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A Thallium NMR Determination of Polyether Cation Selectivity Sequences and Their Solvent Dependences

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Abstract: An NMR method of measuring the stability constants relative to the thallous ion of the univalent cations Li^+, Na^+, K^+, Rb^+, Cs^+, NH_4^+, Ag^+, and Tl^+ with the macrocyclic polyethers 15-crown-5, 18-crown-6, dibenzo-18-crown-6, and dicyclohexo-18-crown-6 in methanol, dimethylformamide, and dimethyl sulfoxide has been developed. The NMR method provides a convenient means of measuring the effects of solvation on the ion selectivity sequences of ionophores. The precision of the stability constant ratios obtained by the NMR method is about ±6%. The stability constants determined in methanol agree with those determined by ion-selective potentiometry. The complex between the thallous ion and 18-crown-6 has 1:1 stoichiometry in a variety of solvents. The effect of the solvents on the binding constants is discussed in terms of solvation of the ions and the crown ether. The chemical shift of the bound thallous ion is diagnostic of the ether oxygen donor atoms of the macrocycle.

The macrocyclic polyethers synthesized by Pedersen[1] have aroused much interest because of the high stability of the complexes they form with the alkali and alkaline earth metal ions.[2-20] Complexation of alkali and alkaline earth metal ions by crown ethers has been studied by ultraviolet spectroscopy,[2] solvent extraction,[2] ion-selective electrode potentiometry,[3] calorimetric measurements,[4] ^1H[5] and alkali metal[6-9] NMR spectroscopy, and ultrasonic absorption methods.[10-12] Reviews covering various aspects of ion binding by crown ethers have recently appeared.[13-20]

Because the complexing ability of alkali metal ions by the crown ethers is highly selective, the crown ethers have been used as models for macrocyclic antibiotics believed to be responsible for alkali ion transport across membranes.[21-25] The ion-selectivity sequences are explained as a superposition of the effects shown in eq 1,[15]

$$-RT \ln K = \Delta G_{\text{bind}} - \Delta G_{\text{solv}}(M^+) - \Delta G_{\text{solv}}(L) - \Delta G_{\text{conf}}(L) - \Delta G_{\text{solv}}(ML^+) \quad (1)$$

where K is the stability constant, i.e., the equilibrium constant for complexing, and the other terms are respectively the free energies of metal–ligand bonds, metal ion solvation, ligand solvation, ligand conformational changes, and solvation of the metal–ligand complex.

The stability constants should be strongly affected by the solvent because of the terms involving solvation of the ion and ligand. Previous measurements of the binding constants as a function of solvent have been restricted primarily to water and methanol because of the limitations in the methods of measurement. A knowledge of the direction and magnitude of the solvent effects is important for theoretical interpretations of ion selectivity and practical applications to synthesis and separations.

In this paper we develop, test, and apply a method of determining binding constants in a variety of solvents using the thallous ion NMR chemical shift. The thallous ion is a useful probe because its chemistry is very similar to that of the alkali metal ions,[26] it has spin $I = \frac{1}{2}$, and its chemical shift is extremely sensitive to its environment. For example, the solvent dependence of its chemical shift is over 2600 ppm[27] in contrast to a shift range of 8 ppm for ^7Li,[28-31] 30 ppm for ^{23}Na,[32-34] and 120 ppm for ^{133}Cs.[35] Because the chemical shift is often diagnostic of the environment of the thallous ion, the NMR method developed here has the potential of being able to determine the nature of the donor atoms of the binding ligand and some aspects of the geometry of the complex. In principle, the methodology described here could be applied using the NMR shifts of any of the alkali metal nuclei. In practice, severe quadrupolar broadening may strongly limit the applicability of alkali metal NMR. A preliminary communication of the method has been published.[36]

Experimental Section

Thallous perchlorate was obtained commercially and was recrystallized from deionized water and dried under vacuum before use. Thallous acetate and all other salts were dried under vacuum before use. Perchlorate salts were used for the studies in DMSO and DMF. Because of limited solubility of perchlorate salts in methanol, acetate salts were used for the studies in that solvent.

Dibenzo-18-crown-6, dicyclohexo-18-crown-6, and 15-crown-5 were purchased from Aldrich. 18-Crown-6 was purchased from PCR. Dibenzo-18-crown-6 was recrystallized from DMF and dried under vacuum over P_2O_5. Dicyclohexo-18-crown-6, 18-crown-6, and 15-crown-5 were dried under vacuum before use. Binaphthyl-2-crown-6 and the dicarboxylic derivatives were the generous gift of Professor Donald J. Cram of UCLA. The [222] cryptand was a gift from Professor J. M. Lehn of the University Louis Pasteur, Strasbourg, France.

The solvents were dried by refluxing over BaO or CaH_2 and distilled under reduced pressure just prior to use. DMF was refluxed over anhydrous $MgSO_4$ and distilled. No effort was made to exclude atmospheric moisture during sample preparation.

Computations were performed using the IBM 360/91 computer of the UCLA Campus Computing Network.

Instrumental. Spectra were obtained using an HR 60 modified with an external field/frequency proton lock. The lock signal is cyclohexane contained in a degassed and sealed capillary displaced along the z axis from the sample coils. The capillary dimension is 0.25 cm in outer diameter and about 2.5 cm in length. The lock channel frequency of 55.5 MHz is produced by a crystal and is modulated by a VFO. Maximum lock stability is obtained when the lock channel modulation is 1600 Hz. The observation channel frequency of approximately 32.0 MHz is produced by a frequency synthesizer and can be varied to cover the full ^{205}Tl chemical shift range. It is modulated by a second VFO; for Tl^+ the observation channel modulation frequency is 3000 Hz.

Samples were contained in 15 mm o.d. NMR tubes. Resonance signals in the presence of the crown ethers were all too broad for single scan detection at 0.1 M Tl^+ ion concentration. All spectra were recorded with at least 200 signal accumulations of successive scans through resonance via a computer of average transients (CAT). Chemical shifts are reported in ppm from the infinite dilution resonance of thallous formate in water.[27] Downfield shifts are positive. No bulk susceptibility corrections are made since these are estimated to be within the experimental error of the shifts.

Method of Calculation. The selectivity sequence of crown ethers toward a series of cations was measured by ^{205}Tl NMR. The sequences are determined quantitatively as the ratio of stability constants of Tl^+-crown to M^+-crown where M^+ represents a cation. The ratios are calculated by fitting the experimental shifts to the stoichiometric equilibrium expression by a method of successive approximations. For a 1:1 stoichiometry of both the Tl^+ and M^+ complexes, the overall competition for coordination is represented by eq 2, where I is the ionophore representing the crown ether,

$$Tl^+\text{-}I + M^+ \rightleftharpoons Tl^+ + M^+\text{-}I \qquad (2)$$

Because the activity coefficients of the species shown in eq 2 are unknown, the quantities reported in this paper are the concentration stability constant ratios and not the thermodynamic stability constant ratios. The concentration stability constant ratio is given by eq 3,

$$K^M/K^{Tl} = \frac{[Tl^+][M^+\text{-}I]}{[M^+][Tl^+\text{-}I]} \qquad (3)$$

If P is the population of Tl^+ in the uncomplexed or free form, then

$$[Tl^+] = P[Tl^+]_{tot} \qquad (4A)$$

and

$$[Tl^+\text{-}I] = (1 - P)[Tl^+]_{tot} \qquad (4B)$$

The concentration of the M^+-I complex is the total concentration of the ionophore minus the amount complexed to Tl^+ minus the amount that is uncomplexed. If the stability constants are large and/or the total concentration of ionophore is kept well below the total concentration of Tl^+ and M^+, the concentration of free, uncomplexed ionophore is small and can be neglected. The concentrations of M^+ and M^+-I are then,

$$[M^+\text{-}I] = [I]_{tot} - (1 - P)[Tl^+]_{tot} \qquad (5A)$$

$$[M^+] = [M^+]_{tot} - [I]_{tot} + (1 - P)[Tl^+]_{tot} \qquad (5B)$$

Substituting these expressions into eq 3 yields eq 6,

$$\frac{K^M}{K^{Tl}} = \frac{P\{[I]_{tot} - (1 - P)[Tl^+]_{tot}\}}{\{[M^+]_{tot} - [I]_{tot} + (1 - P)[Tl^+]_{tot}\}(1 - P)} \qquad (6)$$

Under conditions of fast exchange on the NMR time scale, the population of uncomplexed Tl^+, P, is calculated from the chemical shift information using eq 7,

$$P = (\delta - \delta_i)/(\delta_f - \delta_i) \qquad (7)$$

where δ is the chemical shift at the concentration of ionophore for which P is being calculated, δ_i is the chemical shift of the Tl-ionophore complex, and δ_f is the shift of the free or uncomplexed Tl^+.

In order to calculate a stability constant ratio, eq 6 was fit to the experimental data using a locally written program. The fitting procedure requires constant experimental values of $[Tl^+]_{tot}$ and $[M^+]_{tot}$ and fits eq 6 to the experimentally determined concentration $[I]_{tot}$ and chemical shift δ by successively varying δ_f and δ_i. The initial values of δ_f and δ_i are chosen as just outside the experimental range of δ values. Using these values and the experimental $[I]_{tot}$ and δ, the procedure calculates K^M/K^{Tl} for each experiment point, finds the average K^M/K^{Tl}, and then calculates a chemical shift for each experimental $[I]_{tot}$ based on this average K^M/K^{Tl}. The deviation between the experimental and calculated shifts is calculated. The procedure then increases by increments the complexed ion shift until the deviation is minimized. Then the solvated or free ion shift is stepped by one increment and the complexed ion shift is adjusted again until the minimum total deviation for the current adjusted value of the solvated ion shift is obtained. This last step is repeated until the best values of the solvated and complexed ion shifts are found based upon the minimum total deviation between calculated and experimental shifts. Local minima are avoided by repeating the procedure with a different size increment and by allowing the program to adjust the solvated and complexed ion shifts in the opposite direction. Several runs are made until the best result, based on the minimum standard deviation of chemical shifts, is obtained. In the initial run, a large increment of 10 ppm for both the solvated and complexed ion shifts is used. The final fitting is obtained with an increment of 1 ppm. The stability constant ratio for the fixed thallium and alkali metal ion concentrations is calculated on the basis of a fit to at least four experimental points. The calculations are then repeated for different combinations of thallium and alkali metal ion concentrations. Better fits are usually obtained when the experimental points are collected at low concentration ratios of crown to total metal ion concentration in accord with the assumption that the free crown concentration is negligible. The coefficients of variation of the stability constant ratio for the fixed thallium and metal ion concentration runs were 0.005 on the average.

The error analysis is based on artificially producing the maximum relative error in the population, P, used to calculate the stability constant ratio. The relative error in P, dP, is

$$\frac{dP}{P} = \frac{d\delta + d\delta_i}{\delta - \delta_i} + \frac{d\delta_f + d\delta_i}{\delta_f - \delta_i} \qquad (8)$$

The largest relative error in P is determined by adjusting the experimental values of the shifts, δ_f and δ_i. This can be accomplished by rotating the shift vs. concentration of ionophore curve first in one direction and then in the other by first adding the estimated deviation in δ (1.0 ppm) to the upper portion and then doing the reverse. The error analysis gives the largest possible error in the stability constant ratios which average to ±6%. The 1.0 ppm estimated deviation in δ encompasses the uncertainties in measuring the chemical shifts and in preparing solutions.

Table I. Stability Constants of Crown Ether-Cation Complexes Relative to That of Tl^+, K^M/K^{Tl} [a,d]

Crown	Solvent	Li^+	Na^+	K^+	Rb^+	Cs^+	NH_4^+	Ag^+
15C5[b]	DMSO	0.9	1.4	1.1	1.3	1.0	0.5	0.6
18C6	DMSO	<0.1	0.2	16.3 ± 1.7	8.8 ± 0.6	1.4 ± 0.1	0.4 ± 0.1	<0.1
	DMF		0.1	2.3 ± 0.3	1.4	1.0		
	MeOH		0.7	25.4 ± 2.6	3.5 ± 0.3	0.7 ± 0.1		
DB18C6	DMSO	0.1	5.4 ± 0.9	24.6 ± 3.7	5.3 ± 0.7	1.5	0.5 ± 0.1	0.4
	DMF		6.3	15.5 ± 1.8	2.8	0.8		
	MeOH		13.9	44.4 ± 5.8	5.3 ± 0.5	1.2		
DCH18C6[c]	DMSO	0.5 ± 0.4	0.1	11.0 ± 1.8	5.2 ± 0.5	2.1 ± 0.3	0.4	0.5

[a] All values are ±6% unless otherwise indicated. [b] The values for 15C5 are less accurate than the others because of difficulties in drying the crown. [c] DCH18C6 is a mixture of syn and anti isomers. The stability constant ratios were not determined for the individual isomers. [d] The relative stability constants are reported because they are the measured quantity using the NMR method. They can be converted to absolute stability constants when K^{Tl} is known. As discussed in the text, K^{Tl} can be measured directly using NMR only when $K^{Tl} < 10^3$. The only values directly measured in the work were those for DB18C6 in DMF at 29 °C where K^{Tl} = 280 L/mol and for binaphthyl-20C6 in DMF at 29 °C where K^{Tl} = 3.6 L/mol.

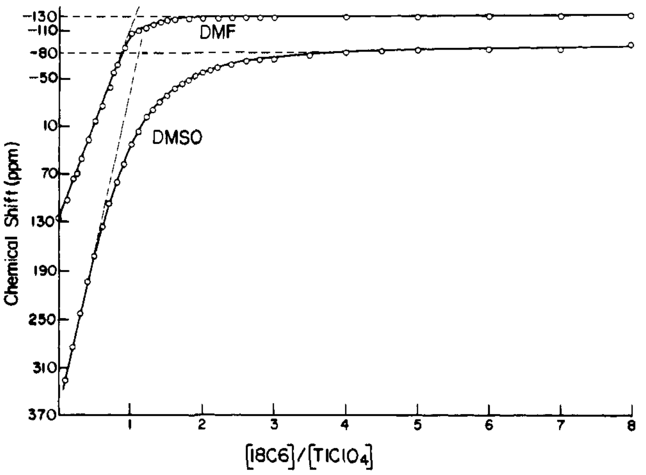


Figure 1. Chemical shift of ^{205}Tl vs. the $18C6/TlClO_4$ mol ratio in DMF (upper curve) and DMSO (lower curve). The concentration of $TlClO_4$ is 10^{-1} M.

The absolute value of the stability constant of a Tl^+-ionophore complex in the absence of M^+ can also be determined under certain conditions. For a 1:1 stoichiometry, the stability constant for Tl^+, K^{Tl}, is

$$K^{Tl} = \frac{1 - P}{P\{[I]_{tot} - (1 - P)[Tl^+]_{tot}\}} \tag{9}$$

The same type of fitting procedure is used. The total ionophore concentration can now take on any value since the assumption is no longer made that the concentration of free ionophore is negligible. The lower limit of the thallium ion concentration that can be used is about 0.10 M because of broadening of the resonance upon complexation. Because of this limitation, the stability constant of the Tl^+-ionophore complex in the absence of M^+ can only be measured when the constants are less than about 10^3 M^{-1}.

Results

(I) Stoichiometry. In order to use the NMR method to determine the binding constants and the selectivity sequences, the stoichiometry of the complex between the cation and the macrocycle must be known. Ion-selective electrode measurements in water and methanol have suggested that the complexes are 1:1 metal:macrocycle in those solvents.[3] The stoichiometry of the thallous ion-macrocycle complex can be determined in a variety of solvents by plotting the chemical shift as a function of the macrocycle concentration.

The plots of the thallous ion chemical shifts vs. the concentrations of the macrocycle are shown in Figure 1 for 18C6 in DMF and DMSO. In both cases the thallous ion resonance shifts upfield with increasing concentration of macrocycle with a break at a 1:1 mol ratio. No other break is found, indicating that if any 2:1 or other higher 18C6/Tl mol ratio complex formation occurs it is negligible. The more pronounced break in the DMF curve in Figure 1 compared to that in the DMSO curve is indicative of a stronger polyether complex formation in DMF than in DMSO. This result is consistent with previous studies of the solvation of the thallous ion which showed that DMSO is a more strongly solvating solvent.[37] Thus, the stability constant for complex formation in DMF is larger than that in DMSO.

The experimental value of the chemical shift of the bound thallous ion in the 1:1 complex can be obtained from the point of intersection between the linear extrapolation of the linear portions of the plot. In DMSO the chemical shift of the fully complexed thallous ion is −80 ppm and in DMF the shift is −130 ppm. The difference between the complexed ion chemical shifts is primarily due to the difference between the solvent and anion interactions in the vacant coordination site in the complexed species (vide infra).

Studies similar to those above were attempted in the more strongly coordinating solvents pyridine and ethylenediamine. In these solvents, the NMR line widths were extremely broad and at 0.01 M 18C6 became too broad to be measured. The broadening is consistent with a previously proposed model for the solvated species.[37]

The thallium NMR studies do not provide direct information concerning 2:1 or 1:2 complexes of the alkali metal ions. Good fits were obtained assuming 1:1 stoichiometry.

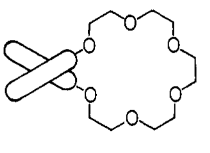
(II) Selectivity Sequences. The relative stability constants of the complexes of the alkali metal ions, silver ion, and the ammonium ion with four crown ethers in three different nonaqueous solvent systems are shown in Table I. These stability constant ratios relative to that of the thallous ion are calculated from the ^{205}Tl chemical shift as described in the previous section. The uncertainty in the stability constant ratio is less than ±6% of the value unless otherwise indicated.

The absolute values of the stability constants can be determined using the NMR method only if they are less than 10^3 L/mol. This upper limit arises from the lower limit on the thallous ion concentration that can be detected (about 10^{-1} M under the experimental conditions on our instrument) and the accuracy of measuring the macrocycle concentrations. At ambient probe temperature (29 °C) in DMF, the thallous ion-DB18C6 complex has a binding constant of 280 L/mol and the binaphthyl-20C6 (I) complex a binding constant of 3.6 L/mol. The complexes with 18C6 and with II have constants greater than 10^3 in both DMSO and DMF.

(III) Comparisons with Ion-Selective Electrode Values. The relative stability constants determined by NMR are compared to those obtained by ion-selective electrode potentiometry[3] in Table II. The values determined by the two methods are normalized to that of potassium ion to facilitate comparison. The

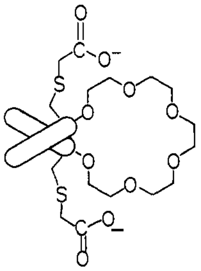
Table II. Comparison of Stability Constants Relative to that of K^+ in Methanol

Crown	Na^+	K^+	Cs^+	Method
18C6	0.030 ± 0.006	1.00 ± 0.2	0.026 ± 0.005	Tl NMR (this study)
	0.017 ± 0.003	1.00 ± 0.2	0.033 ± 0.007	Ion-selective potentiometry (ref 3)
DB18C6	0.31 ± 0.06	1.00 ± 0.2	0.027 ± 0.005	Tl NMR (this study)
	0.23 ± 0.04	1.00 ± 0.2	0.036 ± 0.007	Ion-selective potentiometry (ref 3)



Binophthyl-20-C-6

I



II

error limits for the ion-selective electrode values were taken from ref 3.

(IV) Concentration and Anion Effects. The effects of varying the thallium and potassium concentrations on the values of the relative stability constants are tested by independently varying the thallous ion and the potassium ion concentrations between 0.05 and 0.20 M. No systematic variations of the stability constant with changes in either the thallium ion concentration or the potassium ion concentration are found. The standard deviation of the stability constant ratios for the different concentrations is 1.09. The differences in the stability constants are not significant within experimental error. The effect of changing the anion from perchlorate to tetrafluoroborate is also insignificant within experimental error. We have previously found that solvation equilibrium constants are not changed within experimental error by changing the anion although the chemical shifts can be significantly affected. Within the concentration ranges studied, ionic strength and anion effects are insignificant within experimental error.

Using the potentiometric method,[3] Frensdorff found a variation of the stability constant from 14 to 44 L/mol with a change of the metal ion concentration from 1.0 to 8.2 mM for the complexation of sodium ion by DCH18C6 in water. The large variation was attributed to an unidentified competing or coupled equilibrium. However, only a slight variation in the equilibrium constant was observed at a constant sodium ion concentration as the crown ether concentration was varied.

(V) Chemical Shifts. The fitting procedure which is used to calculate the relative binding constants is also used to calculate the chemical shifts of the bound thallous ions in the 1:1 complexes and those of the free, solvated ion. The chemical shifts of the thallous ion bound to a crown ether are expected to be sensitive to the solvent and the anion because the crown ether only occupies the equatorial coordination sites of the cation. The chemical shifts of the free, solvated ion can be measured independently. The solvent dependence of the bound thallous ion chemical shift and the free ion values are given in Table III and compared with the independently measured free ion values.

The calculated chemical shifts of the solvated ion and the fully complexed ion are average values of all of the experimental determinations of relative binding constants using different cations. In the case of the calculated free ion chemical shifts, the values were independent of the competing cation and were all within 2 ppm of the average value. However, the calculated shifts of the complexed ion were strongly dependent on the competing cation and were spread out over a much larger range. For example, for 18C6 in DMSO, the calculated shifts of the complexed ion varied from −78 ppm with lithium as the competing cation to +87 ppm with cesium as the competing ion. In DMF the range varied from −250 ppm (K^+) to −110 ppm (Na^+) and in methanol it varied from −135 (Na^+) to −30 ppm (K^+).

Table III. Chemical Shifts of Tl^+-Crown Ether Complexes and of Solvated Tl^+

Crown	Solvent	Complexed ion shift[a]	Calcd solvated ion shift	Exptl solvated ion shift
15C5	DMSO	215	365	366
18C6	DMSO	−27	363	366
	DMF	−180	122	124
	MeOH	−70	500	512
DB18C6	DMSO	199	362	366
	DMF	−110	120	124
	MeOH	−35	497	512
DCH18C6	DMSO	113	364	366
[222]	DMSO	62		
	Pyridine	44		

[a] All values are calculated except those for [222].

When the ionophore totally occupies all of the coordination sites on the thallous ion, the solvent and anion effects would be expected to be much smaller and would arise from the effects of the secondary solvation sphere. Using the [222] cryptand, the effect of the solvent on the chemical shift was only 18 ppm as shown in Table III compared to 295 ppm for $TlClO_4$.[37]

Discussion

(I) Solvent Effects on the Binding Constants. Three solvents, DMSO, DMF, and methanol, were chosen for studies of the solvent effects on cation binding by crown ethers and a cryptate. These three solvents were chosen because they encompass a wide range of thallium-solvent interaction strength as measured by NMR[37] and because one of them is common to our NMR study and previous ion selective electrode studies[3] of cation binding. The solvating ability of the three solvents toward the thallous ion is DMSO > DMF > methanol with relative equilibrium constants of 3.6:1.0:0.34, respectively.[37]

The relative binding constants, given in Table I, are strongly affected by the relative solvating ability of the solvents. Two striking examples are Na^+ and Cs^+ with 18C6 and Na^+ and Rb^+ with DB18C6. In the former case, the relative binding constants of Na^+ and Cs^+ by 18C6 are about equal in methanol but differ by an order of magnitude in DMF. In the latter case, the relative binding constants of Na^+ and Rb^+ by DB18C6 are equal in DMSO but differ by over a factor of 2 in both DMF and methanol. The binding of the thallous ion relative to the other ions is also strongly affected. For example, with 18C6 in methanol, the thallous ion is more strongly bound than the cesium ion, while in DMSO, the cesium ion is more strongly bound than the thallous ion.

The effect of the solvent on the binding constants can, in principle, be quantitatively determined using eq 1. In practice, however, too many of the terms are unknown to allow quantitative treatments to be made. Even qualitative predictions of trends are sometimes difficult to make because the solvating strength of a series of solvents toward one cation may be different toward a second cation. Examples of reversals of solvating ability can be found between the thallous ion and the sodium ion.

In spite of these difficulties, certain trends in the data can be observed. The clearest example is provided by comparing binding constants in methanol, which is a poorly solvating solvent, with those in the more strongly solvating solvents, DMSO or DMF. In methanol, 18C6 binds Na^+ and Cs^+ ions equally and Rb^+ only slightly more strongly. In DMF, the solvation of the ions is much more important and probably follows the charge/radius trend of solvation $Na^+ > Rb^+ > Cs^+$. Thus, in DMF, the binding constants to the ionophore would be expected to be more widely separated, with sodium having a smaller value than rubidium. In addition, the binding constants of Rb^+ and Cs^+ to the ionophore would be expected to be much closer in magnitude to that of K^+ because the potassium ion should be more strongly solvated. Both of these trends are observed. Similar reasoning should apply to cation binding by DB18C6. In methanol, the observed order of the binding constants to the ionophore is $Na^+ > Rb^+ > Cs^+$. In the better solvating solvents, the binding constant of Na^+ would be expected to become smaller relative to those of Rb^+ and Cs^+ because the cation is more strongly solvated. Correspondingly, the binding constant of Rb^+ would be expected to become smaller relative to that of Cs^+. The measured binding constants support this reasoning. The relative values of the constants for Na:Rb:Cs are 11.6:4.4:1 in methanol, 3.6:3.5:1 in DMSO, and 7.9:3.5:1 in DMF.

A second trend which is observed in all three of the nonaqueous solvents and which may occur in water is the constancy of the order of the binding constants by a given crown ether and the changed order found for DB18C6 compared to the other ionophores. For 18C6, the observed order is $K^+ \gg Rb^+ > Cs^+ \gg Na^+$ in the three solvents studied here and in water.[3] (The position of Rb^+ is not known in water.) For DCH18C6 the observed order was almost identical in the one solvent studied here and in water:[3] $K^+ \gg Rb^+ > Cs^+ > Na^+$. In contrast, DB18C6 has a selectivity sequence $K^+ \gg Na^+ > Rb^+ > Cs^+$ in the three nonaqueous solvents. The differences in selectivities caused by the side chains have been previously suggested to result from differences in electrostatic and steric effects.[3] In addition, the side chains may play an important role in the solvation of the ionophore. These effects cannot yet be quantitatively analyzed.

The relative stability constants of the lithium, silver, and ammonium ions with all the polyethers studied here are small. In the case of Li^+, the small radius causes strong solvation and a poor fit in the cavity of the crown. The ammonium ion probably requires a tetrahedral coordination environment in order to be more strongly complexed than the thallous ion. Macrotetrolides such as nonactin and monactin, which can adopt a tetrahedral coordination configuration, form very stable complexes with NH_4^+.[39] The small stability constants for silver are not easy to rationalize. They may be related to either the preference of silver(I) for "soft" donor atom ligands such as sulfur[40-42] or to strong solvation of the silver ion by DMSO and DMF.

15C5 exhibits very poor selectivity toward the ions in Table I compared to those exhibited by the crown-6 ionophores. Similar poor selectivity was observed in water and methanol.[4,20,38] The poor selectivity and the low binding constants are generally agreed to result from the small polyether ring "hole size".

(II) Chemical Shifts of Bound Thallium. The thallium 205 chemical shifts of the thallous ion free in solution and fully bound to the ionophore are simultaneously determined by the fitting procedure when the stability constants are calculated. The chemical shift of the free, solvated ion can readily be compared with experimental NMR results as shown in Table III. The chemical shift of the free thallous ion is not very sensitive to the concentration of added alkali metal perchlorate salts and varies by a maximum of 2 ppm in the solvents and concentration ranges used in this study.[27] The chemical shift of the thallous ion bound to the ionophore is a more complicated quantity which can potentially give information about the binding site and geometry of the complex.

According to a recently developed model of the thallous ion chemical shift,[37] several predictions regarding the relationship between shift and the structure of the complex can be made. First, if the crown ether totally surrounded the thallous ion, the field would be roughly symmetrical and the chemical shift would be expected to be at the extreme shielded end of the shift range, i.e., close to −500 ppm. If the solvent or the anion can enter the primary coordination shell of the ion when it is complexed, significant metal p character could be mixed into the ground state and deshielding could occur. If the perchlorate anion were in the primary coordination shell, the shift would be expected to be in the same region as was found for the ion-paired thallous ion with ether oxygen donor atoms, i.e., around −100 ppm. If the solvent were in the primary coordination sphere, even more deshielding would occur. The value of the chemical shift would depend on the coordinating ability of the solvent and would be expected to occur downfield of the ether region, i.e., more positive than −100 ppm.

The solid state structures of Na^+/18C6,[18] Na^+/DB18C6,[43,44] Na^+/DCH18C6,[45] K^+/18C6,[18] and Rb^+/DB18C6[43] have been determined. The crown ether only occupies the equatorial coordination sites of the cation. Thus, the solvent and the anion should be able to interact with the metal in the axial positions and the chemical shifts of the bound thallous ion should exhibit solvent and anion dependences.

The average chemical shifts of the bound thallous ion, determined from all of the determinations of the binding constants for the alkali metals, silver, and ammonium, are shown in Table III. As expected, a strong solvent dependence is observed. All of the shifts are in the ether region or downfield from it. Thus, the shifts are consistent with a solution geometry similar to the solid state geometry with the anion and the solvent interacting with the thallous ion at the sites unoccupied by the crown ether. The amount of the anion which can interact with the bound thallous ion will depend upon the ion pairing equilibrium constant of the added alkali ion salt.

An independent method of determining the chemical shifts of the bound thallous ion is shown in Figure 1. The observed chemical shift is plotted as a function of the crown ether–thallous ion concentration ratio, and the chemical shift is extrapolated back to the 1:1 thallous ion-crown mole ratio. The chemical shifts determined in this way are −80 ppm for the bound thallous ion with 18C6 in DMSO and −130 ppm for the bound thallous ion with 18C6 in DMF. These values are in good agreement with the average values obtained from the fitting procedure. As was mentioned earlier, the chemical shift values obtained from the fitting procedure vary quite markedly with the competing anion. It is thus apparent that ion pairing, in addition to solvation of the cation, contributes to the bound chemical shift.

According to the model of the chemical shifts,[37] a thallous ion which is totally surrounded by the ionophore should exhibit a chemical shift indicative of the donor atoms of the ionophore independent of the solvent or anion. As a test of this idea, the chemical shift of the thallous ion bound to the [222] cryptand was measured. This ionophore has potential donor atoms consisting of two nitrogens and six ether oxygens. The observed chemical shifts, 62 ppm in DMSO and 44 ppm in pyridine, are in the expected region and are much less dependent on solvent than those for the crown ether complexes. The small solvent dependence probably reflects changes in the secondary solvation shell. Further studies are in progress using thallium NMR to measure these subtle effects.

The results of the chemical shift study of the bound thallous ion indicate that the use of the chemical shift to "fingerprint" the type of donor atoms binding the monovalent cation can be complicated by effects of the surrounding medium. However, the shifts in these studies provide qualitative structural information. The expected ether region is −80 to −170 ppm. The chemical shifts determined by the direct concentration study in Figure 1 are within this region as are many of the shifts determined by the fitting procedure. Furthermore, the trends in the shifts are indicative of the interactions. For example, the extent of the deviation from the ether region is dependent on how strongly the crown ether binds the thallous ion. The stronger the binding, the smaller the deviation from the expected region. In DMSO, for example, the deviation from the ether region decreases in the order 15C5 > DB18C6 > DCH18C6 > 18C6. This order is the same as that for increasing stability constants.

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Supplementary Material Available: A listing of $[Tl^+]_{tot}$, $[M^+]_{tot}$, $[I]_{tot}$, δ, δ_{calcd}, K^M/K^{Tl}, the standard deviation of the stability constants, and the standard deviation of the shifts (8 pages). Ordering information is given on any current masthead page.

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