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Cation Complexes of Crown Ether Diesters. Stabilities, Selectivities, Enthalpies, and Entropies of Reaction at 25 °C in Methanol[1]

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Abstract: Log K, ΔH, and $T\Delta S$ for the reaction of alkali and alkaline-earth cations, Ag^+, and 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 $K^+ > Ba^{2+}$ 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.[2] For this reason, the synthesis of simple, inexpensive macrocycles with various cation selectivities is desirable. In recent years, considerable effort has been devoted[3] 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.[4] Several of these ligands, which we have named crown ether diesters, appear in Figure 1 (**1–14**). In this paper are reported log K, ΔH, and $T\Delta S$ values in methanol for several reactions between **1–14** and the alkali cations, alkaline earth cations, Ag^+, and 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.[5]

Experimental Section

Materials. Crown ether diesters were synthesized and purified as described earlier.[6] 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: NaCl, KCl, RbCl, $Mg(NO_3)_2$, $Sr(NO_3)_2$, NH_4I (Baker); $Ba(ClO_4)_2$, $Ca(NO_3)_2$, CsCl, CH_3OH (Fisher); LiCl (Baker and Adamson); $AgNO_3$ (Matheson Coleman and Bell); $Cu(ClO_4)_2$ (G. F. Smith).

The concentrations of methanol solutions of NaCl and KCl were given directly from the weight of salt which had been dried overnight at 120 °C and desiccated over P_2O_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 KCl: RbCl, $Ca(NO_3)_2$, $Sr(NO_3)_2$, $Ba(ClO_4)_2$, $AgNO_3$, NH_4I (18-crown-6); $Cu(ClO_4)_2$ (**6**); CsCl (21-crown-7). Solutions of LiCl and $Mg(NO_3)_2$ were not standardized since no numerical results were calculated. Ligand **6** was standardized in methanol by thermometric titration to an end point against KCl. The methanol was found by Karl Fischer titration to contain less than 0.05% water.

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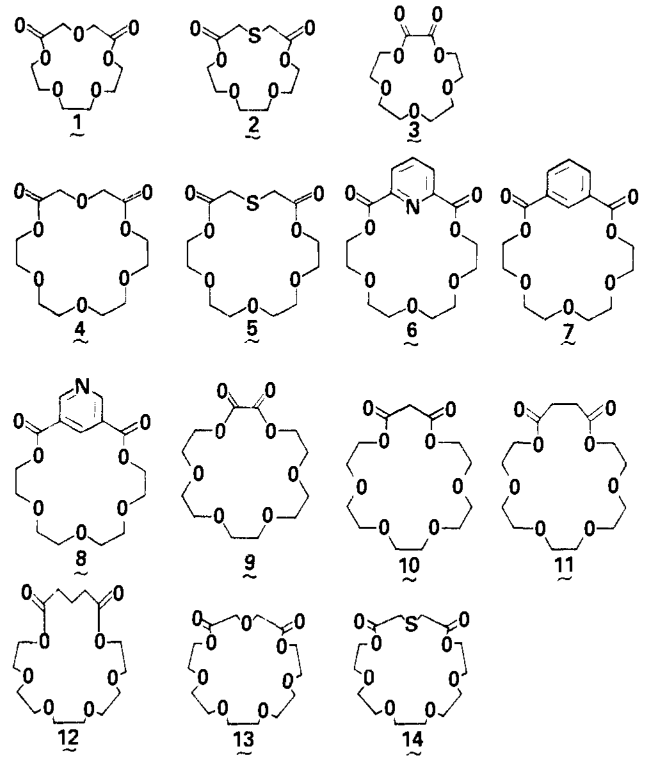

Figure 1. Structures of various macrocyclic ligands.

Procedure and Calculations. Log K, ΔH, and $T\Delta S$ values for the reaction of the macrocycles with cations were determined by the titration calorimetric procedure outlined previously.[5] Results are reported as the average and standard deviation from the average of four–six independent experimental determinations. For reactions involving Cs^+ and also those involving the ligands **1–5** and **7–14** for which direct standardization of solutions was not feasible, a data processing program, EQDHAD, allowed variation of the concentrations of these species to give the best fit of the experimental data.

Results and Discussion

Preliminary thermometric titration experiments showed little or no heat of reaction between alkali or alkaline-earth cations and a large number of crown ether diester ligands in water. However, as had been observed earlier for similar systems,[7,8] reaction in methanol produced sufficient heat to allow calculation of log K and ΔH values. Therefore this solvent was chosen for the study and the results are listed in Table I.

Comparisons between data reported in Table I for crown ether diester reactions and those reported elsewhere for reactions of unsubstituted crown ethers[5] illustrate the effect on complexation of introducing carbonyl oxygens into the crown ether ring. Addition of carbonyl oxygens to the 2 and 6 position carbon atoms of 15-crown-5, 18-crown-6, and 21-crown-7 to give **1**, **4**, and **13**, respectively, results in a significant decrease in complex stability among cations studied. For the diester ligands based on the 18-crown-6 and 21-crown-7 structures, the stability constant is lowered between two and three orders of magnitude for monovalent cation complexes (see Figure 2) and between three and four orders of magnitude for complexes of Ba^{2+}, the only divalent cation for which numerical results were obtained. Similarly, the stability constants of 15-crown-5 complexes are lowered with the introduction of ester groups. Since these constants are low (of the order 10^2–10^4) for the parent ligand, 15-crown-5, they drop below the measurable limit for the diester ligands **1** and **3**. In the following paragraphs we will explore three possible causes of this large stability loss.

The data in Table I indicate that the ΔH contribution to ΔG is responsible for the difference in stabilities between **4** and 18-crown-6.[5] Indeed, the entropy term is more favorable for the reactions of **4** than of 18-crown-6 with every cation studied. A similar trend in ΔH and $T\Delta S$ has been noted[7,8] when comparing 18-crown-6 to its cyclohexano- or benzo-substituted analogues dicyclohexano- or dibenzo-18-crown-6. In the latter two ligands, the bulky substituent groups inhibit the close approach of solvent molecules to the complexed cation, resulting in some loss of complex stability. The presence of the carbonyl groups in **4** may be destabilizing for similar reasons. This first possible explanation is consistent with the ΔH and $T\Delta S$ changes produced.

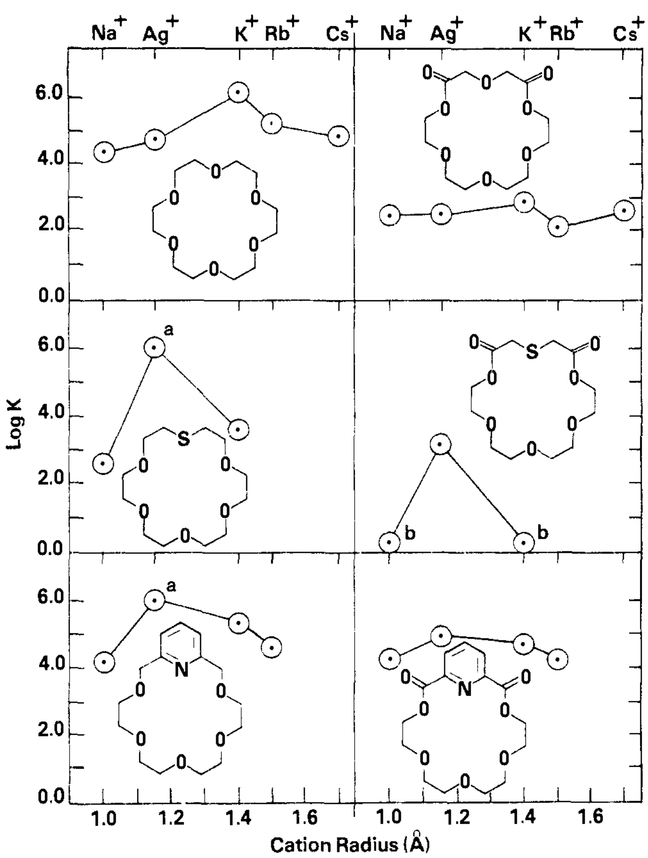

Figure 2. Log K for reaction of monovalent cations with 18-crown-6, thia-18-crown-6, and pyridino-18-crown-6 (left) and their crown ether diester analogues (right) vs. cation radius.[5] (a) Reported >5.5. (b) See Table I, footnote *a*.

The second possible reason for the low stability of complexes of crown ether diesters involves ligand conformation. Dalley has determined the crystal structures of **4**[9a] and of its K^+ complex.[9b] His results show that, in the uncomplexed form, the ligand is nearly planar with one carbonyl oxygen lying out of the ligand plane and the ring open to receive the cation. Both carbonyl groups are found in the plane of the ligand pointing away from the ring in the K^+ complex form. The energy required for this conformational change is expected to be more destabilizing in the case of **4** than for 18-crown-6 (which also undergoes a small conformational change upon complexation[8]). The energy involved in this conformational change may contribute to the low stability of the complexes of **4**.

A third possibility to explain our results involves electronic effects on ring donor atoms. Dalley's crystal structure of the K^+ complex of **4**, having the cation sequestered within the ligand cavity and the carbonyl oxygens pointing away from the cation, shows that the carbonyl oxygens of **4** do not participate in complexation. Nevertheless these oxygens are expected to withdraw electron density away from ester oxygens at the 1 and 7 positions in the ring. A similar inductive effect has been noted previously when benzo crowns were substituted with

Table I. Log *K*, ΔH (kcal/mol), and $T\Delta S$ (kcal/mol) Values for Reactions of Several Crown Ether Diesters with Several Mono- and Divalent Cations in Methanol at 25 °C

macrocycle		Monovalent Cations Li$^+$	Na$^+$	K$^+$	Rb$^+$	Cs$^+$	Ag$^+$	NH$_4^+$
1, 2, 3, 7		*a*	*a*	*a*	*a*	*a*	*a*	*a*
4	log *K*		2.5 ± 0.1	2.79 ± 0.02	2.09 ± 0.04	2.55 ± 0.05	2.50 ± 0.07	
	ΔH	*a*	−2.27 ± 0.18	−5.87 ± 0.01	−6.99 ± 0.26	−1.52 ± 0.10	−1.53 ± 0.12	*a*
	$T\Delta S$		1.1	−2.06	−4.1	2.0	1.88	
5	log *K*						3.05 ± 0.05	
	ΔH		*a*	*a*			−6.97 ± 0.08	
	$T\Delta S$						−2.81	
6	log *K*		4.29 ± 0.06	4.66 ± 0.02	4.24 ± 0.02		4.88 ± 0.05	2.93 ± 0.04
	ΔH	*a*	−6.19 ± 0.08	−9.3 ± 0.2	−9.07 ± 0.29	*b*	−7.83 ± 0.03	−7.75 ± 0.13
	$T\Delta S$		−0.34	−3.0	−3.3		−1.17	~3.8
8		*a*	*a*	*a*				
10	log *K*		1.8 ± 0.2	2.55 ± 0.03				
	ΔH		−1.1 ± 0.2	−7.91 ± 0.06				
	$T\Delta S$		1.4	−4.43				
11	log *K*		1.7 ± 0.1	1.94 ± 0.08	1.74 ± 0.01			
	ΔH	*a*	−1.0 ± 0.4	−5.6 ± 0.3	−7.0 ± 0.3		*a*	*a*
	$T\Delta S$		1.3	−3.0	−4.6			
12	log *K*			1.71 ± 0.05	1.63 ± 0.3	1.02[d]		
	ΔH	*a*	*a*	−4.9 ± 0.2	−6.6 ± 0.3	−11.5[d]	*a*	*a*
	$T\Delta S$			−2.6	−4.4	−10.1		
13	log *K*			2.32[d]	2.27[d]			
	ΔH	*a*	*c*	−6.46[d]	−9.86[d]			
	$T\Delta S$			−3.29	−6.76			
14	log *K*			2.09[d]	2.52[d]	1.91[d]		
	ΔH		*c*	−3.84[d]	−5.49[d]	−3.03[d]		*a*
	$T\Delta S$			−0.99	−2.05	−0.42		

macrocycle		Divalent Cations Mg^{2+}	Ca^{2+}	Sr^{2+}	Ba^{2+}	Cu^{2+}
1, 2, 3, 5, 7, 8, 11, 14		*e*	*e*	*e*	*e*	*e*
4	log *K*				3.1 ± 0.2	
	ΔH	*a*			−0.4 ± 0.1	*a*
	$T\Delta S$				3.9	
6	log *K*				4.34 ± 0.02	
	ΔH				−6.03 ± 0.03	*a*
	$T\Delta S$				−0.11	
10	log *K*				1.41 ± 0.11	
	ΔH	*a*	*a*		−4.88 ± 0.13	
	$T\Delta S$				−3.0	
12		*a*	*a*	*a*	*c*	*a*
13	log *K*				1.73[d]	
	ΔH	*a*	*a*	*c*	−8.34[d]	
	$T\Delta S$				5.98	

[a] No measurable heat other than heat of dilution indicating that ΔH and/or log *K* are very small. [b] Reaction of stoichiometry other than 1:1 which was not resolved. [c] Heat produced but insufficient to calculate ΔH and log *K*. [d] Sufficient ligand available to make only one experimental determination. [e] Among these ligands, footnote *a* applies to the following reactions: Mg^{2+} with **1, 2, 3, 7, 11**, and **14**; Ca^{2+} with **3** and **11**; Sr^{2+} with **1, 11, 12**, and **14**; Ba^{2+} and Cu^{2+} with all. Determinations involving other combinations were not made.

electron-withdrawing or -donating groups. The presence of such substituents on benzo-15-crown-5 or dibenzo-18-crown-6 altered the binding constant with alkali-metal cations due to the inductive effect on ether oxygens adjacent to the benzene rings.[10] If such an effect operates among the crown ether diesters, it would explain why the difference between the log *K* values for the complexes of Na$^+$ with **4** and with 18-crown-6 is less than that between the complex stabilities of K$^+$ with **4** and with 18-crown-6. Since the K$^+$ ion fills the ligand cavity,[5] it must feel the full effect of any decrease of electron density on the oxygen atoms at positions 1 and 7. On the other hand, Na$^+$ ion is smaller than the ring cavity and may shift its position in that cavity so as to offset such a change in electron density.

The complexes of ligand **6** shed some light on the reasons for the low stabilities of crown ether diester complexes. In contrast to **4**, the complexes of **6** are only slightly less stable than those of its nonester analogue, pyridino-18-crown-6[5] (see Figure 2). The higher stabilities of complexes of **6** over those of **4** are surprising in that classical chemistry predicts that nitrogen should have a lower affinity than oxygen for alkali and alkaline-earth cations (as borne out when comparing the more stable complexes of 18-crown-6 to the less stable complexes of pyridino-18-crown-6[5]). The source of the superior stabilities of complexes of **6** possibly lies in the reversal of the electron-withdrawing effect described above due to the presence of the pyridine aromatic ring. Alternatively, the aromatic ring may hold the carbonyl oxygens in the ligand plane, alleviating the necessity of turning them into the plane when the complex is formed, as described for **4**. These arguments suggest that the lower stabilities of metal complexes of crown ether diesters compared to those of crown ethers result from one or both of two factors: electron delocalization away from the macrocyclic ring oxygen atoms and conformational energies.

As noted above, a smaller difference is observed between the stabilities of the Na$^+$ complexes of **4** and of 18-crown-6 than for the corresponding K$^+$ complexes. Thus, **4** is much less selective for K$^+$ over Na$^+$ than is 18-crown-6. Indeed, the data in Table I indicate that crown ether diesters are less selective in general than corresponding crown ethers. The selectivities among monovalent cations of crown ethers are compared to those of corresponding crown ether diesters in Figure 2. Even **6**, which forms complexes of relatively high stabilities, does not exhibit selectivity as high as that of pyridino-18-crown-6.

Ligands **7** and **8** were studied to determine the effect of the presence of the aromatic ring on cation complexation and to examine the effect of removal of one donor atom from the crown-6 structure. No heat of reaction was found for **7** or **8** with any cation studied. This result shows that presence of the aromatic ring does not in itself promote complexation, since measurable heats of formation are found for complexes with the analogous pentaglyme under these conditions.[8] In addition, it is shown that the presence of all six donor atoms in ligands such as **4** and **6** is essential to complexation.

Despite relatively low complex stability constants, ligands **10–12** have interesting cation selectivity properties as outlined in a previous communication.[11] In contrast to 18-crown-6, **4**, and many other simple crown ethers,[8] these ligands complex K^+ more strongly than Ba^{2+} in methanol. In this respect, their behavior is similar to that of valinomycin in which ester carbonyl oxygens serve as donor atoms. In the case of valinomycin, and of hydrophobic synthetic ligands such as dibenzo-18-crown-6,[8] effective isolation of the cation charge from the solvent may explain the $K^+ > Ba^{2+}$ selectivity sequence since the cation solvation energy which is partly lost in the complexation process is higher for the divalent cation. The origin of this selectivity sequence (Table I) among ligands **10–12** is not understood. Among Ba^{2+} complexes with these ligands, entropy and enthalpy data are available for **10** only, making it difficult to find reproducible trends.

No complexation data are reported for **9** because reaction curves with all cations indicated cation-catalyzed decomposition of the ligand (production of heat continued after the end of the titration). This hypothesis was confirmed by NMR studies which showed the ligand decomposition rate to be a function of the cation present. This ligand is known to decompose upon sitting, even in pure form.

As detailed in the previous paper,[5] replacement of an oxygen atom of a crown ether by sulfur destabilizes the complexes of alkali and alkaline-earth cations. This destabilization coupled with that resulting from the presence of carbonyl groups results in a total lack of affinity of alkali and alkaline-earth cations for either **2** or **5**. It is somewhat surprising that ligand **14** shows measurable affinity for K^+, Rb^+, and Cs^+, but not for the alkaline-earth cations. It is expected that association of this ligand with these cations involves only the six ether oxygen donors.

The affinity of **5** for Ag^+ is lower than that of the corresponding nonester ligand, thia-18-crown-6, in keeping with the general lowering of cation affinity among crown ether diesters below that of crown ethers. Selectivity of **5** for Ag^+ over Na^+ and K^+ is similar to that of thia-18-crown-6, as shown in Figure 2. To a smaller degree than the sulfur-containing ligands, those containing the pyridino nitrogen donor atom are also selective for Ag^+ over the alkali metal cations (Figure 2).

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