

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 stoichiometric 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, dithiocarbamate, 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^{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^1) and *N,N'*-bis(2-aminophenyl) malonamide (H_2L^2) by a new method, and their copper(II) complexes characterized by elemental analyses, mass, UV-Vis, IR, ¹H- and ¹³C-NMR spectra, and magnetic susceptibilities.

Experimental

¹H- and ¹³C-NMR spectra were recorded on a Varian Gemini 200 spectrometer using DMSO-d₆ and CDCl₃ as solvents. Chemical shifts (δ) are reported in ppm relative to Me₄Si, using the solvent signal as an internal reference. The metals were determined by complexometric titration against EDTA¹⁵. 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 Mayıs 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^1 ;C₁₅H₁₀N₂S₂)

Sodium ethoxide, produced by mixing 0.92 g (40 mmol) of metallic sodium with 50 cm³ 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^1) was filtered while hot, and evaporated and then crystallized in ethanol. The paleyellow crystalline solid (L^1) is airstable, m.p. 204 °C (yield 70%).

N,N'-Bis(2-aminophenyl)malonamide, (H_2L^2 ;C₁₅H₁₆N₄O₂)

A solution of 2.82 g (20 mmol) of malonyl dichloride in dichloromethane (10 cm³) was slowly added to a suspension of 1,2-phenylenediamine (4.32 g, 40 mmol) in dichloromethane (80 cm³) 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 Et₂O, and then crystallized in ethanol and dried *in vacuo* over P₂O₅. m.p. 220-222 °C (yield 40%).

Preparation of [Cu(L^1)](ClO₄)₂, (**2**;C₁₅H₁₀N₂S₂O₈Cl₂Cu)

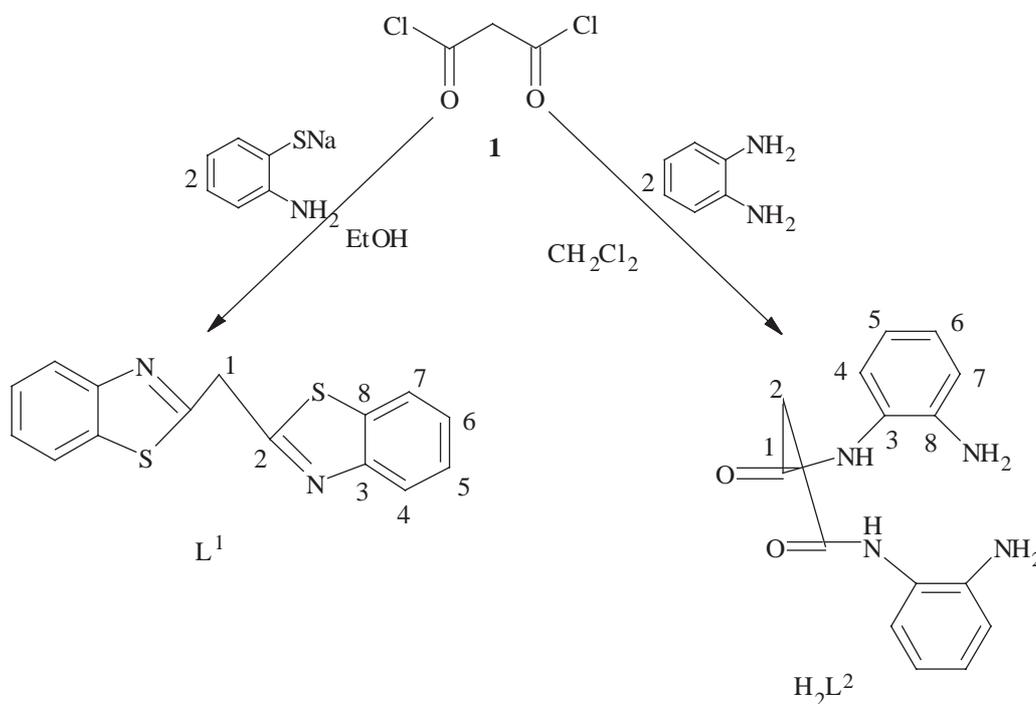
A solution of Cu(ClO₄)₂.6H₂O (4 mmol, 1.5 g) in Me₂CO (25 cm³) was added to the ligand (4 mmol) suspended in Me₂CO (50 cm³), and the mixture was boiled under reflux with stirring for 4 h. The purple-violet product was filtered off, washed successively with H₂O, MeOH and Et₂O and dried over P₄O₁₀. m.p. >300 °C.

Preparation of [Cu (H_2L^2)](ClO₄)₂, (**3**;C₁₅H₁₆N₄O₁₀Cl₂Cu)

A solution of Cu(ClO₄)₂.6H₂O (4 mmol, 1.5 g) in EtOH (10 cm³) was added to the ligand (4 mmol) suspended in EtOH (40 cm³), and the mixture was boiled under reflux with stirring for 4 h. The brown product was filtered off, washed successively with H₂O, EtOH and Et₂O and dried over P₄O₁₀. 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 catalysis¹⁶. 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 detail¹⁷. *N, N'*-bis(2-aminophenyl)malonamide, (H_2L^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 malonamide-tosylate derivative from the reaction of malonyldichloride with an adduct of *p*-toluenesulphonyl chloride with 1,2-phenylenediamine¹⁸. Al(III) complex of this compound was electrochemically converted to Al(III) complex of malonamide, (H_2L^2) upon the removal of tosylate groups.



Scheme 1

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_2L^2 , N_2S_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_2L^2) derivatives were verified by elemental analyses, 1H - and ^{13}C -NMR, IR and mass spectral data, as presented in Tables 1-3.

The 1H -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

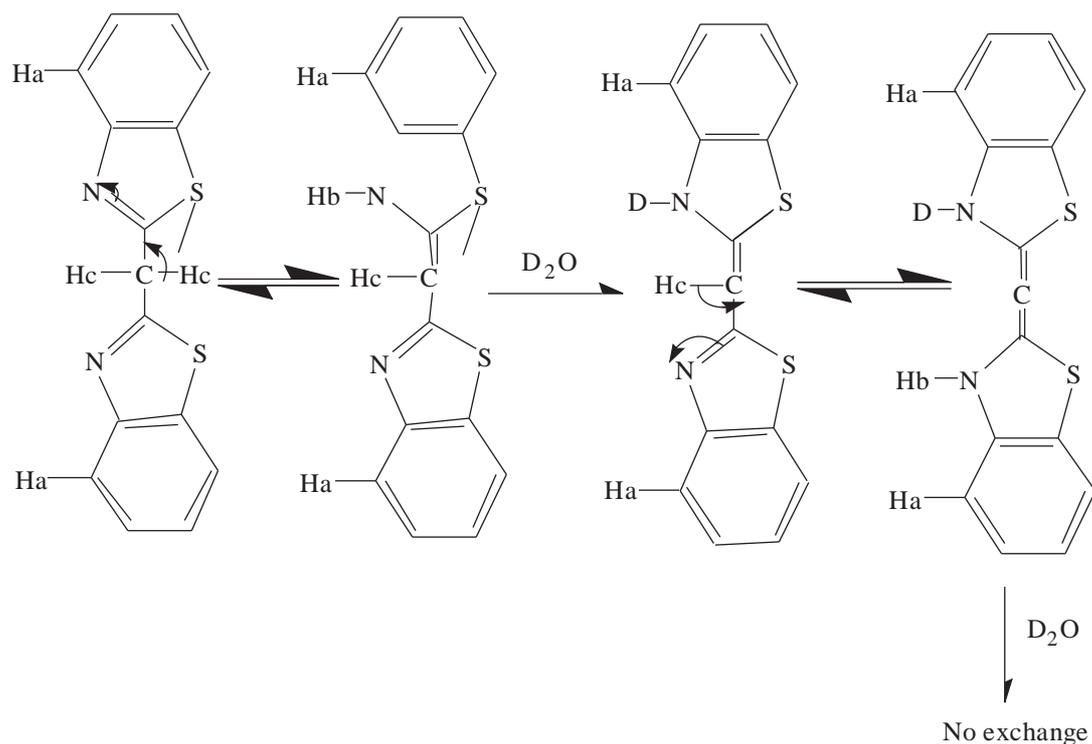
(Ar-H, 8H) and a doublets of doublet at 7.80 ppm (-NH, 1H), corresponding to the aliphatic, aromatic and imine proton resonances, respectively (Table 1). After D₂O was added, the doublet at 4.65 ppm belonging to the H_c proton was converted to a singlet, and the doublet of doublets at 7.80 ppm belonging to H_b was converted to a single doublet. These results indicate that a tautomeric equilibrium was reached. It may be proposed that the H_b proton of the ligand is split into doublets by H_a, ($J_{ab}=7.6$) and H_c, ($J_{bc}=5.2$) protons, separately. At the same time, the H_c proton is split only by the H_b 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 1. ¹H- and ¹³C-NMR data for L¹ and H₂L².

¹ H- data for L ¹	¹³ C- data for L ¹	¹ H- data for H ₂ L ²	¹³ C- data for H ₂ L ²
4.65 d. (-CH ₂ , 1H)	C-1, 38.07	3.60 s. (-CH ₂ , 2H)	C-1, 166.2
7.0-7.6 m. (Ar-H, 8H)	C-2, 120.4	7.0-7.65 m. (Ar-H, 8H)	C-2, 40.4
7.80 d.d. (-NH, 1H)	C-3, 135.1	4.10 br. s. (-NH ₂ , 4H)	C-3, 140.1
	C-4, 130.4	9.95 br. s. (-NH, 2H)	C-4, 124.9
	C-5, 123.6		C-5, 121.6
	C-6, 122.7		C-6, 115.5
	C-7, 127.4		C-7, 122.14
	C-8, 131.9		C-8, 126.1

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) complex **3**. 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.


Scheme 2

In the IR spectrum of benzothiazole (L^1), $-C=N$, $N-H$ and $C-N$ bands were observed at ca. 1605, 3339 and 1473 cm^{-1} , respectively. In the IR spectrum of malonamide, (H_2L^2), $C=O$, $N-H$ and $C-N$ bands were observed at ca. 1655, 3252 and 1451 cm^{-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. $10\text{-}30\text{ cm}^{-1}$).

Table 2. Observed frequencies and proposed mode of assignments and magnetic moment data for L^1 and H_2L^2 and their copper(II) complexes.

Compound	(N-H)	(C=N)	(C=O)	(C-N)	(ClO ₄)	(Cu-N)	(Cu-S)	$\mu_{\text{eff}}/\text{atom}$ (B.M.)
L^1	3339	1605	-	1473	-	-	-	
2	3351	1621	-	1487	1143 1118 1084 624	450	610	1.91
H_2L^2	br 3252	-	1655	1451	-	-	-	
3	br 3283	-	1656	1442	1095 626	615	-	1.80

The perchlorate salt (**2**) of the complex of L^1 shows a triplet (ν_3 mode) at 1143, 1118 and 1084 cm^{-1} due to antisymmetric stretch, which is indicative of the weakly coordinated perchlorate ion. There is also a sharp band at 624 cm^{-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_2L^2) were assigned to $\nu(\text{CN})$ vibrations. The $\nu(\text{CN})$ 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_2S_2 donor groups of the present ligands and support the tentative structure of the complexes (Figure 1).

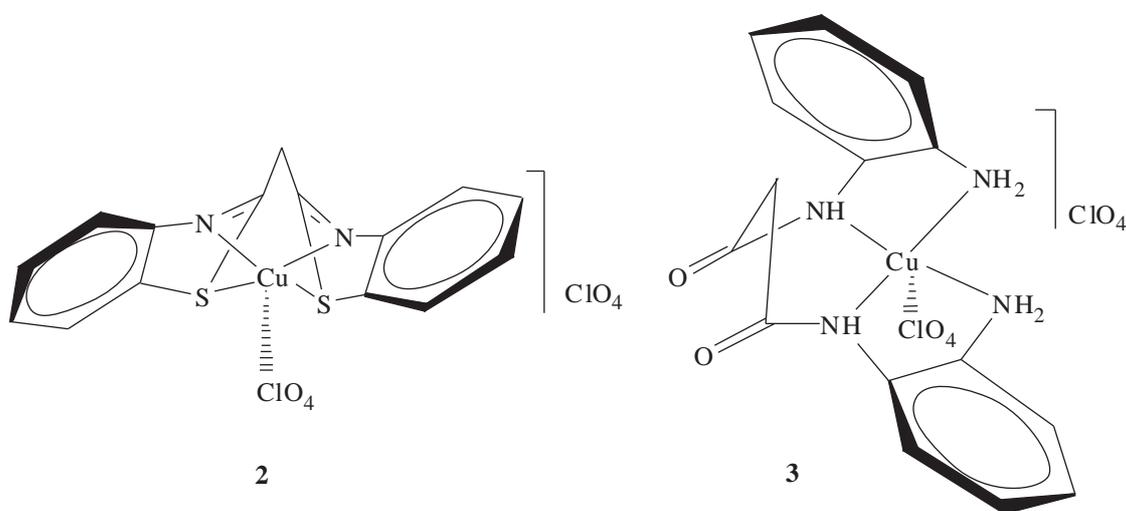


Figure 1. Proposed structure of copper(II) complexes **2** and **3** of L^1 and H_2L^2 ligands.

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) chromophore²³. The DMF solution of complex **2** displays a band due to a d-d transition at 566 nm. This indicates a square pyramidal geometry²⁴ around Cu(II) and complex **3** displays a visible band at 485 nm, suggestive of a predominantly square planar stereochemistry²⁴. 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 calculations²⁵ 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_2L^2 , and their mononuclear copper(II) complexes. Moreover, copper(II) complexes of L^1 and H_2L^2 have a 1:1 metal to ligand ratio.

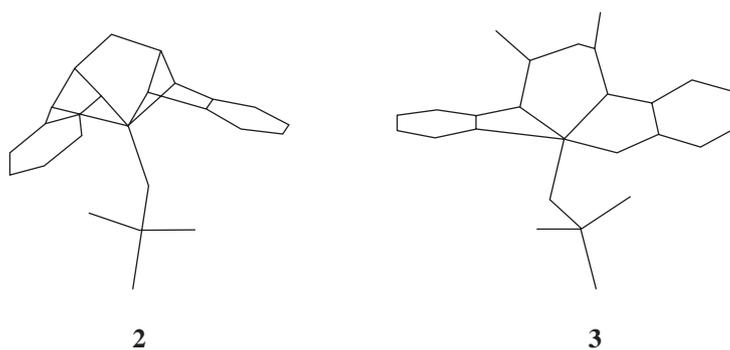


Figure 2. The lowest energy conformations by ZINDO/1 optimized geometries of copper(II) complexes (**2**, **3**).

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

Color	Yield (%)	Found (Calcd.) (%)				Cu	Comp M ⁺	λ_{max} (nm)
		C	H	N				
L ¹	Paleyellow	70	61.9 (62.2)	3.8 (3.7)	10.6 (10.4)	-	282	208, 254, 380
H ₂ L ²	Whitebrown	40	63.1 (63.4)	5.6 (5.7)	20.1 (19.7)	-	284	257, 377
2	Deeppurple	70	33.1 (33.4)	1.85 (1.6)	5.2 (5.1)	11.5 (12.7)	546[M+1] ⁺	370, 566
3	Brown	75	32.5 (32.95)	4.1 (2.95)	10.5 (10.25)	11.4 (11.6)	548[M+1] ⁺	375, 485

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