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Syntheses and Structures of Synthetic Carboxylic Ionophores Containing 2,3-Naphthylene Groups

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Two derivatives of ω-hydroxy carboxylic ionophore 2-[[2-[2-[2-[2-[2-[2-[2-(2-hydroxyethoxy)phenoxy]ethoxy]phenoxy]ethoxy]phenoxy]ethoxy]phenoxy]methyl]benzoic acid **1**, 2-[[3-[2-[2-[2-[2-[2-[3-(2-hydroxyethoxy)-2-naphthyloxy]-ethoxy]phenoxy]ethoxy]phenoxy]ethoxy]-2-naphthyloxy]methyl]benzoic acid **2** and 2-[[3-[2-[2-[2-[3-[2-[2-(2-hydroxyethoxy)phenoxy]ethoxy]-2-naphthyloxy]ethoxy]phenoxy]ethoxy]-2-naphthyloxy]methyl]benzoic acid **3**, were prepared. Both compounds exhibited high K^+ selectivity over Na^+, as did **1**. The structures of the Rb salt of **2** and the K salt of **3** were determined by single-crystal X-ray analyses. Both ionophores formed psuedocycles by a head-to-tail hydrogen bond between the hydroxy and carboxylato groups and enclosed each cation like the seam of a tennis ball to make lipophilic complexes. However, the three-dimensional structures of the two hydrophobic salts differed from each other in spite of the similarity of the primary structures, which might be due to the interaction of the aromatic rings.

Ionophores are compounds which carry ions selectively through artificial and biological membranes by forming complexes with a hydrophobic exterior. A large number of natural cyclic and acyclic compounds are already known.[1] Synthetic cyclic compounds, such as crown ethers and cryptands, are extensively studied[2] and they are used as architecture to build larger molecules.[3] For linear synthetic ionophores, compounds with a rigid poly-THF/THP backbone[4] or with various functional groups at the terminal have been studied.[5] Acyclic compounds are considered to have less ion-selectivity because of their mobility; however, they have the advantages of facile synthesis, versatility of the ligand structure, and fast complex formation.[6] Several studies on the control of the three-dimensional structures of such host–guest complexes by chemical modification have been reported.[5d,5e]

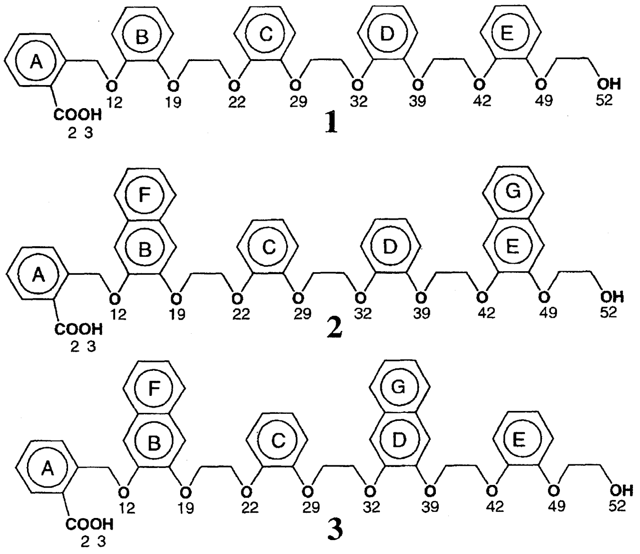
As analogs of the natural acyclic ionophores, such as nigericin, we have already reported a series of linear carboxylic acids whose backbones were composed only of repeating ether units derived from catechol and ethylene glycol.[7] These compounds transport alkali metal cations against their concentration gradient by a coupled counterflow of protons, which is seen for the naturally occurring carboxylic ionophores. Among our synthetic ionophores, 2-[[2-[2-[2-[2-[2-[2-[2-(2-hydroxyethoxy)phenoxy]ethoxy]phenoxy]ethoxy]phenoxy]ethoxy]phenoxy]methyl]benzoic acid, **1**, consisting of 30 atoms in the backbone exhibits high selectivities for K^+, Rb^+, and Cs^+ over Na^+ and Li^+ through a 1,2-dichloroethane liquid membrane.[7d,7g] NMR and X-ray studies revealed that the anion of **1** formed a head-to-tail hydrogen bonding to enclose the ions in the pseudocyclic cavity like the seam of a tennis ball for K^+, Rb^+, and Cs^+, but it would not form such a definite structure with Na^+ or Li^+ in $CDCl_3$ solution.[8] Free acid **1** itself is a flexible molecule in chloroform solution and the molecule changes its conformation upon complexation of the specific ions: K^+, Rb^+, and Cs^+.

In such an induced-fit system, structures of ligand-cation complexes will be influenced by various noncovalent interactions: electrostatic interaction, steric repulsion, hydrogen bonding, hydrophobic interaction, and so on.[9,10] To investigate the effects of such noncovalent interaction on the conformation of host–guest complexes, especially with regard to steric or hydrophobic interaction, we prepared **2** and **3**, by replacing two 1,2-phenylene groups of the ether chain of **1** with two 2,3-naphthylene groups (Scheme 1) and examined their ion transport properties. We report the molecular structures of two alkali metal salts, Rb salt of **2** and K salt of **3**, determined by single-crystal X-ray analysis and discuss their three-dimensional structures.

Results and Discussion

As shown in Scheme 1, one of the naphthylene groups locates next to the toluic acid moiety in the two derivatives. However, the other naphthylene group is in a different place. These two derivatives were prepared using successive Williamson's method according to Scheme 2 and were characterized by EA, IR, and ^{1}H NMR.

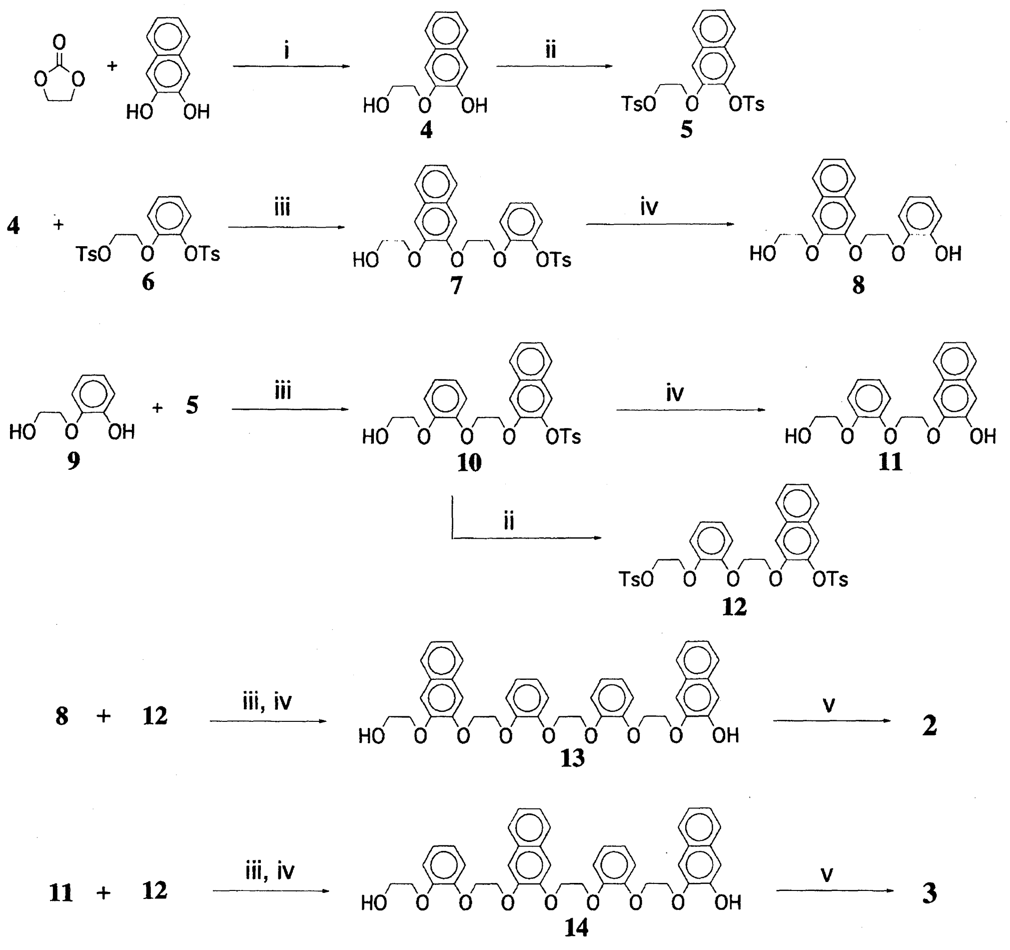
Active ion transport experiments with these synthetic ionophores were carried out using a U-tube apparatus as described before.[7d)] However, the amounts of the alkali metal ions transported through a liquid membrane containing synthetic ionophores were determined by atomic absorption spectrometry instead of flame analysis which was used in the previous work.[7d)] We made sure that the amount of increased and decreased ions was balanced by measuring the ion-concentration of the receiving and source phases. Table 1 shows the results of competitive active transport of alkali metal ions with **1** to **3** through 1,2-dichloroethane at 35 °C for 5 d. In the Na^+–K^+ competitive transport system, all derivatives exhibited high K^+ selectivity over Na^+. In the K^+–Rb^+–Cs^+ competitive transport system, transported



Scheme 1. The structures of synthetic ionophores.

Table 1. Active Transport of Alkali Metal Ions with **1** to **3** through 1,2-Dichloroethane Liquid Membrane

Ionophore	Ion transported/%				
	Na^+	K^+	Rb^+	Cs^+	Total
1	6	90	—	—	96
	—	29	41	22	92
2	4	89	—	—	93
	—	31	50	16	97
3	7	87	—	—	94
	—	28	43	25	96



Scheme 2. Synthetic route of **2** and **3**. Reagents and conditions; *i* Bu_4NI, 170 °C, *ii* *p*-$MeC_6H_4SO_2Cl$, NEt_3, in THF, *iii* NaH in DMF at 80 °C, *iv* alkali hydrolysis and acidification, *v* coupling with methyl 2-(bromomethyl)benzoate by NaH in DMF. (Ts represents *p*-tolylsulfonyl).

ion decreases in the order of $Rb^+ > K^+ > Cs^+$ and the ion selectivity becomes lower than that for K^+ over Na^+. These transport properties of **2** and **3** are similar to those with **1**.

Among the alkali metal salts of two derivatives of **1**, crystal structures of the Rb salt of **2** and the K salt of **3** were determined by single-crystal X-ray analysis. Table 2 lists the crystal data. The selected distances and torsion angles are listed in Tables 3 and 4. The bond distances and angles are normal. ORTEP drawings of the Rb salt of **2** and the K salt of **3** are shown in Figs. 1 and 2, respectively. Their atomic coordinates, thermal parameters, and $F_o - F_c$ tables are deposited as Document No. 70027. The crystals of the K salt of **2** were also prepared and the structure was analyzed. Although the refined structure is not so clear because of heavy disordering of the solvent molecules,[11] the molecular structure is very similar to that of the Rb salt of **2**. These K–O distances show that the K salt of **2** has a coordination manner similar to that of the Rb salt of **2**. The atomic coordinates of the K salt of **2** are also deposited as Document No. 70027.

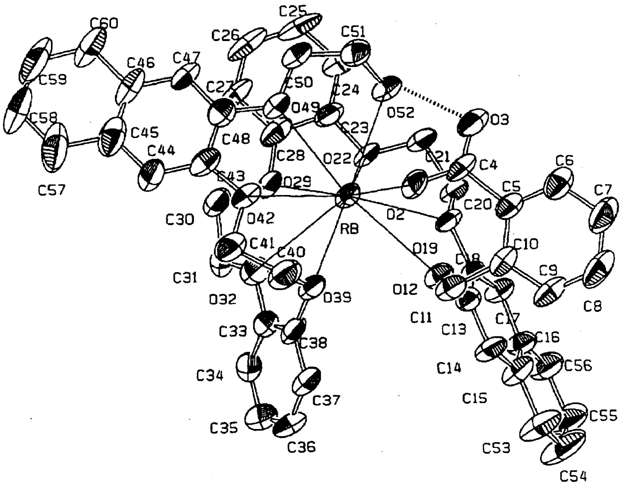


Fig. 1. Molecular structures of the Rb salt of **2** with 40% probability ellipsoids.

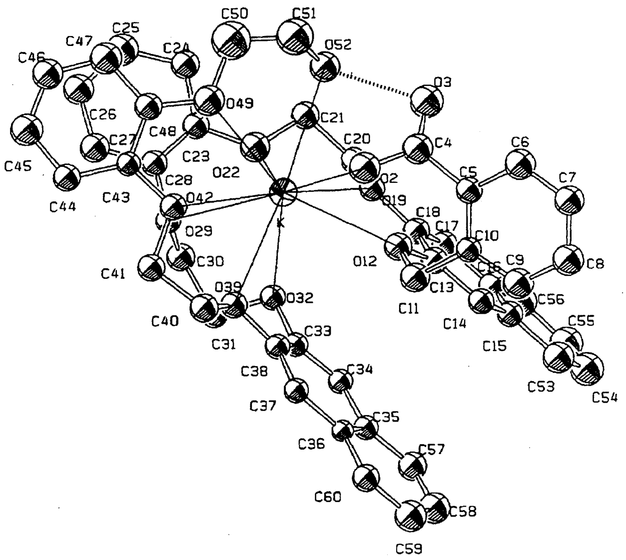


Fig. 2. Molecular structure of the K salt of **3** with 30% probability ellipsoids.

The distance between O3 and O52 of the Rb salt of **2** (2.72(1) Å) in Table 3 shows that the intramolecular hydrogen bonding between the carboxylato and hydroxy groups at the two ends of the molecule is formed to make a pseudocyclic conformation, as observed in the alkali metal salts of **1** and naturally occurring carboxylic ionophores.[12] Torsion angles of the backbone of the Rb salt of **2** are given in Table 4. Torsion angles around the aliphatic C–O bonds are about 180°, except for C10–C11–O12–C13 (+73°) and C38–O39–C40–C41 (−77°). The torsion angles around the aromatic C–O bonds are approximately 0°, except for C11–O12–C13–C14 (+30°) and C37–C38–O39–C40 (−79°). The dihedral angles around the aliphatic C–C bonds

Table 2. Crystal Data and Details of Structure Refinement of the Rb Salt of **2** and the K Salt of **3**

	Rb salt of **2**	K salt of **3**
Formula	$C_{48}H_{44}O_{11}Rb \cdot H_2O \cdot 2CHCl_3$	$C_{48}H_{44}O_{11}K \cdot 2H_2O \cdot CHCl_3$
Formula weight	1140.1	991.4
Crystal size/mm	0.4×0.2×0.3	0.2×0.2×0.2
Crystal system	Monoclinic	Monoclinic
Space group	$P2_1/c$ (#14)	$P2_1/c$ (#14)
a/Å	16.731(5)	10.20(2)
b/Å	13.647(6)	27.72(2)
c/Å	22.640(4)	17.60(3)
β/°	94.27(2)	103.0(3)
V/Å^3	5155(2)	4846(13)
D_{calcd}/g cm^{-3}	1.47	1.36
Z	4	4
μ/cm^{-1}	46.86	30.15
F 000	2236	2068
Unique reflections	8586	5333
Used reflections ($I > 3\sigma(I)$)	4062	1364
Max. Δ/σ	0.09	0.06
$\Delta\rho$/eÅ^{-3}	0.60	0.57
R, R_w	0.091, 0.105	0.096, 0.096

Table 3. Selected Distances (Å) and Angles (°) of the Rb Salt of **2** and the K Salt of **3**

	Rb salt of **2**	K salt of **3**		Rb salt of **2**	K salt of **3**
$M^+\cdots O2$	2.856(9)	2.82(2)	C41–O42	1.44(2)	1.46(3)
$M^+\cdots O3$	3.96(1)	3.93(2)	O42–C43	1.39(1)	1.39(3)
$M^+\cdots O12$	3.051(7)	2.83(2)	C48–O49	1.37(1)	1.34(3)
$M^+\cdots O19$	3.155(7)	2.92(2)	O49–C50	1.42(2)	1.44(3)
$M^+\cdots O22$	3.026(9)	2.78(2)	C50–O51	1.50(2)	1.41(4)
$M^+\cdots O29$	3.175(9)	3.10(2)	C51–O52	1.42(1)	1.43(3)
$M^+\cdots O32$	3.076(9)	2.98(2)			
$M^+\cdots O39$	2.855(9)	2.84(2)	O2–C4–O3	125(1)	122(3)
$M^+\cdots O42$	3.126(9)	3.03(2)	O2–C4–C5	118(1)	116(3)
$M^+\cdots O49$	3.052(8)	2.95(2)	C11–O12–C13	120.0(9)	115(2)
$M^+\cdots O52$	2.884(8)	2.94(2)	O12–C13–C18	117(1)	114(3)
$O3\cdots O52$	2.71(1)	2.64(2)	C18–O19–C20	117.0(9)	113(2)
O2–C4	1.25(2)	1.27(3)	O19–C20–C21	109(1)	106(2)
O3–C4	1.23(2)	1.26(3)	C21–O22–C23	117(1)	125(2)
C4–C5	1.55(2)	1.50(3)	O22–C23–C24	125(1)	119(3)
C10–C11	1.51(2)	1.50(3)	O22–C23–C28	114(1)	117(3)
C11–O12	1.41(1)	1.46(3)	C28–O29–C30	118(1)	113(2)
O12–C13	1.38(1)	1.39(3)	O29–C30–C31	106(1)	108(2)
C18–O19	1.40(1)	1.39(3)	C31–O32–C33	120(1)	109(2)
O19–C20	1.41(1)	1.45(3)	O32–C33–C34	121(1)	125(3)
C20–C21	1.53(1)	1.52(3)	O32–C33–C38	117(1)	116(3)
C21–O22	1.41(1)	1.41(3)	C38–O39–C40	115(1)	120(2)
O22–C23	1.40(1)	1.40(3)	O39–C40–C41	111(1)	107(2)
C28–O29	1.37(1)	1.39(3)	C41–O42–C43	116(1)	115(2)
O29–C30	1.40(2)	1.40(3)	O42–C43–C44	124(1)	122(3)
C30–C31	1.50(2)	1.57(3)	O42–C43–C48	115(1)	117(3)
C31–O32	1.41(2)	1.43(3)	C48–O49–C50	118(1)	115(3)
O32–C33	1.42(1)	1.40(3)	O49–C50–C51	108(1)	112(3)
C38–O39	1.37(1)	1.37(3)			
O39–C40	1.45(2)	1.47(3)			
C40–C41	1.54(2)	1.48(3)			

Table 4. Torsion Angles (°) of the Rb Salt of **2** and the K Salt of **3**

	Rb salt of **2**	K salt of **3**
C10–C11–O12–C13	+73	+80
C18–O19–C20–C21	+176	+179
C20–C21–O22–C23	−169	−158
C28–O29–C30–C31	+180	+163
C30–C31–O32–C33	−177	+164
C38–O39–C40–C41	−77	−168
C40–C41–O42–C43	−178	+177
C48–O49–C50–C51	+164	+172
C11–O12–C13–C14	+30	+2
C17–C18–O19–C20	−3	+5
C21–O22–C23–C24	+5	−9
C27–C28–O29–C30	−5	+107
C31–O32–C33–C34	+6	+107
C37–C38–O39–C40	−79	−2
C41–O42–C43–C44	−1	+6
C47–C48–O49–C50	+5	+0
O19–C20–C21–O22	−66	−65
O29–C30–C31–O32	+63	−68
O39–C40–C41–O42	−69	−66
O49–C50–C51–O52	+67	+71

are all gauche, as observed in the alkali metal salts of **1**. Consequently, the backbone of the Rb salt of **2** is bent at O12 and O39 to enclose the cation in the cavity like the seam of a tennis ball, as shown in Fig. 1; this is also seen for the K, Rb, and Cs salts of **1**.[7a] Approximately the same structure is found in the K salt of **2**. This suggests that the replacement of the two phenylene rings, B and E, with naphthylene rings, BF and EG, does not significantly effect the three-dimensional structure of the alkali metal salts. The Rb–O distances in Table 3 show that ten oxygen atoms coordinate to the cation according to the Shannon ionic radii[13] and the van der Waals radius of oxygen (1.4 Å). The Rb–O distances of the Rb salt of **2** (2.86—3.18 Å) are rather shorter than those of the Rb salt of **1** (2.92—3.20 Å). The Rb–O distances show that O2, O12, O39, and O52, locating at the hinge of the backbone and at the terminal, coordinate to the cation more strongly than the other oxygens. The O3 which participates in intramolecular hydrogen bonding does not coordinate to the cation.

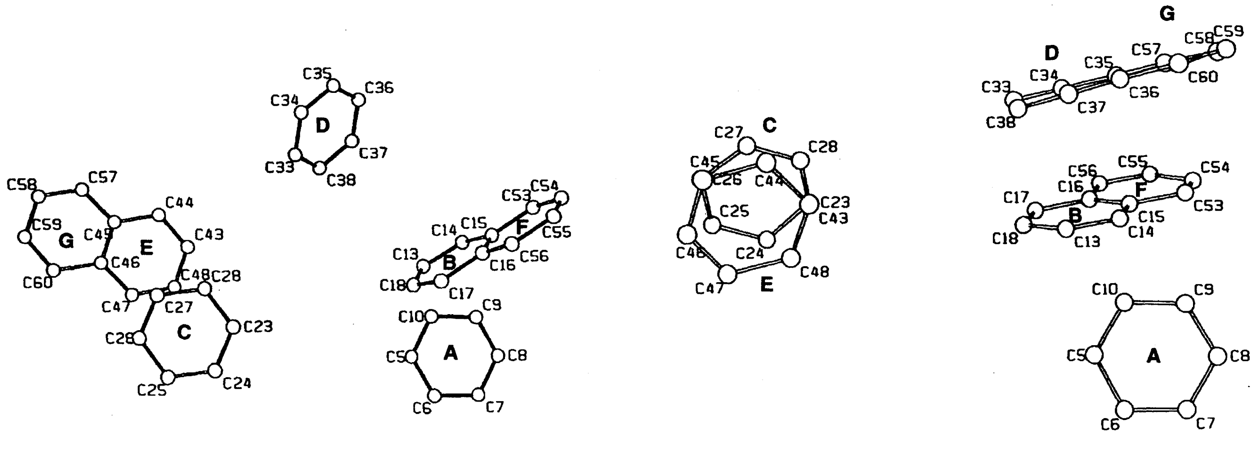
The distance between O3 and O52 of the K salt of **3** (2.64(2) Å) indicates that the head-to-tail hydrogen bonding is formed. Torsion angles around the aliphatic C–O bonds are approximately 180°, except for C10–C11–O12–C13 (+80°). The torsion angles around the aromatic C–O bonds are nearly 0°, except for C27–C28–O29–C30 (+107°) and C31–O32–C33–C34 (+107°). All the four torsion angles around the aliphatic C–C bonds are *gauche*. The signs of these torsion angles of the alkali metal salts of **1** and **2** are changed alternately along the main chain; however, those for the K salt of **3** are not: three negative and one positive signs. These torsion angles show that the backbone of the K salt of **3** is bent at O12, O22, and O32, so the overall conformation of this salt in Fig. 2 is different from those of the alkali metal salts of **1** and **2**. The backbone bending at O22 and O32 is less steep than that at O12. From the K–O distances, ten oxygen atoms coordinate to K$^+$. The K–O distances of the K salt of **3** become shorter at O2, O52, and O12, which are located at the terminal and at one of the hinges. However, at O32, where the backbone is bent, the distance is longer than the others. The O3 which participates in the intramolecular hydrogen bonding dose not coordinate to the cation, as observed in the above two salts.

The molecular structures of the alkali metal salts of **1**, **2**, and **3** were compared with each other. The conformations of the Rb and K salts of **2** are similar to each other and their structures also resemble those of the K, Rb, and Cs salts of **1**. However, the structure of the K salt of **3** is different from those of the alkali metal salts of **1** and **2**. Figure 3 shows the relative positions of the aromatic rings of the Rb salt of **2** and the K salt of **3** projected on the A ring. The distances between the center of two aromatic rings and the dihedral angles are given in Table 5. Most of the distances in the K salt of **3** are slightly shorter than those of the Rb salt of **2**. Pairs of the aromatic rings with the distance less than 6 Å for the Rb salt of **2** are A---B, B---D, and C---E and the corresponding pairs for the K salt of **3** are A---B, B---DG, C---E, and F---G. In the two salts, the distances between the A and B rings, which are connected through the CH$_2$O moiety, are about 5 Å and the dihedral angles are 100°, close to perpendicular. The distances between the B and DG rings for the K salt of **3** are shorter (4.6 and 5.4 Å) than the distance between the B and D rings for the Rb salt of **2** (5.8 Å). The dihedral angles of B and DG rings for the K salt of **3** are 9 and 11°, nearly parallel, but that for the Rb salt of **2** is 54°. The distances of the F and DG rings for the K salt of **3** are shorter (6.1 and 6.0 Å) than that of the F and D rings for the Rb salt of **2** (7.1 Å). The dihedral angles of the F and DG rings for the K salt of **3** and that for the F and D rings for the Rb salt of **2** are 10, 12, and 51°, respectively. The model of aromatic–aromatic interactions of the benzene dimer in chloroform indicates that the contact dimer with a ring center–ring center separation of ca. 5.5 Å is energetically preferred and face-to-face stacked structures are not repulsive.[14] Even if the D ring is replaced with another naphthylene ring in the Rb salt of **2** conformation in Fig. 3, the aromatic rings will not cause much steric repulsion and no additional aromatic–aromatic interaction will occur (the distances of B and G, and F and G are 6.4 and 7.0 Å, respectively). Although the conformation of the main chain observed in the K salt of **3** is likely to be less stable than those of alkali metal salts of **1** and **2**, the intramolecular interaction of aromatic rings between BF and DG rings may stabilize the three-dimensional structure of K salt of **3**. Although the position of two naphthylene rings caused partial conformational change as described above, two derivatives of **1** enclose K$^+$ in their pseudocyclic cavity to form lipophilic complexes. Similar hydrophobic complexes will be formed in the liquid membrane used for the ion transport.

In summary, the two derivatives of **1**, **2**, and **3**, are found to exhibit high K$^+$ selectivity over Na$^+$ in a Na$^+$–K$^+$ competitive transport system. The structures of the Rb salt of **2** and the K salt of **3** determined by X-ray analyses show that both ionophores enclose each cation like the seam of a tennis ball to make lipophilic complexes, which is in agreement with their ion-transport properties. However, the positional difference of the naphthylene rings caused a change in the three-dimensional structure of the salts in spite of the similarity of the primary structures of the ionophores, which may be due to the noncovalent aromatic–aromatic interaction.

Experimental

Materials. Unless otherwise stated, reactants and solvents are reagent grade. They were obtained from commercial supplies and used as received. 2,3-Naphthalenediol, ethylene carbonate,



Rb salt of **2**   K salt of **3**

Fig. 3. Relative positions of the aromatic rings of the Rb salt of **2** and the K salt of **3** projected on their plane of A rings.

Table 5. Dihedral Angles (°) and Distances (Å) between the Center of the Aromatic Rings

	Rb salt of **2**		K salt of **3**	
Ring–Ring	Distance/Å	Dihedral angles/°	Distance/Å	Dihedral angles/°
A–B	4.9	97	5.1	103
A–C	9.5	19	10.0	41
A–D	8.0	47	6.2	97
A–E	10.1	26	9.9	32
A–F	6.5	95	6.6	105
A–G	12.5	24	6.6	95
B–C	8.1	115	8.1	62
B–D	5.8	54	4.6	9
B–E	10.0	116	9.8	72
B–G	12.2	116	5.4	11
C–D	8.0	62	7.8	56
C–E	5.3	11	4.0	9
C–F	10.2	112	10.2	64
C–G	6.3	95	10.2	3
D–E	7.0	63	8.1	65
D–F	7.1	51	6.1	10
D–G	8.7	62	—	—
E–F	12.2	114	12.2	73
E–G	—	—	10.4	63
F–G	14.3	113	6.0	12

60% NaH in oil, Et_3N, Br_2 (99%), LiOH, NaOH, KOH, HCl, KCl, NaCl, KBr, $MgSO_4$, hexane, MeOH, $CHCl_3$, AcOEt, 1,2-dichloroethane, Wakogel C-300, Na, K, Rb, and Cs standard solutions for atomic absorption spectrometry (Wako Pure Chemical Industries, Ltd.); Bu_4NI, catechol, *p*-toluenesulfonyl chloride (TsCl), methyl 2-methylbenzoate, RbOH, CsOH (Kanto Chemical Co., Inc.); THF anhydrous (Aldrich); $CDCl_3$ (99.5%) and tetramethylsilane (TMS) (E. Merck). Et_3N, DMF, and CCl_4 were dried over molecular sieves 3A 1/8. 2-(2-Tosyloxyphenoxy)ethyl *p*-toluenesulfonate, **6** and 2-(2-Hydoxyphenoxy)ethanol, **9**, were obtained according to the literature.[7)] Preparation of the alkali metal salts of the ionophores has been previously described.[8a)]

Instrumentation. Infrared spectra (KBr discs) were recorded on a JEOL JIR-AQS20M FT-IR spectrometer at 25 °C. Atomic absorption measurements were performed with a Hitachi Z8100. Elemental analyses were obtained by a Perkin–Elmer 2400 HCN elemental analyzer. NMR samples were prepared at concentrations of 10 to 20 mM $CDCl_3$ solution ($1\ M = 1\ mol\,dm^{-3}$) in 5 mmϕ tubes. ^1H NMR spectra of **4** to **14** were recorded on a JEOL EX-90 and those of **2** and **3** were measured with a JEOL EX-400 FT-NMR spectrometer. Chemical shifts of ^1H NMR were measured from TMS as an internal standard in $CDCl_3$ and CD_3OD solutions.

2-(3-Hydroxy-2-naphthyloxy)ethanol (4); Procedure i. A mixture of 2,3-dihydroxynaphthalene (110 g, 0.69 mol), ethylene carbonate (60.5 g, 0.69 mol), and Bu_4NI (20 g, 54 mmol) was heated at 170 °C for about 3 h until evolution of CO_2 ceased. The gray crude product was recrystallized from MeOH to give **4** (85.4 g, 61%). ^1H NMR (CD_3OD) $\delta = 3.90$—4.23 (4H, m, OCH_2CH_2OH), 7.14—7.69 (6H, m, aromatic). Found: C, 70.54; H, 5.97%. Calcd for $C_{12}H_{12}O_3$: C, 70.58; H, 5.92%. Mp 159—160 °C.

2-(3-Tosyloxy-2-naphthyloxy)ethyl *p*-Toluenesulfonate (5); Procedure ii. TsCl (83.9 g, 0.44 mol) was added in small portions to a mixture of **4** (40.8 g, 0.20 mol) and Et_3N (100 mL, 0.72 mol) in 800-mL THF at 0 °C. After the solution was stirred for 24 h at room temperature, $[Et_3NH]Cl$ was removed by filtration. The filtrate was evaporated to dryness. The resulting solid was washed with MeOH and diethyl ether to produce the white solid, **5** (89.3 g, 85%). ^1H NMR ($CDCl_3$) $\delta = 2.42$ (6H, s, CH_3), 4.00—4.30 (4H, m, OCH_2CH_2OH), 7.00—7.89 (14H, m, aromatic). Found: C, 61.00; H, 4.67%. Calcd for $C_{26}H_{24}O_7S$: C, 60.92; H, 4.72%.

2-[2-[3-(2-Hydroxyethoxy)-2-naphthyloxy]ethoxy]phenyl *p*-Toluenesulfonate (7); Procedure iii. The α, ω-diol, **4** (12.3 g, 60 mmol) dissolved in 200-mL DMF was dropwise added to a suspension of NaH (2.4 g, 60 mmol) in 50 mL DMF at 0 °C, followed by stirring for 2 h at room temperature. Dropwise addition of **6** (27.8 g, 60 mmol) dissolved in 200-mL DMF to the former solution was done and the mixture was stirred at 80 °C for 20 h. After DMF was evaporated under reduced pressure, the remaining oil was neutralized with 2 M HCl and extracted with $CHCl_3$. The organic phase was washed twice with 2 M HCl and then dried over $MgSO_4$. The solution was evaporated and the residual mixture was purified by silica-gel column chromatography with hexane–AcOEt (1 : 1) as an eluent to yield 23.3 g of **7** (78%). ^1H NMR $\delta = 2.25$ (3H, s, CH_3), 3.96—4.29 (4H, m, OCH_2CH_2OH), 4.30 (4H, s, OCH_2CH_2O), 6.92—7.84 (14H, m, aromatic). Found: C, 65.71; H, 5.30%. Calcd for $C_{27}H_{26}O_7S$: C, 65.57; H, 5.30%.

2-[3-[2-(2-Hydroxyphenoxy)ethoxy]-2-naphthyloxy]ethanol (8); Procedure iv. **7** (11.5 g, 23 mmol) was dissolved in mixed solvent of 100 mL of THF, 100 mL of ethanol, and 100 mL of 2 M NaOH. The solution was refluxed for 3 h. After the organic solvents were evaporated, the solution was neutralized with 2 M HCl. The product was extracted with $CHCl_3$ and the organic layer was dried over $MgSO_4$. After $CHCl_3$ was evaporated, the crude product was purified by silica-gel column chromatography with hexane–AcOEt (1 : 1) to yield 6.1 g of **8** (78%). ^1H NMR ($CDCl_3$) $\delta = 3.96$—4.21 (4H, m, OCH_2CH_2OH), 4.25 (4H, s, OCH_2CH_2O), 6.78—7.82 (10H, m, aromatic). Found: C, 68.45; H, 6.25%. Calcd for $C_{20}H_{20}O_5 \cdot 0.5AcOEt$: C, 68.74; H, 6.29%.

3-[2-[2-(2-Hydroxyethoxy)phenoxy]ethoxy]-2-naphthyl *p*-Toluenesulfonate (10). By a synthetic procedure similar to that of **7**, **10** was prepared from **9** (10.8 g, 23 mmol) and **5** (35.9 g, 70 mmol). Yield 18.7 g, 54%. ^1H NMR ($CDCl_3$) $\delta = 2.34$ (3H, s, CH_3), 3.75—4.24 (4H, m, OCH_2CH_2OH), 4.28 (4H, s, OCH_2CH_2O), 6.99—7.85 (14H, m, aromatic). Found: C, 64.70;

H, 5.52%. Calcd for $C_{27}H_{26}O_7S\cdot 0.5AcOEt$: C, 64.67; H, 5.61%.

2-[2-[2-(3-Hydroxy-2-naphthyloxy)ethoxy]phenoxy]ethanol (11). By a synthetic procedure similar to that of **8**, **11** was prepared from **10** (10.0 g, 20 mmol). Yield 5.15 g, 75%. ^{1}H NMR ($CDCl_3$) $\delta = 3.83$—4.30 (4H, m, OCH_2CH_2OH), 4.37—4.54 (4H, m, OCH_2CH_2O), 6.93—8.02 (10H, m, aromatic). Found: C, 70.89; H, 6.41%. Calcd for $C_{20}H_{20}O_5$: C, 70.58; H, 5.92%.

2-[2-[2-(3-Tosyloxy-2-naphthyloxy)ethoxy]phenoxy]ethyl *p*-Toluenesulfonate (12). By a synthetic procedure similar to that of **5**, **12** was prepared from **10** (8.66 g, 18 mmol) and TsCl (5.00 g, 26 mmol). Yield 9.67 g, 83%. ^{1}H NMR ($CDCl_3$) $\delta = 2.35$ (6H, s, CH_3) 4.24—4.44 (8H, m, CH_2), 6.88—7.80 (18H, m, aromatic). Found: C, 63.14; H, 4.95%. Calcd for $C_{34}H_{32}O_9S_2$: C, 62.95; H, 4.97%.

2-[3-[2-[2-[2-[2-[2-(3-Hydroxy-2-naphthyloxy)ethoxy]phenoxy]ethoxy]phenoxy]ethoxy]-2-naphthyloxy]ethanol (13). By a synthetic procedure similar to that of **7**, **13** was prepared from **8** (7.83 g, 23 mmol) and **12** (14.9 g, 23 mmol). Purification by silica-gel column chromatography with $CHCl_3$–MeOH (100 : 1). Yield 5.61 g, 37%. ^{1}H NMR ($CDCl_3$) $\delta = 4.00$—4.25 (4H, m, OCH_2CH_2OH), 4.43—4.51 (12H, m, OCH_2CH_2O), 6.79—7.76 (20H, m, aromatic).

2-[2-[2-[3-[2-[2-[2-(3-Hydroxy-2-naphthyloxy)ethoxy]phenoxy]ethoxy]-2-naphthyloxy]ethoxy]phenoxy]ethanol (14). By a synthetic procedure similar to that of **7**, **14** was prepared from **11** (4.77 g, 14 mmol) and **12** (9.08 g, 14 mmol). Purification by silica-gel column chromatography with $CHCl_3$–MeOH (100 : 1). Yield 2.48 g, 27%. ^{1}H NMR ($CDCl_3$) $\delta = 3.75$—4.29 (4H, m, OCH_2CH_2OH), 4.34—4.54 (12H, m, OCH_2CH_2O), 6.83—7.66 (20H, m, aromatic).

2-[[3-[2-[2-[2-[2-[2-[3-(2-Hydroxyethoxy)-2-naphthyloxy]ethoxy]phenoxy]ethoxy]phenoxy]ethoxy]-2-naphthyloxy]methyl]benzoic Acid (2); Procedure v. The α, ω-diol, **13** (5.30 g, 8.0 mmol) dissolved in 100-mL DMF was dropwise added to suspension of NaH (ca. 60% 0.32 g, 8.00 mmol) in 50 mL DMF at 0 °C. The reaction mixture was stirred for 2 h at room temperature. Methyl 2-(bromomethyl)benzoate **15** (1.83 g, 8.0 mmol) dissolved in 50-mL DMF was added to the former solution. The resulting solution was stirred at 90 °C for 20 h. After DMF was removed, the remaining oil was neutralized with 2 M HCl. Then 70 mL of THF, 140 mL of EtOH, and 70 mL of 2 M NaOH were added and the mixture was refluxed for 4 h. After $CHCl_3$ was evaporated, the crude product was purified by silica-gel column chromatography with $CHCl_3$–MeOH (100 : 2). Yield 4.13 g, 65%. ^{1}H NMR ($CDCl_3$) $\delta = 3.94$—4.20 (4H, m, OCH_2CH_2OH), 4.25—4.49 (12H, m, OCH_2CH_2O), 5.49 (2H, s, CH_2), 6.78—7.91 (24H, m, aromatic). IR (KBr) 1695 cm^{-1} (C=O). Found: C, 72.30; H, 5.58%. Calcd for $C_{48}H_{44}O_{11}$: C, 72.35; H, 5.57%.

2-[[3-[2-[2-[2-[3-[2-[2-(2-Hydroxyethoxy)phenoxy]ethoxy]-2-naphthyloxy]ethoxy]phenoxy]ethoxy]-2-naphthyloxy]methyl]benzoic Acid (3). By a synthetic procedure similar to that of **2**, **3** was prepared from **14** (5.96 g, 9.0 mmol) and **15** (2.06 g, 9.0 mmol). Purification by column chromatography with $CHCl_3$–MeOH (100 : 2). Yield 4.28 g, 60%. ^{1}H NMR ($CDCl_3$) $\delta = 3.75$—4.19 (4H, m, OCH_2CH_2OH), 4.30—4.48 (12H, m, OCH_2CH_2O), 5.50 (2H, s, benzyl), 6.87—7.92 (24H, m, aromatic). IR (KBr) 1692 cm^{-1} (C=O). Found: C, 72.08; H, 5.63%. Calcd for $C_{48}H_{44}O_{11}$: C, 72.35; H, 5.57%.

Ion Transport Experiment. The ion transport experiments were carried out in a U-tube cell at 35±1°C for 5 d in the same manner as reported previously.[7e,7f,7g] The concentrations of alkali metal ions in Acceptor phase II before and after transport experiment (C_{a0} and C_{a1}) as well as those in Donor phase I (C_{d0} and C_{d1}) were obtained as follows: To an aliquot of both phases were added water and 1 M HCl to prepare 250-times diluted solution in 0.02 M HCl. Concentrations of alkali metal ions of the diluted solutions were determined by atomic absorption spectrometry at wavelengths of 589.0, 766.5, 780.0, and 852.1 nms for Na^+, K^+, Rb^+, and Cs^+, respectively, using calibration curves made with diluted solutions of Na^+ (0.0—2.0 ppm), K^+ (0.0—5.0 ppm), Rb^+ (0.0—7.0 ppm), and Cs^+ (0.0—10.0 ppm) from 1000-ppm standard solutions for atomic absorption spectrometry. The transported ion (%) was calculated by an equation of $[(C_{a1}-C_{a0})/C_{a0}]\times 100$ or $[(C_{d0}-C_{d1})/C_{d0}]\times 100$. The difference between those two values obtained from two equations is less than 9%. The averaged values of transported ion obtained from Acceptor phase II are shown in Table 1.

Structure Analyses. The crystals were obtained from a chloroform solution. A crystal suitable for X-ray analysis was sealed in a glass capillary with a drop of chloroform. Intensities were collected on a Rigaku AFC5S four-circle diffractometer; graphite-monochromatered Cu $K\alpha$ radiation (40 kV, 30 mA, $\lambda = 1.54184$ Å) in the range of 6—125° for the Rb salt of **2** and the K salt of **3**. Cell parameters were obtained by least-squares method using 25 reflections. In all measurements, intensity data were measured by 2θ–ω scan technique monitoring three standard reflections every 150 reflections. Corrections were made for Lorentz, polarization, and absorption using Ψ-scan. Transition factors were 0.62—1.00 for the Rb salt of **2** and 0.60—1.00 for the K salt of **3**. The structure was solved by the direct method and refinement was performed by full-matrix calculation using program package, TEXSAN.[15] The quantity minimized was $\Sigma\omega(|F_o|-|F_c|)^2$ with the weight scheme of $\omega = 4F_o^2/\sigma^2(F_o^2)$. Some hydrogen atoms of the Rb salt of **2** were found on difference Fourier maps and the others and those of the K salt of **3** were derived geometrically (C–H = 0.95 Å). Although several measurements were carried out, it was difficult to collect a sufficient number of the observed reflections with $I > 3\sigma(I)$, probably due to the disordered structures of the solvent molecules. For that reason, only K was refined anisotropically and the other non-hydrogen atoms were refined with isotropic thermal parameters for the K salt of **3**. Tables of the fractional atomic coordinates, anisotropic thermal parameters, bond lengths and angles, and the F_o–F_c data of Rb salt of **2** and K salt of **3** with table of the fractional atomic coordinates of K salt of **2** are deposited as Document No. 70027 at the Office of the Editor of Bull. Chem. Soc. Jpn.

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