SYNTHESIS OF NEW BIS-CROWN ETHERS THAT SHOW SPECIFIC METAL ION TRANSPORT PROPERTIES

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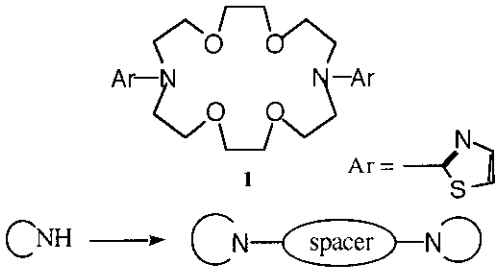
Abstract-A variety of bis-crown ethers were prepared in moderate to good yields (46-95%) by high pressure S_NAr reactions (0.8 GPa, 100°C). Some of them have indicated specific transport properties for Ag^+ ion.

Because of the continuing interests in host-guest chemistry,[1-8] there were many reports regarding crown ether and related compounds that have interesting gust selectivities in metal ion binding and transport properties Recently, based upon the high-pressure S_NAr reactions, we have prepared functionalized mono- and diaza-crown ethers which are directly connected to aromatic heterocycles. Certain of them such as **1**, show specific binding and transport properties towards Ag^+ ion.[9,10]



As an extension of these studies, we designed bis (single-armed crown ethers) possessing an appropriate heteroaromatic spacer. In this paper , we describe the synthesis of the new bis (single-armed crown ethers) and their binding properties. First, activated 2,6-dichloropyridines were used as spacers. A mixture of monoaza-crown (2.5 mmol), **2** (1.5 mmol), and triethylamine (9 mmol) was diluted with THF (4 ml) in a polytetrafluoroethylene vessel (8 ml) which was maintained at 0.8 GPa and 100°C for several days. Next, piperidine and homopiperadine were employed as spacers. Thus, a mixture of **4** (3 mmol), piperazine or homopiperadine (1.5 mmol), and triethylamine (6 mmol) was treated as above. Typical results were summarized in Table 1.[11]

Using the bis (single-armed crown ethers) (**3a - 5j**) as a cation carrier, single cation transport experiments were performed in a CH_2Cl_2 liquid membrane system. The results are summerized in Table 2. **3a** and **3b** spacers of which are connected to mono-aza 18-crown-6, proved to be effective and specific in transport

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This paper is dedicated to Professor Rolf Huisgen on the occasion of his 75 th birthday.

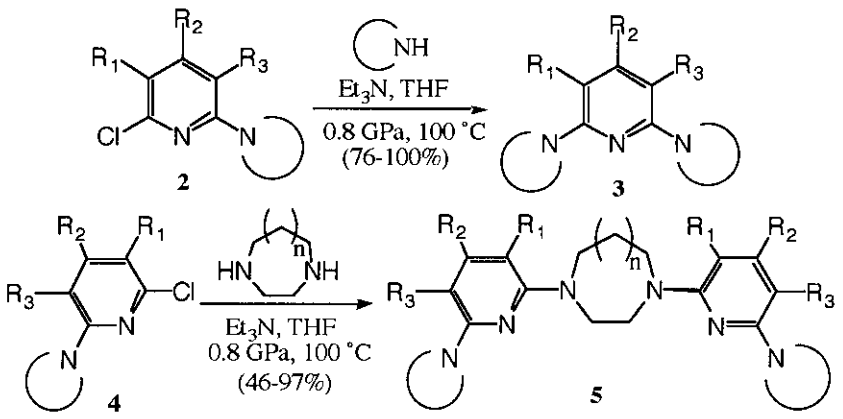

Table 1. Preparation of bis (single-armed crown ethers) (**3a** - **5j**) at 0.8 GPa and 100°C

	crown[a)]	R_1	R_2	R_3	n	days	yield
3a	18	Cl	CF_3	Cl	-	4	76
3b	18	H	H	NO_2	-	4	93
3c	15	Cl	CF_3	Cl	-	30	80
3d	15	H	H	NO_2	-	4	100
5a	18	Cl	CF_3	Cl	0	8	75
5b	18	Cl	CF_3	Cl	1	4	97
5c	18	H	H	NO_2	0	4	89
5d	18	H	H	NO_2	1	6	95
5e	18	NO_2	H	H	1	4	46
5f	15	Cl	CF_3	Cl	0	4	81
5g	15	Cl	CF_3	Cl	1	6	78
5h	15	H	H	NO_2	0	6	56
5i	15	H	H	NO_2	1	6	57
5j	15	NO_2	H	H	1	7	48

a) 18 and 15 are monoaza-18-crown-6 (**6**) and monoaza-15-crown-5 (**7**), respectively.

properties for Ag^+ ion, whereas **3c** and **3d** showed less effective transport properties because of small cavity of monoaza 15-crown-5. It is interesting to note that the parent monaza-18-crown-6 (**6**) shows K^+ ion specific transport properties.

Compounds (**5a**, **5c**, and **5d**) spacers of which are connected to mono-aza 18-crown-6 also show, though less specific, Ag^+ ion transport properties, while **5b** transports K^+ ion effectively together with Ag^+ ion. **5b** presumably forms either the sandwich-type 1:2 K^+/crown complex as was observed in (Z)-azobis(crown ethers)[12] or forms the complex in a molecular cleft fashion[13] due to more flexible structure of homopiperazine than piperazine as a spacer. In accord with the results of **3**, **5f**-**5j** did not transport any metal cations effectively, though the parent monoaza-15-crown-5 (**7**) transports Ag^+ ion pretty effective. Further studies are

underway designed to enhance the metal ion binding selectivity and transport properties of these novel agents and will be reported in due course.

Table 2 Transport properties of bis (single-armed crown ethers) (**3a** - **5j**) and monoaza-crown ethers (**6**, **7**)

	(Transport rate x 10^6 mol/h)							
	Na	K	Li	Hg	Cu	Pb	Cd	Ag
3a	0.2	2.8	*	0.4	*	*	*	3.5
3b	0.1	0.3	*	*	*	0.2	*	2.4
3c	*	*	*	*	*	*	*	0.3
3d	*	*	*	*	*	*	*	1.0
5a	*	1.2	*	*	*	0.2	*	3.8
5b	0.3	3.8	*	0.1	*	*	*	4.3
5c	*	0.7	*	0.1	*	0.1	*	1.6
5d	0.1	0.4	*	0.1	*	0.1	*	2.1
5e	*	*	*	*	*	*	*	0.4
6	0.6	4.2	0.3	-	*	0.3	*	1.1
5f	0.6	0 5	0.5	0.3	0 1	0.2	0.2	0.9
5g	*	*	*	*	*	*	*	0.7
5h	0.1	0 2	0.1	*	*	*	*	0.1
5i	0.1	0.2	0.1	*	*	*	*	0 1
5j	0.1	0.2	0.1	*	*	*	*	0.1
7	0.3	0.2	*	-	*	*	*	1 9
1	*	*	*	-	*	*	-	3 4

Conditions. Aq.: guest perchlorate, 0.5 mmol/H_2O, 5 ml.
Org.: crown, 0.0372 mmol/CH_2Cl_2, 12 ml

ACKNOWLEDGMENTS

This work was supported in part by Grant-in-Aid for Scientific Research from the Ministry of Education, Science, and Culture, Japan (No. 04453023). The authors are also grateful to the Ministry of Education, Science, and Culture, Japan for purchasing the high-field NMR instruments (JEOL JNM-A500 and JNM-EX270) by the special fund (to K. M. as a representative in 1992). This work was also supported in part by the Sasakawa Scientific Research Grant (No. 6-182) from The Japan Science Society (to H. I.) and by the research grant (to J. W. L.) from the Natural Sciences and Engineering Reserach Council of Canada.

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11. Typical procedure: A solution of monoaza-18-crown (0.40g, 1.3 mmol), **2a**[10] (0.51g, 1 mmol), and triethylamine (0.61g, 6 mmol) in dry THF (4 ml) was compresed to 0.8 GPa (8 kbar) and heated at 100 °C for 4 days. After evaparation of solvent and excess triethylamine, the residue was chromatographed on alumina using haxane, hexane/ethyl acetate, and ethyl acetate as eluent to give **3a** as yellow oil (0.56 g, 76%). Satisfactory elemental and/or high resolution mass spectral analyses were obtained for all new compounds.
2,6-bis(16'-(1,4,7,10,13-pentaoxa-16-azacyclooctadecane))-3,5-dichloro-4-trifluoromethylpyridine (**3a**) : mp 158°C;^{1}H nmr ($CDCl_3$) δ 3.78-3.50 (m, 48H); ^{13}C nmr ($CDCl_3$) δ 153.6 (J_{CF} = 37 Hz), 155.1, 109 9 (J_{CF} = 277 Hz), 107 5, 70.8, 70.6, 70.2, 51.4
1,4-bis(6'-(2-(16"-(1,4,7,10,13-pentaoxa-16-azacyclooctadecane))-3,5-dichloro-4-trifluoromethyl-pyridyl))-1,4-diazacyclohexane (**5a**): mp 115-116 °C, ^{1}H nmr ($CDCl_3$) δ 3.69-3 55 (m, 48H), 3.41 (s, 8H); ^{13}C nmr ($CDCl_3$) δ 155.8, 155.7, 136.4 (J_{CF} = 30 Hz), 122.5 (J_{CF} = 278 Hz), 109.8, 109.5, 71.0, 70 8, 70.4, 51.7, 49.4.
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Received, 9th June, 1994