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HIGH PRESSURE SYNTHESIS OF NEW Ag^+ ION-SPECIFIC CROWN ETHERS

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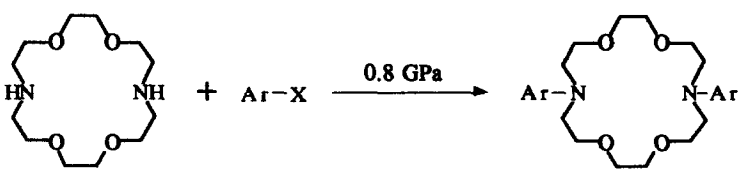
Abstract: A variety of double-armed diaza-crown ethers were first prepared through high pressure S_NAr reaction, in which unique aromatic heterocycles were successfully attached as secondary binding sites. Direct introduction of aromatic heterocycles such as pyridazine, oxazole, and thiazole rings upon nitrogen atom of the diaza-18-crown-6 provided remarkably high binding and transport selectivity for Ag^+ ion.

Double-armed crown ether and related macrocycles represent a new class of synthetic cation-binders which are characterized by a parent macrocyclic ligand and a cation ligating functionalized arm.[1] They are expected to occupy an intermediate position between macrocyclic crowns and bicyclic cryptands. Since they are better cation-binders than the crowns and more dynamic than the cryptands, they can be promising candidates for use in the design of new synthetic ion-carriers.[2] However, there are a few examples of armed azamacrocycles that are directly connected to an aromatic heterocycle such as pyridine.[3] This is probably because of difficulty in the aminolysis of heteroaromatic halides under conventional conditions.

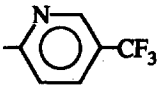
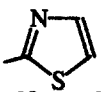
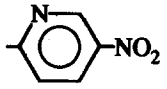
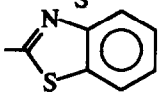
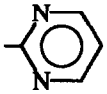
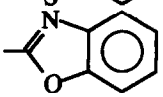
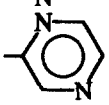
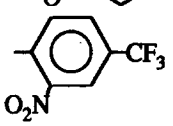
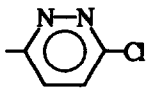
Scheme



1 2~10

We now report successful synthesis of a new series of double-armed diaza-crown ethers based upon high pressure S_NAr reactions,[4~6] which showed remarkably high Ag^+ ion binding and transporting specificity. General reaction procedure: A mixture of diaza-18-crown-6 (1 mmol), the halogenoheterocycles (4 mmol), and triethylamine (5 mmol) was diluted with THF in an 8 ml of PTFE capsule which was stored at 0.8 GPa and 100°C for several days. A variety of double-armed diaza-crown ethers **2~10** that are directly connected to aromatic heterocycles were prepared from commercially available unsubstituted diaza-18-crown-6 **1** and the corresponding halogenoheterocycles (Table 1). The cation transport properties of these crown ethers were characterized by using a CH_2Cl_2 liquid membrane experiment.[7]

Table 1. Synthesis of Double-Armed Crown Ether at 0.8 GPa and 100°C

Prod.	Ar	X	Time (day)	Yield (%)	Prod.	Ar	X	Time (day)	Yield (%)
2		Cl	4	85	7		Br	4	51
3		Cl	3	77	8		Cl	4	74
4		Cl	4	100	9		Cl	4	64
5		Cl	3	86	10		Cl	6	79
6		Cl	4	81					

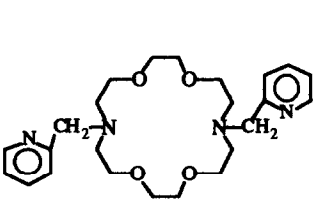
Double-armed crown ethers **5~9** possessing pyrimidine, pyrazine, oxazole, and thiazole heterocycles selectivity and efficiently transported soft Ag^+ ion, while they rarely carried hard Na^+, K^+, and Cs^+ ions and divalent Pb^{2+} ion having similar ion sizes (Table 2). In contrast, the double-armed crown ethers **2~4** were unable to mediate membrane transport of any metal cations examined so far. The heterocyclic moieties of **2~4** apparently act only as electron-withdrawing groups and thus reduce cation-ligating power of two pivot-positioned nitrogen atoms.[8] The pyridine-functionalized crown ethers **11** and **12** were also investigated, because they have been reported as excellent carriers for soft metal cations.[9] Intriguingly, their transport selectivities for Ag^+ ion were much lower than those of the crown ethers **5~9**. Since the simple crown ether **10** and the macrocyclic polyamine **13** have proven to be ineffective carriers, a combination of the parent macroring and heteroaromatic functionalized arm constitutes one of the most important factors in designing a new carrier molecule.

Ag^+ ion-selective binding property of the double-armed crown ether **7** was further demonstrated in DMF/D_2O solution (4/1, v/v) by means of ^{13}C-NMR spectroscopy (Fig.). The addition of $AgClO_4$ salt to the crown **7** solution resulted in remarkable spectral changes due to complexation, whereas $KClO_4$ salt induced only slight changes.[10] Since the signals for 2- and 4-position carbons of the heterocyclic ring significantly shifted, the side-arm participation in complexation is strongly supported to offer a unique and high cation-selectivity as observed in several other types of the double-armed crown ethers.[2]

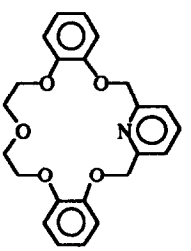
Table 2. Transport Properties of Double-Armed Crown Ethers and Related Macrocycles

Crown Ether	Transport Rate x 10^6 (mol/h)				
	Na^+	K^+	Ag^+	Cs^+	Pb^{2+}
2	*	*	*	*	*
3	*	*	*	*	*
4	*	*	*	*	*
5	*	*	1.4 [a)]	*	*
6	*	*	2.9	*	*
7	*	*	4.9	*	*
8	*	*	1.7	*	*
9	*	*	1.4 [a)]	*	*
10	*	*	*	*	*
11	10.5	7.9	*	7.3	3.2
12	0.4	5.9	8.2	3.7	*
13	*	*	*	*	*

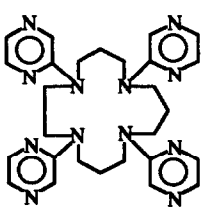
(Conditions) Aq I: Guest perchlorate, 0.50 mmol / H_2O, 0.5 ml.
Membrane: Macrocycle, 0.0372 mmol / CH_2Cl_2, 12 ml.
Aq II: H_2O, 5 ml. Initial transport rates of guest cations were indicated.
*Below limit of detection (< 0.3)
a) Considerable amounts of precipitates appeared in these cases.



11



12



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In conclusion, the present study provides a useful synthetic methodology for a new type of the crown compounds that exhibit excellent binding and transport selectivity for a particular cation. Further applications for exploitation of a variety of unique and specific host molecules based upon high pressure tactics are in progress.

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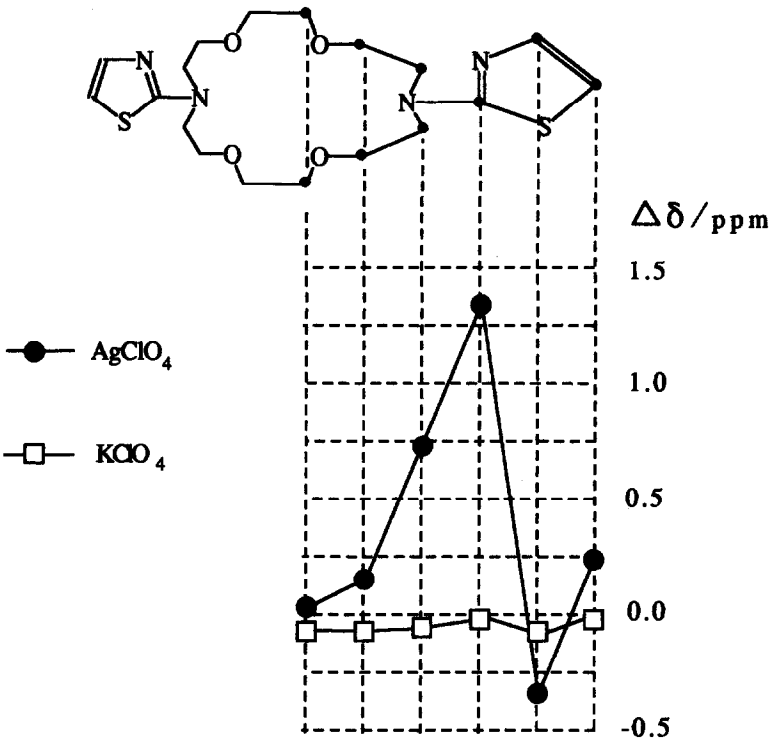
Figure. Guest-Induced Changes in ^{13}C-NMR Chemical Shifts of Double-Armed Crown Ether 7



Host ; 0.025 mmol, $MClO_4$; 0.025 mmol. in DMF/D_2O (4:1) 0.5 ml

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7) CH_2Cl_2 liquid membrane experiments were performed by using a U-tube glass cell (2.0 cm, i.d.) as described before, and the transported amount of guest cations and co-transported anion(ClO_4^-) were determined by atomic absorption spectroscopy and ion-selective electrode techniques: H. Tsukube, H. Adachi, S. Morosawa, *J. Chem. Soc., Perkin 1*, 89 (1989).
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9) H. Tsukube, K. Yamashita, T. Iwachido, M. Zenki, *Tetrahedron Lett.*, **59**, 569 (1988).
10) ^{13}C-NMR titration curves showed clear saturation behaviors, indicating that double-armed crown ether 7 formed a dynamic and 1:1 complex with Ag^+ ion.

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