Some Observations on the Mechanism of Passive Transport *

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Certain mixtures of crown ethers are shown to be synergic in promoting three-phase passive transport of alkali-metal picrates. An explanation in terms of rates of crossing the membrane barriers is proposed. For a series of propeller crowns (dinaphthophenylpolycycloalkins) transport is faster for those with steric hindrance (rigid or locked propellers) and a hypothesis consistent with these results is made.

Passive transport of alkali-metal picrate, M^+ pic$^-$, from one aqueous phase to another separated by an immiscible organic layer, may be brought about by neutral macrocycles [examples are the macrocycles (**1**)—(**4**)] as carriers in the organic phase.[1–3] Such transport should be dominated by three main features, the net rate at which alkali-metal picrate, M^+ pic$^-$, (*i*) crosses the 'in' interface, AB; (*ii*) moves through phase B; and (*iii*) crosses the 'out' interface, BC. The first and third features should be related to the balance between the rate at which the macrocycle can complex the cation at the interface AB, and the rate at which the cation can dissociate from the complex carrier at the interface BC. The second feature may depend on the rate of transfer of cations between ligands in the organic phase (if the carrier is not fully loaded), but may be diffusion controlled.

Recent models have explained the function of the macrocycle in equilibrium terms, but have made clear that this is not a simple equilibrium matter.[3,4] Two situations are presented here where the description in terms of rate seems more natural. Since the equilibrium constant is simply a ratio of rate constants, this may seem pedantic; however, the same equilibrium constant can apply to systems with very different rates. Consequently, correlations with equilibrium constants are faulty if the complex crosses the BC interface too slowly relative to the diffusion through B, so that the cation never gets discharged from the organic membrane, or if the dissociation rate of the complex is so fast, and it moves back across the interface AB to A so fast (relative to the diffusion) that it never gets into the membrane.

A recent analysis by Lehn and co-workers[3] describes how the selectivity of a system between two cations (extracted as ion pairs) needs to be measured in competition and not in single experiments; the experimental findings, for example, of Izatt and co-workers[2] on Pb *versus* K extraction show this clearly. In the first part of this paper, a novel competitive experiment is described, namely transport by mixtures of ligands, some of which prove to be synergic. In the second part, transport by a range of propeller crowns, with different propensities for flexing of crown-ether segments attached directly to the propeller blades is described.[5] The more rigid (locked) propellers were found to promote faster transport than fluxional ones, for the series Na, K, Rb, and Cs with a range of crowns, (**5**), having five, six, or seven oxygen donors in the ether ring.

Experimental

The crown ethers used were purchased [(**1**), (**6**)] or prepared by known routes [(**2**)—(**5**)].[6–8] Alkali-metal picrates were made by neutralising a solution of metal hydroxide with picric acid solution and dilution to 0.01 mol dm^{-3}, except for caesium where 0.005 mol dm^{-3} solutions were used.

Transport Measurements.—Two types of cell were used. An unstirred cell (type b) with a 1-cm u.v. cell fused to the portion containing the receiving phase could be monitored directly in a spectrometer (P.E. 402). This enabled a check on linearity of rate over long periods, sometimes several days. Membrane, source, and receiving phases were chloroform (5 cm^3, 7×10^{-4} mol dm^{-3}) in ligand, water (1 cm^3, 0.01 mol dm^{-3}) in metal picrate, and pure water (20 cm^3) respectively.

In two versions of the Pressman cell, as described in refs. 1 and 2, the temperature was maintained at 25 °C by a water jacket, and the stirring rate was 120 r.p.m., provided by means of a miniature electronic stirrer (Rank Brothers). Membrane, source, and receiving phases were chloroform (20 or 5 cm^3, 7×10^{-4} mol dm^{-3}) in ligand, water (4 or 0.3 cm^3, 0.01 mol dm^{-3}) in metal picrate, and pure water (20 or 5 cm^3) in c or d cell types respectively. Transport measurements were run in triplicate in cells of this design. Aliquots of the receiving phase were analysed using measurements of picrate absorbance as described,[6] with a P.E. 550S spectrophotometer. Experiments were usually followed during the transport of the first 1% of the theoretically possible transport, within the limits shown to be realistic for a linear transport rate by the theory of Lehn and co-workers.[3]

Results and Discussion

Using the cell with the u.v. attachment (type b), I have examined the synergic combination of ligands (**1**) and (**3**). A typical result is shown in Figure 1. The mixture (*b*), containing a 1:6 ratio of 18-crown-6 [(**1**)] to benzo-15-crown-5 [(**3**)] † exhibits enhanced passive transport over the sum of the values expected for the two ligands at the same concentration, acting separately. A range of mixtures was examined in the Pressman type of cell, and the results are given in Table 1. In most cases cited, the combination is synergic. It was not possible to obtain synergism (with this anion) with cryptands (**6**) (n = 1 or 2).

Many facets of carrier-mediated transport through thick liquid membranes have been explained in terms of diffusion-controlled kinetics.[2–4] The novel situation described here in which one ligand acts in concert with a second to improve transport kinetics has not been treated. The greater efficacy of the mixture can be explained in similar terms to those of Lehn's hypothesis on selectivity of the carrier between different substrates.

According to this treatment, the ligand (L), substrate (S), and ligand–substrate complex (LS) concentrations are related by the overall extraction-equilibrium constant K_e. There are three identifiable cases, (*a*)—(*c*), in which the extraction-equilibrium coefficients of a ligand for two substrates A and B (K_{eA} and K_{eB}

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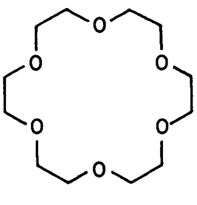
† 18-Crown-6 = 1,4,7,10,13,16-hexaoxacyclo-octadecane, benzo-15-crown-5 = 2,3,5,6,8,9,11,12-octahydrobenzo-1,4,7,10,13-pentaoxacyclopentadecine.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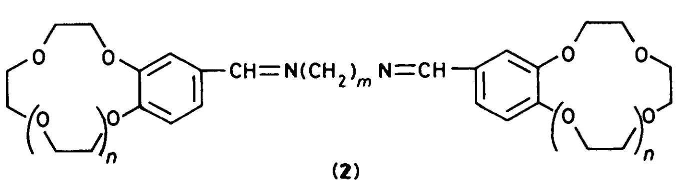

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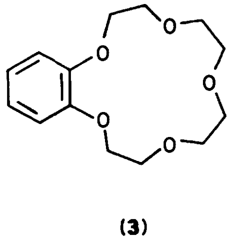
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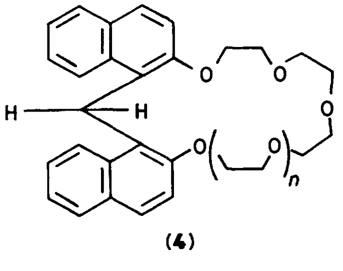

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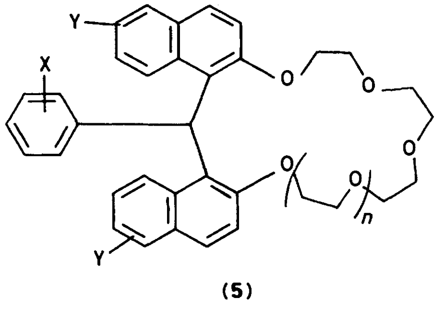

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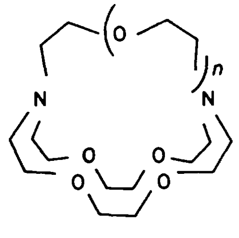
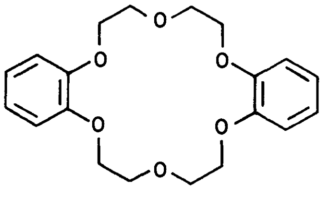


(6a); n = 1
(6b); n = 2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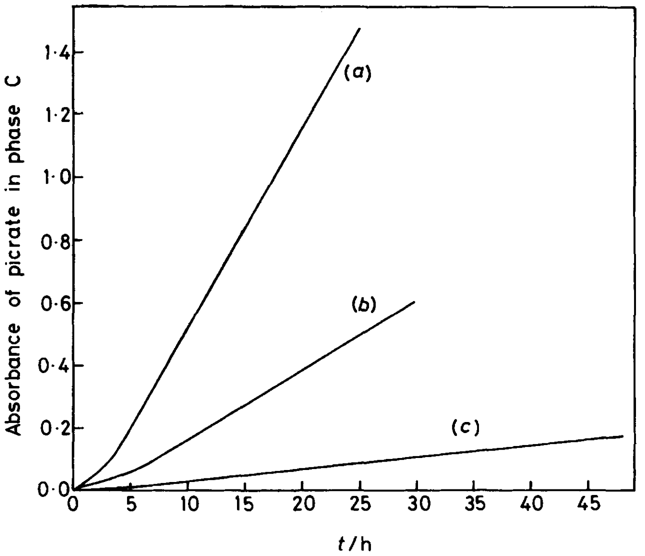

Figure 1. Transport of potassium picrate in cell type b: (*a*) (**1**), (*b*) (**1**):(**3**) = 1:6, (*c*) (**3**); total ligand concentration in each case 7 × 10^{-4} mol dm^{-3}

respectively) are classified relative to an optimum K_e(max.) given by equation (1) (subscript i = interface). The transport rates of the substrates, V_A and V_B, derived from the Lehn[3] treatment, are found to have the relative ordering shown. If we consider two ligands, L′ and L″, having extraction coefficients for the same cation $K_{eL'}$ and $K_{eL''}$ there are similar considerations, cases (*d*)—(*f*).

$$K_e = \frac{LS_{i,in}}{L_{i,in}S_{i,in}}\,\frac{LS_{i,out}}{L_{i,out}S_{i,out}} \qquad (1)$$

case (*a*) $K_{eB} \ll K_{eA} \ll |K_e|(\text{max.})$: $V_B < V_A$
case (*b*) $K_{eB} \ll |K_e|(\text{max.}) \ll K_{eA}$: $V_B \leqslant V_A$; or $V_B \geqslant V_A$
case (*c*) $|K_e|(\text{max.}) \ll K_{eB} \ll K_{eA}$: $V_B > V_A$
case (*d*) $K_{eL'} \ll K_{eL''} \ll |K_e|(\text{max.})$
case (*e*) $K_{eL'} \ll |K_e|(\text{max.}) \ll K_{eL''}$
case (*f*) $|K_e|(\text{max.}) \ll K_{eL'} \ll K_{eL''}$

We are concerned here, not with transport of carriers L′ and L″, but with the metal cation (actually K$^+$), so we consider V_{K^+}. The mixtures considered mostly correspond to case (*d*), *e.g.* L′ = benzo-15-crown-5 and L″ = 18-crown-6, and 18-crown-6 is probably close to the optimum ligand for potassium, thus its K_e value is close to $|K_e|$(max.). The transport rate V_{K^+} for L′ is less than that for L″ in separate experiments, but in the mixture the concerted effect of L′ + L″ is greater than for the expected sum of effects of the two separately, at the same concentrations present in the mixture. Thus, $V_{K^+}(L') < V_{K^+}(L'') \geqslant V_{K^+}(L' + L'')$. It could be seen that the loading depended on L″ (from the absorbance of the picrate in the organic layer). Despite this, L′ must be involved somewhere, and must pick up the substrate at some point; it seems reasonable to suppose that this is by displacement of L″ on the complex. This would give a proportion of the L′ complex, which, since it dissociates faster, is better able to discharge the cation from the membrane at the 'out' interface. The synergism of the mixture in case (*d*) thus

Table 1. Transport of potassium picrate by mixtures of two ligands L′ and L″[a]

L′	J_{K+}	L″	J_{K+}	Ratio L′:L″	J mixture	Cell-type[b]
(3)	0.3	(**1**)	38	6:1	9.7	b
(5)	0.1	(**1**)	38	1:1	30	b
$n = 2$, X = *m*-Me, Y = H						
(1)	150	**(6a)**	<0.1	3:1	96	c
(7)	120	**(6a)**	<0.1	1:3	22	c
(2)	0.35	(**1**)	18	4:1	10	d
$n = 1$, $m = 8$						
(4)	7.9	(**1**)	18	4:1	14.3	d
$n = 2$						
(3)	3.6	(**1**)	18	3:2	15	d
(2)	9	(**1**)	18	4:1	10	d
$n = 2$, $m = 6$						
(3)	11	(**7**)	120	4:1	49	c

[a] Results are for three different cell designs, b, c, d and are quoted as moles ($\times 10^7$) of potassium picrate transported in 24 h, reproducible to ±25%. Comparisons are possible along rows; comparisons down columns should only be made for the same cell type. [b] Cell-type: b, direct-reading u.v. cell; c, Pressman cell, 20 cm^3 receiving phase; d, Pressman cell, 5 cm^3 receiving phase.

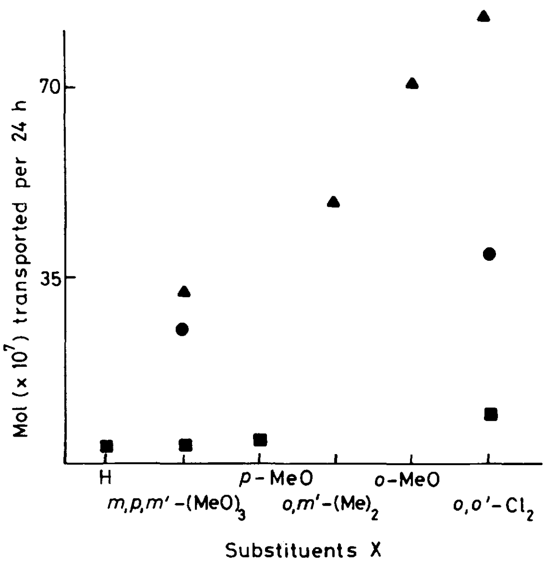

Figure 2. Transport of potassium picrate by propeller crown (**5**); (▲) crown-6, (●) crown 7, (■) crown-5

appears to involve the ligand L″ acting as a 'fisher' ligand and L′ acting as a 'bouncer'. Probably both can act as carriers in the organic phase.* A natural concentration gradient involving the two ligands may develop in the membrane, and could, with advantage, be introduced by some means. When L″ is a cryptand [*e.g.* (**6b**)] the picrate ion pair never gets past the organic phase and again dominates the transport. This is antergic, and an example of case (*e*). No example of case (*f*) was found. The observation of synergism is interesting in relation to mechanism, although it could be detrimental to selectivity between cations.

Table 2. Results obtained in Pressman cell type c, quoted as moles ($\times 10^7$) potassium picrate transported in 24 h, reproducible within ±25%

	Ligand			Metal		
	X	n	Y	Na	K	Rb
(4)		1		3.5	2.6	
(4)		2		3.1	100.0	
(4)		3		1.2	8.7	
Dimer of **(4)**		1		0.3	8.7	
(5)	(MeO)$_3$	1	Bu^t	5.7	2.3	
(5)	(MeO)$_3$	2	Bu^t	2.9	32.5	21.9
(5)	(MeO)$_3$	3	Bu^t	5.0	30.0	40.1
(5)	Cl$_2$	1	Bu^t	7.0	10.0	7.5
(5)	Cl$_2$	2	Bu^t	2.6	85.0	—
(5)	Cl$_2$	3	Bu^t	2.5	40.0	72.5
(5)	Me$_2$	2	Bu^t	3.9	53	33.5
(5)	*o*-MeO	2	Bu^t		72	42.5
(5)	*o*-MeO	1		10.0		5.8
(5)	H	1		6.5	3.0	
(5)	C$_6$H$_4$	1		7.1	4.0	
(5)	*p*-MeO	1			2.7	

Steric Hindrances to Ligand Flexing.—The series of propeller crowns (**4**) and (**5**) was investigated, the variables being (*a*) the size of the propeller ring, and (*b*) the steric hindrance of the substituents on the phenyl ring.[5,8] A typical set of results is displayed in the graph in Figure 2 and in Table 2. It can be seen that five-donor crowns transport Na best, six-donor crowns transport K, and seven-donor crowns transport Rb or Cs best. The best overall transport was by crown (**5**) (X = *o*, *o*′-Cl$_2$, Y = Bu^t, $n = 2$) for K. It is difficult to assess the steric effect of the phenyl substituents; there is no relation with the conventional steric substituent constants of Taft.[9] Recent analysis of the possible path of the flip mechanism for rearrangement of triarylmethanes[10] using the Burgi–Dunitz–Murray-Rust[11] structural correlation method has suggested that bond stretching and angle bending are probably important factors in reducing the steric crowding, and that the minimum energy path probably involves the rings described in the original two-ring flip mechanism, with all three rings moving at different rates.

Why should the 'locked' propeller improve transport? It has been shown (in crystal structures, and through n.m.r. kinetics on the free ligand) to provide a partially pre-organised environment for the cation, reducing the number of conformational options, as proposed by Cram and Rein.[12] We know that the liminal temperature for exchange of sodium from the locked propellers on the ^{23}Na n.m.r. time-scale is *ca.* 280 K, while the corresponding temperature for fluxional propellers is *ca.* 250 K. This slower rate of exchange of sodium cation must be critical in the exchange of sodium in the three-phase transport, and its effect must be at the 'in' interface AB, or in the chloroform membrane itself, since it would have a deleterious effect at the 'out' interface BC. It is noteworthy that the absorbance of picrate in the organic phase is very small for this set of ligands, but the concentration of 'crowned' metal picrate ion pairs, the 'loading' of the organic phase, as measured by the absorbance, is related to the rate of transport J_{K^+}.

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* Alternatively, as suggested by a referee, synergism may involve some type of sandwich complex, which is more favourable to transport when formed from mixed ligands.

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