Synthesis of Double-Armed Benzo-15-crown-5 and Their Complexation Thermodynamics with Alkali Cations

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Abstract

A series of double-armed benzo-15-crown-5 lariats (**3–8**) have been synthesized by the reaction of 4′, 5′-bis(bromomethyl)-benzo-15-crown-5 (**2**) with 4-hydroxybenzaldehyde, phenol, 4-chlorophenol, 4-methoxy-phenol, 2-hydroxybenzaldehyde, and 4-acetamidophenol in $43 \sim 82\%$ yields, respectively. The complex stability constants (K_S) and thermodynamic parameters for the stoichiometric 1:1 and/or 1:2 complexes of benzo-15-crown-5 **1** and double-armed crown ethers **3–8** with alkali cations (Na^+, K^+, Rb^+) have been determined in methanol–water (V/V = 8:2) at 25 °C by means of microcalorimetric titrations. As compared with the parent benzo-15-crown-5 **1**, double-armed crown ethers **3–8** show unremarkable changes in the complex stability constants upon complexation with Na^+, but present significantly enhanced binding ability toward cations larger than the crown cavity by the secondly sandwich complexation. Thermodynamically, the sandwich complexations of crown ethers **3-8** with cations are mostly enthalpy-driven processes accompanied with a moderate entropy loss. The binding ability and selectivity of cations by the double-armed crown ethers are discussed from the viewpoints of the electron density, additional binding site, softness, spatial arrangement, and especially the cooperative binding of two crown ether molecules toward one metal ion.

Introduction

The ion selective binding by synthetic acceptors, such as glyme/podand, crown ether, cryptand, lariat ether, and bis(crown ether)s, is of current interest in host–guest chemistry and supramolecular chemistry. Possessing additional donor atom(s) and/or other functional group(s), lariat ethers have been designed and synthesized not only to alter the original ionic binding ability and selectivity, but also to form functional assembly by sandwich complexation and/or intermolecular interactions. These have been successfully applied to many investigation fields of science and technology [1–3]. Recently, a side-armed benzo-15-crown-5 fluoroionophore bearing a pyrenyl moiety was synthesized and used as an ion probe to exhibit remarkably high sensitivity and selectivity for potassium in the presence of γ-cyclodextrin, which can be applied to various lipophilic chromo- and fluoroionophores to develop further superior sensing functions [4]. Minoura [5] demonstrated that the helix-helix association formed by sandwich complexation in α-helical polypeptide possessing a terminal benzo-15-crown-5 could be con-trolled by its complexation with alkali metal ions. Nakahara *et al.* [6] reported the synthesis of some lariat ethers with plural pyrenylmethyl groups on the electron-donating sidearms, which displayed the fluorometric sensing behavior toward alkaline earth metal cations. In addition, many studies showed that certain azacrown-appended cholesterol derivatives could change from vesicular to lamellar structures in the presence of metal salts in aqueous solution [7, 8]. In the previous study, we have shown that the introduction of both non-donating alkyl/aromatic group and donating oxyethylene group(s) alters not only the cation binding ability but also the relative cation selectivity of the carbon/nitrogen-pivot crown ethers significantly [9, 10]. It has also been demonstrated that the carbon-pivot lariats are less flexible than the corresponding nitrogen-pivot lariats in adjusting their conformations upon complexation with cations [11]. The relevant thermodynamic parameters clearly indicated that the binding ability and selectivity of lariat ethers are governed by the cavity size of ligand, the pivot atom, as well as the type and number of additional donor atoms in side arms. Unfortunately, less attention has been paid to the sandwich complexation thermodynamics of double-armed crown ethers with donating and/or non-donating side arms, though it is of

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great importance to further understand the factors governing the ion binding and molecular assembly behavior of crown ethers.

In the present work, we wish to report our results on the synthesis of six double-armed benzo-15-crown-5 compounds **3-8** and their complexation thermodynamics with some alkali metal ions (Na$^+$, K$^+$, Rb$^+$). It is our special interest to examine the sandwich complexation interactions of double-armed crown ethers with alkali metal ions from the thermodynamic point of view. The results revealed that electron effect of the double arms tethered to parent crown ether is of great important in determining the binding sequence of host crown ethers upon complexation with cations. They also indicated that the sandwich 2:1 complexation of double-armed crown ethers greatly enhance the original cation binding ability and relative cation selectivity of parent benzo-15-crown-5 **1** by forming strong ion-dipole and π–π interactions with the participation of the second ligand molecule.

Experimental section

General

Melting points, measured with an XT-4 apparatus, are uncorrected. ^{1}H NMR spectra were recorded on a Varian Mercury VX300 instrument in CDCl$_3$ solution, using tetramethylsilane as an internal reference. Ultraviolet spectra were recorded on a Shimadzu UV-2401/PC instrument. Elemental analyses were performed on a Perkin–Elmer 2400C instrument.

Materials

Starting materials were commercially available unless otherwise noted. All metal salts (NaCl, KCl, RbCl) were dried in *vacuo* for 24 h at 120 °C prior to use. The methanol was refluxed over magnesium turnings and then distilled. The purified methanol was mixed with distilled, deionized water [(1.0–1.2) × 10^{-6} S/cm] to make a mixed solvent (8:2/V:V) for calorimetric titration experiment. Benzo-15-crown-5 (2,3-benzo-1,4,7,10,13-pentaoxa-2-cyclopentadecene (**1**)) [12], 4′,5′-bis(bromomethyl)-benzo-15-crown-5 (2,3-[4′,5′-bis(bromomethyl)-benzo]-1,4,7,10,13-pentaoxa-2-cyclopentadecene (**2**)) [13] and 2,3-[4′,5′-bis[[(4-formoylphenyl)oxy]methyl]-benzo]-1,4,7,10,13-pentaoxa-2-cyclopentadecene (**3**) [14] were prepared according to the literature procedures.

2,3-[4′,5′-Bis[(phenyloxy)methyl]-benzo]-1,4,7,10,13-pentaoxa-2-cyclopentadecene (4). Phenol (4 mmol), anhydrous K$_2$CO$_3$ (4 mmol) and 50 ml THF were added in a 100 ml reaction flask, which was fitted with a magnetically stirrer, reflux condenser, nitrogen gas inlet. After the mixture was stirred magnetically for 10 min in an inert atmosphere of dry nitrogen, **2** (2 mmol) was added to

reaction flask, and then the reaction was carried out under reflux for 9 h. After cooling, the solvents were removed *in vacuo*. The residue obtained was added to a mixture of water (100 ml) and chloroform (60 ml), the resultant binary mixture was stirred vigorously, and the chloroform layer was separated and dried over MgSO$_4$. The residue obtained upon evaporation of the chloroform was recrystallized from ethyl acetate to give white crystal of **4** (yield 62%): mp. 132–134 °C. UV–Vis λ_{max} (CHCl$_3$)/nm (ε/ m^{-1} cm^{-1}) 272.8 (8,600), 243.2 (16,800). ^{1}H NMR δ 3.75 (s, 8H), 3.90 (dd, $J_1 = 4.2$ Hz, $J_2 = 3.0$ Hz, 4H), 4.15 (dd, $J_1 = 4.2$ Hz, $J_2 = 3.0$ Hz, 4H), 5.07 (s, 4H), 6.94 (m, 6H), 6.97 (m, 2H), 7.27 (m, 4H). Anal. Calcd for C$_{28}$H$_{32}$O$_7$: C, 69.98; H, 6.71. Found: C, 69.84; H, 6.86.

2,3-[4′,5′-Bis[[(4-chlorophenyl)oxy]methyl]-benzo]-1,4,7,10,13-pentaoxa-2-cyclopentadecene (5). This compound was prepared from **2** and 4-chlorophenol according to the procedure described above for **4** in 55% yield after recrystallization from ethyl acetate: mp. 131–132 °C. UV–Vis λ_{max} (CHCl$_3$)/nm (ε/m^{-1}cm^{-1}) 282.4 (10,400), 244.6 (22,000). ^{1}HNMR δ 3.75 (s, 8H), 3.90 (dd, $J_1 = 4.5$ Hz, $J_2 = 3.0$ Hz, 4H), 4.15 (dd, $J_1 = 4.5$ Hz, $J_2 = 3.0$ Hz, 4H), 5.01 (s, 4H), 6.85 (m, 4H), 6.99 (s, 2H), 7.22 (m, 4H). Anal. Calcd for C$_{28}$H$_{30}$O$_7$Cl$_2$: C, 61.21; H, 5.50. Found: C, 61.28; H, 5.55.

2,3-[4′,5′-Bis[[(4-methoxyphenyl)oxy]methyl]-benzo]-1,4,7,10,13-pentaoxa-2-cyclopentadecene (6). This compound was prepared from 4-methoxyphenol according to the procedure described above for **4** in 65% yield after recrystallization from acetone: mp. 100–102 °C. UV–Vis λ_{max} (CHCl$_3$)/nm (ε/m^{-1} cm^{-1}) 288.8 (10,200), 243.0 (20,000). ^{1}HNMR δ 3.75 (s, 6H), 3.76 (d, J = 3.9 Hz, 8H), 3.90 (dd, $J_1 = 3.9$ Hz, $J_2 = 3.0$ Hz, 4H), 4.14 (dd, $J_1 = 3.9$ Hz, $J_2 = 3.0$ Hz, 4H), 5.00 (s, 4H), 6.87 (m, 8H), 7.01 (s, 2H). Anal. Calcd for C$_{30}$H$_{36}$O$_9$: C, 66.65; H, 6.71. Found: C, 66.86; H, 6.63.

2,3-[4′,5′-Bis[[(2-formoylphenyl)oxy]methyl]-benzo]-1,4,7,10,13-pentaoxa-2-cyclopentadecene (7). This compound was prepared from **2** and 2-hydroxybenzadehyde according to the procedure described above for **4** in 65% after recrystallization from acetone: mp. 135–136 °C. Ms m/z: 536 (M$^+$). UV–Vis λ_{max}(CHCl$_3$)/nm (ε/m^{-1} cm^{-1}) 319 (8,800), 250.2 (22,100). ^{1}HNMR δ 3.76 (s, 8H), 3.92 (dd, $J_1 = 4.5$ Hz, $J_2 = 2.7$ Hz, 4H), 4.17 (dd, $J_1 = 4.5$ Hz, $J_2 = 2.7$ Hz, 4H), 5.21 (s , 4H), 7.04 (m, 6H), 7.52 (m, 2H), 7.82 (m, 2H), 10.42 (s, 2H). Anal. Calcd for C$_{30}$H$_{32}$O$_9$: C, 67.15; H, 6.01. Found: C, 66.86; H, 5.91.

2,3-[4′,5′-Bis[[(4-acetamidephenyl)oxy]methyl]-benzo]-1,4,7,10,13-pentaoxa-2-cyclopentadecene (8). This compound was prepared from **2** and 4-acetamidophenol according to the procedure described above for **4** in 43% yield after recrystallization from ethyl acetate:

mp.204–206 °C. UV–Vis $\lambda_{\max}$ (CHCl$_3$)/nm(ε/m^{-1}cm^{-1}) 248.6 (38,500), 278.8 (9,200). ^{1}H NMR δ 2.14 (s, 6H) 3.75 (s, 8H), 3.90 (m, 4H), 4.13 (m, 4H), 4.99 (s, 4H), 6.83 (d, $J = 9.0$ Hz, 4H), 6.99 (s, 2H), 7.30 (d, $J = 9.0$ Hz, 4H), 7.51 (s, 2H). Anal. Calcd for C$_{32}$H$_{38}$O$_9$N$_2$: C, 64.63; H, 6.44; N, 4.71. Found: C, 64.43; H, 6.22; N, 4.71.

Isothermal titration

An isothermal titration calorimeter (VP-ITC), purchased from Microcal Inc. (Northampton MA), was used for microcalorimetric experiments. The reliability of the whole system and the calculation procedures was doubly checked by earlier [15–17] by test runs using the reported reaction systems, such as, logK_S and ΔH (2.83 ± 0.02, −6.51 ± 0.03 kJ mol^{-1} at 25 °C) for the complexation of β-CD with cyclohexanol are in agreement with the reported values (2.85 ± 0.01, −6.6 ± 0.1 kJ mol^{-1}) [16b]. The microcalorimetric titrations were performed at the atmospheric pressure and 298.15 K in methanol-water mixed solution (8:2/ V:V). All solutions are degassed and thermostatted using a ThermoVac accessory before titration experiments. In each run, a constant volume (10 μl/injection) of metal ion solution (20–40 mmol l^{-1}) in the 0.250 ml syringe is injected into the 1.4227 ml stirred (300 rpm) sample cell containing crown ether solution (0.50–2.03 mmol l^{-1}). Each titration experiment contains of 25 successive injections. A typical titration curve is shown as Figure 1 and 2. The entire experiment, including automated titration and data acquisition, takes place under computer control.

The control experiment in each run is performed to determine the dilution heat of metal ions in methanol–water (8:2/V:V) mixed solution without any crown ether present using the same number of injections and concentration of metal ions as used in the titration experiment. The dilution enthalpy measured in the control experiment was subtracted from the enthalpy determined in the titration experiment for data analysis.

The ORIGIN software (Microcal Inc.) was used to calculate simultaneously the binding constant (K_S) and the enthalpy change (ΔH°) of reaction in a single titration experiment with a standard derivation based on the scatter of the data points in a single titration curve. All thermodynamic parameters in this work were obtained in the case of the 'one set of sites' model (for Na$^+$), and 'sequential binding sites ($N = 2$)' model (for K$^+$ and Rb$^+$). Several independent titration experiments were performed to examine the reproducibility of these calculated parameters, and the results and uncertainties were calculated as weighted averages of the results of three titration experiments.

Results and discussions

Synthesis

The double-armed benzo-15-crown-5 compounds **4–8** were prepared in 43–65% yields by treating the dibromo precursor **2** with the corresponding reactant in the presence of anhydrous K$_2$CO$_3$, using THF as solvent,
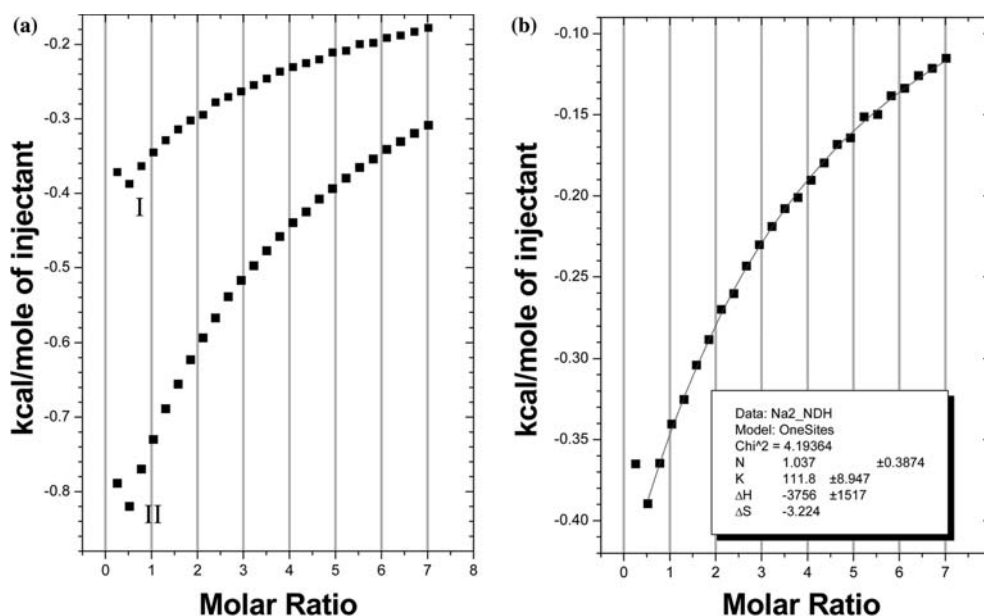

Figure 1. (a) Heat effects of the dilution (I) and of the complexation reactions (II) of Na$^+$ and host **5** for each injection during titration microcalorimetric experiment. (b) 'Net' heat effects of complexation of Na$^+$ and host **5** for each injection, obtained by subtracting the heat of dilution from the heat of reaction, which is fitted by computer simulation using the one set of sites model. The units of thermodynamic parameters obtained are calories.
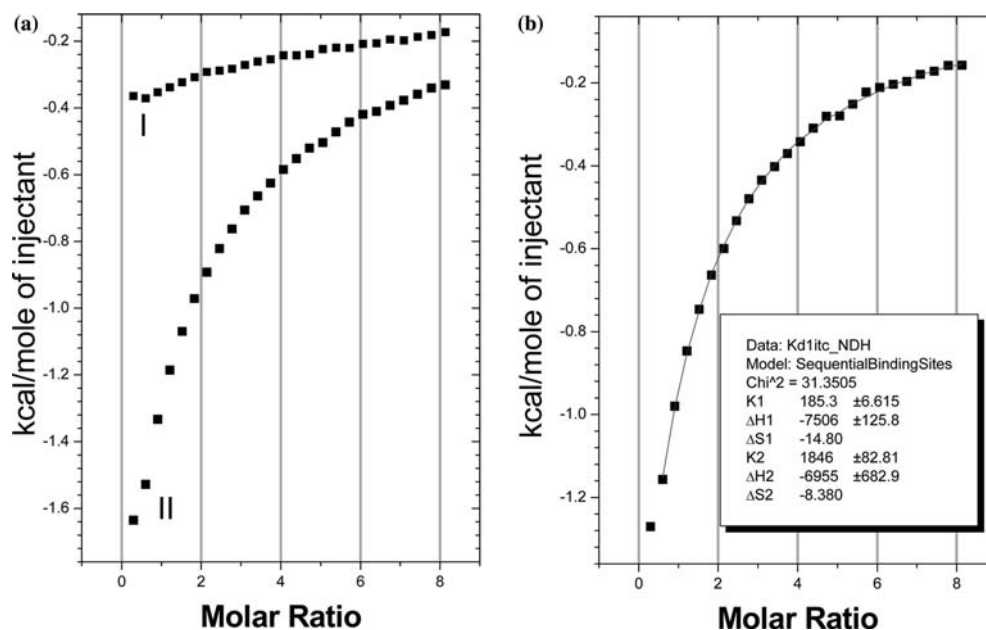
Figure 2. (a) Heat effects of the dilution (I) and of the complexation reactions (II) of K^+ and lariat ether **7** for each injection during titration microcalorimetric experiment at 298 K. (b) 'Net' heat effects of complexation of **7** with K^+ for injection, obtained by subtracting the heat of dilution the heat of reaction, both of which are fitted to the theoretical curve obtained by compute simulation using the two steps sequential binding sites model. The units of thermodynamic parameters obtained are calories.
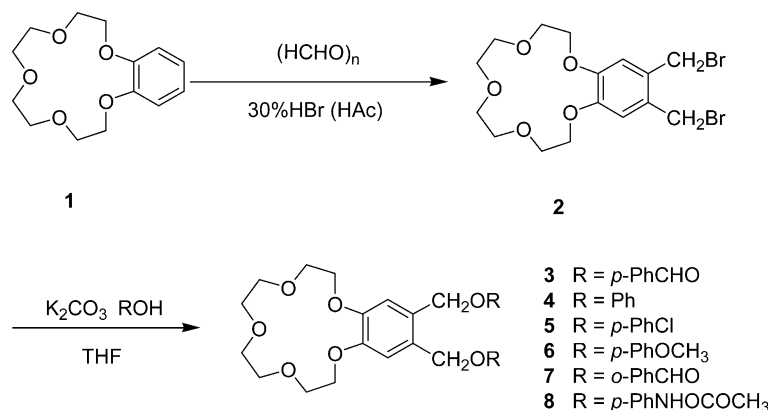

Scheme 1. The synthetic routes of host 3–8.

respectively (Scheme 1). Crown ethers **3-8** obtained were characterized by elemental analysis, UV–Vis, IR, and ^1H NMR spectroscopy.

Calorimetry

It is well-documented that size-fitting combinations of benzo-15-crown-5 with alkali metal cations lead to the stoichiometric 1:1 complex, while cations larger in size than the crown ether's cavity give the stoichiometric 1:2 sandwich complex in solution, [18] and the latter is also validated by the crystal structures of **3** with K^+ [14]. Therefore, crown ethers **3–8**, possessing the same benzo-15-crown-5 skeleton, should form the stoichiometric 1:1 or 1:2 complexes upon complexation with cations of different sizes in methanol–water (8/2 = V/V) mixed solution. For the complexation with Na^+, the satisfactory results are obtained within the experiment error by assuming the 1:1 stoichiometry and using the 'one set of sites' fitting model, and the same results can also be obtained while the titrant and titrate are exchanged for the same reaction. The stability constants and standard molar enthalpies of crown ethers upon complexation with Na^+ are obtained according to following equilibrium:

$$CE + Na^+ \overset{K}{\rightleftharpoons} CE \cdot Na^+$$
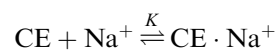
$$K = \frac{\gamma[CE\ Na^+]}{\gamma[CE]\gamma[Na^+]}$$

where γ is the activity coefficient of the corresponding substance. Non-ideality corrections are assumed to be negligible for both the measured stability constants and the standard molar enthalpies of the reaction. Even for the charged ligand (Na$^+$), since the reaction is charge symmetric and the activity coefficients in the numerator and denominator should cancel to a great extent at low and moderate ionic strengths, this approximation should also be reasonable.

For the 2:1 stoichiometric complexation of parent **1** and crown ethers **3–8** with K$^+$ and Rb$^+$, the stepwise complex stability constant(s) (K_n; $N = 1$ or 2) and the enthalpy change(s) (ΔH_n), were determined by using the 'sequential binding sites ($N = 2$)' model. The stepwise complexation of crown ether (CE) with metal cation (M$^+$) is expressed by the following equilibrium:

$$CE + M^+ \overset{K_1}{\rightleftharpoons} CE \cdot M^+$$

$$CE \cdot M^+ + CE \overset{K_2}{\rightleftharpoons} CE_2 \cdot M^+$$
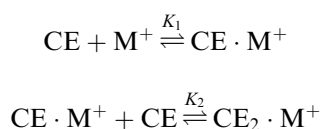
To obtain the optimized sets of K_1 and ΔH_1, together with K_2 and ΔH_2, the computer simulations were repeated several times with various initial sets of the four parameters, using the constancy of chi^2 value as a criterion. The obtained apparent stability constants ($K = K_1 \times K_2$) and the thermodynamic parameters ($\Delta H = \Delta H_1 + \Delta H_2$, $T\Delta S = T\Delta S_1 + T\Delta S_2$) are listed in Table 1. No other sets of the parameters could better

describe the experimental data without increasing the chi^2 value. Since the thermodynamic parameters obtained by using parent **1** as the titrant or titrate are identical upon complexation with K$^+$, in the present experiment, the metal salt solution was titrated into the crown ether solutions considering the solubility limitation of the lariat ethers **3–8**.

Binding ability, selectivity and thermodynamic parameters

It is well-known that complexations of benzo-15-crown-5 and its derivatives with Na$^+$ usually lead to the stoichiometric 1:1 complexes, because the size of the 15-crown-5 cavity is nearly the same as the diameter of Na$^+$. In this text, the introduction of different sidearms to the parent benzo-15-crown-5 alters the original cavity environment and electron cloud density. During the complexation process of crown ethers and metal ions, benzyl oxygen atoms (corresponding to the benzene ring of the parent crown ether) always served as an electron-donor contributing to the binding of metal cation. Therefore, the binding abilities of hosts **4**, **6** and **8** toward Na$^+$ are all enhanced to certain degrees. Possessing the additional electron-donating group at sidearms, i.e., the amido and methoxyl groups, the binding ability of hosts **6** and **8** toward Na$^+$ are further enhanced and consequently give the higher complex stability constants than the parent benzo-15-crown-5 does ($K_6/K_1 = 1.25$, $K_8/K_1 = 1.77$) as shown in Table 1. However, hosts **3**, **5**, and **7**, possessing the additional electron-withdrawing and/or

Table 1. Complex stability constants (K) and thermodynamic parameters for complexation of metal cations with benzo-15-crown-5(**1**) and its derivatives **3–8** in methanol–water (8:2/V:V) mixed solution 298.15 K

| ligand[a]	cation[b]	N	K / M^{-1}	$\Delta H°$/kJ · mol^{-1}	$T\Delta S°$/kJ · mol^{-1}
1	Na$^+$	1	110 ± 5	−32.85 ± 0.04	−21.19 ± 0.16
	K$^+$	2	28180 ± 560	−87.07 ± 0.58	−61.83 ± 0.53
	Rb$^+$	2	1850 ± 9	−99.32 ± 0.22	−80.70 ± 0.36
3	[c]Na$^+$	1	98 ± 2	−21.82 ± 0.04	−10.49 ± 0.08
	[c]K$^+$	2	237190 ± 1350	−70.42 ± 0.40	−39.77 ± 0.11
	Rb$^+$	2	69110 ± 1120	−38.58 ± 1.15	−10.98 ± 1.02
4	Na$^+$	1	135 ± 3	−19.72 ± 0.25	−7.57 ± 0.32
	K$^+$	2	745500 ± 24170	−91.87 ± 1.21	−58.45 ± 1.29
	Rb$^+$	2	195640 ± 20750	−33.19 ± 0.48	−3.14 ± 0.65
5	Na$^+$	1	110 ± 2	−20.35 ± 0.40	−8.53 ± 0.44
	K$^+$	2	369180 ± 2770	−57.01 ± 0.79	−25.52 ± 0.51
	Rb$^+$	2	83140 ± 4720	−48.81 ± 1.02	−20.69 ± 0.34
6	Na$^+$	1	138 ± 3	−18.22 ± 0.38	−6.02 ± 0.36
	K$^+$	2	565230 ± 5320	−66.69 ± 0.42	−33.94 ± 0.45
	Rb$^+$	2	101283 ± 67230	−4.68 ± 0.20	29.52 ± 0.37
7	Na$^+$	1	112 ± 5	−17.47 ± 0.21	−5.81 ± 0.28
	K$^+$	2	369190 ± 5120	−62.22 ± 0.83	−30.68 ± 0.92
	Rb$^+$	2	118780 ± 1850	−29.34 ± 1.73	−0.38 ± 0.02
8	Na$^+$	1	197 ± 23	−6.81 ± 0.16	6.22 ± 0.09
	K$^+$	2	1221010 ± 7000	−29.27 ± 0.31	5.43 ± 0.32
	Rb$^+$	2	321540 ± 10380	−28.68 ± 1.11	2.86 ± 0.45

[a] The concentration of cations is 20–40 mmol dm^{-3}.
[b] The concentration of lariat ethers is 0.5–2 mmol dm^{-3}.
[c] Ref. [14].

non-electron-donating groups, give the unchangeable or decreased binding ability toward Na^+. Though hosts with different sidearms display distinguishable complex stability constants toward Na^+, the binding abilities for all hosts upon complexation with Na^+ seem to be limited to the range ($K = 98\sim197$ M^{-1}), which indicates that the attached sidearms have little effect on the 1:1 binding of the crown ether ring to the metal cation.

It can be seen from Table 1, the binding abilities toward K^+ and Rb^+ of double-armed crown ethers 3-8 are strongly enhanced as compared with parent benzo-15-crown-5 1, showing the much higher effective binding constant ($K = K_1 \times K_2$). Simultaneously, it is found that the cations display the different host selectivity upon complexation with crown ethers 3–8:

$$K^+ : 8 > 4 > 6 > 7 > 5 > 3;$$
$$Rb^+ : 6 > 8 > 4 > 7 > 3 > 5;$$
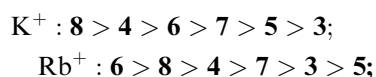
The hosts 6 and 8, possessing the additional electron-donating group at the sidearms, give the relative higher complex stability constants toward both K^+ and Rb^+ than other hosts, i.e., crown ether 8 gives the highest enhancement in binding ability for K^+ ($K_8/K_1 = 43$) and crown ether 6 gives the highest enhancement of binding ability for Rb^+ ($K_6/K_1 = 526$), which mean that the electron effect of double-armed crown ethers still plays an important role in the 2:1 sandwich complexation with cations.

Meanwhile, almost all hosts give the higher binding abilities for K^+ than for Rb^+ except for hosts 3 and 6. As can be seen from Table 1, the sandwich complexation of hosts 3–8 with K^+ and Rb^+ are mostly the enthalpy-driven processes accompanying with the entropy loss. Typically, for the resulting complexes of crown ethers 3–8 with K^+, the strong ion-dipole and π-π interactions result in large enthalpy changes ($-\Delta H° = 29.0 \sim 96.9$ kJ mol^{-1}) and relative smaller entropy losses or entropy gain ($T\Delta S° = -58.5 \sim 5.7$ kJ mol^{-1}), showing higher complex stability constants ($K = 2.4 \times 10^5 \sim 1.2 \times 10^6$ M^{-2}). Different from other hosts, the second, stepwise reactions of crown ethers 3, 6 and 8 with Rb^+ show large positive entropy changes, meaning that there may exist more extensive desolvation effects during the complexation. By comparing the thermo-dynamic data for the complexation of crown ethers with K^+ and Rb^+, it is found that almost all the enthalpic changes and entropic changes become less negative with the increased cation diameter from K^+ to Rb^+, which means that the increase of cation diameter results in the unfavorable enthalpy changes and favorable entropy changes. It has been mentioned that the participation of the second ligand molecule gives a significant contribution for coordinating with K^+ and Rb^+. Therefore, the larger ionic diameter of Rb^+ (3.04 Å) is unfavorable for its size fitting combination with the two crown ether rings as compared with K^+ (2.76 Å), which will

consequently result relative weak ion-dipole interactions between them and simultaneously make it difficult to form strong π–π interactions between the two benzene rings. On the other hand, the strong binding abilities for K^+ can also be reasonably explained by Hard–Soft Acid–Base principle. Comparing to the relative soft cation Rb^+, K^+ is easy to bind with hard oxygen atoms on the crown ether rings forming more stable sandwich complexes.

It is interesting and some puzzling that the relative cation selectivity between K^+ and Rb^+ reversed for host 6, that is to say, it switched from the K^+/Rb^+ of 4.5 for 5 to the Rb^+/K^+ of 1.8 for 6. Compared with the thermodynamic parameters of crown ethers 5 and 6 upon complexation with K^+ and Rb^+, it can be found that the relative cation selectivity for K^+/Rb^+ or Rb^+/K^+ is mainly governed by the entropy term. The host 5 shows the larger complex stability constant ($K = 3.7 \times 10^5$ M^{-2}) for K^+ than for Rb^+ ($K = 8.3 \times 10^4$ M^{-2}) with a larger enthalpy contribution ($\Delta\Delta H° = -8.2$ kJ mol^{-1}) and relative smaller entropy loss ($\Delta T\Delta S° = -4.8$ kJ mol^{-1}), displaying higher K^+/Rb^+ selectivity up to 4.5. However, crown ether 6 shows a much larger entropy gain upon complexation with Rb^+ than K^+ ($\Delta T\Delta S° = 63.5$ kJ mol^{-1}), which makes the stability constant for the resulting complex of crown ether 6 with Rb^+ ($K = 1.0 \times 10^6$ M^{-2}) is larger than that of K^+ ($K = 5.7 \times 10^5$ M^{-2}). Therefore, a plausible explanation for the reversed cation selectivity is that the overall steric hindrance arising from the benzene ring and the side arm play an important role influencing the relative arrangement and orientation of the donor atom and cations, consequently result in the different entropy changes.

Conclusion

Newly synthesized double-armed crown ethers 3–8, possessing the electron-donating or electron-withdrawing double-arms tethered at parent benzo-15-crown-5 skeleton, show unremarkable enhanced binding ability of parent benzo-15-crown-5 1 while forming stoichiometric 1:1 complexes with Na^+, but greatly enhance the original cation binding ability and relative cation selectivity of parent benzo-15-crown-5 1 upon complexation with the cations K^+ and Rb^+ of larger size as compared with the crown ether's cavity. These results indicate the electron effect of double-armed crown ethers plays an important role upon complexation with cations, especially for the 2:1 sandwich complexes, and therefore the functional side arms attached to parent crown ethers can be used as an effective tool to control the cation binding ability and cationic selectivity. Thermodynamically, the 2:1 sandwich complexation of the double-armed crown ethers with metal ions is mostly enthalpy-driven

processes accompanying with moderate entropy loss, which suggest that the participation of the second ligand molecule by forming strong ion-dipole and π–π interactions gives a significant contribution for coordinating with cations with larger size.

Acknowledgement

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Graphical Abstract

Synthesis of Double-Armed Benzo-15-crown-5 and Their Complexation Thermodynamics with Alkali Cations

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R = p-PhCHO, Ph, p-PhCl, p-PhOCH₃, o-PhCHO, p-PhNHOCOCH₃