Complex stability constants ($K_c$) and thermodynamic parameters ($\Delta H^o$ and $\Delta S^o$) were determined in methanol at 25 °C for the stoichiometric 1:1 complexation of some alkali metal ions (Na$^+$, K$^+$, and Cs$^+$) with N-phenylaza-15-crown-5 (1), N-octylaza-15-crown-5 (2), and N-benzylaza-15-crown-5 to N-benzylaza-24-crown-8 (3–6). The N-substituent was shown to have a drastic effect upon complex stability of the aza-15-crown-5 series (1–3). The aza-15-crown-5 possessing the least-bulky substituent afforded the most stable complexes with all cations examined and the highest Na$^+$/K$^+$ selectivity up to 13. The larger-sized aza crown ethers 4–6 gave the highest complex stabilities for the size-matched cations; i.e., 4 showed the highest K$^+$/Cs$^+$ selectivity up to 40, while 6 showed the highest Cs$^+$/K$^+$ selectivity of 10. These results indicate that the N-substituent plays crucial roles in addition to the size-fit concept in the complexation of aza crown ethers with a nondonating side-chain. Thermodynamically, the complexation of alkali metal ions with aza crown ethers is enthalpy-driven, but the cation selectivity is mostly entropy-governed in methanol.

Introduction

Since the first synthesis of crown ethers with side-chain(s) attached through a carbon- or nitrogen-pivot, thermodynamic studies on the complexation of lariat ethers with cations were performed in order to elucidate the nature of the cation-binding behavior from a thermodynamic point of view and also to gain insight into the factors governing cation–ligand complexation phenomena.3–7 Lariat ethers with additional binding sites in the side-chain(s) are known to give significantly enhanced cation-binding ability and selectivity as compared with the parent crown ether.8–15

We have shown that the introduction of both nondonating alkyl16 and donating oxyethylene group(s)17 to the carbon-pivot 16-crown-5 alter not only the cation-binding constant but also the relative cation selectivity significantly. More recently, we have demonstrated that the carbon-pivot lariats are less flexible in adjusting their conformations upon complexation than the corresponding nitrogen-pivot lariats.2,18 The relevant thermodynamic quantities clearly indicate that the binding ability and selectivity of lariat ethers are governed by the ligand’s cavity size, the type and number of additional donor atom(s) in the side-chain, and the pivot atom. However, less attention has been paid to the complexation thermodynamics of aza crown ethers with nondonating side-chain(s). In particular, the influence of substitution and ring size on the cation-binding ability/selectivity of aza crown ethers has not been investigated systematically from a thermodynamic point of view, despite the potential importance of such studies in discussing the complexation behavior of lariat ethers.

In the present study, we report our results of a thermodynamic study on the complexation of alkali metal ions (Na$^+$, K$^+$, and Cs$^+$) with N-phenyl-aza-15-crown-5 (1), N-octylaza-15-crown-5 (2), and N-benzylaza-15-crown-5 (3), N-benzylaza-18-crown-6 (4), N-benzylaza-21-crown-7 (5), and N-benzylaza-24-crown-8 (6) (Chart 1) in methanol at 25 °C. In this study, we discuss the
Experimental Section

Materials. Azacrown ethers 1–6 were prepared according to the procedures reported previously.19–20 Reagent-grade methanol was refluxed over magnesium turnings and then distilled fractionally to give dry methanol for calorimetry. Analytical grade sodium chloride, potassium thiocyanate, and cesium chloride were used as received. All metal salts were dried in vacuo prior to use. The ligands 1–6 were dissolved in the purified methanol to make a titrate solution of 3.0–6.0 mM concentration, while the alkali metal salts were dissolved in the same solvent to make a titrant solution in 0.12–0.15 M concentration.

Apparatus and Procedures. Calorimetric titrations were performed at the atmospheric pressure in a temperature-controlled water bath maintained at 25.0 °C by using an LKB-8721.2 precision titration calorimeter connected to a personal computer for automated titration and data processing.1 The principle of measurement and the detailed experimental procedures were reported elsewhere.21,22 In a typical run, a solution of alkali metal salt (0.12–0.15 M) was continuously added to 6.0 mM placed in the calorimeter. To obtain the net heat of complexation (Qnet), the total apparent heat observed (Qobs) was corrected for the dilution of titrant (Qd), the nonchemical contributions (Qnc), including agitation, heat flow between the vessel and its surrounding, and resistance heating by the thermistor used, and the temperature difference between titrant and titrate (Qtc) in each run: $Q_{\text{net}} = Q_{\text{obs}} - Q_{\text{d}} - Q_{\text{nc}} - Q_{\text{tc}}$. A titration curve was obtained by plotting the temperature change (measured by voltage) against the amount of the azacrown ether solution added, from which the complex stability constant ($K_s$) and the enthalpy change ($\Delta H^\circ$) were directly calculated. Reliability of the whole system and the calculation procedures were doubly checked as previously1 by comparison of the obtained thermodynamic data with the reported values2,23 to give satisfactory results.

Results

Assuming the 1:1 stoichiometry for the complexation of alkali metal ions (M = Na+, K+, and Cs+) with the azacrown ethers 1–6 (ACE in eq 1), the complex stability constant ($K_s$) and the enthalpy change ($\Delta H^\circ$) were calculated by using the least-squares method to minimize the U value (eq 2).24,25

$$ACE + M \rightleftharpoons ACE\cdot M$$

(1)

$$U(K_s\Delta H^\circ) = \sum_{i=1}^{m} (Q_i - \Delta H^\circ \times N_i)^2$$

(2)

where $Q_i$ refers to the net heat of complexation measured at time $t$ in minutes, and $N_i$ denotes the amount in moles of the complex formed at time $t$ and is directly related to the complex stability constant $K_s$.

The stability constant $K_s$ and the enthalpy change $\Delta H^\circ$ for the complexation of Na+, K+, and Cs+ with 1–6 were calculated by computer simulation by continuously changing $K_s$, i.e., $N_0$, to minimize the U value. For each cation–azacrown ether combination, the measurement was repeated more than three times, and the U value obtained was minimized satisfactorily in each case to give the optimized set of $K_s$ and $\Delta H^\circ$. No serious deviation was found in the fitting process, verifying the 1:1 stoichiometry of complexation as assumed above. The values obtained by the repeated measurements were averaged to give the complex stability constants and thermodynamic parameters with standard deviations (Table 1).

Discussion

Complex Stability and Cation Selectivity. As can be seen from Table 1, the complex stability constant, relative cation selectivity, and thermodynamic parameters for the complexation reactions of alkali metal ions

![Chart 1](image-url)

**Table 1. Complex Stability Constant (log $K_s$) and Thermodynamic Parameters (in kcal/mol) for Complexation of Alkali Metal Ions with Azacrown Ethers 1–6 in Methanol at 25 °C**

<table>
<thead>
<tr>
<th>crown ether</th>
<th>lanthanoid</th>
<th>log $K_s$</th>
<th>$-\Delta G^\circ$</th>
<th>$-\Delta H^\circ$</th>
<th>$\Delta S^\circ$</th>
<th>ref</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Na+</td>
<td>1.80 ± 0.03</td>
<td>2.46</td>
<td>6.52 ± 0.07</td>
<td>4.06</td>
<td>a</td>
</tr>
<tr>
<td>2</td>
<td>Na+</td>
<td>1.72 ± 0.03</td>
<td>2.35</td>
<td>8.15 ± 0.05</td>
<td>5.80</td>
<td>a</td>
</tr>
<tr>
<td>3</td>
<td>Na+</td>
<td>3.31 ± 0.06</td>
<td>4.27</td>
<td>4.63 ± 0.08</td>
<td>3.06</td>
<td>a</td>
</tr>
<tr>
<td>4</td>
<td>Na+</td>
<td>2.20 ± 0.07</td>
<td>3.00</td>
<td>11.69 ± 0.09</td>
<td>5.86</td>
<td>a</td>
</tr>
<tr>
<td>5</td>
<td>Na+</td>
<td>1.83 ± 0.03</td>
<td>2.50</td>
<td>16.12 ± 0.12</td>
<td>6.22</td>
<td>b</td>
</tr>
<tr>
<td>6</td>
<td>Na+</td>
<td>1.37 ± 0.03</td>
<td>1.87</td>
<td>15.74 ± 0.06</td>
<td>13.87</td>
<td>b</td>
</tr>
<tr>
<td>7</td>
<td>Na+</td>
<td>5.57 ± 0.03</td>
<td>4.87</td>
<td>5.89 ± 0.09</td>
<td>10.02</td>
<td>b</td>
</tr>
<tr>
<td>8</td>
<td>Na+</td>
<td>5.00 ± 0.07</td>
<td>6.82</td>
<td>11.27 ± 0.14</td>
<td>4.44</td>
<td>b</td>
</tr>
<tr>
<td>9</td>
<td>Na+</td>
<td>3.39 ± 0.06</td>
<td>5.62</td>
<td>11.84 ± 0.05</td>
<td>7.22</td>
<td>b</td>
</tr>
<tr>
<td>10</td>
<td>Na+</td>
<td>2.00 ± 0.06</td>
<td>2.73</td>
<td>3.66 ± 0.05</td>
<td>0.93</td>
<td>b</td>
</tr>
<tr>
<td>11</td>
<td>Na+</td>
<td>4.67 ± 0.06</td>
<td>6.34</td>
<td>9.01 ± 0.07</td>
<td>2.67</td>
<td>b</td>
</tr>
<tr>
<td>12</td>
<td>Na+</td>
<td>3.97 ± 0.08</td>
<td>5.42</td>
<td>8.63 ± 0.04</td>
<td>3.21</td>
<td>b</td>
</tr>
<tr>
<td>13</td>
<td>Na+</td>
<td>1.67 ± 0.06</td>
<td>2.28</td>
<td>4.62 ± 0.03</td>
<td>2.34</td>
<td>b</td>
</tr>
<tr>
<td>14</td>
<td>Na+</td>
<td>2.66 ± 0.03</td>
<td>3.63</td>
<td>10.73 ± 0.04</td>
<td>7.10</td>
<td>b</td>
</tr>
<tr>
<td>15</td>
<td>Na+</td>
<td>3.65 ± 0.06</td>
<td>4.98</td>
<td>7.91 ± 0.07</td>
<td>4.73</td>
<td>b</td>
</tr>
</tbody>
</table>

a Reference 1. b This work; values are the averages of more than three independent measurements.
plexation behavior, which may be attributed to the aza-15-crown-5 plotted in Figure 1.

Na

ence for Na

considered to arise from the other factors. Although all

diameter in Figure 1. As a control, the data28 for the parent 15-crown-5, 18-crown-6, and 21-crown-7 are also affect

ingly, the

The changing profile of complex stability constant (K_s) is plotted against the cation diameter in Figure 1. As a control, the data28 for the parent 15-crown-5, 18-crown-6, and 21-crown-7 are also plotted in Figure 1.

It is noted that, possessing similar cavity sizes, three aza-15-crown-5 1–3 display completely different complexation behavior, which may be attributed to the different substituent introduced at the N-pivot and the relative size between the ligand’s cavity and the cation’s diameter. The changing profile of complex stability constant (K_s) is plotted against the cation diameter in Figure 1. As a control, the data28 for the parent 15-crown-5, 18-crown-6, and 21-crown-7 are also plotted in Figure 1.

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It is interesting to compare the thermodynamic parameters for the complexation of a series of benzylaza-crown ethers 3–6 with K^+ and Cs^+. As can be seen from Table 1 and Figure 2, the enthalpy changes for K^+ and Cs^+ are nearly equal to each other within <1 kcal/mol for these azacrown ethers (3–6), indicating comparable ion–dipole interaction for these cations, irrespective of the ligand’s ring size. However, the entropy changes differ substantially between these two cations except for the size-mismatched ligand 3. Thus, the cations size-fitted to the ligand’s cavity, i.e., K^+ for 4, and 5, and Cs^+

Figure 1. Complex stability constants (K_s) as a function of cation diameter for the complexation of azacrown ethers 1–6 and 15-crown-5 (15C5), 18-crown-6 (18C6), and 21-crown-7 (21C7) with alkali metal ions in methanol at 25 °C.

with azacrown ethers 1–6 are evidently influenced by several factors, particularly the bulkiness and/or flexibility of the substituent introduced at the N-pivot and the relative size between the ligand’s cavity and the cation’s diameter. The changing profile of complex stability constant (K_s) is plotted against the cation diameter in Figure 1. As a control, the data28 for the parent 15-crown-5, 18-crown-6, and 21-crown-7 are also plotted in Figure 1.

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for 6, afford much reduced entropic losses. The mini-
mized entropic loss may be rationalized by the fact that
the size-fitted cation suffers more extensive desolvation
upon complexation than the mismatched one, compen-
sating for a substantial part of the inherent entropic
decrease from the complex formation.

Another interesting thermodynamic feature is the
changing profile of the $\Delta H^\circ$ and $\Delta S^\circ$ values observed for
ligands 3–6 and the compensation between these terms.
For this series of ligands, the enthalpic gain ($-\Delta H^\circ$) and
the entropic loss ($T\Delta S^\circ$) obtained for ligands 3–6 increase
simultaneously with increasing cation diameter in a
compensatory manner. This kind of enthalpy–entropy
compensation effect has been observed widely in su-
pramolecular interactions and discussed earlier from a
more global point of view.24,25,29 In general, the larger
enthalpic gain leads to stronger host–guest interaction
producing a more rigid complex with reduced freedom,
which entropically cancels the enthalpic gain at least in part.
In the present case, it is somewhat unexpected
however that the size-matched cation–ligand combina-
tions do not necessarily give the largest enthalpic gains;
see data for K$^+$–4 and Cs$^+$–6 combinations. Further-
more, it is a general tendency that the complexes
with larger cations (K$^+$ and Cs$^+$) afford greater enthalpic
gains (and entropic losses), irrespective of the ligand's
ring size. Typically, aza-15-crown-5 3 affords the largest
enthalpic gain not with the size-matched Na$^+$ but with
much larger-sized Cs$^+$. A plausible explanation of this
general tendency is that the complex formation of aza-
crown ethers is not driven by equal participation of all
donor atoms but by preferential interaction with the
nitrogen donor which is assisted by the oxygen donors.
Hence, the interaction of a soft nitrogen donor with soft
cations (K$^+$ and Cs$^+$) produces more heat ($-\Delta H^\circ$) and
accompanying entropic loss ($T\Delta S^\circ$) than a hard cation
(Na$^+$).

This simple idea may also explain the changing profile of
thermodynamic parameters obtained for the comple-
Xation of 3–6 with soft cations. Regardless of the in-
creased number of formal donor atoms, the enthalpic gain
and entropic loss gradually decrease with the ligand's
increasing size up to 21 and then increase to some extent
(Figure 2). This behavior suggests that the oxygen atoms
in smaller ligand are situated in the correct position and/or
orientation to be suitable for cation binding and only
a limited number of oxygen atoms around the N-pivot
can coordinate to the cation accommodated in larger
ligands up to 21-crown-7, while the donor atoms in the
largest 24-crown-8 can wrap around the cation, showing
recovery in $\Delta H^\circ$ and $T\Delta S^\circ$.

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Supporting Information Available: Calorimetric titra-
tion data and detailed calculation procedures for the 1:1
complexation of sodium chloride with N-benzylaza-18-crown-6
(4) (4 pages). This material is contained in libraries on
microfiche, immediately follows this article in the microfilm
version of the journal, and can be ordered from the ACS; see
any current masthead page for ordering information.

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Chapter 1.