

Synthesis and Complexing Ability of a C-Pivot Type of Double-Armed 15-Crown-5 Ethers toward Alkali Metal Cations

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Three kinds of positional isomers of the C-pivot type of double-armed 15-crown-5 ethers (*cis* and *trans* isomers for each positional isomer) bearing two 8-quinolyloxy moieties as part of the electron-donating sidearms were prepared, and their complexation properties were evaluated by measuring the stability constant in THF, the extractability, and passive transport velocity. *Cis* isomers were found to be much better host compounds toward alkali metal cations than *trans* isomers possibly because of the potential cooperative coordination of two electron-donating sidearms. All *trans* isomers showed almost the same stability constants toward Na^+ and K^+. On the other hand, in the case of *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.

Crown ethers have been used as the primary host molecule toward a variety of guest molecules, including hard cations, such as alkali metal and alkaline earth metal cations in the area of molecular recognition chemistry.[1,2] The realization of both a high complexing ability and a high selectivity must be of prime importance in the molecular design of new host molecules. As for a modification of the structure of crown ether derivatives, a change in the crown ring size should first be targeted. In addition to this modification, the introduction of electron-donating sidearms to the crown ring has also been successfully used as an effective strategy for improving the complexation properties toward alkali metal cations.[3] Several types of C-pivot[4] and N-pivot[5] lariat ethers, which are crown ether derivatives having an electron-donating sidearm, have been developed for verifying the function of the sidearm in cation recognition. With respect to the molecular design of C-pivot lariat ethers, we found that the presence of a methyl group on the C-pivot carbon atom containing an electron-donating sidearm remarkably raised the complexing ability and selectivity toward alkali metal cations.[4c–4e] Accordingly, it should be interesting for this strategy to be applied to the C-pivot type of double-armed crown ether derivatives. We previously prepared some derivatives of this series of crown ethers,[6] but the coordination properties of the sidearms were insufficiently clarified at that time because the selection of sidearms was not appropriate for this purpose. Another reason that has retarded this study was a difficulty to separate the *cis* (meso) and *trans* (a racemic mixture) isomers of the bis(bromomethyl) dimethyl crown ethers as the key starting material for further modifications. Recently, we developed an easy separation method for one of the key intermediates for the C-pivot type of double-armed crowns.[7] From this point of view, we describe the synthesis and complexation properties of three kinds of positional isomers of dimethyl bis[(8-quinolyloxy)methyl] 15-crown-5 ethers (*cis* and *trans* isomers for each positional isomer) toward alkali metal cations.[8]

Results and Discussion

Design and Synthesis of C-Pivot Type Double-Armed Crown Ethers. Since 18-crown-6 is well known to be a quite effective host for K^+, it should be less important to modify the 18-crown-6 ring. In addition, 15-crown-5 derivatives were found to be excellent host molecules for Na^+ in our previous work concerning the molecular design of C-pivot lariat ethers.[4d] Thus, three kinds of positional isomers of the C-pivot type of double-armed 15-crown-5 ethers (*cis* and *trans* isomers for each positional isomer) bearing 8-quinolyloxy moieties as part of the two electron-donating sidearms were synthesized in this study (Fig. 1). The presence of a methyl group at the pivot position is essential for increasing the complexation ability toward alkali metal cations, as verified by us[4c–4e] and others.[9] The 8-quinolyloxy moiety was selected as an electron-donating sidearm based on our study concerning C-pivot lariat ethers.[4d,4e] As key intermediates, we chose bis(bromomethyl)dimethyl 15-crown-5 ethers because the separation method of *cis*- and *trans*-isomers was developed recently.[7] Compound **8**, 2,9-bis(bromomethyl)-2,9-dimethyl-15-crown-5, was prepared by an intramolecular cyclization reaction of the corresponding pentaethylene glycol derivative, which was obtained by a bromoalkoxylation reaction of ethylene glycol bis(2-methylallyl) ether with ethylene glycol, by using benzenesulfonyl chloride under basic conditions.[6,7,10] Compound **7**, 2,6-bis(bromomethyl)-2,6-dimethyl-15-crown-5, was prepared by a bromoalkoxylation reaction of bis(2-methylallyl) ether with triethylene glycol in the presence of $NaBF_4$ as the template ion.[6] According to a similar procedure, compound **9**, 2,12-bis(bromomethyl)-2,12-dimethyl-15-crown-5, was prepared by a bromoalkoxylation reaction of diethylene glycol bis(2-

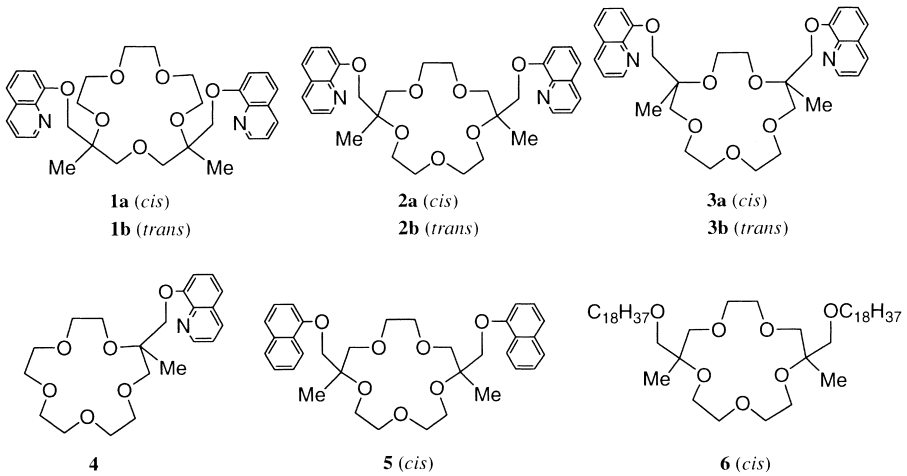
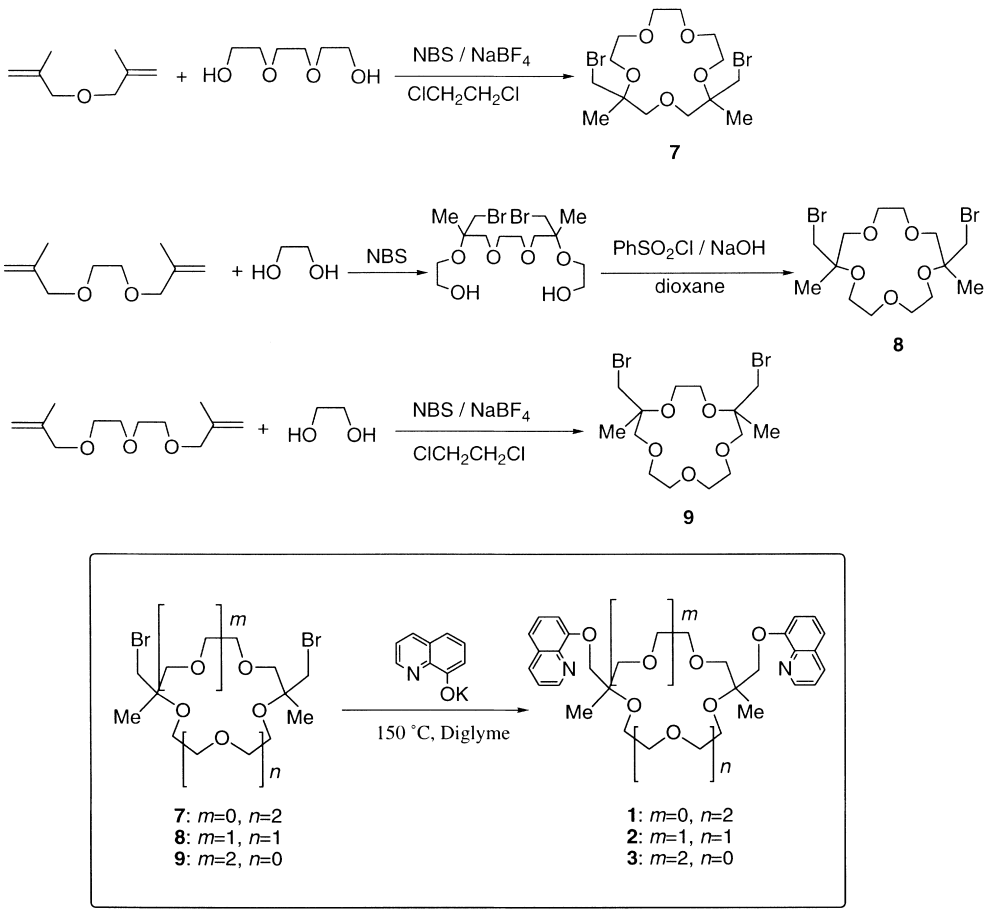


Fig. 1. Structure of host compounds.



Scheme 1.

methylallyl) ether with ethylene glycol (Scheme 1). Compounds **7**–**9**, obtained as a mixture, were separated into *cis* (**7a**–**9a**) and *trans* (**7b**–**9b**) isomers by silica-gel column chromatography using a mixed solvent of ethyl acetate and hexane as an eluent. Compounds **1a** and **1b** were prepared by the reaction of *cis*-2,6-bis(bromomethyl)-2,6-dimethyl-15-crown-5 (**7a**) and *trans*-2,6-bis(bromomethyl)-2,6-dimethyl-15-crown-5 (**7b**) with the potassium salt of 8-quinolinol at 150 °C for 48 h, respectively. Compounds **2a** and **2b** were obtained from the corresponding *cis*-(**8a**) and *trans*-2,9-bis(bromomethyl)-2,9-dimethyl-15-crown-5 (**8b**) according to a similar procedure to that used for **1a** and **1b**. Compounds **3a** and **3b** were also obtained from *cis*-(**9a**) and *trans*-2,12-bis(bromomethyl)-2,12-dimethyl-15-crown-5 (**9b**).

Stability Constants in THF. The stability constants of ligands **1**–**6** toward Na^+ and K^+ measured in THF at 25 °C are

Table 1. Stability Constants in THF[a)]

Ligand	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
3a (*cis*)	6.27	4.84	27
3b (*trans*)	5.63	4.28	22
4	5.30	4.10	16
5 (*cis*)	4.12	3.87	1.8
6 (*cis*)[b)]	4.33	4.37	0.91
15-Crown-5	3.64	3.80	0.71
16-Crown-5[c)]	3.83	3.02	6.5
18-Crown-6[c)]	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) Ref. 11. c) Ref. 12.

summarized in Table 1 along with some reference data. Compound **4**, containing one 8-quinolyloxy moiety as an electron-donating sidearm, was the most effective ligand for Na^+ among the C-pivot lariat ethers examined in previous work.[4d] Compounds **5** and **6** showed somewhat higher stability constants toward Na^+ and K^+ in comparison with 15-crown-5. This result shows that the oxygen atom of the sidearm contributes to an increase in the stability constant, albeit to a limited extent. The fact that all crowns containing quinoline sidearm(s) (**1**–**4**) showed much higher stability constants than other crowns (**5** and **6**) clearly indicates that the quinoline nitrogen plays an important role in the coordination with the cation. As expected, all *trans* isomers (**1b**, **2b**, and **3b**) showed about the same complexing ability toward Na^+ and K^+, and their stability constants were about twice that of compound **4** containing one sidearm, which may be ascribed to a difference in the probability of using the sidearm for the coordination to the cation. The stability constants of all *cis* isomers (**1a**, **2a**, and **3a**) were found to be superior to those of the *trans* isomers (**1b**, **2b**, and **3b**). In the case of *cis* isomers, 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** or **3a**. This finding strongly suggests that the coordination styles of these isomers are different, that is, both electron-donating sidearms cooperatively work for complexation toward K^+ in the case of **2a**. Among all of ligands examined in this work, **2a** showed the highest stability constants toward 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 considered to be the best combination of a simple crown ether and an alkali metal cation; 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. Thus, in a comparison of the stability constants of three *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 **4**, which is the best Na^+ selective ligand among C-pivot lariat ethers.[4d]

^{1}H NMR Studies. ^{1}H NMR studies afforded additional evidence for the participation of two electron-donating sidearms in the complexation of **2a** with K^+. The changes in the chemical shifts of the quinoline protons upon the addition of NaSCN or KSCN in $CDCl_3$ are shown in Table 2. Individual assignments were made based on their 2-dimensional H–H COSY and NOE difference spectra. Ligand **2a**, which possessed an excellent complexing ability toward K^+, showed a fairly large upfield shift in H2, H3, and H4 protons of the quinoline ring when KSCN was added. This result shows that the two quinoline rings are in the same vicinity to each other, and are effectively coordinated to K^+.[12,13] 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 the vicinity of each other, possibly because of a steric hindrance between the two 8-quinolyloxy 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^+. Another a bit of evidence was given by an NOE experiment. The NOE difference spectra of **1a** and **2a** were measured in both the presence and absence of KSCN. Irradiation of the methyl proton at the pivot position of **1a** led to no detectable enhancement of the H-2 proton of the quinoline ring; however, in the presence of KSCN an enhancement of 2.4% was observed On the other hand, compound **2a** showed no detectable enhance-

Table 2. Change in Chemical Shift[a)] in ^{1}H NMR

		Quinoline protons					
Ligand	Salt	H2	H3	H4	H5	H6	H7
1a (*cis*)	NaSCN	0.04	0.10	0.17	0.11	0.10	0.08
	KSCN	0.29	0.14	0.07	0.04	0.03	−0.05
2a (*cis*)	NaSCN	0.01	−0.26	−0.13	−0.01	0.00	0.05
	KSCN	−0.99	−0.76	−0.36	−0.08	0.02	0.08

a) $\Delta\delta$ (ppm) = δ (MSCN) − δ (None); [ligand] = [MSCN]; $CDCl_3$; −60 °C

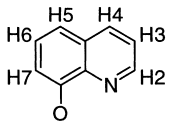


Table 3. Solvent Extraction of Alkali Metal Picrates[a)]

Ligand	Extractability (%)				
	Li^+	Na^+	K^+	Rb^+	Cs^+
1a	36	84	58	38	5
2a	46	90	77	50	19
2b	29	77	47	28	9
3a	42	79	56	40	11
4	26	70	42	34	15
6	1	25[b)]	6[b)]	3	3

a) Extraction conditions: dichloromethane (10 mL)/water (10 mL); [MOH] = 5×10^{-2} M; [extractant] = [picric acid] = 5×10^{-4} M, 25 °C, 9 h. b) Ref. 11.

ment of the H-2 proton in both the presence and absence of KSCN. This result suggests that one sidearm of **1a** is free from coordination to K^+, and thus the quinoline ring is able to be in the vicinity of the methyl group at the pivot position. On the contrary, a lack of enhancement of the H-2 proton of **2a** in the presence of KSCN is reasonably explained by considering that both sidearms are used for the coordination to K^+.

Solvent Extraction. In order to survey the complexation properties of the C-pivot type of double-armed crown ethers toward alkali metal cations, the extraction data conducted under conditions using equimolar amounts of the ligand and alkali metal picrate at 25 °C are summarized in Table 3, along with the data of some reference compounds. Dichloromethane was used as an organic solvent. All compounds showed Na^+ selectivity. Compound **6** is a highly lipophilic crown ether and is considered to be suitable for the solvent extraction, but its extractability is relatively low in comparison with other crown ethers containing 8-quinolyloxy sidearm(s). This result suggests that an effective encapsulation of the cation by the electron-donating sidearm(s) contributes to an increase of the extractability. In accordance with the trend observed concerning the stability constants in THF, the *cis* isomer (**2a**) showed a higher extractability than the corresponding *trans* isomer (**2b**) toward alkali metal cations. The extractability of **2a** was the highest among the compounds examined in this study.

Bulk Liquid Membrane Transport. Membrane transport is an intriguing method for the separation of metal cations.[14] Selective separation of alkali metal cations was carried out by the liquid membrane transport method. The passive transport conditions and the results are summarized in Table 4. Although compound **2a** attained the highest velocity for Na^+, the Na^+/K^+ selectivity was moderate in reflection of the stability constants toward Na^+ and K^+. The low Na^+/K^+ selectivity also supports the effective coordination of two sidearms toward K^+ captured in the crown ring. As expected, the highest Na^+/K^+ selectivity (75) was observed in compound **1a**. Although it is inappropriate to compare transport data obtained under different conditions, this Na^+/K^+ selectivity is among the best for selective carriers. For example, the Na^+/K^+ selectivities of lipophilic 16-crown-5 monocarboxylic acid[15] and monoaza-15-crown-5[16] were reported to be 13 and 15, respectively. The high selectivity must be useful for the recent research on the molecular design of novel transporters, such as the Na^+/K^+ ATPase model.[17]

Table 4. Competitive Passive Transport Data[a)] toward Li^+, Na^+, and K^+

Ligand	Li^+	Na^+	K^+	Selectivity	
				Na^+/Li^+	Na^+/K^+
1a	0.08	28	0.37	349	75
2a	0.36	46	9.1	127	5
2b	0.29	26	0.77	90	33

a) $\times 10^7$ mol/h. Transport conditions: aqueous phase 1 (10 mL), [LiCl] = [NaSCN] = [KSCN] = [Me_4NOH] = 0.1 M, organic phase (CH_2Cl_2, 20 mL), [carrier] = 2.5 mM, aqueous phase 2 (10 mL), 25 °C.

Conclusion

In the molecular design of a C-pivot type of double-armed crown ethers, the position of the electron-donating sidearms on the crown ring was found to be a dominating factor for determining their complexation properties toward alkali metal cations when both sidearms have a *cis* configuration to the crown ring. Based on a strategy of introducing plural electron-donating sidearms to the 15-crown-5 ring, an excellent host for Na^+ was developed.

Experimental

General Methods. ^{1}H NMR spectra were recorded with a JEOL-GSX-400 (400 MHz) spectrometer using tetramethylsilane as the internal standard. IR spectra were measured on a Horiba FT-710 spectrometer. Mass spectra were measured on a JEOL JMS-DX-303 mass spectrometer. Elemental Analyses were measured with a Yanagimoto CHN-Corder. *cis*- and *trans*-2,9-Bis(bromomethyl)-2,9-dimethyl-15-crown-5 ethers (**8a** and **8b**) were prepared according to method, previously reported.[7]

2,6-Bis(bromomethyl)-2,6-dimethyl-15-crown-5 (7). To a stirred suspension of *N*-bromosuccinimide (NBS) (104.3 g, 0.586 mol), triethylene glycol (44.0 g, 0.293 mol), and $NaBF_4$ (128.7 g, 1.17 mol) as a template in 300 mL of 1,2-dichloroethane was added bis(2-methylallyl) ether (36.9 g, 0.293 mol) in 200 mL of 1,2-dichloroethane cooled in an ice bath over a period of 2 h. The resulting mixture was further stirred at 50 °C for another 24 h. After the mixture was cooled to room temperature, insoluble matter was removed by filtration and washed with a small portion of dichloromethane. Then, 300 mL of aq Na_2CO_3 (5%) was added, and the mixture was extracted with dichloromethane (300 mL × 3). The organic layer was dried over $MgSO_4$ and concentrated to give a brown viscous liquid. Triethylene glycol and succinimide as a byproduct were removed by distillation in a Kugelrohr apparatus (90 °C, 0.07 Torr). The crude product was purified by silica-gel column chromatography (acetone/hexane = 1/19) to give **7** as a colorless viscous liquid (14.0 g, 18%). ^{1}H NMR ($CDCl_3$) δ 1.25 (s, 3H), 1.30 (s, 3H), 3.42–3.80 (m, 20H); IR 2870, 1460, 1380, 1300, 1260, 1190, 1130, 960, 670 cm^{-1}; MS(CI) (*m/z*) 435 (M^+ + 3, 97), 365 (50), 355(100), 353 (97). Found: C, 38.53; H, 6.06; Br, 37.10%. Calcd for $C_{14}H_{26}Br_2O_5$: C, 38.73; H, 6.04; Br, 36.81%.

This product was a mixture of the *cis* and *trans* isomers of 2,6-bis(bromomethyl)-2,6-dimethyl-15-crown-5 (**7**). Two stereoisomers were separated by silica-gel column chromatography (ethyl acetate/hexane = 1/4). The *trans* isomer (**7b**)was eluted before the *cis* isomer (**7a**). *Cis* isomer (**7a**): ^{1}H NMR ($CDCl_3$) δ 1.25 (s, 6H), 3.42–3.79 (m, 20H); ^{13}C NMR ($CDCl_3$) δ 19.62, 37.62,

62.85, 70.44, 70.88, 73.47, 76.39. *Trans* isomer (**7b**): ^{1}H NMR ($CDCl_3$) δ 1.30 (s, 6H), 3.41–3.75 (m, 20H); ^{13}C NMR ($CDCl_3$) δ 19.71, 37.76, 62.82, 70.52, 70.90, 74.12, 76.43.

2,12-Bis(bromomethyl)-2,12-dimethyl-15-crown-5 (9). The synthetic procedure was almost the same as that used for **7**. The crude compound was purified by silica-gel column chromatography (acetone/hexane = 1/19) to give **9** as a colorless liquid in 11% yield. ^{1}H NMR ($CDCl_3$) δ 1.24 (s, 6H), 3.34–3.69 (m, 20H); IR 2973, 1460, 1370, 1290, 1250, 1130, 990, 670 cm^{-1}; MS(CI) (*m/z*) 435 (M^+ + 3, 17), 373 (27), 353 (100), 159 (65). . Found: C, 38.50; H, 5.74; Br, 36.83%. Calcd for $C_{14}H_{26}Br_2O_5$: C, 38.73; H, 6.04; Br, 36.81%.

This product was a mixture of the *cis* and *trans* isomers of 2,12-bis(bromomethyl)-2,12-dimethyl-15-crown-5 (**9**). Two stereoisomers were separated by silica-gel column chromatography (ethyl acetate/hexane = 3/17). The *trans* isomer (**9b**) was eluted before the *cis* isomer (**9a**). In this case, both isomers were identified by ^{13}C NMR. *cis*-Isomer (**9a**): ^{13}C NMR ($CDCl_3$) δ 20.36, 37.38, 62.62, 70.36, 70.43, 73.50, 76.07. *Trans* isomer (**9b**): ^{13}C NMR ($CDCl_3$) δ 19.74, 37.69, 62.45, 70.12, 70.25, 72.99, 75.85.

***cis*-2,6-Dimethyl-2,6-bis[(8-quinolyloxy)methyl]-15-crown-5 (1a).** Potassium *t*-butoxide (0.75 g, 8.1 mmol) was added to 8-quinolinol (1.94 g, 13.4 mmol) in diglyme (20 mL) and the *t*-butyl alcohol formed was removed by distillation. To the resulting mixture was added **7a** (0.29 g, 8.1 mmol) in 10 mL of diglyme, the mixture was stirred at 150 °C for 48 h. After the mixture was cooled to room temperature, water (100 mL) was added to the residue and extracted with dichloromethane (100 mL × 3). After evaporation, the lower-boiling point matter was removed under reduced pressure (110 °C/0.07 Torr), and then the residue was purified by chromatography over alumina (chloroform/dichloromethane = 1/19) to give **1a** as a slightly yellow, viscous liquid (0.24 g, 43%). ^{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); IR 3050, 2930, 2880, 1660, 1580, 1500, 1460, 1380, 1320, 1270, 1110, 960, 830, 790, 730 cm^{-1}; FABMS *m/z* 563 (M^+ + 1, 40), 391 (25), 307 (38), 154 (100). Found: C, 66.31; H, 6.65; N, 4.68%. Calcd for $C_{32}H_{38}N_2O_7\cdot H_2O$: C, 66.19; H, 6.94; N, 4.82%.

***trans*-2,6-Dimethyl-2,6-bis[(8-quinolyloxy)methyl]-15-crown-5 (1b).** The synthetic procedure was almost the same as that used for **1a**. A crude compound was purified by chromatography over alumina (chloroform/dichloromethane = 1/19) to give **1b** as a slightly yellow, viscous liquid in 55% yield. ^{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); IR 3060, 2930, 2860, 1650, 1570, 1500, 1460, 1380, 1320, 1270, 1110, 960, 820, 790, 750 cm^{-1}; FABMS *m/z* 563 (M^+ + 1, 20), 391 (52), 363 (18), 154 (100). Found: C, 66.10; H, 7.19; N, 4.43%. Calcd for $C_{32}H_{38}N_2O_7\cdot H_2O$: C, 66.19; H, 6.94; N, 4.82%.

***cis*-2,9-Dimethyl-2,9-bis[(8-quinolyloxy)methyl]-15-crown-5 (2a).** The synthetic procedure was almost the same as that used for **1a**. A crude compound was purified by chromatography over alumina with dichloromethane as an eluent to give **2a** as a slightly yellow, viscous liquid in 81% yield. ^{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); IR 3050, 2870, 1620, 1600, 1570, 1500, 1470, 1425, 1380, 1320, 1300, 1260, 1180, 1130, 1110, 950, 820, 790, 730 cm^{-1}; FABMS *m/z* 563 (M^+ + 1, 89), 307 (27), 198 (41), 154 (100), 136 (68). Found: C, 64.00; H, 6.74; N, 4.36%. Calcd for $C_{32}H_{38}N_2O_7\cdot 2H_2O$: C, 64.20; H, 7.07; N, 4.68%.

***trans*-2,9-Dimethyl-2,9-bis[(8-quinolyloxy)methyl]-15-crown-5 (2b).** The synthetic procedure was almost the same as that used for **1a**. A crude compound was purified by chromatography over alumina with dichloromethane as an eluent to give **2b** as a slightly yellow, viscous liquid in 29% yield. ^{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); IR 3050, 2870, 1620, 1590, 1570, 1500, 1465, 1425, 1380, 1320, 1260, 1190, 1130, 1070, 960, 820, 790, 730 cm^{-1}; FABMS *m/z* 563 (M^+ + 1, 50), 307 (21), 198 (35), 154 (100). Found: C, 65.81; H, 6.95; N, 4.51%. Calcd for $C_{32}H_{38}N_2O_7\cdot H_2O$: C, 66.19; H, 6.94; N, 4.82%.

***cis*-2,12-Dimethyl-2,12-bis[(8-quinolyloxy)methyl]-15-crown-5 (3a).** The synthetic procedure was almost the same as that used for **1a**. A crude compound was purified by chromatography over alumina (chloroform/dichloromethane = 1/19) to give **3a** as a slightly yellow, viscous liquid in 38% yield. ^{1}H NMR ($CDCl_3$) δ 1.48 (s, 6H), 3.64–3.85 (m, 16H), 4.14 (d, 2H, J = 9.2 Hz), 4.39 (d, 2H, J = 9.2 Hz), 7.16 (dd, 2H, J = 7.0, 1.8 Hz), 7.38 (dd, 2H, J = 8.1, 1.5 Hz), 7.40 (dd, 2H, J = 8.1, 4.4 Hz), 7.42 (dd, 2H, J = 8.1, 7.0 Hz), 8.11 (dd, 2H, J = 8.1, 1.8 Hz), 8.92 (dd, 2H, J = 4.4, 1.8 Hz); IR 3060, 2920, 1650, 1570, 1500, 1480, 1380, 1320, 1260, 1110, 820, 790 cm^{-1}; FABMS *m/z* 563 (M^+ + 1, 18), 391 (66), 307 (65), 154 (100). Found: C, 66.01; H, 6.99; N, 4.65%. Calcd for $C_{32}H_{38}N_2O_7\cdot H_2O$: C, 66.19; H, 6.94; N, 4.82%.

***trans*-2,12-Dimethyl-2,12-bis[(8-quinolyloxy)methyl]-15-crown-5 (3b).** The synthetic procedure was almost the same as that used for **1a**. A crude compound was purified by chromatography over alumina with dichloromethane as an eluent to give **3b** as a slightly yellow, viscous liquid in 49% yield. ^{1}H NMR ($CDCl_3$) δ 1.47 (s, 6H), 3.59–3.91 (m, 16H), 4.07 (d, 2H, J = 9.2 Hz), 4.38 (d, 2H, J = 9.2 Hz), 7.19 (dd, 2H, J = 7.3, 1.5 Hz), 7.39 (dd, 2H, J = 8.1, 1.5 Hz), 7.41 (dd, 2H, J = 8.4, 4.0 Hz), 7.45 (dd, 2H, J = 8.1, 7.3 Hz), 8.12 (dd, 2H, J = 8.4, 1.8 Hz), 8.93 (dd, 2H, J = 4.0, 1.8 Hz); IR 3060, 2925-2870, 1650, 1570, 1500, 1465, 1380, 1320, 1260, 1110-1020, 960, 820, 790, 750 cm^{-1}; FABMS *m/z* 563 (M^+ + 1, 49), 391 (49), 363 (23), 154 (100). Found: C, 66.51; H, 6.71; N, 5.01%. Calcd for $C_{32}H_{38}N_2O_7\cdot H_2O$: C, 66.19; H, 6.94; N, 4.82%.

***cis*-2,9-Dimethyl-2,9-bis[(1-naphthyloxy)methyl]-15-crown-5 (5).** The synthetic procedure was almost the same as that used for **1a**. 1-Naphthol was used in place of 8-quinolinol. The crude compound was purified by chromatography over alumina with dichloromethane as an eluent to give **5** as a slightly yellow, viscous liquid in 58% yield. ^{1}H NMR ($CDCl_3$) δ 1.43 (s, 6H), 3.64 (d, 2H, J = 9.9 Hz), 3.79 (d, 2H, J = 9.9 Hz), 3.97–4.26 (m, 16H), 6.77 (dd, 2H, J = 7.7, 2.2 Hz), 7.33 (dd, 2H, J = 7.7, 3.7 Hz), 7.40 (dd, 2H, J = 8.4, 5.8 Hz), 7.44 (dd, 2H, J = 8.2, 2.2 Hz), 7.48 (dd, 2H, J = 5.8, 3.7 Hz), 7.79 (dd, 2H, J = 8.4, 4.1 Hz), 8.29 (dd, 2H, J = 8.2, 4.1 Hz); ^{13}C NMR ($CDCl_3$) δ 18.78, 61.51, 68.02, 70.21, 71.20, 73.98, 76.92, 104.97, 120.35, 122.25, 125.22,

125.68, 125.97, 126.44, 127.48, 134.58, 154.63; IR 3050, 2930, 2880, 2360, 1630, 1580, 1510, 1460, 1400, 1270, 1240, 1100, 960, 790, 770 cm^{-1}; FABMS *m/z* 561 ($M^+ + 1$, 51), 281 (60), 207 (89), 167 (100), 149 (85). Found: C, 72.68; H, 7.26%. Calcd for $C_{34}H_{40}O_7$: C, 72.83; H, 7.19%.

Extraction Procedure. A mixture of aqueous solution (10 mL) of alkali metal hydroxide (5×10^{-2} M) and picric acid (5×10^{-4} M) with a dichloromethane solution (10 mL) of an appropriate extractant (5×10^{-4} M) was shaken at 25 °C for 9 h. The extractability was obtained from a calculation based on the absorption of the picrate anion in the aqueous phase at 354 nm in the UV spectrum.

Measurement of Stability Constants. All of the stability constants herein reported were determined for sodium picrate or potassium picrate in THF at 25 °C and the absorption of the picrate anion in THF at 380 nm in the UV spectrum was used for calculating the stability constants. Typically, the concentration of the guest compound was fixed to be 5×10^{-5} M in THF and the molar ratios of host to guest were changed in the range from 0 to 10 by changing the concentrations of the host compound. Eight data were collected for each host-guest system and the stability constant (K) was calculated using an iterative nonlinear least-squares curve-fitting program. In this case, 1:1 complexation was postulated.

Liquid Membrane Transport. Transport experiments were carried out in a U-shaped cell at 25 °C, as described in the literature.[18] The details of the transport conditions are summarized in the footnotes of Table 4. The receiving phase was sampled from four different cells after 12, 24, 36, and 48 h and analyzed for cation concentration using a Nippon Jarrel-Ash AA-8500 atomic absorption spectrometer. The value reported in Table 4 was the mean of four samples and the deviations from the mean were less than 10%.

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