Synthesis and Characterization of Cu(II) Complexes of Two Ligands Derived from Malonyl Dichloride

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Two different mononucleating ligands incorporating N4 and N2S2 donor units, 2-(1,3-benzothiazole-2-yl-methyl)-1,3-benzothiazole (L1) and N,N’-bis-(2-amino-phenyl)-malonamide (H2L2) were synthesized by a new method from malonyl dichloride as starting material, and their mononuclear copper(II) complexes were prepared and characterized by elemental analyses, 1H- and 13C-NMR, IR, magnetic moments and mass spectral studies. Elemental analyses, and stochiometric and spectroscopic data of the metal complexes indicate that the metal ions are coordinated to the nitrogen and sulfur atoms and the data support the proposed structure of L1, H2L2 and their mononuclear copper(II) complexes. Moreover, the copper(II) complexes of L1 and H2L2 have a 1:1 metal to ligand ratio. In addition, the total energy and heat of formation calculated for complexes (2-3) by the semiempirical ZINDO/1 calculations showed that complexes 2 and 3 having penta coordinations are more stable than complexes of tetra coordinations.

Key Words: Copper(II) complexes, malonamide, benzothiazole, mononucleating ligands

Introduction

The biological activities of some transition metal complexes with thiosemicarbazide, thiosemicarbazone, dithiocarbazate, thiohydrazides, thiosemicarbazides and Schiff bases have been reported previously1−5. Most of them display very interesting biological properties such as antitumor6, antibacterial7 and antifungal activity8. Their properties have been correlated with the chemical nature of the moiety attached to the C=S or C≡N carbon atom of the ligand. Moreover, interesting biological activities have been observed with some nitrogen-sulfur compounds by varying the ligation behavior of specific ligands9−11.

In order to understand the correlation between the structure and biological properties of such compounds, small nitrogen and sulfur-donor low-molecular-weight Cu(II) coordination compounds have been designed and most of them have been shown to possess or to mimic the activities of copper proteins12−14. It has been observed that the addition of specific structural elements to such ligands or modifications to

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the coordination sphere of the metal ion may affect the biological activities\textsuperscript{9–11}. Therefore, several attempts have been made to explore the reactions of copper-nitrogen/sulfur ligand complexes.

In this paper, we describe the synthesis of 2 different mononucleating ligands incorporating nitrogen-sulfur donor atoms, 2-(1,3-benzothiazole-2-yl-methyl)-1,3-benzothiazole (L\textsuperscript{1}) and N,N’-bis(2-aminophenyl) malonamide (H\textsubscript{2}L\textsubscript{2}) by a new method, and their copper(II) complexes characterized by elemental analyses, mass, UV-Vis, IR, \textsuperscript{1}H- and \textsuperscript{13}C-NMR spectra, and magnetic susceptibilities.

**Experimental**

\textsuperscript{1}H- and \textsuperscript{13}C-NMR spectra were recorded on a Varian Gemini 200 spectrometer using DMSO-d\textsubscript{6} and CDCl\textsubscript{3} as solvents. Chemical shifts (\(\delta\)) are reported in ppm relative to Me\textsubscript{4}Si, using the solvent signal as an internal reference. The metals were determined by complexometric titration against EDTA\textsuperscript{15}. Electronic spectra were obtained on an ATI Unicam UV2 model UV-Vis spectrophotometer. IR spectra were recorded on a Matson 1000 model FTIR spectrophotometer as KBr pellets. Room temperature magnetic susceptibility measurements were recorded at 19 Mayas University’s Department of Chemistry (Samsun, Turkey). C, H and N contents were recorded at TÜBİTAK (Ankara, Turkey). Mass spectra using electron impact (e.i.) and FAB(positive) were recorded at TÜBİTAK (Gebze, Turkey). Geometry optimization of the complexes was performed using the molecular mechanics MM+ module and ZINDO/1 semiempirical calculations in HyperChem 6.03.

**2-(1,3- Benzothiazole-2-yl-methyl)-1,3-benzothiazole** (L\textsuperscript{1}; C\textsubscript{15}H\textsubscript{10}N\textsubscript{2}S\textsubscript{2})

Sodium ethoxide, produced by mixing 0.92 g (40 mmol) of metallic sodium with 50 cm\textsuperscript{3} of absolute ethanol under nitrogen atmosphere was allowed to react with 5.01 g (40 mmol) of 2-amino thiophenol. Then 2.82 g (20 mmol) of malonyl dichloride was slowly added to this solution followed by mixing for 2 h at room temperature, and then refluxing for 1 h. The product (L\textsuperscript{1}) was filtered while hot, and evaporated and then crystallized in ethanol. The paleyellow crystalline solid (L\textsuperscript{1}) is airstable, m.p. 204 °C (yield 70% ).

**N,N’-Bis(2-aminophenyl)malonamide**,(H\textsubscript{2}L\textsubscript{2}; C\textsubscript{15}H\textsubscript{16}N\textsubscript{4}O\textsubscript{2})

A solution of 2.82 g (20 mmol) of malonyl dichloride in dichloromethane (10 cm\textsuperscript{3}) was slowly added to a suspension of 1,2-phenylenediamine (4.32 g, 40 mmol) in dichloromethane (80 cm\textsuperscript{3}) over 1 h. The mixture was stirred for 12 h at \(-5\) °C and then for 2 h at room temperature. The resulting precipitate was filtered, washed with Et\textsubscript{2}O, and then crystallized in ethanol and dried in vacuo over P\textsubscript{2}O\textsubscript{5}. m.p. 220-222 °C (yield 40%).

**Preparation of** [Cu(L\textsuperscript{1})](ClO\textsubscript{4})\textsubscript{2}, (2; C\textsubscript{15}H\textsubscript{10}N\textsubscript{2}S\textsubscript{2}O\textsubscript{8}Cl\textsubscript{2}Cu)

A solution of Cu(ClO\textsubscript{4})\textsubscript{2}.6H\textsubscript{2}O (4 mmol, 1.5 g) in Me\textsubscript{2}CO (25 cm\textsuperscript{3}) was added to the ligand (4 mmol) suspended in Me\textsubscript{2}CO (50 cm\textsuperscript{3}), and the mixture was boiled under reflux with stirring for 4 h. The purple-violet product was filtered off, washed successively with H\textsubscript{2}O, MeOH and Et\textsubscript{2}O and dried over P\textsubscript{2}O\textsubscript{5}. m.p. >300 °C.

**Preparation of** [Cu (H\textsubscript{2}L\textsubscript{2})](ClO\textsubscript{4})\textsubscript{2}, (3; C\textsubscript{15}H\textsubscript{16}N\textsubscript{4}O\textsubscript{10}Cl\textsubscript{2}Cu)

A solution of Cu(ClO\textsubscript{4})\textsubscript{2}.6H\textsubscript{2}O (4 mmol, 1.5 g) in EtOH (10 cm\textsuperscript{3}) was added to the ligand (4 mmol) suspended in EtOH (40 cm\textsuperscript{3}), and the mixture was boiled under reflux with stirring for 4 h. The brown product was filtered off, washed successively with H\textsubscript{2}O, EtOH and Et\textsubscript{2}O and dried over P\textsubscript{2}O\textsubscript{5}. m.p. >300 °C.
Results and Discussion

2-(1,3-Benzothiazole-2-yl-methyl)-1,3-benzothiazole (L$^1$) was prepared under nitrogen atmosphere by reacting sodium salts of 2-amino thiophenol with malonyl dichloride in absolute ethanol by a new method (Scheme 1). Previously, 2-(1,3-benzothiazole-2-yl-methyl)-1,3-benzothiazole (L$^1$) was synthesized from dibasic acids and $o$-aminothiophenol in the presence of polyphosphoric acid catalysis$^{16}$. Although the method involves a one-step procedure, there are several time-consuming purification steps. The tautomerism of such compounds was also investigated in some detail$^{17}$. $N,N'$-bis(2-aminophenyl)malonamide, (H$_2$L$^2$) was prepared under nitrogen atmosphere by reacting a dichloromethane solution of malonyl dichloride with 1,2-phenylenediamine by a new method (Scheme 1). Recently, Lu reported the synthesis of a maloamide-tosylate derivative from the reaction of malonyldichloride with an adduct of $p$-toluenesulphonyl chloride with 1,2-phenylenediamine$^{18}$. Al(III) complex of this compound was electrochemically converted to Al(III) complex of malonamide, (H$_2$L$^2$) upon the removal of tosylate groups.

The method described in this work is easier and shorter than those used previously for the synthesis of both types of compounds$^{16,18}$. In the proposed structures of L$^1$ and H$_2$L$^2$, N$_2$S$_2$ and N$_4$ units are available for the complexation of one metal ion in a square-planar coordination geometry. The corresponding mononuclear copper(II) complexes, 2 and 3, were prepared by the reaction of the ligands with copper(II) perchlorate salts in dry acetone/ethanol. The structures of benzothiazole (L$^1$) and malonamide (H$_2$L$^2$) derivatives were verified by elemental analyses, $^1$H- and $^{13}$C-NMR, IR and mass spectral data, as presented in Tables 1-3.

The $^1$H-NMR spectra of a DMSO-$d_6$ solution of 2-(1,3-benzothiazole-2-yl-methyl)-1,3-benzothiazole (L$^1$) show 3 well resolved proton signals as a doublet at 4.65 ppm (-CH, 1H), a multiplet at 7.0-7.6 ppm
(Ar-H, 8H) and a doublets of doublet at 7.80 ppm (-NH, 1H), corresponding to the aliphatic, aromatic and imine proton resonances, respectively (Table 1). After D2O was added, the doublet at 4.65 ppm belonging to the Hc proton was converted to a singlet, and the doublet of doublets at 7.80 ppm belonging to Hb was converted to a single doublet. These results indicate that a tautomeric equilibrium was reached. It may be proposed that the Hb proton of the ligand is split into doublets by Ha, (J_ab=7.6) and Hc, (J_bc=5.2) protons, separately. At the same time, the Hc proton is split only by the Hb proton into a doublet (J_bc = 5.2).

Moreover, water proton signals at 6.5 ppm shift to a higher field as observed at 4.4 ppm upon the addition of D2O. The signals observed at 6.5 ppm indicate that the tautomerized protons form strong hydrogen bonds with water molecules. The hydrogen bonds were not formed after exchanging with D2O and therefore proton signals belonging to water molecules appear at 4.4 ppm as expected.

<table>
<thead>
<tr>
<th>Table 1.</th>
<th>1H- and 13C-NMR data for L1 and H2L2.</th>
</tr>
</thead>
<tbody>
<tr>
<td>1H- data for L1</td>
<td>13C- data for L1</td>
</tr>
<tr>
<td>4.65 d.(-CH2, 1H)</td>
<td>C-1, 38.07</td>
</tr>
<tr>
<td>7.0-7.6 m. (Ar-H, 8H)</td>
<td>C-2, 120.4</td>
</tr>
<tr>
<td>7.80 d.d. (-NH, 1H)</td>
<td>C-3, 135.1</td>
</tr>
<tr>
<td>C-4, 130.4</td>
<td>9.95 br. s. (-NH, 2H)</td>
</tr>
<tr>
<td>C-5, 123.6</td>
<td>C-5, 121.6</td>
</tr>
<tr>
<td>C-6, 122.7</td>
<td>C-6, 115.5</td>
</tr>
<tr>
<td>C-7, 127.4</td>
<td>C-7, 122.14</td>
</tr>
<tr>
<td>C-8, 131.9</td>
<td>C-8, 126.1</td>
</tr>
</tbody>
</table>

The 1H-NMR spectra of a CDCl3 solution of malonamide (H2L2) show well resolved signals as expected (Table 1). The spectrum of malonamide shows a singlet at 3.60 ppm (-CH2-, 2H), a broad singlet at 4.10 ppm (-NH2, 4H), a multiplet at 7.0-7.65 ppm (Ar-H, 8H), and a broad singlet at 9.95 ppm (NH, 2H), corresponding to the aliphatic, amine, aromatic and imine proton resonances, respectively. The 1H-NMR spectral data of a DMSO-d6 solution of benzothiazole and a CDCl3 solution of malonamide support the proposed structures and indicate the formation of L1 and H2L2 (Scheme 1). The data are also consistent with the structures of previously reported compounds16−18.

The imine and amine proton signals at δ 7.80, 9.95 and 4.10 ppm disappear on deuterium exchange. The 8 resonances (Table 1) observed in the 13C- NMR spectra of L1 and H2L2 are also consistent with the proposed structure (Scheme 1). Analysis by e.i. and FAB data of the molecular ions of the ligands and complexes indicated strong parent ions at m/z (e.i.) 282 (100%) M+ for L1 and 284 (100%) M+ for H2L2, at m/z (FAB-positive) 546 [M+1]+ for L1Cu(II) 2 complex and at m/z (FAB-positive) 548 [M+1]+ for H2L2Cu(II) 3 complex. Moreover, the signal that appeared at m/z = 296 (15%) for L1 can be attributed to [M+CH2]+. All these mass spectral data support the formation of the ligands and their copper(II) complex. The abundancy of the other fragmentation products is below 15% for the ligands L1 and H2L2.
In the IR spectrum of benzothiazole (L\textsubscript{1}), -C=N, N-H and C-N bands were observed at ca. 1605, 3339 and 1473 cm\textsuperscript{-1}, respectively. In the IR spectrum of malonamide, (H\textsubscript{2}L\textsubscript{2}), C=O, N-H and C-N bands were observed at ca. 1655, 3252 and 1451 cm\textsuperscript{-1}, respectively. The IR spectra of the complexes were compared with those of similar structures for the coordination modes of the benzothiazole and malonamide ligands in the complexes. The more relevant NH, C=N, C-N and C=O absorption bands are listed in Table 2. In these complexes, the NH, C=N, C-N and C=O absorption bands shifted considerably toward lower or higher wavenumbers (ca. 10-30 cm\textsuperscript{-1}).

Table 2. Observed frequencies and proposed mode of assignments and magnetic moment data for L\textsubscript{1} and H\textsubscript{2}L\textsubscript{2} and their copper(II) complexes.

<table>
<thead>
<tr>
<th>Compound</th>
<th>(N-H)</th>
<th>(C=N)</th>
<th>(C=O)</th>
<th>(C-N)</th>
<th>(ClO\textsubscript{4})</th>
<th>(Cu-N)</th>
<th>(Cu-S)</th>
<th>(\mu_{\text{eff}})/atom(B.M.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>L\textsubscript{1}</td>
<td>3339</td>
<td>1605</td>
<td>-</td>
<td>1473</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>3351</td>
<td>1621</td>
<td>-</td>
<td>1487</td>
<td>1143</td>
<td>450</td>
<td>610</td>
<td>1.91</td>
</tr>
<tr>
<td>3</td>
<td>br 3252</td>
<td>-</td>
<td>1655</td>
<td>1451</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>624</td>
<td>1084</td>
<td>1118</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>H\textsubscript{2}L\textsubscript{2}</td>
<td>br 3283</td>
<td>-</td>
<td>1656</td>
<td>1442</td>
<td>1095</td>
<td>615</td>
<td>-</td>
<td>1.80</td>
</tr>
<tr>
<td>3</td>
<td>br 626</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

The perchlorate salt (2) of the complex of L\textsubscript{1} shows a triplet (\(\nu_3\) mode) at 1143, 1118 and 1084 cm\textsuperscript{-1} due to antisymmetric stretch, which is indicative of the weakly coordinated perchlorate ion. There is also a sharp band at 624 cm\textsuperscript{-1} due to antisymmetric bend, which can be attributed to the uncoordinated
perchlorate ion. Complex 3 shows strong broad antisymmetric stretching bands and a sharp antisymmetric bending band at ca. 1095 and 626 cm\(^{-1}\), indicating ionic perchlorate anions\(^{19,20}\).

The sharp and intense bands at 1605 cm\(^{-1}\) for the imine, at 1473 cm\(^{-1}\) for the thiazole groups of L\(^1\) at 1451 cm\(^{-1}\) for the malonamide, (H\(_2\)L\(^2\)) were assigned to \(\nu(CN)\) vibrations. The \(\nu(CN)\) stretching vibrations for the metal complexes 2 and 3 shift to lower or higher frequencies, suggesting that the amine and imine groups are nitrogen coordinated\(^{21,22}\) in copper(II) 2 and 3 complexes. The IR data confirm the binding of copper(II) ions to N\(_4\) and N\(_2\)S\(_2\) donor groups of the present ligands and support the tentative structure of the complexes (Figure 1).

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure1.png}
\caption{Proposed structure of copper(II) complexes 2 and 3 of L\(^1\) and H\(_2\)L\(^2\) ligands.}
\end{figure}

The electronic spectra of the copper(II) complexes in DMF below 400 nm are dominated by intense bands due to intraligand and charge-transfer transitions in the copper(II) chromophore\(^{23}\). The DMF solution of complex 2 displays a band due to a d-d transition at 566 nm. This indicates a square pyramidal geometry\(^{24}\) around Cu(II) and complex 3 displays a visible band at 485 nm, suggestive of a predominantly square planar stereochemistry\(^{24}\). The room magnetic moment data of the copper complexes 2 and 3 show normal magnetic moments, 1.91 and 1.80 B.M., respectively (Table 2). In addition, total energy (for 2 -177,781.13 and for 3 -200,185.25 kcal/mol) and heat of formation (for 2 -8080.92 and for 3 -8595.71 kcal/mol) calculated for the copper(II) complexes 2 and 3 by semiempirical ZINDO/1 calculations\(^{25}\) showed that complexes having penta coordination are more stable than those having tetra coordination (Figure 2).

Elemental analyses (Table 3) and the stoichiometric and spectroscopic data of the metal complexes indicate that the metal ions are coordinated to the nitrogen and sulfur or nitrogen atoms and the data support the proposed structures of L\(^1\) and H\(_2\)L\(^2\), and their mononuclear copper(II) complexes. Moreover, copper(II) complexes of L\(^1\) and H\(_2\)L\(^2\) have a 1:1 metal to ligand ratio.
Figure 2. The lowest energy conformations by ZINDO/1 optimized geometries of copper(II) complexes (2, 3).

Table 3. Elemental analyses, mass, UV-Vis spectral data of L₁ and H₂L² and their copper(II) complexes.

<table>
<thead>
<tr>
<th>Color</th>
<th>Yield (%)</th>
<th>Found (Calcld.) (%)</th>
<th>Comp</th>
<th>λ_max (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>L₁ Paleyellow</td>
<td>70</td>
<td>61.9 (62.2) 3.8 (3.7) 10.6 (10.4) -</td>
<td>282</td>
<td>208, 254, 380</td>
</tr>
<tr>
<td>H₂L² Whitebrown</td>
<td>40</td>
<td>63.1 (63.4) 5.6 (5.7) 20.1 (19.7) -</td>
<td>284</td>
<td>257, 377</td>
</tr>
<tr>
<td>2 Deeppurple</td>
<td>70</td>
<td>33.1 (33.4) 1.85 (1.6) 5.2 (5.1) 11.5 (12.7) 546[M+1]⁺</td>
<td>370, 566</td>
<td></td>
</tr>
<tr>
<td>3 Brown</td>
<td>75</td>
<td>32.5 (32.95) 4.1 (2.95) 10.5 (10.25) 11.4 (11.6) 548[M+1]⁺</td>
<td>375, 485</td>
<td></td>
</tr>
</tbody>
</table>

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References