peak and the midpoint of the second doublet are predicted within about 0.1 eV, but the observed separation of the 9e and 8e ionizations is about 0.5 eV greater than that calculated. This should be considered as fairly good agreement for such a complex molecule.

A careful examination of the second, split peak in the PE spectrum, which we assign to ionization of the W-W π electrons, leaves little doubt that the two spin-orbit components have different band envelopes and cross sections, as shown in Figure 15. This is not anomalous since the two components of the split π level are rendered inequivalent by their different couplings to the σ and δ levels. The π level with $j = {}^3/_2$ is coupled to the δ level while the π level with $j = {}^1/_2$ is coupled to the σ level.

Figure 7 shows that the only substantial differences between the ionizations of the Mo and W complexes involve the predominantly metal levels. These particular differences are large in comparison to the normal changes found between the ionizations of mononuclear complexes from the first, second, and third transition-metal series. The first ionization of the W complex occurs at 0.63 eV lower binding energy than the first ionization of the Mo complex, and hence the W complex is much more easily oxidized. The predominantly metal π ionization of the W complex occurs at 0.25-0.65 eV lower binding energy than the corresponding ionization of the Mo complex. In contrast to these substantial changes in the metal ionizations, the changes in the M-P σ, M-Cl σ, and Cl lone pair ionizations are quite small (less than 0.1 eV). This indicates that the destabilization of the predominantly metal levels of the W complex is not a simple result of the inherent atomic orbital energy or "electronegativity" for the W atom, since this would also result in a greater negative charge on the ligands and a shift of their ionizations.

Apparently the instability of the W systems resides with the metal atoms and the metal-metal interactions, and not with metal-ligand or ligand-ligand interactions. It seems likely that the ultimate reason there is a difference in M-M bonding while the M-L bonding is essentially the same on going from Mo_2 to W_2 is the presence of much larger cores (by 32 e) in the tungsten atoms. This has a negligible effect on the M-L bonds, but it causes the W-W bonds to be ca. 0.10 Å longer than the Mo-Mo bonds. The greater length considerably reduces the δ overlap, has a smaller but still significant adverse effect on the π overlaps, and may also be responsible for reallocating d character among several orbitals with the symmetry appropriate for M-M σ bonding.

Acknowledgment. We thank the National Science Foundation and the Department of Energy for financial support. Dr. Bruce E. Bursten and Mr. Jan Larsen carried out some preliminary calculations and Dr. B. W. S. Kolthammer prepared the samples used to record the PE spectra. D.L.L. is an Alfred P. Sloan Fellow, 1979-1981.

Na^+ Complexes with Spiro-Bis-Crown Ethers: Stoichiometries, Stabilities, and Labilities in Pyridine Solution

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Abstract: Complex formation between $NaClO_4$ and a series of crown ethers **1-4** has been studied by means of sodium-23 nuclear magnetic resonance, in pyridine solution. With the spiro-bis-crown ethers **2** and **3**, both 1:1 and 2:1 complexes are found to be present, corresponding to single and double occupation of the two equivalent binding sites offered by these dicoronands. With the monocrown ether **1**, as with the dicoronand **4** which presents an "O_4" ring interacting but weakly with Na^+, only 1:1 complexes form, in coexistence for **4** at high ligand ratios with 2:1 complexes. The 1:2 complexes are characterized by binding constants smaller by one order of magnitude, because of electrostatic repulsion between the two bound ions. Sodium ions appear to attach themselves to the first binding site at rates above 10^8 M^{-1} s^{-1}, close to diffusion control.

That crown ethers enjoy widespread use since their introduction[2] is almost an understatement. Therefore, it comes as no surprise that a number of studies have been directed at the precise determination of thermodynamic parameters[3] —and, also, of kinetic parameters[4] —for cation binding. Most of these studies[3,4] have relied upon ion-selective electrodes, calorimetry, or nuclear magnetic resonance methods. In an earlier article,[5] we have used multinuclear probes (^1H, ^{13}C, and ^{23}Na[6]) to investigate Na^+ complexation by linear polyethers. These mimic crown ethers by wrapping themselves around the alkali metal ion.[7] We report here on another structural variation, with respect to the main theme of crown ethers, when two such cyclic polyethers are linked together via a spiro junction.

One or two metallic ions will be able to attach themselves to such spiro bicycles (which have been named "dicoronands"). Presumably, the cavitites associated with the individual rings will be the sites of attachment. One would expect a decreased binding constant and a smaller association rate (or a larger dissociation rate) for interaction of the cation to the second ring, due to Coulombic repulsion with the occupant of the first site. One may also expect small conformation changes in the first ring, due to the presence of the second ring. In order to answer these and other questions, we have examined the organic ionophores listed in Scheme I. These ligands **1-4**, synthesized by Dr. E. Weber at the University of Bonn,[7] offer cavities of various sizes: from

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[1] Laboratoire de chimie organique physique, UER Sciences, Université de Reims, BP 347, F-51962 Reims Cedex, France.

[2] Pedersen, C. J. *J. Am. Chem. Soc.* **1967**, *89*, 7017-7036. In "Synthetic Multidentate Macrocylic Compounds," Izatt, R. M., Christensen, J. J., Eds.; Academic Press: New York, 1978; pp 1-51.

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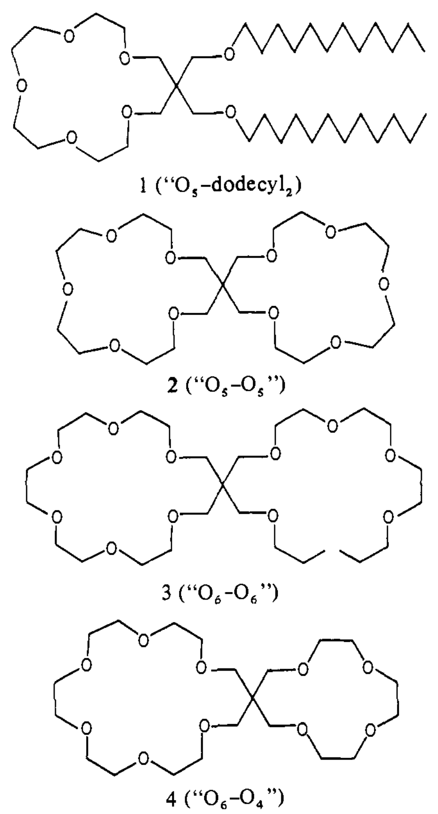
Scheme I



1 ("O_5-dodecyl$_2$")

2 ("O_5-O_5")

3 ("O_6-O_6")

4 ("O_6-O_4")

13-crown-4 to 19-crown-6 through 16-crown-5. We report here on the complexation by these crown ethers **1–4** of sodium perchlorate, in pyridine solution. The perchlorate salt was selected, as in earlier studies,[5] in order to minimize perturbation by the counterions; only loose and dissociated ion pairs are likely to be abundant in pyridine solution. Pyridine was chosen as solvent, as in previous studies from this laboratory:[5,6] sizeable quadrupolar couplings result when the Na^+ cation coordinates to atoms of differing electron-donor ability, for instance oxygens from the ligands and nitrogens from the solvent molecules. There is one drawback to this choice, however: our attempts at independent confirmation by calorimetry of the ΔH values derived from the ^{23}Na NMR results were foiled by the high hygroscopy of this solvent.[5]

Experimental and Data Analysis

Compounds 1–4 were prepared following the procedure described elsewhere.[8] All solutions were prepared under a dry argon atmosphere. Sodium perchlorate (Merck P.A.) was dried under vacuum at 110 °C for several hours. Pyridine (Baker P.A.) was dried by refluxing over potassium hydroxide and distilled under argon. The samples were sealed in NMR tubes under vacuum. ^{23}Na spectra were obtained on a Bruker-WP-80 spectrometer at 21.16 MHz. Line widths are measured at half-height with a maximum uncertainity of ±5%. We have point-checked the Lorentzian character of the absorptions, and relied only on spectra with a better than 50:1 signal-to-noise ratio. Longitudinal relaxation times, T_1, were measured using the $(180°-\tau-90°)_n$ sequence, with a delay $T = 5 \times T_1$ between acquisitions. T_1s were calculated using a nonlinear least-squares analysis with 12 τ values. The ^{23}Na line widths were reduced to unit viscosity using measured bulk viscosities. The resulting reduced line widths $\Delta\upsilon_{1/2}$ were adjusted to equations of the type:

$$\Delta\upsilon_{1/2}^{\text{obsd}} = p_F\Delta\upsilon_{1/2}^{F} + \sum_i p_i(\Delta\upsilon_{1/2}^{B})_i \qquad (1)$$

where the superscripts F and B refer to the free and bound states, and the subscript i to the i bound states, and the ps are mole fractions. Iterative fitting of the data points to eq 1, transformed by expressing these mole fractions in terms of binding constant and concentrations, is performed till self-consistency. In practice, a difference smaller than 5% between experimental and calculated $\Delta\upsilon_{1/2}$ values was obtained for all data points.

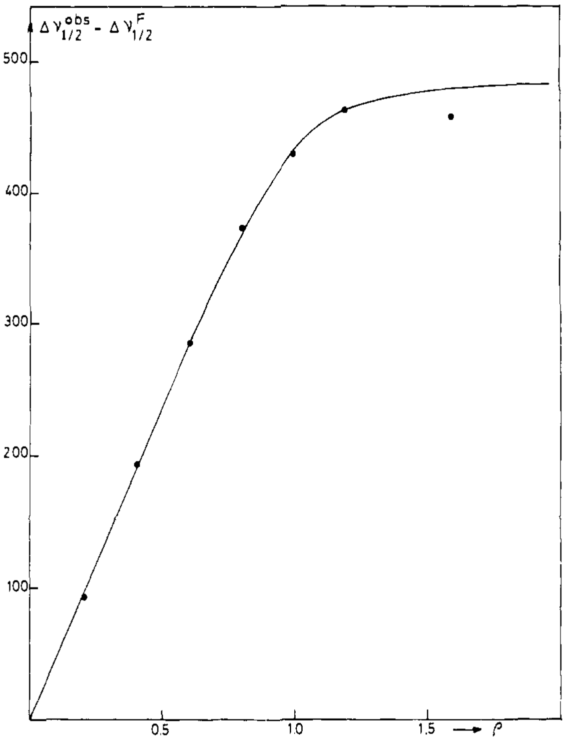


Figure 1. Plot of the variation of the line broadening $\Delta\nu_{1/2}$ (Hz/cP) [$=\Delta\nu_{1/2}^{\text{obsd}} - \Delta\nu_{1/2}^{F}$] against the molar ratio $\rho = [\mathbf{1}]/[NaClO_4]$ at 338.2 K.

Temperature was measured directly in a sample tube using a thermocouple, and temperature readings are good to ±0.2 °C.

For ligand **1**, a single equilibrium

$$Na^+ + \mathbf{1} \underset{}{\overset{K_1}{\rightleftharpoons}} \mathbf{1}\cdot Na^+ \qquad (2)$$

serves to analyze the data. The line width at half-height $\Delta\upsilon_{1/2}$ is measured as a function of the molar ratio $\rho = [\mathbf{1}]/[NaClO_4]$, for values of ρ between 0.3 and 1.6, at constant ionic strength, with $[NaClO_4] = 70$ mM (Figure 1).

The rates of the forward (k_+) and of the reverse (k_-) reaction in eq 2 ($K_1 = k_+/k_-$) are determined from the variation of the transverse relaxation rate $R = T_2^{-1} = \pi\Delta\upsilon_{1/2}$ as a function of the reciprocal temperature T^{-1} (Figure 2). As seen from Figure 2, below −40 °C the chemical exchange rates are very low with respect to the NMR relaxation rates. In this low-temperature range, the variations of R parallel those of R_F for a reference solution of free sodium ions $Na^+ = 70$ mM, devoid of any ligand. Conversely, above 20 °C, fast exchange prevails and a single resonance results. Its width is the weighted average between those for free and complexed species. In the intermediate temperature range, between −40 and +20 °C, the exchange rate becomes of comparable magnitude to the nuclear relaxation rate. The exchange rate constant is obtained from the relation[4]

$$1/\tau = \frac{(R_{\text{av}} - p_F R_F - p_B R_{\text{obsd}})(R_{\text{obsd}} - R_F)}{(R_{\text{av}} - R_{\text{obsd}})} \qquad (3)$$

where R_{obsd} is the transverse relaxation rate observed in the region of intermediate exchange, R_F is the relaxation rate for free (solvated) sodium ions, and R_{av} is the mean relaxation rate determined by extrapolation to the fast exchange limit (Figure 2). The mole fractions p_F and p_B are the fractional populations of free (Na^+) and bound ($\mathbf{1}\cdot Na^+$) sodium ions, respectively. The rate constant k_- is given, according to (2), by

$$k_- = \frac{1}{\tau}\frac{[Na^+]}{[\mathbf{1}\cdot Na^+]} \qquad (4)$$

Complexation of the Na^+ ions to bicyclic ligand **2** could only be accounted for by considering the two coexisting equilibria:

$$Na^+ + \mathbf{2} \overset{K_1}{\rightleftharpoons} Na^+\cdot\mathbf{2} \qquad (5)$$

$$Na^+ + Na^+\cdot\mathbf{2} \overset{K_2}{\rightleftharpoons} Na^+\cdot\mathbf{2}\cdot Na^+ \qquad (6)$$

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(8) Weber, E. *Angew. Chem., Intg. Ed. Engl.* **1979**, *18*, 219–220.

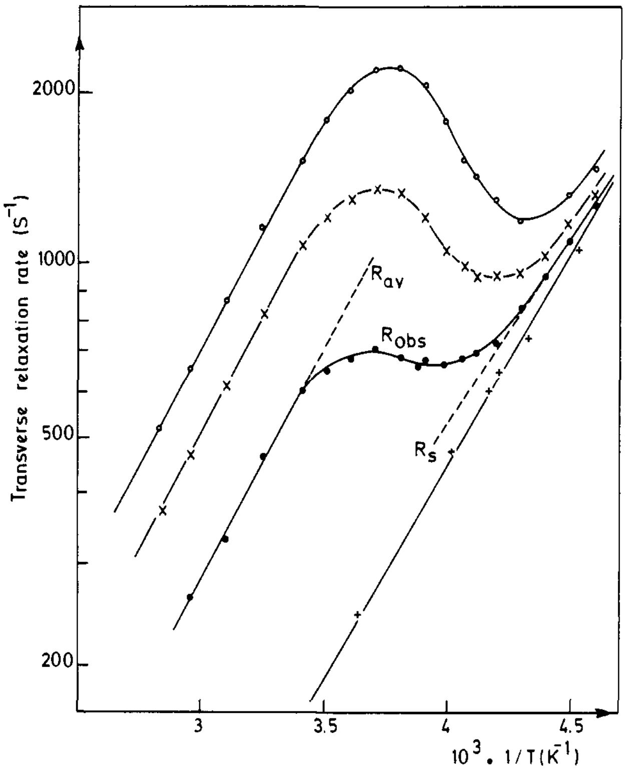
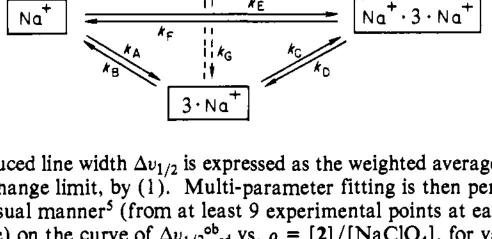


Figure 2. Plot of the transverse relaxation rate $R = 1/T_2$ against the reciprocal temperature $1/T$ for $NaClO_4$ in the presence of ligand **1**. The curved portion with a maximum and a minimum is highly characteristic of chemical exchange at intermediate rates, as explained in the text. (●) $\rho = 0.2$; (×) $\rho = 0.4$; (○) $\rho = 0.6$.

Scheme II



The reduced line width $\Delta\upsilon_{1/2}$ is expressed as the weighted average, in the fast exchange limit, by (1). Multi-parameter fitting is then performed in the usual manner[5] (from at least 9 experimental points at each temperature) on the curve of $\Delta\upsilon_{1/2}{}^{ob}{}_{sd}$ vs. $\rho = [\mathbf{2}]/[NaClO_4]$, for values of ρ between 0.1 and 1.6, at constant Na^+ concentration of 70 mM. We could not obtain reliable values for the kinetic parameters applicable to equilibria 5 and 6 for compound **2**.

Interaction of the sodium ions with ligand **3** was treated in very similar terms: coexistence of the two equilibria corresponding to eq 5 and 6 above. Curves of $\Delta\upsilon_{1/2}$ vs. $\rho = [\mathbf{3}]/[NaClO_4]$ were obtained for values of ρ between 0.05 and 2.5, at constant $[NaClO_4]$ = 85 mM, for at least 13 experimental points at each temperature (Figure 3). These equilibria have also been described in terms of chemical shifts. The observed variations were consistent with the values of the stability constants obtained from the line widths. Kinetically, data could be obtained reproducibly in the slow and in the moderately slow exchange ranges. Analysis was then attempted in terms of the model to be outlined below, in order to account for the change of $1/T_2$, obtained from the FIDs, vs. $1/T$. The equations were derived following the procedure described for a two-sites model.[9] There are four states available to the sodium ions: the free state $(Na^+)_F$, plus three bound states, Na^+·**3**, **3**·Na^+, and Na^+·**3**·Na^+. One has to distinguish between Na^+·**3** and **3**·Na^+, which are the singly occupied states, because their interconversion is effected by a jump of the sodium cation from site 1 to site 2. These four equilibrium states are connected by six elementary steps, corresponding to the rate constants listed in Scheme II.

Table I. Limiting Line Widths (Reduced to Unit Viscosity) and Formation Constant for the 1:1 Complex of Na^+ and **1**

T, K	$\Delta\nu_{1/2}{}^{F\,a}$	$\Delta\nu_{1/2}{}^{B\,a}$	$K_1{}^b$
293.2	58.4	603.4	3300
308.2	55.1	576.8	2400
323.2	51.7	527.5	1400
338.2	48.3	493.0	600
353.2	44.9	453.7	60

[a] Hz (cP)$^{-1}$, ±5%. [b] M^{-1}, ±20%.

Table II. Limiting Line Widths (Reduced to Unit Viscosity) and Formation Constants for the 1:1 Complex (Subscript 1) and for the 1:2 Complex (Subscript 2) of Na^+ and **2**

T, K	$\Delta\nu_{1/2}{}^{F\,a}$	$(\Delta\nu_{1/2}{}^{B})_1{}^a$	$(\Delta\nu_{1/2}{}^{B})_2{}^a$	$K_1{}^{b,c}$	$K_2{}^b$
278.2	61.8	491	614	800	26
293.2	58.4	446	579	750	18
307.2	55.4	424	487	550	31
323.2	51.7	388	484	475	24.5
338.2	48.3	370	407	380	40
353.2	44.9	346	433	350	25.5

[a] Hz (cP)$^{-1}$, ±5%. [b] M^{-1}, ±20%. [c] $\Delta H° = -2.3 \pm 0.2$ kcal mol^{-1}, $\Delta S° = +5.1 \pm 0.8$ eu.

In order to reduce the number of parameters, we made the simplifying assumptions that these seven rate constants reduce in fact to a single rate constant k_A, according to the equations: $k_B = K_1^{-1}k_A$; $k_C = k_A$; $k_D = K_2^{-1}k_A$; $k_E = k_A^2$; $k_F = (K_1K_2)^{-1}k_A^2$. The degenerate equilibrium **3**·Na^+ $\rightleftarrows^{k_G}$ Na^+·**3** does not affect the variations of the transverse relaxation rates. These assumptions turn out to be too drastic, since they do not lead to a self-consistent set of parameters. For instance, using the high-temperature data it was not possible to obtain the value of R_{av} (fast exchange), despite the linearity of log $(1/T_2)$ vs. $1/T$ at these temperatures, which appeared to be consistent with fast exchange. The criterion of a reduction of the line width upon increasing the temperature is not an unambiguous indication for fast exchange.[10] Indeed, a careful scrutiny of the plots of log R vs. T^{-1} showed a lack of parallelism between the linear segments observed for the solutions devoid of ligand, and for the high-temperature asymptote in the presence of ligand **3** (see Figure 2 for an example of the normal behavior). This could be due to nonfulfillment of the fast exchange condition. In order to test for the possibility of moderately slow exchange, rather than fast exchange, at the highest temperatures used, we resorted to a T_1–T_2 comparison. Considering a two-site AB exchange problem, at moderately slow exchange, the transverse relaxation rate is given by the approximate expression:

$$1/T_2 = p_A/T_{2A} + p_B/T_{2B} + p_A{}^2p_B{}^2(\omega_A - \omega_B)^2(\tau_A + \tau_B) \qquad (7)$$

As for the longitudinal relaxation rate $1/T_1$, it is not affected by exchange between the anisochronous A and B sites. In the case at hand, the chemical shift differences $1/2\pi(\omega_A - \omega_B) \sim 200$ Hz is nonzero, but remains inferior to the line width (typically 500 Hz). Hence, exchange at an intermediate rate would translate into a longitudinal relaxation rate $1/T_1$ *inferior* to the transverse relaxation rate $1/T_2$, which could account for the small discrepancy noted above. However, direct measurements of T_1, with the usual (180°–waiting time–90°) pulse sequence, showed similarity of T_1 and T_2, and confirmed the reality of fast exchange in the high-temperature range.

Interaction of sodium ions with ligand **4** was analyzed in terms of the two coexisting equlibria:

$$Na^+ + \mathbf{4} \overset{K_1}{\rightleftarrows} \mathbf{4}\cdot Na^+ \qquad (8)$$

$$\mathbf{4}\cdot Na^+ + \mathbf{4} \overset{K_{1/2}}{\rightleftarrows} \mathbf{4}\cdot Na^+\cdot\mathbf{4} \qquad (9)$$

Analysis of the data was also attempted in terms of the same equilibria as with ligands **2** and **3**, i.e., joint formation of 1:1 and 1:2 complexes: this procedure fails totally. As for obtaining kinetic parameters, this is rendered impossible by fast exchange conditions prevailing throughout the accessible temperature range, down to ca. −40 °C. The reduced line width was monitored as a function of $\rho = [\mathbf{4}]/[Na^+]$ for ρ values between 0.34 and 2.1, at constant sodium concentration $[NaClO_4]$ = 83 mM (Figure 4).

The formation constants K derived for complexes between Na^+ and ligands **1**–**4** are all true formation constants at the low ionic strength (I < 0.08) of our solutions.[11] The error limits stated in the tables were

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(9) Woessner, D. E. *J. Chem. Phys.* **1961**, *35*, 41–48.

(10) Feeney, J.; Batchelor, J. G.; Albrand, J. P.; Roberts, G. C. K. *J. Magn. Reson.* **1979**, *33*, 519–529.

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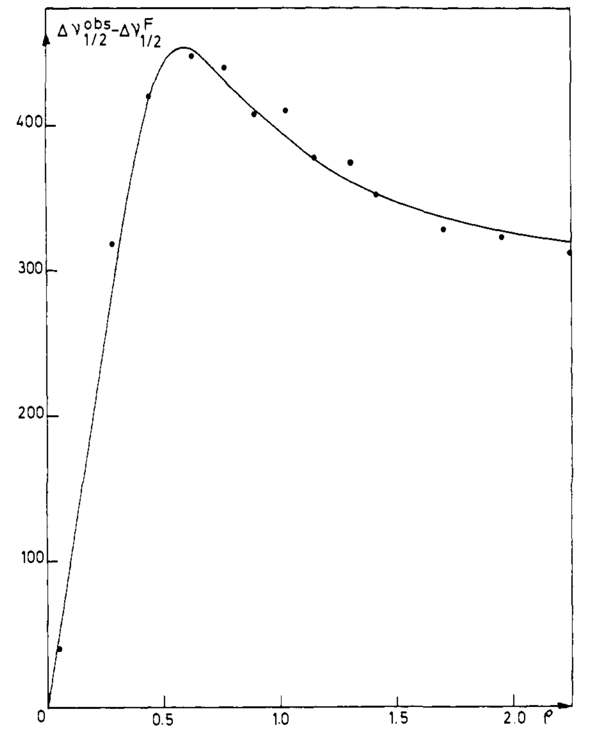

Figure 3. Typical curve of $\Delta\nu_{1/2}$ vs. ρ = [3]/[NaClO$_4$] at 304.4 K.

Table III. Limiting Line Widths (Reduced to Unit Viscosity) and Formation Constants for the 1:1 Complex (Subscript 1) and for the 1:2 Complex (Subscript 2) of Na⁺ and 3

T, K	$\Delta\nu_{1/2}{}^{F\,a}$	$(\Delta\nu_{1/2}{}^{B})_1{}^{a}$	$(\Delta\nu_{1/2}{}^{B})_2{}^{a}$	$K_1{}^{b}$	$K_2{}^{b}$
291.8	55.8	423	837	1,760	185
304.4	54.2	320	655	920	140
318.5	52.6	235	499	450	105

[a] Hz (cP)$^{-1}$, ±5%. [b] M^{-1}, ±30%.

obtained after confirming the results of Simplex optimization with least-squares multiple regressions: the latter yielded the uncertainties quoted for the various parameters.

Results and Discussion

Formation constants for the various complexes formed (1:1, 1:2, and 2:1) between Na⁺ ions and ligands **1**–**4** in pyridine solutions, together with values for the limiting line widths, are listed in Tables I–IV. The limiting line widths for free sodium ions $\Delta\nu_{1/2}{}^{F}$ have values in the range 45–65 Hz (cP)$^{-1}$, which is as expected for NaClO$_4$ solutions at 70–90 mM concentrations in pyridine, in the 278–353 K temperature range.

The O$_5$–dodecyl$_2$ ligand **1** interacts strongly with sodium ions—the binding constant is large (Table I). This result accords with the expectations: by analysis with 15-crown-5, ligand **1** (a 16-crown-5 derivative) should indeed display strong sodium binding. The presence of the two *n*-dodecyl side chains does not appear to affect much the binding constant. This ligand **1** serves as a reference, for comparison of the results for the spiro-bicyclic ligand **2**. With this O$_5$–O$_5$ molecule, sodium complexation by the first O$_5$ ring occurs with a binding constant rather similar, at the same temperatures, to that for the monocyclic ligand **1**; we note only that the values for **2** are systematically smaller, by a factor of 2–4, than the values for **1**. Both steric hindrance to complexation by the dangling *n*-dodecyl chains in **1** and participation by the oxygen heteroatoms in the second O$_5$ ring of **2** in the 1:1 complex formation would have led to the converse. This finding is thus consistent with (weak) participation by the oxygen heteroatoms in the ether side chains of **1**, and/or a small conformational change rendering the O$_5$ ring less apt to sodium com-

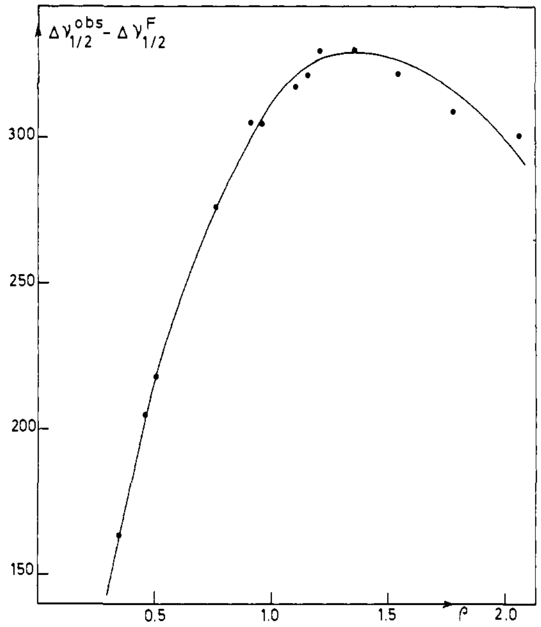

Figure 4. Typical curve of $\Delta\nu_{1/2}$ vs. ρ = [4]/[NaClO$_4$] at 306.3 K.

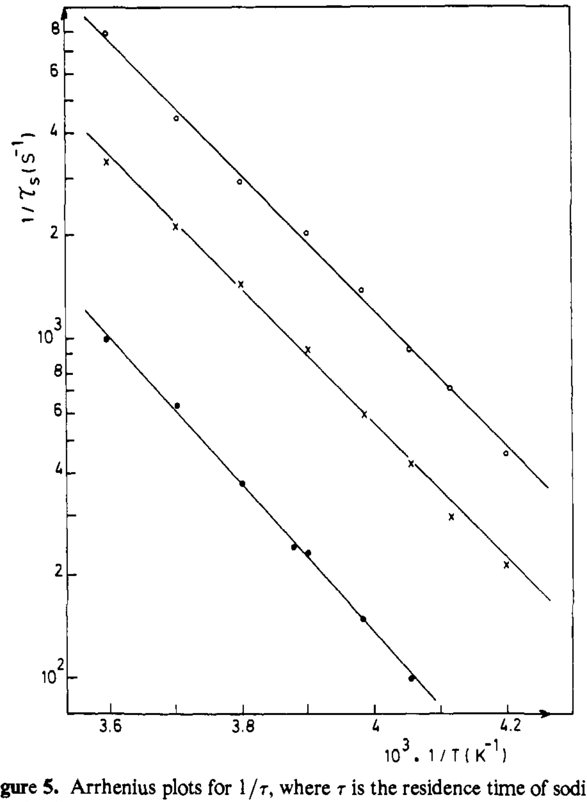

Figure 5. Arrhenius plots for $1/\tau$, where τ is the residence time of sodium ions in the state where they are bound to ligand **1**. (●) ρ = 0.2; (×) ρ = 0.4; (○) ρ = 0.6.

Table IV. Limiting Line Widths (Reduced to Unit Viscosity) and Formation Constants for the 1:1 Complex (Subscript 1) and for the 2:1 Complex (Subscript 1/2) of Na⁺ and 4

T, K	$\Delta\nu_{1/2}{}^{F\,a}$	$(\Delta\nu_{1/2}{}^{B})_1{}^{a}$	$(\Delta\nu_{1/2}{}^{B})_{1/2}{}^{a}$	$K_1{}^{b}$	$K_{1/2}{}^{b}$
286.6	56.5	823	235	140	20
296.9	55.2	766	122	80	18
306.3	54.0	789	100	60	26

[a] Hz (cP)$^{-1}$, ±5%. [b] M^{-1}, ±20%.

plexation in **2** as compared to **1**. The latter would be consistent with other reports in the literature of significant changes in complex stability due to small deviations with respect to an ideal conformation.[12] Examination of the limiting line widths for the 1:1 complexes formed between **1** or **2** and Na$^+$ shows indeed significantly lower values for the **2**·Na$^+$ complex as compared to the **1**·Na$^+$ complex, by 20–30%. This would appear to indicate—if the reorientational correlation time for **2** is at least equal to that for **1**, which is to be expected—that the complex formed by the O_5 ring with Na$^+$ is both more symmetrical and/or weaker in **2** as compared to **1**.

Noteworthy, of course, is the reduction in binding constant when the second sodium ion affixes itself to the second O_5 ring in **2**. There is one order of magnitude difference between the binding constants K_1 and K_2, characteristic of 1:1 and 1:2 complex formation (Table II). The limiting line width for the disodium species exceeds significantly (by 15–20%) that for the complex with a single bound sodium: this is due to an additional electrostatic field gradient component from the presence of a nearby electric charge, with time fluctuations because of internal motions in the two rings; or to increased solvation of the sodium complex leading to a greater reorientational correlation time; or to both these factors jointly.

Turning now to the static parameters for complex formation by the O_6–O_6 ligand **3**, which just like its lower homologue O_5–O_5 **2** forms both 1:1 and 1:2 Na$^+$ inclusion complexes, one notes the greater affinity for sodium ions of **3** as compared to **2**, for each of these two stoichiometries. That the O_6–O_6 system shows somewhat greater binding strength than the O_5–O_5 system is not unprecedented: for instance, Izatt et al.[3] have determined log K = 4.36 for 18-crown-6 against log K = 3.48 for 15-crown-5 in *methanol* solution (in chloroform 15-crown-5 binds Na$^+$ stronger, at least judged from extraction experiments). As with O_5–O_5, attachment of the first sodium ion to O_6–O_6 diminishes the binding constant at the second site, by nearly one order of magnitude. The greater stability of the complexes with **3** may be due to a factor pointed out by Pannell et al.:[13] the Na$^+$ cation, with an ionic radius of 0.95 Å, is too small for each of the cavities of O_6–O_6 which, by analogy with related compounds,[14] have a radius of 1.34–1.43 Å. Hence, Na$^+$ can occupy an excentric position within the cavity so as to coordinate more strongly with five oxygen heteroatoms, and more weakly with the sixth oxygen, as found in the X-ray structure of the Na$^+$-18-crown-6 complex in the crystal.[14] By contrast, Na$^+$ fits only above the plane of ligand oxygen atoms of benzo-15-crown-5,[15] and interacts equally with the five coordinating oxygens, where the cavity radius (0.86–0.92 Å)[14] is too small for inclusion. This could explain the greater strength of the **3**·Na$^+$ complex with respect to the **2**·Na$^+$ complex; in the 1:2 complex Na$^+$·**3**·Na$^+$, a compromise has to be struck. It is likely that electrostatic repulsion forces the two sodium cations into distal positions, in which coordination by the oxygen heteroatoms is not at its maximum, as in the 1:1 complex **3**·Na$^+$. Noteworthy is the increase, by a factor 2, of the limiting line width in the 1:2 complex as compared to the 1:1 complex (Table III).

Indeed, little did we expect to find, when launching upon this study, a negative cooperativity by one order of magnitude only, when two univalent ions occupy two cavities which touch. This finding should be extremely encouraging for the design of inclusion complexes featuring several encapsulated metallic ions, such as exist in Nature, the metallothioneins being just one instance. With respect to the cooperativity displayed in the formation of bimetallic complexes, we note that a more strongly negative cooperativity occurs in the binding of two lithium ions by a tetradentate amido ether.[16] On the other hand, Rebek et al.[17] have reported recently the complexation properties of a bis-crown ether (bis-22-C-6) toward $Hg(CF_3)_2$, where binding occurs independently at the two sites.

Table V. Rate Constant for the Release (k_-) and Corresponding Activation Energy (E_a) of the Sodium Ion from the 1·Na$^+$ Complex

$\rho = [1]/[NaClO_4]$	$1/\tau_s$,^{a} s^{-1}	$k_-{}^a$	$E_a{}^b$
0.200	366	1466	42
0.408	1438	2083	38.5
0.602	2889	1910	38

^{a} At 263 K. ^{b} kJ mol^{-1}.

The O_6–O_4 ligand **4** is characterized by a distinctive stoichiometry: once the 1:1 complex is formed, the 1:2 complex is precluded by the very small size of the O_4 cavity. One would expect the binding constants for the O_6 and for the O_4 ring to differ by as much as three orders of magnitude, on the basis of the determinations by Frensdorff.[3] It is quite interesting to note that a complex of 2:1 stoichiometry is formed instead. Structures that can be envisaged have two O_6 rings from two separate ligand molecules sandwiching a central Na$^+$ ion, or they involve participation of the O_4 ring as in the 2:1 complex formed between Na$^+$ and 12-crown-4. Clearly, ligand **4** binds Na$^+$ ions much more weakly with its O_6 ring than ionophore **3** (Table IV), a manifestation of conformational changes presumably. The limiting line widths for the 1:1 complex are also significantly larger for **4**·Na$^+$ than for **3**·Na$^+$, which may reflect a less symmetrical arrangement of the coordinating oxygen heteroatoms around the cation. This interpretation would appear to be borne out by the marked *reduction* in the limiting line width in the change from the 1:1 to the 2:1 complex, despite as assuredly greater orientational correlation time for the 2:1 complex. In the latter the Na$^+$ ion is likely to be more symmetrically coordinated, to a maximum of 12 oxygens.

Similar effects have been noted by other workers: for the interaction of Na$^+$ with crown ethers, studied by ^{23}Na NMR[18] and for the interaction of Li$^+$ with the diamine–diether NDA studied by ^{7}Li NMR[16]. In these studies,[16,18] the 2:1 "sandwich"-type complex is also characterized by a smaller limiting line width than the 1:1 complex. In other terms, the distribution of electric charges around the quadrupolar ion deviates less from cubic symmetry in the 2:1 than in the 1:1 complex.

Turning now to the kinetic results, they are listed for the O_5–dodecyl$_2$ system **1** in Table V. Plots of $1/\tau$ vs. $1/T$ are shown in Figure 4, from which the activation energies also indicated in Table V have been drawn. From the binding constant K which, extrapolated down to 263 K (see Table I), has the value 11 620 the rate constant for sodium binding $k_+ = K_1\, k_- = 1.3^5 \times 10^8$ M^{-1} s^{-1} is close to the diffusion limit. Hence, in pyridine solution as in protic solvents,[4,19] binding of the univalent Na$^+$ to an ionophore is diffusion controlled (rather than being controlled by desolvation as the slow step). The rate constants k_+ and k_- obtained here for Na$^+$ binding and release by **1** in pyridine are very close to those characteristic of polyether antibiotics: the Eigen group[20] has reported $k_+ = 1.6 \times 10^8$ M^{-1} s^{-1} and $k_- = 4.2 \times 10^4$ s^{-1} for trinactin in methanol. From the activation energies E_a for Na$^+$ release from the **1**·Na$^+$ complex (Table V), and since $E_a = \Delta H^{\ddagger} + RT$, taken together with the enthalpy of formation of the **1**·Na$^+$ complex (ca. −25 kJ mol^{-1}), the activation enthalpy for the forward binding step $\Delta H^{\ddagger}{}_{+} = 12.5 \pm 7$ kJ mol^{-1}. This value, of modest size, appears as quite reasonable for a mechanism in which in the transition state the univalent alkali metal ion is partly desolvated

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and at the same time partly coordinated to its crown ether host.

As indicated in the Experimental section, despite numerous and extensive computational efforts, we could not extract from the experimental data kinetic parameters appropriate to the **3**·Na^+ and to the Na^+·**3**·Na^+ systems. We were left in the quandary of having either too many parameters to extract from a limited number of experimental points or of cutting down drastically upon the number of rate constants to be determined, and finding that in the process of constraining our model on such a Procustean bed we killed it! Back of the envelope calculations show further that with diffusion-controlled values of k_+ in the 10^7–10^8 M^{-1} s^{-1} range, k_- for compounds **2** and **4** as estimated from the K_1 values (Tables II and IV) would be in the range of 10^4–10^6 s^{-1}, i.e., too fast to display intermediate exchange behavior—exactly as is found qualitatively in the temperature range accessible with pyridine solutions.

Conclusion

Like other crown ethers, spiro-bis-crown ethers form, at high ligand concentration, sandwich complexes having one Na^+ ion in between two ligand molecules. These 2:1 complexes coexist with 1:1 complexes. Conformational factors are important, besides cavity size, in determining the magnitude of K for these 1:1 complexes. But the distinctive feature of these ligands, with their two cavities offered as cation-binding sites, is formation of dicationic 1:2 complexes. These doubly occupied complexes of spiro-bis-crown ethers are *less* disfavored than could have been feared on the basis of strong electrostatic repulsions; furthermore, entropy variations appear to be more favorable to double occupancy than to single occupancy of the two binding sites. Hence, direct examination of the thermodynamics and kinetics of cation binding from nuclear magnetic resonance of the cation itself proves to be rewarding and to provide a wealth of information.

Note Added in Proof. The recent X-ray structure of the complex formed between O_6–O_6 and 2LiI, $4H_2O$ shows that each of the macrorings binds one of the water solvation molecules and an Li^+ ion in the same cavity, the metal ion being coordinated to three oxygens from the macroring and to two oxygens from water molecules.[21] This observation is consistent with our description of complex formation between O_6–O_6 and two Na^+ ions.

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Ab Initio SCF Studies of Interactions of Li^+, Na^+, Be^{2+}, and Mg^{2+} with $H_2PO_4^-$: Model for Cation Binding to Nucleic Acids

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Abstract: Phosphate anion–metal cation complexes of $(OH)_2PO_2^-$ with Li^+, Na^+, Be^{2+}, and Mg^{2+} have been studied by using ab initio self-consistent field methods with an extended, double ζ plus polarization, basis set. The most stable binding site for all cations is a symmetric C_{2v} complex with the metal interacting with two phosphate oxygen atoms, consistent with previous calculations. Significant electron transfer was found for all complexes except that involving Na^+, implying that Li^+, Be^{2+}, and Mg^{2+} interactions with phosphate are not totally electrostatic. Hydration of Li^+ and Be^{2+} does not significantly alter the extent of covalency of the metal–phosphate bond, although it weakens the direct complex formation by partial neutralization of the cation. All cations are found to affect both the geometry and electronic charge distribution of the phosphate group, consistent with their key role in determining nucleic acid conformational stability.

Nucleic acid structure is greatly influenced by the intrapolymer electrostatic forces involving the ionized phosphate groups of the backbone. Since the charges of these groups can be shielded by associated counterions, changes in ionic strength and ion type can trigger functionally important conformation changes in the polymer.

The sensitivity of nuclei acid structure to the concentration and type of cation with which it is associated has been established by a variety of experimental techniques. Well-defined conditions for obtaining DNA fibers in the A, B, and C forms have been determined by X-ray crystallographers.[1d] More recently, the identification of the circular dichroism spectrum for each of these forms in solution has allowed the observation of B → C + A transconformational reactions as a function of ion type and ionic strength.[2-4] The duplex rotation angle of closed circular DNA has been shown to depend on ion type and concentration.[5,6] The

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