

# The First Synthesis of a Pd(IV) Complex by Oxidative Addition of an Aryl Halide to Pd(II) and its Use as Precatalyst in a C–C Coupling Reaction.

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((Dedication----optional))

The complex  $[Pd(O,N,C-L)Cl]$  (**1-Cl**), where *L* is the monoanionic ligand resulting from deprotonation of the acetyl group of the dimethylmonoketal of 2,6-diacetylpyridine, reacts with one equiv of  $AgOAc$  to give  $[Pd(N,C-L)OAc]$  (**1-OAc**). This, in turn, reacts with 2-iodobenzoic acid at room temperature in  $CH_2Cl_2$  to afford the very stable pair of Pd(IV) complexes (OC-6-54)- and (OC-6-26)- $[Pd(O,N,C-L)(O,C-C_6H_4CO_2-2)I]$  (**2a** and **2b**, respectively, in 1.5:1 molar ratio, respectively). Complexes **2** are precatalysts for the room temperature *ortho*-vinylation of 2-iodobenzoic acid with  $CH_2=CHCO_2Me$  and  $AgClO_4$ . The reaction neither quenches by addition of 4000 equiv of Hg per Pd nor affords dibenzyl when benzyl chloride is added to the reaction mixture. These results, suggest that neither palladium nanoparticles nor some Pd(0) is involved in the process, leaving a Pd(II)/Pd(IV) catalytic cycle with the participation of some derivative of **2** as an reasonable alternative to the classical Pd(0)/Pd(II) cycle.

The recent award of the 2010 Nobel Prize in Chemistry to Heck, Negishi and Suzuki for their studies on catalytic cross couplings has recognized the important role of palladium in organic synthesis.<sup>[1,2]</sup> Their methods were improved, later on, by the use of Herrmann's palladacycles as precatalysts.<sup>[3]</sup> Most of both types of reactions involve a Pd(0)/Pd(II) catalytic cycle.<sup>[4,5]</sup> Pd(0) species are the precatalysts in the classical reactions<sup>[1]</sup> or form *in situ* from the Pd(II) precatalyst as a Pd(0) complex or in form of Pd nanoparticles.<sup>[6-8]</sup> However, based on various experimental data, Pd(II)/Pd(IV) catalytic cycles have been proposed.<sup>[9,10]</sup> Some computational studies also support this proposal.<sup>[7,11,12]</sup> However, since the oxidative addition of an aryl halide to a Pd(II) complex<sup>[13]</sup> and the existence of Pd(IV) complexes in these catalytic processes<sup>[14]</sup> have not yet been proved, the Pd(II)/Pd(IV) catalytic cycle has become one of the most intriguing open problems in catalysis.<sup>[15]</sup> The present work deals with the first of these two topics.

Only a few aryl palladium(IV) complexes have been isolated -or characterized in solution- from aryliodonium salts<sup>[16]</sup> or by oxidizing the corresponding aryl palladium(II) derivatives<sup>[17,18]</sup> but never from an aryl halide as required in the coupling reactions in which a Pd(II)/Pd(IV) catalytic cycle is invoked, which is one of the weaknesses of the proposal. A computational study has shown that oxidation of a N<sup>^</sup>C<sup>^</sup>N pincer Pd(II) complex with PhI is a highly endothermic reaction<sup>[19]</sup>, while another work<sup>[11]</sup> shows that not only the oxidation of various P<sup>^</sup>C<sup>^</sup>P pincer Pd(II) complexes with PhBr but also a Pd(II)/Pd(IV) Heck-type catalytic cycle are viable. Similar conclusions were attained from a previous work based on a C<sup>^</sup>N chelating Pd(II) complex, suggesting that the presence of a weakly coordinating ligand would favor a Pd(II)/Pd(IV) mechanism.<sup>[12]</sup> Therefore, the nature of the aryl halide and the ligands around Pd(II) seem to greatly influence the viability of

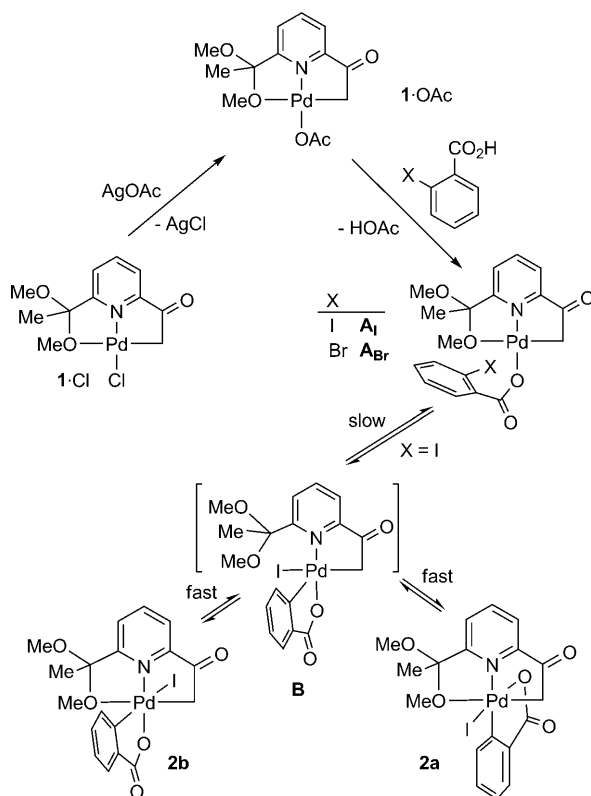
the crucial oxidative addition step in this alternative catalytic cycle

Recently, we have reported the reaction of  $PdCl_2$  with 2,6-diacetylpyridine in refluxing MeOH to give  $[Pd(O,N,C-L)Cl]$  (**1-Cl**, Scheme 1)<sup>[20]</sup> which, in turn, reacts with NaBr,  $Cl_2$  or  $Br_2$  leading to  $[Pd(O,N,C-L)Br]$  or to stable Pd(IV) complexes  $[Pd(O,N,C-L)X_3]$  (X = Cl, Br),<sup>[21]</sup> respectively. The stability of these Pd(IV) complexes, which was attributed to the pincer ligand, and the weakly coordinating ability of the MeO group in the Pd(II) complexes, expected to help its oxidation to Pd(IV) (see above), moved us to attempt the synthesis of a stable and unprecedented aryl Pd(IV) complex from an aryl iodide and a  $[Pd(O,N,C-L)X]$  complex. Because Pd(IV) complexes are thermally unstable and we also set out to use such Pd(IV) complex as a precatalyst in a C–C coupling process, we decide to prepare and test its catalytic ability at room temperature. We chose as reagents the new complex  $[Pd(O,N,C-L)(OAc)]$  (**1-OAc**, Scheme 1), prepared by reacting **1-Cl**<sup>[20]</sup> with  $AgOAc$ , and 2-iodobenzoic acid. Coordination of the benzoate moiety, after deprotonation, would bring the iodo atom close to the palladium atom and this, along with the presence of the electronwithdrawing ortho-substituent,<sup>[4,22]</sup> would give a chance to the oxidative addition reaction to occur at room temperature. Additionally, the resulting chelating phenyl benzoato ligand would increase the stability of the Pd(IV) complex. The product obtained was the expected Pd(IV) complex  $[Pd(O,N,C-L)(O,C-C_6H_4CO_2-2)I]$  (**2**), which is indefinitely stable in the solid state. This first Pd(II) to Pd(IV) oxidative addition using an aryl halide does not contradict the works proving that other aryl halides do not oxidatively add to other Pd(II) complexes.<sup>[23]</sup>

A  $CDCl_3$  solution of **2** at room temperature shows the presence of traces of two non-identified decomposition products after 5 h and 24% decomposition 30 h later. Complexes **1-OAc** and **2** were characterized by X-ray diffraction (Figure 1), NMR spectroscopy and elemental analyses. The crystal structure of **1-OAc** showed it to be a dimer with bridging acetato ligands (Figure 1); the Pd–Pd distance 3.0315(5) Å<sup>[24]</sup> is significantly longer than the double of the Pd covalent radius (1.39 Å).<sup>[25]</sup> However, its <sup>1</sup>H and <sup>13</sup>C NMR spectra (in particular, the MeO resonances) are similar to other Pd(O,N,C-L) complexes and different from those containing the chelating ligand N,C-L<sup>[20]</sup> suggesting that in solution, its structure is that shown Scheme 1. Oxidative addition of aryl halides to Pt(II) complexes has been reported to be assisted by coordination,<sup>[26]</sup> but nothing similar had been found in the chemistry of Pd. The different nature of the assistant group in our case (anionic) with respect to those present in Pt(II) (neutral) merits to be emphasized.

During this reaction, an intermediate was detected, which remained in solution until the end. Its  $CH_2$  protons resonate at a value (3.69 ppm) similar to those found in the other Pd(II)(O,N,C-L) complexes (3.73–3.27 ppm)<sup>[20,21]</sup> and lower than

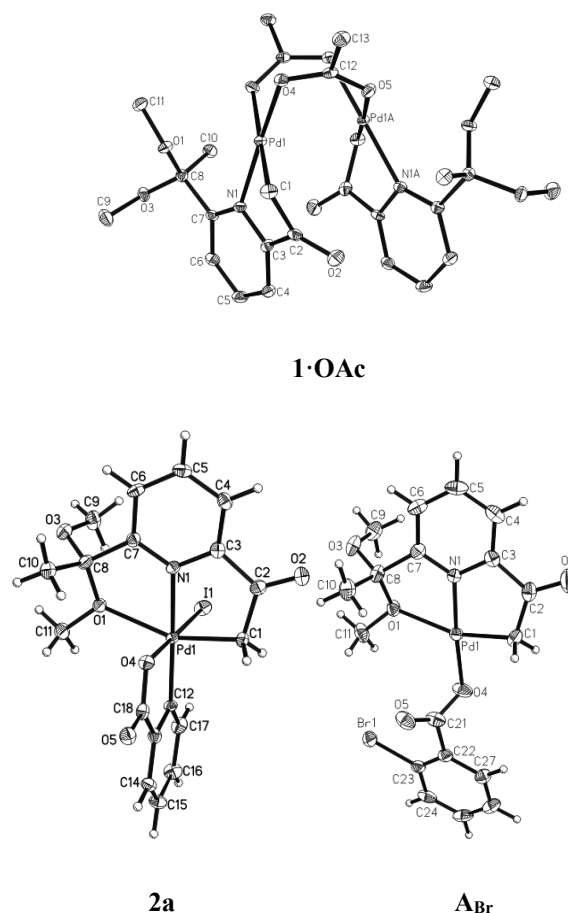
those in **2** ( $\delta_A$ , 4.95,  $\delta_B$ , 4.55 ( $^2J_{HH}$  = 12.4 Hz)) and their homologues (6.06–6.04 ppm)<sup>[21]</sup>. Therefore, we propose that this intermediate is the Pd(II) benzoato complex [Pd(*O,N,C-L*)(O<sub>2</sub>CC<sub>6</sub>H<sub>4</sub>I-2)] (**A<sub>I</sub>**, Scheme 1), which is also observed when **2** is dissolved in CDCl<sub>3</sub>. An additional evidence on the nature of **A<sub>I</sub>** was obtained when, attempting to prepare at room temperature the Br homologue of **2** by reacting **1**·OAc with 2-bromobenzoic acid, we only isolated the complex **A<sub>Br</sub>** (Scheme 1 and Figure 1) which we fully characterized, including its X-ray structure.



**Scheme 1.** Synthesis of complexes **1**·OAc, **A<sub>x</sub>** and **2** and a proposal for the equilibrium between **A<sub>I</sub>** and the two isomers of complex **2**.

The <sup>1</sup>H NMR of **2** was studied in CDCl<sub>3</sub> between –55 and 35 °C, its upper limit of stability, showing a slow **2** ⇌ **A<sub>I</sub>** equilibrium in the NMR time scale. The **2**:**A<sub>I</sub>** molar ratios decrease from *ca.* 9 in the range –55 to –5 °C to *ca.* 2.3 at 25 °C and 1.9 at 35 °C. In addition, the AB system corresponding to the CH<sub>2</sub> protons in **2** at room temperature coalesces at –20 °C and splits into two AB systems below –35 °C, indicating the existence of the two possible Pd(IV) geometrical isomers **2a** and **2b** in equilibrium (Scheme 1; 1.5:1 molar ratio; **2a**:  $\delta_A$ , 4.84,  $\delta_B$ , 4.71 ( $^2J_{HH}$  = 12 Hz); **2b**:  $\delta_A$ , 5.08,  $\delta_B$ , 4.38 ( $^2J_{HH}$  = 13.2 Hz)), probably interconverting through the unobserved intermediate **B** (Scheme 1).<sup>[27]</sup> The isomer with the greater  $\delta_A - \delta_B$  value is assigned to the isomer bearing the iodo ligand trans to the aryl group (**2b**), which shields the nearest CH<sub>2</sub> proton. A line-shape analysis of the CH<sub>2</sub> protons resonances of the equilibrium **2a** ⇌ **2b** did not allow the determination of its activation parameters. Scheme 1 shows a proposal to give account of the formation of **2a** and **2b** and their equilibrium. Oxidative addition reactions

giving two Pd(IV) geometrical isomers have been reported,<sup>[18,28]</sup> but they were not in equilibrium.

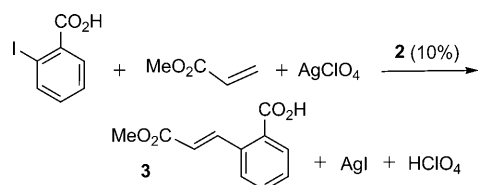


**Figure 1.** X-ray crystal structures of complexes **1**·OAc (CCDC 807142), **2** (CCDC 807142) and **A<sub>Br</sub>** (CCDC 807144).

Complex **2** did not react with CH<sub>2</sub>=CHCO<sub>2</sub>Me in acetone-*d*<sub>6</sub> at room temperature but when it was treated in the presence of one equiv of AgClO<sub>4</sub>, to remove the iodo ligand, with 2 equiv of CH<sub>2</sub>=CHCO<sub>2</sub>Me in acetone-*d*<sub>6</sub> at room temperature, the desired (*E*)-methyl 2-carboxycinnamate (**3**) was quantitatively obtained in less than 1h (Scheme 2). The Heck synthesis of **3**, using the corresponding diazonium salts instead of 2-iodobenzoic acid, has been reported.<sup>[29]</sup> Complex **2** is a precatalyst for this reaction using 10% of the stoichiometric amount (83% yield of **3** after 6h). It is clear that the interest of this result is not synthetic but associated to the use of a Pd(IV) complex as precatalyst in a C–C coupling process, which only related precedent is a recently reported Pd(IV)-catalyzed C–H trifluoromethylation reaction.<sup>[30]</sup> The same reaction mixture excluding **2** did not afford **3** after 4 days. The addition of a strong excess of Hg (4000 equiv per Pd) to the catalytic reaction mixture did not quench the process, suggesting that Pd nanoparticles are not involved in the catalytic cycle,<sup>[8,9]</sup> and adding 0.5 equiv/Pd of benzyl chloride to the reaction mixture gave 80% yield of **3** after 5 h at room temperature but dibenzyl was not detected, excluding any Pd(0) complex to be involved in the catalytic cycle.<sup>[7]</sup>

The above data suggest that Pd(II)/Pd(IV) species are involved in the catalytic synthesis of **3**. Detailed studies on this reaction catalyzed by various Pd pincer complexes and attempts

to detect Pd(IV) in the catalytic cycle are currently in progress. In the absence of AgClO<sub>4</sub>, complex **2** reacted with 2 equiv of CH<sub>2</sub>=CHCO<sub>2</sub>Me in DMSO-d<sub>6</sub> at 140 °C giving quantitatively **3** in 1h. If 10% of the stoichiometric amount of **2** is used, 25 or 6% yield of **3** is obtained after 1 h depending on the solvent and the temperature (140 °C in DMSO-d<sub>6</sub> or 120 °C in DMF-d<sub>7</sub>, respectively). However, **3** did not form when any of these high-temperature reactions were carried out in the presence of a strong excess of Hg (4900 equiv), which suggests that they are mediated by Pd nanoparticles.



**Scheme 2.** Catalytic synthesis of **3** using complex **2** as precatalyst.

In conclusion, we report on several *unprecedented results in the chemistry of Pd*: (1) the synthesis of two Pd(IV) isomeric complexes, **2**, by oxidative addition of an aryl halide to Pd(II), (2) the intramolecular nature of the oxidative addition reaction, as suggested by the detection in solution of the precursor **A<sub>1</sub>**, (3) the isolation and full characterization of the bromo homologue **A<sub>Br</sub>**, (4) the anionic nature of the assistant group (benzoato) in the oxidative addition reaction, which makes a difference with the analogous reactions in Pt chemistry, assisted by neutral groups, (5) Pd(IV) complexes **2** and the precursor **A<sub>1</sub>** are in equilibrium in solution, (6) complexes **2** react with AgClO<sub>4</sub> and 2 equiv CH<sub>2</sub>=CHCO<sub>2</sub>Me at room temperature, to afford quantitatively **3** in less than 1h, (7) they are also precatalysts for this reaction using 10% of the stoichiometric amount, (8) experimental data suggest to occurs through a Pd(II)/Pd(IV) catalytic cycle and (9) in the absence of AgClO<sub>4</sub>, stoichiometric or catalytic reactions of **2** and CH<sub>2</sub>=CHCO<sub>2</sub>Me at high temperatures in DMSO or DMF afford **3** through the mediation of Pd nanoparticles.

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