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Na^+ Ion-Specific Binding and Extraction by Lipophilic Armed Cyclens *via* Octadentate Encapsulation

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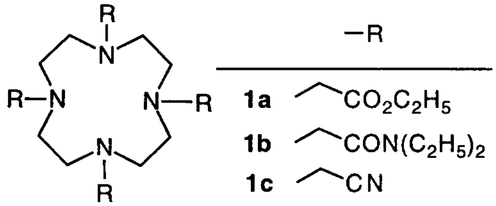
Abstract: 1,4,7,10-Tetraazacyclododecane derivatives having ester- and amide-functionalized sidearms predominantly extracted Na^+ ion from an aqueous mixture of Li^+, Na^+ and K^+ ions into a CH_2Cl_2 *via* specific octadentate complexation. © 1997 Elsevier Science Ltd.

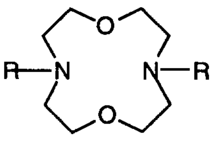
Although a variety of macrocyclic polyamines have been developed as effective ligands of transition metal cations,[1-3] they also have potential as specific ligands of alkali metal cations. In particular, 1,4,7,10-tetraazacyclododecane, cyclen, adopts a well-defined square conformation which provides a macrocyclic skeleton effective for construction of three-dimensional ligands of alkali metal cations.[4,5] Since attachment of cation-ligating sidearm to the cyclen ring can increase coordination number and complex stability, a new series of specific ligands for alkali metal ions can be derived by arm-functionalization of the cyclen.

Here, we report that ester- and amide-armed cyclens predominantly extract Na^+ ion from an aqueous mixture of Li^+, Na^+ and K^+ ions into a CH_2Cl_2. X-ray diffraction, ^{23}Na-NMR and FAB-MS spectroscopic studies reveal that these armed cyclens specifically accommodate Na^+ ion in a unique octacoordination fashion. Although other types of cyclen derivatives have been characterized as ligands of alkali metal cations,[6,7] this is the first example of the armed cyclens offering perfect Na^+ ion-selective extraction functions.

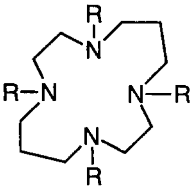
We examined several kinds of armed cyclens and related macrocycles in the binding and extraction of alkali metal cations: 12-membered cyclens **1a** - **1c**, 12-membered diaza-crown ether **2a**,[8] and 14-membered cyclam **3a**.[9] Ester-armed calixarene **4** was also employed which was reported as a Na^+ ion-specific extracting reagent.[10] The crystal structures of alkali metal complexes with hydroxylethyl- and pyrazoylmethyl-armed cyclens have been reported.[6,7] In these complexes, a varying number of ligating sidearms and cyclen nitrogen atoms cooperatively bound guest cations. Although their cation selectivity was not high, further combination of cyclen and functionalized sidearm provides promising possibilities in development of cation-specific, three-dimensional ligands.[11]

Ester- and amide-armed cyclens **1a** and **1b** specifically bound Na^+ ion and predominantly extracted it (Table). Extraction experiments were carried out by adding a CH_2Cl_2 solution of the macrocycle (0.015 mmol in 1.5 ml) to an aqueous mixture of Li^+, Na^+ and K^+ perchlorates (0.015 mmol, each in 1.5 ml). After the mixture had been stirred for 2 h, the concentrations of these metal cations in the aqueous phase were determined by atomic absorption or flame spectroscopic method. Cyclen derivatives having ester- and amide-functionalized sidearms **1a** and **1b** offered excellent extraction efficiencies and perfect selectivity toward Na^+ ion. Under the employed conditions, these cyclens extracted 65 and 86 % of the added Na^+ ion, while all of the added Li^+ and

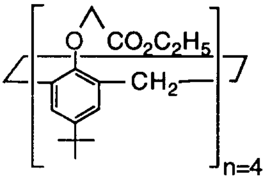




2a R: $CO_2C_2H_5$



3a R: $CO_2C_2H_5$



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K^+ ions remained in the aqueous phase. In contrast, nitrile-armed cyclen **1c**, ester-armed diaza-12-crown-4 **2a** and 14-membered cyclam **3a** could not extract these alkali metal cations at all. Thus, cooperative actions of parent cyclen ring and carbonyl-functionalized sidearms offered Na^+ ion-specific extraction. Table also includes the extraction behaviors of calixarene **4**. It exhibited a good Na^+ ion-selectivity but its extraction efficiency (35%) was greatly inferior to those of cyclens **1a** and **1b**.

Table. Competitive Extraction of Metal Ions by Armed Cyclens and References.

Macrocycle	Extraction %[a]		
	Li^+	Na^+	K^+
1a	<3	65	<3
1b	<3	86	<3
1c	<3	<3	<3
2a	<3	<3	<3
3a	<3	<3	<3
4	<3	35	4

[a] $MClO_4$ (0.015 mmol, each) in H_2O 1.5 ml // Macrocycle (0.015 mmol) in CH_2Cl_2 1.5 ml.

The cation binding properties of the armed cyclens were further characterized using positive FAB-MS spectroscopy.[12] Competitive binding of Li^+, Na^+ and K^+ ions by cyclen **1a** was typically studied in *m*-nitrobenzyl alcohol. The relative peak heights of [**1a** + cation] ions were measured as follows: [**1a** + H^+], 0;

[**1a** + Li$^+$], 0.07; [**1a** + Na$^+$], 1.00; [**1a** + K$^+$], 0.04. These results provided the order parallel to that observed in the extraction experiments.

Figure 1 shows a crystal structure of amide-armed cyclen **1b** - Na$^+$ complex, in which the Na$^+$ ion is octacoordinated by four carbonyl oxygen atoms on the sidearms as well as four nitrogen atoms of the cyclen ring.[13] This has close to twisted prismatic coordination geometry and counter-anion does not directly interact with Na$^+$ ion. Although the parent cyclen is a tetradentate ligand effective for transition metal cations, introduction of pendent amide groups to the cyclen offers an octadentate ligand topology, best suited for the complete encapsulation of the Na$^+$ ion. The mean lengths between Na - O and Na - N are 2.57 and 2.56 Å, which are comparable to those expected from *van der Waals* contact distances. Thus, the Na$^+$ ion was very nicely accommodated in the armed cyclen **1b** and well solubilized in CH_2Cl_2.

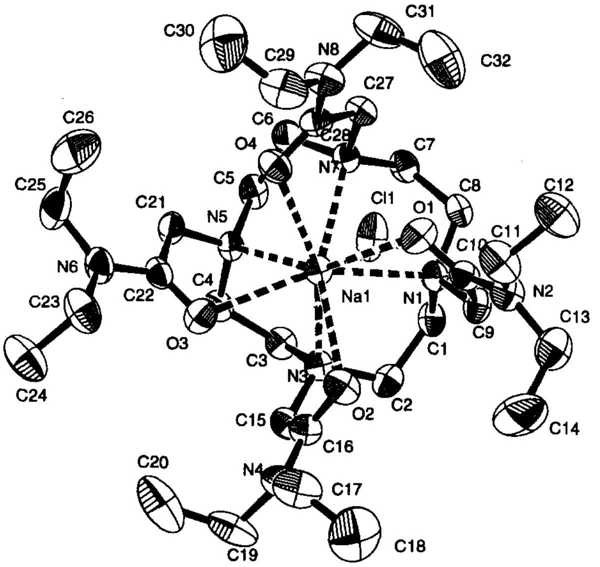

Fig. 1. X-ray crystal structure of amide-armed cyclen 1b - Na$^+$ complex

X-ray diffraction analysis demonstrated that ester-armed cyclen **1a** similarly formed an octacoordinated complex with Na$^+$ ion, indicating that armed cyclens have ligand topology specific for spherical Na$^+$ ion. ^{23}Na-NMR spectroscopic studies also revealed effective encapsulation of the Na$^+$ ion with armed cyclens **1a** and **1b**. Because the chemical shift of Na signal is largely dependent on its coordination circumstance, we determined chemical shifts of the Na signal in the presence and absence of macrocycle in CD_3CN and calculated their differences ($\Delta\delta$). Ester- and amide-armed cyclens **1a** and **1b** showed greater $\Delta\delta$ values (13.9 and 11.7 ppm) than nitrile-armed cyclen **1c** ($\Delta\delta$=7.7 ppm). Since these values were much larger than that in the case of calixarene **4** ($\Delta\delta$=2.8 ppm),[14] ester- and amide-armed cyclens were confirmed to very nicely encapsulate the Na$^+$ ion in the solution. Further extension of the present armed cyclen strategy may lead to the design of new and specific ligands of Ca^{2+}, La^{3+} and other metal cations.

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13. *Crystal data* for **1b**·NaCl·CH_2Cl_2: $C_{33}H_{66}O_4N_8NaCl_3$, Mw=768.28, triclinic, space group *P*-1(#2), a=12.021(3), b=14.668(4), c=12.023(3) Å, α=91.94(2)°, β=90.61(2)°, γ=91.96(2)°, Z=2, D_{calc}= 1.205 g cm^{-3}. Structure solution based on 4272 reflections ($I > 4.0\sigma(I)$) converged to R=0.053.
14. Although direct comparison is difficult, $\Delta\delta$ values were observed as 9.2 ppm for **2a** and 12.8 ppm for **3a**.

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