CHEMISTRY & CHEMICAL TECHNOLOGY

Chem. Chem. Technol., 2025,
Vol. 20, No. 4, pp. 628–634

Chemistry

SYNTHESIS OF COPPER(I) CHELATES BASED ON HETEROCYCLIC THIOAMIDES

***Anatoliy Ranskiy*[1], *Natalia Didenko*[2], *Olga Gordienko*[1], *Taras Titov*[1,✉]**

[1] Vinnytsia National Technical University, Department of Ecology, Chemistry and Environmental Protection Technologies, 95 Khmelnytske Road, Vinnytsia 21021, Ukraine
[2] National Pirogov Memorial Medical University, Department of Pharmaceutical Chemistry, 56 Pirogov St., Vinnytsia 21018, Ukraine
✉ *tarastitov88@gmail.com*

https://

Abstract. The paper presents modern data on the complexation of CuHal halides (Hal = Cl, Br, I; duration - 5 hours; temperature – 60-70°C) with arylamides of benzimidazole-2-thiocarboxylic acid $HL^{I\text{-}X}$ in alkaline aqueous-methanol solution. Such interaction forms $CuL^{I\text{-}X}$ chelates with a yield of 96–99% (method A), while the interaction of Cu_2O (duration - 8 hours; temperature – 70-75°C) with thioamides $HL^{I\text{-}X}$ in methanol forms $CuL^{I\text{-}X}$ chelates with a yield of 90–95% (method B). The composition and structure of the new synthesized copper(I) chelates were studied by elemental analysis and IR spectroscopy. The use of copper(I) chelates as synthons in the production of biologically active compounds and new materials for technology is proposed.

Keywords: copper(I) chelates, heterocyclic thioamides, complexation, wear, lubricant compositions, biologically active and medical drugs.

1. Introduction

The chemistry of thioamides[1-4] and their coordination compounds of copper(I, II)[5-10] is actively developing, as evidenced by original works and limited thematic reviews[11,12] on this subject. This is due to the wide range of practical uses of both thioamides and their coordination compounds, primarily in the development of new drugs, as well as in various technical fields. Thus, the main direction of the development of new drugs is the structural modification of already active bioactive molecules, which improves their efficiency, selectivity, physicochemical and pharmacological properties, and reduces potential toxicity.[13] Regarding thioamides, as biologically active molecules, the strategy of biosterism is of great importance. Thioamides, which themselves have antitumor, antimicrobial, antiviral, and anti-inflammatory activity,[14] are used as isosteres of medical drugs containing amide, sulfamide, or carboxyl functional groups. At the same time, thioamides, as the closest isosteres of amides, are widely used in the development of new medicines. Apparently, this is due to the difference in the physical properties of the amide and thioamide groups in the composition of the initial synthons (Table 1). The difference in the radii of Sulfur and Oxygen atoms and the presence, respectively, of 3d- and 2p-outer orbitals determine the change in the length of the C=X bond, nucleophilicity, and valence of hydrogen bonds, which is important both for the chemical reactivity of the specified centers and for their non-covalent interactions. It should be noted that the presence of N,S-coordinating centers in the composition of thioamides determines their high chelating activity towards a number of biologically important metals.

At the same time, thioamides have increased lipophilicity, which allows them to perform a transport function during the penetration of metals through biological membranes. For example, Elesclomol (STA-4783), developed by Synta Pharmaceuticals Corp. as an oncological drug, selectively transports copper to mitochondria, where it induces the oxidative process in cancer cells.[16] In research,[17] the azepine derivative T4FAT was studied, which effectively blocks the catalytic activity of tyrosinase and reduces melanogenesis in B16 F10 cells. At the same time, the thioamide group in the composition of T4FAT plays an important role in chelating copper and inhibiting tyrosinase. In research,[18] Ru and Os complexes based on pyridine-2-carbothioamide ligands were also synthesized, which demonstrated high anticancer activity. In addition to high specific bioactivity, complex copper compounds also exhibit broad-spectrum biological activity. Thus, complex compounds of copper (I, II) are widely used as disinfectant solutions, antimicrobial, antibacterial, and antiviral drugs.[19-22]

Another important area of application of complex compounds of 3d-metal based on thioamides of various substitutions is their use in various technical fields, primarily in the automotive and transport industries.

Table 1. Physical properties of the amide and thioamide groups in the composition of the initial synthons

Characteristic	Unit	Group –C(=X)NH–		References
		Thioamide X=S	Amide X=O	
Atomic radius	Angstrom /Å	1.85	1.40	14
Bond length C=S	Angstrom /Å	1.71	1.23	14
Hydrogen bond C=X···H–N–C=O		4.80	6.10	15
Hydrogen bond C=O···H–N–C=X		7.30	6.10	15
Inversion barrier C–N		22.00	17.00	4

Thus, several reserachers[23,24] investigated I-20A oil + Cu(II) chelates + DMFA lubricating compositions in the bronze BrAZh 9-4 – thioamide – I-20A oil – steel 45 tribochemical system and determined their anti-wear and antifriction properties. Copper(II) chelates were found to be the active component in the studied compositions, ensuring high-performance properties of friction pairs. The role of copper(II) chelates is determined by the formation of organometallic compounds in the friction process, the formation of a servite layer and a polymer film, which ensures the operation of the friction unit in the selective transfer mode.[23-25] However, the rapid development of nanotribology allows us to consider friction not only from the scientific standpoint as a self-regulating process but also to obtain the necessary effective components of modern lubricants (fullerenes, carbon nanotubes, MoS_2, BN, and other ultrafine materials).[26] At the same time, it is necessary to note several modern technologies that provide protective coatings in the friction layers of various machines and mechanisms. Among them, the most promising is the development of composite materials using the CVD (Chemical Vapor Deposition) method,[27,28] the essence of which is the chemical gas-phase deposition/emission of metals when heating metal-organic or coordination compounds:

$$Cu(C_5H_7O_2)_2 \xrightarrow{400\text{-}450\ ^{o}C} Cu^{o} + CH_3C(=O)CH_3 + CH_3C(=O)CH_2C(=O)CH_3 + CH_3COOH + CO_2 + CO \quad (1)$$

$$Ni(C_5H_5)_2 \xrightarrow{300\text{-}350\ ^{o}C} Ni^{o} + 2CH_4 + 8CO_2 + H_2 \quad (2)$$

where $Cu(C_5H_7O_2)_2$ is copper(II) acetylacetonate; $Ni(C_5H_5)_2$ is cyclopentadienyl nickel(II).

Such systems are designed for optimal temperature parameters of thermal dissociation, which ensures the formation of a high-quality metal substrate. Obviously, the metals that make up organometallic or coordination compounds should have a reasonably minimal degree of oxidation. That is, monovalent copper coordination compounds are promising research objects for obtaining protective coatings for friction pairs of various machines and mechanisms using the CVD method.

However, it should be noted that the use of copper chelates in technical, biological fields and medicine concerns mainly divalent copper compounds (copper(II) chelates), while the synthesis of monovalent copper compounds (copper(I) chelates) is much more difficult, and such compounds are less stable and less studied in various fields of human activity. Solving the issue of the synthesis of monovalent copper chelates based on substituted thioamides, as objects of further research, became an additional incentive for this work.

The aim of this work is the synthesis of new copper(I) chelates based on heterocyclic thioamides, research of their composition and structure, and determination of possible practical application areas.

2. Experimental

2.1. Materials and Methods

The coordination compounds of the general formula CuL^{I-X} (Scheme 3) were synthesized using benzimidazole-2-thiocarboxylic acid arylamides ($HL^{I-VII, IX, X}$) obtained previously by a modified Willgerodt-Kindler reaction.[8-10] In this work, the new thioamide ligand HL^{VIII} was additionally synthesized. The generalized physicochemical properties of the used thioamide ligands are shown in Table 3 (*vide* Section 3). The inorganic compounds of copper(I), potassium hydroxide, 2-methoxy-5-methylaniline, anhydrous alcohols CH_3OH, and *i*-C_3H_7OH used in the synthesis were of reagent grade. The content of copper(I) in the synthesized coordination compounds was determined by complexometric titration with EDTA. The elemental analysis for Nitrogen was performed by the Kjeldahl method, and Sulfur – by the Schöniger method[24]. The IR spectra of coordination compounds I-X in the range of 4000–400 cm^{-1} were recorded using a Specord 75 IR instrument. The samples were prepared in the form of KBr tablets. The ^1H NMR spectra of thioamide ligands were recorded by Varian VXR-200 (200 MHz) and Varian VXR-400 (400 MHz) radiospectrometers for DMSO-d6 solutions using the internal TMS standard. The obtained ^1H NMR spectral data of the used thioamides are given in Table 2 (*vide* Section 3), and their discussion – in Section 3.

2.2. Synthesis of benzimidazole–2–N–(2–methoxy–5–methylphenyl) carbothioamide, VIII

A reactor equipped with a mechanical stirrer, thermometer, and reflux condenser was loaded with 26.4 g (0.2 mol) of 2-methylbenzimidazole, 28.8 g (0.21 mol) of 2-methoxy-5-methylaniline, 19.2 g (0.6 mol) of sulfur, 3.6 g (15 mmol) of $Na_2S{\cdot}9H_2O$, and 30 mL of DMSO. The reaction mixture was heated at 110–120 °C for 1.5 h without a reflux condenser. Then the reflux condenser was attached and the reaction mixture was heated at 130-140 °C for 10 h. The mixture was cooled to 70-80 °C and extracted with a 5% NaOH solution (3 × 250 mL). The alkaline extracts were combined, the hot solution was filtered, cooled to room temperature, and acidified with dilute sulfuric acid to pH = 5-6. The resulting yellow precipitate was filtered, dried, and recrystallized from an aqueous solution of i-C_3H_7OH, precipitated from a dilute solution of NaOH, and recrystallized from an aqueous solution of CH_3OH. The yield was 54.7 g (92 %). The melting point was 285-290 °C. For comparison, the yields of other arylamides of benzimidazole-2-thiocarboxylic acid used in this work are given in Table 2 (*vide* Section 3).

2.3. A general method of the synthesis of copper(I) chelates

2.3.1. Synthesis of [benzimidazole–2–N–(4–methoxyphenyl)carbothioamidato] copper(I), V

Method A. A solution of 0.28 g (5.0 mmol) of KOH in 2 mL of water was added under stirring to a solution of 1.42 g (5.0 mmol) of benzimidazole-2-N-(4-methoxyphenyl)carbothioamide in 100 mL of hot methanol. After that, 0.50 g (5.0 mmol) of copper(I) chloride was added to the reaction mass, and the heterogeneous reaction mixture was stirred at 60-70 °C for 5 h and then cooled to room temperature. The resulting dark brown precipitate was filtered using a Schott filter, washed repeatedly with hot water, then with alcohol (2 × 10 mL), and dried in an oven at 80-90 °C. The yield was 1.66 g (96 %). The melting point was 285-290 °C.

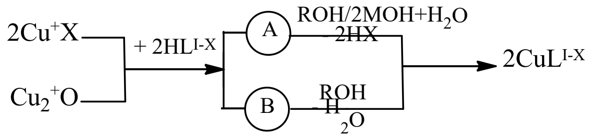
2.3.2. Synthesis of [benzimidazole–2–N–(2–methylphenyl)carbothioamidato] copper(I), II

Method B. 0.72 g (5.0 mmol) of copper(I) oxide was added under stirring to a solution of 1.20 g (5.0 mmol) of benzimidazole-2-N-(2-methylphenyl)carbothioamide in 100 mL of hot methanol. The heterogeneous reaction mixture was stirred at 70-75 °C for 8 h and then cooled to room temperature. The resulting red-brown precipitate was filtered using a Schott filter, washed repeatedly with hot water, then with methanol (2 × 10 mL), and dried in an oven at 80-90 °C. The yield was 1.42 g (94 %). The melting point was 259-262 °C.

Other coordination compounds of copper(I) I, III, IV, VI-X were synthesized similarly by methods A or B. Some properties of the obtained copper(I) chelates are given in Table 3 (*vide* Section 3).

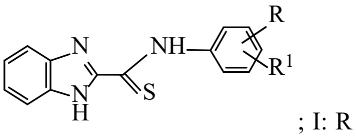
3. Results and Discussion

The complexation reactions of heterocyclic thioamides HL^{I-X} were studied according to the scheme:



(3)

HL^{I-X}:

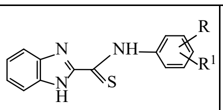


; I: R = R^1 = H; II: R = H, R^1 = 2-CH_3; III: R = H, R^1 = 2-CH_3; IV: R = H, R^1 = 2-OCH_3; V: R = H, R^1 = 4-OCH_3; VI: R = H, R^1 = 4-OC_2H_5; VII: R = 2-CH_3, R^1 = 4-CH_3; VIII: R = 2-OCH_3, R^1 = 5-CH_3; IX: R = H, R^1 = 4-Cl; X: R = H, R^1 = 4-Br.

X^- = Cl, Br, I; M^+ = K, Na; ROH: CH_3OH, i-C_3H_7OH.

The peculiarities of this reaction are that copper(I) compounds are poorly soluble in water and, if present in the aqueous medium, can disproportionate as follows: $2Cu^{+} \rightleftarrows Cu^{2+} + Cu_{0}$. That is, water as a solvent should be present in the reaction medium in a minimal amount. It is possible to effectively stabilize ("hold") the ionic state of the formed copper(I) by a complexation reaction, for example, with the heterocyclic thioamides $HL^{I\text{-}X}$ studied by us (Scheme 3). In this case, complexation and the formation of $CuL^{I\text{-}X}$ chelates (coordination number 2) can be considered as a result of the chemical reaction of the sp-hybridized copper(I) orbital (4s + 4p orbitals) and the N,S electron donor centers of the thioamide ligand. In addition, an important factor is that in the case of disproportionation of the starting copper(I) compounds, the subsequent complexation of thioamide ligands will already correspond equally to a mixture of Cu^{+} and Cu^{2+} cations and also to the formation of various complexes. To prevent the disproportionation of copper(I) compounds, the reaction was carried out with a minimum amount of water (method A) or in a medium of anhydrous alcohol (method B). Some properties of the obtained copper(I) chelates are shown in Table 3.

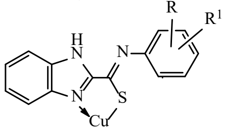
Table 2. ^{1}H NMR spectral data of benzimidazolyl-2-thiocarboxylic acid arylamides[2,10]

Compound			Brutto-formula	$\frac{\text{Found}}{\text{Calculated}}$, %		^{1}H NMR, δ, ppm	Melting point, °C	Yield, %
	R	R^1		N	S			
HL^{I}	H	H	$C_{14}H_{11}N_3S$	$\frac{16.25}{16.59}$	$\frac{12.34}{12.66}$	7.29t, 8.02d (5H, C_6H_5); 7.45-7.70d (4H, $C_6H_{4\,Het}$); 12,00c (1H, NH); 12,40c (1H, NH_{Het})	151–153	17.0
HL^{II}	H	OCH_3-2	$C_{15}H_{13}N_3OS$	$\frac{14.60}{14.83}$	$\frac{11.74}{11.32}$	4.00s (3H, CH_3); 7.04t, 7.17d, 7.30t, 7.62d, 7.76d, 8.98d (8H, C_{Ar}-H, C_{Ar}-H); 11,77c, 12,92c (2H, NH, NH)	171.5–173	25.0
HL^{IV}	H	OC_2H_5-4	$C_{16}H_{15}N_3OS$	$\frac{14.51}{14.13}$	$\frac{10.45}{10.78}$	1.40m (3H, CH_3), 4.00 – 4.10m (2H, CH_3); 6.97d, 7.92d (4H, C_{Het}-H); 12.05s, 12.85s (2H, NH, NH)	171–172	17.0
HL^{VI}	CH_3-2	CH_3-4	$C_{16}H_{15}N_3S$	$\frac{14.54}{14.93}$	$\frac{11.75}{11.40}$	2.26s, 2.35s (6H, CH_3, CH_3); 7.08t, 7.30t, 7.62d, 7.74d (7H, C_{Ar}-H, C_{Ar}-H); 11.90s (1H, NH), 12.85s (1H, NH_{Het})	142–144	11.5
HL^{VII}	H	Cl-4	$C_{14}H_{10}ClN_3S$	$\frac{14.88}{14.60}$	$\frac{11.45}{11.14}$	7.42d, 7.06d, (4H, C_6H_4); 7.28t, 7.68s (4H, C_{Het}-H); 12.22s (1H, NH), 12.90s (1H, NH_{Het})	168–169	32.0
HL^{IX}	H	Br-4	$C_{14}H_{10}BrN_3S$	$\frac{12.41}{12.65}$	$\frac{9.82}{9.65}$	7.59d, 8.00d, (4H, C_{Ar}-H); 7.30d, 7.62 – 7.82m (4H, C_{Het}-H); 12.20s, (1H, NH); 12.92s (1H, NH_{Het})	159.5–160.5	70.5
HL^{X}	H	F-4	$C_{14}H_{10}FN_3S$	$\frac{15.31}{15.49}$	$\frac{11.42}{11.82}$	2.50d, 3.04cs(3H, CH_3); 7.27m, 7.68m, (4H, C_{Het}-H); 7.55s, 7.88d (3H, C_{Ar}-H); 11.80s, (1H, NH); 12.90s (1H, NH_{Het})	173–175	19.0

Note: the yield of $HL^{I\text{-}X}$ compounds was obtained after triple recrystallization in the following sequence: I – i-C_3H_7OH aqueous solution; II – aqueous 5 % NaOH solution; III – CH_3OH aqueous solution.

The data presented in Table 3 indicate a high yield (90-99 %) of the final $CuL^{I\text{-}X}$ chelates and the indirect absence of disproportionation of copper(I) compounds at the first stage of chemical reaction, because otherwise, the yield of the final chelates would be much lower. The composition and structure of benzimidazole-2-thiocarboxylic acid arylamides used in the complexation reaction (1) were confirmed by elemental analysis and ^{1}H NMR spectroscopy (Table 2). The ^{1}H NMR spectra of the $HL^{I\text{-}X}$ thioamides are quite similar. The signal in the region of 1.30–2.30 ppm (mostly a singlet) refers to the protons of the CH_3 group, with the highest value (2.30 s) referring to the corresponding protons of *o*-methylanilide (HL^{II}). An even higher value of the singlet of the three protons at 4.00–4.10 ppm is found in the spectrum of *p*-ethoxyanilide (HL^{VI}). The signal in the region of 7.04–7.92 ppm (doublet, triplet) refers to the protons of thioamide ligands of $HL^{I\text{-}X}$ in the presence of both aryl/amide and hetaryl/benzimidazole fragments in the molecule. The protons of the NH group of the aromatic fragment appear in the region of 11.77–12.20 ppm (singlet), and those of the imidazole fragment in the region of 12.40–12.92 ppm (singlet).

Table 3. Some properties of copper(I) chelates of the general formula



Complex compound	R	R¹	Color of the complex	$\frac{\text{Found}}{\text{Calculated}}$, %			Brutto-formula	Melting point, °C	Yield, %
				N	S	Cu			
CuL^{I}	H	H	dark brown	$\frac{13.02}{13.30}$	$\frac{10.18}{10.15}$	$\frac{20.06}{20.12}$	$C_{14}H_{10}N_3SCu$	> 300	95
CuL^{II}	H	$2\text{-}CH_3$	reddish-brown	$\frac{12.21}{12.74}$	$\frac{9.40}{9.72}$	$\frac{19.11}{19.26}$	$C_{15}H_{12}N_3SCu$	259-262	94
CuL^{III}	H	$4\text{-}CH_3$	dark brown	$\frac{12.34}{12.74}$	$\frac{9.26}{9.72}$	$\frac{19.10}{19.26}$	$C_{15}H_{12}N_3SCu$	220-250	94
CuL^{IV}	H	$2\text{-}OCH_3$	dark brown	$\frac{11.38}{12.14}$	$\frac{9.01}{9.27}$	$\frac{18.14}{18.37}$	$C_{15}H_{12}N_3OSCu$	212-215	91
CuL^{V}	H	$4\text{-}OCH_3$	dark brown	$\frac{12.04}{12.14}$	$\frac{8.88}{9.27}$	$\frac{18.24}{18.37}$	$C_{15}H_{12}N_3OSCu$	290-300	96
CuL^{VI}	H	$4\text{-}OC_2H_5$	burgundy-brown	$\frac{11.41}{11.68}$	$\frac{8.66}{8.91}$	$\frac{17.35}{17.66}$	$C_{16}H_{14}N_3OSCu$	285-293	97
CuL^{VII}	$2\text{-}CH_3$	$4\text{-}CH_3$	brown	$\frac{12.14}{12.22}$	$\frac{9.29}{9.32}$	$\frac{18.10}{18.48}$	$C_{16}H_{14}N_3SCu$	260-270	92
CuL^{VIII}	$2\text{-}OCH_3$	$5\text{-}CH_3$	burgundy	$\frac{11.41}{11.68}$	$\frac{8.40}{8.91}$	$\frac{17.34}{17.66}$	$C_{16}H_{14}N_3OSCu$	285-290	92
CuL^{IX}	H	4-Cl	dark brown	$\frac{11.78}{12.00}$	$\frac{8.84}{9.15}$	$\frac{17.75}{18.14}$	$C_{14}H_9ClN_3SCu$	265-270	90
CuL^{X}	H	4-Br	dark brown	$\frac{10.35}{10.64}$	$\frac{8.23}{8.12}$	$\frac{15.63}{16.10}$	$C_{14}H_9BrN_3SCu$	230-240	99

Table 4. IR-spectra of some heterocyclic thioamides and copper(I) coordination compounds based on them

Compound	Vibrations of NH-group, cm^{-1}		Vibrations of –C(=S)NH-group, cm^{-1}						Other vibrations, cm^{-1}
	$\nu(NH_{thio})$	$\nu(NH_{Het})$	B-band		D-band		E-band		
			C–N	N–H	C–N	C=S	C=S	C–N	
1	2	3	4	5	6	7	8	9	10
HL^{II}	3370 3270	3045	1555 1510	1395 1315	1240 1185	1085	850	755	1287, 1150, 1240, 950, 775, 880
HL^{IV}	3300 3260	3063	1536	1380 1320	1280	1110	944	762 745	1598, 1465, 1423
HL^{VI}	3330 3260	3075	1532 1515	1390 1315	1280 1185	965	832	750	1225, 1125 870, 680
HL^{VII}	3324 3290	3065	1540 1506	1387 1316	1287 1194	933	812	738 732	1575, 1146 900, 700
HL^{IX}	3260	3015	1546 1500	1387 1320	1290 1196	960	870	745	2975, 1455, 772, 1085, 870, 695

Table 4. *(Ccontinuation)* IR-spectra of some heterocyclic thioamides and copper(I) coordination compounds based on them

1	2	3	4	5	6	7	8	9	10
HL^{X}	3260	3015	1596 1535	1384 1316	1280	1072 1006	820	730	1610, 1488, 950, 930, 620
CuL^{II}		3080m 3015m	1525s	1390m 1312m	1220m	1170m 1125s	935m 810w	760s	1597m, 1465s, 1255s, 1035s
CuL^{V}		3080s 3020m	1510vs	1320m	1227m	1140m 1115w	965s 825m	745s	1625m, 1608s, 1260s, 1026s
CuL^{VIII}		3035m	1550m	1310m	1230m	1185m 1130s	850m	750m	1620m, 1575m, 1465s

Note: B-band (C–N + N–H) with a greater contribution of the N-H group; D-band (C–N + C=S) with a greater contribution of the C–N group; E-band (C=S + C–N) with a greater contribution of the C=S group.

Vibration intensity: vs – very strong; s – strong; m – moderate; w – weak.

The structure of the obtained $CuL^{I\text{-}X}$ chelates was investigated using IR spectroscopy by comparing the characteristic absorption frequencies of the thioamide group of the "pure" ligand and the complex compound (Table 4).

The spectra of the used thioamide ligands contain stretching vibrations of the thioamide fragment NH group in the region of 3370–3260 cm^{-1}, as well as several complex stretching and bending vibrations of the –C(=S)NH group: B-band: 1596–1506 cm^{-1} (C–N) + 1395–1315 cm^{-1} (N–H); D-band 1290–1185 cm^{-1} (C–N) + 1110–933 cm^{-1} (C=S); E-band: 944–812 cm^{-1} (C=S) + 762–730 cm^{-1} (C–N). In addition, the studied $HL^{I\text{-}X}$ ligands have weak stretching vibrations of the N–H bond of the benzimidazole fragment in the region of 3075–3015 cm^{-1}. In the case of the synthesized copper(I) chelates, the IR spectra do not show stretching vibrations of $\nu(NH_{thio})$ of the ligands, which clearly indicates the deprotonation of the thioamide group and the formation of deprotonated $CuL^{I\text{-}X}$ chelates, respectively. The displacements of other stretching vibrations of the thioamide group of the studied ligands with their vibrations in the composition of the synthesized $CuL^{I\text{-}X}$ chelates (Table 4) are insignificant and coincide with those described earlier in works.[8-10,29]

Thus, in this work, new copper(I) chelates based on heterocyclic thioamides were synthesized, isolated, and investigated as potentially promising synthons for the development of new medical drugs or obtaining multifunctional additives to lubricants and technical oils.

4. Conclusions

The formation of stable chelates of monovalent copper with N,S-bidentate heterocyclic thioamides of the general formula $CuL^{I\text{-}X}$ has been established. At the same time, for the first time, new coordination compounds of copper(I) based on benzimidazole-2-N-arylcarbothioamides of the general formula $CuL^{I\text{-}X}$ were synthesized, the composition and structure of which were established by elemental analysis and IR spectroscopy. It is shown that the formation of $CuL^{I\text{-}X}$ coordination compounds occurs during the interaction of copper(I) salts with heterocyclic thioamides in alkaline aqueous-methanol solution (method A) or the interaction of copper(I) oxide with the same ligands in anhydrous methanol (method B) and at a stoichiometric ratio: $Cu^{+} : H^{I\text{-}X} = 1{:}1$. The optimal conditions for the synthesis of $CuL^{I\text{-}X}$ coordination compounds have been substantiated. According to method A: duration - 5 hours; temperature - 60-70 °C; the yield of the complexes was 96-99%. According to method B: duration - 8 hours; temperature - 70-75 °C; the yield of the complexes was 90-95%. The prospects of the study and possible use of the synthesized complexes $CuL^{I\text{-}X}$ as initial synthons in the development of new medical drugs and multifunctional additives to lubricants are shown.

References

[1] Priebbenow, D. L.; Bolm, C. Recent Advances in the Willgerodt-Kindler Reaction. *Chem. Soc. Rev.* **2013**, *42*, 7870–7880. https://doi.org/10.1039/C3CS60154D

[2] Zhang, Q.; Soulere, L.; Queneau, Y. Toward More Practical Methods of the Chemical Synthesis of Thioamides Using Sulfuration Agents: A Decade Update. *Molecules* **2023**, *28*, 3527. https://doi.org/10.3390/molecules28083527

[3] Murai, T. Synthesis of Thioamides. *Chemistry of Thioamides*; Springer: Singapore, 2019. https://doi.org/10.1007/978-981-13-7828-7_3

[4] Hansen, T. N.; Olsen, Ch. A. Contemporary Application of Thioamides and Methods for Their Synthesis. *Chem. Eur. J.* **2024**, *30*, e202303770. https://doi.org/10.1002/chem.202303770

[5] Chojnacki, I.; Monka, M.; Serdiuk, I. E.; Bojarski, P.; Połoński, T., Olszewska, T. Copper(I) Halide Cluster-Based Coordination Polymers Modulated by Chiral Ditopic Dithiodianthranilide Ligands: Synthesis, Crystal Structure and Photoluminescence. *CrystEngComm*. **2021**, *23*, 299–307. https://doi.org/10.1039/D0CE01589J

[6] Lobana, T. S.; Sultana, R.; Hundal, G. Heterocyclic Thioamides of Copper(I): Synthesis and Crystal Structures of

Copper Complexes with 1,3-Imidazoline-2-thiones in the Presence of Triphenyl Phosphine. *Polyhedron* **2008**, *27*, 1008–1016. https://doi.org/10.1016/j.poly.2007.11.036

[7] Long, D. L.; Zeng, D. X.; Xin, X. G.; Huang, X. Y.; Kang, B. Sh. Synthesis and Characterization of Copper(I) and Silver(I) Complexes Containing Thioamide Ligands. *Synth. React. Inorg. Met.-Org. Chem.* **1996**, *26*, 723–733. https://doi.org/10.1080/00945719608004331

[8] Gordienko, O.; Titov, T.; Ranskiy, A.; Gumenchuk, O. Synthesis, Structure and Properties of Copper(II) Chelates with Benzimidazole-2-N-arylcarbothioamides. *Chem. Chem. Technol.* **2018**, *12*, 176–181. https://doi.org/10.23939/chcht12.02.176

[9] Ranskiy, A.; Didenko, N.; Gordienko, O. Synthesis of Heterocyclic Thioamides and Copper(II) Coordination Compounds Based on Them. *Chem. Chem. Technol.* **2017**, *11*, 11–18. https://doi.org/10.23939/chcht11.01.011

[10] Ranskiy, A.; Gordienko, O.; Didenko, N.; Titov, T.; Khutko, M. Synthesis, Structure and Application of Mixed-Ligand Coordination Compounds of Copper(II) with Substituted Thioamides. *Chem. Chem. Technol.* **2020**, *14*, 55–61. https://doi.org/10.23939/chcht14.01.055

[11] Orysyk, S.; Pekhnyo, V.; Orysyk, V.; Zborovskii, Y.; Borovyk, P.; Mykhailo, V. Fundamental Aspects of the Coordination Chemistry of Transition Metals with Functionally Substituted Thioamides (Part 1). *Ukrainian Chemistry Journal* **2022**, *88*, 85–115. https://doi.org/10.33609/2708-129X.88.02.2022.85-115

[12] Orysyk, S.; Pekhnyo, V.; Orysyk, V.; Zborovskii, Y.; Borovyk, P.; Vovk, M. Fundamental Aspects of Coordination Chemistry of Transition Metals with Functionally Substituted Thioamides (Part 2). *Ukrainian Chemistry Journal* **2022**, *88*, 3–27. https://doi.org/10.33609/2708-129X.88.03.2022.3-27

[13] Huang, G.; Cierpicki, T.; Grembecka, J. Unlocking the Potential of the Thioamide Group in Drug Design and Development. *Future Med. Chem.* **2025**, *17*, 1–3. https://doi.org/10.1080/17568919.2024.2435245

[14] Huang, G.; Cierpicki, T.; Grembecka, J. Thioamides in medicinal chemistry and as small molecule therapeutic agents. *Eur. J. Med. Chem*. **2024**, *277*, 116732. https://doi.org/10.1016/j.ejmech.2024.116732

[15] Iagodzinski, T. S. Thioamides as Useful Synthons in the Synthesis of Heterocycles. *Chem. Rev.* **2003**, *103*, 197–228. https://doi.org/10.1021/cr0200015

[16] Zheng, P.; Zhou, C.; Lu, L.; Liu, B.; Ding, Y. Elesclomol: A Copper Ionophore Targeting Mitochondrial Metabolism for Cancer Therapy. *J Exp Clin Cancer Res* **2022**, *41*, 271. https://doi.org/10.1186/s13046-022-02485-0

[17] Okajima, S.; Hamamoto, A.; Asano, M.; Isogawa, K.; Ito, H.; Kato, S.; Hirata, Y.; Furuta, K.; Takemori, H. Azepine Derivative T4FAT, a New Copper Chelator, Inhibits Tyrosinase. *Biocem. Biophys. Res. Commun*. **2019**, *509*, 209–215. https://doi.org/10.1016/j.bbrc.2018.12.105

[18] Riaz, Z.; Lee, Y.T.B.; Stjärnhage, J.; Movassaghi, S.; Söhnel, T.; Jamieson, M.F.S.; Shaheen, A.M.; Hanif, M.; Hartinger, G.C. Anticancer Ru and Os Complexes of *N*-(4-chlorophenyl)pyridine-2-carbothioamide: Substitution of the Labile Chlorido Ligand with Phosphines. *J. Inorg. Biochem*. **2023**, *241*, 112115. https://doi.org/10.1016/j.jinorgbio.2022.112115

[19] Borkow, G.; Gabbay, J. Copper as a Biocidal Tool. *Curr. Med. Chem.* **2005**, *12*, 2163–2175. http://dx.doi.org/10.2174/0929867054637617

[20] Tarik, A.; Yahia, H.; Lahcen, L. Determination of Ultra Trace Levels of Copper in Whole Blood by Adsorptive Stripping Voltammetry. *J. Korean Chem. Soc*. **2013**, *57*, 568–573. https://doi.org/10.5012/jkcs.2013.57.5.568

[21] Boulanouar, M.; Tarik, A.; Naceur, B. DFT Study of Some Copper Complexes and Their Derection Limit. *Chem. Chem. Technol*. **2022**, *16*, 185–194. https://doi.org/10.23939/chcht16.02.185

[22] Hassan, Z.M.; Alattar, R.A.; Abass, S.K.; Mihsen H.H.; Abbas, Z.F.; Hussain. K.A. Synthesis, Characterization and Biological Activity of Mixed Ligand (Imine of Benzidine and 1,10-Phenanthroline) Complexes with Fe(II), Co(II), Ni(II) and Cu(II) Ions. *Chem. Chem. Technol*. **2022**, *16*, 15–24. https://doi.org/10.23939/chcht16.01.015

[23] Ranskiy, A. P.; Boychenko, S. V.; Gordienko, O. A.; Didenko, N. O.; Voloshynets', V. A. *Kompozytsiyni mastyl'ni materialy na osnovi tioamidiv ta yikh kompleksnykh spoluk. Syntez. Doslidzhennya. Vykorystannya*; VNTU: Vinnytsia, 2012. https://press.vntu.edu.ua/index.php/vntu/catalog/book/207

[24] Didenko, N. O.; Ranskiy, A. P. *Pryamyy syntez koordynatsiynykh spoluk kuprumu(II) iz zamishchenymy tioamidamy*; VNTU: Vinnytsia, 2021. https://press.vntu.edu.ua/index.php/vntu/catalog/book/623

[25] Ranskiy, A. P.; Didenko, N. O.; Titov, T. S.; Bezvozyuk, I. I. Mekhanizm vybirkovoho perenesennya z tochky zoru rezonansnoho potentsialu za Nechayevym [Online]. *Scientific Works of Vinnytsia National Technical University.* **2010**, *4*. https://praci.vntu.edu.ua/index.php/praci/article/view/230/228

[26] Bukvić, M.; Gajević, S.; Skulić, A.; Savić, S.; Ašonja, A.; Stojanović, B. Tribological Application of Nanocomposite Additives in Industrial Oils. *Lubricants* **2024**, *12*, 21. https://doi.org/10.3390/lubricants12010006

[27] Vahlas, C.; Caussat. B.; Serp, Ph.; Angelopoulos, G.N. Principles and applications of CVD powder technology. *Mater. Sci. Eng.: R: Rep..* **2006**, *53*, 1–72. https://doi.org/10.1016/j.mser.2006.05.001

[28] Izyumskiy, M. S.; Neykovskiy, S. I.; Mel'nik, S. G.; Shtemenko, A. V. Klasternye khlorkarboksilaty direniya(III) kak novye iskhodnye veshchestva dlya khimicheskogo gazofaznogo metoda naneseniya renievykh pokrytiy. *Issues of Chemistry and Chemical Technology* **2013**, *1*, 134–136.

[29] Jensen, K. A.; Nielsen, P. H. Infrared Spectra of Thioamides and Selenoamides. *Acta Chem. Scand*. **1966**, *20*, 597–629.

Received: February 25, 2025 / Revised: April 24, 2025 / Accepted: June 05, 2025

СИНТЕЗ ХЕЛАТІВ КУПРУМУ(І) НА ОСНОВІ ГЕТЕРОЦИКЛІЧНИХ ТІОАМІДІВ

Анотація. *Комплексоутворенням галогенідів CuHal (Hal = Cl, Br, I; час реакції – 5 год.; температура – 60–70°С) з ариламідами бензімідазол-2-тіокарбонової кислоти* HL^{I-X} *в лужному водно-метанольному розчині отримано хелати* CuL^{I-X} *з виходом 96–99 % (метод А), тоді як взаємодія* Cu_2O *(час реакції – 8 год.; температура – 70–75°С) з тіоамідами* HL^{I-X} *в метанолі проходить з утворенням хелатів* CuL^{I-X} *з виходом 90–95 % (метод Б). Склад і будову нових синтезованих хелатів купруму(І) досліджено елементним аналізом та ІЧ-спектроскопією. Запропоновано використання хелатів купруму(І) як синтонів для отримання біологічно активних сполук і нових матеріалів до техніки.*

Ключові слова: *хелати купруму(І), гетероциклічні тіоаміди, комплексоутворення, зношування, мастильні композиції, біологічно активні та лікарські препарати.*