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Synthetic Ionophores. 2.* Effect of Incorporation of Sulphur and Ester Moieties on the Ionophore Character of 18-Crown-6

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Abstract. In 18-crown-6, the replacement of two methylene groups by two carbonyl groups or one oxygen with sulphur, increases the transport selectivity of K^+/Na^+ and Tl^+/Na^+ picrates. However, the presence of a combination of two carbonyl and one sulphur moiety or their multiples adversely affects the transport rates and selectivity.

Key words. 18-Crown-6, transport selectivity, cation transport, picrate.

1. Introduction

The selective complexation character of macrocycles [2] towards cations like that of naturally occurring ionophores [3] was responsible for a myriad of investigations on the synthesis [4], complexation [5] and ionophore character of macroheterocycles [6] including 18-crown-6 [7]. Here, we have studied the effect of peripheral changes in 18-crown-6, involving replacement of (i) two/four methylene groups with carbonyl groups, (ii) one/two oxygens with sulphur or methylene groups, on its ionophore character towards Na^+, K^+ and Tl^+ picrates.

2. Experimental

2.1. MATERIALS

18-Crown-6 was obtained from Aldrich. Compounds **II – IV** and **VI – VII** were synthesized by phase transfer catalysed condensations of appropriate dicarboxylic acid halides and diols, details of which are being reported elsewhere. Sodium and potassium picrates were prepared by the method of Fuoss [8] and thallium picrate was obtained by mixing saturated solutions of thallium carbonate and picric acid in ethanol : water (1 : 1).

2.1.1. *Preparation of Compound V*

A solution of equimolar quantities of thiodiethylene glycol and the ditosylate of tetraethylene glycol in dry DMF containing pulverized potassium hydroxide and

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* For part 1 see ref. 1.

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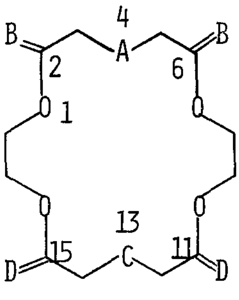
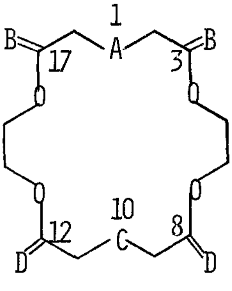


I-IV



V-VII

triethylbenzylammonium chloride (TEBA) was stirred at ambient temperature. After the completion of the reaction, indicated by consumption of ditosylate (tlc), DMF was removed under vacuum. The residue was dissolved in chloroform, washed with water, dried (Na_2SO_4) and the chloroform was distilled off. The product was chromatographed over a silica gel column using benzene : ethyl acetate as eluent and was obtained as a thick liquid in 10% yield. Its ^1H NMR spectrum – ($CDCl_3$) δ 2.66 (t, 4H, 2 × SCH_2), 3.42 (s, 2OH 10 × CH_2) – was comparable with the one reported in the literature [9].

Table I. Rates of transport of metal ions (K^+, Na^+, Tl^+) with 18-membered macrocycles (**I–VII**)[a]

Ligand	Transport rates × 10^8(mol/24 hr)			Selectivity Ratio		
	Na^+	K^+	Tl^+	K^+/Na^+	Tl^+/Na^+	K^+Tl^+
I						
$A = C = O$	1650	940	680	0.6	0.4	1.4
$B = D = 2H$	(1140)[b]	(840)[b]	(430)[b]			
II						
$A = B = O$	53	590	280	11	5.3	2.1
$C = O, D = 2H$	(31)[b]	(450)[b]	(201)[b]			
III						
$A = CH_2, B = O$	110	240	280	2.20	2.5	0.9
$C = O, D = 2H$						
IV						
$A = C = CH_2$	16	16	15	1	0.9	1.1
$B = D = O$						
V						
$A = S, B = 2H$	280	2240	3520	7.9	12.6	0.6
$C = O, D = 2H$						
VI						
$A = S, B = O$	9	9	50	1.0	5.5	0.2
$C = O, D = 2H$						
VII						
$A = C = S$	11	70	30	6.4	2.7	2.3
$B = D = O$						

[a] Concentration of the ligand 1×10^{-3} M (b) 0.625×10^{-3} M. Each experiment was performed thrice and the values reported are within ±5% to ±15% error.

2.2. DETERMINATION OF ION TRANSPORT

The method of Maruyama *et al.* [10] was used (Table I). All experiments were carried out at 26 ± 1°C in a cylindrical glass cell (inside diameter, 3.8 cm) holding a glass tube (inside diameter, 1.9 cm). The inner aqueous phase contained (0.1 M) metal chloride (K, Na)/metal nitrate (Tl) and metal picrate (2×10^{-3} M) (5 mL) and the outer aqueous phase contained only metal chloride/metal nitrate (Tl) (0.1 M, 10 ml). The lower chloroform layer (15 mL) bridging the two aqueous layers containing the ligand (1×10^{-3} M) was stirred at constant speed. The concentration of the metal picrate in the outer aqueous phase was determined from the u.v. absorption band at λ max.357 nm, (ε; Na^+ 15200 $L mol^{-1} cm^{-1}$; K^+ 1500 $L mol^{-1} cm^{-1}$; Tl^+ 13900 $L mol^{-1} cm^{-1}$) [11] either by withdrawing samples at different intervals or by determining the total concentration after 6 to 9 hours. The blank experiments in the absence of ligand did not show any leakage in the case of Na^+ and K^+ and for the leakage determined in the case of Tl^+, a correction factor was applied.

3. Results and Discussion

18-Crown-6 (**I**) transports the picrates of K^+, Na^+ and Tl^+ in the order $Na^+ > K^+ > Tl^+$ (Table I) which is in disregard of their association constants* ($Tl^+ > K^+ > Na^+$) [12]. This change in the order could be attributed to the high stabilities of complexes of K^+ and Tl^+ which inhibit release of the cations from the membrane. These results indicate that the change of the co-anion (nitrate to picrate) alters the ion transport selectivity order towards cations. Ligand **II**, having two carbonyl moieties at C-2 and C-6 in place of methylene groups in 18-crown-6 however transports the picrates at a rate slower than with **I** but in the order $K^+ > Tl^+ > Na^+$ which is in accordance with their association constants. This structural change has significantly increased the selectivity in transport of K^+/Na^+ from 0.6 to 11 and of Tl^+/Na^+ from 0.4 to 5.3. Thus **II**, which lacks ionophoric character towards K^+ and Na^+ nitrates [13, 14], induces the transport of their picrates with a fair degree of selectivity.

The optimum number of donor oxygens required for complexation of K^+ and Na^+ is six and five, respectively [14]. Accordingly, the decrease in effective number of donor atoms from six to five by replacing O(4) of **II** with one methylene group in ligand **III**, decreases the transport rate of K^+ and increases that of Na^+ in comparison with ligand **II**.

Ligand **IV**, having a methylene for O(13) and two carbonyl groups for methylenes (C-11 and C-15) of ligand **III**, transports these picrates at rates lower than those with ligand **III**. The selectivity in transport of metal ions with respect to each other is also insignificant.

Ligand **V**, incorporating a sulphur atom in place of O(4) of 18-crown-6 transports these picrates in the order $Tl^+ > K^+ > Na^+$ as against $Na^+ > K^+ > Tl^+$ in the case of 18-crown-6. The increase in transport rate of Tl^+ could be due to its

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* From 2×10^{-3} M aqueous solutions of K^+ and Na^+ picrates, 18-crown-6 (3×10^{-3} M) extracted K^+, 1.95×10^{-3} M and Na^+ 0.75×10^{-3} M in chloroform layer.

better complexation with ligand **V** containing the softer sulphur and for K^+ due to weaker association but increased decomplexation of the complex formed. As a result, the selectivity in transport of K^+/Na^+ is increased to 7.9 and that of Tl^+/Na^+ to 12.6 with ligand **V** from 0.6 and 0.4 with ligand **I**.

Ligand **VI**, having two carbonyl groups in place of methylene groups at C-3 and C-17 of ligand **V**, transports the picrates of Na^+, K^+ and Tl^+ in the order $Tl^+ > Na^+ > K^+$ but the rates are lower than with ligand **V**. Thus the replacement of two methylene groups with two carbonyl groups in ligand **I** and **V** decreases the transport rates but the decrease is much more conspicuous in thioether **V**. Ligand **VII**, having four carbonyl and two sulphur moieties, transports Na^+ and Tl^+ picrates at comparable or lower rates than ligand **VI**, but its behaviour in the transport of K^+ is anomalous.

Thus, with 18-crown-6 as the carrier, on replacing the coanion nitrate by picrate, the rate of transport of Na^+ is increased sharply. Ligand **II**, which does not induce the transport of metal nitrates transfers their picrates with a fair degree of K^+/Na^+ selectivity. The replacements of (i) two methylene groups by two carbonyl groups (ligand **II**) and (ii) one oxygen with sulphur (ligand **V**) in 18-crown-6 increase the selectivity of K^+/Na^+ and Tl^+/Na^+ picrates. But the presence of two carbonyl and one sulphur moieties or their multiples in the same macrocycle adversely affects the transport rate and selectivity.

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