

# Synthesis and reactivity of a new type of crown ether thiosemicarbazone

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**Abstract:** Palladacycle compounds containing a crown-ether moiety in their structure have been scarcely studied in the past years, although they offer the possibility of combining the crown-ether application as sensors with the catalytic behavior of palladacycles. Maybe the reason for this is because they present a strong interaction with silica making the purification of the new products a difficult task. Nevertheless, in this communication we present the synthesis and characterization of a new palladacycle bearing a 15-crown-5-ether.

**Keywords:** crown-ether; palladacycle; cyclometallation

## 1. Introduction

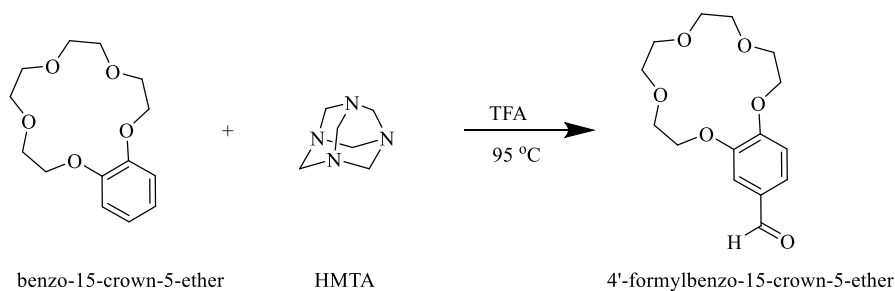
Palladacycles are very versatile compounds and they are known for a good number of ligands. Their main applications are as catalysts,<sup>[1,2]</sup> sensors<sup>[3]</sup> or as antitumor agents.<sup>[4]</sup> In the particular case of the thiosemicarbazone ligands, these react with palladium salts to give very robust cyclometallated compounds,<sup>[5]</sup> which present great air and thermal stability; the ligands themselves show a high biological activity. Moreover, when the corresponding thiosemicarbazone is functionalized with a crown-ether moiety, the resulting palladacycle behaves as a new type of sensor.<sup>[6]</sup>

Once palladated the thiosemicarbazone ligand behaves as tridentate, thus occupying all but one of the coordination positions in the square planar environment of the palladium atom.<sup>[7]</sup> If the ligand is forced to react in the thione fashion with respect to the sulfur atom, the resulting palladacycle is a mononuclear species with the fourth coordination position readily accessible for further modifications.<sup>[8]</sup>

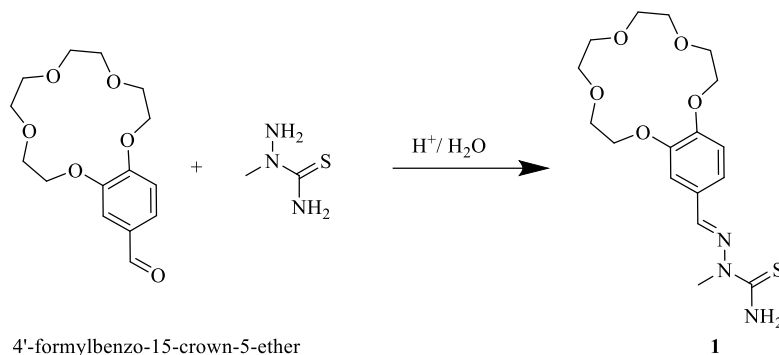
In this communication we present the synthesis of [3,4-(C<sub>8</sub>H<sub>16</sub>O<sub>5</sub>) C<sub>6</sub>H<sub>3</sub>C(H)=NN(Me)C(=S)NH<sub>2</sub>] (1) and its reactivity towards a palladium salt to obtain the mononuclear cyclometallated compound [Pd{3,4-(C<sub>8</sub>H<sub>16</sub>O<sub>5</sub>)C<sub>6</sub>H<sub>3</sub>C(H)=NN(Me)C(=S)NH<sub>2</sub>}(Cl)] (1Pd). The characterization of the compounds was carried out using IR and <sup>1</sup>H NMR spectroscopies.

## 2. Discussion

The compounds described in this proceeding were characterized by elemental analysis (C, H, N, S), IR and <sup>1</sup>H NMR spectroscopies (see experimental section). The syntheses of all the compounds are depicted in Schemes 1 to 3 for the clarity of the reader. Ligand 1 was obtained by the reaction of precursor a, previously obtained by the Smith modification of the Duff reaction for the formylation of aromatic rings (Scheme 1),<sup>[9]</sup> and 2-methyl-3-thiosemicarbazide, in acidic solution (Scheme 2). The formation was monitored by the disappearance of the ν(C=O) stretching band in the IR spectra of compound 1 and the downfield shift of the signal corresponding to the HC=N proton due to the anisotropic deshielding of the iminic bond in the <sup>1</sup>H NMR spectra (see experimental section).

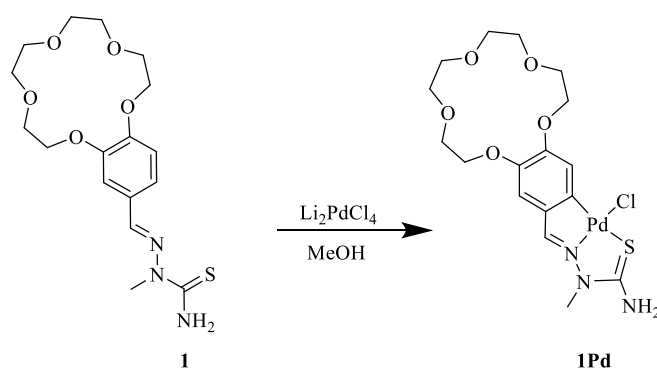


**Scheme 1:** Synthesis of the precursor **a**.



**Scheme 2:** Synthesis of the ligand **1**.

The cyclometallation of **1** was carried out using a round bottom flask in a Radleys carousel in inert atmosphere at 80° C for 1h. The, NaOAc was added to the solution. Finally, the mixture is stirred at room temperature (Scheme 3). Compound **1Pd** is a brown solid, highly insoluble in the common NMR solvents, thus its characterization was performed using IR spectroscopy. The value of the  $\nu(\text{Pd-Cl})$  band (384  $\text{cm}^{-1}$ ) is in accordance with a chlorine acting as terminal ligand suggesting the formation of a mononuclear species.<sup>[8]</sup> In addition, the increase of the value of the  $\nu(\text{C=N})$  is 67  $\text{cm}^{-1}$  indicative of a coordination by the non-binding electron pair on the nitrogen atom.



**Scheme 3:** Synthesis of the palladacycle **1Pd**.

### 3. Experimental Section

All the solvents were purified using the standard methods,<sup>[10]</sup> chemicals were reagent grade.

**Synthesis of [3,4-(C<sub>8</sub>H<sub>16</sub>O<sub>5</sub>)C<sub>6</sub>H<sub>3</sub>C(H)=O] (a):** the product has been synthesized using the Smith modification for the Duff reaction,<sup>[9]</sup> yield 60.6 %. **Molecular formula:** C<sub>15</sub>H<sub>20</sub>O<sub>6</sub> (296.32 g/mol). **Elemental analysis:** exp. C, 60.7; H, 6.9; O, 32.0 % calculated C, 60.8; H, 6.8; O, 32.4 %. **IR (cm<sup>-1</sup>):** 1686  $\nu(\text{C=O})$ . **<sup>1</sup>H NMR** (250 MHz, CDCl<sub>3</sub>,  $\delta$ /ppm): 9.82 (s, 1H, CHO), 7.45 (dd, 1H, H<sub>6</sub>, <sup>3</sup>J(H<sub>6</sub>H<sub>5</sub>) = 8.2 Hz, <sup>4</sup>J(H<sub>6</sub>H<sub>2</sub>) = 1.9 Hz), 7.38 (d, 1H, H<sub>2</sub>, <sup>4</sup>J(H<sub>2</sub>H<sub>6</sub>) = 1.9 Hz), 6.94 (d, 1H, H<sub>5</sub>, <sup>3</sup>J(H<sub>5</sub>H<sub>6</sub>) = 8.2 Hz), 4.19 (m, 4H, H<sub>a</sub>, H<sub>a'</sub>), 3.94 (m, H<sub>b</sub>, H<sub>b'</sub>), 3.74 (m, 8H, H<sub>c</sub>).

**Synthesis of [3,4-(C<sub>8</sub>H<sub>16</sub>O<sub>5</sub>)C<sub>6</sub>H<sub>3</sub>C(H)=NN(Me)C(=S)NH<sub>2</sub>] (1):** To a solution of precursor a in water, the necessary amount of thiosemicarbazide is added. The reaction is stirred for 8 h at room temperature and the white precipitate is filtered and dried, yield 65.7 %. **Molecular formula:** C<sub>18</sub>H<sub>27</sub>N<sub>3</sub>O<sub>5</sub>S (397.49 g/mol). **Elemental analysis:** exp. C, 53.4; H, 6.6; N, 10.7; O, 20.4; S, 8.3 % calculated: C, 54.4; H, 6.8; N, 10.6; O, 20.1; S, 8.1 %. **IR (cm<sup>-1</sup>):** 3289  $\nu$ (N–H), 1590  $\delta$ (NH<sub>2</sub>), 1577  $\nu$ (C=N), 808  $\nu$ (C=S). **<sup>1</sup>H NMR** (250 MHz, CDCl<sub>3</sub>,  $\delta$ /ppm): 7.62 (s, 1H, HC=N), 7.23 (d, 1H, H<sub>2</sub>, <sup>3</sup>J(H<sub>2</sub>H<sub>6</sub>) = 1.6 Hz), 7.17 (dd, 1H, H<sub>6</sub>, <sup>3</sup>J(H<sub>6</sub>H<sub>5</sub>) = 8.2 Hz, <sup>4</sup>J(H<sub>6</sub>H<sub>2</sub>) = 1.6 Hz), 6.87 (d, 1H, H<sub>5</sub>, <sup>3</sup>J(H<sub>5</sub>H<sub>6</sub>) = 8.2 Hz), 4.18 (m, 4H, Ha, Ha'), 3.94 (m, 4H, Hb, Hb'), 3.76 (s, 8H, Hc), 3.49 (s, 2H, NH<sub>2</sub>), 2.17 (s, 3H, MeN).

**Synthesis of [Pd{3,4-(C<sub>8</sub>H<sub>16</sub>O<sub>5</sub>)C<sub>6</sub>H<sub>3</sub>C(H)=NN(Me)C(=S)NH<sub>2</sub>}Cl] (1Pd):** Ligand 1 is added to a solution of Li<sub>2</sub>PdCl<sub>4</sub><sup>[11]</sup> in methanol, the reaction is stirred under N<sub>2</sub> atmosphere during 1 h, after that it is cooled until room temperature getting a brownish solution. The solvent is removed under reduced pressure obtaining a brown solid. **Molecular formula:** C<sub>17</sub>H<sub>24</sub>ClN<sub>3</sub>O<sub>5</sub>PdS (524.33 g/mol). **IR (cm<sup>-1</sup>):** 2925  $\nu$ (N–H), 1597  $\delta$ (NH<sub>2</sub>), 1510  $\nu$ (C=N), 851  $\nu$ (C=S), 384  $\nu$ (Pd-Cl).

#### 4. Conclusions

The first synthetic strategy to obtain mononuclear palladacycles derived from thiosemicarbazones containing a crown-ether in their structure has been described. It is worth noting that these new mononuclear species offer a switchable fourth coordination position at the palladium atom. This situation allows the system to be modified in order to improve the solubility and to be used as a sensor according to the size-selectivity of the entrapping application of 15-crown-5-ether functionality. More experiments in this line are undergoing.

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

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