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# ION TRANSPORT ABILITY AND SELECTIVITY RELATING TO THE STRUCTURE OF SYNTHETIC IONOPHORES[1)]

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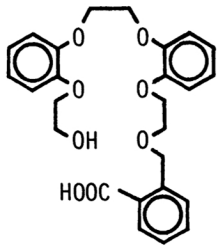
o-, m-, p-Substituted benzoic acids (1, 2, 3) with polyether chain bearing hydroxy group at the end and the methylether of 1 (4) were prepared. With active transport of $Na^+$ and $K^+$ by 1~4, 1 and 4 exhibited $K^+$-selectivity over $Na^+$, while 2 and 3 had no transport ability. From the results of ion transport and $^1$H-NMR study, relationship between the structure and transport ability was discussed.

Recently, much research concerning the membrane transport of metal cations mediated by natural or synthetic ionophores has been carried out[2)]. Naturally occurring carboxyl polyether ionophores such as nigericin and monensin are known to mediate the coupled counter-transport of metal cations and proton, that is active transport[3)]. It is known that remarkable conformational changes of natural acyclic ionophores are induced during ion transport[4)] and are related to the cation selectivity[5)]. On the other hand, only a few synthetic acyclic carboxyl polyethers which have the ability of active transport of cations are reported[6)]. However, the relationship between conformation and cation selectivity of synthetic ionophores has not been clarified.

We report here the synthetic acyclic ionophore, 1~4, to transport alkali metal cations, and present that the conformation of their metal complex in the liquid membrane influences the ion transport ability and selectivity.

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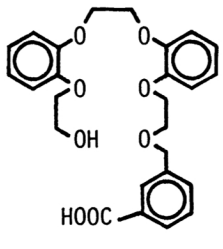


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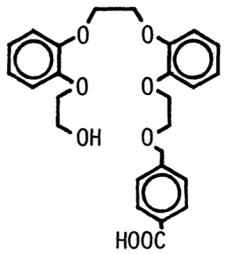


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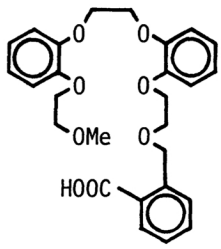


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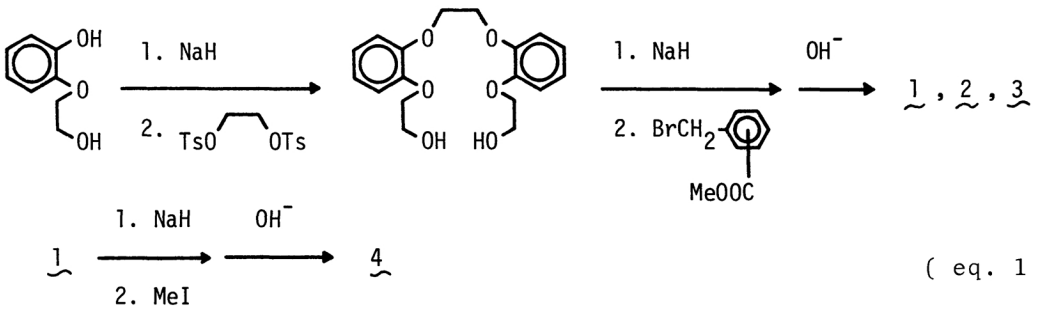



( eq. 1 )

Ionophores 1~4 were prepared according to the reactions (eq. 1) and their structures were identified by NMR and MS[7]. Using 1~4, active ion transport was carried out in a similar manner described previously[8] except for employment of dichloroethane in place of 1-hexanol as a liquid membrane. The results of $Na^+$-$K^+$ competing transport are shown in Table 1. Active and $K^+$-selective ion transport was observed with 1 and 4, while no ion was transported by 2 and 3, m- and p-isomers of 1 respectively. These results indicate that the relative position of carboxyl group and hetero atoms as ligands is very important factor for the ion transport ability and selectivity and that synthetic ionophore 1 adopts pseudocyclic conformation as was reported in case of the nigericin-$K^+$ complex[9]. Assuming the ring closure caused by the head-to-tail hydrogen bonding (by CPK models), the inner cabity size of 1 was estimated to be 2.5 ± 0.5 Å in a diameter which suited for potassium ion (2.66 Å). On the other hand, it is apparent by CPK models that ionophore 2 and 3 could not form pseudocyclic conformation because the metal cation held by carboxyl group and polyether chain are far apart each other. Consequently, potassium salts of 2 and 3 which could not make hydrophobic complexes were insoluble in dichloroethane and showed no transport ability, while pseudocyclized 1-$K^+$ complex

Table 1. Active transport of $Na^+$ and $K^+$ with ionophores 1 - 4

| Ionophore | Transported cation (%) | | Total (%) |
|---|---|---|---|
| | $Na^+$ | $K^+$ | |
| 1 | 13 | 60 | 73 |
| 2 | 0 | 0 | 0 |
| 3 | 0 | 0 | 0 |
| 4 | 28 | 41 | 69 |
| control | 0 | 0 | 0 |

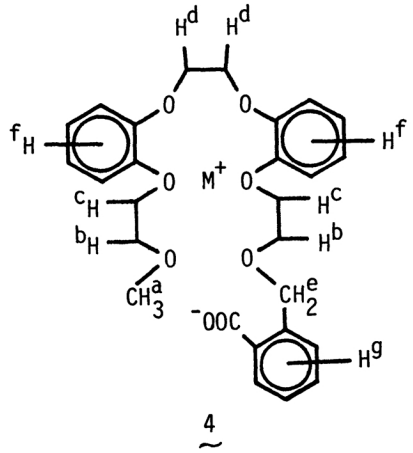
Active transport was carried out at 35 ± 1°C for 5 days. A 10 ml donor aqueous phase I (0.1N NaOH, 0.1N KCl) is separated from the 10 ml acceptor phase II (0.1N HCl, 0.1N NaCl, 0.1N KCl) by dichroloethane liquid membrane (20 ml) containing the ionophore ($10^{-4}$ mol). Each phase was stirred at 200 Hz. The amount of the transported cation was determined by flame analysis.

having hydrophobic exterior was soluble in the liquid membrane and exhibited transport ability. Ionophore 4 prepared by methylation of terminal group of 1 exhibits active transport ability though $K^+$-selectivity was not so high as that of 1. On the basis of the results with 1 and 4, it is considered that the active and selective transport ability was chiefly due to coordination of polyether chain, while lack of terminal hydrogen bonding caused some lowering of selectivity.

The NMR measurement could be performed in $CDCl_3$ with alkali metal salts of ionophore 4, but not with those of 1, 2, and 3 because of poor solubility of the latter ionophores. As shown in Figure 1 and Table 2, all the proton signals of 4 shifted to the upfield[10] and the d-proton signal of the salts splitted into two peaks by complexation with $Na^+$ and $K^+$ ions. These spectral changes reveal that all ethereal oxygen atoms in the ionophore 4 have more or less the interaction with metal ion and that both of $Na^+$ and $K^+$ seem to become adequately wrapped into the ionophore 4. The splitting of the signal results from the nonequivalency of the d-proton, which is caused by the pseudocyclic complex formation. Moreover, the peak width of the d-proton signal of 4-$K^+$ is larger than that of 4-$Na^+$. Therefore, the ionophore seems to make more stable complex with $K^+$ than $Na^+$ leading $K^+$-selectivity over $Na^+$ in the ion transport experiment.

Table 2. Chemical shift of $^1H$ NMR of 4

| M | a | e | f | g |
|---|---|---|---|---|
| H | 3.38 | 5.00 | 6.89<br>6.92 | 7.1-8.0 |
| Na | 3.18 | 4.72 | 6.86 | 7.0-7.6 |
| K | 3.16 | 4.80 | 6.84<br>6.88 | 7.0-7.7 |



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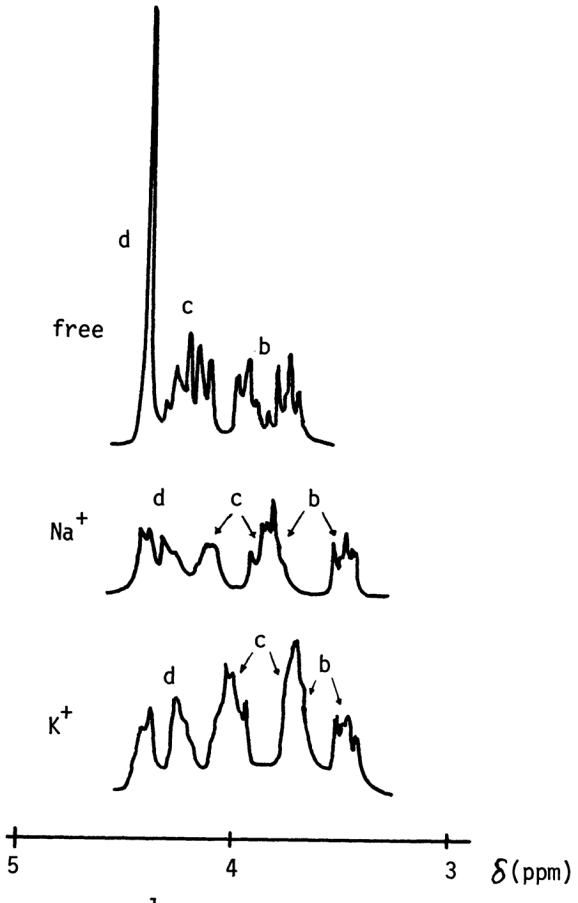


Figure 1. $^1H$ NMR spectra of 4

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7) 1: NMR($d^6$-DMSO)$\delta$=7.4-7.8(4H, m, aromatic toluic acid), 6.9(8H, s, aromatic phenylene), 4.85(2H, s, benzyl), 3.5-4.4(12H, m, ethylene); MS, m/e=468.
2: NMR($CDCl_3$)$\delta$=7.4-8.1(4H, m, aromatic toluic acid), 7.0(8H, s, aromatic phenylene), 4.6(2H, s, benzyl), 3.6-4.4(12H, m, ethylene); MS, m/e=468.
3: NMR($d^6$-DMSO)$\delta$=7.3-8.0(4H, m, aromatic toluic acid), 6.9(8H, s, aromatic phenylene), 4.6(2H, s, benzyl), 3.5-4.4(12H, m, ethylene); MS, m/e=468.
4: NMR($CDCl_3$)$\delta$=7.3-8.1(4H, m, aromatic toluic acid), 6.9(8H, s, aromatic phenylene), 5.0(2H, s, benzyl), 3.6-4.4(12H, m, ethylene), 3.4(3H, s, $OCH_3$); MS, m/e=482.

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