Efficient Transport of Alkali and Ammonium Ions by Proton-ionizable Ester Crowns Containing 1*H*-Pyrazole Units. Symmetric Complexing Behaviour towards Europium observed by ^{13}C N.M.R. Spectroscopy

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The alkali and ammonium ion transport properties in a H_2O–$CHCl_3$–H_2O bulk liquid membrane system have been evaluated for ester crowns containing 1*H*-pyrazole units, and their symmetric complexing behaviour towards 1,1,1,2,2,3,3-heptafluoro-7,7-dimethyloctane-4,6-dionatoeuropium(III) observed by ^{13}C n.m.r. spectroscopy; crown **(4)** (38-membered ring) is an efficient carrier of K^+ and NH_4^+ ions.

The 1*H*-pyrazole unit of heteroaromatic crown ethers can assist cation transport in two different ways. It can take part in ion complexation through its sp^2 nitrogen; however, when deprotonated, it can also behave as a proton-ionizable function promoting ion transport without an independent counterion.[1,2]

We have previously reported the synthesis and complexing properties of ester crowns containing 1-methyl- and 1*H*-substituted pyrazole units.[3,4] The alkali cation transport evaluation of crowns **(1)** and **(2)** using a transport system composed of a neutral aqueous salt solution, a chloroform membrane, and a receiving water phase, showed that neither is an efficient carrier of alkali cations, mainly because of their asymmetric structure. However, according to the size of their respective macrocyclic cavities, the smaller crown **(1)** (18-membered ring) is selective for Li^+ ions while the larger one **(2)** (36-membered ring) showed selectivity for K^+ ions.[5] Crowns **(3)** and **(4)** are difficult to prepare following the synthetic procedure described in reference 3. However, since the symmetry factor contributes greatly to efficient ion transport we have recently carried out an alternative synthesis of both symmetric crowns by Lewis acid-catalysed debenzylation of crowns **(5)** (m.p. 134—135 °C) and **(6)** (m.p. 103—104 °C) with aluminium chloride in refluxing benzene under similar conditions to those reported by Murakami and co-workers for *N*-benzylindoles.[6] This debenzylation afforded crowns **(3)** and **(4)** in 23% and 20% yields, respectively.†

Table 1. Transport rates of alkali and ammonium ions ($\times 10^{-7}$ mol l^{-1} h^{-1}) through a chloroform phase containing 10^{-3} M of ligand.

Ligand	Li^+	Na^+	K^+	Rb^+	Cs^+	NH_4^+
(1)	5.5[a]	0.3[a]	0.1[a]	—[a,b]	—[a,b]	10.7
(2)	0.3[a]	0.6[a]	13.7[a]	6.6[a]	0.4[a]	15.2
(3)	89.8	76.9	58.6	15.3	2.4	52.7
(4)	135.6	70.0	476.2	269.8	45.1	335.4

[a] Experimental data from ref. 5.

[b] Measured transport rate equivalent to that of a blank experiment with no ligand in the organic phase (rate lower than 0.01×10^{-7} mol^{-1} h^{-1}).

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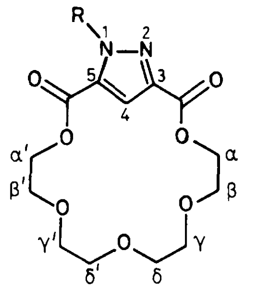
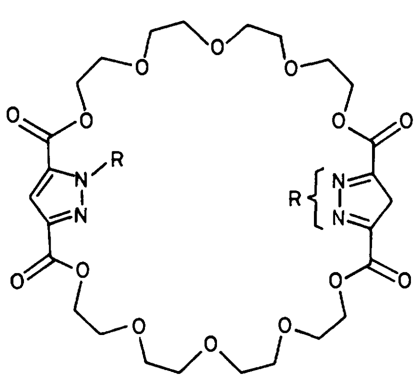
† The synthesis of *N*-benzyl substituted crowns **(5)** and **(6)** and other larger analogues will be reported elsewhere, together with a more detailed description of their debenzylation.



(1) R = Me
(3) R = H
(5) R = CH_2Ph



(2) R = Me
(4) R = H
(6) R = CH_2Ph

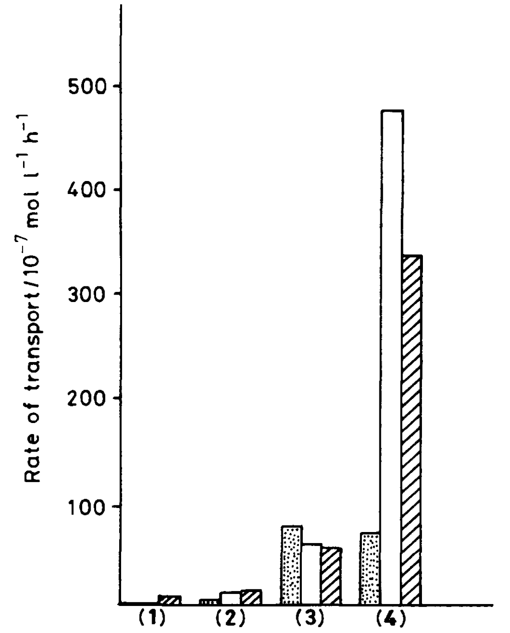


Figure 1. Transport rates for crowns (**1**)—(**4**) of Na^+ (dotted areas), K^+ (empty), and NH_4^+ (hatched).

Using the same membrane system and conditions as previously reported for crowns (**1**) and (**2**)[5,7] we have now measured the transport rates of alkali picrates for (**3**) and (**4**) and those of ammonium picrates for crowns (**1**)—(**4**). The results are presented in Table 1, with those previously obtained for (**1**) and (**2**) for comparison. Both *N*-methyl substituted ligands (R = Me) are more efficient for NH_4^+ than for alkali cation transport. Furthermore, after removal of the *N*-methyl group the NH_4^+ transport rates are enhanced significantly both for (**3**) [≈5 times higher than (**1**)] and (**4**) [22 times higher than (**2**)].

Similarly, both NH substituted crowns (R = H) are much better carriers of alkali metal ions than their *N*-methyl substituted analogues. According to the size of their macrocyclic cavities, crown (**3**) is a selective carrier of Li^+ ions [≈16 times more efficient than (**1**)] and crown (**4**) is a selective and efficient carrier of K^+ ions [≈35 times higher than (**2**)]. Figure 1 compares the Na^+, K^+, and NH_4^+ transport rates for crowns (**1**)—(**4**). In fact, crown (**4**) shows a high selectivity K^+/Na^+ = 6.8 and a lower selectivity K^+/NH_4^+ = 1.4, very close to those exhibited by dibenzo-18-crown-6 (DB18C6) (K^+/Na^+ = 8.8 and K^+/NH_4^+ = 1.5).‡ Since crown (**4**) is a proton-ionizable ligand its K^+/Na^+ selectivity could be applied to the proton-coupled transport of alkali metal cations.[8]

Table 2. Eu(fod)$_3$-induced shifts (p.p.m.) in the ^{13}C n.m.r. spectra of crowns (**1**)—(**4**).

Ligands	(**1**)[a]	(**2**)	(**3**)	(**4**)
C-3	27.0	11.9	13.3	4.3
C-4	1.4	0.3	−9.4	−2.1
C-5	2.8	2.1	13.3	4.3
*C*H$_3$	4.8	2.9	—	—
CO(3)	36.6	16.8	20.4	6.2
CO(5)	1.3	1.6	20.4	6.2
C-α	4.8	4.2	8.0	5.3
C-α'	4.0	3.8	8.0	5.3
C-β	4.5	7.4	4.7	7.5
C-β'	3.8	5.6	4.7	7.5
C-γ	9.3	12.4	7.4	14.6
C-γ'	9.3	10.2	7.4	14.6
C-δ,δ'	10.0	13.1	7.7	19.9

[a] Data taken from ref. 5.

In order to obtain more information on potential site(s) of metal ion complexation of (**3**) and (**4**) in relation to (**1**) and (**2**), the lanthanide induced shifts produced by 1,1,1,2,2,3,3-heptafluoro-7,7-dimethyloctane-4,6-dionatoeuropium(III) [Eu(fod)$_3$] in the ^{13}C n.m.r. spectra of (**2**), (**3**), and (**4**) were studied.§ The results are shown in Table 2 and compared with those previously reported for crown (**1**).[5] Positive and negative signs are used for downfield and upfield induced shifts, respectively.

The upfield shifts for carbon C-4 in (**3**) and (**4**), the other carbons being shifted downfield, are in agreement with the 'wrong-way' shifts found for carbons in position β relative to the complexation sites due to contact terms.[9]

In the complex of (**2**) with Eu(fod)$_3$, as for (**1**), larger induced shifts are observed for carbons C-3 and CO(3) in relation to C-5 and CO(5) as well as little deshielding difference between carbons α, β, γ in relation to carbons α', β' and γ'. These facts suggest a preferential interaction with sp^2

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‡ These data were determined from the Na^+, K^+, and NH_4^+ transport rates for DB18C6 which was taken as the reference carrier in relation to crowns (**1**)—(**4**) using the same membrane system.

§ Registered in Cl_3CD solution using [Eu(fod)$_3$]/[Ligand] concentration ratio between 0.03 and 0.2. These data were extrapolated for a limiting concentration of [Eu(fod)$_3$]/[Ligand] = 1.

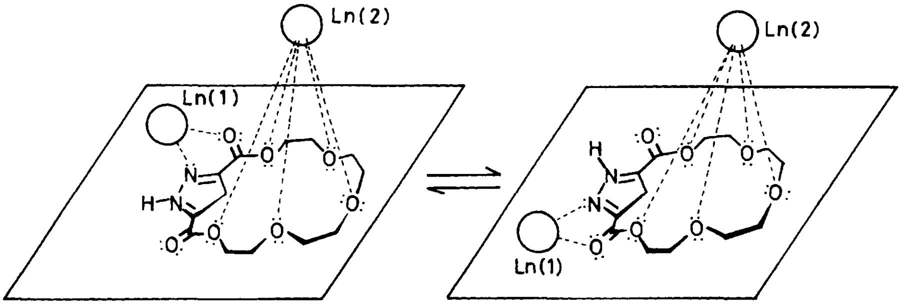

Figure 2. Possible binding of lanthanide cation by crown (**3**), showing tautomerism.

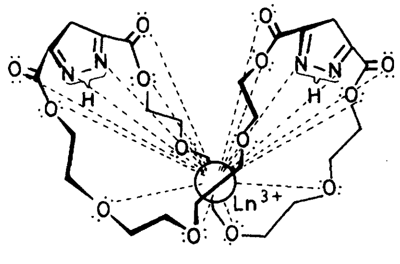

Figure 3. Proposed binding of lanthanide cation by crown (**4**).

pyrazolic nitrogen, the neighbouring ester group, and the ether oxygens of the crown ether cavity on the side less hindered by the methyl group.

However, in crowns (**3**) and (**4**), owing to their symmetrical character, these differences disappear. The Corey–Pauling–Koltun (CPK) model of (**3**) shows that the pyrazolic nitrogens are turned outside their intramolecular cavity, whereas in (**4**) in the presence of Eu(fod)$_3$ they can turn inside to the cavity. Crown (**3**) may bind to the lanthanide cation through two different complexation sites as indicated in Figure 2. Owing to the tautomerism in NH pyrazoles the first one, Ln(1), may be in rapid equilibrium between N(1) or N(2), having therefore a symmetry plane perpendicular to the molecule. The second one, Ln(2), is above the molecular plane in a similar manner to that proposed for (**1**) and for other triazole analogues.[10]

Comparing the data for (**3**) and (**4**) in Table 2 it can be deduced that in the Eu(fod)$_3$ complex of (**4**), the pyrazolic nitrogens and the ester groups seem to play a less important role in complexation than the ether oxygens located in the centre of both tetraethylene chains. This situation suggests a single complexation site with the lanthanide cation located in the middle of the macrocyclic cavity as suggested in Figure 3.

Since it has recently been demonstrated that cation transport increases when the source phase pH is high enough to allow deprotonation of the carrier,[2] crowns (**3**) and (**4**) may be useful as proton-ionizable carriers of ions using an alkaline source phase.

Received, 18th April 1988; Com. 8/01680A

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