Proton-Ionizable Crown Compounds. 12. Proton-Coupled Selective Membrane Transport of Li⁺ Using a Proton-Ionizable Pyridono Macrocycle

REED M IZATT*, GYPZY C. LINDH, RONALD L. BRUENING, PETER HUSZTHY, JOHN D. LAMB, JERALD S. BRADSHAW, AND JAMES J. CHRISTENSEN
Departments of Chemistry and Chemical Engineering, Brigham Young University, Provo, UT 84602, U.S.A.

Abstract. The macrocycle-mediated fluxes of several alkali metal cations have been determined in a $H_2O-CH_2Cl_2-H_2O$ liquid membrane system. Water-insoluble proton-ionizable macrocycles of the pyridono type were used. The proton-ionizable feature allows the coupling of cation transport to reverse H^+ transport. This feature offers promise for the effective separation and/or concentration of alkali metal ions with the metal transport being driven by a pH gradient. A counter anion in the source phase is not co-transported. The desired separation of a particular metal ion involves its selective complexation with the macrocycle, subsequent extraction from the aqueous phase to the organic phase, and exchange for H^+ at the organic phase-receiving phase interface. Factors affecting transport which were studied include ring size, source phase pH, and receiving phase pH. Lithium was transported at a rate higher than that of the other alkali metals in both single and competitive systems using a 15-crown-5 pyridono carrier.
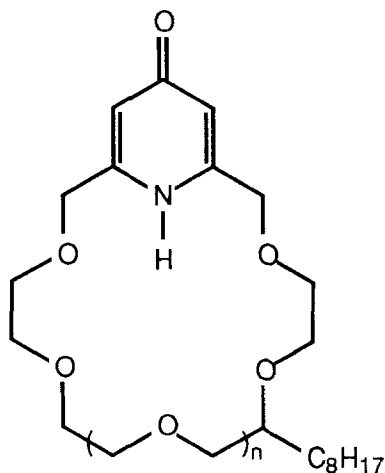
Key words: Pyridono macrocycles, proton-ionizable, selective alkali cation transport, liquid membrane, coupled M^+-H^+ transport.

1. Introduction

Earlier [1, 2], we described the use of a new water-insoluble proton-ionizable pyridono macrocycle (**1**) to transport K^+ selectively over other alkali metal cations in a $H_2O-CH_2Cl_2-H_2O$ bulk liquid membrane system. Previous work on cation transport using proton-ionizable macrocycles was referenced in those communications and in a recent communication by Kimura, *et al.* [3] on selective Cu^{2+} transport by a proton-driven mechanism. Our previous work [2] with **1** showed that proton-coupled transport of Li^+ occurred, but the magnitude of the transport was low compared to that of Na^+ and K^+. It seemed reasonable to expect that a macrocycle of smaller cavity size should show improved selectivity for Li^+ and Na^+. This was the motivation for the synthesis of **2**.

The design of reagents capable of selective recognition of Li^+, particularly in the presence of Na^+, is desirable [4] because of the need to recover Li^+ from waste solutions, process its ores, monitor its presence in blood, and increase the permeability of Li^+ salts in lipid layers for reasons of biological significance. Several workers [5] have designed macrocycles which show Li^+ selectivity in a given solvent and Bartsch, *et al.* [6] obtained selective Li^+ extraction by using a crown ether type macrocycle

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* Author for correspondence.

1, n = 1
2, n = 0

of appropriate size containing a proton-ionizable group as part of a pendant arm. In the present study, alkali cation (M^+) transport by the 15-crown-5 type proton-ionizable pyridono macrocycle (**2**) has been investigated and the results compared to those for the 18-crown-6 type macrocycle (**1**).

2. Experimental

2.1. MATERIALS

Compound **2** was prepared as reported for the synthesis of **1** from an octyl-substituted methylene glycol [7, 8]. The following metal compounds were obtained in the highest grade available from the indicated suppliers and were used without further purification: hydroxides of Li^+ and K^+ (Spectrum), Rb^+ and Cs^+ (Aldrich), and Na^+ (Anachemia–carbonate free, Harleco–carbonate free); nitrates of Li^+ (Baker), Na^+ (Mallinckrodt), K^+ (Fisher, Baker), and Rb^+ and Cs^+ (Fisher, Mallinckrodt, Aldrich). Reagent grade HNO_3 (Fisher, Mallinckrodt, Ashland) and spectroquality methylene chloride (CH_2Cl_2) (EM) were used. All aqueous solutions were prepared using distilled deionized water.

2.2. PROCEDURE

The membrane transport experiments were carried out using bulk liquid membranes as described previously [9–11]. Each cell (Figure 1) consisted of a 3.0 mL membrane phase (CH_2Cl_2, 1.0 mM in carrier, stirred at 120 rpm by a magnetic stirrer) interfaced to both a 0.8 mL source phase (consisting of either 1.00 M total cation or an equal-molar cation mixture of known pH) and a 5.0 mL receiving phase (consisting of either distilled deionized water or an HNO_3 solution of pH 1.5). Source phases of
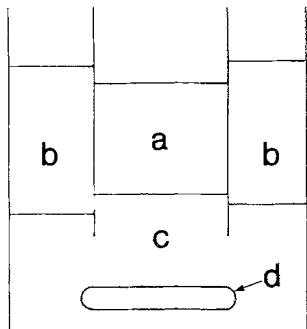
Fig. 1. Liquid membrane cell. (a) Source phase. M^+ (NO_3^-, OH^-) mixtures, H_2O; (b) Receiving phase. H_2O or HNO_3 (pH = 1.5); (c) Membrane. CH_2Cl_2, 1 mM macrocycle; (d) Magnetic stirrer. 120 rpm/24 h.
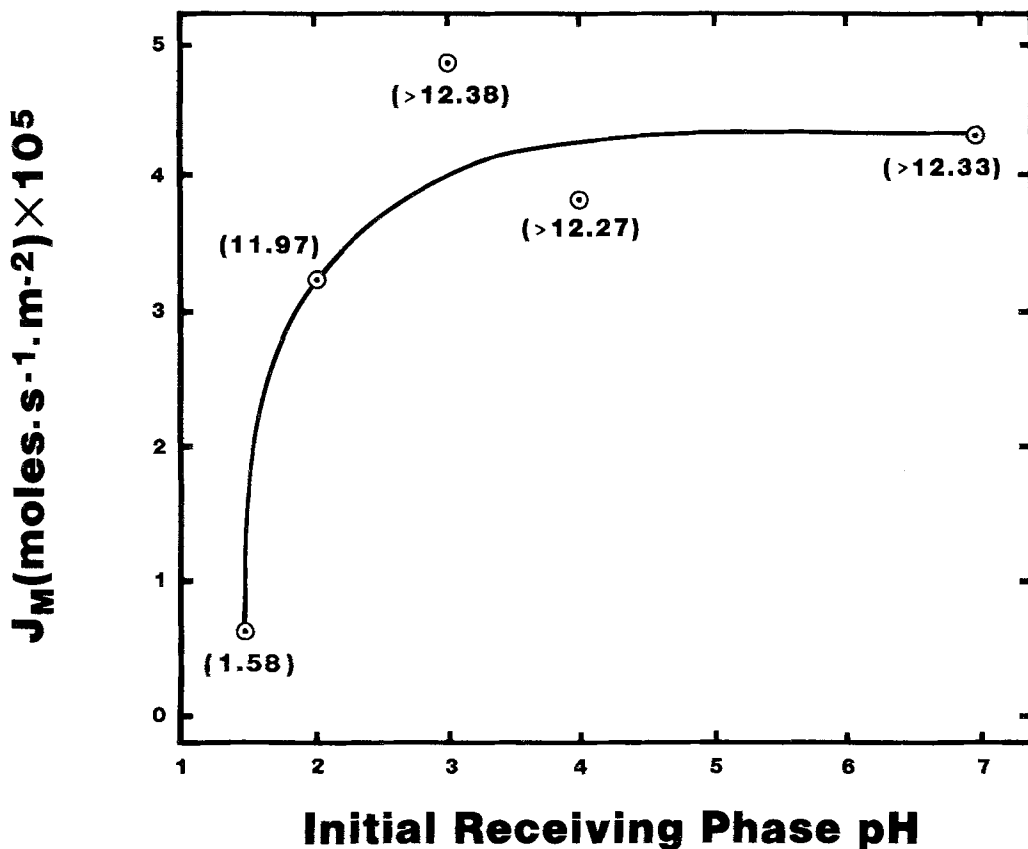

Initial Receiving Phase pH

Fig. 2. Plot of Li^+ flux vs. initial receiving phase pH using 2 as carrier. The numbers in parentheses. are the final pH values of the receiving phase solutions.

different pH were prepared using the appropriate amounts of MNO_3 and MOH. After 24 hours, the receiving phase was sampled and analyzed for cation concentration using a Perkin Elmer model 603 atomic absorption spectrophotometer and for nitrate ion concentration using a Dionex model 20000 ion chromatograph. The

pH values of the aqueous solutions were measured using a Sargent Welch miniature combination pH electrode. The initial source phase pH values were found to correspond closely to the calculated values. The pH values of 1.0 M M$^+$ solutions listed in the Tables (see below) and in Figure 2 are the calculated values based upon the initial MOH concentration.

2.3. CALCULATIONS

Each experiment was repeated at least 3 times, and the results are reported as the average of the three determinations. The standard deviations from the mean among the values in each experiment are less than ±25%. Experiments performed in which no carrier was present in the membrane showed cation fluxes to be less than 0.3 × 10^{-8} mol s^{-1} m^{-2}.

3. Results and Discussion

In those systems where appreciable cation transport occurred, the organic phase turned cloudy approximately one-half hour after stirring began. The cloudiness was much more intense for systems in which the receiving phase pH was 1.5 than for those containing water except in the case of Li$^+$ where the reverse was true. This correlation between cloudiness and cation flux was not investigated further. The cloudiness may be a result of water being extracted with the cation into the membrane phase.

In Table I, flux values are given for the transport of M$^+$ with 2 as carrier. The results in Table I show that M$^+$ transport was small below source phase pH 13 but increased dramatically between pH 13 and 14. As was shown [1, 2] in the case of M$^+$ transport by 1, these results suggest that alkali cation transport of Li$^+$ compared to that of the other M$^+$ at high pH values suggested that 2 might be used to selectively transport Li$^+$ over other M$^+$ in competitive transport experiments. The data in

Table I. Single M$^+$ fluxes[a] in a bulk H$_2$O–CH$_2$Cl$_2$–H$_2$O liquid membrane[b] system using 2 as carrier

M$^+$	Receiving Phase pH	Source Phase pH				
		11	12	13	13.5	14
Li$^+$	7	2	4	50	2313	4254
	1.5	0	0	32	785	929
Na$^+$	7	3	5	16	74	309
	1.5	<1	<1	7	209	641
K$^+$	7	2	4	28	113	421
	1.5	<1	<1	5	111	461
Rb$^+$	7	<1	<1	24	86	124
	1.5	<1	<1	5	83	135
Cs$^+$	7	<1	2	20	47	133
	1.5	<1	<1	4	174	246

[a] $J_M = (\text{mol s}^{-1}\ \text{m}^{-2}) \times 10^8$.
[b] Phase compositions: Source: 1.0 M in each metal cation using appropriate amounts of MNO$_3$ and MOH to achieve the initial source phase pH. Membrane: 0.001 M 2 in CH$_2$Cl$_2$. Receiving: initial pH of 7 (H$_2$O) or 1.5 (HNO$_3$), as indicated.

Table II. Competitive M^+ fluxes[a] in a bulk H_2O–CH_2Cl_2–H_2O liquid membrane[b] system using **2** as carrier

Metal Ions $\left(\dfrac{M_1^+}{M_2^+}\right)$	Aqueous Receiving Phase			
	pH = 7		pH = 1.5	
	Flux	*Ratio*	*Flux*	*Ratio*
$\dfrac{Li}{Na}$	$\dfrac{449}{228}$	2.0	$\dfrac{1443}{630}$	2.3
$\dfrac{Li}{K}$	$\dfrac{474}{184}$	2.6	$\dfrac{1074}{237}$	4.5
$\dfrac{Li}{Rb}$	$\dfrac{753}{353}$	2.1	$\dfrac{545}{232}$	2.4
$\dfrac{Li}{Cs}$	$\dfrac{507}{172}$	2.9	$\dfrac{892}{317}$	2.8
$\dfrac{Na}{K}$	$\dfrac{193}{181}$	1.1	$\dfrac{519}{245}$	2.1
$\dfrac{Na}{Rb}$	$\dfrac{612}{767}$	0.8	$\dfrac{339}{79}$	4.3
$\dfrac{Na}{Cs}$	$\dfrac{857}{833}$	1.0	$\dfrac{302}{147}$	2.1
$\dfrac{K}{Rb}$	$\dfrac{223}{335}$	0.7	$\dfrac{310}{384}$	0.8
$\dfrac{K}{Cs}$	$\dfrac{138}{215}$	0.6	$\dfrac{178}{219}$	0.8
$\dfrac{Rb}{Cs}$	$\dfrac{268}{242}$	1.1	$\dfrac{237}{256}$	0.9

[a] $J_M = (\text{mol s}^{-1}\ \text{m}^{-2}) \times 10^8$.
[b] Phase compositions. Source: initial pH of 14, 0.5 M in each metal hydroxide. Membrane: 0.001 M **2** in CH_2Cl_2. Receiving: initial pH of 7 (H_2O) or 1.5 (HNO_3), as indicated.

Table II show that this is the case. Selective transport of Li^+ was found for all mixtures of it with other M^+. With few exceptions, no appreciable selectivity was found among the remaining cation mixtures.

Competitive transport experiments have shown [1, 2] that K^+ is transported selectively over other M^+ by **1**. It is apparent that reduction of the macrocycle cavity size has altered markedly the interaction of M^+ with these pyridono-type macrocycles. No M^+ transport was observed with **2** present in the membrane and with a source phase pH below 12. A similar result was found for **1** [1, 2]. These results are a consequence of the proton coupled nature of the transport process. For transport to proceed, there must be sufficient OH^- in the source phase to remove the proton from the HL form of the macrocycle. The pK_a value of **2** is expected to be about 11 by analogy with the pK_a value (10.98) [12] measured for the water-soluble (no C_8H_{17}) analog of **1**. Thus, removal of the proton from HL at the source phase-membrane interface occurs readily at source phase pH values of 13 and above.

Table III. Comparison of Li$^+$ and K$^+$ fluxes[a] with **2** and **1**, respectively as a function of receiving phase pH in a bulk liquid membrane system[b]

Receiving phase pH	Li$^+$ Flux with **2**	K$^+$ Flux with **1**
1.5	929	1631
7	4254	803

[a] $J_M = (\text{mol s}^{-1}\ \text{m}^{-2}) \times 10^8$.
[b] Phase compositions: Source: 1.0 M M$^+$ with initial source phase pH of 14. Membrane: 0.001 M **1** or **2** in CH$_2$Cl$_2$. Receiving: initial pH of 7 (H$_2$O) or 1.5 (HNO$_3$), as indicated.

Mechanisms for macrocycle-mediated M$^+$ transport other than the H$^+$-coupled transport require that a co-anion accompany an M—(2)$^+$ complex across the membrane. The possibility of such transport occurring was checked by measuring the receiving phase NO$_3^-$ concentration after 24 hours for all experiments where the initial source phase pH was 13.5 ([NO$_3^-$] = 0.5 M) and the initial receiving phase was water. The concentration of NO$_3^-$ in the receiving phase was never greater than 2% of the sum of the receiving phase concentrations of the cations transported.

The counter transport of H$^+$ and M$^+$ was further substantiated by checking the mass balance for Li$^+$ and H$^+$ when the initial receiving and source phase pH values were 1.58 and 14, respectively. Over a 24 hour period, 3.3×10^{-5} moles of Li$^+$ appeared in the receiving phase and the pH of that phase increased by 0.14 pH unit corresponding to 5.0×10^{-5} moles of H$^+$ being transported from the receiving phase.

The effect of initial receiving phase pH on Li$^+$ transport in the single cation system is shown in Figure 2. It is seen that Li$^+$ flux increased as the initial receiving phase pH was increased. The high final receiving phase pH obtained in most of the cases indicates that counter-transporting H$^+$ was supplied from water dissociation at the receiving phase-membrane interface. When the initial receiving phase pH was 1.5, a sufficient [H$^+$] was present for counter transport with Li$^+$ over 24 h and water dissociation was not required. The increased Li$^+$ flux as receiving phase pH increases is opposite to the pH effect observed for K$^+$ flux in the single cation system as is seen in Table III. The expected order of flux is that seen for K$^+$ since increasing the receiving phase [H$^+$] should increase the rate of protonation of L$^-$ at the receiving phase-membrane interface. The expected order of flux with varying receiving phase pH was observed for Li$^+$ in competitive transport experiments (Table II). Further investigation is underway to understand these phenomena.

4. Conclusions

The results show that alkali cation transport in the bulk liquid membrane system used is proton-coupled when macrocycle **2** is the carrier. A source phase co-anion is not involved in the transport process. Selective transport of Li$^+$ over other alkali cations in competitive transport experiments is obtained by using a pyridono-15-

crown-5 macrocycle. This selective transport is switched 'on' or 'off' by altering the pH of the source phase and is enhanced by altering the receiving phase pH.

Acknowledgements

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