Solvent Effects on Crown Ether Complexations[1]

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A comprehensive study of complexation between potassium salts and 18-crown-6 in 14 different solvents shows stability constant K increases by $>10^4$ from water to pure methanol or to propylene carbonate (PC), with constants increasing in the order H_2O < HMPT < DMSO < DMF < MeCHOHMe < MeCN < Me_2CO < MeOH < PC. The mostly calorimetrically determined thermodynamic values of complexation between metal ion m and ligand l (ΔG_{ml}, ΔH_{ml}, ΔS_{ml}) are compared with a large range of available solvent properties. Linear correlations (with coefficients $R \approx >0.95$) are obtained for ΔG_{ml} with standard Gibbs transfer energies $\Delta G°_t$ of the metal ion from water to the given solvent. Analyses of literature data with some other cations and ligands, including the [222] cryptand, also revealed , that the complexation constant changes are essentially a linear function of the cation desolvation free energies. Less meaningful correlations ($R \approx <0.9$) are obtained with values characterizing the electron donor capacity of the solvent. Parameters characterizing the solvent polarity, such as E_T, are extremely poor descriptors ($R = 0.3$) of the medium effects. In binary dioxane−water mixtures ΔG_{ml} and even ΔH_{ml} correlates well with the vol % of water, or with corresponding solvophobicity parameters S_p ($R = 0.97$). The reaction enthalpies ΔH vary much more than ΔG, for instance from 12 kJ/mol (in MeCN) to 68 kJ/mol (in Me_2CHOH), without meaningful correlations to known solvent properties, or between ΔG and ΔH. An exception is the correlation of ΔH with the solvent polarity index π^* (with $R = 0.996$, if MeCN is excluded). Solvent effects on the ligands are studied by NMR in view of the possible geometry changes of crown ethers from oxygen-in (with aprotic solvents) to oxygen-out (with water) conformations of the macrocycles. Preliminary NMR results, however, point to similar oxygen-in conformations in water as well as in chloroform, in line with molecular mechanics calculations.

Introduction

Solvents are known to have a profound effect on the stability of supramolecular complexes. Cram has pointed out early[2] that the preorganization principle indeed includes minimization also of solvation energy changes during complexation. Literature data on crown ethers show that stability constants K can vary over many orders of magnitude with the medium. The orders of stabilities do not at all conform to usual expectations, based e.g. on solvent polarities. This is evident with K^+/18-crown-6 in methanol showing the most extreme K increase by 10^4 compared to water, with factors of only around 10^2 to 10^3 for dimethylformamide, or for 2-propanol (see below). It even has been postulated that uncomplexed crown ethers may be present in an oxygen-out conformation if they are exposed to water.[3]

Wipff et al.[4] have aptly reviewed MM and MD calculations of solvent effects on ionophore complexes and have stressed the significance of solvent-induced structural reorganization of also the free ligand. MD calculations also indicate the special role of water in solvating ligand sites, as well as a second shell binder to a cation. On the other hand, the applied force fields do not yet allow prediction of the relative free complexation energies in different solvents; they even predict *de*complexation of some highly charged ions[4] which are known experimentally to complex quite efficiently.

We have undertaken a systematic evaluation of medium effects on crown ether complexes also with the aim to arrive at practically useful predictions of stabilities on the basis of sound experimental data. This should extend our approach to predict stabilities from empirical increments which are taken from electron donor factors ED on the basis of many hydrogen bonded associations measured in carbon tetrachloride.[5,6] We also present preliminary NMR studies on possible structural changes of the ligands in water and in chloroform as solvent.

The literature[7] contains a wealth of data on crown ether complexes in various solvents, although to the best of our knowledge no attempt has been made until now to describe the change of stability constants comprehensively for a large number of solvents by a single parameter. Selected systems were reported to show direct[7d−f] or inverse[7g,h] correlations with Gutmann donor number (DN) of solvents. Other correlations were described with polarity,[7i] permittivity,[7j] solvation ability,[7k] Kirkwood parameters,[7l] and dieelectric constants.[7k] Generally, one finds as expected an increase of complex stabilities in organic solvents, which is also reflected in binary mixtures with water.[7] Abraham et al.[8ab] have analyzed the different contributions of ligand, ion, and complex sol-

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vation on the basis of extensive studies of solution enthalpies in water and in methanol. The enthalpy data obtained from direct measurements agreed well with those derived from the corresponding thermodynamic cycle.[8a] In line with more recent MM and MD calculations[4] it was concluded that the central metal is still in contact with the solvent, not only in crown ether,[8b] but even in cryptand[8a] complexes.[8c] In contrast, earlier studies, based e.g. on partial molal volume and compressiblity changes concluded,[8d] that e.g. 18C6 screens the potassium ion well from water. The unknown partial resolvation processes in the complexes make the analysis of the single contributions from ion and ligands on the basis of the corresponding thermodynamic cycle difficult. Instead, we set out to describe the medium effect by as few parameters as possible.

Unfortunately, many literature data show discrepancies which led us to remeasure many equilibria under well defined conditions. Thus, for the potassium/18-crown-6 complex the reported values are log $K = 5.93$ vs 6.66 in MeOH, or 1.83 vs 2.27 in H_2O, or 4.49 vs 6.3 in MeCN[7] at 298 K. As salt we used potassium thiocyanate as this turned out to be enough soluble and stable in many different media (Table 1). 18C6 as host and the potassium ion as guest was chosen in view of the perfect fit between hole size (1.385 Å[9]), and guest diameter (1.38 Å[10,11]). Calorimetry was used for the determination of all thermodynamic parameters which may give further informations on the origin of medium effects. Furthermore, this method is applicable to a wide range of solvents, and has until now not been used comprehensively for all the media used in the present investigation. The chosen anion may affect the observed sensitivities of complexation constants against solvent changes, as suggested in particular for aprotic media by MD calculations.[4] Preliminary studies with DMSO, however, indicate that a change from ClO_4^- to Cl^- as anion changes log K only by 0.3 units.

Table 1. Stability Constants and Thermodynamic Parameters (kJ/mol) for 1:1 Complexation of KSCN with 18C6 in Different Solvents at 298 K[a]

no.	salt	solvent	lg K[b]	$-\Delta G$	$-\Delta H$	$T\Delta S$
1	KSCN	H_2O	1.98	11.3	24.7	−13.4
	KCl	H_2O	1.98[c]	11.3[k,d]		
2	KSCN	MeOH	>5.7		54.7[c]	
	K^+	MeOH	6.07[21]	34.6[21]	56.8[21]	−22.2[21]
3	KSCN	i-PrOH	4.92	28.1	68.1	−40.0
4	KSCN	MeCN	5.52[f]	31.5[g]	15.9	15.6[g]
5	KSCN	Me_2CO	>5.7		50.2	
	$KClO_4$	Me_2CO	5.89[22]	33.6[22]	50.9[22]	−17.4[22]
6	$KClO_4$	PC	6.24[23]	35.6[23]		
7	KSCN	DMF	4.19	23.9[h]	36.8[i]	−12.9[g]
8	KSCN	HMPT	3.24	18.5	37.4	−18.9
	KSCN	HMPT (M_2L)[1]	4.90	27.9	40.7	−12.8
9	KSCN	DMSO	3.35[f]	19.1[g]	27.6[i]	−8.5[j]
10	KSCN	$C_4H_8O_2 + H_2O$ (2:8 v/v)	2.47	14.1	24.7	−10.6
11	KSCN	$C_4H_8O_2 + H_2O$ (4:6 v/v)	3.01	17.2	27.1	−9.9
12	KSCN	$C_4H_8O_2 + H_2O$ (6:4 v/v)	3.59	20.5	31.7	−11.2
13	KSCN	$C_4H_8O_2 + H_2O$ (8:2 v/v)	4.21	24.0	37.6	−13.6
14	KSCN	$C_4H_8O_2 + H_2O$ (19:2 v/v)[m]				
15	$KClO_4$	MeCN	>5.7		11.7	

[a] Thermodynamic values are given for reaction: $M^+ + L = ML^+$, where M^+ is cation and L is ligand. The concentration unit is mol/L in log K calculations. log K and ΔH values were determined using the calorimetric titration technique. Abbreviations: DMF, *N*,*N*-dimethylformamide; HMPT, hexamethylphosphoric triamide; DMSO, dimethyl sulfoxide; $C_4H_8O_2$, dioxane; PC, propylene carbonate. [b] Values are averages taken from two to three determinations. Unless noted, uncertainties are given as standard deviations: in log K 0.05; in ΔG 0.3; in ΔH 0.2; in $T\Delta S$ 0.4; otherwise: [c] 0.02. [d] 0.1. [e] 1.0. [f] 0.15. [g] 0.8. [h] 0.6. [i] 0.5. [j] 0.9; solvent parameters see supporting information (Table 1). [k] Potentiometric titration. [l] Values log β, ΔG, ΔH, and $T\Delta S$ are given for the complexation: $2M^+ + L = M_2L^{2+}$. [m] Anion SCN^- was decomposed in $C_4H_8O_2 + H_2O$ (19:1 v/v) media.

Experimental Section

18C6 was purified by sublimation vapor crystallization at 290 K from samples melting at 330 K. KSCN was analytical grade and was dried in vacuo for 20 h, raising the temperature from 293 K to 330 K. Analytical grade $KClO_4$ was used without additional purification. Solvents were analytical grade and were purified as described in the literature.[10] Acetonitrile was dried over P_2O_5; the water content was monitored by IR (ν(OH) at 3450−3600 cm^{-1}). Water was double distilled.

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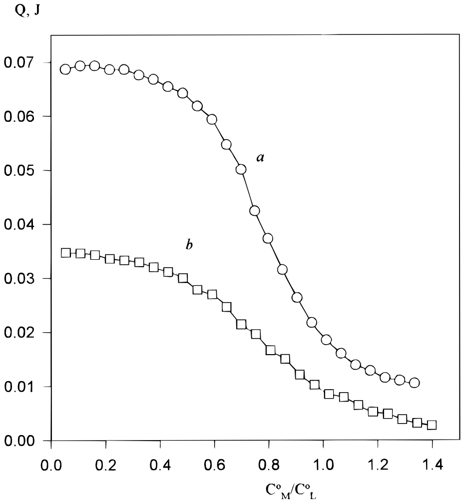

Figure 1. Calorimetric titration curves for the complexation of 18C6 with KNCS in DMSO at 298 K. Interaction heat *Q* (J) vs the reagents concentration ratio $C°_M/C°_L$. Experimental data: salt solution ($C°_M$ 0.2256 M (*a*,*b*) and ΔV 0.0106 (*a*), 0.0053 mL (*b*) for each point) was added into the ligand solution ($C°_L$ 0.0222 M (*a*), 0.0111 M (*b*) and V_o 2.00 mL (*a*,*b*)).

Calorimetric measurements were performed at 298.15 K as described earlier[7c,12] with a LKB microcalorimetry system (Model 2107/112). Typical titration curves are given in Figure 1.

Potentiometric titrations of 18C6 with KSCN in H_2O were carried out at 298 K and at constant ionic strength of 0.025 M NMe_4Cl, using an Orion 901 potentiometer and a solid state potassium selective electrode (from Moscow Institute of General and Inorganic Chemistry). The electrode response in pure H_2O was 53.0 mV. Typically, two different titrations were used to detect the formation of all possible complexes: (a) A solution of an appropriate salt (0.1−0.4 M, 0.01 mL for each titration point) was titrated into a ligand solution (0.005−0.02 M, 2 mL initial volume) until the total concentration of the salt was about two times larger than that of the ligand. (b) A solution of 18C6 (0.1−0.4 M, 0.01 mL for each titration point) was titrated into a cation solution (0.005−0.02 M, 2 mL initial volume) until the total concentration of the ligand was about twice as large as that of the salt.

Concentrations used in the different experiments are described in Table 2 of the supporting information.

The reproducibility of the determinations as judged from two calorimetric titrations (KSCN + 18C6 in H_2O) is within 0.05 (standard deviation) for log *K*, or 0.2 kJ/mol for ΔH, or 0.4 kJ/mol for $T\Delta S$. Standard deviations obtained from curve fitting are given in Table 1. Furthermore, the calorimetrically determined values for the reaction between 18C6 and K^+ in H_2O at 298 K ($\lg K = 1.98$ and $\Delta H = -24.7$ kJ/mol) were close to those obtained from potentiometric data ($\lg K = 1.98$), as well as to published[13] calorimetric data ($\lg K = 2.03$, $\Delta H = -26.0$ kJ/mol). For the complexation of 15-crown-5 with KI in MeOH at 298 K values log K_1 3.46(0.05), ΔH_1 −29.6(0.3) kJ/mol, log K_2 2.49(0.05), and ΔH_2 −36.9(0.5) kJ/mol were obtained from calorimetric data of this work for $M^+ + L = ML^+$ and $ML^+ + L = ML^+_2$ reactions, respectively; published calorimetric data for the 15C5/KI/MeOH system are the following: log K_1 3.35, ΔH_1 −32.6 kJ/mol, log K_2 2.65 and ΔH_2 − 36.8 kJ/mol.[13c]

Table 2. Solvent Effects on NMR Shifts of Crown Ethers 18C6 and Me-18C6a

	18C6			Me-18C6[b]	
	D_2O	$CDCl_3$		D_2O	$CDCl_3$
^{13}C	69.30	70.46	C-2	73.80	74.57
			C-3	74.13	75.05
			C-18	66.82	68.13
			Me	14.60	16.29
			C-n[b,c]	69.19	70.15
^1H	2.69	2.71	H_3A	3.53	3.47
			H_3B	3.59	3.53
			Me	1.18	1.13

[a] In ppm vs external TMS measured at 0.05 M concentration at 300 K. [b] Numbering for Me-18C6 starts at O atom 1. [c] Unresolved signals all other carbon atoms.

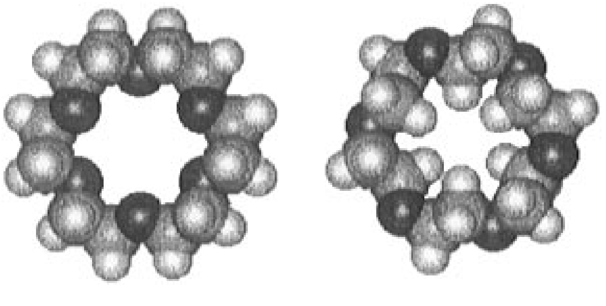

Figure 2. Conformations **1i** and **1o** of 18C6 with oxygens in and out, respectively, from CHARMm simulations.

Stability constants and reaction enthalpies were calculated from experimental titration curves using the multipurpose computer program CHEM-EQUI.[7c] The program is written in FORTRAN 77 and/or PASCAL and can be used with MS DOS on any PC 386 or higher. The nonlinear least-squares fitting program uses several algorithms for minimization including gradient, simplex, as well as Monte-Carlo methods. (The program is available from Dr. V. P. Solov'ev at IPAC). With the exception of HMPT as solvent, where there is a small contribution of a M_2L complex, the fit was perfect with a 1:1 calculational model (ML).

NMR Measurements. NMR-measurements were carried out on a 500 MHz spectrometer Bruker-DRX-500 using D_2O and $CDCl_3$ as solvents; for measuring conditions see Table 2. Assignments for the monomethyl crown ether Me-18C6 were secured by COSY 45, HETCOR, and NOESY experiments.

Results and Discussion

A thermodynamic cycle describes the free energy of complex formation in solution (ΔG_{tml}) as a function of ΔG_{gml} in the gas state, of $\Delta G_{\mathrm{msolv}}$ (desolvation of metal cation), of $\Delta G_{\mathrm{lsolv}}$ (desolvation of the ligand), and of $\Delta G_{\mathrm{mlsolv}}$ (solvation of the complex):

$$\Delta G_{\mathrm{ml}} = \Delta G_{\mathrm{gml}} - \Delta G_{\mathrm{msolv}} - \Delta G_{\mathrm{lsolv}} + \Delta G_{\mathrm{mlsolv}} \quad (1)$$

We first address the possible conformational changes of the ligand in different solvents. Figures 2 and 3 illustrate the alternative conformations **1o** and **1i** with oxygen atoms out or in, respectively, as proposed earlier[3] for 18C6 in alternatively hydrophilic or lipophilic solvents. Computer-aided molecular modeling shows that the oxygen-out geometry **1o** indeed cannot be dismissed entirely: the relative strain energy for **1o** is only 3.7 kJ/mol higher than that for **1i** as calculated with the Hyperchem MM+ forcefield, using charges calculated with AM1. NMR is the method of choice for establishing such differences of crown conformations, but has been rarely used for this until now. The NMR shifts of 18C6 (Table 2) show only a difference below 0.015 ppm for the

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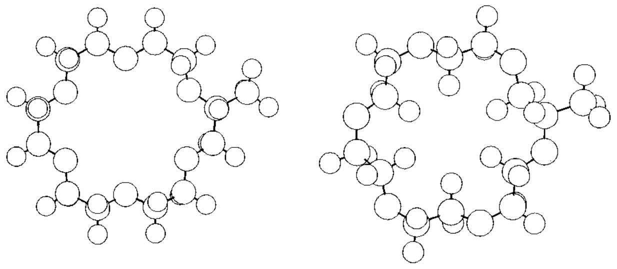

Figure 3. Conformations of methyl-18C6 with oxygens in and out, respectively, from CHARMm simulations.

CH protons, and 1.2 ppm for the ^{13}C signals between D_2O and $CDCl_3$ as solvent. In order to observe not only 1 signal, we have also analyzed the shift changes with the monomethyl crown ether. Molecular mechanics simulations establish that the additional methyl group, which was introduced to relieve the symmetry of the unsubstituted 18C6, can be accommodated in pseudoequatorial positions (Figure 3) with a concomitant strain increase below 6%. This agrees with the complexation energies observed between Me-18C6 and KCl in water, showing differences to the unsubstituted 18C6 in $\Delta\Delta G$ below 6%. Unfortunately, even 2D NOESY spectra of Me-18C6 were too complex with too many overlapping signals for safe interpretation. However, the very small observed shift changes between $CDCl_3$ and D_2O as solvents found also with Me-18C6 (Table 2) rule out the conformational changes predicted in the literature,[3] although no data for shift differences between alternative *anti* O−C−C−O conformations (for the O-*out* structure), and *gauche* arrangements (for the O-*in* structure) are available. However, related structures with X−C−C−X arrangements in well defined antiperiplanar (diaxial) or gauche (diequatorial) cyclohexane conformations are known for X = Hal.[14] They invariably show for the gauche fragments ^{13}C NMR shifts which for the functional C_α are higher by approximately 5 ppm, for the C_β even by about 10 ppm. The much smaller shielding variations observed with the crown ethers are only consistent with the presence of the *same* basic conformation in all solvents, which for enabling complexation must be the oxygen-*in* structure **1i** also in water. We also note, that complexation with K^+ leads to shift change below 0.1 ppm both in MeOD and D_2O (Table 2). In conclusion, there is no evidence for significant conformational reorganization upon complexation, which otherwise would lead to a decrease of the free energy of complexation by a concommitant build-up of strain.

As with earlier studies on solvent effects on supramolecular equilibria[15,16] the most direct approach to quantification is the comparison of complexation energies with established solvent properties. Table 3 shows the result of correlations for a range of potentially usable medium properties. It is gratifying that quite satisfactory descriptions (with linear correlation coefficients $R > 0.9$) are obtained even with single properties like ΔG°_t, *b*, C_a, or, to a lesser degree, with Gutman donor numbers DN (Figure 4, parts a−d). These all characterize the electron-donating capacity of the medium. Correlations with a smaller number of solvents tend to be better, as seen with β values, or C_a values if restricted to the same five solvents as with the β values (see Table 3).

Table 3. Correlations of log *K* with Different Solvent Parameters for K^+-18C6 Complexation[a]

no.	prop.	*R*	*F*	SD	*N*	*A* (Δ*A*)	*B* (Δ*B*)	systems in Table 1
1	ΔG°_t	0.960	58.3	0.401	7	5.13 (0.40)	0.115 (0.039)	2,4−9
2	*b*	0.941	31.1	0.482	6	8.2 (1.8)	−5.5 (2.7)	2,4,5,7−9
3	ΔH°_t	0.943	23.9	0.484	5	9.2 (2.7)	0.150 (0.098)	2,4,6,7,9
4	C_a	0.904	26.7	0.558	8	7.9 (1.5)	−1.27 (0.60)	2−9
5	DN	0.897	24.8	0.760	8	8.3 (2.0)	−0.156 (0.076)	1,2,4−9
6	*g*	0.738	8.35	1.080	9	7.1 (2.2)	−0.69 (0.57)	1−9
7	*e*	0.403	1.36	1.464	9	5.8 (2.8)	−0.030 (0.062)	1−9
8	E_T	0.298	0.68	1.527	9	7.6 (8.8)	−0.06 (0.18)	1−9

[a] Coefficients A and B with random errors (Δ*A* and Δ*B*) for 95% confidence interval for equationlog $K = A + BX$, were X = solvent property; R = linear correlation coefficient; F = Fisher's criterion; SD = standard deviation; N = number fo points, as identified in Table 1. Names of solvent properties: ΔG°_t ΔH°_t standard free energy and enthalpy transfer of the potassium cation from water to the given solvent. [b] Basicity constant; C_a: H-bond acceptor factor; DN: Gutman Donor Number; *g*: surface tension coefficient; *e*: dielectric constant; E_T: Dimroth−Reichardt polarity parameter.[24]

The best correlation with $R = 0.96$ for the K^+/18C6 system, however, exists with the standard Gibbs transfer energies ΔG°_t of the potassium cation from water to the given solvent[17] which were recently reviewed by Marcus and Gritzner.[18] These ΔG°_t values essentially represent the ΔG_{msolv} factor in eq 1, although some cation solvation may also occur in the complexed state. Obviously no extra term is needed to account for ligand solvation/desolvation changes with the medium. This is in line with the much larger solvation contributions of charged species as compared to the electroneutral ligands, and as well with the absence of significant solvent-induced conformational changes in the ligand.

Other solvent properties which, like the Dimroth−Reichardt factor $E_{T,}$ characterize polarities show ***no*** ($R < 0.3$, see Table 3), or poor, correlations. This is in line with their poor correlations with cation ΔG°_t values. Multiple correlations with more than one parameter do not show any significant improvement (see Table 2, supporting information).

Measurements in binary solvent mixtures can also be correlated, in the absence of suitable ΔG°_t parameters e.g. with the solvophicity parameter S_p[19] (Figure 4e). Decomposition of the salt prevented the study in pure dioxane; the observed linear dependencies (Figure 4e), however, allow us in such cases to extrapolate to solvents which are not accessible to direct measurements. However, extrapolations to neat solvents like dioxane are less reliable in view of the lack of experimental data for corresponding ΔG_t values and of the expected large increase of tight ion pairing in aprotic solvents.

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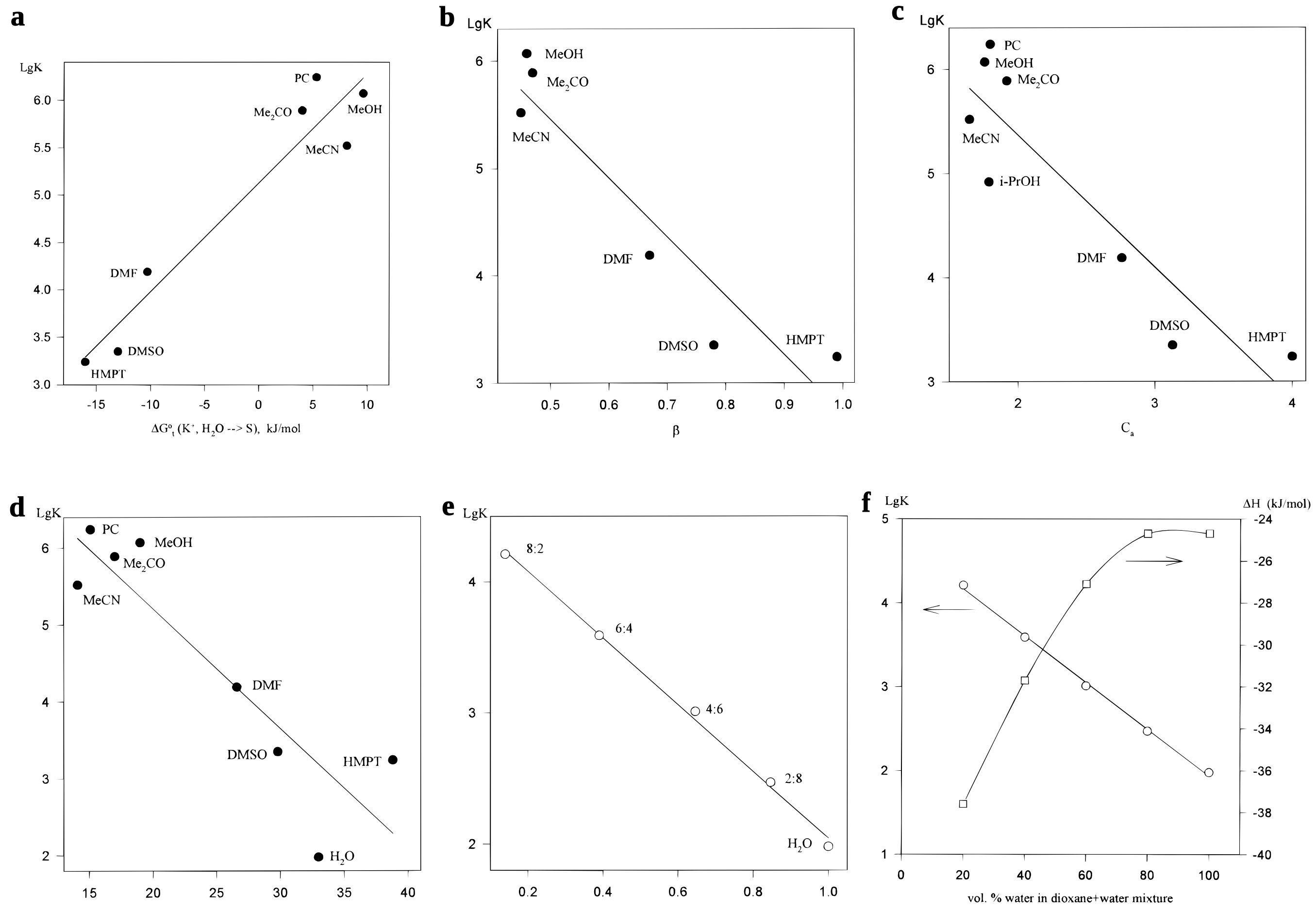

Figure 4. (a) Plot of log K versus free energy of transfer ΔG°_{t} (K^+, $H_2O \rightarrow S$) for the complexation of K^+ with 18-crown-6 in several pure solvents. (b) Plot of log K versus solvent basicity constant β for the complexation of K^+ with 18-crown-6 in several pure solvents. (c) Plot of log K versus solvent H-bond acceptor factor C_a for the complexation of K^+ with 18-crown-6 in several pure solvents. (d) Plot of log K versus Gutman Donor Number DN for the complexation of K^+ with 18-crown-6 in several pure solvents. (e) Plot of log K versus solvophobicity parameter S_p for the complexation of K^+ with 18-crown-6 in dioxane−water mixtures ($C_4H_8O_2$:H_2O v/v). (f) Plot of K and ΔH versus vol % water for the complexation of K^+ with 18-crown-6 in dioxane−water mixtures.

The enthalpies ΔH_{ml} show much larger variations than the ΔG_{ml} values (Table 1). The enthalpies obtained in pure solvents correlate with the solvent polarity index π^* as follows: $-\Delta H = 101.7(6.4) - 72.7(7.7)^*\pi^*$ with $R = 0.996$; $F = 584.9$; SD = 1.6; $N = 7$, however, only if MeCN is excluded. That MeCN does not fit is to be expected in view of its strong interaction with 18C6.[20−25]

In contrast to log K the ΔH values in binary dioxane−water mixtures show poor correlations to S_p, or to vol % (Figure 4f) which are almost linear[19] in S_p values: $\Delta H = -38.5(4.9) + 15.4(7.2)^*S_p$ with $R = 0.969$, $F = 46.3$, SD = 1.6, $N = 5$.

This is in contrast to available data for hydration of ions which generally shows smaller differences between ΔG and ΔH.[18] The data in Table 1 indicate that as expected the complexation is invariably accompanied by sizeable entropy disadvantages; these often amount to 50% of the ΔH gained by the complex formation.

After finding that all medium effects on complexes of K^+ and 18C6 can be quantitatively described by the dependence of the cation K^+ transfer energies ΔG_t from water to a given solvent, we explored whether similar correlations hold for other cations and ligands. Although the number of reliable data from the literature is limited to not as many solvents as in Table 1, we again find gratifyingly linear correlations (Table 4), indicating that the cation ΔG_t values indeed allow to prediction of medium effects for all kind of electroneutral ligands, including cryptands. Unfortunately, for some cations such as Rb^+ or Cs^+, there is a lack of accurate ΔG_t parameters in the literature.

A different solvent effect may be expected by contributions of complexes other than the ML associations with a 1:1 stoichiometry. The latter model gave a satisfactory fit for calorimetric titrations with all solvents except HMPT. Here, a sizeable contribution of a M_2L (2:1) complex was observed, which is in line with the superior electron-donating capacity of this solvent, allowing for extra stabilization of only two partially complexed cations, which are more exposed to the solvent.

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Table 4. Correlations (lg $K = A + B\Delta G°_t$) for the Complexation of Crown Ethers and Cryptand (222) with Metal Cations in Different Solvents[a]

no.	ligand	cation	solvent set	*R*	*F*	SD	*N*	*A* (Δ*A*)	*B* (Δ*B*)	ref
1	18C6	Na^+	MeOH, MeCN, PC, DMF, DMSO	0.964	39.5	0.53	5	3.31(0.77)	0.122(0.062)	25
2	18C6	K^+	MeOH, MeCN, Me_2CO, PC, DMF, HMPT	0.960	58.3	0.40	7	5.13(0.40)	0.115(0.039)	b
3	B18C6	Na^+	MeOH, MeCN, PC, DMF, DMSO	0.988	81.4	0.24	4	3.55(0.62)	0.106(0.051)	7
4	B18C6	K^+	MeOH, MeCN, PC, DMF, DMSO	0.984	91.5	0.26	5	4.57(0.38)	0.117(0.039)	7
5	DB18C6	Na^+	MeOH, MeCN, PC, DMF, DMSO	0.998	786.2	0.11	5	3.45(0.16)	0.112(0.013)	25
6	DB18C6	K^+	MeOH, MeCN, PC, DMF, DMSO	0.980	72.7	0.30	5	4.06(0.43)	0.119(0.044)	25
7	DB21C7	K^+	MeOH, Me_2CO, PC, MeCN, DMF	0.947	26.2	0.32	5	3.60(0.51)	0.104(0.065)	7a
8	DB24C8	K^+	MeOH, Me2CO, PC, MeCN, DMF	0.949	27.3	0.31	5	2.98(0.49)	0.103(0.063)	7a
9	DB30C10	K^+	MeOH, DMSO, PC, MeCN, DMF	0.941	23.3	0.49	5	3.53(0.70)	0.111(0.073)	7a
10	222	Li^+	MeOH, MeCN, $MeNO_2$, PC	0.999	793.5	0.22	4	1.86(0.92)	0.203(0.031)	26
11	222	Na^+	MeOH, EtOH, MeCN, PC, DMF, DMSO, $MeNO_2$	0.937	35.7	1.06	7	7.4(1.2)	0.182(0.78)	26
12	222	K^+	MeOH, EtOH, MeCN, PC, DMF, DMSO, $MeNO_2$	0.914	25.3	0.86	7	9.44(0.910)	0.143(0.073)	26
13	222	Ag^+	MeOH, EtOH, MeCN, PC, DMF, DMSO, $MeNO_2$	0.941	38.6	1.41	7	12.7(1.4)	0.162(0.067)	26

[a] Coefficients *A* and *B* with random errors (Δ*A* and Δ*B*) for 95% confidence interval are given for equationlog $K = A + B\Delta G°_t$, where R = linear correlation coefficient; F = Fisher's criterion; SD = standard deviation; N = number of points (solvents), $\Delta G°_t$ = standard free energy transfer of the metal cation from water to the given solvent. [b] log *K* values from Table 1.

Conclusions

We believe we have given for the first time a quantitative and empirically derived description of the influence of many different solvents on a crown ether and related complexes based on a single solvent parameter. Often in real chemical systems only empirical parameters give satisfactory correlations of practical use, in contrast to fundamental properties. The discovered simple correlation with free energies $\Delta G°_t$ of the cation alone in a given solvent will allow to prediction of complex stability changes for a wide range of media and of cations. The results lead to the conclusion that contact of the complexed cations with the solvent is largely reduced in comparison to the free state before complexation. The possible change of ligand conformations with the solvent has been checked for the first time by NMR methods, although less symmetric ligands should in the future allow better insight into the underlying geometries, based mostly on NOE measurements.

A variation of the present approach will be necessary if one wants to predict solvent effects on complexes with ionophores bearing charges close to the complexed ion,[26,27] or with those where geometrical mismatch[5,6] will lead to larger differences also in ligand solvation. With extremely hydrophobic solvents such as chloroform associations, constants may in comparison to water (Table 1) increase by a factor of 10^9, as judged from extraction constants;[28] such lipophilic media may in the future be correlated by measurements in binary solvent mixtures.

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Supporting Information Available: Figures 5−16: Correlations of equilibriumlog *K* vs free energies ΔG_t of transfer of metal cations to a given solvent (similar to Figure 4a) for different metal ions and ligands; see Table 4 and text for explanations and correlation parameters; Table 1 with concentrations used in the calorimetric titrations; Table 2 with results from multiparameter correlations (14 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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