Rates and Equilibria of Alkali Metal and Silver Ion Complex Formation with Monensin in Ethanol

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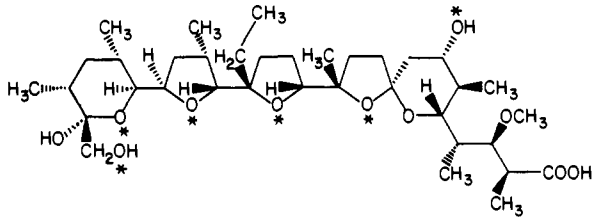
Abstract: Measurements are reported on the stability constants and the rates of formation and dissociation of alkali metal and silver complexes of monensin in ethanol. Among the alkali metal complexes the order of stability is $Li^+ < Na^+ > K^+ > Rb^+ > Cs^+$ (with $Cs^+ \sim Li^+$). Compared with the neutral antibiotic ionophores, the stability constants of monensin complexes are in general higher and show a much sharper peak selectivity. Dissociation rate constants are very sensitive to cation size and reflect a similar (inverse) variation with cation size of the stability constants; the formation rate constants increase monotonically with increasing cation size from Li^+ (9.0×10^7 M^{-1} s^{-1}) to Cs^+ (2.5×10^9 M^{-1} s^{-1}). The silver complex, AgMon, has a stability constant slightly higher than that of the most stable alkali metal complex, NaMon, and a remarkably high formation rate constant, $k_f = 3.5 \times 10^{10}$ M^{-1} s^{-1}, approaching that of a diffusion-controlled reaction, despite the high solvation energy of Ag^+. The kinetic and thermodynamic properties of monensin complexes are compared with those of other naturally occurring and synthetic macrocyclic ionophores.

Monensin (I) is a linear monocarboxylic acid antibiotic of the Nigericin group, first isolated by Agtagrap et al.[1] from cultures of *streptomyces cinnamonensis* in 1967. In recent years a number of investigations of the molecular structure,[2-4] biological activity,[5,6] and chemical properties[7-9] of monensin have been reported. Of major interest have been the specific alkali cation transport properties of the ionophore in biological[5,6] and artificial[6] membrane systems.



I

The stability constants of metal ion complexes of monensin in methanol have been measured by using various techniques including potentiometry,[7] calorimetry,[8] cyclic voltammetry,[7] and fluorescence.[9] The results show that monensin forms stable complexes with several monovalent metal cations and among the alkali cations shows a marked specificity for the sodium cation.[7,8] Cation transport studies have shown a close correlation between the transport and complexing properties of the ligand.[3,5]

Crystallographic studies of the free acid and various metal complexes[2,4] reveal a pseudocyclic conformation in which the ends of the chain are linked by intramolecular head-to-tail hydrogen bonds involving the carboxylate group and suitably placed OH groups. The cations are located at the center of the pseudocavity and coordinated by six oxygen atoms. In this respect the complexes are very similar to those of various synthetic macrocyclic ligands such as crown ethers[10] and cryptands[11] and other naturally occurring ionophores such as valinomycin, ennantian B, macrotetralides, etc.[12]

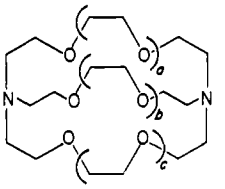
To date, almost no information on the kinetic properties of monensin complexes is available, despite the importance of the complexation–decomplexation steps in the overall cation transport process. The kinetics of Na^+ exchange between free and complexed sites in the Na^+/monensin system in methanol have been studied by using ^{23}Na NMR, with the rate-determining step being ascribed to the dissociation reaction.[13] We have also recently studied the kinetic and thermodynamic properties of silver monensin in several different solvents.[14]

In this work we report the stability constants and the rates of formation and dissociation of alkali metal and silver complexes in ethanol. Ethanol was chosen as an example of a protic solvent because the high stabilities and relatively low dissociation rates of the complexes in this solvent permit a systematic investigation of complex formation over the full range of alkali metal cations.

We also describe the preparation of tetraalkylammonium salts of monensin. These are particularly convenient for the study of different cationic complexes in various solvents.

Experimental and Results

Materials. The inorganic salts $LiClO_4$, $NaClO_4$, $AgClO_4$, KF, RbF, and CsF were high-purity commercial samples, used without further purification. Cryptands (2,1,1), (2,2,1), and (2,2,2) (II–IV) were used as cation scavengers in kinetic measurements. They were commercial



II, $a = 1$; $b = c = 0$ (2,1,1)
III, $a = b = 1$; $c = 0$ (2,2,1)
IV, $a = b = c = 1$ (2,2,2)

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samples (Merck) used as purchased. Ethanol was purified by distillation from magnesium turnings and iodine.

For potentiometric measurements of the stability constants, both tetraethylammonium picrate and tetraethylammonium perchlorate were used as salt bridge electrolytes. They were prepared by reaction of tetraethylammonium hydroxide (Aldrich, 20% solution in water) with the corresponding acid and purified by successive recrystallizations from water followed by drying under vacuum (70 °C).

The anion of monensin (Mon^-) as its tetrabutylammonium (or tetraethylammonium) salt was prepared by the following procedure. Sodium monensin (Sigma, NaMon) was dissolved in hot methanol and the solution filtered. It was precipitated by the addition of water to the cooled methanolic solution. This purification step was repeated twice in order to rid the salt of an unidentified yellow impurity. The white salt obtained was dried under vacuum for several hours. It was then dissolved in chloroform and stirred vigorously for 1 h with a layer of aqueous perchloric acid (1 M) to convert NaMon into the acid form of monensin (MonH). The chloroform layer containing MonH was washed with distilled water until the washings were neutral and then evaporated to dryness. The resulting crystals were dried under vacuum. MonH was dissolved in methanol and carefully neutralized (pH control) with tetrabutylammonium hydroxide (BDH 40% solution in water). This solution was evaporated at 30 °C and dried under vacuum for several hours. The final product had a very pale yellow color and was stored in a desiccator. The carbonyl stretch in the IR provided a very useful conformation of the conversion of MonH into its salt: $\bar{\nu}_{C=O}$ (MonH) = 1710 cm^{-1}; $\bar{\nu}_{C=O}$ (Mon^-M^+) = 1570 cm^{-1}.

Bu_4NMon is readily soluble in water, and various metal salts of MonH could be easily prepared by adding an appropriate electrolyte (e.g., KCl, RbCl, etc.) to aqueous Bu_4NMon, as all of the simple metal monensin salts are only slightly soluble in water.

The purity of Bu_4NMon prepared by the above method was checked by elemental analysis and by measuring the stability constants of alkali metal and silver complexes in methanol, using the potentiometric method described below. The results obtained in methanol[15] were in good agreement with literature values.[7,8,16]

Stability Constant Measurements. The stability constants, K_s, of the silver and alkali metal monensin complexes (M·Mon) were determined by pAg potentiometry using a three-compartment cell, as described previously, for cryptate systems in different solvents.[17,18] The stability constant for AgMon, i.e., the equilibrium constant for reaction 1, was

$$Ag^+ + Mon^- \overset{K_s}{\rightleftharpoons} AgMon \quad (1)$$

$$\text{where} \quad K_s = \frac{[AgMon]}{[Ag^+][Mon^-]\gamma_\pm^2} \quad (2)$$

determined by a direct titration of silver perchlorate solution with Bu_4N Mon. Total Ag^+ concentrations were in the range 1.5×10^{-4} to 5.0×10^{-4} M, and [Mon^-] was in the range 4.0×10^{-4} to 2.0×10^{-3} M. The required activity coefficients, $\gamma_\pm$, which refer to infinite dilution in ethanol, were calculated by using the Davies equation (eq 3),[19] where I is the ionic strength and A ($=1.825 \times 10^6/(\epsilon T)^{3/2}$) is the Debye–Hückel function. In most cases corrections were very small (<0.1 log unit)

$$\log \gamma_\pm = \frac{-AI^{1/2}}{1 + I^{1/2}} + 0.3AI \quad (3)$$

because of the low ionic strengths employed. In these measurements we have assumed that at the concentrations used, Bu_4NMon is completely dissociated and that there is no tendency for complex formation between Bu_4N^+ and Mon^-. This was checked by adding Bu_4NClO_4 or Et_4NClO_4 to the various solutions used in stability constant measurements. This had no effect on the results, apart from small changes in potential consistent with expected variations in activity coefficients.

The stability constants of AgMon were used in conjunction with equilibrium constants for the exchange reactions 4[17,18] to determine the

$$AgMon + M^+ \overset{K_e}{\rightleftharpoons} M\cdot Mon + Ag^+ \quad (4)$$

stability constant for M·Mon (cf. eq 1 and 2) for M^+ = Li^+, Na^+, K^+, Rb^+, and Cs^+. For these measurements, total metal ion concentrations used were ca. 1×10^{-3} to 7×10^{-3} M, [Mon^-] ca. 4×10^{-4} to 1×10^{-3} M, and [Ag^+] ca. 1.5×10^{-4} to 5×10^{-4} M, although concentrations at the lower end of these ranges (where activity coefficient corrections are small) were generally used.

Table I. Stability Constants of Metal Ion Complexes of Ionophores in Ethanol at 25 °C

	log K_s (M^{-1})					
ligand	Li^+	Na^+	K^+	Rb^+	Cs^+	Ag^+
monensin[a]	5.35	8.82	7.28	6.23	5.18	8.94
nonactin[b]		3.53	4.28			
valinomycin[b]		2.3[c]	6.3	6.4	5.8	
beauvericin[b]	2.0	2.5	3.49	3.54	3.54	
(2,2,1)[d]	5.38	10.20	8.56	6.88	4.77	13.84
(2,2,2)[d]	2.3	8.57	10.50	9.28	4.17	11.51

[a] This work, ±0.1 in log K_s. [b] References 12 and 23. [c] Estimated from results in MeOH, ref 12. [d] Reference 20.

The potentiometric titrations (eq 1 and 4) were always repeated at least three times. The values of K_s(AgMon) and K_e obtained were reproducible within ±0.1 in log K. For sodium monensin the stability constant was also measured by direct titration of NaMon with Ag^+ solution, and the result was in good agreement with that determined from Bu_4NMon. The various stability constants are reported in Table I, together with those of other alkali metal ionophores in ethanol for comparison.

The effect of trace water in EtOH on the stability constants was tested for AgMon, LiMon, and NaMon by adding known amounts of water to the system. The results show that addition of 0.2% v/v water led to an ca. 4% decrease in the stabilities of AgMon and LiMon, and further addition up to 1.5% v/v H_2O reduced the stabilities by ca. 18% and 22%, respectively. As the latter only correspond to 0.1 in log K_s, it may be concluded that the small amount of water in the ethanol (ca. 0.05% v/v)[20] has a negligible effect on the measured log K_s values. The stability of NaMon was rather more sensitive to added water, with decreases in log K_s of 0.17 and 0.3 on addition of 0.7% and 1.5% v/v water, respectively. Again, however, the effects of trace amounts of water in the purified ethanol should be well within experimental error.

Kinetic Measurements. The rates of formation and dissociation of the various metal monensin complexes were determined by using the stopped-flow technique to monitor competitive reactions of monensin and cryptands for the cations as follows. When a large excess of an appropriate cryptand (Cry) is mixed with a M·Mon solution, an increase in conductance is observed due to the production of ionic species as in (5).

$$M\cdot Mon + Cry \xrightarrow{k_e} M\,Cry^+ + Mon^- \quad (5)$$

The reaction is kinetically pseudo first order, and provided that the cryptand is chosen such that $K_s(MCry^+) > K_s(M\cdot Mon)$, the reverse reaction corresponding to eq 5 can be neglected.

In the absence of direct exchange of the cation between Mon^- and Cry, reaction 5 may be written in a stepwise manner as in eq 6 and 7. Application of the steady-state assumption to [M^+] (very low in the presence of excess Cry, Mon^-) gives eq 8 and 9

$$M\cdot Mon \underset{k_f}{\overset{k_d}{\rightleftharpoons}} M^+ + Mon^- \quad (6)$$

$$M^+ + Cry \xrightarrow{k} M\cdot Cry^+ \quad (7)$$

$$\frac{-d[M\cdot Mon]}{dt} = k_e[M\cdot Mon] \quad (8)$$

$$\text{where} \quad k_e = \frac{k_d k[Cry]}{k_f[Mon^-] + k[Cry]} \quad (9)$$

In general, the formation rate constants of the monensin complexes, k_f, are significantly larger than those of the cryptates, k. Where the difference is so large that $k_f[Mon^-] \gg k[Cry]$, eq 9 reduces to eq 10. In this case combining the stability constant, K_s, of M·Mon and the slope of a plot of k_e vs. [Cry]/[Mon^-] gives the rate constant for cryptate formation. More often, however, because of the large excess of cryptand

$$k_e = \frac{k_d k[Cry]}{k_f[Mon^-]} = \frac{k[Cry]}{K_s[Mon^-]} \quad (10)$$

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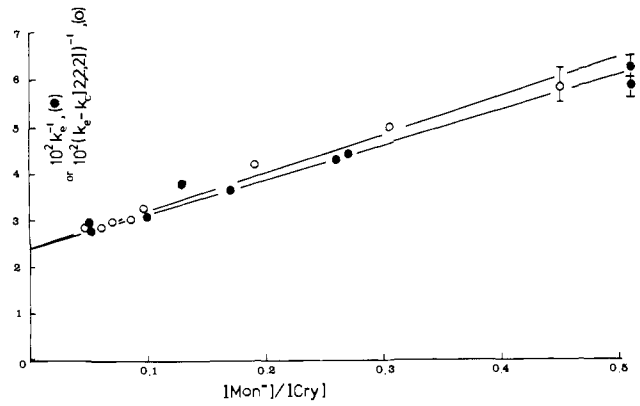

Figure 1. Rates of exchange of Ag^+ between AgMon and $Ag(2,2,1)^+$ (●) or $Ag(2,2,2)^+$ (○) in ethanol at 25 °C.

([Cry] ≫ [Mon⁻]), k[Cry] ≃ k_f[Mon⁻]. Then eq 9 can be rewritten as eq 11 and k_d, the dissociation rate constant for M·Mon, may be obtained

$$\frac{1}{k_e} = \frac{1}{k_d} + \frac{k_f}{k_d k}\frac{[\text{Mon}^-]}{[\text{Cry}]} \tag{11}$$

from the intercept of a plot of $(k_e)^{-1}$ vs. [Mon⁻]/[Cry]. The slope of this plot, $k_f/(k_d k)$ gives k_f if k is known;[21] alternatively, k may be determined by using the stability constant of M·Mon ($K_s = k_f/k_d$). It should also be noted that the internal consistency of K_s, k_f, k_d, and k values obtained in this work and earlier work on cryptate complexes in ethanol[21] may be used as a check on the reliability of the various results.

Earlier studies of AgMon complexes in various solvents[14] have shown that in a number of cases there is a direct bimolecular reaction between the complex and the displacing ligand, eq 12, in addition to the normal

$$\text{AgMon} + \text{Cry} \xrightarrow{k_c} \text{AgCry}^+ + \text{Mon}^- \tag{12}$$

mechanism proceeding via dissociation of the complex, eq 6 and 7. In this case the observed rate constant is given by eq 13, and values of k_d,

$$k_e = \frac{k_d k[\text{Cry}]}{k_f[\text{Mon}^-] + k[\text{Cry}]} + k_c[\text{Cry}] \tag{13}$$

k_f, and k_c were obtained by an iterative procedure based on eq 14 as described earlier.[14]

$$(k_e - k_c[\text{Cry}])^{-1} = k_d^{-1} + \frac{k_f[\text{Mon}^-]}{k_d k[\text{Cry}]} \tag{14}$$

The concentrations of [Cry] were in the range 1×10^{-4} to 2×10^{-2} M, [M⁺] 2×10^{-5} to 1.5×10^{-4} M, and [Mon⁻] 3×10^{-5} to 2×10^{-4} M. All kinetic measurements were made at 25 (± 0.2) °C, using a Durrum–Gibson stopped-flow apparatus with conductance detection. The rate constants for the different complexes were determined as follows.

AgMon. Cryptands (2,2,2) and (2,2,1) were used as scavengers. When cryptand (2,2,2) was used, direct Ag^+ exchange (eq 12) was important at higher concentrations and was allowed for via eq 14. The data for the two cryptands plotted according to eq 11 and 14 are shown in Figure 1. Formation rate constants of $Ag(2,2,1)^+$ and $Ag(2,2,2)^+$ have not previously been reported, but from the slopes of the plots combined with K_s(AgMon) from Table I, the values obtained were $k = 9.9$ (± 2.0) $\times 10^9$ M^{-1} s^{-1} and 1.0 (± 0.2) $\times 10^{10}$ M^{-1} s^{-1}, respectively

LiMon. Initial kinetic measurements were carried out with cryptand (2,1,1) as scavenger. In this case k_e was directly proportional to [2,1,1] (eq 10), i.e., under the conditions studied k_f[Mon⁻] ≫ k[2,1,1]. The slope of a plot of k_e vs. [2,1,1]/[Mon⁻], combined with the measured stability constant K_s for LiMon, gave a value of $k = 2.2$ (± 0.4) $\times 10^5$ M^{-1} s^{-1} for the rate constant of formation of $Li(2,1,1)^+$. This compares favorably with the earlier reported value in ethanol[21] of $k = 1.8$ (± 0.4) $\times 10^5$ M^{-1} s^{-1}.

The use of (2,2,1), which has a higher formation rate with Li^+, as a scavenger was more successful and allowed determinations of k_d and K_s/k values via eq 11. The slope (K_s/k) corresponds to $k(Li(2,2,1)^+) = 3.3$ (±0.5) $\times 10^6$ M^{-1} s^{-1} which again agrees well with an approximate literature value[21] of $k = 3 \times 10^6$ M^{-1} s^{-1}.

NaMon. Cryptands (2,2,1) and (2,2,2) were used as scavengers as in reaction 5. Results for both cryptands gave the same k_d values from the intercept of k_e^{-1} vs. [Mon⁻]/[2,2,1] (eq 11) as shown in Figure 2. From the slopes of the two plots and the known k values for $Na(2,2,1)^+$ and $Na(2,2,2)^+$,[21] rate constants for formation of NaMon were obtained as $k_f = 1.1 \times 10^9$ M^{-1} s^{-1} (using (2,2,1)) and 1.05×10^9 M^{-1} s^{-1} (using (2,2,2)).

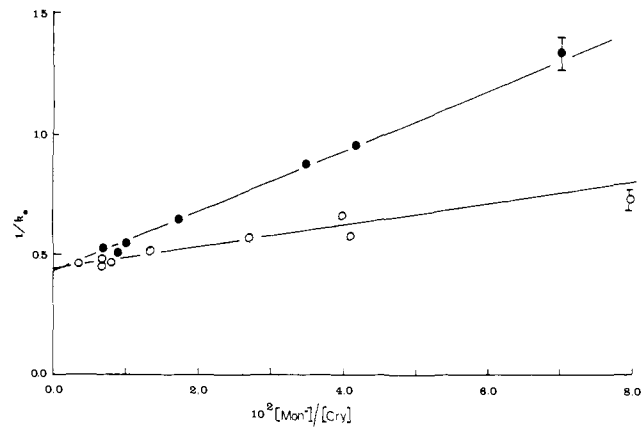

Figure 2. Rates of exchange of Na^+ between NaMon and $Na(2,2,1)^+$ (●) or $Na(2,2,2)^+$ (○) in ethanol at 25 °C.

Table II. Rate Constants for Formation and Dissociation of Monensin Complexes in Ethanol at 25 °C

complex	k_d,[a] s^{-1}	k_f,[b] M^{-1} s^{-1}	log (k_f/k_d)[c]
LiMon	4.0×10^2	9.0×10^7 [d]	
NaMon	2.2	1.11×10^9	8.70
KMon	6.7×10	1.3×10^9	7.27
RbMon	1.0×10^3	2.2×10^9	6.34
CsMon	$\sim 1.6 \times 10^4$ [e]	$\sim 2.5 \times 10^9$ [d,e]	
AgMon[f]	4.0×10	3.5×10^{10} [d]	

[a] k_d values ±8% except for RbMon, ±20%. [b] k_f values ±20%. [c] Values determined independently of measured stability constants of M·Mon; cf. potentiometrically measured K_s values in Table I. [d] Obtained from $k_f = K_s k_d$. [e] Estimated from a plot of log k_f vs. $1/r_m^+$ (see text). [f] In conjunction with these measurements, kinetic values for Ag^+–cryptates were obtained as follows: (2,2,1), $k_f = 9.9 \times 10^9$ M^{-1} s^{-1}, $k_d = 1.4 \times 10^{-4}$ s^{-1}, (2,2,2), $k_f = 1.0 \times 10^{10}$ M^{-1} s^{-1}, $k_d = 3.1 \times 10^{-2}$ s^{-1} (see text).

KMon, RbMon. The rate constants for these complexes were determined by using (2,2,2) as a scavenger and treating the data according to eq 11. The k_f values were again obtained by using known formation rate constants for the corresponding cryptates in ethanol.[21] The results for RbMon are somewhat less accurate because the rates were approaching the stopped-flow limit.

CsMon. Rate constants for reaction between CsMon and (2,2,2) were too fast to follow by stopped-flow. However, a reasonable estimate of k_f for CsMon (and hence k_d from $K_s = k_f/k_d$) may be made from a consideration of k_f values of the other alkali metal complexes. It has been noted earlier for cryptand complexes that k_f values for a series of alkali metal[21] (and alkaline earth)[22] complexes show a monotonic increase with increasing cation size and a linear dependence of log k_f vs. (cation radii)$^{-1}$. Similar behavior is observed here for the series LiMon–RbMon (see below), and this combined with the narrow range of k_f values observed suggests that k_f and k_d values for CsMon may be estimated with some confidence.

The formation and dissociation rate constants for the monensin complexes are listed in Table II. Where indicated the k_f values were obtained from measured k_d values with use of $k_f = K_s k_d$. In other cases where both k_f and k_d values were measured, the stability constants ($K_s = k_f/k_d$) calculated from the kinetic data are in good agreement with those obtained from the potentiometric technique.

Discussion

Monensin is formally an open-chain ligand, but in complexes (as the anion) and in the free acid form it adopts a cyclic structure comparable to that of other neutral macrocyclic antibiotic ionophores. There are, however, significant quantitative differences between complexes of monensin and the neutral ligands such as

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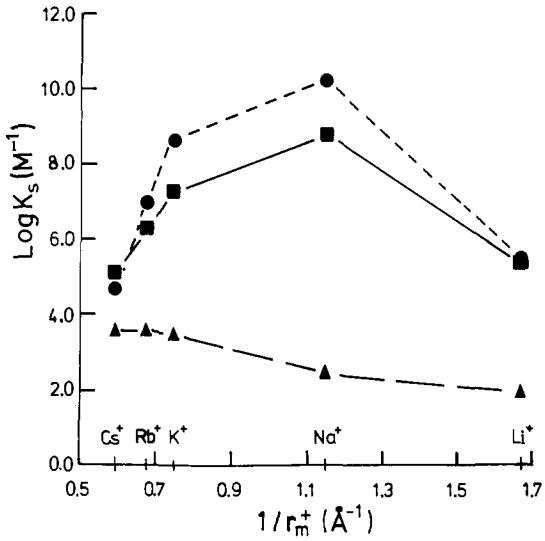

Figure 3. Dependence of stability constants of alkali metal cations and ionophores in ethanol upon cation size: (2,2,1) (●); monensin (■); beauvericin (▲).

beauvericin, the macrotetralides (nonactin, monactin, etc), enniatin, and valinomycin,[12,23-25] as illustrated in Table I and Figure 3. The monensin complexes have a significantly higher maximum stability and a much sharper peak selectivity. The occurrence of a stability maximum for the Na^+ complex is also unusual among naturally occurring ligands. The stabilities of most complexes of the neutral antiobiotics increase sharply from Li^+ to Na^+ to K^+, but thereafter remain approximately constant for Rb^+ and Cs^+.

Two factors may be important in determining these differences: the negative change of the ionized monensin ligand and the somewhat smaller cavity size. On the basis of purely electrostatic effects, a monotonic decrease in complex stability from Li^+ to Cs^+ would be expected. However, the ligand cavity, consisting of an approximately 17-membered ring[4] with six oxygen donor atoms (structure I), should favor a cation of about the size of K^+, assuming the crown ethers to be a reasonable model for size-dependent effects.[26] Thus Rb^+ and Cs^+ are probably discriminated against both on grounds of size and reduced electrostatic interactions, whereas the relatively low stability of LiMon, despite its stronger electrostatic forces, presumably results from Li^+ being too small to interact effectively with sufficient of the donor atoms. The higher stability of NaMon relative to KMon may be attributed predominantly to stronger electrostatic interactions. By contrast, the neutral macrocyclic antibiotics, which generally have 30-membered or larger rings, can adopt conformations which allow relatively strong cation–donor interactions only with the larger cations, K^+–Cs^+, and do not have the compensating stronger electrostatic interactions for Li^+ and Na^+ exhibited by the monensin anion.

The selectivity and maximum stability of the monensin complexes, however, are still somewhat lower than those of the more rigid bicyclic cryptand ligands (Table I, Figure 3). A comparison with (2,2,1) complexes, which also show a maximum stability for the Na^+ complex, reveals the overall range of stabilities to be lower for M·Mon complexes (2.6 log units compared with 5.4 log units for $M(2,2,1)^+$) and the absolute stability of NaMon to be lower than that of $Na(2,2,1)^+$ by 1.4 log units. Thus the pre-formed spherical cavity of the cryptand ligand enables it more effectively

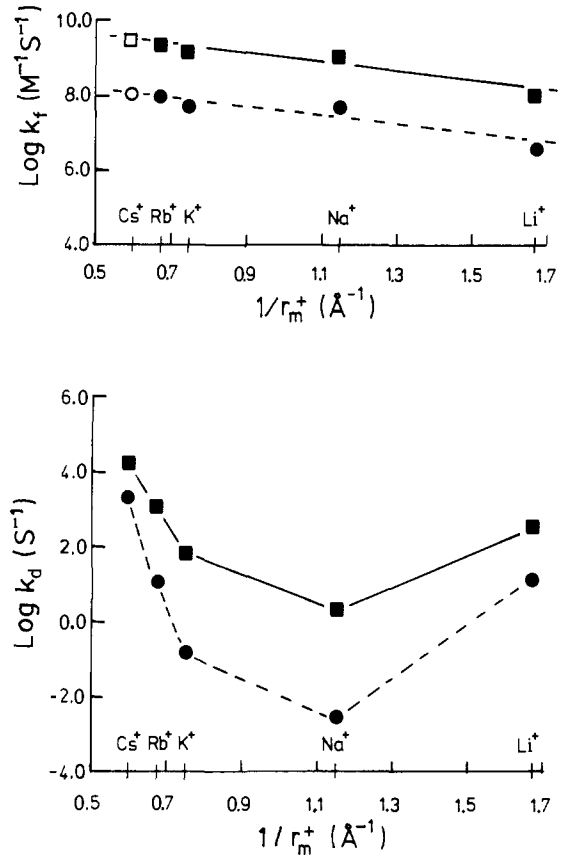

Figure 4. Rates of formation (top, a) and dissociation (bottom, b) of alkali metal complexes of monensin (■) and 2,2,1 (●) in ethanol at 25 °C.

to discriminate between cations of different size and gives rise to higher maximum stabilities, despite the additional electrostatic attraction involved in the monensin complexes.

The stabilities of M·Mon complexes are on average about 1.8 log units higher in ethanol than in methanol.[7-9,16] This is broadly in line with expectations based on the lower solvation of cations in ethanol, but comparisons with other macrocyclic ligand systems also show that the solvation of the free and complexed ligand cannot be neglected. This point will be discussed in greater detail in conjunction with stability constant measurements covering a wider range of solvents.[15]

The formation rate constants (Table II) for the various monensin complexes are high but, except for the Ag^+ complex, somewhat lower than those of diffusion-controlled reactions (ca. 3×10^{10} M^{-1} s^{-1}).[27] This, together with the monotonic increase of k_f with cation size for the alkali metal cations, suggests that partial desolvation of the cation is important in the rate-limiting step for complex formation. As with other naturally occurring and synthetic macrocyclic ligands, the formation rate constants are not directly related to the stability of the complex being formed.[12,21] However, the rate constants are sufficiently high and the variation among cations sufficiently small (e.g., less than a factor of 3 between Na^+ and Cs^+) to indicate that replacement of coordinating solvent molecules by ligand donor atoms occurs by an efficient stepwise procedure. This is characteristic of the behavior of the flexible macrocyclic ionophores.[12]

The dissociation rate constants vary over a much wider range (four orders of magnitude) and are closely correlated with the variations in stability constants. This shows that the size-dependent interactions between the cations and ligand, which play a major role in cation selectivity, influence primarily the rates at which the cations can dissociate from the complex. This further implies that in the transition-state interactions between the cations and ligand-donor atoms are of a more general nature, i.e., they depend

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on the overall charge and the nature of the donor atoms but not on a precise geometrical arrangement of donor atoms, in contrast to the stable complex.

An interesting comparison may be made between the kinetic behavior of the monensin and cryptand (2,2,1) complexes. This is illustrated in Figure 4. The k_f values of (2,2,1) complexes[21] are, within experimental error, slower by a constant factor of 28, independent of the cation involved. Both systems also show an approximately linear relationship between log k_f and $(r_m)^{-1}$, where r_m is the ionic radius[28] of the cation involved. This constant difference between the formation rate constants for the two ligands can most readily be explained in terms of a difference in conformational energy required to allow replacement of cation–solvent with cation–ligand donor atom interactions during complexation. The cryptand (2,2,1) has a more rigid structure and so greater resistance to conformational change. The difference in energy required does not appear to depend upon the incoming cation. It should also be noted that the formation rates make no contribution to the relative selectivities of the two ligands.

The dissociation rates, on the other hand, show a rather sharper minimum for the Na^+ complex of (2,2,1) compared with that of monensin. Thus k_d values for $Na(2,2,1)^+$ vary over some 6 orders of magnitude and increase more sharply with both increasing and decreasing cation size on either side of Na^+. This is again in keeping with the relative flexibilities of the two ligands, as monensin should be able to adjust more easily to accommodate cations of non-optimum size and so show a somewhat smaller dependence upon the nature of the cation. The spherical cavity of the bicyclic cryptand, which leads to higher overall stabilities and lower cation dissociation rates, cannot adjust so easily to cations of different sizes, and this produces a larger variation in the dissociation rates among the cations.

Finally, a comment may be made concerning the formation rate constants for the Ag^+ complexes. These are at least 10 times higher than k_f values of alkali metal complexes of monensin and the cryptands (2,2,2) and (2,2,1) and approach the limit expected for a diffusion-controlled reaction. Similar results have also been found for AgMon complexes in other solvents[14] and $Ag(2,2,2)^+$ in water;[29] only in acetonitrile which is known to solvate Ag^+ very strongly do formation rates of Ag^+ and K^+ complexes become comparable.[29] This seems rather surprising as the overall solvation energies of Ag^+ cations are significantly higher than those of all alkali metal cations except lithium.[30,31] The reason for this apparent contradiction may lie in the fact that Ag^+ tends to form predominantly linear complexes with two ligands (or solvent molecules), involving partial covalent interactions.[32,33] It is possible that other coordinating positions are labilized by these stronger interactions and therefore can become coordinated to donor atoms of the macrocyclic ligands in the initial stages of the complexation reaction more readily than for the alkali metal cations. The dissociation rate constant for $Ag(2,2,1)^+$ is 4×10^5 times smaller than that of AgMon; this may be attributed to the strong $Ag^+ \cdots N$ interactions in the cryptand complex.

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Registry No. Li, 7439-93-2; Na, 7440-23-5; K, 7440-09-7; Rb, 7440-17-7; Cs, 7440-46-2; Ag, 7440-22-4; monensin, 17090-79-8.

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Spectroscopy and Dynamics of 9-Hydroxyphenalenone and of Its 5-Methyl Derivative in Solid Neon: Effect of Methyl Group upon Vibrational Relaxation

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Abstract: Spectroscopy and vibrational relaxation of 9-hydroxyphenalenone (9-HPLN) and of its 5-methyl derivative are examined and compared. Extensive vibrationally unrelaxed fluorescence is found for the unsubstituted 9-HPLN, which gives some qualitative insight into the pathways of vibrational relaxation in the S_1 state. Introduction of the methyl substituent results in at least an order of magnitude increase in the vibrational relaxation rates.

Low-temperature rare-gas matrices represent very useful model systems for studies of molecular relaxation processes.[1,2] Vibrational relaxation of small molecules in these weakly interacting inert "solvents" is often relatively slow, and one frequently observes unrelaxed electronic fluorescence originating from excited vibrational levels.[1] In larger molecules, however, with high intramolecular densities of states, vibrational relaxation is fast even in these cryogenic systems, and usually only fully relaxed fluorescence is reported. Very recently we have demonstrated that by using tunable pulsed dye laser excitation, coupled with time-resolved fluorescence detection, vibrationally unrelaxed emission may often be observable even in large molecular species. Thus, for example, unrelaxed fluorescence was observed for a variety of halobenzene radical cations.[3] Similarly, extensive vibrationally unrelaxed emission was reported for the even larger naphthazarin molecule.[4] The importance of such observations is that, in addition to the spectroscopic information obtained, one can also gain insight into the molecular relaxation and energy redistribution mecha-

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