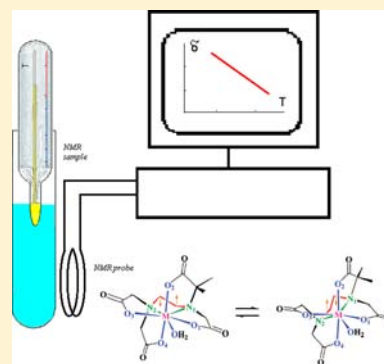


# Lanthanides as NMR Probes of Fast Molecular Dynamics at High Magnetic Fields and Temperature Sensors: Conformational Interconversion of Erbium Ethylenediaminetetraacetate Complexes

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**ABSTRACT:**  $^1\text{H}$  NMR measurements are reported for  $\text{D}_2\text{O}$  solutions of paramagnetic complex  $[\text{Er}(\text{H}_2\text{O})(\text{EDTA}^{4-})]^-$  (I) for temperature interval 273–319 K. Diamagnetic complex  $[\text{Lu}(\text{H}_2\text{O})(\text{EDTA}^{4-})]^-$  (II) was used as an NMR reference compound. The spectra obtained have been analyzed using a band-shape analysis technique in the framework of dynamic NMR (DNMR) taking into account the temperature dependence of lanthanide-induced shifts. Intramolecular dynamics in I was assigned to the interconversion of  $\Delta\text{-}\lambda_{\text{E}}\text{-}\delta\delta\delta\delta$  and  $\Delta\text{-}\delta_{\text{E}}\text{-}\delta\delta\delta\delta$  conformers with estimated activation free energy  $\Delta G^\ddagger(298\text{ K}) = 50 \pm 4\text{ kJ/mol}$ . The methodology of paramagnetic 4f-element probe applications on the example of  $\text{Er}^{3+}$  for the study of free-energy changes in chemical exchange processes, as well as the advantages of this method in comparison with DNMR studies of diamagnetic substances, is discussed. In accordance with the literature reviewed, the fulfilled experimental study is the first example of intramolecular dynamics determination for erbium complexes. An additional advantage of the investigation is in the approach proposed which extends the range of measurement of the NMR rate constants for paramagnetic 4f-element complexes compared to diamagnetic ones. Coordination compounds investigated represent a new type of thermometric NMR sensors and lanthanide paramagnetic probes for *in situ* temperature control in solutions.



## INTRODUCTION

Currently, the number of publications concerned with NMR investigation of the molecular structure and dynamics of rare-earth coordination compounds is constantly increasing.<sup>1–6</sup> One of the reasons for that is due to the fact that the information on the molecular structure and dynamics of rare-earth coordination compounds in solutions underlies the existing technologies for the production of photoresists in microelectronics, sensitizers for photodynamic therapy, contrast reagents for magnetic resonance imaging (MRI), synthetic models of natural ionophores, and sensors for biology and medicine.<sup>7–10</sup>

Dynamic NMR (DNMR) is known to be a routine tool for the investigation of chemical exchange (CE) processes.<sup>1,9–11</sup> The DNMR method is a useful tool for the investigation of CE kinetics in thermodynamic equilibrium.<sup>1,5,9–15</sup> Peculiarities and advantages of DNMR in application for paramagnetic lanthanide complexes in comparison with other physicochemical techniques are discussed in details in refs 9 and 14.

In the literature reviewed, among the objects for NMR researches, lanthanide (Ln) complexes with aminopolycarboxylate ligands, in particular with DOTA, diethylenetriaminepentaacetic acid (DTPA), and ethylenediaminetetraacetate anions ( $\text{EDTA}^{4-}$ ), are cited frequently.<sup>1,5,9,14,16</sup> Mainly, it is because of the application of aminopolycarboxylate ligands that gadolinium complexes are used as MRI contrast relaxation reagents.<sup>1,2,6–9,17–23</sup> EDTA complexes of lanthanides can also be considered as models for MRI contrast agents. Besides, EDTA is an important chelating agent widely used in

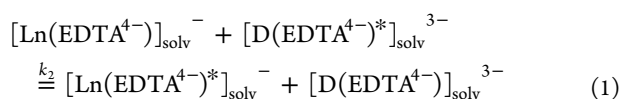
complexometric titrations. Metal chelation is also used therapeutically to treat lead and mercury poisoning. EDTA is applied in the food industry, in soap boiling, etc. Although knowledge of EDTA metal complex structures and applications of EDTA is gained in undergraduate general and analytical chemistry courses, little about the intramolecular CE processes of EDTA paramagnetic lanthanide complexes is introduced.

Water molecule intermolecular exchange at six-coordinate paramagnetic  $3d\text{ M}^{3+}$  or  $M^{2+}$  centers bound to a EDTA-like ligands has been investigated by  $^{17}\text{O}$  NMR measurements.<sup>24,25</sup> Intermolecular process kinetics in aqueous and organic solutions of lanthanide complexes were studied by spectrophotometric<sup>26</sup> and NMR methods.<sup>26–28</sup> Some  $\beta$ -diketonate complexes of paramagnetic lanthanides were proposed as NMR lanthanide paramagnetic shift reagents (LSRs) for organic media.<sup>27,28</sup>  $[\text{Ln}(\text{EDTA}^{4-})]^-$  complexes were employed as LSRs for aqueous media.<sup>27</sup> Peculiarities of NMR applications for the investigation of lanthanide complexes as LSRs and paramagnetic relaxation reagents are discussed in detail in refs 9 and 10. Earlier first attempts to measure  $[\text{Ln}(\text{EDTA}^{4-})]^-$  complexes (where  $\text{Ln} = \text{La}^{3+}, \text{Lu}^{3+}$ ) dissociation rate constants in aqueous solutions were made in refs 26 and 27. Concurrent processes in multicomponent systems containing Ln-Cu-EDTA-Cl were investigated.<sup>26,27</sup> Recently,<sup>29–32</sup> EDTA intermolecular CE processes for  $[\text{Ln}(\text{EDTA}^{4-})]^-$  complexes (where

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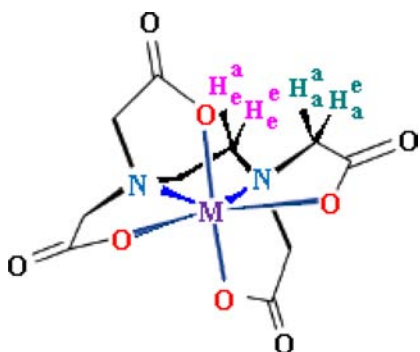
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$\text{Ln} = \text{Tb}^{3+}, \text{Ho}^{3+}, \text{Tm}^{3+}, \text{Yb}^{3+}, \text{and } \text{Lu}^{3+}$ ) have been analyzed by us using  $^1\text{H}$  NMR experiments:<sup>31,35</sup>



Previously, intramolecular conformation dynamics of diamagnetic complexes  $[\text{M}(\text{EDTA}^{4-})]^-$ , where  $\text{M} = \text{Sc}^{3+}, \text{Y}^{3+}, \text{and } \text{La}^{3+}$ , has been studied.<sup>24</sup> Two types of conformational dynamic processes were proposed in the paper. The first was referred to nitrogen inversion processes, and the second was attributed to enantiomerization.<sup>24</sup> However, intramolecular dynamics in EDTA (paramagnetic lanthanide cations) systems was not found. Furthermore, from the literature reviewed, we did not find a paper in which the erbium complex intramolecular dynamics was presented.

In early works, the DNMR of EDTA diamagnetic metal complexes was studied by a low-field NMR spectrometer (60 MHz).<sup>32</sup> Accurate line-shape analysis was hindered by poor spectral resolution. Recently, intramolecular dynamics of diamagnetic EDTA complexes of  $\text{Sc}^{3+}, \text{Y}^{3+}, \text{and } \text{La}^{3+}$  has been studied more precisely using a 400 MHz NMR spectrometer.<sup>24</sup> Molecular dynamics measurements in the articles cited were based on the temperature transformation of the AB signal of acetate hydrogen atoms (acetate protons). However, separate signals of the axial- and equatorial-oriented hydrogen atoms ( $\text{H}_c^a$  and  $\text{H}_e^c$ ) of the ethylene fragment (see Figure 1) have not



**Figure 1.** Proposed coordination of the EDTA ligand in  $[\text{M}(\text{EDTA}^{4-})]^-$  complexes (where  $\text{H}_c^a$  and  $\text{H}_e^c$  are axial and equatorial ethylenic protons and  $\text{H}_a^a$  and  $\text{H}_a^e$  are axial and equatorial acetate protons, respectively).

been found either in these complexes or in paramagnetic EDTA with iron complexes.<sup>33</sup> Moreover, in paramagnetic iron complexes, separate signals of axial- and equatorial-oriented hydrogen atoms ( $\text{H}_a^a$  and  $\text{H}_e^e$ ) in the acetate fragment have not been found either.

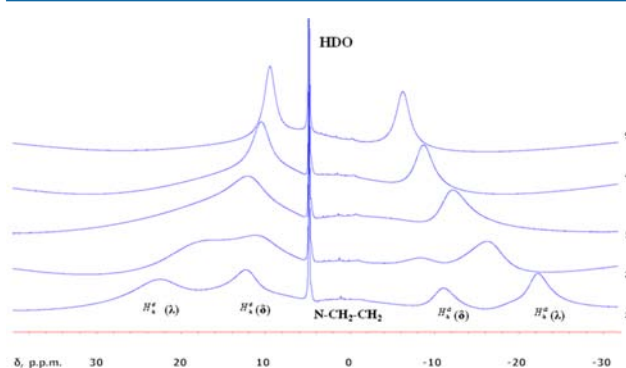
In order to observe separate signals, we tried to use the effect of paramagnetic lanthanide-induced shifts (LISs) in NMR spectra of lanthanide complexes and a strong magnetic field (18.79 T, OFP 800 MHz). The combination of these conditions gives us slow (in terms of the NMR time scale) CE of acetate protons in EDTA ( $\text{H}_a^a$  and  $\text{H}_e^e$ ). The objectives of the present work were to analyze the kinetics of CE processes between  $\Delta\text{-}\lambda_{\text{E}}\text{-}\delta\delta\delta\delta$  and  $\Delta\text{-}\delta_{\text{E}}\text{-}\delta\delta\delta\delta$  conformers in aqueous media. The terms were introduced according to the classification presented in ref 33. In the course of the present work, we planned to study NMR spectra of erbium complexes with EDTA using the band-shape analysis technique in the

framework of DNMR while taking into account the temperature dependence of LISs.<sup>9,13,14,29–31</sup> One can emphasize that our investigation is the first example of a detailed intramolecular dynamics study of paramagnetic erbium complexes. Another advantage of the approach proposed in the paper is in extending the rate constant range measured by NMR for paramagnetic 4f complexes compared to diamagnetic compounds.<sup>9,13,14</sup>

## RESULTS AND DISCUSSION

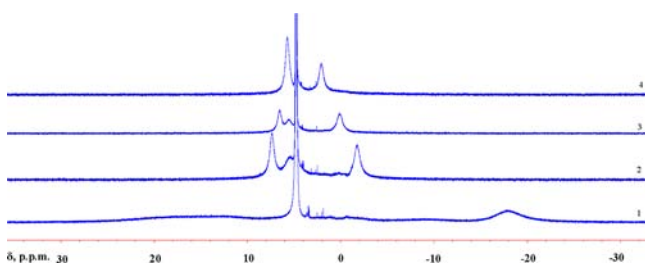
**Intramolecular Dynamics.** We have investigated the band shape of the zero-order  $^1\text{H}$  NMR spectra of the  $[\text{Er}(\text{H}_2\text{O})(\text{EDTA}^{4-})]^-$  complex over a temperature range ( $T = 273\text{--}319$  K) in order to evaluate the magnitude of the activation free energy of the molecular dynamics of  $[\text{Er}(\text{H}_2\text{O})(\text{EDTA}^{4-})]^-$  and to compare the thermodynamic parameters of molecular dynamic processes within a series of analogous metal complexes. The  $^1\text{H}$  NMR band-shape analysis technique, which takes into account the temperature variation of LISs, was employed for the detailed analysis of an effective two-site proton exchange.

In Figure 2, the  $^1\text{H}$  NMR spectra of the complex at different temperatures and 800 MHz are presented. In the spectrum



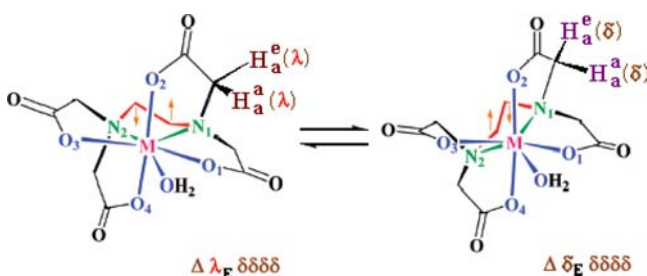
**Figure 2.** Variable-temperature dependence of 800 MHz  $^1\text{H}$  NMR spectra of  $[\text{Er}(\text{H}_2\text{O})(\text{EDTA}^{4-})]^-$  in  $\text{D}_2\text{O}$ . Chemical shift values are relative to DSS ( $\delta$  scale) at temperatures ( $T$ , K) of 273.2 (1), 288 (2), 300 (3), 310 (4), and 319 (5).

obtained at low temperature (273.2 K), there are four signals corresponding to the protons of the acetate groups and at least one broadened signal of the ethylenic protons. Three signals were observed at higher temperature. Among them, two signals correspond to the protons of the acetate groups and one broadened signal to the ethylenic protons. We explained the dramatic change in the NMR line shape by the existence of the complex in two conformational states,  $\Delta\text{-}\lambda_{\text{E}}\text{-}\delta\delta\delta\delta$  and  $\Delta\text{-}\delta_{\text{E}}\text{-}\delta\delta\delta\delta$ , with a concentration ratio of 2.3:1 at 273.2 K. Actually, the ethylene proton signals in NMR spectra obtained by a 800 MHz NMR spectrometer are broadened and relatively difficult to observe probably because of molecular dynamics. It should be noted that, for increasing sensitivity of the experiment, we used a cryoprobe on a Bruker-Avance-800 spectrometer. However, it has technical limitations in a maximal temperature of 319 K. The signal existence is evident from the spectra obtained by a 400 MHz NMR spectrometer (see Figure 3). As we can find from the figure, the signals of the ethylene protons appeared well at 5.5 and 6.0 ppm for temperatures of 353 and 363 K, respectively.



**Figure 3.** Variable-temperature dependence of 400 MHz  $^1\text{H}$  NMR spectra of  $[\text{Er}(\text{H}_2\text{O})(\text{EDTA}^{4-})]^-$  in  $\text{D}_2\text{O}$ . Chemical shift values are relative to DSS ( $\delta$  scale) at temperatures ( $T$ , K) of 283 (1), 353 (2), 363 (3), and 370 (4).

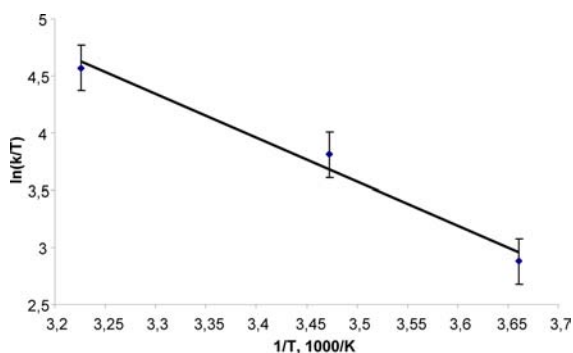
Conformational dynamics presented in Figure 4 takes place in aqueous solutions of EDTA complexes. Inversion of the



**Figure 4.** Detailed scheme of intramolecular conformational dynamics in the  $[\text{Er}(\text{H}_2\text{O})(\text{EDTA}^{4-})]^-$  dynamic system [where  $\text{H}_a^e(\lambda)$  and  $\text{H}_a^a(\lambda)$  are axial and equatorial acetate protons of the  $\Delta\text{-}\lambda\text{-E-}\delta\delta\delta\delta$  conformer, respectively, and  $\text{H}_a^e(\delta)$  and  $\text{H}_a^a(\delta)$  are axial and equatorial acetate protons of the  $\Delta\text{-}\delta\text{-E-}\delta\delta\delta\delta$  conformer, respectively].

central diamine ring in the five-membered E ring of N–C–N–M in EDTA is accompanied by exchanges between the following protons:  $\text{H}_a^e(\lambda) \leftrightarrow \text{H}_a^a(\delta)$  and  $\text{H}_a^e(\delta) \leftrightarrow \text{H}_a^a(\lambda)$ . Here, we use the double-directed vector “ $\leftrightarrow$ ” as a symbol of the exchange process. The calculated fractional population ( $p$ ) of nuclei in pairs of  $\text{H}_a^e(\lambda)$ ,  $\text{H}_a^a(\delta)$  and  $\text{H}_a^e(\delta)$ ,  $\text{H}_a^a(\lambda)$  were respectively 0.7, 0.3 and 0.7, 0.3. The values of the fractional populations were calculated according to ref 34.

Quantitative analysis in the shape change of these signals enabled us to estimate the exchange process rate constants at different temperatures. The data obtained are presented in Figure 5. From Figure 5, we calculated the activation free energy according to eq 4 in the Experimental Section. The



**Figure 5.** Dependence of  $\ln(k/T)$  on  $1/T$ , where  $k$  is the rate constant of the intramolecular dynamics process in  $[\text{Er}(\text{H}_2\text{O})(\text{EDTA}^{4-})]^-$ ,  $T$  is the temperature, and  $\text{D}_2\text{O}$  is the solvent.

estimated activation free energy [ $\Delta G^\ddagger(298 \text{ K})$ ] is equal to  $50 \pm 4$  kJ/mol. As it can be seen from Table 1, the value of the

**Table 1. Activation Energies and Activation Free Energies for Intramolecular Dynamics in EDTA Metal Complexes**

metal ion	radius/Å	activation energy $\Delta E_a^\ddagger$ , kJ/mol	activation enthalpy $\Delta H^\ddagger$ , kJ/mol <sup>a</sup>	intramolecular activation free energy $\Delta G^\ddagger(298 \text{ K})$ , kJ/mol	ref
$\text{Sc}^{3+}$	0.89	69.5	67		24
$\text{Er}^{3+}$	1.03			50	this paper
$\text{Y}^{3+}$	1.04	42.0	39.6		24
$\text{La}^{3+}$	1.17	34.9	32.5		24

<sup>a</sup>Our calculations.

activation free energy is comparable to the values of the energetic barriers of conformational transitions in EDTA complexes with diamagnetic metal cations obtained by other authors.<sup>24</sup> Additionally, in Table 1, the ionic radii for metal cations are given.

It should be noted that experimental data obtained by exchange spectroscopy (2D-EXSY) of DNMR for investigation of this dynamic system confirms the kinetic scheme of processes shown in Figure 3.

From Table 1, one can conclude that the values of the activation free energies monotonically increase with increasing ionic radius. This free-energy monotonic increase in  $[\text{M}(\text{EDTA}^{4-})]^-$  complexes is observed in metal series of different character. The regularity found is analogous to the lanthanide contraction effect.<sup>9,13,14</sup> When discussing the obtained values of the activation free energies for EDTA intramolecular dynamics in the complexes under investigation, we have to note the following. The estimated activation free energy can be compared to  $\Delta G^\ddagger$  of water intermolecular exchange in  $[\text{Fe}(\text{CyDTA})(\text{H}_2\text{O})]^{2-}$  [ $\Delta G^\ddagger(298 \text{ K}) = 38$  kJ/mol]. The value of the intramolecular exchange free energy is much larger than the  $\Delta G^\ddagger$  values of water intermolecular exchange in  $[\text{Fe}(\text{CyDTA})(\text{H}_2\text{O})]^{2-}$ . The last value was found by  $^{17}\text{O}$  NMR relaxation measurements.<sup>33</sup>

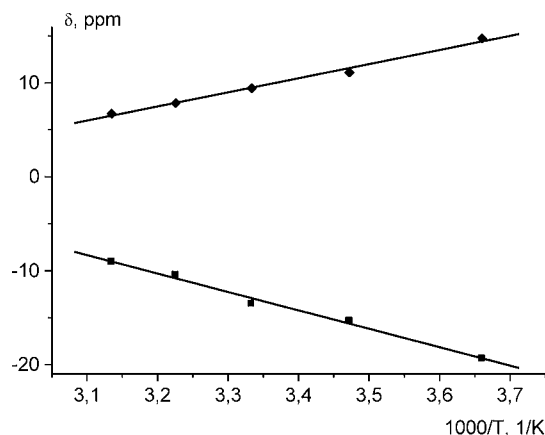
**Paramagnetic Probes Based on 4f Elements for DNMR at High Magnetic Fields.** The following peculiarity of using DNMR for studies of the paramagnetic compounds of 4f elements deserves special attention. The range of measurable paramagnetic LISs is known to be larger than 100 ppm. As a result of paramagnetic chemical shifts ( $\delta\nu$ ) in 4f complexes, the range of measurable rate constants expands considerably compared to the analogous range in diamagnetic compounds. This may be illustrated by a system with a degenerate two-site exchange process. For an NMR spectrometer with an operating frequency for protons of 800 MHz, the largest value of the rate constant that can be measured is  $k_{\text{max}} \sim 10^{10}$  Hz (upper boundary). It can be assumed that the value of  $\delta\nu$  is equal to  $8 \times 10^4$  Hz, which corresponds to 100 ppm in paramagnetic compounds. We consider also that the error of the half-width determination is about  $\sim 1$  Hz. The  $k_{\text{max}}$  value in paramagnetic compounds is much larger than the  $k_{\text{max}}$  value ( $\sim 10^8$  Hz) in diamagnetic compounds ( $\delta\nu \sim 8 \times 10^3$  Hz). The lower boundary of the range of rate constant measurement is  $k_{\text{min}} \sim 1$  Hz.

In the present paper using variable-temperature  $^1\text{H}$  NMR at high magnetic field, evidence of spectral coalescence was found for conformational dynamics of the  $\text{Er}^{3+}$  complex at 300 K (see

Figure 2). Fast molecular dynamics (in an NMR time scale<sup>9,34</sup>) is observed at 319 K. Under these conditions, the rate constant value was estimated to be  $3.2 \times 10^4 \text{ s}^{-1}$ .

Thus, using the paramagnetic probe method for investigation of the intramolecular dynamics of ligands coordinated to this metal cation is equivalent to using an NMR spectrometer with an operating frequency of 8 GHz, which is unavailable at present for commercial instruments. Therefore, the potential of this method in the study of 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 area of application of the NMR-based methods of CE studies will not be limited by the investigations of the presented ligand. In the near future, this technical approach 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 LISs and Thermometric NMR Sensors.** The temperature dependences of paramagnetic LISs of  $[\text{Er}(\text{H}_2\text{O})(\text{EDTA}^{4-})]^-$  for protons of different groups are presented in Figure 6. Both dependences in



**Figure 6.** Temperature dependence of the average paramagnetic LISs in 800 MHz  $^1\text{H}$  NMR spectra for  $\text{H}_\alpha^e$  (◆) and  $\text{H}_\beta^a$  (■) protons of the  $[\text{Er}(\text{H}_2\text{O})(\text{EDTA}^{4-})]^-$  dynamic system, with  $\text{D}_2\text{O}$  as the solvent.

coordinates LIS versus inverse temperature value ( $1/T$ ) can be approximated by linear anamorphose. This result is similar to that of earlier investigated complexes of  $[\text{Ho}(\text{H}_2\text{O})(\text{EDTA}^{4-})]^-$ ,<sup>30,35</sup>  $[\text{Tb}(\text{H}_2\text{O})(\text{EDTA}^{4-})]^-$ ,<sup>31,35</sup>  $[\text{Ln}(18\text{-crown-6})(\text{ptfa})_2]^+$ ,<sup>9,35-39</sup>  $[\text{Ln}(\text{diaza-18-crown-6})(\text{NO}_3)_3]^9$   $[\text{Ln}(18\text{-crown-6})(\text{NO}_3)_3]^9$ ,<sup>9,14,35</sup> and  $[\text{LnH}(\text{oep})(\text{tpp})]^9$ ,<sup>13</sup> where ptfa is 1,1,1-trifluoro-5,5-dimethyl-2,4-hexanedione, tpp is tetraphenylporphyrin, and oep is octaethylporphyrin. From the slopes of both curves, one can conclude that these dependences are substantial.

Our previous NMR investigations of lanthanide complexes were carried out mainly in organic solutions. In this paper, we discuss results obtained in aqueous solutions. Temperature dependences of LISs found for lanthanide complexes in aqueous solutions have more interest for application in biology and medicine.

We propose to use the effect of the temperature dependence of paramagnetic LISs in NMR spectra for temperature control of samples placed directly in an NMR spectrometer in both aqueous and nonaqueous media.<sup>14,27,31,35</sup> In particular, the studied complex  $[\text{Er}(\text{H}_2\text{O})(\text{EDTA}^{4-})]^-$  may be the most promising subnanoscale NMR spectroscopic probe to

determine the temperature in aqueous media at the moment. The effects found are prospective for applications of lanthanide complexes as thermometric NMR sensors directly in reaction media at *in situ* studies of exothermic or endothermic processes and also in medical MRI 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.

## EXPERIMENTAL SECTION

Complexes  $[\text{NaEr}(\text{H}_2\text{O})(\text{EDTA}^{4-})]$  were prepared according to ref 40. In the present work, we used  $\text{Na}_2\text{C}_{10}\text{O}_8\text{N}_2\text{H}_{14} \cdot 2\text{H}_2\text{O}$  (the disodium salt of ethylenediaminetetraacetic acid) of analytical grade. In order to obtain  $\text{ErCl}_3 \cdot 6\text{H}_2\text{O}$ , the corresponding oxide was dissolved in hydrochloric acid of high purity. The salts were purified by recrystallization from hydrochloric acid. Heavy water  $\text{D}_2\text{O}$  Izotop (Cherkassk) produced was enriched to 99.8% (TOR 95.669-79).

Solutions in  $\text{D}_2\text{O}$  had a concentration of complexes  $C = 10^{-2} \text{ mol/L}$  (at pD = 7.0). The pD values were measured in a galvanic cell containing a glass electrode combined with a silver/silver chloride reference electrode filled within a saturated potassium chloride solution by a microprocessor pH meter/ionomer Anion-410 of Infrapak-Analyt (Novosibirsk) and a pocket-sized pH meter with a replaceable electrode of Hanna Instruments. The cell volume was 2 mL. The pD measurement precision was  $\pm 0.05 \text{ log } u$ . The combined electrode was calibrated by solutions in  $\text{D}_2\text{O}$ : (1) 0.05 M potassium citrate, (2) a 0.025 M  $\text{KH}_2\text{PO}_4$  and 0.025 M  $\text{Na}_2\text{HPO}_4$  mixture of phosphates, and also (3) a 0.025 M  $\text{NaHCO}_3$  and 0.025 M  $\text{Na}_2\text{CO}_3$  mixture of carbonates. The volume of solutions was 10–20 mL. For these solutions, the pD values (25 °C) of 4.29, 7.43, and 10.74  $\text{log } u$ , respectively, were used.<sup>41,42</sup>

The  $^1\text{H}$  NMR spectra were measured on Bruker-Avance-400 and Bruker-Avance-800 pulse spectrometers at operating frequencies of 400.03 and 800 MHz, respectively. A cryoprobe was used for experiments on a Bruker-Avance-800 spectrometer. In measuring the  $^1\text{H}$  spectra, we used the residual proton signal in  $\text{D}_2\text{O}$  as an internal standard to which the chemical shift value of 4.8 ppm was assigned. The constant magnetic field stabilization was performed by  $^2\text{D}$  NMR signals of deuterium-enriched heavy water. The spectra were measured in ampules with a diameter of 5 mm. In order to set the desired temperature, we used a B-VT-1000 temperature controller with an accuracy of  $\pm 1 \text{ K}$  and a stability of  $\pm 0.2 \text{ K/h}$ . The unit was calibrated experimentally using standard samples with known chemical shift temperature dependences. Studies of exchange-broadened NMR spectra have been carried out by a line-shape analysis technique within the framework of DNMR.<sup>9,11,14,35</sup>

The rate constants of intramolecular dynamics were evaluated by the complete band-shape method<sup>11</sup> for a two-site exchange<sup>9,14,35-39</sup> in the following procedure. LIS values in the intermediate and fast-exchange regions were extrapolated from the low-temperature range using the Curie–Weiss model.<sup>9,35</sup> Assuming that there are two conformers,  $\Delta\lambda_E\text{-}\delta\delta\delta\delta$  and  $\Delta\delta_E\text{-}\delta\delta\delta\delta$ , that are in exchange, the observed average LIS value is given as

$$\Delta\delta_{av} = p_\lambda \Delta\delta_\lambda + p_\delta \Delta\delta_\delta \quad (2)$$

where  $\Delta\delta_\lambda$  and  $\Delta\delta_\delta$  are the intrinsic LISs in the absence of exchange and  $p_\lambda$  and  $p_\delta$  are the molar fractions of the isomers. It should be noted that paramagnetic LISs were determined relative to the diamagnetic complex II, which served as a reference.<sup>9,10</sup> As can be seen in Figure 6, experimental LIS values are well fitted by a linear dependence on  $1/T$ . Required for NMR signal shape analysis, LIS values of  $\text{H}_\alpha^e(\lambda)$ ,  $\text{H}_\alpha^a(\delta)$ ,  $\text{H}_\beta^e(\lambda)$ , and  $\text{H}_\beta^a(\delta)$  proton signals in the absence of exchange in cases of intermediate and fast exchange (NMR time scaling<sup>9,14,35</sup>) were calculated as

$$\Delta\delta_i(T) = \Delta\delta_i(T_0)(1/T + A)/(1/T_0 + A) \quad (3)$$

Parameter  $A$  in eq 3 was defined by analysis of the average LIS value for  $\text{H}_\alpha^a$  proton at  $T_0 = 273.2 \text{ K}$ .

The free energy of activation,  $\Delta G^\ddagger$ , of molecular dynamics in  $[\text{Er}(\text{H}_2\text{O})(\text{EDTA})]^-$  was calculated according to the Eyring equation<sup>9,11,14</sup>

$$k = (Kk_{\text{B}}T/h) \exp(-\Delta G^\ddagger/RT) \quad (4)$$

where  $k$  is the rate constant of the CE reaction,  $T$  is the absolute temperature,  $R$  is the gas constant,  $k_{\text{B}}$  is Boltzmann's constant,  $h$  is Planck's constant, and  $K$  is the transmission coefficient.

**<sup>1</sup>H NMR Spectral Data.**  $[\text{Er}(\text{H}_2\text{O})(\text{EDTA}^{4-})]^-$  ( $\Delta\lambda_{\text{E}}\delta\delta\delta\delta$ ).  $\delta_{\text{H}}$  (ppm, D<sub>2</sub>O, pD = 7,  $T = 273.2$  K): 23.1 (NCH<sub>2</sub>COO, H, s), -22.6 (NCH<sub>2</sub>COO, H, s), 0.5 (NCH<sub>2</sub>CH<sub>2</sub>N, 1H, s).

$[\text{Er}(\text{H}_2\text{O})(\text{EDTA}^{4-})]^-$  ( $\Delta\delta_{\text{E}}\delta\delta\delta\delta$ ).  $\delta_{\text{H}}$  (ppm, D<sub>2</sub>O, pD = 7,  $T = 273.2$  K): 12.2 (NCH<sub>2</sub>COO, H, s), -11.3 (NCH<sub>2</sub>COO, H, s), 0.5 (NCH<sub>2</sub>CH<sub>2</sub>N, 1H, s).

$[\text{Lu}(\text{H}_2\text{O})(\text{EDTA}^{4-})]^-$ .  $\delta_{\text{H}}$  (ppm, D<sub>2</sub>O, pD = 7,  $T = 300$  K): 3.2 (NCH<sub>2</sub>COO, 2H, s), 2.3 (NCH<sub>2</sub>CH<sub>2</sub>N, 1H, s).

**EDTA.**  $\delta_{\text{H}}$  (ppm, D<sub>2</sub>O, pD = 7,  $T = 298$  K): 4.2 (NCH<sub>2</sub>COO, 2H, s), 3.6 (NCH<sub>2</sub>CH<sub>2</sub>N, 1H, s).

## CONCLUSION

This work presents the features of intramolecular conformational dynamics of paramagnetic erbium complexes with EDTA<sup>4-</sup> in aqueous media by the <sup>1</sup>H NMR method. A change in the shape of the <sup>1</sup>H NMR signals of the  $[\text{Er}(\text{H}_2\text{O})(\text{EDTA}^{4-})]^-$  complex is shown to provide an estimation of the rate constants of conformational dynamics. Complexes of EDTA<sup>4-</sup> with Er<sup>3+</sup> may serve as nanoscale NMR spectroscopic probes to determine the temperature in aqueous media. The described aspect represents a practical application of the study.

A fundamental aspect of the investigation is determination of the energetic characteristics of intramolecular processes for a paramagnetic system. It should be noted that our investigation is the first example of an intramolecular dynamics study of erbium paramagnetic complexes. The method of NMR line-shape analysis taking into account the temperature dependence of the paramagnetic chemical shift was used in the present investigation. On the example of erbium complexes, this method shows its high effectiveness for the study of molecular dynamics in paramagnetic systems. Besides erbium, other lanthanide cations can be used for conducting analogous investigations. As a result, in the lanthanide series, we can expect that the range of experimental rate constants of CE may vary because of variation of the paramagnetic properties of the metal cations.

Summarizing the result of the study and our previous publications, we can propose the use of different lanthanide cations as adjustable probes for the study of dynamic processes occurring in substrate molecules bonded to the cations.

Of course, in the near future, the field of application of the NMR-based methods of CE studies will not be limited to the investigation of the presented polydentate ligand. These techniques will possibly be used in the studies of complexes of many other classes of chemical compounds (in particular, such biomacromolecules as RNA and DNA).

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### Notes

The authors declare no competing financial interest.

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