Inorg. Chem. **1988**, *27*, 4018-4021

Table VI. Relative Energies (kcal/mol) for **6-8**

molecule	ΔE(SCF)[a] basis set 2	ΔE(SCF)[b] basis set 3	ΔE(MP-2)[c] basis set 2	ΔE(MP-2)[d] basis set 3
6a	0.0	0.0	0.0	0.0
7a	-0.7	-1.0	2.5	1.9
8a	-0.9	-1.6	5.2	4.0
6b	13.6	13.7	11.9	11.8
7b	14.6	14.4	18.0	17.3
7c	12.3	12.0	13.5	12.7
8b	13.9	13.3	19.8	18.5

[a] E(SCF) for $H_3Si(CN)_2^-$ -475.407 986 au (basis set 2). [b] E(SCF) for $H_3Si(CN)_2^-$ -475.409 294 au (basis set 3). [c] E(MP-2) for $H_3Si(CN)_2^-$ -476.103 266 au (basis set 2). [d] E(MP-2) for $H_3Si(CN)_2^-$ -476.106 268 au (basis set 3).

stable than **8a**. Making the good approximation that $\Delta\Delta H^{0K} = \Delta\Delta G^{300K}$ for their relative energies, we predict that there are 4.1% of **7a** and 0.2% of **8a** at room temperature relative to the amount of **6a**. We can use the previously obtained values of ΔH and ΔS for eq 2 together with our calculated relative energies to calculate values of $K^{24 °C} = 1.3 \times 10^{-1}$ M^{-1} for eq 6 and $K^{24 °C} = 3.6 \times 10^{-3}$ M^{-1} for eq 7.

$$\mathbf{1} + \mathbf{2} \rightleftharpoons Bu_4N^+Me_3Si(CN)(NC)^- \tag{6}$$

$$\mathbf{1} + \mathbf{2} \rightleftharpoons Bu_4N^+Me_3Si(NC)_2^- \tag{7}$$

The structures with one axial substituent and one equatorial substituent are clearly less stable than those with two axial substituents. Thus, we did not study structures with two equatorial substituents. The most stable structure with one axial substituent and one equatorial substituent is **6b** with two cyano groups. Structure **6b** is 11.8 kcal/mol less stable than **6a** with two axial cyano groups. Structure **7c** with an axial cyano and an equatorial isocyano substituent is the next most stable structure. The least stable structures are **7b** and **8b** with an axial isocyano substituent. The ions with an isocyano axial substituent and an equatorial substituent are destabilized by ~6 kcal/mol with respect to the ions with an axial cyano substituent and an equatorial substituent; e.g., ΔE(**7b**-**6b**) = 5.5 kcal/mol, and ΔE(**8b**-**7c**) = 5.8 kcal/mol.

Supplementary Material Available: Crystal structure data for Et_4N-**4a**, including tables of atomic positional parameters, general displacement parameters, root-mean-square amplitudes, bond distances, bond angles, torsional angles, and least-squares planes and ORTEP figures and ball and stick diagrams (16 pages). Ordering information is given on any current masthead page.

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Rates and Equilibria of Alkaline-Earth-Metal Complexes with Diaza Crown Ethers in Methanol

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The stability constants and rate constants of formation and dissociation of alkaline earth complexes with a series of diaza crown ethers, (2,1), (2,2), $(2_B,2)$, $(2,2\text{-}Me_2)$, and (2,3), in methanol are reported [(2,1) ≡ 1,4,10-trioxa-7,13-diazacyclopentadecane; (2,2) ≡ 1,4,10,13-tetraoxa-6,16-diazacyclooctadecane; $(2_B,2)$ ≡ 2,3-benzo-1,4,10,13-tetraoxa-7,16-diazacyclooctadecane; $(2,2\text{-}Me_2)$ ≡ 7,16-dimethyl-1,4,10,13-tetraoxa-7,16-diazacyclooctadecane; (2,3) ≡ 1,4,7,13,16-pentaoxa-10,19-diazacycloheneicosane]. The diaza crown ethers, like the corresponding fully oxygenated crown ethers, do not show strong selectivity between the alkaline-earth-metal cations Ca^{2+}, Sr^{2+}, and Ba^{2+} or large variations in complex stability with ligand structure and ring size, except when considerable differences between the size of the cation and the ligand cavity are involved. The dissociation rate constants are sufficiently low to allow rate measurements over a range of temperatures with a stopped-flow apparatus. The dissociation reactions of several of the complexes are susceptible to acid catalysis, and those of all nine diaza-18-crown-6 complexes are strongly accelerated by nitrate ions. Complexes of (2,2) and $(2_B,2)$ are up to 7 orders of magnitude less stable than those of the corresponding macrobicyclic cryptands ((2,2,2) and $(2_B,2,2)$, respectively) [(2,2,2) ≡ 4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane; $(2_B,2,2)$ ≡ 5,6-benzo-4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane]. This macrobicyclic or cryptate effect shows up virtually entirely in the dissociation rate constants of the two classes of complexes, with formation rate constants for a given cation being almost identical for mono- and bicyclic ligands.

Introduction

The rate of formation of complexes between alkaline-earth-metal ions and cyclic macromolecular ligands in solution is always several orders of magnitude lower than that of a diffusion-controlled reaction. This means that the dissociation rates of complexes of relatively high stability, such as those of the macrobicyclic cryptand ligands (cryptates),[1] can be followed by conventional techniques, even in water.[2,3] For the less stable, more mobile monocyclic crown ether complexes, it is necessary to use ultrasonic relaxation techniques to determine the complexation kinetics in water.[4] In methanol, however, the stabilities of crown ether complexes are several orders of magnitude higher than those in water with a consequent reduction in the dissociation rate constants. In particular, we have found that for alkaline-earth-metal complexes for diaza-18-crown-6 the dissociation rate constants are sufficiently low to enable rate measurements to be made with a stopped-flow apparatus over a range of temperatures (−10 to +20 °C).[5]

Chart I

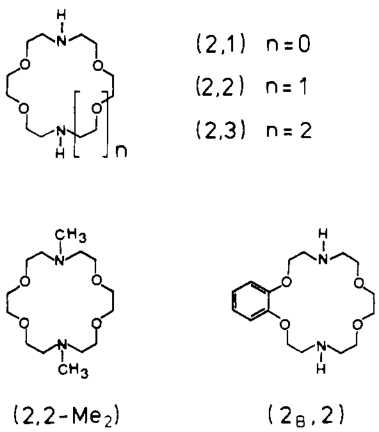

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Table I. Stability Constants, log K_s, in Methanol at 25 °C

	(2,1)	(2,2)[a]	(2_B,2)	(2,2-Me_2)[a]	(2,3)
Ca^{2+}	3.1_3	3.5	3.8	4.2	2.5
Sr^{2+}	2.9_7	5.7	4.9	6.5	3.5
Ba^{2+}	2.7_8	5.9	4.5	6.9	5.1

[a] Reference 5.

In the present paper we present an extended investigation of the kinetics and stabilities in methanol of Ca^{2+}, Sr^{2+}, and Ba^{2+} complexes of various diaza crown ligands: diaza-18-crown-6 (2,2)[5,6] and its dimethyl derivative (2,2-Me_2);[5,6] a benzo-substituted diaza-18-crown-6 (2_B,2);[6] diaza-15-crown-5 (2,1);[6] and diaza-21-crown-7 (2,3)[6] (see Chart I). The benzo group (2_B,2) allowed an independent but consistent determination of the dissociation rate constant using optical detection in addition to the less specific conductimetric detection used for the remainder of the reactions.

Experimental Section and Results

The ligand (2_B,2) was a gift from Merck. It was used without further purification, as were the ligands (2,1) and (2,3).[6] The hydrates of $Ca(ClO_4)_2$ (Ventron) and $Sr(ClO_4)_2$ (Ventron) were dried under vacuum for 20 h at 160 °C, and the residual water content was negligibly small. Tetraethylammonium nitrate (Fluka) was used as purchased. Tetraethylammonium perchlorate (Fluka) was recrystallized from ethanol and dried under vacuum. The origin and purification of the other substances used have been described previously.[5]

The stability constants, K_s, of complexes of Ca^{2+}, Sr^{2+}, and Ba^{2+} (Table I) with a ligand L were determined by potentiometric Ag/Ag^+ titration from the equilibrium constant $K_e = K_s(AgL^+)/K_s(ML^{2+})$ for the reaction

$$ML^{2+} + Ag^+ \rightleftharpoons M^{2+} + AgL^+ \qquad (1)$$

together with the stability constants log $K_s(Ag(2_B,2)^+) = 9.74$, log $K_s(Ag(2.1)^+) = 7.45$, and log $K_s(Ag(2,3)^+) = 9.29$, obtained from direct titrations of Ag^+ with the ligands. The protonation of the basic nitrogen donor atoms of the ligands was not taken into account in the disproportion reaction, eq 1, because the total metal ion concentration was always much larger than the ligand concentration. In the determination of stability constants of the silver complexes, when the total Ag^+ concentration was smaller than the ligand concentration, the stability constants were also calculated, neglecting ligand protonation. It could be shown that the consideration of protonation constants of ligand molecules[7] changes the silver complex stabilities by less than 0.03 unit in log K_s.

The dissociation reactions of the (2_B,2) complexes (eq 2) were measured under pseudo-first-order conditions by mixing an equilibrated $M(2_B,2)^{2+}/M^{2+}$ sample with an excess of trifluoromethane sulfonic acid (used as a scavenger for (2_B,2)) in an all-glass, stopped-flow apparatus. Detection was either conductimetric or optical at 280 nm. The temperature was varied between −10 and +20 °C in steps of 5 °C, covering a range of at least 15 °C for each individual system. The nitrate catalysis of the (2_B,2) complexes was investigated at +5 °C by using alkaline-earth-metal nitrates and perchlorates, together with added tetraethylammonium nitrate. The inertness of ClO_4^- was shown by addition of tetraethylammonium perchlorate to alkaline-earth-metal perchlorates. The results of a previous investigation,[5] in which the influence of NO_3^- was unknown and the nitrate salts of Ca^{2+} and Sr^{2+} were used, have been rechecked by using perchlorate salts. No influence of NO_3^- on K_s values was observed (Table I), but k_d and k_H for the (2,2) and (2,2-Me_2) complexes of Ca^{2+} and Sr^{2+} required correction because of the influence of the nitrate catalysis on the extrapolation of H^+-catalyzed reactions to zero [H^+].

$$M(2_B,2)^{2+} \xrightarrow{k_d} M^{2+} + (2_B,2) \qquad (2)$$

Table II. Rate Constants of Dissociation (k_d/s^{-1}), of Formation ($k_f/M^{-1}\ s^{-1}$), and of Catalysis ($k_H/M^{-1}\ s^{-1}$) and Activation Parameters of Dissociation in Methanol at 25 °C

ligand	M^{2+}	log k_d	log k_f	log k_H	ΔH_d^*/ kJ mol^{-1}	298 ΔS_d^*/ kJ mol^{-1}
(2,1)	Ca^{2+}	1.97	5.1		37.4	−24.4
(2,1)[a]	Sr^{2+}	1.91				
(2_B,2)	Ca^{2+}	1.70	5.5		43.1	−20.2
(2_B,2)	Sr^{2+}	1.18	6.1		50.5	−15.8
(2_B,2)	Ba^{2+}	2.07	6.6		47.4	−13.8
(2,2)	Ca^{2+}	1.48	5.0	2.14	49.0	−15.6
(2,2)	Sr^{2+}	0.041	5.7	2.12	57.1	−15.7
(2,2)	Ba^{2+}	0.90	6.8	3.09	45.0	−22.9
(2,2-Me_2)	Ca^{2+}	1.25	5.5	3.20	35.3	−30.6
(2,2-Me_2)	Sr^{2+}	-0.66_6	5.8	0.87	58.6	−18.2
(2,2-Me_2)	Ba^{2+}	0.14_6	7.0	1.86	59.1	−13.1
(2,3)	Ba^{2+}	2.20	7.6		22.4	−38.10

[a] At −8.5 °C.

For the ligands (2,1) and (2,3), only the dissociation reactions of $Ca(2,1)^{2+}$ and $Ba(2,3)^{2+}$ could be measured over a sufficiently wide temperature range (around 0 °C) to enable a reliable extrapolation to 25 °C. The dissociation of $Sr(2,1)^{2+}$ was measured only at −8.5 °C: above this temperature reactions were too rapid for measurement by stopped-flow. The dissociation reactions of the two (2,1) complexes were independent of [CF_3SO_3H]. The dissociation reaction of $Ba(2,3)^{2+}$ was measured by using Ag^+ as a scavenging ion for (2,3) instead of CF_3SO_3H because of a larger conductance change, and the reaction was also catalyzed by Ag^+.

Values of k_f, k_d and its associated activation parameters, ΔH_d^* and ΔS_d^*, and, where appropriate, the catalytic constant for proton catalysis, k_H are listed in Table II. Details of the influence of NO_3^- on the dissociation reactions are included in the Discussion.

Discussion

The stability constants of all of the Ca^{2+} complexes with the diaza-18-crown-6 ligands are lower than those of the Sr^{2+} and Ba^{2+} complexes (Table I). There is very little difference between the stabilities of the Ba^{2+} and Sr^{2+} complexes, and this suggests that the ring size of the three ligands lies between the diameters of Sr^{2+} and Ba^{2+}. The addition of the benzo substituent, although not having a very large effect, leads to a progressively unfavorable effect as the cation size increases: log $K_s(M(2_B,2)^{2+})$ − log $K_s(M(2,2)^{2+})$ values are +0.3, −0.8, and −1.4 for M^{2+} = Ca^{2+}, Sr^{2+}, and Ba^{2+}, respectively. This would be consistent with the major influence of the benzo substituent being a reduction in the effective ring size of the ligand, thus favoring complexation of Ca^{2+} relative to Ba^{2+}. *N*-Methyl substitution leads to a significant, but relative constant increase in K_s of ca. 0.8 log unit.

The results for the (2,1) and (2,3) complexes in comparison with those for the (2,2) complexes show that there is no striking effect of ring size on the stabilities of the complexes, except where the difference between formal ring and cation diameters is considerable. The small variations of log $K_s(M(2,1)^{2+})$ for the alkaline-earth-metal ions may result from partial compensation of decreasing ion solvation by a growing discrepancy in the sizes of ligand and ion. Nevertheless, as with the fully oxygenated parent crown ethers,[8,9] it may be concluded that the diaza crown systems

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(6) (2,1) ≡ 1,4,10-trioxa-7,13-diazacyclopentadecane; (2,2) ≡ 1,4,10,13-tetraoxa-7,16-diazacyclooctadecane; (2_B,2) ≡ 2,3-benzo-1,4,10,13-tetraoxa-7,16-diazacyclooctadecane; (2,2-Me_2) ≡ 7,16-dimethyl-1,4,10,13-tetraoxa-7,16-diazacyclooctadecane; (2,3) ≡ 1,4,7,13,16-pentaoxa-10,19-diazacycloheneicosane; (2,2,2) ≡ 4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane; (2_B,2,2) ≡ 5,6-benzo-4,7,13,16,21,24-hexaoxa-1,10-diazabicyclo[8.8.8]hexacosane.

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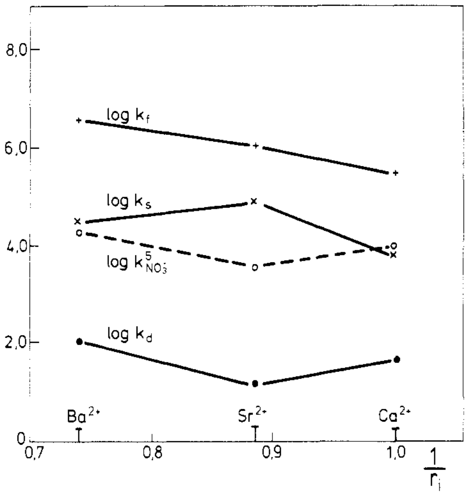

Figure 1. Stability constant, K_s, and rate constants of dissociation, k_d, and of formation, k_f, at 25 °C and of nitrate ion catalysis, k_{NO_3}, for $(2_B,2)$ complexes at 5 °C in methanol.

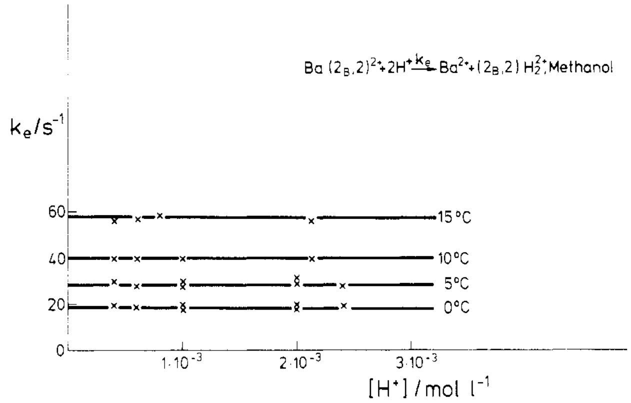

Figure 2. Dissociation of $Ba(2_B,2)^{2+}$ in methanol.

do not show strong selectivity between alkaline-earth-metal cations or strong variations in stability with ligand structure and ring size. The stability constants of corresponding crown ether and diaza crown ether complexes are often the same within experimental error, and any observed differences do not show systematic trends in sign or magnitude with cation or ligand size.

A comparison of the stability constants, K_s (Table I), and dissociation rate constants, k_d (Table II), of the alkaline-earth-metal diaza-18-crown-6 complexes shows a very similar dependence of K_s and $1/k_d$ upon cation radius, r_i. This is exemplified for complexes of $(2_B,2)$ in Figure 1. The formation rate constants, $k_f = K_s k_d$, on the other hand show an almost linear decrease of log k_f with $1/r_i$. This behavior is considered more fully below in connection with results for other macrocyclic systems.

The dissociation reactions of (2,2) and $(2,2\text{-}Me_2)$ are all subject to acid catalysis. In contrast, however, the dissociation rate constants of the $(2_B,2)$ complexes are independent of the concentration of the scavenging acid, as illustrated, for example, by the results in Figure 2. Proton-catalyzed dissociation of metal ions from complexes with macrobicyclic diaza polyethers (cryptands)[1] has been observed earlier,[2,10,11] and this has been explained in terms of formation of a protonated complex that releases the metal ion more rapidly than the original complex. For the cryptates the relative contribution of the proton-catalyzed dissociation to the overall dissociation reaction decreases as the ratio of cation size to ligand size increases. No acid catalysis was observed for (2.1) complexes. The results presumably reflect the ability of a nitrogen atom within the complex to adopt an exo-conformation in which the lone pair is directed outward and is available for protonation.

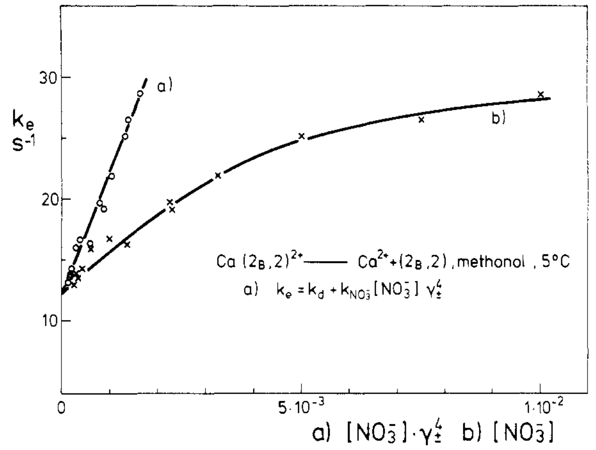

Figure 3. NO_3^- enhanced dissociation of $Ca(2_B,2)^{2+}$ in methanol at 5 °C.

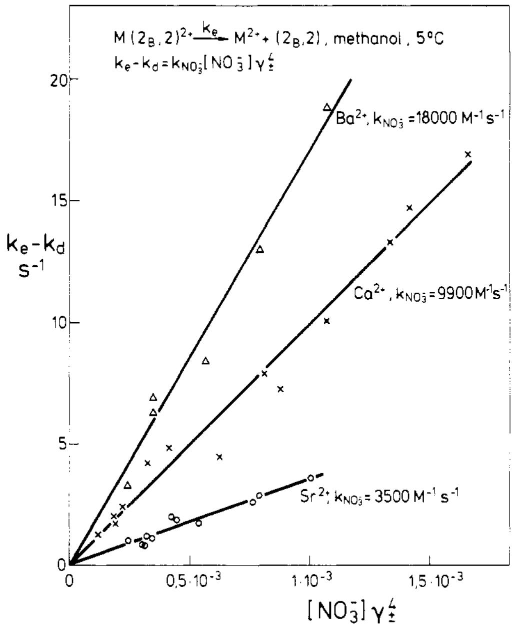

Figure 4. Contribution of the NO_3^--catalyzed dissociation pathway of alkaline-earth-metal complexes with $(2_B,2)$ in methanol at 5 °C.

This process may involve reactions analogous to those occurring in the protonation of the free cryptands[12,13] in their various conformational states.[1,14] Thus it seems that the monocyclic diaza-18-crown-6 ligands (2,2) and $(2,2\text{-}Me_2)$ still retain sufficient flexibility in their complexes, especially with smaller cations, to allow interactions between a nitrogen atom and a proton in solution. No catalysis was observed for $(2_B,2)$ complexes, even at acid concentrations up to 4×10^{-3} M, and this suggests that the benzo substituent tends to immobilize the ligand structure in the complex.

A very unexpected observation was the increase in dissociation rates in the presence of nitrate ions. This is illustrated in Figure 3 where the dissociation rate constant for $Ca(2_B,2)^{2+}$ is plotted against the nitrate concentration. The results are independent of whether nitrate concentrations are varied by adding different amounts of $Ca(NO_3)_2$ or by mixing $Ca(ClO_4)_2$ with tetraethylammonium nitrate. There is no convincing evidence in the experimental results for any strong degree of ion-pair formation

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Table III. The Macrobicyclic Effect: (2,2) versus (2,2,2)[a] Complexes in Methanol at 25 °C

	log (K_s/M^{-1})		log (k_f/M^{-1} s^{-1})		log (k_d/s^{-1})	
cation	(2,2)	(2,2,2)	(2,2)	(2,2,2)	(2,2)	(2,2,2)
Ca^{2+}	3.5	8.1	5.0	4.5	1.48	−3.66
Sr^{2+}	5.7	11.8	5.7	5.5	0.04	−6.26
Ba^{2+}	5.9	12.9	6.8	6.7	0.90	−6.20

[a] Reference 20.

between the complexes and NO_3^-, so the process may be described as catalytic. A reaction of the form shown in eq 3, on application

$$M(2_B,2)^{2+} + NO_3^- \rightleftharpoons [M(2_B,2)NO_3]^+ \rightarrow M^{2+} + (2_B,2) + NO_3^- \quad (3)$$

of the steady-state approximation to $[M(2_B,2)NO_3]^+$, together with the contribution from the direct dissociation (eq 2), leads to eq 4 for the observed rate constant. The required activity

$$k_e = k_d + k_{NO_3}[NO_3^-]\gamma_\pm^4 \quad (4)$$

coefficients, $\gamma_\pm$, have been calculated by using the Davies equation[15] and are quite small, varying between 0.65 and 0.86 in the different solutions. The results presented in Figure 3 show that there is a nice linear relationship between k_e and the function $[NO_3^-]\gamma_\pm^4$. Results for the three alkaline-earth-metal complexes of $(2_B,2)$ are shown in Figure 4, where in order to present a simple comparison, values of $k_e - k_d$ are plotted against $[NO_3^-]\gamma_\pm^4$. There is clearly a very substantial influence of NO_3^- on the rates, and the numerical values of k_{NO_3} are larger than any of those of k_H in Table II. It is interesting to note that the variation of k_{NO_3} with cation size parallels that of the simple dissociation reactions (Figure 1).

Independent experiments with Cl^- and Br^- over a concentration range similar to that of NO_3^- failed to show any catalysis. However, it is to be expected that catalysis of the dissociation reaction by these ions would be measurable at sufficiently high concentrations, as has been found for Ca^{2+}–cryptates in methanol.[16] It has also been reported that SCN^- has a strong catalysis effect on Na^+ exchange with the crown ether 18-crown-6 in tetrahydrofuran.[17] Thus, although the magnitude of NO_3^- catalysis of the $M(2_B,2)^{2+}$ systems is perhaps surprisingly large, the observation of anion catalysis of the dissociation reactions is not unique among macrocyclic systems. It should be noted that the dissociation rates of the alkaline-earth-metal complexes of (2,2) and (2,2-Me$_2$) also show a nitrate dependence. However, for these systems, k_{NO_3} has not been determined because of the additional acid catalysis, which makes a sufficiently accurate separation of the two pathways rather difficult.

The activation parameters in Table II are unremarkable for dissociation reactions of macrocyclic complexes,[18] and only a relatively small set of values for other systems is available for comparison, but almost all show negative $\Delta S_d^\ddagger$. This is especially true for ions of high charge density,[2,19] for which $\Delta S_d^\ddagger$ values are generally large and negative, presumably because of the formation of a solvation shell around the emerging cation. Activation entropies for the formation reaction, $\Delta S_f^\ddagger$, for (2,2-Me$_2$) complexes, obtained from a combination of the present $\Delta S_d^\ddagger$ values with earlier values[5] for the overall entropies of complexation ($\Delta S_c = \Delta S_d^\ddagger - \Delta S_f^\ddagger$), are also negative. Thus the entropy of the transition state is at a minimum with respect to reactants and products for complexes of all three cations. The simplest explanation for this is that in the transition state the cations have their solvation shells largely intact, so that the loss of translational entropy on association of the cations and ligands is only partially compensated for by release of solvent molecules from the coordination spheres of the cations.

Finally, the present results allow a more detailed consideration of the so-called macrobicyclic or cryptate effect than has hitherto been possible. In Table III, log K_s, log k_f, and log k_d values for (2,2) and (2,2,2)[6,20] alkaline-earth-metal ion complexes in methanol are compared. Two features of the results stand out. The first is the very large increase in complex stability resulting from addition of the third bridge to (2,2) to form (2,2,2): 4.6, 6.1, and 7.0 units in log K_s for Ca^{2+}, Sr^{2+}, and Ba^{2+}, respectively. These increases are much too large to be accounted for simply in terms of the increase in the number of donor atoms in (2,2,2) relative to (2,2), as it has been shown for a number of crown ethers and aza crown ethers that additional substituents in the form of oxygen-containing side arms (e.g. CH_2CH_2OH) have only a relatively small effect on complex stabilities.[18] More striking, however, is the observation that the formation rate constants for complexes of the two ligands are almost identical. The major difference between the two systems then occurs in the dissociation reactions. The differences are very large as may be seen from the results in Table III, which show that k_d values for (2,2,2) are some 5–7 orders of magnitude lower than those for (2,2) complexes.

The close agreement between the k_f values of mono- and bicyclic ligands (Table III), which holds also for $(2_B,2)$ and $(2_B,2,2)$[6] with all values being 1.5 log units lower than those of the corresponding complexes of the unsubstituted ligands, has some implications for the mechanism of formation of macrocyclic complexes. Formally the (2,2) ring and one of the faces of (2,2,2) will present structures very similar to those of the incoming cation. However, (2,2,2) has much greater conformational rigidity than (2,2) so that previously discussed proposals of a rate-determining conformational change in the ligand prior to complex formation[2,21,22] may be excluded. Similarly, the simultaneous separation of two or more solvent molecules before entry of the metal ion into the cryptand cavity[23] may be considered very unlikely as a rate-deteming step in cryptate formation. Probably the formation of the first or second chelate ring, a process common to both types of ligand, is rate-determining as suggested by Rorabacher and co-workers.[24]

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