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Supported palladium nanoparticles: A general sustainable catalyst for microwave enhanced carbon-carbon coupling reactions

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GRAPHICAL ABSTRACT



Highlights of the work

- Palladium nanoparticle catalyzed Suzuki, Hiyama, Heck and Sonogashira reactions.
- Synergism between microwave and recyclable palladium nanoparticles on inert support
- Reaction time 6 to 35 min with catalyst quantity less than 0.1 %.
- A versatile recyclable catalyst with general applicability
- The catalyst can be used for facile synthesis of asymmetric terphenyls.

Abstract

Synergism between nanocatalysts and microwave heating has emerged as a tool for sustainable organic synthesis. In the present investigation scope of palladium nanoparticle for ligand free carbon-carbon coupling reactions namely Suzuki, Hiyama, Heck and Sonogashira under microwave heating is investigated. Palladium nanoparticles of less than 10 nm dimension were impregnated onto a commercially available, non-functional, microporous polystyrene resin and were characterized by UV-Vis spectroscopy, HRTEM attached with EDX, powder X-ray Diffraction (XRD) and ICP-AES. Highly pure coupled products in various reactions were obtained in 6 to 35 min using microwave heating in closed vials using benign mixed low boiling solvents, which otherwise require 4 to 30 h of inert atmosphere under conventional heating. Reaction parameters such as temperature, time and concentration of catalyst were optimized and catalyst was successfully recycled five to six times without any noticeable leaching or decrease in performance. Post reaction TEM analysis showed that size of the nanoparticles was still in the range of 3 to 10 nm. The catalyst was successfully used to synthesize asymmetric terphenyls in a single pot by sequential addition of aryl boronic acids.

Keywords: Supported Palladium nanoparticles, Heck reaction, Sonogashira reaction, Microwave heating, Terphenyl, Recycling

1. Introduction

Today, palladium is widely accepted as one of the most versatile and beneficial metal used in a variety of catalytic applications ranging from organic synthesis to fuel cells, oil refining etc. In chemistry, this silvery-white precious metal as catalyst was first reported in Wacker process developed for the oxidation of ethylene to acetaldehyde in 1959. Study of nucleophilic allylation and its mechanistic studies performed by Tsuji et al. started the modern era in organo-palladium chemistry [1]. Since then, several palladium catalyzed organic transformations were developed. Especially noteworthy are those involving carboncarbon bond formation such as Suzuki, Hiyama, Heck, Kumada, Negishi, Stille, Sonogashira etc. which changed the way in which organic synthesis is conceptualized. These highly important reactions were carried out in high boiling organic solvents and required phosphine ligands which were expensive and toxic. Moreover, separation of palladium metal ions especially from pharmaceuticals is a cumbersome necessity. Eventually, efforts for greening of reaction protocols for these reactions became important which led to synthesis of water soluble ligands on one hand and polymer supported ligand or palladium catalysts on the other hand [2].

In the last two decades which saw intense research in the field of metal nanoparticle synthesis, palladium catalyzed carbon-carbon reactions have witnessed a complete revolution. PdNPs catalyzed C-C coupling reaction and its mechanistic issues were first reported by Beller et al. in 1996. They prepared Pd colloids stabilized by tetra-octylammonium bromide following the Bonne-man procedure and used it to study Heck arylation [3]. Reetz et al. also reported independently in 1996 the preparation of nanostructured PdNPs of sizes 8-10 nm on propylene carbonate which were highly stable under the Heck reaction conditions (140-155°C) [4]. A lot of research in the field of PdNPs catalyzed C-C coupling reactions followed which resulted in ligandless reactions in water at

temperatures ranging from RT to moderate. To facilitate separation of nanoparticles, supporting them on insoluble supports is very attractive but supports can decrease the accessibility of the catalytic sites. As nanoparticles are extremely structure-sensitive, their catalytic activity not only depends upon their size and shape but also on their support [5]. A support that can stabilize nanoparticles, without hindering catalytic sites is highly desirous. Challenge also lies in the facile synthesis and uniform or narrow distribution of sizes of nanoparticles on supports that allow facile movement of materials in the reaction medium. Therefore, innumerable and extremely varied approaches to synthesize supported nanoparticles have been pursued [6]. Supporting nanoparticles on supports can further enhance the sustainability of catalyst by facilitating recovery and reuse.

Microwave induced heating in closed vessels for organic synthesis has emerged as one of the most efficient ways of carrying organic synthesis. Combining microwave heating with Pd nanoparticle catalysis has led to ligand-free carbon-carbon coupling reactions with unprecedented reaction rates using catalyst in such miniscule amounts called homeopathic doses, thus, enhancing the sustainability of these procedures. We have earlier reported palladium nanoparticles supported on nonfunctional inert commercial polystyrene resin Amberlite XAD-4 for microwave enhanced Suzuki and Hiyama coupling reactions. Herein, we first report some more developments in the catalytic activity of resin-PdNPs in different C-C coupling reactions and then discuss the general advantages in terms of time and yield for reactions carried under microwave heating over those carried out under conventional heating. All the reaction parameters were studied and reaction conditions optimized for the best Turnover numbers (TON) and Turnover frequencies (TOF) in benign organic solvents. Further, the reusability of the resin was checked and post reaction TEM analysis was carried out to check the stability of nanoparticles.

2. 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/HNO₃ (aqua regia) and rinsed thoroughly with Millipore-Q water. Styrene, phenyl boronic acid. phenyltrimethoxysilane, methyl acrylate, phenyl acetylene, Iodobenzene, 4-iodoanisole, 4iodoacetophenone, 4-iodonitrobenzene, 4-iodotoulene, bromobenzene, 4-bromoanisole, 4-4-bromonitrobenzene bromoacetophenone, 4-bromotoulene, chlorobenzene, 4chloronitrobenzene were purchased from Aldrich. All aryl halides standards were of 98-99% purity. Dichloromethane (DCM), diethyl ether (Et₂O), Na₂CO₃ and K₂CO₃ were purchased from Finar chemicals. The resin supported palladium nanoparticles were synthesized by a method developed in our lab [7] and further characterized by TEM-EDX.

High resolution Transmission electron microscopy (HR-TEM-EDX) pictures were taken using a JEOL, JEM 2100 instrument with EDX analyzer facility. The swollen resin beads were milled and a drop of alcoholic suspension was placed onto a 200 mesh carbon coated copper grid. It was then dried to evaporate the solvent and used for microscopy. Inductively coupled plasma atomic emission spectroscopy (ICP-AES) measurements was carried out on a HJY Ultima-2 instrument: power 1000 W, nebulizer flow 1.29, nebulizer pressure 2.96, wave length 340.458 nm. GC–MS measurements were carried on Perkin Elmer USA Auto system XL. The GC-MS programs applied throughout the analysis was as follows: the column temperature was 40 °C at the beginning of the program and it was heated with a rate of 5 °C/min up to 250 °C. UV-Visible absorption spectra were acquired on a Jasco V-570 UV-Vis spectrophotometer. ¹H NMR spectra were recorded on a Bruker Advance II 400 NMR spectrometer. Reactions were carried out in CEM Microwave synthesizer (benchemate), in closed vessels with external cooling under aerobic conditions.

2.1 Protocol for sequential synthesis of asymmetric terphenyl

Into a 10 mL vial 4-iodo bromobenzene (1.0 mmol) phenylboronic acid (1.0 mmol) sodium carbonate (2.0 mmol), 200 mg resin-PdNPs (Pat dried between the folds of filter paper), 1.5 mL ethanol, 1.0 mL water was taken and heated at 140 °C at 100 watt in a CEM benchmate microwave reactor. After 10 minutes 1.0 mmol of substituted phenylboronic acid was added and reaction mixture heated for another 10 min under same conditions. The reaction was quenched by filtering the hot solution into 10 mL of cold water. The resulting solution was extracted with Et_2O (2×5 mL). The combined ether extract was dried over anhydrous MgSO4 and crude isolated after removing the solvent. The product was recrystallized from appropriate solvent.

2.2 Protocol for Mizoroki-Heck cross-coupling reaction using Resin_PdNPs

Into a 10 mL vial, aryl halide (1.0 mmol), alkenes (1.5 mmol), base (2.0 mmol), ethanol (3.0 mL), water (1.0 mL) and resin - PdNPs catalyst (300 mg) were taken and heated in a CEM microwave (120 w, 120 °C) for different intervals of time (Scheme 5.1). The reaction was quenched by pouring the reaction mixture in 10 mL cold water. The resulting solution was extracted with Et₂O. The combined ether extract was dried over anhydrous MgSO₄ and the solvent removed using a rotaevaporator. The crude products thus isolated were recrystallized from appropriate solvents and analyzed by ¹H NMR.

The effect of various parameters such as base, solvent, temperature, catalyst concentration, time and recyclability was studied taking coupling of iodobenzene and styrene as the standard reaction

2.3 Protocol for Sonogashira cross-coupling reaction using Resin_PdNPs

Into a 10 mL vial, aryl halide (1.0 mmol), phenylacetylene (1.2 mmol), K₂CO₃ (3.0 mmol), ethanol (3.0 mL), water (1.0 mL) and resin-PdNPs catalyst (300 mg) were taken and heated in a CEM microwave (150 w, 90 °C) for different intervals of time (Scheme 6.1).

The reaction was quenched in 10 mL cold water. The resulting solution was extracted with Et₂O. The combined ether extract dried over anhydrous MgSO₄ and solvent removed using a rotaevaporator. The crude product thus isolated was recrystallized from appropriate solvents.

The effect of various parameters was studied taking coupling of iodobenzene and phenylacetylene as the standard reaction

3. Result and Discussion

Amberlite XAD-4 resin is a microporous material with high surface area, durability and chemical stability towards acids, bases and oxidizing agents. This makes it an ideal solid support for the immobilization of the metal nanoparticles [8-9]. The resin is thermally stable under microwave conditions and due to its inert nature there is no interference with reaction conditions. The resin was impregnated with nanoparticles by a protocol mentioned before. Diffusion of precursor ion takes place into the polymer matrix which is passive as no chelating or ion exchange groups are present. Sajiki et al. [10] were of the opinion that some complexation occurs with electron rich benzene ring. But we observed that absorption of metal precursor was not complete even after equilibrating the resin with 1 molar solution for 24 h. So, these interactions must be very weak. After excess of precursor solution was filtered off, palladium ions were reduced by passing cold sodium borohydride solution quickly (Fig. 1). Microporous resins such as XAD-4 has two types of porosities: micropores which are permanent and nanopores that develop only after swelling with solvent. Size of nanopores is dependent on the degree of cross linking and the nature of solvent used for swelling. Hanson and co-workers [11] showed that if low concentration of metal precursor is used small nanoparticles are formed in the nanopores. The size of nanopores can control the growth of metal particles which resulted in very small distribution in the size of PdNPs. Micropores present in the resin facilitate movement of material through the resin that

enhances contact with catalytic sites. This makes these microporous polymer resins highly suitable for supporting nanoparticles for solution phase reactions. After impregnation with PdNPs colorless resin beads turn brown. HRTEM images (Fig. 2) revealed that palladium nanoparticles were uniformly embedded in the matrix of resin with narrow distribution of particles size (3-10 nm in diameter) and d-lattice spacing as measured from HR-TEM was 0.2118 nm which is close to d-spacing of the (1 1 1) planes of fcc Pd crystal [12]. The UV-Visible spectroscopy was also used to check the reduction of Pd(OAc)₂. UV-visible spectrum (Fig. 3) of Pd(OAc)₂ showed a peak at 400 nm which indicated the existence of Pd(II). This peak disappeared completely after passing sodium borohydride indicating complete reduction of Pd (II) to Pd(0). Resin was incinerated in a furnace and the amount of palladium in the residue was determined by ICP-AES after preparing its solution [8]. It was found to be 0.00235 mmol/g (0.249 mg/g) of the resin for resin-PdNPs. It is noteworthy to mention here that this technique can be used to recover precious palladium from the catalyst once it becomes inactive. Though, it is possible to load higher concentration of metal, we kept it low for two reasons: one to prevent overheating of the catalyst during microwave heating and two, over loading can hinder mass transfer through the resin matrix.

3.1 Catalytic activity of Resin_PdNPs

The synergism between nano-catalysts and microwave heating is leading to highly efficient protocols in terms of both turn over number and turn over frequency. Also, the ability to heat low boiling solvents above their boiling points in microwave assisted closed vessel reactions have diminished the need for high boiling organic solvents to conduct reactions at high temperatures. Judicious choice of mixed solvents can further enhance general applicability of the protocols. It also minimized the need for usage of surfactants such as TBAB leading to truly green protocols.

3.1.1 Catalytic activity of Resin_PdNPs for Suzuki and Hiyama reactions

We have already demonstrated the huge potential of microwave heating to carry out Hiyama and Suzuki reactions using Resin_PdNPs [for details see references 7-8]. Excellent results were obtained in both the cases using less reactive bromo derivatives. We further used these protocols to synthesize terphenyl a chemical used industrially as heat storage and transfer agents. Terphenyl can be easily synthesized by using either Suzuki or Hiyama coupling of di-iodo or 4-bromo iodobenzene with appropriate reagent. When 4bromo iodobenzene was reacted with equivalent amount of phenylboronic acid or phenyltrimethoxysilane, major isolated coupled product was 4-bromobiphenyl. However, when two moles of phenylboronic acid or phenyltrimethoxysilane were used terphenyl was isolated in high yield (Fig. 4). We used this selectivity to synthesize asymmetric terphenyls in one pot by sequential addition of different boronic acids. The products were identified by their NMR data (See supplementary data).

3.1.2 Catalytic activity of Resin_PdNPs for Mizoroki-Heck reactions

"Heck Reaction" refers to the C-C coupling reaction between aryl halides or vinyl halides and activated alkenes catalyzed by palladium in the presence of a base. It was first discovered by Mizoroki [13] and further developed by Richard F. Heck [14] in the early 1970's. Soluble Pd complexes with phosphine ligands were used to be general catalysts for Heck Reaction [15-16] as active sites are more accessible. However, separation and recycling of the homogeneous catalysts is extremely difficult and in consideration of economic, as well as environmental issues, heterogenization of catalyst was an obvious necessity. Thus, palladium complexes or nanoparticles were immobilized on various supports such as silica [17-21], alumina [22], zeolite [23], organic polymers [24, 25], carbon nanotube [26], grapheme [27, 28] and biological materials [29] to create heterogeneous catalysts. Although

many of them were reported to be effective for Heck reactions, very few catalysts showed high stability of Pd species and successful recyclability. Mehnert et al. reported that Pd nanoparticles supported on mesoporous silica showed good yield for Heck reaction of aryl bromides, but recycling of this catalyst was hampered by significant agglomeration of PdNPs [30]. Dams et al. published Pd-exchanged zeolites with obvious formation of Pd cluster. Structural damage to the support were reported after use in Heck reaction as catalyst [31]. Köhler et al. synthesized Pd/C catalysts for Heck reaction and showed that the average Pd crystallite size significantly increased after reactions [32]. Therefore, heterogeneous catalysts with excellent catalytic activity and recyclability, which is the key factor for the practical applications, are still limited and remain a challenge.

In the present study resin-PdNPs were used to study Mizoroki-Heck reaction and the effect of solvent, catalyst quantity, time, nature of base, etc. were studied and reaction conditions optimized for the coupling between iodobenzene and styrene. Optimization of the conditions is summarized in Table 1. The solvents play an important role in this reaction. Literature showed that many organic solvent such as DMSO, DMF, toluene, dioxane etc. have been used. Under microwave heating the choice of solvent is even more important as they not only provide a medium for reaction but also affect the rate at which microwaves are absorbed. So, polar solvents such as alcohols, DMF and DMSO are more efficient compared to nonpolar solvents like toluene and dioxane. Based on our earlier studies we carried out the reactions at a temperature of 120 °C using ethanol/ water mixture in a closed vessel protocol. A mixture of ethanol water was tried in different proportions and best resulted were obtained when EtOH: H₂O in 3:1 ratio was used. The presence of base was essential for reaction as no reaction took place in its absence. Both nature and quantity of base are reported to have a great effect on the yield of the Mizoroki-Heck reaction [33-35]. Many bases such as Na₂CO₃,

Et₃N, NaHCO₃ and CH₃COONa were tried and among them Na₂CO₃ was found to be the most effective (Table 1).

The catalytic activity of the nanoparticle systems was investigated by varying the amount of catalyst while keeping the other parameters constant. It was observed that 300 mg resin (≈ 0.0007 mmol of Pd, 0.07 mol % with respect to aryl halide) was sufficient for completing the reaction. Using the obtained results, we calculated the, TON and TOF (h⁻¹) values which were found to be 1,430 and 7,150 respectively. To study the effect of time the reaction mixture was analyzed at different intervals of time. The reactions were quenched by filtering the hot solutions in water after appropriate time. The product extracted into ether and was analyzed by GC-MS (Fig. 5). The analysis of the ether extract showed a peak for unreacted iodobenzene at retention time of 10.40 min whereas the peak for stilbene appeared at retention time of 16.60 min. Total conversation of iodobenzene was obtained after 12 min as the peak for iodo benzene disappeared completely at this point. It was also observed that trans-stilbene was produced exclusively. No homocoupling product was observed

After optimizing the reaction conditions, we checked the versatility of protocol by coupling various aryl halides with styrene or methyl acrylate (Table 2). The course of the reaction was monitored periodically by analyzing reaction mixture by means of TLC (or GC if necessary). Characterization of the products was performed by their melting points and comparison of their NMR spectra with the reported data. The results demonstrate that aryl iodides with either electron withdrawing or electron donating substituents react with olefins rapidly and generate the coupled products with excellent yields in EtOH/water mixture at 120 °C. A wide range of substituents, which included –CH₃, -OCH₃, -NO₂, and – COCH₃, were compatible with this procedure. The chemo-selectivity for the reaction was

totally in the favour of trans cross-coupled product. We also tried reaction with aryl bromide (entry 6-10) and found that under the present set of conditions reaction with bromobenzene (entry 6), did not proceed to completion. However, on increasing the reaction time from 12 to 20 min, we could isolate the products in high yields. We successfully carried out reaction with less active chlorobenzene (entry 11) with good yield by increasing the reaction time to 30 min. This difference in reactivity of various aryl halides can be attributed to the differences in the strengths of C-I bond, C-Br bond and C-Cl bond. We also applied this protocol to coupling of methyl acrylate (12-14) and iodobenzene using sodium acetate as base. The product isolated in all the reactions were of high purity as no stabilizers, surfactants or ligands were used in the nanoparticle synthesis or in the reaction mixture.

A comparison of the present protocol with others reported in the literature under microwave heating was carried out and the results are reported in Table 3. It can be seen that the present catalyst exhibited equally high conversions and yields without using any surfactant or ligand. Reactions were completed in short time compared to others. Moreover the Resin-PdNPs were easily separated and recycled many times.

3.1.3 Catalytic activity of resin supported PdNPs for Sonogashira reaction

Sonogashira cross-coupling, a palladium-copper catalyzed reaction of aryl halides and terminal acetylenes, is another important and widely used reaction for $sp-sp^2 C - C$ bond formation. It provides an efficient route for the synthesis of diaryl-substituted acetylenes [36], an important intermediate for the synthesis of natural products [37], pharmaceutical agents [38], dendrimers and conjugated polymers [39–41] etc. The reaction is generally conducted in organic solvents in the presence of amine base, copper(I) iodide as a co-catalyst and like other palladium catalyzed reactions, it showed a wide tolerance to functional groups. Both homogeneous palladium catalyst such as Pd (PPh₃)₂Cl₂ or Pd(PPh₃)₄,

and heterogeneous palladium catalysts which are supported on charcoal, zeolites and magnesium oxide [42-47], etc. has been reported. Cu(I) which is used as activator in these reactions, also promotes Glaser-type homocoupling reactions of terminal alkynes to divnes in the presence of oxygen. These undesirable by-products reduce yield and are also difficult to separate from the target products [48-50]. Hence, considerable effort is devoted to developing copper-free Sonogashira cross-coupling reactions under mild conditions. These reactions are reported in a variety of solvents using a variety of supports [51, 52]. Thathagar et al. used Cu and Pd mixed metal clusters in DMF for this reaction [53, 54]. Gao et al. used palladium nanowires for efficient coupling reaction in isopropanol at 75 °C [55]. We studied the effect of solvent, catalyst quantity, time, nature of base etc. on coupling between iodobenzene and phenylacetylene and the results are tabulated in Table 4.. It was observed that in the absence of base reaction does not proceed. Previous researchers have found that the reaction rate depends on the nature of the base also. In our lab we tried Et₃N, Na₂CO₃, K₂CO₃ and CH₃COONa and obtained best results with K₂CO₃. Though, in conventional methods protic polar solvents such as DMF and CH₃CN are common [56], we were successful in conducting the reactions at 90 °C using 3:1 ethanol/water mixture in a closed vessel protocol. The catalytic activity of the nanoparticle system was investigated by varying the amount of catalyst while keeping the other parameters constant. It was observed that 300 mg resin (≈ 0.0007 mmol of Pd, 0.07 mol % with respect to aryl halide) was sufficient for completing the reaction. Using the obtained result, TON and TOF (h⁻¹) were calculated and the values were found to be 1,430 and 3,489 respectively. The kinetic of reaction was studied by taking GC-MS of the reaction mixture at different intervals of time and results are presented in Fig. 6. Total conversion of iodobenzene was obtained in 25 min. GC-MS analysis of the ether extract showed that diphenylacetylene was the sole product. The mass spectrum of the peak at retention time = 10.098 min was identified as diphenylacetylene from

its molecular peak in the highest mass region at m/z 178. The other prominent peaks were found at m/z 176, 152, 126, 76 and 61.

After optimizing the reaction conditions, we performed the Sonogashira reaction of various aryl iodide and bromide with phenylacetylene and results are shown in Table 4. Trend similar to those observed in Heck reaction were observed here also. A total of twelve reactions were tried and 25 to 35 minutes of microwave heating was sufficient to complete the reactions. Reaction of chlorobenzene (entry 12) with phenyl acetylene was very slow and only 50% yield was obtained even after 45 min of microwave heating.

Very few examples of microwave enhanced Sonogashira reaction catalyzed by PdNPs are reported in literature. A comparison of the protocol with other reported methods under microwave heating is shown in Table 5.

3.2 Recycling of the catalyst after Heck and Sonogashira Reactions

Easy catalyst separation and recycling in successive batch operations can greatly increase efficiency of any reaction protocol. In this study we found that Resin-PdNPs were highly recyclable. At the completion of the reaction, the catalyst was recovered by simple filtration. The resin beads were collected and washed with hot alcohol/water to remove the product sorbed onto the resin and reused. The recovered catalyst was employed in the next run after further addition of substrates in appropriate amount and results are reported in Fig. 7. To check the agglomeration of particles during the reaction TEM images of the resin beads were taken after sixth cycle and the results were compared with those of freshly synthesized catalyst and the results are shown in Fig. 8. It was observed that most of the particles were still in the size range of 3 to 10 only.

Additionally, leaching of the catalyst was probed by hot filteration test. The reactions were stopped after some time and the resin beads were filtered off while the solution was still hot. The filterate was further heated and the reaction mixture analyzed by GC–MS after various intervals of time. The results are shown in Fig. 9. It was observed that the reaction stopped after the resin was filtered off. Which indicated that there were no soluble active species in the reaction mixture. Further, the reaction mixture was extracted with ether and aqueous layer was analyzed for palladium by ICP-AES. Total palladium concentration was found to be 65 ± 10 ppb in case of Heck reaction and 45 ± 10 ppb in case of Sonogashira reaction. Thus leaching of palladium was negligible.

3.3 Efficiency of microwave heating

Microwave heating is not only very efficient but also green. Thus, using microwave heating, the reactions can be performed at a faster pace with higher yield as compared to conventional heating [59]. In majority of the reactions, power of microwave was maintained between 120 to 150 W and appropriate temperature was maintained by external cooling. The temperature and potency profile for the Sonogashira reaction under microwave irradiation is shown in Fig. 10.

We have earlier reported Suzuki [7] and Hiyama [8] coupling reactions under microwave heating using resin-PdNPs. Presently, we carried out the standard reactions for all the four coupling reactions under conventional heating also (see supplementary information for protocols) and compared reaction time and yield with those obtained under microwave heating as shown in Fig. 11 (see ref. 7 and 8 for Suzuki and Hiyama reaction conditions). As expected the reaction times were greatly reduced under microwave heating (6-35 min) as compared to conventional heating (4-30 h). Isolated yields of products under conventional heating were only 65 to 85% in contrast to 88 to 95% isolated under microwave heating. It is also noteworthy that under microwave heating continuous purging of inert gas through the reaction mixture was not required. No side products were observed and in most cases the products were purified by simple crystallization. The simplicity of protocol and

efficiency of catalyst coupled with its recyclability can lead to truly sustainable and green protocols for C-C coupling reactions.

4. Conclusions

Cross-linked polystyrene resins are ideal for supporting palladium nanoparticles for microwave heating that can tremendously reduce the reaction times for C-C coupling reactions such as Suzuki, Hiyama, Heck and Sonogashira. The catalyst was successfully used to synthesize asymmetric terphenyls a useful industrial commodity. The choice of nonfunctional resin probably increased the accessibility of reaction sites as there were no strongly coordinating groups on the surface of the nanoparticles and less than 0.1 % of palladium was sufficient to carry out any of the C-C coupling reactions. The presence of permanent pores and hydrophobic nature or the resin creates a favorable mass transfer of the materials (generally non polar in C-C couplings) inside the resin matrix which allows the reactants to come in contact with the catalyst leading to high reaction rates (TOFs of the order of >103) for bromo derivatives. In comparison to direct usage of palladium salts as catalyst [60], converting them to well dispersed nanoparticles on a support is advantageous as the amount of catalyst required is much less. Besides the ease of separation of catalyst, its reuse and recovery of metal from the used catalyst are other useful benefits. Thus, synergism between microwaves and palladium nanoparticles can lead to truly green and sustainable protocols for C-C coupling reactions in general.

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Figure 1. Sorption reduction method for nanoparticle synthesis



Figure 2. HRTEM image and ED patterns of Resin_PdNPs



Figure 3. UV–visible spectrum for the resin supported PdNPs



Figure 4. Synthesis of asymmetric terphenyls



Figure 5. Time course of Heck reaction between iodobenzene and styrene



Figure 6. Time course of Sonogashira reaction between iodobenzene and phenylacetylene



Figure 7. Recycling of the catalyst for the standard Mizoroki-Heck and Sonogashira reaction



Figure 8. TEM image of freshly prepared Resin_PdNPs [A], and after sixth recycle of Heck reaction [B]



Figure 9. Results of hot filteration test [A] reaction between styrene and iodobenzene [B] reaction between phenylacetylene and iodobenzene



Figure 10. Temperature and potency profile for the microwave-assisted Sonogashira reactions catalyzed by resin-PdNPs



Figure 11. A comparison of time and yield for standard protocols of various coupling reactions

Entry	Reaction Condition	Yield (%)
1	Na ₂ CO ₃ , EtOH:water(3:1), 120 °C	-
2	Catalyst 300 mg, Na ₂ CO ₃ , EtOH:water(3:1), 120 °C	95
3	Catalyst 300 mg, Et ₃ N, EtOH:water(3:1), 120 °C	40
4	Catalyst 300 mg, NaOAC, EtOH:water(3:1), 120 °C	55
5	Catalyst 300 mg, NaHCO ₃ , EtOH:water(3:1), 120 °C	60
6	Catalyst 200 mg, Na ₂ CO ₃ , EtOH:water(3:1), 120 °C	35
7	Catalyst 100 mg, Na ₂ CO ₃ , EtOH:water(3:1), 120 °C	75
8	Catalyst 300 mg, Na ₂ CO ₃ , EtOH:water(1:1), 120 °C	65
9	Catalyst 300 mg, Na ₂ CO ₃ , EtOH:water(2:1), 120 °C	78
10	Catalyst 300 mg, Na ₂ CO ₃ , EtOH:water(2:3), 120 °C	48
11	Catalyst 300 mg, Na ₂ CO ₃ , EtOH:water(3:1), 100 °C	80
12	Catalyst 300 mg, Na ₂ CO ₃ , EtOH:water(3:1), 80 °C	67

Table 1 Optimization of reaction condition on the Mizoroki-Heck reaction

Reaction Conditions: Iodobenzene (1.0 mmol); styrene (1.5 mmol); base (2.0 mmol);(Microwave conditions 120 w, 12 min). *Isolated yields.

Entry	Aryl halide	Product	Time (min)	*Yield %
	Iodobenzene		12	95
2	4-iodoanisole	осн3	12	92
3	4-iodoacetophenone	Сосн3	12	85
4	4-iodonitrobenzene		12	90
5	4-iodotoulene	С СН3	12	82
6	Bromobenzene		18	90
7	4-bromoanisole	ОСН3	20	87
8	4-bromoacetophenone	COCH3	20	82
9	4-bromonitrobenzene	NO ₂	20	88
10	4-bromotoulene	CH3	20	80
11	Chlorobenzene		20	25(86)

Table 2: Resin-PdNPs Catalyst Mizoroki-Heck cross-coupling reaction with various aryl halides with alkenes



Conditions: Aryl halide (1.0 mmol); alkenes (1.5 mmol); Resin-PdNPs (300 mg); base (2.0 mmol); EtOH (3.0 mL); H₂O (1.0 mL) (Microwave conditions, 120 °C, 120 w). *Isolated yields, ** using sodium acetate base.

Entry	Catalyst	Reaction Condition	Yield %	Ref.
1	Resin-PdNPs	Na ₂ CO ₃ , EtOH:H ₂ O (3:1), 120 W, 120 °C, 12-20 min.	95	Present
2	Pd(0)-PVP	K ₂ CO ₃ , EtOH, 120 °C, 300 W, 5-12 min.	65-85	33
3	Pd@Cs ⁺ -(Al)MCM-41	NaOAc, DMA, 165 °C, 300 W, 10 h.	45 (Conv. %)	34
4	PdNPs@laponite	NEt ₃ , Solvent less, 25-75 W MW, 5-10 min	94	35

Table 3: A comparison of the present method for Heck coupling with other methods

Entry	Reaction Condition	Yield (%)
1.	K ₂ CO ₃ , EtOH:Water(3:1), 90 °C	-
2	Catalyst 300 mg, K ₂ CO ₃ , EtOH:Water (3:1), 90 °C	95
3	Catalyst 300 mg, Et ₃ N, EtOH:Water (3:1), 90 °C	55
4	Catalyst 300 mg, NaOAC, EtOH:Water(3:1), 90 °C	45
5	Catalyst 300 mg, Na₂CO ₃ , EtOH:Water(3:1), 90 ℃	65
6	Catalyst 200 mg, K ₂ CO ₃ , EtOH:Water(3:1), 90 °C	68
7	Catalyst 100 mg, K ₂ CO ₃ , EtOH:Water(3:1), 90 °C	22
8	Catalyst 300 mg, K₂CO ₃ , EtOH:Water(1:1), 90 ℃	55
9	Catalyst 300 mg, K ₂ CO ₃ , EtOH:Water(2:1), 90 °C	75
10	Catalyst 300 mg, K ₂ CO ₃ , EtOH:Water(2:3), 90 °C	35
11	Catalyst 300 mg, K ₂ CO ₃ , EtOH:Water(3:1), 70 °C	70
12	Catalyst 300 mg, K ₂ CO ₃ , EtOH:Water(3:1), 50 °C	57

Table 4. Optimization of reaction condition on the Sonogashira reaction

Conditions: Aryl halide (1.0 mmol); phenylacetylene (1.2 mmol); base (3.0 mmol); (microwave conditions, 90 °C, 150 w). *Isolated yields.

Table 5: Resin-PdNPs	catalyst	Sonogashira	coupling	reaction	various	aryl	halides	with
phenylacetylene								

Entry	Aryl halide	Product	Time (min)	*Yield %
1	Iodobenzene		25	95
2	4-iodoanisole	√ — — √ — осн,	25	92
3	4-iodoacetophenone	ССосн3	25	85
4	4-iodonitrobenzene		25	90
5	4-iodotoulene	⟨Сн,	25	82
6	Bromobenzene		35	90
7	4-bromobenzaldehyde	⟨сно	35	85
8	4-bromoanisole	⟨осн₃	35	87
9	4-bromoacetophenone		35	82
10	4-bromonitrobenzene	√	35	88
11	4-bromotoulene	√————————————————————————————————————	35	80
12	Chlorobenzene		45	50

Conditions: Aryl halide (1.0 mmol); phenylacetylene (1.2 mmol); resin-PdNPs (300 mg); base (3.0 mmol); EtOH (3.0 mL); H₂O (1.0 mL) (Microwave conditions, 90 °C, 150 w). *Isolated yields.

Entry	Catalyst	Reaction Condition	Yield %	Ref.
1	Resin-PdNPs	K ₂ CO ₃ , EtOH:H ₂ O, 90 °C, 150 W, 25-45 min.	95	Present
2	Pd-starch	DABCO, solvent free, 300 W, 130 °C, 2 min.	55-65	57
3	Pd/G	DBU, 300 W, 120 °C, 10 min.	89	58

Table 6. A comparison of the present method for Sonogashira reaction with other methods