The Nature of the Exchange of Free Crowns with a Cation Crown Complex Studied by ^{1}H N.M.R.

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In the ^{1}H n.m.r. spectra of propeller crown ligands and their salt complexes, the OCH_2CH_2O segments next to the naphthyl rings have ABCD spectra (interpreted in terms of the fluxional process averaging *gauche* and *anti* placements of the two oxygens) which have been completely assigned (NUMARIT), defining in detail the stereochemistry of these segments. The exchange of excess ligand with salt complex, studied by dynamic ^{1}H n.m.r. spectroscopy in a mixed solvent, was found to have a second-order and a first-order component, by the Shchori method, and the results are discussed in relation to the kinetic basis of selectivity of macrocycles for cations. The rearrangement of one OCH_2CH_2O segment between two *gauche* forms is shown to occur on a KSCN salt complex at a rate much faster than the overall ligand exchange, showing that such a rearrangement is a feasible fast preliminary step for exchange.

When we analysed the ^{1}H n.m.r. spectra of propeller crown ether† segments [compound (**1**)] and took a preliminary look at the same features for their salt complexes, we realised the potential of the dynamic n.m.r. method to bring the kinetics of exchange processes involving the ligands on to an n.m.r. timescale.[1,2] In this paper we exploit the dynamic n.m.r. method in order to investigate the exchange of propeller crown ligands (**2**)–(**5**) with their salt complexes, and the mechanism of ligand exchange.[2] The ligands have been extensively studied in Newcastle to determine their role in passive transport[3] and in ISE membranes,[4] for which we need as detailed a look as possible at the kinetics and equilibria of the processes which may be relevant to the selectivity process especially in the crossing of any aqueous/organic phase boundary. Some processes regarded as relevant are described in equations (1)–(3).

$$M^+(solv) + L \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ML^+ + solv \qquad (1)$$

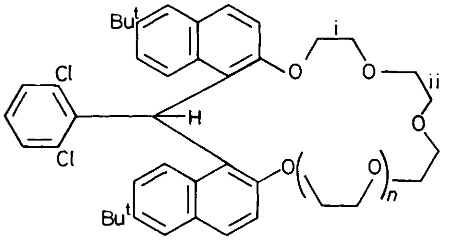
$$ML^+ + {}^*M^+ \rightleftharpoons {}^*ML^+ + M^+ \qquad (2)$$

$$^*L + ML^+ \overset{k_2}{\rightleftharpoons} M^*L^+ + L \qquad (3)$$

The exchange of Na^+ cations with propeller crown complexes has already been studied and shown to proceed mainly by the dissociative route shown as the reverse step in equation (1), in media intended to simulate a typical plasticised PVC membrane,[5] and at 300 K. We did not find any evidence at normal temperatures for bimolecular cation exchange with complex as depicted in equation (2). In this paper we investigate the exchange of ligand with the same solvent system;[5] this might be expected to occur by process (3), or by the dissociative process in equation (1).

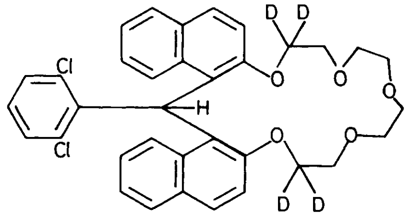
Experimental

The ligands (**2**)–(**5**), and metal salts, and n.m.r. solvents were prepared as described previously.[5,6] ^{1}H N.m.r. spectra were obtained on a Bruker WM300WB instrument at 300 MHz. The solvent eventually used for most of the n.m.r. kinetic studies was a mixture of [$^2H_5$]pyridine–[$^2H_2$]methylene chloride–[$^2H_4$]methanol (45:45:10); this is not the same composition as

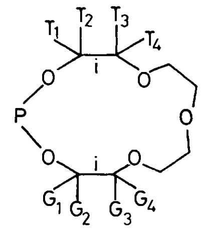


(**1**)

(**2**) $n = 1$
(**4**) $n = 2$
(**5**) $n = 3$



(**3**)



(**6**)

P = propeller
T = proton on segment iT
G = proton on segment iG

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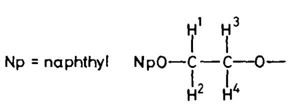
† Dinaphthopolycycloalkin.

Table 1. Chemical shifts[a] of segments for crowns.



Np = naphthyl $\mathrm{NpO{-}\overset{H^1}{\underset{H^2}{C}}{-}\overset{H^3}{\underset{H^4}{C}}{-}O{-}}$

segment i

Segment	Crown	δ(ppm) 1	2	3	4
iG	4	4.171	3.464	3.233	3.358
iG	4, KSCN[b]	4.460	2.711	3.150	3.116
iG	4, NaSCN[b]	4.497	3.117	2.630	3.307
iT	4	3.944	3.091	3.360	3.287
iT	4, KSCN[b]	3.540	2.180	3.240	2.617
iT	4, NaSCN[b]	4.123	2.267	2.983	2.720
iG	2	4.186	2.907	3.356	*ca.* 3.59
iG	2, $NaBPh_4$	4.421	2.386	3.221	3.553
iT	2	3.907	3.096	3.021	3.510
iT	2, $NaBPh_4$	4.001	2.452	2.915	1.962

[a] ^1H N.m.r. spectra taken at 300 MHz in 1:1 mixture of $[^2H_5]$pyridine and CD_2Cl_2 unless otherwise stated. [b] Solvent with 10% CD_3OD added.

Table 2. Coupling constants[a] obtained for crowns (segment i).

Segment	Crown	$J_{1.2}$	$J_{1.3}$	$J_{1.4}$	$J_{2.3}$	$J_{2,4}$	$J_{3.4}$
iG	4	−10.10	8.13	4.42	3.87	4.13	−10.17
iG	4, KSCN[c]	−10.75	10.69	2.20	1.43	2.20	−10.37
iG	4, NaSCN[c]	−10.35	10.46	2.55	2.29	2.08	−10.13
iT	4	−9.57	6.24	6.06	5.80	4.87	−10.09
iT	4, KSCN[c]	−11.85	2.03	6.91	5.72	2.00	−11.00
iT	4, NaSCN[c]	−10.35	2.37	10.49	2.13	2.39	−9.78
iG	2	−10.84	3.53	9.25	2.92	3.56	−10.86
iG	2, $NaBPh_4$	*b*	2.81	10.94	1.79	2.92	−13.23
iT	2	−9.18	6.36	6.88	4.76	6.26	−10.22
iT	2, $NaBPh_4$	−10.85	2.58	9.00	3.76	2.43	−10.31

[a] Spectra run at 300 MHz in 1:1 mixture of $[^2H_5]$pyridine and CD_2Cl_2 unless otherwise stated. [b] Not accessible. [c] Solvent with 10% CD_3OD added.

Table 3. Rate of ligand exchange with sodium complexes[a]/s^{-1}.

T/K	$1/\tau^b$	$1/\tau^c$	$1/\tau^d$
210	4.0×10^3		
220	6.0×10^3		
230	10.0×10^3		
250			26.0×10^3
260		16.0×10^3	40.0×10^3
280		31.0×10^3	70.0×10^3
300		52.0×10^3	110.0×10^3

[a] Exchange rates from simulation of ^1H n.m.r. spectra (DNMR3). Solvent $[^2H_5]$pyridine–$[^2H_2]$methylene chloride–CD_3OD, (45:45:10). [b] Ligand (**4**), 0.05 mol dm^{-3} [NaSCN] 0.025 mol dm^{-3}. [c] Ligand (**3**), 0.02 mol dm^{-3} $[NaBPh_4]$ 0.01 mol dm^{-3}. [d] Ligand (**3**), 0.02 mol dm^{-3} $[NaBPh_4]$ 0.015 mol dm^{-3}. Solvent 1:1 $[^2H_5]$pyridine–CD_2Cl_2.

Table 4. Rates of ligand (**4**) exchange with KSCN complexes[a]/s^{-1}.

T/K	$1/\tau^b$	$1/\tau^c$	$1/\tau^d$
210		0.4×10^2	0.08×10^3
220		0.7×10^2	0.16×10^3
230	0.09×10^3	1.3×10^2	0.32×10^3
250	0.25×10^3		1.20×10^3
270	1.0×10^3		2.50×10^3
280	1.5×10^3		5.0×10^3
290	3.0×10^3		10.0×10^3
297			30.0×10^3
E_A/kcalmol^{-1}	7.3	7.5	7.6

[a] Exchange rates from simulation of ^1H n.m.r. spectra (DNMR3). Initial ligand 0.05 mol dm^{-3}. [b] $[KSCN]_0 = 0.0125$ mol dm^{-3}. [c] $[KSCN]_0 =$ 0.025 mol dm^{-3}. [d] $[KSCN]_0 = 0.0375$ mol dm^{-3}.

used in the earlier sodium n.m.r. studies {where the solvent was pyridine–methylene chloride–$[^2H_2]$methylene chloride (4:3:1), deuteriated solvent being required as lock}. This latter mixture, found suitable for some work with sodium salts, turned out to be unsuitable for the potassium analogues. The solvent choice was extremely limited because of the relevant solubilities of salts and ligands at the lowest temperatures needed for the n.m.r. kinetics, and the trace of methanol eventually used was needed to keep the potassium complex in solution. The original intention to use a typical ISE plasticiser as n.m.r. solvent was thwarted because (*a*) no deuteriated version was available and (*b*) the viscosity of a typical plasticiser was too high for high resolution proton n.m.r. work.

N.m.r. spectra were simulated using NUMARIT[7] to give the shifts and coupling constants in Tables 1 and 2. The proton assignments were checked by spin-decoupling experiments on the easily accessible protons. The kinetic data in Tables 3 and 4 were obtained by visual comparison of the observed spectra with computer-generated spectra, using the computer package DNMR3.[7]

Results and Disscussion

The exchange of other crown-ether ligands with their respective complexes, has been examined previously by use of fast kinetic methods,[8] but very few crown ethers have suitable ^1H n.m.r. shift changes for the application of dynamic n.m.r. methods. This paper reports the results of a detailed ^1H n.m.r. study giving information on structure and mechanism in solution. Data that pertain to mechanism are important in the interpretation of many processes which occur in and at the interface of membranes, such as solvent extraction, three-phase transport, and ISE membranes. Our data refer to kinetics in a single phase, not interphase transfers. However, the relevant interphase processes may have similar mechanisms.

Analysis of the complex proton spectra of propeller crowns[2] enabled complete identification of ether protons of segment i in free and in complexed ligands. For convenience, as in ref. 1, the two differentiable segments i [see formula (**6**)] are referred to by the labels T and G, although it should be appreciated that each is a fluxional mix of *anti* and *gauche* conformers. In Tables 1 and 2 are collected the shifts and coupling constants for the free and complexes crowns (**2**)–(**5**) which are used in this study. Details for some of the free crowns have already been reported.[2] A remarkable feature of these coupling constants is the light they shed on the conformations of the segment i portions. Thus, the free crown-5 (**2**) has been shown to have a proportion of *anti*-conformer in the T segment, but not in the G, while the corresponding crown-6 (**4**) has a proportion of *anti* in both segments.[2] In this work, the coupling constants determined from the n.m.r. spectra of the sodium complex of the crown-6, ligand (**4**), suggest a complete fixed *gauche*-conformer for each segment i [iG and iT, see (**6**)] as expected for co-ordination of all the relevant oxygens to the cation. This is also true for the iG segment of the potassium complex of (**4**), (see Table 2). Unexpectedly, the coupling constants calculated for the iT segment of the potassium complex of this crown, correspond to the average value for two gauche conformers in almost equal population; the inference from this is that the iT segment (but not the iG) is rearranging the complex, since the ligand is lost

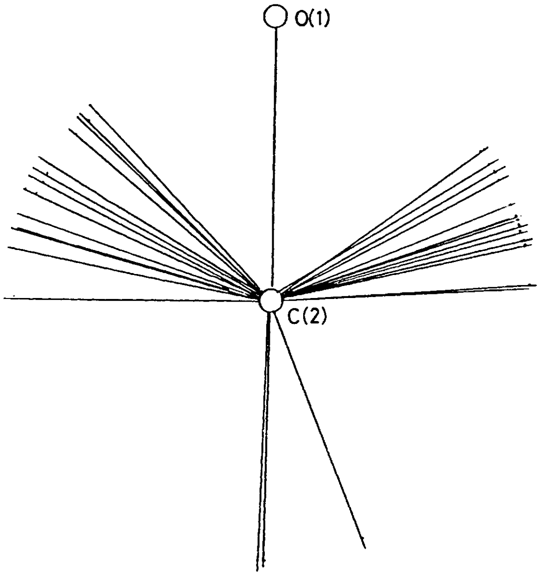


Figure 1. Representation of the torsion of O(1)–C(1)–C(2)–O(2) segments from crystal-structure data for propellers, viewed down the C(2)–C(1) bond and perpendicular to the O(1)–C(1) bond. The position of C(2)–O(2) for each structure is represented by a line at the appropriate angle to O(1)–C(1).

at a slow rate in these systems (see below). The process can be described as ML′ = ML″. It could conceivably take place either by dissociation of one oxygen, which would make the torsional movement energetically easier, with reassociation after rearrangement, or by the torsional change occurring while the ligand is fully bonded to the cation; the results do not differentiate between these two possibilities. It is unlikely that the ligand is fully dissociated to allow the rearrangement, since this would permit both differentiable segments i to have averaged spectra which is not the case. It is seldom that movement of the ligand, while it is still co-ordinated to the cation, has been observed for a crown system; that it has actually been observed in the room-temperature spectra, is a result of the unusually large shifts between protons in the free and complexed ligand. Although the phenomenon is not observed for the NaSCN complex of ligand (**4**), it is possible that a similar, but n.m.r.-transparent, movement occurs in segment ii. It is certainly curious that the movement is observed for the larger, better-fit cation K^+, rather than Na^+. A possible involvement of this segment switch at low temperatures is described in the earlier sodium paper.[5] Structural implications for the corresponding crown-7 (**5**) and its salts were similar to those for (**4**), but the overlap of spectra prevented a complete analysis.

In Figure 1 are displayed the data obtained to date on torsion angles of the ether ring segments O–C–C–O from the crystal structures of propeller crowns and their salt complexes.[9] Free crowns have *gauche* oxygens, except in segment i, where three of the observed torsion angles are *anti.* In the complexes the O–C–C–O torsion angles are all *gauche.* The striking visual display of the occurrence of *gauche* and *anti* segments for propeller crowns, in a series of superposed O–C–C–O segments taken from the crystal data already published shows that the distribution is overwhelmingly between the two possible *gauche* placements, except for the three *anti* placements already referred to; it is consistent with the proportion of *anti* segments estimated from the averaged n.m.r. spectra.

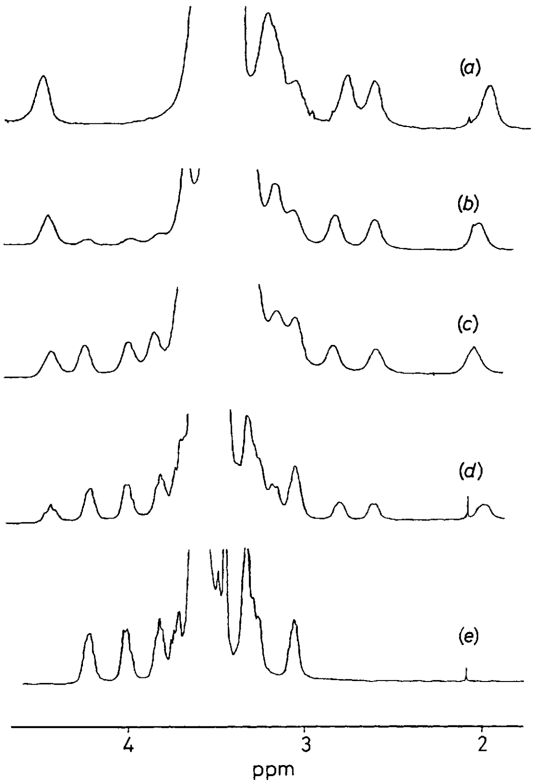


Figure 2. ^1H N.m.r. spectra of ether segment at 200 K for 0.05 mol dm^{-3} of ligand (**4**) in $[^2H_5]$pyridine/CD_2Cl_2, containing the following amounts of KSCN: (*a*) 0.05 mol dm^{-3} (*b*) 0.075 mol dm^{-3} (*c*) 0.025 mol dm^{-3} (*d*) 0.0125 mol dm^{-3} (*e*) Free crown.

It was also possible to make a kinetic investigation. The free ligands were shown to have a proportion of *anti*-conformer (appropriate averaged coupling constants) for their segments i, such that a T–G equilibrium just began to slow at low temperatures on the n.m.r. timescale. In the complex, the segments are likely to have *gauche* oxygens, when co-ordinated to the metal cation, so that the n.m.r. chemical shifts change (hundreds of Hz in the most dramatic case). This fortunate circumstance located the ligand exchange on the n.m.r. timescale. In Figure 2 we show portions of the ether spectra for mixtures of ligand (**4**), the dichloro substituted crown-6, and KNCS, at various temperatures. The protons numbered T2 and G1 *etc.* on formula (**6**) provided several different windows with which to view the timescale of the exchange. Additional rate information could be obtained from the t-butyl signals and the phenyl ABC protons of the triaryl section. In Figure 3 are shown the spectra of the free ligand (**2**), and its complex with $NaBPh_4$ indicating the shift changes which occurred on complexation. In this instance, the kinetics were determined using the deuteriated segment i [ligand (**3**), used earlier in ref. 2], which simplified the segment i spectra to AB systems. The several sets of rate constants and activation parameters are collected in Tables 3 and 4. The exchange rates for the free ligand (**4**) with either its sodium or potassium complex show that the exchange on the potassium complex is slower than on the sodium complex. The rate ratio Na:K (by extrapolation) is approximately 100 at room temperature for this ionophore, the crown-6 (**4**).

Concentration Variation.—A set of solutions with a constant concentration of crown ligand but with different ratios of ligand to metal salt, was analysed by n.m.r. using the DNMR3 package to determine the dependence of the exchange rate on concentration, for ligands (**3**) and (**4**). The Shchori[10] treatment is applicable here {[equation (4)], derived from the mechanism represented by equations (1) and (3), for excess ligand L}, for ligands (**3**) with $NaBPh_4$ and (**4**) with KNCS only, since the overlap of signals, or high rates, prevented full analysis of other reactions.

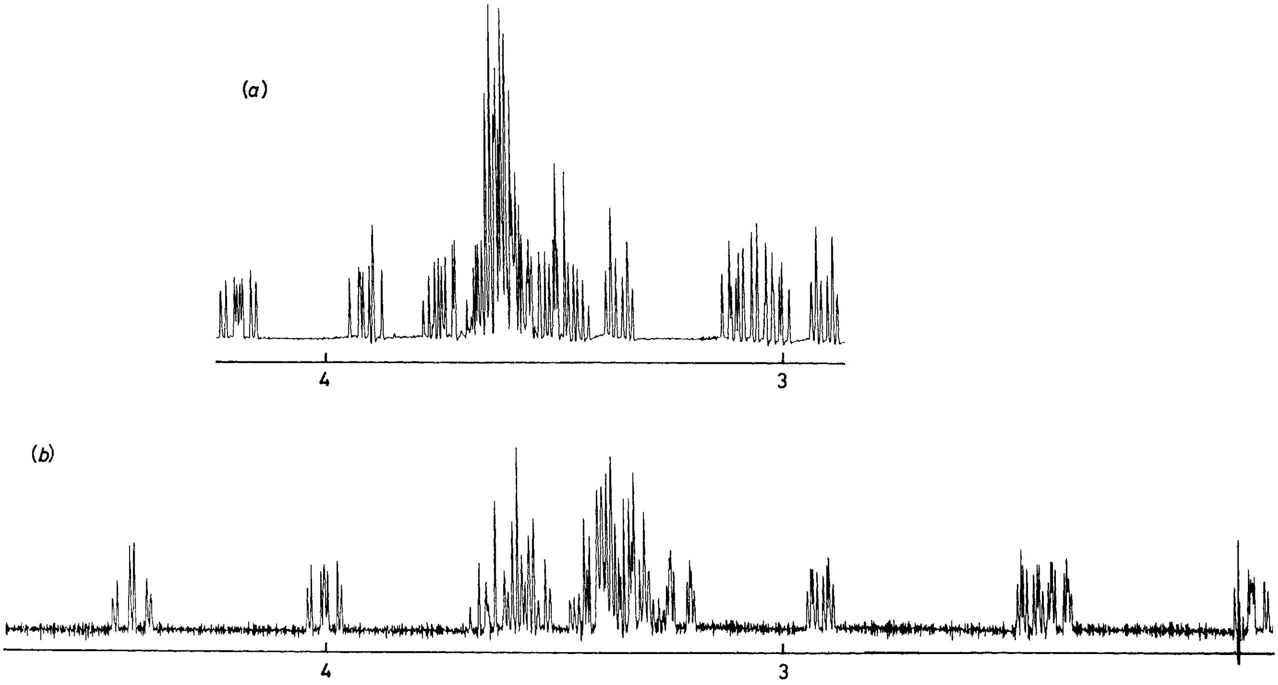


Figure 3. Comparison of ^1H n.m.r. spectra (ether region) of (*a*) crown 2 in $CD_2Cl_2/[^2H_5]$pyridine; (*b*) crown 2 and excess $NaBPh_4$ in $CD_2Cl_2/[^2H_5]$pyridine.

Table 5. Rate constants derived from Shchori plots for ligands (**3**) and (**4**), derived from data in Tables 3 and 4.

	Ligand (**4**), KNCS		Ligand (**3**), $NaBPh_4$	
T/K	k_{-1}/s^{-1}	$k_2/dm^3\ mol^{-1}\ s^{-1}$	k_{-1}/s^{-1}	$k_2/dm^3\ mol^{-1}\ s^{-1}$
210	3	1.4×10^3		
220	1×10	3.0×10^3		
230	2.5×10	6.2×10^3		
240	6.0×10	1.2×10^4		
250	1.2×10^2	2.2×10^4		
260	2.3×10^2	3.7×10^4	1.1×10^4	5×10^5
270	4.2×10^2	6.2×10^4		
280	7.4×10^2	1.0×10^5	1.6×10^4	1.5×10^6
290	1.3×10^3	1.5×10^5		
300	2.0×10^3	2.4×10^5	2.2×10^4	3.0×10^6

[a] k_{-1} values $\pm 25\%$, k_2 values $\pm 10\%$ from regression at room temperature; progressively higher at lower temperatures.

For dissociative and bimolecular steps operating together:

$$1/\tau = k_{obs} = k_2[B] + k_{-1}[B]/[A] \qquad (4)$$

where B = [ML] and A = [L] (excess L). A plot of $k_{obs}/[B]$ *versus* $1/[A]$ gives k_{-1} and k_2.

From the intercepts on the Shchori plots of $1/\tau_A[B]$ *versus* $1/[A]$ at various temperatures the second-order rate constants k_2 [corresponding to equation (3)] may be determined. The slopes correspond to first-order dissociation rate constants k_{-1} [from equation (1)]. This secondary data (k values) is shown in Table 5, and potential errors in the derivation of rate constants from primary data, and in the experimental procedure are quoted. For ligand (**4**) with KNCS, the Arrhenius activation energy for k_2 is 7.3 kcal mol^{-1} * essentially the same as that obtained for the observed exchange rates $^1/\tau_A$. Any contribution from the dissociative rate (rate constant k_{-1}, obtained from the slopes) is small at the relatively high concentrations required for n.m.r. work. The mechanistic path of equation (3), ligand displacement on metal ion, is, thus, the appropriate one in this system. This is envisaged as the most realistic way to transfer ligand in, for example a mobile membrane, where there is high concentration of ligand and complex. However, for crown (**3**) in reaction with its $NaBPh_4$ complex, the dissociative path contributes relatively more.

Competition.—There is a competition between second-order routes for the exchange, dependent both on concentration and on temperature. The Arrhenius energies show that at low temperatures the exchange process [equation (3)] is significant, while at higher temperatures, the dissociative path becomes relatively more important. Clearly, the competition between the two processes will depend on the concentrations in the mixture. The competition will, thus, be at different levels in each mixture to be considered.

Comparisons.—It is possible to compare the dissociative rate constant at 260 K for crown (**3**) from the data in Table 5 with the value for ligand (**2**) obtained in the work on sodium,[5] in virtually the same solvent; the present results were obtained at one tenth the concentration of $NaBPh_4$ used in the sodium n.m.r. work. The relevant rate constants are 11×10^3 for crown (**3**) obtained from the ^1H n.m.r. data in this work, and 3.4×10^3 s^{-1} from the sodium n.m.r. data. While these values are for ligands differing in the naphthyl substituent in the 6 position, they agree within an order of magnitude, providing a check on consistency. Unfortunately, we were unable to make a direct comparison of the dissociative rate constants for K and Na complexed to the same ligand. Note that the magnitude of the Na dissociative rate constants at one particular temperature (range of ligands in ref. 5), is considerably greater than for the K dissociation rates for (**4**).

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* 1 cal = 4.184 J.

Implications for Selectivity in ISE and Three-phase Membranes.—The discoveries made show that where there is excess ligand, there is a second-order exchange which will be dependent on localised concentration of ligand. This is likely to occur in the membrane interior, and the exchange rate is likely to be faster for Na than K [at least for ligand (**4**)]. If this process is significant in transmitting the electrical effect of an entrant cation through the membrane of a potassium-selective ISE for example, conceivably it could reduce the overall K/Na selectivity over that obtained at the membrane interface, since the effect will be transmitted faster for Na than for K by a factor of *ca.* 100. However, the concentration of species within the membrane is an over-riding factor, and the following arguments will show that the dissociation path [reverse of equation (1)] is actually more likely than the ligand exchange path [equation (3)] in real selective devices. We consider several cases, relating to ISE and three-phase transport.[3,4] Some data relating to selectivity of these or similar ligands for K and Na is available. If we suppose we have a typical K-selective membrane, with ionophore [ligand (**4**)] at the usual concentration, containing $KBPh_4$ (0.5 mol equiv.) and assume (*i*) rate constants similar to those in Table 5 (*ii*) that the membrane is homogeneous and (*iii*) that it has the density of the plasticiser (*iv*) [ligand] = [Kcomplex] = 0.007 mol dm^{-3}, then the half life of ligand reacting by the second-order route at this concentration is *ca.* 0.0009 s at 290 K. A first-order process with a rate constant of 770 s^{-1} would give an equal half life, so that for first-order components of higher rate constant, the process is increasingly dissociative in character. In the three-phase transport, however, the concentration of ligand is *ca.* 0.001 mol dm^{-3}, giving a half-life of 0.0067 s for the second-order process; in this instance a first-order process becomes competitive at a rate constant of 104 s^{-1}. This is also the concentration used by Todd and Armstrong in their impedance studies[11] with specimen ISE membranes rather than the seven fold higher concentration mentioned above. Thus it seems likely that at the concentrations prevailing in practice, the turnover in the exchange process is by a dissociative route for all these selective systems. Efforts to find a system in which a direct comparison of rates for K and Na systems can be made, continue. However, the arguments given in ref. 1 are still appropriate.

Acknowledgements

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