Complexation of the Sodium Ion by a Pendant-arm Tetraaza Macrocyclic Ligand in Aqueous Solution

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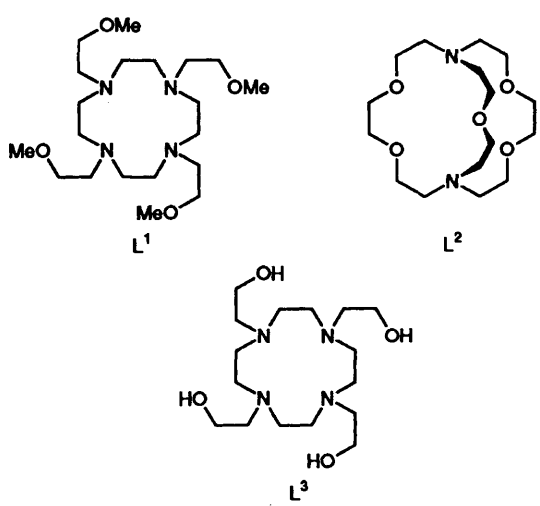
The first pendant-arm tetraaza macrocyclic sodium(I) complex to be quantitatively kinetically characterized in aqueous solution, *N,N',N'',N'''*-tetrakis(2-methoxyethyl)-1,4,7,10-tetraazacyclododecanesodium(I), has an apparent stability constant K = 159 ± 18 dm^3 mol^{-1} in aqueous 0.100 mol dm^{-3} NEt_4ClO_4 at 298.2 K, and is more stable than its other alkali-metal ion analogues, as shown by potentiometric titration methods. Variable-temperature ^{23}Na NMR spectroscopy showed sodium ion exchange on this complex to be characterized by k_d (298.2 K) = 70.3 ± 2.3 s^{-1}, $\Delta H_d^{\ddagger}$ = 64.0 ± 0.7 kJ mol^{-1} and $\Delta S_d^{\ddagger}$ = 5.1 ± 2.1 J K^{-1} mol^{-1}, where k_d is a monomolecular decomplexation rate constant. The protonation of *N,N',N'',N'''*-tetrakis(2-methoxyethyl)-1,4,7,10-tetraazacyclododecane is characterized by pK_a values (±0.05) of 10.92, 8.04 and 2.17, and the log(K/dm^3 mol^{-1}) values for its complexes with Mg^{2+}, Ca^{2+}, Sr^{2+} and Ba^{2+} are 2.47, 5.47, 5.00 and 4.72 (all ±0.05), respectively.

Studies of the fast substitution of ligands of either low denticity or of high flexibility on the hydrated alkali-metal ions indicate that water exchange on these ions is characterized by rate constants ranging from 5 × 10^8–8 × 10^9 s^{-1} at 298.2 K as a consequence of their low surface charge densities.[1] However, for less flexible multidentate ligands where either a preformed cavity exists (as exemplified by cryptands) whose size may match that of the alkali-metal ions, or such a cavity is formed during complexation (as exemplified by coronands and ionophoric antibiotics), the rates of complexation and decomplexation of alkali-metal ions are less and a ligand selectivity for the complexation of alkali-metal ions is exhibited through the substantial variations in the stabilities of the complexes formed.[2–7] The factors affecting such selectivity are currently of considerable interest and accordingly we report a study of *N,N',N'',N'''*-tetrakis(2-methoxyethyl)-1,4,7,10-tetraazacyclododecanesodium(I), $[NaL^1]^+$, which appears to be the first pendant-arm tetraaza macrocyclic alkali-metal complex to be quantitatively kinetically characterized in aqueous solution. Pendant-arm polyaza macrocyclic ligand complexes of divalent metal ions have been studied in aqueous and non-aqueous solutions and their complexation and decomplexation reactions are usually considerably slower than is found for $[NaL^1]^+$ in this study.[8–12]

Experimental

Preparation of Materials.—*N,N',N'',N'''*-Tetrakis(2-methoxyethyl)-1,4,7,10-tetraazacyclododecane (L^1) was prepared by refluxing 1,4,7,10-tetraazacyclododecane[13] (0.57 g) with 2-chloroethyl methyl ether (12.4 g) and NaOH (0.53 g) in 50% aqueous ethanol (25 cm^3) for 7 d. A pH > 11 was maintained by regular addition of solid NaOH. The solvent was removed under vacuum, the solid residue was dissolved in water (30 cm^3), made basic with NaOH, and the resulting solution was extracted with chloroform (5 × 50 cm^3). The chloroform was removed under vacuum yielding crude $[NaL^1]Cl$. Free L^1 was obtained as a colourless oil (0.78 g) by fractional distillation (b.p. *ca.* 413 K at 0.015 mmHg, *ca.* 2 Pa), and was shown to be >98% pure by ^{13}C NMR spectroscopy (75.5 MHz) in $CDCl_3$: δ 52.6 (ring carbons), 55.0 ($NCH_2CH_2OCH_3$), 58.7 ($NCH_2CH_2OCH_3$) and 71.0 (methyl carbon). Lithium and sodium perchlorate (Fluka) were used as received after drying. Potassium perchlorate (BDH) was recrystallized from water.



Rubidium and caesium perchlorates were precipitated from solutions of their chlorides (BDH) by the addition of concentrated $HClO_4$ (May and Baker AR) and were recrystallized from water until chloride was absent. Tetraethylammonium perchlorate was prepared by treating NEt_4Br (BDH) with an excess of $HClO_4$ in water and the resultant NEt_4ClO_4 precipitate was recrystallized from water until no acid or bromide was detectable. All of the metal perchlorates and NEt_4ClO_4 were vacuum dried at 353–363 K for 48 h, and were stored over P_2O_5 under vacuum. (**CAUTION**: Anhydrous perchlorate salts are potentially powerful oxidants and should be handled with care.) Water was purified with a MilliQ-Reagent system to a resistance of >15 MΩ cm. The $HClO_4$, NEt_4OH (Aldrich) and metal perchlorate titration solutions (all with I adjusted to 0.100 mol dm^{-3} with NEt_4ClO_4) were prepared under nitrogen and were standardized by conventional methods. The solutions of $NaClO_4$ and L^1 for ^{23}Na NMR studies were degassed and sealed under vacuum in 5 mm NMR tubes which were coaxially mounted in 10 mm NMR tubes containing D_2O which provided the deuterium lock signal.

Potentiometric Titrations.—Potentiometric titrations were

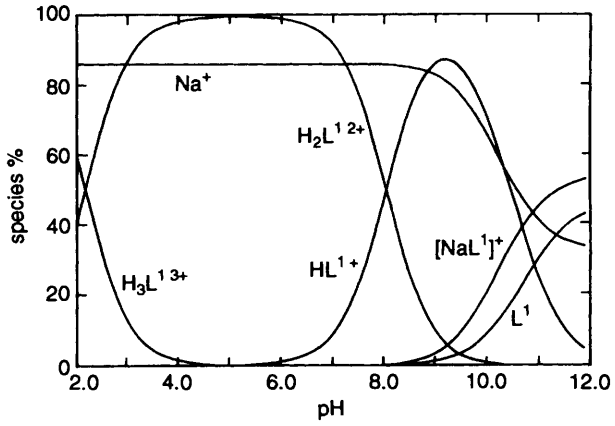


Fig. 1 Speciation curves for the Na^+–$H_nL^{1\,n+}$ (n = 0, 1, 2 or 3) system in aqueous 0.100 mol dm^{-3} NEt_4ClO_4 solution. The total $[Na^+]$ and $[L^1]$ are 0.0201 and 0.0237 mol dm^{-3}, respectively

carried out with a Metrohm E665 Dosimat autoburette interfaced to a Laser XT/3-8086 personal computer in conjunction with an Orion SA720 potentiometer and an Orion Ross Sureflow combination electrode. All titrations were performed at 298.2 ± 0.05 K in a water-jacketted vessel which was closed apart from a vent to allow egress of nitrogen. A stream of nitrogen was passed through the titration solution to exclude atmospheric carbon dioxide, and the solution was stirred using a magnetic stirrer. The electrode was calibrated by titration of 0.100 mol dm^{-3} NEt_4OH from the autoburette against 0.005 mol dm^{-3} $HClO_4$ (10.00 cm^3). The protonation constants of L^1 were determined by titration of a solution (10.00 cm^3) 0.005 and 0.001 mol dm^{-3} in $HClO_4$ and L^1, respectively, with 0.100 mol dm^{-3} NEt_4OH. The apparent stability constants of $[ML^1]^{n+}$ (M^{n+} = Li^+, Na^+, K^+, Rb^+, Cs^+, Mg^{2+}, Ca^{2+}, Sr^{2+} or Ba^{2+}) were determined by titrations of solutions (10.00 cm^3) 0.005, 0.001 and 0.0005–0.0020 mol dm^{-3} in $HClO_4$, L^1 and $M(ClO_4)_n$, respectively, with 0.100 mol dm^{-3} NEt_4OH. All titrations were carried out in duplicate at least. The protonation constants and apparent stability constant values were determined using the program SUPERQUAD.[14]

NMR Kinetic Studies.—Sodium-23 NMR spectra were run at 79.39 MHz on a Bruker CXP-300 spectrometer, and 1000–6000 transients were accumulated in a 2048 data point base over a 8064 Hz spectral width for each solution. The solution temperatures were controlled to within ±0.3 K using a Bruker B-VT 1000 temperature controller. The Fourier-transformed spectra were subjected to complete line shape analysis[15] on a VAX 11-780 computer. The temperature-dependent ^{23}Na linewidths, chemical shifts and species populations employed in the line shape analysis were obtained by extrapolation from low temperatures where no exchange induced modification occurred.

Results and Discussion

Equilibrium Studies.—Potentiometric titration shows the protonated ligand, $(H_3L^1)^{3+}$, to be characterized by pK_a values (±0.05) of 10.92, 8.04 and 2.17 in aqueous 0.100 mol dm^{-3} NEt_4ClO_4 at 298.2 K. These pK_a variations are consistent with the first two protonations occurring at the amine groups diagonally opposed across the tetraaza ring such that electrostatic interactions are minimized. The markedly decreased value of the third pK_a is largely attributable to the third protonation occurring on an amine group adjacent to those already protonated with a consequently considerable increase in electrostatic interaction. Under the same conditions, L^1 shows a small selectivity for Na^+ as indicated by the

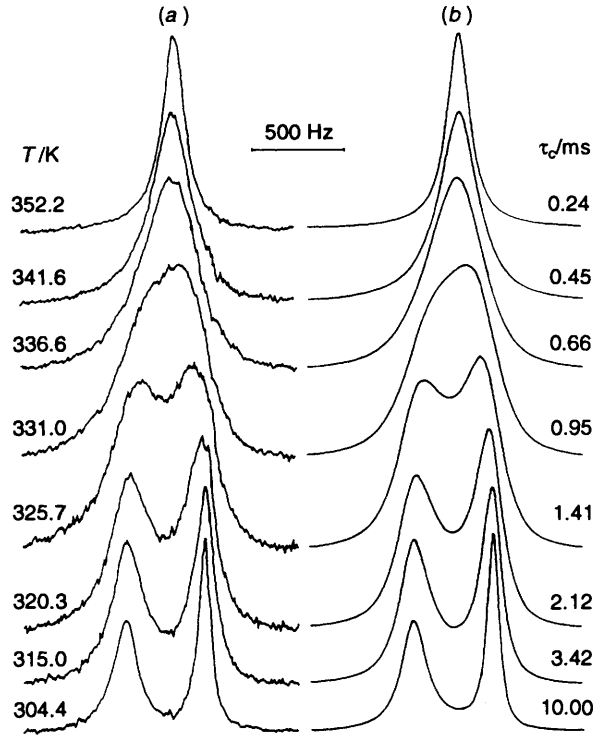


Fig. 2 The temperature variation of the ^{23}Na 79.39 MHz NMR spectrum of an aqueous solution of $[Na^+]_{hydrated}$ = 0.0085, $[NaL^{1+}]$ = 0.0116, $[L^1]_{free}$ = 0.0087 and $[HL^{1+}]_{free}$ = 0.0035 mol dm^{-3}. The ^{23}Na resonance of $[NaL^1]^+$ appears downfield of that of hydrated Na^+. The experimental temperatures and the mean site lifetimes, τ_c, derived from complete line shape analyses of the exchange modified resonances, appear to the left and right of the Figure, respectively (*a*) experimental, (*b*) calculated spectra

variation of $\log(K/dm^3\ mol^{-1})$ for $[ML^1]^+$ in the sequence < 2, 2.20 ± 0.05, < 2, < 2 and < 2 where M = Li, Na, K, Rb and Cs, respectively, where $K = [ML^{1+}]/[M^+][L^1]$. (It is seen in Fig. 1 that $[NaL^1]^+$ is only formed at high pH as a consequence of L^1 being the only ligand species to complex Na^+.) This selectivity pattern may be compared with that of the cryptand 4,7,13,16,21-pentaaoxa-1,10-diazabicyclo[8.8.5]triicosane (L^2) for which the analogous $\log(K/dm^3\ mol^{-1})$ varies in the sequence: 2.50, 5.40, 3.95, 2.55 and < 2.0 where M = Li, Na, K, Rb and Cs,[4] respectively. This demonstrates the greater selectivity and complex stability arising from the matching of the radius (1.1 Å)[2] of the preformed L^2 cavity and that of seven-co-ordinate Na^+ (1.12 Å)[16] consistent with extensive studies which show that cryptate thermodynamic stability is very dependent on the match of the cation and cryptand cavity radii.[2,6,7]

The $\log(K/dm^3\ mol^{-1})$ for $[ML^1]^{2+}$ vary in the sequence: 2.47, 5.47, 5.00 and 4.72 (all ±0.05) where M = Mg, Ca, Sr and Ba, respectively, consistent with the higher surface charge density of the alkaline-earth ions producing a stronger ion–dipole interaction with L^1, and a selectivity for Ca^{2+} which possesses a seven-co-ordinate ionic radius (1.06 Å)[16] similar to that of Na^+. This order of relative stability contrasts with the Irving–Williams order[17] where a decrease in stability in the sequence $Mg^{2+} > Ca^{2+} > Sr^{2+} > Ba^{2+}$ is observed for complexes with a range of bidentate ligands in water, and which mainly reflects electrostatic effects. This emphasizes the selectivity exhibited by L^1 for Ca^{2+} in the alkaline-earth $[ML^1]^{2+}$ complexes.

Kinetic Studies.—The coalescence of the ^{23}Na resonances characterizing $[NaL^1]^+$ and hydrated Na^+ with increase in temperature (Fig. 2) is consistent with exchange of Na^+ between the complexed and hydrated environments. Complete line shape analysis[15] yields the mean lifetime of $[NaL^1]^+$, τ_c,

Table 1 Solution compositions[a] and kinetic parameters[b] for $[NaL^1]$ in aqueous solution

Solution	$[Na^+]_{hydrated}$ / mol dm^{-3}	$[NaL^{1+}]$ / mol dm^{-3}	$[L^1]_{free}$ / mol dm^{-3}	$[HL^{1+}]_{free}$ / mol dm^{-3}	k_d(325.7 K)[c]/s^{-1}	$\Delta H_d^{\ddagger}$/kJ mol^{-1}	$\Delta S_d^{\ddagger}$/J K^{-1} mol^{-1}
i	0.0062	0.0139	0.0141	0.0044	676 ± 17	66.3 ± 1.7	1.2 ± 4.8
ii	0.0085	0.0116	0.0087	0.0035	664 ± 15	64.3 ± 1.1	5.8 ± 3.0
iii	0.0114	0.0087	0.0048	0.0025	689 ± 21	62.7 ± 1.5	1.1 ± 4.3
iv	0.0143	0.0058	0.0025	0.0018	680 ± 26	63.9 ± 1.9	4.8 ± 5.3
(i–iv)					677 ± 9	64.0 ± 0.7	5.1 ± 2.1

[a] The solution pH at 298.2 K for solutions i–iv were 11.42, 11.32, 11.20 and 11.06, respectively. [b] The quoted errors are the standard deviations of the fit of the τ_c data to equation (2). [c] The temperature 325.7 K is in the midst of the spectral coalescence region where the most accurate data are obtained.

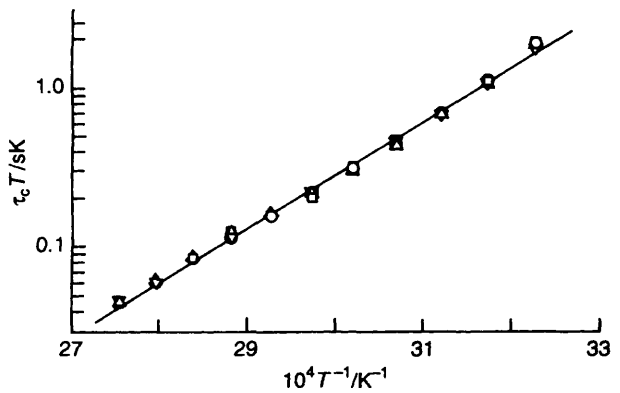


Fig. 3 The temperature variation of τ_c for solutions i–iv which are indicated by circles, squares, triangles and inverted triangles, respectively. The solid line represents the simultaneous best fit of these data by equation (2)

which is related to the mean lifetime of hydrated Na^+, τ_h, and the mole fractions of Na^+ in the complexed and hydrated environments, X_c and X_h, through equation (1). The de-

$$\tau_c/X_c = \tau_h/X_h \quad (1)$$

complexation rate constant k_d and the associated activation parameters are derived from equation (2). For solutions i–iv, τ_c

$$1/\tau_c = k_d = (k_B T/h)e^{-\Delta H_d^{\ddagger}/RT} e^{\Delta S_d^{\ddagger}/R} \quad (2)$$

is independent of both $[Na^+]_{hydrated}$ and $[L^1]_{free}$ (Table 1 and Fig. 3) consistent with the rate-determining step of the dominant decomplexation mechanism involving $[NaL^1]^+$ alone as shown in equation (3) where the complexation rate constant $k_c = k_d K$.

$$Na^+ + H_nL^{1\,n+} \underset{k_d}{\overset{k_c}{\rightleftharpoons}} [NaL^1]^+ + nH^+ \quad (3)$$

When the combined data from solutions i–iv are simultaneously fitted to equation (2), k_d (298.2 K) = 70.3 ± 2.3 s^{-1}, $\Delta H_d^{\ddagger}$ = 64.0 ± 0.7 kJ mol^{-1} and $\Delta S_d^{\ddagger}$ = 5.1 ± 2.1 J K^{-1} mol^{-1} are obtained, from which k_c (298.2 K) = 1.1 × 10^4 dm^3 mol^{-1} s^{-1} is calculated.

Mechanistic Aspects.—As L^1 is octadentate, Na^+ may be eight-co-ordinated in $[NaL^1]^+$ as is the case for K^+ in $[KL^3]^+$ [where L^3 is closely related *N,N′,N″,N‴*-tetrakis(2-hydroxyethyl)-1,4,7,10-tetraazacyclododecane] in the solid state[18] and for Pb^{2+} in $[PbL^3]^{2+}$ in solution.[7] However, seven-co-ordinate Na^+ is bound above the tetraaza plane by four nitrogens and three hydroxo groups in $[NaL^3]^+$ in the solid state,[18] and a similar co-ordination may exist in $[NaL^1]^+$. Despite this uncertainty as to the structure of $[NaL^1]^+$, a complexation sequence may be envisaged in which the diffusion controlled formation of an outer-sphere complex is followed by the rapid displacement of the first aqua ligand from the alkali-metal ion and the rates of some of the subsequent slower steps are substantially controlled by conformational changes in the multidentate ligand. Thus k_d observed for $[NaL^1]^+$ may characterize an inversion about an L^1 amine nitrogen as has been suggested for the decomplexation and complexation of divalent metal ions by *N,N′,N″,N‴*-tetramethyl-1,4,7,10-tetraazacyclotetradecane.[19] (Similar rate-limiting conformational changes have been postulated in the Eigen–Winkler mechanism[20] originally proposed for the complexation of metal ions by ionophoric antibiotics, and also for the complexation of Li^+ and Na^+ by lariat ethers.[21]) The second-order k_c is a composite rate constant which includes an intermolecular equilibrium constant characterizing a preequilibrium which is rapidly established prior to the rate-determining intramolecular step. For the cryptate $[NaL^2]^+$, k_c = 3.6 × 10^6 dm^3 mol^{-1} s^{-1} and k_d = 14.5 s^{-1} in water at 298.2 K,[5] indicating that the kinetic basis for greater stability of this cryptate by comparison with that of $[NaL^1]^+$ is a consequence of its greater k_c.

In aqueous solution, L^1 and L^2 preferentially complex Na^+ which suggests that L^1 is capable of forming a cavity of similar dimensions to the preformed cavity of L^2. However, the smaller magnitudes of K for $[ML^1]^+$ indicate that water more readily competes for the alkali-metal ion with L^1 than with L^2. This suggests that the restricted movement of the donor atoms in the preformed cavity of L^2, optimized in size for Na^+, engenders a greater stability for $[NaL^2]^+$ by comparison with that of $[NaL^1]^+$ despite the relatively flexible L^1 being able to adjust its stereochemistry to produce the highest stability for $[NaL^1]^+$ in the alkali-metal $[ML^1]^+$ series. (As a consequence of this flexibility of L^1, the possibility that a different selectivity pattern for alkali-metal ions may arise in other solvents cannot be excluded.) This also suggests that the more rigid array of the donor atoms of L^2 is particularly well positioned for the sequential co-ordination of Na^+ and that this accounts for the greater k_c for $[NaL^2]^+$.

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