(8) A solution of 1 (921 mg, 3 mmol) and *p*-toluic anhydride (2.54 g, 10 mmol) in *p*-dioxane (50 mL) was refluxed for 24 h, and the reaction mixture was treated as described in (5), (6), and (7). From a silica gel column (4:1 C_6H_6–EtOAc) 6 was eluted first; yield 40 mg (2%).

7,8-Dihydro-*N*^{6},7-di-*p*-toluyl-2′,3′-*O*-isopropylidene-8-5′-*O*-cycloadenosine (20) was eluted with 1:1 benzene–EtOAc: yield 320 mg (20%); mp 229–30 °C (C_6H_6); for ^{1}H NMR and ^{13}C NMR data, see Tables II and III.

Anal. Calcd for $C_{29}H_{29}O_6N_5$: C, 64.08; H, 5.38; N, 12.89. Found: C, 64.35; H, 5.37; N, 12.75.

***N*^{6},5′-*O*-Di-*p*-toluyl-2′,3′-*O*-ispropylideneadenosine (18)** was eluted from a silica gel column with EtOAc: yield 430 mg (26%); glassy solid from toluene–ligroin; ^{1}H NMR δ 2.35 and 2.41 (2 s, 6 H, two toluyl methyls), 6.10 (d, 1 H, H-1′, $J_{1',2'}$ = 2 Hz), 8.13 (s, 1 H, H-8), 8.75 (s, 1 H, H-2); for ^{13}C NMR, see Table III.

Anal. Calcd for $C_{29}H_{29}O_6N_5$: C, 64.08; H, 5.38; N, 12.89. Found: C, 64.13; H, 5.46; N, 12.67.

2′,3′-*O*-Isopropylidene-5′-*O*-*p*-toluyladenosine (19) was eluted from a silica gel column with 9:1 EtOAc–MeOH: yield 470 mg (37%); mp 165–6 °C (BuOAc); ^{1}H NMR δ 2.44 (s, 3 H, toluyl), 6.00 (d, 1 H, H-1′, $J_{1',2'}$ = 3 Hz), 8.16 (s, 1 H, H-8), 8.72 (s, 1 H, H-2).

Anal. Calcd for $C_{21}H_{23}O_5N_5$: C, 59.28; H, 5.45; N, 16.46. Found: C, 58.98; N, 5.43; N, 16.23.

Reaction of 2′,3′-*O*-Isopropylideneadenosine with *p*-Toluyl Chloride in CH_2Cl_2–Et_3N. (9) To an ice-cooled and stirred solution of 1 (1.54 g, 5 mmol) in a mixture of CH_2Cl_2 (75 mL) and Et_3N (12 mL) was added *p*-toluyl chloride (5 g, 32 mmol) dropwise, and the solution was left at room temperature overnight with stirring. The reaction mixture, after washing with aqueous $NaHCO_3$ to quench the reagent, was applied to a silica gel chromatography column. The least polar product, 7, was eluted with 4:1 C_6H_6–EtOAc (yield 1.11 g, 34%), and 6 (yield 1.0 g, 30%) was eluted with 4:1 to 2:1 C_6H_6–EtOAc. Further chromatography was needed to separate 7 and 6 completely.

4-Cyano-1-(2,3-*O*-isopropylidene-5-*O*-*p*-toluyl-β-D-ribofuranosyl)-5-(*p*-toluylamino)imidazole (21) was eluted from a silica gel column with 1:1 C_6H_6–EtOAc: yield 300 mg (12%); mp 95–7 °C (toluene); ^{1}H NMR δ 2.39 and 2.43 (2 s, 6 H, two toluyl), 5.86 (d, 1 H, H-1′, $J_{1',2'}$ = 3 Hz), 7.64 (s, 1 H, H-2), 8.84 (s, 1 H, NH, collapsed on addition of D_2O); for ^{13}C NMR data, see Table III.

Anal. Calcd for $C_{28}H_{28}O_6N_4$: C, 65.10; H, 5.46; N, 10.85. Found: C, 65.13; H, 5.50; N, 10.77.

Compound **20** was eluted from a silica gel column with 1:1 C_6H_6–EtOAc contaminated by **21**, and complete separation of **20** from **21** was unsuccessful even after additional chromatography. However, **21** was hardly soluble in toluene and, after crystallization of **21** from toluene, the filtrate was condensed and the residue was triturated in benzene to obtain crystals of **20**; yield 300 mg (11%).

Registry No. 1, 362-75-4; 2, 93135-57-0; 3, 93135-58-1; 4, 93135-59-2; 5, 93135-60-5; 6, 51008-69-6; 7, 93135-61-6; 8, 93135-62-7; 9, 93135-63-8; 10, 93135-64-9; 11, 93135-65-0; 12, 93135-66-1; 13, 93135-67-2; 14, 93135-68-3; 15, 93135-69-4; 16, 93135-70-7; 17, 93135-71-8; 18, 93135-72-9; 19, 93135-73-0; 20, 93135-74-1; 21, 93135-75-2; phenyl chloroformate, 1885-14-9; benzoyl chloride, 98-88-4; *p*-toluyl chloride, 874-60-2; *p*-methoxybenzoyl chloride, 100-07-2; *p*-cyanobenzoyl chloride, 6068-72-0; benzoic anhydride, 93-97-0; *p*-toluic anhydride, 13222-85-0.

Stability Constants, Enthalpies, and Entropies for Metal Ion-Lariat Ether Interactions in Methanol Solution[1]

Richard B. Davidson, Reed M. Izatt,* and James J. Christensen

Departments of Chemistry and Chemical Engineering and the Thermochemical Institute,[†]
Brigham Young University, Provo, Utah 84602

Rose Ann Schultz, Dennis M. Dishong, and George W. Gokel

Department of Chemistry, University of Maryland, College Park, Maryland 20742

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Log K_n, ΔH_n, and $T\Delta S_n$ values valid in CH_3OH at 25 °C have been determined for the interaction of Na^+, K^+, Cs^+, and Ca^{2+} with 15-crown-5 and several lariat ethers. The lariat ethers studied are based on both 15-crown-5 and 18-crown-6 frameworks and contain various pendant arms extending from either carbon or nitrogen atoms on the crown framework. In comparable cases, enlarging the ring size from 15 to 18 members resulted in increased stability. The inclusion on the aza-15-crown-5 ring of a pendant arm bound to nitrogen and having an oxygen atom in the 3 position increases complex stability about ten-fold for Na^+, K^+, and Ca^{2+} compared to the crown ether with the same ring structure but lacking a heteroatom in the side arm. Generally, little effect on the log K_n value is found either by lengthening the pendant arm (and by including an additional donor atom) on the 18-crown-6 compounds or by appending pendant arms having oxygen atoms on the carbon pivot atom of the 15-crown-5 macrocycles.

Recently, one of us reported the preparation and cation binding properties of a series of compounds named "lariat ethers".[2-4] These compounds (1–6) contain a cyclic polyether macroring with an attached, conformationally mobile side chain. The side chains carry heteroatoms (oxygen, nitrogen) which are expected to participate with the macroring in the binding of cations. Thus, these compounds might be expected to be intermediate in their binding and dynamic properties between crown ethers and cryptands.[5-9] Similar molecules having secondary binding arms have been reported by others.[10-16]

[†] Contribution No. 328.

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Table I. Log K, ΔH (kcal/mol), and $T\Delta S$ (kcal/mol) Values[a] for the Interaction in CH_3OH at 25 °C of Lariat Ethers with Metal Cations Using the Cation as Titrant

	1	2	5	6	3	4	7[b]	8[c,22]
				Na^+				
log K_1	3.22 ± 0.01	4.33 ± 0.01	5.6 ± 0.1	5.7 ± 0.2	3.24 ± 0.01	2.90 ± 0.01	3.30 ± 0.01	4.36
ΔH_1	−4.15 ± 0.08	−6.39 ± 0.01	−7.44 ± 0.01	−6.70 ± 0.05	−5.34 ± 0.03	−5.41 ± 0.02	−5.40 ± 0.05	−8.4
$T\Delta S_1$	0.24	−0.48	0.2	1.0	−0.92	−1.46	−0.90	−2.4
log K_2	*d*	2.30 ± 0.04	2.7 ± 0.2	3.7 ± 0.2	*d*	*d*	*d*	
ΔH_2	*d*	−0.5 ± 0.2	−1.4 ± 0.5	−0.44 ± 0.08	*d*	*d*	*d*	
$T\Delta S_2$	*d*	2.6	2.3	4.7	*d*	*d*	*d*	
				K^+				
log K_1	2.99 ± 0.01	4.20 ± 0.01	5.35 ± 0.07[e]	*f*	3.32 ± 0.06	3.17 ± 0.07	3.35 ± 0.05	6.06
ΔH_1	−6.36 ± 0.06	−9.08 ± 0.02	−12.38 ± 0.03	−12.54 ± 0.03	−7.8 ± 0.1	−8.08 ± 0.07	−7.79 ± 0.01	−13.41
$T\Delta S_1$	−2.28	−3.35	−5.08[e]	*f*	−3.2	−3.76	−3.21	−5.14
log K_2	*d*	2.19 ± 0.03	*d*	*d*	2.53 ± 0.04	2.77 ± 0.04	2.65 ± 0.03	
ΔH_2	*d*	−0.6 ± 0.02	*d*	*d*	−8.8 ± 0.8	−7.4 ± 0.9	−8.8 ± 0.7	
$T\Delta S_2$	*d*	2.4	*d*	*d*	−5.4	−3.7	−5.2	
				Cs^+				
log K_1	*e*	2.79 ± 0.02	4.24 ± 0.01[g]	4.34 ± 0.01	*g*	2.63 ± 0.05	2.62 ± 0.02	4.79
ΔH_1	*e*	−7.87 ± 0.05	−10.72 ± 0.01[g]	−11.8 ± 0.4	*g*	−7.8 ± 0.1	−7.63 ± 0.03	−11.29
$T\Delta S_1$	*e*	−4.06	−4.93[g]	−5.9	*g*	−4.2	−4.06	−4.75
log K_2	*e*	*e*	2.10 ± 0.06[h]	*d*	*g*	2.37 ± 0.09	*e*	
ΔH_2	*e*	*e*	−0.9 ± 0.1[h]	*d*	*g*	3.2 ± 0.9	*e*	
$T\Delta S_2$	*e*	*e*	1.9[h]	*d*	*g*	6	*e*	
				Ca^{2+}				
log K_1	2.83 ± 0.03	3.78 ± 0.03	4.83 ± 0.06	4.23 ± 0.04	*i*	*i*	2.55 ± 0.03[i]	3.86
ΔH_1	−3.3 ± 0.2	−2.58 ± 0.03	−3.17 ± 0.05	−2.78 ± 0.05	*i*	*i*	−2.8 ± 0.1[i]	−2.75
$T\Delta S_1$	0.6	2.58	3.4	2.99	*i*	*i*	0.7	2.52
log K_2	2.8 ± 0.1	2.71 ± 0.05	3.45 ± 0.02	3.08 ± 0.07	*i*	*i*	2.1 ± 0.1[i]	
ΔH_2	3.5 ± 0.2	1.8 ± 0.1	0.73 ± 0.7	1.10 ± 0.09	*i*	*i*	4.8 ± 0.7[i]	
$T\Delta S_2$	7	5.5	5	5.3	*i*	*i*	7	

[a] Averages of three determinations except as indicated by footnote *h*. Uncertainties are given as the standard deviation in each case. [b] 15-Crown-5. [c] 18-Crown-6. [d] Reaction could not be characterized as 1:2, second equilibrium constant unimportant. [e] Large uncertainty in these values. [f] Sharp endpoint indicates a large value of log K not accurately determinable by calorimetric methods. [g] Thermograms from three calorimeter runs were practically superimposable, indicating good repeatability, but neither assumption of 1:1 nor of combined 1:1 and 1:2 stoichiometry could characterize the reaction. [h] Average of two determinations. [i] Small amount of heat produced makes these values uncertain.

Altering the side-chain structure, adjusting the size of the macrocycle ring, and varying the component heteroatoms makes it possible to vary both cation binding strength and cation selectivity. Thus, the lariat ethers offer the opportunity to design selectivity for specific cations into macrocyclic systems. Implementation of such designs could prove useful in areas of chemistry where cation selectivity is important, such as membrane separation processes and preparation of synthetic enzymes.

In earlier studies,[2] comparison of the respective abilities of **3** and **4** to extract either Na^+ or K^+ from water into $CHCl_3$ produced interesting results. Both compounds extracted K^+ to a similar extent and either was better than 15C5 at this task. In contrast, about twice as much Na^+ was extracted by **3** as by either **4** or 15-crown-5 (**7**).

Log K_1 values for the 1:1 reactions of Na^+ with **3**, **4**, and **7** in 90% methanol–10% water (v/v) solution were determined earlier by using an ion-selective electrode procedure.[17,18] The order of binding strength was found to be **7** ≃ **3** > **4**. The objective of the present investigation was to extend this study to include a wider range of cations (Na^+, K^+, Cs^+, Ca^{2+}) and lariat ethers (Figure 1) and to determine ΔH_n and $T\Delta S_n$ values for the interactions as well.

Experimental Section

Materials. Methanol (Fisher, reagent, H_2O <0.05%), sodium chloride (Fisher, reagent), cesium chloride (Cerac 99.9%), calcium chloride (Allied Chemical, reagent A.C.S.), and potassium iodide (Mallinckrodt, reagent) were used as received. Compound **7** (Parish Chemical) was used as supplied. The syntheses of the remaining crown ethers have been reported: [*N*-butylmonoaza]-15-crown-5 (**1**),[4] [*N*-(2-methoxyethyl)monoaza]-15-crown-5 (**2**),[19] 2-[(2-methoxyphenoxy)methyl]-15-crown-5 (**3**),[2] 2-[(4-methoxyphenoxy)methyl]-15-crown-5 (**4**),[2] [*N*-(2-methoxyethyl)monoaza]-18-crown-6 (**5**),[19] and [*N*-(3,6-dioxaheptyl)-monoaza]-18-crown-6 (**6**).[19] All of the crown ether solutions were standardized by titration with silver nitrate (Sargent-Welch, reagent) using the method of Lamb et al.[20]

Procedure. The calorimetric titration data were determined as described earlier.[21,22] A new computer program, 12AUTO,[21] was developed to analyze the calorimetric data in order to accom-

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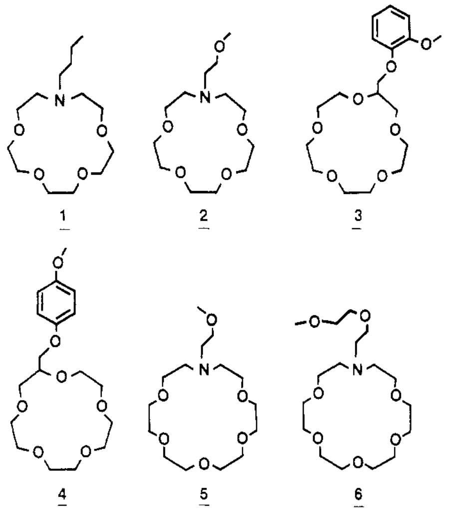

Figure 1. Macrocycles used in the study. The compounds are identified by name in the Experimental Section.

modate both 1:1 and 1:2 metal–ligand (M:L) interactions. The program used in past work, EQDH, assumes that only 1:1 interaction occurs.[22] Usually, the titrations were performed with the macrocycle in the Dewar since in that way only 100 μmol of macrocycle are required per calorimeter run. The titrations were carried out to an excess of more than 2 to 1 molar equiv in order to study 1:2 reactions. The anion used was chloride in all cases except potassium where it was iodide. Potassium chloride is not soluble in methanol to the extent required in the titrations.

Since the computer program developed to analyze for 1:1 and 1:2 M:L coupled reactions was new, it was important to verify the accuracy of the coding in its case. This was done by analyzing the data from titrations in which the positions of the reactants were reversed. If the correct assumptions have been made with regard to reaction stoichiometry, then it is unimportant which compound, host or guest, is in the reaction vessel; the calculated values of log K and ΔH should be identical. For this purpose, additional runs were made in which the macrocycle was titrated into the cation.

Results and Discussion

The log K_n, ΔH_n, and $T\Delta S_n$ values determined in the study are given in Tables I and II. In these tables, K_1 and K_2 refer to the reactions $M^+ + L = ML^+$ and $ML^+ + L = ML_2^+$, respectively, where L is the macrocycle ligand. Corresponding ΔH_n and ΔS_n values are designated in a similar manner. The presentation and discussion of these data are found under the headings: macrocycles with oxygen donor atoms, macrocycles with oxygen and nitrogen donor atoms, and cation effects.

Macrocycles with Oxygen Donor Atoms. The log K_1 value of 3.30 for Na^+:7 interaction determined in this study is in good agreement with that determined earlier by ion-selective electrode (3.25,[19] 3.27[23]) and calorimetric (3.48[22]) methods. No evidence for 1:2 stoichiometry was found in the Na^+:7 system.

Log K_1 for K^+:7 interactions was reported previously by us[22] to be 3.77 ± 0.18. Using the same computer program to analyze the present data, a value of 3.47 ± 0.01 was obtained. However, it was noticed that agreement between the observed and the theoretical enthalpograms was only fair, indicating that contributions to the reaction heat from another reaction were significant. When the assumption of 1:1 in conjunction with 1:2 stoichiometry is made, program 12AUTO produces excellent agreement between observed and theoretical enthalpograms. For example, theoretical curves were obtained with root-mean-square errors of deviation from the observed data of 0.0013, 0.0009, and 0.0009 cal for three consecutive runs having reaction heats of 0.705, 0.702, and 0.703 cal, respectively. The calculated log K_1 value in this case (3.35) is in fair agreement with that reported by Nakatsuji, Nakamura, and Okahara (3.3–3.6).[23]

Table II. Log K, ΔH (kcal/mol), and $T\Delta S$ (kcal/mol) Values[a] Obtained Using Crown Ethers as Titrant

	3	7[b]
	K^+	
log K_1	3.30 ± 0.02	2.96 ± 0.12
ΔH_1	-7.97 ± 0.09	-8.1 ± 0.5
$T\Delta S_1$	-3.5	-4.0
log K_2	2.46 ± 0.01	2.63 ± 0.08
ΔH_2	-9.44 ± 0.08	-8.4 ± 0.9
$T\Delta S_2$	-6.09	-5
	Ca^{2+}	
log K_1		2.50 ± 0.04
ΔH_1		-1.82 ± 0.09
$T\Delta S_1$		1.6
log K_2		1.7 ± 0.4
ΔH_2		0.9 ± 0.2
$T\Delta S_2$		3

[a] Averages of three determinations. Uncertainties are given as the standard deviation in each case. Thermograms from three calorimeter runs in the case of the Cs^+:3 system were practically superimposable, indicating good repeatability, but neither assumption of 1:1 nor of combined 1:1 and 1:2 stoichiometry could characterize the reaction. [b] 15-Crown-5.

When the titrant and titrate were exchanged, titrating 15C5 into K^+ and analyzing the data with EQDH, the value of log K_1 was calculated to be 1.75 ± 0.09. Again, the fit to the data was poor. Analyzing the same data with program 12AUTO gave the log K_1 and log K_2 values listed in Table II. The log K_2 value in Table II is in excellent agreement with that tabulated in Table I for the same reaction. The log K_1 values differ by 0.39. Corresponding ΔH_1 and ΔH_2 values are in good agreement.

Comparison of the results of titrations of Ca^{2+} into 7 and the reverse shows that the log K_n values agree within limits of uncertainty (Tables I and II). The reported ΔH values in the case of this system have large uncertainties associated with them. One difficulty in titrations involving Ca^{2+} as titrant is a large heat of dilution relative to the heat of reaction. For the solution concentrations used, the heat of dilution was 665 mcal. This is to be compared with a reaction heat (exclusive of heats of dilution) of approximately 150 mcal. The difficulty appears to be due to round-off error as large values of total heat, in the neighborhood of 800 mcal, are subtracted to yield reaction heats approximately one-fifth as great.

Log K_1 values determined earlier[17,18] and valid in 90% methanol–10% water solution for 1:1 Na^+ binding with 7 and 3 were equal within the limits of experimental error (2.97), while that for 1:1 Na^+ binding with 4 (2.56) was somewhat less. The log K_1 values found in the present study are larger as would be expected based on results from earlier studies of Na^+–macrocycle complexation in CH_3OH and CH_3OH–H_2O solvents.[24,25] However, the trend is the same (Table I). The corresponding ΔH_1 values for the three systems are equal within the limits of experimental error.

Replacement of Na^+ by K^+ results in little change in the log K_1 values, except in the case of 4. Significant changes

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are seen in the corresponding ΔH_1 and ΔS_1 values, but these counterbalance each other. The larger change in log K_1 in the case of 4 is a result of the greater change of ΔH_1. The less negative $T\Delta S_1$ values in the case of Na^+ could be due to the larger charge density of Na^+ which would attract a larger number of methanol molecules to its solvation sphere so that more are replaced in the complexation reaction. From the standpoint of the macrocycle, it is likely that less conformational change is required to accommodate the smaller ion and/or the resulting complex is less rigid. Similar arguments account for the opposing changes in ΔH_1.

The reaction of Cs^+ with **3** is neither well characterized stoichiometrically as 1:1 nor as combined 1:1 and 1:2. Run to run agreement of reaction heat vs. titrant volume was excellent in these cases, but during the data analysis it was noticed that arriving at a solution was more difficult and larger than normal standard deviations were the rule. The root-mean-square error surface in log K_1, log K_2 space in the vicinity of the solution typically showed the presence of a long narrow channel having a gradually rising bottom on each side of the minimum. The existence of this kind of formation makes for the large standard deviation mentioned above. In these cases, it is possible that reactions are occurring other than those assumed. For instance, Pedersen and Frensdorff reported 2:3 species in a similar case where the cation was large compared to the macrocycle cavity.[8]

Heats of reaction of Ca^{2+} with all the macrocycles under study were much less than thooe for the other cations studied. In addition, a large heat of dilution was found for $CaCl_2$.

It is instructive to compare the values of log K_1 for the reactions of Ca^{2+} and Cs^+ with **7**. They are nearly equal but for different reasons. Complexation of Ca^{2+} by **7** is stabilized by the increase in entropy while the decrease in enthalpy is of minor importance in comparison to the contributions of the enthalpy change to the stability of the Cs^+:**7** complex. The entropy change is destabilizing in the latter case. The stabilization of the 1:2 complex of Ca^{2+} with **7** is entirely an entropy effect, the ΔH_2 value being positive. The large positive $T\Delta S_2$ value may result, in part, from the replacement of the remaining solvent molecules from Ca^{2+} as it is sandwiched between two molecules of **7**. The large solvation energy of Ca^{2+} (compared to Cs^+) is likely to cause both of the less negative ΔH_1 value (replacement of solvent by **7** requires energy) and of the more positive $T\Delta S_1$ value (more solvent replaced per **7** bound). The endothermic reaction resulting in the positive ΔH_2 value is seen clearly in the enthalpograms, all of which exhibited a sigmoidal shape being convex upward for about the first 60 s of the run. During this time Ca^{2+} is scarce in the reaction vessel and the formation of 1:2 complexes is more likely. Their formation consumes heat so a lesser temperature rise is noticed. The temperature does rise even though the 1:2 reaction is endothermic because the equilibrium constant for the 1:1 reaction is dominant.

The uniformity of values for log K_1 and log K_2 in the reaction of K^+ with the 15-crown-5-type macrocycles bearing oxygen only as heteroatoms (**3**, **4**, **7**) is surprising. One would expect to see some effect of the side chains reflected in the thermodynamic properties of complexation. On the contrary, all three macrocycles are about equal not only with regard to log K_n but ΔH_n and $T\Delta S_n$ as well. In these cases, it is possible that the side chains are physically uninvolved in the reactions.

It was hoped that evidence would be found for interaction of the side chains with the guest cations from a comparison of the values of K_2. One would expect sandwich compounds for the unencumbered **7** to form more easily than for **3** and **4** where the side chain is bound to a carbon pivot atom and somewhat more easily than for **1** and **2** where the side chain is bound to a nitrogen pivot atom. A complete set of data is available only for those systems involving K^+. The results are disappointing. Log K_2 is greatest for complexation with **4** instead of with **7** and, in fact, all the values are much more nearly equal than statistical considerations would suggest. Thus, our data do not provide evidence for interaction of the side chain with K^+.

Macrocycles with Oxygen and Nitrogen Donor Atoms. Examination of the results obtained by using **1** and **2** (Table I) shows a trend pointed out previously;[19] namely, the presence of oxygen in the side chain of these ligands enhances the binding capability of the host. The larger binding constants (by about an order of magnitude) in the reactions with **2** compared to those with **1** suggest that the oxygen in the side chain is involved in the binding.

The macrocycles **7**, **1**, and **2** constitute a series in which there may be evidence for side-chain interaction with K^+. The data in the case of **7** show well-defined 1:1 and 1:2 complexes which are enthalpy stabilized. Addition of the butyl arm on the pivot nitrogen atom effectively eliminates the 1:2 complex and results in about a two-fold decrease in stability. In the case of the K^+–**2** complex, one might expect enhanced binding involving the oxygen on the pendant arm. In this case, the log K_1 value (4.20) is nearly an order of magnitude larger than that (3.35) for K^+:**7** binding. The enhanced binding is an enthalpy effect. In addition, a second **2** macrocycle binds to the K^+, but, in this case, the magnitude of ΔH_2 is very small in contrast to that in the case of **7**. The 1:2 complex of K^+ with **2** is entropy stabilized. (It would be useful to have X-ray crystallography data to characterize this set of complexes further. Side-arm involvement has been shown by single-crystal X-ray analysis of two other alkali metal–nitrogen–pivot lariat ether complexes.[3])

Comparison of **2** with **5** shows larger log K_n values for M^{n+}–**5** interaction, in each case. Addition of an EtO group to the pendant arm to form **6** has little effect on any of the thermodynamic quantities in the cases of either Na^+ or Cs^+ but results in decreased stability in the case of Ca^{2+}. Log K_1 appears to increase significantly in the case of K^+ which is also the cation having the best fit in the macrocycle cavity and the one for which no 1:2 species are found.

When 18-crown-6 (**8**) is compared to **5** and **6**, addition of the pendant arms results in increased log K_1 values in the case of Na^+, but decreased log K_1 values in the case of Cs^+ for both ligands. The effect in the case of K^+ appears to be intermediate with log K_1 being smaller for **5** and probably larger for **6**. These log K_n changes follow the order of decreasing charge density for the alkali metal cations. These data suggest that interaction between the cation and the pendant arm increases with increasing cation charge density. The increased log K_1 value for the interaction of the high charge density cation Ca^{2+} with the crowns having pendant arms relative to that with **8** is consistent with this idea, also. These results may have implications for the design of selective complexing agents for high charge density cations since the presence of appropriate pendant arms may enhance complexation with these cations.

The type of donor atom is an important factor influencing the binding. For example, log K_1 for Ag^+:**7** interaction was found to be 3.62 ± 0.03 compared to log K_1 = 5.75 ± 0.11 for Ag^+:**1** interaction. The difference in log K_n

values would be expected to be due to the presence of nitrogen. It seems unreasonable that the presence of an *n*-butyl side chain could cause the difference noticed in this case. Evidence that the effect is related to the change in cation type is seen by comparing the Ag^+ results with those of Na^+. The log K_1 values for complexation of Na^+ with **1** and **7** are comparable (3.22 and 3.30, respectively), whereas the log K_1 value for Ag^+:**1** interaction is much greater than that for Ag^+:**7** interaction. Furthermore, K^+ shows a smaller log K_n value in its complexation with **1** than with **7**. Ag^+ is intermediate between Na^+ and K^+ in ionic radus,[22] so the observed changes in log K cannot be attributed to size effects. The effect of donor atom type on equilibrium constant is discussed in detail by Lamb et al.[22]

Cation Effects. Among the alkali metal cations, log K_1 decreases with increasing ion size when the host contains nitrogen in the macrocycle ring. A possible exception to this is the binding of the cations by **6** where log K_1 for binding of K^+ is large and not determined accurately. For the lariat ether hosts that contain only oxygen donor atoms, the largest log K_1 values are found in the case of K^+ and the smallest in the case of Cs^+.

Of the cations studied, K^+ and Ca^{2+} showed the greatest propensity to form 1:2 complexes with the macrocycles studied. In some cases, principally those for Ca^{2+} reacting with **1** and **7**, log K_2 rivals log K_1 in magnitude. The largest cation, Cs^+, formed well-defined 1:2 complexes only with **5** and **4**. In the remaining cases, either the reactions with Cs^+ could not be well characterized as including 1:2 complexes or K_2 was at least 2 orders of magnitude less than K_1. The reaction of Cs^+ with **3** could not be characterized at all. Examining the plots of heat produced vs. titrant volume showed them to be practically superimposable. In this case, the problem is not run to run inconsistency in the calorimeter output but in the theory applied to explain the shape of the enthalpogram.

Conclusions

In comparable cases, enlarging the ring size from 15 to 18 atoms results in increased log K values. The inclusion on the aza-15C5 ring of a side chain bound to nitrogen and having an oxygen atom in the number 3 position (compound **2**) improves the stability of the complexes formed with the cations studied here by about an order of magnitude. These results indicate that the side chain is involved in the binding although it is not clear by what mechanism the improved stability is achieved. Lengthening the side chain and including more donor atoms in it has little if any perceptible effect on the binding with the 18-crown-6 variety of macrocycles. Finally, the effect on the equilibrium constant produced by appending side chains to a carbon pivot atom of **7** is small. Such a gross structural variation must result in some alteration of the characteristics of the molecule. Possibly, an enlarged set of cations might include one which could "see" the difference in the ligands. Organic ammonium cations with groups that could interact with the donor atoms on the side chain would be an obvious choice.

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4,4′-Methylenebis(benzyne) [4,4′-Methylenebis(1,2-didehydrobenzene)] Equivalent

Juzo Nakayama,* Atsuhiro Sakai, and Masamatsu Hoshino

Department of Chemistry, Faculty of Science, Saitama University, Urawa, Saitama 338, Japan

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The aprotic diazotization of 5,5′-methylenebis(anthranilic acid) (**4**) by isoamyl nitrite in refluxing 1,2-dichloroethane functions as a 4,4′-methylenebis(benzyne) (**5**) equivalent. **5** undergoes Diels–Alder reaction with tetraphenylcyclopentadienone, anthracene, and 2,5-dimethylfuran and [2 + 2] cycloaddition with *trans*-1,2-dichloroethylene to give the corresponding bis-adducts in moderate to low yields. Reactions of **5** with iodine, carbon disulfide, and ethyl phenyl sulfide are also described.

Although diaryne synthons have been sporadically described in the literature,[1-3] it is in recent years that their synthetic utility has attracted much attention. Hart and co-workers showed that 1,2,4,5- and 1,2,3,4-tetrahalobenzenes are synthetically useful diaryne (**1** and **2**) equivalents.[4] For example, when they are treated with 2 equiv of an organolithium reagent in the presence of a receptor diene, they form products which correspond formally to bis-adducts of **1** and **2**. 1,5-Naphthodiyne (**3**) synthon was recently utilized for the preparation of chrysenes.[5] Very recently it was shown that oxidation of

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