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Design, Synthesis and Structural Characterisation of a Bicompartimental *Bis*hydrazone Ligand †

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Abstract: In recent decades, hydrazone ligands have been extensively studied due to their versatility in coordination chemistry and because of their important biological properties (anticancer, antifungal, antimicrobial, etc.). These types of ligands are widely used in coordination chemistry, due to the variety of metallo-supramolecular architectures they can form. These include the formation of helicates, mesocates and clusters. Among the most relevant properties of metal complexes derived from hydrazone ligands are their interaction with biomolecules such as DNA, as well as their magnetic or antioxidant properties. In this work, we present the design and synthesis of the *bis*hydrazone ligand H_3L generated through an iminic condensation reaction between 2-hydroxyisophthalaldehyde and 2-hydroxybenzohydrazide. This synthesis is carried out using acid catalysis and ethanol as solvent. This ligand is bicompartimental, potentially pentadentate [N_2O_3] and trianionic. The presence of a spacer consisting of a phenolic group facilitates the coordination of transition and post-transition metal ions, resulting in a wide variety of metallo-supramolecular structures. Several characterisation techniques in solid state and in solution were used to confirm the formation and purity of the ligand, including elemental analysis, mass spectrometry, infrared spectroscopy and nuclear magnetic resonance. Moreover, it was also possible to analyse the structure of H_3L by X-ray diffraction studies.

Keywords: *bis*hydrazone; coordination chemistry; X-ray diffraction

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1. Introduction

Hydrazones and *bis*hydrazones are organic ligands with a skeleton containing donor atoms such as nitrogen and oxygen. These compounds are obtained by the reaction of a hydrazide with aldehydes or ketones [1]. The design and synthesis of this type of ligands has been extensively studied in the last decades due to their important biological properties and their versatility in coordination chemistry with different metal ions [2].

Thus, in this work we report the design, synthesis and characterization of a *bis*hydrazone ligand, H_3L, a potential precursor of dinuclear metal-derived complexes.

2. Experimental Section

The synthesis of the *bis*hydrazone ligand H_3L was carried out by means of the imine condensation reaction between 2-hydroxyisophthalaldehyde and 2-hydroxybenzohydrazide in a ratio of 1:2, using absolute ethanol as solvent (Figure 1). Acid catalysis by the addition of p-toluensulfonic acid was used to promote the formation of the imine bond. The reaction mixture was refluxed for 4 h using a Dean−Stark trap to remove the released water [3].

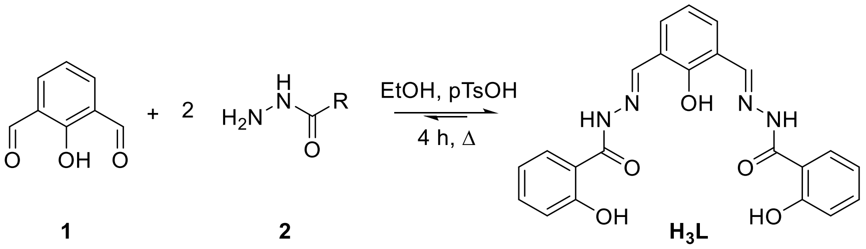

Figure 1. Synthesis of the *bis*hydrazone ligand H_3L.

H_3L: Yield 0.439 g, (84%). Elemental analysis, Calc. for $C_{22}H_{18}N_4O_5$: C, 63.2; H, 4.3; N, 13.4%. Found: C, 63.2; H, 4.4; N, 13.4 %. MS ESI+ (*m*/*z*): 419.1 $[H_3L + H^+]^+$. IR (KBr, cm^{-1}): $\upsilon_{(O\text{-}H)}$ 3468 (a), $\upsilon_{(N\text{-}H)}$ 3258 (d); $\upsilon_{(C=O)}$ 1640 (f); $\upsilon_{(C=N)}$ 1603 (f); $\delta_{(NH)} + \nu_{(N\text{-}CO)}$ 1545 (f); $\delta_{(NH)} + \nu_{(CO)}$ 1306 (m). RMN ^1H (400 MHz, dmso-d_6) δ 12.52 (s, 1H), 12.08 (s, 2H), 11.77 (s, 2H), 8.80 (s, 2H), 7.92 (d, *J* = 6.3 Hz, 2H), 7.78 (d, *J* = 7.7 Hz, 2H), 7.47 (t, *J* = 6.9 Hz, 2H), 7.09 (t, *J* = 7.7 Hz, 1H), 7.00 (m, 4H). RMN ^{13}C (101 MHz, dmso-d_6) δ 165.55 (C, 2C), 159.85 (C, 3C), 146.67 (C, 2C), 133.39 (C, 2C), 130.30 (CH, 2C), 128.67 (CH, 3C), 120.16 (CH, 2C), 118.28 (CH, 2C), 117.29 (CH, 2C), 116.53 (C, 2C).

Crystallographic Data

$H_3L \cdot C_2H_6O$: $C_{24}H_{24}N_4O_6$; MW: 464.47 g·mol^{-1}; crystal dimensions: 0.10 × 0.07 × 0.02 mm; orthorhombic; P*ca*2_1; a = 24.662 (5), b = 4.9645 (9), c = 18.105 (3) Å; $\alpha = 90°$; $\beta = 90°$, $\gamma = 90°$; V = 2216.7 (7) Å^3; z = 4; $\mu = 0.10$ mm^{-1}; measured reflections = 27,415; independent reflections [Rint] = 3103 [0.096]; R = 0.062; wR = 0.174.

3. Results and Discussion

The bishydrazone ligand H_3L can be described as bicompartimental, potentially trianionic and pentadentate $[N_2O_3]$, showing two [NO] binding domains separated by a short spacer with an oxygen donor atom. The ligand H_3L was fully characterized by the usual techniques for organic compounds.

3.1. IR Spectroscopy

Infrared spectra was performed in solid state using the KBr pellet transmission technique in the range 4000–500 cm^{-1} (Figure 2). Band assignments were carried out based on the literature [4].

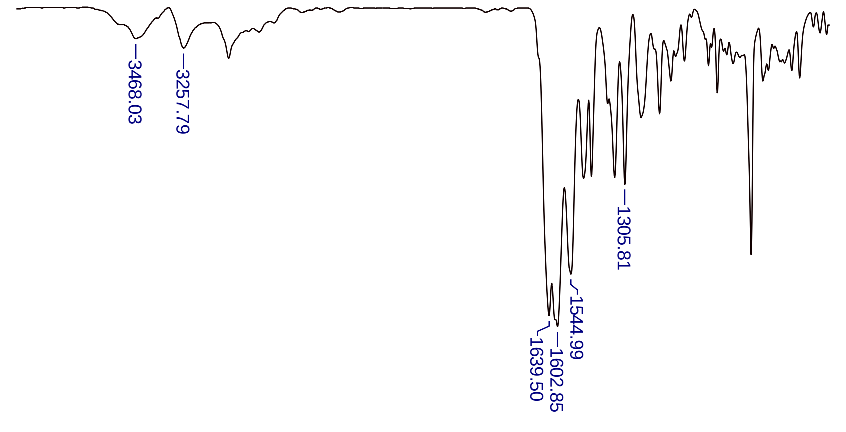

Figure 2. IR spectrum (cm^{-1}) of the bishydrazone ligand H_3L.

In this spectrum should be highlighted the appearance of a new band around 1603 cm^{-1} attributed to the imine ν(C=N) bonds, confirming the formation of the ligand H$_3$L.

3.2. X-Ray Diffraction

Slow evaporation of the mother liquors from the synthesis of the bishydrazone ligand H$_3$L yielded yellow crystals suitable for single-crystal X-ray diffraction studies. The asymmetric unit of the H$_3$L ligand consists of a ligand molecule solvated by a methanol molecule (Figure 3). The main bond distances and angles given in Tables 1 and 2 are in the expected range for bishydrazone ligands [5].

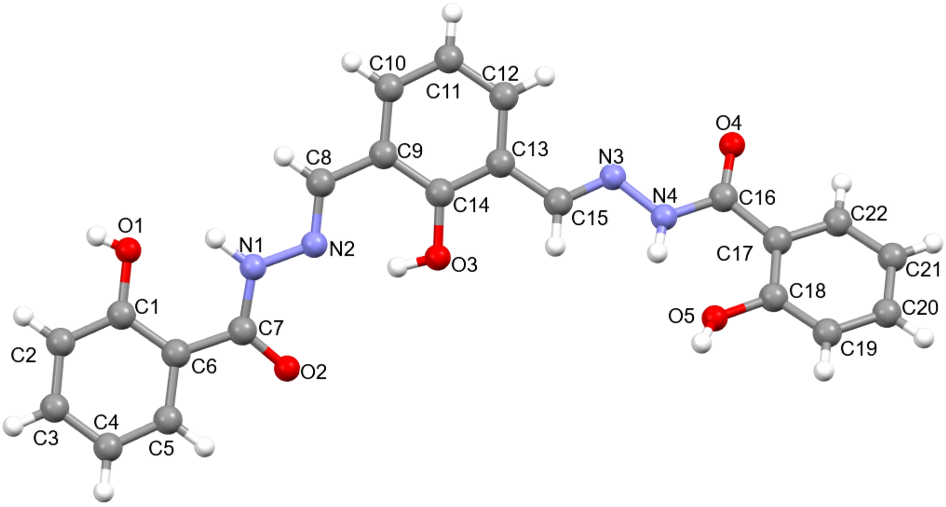

Figure 3. Crystal structure of the bishydrazone ligand H$_3$L·C$_2$H$_6$O. Solvent molecule was omited for clarity.

The ligand shows an E configuration with respect to the imine bonds and an anti conformation with both branches located on opposite sides. This arrangement is conditioned by the existence of intramolecular hydrogen bonds between the imine nitrogen atom (N2) and the hydroxyl group of the spacer (O3-H3O); as well as between the hydrazidic NH (N4) and the phenolic oxygen atom (O5) of a branch. In addition, there are intermolecular hydrogen bonds between the phenolic hydrogen (O5-H5O) of that branch and the oxygen atom of the solvating molecule (O6). There are also hydrogen bonding type interactions between the phenolic oxygen (O1-H1O) of the the other arm and the oxygen of the carbonyl group (O4) and the iminic nitrogen (N3) of an adjacent ligand. These interactions result in the ligand molecules being connected throughout the crystal lattice (Figure 4).

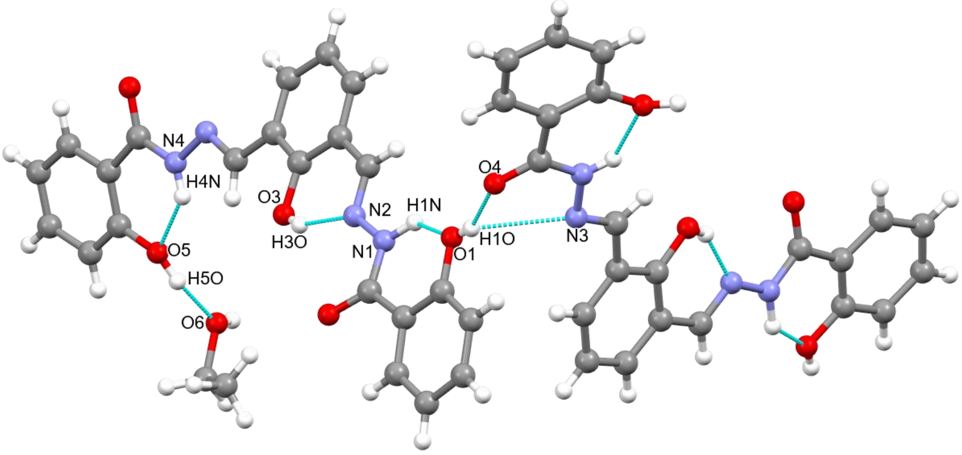

Figure 4. Intra- and intermolecular hydrogen bonds established in the crystal lattice of the ligand $H_3L{\cdot}C_2H_6O$ (O1-H1O···O4^{i} 2.02 Å, O1-H1O···N3^{i} 2.59 Å, O3-H3O···N2 1.81 Å, N1-H1N···O1 1.85 Å, N4-H4N···O5 1.96 Å, O5-H5O···O6 1.82 Å).

Table 1. Main crystallographic data for H_3L.

Crystallographic Data	
Formula	$C_{24}H_{24}N_4O_6$
Molecular weight	464.47
Crystal system	Orthorhombic
Crystal size/mm	0.10 × 0.07 × 0.02
Volume/Å	2216.7 (7)
Space group	$Pca2_1$
Z	4
a/Å	24.662 (5),
b/Å	4.9645 (9)
c/Å	18.105 (3)
α/°	90
β/°	90
γ/°	90
μ/mm^{-1}	0.10
Measured reflexions	27,415
Independent reflexions [R_{int}]	3103 [0.096]
Residues/e·Å^{-3}	0.55 and −0.43
R	0.062
wR	0.174

Table 2. Selected bond length (Å) for H_3L.

Main Bond Distances (Å)			
C8=N2	1.292 (10)	C15=N3	1.271 (10)
N2-N1	1.368 (8)	N3-N4	1.378 (9)
C7=O2	1.252 (10)	C16=O4	1.247 (9)
C7-N1	1.353 (10)	C18-O5	1.372 (10)
C14-O3	1.349 (10)	C16-N4	1.352 (10)

Table 3. Selected bond angles (°) for H_3L.

Main Bond Angles (°)			
O4=C16-N4	121.4 (7)	N4-C16=O4	106 (4)
O3-C14-C9	122.2 (7)	O3-C14-C13	118.1 (7)
N3=C15-C13	120.4 (7)	N2=C8-C9	120.1 (7)
C16-N4-N3	119.1 (2)	C7-N1-N2	119.2 (7)
C15=N3-N4	114.8 (6)	C8=N2-N1	116.2 (6)
O5-C18-C17	119.0 (7)	O1-C1-C6	119.1 (7)

4. Conclusions

The new bishydrazone ligand H_3L has been synthesized and isolated with high purity and yield. The structure of the ligand was determined by X-ray diffraction study of the crystals obtained. The crystallographic studies show that the [NO] donor atoms are oriented in different directions in both ligand branches, suggesting a conformational rotation to obtain dinuclear metal-derived complexes.

Author Contributions: Conceptualization, L.R.-S. and A.M.G.-N.; methodology, I.V.-H., L.R.-S. and A.M.G.-N.; formal analysis, I.V.-H.; investigation, I.V.-H., L.R.-S. and A.M.G.-N.; resources A.M.G.-N.; data curation, I.V.-H., L.R.-S. and A.M.G.-N.; writing—original draft preparation, I.V.-H., L.R.-S. and A.M.G.-N.; writing—review and editing, I.V.-H., L.R.-S. and A.M.G.-N.; supervision, L.R.-S. and A.M.G.-N.; project administration, L.R.-S. and A.M.G.-N.; funding acquisition, A.M.G.-N. All authors have read and agreed to the published version of the manuscript.

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References

1. (a) Bermejo, M.R.; Fondo, M.; González, A.M.; Hoyos, O.L.; Sousa, A.; McAuliffe, C.A.; Hussain, W.; Pritchard, R.; Novotorsev, V.M.J. *Chem. Soc. Dalt. Trans.* **1999**, *13*, 2211–2218. (b) Jiang, H.; Chen, L.; Li, Z.; Li, J.; Ma, H.; Ning, L.; Li, N.; Liu, X.J. *Lumin* **2022**, *243*, 118672. (c) Choudhury, A.; Mudoi, P.P.; Eshore, K.N.; Lahkar, D.J.; Sarma, B.; Long, J.; Gogoi, N. *Polyhedron* **2022**, *212*, 115603.
2. (a) Pedrido, R.; Romero, M.J.; Bermejo, M.R.; González-Noya, A.M.; Maneiro, M.; Rodríguez, M.J.; Zaragoza, G. *Dalt. Trans.* **2006**, *44*, 5304–5314. (b) Bermejo, M.R.; Pedrido, R.; González-Noya, A.M.; Romero, M.J.; Vázquez, M.; Sorace, L. *New J. Chem.* **2003**, *27*, 1753–1759. (c) Andjelković, K.; Šumar, M.; Ivanović-Burmazović, I.J. *Therm. Anal. Calorim.* **2001**, *66*, 759–778.
3. (a) Rodríguez-Hermida, S.; Wende, C.; Lago, A.B.; Carballo, R.; Kulak, N.; Vázquez-Lõpez, E.M. *Eur. J. Inorg. Chem.* **2013**, *2*, 5843–5853. (b) Romero, M.J.; Carballido, R.; Rodríguez-Silva, L.; Maneiro, M.; Zaragoza, G.; González-Noya, A.M.; Pedrido, R. *Dalt. Trans.* **2016**, *45*, 16162–16165. (c) Datta, B.K.; Thiyagarajan, D.; Ramesh, A.; Das, G. *Dalton Trans.* **2015**, *44*, 13093–13099.
4. (a) Pretsch, E.; Bühlmann, P.; Affolter, C.; Herrera, A.; Martínez, R. *Structure Determination of Organic Compounds*, 4th ed.; Springer: Basingstoke, UK, 2009. (b) Kokare, D.G.; Kamat, V.; Naik, K.; Nevrekar, A.; Kotian, A.; Revankar, V.K. *J. Mol. Struct.* **2017**, *1127*, 289–295.
5. (a) Foster, J.S.; Zurek, J.M.; Almeida, N.M.S.; Hendriksen, W.E.; Le Sage, V.A.A.; Lakshminarayanan, V.; Thompson, A.L.; Banerjee, R.; Eelkema, R.; Mulvana, H.; et al. *Am. Chem. Soc.* **2015**, *137*, 14236–14239. (b) Liu, E.; Li, L.; Davis, K.; Zhang, G.J. *Mol. Struct.* **2019**, *1188*, 1–6. (c) Rodríguez-Hermida, S.; Lago, A.B.; Carballo, R.; Fabelo, O.; Vázquez-Lõpez, E.M. *Chem. Eur. J.* **2015**, *21*, 6605–6616.