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Thermochemical Study of the Complex Formation of Copper(II)
and Nickel(II) Iminodiacetates with Amino Acids
in Aqueous Solutions

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Abstract—The formation of mixed-ligand complexes in the M(II)–Ida–L systems (M = Cu, Ni, L = His, Orn, Lys), where Ida is the iminodiacetic acid residue, was studied by pH-metry, calorimetry, and spectrophotometry. The thermodynamic parameters ($\log K$, $\Delta_r G^0$, $\Delta_r H$, $\Delta_r S$) of formation of the complexes were determined at 298.15 K and the ionic strength $I = 0.5$ (KNO₃). The most probable mode of coordination of the chelating agent and the amino acid in the mixed-ligand complexes was elucidated.

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The active use of chelating agents (Dtpa, Edta, Nta, etc.) for the removal of toxic metal cations from a human body (chelation therapy) accounts for the interest in the reactions between metal chelates and biomolecules. Taking account of the formation of mixed metal chelates with amino acids and oligopeptides can make the existing chelation therapy protocols more efficient and make the proposed models for metal cation behavior and binding in the human body more correct [1]. Immobilization of metal chelates (Ida, Nta) is used for separation of proteins by immobilized metal-ion affinity chromatography (IMAC), which also implies elucidation of the coordination modes of ligands (chelating agent and protein molecule) in the mixed complexes thus formed [2].

Unfortunately, most papers devoted to the mixed complex formation involving 3d-metal nitrilotriacetates or iminodiacetates and amino acids [3–6] are restricted to calculation of the constants without determining full thermodynamic characteristics of the processes. Studies often lack a critical choice of a complexation model (complex compositions) adequate to the experiment and do not indicate the most likely structure of the complexes. Determination of the composition of mixed complexes in these studies cannot be recognized as completely well-posed and selection of investigation objects (amino acids) is not systematic in most cases.

Therefore, it appeared pertinent to study the M–Nta(Ida)–amino acid(oligopeptide) systems in aqueous

solutions over a broad range of concentration ratios and pH in order to elucidate the coordination modes of the chelating agent and the amino acid in the mixed complex. Previously, the stabilities of mixed-ligand Cu(II), Ni, Zn, and Cd nitrilotriacetate complexes with ethylenediamine, glycine [7], histidine, ornithine, and lysine [8] have been studied and the efficiency of thermodynamic approach to estimation of structures of mixed-ligand complexes has been demonstrated.

EXPERIMENTAL

The synthesis of copper(II) and nickel(II) iminodiacetates, CuIda · 2H₂O and NiIda · 3H₂O, consisted of dissolving freshly precipitated basic copper (or nickel) carbonate in a solution containing an equimolar amount of analytical grade iminodiacetic acid H₂Ida, thorough filtering of the solution, concentrating to a substantially smaller volume, and product crystallization. The water content in the chelating agents was confirmed by thermogravimetry. The working solution of the chelating agent was prepared from an exact weighed portion of the chemical. The carbonate-free solution of sodium hydroxide was prepared by a usual procedure from CO₂-free distilled water. Analytical grade L-histidine (Reanal), L-ornithine (Acros), and L-lysine (Acros) hydrochlorides were used as received. Imidazole was recrystallized from benzene. Analytical grade potassium nitrate serving to produce the desired ionic strength was twice recrystallized from water.

A series of pH-potentiometric titrations of solutions (MIda + HL · HCl + KNO₃) with aqueous

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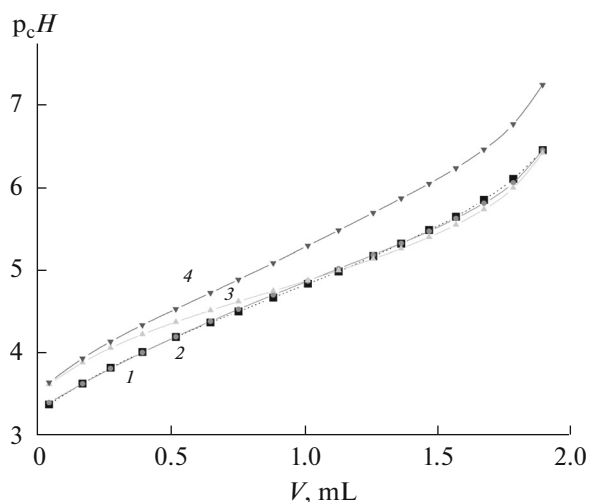
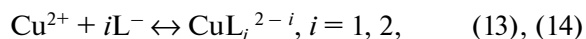
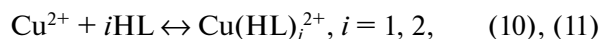
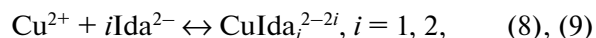
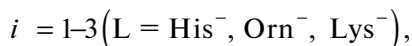
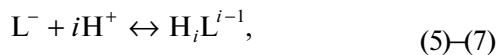
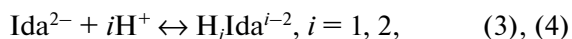
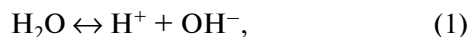


Fig. 1. (1) Curve of potentiometric titration of 20.09 mL of a solution (0.01002 M CuIda + 0.01022 M HHis · HCl + 0.48 M KNO₃) with a 0.2012 M solution of NaOH and (2, 3, 4) calculated titration curves taking into account the formation of (3) CuIdaHis⁻ ($F_{\min} = 1.36$), (4) CuIdaHHis ($F_{\min} = 17.8$), and (2) both CuIdaHis⁻ and CuIdaHHis ($F_{\min} = 0.092$).

NaOH was performed at 25°C and ionic strength of 0.5 (KNO₃) and at MIda : L ratios of 2 : 1 and 1 : 1. The amino acid (L) concentration was 0.01 mol/L in all experiments (Fig. 1). The e.m.f. of the galvanic circuit including glass and silver chloride electrodes was measured by the zero method. The correspondence of the experimental slope of the hydrogen function of the glass electrode (η) to the theoretical value was checked using three standard buffer solutions in the pH range of 2–9. The pH-metric data were treated using the PHMETR program [9] based on minimizing the likelihood function $F = \sum (p_c H_{\text{exp}} - p_c H_{\text{calcd}})^2$, where $p_c H = -\log[H^+]$ are, respectively, experimental values and the values calculated according to the model considering the following reactions:



As a rule, agreement between the calculated curve and experimental data was achieved only by taking into account the formation of not only MIdaL⁻ but also mixed MIdaHL complex according to the reaction



The possibility of formation of complexes with dissociated imidazole moiety, CuHisHisH₋₁⁻ and Cu(HisH₋₁)₂²⁻, at high pH brought about the necessity to perform an additional potentiometric experiment. Treatment of the titration data, in which the value $a = n(\text{NaOH})/n(\text{His})$ reached 3, revealed the formation of the mixed complex CuIdaHisH₋₁²⁻, in addition to the above-indicated complexes. In the case of the Ni–Ida–His system, no mixed protonated NiIdaHHis complex was identified by pH-metric titration.

The log*K* values for the protonation of iminodiacetate ion were taken from a critical review [10]. The log*K* values for reactions (6) and (7) for histidine (9.02 and 15.07, respectively), lysine (10.66 and 19.86, respectively), and ornithine (10.52 and 19.35, respectively) were taken from critical reviews [11, 12]. The stability constants of the hydroxy chelates MIdaOH⁻ were determined more precisely in a separate potentiometric titration. The recommended values for the stability constants of Cu and Ni complexes with amino acids were also taken from the reviews [11, 12]. The contribution of reactions (9)–(14) to the observed $p_c H$ and to the heats of mixing proved to be rather low and was adequately taken into account. The species abundance curves for the CuIda–His⁻–H⁺ and NiIda–Orn⁻–H⁺ systems at the MIda : L ratio of 1 : 1 are shown in Figs. 2 and 3.

The heats of reactions were determined on an ampoule isothermal-shell mixing calorimeter with a resistance temperature detector. The calorimeter operation was checked by the heat of dissolution of KCl in water at 298.15 K. The heats of mixing $\Delta_{\text{mix}}H$ of alkaline solutions of amino acids with solutions of Cu(II) and Ni(II) chelates containing a supporting electrolyte (KNO₃) were measured. A solution of amino acid hydrochloride completely or half neutralized with alkali was placed into a tightly sealed glass tube. The amino acid concentration after mixing was 0.005–0.01 mol/L. The optimal conditions for thermochemical experiment were selected using computer simulation of equilibria by the RRSU program [9]. Selected heats of mixing in the systems in question are presented in Tables 1–5. The data of calorimetric measurements were treated by the HEAT program [9] with inclusion of contributions of water ionization, $\Delta_r H_{(1)} = -56.90$ kJ/mol [13], amino acid protonation ($\Delta_r H_{(5)} = -45.15$ kJ/mol and $\Delta_r H_{(6)} = -75.65$ kJ/mol [14] for histidine; $\Delta_r H_{(5)} = -53.55$ kJ/mol and $\Delta_r H_{(6)} = -100.80$ kJ/mol [15] for

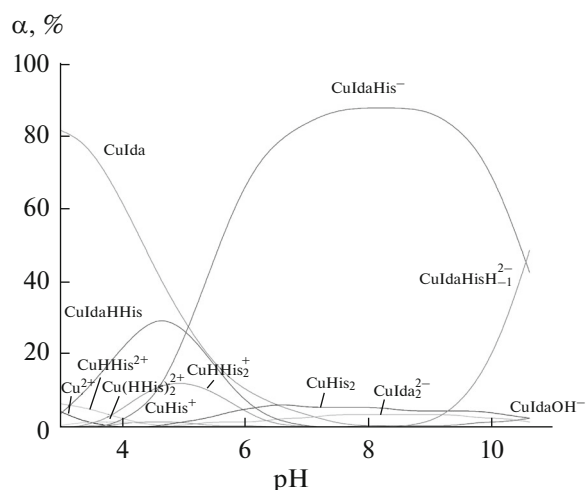


Fig. 2. Species abundance curves for the CuIda–His–H⁺ system at CuIda : His = 1 : 1 ($C_{\text{His}} = 0.01$ mol/L).

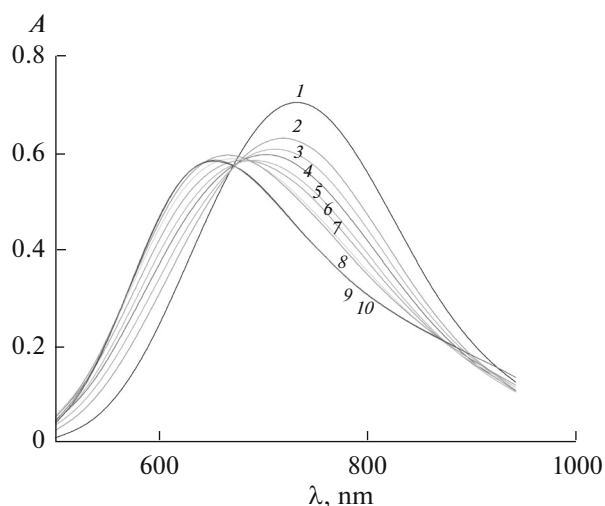


Fig. 4. UV/Vis spectra of solutions in the Cu–Ida–His system at 1 : 1 : 1 ratio and pH (1, $C_{\text{His}} = 0$) 5.97, (2) 4.45, (3) 4.71, (4) 4.95, (5) 5.17, (6) 5.41, (7) 5.66, (8) 5.99, (9) 9.00, (10) 9.83. $C_{\text{CuIda}} = 0.002$ mol/L; $l = 5$ cm, 20°C, $I = 0.5$ (KNO₃).

lysine; and $\Delta_r H_{(5)} = -51.92$ kJ/mol and $\Delta_r H_{(6)} = -99.00$ kJ/mol [15] for ornithine), and the formation of hydroxy chelate and mixed complexes of the above-indicated composition to the overall heat. The contributions of all other reactions did not exceed the experimental error under these conditions.

For the MIda–L systems (M = Cu, Ni; L = His, Orn, Im), UV/Vis spectra were recorded, which are presented in Figs 4–7. A series of solutions were prepared that contained a metal chelate and an amino acid and corresponded to different degrees of amino acid neutralization and, as a consequence, different contents of mixed-ligand species. The absorption was measured on a KFK-3 spectrophotometer in 5-cm

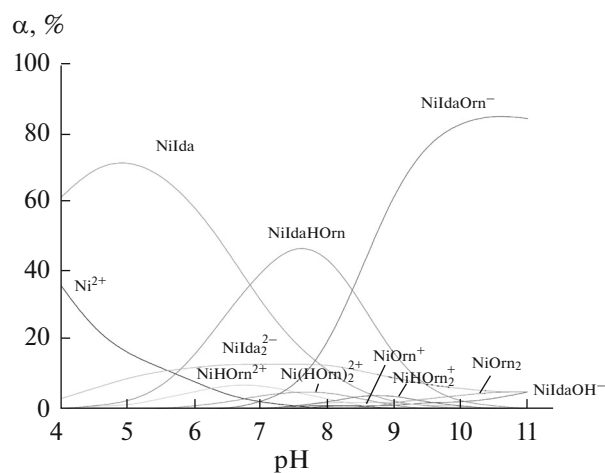


Fig. 3. Species abundance curves for the NiIda–Orn–H⁺ system at NiIda : Orn = 1 : 1 ($C_{\text{Orn}} = 0.01$ mol/L).

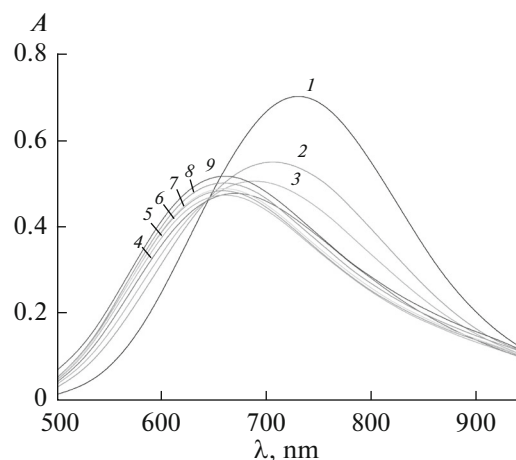


Fig. 5. UV/Vis spectra of solutions in the Cu–Ida–Orn system at 1 : 1 : 1 ratio and pH (1, $C_{\text{Orn}} = 0$) 5.97, (2) 5.96, (3) 6.50, (4) 7.21, (5) 8.16, (6) 8.74, (7) 9.12, (8) 9.44, (9) 10.11. $C_{\text{CuIda}} = 0.002$ mol/L; $l = 5$ cm, 20°C, $I = 0.5$ (KNO₃).

cells. A 0.5 M solution of KNO₃ served as the reference solution. The spectrophotometric data were treated by the FTMT program [9]. The spectra of single mixed-ligand species for Cu(II) are shown in Fig. 8.

RESULTS AND DISCUSSION

The complex formation involving histidine is the subject of numerous papers and reviews. Owing to the presence of three functional groups (–NH₂, –COOH, and –N_{Im}), histidine is a potentially tridentate ligand. However, very often, depending on the pH or steric hindrance, histidine is coordinated in a bidentate fashion in three different modes: {N_{am}, N_{Im}}, {N_{am}, O},

Table 1. Heats of mixing of an alkaline solution of histidine (HHis · HCl, 0.7544 mol/kg of solution + NaOH, 1.510 mol/kg of solution) with solutions of MIda at 298.15 K and $I = 0.5$ (KNO₃)

Weight of His solution, g	Concentration after mixing, mol/L		$\Delta_{\text{mix}}H$, kJ/mol His	$\Delta_{\text{mix}}H - \Delta_{\text{dil}}H$, kJ/mol His
	His ⁻	H ⁺		
$C_{\text{CuIIda}} = 0.005051$ mol/L				
0.33895	0.005106	-0.0000104	-50.43	-49.25
0.33955	0.005115	-0.0000104	-50.10	-48.91
0.35625	0.005367	-0.0000109	-48.70	-47.52
0.31805	0.004791	-0.0000098	-50.76	-49.57
0.32235	0.004856	-0.0000099	-50.33	-49.14
$C_{\text{NiIIda}} = 0.005063$ mol/L				
0.32535	0.004901	-0.0000100	-37.08	-35.89
0.34005	0.005122	-0.0000104	-36.72	-35.53

Table 2. Heats of mixing of an alkaline solution of ornithine (HOrn · HCl, 0.7947 mol/kg of solution + NaOH 1.554, mol/kg of solution) with solutions of MIda at 298.15 K and $I = 0.5$ (KNO₃)

Weight of Orn solution, g	Concentration after mixing, mol/L		$\Delta_{\text{mix}}H$, kJ/mol Orn	$\Delta_{\text{mix}}H - \Delta_{\text{dil}}H$, kJ/mol Orn
	Orn ⁻	H ⁺		
$C_{\text{CuIIda}} = 0.005014$ mol/L				
0.32040	0.005084	0.0002296	-32.07	-30.76
0.31790	0.005045	0.0002278	-32.46	-31.16
0.35925	0.005701	0.0002575	-29.61	-28.31
$C_{\text{NiIIda}} = 0.005055$ mol/L				
0.34475	0.005471	0.0002471	-31.89	-30.59
0.31605	0.005015	0.0002265	-29.97	-28.67
0.24180	0.003837	0.0001733	-31.03	-29.72

Table 3. Heats of mixing of an alkaline solution of ornithine (HOrn · HCl, 1.351 mol/kg of solution + NaOH, 1.385 mol/kg of solution) with solutions of MIda at 298.15 K and $I = 0.5$ (KNO₃)

Weight of Orn solution, g	Concentration after mixing, mol/L		$\Delta_{\text{mix}}H$, kJ/mol Orn	$\Delta_{\text{mix}}H - \Delta_{\text{dil}}H$, kJ/mol Orn
	Orn ⁻	H ⁺		
$C_{\text{CuIIda}} = 0.005014$ mol/L				
0.17550	0.004734	0.004614	-32.56	-31.34
0.18230	0.004918	0.004793	-31.51	-30.28
$C_{\text{NiIIda}} = 0.005055$ mol/L				
0.19045	0.005138	0.005007	-18.39	-17.16
0.16910	0.004562	0.004446	-18.67	-17.44

and {N_{lm},O}. In recent studies thoroughly carried out using various sorts of spectroscopy, first of all, ESR [16, 17], the structure of the CuH_nHis₂ complexes ($n = 0, 1, 2$) in solution was established reliably. Lysine and ornithine are so-called basic amino acids. The presence of a highly basic additional amino group together with the glycinate moiety not only increases the potential (actual) denticity of these amino acids but also promotes their polyvariant coordination. In neu-

tral solutions, ornithine and lysine form protonated complexes of the M(HL)₂ type. The deprotonated MHL₂ and ML₂ complexes are formed in alkaline solutions. Ornithine behaves similarly to lysine in which the second δ -amino group is rarely if at all involved in coordination, as indicated by most publications [12]. The details of coordination of diamino-carboxylate ligands to copper(II) cations were studied [15] by potentiometry, calorimetry, and NMR relax-

Table 4. Thermodynamic parameters of the formation reactions of mixed-ligand complexes in the MIda–L[–]–H⁺ systems (L = His, Lys, Orn, Im) at 298.15 K and I = 0.5 (KNO₃)

Equilibrium	logK	–Δ _r G ⁰ , kJ/mol	Δ _r H, kJ/mol	Δ _r S, J/mol K
CuIda + His [–] = CuIdaHis [–]	7.81 ± 0.02	44.58 ± 0.11	–49.88 ± 0.56	–17.8 ± 1.9
CuIda + His [–] + H ⁺ = CuIdaHHis	12.88 ± 0.04	73.52 ± 0.23	–67.3 ± 1.5	20.9 ± 5.1
CuIda + HHis = CuIdaHis	3.86 ± 0.04	22.03 ± 0.23	–22.2 ± 1.5	–0.6 ± 5.1
2CuIda + His [–] = (CuIda) ₂ His [–]	10.25 ± 0.08	58.51 ± 0.46	–57.4 ± 1.3	3.8 ± 4.6
CuIda + Im = CuIdaIm	4.16 ± 0.11	23.74 ± 0.63	–33.51 ± 0.77	–32.8 ± 3.3
CuIda + 2Im = CuIdaIm ₂	6.01 ± 0.10	34.30 ± 0.57	–47.8 ± 4.0	–45 ± 14
CuIda + Gly [–] = CuIdaGly [–]	6.09 ± 0.04	34.76 ± 0.23	–31.67 ± 0.88	10.4 ± 3.1
CuIda + Orn [–] = CuIdaOrn [–]	6.88 ± 0.05	39.27 ± 0.29	–31.03 ± 0.60	27.6 ± 2.2
CuIda + Orn [–] + H ⁺ = CuIdaHOrn	16.15 ± 0.03	92.18 ± 0.17	–83.54 ± 0.65	29.0 ± 2.3
CuIda + HOrn = CuIdaHOrn	5.63 ± 0.03	32.14 ± 0.17	–31.62 ± 0.65	1.7 ± 2.3
CuIda + Lys [–] = CuIdaLys [–]	7.00 ± 0.09	39.96 ± 0.51	–30.13 ± 0.35	33.0 ± 2.1
CuIda + Lys [–] + H ⁺ = CuIdaHLys	16.67 ± 0.06	95.15 ± 0.34	–84.26 ± 0.31	36.5 ± 1.5
CuIda + HLys = CuIdaHLys	5.96 ± 0.06	34.02 ± 0.34	–30.66 ± 0.31	11.3 ± 1.5
NiIda + His [–] = NiIdaHis [–]	7.27 ± 0.03	41.50 ± 0.17	–35.26 ± 0.13	20.9 ± 0.7
NiIda + Orn [–] = NiIdaOrn [–]	6.46 ± 0.04	36.87 ± 0.23	–28.71 ± 0.12	27.4 ± 0.9
NiIda + Orn [–] + H ⁺ = NiIdaHOrn	14.85 ± 0.04	84.76 ± 0.23	–71.83 ± 0.17	43.4 ± 1.0
NiIda + HOrn = NiIdaHOrn	4.33 ± 0.04	24.72 ± 0.23	–19.91 ± 0.17	16.1 ± 1.0
NiIda + Lys [–] = NiIdaLys [–]	5.49 ± 0.07	31.34 ± 0.40	–22.36 ± 0.54	30.1 ± 2.3
NiIda + Lys [–] + H ⁺ = NiIdaHLys	15.24 ± 0.06	86.99 ± 0.34	–73.90 ± 0.61	43.9 ± 2.3
NiIda + HLys = NiIdaHLys	4.53 ± 0.06	25.86 ± 0.34	–20.30 ± 0.61	18.6 ± 2.3

Table 5. Thermodynamic parameters of the formation reactions of complexes in the M²⁺–Ida^{2–}–L–H⁺ systems (M = Cu, Ni; L = His[–], Lys[–], Orn[–], Im, Gly[–], En) (Δ_rH in kJ/mol, Δ_rS in J/mol K)

Reaction	Cu			Ref.	Ni			Ref.
	log K	Δ _r H	Δ _r S		log K	Δ _r H	Δ _r S	
MIda + His = MIdaHis	7.8	–49.9	–18	*	7.3	–35.3	21	*
MIda + HHis = MIdaHHis	3.9	–22.2	–1	*				*
MIda + Im = MIdaIm	4.2	–33.5	–33	*				*
M + His = MHis	10.2	–48.4	33	[11]	8.7	–33.4	54	[21]
					8.6	–31.5	58	[8]
MIda + Orn = MIdaOrn	6.9	–31.0	28	*	6.5	–28.7	27	*
MIda + HOrn = MIdaHOrn	5.6	–31.6	2	*	4.3	–19.9	16	*
MIda + Lys = MIdaLys	7.0	–30.1	33	*	5.5	–22.4	30	*
MIda + HLys = MIdaHLys	6.0	–30.7	11	*	4.5	–20.3	19	*
MGly + Gly = MGly ₂	6.9	–28.7	35	[22]	5.0	–20.3	28	[22]
MGly + En = MNtaEn	9.4	–55.5	–7	[19]				
MNta + En = MNtaEn	7.7	–61.7	–59	[7]	7.2	–34.1	24	[7]
MIda + En = MIdaEn	7.9	–44.9	1	[20]	6.3	–32.3	13	[20]

* This work.

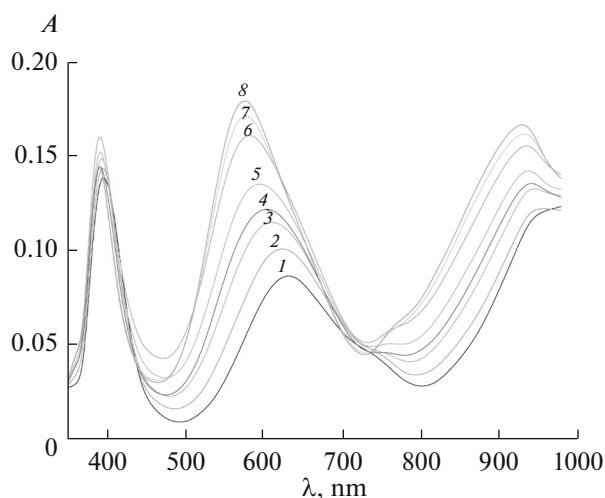


Fig. 6. UV/Vis spectra of solutions in the Ni–Ida–His system at 1 : 1 : 1 ratio and pH (1, $C_{\text{His}} = 0$) 6.88, (2) 4.71, (3) 5.03, (4) 5.21, (5) 5.38, (6) 5.93, (7) 6.91, (8) 10.11. $C_{\text{NiIda}} = 0.005$ mol/L; $l = 5$ cm, 20°C , $I = 0.5$ (KNO₃).

ation. It was shown that lysine is coordinated according to the glycinate type, while in the complexes of other diaminocarboxylates (dapa, daba, orn), the second amino group is involved in coordination. In [18], differences between the coordination (denticity) of ornithine and lysine were demonstrated on the basis of thermochemical data. Thus, in most cases of complex formation, the lysine denticity is less than three.

Mixed complex formation involving 3*d*-metal iminodiacetates and amino acids has been studied previously in a number of papers [3–6]. In particular, in [3–5], the stability constants of the MIdaL complexes

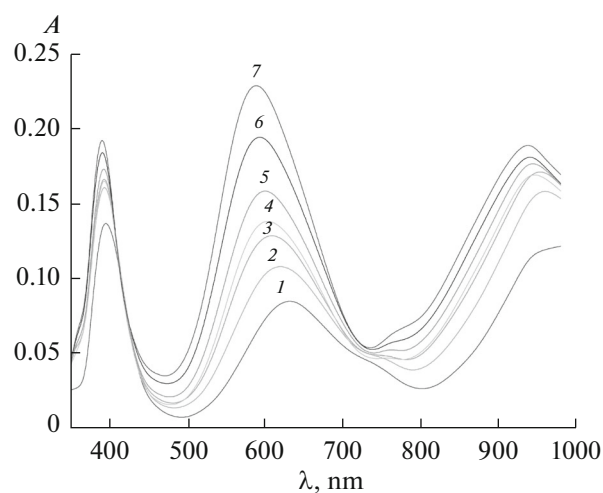


Fig. 7. UV/Vis spectra of solutions in the Ni–Ida–Orn system at 1 : 1 : 1 ratio and pH (1, $C_{\text{Orn}} = 0$) 6.88, (2) 6.81, (3) 7.63, (4) 7.95, (5) 8.26, (6) 8.87, (7) 10.16. $C_{\text{NiIda}} = 0.005$ mol/L; $l = 5$ cm, 20°C , $I = 0.5$ (KNO₃).

(M = Cu, Ni, Zn, Cd; L = Gly, Ala, Phe, Leu, Aln, Asp) were calculated from the results of potentiometric measurements. In [6], the Cu(L-/D-His)(AA) complexes (AA = L-/D-Asn, L-Gln, L-Ser, L-homoserine, L-citrulline (L-Cit)) involving L- or D-amino acids were isolated in the crystalline state. The authors also studied mixed complex formation of Cu(II) histidinate with iminodiacetate and ethylenediamine. For most amino acids, the absorption maximum of the mixed complexes is in the range of 610–620 nm, whereas for CuIdaHis and CuHisEn⁺, the absorption maxima are at 656 and 585 nm, respectively. The stability constants of the ternary Cu(II) complexes with L-His and L-Asn, L-Gln, L-Ser, or L-Thr were determined by potentiometric titration at 25°C and ionic strength of 0.1 M (KNO₃). The stereoselectivity of formation of these complexes detected by the authors is caused by hydrogen bonding between the histidine carboxyl group and amide or alcohol group present in the amino acid side chain. The ϵ and λ_{max} values for CuIdaHis and CuHisEn⁺ (656 and 585 nm, respectively) found in [6] are in good agreement with the values obtained in the present work. Thus, the stability constants and the heats of formation of MIdaL (M = Cu, Ni; L = His, Orn, Lys) were obtained here for the first time.

The calculated thermodynamic parameters of the reactions are given in Table 4. The addition of the amino acid residue is accompanied by a negative enthalpy change and either positive or negative entropy change. Since the 3*d*-metal(II) iminodiacetate complexes are coordinatively unsaturated, the attachment of a second ligand to MIda(H₂O)_{*n*} (*n* = 2, 3) leads to displacement of water molecules from the inner coordination sphere, which accounts for generally positive $\Delta_r S$ value. For Ni complexes, the $\Delta_r S$ value is much greater than for Cu(II) complexes. The

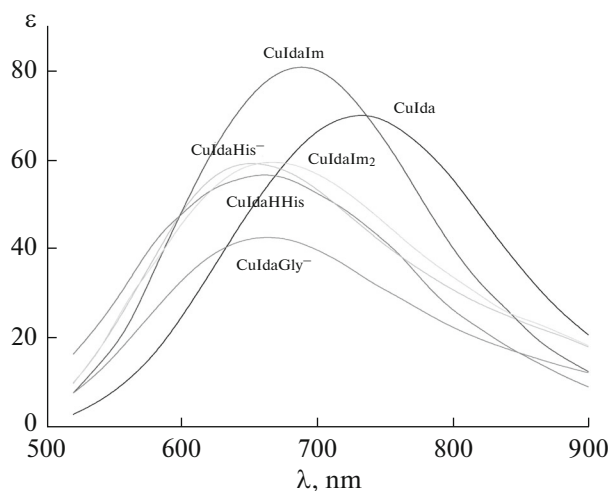


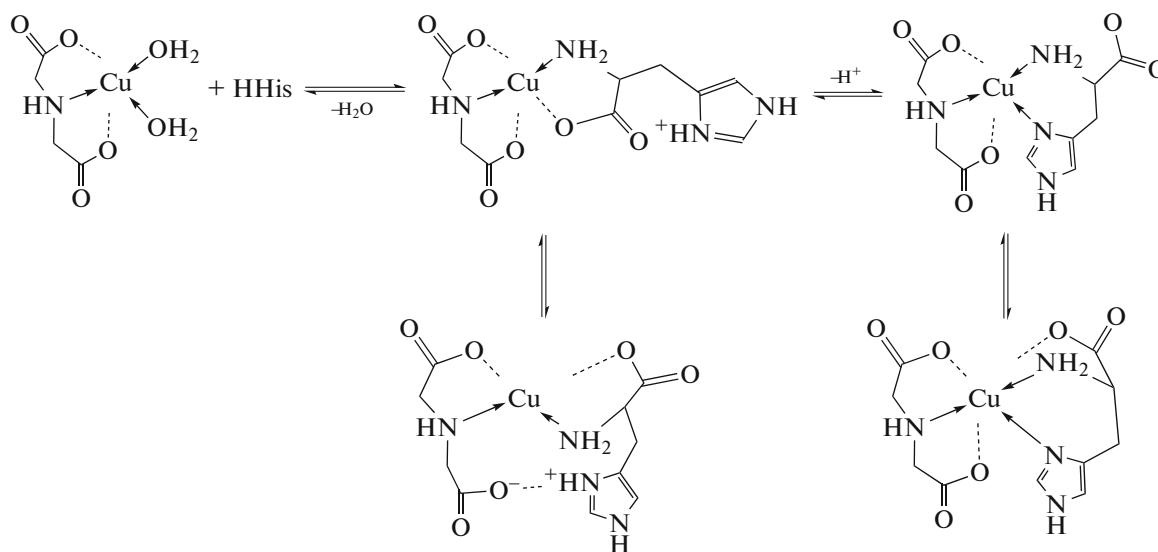
Fig. 8. UV/Vis spectra of mixed-ligand Cu(II) complexes; 20°C , $I = 0.5$ (KNO₃).

tetragonal distortion of the Cu(II) cation results in two more, strongly bound, water molecules being actually displaced from the equatorial position. The heat of formation of the MIdaL complexes is mainly composed of contributions of bond cleavage between the central ion and two or three water molecules, displacement of some water molecules from the hydrate shells of the ligands, and bond formation between the central ion and the ligands. Heat evolution upon the attachment of amino acid residues to MIda indicates that bonding between the metal chelate and the additional ligand L is an enthalpically favorable process, which compensates for heat expenditure for dehydration of the central ion and ligands.

While comparing the thermodynamic characteristics of these reactions involving the indicated amino acids, one should note that the values obtained for ornithine and lysine differ little (Table 4). The values obtained for His differ markedly both for Cu and Ni complexes. The reason is the possibility of both (N_{am} , N_{im}) and (N_{am} , COO) bidentate coordination as well as (N_{am} , N_{im} , COO) tridentate coordination for the histidine residue. The heat of reactions (16) is much higher for His than for the attachment of Orn or Lys. This implies that the histidine residue is coordinated in the MIdaHis⁻ complexes via the nitrogen atoms of the amino group and the imidazole ring. In most studies devoted to the structure of Cu(II) complexes with histidine [17, 18], the histidine anion is shown to be coordinated, most often, via two donor nitrogen atoms (so-called histamine-like coordination). This is accompanied by closure of a six-membered metal-containing ring. Indeed, the heat of reaction (16) with histidine is

very close to the heat of formation of MHis⁺, on the one hand, and to the heat of addition of ethylenediamine En to MIda, on the other hand (Table 5).

The earlier results on the thermodynamics of mixed complex formation involving metal nitrilotriacetates show that in the protonated MNtaHHis⁻ complexes, the zwitter-ion form of histidine is coordinated via the less basic imidazole moiety. The similar values for the addition constants for HHis[±] and Im to MNta⁻, as well as the similar patterns of the absorption spectra and close molar absorption coefficients of MNtaIm⁻ and MNtaHHis⁻ support the assumed histidine coordination via the imidazole moiety. In CuIdaHHis, the histidine residue can also be coordinated via the imidazole nitrogen atom. This assumption was verified by additional investigation of the CuIda-Im system. The stability constants of the CuIdaIm_i complexes, $i = 1, 2$, were calculated from spectrophotometric data, while the heats were found from the calorimetric data. The CuIdaIm_i stability constants that we found are in reasonable agreement with the potentiometric data reported in [23]. The close heats of glycinate ion and imidazole addition to CuIda preclude unambiguous determination of the HHis[±] coordination mode from the thermodynamic data alone. However, the spectra of solutions of CuIdaIm and CuIdaHHis are markedly different. Meanwhile, similarity of the spectra of solutions of single mixed-ligand species, CuIdaGly⁻ and CuIdaHHis (Fig. 8), is indicative of glycinate type histidine coordination in CuIdaHHis rather than coordination via the imidazole moiety (Scheme 1).



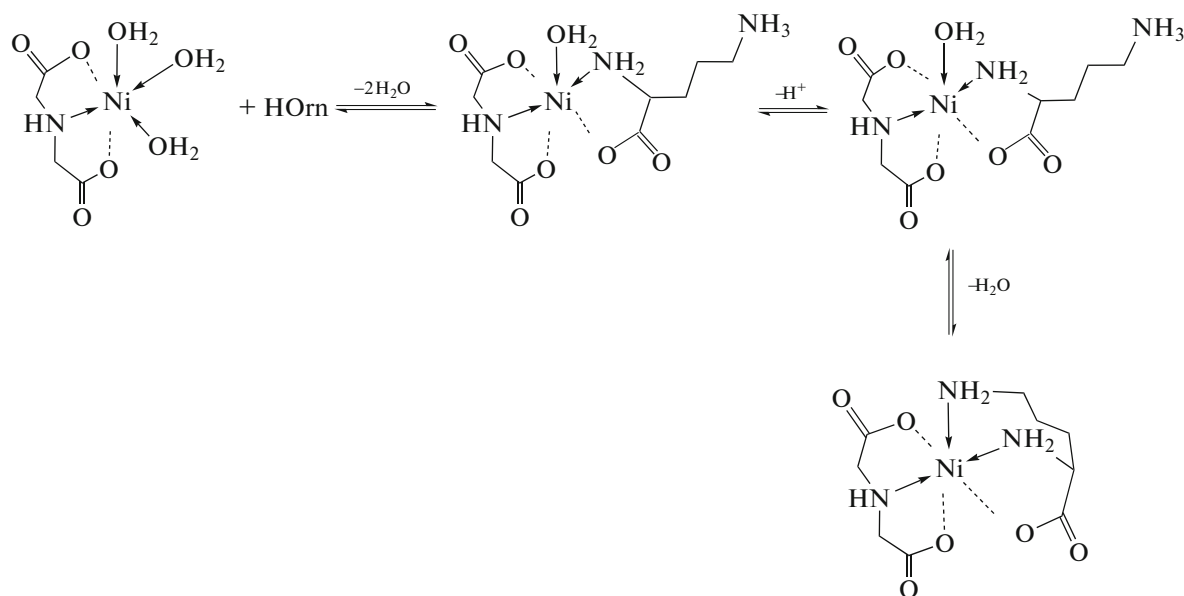
Scheme 1.

The heats of addition of L⁻ and HL[±] (L = Lys, Orn) to CuIda coincide within the confidence inter-

vals, which suggests similar modes of coordination in the mixed complexes. The fact that these heats are

close to both the heat of formation of the glycinate complexes in the second stage, which is considered as the model reaction, and the heat of reaction (16) for Gly (Table 5) attests to the glycinate type N,O-coordination of these amino acid residues. The addition of the ornithine anion to Ni iminodiacetate was found to be somewhat more exothermic than that for the zwitter-ion form. In the case of lysine, these values are virtually equal. The spectra of solutions containing NiIdaHis⁻, NiIdaEn, and NiIdaOrn⁻ show a similar growth of the absorption band at 600 nm. This also points to participation of two amino groups in the coordination of the ornithine residue. This provides

evidence for the tridentate (N, N, O) coordination of ornithine in NiIdaOrn⁻. Presumably, the equilibrium between the bi- and tridentate ornithine forms of the mixed complex is shifted toward the latter (Scheme 2). Thus, the average denticity of ornithine in this complex is greater than two. Lysine, apparently, is not coordinated in this fashion because of the lower stability of larger chelate ring. In NiIdaLys⁻ and NiIdaHLys, the lysine residue is coordinated according to the glycinate type. Evidently, on going from NiIdaLys⁻ to NiIdaHLys, the uncoordinated ε-amino group is protonated.



Scheme 2.

We used the obtained results and published data on the formation of Cu(II) and Ni complexes with amino acids to calculate the thermodynamic parameters of co-proportionation reactions



Table 6. Thermodynamic parameters of the reactions $\text{MY}_2 + \text{ML}_2 = 2\text{MYL}$ ($\text{Y} = \text{Nta, Ida}$; $\text{L} = \text{His, Lys, Orn}$) at 298.15 K and $I = 0.5$ (KNO_3) ($\Delta_r H$ in kJ/mol; $\Delta_r S$ in J/mol K)

M	L	Nta			Ida		
		log K	$\Delta_r H$	$\Delta_r S$	log K	$\Delta_r H$	$\Delta_r S$
Cu	His	3.7	7.8	97	2.5	-6.2	28
	Orn	5.9	0.2	113	3.4	0.6	67
	Lys	7.4	-6.8	118	4.1	-4.7	63
Ni	His	1.3	35.2	144	0.8	35.3	133
	Orn	4.8	25.2	176	3.1	15.2	111
	Lys	6.0	8.0	142	2.5	7.8	75

Previously, we showed, in relation to M–Nta–En systems [7], that the equilibrium constants of co-proportionation reaction (18) are high, that is, the mixed MNtaEn⁻ complexes are fairly stable against decomposition to complexes with identical ligands. The key reason for this is the increase in the Nta denticity in MNtaEn⁻ with respect to $\text{M}(\text{Nta})_2^{4-}$. The thermochemical data obtained in [7] confirmed this conclusion. It can be seen from Table 6 that on going from His to Lys, the equilibrium constant of reaction (18) for Nta sharply increases, which can also be due to increase in the Nta denticity in the mixed complex. In the series His–Orn–Lys, the actual denticity of the amino acid residue in Cu(II) and Ni complexes decreases from 3 to 2, which allows the potentially tetradentate nitrilotriacetate ion to fully implement its denticity. The considered co-proportionation reactions are entropically favorable. Their large positive entropy is due to both displacement of the inner-sphere water molecules (in the case of Orn and Lys) and liberation of the outer-sphere water molecules

from the hydrate shells of $M(\text{Nta})_2^{4-}$ upon the formation of mixed complexes. For metal iminodiacetates, there is no effect of increasing denticity of the chelating agent in the mixed MIdaL complex with respect to the $M(\text{Ida})_2^{2-}$. This results in lower $\log K_{18}$ and $\Delta_r S_{18}$ values for reactions involving metal iminodiacetates (Table 6).

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