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**Registry No.** **4**, 125877-64-7; **5**, 125877-59-0; **6**, 125877-74-9; **7**, 125877-65-8; **8**, 34748-64-6; **8** dithiane derivative, 125877-70-5; **9**, 53495-28-6; **10**, 31351-12-9; **10** dithiane derivative, 125949-38-4; **11**, 54676-38-9; **12**, 125877-61-4; **13**, 125949-32-8; **16** (exo isomer), 126059-67-4; **16** (endo isomer), 125877-67-0; methallyl alcohol, 513-42-8; 6-(*tert*-butyldimethylsiloxy)-2-methylidenehexan-1-ol, 125877-52-3; 1-(benzoyloxy)-2-methylidene-6-(*tert*-butyldimethylsiloxy)hexane, 125877-53-4; 1-(benzoyloxy)-2-methylidenehexan-6-ol, 125877-54-5; 1-(benzoyloxy)-2-methylidenehexan-6-al, 125877-55-6; 6-(4-((benzoyloxy)methyl)-4-pentenyl)fulvene, 125877-56-7; dimethyl 2,3-diazo-7-(5′-((benzoyloxy)methyl)hex-5′-enylidene)bicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate, 125877-57-8; dimethyl 2,3-diaza-7-(5′-((benzoyloxy)methyl)hex-5′-enylidene)bicyclo[2.2.1]heptane-2,3-dicarboxylate, 125877-58-9; (3a$\alpha$,6a$\alpha$,7a$\beta$)-2,3,3a,5,6,6a,7,7a-octahydro-1*H*-cyclopenta[*a*]pentalene-7a-methanol, 125877-60-3; (3a$\alpha$,6a$\beta$,7a$\beta$)-2,3,3a,5,6,6a,7,7a-octahydro-1*H*-cyclopenta[*a*]pentalene-7a-methanol, 125949-33-9; 2,3-diaza-7-[5′-formyl-5′-methylidenepentanylidene]bicyclo[2.2.1]hept-2-ene, 125877-62-5; 2,3-diaza-7-(5′-methylene-6′-hydroxyheptanylidene)bicyclo-[2.2.1]hept-2-ene, 125877-63-6; ((3a$\beta$,6a$\alpha$,7a$\beta$)-2,3,3a,5,6,6a,7,7a-octahydro-1*H*-cyclopenta[*a*]pentalen-7a-yl)-1-ethanone, 125877-66-9; ((3a$\alpha$,6a$\alpha$,7a$\alpha$)-2,3,3a,5,6,6a,7,7a-octahydro-1*H*-cyclopenta-[*a*]pentalen-7a-yl)-1-ethanone, 125949-34-0; (3a$\alpha$,6a$\alpha$,7a$\beta$)-2,3,3a,5,6,6a,7,7a-octahydro-7a-(dimethoxymethyl)-1*H*-cyclopenta[*a*]pentalene, 125877-68-1; (3a$\alpha$,4a$\alpha$,8$\alpha$)-2,3,3a,4,5,6,7,8-octahydro-4-(dimethoxymethyl)-4,6-methanoazulene, 125877-69-2; (3a$\beta$,4$\alpha$,8$\alpha$)-2,3,3a,4,5,6,7,8-octahydro-4-(dimethoxymethyl)-4,6-methanoazulene, 125949-35-1; (3a*S**,4*S**,7*R**,7a*S**)-trimethyl-[(2,3,3a,4,7,7a-hexahydro-4,7-methano-1*H*-inden-5-yl)oxy]silane, 85652-69-3; (1a*R**,2*S**,2a*S**,5a*R**,6*R**,6a*S**)-trimethyl[(octahydro-2,3-methano-1*H*-cycloprop[*f*]inden-1a-yl)oxy]silane, 125949-36-2; (3a*S**,4*S**,8*R**,8a*S**)-1,2,3,3a,4,5,6,7,8,8a-decahydro-4,8-methanoazulen-5-one, 53432-49-8; (3a*R**,4*S**,8*S**,8a*R**)-1,2,3,3a,4,5,6,7,8,8a-decahydro-4,8-methanoazulene-4-methanol, 125877-71-6; (3a*R**,4*S**,8*S**,8a*R**)-1,2,3,3a,4,5,6,7,8,8a-decahydro-4,8-methanoazulene-4-carboxylic acid, 125877-72-7; (3a*S**,4*R**,7*S**,7a*R**)-2,3,3a,4,7,7a-hexahydro-4,7-methano-1*H*-inden-1-one, 22981-84-6; (1*R**,3a*S**,4*R**,7*S**,-7a*R**)-2,3,3a,4,7,7a-hexahydro-4,7-methano-1*H*-inden-1-ol, 65470-96-4; (1*R**,3a*S**,4*R**,7*S**,7a*R**)-2,3,3a,4,7,7a-hexahydro-1-((methylsulfonyl)oxy)-4,7-methano-1*H*-indene, 125877-73-8; (3a*S**,4*R**,7*S**,7a*R**)-2,3,3a,4,7,7a-hexahydro-4,7-methano-1*H*-indene, 2826-19-9; (3a*R**,4*S*,5*R**,7*S**,7a*R**)-2,3,3a,4,5,6,7,7a-octahydro-5-hydroxy-4,7-methano-1*H*-indene, 10271-45-1; (3a*R**,4*S**,7*R**,7a*R**)-trimethyl[(2,3,3a,4,7,7a-hexahydro-4,7-methano-1*H*-inden-5-yl)oxy]silane, 85700-83-0; (1a*R**,2*S**,2a*R**,5a*S**,6*R**,6a*S**)-trimethyl[(octahydro-2,6-methano-1*H*-cycloprop[*f*]inden-1a-yl)oxy]silane, 125949-37-3; (3a*R**,4*S**,8*R**,8a*R**)-1,2,3,3a,4,5,6,7,8,8a-decahydro-4,8-methanoazulen-5-one, 85700-85-2; (3a*S**,4*S**,8*S**,8a*S**)-1,2,3,3a,4,5,6,7,8,8a-decahydro-4-(hydroxymethyl)-4,8-methanoazulene, 125949-39-5; (3a*S**,4*S**,8*S**,8a*S**)-1,2,3,3a,4,5,6,7,8,8a-decahydro-4-carboxy-4,8-methanoazulene, 125949-40-8; *trans*-2-[2-(hydroxymethyl)-2-methylenecyclopentyl]cyclopentenyl diradical, 125926-41-2; *trans*-2-[2-(dimethoxymethyl)-2-methylenecyclopentyl]cyclopentenyl diradical, 125926-43-4; *trans*-2-[2-(1,1-dimethoxyethyl)-2-methylenecyclopentyl]cyclopentenyl diradical, 125926-45-6; 1-(hydroxymethyl)-3-(5-cyclopentene-2,1-diyl)cyclohexyl diradical, 125926-42-3; 1-(dimethoxymethyl)-3-[5-cyclopetene-2,1-diyl)cyclohexyl diradical, 125926-44-5; 1-(1,1-dimethoxyethyl)-3-(5-cyclopentene-2,1-diyl)cyclohexyl diradical, 125926-46-7.

**Supplementary Material Available:** $^1H$ and $^{13}C$ NMR spectra (22 pages). Ordering information is given on any current masthead page.

# C-Pivot Lariat Ethers Bearing an Electron-Donating Side Arm as $Li^+$-Selective Extractants

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A new series of methyl-substituted lariat ethers having a 12-, 13-, or 14-crown-4 ring was prepared by the reaction of the corresponding bromomethyl methyl crown ethers (**1-3**), with an appropriate sodium alkoxide or potassium phenoxide. Their complexation properties toward alkali metal cations were evaluated by the solvent extraction method. The lariat ether based on 13-crown-4 with a quinolinyloxy side arm (**5a**) shows a good affinity toward lithium cation over other alkali metal cations. The high extraction efficiency of **5a** was ascertained by comparing its extraction equilibrium constant ($K_{ex}$) with those of some representative compounds known as good extractants for lithium ion. The relationship between the structure of the ligand and the cation selectivity is also discussed.

## Introduction

Lariat ethers show different complexation properties from normal crown ethers toward a variety of cations because of effective coordination of the electron-donating side arm.[1] Recently, we found that complexing ability toward $Na^+$ and $Na^+/K^+$ selectivity was dramatically raised by introducing a methyl group on the pivot position of Gokel's C-pivot lariat ether having a 15-crown-5 ring.[2] One of these lariat ethers having an 18-crown-6 ring displayed a higher stability constant for $K^+$ than an unsubstituted 18-crown-6.[2c]

(1) (a) Gokel, G. W.; Dishong D. M.; Diamond, C. J. *J. Chem. Soc., Chem. Commun.* **1980**, 1053. (b) Dishong, D. M.; Diamond, C. J.; Cinoman, M. I.; Gokel, G. W. *J. Am. Chem. Soc.* **1983**, *105*, 586. (c) Echegoyen, L.; Kaifer, A.; Durst, H.; Schultz, R. A.; Dishong, D. M.; Goli, D. M.; Gokel, G. W. *Ibid.* **1984**, *106*, 5100.

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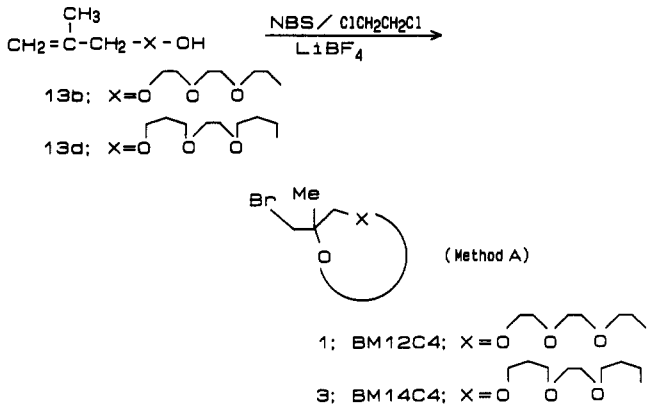
0022-3263/90/1955-2752$02.50/0 

**Table I. Solvent Extraction of Alkali Metal Picrates by Several Crown Ethers[a]**

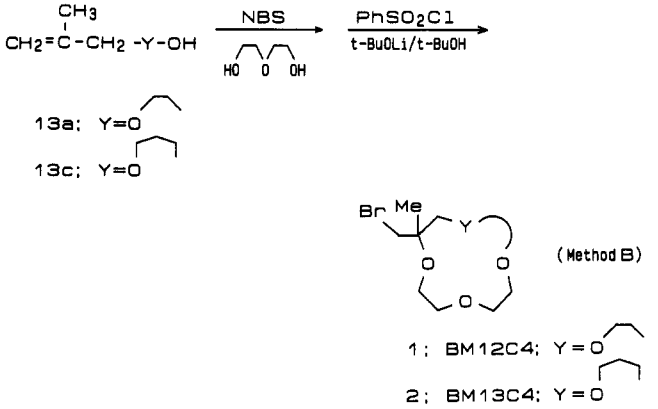
| crown ether | | | extraction, % | | | | |
|---|---|---|---|---|---|---|---|
| compd | ring size | DN[b] | $Li^+$ | $Na^+$ | $K^+$ | $Rb^+$ | $Cs^+$ |
| 1 | 12C4 | 4 | <0.3 | <0.3 | <0.3 | <0.3 | <0.3 |
| 2 | 13C4 | 4 | <0.3 | <0.3 | <0.3 | <0.3 | <0.3 |
| 3 | 14C4 | 4 | <0.3 | <0.3 | <0.3 | <0.3 | <0.3 |
| 4a | 12C4 | 6 | 13.3 | 12.5 | 3.4 | 1.2 | 2.5 |
| 4b | 12C4 | 6 | <0.3 | 0.8 | <0.3 | <0.3 | <0.3 |
| 4c | 12C4 | 5 | <0.3 | 2.4 | 1.3 | <0.3 | 1.1 |
| 5a | 13C4 | 6 | 50.0 | 24.7 | 3.4 | 2.1 | 1.9 |
| 5b | 13C4 | 6 | 5.3 | 2.9 | 1.6 | <0.3 | <0.3 |
| 5c | 13C4 | 5 | 1.0 | 1.9 | 1.0 | <0.3 | <0.3 |
| 6a | 14C4 | 6 | 27.8 | 6.5 | <0.3 | <0.3 | <0.3 |
| 7 | 14C4 | 5 | 14.3 | <0.3 | 1.4 | <0.3 | 0.8 |

[a] Organic phase ($CH_2Cl_2$, 10 mL)/aqueous phase (10 mL); [MOH] = 50 mM; [extractant] = [picric acid] = 0.5 mM; 22 °C; 9 h. [b] The number of donor atoms.

**Scheme I**



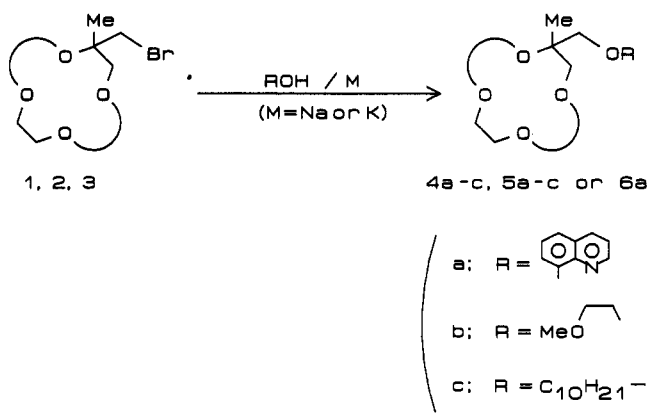

**Scheme II**




Considerable effort has been devoted to developing useful ligands for lithium ion[3-7] for use as extractants, carriers through the lipophilic membranes, or sensors for ion-selective electrodes. Lithium ion selective extractants, which are able to extract $Li^+$ into the lipophilic phase from an aqueous phase and to concentrate it from dilute aqueous media, have been of much interest in lithium therapy.[4a]

In this paper, we describe the syntheses of methyl-substituted lariat ethers, having 12–14-membered rings (Chart I), and the evaluation of their ability to extract lithium and alkali metal picrates. The relationship between the structure of the extractants and their complexation properties toward lithium ion will also be discussed in comparison with the reference compounds shown in Chart I.

**Scheme III**




## Results and Discussion

**Synthesis.** We used two methods for preparing 2-(bromomethyl)-2-methyl-12-crown-4 (**1**) (Schemes I and II). One is intramolecular bromoalkoxylation of triethylene glycol 2-methylallyl ether (**13b**) with *N*-bromosuccinimide (NBS) using $LiBF_4$ as the template in 1,2-dichloroethane (method A).[2] The other is intermolecular bromoalkoxylation of ethylene glycol 2-methylallyl ether (**13a**) with NBS and diethylene glycol, followed by intramolecular cyclization with benzenesulfonyl chloride using lithium *tert*-butoxide as the base in *tert*-butyl alcohol (method B).[2] Method A was superior to method B from the viewpoint of a higher yield (36% vs 15%) and a smaller number of steps. A combination of diethylene glycol 2-methylallyl ether and ethylene glycol was not chosen because it was suspected that formation of a stable dioxane derivative would be preferred in the cyclization step. Method A was also applied for preparing 2-(bromomethyl)-2-methyl-14-crown-4 (**3**).

On the other hand, we used method B in the synthesis of 3-(bromomethyl)-3-methyl-13-crown-4 (**2**). Though intramolecular bromoalkyloxylation was expected to give a better result, it is rather tedious to prepare the precursor,

(3) (a) Olsher, U.; Jagur-Grodzinski, J. *J. Chem. Soc., Dalton Trans.* **1981**, 501. (b) Czech, B. P.; Babb, D. A.; Son, B.; Bartsch, R. A. *J. Org. Chem.* **1984**, *49*, 4805. (c) Bartsch, R. A.; Czech, B. P.; Kang, S. I.; Stewart, L. E.; Walkowiak, W.; Charewicz, W. A.; Heo, G. S.; Son, B. *J. Am. Chem. Soc.* **1985**, *107*, 4997. (d) Kobiro, K.; Matsuoka, T.; Takeda, S.; Kakiuchi, K.; Tobe, Y.; Odaira, Y. *Chem. Lett.* **1986**, 713.

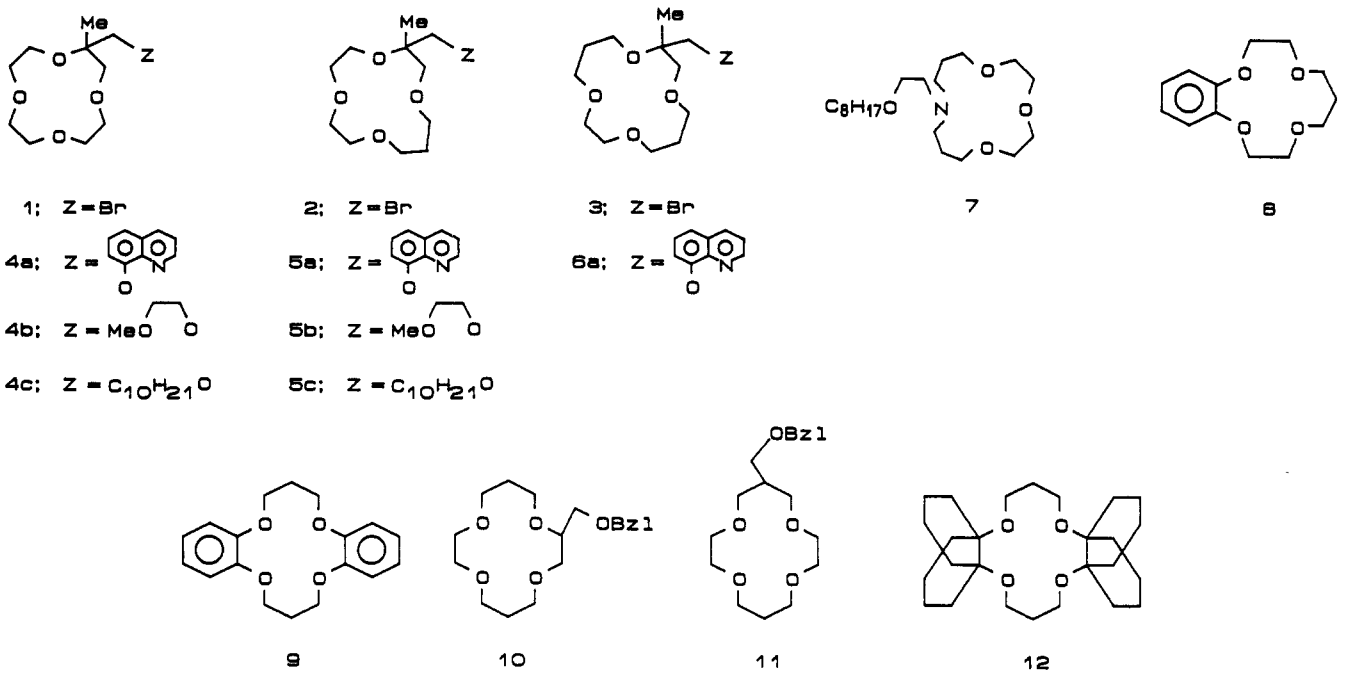
(4) (a) Shanzer, A.; Samuel, D.; Korenstein, R. *J. Am. Chem. Soc.* **1983**, *105*, 3815. (b) Nakatsuji, Y.; Wakita, R.; Harada, Y.; Okahara, M. *J. Org. Chem.* **1989**, *54*, 2988.

(5) Walkowiak, W.; Brown, P. R.; Shukla, J. P.; Bartsch, R. A. *J. Membr. Sci.* **1987**, *32*, 59.

(6) Izatt, R. M.; LindH, G. C.; Bruening, R. L.; Huszthy, P.; Lamb, J. D.; Bradshaw, J. S.; Christensen, J. J. *J. Incl. Phenom.* **1987**, *5*, 739.

(7) (a) Kitazawa, S.; Kimura, K.; Yano, H.; T. Shono, T. *J. Am. Chem. Soc.* **1984**, *106*, 6978. (b) Kimura, K.; Sakamoto, S.; Kitawaza, S.; Shono, T. *J. Chem. Soc., Chem. Commun.* **1985**, 669.

**Chart I**



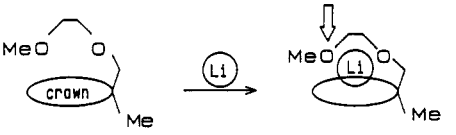

oligoalkylene glycol 2-methylallyl ether.

The modification of bromomethyl methyl crown ethers (**1–3**) was carried out according to the literature[2] (Scheme III). The reaction was usually carried out using sodium alkoxide in an excess of the corresponding alcohol at 120 °C for 24 h. The reaction with 8-hydroxyquinoline was carried out by using the corresponding potassium salt at 140 °C for 48 h. The presence of the methyl substituent at the pivot carbon prevents the undesirable elimination reaction. The structures of all new compounds were ascertained by NMR, mass, and IR spectroscopy, and elemental analyses (Experimental Section).

**Solvent Extraction.** The complexation properties of lariat ethers toward alkali metal cations were evaluated by solvent extraction (Table I.)[8] The side arms examined in this study are the quinolinyloxy, methoxyethoxy, and decyloxy groups. The last one has one donor atom, but the others have two donor atoms. Though all bromomethyl methyl crown ethers (**1–3**) showed low complexing ability toward alkali metal cations under these conditions, lariat ethers showed some affinity for these cations. This result shows an effective coordination of the electron-donating side arm for cations. As for 12-crown-4 derivatives, only **4a**, with a quinolinyloxy side arm, extracted over 10% of ions in the case of lithium ion or sodium ion. Since the extraction of cations by **4b** and **4c** was very small, it was difficult to find some trend concerning the effect of the electron-donating side arm on complexation.

In the case of 13-crown-4 ethers, however, a trend was clearly observed. The order of complexing ability of lariat ethers toward lithium ion was **5a** > **5b** > **5c**. The higher extraction efficiency of **5b** compared to that of **5c** reflects the effective coordination of the second oxygen atom of the side arm toward lithium ion (shown by arrow in Chart II). The extraction efficiency of **5a** reached 50% using equimolar amounts of picrate anion and the ligand. Although the extraction efficiency of **5a** (13-crown-4) for lithium ion was higher than that of **6a** (14-crown-4), its $Li^+/Na^+$ selectivity was lower than that of the latter. It

**Chart II**




is interesting that a maximum extraction efficiency is attained not by the 14-crown-4 derivative (**6a**) but by the 13-crown-4 derivatives (**5a**) in this series of C-pivot lariat ethers. The ring size of the 14-crown-4 is more suitable for lithium ion than that of the 13-crown-4 or the 12-crown-4.[7a] In the case of lariat ethers, however, the cooperative function of the crown ring and the electron-donating side arm should be considered. This result means that 14-crown-4 ring does not necessarily have the most favorable coordination geometry for lithium ion. $^1H$ NMR spectral data provide additional evidence for the contribution of the side arm. The methylene protons of the electron-donating side arm of **4a**, **5a**, and **6a** exhibited downfield shifts (0.26, 0.29, and 0.19 ppm, respectively) with the addition of lithium perchlorate in $CDCl_3$.

We can compare the extraction efficiency of the new lariat ethers with those of compounds reported in the literature. In order to compare with cylindrical 14-crown-4 (**12**),[3d] which is the most effective neutral ligand for lithium ion among the crown ether derivatives reported in the literature to the best of our knowledge, another set of extraction conditions was examined. The extraction profiles for **4a**, **5a**, **6a**, and **12** are summarized in Figure 1. In this case, the concentrations of picrate ion and the ligand are low compared with the conditions shown in the footnotes of Table I. This change of extraction conditions generally enhanced the $Li^+$ selectivity over other alkali metal cations, especially in the case of **4a**. It is known that an increase in the concentration of the crown tends to increase the amounts of the 2:1 (ionophore:metal ion) complex. The contribution of this type of complex may have increased the extraction efficiency of **4a** toward sodium ion under the conditions shown in Table I. Figure 1 clearly shows that the extraction efficiency of **5a** toward lithium ion is about twice that of **12**. The extraction ef-

(8) Nakatsuji, Y.; Sakamoto, M.; Okahara, M.; Matsuhisma, K., *Nippon Kagaku Kaishi* **1987**, 430.

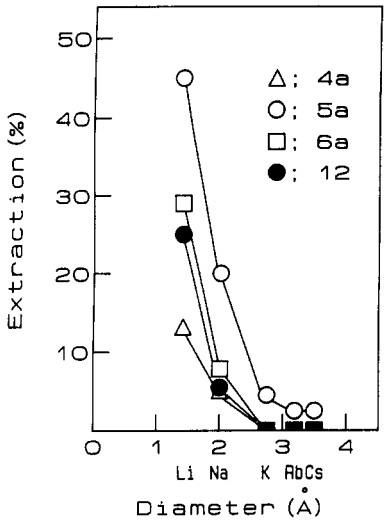



**Figure 1.** Extraction data toward alkali metal picrate. Extraction conditions: Organic phase ($CH_2Cl_2$, 10 mL)/aqueous phase (10 mL); [MOH] = 100 mM; [extractant] = [picric acid] = 0.07 mM; 22 °C; 9 h.

**Table II. Extraction Constants ($K_{ex}$)[a] for Lithium Ion by Several Crown Ethers**

| compd | crown ether ring size | DN[b] | log $K_{ex}$ |
|---|---|---|---|
| **4a** | 12C4 | 6 | 3.72 |
| **5a** | 13C4 | 6 | 4.87 |
| **5b** | 13C4 | 6 | 2.83 |
| **6a** | 14C4 | 6 | 4.45 |
| **7** | 14C4 | 5 | 3.67 |
| **8** | benzo-13C4 | 4 | 3.18[c] |
| **9** | dibenzo-14C4 | 4 | 2.97[c] |
| **10** | 14C4 | 5 | 3.29[d] |
| **11** | 14C4 | 5 | 2.69[d] |

[a] Tricresyl phosphate and 1,2-dichloroethane/water system at room temperature (23–26 °C). [b] The number of donor atoms. [c] Data from ref 3a. [d] Data from ref 3b.

ficiency of **6a** is very similar to that of **12** for lithium ion.

The determination of extraction equilibrium constants ($K_{ex}$) for the new lariat ethers makes possible a direct comparison with literature data for other crown ethers. Lithium picrate was extracted from the aqueous phase into a 1:1 mixture of 1,2-dichloroethane and tricresyl phosphate according to the literature.[3a,b] The results are shown in Table II along with the data for reference compounds. Among the new lariat ethers, the largest $K_{ex}$ was obtained with **5a**, as expected on the basis of the data in Table I using dichloromethane as the organic layer. It is noteworthy that the $K_{ex}$ of **5a** is 30 times that of **10**.

**Liquid Membrane Transport.** N-Pivot lariat ethers based on monoaza-14-crown-4 ether have recently been shown to be excellent selective ionophores for lithium ion in an artificial membrane system.[4b] The transport velocity of **7** for lithium ion, however, was slower than that of *N*-octylmonoaza-15-crown-5 for sodium ion.[8] This finding is reasonably explained by considering that the complexing ability of **7** for lithium ion is rather low compared with that of the latter for sodium ion. Accordingly, the development of a ligand having a higher complexing ability toward lithium ion is desirable. Transport experiments using our new ligands were carried out in a U-type cell under the conditions described in the footnotes in Table III. The results are also summarized in Table III. An increase in the transport velocity was successfully attained by **5a**, judging from the total cations transported, although its selectivity was moderate.

In conclusion, strong complexation properties for lithium ion were achieved by adding a quinolinyloxy side arm to the crown ring. The side arm may lock the coordination sites into a rigid arrangement around the cavity. The data presented in this work clearly show that introduction of an electron-donating side arm to the crown ring is an effective method for developing a host for lithium ion as well as for other alkali metal cations.

## Experimental Section

$^1H$ NMR spectra were taken at 400 MHz, and mass spectra were measured at an ionization potential of 70 eV. Ethylene glycol mono-2-methylallyl ether (**13a**), triethylene glycol mono-2-methylallyl ether (**13b**), trimethylene glycol mono-2-methylallyl ether (**13c**), and 4,7-dioxa-1,10-decanediol mono-2-methylallyl ether (**13d**) were prepared according to the literature.[2] Merck silica gel 60 (70–230 mesh) was used for the chromatography.

**2-(Bromomethyl)-2-methyl-1,4,7,10-tetraoxacyclododecane (1). Method A (via Intramolecular Bromoalkoxylation).** Compound **13b** (20.5 g, 0.1 mol) in 1,2-dichloroethane (100 mL) was added dropwise to a stirred suspension of *N*-bromosuccinimide (NBS; 17.8 g, 0.1 mol) and $LiBF_4$ (37.5 g, 0.4 mol) in 1,2-dichloroethane (300 mL) over a period of 2 h at 45 °C, and the mixture was stirred at 50 °C for another 6 h. The mixture was filtered, and the solvent was evaporated. Water (200 mL) was added to the residue and extracted with dichloromethane (200 mL × 3). After evaporation, the viscous oil was purified by chromatography over silica gel (acetone/hexane = 3/97) and then distilled to give **1** (10.2 g, 36%) as a slightly yellow oil. The analytical data of **1** are as follows: bp 80 °C (0.01 Torr) (Kugelrohr); IR (neat) 2920, 2860, 1450, 1370, 1300, 1250, 1140, 920 $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 1.24 (s, 3 H), 3.46–3.80 (m 16 H); MS *m/e* (relative intensity) 284 ($M^+ + 2$), 282 ($M^+$), 203 (4), 189 (8), 145 (8), 138 (15), 101 (31), 87 (31), 45 (100).

Anal. Calcd for $C_{10}H_{19}O_4Br$: C, 42.42; H, 6.76; Br, 28.22. Found: C, 42.81; H, 6.91; Br, 28.24.

**Method B (via Intermolecular Bromoalkoxylation).** To a stirred suspension of NBS (18.4 g, 0.103 mol) in diethylene glycol (43.9 g, 0.414 mol) was added **13a** (12.0 g, 0.103 mol) at 40 °C over 1 h. The resulting mixture was further stirred at 50 °C for 6 h. After cooling to room temperature, water (100 mL) was added to the mixture, and the product was extracted with dichloromethane (100 mL × 2). The solvent was evaporated to give a viscous brown oil. Some diethylene glycol and byproducts such as succinimide were removed by distillation in a Kugelrohr apparatus (150 °C/0.01 Torr) to give a viscous brown oil (16.8 g, 56%). The crude intermediate was used for the next step without further purification. After dissolving lithium metal (1.10 g, 0.159 mol) in *tert*-butyl alcohol (150 mL) a solution of diol (6.20 g, 0.0206 mol) and benzenesulfonyl chloride (3.80 g, 0.0213 mol) in *tert*-butyl alcohol (150 mL) was added dropwise to the mixture over a 4-h period with continuing gentle reflux, and the mixture was held at reflux for another 2 h. The mixture was filtered and washed

**Table III. Competitive Passive Transport Data[a] toward $Li^+$, $Na^+$, and $K^+$**

| compd | $Li^+$ | $Na^+$ | $K^+$ | $\sum M^+$[b] | selectivity $Li^+/Na^+$ | selectivity $Li^+/K^+$ |
|---|---|---|---|---|---|---|
| **4a** | 4.4 | 5.0 | 0.74 | 10.1 | 0.9 | 5.9 |
| **5a** | 8.9 | 2.4 | 0.17 | 11.5 | 3.5 | 52 |
| **7** | 7.8 | 0.3 | 0.074 | 8.2 | 24 | 97 |

[a] $10^6$ mol/h. [b] Total amount of transported cations. Transport conditions: aqueous phase 1 (10 mL), [LiCl] = [NaCl] = [KCl] = [$Me_4NOH$] = 0.1 M; organic phase ($CH_2Cl_2$, 20 mL) carrier and picric acid, $5 \times 10^{-5}$ mol; aqueous phase 2 (10 mL) [HCl] = 0.1 M; 25 °C.

with dichloromethane. The solvent was evaporated. Water (100 mL) was added to the residue, and the mixture was extracted with dichloromethane (200 mL). After evaporation, the residue was distilled under reduced pressure (100 °C/0.04 Torr) and purified by chromatography over silica gel (acetone/hexane) to give a slightly yellow oil (1.52 g, 26% based on intermediate diol). All spectral data agree with the data shown above.

**3-(Bromomethyl)-3-methyl-1,4,7,10-tetraoxacyclotridecane (2).** The synthetic procedure was almost the same as that used for **1** (method B). The yield was calculated based on the starting **13c** (6.8 g, 23%): bp 90 °C (0.01 Torr) (Kugelrohr); IR (neat) 2910, 2860, 1440, 1370, 1250, 1120, 900 $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 1.26 (s, 3 H), 1.68–1.88 (m, 2 H), 3.50–3.70 (m, 16 H); MS *m/e* (relative intensity) 298 ($M^+ + 2$), 296 ($M^+$), 217 (12), 203 (8), 147 (33), 115 (40), 103 (38), 87 (21), 59 (44), 45 (100).

Anal. Calcd for $C_{11}H_{21}O_4Br$: C, 44.46; H, 7.12; Br, 26.89. Found: C, 44.58; H, 7.16; Br, 26.52.

**2-(Bromomethyl)-2-methyl-1,4,8,11-tetraoxacyclotetradecane (3).** The synthetic procedure was almost the same as that used for **1** (method A). The preparation of 4,7-dioxa-1,10-decanediol was performed according to the literature.[7a] The crude product of **3** was purified by chromatography over silica gel (acetone/hexane = 5/95) and then used in the next step without further purification. The crude yield was calculated based on the starting **13d** (12.1 g, 39%). IR (neat): 2950, 2870, 1460, 1300, 1240, 1120, 900 $cm^{-1}$.

**General Procedure for the Synthesis of Lariat Ethers.** A simple substitution reaction of bromomethyl methyl crown ether with an appropriate sodium alkoxide or potassium phenoxide was carried out. After sodium metal (0.2 g, 9 mmol) was dissolved in the alcohol (60 mmol), bromomethyl methyl crown ether (3 mmol) was added to the mixture, and the mixture was stirred at 120 °C for 24 h. 8-Hydroxyquinoline was used as a solution in 20 mL of diethylene glycol dimethyl ether when potassium metal was employed instead of sodium, and the mixture was stirred at 140 °C for 48 h. After the mixture was cooled to room temperature, dichloromethane (20–50 mL) was added to the residue and the insoluble matter was removed by filtration. Then the resulting mixture was concentrated and distilled under reduced pressure (150–200 °C/0.01 Torr). The volatiles were redistilled by using a Kugelrohr apparatus.

**8-[(2-Methyl-1,4,7,10-tetraoxacyclododec-2-yl)methoxy]quinoline (4a)**: yield 0.58 g (56%); bp 180 °C (0.02 Torr) (Kugelrohr); IR (neat) 2920, 2860, 1500, 1370, 1260, 1100 $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 1.45 (s, 3 H), 3.57–4.00 (m, 14 H), 4.12 (d, 1 H, $J$ = 9 Hz), 4.38 (d, 1 H, $J$ = 9 Hz), 7.12–7.54 (m, 4 H), 8.04–8.40 (m, 1 H), 8.90–9.00 (m, 1 H); MS *m/e* (relative intensity) 347 ($M^+$, 9), 184 (90), 158 (100), 145 (95), 101 (36), 45 (60).

Anal. Calcd for $C_{19}H_{25}O_5N \cdot 0.5H_2O$: C, 64.03; H, 7.35; N, 3.93. Found: C, 63.83; H, 7.26; N, 4.15.

**2-[(2-Methoxyethoxy)methyl]-2-methyl-1,4,7,10-tetraoxacyclododecane (4b)**: yield 0.35 g (79%); bp 80 °C (0.005 Torr) (Kugelrohr); IR (neat) 2930, 2860, 1450, 1370, 1250, 1140 $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 1.16 (s, 3 H), 3.34 (s, 3 H), 3.42–3.88 (m, 20 H); MS *m/e* (relative intensity) 278 ($M^+$, 6) 189 (67), 147 (26), 101 (64), 59 (100).

Anal. Calcd for $C_{13}H_{26}O_6$: C, 56.10; H, 9.42. Found: C, 56.41; H, 9.82.

**2-[(Decyloxy)methyl]-2-methyl-1,4,7,10-tetraoxacyclododecane (4c)**: yield 0.35 g (32%); bp 95 °C (0.02 Torr) (Kugelrohr); IR (neat) 2920, 2860, 1450, 1360, 1250, 1120, 930 $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 0.78–1.08 (t, 3 H), 1.10 (s, 3 H), 1.22–1.56 (m, 16 H), 3.46–3.90 (m, 18 H); MS *m/e* (relative intensity) 360 ($M^+$, 8), 189 (62), 101 (100), 59 (65), 45 (70).

Anal. Calcd for $C_{20}H_{40}O_5$: C, 66.63; H, 11.18. Found: C, 66.26; H, 11.22.

**8-[(3-Methyl-1,4,7,10-tetraoxacyclotridec-3-yl)methoxy]quinoline (5a)**: yield 0.38 g (35%); bp 145 °C (0.03 Torr) (Kugelrohr); IR (neat) 3050, 2920, 2860, 1570, 1500, 1460, 1375, 1320, 1260, 1120, 820, 790 $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 1.46 (s, 3 H), 1.64–2.06 (m, 2 H), 3.48–4.10 (m, 14 H), 4.14 (d, 1 H, $J$ = 9 Hz), 4.36 (d, 1 H, $J$ = 9 Hz), 7.06–7.60 (m, 4 H), 7.98–8.28 (m, 1 H), 8.82–9.06 (m, 1 H); MS *m/e* (relative intensity) 361 ($M^+$, 5), 184 (71), 158 (54), 145 (100), 59 (31), 45 (53).

Anal. Calcd for $C_{20}H_{27}O_5N \cdot 0.5H_2O$: C, 64.85; H, 7.62; N, 3.78. Found: C, 64.83; H, 7.50; N, 3.71.

**3-[(2-Methoxyethoxy)methyl]-3-methyl-1,4,7,10-tetraoxacyclotridecane (5b)**: yield 0.60 g (68%); bp 80 °C (0.01 Torr) (Kugelrohr); IR (neat) 2920, 2860, 1470, 1360, 1250, 1120 $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 1.16 (s, 3 H), 1.60–1.90 (m, 2 H), 3.34 (s, 3 H), 3.40–3.86 (m, 20 H); MS *m/e* (relative intensity) 292 ($M^+$, 13), 203 (99), 147 (38), 115 (33), 101 (24), 89 (44), 87 (44), 73 (70), 59 (98), 45 (100).

Anal. Calcd for $C_{14}H_{28}O_6$: C, 57.51; H, 9.65. Found: C, 57.58; H, 9.65.

**3-[(Decyloxy)methyl]-3-methyl-1,4,7,10-tetraoxacyclotridecane (5c)**: yield 0.48 g (43%); bp 100 °C (0.02 Torr) (Kugelrohr); IR (neat) 2930, 2850, 1470, 1360, 1240, 1110 $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 0.76–1.10 (t, 3 H), 1.20 (s, 3 H), 1.28–1.54 (m, 16 H), 1.62–1.90 (m, 2 H), 3.46–3.92 (m, 18 H); MS *m/e* (relative intensity) 374 ($M^+$, 8), 203 (80), 115 (24), 101 (42), 59 (86), 45 (100).

Anal. Calcd for $C_{21}H_{42}O_5$: C, 67.34; H, 11.30. Found: C, 67.60; H, 11.18.

**8-[(2-Methyl-1,4,8,11-tetraoxacyclotetradec-2-yl)methoxy]quinoline (6a)**: yield 0.35 g (31%); bp 125 °C (0.02 Torr) (Kugelrohr); IR (neat) 2950, 2850, 1570, 1500, 1110, 890 $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 1.46 (s, 3 H), 1.75–1.95 (m, 4 H), 3.50–3.85 (m, 14 H), 4.24 (s, 2 H), 7.14–7.16 (m, 1 H), 7.37–7.46 (m, 3 H), 8.11–8.14 (m, 1 H), 8.90–8.92 (m, 1 H); MS *m/e* (relative intensity) 375 ($M^+$, 6) 345 (7), 145 (100).

Anal. Calcd for $C_{21}H_{29}O_5N \cdot 0.5H_2O$: C, 65.60; H, 7.87; N, 3.64. Found: C, 65.26; H, 7.59; N, 3.75.

**Extraction of Alkali Metal Picrate into Methylene Chloride.** A mixture of an aqueous solution (10 mL) of alkali metal hydroxide (50 or 100 mM) and picric acid (0.5 or 0.07 mM) and a dichloromethane solution (10 mL) of an appropriate extractant (0.5 or 0.07 mM) was shaken at 22 °C for 9 h. The extraction efficiency was calculated from on the absorption of picrate anion in the aqueous phase at 354 nm in the UV spectrum.[9]

**Extraction of Alkali Metal Picrate into Tricresyl Phosphate/1,2-Dichloroethane.** A mixture of an aqueous solution (3.0 mL) of alkali metal hydroxide (100 mM) and picric acid (0.1 mM) and a tricresyl phosphate/1,2-dichloroethane (1/1 = vol/vol) solution (3.0 mL) of an appropriate extractant (0.03–10.0 mM) was agitated for 2 min with a vortex mixer. The resulting mixture was centrifuged for 10 min to separate the layers. In all cases, the absorption of picrate anion in the aqueous phase was measured at 354 nm in the UV spectrum. The concentrations of lithium picrates in the organic phase were calculated by difference and were used in calculating the $K_{ex}$ (extraction constant) value. Each experiment was repeated at least three times, and the results are reported as the average of three determinations.

**Liquid Membrane Transport.** Transport experiments were carried out in a U-type cell at 25 °C. The details of the transport conditions are summarized in the footnotes of Table III. The cation concentrations were determined by using a Nippon Jarrel Ash AA-8500 atomic absorption spectrophotometer.

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**Registry No.** **1**, 126063-36-3; **2**, 126063-37-4; **3**, 126063-38-5; **4a**, 126063-41-0; **4b**, 126063-42-1; **4c**, 126063-43-2; **5a**, 126063-44-3; **5b**, 126063-45-4; **5c**, 126063-46-5; **6a**, 126063-47-6; **13a**, 5175-48-4; **13b**, 111719-00-7; **13c**, 111718-99-1; **13d**, 126063-39-6; $Li^+$, 7439-93-2; $Na^+$, 7440-23-5; $K^+$, 7440-09-7; $HO(CH_2CH_2O)_2C(CH_3)(CH_2Br)CH_2O(CH_2)_2OH$, 126063-40-9; diethylene glycol, 111-46-6; 8-hydroxyquinoline, 148-24-3; 2-methoxyethanol, 109-86-4; 1-decanol, 112-30-1.

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