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Design, Synthesis and Structural Characterization of a Novel Asymmetric Hydrazone-Thiosemicarbazone Ligand with the Aim of Obtaining Interesting Metallosupramolecular Architectures †

Sandra Fernández-Fariña, Isabel Velo-Heleno, Miguel Martínez-Calvo, Ana M. González-Noya * and Rosa Pedrido *

Departamento de Química Inorgánica, Facultade de Química, Campus Vida, Universidade de Santiago de Compostela, 15782 Santiago de Compostela, Spain; sandra.fernandez.farina@usc.es (S.F.-F.); email1 (I.V.-H.); email2 (M.M.-C.)

* Correspondence: ana.gonzalez.noya@usc.es (A.M.G.-N.); rosa.pedrido@usc.es (R.P.)

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Abstract: The asymmetric hydrazone-thiosemicarbazone ligand H_2L was synthesized in two stages by means of a double condensation reaction. The potentially dianionic and pentadentate [N_3SO] organic ligand H_2L possesses two flexibles bidentate [NS/NO] domains separated by a pyridine spacer which could stabilize a wide variety of metal ions, giving rise to different supramolecular architectures. This ligand was fully characterized by different techniques such as elemental analysis, infrared spectroscopy, mass spectrometry and $^1H/^{13}C$ NMR confirming that it was obtained with high purity.

Keywords: hydrazone; thiosemicarbazone; ligand; metallosupramolecular architectures

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1. Introduction

Among the wide variety of organic ligands reported to date, the design and synthesis of hydrazone and thiosemicarbazone ligands is an interesting field of study because of their potential biological properties such as antitumoral, antiviral, antibacterial or antifungal, both as free ligands and as derived metal complexes [1]. Furthermore, their fascinating structural versatility give rise to different coordination modes and thus, to a wide variety of metallosupramolecular architectures [2].

In this point, our research group has carried out an extensive study on the effect that the type of ligand has on the assembly of different metallosupramolecular architectures [2b,c]. For further study, we report here the design and synthesis of a novel hydrazone-thiosemicarbazone asymmetric ligand H_2L (Figure 1).

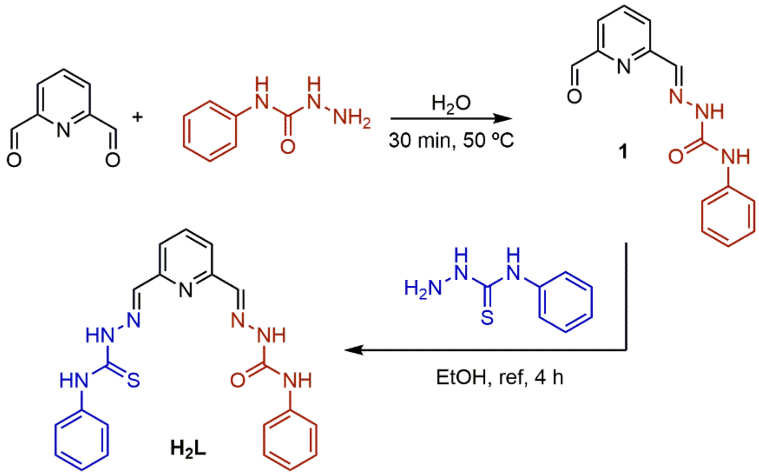

Figure 1. Synthesis of the hydrazone-thiosemicarbazone ligand H_2L.

2. Experimental Section

The [N_3SO] hydrazone-thiosemicarbazone asymmetric ligand H_2L was obtained in two steps by means of a double condensation (Figure 1). First, 4-phenylsemicarbazide (1.12 g, 7.4 mmol) was dissolved in water and added to an aqueous solution of 2,6-diformylpyridine (1 g, 7.4 mmol) in a 1:1 molar ratio. The mixture was stirred during 30 min at ca. 50 °C and the precipitate formed was filtered off and redissolved in chloroform. The final white solid was isolated by filtration and the remaining solution was concentrated to dryness under reduced pressure, giving rise to product **1**.

In a second step, **1** (0.3 g, 1.1 mmol) was mixed with 4-phenylthiosemicarbazide (0.2 g, 1.2 mmol) in ethanol. The resulting solution was refluxed for 4 h. Afterwards, the solution was cooled and a yellow powder was obtained. This solid was filtered off, washed with diethyl ether, dried under vacuo and was fully characterized as shown below.

H_2L: Yield 0.43 g (98%). Elemental analysis, Calc. for $C_{21}H_{19}N_7OS$: C, 60.4; H, 4.6; N, 23.5; S, 7.7. Found: C, 60.4; H, 4.5; N, 23.5; S, 7.7%. MS ESI$^+$ (m/z): 418.15 $[L+H]^+$. IR (KBr, cm^{-1}): ν(N-H) 3386, 3313, ν (C=O) 1689, ν((C=N) + (C-N)) 1596, 1543, 1499, ν((N-H) + (C-O)) 1396, ν(C=S) 1080, 759, ν(N-N) 1036. ^1H NMR (DMSO-d_6, ppm): 12.08 (s, 1H, NH), 11.06 (s, 1H, NH), 10.33 (s, 1H, NH), 9.09 (s, 1H, NH), 8.38 (d, 1H, Ar), 8.30 (d, 1H, Ar), 8.18 (s, 1H, CH), 7.99 (s, 1H, CH), 7.91 (t, 1H, Ar), 7.63 (d, 2H, Ar), 7.54 (d, 2H, Ar), 7.65-7.52 (m, 5H, Ar), 7.01 (t, 1H, Ar). ^{13}C NMR (DMSO-d_6, ppm) 177.7(C=S), 153.4 (C=O), 150.1(C=N), 120.1-145.2(C_{Ar}).

3. Results and Discussion

The crystal structure of H_2L is shown in Figure 2. Main crystallographic data are summarised in Table 1 while the bond lengths and angles are listed in Table 2.

The crystal structure of H_2L consists of discrete molecules with the thiosemicarbazone and the hydrazone arms adopting a *syn-close* arrangement and an *E* conformation in relation to the two imine bonds (Figure 2).

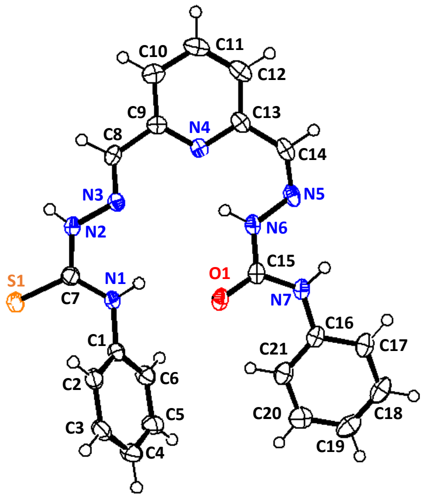

Figure 2. Crystal structure of the hydrazone-thiosemicarbazone ligand H_2L.

Table 1. Main crystallographic data for H_2L.

Crystallographic Data	
Formula	$C_{21}H_{19}N_7OS$
Molecular weight	417.49
Crystal system	Monoclinic
Crystal size/mm	0.22 × 0.14 × 0.13
Volume/Å3	1996.63(18)
Space group	P 21/n
Z	4
a/Å	11.5094(6)
b/Å	7.4248(4)
c/Å	23.3671(11)
α/º	90
β/º	90.819(2)
γ/º	90
d/g·cm^{-3}	1.389
μ/mm^{-1}	0.191
F(000)	432
Interval θ/º	1.74–26.01
Measured reflexions	25719
Independent reflexions [Rint]	3923 [0.042]
Residues/e·Å^{-3}	0.88 and −0.98
R	0.0443
wR	0.1183

Table 2. Selected bond length (Å) and angles (º) for H_2L.

Main bond distances (Å)			
C15–O1	1.247	C7–S1	1.687
C8–C9	1.462	C13–C14	1.462
N7–C15	1.368	N1–C7	1.336
C15–N6	1.360	C7–N2	1.361
N6–N5	1.364	N2–N3	1.374
N5–C14	1.286	N3–C8	1.280
Main bond angles (º)			

N7–C15–O1	125.27	N1–C7–S1	124.72
O1–C15–N6	119.68	S1–C7–N2	118.18
C15–N6–N5	121.00	C7–N2–N3	121.41
N6–N5–C14	117.56	N2–N3–C8	115.14

As expected, the *syn-close* arrangement is mainly determined by the existence of both intra- and intermolecular hydrogen bonds (Figure 3). The intramolecular bonds are established between the pyridine's nitrogen atom as acceptor and one of the hydrazone's (NH) groups [N6–H6···N4 2.581 Å] as donor, giving rise to one six-membered quelate ring *per* ligand. Also, the oxygen atom of the hydrazone arm and the thioamidic proton of the thiosemicarbazone arm are involved in intramolecular hydrogen bonds [N1–H1···O1 3.008 Å]. Moreover, two intermolecular hydrogen bonds are established between the sulphur atom of the thiosemicarbazone ligand arm as acceptor and the imine or one of the thiosemicarbazone (NH) groups of one neighbour molecule as donors [C8–H8···S1 3.652 Å; N2–H2···S1 3.396 Å] (Figure 3).

The imine bond distances are in the interval 1.280–1.286 Å, similar to those expected for conjugated imine bonds (1.279 Å). The charge delocalization give rise to some double bond character for the C8–C9, C13–C14, N2–N3 and N5–N6 bonds as they have smaller values than those usual for the corresponding single bonds, C–C (1.530 Å) and N–N (1.420 Å). In both cases, thiosemicarbazone and hydrazone arms, the bond distances C–N, C–S and C–O are in the expected range [C–N (1.346 Å) [2b], C=S thiourea (1.681 Å) [1] and C=O (1.220 Å)] [3].

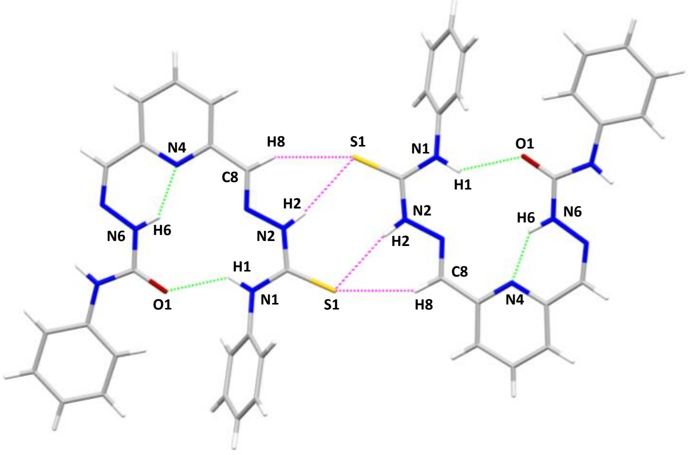

Figure 3. Intra- (green) and intermolecular (pink) hydrogen bonds in H_2L.

The study the ligand H_2L in solid state is interesting to know what kind of changes are needed in its conformation to form a metallosupramolecular architecture. The *syn-close* arrangement of H_2L would be appropriate for the coordination of one ligand to one metal ion. Regarding to this arrangement it must be noted that the N/S and N/O donor atoms of both ligand arms are oriented in opposite directions. For that reason, the coordination of these two donor atoms to the same metal ion would need a conformational rotation that places the donor atoms pointing to the same metal ion.

4. Conclusions

The novel hydrazone-thiocarbohydrazone ligand H_2L could be obtained with high purity and yield. Its crystal structure reveals that donor atoms (nitrogen, oxygen and sulphur) are oriented to opposite directions in both ligand arms. This fact indicates a necessary conformational rotation to coordinate to the metal ion. Therefore, considering the *syn-close* conformation taken by the H_2L, [ML] metallosupramolecular assemblies are expected.

Institutional Review Board Statement:

Informed Consent Statement:

Data Availability Statement:

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