two phenoxy oxygen atoms of these ion clefts cannot work as ligating sites, because of the steric hindrance of the *o*-methylene groups, so that they must bind cations with the other oxygen atoms. This disadvantage resulted in the weak dehydration of the cations in aqueous media and in insufficient lipophilicity of the complexes to move into the organic layer. Therefore, **15a**, with only three contributable ligating oxygen atoms, did not show any extractability. On the other hand, crownopaddlanes **15b** and **15c**, having a larger crown ring, did show a satisfactory extractability toward larger alkali metal cations. In these cases, **15b** and **15c** are considered not only to have enough oxygen atoms for binding, but also to show lower hydration energy for larger cations which may contribute to the extractability significantly.

3.2.2. *The extraction of heavy metal nitrates*

Results are summarized in Table III. As crown ethers with oxygen atoms as ligating sites are known to interact weakly with Ag^+ cation [14], it is reasonable that the same kind of ionophores, esters **4** and **5**, and polyether **7** in the present work, extracted only a small amount of the cation. Amides **8** and **9** showed a somewhat higher affinity for the cation than the above esters and polyether. This phenomenon is considered to be due to the fact that the soft nitrogen atoms play a role in this complexation, in contrast to the extraction of alkali metal cations. Cleft **9** extracted Ag^+ cation less than **8** and pyridine derivatives **11–13**, because the pyridine rings of **9** attach far from its rigid paddlane part and are not easily preorganized for the incoming cation.

We have already found that the affinity toward heavy metal cations can be enhanced, when two aminimide groups are properly arranged or second additional ligating groups are introduced [15]. Cleft **10** was designed according to this finding. Since its two aminimide groups are properly arranged on the rigid paddlane skeleton, cleft **10** extracted Ag^+ cation with high efficiency as well as high selectivity. This is one of the well-designed ion clefts.

Crown compounds, modified by pyridyl groups as lariats, generally show high extractability toward some heavy metal cations, especially Ag^+ cation, as reported in [16]. Despite the absence of a cyclic polyether moiety, compounds **11–13**, possessing two pyridine moieties, extracted the cation efficiently and almost exclusively. In order to clarify the π -electron effect to the Ag^+ cation binding, **14**, having benzene rings instead of pyridine rings, was prepared and investigated for its cation binding ability. As shown in Table III, **14** did not extract Ag^+ cation at all. Hence, clefts **11–13** are clarified to bind Ag^+ cation by their nitrogen-atom lone pairs. This is the best case to demonstrate the characteristics of our ion-clefts; they have two

Table III. Extraction of metal nitrates with ion cleft.

Cleft	Extractability(%) ^a							
	Ag ⁺	Pb ²⁺	Ni ²⁺	Cu ²⁺	Mn ²⁺	Zn ²⁺	Co ²⁺	Fe ³⁺
3	1(7.2)	0(4.7)	0(4.7)	0(4.6)	0(4.5)	0(5.0)	0(6.7)	0(2.3)
4	6(6.7)	0(4.6)	0(4.0)	0(4.4)	0(4.7)	0(5.2)	0(6.6)	0(2.2)
7	3(7.3)	0(4.2)	0(3.8)	0(4.0)	0(6.0)	0(5.8)	0(6.2)	0(2.2)
8	13(6.0)	0(4.1)	0(3.3)	1(3.8)	0(6.9)	0(5.8)	0(6.5)	0(1.2)
9	10(7.3)	1(4.4)	0(4.5)	0(4.3)	0(6.1)	0(5.7)	0(6.4)	0(1.2)
10	74(5.8)	0(3.9)	0(3.0)	5(3.5)	0(5.7)	1(5.7)	0(6.3)	0(1.1)
11	88(7.4)	2(4.9)	0(4.4)	0(3.8)	0(5.0)	0(6.5)	0(4.5)	1(2.2)
12	76(5.4)	0(4.4)	0(6.7)	1(4.3)	0(5.8)	0(5.1)	1(6.2)	1(1.2)
13	71(5.3)	0(4.2)	0(6.6)	1(4.7)	0(5.5)	0(5.2)	0(5.6)	0(1.2)
14	0(5.9)	0(3.7)	0(3.0)	2(3.8)	0(6.1)	0(5.6)	0(6.0)	0(1.3)
15a	0(7.4)	0(4.6)	3(4.2)	2(4.4)	0(5.2)	0(6.0)	0(6.3)	1(2.7)
15b	4(7.8)	4(4.9)	0(4.4)	0(4.5)	2(5.3)	0(5.9)	0(5.0)	0(2.8)
15c	1(7.5)	1(4.8)	0(4.4)	0(4.4)	0(5.3)	0(6.2)	0(6.5)	0(1.7)
18^b	2(7.1)	2(4.7)	0(4.6)	0(4.7)	0(4.6)	0(5.0)	0(6.8)	0(2.1)

^a Extraction conditions: Aq. phase (5 mL), [metal nitrate]= 1.0×10^{-1} M; Org. phase, CH₂Cl₂ (5 mL), [cleft]= 1.0×10^{-4} M; ca. 20 °C, shaken for 1 h. Values in parentheses were equilibrium pH of aqueous phase. The values were based on the concentration of the cleft compounds.

^b Dibenzo-18-crown-6.

properly arranged ligating sites on a rigid framework to fit the size of the subject metal cation, Ag⁺ cation in this case.

3.2.3. Stoichiometry of cleft-ion complex

In order to examine the fundamental properties of the cleft-ion complexes formed, we measured their stoichiometry. The experiments were carried out in polar homogeneous media and also in nonpolar organic media of binary system with water. The molar ratios were measured by UV, ¹H NMR, and ¹³C NMR spectroscopic methods. Moreover, the continuous variation method was applied to the extraction experiment. Data are listed in Table II.

Although their stoichiometry is 2 : 1 in polar media and their theoretical extractability should be less than 50% if the stoichiometry is maintained in all kinds of media, some clefts extracted metal cations to the extent of 70% based on their molar amount (see Tables I, II, and III for **15c**-Cs⁺, **10**-Ag⁺, and **13**-Ag⁺). The discrepancy was solved upon measuring the stoichiometry in the extraction solvent system. In fact, all the systems mentioned above suggested the presence of 1 : 1 complexes under the extraction conditions.

The results for **15c**-Cs⁺, **10**-Ag⁺, and **13**-Ag⁺ combinations probably mean that their complexation or stoichiometry is changed depending on the solvent

polarity. This solvent effect can be rationalized as follows: in nonpolar solvents, the counter anions of metal cations become rather 'bared' and work as a kind of strong ligating species, so that the complexes are composed of the metal ion, the cleft molecule, and the counter anion. If the complexes are sufficiently lipophilic, they could be extracted into organic media. This is the case in the present work with remarkably lipophilic picrate and nitrate [17]. On the other hand, in polar systems, the counter anion is well solvated and does not work as a ligating species. Therefore, two host molecules must bind the metal, in order to occupy its coordination sites.

The behavior of clefts **15b** and **15c** towards alkali metal cations, K^+ , Rb^+ , and Cs^+ , is interesting, as is shown in Table II. The former formed 1 : 1 complexes with the three metals in acetonitrile, while the latter bound them in a ratio of 2 : 1 in the same solvent. The results can reasonably be explained by the behavior of **15c**, which is altered with the solvent polarity: **15c** is a rather flexible molecule in polar media and cannot create a ligating site by itself, and two molecules are required to form an effective cavity for a metal ion. On the other hand, its flexibility decreases in a nonpolar solvent, because the lipophilic ethano bridges of the oligooxyethylene are apt to be forced to the outside and the hydrophilic oxygens to the inside in order to decrease its dipole moment. As a result, it may serve as a reasonably preorganized cyclic ligating site for the alkali metal cations in a nonpolar solvent, such as methylene chloride. Moreover, the picrate anion behaves as a ligand in this nonpolar solvent. Eventually, the intermolecularly suitable cooperation between the counter anion and the cleft's ligating site is considered to reflect this 1 : 1 complexation.

4. Conclusion

New ion clefts **4–15**, based on a three-bridged cyclophane, have been synthesized, and their binding ability with alkali metal and heavy metal cations have been examined by the liquid–liquid extraction method. Most of these clefts acted as efficient cation-binding ionophores.

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