Thermodynamics of Solvent Extraction of Metal Picrates with Crown Ethers: Enthalpy–Entropy Compensation. Part 1. Stoicheiometric 1 : 1 Complexation

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Quantitative solvent extractions were performed in the water–dichloromethane system at 10–25 °C to give the extraction equilibrium constants (K_{ex}) and the thermodynamic quantities (ΔH° and ΔS°) for the ion-pair extraction of aqueous alkali (Li^+–Cs^+), alkaline earth (Ca^{2+}–Ba^{2+}), and some heavy metal (Ag^+, Tl^+) picrates with 15-crown-5, benzo-15-crown-5, *cis*-cyclohexano-15-crown-5, 16-crown-5, 15-(2-methoxyethoxy)methyl-15-methyl-16-crown-5, 18-crown-6, dibenzo-18-crown-6, and dibenzo-24-crown-8. The cation-binding abilities and relative cation selectivities of the ligands are discussed from the thermodynamic point of view. Global treatment of the thermodynamic data obtained in the present and previous works reveals not only that, as is the case with the complexation in the homogeneous phase, the enthalpy–entropy compensation effect holds in the solvent extraction system, but also the ΔH° *vs.* $T\Delta S^\circ$ plot affords the characteristic slope (α) and intercept ($T\Delta S_0$) which are comparable to the corresponding values obtained for the homogeneous-phase complexation. This indicates that the conformational change and the extent of desolvation upon cation binding by crown ethers are quite analogous both in the homogeneous phase and in the solvent extraction beyond the apparent differences in the phase and the complexed species involved.

Enormous endeavours have been devoted to the thermodynamic studies of cation binding by macrocyclic polyethers such crown ethers and their acyclic and bicyclic analogues over the past two decades, and a great deal of thermodynamic data has hitherto been compiled for the complexation process in homogeneous solutions.[1] However, the thermodynamic data obtained have long been used to explain the stability and relative cation selectivity of only a particular individual cation–ligand combination from the enthalpic or entropic points of view. Each rationale given appears convincing for the particular case but cannot be applied in general to the other systems, so that the explanations seem *ad hoc*.

A more general approach has been proposed by Kauffmann *et al.*[2] and by Vögtle and Weber,[3] who classified the processes into four categories by the sign of the enthalpy and entropy changes upon complexation. However, the classification *per se* leads nowhere in particular and does not seem essential for a global understanding of the complexation process.

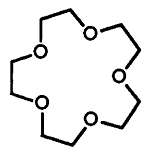
In their thermodynamic studies on cation binding by some crown ethers, Izatt *et al.*,[4] Michaux and Reisse,[5] Choi *et al.*,[6] and Ouchi *et al.*[7] have incidentally suggested that the enthalpy change (ΔH°) and the entropy change (ΔS°) compensate each other with ΔH° being the dominant factor determining the magnitude of the stability constant (K) of the complex. Examining the universal validity of the compensatory ΔH°–ΔS° relationship from the comprehensive and quantitative points of view by using all the compiled thermodynamic data,[8,9] we demonstrated that good linear relationships are found between ΔH° and $T\Delta S^\circ$ for the homogeneous-phase complexation of cations with a variety of synthetic and natural ligands, including glymes/podands,[8] crown ethers,[8] cryptands,[8] macrocyclic antibiotics,[8] and bis(crown ether)s.[9] Importantly, this linear relationship has been shown to serve our global understanding of the complexation phenomenon. The slope (α) and the intercept ($T\Delta S_0$), which are characteristic of the type of ligand used, can be rationalized in terms of the change in ligand conformation and the extent of desolvation upon complex formation, respectively.

In sharp contrast to the numerous thermodynamic studies on the homogeneous-phase complexation, surprisingly little work has been reported on the thermodynamics of solvent extraction with crown ethers.[7,10–15] In the present study, we report the thermodynamics of the solvent extraction of aqueous alkali, alkaline earth, and some heavy metal picrates with 15-crown-5 (**1**), benzo-15-crown-5 (**2**), *cis*-cyclohexano-15-crown-5 (**3**), 16-crown-5 (**4**), 15-(2-methoxyethoxy)methyl-15-methyl-16-crown-5 (**5**), 18-crown-6 (**6**), dibenzo-18-crown-6 (**7**), and dibenzo-24-crown-8 (**8**) in dichloromethane. The effects of ring substitution, molecular symmetry, additional binding sites, and ring size upon cation-binding abilities and relative cation selectivities are discussed from the thermodynamic viewpoint. The thermodynamic parameters obtained are further discussed in comparison with those for the homogeneous-phase complexation and also for the solvent extraction systems using different organic phases. We also reveal that the ΔH°–$T\Delta S^\circ$ complexation effect, demonstrated in the homogeneous phase,[8] holds again in the solvent extraction systems and that the ΔH° *vs.* $T\Delta S^\circ$ plot affords the characteristic slope (α) and intercept ($T\Delta S_0$) which are comparable to those for the complexation of crown ethers in the homogeneous phase.

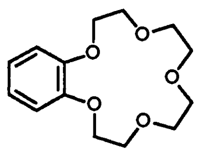
Experimental

Spectroscopy.—IR Spectra were recorded on a JASCO A-100 spectrometer. Mass spectra were obtained on a Hitachi RMU-6E instrument. ^1H NMR spectra were recorded on a JEOL GX-400 spectrometer.

Materials.—Commercially available 15-crown-5 (**1**) (Nisso), 18-crown-6 (**6**) (Nisso), and dibenzo-18-crown-6 (**7**) (Merck)



(1)



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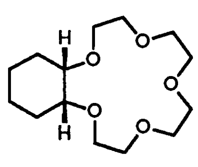

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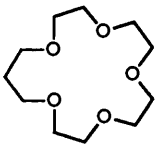

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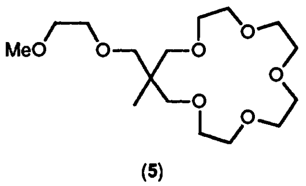

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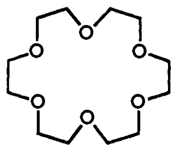

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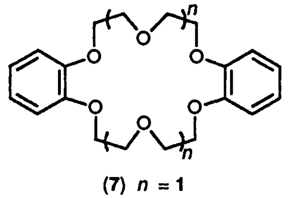


(7) $n = 1$
(8) $n = 2$

were used without further purification. Dibenzo-24-crown-8 (**8**) (Merck) was purified by repeated recrystallization from methanol. 16-Crown-5 (**4**) and its lariat derivative (**5**) were synthesized from tetraethylene glycol bis(toluene-*p*-sulphonate) and the appropriate trimethylene glycols according to the method reported previously.[16,17] Benzo-15-crown-5 (**2**) was synthesized in the reaction of tetraethylene glycol bis(toluene-*p*-sulphonate) with pyrocatechol in the presence of sodium hydroxide as base in tetrahydrofuran (THF), the subsequent recrystallization of the product from heptane gave white crystals in 40% yield. *cis*-Cyclohexano-15-crown-5 (**3**) was prepared from benzo-15-crown-5 by catalytic hydrogenation over Rh on charcoal as follows. A stainless steel autoclave was charged with benzo-15-crown-5 (2.5 g), acetic acid (0.5 g), 5% Rh/C (0.5 g), and methanol (100 cm^3) and the vigorously stirred mixture was hydrogenated at a hydrogen pressure of 5 atm for 5 h at room temperature (*ca.* 25 °C). The catalyst was removed by filtration and the solvent was evaporated off under reduced pressure to give a crude product, which was purified by distillation and subsequent column chromatography over alumina with heptane eluant to afford pure product (**3**) (1.4 g, 55%) (Found: C, 61.0; H, 9.7. Calc. for $C_{14}H_{26}O_5$: C, 61.31; H, 9.49%; MS (70 eV) *m/z* 274 (M^+); δ_H(400 MHz; CDCl$_3$) 1.23–1.35 (m, 2 H), 1.40–1.50 (m, 2 H), 1.55–1.65 (m, 2 H), 1.82–1.90 (m, 2 H), 3.54–3.56 (m, 2 H), and 3.62–3.78 (m, 16 H); ν_{max}(neat) 2 950, 2 850, 1 460, 1 360, and 1 120 cm^{-1}.

All metal picrates were prepared and purified according to the procedures reported elsewhere.[17–19]

Solvent Extraction.—The quantitative solvent extraction and the determination of the extraction equilibrium constants (K_{ex}) were carried out in the dichloromethane–water two-phase system according to the procedures reported previously.[17,19] Distilled dichloromethane and water were saturated with each other prior to use in order to prevent volume change during extraction. Dichloromethane solutions (10 cm^3) of a ligand over various concentration ranges (0.08–12 mmol dm^{-3}, depending upon its extractability) and aqueous solutions (10 cm^3) of each metal picrate (3 mmol dm^{-3}) were introduced into Erlenmeyer flasks, which were then stoppered and shaken reciprocally for 10 min in a Taiyo M100L incubator thermostatted at 25.0 ± 0.1 °C. The concentrations of picrate extracted into the organic phase were determined spectrophotometrically.[17,18] In order to determine thermodynamic parameters for the extraction equilibrium, the extraction experiments were repeated at 10, 15, 20, and 25 °C. In control runs, no detectable amounts of any picrates were extracted into the organic phase in the absence of crown ethers.

Distribution of Ligand.—Less lipophilic crown ethers are prone to distribute to the aqueous phase under the solvent extraction conditions. We, therefore, determined gravimetrically the distribution ratios (K_d) of the crown ethers between water and dichloromethane. Equal volumes (10 cm^3) of distilled water and dichloromethane solution containing a crown ether (300 mg) in a stoppered flask were brought into equilibrium by being shaken at each temperature investigated. After storage for 2 h at that temperature, the resultant mixture was separated. The organic phase was evaporated to dryness under reduced pressure to recover the organic fraction of crown ether remaining in dichloromethane, while the aqueous phase was back-extracted three or four times with fresh dichloromethane and the combined extracts were evaporated similarly to leave the fraction of crown ether from the original aqueous phase. Both fractions were weighed and the distribution ratio K_d was calculated.

Results

Extraction Equilibrium Constant.—Assuming a 1:1 cation:ligand stoicheiometry, the overall extraction equilibrium between an aqueous (aq) phase containing mono- or di-valent metal picrate (MA_m) and an organic (org) phase containing ligand (L) is expressed by equation (1).

$$M^{m+}_{aq} + mA^-_{aq} + L_{org} \rightleftharpoons [MLA_m]_{org} \qquad (1)$$

The extraction equilibrium constant (K_{ex}) is given by equation (2), where $[A^-]_{aq} = [A^-]_i - m[MLA_m]_{org}$; $[A^-]_i = 3m$ mmol dm^{-3}. The distribution coefficient of metal ion (D_M) and the concentration of free ligand in the organic phase ($[L]_{org}$) after the equilibrium is attained are calculated by equations (3) and (4), respectively, where $[M^{m+}]_{aq} = [A^-]_{aq}/m$ and $[L]_i$ represents the initial concentration of ligand dissolved in the organic phase, and K_d the distribution coefficient of ligand between the aqueous and organic phases ($K_d = [L]_{aq}/[L]_{org}$), which was determined in the experiment described below. Modification of equation (2) leads to equation (5). Thus, a plot of log ($D_M/[A^-]_{aq}{}^m$) as a function of log $[L]_{org}$ gives a straight line of unit slope and the extraction equilibrium constant K_{ex} is calculated from the intercept.

$$K_{ex} = \frac{D_M}{[A^-]_{aq}{}^m[L]_{org}} \qquad (2)$$

$$D_M = [MLA_m]_{org}/[M^{m+}]_{aq} \qquad (3)$$

$$[L]_{org} = ([L]_i - [MLA_m]_{org})/(1 + K_d) \qquad (4)$$

$$\log (D_M/[A^-]_{aq}{}^m) = \log [L]_{org} + \log K_{ex} \qquad (5)$$

Quantitative solvent extraction studies with aqueous alkali, alkaline earth, and heavy metal picrates were carried out at a variety of ligand concentrations to determine extraction equilibrium constants K_{ex}. A set of extraction data obtained for each cation–ligand combination was analysed according to equation (5). Typical plots for 18-crown-6 (**6**) are shown in Figure 1. The experiments were performed at 10, 15, 20, and

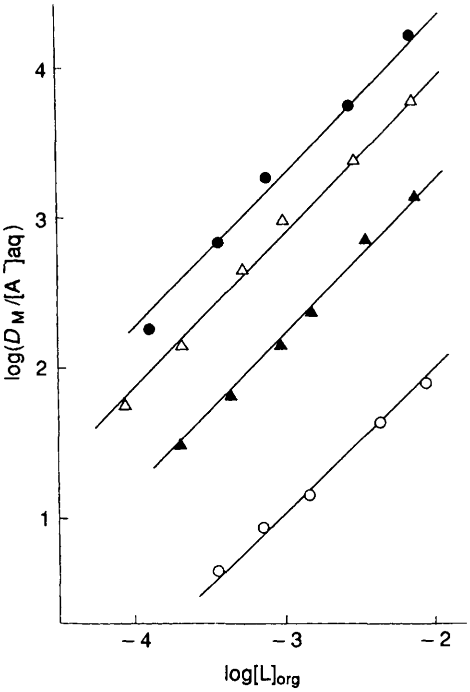


Figure 1. Typical plots of $\log(D_M/[A^-]_{aq}{}^m)$ *vs.* $\log[L]_{org}$ in solvent extraction of aqueous sodium (○), potassium (●), rubidium (△), and caesium (▲) picrates (3 mmol dm^{-3}) with 18-crown-6 (**6**) at various concentrations in dichloromethane at 25 °C.

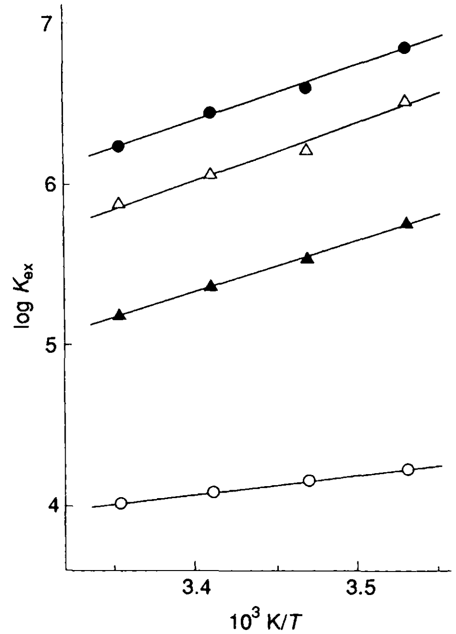


Figure 2. Typical plots of $\log K_{ex}$ *versus* $1/T$ in solvent extraction of sodium (○), potassium (●), rubidium (△), and caesium (▲) picrates with 18-crown-6 (**6**).

25 °C and the K_{ex}-values obtained at every temperature are listed in Table 1.

Distribution of Crown Ether.—Since some of the crown ethers used are water soluble, the distribution coefficients K_d of free crown ethers were determined gravimetrically at each temperature investigated. The K_d-values determined from three independent runs are listed in Table 2. The benzo- or cyclohexano-crown ethers were shown to be practically insoluble ($K_d \ll 0.01$) in water, although their distributions to the aqueous phase were examined by spectrophotometric or gravimetric analyses of the aqueous and organic phases separated from the equilibrated mixture.

Thermodynamic Parameters.—The free-energy change ($\Delta G°$) for the extraction equilibrium [equation (1)] is calculated from the equilibrium constant K_{ex} by equation (6) and is related to

$$\Delta G° = -RT\ln K_{ex} \qquad (6)$$

the enthalpic and entropic changes ($\Delta H°$ and $\Delta S°$) through the Gibbs–Helmholtz equation (7). Combining equations (6) and

$$\Delta G° = \Delta H° - T\Delta S° \qquad (7)$$

(7), we obtain equation (8) which describes the temperature

$$\log K_{ex} = (1/2.303R)(\Delta S° - \Delta H°/T) \qquad (8)$$

dependence of K_{ex}.

Plots of the log K_{ex} value, shown in Table 1, as a function of the inverse temperature gave good straight lines as exemplified by 18-crown-6 (**6**) in Figure 2. The thermodynamic parameters obtained for each crown ether are listed in Table 3.

Discussion

As the solvent extraction involves transfer of hydrated ion pairs from the aqueous to the organic phase, the feasibility of dehydration upon extraction becomes a crucial factor determining the extractability of the ligand.[20] Taking into account the participation of water of hydration in the solvent extraction system, we can rewrite equation (1) in a more detailed form [equation (9)].

$$[M^{m+}\cdot jH_2O]_{aq} + m[A^-\cdot kH_2O]_{aq} + L_{org} \rightleftharpoons [MLA_m\cdot(j + mk - x)H_2O]_{org} + xH_2O_{aq} \qquad (9)$$

In the ion-pair extraction process, the hydrated metal ($M^{m+}\cdot jH_2O$) and picrate ($A^-\cdot kH_2O$) ions in the aqueous phase are simultaneously extracted with the ligand (L) in the organic phase, giving rise to the ion-pair complex $MLA\cdot(j + mk - x)$ H_2O and the liberated water of hydration (xH_2O). Upon extraction into the highly hydrophobic organic solvents, the dehydration fron the ion's first solvation shell must be fairly extensive but, still, the resulting ion-pair complex in the organic phase has been shown to carry a certain number of water molecules: $j + mk - x = 1$–5.[21,22]

Thermodynamically, the solvent extraction process is governed by several self-conflicting factors. The molecular association process, which is inherently unfavourable from the entropic point of view, is driven by the enthalpic gain from the favourable ion–dipole and electrostatic interactions of the metal ion with the pre-organized ligand donors and the counteranion, respectively. The extensive desolvation of the ion pair upon extraction may compensate the unfavourable entropic contribution from the molecular association and the frozen ligand conformation. It should be noted, however, that, as shown in Table 3, the entropy changes ($\Delta S°$), as well as the enthalpy changes ($\Delta H°$), are all negative throughout the combinations of cation and ligand employed, in contrast to the corresponding data in the homogeneous phase listed in Table 4.[23–27]

Cation-binding Ability and Cation Selectivity.—As can be seen from Table 3, both the cation-binding ability and the relative

Table 1. Extraction equilibrium constants (K_{ex}) at 10–25 °C for solvent extraction of aqueous mono- and di-valent metal picrates with some crown ethers in dichloromethane.

Ligand	Cation	log K_{ex}			
		25 °C	20 °C	15 °C	10 °C
15-Crown-5 (**1**)	Li^+	2.78	2.84	2.90	2.97
	Na^+	4.48	4.63	4.83	5.03
	K^+	4.33	4.45	4.59	4.73
	Rb^+	4.14	4.25	4.40	4.55
	Cs^+	3.67	3.83	3.93	4.06
	Ag^+	4.94	5.10	5.30	5.52
	Tl^+	5.08	5.21	5.39	5.57
	Ca^{2+}	5.50	5.66	5.72	5.84
	Sr^{2+}	6.06	6.24	6.49	6.68
	Ba^{2+}	6.72	6.90	7.16	7.43
Benzo-15-crown-5 (**2**)	Na^+	3.74	3.78	3.94	4.10
	K^+	3.99	4.09	4.21	4.37
	Rb^+	3.70	3.77	3.89	4.03
	Cs^+	3.31	3.43	3.52	3.60
	Ag^+	3.98	4.07	4.24	4.38
	Tl^+	4.30	4.39	4.56	4.72
	Ca^{2+}	4.45	4.53	4.60	4.75
	Sr^{2+}	4.93	5.10	5.21	5.32
	Ba^{2+}	5.62	5.70	5.83	5.99
Cyclohexano-15-crown-5 (**3**)	Na^+	4.85	5.04	5.15	5.26
	K^+	4.23	4.38	4.49	4.59
	Rb^+	4.16	4.30	4.40	4.50
	Cs^+	3.81	3.95	4.06	4.20
	Tl^+	5.27	5.39	5.41	5.46
16-Crown-5 (**4**)	Na^+	4.54	4.71	4.88	5.04
	K^+	3.60	3.77	3.94	4.09
	Rb^+	3.48	3.63	3.72	3.89
	Ag^+	5.19	5.37	5.56	5.73
	Tl^+	4.79	4.98	5.10	5.32
	Sr^{2+}	5.81	6.00	6.19	6.35
	Ba^{2+}	6.32	6.52	6.77	6.96
16-Crown-5 lariat (**5**)	Na^+	4.70	4.86	5.02	5.15
	K^+	3.40	3.55	3.69	3.84
	Rb^+	3.25	3.33	3.54	3.81
	Ag^+	5.18	5.33	5.45	5.65
	Tl^+	4.37	4.54	4.71	4.85
18-Crown-6 (**6**)	Na^+	4.02	4.09	4.16	4.23
	K^+	6.24	6.45	6.59	6.85
	Rb^+	5.89	6.07	6.21	6.53
	Cs^+	5.19	5.37	5.54	5.77
	Ag^+	5.14	5.28	5.36	5.54
Dibenzo-18-crown-6 (**7**)	Na^+	2.83	2.94	3.05	3.14
	K^+	4.80	4.97	5.18	5.34
	Rb^+	4.44	4.58	4.77	4.99
	Cs^+	4.09	4.18	4.36	4.53
	Ag^+	3.72	3.83	3.98	4.10
	Tl^+	5.02	5.20	5.42	5.61
	Sr^{2+}	5.68	5.80	5.93	6.09
Dibenzo-24-crown-8 (**8**)	Rb^+	4.33	4.45	4.65	4.80
	Cs^+	4.55	4.69	4.89	5.03
	Tl^+	5.04	5.25	5.40	5.56
	Ba^{2+}	7.15	7.25	7.65	7.95

cation selectivity are affected drastically by several structural factors of the ligand as is the case with the homogeneous-phase complexation.[3,28]

Size–fit concept. The cation-binding ability and relative cation selectivity of macrocyclic ligands such as crown ethers have long been discussed from the size-relationship between the ligand cavity and the cation diameter,[3,28] while the size–fit concept has recently been shown to be unsuccessful in explaining the cation selectivities of some flexible macrocycles and *N*-pivot lariat ethers.[5,29] However, as far as the data obtained in the present study are concerned, the size–fit concept still functions as a valid working hypothesis. With each crown ether, the largest enthalpy changes are found almost always in the complexation with the size-matched cations: Na^+ and Ag^+ for crown-5; K^+ or Rb^+ and Tl^+ for crown-6; Cs^+ for crown-8. Thus, the cation-binding ability and cation selectivity are apparently enthalpy driven. This is probably because the size-fitted combinations give the strongest ion–dipole interaction and, therefore, the largest enthalpic gain, part of which is cancelled to a certain extent by the accompanying entropic loss from the structural freezing of the resulting complex.

It is also interesting to discuss the complexation of size-mismatched cation–ligand combinations from the thermodynamic viewpoint. As the cation size becomes larger than

Table 2. Distribution coefficients (K_d)[a] of some crown ethers between aqueous and dichloromethane phases at 10–25 °C.

Ligand	K_d 25 °C	20 °C	15 °C	10 °C
15-Crown-5 (**1**)	0.305	0.336	0.394	0.461
16-Crown-5 (**4**)	0.149	0.163	0.187	0.212
16-Crown-5 lariat (**5**)	0.017	0.018	0.019	0.020
18-Crown-6 (**6**)	0.289	0.334	0.394	0.462

[a] $K_d = [L]_{aq}/[L]_{org}$.

Table 3. Thermodynamic parameters at 25 °C in kcal mol^{-1} for solvent extraction of aqueous mono- and di-valent metal picrates with some crown ethers in dichloromethane.

Ligand	Cation	$-\Delta G°$	$-\Delta H°$	$-T\Delta S°$
15-Crown-5 (**1**)	Li^+	3.79	4.86	1.07
	Na^+	6.09	14.30	8.21
	K^+	5.91	10.35	4.44
	Rb^+	5.7	10.7	5.0
	Cs^+	5.03	9.79	4.76
	Ag^+	6.72	15.00	8.28
	Tl^+	6.92	12.75	5.83
	Ca^{2+}	7.53	8.33	0.80
	Sr^{2+}	8.26	16.30	8.04
	Ba^{2+}	9.1	18.5	9.3
Benzo-15-crown-5 (**2**)	Na^+	5.1	9.6	4.5
	K^+	5.43	9.74	4.31
	Rb^+	5.03	8.59	3.56
	Cs^+	4.53	7.39	2.86
	Ag^+	5.41	10.59	5.18
	Tl^+	5.84	11.05	5.21
	Ca^{2+}	6.06	7.51	1.45
	Sr^{2+}	6.76	9.63	2.87
	Ba^{2+}	7.64	9.59	1.95
Cyclohexano-15-crown-5 (**3**)	Na^+	6.65	10.31	3.66
	K^+	5.80	9.17	3.37
	Rb^+	5.70	8.63	2.93
	Cs^+	5.21	9.88	4.67
	Tl^+	7.2	4.5	−2.7
16-Crown-5 (**4**)	Na^+	6.20	12.90	6.70
	K^+	4.92	12.65	7.73
	Rb^+	4.75	10.19	5.44
	Ag^+	7.08	13.96	6.88
	Tl^+	6.54	13.21	6.67
	Sr^{2+}	7.94	13.96	6.02
	Ba^{2+}	8.63	16.74	8.11
16-Crown-5 lariat (**5**)	Na^+	6.43	11.66	5.23
	K^+	4.65	11.27	6.62
	Rb^+	4.3	14.6	10.3
	Ag^+	7.06	11.82	4.76
	Tl^+	5.97	12.41	6.44
18-Crown-6 (**6**)	Na^+	5.49	5.40	−0.09
	K^+	8.51	15.22	6.71
	Rb^+	8.0	15.9	7.9
	Cs^+	7.08	14.76	7.68
	Ag^+	7.01	9.89	2.88
	Tl^+	8.96	18.56	9.60
Dibenzo-18-crown-6 (**7**)	Na^+	3.87	8.03	4.16
	K^+	6.55	14.12	7.57
	Rb^+	6.03	14.22	8.19
	Cs^+	5.55	11.60	6.05
	Ag^+	5.07	9.96	4.89
	Tl^+	6.85	15.36	8.51
	Sr^{2+}	7.74	10.51	2.77
Dibenzo-24-crown-8 (**8**)	Rb^+	5.89	12.43	6.54
	Cs^+	6.19	12.88	6.69
	Tl^+	6.90	13.18	6.28
	Ba^{2+}	9.7	21.7	12.0

the cavity size, the enthalpy and entropy changes decrease only slightly or gradually to a limited extent; see the parameters for K^+–Cs^+ and Tl^+ with crown-5 and those for Rb^+ and Cs^+ with crown-6 in Table 3. By contrast, for the cations smaller in size than the cavity, the enthalpy change in particular, and the entropy change to a smaller extent, are reduced quite abruptly to give much smaller free-energy changes; see the values for Li^+ with 15-crown-5 and those for Na^+ with crown-6. Consequently the relative cation selectivities for the size-matched cation toward smaller cation(s) become satisfactorily high, while those toward larger cations are disappointingly low, except for the less symmetrical 16-crown-5 ethers (**4**) and (**5**). The abrupt decrease, especially in enthalpy change, may indicate that the small cation in a large cavity interacts insufficiently in strength and/or number with the donor oxygens owing to the limited structural adjustability of the ligand.

Substituent Effect. The ring substitutions of 15-crown-5 (**1**) with the benzo and cyclohexano groups resulted in distinctly different changes in the extraction equilibrium constant K_{ex} or $-\Delta G°$. The decreased extractabilities or smaller $\Delta G°$-values for benzo-15-crown-5 (**2**) are attributed to the much reduced enthalpic gains, which far exceed the favourable entropic contributions. On the other hand, cyclohexano-15-crown-5 (**3**) showed somewhat greater enthalpic gains and smaller entropic losses for most cations as compared with the benzo derivative, thus, affording higher extractabilities than the benzo- and the parent 15-crown-5. This effect is notable particularly for the size-matched cations, *i.e.* Na^+ and Ag^+, and, therefore, the cation selectivity increases in the order (**2**) < (**1**) < (**3**).

It is interesting to compare the entropy change upon complexation of the size-matched Na^+ and Ag^+ cations with compounds (**1**)–(**3**). Since the complex geometry does not substantially differ for these 15-crown-5 derivatives, the entropic gain arising from desolvation is inferred to be about equal for each complex. Thus, the entropy change may be taken as a measure of the crown ether's conformational change upon complexation. In this context, the large entropy loss for compound (**1**) indicates substantial conformational change upon complexation, suggesting that the original structure of free (**1**) is not suitable for complexation. The partially fixed structures, and possibly the favourable original structures, of crown ethers (**2**) and (**3**) may be responsible for the smaller entropy change for these ligands.

Molecular symmetry. In previous papers, we have demonstrated that the ring-enlarged 16-crown-5 (**4**) shows much higher cation selectivities for Na^+ and Ag^+ than does the more common 15-crown-5 (**3**) in the solvent extraction[7,16,17,20] as well as the homogeneous-phase complexation.[30] As shown in Table 3, the introduction of an extra methylene group into compound (**3**), affording the less symmetrical ligand (**4**), does not substantially enhance the extractabilities or $-\Delta G°$-values for the size-matched cations but does drastically diminish the cation-binding abilities for the size-mismatched larger cations, endowing this less symmetrical crown ether with high cation selectivities. Upon ring enlargement, the enthalpic gains decrease uniformly for all monovalent cations except for Tl^+, while the entropic losses concurrently decrease for the size-matched cations but increase for the larger cations. This result indicates that, in spite of its increased conformational freedom, the ring-enlarged crown ether (**4**) suffers unexpectedly small conformational change upon complexation with the size-matched cations and therefore the conformation of free ligand (**4**) is originally more suitable for complexation.

Lariat effect. The introduction of an additional binding site in 16-crown-5 affording lariat ether (**5**)[17] does not greatly alter the extractabilities of the size-matched cations Na^+ and Ag^+ but diminishes those for the larger cations to some extent, resulting in the appreciably enhanced Na^+/K^+ and Ag^+/Tl^+ selectivities

Table 4. Reported thermodynamic parameters at 25 °C, in kcal mol^{-1}, for homogeneous-phase 1:1 complexation of mono- and di-valent cations with some crown ethers in methanol.

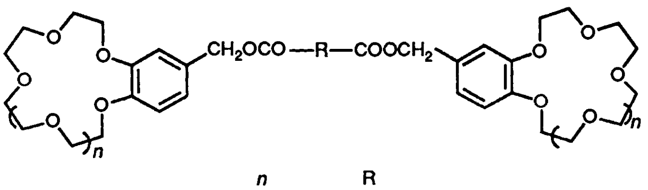
Ligand	Cation	$-\Delta G°$	$-\Delta H°$	$-T\Delta S°$	Ref.
15-Crown-5 (**1**)	Li^+	1.68	2.70	1.10	*a*
	Na^+	4.67	5.25	0.64	*b*
	K^+	5.26	7.41	2.21	*b*
	Rb^+	5.55	6.76	0.50	*b*
	Cs^+	4.88	5.07	0.21	*b*
	Ag^+	4.97	6.42	1.45	*b*
	Tl^+	4.41	8.71	4.30	*c*
	Ca^{2+}	2.73	2.22	−0.50	*b*
	Sr^{2+}	4.37	3.47	0.86	*b*
	Ba^{2+}	5.58	5.00	−0.57	*b*
Benzo-15-crown-5 (**2**)	Na^+	4.13	5.04	0.93	*b*
	K^+	5.34	6.48	1.14	*b*
	Rb^+	5.40	5.40	0.00	*b*
	Cs^+	4.75	3.32	−1.43	*b*
	Ag^+	4.17	3.96	−0.21	*b*
	Sr^{2+}	3.98	0.55	−3.57	*b*
	Ba^{2+}	4.95	1.14	−3.49	*b*
Cyclohexano-15-crown-5 (**3**)	Na^+	5.32	4.80	−0.50	*b*
	K^+	5.40	5.59	0.21	*b*
	Rb^+	5.96	5.91	0.00	*b*
	Cs^+	4.81	5.31	0.50	*b*
18-Crown-6 (**6**)	Na^+	5.89	8.13	2.28	*b*
	K^+	8.27	13.12	4.85	*b*
	Rb^+	7.26	11.85	4.56	*b*
	Cs^+	6.06	11.93	5.91	*b*
	Ag^+	6.34	9.33	3.13	*b*
Dibenzo-18-crown-6 (**7**)	Na^+	6.14	7.48	1.34	*d*
	K^+	6.98	9.58	2.62	*d*
	Rb^+	5.95	6.84	0.89	*c*
Dibenzo-24-crown-8 (**8**)	Rb^+	5.32	9.42	4.10	*e*
	Cs^+	5.24	8.80	3.49	*e*
	Tl^+	4.64	7.17	2.53	*c*
	Ba^{2+}	5.52	5.88	0.36	*c*

[a] Ref. 23. [b] Ref. 24. [c] Ref. 25. [d] Ref. 26. [e] Ref. 27.

(Table 3). Unlike simple crown ethers, the lariat ethers bind cations in the three-dimensional cavity surrounded by the donor atoms in the ring and the sidearm.[31,32] This complexation process apparently requires conformational fixation of the sidearm, accompanying a substantial entropic loss. On the other hand, the cation accommodated in the three-dimensional cavity suffers thorough dehydration upon complexation. The entropic gain from the dehydration well exceeds the entropic loss from the conformational fixation to give the less negative entropy changes for the lariat ether (**5**) as compared with 16-crown-5 (**4**) except for Tl^+.

Homogeneous vs. *Heterogeneous Phase.*—In Table 4, the latest thermodynamic parameters for methanol solution are listed for the same cation–ligand combinations as Table 3. Although the free-energy changes for the homogeneous and heterogeneous systems are incidentally in the comparable orders of magnitude for most cations, solvent extraction gives much larger enthalpy and entropy changes than the homogeneous-phase complexation. This is simply because the solvent extraction process involves the molecular association of three, rather than two, components, resulting in a larger entropic loss, and also because of the Coulombic, in addition to ion–dipole, interaction between the complexed cation and the counteranion picrate, leading to a larger enthalpic gain. However, the two opposite contributions appear to compensate each other, and give comparable free-energy changes in the homogeneous and heterogeneous systems. It is inferred, therefore, that the enthalpy and entropy changes in the solvent extraction are merely exaggerated by the participation of counteranion in the complex formed, but the net change upon complexation does not substantially differ between the systems.

Solvent Effect.—Apart from the pioneering work by Sadakane *et al.*,[10] the thermodynamics of solvent extraction have only recently been investigated with a limited number of cation–ligand combinations in the benzene–water or chloroform–water system.[7,11–15] All of the thermodynamic parameters reported for these solvent extraction systems are listed in Table 5. It is noted that these parameters were obtained in the presence of dense background salt, *i.e.* metal hydroxide or nitrate, in the aqueous phase, while our work was done with dilute, pure metal picrate solutions in the absence of any background salts.



	n	R
(**9t**)	1	CH=CH(*trans*)
(**9c**)	1	CH=CH(*cis*)
(**9s**)	1	CH_2CH_2
(**10t**)	2	CH=CH(*trans*)
(**10c**)	2	CH=CH(*cis*)
(**10s**)	2	CH_2CH_2

In the homogeneous-phase complexation, the stability constant for the complex often varies over several orders of

Table 5. Reported thermodynamic parameters at 25 °C in kcal mol^{-1} for solvent extraction of aqueous alkali metal picrates with some crown ethers in chloroform or benzene in the presence of excess of metal hydroxides in aqueous phase.

Ligand	System	Cation	$-\Delta G^\circ$	$-\Delta H^\circ$	$-T\Delta S^\circ$	Ref.
15-Crown-5 (**1**)	water–C_6H_6	Na$^+$	5.32	10.83	5.47	*a*
		K$^+$	3.52	6.52	2.99	*a*
		Rb$^+$	2.92	8.91	6.05	*a*
		Cs$^+$	2.59	10.16	7.55	*a*
Benzo-15-crown-5 (**2**)	water–C_6H_6	Na$^+$	4.49	17.7	13.1	*b*
		K$^+$	2.80	12.0	9.1	*b*
18-Crown-6 (**6**)	water–C_6H_6	Na$^+$	4.62	8.22	3.51	*c*
		K$^+$	8.14	18.48	10.23	*c*
		Rb$^+$	7.40	18.55	11.02	*c*
		Cs$^+$	5.97	15.85	9.78	*c*
	water–$CHCl_3$	Na$^+$	4.73	10.92	6.21	*d*
		K$^+$	8.28	18.26	9.99	*d*
		Rb$^+$	7.70	18.91	11.21	*d*
		Cs$^+$	6.30	18.28	11.97	*d*
Dibenzo-18-crown-6 (**7**)	water–C_6H_6	Na$^+$	2.9	8.9	6.0	*e*
		K$^+$	6.3	16.3	10.0	*e*
		Rb$^+$	5.1	16.4	11.3	*e*
		Cs$^+$	4.2	16.0	11.8	*e*
(*E*)- or *trans*-Bis-(benzo-15-crown-5) (**9t**)	water–$CHCl_3$	Na$^+$	4.20	7.80	3.61	*f*
		K$^+$	3.49	9.02	5.54	*f*
(*Z*)- or *cis*-Bis(benzo-15-crown-5) (**9c**)	water–$CHCl_3$	Na$^+$	4.27	7.74	3.46	*f*
		K$^+$	5.77	6.18	0.41	*f*
Bis(benzo-15-crown-5) (**9s**)	water–$CHCl_3$	Na$^+$	4.21	7.76	3.55	*f*
		K$^+$	5.73	8.88	3.12	*f*
(*E*)- or *trans*-Bis(benzo-18-crown-6) (**10t**)	water–$CHCl_3$	K$^+$	7.09	16.1	9.0	*f*
		Cs$^+$	5.14	15.3	10.2	*f*
(*Z*)- or *cis*-Bis(benzo-18-crown-6) (**10c**)	water–$CHCl_3$	K$^+$	7.20	16.0	8.79	*f*
		Cs$^+$	6.57	11.0	4.44	*f*
Bis(benzo-18-crown-6) (**10s**)	water–$CHCl_3$	K$^+$	7.19	16.30	9.12	*f*
		Cs$^+$	6.47	12.72	6.23	*f*

[a] Ref. 13. [b] Ref. 12. [c] Ref. 15. [d] Ref. 14. [e] Ref. 10. [f] Ref. 11.

magnitude upon changing of the solvent polarity.[1,28] In contrast, the free-energy change in solvent extraction does not vary over such a wide range upon changing of the extraction solvent, especially for the size-matched cations. Thus, the free-energy gains ($-\Delta G^\circ$) for Na$^+$ with crown-5 and for K$^+$ with crown-6 increase by less than 0.7 and 0.3 kcal mol^{-1},* respectively, on going from benzene to chloroform, and then to dichloromethane. This is attributed in part to the smaller polarity range of the extraction solvent used. However, the relative cation selectivity is much more sensitive to the polarity change, as the free-energy gains for the size-mismatched cations rapidly decrease with decreasing solvent polarity. The benzene–water system exhibits the highest cation selectivities for most crown ethers.

Further examination of the individual enthalpy and entropy changes does not lead to a general conclusion with respect to the solvent effect, since apparently both thermodynamic parameters vary arbitrarily when the solvent polarity is changed. However, we note that the enthalpy and entropy changes are affected in a related and compensatory manner, resulting in the analogous ultimate free-energy changes in all solvents.

Enthalpy–Entropy Compensation.—From our systematic study of the solvent extraction at different temperatures, we obtained the invaluable thermodynamic parameters for the ion-pair extraction of aqueous metal picrates with a series of crown ethers in dichloromethane. Using the data obtained, we have discussed the observed cation-binding ability, relative cation selectivity, and other features of the individual crown ethers from the thermodynamic point of view, and the conclusions derived are convincing (we believe) in these specific cases. However, as was indicated in our first paper on the enthalpy–entropy compensation effect in the homogeneous-phase complexation,[8,9] the rationalizations given in the literature are often oversimplified and/or highly specialized, and do not appear to contribute significantly to the global understanding of the nature of cation–ligand complexation. Here we concentrate on the possible extension of the enthalpy–entropy compensation effect to the solvent extraction system.

Table 6. The slope (α) and the intercept ($T\Delta S_0$) of the ΔH°–$T\Delta S^\circ$ plots for 1:1 complexation with various ligands in homogeneous phase and solvent extraction.

	Homogeneous phase[a]		Solvent extraction[b]	
Ligand	α	$T\Delta S_0$	α	$T\Delta S_0$
Glyme/podand	0.86	2.3		
Crown ether	0.76	2.4	0.73	2.6
Cryptand	0.51	4.0		
Antibiotic	0.95	5.6		
Bis(crown ether)	1.03	4.6		

[a] Refs. 8 and 9. [b] This work.

In addition to the data obtained in the present study (Table 3), Sadakane *et al.*,[10] Kimura *et al.*,[11] and Takeda *et al.*[12–15] have reported the thermodynamic parameters for the solvent extraction of alkali and alkaline earth metal picrates with some crown ethers and bis(crown ethers). These data, listed in Table 5, were obtained under somewhat different conditions, using benzene or chloroform as the organic solvent and higher ionic strength of excess of metal hydroxide or nitrate in the aqueous phase.

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* 1 cal = 4.184 J.

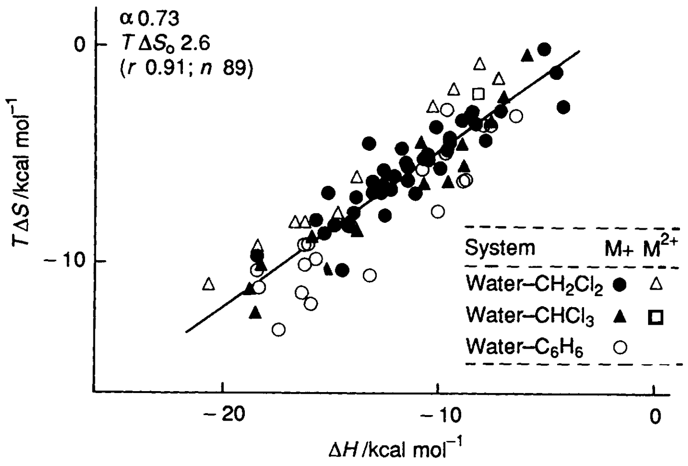

Figure 3. Enthalpy–entropy compensation effect for 1:1 stoicheiometric extraction of aqueous metal picrates with some crown ethers in dichloromethane–water (●), chloroform–water (▲), and benzene–water (○) systems; △ and □ refer to divalent cations; see Tables 3 and 5 for original data.

Using the present and reported thermodynamic parameters except for those for sandwich complexation of bis(crown ethers) (**9c**), (**9s**), (**10c**), and (**10s**), the $T\Delta S°$ values were plotted as a function of $\Delta H°$. The plot affords a good linear relationship with a correlation coefficient of 0.91 as shown in Figure 3. Quite interestingly, the slope (α) and the intercept ($T\Delta S_0$) obtained for the solvent extraction coincide nicely with those for the homogeneous-phase complexation, as shown in Table 6. It has been shown previously that the slope (α) and the intercept ($T\Delta S_0$) of the $\Delta H°$ *vs.* $T\Delta S°$ plot are the quantitative measures of the ligand's conformational change and the extent of desolvation upon complex formation, respectively.[8,9] Hence, the comparable slope and intercept indicate that the conformational change and the desolvation are much the same both in the solvent extraction and in the homogeneous-phase complexation as far as the same type of ligand is concerned. It is, therefore, concluded that, in spite of the apparent difference, the nature of cation–ligand complexation does not significantly differ between the homogeneous and the heterogeneous system.

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