

Synthesis, Structure and Properties of Complex Compounds of Cobalt, Nickel, Copper and Zinc with 2-Formylpyridine Semicarbazone

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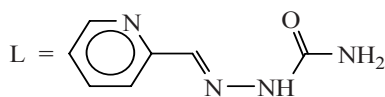
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Abstract—2-Formylpyridine semicarbazone L reacts with cobalt, nickel, copper and zinc chlorides, nitrates and perchlorates to form coordination compounds of compositions $ML_2X_2 \cdot nH_2O$ ($M=Co, Ni, Cu, Zn$; $X=Cl, NO_3, ClO_4$; $L=NC_5H_4-CH=N-NH-C(O)-NH_2$; $n=0, 1$) and $CuLX_2 \cdot nH_2O$ ($X=Cl, Br, NO_3$; $n=0-0.5$). Complex $CuL(NO_3)_2$ has polynuclear, $CuLX_2 \cdot 0.5H_2O$ ($X=Cl, Br$), binuclear, and other compounds, mononuclear structures. Azomethine L behaves in them as tridentate N,N,O-ligand. Thermolysis of these complexes proceeds through such stages as dehydration (80–95°C), deactivation (145–155°C) and complete thermal degradation (170–590°C). Complexes $CuLX_2 \cdot nH_2O$ ($X=Cl, NO_3$; $n=0-0.5$) were established to inhibit in vitro the growth and reproduction of 100% of cancer cells of human myeloid leukaemia HL-60 at 10^{-4} M concentration. At 10^{-5} M concentration they inhibit only 10% of cells, and at 10^{-6} M concentration they do not possess anticancer activity.

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Semicarbazones of aromatic aldehydes and ketones contain wide set of donor atoms and form with transition metals ions some complex compounds of diverse composition, structure, and properties [1–5]. Many of them are biologically active [6–8], that allows to use them as a matrix for creation of a selectively acting microbiologic nutrient medium as well as potential disinfectants and anti-infective agents. In this connection synthesis and study of the new complex compounds of biometals with semicarbazones are of both scientific and practical interest.

The aim of this work is to develop optimal synthesis conditions and to study structure and properties of coordination compounds of cobalt, nickel, copper, and zinc with 2-formylsemicarbazone L.



The experiment showed that the reaction of hot (50°–55°) ethanol solutions of hydrates of the above

mentioned metal chlorides, bromides, and perchlorates with azomethine L in the molar ratio 1:2 provided fine-crystalline compounds I–IV, VIII, and IX. By elemental analysis data (Table 1) they have composition $ML_2X_2 \cdot nH_2O$ [$M=Co$ (I, II), Ni (III, IV), Cu (VIII), Zn (IX); $X=Cl$ (I, III, IX), NO_3 (II, IV), ClO_4 (VIII), $n=0$ (I–IV, IX), $n=1$ (VIII)]. The hydrates of copper chloride, bromide, and nitrate react with semicarbazone in the molar ratio 1:1 under these conditions to form complexes V–VII having composition $CuLX_2 \cdot nH_2O$ [$X=Cl$ (V), Br (VI), NO_3 (VII); $n=0$ (VII), 0.5 (V, VI)].

The coordination compounds I–IX obtained are not soluble in diethyl ether, poorly soluble in water, better soluble in alcohols, well soluble in DMF, DMSO, and acetonitrile. Their yields and some physicochemical characteristics are given in the table.

On recrystallization of the studied compounds from ethanol, we succeeded to grow single crystals of complexes V, VII, and VIII, whose structure was determined by XRD analysis. The crystals of V are

Physicochemical properties of coordination compounds of cobalt, nickel, copper, and zinc with 2-formylpyridine semicarbazone

Comp. no.	Yield, %	$\mu_{\text{eff.}}^a$, BM	ε^a , $\Omega^{-1} \text{ cm}^2 \text{ mol}^{-1}$	Found, %			Formula	Calculated, %			T , °C ^d
				Cl (Br)	M ^b	N		Cl (Br)	M ^b	N	
I	68	5.04	131	15.25	12.59	24.30	C ₁₄ H ₁₆ Cl ₂ CoN ₈ O ₂	15.48	12.86	24.46	570
II	62	4.93	145	–	11.29	27.11	C ₁₄ H ₁₆ CoN ₁₀ O ₈	–	11.53	27.40	190
III	65	2.87	134	15.19	12.74	24.17	C ₁₄ H ₁₆ Cl ₂ N ₈ NiO ₂	15.48	12.86	24.46	550
IV	60	3.07	144	–	11.41	27.28	C ₁₄ H ₁₆ N ₁₀ NiO ₈	–	11.53	27.40	185
V	73	1.51	72	22.90	20.41	18.00	C ₁₄ H ₁₈ Cl ₄ Cu ₂ N ₈ O ₃	23.05	20.66	18.22	550
VI	76	1.44	76	40.02	15.90	13.87	C ₁₄ H ₁₈ Br ₄ Cu ₂ N ₈ O ₃	40.30	16.12	14.11	550
VII	70	1.62	9	–	17.79	24.09	C ₇ H ₈ CuN ₆ O ₇	–	18.07	23.90	170
VIII	75	1.96	140	11.40	10.27	18.21	C ₁₄ H ₁₈ Cl ₂ CuN ₈ O ₁₁	11.65	10.44	18.41	210
IX	63	^c	137	15.01	13.95	23.87	C ₁₄ H ₁₆ Cl ₂ N ₈ O ₂ Zn	15.26	14.07	24.12	590

^a At 293 K. ^b M is metal. ^c Complex is diamagnetic. ^d T is the temperature of the complete thermal degradation of the complex.

triclinic, space group P-1, the cell parameters are as follows: a 9.580(3), b 10.1530(19), c 12.296(2) Å, α 106.71(3), β 102.40(3), γ 93.65(3)°, Z 2; the crystals of **VII** are monoclinic, space group $P2_1/c$, the cell parameters are as follows: a 7.6870(15), b 15.553(3), c 12.107(4) Å, α 90, β 124.56(2), γ 90°, Z 4; the crystals of **VIII** are triclinic, space group P-1, cell parameters are as follows: a 10.000(2), b 11.279(2), c 12.232(2) Å, α 113.77(2), β 110.02(2), γ 93.62(3)°, Z 2. In all of the studied complex compounds **V**, **VII** and **VIII** neutral molecule of 2-formylpyridine semicarbazone L was found to add tridentately to the copper atom through N,N,O donor atoms. In this case the ratio copper:semicarbazone in **V** and **VII** is 1:1, and in **VIII**, 1:2. Complex **V**, whose composition is better described by the formula $[\text{CuLCl}_2 \cdot \text{Cu}(\text{H}_2\text{O})\text{LCl}]\text{Cl}$, has a ionic structure. The base of its structure is a dimer complex cation $[\text{CuLCl}_2 \cdot \text{Cu}(\text{H}_2\text{O})\text{LCl}]^+$. The bonding between the copper atoms occurs through the one of μ_2 -bridge chlorine atoms of CuLCl_2 fragment. Coordination polyhedron of the central atom of complex fragment $\text{Cu}(\text{H}_2\text{O})\text{LCl}$ is bipyramide (4 + 1 + 1), the base of which consists of the carbamide oxygen atoms, azomethine and pyridine nitrogen atoms of organic ligand L and chlorine atom. The bipyramide vertices are occupied by the oxygen atoms of water molecule and by the bridge chlorine atom. The coordination polyhedron of the complex fragment CuLCl_2 copper atom can be described as a distorted tetragonal pyramid, in the base of which the carbamide oxygen atoms, azomethine and pyridine nitrogen atoms of semicarbazone L and chlorine atom lie. Coordination pyramid apical vertex of the copper atom

is occupied with the chlorine atom. In the complex **VII** besides azomethine L two nitrate-ions, structural functions of which are different, are involved into the inner coordination sphere of copper atom. The structure is constructed as a one-dimensional coordination polymer. Bidental nitrate-group performs the bridge function. The coordination polyhedron of central atom may be regarded as a distorted tetragonal bipyramide with (4 + 1 + 1) way of the copper atom coordination. The bipyramid base is formed by the carbamide oxygen atoms, azomethine and pyridine nitrogen atoms of semicarbazone L and nitrate-group oxygen atom. The bipyramid axial vertices are occupied with the bridge nitrate-group oxygen atoms. In compound **VIII** the central copper atom is octahedrally surrounded by two ligands L in *mer*-configuration. Coordination bonds of the complexing ion with the ligand donor atoms as well as distances between analogous atoms in the molecules are conformed among themselves within three standard deviations. The exception is the copper-oxygen bonds, which differ by 0.041 Å.

Visual microscopic study of the rest of complex compounds **I–IV**, **VI**, and **IX** showed that their powders possess phase homogeneity and are composed by crystal grains of various forms. Due to their small sizes and the absence of single crystals of these compounds, we used elemental and thermal analyses, magnetochemistry, and IR spectroscopy to establish the individuality of their composition and structure.

The molar conductivity measurement of the complex obtained in DMF showed that at the moment of

dissolution complex **IX** is nonelectrolyte, compounds **V** and **VI** are two-ionic and other substances are three-ionic electrolytes (see the table).

By the magnetochemical data all the cobalt and nickel compounds were established to be paramagnetic. The central atoms in their composition have a pseudooctahedral structure of coordination node judging by the values of the effective magnetic moment. Magnetochemical characteristics of the copper compound **VIII** correspond to spin value for one unpaired electron and indicate that it is monomeric. As regards the copper complexes **V** and **VI**, they are polynuclear since the effective magnetic moment values are underrated in comparison with the spin value for the one unpaired electron.

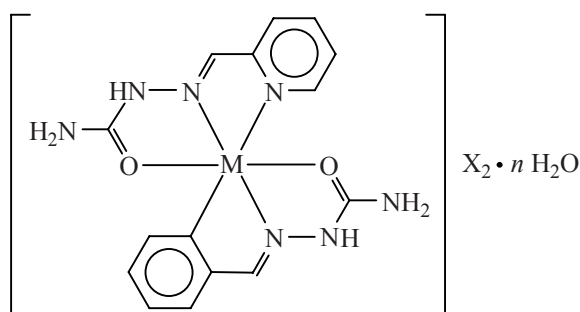
Aiming at establishing the coordination mode of semicarbazone L with central ions, we carried out comparative analysis of the IR spectra of the initial azomethine L, complexes **I–IX**, and coordination compounds of transition metals with similar Schiff bases described in the literature [9–11]. Carbazone L in the substances studied was established to behave as tridentate N,N,O-ligand and to add to complexing ion through pyridine and azomethine nitrogen atoms and also through carbamide oxygen to form the two five-membered metallocycles. This is supported by the shift to low frequencies by 20–10 cm^{-1} of absorption bands C=N and C=O in comparison with the analogous absorption bands of the initial semicarbazone where they are at 1630–1620 and 1660 cm^{-1} respectively. The coordination cited above is also supported by the appearance of some new absorption bands in the IR spectra of all the complexes at 550–400 cm^{-1} due to M–N (535–510 and 430–405 cm^{-1}) and M–O (490–450 cm^{-1}). The participation of the other functional groups of Schiff base L in the coordination with the

metal ions is excluded since its characteristic absorption bands are in the same regions as in the initial semicarbazone spectrum. The presence of the coordinated water molecules in complexes **V** and **VI** is confirmed by the presence of the corresponding absorption bands in their IR spectra: $\nu(\text{H}_2\text{O})$ 3590–3580, $\delta(\text{H}_2\text{O})$ 1580–1575 and $\gamma(\text{H}_2\text{O})$ 925–920 cm^{-1} . In the case of compound **VII** the absorption bands of inner-sphere nitrate-ions were observed at 1295, 1020, 1530 and 800 cm^{-1} .

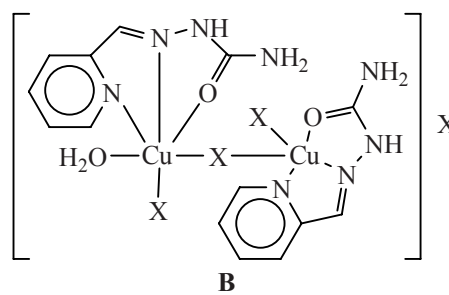
Thermal analysis of the complexes **I–IX** showed (see the table) that their thermolysis proceeds through dehydration (80–95°C) and deaquaation stages (155–180°C) to full thermal-oxidative destruction (370–585°C). The full destruction temperature (t) of compound depends on the central atom nature. When the inner and outer sphere compositions of complexes are identical, this temperature changes in the following sequence: Zn > Co > Ni. The acid residue nature affects the compound destruction temperature: the latter increases, if nitrate-ion is replaced by halide-ions.

Physicochemical data cited above allows representation of the chemical bonds distribution for coordination compounds **I–IX** as **A**, **B** and **C** schemes.

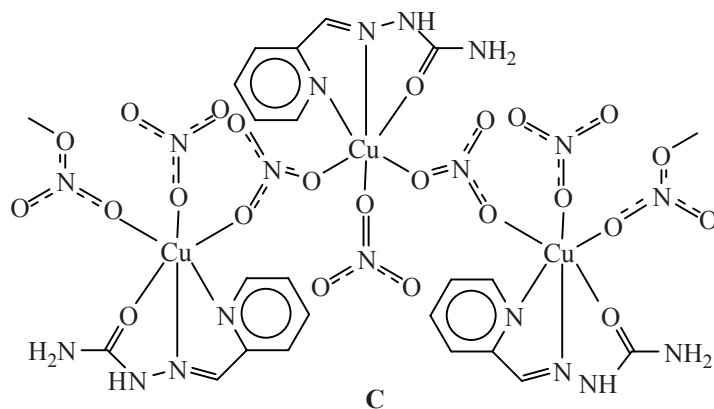
It was showed in [12–14] that many of 3d-elements coordination compounds with ligands obtained from hydrazine derivatives inhibit selectively the malignant neoplasms growth. In this connection with anticancer activity of complexes **V** and **VII** was examined *in vitro* on the human mieloid leukaemia HL-60 cells. The substances studied were established to inhibit growth of this type cells as chemotherapeutic agents used in medicine on leukosis prophylaxis and cure. At 10^{-4} M concentration these complexes inhibit growth and reproduction of 100% of cancer cells, at 10^{-5} M



M = Co, Ni, Cu; X = Cl, NO₃, ClO₄; n = 0, 1



X = Cl, Br



concentration they inhibit only 10% of cells and at 10^{-6} M, they do not possess anticancer activity.

EXPERIMENTAL

The X-ray analysis of complex compounds **V**, **VII** and **VIII** was carried out on a Siemens AED diffractometer. Structures were solved by the direct method and refined by full-matrix least-squares procedure in anisotropic approximation for nonhydrogen atoms using SHELX-97 package [15]. The main crystallographic data were deposited into the Cambridge Database of Crystallographic Data (CCDC 680877-680879). The solution resistance for **I–IX** in DMF (20°C, 0.001M) was measured by means of a P-38 slidewire bridge. The IR spectra for substances preliminary kept in drying box at 105°C to constant weight were registered on a Specord M-80 spectrophotometer from suspension in mineral oil. The effective magnetic moments of **I–VIII** were determined by Gouy method. Molar magnetic susceptibility calculation corrected for diamagnetism was carried out on the basis of theoretical values of organic compounds magnetic susceptibility. The derivatograms of complexes **I–IX** were taken on a Paulik-Paulik-Erdey system derivatograph in the range 20–1000°C under air atmosphere (reference is Al₂O₃, corundum crucible). The anticancer activity of compounds **V** and **VII** was examined *in vitro* on the human mieloid leukaemia HL-60 cells by the standard procedure [16].

The initial 2-formylpyridine semicarbazone **L** was prepared by procedure described in [17].

Bis(2-formylpyridine semicarbazone)cobalt(2+) chloride (I). 30 ml of a hot (50–55°C) ethanol solution containing 10 mmol of 2-formylpyridine semicar-

bazone was mixed with a solution of 5 mmol of cobalt chloride hexahydrate in 20 ml of alcohol. The obtained reaction mixture was refluxed under continuous stirring on a magnetic stirrer for 45–50 min. In so doing, the rose-coloured solution is formed, from which on cooling a pale pink fine-crystalline substance precipitates. It was filtered off on a glass frit, washed with alcohol and ether, and dried in air.

Similarly, complexes **II–IV**, **VIII**, **IX** were obtained, starting from hydrates of cobalt, nickel, copper and zinc chloride, nitrate, and perchlorate and semicarbazone **L** taken in molar ratio 1:2. The coordination compounds were synthesized by the mentioned above procedure on reaction of hydrate of copper(2+) chloride, bromide and nitrate with azomethine **L** (molar ratio 1:1). Yields and some physicochemical characteristics of compounds obtained are given in the table.

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