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Study of the Influence of the Solvent on the Crystal Structure of an Ethyl-Substituted *Bis*thiosemicarbazone Ligand †

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Abstract: A potentially dianionic symmetric *bis*thiosemicarbazone ligand H_2L^{Et} has been prepared by a condensation reaction between two equivalents of 4-N-ethyl-3-thiosemicarbazide and one equivalent of 4,4′-methylenebis(acetophenone). The crystal structures obtained from solvents with different donor ability were studied. Recrystallization of H_2L^{Et} from methanol and dimethylsulfoxide allows the isolation of single crystals suitable for X-ray diffraction studies of $[H_2L^{Et}]$ **1** and $[H_2L^{Et}]\cdot CH_3SOCH_3$ **2**, respectively. This study shows that the solvent does not affect the macrostructure but influences the microstructure of the ethyl-substituted *bis*thiosemicarbazone ligand H_2L^{Et}.

Keywords: *bis*thiosemicarbazone; X-ray diffraction; solvent

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1. Introduction

To date, a vast family of thiosemicarbazone ligands have been synthesized because of their high versatility in coordination chemistry and their interesting properties related with biomedical and pharmacological activities [1,2]. These ligands can be obtained easily by a condensation reaction between an appropriate carbonyl compound and a thiosemicarbazide [3], giving rise to the formation of an imine bond and the liberation of a water molecule.

In the case of thiosemicarbazone ligands, the influence of different factors such as the presence of metal ions [4], the pH of the medium [5] or the solvent [6], among others, can lead to a desulfurization process, giving rise to the loss of the sulfur atom. Having this in mind, in this work we decided to study the influence of the recrystallization solvent on the desulfurization process and the concomitant modification of the macrostructure of the *bis*thiosemicarbazone ligand H_2L^{Et}. For this reason, we have prepared again the ethyl-substituted *bis*thiosemicarbazone published [7] and it was recrystallized in solvents with different donor ability.

2. Experimental Section

2.1. Reactants and Solvents

All solvents, 4,4′-methylenebis(acetophenone) and 4-N-ethyl-3-thiosemicarbazide are commercially available ant they were used without further purification.

2.2. Preparation of the Bisthiosemicarbazone Ligand H_2L^{Et}

The $[N_2S_2]$ *bis*thiosemicarbazone ligand H_2L^{Et} was obtained by means of a condensation reaction between two equivalents of 4-N-ethyl-3-thiosemicarbazide and one equivalent of 4,4′-methylenebis(acetophenone) using absolute ethanol as solvent (*ca.* 50 mL) and *p*-toluensulfonic acid as catalyst [8]. Recrystallization of H_2L^{Et} from dimethylsulfoxide yielded yellow needle-shaped crystals that were suitable for monocristal X-ray-crystallographic studies.

2.3. Crystallographic Data

$[H_2L^{Et}]\cdot CH_3SOCH_3$ **2**: $C_{23}H_{30}N_6S_2\cdot C_2H_6OS$, *MW*: 532.78; crystal dimensions: 0.53 × 0.14 × 0.1; monoclinic; $P2_1/c$; a = 17.8816(15); b = 14.0286(11); c = 10.9880(9) Å; α = 90; β = 91.617(3); γ = 90°; V = 2755.3(4) Å^3; Z = 4; μ = 0.30 mm^{-1}; measured reflexions = 21262678; independent reflexions [R_{int}] = 5642 [0.040]; R = 0.048; *w*R = 0.131.

3. Results and Discussion

The ethyl-substituted *bis*thiosemicarbazone ligand H_2L^{Et} have been prepared by means of a condensation reaction between 4-N-ethyl-3-thiosemicarbazide and 4,4′-methylenebis(acetophenone), as previously reported [7].

Recrystallization of H_2L^{Et} from methanol allows discrete molecules of H_2L^{Et} **1** to be isolated [7]. In the ligand both thiosemicarbazone arms adopt an *E* configuration with respect to the imine bonds and an *anti* conformation, with the two thiosemicarbazone arms facing different sides.

With the aim of explore if the solvent of recrystallization influences in the macro- and microstructure of the ligand H_2L^{Et}, we have used dimethylsulfoxide to recrystallize the solid obtained from the synthesis. Recrystallization of the ligand solid in dimethylsulfoxide allowed us to obtain yellow needle-shaped crystals suitable for X-ray diffraction studies. The crystal structure of $[H_2L^{Et}]\cdot CH_3SOCH_3$ **2** is shown in Figure 1.

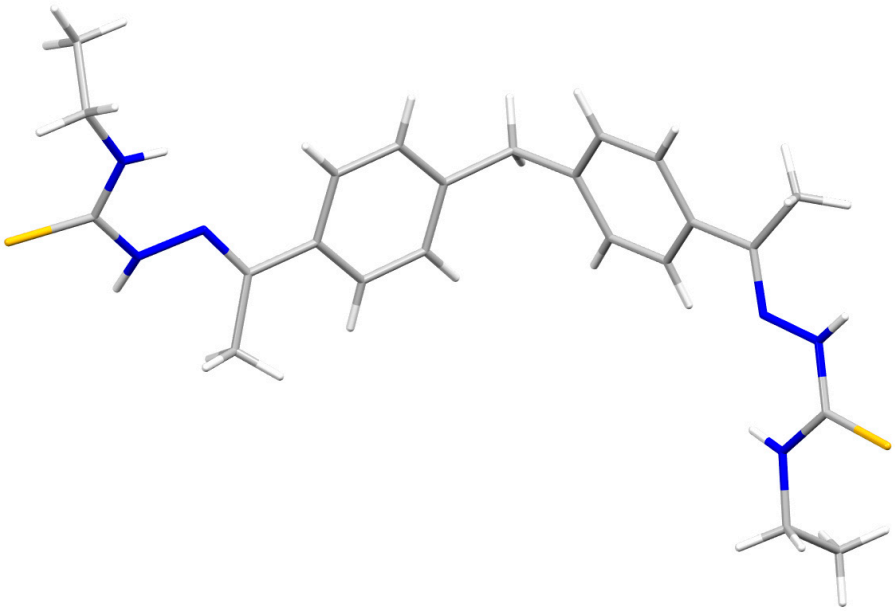

Figure 1. Crystal structure of the ethyl-substituted *bis*thiosemicarbazone ligand $[H_2L^{Et}]\cdot CH_3SOCH_3$ **2**. The solvent molecule was omitted for clarity.

Compound $[H_2L^{Et}]\cdot CH_3SOCH_3$ **2** (Figure 1) crystallized solvated by one molecule of dimethylsulfoxide. The crystal structure consists of discrete molecules in which both thiosemicarbazone arms adopt an *E* configuration with respect to the imine bonds and an *anti* configuration with the two thiosemicarbazone arms oriented in opposite sides, similar

to the previously published ethyl-substituted *bis*thiosemicarbazone ligand crystal structure obtained using methanol as solvent [7]. Main bond distances C=N, N-N and C-S and angles given in Table 1 are very similar to H_2L^{Et} **1** being in the expected range for thiosemicarbazone ligands and need no further discussion [7].

Table 1. Selected bond lengths (Å) for $[H_2L^{Et}]\cdot CH_3SOCH_3$ **2**.

Main Bond Distances (Å)			
C3—S1	1.685 (2)	C21—S2	1.387 (3)
C5—N3	1.290 (3)	C22—N8	1.288 (4)
N2—N3	1.381 (3)	N4—N7	1.383 (3)

However, the comparison of **1** and **2** shows that there are some differences related to the hydrogen bonds established in the crystal lattice.

In the case of H_2L^{Et} **1**, moderate intermolecular hydrogen bonds are observed between the thioamidic sulfur atom of one of the ligand arms and one of the thioamidic NH groups of the adjacent unit ligand, connecting the molecules along the crystal lattice. Also, intramolecular hydrogen bonds between the iminic nitrogen and the thioamidic nitrogen atom of one branch are observed [7].

On the other hand, in the case of $H_2L^{Et}\cdot CH_3SOCH_3$ **2** the ligand establishes a moderate intermolecular hydrogen bond between the thioamidic nitrogen atom of one of their branches and the oxygen atom of the solvation dimethylsulfoxide molecule. Also, a weak intermolecular hydrogen bond exists between one methyl group of dimethylsulfoxide molecule and the hydrazidic nitrogen of another ligand unit (Figure 2). However, in this case there are no intramolecular hydrogen bonds.

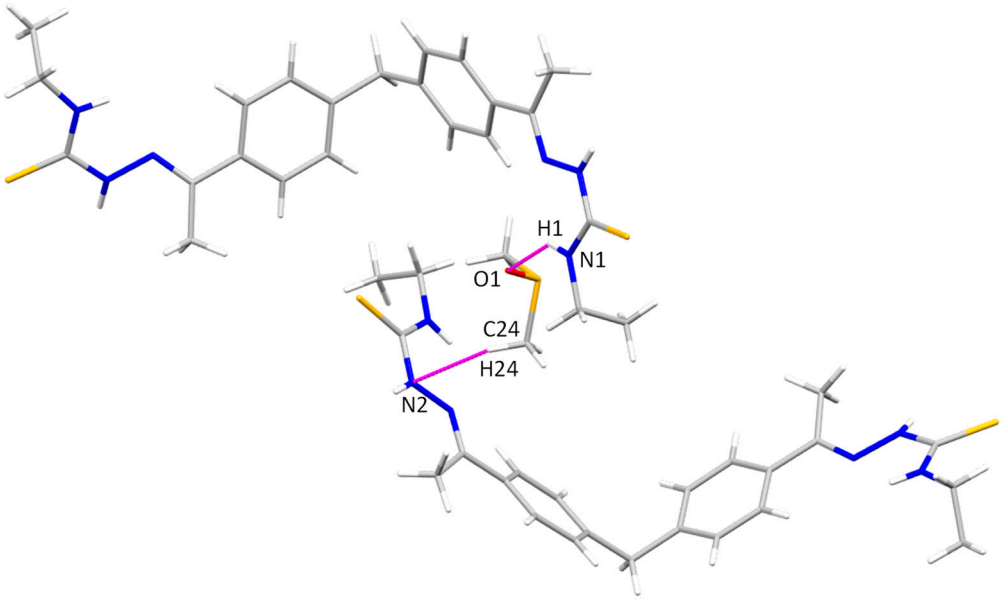

Figure 2. Intermolecular hydrogen bonds *[N1–H1···O1 2.924 Å; C24–H24···N2 3.516]* in $H_2L^{Et}\cdot CH_3SOCH_3$ **2**.

4. Conclusions

The recrystallization of the ethyl-substituted bisthiosemicarbazone ligand H_2L^{Et} in methanol [7] and in dimethylsulfoxide allowed to explore the influence of the solvent with different donor ability in the structure of the compound. It is clear from the crystal data obtained that the solvents used do not have an influence on the macrostructure of the bisthiosemicarbazone compound, confirming that there is no evidence of a

desulfurization process. However, the solvent affects the microstructure showing a higher number of hydrogen bonds in the case of the crystal structure obtained in methanol, H_2L^{Et} **1**, compared with the crystal structure obtained in dimethylsulfoxide, $H_2L^{Et}{\cdot}CH_3SOCH_3$ **2**.

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