A Coiled Synthetic Carboxylic Ionophore capable of Encapsulating a Potassium Ion[1]

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A synthetic carboxylic ionophore with eight ether oxygens and five aromatic rings mediated selective K^+ ion transport through a liquid membrane; the coiled carboxylate-encapsulated potassium ion is highly lipophilic.

Naturally occurring carboxylate ionophores are known to mediate active ion transport through lipophilic biological membranes by formation of hydrophobic complexes with metal cations. The ionophores adopt a cyclic conformation by head-to-tail hydrogen bonding between terminal carboxy and hydroxy groups forming pseudo cavities which selectively bind metal ions.[2] Recently we found that the high potassium selectivity of ionophore (**1**) originated from the stability of the cyclic conformers of its potassium salt[1] in a similar manner to natural ionophores.

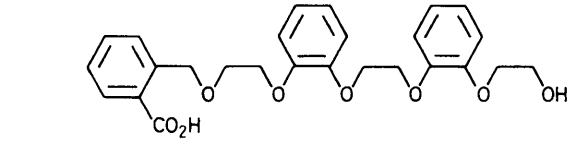
In this communication, we describe a new synthetic ionophore (**2**) which shows higher selectivity for K^+ than any other synthetic ionophore reported previously[1,3—5] with K^+ encapsulated in a coil of (**2**).

Ionophore (**2**) was prepared by a modification of the Williamson reaction starting from 2-(2-hydroxyethoxy)phenol (**3**)[6] according to Scheme 1.† Sodium and potassium salts were prepared by neutralization of (**2**) with NaOH and KOH respectively. Solubility of K^+-(**2**) in dichloroethane at 28 °C was 6.0×10^{-1} mol dm^{-3}, whereas the solubilities of Na^+-(**2**) and (**2**) were 1.0×10^{-2} and 2.1×10^{-2} mol dm^{-3} respectively. The high solubility of K^+-(**2**) suggests the formation of a hydrophobic complex.

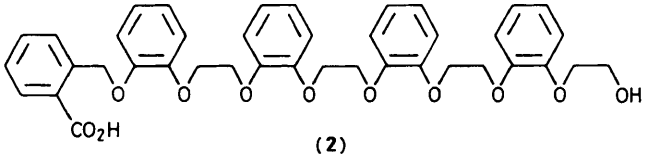
Table 1. Active ion transport through a dichloroethane liquid membrane.[a]

Ionophore	Ion transported, %		
	Na^+	K^+	Total
(**1**)	13	60	73
(**2**)	10	81	91
Control	0	0	0

[a] The conditions were same as those reported previously (ref. 1).



(**1**)

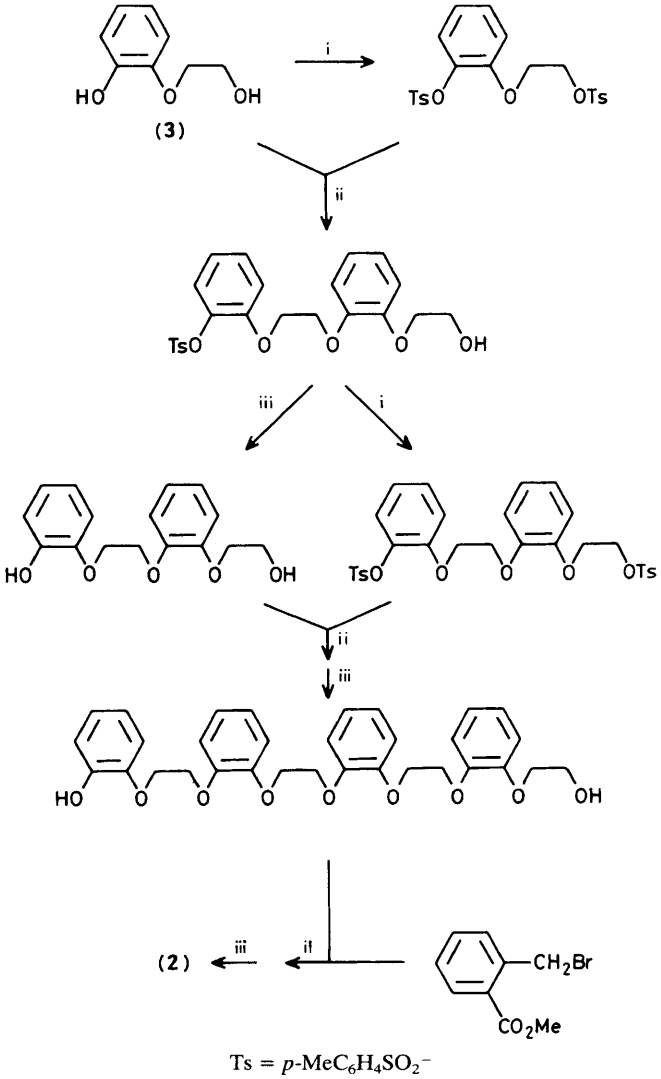


(**2**)

† The compound (**2**) was fully characterized by elemental analysis and i.r. and ^{1}H n.m.r. spectroscopy.

Active transport of sodium and potassium ions by (**2**) occurred through a dichloroethane liquid membrane; the results are shown in Table 1. The ionophore (**2**) exhibits the highest selectivity for K^+ over Na^+ of all the synthetic ionophores reported. The high selectivity for K^+ over Na^+ can be accounted for by the differences in solubility in dichloroethane.

400 MHz ^{1}H N.m.r. spectra of (**2**) and the alkali metal salts in $CDCl_3$ are shown in Figure 1. The spectra of (**2**) and Na^+-(**2**) are similar, but are quite different from those of K^+-(**2**). For both (**2**) and Na^+-(**2**), the moderately sharp



Ts = *p*-$MeC_6H_4SO_2^-$

Scheme 1. *Reagents and conditions:* i, *p*-$MeC_6H_4SO_2Cl$, NEt_3; ii, NaH, dimethylformamide, 80 °C; iii, alkaline hydrolysis and acidification.

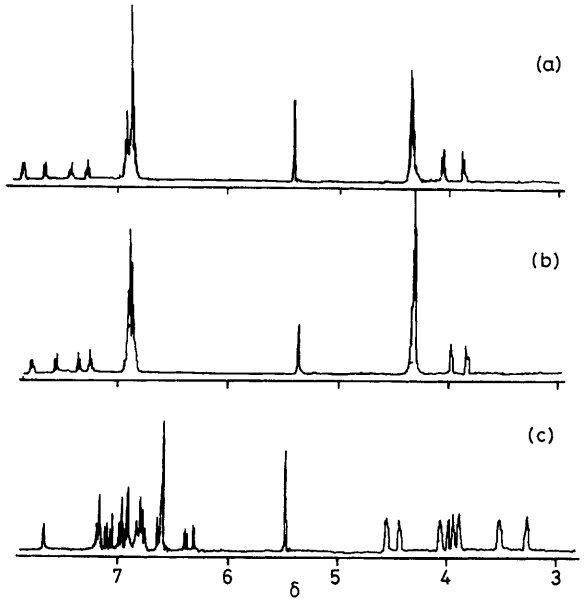


Figure 1. ^{1}H N.m.r. (400 MHz) spectra in $CDCl_3$: (a) (**2**), (b) Na^+-(**2**), (c) K^+-(**2**).

singlet resonances at *ca.* δ 4.3 can be assigned to oxyethylene protons by the chemical shift and intensity.‡ The non-terminal oxyethylene protons are equivalent on the n.m.r. time scale because of rapid interconversion between the conformers. The poorly-resolved, non-terminal aromatic resonance at *ca.* δ 6.9 also suggests conformational flexibility of the molecule at ambient temperature.§ Eight resolved signals with identical intensities were observed at δ 3.26, 3.51, 3.88, 3.93, 3.96, 4.04, 4.42, and 4.53 for K^+-(**2**). This separation of the aliphatic resonances results from the different environments of the methylene protons when fixed in a three-dimensional structure in K^+-(**2**). Additionally, the multiplicity of the aromatic resonance is probably caused by a mutual ring current effect of the aromatic rings held at definite positions in the complex. From these results, it is inferred that the K^+-(**2**) complex has a definite coiled conformation with co-ordination of the ether oxygen atoms to the potassium ion.

A CPK (Corey–Pauling–Koltun) model of (**2**) in a *gauche* conformation gave a coiled structure with a cavity (2.9 Å diameter) which did not require head-to-tail hydrogen bonding to form the pseudo cyclic structure found in natural ionophores and (**1**).[1,2] The size of the cavity of the coil corresponds well with the diameter of K^+ (2.66 Å) but is larger than Na^+ (1.96 Å), as in the case of (**1**). The longer polyether chain of (**2**) over (**1**) makes K^+-(**2**) more lipophilic than the pseudo cyclic polyether chain structure of K^+-(**1**). The high solubility of the complex in the dichloroethane liquid membrane is probably due to the stability of the coiled structure which in turn causes the high K^+-selectivity.

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‡ The A_2B_2 pattern at *ca.* δ 3.9—4.1 and the sharp singlet signals at δ 5.3—5.5 were assigned to the terminal oxyethylene protons and the methylene protons of the oxybenzyl group, respectively.

§ Resonances of terminal aromatic protons for (**2**) and Na^+-(**2**) appeared in the range δ 7.2—7.9.

References

1 For part 3 of this series see H. Kuboniwa, K. Yamaguchi, A. Hirao, S. Nakahama, and N. Yamazaki, *Chem. Lett.*, 1982, 1937.
2 A. Agtarap, J. W. Chamberlin, and M. Pinkerton, *J. Am. Chem. Soc.*, 1969, **89**, 5737.
3 N. Yamazaki, A. Hirao, and S. Nakahama, *J. Macromol. Sci., Chem.*, 1979, **A13**, 321; N. Yamazaki, S. Nakahama, A. Hirao, and S. Negi, *Tetrahedron Lett.*, 1978, 2429.
4 W. Wierenga, B. R. Evans, and J. A. Wolerson, *J. Am. Chem. Soc.*, 1979, **101**, 1334; K. Hiratani, *Chem. Lett.*, 1981, 21; K. Hiratani, *Bull. Chem. Soc. Jpn.*, 1982, **55**, 1963; K. Hiratani, *Chem. Lett.*, 1982, 1021.
5 Recently co-operative carriers composed of alkanoic acid and crown ether are reported to exhibit excellent selectivity for K^+ over Na^+: S. Inokuma, K. Yabusa, and T. Kuwamura, *Chem. Lett.*, 1984, 607.
6 K. Ziegler, A. Lüttringhaus, and K. Wohlgemuth, *Liebigs Ann. Chem.*, 1937, **528**, 162.