

Efficient Sonogashira and Suzuki-Miyaura coupling reaction catalyzed by Pd-Nanoparticles

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Abstract. The Pd nano particles were electrochemically deposited on nafion-graphene. They showed excellent catalytic activity towards Sonogashira and Suzuki-Miyaura cross-coupling reaction. Benzenediazonium salts were used as alternative to aromatic halide. The developed protocol offers recyclability, easy workups with short reaction time and good-to-excellent product yield.

Keywords. Electrochemistry; Palladium nanoparticles; Nafion-graphene; heterogeneous recyclable catalyst.

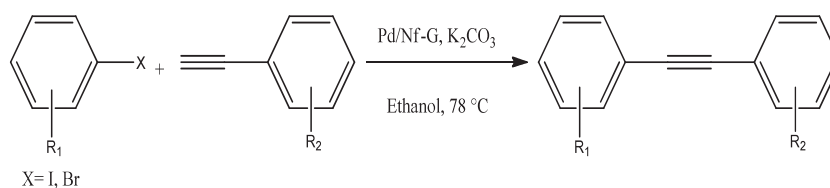
1. Introduction

Various cross-coupling reactions such as Suzuki, Heck and Sonogashira have been used in organic synthesis.¹ These reactions have wide industrial applications in synthesizing pharmaceutical and agrochemical compounds.² Recently, Sonogashira and Suzuki cross-coupling reactions were extensively studied for the C-C bond forming transformations. A number of homogeneous palladium catalysts such as Pd(II) phosphine-ylide complexes,³ Pd(II)diamino carbene,⁴ oxime-based palladacycle⁵ and Pd(OAc)₂, Pd₂dba₃ with appropriate ligands,⁶ have been reported to achieve these transformations with the advantages of fast reaction rates, good selectivity and high product yield.⁷ However, these homogeneous catalytic systems have some limitations. The ligands used in the above reported methods are either very expensive or their synthesis is very tedious. Moreover, the catalysts are not reusable. Heterogeneous catalysts can be recovered and reused at least for a few cycles as compared to homogeneous catalytic systems. A number of heterogeneous catalysts such as Pd on MOF-5,⁸ hybrid silica based Pd(II)complex,⁹ organosilica-SBA-15,¹⁰ Pd-grafted mesoporous silica,¹¹ and Pd(0)/BaSO₄,¹² were reported. Polymer-supported N-heterocyclic carbene-palladium,¹³ palladium on charcoal¹⁴ and aluminum hydroxide-supported palladium nanoparticles¹⁵ have also been reported as catalysts. It is observed that the supporting material plays an important role in catalytic activity of heterogeneous catalyst. In most of the cases, the supported heterogeneous Pd catalyst suffers from problems such as

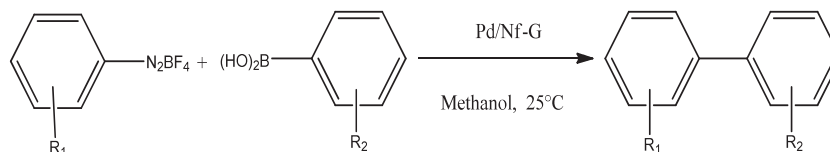
thermal instability, high surface area and agglomeration of nanoparticles. Graphene has wide scope in catalysis as a support material due to its high surface area, thermal as well as mechanical stability, and electrical conductivity.^{16,17} Additionally, graphene has applications in various fields such as fuel cell, nanocomposite materials and electronic devices.^{18–20} The electrochemically synthesized catalyst is environmentally favourable having high stability and large surface area with dispersed Pd nanoparticles. Besides these advantages, electrochemical processes are heterogeneous in nature which regulates the size and morphology of Pd nano particles. Various coupling reactions were carried out by using electrochemically synthesized nano-Pd catalysts.^{21,22} Earlier, we have reported electrochemically synthesized nano-Pd particles on nafion-graphene support (Pd/Nf-G) as an efficient heterogeneous catalyst for Suzuki coupling reaction.²³ Herein we report the Sonogashira and Suzuki-miyaura coupling reactions by using electrochemically synthesized Pd on nafion-graphene support as a catalyst. The Sonogashira cross coupling between aryl halides and terminal alkynes is one of the important reactions in organic chemistry. We have carried out the ligand-free, copper co-catalyst-free and amine-free synthesis of aryl alkynes from substituted iodobenzenes and bromobenzenes with phenyl acetylene derivatives in ethanol as the solvent and K₂CO₃ as the base at 78°C. The reaction time varies from 6–12 h depending on the nature of substituted aryl halide (scheme 1).

The research work was further extended to explore the catalytic activity of Pd/Nf-G for Suzuki-Miyuara cross coupling reactions. Benzenediazonium tetrafluoroborate salts are the best alternative to the very

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Scheme 1. Sonogashira coupling reaction catalyzed by Pd/Nf-G.



Scheme 2. Suzuki-Miyaura coupling reaction catalyzed by Pd/Nf-G.

Table 1. Optimization of reaction parameters for Sonogashira reaction catalyzed by Pd/Nf-G.^a

Entry	Solvent	Base	Temp °C	Catalyst loading (mol%)	Time (h)	Yield ^b (%)
1.	CH ₃ CN	K ₂ CO ₃	80	0.3	9	45
2.	DMF	K ₂ CO ₃	100	0.3	8	65
3.	Water	K ₂ CO ₃	100	0.3	10	50
4.	Ethanol-Water (1:1)	K ₂ CO ₃	78	0.3	9	66
5.	Dioxane	K ₂ CO ₃	100	0.3	8	70
6.	Ethanol	Pyrolidine	78	0.3	6	58
7.	Ethanol	TEA	78	0.3	6	65
8.	Ethanol	K ₂ CO ₃	78	0.3	6	97
9.	Ethanol	K ₂ CO ₃	78	0.2	6	92
10.	Ethanol	K ₂ CO ₃	78	0.1	8	88
11.	Ethanol	K ₂ CO ₃	78	0.4	6	97

^aReaction conditions: iodobenzene (0.5 mmol), phenyl acetylene (0.75 mmol), base (1.25 mmol), solvent (3 mL), catalyst Pd/Nf-G (0.3 mol%), temperature (78°C).

^bIsolated yield based on column chromatography.

expensive aryl halides. Hence, the Suzuki-Miyaura cross-coupling reactions were carried out by using substituted boronic acids and various benzenediazonium tetrafluoroborate salts in methanol as solvent. The reactions were carried out at ambient temperature with reaction time varying from 2–4 h (scheme 2).

2. Experimental

2.1 Chemicals

All chemicals are of analytical grade and are used without further purification. Graphite powder, sulphuric acid, sodium nitrate, hydrogen peroxide (30 wt%), ammonia solution, hydrochloric acid, hydrazine hydrate, ethanol were procured from Merck. 5 wt% Nafion solution in lower aliphatic alcohols (Alfa

Aesar), palladium (II) chloride (99.9%) were purchased from Sigma-Aldrich.

2.2 Preparation of graphene oxide

The graphene oxide (GO) was prepared from graphite by using Hummers method.²⁴ Initially 1 gm of graphite powder was added to previously cooled 50 mL concentrated H₂SO₄ in round bottom flask, followed by addition of 0.8 g of NaNO₃. Then 3 g of KMnO₄ was added slowly and by maintaining the temperature of reaction mass below 20°C. The reaction mixture was stirred for 30 min at 35°C followed by addition of 46 mL distilled water with continuous stirring. The resulting suspension was heated at 97°C for 15 min. The suspension was cooled to room temperature and then 10 mL of 30% H₂O₂ was slowly added to it with constant stirring. The entire suspension was centrifuged to get GO. It was

washed with 5% HCl followed by distilled water and finally with ethanol. The obtained GO was dried under vacuum for 12 h at 60°C.

2.3 Synthesis of graphene


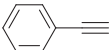
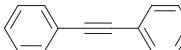
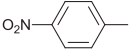
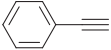
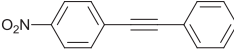
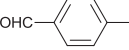
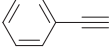
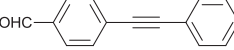
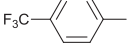
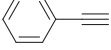
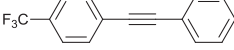
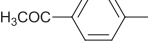
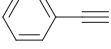
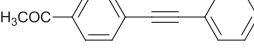
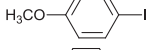
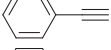
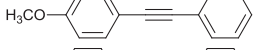
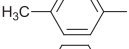
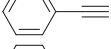
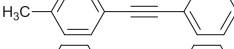
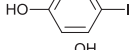
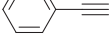
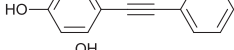

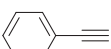
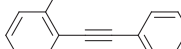
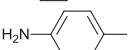
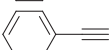
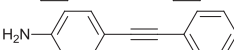


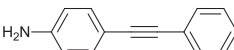

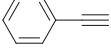
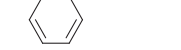

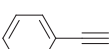
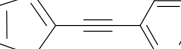

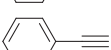
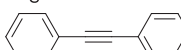
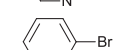
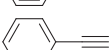
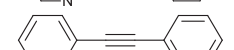
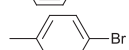
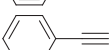
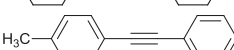

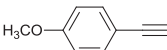
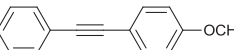


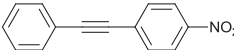
The GO powder was dispersed in distilled water (0.05 wt%) and subjected to ultrasonication for 10 min. 25 mL of dispersion was transferred to 100 mL round bottom flask followed by addition of 44 mL of distilled water, 154 μ L of ammonia and 22 μ L of hydrazine hydrate. The reaction mass was refluxed

at 95°C for 1 h to get a homogeneous dispersion of graphene.

2.4 Preparation of Nf-G platinum plate

From above solution, 50 μ L graphene dispersion having concentration (0.18 μ g/ μ L) was added to the 100 μ L of 5 wt% Nafion-ethanol solution and the mixture was sonicated for 100 s to get the homogeneous dispersion. Nf-G dispersion was spread over the platinum plate by using syringe and the plate was subsequently dried in air to get thin film of Nf-G.

Table 2. Pd/Nf-G catalyzed Sonogashira reaction of various aryl iodide and bromide with various phenyl acetylene.^a

Entry	Aryl halides	Phenyl Acetylene	Products	Time (h)	Yield ^b (%)
1.				6	97
2.				6	97
3.				7.5	95
4.				6	96
5.				7	94
6.				8	94
7.				9	93
8.				10	91
9.				10	89
10.				10	89
11.				8	93
12.				10	94
13.				11	92
14.				12	65
15.				12	58
16.				10	75
18.				6	97
19.				8	90

^aReaction conditions: aryl halide (0.5 mmol), phenyl acetylene (0.75 mmol), K₂CO₃ (1.25 mmol), ethanol (3 mL), catalyst Pd/Nf-G (0.3 mol%), temperature 78°C.

^bIsolated yield based on column chromatography.

2.5 Electrochemical deposition of Pd NPs on Nf-G modified Pt plate

The electrochemical deposition of Pd was carried out in aqueous solution of 10 mM PdCl₂ at -0.2 V for the period of 60 s by using three electrode cyclic voltammetry technique. In this system, the Nf-G modified Pt plate as the working electrode, saturated calomel (SCE) as the reference and platinum rod as the counter electrode were used. Pt plate was removed from solution after 60 s and dried in the air. The deposited Pd NPs on to Nf-G film were scrapped with stainless steel blade and preserved for further use.

3. Result and Discussion

3.1 Sonogashira reaction

Our first approach was to optimize reaction conditions for the reaction between iodobenzene and phenylacetylene as a model reaction. The results are summarized in table 1. We started optimization study with variety of solvents (table 1, entry 1–6). All the solvents gave good conversion but the excellent results were obtained with ethanol. Ethanol also helped in reducing the leaching of Pd nano particles (table 1, entry 8). Ethanol-water or water as solvent gave lower product yield (table 1, entries 3–4). Sonogashira coupling is strongly influenced by the nature of the base. We have applied several bases (table 1, entries 6–8) among which K₂CO₃ gave maximum conversion and selectivity (table 1, entry 8). Increase in Pd content from 0.3 mol% to 0.4 mol%

did not show any significant increase in product yield (table 1, entries 8 and 11). Therefore, 0.3 mol% Pd loading at 78°C temperature and 6 h reaction time were the optimized reaction parameters for the model reaction (table 1, entry 8).

Under these optimized conditions, we carried out substrate study using various substituted iodo and bromo benzene derivatives and phenyl acetylene as starting materials. We tried reaction of both electron donating as well as electron withdrawing substituents of iodobenzene and bromobenzene with substituted phenyl acetylene which exhibits excellent reactivity towards the Pd/Nf-G. The electron withdrawing substituents (table 2 entries 2–5, 16) gave greater yield as compared to electron donating groups (table 2 entries 6–10, 12–13). The electron withdrawing groups facilitate the removal of iodide and bromo group. Some heterocyclic iodo derivatives also gave excellent yields (table 2 entries 12–13). The 2-hydroxy iodobenzene gave lower yield as compared to that of 4-hydroxy iodobenzene which may be due to steric hindrance (table 2, entries 8–9). Excellent product yields were obtained when we carried out experiments using substituted phenyl acetylene. It was found that the catalyst showed good activity for electron donating group as compared to electron withdrawing group (table 2, entries 18–19).

3.2 Suzuki-Miyaura coupling reaction

We further explored the applicability of catalyst Pd/Nf-G for the Suzuki-Miyaura reaction between

Table 3. Optimization of reaction parameters for Suzuki-Miyaura reaction between benzenediazonium tetrafluoroborate salt with boronic acid catalyzed by Pd/Nf-G.^a

Entry	Solvent	Temp.(°C)	Pd Loading (mol%)	Time (h)	Yield ^b (%)
1.	Water	25	0.2	3	75
2.	Ethanol	25	0.2	4	85
3.	Dioxane	25	0.2	9	Traces
4.	DCM	25	0.2	12	Traces
5.	DMSO	25	0.2	4	80
6.	DMF	25	0.2	4	65
7.	i-PrOH	25	0.2	4	89
8.	DME-H ₂ O (1:1)	25	0.2	4	50
9.	THF	25	0.2	2	67
10.	MeOH	25	0.2	2	95
11.	MeOH	25	0.1	3	91
12.	MeOH	25	0.3	2	95
13.	MeOH	40	0.2	1.5	58
14.	MeOH	15	0.2	5	77

^aReaction conditions: Benzenediazonium tetrafluoroborate salt (0.3 mmol), phenyl boronic acid (0.36 mmol), solvent (2 mL), Catalyst Pd/Nf-G (0.2 mmol).

^bIsolated yield based on column chromatography.

Table 4. Pd/Nf-G catalyzed Suzuki reactions of substituted arenediazonium salt with various boronic acids.^a

Entry	Arenediazonium salt	Boronic acid	Product	Time (h)	Yield ^b (%)
1.				2	95
2.				4	93
3.				4	92
4.				3	96
5.				4	94
6.				2	93
7.				4	90
8.				4	91
9.				2	94
10.				3.5	92
11.				4	87
12.				4	89
13.				4	85

^aReaction conditions: arenediazonium tetrafluoroborate salt (0.3 mmol), phenyl boronic acid (0.36 mmol), methanol (2 mL), Catalyst Pd/Nf-G (0.2 mmol). ^bIsolated yield based on column chromatography.

Table 5. Recyclability study of catalyst for Sonogashira coupling reaction and Suzuki coupling reaction.^a

Run		1 st	2 nd	3 rd	4 th	5 th
Yield (%) ^b	Scheme 1	97	97	96	95	93
	Scheme 2	95	95	94	94	92

^aReaction condition: iodobenzene (0.5 mmol), phenyl acetylene (0.75 mmol), K₂CO₃ (1.25 mmol), ethanol (3 mL), catalyst Pd/Nf-G (0.3 mol%), temperature 78°C.

^bIsolated yield based on column chromatography.

^aReaction condition: benzenediazonium tetrafluoroborate salt (0.3 mmol), phenyl boronic acid (0.36 mmol), Methanol (2 mL), Catalyst Pd/Nf-G (0.2 mmol).

^bIsolated yield based on column chromatography (scheme 2).

benzenediazonium tetrafluoroborate salts with phenyl boronic acid in methanol as a solvent at 25°C (scheme 2). This was treated as a model reaction for optimization of various parameters and the results are summarized in table 3. Methanol was found to be the most suitable solvent for the reaction and it gave higher conversion as well as yield of desired product (table 3, entries 10). When the reaction temperature was increased to 40°C, the reactants were completely consumed within short time with the formation of impurities which consequently decreased the yield drastically (table 3, entry 13). The reaction was also carried out at 15°C, and no significant increase in the product yield was observed even after longer reaction time. Hence the appropriate temperature for model reaction was 25°C. Catalyst loading was also optimized and it was found that 0.2 mol% of Pd/Nf-G catalyst gave higher yield of product (table 3, entries 10) as compared to 0.3% and 0.1 mol% (table 3, entries 11–12).

We further examined catalytic activity of Pd/Nf-G for variety of arenediazonium tetrafluoroborate salts with various boronic acids which gave biaryl products in good yields. We screened phenyl boronic acid and chloro substituted phenyl boronic acid with variety of arenediazonium tetrafluoroborate salts having electron donating as well as electron withdrawing substituents. The product obtained from the coupling reactions of phenyl boronic acid with arenediazonium tetrafluoroborate salts gave better yield (table 4, entries 1–5) as compared to chloro-substituted boronic acid (table 4, entries 6–11). The nature of the substituted arenediazonium tetrafluoroborate salt also has greater effect on the yield of product. The substituent having electron withdrawing nature was more reactive (table 4, entries 4, 5, 9, 10) than electron donating ones giving higher yields (table 4, entries 2, 3, 7, 8). We also carried out reaction using 4-methoxy boronic acid and obtained good yield (table 4, entries 12–13). This study clears that the catalyst Pd/Nf-G can be applied efficiently for these coupling reactions.

3.3 Recyclability of Pd/Nf-G for Sonogashira (scheme 1) and Suzuki-Miyaura (scheme 2) coupling reactions

Recyclability of catalyst has greater importance for industrial applications. We also examined the recyclability of catalyst for scheme 1 and scheme 2 up to fifth cycle and catalyst showed excellent efficiency for these coupling reactions (table 5). After completion of reaction, catalyst was separated by simple filtration and was washed with ethyl acetate followed by drying at 60°C for 1 h. The recovered catalyst was again reused for next run with fresh starting compounds under the similar reaction conditions. This procedure was repeated for next four batches. It was found that catalyst showed excellent activity up to fifth cycle. The palladium leaching was also investigated after 5th run by ICP-AES which demonstrated 1.1 wt% and 0.9 wt% leaching of Pd for scheme 1 and scheme 2 respectively. This was also confirmed by hot filtration test for scheme 1.

3.4 Hot filtration test

This test was carried out for scheme 1 (table 1, entry 1). Reaction mass was filtered after 3 h under hot condition and the filtrate was subjected to GC analysis which gave 58% conversion. The resultant filtrate was heated again at 78°C for 3 h and then subjected to GC analysis. The GC results did not show any increase in the product conversion. This confirms that there was no significant amount of Pd leaching during the reaction.

4. Conclusion

In conclusion, we report the heterogeneous, Pd/Nf-G catalyst which can be efficiently applied for Sonogashira and Suzuki-Miyaura coupling reactions. The catalyst was easily recoverable and reused without loss in the activity up to 5th cycle.

Supplementary Information

Experimental details, characterization techniques, TEM, NMR spectra, mass spectra are given as supplementary information and are available at www.ias.ac.in/chemsci.

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