^{1}H NMR study of *N*-(*o*-hydroxybenzyl)iminodiacetic acid and its complexes with lanthanum and lutetium

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Dependence of chemical shifts of the ^{1}H NMR signals of nonlabile protons in *N*-(*o*-hydroxybenzyl)iminodiacetic acid (HBIDA) in its D_2O solutions on pD was utilized for investigation of successive dissociation of three protons of the HBIDA functional groups. In a HBIDA anion HL^{2-} there is supposed the formation of a hydrogen bond between the phenolic group and nitrogen atom of the amino group. The formation of LaL, LaL_2, LuL, and LuL_2 complexes was found from the pD dependence of proton chemical shifts in the systems where the ratio of *c*(La(III)) and/or *c*(Lu(III)) to *c*(HBIDA) equals 1 : 1 and 1 : 2, respectively. In all these complexes the oxygen atoms of two carboxylate groups are coordinated, as well as the amino group nitrogen atom and oxygen one of the phenolic group. The bonds Lu—N are nonlabile in LuL_2 complex, in the other complexes all coordination bonds were found to be labile. Two molecules of HBIDA bonded to Lu in the LuL_2 complex are equivalent, while two glycinate rings of each HBIDA molecule are mutually nonequivalent.

Использована зависимость химических сдвигов ^{1}H ЯМР сигналов нелабильных протонов *N*-(*o*-гидроксибензил)иминодиуксусной кислоты (ГБИДУ) в растворах D_2O от pD для исследования последовательной диссоциации трёх протонов функциональных групп ГБИДУ В анионе ГБИДУ HL^{2-} предполагается образование водородной связи между фенольной группой и атомом азота аминогруппы. Обнаружено образование комплексов LaL, LaL_2, LuL и LuL_2 на основании зависимости химических сдвигов протонов от pD в системах, где отношение *c*(La(III)) или *c*(Lu(III)) к *c*(ГБИДУ) равнялось 1 : 1 и 1 : 2 соответственно. Во всех этих комплексах кислородные атомы двух карбоксильных групп координированы, также, как и атом азота аминогруппы и атом кислорода фенольной группы. Связи Lu—N нелабильны в комплексе LuL_2, в других же комплексах все координационные связи являются лабильными. Две молекулы ГБИДУ, связанные с Lu в комплексе LuL_2 являются эквивалентными, в то время как два глицинатных кольца в каждой молекуле ГБИДУ, взаимно неэквивалентны.

Compounds of the complexane type, which contain an *N*-(*o*-hydroxybenzyl)amino group in their molecule, reveal selective chelation with trivalent ions, especially with iron [1]. Ligand with this functional group, *e.g.* *N*-(*o*-hydroxybenzyl)iminodiacetic acid (HBIDA) was synthesized for the first time by *Schwarzenbach* [2], its improved synthesis is described by *Martell et al.* [3]. In our previous paper [4] are published the stability constants of HBIDA complexes with lanthanides obtained by potentiometric measurements together with the information about composition of complexes thus formed obtained by means of paper electrophoresis method. This work has been aimed to gain the information about the structure of individual ionic forms of HBIDA in aqueous solutions and the mode of HBIDA coordination in the systems where the ratio of c(La(III)) and/or c(Lu(III)) to c(HBIDA) equals to 1:1 and 1:2, respectively.

Experimental

HBIDA was prepared in the reaction of iminodiacetic acid with *o*-acetoxybenzylbromide [3]. The identity and purity of the synthesized product were verified by ^{1}H NMR spectrum, elemental analysis, and by potentiometric neutralization.

The solutions of HBIDA, $La(NO_3)_3 \cdot 6H_2O$, anal. grade, and Lu_2O_3, anal. grade (after dissolving in diluted hydrochloric acid and subsequent evaporation to dryness) were prepared in D_2O. The pD adjustment was provided by addition of KOD or DCl solutions in D_2O. Ligand concentration in the measured solutions was about 0.1 mol dm^{-3}, and deuterated *tert*-butyl alcohol $(CH_3)_3COD$ (TBA) was used as an internal reference. pD values of solutions were determined from the pH readout (pH_m) according to relationship $pD = pH_m + 0.40$ [5].

^{1}H NMR spectra were measured on a Tesla BS 487 A spectrometer operating at 80 MHz and ambient temperature. The chemical shift values are in ppm (with an accuracy of ± 0.02 ppm) in δ_r scale relative to DSS ($\delta_{r,TBA} = 1.233$ ppm).

Results and discussion

In the ^{1}H NMR spectrum of HBIDA solution in D_2O there are observed signals of nonlabile protons of methylene and methine groups, respectively. The appearance of spectrum does not reveal remarkable changes in the whole pD range studied. There is a singlet of four protons of carboxymethyl groups positioned upfield, protons of methylene group bonded to an aromatic ring are less shielded and their signal is observed also as a singlet. Protons of aromatic ring gave the signals, as observed, forming two multiplets of the same intensity. As implied from the changes of chemical shifts due to the dependence on pD, the effect which mainly influences the electron density at aromatic protons is the $+M$ effect of the phenolic group. At these protons in *ortho* and *para* position to the phenolic group, the electron density is higher in the whole pD range applied when compared with that

of *meta*-positioned protons. Fig. 1 shows the dependence of chemical shifts of nonlabile protons of HBIDA on pD. An increase in pD causes the successive dissociation of three protons (or D^+ ions) from the functional groups of amino acid under study, with subsequent increase in the electron density at nonlabile protons, which is observed as the decrease of their chemical shift values. In the region of pD = 1.5—4 there is observed the greatest change of chemical shift of protons of carboxymethyl —CH_2— groups due to dissociation of the proton from that group in the given region of pD. Since carboxymethyl groups are observed as equivalent ones also at pD < 1.5, one may conclude that the proton which dissociates at pD = 1.5—4 is either simultaneously bonded to both carboxyl groups or there exists a rapid exchange of this proton between them. At pD = 4—7.5 the HBIDA in D_2O solution exists as a H_2L^- anion. At pD = 7.5—10 there are observed significant changes of chemical shifts of protons of methylene groups attached to the amino-nitrogen atom. These changes are characteristic of the dissociation of protons from nitrogen atom. The further changes of chemical shifts are observed at

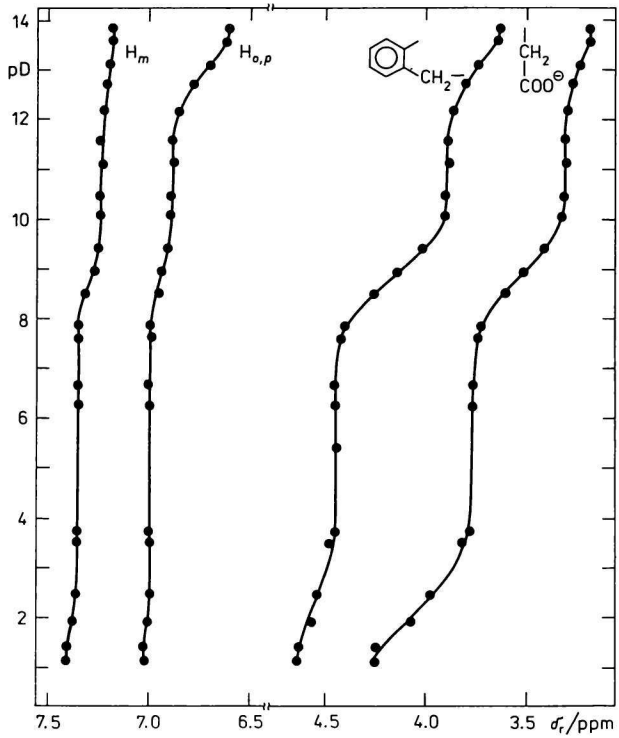
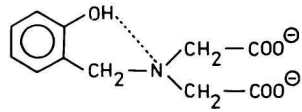


Fig. 1. Dependence of the chemical shifts of resonance signals of HBIDA protons on pD of solution, c(HBIDA) ≈ 0.1 mol dm^{-3}, temperature 25 °C.

pD = 12—13.5 and the most pronounced ones are in the case of protons positioned *ortho* and *para* to phenolic group as well as the protons of CH_2— group attached to aromatic ring. These changes are due to the proton dissociation from phenolic group. As the proton of phenolic group dissociates producing thus phenolate anion, as expected, the electron density is increased mainly at *ortho* and *para* aromatic protons, which is consequence of increased $+M$ effect and conversion of $-I$ effect to $+I$ one of phenolic group being ionized. Slight increase in electron density due to these effects may be expected also at the protons of methylene group attached to the aromatic ring. In this region of pD is, however, observed also the shift (0.13 ppm) of signals of the carboxymethylate group protons regardless of their relative great distance from the place of dissociation. It points out the fact that in the pD region of 10—12 in the HBIDA HL^{2-} anion there is formed a hydrogen bond between the phenolic group and the amino one. As the phenolic group proton dissociates the hydrogen bond is interrupted, which



probably causes an increase in electron density also at protons of carboxylate groups. This hydrogen bond influences to a significant extent the acid-base properties of HBIDA and it was predicted by *Martell* [3], basing on the unusually low value of $pK(a_2)$ when compared with those of similar compounds.

Comparison of the chemical shifts of nonlabile protons of individual ionic forms of HBIDA (Table 1) enables to construct the following scheme of the proton dissociation of amino acid under study

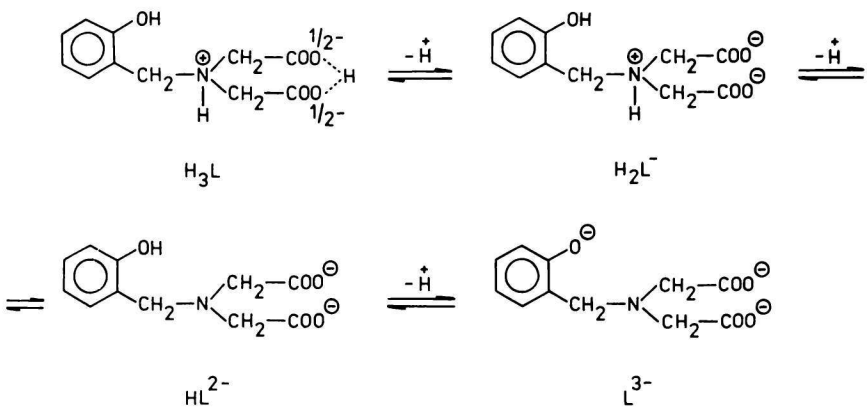


Table 1

Chemical shifts of nonlabile protons of ionic forms of HBIDA and their changes caused by the dissociation of protons of functional groups

	$-CH_2-CO$		$-CH_2-Ar$		$H_{o,p}$		H_m	
	δ_r/ppm	$\Delta\delta_r$/ppm	δ_r/ppm	$\Delta\delta_r$/ppm	δ_r/ppm	$\Delta\delta_r$/ppm	δ_r/ppm	$\Delta\delta_r$/ppm
H_3L	4.24		4.63		7.00		7.40	
		0.49		0.19		0.02		0.07
H_2L^-	3.75		4.44		6.98		7.33	
		0.45		0.56		0.11		0.12
HL^{2-}	3.30		3.88		6.87		7.21	
		0.13		0.26		0.27		0.05
L^{3-}	3.17		3.62		6.60		7.16	

The complex formation and their structure in solution was studied in the systems involving c(La(III)) and/or c(Lu(III)) to c(HBIDA) = 1:1 and 1:2 ratios, respectively. The ^{1}H NMR signals of nonlabile protons of HBIDA in the system with lanthanum remain practically unchanged in the whole pD region studied. Fig. 2 shows the spectrum of c(La(III)) to c(HBIDA) = 1:2 at pD = 11.5. The chemical shift dependence on pD is shown in Fig. 3. In c(La(III)) to c(HBIDA) = 1:2 solution at pD > 10 the chemical shifts and shape of signals remain unchanged. These facts point out that HBIDA is bonded to a LaL_2 complex (values of chemical shifts are listed in Table 2). Multiplicity of signals of HBIDA coordinated in this complex is the same as that on noncoordinated ligand. It is a proof of kinetic lability of all the lanthanum—HBIDA bonds. This lability enables a rapid inversion of nitrogen atom as well as the rapid intraligand exchange of donor atoms of HBIDA in coordination polyhedron. Comparing the values of chemical shifts of nonlabile protons of HBIDA in its LaL_2 complex with those of L^{3-} anion there is observed a substantial decrease in electron density at these protons as the ligand became coordinated. The central atom—carboxylate oxygen bond has a ionic nature and the electron density of nonlabile protons of carboxymethyl groups in the complex depends mainly on an electrostatic potential of the central ion [6]. Signals of the other protons of LaL_2 complex are observed upfield when compared with those for noncomplexed L^{3-} anion. Such a mutual position of proton signals of the ligand anion and of ligand in its La(III) or Lu(III) complex was not observed in the case of iminodiacetic acid, *N*-methyliminodiacetic acid, and *N*-(2-hydroxyethyl)iminodiacetic acid [7]. One may expect a decrease in diamagnetic contribution to shielding constant of protons when the ligand is coordinated. Decreased value of chemical shift of aromatic protons as well as that of the protons of methylene group attached to aromatic ring is thus connected with

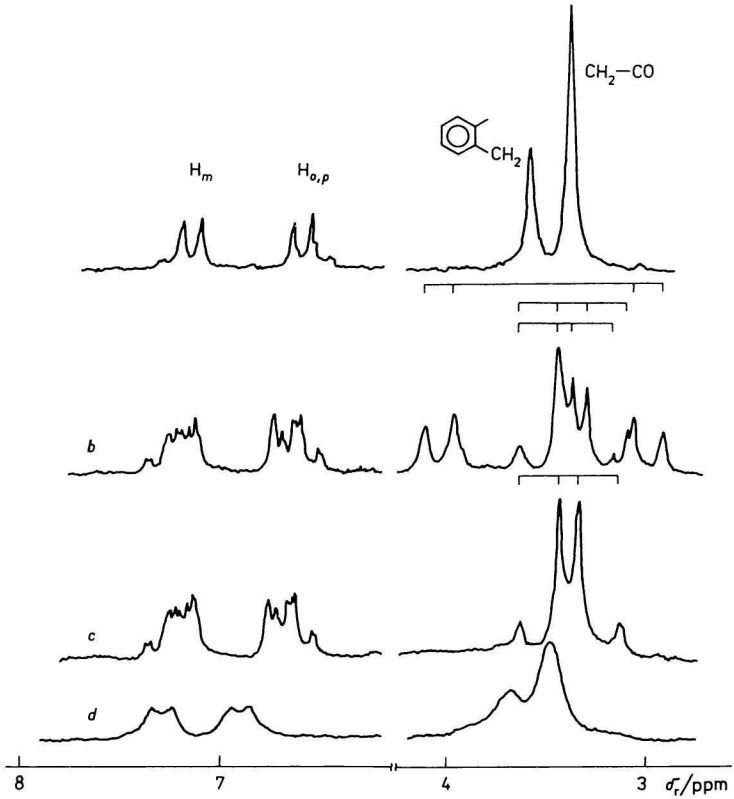


Fig. 2. Typical spectra of c(Ln(III)) : c(HBIDA) = 1 : 2 solutions in D_2O, c(HBIDA) ≈ 0.1 mol dm^{-3}, temperature 25 °C.

a) c(La(III)) : c(HBIDA) = 1 : 2, pD = 11.5;
b) c(Lu(III)) : c(HBIDA) = 1 : 2, pD = 11.3;
c) c(Lu(III)) : c(HBIDA) = 1 : 2, pD = 7.1;
d) c(Lu(III)) : c(HBIDA) = 1 : 2, pD = 5.4.

the increase in contribution to the shielding constant of protons due to magnetic anisotropy of bonds and ring currents in aromatic ring induced by the magnetic field. Comparing the chemical shifts of protons in c(La(III)) : c(HBIDA) = 1 : 2 system and those of protons of HBIDA in the absence of lanthanum one may suppose that in complex LaL_2 there are coordinated the oxygen atoms of carboxyl groups, nitrogen atom of amino group, and oxygen atom of phenolic group, from which the proton is dissociated as the latter group is coordinated. These conclusions are in agreement with the results reported in our previous paper [4].

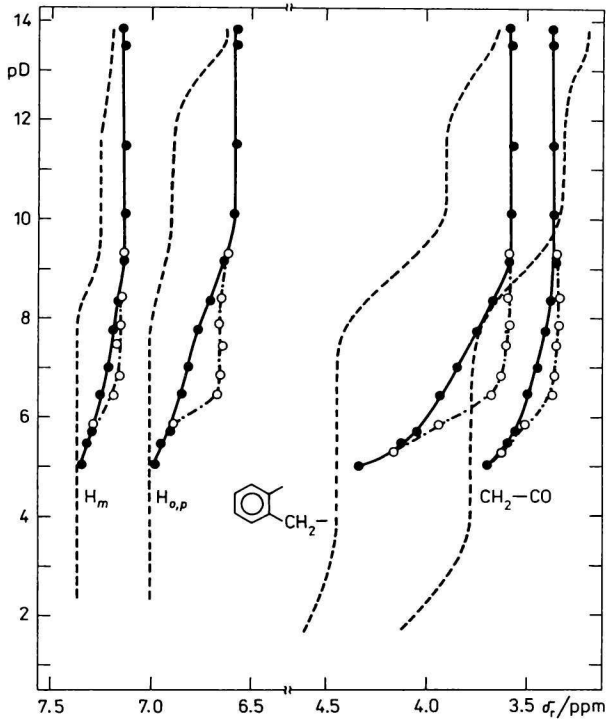


Fig. 3. Dependence of the chemical shifts of resonance signals of protons in the systems La(III) + HBIDA in solution on pD.
● c(La(III)) : c(HBIDA) = 1 : 2 ; ○ c(La(III)) : c(HBIDA) = 1 : 1 ; ---- HBIDA.

Table 2

Chemical shifts (δ_r/ppm) of protons of HBIDA coordinated in its La(III) and Lu(III) complexes

Complex	—CH_2—CO	—CH_2—Ar	$H_{o,p}$	H_m
LaL_2	3.35	3.56	6.56	7.11
LaL	3.33	3.59	6.63	7.14
LuL_2	3.36	3.50	6.63	7.17
LuL	3.38	3.61	6.64	7.15

Acidifying the solution containing LaL_2 complex there is observed the upfield shift of all chemical shifts in the spectra, and the signals become slightly broadened when compared with those of LaL_2 complex. The relatively greatest change of chemical shift (relative to the difference of chemical shifts in LaL_2 complex and free

ligand) is exhibited in the case of aromatic protons $H_{o,p}$ at pD < 10. Changes in the spectra in this region of pD may be explained by statement that the complex is decomposed and thus the released HBIDA exists in several forms amongst which proceeds a rapid exchange. One of these HBIDA forms is probably a complex in which the phenolic group is not coordinated.

The shape of HBIDA signals in $c(La(III)):c(HBIDA) = 1:1$ system is the same as that in 1:2 ratio, also the position of all signals observed at pD > 9.5 is identical. In alkaline region even at $c(La(III)):c(HBIDA) = 1:1$ ratio there is present a complex of LaL_2 type and the slight turbidity of solution due to suspended $La(OH)_3$ is observable. Fig. 3 shows that at pD < 9.5 the chemical shifts of protons are different for both systems under study. At pD = 7—9 the HBIDA is bonded in its lanthanum complex. It was found by potentiometric measurements that three protons are released from the HBIDA molecule, and the normal LaL complex is thus formed in this pD region. Small differences of chemical shifts of HBIDA bonded in its LaL and LaL_2 complexes (Table 2) pointed out the same mode of the ligand coordination in both complexes. The more pronounced difference is observed only for the chemical shifts of atomatic protons $H_{o,p}$ (0.07 ppm). This difference may be consequence of reduced length of the lanthanum—phenolate oxygen bond in LaL complex when compared with that in LaL_2 one.

The spectra of nonlabile protons of HBIDA in $c(Lu(III)):c(HBIDA) = 1:2$ are different from those of $c(La(III)):c(HBIDA) = 1:2$ system. Fig. 2 shows the typical spectra of the former system. Appearance of the spectra remains unchanged at pD > 8, and HBIDA is bonded in its LuL_2 complex. There are observed six nonequivalent protons of methylene groups, arranged in three AB-quartets (Fig. 2). The spectrum was interpreted with the aid of an INDOR technique. The following values of chemical shifts and coupling constants were calculated for the above-mentioned part of spectrum

the 1st group —CH_2—CO	$\delta_{r,A} = 3.47$ ppm
	$\delta_{r,B} = 3.29$ ppm
	$J_{AB} = 16.4$ Hz
the 2nd group —CH_2—CO	$\delta_{r,A} = 3.49$ ppm
	$\delta_{r,B} = 3.20$ ppm
	$J_{AB} = 16.3$ Hz
group —CH_2—Ar	$\delta_{r,A} = 4.02$ ppm
	$\delta_{r,B} = 2.97$ ppm
	$J_{AB} = 11.4$ Hz

The graphical expression of chemical shifts (Fig. 4) contains only the average values for protons of a given methylene group because of simplicity. Chemical shifts of aromatic protons were determined as the centre of multiplet using the

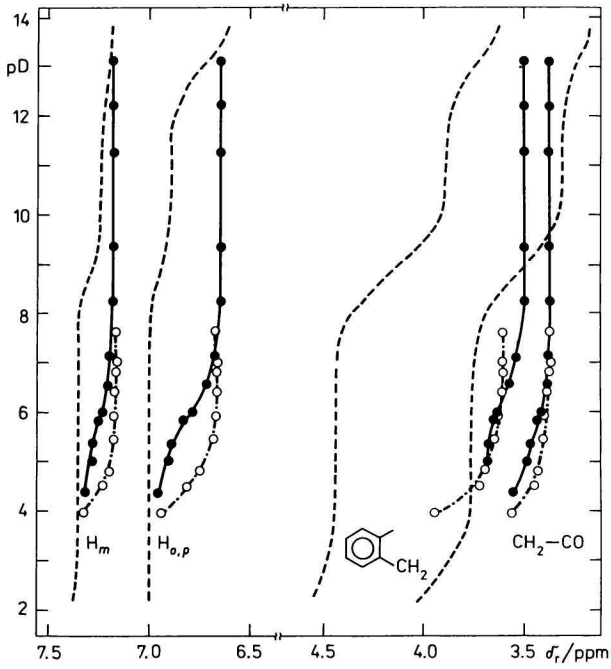


Fig. 4. Dependence of the chemical shifts of resonance signals of protons in the systems Lu(III) + HBIDA in solution on pD.
● c(Lu(III)) : c(HBIDA) = 1 : 2; ○ c(Lu(III)) : c(HBIDA) = 1 : 1; ---- HBIDA.

integral record of spectra. Comparing the chemical shifts for protons in free ligand and those in LuL_2 one may, analogically to LaL_2 complex, suppose the coordination of four donor atoms of HBIDA. The only one system of signals is a proof of the fact that both molecules of HBIDA are coordinated in the same way and they are equivalent. The Lu—N bonds in this complex are nonlabile without the possibility of rapid inversion of nitrogen atom, therefore protons of each methylene group are observed as nonequivalent. There is also observed the nonequivalence of carboxymethyl groups, which might be the consequence of nonlability of Lu—O bonds. According to our knowledge, the nonlabile Lu—O bonds in complexes of similar compounds have not been observed so far. Nonequivalence of carboxymethyl groups is probably caused by the hindrance of the hydroxybenzyl group rotation around C—N bond, having connection with the Lu-phenolate oxygen bond. In the spectrum there is an interestingly great difference of chemical shifts of protons of methylene group attached to aromatic ring (1.05 ppm). We suppose that difference is caused by a magnetic anisotropy of the environment surrounding that methylene group, especially by the ring currents of aromatic ring. Regarding this

one may conclude that the benzyl group possesses a conformation in which one of the —CH_2—Ar protons lies in the plate of aromatic ring.

Lowering the pD of solution containing LuL_2 complex (pD < 8), the increased values of chemical shifts are observed and the greatest one is observed for aromatic protons $H_{o,p}$ (Fig. 4). It is a consequence of interruption of the lutetium—phenolate oxygen bond, with simultaneous protonation of the phenolate group. After interruption of this coordination bond there is renewed the possibility of rotation of hydroxybenzyl group causing thus the chemical shifts of protons of both carboxymethyl groups to be averaged. Signal of these protons is the AB-quartet (Fig. 2*c*), so that the Lu—N bonds in the complex formed are nonequivalent as well. Signal of the —CH_2—Ar protons, when measured at laboratory temperature, is very broad and superposed on the AB-quartet. Warming up the solution to 50 °C the rate of rotation of hydroxybenzyl group is increased and the signal of its protons is observed as a singlet. After further lowering the pD (pD < 5.5) the signals of protons of methylene groups are observed as broadened singlets (Fig. 2*d*). Fig. 4 shows that chemical shifts of HBIDA in c(Lu(III)):c(HBIDA) = 1:2 system in a given area of spectrum differ from those for free ligand. Worth of note is the difference of chemical shifts of —CH_2—Ar protons (0.75 ppm). Basing on the spectra one may suppose that in this region the HBIDA is predominantly present as the hydrogen complexes of LuH_nL_2 type, in which the Lu—N bond remains unaffected.

In equimolar solutions of Lu(III) and HBIDA at pD > 8 the same complex of LuL_2 type is formed, as it was described earlier. In the spectra of c(Lu(III)):c(HBIDA) = 1:1 solutions at pD < 8 there are observed the broadened singlets of protons of methylene groups and multiplets of aromatic protons. Chemical shifts of protons of this system in dependence on pD are shown in Fig. 4. The formation of normal complex LuL might be expected in the pD region 5.5—7.6. The values of chemical shifts of HBIDA coordinated in this complex are listed in Table 2. Comparing the chemical shifts of protons of various forms of HBIDA one may conclude that in the LuL complex are coordinated also four donor atoms of the ligand under study. Difference in the structure of HBIDA bonded in its LuL and LuL_2 complexes is mainly in the conformation of hydroxybenzyl chelate ring.

Conclusion

Results of the study of complex formation of HBIDA with lanthanides, as presented in this paper and the previous one [4], have confirmed that HBIDA possesses suitable arrangement of donor atoms and is capable to form the stable complexes with lanthanides. In complexes of the LnL and LnL_2 type HBIDA acts

as a four-donor ligand. The typical complexes for this ligand are those of $c(\mathrm{Ln}):c(\mathrm{L}) = 1:2$ composition, which are present in alkaline solutions. HBIDA is particularly suitable ligand for coordination with heavier lanthanides, as demonstrated by the LuL_2 complex, which is the most stable one owing to nonlabile Lu—N bonds, and which is formed in solutions containing an excess of both lutetium and ligand.

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