# Novel Lithium-selective Ionophores bearing an Easily Ionizable Moiety

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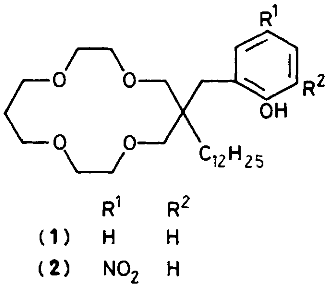
Lipophilic 14-crown-4 derivatives incorporating a nitrophenol substituent are excellent lithium ionophores for proton-driven cation transport, in which extremely high selectivity ratios of lithium over sodium are realized.

Considerable efforts are presently being directed towards syntheses of ionophores selective for $Li^+$, which are of importance for its separation and analysis.[1—8] Lithium ionophores incorporating a proton-dissociative group are able to form intramolecular ion-pairs on complexing the cation under basic conditions.[4—7] The ionizable ionophores may, therefore, be applied to solvent extraction[4—6] and membrane transport[7] which do not involve transfer of the aqueous-phase counter anion into the organic phase. A special counter anion such as the picrate ion which enhances the cation distribution to the organic phase is not required in those cases. Also, in proton-driven cation transport, selective lithium enrichment is considered to be feasible. We have recently reported that lipophilic 14-crown-4 derivatives are highly selective for $Li^+$, being promising candidates as neutral carriers for $Li^+$-selective electrodes.[8] It occurred to us that incorporation of an ionizable substituent into the lipophilic 14-crown-4 cycle would lead to novel $Li^+$-selective ionophores which would permit proton-driven cation transport.

Cyclization of 2-dodecyl-2-(2-methoxybenzyl)propane-1,3-diol with 3,7-dioxanonane-1,9-diylbis(toluene-*p*-sulphonate) (dioxane, NaH, $LiClO_4$, reflux) afforded 6-dodecyl-6-(2-methoxybenzyl)-1,4,8,11-tetraoxacyclotetradecane, which was then converted into the lipophilic crown phenol (**1**) by demethylation ($LiAlH_4$, heptane, reflux). Nitration of the 14-crown-4 phenol ($HNO_3$, $CHCl_3$, room temp.) yielded the corresponding *p*-nitrophenol (**2**), *o*-nitrophenol (**3**), and dinitrophenol (**4**) derivatives.

A disc of microporous polypropylene film (maximum pore size of 0.04 × 0.4 μm) was impregnated with an *o*-nitrophenyl octyl ether (NPOE) solution of the appropriate crown phenol and then the external solution on the membrane was carefully wiped off with filter paper. Competitive transport of alkali metal ions was carried out at 25 °C in a glass cell where two aqueous phases possessing identical alkali metal ion concentrations and different proton concentrations were divided by the crown ether-impregnated membrane (see Figure 1).

Figure 1(a) illustrates clearly that the membrane containing the lipophilic 14-crown-4 *p*-nitrophenol (**2**) acts as a cation pump selective for $Li^+$. The lithium selectivity in the proton-driven cation transport is extremely high, the selectivity order being $Li^+ \gg Na^+ > K^+ \sim Rb^+ \sim Cs^+$. The crown *o*-nitrophenol (**3**) and the crown dinitrophenol (**4**) also exhibited similar membrane transport behaviour. The crown phenol (**1**), however, did not lead to proton-driven cation transport of any alkali metal ion, probably owing to the high $pK_a$ value of the phenol proton.



| | $R^1$ | $R^2$ |
|---|---|---|
| (**1**) | H | H |
| (**2**) | $NO_2$ | H |
| (**3**) | H | $NO_2$ |
| (**4**) | $NO_2$ | $NO_2$ |

Most outstanding is the high preference of $Li^+$ over $Na^+$ in the proton-driven transport using the crown nitrophenol derivatives (**2**)—(**4**), because the selectivity ratio of $Li^+/Na^+$ for lithium ionophores is a very important factor for their

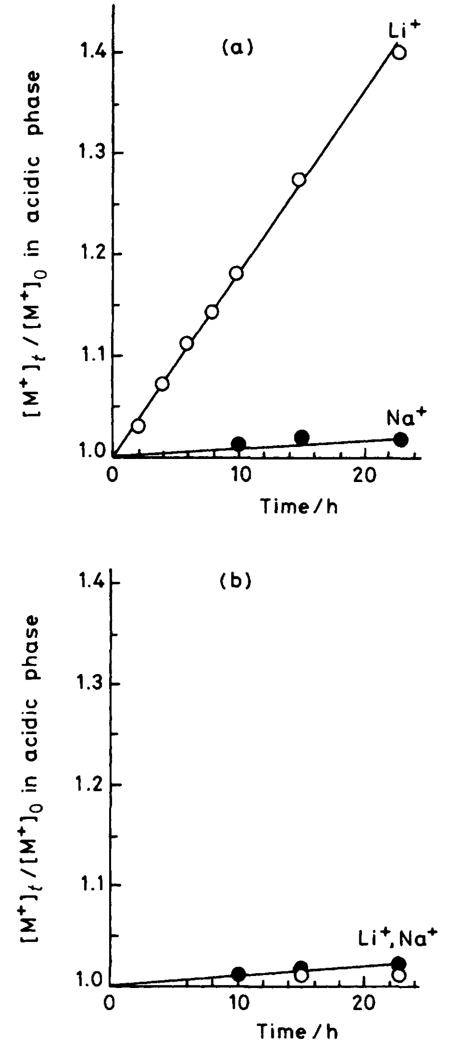


**Figure 1.** Proton-driven transport of alkali metal ions through a membrane impregnated with (a) crown *p*-nitrophenol–NPOE solution or (b) NPOE. Membrane: film disc of 3.3 cm diameter containing 13 μl of $4.5 \times 10^{-2}$ M crown ether–NPOE solution or NPOE; exposed membrane area: 1 $cm^2$; basic phase (pH 13): LiOH, NaOH, KOH, RbOH, and CsOH ($2 \times 10^{-2}$ M), 20 ml; acidic phase (pH 1): the alkali metal hydroxides ($2 \times 10^{-2}$ M) and $2 \times 10^{-1}$ M HCl, 20 ml; $[M^+]_t$ and $[M^+]_0$ refer to metal ion concentrations at time = *t* and 0, respectively, which were determined by flame photometry.

practical applications. The $Li^+/Na^+$ ratio in the cation transport, although not very accurate because only a trace of $Na^+$ was transferred, was determined to be at least 20 (calculated from the ratio of the average flux during 23 h) for the membrane system including the crown *p*-nitrophenol (**2**). However, even in transport experiments using an NPOE membrane without any ionophore under identical conditions, a slight increase of $Li^+$ and $Na^+$ concentrations in the acidic phase was observed as shown in Figure 1(b). Thus the real $Li^+/Na^+$ selectivity ratio for the crown nitrophenols must be greater than the apparent value. The excellent lithium selectivity of the lipophilic 14-crown-4 nitrophenol derivatives in proton-driven cation transport should have wide applicability.

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