Effective Coordination of Electron-Donating Sidearms of Double-Armed 15-Crown-5 Ethers toward Alkali Metal Cations

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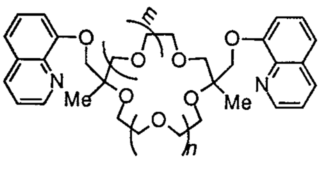
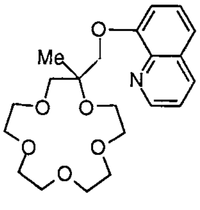
Two kinds of positional isomers of double-armed crown ethers containing quinoline moieties in the sidearms were prepared and the participation of their sidearms in the complexation with alkali metal cations was examined. The difference in the position of the two sidearms on the crown ring was found to remarkably affect the complexation properties toward alkali metal cations when both sidearms are *cis* configuration to the crown ring.

In the molecular design of a crown ether structure, introduction of electron-donating sidearms to the crown ring is an effective method for improving the complexation properties toward alkali metal cations.[1] A variety of N-pivot and C-pivot lariat ethers, which are crown ether derivatives having an electron-donating sidearm, have been developed for verifying the function of the sidearm. With respect to the double-armed crown ethers, extensive studies were done by Gokel *et al.*, but the work was mostly limited to modification of diazacrown ethers, that is, the N-pivot type of double-armed crowns.[2] Accordingly, it should be interesting for this strategy to be applied to the C-pivot type of double-armed crowns. We previously prepared some derivatives of this series of crown ether derivatives, but the coordination properties of the sidearms were insufficiently clarified at that time because the selection of the sidearm was not appropriate for this purpose.[3] From this standpoint, we here describe the complexation properties of two kinds of positional isomers of bis(quinolinyloxymethyl) dimethyl 15-crown-5 ethers (*cis* and *trans* isomers for each positional isomer) (**1**, **2**) toward sodium and potassium cations.

We chose an oxyquinoline moiety as the sidearm because it showed the highest coordination ability toward alkali metal cations among several electron-donating sidearms examined in the case of C-pivot lariat ethers containing a methyl group at the pivot position.[4] Another reason is that this group is a potent probe for NMR studies because of its paramagnetic effect.[5] Compounds **1a** and **1b** were prepared by the reaction of *cis*-2,6-bis(bromomethyl)-2,6-dimethyl-15-crown-5[3] and *trans*-2,6-bis(bromomethyl)-2,6-dimethyl-15-crown-5[3] with 8-quinolinol in diglyme in the presence of *t*-BuOK at 120 °C for 48 h, respectively.[4] Compounds **2a** and **2b** were also obtained from the corresponding *cis*- and *trans*-2,9-bis(bromomethyl)-2,9-dimethyl-15-crown-5[3] according to a similar procedure to that used for **1a** and **1b**.[6]



m=0, *n*=2 : **1a** (*cis*), **1b** (*trans*)
m=1, *n*=1 : **2a** (*cis*), **2b** (*trans*)



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The stability constants of the *cis* and *trans* isomers of ligand **1** and **2** toward Na$^+$ and K$^+$ measured in THF at 25 °C[7] using the UV spectroscopy are summarized in Table 1 along with the data of reference compounds. The stability constants of all the double-armed crown ethers (**1**, **2**) were found to be higher than those of the corresponding C-pivot lariat ether containing one sidearm (**3**). As expected, both *trans* isomers (**1b**, **2b**) showed about the same stability constants for Na$^+$ and K$^+$. In the case of *cis* isomers (**1a**, **2a**), a remarkable difference in the stability constants was observed, especially for K$^+$. It is noteworthy that the stability constant of **2a** toward K$^+$ is more than tenfold that of **1a**. In addition, *cis* isomers gave higher stability constants than *trans* isomers did. These findings suggest that both electron-donating sidearms cooperatively work for the complexation toward K$^+$ in the case of **2a**. Among four ligands examined in this work, **2a** showed the highest stability constants toward both Na$^+$ and K$^+$. It should be noted that the stability constant of **2a** for Na$^+$ is about a thousand times that of 15-crown-5 for Na$^+$ and is higher than that of 18-crown-6 for K$^+$, which is the best value attained by simple crown ethers toward alkali metal cations; to the best of our knowledge, the value of **2a** for Na$^+$ is the highest among the data reported for Na$^+$ selective crown ether derivatives. Therefore, by comparing the stability constants of two *cis* isomers, the difference in the position of the two sidearms on the crown ring was found to remarkably affect the complexation properties toward alkali metal cations. It is also interesting that the Na$^+$/K$^+$ selectivity (34) of **1a** is higher than that (16) of **3**, which is the best Na$^+$ selective ligand among C-pivot lariat ethers.[4]

Table 1. Stability constants of 15-crown-5 derivatives[a]

Compd	Log *K* (Na$^+$)	Log *K* (K$^+$)	Selectivity (Na$^+$/K$^+$)
1a (*cis*)	6.41	4.88	34
1b (*trans*)	5.60	4.26	22
2a (*cis*)	6.66	5.98	4.9
2b (*trans*)	5.57	4.22	23
3	5.30	4.10	16
15-crown-5	3.64	3.80	0.71
16-crown-5[b]	3.83	3.02	6.5
18-crown-6[b]	4.49	6.26	0.017

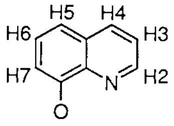
[a] Obtained from the calculation based on the absorption of the picrate anion in THF at 380 nm in the UV spectrum. [b] Reference 8.

^{1}H NMR studies afforded further evidence for the participation of two sidearms in the complexation of **2a** with K$^+$. The changes in the chemical shifts of the quinoline protons upon the addition of KSCN in CDCl$_3$ are shown in Table 2. Individual proton assignments were done on the basis of their 2-dimensional H-H COSY and NOE difference spectra. Ligand **2a**, which possessed an excellent complexation ability toward K$^+$, showed fairly large upfield shifts in H2, H3, and H4 protons of the quinoline ring when KSCN was added. In this case, π–π stacking of the two quinoline rings contributes to the upfield shifts.[9] This result clearly shows that the two quinoline rings are in vicinity to each other and are effectively coordinated to K^+.[2c-d, 10] On the other hand, no upfield shifts of the quinoline protons were observed in the case of **1a** upon the addition of KSCN. This finding indicates that the two quinoline rings are not in vicinity to each other, possibly because of the steric hindrance between the two oxyquinoline moieties as suggested by an examination of CPK models. Thus, the moderate complexation ability of **1a** toward K^+ may be reasonably explained by considering that only one of the two quinoline moieties coordinated with K^+.

Table 2. Changes in chemical shift of quinoline protons in ^{1}H NMR in the presence of KSCN

Compd	H2	H3	H4	H5	H6	H7
1a (*cis*)	0.29	0.19	0.10	0.02	0.00	-0.05
2a (*cis*)	-0.99	-0.76	-0.36	-0.08	0.02	0.08

$\Delta\delta$(ppm) = δ(KSCN) - δ(none); [ligand] = [KSCN]; $CDCl_3$.
Assignment of quinoline protons was as follows.



Molecular mechanics calculations have been successfully used for investigating the stable conformations of crown ether derivatives.[11] So we computed the potential energies for the K^+ complexes of **1a** and **2a** by MM2 calculations.[11b] It has been assumed that both or only one of two electron-donating sidearms are coordinated to K^+, respectively. In the case of **2a**, about the same potential energies (25 kcal mol^{-1}) were calculated for both assumptions. On the contrary, the MM2 calculation for **1a** demonstrated that the conformation having the coordination of only one sidearm with K^+ (40 kcal mol^{-1}) is more stable than the conformation having the coordination of both sidearms with K^+ (48 kcal mol^{-1}). This result is in good accordance with the expectation based on the stability constants and the ^{1}H NMR studies mentioned above.

In conclusion, an appropriate arrangement of the position of two electron-donating sidearms on the crown ring is found to be very important for the molecular design of the C-pivot type of double-armed crown ethers.

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6 Compound **1a**: a slightly yellow viscous liquid, ^{1}H NMR ($CDCl_3$) δ 1.41 (s, 6H), 3.68-3.89 (m, 16H), 4.16 (d, 2H, *J*=9.5 Hz), 4.31 (d, 2H, *J*=9.5 Hz), 7.16 (dd, 2H, *J*=7.3, 1.1 Hz), 7.39 (dd, 2H, *J*=8.6, 1.1 Hz), 7.41 (dd, 2H, *J*=7.3, 4.4 Hz), 7.44 (dd, 2H, *J*=8.6, 7.3 Hz), 8.11 (dd, 2H, *J*=8.6, 1.8 Hz), 8.91 (dd, 2H, *J*=4.4, 1.8 Hz). Compound **1b**: a slightly yellow viscous liquid, ^{1}H NMR ($CDCl_3$) δ 1.40 (s, 6H), 3.64-3.89 (m, 16H), 4.15 (d, 2H, *J*=9.5 Hz), 4.29 (d, 2H, *J*=9.5 Hz), 7.23 (dd, 2H, *J*=7.3, 1.5 Hz), 7.38 (dd, 2H, *J*=8.1, 1.5 Hz), 7.41 (dd, 2H, *J*=8.4, 4.0 Hz), 7.44 (dd, 2H, *J*=8.1, 7.3 Hz), 8.11 (dd, 2H, *J*=8.4, 1.8 Hz), 8.91 (dd, 2H, *J*=4.0, 1.8 Hz). Compound **2a**: a slightly yellow viscous liquid, ^{1}H NMR ($CDCl_3$) δ 1.48 (s, 6H), 3.63-3.85 (m, 16H), 4.15 (d, 2H, *J*=9.5 Hz), 4.36 (d, 2H, *J*=9.5 Hz), 7.15 (dd, 2H, *J*=7.0, 1.7 Hz), 7.37 (dd, 2H, *J*=8.2, 1.7 Hz), 7.40 (dd, 2H, *J*=7.4, 4.2 Hz), 7.42 (dd, 2H, *J*=8.2, 7.0 Hz), 8.11 (dd, 2H, *J*=7.4, 1.8 Hz), 8.92 (dd, 2H, *J*=4.2, 1.8 Hz). Compound **2b**: a slightly yellow viscous liquid, ^{1}H NMR ($CDCl_3$) δ 1.46 (s, 6H), 3.59-3.90 (m, 16H), 4.11 (d, 2H, *J*=9.4 Hz), 4.37 (d, 2H, *J*=9.4 Hz), 7.17 (dd, 2H, *J*=7.3, 1.5 Hz), 7.38 (dd, 2H, *J*=8.1, 1.5 Hz), 7.40 (dd, 2H, *J*=8.4, 4.0 Hz), 7.44 (dd, 2H, *J*=8.1, 7.3 Hz), 8.11 (dd, 2H, *J*=8.4, 1.8 Hz), 8.91 (dd, 2H, *J*=4.0, 1.8 Hz).

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