

Oxidation Processes in a Phosphine-Thiocarbohydrazone Ligand [†]

Sandra Fernández-Fariña ^{1,*} , Isabel Velo-Helena ¹ , Lara Rouco ², Miguel Martínez-Calvo ¹ 
and Ana M. González-Noya ¹ 

¹ Departamento de Química Inorgánica, Facultade de Química, Campus Vida, Universidade de Santiago de Compostela, 15782 Santiago de Compostela, Spain

² Departamento de Química Inorgánica, Facultade de Ciencias, Campus Terra, Universidade de Santiago de Compostela, 27002 Lugo, Spain

* Correspondence: sandra.fernandez.farina@usc.es

[†] Presented at the 26th International Electronic Conference on Synthetic Organic Chemistry, 15–30 November 2022; Available online: <https://sciforum.net/event/ecsoc-26>.

Abstract: In this work, we isolated a pentadentate [P₂N₂S] phosphine-thiocarbohydrazone ligand H₂L with a bulky phosphine group in both linker domains that undergoes an oxidation process in solution. This ligand was synthesized by a direct reaction between two equivalents of 2-diphenylphosphinebenzaldehyde and one equivalent of thiocarbohydrazide. Two types of crystals derived from this ligand were obtained and studied using X-ray diffraction spectroscopy. One structure corresponds to the monooxidized ligand H₂L(O) while the other indicates a dioxidation of the compound, H₂L(OO).

Keywords: thiocarbohidrazone; phosphine; oxidation; X-ray diffraction



Citation: Fernández-Fariña, S.; Velo-Helena, I.; Rouco, L.; Martínez-Calvo, M.; González-Noya, A.M. Oxidation Processes in a Phosphine-Thiocarbohydrazone Ligand. *Chem. Proc.* **2022**, *12*, 57. <https://doi.org/10.3390/ecsoc-26-13559>

Academic Editor: Julio A. Seijas

Published: 14 November 2022

Publisher's Note: MDPI stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.



Copyright: © 2022 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

1. Introduction

Thiocarbohydrazones are compounds of great interest in health-related fields such as pharmacology, as several studies have shown that these compounds possess promising antifungal [1], antimicrobial [1] and even antitumoral properties [2]. Nevertheless, the co-ordination chemistry of this type of ligand has been less studied than that of its thiosemicarbazone analogues.

In general, the thiocarbohydrazones found in the literature act as [NS] or [ONS] donor ligands, giving rise to structures of different nuclearities [3]. However, our group recently reported the first examples of complexes derived from a phosphine-thiocarbohydrazone ligand, H₂L [4], confirming that the presence of bulky groups gives rise to the formation of mesocate species. At this point, we decided to synthesize the phosphine-thiocarbohydrazone ligand H₂L with the aim of obtaining the first example of a [NSP] thiocarbohydrazone crystal structure.

2. Experimental Section

The [P₂N₂S] phosphine-thiocarbohydrazone ligand H₂L was obtained by means of a condensation reaction, as reported before [4]. Yellow X-ray-quality crystals of the monooxidized ligand H₂L(O)·CH₃CH₂OH were collected by slow evaporation of the mother liquors after 24 h.

With the aim of obtaining the non-oxidized crystal structure of the ligand H₂L, recrystallization experiments of the solid obtained during the synthesis were carried out using acetonitrile, acetone, methanol, or a mixture of dichloromethane–methanol solvents. Thus, X-ray-quality crystals of H₂L(OO)·3CH₃CN were obtained by recrystallization of the solid in acetonitrile. It should be noted that H₂L(OO)·3CH₃CN crystals were obtained after 7 days.

spectively. In both ligands, the two imino-phosphine branches adopt an E configuration relative to the imino bonds and a syn-type conformation, with the two phosphine branches oriented towards the same side. The different arrangement of the thioamidic NH gives rise to a *syn* conformation in the C=S bond with respect to the N₃–H₃ bond and an *anti* conformation with respect to the N₂–H₂ bond.

The conformation adopted by the ligands is mainly conditioned by the existence of moderate intramolecular hydrogen bonds between one of the thioamide nitrogens and the oxygen atom. In addition, weak intermolecular hydrogen bonds exist in both ligands. In the case of the monooxidized ligand, H₂L(O)·CH₃CH₂OH, these interactions occur between the sulfur atom of one ligand molecule and one of the thioamide nitrogens of another ligand unit (Figure 3). In the case of the dioxidized ligand, H₂L(OO)·3CH₃CN, a hydrogen bond is observed between one of the thioamide nitrogens and the nitrogen of one of the solvating acetonitrile molecules (Figure 4).

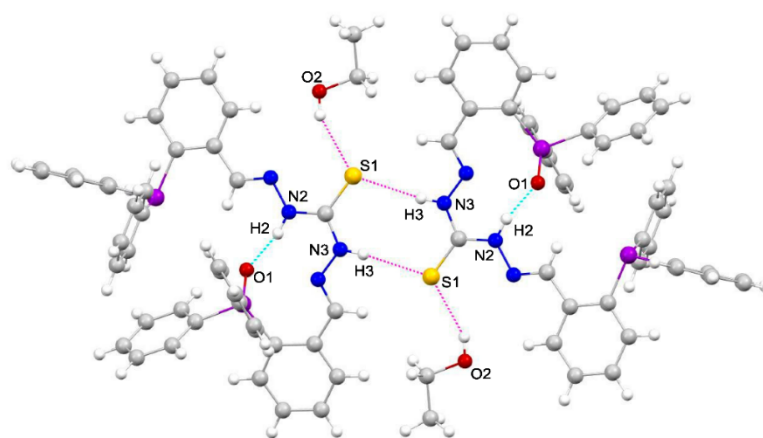


Figure 3. Intramolecular hydrogen bonds (blue) [N₂–H₂···O1 2.86 (7) Å] and intermolecular hydrogen bonds (pink) [N₃–H₃···S1 3.332 (2) Å; O₂–H₂···S1 3.23 (4)] in H₂L(O)·CH₃CH₂OH.

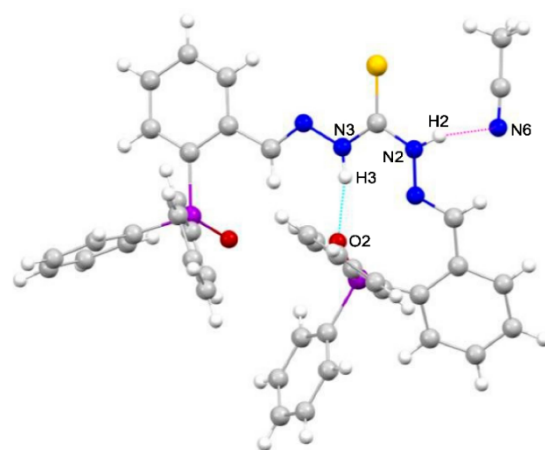


Figure 4. Intramolecular hydrogen bonds (blue) [N₃–H₃···O₂ 2.78 (4) Å] and intermolecular hydrogen bonds (pink) [N₂–H₂···N₆ 3.09 (4) Å] in H₂L(OO)·3CH₃CN.

The main bond lengths, C=N, N–N and C–S, given in Tables 1 and 2 are in the expected range for thiocarbohydrazone ligands and do not need further discussion [5].

Table 1. Selected bond lengths (Å) for H₂L(O)·CH₃CH₂OH.

Main Bond Distances (Å)			
C1—N1	1.456 (4)	N2—N3	1.387 (3)
N1—C2	1.338 (4)	N3—C4	1.288 (4)
C2—N2	1.365 (4)	C8—O1	1.399 (3)
N6—C20	1.451 (4)	C39—S4	1.695 (3)

Table 2. Selected bond lengths (Å) for H₂L(OO)·3CH₃CN.

Main Bond Distances (Å)			
C19—N1	1.280 (4)	C20—S1	1.674 (4)
C20—N2	1.352 (4)	C21—N4	1.278 (4)
C20—N3	1.348 (4)	N1—N2	1.368 (4)
P2—O1	1.578 (5)	N3—N4	1.378 (4)
P1—O2	1.478 (3)		

4. Conclusions

The obtainment of two different crystal structures derived from the phosphine-thio-carbohydrazone ligand H₂L lead us to discover that the compound undergoes an oxidation process in solution. It is clear from the crystal structures obtained that both solvent and time have an effect on the final crystal structure of the ligand and therefore on the oxidation process; thus, we obtained the monooxidized structure, H₂L(O)·CH₃CH₂OH, in ethanol after 24 h, and the dioxidized structure, H₂L(OO)·3CH₃CN, in acetonitrile after 1 week.

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

Funding: This research was funded by the following FEDER co-funded grants. From Consellería de Cultura, Educación e Ordenación Universitaria, Xunta de Galicia, 2017GRCGI-1682 (ED431C2017/01), 2018GRCGI-1584 (ED431C2018/13), MetalBIONetwork (ED431D2017/01). From Ministerio de Ciencia, Innovación y Universidades, METALBIO (CTQ2017-90802-REDT). From Ministerio de Ciencia e Innovación, MultiMetDRUGS (RED2018-102471-T) and Project PID2021-127531NB-I00 (AEI/10.13039/501100011033/FEDER, UE).

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Crystallographic data for H₂L(O) and H₂L(OO) were deposited into the Cambridge Crystallographic Data Centre, CCDC 2237161 and 2237162. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: +44-1223-336033.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Gabr, M.T.; El-Gohary, N.S.; El-Bendary, E.R.; Ni, N.; Shaaban, M.I.; El-Kerdawy, M.M. Microwave-Assisted Synthesis, Antimicrobial, Antiquorum-Sensing and Cytotoxic Activities of a New Series of Isatin-β-Thiocarbohydrazones. *Synth. Commun.* **2018**, *48*, 2899–2911. [CrossRef]
2. Bonaccorso, C.; Marzo, T.; La Mendola, D. Biological Applications of Thiocarbohydrazones and Their Metal Complexes: A Perspective Review. *Pharmaceuticals* **2020**, *13*, 4. [CrossRef] [PubMed]
3. Kaya, Y.; Erçağ, A.; Koca, A. New Square-Planar Nickel(II)-Triphenylphosphine Complexes Containing ONS Donor Ligands: Synthesis, Characterization, Electrochemical and Antioxidant Properties. *J. Mol. Struct.* **2020**, *1206*, 127653. [CrossRef]

4. Fernández-Fariña, S.; Martínez-Calvo, M.; Maneiro, M.; Seco, J.M.; Zaragoza, G.; González-Noya, A.M.; Pedrido, R. Two Synthetic Approaches to Coinage Metal(I) Mesocates: Electrochemical versus Chemical Synthesis. *Inorg. Chem.* **2022**, *61*, 14121–14130. [[CrossRef](#)] [[PubMed](#)]
5. Ibrahim, A.A.; Khaledi, H.; Ali, H.M. A multiprotic indole-based thiocarbohydrazone in the formation of mono-, di- and hexa-nuclear metal complexes. *Polyhedron* **2014**, *81*, 457–464. [[CrossRef](#)]