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NEW SYNTHETIC IONOPHORES EXHIBITING SELECTIVITY FOR ALKALINE EARTH METAL IONS[1)]

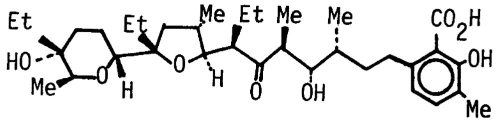
Kazuhiro TAGUCHI,* Kazuhisa HIRATANI,* Hideki SUGIHARA,
and Kokoro IIO
Industrial Products Research Institute,
1-1-4, Yatabe-machi Higashi, Tsukuba-gun, Ibaraki 305

New noncyclic polyethers, which contain 3-carboxy-2-hydroxyphenyl group as one terminal group were prepared. These polyethers exhibit the ability to transport alkaline earth metal ions through chloroform liquid membrane, but not to transport alkali metal ions. Highly Ba^{++}-selective ionophores were synthesized in this series.

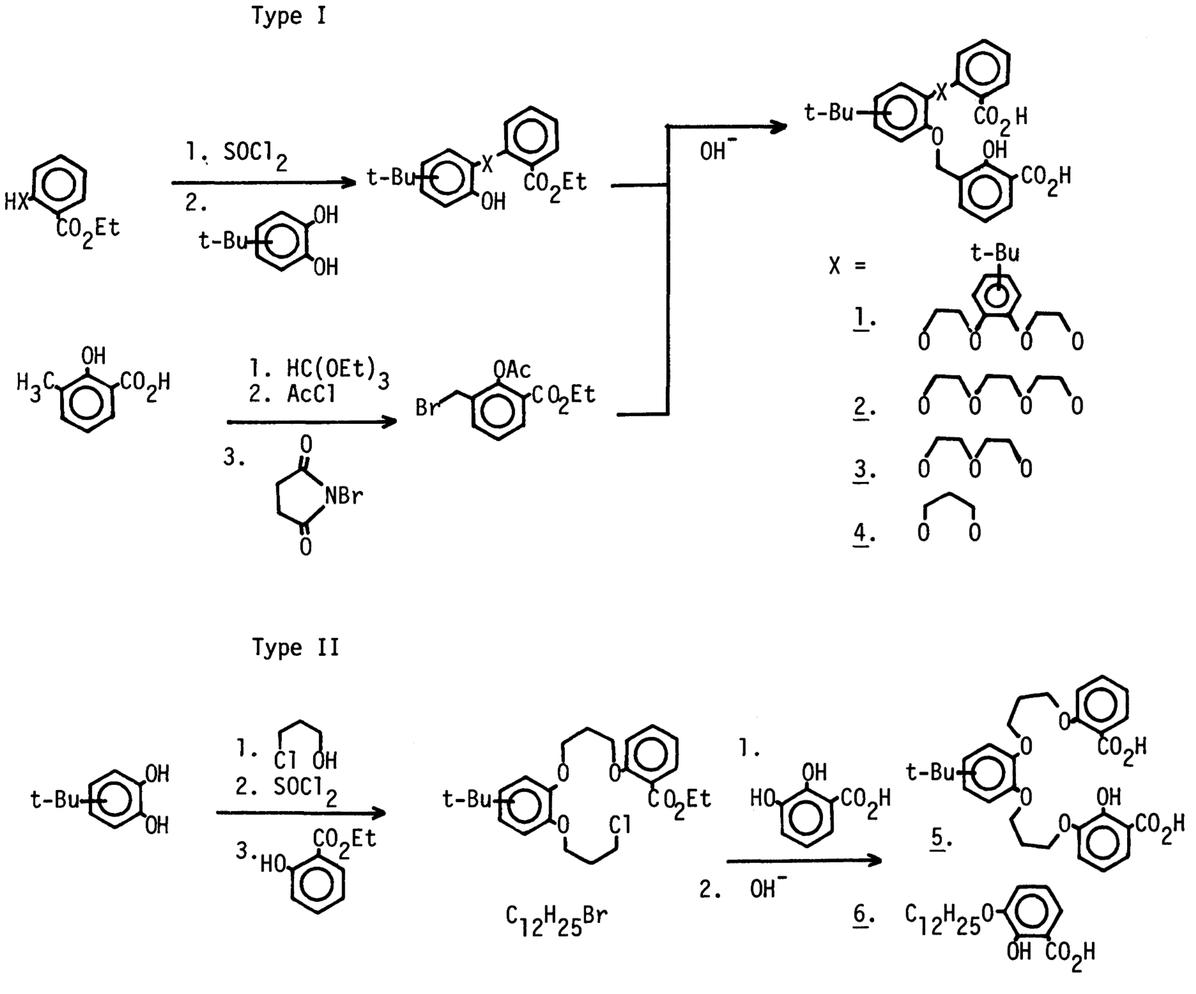
The structure and properties of noncyclic natural ionophores, e.g., nigericin, monensin, and lasalocid, have been studied in detail, and also a number of their total synthesis were succeeded.[2,3)] It is, however, not easy to obtain them in quantity and not advantageous to investigate the properties as ion-transport carriers owing to the complexity of chemical structures. So far many synthetic noncyclic ionophores containing the same or similar moiety as that of natural ones were prepared to elucidate the relationship between the structures and ion-transport ability. Consequently, it was found that their transport ability and selectivity for cations were greatly dependent on their chain structures and terminal groups.[2,4)]

In this paper we wish to report the synthesis and the ion transport ability of several new type polyether ionophores containing 3-carboxy-2-hydroxyphenyl group as one end group. Several natural ionophores, e.g., highly Ba^{++}-selective ionophore, lasalocid, contain both carboxy and hydroxy groups, which are adjacent each other on the terminal benzene ring. It is assumed that these two groups play an important role to exhibit selective transport ability for cations. So, it could be expected that new type polyether compounds having these two groups exhibit unique ion-selective transport ability.

Polyether compounds, type I (1, 2, 3, and 4) and type II (5 and 6), were prepared by the procedures as depicted in Scheme 1, and purified by column chromatography(silica gel-chloroform), and identified with IR and NMR spectroscopic methods.[6)] The competitive transport experiment of alkaline earth metal ions (Mg^{++}, Ca^{++}, and Ba^{++}) or alkali metal ions (Li^{+}, Na^{+}, and K^{+}) by these polyether carriers through chloroform liquid membrane was carried out using previously-reported U-type glass tube at 25 ± 0.2 °C.[4)] The initial transport conditions are shown in Table 1 and the amounts of cations transported were determined by atomic absorption analysis. In Table 1 are summarized the amounts of cations transported after 2 days by each carrier. For comparison, the result of the transport by lasalocid under the same conditions is also shown.



lasalocid



Scheme 1.

In Table 1, it is noteworthy that the new type polyether compounds can transport only alkaline earth metal ions, but not alkali metal ions, whereas lasalocid and most of the other natural ionophores transport both of them. The ionophores, 1 and 2, can transport Ba^{++} and 5 can transport Ca^{++} selectivity, while the ionophores, 3 and 4, transport Ca^{++} and Ba^{++} with low degree of selectivity, respectively. Nonpolyether compound 6 has no transport ability for both alkaline earth metal ions and alkali metal ions under the same conditions. Thus, the selectivity for alkaline earth metal ions apparently depends on their structures. That is, the longer the chain length, the better selectivity for Ba^{++} which has the largest ion radius among these cations used. The amount of alkaline earth metal ions transported by 1 and 2 was not extremely large, but their Ba^{++}-selectivity is almost comparable to that of lasalocid.

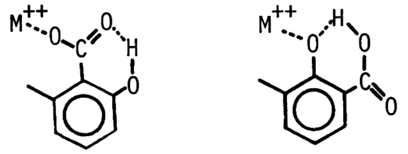
Table 1. Cation Transported through Liquid Membranes

Polyether	Cation transported after 2 d x 10^6 mol					
	Mg	Ca	Ba	Li	Na	K
1	0	60	240	0	0	0
2	0	30	180	0	0	0
3	0	120	195	0	0	0
4	0	150	135	0	0	0
5	15	120	30	0	0	0
6	0	0	0	0	0	0
Lasalocid	0	15	320	75	110	840

Initial transport conditions (25°C):

	Source phase	Chloroform membrane	Receiving phase
Alkaline earth metal	0.1 M $MgCl_2$ 0.1 M $CaCl_2$ 0.1 M $BaCl_2$ Trisbuffer pH 9.10 15 ml	Polyether 1.5×10^{-4} mol $CHCl_3$ 30 ml	0.1 M H_3PO_4 15 ml
Alkali metal	0.1 M LiOH 0.1 M NaOH 0.1 M KOH 0.1 M H_2SO_4 15 ml	Polyether 1.5×10^{-4} mol $CHCl_3$ 30 ml	0.05 M H_2SO_4 15 ml

The inspection of CPK model of 1 and 2 suggests that these ionphores having triethylene glycol chain unit can form pseudocyclic conformation to wrap around Ba^{++} most adequately in its cavity. On the other hand, 3 and 4 with short oxyalkylene chain, which is insufficient to form pseudocyclic cavity for the size of Ba^{++}, exhibit poor selectivity for Ba^{++}. Polyether 5 having oxytrimethylene chain unit and forming smaller cavity than 1 and 2 can predominantly transport smaller cations.[7)] It has been elucidated by X-ray diffraction study that the terminal carboxy group of lasalocid is one of the ligands for cations incorporated into its cavity, whereas the hydroxy group doesn't play directly a role as a ligand and only forms hydrogen bonding with the neighboring carboxy group (Fig. 1a).[2)] On the contrary, on the basis of CPK model building, new type ionophores, which we have synthesized, are presumed that oxygen atom of the hydroxy group can take part in the coordination to metal



a. lasalocid type b. synthetic polyether type

Fig. 1. Proposed terminal structure of ionophore.

ion incorporated into the pseudo-cavity of the polyethers (Fig. 1 b). Their ion selectivity seems to be remarkably influenced by the substituted position of hydroxy and carboxy groups on the terminal aromatic ring.

Further investigation concerning to new polyether compounds containig lasalocid-type terminal group is now in progress.

References

1) Part IX on "Synthesis and Properties of Noncyclic Polyether Compounds."

2) Max Dobler, "Ionophoeres and Their Structures," John Wiley & Sons, New York (1981), Chap. 7, pp.77-120 and references cited therein.

3) J. ApSimon, "The Total Synthesis of Natural Products," John Wiley & Sons (1981), Vol.4, pp.263-351.

4) K. Hiratani, Chem. Lett., 1982, 1021; Bull. Chem. Soc. Jpn., 55, 1963 (1982); K. Hiratani, K. Taguchi, H. Sugihara, and K. Iio, ibid., 57, 1976 (1984).

5) H. Kuboniwa, K. Yamaguchi, A. Hirao, S. Nakahama, and N. Yamazaki, Chem. Lett., 1982, 1937.

6) NMR (δ , $CDCl_3$) 1: 1.34 (18H,bs,$C\text{-}C\underline{H}_3$), 4.32-4.75 (10H,m,$O\text{-}C\underline{H}_2$), 6.42-7.74 (12H,m,aromatic), 8.10-8.30 (1H,m,aromatic);

2: 1.22 (9H,s,$C\text{-}C\underline{H}_3$), 3.59-4.38 (14H,m,$O\text{-}C\underline{H}_2$), 6.58-7.35 (9H,m,aromatic), 7.95-8.12 (1H,m,aromatic);

3; 1.27 (9H,s,$C\text{-}C\underline{H}_3$), 3.78-4.43 (10H,m,$O\text{-}C\underline{H}_3$), 6.80-7.72 (9H,m,aromatic), 8.09-8.82 (1H,m,aromatic);

4: 1.30 (9H,s,$C\text{-}C\underline{H}_3$), 2.17-2.50 (2H,m,$CH_2\text{-}C\underline{H}_2\text{-}CH_2$), 4.00-4.53 (6H,m, $O\text{-}C\underline{H}_2$), 6.85-7.75 (9H,m,aromatic), 8.14-8.35 (1H,m,aromatic);

5: 1.26 (9H,s,$C\text{-}C\underline{H}_3$), 2.02-2.52 (4H,m,$CH_2\text{-}C\underline{H}_2\text{-}CH_2$), 3.94-4.58 (8H,m,$O\text{-}C\underline{H}_2$), 6.77-8.08 (10H,m,aromatic);

6: 0.96 (3H,m,$CH_2\text{-}C\underline{H}_3$), 1.36 (12H,bs,$\text{-}C\underline{H}_2\text{-}$), 4.00 (2H,t,$O\text{-}C\underline{H}_2$), 6.74 -7.66 (3H,m,aromatic).

7) As previously-reported, 1,2-bis 3-(o-carboxyphenyl)propyloxy -4-t-butylbenzene (7) can transport either Ca^{++} or Mg^{++} with high selectivity which depends on the transport conditions. Polyether 7 transports Ca^{++} selectively under the same conditions as described in this paper; K. Hiratani, K. Taguchi, H. Sugihara, and K. Iio, Chem. Lett., 1983, 1657.

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