Partition Coefficients and Equilibrium Constants of Crown Ethers between Water and Organic Solvents Determined by Proton Nuclear Magnetic Resonance

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The extraction of water by several crown ethers into chloroform + carbon tetrachloride mixtures has been investigated using a proton NMR technique. The equilibrium is well described by formation of a 1:1 water−crown complex in rapid exchange with uncomplexed ligand and water. The fraction (k) of crown ether complexed with water increases with crown cavity size, varying from (15 ±1)% for 12-crown-4 to (97 ± 5)% for 18-crown-6. Addition of carbon tetrachloride to chloroform lowers the k value for all crown ethers in equilibrium with water, and the value is close to zero in pure CCl_4. The partition coefficient follows the opposite trend: the amount of crown ether in the organic phase increases with the percentage of CCl_4 in this phase. The chemical shifts of free and complexed water also vary with solvent composition. Interaction of water with crown ether depends on solvation environment and may play a significant role in liquid−liquid extraction of metal ions using macrocyclic polyethers as extractants.

Introduction

Solvent extraction processes for the removal or separation of metal ions from aqueous solutions have been extensively studied using a variety of acidic, anionic, or neutral extractants.[1−6] Macrocyclic compounds, such as crown ethers and calixarene-crowns, are excellent neutral extractants with high efficiency and selectivity for a number of metal cations, including the alkali metal ions.[1,7−9] We are interested in the equilibria involved in the extraction of cesium ions from aqueous solution into a supercritical CO_2 phase, using crown ethers and calixarene-crowns. As part of this project, we are studying extraction of cesium salts into solvents of low dielectric constant, with solubility parameters in the range of possible solubility parameters for supercritical CO_2.[3] The equilibria of cesium salts with the above ligands have been studied extensively in organic solvents, usually with relatively high relative permittivity (>10).[10] In these studies, the specific role of the water which is dissolved in the organic solvents is generally not discussed in detail. In one study, it was noted that the description of the resulting equilibria must take into account the fact that the organic phase is saturated with water.[11] In a second study, it was found that the extraction efficiency of alkali metal ions increases with the solubility of water in the organic phase.[12] This is ascribed to increased solubility of the counteranion in the water-saturated organic phase. In another study,[13] the equilibrium constant between water and 18-crown-6 (18C6) has been determined in CCl_4 by FTIR. The effects of solvent polarity or crown ether cavity size have not been discussed. Neither was the partition coefficient.

For organic solvents with a high relative permittivity, equilibration of the solvent with water yields a water concentration in the solvent which is high compared to the typical concentrations of the extracting agents and the extracted ions. Therefore, the water concentration is relatively independent of the concentrations of these other components. By contrast, the solubility of water in chloroform (relative permittivity 4.8 at 20 °C) is about 0.06 $mol \cdot L^{-1}$ at normal ambient temperature, which is more comparable to the concentrations of other species extracted from a water phase. Water solubility varies from 0.02 to 0.2 $mol \cdot L^{-1}$ in supercritical CO_2, depending on the temperature and the pressure applied.

Proton nuclear magnetic resonance (NMR) is a very precise analytical technique for measuring the amount and chemical environment of water in organic solvents. Early NMR studies by de Jong et al.[14] and Golovkova et al.[15] have shown that various crown ethers interact with water to form 1:1 complexes in $CHCl_3$. An IR study by Moyer et al. has likewise demonstrated formation of a 1:1 water−crown ether complex in CCl_4.[13] A compilation of data for complexes of crown ethers with neutral molecules has been carried out by Izatt et al.[16]

The purpose of this paper is to determine the influence of solvent (mixtures of $CHCl_3$ and CCl_4) on those interactions using NMR techniques. These solvent mixtures cover a wide range of solvent parameters which are comparable to those of liquid and supercritical CO_2 at different densities. Some of the crown ethers used in this study are appreciably soluble in water, leading to their partitioning between the water and organic phases. NMR measurements also enable us to obtain partition coefficients of crown ethers between water and organic phases.

Experimental Section

The crown ethers dibenzyl-24-crown-8 (DB24C8), dicyclohexano-24-crown-8 (DCH24C8), dicyclohexano-18-crown-6 (DCH18C6), 12-crown-4 (12C4), 15-crown-5 (15C5), and 18-crown-6 (18C6) were purchased from Aldrich Chemical Co. and used without further purification. To carry out the NMR measurement, chloroform was used in its deuterated form (99.5% $CDCl_3$). The water phase contained 5% D_2O by volume.

Solutions of the crown ethers, in the concentration range (0.02 to 0.2) $mol \cdot L^{-1}$, in the $CDCl_3$ + CCl_4 mixtures were

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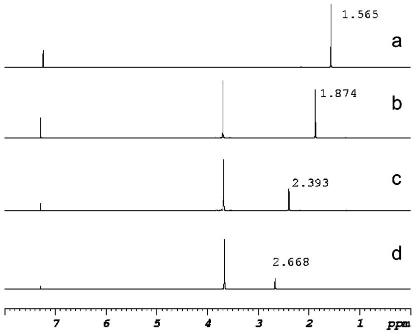

Figure 1. Typical NMR spectra of 18-crown-6 in the $CDCl_3$ phase. The concentrations of 18-crown-6 after equilibration with water are 0.00 M, 0.002 M, 0.075 M, and 0.153 M (from top to bottom) for the water peaks at (1.565, 1.874, 2.393, and 2.668) ppm, respectively.

equilibrated with an equal volume of the D_2O-enriched water by shaking with a wrist-type shaker for 2 h or more. The mixtures were then centrifuged for 1 h. The studies involving 15C5, 18C6, and DCH18C6 in solvents containing high percentages of CCl_4 required longer shaking time to get consistent data. Several shaking times (from 2 h to 24 h) were tested; after 12 h no change was observed. These procedures were conducted at ambient temperatures which were within the range (25 ± 1) °C.

NMR measurements for the solvent experiments were carried out using a 500 MHz Bruker DRX500 spectrometer. To obtain quantitative results, the pulse interval was set to 11.3 s (acquisition time 3.3 s, relaxation delay 8 s) and the pulse width was 30° (corresponding to a 2 μs relation time) in all systems (organic, aqueous, with or without chelator agent). Chemical shifts in the organic phase were calibrated by setting the chloroform chemical shift to 7.24 ppm. For the solvent mixtures containing CCl_4, the chloroform resonance shifts upfield (lower ppm) as CCl_4 is added. The magnitude of this effect was measured by comparing the solvent mixtures at constant field, that is, with the field lock turned off. The shift between 100% $CHCl_3$ and 25% $CHCl_3$ was 0.14 ppm. Therefore, an upfield correction was added for the mixed solvent samples run with a $CDCl_3$ field lock. The intensity (based on integrated area calculations for all data) of the water peaks in the NMR spectra was corrected for the 5% D_2O (by volume) present in the water phase. For the 100% CCl_4 mixture, an insert filled up with benzene-d_6 has been used as a reference for the intensity and the chemical shift, which was set at 7.15 ppm.

Typical NMR spectra for 18C6 in the $CDCl_3$ phase are shown in Figure 1. For the unsubstituted crown ethers, there is only a single resonance for the ring protons, generally in the region between (3 and 4) ppm. A singlet resonance for water appears at a chemical shift which moves downfield as the ligand concentration is increased. As noted above, the observed water and ligand resonances are averages which result from the rapid equilibrium between uncomplexed ligand and water and the complex $L\cdot H_2O_{(org)}$. Figure 1 shows the trend of the chemical shift for the water resonance associated with 18C6 concentration in $CDCl_3$. The concentration of the ligand in the organic phase has been corrected for its solubility in the aqueous phase on the basis of NMR measurements of its partition between the two phases.

The purities of the substituted crown ethers were assessed by determining the relative areas of the various resonances of the crown ethers, under conditions such that there is no overlap with the water peak. The ratios agreed with the theoretical values to better than 1%. All spectra were relatively free of artifacts, indicating a purity of crown ethers of 99% or better.

Calculations

The equilibrium model for the extraction is straightforward. Representing the crown ether ligand by L and the organic phase by (org), we have

$$H_2O_{(aq)} \leftrightarrow H_2O_{(org)} \qquad (1)$$

$$L_{(aq)} \leftrightarrow L_{(org)} \qquad (2)$$

$$H_2O_{(org)} + L_{(org)} \leftrightarrow L\cdot H_2O_{(org)} \qquad (3)$$

where $L\cdot H_2O_{(org)}$ represents a ligand−water complex. We define

$$K = [L\cdot H_2O_{(org)}]/\{[L_{(org)}][H_2O_{(org)}]\} \qquad (4)$$

to be the equilibrium constant corresponding to eq 3 on the basis of concentrations ([ ], in $mol\cdot L^{-1}$). Because of equilibrium 1, the concentration $[H_2O_{(org)}]$ is independent of the ligand concentration. Therefore, the ratio $[L\cdot H_2O_{(org)}]/[L_{(org)}]$ is independent of the ligand concentration. Likewise, k, the fraction of ligand molecules complexed to water as defined in eq 5 is independent of the ligand concentration.

$$k = [L\cdot H_2O_{(org)}]/\{[L_{(org)}] + [L\cdot H_2O_{(org)}]\} \qquad (5)$$

When $[L\cdot H_2O_{(org)}]$ is expressed in terms of $K[L_{(org)}][H_2O_{(org)}]$, the constant k is related to K by

$$k = K[H_2O_{(org)}]/\{1 + K[H_2O_{(org)}]\} \qquad (6)$$

The initial total ligand concentration $[L_{(init)}]^\circ$ is calculated from the total mass of ligand dissolved in a known volume of the organic phase during the preparation of the solutions. By material balance, at equilibrium

$$[L_{init}]^\circ = [L_{(aq)}] + [L_{(org)}] + [L\cdot H_2O_{(org)}] \qquad (7)$$

For the crown ethers containing additional organic groups (benzyl and cyclohexyl), the term $[L_{(aq)}]$, representing extraction of the ligand into the aqueous phase, is negligible. Because of the rapid exchange of complexed and uncomplexed water in the organic phase, only the totals

$$[L_{(org)}]^\circ = [L_{(org)}] + [L\cdot H_2O_{(org)}] \qquad (8)$$

and

$$[H_2O_{(org)}]^\circ = [H_2O_{(org)}] + [L\cdot H_2O_{(org)}] \qquad (9)$$

can be measured directly, where $[H_2O_{(org)}]^\circ$ and $[L_{(org)}]^\circ$ are the total concentrations of water (uncomplexed and complexed water) and ligand (free and complexed ligand) present in the organic phase, respectively.

When the material balance relations (eqs 8 and 9) are combined with eq 5, the linear relation

$$[H_2O_{(org)}]^\circ = k[L_{(org)}]^\circ + [H_2O_{(org)}] \qquad (10)$$

can be derived. According to eq 10, a plot of $[H_2O_{(org)}]^\circ$ versus $[L_{(org)}]^\circ$ should yield a straight line and the slope gives the value k. From k and $[H_2O_{(org)}]$, the equilibrium constant K can be obtained from eq 6.

As noted above, the equilibrium between $H_2O_{(org)}$ and $L\cdot H_2O_{(org)}$ determines the observed NMR chemical shift δ of

Table 1. Equilibrium and Chemical Shift Parameters of Various Crown Ethers[a]

crown	% vol $CDCl_3$[b]	k	K ($L \cdot mol^{-1}$)	$[H_2O]_{org}$[c]	D	δ_0/ppm	δ_1/ppm
12C4	100	0.15	2.78	0.065	0.25	1.55	3.0
	75	0.10	2.79	0.039	0.34	1.43	3.0
15C5	100	0.54	25.6	0.045	0.18	1.49	2.8
	75	0.35	19.9	0.027	0.29	1.40	2.7
	50	0.25	14.2	0.024	0.71	1.29	2.8
	25	0.21	35	0.008	2.13	1.11	2.0
	0			0.00[d]	2.450	1.36	
18C6	100	0.97	545	0.060	0.25	1.52	3.1
	75	0.79	102	0.037	0.42	1.40	2.8
	50	0.63	97	0.017	1.16	1.28	2.6
	25	0.61	141	0.011	3.83	1.08	2.2
	0			0.00[d]	48.04	1.31	
DCH18C6	100	0.70	32	0.072	0.00	1.52	3.3
	50	0.58	81	0.017	0.00[d]	1.25	2.6
	25	0.40	36	0.018	0.00[d]	1.13	2.6
DCH24C8	100	0.850	93	0.060	0.00[d]	1.57	3.2
DB24C8	100	0.37	9.03	0.064	0.00[d]	1.57	2.7

[a] Typical statistical errors (based on linear regressions): k, ±5%; K, ±10%; $[H_2O]_{org}$, ±0.003 $mol \cdot L^{-1}$; D, ±5%; δ_0, ±0.04 ppm; δ_1, ±0.3 ppm. [b] Volume percentage of $CDCl_3$ in CCl_4. [c] Concentration in moles per liter. [d] <0.01 for the ligand concentration range 0.02−0.2 $mol \cdot L^{-1}$.

water in chloroform. Denoting δ_0 = the chemical shift of pure water in the organic solvent and δ_1 = the chemical shift of complexed water, we have

$$(\delta - \delta_0)/(\delta_1 - \delta_0) = [L \cdot H_2O_{(org)}]/[H_2O_{(org)}]^\circ \qquad (11)$$

Combining eq 11 with eqs 6 and 8 and rearranging produces the linear relation between δ and $[L_{(org)}]^\circ/[H_2O_{(org)}]^\circ$

$$\delta = \delta_0 + k(\delta_1 - \delta_0)[L_{(org)}]^\circ/[H_2O_{(org)}]^\circ \qquad (12)$$

According to eq 12, δ_0 and δ_1 can be determined by linear regression once k is known.

The NMR data required for obtaining equilibrium (k and K) and chemical shift parameters (δ_0 and δ_1) are the intensities of the water and the ligand peaks ($[H_2O_{(org)}]^\circ$ and $[L_{(org)}]^\circ$) and the chemical shift (δ) of the water peak in the organic phase. For the NMR intensity measurements, the water peak in the aqueous phase or the $CHCl_3$ peak in the organic phase can be used as the reference. At 25 °C, the density of water is known and the concentration of 95% water by volume is 52.8 $mol \cdot L^{-1}$. Using the $CHCl_3$ peak as the reference, the amount of $CHCl_3$ in $CDCl_3$ must be known. The results represented in Table 1 were obtained using the water peak as the reference. A few experiments were done by adding a known amount of $CHCl_3$ to $CDCl_3$ as the reference. The results are consistent with those obtained using the water peak as the reference within the experimental uncertainty. The intensities of the ligand peaks in the aqueous phase were also measured to evaluate their partition coefficients (D) and for correction of ligand concentrations in the organic phase.

It should be noted that eq 12 differs from the classic complex equilibrium equations derived from the work of Benesi and Hildebrand[20] and Deranleau,[21] which are derived for a single-phase system containing two interacting components. As pointed out in the Calculations section, because of equilibrium 1, $[H_2O_{(org)}]$ is constant. As an incidental consequence, $[H_2O_{(org)}]^\circ$ cannot go to zero. This enables an extrapolation of eq 12 to zero ligand concentration to get the value of δ_0. Also, two separate quantities $[H_2O_{(org)}]^\circ$ and $[L_{(org)}]^\circ$ appear which vary together, since increasing $[H_2O_{(org)}]^\circ$ increases $[L_{(org)}]^\circ$. Unlike the case in the previous work, none of the individual species can be measured.

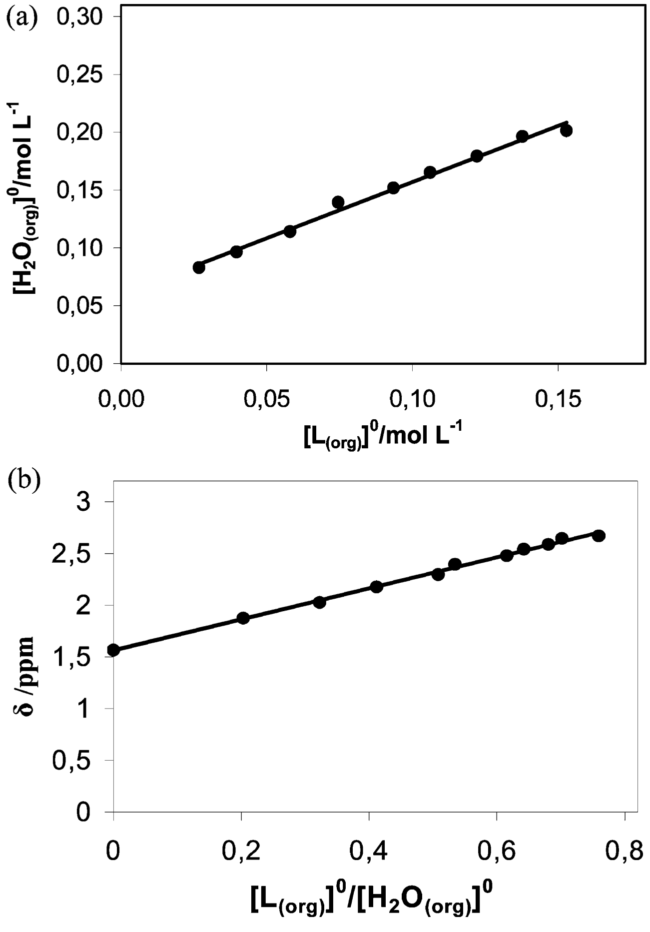

Figure 2. Linear relationship between (a) the total water and 18-crown-6 concentrations in chloroform ($[H_2O_{(org)}]^\circ = 0.9704[L_{(org)}]^\circ + 0.0601$; correlation coefficient $r = 0.9955$) and between (b) the observed chemical shift of water and the ratio $[L_{(org)}]^\circ/[H_2O_{(org)}]^\circ$ in chloroform (eq 7) ($\delta = 1.5015[L_{(org)}]^\circ/[H_2O_{(org)}]^\circ + 1.5611$; $r = 0.9982$).

Results and Discussion

Parts a and b of Figure 2 show plots based on eqs 10 and 12, respectively, for 18C6 in $CDCl_3$. Results for the other ligands are similar. The linear relations obtained in every case verify that the water−ligand equilibrium is well described by formation of a 1:1 complex. Figure 2a yields a slope of 0.970 ± 0.04 (corresponding to k) and an intercept of 0.060 ± 0.003 (corresponding to $[H_2O]_{org}$) based on our regression analysis ($R^2 = 0.991$) and according to eq 10. The free (uncomplexed) water dissolved in chloroform is about 0.06 $mol \cdot L^{-1}$ for the $H_2O + CDCl_3 + 18C6$ system at room temperature (25 ± 1) °C. This value is confirmed by the analysis of a solution of water saturated chloroform-*d*. The concentration of the total water in the organic phase, $[H_2O]_{org} + L \cdot [H_2O]_{org}$, depends on the ligand concentration as shown in Figure 2a. About 97% of the ligands in the organic phase are complexed with water. The intercept of Figure 2b gives the chemical shift of uncomplexed water in chloroform $\delta_0 = (1.56 \pm 0.02)$ ppm. From the slope of Figure 2b, the chemical shift of the water complexed with 18C6 in $CDCl_3$, δ_1, was calculated to be (3.1 ± 0.3) ppm.

Results for the equilibrium and NMR chemical shift parameters for the six crown ethers studied by this work are summarized in Table 1. In $CDCl_3$, the *k* values for unsubstituted crown ethers 12C4, 15C5, and 18C6 are 0.15, 0.54, and 0.97, respectively. This trend shows strong binding of water for 18C6 relative to the smaller rings. Substitution in crown ethers tends to lower the *k* value. Thus, for DCH18C6, the *k* value in chloroform is lowered to 0.70 compared with a value of 0.97 for the unsubstituted 18C6. In the case of DCH24C8 and DB24C8, benzyl substitution further lowers the *k* value compared with cyclohexyl substitution in 24C8. The equilibrium constant (K) defined by eq 4 varies from 2.78 for 12C4 to 545 for 18C6 in chloroform. The *K* value for the substituted (DCH18C6) crown is much lower than that of the unsubstituted (18C6) one (32 versus 545). The δ_0 values for the three unsubstituted crown ethers are approximately constant (in the range 1.53 ± 0.04 ppm), as expected. Considering the experimental error, the δ_1 value is stable.

For the individual ligands, there are several clear trends with respect to the variation of solvent composition ($CDCl_3 + CCl_4$). First, the amount of free water dissolved in the organic phase decreases with increasing CCl_4 fraction in the solvent. This is expected, since decreasing the solvent polarity should result in lower solubility of water in the organic phase. In all cases, the parameter *k* representing the fraction of ligand bound to water also decreases monotonically as the proportion of CCl_4 increases. Thus, decreasing solvent polarity also reduces water−crown complexation $[L \cdot H_2O_{(org)}]$, leading to lower *k* values. This is probably caused by the combination of a lower solubility of free water in the organic phase and intrinsic solvation effects on the crown−water complex. The equilibrium constant *K*, which includes the concentration of unbound water and the ligand in the mixed organic phase, changes less and in an irregular fashion. Because both $[H_2O]_{org}$ and $[L]_{org}$ vary drastically with the solvent composition, the *K* values defined by eq 4 are not as useful as the *k* values for discussion in the $CHCl_3 + CCl_4$ system. In the binary solvent systems, $[H_2O]_{org}$ decreases with increasing CCl_4 fraction whereas $[L]_{org}$ changes independently in the opposite direction, resulting in irregular trends for the *K* values.

From the crown ether NMR peak intensities in the organic and in the aqueous phases, we also calculated the partition coefficients $D = [L_{(aq)}]^\circ/[L_{(org)}]^\circ$ as shown in Table 1. The *D* values for 12C4 and 18C6 between water and chloroform are around 0.25, and that for 15C5 is somewhat lower. For the crown ethers that are appreciably soluble in water, the partition coefficients show that extraction into the aqueous phase increases exponentially as the organic solvent polarity decreases. In the case of 18C6, the *D* value starts at 0.25 in 100% $CHCl_3$, becomes 1.16 with a 50:50 mixture of $CHCl_3$ and CCl_4, and rises up to 48 for a 100% CCl_4 solution (Figure 3). For the substituted crown ethers DCH18C6, DCH24C8, and DB24C8, the *D* values are below detection (<0.01) in the concentration range (0.06 to 0.2) $mol \cdot L^{-1}$. Partitioning of 18-crown-6 between water and various organic solvents has been determined by several different methods including gravimetric and conductivity measurements.[17−19] NMR actually provides a simple and rapid method for determination of crown ether partition coefficients between water and organic solvents. The *D* values given in Table 1 represent the first systematic measurements of such data using a NMR technique.

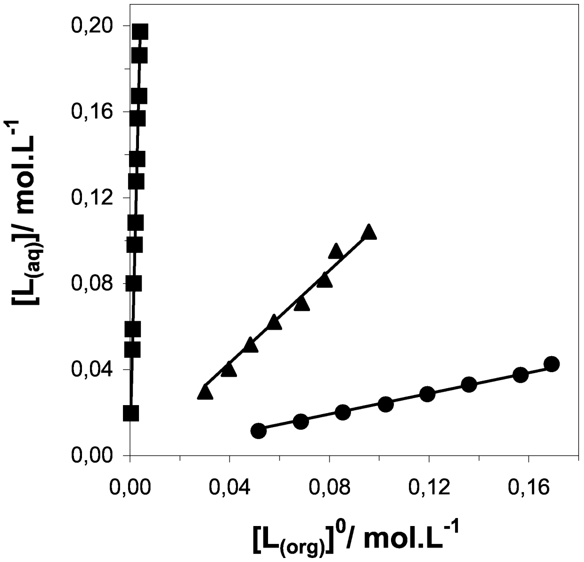

Figure 3. Determination of the partition coefficient for 18-crown-6 in (●) $CDCl_3$, (▲) 50% $CDCl_3 + CCl_4$, and (■) CCl_4.

The NMR studies performed by Golovkova et al.[15] in $CDCl_3$ investigated several compounds also covered in our work (15C5, 18C6, and DCH18C6). In their work, single-phase measurements were made with a constant water concentration and varying ligand concentrations. Analysis was based on the chemical shift employing eq 11. The chemical shift δ_1 for the pure complex $L \cdot H_2O$ was determined by extrapolation to infinite ligand concentration. Their results for *K* deviate widely from ours, sometimes by an order of magnitude. We feel that their extrapolation method is subject to considerable error because (1) the dependence of the chemical shift on ligand concentration is nonlinear and, (2) on the basis of the δ_1 values we obtained, the range of concentrations they employed was insufficient. Our calculational method involved only the use of linear regression analysis; thus, it is more accurate.

The chemical shifts δ_0, representing isolated water molecules in the organic solvent, can be measured by equilibrating the organic solvent with pure water. For 18C6, the δ_0 values decrease from 1.56 ppm in pure chloroform to 1.08 ppm in the $CHCl_3 + CCl_4$ mixture with 25% $CHCl_3$ by volume. Similar trends are observed for the other crown ether systems. For 15C5 and DCH18C6, the δ_0 values decrease, respectively, from 1.49 ppm to 1.52 ppm in pure chloroform and from 1.11 ppm to 1.08 ppm in the $CHCl_3 + CCl_4$ mixture with 25% $CHCl_3$ by volume. Those results follow the general trend of an upfield shift for water in solvents of decreasing polarity. The values of δ_0 and δ_1 in Table 1 were found using a linear regression plot of δ versus $[L_{(org)}]^\circ/[H_2O_{(org)}]^\circ$ according to eq 12 and using the *k* values predetermined. Those results agree well with preceding measurements involving no crown ethers.

δ_1 represents the chemical shift of water in the crown−water complex. The error on δ_1 values includes the error on k; therefore, the δ_1 value is less accurate than the δ_0 one. In the 18C6 series, δ_1 decreases monotonically with decreasing solvent polarity from 3.1 ppm in pure chloroform to 2.2 ppm in the $CHCl_3 + CCl_4$ mixture with 25% $CHCl_3$ by volume. The trends of δ_1 for the other crown ethers are less clear. Generally, there is an upfield shift as the solvent polarity decreases. This does not seem obvious, however, for the weakly binding ligands 12C4 and 15C5.

Complexation of water with crown ether depends strongly on the nature of the solvents. The difference in solvation environment of chloroform and carbon tetrachloride is reflected in the degree of crown−water complexation and the chemical shifts of free water and the crown−water complex described in this NMR study. Interaction between water and crown ether is likely to affect complex formation of the crown ether with metal ions during liquid−liquid extraction. Crown ethers have been extensively investigated for selective extraction of the alkali metal and the alkaline earth metal ions from aqueous solutions. The solvation effects of water and solvent molecules on metal−crown complexation are not well understood. NMR studies may provide very useful information for understanding such interactions. Solvation effects can be studied using different conventional solvents. Conventional solvents offer discontinued changes in solvation environment and often involve other variables that are difficult to control experimentally. Further studies of water−crown interactions in a system with a tunable solvation environment, supercritical fluid carbon dioxide, are currently in progress in our laboratory.

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