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Lanthanide Paramagnetic Probes for NMR Spectroscopic Studies of Fast Molecular Conformational Dynamics and Temperature Control. Effective Six-Site Proton Exchange in 18-Crown-6 by Exchange Spectroscopy

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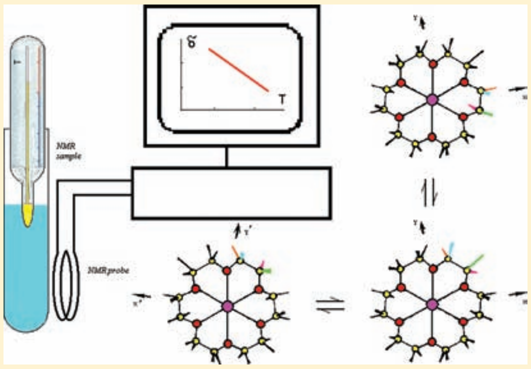
S Supporting Information



ABSTRACT: ^{1}H and ^{13}C NMR measurements are reported for the $CDCl_3$ and CD_2Cl_2 solutions of [La(18-crown-6)$(NO_3)_3$] (**I**), [Pr(18-crown-6) $(NO_3)_3$] (**II**), [Ce(18-crown-6)$(NO_3)_3$] (**III**), and [Nd(18-crown-6)$(NO_3)_3$] (**IV**) complexes. Temperature dependencies of the ^{1}H NMR spectra of paramagnetic **II**−**IV** have been analyzed using the dynamic NMR (DNMR) methods for six-site exchange. Two types of conformational dynamic processes were identified (the first one is conditioned by interconversion of complex enantiomeric forms and pseudorotation of a macrocycle molecule upon the C_2 symmetry axis; the second one is conditioned by macrocycle molecule inversion). Application of exchange spectroscopy (2D-EXSY) of DNMR for investigation of this dynamic system (**II**−**IV**) simplifies the assignment of the NMR signals and represents the first experimental study of multisite exchange. In the present work, the methodology of paramagnetic 4f (Ce, Pr, and Nd) probe applications for the study of free-energy, enthalpy, and entropy changes in chemical exchange processes, as well as the advantages of this method in a comparison with DNMR studies of diamagnetic substances, is discussed. In particular, as a result of paramagnetic chemical shifts in 4f complexes, the range of measurable rate constants expands considerably compared to the analogous range in diamagnetic compounds. Coordination compounds investigated in the paper represent new types of thermometric NMR sensors and lanthanide paramagnetic probes for in situ temperature control in solution.

1. INTRODUCTION

During the last decades, an increase in the number of publications devoted to the molecular structure and to the dynamics of the rare-earth coordination compounds has been observed.[1−11] The information about the molecular structure and the dynamics of the rare-earth coordination compounds in solutions underlies the existing technologies for photoresist production in microelectronics, sensitizers for photodynamic therapy, contrast reagents for magnetic resonance imaging (MRI), synthetic models of natural ionofores, and sensors for biology and medicine. Studies of the paramagnetic chemical shifts in NMR spectra allow us to gain qualitative and quantitative information about the molecular structure as well as the kinetic and thermodynamic stability of paramagnetic complexes in solutions.[11−23]

Recently, the growth of interest in studies of lanthanide (Ln) cations with macrocyclic ligands [in particular with macrocyclic polyethers (MCPEs)][11,12] has been noticed. MCPEs are promising as extractants and NMR analytical reagents and are regarded by many researchers as model compounds for natural ionophores.[11] The lanthanide salt complexes of the cerium subgroup with 18-membered MCPEs are compounds for which the possibility of forming saturated 12-coordinated inclusion complexes of the lanthanides has been found.[1−4,11] Presently, the thermodynamic, structural, and electronic properties of 18-membered macrocyclic ether complexes with the Ln cations are well-known both in solution and in the solid state.[3−9] In particular, studies of the lanthanide-induced shift (LIS) values revealed that the structure of complex [Pr(18-crown-6)-$(NO_3)_3$)] (**III**) in solution is similar to that reported for the [La(18-crown-6)$(NO_3)_3$] complex (**I**) in the crystal state.[4,10−12] On the other hand, the paramagnetic properties, the complex formation thermodynamics, and the conformation dynamics of these complexes in solution have been studied insufficiently.[2,5,6,10−12] The investigation of the dynamic properties of these complexes represents an interesting area in chemistry of the inclusion compounds and attracts the interest of researchers.[6,10−12] Although we reported the proposed model of conformational dynamics in **III** (Ln = Pr),[10,11] the applicability of this model to the complexes of other Ln cations has not been verified yet. In the present work,

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the structure of the kinetically stable complexes [Ln(18-crown-6)$(NO_3)_3$] in $CDCl_3$ and CD_2Cl_2 solutions is investigated by ^1H NMR [where Ln = La, Ce (**II**) and Nd (**IV**)]. The molecular dynamics of the complexes **II**−**IV** is studied in detail by ^1H dynamic NMR (DNMR) spectroscopy, and the results found are discussed. It has been found that the dynamics was conditioned by two dynamic processes. The first one with the activation free energy $\Delta G^{\ddagger} \approx 30$ kJ/mol is caused by interconversion of the complex enantiomeric forms and pseudorotation of the macrocycle molecule upon the C_2 symmetry axis. The second one with $\Delta G^{\ddagger} \approx 50$ kJ/mol is conditioned by macrocycle molecule inversion. The nature of the dynamics is very similar to the moving of the electric ray fins. It should be noted that an investigation of this kind is of interest both for coordination chemistry and for organic chemistry because pseudorotation of the 18-crown-6 molecule studied in detail in this paper represents a first experimental investigation of an effective multisite (concretely six-site) exchange by 2D-EXSY.

In the past several years, many excellent original papers and reviews have appeared. In these works, more precise definitions to the aspects of paramagnetic lanthanide contrast agent structure and solution dynamics,[1−9,23] biomedical[11,23] and NMR applications,[22,31] complex design features,[23] thermodynamic aspects of complex formation,[11,23,29,31−35] and the diagnostic and therapeutic uses of lanthanide texaphyrin, crown ethers, and porphyrin complexes[23] have been presented. In the review[23] dedicated to the analysis of NMR investigation results in the field of intramolecular chemical exchange (CE) processes for lanthanide complexes in aqueous solution, the numerous examples of conformational dynamics studies in diamagnetic lanthanum complexes were considered in detail. The kinetics data were obtained initially by using the complete NMR line-shape analysis method. There were only a few examples of dynamics studies in paramagnetic lanthanide complexes (in aqueous solution), with the initial kinetics data being obtained by using the exchange spectroscopy (EXSY) for two-site nuclear exchange.[11,23,36] At the same time, we did not find in the literature examples of the EXSY investigation of the multisite nuclear exchange in paramagnetic lanthanide complexes in nonaqueous solution. Moreover, such methods as line-shape analysis, which takes into account temperature variation of the LIS, and the EXSY method of studying the paramagnetic lanthanide complexes with MCPE and other ligands in nonaqueous solutions have not been systematically discussed yet.

We solve the problem of the substrate molecule intramolecular dynamics study with the help of the paramagnetic probe application. It is used for studying the conformational dynamics of such polydentate complex reagents as crown ethers in nonaqueous solutions. In the present work, the advantages of this approach's application for paramagnetic complexes are briefly discussed in comparison with DNMR studies of the diamagnetic substances. In particular, the relative ranges of the CE rate constants to be measured are considered. As a result of paramagnetic chemical shifts in 4f complexes, the range of measurable rate constants expands considerably compared to the analogous range in the diamagnetic compounds.

It is known that Fermi contact contributions to LIS are proportional to $1/T$ (Curie's law), and in a theoretical paper by Bleaney, it was predicted that pseudocontact contributions to LIS should be proportional to $1/T^2$. Concerning experimental investigations, some of them confirmed the $1/T^2$ dependence (nevertheless, in many cases, there was no control of the thermodynamic and kinetic stability of complexes), but some of them did not confirm such a dependence. We support the viewpoint[21] that the temperature relationship of LIS depends heavily on higher-order states, but for practical purposes, the experimental dependence in the working range from 200 to 350K is adequately described by the Curie−Weiss approximation:[11,34]

$$\delta_{\mathrm{LIS}} = a + b/T \tag{1}$$

One can use this substantial temperature relationship of LIS in practice. Recently, we suggested applying the paramagnetic lanthanide complexes with polydentate ligands as thermometric NMR sensors[35] for in situ temperature determination in solution and MRI diagnostics. Coordination compounds investigated in the paper represent the new types of thermometric NMR sensors and lanthanide paramagnetic probes for in situ temperature control in solution.

2. EXPERIMENTAL SECTION

Complexes **I**−**IV** were prepared by methods similar to those in refs 1, 2, and 11. The ^1H and ^{13}C NMR spectra were recorded by Bruker DPX-200, MSL-300, and Avance-III-500 spectrometers (with ^1H operating frequencies of 200, 300, and 500 MHz, respectively). Solutions were 0.01 M in $CDCl_3$ and CD_2Cl_2 for NMR spectroscopy with a tetramethylsilane (TMS) internal standard. The solution temperature was controlled by using a Bruker B-VT 1000 temperature controller (MSL-300). Fourier-transformed spectra were subjected to complete line-shape analysis[11,19,34] on a personal computer (Windows-XP) to obtain rate data for complexes **II**−**IV**. Temperature calibration was carried out using ethylene glycol and methanol samples.

The isotropic LISs (δ_{LIS}) in NMR spectra on ligand nuclei and resulting from association of the ligand with the paramagnetic cation were expressed as the sum of diamagnetic shifts (δ^{dia}) and paramagnetic shifts ($\delta^{\mathrm{para}}_{\mathrm{calc}}$):[11,20,21,34]

$$\delta_{\mathrm{LIS}} = \delta^{\mathrm{dia}} + \delta^{\mathrm{para}}_{\mathrm{calc}} \tag{2}$$

The paramagnetic shifts were expressed as the sum of pseudocontact contributions (δ_{PC}) and Fermi contact contributions (δ_{FC}) by the equality

$$\delta^{\mathrm{para}}_{\mathrm{calc}} = \delta_{\mathrm{PC}} + \delta_{\mathrm{FC}} \tag{3}$$

The pseudocontact contributions to the LIS were calculated from eq 3:[11,21]

$$\begin{aligned}\delta_{\mathrm{PC}} = 10^{30}[(\chi_Z - \chi_{\mathrm{av}})\left\langle(3\cos^2\theta - 1)/r^3\right\rangle \\ + (\chi_X - \chi_Y)\left\langle\sin^2\theta\cos 2\phi/r^3\right\rangle]/2N_A\end{aligned} \tag{4}$$

where δ_{PC} is expressed in ppm, r in Å, and χ_i in cgs units. The Fermi contact contributions to the LIS were expressed as[11,18,20,21,30,33]

$$\delta_{\mathrm{FC}} = \frac{2\pi\beta}{3kT\gamma}\frac{A}{h}\langle S_z\rangle = F\langle S_z\rangle \tag{5}$$

where β is the Bohr magneton, k is the Boltzmann constant, γ is the gyromagnetic ratio, A/h is the hyperfine coupling constant in frequency units, F is a metal-independent parameter of each nucleus for a series of isostructural complexes, and S_z is the electron-spin expectation value, which has been tabulated for each Ln ion.

In the calculation of the paramagnetic LISs of **II**−**IV** at low temperature, the Fermi contact contributions were neglected compared to pseudocontact contributions (because of the predicted domination of pseudocontact contributions).[5,11,12,20,31,32] The diamagnetic contributions to the LISs were allowed for by means of the diamagnetic lanthanum complexes.[5,11,21,31,32] The values of $\chi_Z - \chi_{\mathrm{av}}$, $\chi_X - \chi_Y$, and α were treated as parameters and were fit using eq 5 to the observed shift values ($\delta_{\text{obs}}^{\text{para}}$) for protons of the CH_2 groups using values of r, φ, and θ for the atomic coordinates that were obtained from the X-ray structure[2] of solid $[La(NO_3)_3(18\text{-crown-}6)]$:[5,10,11,21,31,32]

$$\mathrm{AF} = \left[\sum w_i(\delta_{\text{calc}}^{\text{para}} - \delta_{\text{obs}}^{\text{para}})^2 / \sum w_i(\delta_{\text{obs}}^{\text{para}})^2 \right]^{0.5} \tag{6}$$

where w_i are the reciprocals of squares of the experimental errors. A procedure of the so-called "permutation of the pseudocontact shifts" was used for assignment of the peaks in the spectrum to their respective atoms.[17,32]

The rate constants of the intramolecular dynamics were evaluated by the complete band-shape method[19] for a multisite exchange:[4,10,11]

$$V(\nu) = \mathrm{Im} - [iC_0\mathbf{I}(i2\pi\nu\mathbf{E}_n - i\mathbf{\Omega} + \mathbf{R} + \mathbf{X})^{-1}\mathbf{P}] \tag{7}$$

Here $\mathbf{\Omega}$ and $\mathbf{R}$ are diagonal matrices (of the dimensions $n = 12$) with elements $w_i = 2\pi\nu_i$ and T_{2i}^{-1}, respectively, and $\mathbf{X}$ is the exchange matrix. $\mathbf{P}$ is a column vector of the fractional populations. The temperature dependence of the LIS was taken into account by extrapolation[19] of the low-temperature dependence to the intermediate- and fast-exchange regions according to the Curie−Weiss law.[11,21,32] We have taken into account the temperature dependence of LISs by applying the Curie−Weiss approximation[11,21,32] during examination of the NMR signal shape temperature dependence. As can be seen in Figure 1, experimental LIS values are well approximated by the linear dependence on $1/T$, and on the diagram, the average values for a_1, a_2, ..., f_2 protons correspond to the $-CH_2-$ groups. Required for NMR signal shape analysis, LIS values of a_1, a_2, ..., f_2 proton signals "without exchange" in the cases of intermediate and fast exchange (NMR time scaling[32]) were calculated as

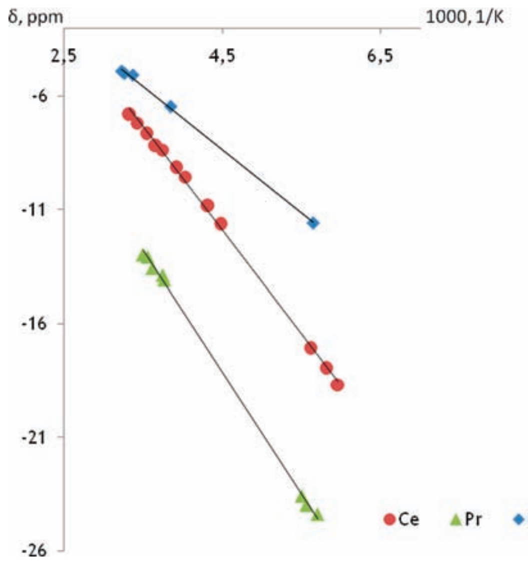

Figure 1. Temperature dependence of the average paramagnetic LISs in 500 MHz ^{1}H NMR spectra of $[Ln(18\text{-crown-}6)(NO_3)_3]$, with CD_2Cl_2 as the solvent [here Ln = Ce (●), Pr (Δ), and Nd (◇)].

$$\Delta\delta_i(T) = \Delta\delta_i(T_0)\ (1/T + A)/(1/T_0 + A) \tag{8}$$

where A is a constant defined by analysis of the average LIS value for the $-CH_2-$ groups and $T_0 = 179$ K.

Typical pulse sequence D1-P1-D0$_1$-P1-D9-P1-D0$_2$-FID was used to carry out the EXSY experiments (here D1 is the relaxation delay, D0$_1$ and D0$_2$ are incrementable delays, P1 is a 90° transmitter pulse, and D9 is the mixing time).

^{1}H NMR Spectral Data. $[Ce(18\text{-crown-}6)(NO_3)_3]$. δ_H (ppm, CD_2Cl_2, 179 K): −18.93 (a_1, 1H, s), −20.17 (a_2, 1H, s), −1.9 (b_1, 1H, s), −24.63 (b_2, 1H, s), −1.7 (c_1, 1H, s), −19.48 (c_2, 1H, s), −18.29 (d_1, 1H, s), −34.75 (d_2, 1H, s), −8.22 (e_1, 1H, s), −28.63 (e_2, 1H, s), 3.79 (f_1, 1H, s), −9.04 (f_2, 1H, s).

$[Pr(18\text{-crown-}6)(NO_3)_3]$. δ_H (CD_2Cl_2, ppm, 179 K): −25.9 (a_1, 1H, s), −28.1 (a_2, 1H, s), −12.2 (b_1, 1H, s), −39.04 (b_2, 1H, s), −9.62 (c_1, 1H, s), −27.6 (c_2, 1H, s), −22.5 (d_1, 1H, s), −51.0 (d_2, 1H, s), −13.4 (e_1, 1H, s), −45.0 (e_2, 1H, s), −0.4 (f_1, 1H, s), −22.3 (f_2, 1H, s).

$[Nd(18\text{-crown-}6)(NO_3)_3]$. δ_H (CD_2Cl_2, ppm, 177 K): −10.26 (a_1, 1H, s), −12.63 (a_2, 1H, s), 4.2 (b_1, 1H, s), −13.32 (b_2, 1H, s), 4.3 (c_1, 1H, s), −11.49 (c_2, 1H, s), −5.42 (d_1, 1H, s), −26.64 (d_2, 1H, s), −1.5 (e_1, 1H, s), −16.61 (e_2, 1H, s), 5.88 (f_1, 1H, s), −2.7 (f_2, 1H, s).

$[Nd(18\text{-crown-}6)(NO_3)_2]^+$ $[NO_3]^-$. δ_H (CD_2Cl_2, ppm, 260 K): 41.

3. RESULTS AND DISCUSSION

Molecular Dynamics. The ^{1}H NMR line-shape analysis technique (which takes into account the temperature variation of LIS) was employed for the detailed analysis of an effective six-site proton exchange caused by the intramolecular dynamics of lanthanide complexes with 18-membered MCPEs with saturated coordination.[11,34] We have investigated the band shape of the zero-order ^{1}H NMR spectra of **II**−**IV** over a wide temperature range (T = 179−310 K) in order to evaluate the magnitude of the activation free energy of the degenerate molecular dynamics of $[Ln(18\text{-crown-}6)(NO_3)_3]$ and to compare the thermodynamic parameters of molecular dynamics processes within the lanthanide series (Figure 2).

In the ^{1}H NMR spectrum of complex **II** at low temperature (179 K, Figure 2), there are 12 signals corresponding to the protons of the CH_2 groups. Two step increases of effective symmetry of the spin system were observed upon heating. Two signals were observed at 275 K (an effective C_{6v} symmetry appears due to the dynamic process of the first type). Finally, a single signal was found at higher temperature [an additional plane of effective symmetry perpendicular to the C_2 symmetry axis (Figure 3 and the Supporting Information) appeared at 310 K]. Two types of molecular dynamics processes were found for $[Ln(18\text{-crown-}6)(NO_3)_3]$ complexes; the dynamic system of these complexes was characterized by 12 structural forms (Figures 3 and 4).[11] The first type of dynamics was due to mutual interconversion of the enantiomeric forms of the complexes and pseudorotation of the 18-crown-6 molecule about the C_2 symmetry axis. The activation free energies [$\Delta G^{\ddagger}(210\text{ K})$] established for the first type of dynamics (first-order reaction) at 210 K are 28 ± 4, 39 ± 5, and 33 ± 4 kJ/mol for **II**−**IV**, respectively (Figures 5 and 6). The second type is due to the cooperative ring inversion of the MCPE molecule. The activation free energies [$\Delta G^{\ddagger}(310\text{ K})$, second-order reaction] appear to be 58 ± 6, 49 ± 6, and 45 ± 5 kJ/mol for **II**−**IV**, respectively. For this dynamic system, interconversion of the enantiomers was accompanied by the exchange of proton sites, which are marked in Figure 3 as a_1, a_2, ..., f_2. For example, the permutations of methylene protons a_1', a_2', b_1', and b_2' between the set of sites a_1, a_2, b_1, and b_2 and the set of sites f_1, f_2, e_1, and e_2 are shown in Figure 3.

Interconversion of the enantiomers and pseudorotation of macrocycle molecules about the C_2 symmetry axis (dynamic process of the first type) lead to chemical exchange between molecular forms S_1, S_2, S_3, S_4, S_5, and S_6 (see Figure 4). Labeling of the proton sites a_1, a_2, ..., f_2 is omitted in Figure 4. The proposed kinetic scheme of the reactions can be presented as

$$S_i \xrightarrow{k_1} S^* \xrightarrow{k_1'} S_k \tag{9}$$

where i, k = 1−6 and S^* is a transition state. Thus, the intramolecular dynamics of the first type causes effective exchange

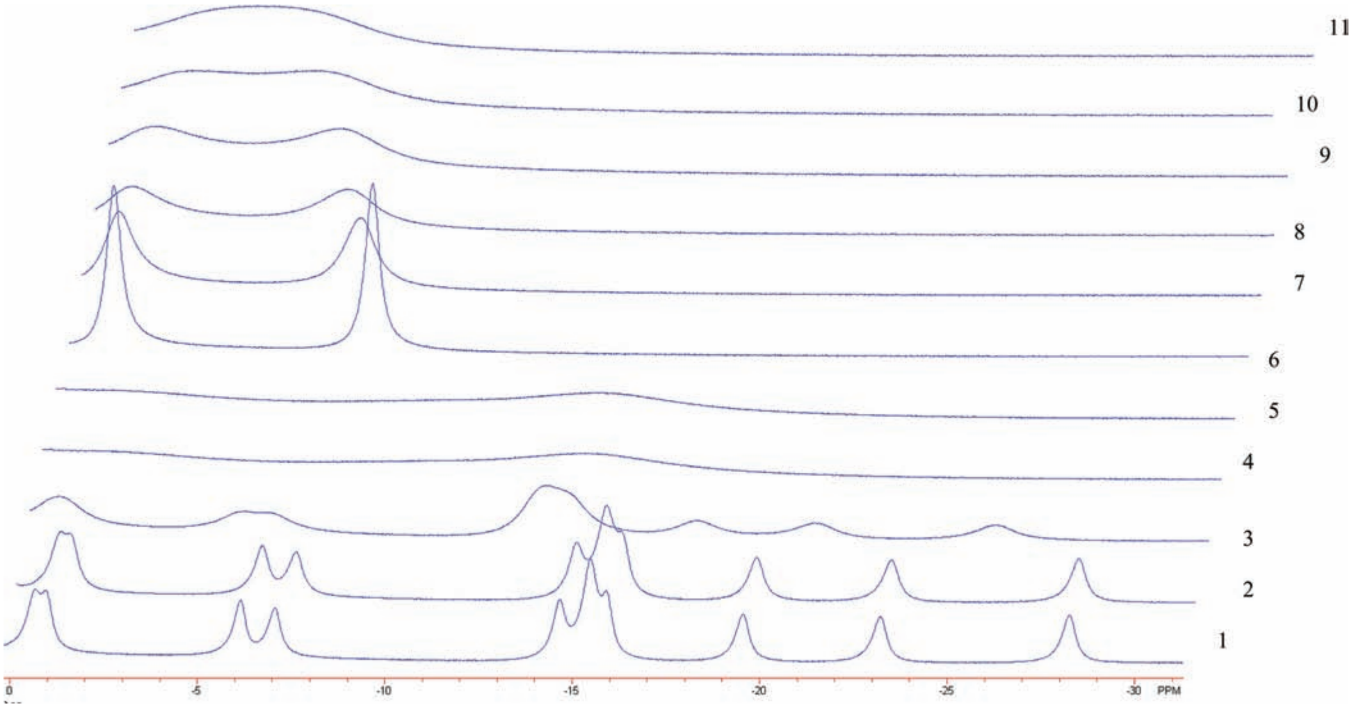

Figure 2. Variable temperature dependence of 500 MHz ^{1}H NMR spectra of [Ce(18-crown-6)(NO_3)$_3$] in CD_2Cl_2; chemical shift values are relative to TMS (δ scale); at temperatures 179.1 K (1), 181.4 K (2), 188.1 K (3), 210 K (4), 270 K (5), 275.7 K (6), 287.2 K (7), 297 K (8), 302.1 K (9), 307.3 K (10), and 310 K (11).

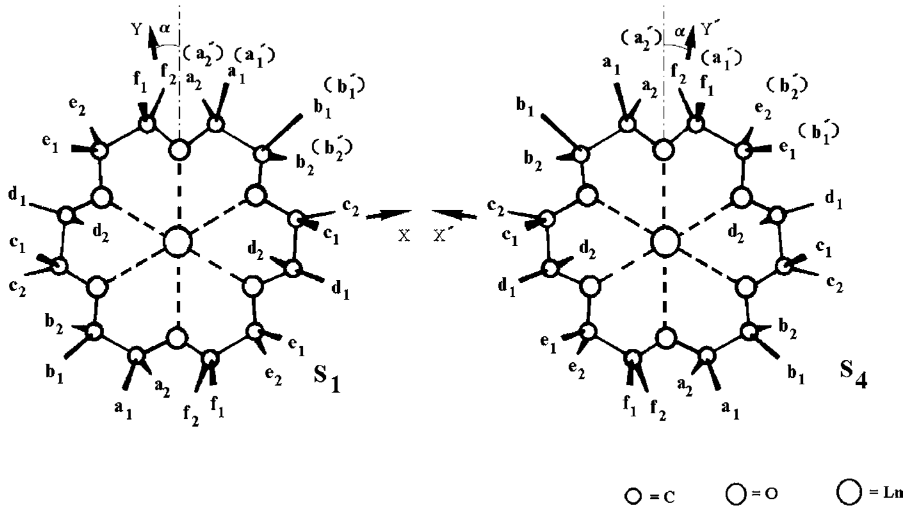

Figure 3. Detailed scheme of enantiomeric isomer (S_1 and S_4) interconversion in the [Ln(18-crown-6)(NO_3)$_3$] dynamic system; here coordination bonds are denoted by dashed lines and NO_3 groups are omitted (the plane perpendicular to the C_2 axis of symmetry).

between sites within the following two groupes: a_1, b_1, c_1, d_1, e_1, and f_1 (exo sites) and a_2, b_2, c_2, d_2, e_2, and f_2 (endo sites).

^{1}H NMR signals corresponding to endo and exo protons are broadened with rising temperature, which is consistent with 18-crown-6 molecule inversion (see Figure 2, spectrum obtained at 287 K compared to that found at 275 K). The kinetic scheme of the reactions can be presented as

$$S_n + [\mathrm{Ln(NO_3)_3}] \overset{k_2}{\rightarrow} [\mathrm{Ln(NO_3)_4}]^-[\mathrm{Ln(NO_3)_2(18\text{-}crown\text{-}6)}]^+ \xrightarrow{k_2^{©}} S_j + [\mathrm{Ln(NO_3)_3}] \quad (10)$$

If n = 1−6, then j = 7−12, and if n = 7−12, then j = 1−6.

In order to obtain further support for the molecular dynamics of complexes **II**−**IV** and the assignment of NMR signals obtained by calculating LIS, we have investigated complexes using 2D-EXSY (Figure 7). In Figure 7, the 2D-EXSY spectrum of **III** in CD_2Cl_2 is shown. Only five well-defined cross signals are observed for each site of the C−H proton of crown ether. We should note that the exchange within the two groups of signals experimentally found by 2D-EXSY clearly confirms the used model of dynamic processes in the [Ln(18-crown-6)(NO_3)$_3$] system.

Discussing the obtained values of the activation enthalpy for 18-crown-6 molecular dynamics in the complexes under investigation, we have to note the following. The discovered

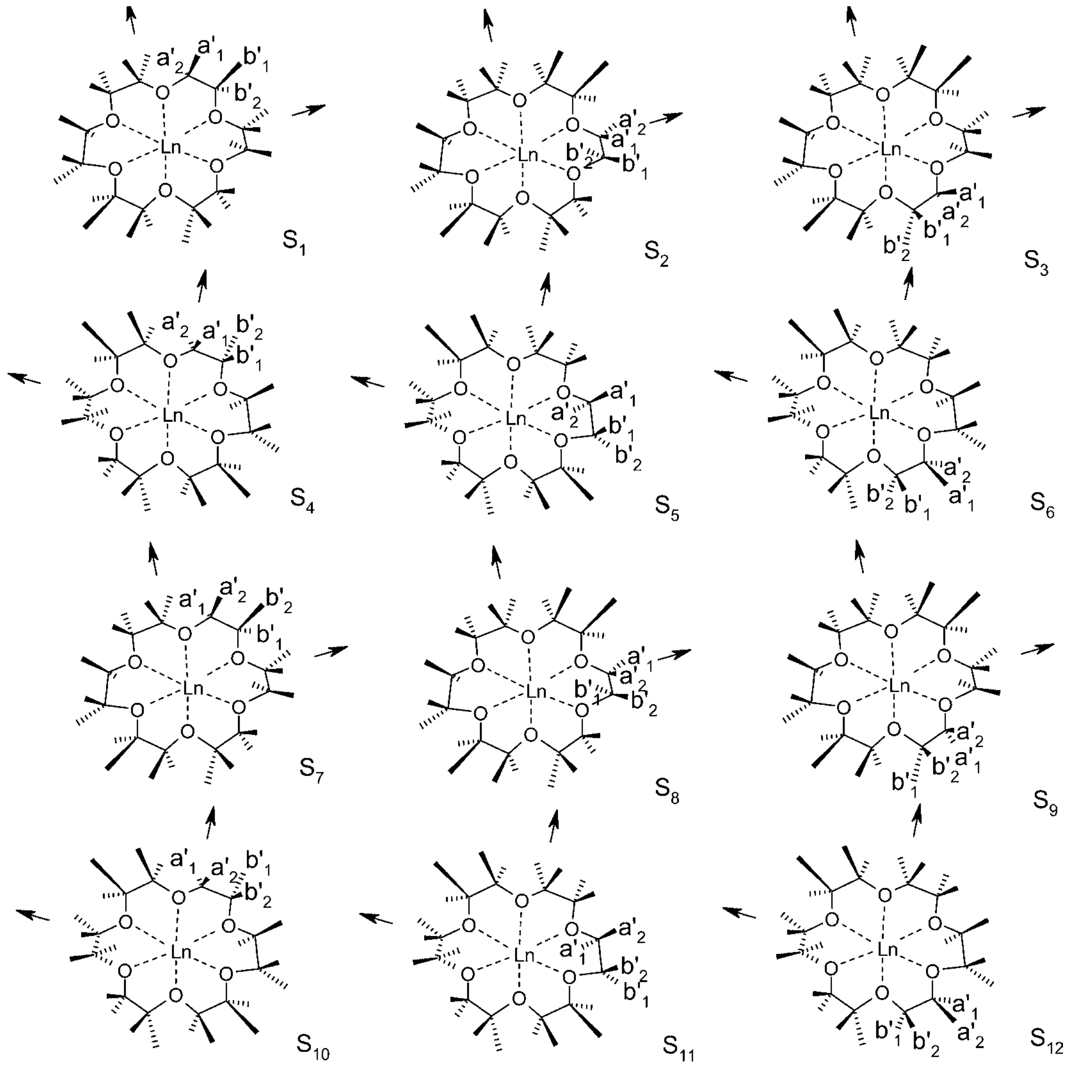

Figure 4. Structure forms of the [Ln(18-crown-6)$(NO_3)_3$] dynamic system.

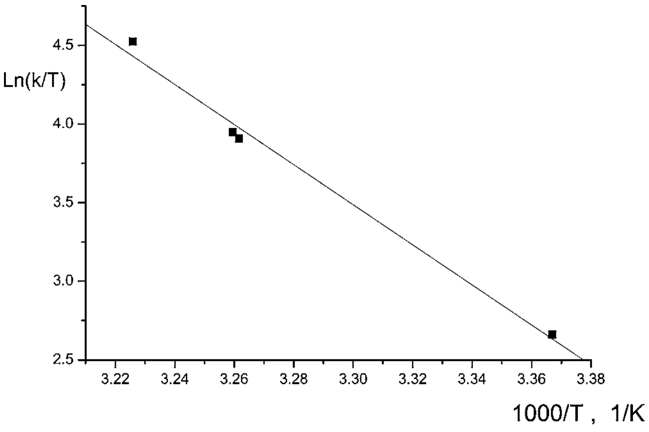

Figure 5. Dependence of ln(k/T) on $1/T$, where k is the rate constant of the 18-crown-6 molecular dynamic process of the first type in [Nd(18-crown-6)$(NO_3)_3$], T is the temperature, and CD_2Cl_2 as the solvent.

magnitude of the activation enthalpy of the first type is commensurable with the values of the energetic barriers of conformational transitions in 18-membered MCPE molecules ($\Delta H^{\ddagger}$ = 22 kJ/mol) and their alkali complexes[25] and in

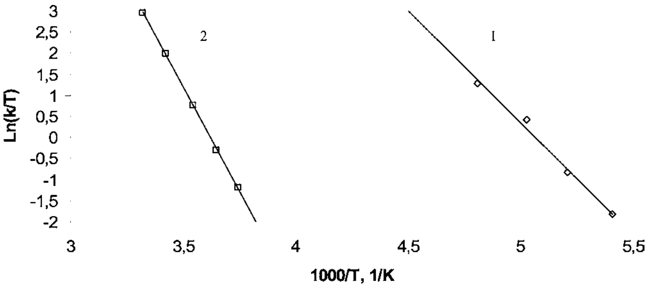

Figure 6. Dependence of ln(k/T) on $1/T$ for the first (1) and second (2) types of molecular dynamics in [Ce(18-crown-6)$(NO_3)_3$] complexes (where k is the rate constant); solvent 8:1 (v/v) $CD_2Cl_2/CDCl_3$.

[Pr(diaza-18-crown-6)$(NO_3)_3$].[32] A monotonic decrease of the free energy of the ring inversion of the MCPE molecule along the series of lanthanide [Ln(18-crown-6)$(NO_3)_3$] complexes may be related to the ionic radius decrease along the series of lanthanide metals, known as the "lanthanide contraction".

The concentration of **II–IV** appeared to have no influence on the rate constant of the first type of molecular dynamics (studied between 10^{-3} and 1.2 × 10^{-2} mol/dm^3), i.e., interconversion of the enantiomeric forms and pseudorotation

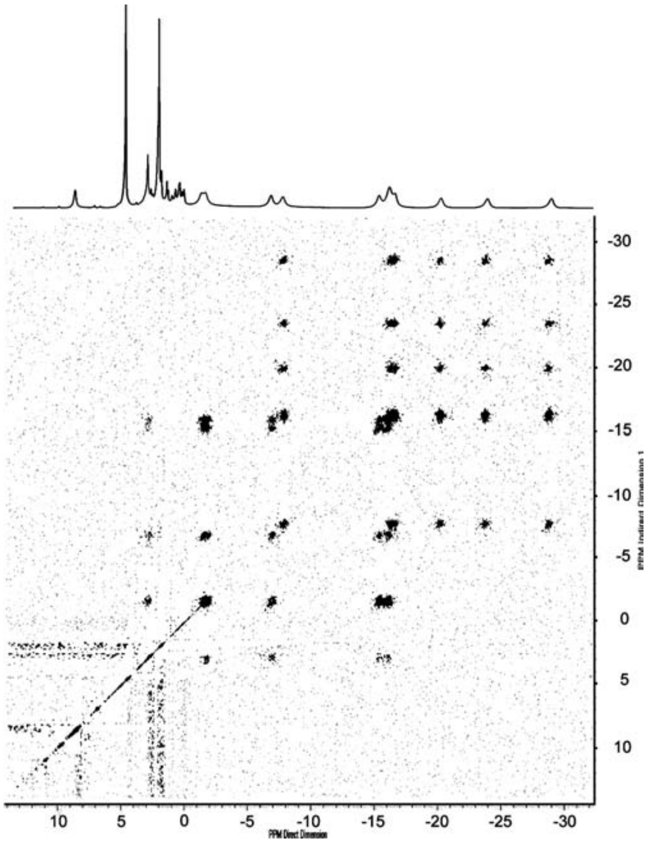

Figure 7. 500 MHz ^1H 2D-EXSY spectrum of the [Ce(18-crown-6)(NO_3)$_3$] in solvent 8:1 (v/v) CD_2Cl_2/$CDCl_3$ at temperature 179 K; chemical shifts values are relative to TMS.

of the macrocycle molecule upon the C_2 symmetry axis of investigated complexes are obviously a first-order reaction. It was found experimentally that the rate constant of the dynamic process of the second type decreases with a decrease of the concentration of the complexes.

The intramolecular dynamics in the macrocyclic molecule investigation results may be relevant for understanding some of their other physicochemical properties, for example, reactivity, volatility, reaction mechanism, etc.

Paramagnetic Probes Based on 4f Elements for Dynamic NMR. The following peculiarity of using DNMR for studies of the paramagnetic compounds of 4f elements deserves special attention. The range of measurable paramagnetic LISs is known to be larger than 100 ppm.[11] For example, the ranges of LISs, $\Delta\delta_{\mathrm{LIS}}$, for protons of [Pr(18-crown-6)] (NO_3)$_3$] and [Pr(diaza-18-crown-6)] (NO_3)$_3$][11,12,34] are 50 and 135 ppm at 179 K, respectively. Moreover, the ranges of LISs, $\Delta\delta_{\mathrm{LIS}}$, of [Pr(18-crown-6)(ptfa)$_2$]$^+$[11,12,34] and [Tm(12-crown-4)(ClO_4)$_3$][11,34] complexes are 99 and 215 ppm at ambient temperature, respectively.

As a result of paramagnetic chemical shifts in 4f complexes, the range of measurable rate constants expands considerably compared to the analogous range in diamagnetic compounds. This may be illustrated by reference to a degenerate two-site exchange. For an instrument with an operating frequency for protons of 500 MHz and assuming a value of $\delta\nu = 5 \times 10^4$ Hz corresponding to 100 ppm in paramagnetic compounds and having an error of half-width determination of ~1 Hz, the largest value of a rate constant that can be measured is $k_{\max} \sim 3 \times 10^9$ Hz. This value is much larger than the value ~3×10^7 Hz measurable in diamagnetic compounds ($\delta\nu \sim 3 \times 10^3$ Hz). The lower bound of the range of rate constant measurement is $k_{\min} \sim 1$ Hz. Thus, using the paramagnetic probe method for investigation of the intramolecular dynamics of ligands coordinated to this metal cation is equivalent to using a NMR spectrometer with an operating frequency of 5 GHz, which is unavailable for present commercial instruments. Therefore, the potential of this method in the study of the structure and intramolecular dynamics of various ligand complexes with paramagnetic metal cations is higher than that in the case of complexes with diamagnetic cations.

Of course, the field of application of the NMR-based methods of CE studies will not be limited by the investigations of presented macroheterocycles. In the near future, these techniques will possibly be used in the study of complexes of paramagnetic cations with phthalocyanines, calixarenes, and many other classes of chemical compounds.

Temperature Dependence of Paramagnetic LIS and Thermometric NMR Sensors. Analysis of the temperature dependence of paramagnetic LISs of **II** in Figure 1 shows that it is substantial and well approximated by a linear anamorphose of the inverse temperature value (1/*T*) (like for [Ln(18-crown-6)(ptfa)$_2$]$^+$,[11,12,14,34] [Ln(diaza-18-crown-6)(NO_3)$_3$],[11,32,34] [Ln(EDTA)],[35] and [LnH(oep)(tpp)],[11,29] where ptfa is 1,1,1-trifluoro-5,5-dimethyl-2,4-hexanedione, tpp is tetraphenylporphyrin, and oep is octaethylporphyrin). We propose to use this temperature dependence of paramagnetic LISs in NMR spectra to detect the temperatures of the samples placed directly in an NMR spectrometer in both aqueous and nonaqueous media.[35] Complexes **II**–**IV** can be in particular the most promising subnanoscale NMR spectroscopic probes to determine the temperature in nonaqueous media. These effects are prospective for applications (of Ln complexes) as thermometric NMR sensors directly in reaction media (for in situ studies of exothermic or endothermic processes) and also in medical magnetic resonance tomography for in vivo three-dimensional mapping of the body-temperature distribution and the temperature of different body parts in diseases, including some related to cancer.[35]

4. CONCLUSION

The results of the present work demonstrate that there are two types of conformational dynamic processes in [Ln(18-crown-6)(NO_3)$_3$] complexes (the first one with the activation free energy $\Delta G^{\ddagger} \approx 30$ kJ/mol is conditioned by interconversion of the complex enantiomeric forms and pseudorotation of the macrocycle molecule upon the C_2 symmetry axis; the second one with $\Delta G^{\ddagger} \approx 50$ kJ/mol is conditioned by macrocycle molecule inversion, where Ln = La, Ce, Pr, and Nd). The [Ln(18-crown-6)(NO_3)$_3$] complexes represent a model system of the effective multisite exchange for the dynamic NMR. These complexes are promising subnanoscale NMR spectroscopic probes to determine the temperature in nonaqueous media.

Paramagnetic 4f metal cations may be considered as adjustable probes for the study of the dynamic processes occurring in substrate molecules, which can form complexes with these cations in solution. This paramagnetic probe provides an extension of the range of values of the rate constants for CE in comparison with dynamic NMR application to diamagnetic substances. The following two dynamic NMR techniques are distinguished for effective investigation of intramolecular dynamics in substrate molecules: line-shape analysis, taking into account the temperature dependence of the paramagnetic chemical shift, and exchange spectroscopy.

Of course, the field of application of the NMR-based methods of CE studies will not be limited to investigation of the presented macroheterocycles. In the near future, these techniques will possibly be used in studies of complexes of paramagnetic cations with phthalocyanines, calixarenes, anthraquinones, stilbene derivatives, indigoids, photosensitive styryl dyes, and of many other classes of chemical compounds (in particular, such biomacromolecules as RNA and DNA).

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Molecular structure of the [Ln(18-crown-6)(NO_3)$_3$] complexes. This material is available free of charge via the Internet at http://pubs.acs.org.

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