investigation were found to obey Beer's law up to a concentration of 10^{-5} M. For the rapid fading reaction of less than 2-3 min, we used the high-pressure stopped flow apparatus.

High-Pressure Stopped Flow Technique. The schematic diagram of the high-pressure stopped flow (HPSF) apparatus is shown in Figure 5. The high-pressure optical and mixing chamber (SUS 630 stainless steel) was a T-jet type with two quartz windows (Figure 6). The spectrophotometric system was a Union Giken stopped flow apparatus. Pressure was measured by a strain gauge (Kyowa KPC-5C1-11) which was calibrated against a Heise precision bourdon gauge (full scale 50 000 psi, unit scale 50 psi). The temperature was kept constant by circulating the thermostated water surrounding the solution reservoirs and the mixing chamber. The temperature of the mixing chamber was monitored by the thermocouple ±0.1 °C.

The operation was carried out as follows. First, the valves V_1 and V_3 were closed and the valve V_2 was opened after filling the high-pressure sample reservoir B with each reactant solution. Then, as soon as the solenoid valve E was opened in order to push the piston P upward through the intensifier D, each reactant solution was mixed up in the mixing chamber and was immediately compressed. The desired pressure was set up by controlling the gaseous pressure in the gas reservoir G and it took 2 s at least to generate a constant pressure in the mixing chamber. The temperature of the solution accompanying the compression up to 1 kbar increased about 2 °C more than in the experimental condition and 2 s was needed before the constant temperature was recovered. With this operation, the reliable kinetic data were obtained 2 s after the operation of E. Figure 7 is a typical example of the alkaline fading reaction of **2b** at 150 and 750 bar.

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Registry No. 1a, 2390-59-2; **1b**, 548-62-9; **2a**, 633-03-4; **2b**, 569-64-2; OH^-, 14280-30-9; H_2O, 7732-18-5.

Clarification of the Hole-Size Cation-Diameter Relationship in Crown Ethers and a New Method for Determining Calcium Cation Homogeneous Equilibrium Binding Constants

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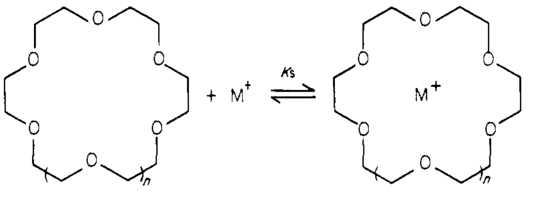
Abstract: The equilibrium stability constants for the homologous series of crown ethers ranging from 12-crown-4 to 24-crown-8 with sodium, potassium, ammonium, and calcium cations have been determined in anhydrous methanol solution. The key finding of this study is that the widely recounted "hole-size-selectivity" principle is not applicable to this series of simple macrocycles. Instead, it is observed that the K^+ cation is bound most strongly by all of the macrocycles in this series and that the strongest binding for all of the cations in this study is observed with 18-crown-6. In order to determine the stability constants for Ca^{2+} in MeOH by ion selective electrode methods, it was necessary to develop a new, competitive technique utilizing the Na^+-selective glass electrode. We report such a method here which is rapid, reliable, and applicable in organic solvents that are incompatible with commercial Ca^{2+}-selective electrodes.

Not long after Pedersen's discovery of cation binding by crown ethers,[1] he and Frensdorff reported that picrate extraction constants showed an apparent relationship between cation diameter and crown ether hole size.[2] The same sort of relationship was observed for the relatively inflexible, three-dimensional cation binders devised by Lehn and called cryptands.[3] The hole-size concept was widely accepted and led to the design and synthesis of a remarkable variety of cation and molecule hosts including the spherands[4] and cavitands.[5] These inflexible cation binders appeared to affirm the hole-size concept as well. In contrast to this, Reisse and Michaux recently reported that the enthalpies of binding between Na^+ and K^+ and the 12-18-membered crown rings do not correlate with hole sizes.[6]

Some of our previous work with the macrocycles we have called "lariat ethers" has suggested that the more flexible polyether systems do not abide by this "hole-size rule".[7] We therefore felt it would be useful to survey stability constants, K_s (see eq 1), for as broad a range as possible of homologous crowns. Since much



(1)

$n = -1, 0, 1, 2, 3$
$M = Na^+, K^+, NH_4^+, Ca^{2+}$

of the binding data thus far accumulated have been taken in anhydrous MeOH solution, we wished to conduct our studies in this solvent. Furthermore, we were anxious to have a full set of Ca^{2+} binding, as well as Na^+, K^+, and NH_4^+, data in this solvent. To date, virtually all of the Ca^{2+} stability constants that are available have been determined by calorimetric methods[8] since commercial, Ca^{2+}-selective ion selective electrodes (ISE) are incompatible with organic solvents.[9] We have therefore developed a convenient method for determining Ca^{2+} stability constants in solvents other than water. We have applied the method to the 12-crown-4 to 24-crown-8 series of crown ethers in anhydrous

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(9) This is due to their construction. The epoxy body of the electrode is unstable to the nonaqueous solvent, and the ionophore contained within it dissolves away.

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MeOH solution and report the results of these studies below.

Experimental Section

12-Crown-4 was prepared by the method of Stewart et al.[10] 15-Crown-5 was purchased from the Aldrich Chemical Co. and vacuum distilled prior to use. We have previously published procedures for the preparations of 18-crown-6,[11] 21-crown-7,[12] and 24-crown-8.[12]

The binding constants were determined potentiometrically. A Na^+-ISE (Corning catalog No. 476210) was used for Na^+ and a monovalent cation electrode (Corning catalog No. 476220) was used for K^+ and NH_4^+. Emf against a Ag/AgCl electrode was measured with use of an Orion Research Model 701A digital "Ionalyzer". All the measurements were conducted in a water-free glovebox under a N_2 atmosphere. The temperature of the system was maintained at 25.0 ± 0.1 °C with a bath of circulating di-*n*-butyl phthalate.

Since the bodies of currently available Ca^2-ISEs are damaged by many organic solvents,[9] a Na^+-ISE was used for Ca^{2+}–crown binding studies. Free Na^+ concentration is measured in the presence of known amounts of Ca^{2+} and crown, i.e., the Ca^{2+}–crown binding is studied in competition with Na^+–crown binding.

Na^+, K^+, or NH_4^+ binding constants were determined by measuring the emf for the respective electrode (see above) against a Ag/AgCl reference electrode. This was done (1) for a solution containing only the $cation^+Cl^-$ salt (standard) and (2) for solutions containing the salt with differing amounts of crown present as well.

The competitive method for determining the Ca^{2+}–crown binding constant involves measurement of the Na^+-ISE's emf vs. Ag/AgCl (1) for a solution containing a known concentration of NaCl alone, (2) for a solution containing NaCl and crown, and (3) for a solution containing NaCl, crown, and $CaCl_2$. Ion concentrations were measured (1) alone for the standard, (2) in the presence of the crown ether, and (3) in the presence of $CaCl_2$. Binding constants were then determined as discussed below.

Results and Discussion

Binding Constant Determinations. The homogeneous stability constants for Na^+, K^+, and NH_4^+ were determined in anhydrous MeOH solution with use of a Na^+ or monovalent cation (K^+, NH_4^+) electrode. Since the commercially available ISEs for Ca^{2+} can be used only in water or aqueous solutions containing no more than a small percentage of organic solvent,[9] a new method was developed to determine the stability constants in MeOH (see Experimental Section). The method is based on a competition for the crown by calcium and sodium; the latter is detected by using the sodium selective glass electrode. The sodium binding constant is determined first and is then used to calculate calcium binding with use of the following equations.

For crown (Cr) and Na^+ alone, the total Na^+ concentration is found as follows, $[Na^+]_T = [Na^+]_F + [CrNa^+]$, and the total crown concentration is found as follows, $[Cr]_T = [Cr]_F + [CrNa^+]$. Na^+ ion concentration was calculated from the measured emf for the solution and the emf for the standard with use of the usual electrode equation. The Na^+–crown binding constant (K_s) is determined from the $[Cr]_F$ and $[CrNa^+]$ concentrations calculated from the above mass balance equations and by using the formula

$$K_s = [CrNa^+]/\{[Na^+]_F[Cr]_F\}$$

Note that this is the common procedure for determining Na^+, K^+, and NH_4^+ binding constants.[13]

For a solution containing Na^+, Ca^{2+}, and crown (Cr), the total concentrations can be written as:

$$[Na]_T = [Na^+]_F + [CrNa^+]$$

$$[Cr]_T = [Cr]_F + [CrNa^+] + [CrCa^{2+}]$$

$$[Ca^{2+}]_T = [Ca^{2+}]_F + [CrCa^{2+}]$$

$[Na^+]_F$ is calculated as before, from the measured emf for the solution. These mass balance equations, along with the relationship for K_s illustrated above, can be used to calculate $[Cr]_F$, $[Ca^{2+}]_F$, and $[CrCa^{2+}]$. The binding constant for the Ca^{2+}–crown interaction can therefore be calculated as follows:

$$K_s[Cr{\cdot}Ca^{2+}] = \frac{[CrCa^{2+}]}{[Ca^{2+}]_F[Cr]_F}$$

Table I. Stability Constants [log K_s] for Crowns and Cations in Anhydrous Methanol at 25.0 °C[a]

	binding constants							
crown	Na^+	lit.	K^+	lit.	NH_4^+	lit.	Ca^{2+}	lit.
12-C-4	1.7	1.47[6]	1.74	1.58[6]	1.3	na	nd	na
15-C-5	3.24[b]	3.16[6] 3.48[8]	3.43	3.59[6] 3.76[8]	3.03	na	2.36	2.18
18-C-6	4.35	4.36[6] 4.36[8] 4.32[13]	6.08	6.16[6] 6.06[8] 6.10[13]	4.14	4.27[17]	3.90	3.86
21-C-7	2.54	1.73[8]	4.35	4.22[8] 4.41[18]	3.27	na	2.80	na
24-C-8	2.35	na	3.53	3.48[18]	2.63	na	2.66	na

[a] na = not available; nd = not determined. [b] We have previously reported this value as 3.25.[16] We do not believe that this difference is significant.

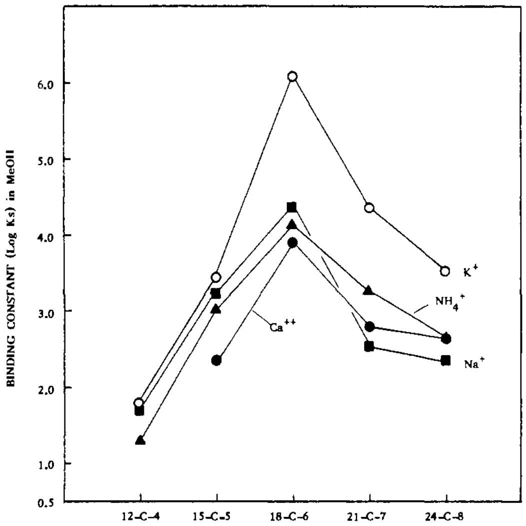

Figure 1. Cation binding by simple crown ethers.

Our data and comparable literature values from a variety of sources are shown in Table I and our observations are further summarized in graphical form in Figure 1. With one exception, our potentiometrically (ISE) determined values correlate well with those of others, many of which were determined calorimetrically. Despite this good agreement, we have noted a limitation in our system: When the Na^+-selective electrode is used in the presence of Ca^{2+} for several weeks, its reponse begins to fade. Fortunately, when bathed for several days in a Na^+-rich MeOH solution, the difficulty is completely reversed and the normal response pattern returns. Details of the method are recorded in the Experimental Section (above).

Stability Constant Determinations. The homogeneous stability constant values for the series of macrocycles 12-crown-4 to 24-crown-8 in anhydrous MeOH are shown in Table I and graphically in Figure 1. As noted above, our data generally agree with comparable literature values, whether determined by ISE or calorimetric methods. The single exception to this is the stability constant between 21-crown-7 and Na^+. The literature value seems unusually low in light of the other values for binding by this macrocycle, but we have no clear explanation to account for this discrepancy.

Although some of the values reported in Table I have been available for over a decade, the cation-diameter–hole-size relationship is still widely accepted. The homogeneous binding constants reported here and by others contradict this for a variety of cations and crowns. The crown–cation relationship can be

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viewed in two ways: ligand selectivity for cations of a certain size, or cation selectivity for ligands of a certain size. This would suggest that, for example, 15-crown-5 is selective for Na$^+$ over K$^+$. This is not the case (see Table I). On the other hand, according to this principle, Na$^+$ should select "appropriately sized" 15-crown-5 over the larger 18-crown-6. This is not the case either, suggesting that the hole-size correlation, while not without some foundation, is not true in general.

As mentioned above, the most important point to note about the binding constant data is that the hole-size relationship is simply not obeyed for this group of unsubstituted, flexible crown ethers. Instead, the two rules that can be formulated are the following: (1) For this series of crowns and cations, K$^+$ is bound more strongly than Na$^+$, Ca$^+$, or NH$_4^+$ by all of the crowns irrespective of hole size. (2) For this series of crowns and cations, the strongest binding is observed with 18-crown-6, irrespective of cation size or geometry (i.e., spherical for metals and tetrahedral for ammonium).

It has been reported previously that the K$^+$·18-crown-6 complex is intrinsically less stable than the corresponding Na$^+$ complex, and that the K$^+$ selectivity in this case is due to solvation and conformation differences between these two complexes.[6,14,15] In this group of crowns, the special stability of the K$^+$·18-crown-6 complex may be due to a combination of a high complexation enthalpy for K$^+$[6,8] and the ligand's symmetry,[14] planarity, and absence of eclipsing interactions in the backbone.[15]

There are at least four factors that make significant contributions to the binding of cations by crowns. These are the following: (1) the cation-diameter–hole-size relationship, (2) the solvation enthalpies and entropies of the cation and ligand, (3) the number of donor atoms participating in binding, and related to the latter, (4) the conformation of the bound and unbound macrorings. Of these factors, the hole-size relationship probably plays its greatest role when the ligands are relatively inflexible (not the case here) or when cation–crown affinity is determined by the picrate extraction technique. In this experiment, the ligand draws a cation across an organic–aqueous phase boundary and the colored anion that accompanies the cation is detected colorimetrically.[2,13] In this two-phase system, it is obviously more difficult to sort out the question of hole size vs. solvation enthalpy and entropy contributions. The key point, however, is that while both picrate extraction and homogeneous binding constant determinations provide useful information, they do not provide the same information.

Summary

The new, competitive ISE-based method we present here allows Ca^{2+}–cation equilibrium stability constants to be determined in solvents outside water or the usual aqueous solvent mixtures. Although we have applied the method only to anhydrous methanol, it should be applicable in any solvent system compatible with the Na$^+$-selective glass electrode.

We have used this new technique to complete the series of Na$^+$, K$^+$, NH$_4^+$, and Ca^{2+} binding constants (in anhydrous MeOH) for the 12- through 24-membered homologues of 18-crown-6. The binding constants do not obey the much publicized "hole-size relationship". Instead, for this group of crowns and cation, the strongest binding for each cation is observed with 18-crown-6 irrespective of diameter or charge. Further, it is found that K$^+$ is bound more strongly by all of the crowns than is any other cation in this group.

Acknowledgment. We thank the National Institutes of Health for grants (GM 29150, GM 29706, and GM 31846) that supported this work.

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Identification of the Gas-Phase Trimer $(CH_3)_2S{\cdot}(HF)_2$ by Photoelectron Spectroscopy

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Abstract: Analysis of the He I photoelectron spectrum measured for the binary intermolecular complex $(CH_3)_2S{\cdot}HF$ indicates the presence of another gas-phase species that is assigned as the trimeric system $(CH_3)_2S{\cdot}(HF)_2$. The first ionization energy of $(CH_3)_2{\cdot}(HF)_2$, measured at 10.3 eV, is higher than that for $(CH_3)_2S{\cdot}HF$, which is 9.5 eV. Molecular orbital calculations that suggest that $(CH_3)_2S{\cdot}HF$ has a nonplanar equilibrium geometry of C_s symmetry indicate that the addition of the second hydrogen-bonded HF moiety is achieved with little change in the structure of the dimer.

In a recent paper[1] we described how, on the basis of the He I photoelectron spectra measured for the dimeric complexes $(CH_3)_2O{\cdot}HF$ and $(CH_3)_2O{\cdot}HCl$, we were able to identify the weaker gas-phase complex $(CH_3)_2S{\cdot}HF$ from its He I spectrum. The measurements involved the use of a pinhole inlet system with high-pressure equilibrium mixtures of the respective monomer gases. A spectrum-stripping procedure that subtracts the appropriate monomer spectra is used to reveal the spectrum of the intermolecular complex.

An important aspect of this analysis concerns the effect of the intermolecular hydrogen bond in stabilizing the nonbonding n_s electrons of $(CH_3)_2S$ as indicated by a 0.8-eV increase in their vertical ionization energy (IE) on complexation. The appearance of this first ionization band of $(CH_3)_2S{\cdot}HF$ between the first and second bands of $(CH_3)_2S$ assisted in its identification. Molecular

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