Active Transport of Alkali Metal Cations: A New Type of Synthetic Ionophore Derived from a Crown Ether

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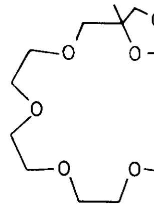
A new type of synthetic ionophore having both an 18-crown-6 ring and a primary amino group in the same molecule displayed an excellent K^+/Na^+ selective and active transport across a liquid membrane based on the reversible intramolecular complexation of the crown ring and the ammonium ion.

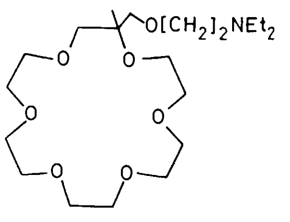
The development of noncyclic[1-3] and cyclic carboxylic ionophores[4-6] has been stimulated by attempts to mimic the function of monensin-type antibiotics, which selectively transport alkali metal cations against the concentration gradient.[7] In this case, intramolecular complexation is used in the uptake process of the cation. We now report a new ion transport system incorporating a structural device assisting in the release process using intramolecular complexation of an 18-crown-6 ring and a primary ammonium ion.

The ionophores (**1**) and (**2**) (which both have a primary amino group) and the ionophore (**3**) (which has a tertiary amino group) were prepared by the reaction of 2-bromomethyl-2-methyl-18-crown-6[8] with the sodium alkoxide of the appropriate amino-alcohol according to the literature procedure:[9] (**1**): yield 75%; b.p. 180 °C at 0.05 Torr (Kugelrohr); δ ($CDCl_3$) 1.16 (s, 3H), 1.26—1.76 (m, 8H), 2.66 (t, 2H), and 3.34—3.80 (m, 26H); ν_{max} (neat) 3350(s), 2870(s), 1640(m), 1460(m), 1100(s), and 950(m) cm^{-1}; *m/z* 393 (M^+), 277 (11%), 102 (24), 101 (100), 86 (37), 57 (30), 45 (41), and 44 (24); (**2**): yield 58%, b.p. 140 °C at 0.03 Torr; (**3**): yield 68%; b.p. 165 °C at 0.01 Torr.

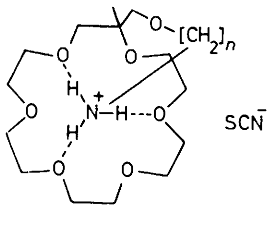
Transport experiments were performed at 25 °C in a U-type cell[1] under the conditions shown in Figure 1 and the quantity of the transported cation was determined by atomic absorption analysis. The stability constants (log K_S) of (**1**) and (**3**) towards K^+ were 5.43 and 5.77 respectively (in methanol, 25 °C). As these two ionophores have almost the same lipophilicity and complexing ability, their transport abilities in transport system I are expected to be similar.[10] In fact, the ionophores (**1**) and (**3**) did transport almost the same amounts of cations after 48 h in transport system I [(**1**): for K^+, 60%; for Na^+, 6%; (**3**): for K^+, 61%; for Na^+, 6%]. In transport system II, on the other hand, ionophores (**1**) and (**2**) (which both have a primary amino group) displayed much better transport ability towards K^+ than ionophore (**3**) (which has a tertiary amino group), as shown in Figure 2. The measurement of the pH in both aqueous phases after 48 h demonstrated that ionophore (**3**) performed little reverse



(1): n = 5
(2): n = 2



(3)



(1a): n = 5
(2a): n = 2

Phase 1 (H_2O, 10 ml)	Liquid membrane (CH_2Cl_2, 20 ml)	Phase 2 (H_2O, 10 ml)
Transport system I and II KSCN 0.1 M NaSCN 0.1 M Me_4NOH 0.1 M	Ionophore: 5×10^{-5} mol	Transport system I Me_4NOH, 0.1 M Transport system II KSCN 0.1 M NaSCN 0.1 M HCl 0.1 M

Figure 1. Conditions for competitive transport of K^+ and Na^+.

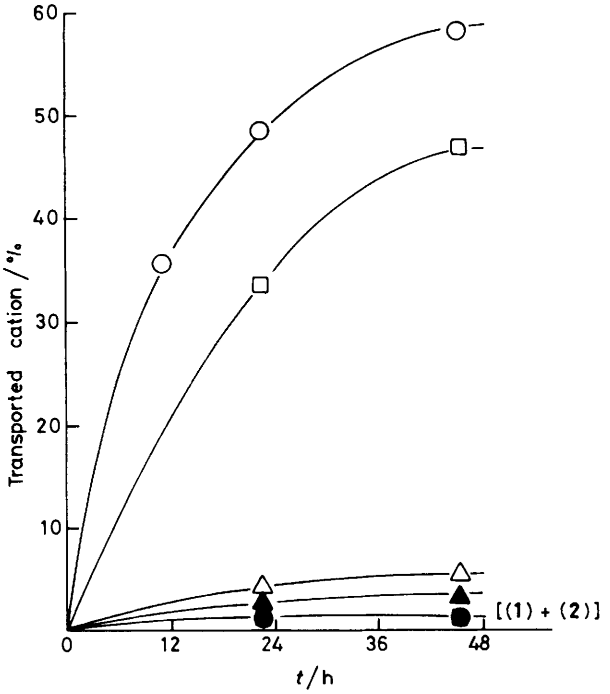


Figure 2. Competitive transport of K^+ and Na^+ in transport system II. Open symbols, K^+; filled symbols, Na^+; ○, ●, (**1**); □, ■, (**2**); △, ▲, (**3**).

transport of protons, whereas ionophores (**1**) and (**2**) could efficiently transport protons to phase 1. This means that the primary ammonium ion derived from ionophore (**1**) or (**2**) is lipophilic to some extent, while the tertiary ion derived from ionophore (**3**) is hydrophilic and scarcely distributed in the organic layer (CH_2Cl_2).

It is well known that 18-crown-6 derivatives can effectively complex with primary ammonium ions,[11,12] but hardly complex at all with tertiary ones.[11] On the basis of the above facts, ionophores (**1**) and (**2**) (which both have a primary amino group) may form intramolecular complexes such as (**1a**) and (**2a**), in the acidic region, and these are lipophilic enough to dissolve in the liquid membrane. Consequently, the marked difference in the transport ability among these ionophores seems to be resonably explained by considering intramolecular complexation between the 18-crown-6 ring and the primary ammonium ion. Thus, ionophore (**1**) or (**2**) complexes with K^+ in the basic region (phase 1) and transfers it with the counter anion (thiocyanate) to the acidic region (phase 2) across the liquid membrane. In phase 2, the amino group is protonated and the primary ammonium ion formed *in situ* competes with K^+ for complexation. The intramolecular complex with primary ammonium thiocyanate (**1a**) or (**2a**) is soluble in the liquid membrane and is transferred to phase 1. The active transport cycle is completed by deprotonation of the ammonium ion in phase 1.

The transport of Na^+ using synthetic ionophores which possess an 18-crown-6 ring was rather difficult, as expected, since the characteristic complexation property is based on the relative sizes of the ring and the cation.[10,13] As a result, ionophores (**1**) and (**2**) showed an excellent K^+/Na^+ selectivity.

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