Crown Ether–Ammonium Complexes: Binding Mechanisms and Solvent Effects

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Thermodynamics of 18-crown-6 complexes with ammonium cations (NH_4, $MeNH_3$, Me_2NH_2, Me_3NH, Me_4N, Et_4N, $PhNH_3$, and $PhCH_2NH_3$) in methanol were determined by titration calorimetry. The results show strong contributions from entropy terms counteracting the enthalpy of complexation, and a linear decrease of the complexation free energy ΔG with the number of available N–H hydrogen bonds. In several cases formation of relatively strong complexes containing two ammonium ions per crown unit was observed. Tetramethylammonium ions show no detectable association with the crown ether, demonstrating the absence of significant Coulomb-type interaction between the partial charges at the crown ether oxygen and the N$^+$–C–H atoms. Ammonium ions bind to *aza* crown ethers with almost equal affinity as to the *all*-oxygen anologs only, if methyl groups at the nitrogen atoms force the lone pairs into equatorial position. Molecular mechanics calculations (CHARMm) of corresponding gas-phase complexes yield geometries and energies in agreement with this, with energetically equally good conformations of an essentially undistorted D_{3d} crown accepting either 3 linear hydrogen bonds, or 6 bifurcated bonds from the primary ammonium cations. Complexation equilibria were measured with $PhNH_3$, and $PhCH_2NH_3$ in water, 2-propanol, *tert*-butyl alcohol, *n*-octanol, DMF, DMSO, pyridine, HMPT and acetone mostly by calorimetry, in some cases by potentiometry. The observed association constants varied by factors of up to 1000; the solvent effects can be described generally as a linear function of the hydrogen bond accepting power of the solvent molecules, in line with the mechanisms derived above. The lg$K$ and ΔH values of the complexation of the $PhNH_3$ or $PHCH_2NH_3$ cation with 18-crown-6 ligand are compared with a large range of available solvent properties. The best correlations ($R \approx 0.9$) for lg$K$ (or ΔG) are obtained with values characterizing the electron donor capacity of the solvent (C_a, β*, DN) for lg$K$, as found earlier for complexes between K$^+$ and 18C6.

Introduction

The complexation of ammonium compounds with crown ethers has been studied very early[1] and forms the basis of many promising applications.[2] Calorimetric measurements, which are also the basis of the present work, have already provided much insight into the dominating binding contributions.[3] Thus, the complexation of primary protonated amines has been shown to be due mostly to an enthalpic driving force, which is set off by negative $T\Delta S$ values, reducing the total free energy ΔG by usually 50% in polar solvents. This seems to be even more so for secondary amines, although less data are available for these. Most of the available data stem from measurements in methanol. The extraction methods often used early,[2a] essentially reflect complexation in the chloroform phase, but are difficult to compare to true equilibrium constants in homogenous phase. Studies with a variety of other solvents such as nitrobenzene, acetonitrile, *N,N*-dimethylformamide[4] or in mixed solvents such as $MeOH/H_2O$[4c] and $CD_3OD/CDCl_3$, including also aqueous systems,[4d] have already shown a strong variation of binding constants. The only correlation between solvent properties and binding affinity reported[4a] until now was that with Gutman donor numbers for a limited range of solvents (nitrobenzene, acetonitrile, *N,N*-dimethylformamide). In a comprehensive study of medium effects on crown ether−metal ion complex stabilities we found[5] that Gutman donor numbers provided correlations of lesser quality than those with some other solvent parameters. In the present paper we describe solvent effects on ammonium complexes on a broader basis, including the calorimetric evaluation of enthalpic versus entropic changes.

We also wanted to explore the possibility to predict ammonium complex stabilities with empirical free energy increments, using a strategy which was successfully for alkali metal ion complexes[6] within limitations given by steric[7] or stereoelectronic[8] factors. Such correlations also shed light on the binding mechanisms in the complexes; linear correlations within one series indicate that the underlying mechanism does not change significantly. The noncovalent bonds between protonated nitrogen groups and crown ethers have been attributed early to hydrogen bonds between the ^+N-H groups and the lone pairs of the oxygen and/or nitrogen atoms in the ligand.[1] For the solid state this is supported by several X-ray studies, showing usually a tripod arrangement of three close to linear $^+N-H\cdots O$ bonds.[9−13] Bifurcated hydrogen bonds have also been located. The complex stability dependence on the number of available NH protons, going from primary to tertiary protonated amines, support that the number of hydrogen bonds is decisive.[3j,10]

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Results and Discussion

The complexation of seven different ammonium salts with 18C6 was studied mostly by titration calorimetry in a series of solvents (Tables 1−5), with methods described before.[5,7,8] The lg$K$ values obtained in selected cases also by titrations with ion-selective electrodes showed satisfactory agreement with ΔG from calorimetry and with literature data, where available. Somewhat larger differences were only found with ΔH for $BzNH_3Cl$/18C6 in MeOH, or with lg$K$ and ΔH for $MeNH_3Cl$ and Me_2NHCl/18C6 in MeOH.

Table 1. Stability constants and thermodynamic parameters [kJ/mol] for 1:1 (M/L) complexation of benzylammonium chloride ($BzNH_3Cl$) (M) with 18-crown-6 (L) in different solvents at 298 K[a,b]

Entry	Solvent	lg$K$	$-\Delta G$	$-\Delta H$	$T\Delta S$
1	H_2O	1.44[c]	8.2[d]	6.5[e]	1.7[f]
2	MeOH	4.22	24.1	43.2	−19.1
		4.37(0.17)[q]	[q]	47.7(0.9)[q]	−2.9(1.8)[q]
	MeOH	4.43 (ISE)	25.3 (ISE)	−	−
3	*i*PrOH	4.14	23.6	50.0[g]	−26.4[g]
4	*t*BuOH	2.79[h]	15.9[f]	52.8[i]	−36.9[i]
5	OctOH	3.25[h]	18.6[f]	43[j]	−24.4[k]
6	DMF	2.50[d]	14.3[g]	36[l]	−22[i]
7	Py	2.34[d]	13.4[g]	22.0[m]	−9[m]
8	DMSO	1.34[c]	7.6[d]	31.3[n]	−23.7[n]
9	HMPT	[o]	−	−	−
10	Me_2CO	[o]	−	−	−
11	MeCN	[p]	−	−	−

[a] Concentration unit for lg$K$: mol/l. lg$K$ and ΔH values from calorimetric titrations. Abbreviations: *i*PrOH, 2-propanol; *t*BuOH, *tert*-butyl alcohol; OctOH, 1-octanol; DMF, *N*,*N*-dimethylformamide; Py, pyridine; DMSO, dimethyl sulfoxide; HMPT, hexamethylphosphoric triamide. − [b] Thermodynamic values are given for the (1:1) reaction $M^+ + L = ML^+$, where M^+ is the cation and L is the crown ether ligand. Unless noted, uncertainties are given as standard deviations: in lg$K$ 0.10; in ΔG 0.6; in ΔH 1.5; in $T\Delta S$ 1.6; otherwise: [c] 0.04; [d] 0.2; [e] 0.3; [f] 0.4; [g] 1.0; [h] 0.07; [i] 2.3; [j] 1.3; [k] 1.4; [l] 2.0; [m] 3.5; [n] 0.6. − [o] Titration heat effect unsufficient for measurement. − [p] Solubility of the salt too low for calorimetric titration. − [q] Ref.[7]; ISE, lg$K$ and ΔG values were obtained from potentiometric measurements using a potassium-ion-selective electrode.

Table 2. Stability constants and thermodynamic parameters [kJ/mol] for 1:1 (M/L) complexation of phenylammonium chloride ($PhNH_3Cl$) (M) with 18-crown-6 (L) in different solvents at 298 K[a,b]

Entry	Solvent	lg$K$	$-\Delta G$	$-\Delta H$	$T\Delta S$
1	H_2O	1.77[c]	10.1[d]	1.0[e]	9.1[d]
	H_2O	1.49[f] (ISE)	8.5[e] (ISE)	−	−
2	MeOH	3.76	21.5	40.2	−18.7
		3.85(0.21)[m]	[m]	41.6(0.3)[m]	−19.7(0.8)[m]
		3.80(0.03)[n]	21.7[n]	39.9(0.6)[n]	−18.2[n]
3	*i*PrOH	3.50[f]	20.5[e]	42.0	−22.0[g]
4	DMF	2.03[c]	11.6[d]	19.7[h]	−8[i]
5	DMSO	1.53	8.7	4.5	4.2
6	Me_2CO	2.30	13.1	18.7[j]	−6[j]
7	HMPT	[k]	−	−	−
8	MeCN	[l]	−	−	−

[a,b] ISE: See footnotes to Table 1. Unless noted, uncertainties are given as standard deviations: in lg$K$ 0.20; in ΔG 1.1; in ΔH 1.5; in $T\Delta S$ 1.9; otherwise: [c] 0.15; [d] 0.9; [e] 0.5; [f] 0.1; [g] 1.6; [h] 2.0; [i] 2.2; [j] 7.0. − [k] Titration heat effect not sufficient for measurement. − [l] Solubility of the salt too low for calorimetric titration measurements. − [m] Ref.[7] − [n] Ref.[3f,3g,3h]

Table 3. Stability constants and thermodynamic parameters [kJ/mol] for 1:1 (M/L) complexation of ammonium cations $NH_{4-n}Me_n^+$ ($n = 0-4$) and Et_4N^+ (M^+) with 18-crown-6 (L) in MeOH at 298 K[a,b]

Entry	Salt	lg$K$	$-\Delta G$	$-\Delta H$	$T\Delta S$
1.	NH_4Cl	3.84	21.9	40.0	−18.1
		4.27[c]	24.4[c]	38.8[c]	−14.4[c]
		4.32[d]	24.7[d]	39.6[d]	−14.9[d]
2.	$MeNH_3Cl$	3.98[e]	22.7[f]	49[g]	−26[h]
		4.25[c]	24.3[c]	44.8[c]	−20.5[c]
3.	Me_2NH_2Cl	1.43[i]	8.2[j]	32.1[k]	−23.9[k]
		1.76[c]	10.0[c]	27.9[c]	−17.9[c]
4.	Me_3NHCl	0.4	2.3	19.3	−17.0
5.	NMe_4Cl	[e]		[e]	
6.	Net_4Cl	[e]		[e]	

[a,b] See footnotes to Table 1. Unless noted, uncertainties are given as standard deviations: in lg$K$ 0.25; in ΔG 1.4; in ΔH 2.0; in $T\Delta S$ 2.5; otherwise: [e] 0.38; [f] 2.2; [g] 4.3; [h] 4.8; [i] 0.02; [j] 0.1; [k] 0.8. − [c] Ref.[3i,3f] − [d] Ref.[3k] − [e] Heat effect too low for measurement.

Table 4. Stability constants and thermodynamic parameters [kJ/mol] for 2:1 (M/L) complexation of benzylammonium chloride ($BzNH_3Cl$) (M) and phenylammonium chloride ($PhNH_3Cl$) (M) with 18-crown-6 (L) in different solvents at 298 K[a]

Solvent	lg$K$	$-\Delta G$	$-\Delta H$	$T\Delta S$
Benzylammonium chloride as guest				
MeOH	5.7[c]	32.5[d]	12.0[e]	20[d]
*i*PrOH	6.56[f]	37.4[g]	51[h]	−14[i]
*t*BuOH	4.97[j]	28.4[c]	39.6[k]	−11.2[k]
OctOH	5.27[j]	30.1[c]	43.5[l]	−13.4[k]
Py	2.11[m]	12.0[e]	97.5[n]	−85[n]
Phenylammonium chloride as guest				
H_2O	1.80	10.3	15.0	−4.7
MeOH	7.16	40.9	49.2	−8.4
*i*PrOH	5.38	30.7	20.6	10.1
Me_2CO	3.7	21	16	5

[a,b] See footnotes to Table 1, except here thermodynamic values for the 2:1 complex $2\ M^+ + L = M_2L^{2+}$, where M^+ is the $BzNH_3^+$ or $PhNH_3^+$ cation and L is the 18-crown-6 ligand. Unless noted, uncertainties are given as standard deviations: in lg$K$ 0.20; in ΔG 1.1; in ΔH 3.0; in $T\Delta S$ 3.2; otherwise: [c] 0.6; [d] 3.5; [e] 2.0; [f] 0.5; [g] 2.5; [h] 4.0; [i] 4.8; [j] 0.1; [k] 1.5; [l] 1.1; [m]0.35; [n] 9.5. Small systematic deviations could be removed by assuming also additional 3:1 (M/L) complexes, which are considered to be artifacts for the following systems: 1. $BzNH_3Cl$ + 18C6: 1a) MeOH: lg$K$ = 9.43 ± 0.60, $\Delta H = -34.1 \pm 2.0$ kJ/mol; 1b) *t*BuOH: lg$K$ = 7.93 ± 0.10, $\Delta H = -37.7 \pm 2.5$; 1c) DMF: lg$K$ = 7.43 ± 0.10, $\Delta H = -27.5 \pm 0.5$; 1d) Py: lg$K$ = 6.30 ± 0.35, $\Delta H = -24.2 \pm 9.5$; 2. $PhNH_3Cl$ + 18C6: 2a) H_2O: lg$K$ = 2.60 ± 0.50, $\Delta H = -30.0 \pm 0.5$; 2b) MeOH: lg$K$ = 9.27 ± 0.10, $\Delta H = -23.6 \pm 1.0$; 2c) *i*PrOH: lg$K$ = 8.51 ± 0.20, $\Delta H = -39.7 \pm 3.0$; 2d) DMF: lg$K$ = 6.30 ± 0.20, $\Delta H = -15.0 \pm 1.0$; 2e) DMSO: lg$K$ = 2.56 ± 0.20, $\Delta H = -1.0 \pm 0.5$; 2f) Me_2CO: lg$K$ = 5.6 ± 0.20, $\Delta H = -16 \pm 3.0$ kJ/mol.

In many cases an acceptable fit for the calorimetric titration curves could only be obtained by taking into account not only formation of 1:1 complexes, but also 1:2 stochiometries (see Figure 1). Solid-state structures of complexes between crown ethers and compounds with ^+N-H groups most often show a 1:1 stochiometry, however with noticeable exceptions and sometimes discrepancies between solution and solid state.[9]

Table 5. Association constants (lg*K* values) for the complexes of ammonium salts ($BzNH_3Cl$ and $PhNH_3Cl$) with crown ethers other than 18-crown-6 itself[a]

Entry	Ligand	Salt	Solvent	lg*K*	C_L [mmol/L]	C_M [mmol/L]	$C_{\mathrm{Mcompet.}}$ [mmol/L]
1	Me18C6	$BzNH_3Cl$	MeOH	3.86(0.07)	3.83	8.11	1.05
				ISE(K^+)	3.44	7.73	11.3
2	Me18C6	$PhNH_3Cl$	H_2O	1.50(0.21)	9.96	10.3	0.74
				ISE(K^+)	9.10	9.41	13.5
3	Me18C6	$BzNH_3Cl$	H_2O	1.51(0.19)	9.96	10.3	0.74
				ISE(K^+)	9.10	9.10	13.5
4	2,3-$Me_2$18C6	$BzNH_3Cl$	MeOH	3.54(0.03)	3.85	8.11	1.05
				ISE(K^+)	3.44	7.27	11.3
5	15C5	$BzNH_3Cl$	MeOH	2.74(0.06)	3.92	8.11	1.05
				ISE(K^+)	3.51	7.27	11.3
6	Me15C5	$BzNH_3Cl$	MeOH	2.27(0.09)	4.01	7.92	1.05
				ISE(K^+)	3.62	7.17	10.5
7	12C4	$BzNH_3Cl$	MeOH	0.80(0.05)	4.07	8.05	1.05
				ISE(K^+)	3.72	7.36	9.59
8	18C5	$BzNH_3Cl$	MeOH	1.55(0.08)	3.99	8.11	1.05
				ISE(K^+)	3.59	7.27	11.3
9	N18C6	$BzNH_3Cl$	MeOH	0.81(0.20)	3.78	9.65	1.06
				ISE(Na^+)	3.45	8.81	9.64
10	1,10-$N_2$18C6	$BzNH_3Cl$	MeOH	0.76(0.11)	3.93	8.05	1.05
				ISE(K^+)	3.58	7.36	9.59
11	MeN18C6	$BzNH_3Cl$	MeOH	3.94(0.10)	3.80	8.05	1.05
				ISE(K^+)	3.41	7.22	11.3
12	1,10-$(MeN)_2$18C6	$BzNH_3Cl$	MeOH	3.31(0.09)	3.83	7.73	5.05
				ISE(K^+)	3.54	7.15	12.2
13	1,10-$(AcN)_2$18C6	$BzNH_3Cl$	MeOH	2.45(0.06)	3.97	7.94	1.09
				ISE(Na^+)	3.70	7.41	10.3
14	DCH18C6	$BzNH_3Cl$	MeOH	4.22(0.07)	3.99	7.95	1.05
	cis-syn-cis			ISE(K^+)	3.52	7.01	12.6
					9.07	1.32	
					9.88	13.5	
15	DCH18C6	$BzNH_3Cl$	MeOH	3.16(0.12)	4.48	7.87	2.08
	cis-anti-cis			ISE(K^+)	3.95	6.93	13.7
					6.01	0.98	
					6.55	9.00	

[a] Potentiometric titration with ISE electrodes; logarithms of stability constants with standard deviations in parentheses are given for the reaction $M^+ + L = ML^+$. Background electrolytes: Et_4NI, Et_4BF_4, Bu_4NClO_4, and Me_4NClO_4 at 0.05 M concentration. C_L, C_M and $C_{\mathrm{Mcompet.}}$ are total (analytical) ligand, cation and electrode cation salt concentrations in solution, respectively.

Our titrations show that indeed complexes containing two RNH_3 derivatives per crown ether unit can contribute significantly in solution (Table 4), as expected less in water, than in more lipophilic solvents. The $\Delta\Delta G$ values (for 1:1 complexes) for binding the second ammonium salt vary, e.g. for benzylammonium ions between at least 8 kJ/mol in methanol (lower value considering the errors, see Tables 1 and 4) and 12 kJ/mol to 14 kJ/mol in *i*PrOH. The CHEMEQUILI program used in this work also allows to use 1:3 stochiometries in addition to 1:1 and 1:2; although calculations including also a 1:3 model improved the quality of the fit furthermore (particularly with complexes in DMF, DMSO or Me_2CO), contributions of such chemically unreasonable complexes were considered to be artifacts and are omitted in the tables.

Structure and Stabilities of Complexes Between 18-Crown-6 and Ammonium Salts

The structures of these complexes were simulated with the CHARMm force field in the gas state; they show that the ligand can essentially retain its D_{3d} symmetry without significant distortions by building up three almost linear $^+N-H\cdots O$ hydrogen bonds, as it was visible in most but not all solid-state structures,[9] including structures of 18C6 and R^+NH_3 with R = hydrogen,[13] R = methyl,[14] and R = benzyl.[15]

Gas-phase measurements of ammonion ion−crown ether complexes also suggest the presence of three hydrogen bonds.[16] However, an equally symmetric orientation with bifurcated hydrogen bonds to all six oxygen atoms yielded for this complex a calculated energy which differed negligibly (by 3 kJ/mol out of a total of 94 kJ/mol gas-state complexation energy) from the classical three-bond situation (Figure 2). It should be noted that the CHARMm-calculated complexation of 94 kJ/mol for RNH_3 + 18C6 is not far from an experimental value of ΔH = 88 kJ/mol determined in the gas phase, where at the same time counteracting entropic contributions were found to be as large as $T\Delta S$ = 48 kJ/mol. The CHARMm-calculated enthalpies for other ammonium−18C6 complexes (Table 6) follow the sequence of the experimental stabilities. The results are essentially in line with other force-field calculations on similar complexes.[17]

It is, however, well known that such calculations are fraught with substantial problems regarding the choice of

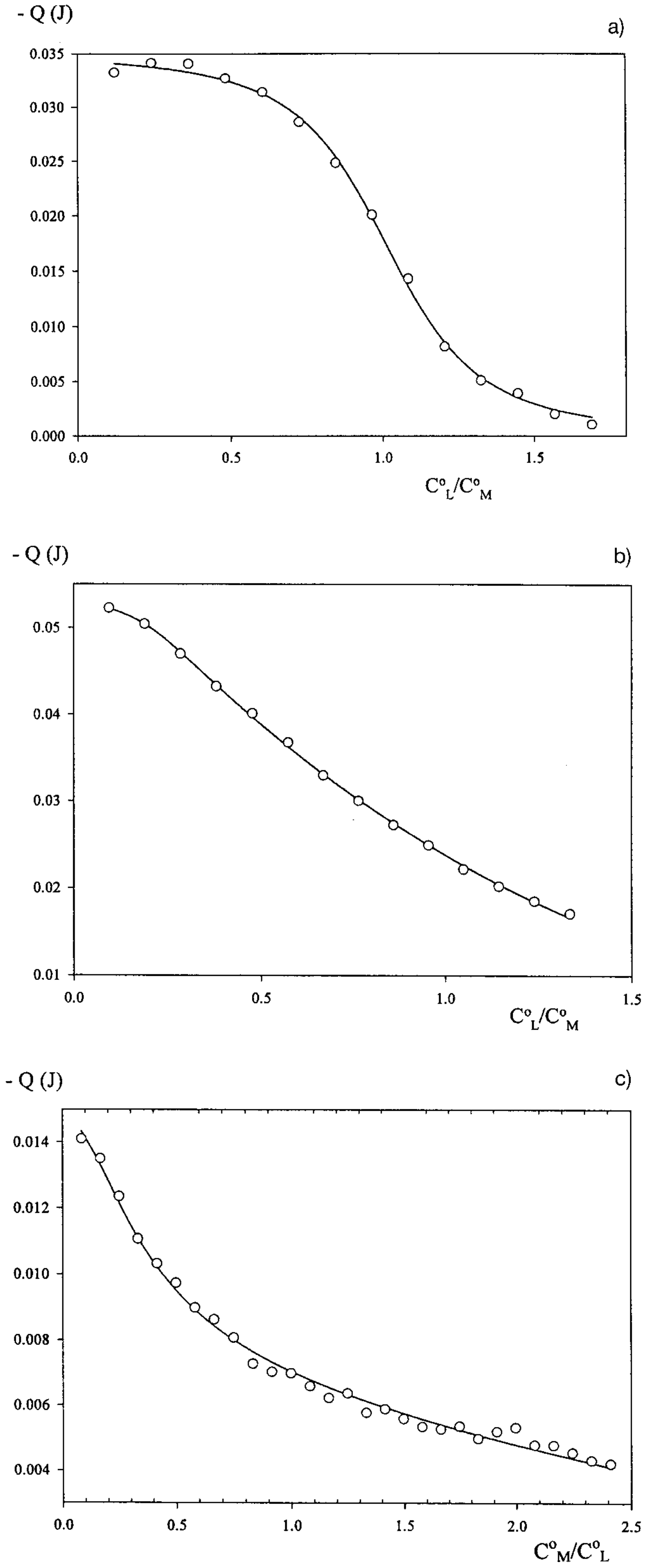


Figure 1. Calorimetric titration curves for the complexation with ammonium salts; interaction heat Q [J] versus reagent concentration ratios of ligand L to guest; 298 K; a) proportions of 0.016 mL solution of [L] = 0.0658 M were added to 2.00 of salt solution ([M] = 0.002925 M) (M = benzylammonium chloride, solvent = 2-propanol); b) as for a) but [L] = 0.1785 M, [M] = 0.009906 M [M = benzylammonium chloride, solvent = *N*,*N*-dimethylformamide (DMF)]; c) as for a) but the salt M was added in volume portions of 0.0053 mL each ([M] = 0.2940 M) to the ligand ([L] = 0.00937 M, 2.00 mL), [M] = 0.009906 M [M = phenylammonium chloride, solvent = *N*,*N*-dimethylformamide (DMF)]

local charges or dipoles, of the local dielectrics and of the simulation of the micro environment. Our experimental results emphasize the strong dependence of complexation strength on the chosen solvents. They also illustrate the very large entropic contributions, which, depending on the solvent, can be as large as the enthalpic contributions. Also for these reasons the development of an empirical increment is one aim of the present study, in which gas-phase simulations only provide models for the rationalization of the observed thermodynamics.

In line with our earlier approach, the most simple description of complex stability is the summation of all non-

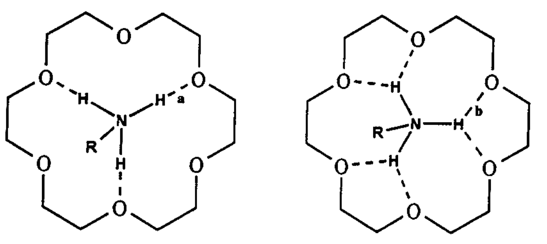
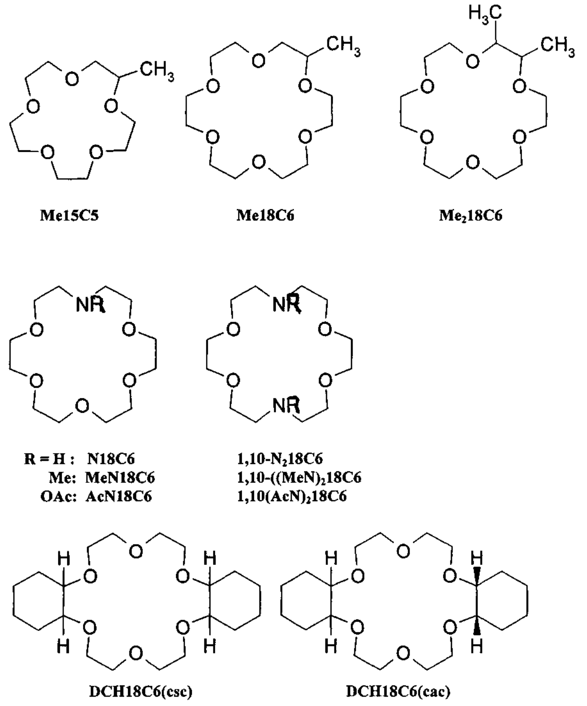


Figure 2. Complex between 18-crown-6 and methylammonium ion; with either linear or bifurcated hydrogen bonds; O···H distances a = 1.88 Å; b = 2.06 Å (CHARMm calculations)

Table 6. CHARMm-calculated energies[a] of complexes between 18-crown-6 and NH_4^+, $MeNH_3^+$, $Me_2NH_2^+$ and Me_3NH^+ ions (gas-phase simulations)



Me15C5 **Me18C6** **Me₂18C6**

R = H : N18C6
Me: MeN18C6
OAc: AcN18C6

1,10-N₂18C6
1,10-((MeN)₂18C6
1,10(AcN)₂18C6

DCH18C6(csc) **DCH18C6(cac)**

Guest	FSE_{crown}	FSE_{guest}	FSE_{cplx}	FSE_{incplx}[b]	E_{cplx}[c]	SE	H bonds[d]	ΔG_{exp}
NH_4^+	10.6	0	−113.2	12.0	−123.8	1.4	6 (3 × 2s)	24.4
$MeNH_3^+$	10.6	3 .6	−109.0	12.0	−123.2	1.4	6 (3 × 2s)	24.3
$Me_2NH_2^+$	10.6	6.1	−64.9	18.6	−81.6	8.0	4 (2 × 2s)	10.1
Me_3NH^+	10.6	4.7	−49.7	13.0	−65.0	2.4	2 (1 × 2s)	2.28
NMe_4^+	–	–	–[e]	–	–	–	–	< 0.05
NEt_4^+	–	–	–[e]	–	–	–	–	< 0.05
$PhNH_3^+$	10.6	46.1	−31.4	13.4	−88.4	2.8	5 (3s/2l)	21.7
$BzNH_3^+$	10.6	43.2	−41.1	12.6	−95.1	2.0	6 (3s/3l)	25.4

[a] In kJ/mol; ΔG_{exp}: experimental complexation free energies in MeOH, see Table 1. – [b] FSE: final steric energies; FSE: of the crown alone; FSE_{cplx}: of the crown after complexation; FSE_{guest}: of the guest alone; FSE_{incplx}: of the complex. – [c] Calculated gas-phase complexation enthalpy $E_{cplx} = (FSE_{crown} + FSE_{guest}) - FSE_{cplx}$. – [d] The number of hydrogen bond is given as observed in the simulations with the more stable bifurcated bonds (see text and Figure 2); s: short bonds (1.85–2.1 Å); l = longer bonds (2.1–2.5 Å). – [e] Not even partial inclusion obtained by the simulations.

covalent bonds participating in binding the guest molecule. Figure 3 illustrates that indeed the observed free complexation energies ΔG are a linear function of the available number of hydrogen bonds, due to the symmetry mentioned above independent of the underlying model with either three (calculated O···H distance 1.88 Å) or six (O···H distance 2.06 Å) bridges (Figure 2). An equally linear correlation is obtained with the CHARMm-calculated gas-phase complexation enthalpies (Figure 4). Remarkably, the absence of hydrogen bonds as in the tetramethylammonium salt leads to the absence of any detectable complex (Table 3), even though it is known that the peripheric hydrogen atoms of the methyl groups and not the central nitrogen atom bear considerable positive charges. Even gas-phase measurements with electrohydrodynamic mass spectrometry showed for the tetramethylammonium ion complexes about 250 times weaker constants than with e.g. potassium ions.[18]

This result clearly shows the dominance of hydrogen bonding over any other contributions in these complexes. The ΔG values for the alkyl- and benzylammonium salts are within the error the same, and the phenyl derivative (aniline) is smaller by only 3 kJ/mol, indicating small steric

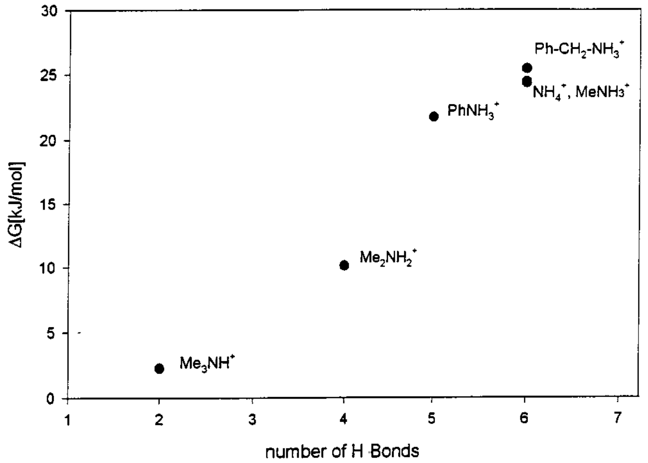


Figure 3. Free energies of complexation ΔG in MeOH of NH_xMe_y (x,y = 1−4) with 18C6 in MeOH (see Table 1) as a function of the number of participating hydrogen bonds (configuration with the more stable bifurcated bonds, see text and Figure 2

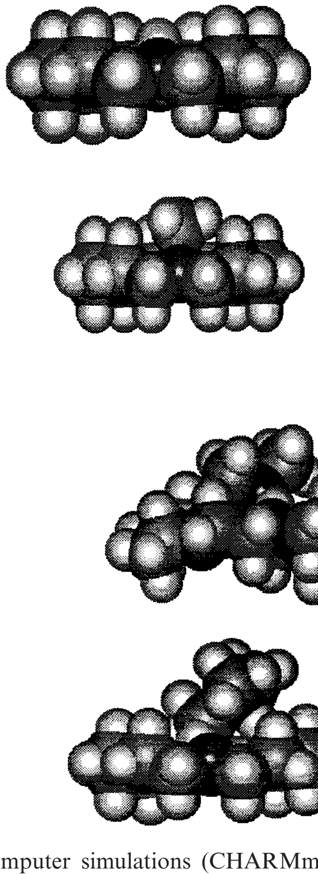


Figure 4. Computer simulations (CHARMm) of complexes between 18-crown-6 and NH_4^+, $MeNH_3^+$, $Me_2NH_2^+$ und Me_3NH^+ ions

hindrance of complexation. The protonated secondary and tertiary amines are on the linear correlation line (Figure 3) in agreement with the CHARMm-simulated structures, which indicate an almost strainfree insertion into the 18C6 cavity (Figure 4).

The assocation constants of benzylammonium chloride with aza crown ethers show a large drop from 18C6 itself with lg$K$ = 4.2 (Table 1) to lg$K$ = 0.81 with the monoaza crown N18C6, and lg$K$ = 0.76 with 1,10-diaza crown $N_2$18C6 (Table 5). However, a similar decrease is seen with potassium complexes, and we have shown earlier, that this is only due to the axial orientation of the N lone pairs, which must convert into the equatorial position for complexation at the expense of considerable strain. As in our early studies with K complexes, nitrogen methylation results in a strong increase of complexation: The methyl derivative MeN18C6 shows with benzylammonium chloride an increase which amounts to lg$K$ = 3.94, close to 18C6 itself, and with the dimethyl derivative $Me_2N_2$18C6 still to lg$K$ = 3.31. As shown earlier this can only be explained by the predominance of equatorial lone pairs in the *N*-methyl derivatives, resulting from the relative instability of axial methyl groups in these ligands. The results demonstrate, that a general preference of oxygen over nitrogen atom as hydrogen-bond acceptor, or the reverse, cannot be derived independent of the lone-pair orientations. These findings shed a different light on recent analyses of the competition of nitrogen and oxygen atom as hydrogen-bond acceptor.[19] Other crown ethers (Table 5), such as the *C*-methyl derivatives show similar affinities towards benzylammonium ions as towards potassium cations; with significant exceptions of dicyclohexyl crown ethers where the attached rings can interfer with the phenyl group.

Enthalpy-entropy correlations have been discussed for many ionophore complexes, showing characteristic differences in the slopes, which have been ascribed to the different degree of preorganization in the ligands.[20] However, many of these data are based on measurements of the temperature dependence of equilibrium constants, and are therefore fraught with systematical errors.[21] Calorimetric data provide more reliable grounds for such studies, and have been applied in the present work. Correlations with satisfactory linearity (n: number of points; r: linear correlation coefficient; SD: standard deviation) were observed between ΔH and $T\Delta S$ in different solvents for the complexes with benzylammonium ions, with

$$T\Delta S = 0.71\ \Delta H + 5.3\ (n = 8,\ r = 0.931,\ \mathrm{SD} = 4.6),$$

in H_2O, MeOH, *i*PrOH, *t*BuOH, OctOH, DMF, Py and DMSO as solvent and for the anilinium complexes with

$$T\Delta S = 0.70\cdot\Delta H + 7.9\ (n = 6,\ r = 0.992,\ \mathrm{SD} = 1.7)$$

in H_2O, MeOH, *i*PrOH, DMF, DMSO and Me_2CO as solvent.

For $NH_{4-n}Me_n^+$ (n = 0−3) cations the correlations were much worse, e.g. like

$$T\Delta S = 0.24\cdot\Delta H - 12.8\ (n = 4,\ r = 0.675,\ \mathrm{SD} = 4.1)$$

in MeOH as solvent.

The correlations (see Figure 5) are partially poor, but nevertheless demonstrate, that the large solvent dependence of the complexation constants (see below) is essentially due to roughly proportional enthalpy and entropy contributions.

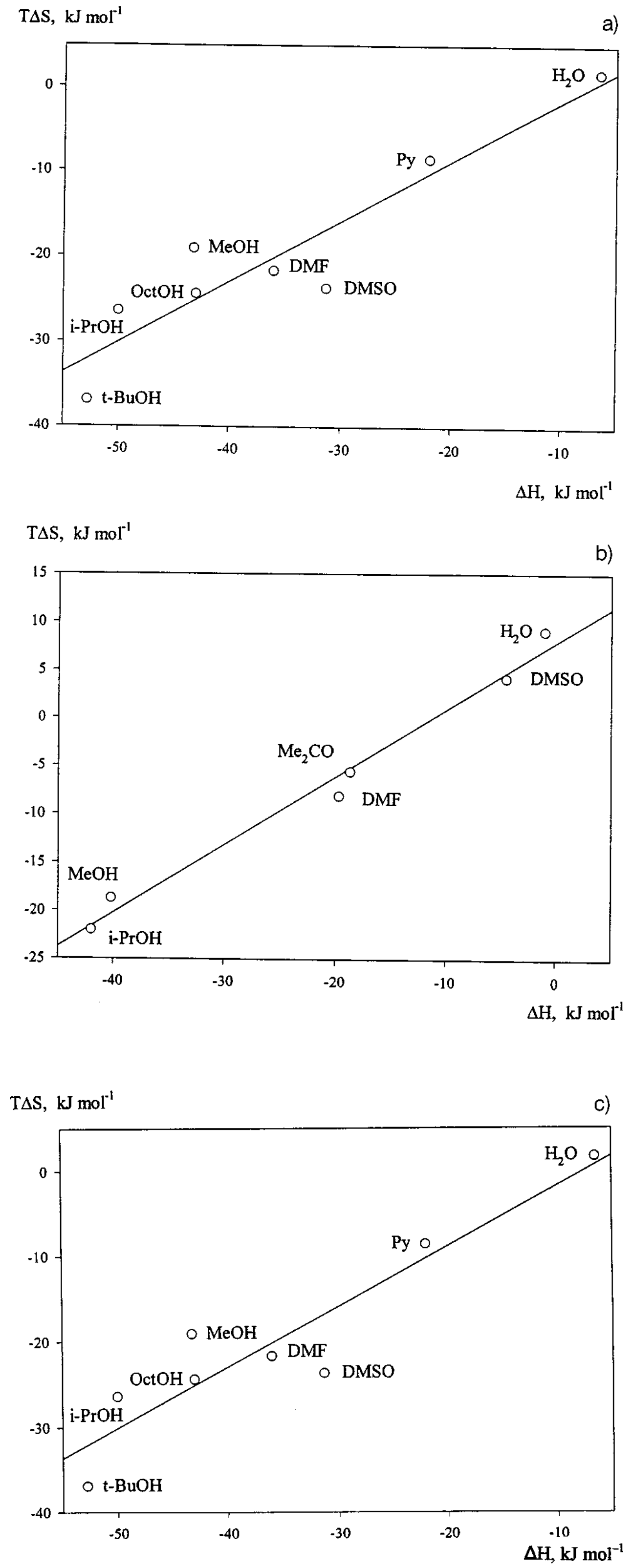


Figure 5. Plots of $T\Delta S$ versus ΔH of 18-crown-6 complexes at 298 K in different solvents; a) for benzylammonium chloride; b) for phenylammonium chloride; c) for the ammonium salts $NH_{4-n}Me_n$

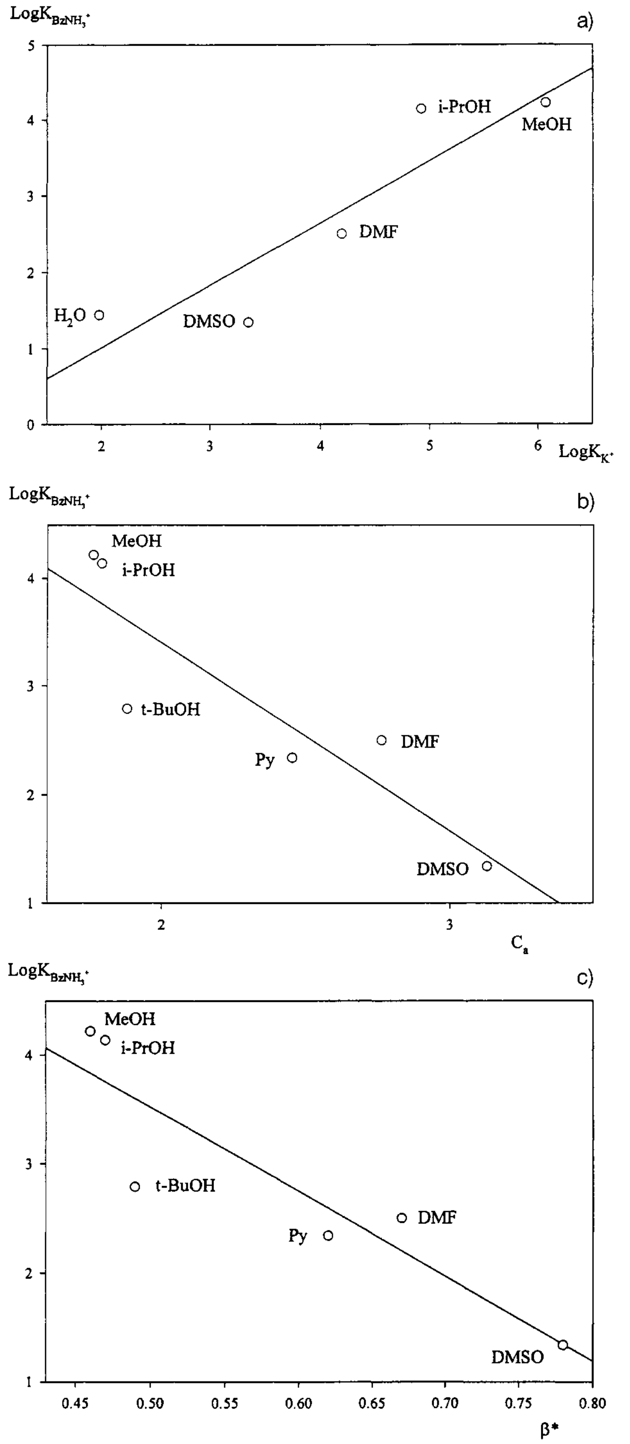


Figure 6. Solvent-effect correlations; a) plot of lg$K$ values for 18-crown-6 complexes with benzylammonium chloride against lg$K$ values of 18C6 complexes with potassium ions in different solvents; b) plot of lg$K$ values for 18-crown-6 complexes with benzylammonium chloride against hydrogen-bond acceptor values C_a; c) plot of lg$K$ values for 18-crown-6 complexes with benzylammonium chloride against solvent basicity constants β*

Solvent Effects

As found in earlier investigations the change of solvent can increase the complexations constants by the power of

Table 7. The solvent influence on the stability constants K of complexation; correlation equation $\lg K = A + B \cdot X$ for the complexation of $BzNH_3Cl$ with 18-crown-6 in different solvents[a]

Entry	Property	R	F	SD	N	A	B	Table 1: point no.
1	$\lg K(K^+)$[b]	0.903	13.2	0.70	5	−0.62	0.82	1−3,6,8
2	β^*	0.906	18.4	0.53	6	7.4	−7.8	2−4,6−8
3	C_a	0.895	16.0	0.56	6	6.9	−1.7	2−4,6−8
4	D	0.890	22.9	0.54	8	9.9	−8.0	1−8
5	K_T	0.888	22.3	0.54	8	0.22	0.32	1−8
5a	K_T	0.958	55.2	0.37	7	−0.063	0.38	1−3,5−8
6	DN	0.867	12.1	0.61	6	6.7	−0.16	1,2,5−8
7	π^*	0.810	9.5	0.74	7	5.4	−3.5	1−4,6−8

[a] $\lg K$: logarithm of the stability constant for the complexation; X: solvent property; A and B are coefficients of the linear equation $\lg K = A + B \cdot X$; R: the correlation coefficient; F: Fisher′s criterion; SD: standard deviation, N: number of points in the correlation. Names of solvent properties: see text. − [b] $\lg K(K^+)$ refers to stability constants for the 1:1 complexation of the potassium cation with 18-crown-6 in the corresponding solvents.

Table 8. The solvent influence on the complexation enthalpies; correlation equation $\Delta H = A + B \cdot X$ for the complexation of $BzNH_3Cl$ with 18-crown-6 in different solvents[a]

Entry	Property	R	F	SD	N	A	B	Points used
1	$\Delta H(K^+)$[b]	0.995	199.2	1.0	4	−19.2	0.44	2,3,6,8
2	γ	0.937	43.4	5.8	8	−64.4	8.4	1−8
3	π^*	0.900	21.3	7.8	7	−77.0	55.6	1−4,6−8
4	DN	0.877	13.3	7.6	6	−84.7	2.0	1,2,5−8
5	K_T	0.832	13.5	9.2	8	−1.9	−4.3	1−8
6	α_P	0.830	13.2	9.3	8	1.7	−38.4	1−8
7	$-\varepsilon_T$	0.817	8.0	9.9	6	−58.1	129.4	1−3,5,6,8

[a] ΔH: complexation enthalpy; X: solvent property; coefficients A and B of the linear equation $\Delta H = A + B \cdot X$. − [b] $\Delta H(K^+)$ is the enthalpy change for the 1:1 complexation of the potassium cation with 18-crown-6 in different solvents.

Table 9. Solvent influence on stability constants K of complexation; correlation equations $\lg K = A + B \cdot X$ for the complexation of $PhNH_3Cl$ with 18-crown-6 in different solvents[a]

Entry	Property	R	F	SD	N	A	B	Point no.
1	$\lg K(K^+)$[b]	0.715	4.2	0.726	6	0.62	0.42	1−6
2	π^*	0.906	18.4	0.439	6	5.3	−3.6	1−6
3	C_a	0.871	9.4	0.546	5	5.6	−1.3	2−6
4	D	0.834	9.2	0.573	6	7.7	−5.8	1−6
5	β^*	0.830	6.6	0.621	5	5.7	−5.4	2−6
6	K_T	0.789	6.6	0.638	6	0.77	0.20	1−6
7	DN	0.705	3.0	0.718	5	4.5	−0.090	1,2,4−6

[a] See footnote to Table 7. − [b] $\lg K(K^+)$ is the logarithm of the stability constant for the 1:1 complexation of the potassium cation with 18-crown-6 in different solvents.

Table 10. Solvent influence on the complexation enthalpy; correlation equations $\Delta H = A + B \cdot X$ for the complexation of $PhNH_3Cl$ with 18-crown-6 in different solvents[a]

Entry	Property	R	F	SD	N	A	B	Point no.
1	$\Delta H(K^+)$[b]	0.943	31.9	6.4	6	20.6	0.94	1−6
2	π^*	0.957	43.1	5.6	6	−76.3	69.7	1−6
3	C_a	0.847	7.6	9.7	5	−73.4	21.3	2−6
4	d	0.832	9.0	10	6	−117.1	107.0	1−6
5	γ	0.813	7.8	11	6	−46.8	7.2	1−6
6	K_T	0.794	6.8	12	6	11.0	−3.7	1−6
7	DN	0.785	4.8	11	5	−61.3	1.8	1,2,4−6

[a] See footnote to Table 8. − [b] $\Delta H(K^+)$ is the enthalpy change for the 1:1 complexation of the potassium cation with 18-crown-6 in different solvents.

10^3, e.g. between DMSO and methanol (see Tables 1−4). That this is not a function of solvent polarity is obvious from the complexes in methanol, which are about 10 times *stronger* than those in, e.g, 1-octanol. Consequently, the complexation energies show very poor correlations with solvent-polarity parameters. As in the case of alkali metal complexation,[5] acceptable correlations are found only with parameters which relate to the electron donor or Lewis base capacity of the solvent. A correlation of lg$K$ values of 18C6−potassium ion complexes in different solvents and the corresponding benzylammonium complexes is satisfactorily linear (Figure 6a); the sensitivity against solvent changes, measurable by the slope of the correlations (see Tables 6−9), is, however, distinctly lower for the ammonium complexes. In line with hydrogen bonds as dominating binding mechanisms in crown ether−ammonium ion complexes solvents which compete efficiently with the ligand oxygen atoms lead to strong affinity decrease. Corresponding parameters, such as C_a or β values, have been derived from thousands of hydrogen-bonded associations, mostly in carbon tetrachloride as solvent; as expected, these show acceptable linear correlations with lg$K$ values of benzyl-, less with phenylammonium ion complexes (Figure 6b,c). From the large number of solvent parameters tested furthermore, some like Gutmann donor numbers DN, the polarity index π^*, the isothermal compressiblity K_T, even the density d or the surface tension coefficient γ also yield linear correlation coefficients close, or above $r = 0.9$. The solvent dependence of the measured ΔH values (Table 10) showed less linear correlations, acceptable only with the values of the corresponding affinity changes of potassium ion complexes, and with, e.g., the polarity index π^*.

Experimental Section

Materials: The ligand 18-crown-6 was a commercial sample, and was purified before use by vapor crystallization at 290 K with evaporation from a molten sample at 330 K under vacuum. Benzylammonium chloride was obtained by adding HCl to freshly distilled benzylamine; the salt $BzNH_3Cl$ was recrystallized twice from methanol and dried under vacuum. Anilinium chloride ($PhNH_3Cl$) was obtained by adding HCl to freshly distilled aniline; the salt $PhNH_3Cl$ was recrystallized twice from a mixture of acetone and water; m.p. 198 °C. Water was double distilled. Methanol (MeOH) was distilled from magnesium methoxide under nitrogen. Acetonitrile was dried over P_2O_5 according to a standard procedure. The water content in acetonitrile was monitored by IR spectroscopy for ν(OH) at 3450−3600 cm^{-1}. The commercially available solvents 2-propanol, *tert*-butyl alcohol, 1-octanol, *N*,*N*-dimethylformamide (DMF), dimethyl sulfoxide (DMSO), pyridine and hexamethylphosphoric triamide (HMPT) were dried and/or purified according to standard procedures. Acetone and ammonium hydrochloride were commercial high-purity grade samples used without additional purification. Methylamine hydrochloride (99%, m.p. 232−234 °C), dimethylamine hydrochloride (99%, m.p. 170−173 °C), trimethylamine hydrochloride (Me_3NHCl) (98%, m.p. 283−284 °C), all from Aldrich, and tetramethyl- (Me_4NCl) and tetraethylammonium hydrochloride (Et_4NCl) were dried for about 3 h under vacuum at 320 K.

Calorimetric Measurements, Evaluations of Thermodynamic Parameters, and Potentiometric Titrations: Carried out as described before with the program CHEM-EQILII and with ISE electrodes, respectively.[5,7,9] Concentrations for the titrations are given in Table 11. The reliability of the experimental procedure was tested as described before also by comparison with literature values.

Table 11. Experimental conditions for the calorimetric titrations

Entry	Salt	Ligand	Solvent	C^o_S [mmol/L]	C^o_L [mmol/L]
1	$PhCH_2NH_3Cl$	18C6	H_2O	18.4−19.7	1.6−20.8
2			MeOH	4.5−4.8	0.5−7.0
				3.9−4.2	0.2−5.3
3			*i*PrOH	2.7−2.9	0.4−4.6
4			*t*BuOH	4.2−4.5	0.5−6.9
5			OctOH	9.6−10.2	1.3−15.5
6			DMF	9.2−9.9	0.9−12.3
7			Py	11.0−11.7	1.1−13.7
8			DMSO	15.3−16.3	2.1−28.1
9			HMPT	8.7−9.0	1.0−8.9
10			Me_2CO	3.0	1.1
11			MeCN	insoluble	
12	$PhNH_3Cl$	18C6	H_2O	27.1−28.6	1.7−19.0
13			MeOH	0.9−20.4	14.0−14.8
				6.4−6.8	0.4−7.5
14			*i*PrOH	8.6−9.2	0.8−9.9
15			DMF	7.4−7.9	0.4−10.9
				0.8−21.0	8.7−9.3
16			DMSO	8.0−8.1	0.4−2.9
				29.3−30.8	0.8−15.2
				37.7−40.4	0.8−20.9
17			Me_2CO	3.9−4.2	0.6−7.6
				13.7−14.6	0.6−7.1
18			HMPT	38.6−39.4	0.8−7.2
19			MeCN	insoluble	
20	NH_4Cl	18C6	MeOH	10.3−11.4	0.7−15.1
21	$MeNH_3Cl$			4.0−4.3	0.5−6.5
22	Me_2NH_2Cl			18.5−19.8	1.1−27.8
				4.6−4.8	0.5−5.5
23	Me_3NHCl			17.9−19.1	2.1−27.8
				17.9−19.2	1.5−37.8
				6.0−37.0	18.3−19.3
24	Me_4NCl			9.4	0.4−1.6
25	Et_4NCl			0.7−5.9	13.2−13.5

Molecular Mechanics Calculations: Performed as described before,[8] using version 3.3 from MSI of CHARMm,[22] with Gasteiger point charges and $\varepsilon = 3$ (constant).

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