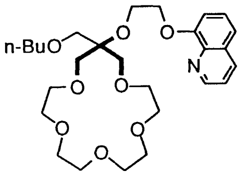
Importance of the Glycerol Structure of C-Pivot Lariat Ethers Containing a 16-Crown-5 Ring for Effective Complexation toward Alkali Metal Cations

Kohji Kita, Toshiyuki Kida, Yohji Nakatsuji, and Isao Ikeda*
Department of Applied Chemistry, Faculty of Engineering, Osaka University, 2-1, Yamada-oka, Suita, Osaka 565

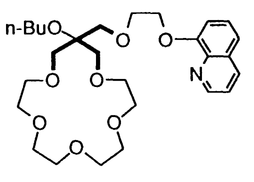
(Received January 6, 1997; CL-970005)

The effect of the skeletal structure of the pivot position of the C-pivot lariat ethers containing a 16-crown-5 ring on their complexation properties toward alkali metal cations was examined. The glycerol structure was found to be necessary for the effective coordination toward the potassium ion.

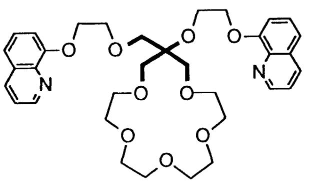
Lariat ethers are interesting host molecules for alkali metal and alkaline earth metal cations because they possess unique complexation properties based on the effective coordination of the electron-donating sidearm with the cation.[1] Concerning 16-crown-5 derivatives, a variety of lariat ethers have been synthesized in order to clarify the relation between the structure and the complexation property.[2, 3] Among them, when the electron-donating sidearm is connected with the central carbon of the trimethylene moiety, two types are known. One type, such as **1**, directly connects the oxygen atom to the pivot carbon. The other type, such as **2**, mediates one carbon atom between the pivot carbon and the oxygen atom. Which is more effective for the complexation toward metal cations? Although the complexation properties of such types of compounds have been reported, the direct comparison between these two types has never been done to the best of our knowledge. From this point of view, we describe the synthesis of such two types of lariat ethers (**1**-**3**) and the comparison in their complexation properties for alkali metal cations.



1



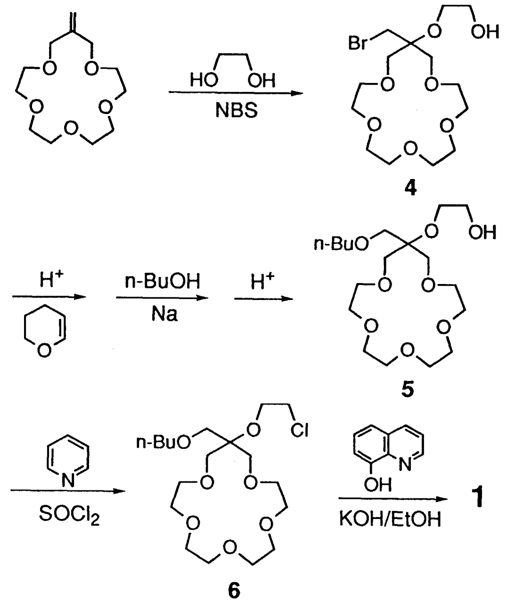
2



3

The synthetic procedure for compound **1** is summarized in Scheme 1. Compound **4** was obtained from the bromoalkoxylation reaction of 15-methylene-16-crown-5[4] using N-bromosuccinimide (NBS) and ethylene glycol. The hydroxyl group of **4** was protected by the treatment with dihydropyrane according to the conventional method and then the compound was reacted with *n*-butyl alcohol under the basic conditions, followed by the deprotection to give **5**. After compound **5** was converted to the corresponding chloride (**6**), the reaction of **6** and 8-hydroxyquinoline was carried out in ethanol in the presence of KOH at refluxed temperature for 2 days[5] to afford **1**. On the other hand, compound **2** was prepared by changing the reaction sequence used in the case of **1**, that is, the bromoalkoxylation of 15-methylene-16-crown-5 with NBS and *n*-butyl alcohol was done at the first step. All structures were ascertained by ^{1}H NMR and IR spectroscopy, mass spectrometry and elemental analysis.[6]

Scheme 1. Preparation of compound **1**.



Extraction profiles conducted under the conditions using equimolar amounts of the ligand and alkali metal picrate[3, 7] are shown in Figure 1. Ligands **1** and **2** are structurally regarded to be derived from glycerol and trimethanolmethane, respectively.[8] Although both ligands **1** and **2** possess the same hetero atoms (nine) and almost the same structure, their extractabilities toward alkali metal picrates are remarkably different. For example, ligand **1** showed much higher extractability toward K^+ than ligand **2** did. In the former case, the original Na^+ selectivity of 16-crown-5 ring was changed to the K^+ selectivity. This finding strongly suggests that the electron-donating side arm of ligand **1** effectively coordinates with K^+ and that the side arm of **2** hardly interacts with the cation. In order to verify the effectiveness of the glycerol structure, ligand **3** was designed and the extractability was examined. As expected, the extraction profile of **3** was very similar to that of **1**. This result indicates that only the side arm constituting the glycerol structure at the pivot position participates in the complexation with the cation.

The stability constants of ligand **1**-**3** toward Na^+ and K^+ measured in THF at 25 °C[9] are summarized in Table 1 along with

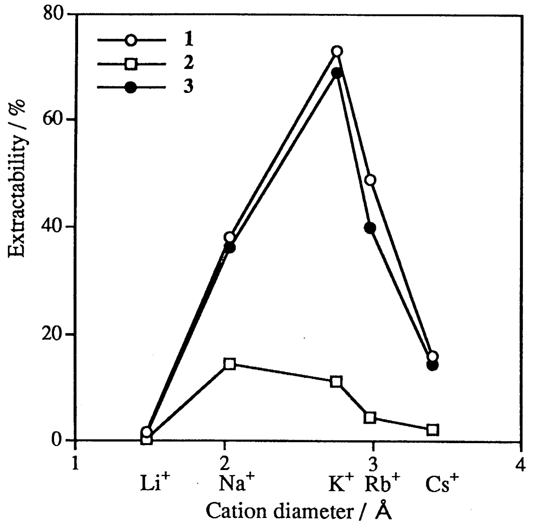


Figure 1. Extractability of compounds **1**-**3** for Alkali metal picrates.
Extraction conditions: dichloromethane(10 ml) / water (10 ml); [MOH]=5×10^{-2} M; [extractant]=[picric acid]= 5×10^{-4} M; 25 ℃; 9 h.

data of the reference compound. It is noteworthy that the stability constant of **1** toward K^+ is about 180 times that of **2** and the K^+/Na^+ selectivity is about 17. As expected from the extraction data, ligand **3** showed about the same stability constants as ligand **1** did.

Another evidence for the effective coordination of ligands **1** and **3** toward K^+ was given by the UV spectroscopy study. The position of the UV spectrum of the picrate anion is a measure of the type of the ion pair.[10] When **1** complexed with potassium picrate in THF, a peak at 381 nm was observed (Table 2). This absorption was assigned to the loose ion pair. On the other hand, the combination of **2** and potassium picrate showed the absorption at 359 nm, assigned to the contact ion pair. The large difference between **1** and **2** should be attributable to the three-dimensional coordination of **1** toward potassium cation.

Table 1. Stability constants of 16-crown-5 derivatives[a]

Compd.	logK(Na^+)	logK(K^+)	selectivity(K^+/Na^+)
1	4.21	5.45	17.4
2	3.26	3.18	0.8
3	4.03	5.01	9.3
16-Crown-5	3.83	3.02	0.15
	3.51[b]	2.63[b]	0.13

[a] Obtained from the calculation based on the absorption of picrate anion in THF at 380 nm in the UV spectrum.
[b] Measured by ion-selective electrode; Ref. 3.

Table 2. UV absorption maximum of picrate anion in THF

Compd.	Na^+		K^+	
	[L]/[P]=1[a]	[L]/[P]=5	[L]/[P]=1	[L]/[P]=5
1	355[b]	363	381	381
2	353	355	359	364
3	355	362	380	380

[a] [L]=[Ligand]; [P]=[Picrate anion]=5×10^{-3} M [b] In nm.

In conclusion, an appropriate arrangement of the coordination sphere including the electron-donating sidearm around the pivot position was found to be of importance in molecular design of lariat ethers. Further modification of the structure of ligands to improve the complexing ability is now in progress.

We thank Dr. Keiji Hirose of Osaka University concerning the estimate of stability constants. The Ministry of Education, Science, Sports, and Culture is acknowledged for the partial support of this work through a Grant in Aid for Scientific Research.

References and Notes

1 G. W. Gokel, *Chem. Soc. Rev*, **21**, 39 (1992).
2 a) Y. Inoue and G. W. Gokel, "Cation Binding by Macrocycles," Marcel Dekker, Inc., New York (1990), pp549-579. b) M. Ouchi, Y. Inoue, K. Wada, S. Iketani, T. Hakushi, and E. Weber, *J. Org. Chem.*, **52**, 2420 (1987).
3 Y. Nakatsuji, T. Nakamura, M. Yonetani, H. Yuya, and M. Okahara, *J. Am. Chem. Soc.*, **110**, 531 (1988).
4 M. Tomoi, O. Abe, M. Ikeda, K. Kihara, and H. Kakiuchi, *Tetrahedron Lett.*, **1978**, 3031.
5 R. Wakita, M. Miyakoshi, Y. Nakatsuji, and M. Okahara, *J. Incl. Phenom.*, **10**, 127 (1991).
6 Satisfactory spectral and microanalytical data were obtained for new compounds. Representative data are as follows. Compound **1**: a slightly yellow viscous liquid, ^{1}H NMR($CDCl_3$) δ 0.84-0.95(t,3H), 1.24-1.41(m,2H), 1.45-1.58(m,2H), 3.24-4.58(m,28H), 7.17-7.19(m,1H), 7.36-7.44(m,3H), 8.11-8.13(m,1H), 8.92-8.94(m,1H). Anal. Found: C, 63.56; H, 7.99; N, 3.09%. Calcd for $C_{27}H_{41}NO_8$: C, 63.89; H, 8.14; N, 2.76%. Compound **2**: a slightly yellow viscous liquid, ^{1}H NMR($CDCl_3$) δ 0.83-0.92(t,3H), 1.26-1.31(m,2H), 1.45-1.49(m,2H), 3.56-4.46(m,28H), 7.15-7.18(m,1H), 7.39-7.47(m,3H), 8.11-8.14(m,1H), 8.92-8.94(m,1H). Anal. Found: C, 63.86; H, 8.05; N, 3.07%. Calcd for $C_{27}H_{41}NO_8$: C, 63.89; H, 8.14; N, 2.76%. Compound **3**: a slightly yellow viscous liquid, ^{1}H NMR($CDCl_3$) δ 3.56-4.43(m,30H), 7.10-7.13(m,2H), 7.33-7.43(m,6H), 8.08-8.12(m,2H), 8.90-8.94(m,2H). Anal. Found: C, 63.67; H, 6.62; N, 4.50%. Calcd for $C_{34}H_{42}N_2O_9 \cdot H_2O$: C, 63.74; H, 6.92; N, 4.37%.
7 Y. Nakatsuji, T. Nakamura, M. Okahara, D. M. Dishong, and G. W. Gokel, *J. Org. Chem.*, **48**, 1237 (1983).
8 Y. Nakatuji, K. Kita, T. Kida, and A. Masuyama, *Chem. Lett.*, **1995**, 51.
9 K. H. Wong, M. Bourgoin, and J. Smid, *J. Chem. Soc., Chem. Commun.*, **1974**, 715.
10 M. Bourgoin, K. H. Wong, J. Y. Hui, and J. Smid, *J. Am. Chem. Soc.*, **97**, 3462 (1975).