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Catalysis Communications

journal homepage: www.elsevier.com/locate/catcom

Short Communication

Resin encapsulated palladium nanoparticles: An efficient and robust catalyst for microwave enhanced Suzuki–Miyaura coupling

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ARTICLE INFO

Article history:

Received 26 March 2011

Received in revised form 11 May 2011

Accepted 12 May 2011

Available online xxxx

Keywords:

Palladium nanoparticle catalysis

Amberlite XAD-4

Suzuki–Miyaura cross-coupling

Microwave heating

ABSTRACT

A simple and rapid method for synthesizing highly accessible supported palladium nanoparticles inside the matrix of a commercial resin is reported. The encapsulated palladium nanoparticles were observed by TEM. The prepared catalyst has shown very high turnover frequency (TOF) in the coupling of aryl bromides with phenylboronic acid, under microwave heating. The encapsulated nanoparticles show excellent reusability and remarkable stability. The protocol is environmentally benign as no ligands, surfactants or toxic solvent were used.

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1. Introduction

The Suzuki–Miyaura cross-coupling reaction of aryl halides with arylboronic acids is one of the most important and convenient synthetic protocol for the generation of biaryls and is widely used for the synthesis of fine chemicals, pharmaceuticals, dyes etc. [1–3]. In general, these reactions are carried out in organic solvents using homogeneous or heterogeneous palladium catalysts, in the presence of a variety of phosphine based ligands [4,5]. The problem of catalyst recovery and pollution by phosphine ligands is a matter of concern, especially for the pharmaceutical industry. In the last few years nanoparticle synthesis and applications have attracted a great deal of attention. Nanoparticles possess properties, which are distinct both from the bulk material and from isolated atoms or molecules. Nanoparticle catalysis is more efficient compared to heterogeneous catalysis and has recyclability, which is not possible in homogeneous catalysis [6]. Palladium nanoparticles stabilised by polymers [7,8], porous silica [9] dendrimers [10] biomaterials [11], resins [12–14], zeolites [15], carbon nanotubes [16] graphene/graphite oxide [17] etc., have been reported to catalyse Suzuki reactions in the absence of ligands and in most cases, reactions are carried out in green solvents using extremely low concentrations of palladium catalyst.

Microwave-assisted heating under controlled conditions, has been proven as an invaluable technology for organic synthesis and its application in several cases has led to an acceleration of reaction rate, improvement of yield, and selectivity. Dramatic reduction in time

enables medicinal chemists to optimize chemistry and synthesize compound libraries very rapidly. Recent innovation in microwave assisted organic synthesis (MAOS) in sealed vessels allows solvents to be heated far above their boiling points, thus, eliminating the need for high boiling solvents to reach high temperatures [18]. The first report of microwave mediated Suzuki reaction came in 1996, using Pd(PPh)₃ as catalyst by Hallberg and Lorhed [19]. Leadbeater and co-workers have explored microwave induced Suzuki reactions under many different conditions using different catalysts [20]. Recently, usage of nanoparticles in microwave induced reactions has attracted considerable interest [21]. Martin et al. [22] reported very high TOF (10⁴–10⁵) for the Suzuki reaction under microwave conditions using PVP stabilised colloidal PdNPs. Our own work with PVP stabilized nanoparticles [23] showed that Pd(0) black precipitated at the end of reaction and hence, no recycling was possible. Astunes and co-workers [24] have also reported similar results. This can be due to the unstable nature of the nanoparticles at high temperature or the movement of polymer segments upon microwave absorption may have led to ineffective capping and hence, coagulation of the particles. In contrast, supported nanoparticles [25,26] have been reported to be recyclable but catalyst concentration required is relatively high. In most of the reports concerning supported nanoparticle catalysis, functional microporous or macroporous resin has been selected as support [27]. We decided to investigate the behaviour of nanoparticles, supported on an inert nonfunctional polymer resin for microwave induced reaction.

Amberlite XAD-4 is a commercial polystyrene–divinylbenzene cross-linked macroporous resin, that is widely used as solid phase support for organic synthesis. Apart from the freedom to use in a variety of solvents, its low degree of cross-linking allows easy mass

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transfer. The resin is devoid of any functional groups and is found to be chemically and mechanically stable under microwave heating [18]. So, we selected this resin as a support for palladium nanoparticles. Here, we demonstrate the synthesis of PdNPs encapsulated inside the matrix of Amberlite XAD-4 and observed that they provide a very simple, robust, efficient and recyclable catalytic system for the microwave enhanced Suzuki reaction.

2. Experimental section

2.1. Preparation of palladium nanoparticles in resin matrix

Amberlite XAD-4 beads (5.0 g) were thoroughly washed with hot water to remove salts and then washed with ethanol (20 mL \times 2). The Resin beads were filtered and then equilibrated with 25 mL of 1.0 mmol palladium acetate solution prepared in ethanol at 10 °C. After 1 h, excess solution was filtered off and 10 mL of cold aqueous NaBH₄ (0.1 mol dm⁻³) solution was passed through the beads. The grey coloured beads thus obtained (Fig. 1), were washed with water to remove excess reagent and were stored in ethanol.

2.2. Typical protocol for the Suzuki–Miyaura reaction

Into a 10 mL vial, phenylboronic acid (1.8 mmol), aryl bromide (1.5 mmol), sodium carbonate (2.0 mmol), ethanol (1.5 mL), water (1.0 mL) and catalyst (200 mg wet resin) were taken and heated in a CEM microwave (140 °C, 100 w) for 8 min. The reaction was quenched by filtering the hot solution in 10 mL of cold water. The resulting solution was extracted with ET₂O/DCM (2 \times 5 mL). The combined

extracts were dried over anhydrous MgSO₄ and the solvents were removed under vacuum. The crude products were then recrystallized from appropriate solvent and characterized by ¹H NMR.

2.3. Kinetic studies

Kinetics studies were carried out for the coupling reaction between 4-bromoanisole and phenylboronic acid. Into a set of 10 mL vials, phenylboronic acid (1.8 mmol), 4-bromoanisole (1.5 mmol), sodium carbonate (2.0 mmol), ethanol (1.5 mL), water (1.0 mL) and catalyst (200 mg wet resin) were taken and heated in a CEM microwave reactor for a hold time of 2, 4, 6, 8 and 10 min respectively. The reactions were quenched by filtering the hot solution in 10 mL cold water and the aqueous solution for each run was extracted with ET₂O (2 \times 5 mL). The combined ether extracts were dried over anhydrous MgSO₄, and products analyzed by GC–MS.

The effect of catalyst concentration was also studied by taking different amounts of resin while keeping the other parameters constant.

3. Results and discussion

3.1. Synthesis and characterization of resin encapsulated PdNPs

The immobilization of nanoparticles on solid support is desirable because the catalysts can be separated by simple filtration. Recent literature shows that micropores of nonfunctional crosslinked polystyrene resins, can also be used to synthesize fairly uniform nanoparticles [28,29] without using any other stabilizing agent. Many different methods have been reported to synthesize supported PdNPs [30]. In the present case PdNPs were synthesized in situ by reduction of impregnated metal ions with NaBH₄. The method is faster compared to alcoholic reduction used by Sajiki et. al. [29].

The amount of palladium loaded onto the resin was determined spectrophotometrically [31]. 500 mg of resin was incinerated in a crucible for 4 h at 550 °C. The residue was dissolved in 1 mL of conc. HCl and diluted to 10 mL with distilled water. The average concentration of palladium (3 trials) as determined by iodide method was found to be 0.00235 mmol/g (0.250 mg/g) of the resin.

SEM image of the resin beads did not show any particles or agglomerations on the surface (Figure S1). Tunneling Electron Microscopy was used to study the shape and size of nanoparticles. Polymer beads were milled, the powder thus obtained was dispersed in ethanol and was deposited onto carbon coated copper grids. Fig. 2 shows TEM and HRTEM pictures of PdNPs embedded in polymer matrix. The nanoparticles are spherical in shape and the size for most of the particles varies between 5 and 10 nm.

3.2. Catalytic activity of resin encapsulated PdNPs under microwave heating

We examined the activity of the catalyst for the reaction between p-bromoanisole and phenylboronic acid under aerobic conditions using microwave heating. Ethanol/water mixture which is a green solvent and in which, Amberlite XAD-4 shows little swelling, was chosen as the reaction medium. GC–MS analysis (Figure S2) of the reaction mixture shows that after 8 min 4-methoxy biphenyl is the sole product, which was identified by its mass spectrum. Time course of reaction is shown in Fig. 3. Some blank tests were also performed and the results show that reaction takes place only in the presence of resin encapsulating nanoparticles (Table 1).

The effect of catalyst concentration was carried out by varying the amount of catalyst (resin encapsulating PdNPs) while keeping the other parameters constant. It was observed that 200 mg of resin (\approx 0.0005 mmol of Pd, 0.03 mol.% with respect to arylhalide) was sufficient to complete the reaction (Fig. 4). The TON and TOF (h⁻¹) were calculated to be 3000 and 22,500 respectively. They are

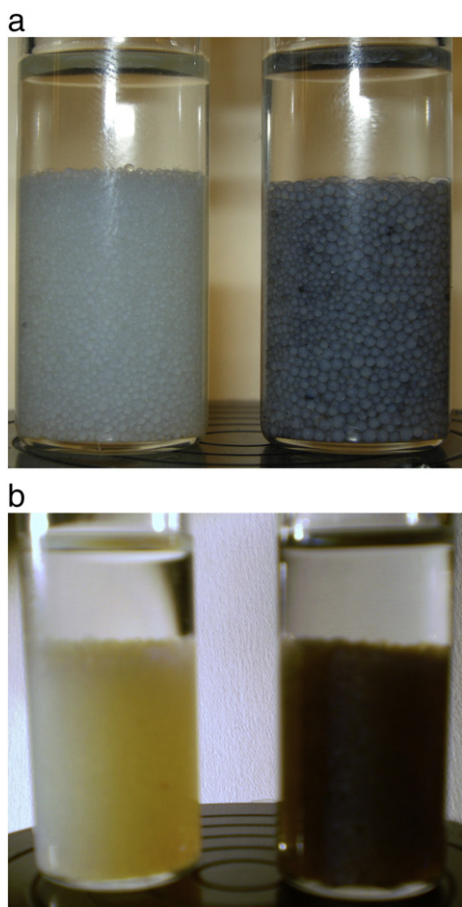


Fig. 1. a) Photograph of Amberlite XAD-4 beads before and after encapsulating PdNPs. a) without b) with lateral illumination.

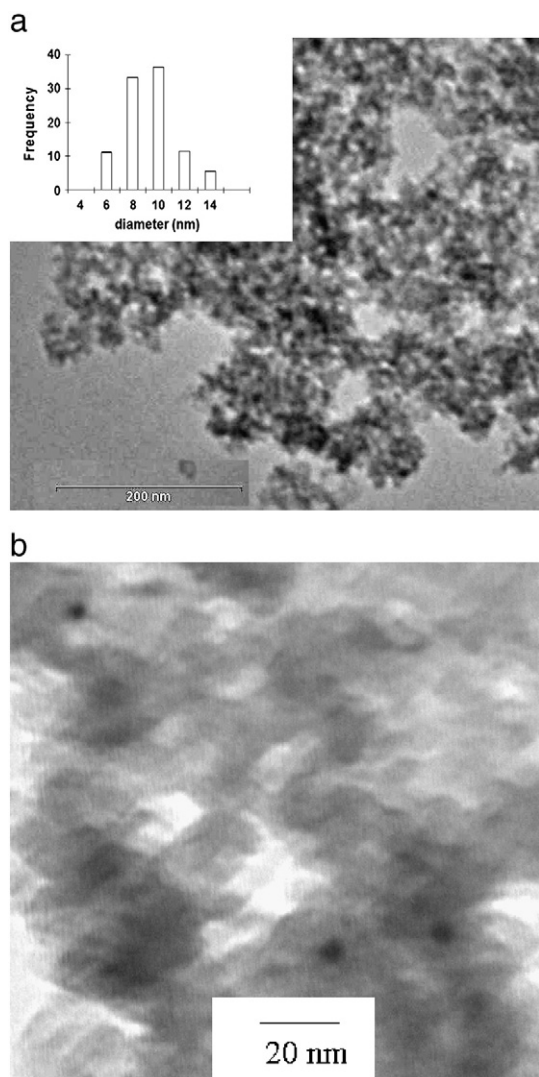


Fig. 2. a) TEM image of the resin supported PdNPs. Scale bar 200 nm b). HRTEM scale bar 20 nm.

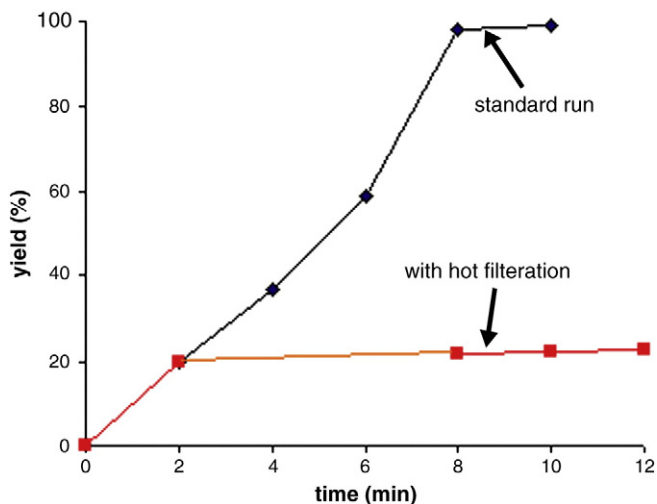


Fig. 3. Time course of the Suzuki reaction between phenylboronic acid and 4-bromoanisole catalysed by resin supported PdNPs (Standard run) and application of hot filtration of the resin after 2 min.

Table 1
Suzuki reaction between 4-bromoanisole and phenylboronic acid.

Entry	Conditions	Yield ^a (%)
1.	Na ₂ CO ₃ 8 min	Trace
2.	200 mg resin, Na ₂ CO ₃ 8 min	Trace
3.	200 mg Pd catalyst, Na ₂ CO ₃ 2 min	20
4.	200 mg Pd catalyst, Na ₂ CO ₃ 4 min	37
5.	200 mg Pd catalyst, Na ₂ CO ₃ 6 min	60
6.	200 mg Pd catalyst, Na ₂ CO ₃ 8 min	96

4-bromoanisole (1.5 mmol); phenylboronic acid (1.8 mmol); Pd Catalyst (200 mg resin ≈ 0.0005 mmol of Pd); Na₂CO₃ (2.0 mmol); EtOH (1.5 mL); H₂O (1 mL), (Microwave conditions, 140 °C, 100 w).

^a GC yields.

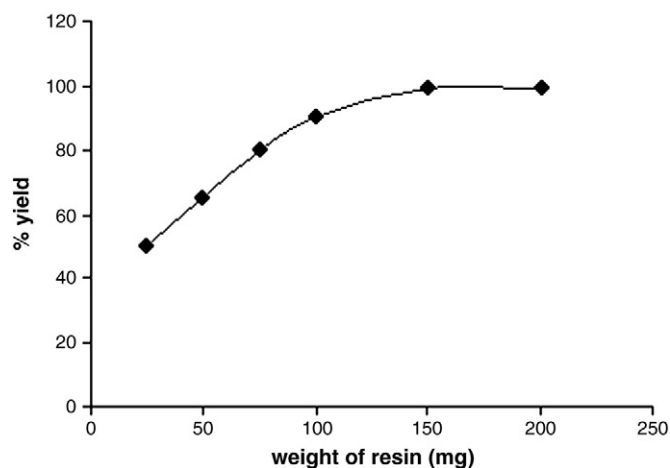


Fig. 4. Effect of catalyst concentration on the % yield of reaction.

comparable to those, reported for microwave induced suzuki reaction using colloidal PdNPs by Martin et al. [22].

3.3. Recycling of the catalyst

The resin beads after each cycle were extracted by boiling in 5 mL of ethanol to remove any product sorbed inside the resin and reused. The subsequent use of resin encapsulated PdNPs, did not show any loss in activity (Fig. 5).

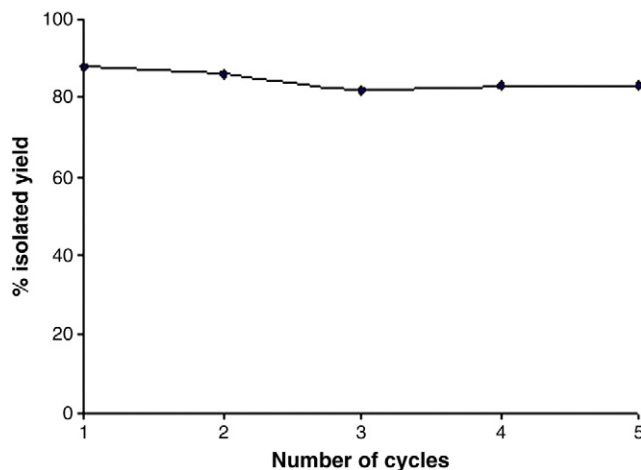
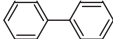
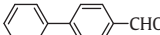
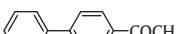
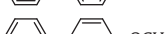
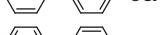

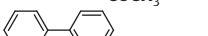
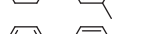

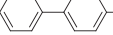


Fig. 5. Recycles of catalyst.

Table 2
Suzuki cross-coupling with phenylboronic acid under MW.

Entry	Aryl halide	T, min	Yield*, %	Product
1	Bromobenzene	8	82	
2	4-bromobenzaldehyde	8	91	
3	4-bromoacetophenone	8	90	
4	4-bromoanisole	8	88	
5	2-bromoacetophenone	12	80	
6	3-bromotoulene	8	86	
7	4-bromoacetanilide	8	62	
8	4-bromonitrobenzene	8	94	
9	2-bromothiophene	20	82	
10	Chlorobenzene	8	54	

Aryl halide (1.5 mmol); phenylboronic acid (1.8 mmol); Pd Catalyst (200 mg resin); Na₂CO₃ (2.0 mmol); EtOH (1.5 mL); H₂O (1 mL), (Microwave conditions, 140 °C, 100 w, 8 min).

*Isolated yields.

To probe the leaching of the catalyst, hot filtration test was performed. The reaction between p-bromoanisole and phenylboronic acid was stopped after 2 min and the resin filtered off while the solution was still hot. The filtrate was heated further and the reaction mixture analysed by GC after 6, 8 and 10 min. The results shown in Fig. 3, indicate that reaction stops after the resin is filtered off. Additionally the reaction mixture was extracted with ether and aqueous layer analysed for palladium by ICP-AES. Total palladium concentration was found to be 160 ± 10 ppb. The negative results of hot filtration test indicate that the leaching of palladium is negligible and most probably the reaction is heterogeneous in nature.

3.4. Suzuki–Miyaura cross-coupling reactions

After optimising the reaction conditions, we performed the Suzuki cross-coupling of various arylbromides with phenylboronic acid. Very high yields of cross-coupling products were obtained (Table 2). The products were characterized by matching their ¹H NMR spectra with the reported data and the results are reported in the supporting information. Both electron deficient as well as electron rich arylbromides afforded the corresponding biphenyls in very good yields. The catalytic property was preserved even in the presence of a thio containing substrate (entry 8). We also performed the reaction with chlorobenzene and isolated biphenyl in 54% yield. As it is possible to carry out reactions

at higher temperature in a microwave synthesizer, we are trying to optimize conditions for optimum yields with the less reactive arylchlorides too. The biaryls isolated in all the reactions were of high purity as no leachable material such as stabilizers, surfactants or ligands were used in the nanoparticle synthesis or in the reaction mixture.

A comparison of the present method with others reported in the literature using nanoparticles and microwave heating was done and the results are summarized in Table 3. Charcoal is another neutral support which is widely used to support palladium. Leadbeater et al. [32] and Cravotto et al. [33] have used Pd/C for the microwave induced Suzuki reaction in water and DME but no recycling was reported. Also, charcoal requires pretreatment and conditioning to obtain adequate surface area and porosity. In a recent publication, monodisperse palladium in SBA-15 has been reported as catalyst for microwave induced Suzuki reaction by Cao et al. [34]. However, they used dendrimers to support the particles onto the inorganic support. In case of Macronet MN 100 and Tentagel (entries 4 and 6) extra crosslinking steps were carried out to reduce leaching of metal from the resin. Chitosan supported nanoparticles reported by Lee and co-workers, showed higher yields after phase transfer agent TBAB was added to the reaction mixture [35]. The authors reasoned that poor compatibility of hydrophobic substrate (aryl halide) with hydrophilic support might have lowered the reaction performance, which increased after adding TBAB. Possibly favourable mass transfer of the materials inside the hydrophobic resin matrix, is the reason that in the present case amount of catalyst required is much lower compared to others. Another benefit of nonfunctional support is that reaction conditions does not have any effect on the nanoparticle stability especially in solvents where swelling is not much.

4. Conclusion

In conclusion, the present method provides a very simple process for impregnating PdNPs inside the resin matrix. The encapsulated nanoparticles, can be effectively used for ligandless Suzuki–Miyaura cross-coupling reactions of a variety of aryl bromides under microwave heating conditions with high yields. The main key issues of nanoparticle catalysis such as accessibility, stability and recyclability have been successfully realised.

Acknowledgements

Authors are grateful to the UGC, New Delhi for the financial support to carry out this work and to SAIF, Panjab University, Chandigarh for the NMR spectra and HRTEM pictures. Sicart, Vallabh Vidhya Nagar, Gujarat for GC–MS; Dr Sareen, PRL, Ahmedabad for ICP-AES studies.

Appendix A. Supplementary data

Supplementary data to this article can be found online at doi:10.1016/j.catcom.2011.05.012.

Table 3
A comparison of the present method with the other reported methods using supported PdNPs under microwave heating.

Entry	Catalyst support	Pd (mol.%)	Phase transfer agent/solvent	Ref.
1	Pd/C	1.0	DME/H ₂ O	[32,33]
2	SBA-15/dendrimers	0.5	H ₂ O/ETOH	[34]
4	Chitosan	0.5	TBAB/dioxane	[35]
4	Macronet MN100 HPS	2.0	H ₂ O	[26]
5	Poly(N,N dialkylcarbidimide)	0.5	Dioxane	[12]
6	Aminomethylated tentagel	10.0	H ₂ O	[14]
7.	Mesoporous starch	2.3	–	[11]
8.	Amberlite XAD-4	0.03	H ₂ O/ETOH	Present

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