

# Alkaline Earth Cryptates: Dynamics and Stabilities in Different Solvents

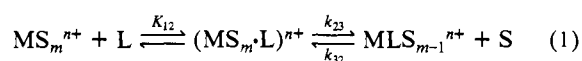
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**Abstract:** The stability constants and rates of formation and dissociation of alkaline earth cryptates with (2,1,1), (2,2,1), (2,2,2), (2<sub>B</sub>,2,2), and (2<sub>B</sub>,2<sub>B</sub>,2) have been measured in several solvents. The stability constants,  $K_s$ , are considerably larger and display higher selectivity than those of the monocyclic crown and diaza crown ethers and anionic ionophores. Values of  $K_s$  vary by over 10 orders of magnitude in the different solvents, increasing in the order  $\text{Me}_2\text{SO} < \text{DMF} \approx \text{H}_2\text{O} < \text{MeOH} < \text{PC}$ . Ligand selectivity is based predominantly on variations in dissociation rates, both within the series of cryptands and in comparison to other macrocyclic ligands. Formation rates do not conform to the simple Eigen–Wilkins dissociative-interchange mechanism ( $I_d$ ). The rates show no correlation with solvent exchange rates, and are sensitive to cation size, cation–solvent interactions, and ligand flexibility. In strongly solvating media such as  $\text{Me}_2\text{SO}$ , rates are up to  $10^6$  lower than predicted by a simple  $I_d$  mechanism. The results suggest that the complexation reaction involves essentially stepwise replacement of solvent by ligand donor atoms, but that even for relatively flexible macrocyclic ligands compensation for loss in solvation by ligand binding energy in the transition state is not complete.

## Introduction

Ligand substitution reactions may be discussed in terms of eq 1, in which S represents the solvent and  $(\text{MS}_m\cdot\text{L})^{n+}$  an outer-sphere



complex.<sup>1-3</sup> For reactions involving multidentate ligands the step represented by rate constants  $k_{23}$  and  $k_{32}$  may be repeated several times or may involve replacement of more than one solvent molecule. The results in aqueous solution are generally consistent with a simple dissociative interchange mechanism ( $I_d$ ) in which the formation rate constant is given by eq 2, where  $K_{ES}$  is an

$$k_f = K_{12}k_{23} = K_{ES}k_s \quad (2)$$

association constant calculated on the basis of electrostatic interactions (or by random encounters if L is uncharged) and  $k_s$  is the rate constant for solvent exchange determined by NMR methods. Equation 2 is modified slightly if  $k_{23}$  and  $k_{32}$  are sufficiently rapid such that the diffusional encounter and separation of  $\text{MS}_m^{n+}$  and L become partially rate determining,<sup>4</sup> but the same general conclusions hold. In nonaqueous solvents, however, the complexation rates exhibit a marked ligand dependence, especially for bidentate and tridentate ligands. This has been discussed in terms of specific solvent dependent interactions and ligand orientations in the first step,<sup>3</sup> or of the influence of L on the rate constant  $k_{23}$ , which cannot then be identified with the rate constant for solvent exchange in the absence of L.<sup>2</sup>

Complex formation with ion-specific macrocyclic ligands such as the ionophorous antibiotics<sup>4</sup> and the synthetic crown ethers<sup>5</sup> and cryptands<sup>6</sup> represent a very important class of ligand substitution reactions, which may not follow the simple behavior described by (1) and (2). In particular, complex formation with the naturally occurring antibiotics and the cryptands involves removal of all of the coordinated solvent molecules and might be expected to show a strong dependence upon ion–solvent interactions that cannot be simply related to the solvent exchange rates of the free cations.

Formation rates of alkali metal complexes of crown ethers,<sup>7</sup> naturally occurring ionophores such as valinomycin<sup>8</sup> and the macrotetralides,<sup>9</sup> and cryptands<sup>10</sup> in methanol are all fast and approach the rates expected for exchange of methanol in the inner sphere of the cations. However, the corresponding values for the complexes of valinomycin<sup>4</sup> and cryptands<sup>11</sup> in aqueous solutions are considerably lower than those in methanol. In nonaqueous

solvents the formation rates of alkali metal cryptand complexes (cryptates) are relatively insensitive to solvent variation<sup>12</sup> but show a dependence upon the strength of ion–solvent interactions rather than the solvent exchange rates. Kinetic and thermodynamic data for alkaline earth complexes are scarce. The anionic antibiotics of the nigericin group form strong complexes with alkaline earth cations,<sup>13,14</sup> but kinetic data are not available. Alkaline earth cryptates in water<sup>11,15</sup> and methanol<sup>16</sup> are characterized by slow formation and dissociation rates that are strongly dependent upon cation size. Formation rates of  $\text{Sr}^{2+}$  and  $\text{Ba}^{2+}$  crown ethers in methanol,<sup>17</sup> however, are comparable to the corresponding values for the alkali metal complexes.

In the present paper we report the stabilities and formation and dissociation rates of alkaline earth cryptates (I–V) in several solvents: water, methanol, dimethylformamide (DMF), dimethyl sulfoxide ( $\text{Me}_2\text{SO}$ ), and propylene carbonate (PC). The high solvation energies of the cations influence strongly the stabilities and kinetics of complex formation in the different solvents.

## Experimental Section and Results

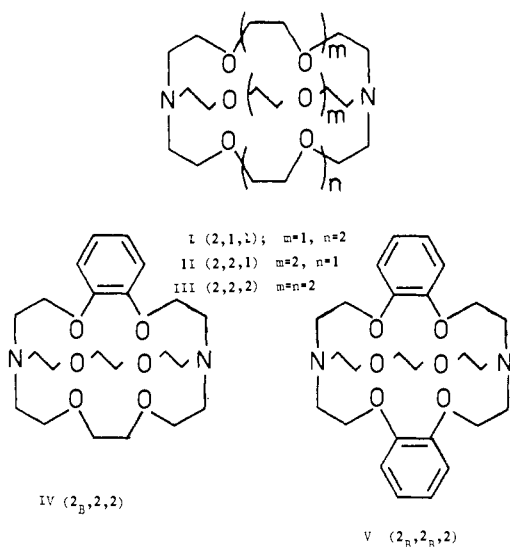
**Materials.** Cryptands (2,1,1), (2,2,1), (2,2,2), (2<sub>B</sub>,2,2) and (2<sub>B</sub>,2<sub>B</sub>,2) were commercial samples (Merck) used without further purification. Their purities have been checked by pH-metric, conductometric, and NMR methods.<sup>18</sup>

The following reagents were used:  $\text{AgClO}_4$ ,  $\text{AgNO}_3$ ,  $\text{CaCl}_2$ ,  $\text{Ca}(\text{N}-$

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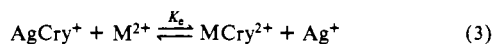
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$O_3)_2 \cdot 4H_2O$ ,  $Ca(ClO_4)_2 \cdot 4H_2O$ ,  $Sr(NO_3)_2$ ,  $Sr(ClO_4)_2 \cdot 6H_2O$ ,  $Ba(ClO_4)_2 \cdot 3H_2O$ ,  $HCl$ ,  $CH_3SO_3H$ ,  $CHCl_2CO_2H$ , and  $Et_4NClO_4$ . All were high purity commercial grades except for  $Et_4NClO_4$  which was prepared from aqueous  $NET_4OH$  and  $HClO_4$  and purified by several recrystallizations from water, followed by drying under vacuum. Solutions of hydrated salts were dried over molecular sieves, type 5A, except for very dilute solutions where the amount of water added was negligible.

The methods of purification of the solvents and tests for their purity and water content have been described previously.<sup>19</sup>

**Stability Constant Measurements.** The stability constants of all of the alkaline earth cryptates were determined by disproportionative reaction of alkaline earth metal ions with the corresponding  $Ag^+$  complex (eq 3),



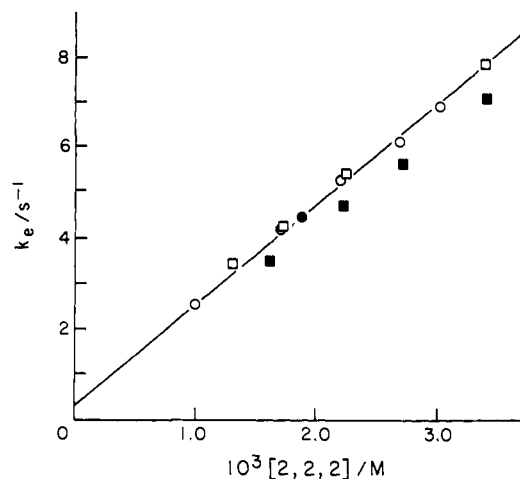
using the stability constants of  $Ag^+$  complexes obtained by direct potentiometry. The reference electrode was an  $Ag/Ag^+$  electrode, immersed in the solvent S and separated from the test cell by a salt bridge containing 0.1 M  $NET_4ClO_4$  in S. Total metal ion concentrations were ca.  $1 \times 10^{-3}$ – $7 \times 10^{-3}$  M ( $[Ag^+] = 1 \times 10^{-4}$ – $7 \times 10^{-4}$  M) and cryptand concentrations were in the range  $4 \times 10^{-4}$ – $2 \times 10^{-3}$  M. Establishment of equilibrium was fast in all solvents except PC, where for most  $Sr^{2+}$  and  $Ba^{2+}$  cryptates the rate of equilibration was so slow that reliable equilibrium constants could not be measured. It was assumed that equilibrium 3 was independent of ionic strength at the relatively low concentrations used, as the reactants and products have the same charge. The detailed experimental procedure has been published previously.<sup>10,20</sup>

The measured stability constants are given in Table I. In most cases the required stability constants of the  $Ag^+$  complexes ( $K_s(AgCry^+)$ ) were available from previous work,<sup>10,19,21</sup> and values determined in the present work were in excellent agreement with these. Where  $K_s(AgCry^+)$  values were determined for the first time they are included as footnotes in Table I. The effect of trace water in the nonaqueous solvents was tested in several cases. In  $Me_2SO$  the effect of adding known amounts of water on the stabilities of  $Sr(2,2,1)^{2+}$ ,  $Sr(2_B,2,2)^{2+}$ ,  $Sr(2_B,2_B,2)^{2+}$ ,  $Ba(2,2,1)^{2+}$ ,  $Ba(2_B,2,2)^{2+}$ , and  $Ba(2_B,2_B,2)^{2+}$  was found to be extremely small. In all cases the stability constants increased with increasing water content of the solvent, but the addition of even 2% v/v water resulted in an increase in stability of only 18% (0.07 in  $\log K_s$ ). Similar results were obtained in DMF, where, for example, the addition of 1% water increased  $K_s$  ( $Sr(2_B,2_B,2)^{2+}$ ) by 12% (0.05 in  $\log K_s$ ). Slightly different behavior was observed in PC where the effect of added water on the stability of  $Ca(2_B,2_B,2)^{2+}$  was studied. The results showed that addition of 0.2% v/v water led to a small increase in stability of ca. 5%, but further addition of 0.5% and 1.0%  $H_2O$  reduced the stability of about 12% and 20% (0.1 in  $\log K$ ), respectively. As the solvents used in this work contained  $\leq 0.01\%$  water, any effects due to water will be well within experimental error, and the stability constants in Table I may be taken to refer to the anhydrous solvent.

**Table I.** Stability Constants ( $\log K_s$ ) of Alkaline Earth Cryptates in Various Solvents at 25 °C<sup>a</sup>

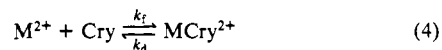
cation	cryptand	solvent <sup>b</sup>				
		$H_2O^c$	$MeOH^d$	$Me_2SO^e$	$DMF^f$	PC
$Ca^{2+}$	(2,1,1)	2.5 <sup>g</sup>	5.4 <sub>3</sub>	$\leq 2$	3.0 <sub>9</sub> (3.08) <sup>h</sup>	8.6 <sub>3</sub>
$Ca^{2+}$	(2,2,1)	6.9 <sub>5</sub> <sup>g</sup>	9.9 <sub>2</sub>	3.9 <sub>0</sub>	6.5 <sub>8</sub> (6.66) <sup>h</sup>	11.4 <sub>8</sub>
$Sr^{2+}$	(2,2,1)	7.3 <sub>5</sub> <sup>g</sup>	11.0 <sub>4</sub>	6.1 <sub>0</sub>	7.9 <sub>4</sub>	
$Ba^{2+}$	(2,2,1)	6.3 <sub>0</sub> <sup>g</sup>	10.6 <sub>2</sub>	5.3 <sub>0</sub>	6.9 <sub>6</sub>	
$Ca^{2+}$	(2,2,2)	4.5 <sub>7</sub> <sup>i</sup>	8.1 <sub>4</sub>	$\leq 2.1$	3.7 <sub>9</sub> (3.84) <sup>h</sup>	10.7 <sub>6</sub>
$Sr^{2+}$	(2,2,2)	8.2 <sub>6</sub> <sup>i</sup>	11.7 <sub>5</sub>	5.2 <sub>6</sub>	7.3 <sub>0</sub>	
$Ba^{2+}$	(2,2,2)	9.7 <sub>1</sub> <sup>i</sup>	12.9 <sub>1</sub>	6.5 <sub>0</sub>	8.3 <sub>9</sub>	
$Ca^{2+}$	(2 <sub>B</sub> ,2,2)	4.0 <sub>5</sub> (3.8) <sup>k</sup>	7.1 <sub>9</sub>	$\leq 2$	2.6 <sub>0</sub>	10.1 <sub>0</sub>
$Sr^{2+}$	(2 <sub>B</sub> ,2,2)	7.5 <sub>0</sub> (6.9) <sup>k</sup>	10.5 <sub>2</sub>	4.3 <sub>3</sub>	6.1 <sub>0</sub>	
$Ba^{2+}$	(2 <sub>B</sub> ,2,2)	7.9 <sub>1</sub> (7.4) <sup>k</sup>	11.0 <sub>5</sub>	5.1 <sub>0</sub>	6.4 <sub>6</sub>	
$Ca^{2+}$	(2 <sub>B</sub> ,2 <sub>B</sub> ,2)	3.4 <sub>5</sub>	5.9 <sub>4</sub>	$\leq 2$	$\leq 2$	9.7 <sub>4</sub>
$Sr^{2+}$	(2 <sub>B</sub> ,2 <sub>B</sub> ,2)	6.3 <sub>8</sub>	9.0 <sub>5</sub>	3.5 <sub>8</sub>	4.8 <sub>9</sub>	13.4 <sub>1</sub>
$Ba^{2+}$	(2 <sub>B</sub> ,2 <sub>B</sub> ,2)	5.6 <sub>5</sub>	8.8 <sub>5</sub> <sup>j</sup>	3.4 <sub>6</sub>	4.6 <sub>7</sub>	

<sup>a</sup>  $\log K_s \pm 0.1$ . <sup>b</sup> Abbreviations: DMF, *N,N*-dimethylformamide; PC, propylene carbonate. <sup>c</sup>  $\log K_s (Ag(2_B,2,2)^+) = 9.2_8 (\pm 0.05)$ . <sup>d</sup> Reference 16. <sup>e</sup>  $\log K_s (Ag(2_B,2,2)^+) = 6.9_5 (\pm 0.05)$ ;  $\log K_s (Ag(2_B,2_B,2)^+) = 6.7_6 (\pm 0.05)$ . <sup>f</sup>  $\log K_s (Ag(2_B,2,2)^+) = 9.7_4 (\pm 0.05)$ ;  $\log K_s (Ag(2_B,2_B,2)^+) = 9.4_7 (\pm 0.05)$ . <sup>g</sup> Reference 22. <sup>h</sup> Reference 19. <sup>i</sup> Reference 31. <sup>j</sup> Reference 21. <sup>k</sup> Reference 37. <sup>l</sup>  $\pm 0.2$ .



**Figure 1.** Rate of formation of  $Ca(2,2,2)^{2+}$  in DMF at 25 °C: (○),  $1 \times 10^{-4}$  M  $Ca(NO_3)_2$ ; (●),  $1 \times 10^{-4}$  M  $Ca(ClO_4)_2$ ; (□),  $5 \times 10^{-5}$  M  $CaCl_2$ .

**Kinetic Measurements. (i) Formation Rates.** The rates of formation of the  $M^{2+}$  cryptates were normally obtained from a direct determination of the rate of approach to equilibrium as in eq 4. The reactions were



monitored conductometrically ( $M^{2+}$  and  $MCry^{2+}$  in general have different mobility) on a Durrum-Gibson stopped-flow apparatus. Reactions of the benzo-substituted cryptands ( $2_B,2,2$ ) and ( $2_B,2_B,2$ ) could also be measured by using optical detection<sup>16</sup> as there is a difference in the absorption spectra of the free and complexed ligand. Where the two methods were compared, the results were in good agreement.<sup>16</sup>

Solutions of  $M^{2+}$  ( $\leq 10^{-4}$  M) were reacted with an excess ( $\geq 10$ -fold) of the required cryptand, and under these conditions the observed rate law was of the form shown in eq 5 and 6. Values of  $k_f$  were obtained

$$-d([MCry^{2+}]_0 - [MCry^{2+}])/dt = k_f([MCry^{2+}]_0 - [MCry^{2+}]) \quad (5)$$

$$k_e = k_f[Cry] + k_d \quad (6)$$

from plots of  $k_e$  vs.  $[Cry]$ . For most of the cryptates  $k_f[Cry] \gg k_d$  over the concentration range employed, and so  $k_d$  values could not be estimated from these measurements. The results are listed in Table II.

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Table II. Rates of Formation of Alkaline Earth Cryptates in Several Solvents at 25 °C<sup>a,b</sup>

cation	cryptand	$k_f/M^{-1} s^{-1}$				
		H <sub>2</sub> O <sup>c</sup>	MeOH <sup>d</sup>	Me <sub>2</sub> SO	DMF	PC
Ca <sup>2+</sup>	(2,1,1)	2.6 × 10 <sup>2</sup> <sup>e</sup> (1.1 × 10 <sup>2</sup> ) <sup>f</sup>	9.0 × 10 <sup>3</sup>		1.05 × 10 <sup>3</sup>	2.2 × 10 <sup>4</sup>
Ca <sup>2+</sup>	(2,2,1)	5.9 × 10 <sup>3</sup> <sup>e</sup> (1.6 × 10 <sup>4</sup> ) <sup>f</sup>	1.9 × 10 <sup>4</sup>	2.0 × 10	1.3 × 10 <sup>3</sup>	1.1 × 10 <sup>5</sup>
Sr <sup>2+</sup>	(2,2,1)	3.3 × 10 <sup>4</sup> <sup>e</sup> (5.7 × 10 <sup>4</sup> ) <sup>f</sup>	9.2 × 10 <sup>4</sup>	5.3 × 10 <sup>2</sup>	1.4 × 10 <sup>4</sup>	
Ba <sup>2+</sup>	(2,2,1)	1.2 × 10 <sup>5</sup> <sup>e</sup>	1.9 × 10 <sup>6</sup>	7.6 × 10 <sup>3</sup>	1.8 × 10 <sup>5</sup>	
Ca <sup>2+</sup>	(2,2,2)	7.8 × 10 <sup>3</sup> <sup>e</sup> (7.3 × 10 <sup>3</sup> ) <sup>f</sup>	3.4 × 10 <sup>4</sup>		2.2 × 10 <sup>3</sup>	ca. 6 × 10 <sup>5</sup>
Sr <sup>2+</sup>	(2,2,2)	1.4 × 10 <sup>4</sup> <sup>e</sup> (1.0 × 10 <sup>4</sup> ) <sup>f</sup>	3.1 × 10 <sup>5</sup>	6.6 × 10 <sup>2</sup>	2.9 × 10 <sup>4</sup>	
Ba <sup>2+</sup>	(2,2,2)	9.0 × 10 <sup>4</sup> <sup>e</sup> (7.0 × 10 <sup>4</sup> ) <sup>f</sup>	ca. 5 × 10 <sup>6</sup>	2.3 × 10 <sup>4</sup>	6.1 × 10 <sup>5</sup>	
Ca <sup>2+</sup>	(2 <sub>B</sub> ,2,2)	3.9 × 10 <sup>3</sup>	6.4 × 10 <sup>3</sup>		1.9 × 10 <sup>2</sup>	1.8 × 10 <sup>5</sup>
Sr <sup>2+</sup>	(2 <sub>B</sub> ,2,2)	9.2 × 10 <sup>3</sup>	4.6 × 10 <sup>4</sup>	1.6 × 10 <sup>2</sup>	3.8 × 10 <sup>3</sup>	
Ba <sup>2+</sup>	(2 <sub>B</sub> ,2,2)	4.5 × 10 <sup>4</sup>	4.1 × 10 <sup>5</sup>	5.8 × 10 <sup>3</sup>	6.7 × 10 <sup>4</sup>	
Ca <sup>2+</sup>	(2 <sub>B</sub> ,2 <sub>B</sub> ,2)	5.1 × 10 <sup>2</sup>	5.0 × 10 <sup>2</sup>			4.4 × 10 <sup>4</sup>
Sr <sup>2+</sup>	(2 <sub>B</sub> ,2 <sub>B</sub> ,2)	1.4 × 10 <sup>3</sup>	4.8 × 10 <sup>3</sup>	2.5 × 10	4.2 × 10 <sup>2</sup>	
Ba <sup>2+</sup>	(2 <sub>B</sub> ,2 <sub>B</sub> ,2)	6.4 × 10 <sup>3</sup>	5.6 × 10 <sup>4</sup>	9.9 × 10 <sup>2</sup>	1.1 × 10 <sup>4</sup>	

<sup>a</sup> Abbreviations as in Table I. <sup>b</sup>  $k_f \pm 5\%$  Unless otherwise indicated. <sup>c</sup> Values obtained from  $k_f = k_d K_s$ ,  $k_f \pm 20\%$ . <sup>d</sup> Reference 16. <sup>e</sup> Reference 11. <sup>f</sup> Stopped-flow determination at pH = 11.5, ref 15.

Individual comments on measurements in the various solvents follows.

**Water.** Rates of formation of alkaline earth cryptates of (2,1,1), (2,2,1), and (2,2,2) have been reported previously,<sup>11,15</sup> and only values for complexes of (2<sub>B</sub>,2,2) and (2<sub>B</sub>,2<sub>B</sub>,2) were determined here. Direct determination of the formation rates are complicated by competing protonation of the cryptands, which are quite strong bases.<sup>18,22</sup> For this reason  $k_f$  values in water were obtained by combining the stability constants with measured dissociation rates (see below),  $k_f = K_s k_d$ .

**Dimethylformamide.** The formation rates were followed conductometrically and  $k_f$  values obtained from plots according to eq 6. Cryptand concentrations were in the range  $2 \times 10^{-4}$ – $1 \times 10^{-2}$  M. For Ca(2,2,2)<sup>2+</sup> the influence of anions on the formation rate constant was also checked using the following salts: CaCl<sub>2</sub>, Ca(NO<sub>3</sub>)<sub>2</sub>, and Ca(ClO<sub>4</sub>)<sub>2</sub>. At salt concentrations of  $1 \times 10^{-4}$  M, both Ca(NO<sub>3</sub>)<sub>2</sub> and Ca(ClO<sub>4</sub>)<sub>2</sub> gave similar values of  $k_e$ , but those obtained for CaCl<sub>2</sub> were somewhat lower (Figure 1). However, at [CaCl<sub>2</sub>] = ca.  $5 \times 10^{-5}$  M the results are in agreement with those for Ca(NO<sub>3</sub>)<sub>2</sub> and Ca(ClO<sub>4</sub>)<sub>2</sub>. It seems likely that ion-pair formation in solutions of CaCl<sub>2</sub> at higher concentrations in DMF is responsible for the lower reactivity. This suggestion was supported by conductance measurements on the various salts in DMF. Conductances of Ca(NO<sub>3</sub>)<sub>2</sub> and Ca(ClO<sub>4</sub>)<sub>2</sub> solutions were linear in concentration up to ca.  $2 \times 10^{-4}$  M whereas those of CaCl<sub>2</sub> showed distinct curvature at concentrations > ca.  $7 \times 10^{-5}$  M. At [CaCl<sub>2</sub>] ≥  $10^{-4}$  M measured conductances are significantly below those obtained by linear extrapolation of data obtained at lower concentrations. The results for Ca(NO<sub>3</sub>)<sub>2</sub> and Ca(ClO<sub>4</sub>)<sub>2</sub> are in agreement with those of Farmer and Popov,<sup>23</sup> who have shown that ion-pair formation between Ca<sup>2+</sup> and NO<sub>3</sub><sup>-</sup> and ClO<sub>4</sub><sup>-</sup> is not significant in strongly solvating media such as DMF and Me<sub>2</sub>SO. For the other cations and cryptates, NO<sub>3</sub><sup>-</sup> and ClO<sub>4</sub><sup>-</sup> salts were used at concentrations in the range  $1.5 \times 10^{-5}$ – $1 \times 10^{-4}$  M, and no evidence of effects due to ion-pair formation was observed.

**Dimethyl Sulfoxide.** The formation rates were determined directly, as described for DMF. Cryptand concentrations were in the range  $5 \times 10^{-4}$ – $5 \times 10^{-2}$  M and [M<sup>2+</sup>] ≤  $10^{-4}$  M. Identical behavior was obtained for NO<sub>3</sub><sup>-</sup> and ClO<sub>4</sub><sup>-</sup> salts, and there was no evidence of ion-pair formation. Excellent linear plots of  $k_e$  against [Cry] according to (6) were obtained in all cases (e.g., Figure 2).

**Propylene Carbonate.** PC is a relatively poor solvent for cations, and the stability constants (Table I) and formation rates were very high. Except for Ca<sup>2+</sup> complexes the formation rates were too high to be measured by stopped-flow ( $k_f > ca. 10^6 M^{-1} s^{-1}$ ). For Ca(2,1,1)<sup>2+</sup>, Ca<sup>2+</sup> concentrations were in the range  $2 \times 10^{-5}$ – $5 \times 10^{-5}$  M, and [Cry] in the range  $2 \times 10^{-4}$ – $1.2 \times 10^{-3}$  M. Good linear plots of  $k_e$  against [Cry] passing through the origin ( $k_d$  very small) were obtained. The formation rate constant of Ca(2,2,2)<sup>2+</sup> was very high, and the change in conductance on complex formation was small. The first-order rate constant for formation of Ca(2,2,2)<sup>+</sup> at [Ca<sup>2+</sup>] ca.  $3.8 \times 10^{-6}$  M and [Cry] =  $2.9 \times 10^{-5}$  M was found to be  $k_e = 17.6 s^{-1}$ . From this a  $k_f$  value of ca.  $6 \times 10^5 M^{-1} s^{-1}$  was established. The formation rates of Ca(2<sub>B</sub>,2,2)<sup>2+</sup> and

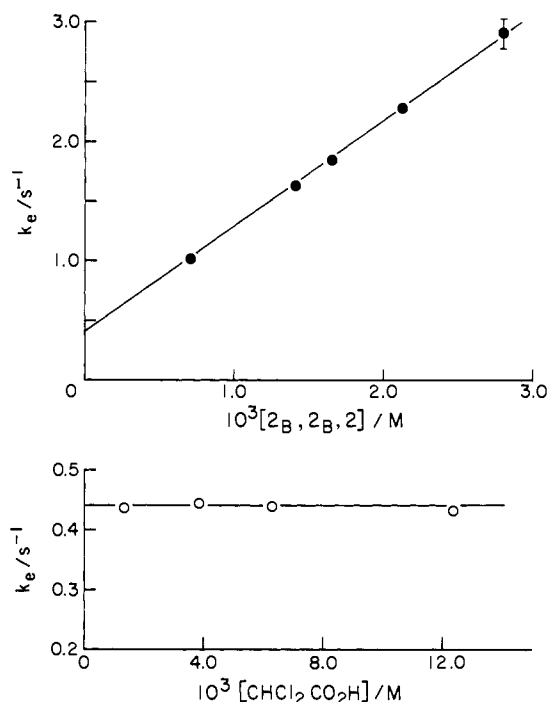


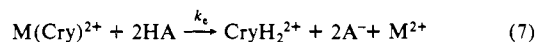
Figure 2. Rates of formation and dissociation of Ba(2<sub>B</sub>,2<sub>B</sub>,2)<sup>2+</sup>: (a) direct equilibration of Ba<sup>2+</sup> and (2<sub>B</sub>,2<sub>B</sub>,2) eq 4–6; (b) dissociation rate measured by acid scavenging, eq 9.

Ca(2<sub>B</sub>,2<sub>B</sub>,2)<sup>2+</sup> were measured with [Ca<sup>2+</sup>] in the range  $10^{-5}$ – $5 \times 10^{-5}$  M and [Cry] in the range  $8 \times 10^{-5}$ – $7 \times 10^{-4}$  M. The observed first-order rate constants showed an excellent linear dependence upon [Cry].

Preliminary measurements have also been made in acetonitrile. Formation rates were too high to be measured by the stopped flow, except for Ca(2,1,1)<sup>2+</sup>,  $k_f = 1.0(\pm 0.1) \times 10^5 M^{-1} s^{-1}$ , and Ca(2<sub>B</sub>,2<sub>B</sub>,2)<sup>2+</sup>,  $k_f = 5(\pm 1) \times 10^4 M^{-1} s^{-1}$ .

(ii) **Dissociation rates.** The rates of dissociation of the alkaline earth cryptates were obtained by using several different techniques as follows: (a) From the intercepts of plots of the observed first order rate constant for equilibration of M<sup>2+</sup> and Cry against [Cry] according to (6): This method could only be used for complexes of relatively low stability where  $k_f[M^{2+}]$  and  $k_d$  values were comparable under the conditions used.

(b) By observing the conductance change when an excess of acid HA (HCl or CHCl<sub>2</sub>CO<sub>2</sub>H) is added to an equilibrium cation-cryptand mixture:<sup>10-12</sup> The rate of the overall reaction, eq 7, is given by eq 8, and



$$k_e = k_d + k_{\text{HA}}[\text{HA}] \quad (8)$$

(22) Lehn, J. M.; Sauvage, J. P. *J. Am. Chem. Soc.* **1975**, *97*, 6700.

(23) Farmer, R. M.; Popov, A. I. *Inorg. Nucl. Chem. Lett.* **1981**, *17*, 51.

Table III. Rates of Dissociation of Alkaline Earth Cryptates in Several Solvents at 25 °C<sup>a,b</sup>

cation	cryptand	$k_d/s^{-1}$				
		H <sub>2</sub> O	MeOH <sup>c</sup>	Me <sub>2</sub> SO	DMF	PC
Ca <sup>2+</sup>	(2,1,1)	$8.2 \times 10^{-1}$ <sup>d</sup>	$3.6 \times 10^{-2}$		$8.0 \times 10^{-1}$	$4.9 \times 10^{-5}$ <sup>e</sup>
Ca <sup>2+</sup>	(2,2,1)	$6.4 \times 10^{-4}$ <sup>f</sup>	$2.3 \times 10^{-6}$	$1.9 \times 10^{-3}$	$8.3 \times 10^{-4}$	$3.4 \times 10^{-7}$ <sup>e</sup>
Sr <sup>2+</sup>	(2,2,1)	$1.4 \times 10^{-3}$ <sup>f</sup>	$8.2 \times 10^{-7}$	$4.2 \times 10^{-4}$	$3.5 \times 10^{-4}$	
Ba <sup>2+</sup>	(2,2,1)	$6.1 \times 10^{-2}$ <sup>d</sup>	$4.6 \times 10^{-5}$	$5.4 \times 10^{-2}$	$1.4 \times 10^{-2}$	
Ca <sup>2+</sup>	(2,2,2)	$2.1 \times 10^{-1}$ <sup>d</sup>	$2.2 \times 10^{-4}$		$3.0 \times 10^{-1}$	$1.0 \times 10^{-5}$ <sup>e</sup>
Sr <sup>2+</sup>	(2,2,2)	$8.4 \times 10^{-5}$ <sup>f</sup>	$5.5 \times 10^{-7}$	$5.2 \times 10^{-3}$	$2.0 \times 10^{-3}$	
Ba <sup>2+</sup>	(2,2,2)	$1.8 \times 10^{-5}$ <sup>d</sup>	$6.3 \times 10^{-7}$	$8.0 \times 10^{-3}$	$2.5 \times 10^{-3}$	
Ca <sup>2+</sup>	(2 <sub>B</sub> ,2,2)	$5.2 \times 10^{-1}$	$5.0 \times 10^{-4}$		$6.0 \times 10^{-1}$	$1.4 \times 10^{-5}$ <sup>e</sup>
Sr <sup>2+</sup>	(2 <sub>B</sub> ,2,2)	$2.9 \times 10^{-4}$	$1.4 \times 10^{-6}$	$9.6 \times 10^{-3}$	$4.5 \times 10^{-3}$	
Ba <sup>2+</sup>	(2 <sub>B</sub> ,2,2)	$5.5 \times 10^{-4}$	$3.5 \times 10^{-6}$	$1.0 \times 10^{-1}$	$2.2 \times 10^{-2}$	
Ca <sup>2+</sup>	(2 <sub>B</sub> ,2 <sub>B</sub> ,2)	$1.9 \times 10^{-1}$	$4.7 \times 10^{-4}$			$1.1 \times 10^{-5}$
Sr <sup>2+</sup>	(2 <sub>B</sub> ,2 <sub>B</sub> ,2)	$5.8 \times 10^{-4}$	$4.3 \times 10^{-6}$	$9.1 \times 10^{-3}$	$7.9 \times 10^{-3}$	
Ba <sup>2+</sup>	(2 <sub>B</sub> ,2 <sub>B</sub> ,2)	$1.5 \times 10^{-2}$	$1.8 \times 10^{-4}$	$4.0 \times 10^{-1}$	$2.2 \times 10^{-1}$	

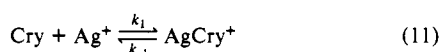
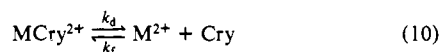
<sup>a</sup> Abbreviations as in Table I. <sup>b</sup>  $k_d \pm 10\%$  Unless otherwise indicated. <sup>c</sup> Reference 16. <sup>d</sup> Reference 11. <sup>e</sup>  $k_d \pm 20\%$ , Obtained from  $k_d = k_f/K_s$ . <sup>f</sup> Reference 11, and J. Garcia-Rosas, Ph.D. Thesis, University of Stirling, 1980.

is independent of  $[M^{2+}]$  provided that the rate of protonation of the free cryptand (formed by dissociation of  $MCry^{2+}$ ) is much faster than the rate of cryptate formation.<sup>10-12</sup> Because of the slow rates of complex formation for alkaline earth cryptates (Table II), this was always true under the reaction conditions used in the present study ( $[M^{2+}]$  ca.  $10^{-4}$ – $10^{-3}$  M in slight excess over  $[Cry]$ ,  $[HA] \geq$  ca.  $10 [Cry]$ ). When HA is a strong acid, as in the case of HCl in water, eq 8 must be modified to eq 9 to

$$k_e = k_d + k_H [H^+] / \gamma_{\pm}^4 \quad (9)$$

allow for the effect of ionic strength on the reaction between  $H^+$  and  $MCry^{2+}$ . The required activity coefficients were calculated by using the Davies equation.<sup>24</sup>

(c) Potentiometrically, using  $Ag^+$  as a scavenger for the free cryptand. This method is based on the reaction (eq 3) used in the determination of the stability constants. The reactions were monitored by using a Radiometer automatic titrator (Type TTT 11) in the EMF-stat mode, in which the volume of an  $Ag^+$  solution required to maintain a constant  $[Ag^+]$  in the reaction cell (measured potentiometrically against a  $Ag^+/Ag$  reference cell) is recorded. If the displacement reaction occurs via the free cryptand, reaction 3 (considered in the reverse direction) may be divided into two steps as in eq 10 and eq 11, where  $k_1$  and  $k_{-1}$  are the



formation and dissociation rate constants of  $AgCry^+$ , respectively. The concentration of free cryptand was always very low (excess  $M^{2+}$  was used), and so by applying the steady-state assumption to  $[Cry]$  and allowing for the fact that  $k_1$  is several orders of magnitude larger than  $k_f$ ,<sup>25</sup> it may be shown that the approach to equilibrium is first order with a rate constant  $k_e$  given by eq 12 or eq 13, where  $K_s(MCry^{2+}) = k_f/k_d$

$$k_e = k_d + \frac{k_f k_{-1} [M^{2+}]}{k_1 [Ag^+]} \quad (12)$$

$$k_e = k_d \left\{ 1 + \frac{K_s(MCry^{2+}) [M^{2+}]}{K_s(AgCry^+) [Ag^+]} \right\} \quad (13)$$

is the stability constant of  $MCry^{2+}$  and  $K_s(AgCry^+) = k_1/k_{-1}$  is the stability constant of  $AgCry^+$ . When the stability constant of  $AgCry^+$  is considerably higher than that of  $MCry^{2+}$ ,  $k_e \sim k_d$  and is independent of  $[M^{2+}]$ . Otherwise  $k_d$  may be obtained from the intercept of a plot of  $k_e$  against  $[M^{2+}]$  at constant  $[Ag^+]$ . In all cases the observed behavior was consistent with eq 12 and 13 and no evidence of any alternative cation exchange mechanism, such as a direct bimolecular exchange reaction, was found for the alkaline earth cryptates.

(d) From  $k_d = k_f/K_s$ , using previously measured  $k_f$  and  $K_s$  values (Tables I and II): This method was used to determine  $k_d$  for only a few complexes in PC where determination by more direct methods was not possible (see below).

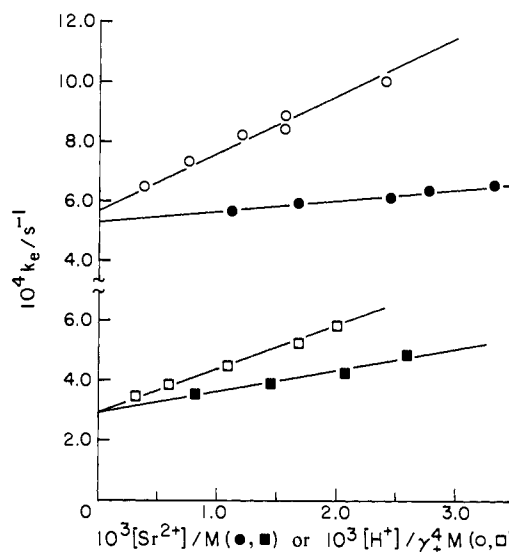


Figure 3. Rates of dissociation of  $Sr(2B,2B,2)^{2+}$  (●, ◻) and  $Sr(2B,2,2)^{2+}$  (◻, ◻) in water at 25 °C, using  $Ag^+$  (filled symbols, eq 12) or  $H^+$  (open symbols, eq 9) as scavenger.  $[Ag^+] = 1 \times 10^{-5}$  M.

For most complexes more than one of the above methods was used to determine  $k_d$ , and agreement between the values obtained by the different methods was good.

The results are listed in Table III. Detailed comments on the reaction conditions and the individual various methods used in the various solvents follows.

**Water.** Dissociation rates for complexes of (2,1,1), (2,2,1), and (2,2,2) have been determined earlier<sup>11,15</sup> and only the benzo-substituted complexes were studied here. Dissociation reactions of  $Ca^{2+}$  complexes were too fast to be monitored by the potentiometric method and were measured by using method b only. For  $Ca(2B,2,2)^{2+}$ ,  $k_d$  was in excellent agreement with that determined from ligand exchange reactions.<sup>26</sup>  $Sr^{2+}$  cryptates could be studied by using scavenging by  $H^+$  and  $Ag^+$ . The results obtained for the (2<sub>B</sub>,2,2) and (2<sub>B</sub>,2<sub>B</sub>,2) complexes, plotted according to eq 9 and 12, are shown in Figure 3.  $Ba(2B,2,2)^{2+}$  was also studied by using methods b and c, and the same result was obtained from each method. The rate of dissociation of  $Ba(2B,2B,2)^{2+}$  was too fast to be monitored potentiometrically and was measured by using method b. The experimentally determined rate constant,  $k_e$  (eq 7, 8), was independent of  $[Ba^{2+}]$  (in the range  $1.2 \times 10^{-4}$ – $8 \times 10^{-4}$  M) and  $[H^+]$  (in the range  $6 \times 10^{-4}$ – $3 \times 10^{-3}$  M) and was identified with  $k_d$ .

**Dimethyl Sulfoxide.**  $Ca^{2+}$  and  $Sr^{2+}$  cryptates were studied by using both methods b and c. In the former case (method b) the measured rates were independent of  $[M^{2+}]$  and  $[CHCl_2CO_2H]$  (=HA). Good agreement ( $\leq 10\%$ ) was obtained in all cases except for  $Sr(2,2,2)^{2+}$  where  $k_d$  (HA<sup>+</sup> scavenging) =  $1.0 \times 10^{-2}$  s<sup>-1</sup> differs considerably from  $k_d$  ( $Ag^+$  scavenging) =  $5.2 \times 10^{-3}$  s<sup>-1</sup>. The reason for this is not clear but the latter value when combined with  $k_f = 6.6 \times 10^2$  M<sup>-1</sup> s<sup>-1</sup> (Table II) gives a stability constant ( $\log K_s = \log(k_f/k_d) = 5.10$ ) that is much more consistent with the potentiometric value ( $\log K_s = 5.2_6$ , Table I), and is the

(24) Davies, C. W. "Ion Association," Butterworths: London 1962.

(25) J. Stroka, unpublished results.

(26) N. van Truong, unpublished results.

Table IV, Comparison of Kinetic ( $\log k_f/k_d$ ) and Thermodynamic ( $\log K_s$ ) Parameters for Alkaline Earth Cryptate Formation at 25 °C

cryptate	solvent <sup>a</sup>	$\log K_s$	$\log (k_f/k_d)$	cryptate	solvent	$\log K_s$	$\log (k_f/k_d)$
Ca(2,2,1) <sup>2+</sup>	Me <sub>2</sub> SO	3.9 <sub>0</sub>	4.0 <sub>2</sub>	Ca(2,2,1) <sup>2+</sup>	DMF	6.5 <sub>8</sub>	6.2 <sub>0</sub>
Sr(2,2,1) <sup>2+</sup>	Me <sub>2</sub> SO	6.1 <sub>0</sub>	6.0 <sub>9</sub>	Ca(2,2,2) <sup>2+</sup>	DMF	3.7 <sub>9</sub>	3.8 <sub>7</sub>
Sr(2,2,2) <sup>2+</sup>	Me <sub>2</sub> SO	5.2 <sub>6</sub>	5.1 <sub>1</sub>	Ca(2 <sub>B</sub> ,2,2) <sup>2+</sup>	DMF	2.6 <sub>0</sub>	2.5 <sub>0</sub>
Sr(2 <sub>B</sub> ,2,2) <sup>2+</sup>	Me <sub>2</sub> SO	4.3 <sub>3</sub>	4.2 <sub>2</sub>	Sr(2,2,1) <sup>2+</sup>	DMF	7.9 <sub>5</sub>	7.6 <sub>0</sub>
Sr(2 <sub>B</sub> ,2 <sub>B</sub> ,2) <sup>2+</sup>	Me <sub>2</sub> SO	3.5 <sub>8</sub>	3.4 <sub>5</sub>	Sr(2,2,2) <sup>2+</sup>	DMF	7.3 <sub>0</sub>	7.1 <sub>5</sub>
Ba(2,2,1) <sup>2+</sup>	Me <sub>2</sub> SO	5.3 <sub>0</sub>	5.1 <sub>5</sub>	Sr(2 <sub>B</sub> ,2,2) <sup>2+</sup>	DMF	6.1 <sub>0</sub>	5.9 <sub>4</sub>
Ba(2,2,2) <sup>2+</sup>	Me <sub>2</sub> SO	6.5 <sub>0</sub>	6.4 <sub>5</sub>	Sr(2 <sub>B</sub> ,2 <sub>B</sub> ,2) <sup>2+</sup>	DMF	4.8 <sub>9</sub>	4.7 <sub>3</sub>
Ba(2 <sub>B</sub> ,2,2) <sup>2+</sup>	Me <sub>2</sub> SO	5.1 <sub>0</sub>	4.7 <sub>6</sub>	Ba(2 <sub>B</sub> ,2,2) <sup>2+</sup>	DMF	6.4 <sub>6</sub>	6.4 <sub>8</sub>
Ba(2 <sub>B</sub> ,2 <sub>B</sub> ,2) <sup>2+</sup>	Me <sub>2</sub> SO	3.4 <sub>6</sub>	3.3 <sub>9</sub>	Ba(2 <sub>B</sub> ,2 <sub>B</sub> ,2) <sup>2+</sup>	DMF	4.6 <sub>3</sub>	4.7 <sub>0</sub>
Ca(2,1,1)	DMF	3.0 <sub>9</sub>	3.1 <sub>2</sub>	Ca(2 <sub>B</sub> ,2 <sub>B</sub> ,2) <sup>2+</sup>	PC	9.7 <sub>4</sub>	9.5 <sub>9</sub>

<sup>a</sup> Abbreviations as in Table I.

value listed in Table III. Ba(2,2,1)<sup>2+</sup> and Ba(2,2,2)<sup>2+</sup> were studied by methods c and b, respectively. For the benzo-substituted Ba<sup>2+</sup> cryptates, a reasonable estimate of  $k_d$  could be obtained from the intercept of  $k_e$  vs [Cry] plots according to eq 6, under formation rates. Figure 2 illustrates the results for Ba(2<sub>B</sub>,2<sub>B</sub>,2)<sup>2+</sup> ( $k_d = 0.39 \text{ s}^{-1}$ ); also included are the results of an alternative determination of  $k_d$  using method b ( $k_d = 0.43 \text{ s}^{-1}$ ). Good agreement between  $k_d$  values determined by the same two methods was also found for Ba(2<sub>B</sub>,2,2)<sup>2+</sup>:  $k_d = 9.0 \times 10^{-2} \text{ s}^{-1}$  (eq 6) and  $k_d = 10.0 \times 10^{-2} \text{ s}^{-1}$  (eq 8).

**Dimethylformamide.** Dissociation rate constants were determined by using Ag<sup>+</sup> scavenging (method c) or from intercepts of plots of  $k_e$  against [Cry], according to eq 6 (Ca(2,1,1)<sup>2+</sup>, Ca(2,2,2)<sup>2+</sup>, and Ca(2<sub>B</sub>,2,2)<sup>2+</sup>). For Ba(2<sub>B</sub>,2<sub>B</sub>,2)<sup>2+</sup> a value of  $k_d = 0.22 \text{ s}^{-1}$  was obtained from a study of cryptand exchange kinetics,<sup>26</sup> and this is in good agreement with  $k_d = 0.24 \text{ s}^{-1}$  obtained from  $k_d = k_f/K_s$  using the data in Tables I and II.

**Propylene Carbonate.** The dissociation rates were for the most part too slow to be determined with any accuracy ( $t_{1/2} > 30$  days for the more stable complexes). Rates of dissociation of Ca(2,2,2)<sup>2+</sup>, Ca(2<sub>B</sub>,2,2)<sup>2+</sup>, and Ca(2<sub>B</sub>,2<sub>B</sub>,2)<sup>2+</sup> were determined in the presence of excess dichloroacetic acid (method b). However, reactions of the former two cryptates were so strongly acid catalyzed that it was not possible to obtain  $k_d$  from a plot of  $k_e$  against [HA]. Therefore, for these and also Ca(2,1,1)<sup>2+</sup> and Ca(2,2,1)<sup>2+</sup>  $k_d$  values were obtained from  $k_d = k_f/K_s$ . The value obtained for the dissociation of Ca(2<sub>B</sub>,2<sub>B</sub>,2)<sup>2+</sup>,  $k_d = 1.1 \times 10^{-5} \text{ s}^{-1}$ , was not checked by measurement using an alternative technique, but when combined with  $k_f = 4.4 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$  (Table II), corresponds to  $\log (k_f/k_d) = 9.6_0$ , which is in quite good agreement with the potentiometrically determined stability constant ( $\log K_s = 9.7_4$ ).

In a number of cases where  $k_f$  and  $k_d$  values were measured independently, it is possible to check the internal consistency of the kinetic and thermodynamic parameters reported in Tables I-III. This is done in Table IV, where  $\log (k_f/k_d)$  values are compared with  $\log K_s$  values. Considering the number of independent measurements involved, the agreement is generally very good. There is perhaps a tendency for  $\log K_s$  values to be slightly higher than  $\log (k_f/k_d)$ , but differences are normally within the combined experimental uncertainty, and it is difficult to know whether this is a real effect.

## Discussion

**Stability Constants.** The particular 3-D structure of the cryptand ligands shows up strongly in two aspects of alkaline-earth cryptates: a very high stability, and a high selectivity among alkaline-earth cations. For example, the stability constants of the alkaline earth cryptates are larger by a factor of about  $10^6$  than those of other neutral ligands such as the crown ethers<sup>27</sup> and diaza crown ethers<sup>28,29</sup> (with similar ligand cavity size). They are also much larger than those of the naturally occurring anionic antibiotics X-14547A<sup>13</sup> and lasalocid (X 537 A).<sup>13</sup> Even the complexes of calcimycin (A, 23187),<sup>13</sup> the most effective of the anionic antibiotics with respect to alkaline earth complexation, are  $10^{1.5}$ – $10^4$  times less stable in methanol than the corresponding (2,2,1) complexes, despite the additional stabilization that must result from Coulombic attraction between the cations and ligand in the calcimycin complexes. The cryptand's cavity allows for maximum replacement of solvent molecules in the inner coordination sphere of the cations by the donor atoms of the ligand,

In addition, very little conformational rearrangement is required compared to the (more flexible) crown ethers and the noncyclic anionic ionophores. This "preformed" geometry and the relative rigidity, however, although leading to higher complex stability, might be expected to slow down the rates of the complexation/decomplexation process (see below).

The stabilities of the cryptates depend strongly upon the relative size of the cation and the ligand's cavity ( $r(M^{n+})/r(\text{Cry})$ ), and for a given cryptand the complexes are more stable when  $r(M^{n+})/r(\text{Cry})$  is nearer to unity. Thus, the alkaline-earth cations forming the most stable complexes with (2,2,1) and (2,2,2) are Sr<sup>2+</sup> and Ba<sup>2+</sup>, respectively, independent of solvent. Cryptand (2,2,2) is highly selective toward Sr<sup>2+</sup> and Ba<sup>2+</sup> relative to Ca<sup>2+</sup> (stability ratios are, for example,  $4 \times 10^3$  for Sr<sup>2+</sup>/Ca<sup>2+</sup> and  $6 \times 10^4$  for Ba<sup>2+</sup>/Ca<sup>2+</sup> in methanol). These values may be compared with the corresponding values for diaza crown ethers (ca.  $10^2$  for both ratios)<sup>22</sup> and the various anionic ionophores ( $\leq 10^2$ ).<sup>13</sup> Simple size-dependent relationships, however, no longer hold when transition-metal cations are involved, particularly for ions such as Cu<sup>2+</sup>, Pb<sup>2+</sup>, and Hg<sup>2+</sup>, which are capable of strong interaction with nitrogen.<sup>30,31</sup>

The stability constants of the M<sup>2+</sup> cryptates are sensitive to solvent variation, with variations in  $K_s$  of over 10 orders of magnitude being observed for some complexes (Table I). In all cases the stability constants increase in the order Me<sub>2</sub>SO < DMF  $\approx$  H<sub>2</sub>O < MeOH < PC. The same order (not including DMF) has been reported for complexes of Pb<sup>2+</sup>, Cd<sup>2+</sup>, Cu<sup>2+</sup>, and Zn<sup>2+</sup>.<sup>30</sup> For alkali metal cryptates the relative positions of H<sub>2</sub>O and Me<sub>2</sub>SO are reversed, but otherwise the order is the same. The overall range of the stability constant variations for the alkali metal cryptates (ca. 7 orders of magnitude in  $K_s$ )<sup>19</sup> is, however, somewhat smaller.

The solvent dependence of the stability constants contains information on the solvation of the free cations, the ligands, and the complexes. This is shown in eq 14 where the stability constants

$$RT \ln [K_s(S2)/K_s(S1)] = \Delta G_{tr}(M^{2+}) + \Delta G_{tr}(\text{Cry}) - \Delta G_{tr}(\text{MCry}^{2+}) \quad (14)$$

in solvents S1 and S2 are related to the free energies of transfer,  $\Delta G_{tr}$ , of the various species from S1 and S2.  $\Delta G_{tr}(\text{Cry})$  values are small ( $\leq$  ca. 8 kJ mol<sup>-1</sup>),<sup>19,21,32</sup> especially for transfer between nonaqueous solvents, and do not make a large contribution to the variations in  $\log K_s$ . Depending upon how effectively the cation in the cryptate is shielded from the solvent,  $\Delta G_{tr}(\text{MCry}^{2+})$  might be expected to be relatively small, in which case the change in free energy of M<sup>2+</sup> with solvent would dominate the stability constant behavior. Thus, the wider range of  $\log K_s(M^{2+})$  values compared with  $\log K_s(M^+)$  values on solvent transfer probably reflects primarily the much larger variations in the solvation of M<sup>2+</sup> cations<sup>33-35</sup> relative to M<sup>+</sup> cations.<sup>36</sup> Estimates of  $\Delta G_{tr}(\text{Ca}^{2+})$

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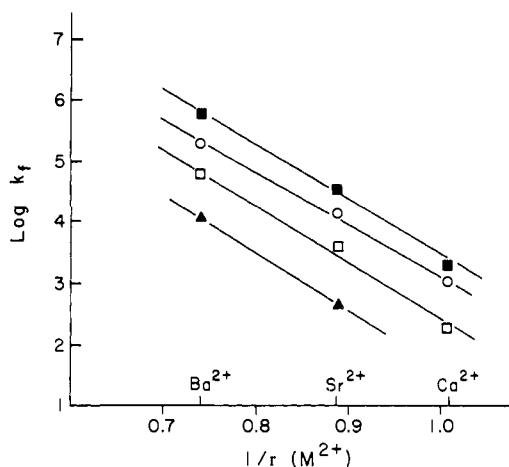
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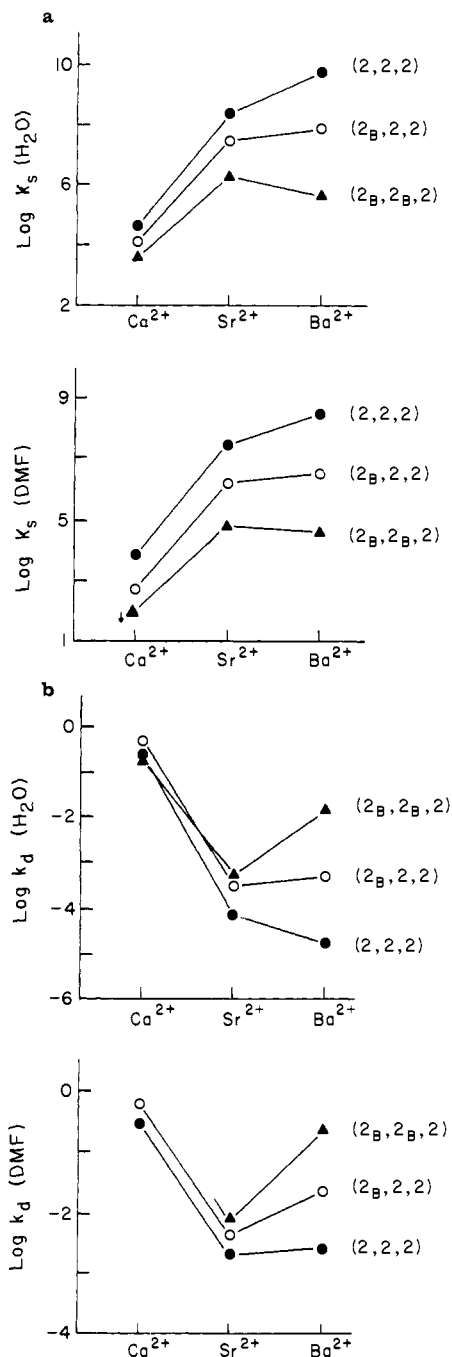


**Figure 4.** Rates of formation of alkaline earth cryptates in dimethylformamide at 25 °C: (■) (2,2,2); (○) (2,2,1); (□) (2<sub>B</sub>,2,2); (▲) (2<sub>B</sub>,2<sub>B</sub>,2).

and  $\Delta G_{tr}(Sr^{2+})$  are not available, but on the basis of published  $\Delta G_{tr}$  for  $Ba^{2+}$  and other  $M^{2+}$  cations<sup>33-35</sup> it seems that differences in the behavior of  $M^{2+}$  and  $M^+$  cryptates<sup>19</sup> on solvent transfer are significantly less than those expected on the basis of solvation of the free cations. Therefore, some attenuation due to solvation of the complexed cations must occur. It seems, then, that at least for the simple cryptand ligands, the shielding of  $M^{2+}$  cation/solvent interactions is not very effective. Lehn and co-workers<sup>37</sup> have earlier reported quite larger variations in  $M^+/M^{2+}$  selectivity in the series (2,2,2), (2<sub>B</sub>,2,2), and (2<sub>B</sub>,2<sub>B</sub>,2), attributable to increasingly effective shielding of cation/solvent interactions as the thickness of the organic ligand layer increases. The use of eq 14 and analogous equations, in conjunction with various assumptions regarding the solvation of  $MCr^{2+}$ , to determine single-ion  $\Delta G_{tr}(M^{2+})$  values for several transition-metal cations has also been discussed recently.<sup>30</sup>

**Reaction Rates.** Observed variations in formation and dissociation rate constants within a given solvent for the alkaline-earth cryptates are characteristic of the behavior of complexes of macrocyclic ligands. The dominant influence on the stabilities, in terms of the selectivity of the ligands, is the dissociation rate. It has been shown earlier for alkali cryptates<sup>12</sup> that there is a good correlation of the dissociation rate constants with the stability constants, covering a wide range of cations, ligands, and solvents. Furthermore, a recent survey by Lockhart<sup>38</sup> shows that this correlation may be extended to include crown ether complexes. Such a relationship exists because the formation rate constants of the various complexes are relatively insensitive to solvent and ligand and increase slowly and monotonically with increasing cation size.

Similar behavior is observed for the  $M^{2+}$  cations (Tables II and III). The formation rate constants show a monotonic increase with cation size, irrespective of the ligand, and there is an approximately linear relationship between  $\log k_f$  and the inverse of the cationic radius (e.g., Figure 4 for complexes in DMF). Where comparison with ligands of different structure is possible, the formation rate constants are similar. Thus, for the (2,2) diaza crown ethers,<sup>28</sup>  $k_f$  values for  $Ca^{2+}$ ,  $Sr^{2+}$ , and  $Ba^{2+}$  complexes in MeOH are  $2.5 \times 10^5$ ,  $2.1 \times 10^6$ , and  $6.4 \times 10^6 M^{-1} s^{-1}$ , respectively, compared with the corresponding values of  $3.4 \times 10^4$ ,  $3.1 \times 10^5$ , and  $5 \times 10^6 M^{-1} s^{-1}$  for the (2,2,2) cryptates (Table II). The  $k_f$  values for  $Sr^{2+}$  complexes of (2,2,2) and dibenzo-18-crown-6 in methanol differ by less than a factor of two (at -15 °C).<sup>39</sup> Similarly, the  $Ca^{2+}$  complex of the cyclodecapeptide



**Figure 5.** Stability constants (a) and dissociation rate constants (b) for (2,2,2), (2<sub>B</sub>,2,2) and (2<sub>B</sub>,2<sub>B</sub>,2) complexes in H<sub>2</sub>O and DMF.

antamanide<sup>40</sup> has a formation rate constant ( $k_f = 5 \times 10^3 M^{-1} s^{-1}$ ) in methanol close to those of the  $Ca^{2+}$  cryptates. These relatively similar formation rate constants for the different complexes (within ca.  $10^2$ ) contrast strikingly with the dissociation rate constants, which for the same ligands vary by more than  $10^8$ .

The results for (2,2,2), (2<sub>B</sub>,2,2), and (2<sub>B</sub>,2<sub>B</sub>,2) show a nice example of systematic trends in  $\log K_s$  and  $\log k_d$  as a result of changing electrostatic and cavity-size interactions on benzo substitution. The results shown in Figure 5a,b for solvents H<sub>2</sub>O and DMF are typical. The increase in  $\log K_s$  from  $Ca^{2+}$  to  $Sr^{2+}$  is almost constant, while the line connecting  $\log K_s$  values for  $Ba^{2+}$  decreases from positive to negative values in the series (2,2,2), (2<sub>B</sub>,2,2), (2<sub>B</sub>,2<sub>B</sub>,2). Similar behavior is found in the  $\log k_d$  plots, except that the minimum in  $\log k_d$  for  $Sr^{2+}$  has already occurred at (2<sub>B</sub>,2,2). Over the same series,  $\log k_f$  values in all cases show

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a monotonic decrease in the order  $(2,2,2) > (2_B,2,2) > (2_B,2_B,2)$ .

Despite the qualitative similarity between the  $M^+$  and  $M^{2+}$  cryptates, there is a quantitative difference between the two groups in terms of the absolute magnitudes of the rate constants. When cations of similar size are compared ( $Na^+$  and  $Ca^{2+}$ , or  $K^+$  and  $Ba^{2+}$ ) formation and dissociation rate constants of  $M^{2+}$  cations are lower by as much as  $10^5$  and normally at least  $10^3$ . Variations between the cations within a group are also larger for  $M^{2+}$  cations:  $k_f(Ba^{2+}/Ca^{2+}) \approx 100$ ; cf.  $k_f(K^+/Na^+) \approx 3$ .<sup>12</sup> These differences, however, should be considered in light of the enormous changes in the absolute solvation energies on going from  $M^+$  to  $M^{2+}$  cations (cf., for example,  $\Delta G_{hydr}^\circ(Na^+) = -411 \text{ kJ mol}^{-1}$  and  $\Delta G_{hydr}^\circ(Ca^{2+}) = -1598 \text{ kJ mol}^{-1}$ ).<sup>41</sup> Large variations in kinetic parameters with cationic charge have earlier been observed for europium 2+ and 3+ cryptates in water.<sup>42</sup>

The formation rate constants differ significantly from the simple predictions of eq 2 in at least three respects: the absolute values of  $k_f$  are lower than  $k_s K_{ES}$  by factors of up to  $10^6$ , they are quite sensitive to solvent composition, and they are also more sensitive to cation size and ligand structure than predicted. This disagreement extends to results in aqueous solution, where it has been previously shown that the data for complexation of bidentate and tridentate ligands may be accommodated by a simple  $I_d$  mechanism.<sup>2,3</sup>

For neutral ligands the stability constant of the outer-sphere complex may be estimated from eq 15, where  $a_1$  represents the

$$K_{ES} = 10^3(4\pi N/3)a_1^3 \quad (15)$$

center-to-center distance of closest approach of the solvated metal ion and the reaction site on the ligand.<sup>2,3</sup> Values of  $K_{ES}$  will be insensitive to solvent and cation variation. For the nonaqueous solvents studied, using a typical  $a_1$  value of ca.  $7 \times 10^{-10} \text{ M}$  for the distance between the centers of the cation and nearest donor atoms<sup>43</sup> gives  $K_{ES} = 0.89 \text{ M}^{-1}$ .  $K_{ES}$  should vary by only 70% from  $Ca^{2+}$  to  $Ba^{2+}$ , because of the relatively small contribution of the ionic radii of the cations to the separation of cation and ligand sites in the outer-sphere complex; values in water should be somewhat smaller (ca.  $0.3 \text{ M}^{-1}$ ). Rate constants for solvent exchange at alkaline earth cations are available only in water, with the following values:<sup>44</sup>  $Ca^{2+}$ ,  $3 \times 10^8 \text{ s}^{-1}$ ;  $Sr^{2+}$ ,  $4 \times 10^8 \text{ s}^{-1}$ ;  $Ba^{2+}$ ,  $8 \times 10^8 \text{ s}^{-1}$ . However,  $k_s$  values for  $M^{2+}$  transition-metal cations of varying electronic structure have been measured in a number of solvents,<sup>44,45</sup> and the solvent dependence of  $k_s$  is almost independent of  $M^{2+}$ . On the basis of the results for these cations we estimate the following rate constants for solvent exchange of  $Ca^{2+}$  in the various solvents:  $H_2O$ ,  $3 \times 10^8 \text{ s}^{-1}$ ;  $MeOH$ ,  $6 \times 10^6 \text{ s}^{-1}$ ;  $DMF$ ,  $3 \times 10^7 \text{ s}^{-1}$ ;  $Me_2SO$ ,  $6 \times 10^7 \text{ s}^{-1}$ ;  $CH_3CH$ ,  $3 \times 10^7 \text{ s}^{-1}$  (results for PC should be very similar to those for  $CH_3CN$ ).<sup>36</sup> Values of  $k_s$  for  $Sr^{2+}$  and  $Ba^{2+}$  should be higher than for  $Ca^{2+}$  by a similar ratio to those observed in  $H_2O$ .

It is clear that a simple combination of  $k_s$  and  $K_{ES}$  values as in eq 2 cannot account for the data in Table II, even allowing for a large degree of uncertainty in the estimation of  $k_s$  and  $K_{ES}$ . Experimental values are in all cases substantially lower than the calculated values, and in  $Me_2SO$  by a factor of more than  $10^6$ . Part of this discrepancy could be accounted for by a requirement for a conformational change to occur *prior* to complexation,<sup>15</sup> and indeed evidence for the existence of different conformations in  $(2,2,2)$  has been obtained from ultrasonic relaxation studies.<sup>46</sup>

However, it would be very difficult to explain in this way, for example, the observed variations in  $k_f$  with cation size or the fact that in the nonaqueous solvents the formation rates vary systematically and substantially with the cation-solvating abilities of the various solvents. The large differences between formation rates of  $M^+$  and  $M^{2+}$  cryptates also cannot be accounted for in this way.

A more likely explanation for the low and variable formation rates is incomplete compensation for the loss of solvation of the cation, because of difficulties that the ligand has in adopting optimal conformations at various stages during complexation. Strehlow and Knoche<sup>47</sup> have shown, using a simple electrostatic model, that substitution reactions at polyvalent nontransition cations do not proceed by a purely dissociative mechanism. A considerable reduction in activation energy is achieved by adopting a concerted mechanism in which the incoming ligand helps to stabilize the cation. Such a process would undoubtedly be more difficult for a macrocyclic ligand, depending upon the ligand flexibility and geometry, and so the complexation rates are expected to be slower than those of simple solvent exchange. In particular, lower rates should occur for higher charge density cations, solvents in which cation-solvent interactions are particularly strong (e.g.,  $Me_2SO$ ), and for more rigid ligands [e.g.,  $(2,1,1)$ ,  $(2_B,2_B,2)$ ]. The effects are large, as may be seen, for example, from  $k_f/k_s K_{ES}$  values estimated for  $Ca(2,2,1)^{2+}$  complexes in the various solvents:  $Me_2SO$ ,  $3.8 \times 10^{-7} < DMF$ ,  $4.1 \times 10^{-5} \sim H_2O$ ,  $6.6 \times 10^{-5} < MeOH$ ,  $3.6 \times 10^{-3} \sim PC$ ,  $4 \times 10^{-3} < CH_3CN$ ,  $2 \times 10^{-2}$ . This order is in accord with the cation solvating abilities of the different solvents.<sup>36</sup> Similarly,  $k_f/k_s K_{ES}$  values decrease ca. 50-fold in the series  $(2,2,2)$ ,  $(2_B,2,2)$ ,  $(2_B,2_B,2)$ , corresponding to increasing rigidity of the ligands.

Grell and Oberbäumer<sup>48</sup> in a comparison of  $k_f$  values for alkali-metal complexes of mono- and bicyclic ligands make a more specific suggestion that in the multistep process of cryptate formation, there is a rate-limiting step in which two or more remaining solvent molecules of a partially complexed cation have to be removed prior to entry of the cation into the ligand cavity. It is difficult to distinguish experimentally between this possibility and that of a simple stepwise process with incomplete compensation for loss of solvation, as discussed above. However, an analysis of the solvent effects on  $M^+$ -cryptate formation suggested that the transition state occurs very early in the substitution process, with most of the cation-solvent interactions remaining intact.<sup>12</sup>

In a recent comprehensive study of the solvent effects on the kinetics of formation of copper(II)-cyclic polythiaether complexes, Rorabacher and co-workers<sup>49</sup> found formation rate constants significantly below those estimated from the  $Cu^{2+}$ - $NH_3$  reaction, even after allowing for statistical, steric, and ligand conformational effects. They suggested that this may be due to a shift in the rate-determining step from the first bond formation to that of the second bond formation, owing to difficulty in achieving chelate ring closure. Such a conclusion could also apply to our results; i.e., the rate-determining step may not correspond to loss of the first solvent molecule. However, the very large variations in  $k_f$  with solvent and the differences between  $M^+$  and  $M^{2+}$  cations for cryptate formation would suggest that, at whatever point the rate-determining step occurs, the energetics associated with the required desolvation of the metal ion must be of major importance.

Although the present results refer to the relatively rigid cryptand ligands, it is clear from the similarity of formation rates for the other macrocyclic ligands considered earlier, including the crown ethers, diaza crown ethers, and antamanide, that similar comments pertain to a variety of macrocyclic complexing agents. It should be emphasized, however, that the formation rate constants are sufficiently large that only a small fraction of the total solvation energy can be lost during complexation. Thus, the overall com-

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plexation process should still be viewed essentially as one in which the solvent molecules are replaced in a stepwise fashion by ligand donor atoms, with a significant amount of the solvation energy being compensated for by the ligand binding energy during complexation.<sup>50</sup>

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**Registry No.** Ca, 7440-70-2; Sr, 7440-24-6; Ba, 7440-39-3; Me<sub>2</sub>SO, 67-68-5; MeOH, 67-56-1; DMF, 68-12-2; PC, 108-32-7; (2,1,1), 31250-06-3; (2,2,1), 31364-42-8; (2,2,2), 23978-09-8; (2<sub>B</sub>,2,2), 31250-18-7; (2<sub>B</sub>,2<sub>B</sub>,2), 40471-97-4.

## Crystal and Molecular Structure of the Complex between *sym*-Dibenzo-14-crown-4-oxyacetate and Li<sup>+</sup>, [C<sub>20</sub>H<sub>21</sub>O<sub>7</sub>]<sup>-</sup>·Li<sup>+</sup>·7.5H<sub>2</sub>O

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**Abstract:** The synthesis and crystal structure of the title compound are described. Single crystal X-ray diffractometry indicates 8 formula units in the unit cell of parameters  $a = 20.779 \text{ \AA}$ ,  $b = 17.845 \text{ \AA}$ ,  $c = 13.903 \text{ \AA}$ ,  $\beta = 98.19^\circ$ . The space group is monoclinic  $C2/c$ . Direct methods yielded the structure, which was refined by least-squares techniques to a final  $R$  factor of 0.077 for 3124 independent observations. The lithium cation forms a 1:1 neutral complex with the carboxylic crown ether. In this complex, Li<sup>+</sup> is pentacoordinated with 4 crown oxygens (av. Li-O is 2.06 Å) and an apical water molecule (Li-O, 1.91 Å) in a nearly square pyramidal geometry. This apical water molecule forms a bridge between the Li<sup>+</sup> cation and the negatively charged carboxylate group. In the crystal structure we find an extensively ordered solvent (water) network which is dominated by O<sub>5</sub> pentagons. The crystal packing is formed of hydrophilic regions, linked together by water "channels", and hydrophobic regions, consisting mainly of the benzo rings.

Since Pedersen's introduction<sup>1</sup> of synthetic macrocyclic ionophores capable of forming stable complexes with alkali and alkali earth metal ions, considerable attention has been devoted to the exploitation of the cationic selectivity of these neutral coronands.<sup>2-6</sup> Crown ethers are of potential utility for many applications where cationic selectivity and solubility in nonpolar solvents or membranes are necessary. Properties that influence this selectivity include the charge, size, and electronic structure of the cations as well as the associated counterions. However, it is usually found that the strongest complex of an ionophore and a cation is one where the diameter of the cation best matches the diameter of the cavity formed by the polyether ring upon complexation.<sup>1</sup>

The nature of the interaction of lithium cations with neutral ionophores has received relatively little attention. Complexation tendencies toward lithium have been reported for 12- to 18-membered-ring crown ethers,<sup>1,7-12</sup> as well as (2.1.1) cryptand<sup>13,14</sup> and some acyclic quadridentate amido ethers.<sup>15,16</sup> Some of these complexing agents display a significant selectivity toward lithium cations.<sup>11,12,15,16</sup> In addition, crystal structure analyses have been presented for lithium complexes with the (2.1.1) cryptand,<sup>14</sup> some 12-18-membered-ring macrocycles,<sup>17-20</sup> and recently the crown ethers benzo-13-crown-4 (B-13-C-4)<sup>21</sup> and dibenzo-14-crown-4 (DB-14-C-4) (**1**).<sup>22</sup> In the latter two crystal structures, the coordination polyhedron of the lithium cation is 5-coordinate square pyramidal with the metal ion being positioned 0.7-0.8 Å above the plane of the four ethereal oxygens of the coronand. The counterion occupies the fifth (apical) coordination site.

A series of macrocyclic polyethers possessing ligating arms was reported recently by Gokel,<sup>23</sup> who identifies such compounds as

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