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Synthetic Polyether Dicarboxylic Acids Exhibiting Lithium Ion-Selective Transport[1]

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Polyether dicarboxylic acid carriers with several alternate units of oxytrimethylene and oxy-*o*-phenylene groups have been synthesized. They exhibit lithium ion selectivity in the competitive cation transport among lithium, sodium, and potassium ions through liquid membranes. On the basis of the cation extraction and the spectroscopic behavior, it is proposed that these carriers form a coiled structure into which the lithium ion becomes selectively incorporated to exhibit lithium ion-selective transport.

Since Pedersen has reported for the macrocyclic polyethers, the so-called crown ethers,[2] a large number of macrocyclic polyethers exhibiting cation-selectivity have been synthesized.[3] On the other hand, it has attracted considerable attention that naturally-occurring antibiotic ionophores can transport cations through biomembranes.[4] One of the properties of both such artificial and natural ionophores is that they incorporate cations into the cavity by means of the electrostatic interactions of electron-donating hetero atoms. It should be noted that there are a number of noncyclic polyether carboxylic acids among such natural ionophores which exhibit a high selectivity toward alkali and alkaline earth metal ions. We have now studied these structures and functions and have synthesized a series of noncyclic polyether compounds.[5]

In general, the cation complexes of synthetic and noncyclic polyethers have low stability constants and have less ability to extract cation from aqueous to organic solutions compared with cyclic ones.[6] Therefore, these compounds have attracted less attention than have macrocyclic polyethers. However, as has been reported by the works of Vögtle, Simon, and other groups, various functionalized noncyclic polyethers have been synthesized.[7,8] Noncyclic polyethers with carboxyl end groups have been reported as carriers for the cation transport through liquid membranes.[9–12] The introduction of carboxyl groups results in the rapid formation of salts with cations, and it is particularly useful for cation transport and also for cation extraction into an organic solvent from an aqueous solution. It has been found that cation selectivity with the polyether carboxylic acids depends on the residual parts of polyether structures.

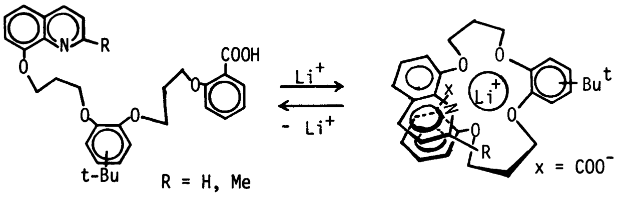


Fig. 1. Uptake of Li^+ ion by the conformational change of **5**.

As previously reported, the noncyclic polyether **5** is an ionophore which can selectively transport lithium ions through liquid membranes against the concentration gradient.[13] In this case, it has been inferred that lithium ions form the salt with the carboxyl group and become incorporated into the pseudocavity thus formed, as is shown in Fig. 1. Such a conformation has been suggested on the basis of the CPK model building and supported spectroscopically.[14]

By the way, the lithium ion has the smallest naked ionic radius among the alkali metal ions, while it has the largest hydrated ionic radius and the largest hydration energy. There is no naturally-occurring ionophore which exhibits an excellent lithium ion-selectivity, but several synthetic lithium ion-selective ionophores have been reported in noncyclic,[15,16] cyclic,[17–21] and bicyclic[22] compounds. Wide applications can be expected for lithium ion-selective ionophores, e.g., in the selective separation of lithium ions by transport through liquid membranes and by solvent extraction, and also in monitoring lithium-ion activity in blood during therapy for manic-depressive psychosis.[23]

If the carrier **5** can wrap around the lithium ion by means of conformational change, as is shown in Fig. 1, even polyethers with fairly long chain structures can be expected to transport lithium ions selectively. In this paper, we wish to report on the synthesis of polyethers with long polyether chains and on their transport of alkali metal ions through liquid membranes.

Experimental

General. The IR and the UV spectra were recorded with JASCO A-3 Infrared and Hitachi 330 spectrophotometers respectively. The ^1H NMR spectrum was recorded with a Varian EM-360 spectrometer. The chemical shifts for the $CDCl_3$ solution are reported from internal tetramethylsilane (TMS).

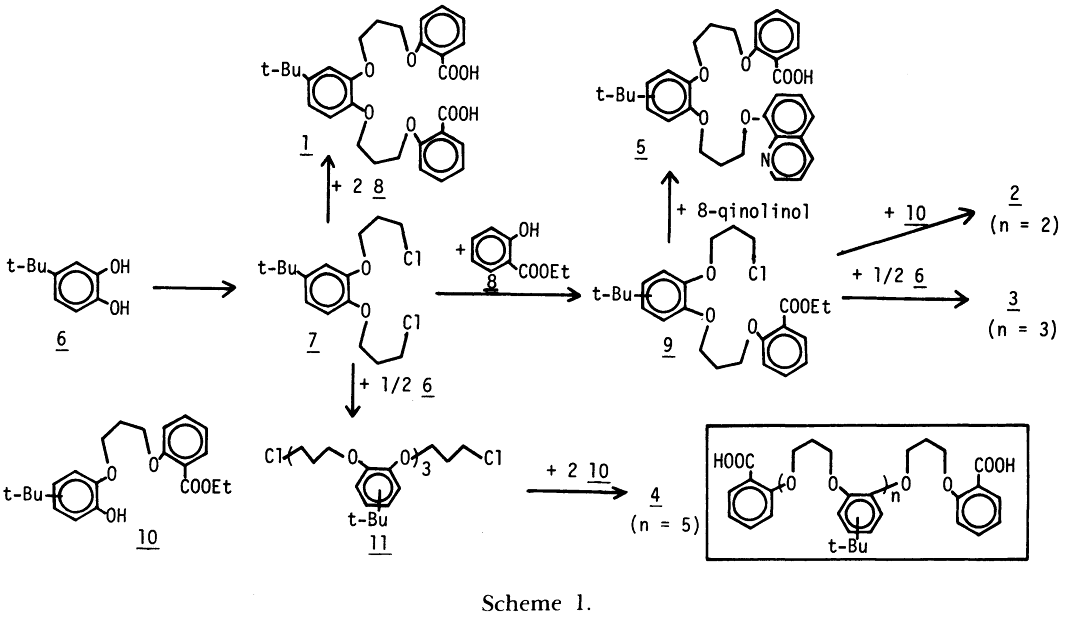
Synthesis of Noncyclic Polyethers. The ethyl salicylate, 4-*t*-butylcatechol, and potassium *t*-butoxide used were extra-pure-grade reagents of Wako Pure Chemical Industries, Ltd.

Extra pure-grade *N*,*N*-dimethylformamide (DMF) was used as the solvent after having been dried with molecular sieves. The 1,2-bis(3-chloropropoxy)-4-*t*-butylbenzene (**7**), 1-[3-(*o*-ethoxycarbonylphenoxy)propoxy]-2-(3-chloropropoxy)-4(or 5)-*t*-butylbenzene (**9**), and 2-[3-(*o*-ethoxycarbonylphenoxy)-propoxy]-4(or 5)-*t*-butylphenol (**10**) were prepared as previously reported.[13] The 1,2-bis[3-(*o*-carboxyphenoxy)-propoxy]-4-*t*-butylbenzene (**1**)[22] and 1-[3-(*o*-carboxyphenoxy)propoxy]-2-[3-(8-quinolyloxy)propoxy]-4(or 5)-*t*-butylbenzene (**5**)[13] which were used in the transport experiment for comparison were also prepared as previously reported. Compounds **2**—**4**, with long polyether chains, were prepared by the reaction process shown in Scheme 1.

1,3-Bis[1-[2-(*o*-carboxyphenoxy)propoxy]-4(or 5)-*t*-butylphenoxy]propane (2). A mixture of 1.9 g (5 mmol) of 2-[3-(*o*-ethoxycarbonylphenoxy)propoxy]-4(or 5)-*t*-butylphenol (**10**) and 0.56 g (5 mmol) of potassium *t*-butoxide was stirred in 30 ml of DMF until it became homogeneous. To the solution we then added 2.3 g (5 mmol) of 1-[3-(*o*-ethoxycarbonylphenoxy)propoxy]-2-(3-chloropropoxy)-4(or 5)-*t*-butylbenzene (**9**) and a small amount of KI, after which the mixture was stirred at 80 °C for 24 h. Then, after cooling, 150 ml of water was added to the solution after and extraction with benzene (100 ml) was carried out. The benzene layer was washed with water three times and dried with $MgSO_4$. After the removal of the benzene, the residue was submitted to column chromatography on silica gel, with ethyl acetate–hexane as the eluent, to give 1.4 g (36%) of the ethyl ester of **2** as a viscous, clear oil. A solution of the diethyl ester of **2** (1.0 g, 1.3 mmol) in ethanol (70 ml) and potassium hydroxide (0.5 g) was mixed and heated at reflux overnight. After the solvent has evaporated, water (100 ml) was added. The aqueous phase was acidified with concentrated hydrochloric acid and extracted with chloroform (3×50 ml). The combined organic phase was washed with water, dried with $MgSO_4$, and evaporated. The residue was submitted to column chromatography on silica gel, with chloroform–ethanol as the eluent, to give 0.8 g (85%) of **2** as a pale yellow, glassy solid: IR (KBr) 3300 and 2600 (COOH), 1735 and 1700 (C=O), 1605 and 1580 (aromatic C=C), 1055 cm^{-1} (C–O); ^{1}H NMR ($CDCl_3$) δ=1.29 (18H, s, $C(CH_3)_3$), 2.0—2.6 (6H, m, $OCH_2C\underline{H}_2CH_2O$), 4.0—4.7 (12H, m, $OC\underline{H}_2CH_2C\underline{H}_2O$), 6.8—7.8 (12H, m, aromatic), 8.17—8.4 (2H, m, aromatic); UV ($CHCl_3$), λ_{max}=283 nm, ε=10000. Found: C, 70.25; H, 6.98%. Calcd for $C_{43}H_{52}O_{10}$ (MW 728.88): C, 70.86; H, 7.19%.

1,2-Bis[3-[2-[3-(*o*-carboxyphenoxy)propoxy]-4(or 5)-*t*-butylphenoxy]propoxy]-4(or 5)-*t*-butylbenzene (3). A mixture of 3.7 g (10 mmol) of 2-[3-(*o*-ethoxycarbonylphenoxy)propoxy]-4(or 5)-*t*-butylphenol (**10**) and 1.1 g (10 mmol) of potassium *t*-butoxide was stirred in 30 ml of DMF until it became homogeneous. To the solution we then added 1.6 g (5 mmol) of 1,2-bis(3-chloropropoxy)-4-*t*-butylbenzene (**7**) and a small smount of KI, after which the mixture was stirred at 80 °C for 48 h. After the same post-treatment as in the case of **2**, 1.5 g (32%) of the ethyl ester of **3** was obtained as a viscous, pale yellow oil. In a manner similar to the hydrolysis described above, **3** (1.2 g, 85%) was obtained as a pale yellow, glassy solid: IR (KBr) 3300 and 2500 (COOH), 1740 and 1700 (C=O), 1605 and 1580 (aromatic C=C), 1050 cm^{-1} (C–O); ^{1}H NMR ($CDCl_3$) δ=1.30 (27H, s, $C(CH_3)_3$), 2.0—2.6 (8H, m, $OCH_2C\underline{H}_2CH_2O$), 4.0—4.7 (16H, m, $OC\underline{H}_2CH_2C\underline{H}_2O$), 6.8—7.8 (15H, m, aromatic), 8.2—8.45 (2H, m, aromatic); UV ($CHCl_3$) λ_{max}=282 nm, ε=12000. Found: C, 71.23; H, 7.84%. Calcd for $C_{56}H_{70}O_{12}$ (MW 935.16): C, 71.93; H, 7.55%.

1,2-Bis[3-[2-[3-[2-[3-(*o*-carboxyphenoxy)propoxy]-4(or 5)-*t*-butylphenoxy]propoxy]-4(or 5)-*t*-butylphenoxy]propoxy]-4(or 5)-*t*-butylbenzene (4). A mixture of 1.7 g (10 mmol) of *t*-butylcatechol (**6**) and 2.3 g (20 mmol) of potassium *t*-butoxide was stirred in 50 ml of DMF under a nitrogen atmosphere until it became homogeneous. To the solution we then added 10 g (31 mmol) of 1,2-bis(3-chloropropoxy)-4-*t*-butylbenzene (**7**) and a small amount of KI, after which the mixture was stirred at 80 °C for 24 h. After the post-treatment described above, 3.1 g (42%) of 1,2-bis[3-[2-(3-chloropropoxy)-4(or 5)-*t*-butylphenoxy]propoxy]-4(or 5)-*t*-butylbenzene (**11**) were obtained. Then a mixture of 2.8 g



Scheme 1.

(7.5 mmol) of 2-[3-(*o*-ethoxycarbonylphenoxy)propoxy]-4-(or 5)-*t*-butylphenol (**10**) and potassium *t*-butoxide (0.85 g, 7.5 mmol) was stirred in 50 ml of DMF until it became homogeneous. To the solution we then added 1.8 g (2.5 mmol) of **11** and a small amount of KI, after which the mixture was stirred at 80 °C for 48 h. After the same post-treatment, 1.2 g (34%) of the ethyl ester of **4** were obtained. The hydrolysis of the ethyl ester as described above gave **4** (0.9 g, 78%) as a pale yellow, glassy solid: IR (KBr) 3300 and 2550 (COOH), 1740 and 1700 (C=O), 1605 and 1580 (aromatic C=C), 1050 cm^{-1} (C–O); ^{1}H NMR (CDCl$_3$) δ=1.30 (45H, s, C(CH$_3$)$_3$), 2.0—2.6 (12H, m, $OCH_2\underline{CH_2}CH_2O$), 4.05—4.7 (24H, m, $O\underline{CH_2}CH_2\underline{CH_2}O$), 6.9—7.8 (18H, m, aromatic), 8.25—8.5 (2H, m, aromatic); UV (CHCl$_3$) λ_{max}=282 nm, ε=17000. Found: C, 72.69; H, 8.26%. Calcd for $C_{82}H_{106}O_{16}$ (MW 1347.73): C, 73.08; H, 7.93%.

General Procedure of Cation Transport. Reagents: Chloroform (extra-pure grade) was used without further purification. Each aqueous solution which was used in either the source or receiving phase was prepared by the dilution of one normal alkali hydroxide and/or one normal acid.

Procedure: A U-type or H-type glass tube as previously reported was used for measuring the transport of alkali metal ions.[13] In the case of the use of chloroform as the membrane solvent, a U-type glass tube was used. First, 30 ml of chloroform containing the carrier (0.03—0.15 mmol) was poured into the tube. Then, 15 ml of a solution of 0.1 M[†] LiOH+0.1 M NaOH+0.1 M KOH+0.1 M H$_2$SO$_4$ and 15 ml of a solution of 0.05 M H$_2$SO$_4$ were simultaneously poured into the source and receiving phases respectively. The tube was then placed in a water bath whose temperature was kept at 25±0.2 °C. Each phase was agitated at 200 min^{-1} mechanically with a pair of glass stirrers. On the other hand, in the case of the use of toluene, an H-type glass tube was used. In this case, first the aqueous solution containing metal hydroxides described above and an acidic solution (0.05 M H$_2$SO$_4$) were poured into the source and receiving phases respectively. Subsequently, a 30-ml portion of chloroform containing the carrier was poured into the tube.

The transport of cations was initiated by the addition of the solutions and by then stirring each phase. At each time point, 50 μl of the solution was withdrawn from each aqueous phase and the concentration of each cation was adjusted by using a measuring flask and determined by means of a Shimadzu AA-646 atomic absorption spectrometer.

The transport of cations in the blank systems was negligible. The detailed conditions are shown in the table.

Extraction of Cations. Polyether (0.05 mmol) was added to 5 ml of a 0.1 M LiOH aqueous solution in a 30-ml Erlenmeyer flask. The mixture was stirred overnight at room temperature. Then, 10 ml of chloroform was added to it. After the mixture had been vigorously stirred for 6 h, the amounts of the lithium salt of the polyethers in the aqueous solution were measured by means of the UV spectrum.

Results and Discussion

Cation Transport through Liquid Membranes.

Cation transport through liquid membranes was carried out by using the **2**—**4** carriers, and also for the sake of comparison, **1** and **5** which were previously reported. Figure 2 shows the plots of the amounts of cation transported versus the running time in the case of carrier **4**, which has five repeating units of the 2-propoxy-4(or 5)-*t*-butylphenoxy group. Apparently, among the three alkali metal ions, the lithium ion can be transported with the most appreciable selectivity in the competitive transport. The cation transport by this carrier ceased within 1 day under these conditions because of the pH-decrease in the source phase. The results for cation transport by **1**—**5** are summarized in Table 1. Carrier **1**, which has the shortest chain structure, with two carboxyphenyl terminal groups, transported hardly any alkali metal ions although **1** can selectively transport either Ca^{2+} or Mg^{2+}, depending on the transport conditions[24] It should be noted that the longer the polyether chain, the better the ability of transport for monovalent cations, especially the lithium ion, by carriers which have two

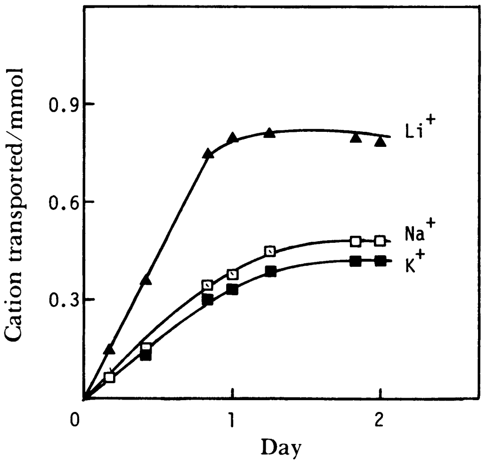


Fig. 2. Plots of amounts of cation transported by carrier **4** vs. the running time.

Table 1. Cation Transport through Liquid Membranes

Carrier	Transport rate/μmol h^{-1} Li	Na	K	Selectivity Li/Na	Li/K
1	0.1	<0.1	0	—	—
2	11.3	3.4	2.6	3.3	4.3
3	35.6	18.7	16.9	1.9	2.1
4	36.6	15.0	13.1	2.4	2.8
5	18.8	6.3	3.4	3.0	5.5

Reproducibility: ±10% or better.

Initial transport conditions (25 °C):

Source phase	Chloroform membrane	Receiving phase
0.1 M LiOH	Carrier	0.05 M H$_2$SO$_4$
0.1 M NaOH	1.5×10^{-4} mol	15 ml
0.1 M KOH	CHCl$_3$ 30 ml	
0.1 M H$_2$SO$_4$		
15 ml		

[†] 1 M=1 mol dm^{-3}.

carboxyphenyl terminal groups. Carrier **5**, which can selectively transport the lithium ion, as has previously been reported,[13] exhibits the selectivity ratios of Li/Na=3.0 and Li/K=5.5 under these transport conditions. Carrier **2**, with a relatively short chain, has a small cation-transport rate compared with carrier **5**, which has one carboxyl group, whereas carriers **3** and **4**, which have longer polyether chains, show a more than 2-fold enhancement in the transport of monovalent cations over **5**. However, the lithium-ion selectivity has a tendency to be reduced as the polyether chain lengthens. The lithium-ion transport rate by **3** and **4** is nearly two times larger than that by **5**. It is presumed that the two carboxyl groups on **3** and **4** act effectively in cation transport. That is, it is probable that one carrier has the ability to carry two cations at the same time in the case of carriers **3** and **4**. The relatively long polyether chain in these carriers, which can form a looser conformation for the uptake of cations, may be responsible for the increase in the ability of sodium- and potassium-ions transport.

In Table 2, the influence of the carrier concentration and the liquid-membrane solvent on the cation transport are summarized. The greater the concentration of **4** in chloroform, the larger both the transport rate and the amounts of cations transported after 2 days. When toluene was used as the liquid-membrane solvent in the H-type glass tube, the transport rates of cations by **4** are relatively small compared with those in the same concentration of **4** in chloroform (see Runs 2 and 3 in Table 2). However, it should be noted that appreciable cation transport by **4** through toluene (Run 3) can occur, whereas **5** in toluene transports scarcely no cations. This means that carriers with long polyether chains, such as **4**, can selectively transport lithium ion even in the more nonpolar solvent, toluene.

Thus, it is noteworthy that compounds **3** and **4**, with relatively long polyether chains can exhibit the selective transport of the lithium ion, which has the smallest naked ion radius among alkali metal ions. We have proposed the hypothesis that carrier **5** forms a pseudocyclic conformation to pass through an organic solvent, and that then the ion (i.e., the lithium ion), which can be well incorporated into the pseudocavity[13], can be selectively transported. Can compounds **3** and **4**, with long polyether chains, form such a conformation? The length between the two carboxyl groups of **1** is too short to take the conformation incorporating the lithium ion. In this case, the electrostatic repulsion between the two terminal carboxylato anions occurs inevitable when **1** forms a complex with two lithium ions. In the case of **2**, with a polyether chain of an intermediate length, it is also difficult for the carrier to wrap two lithium ions at the same time. Nevertheless, it is possible for one cation to be incorporated by **2**, though the salt of **2** with the lithium ion might not have enough solubility in organic solvents. Therefore, the transport ability of **2** is considered to decrease compared with that of **5**. On the contrary, carriers **3** and **4** are expected to have chains long enough to be able to wrap two lithium ions inside the pseudocavity formed. Recently, Nakahama et al. have also reported that a synthetic carboxylic ionophore with eight ether oxygens and five aromatic rings can complex with the potassium ion, and that the resulting complex has a coiled conformation, with coordination of the ether oxygen atoms to the potassium ion. This was presumed by means of the NMR spectrum.[25]

Table 2. Effects of Carrier Concentration and Membrane Solvent on the Cation Transport

Run	Concn of carrier	(mM)	Membrane solvent	Transport rate/μmol h^{-1} Li	Na	K
1	**4**	1.0	$CHCl_3$	5.5	1.7	1.3
2	**4**	2.5	$CHCl_3$	13.1	4.4	3.0
3	**4**	2.5	Toluene	9.7	4.4	3.4
4	**4**	5.0	$CHCl_3$	36.6	15	13.1
5	**5**	5.0	Toluene	0	0	0

Initial transport conditions: see Table 1.
Reproducibility: ±10% or better.

From these results, it can be inferred that the lithium complex of carriers **3** and **4** becomes more lipophilic than that of **1** and **2**. The lithium-ion complexes of **3** and **4** can be expected to dissolve more easily in an organic solvent than in water because of their lipophilicity. Therefore, their ability of cation extraction was investigated.

Cation Extraction. All carriers except **4** (0.05 mmol) are completely soluble in 5 ml of an aqueous solution containing 0.1 M LiOH after it has been stirred overnight at room temperature. Carrier **4**, with sufficiently hydrophobic groups, is insoluble in such a solution, while carrier **3** becomes foamy on the surface of an aqueous solution; that is, **3** seems to have surface activity. Then, chloroform (10 ml) was added to this alkaline solution or mixture containing the carrier, and the mixture was stirred. After that, the amounts of lithium salt of carriers remaining in the aqueous solution were determined by means of the UV spectrum. It was confirmed that one polyether formed

Table 3. Partition of Li^+ Salt of Polyethers between Aqueous and Chloroform Phases

Polyether	**1**	**2**	**3**	**4**	**5**
In aqueous phases/%	100	51	8	≈3	≈1

Initial conditions
Aqueous phase: 5 ml of 0.1 M LiOH solution.
$CHCl_3$ phase: 10 ml of $CHCl_3$ containing 0.5×10^{-4} mol of carrier.

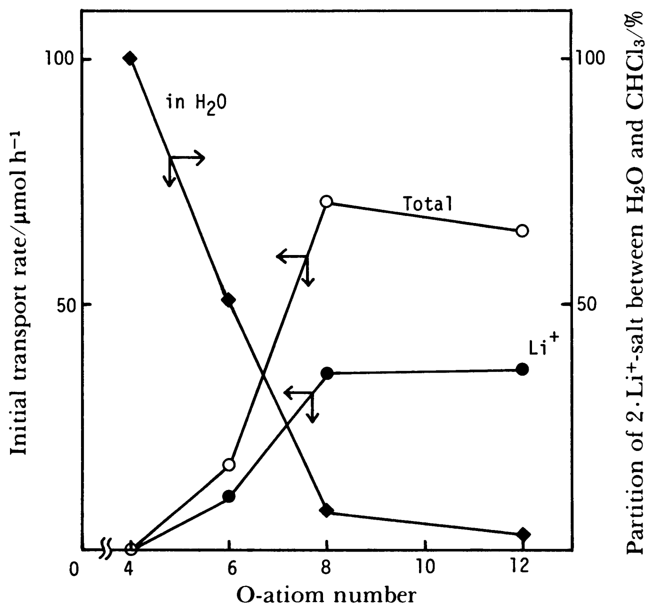


Fig. 3. Plots of initial transport rate and partition ratio of lithium salt of carriers vs. the number of ether oxygen atom of each carrier; O-atom number=4: **1**, 6: **2**, 8: **3**, 12: **4**.

salts with two lithium ions under these conditions. These results, shown in Table 3, are in good agreement with favorably those of the cation transport. Two equimolar lithium salts of **1** are not at all removed from the aqueous to the chloroform phase. The lithium salt of **2** has small solubility in chloroform. On the contrary, carriers **3** and **4** can extract two equimolar lithium ions almost quantitatively from aqueous to chloroform phase. Carrier **5**, with one carboxyl group, can also extract the lithium ion completely to the chloroform phase. These results reflect the cation-transport rate and the amounts of cation transported, as is shown in Table 1.

Figure 3 depicts the plots of the initial lithium ion-transport rate and the partition ratio of lithium salt of carriers between chloroform and aqueous solutions versus the number of ether oxygen atoms of each carrier. Apparently carriers **3** and **4** are superior to carriers **1** and **2** in both the distribution to chloroform and in the ability of lithium ion transport through liquid membranes.

Conformations of Cation Salts of Carriers in Chloroform. As has been indicated for the cation transport and cation extraction, **3** and **4** exhibited an appreciable selectivity toward the lithium ion, although **3** and **4** have rather long polyether chains, containing 8 and 12 ether oxygens respectively. Furthermore, carriers **3** and **4** can transport about twice as many cations as the polyether monocarboxylic acid **5** and can capture two equivalent lithium ions at the same time by means of the two carboxyl terminal groups.

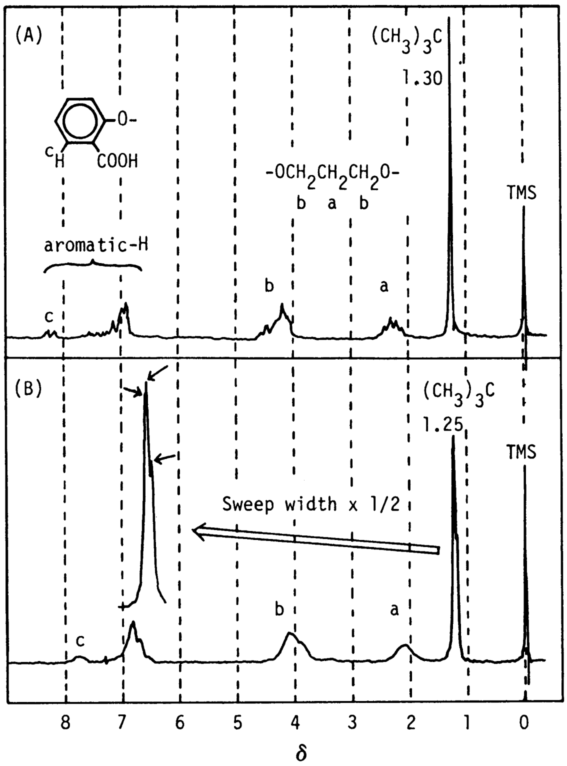


Fig. 4. Proton NMR spectrum of **3** and Li⁺ salt of **3** in CDCl₃; (A): **3**, (B): Li⁺ salt of **3**.

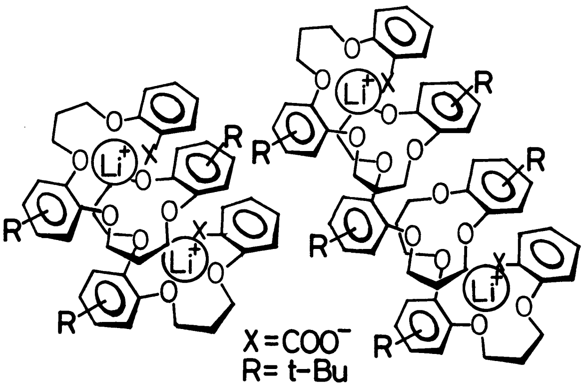


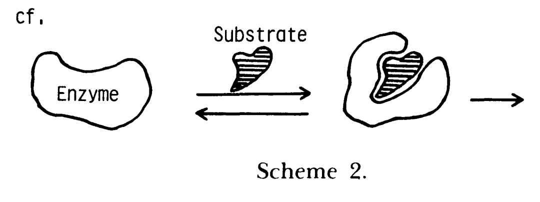
Fig. 5. Posturated strucutre of Li⁺ salts of polyethers **3** and **4** in chloroform liquid membrane.

Figure 4 shows the signal for the methyl protons on three *t*-butyl groups in **3** and its lithium salt. One sharp singlet for the methyl protons in free **3** becomes appreciably broad, when free **3** becomes its lithium salt. It can be inferred that the splitting of the proton signal for *t*-butyl groups is attributable to the proton-nonequivalency of each *t*-butyl group when **3** forms a complex with the lithium ion in chloroform. Such a change in the NMR spectrum was also observed in the case of carrier **4**. Additionally, a study of the NMR spectra confirms that the lithium salts of **3** and **4** do not contain water.

From these results, we would like to propose that **3** and **4** take the conformation shown in Fig. 5, where two lithium ions become incorporated into the pseudocavity formed and can selectively transport lithium ions through liquid membranes. When the carriers take such a conformation, the protons for the *t*-butyl groups situated adjacent to the carboxyl terminal groups and those in the middle position seem to be at least nonequivalent. Therefore, the lithium salts can dissolve in a hydrophobic solvent and transport lithium ions selectively. An inspection of the CPK models suggests the formation of a small pseudocavity in which the lithium ion best fits. However, in carrier **1**, with the shortest polyether chain, electrostatic repulsion between lithium salts of two terminal carboxylato groups results in the deformation of the pseudocavity. Therefore, water molecules around the lithium ion presumably cannot be removed, and the salt of **1** does not dissolve in organic liquid membranes. Because the lithium salt of carrier **2**, with a medium chain length, is soluble in the organic phase, at least to some extent, it is considered that **2** can transport cations, although the ability of ion-transport is smaller even than that of monocarboxylic acid **5**.

Conclusion

Thus, we could show that compounds with rather long polyether chains can recognize the lithium ion as a guest, accompanied by a drastic conformational change. Cyclic polyether (crown ethers), cryptands, and spherands,[26] which have a preorganized cavity, can selectively incorporate ions which fit well inside. On the contrary, the noncyclic compounds with long polyether chains used in this study can wrap around cations by changing their conformation, as is shown in Scheme 2. Such a conformational change accompanies a large energetic loss and causes a decrease in the complex stability and in the rate of cation uptake compared with those of preorganized compounds. Such a dynamic conformational change reminds us of the induced-fit theory in enzymatic reactions proposed by Koshland,[27] although an enzyme has a much larger molecular weight and can recognize a substrate much more precisely compared with the noncyclic polyethers reported here.



Scheme 2.

It should be noted that the selectivity for cations can change when the chain structures on the carriers change appropriately. In this study, the chain structures containing oxytrimethylene groups can result in the lithium-ion selectivity, whereas those containing oxyethylene groups can exhibit potassium- ion selectivity, as has been reported by Nakahama et al.[25] Thus, the importance of the chain structure in producing ion-selectivity should also be pointed out.

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