Molecular Design of Crown Ethers. 13. Complexation Thermodynamics of Light Lanthanoid Nitrates with Aza-16-Crown-5 Lariat in Acetonitrile: Enhanced Selectivity for Nd³⁺ [†]

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Calorimetric titrations have been performed in anhydrous acetonitrile at 25 °C to give the complex stability constants (K_s) and the thermodynamic parameters for the stoichiometric 1:1 complexation of light lanthanoid-(III) nitrates (La−Gd) with *N*-methoxyethylaza-4,7,11,14-tetraoxacyclohexadecane (aza-16-crown-5 lariat) (**1**). Using the present and reported data, the complexation behavior of *C*- and *N*-pivot lariats with 16-crown-5 skeletons is discussed comparatively and globally from the thermodynamic point of view. Possessing structural flexibility as compared with lariat ether 15-(2,5-dioxahexyl)-15-methyl-1,4,7,10,13-pentaoxacyclo-hexadecane (16-crown-5 lariat) (**2**), aza-16-crown-5 lariat gave the highest K_s for Nd³⁺ among the light lanthanoid nitrates. The complex stability sequence as a function of reciprocal ionic diameter of lanthanoid showed a characteristic peak profile at Nd³⁺ for **1**, the relative cation selectivity for Nd³⁺ over the neighboring Pr³⁺ and Sm³⁺ amounted to 9. Thermodynamically, the complexation of light lanthanoid nitrates with the lariat ethers is mainly enthalpy-driven in acetonitrile, but the cation selectivity is entropy-governed. The high cation selectivity of aza-16-crown lariat (**1**) is attributed to the entropic loss that is minimized only when a strict size match is materialized between the ionic diameter of the lanthanoids and the relatively flexible three-dimensional cavity induced upon lariat ligation. Therefore, the three-dimensional induced fit plays an important role in the recognition of trivalent lanthanoid ions by lariat ethers with structural flexibility.

Introduction

Lariat ethers with additional donor atom(s) in the side arm-(s) have been designed and synthesized to enhance the cation binding ability and selectivity of the parent crown ether through further ligation of the sidearm donor(s) to a cation accommodated in the crown cavity.[1−8] On the other hand, the introduction of extra methylene(s) into small-sized 12-crown-4 and 15-crown-5 endows the resulting less-symmetrical 14-crown-4[9−11] and 16-crown-5[11−13] with much higher cation selectivities for lithium and sodium ions, respectively, than the parent crown ethers. In particular, the carbon-pivot 16-crown-5 lariat, which carries a donating side arm, shows specific enhancement in complex stability and cation selectivity for the size-fitted Na⁺.[14] Thus the tailoring of crown ether's ring size by introducing extra methylene(s) and adding donating side arm-(s) has been demonstrated to be a convenient and powerful tool to enhance the cation-binding ability and relative cation selectivity of crown ethers.[14] However, the work on the complexation thermodynamics with these crown ethers has been concentrated mainly on alkali, alkaline earth, and some heavy metal salts. So far, less attention has been paid to the complexation thermodynamics of trivalent lanthanoids.

We have recently shown that the complexation in induced three-dimensional cavity of carbon-pivot 16-crown-5 lariat(s) shows a poor cation selectivity for the light lanthanoid series.[15] More recently, however, we have demonstrated that the nitrogen-pivot 16-crown-5 lariat (**1**) possesses much higher cation-binding ability and selectivity compared with the carbon-pivot 16-

crown-5 (**2**).[16] This indicates that the increased conformational freedom of the ligand is more suitable for the complexation of size-matched cation. These results prompted us to investigate the complexation behavior of less-symmetrical aza-16-crown-5 lariat with lanthanoid nitrates.

In the present study, we synthesized nitrogen-pivot 16-crown-5 lariat (**1**) (Chart 1) and investigated the thermodynamics of the complexation with aza-16-crown-5 lariat in acetonitrile of light lanthanoid(III) nitrates (Ln = La, Ce, Pr, Nd, Sm, Eu, and Gd), using titration calorimetry. The thermodynamic parameters for the complexation of light lanthanoid nitrates with aza-16-crown-5 lariat, together with those for 16-crown-5 (**3**) and the lariat ether (**2**),[15] will serve our further understanding of this thermodynamically less investigated area of crown ether chemistry.[17,18] It is another point of interest to examine the scope and limitations of the lariat effect with the relatively flexible *N*-pivot lariat ether from the thermodynamic point of view.

Experimental Section

Materials. Less-symmetrical aza-16-crown-5 lariat (**1**) was synthesized in 29% yield by the reaction of *N*-methoxyethyldi-ethanolamine with the ditosylate of 3,7-dioxanonane-1,9-diol in the presence of NaH as a base in tetrahydrofuran, according to the procedures reported previously.[19] Analytical-grade ac-etonitrile was dried over calcium hydride and then distilled fractionally to give the anhydrous solvent ($<5 \times 10^{-7}$ S cm⁻¹) for calorimetry. Light lanthanoid(III) nitrates (La−Gd) were prepared by dissolving the corresponding oxides of 99.9% purity (Baotou Rare Earth Chemical Co.) in 50% aqueous nitric acid while heating for about 10 min. After evaporation, the solid residue was dehydrated with P₂O₅ in vacuo for several days to give a powdery product. Lanthanoid nitrate was dissolved in

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CHART 1

(1)

(2)   **(3)**

anhydrous acetonitrile and refluxed for 24 h over molecular sieves for further removal of water. The concentrations of lanthanoid nitrate solutions in acetonitrile were determined by the EDTA titration using xylenol orange as an indicator. The conductometric measurements showed that these light lanthanoid nitrates behave as nonelectrolytes in anhydrous acetonitrile solution.[20]

Apparatus and Procedures. Calorimetric titrations were performed at atmospheric pressure in a temperature-controlled water bath maintained at 25.0 °C, by using a TRONAC model 458 isoperibol titration calorimeter connected to a personal computer for automated titration and data processing.[21] The principle of the measurement and the detailed experimental procedures have been described previously.[22,23] Typically, a crown ether solution (20–30 mM) in anhydrous acetonitrile was continuously introduced at a rate of 0.3321 cm^3 min^{-1} into a lanthanoid nitrate solution (0.9–1.5 mM) placed in the calorimeter. In order to obtain the net heat of complexation (Q_{net}), the total apparent heat observed (Q_{obs}) was corrected for the dilution of titrant (Q_D), the non-chemical contributions (Q_{HL}), including agitation, heat flow between the vessel and its surroundings, and resistance heating by the thermistor used, and the temperature difference between titrant and titrate (Q_{TC}) in each run: $Q_{net} = Q_{obs} - Q_D - Q_{HL} - Q_{TC}$. A titration curve was obtained by plotting the temperature change (measured by voltage) against the amount of the crown ether solution added, from which the complex stability constant (K_s) and the enthalpy change ($\Delta H°$) were calculated. Reliability of the whole system and the calculation procedures were doubly checked as previous[24] by comparison of the obtained thermodynamic data with the reported values,[25,26] and satisfactory results were obtained.

Results

Assuming the 1:1 stoichiometry[27,28] for the complexation of Ln(NO$_3$)$_3$ (Ln = La, Ce, Pr, Nd, Sm, Eu, and Gd) for the aza-16-crown-5 lariat, the complex stability constant (K_s) and the enthalpy change ($\Delta H°$) were calculated by using the least-squares method to minimize the U value:[29,30]

$$H + G \underset{}{\overset{K_s}{\rightleftharpoons}} H{\cdot}G \qquad (1)$$

$$U(K_s, \Delta H°) = \sum_{t=1}^{m} (Q_t - \Delta H° N_t)^2 \qquad (2)$$

where Q_t refers to the net heat of complexation measured at time t in minutes and N_t denotes the amount in moles of the

TABLE 1: Complex Stability Constant (log K_s) and Thermodynamic Parameters (in kcal/mol^{-1}) for Complexation of Light Lanthanoid(III) Nitrates with *N*-Pivot 16-Crown-5 Lariat (1), *C*-Pivot 16-Crown-5 (2), and 16-Crown-5 (3) in Anhydrous Acetonitrile at 25 °C

ligand	cation	log K_s	$-\Delta G°$	$-\Delta H°$	$T\Delta S°$	ref
1	La^{3+}	2.82 ± 0.07	3.85	8.20 ± 0.10	-4.35	a
	Ce^{3+}	3.01 ± 0.08	4.11	5.14 ± 0.07	-1.03	a
	Pr^{3+}	3.47 ± 0.06	4.73	2.98 ± 0.20	1.75	a
	Nd^{3+}	4.41 ± 0.07	6.02	1.59 ± 0.11	4.43	a
	Sm^{3+}	3.50 ± 0.09	4.77	4.70 ± 0.27	0.77	a
	Eu^{3+}	2.71 ± 0.09	3.70	8.33 ± 0.13	-4.63	a
	Gd^{3+}	2.82 ± 0.03	3.85	10.24 ± 0.14	-6.39	a
2	La^{3+}	3.76 ± 0.07	5.13	6.99 ± 0.03	-1.86	b
	Ce^{3+}	3.18 ± 0.03	4.34	5.05 ± 0.05	-0.71	b
	Pr^{3+}	3.07 ± 0.02	4.19	5.57 ± 0.04	-1.38	b
	Nd^{3+}	3.04 ± 0.02	4.15	2.49 ± 0.09	1.66	b
	Sm^{3+}	3.01 ± 0.05	4.11	7.54 ± 0.06	-3.43	b
	Gd^{3+}	3.10 ± 0.01	4.23	7.63 ± 0.01	-3.40	b
3	La^{3+}	2.54 ± 0.03	3.46	14.51 ± 0.09	-11.05	b
	Ce^{3+}	2.49 ± 0.01	3.40	8.47 ± 0.11	-5.07	b
	Pr^{3+}	2.76 ± 0.03	3.76	8.55 ± 0.01	-4.79	b
	Nd^{3+}	3.81 ± 0.04	5.20	3.72 ± 0.05	1.48	b
	Sm^{3+}	4.14 ± 0.08	5.65	5.75 ± 0.08	-0.10	b
	Gd^{3+}	3.66 ± 0.07	4.99	5.46 ± 0.05	-0.47	b

a This work; values are the averages of more than three independent measurements. *b* Reference 15.

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 $\Delta H°$ for the complexation of lanthanoid nitrate with lariat ether (**1**) were calculated by computer simulation by continuously changing K_s, i.e., N_t to minimize the U value. For each lanthanoid–ligand combination, the measurement was repeated more than three times and the U value obtained was minimized satisfactorily to give the optimized set of K_s and $\Delta H°$ with standard deviations. No serious deviation was found in the fitting process, verifying the 1:1 stoichiometry of complexation as assumed above. The complex stability constants and thermodynamic parameters obtained are listed in Table 1. For the comparison purpose, the thermodynamic quantities reported for the complexation with 16-crown-5 (**3**) and its lariat derivative (**2**) in acetonitrile are also included in Table 1.

Discussion

Binding Constants and Selectivity. As can be seen from Table 1, the complex stability constants, the relative cation selectivity, and the thermodynamic parameters for the complexation reactions of light lanthanoid nitrates with ligands **1**–**3** are influenced by several factors: relative size of the ligand's cavity to the cation's diameter, surface charge density, ligand's structural rigidity, spatial arrangement of the donor atoms, molecular symmetry, size of the induced three-dimensional cavity of lariat ether, and so on. In order to visualize the cation-binding properties of ligands **1**–**3**, the changing profile of the complex stability constant (K_s) is plotted as a function of reciprocal ionic diameter of lanthanoid in Figure 1.

As can be seen from Figure 1, the profile of K_s for the less-symmetrical 16-crown-5 (**3**) shows a sudden jump at Nd^{3+} and keeps high K_s values over Nd–Gd, probably owing to their fitted cavity size and proper donated orientations. This result may indicate that the size-fit concept is more rigorous in the complexation of trivalent lanthanoid ions, since the ionic diameters (1.88–1.97 Å)[31] of Nd^{3+} through Gd^{3+} apparently match to the cavity of 16-crown-5 (**3**) (1.8–1.9 Å).[32,33] On the other hand, the carbon-pivot 16-crown lariat (**2**) shows a very flat K_s profile. This poor cation selectivity for (**2**) would

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Figure 1. Complex stability constant (K_s) at 25 °C as a function of reciprocal ionic radius (r^{-1}, Å^{-1}) for the complexation of light lanthanoids with *N*-pivot 16-crown-5 lariat (**1**) (●), *C*-pivot 16-crown-5 lariat (**2**) (△), and 16-crown-5 (**3**) (□) in acetonitrile.

be ascribed to the difficulty in adjusting strictly the three-dimensional cavity induced upon lariat ligation to the size of lanthanoids, probably due to its rigid framework. However, it is very interesting and significant that the cation binding constants and the relative cation selectivities exhibited by the nitrogen-pivot 16-crown-5 lariat (**1**), shown in Figure 1, are totally different from those of the reference compounds **2** and **3**. Possessing a relatively flexible molecular structure as compared with the carbon-pivot 16-crown-5 lariat (**2**), the nitrogen-pivot 16-crown-5 lariat (**1**) gave the highest K_s for Nd^{3+} and the lowest for La^{3+} and Eu^{3+} among the light lanthanoid ions, eventually showing the highest cation selectivity for Nd^{3+}. It is noted that the relative cation selectivity for Nd^{3+} over the neighboring Pr^{3+} and Sm^{3+} amounted to 8−9, which is exceptionally high for the lanthanoid series possessing quite similar chemical and physical properties. This is reasonably

accounted for in terms of the steric requirement upon sidearm ligation; only the most size-fitted lanthanoid ion accommodated in the cavity of 16-crown-5 fully enjoys further ligation by the donating sidearm with relatively large structural flexibility, making the operation of exact size-matching easy. Therefore, the increased conformational freedom of the lariat ether is essentially for the highly selective complexation of the size-matched trivalent lanthanoid ions.

Thermodynamic Parameters. In order to discuss the changing profile of K_s and the relative cation selectivity from the thermodynamic point of view, the thermodynamic quantities for the complexation with ligands **1**−**3** are plotted against the lanthanoids in Figure 2. As can be recognized more easily from Figure 2, the $\Delta H°$ values of the complex formation are all negative with either negative or slightly positive entropic changes. This means that these reactions are chiefly enthalpy-driven in acetonitrile. However, the large enthalpic gain ($\Delta H°$) does not immediately mean high complex stability and is often canceled by the larger entropic loss, as is the case with 16-crown-5 (**3**) for the first half of the lanthanoids. Instead, the cation−ligand combinations accompanying smaller entropic losses lead to higher complex stabilities. Thermodynamically, the entropic loss arising from the structural freezing upon lariat ligand to lanthanoid ion accommodated in the cavity is often compensated by the gain from the accompanying extensive desolvation, giving rise to the positive $T\Delta S$ value as high as 4.43 kcal mol^{-1} for the complexation of lariat ether **1** with Nd^{3+}. Thus, it is concluded that the complexation itself is mainly enthalpy-driven in acetonitrile but that the cation selectivity is governed by the entropy change for all ligands.

Differing from the inherent two-dimensional cavity of the parent crown ether, the lariat ether forms an induced three-dimensional cavity upon complexation. Therefore, it is interesting to compare the thermodynamic parameters for the nitrogen-pivot 16-crown-5 lariat (**1**) with those for the carbon-pivot 16-crown-5 (**2**), since these two lariats, possessing *C*- and *N*-pivot, suffer substantially different structural changes upon lariat ligation. As can be seen from Figures 1 and 2, the cation selectivity sequences and the thermodynamic profiles observed for two lariat ethers are distinctly different. One possible explanation for the relatively small and mutually resembling parameters obtained for **2** throughout the light lanthanoid series would be found in the presence of the methyl group at C-15 that may contribute to the lock of the 16-crown-5 lariat framework in a conformation favorable for complexation of some cation but makes the operation of strict size-fitting difficult. In contrast
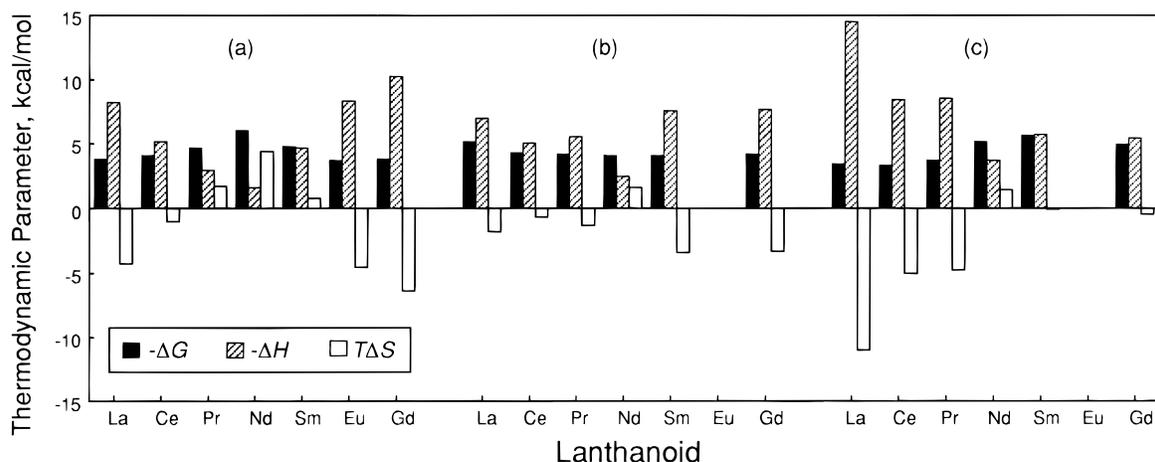
Figure 2. Thermodynamic parameters for the complexation of light lanthanoids (La−Gd) with (a) *N*-pivot 16-crown-5 lariat (**1**), (b) *C*-pivot 16-crown-5 lariat (**2**), and (c) 16-crown-5 (**3**) in acetonitrile at 25 °C.

to the reference lariat ether **2**, *N*-pivot 16-crown-5, possessing the relatively large structural flexibility, can strictly adjust the induced three-dimensional cavity to the size of the most favorable lanthanoid ion, i.e., Nd^{3+}. In this case, the desolvation becomes more extensive upon complexation with $Pr^{3+}-Sm^{3+}$ to give the positive entropy changes ($T\Delta S$), which lead to the higher cation-binding ability. Thus the *N*-pivot 16-crown-5 (**1**) is shown to possess the most advantageous structure from the viewpoint of the strict size-matching required for highly selective complexation of lanthanoids. Thermodynamically, this drastic change in the cation selectivity sequence is attributed to the positive entropy change that is maximized when a very strict size-fit relationship is attained between the induced 3-D cavity of *N*-pivot lariat ether and the ionic diameter of the lanthanoids. In this context, the tailoring of lariat ether's 3-D cavity by introducing a donating side arm to a less-symmetric aza-crown ether is a convenient and powerful tool to enhance the cation-binding ability and relative cation selectivity for lanthanoid ions.

Supporting Information Available: Calorimetric titration data and detailed calculation procedures for the 1:1 complexation of light lanthanoid(III) nitrates and aza-16-crown-5 lariat (**1**) (6 pages). Ordering information is given on any current masthead page.

References and Notes

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