Magnetic, Optical and Biological Studies on Copper(II) Complexes with 2-benzothiazolyl Hydrazones. II

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Abstract

Three Cu(II) complex compounds with 4-methoxybenzaldehyde-2-benzothiazolyl hydrazone (HL) have been prepared and characterized by elemental and thermogravimetical analysis, infrared, electronic and EPR spectra. The complex compounds have various composition and stereochemistry, depending on the reaction conditions and the metal salt used. The ligand acts as neutral bidentate NN donor in the complexes [Cu(HL)2(H2O)Cl] . Cl, and [Cu(HL)2(H2O)Br] . Br and monobasic bidentate donor in the complex ([CuL]2). EPR studies of the complexes gave axial symmetry, with g|| = 2.0, the ground state. The bonding parameters calculated from the electronic and EPR spectra indicate strong in-plane π-bonding for all the complexes. Investigations on antibacterial and antifungal activities show that the complexes are more active than the free ligand.

Keywords: hydrazones, complexes, copper(II)

During the last years the chemical properties of hydrazones have been intensively investigated because of their chelating capability and their pharmacological applications [1-4]. Thus, a great number of hydrazones and their complexes with some first transition metal ions show tuberculostatic [5-7], antitumor [8-11], antibacterial and antifungal activity [12-14]. Several researches are focusing on the aromatic and heterocyclic hydrazones, like those derived from 2-hydrazinobenzothiazole and aromatic aldehydes or ketones, due to the presence of various donor sites: nitrogen, sulphur or oxygen atoms [15-17]. Thiazole itself and its derivatives are known as antiinflamatory, analgesic and antimicrobial agents [18,19]. In addition, the thiazole and benzothiazole hydrazones and their metal complexes show an increasing of biological activity comparatively with simple hydrazones [20, 21].

As a continuation of our studies on the complex compounds of transition metals with 2-benzothiazolyl hydrazones [22-25], we report here the synthesis, characterization and biological activity of three new complexes of Cu(II) with 4-methoxybenzaldehyde-2-benzothiazolyl hydrazone.

The literature reports the synthesis and characterization of two complex compounds of Cu(II) with 4-methoxybenzaldehyde-2-benzothiazolyl hydrazone, having the formulas: [Cu(HL)Cl] . H2O and [Cu(HL)]Cl [17] (both black, m.p. > 300°C), but no detailed spectral investigations have been made.

Experimental part

Preparation of the ligand

All the chemicals used were of A.R. grade. The ligand 4-methoxybenzaldehyde-2-benzothiazolyl hydrazone (HL) was synthesized by a procedure reported in the literature [26], by condensation reaction of 2-hydrazinobenzothiazole with 4-methoxybenzaldehyde, in equimolar quantities; m.p. = 189°C.

Preparation of the complexes

A quantity of 0.283 g (1 mmol) of the ligand was dissolved in 25 mL methanol, under heating. To this solution was added the corresponding metal salt: 0.0855 g (0.5 mmol) of CuCl2 . 2H2O for the complex (1), 0.0998 g (0.5 mmol) of Cu(CH3COO)2 . H2O for the complex (2) and 0.1120 g (0.5 mmol) of CuBr2 for the complex (3). The resulting solution was refluxed for 2-3 h and then cooled to room temperature, when solid products separated out. These were filtered, washed with methanol and dried in air.

The purity of the hydrazone Schiff base and its complexes was confirmed by C, H and N analyses, using a Carlo Erba 1180 analyzer. The metal content was determined by standard procedures.

Elemental analysis:

[Cu(HL)2(H2O)Cl] . Cl (1) brown; found (%): C-48.20; N-11.02; Cu-8.85; calc. (%): C-48.84; N-11.39; Cu-8.68; λM(DMF) = 137 Ω cm2 mol-1; p.f. > 150°C, decomposition.

[Cu(L)]2 (2) yellow; found (%): C-57.65; N-13.88; Cu-9.90; calc. (%): C-57.32; N-13.37; Cu10.19; λM (DMF) = 45 Ω cm2 mol-1; p.f. > 220°C, decomposition.

[Cu(HL)2(H2O)Br] . Br (3), green; found (%): C-43.11; N-10.42; Cu-7.98; calc. (%): C-43.58; N-10.17; Cu-7.75; λM(DMF) = 85 Ω cm2 mol-1; p.f. > 240°C, decomposition.

Thermogravimetric analysis were carried out in static air atmosphere, at a heating rate of 10°C/min, using a MOM Q-1500 derivatograph. Molar conductance measurements were made on Consort C-533 conductometer. Infrared spectra (in KBr pellets) were recorded on a Perkin Elmer Specord M-40 spectrophotometer, in the range 200-900 nm. VIS diffuse reflectance spectra were measured on a Spectord M-40 spectrophotometer, in the range 200-900 nm. The EPR spectra were recorded on an ART-6-IFIN spectrophotometer, in K band.

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Results and discussion

Infrared spectral studies

Table 1 gives the most important IR frequencies of the ligand and its chelates for decide the coordination of the hydrazone to the metal ion.

**Table 1**

| Assignments | H | L | C
<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>v(NH\text{am})</td>
<td>3189 m</td>
<td>3212 m</td>
<td>-</td>
</tr>
<tr>
<td>v(OH)</td>
<td>-</td>
<td>3451 m</td>
<td>-</td>
</tr>
<tr>
<td>v(C=N\text{exoc})</td>
<td>1618 s</td>
<td>1610 s</td>
<td>1607 vs</td>
</tr>
<tr>
<td>v(C=N\text{enoc})</td>
<td>1610 s</td>
<td>1569 m</td>
<td>1606 m</td>
</tr>
<tr>
<td>v(C=N-N=C&lt;)</td>
<td>-</td>
<td>-</td>
<td>1499 vs</td>
</tr>
<tr>
<td>v(CuN\text{N})</td>
<td>-</td>
<td>-</td>
<td>777 m</td>
</tr>
<tr>
<td>(\rho\text{(H}_2\text{O}))</td>
<td>-</td>
<td>650 w</td>
<td>-</td>
</tr>
</tbody>
</table>

The medium absorption band appearing in the IR spectrum of the free ligand at 3189 cm\(^{-1}\) (fig. 1) may be assigned to v(NH) and suggests that the ligand is in the tautomeric form a in the solid state [2, 8].

![Fig. 1. Tautomeric forms of the ligand](image)

This band disappears in the spectrum of the complex (2), but remains in the IR spectra of the complexes (1) and (3). These observations suggest that the ligand exists in the tautomeric form a in the complexes (1) and (3) and in the tautomeric form b in the complex (2).

The IR spectrum of the ligand shows two strong absorption bands, at 1618 and 1610 cm\(^{-1}\), due to the stretching vibration of the hydrazone function, v(C=N)\text{exoc} and benzothiazole group, v(C=N)\text{enoc} respectively [20, 26]. In the spectra of the complexes (1) and (3) these bands shift to lower wave numbers, indicating the coordination of the ligand through the azomethinic nitrogen atoms [2, 26]. In the IR spectrum of the complex (2) the stretching vibration of the exocyclic azomethine group shows also downshift; in addition, a very strong band, at 1499 cm\(^{-1}\), which may be assigned to the function \(\rightarrow\text{C-N-C}<\), confirms the tautomerisation and subsequent deprotonation of the ligand at the formation of this complex [2, 8, 20].

Supplementary bands appearing in the IR spectra of the complexes (1) and (3) in the ranges 3448-3451 cm\(^{-1}\) and 650-651 cm\(^{-1}\) are attributed to v(OH) and \(\rho\text{(H}_2\text{O})\) modes of coordinated water, respectively [2, 27]. Another new band, at 777 cm\(^{-1}\), in the IR spectrum of the complex (2), is due to the vibration \(\nu\text{CuN}_2\), confirming the dimeric nature of this complex [8].

On the base of the IR spectra we can conclude that the ligand acts as neutral bidentate NN donor in the complexes (1) and (3) and monobasic bidentate NN donor in the complex (2).

**Thermogravimetric analysis**

The TG curves of the compounds (1) and (3) show an endothermic peak at 160 °C and 200 °C, respectively, due to the loss of coordinated water [28], which is in agreement with the results obtained from the IR spectra. The endothermic peaks observed at 340 °C correspond to the removal of the anionic chloride (1) and anionic and coordinated bromide (3) [28]. All the complexes lose the organic ligand in a large exothermic process, in the range of 400-800 °C.

The dimeric nature of the complex (2) is also supported by the determinations of molar weight using the cryoscopic method with chloroform as solvent.

The analytical and thermogravimetical data, correlated with the observations from IR spectra permitted to attribute for the complex compounds the formulas written above, with the metal ion six coordinated in the complexes (1) and (3) and five coordinated in the complex (2).

**Electronic and EPR spectral data**

The EPR spectra of the Cu(II) complexes, recorded on powdered samples, in K band, show axial symmetry, with \(g_\parallel > g_\perp\). The EPR spectra of the complexes are presented in figures 2 and 3 and the parameters are listen in table 2.

**Table 2**

<table>
<thead>
<tr>
<th>Complex</th>
<th>(g_\parallel)</th>
<th>(g_\perp)</th>
<th>(A_\parallel \times 10^4) cm(^{-1})</th>
</tr>
</thead>
<tbody>
<tr>
<td>[Cu(HL)\text{H}_2\text{O}]\text{Cl}_2\ (1)</td>
<td>2.35</td>
<td>2.10</td>
<td>190</td>
</tr>
<tr>
<td>[Cu(C\text{N})\ (2)</td>
<td>2.132</td>
<td>2.053</td>
<td>132</td>
</tr>
<tr>
<td>[Cu(HL)\text{H}_2\text{O}]\text{Br}–\text{Br}\ (3)</td>
<td>2.153</td>
<td>2.05</td>
<td>-</td>
</tr>
</tbody>
</table>

![Fig. 2. K-band EPR spectra of the complexes at room temperature](image)
The EPR spectrum of $[\text{Cu}(\text{HL})_2(\text{H}_2\text{O})_2]\text{Cl}_2$ (1) indicates a symmetry almost octahedral, with a weak axial distortion, poorly resolved. The complex $[\text{Cu}_2\text{L}_4]$ (2) shows a large signal, with axial symmetry, so we can see better in figure 3. For the complex $[\text{Cu}(\text{HL})_2(\text{H}_2\text{O})\text{Br}]\text{Br}$ (3), the EPR spectrum shows an anisotrop signal, without hyperfine structure.

The $g_\parallel > g_\perp$ values suggest distorted octahedral symmetry with elongation along $z$ axis for the complexes (1) and (3) and square pyramidal geometry for the complex (2) [20]. In this assumption, the significant electronic absorption bands in the diffusion reflectance spectra of complexes, in the visible region, may be attributed to the transitions written in table 3.

A correlation between the EPR spectral data and the observed bands in the electronic spectra gave important informations on the stereochemistry of the complexes and on the character of the metal-ligand bonds.

The $\alpha_2$, $\beta_1^2$ and $\beta_2^2$ characterizes the in-plane $\sigma$-bonding, in-plane $\pi$-bonding and out-of-plane $\pi$-bonding of Cu$^{2+}$, respectively. $\alpha_2$ can take the values between 0.5 and 1, corresponding to pure covalent and pure ionic metal-ligand bond, respectively.

Using the approximation: $(4/7 + k) = 1$ in the equation (3), we can calculate $\alpha_2$ which is then utilized for the calculation of $\beta_1^2$ and $\beta_2^2$, using the relations (1) and (2).

The parameter $f = g_\parallel / g_\perp$ is an index of tetragonal distortion and its values may vary from 105 to 135 for small to extreme distortion [20, 32].

The orbital parameters which can be calculated from the relations (1) and (2) are a guide of the metal-ligand bonding nature [32]: $K_\parallel = K_\perp$ for the pure $\sigma$ bonding, $K_\parallel < K_\perp$ for strong in-plane $\pi$ bonding and $K_\parallel > K_\perp$ for strong out-of-plane $\pi$ bonding.

The values of the bonding parameters calculated for the three Cu(II) complexes are listed in table 4.

The $\alpha_2$ values indicate an important covalent character for the in-plane $\sigma$-bonding in the complex (2), in accordance with the deprotonation of the ligand and a preponderent ionic metal-ligand bonding in the complex (1). For all the three complexes, $K_\parallel < K_\perp$, in accordance with strong in-plane $\pi$ bonding, showing that the hydrazone ligand is a better $\pi$-donor than the water or the bromide.

The $f$ value calculated for the complex (1) is in accordance with a moderate distortion from the octahedral symmetry, suggesting that the ligand field of the hydrazone ligand is only a little stronger than the ligand field of the water. For the complex (2) the value of the factor excedes the limit for the octahedral distortion, which confirms the square pyramidal geometry, with the axial bond weaker than the in-plane bonds.

### Table 3

**Electronic Transitions in the Visible Region for Cu(II) Complexes**

<table>
<thead>
<tr>
<th>Complex</th>
<th>Observed bands (v&lt;sub&gt;max&lt;/sub&gt;, cm&lt;sup&gt;-1&lt;/sup&gt;)</th>
<th>Assignments</th>
</tr>
</thead>
<tbody>
<tr>
<td>$[\text{Cu}(\text{HL})_2(\text{H}_2\text{O})_2]\text{Cl}_2$ (1)</td>
<td>11100, 13200, 18600</td>
<td>$2^2\text{B}<em>{1g} \rightarrow 2^2\text{B}</em>{2g}$, $2^2\text{B}<em>{1g} \rightarrow 2^2\text{E}</em>{g}$, CT</td>
</tr>
<tr>
<td>$[\text{Cu}_2\text{L}_4]$ (2)</td>
<td>12600, 15800, 16200, 17200</td>
<td>$2^2\text{B}<em>{1g} \rightarrow 2^2\text{A}</em>{1g}$, $2^2\text{B}<em>{1g} \rightarrow 2^2\text{B}</em>{2g}$, $2^2\text{B}<em>{1g} \rightarrow 2^2\text{E}</em>{g}$, CT</td>
</tr>
<tr>
<td>$[\text{Cu}(\text{HL})_2(\text{H}_2\text{O})\text{Br}]\text{Br}$ (3)</td>
<td>13514, 15150, 16260, 18350</td>
<td>$2^2\text{B}<em>{1g} \rightarrow 2^2\text{A}</em>{1g}$, $2^2\text{B}<em>{1g} \rightarrow 2^2\text{B}</em>{2g}$, $2^2\text{B}<em>{1g} \rightarrow 2^2\text{E}</em>{g}$, CT</td>
</tr>
</tbody>
</table>

The coefficients $\alpha_2, \beta_1^2$ and $\beta_2^2$ characterize the in-plane $\sigma$-bonding, in-plane $\pi$-bonding and out-of-plane $\pi$-bonding of Cu$^{2+}$, respectively.

The parameters $\lambda_0$ is the spin-orbit coupling constant for the free Cu$^{2+}$ ion (-828 cm<sup>-1</sup>), $k$ is the Fermi contact term and characterizes the isotropic (s-electron) contribution to the hyperfine interaction: $p = 2\sqrt{3} \beta_0 < r^2 > = 0.036$ cm<sup>-1</sup>;

$\Delta E_{\sigma} = \Delta(E_{\sigma} - E_{\sigma})$, $\Delta E_{\pi,\sigma} = \Delta(E_{\pi,\sigma} - E_{\pi,\sigma})$. The values of the bonding parameters calculated for the three Cu(II) complexes are listed in table 4.
\[
G = \frac{g_\| - 2}{g_\perp - 2} \text{ is smaller than 4 for all the complexes, suggesting the strong spin-spin interactions between the copper centers.}
\]

According to the determinations presented above, the following structures have been proposed for the complexes (fig. 4):

\[
\begin{align*}
\text{Gram negative bacteria:} & \\
\text{Escherichia coli} & \\
\text{Pseudomonas aeruginosa} & \\
\text{Gram positive bacteria:} & \\
\text{Staphylococcus coagulase positive} & \\
\text{Streptococcus \( \beta \)-haemolytic type A} & \\
\text{Streptococcus \( \beta \)-haemolytic type B} & \\
\text{Staphylococcus aureus} & \\
\text{Fungi:} & \\
\text{Candida albicans} & \\
\end{align*}
\]

**Fig. 4. Structures of Cu(II) complexes**

### Biological activity

Antibacterial and antifungal activity was determined by the disk diffusion technique, against Gram negative bacteria (E. coli, Pseudomonas aeruginosa serotip IV), Gram positive bacteria (Staphylococcus coagulase positive, Staphylococcus aureus, Streptococcus \( \beta \)-haemolytic type A and type B) and fungi (Candida albicans). A solution 10\(^{-4}\)M of each compound in acetone was used. The culture medium and microbial strains were laid in petri plates. The 10\(\mu\)L solution compound (ligand or complex) impregnated disks were applied to the surface of inoculated plates. The petri plates were placed in an incubator at 37\(^\circ\)C for 24 h. After incubation the diameter of the zone of inhibition was measured. The results are presented in the table 5.

The ligand is biologically inactive against the test bacteria and fungi used. All the copper(II) complexes are moderately active, especially against the Gram positive bacteria. They are also found a little active against the test fungi used. The increasing in the antimicrobial activity is more intensive for the cationic complexes (1) and (3) and is probably due to faster diffusion of the electrolyte metal complexes through the cell membrane.

### Conclusions

We have prepared three new complex compounds of copper(II) with 4-metoxybenzaldehyde-2-benzothiazolyl hydrazone, using the copper(II) chloride, bromide and acetate, respectively. The values of bonding parameters calculated from the electronic and EPR spectra are in accordance with strong in-plane \( \pi \) bonding for these complexes. All the complexes are more active than the ligand against the bacteria and fungi used.

### References

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