1384 J. Am. Chem. Soc. 1981, 103, 1384-1389

Solvent Dependence of the Stability of Cryptate Complexes

B. G. Cox,* J. Garcia-Rosas, and H. Schneider*

Contribution from the Department of Chemistry, University of Stirling, Stirling, FK9 4LA, Scotland, and the Max-Planck-Institut für Biophysikalische Chemie, D-3400 Göttingen, West Germany. *Received June 20, 1980*

Abstract: Stability constants of (2,1,1), (2,2,1), and (2,2,2) cryptates of alkali-metal cations, Ag^+ and Ca^{2+}, have been measured in several solvents, both protic and aprotic. There is a large variation with solvent of the stability constants, but qualitatively the same selectivity pattern is observed in all solvents. Free energies of transfer of $MCry^+I^-$ between the solvents have been obtained by combining measured stability constants with free energies of transfer of the corresponding MI salts. For transfer from water to nonaqueous solvents, (2,2,2) cryptates show distinct minima corresponding to transfer of the $K(2,2,2)^+$ cryptate. Similar behavior is observed for (2,2,1) and (2,1,1) cryptates, but as the size of the ligand decreases, transfer of cryptates containing the smaller cations becomes progressively favored. Free energies of transfer of cryptate salts between nonaqueous solvents are essentially independent of the included cation. The implications of the results for the extraction of alkali-metal salts from water into nonaqueous media by cryptands and related ligands are discussed.

Introduction

Complex formation between cations and ligands involves the substitution of one or more solvent molecules from the inner coordination sphere of the metal ion. Thus the differences of the two binding energies due to competition between the ligand and solvent molecules for the cation should constitute a major contribution to the overall stability of a complex. In the particular case of macrocyclic or macropolycyclic ligands, which in the most favorable cases can completely replace the solvent in the immediate neighborhood of the ion, the stability constants for complex formation might be expected to be very sensitive to solvent variation.

The majority of studies concerned with equilibria of complex formation between naturally occurring or synthetic macrocyclic ligands and cations (particularly alkali or alkaline earth cations) have involved water or methanol as solvent(1) and refer to a single-solvent reaction as in eq 1. Such studies have shown that

$$M^{n+}(aq) + L(aq) \rightleftharpoons ML^{n+}(aq) \qquad (1)$$

many of the ligands show considerable selectivity in complex formation. However, both the overall stabilities of the complexes and the selectivity patterns of the ligands might be expected to be solvent dependent. In addition, in considering problems relevant to the extraction of metal ions from aqueous into nonaqueous environments using macrocyclic ligands, information on equilibria represented in eq 2, where S represents a nonaqueous solvent, might be of more importance.

$$M^{n+}(aq) + L(aq\ or\ s) \rightleftharpoons ML^{n+}(s) \qquad (2)$$

For complex formation, as defined by eq 3 and 4, the difference

$$M^{n+} + L \overset{K_s}{\rightleftharpoons} ML^{n+} \qquad (3)$$

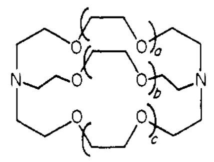
$$K_s = [ML^{n+}]/[L][M^{n+}] \qquad (4)$$

between K_s in solvent S1 (K_{S1}) and solvent S2 (K_{S2}) is simply related to the free energies of transfer of the species involved, M^{n+}, L, and ML^{n+}, by eq 5. In eq 5, ΔG_{tr} values refer to the free

$$RT[\ln K_{S2} - \ln K_{S1}] = \Delta G_{tr}(M^{n+}) + \Delta G_{tr}(L) - \Delta G_{tr}(ML^{n+}) \qquad (5)$$

energies of transfer from S1 to S2. Thus by combining stability constants measured in different solvents with thermodynamic data on the solvation of M^{n+} and L, it is possible to gain information both on the solvent dependence of equilibria 3 and on the equilibrium extraction processes as defined by eq 2.

In this paper we report a study of the solvent dependence of stability constants of complexes formed between the macrobicyclic cryptand ligands **1**-**3** (Cry)(2) and a series of metal ions including alkali-metal ions, Ca^{2+} and Ag^+. The solvents chosen include protic solvents, water, methanol, and ethanol, and the high-dielectric solvent *N*-methylpropionamide (NMP), as well as dipolar aprotic solvents, dimethyl sulfoxide (Me_2SO), acetonitrile (AN), and dimethylformamide (DMF). Results of kinetic and thermodynamic studies in propylene carbonate (PC) have already been reported.(3) A considerable amount of thermodynamic data on ion-solvent interactions in these solvents exists.(4) The results are analyzed according to the solvent dependence of the free energies of the various species M^{n+}, L (≡Cry), and ML^{n+} (≡$MCry^{n+}$) in eq 3.



1, $a = 1, b = c = 0$ (2,1,1)
2, $a = b = 1, c = 0$ (2,2,1)
3, $a = b = c = 1$ (2,2,2)

Experimental Data and Results

Materials. Cryptands (2,1,1), (2,2,1), and (2,2,2) were commercial samples (Merck) used without further purification. Checks for purity have been described previously.(5)

Unless otherwise stated, inorganic salts used in all solvents were $LiClO_4$ (Fluka, purum, water free), $NaClO_4$ (Koch-Light, crystal puriss), $KClO_4$ (Fisons, SLR), $RbNO_3$ (Hopkins and Williams, LR), $CsNO_3$ (Hopkins and Williams, LR), and $AgClO_4$ (BDH, LR). In Me_2SO, $AgNO_3$ (Fisons, AR) and KNO_3 (Fisons, AR) were also used. In EtOH, KF (Hopkins and Williams, purified), RbF (Koch Light, 99.8%), and CsF (BDH, LR) were also used. The salts were dried, where necessary, under vacuum.

Anhydrous solutions of $Ca(NO_3)_2$ were prepared by drying solutions of the hydrated salt (Fisons, SLR) in the appropriate solvent over molecular sieves (BDH, Type 4A).

For emf measurements in Me_2SO and DMF, Et_4NClO_4 was used in the salt bridge. Tetraethylammonium picrate was used in EtOH and NMP. Both salts were prepared by reaction of tetraethylammonium hydroxide (Aldrich Chem. Co., 20% solution in water) with the corresponding acid. They were purified by successive recrystallizations from water and dried under vacuum.

---

*Address correspondence as follows: B.G.C., University of Stirling; Max-Planck-Institut für Biophysikalishe Chemie.

(1) W. Burgermeister and R. Winkler-Oswatitsch, *Top. Curr. Chem.*, **69**, 91 (1977).

(2) J. M. Lehn, *Struct. Bonding (Berlin)*, **16** (1973).

(3) B. G. Cox, J. Garcia-Rosas, and H. Schneider, *J. Phys. Chem.*, **84**, 3178 (1980).

(4) B. G. Cox, *Annu. Rep. Prog. Chem., Sect. A, Phys. Inorg. Chem.*, **70**, 249 (1973).

(5) B. G. Cox, D. Knop, and H. Schneider, *J. Am. Chem. Soc.*, **100**, 6002 (1978).

0002-7863/81/1503-1384$01.25/0

Table I. Stability Constants ($\log K_S$)[a] of Silver Cryptates in Different Solvents at 25 °C

complex	solvent[b]							
	H_2O	MeOH	EtOH	MeCN	PC	NMP	DMF	Me_2SO
$Ag(2,1,1)^+$	8.5[c]	10.6_0[d]	9.70	7.7_0 7.8[e]	14.4_4	7.6_4	8.60 8.6_2[f]	6.1_7
$Ag(2,2,1)^+$	10.6[c] 11.8[f]	14.6_4[d]	13.8_4	11.2_4 11.2[e]	18.5_0	10.4_5	12.4_1 12.4_3[f]	9.6_1
$Ag(2,2,2)^+$	9.6[g,h]	12.2_0[d] 12.3[i]	11.5_1	8.9_9 8.9_2,[f] 9.3[i]	16.3_3 16.2_9[f]	9.1_7	10.0_7 10.0_3[f]	7.3_0 7.1_5,[f] 7.2[i]

[a] Precision: ±0.1 in $\log K_S$. [b] Abbreviations: MeCN, acetonitrile; PC, propylene carbonate; NMP, *N*-methylpropionamide; DMF, dimethylformamide; Me_2SO, dimethyl sulfoxide. [c] Reference 15. [d] Reference 11. [e] Reference 23. [f] Reference 12. [g] Reference 13. [h] Reference 14. [i] Reference 20.

Table II. Stability Constants ($\log K_S$)[a] of Cryptates in Various Solvents at 25 °C

cation	cryptand	solvent[b]							
		H_2O[c]	MeOH[d]	EtOH	MeCN	PC[e]	NMP	DMF	Me_2SO
Li^+	2,1,1	5.5	8.0_4	8.4_7	>10	12.4_4	6.4_3	6.9_9 6.73[f]	5.8_4
Na^+	2,1,1	3.2	6.1[g]	7.0_9	>9	8.7_6	5.0_6	5.2_3 5.10[f]	4.6_3 4.3[h]
K^+	2,1,1	<2	2.3[g]	⩽2.6	2.84	3.3_5	2.4_6	<2.5	<2.0
Rb^+	2,1,1	<2	1.9[g]			⩽2.2			
Ca^{2+}	2,1,1	2.5_0				8.6_5		3.0_8	
Li^+	2,2,1	2.5_0	5.3_8	5.3_8	10.3_3 10.3[f]	9.6_0	3.4_8	3.5_8 3.58[f]	2.7_7
Na^+	2,2,1	5.4	8.6_5 9.3[h]	10.2_0	>11.3	12.0_9	6.5_5	7.9_3 8.03[f]	6.9_8 6.9[h]
K^+	2,2,1	3.9_5	8.5_4	8.5_6	9.5[f]	9.8_8	6.1_1	6.6_6 6.65[f]	5.97
Rb^+	2,2,1	2.5_5	6.7_4	6.8_8	7.27[f]	7.0_3	5.5_5	5.3_5 5.26[f]	4.6_4
Cs^+	2,2,1	<2.0	4.3_3	4.7_7	5.15[f]	4.9_2	3.8_7	3.6_1 3.56[f]	3.2_3
Ca^{2+}	2,2,1	6.9_5				11.4_8		6.6_7	
Li^+	2,2,2	0.9_8	2.6	⩽2.3	6.9_7 7.00[f]	6.9_4	2.9_7		<1.0
Na^+	2,2,2	3.98	7.9_8 7.8[h] 7.9[i]	8.5_7	9.63[f]	10.5_4	5.8_2	6.1_7 5.92[f]	5.3_2 5.4[i]
K^+	2,2,2	5.47	10.4_1 10.8[i]	10.5_0	11.3_1 10.7_1[j]	11.1_9 11.1_0[j]	ca. 8.4	7.9_8 7.8_9[j]	7.1_1, 6.9_2[j] 6.9_2[h], 6.0[i]
Rb^+	2,2,2	4.24	8.9_8	9.2_8	9.50[f]	9.0_2	7.2_8	6.7_8 6.68[f]	5.8_5 5.7[i]
Cs^+	2,2,2	1.4_7	4.4	4.1_7	4.5_7 4.53[f]	4.1_8 4.2[k] 4.0[l]	ca. 4.4	2.1_6	1.4[i] 1.45[m]
Ca^{2+}	2,2,2	4.5				10.7_6		3.8_4	

[a] Precision ±0.1 in $\log K_S$. [b] Abbreviations for solvents as in Table I. [c] Values in water averaged where appropriate from values in reference 13, 14, 17, 18, and 20. [d] Reference 11. [e] Reference 3. [f] Reference 23. [g] Reference 13. [h] Reference 20. [i] Reference 19. [j] Reference 12. [k] F. Peter, J. Gisselbrecht, and M. Gross, *J. Electroanal. Chem.*, 86, 115 (1978). [l] E. Mei, A. I. Popov and J. Dye, *J. Am. Chem. Soc.*, 99, 6532 (1977). [m] Reference 21.

Ethanol was purified by refluxing with magnesium turnings and iodine, followed by distillation as described by Vogel.[6]

Me_2SO was distilled under reduced pressure from CaH_2.

DMF was dried over molecular sieves or Na_2SO_4. It was distilled from CaH_2 under reduced pressure in a pure nitrogen atmosphere.[7] The middle 60% was collected and had a specific conductance of 1×10^{-7} Ω^{-1} cm^{-1} at 25 °C.

NMP was prepared by the reaction of methylamine and propionic acid (Koch-Light, puriss).[8] One sample was made by using 40% aqueous methylamine (Koch-Light) and the other by passing anhydrous methylamine gas (BOC) rapidly into well-stirred propionic acid. Following rapid heating to 120–140 °C to remove water, the crude NMP was fractionally distilled at 5 torr several times under a nitrogen atmosphere. After five distillations, the specific conductance was reduced to 2.7×10^{-7} Ω^{-1} cm^{-1} at 25 °C. This compares favorably with earlier reported values of 10^{-6}–10^{-7} Ω^{-1} cm^{-1}.[8]

Acetonitrile was purified by successive distillations from CaH_2 and P_2O_5.[9]

The water content of the solvents, except for NMP whose purity was checked as described above, was determined by coulometric titration of H_2O, based on the Karl Fischer method.[10] The water content was found to be less than 0.01% w/v (5.6×10^{-3} M) in all cases except ethanol where it was found to be 0.05% w/v. A detailed study of the effect of added water on complex stabilities in acetonitrile and dimethyl sulfoxide was carried out (see below).

Stability Constant Measurements. The stability constants of Ag^+ cryptates were determined by simple potentiometric titration of Ag^+ solutions of the cryptates, as previously described.[11,12] Total Ag^+ concentrations were in the range 10^{-4}–10^{-3} M and cryptand concentrations in the range 5×10^{-4}–5×10^{-3} M. The results are shown in Table I, together with earlier reported values in water,[13-15] methanol,[11] and PC[3] for comparison.

---

(6) A. I. Vogel, "Practical Organic Chemistry", Longmans, London, 1956.

(7) J. Juillaid, *Pure Appl. Chem.*, **49**, 885 (1977).

(8) T. B. Hoover, *Pure Appl. Chem.*, **37**, 579 (1974).

(9) J. F. Coetzee, G. P. Cunningham, D. K. McGuire, and G. R. Podmanashan, *Anal. Chem.*, **34**, 1139 (1962).

(10) W. Pawlowski and W. Jedral, *Chem. Anal. (Warsaw)*, **25**, 151 (1980).

(11) B. G. Cox, H. Schneider, and J. Stroka, *J. Am. Chem. Soc.*, **100**, 4746 (1978).

(12) J. Gutknecht, H. Schneider, and J. Stroka, *Inorg. Chem.*, **17**, 3326 (1978).

(13) J. M. Lehn and J. P. Sauvage, *J. Am. Chem. Soc.*, **97**, 6700 (1975).

(14) G. Anderegg, *Helv. Chim. Acta*, **58**, 1218 (1975).

(15) F. Arnaud-Neu, B. Spiess, and M. Schwing-Weill, *Helv. Chim. Acta*, **60**, 2633 (1977).

Stability constants for other metal ions were determined by disproportionative reaction of the ions with the corresponding Ag^+ cryptates. The experimental procedure has been published previously.[11,12] In some cases when the stability constants were relatively low (log $K_s \leq 6$), the results were checked by direct titration of the cryptand and metal ions, using a cationic glass electrode (Beckman Cation Selective Electrode No. 39137) to monitor the titrations. Total metal ion concentrations were ca. 10^{-3}–5×10^{-3} M and total cryptand concentrations in the range ca. 5×10^{-4}–10^{-3} M. Activity coefficients used in calculating silver ion concentrations from measured cell potentials were determined from the Davies equation.[16] The results are given in Table II, along with earlier results in H_2O,[13-15,17,18] MeOH,[11] and PC.[3]

In order to test for possible effects due to the presence of trace amounts of water in the non-aqueous solvents, results in acetonitrile (AN) which solvates cations (except for Ag^+) poorly and dimethyl sulfoxide (Me_2SO) which strongly solvates cations[4] were chosen for study. The effect of added water on stability constants of $Ag(2,2,1)^+$, $K(2,2,1)^+$, $Ag(2,2,2)^+$, and $Li(2,2,2)^+$ cryptates measured in acetonitrile containing initially 0.0045% w/v water (Tables I and II) was tested. For the Ag^+ complexes, effects of adding up to 0.4% H_2O were negligible (<2%). $K(2,2,1)^+$ stabilities were also relatively insensitive to added water, with addition of 0.054% and 0.11% H_2O causing reductions in stability of 1% and 2.5%, respectively. Further addition of water led to larger decreases in stability, e.g., 0.27% H_2O reduced the stability by 7.5% and 0.5% H_2O by 19%. This latter result, however, only corresponds to a reduction of 0.08 in log K_s which is lower than the overall uncertainty quoted in Tables I and II.

As expected $Li(2,2,2)^+$ was much more sensitive to the presence of trace amounts of water in the acetonitrile. Thus additions of 0.037% and 0.074% H_2O resulted in reductions of 15% and 29% in the stability of $Li(2,2,2)^+$. Further addition of water led to correspondingly large decreases in complex stability; e.g., 0.2% H_2O reduced the stability by a factor of 2 and 0.5% H_2O by a factor of ca. 5. Again, however, the effects at levels below 0.01% H_2O are within experimental error.

Results in Me_2SO were very insensitive to added amounts of H_2O. Both $Ag(2,2,2)^+$ and $K(2,2,2)^+$ showed slight increases in stability on addition of water to the Me_2SO, but the effects were small. The addition of even 1% water resulted in increases of stability of only 10%.

Few results for alkali-metal cryptates are available in the literature for comparison. Weaver and co-workers,[19] using an electrochemical method similar in principle to the one used here but based on the Tl^+/Tl(Hg) electrode, have reported stability constants for several 2,2,2 cryptates in Me_2SO. The agreement with the present values is good (Table II) except for $K(2,2,2)^+$, for which they obtain a value of log K_s = 6.0 compared with the present value of log $K_s = 7.1_1$. If our value is correct, the stability of $K(2,2,2)^+$ in Me_2SO is greater than that of $Tl(2,2,2)^+$, which would invalidate Weaver's measurements for this particular cryptate. Lejaille et al.[20] report a value of log K_s = 6.92 for $K(2,2,2)^+$ in Me_2SO, in quite good agreement with the present results. They also report other values in Me_2SO and a K_s value for $Ag(2,2,2)^+$ cryptates in several solvents, the results of which are in good agreement with our values. Popov and co-workers[21] have determined the stability constants of some $Cs(2,2,2)^+$ complexes in different solvents using ^{133}Cs NMR. Where comparison is possible, agreement between the two sets of results is good (Table II). Shih and Popov's value[22] of log K_s = 2.8 ± 0.2 for $K(2,1,1)^+$ in AN, determined by ^{39}K NMR is also in excellent agreement with the present value (log K_s = 2.84).

Similarly, the results of independent measurements[12,23] carried out in a different laboratory, but by using the same methods as in the present work, agree very well with those reported here (see Tables I and II).

Discussion

The results in Table I and II show the stability constants for the cryptates to be quite sensitive to solvent variation. Thus for a given cryptate, variations in stability constants of up to 9 orders of magnitude are observed. It is noticeable that the stability constants of the alkali-metal cryptates are lower in water than in any of the nonaqueous solvents. Among the nonaqueous solvents, the stability constants are qualitatively in line with trends expected from ion–solvent interactions in the solvents; stability constants are highest in acetonitrile and propylene carbonate where cation–solvent interactions are relatively weak, lowest in dimethylformamide and dimethyl sulfoxide, and occupy intermediate positions in methanol and ethanol. The larger variations in the free energies of Ag^+ compared with the alkali-metal cations on solvent transfer (see Table III below) are also reflected in larger variations in the stability of Ag^+ cryptates.

Table III. Free Energies of Transfer of Iodides from Water to Solvents[a] at 25 °C

	$\Delta G_{tr}(MI)^b$/kJ mol^{-1}					
MI	MeOH	EtOH	PC	MeCN	Me_2SO	DMF
LiI	10.8	20.3	36.0	41.6	−4.1	9.7
NaI	15.9	25.7	29.8	32.4	−1.6	10.1
KI	17.1	28.0	21.3	26.1	−0.9	11.0
RbI	17.8	29.8	18.9	25.2	1.0	11.2
CsI	17.3	28.6	17.4	22.8	−1.8	10.8
AgI	14.5	18.8	33.6	−4.2	−21.5	2.2
Ph_4AsI^c	−16.4	−7.9	−19.4	−14.2	−25.5	−18.2

[a] Abbreviations for solvents as in Table I. [b] Values from ref 4 and 24 (see text). [c] Reference 25.

Despite the large changes in ion–solvent interactions and stability constants in the various solvents, the selectivity pattern displayed by the cryptands is essentially independent of solvent. In all solvents, the alkali-metal cation forming the most stable complexes with the cryptands 2,1,1, 2,2,1, and 2,2,2 respectively are Li^+, Na^+, and K^+. This is in agreement with the simple concept of maximum stability resulting from optimum correspondence of the sizes of the cation and the intramolecular cavity of the ligand.[2] Complexes with Ag^+ are more stable than those of the alkali-metal cations in all solvents except acetonitrile. The ion–solvent interaction of Ag^+ compared with the alkali-metal cations are much stronger in acetonitrile than in any other of the solvents (see Table III).

A comparison of the results in dimethylformamide ($\epsilon = 36.7$)[7] and *N*-methylpropionamide ($\epsilon = 176$)$_8$ suggests that the dielectric constant of the medium does not play a large part in determining the stabilities of the complexes. Both solvents are expected to interact similarly with cations, predominantly through the oxygens of the amide carbonyl groups, and in the majority of cases, the stability constants in the two solvents are within 0.5 log unit, despite the very large difference in dielectric constants.

A more qualitative analysis of the results may be carried out in terms of eq 5, which relates the difference in stability constants between any two solvents to the free energies of transfer, ΔG_{tr}, of the species involved. In order to avoid discussion in terms of single-ion quantities (M^+ and $MCry^+$), we discuss the results with reference to the transfer of the corresponding iodide salts. Rearranging eq 5, and including I^-, leads to eq 6 for cryptate equilibria on transfer from water to solvent S. $\Delta G_{tr}(M^+I^-)$ values

$$\Delta G_{tr}(MCry^+I^-) = \Delta G_{tr}(M^+I^-) + \Delta G_{tr}(Cry) - RT \ln [K_s(s)/K_s(H_2O)] \quad (6)$$

for transfer from water to the various solvents (except for NMP) have been obtained from published solubility and electrochemical data in the solvents as described earlier[4] but modified where appropriate in light of more recent literature data[24] (particularly values in propylene carbonate[25,26]). The results are given in Table III, along with values of $\Delta G_{tr}(Ph_4As^+I^-)$.[27] $\Delta G_{tr}(2,2,2)$ values for transfer to MeOH, DMF, MeCN, and Me_2SO, respectively,

---

(16) C. W. Davies, "Ion Association", Butterworths, London, 1962.

(17) Y. M. Cahen, J. L. Dye, and A. I. Popov, *J. Phys. Chem.*, **79**, 1289 (1975).

(18) M. H. Abraham, E. C. Viguria, and A. F. Danil de Namor, *J. Chem. Soc., Chem. Commun.*, 374 (1979).

(19) E. L. Yee, J. Tabib, and M. J. Weaver, *J. Electroanal. Chem.*, **96**, 241 (1979).

(20) M. Lejaille, M. Livertoux, C. Guidon, and J. Bessiere, *Bull. Soc. Chim. Fr.*, I-373 (1978).

(21) E. Mei, L. Liu, J. L. Dye, and A. I. Popov, *J. Solution Chem.*, **6**, 771 (1977).

(22) J. S. Shinard and A. I. Popov, *Inorg. Chem.*, **19**, 1689 (1980).

(23) P. Firman, H. Schneider, and I. Schneider, unpublished results.

(24) B. G. Cox and W. E. Waghorne, *Chem. Soc. Rev.*, **9**, 381 (1980).

(25) M. L'Her, D. Morin-Bozec, and J. Courtot-Coupez, *J. Electroanal. Chem.*, **61**, 99 (1975).

(26) G. Gritzner, *Inorg. Chim. Acta*, **24**, 5 (1977).

(27) F. Alexander, A. J. Parker, J. H. Sharp, and W. E. Waghorne, *J. Am. Chem. Soc.*, **94**, 1148 (1972).

Table IV. Free Energies of Transfer of Metal Cryptate Iodides from Water to Solvents[a] at 25 °C

		$\Delta G_{tr}(MCry^+I^-)$[b]/kJ mol^{-1}					
M^+	Cry	MeOH	EtOH	PC	MeCN	Me_2SO	DMF
Li^+	2,2,2	5.8	18.4	8.0	12.3		
Na^+	2,2,2	−2.7	4.7	−2.4	4.8	−3.0	3.9
K^+	2,2,2	−7.8	4.5	−6.1	−2.4	−4.0	3.0
Rb^+	2,2,2	−4.7	5.3	−3.4	−0.2	−1.2	4.2
Cs^+	2,2,2	4.8	18.3	7.1	9.7	4.5	13.6
Ag^+	2,2,2	4.4	13.7	0.4	0.0	−1.6	6.9
Li^+	2,2,1	−3.5	6.0	−2.4	−0.9	−3.5	5.7
Na^+	2,2,1	−6.2	2.5	−6.3		−8.5	−2.5
K^+	2,2,1	−7.0	3.8	−10.5	−3.4	−10.3	−2.3
Rb^+	2,2,1	−4.0	6.2	−4.6	0.4	−8.8	−2.3
Ag^+	2,2,1	−2.8	5.9	−6.0	−2.6	−10.3	−2.7
Li^+	2,1,1	−1.4	5.7	−1.3		−3.7	3.5
Na^+	2,1,1	10.5	5.8	0.4		−6.5	1.3
Ag^+	2,1,1	4.8	14.3	1.7	2.4	−5.9	3.9

[a] Abbreviations for solvents as in Table I. [b] Values obtained by using eq 6, see text.

of 4.2, 6.7, 4.6, and 6.3 kJ mol^{-1} have been obtained from solubility studies of perchlorate salts of alkali-metal and Ag^+ cryptates.[28] Abraham and co-workers[18] also report a value of $\Delta G_{tr}(2,2,2)$ = 4.6 kJ mol^{-1} for transfer to methanol. For transfer to the other solvents we use an average value of $\Delta G_{tr}(2,2,2)$ = 5.2 kJ mol^{-1}, on the basis of those given above. Similarly $\Delta G_{tr}(2,2,1)$ and $\Delta G_{tr}(2,1,1)$ values for transfer to methanol of 2.1 and 2.3 kJ mol^{-1} have been obtained, but values for transfer of these ligands to other nonaqueous solvents are not available. We have used the values obtained in methanol for the analysis of results in the other solvents. It may be noted that the values chosen for $\Delta G_{tr}(Cry)$ will of course not affect the relative values of $\Delta G_{tr}(MCry^+I^-)$ for different metal ions with a given ligand. The application of eq 6 to the $\Delta G_{tr}(Cry)$ values above, together with $\Delta G_{tr}(MI)$ from Table III and log K_s from Tables I and II, gives $\Delta G_{tr}(MCry^+I^-)$ values shown in Table IV.

Considering first the results for 2,2,2 cryptates, for which the most comprehensive set of data exists, the large variations in $\Delta G_{tr}(MCry^+I^-)$ with M^+ in a given solvent are quite striking. Similar trends for 2,2,2[18] and 2B,2,2 cryptates in methanol[29] have been reported earlier. It is also noticeable that in all cases, ΔG_{tr} values are most favorable for $K(2,2,2)^+$ cryptates. Also, the trend with M^+ of $\Delta G_{tr}(M(2,2,2)^+I^-)$ values in a given solvent shows the same type of selectivity pattern as the stability constants. This is illustrated in Figures 1 and 2 for transfer to MeOH and PC. Figure 1 also includes $\Delta G_{tr}(HCry^+I^-)$ obtained from the pK_a's in water[5] and methanol[30] together with $\Delta G_{tr}(HI)$.[31] It may be seen that with respect to transfer of cryptates from water to methanol, H^+ acts in a manner qualitatively expected of a small alkali-metal cation. In contrast to this behavior, transfer between nonaqueous solvents shows no systematic trends with the metal ion, the differences between $\Delta G_{tr}(M(2,2,2)^+)$ values for different M^+ between two solvents being constant to within ca. ±2 kJ mol^{-1}. Values for transfer from DMF to PC and DMF to Me_2SO are shown in Figure 3 and are typical of the values for other pairs of nonaqueous solvents.

We would argue[3,29] that the variation of $\Delta G_{tr}(M(2,2,2)^+)$ for transfer from H_2O to S arise predominantly from interactions (H bonded) between water and the donor atoms of the ligands rather than between the solvents and cations within the ligand cavity. Thus for $K(2,2,2)^+$, the excellent fit of K^+ within the ligand cavity should result in all of the donor atoms being directed toward K^+, thus reducing ligand flexibility and allowing only hydrophobic CH_2 groups to come into contact with the solvent. Its transfer to nonaqueous solvents should then be relatively favorable. However, with a smaller cation such as Li^+, much of the ligand

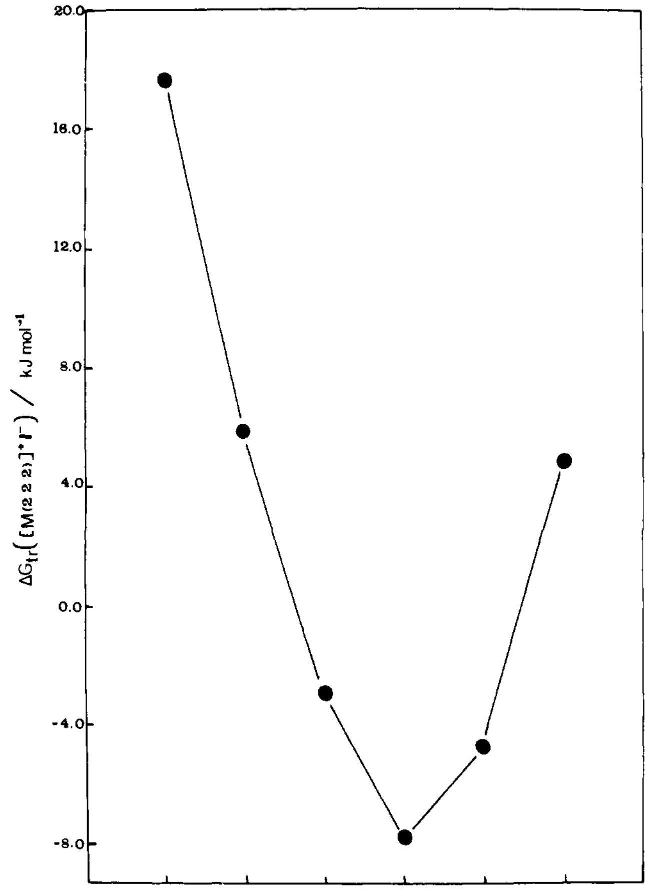


Figure 1. Free energies of transfer of $M(2,2,2)^+I^-$ from water to methanol.

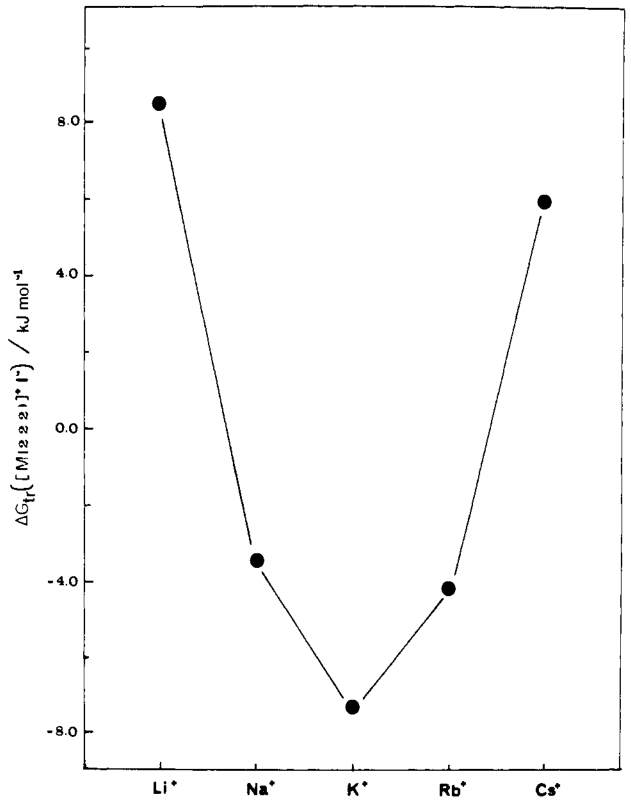


Figure 2. Free energies of transfer of $M(2,2,2)^+I^-$ from water to propylene carbonate.

---

[28] B. G. Cox, D. Knop, and H. Schneider, unpublished results.

[29] B. G. Cox, D. Knop, and H. Schneider, *J. Phys. Chem.*, **84**, 320 (1980).

[30] B. Spiess, E. Arnaud-Nai, and M.-J. Schwing-Weill, *Helv. Chim. Acta*, **62**, 1531 (1979).

[31] A. L. Andrews, H. P. Bennetto, D. Feakins, K. G. Lawrence, and R. P. T. Tomkins, *J. Chem. Soc. A*, 1486 (1968).

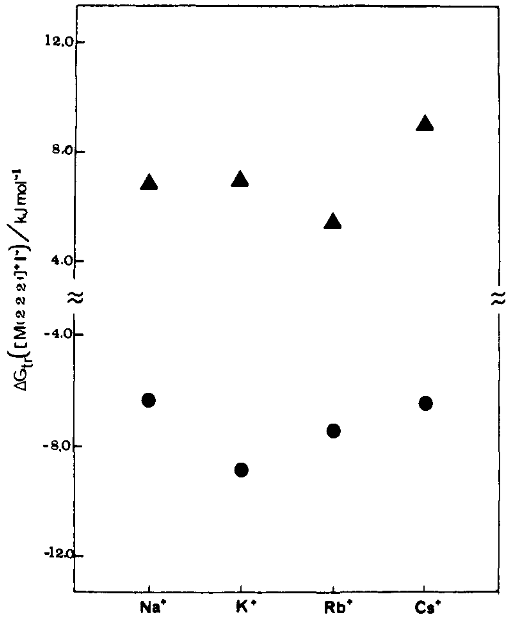


Figure 3. Free energies of transfer of $M(2,2,2)^+I^-$ from dimethylformamide to propylene carbonate (●) and from dimethyl sulfoxide to dimethylformamide (▲).

flexibility should be retained, allowing relatively free rotation of some of the donor groups to come into contact with the solvent, without greatly affecting the overall strength of cation–donor atom bonds. Similarly for a cation such as Cs^+, which is too large to fit properly into the cavity, some of the ligand donor groups will again be free to interact with the solvent. There is also the possibility of interaction between the only partially cryptated Cs^+ and the surrounding medium leading to variations in $\Delta G_{tr}(Cs(2,2,2)^+)$ relative to other metal cryptates. This, however, does not seem to be an important factor, as there is no evidence for this among transfers between the various nonaqueous solvents. This is perhaps not surprising, as interactions between a large cation such as Cs^+ and the solvent are not expected to be very large even when the cation is completely free and should certainly be smaller when Cs^+ is partially enclosed by a cryptand ligand.

Results for ligands 2,2,1 and 2,1,1 are in broad agreement with the discussion above. Again there is significant variation with M^+ of $\Delta G_{tr}(M(Cry)^+)$, but the minima in $\Delta G_{tr}(MCry^+)$ shift toward Li^+ in all solvents as Cry is reduced in size from 2,2,2 to 2,2,1 to 2,1,1. This is to be expected, as the cation most closely fitting into the ligand cavity changes from K^+ to Na^+ to Li^+ as the size of the ligand decreases. $\Delta G_{tr}(AgCry^+)$ values are generally close to those of $\Delta G_{tr}(Na(Cry)^+)$ or between those of Na^+ and Li^+ cryptates and show no particular trend with solvent relative to those of the alkali-metal cations. It is difficult to predict what might be expected for Ag^+ cryptates, as Ag^+ presumably interacts predominantly with the nitrogen atoms of the ligand. The crystallographic radius of Ag^+ lies between that of Na^+ and K^+.[32]

Although, as discussed above, there is a significant and systematic variation with M^+ of $\Delta G_{tr}(MCry^+I^-)$ for transfer from water to nonaqueous solvents, the variations in $G_{tr}(MCry^+I^-)$ are in general considerably less than those of the corresponding $\Delta G_{tr}(MI)$, particularly among the nonaqueous solvents. For transfer between PC and Me_2SO, to take an extreme example, $\Delta G_{tr}(MI)$ values vary between −54 and −18 kJ mol^{-1}, depending upon M^+, whereas $\Delta G_{tr}(MCry^+I^-)$ are close to 0 kJ mol^{-1}. Similarly the very strong interactions between Ag^+ and Me_2SO and CH_3CN compared with those of the alkali-metal salts (Table III) are not reflected in the $\Delta G_{tr}(MCry^+)$ values. These results suggest an effective shielding by the ligands of specific interactions between the solvents and cations held within the ligand cavities.

Table V. Effect of Anion on the Free Energies of Transfer of $K(2,2,2)^+X^-$ from Water to Acetonitrile at 25 °C

X^-	$\Delta G_{tr}°(K(2,2,2)^+X^-)$/ kJ mol^{-1}	X^-	$\Delta G_{tr}°(K(2,2,2)^+X^-)$/ kJ mol^{-1}
OAc^-	42.5	CNS^-	−4.5
Cl^-	24.9	ClO_4^-	−12.4
Br^-	12.3	Pic^-	−12.5
I^-	1.0	BPh_4^-	−50.4

[a] Values obtained by using eq 6.

The same does not, however, appear to be true for the difference between singly and doubly charged cations and their cryptates. Here the results suggest large differences between the interactions of $MCry^+$ and $MCry^{2+}$ with the surrounding solvent. Taking the data for Na^+ and Ca^{2+} (which have similar ionic radii[33]), it may be shown from the results in Table II, together with eq 5, that for transfer from water to PC

$$\Delta G_{tr}(CaCry^{2+}) - \Delta G_{tr}(NaCry^+) = \Delta G_{tr}(Ca^{2+}) - \Delta G_{tr}(Na^+) - 4.0 \text{ kJ mol}^{-1} \quad (7)$$

and for transfer from PC to DMF

$$\Delta G_{tr}(CaCry^{2+}) - \Delta G_{tr}(NaCry^+) = \Delta G_{tr}(Ca^{2+}) - \Delta G_{tr}(Na^+) - 10.0 \text{ kJ mol}^{-1} \quad (8)$$

The constants in eq 7 and 8 represent averages for the three ligands 2,2,2, 2,2,1, and 2,1,1. Thus the *difference* between ΔG_{tr} values of the cryptates is very similar to that of the free cations (as may be seen qualitatively from the very similar solvent dependences of the stabilities of Na^+ and Ca^{2+} cryptates). This latter term (i.e., the difference between ΔG_{tr} values of the free cations) is expected to be very large. For example, although results for the transfer of Ca^{2+} from water to PC are not known, Burgess[33] reports a difference between Ca^{2+} and Na^+ on transfer between H_2O and CH_3CN of some 97 kJ mol^{-1}. Also, Parker and co-workers[34] report a difference between Ba^{2+} and Na^+ of 44 kJ mol^{-1} for transfer between the same two solvents and a difference of 64 kJ mol^{-1} for transfer between DMF and CH_3CN; the corresponding differences between Ca^{2+} and Na^+ should be substantially larger. These values (although subject to the uncertainties of extra thermodynamic assumptions), together with eq 7 and 8, suggest strongly that the interactions with the surrounding solvent of cryptates containing singly and doubly charged cations of similar size are very different.

The results in Table IV and Figures 1 and 2 have important implications for the extraction of an electrolyte, MX, from water into nonaqueous media by cryptands and possibly other related macrocycles. It is clear that selective extraction results not only from selective complex formation in water (Table II), but as well there is a degree of selectivity in the equilibration of $MCry^+X^-$ between water and nonaqueous solvents (eq 9). In the case of

$$M^+(aq) + X^- + Cry(aq) \overset{K_s}{\rightleftharpoons} MCry^+(aq) + X^-(aq) \overset{K_{ex}}{\rightleftharpoons} [MCry^+X^-](s) \quad (9)$$

2,2,2 cryptates, this latter term results in an extra factor of ca. 10 in the extraction of K^+ salts relative to Na^+ and Rb^+ salts and of ca. 10^2–10^3 relative to Li^+ and Cs^+ salts, approximately independent of the nonaqueous solvent in question. For 2,2,1 cryptands, while there appears to be little effect in general on Na^+/K^+ ratios, it results in more effective extraction of Na^+ relative to Li^+, Rb^+, and Cs^+. Similarly, the extraction of Li^+ by 2,1,1 appears to be additionally favored by the selective transfer

---

(32) L. Pauling, "The Nature of the Chemical Bond", 3rd ed., Cornell University Press, New York, 1960.

(33) J. Burgess, "Metal Ions in Solution", Ellis Horwood, Chichester, 1978, Chapter 7.

(34) G. R. Hedwig, D. A. Owensby, and A. J. Parker, *J. Am. Chem. Soc.*, **97**, 3888 (1975).

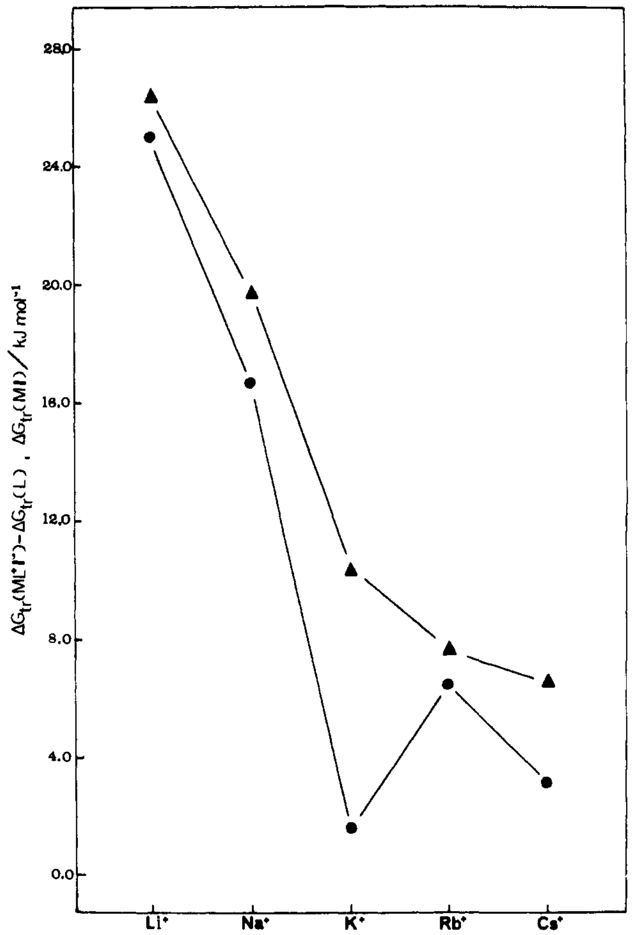


Figure 4. Free energies of transfer of (ML^+I^-–L) (●) and MI (▲) from dimethylformamide to propylene carbonate, with L = dibenzo-18-crown-6.

of $Li(2,1,1)^+$ into nonaqueous media relative to 2,1,1 cryptates of other alkali-metal cations.

In absolute terms, the transfer of alkali-metal iodides by the simple cryptands used here is not particularly effective. ΔG_{tr}($MCry^+I^-$) values are either slightly positive or slightly negative depending upon the system involved. They are, however, more negative than the corresponding ΔG_{tr}(MI) value (Table III), the difference being particularly marked for transfer to poorly solvating media such as PC and MeCN. The difference in the effect of solvent on $\Delta G_{tr}(M^+)$ and $\Delta G_{tr}(MCry^+)$ is reflected in the lower stabilities of the complexes in water compared with those of all of the nonaqueous solvents.

The ability of the cryptate to extract MX from water will also be strongly dependent upon the anion X^-. Table V shows the effect of anion on $\Delta G_{tr}(K(2,2,2)^+X^-)$ from water, the values in Table V coming from $\Delta G_{tr}(K(2,2,2)^+I^-)$ in Table IV, together with $\Delta G_{tr}(X^-) - \Delta G_{tr}(I^-)$ values from ref 3 and 24. The variations are typical for dipolar aprotic solvents, and it is clear from the work of Abraham and Danil de Namor[35] on ion solvation in solvents such as 1,2-dichloroethane that even more positive values for the smaller anions are to be expected in solvents of lower polarity. The very marked effects of anion on the results of crown ether-facilitated transport of cations across liquid membranes have already been noted by Christensen et al.[36] and are in line with the results in Table V (picrate > I^- > Br^- > Cl^- > OAc^-). In order to transport chloride salts effectively, it is necessary to use ligands capable of forming much more "organic" complexes than those of the simple cryptated studied here. These cryptates are much less effective than, for example, Ph_4As^+ (see Table III) in terms of their extraction into organic solvents. The mono- and dibenzo (2,2,2) cryptands[37] should undoubtedly be much better in this respect.

Finally, it is of interest to see the extent to which the behavior observed here for cryptates, particularly the selective extraction of metal cryptates from aqueous to nonaqueous media, is representative of the behavior of other macrocyclic ligands with similar complexing properties to those of cryptands. Some results for complexes of valinomycin in H_2O and MeOH are available (K^+, Rb^+, and Cs^+),[1] but these do not show any particular trend of $\Delta G_{tr}(ML^+)$ with cation. Other results, particularly for Li^+, Na^+, and K^+ complexes in various solvents, would be desirable.

Ligands of the crown-ether type[38] have been more extensively studied. These ligands, in contrast to the cryptands and naturally occurring macrocyclic antibiotics,[1] hold the cation in a two-dimensional cavity, allowing direct interaction between the solvent and the complexed cation. Thus changes in ion–solvent interactions between the solvent and the complexed cation would be expected to be more directly reflected in the $\Delta G_{tr}(ML^+)$ values. This is borne out by the results in Figure 4 for dibenzo-18-crown-6 complexes, which show a good correlation between $\Delta G_{tr}(ML^+I^-)$ and ΔG_{tr}(MI) values for transfer from DMF to PC. The values were obtained as before by the application of eq 5 to the stability constants in the two solvents, measured by Matsuura et al.[39] and ΔG_{tr}(MI) values from Table III. The contrast between these results and those in Figure 3 for transfer of 2,2,2 cryptates between the same pair of solvents is quite striking. The results in Table IV for transfer of various $MCry^+$ also suggest that $\Delta G_{tr}(Li(2,2,2^+))$ should be similar to those of the other cations in Figure 3. It is noticeable that there is a shallow minimum in both systems for the transfer of K^+ complexes (the most stable complex for both ligands), but it is difficult to know how significant this is.[40] The free energies of transfer of crown-ether complex salts from water to nonaqueous solvents also correlate quite well with the free energies of transfer of the corresponding uncomplexed salts. This may be shown, as described above, for complexes of dibenzo-18-crown-6[39,42] on transfer from water to PC, Me_2SO, and DMF and of 18-crown-6[42] and 15-crown-5[43] on transfer from water to PC.

Acknowledgment. We thank the SRC for a grant and the British Council and the National University of Mexico for financial support to J.G.-R.

---

[35] M. H. Abraham and A. F. Danil de Namor, *Chem. Soc., Faraday Trans. 1*, 955 (1976).

[36] J. J. Christensen, J. D. Lamb, S. R. Izatt, S. E. Starr, G. C. Weed, M. S. Austin, B. D. Stitt, and R. M. Izatt, *J. Am. Chem. Soc.*, **100**, 3219 (1978).

[37] B. Dietrich, J. M. Lehn, and J. P. Sauvage, *J. Chem. Soc., Chem. Commun.*, 15 (1973).

[38] C. J. Pederson and H. K. Frensdorff, *Angew, Chem., Int. Ed. Engl.*, **11**, 16 (1972).

[39] N. Matsuvura, K. Umemoto, Y. Takeda, and A. Sasaki, *Bull. Chem. Soc. Jpn.*, **49**, 1246 (1976).

[40] A recent study by Kolthoff and Chantooni[41] in fact questions some of the values reported in ref 39 but also shows a linear relationship between $\Delta G_{tr}(ML^+)$ and $\Delta G_{tr}(M^+)$ for L = dibenzo-18-crown-6 between the same pair of solvents.

[41] I. M. Kolthoff and M. K. Chantooni, *Anal. Chem.*, **52**, 1039 (1980).

[42] E. Shchori, N. Nae, and J. Jagur-Grodzinski, *J. Chem. Soc. Dalton Trans.*, 2381 (1975).

[43] Y. Takeda, H. Yano, M. Iskibashi, and H. Isozumi, *Bull. Chem. Soc. Jpn.*, **53**, 72 (1980).