SYNTHESIS OF DIAZATHIA 15- AND 18-CROWN ETHERS AND THEIR TRANSPORT PROPERTIES FOR METAL CATIONS

Kiyoshi Matsumoto,*[a] Masahiro Nogami,[a] Mitsuo Toda,[b] Hideki Katsura,[a] Naoto Hayashi,[a] and Rui Tamura[a]

[a] Graduate School of Human and Environmental Studies, Kyoto University, Kyoto 606-01, Japan
[b] Faculty of Engineering, Shizuoka University, Hamamatsu 910, Japan

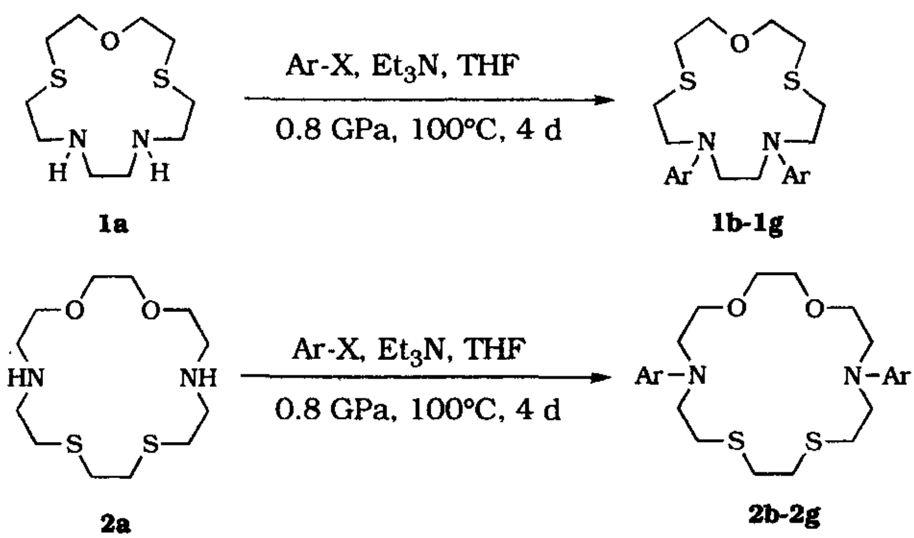
Abstract- A new series of the diazathia 15- and 18-crown ethers were prepared by high pressure S_NAr reaction, in which various heteroaromatics were directly connected to their nitrogens. Liquid membrane transport studies demonstrated that the diazathia 18-crown ethers having benzothiazole, benzoxazole, and pyridine rings on their sidearms exhibited Hg^{2+} and Ag^{+} ion selectivity.

Because of the continuing interests of host-guest chemistry,[1] there were many reports regarding crown ether and related compounds that have interesting guest selectivities in metal ion binding and transport properties. Recently, based upon the high pressure S_NAr reactions, we have prepared functionalized double-armed diaza[2] and single-armed monoaza[3] crown ethers which are directly connected to aromatic heterocycles. Some of them show specific binding and transport properties towards Ag^{+} ion. To utilize these results to design a collection system of hazardous heavy metals, we have further prepared various new kinds of cyclic functionalized compounds such as bis- and tris-crown ethers[4] and polyamines,[5] and have reported their transport and extraction properties for heavy metal cations.

Dedicated to Professor Koji Nakanishi on the occasion of his 75th birthday.

Since sulfur atom is generally known as good ligand of mercury cation, we now describe new diazathia-crown ethers whose nitrogen atoms are connected with aromatic heterocycles by using high pressure S_NAr reaction together with their transport properties for heavy metal cations, especially for mercury cation.

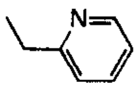
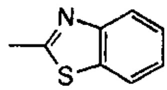
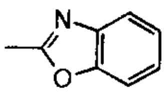
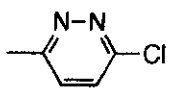
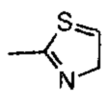
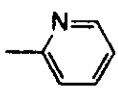
The unsubstituted diazathia 15-crown ether (**1a**) (1-oxa-4.13-dithia-7.10-diazacyclopentadecane)[6] and diazathia 18-crown ether (**2a**) (1,16-dioxa-7,10-dithia-4,13-diazacyclooctadecane)[7] were prepared according to the methods of Pelissaard *et al.* and Lehn *et al.*, respectively. The direct introduction of aromatic heterocycles to the nitrogens of these diazathia 15-crown ether (**1a**) and diazathia 18-crown ether (**2a**) were unsuccessful under atmospheric conditions but achieved under high pressure conditions.[8] (Scheme 1) The results are summarized in Table 1. Only low yields of **1f** and **1g** were obtained, probably because of lower reactivity of **1** rather than triethylamine; indeed in these cases a considerable amount of 2-diethylaminothiazole and 2-diethylaminopyridine were obtained, respectively. More sterically hindered amines such as DBU did not improve the yields, although more attempts should be done in this aspect.



Scheme 1

Using the diazathia 15- and 18-crown ethers (**1a-e**) and (**2a-g**) as a cation carrier, single cation transport experiment is carried out in a CH_2Cl_2 liquid membrane system as described before.[2,3] The results are summarized in Table 2. From the results of cation transport experiments, the transportability of the diazathia15-crown-5 (**1a-g**)

Table 1. High Pressure Synthesis of **1b-g** and **2b-g**

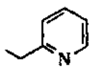
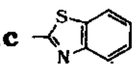
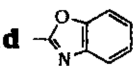
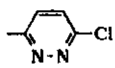
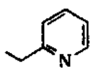
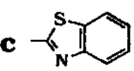
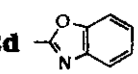
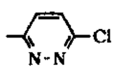
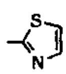
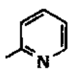
Ar	X	Yield of **1** (%)		Yield of **2** (%)	
	Cl	**1b**	74[a]	**2b**	86[b]
	Cl	**1c**	56	**2c**	73
	Cl	**1d**	49	**2d**	71
	Cl	**1e**	34	**2e**	69
	Br	**1f**	<3	**2f**	64
	F	**1g**	<3	**2g**	30

[a] 27% at normal pressure. [b] 22% at normal pressure.

and 18-crown-6 (**2a-g**) are compared with each other. The functionalized diazathia 15-crown-5 (**1b-g**) did not show high transportability to any metal cations, but the diazathia 18-crown-6 (**2b-g**), except **2e**, showed expected high values to mercury cation (Hg^{2+}). Comparison of the unsubstituted compounds (**1a**) and (**2a**) with each other showed that **1a** can transport mercury cation and small amounts of alkali metal cations, while **2a** transports only heavy metal cations. Therefore, there seems to be no relation between the size of ring pore and the ion selectivity. The 18-crown ring has larger flexibility and its donor atom can more easily coordinate to softer ion than the 15-crown ring, consequently **2a** is considered to show higher selectivity than **1a**.

Regarding the diazathia18-crown compounds, when **2a** is contrasted with the compounds (**2b-g**) containing heteroaromatics, the latter have higher selectivity to transport only silver and mercury cations but not to transport alkali metal cations except **2b**. On difference in substituent groups, for example, in the comparison of **2c**

Table 2. Cation Transport Properties of Functionalized Diazathia Crown Ethers

		trasnport rate 10^6(mol/h)							
Carrier	**R**	Na^+	K^+	Li^+	Hg^{2+}	Cu^{2+}	Pb^{2+}	Cd^{2+}	Ag^+
1a	–H	0.2	0.1	0.1	1.8	*	*	*	*[b]
1b		*	*	*	1.3	*	0.5	0.4	*
1c		*	*	*	*[b]	*	*	*	*[b]
1d		*	*	*	0.4	*	*	*	*[b]
1e		*	*	*	*[b]	*	*	*	0.1[b]
2a	–H	*	*	*	1.4	0.5	0.8	0.5	0.1
2b		1.3	*	*	1.5	*	0.3	0.8	1.3
2c		*	*	*	4.5	*	*	*	3.8
2d		*	*	*	2.6	*	*	*	2.1
2e		*	*	*	1.0	*	*	*	0.6[b]
2f		*	*	*	*	*	*	*	1.7
2g		*	*	*	2.7	*	*	*	2.3

[a] Asterisk shows below limit of detection(<0.1); [b] A precipitate was observed.

with **2d, 2c** having sulfur in the substituent groups shows higher transportability to mercury ion than **2d**. The only difference between them is one heteroatom in the substituent groups and their large different transportabilities apparently originate from whether it is oxygen or sulfur. From the above fact, sulfur atom is estimated to perform its duties on binding of mercury ion. Unexpectedly, the diazathia18-crown compounds (**2d**), (**2e**), and (**2g**) not containing sulfur in the substituent group indicated comparatively high transportability to mercury cation, whereas the crown ether (**2f**) modified with thiazolyl group did not transport whole mercury ion in spite of containing sulfur atom in the substituent group. On the contrary, **2c** modified with benzothiazolyl group shows the highest value in the Table. Presumably, at the transport experiment of **2f**, insoluble membrane (probably complex) is formed immediately in the interface between the organic layer and the aqueous layer, consequently mass transfer may not occur.

Next, the compounds (**1b**) and (**2b**) with methylene group between crown ring and heteroaromatic ring are compared; both can transport cadmium cation with higher value than other compounds, though both transportabilities and selectivities are not high. It is reported[2-5] that the crown ethers having pyridylmethyl group (picolyl group) as a side arm can transport cadmium cation, so that pyridylmethyl group seems to be better group to realize capture of cadmium cation.

Further studies on extraction properties for metal ions, NMR titration experiments as well as X-ray analyses of the diazathia crown ethers are currently underway.

ACKNOWLEDGEMENT

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8. Typical procedure: A solution of **1a** (0.50 g, 2 mmol), 2-chlorobenzothiazole (0.68 g, 4 mmol), and triethylamine (1.21 g, 12 mmol) in tetrahydrofuran (6 mL) was compressed to 0.8 GPa and heated at 100 °C for 4 days. After evaporation of the solvent, the residue was chromatographed on silica gel using hexane/ethyl acetate (2/1) and ethyl acetate as eluent to give **1c** (0.57 g, 56%). Satisfactory elemental and/or high resolution mass spectral analyses were obtained for all the new compounds.

7,10-Bis(2'-benzothiazolyl)-1-oxa-4,13-dithia-7,10-diazacyclopentadecane (**1c**) mp 146.5-147.5°C (ethanol); ^{1}H NMR(270.05 MHz, $CDCl_3$) δ 2.82(t, 4H, *J*=5.1 Hz), 3.06(t, 4H, *J*=7.0 Hz), 3.75(t, 4H, *J*=5.1 Hz), 3.86(t, 4H, *J*=7.0 Hz), 4.01(s, 4H), 7.05-7.11(m, 2H), 7.28-7.34(m, 2H), 7.58-7.64(m, 4H); ^{13}C NMR(67.51 MHz) δ 31.04, 32.54, 50.60, 52.72, 72.20, 119.14, 120.72, 121.29, 125.89, 131.05, 152.92, 167.58. Anal. Calcd for $C_{24}H_{28}N_4OS_4$: C, 55.78; H, 5.46; N, 10.84. Found: C, 55.67; H,5.38; N,10.96.

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