Synthesis and complexation properties of C-pivot lariat ethers containing 16-crown-5, 19-crown-6 and 22-crown-7 rings toward alkali metal cations

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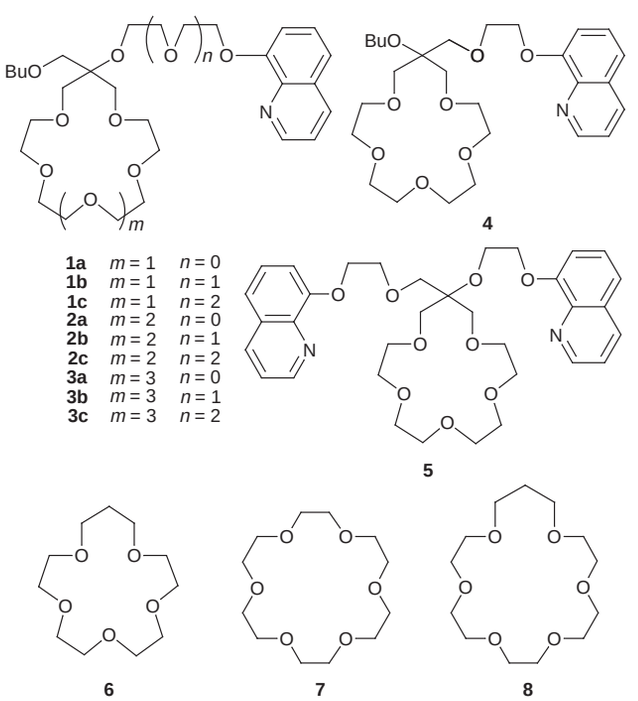
A new series of C-pivot lariat ethers **1**–**5** having an oxyquinoline moiety as part of the electron-donating sidearm were obtained from crown ether derivatives of low symmetry such as 3*n*-methylene-(3*n* + 1)-crown-*n* (*n* = 5, 6, 7) and their complexation properties toward alkali metal cations were evaluated by measuring the extractability, stability constant in THF, characteristic absorption in the UV spectrum in THF, and passive transport ability. The difference in the skeletal structure of the pivot position of the lariat ethers **1a** and **4** was found to remarkably affect their complexation properties; that is, the former having a 2-methylglycerol structure around the pivot carbon showed much higher complexing ability than did the latter. The effect of the crown ring size and the number of heteroatoms of the electron-donating sidearm on the complexation properties was also examined and discussed. As a result, K^+ selectivity was attained by 16-crown-5 and 19-crown-6 derivatives (**1** and **2**), whereas 22-crown-7 derivatives **3** showed Rb^+ selectivity.

Introduction

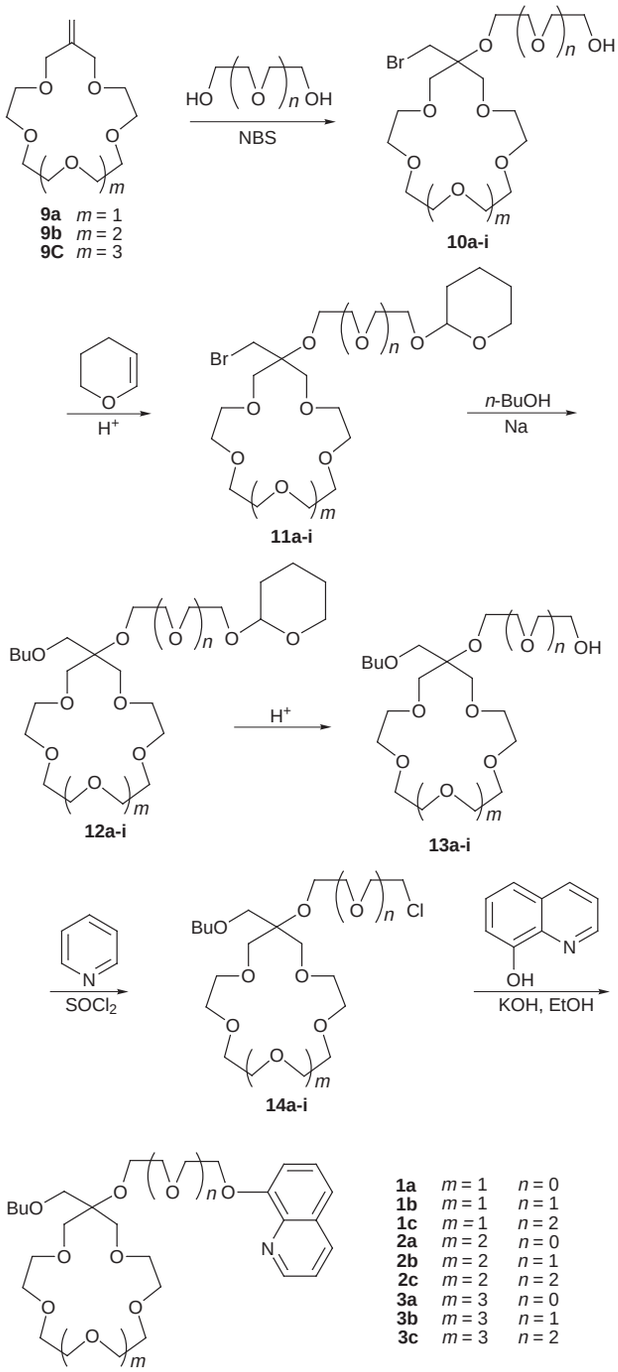
A variety of artificial macrocyclic multidentate ligands and related acyclic analogues have been developed to achieve high complexing ability for specific guest molecules, such as cations, anions and organic molecules.[1,2] Among them, lariat ethers are known to be an effective host molecule for alkali metal and alkaline earth metal cations in connection with their cooperative coordination function of the crown ring and the electron-donating sidearm with the cation.[3–7] As regards (3*n* + 1)-crown-*n* derivatives of low symmetry, much attention has been concentrated on the molecular design of 16-crown-5 ethers to create efficient Na^+-selective complexants because 16-crown-5 possesses a higher complexing ability toward Na^+ than 15-crown-5 does.[6–8] On the other hand, we previously reported that a 16-crown-5 having an electron-donating sidearm on the central carbon of the trimethylene unit showed K^+/Na^+ selectivity.[8] Recently, the 2-methylglycerol structure around the pivot position of C-pivot lariat ethers containing a 16-crown-5 ring was found to play an important role in increasing the complexing ability.[9] It would be interesting to examine whether this strategy can be applied to larger crown derivatives. In this paper, we describe the synthesis of a new series of lariat ethers **1**–**3** derived from 3*n*-methylene-(3*n* + 1)-crown-*n* (*n* = 5, 6, 7) with different lengths of oxyethylene sidearm and their complexation properties towards alkali metal cations evaluated by using solvent extraction, as well as their stability constants in homogeneous solution, UV spectroscopy, and liquid membrane transport. The relationship between their complexing properties toward alkali metal cations and the structure of the ligands is discussed in terms of the fitness of the cavity size, a function of the cooperation of the crown ring and the sidearm, to coordinate with a particular cation size.



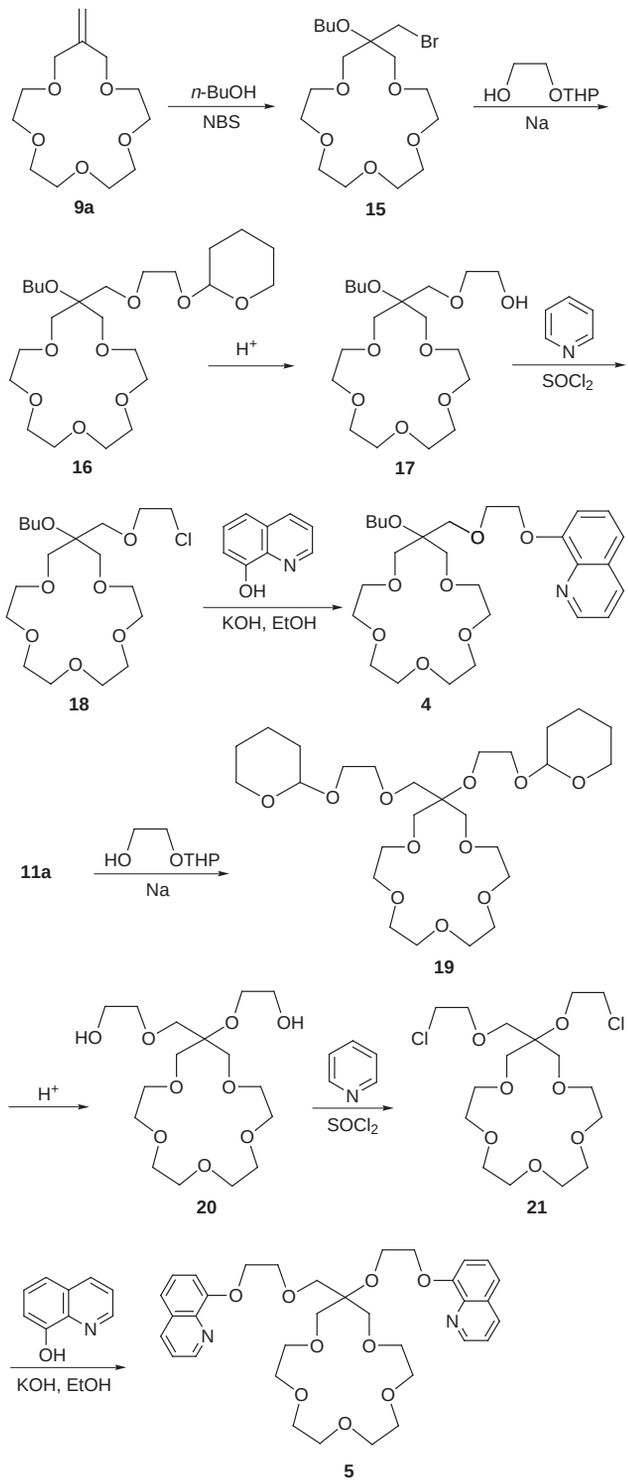
Results and discussion

Design and synthesis of lariat ethers

A series of lariat ethers containing a glycerol unit (compounds **1**–**3**) were designed to afford systematic structural variations of the crown ring size and the length of the oxyethylene sidearm. The 8-oxyquinoline moiety was introduced at the end of the sidearm of lariats **1**–**3** because of its excellent coordination ability toward alkali metal cations.[8b] The presence of the methyl group at the pivot position is expected to play an important role in increasing the complexation ability toward alkali metal cations, as verified in the molecular design of C-pivot lariat ethers by us[8b,10] and others.[11] The general synthetic procedures for compounds **1**–**3** are summarized in Scheme 1. Compounds **10** were obtained from the bromoalkoxylation of 3*n*-methylene-(3*n* + 1)-crown-*n* (*n* = 5, 6, 7) **9**[12] using *N*-bromosuccinimide (NBS) and oligoethylene glycols. The hydroxy group of compounds **10** was protected by treatment with 3,4-dihydro-*2H*-



Scheme 1



Scheme 2

pyran, according to the conventional method, to give the corresponding tetrahydropyranyl ethers **11**, which were then treated with *n*-butyl alcohol under basic conditions, to give the butoxymethyl derivatives **12**, followed by the deprotection under acidic conditions to give butoxymethyl alcohols **13**. The chlorides **14** obtained from the chlorination of alcohols **13** by use of thionyl chloride were further treated with 8-hydroxyquinoline in ethanol in the presence of KOH at reflux temperature for 2 days[13] to give the corresponding lariat ethers **1**–**3**.

On the other hand, another type of compound, **4**, was prepared by changing the reaction sequence used in the case of lariat **1a**; that is, the bromoalkoxylation of 15-methylene-16-crown-5 **9a** with NBS and *n*-butyl alcohol was performed as the first step as shown in Scheme 2. The trimethylolmethane structure of the crown ring together with the side chain around the pivot carbon was constructed according to this synthetic route. The lariat ether **5**, with two oxyquinoline moieties, was also obtained from substrate **9a** in a similar way as shown in Scheme 2. All structures were ascertained by ^{1}H NMR and IR spectroscopy, mass spectrometry, and elemental analysis.

Solvent extraction of alkali metal cations

Extraction data conducted under conditions using equimolar amounts of the ligand and alkali metal picrate[8b,14] at 25 °C are summarized in Table 1. Dichloromethane was used as the organic solvent. First, the effect of the difference in the structure around the pivot position of the ligands on the extractability was evaluated. The ligands **1a** and **4** are structurally regarded as being derived from 2-methylglycerol and trimethylolmethane, respectively,[15] by considering their respective coordination spheres. Although both isomers **1a** and **4** possess

Table 1 Solvent extraction of alkali metal picrates[a]

	Extractability (%)				
Ligand	Li^+	Na^+	K^+	Rb^+	Cs^+
1a	2	38	73	49	16
1b	3	45	70	53	34
1c	5	33	48	39	31
2a	1	20	70	60	52
2b	2	12	70	66	46
2c	3	11	71	64	46
3a	2	26	51	61	52
3b	3	18	50	49	40
3c	2	15	41	46	42
4	1	14	11	6	3
5	2	36	69	40	14
6	4	24	8	3	1
7	1	7	68	63	44
7[b]		6	69	58	37
8[b]		3	22	17	7

[a] Extraction conditions: dichloromethane (10 cm^3)/water (10 cm^3); [MOH] = 5×10^{-2} mol dm^{-3}; [extractant] = [picric acid] = 5×10^{-4} mol dm^{-3}; 25 °C; 9 h. [b] Ref. 2*a*.

Table 2 Stability constants in THF[a]

	log *K*			
Ligand	Na^+	K^+	Rb^+	Cs^+
1a	4.21	5.45	4.67	3.83
1b	4.08	4.86	4.43	3.82
1c	3.99	4.57	4.22	3.59
2a	4.01	5.13	4.76	4.11
2b	3.79	5.05	4.83	4.18
2c	3.88	5.15	4.83	4.15
3a	3.91	4.22	4.66	4.64
3b	3.59	4.03	4.35	4.23
3c	3.13	3.78	4.32	4.46
4	3.26	3.18		
5	4.03	5.01	4.62	4.01
6	3.83	3.02		
	3.51[b]	2.63[b]		
7	4.49	6.26	5.13	4.67
	4.32[b]	6.10[b]		

[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 in MeOH; ref. 8*b*.

the same number of hetero atoms (nine) and almost the same structure, their extractabilities toward alkali metal picrates are completely different. For example, compound **1a** showed much higher extractability and selectivity toward K^+ than did isomer **4**. In the case of compound **1a**, the original Na^+ selectivity based on the 16-crown-5 ring alone (structure **6**) was completely changed to favour K^+ selectivity, whereas isomer **4** maintained the Na^+ selectivity of its parent crown **6**. This finding suggests that the electron-donating sidearm of lariat **1a** effectively coordinates with K^+ but that the sidearm of compound **4** associates with the cation hardly at all. In order to verify the effectiveness of the glycerol structure of compound **1a**, the structure **5** was designed and the extractability of the compound was examined. As expected, the extraction profile of lariat **5** was very similar to that of compound **1a**. This result indicates that only the sidearm constituting the glycerol structure at the pivot position participates in complexation with the cation. The K^+ extractability of compound **1a** is comparable to that of 18-crown-6 **7**. In addition, the K^+/Rb^+ or the K^+/Cs^+ selectivity of compound **1a** is better than that of crown **7** though the K^+/Na^+ selectivity is moderate. This cation selectivity suggests that the coordination sphere of compound **1a** is estimated to be smaller than that of crown **7**.

Secondly, based on the result mentioned above, we attempted to expand this strategy using a 2-methylglycerol unit as the skeletal structure around the pivot carbon to larger crown ethers. In other words, in order to clarify the relationship between crown ring size and complexing ability, extractabilities of lariat ethers **1a**, **2a** and **3a** were compared. The three ligands have the same sidearm and so the difference among them exists only in the crown ring size. Inoue and Gokel previously reported that the extractability of 19-crown-6 **8** toward K^+ is much lower than that of 18-crown-6 as cited in Table 1.[2a] Ligand **2a**, having a 19-crown-6 ring, however, showed extractability toward K^+ comparable to that of 18-crown-6 **7**, which clearly demonstrates the effective coordination of the electron-donating sidearm. In comparison with compound **1a**, lariat **2a** possesses a better affinity toward larger cations such as Rb^+ and Cs^+, as expected from the increase in ring size. More interestingly, Rb^+ selectivity was observed in the extraction with ligand **3a** having a 22-crown-7 ring. This may be ascribed to the decrease in the affinity toward K^+ because the crown ring size of compound **3a** is too large to accommodate the cation. The effective coordination of the electron-donating sidearm toward Rb^+ is also responsible for the Rb^+ selectivity of lariat **3a**. The crown ether derivatives having Rb^+ selectivity developed so far are very few in comparison with those favouring complexation of other alkali metal cations.[16] Bartsch and co-workers previously reported that another type of C-pivot lariat ether, containing a dibenzo-22-crown-7 ring with a carboxylic acid moiety, showed K^+ selectivity in their extraction experiment.[7d] To our knowledge, this (compound **3a**) is the first example of an Rb^+-selective C-pivot lariat ether.

Thirdly, the effect of the length of the electron-donating sidearm on the complexing ability was examined. In the series of 16-crown-5 ethers **1**, both compounds **1a** and **1b** showed higher extractability toward K^+ and Rb^+ than did compound **1c**, which has the longest sidearm among them. Since the oxyquinoline moiety was one of the most effective alkali metal cation coordination sites, as shown in the preceding work,[8b] this result is reasonably explained upon consideration that the nitrogen atom of the quinoline ring of compound **1c** does not participate in complexation with the smaller cation. In the case of 19-crown-6 ethers **2**, all ligands showed about the same extractability toward K^+, Rb^+ and Cs^+, and much larger than for the unsubstituted one **8**, and thus the effect of the length of the sidearm on the extractability was uncertain in this case, though the necessity of the sidearm is obvious. The effective coordination of the oxyquinoline ring, however, was again observed, especially in the extraction of Rb^+, with lariat **3a**. Although crown ethers of low symmetry such as 19-crown-6, 20-crown-6 and 21-crown-6 are known to show much lower complexing abilities toward alkali metal cations than does 18-crown-6 as mentioned above,[2a] compounds **2a** and **3a** showed good extractability, especially toward K^+, Rb^+ and Cs^+. This result clearly shows that introduction of an electron-donating sidearm to the crown ring contributed to the increase in the complexing ability.

Stability constants in THF

The stability constants of ligands **1**–**5** toward Na^+, K^+, Rb^+ and Cs^+ measured in THF at 25 °C[14] are summarized in Table 2 along with data for the reference compounds **6** and **7**. The profile of the stability constants toward alkali metal cations essentially corresponded to that of the solvent extraction data. The stability constant toward K^+ of ligand **1a** (5.45) was found to be 186-times that of ligand **4** (3.18) and about 270-times that of unsubstituted 16-crown-5 **6** (3.02). In addition, the K^+/Na^+ selectivity of compound **1a** showed a value of ~17 and the original Na^+ selectivity of the 16-crown-5 ring (see data for compound **6**) was completely changed to K^+ selectivity. This finding shows that ligand **1a** effectively coordinates with K^+

with cooperative coordination of the sidearm but that the sidearm of compound **4** hardly interacts with the cation. Thus, the 2-methylglycerol structure around the pivot carbon of C-pivot lariat ethers was verified to play an important role for effective coordination of this type of ligands. The effect of ring size on the complexation properties was clearly observed in the comparison of the stability constants of ligands **1a**, **2a** and **3a** toward Cs^+. The stability constants toward Cs^+ increased with increasing ring size; that is, in the order **1a** < **2a** < **3a**. These three ligands showed about the same stability constant toward Rb^+. In the case of compound **3a** having a 22-crown-7 ring, however, the stability constant toward K^+ is much lower than that of ligands **1a** and **2a** because of the too large crown ring size for capturing the cation. As a result, Rb^+/K^+ selectivity was observed in the case of ligand **3a**. The stability constant of ligand **1a** toward K^+ was found to be lower than that of 18-crown-6 **7** though both ligands possess about the same extractability toward K^+. In the solvent extraction, the transfer of the cation from the aqueous phase to the organic phase is necessary, so the lipophilicity of the complex should be considered in addition to the stability constant. The three-dimensional coordination of ligand **1a** toward K^+ may be advantageous for increasing the lipophilicity of the complex in comparison with the two-dimensional coordination of the simpler crown **7**.

UV spectroscopy study

Further evidence for the three-dimensional coordination of C-pivot lariat ethers **1**–**3** toward alkali metal cations was obtained from the UV spectroscopy study. The position of the UV spectral maximum of the picrate anion is a measure of the type of the ion pair formed.[17,18] When ligand **1a** complexed with potassium picrate in THF, a peak at 381 nm was observed (Table 3). This absorption was assigned to the loose-ion pair. On the other hand, the combination of compound **4** and potassium picrate showed an absorption at 359 nm, assigned to the contact-ion pair. The large difference between ligands **1a** and **4** should be attributable to the three-dimensional coordination of ligand **1a** toward K^+.[8] A relatively small bathochromic shift was observed when equimolar amounts of 18-crown-6 **7** and potassium picrate were mixed, in spite of the fact that this crown possesses the highest stability constant for K^+ among ligands examined in this study. This result also shows the three-dimensional coordination of ligand **1a** for K^+ while ligand **7** is considered to complex with the cation by two-dimensional coordination. Moreover, in spite of the fact that the stability constant of compound **3a** toward K^+ is about one-hundredth that of compound **7**, the ligand formed a loose-ion pair when an equimolar amount of potassium picrate was added, supporting the three-dimensional coordination postulate.

Table 3 UV Absorption maximum of picrate anion in THF

	[L]/[P][a]							
	Na^+		K^+		Rb^+		Cs^+	
Ligand	1	5	1	5	1	5	1	5
1a	355[b]	363	381	381	367	380	362	366
2a	354	360	380	381	369	378	365	370
3a	355	358	380	380	367	380	365	370
4	353	355	359	364	358	359	360	360
5	355	362	380	380	366	380	360	365
6	354	365	358	358	358	358	360	360
7	358	378	370	379	362	365	366	368

[a] [L] = [ligand]; [P] = [picrate anion] = 5×10^{-5} mol dm^{-3}. [b] In nm.

^{1}H NMR spectroscopic study

The coordination of the sidearm of lariat ethers containing a 16-crown-5 ring toward K^+ was evaluated by ^{1}H NMR spectroscopy (Table 4). When a donor atom participates in coordination with a metal cation, the chemical shifts of neighbouring protons generally tend to move downfield. Thus, the extent of the downfield shift of quinoline protons is considered to be a measure of the complexation toward the metal cation. As expected, ligand **1a**, which possesses the highest stability constant for K^+ among a series of 16-crown-5 ethers, showed the largest downfield shifts for all quinoline protons. When the sidearm is lengthened by insertion of the oxyethylene unit, the change in the chemical shifts of quinoline protons is decreased in proportion to the decrease in their stability constants toward K^+. Furthermore, the chemical shifts of ligand **4** hardly moved upon the addition of KSCN. These findings clearly show that the quinoline moiety contributes highly to increasing the complexing ability of lariat ethers. It is noteworthy that all quinoline protons were separated into two sets of signals upon the addition of KSCN in the case of ligand **5**. Based on a comparison with the chemical shifts of ligands **1a** and **4**, one set of proton signals observed in the more downfield region is reasonably assigned to those of the quinoline moiety which belongs to the sidearm constituting the glycerol structure.

Bulk liquid membrane transport

Liquid membrane transport is an effective method for estimating the complexation properties of host compounds toward metal cations.[19] This method also makes possible an actual separation of metal cations. Thus, a competitive passive transport of alkali metal cations through a dichloromethane bulk membrane was carried out. The detailed transport conditions and the results using ligands **1a**, **2a** and **3a** as the ionophore in the presence of Li^+, Na^+, K^+, Rb^+ and Cs^+ are summarized in Table 5. The smallest ligand **1a** clearly showed selectivity for K^+, and the cation selectivity was shifted from K^+ to Rb^+ upon increasing the crown ring size. As expected from the extraction data, ligand **3a** showed Rb^+ selectivity.

Conclusions

In this paper, we describe the synthesis and the complexation properties of two types of C-pivot lariat ethers, which are different in the basic skeleton around the pivot carbon. In the case of lariat ethers containing a 16-crown-5 ring, ligand **1a** having a 2-methylglycerol structure showed not only higher complexing

Table 4 Changes in chemical shifts[a] of quinoline protons of 16-crown-5 ethers with equimolar additions of KSCN

	Quinoline protons					
Ligand	H-2	H-3	H-4	H-5	H-6	H-7
1a	0.08	0.13	0.13	0.13	0.12	0.07
1b	0.05	0.08	0.07	0.06	0.07	0.05
1c	0.03	0.05	0.04	0.03	0.04	0.02
4	0.01	0.01	0.02	0.01	0.01	0.00
5	0.06/0.01	0.07/0.01	0.09/0.02	0.07/0.01	0.08/0.01	0.08/0.02

[a] $\Delta\delta$(ppm) = [L] = δ(KSCN) − δ(None); [ligand] = [KSCN]; $CDCl_3$; 27 °C.

Table 5 Competitive passive transport data[a] toward alkali metal cations

Ligand	Li^+	Na^+	K^+	Rb^+	Cs^+	Selectivity K^+/Na^+	Selectivity K^+/Rb^+	Selectivity Rb^+/Cs^+
1a	<0.01	4.7	29	5.7	0.5	6.2	5.1	11.4
2a	<0.01	1.8	36	19	7.7	20	1.9	2.5
3a	<0.01	0.8	10	16	2.4	12.5	0.63	6.7

[a] $\times 10^7$ mol h^{-1}. Transport conditions: aqueous phase 1 (10 cm^3), [LiCl] = [NaSCN] = [KSCN] = [RbCl] = [CsCl] = [Me_4NOH] = 0.1 M, organic phase (CH_2Cl_2, 20 cm^3), [carrier] = 2.5 mmol dm^{-3}, aqueous phase 2 (10 cm^3), 25 °C.

ability but also a better selectivity toward K^+ than did ligand **4**, which has a trimethylolmethane structure, based on its three-dimensional coordination. In other words, strong complexation properties for alkali metal cations were attained by selecting the 2-methylglycerol skeleton in the design of lariat ethers. By expanding this strategy to larger lariat ethers, Rb^+ selectivity was observed in the 22-crown-7 derivatives. These findings clearly show that proper selection of the structure of the basic skeleton and balance between the crown ring size and the length of sidearm, are important for the molecular design of C-pivot lariat ethers.

Experimental

^{1}H NMR spectra were taken at 400 MHz on a JEOL JNM-GSX-400 spectrometer using tetramethylsilane at the internal standard. *J* Values are given in Hz. IR and UV spectra were obtained on a Hitachi 260-10 spectrophotometer and a Hitachi U-2000 spectrophotometer, respectively. The starting crown ethers, 15-methylene-16-crown-5 **9a**, 18-methylene-19-crown-6 **9b** and 21-methylene-22-crown-7 **9c** were prepared according to the method described in the literature.[12]

General procedure for the bromoalkoxylation of alkenes 9a–c using NBS and oligoethylene glycol to give compounds 10a–i

To an ice-cooled, stirred suspension of NBS (20 mmol) in oligoethylene glycol (0.20 mol) was added an alkene **9** (20 mmol) during 1 h. The resulting mixture was further stirred at 50 °C for 1 h. After cooling of the mixture to rt, 10% aq. sodium carbonate (100 cm^3) was added, and the product was extracted with dichloromethane (100 $cm^3 \times 4$). The solvent was evaporated off to give a slightly yellowish liquid. The crude product **10** was used for the next step without further purification.

General procedure for the synthesis of the protected compounds 11a–i

After dissolution of crude compound **10** (20 mmol) and PTSA (1.2 mmol) in 1,2-dichloroethane (30 cm^3), 3,4-dihydro-2*H*-pyran (30 mmol) was added dropwise to the ice-cooled mixture during 10 min. The resulting mixture was further stirred at rt for 3 h. Aq. sodium carbonate (10%; 100 cm^3) was added to the mixture, and the product was extracted with dichloromethane (100 $cm^3 \times 3$). After evaporation, the residue was purified by silica gel chromatography (acetone–hexane = 3 : 10).

15-Bromomethyl-15-[2-(tetrahydropyran-2-yloxy)ethoxy]-1,4,7,10,13-pentaoxacyclohexadecane 11a. By following the general procedure, compound **11a** was obtained from alcohol **10a** as a slightly yellowish liquid in 76% yield (based on alkene **9a**); $\delta_H(CDCl_3)$ 1.50–1.86 (6H, m, CH_2), 3.48–3.91 (28H, m, OCH_2) and 4.68–4.69 (1H, m, OC*H*CH_2O); ν_{max}(neat)/cm^{-1} 2950, 1460, 1350, 1300, 1200, 1120 and 970; *m*/*z* (CI) 471 ($M^+ + 1$).

15-Bromomethyl-15-{2-[2-(tetrahydropyran-2-yloxy)ethoxy]-ethoxy}-1,4,7,10,13-pentaoxacyclohexadecane 11b. By following the general procedure, compound **11b** was obtained from alcohol **10b** as a slightly yellowish liquid in 73% yield (based on alkene **9a**); $\delta_H(CDCl_3)$ 1.50–1.85 (6H, m, CH_2), 3.52–3.90 (32H, m, OCH_2) and 4.63–4.65 (1H, m, OC*H*CH_2O); ν_{max}(neat)/cm^{-1} 2900, 1450, 1350, 1300, 1200, 1120 and 950; *m*/*z* (FAB) 515 ($M^+ + 1$).

15-Bromomethyl-15-(2-{2-[2-(tetrahydropyran-2-yloxy)-ethoxy]ethoxy}ethoxy)-1,4,7,10,13-pentaoxacyclohexadecane 11c. By following the general procedure, compound **11c** was obtained from alcohol **10c** as a slightly yellowish liquid in 47% yield (based on alkene **9a**); $\delta_H(CDCl_3)$ 1.53–1.89 (6H, m, CH_2), 3.51–3.90 (36H, m, OCH_2) and 4.66–4.68 (1H, m, OC*H*CH_2O); ν_{max}(neat)/cm^{-1} 2900, 1400, 1350, 1300, 1250, 1120 and 970; *m*/*z* (FAB) 559 ($M^+ + 1$).

18-Bromomethyl-18-[2-(tetrahydropyran-2-yloxy)ethoxy]-1,4,7,10,13,16-hexaoxacyclononadecane 11d. By following the general procedure, compound **11d** was obtained from alcohol **10d** as a slightly yellowish liquid in 64% yield (based on alkene **9b**); $\delta_H(CDCl_3)$ 1.50–1.86 (6H, m, CH_2), 3.48–3.91 (32H, m, OCH_2) and 4.67–4.69 (1H, m, OC*H*CH_2O); ν_{max}(neat)/cm^{-1} 2950, 1400, 1360, 1300, 1240, 1100 and 970; *m*/*z* (FAB) 515 ($M^+ + 1$).

18-Bromomethyl-18-{2-[2-(tetrahydropyran-2-yloxy)-ethoxy]ethoxy}-1,4,7,10,13,16-hexaoxacyclononadecane 11e. By following the general procedure, compound **11e** was obtained from alcohol **10e** as a slightly yellowish liquid in 62% yield (based on alkene **9b**); $\delta_H(CDCl_3)$ 1.50–1.85 (6H, m, CH_2), 3.49–3.88 (36H, m, OCH_2) and 4.63–4.65 (1H, m, OC*H*CH_2O); ν_{max}(neat)/cm^{-1} 2950, 1430, 1360, 1300, 1240, 1100 and 970; *m*/*z* (FAB) 559 ($M^+ + 1$).

18-Bromomethyl-18-(2-{2-[2-(tetrahydropyran-2-yloxy)-ethoxy]ethoxy}ethoxy)-1,4,7,10,13,16-hexaoxacyclononadecane 11f. By following the general procedure, compound **11f** was obtained from alcohol **10f** as a slightly yellowish liquid in 63% yield (based on alkene **9b**); $\delta_H(CDCl_3)$ 1.51–1.84 (6H, m, CH_2), 3.43–3.85 (40H, m, OCH_2) and 4.61–4.64 (1H, m, OC*H*CH_2O); ν_{max}(neat)/cm^{-1} 2930, 1460, 1350, 1300 and 1120; *m*/*z* (FAB) 603 ($M^+ + 1$).

21-Bromomethyl-21-[2-(tetrahydropyran-2-yloxy)ethoxy]-1,4,7,10,13,16,19-heptaoxacyclodocosane 11g. By following the general procedure, compound **11g** was obtained from alcohol **10g** as a slightly yellowish liquid in 57% yield (based on alkene **9c**); $\delta_H(CDCl_3)$ 1.49–1.86 (6H, m, CH_2), 3.52–3.88 (36H, m, OCH_2) and 4.58–4.62 (1H, m, OC*H*CH_2O); ν_{max}(neat)/cm^{-1} 2990, 1480, 1380, 1320, 1240, 1100 and 960; *m*/*z* (FAB) 559 ($M^+ + 1$).

21-Bromomethyl-21-{2-[2-(tetrahydropyran-2-yloxy)ethoxy]-ethoxy}-1,4,7,10,13,16,19-heptaoxacyclodocosane 11h. By following the general procedure, compound **11h** was obtained from alcohol **10h** as a slightly yellowish liquid in 79% yield (based on alkene **9c**); $\delta_H(CDCl_3)$ 1.46–1.82 (6H, m, CH_2), 3.48–3.99 (40H, m, OCH_2) and 4.59–4.63 (1H, m, OC*H*CH_2O);

ν_{max}(neat)/cm^{-1} 2900, 1450, 1350, 1300, 1200, 1100 and 950; *m*/*z* (FAB) 603 ($M^+ + 1$).

21-Bromomethyl-21-(2-{2-[2-(tetrahydropyran-2-yloxy)-ethoxy]ethoxy}ethoxy)-1,4,7,10,13,16,19-heptaoxacyclodocosane 11i. By following the general procedure, compound **11i** was obtained from alcohol **10i** as a slightly yellowish liquid in 80% yield (based on alkene **9c**); $\delta_H(CDCl_3)$ 1.53–1.89 (6H, m, CH_2), 3.38–4.18 (44H, m, OCH_2) and 4.66–4.69 (1H, m, OC*H*CH_2O); ν_{max}(neat)/cm^{-1} 2920, 1430, 1320, 1260, 1120 and 950; *m*/*z* (FAB) 669 (M^+ + Na).

General procedure for the synthesis of compounds 12a–i

After sodium metal (0.58 g, 25 mmol) had been dissolved in *n*-butyl alcohol (0.1 mol), a bromide **11** (5 mmol) was added to the solution, which was then stirred at 120 °C for 48 h. After cooling of the mixture to rt, water (100 cm^3) was added and the product was extracted with dichloromethane (150 cm^3 × 3). The solvent was evaporated off to give a yellowish liquid. The crude product was used for the next step without further purification.

General procedure for the deprotection of THP ethers 12a–i to give alcohols 13a–i

After a crude compound **12** had been dissolved in methanol (150 cm^3), conc. H_2SO_4 (10 drops) was added to the solution, which was stirred at rt for 24 h. After neutralization with sodium hydroxide, methanol was evaporated off *in vacuo.* Water (200 cm^3) was added to the residue, and the product was extracted with dichloromethane (150 cm^3 × 4). The solvent was evaporated off to give a yellowish viscous liquid. The crude product was used for the next step without further purification.

General procedure for the chlorination of alcohols 13a–i to give chlorides 14a–i

After dissolution of a crude compound **13** (0.7–2.5 g) and pyridine (5 drops) in chloroform (25 cm^3), thionyl chloride (0.6–1.8 g) was added to the mixture under cooling in an ice-bath. The resulting mixture was further stirred at reflux temperature for 5 h. After cooling of the mixture to rt, 10% aq. sodium carbonate (200 cm^3) was added to the mixture, and the product was extracted with dichloromethane (200 cm^3 × 3). After evaporation, the residue was purified by silica gel chromatography (acetone–dichloromethane = 3 : 97).

15-*n*-Butoxymethyl-15-(2-chloroethoxy)-1,4,7,10,13-pentaoxacyclohexadecane 14a. By following the general procedure, compound **14a** was obtained from alcohol **13a** as a slightly yellowish liquid in 28% yield (based on bromide **11a**); $\delta_H(CDCl_3)$ 0.91 (3H, t, *J* 7.3, Me), 1.33–1.39 (2H, m, CH_2), 1.52–1.56 (2H, m, CH_2) and 3.51–3.99 (28H, m, OCH_2); ν_{max}(neat)/cm^{-1} 2920, 1450, 1300, 1100 and 980; *m*/*z* (FAB) 399 ($M^+ + 1$).

15-*n*-Butoxymethyl-15-[2-(2-chloroethoxy)ethoxy]-1,4,7,10,13-pentaoxacyclohexadecane 14b. By following the general procedure, compound **14b** was obtained from alcohol **13b** as a slightly yellowish liquid in 19% yield (based on bromide **11b**); $\delta_H(CDCl_3)$ 0.93 (3H, t, *J* 7.3, Me), 1.34–1.41 (2H, m, CH_2), 1.52–1.57 (2H, m, CH_2) and 3.41–3.98 (32H, m, OCH_2); ν_{max}(neat)/cm^{-1} 2940, 1450, 1300, 1120 and 950; *m*/*z* (FAB) 443 ($M^+ + 1$).

15-*n*-Butoxymethyl-15-{2-[2-(2-chloroethoxy)ethoxy]ethoxy}-1,4,7,10,13-pentaoxacyclohexadecane 14c. By following the general procedure, compound **14c** was obtained from alcohol **13c** as a slightly yellowish liquid in 31% yield (based on bromide **11c**); $\delta_H(CDCl_3)$ 0.91 (3H, t, *J* 7.3, Me), 1.33–1.39 (2H, m, CH_2), 1.52–1.55 (2H, m, CH_2) and 3.41–3.96 (36H, m, OCH_2); ν_{max}(neat)/cm^{-1} 2900, 1420, 1300, 1100 and 950; *m*/*z* (FAB) 487 ($M^+ + 1$).

18-*n*-Butoxymethyl-18-(2-chloroethoxy)-1,4,7,10,13,16-hexaoxacyclononadecane 14d. By following the general procedure, compound **14d** was obtained from alcohol **13d** as a slightly yellowish liquid in 71% yield (based on bromide **11d**); $\delta_H(CDCl_3)$ 0.92 (3H, t, *J* 7.3, Me), 1.33–1.39 (2H, m, CH_2), 1.50–1.55 (2H, m, CH_2) and 3.41–3.95 (32H, m, OCH_2); ν_{max}(neat)/cm^{-1} 2900, 1450, 1300, 1100 and 920; *m*/*z* (FAB) 443 ($M^+ + 1$).

18-*n*-Butoxymethyl-18-[2-(2-chloroethoxy)ethoxy]-1,4,7,10,13,16-hexaoxacyclononadecane 14e. By following the general procedure, compound **14e** was obtained from alcohol **13e** as a slightly yellowish liquid in 49% yield (based on bromide **11e**); $\delta_H(CDCl_3)$ 0.92 (3H, t, *J* 7.3, Me), 1.33–1.39 (2H, m, CH_2), 1.50–1.55 (2H, m, CH_2) and 3.41–3.95 (36H, m, OCH_2); ν_{max}(neat)/cm^{-1} 2900, 1450, 1300 and 1100; *m*/*z* (FAB) 487 ($M^+ + 1$).

18-*n*-Butoxymethyl-18-{2-[2-(2-chloroethoxy)ethoxy]ethoxy}-1,4,7,10,13,16-hexaoxacyclononadecane 14f. By following the general procedure, compound **14f** was obtained from alcohol **13f** as a slightly yellowish liquid in 23% yield (based on bromide **11f**); $\delta_H(CDCl_3)$ 0.93 (3H, t, *J* 7.3, Me), 1.31–1.37 (2H, m, CH_2), 1.47–1.52 (2H, m, CH_2) and 3.42–3.93 (40H, m, OCH_2); ν_{max}(neat)/cm^{-1} 2930, 1460, 1360, 1250 and 1130; *m*/*z* (FAB) 531 ($M^+ + 1$).

21-*n*-Butoxymethyl-21-(2-chloroethoxy)-1,4,7,10,13,16,19-heptaoxacyclodocosane 14g. By following the general procedure, compound **14g** was obtained from alcohol **13g** as a slightly yellowish liquid in 73% yield (based on bromide **11g**); $\delta_H(CDCl_3)$ 0.91 (3H, t, *J* 7.3, Me), 1.33–1.45 (2H, m, CH_2), 1.52–1.58 (2H, m, CH_2) and 3.36–3.96 (36H, m, OCH_2); ν_{max}(neat)/cm^{-1} 2920, 1460, 1300, 1100 and 920; *m*/*z* (FAB) 487 ($M^+ + 1$).

21-*n*-Butoxymethyl-21-[2-(2-chloroethoxy)ethoxy]-1,4,7,10,13,16,19-heptaoxacyclodocosane 14h. By following the general procedure, compound **14h** was obtained from alcohol **13h** as a slightly yellowish liquid in 19% yield (based on bromide **11h**); $\delta_H(CDCl_3)$ 0.92 (3H, t, *J* 7.3, Me), 1.33–1.39 (2H, m, CH_2), 1.50–1.55 (2H, m, CH_2) and 3.41–3.95 (40H, m, OCH_2); ν_{max}(neat)/cm^{-1} 2900, 1450, 1300, 1100 and 950; *m*/*z* (FAB) 531 ($M^+ + 1$).

21-*n*-Butoxymethyl-21-{2-[2-(2-chloroethoxy)ethoxy]ethoxy}-1,4,7,10,13,16,19-heptaoxacyclodocosane 14i. By following the general procedure, compound **14i** was obtained from alcohol **13i** as a slightly yellowish liquid in 21% yield (based on bromide **11i**); $\delta_H(CDCl_3)$ 0.92 (3H, t, *J* 7.3, Me), 1.31–1.41 (2H, m, CH_2), 1.49–1.55 (2H, m, CH_2) and 3.32–4.12 (44H, m, OCH_2); ν_{max}(neat)/cm^{-1} 2920, 1460, 1320, 1120 and 920; *m*/*z* (FAB) 575 ($M^+ + 1$).

General procedure for the synthesis of lariat ethers 1a–3c

Potassium hydroxide (0.07–0.3 g) and 8-hydroxyquinoline (0.2–0.9 g) were dissolved in ethanol (20 cm^3). The mixture was refluxed for 2 h and then a solution of a chloride **14** (0.1–0.6 g) in ethanol (15 cm^3) was added dropwise over a period of 30 min. The mixture was stirred for another 2 days at reflux temperature. After cooling to rt, the mixture was filtered, and evaporated *in vacuo*. Water (150 cm^3) was added to the residue and the product was extracted with dichloromethane (150 cm^3 × 4). After evaporation, the residue was purified by alumina chromatography (acetone–dichloromethane = 1 : 99–3 : 97).

15-*n*-Butoxymethyl-15-[2-(quinolin-8-yloxy)ethoxy]-1,4,7,10,13-pentaoxacyclohexadecane 1a. By following the general procedure, *lariat ether* **1a** was obtained from chloride **14a** as a slightly yellowish viscous liquid in 83% yield (Found: C, 63.6; H, 8.0; N, 3.1. $C_{27}H_{41}NO_8$ requires C, 63.89; H, 8.14; N, 2.76%); $\delta_H(CDCl_3)$ 0.90 (3H, t, *J* 7.3, Me), 1.24–1.41 (2H, m, CH_2), 1.45–1.58 (2H, m, CH_2), 3.24–4.58 (28H, m, OCH_2), 7.19–7.26 (1H, m, ArH), 7.34–7.50 (3H, m, ArH), 8.09–8.15 (1H, m, ArH) and 8.89–8.98 (1H, m, ArH); ν_{max}(neat)/cm^{-1} 2900, 1390, 1280, 1100 and 820; *m*/*z* (FAB) 508 ($M^+ + 1$).

15-*n*-Butoxymethyl-15-{2-[2-(quinolin-8-yloxy)ethoxy]-ethoxy}-1,4,7,10,13-pentaoxacyclohexadecane 1b. By following the general procedure, *lariat ether* **1b** was obtained from chloride **14b** as a slightly yellowish viscous liquid in 95% yield (Found: C, 61.0; H, 8.0; N, 2.6. $C_{29}H_{45}NO_9\cdot H_2O$ requires C, 61.14; H, 8.32; N, 2.46%); $\delta_H(CDCl_3)$ 0.88 (3H, t, *J* 7.3, Me), 1.32–1.36 (2H, m, CH_2), 1.40–1.51 (2H, m, CH_2), 3.39–4.43 (32H, m, OCH_2), 7.14–7.26 (1H, m, ArH), 7.40–7.50 (3H, m, ArH), 8.11–8.13 (1H, m, ArH) and 8.92–8.94 (1H, m, ArH); ν_{max}(neat)/cm^{-1} 2900, 1450, 1390, 1250, 1150, 1050 and 820; *m*/*z* (FAB) 552 ($M^+ + 1$).

15-*n*-Butoxymethyl-15-(2-{2-[2-(quinolin-8-yloxy)ethoxy]-ethoxy}ethoxy)-1,4,7,10,13-pentaoxacyclohexadecane 1c. By following the general procedure, *lariat ether* **1c** was obtained from chloride **14c** as a slightly yellowish viscous liquid in 82% yield (Found: C, 61.0; H, 8.0; N, 2.55. $C_{31}H_{49}NO_{10}\cdot H_2O$ requires C, 60.67; H, 8.38; N, 2.28%); $\delta_H(CDCl_3)$ 0.88 (3H, t, *J* 7.3, Me), 1.24–1.35 (2H, m, CH_2), 1.45–1.55 (2H, m, CH_2), 3.40–4.58 (36H, m, OCH_2), 7.10–7.26 (1H, m, ArH), 7.34–7.45 (3H, m, ArH), 8.11–8.15 (1H, m, ArH) and 8.94–8.98 (1H, m, ArH); ν_{max}(neat)/cm^{-1} 2900, 1450, 1330, 1260, 1120, 1020 and 820; *m*/*z* (FAB) 596 ($M^+ + 1$).

18-*n*-Butoxymethyl-18-[2-(quinolin-8-yloxy)ethoxy]-1,4,7,10,13,16-hexaoxacyclononadecane 2a. By following the general procedure, *lariat ether* **2a** was obtained from chloride **14d** as a slightly yellowish liquid in 79% yield (Found: C, 61.5; H, 7.95; N, 2.85. $C_{29}H_{45}NO_9\cdot H_2O$ requires C, 61.14; H, 8.32; N, 2.46%); $\delta_H(CDCl_3)$ 0.90 (3H, t, *J* 7.3, Me), 1.24–1.41 (2H, m, CH_2), 1.45–1.58 (2H, m, CH_2), 3.24–4.58 (32H, m, OCH_2), 7.19–7.26 (1H, m, ArH), 7.34–7.50 (3H, m, ArH), 8.09–8.15 (1H, m, ArH) and 8.89–8.98 (1H, m, ArH); ν_{max}(neat)/cm^{-1} 2950, 1450, 1350, 1280, 1180, 1000 and 820; *m*/*z* (FAB) 552 ($M^+ + 1$).

18-*n*-Butoxymethyl-18-{2-[2-(quinolin-8-yloxy)ethoxy]-ethoxy}-1,4,7,10,13,16-hexaoxacyclononadecane 2b. By following the general procedure, *lariat ether* **2b** was obtained from chloride **14e** as a slightly yellowish liquid in 79% yield (Found: C, 60.7; H, 8.8; N, 1.9. $C_{31}H_{49}NO_{10}\cdot H_2O$ requires C, 60.67; H, 8.38; N, 2.28%); $\delta_H(CDCl_3)$ 0.90 (3H, t, *J* 7.3, Me), 1.31–1.38 (2H, m, CH_2) 1.49–1.55 (2H, m, CH_2), 3.39–4.43 (36H, m, OCH_2), 7.13–7.15 (1H, m, ArH), 7.38–7.45 (3H, m, ArH), 8.11–8.13 (1H, m, ArH) and 8.93–8.95 (1H, m, ArH); ν_{max}(neat)/cm^{-1} 2920, 1450, 1300, 1250, 1150, 1060 and 820; *m*/*z* (FAB) 596 ($M^+ + 1$).

18-*n*-Butoxymethyl-18-(2-{2-[2-(quinolin-8-yloxy)ethoxy]-ethoxy}ethoxy)-1,4,7,10,13,16-hexaoxacyclononadecane 2c. By following the general procedure, *lariat ether* **2c** was obtained from chloride **14f** as a slightly yellowish liquid in 26% yield (Found: C, 61.7; H, 8.5; N, 2.0. $C_{33}H_{53}NO_{11}$ requires C, 61.95; H, 8.35; N, 2.19%); $\delta_H(CDCl_3)$ 0.88 (3H, t, *J* 7.3, Me), 1.31–1.37 (2H, m, CH_2), 1.42–1.51 (2H, m, CH_2), 3.49–4.49 (40H, m, OCH_2), 7.18–7.24 (1H, m, ArH), 7.41–7.52 (3H, m, ArH), 8.12–8.15 (1H, m, ArH) and 8.92–8.96 (1H, m, ArH); ν_{max}(neat)/cm^{-1} 2930, 1470, 1380, 1260, 1110 and 950; *m*/*z* (FAB) 640 ($M^+ + 1$).

21-*n*-Butoxymethyl-21-[2-(quinolin-8-yloxy)ethoxy]-1,4,7,10,13,16,19-heptaoxacyclodocosane 3a. By following the general procedure, *lariat ether* **3a** was obtained from chloride **14g** as a slightly yellowish liquid in 33% yield (Found: C, 58.6; H, 8.8; N, 1.9. $C_{31}H_{49}NO_{10}\cdot 2H_2O$ requires C, 58.94; H, 8.46; N, 2.22%); $\delta_H(CDCl_3)$ 0.90 (3H, t, *J* 7.3, Me), 1.24–1.41 (2H, m, CH_2), 1.44–1.59 (2H, m, CH_2), 3.34–4.60 (36H, m, OCH_2), 7.17–7.21 (1H, m, ArH), 7.37–7.48 (3H, m, ArH), 8.10–8.15 (1H, m, ArH) and 8.82–8.94 (1H, m, ArH); ν_{max}(neat)/cm^{-1} 2900, 1340, 1280, 1150 and 820; *m*/*z* (FAB) 596 ($M^+ + 1$).

21-*n*-Butoxymethyl-21-{2-[2-(quinolin-8-yloxy)ethoxy]-ethoxy}-1,4,7,10,13,16,19-heptaoxacyclodocosane 3b. By following the general procedure, *lariat ether* **3b** was obtained from chloride **14h** as a slightly yellowish liquid in 50% yield (Found: C, 60.4; H, 8.35; N, 2.1. $C_{33}H_{53}NO_{11}\cdot H_2O$ requires C, 60.26; H, 8.43; N, 2.13%); $\delta_H(CDCl_3)$ 0.88 (3H, t, *J* 7.3, Me), 1.31–1.37 (2H, m, CH_2), 1.42–1.55 (2H, m, CH_2), 3.49–4.49 (40H, m, OCH_2), 7.18–7.24 (1H, m, ArH), 7.41–7.52 (3H, m, ArH), 8.12–8.15 (1H, m, ArH) and 8.92–8.96 (1H, m, ArH); ν_{max}(neat)/cm^{-1} 2900, 1450, 1390, 1250, 1150, 1050 and 820; *m*/*z* (FAB) 640 ($M^+ + 1$).

21-*n*-Butoxymethyl-21-(2-{2-[2-(quinolin-8-yloxy)ethoxy]-ethoxy}ethoxy)-1,4,7,10,13,16,19-heptaoxacyclodocosane 3c. By following the general procedure, *lariat ether* **3c** was obtained from chloride **14i** as a slightly yellowish liquid in 39% yield (Found: C, 61.1; H, 8.4; N, 1.8. $C_{35}H_{57}NO_{12}$ requires C, 61.47; H, 8.40; N, 2.05%); $\delta_H(CDCl_3)$ 0.88 (3H, t, *J* 7.3, Me), 1.22–1.33 (2H, m, CH_2), 1.45–1.58 (2H, m, CH_2), 3.38–4.68 (44H, m, OCH_2), 7.12–7.29 (1H, m, ArH), 7.34–7.51 (3H, m, ArH), 8.12–8.18 (1H, m, ArH) and 8.90–8.95 (1H, m, ArH); ν_{max}(neat)/cm^{-1} 2920, 1480, 1360, 1260, 1120, 1040 and 820; *m*/*z* (FAB) 684 ($M^+ + 1$).

15-Bromomethyl-15-*n*-butoxy-1,4,7,10,13-pentaoxacyclohexadecane 15

To an ice-cooled stirred suspension of NBS (1.78 g, 0.10 mol) in *n*-butyl alcohol (7.41 g, 0.10 mol) was added a solution of alkene **9a** (2.46 g, 0.10 mol) in 1,2-dichloroethane (20 cm^3) during 2 h. The resulting mixture was further stirred at 50 °C for 18 h. After cooling of the mixture to rt, 10% aq. sodium carbonate (100 cm^3) was added, and the product was extracted with dichloromethane (100 cm^3 × 3). After evaporation, the residue was purified by silica gel chromatography (acetone–dichloromethane = 3 : 97) to give a slightly yellowish liquid (2.55 g, 64%), $\delta_H(CDCl_3)$ 0.91 (3H, t, *J* 7.3, Me), 1.35–1.41 (2H, m, CH_2), 1.50–1.56 (2H, m, CH_2) and 3.46–3.70 (24H, m, OCH_2); ν_{max}(neat)/cm^{-1} 2900, 1480, 1300, 1150 and 1080; *m*/*z* (CI) 399 ($M^+ + 1$).

15-*n*-Butoxy-15-{[2-(tetrahydropyran-2-yloxy)ethoxy]methyl}-1,4,7,10,13-pentaoxacyclohexadecane 16

After sodium metal (0.29 g, 12.5 mmol) had been dissolved in ethylene glycol monotetrahydropyran-2-yl ether (9.15 g, 62.6 mmol), bromide **15** (2.50 g, 6.26 mmol) was added, and the mixture was stirred at 140 °C for 39 h. After cooling to rt, the mixture was filtered and evaporated. Water (100 cm^3) was added, and the product was extracted with dichloromethane (100 cm^3 × 3). The solvent was evaporated off to give a yellowish liquid (5.00 g). The crude product was used for the next step without further purification.

15-*n*-Butoxy-15-[(2-hydroxyethoxy)methyl]-1,4,7,10,13-pentaoxacyclohexadecane 17

The synthetic procedure was almost the same as that used for compounds **13**. The crude product was used for the next step without further purification.

15-*n*-Butoxy-15-[(2-chloroethoxy)methyl]-1,4,7,10,13-pentaoxacyclohexadecane 18

The synthetic procedure was almost the same as that used for compounds **14**. The crude compound was purified by silica gel chromatography (acetone–dichloromethane = 1 : 99) to give a slightly yellowish liquid (0.82 g, 33% based on bromide **15**); $\delta_H(CDCl_3)$ 0.91 (3H, t, *J* 7.3, Me), 1.33–1.44 (2H, m, CH_2), 1.46–1.55 (2H, m, CH_2) and 3.59–3.78 (28H, m, OCH_2); ν_{max}(neat)/cm^{-1} 2950, 1460, 1350, 1300 and 1120; *m*/*z* (CI) 399 ($M^+ + 1$).

15-*n*-Butoxy-15-{[2-(quinolin-8-yloxy)ethoxy]methyl}-1,4,7,10,13-pentaoxacyclohexadecane 4

The synthetic procedure was almost the same as that used for the isomeric lariat ether **1a**. The crude compound was purified by alumina chromatography (acetone–dichloromethane = 1 : 99) to give *compound* **4** as a slightly yellowish viscous liquid (0.75 g, 72%) (Found: C, 63.9; H, 8.05; N, 3.1. $C_{27}H_{41}NO_8$ requires C, 63.89; H, 8.14; N, 2.76%); $\delta_H(CDCl_3)$ 0.88 (3H, t, *J* 7.3, Me), 1.26–1.31 (2H, m, CH_2), 1.45–1.49 (2H, m, CH_2), 3.56–4.46 (28H, m, OCH_2), 7.15–7.18 (1H, m, ArH), 7.39–7.47 (3H, m, ArH), 8.11–8.14 (1H, m, ArH) and 8.92–8.94 (1H, m, ArH); ν_{max}(neat)/cm^{-1} 2950, 1460, 1350, 1200, 1080 and 880; *m*/*z* (CI) 508 ($M^+ + 1$).

15-[2-(Tetrahydropyran-2-yloxy)ethoxy]-15-{[2-(tetrahydropyran-2-yloxy)ethoxy]methyl}-1,4,7,10,13-pentaoxacyclohexadecane 19

After sodium metal (0.35 g, 15 mmol) had been dissolved in ethylene glycol monotetrahydropyran-2-yl ether (9.32 g, 64 mmol), the bromide **11a** (2.00 g, 4.25 mmol) was added to the mixture, which was then stirred at 140 °C for 36 h. After cooling to rt, the mixture was filtered and evaporated. Water (100 cm^3) was added to the residue, and the product was extracted with dichloromethane (100 cm^3 × 3). The solvent was evaporated off to give a yellowish liquid (3.76 g). The crude product was used for the next step without further purification.

15-(2-Hydroxyethoxy)-15-[(2-hydroxyethoxy)methyl]-1,4,7,10,13-pentaoxacyclohexadecane 20

The synthetic procedure was almost the same as that used for compound **13a**. The crude product (1.15 g) was used for the next step without further purification.

15-(2-Chloroethoxy)-15-[(2-chloroethoxy)methyl]-1,4,7,10,13-pentaoxacyclohexadecane 21

The synthetic procedure was almost the same as that used for chlorides **14**. The crude compound was purified by silica gel chromatography (acetone–dichloromethane = 1 : 99) to give a slightly yellowish liquid (0.66 g, 38% based on bromide **11a**); $\delta_H(CDCl_3)$ 3.59–3.98 (30H, m, OCH_2); ν_{max}(neat)/cm^{-1} 2900, 1460, 1350, 1160, 1100 and 820; *m*/*z* (CI) 405 ($M^+ + 1$).

15-{[2-(Quinolin-8-yloxy)ethoxy]-15-{[2-(quinolin-8-yloxy)-ethoxy]methyl}-1,4,7,10,13-pentaoxacyclohexadecane 5

The synthetic procedure was almost the same as that used for lariat ether **1a**. The crude compound was purified by alumina chromatography (acetone–dichloromethane = 1 : 99) to give *compound* **5** as a slightly yellowish viscous liquid (0.75 g, 74%) (Found: C, 63.7; H, 6.6; N, 4.5. $C_{34}H_{42}N_2O_9 \cdot H_2O$ requires C, 63.74; H, 6.92; N, 4.37%); $\delta_H(CDCl_3)$ 3.56–4.43 (30H, m, OCH_2), 7.10–7.13 (2H, m, ArH), 7.33–7.43 (6H, m, ArH), 8.08–8.12 (2H, m, ArH) and 8.90–8.94 (2H, m, ArH); ν_{max}(neat)/cm^{-1} 2900, 1460, 1350, 1160, 1080 and 750; *m*/*z* (EI) 622 (M^+, tr), 478 (10%), 217 (10) and 172 (100).

Extraction procedure

A mixture of an aqueous solution (10 cm^3) of an alkali metal hydroxide (5×10^{-2} mol dm^{-3}) and picric acid (5×10^{-4} mol dm^{-3}) with a dichloromethane solution (10 cm^3) of an appropriate extractant (5×10^{-4} mol dm^{-3}) was shaken at 25 °C for 9 h. The extractability was obtained from the calculation based on the absorption of 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 alkali metal picrate in THF at 25 °C and the absorption of picrate anion in THF at 380 nm in the UV spectrum was used for calculation of the stability constants. Typically, the concentration of the guest compound was fixed at 5×10^{-5} mol dm^{-3} in THF and the molar ratios of the 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.[19] Details of the transport conditions are summarized in the footnotes to Table 5. 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 5 was the mean of four samples and the deviations from the mean were less than 10%.

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