

**NOVEL COPPER COMPLEXES WITH GLYOXIMES, AMINES, SCHIFF BASES, SEMI- AND THIOSEMICARBAZONES; SYNTHESIS AND PHYSICO-CHEMICAL ANALYSIS**

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### Abstract

In our research project new copper(II) complexes were synthesized with  $\alpha$ -dioximes, amines, Schiff bases, semi- and thiosemicarbazones such as  $[\text{Cu}(\text{DioxH})_2\text{L}_2]$ , ( $\text{DioxH}_2$ : methyl-butyl-glyoxime, ethyl-butyl-glyoxime, methyl-phenyl-glyoxime; L: diphenyl-amine, 2-methylimidazole, dibutyl-amine, 2-amino-4-methylpyridine, imidazole, 1-aminonaphthalene),  $[\text{Cu}(\text{octan-2-one})_2\text{AL}_2]$ , (A: hydrazine, phenylhydrazine, *o*-phenylene-diamine; L: 3-amino-1*H*-1,2,4-triazole, 2-aminopyrimidine, 2-methylimidazole),  $[\text{Cu}(\text{ketone-SC})_2]$ ,  $[\text{Cu}(\text{ketone-TSC})_2]$ , (ketone: propiophenone, butyrophenone; SC: semicarbazone; TSC: thiosemicarbazone), by the reaction of copper(II)-acetate in suitable solvent. After a short bibliographical survey, involving the classification and evolution of copper complexes with possible applications, we analyzed their physicochemical properties using FTIR, Raman, ESR, UV-VIS, powder X-ray diffraction (XRD), mass spectrometry, thermal analysis (TG, DTG, DTA) and SEM. The importance of this class of compounds lies in biochemistry as some of them are antibacterial agents and potential anti-tumour drugs.

### Introduction

Copper is one of the oldest and most widely used metal. Its name originates from the Latin name of Cyprus, Cyprium. Copper is an essential element in the life of plants and animals. It is also an industrial metal bearing excellent electrical and thermal conductivity, and easy to work with it, and when is combined with other metals, its technical applications are unlimited.

Among copper coordination compounds, copper(II)-azomethines (Schiff bases, oximes, hydrazones, semi- and thiosemicarbazones, porphyrins, etc.) play very important role in many biological and biochemical processes. Schiff bases show bacteriostatic and antibacterial activities. In addition, its anti-fungal, anti-tumor and anti-cancer effects have also been reported [1]. Copper complexes formed with dioximes are also significant due to their antibacterial effect [2], and some representatives are catalysts in oxidative coupling (polymerization) reactions.

Schiff bases are privileged class of ligands in coordination chemistry, and found numerous applications in different scientific fields. Semicarbazones and thiosemicarbazones are biologically important compounds due to their potential pharmacological properties such as antibacterial, antifungal, antimalarial, anticancer, antineoplastic and antiviral activities. Medicinal chemistry shows a growing interest in the development of metal complexes as drugs

or diagnostic agents. Owing to their wide range of coordination numbers and geometries, as well as kinetic properties, metal compounds offer various mechanisms for drug action [3]. In this paper we report the synthesis and characterization of novel copper complexes with glyoximes, Schiff bases, semi- and thiosemicarbazones.

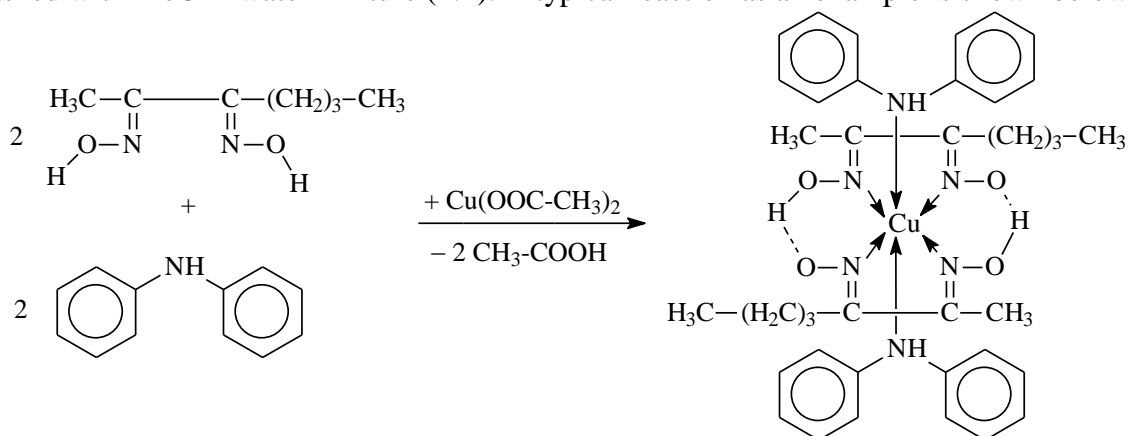
## Experimental

**Used materials:**  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$ , Me-Bu-DioxH<sub>2</sub>, Et-Bu-DioxH<sub>2</sub>, Me-Ph-DioxH<sub>2</sub>, diphenylamine, 2-methylimidazole, dibutyl-amine, 2-amino-4-methylpyridine, imidazole, 1-aminonaphthalene, 3-amino-1*H*-1,2,4-triazole, 2-aminopyrimidine, octan-2-one, hydrazine, phenylhydrazine, *o*-phenylene-diamine, propiophenone, butyrophenone, semicarbazide, thiosemicarbazide, MeOH, EtOH.

### Methods:

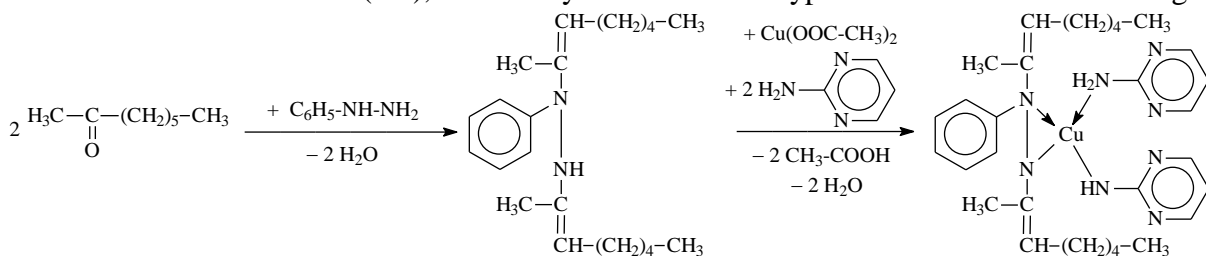
#### - Synthesis of $[\text{Cu}(\text{DioxH})_2\text{L}_2]$ type complexes

2 mmol DioxH<sub>2</sub> (Me-Bu-DioxH<sub>2</sub>, Et-Bu-DioxH<sub>2</sub> or Me-Ph-DioxH<sub>2</sub>) was dissolved in 20 ml EtOH or MeOH, then this solution was added to the aqueous solution of 1 mmol (0.2 g)  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$  dissolved in 10 ml water. Afterwards 2 mmol amine (diphenyl-amine or 2-methylimidazole or dibutyl-amine or 2-amino-4-methylpyridine or imidazole or 1-aminonaphthalene) dissolved in 5 ml EtOH or MeOH was added. The obtained solution was heated for 2–3 hours on a water bath. After cooling the crystalline complexes were filtered, washed with MeOH–water mixture (1:1). A typical reaction as an example is shown below:



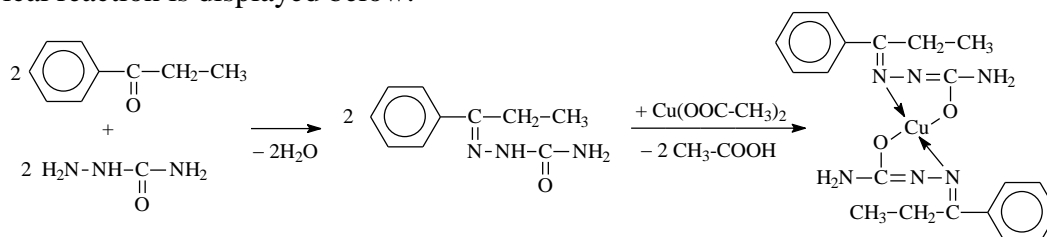
#### - Synthesis of $[\text{Cu}(\text{2-octanone})_2\text{AL}_2]$ type complexes

3 mmol octan-2-one (0.5 ml) and 1.5 mol diamine (hydrazine or phenylhydrazine or *o*-phenylene-diamine) were dissolved in 5 ml MeOH, then refluxed for 1–2 hours. The resulting colored solution was added to the aqueous solution of 1.5 mol (0.3 g)  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$  dissolved in 5 ml water. At last 3 mmol amine (3-amino-1*H*-1,2,4-triazole or 2-amino-pyrimidine or 2-methylimidazole) dissolved in 10 ml MeOH was added. The obtained mixture was refluxed in a water bath for 2–3 hours. After cooling the crystalline complexes were filtered off, washed with MeOH–water mixture (1:1), and finally dried on air. A typical reaction is the following:



- Synthesis of  $[Cu(\text{ketone-SC})_2]$ ,  $[Cu(\text{ketone-TSC})_2]$  type complexes

1.5 mmol propiophenone or butiropfenone was added to 1.5 mmol semi- or thiosemicarbazide dissolved in 5 ml water. In the case of semicarbazide 1.5 mmol  $\text{CH}_3\text{COONa}$  (0.1 g) was added to release the semicarbazide from the salt. The obtained solution was refluxed in a water bath for 1 hour, then 0.75 mmol (0.2 g)  $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$  dissolved in 5 ml distilled water was added. The obtained mixture was refluxed in a water bath for 2–3 hours. After cooling the crystalline complexes were filtered off, washed with  $\text{MeOH}$ –water mixture (1:1), and finally dried on air. A typical reaction is displayed below:

**Results and discussion**

Microscopic characterization and yields of the prepared complexes are presented in Table 1.

Table 1. Microscopic characterization, calculated molar masses and yields of the prepared complexes.

Nr.	Compound	Calc. mol. mass	Yield (%)	Microscopic characterization
1.	$[\text{Cu}(\text{Me-Bu-DioxH})_2(\text{diphenyl-amine})_2]$	716.38	62	Dark brown lamellar crystals
2.	$[\text{Cu}(\text{Me-Bu-DioxH})_2(2\text{-Me-imidazole})_2]$	542.14	17	Brown triangle-based prisms
3.	$[\text{Cu}(\text{Me-Bu-DioxH})_2((n\text{-Bu})_2\text{NH})_2]$	636.42	50	Dark brown triangle-based prisms
4.	$[\text{Cu}(\text{Me-Bu-DioxH})_2(2\text{-amino-4-Me-pyridine})_2]$	594.21	69	Dark brown triangle-based prisms (microcrystals)
5.	$[\text{Cu}(\text{Et-Bu-DioxH})_2(\text{imidazole})_2]$	542.14	56	Dark brown irregular microcrystals
6.	$[\text{Cu}(\text{Ph-Me-DioxH})_2(2\text{-amino-4-Me-pyridine})_2]$	634.19	56	Reddish-brown triangle-based prisms
7.	$[\text{Cu}(\text{Ph-Me-DioxH})_2(1\text{-naphthylamine})_2]$	704.28	50	Black triangle-based prisms, lamellar crystals
8.	$[\text{Cu}(\text{Ph-Me-DioxH})_2(2\text{-Me-imidazole})_2]$	582.12	49	Dark brown triangle-based prisms (microcrystals)
9.	$\text{Cu}(2\text{-oct.})_2(\text{hidrazone}(3\text{-amino-1}H\text{-1,2,4-triazole})_2]$	482.13	21	Green triangle-based prisms (microcrystals)
10.	$[\text{Cu}(2\text{-oct.})_2(\text{Ph-hidrazone}(2\text{-amino-pyrimidine})_2]$	581.28	7	Khaki green, small triangle-based prisms (microcrystals)
11.	$[\text{Cu}(2\text{-octanone})_2(\text{o-fen}(2\text{-Me-imidazole})_2]$	554.28	21	Dark brown triangle-based prisms (microcrystals)
12.	$[\text{Cu}(\text{propiophenone-SC})_2]$	443.99	24	Brown, small triangle-based prisms (microcrystals)
13.	$[\text{Cu}(\text{propiophenone-TSC})_2]$	476.11	41	Brown triangle-based prisms
14.	$[\text{Cu}(\text{butiropfenone-SC})_2]$	472.04	12	Dark gray triangle-based prisms (microcrystals)
15.	$[\text{Cu}(\text{butiropfenone-TSC})_2]$	504.17	43	Black triangle-based prisms (microcrystals)

Infrared spectroscopic study

The mid-IR spectra were recorded with a Bruker Alpha FTIR spectrometer (Platinum single reflection diamond ATR), at room temperature, in the wavenumber range of 4000–400  $\text{cm}^{-1}$ , and the far-IR range of 500–50  $\text{cm}^{-1}$ , respectively, on a Bio Rad – FTS 60A, PIKE Gladi ATR spectrometer, with a resolution of 4  $\text{cm}^{-1}$ . The samples were measured in solid state (in powder form). The data of the most characteristic IR bands for the selected complexes are presented in Table 2.

Table 2. IR data of the selected complexes.

Comp. $\text{cm}^{-1}$	1	5	6	7	9	10	11	12	14	15
$\nu_{\text{N-H}}$	3191 m	3135 m	3205 w	3180 w	3318 m	3386 w	3180 w	3192 m	3169 m	3318 m
$\nu_{\text{C-H}}$	2929 m	2930 s	2918 m	2920 w	2924 w	2924 w	2923 m	2968 w	2929 m	2963 w
$\nu_{\text{C=C}}$	-	-	1579 m	1579 w	1611 m	1655 s	1656 m	1674 vs	1676 s	1592 s
$\nu_{\text{C=N}}$	1589 s	1560 s	1545 s	1544 s	1541 vs	1537 w	1565 vs	1564 vs	1568 vs	1518 vs
$\delta_{\text{CH}_2}$	1457 s	1399 s	1441 m	1440 s	1397 e	1372 vs	1441 vs	1468 vs	1456 s	1489 s
$\delta_{\text{CH}_3}$	1315 m	1327 s	1325 m	1325 m	1338 k	1347 s	1391 vs	1336 s	1344 w	1343 m
$\nu_{\text{N-N}}$	-	-	-	-	-	-	-	1294 m	1307 m	1277 s
$\nu_{\text{N-O}}$	1218 m	1259 w	1240 s	1242 s	-	-	-	-	-	-
$\nu_{\text{N-OH}}$	1116 w	1185 w	1146 s	1148 s	-	-	-	-	-	-
$\tau_{\text{O-H}}$	978 s	1085 vs	951 vs	951 vs	1066 m	1067 w	-	-	-	-
$\gamma_{\text{C-H}}$	741 vs	747 vs	694 vs	694 vs	651 m	665 m	754 vs	694 vs	767 s	697 m
$\nu_{\text{Cu-N}}$	505 s	493 w	474 s	474 m	505 s	506 m	478 m	503 m	541 m	503 w
$\nu_{\text{Cu-O}}$	-	-	-	-	-	-	-	460 vs	461 vs	-
$\nu_{\text{Cu-S}}$	-	-	-	-	-	-	-	-	-	443 m
$\delta_{\text{N-Cu-N}}$	-	-	380 s	374 s	343 w	343 w	-	-	-	-

(Abbreviations: vs = very strong, s = strong, m = medium, w = weak)

The most important bands for the characterization of complexes are  $\nu_{\text{C=N}}$  (1518–1589  $\text{cm}^{-1}$ ) and  $\nu_{\text{Cu-N}}$ ,  $\nu_{\text{Cu-O}}$ ,  $\nu_{\text{Cu-S}}$  (443–541  $\text{cm}^{-1}$ ). In the far IR region  $\delta_{\text{N-Cu-N}}$  deformation vibrations appear (343–380  $\text{cm}^{-1}$ ) [4].

Mass spectrometry

Mass spectra of the samples were recorded using electrospray ionization (ESI). In the spectra we could detect the molecular ions and some decomposition fragments.

ESR measurements

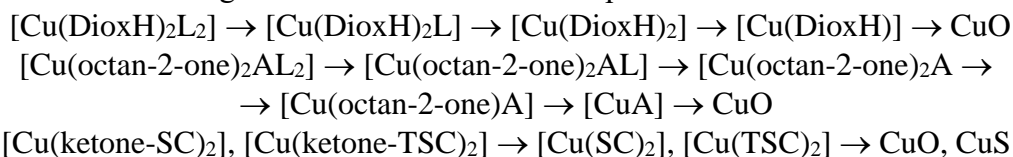
The measurements were performed with a Bruker ELEXSYS 500 type device. By comparing the experimental and calculated spectra, and by calculating the characteristic parameters, the Cu–N couplings can be identified. In some cases, a small amount of cluster formation or two conformations can be observed.

Thermoanalytical measurements (TG-DTG-DTA)

Thermal measurements were performed with a 951 TG and 910 DSC calorimeter (TA Instruments), in Ar or  $\text{N}_2$  at a heating rate of 10  $\text{Kmin}^{-1}$  (sample mass of 4–10 mg).

The thermal stability of complexes is limited within the temperature range of 100–130  $^{\circ}\text{C}$ . In the case of  $[\text{Cu}(\text{DioxH})_2\text{L}_2]$  type complexes the first decomposition step belongs to leaving amino (L) groups, until 240  $^{\circ}\text{C}$ , then the glyoxime units leave. The end of the process is at 470  $^{\circ}\text{C}$ . Subsequently, the decomposition of the glyoxime unit is accompanied by big exothermic peaks. This behavior can be explained with the presence of oxygen in the molecule. In the case of  $[\text{Cu}(\text{octan-2-one})_2\text{AL}_2]$  type complexes the first step of the decomposition

mechanism is the loss of the amino (L) groups between 50–350 °C, then the 2-octanone units leave. Finally the diamine (A) unit is lost between 350–450 °C. The end of the process is at 500 °C. The decomposition of  $[Cu(\textit{ketone-SC})_2]$ ,  $[Cu(\textit{ketone-TSC})_2]$  type complexes begins with leaving of the ketone moieties until 400 °C, then the semicarbazone or thiosemicarbazone unit leaves until 790 °C. The general mechanism for decomposition is as follows:



#### UV–VIS spectroscopy

The electronic spectra were recorded with a Jasco V-670 Spectrophotometer in 10% EtOH/water solutions containing the substance in  $10^{-4}$  mol/dm<sup>3</sup> concentration. Using Sørensen buffer solutions the electronic spectra were also recorded as a function of pH, and then the acidity constants were calculated, too. The obtained values were between  $3.9 \cdot 10^{-12}$  –  $6 \cdot 10^{-10}$ .

#### Powder X-ray diffraction measurements

The crystal structure of the complexes was studied with powder XRD measurements, carried out on a PANalytical X'pert Pro MPD X-ray diffractometer. As being novel compounds their diffractograms can not be found in the Cambridge database. The majority of the complexes exhibits crystalline form, except for  $[Cu(\text{octan-2-one})_2(o\text{-fen})(2\text{-Me-imidazole})_2]$  and  $[Cu(\textit{butiropenone-TSC})_2]$  which are amorphous.

#### SEM (scanning electron microscopy) and EDX (energy dispersive X-ray spectroscopy analysis)

The images were taken with a JEOL JSM-5500LV scanning electron microscope. For all study the beam energy was 20kV in order to obtain the excitation of all the elements and secondary electron detector (SED) were employed for measurement. The morphological study of the sample surface at five significant magnifications 10000x, 5000x, 1000x, 500x and 100x were recorded.

### **Conclusion**

In this work new copper(II) complexes were synthesized and characterized with physico-chemical methods. Thermal decomposition mechanism was monitored with thermoanalytical measurements.

### **Acknowledgement**

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### **References**

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