^{13}C and ^{23}Na n.m.r. studies of the interactions between cations and kryptofix (2,2) bound to soluble or gel polyacrylamide

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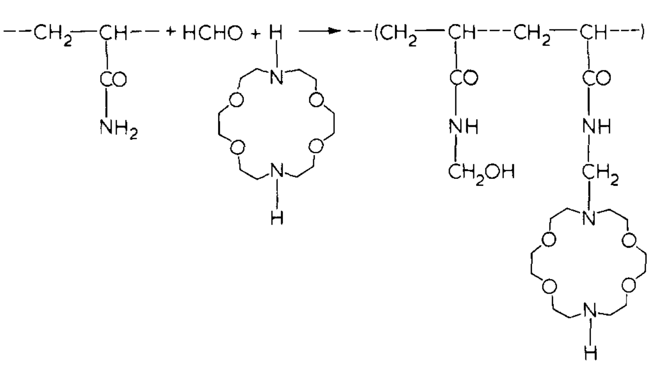
Interactions between univalent cations (Li^+, Na^+, K^+, Ag^+) and bivalent cations (Ba^{2+}, Ca^{2+}) with kryptofix (2,2) substituted polyacrylamide have been investigated using ^{13}C n.m.r. The tendency to form complexes involves the dimensions of both the hydrated ion and the cavity size macrocycle and for Ag^+ the nature of the interaction site. The sensitivity of the ^{23}Na n.m.r. method for detecting complex formation in solution from macromolecular species has been applied to the determination of the conditional formation constants of Na^+ and Ba^{2+} complexes.

Keywords Nuclear magnetic resonance; carbon 13; sodium 23; polyacrylamide; 1,10-diaza-18-crown 6; complexation; formation constant

INTRODUCTION

The synthesis of acrylamide gels with kyptofix (2,2) as the anchor group and their complexing ability have been described in a previous paper[1]. Ion extraction and chromatographic studies have shown that the resins are selective for alkali and alkaline earth cations.

Changes in ^1H, ^{13}C and ^{23}Na resonance spectra of alkali metal complexes of crown ligands and cryptands have been correlated with complex formation[2-9] or conformation[10]. Here we report on data analysis and interpretation of the interaction obtained from ^{13}C and ^{23}Na n.m.r. between some cations and macrocycles grafted to water soluble or gel polyacrylamide. The formation of complexes with several ions is detected and the conditional formation constants with Na^+ and Ba^{2+} ions are determined. The grafting of linear polyacrylamide is made by the Mannich reaction with kryptofix (2,2):



A similar reaction occurs in the preparation of kryptofix (2,2) substituted gel[1].

EXPERIMENTAL

Grafted polymer synthesis

Polyacrylamide was prepared by dissolving in a mixture of H_2O/ethanol (250 ml/100 ml), acrylamide (25 g) and potassium persulphate (0.5 g). The temperature was raised to 70°C and maintained for 4 h. A polymer of rather low molecular weight ($\bar{M}_n = 23\,000$), according to viscosity measurements[11], was recovered by precipitation in EtOH. Polyacrylamide (1.5 g, 21 mmol), was dissolved in 50 ml H_2O and formaldehyde (0.63 g, 21 mmol), LiOH (0.5 g) and kryptofix (2,2) (5.5 g) were added to the polymer solution. The mixture was left at room temperature for 3 h. The modified polymer was recovered by ultrafiltration on a PTGC type Millipore membrane and freeze-drying.

The polymer is characterized by its capacity expressed in meq/g of dry polymer and determined by potentiometric titration. The measurements were performed by back titration with base (0.2 Me_4NOH, so as to avoid complexation of the cation): 0.080 g grafted polymer were dissolved in 20 ml of supporting electrolyte (0.1 M tetramethylammonium chloride) and this solution was previously acidified to pH 2. A TACUSSEL TITRIMAT apparatus was used with TACUSSEL electrodes (glass and calomel reference).

Reagent grade salts were obtained from PROLABO. The metal salts were the chlorides except for Na^+, and Ag^+.

Instrumentation

^{13}C n.m.r. spectra were run in D_2O at 28°C using a VARIAN spectrometer model CFT 20.

The chemical shifts are expressed in ppm downfield from an external TMS reference. A negative shift indicates

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a downfield shift. $\Delta\delta$ values are based on perturbed system minus unperturbed system.

^{23}Na n.m.r. spectra were obtained with a VARIAN spectrometer model FT 80. No chemical shift variation was observed when adding increasing amounts of polymer to a 0.1 M $NaNO_3$ solution. Spin-lattice relaxation times T_1 were measured at 28°C by the conventional (180°, τ, 90°, $5T_1$) sequence with at least 15 τ values between 0.01 T_1 and 3 T_1. Logarithmic plots of the magnetization return to equilibrium always appeared quite linear within the experimentally accessible region for τ, least-square fits of these plots gave correlations superior to 97%. The reproducibility was better than 10%.

Additional measurements were run at 44°C and 53°C in order to get more information about the nature of the exchange processes. Half-width values were used to estimate the spin–spin relaxation T_2.

METHOD OF CALCULATION

In our systems the quadrupolar ($I=3/2$) ^{23}Na ion is exchanging between the free aqueous state and the coordination site of a slowly reorienting macromolecule according to the equilibrium:

$$Na^+ + P \rightleftarrows Na\,P \qquad (1)$$

As we observed that T_2 decreased more than T_1 with increasing amounts of polymer, the extreme-narrowing condition is certainly not fulfilled at the bound site; and the linearity of our logarithmic plots is only then apparent and this means that the two time constants should differ by less than a factor two. For such systems there is an approximate solution from which the real value of the relaxation rates in the bound state cannot be extracted[12].

However, the expression of the observed relaxation rate also depends on the exchange rate. As from previous results[1], the conditional formation constants are not expected to be large and a rapid exchange condition should apply in our systems[13]. Moreover the excess likewidth between 0.1 M $NaNO_3$ and the same solution containing the polymer were observed to decrease from 28°C to 53°C for a given amount of polymer and, as a result, rapid exchange occurs for T_2[14] and accordingly for T_1, and the observed relaxation rate will be given by:

$$\frac{1}{T_1}=\frac{p_f}{T_{1f}}+\frac{p_b}{T_{1b}^*} \qquad (2)$$

where p_f and p_b are the respective mole fractions of free and bound ion, T_{1f} is the spin-lattice relaxation time of the free ion, T_{1b}^* is the linear combination of the two theoretical time constants at the bound state in the above approximation. The same expression holds for T_2 since there is no chemical shift variation.

Defining $[P]_f$ as the concentration of unoccupied sites and K_1 the dissociation constant for equation (1):

$$K_1=\frac{[P]_f[Na]_f}{[P\,Na]} \qquad (3)$$

$[Na]_b$ (concentration of Na^+ bound to the polymer) can be calculated:

$$2[Na]_b=[Na]_t+[P]_t+K_1-[([Na]_t+[P]_t+K_1)^2-4[P]_t[Na]_t]^{1/2} \qquad (4)$$

This equation contains two undetermined parameters $[Na]_b$ and K_1 with 2 independent variables $[R]_t$ and $[Na]_t$. This relationship is solved iteratively using a procedure described by Reuben *et al.*[15]. Since $[Na]_t=[Na]_b+[Na]_f$, equation (2) gives:

$$\frac{1}{T_1}=\frac{1}{T_{1f}}+p_b\left(\frac{1}{T_{1b}^*}-\frac{1}{T_{1f}}\right) \qquad (5)$$

A plot of $\frac{1}{T_1}$ *versus* p_b (calculated from equation (4)) should be linear with a slope of $\left(\frac{1}{T_{1b}^*}-\frac{1}{T_{1f}}\right)$ and an intercept on the ordinate of $1/T_{1f}$. K_1 is the value which gives the best fit to equation (5).

Analysis from competition experiments

When a variable concentration of Ba^{2+} ion is added to a solution of ligand and Na^+ ion at the same concentration, the selectivity of Ba^{2+} *versus* Na^+ can be deduced from ^{23}Na T_1 measurements.

In addition to equation (1), the formation of the complex with Ba^{2+} has to be considered:

$$P+Ba^{2+}\rightleftarrows P\,Ba \qquad (6)$$

The dissociation constant K_2 is given by:

$$K_2=\frac{[P]_f[Ba]_f}{[PBa]} \qquad (7)$$

Using the following relations:

$$[P]_t=[P]_f+[PNa]+[PBa] \qquad (8)$$

$$[Na]_f=[Na]_t(1-p_b) \qquad (9)$$

$$[Ba]_f=[Ba]_t-[P]_t+p_b[Na]_t \qquad (10)$$

$$[PBa]=[P]_t-p_b[Na]_t \qquad (11)$$

The ratio $\frac{K_2}{K_1}=K'$ can be calculated and it depends on three independent variables $[Ba]_t$, $[P]_t$ and $[Na]_t$:

$$K'=\frac{p_b}{1-p_b}\,\frac{([Ba]_t-[P]_t+p_b[Na]_t)}{([P]_t-p_b[Na]_t)} \qquad (12)$$

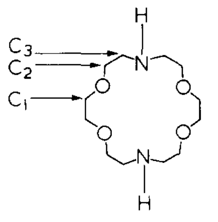
Using the T_{1f} and T_{1b}^* values calculated above for the Na^+/polymer complex, we firstly calculated:

$$p_b=\frac{1/T-1/T_{1f}}{\frac{1}{T_{1b}^*}-\frac{1}{T_{1f}}} \qquad (13)$$

and K' for each value of p_b, found the average K', and calculated p_b based on this average:

$$p_b=\frac{([Ba]_t-(1-K')[P]_t+K'[Na]_t)+\{([Ba]_t-(1-K')[P]_t+K'[Na])_t^2+4(1-K')[Na]_t[P]_tK'\}^{1/2}}{2(1-K')[Na]_t} \qquad (14)$$

Table 1 ^{13}C n.m.r. shifts of the kryptofix (2,2) in D_2O (0.38 mol. dm^{-3}) and in presence of ions. Shifts are in ppm from TMS



Ion	C_1	C_2	C_3
H^+ pH ≈ 10	−71.1	−70.95	−48.97
H^+ pH ≈ 7	−71.05	−66.92	−48.92
H^+ pH < 1	−71.05	−66.88	−48.92
Li^+	−71.06	−70.90	−48.93
Na^+	−71.06	−70.90	−48.92
K^+	−71.06	−70.92	−48.95
$\overset{+}{N}H_4$	−71.06	−71.0	−48.92
$(C_2H_5)_4 N^+$	−71.04	−70.87	−48.90
Ca^{2+}	−70.7	−70.43	−48.77
Ba^{2+}	−72.6	−71.46	−49.96
Ag^+	−70.46	−70.23	−52.0

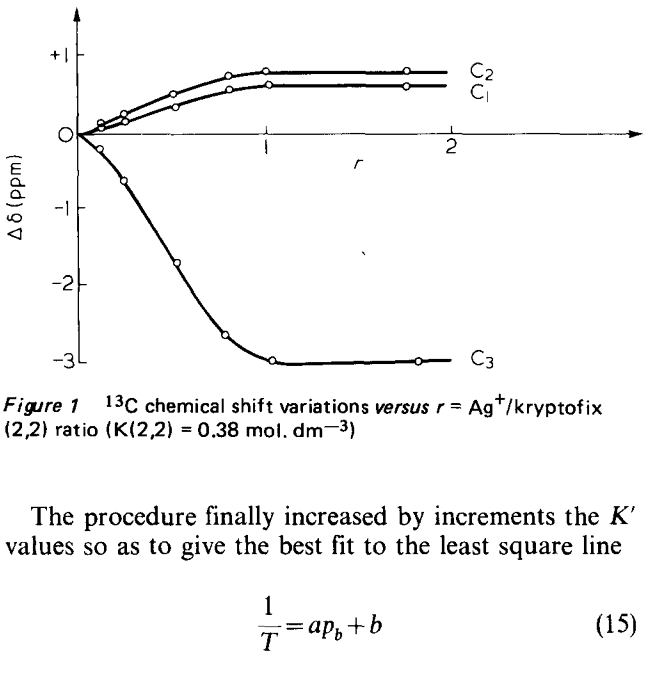


Figure 1 ^{13}C chemical shift variations *versus* $r = Ag^+$/kryptofix (2,2) ratio (K(2,2) = 0.38 mol. dm^{-3})

The procedure finally increased by increments the K' values so as to give the best fit to the least square line

$$\frac{1}{T} = ap_b + b \qquad (15)$$

^{13}C N.M.R. OF KRYPTOFIX (2,2) AND SUBSTITUTED POLYACRYLAMIDE

A number of applications of n.m.r. spectroscopy to complex formation and structure determination of the complexes of macrocyclic compounds have been reported[2–9]. As the ^1H n.m.r. spectra of macrocyclic polyethers are often complex, ^{13}C n.m.r. was more convenient for our study of the interaction of various ions with the kryptofix (2,2), grafted either to the water soluble polymer or to the gel.

When a salt is added to a solution of the polyacrylamide substituted by kryptofix (2,2), a modification of the ^{13}C spectrum is observed. The ion dipole interaction changes the electronic density of the neighbouring atoms which gives a variation in the chemical shift. Interpretation of intensity and direction of the shift is often difficult to make.

Kryptofix (2,2)

The ^{13}C n.m.r. spectrum of kryptofix (2,2)(K(2,2)) shows 3 types of signal. In the presence of various ions, modifications are observed and *Table 1* gives the assignment and the chemical shift of ^{13}C nuclei of K(2,2). The metallic ion/ligand ratio is 1.

The protonation of the nitrogen atoms induces a shielding of the C_2 atom. ($\Delta\delta = +4$ ppm). In the presence of metallic ions, shifts are generally weak and upfield. Large shifts are observed for Ba^{2+} and Ag^+ ions and resonance of the C_3 atom is downfield. These changes are probably due to a stronger interaction of the ions with the ligand. For Ag^+ which is a soft acid, the perturbation is more sensitive for the C_3 nucleus which is near the nitrogen atom (soft base). ($\Delta\delta = -3$ ppm). *Figure 1* shows the variation of chemical shifts for C_1, C_2, C_3 nuclei *versus* $r = Ag^+$/kryptofix. A complex formation of stoichiometry 1/1 is observed.

Water soluble polyacrylamide substituted with K(2,2)

The viscosity of the polymer solutions increases with the addition of ions and gel formation can be obtained with Ba^{2+} and Ag^+. Spectra of the polymer show wide peaks due to the CH and CH_2 atoms of the polymeric chain. Peak assignments are shown in *Figure 2*.

The signal of the amide function is complex. When a salt is added to a polymer solution, only small variations are observed in this region and participation of the amide function in the complexation cannot be deduced from n.m.r. spectra.

Chemical shifts are given in *Table 2*. The resonance position of the C_1 atom, near the centre of the cavity, is not modified by complexation with K^+ but there is an upfield

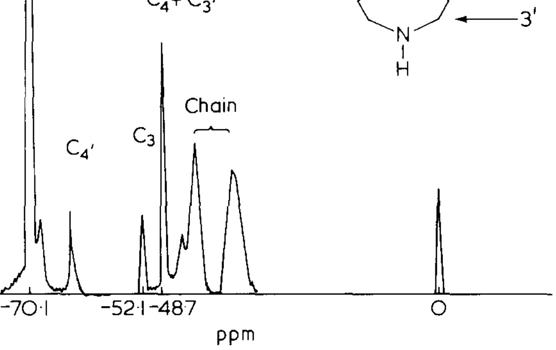


Figure 2 ^{13}C n.m.r. of kryptofix (2,2) (0.15 mol. dm^{-3}) substituted polyacrylamide in D_2O; shifts in ppm from TMS. The position of the small peak at 69.3 ppm is slightly sensitive to the addition of various ions but no interpretation could be given. When NH_4^+ ion is added 3 peaks are present in the C_2 resonance region. Similar phenomena have been ascribed by several authors to a strong complexation with the metal cations[15,16]. However, this splitting may also be ascribed to a possible conformational change[17]

resonance with NH_4^+ and Ag^+ ions and a downfield resonance with Ba^{2+}. When complexation occurs, C_2 is shifted in the same direction as the C_1 resonance peak, but the magnitude is greater: NH_4^+ ($\Delta\delta = +2.8$ ppm), Ba^{2+}($\Delta\delta = -1.1$ ppm).

Interaction of the Ag^+ ion with the macrocycle leads to a deshielding of the C atoms near the nitrogen atom. (C_3: $\Delta\delta = -2.8$ ppm; C_4: $\Delta\delta = -2.4$ ppm).

Experiments with Ba^{2+} ion concerning the variation of the chemical shift with the ion/ligand ratio have demonstrated that this ratio is equal to 1. This ion has a 2.7 Å ionic diameter close to that of the macrocycle (2.8 Å).

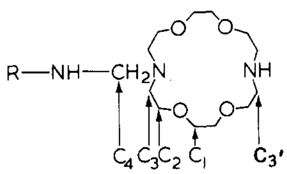
The specificity of the complexation is due to the required fit between the ionic radius and the size of the macrocyclic ring. Nevertheless, it may be affected by the medium as the macrocyclic polyether must compete with the surrounding solvent for the cation.

Acrylamide gel modified with K (2.2)

Spectra of the unmodified acrylamide gel were run in D_2O. The peak at -180.5 ppm is assigned to the C atom of the amide group and those at -43.1 and -36.6 ppm to the C atoms of the polymeric chain.

Because of the flexibility and mobility of the macrocycle grafted to the gel, 3 intense signals are observed which are assigned to the various C atoms of the ligand. The spectrum of the gel, swollen in aqueous salt solution, indicates a change on complexation. In the absence of ions the signal at -71.2 ppm is attributed to the $C_1 + C_2$ resonance of the macrocycle. By addition of an ion, the signal is shifted and a second peak appears, the position of which depends on the nature of the ion. Comparing the results in *Tables 2* and *3*, the evidence for larger chemical shifts of the C_2 carbon atom of the gel is observed. It can be concluded that the gel has a higher affinity for alkaline earth ions than for alkali ions.

Table 2 ^{13}C n.m.r. shifts of the kryptofix (2,2) (0.15 mol. dm^{-3}) substituted polyacrylamide in D_2O, plus salts (0.15 mol. dm^{-3}). Shifts are expressed in ppm from TMS



	C_1	C_2	C_3	$C_4 + C_3'$
Free ligand	−70.70	−70.45	−52.20	−48.70
K^+	−70.70	−70.45	−52.15	−48.70
NH_4^+	−70.40	−68.2 − −67.7 − 67.0	−52.10	−48.20
Ba^{2+}	−71.0	−71.60	−52.40	−49.40
Ag^+	−70.1	−69.80	−54.60	−51.50

^{23}Na n.m.r.

With the ^{13}C n.m.r. study described above, we were able to give evidence for the complex formation and identification of the binding sites of the ligand. The ^{23}Na n.m.r. approach may detect changes of hydration and mobility and analysis of ^{23}Na spin lattice relaxation times permits measurement of the complex dissociation constant $(K_1)^{18-20}$.

Although the correlation time is related to the macroscopic viscosity of the solution, it has been shown[21–23] that ^{23}Na T_1 can remain independent of large viscosity changes. Our T_1 measurements show no difference when Na^+ is dissolved in H_2O or in polymethylol acrylamide solution ($\bar{M}_n = 23\,000$, 1%). At constant sodium concentration and in the presence of variable grafted polymer concentrations, the ^{23}Na T_1 changes in a way unaccounted for by viscosity alterations (low concentration of polymer).

As kryptofix (2,2) is added to a 0.1M Na^+ solution, the ^{23}Na T_1, changes slightly. The variation falls within the error limit. With kryptofix (2,2) we have only the possibility of detecting the formation of a weak complex. Using the grafted polymer as the ligand, large T_1 variations are observed and data can be related to the complex formation constant.

A plot of relaxation rates of ^{23}Na at variable polymer concentrations *versus* $p_b = [Na]_b/[Na]_t$ are shown in *Figure 3*, $[Na]_b$ values were calculated (see method of calculation section) with equation (4) using an iterative procedure for K_1 in order to give the best fit for the result to equation (5).

T_1 measurements were run with various polymer samples. The variation of the two parameters: molecular weight and capacity of the polymers, were studied. Polyacrylamide of molecular weight $\bar{M}_n = 23\,000$ or $\bar{M}_n = 50\,000$ was used and the capacity of the grafted polymer was either 0.8 meq/g or 0.5 meq/g. For all sets of measurements K_1 values were in good agreement. However, T_{1f} and T_{1b}^* values, obtained by the graphical method, were slightly different, depending on the grafted polymer capacity. Macroscopic viscosity change in the polymer solution might account for the observed difference.

The calculation gave a mean value for the conditional formation constant for the Na^+-polymer complex:

$$\log K_f = 1.9 \pm 0.1 \qquad 1/T_{1f} = 19 \pm 1.5\,s^{-1} \qquad \text{and} \qquad 1/T_{1b}^* = 169 \pm 10\,s^{-1}$$

It is a general finding that T_1 and T_2 are unequal for solutions of ions and macromolecules and different values T_1 and T_2 were noted in this work. There is some

Table 3 ^{13}C n.m.r. chemical shifts of the free kryptofix (2,2) (0.15 mol. dm^{-3}) bound to a polyacrylamide gel swollen in D_2O, and in presence of various ions (0.15 mol. dm^{-3}). Shifts are expressed in ppm from TMS

	Ligand bound to the gel	Li^+	Na^+	NH_4^+	Ca^{2+}	Ba^{2+}	Ag^+
C_1	−71.2	−70.4	−70.7	−70.6	−70.7	−70.6	−70.6
C_2	–	−68.1	−68.5	−66.7	−66.9	−66.4	−66.5

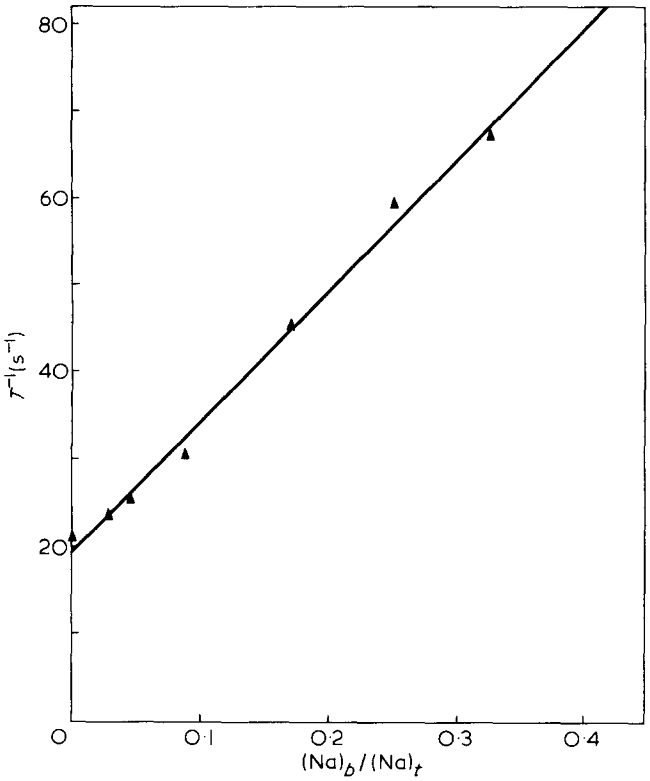


Figure 3 Plot of longitudinal relaxation rate ^{23}Na in solutions containing kryptofix (2,2) substituted polyacrylamide *versus* $(Na)_b/(Na)_f$. The total concentration $(Na)_f$ is 0.1 M

imprecision in the T_2 determination from the line-width measurements but the use of either T_1 or T_2 yields the same conditional formation constant.

No significant ^{23}Na chemical shift was observed with increasing ligand concentration. This might be interpreted as a partial modification of the primary shell of coordination of the hydrated Na^+ ion on complexation.

Competition experiments

J. I. Zink *et al.* reported a Thallium n.m.r. determination of a polyether cation selectivity sequence They have shown that the chemical shift perturbation of Tl^+ ion by various univalent cations can be related to the determination of the macrocyclic polyether-cation stability constants. A similar approach was used here. A convenient way of determining the stability constant of Ba^{2+}, relative to the sodium ion, with the polymer is provided by the ^{23}Na relaxation time measurements.

When an increasing amount of Ba^{2+} ion is added to Na^+-polymer solutions, there is a modification of the solvation sphere of Na^+ ion. The complexation sites of the ligand complete with water molecules and the selectivity corresponds to the polyether ring hole size. ^{23}Na T_1 values are modified and the variation of T_1 *versus* Ba^{2+} concentration is shown in *Figure 4*. As expected, Ba^{2+} gives complexes with the cryptand grafted to the polymer which are more stable than complexes of the corresponding Na^+ ion. A complex of 1/1 stoichiometry is formed.

Using the calculation procedure described in the method of calculation section, the formation constant log $K_{Ba}=4.35$ is obtained.

Similar experiments have been done with K^+ and Cs^+ ions. The results were not reliable, probably because the sequence order of the formation constants of these ions with the polymer is $Cs^+ < K^+ \simeq Na^+$ and Cs^+ does not fit the macrocyclic hole size.

The K^+/Na^+ specificity has been found only for ligands which wrap the ion from all sides and have a high number of oxygen atoms.

CONCLUSION

Previous studies[1] on the complexation of salts with kryptofix (2,2) grafted to an acrylamide gel have shown that there were significant interactions of inorganic ions with the gel. The selectivity of the alkaline earth ions over alkali ions was observed and for cations like Cd^{2+}, Ag^+ and Hg^{2+} ions, high extraction was obtained. The present work aimed to corroborate the results obtained with the gel and with the homologous linear water soluble polymer.

The addition of salts to solutions of kryptofix (2,2) grafted on polyacrylamide, induces modifications of the ^{13}C n.m.r. chemical shift of the cryptand. The intensity of the perturbation of each C atom is in good agreement with the complex formation and it seems reasonable to suppose that the complex formation tendency involves the dimension of both the hydrated ion and the macrocyclic cavity size. When the ligand is bound to the gel, larger ^{13}C chemical shifts are observed and this can be interpreted as a 'gel effect'.

A quantitative study of the interaction of Na^+ and Ba^{2+} ions with the linear polymer has been made using the ^{23}Na n.m.r. relaxation time measurements. The

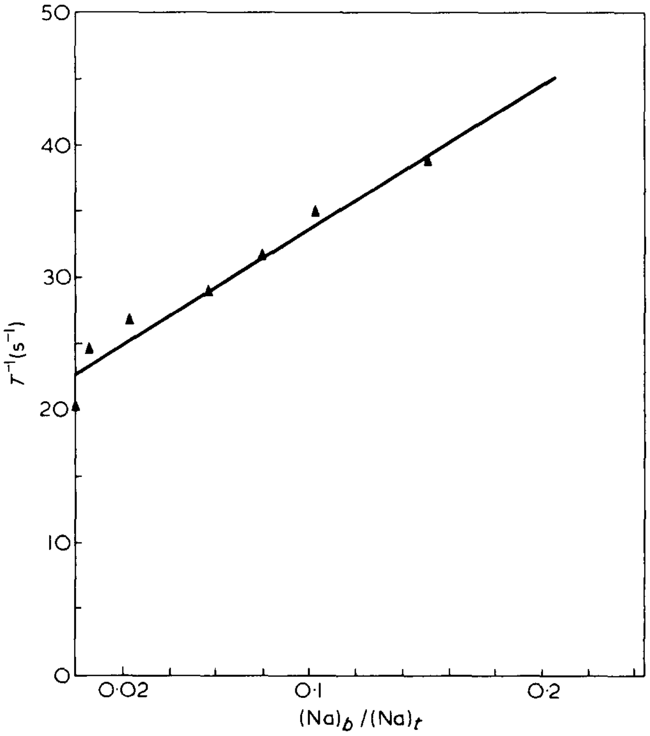


Figure 4 Solutions of kryptofix (2,2) substituted polyacrylamide and Na^+ in D_2O. Concentrations of the cryptand and Na^+ are 0.02 M and 0.1 M respectively. Variable quantity of Ba^{2+} is added. ^{23}Na T^{-1} is plotted *versus* $(Na)_b/(Na)_f$

estimation of the conditional formation constants obtained by this technique is in good agreement with the binding sequence observed with the gel.

Although the binding of metal ions to macromolecules can be studied by dialysis equilibrium, conductimetric methods and cation sensitive glass electrode, these techniques have their limitations. The use of the n.m.r. relaxation technique, outlined in this paper, offers the advantage of providing information on the electronic environment of the ion bound to the macromolecule.

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