

## THE ION–DIPOLE INTERACTION MECHANISM OF MACROCYCLIC ETHERS WITH $^{13}\text{C}$ DIPOLE–DIPOLE RELAXATION TIME MEASUREMENTS.

### Part 9. The stabilities of 18-crown-6 complexes with $\text{Na}^+$ and $\text{K}^+$ in $\text{D}_2\text{O}$ and methanol-d

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#### ABSTRACT

The stabilities of various stoichiometries of the 18-crown-6 ether complexes with  $\text{Na}^+$  and  $\text{K}^+$  in methanol-d and  $\text{D}_2\text{O}$  were estimated by means of an NMR method using  $^{13}\text{C}$   $T_1$  relaxation time measurements. The experimental coordination conditions were established by maintaining an identical ion/ligand concentration. The evidence was evaluated using the expression of dependence of the mole fraction of the bound ligand,  $P_{\text{AE}}$ , to the experimental dipole–dipole relaxation time,  $T_1^{\text{obs}}$ :  $P_{\text{AE}} = (1/T_1^{\text{obs}} - 1/T_E)/(1/T_{\text{AE}} - 1/T_E)$ . The equilibrium constants  $K_e$  for complex formation were obtained through the expression and regression of  $1/K_e[E_0]^{n+m-1} = (1 - nP')^n(1 - mP')^m/P'$  where  $P' = P_{\text{AE}}/(1 + P_{\text{AE}}(m - 1))$ . The existence of various  $n:m$  ratios of complexes in solution has also been verified with the simulation of the  $T_{\text{AE}}$  behaviour for each stoichiometry.

#### INTRODUCTION

The nature of the ion–dipole interactions of macrocyclic ethers and their derivatives has been investigated in several ways [1–3]. Recently, NMR spectroscopy utilizing  $T_1$  relaxation time measurements of the macrocyclic backbone of free and complexed ligands in solution has provided a new way of approaching this topic [4–13]. Accordingly, we have initiated the investigation of the  $^{13}\text{C}$  dipole–dipole relaxation time of cyclic oligo ethers in free and cationic solutions (eqns. (1) and (2) [14–16]. In fact, the effect of the cation on the relaxation time of  $^{13}\text{C}$  nuclei is quite remarkable, as has been shown by Eliasson et al. [5] and by Echevoyen et al. [2].

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Accordingly, the dipole–dipole relaxation time of a carbon nucleus under extreme narrowing conditions can be given as [9,11]

$$T_1^{\text{obs}} = T_1^{\text{DD}} = T_1^{\text{exp}} 1.99 / \eta_{\text{CH}} \quad (1)$$

$$1/T_1^{\text{DD}} = 3/2 h^2 \gamma_{\text{C}}^2 \gamma_{\text{H}}^2 r_{\text{CH}}^{-6} \tau_{\text{eff}} \quad (2)$$

Note that both proton  $T_1$  and  $T_2$  measurements are affected by intermolecular and intramolecular interaction mechanisms and by translational jumps, but  $^{13}\text{C}$  relaxation time measurements allow, in particular, the estimation of intermolecular interactions of internal motions which could be identified with nuclear Overhauser enhancement measurements as described for  $\text{CH}_2$  groups in eqn. (1) [3,11,13].

## EXPERIMENTAL

The 18-crown-6 ether (Aldrich) was purified by redistillation at low pressure and dissolved in methanol-d or  $\text{D}_2\text{O}$  at appropriate concentrations. Alkali salts were dried under vacuum. The semi-micro free and salt/crown ether containing samples were prepared separately to desired concentrations using micro-pipettes with analytical graduations and transferred into 10-mm NMR tubes, which were then degassed under  $10^{-3}$  Torr pressure and sealed.

The  $^{13}\text{C}$  dipole–dipole relaxation time determinations were carried out on a JEOL spectrometer (Model FX-60Q) at 15 MHz and 2000 Hz sweep width, with the inversion recovery method. The inversion recovery measurements were carried out with an autostacking software program supplied by JEOL. Pulse sequences of 180– $t$ –90 were applied with pulse interval times in the range of  $0.1T_1 < t < 5T_1$  [16]. The relaxation time values were obtained from the least-squares slope of the plot of log magnetization vs. pulse interval times.

Measurements of the nuclear Overhauser enhancement (NOE) of the samples were conducted with exactly the same experimental settings used for longest pulse interval time under completely decoupled and pulse modulated decoupled resonance conditions.

## RESULTS AND DISCUSSION

In cationic solutions of macrocyclic ethers a decrease was observed in the  $^{13}\text{C}$   $T_1$  values in going from free to complexed ligands due to the strong ion–dipole interaction. The strength of the ion/ligand complexation is a function of the structure of the ligand sphere and the residence time of the cation; therefore, the observed  $T_1$  difference should be a measure of the binding ability.

The relaxation time of exchanging free and complexed sites has been discussed by Frahm and Strehlow [12] in terms of the lifetimes of both sites and they explained that the increased lifetime of a complexed ligand site results in a short relaxation time for a molecule. Hertz and coworkers [3,13] have shown that the observed inverse relaxation time of a ligand in a salt solution can be given as the sum of the inverse relaxation times of thermodynamically distinct species proportional to their mole fractions.

$$1/T_1^{\text{obs}} = P_1/T_1 + \sum_{m,n} (P_{mn}/T_{mn}) \quad (3)$$

From the ligand/ion complex formation equilibria shown in eqns. (4) and (5), the eqns. (6) and (7) were established for the cases in which there are identical initial ligand/cation concentrations. Equations (8) to (10) are then derived for the estimation of the equilibrium constants,  $K_e$ , where the mole fraction of the complexed ligand,  $P_{AE} = [A_n^+ E_m]/[E] + [A_n^+ E_m]$ , and therefore  $P_{AE} = [A_n^+ E_m]/\{[E_0] - (m-1)[A_n^+ E_m]\}$ , is obtained. If the initial cation concentration  $[A_0^+]$  is kept identical to the initial ligand concentration,  $[E_0]$ , the following relationships apply:



$$K_e = [A_n^+ E_m]/[A^+]^n [E]^m \quad (5)$$

$$K_e = [A_n^+ E_m]/([A_0^+] - n[A_n^+ E_m])^n ([E_0] - m[A_n^+ E_m])^m \quad (6)$$

If  $P' = P_{AE}/(1 + P_{AE}(m-1))$  is used for a simple expression then  $K_e$  is given by

$$K_e = P' [E_0]/([E_0] - nP' [E_0])^n ([E_0] - mP' [E_0])^m \quad (7)$$

Consequently, eqn. (8) can be applied to experimental studies for  $n = 1$  and  $m = 1$  in a 1:1 complex, while eqn. (9) is used for 1:2 complex formation and eqn. (10) can be used for multiple degrees of complex formation.

$$1/K_e [E_0] = (1 - P')^2 / P' \quad (8)$$

$$1/K_e [E_0]^2 = (1 - P')(1 - 2P')^2 / P' \quad (9)$$

$$1/K_e [E_0]^{m+n-1} = (1 - nP')^n (1 - mP')^m / P' \quad (10)$$

The  $P_{AE}$  value of a complexed ion or ligand mole fraction obtained by any analytical measurement may be plotted against the inverse ligand or cation concentration, and the slope gives the inverse of the equilibrium constant of the ion-dipole interaction [10,14,15].

In the case of relaxation-time measurements of cationic ligand solutions, regarding eqn. (3) the mole fraction of complexed ligand  $P_{AE}$  is given by eqn. (11) in terms of the particular relaxation times of complexing sites.

$$P_{AE} = (1/T_1^{\text{obs}} - 1/T_E)/(1/T_{AE} - 1/T_E) \quad (11)$$

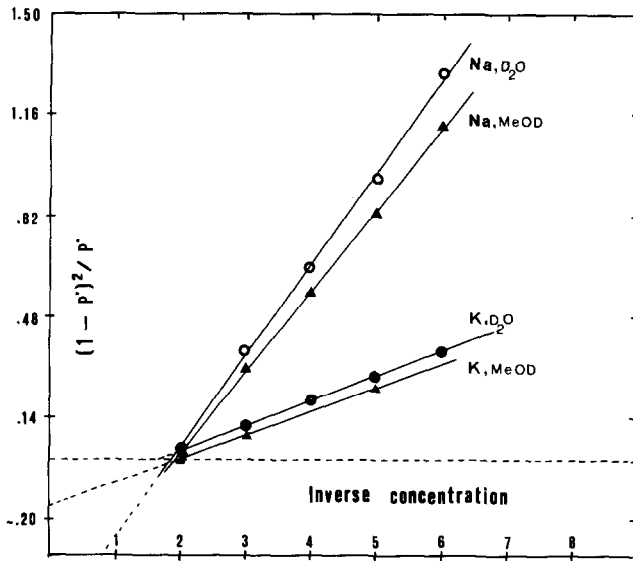


Fig. 1. The dependence of the mole fraction of complexed species,  $(1 - P')^2 / P'$ , on the inverse ligand concentration,  $1/[E_0]$ , for a 1:1 complex of 18-crown-6 ether and cations.

The experimental complex formation conditions were arranged by maintaining an identical ion/ligand concentration; the expression for the dependence of the mole fraction of a bound ligand on the experimental  $T_1^{\text{obs}}$  values was used [3,10] and experimental  $K_e$  values were obtained. For

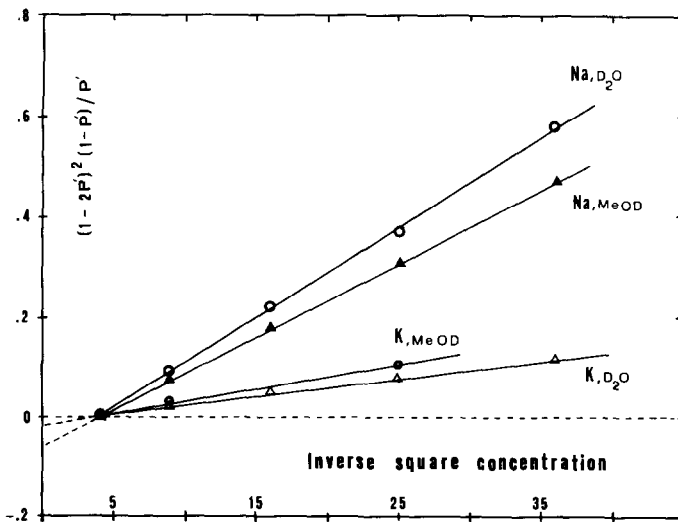


Fig. 2. The dependence of the mole fraction of complexed species,  $(1 - 2P')^2 (1 - P') / P'$ , on the inverse square ligand concentration,  $1/[E_0]^2$ , for a 2:1 complex of 18-crown-6 ether and cations.

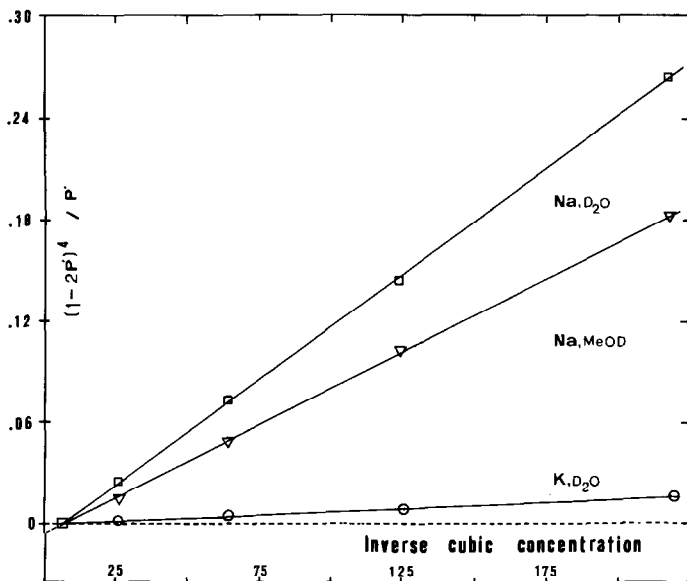


Fig. 3. The dependence of the mole fraction of complexed species,  $(1-2P')^4/P'$ , on the inverse cubic ligand concentration,  $1/[E_0]^3$ , for a 2:2 complex of 18-crown-6 ether and cations.

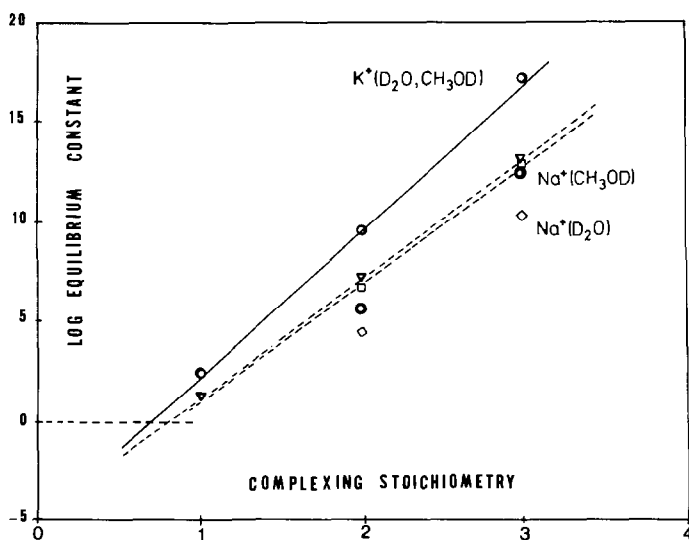


Fig. 4. The dependence of log equilibrium constants on the stoichiometries of the ligand or cation in solution. (—)  $K^+$  and (---)  $Na^+$  ligand/ion ratios of identical  $n$  and  $m$ ; (····) non-identical cases.

TABLE 1

$^{13}\text{C}$   $T_1$  parameters of free and cationic solutions, and mole fraction of complexed ligand of 18-crown-6/sodium chloride for a 1:1 complex stoichiometry in  $\text{D}_2\text{O}$  at 15 MHz:  $\log K_e = -1.182$ ; correlation coefficient = 0.9990;  $y$  intercept =  $-0.5701$

$1/\text{const.}$	$T_1^{\text{obs}}$ <sup>a</sup>	$T_E$ <sup>b</sup>	$P_{\text{AE}}$ <sup>c</sup>	$(1 - P')^2/P'$ <sup>d</sup>	Error <sup>e</sup>
2.000	1.939	2.429	0.818	0.043	0.002
3.030	2.137	2.622	0.549	0.351	0.019
4.000	2.264	2.777	0.456	0.656	0.099
5.000	2.365	2.878	0.394	0.963	0.031
6.024	2.453	2.936	0.338	1.277	0.022

<sup>a</sup> Experimental dipole-dipole relaxation time of cation/crown ether. <sup>b</sup> Experimental dipole-dipole relaxation time of free crown ether in solution. <sup>c</sup> Experimental mole fraction of ligand/crown ether in solution. <sup>d</sup> Least-squares data from the mole fractions of the ligand/crown ether in solution. <sup>e</sup> Error of least-squares data from the experimental mole fractions of the ligand/crown ether in solution.

example, if the inverse of the  $[\text{E}_0]$  and  $[\text{E}_0]^2$  values for a cation are plotted vs.  $(1 - P')^2/P'$  and  $(1 - P')(1 - 2P')^2/P'$  excellent results are obtained, showing the different ligand/ion stoichiometries.

In fact, measurements of the 18-crown-6 complexation have been made in several different ways previously. However, the increasing complex formation stoichiometries gave rise to higher  $K_e$  values, which was also observed in the potentiometric  $K_e$  measurements reported recently [15]. The  $T_{\text{AE}}$

TABLE 2

$^{13}\text{C}$   $T_1$  parameters of free and cationic solutions, and mole fraction of complexed ligand of 18-crown-6/sodium chloride for a 2:1 complex stoichiometry in  $\text{D}_2\text{O}$  at 15 MHz:  $\log K_e = 4.037$ ; correlation coefficient = 0.9997;  $y$  intercept =  $-0.00689$

$1/(\text{const.})^2$	$T_1^{\text{obs}}$ <sup>a</sup>	$T_E$ <sup>b</sup>	$P_{\text{AE}}$ <sup>c</sup>	$(1 - P')$ $(1 - 2P')^2$ $/P'$ <sup>d</sup>	Error <sup>e</sup>
4.000	1.938	2.429	0.942	0.002	0.000
9.295	2.136	2.621	0.615	0.090	0.002
16.000	2.263	2.776	0.504	0.213	0.003
25.000	2.364	2.878	0.432	0.372	0.008
36.289	2.453	2.935	0.369	0.572	0.038

<sup>a</sup> Experimental dipole-dipole relaxation time of cation/crown ether in solution. <sup>b</sup> Experimental dipole-dipole relaxation time of free crown ether in solution. <sup>c</sup> Experimental mole fraction of ligand/crown ether in solution. <sup>d</sup> Least-squares data from the mole fractions of ligand/crown ether in solution. <sup>e</sup> Error of least-squares data obtained from the mole fractions of ligand/crown ether in solution.

TABLE 3

$^{13}\text{C}$  dipole-dipole relaxation time and complex formation parameters of 18-crown-6/NaCl in  $\text{D}_2\text{O}$  at 303 K

Stoichiometry <sup>a</sup>	$T_{\text{AE}}$ <sup>b</sup>	$\log K_e$	$-\Delta G$ <sup>c</sup> (kcal mol <sup>-1</sup> )	Intercept <sup>d</sup>
1:1	1.855	1.182	0.711	-0.5701
2:1	1.915	4.037	2.429	-0.0069
1:2	1.595	3.571	2.148	-0.1083
2:2	1.835	6.685	4.022	-0.0009
3:2	1.925	9.836	5.918	0.0000
3:3	1.820	12.643	7.608	0.0000

<sup>a</sup> The ratio of the ligand to the cation. <sup>b</sup> The simulated relaxation time of fully complexed ligand. <sup>c</sup> The free energy of complex formation at 303 K. <sup>d</sup> The intercept of Figs. 1-3.

values for the complexed ligand obtained by means of linear regression of eqn. (8) or (9) gave quite satisfactory results for ion-ligand interactions and were free of even experimental concentration optimizations. Typical relationships for  $\text{Na}^+$  and  $\text{K}^+$  are shown in Figs. 1-4. The  $y$  intercept of these plots comes closer to zero as the ion/ligand ( $n:m$ ) ratio is increased, providing further evidence for the existence of multiple degrees of complex formation. Changes in the relaxation times of the encapsulated structure were observed and the  $\log K_e$  values change dramatically with complex stoichiometry. It is therefore concluded that the ion/macrocyclic ligand systems are apparently aggregated and what is actually observed when making measurements on complexing is the gradual dissociation of the ion/ligand structure (Tables 1-4 and Figs. 1-4) [17].

TABLE 4

$^{13}\text{C}$  dipole-dipole relaxation time and complex formation parameters of 18-crown-6/KCl in  $\text{D}_2\text{O}$  at 303 K

Stoichiometry <sup>a</sup>	$T_{\text{AE}}$ <sup>b</sup>	$\log K_e$	$-\Delta G$ <sup>c</sup> (kcal mol <sup>-1</sup> )	Intercept <sup>d</sup>
1:1	2.060	2.470	1.486	-0.14190
2:1	2.100	5.641	3.394	-0.00120
2:2	2.075	9.435	5.677	-0.00008
3:2	2.105	12.474	7.506	0.00000
3:3	2.060	16.889	10.889	0.00000

<sup>a</sup> The ratio of the ligand to the cation. <sup>b</sup> The simulated relaxation time of the fully complexed ligand. <sup>c</sup> The free energy of complex formation at 303 K. <sup>d</sup> The intercept of Figs. 1-3.

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