

Preparation and characterization of thiosemicarbazone ligands and study of their iron and palladium derivatives [†]

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Abstract: Transition metal complexes are useful in organic synthesis due to the capability of the metal to activate substrates [1-2]; in particular, cyclometallation reactions may lead to novel routes in organic synthesis. Thiosemicarbazones show a high coordinative capacity given that they possess several potential donor atoms through which they can bind to transition metals. In addition, thiosemicarbazones as well as their semicarbazones analogues have considerable biological and pharmacological interest [3] because of their antibacterial, antiviral and antitumor activity. Their derivatives with ferrocenyl phosphines such as 1,1'-bis(diphenylphosphine)ferrocene (dppf) show a wide range of applications [4].

Keywords: Thiosemicarbazones; palladium; iron; dppf

1. Introduction

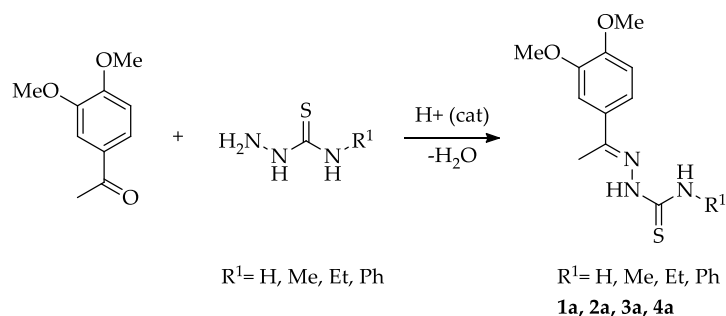
Palladium cyclometallated compounds have cytotoxic properties [5-6] similar to platinum antitumor drugs; in addition, it is well known that palladium also shows catalytic properties in cross-coupling reactions [7-8]. Tertiary phosphines are commonly used as ligands in coordination chemistry [9]. In the present work, we present a family of palladium cyclometallated compounds derived from thiosemicarbazone ligands containing the diphosphine 1,1'-bis(diphenylphosphine)ferrocene, dppf, which shows interesting catalytic, photochemical, photophysical and electrochemical properties [10-13].

2. Materials and Methods

2.1 Synthesis of the ligands

Thiosemicarbazones are obtained by condensation reaction between the aldehyde or ketone carbonyl group and the amino group of a thiosemicarbazide. The synthesis of the thiosemicarbazone

ligands was carried out in aqueous medium because the reaction product precipitates as a white solid. For this process acidification is necessary to activate the carbonyl group.



Scheme 1. Synthesis of the thiosemicarbazone ligands.

2.2 Synthesis of the cyclometallated compounds

Cyclometallated compounds are those contain a σ M-C bond and also a covalent coordinated bond with a donor atom. Palladium and platinum cyclometallated compounds with thiosemicarbazone ligands have been described, these compounds have a very characteristic tetranuclear structure (Figure 1), containing two types of Metal-S bonds: Metal-S_{chelate} and Metal-S_{bridging}. The metal atom, is bonded to the carbon in the *ortho* position and coordinated to a nitrogen atom and two different sulfur atoms.

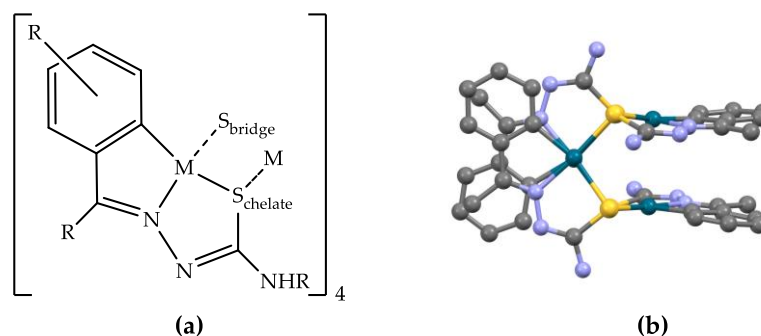
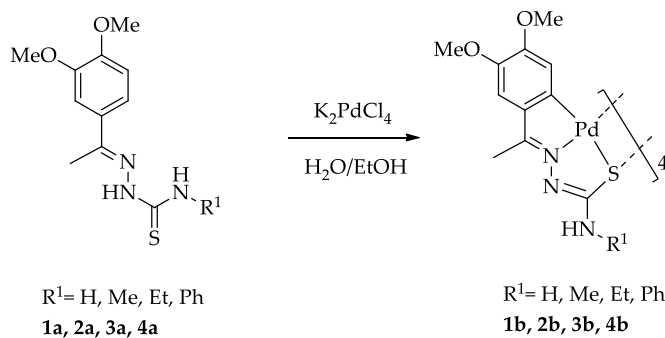


Figure 1. (a) Representation of a tetrameric structure. (b) X-Ray resolution of a tetrameric structure.

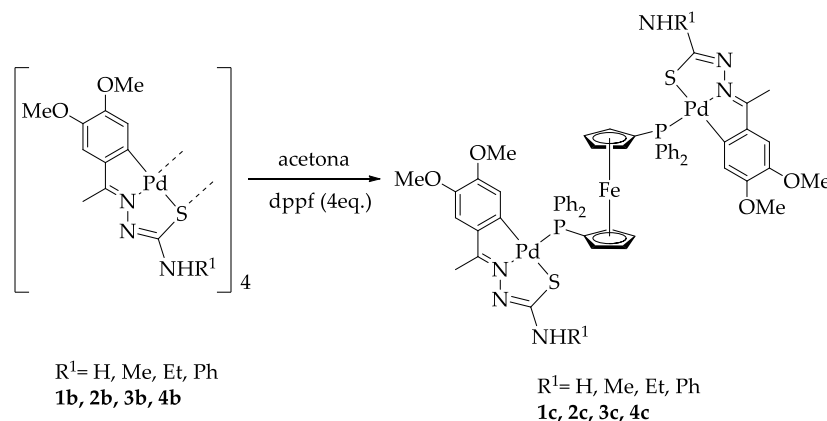
Potassium tetrachloropalladate was used as metallating agent and a water-ethanol mixture as a solvent. The products precipitate within the solution and due to their tetrameric structure they are rather insoluble so they are usually characterized by proton NMR using DMSO-*d*₆ as solvent.



Scheme 2. Synthesis of the cyclometallated compounds.

2.3 Synthesis of the compounds bearing phosphine

The synthesis of the cyclometallated compounds with phosphine ligands was carried out using acetone as solvent at room temperature. It is remarkable that although four equivalents of diphosphine were added, all the products obtained showed the diphosphine acts in a bridging mode. These products precipitate giving a pure product and leaving the diphosphine excess in solution.



Scheme 3. Synthesis of the compounds bearing phosphine.

3. Results and Discussion

Analysis of the $^1\text{H-NMR}$ data confirmed the formation of the ligand mainly due to the chemical shift of the signal of the hydrazinic proton (NNH). Cyclometallation was confirmed due to the differences of the signals in the aromatic zone with respect to those of the free ligand, namely the absence of the proton of the metallated carbon and also the signal for the hydrazinic proton disappears.

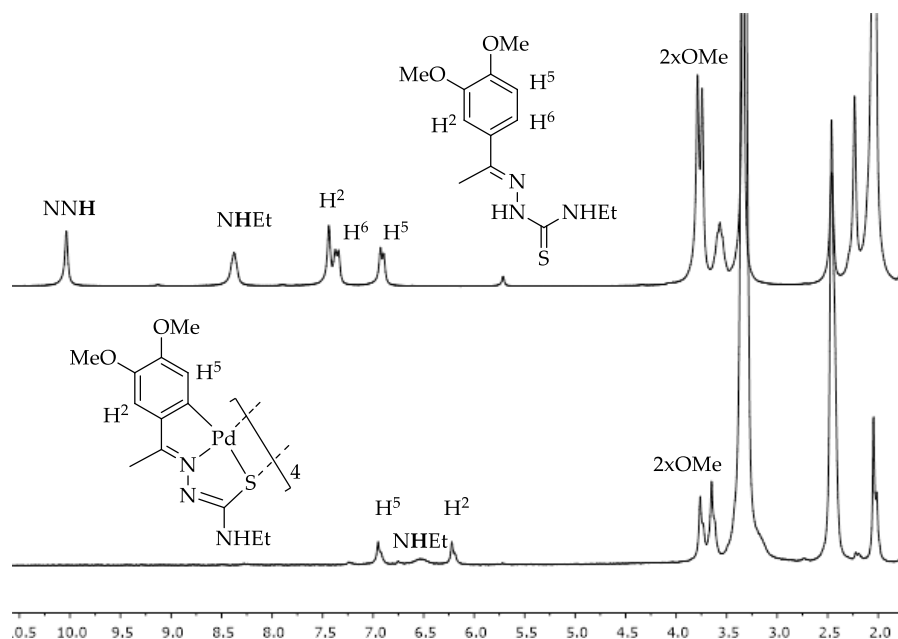


Figure 2. $^1\text{H-NMR}$ spectra of **3a** and **3b** in DMSO-d_6 .

In the IR spectra of the ligands, signals corresponding to ν (N-H) from the NNH and NHR¹ groups were observed, whereas in the cyclometallated compounds the number of signals decreases due to the disappearance of the hydrazinic hydrogen.

Table 1. Infrared data in cm^{-1}

Ligand	ν (N-H)	Cyclometallated	ν (N-H)
1a	3159/3269/3379	1b	3344/3452
2a	3244/3328	2b	3376
3a	3240/3324	3b	3414
4a	3254/3388	4b	3406

The analysis of the ^1H -NMR data confirmed the coordination of the phosphorus atoms to the metal center. There was a large upfield displacement of the signal corresponding to the H⁵ proton and coupling between H⁵ and the phosphorus nucleus. On the other hand the ^{31}P -NMR showed the behavior of this phosphine as bidentate bridging because it showed a singlet signal (*ca.* +28 ppm) which indicates that both phosphorus nuclei are equivalent.

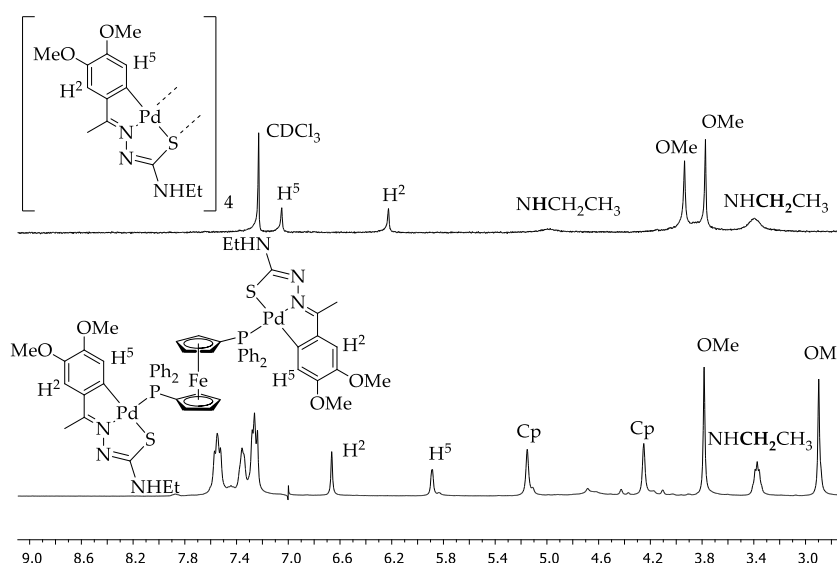


Figure 3. ^1H -NMR spectra of **3b** and **3c** in CDCl_3 .

It has been possible to obtain crystals suitable for the X-ray diffraction of one of the cyclometallated compounds bearing diphosphine dppf (**2c**). The structure of the ligand is almost planar and the ferrocene maintains the alternated sandwich structure.

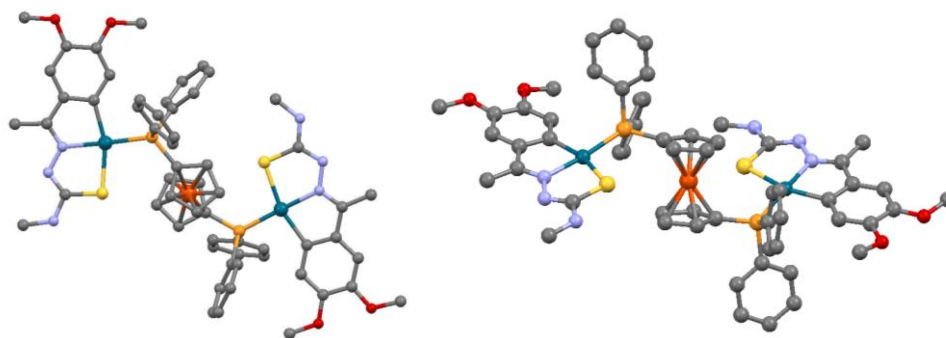


Figure 4. Two different views of the crystal structure of **2c**.

Table 2. Crystallographic data of **2c**.

Empirical formula	C61 H64 Fe N6 O5 P2 Pd2 S2
Formula weight	1355.89
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P-1
Unit cell dimensions	a = 11.148(5) Å; a \angle = 86.251(5) $^\circ$ b = 12.652(5) Å; b \angle = 84.791(5) $^\circ$ c = 20.736(5) Å; g = 78.360(5) $^\circ$
Volume	2849.4(18) Å ³
Z	2
Density (calculated)	1.580 Mg/m ³
Absorption coefficient	1.061 mm ⁻¹
F(000)	1384
Crystal size	0.22 x 0.15 x 0.04 mm ³
Theta range for data collection	0.987 to 26.373 $^\circ$
Index ranges	-13 \leq h \leq 13, -15 \leq k \leq 15, -25 \leq l \leq 25
Reflections collected	87669
Independent reflections	11617 [R(int) = 0.0444]
Data / restraints / parameters	11617 / 0 / 888
Goodness-of-fit on F ²	1.028
Final R indices [I \geq 2 σ (I)]	R1 = 0.0273, wR2 = 0.0588
R indices (all data)	R1 = 0.0405, wR2 = 0.0632
Largest diff. peak and hole	0.675 and -0.662 e.Å ⁻³

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Conflicts of Interest: “The authors declare no conflict of interest”. “The founding sponsors had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, and in the decision to publish the results”.

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