

Enhanced Calcium Ion Selectivity of a Macrocyclic Polyether-amide with Two Polyether Rings

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The macrocyclic polyether-amide (**1**) is shown to be more selective than its corresponding monocyclic analogue (**4**) for the Ca^{2+} ion; the potentiometric selectivity for Ca^{2+} relative to Mg^{2+} is improved by more than one order of magnitude.

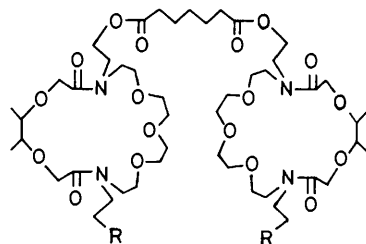
Macrocyclic polyether-diamides¹⁻³ with two amide groups in the macroring of the polyether preferentially complex alkaline earth metal ions, especially Ca^{2+} . Interestingly, their Ca^{2+} complexes almost always have 2:1 (macrocycle:cation) stoichiometry, probably with the cation sandwiched between two macrocycles.³ This prompted us to synthesize a model compound (**1**) with two macrorings, with hopefully a better Ca^{2+} ion selectivity than that of its monocyclic analogues. We report here the Ca^{2+} selectivity of (**1**) as a neutral carrier in a polymeric membrane ion-selective electrode and a comparison with that of its analogue (**4**).

Macrocycle (**2**) was prepared by cyclization of 4,5-dimethyl-3,6-dioxaoctanedioyl chloride with 1,17-dihydroxy-3,15-diaza-6,9,12-trioxaheptadecane in a manner similar to that in the literature.² Treatment of the macrocycle with octanoyl chloride afforded a mixture of the macrocycles (**3**) and (**4**), which were readily separated by silica gel column chromatography. The polyether-amide (**1**) was synthesized by treating a macrocycle (**3**) with pimelic chloride (CHCl_3 , Et_3N , reflux) and then purified by preparative gel permeation chromatography.[†]

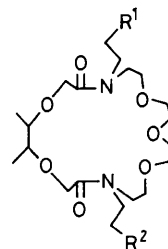
The polymeric membranes for the Ca^{2+} -selective electrodes were cast from tetrahydrofuran solutions of 3% (w/w) macrocycle, 66% *o*-nitrophenyl octyl ether (NPOE), 30% poly(vinyl chloride) (PVC, average polymerization degree of 1100), and 1% potassium tetrakis(*p*-chlorophenyl)borate.

† (**1**): Colourless oil (30%); ν_{max} (neat) 1640 (amide C=O) and 1730 cm^{-1} (ester C=O); δ_{H} (100 MHz, CDCl_3) 0.90 (6H, t, CH_3CH_2), 1.05–1.40 (28H, m, $\text{Me}[\text{CH}_2]_4$ and CH_3CH), 1.40–1.80 (10H, m, $\text{Me}[\text{CH}_2]_4\text{CH}_2$ and $\text{COCH}_2[\text{CH}_2]_3\text{CH}_2\text{CO}$), 2.15 (8H, t, CH_2CO_2), 3.60 (44H, m, $\text{O}[\text{CH}_2]_2\text{O}$, $\text{N}[\text{CH}_2]_2\text{O}$, $\text{CO}_2\text{CH}_2\text{CH}_2\text{N}$, and CHMe), 4.05–4.50 (16H, m, OCH_2CON and CH_2OCO).

The E.M.F. measurements were taken at 25 °C; the composition of the electrochemical cell was $\text{Ag}\cdot\text{AgCl} | 0.001 \text{ mol dm}^{-3} \text{ CaCl}_2 | \text{PVC membrane} | \text{sample solution} | 0.1 \text{ mol dm}^{-3} \text{ NH}_4\text{NO}_3 | \text{KCl (sat.)} | \text{Hg}_2\text{Cl}_2 \text{ (s)} \cdot \text{Hg}$. The potentiometric selectivity coefficients were determined in mixed solutions⁴ of Ca^{2+} and a foreign ion M by varying the concentration of the



(1) $\text{R} = \text{Me}[\text{CH}_2]_6\text{CO}_2^-$



(2) $\text{R}^1 = \text{R}^2 = \text{OH}$

(3) $\text{R}^1 = \text{OH}$, $\text{R}^2 = \text{Me}[\text{CH}_2]_6\text{CO}_2^-$

(4) $\text{R}^1 = \text{R}^2 = \text{Me}[\text{CH}_2]_6\text{CO}_2^-$

Table 1. Selectivity coefficients for PVC membrane Ca²⁺-selective electrodes based on (1) and (4).

Compound	Mg ²⁺	Sr ²⁺	Ba ²⁺	k_{CaM}^{Pot} ^a	Li ⁺	Na ⁺	K ⁺
(1)	1×10^{-5}	5×10^{-2}	5×10^{-2}		1×10^{-4}	9×10^{-6}	3×10^{-5}
(4)	2×10^{-4}	1×10^{-1}	8×10^{-2}		3×10^{-4}	7×10^{-5}	7×10^{-5}

^a Constant concentrations of foreign ions: 0.5 mol dm⁻³ for Mg²⁺, Na⁺, Li⁺, and K⁺; 0.005 mol dm⁻³ for Sr²⁺ and Ba²⁺.

former ion and using a constant background concentration of the latter one.

The selectivity coefficients for Ca²⁺ relative to the ion M (k_{CaM}^{Pot}) in the PVC membrane electrode based on (1) are listed in Table 1, together with those for its monocyclic analogue (4).[‡] The smaller the k_{CaM}^{Pot} value, the higher the preference for Ca²⁺ over M in the electrode. It should be noted that macrocycle (1) has smaller values than (4) for most of the selectivity coefficients, especially those relative to alkaline earth metal ions. The most striking value is that of (1) for preference of Ca²⁺ over Mg²⁺ which is at least an order of magnitude larger than that of (4). Previous studies⁵⁻⁸ indicate that bis(crown ether)s containing two crown ether moieties at the end of a short aliphatic chain, possess excellent complexing abilities compared to monocyclic analogues for particular alkali metal ions which are likely to form 2:1 (crown ring : cation) complexes. This phenomenon was thought to be due to co-operative action of the two adjacent crown ether groups. This also seems to be the case in compound (1). The electrochemical ion-selectivities strongly suggest that the 'bicyclic effect' is significant even in this ligand system.

[‡] For (2) and (3), reliable values for the selectivity coefficients could not be obtained owing to the non-Nernstian response of their electrodes, probably because of the insufficient lipophilicity of the molecules which causes poor solubility in the PVC membrane.

The calibration plots for the Ca²⁺-selective electrode based on (1) showed Nernstian response (30 mV/decade) in the activity range of 3×10^{-2} to 1×10^{-5} mol dm⁻³ CaCl₂. Also, the Ca²⁺ selectivities of the electrode relative to Mg²⁺, Na⁺, and K⁺ are extremely high. Therefore, the (1)-based Ca²⁺-selective electrode may be of great practical use.

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