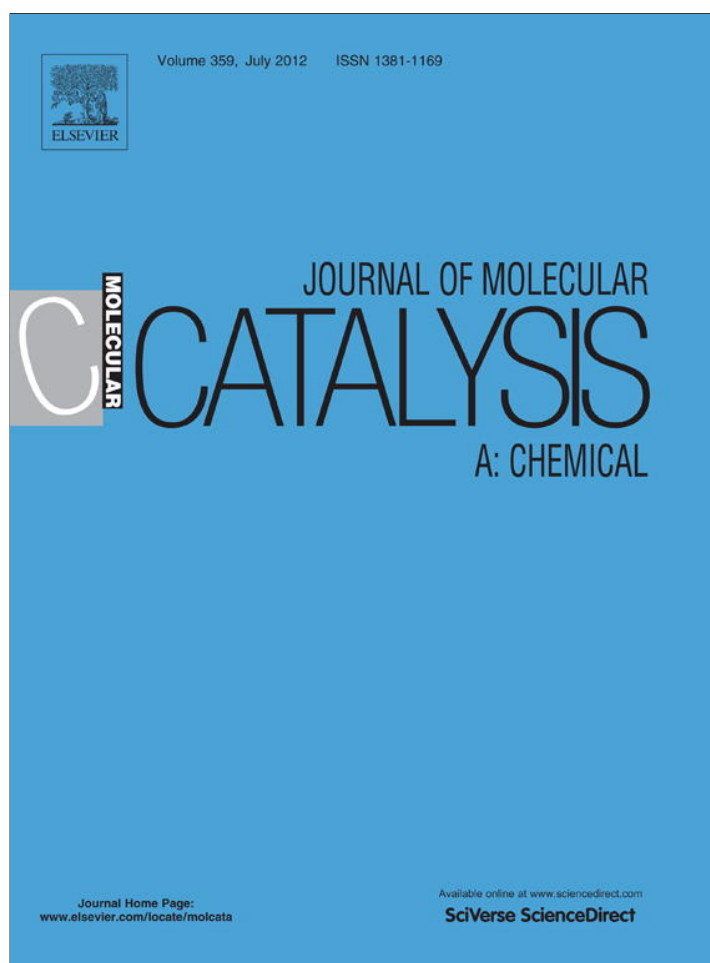


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# Macroporous resin impregnated palladium nanoparticles: Catalyst for a microwave-assisted green Hiyama reaction

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## ABSTRACT

A non-functional macroporous commercial resin, Amberlite XAD-4, was impregnated with palladium nanoparticles of size 5–10 nm. The supported PdNPs, thus prepared, were used to catalyze the sodium hydroxide activated Hiyama cross-coupling reaction of phenyltrimethoxysilane with a variety of bromo and chloro arenes under microwave heating. They were found to have very high efficiency (TOF  $\approx 3 \times 10^4$ ) and excellent recyclability. The procedure, which was carried out in the absence of any additional ligands, surfactants or toxic organic solvents, can lead to the development of a sustainable and green protocol for the production of biaryls.

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## 1. Introduction

Palladium catalyzed cross-coupling reactions have emerged as the most efficient methodologies for the production of unsymmetrical biaryls and are extensively utilized in the synthesis of polymers, agrochemicals, pharmaceutical intermediates, etc. [1]. Among the coupling reactions, three most frequently employed are Stille [2], Suzuki-Miyaura [3], and Hiyama [4,5] reactions. In spite of the excellent yields, high stereoselectivity and superior functional group tolerance, the use of toxic tin reagents in Stille couplings, and the difficulties in the preparation and purification of boron reagents required for the Suzuki reactions, are major disadvantages. Therefore, the Hiyama coupling reaction that uses environmentally benign, cheaper and easy to prepare organosilicon reagents has many advantages in comparison to others. Hiyama et al. [6–8] have developed several methods for this transformation, using various Pd catalysts in the presence of phosphine ligands. Earlier, corrosive fluoride anions were used for the activation of C–Si bond of alkylsilanes but later on, the activity of C–Si bond was enhanced by using alkenylfluorosilanes [9], alkenylalkoxysilanes [10–12], and organosilanols [13–15]. Subsequently, with the development of sodium hydroxide as an effective promoter [16,17] for alkoxysilanes in aqueous media, the potential of Hiyama reaction as a viable synthetic process was demonstrated. Though the aqueous Hiyama reaction made significant progress, either toxic phosphine

ligands or expensive palladocycles were still required. Of late, nanoparticles have emerged as efficient catalysts for coupling reactions in the absence of ligands. Rothenberg et al. [18], first reported the usage of bimetallic core-shell Ni–Pd nanoclusters to catalyze Hiyama cross-coupling reaction between phenyltrimethoxysilane and various halo arenes. High product yields were obtained with a variety of iodo- and bromo-aryls in tetrahydrofuran using tetrabutylammonium fluoride (TBAF) as the activator. Sarkar et al. [19] reported efficient catalysis of NaOH activated ligandless Hiyama cross-coupling reaction using polyethylene glycol (PEG) capped palladium nanoparticles, in aqueous media. Ranu et al. [20] demonstrated that in situ generated Pd (0) nanoparticles can catalyze Hiyama cross-coupling reaction in a very short time. Sodium dodecyl sulphate (SDS) was used as surfactant in this reaction. These methods, which used colloidal nanoparticles, lacked recyclability. Hence, there is a growing need to develop stable and recyclable catalyst systems.

Conventional methods of heating reactions need more time, elaborate and tedious apparatus. This results in higher costs and environmental pollution too. In today's world, microwave induced heating is emerging as a simple, clean, fast, efficient and economical method for the synthesis of organic molecules. This technique can reduce the duration of chemical reaction from hours to minutes. Also, the ability to heat solvents far above their boiling points in closed vessels has reduced the usage of high boiling organic solvents. In other words, microwave heating offers energy efficient and environment-friendly processes [21]. However, there is need to synthesize catalytic systems which have greater stability under microwave heating. Polymer ligands such

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as PVP and PEG [19,22] that can efficiently stabilize nanoparticles under conventional heating, may not be suitable for under microwave heating as nanoparticles tend to coagulate. Supporting nanoparticles on a neutral polymer resin is a viable alternative for stabilizing nanoparticles. Microporous resins are reported to disperse palladium nanoparticles with excellent size control as they have a narrow pore size distribution [23]. However, such resins need to be swollen in appropriate solvents (non polar solvents in case of crosslinked polystyrene) to promote transport of reactants. Polar solvents on the other hand tend to close up the pores and decrease accessibility to the embedded catalyst. In comparison to microporous supports, catalysts supported on macroporous resins remain accessible in a variety of solvents including water and ethanol [24]. In this study, we investigated the behavior of palladium nanoparticles, supported on an inert non-functional macroporous polymer resin for the microwave induced Hiyama reaction.

## 2. Experimental

### 2.1. Materials and instruments

All chemicals used were of analytical grade or of the highest purity available. All glassware was thoroughly cleaned with freshly prepared 3:1 HCl/HNO<sub>3</sub> (aqua regia) and rinsed with Millipore-Q water. Phenyltrimethoxysilane was purchased from Aldrich. The Aryl bromides were obtained from BDH and Merck. All aryl bromides and chlorides were of 98–99% purity. Dichloromethane (DCM), diethyl ether (ET<sub>2</sub>O), and NaOH were purchased from Finar Chemicals. Water used in all experiments was purified by the Millipore system.

GC–MS measurements were carried on Perkin Elmer USA Auto system XL. High resolution transmission electron microscopy (HR-TEM) pictures were taken using a Hitachi (H-7500) Instrument. The swollen resin beads were milled and a drop of alcoholic suspension was placed on a 200 mesh carbon coated copper grid. It was then dried to evaporate the solvent and used for microscopy. <sup>1</sup>H NMR spectra were recorded on a Bruker Advance II 400 NMR spectrometer. Inductively coupled plasma atomic emission spectroscopy (ICP-AES) measurements were carried out on a HJY Ultima-2 instrument: power 1000 W, nebulizer flow 1.29, nebulizer pressure 2.96 min<sup>-1</sup>, wave length 340.458 nm. CEM benchmate microwave reactor was used for microwave heating. The general parameters used were: closed vessel synthesis, stirring on, power 50 W, temperature 110 °C, hold time 6–12 min, external cooling on.

### 2.2. Preparation of resin supported palladium nanoparticles (resin-PdNPs)

The resin supported palladium nanoparticles were synthesized by a method developed in our lab [25]. Amberlite XAD-4 beads (5.0 g) were washed repeatedly with hot water to remove salts, swollen in ethanol and then equilibrated with 25 mL of 1.0 mmol solution of palladium acetate in ethanol at 10 °C. After 1 h, excess solution was drained and the metal was reduced by passing cold aqueous NaBH<sub>4</sub> (0.1 mol dm<sup>-3</sup>) solution. The resin particles were further washed with water to remove excess reagent and stored in ethanol.

### 2.3. Typical protocol for the Hiyama reaction under microwave heating

Into a 10 mL vial phenyltrimethoxysilane (1.5 mmol), resin-PdNPs (150 mg), and ethanol (1.5 mL) were taken. The reaction mixture was stirred vigorously and 3 M NaOH (1 mL, 3 mmol) was

added drop wise. Then aryl halide (1 mmol) was added and the vial heated in CEM microwave (50 W, 110 °C) for different intervals of time. The reaction was quenched by filtering the hot solution in 10 mL cold water. The resulting solution was extracted with ET<sub>2</sub>O/DCM (2 × 5 mL). The combined extract was dried over anhydrous MgSO<sub>4</sub> and the solvent was removed using a rotaevaporator. The crude product, thus isolated, was recrystallised from an appropriate solvent.

### 2.4. Effect of various parameters on catalyst activity

Effect of various parameters such as time, catalyst concentration, base, etc. was studied for the coupling reaction between 4-bromoacetophenone and phenyltrimethoxysilane. Into three 10 mL vials, 4-bromoacetophenone (2.0 mmol), 4-bromoacetophenone (1 mmol), sodium hydroxide (1 mL, 3 M), ethanol (1.5 mL) and catalyst (150 mg wet resin) were taken and heated in a CEM microwave reactor for a hold time of 2, 4, and 6 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 ET<sub>2</sub>O (2 × 5 mL). The combined extracts were dried over anhydrous MgSO<sub>4</sub>, and products analyzed by GC–MS.

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

## 3. Results and discussion

We have synthesized palladium nanoparticles supported on Amberlite XAD-4, a neutral, non-functional, hydrophobic, macroporous, commercial and cross-linked polystyrene resin. The resin is chemically and mechanically stable under microwave conditions and due to its inert nature, there is no interference with reaction conditions. While the presence of ligands/functional groups on a resin can control the size and stability of nanoparticles, they have a negative influence from the catalytic activity point of view, reducing the interaction of catalytic sites with the substrates [26]. This also prompted us to choose a non-functional resin in which nanoparticles are stabilized solely by the steric factor or electrostatic interaction of benzene rings. This probably increases the accessibility of nanoparticles which is reflected by their high turn over number (TON). The hydrophobic nature of the resin can also create a favorable mass transfer for the less polar alkylhalides reactants through the resin and increases interaction with the embedded catalyst. Swelling of such resin in organic solvent can be a problem during the reaction. However, the impregnated resin shows little swelling in ethanol water mixture.

The method used for nanoparticles impregnation was very simple. It involved sorption of palladium acetate in the resin followed by reduction with sodium borohydride. TEM images showed embedded palladium nanoparticles with size ranging from 5 to 10 nm (Fig. 1). The method gave a metal loading of 0.235 mg of palladium per g of resin which was determined spectrophotometrically [25] after incinerating the resin. This is a comparatively low value which makes it desirable for microwave heating. This is because high content of metal may lead to generation of hot spots and degradation of polymer support [21].

### 3.1. Catalytic activity of resin supported PdNPs for Hiyama reaction

Our initial investigation on the evaluation of the catalytic activity started with the cross-coupling of phenyltrimethoxysilane and 4-bromoacetophenone under microwave heating (Scheme 1) using NaOH as the activator. The reaction was carried out in a closed

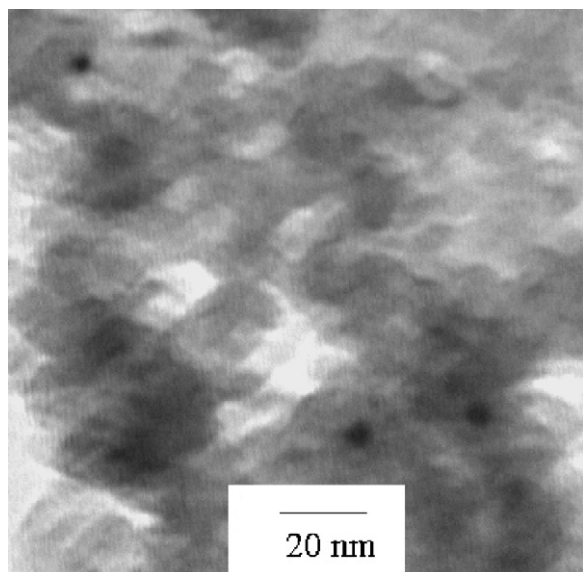
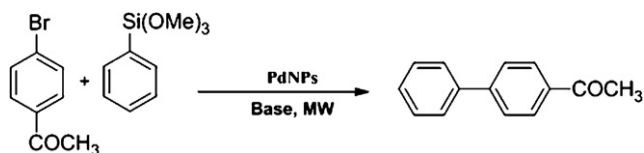


Fig. 1. HRTEM image of the resin encapsulated palladium nanoparticles.



Scheme 1. Hiyama reaction between phenyltrimethoxysilane and 4-bromoacetophenone.

vial. Hiyama reaction has been reported in a variety of organic solvents and water. Water alone cannot solubilize hydrophobic alkyl halides. Surfactants or phase transfer agents such as TBAB are generally used to increase solubility. Ethanol/water mixture [27] in which the reactants dissolve on heating was chosen as the reaction medium. The heating in ethanol/water mixture is also very efficient under microwave heating and the required temperature can be achieved in seconds (Fig. 2).

The time course of the reaction (Fig. 3) was studied by quenching the reaction at different time intervals and the reaction mixture was analyzed by the GC-MS (Fig. S1). It was observed that after 6 min, the peak for 4-bromoacetophenone disappeared completely and 4-biphenyl-4-yl-ethanone was identified as the sole coupling product by its mass spectrum. No homocoupling product was observed. Three moles of NaOH were required for the completion

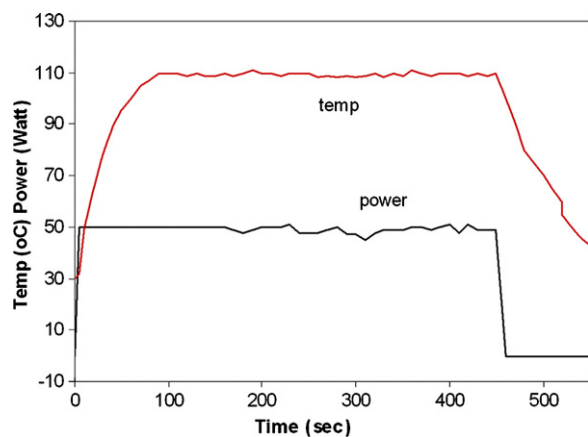


Fig. 2. Temperature and potency profile of the microwave-assisted Hiyama reaction.

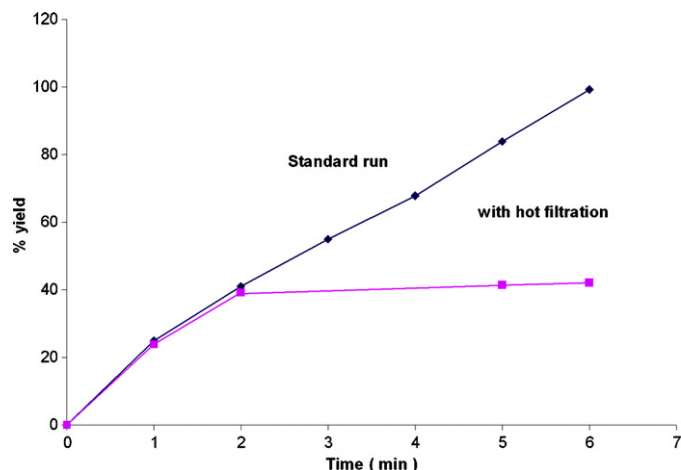


Fig. 3. Time course of the Hiyama reaction between phenyltrimethoxysilane and 4-bromoacetophenone (standard run) and after hot filtration of the resin.

Table 1  
Conditions for Hiyama reaction.

No	Conditions	Yield <sup>a</sup> (%)	TOF (h <sup>-1</sup> )
1	150 mg resin, 3 M NaOH, EtOH, 6 min.	0	–
2	150 mg resin-PdNPs, 1 M NaOH, EtOH, 6 min.	58	17,060
3	150 mg resin-PdNPs, 2 M NaOH, EtOH, 6 min.	80	23,530
4	150 mg resin-PdNPs, 3 M NaOH, EtOH, 6 min.	99	29,120
5	150 mg resin-PdNPs, 3 M NaOH, MeOH, 6 min.	90	26,500
6	150 mg resin-PdNPs, 3 M Na <sub>2</sub> CO <sub>3</sub> , EtOH, 6 min.	35	10,290

Aryl halide (1.0 mmol), phenyltrimethoxysilane (1.5 mmol), resin-PdNPs (150 mg) closed vessel,  $P = 50$  W,  $110$  °C.

<sup>a</sup> GC yields.

of the reaction and reaction was found to be incomplete when Na<sub>2</sub>CO<sub>3</sub> was used as base. Optimization of conditions is summarized in Table 1. It was also observed that 150 mg of resin ( $\approx 0.00035$  mmol of Pd, 0.035 mol% with respect to aryl halide) was sufficient to complete the reaction and no reaction was observed in the absence of the catalyst. The effect of catalyst concentration is shown in Fig. 4. We were able to obtain high TON (2912) and TOF (29,120/h) using microwave heating.

### 3.2. Recycling of the catalyst

Easy catalyst separation and recycling in successive batch operations can greatly increase the efficiency of the reaction. Resin

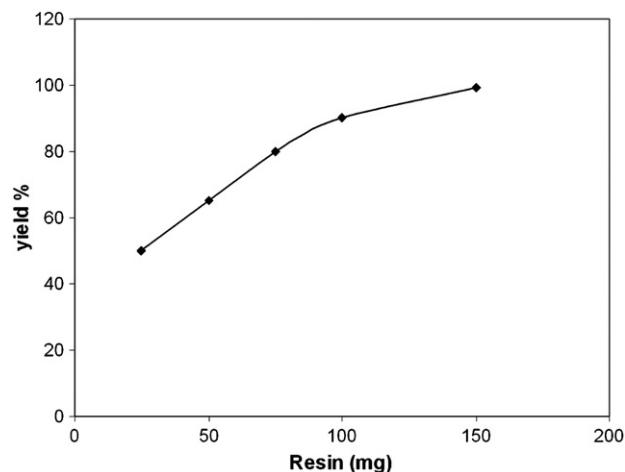
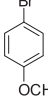


Fig. 4. Effect of catalyst concentration on Hiyama coupling.

**Table 2**  
Hiyama cross-coupling of aryl halides with phenyltrimethoxysilane.

Entry	Aryl halide	Product	T min	Yield <sup>a</sup> (%)
1			6	94
2			6	95
3			6	96
4			6	96
5			6	76
6			12	89
7			12	92
8			12	85
9			6	92
10			6	90
11			8	90

Aryl halide (1.0 mmol), phenyltrimethoxysilane (1.5 mmol), EtOH–H<sub>2</sub>O resin-PdNPs (150 mg) closed vessel, P=50 W, 110 °C.

<sup>a</sup> Isolated yield.

supported nanoparticles were separated from the hot reaction mixture by simple filtration and were recycled many times. The beads, after separation, were extracted with hot water, ethanol or DCM (5 mL) to remove any sorbed products and were reused. Recyclability of the resin is shown in Fig. 5. No change in activity was observed up to five cycles.

Leaching can cause depletion of the metal from the support and limit the service life and reusability of the catalyst. It can also lead to metal contamination of the product. Leaching depends on the solvent used, interaction with reactants, products and the reaction temperature. To probe leaching of the catalyst, hot filtration test was performed. The reaction between 4-bromoacetophenone and phenyltrimethoxysilane was stopped after 2 min and the resin filtered off while the solution was still hot. The filtrate was further heated and the reaction mixture analyzed by GC–MS 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 was analyzed for palladium by ICP–AES. Total palladium concentration was found to

be  $35 \pm 10$  ppb. The negative results of the hot filtration test indicate that the leaching of palladium is negligible and most probably, the reaction is heterogeneous in nature.

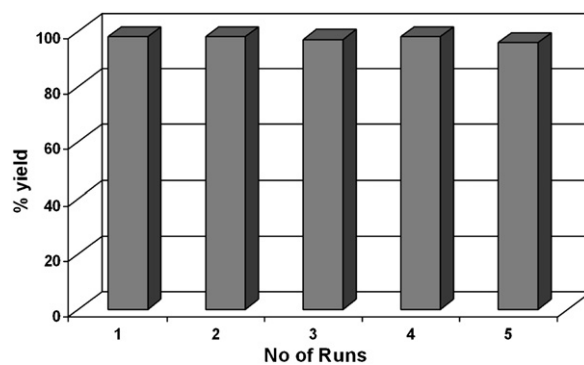


Fig. 5. Recycling of the catalyst.

### 3.3. Hiyama cross-coupling reaction

The excellent results obtained in the cross-coupling of 4-bromoacetophenone with phenyltrimethoxysilane prompted us to carry out the reaction with other aryl bromides. A series of aryl bromides with both electron withdrawing and donating groups were used and the results are summarized in Table 2. The reaction was uniform irrespective of the nature of the substituents (electron withdrawing or electron donating) on the aromatic ring. A wide range of substituents, which included  $-\text{CH}_3$ ,  $-\text{CHO}$ ,  $-\text{OCH}_3$ ,  $-\text{NO}_2$ , and  $-\text{COCH}_3$ , were compatible with this procedure. In case of aldehyde, chemo selectivity was totally in favor of Hiyama cross-coupled product. We also carried out the reaction with 2-bromothiophene (entry 11) and isolated coupled product in good yield. In case of  $-\text{NHCOCH}_3$  group (entry 5), 4-aminobiphenyl was also isolated.  $-\text{CO}_2\text{H}$  and  $-\text{CN}$  groups were found to be incompatible. No reaction occurred with 4-bromobenzoic acid and in case of 4-bromobenzonitrile, only hydrolysis product was isolated. We also tried reaction with arylchlorides (entry 6–8) and found that under the present set of conditions reaction with chlorobenzene (entry 6), did not proceed to completion. However, on increasing the reaction time from 6 to 12 min, we could isolate the products in high yields. All the products were of high purity and were characterized by matching their  $^1\text{H}$  NMR spectra with the reported data and the results are summarized in Supporting Information.

### 4. Conclusion

The role of microwave synthesis is increasing day by day. To the best of our knowledge, this is the first study of Hiyama reaction under microwave heating using supported palladium nanoparticles. Clarke [28] reported first microwave assisted Hiyama cross-coupling reaction using in situ synthesized palladium phosphine ligands as catalyst and TBAF as activator. Alacid and Najera [29] reported coupling of vinyltrialkoxysilane with arylbromides and chlorides in the presence of phenone oxime-derived palladocycles as catalysts. In both the reactions, no isolation of catalyst was reported. The significant improvements offered by the present method are: operational simplicity, general applicability, recyclability and the absence of hazardous organic solvents, fluoride activators, phosphine ligands, surfactants, etc. This can contribute to the development of green strategy for the synthesis of biaryls.

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### Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.molcata.2012.03.022>.

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