

# A Systematic Study of the Effect of Macrocyclic Ring Size and Donor Atom Type on the Log $K$ , $\Delta H$ , and $T\Delta S$ of Reactions at 25 °C in Methanol of Mono- and Divalent Cations with Crown Ethers<sup>1</sup>

J. D. Lamb, R. M. Izatt,\* C. S. Swain, and J. J. Christensen

Contribution from the Departments of Chemistry and Chemical Engineering and Contribution No. 168 from the Thermochemical Institute, Brigham Young University, Provo, Utah 84602. Received August 8, 1979

**Abstract:** The reactions in methanol at 25 °C of Ag<sup>+</sup>, Cu<sup>2+</sup>, and alkali and alkaline earth metal cations with 15-crown-5 (15C5), 18-crown-6 (18C6), 21-crown-7 (21C7), thia-18-crown-6 (T18C6), and pyridino-18-crown-6 (P18C6) were studied by titration calorimetry. Log  $K$ ,  $\Delta H$ , and  $T\Delta S$  values for these reactions are reported in those cases where measurable heat was obtained. Ligand 15C5 shows poor selectivity among the cations studied, its cavity being too small to accommodate Na<sup>+</sup> or larger cations. Ligands 18C6 and 21C7 show selectivity among monovalent cations for K<sup>+</sup> and Cs<sup>+</sup>, respectively, consistent with the expected better fit of each cation in the particular ligand cavity. Substitution of sulfur for one oxygen of 18C6 to give T18C6 causes the stability of complexes of alkali and alkaline-earth cations to drop. A greater loss of stability is noted for Na<sup>+</sup> than for K<sup>+</sup> or Ba<sup>2+</sup> complexes. P18C6 complexes alkali and alkaline earth cations almost as strongly as 18C6 and, unlike the other ligands studied, complexes Cu<sup>2+</sup> as well.

## Introduction

Pedersen<sup>2</sup> early reported that in general crown ether ligands complex most strongly those metal cations whose ionic radii best match the radius of the cavity formed by the polyether ring. Consequently, crown ethers of varying cavity sizes have been synthesized in hopes of selectively binding metal cations of different radii.<sup>3-5</sup> In addition, donor atoms such as sulfur, aza nitrogen, and pyridyl nitrogen have been used to replace oxygen in crown ether rings in order to vary the cation binding characteristics of these ligands.<sup>3-6</sup> In this work we have attempted to clarify the role of ring size and donor-atom type in cation binding by crown ethers.

We present here a systematic study of the effect of ring size and of donor atom type on the log  $K$ ,  $\Delta H$ , and  $T\Delta S$  of interaction of mono- and divalent cations in methanol with several crown ether ligands; 15-crown-5 (15C5), 18-crown-6 (18C6), 21-crown-7 (21C7), thia-18-crown-6 (T18C6), and pyridino-18-crown-6 (P18C6). The structures of these ligands are given in Figure 1. Values of log  $K$  reported for the reactions reflect the stabilities of cation complexes formed. Differences between log  $K$  for the interaction of two or more cations with a given ligand indicate the selectivity of the ligand among these cations. In addition, values of  $\Delta H$  and  $T\Delta S$  give clues concerning the reaction processes which influence stability and selectivity.<sup>7</sup>

To facilitate the discussion of crown-ring and cation sizes we have sought to obtain accurate values for cation and ligand cavity radii. Cation radii used in this study have been taken from Shannon and Prewitt<sup>8</sup> as determined crystallographically for oxides of coordination number 6. The ligand cavity sizes, defined here as the radius of the circular hole created when the crown ether ring is oriented so that all ring donor atoms lie in a plane, have been determined either crystallographically or from space-filling models. Originally<sup>2</sup> space-filling molecular models were used to find a range of values for the radius of this hole. Since that time, X-ray crystallographic studies have made it possible to accurately determine the positions of ring atoms in the complexed and/or uncomplexed form of the ligand. These interatomic distances may be adjusted by subtracting the van der Waals radii of the donor atoms to give what is probably a much better estimation of the correct ring cavity size.<sup>9</sup> Using this method, Dalley<sup>9</sup> found that, for estimating ring cavity diameters, Corey-Pauling-Koltun space-filling

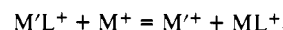
models are the most accurate. Where crystallographic data are not available, these models have been relied upon to estimate ligand cavity sizes in this paper.

## Experimental Section

**Materials.** The ligands 15C5, 18C6, and 21C7 were obtained from Parish Chemical Co. and used without further purification. T18C6 was synthesized in our laboratory<sup>10</sup> and P18C6 was obtained from D. J. Cram.<sup>11</sup> Methanol solutions of the following ligands were standardized by calorimetric titration to an end point against the indicated salt: 18C6, 21C7, and P18C6 against KCl; 15C5 and T18C6 against AgNO<sub>3</sub>. Solutions of Cu(ClO<sub>4</sub>)<sub>2</sub> (G. F. Smith, reagent) were standardized by the same technique against P18C6. All other materials were obtained and used as outlined in the following paper.<sup>12</sup>

**Procedure and Calculations.** The titration calorimetric technique for determining log  $K$ ,  $\Delta H$ , and  $T\Delta S$  has been described.<sup>13</sup> Results are reported as the average and standard deviation from the average of four-six independent experimental determinations. In some cases where reactions of stoichiometry other than 1:1 were detected, the parameters for the multiple reactions were not resolved.

Log  $K$  and  $\Delta H$  values for reactions for which log  $K > 5.5$  were determined by a cation competition technique wherein a solution containing ligand (L) and one cation (M<sup>+</sup>) was titrated with a solution of a second cation (M<sup>+</sup>) having a different complex stability.<sup>14</sup> The  $K$  for the reaction



was combined with  $K$  for the reaction



to give  $K$  for the reaction



## Results and Discussion

In Table I are listed log  $K$ ,  $\Delta H$ , and  $T\Delta S$  values determined for the reaction in methanol at 25 °C of the macrocyclic ligands studied with Ag<sup>+</sup>, Cu<sup>2+</sup>, and several alkali and alkaline-earth metal cations. The reliability of the log  $K$  data in Table I is indicated by the excellent agreement for several systems with log  $K$  data obtained by Frensdorff<sup>3</sup> by an ion selective electrode technique (see Table I, footnote *d*). The ligand-cation systems in Table I illustrate in a systematic fashion the effect on cation binding of macrocycle ring size and donor-atom type. These two ligand structural features will be treated under individual headings.

**Table I.** Log  $K$ ,  $\Delta H$  (kcal/mol), and  $T\Delta S$  (kcal/mol) for Reaction of Mono- and Divalent Cations with Several Macrocyclic Ligands in Methanol at 25 °C

cation		macrocycle				
		15C5	18C6	21C7	T18C6	P18C6
Li <sup>+</sup>		<i>a</i>	<i>a</i>	<i>a</i>	<i>a</i>	<i>a</i>
Na <sup>+</sup>	log $K$	3.48 ± 0.01	4.36 ± 0.02 (4.32 ± 0.4) <sup>d</sup>	1.73 ± 0.11	2.57 ± 0.02	4.09 ± 0.02
	$\Delta H$	-4.99 ± 0.03	-8.4 ± 0.3	-10.37 ± 0.14	-4.99 ± 0.06	-5.44 ± 0.05
	$T\Delta S$	-0.24	-2.4	-8.0	-1.48	0.14
K <sup>+</sup>	log $K$	3.77 ± 0.18 (2.71 ± 0.03) <sup>c</sup>	6.06 ± 0.03 (6.10 ± 0.04) <sup>d</sup>	4.22 ± 0.03 (4.41 ± 0.04) <sup>d</sup>	3.61 ± 0.02	5.35 ± 0.06
	$\Delta H$	-7.7 ± 0.3 (-8.1 ± 0.5) <sup>c</sup>	-13.41 ± 0.06	-8.59 ± 0.02	-9.01 ± 0.16	-9.11 ± 0.11
	$T\Delta S$	-2.57 (-4.4) <sup>c</sup>	-5.14	-2.83	-4.08	-1.81
Rb <sup>+</sup>	log $K$		5.32 ± 0.11	4.86 ± 0.02		4.56 ± 0.02
	$\Delta H$	<i>b</i>	-12.09 ± 0.05	9.66 ± 0.07		-8.7 ± 0.3
	$T\Delta S$		-4.83	-3.03		-2.5
Cs <sup>+</sup>	log $K$	2.18 ± 0.02	4.79 ± 0.05 (4.62) <sup>d</sup> (2.06 ± 0.05)	5.01 ± 0.01 (5.02 ± 0.04) <sup>d</sup>		
	$\Delta H$	-11.7 ± 0.4	-11.29 ± 0.07 (-3.32 ± 0.14)	-11.18 ± 0.01		<i>b</i>
	$T\Delta S$	-8.7	-4.75 (-0.51) <sup>c</sup>	-4.34		
Ag <sup>+</sup>	log $K$	3.62 ± 0.01	4.58 ± 0.03	2.46 ± 0.04	>5.5	>5.5 (2.58 ± 0.08) <sup>c</sup>
	$\Delta H$	-6.58 ± 0.04	-9.15 ± 0.11	-6.9 ± 0.3	-12.3 ± 0.2	-8.33 ± 0.08 (2.58 ± 0.06) <sup>c</sup>
	$T\Delta S$	-1.64	-2.9	-3.5		(0.94) <sup>c</sup>
Mg <sup>2+</sup>		<i>a</i>	<i>a</i>			
Ca <sup>2+</sup>	log $K$	2.18 ± 0.05	3.86 ± 0.02			5.26 <sup>e</sup>
	$\Delta H$	-1.45 ± 0.14	-2.75 ± 0.07	<i>f</i>		-2.90 <sup>e</sup>
	$T\Delta S$	1.52	2.52			4.3
Sr <sup>2+</sup>	log $K$	2.63 ± 0.03	>5.5	1.77 ± 0.06		
	$\Delta H$	-4.69 ± 0.12	-8.61 ± 0.04	-7.10 ± 0.06		
	$T\Delta S$	-1.1		-4.69		
Ba <sup>2+</sup>	log $K$		7.04 ± 0.08	5.44 ± 0.22	3.4 ± 0.1	>5.5
	$\Delta H$	<i>b</i>	-10.41 ± 0.06	-6.81 ± 0.14	-6.1 ± 0.6	-7.72 ± 0.18
	$T\Delta S$		-0.80	0.61	1.45	
Cu <sup>2+</sup>	log $K$					4.63 ± 0.10
	$\Delta H$	<i>a</i>	<i>a</i>			-1.68 ± 0.02
	$T\Delta S$					4.64

<sup>a</sup> No measurable heat other than heat of dilution indicating that  $\Delta H$  and/or log  $K$  are very small. <sup>b</sup> Reaction of stoichiometry other than 1:1 which was not resolved. <sup>c</sup> For reaction  $ML^{2+} + L = ML_2^{2+}$ . <sup>d</sup> Data of Frensdorff.<sup>3</sup> <sup>e</sup> Sufficient ligand available to make only one experimental determination. <sup>f</sup> Heat produced, but insufficient to calculate log  $K$  or  $\Delta H$ .

**Macrocyclic Ring Size.** The three ligands 15C5, 18C6, and 21C7 provide a series of analogous macrocyclic rings of increasing size without the interference of ring substituents which has complicated discussions of ring-size effects in the past.<sup>7</sup> The radii of the cations studied and of the macrocyclic ring cavities as determined by X-ray crystallography or space-filling models are listed in Table II. These data, taken with the stability-constant data presented in Table I, confirm the prevalent theory that correspondence of ligand ring cavity "size" (as defined above) to cation size is an important factor in determining the stabilities of complexes formed among cations small enough to enter the ligand cavity. Specifically, those cations which exactly fit the ligand cavity are bound more strongly than those which are too small. We have noted, however, that, among cations too large to enter the ligand cavity, size correspondence is not predominant in determining cation selectivity, which must therefore be governed by other factors.

The data in Table II for 15C5 predict that the cavity of this

ligand will accommodate only Li<sup>+</sup>, Mg<sup>2+</sup>, and Cu<sup>2+</sup> of the cations listed. These three cations are too small to produce a good fit in the 15C5 cavity. This poor fit combined with the high heats of solvation of these cations probably accounts in part for the lack of any measurable interaction of these cations with 15C5 (Table I). The  $\Delta H$  of complexation must not be sufficient to offset the large heats of solvation of these small cations.

The remaining cations found in Table II, including Na<sup>+</sup>, are too large to enter the cavity of 15C5. This prediction from size considerations agrees with structural data for the Na<sup>+</sup> complex of benzo-15-crown-5 in which the Na<sup>+</sup> ion sits above the plane of ligand oxygen atoms.<sup>15</sup> If the relationship between cation "fit" into the macrocyclic cavity and complex stability is important, the selectivity of 15C5 among the cations too large for the ligand cavity ought to be poor. Figure 2 shows that poor selectivity is indeed observed for 15C5 among monovalent cations. A similar lack of selectivity in water by 15C5 has been noted previously.<sup>16</sup>

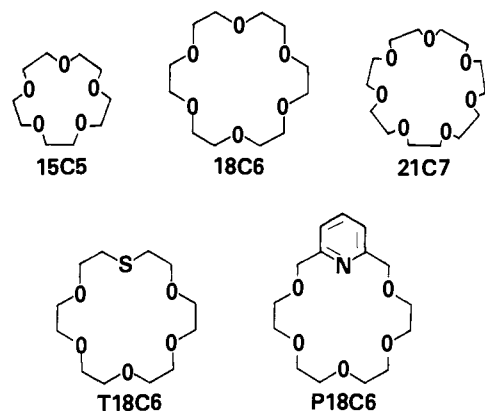


Figure 1. Structures of crown ethers.

Among monovalent cations, the selectivity order of 15C5 in methanol is  $K^+ > Ag^+ > Na^+ > Cs^+$  (Figure 2). (The parameters for  $Rb^+$  were not resolved.) Of these cations, the size of  $Na^+$  most closely corresponds to that of the 15C5 cavity—yet  $K^+$  is bound more strongly. Among divalent cations,  $Sr^{2+}$  is bound more strongly by 15C5 than  $Ca^{2+}$  even though  $Ca^{2+}$  more closely matches the ligand cavity size. Thus, we observe that, among cations too large to enter the 15C5 cavity, selectivity is not governed by the similarity of cation size to ligand cavity size. Other factors must dominate in determining cation selectivity. Some of these factors are cation solvation energies (which in fact, explain the selectivity  $K^+ > Na^+$ ), the formation of complexes of stoichiometry other than 1:1, and the solvation energy of the complex. Since these factors are often difficult to predict, the selectivity of a particular macrocyclic ligand among cations too large to enter its cavity is likewise difficult to predict.

Unlike 15C5, the cavity size of 18C6 is large enough to allow entry of all cations studied except  $Rb^+$  and  $Cs^+$ . The size of  $Rb^+$  is only slightly larger than the upper boundary for the size of the ligand cavity of 18C6. Size considerations for this ligand have been discussed in detail previously.<sup>2-5</sup> The sizes of  $K^+$  and  $Ba^{2+}$  match that of the ligand cavity very closely (Table II) and the selectivity of 18C6 for these two cations over others in their respective groups in the periodic table is well established.<sup>3-5</sup> Selectivity for  $K^+$  is illustrated in Figure 2. Table I shows that the selectivity of 18C6 for  $K^+$  over other alkali-metal cations and for  $Ba^{2+}$  over other alkaline-earth cations is almost entirely enthalpic in origin, probably corresponding to the close approach of the cation to the ring donor atoms without the need to strain any ring bonds.

The data in Table II indicate that the cavity radius of 21C7 corresponds exactly to the radius of  $Cs^+$ , the largest cation studied. The ligand 21C7 therefore presents a case quite different from that of 15C5 in that all cations studied may enter the ligand cavity. As expected on the basis of size considerations, 21C7 is selective for  $Cs^+$  among monovalent cations (Figure 2) and  $Ba^{2+}$  among divalent cations. The large selectivity of 21C7 for  $K^+$  over  $Na^+$  is noteworthy, rivaling that of cryptand [2.2.2].<sup>17</sup> In addition, the selectivity of 21C7 for  $Na^+$  over  $Ca^{2+}$  (which have nearly identical ionic radii; see Table II) is unusual and is opposite to that shown for valinomycin.<sup>5</sup> Selectivity of this ligand for  $Ba^{2+}$  over  $Sr^{2+}$  (ratio of stability constants = 5000) is also unusually large, with  $Ba^{2+} > Ca^{2+}$  selectivity being even larger. The  $K^+ > Na^+$  and  $Ba^{2+} > Sr^{2+}$  selectivities are largely due to differences in the  $T\Delta S$  terms, pointing possibly to differences in complex structure. Since the cavity of 21C7 is larger than any of these cations and since the ligand is quite flexible, variation in ligand conformation induced by the strongly polarizing cations  $Na^+$  and  $Ca^{2+}$  is easily visualized. X-ray crystallographic studies are planned to throw further light on this phenomenon.

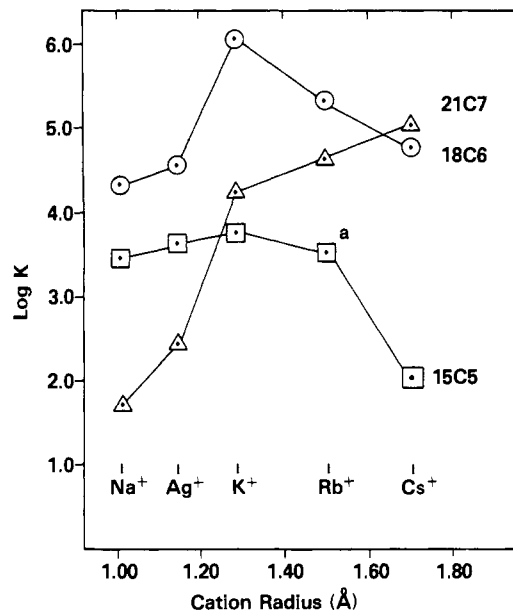


Figure 2. Log  $K$  for interaction of 15C5, 18C6, and 21C7 with monovalent cations in methanol at 25 °C vs. cation radius. (a) Log  $K$  value for 1:1 reaction estimated from data valid in water by addition of 3.0.<sup>4,5</sup>

Table II

cation	radius	cation	radius
Cation Radii, <sup>8</sup> Å			
$Mg^{2+}$	0.72	$Ag^+$	1.15
$Cu^{2+}$	0.73	$Sr^{2+}$	1.16
$Li^+$	0.74	$Ba^{2+}$	1.36
$Ca^{2+}$	1.00	$K^+$	1.38
$Na^+$	1.02	$Rb^+$	1.49
		$Cs^+$	1.70
Macrocyclic Ring Cavity Radii, <sup>9</sup> Å			
15C5 (0.86–0.92) <sup>a</sup>	18C6 (1.34–1.43) <sup>a</sup>	21C7	1.7 <sup>b</sup>

<sup>a</sup> From X-ray crystallographic data. <sup>b</sup> From Corey–Pauling–Koltun models.

In proceeding through the series 15C5, 18C6, 21C7 the cavity sizes of the ligands increase from being smaller than the size of  $Na^+$  in the case of 15C5 to being as large as the largest cation studied,  $Cs^+$ , in the case of 21C7. Differences in cavity size from one ligand to the next are larger than differences in cation sizes from one cation to the next largest. Thus no simple crown ethers exist to selectively bind (on the basis of size alone) the monovalent cations of intermediate size,  $Na^+$ ,  $Ag^+$ , and  $Rb^+$ . By contrast, among cryptand ligands the differences in cavity size from one ligand to the next larger ligand are smaller. Thus among cryptands there exists a ligand which is able to selectively bind each of the alkali-metal ions over the others.<sup>17</sup> Simple crown ethers larger than 21C7 form cavities which are not only large enough to accommodate all cations listed in Table II but too large to allow exact fit of any in a ring-type cavity. Molecular models and X-ray structures<sup>9</sup> show that such large crown ethers are quite flexible so that ligands such as 30-crown-10 can wrap around cations. In this light, however, the selectivity of the ligand will not be due to the “fit” of the cation in the ligand cavity, since the effective “size” of the ligand cavity can vary over a wide range.

From the results with the above-mentioned macrocycles and cations, it can be concluded that (1) the cation selectivity of a macrocyclic ligand is affected by the “fit” of cations in the ligand cavity only among cations which can enter the ligand cavity and (2) the fit of the cations in the ligand cavity cannot be cited to explain the selectivities of larger crown ethers

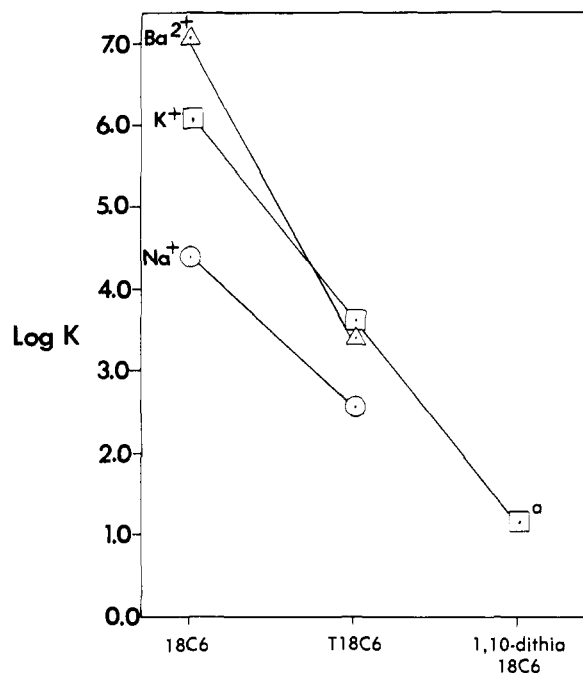


Figure 3. Log  $K$  for interaction in methanol at 25 °C of  $\text{Na}^+$ ,  $\text{K}^+$ , and  $\text{Ba}^{2+}$  with three 18-crown-6 type ligands of varying sulfur content. (a) Data from Frensdorff.<sup>3</sup>

(24-crown-8 and larger) because their cavities are all larger than the largest cation,  $\text{Cs}^+$ . Conclusion (1) precludes using size to explain the selectivities of 15C5 and smaller crowns except among cations smaller than  $\text{Na}^+$ . Indeed size relationships explain very well the selectivities of a very limited number of crown ether macrocycles (e.g., 18C6 and 21C7). Alternate considerations must be used to explain the selectivities of other crown ether ligands as has been pointed out by Poonia.<sup>18</sup>

**Ring Donor Atom Type. Sulfur Substitutions.** Frensdorff<sup>3</sup> first noted a marked decrease in  $\text{K}^+$  complex stability in methanol when two sulfur atoms are substituted for ether oxygens in the 1 and 10 positions of 18C6. Indeed, a resulting drop of four orders of magnitude in the stability constant was observed. Izatt et al.<sup>19</sup> similarly noted no affinity by sulfur-containing derivatives of crown ethers for alkali or alkaline-earth cations in water. In this work, we have studied the effect on cation binding of substitution of one sulfur for oxygen in 18C6 to give T18C6.

Table I lists thermodynamic quantities for the interaction in methanol of T18C6 with several cations. As expected, the stabilities of complexes of  $\text{Na}^+$ ,  $\text{K}^+$ , and  $\text{Ba}^{2+}$  with T18C6 are considerably lower than those with 18C6. The drops in stability upon substitution of sulfur for oxygen in 18C6 are 1.79, 2.45, and 3.63 orders of magnitude for  $\text{Na}^+$ ,  $\text{K}^+$ , and  $\text{Ba}^{2+}$ , respectively. This observation, illustrated in Figure 3, can be explained according to the reasoning of Pannell et al.<sup>20</sup> in terms of the sizes of these three cations. Because the  $\text{Na}^+$  ion is smaller than the cavity of 18C6, it can move in the cavity in such a way as to associate with only a part of the total set of donor atoms in the ligand. Indeed, the crystal structure of the  $\text{Na}^+$  complex of 18C6 shows  $\text{Na}^+$  coordinated equally to five roughly planar oxygen atoms and more weakly to the sixth oxygen which is raised up out of this plane.<sup>9</sup> Introduction of one sulfur atom leaves five oxygens with which  $\text{Na}^+$  may still interact as with 18C6. The  $\text{K}^+$  and  $\text{Ba}^{2+}$  ions, on the other hand, fill the cavity of 18C6 and interact equally with all donors. Introduction of sulfur is thus expected to have a greater effect on the stabilities of the complexes of  $\text{K}^+$  and  $\text{Ba}^{2+}$  than on that of  $\text{Na}^+$ . This is indeed the case, resulting in a change

in ligand selectivity. Whereas the selectivity sequence of 18C6 is  $\text{Ba}^{2+} > \text{K}^+ > \text{Na}^+$ , that of T18C6 is  $\text{K}^+ > \text{Ba}^{2+} > \text{Na}^+$ .

Using the data of Frensdorff<sup>3</sup> for the reaction of 1,10-dithia-18-crown-6 with  $\text{K}^+$ , Figure 3 illustrates that the drop in complex stability (measured as log  $K$ ) upon replacement of two oxygen atoms by sulfur atoms in the 1 and 10 positions of 18C6 is exactly twice that resulting from replacement of one oxygen atom by sulfur. If this trend is true also for  $\text{Ba}^{2+}$  and  $\text{Na}^+$ , the plot in Figure 3 predicts that the selectivity sequence for 1,10-dithia-18-crown-6 should be  $\text{K}^+ > \text{Na}^+ > \text{Ba}^{2+}$  and that the  $\text{Ba}^{2+}$  complex should be extremely weak.

The data in Table I illustrate that the drop in stability for the  $\text{Na}^+$ ,  $\text{K}^+$ , and  $\text{Ba}^{2+}$  complexes between 18C6 and T18C6 is largely due to less favorable  $\Delta H$  values in the complexes of the latter. For the cations of similar size,  $\text{K}^+$  and  $\text{Ba}^{2+}$ , this change in  $\Delta H$  between complexes of the two ligands is almost identical, 4.40 and 4.31 kcal/mol, respectively. At least two factors play an important part in causing this loss of stability. The first is the larger size of sulfur compared to oxygen, which results in a decrease in ligand cavity size and in an alteration in ring conformational energies. The second is the intrinsic lower affinity of alkali and alkaline-earth cations for sulfur than for oxygen.

Introduction of sulfur into a macrocyclic ligand results in increased affinity for  $\text{Ag}^+$  as seen from the log  $K$  data in Table I. An extensive study of this effect has been reported.<sup>19</sup>

**Pyridine Substitution.** Replacement of one ether oxygen in 18C6 by a pyridine moiety having its nitrogen atom pointing into the ring to give P18C6 results in some loss of complex stability, but little change in ligand selectivity with the cations studied.<sup>21</sup> Less favorable  $\Delta H$  and more favorable  $T\Delta S$  terms for the pyridino ligand reactions indicate that differences do exist between its reactions and those of 18C6. Differences between the two ligands are also manifest in the reversal of  $\text{Na}^+/\text{Ca}^{2+}$  selectivity illustrated in Table I, in the occurrence of a 2:1 ligand to metal reaction of the pyridino ligand with  $\text{Ag}^+$ , and in the reaction of the pyridino ligand with  $\text{Cu}^{2+}$ . This ligand is unusual in having nearly equal affinity for  $\text{Cu}^{2+}$  and the alkali-metal cations  $\text{Na}^+$  and  $\text{K}^+$ .

Reaction between macrocycles having nitrogen and sulfur donor atoms and transition-metal cations such as  $\text{Cu}^{2+}$  have been reported previously.<sup>4,5,22</sup> However, this work reports the first observation of reaction in solution between  $\text{Cu}^{2+}$  and P18C6, a macrocycle very similar in structure to 18C6. The thermodynamic reaction parameters for the  $\text{Cu}^{2+}$  interaction are curious in that  $\Delta H$  is small and the complex is highly entropy stabilized. The possibility exists that the pyridine nitrogen is turning out of the crown ring to interact with  $\text{Cu}^{2+}$  and that the cation is not sequestered in the ligand cavity at all. However, three experimental observations are not consistent with this possibility. First, the data show no indication of ligand-metal interaction of stoichiometry other than 1:1 which might be expected if such were the case. Second, the diketo analogue of this pyridyl ligand having the pyridine nitrogen of necessity turned out of the ring, 2,6-diketopyridino-18-crown-5, gives no heat of reaction with  $\text{Cu}^{2+}$ .<sup>12</sup> Third, log  $K$  for the 1:1 reaction between  $\text{Cu}^{2+}$  and pyridine in methanol is reported<sup>23</sup> to be 2.92, which is significantly lower than that found for P18C6. The  $\text{Cu}^{2+}$  cation is considerably smaller than the cavity of P18C6 and it is therefore expected that the cation in the complex is positioned so as to associate to a greater degree with the pyridine nitrogen. Infrared and/or X-ray spectroscopic studies are desirable to determine the nature of the interaction between  $\text{Cu}^{2+}$  and P18C6.

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## References and Notes

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## Cation Complexes of Crown Ether Diesters. Stabilities, Selectivities, Enthalpies, and Entropies of Reaction at 25 °C in Methanol<sup>1</sup>

J. D. Lamb, R. M. Izatt,\* C. S. Swain, J. S. Bradshaw, and J. J. Christensen

*Contribution from the Departments of Chemistry and Chemical Engineering  
and Contribution No. 167 from the Thermochemical Institute, Brigham Young University,  
Provo, Utah 84602. Received August 8, 1979*

**Abstract:** Log  $K$ ,  $\Delta H$ , and  $T\Delta S$  for the reaction of alkali and alkaline-earth cations,  $\text{Ag}^+$ , and  $\text{NH}_4^+$  with several macrocyclic ligands of the crown ether diester type are reported and compared to corresponding values for parent crown ether ligands. The effect of inclusion of the ester carbonyl oxygens in the macrocyclic ring is to reduce the stability constant of complexes of monovalent cations by  $10^2$ - $10^4$  and of divalent cations by  $10^3$ - $10^4$ . This reduction is due to loss of enthalpic stabilization. Complex stability is restored if a pyridine moiety is included in the macrocyclic ring between the carbonyl oxygens. Selectivity of crown ether diesters among cations is lower than that of crown ethers. One class of crown ether diesters derived from malonic, succinic, and glutaric acids shows the unusual  $\text{K}^+ > \text{Ba}^{2+}$  selectivity of valinomycin.

### Introduction

Macrocyclic ligands have demonstrated potential for use in many industrial and chemical processes where cation selectivity and/or solubility in nonpolar solvents are required.<sup>2</sup> For this reason, the synthesis of simple, inexpensive macrocycles with various cation selectivities is desirable. In recent years, considerable effort has been devoted<sup>3</sup> to the design of new synthetic macrocyclic ligands whose cation complex stability and cation selectivity hopefully would match if not surpass those of the naturally occurring antibiotic macrocycles such as valinomycin. In our own laboratories, we have synthesized a large number of low-cost macrocyclic analogues of crown ethers based on the inclusion of ester linkages in the cyclic molecule.<sup>4</sup> Several of these ligands, which we have named crown ether diesters, appear in Figure 1 (1-14). In this paper are reported log  $K$ ,  $\Delta H$ , and  $T\Delta S$  values in methanol for several reactions between 1-14 and the alkali cations, alkaline earth cations,  $\text{Ag}^+$ , and  $\text{NH}_4^+$ . These results combined with comparable data for unsubstituted crown ethers serve to elucidate the effect of ligand carbonyl groups on the complex stability and cation selectivity of cyclic polyethers. The effects

on complex stability of ring size and donor-atom type have been treated in the preceding paper.<sup>5</sup>

### Experimental Section

**Materials.** Crown ether diesters were synthesized and purified as described earlier.<sup>6</sup> Crystalline ligands were dried under vacuum for several hours before weighing. Reagent grade chemicals were obtained from the indicated sources and used without further purification:  $\text{NaCl}$ ,  $\text{KCl}$ ,  $\text{RbCl}$ ,  $\text{Mg}(\text{NO}_3)_2$ ,  $\text{Sr}(\text{NO}_3)_2$ ,  $\text{NH}_4\text{I}$  (Baker);  $\text{Ba}(\text{ClO}_4)_2$ ,  $\text{Ca}(\text{NO}_3)_2$ ,  $\text{CsCl}$ ,  $\text{CH}_3\text{OH}$  (Fisher);  $\text{LiCl}$  (Baker and Adamson);  $\text{AgNO}_3$  (Matheson Coleman and Bell);  $\text{Cu}(\text{ClO}_4)_2$  (G. F. Smith).

The concentrations of methanol solutions of  $\text{NaCl}$  and  $\text{KCl}$  were given directly from the weight of salt which had been dried overnight at 120 °C and desiccated over  $\text{P}_2\text{O}_5$ . The concentrations of solutions of the following salts were obtained by thermometric titration to an end point against the macrocycle given in parentheses, solutions of which had in turn been standardized by the same method against  $\text{KCl}$ :  $\text{RbCl}$ ,  $\text{Ca}(\text{NO}_3)_2$ ,  $\text{Sr}(\text{NO}_3)_2$ ,  $\text{Ba}(\text{ClO}_4)_2$ ,  $\text{AgNO}_3$ ,  $\text{NH}_4\text{I}$  (18-crown-6);  $\text{Cu}(\text{ClO}_4)_2$  (6);  $\text{CsCl}$  (21-crown-7). Solutions of  $\text{LiCl}$  and  $\text{Mg}(\text{NO}_3)_2$  were not standardized since no numerical results were calculated. Ligand 6 was standardized in methanol by thermometric titration to an end point against  $\text{KCl}$ . The methanol was found by Karl Fischer titration to contain less than 0.05% water.