Palladium Complexes

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Synthesis of a Palladium(IV) Complex by Oxidative Addition of an Aryl Halide to Palladium(II) and Its Use as Precatalyst in a C–C Coupling Reaction

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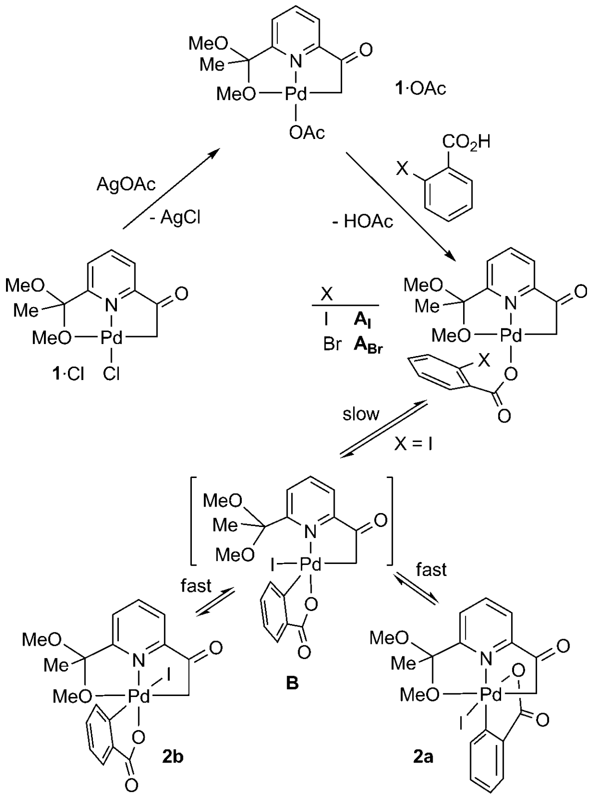
The recent award of the 2010 Nobel Prize in Chemistry to Heck, Negishi, and Suzuki for their studies on catalytic cross couplings has recognized the important role of palladium in organic synthesis.[1,2] Their methods were later improved by the use of Herrmann's palladacycles as precatalysts.[3] Most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

A few aryl palladium(IV) complexes have been isolated (or characterized in solution) from aryliodonium salts[16] or from the oxidation of corresponding aryl palladium(II) derivatives,[17,18] 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 an N^C^N pincer Pd^{II} complex with PhI is a highly endothermic reaction,[19] while another study shows that not only the oxidation of various P^C^P pincer Pd^{II} complexes with PhBr but also a Pd^{II}/Pd^{IV} Heck-type catalytic cycle are viable.[11] Similar conclusions were drawn from a previous investigation based on a C^N chelating Pd^{II} complex, thus suggesting that the presence of a weakly coordinating ligand would favor a Pd^{II}/Pd^{IV} mechanism.[12] 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 reported the reaction of $PdCl_2$ with 2,6-diacetylpyridine in MeOH at reflux to give [Pd(*O*,*N*,*C*-L)Cl] (**1**·Cl, Scheme 1)[20] which reacts with Cl_2 or NaBr to give, respectively, the stable Pd^{IV} complex [Pd(*O*,*N*,*C*-L)Cl_3] or [Pd(*O*,*N*,*C*-L)Br], which, in turn, reacts with Br_2 to afford [Pd(*O*,*N*,*C*-L)Br_3].[21] 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 (which was 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 because we also set out to use such a Pd^{IV} complex as a precatalyst in a C–C coupling process, we decided to prepare and test its catalytic ability at room temperature. We chose as reagents 2-iodobenzoic acid and the new complex [Pd(*O*,*N*,*C*-L)(OAc)] (**1**·OAc, Scheme 1), pre-



Scheme 1. Synthesis of complexes **1**·OAc, $\mathbf{A_X}$, and **2** and a proposal for the equilibrium between $\mathbf{A_I}$ and the two isomers of complex **2**.

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pared by treating **1**·Cl[20] with AgOAc. Coordination of the benzoate moiety, after deprotonation, would bring the iodine atom close to the palladium atom, and this situation, along with the presence of the electron-withdrawing *ortho* substituent,[4,22] would give the oxidative addition reaction a chance 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*-2-$CO_2C_6H_4$)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 studies demonstrating that other aryl halides do not oxidatively add to other Pd^{II} complexes.[23]

The ^{1}H NMR spectrum of a $CDCl_3$ solution of **2** at room temperature shows the presence of traces of two unidentified decomposition products after 5 h and 24 % decomposition 30 h later. Complexes **1**·OAc and **2a** 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 separation of 3.0315(5) Å[24] is significantly longer than twice the covalent radius of Pd (1.39 Å).[25] However, its ^{1}H and ^{13}C NMR spectra (in particular, the MeO resonances) are similar to those of other Pd(*O*,*N*,*C*-L) complexes and different from those of complexes containing the chelating ligand *N*,*C*-L,[20] thus suggesting that in solution, the structure of **1**·OAc is that shown in Scheme 1. Oxidative addition of aryl halides to Pt^{II} complexes has been reported to be assisted by coordination,[26] 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 emphasis.

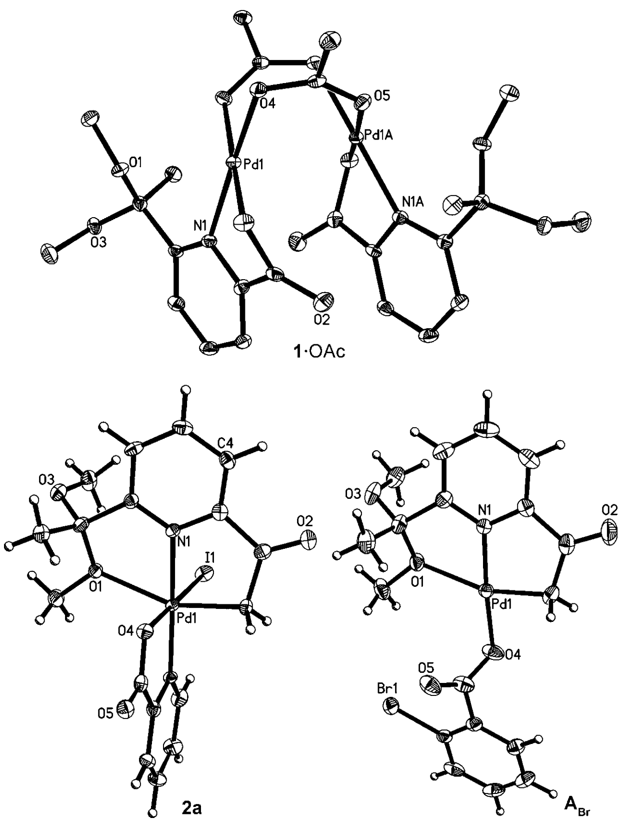
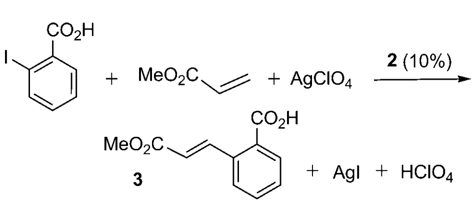


Figure 1. X-ray crystal structures of complexes **1**·OAc, **2a**, and $\mathbf{A_{Br}}$.[31]

During this reaction, an intermediate was detected, which remained in solution until the end. Its CH_2 protons resonate at a value ($\delta = 3.69$ ppm) similar to those found for the other Pd^{II}(*O*,*N*,*C*-L) complexes ($\delta = 3.73$–3.27 ppm)[20,21] and lower than those for **2** ($\delta_A = 4.95$, $\delta_B = 4.55$ ppm ($^2J_{HH} = 12.4$ Hz)) and its homologues ($\delta = 6.06$–6.04 ppm).[21] Therefore, we propose that this intermediate is the Pd^{II} benzoato complex [Pd(*O*,*N*,*C*-L)(O_2C-2-IC_6H_4)] ($\mathbf{A_I}$, Scheme 1), which is also detected when **2** is dissolved in $CDCl_3$. Additional evidence on the nature of $\mathbf{A_I}$ was obtained when, while attempting to prepare the Br homologue of **2** at room temperature by treating **1**·OAc with 2-bromobenzoic acid, we isolated only the complex $\mathbf{A_{Br}}$ (Scheme 1 and Figure 1), which we fully characterized, including by X-ray crystallography.

The ^{1}H NMR spectrum of **2** was studied in $CDCl_3$ between −55 and 35 °C, its upper limit of stability (see the Supporting Information), and a slow $\mathbf{2} \rightleftarrows \mathbf{A_I}$ equilibrium on the NMR time scale was detected. The $\mathbf{2}$:$\mathbf{A_I}$ molar ratio decrease from approximately 9:1 in the range −55 to −5 °C to about 2.3:1 at 25 °C and 1.9:1 at 35 °C. Furthermore, the AB system corresponding to the CH_2 protons in **2** at room temperature coalesces at −20 °C and splits into two AB systems below −35 °C, thus indicating the existence of the two possible Pd^{IV} geometric isomers **2a** and **2b** in equilibrium (Scheme 1; 1.5:1 molar ratio; **2a**: $\delta_A = 4.84$, $\delta_B = 4.71$ ppm ($^2J_{HH} = 12$ Hz); **2b**: $\delta_A = 5.08$, $\delta_B = 4.38$ ppm ($^2J_{HH} = 13.2$ Hz)), which probably interconvert through the unobserved intermediate **B** (Scheme 1).[27] The isomer with the greater $\delta_A - \delta_B$ value is assigned as that bearing the iodo ligand trans to the aryl group (**2b**), which shields the nearest CH_2 proton. A line-shape analysis of the CH_2 proton resonances of the equilibrium $\mathbf{2a} \rightleftarrows \mathbf{2b}$ did not allow the determination of its activation parameters. Scheme 1 shows a proposal to account for the formation of **2a** and **2b** and their equilibrium. Oxidative addition reactions giving two Pd^{IV} geometrical isomers have been reported,[18,28] but those species were not in equilibrium.

Complex **2** did not react with $CH_2{=}CHCO_2Me$ in [D$_6$]acetone at room temperature, but when it was treated with two equivalents $CH_2{=}CHCO_2Me$ in [D$_6$]acetone in the presence of one equivalent $AgClO_4$ to remove the iodo ligand at room temperature, the desired (*E*)-methyl 2-carboxycinnamate (**3**) was quantitatively obtained in less than 1 h (Scheme 2). The Heck synthesis of **3** using the corresponding diazonium salts instead of 2-iodobenzoic acid has been reported.[29] Complex **2** is a precatalyst for this reaction using 10 % of the stoichiometric amount (83 % yield of **3** after



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

6 h). It is clear that the interest of this result is not synthetic but is associated with the use of a Pd^{IV} complex as precatalyst in a C–C coupling process, the only related precedent of which is a recently reported Pd^{IV}-catalyzed C–H trifluoromethylation reaction.[30] The same reaction mixture excluding **2** did not afford **3** after four days. The addition of a large excess of Hg (4000 equiv relative to Pd) to the catalytic reaction mixture did not quench the process, thus suggesting that Pd nanoparticles are not involved in the catalytic cycle,[8,9] and adding 0.5 equiv benzyl chloride relative to Pd to the reaction mixture gave 80 % yield of **3** after 5 h at room temperature, but dibenzyl was not detected, thus excluding the involvement of a Pd^0 complex in the catalytic cycle.[7]

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 $AgClO_4$, complex **2** reacted with two equivalents $CH_2=CHCO_2Me$ in [D$_6$]DMSO at 140 °C to give **3** quantitatively in 1 h. 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 [D$_6$]DMSO or 120 °C in [D$_7$]DMF, respectively). However, **3** did not form when any of these high-temperature reactions were carried out in the presence of a large excess of Hg (4900 equiv), which suggests that they are mediated by Pd nanoparticles.

In conclusion, we report on several unprecedented results in the chemistry of Pd: 1) the synthesis of a mixture of Pd^{IV} 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 $\mathbf{A_I}$, 3) the isolation and full characterization of the bromine homologue $\mathbf{A_{Br}}$, 4) the anionic nature of the assistant group (benzoato) in the oxidative addition reaction, which is different from analogous reactions in Pt chemistry, which are assisted by neutral groups, 5) Pd^{IV} complexes **2** and the precursor $\mathbf{A_I}$ are in equilibrium in solution, 6) complexes **2** react with $AgClO_4$ and two equivalents $CH_2=CHCO_2Me$ at room temperature to afford **3** in quantitative yield in less than 1 h, 7) they also catalyze the same C–C coupling process, 8) experimental data suggest that this process occurs through a Pd^{II}/Pd^{IV} catalytic cycle, and 9) in the absence of $AgClO_4$, stoichiometric or catalytic reactions of **2** and $CH_2=CHCO_2Me$ at high temperatures in DMSO or DMF afford **3** through the mediation of Pd nanoparticles.

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