N,*N*-Bis(2-Hydroxyethyl)taurine: Synthesis, Structure, and Stability of the Complexes with Cobalt(II) and Nickel(II)

E. O. Zemlyakova[a], **A. V. Pestov**[a, b], **P. A. Slepukhin**[a], **E. I. Kapitanova**[b, *],
Yu. S. Petrova[b], **and L. K. Neudachina**[b]

[a]*Postovskii Institute of Organic Synthesis, Ural Branch, Russian Academy of Sciences, Yekaterinburg, Russia*
[b]*Ural Federal University Named after the First President of Russia B.N. Yeltsin, Yekaterinburg, Russia*
**e-mail: bagazeeva.e@gmail.com*

Abstract—The complex formation of *N*,*N*-bis(2-hydroxyethyl)taurine with cobalt(II) and nickel(II) ions is studied. The acidic ionization constant of the ligand is determined by the potentiometric method. The stability constants of the complexes with the metal ions are calculated. Bis(*N*,*N*-di(2-hydroxyethyl)taurinato)cobalt(II) (**II**) and bis(*N*,*N*-di(2-hydroxyethyl)taurinato)nickel(II) monohydrate DMF disolvate (**I**) are synthesized, and their structures are studied by X-ray diffraction analysis (CIF file CCDC no. 1822829 (**II**)).

INTRODUCTION

A regular change in the structures of chelating organic ligands makes it possible to reveal fine dependences of the compositions, structures, and properties of the related coordination compounds containing these ligands [1, 2]. This forms a basis for the target synthesis of coordination compounds of desired compositions and spatial structures [3, 4]. Taurine (2-aminoethanesulfonic acid) is a half indispensable amino acid in living organisms [5]. This makes it possible to use taurine for the preparation of pharmaceuticals [6] and main components of buffer solutions used for biochemical and physiological studies [7]. In the latter case, the N-substituted taurine derivatives are characterized by pK_a in a range of 6.15−8.35, which provides the necessary buffer capacity at physiological values of pH [8].

In the most cases, the biological activity of taurine and its derivatives is related to their complexation properties [9−11]. Logarithms of the stability constants of the taurine complexes with transition and alkaline-earth metal ions range from 5.0 to 6.5 [12]. The taurine derivatives can form stable complexes with metal ions. For example, the logarithm of the stability constant for the 1 : 1 copper(II) complex and 4-(2-hydroxyethyl)-1-piperazinethanesulfonic acid is 3.22 [13]. The complex formation of copper(II), cobalt(II), nickel(II), zinc(II), and manganese(II) with *N*-(2-acetamido)-2-aminoethanesulfonic acid was studied [14, 15]. The stability constants of the 1 : 1 complexes

range from 3.5 to 4.9 [15], and the logarithm of the stability constant for the copper(II) complex with this reagent (1 : 2 metal to ligand composition) reaches 8.04 [14]. One of the compounds used for the preparation of so-called biological Good's buffers is *N*,*N*-bis(2-hydroxyethyl)taurine (HL[1]). Its complexation properties are not described. The present study concerns the synthesis and investigation of the properties of the complexes formed by this compound with nickel(II) and cobalt(II) ions.

EXPERIMENTAL

Diethanolamine (98%, Sigma-Aldrich), a 30% aqueous solution of sodium vinyl sulfate (Sigma-Aldrich), and reagents $Ni(NO_3)_2 \cdot 6H_2O$, $Co(NO_3)_2 \cdot 6H_2O$, KCl, and KNO_3 (reagent grade) were used.

Synthesis of ligand HL[1]. A mixture of diethanolamine (9.6 mL, 0.1 mol) and a 30% solution of sodium vinyl sulfonate (44 mL, 0.1 mol) was refluxed for 24 h, and then the solution was evaporated to dryness on a rotor evaporator. Ethanol (20 mL) was added to the dry residue, and the mixture was brought to boiling and then cooled down at −20°C. The precipitate was filtered off and dried at room temperature to a constant weight. The yield was 19.03 g (81%).

For $C_6H_{14}NO_5SNa \cdot 1.5H_2O$

	C	H	N	S
Anal. calcd., %	27.48	6.48	5.34	12.21
Found, %	27.64	6.03	4.94	12.48

IR (ν, cm^{-1}): 3393 ν(OH), 2959 ν(CH), 1181 ν(S=O). ^{1}H NMR (D$_2$O), δ, ppm: 2.71 t, 4 H, (CH_2CH$_2$OH), 3.01 t, 2 H, (CH_2CH$_2$SO$_3$Na), 3.09 t, 2 H, (CH_2SO$_3$Na), 3.68 t, 4 H, (CH_2OH).

Synthesis of bis(*N,N*-di(2-hydroxyethyl)taurinato)nickel(II) (I). Ligand L^1 (0.376 g, 1.6 mmol) was dissolved in water (5 mL) and mixed with a solution of Ni(NO$_3$)$_2 \cdot$ 6H$_2$O (0.233 g, 0.8 mmol) in water (5 mL). The mixture was kept at room temperature, and the crystals precipitated on slow evaporation.

For C$_{12}$H$_{28}$N$_{22}$O$_{10}$SNi $\cdot$ 6H$_2$O

Anal. C, 24.36 H, 6.76 N, 4.73 S, 10.83 Ni, 9.98 calcd., %

Found, % C, 24.34 H, 6.49 N, 5.09 S, 11.07 Ni, 10.39

IR (ν, cm^{-1}): 3375 ν(OH), 2945 ν(CH), 1173 ν(S=O).

The single crystals for X-ray diffraction analysis were obtained by the slow evaporation of a solution of complex **I** in an H$_2$O−DMF mixture (volume ratio 1 : 2).

Synthesis of bis(*N,N*-di(2-hydroxyethyl)taurinato)cobalt(II) (II). Ligand HL^1 (0.376 g, 1.6 mmol) was dissolved in water (5 mL) and mixed with a solution of Co(NO$_3$)$_2 \cdot$ 6H$_2$O (0.233 g, 0.8 mmol) in water (5 mL). The mixture was kept at room temperature, and the crystals precipitated on slow evaporation.

For C$_{12}$H$_{28}$N$_2$S$_2$O$_{10}$Co $\cdot$ 8H$_2$O

Anal. C, 22.96 H, 7.01 N, 4.46 S, 10.21 Co, 9.40 calcd., %

Found, % C, 22.82 H, 6.82 N, 4.75 S, 10.06 Co, 9.13

IR (ν, cm^{-1}): 3369 ν(OH), 2943 ν(CH), 1170 ν(S=O).

Analyses to C, H, N, and S were carried out on a PerkinElmer automated analyzer, and those to nickel and cobalt were conducted by atomic emission spectroscopy on an Optima 4300 DV spectrometer. IR reflectance spectra were recorded on a Spectrum-One spectrometer (PerkinElmer).

**X-ray diffraction analysis.** Experimental data for complex **I** were obtained on an Xcalibur 3 automated diffractometer (CCD detector, MoK_α, graphite monochromator, $T = 295(2)$ K). The crystallographic data and experimental and structure refinement characteristics are presented in Table 1. An empirical absorption correction was applied [16]. The structure was solved and refined using the SHELX program package [17]. All non-hydrogen atoms were determined by a direct method and refined in the anisotropic approximation. Hydrogen atoms were placed in the geometrically calculated positions and included into refinement with the dependent thermal parameters by the riding model. The coordinates of atoms and thermal parameters were deposited with the Cambridge Crystallographic Data Centre (CIF file CCDC no. 1822829; deposit@ccdc.cam.ac.uk or http://www.ccdc.cam.ac.uk/data_request/cif).

The dissociation constant of HL^1 and stability constants for its complexes **I** and **II** were determined by potentiometric titration. Aqueous solutions were titrated in an inert atmosphere (nitrogen) at the ionic strength $\mu = 0.1$ M KCl (KNO$_3$) and a temperature of 20 ± 1°C using an I-160 MI ionomer equipped with an ESK-10601/7 glass combined electrode. The ionomer was calibrated by standard buffer solutions. The solutions containing L^1 (0.01 mol/dm^3) in the presence and in the absence of the metal salt (0.002 mmol/dm^3) were studied. A carbonate-free solution of potassium hydroxide (0.2116 mol/dm^3) was used as a titrant. At least three titration curves were obtained for each series.

The value of pK_a was calculated by the Henderson−Hasselbach equation, which takes into account corrections to the concentrations of hydroxide ions (at pH > 10) and hydrogen ions (at pH < 4) [18] for the determination of the acidic dissociation constant pK_a of the amino acid in the HL^1 composition at each titration point. The stability constants of the complexes were calculated by the Irving−Rossotti equation [19].

RESULTS AND DISCUSSION

The potentiometric study of L^1 demonstrates the presence of one jump on the titration curve corresponding to the deprotonation of the ammonia group according to the Scheme 1
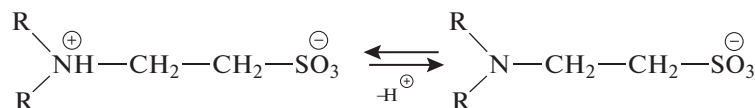
The acidic dissociation constants for the ammonia group of taurine and its derivatives are presented in Table 2.

The obtained value of pK_a for ligand HL^1 is consistent with the published data and indicates a decrease in the basicity of the tertiary amino group of HL^1 compared to that of the primary amino group of taurine.

The stability constants of the complexes of ligand HL^1 with nickel(II) and cobalt(II) ions were calculated according to [18] on the basis of the determined

Table 1. Crystallographic data and experimental and structure refinement parameters for complex **I** monohydrate DMF disolvate

Parameter	Value
Empirical formula	$C_{12}H_{28}N_2O_{10}S_2Ni \cdot 2(C_3H_7NO) \cdot H_2O$
FW	647.40
Sample size, mm	$0.18 \times 0.08 \times 0.01$
Crystal system	Monoclinic
Space group	$P2_1/c$
a, Å	13.1907(12)
b, Å	8.7676(15)
c, Å	12.8930(12)
β, deg	107.826(10)
V, Å^3	1419.5(3)
Z	2
ρ, g/cm^3	1.515
μ, mm^{-1}	0.897
F(000)	688
Scan mode	ω
Scan θ range, deg	2.838–26.092
Range of reflection indices	$-16 \le h \le 16, -10 \le k \le 10, -16 \le l \le 16$
Total number of measured reflections	5752
Number of independent reflections	2895
Number of reflections with $I > 2\sigma(I)$	1560
Number of reflection parameters	233
GOOF	1.000
$R (I > 2\sigma(I))$	$R_1 = 0.0599, wR_2 = 0.1203$
R (for all reflections)	$R_1 = 0.1323, wR_2 = 0.1591$
Residual electron density (min/max), $e/Å^3$	$-0.843/0.570$

Table 2. Acidic dissociation constants of the ammonia group of taurine and its derivatives

Formula of ligand	pK_a	References
$\overset{\oplus}{H_3N}-CH_2-CH_2-\overset{\ominus}{SO_3}$	8.93	[12]
$HO-CH_2-CH_2 \diagdown \overset{\oplus}{N}H-CH_2-CH_2-\overset{\ominus}{SO_3}$ $HO-CH_2-CH_2 \diagup$	7.10	This work
	7.10	[20]
	7.06	[21]
$O \diagdown \overset{CH_2-CH_2}{}\diagup \overset{\oplus}{N}H-CH_2-CH_2-\overset{\ominus}{SO_3}$ $\diagup_{CH_2-CH_2}$	6.10	[22]

Table 3. Logarithms of the stability constants of the complexes formed by taurine and its derivatives with nickel(II) and cobalt(II) ions

Formula of ligand	Ni(II)		Co(II)		References
	$\log\beta_1$	$\log\beta_2$	$\log\beta_1$	$\log\beta_2$	
$H_3\overset{\oplus}{N}-CH_2-CH_2-\overset{\ominus}{SO_3}$	2.77	5.52	2.09	5.37	[12]
$HO-CH_2-CH_2$ $HO-CH_2-CH_2$ $\overset{\oplus}{N}H-CH_2-CH_2-\overset{\ominus}{SO_3}$		4.48		4.54	This work
$O\overset{CH_2-CH_2}{\underset{CH_2-CH_2}{\diagup}}\overset{\oplus}{N}H-CH_2-CH_2-\overset{\ominus}{SO_3}$	2.06		2.04		[22]

acidic dissociation constant and potentiometric titration data. The obtained stability constants in comparison with the published data for taurine and its derivatives are presented in Table 3.

The values of $\log\beta_1$ calculated from the potentiometric titration data for HL^1 are negative, which is related to a low stability of the 1 : 1 complexes. The values of $\log\beta_2$ for cobalt(II) and nickel(II) are relatively low and comparable with each other. The stability of the complexes formed by ligand HL^1 somewhat decreases compared to that of taurine (Table 3) because of the lower donating ability of its amino group. However, the presence of hydroxy groups enhances the total donating ability of HL^1 compared to 2-(N-morpholino)ethanesulfonic acid (HL^2) also containing the tertiary amino group. In fact, the complexation properties of HL^2 are so weak that no 1 : 2 complexes are formed with cobalt(II) and nickel(II) ions but the heteroligand hydroxo complexes are formed [22].

The enhancement of the complexation properties of HL^1 compared to those of ligand HL^2 due to the presence of hydroxy groups is also confirmed by the X-ray diffraction data. A molecule of crystalline complex **I** is symmetric. In complex **I** (Fig. 1) of the formal 1 : 2 composition, the metal atom exists in the octahedral environment. The equatorial plane of the octahedron is formed by four oxygen atoms of the hydroxy groups of two organic ligands, and two nitrogen atoms of the amino groups of both ligands L^1 lie on the axial axis. No sulfo groups are involved in coordination. Thus, each potentially tetradentate ligand is
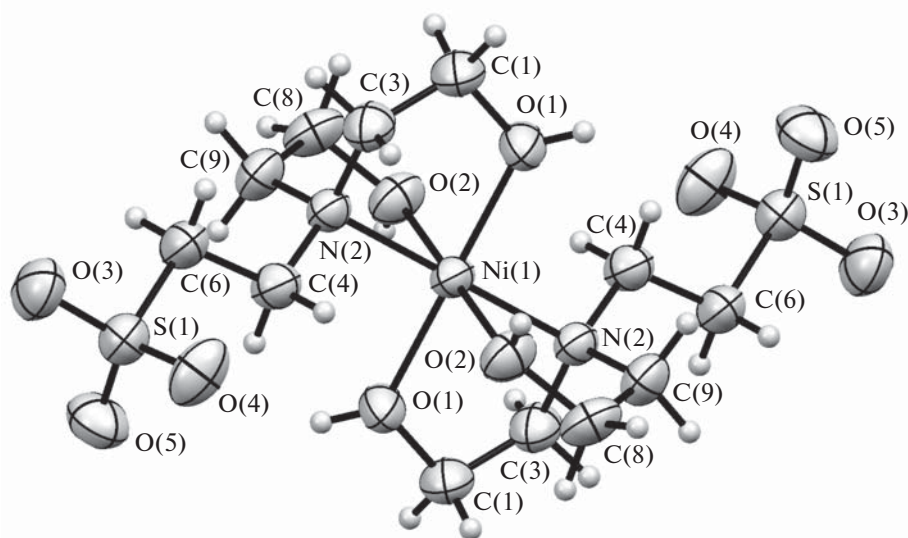
Fig. 1. Molecular structure of bis(N,N-di(2-hydroxyethy)-2-aminoethanesulfonato)nickel(II) (**I**), according to X-ray diffraction analysis data, in thermal ellipsoids of 50% probability. Solvate molecules are omitted.

tridentate. On the whole, the complex is neutral with the bis(betaine) structure. Selected bond lengths in complex **I** are presented in Table 4.

A comparison of the Ni−N bond lengths in the nickel(II) complexes in the series of the taurine derivatives (Table 5) shows that the tertiary amino group has a decreased donating ability than the primary amino group of taurine, since the bond length with the last ligand is minimum. The additional chelating by the hydroxy groups of ligand L^1 slightly shortens the Ni−N bonds compared to other taurine derivatives containing the tertiary amino group, indicating the enhancement of the total donating ability of the ligand.

The solvate shell providing structure formation due to intermolecular hydrogen bonds plays an important role in the formation of crystals (Figs. 2, 3). In spite of participation in intermolecular hydrogen bonds, mol-
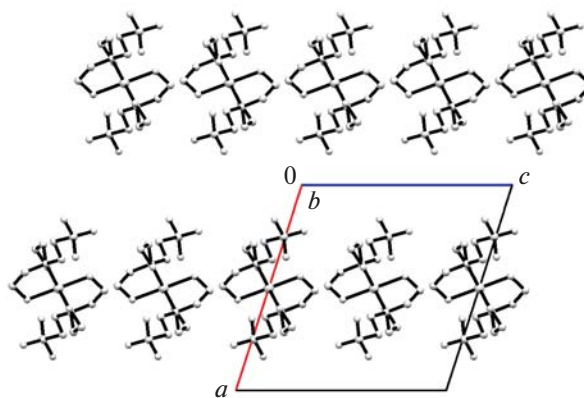

Fig. 2. Crystal packing of molecules of complex **I**. Hydrogen atoms and solvent molecules are omitted.

ecules of H_2O solvate demonstrate serious disordering that does not allow one to exactly estimate their geometric characteristics.

Unfortunately, attempts to obtain single crystals of complex **II** of satisfactory quality were not successful. The monoclinic crystal system was determined for fine twin needle crystals grown from water: space group $P2_1/c$ with the unit cell parameters $a = 9.208(3)$, $b = 6.8246(12)$, $c = 18.909(4)$ Å, and $\beta = 101.98(3)°$. An attempt to solve the structure resulted in the configuration of the complex coinciding on the whole with that of complex **I**. The high divergence factors

Table 4. Selected bond lengths (Å) and bond angles (deg) in the coordination mode of complex **I**

Bond	d, Å	Angle	ω, deg
Ni(1)−O(1)	2.051(3)	N(2)Ni(1)N(2)	180.0(15)
Ni(1)−O(2)	2.060(4)	O(2)Ni(1)N(2)	83.37(15)
Ni(1)−N(2)	2.104(4)	O(1)Ni(1)N(2)	81.88(13)

Table 5. Lengths of the Ni−N bond in the nickel(II) complexes in the series of the taurine derivatives

Formula of ligand	Length of Ni−N bond, Å*	References
$NH_2-CH_2-CH_2-SO_3H$	2.108(4) 2.120(5)	[23]
(see structure)	2.102 2.120	[24]
(see structure)	2.143	[25]
(see structure)	2.104(4)	This work

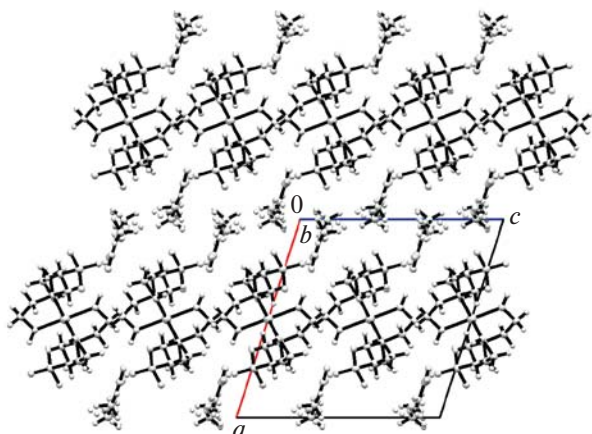* The maximum and minimum values are presented.

Fig. 3. Interlayer binding of molecules of complex **I** in the crystal due to intermolecular hydrogen bonds with the solvent molecules.

obtained by the refinement of the structure of compound **II** ($R_1 > 10\%$ for $I > 2\sigma(I)$) do not allow one to consider this structure as reliably determined. Nevertheless, the obtained information can be useful as a supplement to the spectral data and results of studying complex **I**.

Thus, in spite of the weak complexation properties, the tri- and tetradentate taurine derivatives are promising ligands for the binding of metal ions and formation of coordination compounds with nontrivial structures. The study of the complexation properties of these compounds makes it possible to take into account possible side reactions in biochemical assays and also to significantly enlarge possible areas of their application.

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