

Switching of Cation Selectivity toward Na⁺ and K⁺ by a New Type of pH-Responsive 16-Crown-5 in a Countercurrent Double Uphill Transport System

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Received February 3, 2000

Crown ethers are interesting host compounds in connection with their selective complexation properties toward metal cations, especially the alkali and alkaline earth metal cations.¹ A variety of modifications of crown ether structure have been achieved to search for new functions.^{2,3} We previously examined the potential of crown ethers as models for natural ionophores and succeeded in developing a novel double uphill transport system in which two different cations are transported in opposite directions against their concentration gradients through a bulk liquid membrane by using a pH-responsive crown ether as the ion carrier.^{4,5} For example, the exchange between Na⁺ and K⁺ or between Ca²⁺ and K⁺ was realized by a bis(crown ether) derivative containing monoaza-18-crown-6 and 15-crown-5 rings⁴ or an 18-crown-6 derivative having two carboxylic acid groups.⁵ In addition to being an interesting model for a cation transport system of a cell,⁶ this double uphill transport is regarded as a promising separation method for metal cations⁷ because the desired cation is concentrated in one phase whereas the undesired cation is simultaneously removed from the phase.

Since the target of this study is the exchange of Na⁺ and K⁺ through a bulk liquid membrane by pH control, the ionophore should switch the cation selectivity at two interfaces. Bartsch reported that 16-crown-5 carboxylic acid derivatives are excellent ionophores for Na⁺.⁸ On the other hand, we recently found that introduction of an appropriate electron-donating sidearm to the central carbon atom of the trimethylene chain of the 16-crown-5 ring provides K⁺ selectivity to the 16-crown-5 derivative.⁹ These observations prompted us to design a novel type of ionophore for a double uphill transport system. We herein report the unique transport ability of a lipophilic 16-crown-5 derivative (**1**) containing both a carboxylic acid group and an electron-donating sidearm

Chart 1. Chemical Structure of Ionophore 1

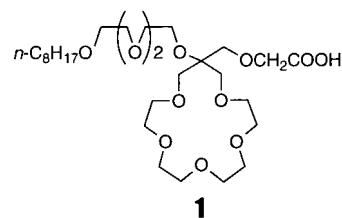


Table 1. Transport Data in the Presence of Sodium Ion and Potassium Ion

entry	initial conditions ^a		results (transport vel. ^b)					
	phase 1		phase 2		phase 1		phase 2	
	salt added	pH ^c	salt added	pH ^c	Na ⁺	K ⁺	Na ⁺	K ⁺
1	NaCl, KCl	13		2.3			3.1	1.4
2	PicNa, PicK	2.3		2.3			0.9	2.1
3	NaCl, KCl	13	PicNa, PicK	2.3		0.8	1.9	
4	NaCl, KCl	10	PicNa, PicK	2.3		2.4	0.7	

^a The initial concentrations of metal salts in the aqueous phases were arranged to be 5×10^{-3} M. In the case of active transport experiments (entries 3 and 4), tetramethylammonium chloride (0.2 and 0.3 M for entries 3 and 4, respectively) was added to phase 1. ^b 10^{-7} mol/h. ^c $[\text{Me}_4\text{N}^+\text{OH}^-] = 0.1$ M (pH 13); $[\text{Tris}] = 0.05$ M (pH 10); $[\text{HCl}] = 5 \times 10^{-3}$ M (pH 2.3).

on the pivot carbon atom.¹⁰ Transport experiments were carried out in a U-type cell at 25 °C.^{5a} Dichloromethane was used as the liquid membrane. The concentrations of metal cations were determined by atomic absorption analysis. The detailed transport conditions and the results are summarized in Table 1.

In the competitive passive transport system for Na⁺ and K⁺, the ionophore selectively transported Na⁺ from the basic phase to the acidic phase (entry 1). In this case, the metal cation is transferred into the liquid membrane as the counterion of the carboxylate anion with the aid of coordination of the crown ring. Thus, this Na⁺ selectivity is reasonably explained by considering that the Na⁺ complex is more lipophilic than the K⁺ complex, which is ascribed to the recognition ability of the 16-crown-5 ring.^{8,11} On the other hand, K⁺ selectivity was realized when the receiving phase was controlled to be acidic (entry 2). This result indicates that the cooperation of the oligooxyethylene sidearm of the ionophore and the 16-crown-5 ring effectively works for giving the K⁺ selectivity.⁹ It should be noted that this ionophore properly uses the two different sidearms for recognizing the kind of cation in response to the pH changes.

A unique double uphill transport was also successfully attained by pH control of aqueous phases (entries 3 and 4). The sodium and potassium cations were concentrated in the acidic and the basic phases, respectively. Although the mechanism is complicated, the phenomenon observed in entries 3 and 4 may be explained as follows (Figure 1). At the basic interface, the ionophore can capture both Na⁺ and K⁺ as the counterion of the carboxylate anion.⁸ However, the ionophore transfers Na⁺ rather than K⁺ into the organic phase as the lipophilic salt by the aid of 16-crown-5 ring, resulting in selective transportation of Na⁺ to the acidic phase. At the acidic interface, the Na⁺ salt of the ionophore is protonated to give a free acid. When the

(10) Ligand **1** is characterized on the basis of its ¹H NMR, mass spectrometry, and IR spectrometry. ¹H NMR (400 MHz, CDCl₃) δ 0.88 (t, *J* = 6.8 Hz, 3H), 1.20–1.40 (m, 10H), 1.55–1.61 (m, 2H), 3.45–3.82 (m, 36H), 4.13 (s, 2H). FABMS *m/z* 583 (*M*⁺ + 1). IR (neat) 1720 cm⁻¹ (*ν*_{C=O}). The elemental analysis was done as the methyl ester of **1**. Anal. Calcd for C₂₉H₅₆O₁₂: C, 58.37; H, 9.46. Found: C, 58.20; H, 9.31.

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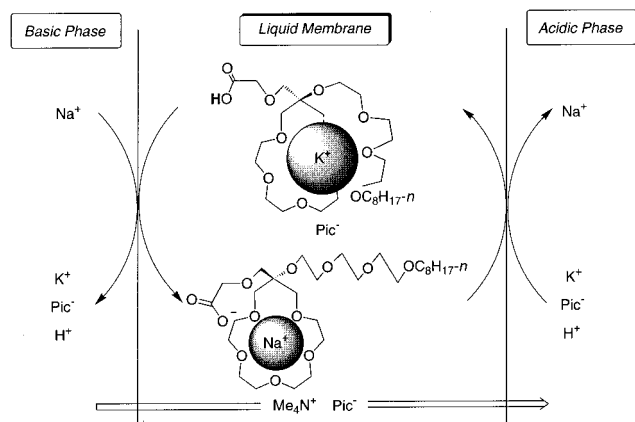


Figure 1. Mechanism of double uphill transport of Na^+ and K^+ in opposite directions by ionophore **1**.

ionophore is present as the free acid, the ionophore selectively complexes with K^+ rather than Na^+ by the cooperative coordination of the 16-crown-5 ring and the oligooxyethylene sidearm.⁹ In this case, the ionophore needs an assistance of the lipophilic counteranion (picrate ion) to transfer the cation from the aqueous phase to the organic phase. Then, the ionophore transports potassium picrate from the acidic to the basic phase. According to this cycle, the picrate anion should be gradually removed from the acidic phase without any devices. In addition, picric acid is also known to move spontaneously from the acidic phase to the

basic phase through the dichloromethane membrane.^{4b} The decrease in the picric acid concentration in the acidic phase is considered to be a drawback because it causes a decrease in the transport velocity of K^+ from the acidic to the basic phase. To solve this problem, tetramethylammonium salt is added into this transport system. A tetramethylammonium ion can transport a picrate ion as the salt from the basic to the acidic phase according to its concentration gradient.^{4b} Then, Na^+ and K^+ are concentrated in the acidic phase and the basic phase, respectively.

It is interesting that the direction of the transport of Na^+ and K^+ by using this type of ionophore through the membrane is just in converse relation to the direction realized by the bis(crown ether)-type ionophore consisting of monoaza-18-crown-6 and 15-crown-5.⁴ Compared to the latter system, the present case is a simple and unique switching system of the cation selectivity, considering that the ionophore contains only one crown ring.

Modification of the ionophore structure is now under way in our laboratory to improve the double uphill transport system.

Acknowledgment. This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, Sports and Culture of Japan and a grant from General Sekiyu Research & Development Encouragement & Assistance Foundation.

Supporting Information Available: Synthesis details and characterization of compound **1** and experimental details for transport studies (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

JA0004229