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# Introducing *N*-Heteroaromatic Bases into Copper(II) Thiosemicarbazon Complexes: A Way to Change their Biological Activity

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Three new copper(II) complexes, [Cu(1,10-Phen)(L)] (**1**), [Cu(2,2′-Bpy)(L)] (**2**) and [Cu(3,4-Lut)(L)] (**3**), where $H_2L$ = 2-[(2,4-dihydroxyphenyl)methylidene]-*N*-(prop-2-en-1-yl)hydrazine-1-carbothioamide, 1,10-Phen = 1,10-phenanthroline, 2,2′-Bpy = 2,2′-bipyridine, 3,4-Lut = 3,4-lutidine, have been synthesized and characterized by elemental analysis, FTIR spectroscopy and single crystal X-ray crystallography (**1**, **2**). All compounds are mononuclear. The introduction of a monodentate *N*-heteroaromatic base (3,4-dimethylpyridine) has led to a significant increase of antimicrobial activity against Gram-negative *Escherichia coli* and antifungal activity against *Candida albicans* compared to the pro-ligand and the precursor complex [Cu(L)$H_2O$]. The introduction of bidentate *N*-heteroaromatic bases did not lead to such increase of antimicrobial and antifungal activities. Moreover, complex **3** surpasses the inhibitory activity of tetracycline toward *Enterobacter cloacae* and the inhibitory activity of fluconazole toward *Candida parapsilosis* and *Cryptococcus neoformans*. The study of antioxidant activity against cation radicals $ABTS^{\bullet+}$ showed that complexes **1**–**3** are more active than Trolox, but only introduction of the monodentate *N*-heteroaromatic base (3,4-dimethylpyridine) led to the increase of antioxidant properties compared to the precursor complex.

## Introduction

The study of new coordination compounds is a relevant direction of chemistry. Thiosemicarbazones represent one of the classes of substances that form complexes using nitrogen, sulfur and other donor atoms. They exhibit a wide range of biological properties such as antitumor, antiviral, antifungal and antibacterial activity.[1–5]

Thiosemicarbazones coordinate to the metal ions forming stable coordination compounds whose biological properties differ from the properties of the initial uncoordinated thiosemicarbazone.[6–10]

Copper is an essential trace metal found in all living organisms. It is found in all body tissues and plays a role in making red blood cells and maintaining nerve cells and the immune system.[11] Copper can inhibit oxidation, promoted by oxygen, peroxides or free radicals as well as accelerate the oxidation of another substance, so it can act as both an antioxidant and prooxidant respectively. When copper acts as an antioxidant, it scavenges or neutralizes free radicals. But as a prooxidant, it promotes free radical damage and contributes to the development of Alzheimer's disease.[12] Therefore, copper coordination compounds with thiosemicarbazones often manifest biological activity and can be potential antibacterial, antifungal and antioxidant therapeutic agents.[13–14]

It has been reported that copper(II) complexes with thiosemicarbazones and *N*-heteroaromatic bases in the inner sphere are less toxic in biological systems than the proligands.[15–19] The higher antimicrobial activity of the complexes is associated with their ability to penetrate better through membranes. The inhibitory effect of these type of complexes may be associated with their interaction with the prosthetic group of the enzyme that inhibits DNA replication.[20]

Previously it was found that copper(II) coordination compounds with 2-[(2,4-dihydroxyphenyl)methylidene]-*N*-(prop-2-en-1-yl)hydrazine-1-carbothioamide (2,4-dihydroxybenzaldehyde *N*(4)-allyl-3-thiosemicarbazone, Figure 1) with 3- and 4-methylpyridine showed moderate antimicrobial and antifungal activity.[21] There are reports that mixed-ligand copper(II) complexes with 1,10-phenanthroline (1,10-Phen) and 2,2′-bipyridine (2,2′-Bpy) are less toxic than the corresponding proligands.[22–23] Based on this, the aim of the present investigation

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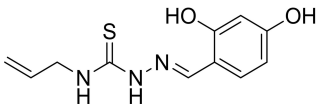

**Figure 1.** 2-[(2,4-dihydroxyphenyl)methylidene]-*N*-(prop-2-en-1-yl)hydrazine-1-carbothioamide ($H_2L$).

is the synthesis of copper(II) complexes with 2-[(2,4-dihydroxyphenyl)methylidene]-*N*-(prop-2-en-1-yl)hydrazine-1-carbothioamide and bidentate *N*-heteroaromatic bases as well as with 3,4-dimethylpyridine (3,4-lutidine, 3,4-Lut); the study of their antimicrobial, antifungal and antioxidant activities; the comparison of their biological activity with the activities of the previously described precursor coordination compound and other mixed-ligand copper(II) coordination compounds with the same thiosemicarbazone pro-ligand.

## Results and Discussion

### Synthesis and characterization

Complex **1** was prepared by the reaction of complex [Cu(L)$H_2O$] with 1,10-phenanthroline in ethanol. Complexes **2** and **3** were prepared by the similar method as complex **1**, but 1,10-phenanthroline was replaced by 2,2′-bipyridine and 3,4-dimethylpyridine, respectively. Single crystals of the complexes **1** and **2** were obtained by recrystallization of the solid products from dimethylformamide. Elemental analyses of the complexes suggest the general formula [Cu(A)L] (A = 1,10-Phen; 2,2′-Bpy; 3,4-Lut) and are in accordance with the molecular structures of **1** and **2** determined by single crystal X-ray analysis. The molar conductivity values of the synthesized complexes are in the range of 9–11 $\Omega^{-1}\,cm^2\,mol^{-1}$ which indicates that complexes are non-electrolytes.[24]

### Spectroscopic studies

The spectra of the synthesized compounds contain absorption bands in the regions of 3343–3167, 1644–1558, and 1213–1171 $cm^{-1}$ which characterize the stretching vibrations of the coordinated molecules of the corresponding ligands.[25] The spectrum of the $H_2L$ pro-ligand contains the absorption bands at 3384 and 3289 $cm^{-1}$, corresponding to two phenol groups. One of the ν(O–H) absorption bands disappears from the IR spectra of the complexes **1**–**3**, which points to deprotonation of $H_2L$. But the position of the absorption band of the second phenol group almost does not change. This fact indicates that the second phenol group is not involved in the coordination to the central atom. In addition, the spectra show shifts of the ν(C=N) absorption band to the low–frequency region by 20–25 $cm^{-1}$ as well as the disappearance of the ν(C=S) and appearance of the ν(C–S) absorption bands in the region of 775–757 $cm^{-1}$.

The disappearance of C=S group indicates that the pro-ligand has transformed from the thione form to a thiol tautomeric form followed by deprotonation. In the IR spectra of complexes **1**–**3**, new absorption bands are found in the region of 510–412 $cm^{-1}$ that correspond to ν(Cu–N), ν(Cu–O) and ν(Cu–S) according to the literature.[26] Based on this, it can be proved that the $H_2L$ pro-ligand coordinates to the copper atom in a doubly deprotonated thiol form ($L^{2-}$) by means of the deprotonated phenolic oxygen atom, azomethine nitrogen atom and deprotonated sulfur atom forming five- and six-membered metallacycles.[27]

Based on the obtained data, the distribution of bonds in the composition of complexes **1**–**3** shown in Figure 2 can be assumed.

### Structural description of the complexes

The X-ray data and the details of the refinement of **1** and **2** are summarized in Table 1, the selected bond lengths and angles as well as hydrogen bond parameters are given in Tables 2, 3, and the structures of complexes **1** and **2** are presented in Figures 3–6.

The outer coordination sphere of these compounds consists of dimethylformamide plus water molecule in **1** plus an additional water molecule in the case of **1**. In both complexes, the $H_2L$ is found in a doubly deprotonated form ($L^{2-}$). It acts as a tridentate ligand and coordinates to the copper atom with a ONS set of donor atoms. In **1** and **2**, the metal coordinates also

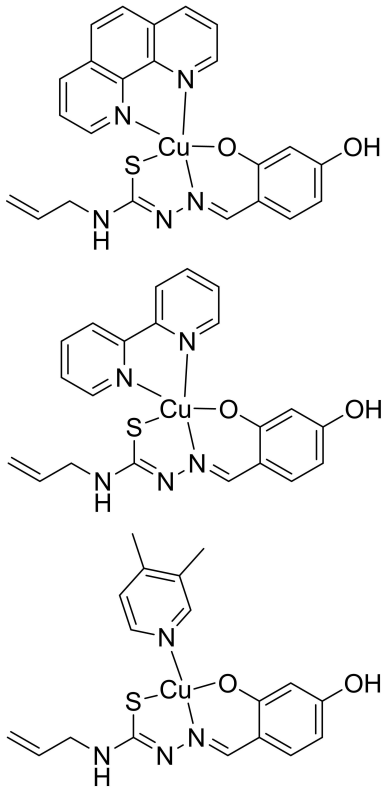

**Figure 2.** Structural formula of complexes **1**–**3**.

**Table 1.** Crystal and Structure Refinement Data for **1** and **2**.

| | **1** | **2** |
|---|---|---|
| Empirical formula | $C_{26}H_{28}CuN_6O_4S$ | $C_{24}H_{26}CuN_6O_3S$ |
| Formula weight | 584.1 | 542.12 |
| Crystal system | monoclinic | triclinic |
| Space group | $P2_1/c$ | $P\bar{1}$ |
| *a* (Å) | 10.6262(7) | 8.9387(5) |
| *b* (Å) | 26.4648(12) | 12.458(1) |
| *c* (Å) | 9.5162(6) | 12.5929(8) |
| α (°) | 90 | 99.760(6) |
| β (°) | 97.001(6) | 107.329(5) |
| γ (°) | 90 | 98.529(5) |
| *V* (Å$^3$) | 2656.2(3) | 1289.51(16) |
| Z | 4 | 2 |
| $\rho_{calc}$ (g cm$^{-3}$) | 1.461 | 1.396 |
| $\mu_{Mo}$ (mm$^{-1}$) | 0.945 | 0.965 |
| *F*(000) | 1212 | 562 |
| Crystal size (mm) | 0.35×0.3×0.25 | 0.37×0.32×0.27 |
| *θ* Range (°) | 3.0–25.5 | 3.1–25.5 |
| Indexes ranges, h | −8–12 | −10-10 |
| k | −29–31 | −15–14 |
| l | −11–11 | −15–14 |
| Reflections collected | 9432 | 8067 |
| Independent reflections | 4923 | 4783 |
| R(int) | 0.056 | 0.032 |
| Reflections with $I > 2\sigma(I)$ | 2737 | 3615 |
| Number of refined parameters | 349 | 312 |
| Goodness-of-fit,F$^2$ (S) | 0.96 | 1.04 |
| *R1* (for $I > 2\sigma(I)$) | 0.065 | 0.0537 |
| *R1w* | 0.1194 | 0.127 |
| *R*(for all reflections) | 0.1304 | 0.0773 |
| *R1w* | 0.1451 | 0.14 |
| $\Delta\rho_{max}/\Delta\rho_{min}$ (e·Å$^{-3}$) | −0.52, 0.56 | −0.42, 0.56 |

the 1,10-phenanthroline and 2,2′-bipyridine, respectively, via the N3 and N4 nitrogen atoms. The central atom in these complexes is five-coordinated in a distorted square-pyramidal coordination geometry. Its basal plane includes three donor atoms of the $L^{2-}$ (S(1), O(1), N(1)) and nitrogen atom N(3) (Figure 3, Table 2).

The deviations of these atoms from their mean planes in **1** and **2** are −0.269(2), −0.308(3), 0.308(4), 0.270(4) Å and −0.123(1), −0.138(3), 0.134(3), 0.126(3) Å, respectively. In these compounds, the Cu atom deviates from this plane by 0.1944(6) and 0.1940(4) Å towards the apices of the respective pyramids. These apices of the metals' coordination pyramids are occupied by nitrogen atoms N(4) with distances of 2.252(4) and 2.253(3) Å, respectively. The polyhedral volume is related to the distortion of coordination polyhedra and its values for the copper atoms in **1** and **2** are 7.407 and 6.895 Å$^3$. In the crystal of **1**, the complexes are linked by hydrogen bonds (HB) C2–H···N5 in helix-like chains along the *c*-direction due to glide plane. These chains are further joined by water molecules forming the 3D hydrogen bonding networks (Table 3, Figures 4a, 5). In the crystal of **2**, the complexes are joined into centrosymmetric dimers by C12–H···O1 hydrogen bonds and these dimers are linked by N5–H···O2 HB in chains along the *b*-direction (Table 3, Figures 4b, 6). In both **1** and **2**, the dimethylformamide molecules form O2–H···O3 hydrogen bonds with the complexes.

**Table 2.** Selected bond lengths and angles in **1** and **2**.

| Bond | d, Å | |
|---|---|---|
| | **1** | **2** |
| Cu1–S1 | 2.2994(15) | 2.2711(13) |
| Cu1–O1 | 1.959(3) | 1.950(3) |
| Cu1–N1 | 1.941(4) | 1.958(2) |
| Cu1–N3 | 2.033(4)) | 2.025(2) |
| Cu1–N4 | 2.252(4) | 2.253(3) |
| S1–C1 | 1.739(5) | 1.741(4) |
| O1–C4 | 1.314(5) | 1.303(4) |
| N1–N2 | 1.397(6) | 1.389(4) |
| N1–C2 | 1.292(6) | 1.295(4) |
| N2–C1 | 1.292(6) | 1.304(5) |
| C2–C3 | 1.419(7) | 1.426(5) |
| C3–C4 | | 1.424(5) |
| Angle | ω° | |
| S1–Cu1–O1 | 153.13(10) | 162.13(9) |
| S1–Cu1–N1 | 84.51(12) | 85.14(8) |
| S1–Cu1–N3 | 94.65(12 | 91.77(8) |
| S1–Cu1–N4 | 100.75(11)) | 101.85(10) |
| O1–Cu1–N1 | 92.45(15) | 92.73(10) |
| O1–Cu1–N3 | 90.86(15) | 89.21(10) |
| O1–Cu1–N4 | 106.12(13) | 95.74(13) |
| N1–Cu1–N3 | 174.22(18) | 175.50(11) |
| N1–Cu1–N4 | 96.68(15) | 107.14(10) |
| N3–Cu1–N4 | 77.84(15) | 76.68(10) |
| Cu1–S1–C1 | 92.73(17) | 94.27(13) |
| Cu1–O1–C4 | 126.9(3) | 125.0(2) |
| Cu1–N1–N2 | 120.7(3) | 121.7(2) |
| Cu1–N1–C2 | 124.6(3) | 123.1(2) |
| N2–N1–C2 | 114.7(4) | 115.1(3) |
| N1–N2–C1 | 112.9(4) | 112.9(3) |
| S1–C1–N2 | 126.2(4) | 125.9(3) |
| N1–C2–C3 | 127.3(4) | 126.2(3) |
| C2–C3–C4 | 123.6(4) | 124.0(3) |
| O1–C4–C3 | 122.5(4) | 123.3(3) |

**Table 3.** Hydrogen bond distances (Å) and Angles (°) in **1** and **2**.

| D–H···A | d(H···A) | d(D···A) | ∠(DHA) | Symmetry transformation for acceptor |
|---|---|---|---|---|
| **1** | | | | |
| O2–H···O3 | 1.9 | 2.706(6) | 169.0 | x,y,1+z |
| O1 W–H···O1 | 2.02 | 2.799(8) | 152.0 | x,y,z |
| O1 W–H1···O2 | 2.16 | 2.977(9) | 161.0 | 1−x,1−y,1−z |
| C5–H···O1 W | 2.58 | 3.293(10) | 134.0 | x,y,z |
| C2–H···N5 | 2.6 | 3.347(7) | 137.0 | x,1/2−y,1/2+z |
| C19–H···O1 W | 2.482 | 3.334(10) | 166.0 | 1−x,1−y,−z |
| **2** | | | | |
| O2–H···O3 | 2.08 | 2.669(8) | 129.0 | x,1+y,z |
| N5–H···O2 | 2.23 | 3.058(5) | 162.0 | x,−1+y,z |
| C5–H···O3 | 2.54 | 3.220(8) | 130.0 | x,1+y,z |
| C12–H···O1 | 2.6 | 3.327(5) | 135.0 | 1−x,2−y,1−z |

## Biological activity

### *Antimicrobial and antifungal activity*

The ligand $H_2L$ and its complexes were tested against Gram-positive bacterial strains (*Staphylococcus aureus* ATCC 25923), Gram-negative bacterial strains (*Escherichia coli* ATCC 25922) and fungal strains (*Candida albicans* ATCC 10231, *Candida krusei* ATCC 6258). The MIC (minimum inhibitory concentration,

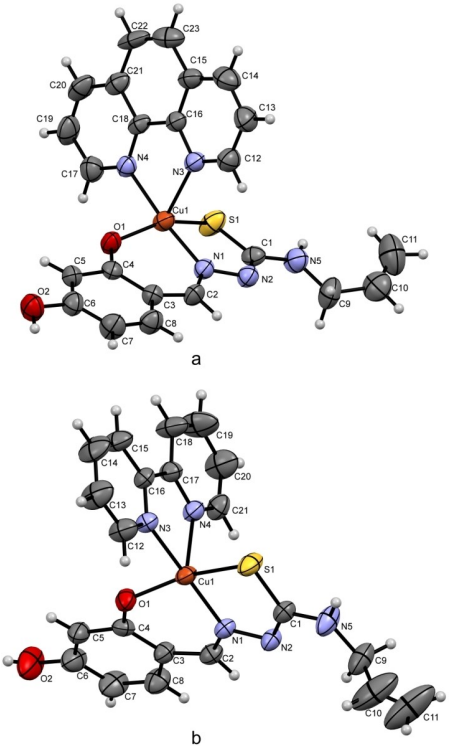


**Figure 3.** View of compounds (a) **1** and (b) **2** with atom numbering. Thermal ellipsoids are drawn at the 50% probability level.

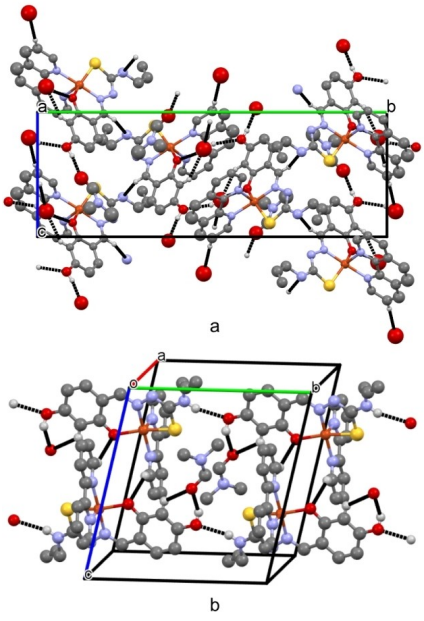


**Figure 4.** The crystal packing fragments of **1** (a) and **2** (b).

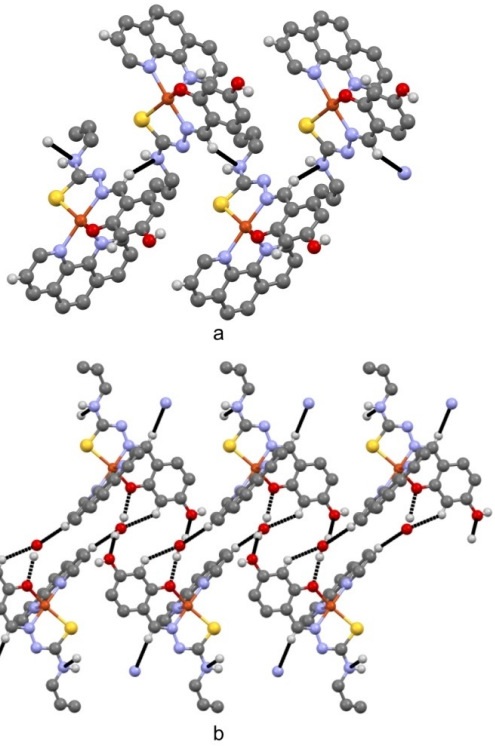


**Figure 5.** The chains in **1** (a) and complexes of **1** linked by water molecules (b).

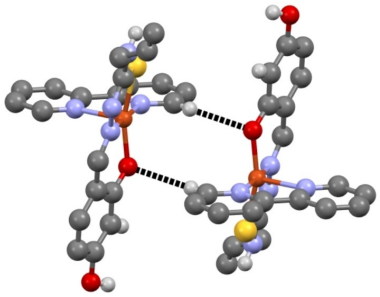

**Figure 6.** The formation of dimers of complexes **2**.

μg mL$^{-1}$) and MBC/MFC (minimum bactericidal/fungicidal concentrations, μg mL$^{-1}$) values of the compounds against bacteria and fungi are listed in Table 4. Tetracycline and fluconazole were used as the standard drugs to compare the activity. The studied complexes show the most pronounced activity towards *S. aureus* and their activity is higher than the activity of the proligand $H_2L$, in case of complex **3** also higher than that of tetracycline. Complex **1** is inactive towards the Gram-negative bacterial strain, complex **2** has medium activity, and complex **3** is the most active one. Complexes **1**, **2** with bidentate *N*-heteroaromatic bases in the internal sphere are inactive towards the fungal strain *C. albicans*, complex **3** has stronger activities than fluconazole. However, all studied complexes show medium activity toward *C. krusei*. The introduction of bidentate *N*-heteroaromatic bases (1,10-Phen and 2,2′-Bpy) into the inner sphere of the complexes **1** and **2** did not affect their activity. The activity value either did not change compared to the precursor in the case of some strains, or the complexes were even less active. Comparing the data obtained with the activity of the previously described complexes, it can be said that complexes **2** and **3** exhibit higher activity than the coordination compounds with 3- and 4-methylpyridine.[21] Complex **3** is the

**Table 4.** Minimal inhibitory concentration (MIC) and bactericidal/fungicidal (MBC/MFC) concentrations of coordination compounds **1**–**3** in relation to test microbes and fungi ($\mu g\,mL^{-1}$).

| Compound | *Staphylococcus aureus* ATCC 25923 | | *Escherichia coli* ATCC 25922 | | *Candida albicans* ATCC 10231 | | *Candida krusei* ATCC 6258 | |
|---|---|---|---|---|---|---|---|---|
| | MIC | MBC | MIC | MBC | MIC | MFC | MIC | MFC |
| $Cu(OAc)_2{\cdot}H_2O$ | >1000 | >1000 | >1000 | >1000 | >1000 | >1000 | >1000 | >1000 |
| $H_2L$ | 15.63 | 31.25 | 500 | >1000 | 250.0 | 500.0 | 62.50 | 125.0 |
| $[Cu(L)H_2O]$ | 0.1221 | 0.2441 | 125 | 250 | 125.0 | 250.0 | 62.50 | 125.0 |
| **1** | 0.9766 | 1.953 | 1000 | >1000 | 500.0 | >1000 | 125.0 | 250.0 |
| **2** | 0.4883 | 0.9766 | 250 | 500 | 500.0 | >1000 | 62.50 | 125.0 |
| **3** | 0.1221 | 0.2441 | 3.906 | 7.813 | 7.813 | 15.63 | 500.0 | >1000 |
| Tetracycline[28–31] | 0.25 | 1.96 | 0.98 | 3.91 | – | – | – | – |
| Fluconazole[32–33] | –[a] | – | – | – | 15.62 | 31.25 | 15.62 | 31.25 |

[a] Not studied.

**Table 5.** Minimal inhibitory concentration (MIC) and bactericidal/fungicidal (MBC/MFC) concentrations of coordination compound **3** in relation to test microbes and fungi ($\mu g\,mL^{-1}$).

| Gram-negative bacterial strains and fungal strains | | Compound **3** | Tetracycline | Fluconazole |
|---|---|---|---|---|
| Acinetobacter baumannii | MIC | 3.906 | 0.5 | – |
| ATCC BAA-747 | MBC | 7.813 | 5.66 | – |
| Enterobacter cloacae | MIC | 7.813 | 29.5 | – |
| ATCC 13047 | MBC | 15.63 | – | – |
| Pseudomonas aeruginosa | MIC | 62.5 | 7.82 | – |
| ATCC 27853 | MBC | 125 | 62.5 | – |
| Candida parapsilosis | MIC | 1.953 | – | 7.81 |
| ATCC 22019 | MFC | 3.906 | – | 15.62 |
| Cryptococcus neoformans | MIC | 1.953 | – | 2.0 |
| ATCC 34877 | MFC | 3.906 | – | 8.0 |

**Table 6.** Antioxidant activity of compounds **1**–**3** against cation radicals $ABTS^{\bullet+}$.

| Compound | $IC_{50}$, μM |
|---|---|
| $H_2L$ | 6.30 |
| $[Cu(L)H_2O]$ | 6.50 |
| **1** | 10.9 |
| **2** | 7.37 |
| **3** | 4.54 |
| Trolox | 33 |

most active among the studied substances. Therefore, its activity was studied on a wider range of Gram-negative bacterial strains and fungal strains (Table 5). This complex showed high activity against this wide spectrum of Gram-negative bacterial strains which is comparable to the activity of Tetracycline. Its activity towards *E. cloacae* is even higher than the activity of tetracycline. Moreover, its activity towards the studied fungal strains is higher than the activity of fluconazole.

### *Antioxidant activity*

The antioxidant activity of the compounds was determined by the $ABTS^{\bullet+}$ method (Table 6). Complexes **1** and **2** are less active than $H_2L$ and $[Cu(L)H_2O]$. The complex **3** shows good results, and is more active than the pro-ligand and Trolox which is used in medical practice as a standard antioxidant.

## Conclusion

Three new complexes with 2-[(2,4-dihydroxyphenyl)methylidene]-*N*-(prop-2-en-1-yl)hydrazine-1-carbothioamide and *N*-heteroaromatic bases were prepared and characterized. The structures of the complexes **1** and **2** are confirmed by single crystal X-ray diffraction analysis. Due to water molecules, the helix-like chains of **1** in the crystal form 3D hydrogen bonding networks while molecules of **2** in the crystal are joined into dimers which are further linked by HB into chains.

The studied complexes show high activity against *Staphylococcus aureus*. Compound **3** is the most active one. It manifests antimicrobial activity towards Gram-positive and Gram-negative microorganism and exceeds the activity of the precursor complex $[Cu(L)H_2O]$ and in some cases of tetracycline and fluconazole. Meanwhile, the introduction of bidentate *N*-heteroaromatic bases (1,10-Phen and 2,2′-Bpy) into the inner sphere of copper complex did not particularly enhance their activity.

The introduction of *N*-heteroaromatic bases changes the antioxidant activity of corresponding complexes toward $ABTS^{\bullet+}$. All studied complexes surpass Trolox that is used as standard antioxidant in medical practice. Nevertheless, only introduction of monodentate *N*-heteroaromatic base (3,4-Lut) leads to an increase of antioxidant activity compared to the activity of precursor complex $[Cu(L)H_2O]$, while introduction of bidentate *N*-heteroaromatic bases leads to a decrease of antioxidant properties. The complex **3** is 1.6–2.4 times more active that the complexes **1** and **2**.

Thus, the introduction of monodentate *N*-heteroaromatic bases is a potential way to enhance the antimicrobial, antifungal, and antioxidant activities of copper(II) complexes.

## Experimental Section

### Materials and Methods

*N*-(Prop-2-en-1-yl)hydrazinecarbothioamide (*N*$^4$-Allyl-3-thiosemicarbazide) was synthesized by the reaction between 3-isothiocyanatoprop-1-ene (allyl isothiocyanate) and hydrazine hydrate.[34]

2-[(2,4-Dihydroxyphenyl)methylidene]-N-(prop-2-en-1-yl)hydrazine-1-carbothioamide (2,4-dihydroxybenzaldehyde *N*$^4$-allyl-3-thiosemicarbazone, $H_2L$) was synthesized by the reaction between 2,4-dihydroxybenzaldehyde and *N*-(prop-2-en-1-yl)hydrazinecarbothioamide in ethanol as described by A. Scott et al.[35] m.p. 186–188 °C; $^1$H NMR (400 MHz, acetone-$d_6$): 10.29 br.s (1H, OH), 9.44 br.s (1H, OH), 8.92 br.s (1H, NH), 8.35 s (1H, CH=N), 8.11 br.s (1H, NH), 7.38 d (1H, $H_{arom}$, $J$ = 8.5 Hz), 6.45 d (1H, $H_{arom}$, $J$ = 8.5 Hz), 6.41 s (1H, $H_{arom}$), 5.98 m (1H, CH=$CH_2$), 5.15 m (2H, $CH_2$=), 4.35 m (2H, $CH_2$N); $^{13}$C NMR (100 MHz, acetone-$d_6$): 177.85 (C=S); 160.84, 158.84, 131.50, 111.22, 108.10, 102.71 ($C_{arom}$); 145.01 (CH=N), 134.86 (CH=$CH_2$), 115.15 ($CH_2$=), 46.41 ($CH_2$N). The melting point and NMR spectra (Figures S1, S2) correspond to the literature data of this pro-ligand.[36]

3-Isothiocyanatoprop-1-ene, hydrazine hydrate, 2,4-dihydroxybenzaldehyde, copper(II) acetate monohydrate, 1,10-phenanthroline, 2,2′-bipyridine, 3,4-dimethylpyridine were obtained from Sigma-Aldrich. FTIR spectra were obtained on a Bruker ALPHA FTIR spectrophotometer at room temperature in the range of 4000–400 cm$^{-1}$. The elemental analysis was performed similarly to the literature procedures.[37] The resistance of solutions of complexes in dimethylformamide (20 °C, c 0.001 M) was measured using an R-38 rheochord bridge.

### Synthesis of coordination compounds

**[Cu(1,10-Phen)(L)] (1)**: The precursor coordination compound [Cu(L)$H_2O$] was obtained by the reaction between $H_2L$ and copper(II) acetate monohydrate in ethanol as it was previously described.[21] The resulting complex [Cu(L)$H_2O$] (0.331 g, 1.00 mmol) was dissolved in ethanol (20 mL) and the 1,10-phenanthroline (0.180 g, 1.00 mmol) was added to the reaction mixture. The green precipitate has formed during stirring. The resulting precipitate was filtered off, washed with a small amount of ethanol and dried. The solid product was recrystallized from dimethylformamide to give green single crystals, suitable for X-ray diffraction. The crystals were isolated by filtration. Yield: 83%. IR data (cm$^{-1}$): 3343, 3203, 1641, 1620, 1601, 1589, 1558, 1204, 1175, 775, 510, 479, 470, 461, 420; $\lambda$ (DMF, $\Omega^{-1}\cdot cm^2\cdot mol^{-1}$): 11; elemental analysis calcd. (%) for $C_{23}H_{19}CuN_5O_2S$: Cu, 12.89; C, 56.03; H, 3.88; N, 14.20; S, 6.50; found: Cu, 12.70; C, 55.90; H, 3.80; N, 14.14; S, 6.44.

**[Cu(2,2′-Bpy)(L)] (2)**: The resulting complex [Cu(L)$H_2O$] (0.331 g, 1.00 mmol) was dissolved in ethanol (20 mL) and the 2,2′-bipyridine (0.156 g, 1.00 mmol) was added to the reaction mixture. The green precipitate has formed during stirring. The resulting precipitate was filtered off, washed with a small amount of ethanol and dried. The solid product was recrystallized from dimethylformamide to give green single crystals, suitable for X-ray diffraction. The crystals were isolated by filtration. Yield: 90%. IR data (cm$^{-1}$): 3260, 3202, 1644, 1613, 1601, 1593, 1563, 1205, 1171, 764, 490, 487, 463, 426, 416; $\lambda$ (DMF, $\Omega^{-1}\cdot cm^2\cdot mol^{-1}$): 10; elemental analysis calcd. (%) for $C_{21}H_{19}CuN_5O_2S$: Cu, 13.55; C, 53.78; H, 4.08; N, 14.93; S, 6.84; found: Cu, 13.22; C, 53.67; H, 3.94; N, 14.78; S, 6.75.

**[Cu(3,4-Lut)(L)] (3)**: The resulting complex [Cu(L)$H_2O$] (0.331 g, 1.00 mmol) was dissolved in ethanol (20 mL) and the 3,4-dimethylpyridine (0.107 g, 1.00 mmol) was added to the reaction mixture. The green precipitate has formed during stirring. The resulting precipitate was filtered off, washed with a small amount of ethanol and dried. Yield: 84%. IR data (cm$^{-1}$): 3342, 3231, 1643, 1612, 1602, 1562, 1201, 1174, 756, 469, 440, 420, 412; $\lambda$ (DMF, $\Omega^{-1}\cdot cm^2\cdot mol^{-1}$): 9; elemental analysis calcd. (%) for $C_{18}H_{20}CuN_4O_2S$: Cu, 15.13; C, 51.48; H, 4.80; N, 13.34; S, 7.63; found: Cu, 15.34; C, 51.37; H, 4.69; N, 13.25; S, 7.51.

### X-ray crystallography

The single crystal X-ray analysis of coordination compounds **1** and **2** were carried out on a Xcalibur E CCD diffractometer equipped with a CCD area detector and a graphite monochromator, Mo$K\alpha$ radiation (0.71073 Å), at room temperature (293 K). Data collection and reduction, unit cell determination were done by CrysAlis PRO CCD (Oxford Diffraction), the SHELXS97 and SHELXL2014 program packages[38–39] were used to solve and refine the structures. The non-hydrogen atoms were treated anisotropically (full-matrix least squares method on $F^2$). The hydrogen atoms were placed in calculated positions and were treated using riding model approximations with $U_{iso}(H) = 1.2U_{eq}(C)$, while the oxygen bounded H-atoms were found from differential Fourier maps at an intermediate stage of the structure refinement. These hydrogen atoms were refined with the isotropic displacement parameter $U_{iso}(H) = 1.5U_{eq}$-(O). The geometric parameters were calculated by PLATON program[40] and Mercury software[41] was used for visualization of structures. The hydrogen atoms that were not involved in the hydrogen bonding were omitted from the generation of the packing diagrams.

Deposition Numbers 2218767 (for **1**), 2218768 (for **2**) contain the supporting crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service.

### Biological activity

The antibacterial properties of the complexes were tested against *Staphylococcus aureus* (ATCC 25923), *Escherichia coli* (ATCC 25922), *Acinetobacter baumannii* (ATCC BAA-747), *Enterobacter cloacae* (ATCC 13047), *Pseudomonas aeruginosa* (ATCC 853). The antifungal activities of the compounds were tested against *Candida albicans* (ATCC 10231), *Candida krusei (*ATCC 6258), *Candida parapsilosis* (ATCC 22019), *Cryptococcus neoformans* (ATCC 34877). The minimum inhibitory concentrations (MICs, μg mL$^{-1}$), minimum bactericidal concentrations (MBCs, μg mL$^{-1}$), and minimum fungicidal concentrations (MFCs, μg mL$^{-1}$) were determined using the method of serial dilutions in liquid broth.[42–43]

The antioxidant activity was studied using the ABTS free radical-scavenging assay according to Re et al.[44]

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## *Conflict of Interest*

The authors declare no conflict of interest.

## Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

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