

Heck reaction catalysed by pyridyl-imine palladium(0) and palladium(II) complexes

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Received 23 July 2004; received in revised form 22 September 2004; accepted 24 September 2004

Available online 6 November 2004

Abstract

Three different palladium(II) complexes Pd(NN')Cl₂ and two different palladium(0) complexes Pd(NN')(dmfu) (dmfu = dimethylfumarate) containing NN' pyridyl-imine ligands, have been prepared and used as pre-catalysts for the coupling between iodobenzene and methyl acrylate (Meac) (Heck reaction). All the reactions have been conducted in DMF at 80 °C, using Et₃N as base and a Pd:PhI:Meac:Et₃N = 1:1000:1100:1000 molar ratio. In all cases the complete conversion of iodobenzene into *trans*-methylcinnamate has been observed within 2.5 h of reaction, with the highest TOF value (1253) obtained with a palladium(II) complex. At the end of the catalytic reactions the dimeric species [Pd₂I₆][Et₃NH]₂ has been recovered, pointing out a partial palladium loss from the starting complex species. A poisoning Hg(0) test has shown a heterogeneous nature of the catalytic reactions and this indicates that the Pd(NN') complexes act as metallic palladium reservoirs. The dimer [Pd₂I₆][Et₃NH]₂ probably forms from soluble palladium(0) particles arising from the complex decomposition once the substrates have been totally consumed. Interestingly, the dimer [Pd₂I₆][DMFH]₂ has been obtained by reacting PdCl₂ with PhI and Meac in DMF at 80 °C.

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Keywords: Heck couplings; Palladium catalysts; Nitrogen ligands; Schiff-bases; Catalysis

1. Introduction

The Heck coupling reaction, to say the palladium catalysed arylation of an alkene with organic halides, is one of the most powerful tool to make new C–C bonds [1–3]. In order to have thermally robust catalysts, phosphine-based palladium complexes [2,3] and palladacycle complexes [4] have been prepared and extensively employed not only with iodo-arenes but also with the less reactive bromo- and chloro-arenes. Palladium complexes with di-nitrogen ligands, not containing any Pd–P or Pd–C bond, have also been used for the Heck coupling [5–11], especially with the aim of overcoming the

drawbacks encountered with phosphine containing catalysts [2].

Some of us have recently shown that zerovalent palladium complexes Pd(NN')(dmfu) of pyridyl-imine ligands (NN') and dimethylfumarate (dmfu) can be successfully employed as pre-catalysts for the stereoselective homogeneous hydrogenation of 1-phenyl-1-propyne to the corresponding Z-olefin [12]. The possibility of easily make dichloride palladium(II) complexes with the same NN' ligands, prompted us to undertake a study on the catalytic behaviour of the Pd(NN') complexes reported in Scheme 1 in the Heck coupling. This allows to compare the catalytic activity of similar pre-catalysts, where the same Pd(NN') fragment contains the metal in two different oxidation states. The coupling between iodobenzene and methyl acrylate has been chosen as a model reaction. In the literature pyridyl-imine [13] or their reduced

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forms [14] have been used as ligands in the Heck reaction as silica-supported palladium catalysts but, curiously, there are not examples of their use in homogeneous conditions.

2. Experimental

2.1. Synthesis

Proton NMR spectra were recorded at 27 °C on a Bruker 300 FT spectrophotometer by using SiMe₄ as internal standard. Elemental analyses were performed by using a Carlo Erba Model EA 1108 apparatus. All the syntheses have been conducted under a nitrogen atmosphere, by using Schlenk techniques. The syntheses of the NN' ligands as well as those of the palladium(0) complexes **4** and **5** have already been reported [12]. Pd(cod)Cl₂ has been prepared by a literature reported method [15]. The solvents have been deaerated and dried according to literature methods.

2.2. Synthesis

2.2.1. General procedure for the synthesis of the palladium(II) complexes 1–3

0.45 mmol of the NN' ligand were dissolved in 40 ml of dichloromethane and a stoichiometric amount of Pd(cod)Cl₂ was added. The solution was stirred at room temperature for at least 5 h, then the solvent was partially removed by vacuum and the product precipitated by diethyl ether. After filtration the solid was washed with diethyl ether and dried under vacuum.

1: light-orange. Yield: 75%. Anal. Calcd. for C₉H₁₂Cl₂N₂Pd (325.5): C 33.21; H 3.72; N 8.61. Found: C 33.15; H 3.58; N 8.59. ¹H NMR (CDCl₃) δ: 9.33 (d, 1H, py, ³J=5.5 Hz), 8.16 (s, 1H, CH=N), 8.12 (t, 1H, py, ³J=7.6 Hz), 7.86 (d, 1H, py, ³J=7.5 Hz), 7.66 (t, 1H, py, ³J=6.5 Hz), 4.84 (m, 1H, *i*-Pr), 1.49 (d, 6H, *i*-Pr, ³J=6.0 Hz).

2: orange. Yield: 74%. Anal. Calcd. for C₁₀H₁₄Cl₂N₂Pd (339.5): C 35.38; H 4.16; N 8.25. Found: C 35.35; H 4.09;

N 8.15. ¹H NMR (CDCl₃) δ: 9.41 (dd, 1H, py, ³J=5.5 Hz, ⁴J=1.3 Hz), 8.14 (td, 1H, py, ³J=7.8 Hz, ⁴J=1.4 Hz), 7.26 (d, 1H, py, ³J=7.3 Hz), 7.62 (td, 1H, py, ³J=6.6 Hz, ⁴J=1.1 Hz), 4.73 (m, 1H, *i*-Pr), 2.60 (s, 3H, C(Me)=N), 1.60 (d, 6H, *i*-Pr, ³J=6.9 Hz).

3: light-orange. Yield: 64%. Anal. Calcd. for C₁₀H₁₄Cl₂N₂Pd (339.5): C 35.38; H 4.16; N 8.25. Found: C 35.43; H 4.20; N 8.21. ¹H NMR (CDCl₃) δ: 9.50 (d, 1H, py, ³J=6.1 Hz), 8.11 (t, 1H, py, ³J=7.5 Hz), 8.05 (s, 1H, CH=N), 7.77 (d, 1H, py, ³J=7.4 Hz), 7.62 (t, 1H, py, ³J=6.5 Hz), 1.25 (s, 9H, *t*-Bu).

2.2.2. Synthesis of [Pd₂I₆][DMFH]₂

Method a. Eighty milligrams (0.451 mmol) of PdCl₂ were dissolved in 5 ml of DMF and the solution was thermostated at 60 °C. PhI and methyl acrylate, 2 ml each, were added and the purple solution was stirred for 3 h without varying the temperature. The volatiles were then removed by vacuum pump and the blackish solid residue repeatedly washed with cyclohexane, filtered off, washed again with cyclohexane and finally dried in vacuum. Yield: 47% (120 mg). Anal. Calcd. for C₆H₁₆I₆N₂O₂Pd₂·2H₂O: C 6.22; H 1.74; N 2.41. Found: C 6.18; H 1.54; N 2.35. TGA (30–400 °C, 5 °C/min): 119 °C, –3.37% (–2H₂O), 256.5 °C, –4.93% (–2CO). ¹H NMR (d₆-DMSO) δ: 8.06 (sbr, 1H, NH), 7.95 (s, 1H, CHO), 2.89 (s, 3H, CH₃), 2.73 (s, 3H, CH₃).

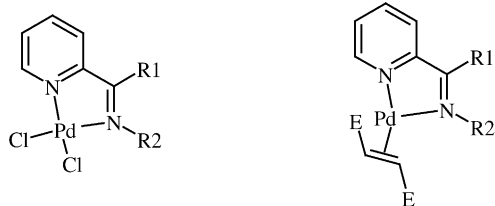
From the cyclohexane solution 65 mg of methyl cinnamate were recovered.

Method b. Twenty eight milligrams (0.086 mmol) of **1** were dissolved in 3 ml of DMF and the solution thermostated at 60 °C. PhI and methyl acrylate, 1 ml each, were added and the purple solution stirred for 3 h without varying the temperature. The volatiles were removed under vacuum and the black oily residue treated with diethyl ether. A black solid was filtered off, washed with diethyl ether and then dried in vacuum. ¹H NMR (d₆-DMSO): **1** δ: 8.98 (d, 1H, py, ³J=5.2 Hz), 8.60 (s, 1H, CH=N), 8.34 (t, 1H, py, ³J=7.5 Hz), 8.11 (d, 1H, py, 7.5 Hz), 7.85 (t, 1H, py, ³J=6.5 Hz), 4.49 (m, 1H, *i*-Pr), 1.38 (s, 3H, *i*-Pr), 1.36 (s, 3H, *i*-Pr). [Pd₂I₆][DMFH]₂ δ: 7.95 (s, 1H, CHO), 2.88 (s, 3H, CH₃), 2.73 (s, 3H, CH₃). The N–H singlet was obscured by signals of **1**. From the ¹H NMR integrals a **1**:[Pd₂I₆][DMFH]₂ = 10:1 ratio has been established.

By slow evaporation of an acetone solution of the black mixture, well shaped orange crystals of **1**, suitable for X-ray analysis, were collected (see Supplementary data).

2.3. Catalysis

All the reactions were carried out under nitrogen, by using standard Schlenk techniques; DMF was dried according to literature methods. PhI and methyl acrylate were used as received, while Et₃N was distilled prior to use. The GC analyses were performed on a Dani HP 3800 flame-ionisation gas chromatograph (OV 101 on CHP column).



Pd(NN')Cl₂

R1 = H, R2 = *i*-Pr **1**

R1 = Me, R2 = *i*-Pr **2**

R1 = H, R2 = *t*-Bu **3**

Pd(NN')(dmfu)

R1 = H, R2 = *i*-Pr **4**

R1 = Me, R2 = *i*-Pr **5**

E = COOMe

Scheme 1.

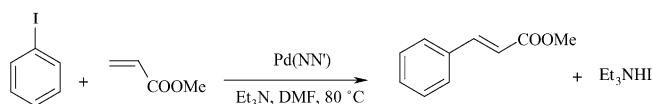
In a dry 100 ml capacity Schlenk tube equipped with a magnetic bar, iodobenzene, methyl acrylate, triethylamine and mesitilene (internal standard) were introduced; a 10 ml DMF solution containing 9×10^{-3} mmol of complex (about 3 mg) or PdCl₂ (1.6 mg) was quantitatively transferred into the reactor and the solution thermostated at 80 °C (oil bath). Microvolumes of the reactant solutions were withdrawn, quenched with brine and extracted with dichloromethane; after drying with anhydrous sodium sulphate and filtration they were analysed by GC.

3. Results and discussion

The palladium(0) complexes **4** and **5** have been prepared by following the literature reported method [12], while the palladium(II) complexes **1–3** have been prepared by reacting Pd(cod)Cl₂ with a slight excess of ligand in dichloromethane at room temperature [16]. The elemental analyses and the spectroscopic data are in agreement with the structures depicted in Scheme 1. The complexes **1–5** have been tested as catalysts in the model coupling reaction of methyl acrylate (Meac) with iodobenzene, using DMF as solvent, Et₃N as base and a temperature of 80 °C. A Pd:PhI:Meac:Et₃N = 1:1000:1100:1000 molar ratio has been kept constant at every catalytic experiment (Scheme 2).

The catalytic results are collected in Table 1.

All the palladium complexes promote the complete conversion of iodobenzene into *trans*-methyl cinnamate (unique product as established by ¹H NMR spectroscopy) within 2.5 h of reaction. In all the catalytic experiments the reactant solutions showed the same chromatic behaviour: once



Scheme 2.

Table 1
Heck couplings catalysed by complexes **1–5**^a

Entry	Cat.	<i>t</i> (h)	Conv. (%)	ton ^b	tof ^c
1	1	1	75 ^d	750	750
2	2	0.75	94 ^e	940	1253
3	3	0.75	88 ^e	882	1176
4	4	2	86 ^f	860	430
5	5	2	100	1000	500
6 ^g	PdCl ₂	1	100	1000	1000
7	3	0.75	35	350	467

^a Solvent: DMF, *T* = 80 °C, Pd:PhI:Meac:Et₃N = 1:1000:1100:1000.

^b ton = mol of product/mol of Pd.

^c tof = ton/h.

^d The reaction is complete within 1.5 h.

^e The reaction is complete within 1 h.

^f The reaction is complete within 2.5 h.

^g The conversion has been determined only after 1 h of reaction.

the complex was dissolved in DMF the solution appeared light-yellow; in contact with the substrates at 80 °C, the solution became light-orange within 10 min, to return light-yellow when iodobenzene was totally converted. Only at this time traces of palladium black deposited on the magnetic barrette, the supernatant solution appearing homogeneous. On standing the reactor at room temperature the solution quickly took a purple colour, without releasing additional solid palladium. This points out a similar behaviour of the complexes **1–5** under the catalytic conditions. Moreover, the observed colour changes unequivocally point out that the starting complexes undergo dramatic changes during the catalytic process; particularly, the final purple solution colour states the presence of a new metal containing species. In order to get more details about the behaviour of the palladium complexes under the applied catalytic conditions, several experiments have been conducted using complex **1**. Thus, at the end of a catalytic process promoted by **1**, all the volatiles were removed under vacuum, and the black residue was repeatedly washed with diethyl ether. The ¹H-NMR spectrum recorded in CDCl₃ (purple solution) shows signals of the starting chloride complex with two additional multiplets centred at 1.49 and 3.28 ppm, respectively, which persisted even after a prolonged vacuum. The formation of a deep-red solution has been reported for the Pd(OAc)₂ catalysed coupling of iodobenzene with 2-methylprop-2-en-1-ol in NMP (NMP = 1-methyl-2-pyrrolidinone); the colour was due to the formation of the dimer [Pd₂I₆][Et₃NH]₂, whose ¹H NMR spectrum recorded in CDCl₃ shows a triplet at 1.4 ppm and a quadruplet at 3.1 ppm, respectively [17]. On the basis of these data we assume that during the catalytic reaction complex **1** partially degrades to the dimeric species [Pd₂I₆][Et₃NH]₂, after ligand dissociation. In order to test the stability of the Pd(NN') complexes under the applied experimental conditions, complex **1** was reacted with PhI and Meac (Pd:PhI:Meac = 1:100:130 molar ratio) in DMF at 60 °C (no Et₃N was added); the solution became purple (the purple colour appeared only after the addition of Meac) and after the work-up (see Section 2) the ¹H NMR spectrum (d₆-DMSO) of the black residue shows the set of signals of **1**, with three additional singlets at 7.95, 2.89 and 2.73 ppm, respectively, corresponding to a DMF molecule. These three signals persist even after a prolonged vacuum. By slow evaporation of an acetone solution of the black residue, well shaped orange crystals separated from the black powder; an X-ray analysis conducted on the crystals confirmed the presence of **1** in the mixture (see Supplementary data) [18], while the ¹H NMR spectrum of the black powder shows again the three singlets of DMF together with some residual signals belonging to **1**. Interestingly, the reaction of PdCl₂ with an excess of PhI and Meac in DMF at 60 °C (no Et₃N was added) quickly brought to a purple solution, from which a black solid was recovered.[§] The ¹H NMR spectrum recorded in d₆-DMSO

[§] A nearly stoichiometric amount, based on palladium, of methyl cinnamate was recovered (see Section 2).

shows the three singlets of the DMF plus a broad singlet centred at 8.06 ppm, pointing out the presence of a DMFH⁺ unit. With our surprise the elemental analysis of this black solid is in accord with the dimeric species [Pd₂I₆][DMFH⁺]₂, where two protonated DMF molecules neutralize the anionic dimer [Pd₂I₆]²⁻. This dimeric species has also been obtained from metallic palladium and iodine in DMF [19]. On the basis of this result, the species [Pd₂I₆][DMFH⁺]₂ must form also in the reaction of **1** with PhI and Meac in DMF in the absence of Et₃N. As expected a Heck coupling promoted by PdCl₂ under our experimental conditions (then in the presence of Et₃N) brought to the complete conversion of the substrates into methyl cinnamate (entry 6 in Table 1), the final reactant solution appearing deep-purple; [Pd₂I₆][Et₃NH]₂ was recovered again. All these reactions underline the high stability of the dimer anion [Pd₂I₆]²⁻. The recovery of the dimer [Pd₂I₆][Et₃NH]₂ at the end of the Pd(NN') catalysed coupling reactions must mean that a part of the starting complex undergoes a ligand dissociation with the likely formation of low-ligated and reactive palladium(0) species. This is supported by the positiveness of a Hg test [20] conducted on a coupling catalysed by complex **3** (entry 7, Table 1), which points out a heterogeneous nature of the reaction. The metal particles probably give rise to the [Pd₂I₆][Et₃NH]₂ dimer at the end of the reaction through a not yet clear pathway. The Pd(NN') complexes would then play the role of palladium reservoirs, releasing the active species upon dissociation [2].

An inspection of Table 1 brings to the following conclusions: (i) ligand being equal, the palladium(II) complexes are more active than the corresponding palladium(0) complexes (compare the entries 1 and 2 with the entries 4 and 5); (ii) the ketimine complexes always result more reactive than the corresponding aldimine complexes (compare entry 1 with entry 2 and entry 4 with entry 5); (iii) the replacing of the *i*-Pr imine substituent with the bulkier *t*-Bu group leads to a more reactive aldimine palladium(II) complex (compare entries 1 and 3).

The reactivity orders **2** > **3** ≫ **1** > **5** > **4** can now be explained in terms of steric reasons: the ligand dissociation, and then the active species formation, is faster with the more hindered complexes. More difficult is to explain the lower activity observed for the palladium(0) complexes **4** and **5** with respect to the palladium(II) complexes **1–3**; in fact it would be obvious to suppose an easier formation of under-ligated palladium(0) species with the Pd(NN')(dmfu) complexes, where a zerovalent metal nucleus is already present in the starting complex. However, the robustness of these complexes is enhanced by the presence of the π-acceptor dmfu ligand, which, even after ligand dissociation, could retard the oxidative addition step.

Finally, the catalytic activities of the reported palladium complexes are superior with respect to those obtained in heterogeneous conditions, where the coupling of iodobenzene with methyl acrylate brought to a 82% conversion after 24 h of reaction [13].

4. Conclusions

Simple palladium(0) and palladium(II) complexes containing pyridyl-aldimine or pyridyl-ketimine ligands promote the Heck coupling between iodobenzene and methyl acrylate. The pre-catalysts probably act as palladium reservoirs during the catalysis, giving rise to active palladium(0) species. This study has allowed the isolation of the dimer [Pd₂I₆][Et₃NH]₂ which forms at the end of the reaction, probably via the palladium metal particles formed during the catalysis. Interestingly, the reaction of PdCl₂ with PhI and methyl acrylate in DMF leads to the dimer [Pd₂I₆][DMFH]₂, where two protonated DMF molecules are the countercations of the very stable anion dimer [Pd₂I₆]²⁻. The same dimer partially forms from the reaction of **1** with PhI and methyl acrylate in DMF.

Acknowledgments

The C.I.M. (Centro Interfacoltà di Misure “Giuseppe Casnati”) of the University of Parma is thanked for the instrument facilities. Mr. Giuseppe Foroni is thanked for his technical support.

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