

Complexation Thermodynamics of Bis(crown ether)s. 4.¹ Calorimetric Titration of Intramolecular Sandwich Complexation of Thallium and Sodium Ions with Bis(15-crown-5)s and Bis(12-crown-4)s: Enthalpy–Entropy Compensation

Yu Liu,^{*,2} Lin-Hui Tong,² Shu Huang,³ Bao-Zhi Tian,³ Yoshihisa Inoue,^{*,4} and Tadao Hakushi⁵

Lanzhou Institute of Chemical Physics, Academia Sinica, Lanzhou, China, Department of Chemistry, Sichuan University, Chengdu, China, and Basic Research Laboratory and Department of Applied Chemistry, Himeji Institute of Technology, 2167 Shosha, Himeji, Hyogo 671-22, Japan (Received: August 1, 1989; In Final Form: October 11, 1989)

Calorimetric titrations were performed in methanol–water (8:2) at 25 °C to give the complex stability constants and thermodynamic parameters for the complexation reactions of thallium ion with a series of bis(benzo-15-crown-5)s **1–3** and bis(15-crown-5) **6**, and of sodium ion with a series of bis(12-crown-4)s **7–11**. Both quantities are critical functions of the chain length (n) of the bridging methylene. The polymethylene-bridged bis(crown ether) **1** and its hydroxy analogue **3** with the same n gave quite similar stability constants and the maximum stabilities were obtained at $n = 5$, while the dioxo derivative **2** and the previously reported bis(crown ether) Schiff base **4** appeared to afford the maximum stability constants at larger n of 8–10. Thermodynamically the formation of the intramolecular sandwich complexes is evidently enthalpy driven for most bis(15-crown-5)s, but the profile of stability change is well accounted for in terms of the entropy change. Partial structural freezing induced by introducing a rigid cyclopentanedyl or xylylene moiety in the bridge dramatically enhances the complex stability of bis(crown ether)s **6–10** primarily through the less negative or even positive entropy change upon complexation. The $\Delta H-T\Delta S$ plot to testify to the enthalpy–entropy compensation effect gave an excellent straight line with a slope of 1.03 and an intercept of 4.6, indicating that the intramolecular sandwich complexation of bis(crown ether)s accompanies substantial conformational changes and extensive desolvation, both of which are inferred to be comparable to those for the antibiotic ionophores.

We have recently reported a thermodynamic study on the complexation of potassium ion with a series of polymethylene-bridged bis(benzo-15-crown-5)s **1** and some dioxo derivatives **2** in the homogeneous solution.^{1b} The thermodynamic parameters obtained clearly indicated that two crown ether units in a ligand molecule cooperatively bind a potassium ion to form an open or closed clamlike intramolecular “1:2” sandwich complex, depending upon the chain length (n) of the bridging methylene. It was demonstrated that, for each series of bis(crown ether), there is the optimum chain length that maximizes the complex stability constant. Although the complexation is primarily enthalpy favored, what maximizes the complex stability at specific n in each series is the less negative entropy change arising from the extensive desolvation of the cation encapsulated and also from the minimal change in the ligand conformation upon sandwich complexation. The effect of derivatization was also discussed to some extent, using a limited number of derivatives. Further examined was the validity of the enthalpy–entropy compensation effect, which had been proposed as a useful concept to understand more globally the complexation phenomenon of various type of ligands including acyclic glyme/podand, cyclic crown ether, bicyclic cryptand, and macrocyclic antibiotic ionophore.⁶

In the present paper, we wish to discuss the complexation thermodynamics of bis(crown ether)s from more general points of view by extending our study to cover other cations and crown ether units, as well as different derivatization and structure of the bridge connecting two crown ether units. The thermodynamic parameters for the complexation of thallium ion with bis(15-crown-5)s and of sodium ion with bis(12-crown-4)s, together with those reported,^{1,7i} will serve our further understanding of this

recently developing, but thermodynamically less investigated, area of the crown ether chemistry.^{7–15} It is of our special interest to test and discuss the general validity and the significance of the enthalpy–entropy compensation effect in the complexation of bis(crown ether)s, using a wider variety of cation, ligand, and/or solvent.

Experimental Section

Materials. Dioxobis(benzocrown ether)s **2b,d–f** were synthesized in the reaction of benzo-15-crown-5 with the respective alkanedioic acids in polyphosphoric acid. The catalytic hydro-

(1) (a) Part 3, Liu, Y.; Tong, L.-H.; Sun, X.-Q.; Wang, D.-F.; Hu, H.-W. Submitted for publication. (b) Part 2, Inoue, Y.; Hakushi, T.; Liu, Y.; Tong, L.-H.; Hu, J.; Zhao, G.-D.; Huang, S.; Tian, B.-Z. *J. Phys. Chem.* **1988**, *92*, 2371. (c) Part 1, Liu, Y.; Wang, Y.; Guo, Z.-Q.; Yang, S.-Y.; Jin, D.-S. *Acta Chim. Sin. (Huaxue Xuebao)* **1986**, *44*, 22.

(2) Lanzhou Institute of Chemical Physics.

(3) Sichuan University.

(4) Basic Research Laboratory, Himeji Institute of Technology.

(5) Department of Applied Chemistry, Himeji Institute of Technology.

(6) Inoue, Y.; Hakushi, T. *J. Chem. Soc., Perkin Trans. 2* **1985**, 935.

(7) (a) Kimura, K.; Sakamoto, H.; Koseki, Y.; Shono, T. *Chem. Lett.* **1985**, 1241. (b) Kimura, K.; Ishikawa, A.; Tamura, H.; Shono, T. *J. Chem. Soc., Perkin Trans. 2* **1984**, 447. (c) Kimura, K.; Tamura, H.; Shono, T. *J. Chem. Soc., Chem. Commun.* **1983**, 492. (d) Kimura, K.; Ishikawa, A.; Tamura, H.; Shono, T. *Bull. Chem. Soc. Jpn.* **1984**, *56*, 1859. (e) Kimura, K.; Kitazawa, S.; Maeda, T.; Shono, T. *Z. Anal. Chem.* **1982**, *331*, 132. (f) Maeda, T.; Kimura, K.; Shono, T. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 3506. (g) Maeda, T.; Ouchi, M.; Kimura, K.; Shono, T. *Chem. Lett.* **1981**, 1573. (h) Ikeda, I.; Katayama, T.; Okahara, M.; Shono, T. *Tetrahedron Lett.* **1981**, *22*, 3615. (i) Kimura, K.; Kitazawa, S.; Maeda, T.; Shono, T. *Talanta* **1980**, *27*, 801.

(8) Bourgoin, M.; Wong, K. H.; Hui, J. Y.; Smid, J. *J. Am. Chem. Soc.* **1975**, *97*, 3462.

(9) Handyside, T. M.; Lockhard, J. C.; MacDonnell, M. B.; Rao, R. V. *S. J. Chem. Soc., Dalton Trans.* **1982**, 2331.

(10) (a) He, G.-X.; Kikukawa, K.; Ohe, H.; Machida, M.; Matsuda, T. *J. Am. Chem. Soc.* **1988**, *110*, 603. (b) Kikukawa, K.; He, G.-X.; Abe, A.; Goto, T.; Arata, R.; Ikeda, T.; Wada, F.; Matsuda, T. *J. Chem. Soc., Perkin Trans. 2* **1987**, 135. (c) Ikeda, T.; Abe, A.; Kikukawa, K.; Matsuda, T. *Chem. Lett.* **1983**, 369. (d) Shinkai, S.; Ogawa, T.; Kusano, Y.; Manabe, O.; Kikukawa, K.; Goto, T.; Matsuda, T. *J. Am. Chem. Soc.* **1982**, *104*, 1960. (e) Wada, R.; Wada, Y.; Goto, T.; Kikukawa, K.; Matsuda, T. *Chem. Lett.* **1980**, 1189.

(11) (a) Beer, P. D.; Crane, C. G. *Polyhedron* **1988**, *7*, 2649. (b) Beer, P. D.; Rothin, A. S. *J. Chem. Soc., Chem. Commun.* **1988**, 52.

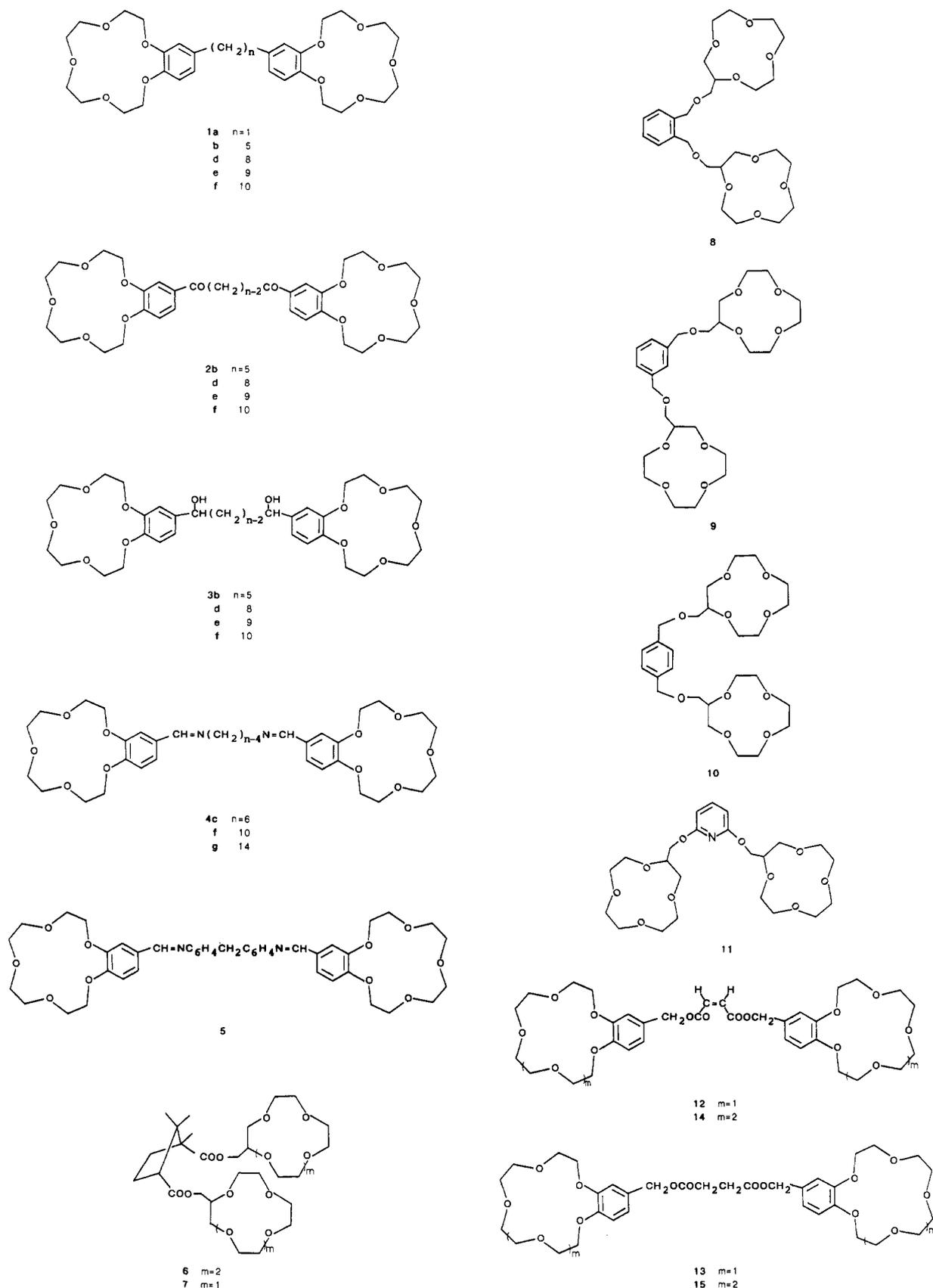
(12) Lukyanenko, N. G.; Nazarova, N. Yu.; Vetrogen, V. I.; Holdt, H. J.; Aurich, J.; Kuntosch, G. *Inorg. Chim. Acta* **1989**, *155*, 35.

(13) (a) Wang, D.-F.; Wang, D.-J.; Du, H.-G.; Sun, X.-Q.; Hu, H.-W. *Gaodeng Xuexiao Huaxue Xuebao* **1988**, *9*, 317. (b) Wang, D.-F.; Sun, X.-Q.; Huan, J.-D.; Hu, H.-W. *Huaxue Xuebao* **1987**, *45*, 92.

(14) (a) Sheldrick, W. S.; Poonia, N. S. *J. Inclusion Phenom.* **1986**, *4*, 93. (b) Momany, C.; Clinger, L.; Hackert, M. L.; Poonia, N. S. *J. Inclusion Phenom.* **1986**, *4*, 61.

(15) Wong, K. H.; Ng, H. L. *Tetrahedron Lett.* **1979**, 4295.

CHART I



genation over Raney nickel or the reduction with lithium aluminum hydride of α,α' -dioxobis(benzocrown ether)s **2** gave the corresponding polymethylene-bridged bis(benzocrown ether)s **1** or α,α' -dihydroxypolymethylenebis(benzocrown ether)s **3**. The full description of the synthetic procedures for these bis(crown ether)s and **1a** has been presented previously.¹⁶

The solvent methanol was refluxed over magnesium turnings and then distilled. The purified methanol was mixed with distilled, deionized water $[(1.0-1.2) \times 10^{-6} \text{ S/cm}]$ to make a mixed solvent

(16) Huang, S.; Tian, B.-Z.; Xie, H. *Org. Chem. (Youji Huaxue)* **1986**, *1*, 24.

TABLE I: Complex Stability Constant (log *K*) and Thermodynamic Parameters in kcal/mol for Complexation of Bis(15-crown-5)s 1–6 and Bis(12-crown-4)s 7–11 with Potassium or Thallium Ions and with Sodium Ion, Respectively, in Methanol–Water (8:2) at 25 °C

compd (<i>n</i>) ^a	cation	log <i>K</i>	–Δ <i>H</i>	–Δ <i>G</i>	<i>T</i> Δ <i>S</i>	ref
Bis(15-crown-5)						
1a (1)	K ⁺	2.92 ± 0.03	15.92 ± 0.05	3.98	–11.94	<i>b</i>
	Tl ⁺	2.04 ± 0.03	24.39 ± 0.09	2.78	–21.61	<i>c</i>
1b (5)	K ⁺	4.36 ± 0.04	10.74 ± 0.13	5.95	–4.79	<i>b</i>
	Tl ⁺	3.17 ± 0.06	12.78 ± 0.19	4.32	–8.46	<i>c</i>
1d (8)	K ⁺	3.24 ± 0.03	14.41 ± 0.23	4.42	–9.99	<i>b</i>
	Tl ⁺	2.32 ± 0.04	20.81 ± 0.27	3.16	–17.65	<i>c</i>
1e (9)	K ⁺	3.40 ± 0.03	13.97 ± 0.02	4.64	–9.33	<i>b</i>
	Tl ⁺	2.49 ± 0.05	18.46 ± 0.05	3.40	–15.06	<i>c</i>
1f (10)	K ⁺	3.68 ± 0.02	13.78 ± 0.06	5.02	–8.76	<i>b</i>
	Tl ⁺	2.69 ± 0.03	18.77 ± 0.17	3.67	–15.10	<i>c</i>
2b (5)	K ⁺	3.47 ± 0.03	8.84 ± 0.25	4.73	–4.11	<i>b</i>
	Tl ⁺	2.10 ± 0.02	19.00 ± 0.46	2.86	–16.14	<i>c</i>
2d (8)	K ⁺	3.73 ± 0.01	9.51 ± 0.03	5.09	–4.42	<i>c</i>
	Tl ⁺	1.90 ± 0.01	25.82 ± 0.87	2.59	–23.23	<i>c</i>
2e (9)	K ⁺	3.31 ± 0.06	11.80 ± 0.20	4.51	–7.28	<i>b</i>
	Tl ⁺	1.99 ± 0.03	20.41 ± 0.19	2.71	–17.70	<i>c</i>
2f (10)	K ⁺	3.13 ± 0.02	12.63 ± 0.50	4.27	–8.36	<i>b</i>
	Tl ⁺	2.13 ± 0.02	19.55 ± 0.41	2.91	–16.64	<i>c</i>
3b (5)	K ⁺	4.54 ± 0.09	10.18 ± 0.04	6.19	–3.99	<i>c</i>
	Tl ⁺	3.37 ± 0.04	12.05 ± 0.36	4.60	–7.45	<i>c</i>
3d (8)	K ⁺	3.08 ± 0.07	10.50 ± 0.07	4.20	–6.30	<i>c</i>
	Tl ⁺	2.29 ± 0.07	14.00 ± 0.07	3.12	–10.88	<i>c</i>
3e (9)	K ⁺	3.21 ± 0.04	12.86 ± 0.03	4.38	–8.48	<i>c</i>
	Tl ⁺	2.62 ± 0.01	9.29 ± 0.20	3.57	–5.72	<i>c</i>
3f (10)	K ⁺	3.50 ± 0.05	12.28 ± 0.01	4.77	–7.51	<i>c</i>
	Tl ⁺	2.80 ± 0.04	11.12 ± 0.44	3.82	–7.30	<i>c</i>
4c (6)	K ⁺	3.14 ± 0.06	18.00 ± 0.66	4.28	–13.72	<i>d</i>
4f (10)	K ⁺	3.56 ± 0.08	16.25 ± 0.22	4.85	–11.40	<i>d</i>
4g (14)	K ⁺	3.12 ± 0.07	17.23 ± 0.44	4.25	–12.98	<i>d</i>
5	K ⁺	2.79 ± 0.01	16.70 ± 0.06	3.80	–12.90	<i>d</i>
6	K ⁺	3.07 ± 0.08	2.59 ± 0.06	4.19	1.60	<i>e</i>
	Tl ⁺	2.37 ± 0.02	9.12 ± 0.05	3.23	–5.89	<i>e</i>
Bis(12-crown-4)						
7	Na ⁺	2.02 ± 0.02	1.64 ± 0.07	2.76	1.12	<i>e</i>
8	Na ⁺	2.14 ± 0.08	5.40 ± 0.11	2.92	–2.48	<i>e</i>
9	Na ⁺	2.33 ± 0.03	1.29 ± 0.07	3.02	1.73	<i>e</i>
10	Na ⁺	2.41 ± 0.04	0.84 ± 0.06	3.29	3.08	<i>e</i>
11	Na ⁺	1.84 ± 0.02	1.89 ± 0.27	2.51	0.62	<i>e</i>
12-Crown-4						
16(1:1) ^{f,g}	Na ⁺	1.47	3.00	2.00	–1.00	<i>h</i>
16(1:2) ^{f,g}	Na ⁺	2.28	6.70	3.11	–3.60	<i>h</i>

^aChain length (*n*); see Chart I. ^bReference 1b. ^cThis work; average of more than three independent runs. ^dReference 1c. ^eReference 1a. ^fComplex stoichiometry (cation:ligand). ^gReported values in pure methanol. ^hMichaux, G.; Reisse, J. *J. Am. Chem. Soc.* **1982**, *104*, 6895.

for calorimetry. Analytical-grade sodium thiocyanate and potassium thiocyanate were recrystallized from water and then from ethanol to give white crystals and analytical-grade thallium(I) nitrate was used as received. All metal salts were dried in vacuo prior to use.

Apparatus and Procedures. Calorimetric titrations were performed at 25 °C in a thermostated water bath, by using an LKB 8721-2 precision calorimeter, which was connected to an Apple II microcomputer for automated titration and data processing.¹⁷ The principle of measurement and the detailed experimental procedures were reported elsewhere.^{18,19} Typically, a thallium nitrate solution (0.041 M) was introduced continuously at a rate of 0.43 mL/min into a bis(crown ether) solution (1.1–5.0 mM) placed in the calorimeter. A titration curve was obtained by plotting the temperature change (measured by *E*/mV) against the amount of thallium nitrate solution added, from which the

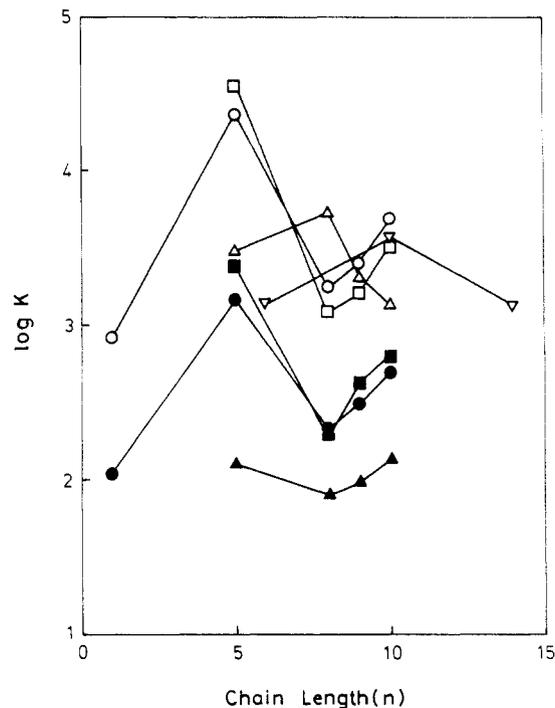


Figure 1. Complex stability constant (log *K*) as a function of bridging chain length (*n*) for complexation of potassium (open symbols) and thallium (closed symbols) ions with bis(benzo-15-crown-5)s 1 (○ and ●), 2 (△ and ▲), 3 (□ and ■), and 4 (▽ and ▼).

complex stability constant (*K*) and the enthalpy change (Δ*H*) were calculated. The reliability of the whole system and the calculation procedures were doubly checked as previous^{1b} by comparison of the thermodynamic data obtained with the reported values,^{20,21} and satisfactory results were obtained in both systems.

Results

Assuming 1:1 stoichiometry for the complexation of sodium, potassium, and thallium ion with bis(crown ether)s 1–11, the complex stability constant (*K*) and the enthalpy change (Δ*H*) were calculated by using the least-squares method to minimize the *U* value:^{1b,c}

$$U(K, \Delta H) = \sum_{p=1}^m (Q_{c,p} - \Delta H \Delta n_p)^2$$

where $Q_{c,p}$ refers to the experimental heat of complexation measured at time *p* in minutes and Δn_p denotes the amount in moles of the complex formed at time *p* and is directly related to the stability constant *K*.

The stability constant *K* and the enthalpy change Δ*H* of complexation for each bis(crown ether) were calculated by computer simulation with continuously changing *K*, i.e., Δn_p , to minimize the *U* value. The *U* value was minimized satisfactorily in each cation–ligand combination to give the optimized set of *K* and Δ*H* listed in Table I, which in turn supports the 1:1 stoichiometry for the complex formation as assumed above.

Discussion

Bis(15-crown-5). Possessing larger ionic diameter (3.00 Å)²² and polarizability (4.3 Å³)²³ as compared with potassium ion (2.76 Å and 1.2 Å³, respectively), thallium ion is bound less effectively by all series of bis(benzo-15-crown-5)s 1–3 examined. The complex stability constants *K* are roughly 1–2 orders of magnitude

(17) Shi, J.-P.; Liu, Y.; Sun, L.-C. *Anal. Instrum. (Fenxi Yiqi)* **1988**, *2*, 42.

(18) Wadsö, I. *Sci. Tools* **1966**, *13*, 33.

(19) Liu, Y.; Hu, J. *Acta Phys. Chim. Sin. (Wuli Huaxue Xuebao)* **1987**, *3*, 11.

(20) Hansen, L. D.; Lewis, E. R. *J. Chem. Thermodyn.* **1971**, *3*, 35.

(21) Izatt, R. M.; Terry, R. E.; Haymore, B. L.; Hansen, L. D.; Dalley, N. K.; Avondet, A. G.; Christensen, J. J. *J. Am. Chem. Soc.* **1976**, *98*, 7620.

(22) Shannon, R. D. *Acta Crystallogr., Sect. A* **1976**, *32*, 751.

(23) Salzmann, J.-J.; Jørgensen, C. K. *Helv. Chim. Acta* **1968**, *51*, 1276.

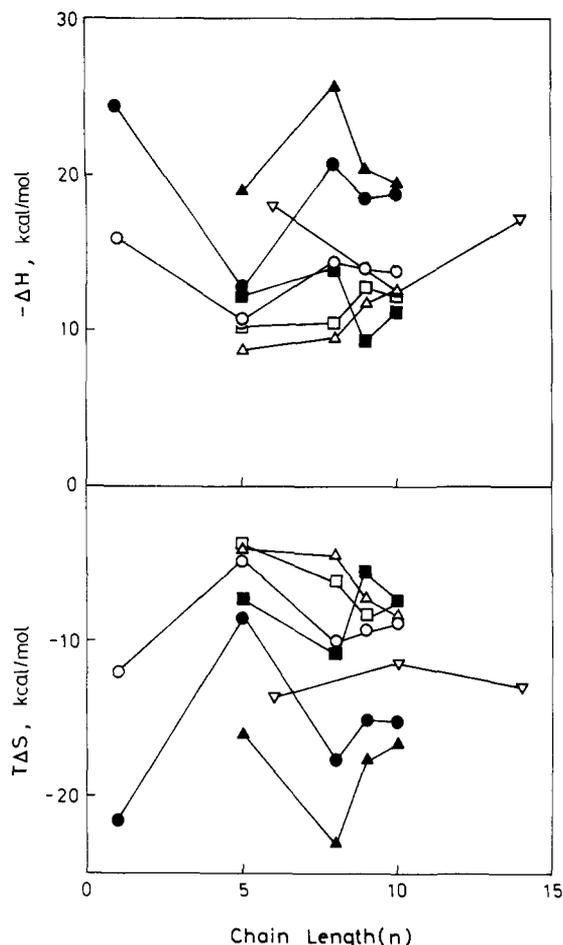


Figure 2. Enthalpic gain ($-\Delta H$) and entropic loss ($T\Delta S$) as a function of bridging chain length (n) for complexation of potassium (open symbols) and thallium (closed symbols) ions with bis(benzo-15-crown-5)s **1** (○ and ●), **2** (△ and ▲), **3** (□ and ■), and **4** (▽ and ▼).

smaller for Tl^{+} than for K^{+} . As to the polymethylene-bridged **1** and the corresponding dihydroxy analogues **3**, the stability constant varies with a close mutual resemblance over a fairly wide range of $\log K$ with the methylene chain length n , and the peak stability is found at $n = 5$ for both Tl^{+} and K^{+} , as can be seen from Figure 1. This seems reasonable since the substitution of **1** with hydroxyl groups does not significantly change the electron density of the donor oxygen or the flexibility of the bridging chain, although the situation is little more complicated in view of the thermodynamic quantities as discussed below.

On the other hand, the dioxo derivatives **2** show much smaller variation in complex stability, which gives a small peak around $n = 8-10$. This is also the case with the Schiff bases **4**, although the data are available for limited n . The diminished stability constants for **2** and **4** are obviously the direct consequence of the decreased electron density, induced by the electron-withdrawing carbonyl or imino group, of donor oxygens attached to the aromatic ring; their smaller variations with n and peak shifts to $n = 8-10$ cannot be rationalized by the decreased electron density. Besides the electron-withdrawing effect, the carbonyl or imino group in direct conjugation with the aromatic ring imposes a fixed conformation at both ends of the bridge. It is more likely that this fixed conformation is responsible for the shift of the peak complex stability to the longer chain lengths of $n = 8-10$ and in part for the smaller variation of **2** in $\log K$. However, the relatively insensitive change in $\log K$ for **2** does not immediately mean that the changes in enthalpy and entropy are also minimal, but rather are taken as a result of the compensation between the dynamically varying enthalpy and entropy changes, as can be seen from Figure 2.

Thermodynamically the complex stability of bis(crown ether)s is exclusively enthalpic in origin, as the major contributor to $-\Delta G$

is the large enthalpic gain ($-\Delta H$), which far exceeds the entropic loss ($T\Delta S$) in each cation-ligand combination. Close examination of these thermodynamic quantities, however, reveals some interesting aspects of the intramolecular sandwich complexation of large cations with bis(crown ether)s. Unexpectedly, for most bis(crown ether)s examined, the profile of the change in $-\Delta G$ as a function of the chain length n is evidently entropy governed. As can be seen from Figures 1 and 2, the enthalpic gain and the entropic loss behave quite contradictorily, so that the resulting free energy change ($-\Delta G$) varies less drastically than would be expected from the dynamic change in $T\Delta S$ or $-\Delta H$. The bis(crown ether)s with $n \geq 4$ are assumed to form intramolecular face-to-face sandwich complexes with K^{+} and Tl^{+} from the CPK space-filling model examinations,^{1b} and therefore the extent of complexation-induced desolvation of cation is analogous for most bis(crown ether)s except for **1a**. Thus, the least negative entropy change at $n = 5$ cannot be attributed to the extensive desolvation of the cation accommodated but rather be accounted for in terms of the minimal change of ligand conformation at $n = 5$, although the more extensive desolvation of ligand itself at $n = 5$ may also be at least partly responsible especially in hydrogen-bonding solvent such as methanol-water.

It is also interesting to compare the polymethylene-bridged **1** and their dihydroxy analogues **3** from the thermodynamic point of view. In sharp contrast to the almost superimposable n - $\log K$ plots for the complexation with **1** and **3** of either K^{+} or Tl^{+} (Figure 1), their enthalpy and entropy changes are distinctly different each other (Figure 2). One possible explanation for the less drastic variation of **3** in both $-\Delta H$ and $T\Delta S$ would be the intramolecular hydrogen bonding, which helps the dihydroxy derivatives **3** taking analogous original conformations irrespective of the chain length n , although we do not have any direct evidence.

Bis(15-crown-5) **6** is another excellent example in which the rigidity of the bridging chain plays a crucial role in determining the thermodynamic parameters. Carrying a conformationally fixed *cis*-1,3-cyclopentandiyl unit in the bridge, **6** gives the least negative or even positive entropy change for K^{+} or Tl^{+} among the bis(15-crown-5)s examined.

Bis(12-crown-4). Sodium ion, which is too large (2.04 Å)²² to fit into the cavity of 12-crown-4 (1.2 Å),²⁴ is known to form intramolecular sandwich complexes with several bis(12-crown-4)s.^{7f-h,9} Analogously the bis(12-crown-4)s **7-11** used in the present study are concluded to form intramolecular sandwich complexes with Na^{+} , since the complex stability constants ($\log K = 1.84-2.41$) obtained for **7-11** in methanol-water (8:2) are much higher than that (1.47) for the 1:1 complexation of the parent 12-crown-4 **16** in pure methanol.

The complex stability is, however, a critical function of the detailed structure of the bridging chain. Of bis(12-crown-4)s **8-10** possessing a rigid isomeric xylylene unit in the chain, the para isomer **10** gives the highest stability, the meta follows, and the ortho comes last. This stability sequence is reasonably accounted for through examination of CPK molecular models. As was the case with polymethylene-bridged bis(benzo-15-crown-5)s,^{1b} there is a critical chain length or spacing which enables two crown ether units being placed fact-to-face, thus optimizing the charge-dipole interaction upon sandwich complexation. In this criterion, *cis*-1,3-cyclopentandiyl-**7** and 2,6-pyridino-**11**, and **8** and **9** as well, possess more or less insufficient chain length or spacing and consequently afford substantially lower complex stabilities than **10**. The pyridine nitrogen of **11** does not appear to function as an additional binding site, enhancing complex stability, just like the lariat ethers^{25,26} and bis(crown ether) with an oligoxyethylene bridge.^{10a}

(24) Estimated from the CPK molecular model.

(25) (a) Schultz, R. A.; White, B. D.; Arnold, K. A.; Gokel, G. W. *J. Am. Chem. Soc.* **1985**, *107*, 6659. (b) Dishong, D. M.; Diamond, C. J.; Cinaman, M. I.; Gokel, G. W. *J. Am. Chem. Soc.* **1983**, *105*, 586.

(26) (a) Ouchi, M.; Inoue, Y.; Wada, K.; Iketani, S.; Hakushi, T.; Weber, E. *J. Org. Chem.* **1987**, *52*, 2420. (b) Ouchi, M.; Inoue, Y.; Wada, K.; Hakushi, T. *Chem. Lett.* **1984**, 1137.

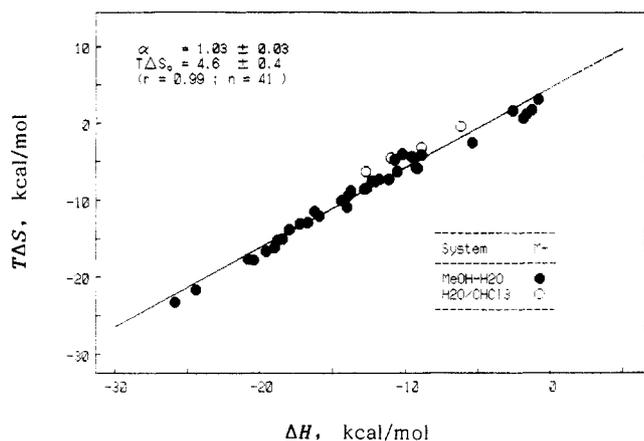


Figure 3. Enthalpy-entropy compensation effect for the intramolecular "1:2" sandwich complexation of metal ions with bis(crown ether)s in the homogeneous phase (●) and in the solvent extraction (○); see Table I and ref 7i for the original data, respectively.

In contrast to the enthalpy-driven complex stabilization of the bis(15-crown-5)s **1–4** with flexible bridges discussed above, the complexation thermodynamics of the bis(12-crown-4)s is characterized by the very small enthalpic gain ($-\Delta H$) and the positive entropy change ($T\Delta S$), except for the ortho isomer **8**. This is ascribed most likely to the highly rigid bridging chain and probably to the intrinsically less flexible skeleton of 12-crown-4 as compared with 15-crown-5. Thus the entropic gain arising from the desolvation of cation and ligand exceeds the entropic loss caused by the conformational change of bis(crown ether) upon complexation. The profile of the stability change of **8–10** is again entropy governed. The extensive desolvation of cation and ligand and the minimal conformational change of ligand upon sandwich complexation must be responsible for the highest stability of the para isomer **10**.

Enthalpy-Entropy Compensation. In our previous paper,^{1b} we have preliminarily examined the validity of the enthalpy-entropy compensation effect⁶ by using a limited number of thermodynamic parameters, 16 sets of data in total, for the intramolecular sandwich complexation of K^+ with some bis(benzo-15-crown-5)s. Although the correlation coefficient was excellent ($r = 0.99$), it is obviously desirable to include other types of cations and bis(crown ether)s in order to demonstrate the general validity. The present study enables us to examine more precisely and comprehensively the enthalpy-entropy relationship for bis(crown ether) as a new class of ligand.

In Figure 3, the entropy change ($T\Delta S$) is plotted as a function of the enthalpy change (ΔH), using the thermodynamic parameters listed in Table I and those reported by Kimura et al.⁷ⁱ for solvent extraction of aqueous K^+ and Cs^+ picrates with bis(benzo-15-crown-5)s **12**, **13** and bis(benzo-18-crown-6)s **14**, **15** in chloroform. The ΔH - $T\Delta S$ plot gives an excellent straight line ($r = 0.99$) with a slope (α) of 1.03 and an intercept ($T\Delta S_0$) of 4.6. These values are somewhat different from those reported previously^{1b} probably due to the larger sample size ($n = 41$) and the diversity of the cation/ligand combinations employed in the present study.²⁷ It

TABLE II: Slope (α) and Intercept ($T\Delta S_0$) of the ΔH - $T\Delta S$ Plots for 1:1 and 1:2 Complexations with Various Ligands in the Homogeneous Phase and in Solvent Extraction

ligand	1:1 complexation		1:2 complexation	
	α	$T\Delta S_0$	α	$T\Delta S_0$
glyme/podand ^a	0.86	2.3		
crown ether ^a	0.76	2.4	0.71	2.7
cryptand ^a	0.51	4.0		
antibiotic ^a	0.95	5.6		
bis(crown ether) ^b	1.03	4.6		

^aReference 6. ^bThis work; this type of ligand forms intramolecular "1:2" sandwich complex.

is noted that the enthalpy-entropy compensation effect does hold for the intramolecular sandwich complexation of bis(crown ether)s not only in the homogeneous solution but also in the solvent extraction system.

The results are summarized in Table II along with the corresponding values for different categories of ligand, i.e., glyme/podand, crown ether, cryptand, and antibiotic.⁶ Each category of ligand with different topology affords distinctly different slope (α) and intercept ($T\Delta S_0$). This clearly indicates that the different degrees of conformational change and desolvation are involved upon complexation in each case, since, from the previous study,⁶ the slope (α) is related to the degree of ligand's conformational change and the intercept ($T\Delta S_0$) to the extent of cation's and ligand's desolvation. Thus the largest α obtained for bis(crown ether) reveals that this class of ligand experiences substantial conformational change, which is comparable to that for macrocyclic antibiotic. The second largest intercept ($T\Delta S_0$) also demonstrates that the cation accommodated in the cavity suffers extensive desolvation, which is characteristic of the three-dimensional complexation by cryptand, antibiotic, and bis(crown ether). Quantitatively, the unit slope ($\alpha = 1$) and the large intrinsic entropic gain ($T\Delta S_0 = 4.6$) jointly indicate that the enthalpic gain arising from cation binding is completely canceled by the entropic loss from the bis(crown ether)'s conformational change required upon complexation, but the sandwich complexation is still favored even in the absence of enthalpic stabilization exclusively owing to the entropic gain arising from the extensive desolvation of both cation and ligand.

It is shown that the enthalpy-entropy compensation effect, derived from the examination of the thermodynamic parameters, enables us to discuss and visualize the complexation behavior of all sorts of ligand in the homogeneous solution and probably in the solvent extraction from the more global and quantitative points of view. Endeavors to measure and compile the thermodynamic quantities in the homogeneous phase and in the solvent extraction system are currently in progress.

Acknowledgment. This work was supported in part by the National Science Fund of China, which is gratefully acknowledged.

(27) The inconsistency in the previous and present studies may require further compilation of the thermodynamic parameters for the cation complexation by bis(crown ether)s in order to obtain more reliable slope (α) and intercept ($T\Delta S_0$).