

1 *Conference Proceedings Paper*

2 **Synthesis and X-ray diffraction study of**
3 **thiosemicarbazone palladacycles with dppm[†]**

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9 † Presented at the title: Synthesis and X-ray diffraction study of thiosemicarbazone palladacycles with dppm,

10 Place: The 2nd International Online Conference on Crystals, Date: Nov. 10th 2020.

11 Published: 6 November 2020

12 **Abstract:** Cyclometallated compounds have been extensively studied, in particular those with
13 palladium and platinum. This is because of their possible applications in medicinal chemistry, as
14 anticancer or antimicrobial agents; in some cases with similar results as cisplatin, carboplatin or
15 oxaliplatin. Also remarkable is their use as homogeneous catalysts, for example, in cross coupling
16 reactions such as Suzuki-Miyaura or Mizoroki-Heck.

17 Herein we report the synthesis of different thiosemicarbazone ligands, which will be reacted with a
18 palladium or platinum salt, to give the corresponding cyclometallated compounds; their reactivity
19 with bis(diphenylphosphino)methane (dppm) will be studied.

20 Characterization has been carried by elemental analysis, IR spectroscopy, ¹H and ³¹P NMR
21 spectroscopy. Also, **1c** has been studied by X-ray diffraction.

22 **Keywords:** cyclometallation, thiosemicarbazone, palladium, platinum, X-ray diffraction

24 **1. Introduction**

25 Palladium and platinum cyclometallated compounds have been studied due to their interesting
26 applications in several chemical fields.

27 On the one hand, they are useful in synthetic organic chemistry, as catalysts in many reactions
28 with formation of C-C and C-N bonds.¹⁻⁶

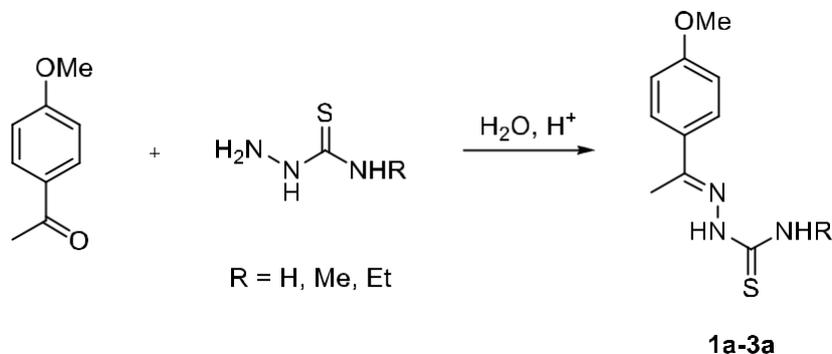
29 On the other hand, their cytotoxic activity has been considered in biological assays,⁷⁻¹¹ showing
30 in some cases really good results in this field.

31 There are many characterization techniques that could be used for this kind of complexes.
32 Probably the most precise one is single crystal X-ray diffraction, which in this research work is given
33 for compound **1c**.

35 2. Experimental

36 2.1. Ligands

37 The thiosemicarbazide and hydrochloric acid (0.4 cm³) were added in water (20 cm³). After
 38 complete solubilization the ketone was added. The mixture was stirred at room temperature for 8 h,
 39 after which a white solid appeared, that was filtered, washed with water and dried under vacuum.



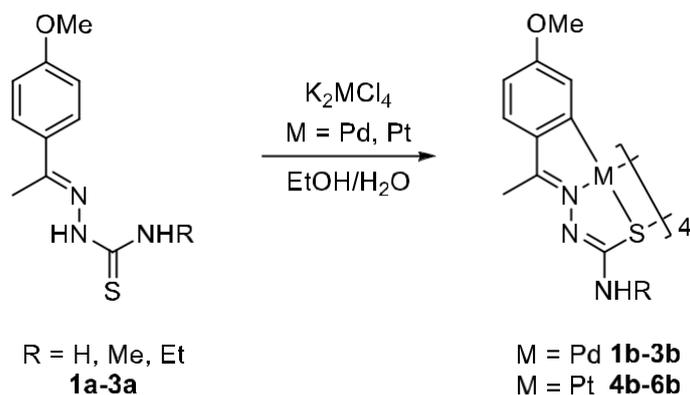
40
41 **Scheme 1.** Synthesis of thiosemicarbazone ligands

42 **Chart 1.** Quantities of reagents added

| Ligand | R | Thiosemicarbazide (mg) | Ketone (mg) | Yield (%) |
|--------|----|------------------------|-------------|-----------|
| 1a | H | 250 | 412 | 90 |
| 2a | Me | 250 | 357 | 98 |
| 3a | Et | 250 | 315 | 88 |

43 2.2. Cyclometallated compounds

44 K₂MCl₄ (M = Pd, Pt) was added in 6 cm³ of water. After total solubilization, the corresponding
 45 thiosemicarbazone ligand was added in ethanol (25 cm³). The mixture was stirred at room temperature
 46 for 24 h. A suspension formed, that was centrifugated and the solid was dried under vacuum.



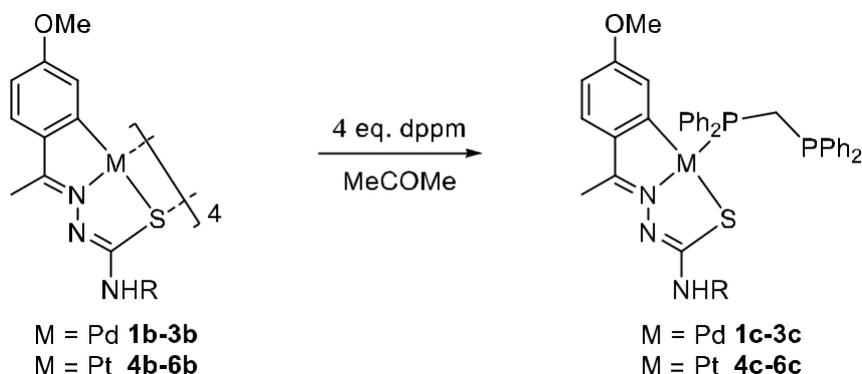
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48 **Scheme 2.** Synthesis of cyclometallated compounds

49 **Chart 2.** Quantities of reagents added

| Compound | R | M | K ₂ MCl ₄ (mg) | Thiosemicarbazone (mg) | Yield (%) |
|----------|----|----|--------------------------------------|------------------------|-----------|
| 1b | H | Pd | 200 | 164 | 71 |
| 2b | Me | Pd | 200 | 174 | 78 |
| 3b | Et | Pd | 200 | 185 | 86 |
| 4b | H | Pt | 150 | 80,7 | 85 |
| 5b | Me | Pt | 150 | 85,8 | 85 |
| 6b | Et | Pt | 150 | 90,8 | 86 |

50 2.3. Reactivity with dppm

51 The cyclometallated compounds and the corresponding amount of
 52 bis(diphenylphosphino)methane were added under nitrogen in 15 cm³ of oxygen-free acetone. After
 53 stirring at 50 °C for 24 h, a solid was obtained, that was centrifugated and dried under vacuum.



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Scheme 3. Reactions with dppm

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Chart 3. Quantities of reagents added

| Compound | R | M | Metallacycle (mg) | dppm (mg) | Efficiency (%) |
|----------|----|----|-------------------|-----------|----------------|
| 1c | H | Pd | 35 | 41,0 | 60 |
| 2c | Me | Pd | 35 | 39,3 | 75 |
| 3c | Et | Pd | 35 | 37,8 | 72 |
| 4c | H | Pt | 35 | 32,3 | 64 |
| 5c | Me | Pt | 35 | 31,3 | 59 |
| 6c | Et | Pt | 35 | 30,2 | 61 |

57 **3. Results and discussion**

58 All the compounds were characterized by IR spectroscopy, ¹H and ³¹P NMR spectroscopy. In
 59 addition, compound **1c** was characterized by single crystal X-ray diffraction.

60 3.1. IR spectroscopy

61 IR spectroscopy characterization data for the thiosemicarbazone ligands and cyclometallated
 62 compounds are shown in **¡Error! No se encuentra el origen de la referencia..**

63 The deprotonation and the loss of the C=S double bond character is required for cyclometallation
 64 to occur.

65
 66

Chart 4. IR spectroscopy characterization

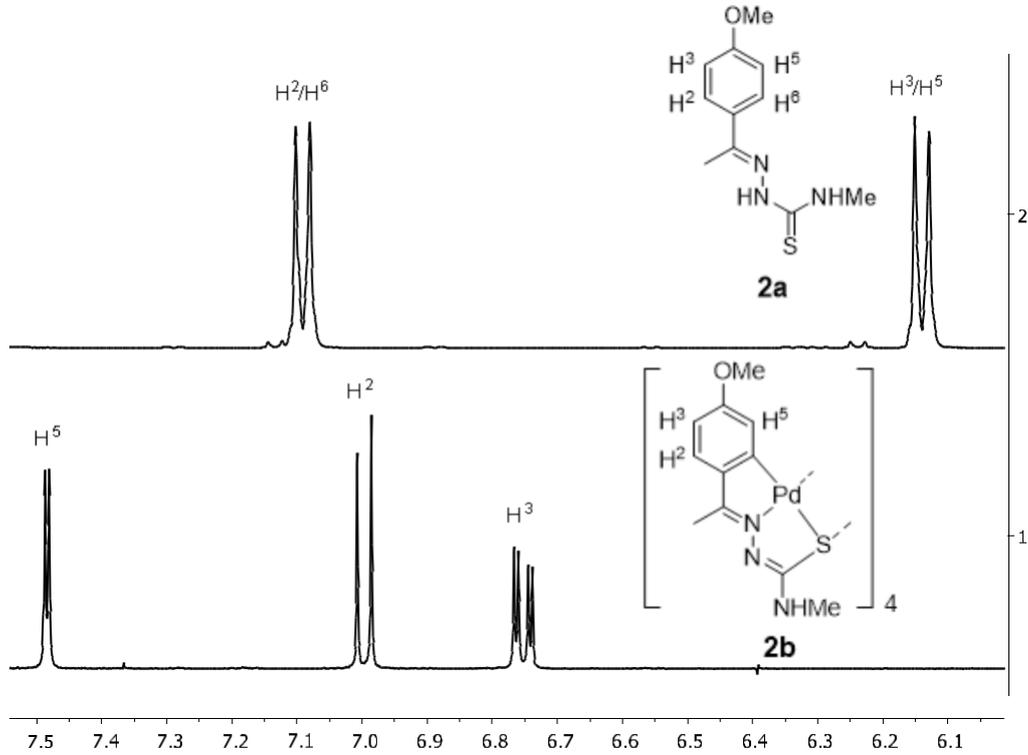
| Compound | R | M | $\nu(\text{N-H})$ | $\nu(\text{C=S})$ |
|----------|----|----|-------------------|-------------------|
| 1a | H | - | 3154/3243/3375 | 826 |
| 2a | Me | - | 3193/3366 | 836 |
| 3a | Et | - | 3201/3299 | 829 |
| 1b | H | Pd | 3159/3292 | - |
| 2b | Me | Pd | 3353 | - |
| 3b | Et | Pd | 3341 | - |
| 4b | H | Pt | 3215/3320 | - |
| 5b | Me | Pt | 3286 | - |
| 6b | Et | Pt | 3303 | - |

67

68 3.2. ^1H NMR spectroscopy

69 The comparison of the spectra for the thiosemicarbazone ligands and cyclometallated
 70 compounds spectrums shows the disappearance of the *ortho* aromatic proton resonance and the
 71 hydrazinic proton resonance in agreement with cyclometallation.
 72

Moreover, aromatic signals change their multiplicity upon formation of the Pd-C bond.

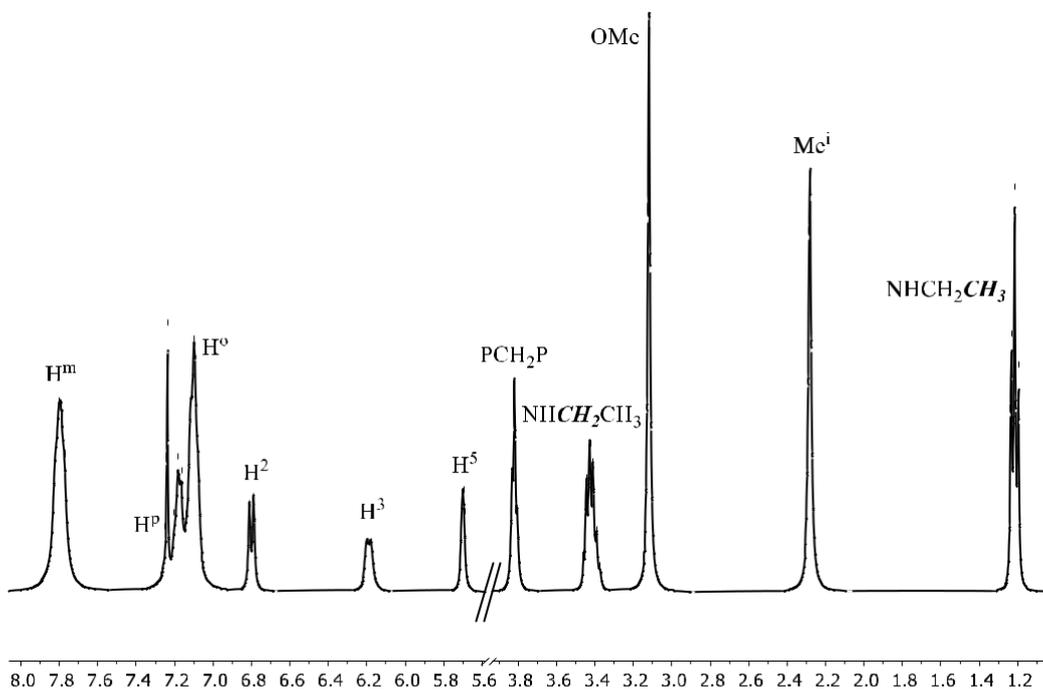


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Figure 1. ^1H NMR stacked spectrum (400 MHz, DMSO- d_6) for compounds 2a and 2b

75 After reaction with dppm the spectra did not show very significant changes. Only remarkable is
 76 the highfield shift of the H_5 proton signal, caused by the phenyl rings of the diposphine that give
 77 producing a strong shielding in that position.



78

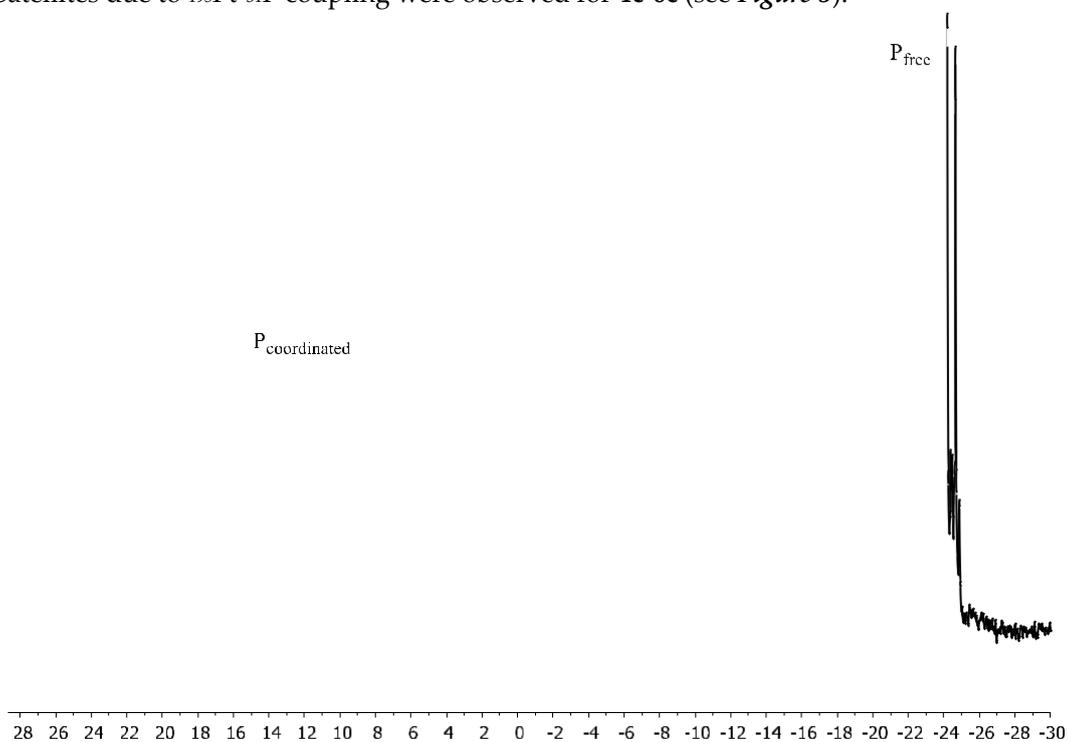
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Figure 2. ^1H NMR spectrum of compound 3c in CDCl_3

80 3.3. $^{31}\text{P}\{-^1\text{H}\}$ NMR spectroscopy

81 The ^{31}P NMR spectrum gives information about the coordinative behavior of the phosphine
82 ligand.

83 In this case, the spectra show two doublets, one for each of the two inequivalent ^{31}P nuclei.
84 Satellites due to $^{195}\text{Pt}\text{-}^{31}\text{P}$ coupling were observed for **4c-6c** (see *Figure 3*).



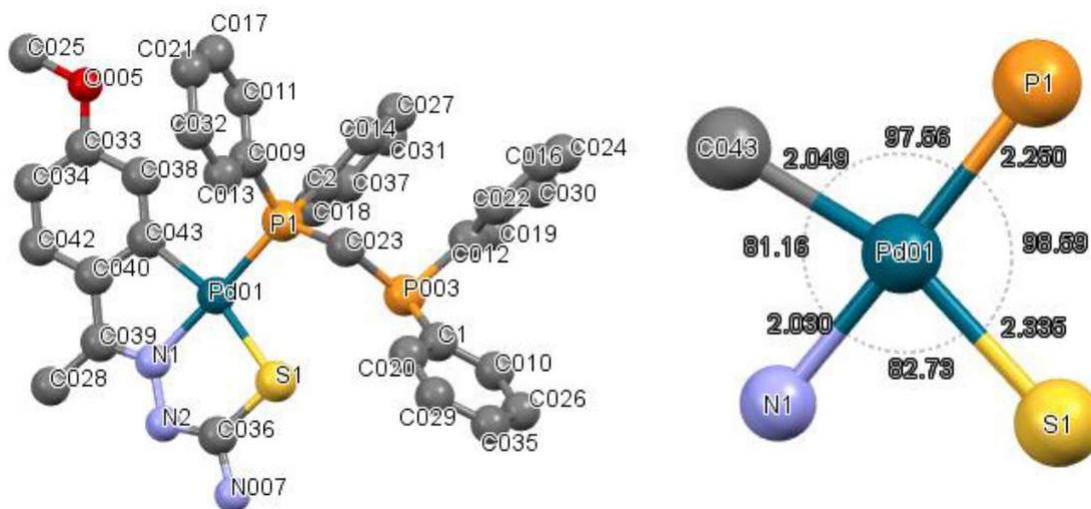
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Figure 3. $^{31}\text{P}\{-^1\text{H}\}$ NMR of compound **5c** in acetone- d_6

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88 3.4. Single crystal X-ray diffraction

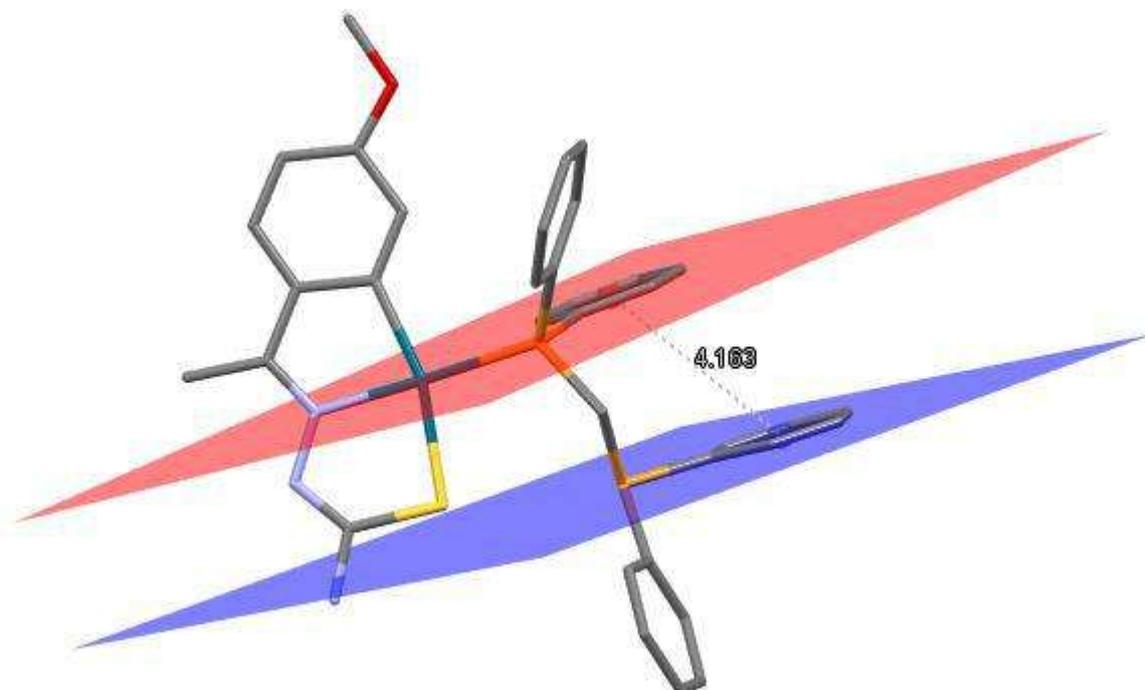
89 Single crystals for compound **1c** were obtained by slow evaporation of an acetone solution.90 Compound **1c** crystallizes in the monoclinic system, $C2/c$ space group. The resolution of the
91 molecular structure confirms the spectroscopic data. The molecular structure of **1c** is shown in **Figure**
92 **4** and selected bond distances (Å) and angles (°) are shown in **;****Error! No se encuentra el origen de la**
93 **referencia..**94 Complex **1c** shows a mononuclear structure, with slightly distorted square-planar geometry
95 around the palladium center, surrounded by the *ortho* carbon atom of the phenyl ring (C043), the
96 iminic nitrogen (N1), the sulfur (S1) and one phosphorus atom (P1). The sum of angles about
97 palladium atom is approximately 360°. Pd01-N1 2.030(3) Å, Pd01-C043 2.049(3) Å and Pd01-S1
98 2.3352(13) Å bond distances are within the expected range, and they are in agreement with similar
99 structures previous presented by us.¹²⁻¹⁴100
101 **Figure 4.** a) Molecular structure of compound **1c**. Hydrogen atoms have been omitted for clarity. b) Bond
102 distances (Å) and angles (°) around the palladium center103 **Chart 5.** Selected bonds (Å) and angles (°) for compound **1c**

| | | | |
|--------------------|------------|--------------------|------------|
| Pd(01)-N(1) | 2.030(3) | S(1)-C(036) | 1.763(3) |
| Pd(01)-C(043) | 2.049(3) | N(2)-C(036) | 1.306(4) |
| Pd(01)-P(1) | 2.2502(8) | N(2)-N(1) | 1.379(4) |
| Pd(01)-S(1) | 2.3352(13) | C(039)-N(1) | 1.304(4) |
| N(1)-Pd(01)-C(043) | 81.16(13) | N(1)-Pd(01)-S(1) | 82.72(9) |
| N(1)-Pd(01)-P(1) | 177.17(8) | C(043)-Pd(01)-S(1) | 163.84(10) |
| C(043)-Pd(01)-P(1) | 97.56(10) | P(1)-Pd(01)-S(1) | 98.59(4) |

104

105 Intramolecular π - π stacking interactions were observed between two phenyl rings, one from
106 each phosphorus atom (see **Figure 5**).

107 The distance between the two centroids is 4.163 Å, and the angle between the ring planes is 3.43°.

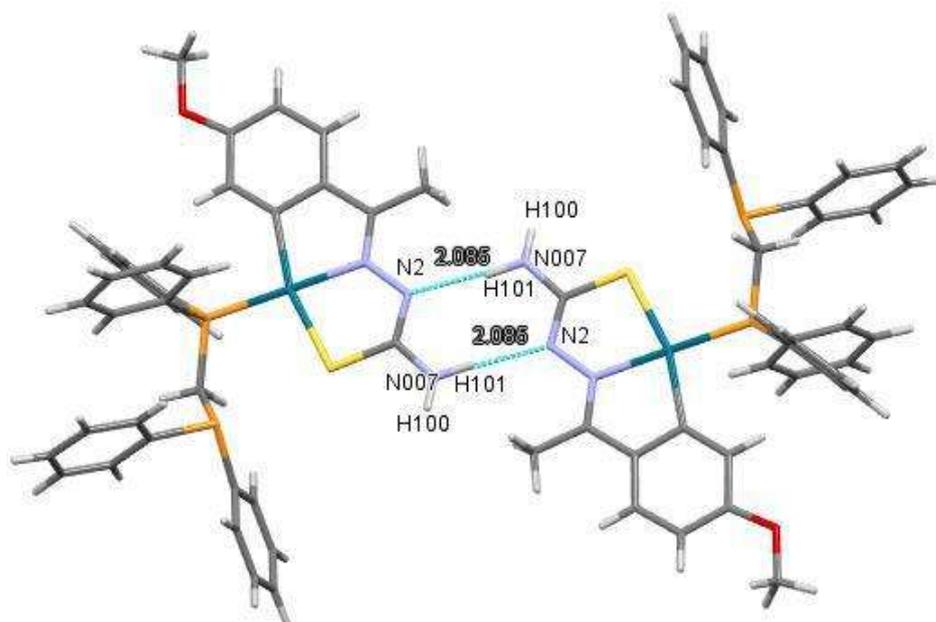


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Figure 5. Intramolecular π - π stacking interaction in 1c

110 In addition, intermolecular hydrogen bond interactions were observed between the hydrazinic
111 nitrogen and the thioamidic nitrogen. The hydrogen bond distances were 2.085 Å, as shown in **Figure**
112 **6**.

113



114
115

Figure 6. Intermolecular hydrogen bonding interaction in 1c

116

117 4. Conclusions

- 118 • Coordination to the metal center occurs in the thiol form of the thiosemicarbazone
119 ligand, as shown by IR spectroscopy.
- 120 • ¹H NMR spectroscopy confirms cyclometallation, with the thiosemicarbazone ligand as
121 tridentate [C, N, S].
- 122 • The cyclometallated compounds show a tetranuclear structure, with two types of bonds
123 between palladium and sulfur: Pd-Schelate and Pd-Sbridging.
- 124 • Reaction with dppm generates mononuclear compounds with one free phosphorus
125 atom.
- 126 • Single crystal X-ray diffraction study of compound **1c** shows the proposed structure,
127 with the palladated thiosemicarbazone ligand and dppm as a monodentate ligand.
128

129 **Supplementary Materials:** The following are available online at www.mdpi.com/xxx/s1, Figure S1: title, Table
130 S1: title, Video S1: title.

131 **Funding:** “Francisco Reigosa wants to thank the financial support to the Spanish Government (AEI) through an
132 FPU grant (number 13/05014)”

133 **Acknowledgments:** The authors thank funding from Xunta de Galicia (Galicia, Spain) under the Grupos de
134 Referencia program (GRC 2019/014)

135 **Conflicts of Interest:** “The authors declare no conflict of interest”

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