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Ligand-free C-C and C-N cross-couplings with Pd /Nf-G nanocomposite

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ARTICLE INFO	ABSTRACT
Article history:	The catalytic activity of electrochemical deposited Pd nanoparticles on nafion-graphene support
Received	was examined for Buchwald-Hartwig amination reaction and Heck coupling reaction. The
Received in revised form	developed protocol is very efficient and ecofriendly, providing excellent product yield. The
Accepted	Pd/Nf-G catalyst can be used up to four cycles with slight decrease in catalytic activity.
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Palladium catalyzed reactions are important in synthetic organic chemistry, especially palladium catalyzed coupling and amination reactions $^{\rm I-4}$. The C-C and C-N bond forming palladium catalyzed reactions are one of the best alternatives for synthesis natural products, pharmaceutically and chemically applicable products⁵⁻⁸. These coupling reactions were carried out by various homogeneous catalysts with an excellent activity⁹⁻¹⁴. However, from industrial point of view, homogeneous systems are not suitable because of issues related to recovery and reusability. To address these issues, solid supported metal nano particles (heterogeneous catalyst) are the best alternative for homogeneous systems. The variety of heterogeneous solid supported palladium catalysts were reported to accomplish these coupling reactions¹⁵⁻¹⁸. Palladium is special metal due to its high catalytic activity at the nanoscale. Now days, Pd-based supported catalysts have been prepared and used as the electrocatalyst for electrochemical oxidation of alcohols^{19, 20}. In addition to this it finds applications in carbon-carbon bond forming coupling reactions^{21, 22}. Although in case of some heterogeneous catalysts, there is difficulty in reducing surface area with agglomeration of nano particles, mechanical and thermal stability of catalyst, use of capping agent, long and non-ecofriendly route of preparation, which have an effect on catalyst activity and environment. In order to overcome these issues, herein we explore catalytic activity of Pd/Nf-G in continuation with our previous report²³ for C-C and C-N coupling reactions as heterogeneous catalyst. It is easiest to control the size and morphology of nano particles by electrochemical method. Electrochemical deposition of metal nano particles is one of the most useful approaches to prepare supported metal nano particles. Furthermore, compared with the chemical reduction methods, no capping reagent is used in the electro deposition method. Consequently, the synthetic procedures can be simplified to a greater extent. Graphene is used as catalyst support due to its good mechanical strength and thermal stability, high conductivity and enormous surface area. Moreover, graphene based composite with different metals like Pd, Pt and Au has been used as electro catalyst for the different kinds of oxidation and reduction reactions²⁴⁻²⁶. However, to the

best of our knowledge, there is no report on application of electrochemically prepared Pd/Nf-G catalyst for Buchwald–Hartwig amination and Heck reactions.

As synthesized nano Pd/Nf-G catalyst has been extensively screened for its catalytic activity against the C-C and C-N bond forming reactions. Initially, the Pd/Nf-G has been employed to catalyzed Buchwald Hartwig amination reactions The model Buchwald Hartwig amination reaction was selected by taking a mixture of iodobenzene (1mmol) and morpholine (1mmol) in DMSO using tBuONa as a base at 110 °C for 12h using Pd/Nf-G as a catalyst (Scheme 1).



Scheme1. Buchwald-Hartwig amination reaction catalyzed by Pd/Nf-G.

To fix the various reaction parameters for this model reaction we have carried out a broad optimization study. Initially, variety of solvents has been screened out such as DMSO, DMF, NMP, dioxane and toluene. It was found that DMSO was the best solvent for the reaction (Table 1, entries 1-5). We have also carried out reaction in mixture solvents with water the product yield was very low (Less than 10%) after 24 hrs. In selection of appropriate base for this reaction, base study also carried out and the obtained results showed that out of K_2CO_3 , K_3PO_4 , NEt₃ and tBuONa, tBuONa gave excellent yield of the product (Table1,

Tetrahedron Letters

entries 1, 6-8). Temperature effect was found significantly; 110 $^{\circ}$ C was the required temperature for this transformation to obtained desire product in high percent (Table 1, entries 1, 9, 10). Then Pd loading was monitored get maximum yield of the product. Pd loading, 0.2 mol% was found to be sufficient for higher yield (Table 1, entries 1, 11, 12). Conversion of the iodobenzene into product is 98 % with above reaction conditions. In this reaction no homocoupling product was observed. The progress of reaction has been monitored by GC and the graph of GC yield versus time showed that after 12h, the yield of desire product was high (Fig. 1).



Fig. 1 The plot of GC yield (%) versus time (h)

 Table 1. Optimization of reaction condition for Buchwald-Hartwig

 amination reaction of iodobenzene and morpholine^a

Entry	Solvent	Base	Catalyst	Temperature	Yield
			loading		$(\%)^{b}$
1.	DMSO	^t BuONa	0.2	110 °C	97
			mol%		
2.	DMF	^t BuONa	0.2	110 °C	93
			mol%		
3.	NMP	^t BuONa	0.2	110 °C	90
			mol%		
4.	Dioxane	^t BuONa	0.2	110 °C	79
			mol%		
5.	Toluene	^t BuONa	0.2	110 °C	84
			mol%		
6.	DMSO	K ₂ CO ₃	0.2	110 °C	68
			mol%		
7.	DMSO	K ₃ PO ₄	0.2	110 °C	76
			mol%		
8.	DMSO	Et ₃ N	0.2	110 °C	64
			mol%		
9.	DMSO	^t BuONa	0.2	80 C	75
			mol%		
10.	DMSO	^t BuONa	0.2	60 °C	51
			mol%		
11.	DMSO	^t BuONa	0.1	110 °C	73
			mol%		
12.	DMSO	^t BuONa	0.3	110 °C	97
			mol%		

^aReaction conditions: Iodobenzene(1mmol), Morpholine(1mmol), Base(1mmol), Solvent(1mL) for 12h. ^bGC yield.

To investigate the catalytic activity of nano sized Pd/Nf-G, we have showed a wide substrate study by using different

substituents on aromatic ring of aryl halides or by changing

Table 2. Buchwald-Hartwig amination reactions of aryl halides with secondary amines by using Pd/Nf-G^a.

Entry	Aryl halides	Secondary amines	Products	Yield (%) ^b
1.				93
2. oʻ				95
3. _{Н₃} сс	x Br	HN O H3CC		84
4.	NC	Br		86
5. н _я с		HN O H ₃ C		89
6.				87
7.		,Br HNO		84
8.	F	.Br HNO	FNO	77
9.				75
10.	\sqrt{s}	HNO		69
11.		HN		94
12.		HNNN- (N	92
13.				89
14.	\bigcirc	HN-		95
15.				91

^aReaction conditions: Aryl halides (1 mmol), Secondary amines (1 mmol), ^bBuONa (1 mmol), DMSO (1 mL) at 110 °C for 12h. 0.7 mg of Pd/Nf-G (0.2 mol% or 0.21 mg of Pd) ^bIsolated yield.

variety of secondary amines and the results are summarized in Table 2. Initially the catalyst efficiency was evaluated for various substituted iodobenzene and bromobenzene with morpholine and moderate to excellent yield of products were obtained. The

Tetrahedron Letters

catalyst afforded good yield of product for both electronwithdrawing substituents (-NO₂, -COCH₃ and -CN) and electrondonating substituents (-OMe, -CH₃ and -F) (Table 2, entries 1-8). However, iodobenzene exhibit greater activity than bromobenzene.

In addition to Buchwald-Hartwig amination reaction, we have also studied catalytic application of nano Pd/Nf-G for Heck cross coupling reactions. The Heck reaction of iodobenzene (1mmol) and ethyl acrylate (2mmol), NEt₃ as a base in DMF at 120 °C for 2h in presence of Pd/Nf-G catalyst was found to be best model reaction after employing various optimized reaction parameters (Scheme 2).



Scheme 2. Heck cross coupling reaction catalyzed by Pd/Nf-G

To confirm various parameters we have screened various solvents, reaction in DMF gave higher yield of the product (Table 3, entries 1-4). We have tried reaction in mixture of solvents with water the product yield was very low after 24 hrs. Base study showed that NEt₃ was suitable base to increase catalyst performance (Table 3, entries 1, 5-7). Variation in temperature also affects the product yield, temp. 120 °C gave higher yield of product (Table 3, entries 1, 8-11). To accomplish this reaction to larger extent, Pd loading has been examined and it showed that 0.3 mol% was enough to achieve maximum yield of the product (Table 3, entries 1, 12, 13). Conversion of iodobenzene into product was 100%. This indicates excellent selectivity towards the reaction product. The graph shown in Fig. 2 is based on GC yield which explain the progress of reaction with increasing time.

Table 3. Optimization of reaction conditions for Heck cross coupling reaction of iodobenzene and ethylacrylate^a.

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Entry	Solvent	Base	Catalyst loading	Temperature	Yield (%) ^a
1.	DMF	Et ₃ N	0.3	120 °C	95
2.	NMP	Et ₃ N	0.3	120 °C	87
3.	Toluene	Et ₃ N	0.3 mol%	120 °C	69
4.	DMSO	Et ₃ N	0.3 mol%	120 °C	88
5.	DMF	K ₂ CO ₃	0.3 mol%	120 °C	75
6.	DMF	K ₃ PO ₄	0.3	120 °C	64
7.	DMF	NaOH	0.3	120 °C	51
8.	DMF	Et ₃ N	0.3 mol%	100 °C	81
9.	DMF	Et ₃ N	0.3 mol%	80 °C	60
10.	DMF	Et ₃ N	0.3	60 °C	38
11.	DMF	Et ₃ N	0.3	RT	<10 ^c
12.	DMF	Et ₃ N	0.2	120 °C	73
13.	DMF	Et ₃ N	mol% 0.4 mol%	120 °C	95

^aReaction conditions: Iodobenzene (1mmol), Ethylacrylate (2mmol), Base (2mmol), Solvent (1mL) for 2h. ^bGC yield. ^cYield after 24h

 Table 4. Heck cross coupling reactions of aryl halides and olefins by using Pd/Nf-G^a.



^aReaction conditions: Aryl halides (1mmol), Olefins (2mmol), Et₃N (2mmol), DMF (1mL) at 120 °C. 1mg of Pd/Nf-G (0.3 mol% or 0.32 mg of Pd) ^bIsolated yield.

Tetrahedron Letters



Fig. 2 The plot of GC yield (%) versus time (h) for scheme 2.

On the basis of above optimized parameters we have also carried out the substrate study for Heck coupling with Pd/Nf-G catalyst. In substrate study, various substituted aryl halides has been successfully coupled with different alkenes. The presence of substituents on aromatic ring of halides has pronounced effect on yield of desire products. Substituents such as -NO₂, -COCH₃ of aryl halides gave good response as compare to -NH₂, -OMe, -OH, -CH₃, substituents (Table 4, entries 1-7). However, substituted aryl bromide afforded excellent yield of corresponding products but required longer reaction time (Table 4, Entries 3, 11 and 15). This is because of high bond energy of the C-Br bond. The heterocyclic 2-iodothiophene derivative easily coupled with alkenes and gives moderate yield of product (Table 4, entry 8). The reactions between iodobenzene and different alkenes has been tested against Pd/Nf-G catalyst and found that all reactions efficiently gave high product yield with 100 % selectivity (Table 4, entries 9-15). However, selectivity of trans styrene (88% and 90%, Table 4 entries 14 and 15) is higher than cis styrene (4% and 5%)

Industrially catalyst recovery and recyclability has greater importance. For this purpose we have assessed recyclability of Pd/Nf-G composite for reaction of iodobenzene with morpholine (Scheme 1) and also for reaction of iodobenzene with ethyl acrylate (Scheme 2). For recyclability study Pd loading was 0.2 mol% and 0.3 mol% for scheme 1 and scheme 2 respectively. After completion of reactions catalyst was separated from reaction mixture by decantation, washed with ethyl acetate and dried at room temperature. The recovered catalyst was successively reused for next five cycles under same reaction conditions. The results showed that the catalytic activity was decreased after fourth cycle due to aggregation and leaching of Pd NPs during recycling experiment (Fig. 3). The amount of Pd lost after fourth cycle is 4% and 5% (0.0084 mg of and Pd 0.02 mg of Pd) for scheme 1 and scheme 2 respectively as determined by ICP-AES. This clearly indicates that Pd/Nf-G has greater stability and activity.



Fig. 3 The plot of GC yield (%) versus Run

In conclusion we have explored catalytic activity of Pd/Nf-G composite as catalyst for Buchwald-Hartwig amination and Heck coupling reactions. The catalyst showed excellent activity against these C-N and C-C bond forming reactions with simple methodology. The stability of catalyst has been confirmed by recyclability. The Pd/Nf-G catalyst can be used up to four cycles with slight decrease in catalytic activity.

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