Three new disubstituted benzo-15-crown-5 derivatives (3–5) have been synthesized from 4’,5’-bis-(bromomethyl)benzo-15-crown-5 (2) and the corresponding alkanols in the presence of Na₂S₂. Their complexation thermodynamics with light lanthanoid(III) nitrates (La³⁺–Gd³⁺) have been studied in anhydrous acetonitrile at 25 °C. Plots of ΔS° against the reciprocal ionic diameter of lanthanoid cations exhibited monotonically declining pattern for the parent benzo-15-crown-5 (1) and 3 but showed a characteristic peak at Ce³⁺ for 4 and 5. It is interesting to note that the simple extension of the alkyl side chains in 4 and 5 can alter the cation selectivity profiles of 1 and 3. Possessing two 2-oxapropyl groups, 3 gave a comparable Kₛ for La³⁺ but a significantly decreased Kₛ for Ce³⁺ compared with the corresponding values for 1, thus exhibiting an exceptionally high La³⁺/Ce³⁺ selectivity of 11. Thermodynamically, the complexation of lanthanoid perchlorates with 1 is absolutely entropy-driven in acetonitrile, while the complexation of lanthanoid nitrates with 3–5 is primarily driven by exothermic enthalpy changes with accompanying moderate entropic gain or small entropic loss.

**Introduction**

Lariat ethers, i.e., crown ethers with additional donor atom(s) in the side arm(s), have been designed and synthesized in order to alter the cation binding ability and selectivity of the parent crown ethers through further ligation of the side arm donor(s) to a cation accommodated in the crown cavity. Indeed, lariat ethers give much enhanced cation-binding abilities and selectivities as compared with the parent crown ethers. However, the foregoing studies on the complexation thermodynamics of lariat ethers have been concentrated mostly on alkali, alkaline earth, and some heavy metal salts, while little attention has been paid to the complexation thermodynamics of trivalent lanthanoid ions. We have recently shown that both carbon- and nitrogen-pivot 16-crown-5 lariats display distinctly different cation-binding abilities and selectivities for the light lanthanoid series. The obtained thermodynamic quantities clearly indicate that the binding abilities and selectivities of lariat ethers are governed by the type and number of additional donor atom(s) in the side arm. Unfortunately, no thermodynamic study has hitherto been reported on the complexation of trivalent lanthanoid ions with lariat benzocrown ethers in which donating side arm(s) are introduced at the benzene ring. Such a situation prompted us to synthesize a series of novel benzocrown ethers with donating side arms and investigate their complexation behavior with lanthanoid nitrates from a thermodynamic point of view.

In the present study, we synthesized a series of 4’,5’-bis-(2-oxaalkyl)benzo-15-crown-5 (3, 4, and 5) (Chart 1) from 4’,5’-bis-(bromomethyl)benzo-15-crown-5 (2) and in

![Chart 1](https://example.com/chart1.png)
vestigated their complexation thermodynamics with light lanthanoid(III) nitrates (Ln = La, Ce, Pr, Nd, Sm, Eu, and Gd) in acetonitrile at 25 °C, using titration calorimetry. The obtained thermodynamic quantities, when compared with the relevant data reported for benzo-15-crown-5 (1),18 will promote further understanding of the complexation behavior of benzo-15-crown-5 lariats with light lanthanoid nitrates. It is also interesting to examine the effects of the introduced side arms and their chain length upon complexation thermodynamics.

**Experimental Section**

Melting points are uncorrected. \(^1\)H NMR spectra were recorded at 200 MHz in CDCl\(_3\). Starting materials were commercially available unless noted otherwise. 2,3-Benzo-[1,4,7,10,13-pentaoxa-2-cyclopentadecene (3). Starting materials were commercially available unless noted otherwise. 2,3-Benzo-[1,4,7,10,13-pentaoxa-2-cyclopentadecene (3). Starting materials were commercially available unless noted otherwise. 2,3-Benzo-[1,4,7,10,13-pentaoxa-2-cyclopentadecene (3). Starting materials were commercially available unless noted otherwise. 2,3-Benzo-[1,4,7,10,13-pentaoxa-2-cyclopentadecene (3). Starting materials were commercially available unless noted otherwise. 2,3-Benzo-[1,4,7,10,13-pentaoxa-2-cyclopentadecene (3). Starting materials were commercially available unless noted otherwise. 2,3-Benzo-[1,4,7,10,13-pentaoxa-2-cyclopentadecene (3). Starting materials were commercially available unless noted otherwise. 2,3-Benzo-[1,4,7,10,13-pentaoxa-2-cyclopentadecene (3). Starting materials were commercially available unless noted otherwise. 2,3-Benzo-[1,4,7,10,13-pentaoxa-2-cyclopentadecene (3). Starting materials were commercially available unless noted otherwise. 2,3-Benzo-[1,4,7,10,13-pentaoxa-2-cyclopentadecene (3). Starting materials were commercially available unless noted otherwise. 2,3-Benzo-[1,4,7,10,13-pentaoxa-2-cyclopentadecene (3). Starting materials were commercially available unless noted otherwise. 2,3-Benzo-[1,4,7,10,13-pentaoxa-2-cyclopentadecene (3). Starting materials were commercially available unless noted otherwise. 2,3-Benzo-[1,4,7,10,13-pentaoxa-2-cyclopentadecene (3). Starting materials were commercially available unless noted otherwise. 2,3-Benzo-[1,4,7,10,13-pentaoxa-2-cyclopentadecene (3). Starting materials were commercially available unless noted otherwise.

**Results**

A 1:1 stoichiometry28,29 was assumed for complexation of Ln(NO\(_3\))\(_2\) (Ln = La, Ce, Pr, Nd, Sm, Eu, and Gd) with lariat ethers 3–5 (CE in eq 1) in calculating the complex stability constant (K\(_s\)) and the enthalpy change (\(\Delta H^\circ\)) by using the least-squares method to minimize the U value (eq 2):28,31

\[
\text{CE} + \text{Ln} \rightleftharpoons \text{CE-Ln} \quad (1)
\]

\[
U(K_s, \Delta H^\circ) = \sum_{t=1}^{m} (Q_t - \Delta H^\circ \times N_t)^2 \quad (2)
\]

(21) Seminara, A.; Musumeci, A. Inorg. Chem. Acta 1980, 39, 9, and ethanol according to the procedure described above for 3 in 91% yield after recrystallization from hexane: mp 69.5–70.5 °C; MS m/z 384 (M\(^+\)); UV–vis \(\lambda_{max} (\text{CHCl}_3) / \text{nm} (\epsilon / M^{-1} \text{cm}^{-1})\) 241.4 (14130), 283.1 (5800); \(^1\)H NMR \(\delta = 3.3 (s, 6 H), 3.73 (s, 8 H), 3.87 (t, J = 4.3 Hz, 4 H), 4.10 (t, J = 4.3 Hz, 4 H), 4.37 (t, J = 4.3 Hz, 4 H). Anal. Calcd for C\(_{18}\)H\(_{28}\)O\(_7\): C, 60.66; H, 7.92. Found: C, 60.95; H, 7.74.

(22) Shi, J.-P.; Liu, Y.; Sun, L.-C. Anal. Instrum. (Fenxi Yiqi) 1988, 2, 42.
Nt computer simulation by continuously changing Pr, Nd, Sm, Eu, and Gd) with

Table 1. Complex Stability Constant (log K₅) and Thermodynamic Parameters (in kcal/mol) for Complexation of Light Lanthanoid(III) Perchlorate with Benzo-15-crown-5 (1) and Light Lanthanoid(III) Nitrates with Benzo-15-crown-5
Lariats (3, 4, and 5) in Anhydrous Acetonitrile at 25 °C

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<th>ligand</th>
<th>cation</th>
<th>log K₅</th>
<th>ΔH°</th>
<th>ΔG°</th>
<th>TAS°</th>
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<td>Gd³⁺</td>
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<td>Ce³⁺</td>
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<td>Pr³⁺</td>
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<td>Eu³⁺</td>
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<td>La³⁺</td>
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<td>Ce³⁺</td>
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<td>2.89 ±0.03</td>
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<tr>
<td>5</td>
<td>La³⁺</td>
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<td>Ce³⁺</td>
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<td>Pr³⁺</td>
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<td>Nd³⁺</td>
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<td>Sm³⁺</td>
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<td>Eu³⁺</td>
<td>2.93 ±0.01</td>
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<td>Gd³⁺</td>
<td>2.76 ±0.07</td>
<td>-2.20 ±0.05</td>
<td>-3.77 ±0.09</td>
<td>1.57 ±0.04</td>
<td>b</td>
</tr>
</tbody>
</table>

a Reference 18. b This work; average of more than three independent measurements.

Scheme 1

Discussion

Syntheses. The disubstituted benzo-15-crown-5 ligands, i.e., 3, 4 and 5, were synthesized in 93%, 91%, and 85% yields, respectively, by treating the dibromo precursor 2 with methanol, ethanol, and propanol in the presence of Na₂S₂ (Scheme 1). The use of sodium sulfide as a mild base appreciably improved product yields over those obtained by using conventional strong bases such as sodium hydroxide or metallic sodium. However, the use of octanol did not give the corresponding octyl derivative, suggesting that the reactant alcohol should be highly soluble in water in this synthetic procedure.

Substituent Effect upon Cation Binding and Selectivity. As shown in Table 1, the introduction of side arms of varying chain lengths into 1, giving the benzo-15-crown-5 lariats 3–5, significantly alters not only the cation binding ability but also the relative cation selectivity for the trivalent lanthanoid ions. To visualize the cation binding abilities and selectivities of crown ethers 1, 3, 4, and 5, the changing profile of the binding constant (K₅) is plotted as a function of reciprocal ionic diameter of lanthanoid in Figure 1.

As shown in Figure 1, the K₅ values obtained for the complexation of lanthanoid perchlorates with 1 show a relatively simple profile, declining with increasing atomic number or decreasing ionic radius throughout the light lanthanoid series La³⁺–Nd³⁺. Thus, the reference host 1 shows the highest cation selectivities, defined as the relative K₅, primarily for La³⁺ and second for Ce³⁺ with a relative La³⁺/Ce³⁺ selectivity of 4.6. The declining profile of K₅ for light lanthanoids may be attributed to the increasing surface charge density due to the lanthanoid contraction and the consequent tighter solvation for heavier lanthanoids, ³⁷ since the size–fit concept does not appear to rationalize the preferred complexation of 1.

Figure 1. Complex stability constant ($K_S$) as a function of reciprocal ionic radius ($r^{-1}, \text{Å}^{-1}$) for the complexation of light lanthanoids with 1 (△), 3 (○), 4 (●), and 5 (▲) in acetonitrile at 25 °C.

(cavity diameter 1.7–1.9 Å) with La$^{3+}$ (ion diameter 2.12 Å) and Ce$^{3+}$ (2.06 Å).

It is interesting that introduction of two 2-oxapropyl groups to 1, affording double-armed lariat 3, alters the original cation binding ability and relative cation selectivity of 1 to give a significantly different binding profile shown in Figure 1. The substitution does not greatly affect the $K_S$ for La$^{3+}$ but significantly lowers the $K_S$ for Ce$^{3+}$ and enhances the $K_S$ for Pr$^{3+}$–Gd$^{3+}$, eventually flatting the $K_S$ profile of 3 through Ce$^{3+}$ to Gd$^{3+}$. Interestingly, such disoriented changes endow 3 an exceptionally high relative selectivity for La$^{3+}$ of $\approx$11 over Ce$^{3+}$ or any other light lanthanoid. This specific cation selectivity for La$^{3+}$ could be attributed to the appropriate steric requirement upon side arm ligation of 3 to La$^{3+}$, although we do not have any direct evidence such as crystallographic structure in support of this possibility.

In contrast, the introduction of longer side arms, affording 4 and 5, causes significant changes in the binding behavior of particularly La$^{3+}$ and Ce$^{3+}$, giving a distinctly different global cation selectivity profiles. As shown in Table 1 and Figure 1, the $K_S$ values for complexation of heavier lanthanoids (Pr$^{3+}$–Gd$^{3+}$) with 4 and 5 resemble each other and are comparable to the relevant values for 3 to give a global average of log $K_S = 2.86 \pm 0.07$. On the other hand, the $K_S$ for La$^{3+}$ gradually decreases with extending the side arm from log $K_S = 4.03$ for 3, to 3.49 for 4, and then to 3.22 for 5, while the $K_S$ for Ce$^{3+}$ shows an opposite tendency, increasing from log $K_S = 2.98$ for 3, to 3.75 for 4, and then to an apparently saturated value of 3.74 for 5. As a consequence of such unique changing profiles of the $K_S$ for 3–5, the relative cation selectivity between La$^{3+}$ and Ce$^{3+}$ is dramatically inverted just by extending the side arm, switching from the La$^{3+}$/Ce$^{3+}$ selectivity of 11 for 3 to the Ce$^{3+}$/La$^{3+}$ selectivity of 3.3 for 5, although the global range of $K_S$ obtained for the light lanthanoids definitely becomes narrower as the side arms are elongated. It is deduced that the overall steric hindrance around the benzene ring and the side arm donors plays an important role in determining the spatial arrangement and orientation of the donor atoms. Probably, the shorter 2-oxapropyl groups can induce the most favorable conformation for the size-matched La$^{3+}$, while the longer 2-oxabutyl or 2-oxapentyl groups may lead to less favorable conformations. It is somewhat unexpected and therefore noteworthy that the apparently similar donating side arms with different alkyl groups can alter not only the binding ability for trivalent lanthanoid ions but also the relative cation selectivity significantly.

**Thermodynamic Parameters.** The reported thermodynamic data clearly indicate that the complexation of light lanthanoid perchlorates with unsubstituted benzo-15-crown-5 1 in acetonitrile is exclusively driven by the large positive entropy changes ($T\Delta S^\circ = 6.32–8.22$ kcal/mol), which are canceled in part by moderately endothermic enthalpy changes ($\Delta H^\circ = 2.92–4.93$ kcal/mol), as shown in Table 1. As a consequence of the compensation between the positive $T\Delta S^\circ$ and $\Delta H^\circ$, the complex stability ($K_S$) in acetonitrile decreases gradually with increasing atomic number, as illustrated in Figure 1.

In contrast, the complexation of lanthanoids with benzo-15-crown-5 lariats 3–5 exhibited completely dif-
different thermodynamic behavior. As can be readily rec-
ognized from Figure 2, all of the $\Delta H^\circ$ values are negative
and the $T \Delta S^\circ$ values are slightly positive or even negative
in some cases. Thus, the complexation of lanthanoids
with $3 - 5$ in acetonitrile is mostly driven by enthalpy with
accompanying minor entropic assist or drawback, al-
though the entropic contribution exceeds the enthalpic
stabilization in some cases.

Despite the apparently similar global profiles of $K_S$ for
1 and for $3 - 5$, the thermodynamic parameters behave
completely oppositely. In this context, it should be
emphasized that lanthanoid salts with different coun-
teranions, i.e., perchlorate and nitrate, were employed
in the previous18 and present studies, respectively. Hence,
the contrasting thermodynamic behavior may be at-
tributed to the nature of the lanthanoid salts used and
also to the ability of lariat ligation by $3 - 5$, both of which
are related to the entropy factors such as solvation/
desolvation and structural freezing upon complexation.
In acetonitrile, lanthanoid perchlorates dissociate to some
extent to give heavily solvated trivalent lanthanoid ions
through ion–dipole interactions. Then, the complexation
with 1 requires fairly extensive desolvation of both cation
and ligand upon complexation, affording the highly
positive entropy changes, as observed (Figure 2). In
contrast, lanthanoid nitrates are not completely dissoci-
ated in acetonitrile,17c forming contact ion pairs, and
therefore the solvation to lanthanoid nitrates is not so
heavy or tight as the perchlorates, which probably
reduces the entropic contributions to the complex stabili-
ties of $3 - 5$.

It is also interesting to discuss the relative cation
selectivity from the thermodynamic point of view. As
shown in Table 1, the benzo-15-crown-5 lariats $3 - 5$
display quite similar changing profiles of $\Delta H^\circ$ and $T \Delta S^\circ$
for Pr$^{3+}$–Gd$^{3+}$, but completely different values for La$^{3+}$
and for Ce$^{3+}$. Thus, the dramatic selectivity change from
La$^{3+}$ to Ce$^{3+}$ by changing the host from 3 to 5 (or 4) is
attributable not to the increased enthalpic gain but to
the enhanced entropic contribution stabilizing the latter
hosts. Upon complexation of La$^{3+}$, 5 affords more exo-
thermic $\Delta H^\circ$ by 1.68 kcal/mol than 3, which is however
canceled out by more negative $T \Delta S^\circ$ by 2.78 kcal/mol,
resulting in a less stable La$^{3+}$–5 complex. In the case of
Ce$^{3+}$, the enthalpic disadvantage for 5 by 2.71 kcal/mol
is overcome by the entropic contribution by 3.66 kcal/
ml, thus providing a more stable Ce$^{3+}$–5 complex with
the Ce$^{3+}$/La$^{3+}$ selectivity of 3.3. Almost the same dis-
cussion can be applied to the thermodynamic behavior of 4
upon complexation with La$^{3+}$ and Ce$^{3+}$. Although the
contrasting thermodynamic behavior observed for La$^{3+}$
and Ce$^{3+}$ is not readily rationalized or attributable to a
single cause at present, probably the slight differences
in cation diameter and surface charge would affect the
conformational changes and solvation/desolvation upon
complexation. It is concluded however that the complex-
ation of lanthanoid nitrates with benzo-15-crown-5 lariats
$3 - 5$ is obviously entropy-driven in acetonitrile, but the
cation selectivity is critically governed by the entropy
term.

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