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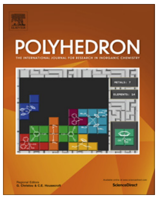

Complex of ytterbium ethylenediaminetetraacetate as combined NMR paramagnetic probe for *in situ* control of temperature and pH in aqueous media

Sergey P. Babailov [a,b,*], Eugeny N. Zapolotsky [a]

[a] *A.V. Nikolaev Institute of Inorganic Chemistry of the Siberian Branch of the Russian Academy of Sciences, Av. Lavrentyev 3, Novosibirsk 630090, Russia*
[b] *National Research Tomsk Polytechnic University, Lenin Avenue 30, Tomsk 634050, Russia*

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ABSTRACT

The paper reports variations in LIS for $[Yb(H_2O)_n(EDTA)]^-$ and $[Yb_2(EDTA)_3]^{6-}$ complexes as a result of variation in pD and temperature. This is the first detection of kinetically stable complexes of the yttrium subgroup with stoichiometric ratio of 2:3. The experimental paramagnetic lanthanide-induced chemical shift values of these compounds are well fitted by linear dependence on 1/T at different pH values. The $[Yb(H_2O)_n(EDTA)]^-$ complex can be considered as one of the most promising combined NMR spectroscopic probe to determine temperature and pH in aqueous media.

1. Introduction

Aminopolycarboxylate ligands (APCL) are, without any doubt, considered some of the most extensively studied chemical structures for many purposes, of which is reputed their applicability in biomedical applications [1–7]. During the last decades, an increase in the number of publications devoted to the physicochemical properties, to the molecular structure, to the inter- and intramolecular dynamics of the rare earth coordination compounds has been observed [1,4–5,7,8]. Recently, the growth of interest in studies of lanthanide (Ln) coordination compounds with APCLs [1–5,7,9–10] (in particular with ethylenediaminetetraacetate anions {EDTA}) has been noticed. This is connected with the using the Gd-complexes with aminopolycarboxylate ligands as MRI contrast relaxation reagents [1,7–8]. 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 food industry, in soap boiling, and so on. Lanthanide complexes with EDTA (compared to complexes with cations of d-elements) are characterized by large coordination numbers (6–12) [1,7]. Consequently, the complexes of lanthanides are possessed of a different stoichiometry in solution (1:1, 1: 2, and 2:3) [1,7–10]. They also have a more rapid intermolecular exchange of ligands [9,11]. The relative proportions of complexes with different stoichiometry in aqueous solution are mainly determined by the ratio of the metal–ligand and pH value. Processes of EDTA complexing with lanthanide cations in solution are currently poorly understood (especially at the stoichiometric excess of EDTA molecules). Two types of conformational dynamic processes were identified (the first one is conditioned by nitrogen inversion processes, and the second one is conditioned by the enantiomerization) [9]. It should be noted that intermolecular dynamics has been also investigated by NMR measurements (both for the light and the heavy [9] lanthanides). Previously, it have been suggested that intermolecular dynamics occur through the formation of intermediates $[Ln_2(EDTA)_3]^{6-}$ [9]. However, the most of the complexes like $[Ln_2(EDTA)_3]^{6-}$ not previously been discovered experimentally (excepting complex of Eu^{3+} [10]). Previously, we have in particular suggested to use paramagnetic lanthanide complexes with APCLs as NMR temperature sensors for control local temperature in solutions and medical applications [9]. Although the structures of EDTA metal complexes and the applications of EDTA are taught in undergraduate courses of general chemistry and analytical chemistry, little about the pH dependence of paramagnetic lanthanide-induced chemical shifts (LISs) [7,9] in aqueous solutions of complexes with the heavy lanthanide ions were introduced. The objectives of the work were to analyze the pD and

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[*] Corresponding author at: A.V. Nikolaev Institute of Inorganic Chemistry of the Siberian Branch of the Russian Academy of Sciences, Av. Lavrentyev 3, Novosibirsk 630090, Russia. Fax: +7 (3832) 3309489.

E-mail address: babajlov@niic.nsc.ru (S.P. Babailov).

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temperature dependences of paramagnetic lanthanide-induced chemical shifts in the ytterbium complexes of EDTA {$[Ln(H_2O)_n(\text{EDTA})]^-$ (I)} in aqueous media where n = 0, 1, 2, 3. To this end, we studied the ^1H NMR spectra of ytterbium(III) complexes with EDTA depending on temperature and pD. In order to find $[Yb_2(\text{EDTA})_3]^{6-}$ (II) experimentally we studied this system in a stoichiometric excess of EDTA molecules.

2. Results and discussion

It was experimentally observed the following. The signals of compounds I, II and the free H_4EDTA are observed in the ^1H NMR spectra at different temperatures and pH values. One can find signals of I and the free H_4EDTA at pD = 0,7 and 1,1. It was found at pD = 7,5 that there are signals of I and II. However signals of the free H_4EDTA are absent at this condition (pD = 7,5).

Signal assignment was directly done by integral intensity analysis in NMR spectra of studied compounds. So, one can distinguish in NMR spectra intensive signals of ethylenic and acetic CH_2 protons of I and less intensive signals of II (see

Supporting Information). In addition, it was observed that the mutual arrangement of signals of ethylenic and acetic CH_2 protons for the complex $[Er(H_2O)_n(\text{EDTA})]^-$ (previously studied by us [13]) is consistent with the same for I, which made it possible to successfully complete the assignment of signals.

It was suggested by us that the excess of the free ligand H_4EDTA is associated with the $[Yb(H_2O)_n(\text{EDTA})]^-$ complex at medium pD values. And, the $[Yb(\text{EDTA})_2]^{5-}$ and II complexes are forming. The proposed structure of II is shown on the Scheme 1. Here one can see two EDTA ions with a hexadentate bonding, and one EDTA ion having a bridged binding with two lanthanide cations (at tetradentate bonding).

It should be noted that this suggestion (on forming of II) is in agreement with the proposed scheme of intermolecular chemical exchange in the system {H_4EDTA} – {$[Ln(H_2O)_n(\text{EDTA})]^-$} presented in Ref. [9]. According to the proposed scheme, ligand exchange occurs via forming the intermediate complex of stoichiometric ratio of 1:2 [9]. The II complex is more or less thermodynamically and kinetically stable as compare to the intermediate $[Yb(\text{EDTA})_2]^{5-}$. It should be noted that this is the first detection of kinetically stable complexes of the yttrium subgroup with stoichiometric ratio of 2:3. It is known that Fermi contact contributions to LIS are proportional to 1/T (Curie's law), and as predicted by Bleaney [12] 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 (presented in Ref. [7]) 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 350 K is adequately described by the Curie–Weiss approximation [7]:

$$\Delta\delta = a + b/T \tag{1}$$

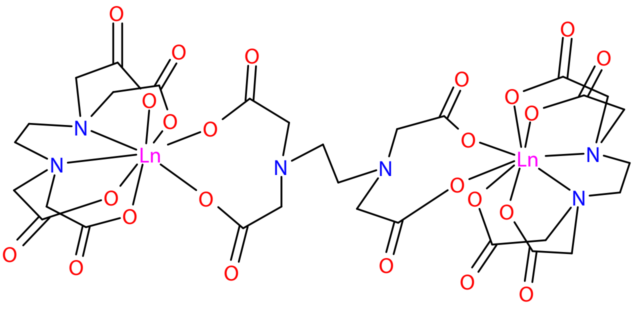
We also investigated the actual temperature dependence of the LIS on temperature. This was done in order to compare the obtained temperature sensitivities (the temperature derivatives) with the corresponding data in the literature. These values for II appeared to be 0.35 p.p.m./K (for $-N-CH_2-COO-$) {a = 36.4 p.p.m., b = −24.1 K × p.p.m.} and 0.464 p.p.m./K (for $-N-CH_2-COO-$) {a = −64.3 p.p.m., b = −37.0 K × p.p.m.} at pD = 7,5. Related values for I are found to be 0.2 p.p.m./K (for H_a^a) {a = −62,4 p.p.m., b = −19,7 K × p.p.m.} and 0.31 p.p.m./K (for H_a^e) {a = −56,7 p.p.m., b = 20,4 K × p.p.m.} at pD = 7,5. It should be noted that other complex compounds, which were earlier investigated by ^1H NMR in both organic and aqueous media, are characterized by the LIS temperature sensitivity in the range from 0 to 1.46 p.p.m./K [7,9,13]. The obtained results indicate that the coordination compounds I and II may be considered as moderately middle sensitive ^1H NMR lanthanide paramagnetic probes for *in situ* temperature control in aqueous media.

According to NMR data, paramagnetic LISs related to the CH_2 groups of I depend significantly not only on temperature but also on pD (Figs. 1, 2). Maximum sensitivity to pD was found to be 0.5 p.p.m./pD at the same time. It may be supposed that the LISs dependence on pD are connected to moderately rapid chemical exchange between the protonated and unprotonated forms of I. Note that this is the first example of a detailed study of paramagnetic LIS depending on two parameters (temperature and pD) for lanthanide complexes with EDTA. One can considered I as a combined ^1H NMR probe for *in situ* control of temperature and pD in aqueous media. Obviously, the actual Ln-(EDTA) complexes cannot be used as *in vivo* MRI reagents because of their moderate toxicity. Nevertheless, Ln complexes with EDTA can be regarded as a model for other APCL compounds. Ln complexes with DTPA and DOTA-like ligands [1,7,13] are possessed for example of low toxicity. In this regard, other aminopolycarboxylate complexes of lanthanides are promising compounds for *in vivo* MRI three-dimensional mapping of the body temperature and pH distribution and the temperature or pH of different body parts in diseases, including some related to cancer (Fig. 2).

NMR spectral data in D_2O. **I** δ_H (p.p.m., pD = 0.7, T = 360 K): 1.6 ($-N-CH_2-COO^-$, 1H, s), 1.9 ($-N-CH_2-COO^-$, 1H, s), 10,0 ($N-CH_2-CH_2-N$, 1H, s).

δ_H (ppm, D_2O, pD = 1.1, T = 360 K): 2.6 ($-N-CH_2-COO-$, 1H, s), 1.6 ($-N-CH_2-COO-$, 1H, s), 7.83 ($N-CH_2-CH_2-N$, 1H, s).

δ_H (ppm, D_2O, pD = 7.5, T = 360 K): 3.0($-N-CH_2-COO-$, 1H, s), 0.7 ($-N-CH_2-COO-$, 1H, s), 5.5 (N—CH2—CH2—N, 1H, s).



Scheme 1.

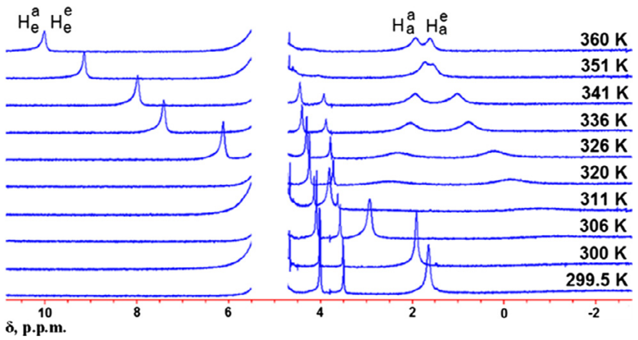


Fig. 1. 300 MHz ^1H NMR spectra of $[Yb(H_2O)_n(\text{EDTA})]^-$ at different temperatures (at pD = 0.7; solvent D_2O).

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