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Studies on Synthetic Ionophores. X.[1)] Transport Behavior of Na^+ and K^+ with an ω-Hydroxy Carboxylic Acid Containing Octaether Linkages as a Synthetic Analog of Natural Carboxylic Acid Ionophores through an Organic Liquid Membrane

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2-[[2-[2-[2-[2-[2-[2-[2-(2-Hydroxyethoxy)phenoxy]ethoxy]phenoxy]ethoxy]phenoxy]ethoxy]phenoxy]methyl]benzoic acid (**1**) was employed as a carrier to transport alkali metal ions. The transport selectivity sequence through 1,2-dichloroethane membrane was $K^+ \geq Rb^+ > Cs^+ > Na^+ \geq Li^+$. The high preference of K^+ to Na^+ in competitive transport through 1,2-dichloroethane–toluene was consistent with the difference of solubility between the potassium and sodium salts of **1**. However, the separate transport rates of K^+ and Na^+ through 1,2-dichloroethane were comparable. The amount of water incorporated from aqueous to organic layer by the sodium salt was much more than by the potassium salt, and the amounts were dependent on the stirring rates of the two layers. The sodium salt lowered the interfacial tension between the aqueous and organic layers, while the potassium salt did not change it. Emulsion-like aggregates of the sodium salt in the organic layer were observed by dynamic light scattering. The above experiments showed that K^+ was transported as the potassium salt of **1**, while Na^+ was incorporated into the organic layer and transported as an aggregate of the sodium salt containing water.

Ionophores are small lipophilic molecules that are dissolved in lipid bilayers and carry ions as hydrophobic complexes across the bilayer barrier. These ionophores have been extensively employed to create increases in membrane permeability to a particular ion in studies on artificial and biological membranes.[2)] The ionophores are classified into cyclic and linear molecules in terms of the structure. A typical example of the cyclic ionophores is valinomycin. Its cavity size is fitted for the diameter of potassium ion, so it forms a hydrophobic and stable complex by coordination of oxygens of the carbonyl groups with the cation.[3)] Linear ionophores are ω-hydroxy carboxylic acids with several polyether oxygens in the backbone. They are called carboxylic acid ionophores or polyether antibiotics.[4)] It has been found by X-ray crystallography[5)] as well as NMR spectroscopy[6)] that compounds such as monensin and nigericin produce pseudo-cyclic structures by head-to-tail hydrogen bonding between the carboxyl and hydroxyl groups at both the terminals and that most of the ether oxygens of the molecules are arranged to coordinate with cations. The ion transport selectivity through artificial and biological membranes is related to the cavity size of the stable pseudo-cyclic conformations.[3,7)] Characteristic of ion transport with the linear ionophores results from the carboxyl group in the molecule different from cyclic ionophores. Thus, the acidic proton is exchanged by a cation to form a salt of the linear ionophore. Since the acidic ionophore in the salt complex has a negative charge from the carboxylato group, an anion from outside does not enter into the complex. This is in contrast with the case of neutral, cyclic ionophores. This structural feature enables acyclic ionophores to transport ions against the concentration gradient using the difference of proton concentration; this is called active ion transport.[7b)]

We have already synthesized a series of ω-hydroxy carboxylic acids with several ether oxygens and aromatic rings as a synthetic analog to the naturally occurring linear ionophores. We examined the relationship between their structures and the ion transport ability and selectivity.[8)] In analogy to natural products, active ion transport was realized. Head-to-tail hydrogen bonding was found to play an important role in exhibiting an ion selectivity. Among these synthetic ionophores, 2-[[2-[2-[2-[2-[2-[2-[2-(2-hydroxyethoxy)phenoxy]ethoxy]phenoxy]ethoxy]phenoxy]ethoxy]phenoxy]methyl]benzoic acid (**1**) exhibited the highest selectivity of K^+/Na^+ through 1,2-dichloroethane liquid membrane corresponding to the large difference of solubility between the potassium and sodium salts of **1** (Chart 1).[8d] In addition, the potassium, rubidium, and cesium salts of **1** are found to adopt hydrophobic conformations with head-to-tail hydrogen bonding in the crystal from x-ray crystal structure analysis[1,9] and the solution conformations of these salts are substantially similar to those in the crystal.[10] Since the single crystals of **1** and the sodium salt have unfortunately not been obtained so far, no information on the molecular structures has yet been obtained. Nevertheless, the conformations of **1** and the sodium salt in solution are expected to be different from those of the potassium, rubidium, and cesium salts from the ^{1}H NMR spectra. Although natural ionophores adopt stable and rigid pseudocycle conformations as described above, our synthetic compound, **1**, retains the flexibility and changes the conformation upon complexation of a specific ion.

In this paper, we describe in detail transport behaviors of Na^+ and K^+ as well as other alkali metal ions with **1**. We discuss the cause of selectivity and the difference between transport mechanisms of Na^+ and K^+.

Results and Discussion

Table 1 shows active transport of alkali metal ions with **1** through 1,2-dichloroethane liquid membrane at 35 °C for 5 d. Although K^+/Na^+ selectivity was very high as previously reported,[8d] the amount of Li^+ transported was comparable to that of Na^+. Among K^+, Rb^+, and Cs^+, **1** transported K^+ more than the other ions. From these results, the selectivity sequence by **1** is found to be $K^+ \geq Rb^+ > Cs^+ > Na^+ \geq Li^+$. We have already reported the structure of potassium salt of **1** with a conformation of the seam of a tennis ball of the backbone in the crystal as well as the rubidium and cesium salts of **1**.[1,9] Single crystals of free acid, **1**, and the lithium and sodium salts have not been obtained so far, and the backbone of **1** may be too flexible to form single crystals. The selectivity sequence is consistent with the difference of the crystal structures of potassium, rubdium, cesium salts of **1**, as determined by X-ray diffraction[1,9] and also with the difference of the solution structures of **1** and its alkali metal salts, as analyzed by NMR spectroscopy.[10]

In a previous paper, we reported that selectivity of active ion transport for K^+ over Na^+ with **1** through 1,2-dichloroethane liquid membrane is high and corresponds to solubility of potassium and sodium salts of **1** in 1,2-dichloroethane.[8d] This correlation suggests that the step of extraction of the cations as salts to the organic membrane dominates the ion transport selectivity. Through mixtures of 1,2-dichloroethane and toluene with different ratios, selectivity of active transport of sodium and potassium ions with **1** was investigated. Results were compared with solubilities of **1**, its sodium, and potassium salts in the same mixed solvents. The result of the active ion transport with **1** through a mixture of 1,2-dichloroethane and toluene is shown in Table 2. The transport experiment at the region of 30—70% contents of toluene was not carried out because the density of such mixed solvents is nearly equal to that of the aqueous solutions used here. At the region of 10—20% content of toluene, the selectivity of K^+ over Na^+ is higher than that through 1,2-dichloroethane itself. However, the preferred ratio of K^+ to Na^+ was much lower with increase in the toluene content (80—90%). The solubilities of **1** and the sodium and potassium salts in the same mixed solvents as well as in each solvent are shown in Table 3. When the solubility was measured in

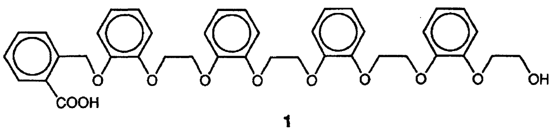

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Chart 1.

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

Ion transported/%					
Li^+	Na^+	K^+	Rb^+	Cs^+	Total
37	43	—	—	—	80
—	10	81	—	—	91
—	—	46	33	17	96

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

Toluene/1,2-Dichloroethane (v/v)	Ion transported/%		
	Na^+	K^+	Total
0/100	10	81	91
10/90	6	91	97
20/80	6	91	97
80/20	35	62	97
90/10	24	64	88

Table 3. Solubility of **1** and Its Alkali Metal Salts

Toluene/1,2-Dichloroethane (v/v)	Solubility/mg g^{-1}		
	1	Na^+salt	K^+salt
0/100	12	6	600
10/90	3	5	1000
20/80	2	3	900
80/20	1	3	4
90/10	2	1	2
100/0	3	0	2

solvents that exhibited high K^+-selectivity, the potassium salt was 100—200 times more soluble than **1** and the sodium salt. On the contrary, in the higher content of toluene, the potassium salts had poor solubility and there was not much difference between the solubilities of the acid and salts. These results show that selectivity of K^+ over Na^+ in the transport experiment roughly corresponds to the difference of solubility between the sodium and potassium salts in mixtures of 1,2-dichloroethane and toluene with different ratios. However, in the case of 0—20% contents of toluene the K^+-selectivity is not as much as the solubility ratio of the potassium to sodium salts. Moreover, **1** still exhibits some K^+-selectivity through liquid membrane with 80—90% content of toluene where the potassium and sodium salts have a solubility comparable to each other. Thus, the solubility of salts to organic liquid membrane (an equilibrium between solid and liquid) alone is not able to explain ion transport ability and selectivity. Other factors associated with partition equilibrium between aqueous and organic layers should be considered.

To investigate the effect of coexisting metal ions on the ion transport selectivity, competitively and separately transported rates of K^+ and Na^+ with **1** through 1,2-dichloroethane were determined. The results are shown in Figs. 1 and 2 respectively. In the competitive transport experiments, about 50% of K^+ preferentially transported for the initial 30 h, and then transport of Na^+ started. The selectivity for K^+ over Na^+ is extremely high for the initial 30 h, but then Na^+ transports gradually and selectivity for K^+ over Na^+ is lowered when the transport is completed (pH gradient is consumed). On the other hand, transported rates of K^+ and Na^+ are almost the same in the separate transport experiments. The organic liquid membrane in separate transport of Na^+ became turbid immediately after starting the experiment. This phenomenon not observed in the separate K^+-transport experiment, will be described in detail below.

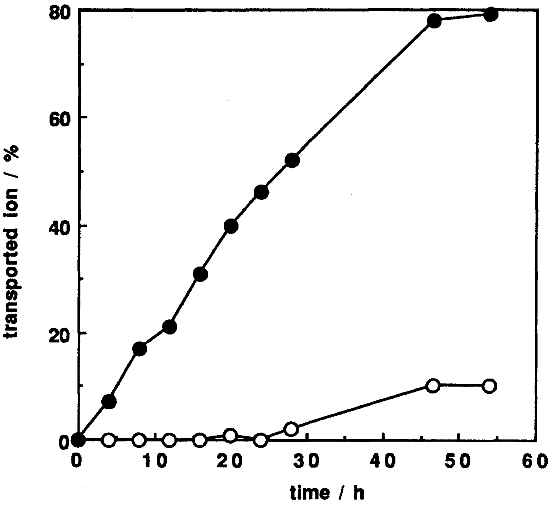

Fig. 1. Amount of Na^+ (○) and K^+ (●) transported competitively as a function of time with **1** through 1,2-dichloroethane liquid membrane.

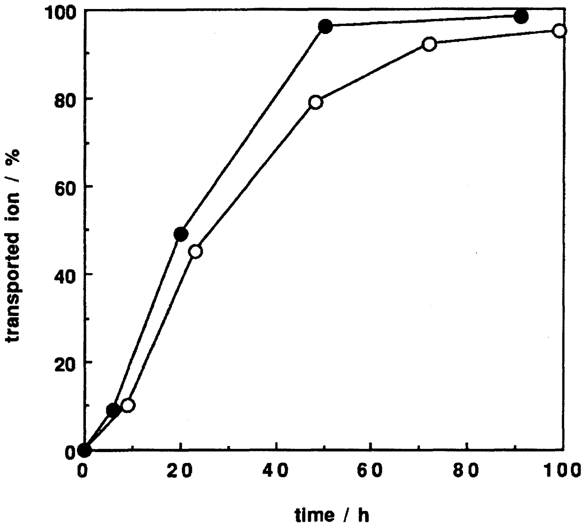

Fig. 2. Amount of Na^+ (○) and K^+ (●) transported separately as a function of time with **1** through 1,2-dichloroethane liquid membrane.

Although the evident selectivity appears in the competitive transport, there is not much difference between the apparent rates of separate transport of K^+ and Na^+. The ratio of transported rates of K^+ to Na^+ is therefore different from the selectivity ratio in the competitive transport. The large difference between the concentration of the potassium and sodium salts in organic liquid membrane is estimated from the data of extraction experiment of these salts from an aqueous to organic layer, as described above. Since only K^+ actually transported for the initial 30 h in the competitive transport, during that time the potassium salt should be preferentially extracted to the organic layer.

Separate transport of Na^+ resulted in turbid organic liquid membrane and transport of water to acidic layer with transport of Na^+ as described above. Amounts of water to acidic layer transported with transported time, determined by increases of volume of the acidic layer, are shown in Fig. 3. Transport of water to the acidic layer started in 24 h, and 16% of water in the basic layer was transported within 50 h. This result corresponds to the amount of Na^+ transported separately from K^+, as shown in Fig. 2. It was expected from the turbid organic layer that, in the case of Na^+ separate transport, the ion was transported as a dispersion of the sodium salts of **1** including a large amount of water in the organic layer. To ascertain it, the amount of water incorporated into organic layer was measured by Karl Fischer titration in the extraction of K^+ and Na^+ with **1** to 1,2-dichloroethane (Table 4). Much more water is incorporated into the organic layer with Na^+ than with K^+. The amount of water extracted into the organic layer increases with decrease in the concentration of NaOH. In the presence

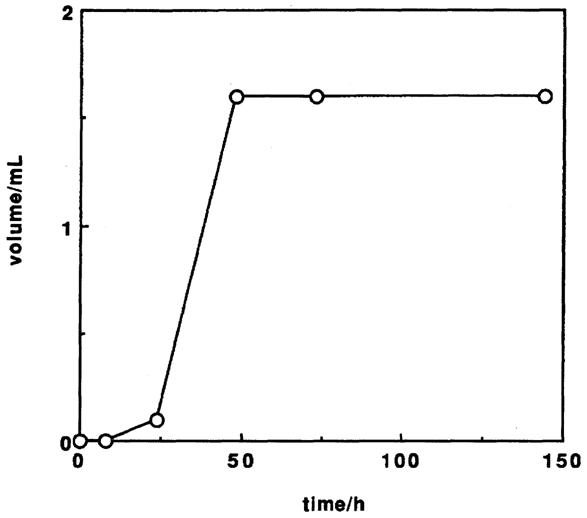

Fig. 3. Amount of water transported from basic to acidic layer in Na^+ transport with **1** through 1,2-dichloroethane liquid membrane.

Table 4. Water Content of 1,2-Dichloroethane Layer in Alkali Metal Ion Extraction with **1**

Aqueous layer	Water content/mg mL^{-1}
0.1 M NaOH	230
0.05 M NaOH	790
0.1 M KOH	20
0.05 M KOH	2
0.1 M KOH + 0.1 M NaCl	28

of both Na^+ and K^+, water is not much transferred into the organic layer. Table 5 shows the amount of water incorporated from 0.1 M NaOH (1 M=1 mol dm^{-3}) or KOH to 1,2-dichloroethane containing **1** with changes of stirring rate of the aqueous and organic layers. Stirring at 700 rpm induced incorporation of water in the presence of NaOH 80 times more than in the presence of KOH. In the presence of K^+, the incorporated amount of water was less, and was affected neither by metal ion concentration nor by disorder of the interface with stirring. These results are consistent with the phenomena of transport of water as well as of cations.

On the basis of the results described above, we hypothesized that while potassium salt of **1** itself was extracted and transported, sodium cation was transported by formation of emulsion-like aggregates of sodium salts of **1** with large amounts of water in the organic liquid membrane. Since an emulsion-like dispersion has a large surface area, such an emulsion is easier to form in the case of lower free energy (lower interfacial tension). Thus, the tension of interface between an aqueous and organic layers should be a measure of the ease of formation of emulsion. To demonstrate the hypothesis, we carried out the measurement of interfacial tension between a basic aqueous solution and 1,2-dichloroethane using **1** and linoleic acid as an emulsifier as shown in Table 6. There is no difference of the interfacial tension between the aqueous solution containing Na^+ and K^+ in the absence of an emulsifier. The presence of **1** lowered the interfacial tension between the organic and the aqueous layers including Na^+, whereas potassium salt of **1** does not change the tension. Linoleic acid with no ether oxygen lowered the tension, irrespective of the kind of cations. These results show that, whereas potassium salt of **1**, a hydrophobic complex, does not function as an emulsifier, the sodium salt which does not form such a complex in the organic layer functions as an emulsifier similar to the sodium and potassium salts of linoleic acid. Incorporation of large amounts of water with the sodium salt into the organic layer is based on the emulsifying property of the sodium salt.

Table 5. Effect of the Stirring Rate on Water Content of 1,2-Dichloroethane Layer in the Alakli Metal Ion Extraction with **1**

Stirring rate/rpm	Water content/mg mL^{-1}	
	0.1 M NaOH	0.1 M KOH
0	2.8	3.1
200	230	20
700	490	6.1

The size of the aggregates formed in 1,2-dichloroethane was determined by dynamic light scattering experiments or by optical microscope observations. The obtained diameter of aggregates is shown in Table 7. The sodium salt became a particle with a large diameter in the organic solution. This is probably a w/o type of emulsion, given the diameter. The size of the particles was dependent on the concentration of metal ions in an aqueous solution and the lower concentration forms the larger particle, consistent with decreases in the interfacial tension. Even in the case of the potassium salt, formation of some particles was detected by the

Table 6. Interfacial Tension between Aqueous and 1,2-Dichloroethane Layers

Compound	Interfacial tension/mN m^{-1}	
	0.1 M NaOH	0.1 M KOH
None	11.2	11.4
1	1.9	11.5
Linoleic acid	0.9	1.9

Table 7. Aggregates Size of Sodium and Potassium Salts of **1** in 1,2-Dichloroethane Determined by Light Scattering

Aqueous layer	Diameter/μm
0.04 M NaOH	30[a)]
0.1 M NaOH	5
3.5 M NaOH	1.9
0.1 M KOH	0.32
0.2 M KOH	0.13

a) Observed by a microscope.

Table 8. Differences of Physicochemical Properties between the Sodium and Potassium Salts of **1** in Transport through 1,2-Dichloroethane Liquid Membrane

Property	Sodium salt	Potassium salt
Appearance of liquid membrane	Turbid	Clear
Water in organic layer	Large amount dependent on the cation concentration	Small amount independent of the cation concentration
Water transport	Transport from basic to acidic layer	No transport
Interfacial tension	Lowered	Almost no change
Particles size	Large dependent on the cation concentration	Small

light scattering measurements, but the particle size was much smaller than that at the same concentration of the sodium salt.

The cause of high selectivity of **1** for K^+ over Na^+ in competitive ion transport will be discussed on the basis of the experimental results, to investigate the effect of factors on ion transport selectivity.

In the competitive transport of Na^+ and K^+ with **1**, high K^+-selectivity is attained by differences of behavior between sodium and potassium salts of **1** in terms of the incorporated amounts and periods. The difference should be due to the physicochemical properties of the sodium and potassium salts of **1**. From the properties summarized in Table 8, the ionophore **1** seems to change its transporting mode depending on the ions. The potassium salt itself is a hydrophobic complex, while the sodium salt is a surfactant molecule which forms emulsion-like aggregates in the organic layer. The mechanism for **1** to exhibit K^+-selectivity can be explained as follows. Potassium salts of **1** are incorporated more and faster, because the molecular complex of potassium salts of **1** is much more stable in organic liquid membrane than an emulsion formed by the sodium salts. Especially at the initial stage of the high ion concentration, no sodium salt of **1** is extracted and no transport occurs, but the lipophilic potassium salt is easily extracted into the organic layer, independent of the interface situation, resulting in exclusive K^+ transport. When the metal ion concentration of the basic aqueous solution is lowered by transport of considerable amounts of K^+, the interfacial tension decreases, resulting in the easier disorder of the interface. The increased ratio of Na^+ to K^+ in the basic solution results in an increase in the relative concentration of the sodium salts at the interface to make the formation of the emulsion-like aggregates easier.

Such a difference of transport behavior of Na^+ and K^+ is not observed by natural carboxylic acid ionophores with less structural flexibility such as monensin.[7b)] The acyclic ionophore, **1**, is highly flexible and able to change its conformation, corresponding to transport conditions such as ions, their concentrations, and the polarity of liquid membrane. Therefore, a hydrophobic complex of the potassium salt is formed in which the cavity size of the ionophore matches the diameter of K^+, whereas emulsion-like aggregates are formed because of the amphiphilic property in the case of the sodium salt.

Experimental

Instrument. IR spectra were run with a JASCO IR-G spectrophotometer. ^{1}H NMR spectra were recorded with a JEOL JNM-PMX 60 instrument using tetramethylsilane as internal standard. Elemental analyses were performed on a Yanaco Model MT-3. Flame spectrochemical analyses were performed with a Hitachi 170-30 Atomic Absorption Spectrophotometer. Karl Fischer titration was performed on a Metrohm E452. Dynamic light scattering was measured on a Helvern Type 7027 with a He–Ne laser (λ=6330 Å) as a light source.

Materials. Unless stated otherwise reagent grade reactants and solvents were obtained from commercial suppliers and used without further purification. Synthesis of **1** was carried out according to the method previously reported.[8d,8e)] The final three steps are described below.

2-[2-[2-(2-Hydroxyphenoxy)ethoxy]phenoxy]ethanol bis(*p*-toluenesulfonate). To a mixture of 2-[2-[2-(2-hydroxyphenoxy)ethoxy]phenoxy]ethanol (1.0 g, 2.2 mmol) and triethylamine (0.35 g, 3.5 mmol) in dry THF (20 mL) with stirring was added portionwise *p*-toluenesulfonyl chloride (0.60 g, 3.1 mmol). The mixture was stirred at room temperature for 48 h. The resulting precipitate of triethylamine hydrochloride was filtered off, and the filtrate was evaporated under reduced pressure. The residue was purified by silica-gel column chromatography ($CHCl_3$) to obtain the product as a white solid (1.0 g, 76%). ^{1}H NMR ($CDCl_3$)

δ=2.37 and 2.42 (6H, s, CH_3), 4.0—4.6 (8H, m, CH_2), 6.8—8.0 (16H, m, aromatic). Found: C, 60.16; H, 5.00%. Calcd for $C_{30}H_{30}O_9S_2$: C, 60.19; H, 5.05%.

2-[2-[2-[2-[2-[2-[2-(2-hydroxyphenoxy)ethoxy]phenoxy]ethoxy]phenoxy]ethoxy]phenoxy]ethanol. A mixture of 2-[2-[2-(2-hydroxyphenoxy)ethoxy]phenoxy]ethanol (1.5 g, 5.2 mmol) and 60% NaH (0.23 g, 5.8 mmol) in dry DMF (30 mL) was stirred at 80—90 °C to form the corresponding phenoxide. To the solution was added dropwise a solution of 2-[2-[2-(2-hydroxyphenoxy)ethoxy]phenoxy]ethanol bis(*p*-toluenesulfonate) (3.1 g, 5.2 mmol) in dry DMF (10 mL) at room temperature. The mixture was stirred at 80—90 °C for 18 h. DMF was removed in vacuo, KOH (2.1 g), H_2O (35 mL), and ethanol (35 mL) were added to the residue, and the solution was refluxed for 1 h. The alkaline solution was neutralized with 2 M HCl and extracted with chloroform. The organic layer dried over sodium sulfate was evaporated and applied to a silica-gel column ($CHCl_3$ to 3% MeOH in $CHCl_3$) to purify the product (1.65 g, 56%). ^{1}H NMR ($CDCl_3$) δ=3.7—4.1 (4H, m, –OCH_2CH_2OH), 4.25 (4H, s, –OCH_2CH_2–), 4.28 (4H, s, –OCH_2CH_2–), 4.35 (4H, s, –OCH_2CH_2–), 6.8 (4H, s, aromatic), 6.9 (12H, s, aromatic). Found: C, 67.82; H, 6.18%. Calcd for $C_{32}H_{34}O_9$: C, 68.32; H, 6.09%.

2-[[2-[2-[2-[2-[2-[2-[2-(2-hydroxyethoxy)phenoxy]ethoxy]phenoxy]ethoxy]phenoxy]ethoxy]phenoxy]methyl]benzoic Acid (1). A mixture of 2-[2-[2-[2-[2-[2-[2-(2-hydroxyphenoxy)ethoxy]phenoxy]ethoxy]phenoxy]ethoxy]phenoxy]ethanol (0.84 g, 1.5 mmol) and 60% NaH (60 mg, 1.5 mmol) in dry DMF (20 mL) was stirred at 80—90 °C for 2 h to form the corresponding phenoxide. To the solution was added dropwise a solution of methyl 2-(bromomethyl)benzoate (0.35 g, 1.5 mmol) in dry DMF (10 mL). The mixture was stirred at 80—90 °C for 18 h. DMF was removed in vacuo and the residue dissolved in 2 M NaOH (50 mL) and ethanol (20 mL) was refluxed for 2 h. The alkaline solution was neutralized with 2 M HCl and extracted with chloroform. The organic layer dried over sodium sulfate was evaporated and applied to a silica-gel column ($CHCl_3$ to 3% MeOH in $CHCl_3$) to isolate **1** as a white solid (0.63 g, 60%). ^{1}H NMR ($CDCl_3$) δ=3.67—4.2 (4H, m, –OCH_2CH_2OH), 4.23—4.40 (12H, m, –OCH_2CH_2O–), 5.40 (2H, s, benzyl), 6.9 (16H, s, aromatic), 7.2—8.1 (4H, m, aromatic). IR (KBr) 1690 cm^{-1} (C=O). Found: C, 69.14; H, 5.78%. Calcd for $C_{40}H_{40}O_{11}$: C, 68.95; H, 5.79%.

Measurement. Alkali metal salts of **1** were prepared by neutralization of **1** in chloroform with 0.1 M metal hydroxide solution, followed by evaporation of the organic layer and freeze-drying.

Ion transport experiments were carried out in U-type or H-type cell at 35±1 °C for 5 d by the same manner as previously reported unless stated otherwise.[8b,8e]

The solubility of alkali metal salts of **1** was determined from a volume of the solvent completely dissolving 0.10 g of the salts. In the case of extremely poor solubility of a salt, a saturated solution of a salt was prepared by addition of 4 mL of solvent to the salt and after 2 h, 1 mL of the saturated solution taken was lyophilized to obtain the weight of the salts.

The content of water in an organic liquid membrane was determined by the Karl Fischer method. In a test tube, 10 mL of appropriately diluted metal hydroxide solution and 10 mL of 1,2-dichloroethane with or without 5.0×10^{-5} mol of **1** were taken, and both the layers were kept at 35 °C for 3 h with stirring at 200 rpm as in the ion transport experiment. A portion of the organic layer taken was titrated to determine the water content. The values of water content in alkali metal ion extraction with **1** were obtained by subtraction of that without **1** as a blank.

Interfacial tension was measured by a capillary rising method. Capillaries with diameters of 0.15 and 0.54 mm were soaked into a test tube containing 0.1 M MOH solution (10 mL) and 1,2-dichloroethane solution of **1** (10 mL) and it stood at 35 °C for 10—24 h until the height of the meniscus became constant. The value of interfacial tension (γ) was calculated from $\gamma=d\cdot\Delta\rho\cdot g(\Delta h+d/3)/2$, where d is a radius of a capillary, $\Delta\rho$ is difference of density between the aqueous and organic solutions, g is gravity constant, and Δh is the height of meniscus.[11)]

To determine a particle size of alkali metal salts of **1** in an organic layer, a sample prepared by the same way as for Karl Fischer titration was used. An aliquot of the organic layer taken was observed by an optical microscope (Olympus PM-6), or dynamic light scattering of 100-times-diluted solution of the organic layer was measured at an angle of 90°.

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