Thermodynamic Characteristics of Complexation between Ho³⁺ and Ethylenediamine-*N,N*'-Disuccinic Acid in Aqueous Solutions at 298.15 K

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Abstract—The thermodynamic characteristics of complexation between ethylenediamine-*N,N*'-disuccinic acid (H_4Y; EDDA) and Ho^{3+} ion were determined calorimetrically and potentiometrically at 298.15 K and ionic strengths of 0.1, 0.5, 1.0, and 1.5 (KNO_3). The $\log K$, $\Delta_r G$, $\Delta_r H$, and $\Delta_r S$ values for the formation of HoY^- and HOHY complexes were calculated at the studied and zero ionic strength values. The changes in thermodynamic parameters of the reactions are discussed.

Ethylenediamine-*N,N*'-disuccinic acid (EDDA) can be regarded as the closest structural analogue of the commonly used ethylenediaminetetraacetic acid (EDTA).

Like EDTA, EDDA forms strong chelate complexes with ions of most metals, while at the same time acting as a stereo-specific ligand by forming complexonates that can have both five- and six-membered chelate rings [1, 2]. These complexing agents are of interest as ligands that can form rather strong water-soluble complexes with metal ions and exhibit high biological activity [3].

Selective extraction of complexes from solutions is the main method for separating lanthanides when producing them in pure form. The formation of lanthanide complexes with complexing agents and amino acids is of interest in terms of bioinorganic chemistry, since Ln(III) ions and their complexes are widely used as efficient relaxants, luminescent tags, and paramagnetic probes in medicine for diagnosing various diseases [3–6].

The thermodynamic characteristics of complexation between EDDA and holmium(III) and especially the formation of protonated complex species remain poorly studied.

The interaction between EDDA and Ho^{3+} at 298.15 K and ionic strength of 0.1 (KCl) was studied by potentiometric titration [8]; the constants were determined for the two particles, HoY^- ($\log\beta_{HoY^-} = 13.10 \pm 0.01$) and HoHY ($\log\beta_{HoHY} = 6.78 \pm 0.04$). Babich and Gorelov [9] conducted a polarographic study of this system at the same ionic strength of 0.1 (KNO_3) and determined the constant $\log\beta_{HoY^-} = 13.60 \pm 0.03$.

It is clear from the literature data that the values of the constant for the HoY^- species are close, but there is the only value for the HoHY species. Neither enthalpy nor entropy characteristics of complexation in the $Ho^{3+}-H_4Y$ system have been reported in the literature.

This study aimed at determining the heat effects and equilibrium constants of complexation between Ho^{3+} and ethylenediamine-*N,N*'-disuccinic acid both calorimetrically and potentiometrically, investigating the effect of concentration of a background electrolyte, and calculating the complete set of thermodynamic parameters of complexation.

EXPERIMENTAL

Ethylenediamine-*N,N*'-disuccinic acid synthesized in the Tver State University was used for this study [11]. The content of the basic substance in EDDA determined by alkalimetric titration was 99.36%. Neodymium(III) nitrate solution was prepared using a recrystallized sample of the compound of chemical purity grade. Holmium(III) concentration in the solution was determined complexonometrically [12]. Twice recrystallized potassium nitrate of pure for analysis grade was used as a background electrolyte.

Nitric acid solution was prepared by diluting concentrated HNO_3 of chemical purity grade. Concentra-

Table 1. Logarithms of the stability constants in the Ho^{3+}–ethylenediamine-N,N'-disuccinic acid system for different ionic strength (KNO_3) values at 298.15 K

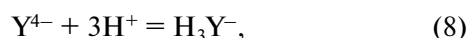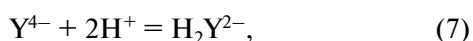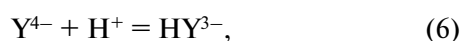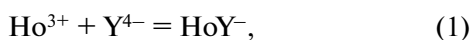| I	$\log\beta$ ($Ho^{3+} + Y^{4-} = HoY^-$)	$\log\beta$ ($Ho^{3+} + HY^{3-} = HoHY$)	$\log\beta$ ($Ho^{3+} + H_2Y^{2-} = HoH_2Y^+$)
0.1	13.02 ± 0.02	7.26 ± 0.02	3.37 ± 0.03
0.5	12.69 ± 0.03	6.68 ± 0.04	3.37 ± 0.03
1.0	11.83 ± 0.04	6.64 ± 0.04	3.73 ± 0.03
0	15.99 ± 0.53	9.44 ± 0.52	4.53 ± 0.10

tions of KOH and HNO_3 were determined using the regular titrimetric methods.

We performed a series of potentiometric titrations of the solutions containing $Ho(NO_3)_3$ and H_4Y at $Ho(III) : H_4Y$ ratios varying from 1 : 1 to 1 : 2 with KOH solution in the pH range 2.3–7.8 at ionic strengths I = 0.1, 0.5, and 1.0 (KNO_3). In all the experiments, ligand concentration was approximately 0.005 mol/L. The details of potentiometric experiment are found in [7]. The titration curves in the Ho^{3+}–EDDA system are similar at different $Ho^{3+} : Y^{4-}$ ratios. Table 1 lists the resulting data.

Heat effects were measured in an ampoule calorimeter that was equipped with an isothermal shell and a thermistor temperature sensor and was capable of automatically recording the temperature–time curve. The reliability of operation of the device was verified based on the heat of solution of KCl in water at 298.15 K. The details of the calorimetry experiment were described earlier [10]. Samples were weighed on a VLR-200 balance with an accuracy of 5×10^{-5} g. The heats of mixing of solutions of holmium nitrate and EDDA were measured at 298.15 K and ionic strength of 0.5, 1.0, and 1.5; the heats of dilution of $Ho(NO_3)_3$ in background electrolyte solutions (KNO_3) were measured at the same concentrations. The pH values of the aqueous solution of background electrolyte remained unchanged. The resulting data are listed in Table 2.

RESULTS and DISCUSSION

The results of potentiometric titration were processed using the scheme that takes into account the occurrence of the following reactions:

$$Ho^{3+} + Y^{4-} = HoY^-, \tag{1}$$

$$Ho^{3+} + HY^{3-} = HoHY, \tag{2}$$

$$Ho^{3+} + H_2Y^{2-} = HoH_2Y^+, \tag{3}$$

$$Ho^{3+} + H_2O = HoOH^{2+} + H^+, \tag{4}$$

$$Ho^{3+} + 2H_2O = Ho(OH)_3 + 2H^+, \tag{5}$$

$$Y^{4-} + H^+ = HY^{3-}, \tag{6}$$

$$Y^{4-} + 2H^+ = H_2Y^{2-}, \tag{7}$$

$$Y^{4-} + 3H^+ = H_3Y^-, \tag{8}$$

$$Y^{4-} + 4H^+ = H_4Y, \tag{9}$$

$$H^+ + OH^- = H_2O. \tag{10}$$
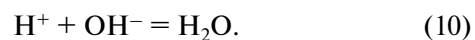
The calculation of the equilibrium compositions of the solutions in the Ho(III)–EDDA system using RRSU software [15] revealed the pH regions that are most informative for calculating $\log K$; the occurrence of the following processes was taken into account: complexation (1)–(3), hydrolysis (4) and (5), and acid–base interactions of the ligand (6)–(10).

The stability constants of the resulting complexes were determined by processing the titration curve data using the PHMETR software [15], which is intended for processing the potentiometric measurements in the systems containing an arbitrary number of reactions according to the measured equilibrium concentration of one of the species.

The constants of acid–base interactions of EDDA were taken from [16]; the stability constants determined in [8] were used as the initial approximations for the calculations in the Ho^{3+}–EDDA system; hydrolysis of the Ho^{3+} ion was taken into account based on the data [17].

It was demonstrated by varying the $\log K$ value that the system is expected to be sensitive to presence of such ionic species as HoY^- $HoHY$, and HoH_2Y^+ in the solution. Data processing has shown that the content of the hydroxo-complex in the studied pH range is negligibly small; the yield of the HoHY complex in the pH range of 2.5–4 is >45%. The yield of the HoY^- complex at pH $\geqslant$ 6.5 is 100%. Table 1 lists the resulting stability constants. The logarithms of the stability constants are given as the weighted mean values obtained in 3–5 parallel experimental runs. The error was determined as a possible arithmetic mean deviation at 95% confidence interval. The close values of the constants determined at different concentration ratios indicate that these values are reliable and the calculation scheme is adequate. The constants were recalculated for the zero ionic strength using the equation with a single individual parameter [14]. The resulting constants (Table 1) differ from the published data. However, since the potentiometric measurements were performed in this study at different ionic strengths and the contributions of most accompanying processes were strictly taken into account, we believe that our data are more reliable.

Table 2. Heats of reaction between $Ho(NO_3)_3$ (0.5166 mol/kg) and ethylenediamine-N,N'-disuccinic acid (H_4Y) solutions at 298.15 K

Ionic strength	Sample, g	$C_Y^0 \times 10^3$	$C_{Nd}^0 \times 10^3$	$C_{H^+}^0 \times 10^3$	$\Delta_{mix}H$	$-\Delta_{dil}H^*$
		mol/L			kJ/mol	
pH_des 10.64–10.69						
0.5	0.50775	9.9780	5.624	3.9620	−20.969	0.5
	0.49365	9.9780	5.467	3.9620	−21.925	
	0.50225	9.9780	5.563	3.9620	−20.753	
	0.52570	9.9780	5.822	3.9620	−20.997	
1.0	0.57240	9.9600	6.339	4.1900	−22.403	1.0
	0.60485	9.9600	6.699	4.1900	−22.327	
	0.58630	9.9600	6.493	4.1900	−23.977	
	0.61190	9.9600	6.777	4.1900	−22.623	
1.5	0.57540	10.000	6.373	1.5330	−29.567	1.5
	0.59310	10.000	6.569	1.5330	−29.610	
	0.57575	10.000	6.377	1.5330	−27.695	
	0.59405	10.000	6.539	1.5330	−28.407	
pH_des 3.7–3.75						
0.5	0.58775	11.930	6.049	7.480	15.543	3.766 ± 0.021
	0.51680	11.930	5.318	7.480	16.246	
	0.55665	11.930	5.729	7.480	15.196	
	0.54380	11.930	5.596	7.480	16.773	
1.0	0.58430	12.150	6.471	7.510	18.175	3.723 ± 0.026
	0.59450	12.150	6.584	7.510	17.138	
	0.59785	12.150	6.621	7.510	17.990	
	0.59695	12.150	6.611	7.510	18.033	
1.5	0.59405	12.200	6.580	7.531	16.539	3.170 ± 0.026
	0.62640	12.200	6.938	7.531	16.967	
	0.57285	12.200	6.345	7.531	17.143	
	0.61525	12.200	6.662	7.531	17.552	

* The mean value from 3 or 4 experimental runs.

The stability of the HoY complex (Table 1) decreases approximately twofold as each sequential proton is attached; this can probably be attributed to weakening of coordination at the nitrogen atom and the corresponding succinic acid residue, which changes the chelate structure and reduces stability.

Calorimetric measurements were performed in the pH ranges corresponding to the maximum content of the complexes under study. The contribution of side reactions (water ionization, hydrolysis of holmium, and formation of hydrolyzed species) to the total heat effect turned out to be low and was properly taken into account. The calorimetric data were processed using the HEAT software [15]; the occurrence of complexation processes (1) and (2) and the acid–base interactions of the ligand were taken into consideration.

The calculations demonstrated that metal ion is 100% bound into the HoY^- complex in the pH range higher than 6.5. The contribution of processes (6) and (10) is ~12% and is taken into account due to correction for the heats of these processes through Eq. (11):

$$\Delta H_{HoY^-} = (\Delta_{mix}H - \Delta_{dil}H) \\ - \alpha_6 \Delta H_{HY^{3-}} - \alpha_{10} \Delta H_W, \qquad (11)$$

where $\Delta_{mix}H$ is the heat of mixing of 0.01 M EDDA solution neutralized to pH 10.7 with $Ho(NO_3)_3$ solution; $\Delta_{dil}H$ is the heat effect of dilution of $Ho(NO_3)_3$ in background electrolyte solutions; and $\alpha_6 \Delta H_{HY^{3-}}$ and $\alpha_{10} \Delta H_W$ are the corrections for the heats of processes (6) and (10), respectively.

The calculations demonstrated that the content of HoHY complex formed in the pH range of ~5.0–5.2 is

Table 3. Thermodynamic characteristics of the reactions of formation of holmium ethylenediamine disuccinate at $T = 298.15$ K

Process	Ionic strength	$-\Delta_r H$	$-\Delta_r G$	$\Delta_r S$, J/mol K
		kJ/mol		
Ethylenediamine-N,N'-disuccinic acid				
$Ho^{3+} + Y^{4-} = HoY^-$	0	6.92 ± 0.35	91.2 ± 3.0	282 ± 9
	0.5	15.27 ± 0.41	72.4 ± 0.1	191 ± 1
	1.0	17.85 ± 0.46	67.5 ± 0.2	166 ± 1
	1.5*	20.19 ± 0.39	67.2 ± 0.2	157 ± 1
$Ho^{3+} + HY^{3-} = HoHY$	0	0.75 ± 0.33	53.8 ± 2.9	177 ± 10
	0.5	7.53 ± 0.32	38.1 ± 0.1	102 ± 1
	1.0	9.03 ± 0.35	37.9 ± 0.2	96 ± 1
	1.5*	10.64 ± 0.42	35.7 ± 0.2	84 ± 2
Ethylenediamine-N,N,N',N'-tetraacetic acid [4]				
$Ho^{3+} + A^{4-} = HoA^-$	0.1	16.4	97.8	273

* The constants at ionic strength 1.5 were recalculated from the ionic strength using the equation with a single individual parameter [14] and were as follows: $\log\beta_{HoY^-} = 11.78 \pm 0.93$, $\log\beta_{HoHY} = 6.26 \pm 0.52$.

~27%; the content of HoY^- is ~30%, while the contribution of processes (1) and (6)–(9) to the heat is ~84%.

The heat of HoHY complex formation was calculated using the equation

$$\Delta H_{HoHY} = \{(\Delta_{mix}H - \Delta_{dil}H) \\ - \alpha_1\Delta H_{HoY^-} - \alpha_6\Delta H_{HY^{3-}} \\ - \alpha_7\Delta H_{H_2Y^{2-}} - \alpha_8\Delta H_{H_3Y^-} - \alpha_9\Delta H_{H_4Y}\}/\alpha_2, \quad (12)$$

where $\Delta_{mix}H$ is the heat of reaction between 0.01 M EDDA solution (pH 6.1) and $Ho(NO_3)_3$ solution; $\Delta_{dil}H$ is the heat of dilution of $Ho(NO_3)_2$ in the background electrolyte solution; α_2 is the degree of completeness of process (2); and $\alpha_1\Delta H_{HoHY^-}$, $\alpha_6\Delta H_{HY^{3-}}$, $\alpha_7\Delta H_{H_2Y^{2-}}$, $\alpha_8\Delta H_{H_3Y^-}$, and $\alpha_9\Delta H_{H_4Y}$ are corrections for heat of processes (1) and (6)–(9). The $\Delta H_{HY^{3-}}$, $\Delta H_{H_2Y^{2-}}$, $\Delta H_{H_3Y^-}$, ΔH_{H_4Y}, and ΔH_W values were taken from [18, 19].

Table 2 lists the ΔH_{HoY^-} and ΔH_{HoHY}, values calculated according to [15] at fixed ionic strengths as the mean values of 4–6 experimental runs. The confidence interval was assessed using the Student's t-test with the confidence level 0.95. The change in enthalpy in the processes (1) and (2) at zero ionic strength was calculated according to [14]. The small stability constant (Table 1) and low yield (~25%) of the complex species HoH_2Y make thermochemical measurements unreasonable as the heat effect is low, while error is high.

Table 3 shows the changes in thermodynamic characteristics of complexation in the Ho–H_4Y system.

The formation of the HoY^- complex is accompanied by the exotherm, whose absolute magnitude increases with ionic strength. There is a significant positive change in entropy.

The heat of formation of the HoY complex mainly consists of the contributions from detachment of bonding between the central ion and two or three water molecules, replacement of some water molecules from hydration shells of the ligand, and formation of bonds between the central ion and the ligand. The exothermicity of the reactions indicates that formation of bonds between the gadolinium ion and ligand (Y) is a favorable process in terms of enthalpy, whose $\Delta_r H$ value compensates for the heat input due to partial desolvation of the central ion and ligand. The close values of the heats of HoY ($\Delta_r H = -15.27 \pm 0.41$ kJ/mol) and HoEDTA ($\Delta_r H = -16.4 \pm 0.5$ kJ/mol [4]) indicates that their coordination spheres have similar structures.

An abrupt decrease in endothermicity upon the formation of protonated complexes is associated with the weakening of metal–nitrogen bond, while the protonation of a complexing agent molecule opens the corresponding glycinate cycle and reduces the ligand denticity, where the metal coordination sphere includes water molecules instead of the protonated acetate group. The thermodynamic functions of the protonated species of HoHY complexes are lower than those for the complexes with composition HoY^-. The N–Ho bond breaks easily during the formation of the

N−H bond, thus changing the chelate structure and reducing the denticity of the ligand and, as a result, decreasing the thermodynamic parameters. The structure of the coordination sphere of the protonated species HoHY becomes similar to that of the holmium−nitrilotriacetic acid (Nta) complex as indicated by the close values of their enthalpies of reactions ($\Delta_r H = -0.75 \pm 0.33$ kJ/mol for HoHY and $\Delta_r H = 0.96 \pm 0.38$ kJ/mol for HoNta [4]).

The significant positive changes in entropy during the formation of holmium complexonate are due to the release of a significant number of water molecules from hydration shells of the initial ions, which substantially overlaps the effect of decreasing number of species due to complexation.

The significant decrease in thermodynamic characteristics of ethylenediamine disuccinate complexes of holmium compared to ethylenediaminetetraacetic ones [3, 4] (Table 3) can be explained by the replacement of two five-membered glycinate metal cycles in EDTA complexes with six-membered β-alaninate cycles in EDDA complexes.

The complexation in the Ho(III)−EDDA system has been completely thermodynamically characterized for the first time.

ACKNOWLEDGMENTS

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