

Pd/C: an efficient, heterogeneous and reusable catalyst for carbon monoxide-free aminocarbonylation of aryl iodides

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Received 12 December 2007; revised 29 January 2008; accepted 10 February 2008

Available online 13 February 2008

Abstract

Carbon monoxide-free aminocarbonylation is carried out efficiently via coupling of *N,N*-dimethylformamide (DMF) with aryl iodides using Pd/C as a heterogeneous catalyst. The catalyst exhibits remarkable activity and is reusable for up to three consecutive cycles. The reaction is applicable to a wide variety of substituted aryl iodides with different steric and electronic properties providing excellent yields of the corresponding tertiary amides.

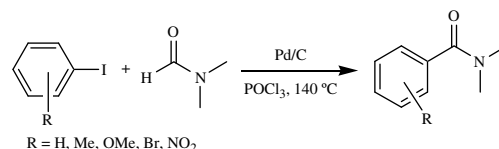
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Keywords: Carbonylation; Aryl iodides; Amides; Palladium; Heterogeneous catalyst

Catalytic reactions are generally classified as homogeneous and heterogeneous depending on the nature of the catalyst employed. It is well known that homogeneous catalysts consisting of soluble metal complexes have high activity and selectivity compared to heterogeneous catalysts.^{1,2} In spite of their potential utility their application is limited due to difficulties encountered in catalyst-product separation. Additionally the ligands (usually phosphine ligands) which are required to stabilize the transition metal ion are air/moisture sensitive, expensive and require special handling techniques. To overcome these drawbacks several modifications of these catalysts have been developed,^{3–5} such as anchoring of the metal complex to a polymeric or mineral support,⁶ supported liquid phase catalysis,^{7,8} biphasic catalysis⁹ and transition metals on activated carbon.^{10–14} As such, these catalysts can be easily recovered from the reaction medium and reused further.

Palladium catalyzed aminocarbonylation (Heck carbonylation) is a selective and useful method for the direct synthesis of amides from aryl, heterocyclic and alkenyl halides

by reaction with primary or secondary amines. Traditionally, carbon monoxide gas is the most commonly employed source of the carbonyl group in these transformations.^{15–17} However, the use of sophisticated instruments such as high pressure reactors, troublesome gas handling procedures and the toxicity of carbon monoxide limits the use of carbonylation reactions for the synthesis of compound libraries. To overcome these difficulties, carbon monoxide-free syntheses of amides using various other sources such as formamide, metal carbonyls and DMF have been reported.^{18–21} Recently, Ju et al. reported aminocarbonylation of aryl halides using Ni/phosphite as the catalytic system.²² However, despite their potential utility, the above methods suffer from the drawback of catalyst-product separation thereby limiting their application. Also, in many cases, the catalysts used are homogeneous and are not



Scheme 1. Pd/C catalyzed aminocarbonylation of aryl iodides.

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recyclable. The loss of a palladium catalyst, even at ppm level, is not desirable due to its high cost. Therefore, the search for a heterogeneous and reusable catalyst which could efficiently catalyze the aminocarbonylation reaction is the subject of the present work.

We herein report an efficient carbon monoxide-free aminocarbonylation of aryl iodides using Pd/C as a heterogeneous and reusable catalyst in the presence of DMF and phosphoryl chloride (Scheme 1). The catalyst showed remarkable activity and the system tolerates a wide variety of functional groups such as NO₂, Br, CH₃ and OCH₃ on the aryl halide. The catalyst was also found to be reusable for up to three consecutive cycles without any significant loss in activity.

To optimize the reaction conditions, the coupling of *N,N*-dimethylformamide with iodobenzene in the presence of POCl₃ was chosen as a model system. The influence of various parameters such as temperature, catalyst and catalyst loading (Table 1) was examined on the model reaction.

The reaction was carried out at five different temperatures (80, 100, 120, 140 and 160 °C). It was observed that at 80 °C the yield of the desired product was too low. On increasing the temperature to 140 °C, a 76% yield was obtained within 24 h. Although a similar result was obtained when the reaction was carried out at 120 °C, at 140 °C thermal redeposition of the catalyst was more effective as discussed later. With further increase of the temperature to 160 °C, the yield of the desired product decreased to 68%. Hence, 140 °C was the optimum temperature for this reaction. The effect of various catalysts on the reaction was investigated (Table 1, entries 6–10). Several homogeneous palladium salts with and without ligands were tested. Both Pd(OAc)₂ and PdCl₂ provided 59% and 73% yields of the desired product. The use of PdCl₂/4PPh₃ was found to be ineffective. Since the reusability of the catalyst was the primary aim of this study 5% and 10% Pd supported on activated carbon (Pd/C) were employed as the catalyst. However, 5% Pd/C afforded only a 16% yield whereas 10% Pd/C gave 76% yield of the desired tertiary amide. In an effort to determine the optimum concentration of the catalyst, various catalyst loadings were studied as shown in Table 1 (entries 11–14). The yield increased on increasing the catalyst concentration. Optimum results with respect to yield (76%) were obtained when 10 mol % of Pd/C was used. Hence, the optimum reaction parameters were: temperature 140 °C, 10% Pd/C, 10 mol % catalyst loading and a time of 24 h.

Table 1
Effect of reaction parameters on the aminocarbonylation of PhI^a

Entry	Catalyst	Temp (°C)	Catalyst loading (mol %)	Yield ^b (%)
<i>Influence of temperature</i>				
1	Pd/C (10%)	80	10	43
2	Pd/C (10%)	100	10	64
3	Pd/C (10%)	120	10	76
4	Pd/C (10%)	140	10	76
5	Pd/C (10%)	160	10	68
<i>Influence of catalyst</i>				
6	Pd(OAc) ₂	140	10	59
7	PdCl ₂	140	10	73
8	Pd/C (10%)	140	10	76
9	Pd/C (5%)	140	10	16
10	PdCl ₂ /4PPh ₃	140	10	No reaction
<i>Influence of catalyst loading</i>				
11	Pd/C (10%)	140	2.5	35
12	Pd/C (10%)	140	5	58
13	Pd/C (10%)	140	10	76
14	Pd/C (10%)	140	15	78

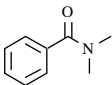
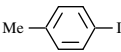
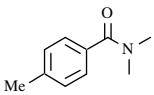
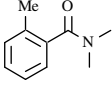
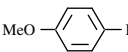
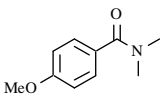
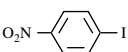
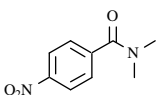
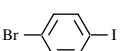
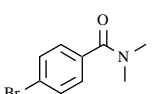
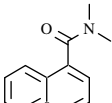
^a Reaction conditions: Iodobenzene (1 mmol), POCl₃ (2 mmol), DMF (10 ml), time = 24 h.

^b Yields based on GC analysis.

The scope of Pd/C as the aminocarbonylation catalyst was further demonstrated in the reaction of various substituted aryl halides with DMF in the presence of POCl₃. The desired products were obtained in good to moderate yields (Table 2, entries 1–7).²³

The reaction of iodobenzene with DMF proceeded smoothly providing a 76% yield of *N,N*-dimethylbenzamide. Various electron-donating and electron-withdrawing groups on the aryl halide such as Me, OMe and Br were well tolerated to give the desired tertiary amides in good yields. 4-Iodonitrobenzene which is a deactivated substrate

Table 2
Pd/C catalyzed aminocarbonylation of aryl iodides^a

Entry	Aryl iodide	Product	Yield ^b (%)
1			76
2			73
3			68
4			70
5			66
6			63
7			67

^a Reaction condition: aryl iodide (1 mmol), Pd/C (0.1 mmol), POCl₃ (2 mmol), DMF (10 ml) at 140 °C, time = 24 h.

^b Isolated yields.

for coupling reactions (since it is easily dehalogenated to the corresponding arene) afforded a satisfactory yield of the desired product (entry 5). *ortho*-Substituents on the aryl halide were also viable partners for the coupling reaction. Encouraged by these results, the catalyst was then utilized for the aminocarbonylation of sterically hindered 1-iodonaphthalene to afford a 67% yield of *N,N*-dimethylnaphthamide. Thus the protocol is effective for the coupling of aryl iodides having different steric and electronic properties.

The methodology was further extended to the coupling of formamide and its derivatives with aryl iodides. However, no coupling product was observed. Similarly, the reaction of bromobenzene with DMF was also attempted, but no product formation was detected. Thus, only aryl iodides and DMF are viable partners for these coupling reactions.

The reusability of the catalyst was also examined in the standard reaction of iodobenzene with DMF. It is well known that the supported palladium leaches out into the solvent and the reaction is catalyzed mainly by these dissolved palladium species. To reuse the catalyst, redeposition of palladium was attempted using methods such as (a) chemical redeposition in which a reducing agent like sodium formate is added to the solution, (b) chemical redeposition using ultrasound,¹³ and (c) thermal redeposition which can occur in situ at higher temperature.¹⁰ Redeposition of the catalyst was monitored using ICP-AES analysis. When chemical redeposition using sodium formate in the presence of ultrasound was performed, ICP-AES analysis of the reaction mixture revealed the palladium content to be 43.65 ppm. We then attempted thermal redeposition. At 120 °C thermal redeposition was not effective and the Pd content of the reaction mixture was found to be 37.79 ppm, whereas at 140 °C efficient redeposition of Pd took place and the Pd content was found to be 4.45 ppm which is also in agreement with literature reports for similar catalyst systems used for the Heck reaction.¹⁰

The redeposited catalyst was then given prior treatment and used for the next cycle.²⁴ The catalyst required activation at 200 °C for 12 h prior to the next recycle and gave a 74% yield of the desired product. Thus the catalyst was successfully recycled and the reusability procedure was tested up to three times and consistent results were obtained (Fig. 1).

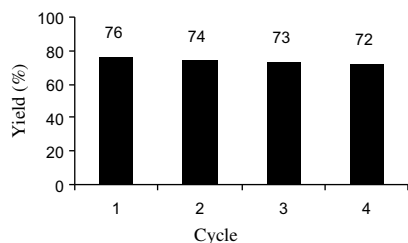
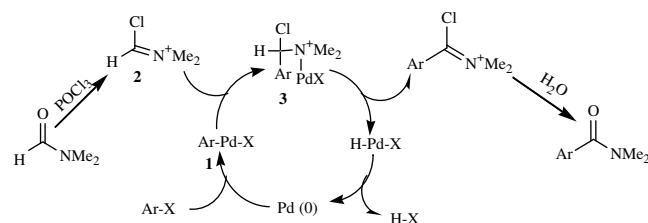


Fig. 1. Catalyst reusability.



Scheme 2. Mechanism of the reaction.

The probable mechanism for the aminocarbonylation of the aryl iodide is shown in Scheme 2. Initially, oxidative insertion of Pd(0) into the C–X bond produces an aryl palladium halide **1** under the present reaction conditions.²⁵ Then nucleophilic addition of the aryl palladium halide to the iminium salt **2** (generated from the reaction of POCl₃ and DMF, also known as the Vilsmeier reagent) occurs to form **3**, which undergoes β-hydride elimination followed by hydrolysis to give the desired product. As earlier reported by Hosoi et al.,²¹ the formation of the Vilsmeier reagent in this case is essential for the reaction to occur and no base is employed to regenerate Pd(0) from hydro palladium halide species (H–Pd–X).

In conclusion, we have reported an efficient, heterogeneous and reusable catalyst system for the carbon monoxide-free synthesis of various substituted tertiary amides. The reaction was optimized with respect to various parameters and could be used for the coupling of electron-rich, electron deficient and sterically hindered aryl iodides. Catalyst reusability and Pd leaching were also examined and effective redeposition of Pd metal on the support was carried out using thermal deposition.

Acknowledgement

Financial assistance from the Technical Education Quality Improvement Programme (TEQIP), Government of India is kindly acknowledged.

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23. *General procedure for the aminocarbonylation of aryl halides:*
A mixture of aryl iodide (1 mmol) and Pd/C (10 mol %) in DMF (10 ml) was taken in a 25 ml two-necked round-bottom flask and stirred for 10 min at room temperature. Then POCl₃ (2 mmol) was added to the reaction mixture with stirring over a period of 15 min. The reaction mixture was magnetically stirred at 140 °C for 24 h under nitrogen. After completion, the reaction mixture was cooled to room temperature and filtered using a sintered funnel. The filtrate was poured into a saturated solution of NaHCO₃. The aqueous layer was then extracted with ethyl acetate. The combined organic layers were dried over Na₂SO₄ and the solvents were removed in vacuo to afford the crude product which was purified by column chromatography using chloroform/methanol as eluent. *Spectral data for selected products:*
Table 2, entry 1: ¹H NMR (300 MHz, CDCl₃, 25 °C, TMS): δ 3.1 (s, 6H), 7.4 (s, 5H) ppm. ¹³C NMR (100 MHz, CDCl₃, 25 °C, TMS): δ 35.4, 127.1, 128.4, 129.6, 136.4, 171.8 ppm. MS (70 eV, EI): *m/z* (%): 149 (27) (M⁺), 148 (59), 105 (100), 77 (62).
Table 2, entry 4: ¹H NMR (300 MHz, CDCl₃, 25 °C, TMS): δ 2.9 (s, 6H), 3.8 (s, 3H), 6.9 (d, *J* = 2.1 Hz, 6.6 Hz, 2H), 7.41 (dd, *J* = 2.1 Hz, 6.6 Hz, 2H) ppm. ¹³C NMR (75 MHz, CDCl₃, 25 °C, TMS): δ 35.3, 55.1, 113.3, 128.1, 128.9, 162.4, 171.3 ppm. MS (70 eV, EI): *m/z* (%): 179 (19) (M⁺), 178 (25), 135 (100), 77 (24).
Table 2, entry 5: ¹H NMR (300 MHz, CDCl₃, 25 °C, TMS): δ 2.9 (s, 6H), 7.7 (dd, *J* = 2.1 Hz, 6.9 Hz, 2H), 8.3 (dd, *J* = 2.1 Hz, 6.9 Hz, 2H), ppm. ¹³C NMR (75 MHz, CDCl₃, 25 °C, TMS): δ 35.3, 123.7, 128.0, 142.5, 148.2, 169.2 ppm. MS (70 eV, EI): *m/z* (%): 194 (35) (M⁺), 193 (100), 150 (82), 104 (55).
24. *Procedure for catalyst recycling:* The catalyst obtained after filtration was washed with saturated NaHCO₃ solution (5 ml × 3) to remove any acidic impurities if present and then with water (5 ml × 3) and finally with dichloromethane (5 ml × 3) to remove any organic impurities. The resulting catalyst was dried in oven at 200 °C for 12 h and used for the next cycle.
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