

Sulfanilamide-containing Coordination Compounds of Cu(II) with Isatin and *N*-Methylisatin Thiosemicarbazones

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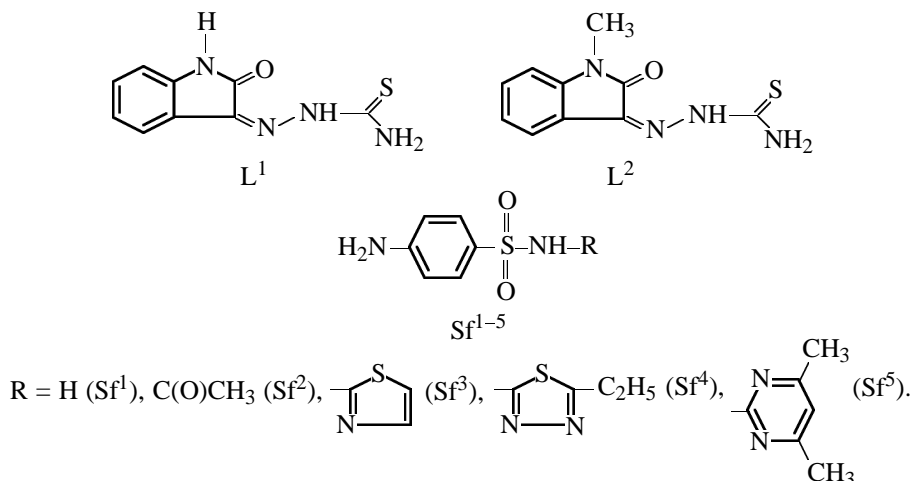
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Abstract—Isatin (L^1) and *N*-methylisatin (L^2) β -thiosemicarbazones react in ethanol with Cu(II) chloride and bromide in the presence of sulfanilamide (Streptocid, Sf^1), *N*-acetylsulfanilamide (Sulfacyl, Sf^2), Norsulfazole (Sf^3), Aethazolum (Sf^4), and Sulfadimesine (Sf^5) to form coordination compounds $Cu(Sf^{1-5})L^{1-2}X_2 \cdot nH_2O$ ($X = Cl, Br; n = 2-5$). All the complexes have a monomeric structure. Thiosemicarbazones L^1 and L^2 in these complexes are tridentate O,N,S ligands, and sulfanilamides Sf^{1-5} are monodentate ligands. Thermolysis of the substances involves the steps of dehydration (70–95°C) and complete decomposition (410–530°C).
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Isatin β -thiosemicarbazide and its derivatives form with transition metal ions coordination compounds of diverse compositions and structures [1–4]. Some of these substances are biologically active [5, 6], which allows their use as a base for the development of selective microbiological media and potential disinfectants and antiseptics. It was found that the physiological activity of these compounds is determined by the simultaneous presence of complexing metal ions and their inner-sphere surrounding. In this connection, synthesis and study of new coordination compounds

of biometals with such ligands is of both scientific and practical interest.

The goal of this study is synthesis and determination of the composition, probable structure, and physicochemical properties of mixed-ligand complexes of copper(II) chloride and bromide with isatin and *N*-methylisatin β -thiosemicarbazones (L^1 and L^2 , respectively) and selected sulfanilamides: sulfanilamide (Streptocid, Sf^1), *N*-acetylsulfanilamide (Sulfacyl, Sf^2), Norsulfazole (Sf^3), Aethazolum (Sf^4), and Sulfadimesine (Sf^5).



It was found that the reaction of hot (50–55°C) ethanol solutions of the above copper(II) halides with thiosemicarbazones L^{1-2} and sulfanilamides Sf^{1-5}

taken in a 1 : 1 : 1 molar ratio yields finely crystalline substances **I–XV**; according to elemental analysis (Table 1), they have the composition $Cu(Sf^{1-5})$.

Table 1. Physicochemical characteristics of sulfanilamide-containing coordination compounds of Cu(II) with isatin and *N*-methylisatin β -thiosemicarbazones

Comp. no.	Yield, %	μ_{ef} , BM (294 K)	Found, %					Formula	Calculated, %				
			C	H	Cl (Br)	Cu	N		C	H	Cl (Br)	Cu	N
I	62	2.09	30.00	3.81	11.64	10.45	13.88	$\text{C}_{15}\text{H}_{24}\text{Cl}_2\text{CuN}_6\text{O}_7\text{S}_2$	30.05	4.01	11.85	10.68	14.02
II	68	1.79	25.38	3.50	22.45	8.88	11.65	$\text{C}_{15}\text{H}_{26}\text{Br}_2\text{CuN}_6\text{O}_8\text{S}_2$	25.50	3.68	22.66	9.07	11.90
III	60	1.75	33.54	3.50	11.50	10.33	13.59	$\text{C}_{17}\text{H}_{22}\text{Cl}_2\text{CuN}_6\text{O}_6\text{S}_2$	33.72	3.64	11.74	10.58	13.88
IV	65	1.84	27.70	3.44	21.70	8.53	11.67	$\text{C}_{17}\text{H}_{26}\text{Br}_2\text{CuN}_6\text{O}_8\text{S}_2$	27.95	3.56	21.92	8.77	11.51
V	69	1.92	32.33	3.40	10.41	9.48	14.50	$\text{C}_{18}\text{H}_{23}\text{Cl}_2\text{CuN}_7\text{O}_6\text{S}_3$	32.53	3.46	10.70	9.64	14.76
VI	73	2.06	28.84	2.87	21.01	8.32	12.84	$\text{C}_{18}\text{H}_{23}\text{Br}_2\text{CuN}_7\text{O}_6\text{S}_3$	28.69	3.05	21.25	8.50	13.01
VII	72	2.18	33.31	3.26	10.75	9.79	16.30	$\text{C}_{18}\text{H}_{22}\text{Cl}_2\text{CuN}_8\text{O}_4\text{S}_3$	33.49	3.41	11.01	9.92	17.36
VIII	77	1.94	27.90	3.14	20.55	8.18	14.44	$\text{C}_{18}\text{H}_{26}\text{Br}_2\text{CuN}_8\text{O}_6\text{S}_3$	28.05	3.38	20.78	8.31	14.54
IX	73	1.88	35.01	4.31	9.61	8.97	15.20	$\text{C}_{21}\text{H}_{32}\text{Cl}_2\text{CuN}_8\text{O}_8\text{S}_2$	34.85	4.43	9.82	8.85	15.49
X	75	1.93	30.90	4.12	19.33	7.99	13.50	$\text{C}_{21}\text{H}_{32}\text{Br}_2\text{CuN}_8\text{O}_8\text{S}_2$	31.03	3.94	19.70	7.88	13.79
XI	66	2.11	33.09	3.65	12.09	12.85	14.30	$\text{C}_{16}\text{H}_{22}\text{Cl}_2\text{CuN}_6\text{O}_5\text{S}_2$	33.28	3.81	12.31	11.09	14.56
XII	67	1.79	32.05	3.94	10.90	9.86	12.90	$\text{C}_{18}\text{H}_{26}\text{Cl}_2\text{CuN}_6\text{O}_7\text{S}_2$	33.91	4.08	11.15	10.05	13.19
XIII	72	1.89	33.47	3.48	10.18	9.25	14.29	$\text{C}_{19}\text{H}_{25}\text{Cl}_2\text{CuN}_7\text{O}_6\text{S}_3$	33.63	3.69	10.47	9.44	14.45
XIV	75	1.75	35.18	4.59	10.21	9.32	16.79	$\text{C}_{20}\text{H}_{32}\text{Cl}_2\text{CuN}_8\text{O}_6\text{S}_2$	35.35	4.71	10.46	9.43	16.49
XV	74	1.78	37.54	4.04	9.88	8.90	16.11	$\text{C}_{22}\text{H}_{30}\text{Cl}_2\text{CuN}_8\text{O}_6\text{S}_2$	37.66	4.28	10.13	9.13	15.98

$(\text{L}^{1-2})\text{X}_2 \cdot n\text{H}_2\text{O}$ [$\text{Sf}^{1-5} = \text{Sf}^1$ (**I**, **II**, **XI**), Sf^2 (**III**, **IV**, **XII**), Sf^3 (**V**, **VI**, **XIII**), Sf^4 (**VII**, **VIII**, **XIV**), Sf^5 (**IX**, **X**, **XV**); $\text{L}^{1-2} = \text{L}^1$ (**I–X**), L^2 (**XI–XV**); $\text{X} = \text{Cl}$ (**I**, **III**, **V**, **VII**, **IX**, **XI–XV**), Br (**II**, **IV**, **VI**, **VIII**, **X**); $n = 1$ (**VII**), 2 (**III**, **XI**), 3 (**V**, **VI**, **VIII**, **XII**, **XIII**, **XV**), 4 (**I**, **IV**), 5 (**II**, **IX**, **X**, **XIV**).

Coordination compounds **I–XV** are insoluble in ether, poorly soluble in water and alcohols, and readily soluble in dimethylformamide (DMF) and dimethyl sulfoxide. Their yields and physicochemical characteristics are given in Tables 1–3.

Visual microscopic examination of complexes **I–XV** showed that their powders exhibited phase uniformity and consisted of crystals of various shapes. We failed to prepare single crystals of X-ray quality; we identified the compounds and examined their structures by elemental and thermal analyses, molar electrolytic conductivity measurements, IR spectroscopy, and magnetic measurements.

All the compounds prepared are nonelectrolytes in DMF ($\kappa = 2\text{--}4 \Omega^{-1} \text{cm}^2 \text{mol}^{-1}$).

A magnetochemical study of complexes **I–XV** at room temperature (Table 1) showed that their effective magnetic moments correspond to the spin values for one unpaired electron. This fact suggests for them a monomeric structure.

Thermal analysis of **I–XV** showed (Table 2) that these compounds decompose in two steps. The DTA

curves of all the complexes exhibit an endothermic effect at 70–95°C corresponding to dehydration. The subsequent thermal effect in the DTA curves, observed in the range 410–530°C, is exothermic and is associated with thermal oxidative degradation of the coordinated sulfanilamides (Sf^{1-5}) and thiosemicarbazones (L^1 , L^2). The temperature (T_{dec}) of complete decomposition of the substances depends on the nature of the inner-sphere ligands and increases on replacement of the isatin moiety in L^1 by *N*-methylisatin moiety and of bromide ion by chloride ion; with the same halide ion and thiosemicarbazone, T_{dec} decreases in the order $\text{Sf}^4 \geq \text{Sf}^5 > \text{Sf}^3 > \text{Sf}^2 > \text{Sf}^1$.

Using the Horowitz–Metzger's method [7] with Topor's modifications [8], we estimated the kinetic parameters of the dehydration of complexes **I–XV**: activation energy E_a and preexponential factor Z . As seen from Table 2, they are close to the parameters of related reactions described in the literature [9–11].

With the aim to determine the mode of ligand coordination with the central ion, we compared the IR spectra of complexes **I–XV** and of the starting thiosemicarbazones $\text{L}^{1,2}$ and sulfanilamides Sf^{1-5} , taking into account the published data [1–6] for coordination compounds of transition metals with related Schiff bases. We found (Table 3) that azomethines L^1 and L^2 in **I–XV** behave as tridentate O,N,S ligands and coordinate with the metal via the carbonyl oxygen atom of the isatin moiety, C=N nitrogen atom, and sulfur atom, forming two five-membered chelate rings. This

Table 2. Results of thermal analysis of sulfanilamide-containing coordination compounds of Cu(II) with isatin and *N*-methylisatin β -thiosemicarbazones

Comp. no.	Dehydration temperature, °C	Weight loss, %			Kinetic parameters		Temperature of complete decomposition, °C
		found, %	calculated, %	elimination of	E_a , kJ mol ⁻¹	log Z	
I	70	11.7	12.0	4H ₂ O	35.1	4.1	430
II	85	12.5	12.7	5H ₂ O	42.6	4.7	410
III	80	6.2	6.0	2H ₂ O	30.9	3.8	440
IV	75	10.0	9.9	4H ₂ O	32.1	3.9	430
V	95	8.5	8.1	3H ₂ O	40.3	4.5	460
VI	80	7.0	7.2	3H ₂ O	26.9	2.9	440
VII	75	3.0	2.7	H ₂ O	30.1	3.7	510
VIII	85	7.0	6.9	3H ₂ O	38.5	4.4	500
IX	70	12.1	12.4	5H ₂ O	35.6	4.2	500
X	80	11.0	11.1	5H ₂ O	37.4	4.3	480
XI	90	6.0	6.2	2H ₂ O	45.1	5.1	450
XII	75	8.2	8.5	3H ₂ O	43.2	4.8	460
XIII	85	8.3	8.0	3H ₂ O	28.8	3.1	480
XIV	80	12.0	12.1	5H ₂ O	31.3	3.8	530
XV	75	7.5	7.7	3H ₂ O	40.1	4.5	520

Table 3. Frequencies (cm⁻¹) of absorption bands in the IR spectra of sulfanilamide-containing coordination compounds of Cu(II) with isatin and *N*-methylisatin β -thiosemicarbazones

Comp. no. ^a	$\nu(\text{NH})$ of isatin	$\nu(\text{NH}_2)$, $\nu(\text{NH})$	$\nu(\text{C}=\text{O})$	$\nu(\text{C}=\text{N})$	$\nu_{\text{as}}(\text{SO}_2)$, $\nu_2(\text{SO}_2)$	$\delta(\text{C}-\text{N})$	$\nu(\text{C}=\text{S})$	$\nu(\text{C}-\text{N})$	$\nu(\text{S}-\text{N})$	$\nu(\text{C}-\text{S})$	$\delta(\text{SO}_2)$	$\nu(\text{M}-\text{N})$, $\nu(\text{M}-\text{O})$, $\nu(\text{M}-\text{S})$
L	3320, 3300	3430, 3315, 3180, 1540	1710	1620	–	1185, 1110	1120	980, 945	–	–	–	–
Sf ¹	–	3440, 3330, 3210, 1530	–	–	1320, 1145	1330, 1115	–	975, 930	860	745	560	–
I	3322, 3300	3425, 3415, 3310, 3305, 3190, 1525	1685	1600	1325, 1140	1325, 1180, 1115	1100	975, 940, 930	855	740	555	530, 490, 475, 415
II	3325, 3305	3425, 3415, 3310, 3305, 3190, 1520	1680	1605	1320, 1140	1325, 1185, 1110	1100	975, 945, 935	855	745	560	520, 485, 470, 435
Sf ²	–	3440, 3320, 3210, 1540	1675	–	1325, 1140	1330, 1115	–	985, 935	865	740	560	–
III	3320, 3305	3420, 3415, 3310, 3305, 3190, 1525	1685, 1670	1605	1320, 1130	1335, 1180, 1115	1105	980, 935, 930	860	740	555	525, 480, 465, 410
IV	3323, 3305	3425, 3415, 3310, 3305, 3190, 1525	1690, 1670	1600	1325, 1135	1330, 1185, 1120	1105	985, 940, 935	860	745	555	530, 475, 470, 430
Sf ³	–	3435, 3335, 3200, 1530	–	1625	1315, 1130	1320, 1110	–	980, 925	870	745	560	–

Table 3. (Contd.)

Comp. no. ^a	$\nu(\text{NH})$ of isatin	$\nu(\text{NH}_2)$, $\nu(\text{NH})$	$\nu(\text{C}=\text{O})$	$\nu(\text{C}=\text{N})$	$\nu_{\text{as}}(\text{SO}_2)$, $\nu_2(\text{SO}_2)$	$\delta(\text{C}-\text{N})$	$\nu(\text{C}=\text{S})$	$\nu(\text{C}-\text{N})$	$\nu(\text{S}-\text{N})$	$\nu(\text{C}-\text{S})$	$\delta(\text{SO}_2)$	$\nu(\text{M}-\text{N})$, $\nu(\text{M}-\text{O})$, $\nu(\text{M}-\text{S})$
V	3321, 3305	3430, 3330, 3320, 3205, 3185, 1535	1695	1605, 1600	1310, 1125	1325, 1180, 1105	1100	985, 945, 930	870	745	555	520, 480, 465, 415
VI	3320, 3305	3435, 3330, 3325, 3200, 3190, 1530	1690	1600, 1595	1315, 1125	1325, 1185, 1110	1105	985, 940, 930	865	745	560	525, 485, 465, 425
Sf ⁴	–	3435, 3330, 3200, 1535	–	1620	1320, 1135	1330, 1120	–	985, 930	870	750	560	–
VII	3322, 3300	3430, 3335, 3315, 3205, 3195, 1535	1695	1615, 1605, 1600	1315, 1130	1325, 1180, 1115	1100	980, 940, 925	865	745	560	530, 480, 470, 420
VIII	3320, 3297	3435, 3330, 3320, 3200, 3190, 1530	1690	1610, 1600, 1595	1315, 1135	1330, 1185, 1125	1100	985, 935, 930	870	745	555	525, 490, 475, 410
Sf ⁵	–	3460, 3350, 3245, 1535	–	1630	1320, 1145	1335, 1110	–	980, 940	870	755	570	–
IX	3323, 3298	3455, 3350, 3320, 3245, 3190, 1535	1695	1625, 1605, 1600	1315, 1140	1330, 1180, 1115	1100	985, 940, 930	865	750	560	530, 480, 460, 415
X	3320, 3299	3460, 3355, 3325, 3240, 3195, 1530	1690	1620, 1600, 1595	1320, 1145	1335, 1185, 1110	1100	980, 945, 930	870	750	565	510, 490, 480, 435
L ¹	–	3435, 3325, 3190, 1545	1700	1615	–	1190, 1120	1115	980, 935	–	–	–	–
XI	–	3420, 3410, 3315, 3310, 3195, 1535	1680	1595	1320, 1140	1320, 1185, 1110	1100	975, 935, 930	850	745	565	510, 485, 470, 435
XII	–	3425, 3415, 3315, 3300, 3195, 1530	1695, 1675	1600	1325, 1135	1330, 1185, 1115	1100	980, 940, 935	860	745	565	515, 490, 475, 430
XIII	–	3430, 3320, 3315, 3200, 3195, 1540	1685	1600, 1595	1315, 1120	1330, 1185, 1105	1100	980, 940, 930	865	750	560	530, 495, 485, 435
XIV	–	3435, 3330, 3320, 3200, 3195, 1530	1690	1610, 1600, 1595	1310, 1125	1320, 1185, 1115	1095	985, 945, 930	860	745	560	515, 475, 470, 410
XV	–	3445, 3355, 3320, 3240, 3200, 1530	1690	1610, 1600, 1585	1315, 1135	1335, 1185, 1110	1100	980, 945, 935	860	750	560	510, 485, 475, 435

^a Complexes were preliminarily kept in an oven at 105°C to constant weight.

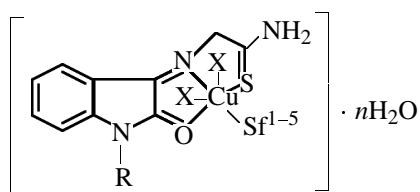
is indicated by a 30–15 cm⁻¹ low-frequency shift of the $\nu(\text{C}=\text{O})$ and $\nu(\text{C}=\text{N})$ bands compared to the related absorption bands of the starting thiosemicarbazones (in L¹ and L² they are manifested at 1710–1700 and 1620–1610 cm⁻¹, respectively). The suggested coordination mode of L¹ and L² is also supported by the appearance of new bands at 530–405 cm⁻¹ in the IR

spectra of all the complexes: $\nu(\text{Cu}-\text{N})$ at 525–505 and 430–405 cm⁻¹, $\nu(\text{Cu}-\text{O})$ at 490–460 cm⁻¹, and $\nu(\text{Cu}-\text{S})$ at 460–445 cm⁻¹. Participation of other functional groups of L¹ and L² in the coordination is unlikely, because the characteristic absorption bands are not noticeably shifted relative to the starting thiosemicarbazones. As for sulfanilamides, their presence

in the complexes is confirmed by the corresponding absorption bands (Table 3). The spectra suggest that Streptocid and Sulfacyl are coordinated via the amine nitrogen atom; Norsulfazole and Aethazolum, via the thiazole and thiadiazole nitrogen atoms; and Sulfadimesine and Sulfapyridazine, via one of pyrimidine and pyridazine nitrogen atoms. In the case of **I–IV**, **XI**, and **XII**, this follows from the 25–15 cm⁻¹ long-wave shift of the $\nu(\text{NH}_2)$ and $\nu(\text{NH})$ absorption bands, and in the case of **V–X** and **XIII–XV**, from the splitting and 25–20 cm⁻¹ long-wave shift of the $\nu(\text{C}=\text{N})$ band (Table 3).

Thus, we have determined the composition and structure of the synthesized compounds by elemental analysis and physicochemical methods.

The following structure can be suggested for **I–XV**:



R = H (**I–X**), CH₃ (**XI–XV**); X = Cl (**I**, **III**, **V**, **VII**, **IX**, **XI–XV**), Br (**II**, **IV**, **VI**, **VIII**, **X**); Sf^{1–5} = Sf¹ (**I**, **II**, **XI**), Sf² (**III**, **IV**, **XII**), Sf³ (**V**, **VI**, **XIII**), Sf⁴ (**VII**, **VIII**, **XIV**), Sf (**IX**, **X**, **XV**); n = 1 (**VII**), 2 (**III**, **XI**), 3 (**V**, **VI**, **VIII**, **XII**, **XIII**, **XV**), 4 (**I**, **IV**), 5 (**II**, **IX**, **X**, **XIV**).

EXPERIMENTAL

The resistance of solutions of **I–XV** in DMF (20°C, c 0.001 M) was measured with an R-38 rheochord bridge. The IR spectra were measured on a Perkin-Elmer FTIR 1650 spectrophotometer (mulls in mineral oil). The effective magnetic moments of **I–XV** were measured by the Gouy method at 294 K. The molar magnetic susceptibility corrected for diamagnetism was calculated using the theoretical magnetic susceptibilities of the organic compounds. The derivatograms of **I–XV** were recorded at a rate of 5 deg min⁻¹ on a Paulik–Paulik–Erdey derivatograph in the temperature range 20–1000°C in air (reference Al₂O₃, corundum crucible). The C and H content was determined by combustion of a weighed portion of a substance in oxygen (Korshun's method [12]); the halogen content, by Schoeniger's method involving combustion of a weighed portion of a substance in oxygen followed by potentiometric titration [13]; the copper content, by complexometric titration [14]; and the nitrogen content, by Dumas' method involving combustion of a weighed portion of a substance in a quartz tube in a CO₂ atmosphere [12]. The starting isatin and *N*-meth-

ylisatin β -thiosemicarbazones (mp 251–253 and 242–244°C, respectively) were prepared by the procedure described in [1].

Dichloro(1*H*-indole-2,3-dione 3-thiosemicarbazone)(4-aminobenzenesulfamide)copper tetrahydrate (I). Hot (50–55°C) ethanolic solutions of 10 mmol of copper(II) chloride dihydrate and 10 mmol of isatin β -thiosemicarbazone (L¹) were mixed with an alcoholic solution of 10 mmol of Streptocid (4-aminobenzenesulfamide). The mixture was refluxed on a water bath for 40–45 min with continuous stirring. A dark green finely crystalline product precipitated on cooling; it was filtered off, washed with ethanol and ether, and dried in air.

Compounds **II–XV** were prepared similarly starting from copper(II) chloride and bromide, thiosemicarbazones L^{1,2}, and sulfanilamides Sf^{1–5} (molar ratio 1 : 1 : 1). Their yields and physicochemical characteristics are given in Tables 1–3.

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