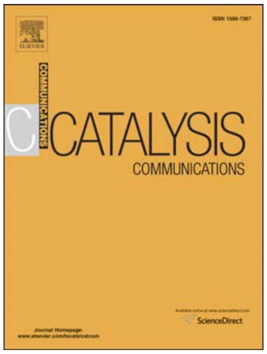

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PII: S1566-7367(13)00090-3
DOI: doi: 10.1016/j.catcom.2013.03.013
Reference: CATCOM 3438

To appear in: *Catalysis Communications*

Received date: 16 January 2013
Revised date: 25 February 2013
Accepted date: 11 March 2013

Please cite this article as: Ardeshir Khazaei, Sadegh Rahmati, Shahnaz Saeednia, An efficient ligand- and copper-free Sonogashira reaction catalyzed by palladium nanoparticles supported on pectin, *Catalysis Communications* (2013), doi: 10.1016/j.catcom.2013.03.013

# An efficient ligand- and copper-free Sonogashira reaction catalyzed by palladium nanoparticles supported on pectin

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## Abstract:

A novel and green procedure for synthesis of Palladium nanoparticles (2-6 nm) supported on pectin, as a reductant and ligand is described. The synthesized catalyst was further successfully explored in copper, ligand- and amine-free Sonogashira-Hagihara coupling of various aryl iodides, bromides and chlorides as well as heteroaryl halides with phenylacetylene under aerobic conditions. It was found that the catalyst exhibited a high activity and selectivity for the Sonogashira-Hagihara reaction. The catalyst can be recovered and recycled by a simple filtration of the reaction solution with some decrease in catalytic activity.

**Keywords**: Coupling reaction, Palladium nanoparticles, Sonogashira-Hagihara reaction, Phenylacetylene, Pectin.

## Introduction

Palladium catalyzed methods for formation of carbon-carbon bonds have been widely studied because of the usefulness and wide applicability to various substrates [1,2]. In recent years, investigators have focused their attention to reduce the cost of the reaction either by replacing palladium with cheap metals [3] or by using palladium nanoparticles immobilized on solid supports [4,5]. In this regard, immobilization of the catalysts to organic [6] or inorganic [7] supports has gained much attention because they offer several advantages such as easy separation, low waste and low cost.

In the last few years, immobilization of the palladium nanoparticles on solid supports to prepare active and stable catalytic systems is an interesting topic, and various supports have been employed to stabilize the nanoparticles, such as silica [8], carbon nanotube [9], metal oxides [10], polymers [11], magnetic-material [12], dendrimer [13] and ionic liquid [14]. Despite significant advances in the use of new supports with various ability for stabilized of palladium nanoparticles, less attention has been paid to bioorganic polymers [15-18] such as carbohydrate-based materials. Carbohydrate-based materials such as polysaccharides are attracting growing interest as substitutes for classical inorganic and organic supports for environmentally friendly catalysts. Along this line, Pd/chitosan [19,20] and Pd/starch [21] have been prepared using polysaccharides as the bed. In addition, they are cheap, non-toxic, environmentally friendly and readily available in the nature.

Pectin is a polysaccharide that is found extensively in all plant primary cells. It is a natural polymer which extensively employed in food industry, as a thickener or stabilizing agent. Pectin is a linear chain of 1,4-linked α-D-galacturonic acid residues in which some of the carboxyl groups are methyl esterified (Figure 1). Eye-catching properties of pectin, such as flexibility, biodegradability, non-toxicity, low price and carrying freely available hydroxyl groups make it suitable and ideal candidate for many practices in different areas of science [22,23]. Pectin contains free carboxyl groups on its backbone which can form complexes with Pd(II) ions in solution and reduce them to Pd(0) without using any extra reducing agent such as $NaBH_4$, hydrazine or molecular hydrogen. This slow rate *in situ* reduction of Pd(II) to Pd(0) causes the formation of small size and well distributed palladium nanoparticles on the surface of pectin.

**<Figure 1>**

Recent development in Pd-catalyzed reactions has revealed that palladium nanoparticles can catalyze various C-C coupling reactions including Mizoroki–Heck, Suzuki–Miyaura and Sonogashira-Hagihara reactions [24]. The Sonogashira-Hagihara coupling reaction is often used as a key step in the sp-sp$^2$ carbon-carbon bond forming reactions [25]. The Sonogashira coupling reaction of terminal alkynes and aryl or alkenyl halides provides an efficient method to the synthesis of aryl alkynes [26]. This reaction is performed in the presence of catalytic amounts of a palladium complex and copper(I) iodide in the presence of a base [27]. Using copper iodide as the co-catalyst sometimes lead to the homo-coupling reaction of terminal alkynes [28]. In order to solve this problem, copper-free systems for this reaction were reported [29]. In this paper, we report a ligand- and copper-free Sonogashira reaction catalyzed by palladium nanoparticles stabilized by pectin as biopolymer support under aerobic conditions.

## Experimental:

### Gram-scale preparation of palladium nanoparticles supported on pectin:

Pectin (1 g) was dissolved in water (100 mL) at ambient temperature. To this solution was added a solution of $PdCl_2$ (100 mL, 1 mM) and diluted with water (100 mL). The reaction mixture was refluxed at 100 °C for 4 h. The mixture was cooled down to room temperature and the solvent was evaporated. The obtained dark grey composite was dried by the flow of air over night and then under vacuum for 24 h.

### General procedure for the Sonogashira-Hagihara reaction in the presence of the nanocatalyst:

Into a conical flask, a mixture of pectin supported Pd nanoparticles (0.05 g of the composite, contains 0.0028 mmol of Pd), aryl halide (1 mmol), terminal acetylene (2 mmol), KOAc (1.5 mmol) and DMF (2 mL) were stirred at 100 °C under aerobic conditions. After completion of the reaction (monitored by TLC or GC), water (10 mL) and ethylacetate (10 mL) was added to the reaction mixture and decanted. The organic layer was dried over anhydrous $Na_2SO_4$. After evaporation of the solvent, the products were purified by column chromatography. Finally, evaporation of the solvent gave the desired pure products in good yields.

## Results and discussion:

The palladium nanoparticles supported on pectin were prepared by addition of aqueous solution $PdCl_2$ (100 mL, 1 mM) to pectin (1 g dissolved in 100 mL water) without using any extra reducing agent. This solution was refluxed for 4 h giving a dark grey solution. Evaporation of the solvent followed by drying gave a dark grey solid.

Our initial efforts were focused on the characterization of the resulting Pd supported nanoparticles. The UV-Vis spectroscopy of the resulted material showed the complete conversion of Pd(II) to Pd(0) which was proved by the disappearance of the peak at around 430 nm (Figure 2).The presence of palladium in the obtained material was confirmed by energy dispersive X-ray analysis (EDX) and its loading amount was measured to be 0.61% w/w. The EDX spectrum also shows other elements, including C and O, which are present in the pectin substrate (Supporting information, Figure 1S). The X-ray diffraction (XRD) spectroscopy of the resulted material shows four peaks at (111), (200), (220) and (311) crystallographic planes related to the formation of Pd(0) (Supporting information, Figure 2S).

**<Figure 2>**

The transmission electron microscopy (TEM) image shows that the average size of the Pd nanoparticles entrapped by pectin is around 2-6 nm (Figure 3). The amount of palladium content deposited on the surface of pectin was detected by ICP and EDX. According to the ICP results the amount of palladium to be 0.056 mmol per gram of the pectin. Energy dispersive X-ray (EDX) results showed that the amount of palladium to be 0.057 mmol per gram of the pectin.

**<Figure 3>**

After characterization of the composite, the catalytic activities of $Pd_{np}$/Pectin were examined in the Sonogashira reaction. Initially, the optimum conditions were investigated for the reaction of iodobenzene with phenylacetylene in the presence of the nanocatalyst (Table 1). The effect of solvents and bases was studied upon the reaction at different temperatures. The results showed that the nanocatalyst was not efficient when the reaction was performed in water as a solvent (Table 1, entry 1). Addition of TBAB as a phase transfer agent to the water was not beneficial to the progress of the reaction (Table 1, entry 2). We have also checked the effect of TBAB as a reaction media in its melt form (100 °C) in the presence of KOAc or NaOAc (Table 1, entries 3 and 4). Employing PEG as the solvent gave 82% conversion of the starting material after 70 min (Table 1, entry 5). Comparison of the results clearly shows that among the tested solvents, DMF was more beneficial solvent compared to other tested solvents. Employing DMF as the solvent in the presence of KOAc at 100 °C gave 100% conversion of the starting material after 25 min (Table 1, entry 8). The reaction was also studied in the presence of various bases. The results demonstrated that the effect of bases on the reaction was significant (Table 1, entries 8–13). A comparative study of different bases, such as KOAc, NaOAc, DABCO, $K_2CO_3$, $Et_3N$, and n-$Pr_3N$ in the reaction showed that

KOAc was more effective for this coupling. Using KOAc as the base, the effect of temperature on the reaction was studied. Decreasing the temperature was accompanied by the elongation of the reaction times as well as lowering the yields of the coupling products (Table 1, entries 6-8). No reaction happens in the absence of the Pd nanoparticle.

**<Table 1>**

Employing the optimized reaction conditions (Table 1, entry 8), a range of aryl iodides, bromides and chlorides with various substituent groups were examined in the Sonogashira coupling reaction in the presence of $Pd_{np}$/Pectin catalytic system (Table 2). All coupling products were easily isolated from the catalyst and solvent by extraction with ethylacetate in high yields. It is citable that, the Sonogashira coupling reaction performed efficiently without utilizing a copper catalyst [30]. It is recognized that the relative reactivity of organic halides in palladium catalyzed reactions is R-Cl<R-Br<R-I. These results reflect the reactivity toward oxidative addition. Therefore, electron-withdrawing substituents (such as $NO_2$, $CH_3CO$ and F) on aromatic halides increase the reaction rate [31]. Aryl iodides with electron-donating substituents on the aromatic ring are reactive substrates in Sonogashira reactions and the related reactions went to completion in

longer reaction times (Table 2, entries 1-5). The coupling reaction of phenylacetylene with *o*-substituted in compare with *p*-substituted aryl iodides performed in longer times (Table 2, entries 2, 3).

The reaction of several aryl bromides and phenylacetylene was tasted at the same conditions. The yields and reaction times depend on the functional groups (electron-donating or electron-withdrawing) in aromatic ring. As expected, in the case of less reactive electron-rich aryl bromides such as 4-bromotoluene and 4-bromoanisole the coupling reaction carried out in longer time (Table 2, entries 7, 8). Very strong electron-withdrawing group (such as $NO_2$) on the aromatic ring led to a high yield at shorter time of coupling product (Table 2, entry 10). Heterocyclic aryl bromides are also suitable substrates for this reaction (Table 2, entries 11, 12). We have also questioned the coupling of aryl chlorides and observed that the Sonogashira coupling reaction can perform at 100 °C with good yields in longer times (Table 2, entries 13,14).

<**Table 2**>

There are many reports in the literature applying palladium nanoparticles for the sonogashira reaction. Some studies have been investigated to compare the catalytic activity of these modified beds in the coupling reactions. Herein we wish to compare the previously reported systems in sonogashira reaction with the system reported in this article. Shu et al. reported the application of palladium nanoparticles supported on MOF-5 in the copper-free sonogashira reaction of 4-iodotoluene with phenylacetylene in the presence of $K_3PO_4.3H_2O$ as a base in $CH_3OH$ at 80 °C. Under these conditions, the reaction was completed within 3 h [32]. Similar reaction under our conditions gave the desired product within 45 min in 93% yield (Table 2, entry 2). The in situ stabilization of Pd-nanoparticles into the nanopores of modified montmorillonite has been reported. This system has been applied as a catalyst in sonogashira reaction of idobenzene with phenylacetylene using $CH_3CN$ as solvent in the presence of $Et_3N$ under copper-free conditions. In the presence of this system the reaction was completed within 3 h [33]. While for the similar reaction, using the pectin supported palladium nanoparticles the reaction was completed after 25 min (Table 2, entry 1). In another try, palladium-polypyrrole nanoparticles were used as a catalyst for sonogashira reaction. The reaction of iodobenzene with phenylacetylene in the presence of this catalyst proceeded to completion within 4 h in the presence of $Na_2CO_3$ in NMP as the solvent at 100 °C [34], whereas, the similar reaction, as mentioned above, went to completion within 25 min. Tsai and coworkers reported the application of nanosized MCM-41 anchored palladium bipyridyl complex in the sonogashira reaction of bromobenzene with phenylacetylene in the presence of

$Bu_3N$ as a base in NMP at 140 °C. Under these conditions, the reaction gave only 30% isolated of product after 24 h [35]. Similar reaction under our conditions gave the desired product within 3 h in 82% yield (Table 2, entry 6).

Recycling of the catalyst was performed upon the reaction of iodobenzene with phenylacetylene employing 0.05 g of the catalyst in the presence of KOAc at 140 °C. After completion of the reaction at the first run, ethylacetate was added to the reaction mixture to extract the organic materials. After drying the residual Pd nanoparticles, the vessel was charged with starting materials and the reaction was repeated under the same conditions. At the first run, the reaction was completed within 25 min. The nanocatalyst has been recovered for three runs with some decrease in the catalytic activity of the catalyst. At the third run, the reaction was completed within 130 min. As the reaction was performed from the first run to the third, the required time for the completion of the reaction was elongated from 25 to 130 min, which indicates that the activity of the catalyst was decreased as the number of the runs was increased (Table 3). The TEM picture of the recovered nanocatalyst showed that the morphology and the size of the particles were not disturbed notably in comparison with the TEM picture of the fresh catalyst (Supporting information, Figure 4S).

<**Table 3**>

## Conclusion:

In conclusion, we have presented a green approach for the preparation and characterization of a novel and high performance catalyst system for the copper-free Sonogashira-Hagihara reaction. Palladium nanoparticles were formed by *in situ* reduction of $PdCl_2$ in the presence of pectin without addition of any external reducing agents. The nanoparticles have been characterized by UV-Vis, XRD and EDX spectra and also by TEM images. The $Pd_{np}$/Pectin system exhibited high catalytic efficiency and air stability in the Sonogashira coupling reaction. The catalyst could be easily separated from the products and reused for several successive runs with some decrease in catalytic activity.

Further studies on the applications of this catalytic system are in progress in our laboratory and will be reported.

## Acknowledgment:

The authors are thankful to Bu-Ali Sina University Research Councils, Center of Excellence in Development of Chemistry Methods (CEDCM) (Grant No. 2472) and National Foundation of Elites (BMN) for their supports.

## References

[1] T. Noel, S.L. Buchwald, Chem. Soc. Rev. 40 (2011) 5010-5029.

[2] N.T.S. Phan, M.V.D. Sluys, C.W. Jones, Adv. Synth. Catal. 348 (2006) 609-679.

[3] R. Loska, C.M.R. Volla, P. Vogel, Adv. Synth. Catal. 350 (2008) 2859-2864.

[4] Q. Du, W. Zhang, H. Ma, J. Zheng, B. Zhou, Y. Li, Tetrahedron 68 (2012) 3577-3584.

[5] H. Firouzabadi, N. Iranpoor, A. Ghaderi, J. Mol. Catal. A: Chem. 347 (2011) 38-45.

[6] B. Clapham, T.S. Reger, K.J. Janda, Tetrahedron 57 (2001) 4637-4662.

[7] F. Hoffmann, M. Cornelius, J. Morell, M. Froba, Angew. Chem. Int. Ed. 45 (2006) 3216-3251.

[8] V. Polshettiwar, A. Molnar, Tetrahedron 63 (2007) 6949-6976.

[9] R. Bernini, S. Cacchi, G. Fabrizi, G. Forte, F. Petrucci, A. Prastaro, S. Niembro, A. Shafir, A. Vallribera, Green Chem.12 (2010) 150-158.

[10] F.Z. Su, Y.M. Liu, Y. Cao, K.N. Fan, Angew. Chem. Int. Ed. 47 (2008) 334-337.

[11] B. Tamami, S. Ghasemi, J. Mol. Catal. A: Chem. 322 (2010) 98-105.

[12] B. Karimi, A. Zamani, S. Abedi, J.H. Clark, Green Chem. 11 (2009) 109-119.

[13] K.R. Gopidas, J.K. Whitesell and M.A. Fox, Nano Lett. 3 (2003) 1757-1760.

[14] V. Calo, A. Nacci, A. Monopoli, F. Montingelli, J. Org. Chem. 70 (2005) 6040-6044.

[15] A. Khalafi-Nezhad, F. Panahi, J. Organome. Chem. 717 (2012) 141-146.

[16] B.C.E. Makhubela, A. Jardine, G.S. Smith, Appl. Catal. A: Gen. 393 (2011) 231-241.

[17] H. Firouzabadi, N. Iranpoor, F. Kazemi, J. Mol. Catal. A: Chem. 348 (2011) 94-99.

[18] E. Sin, S.-Se. Yi, Y.-Sik. Lee, J. Mol. Catal. A: Chem. 315 (2010) 99-104.

[19] V. Calo, A. Nacci, A. Monopoli, A. Fornaro, L. Sabbatini, N. Cioffi, N. Ditaranto, Organometallics 23 (2004) 5154-5158.

[20] A.A. Dabbawala, N. Sudheesh, H.C. Bajaj, Dalton T. 41 (2012) 2910-2917.

[21] V.L. Budarin, J.H. Clark, R. Luque, D.J. Macquarrie, R.J. White, Green Chem. 10 (2008) 382-387.

[22] B.L. Ridley, M.A. O'Neill and D. Mohnen, Phytochemistry 57 (2001) 929-967.

[23] B.R. Thakur, R.K. Singh, A.K. Handa, Crit. Rev. Food Sci. 37 (1997) 47-73.

[24] A. Balanta, C. Godard, C. Claver, Chem. Soc. Rev. 40 (2011) 4973–4985.

[25] K. Sonogashira, Y. Tohda, N. Hagihara, Tetrahedron Lett. 16 (1975) 4467-4470.

[26] S. Ma, Z. Shi, Z.Yu, Tetrahedron 55 (1999) 12137-12148.

[27] K. Sonogashira, in: B. M. Trost, I. Fleming, G. Pattenden (Eds.), Comprehensive Organic Synthesis, Pergamon Press, Oxford 1991, pp. 521-549.

[28] F. Yang, X. Cui, Y. Li, J. Zhang, G. Ren, Y. Wu, Tetrahedron 63 (2007) 1963-1969.

[29] D.A. Alonso, C. Najera, M.C. Pacheso, Adv. Synth. Catal. 345 (2003) 1146-1158.

[30] T. Fukuyama, M. Shinmen, S. Nishitani, M. Sato, I. Ryu, Org. Lett. 4 (2002) 1691-1694.

[31] T. Hundertmark, A.F. Littke, S.L. Buchwald, G.C. Fu, Org. Lett. 2 (2000) 1729-1731.

[32] S. Gao, N. Zhao, M. Shu, S. Che, Appl. Catal. A: Gen. 388 (2010) 196–201.

[33] B. J. Borah, D. K. Dutta, J. Mol. Catal. A: Chem. 366 (2013) 202– 209.

[34] T.V. Magdesieva, O.M. Nikitin, E.V. Zolotukhina, V.A. Zinovieva, M.A. Vorotyntsev, Mendeleev Commun. 22 (2012) 305–306.

[35] B.N. Lin, S.H. Huang, W.Y. Wu, C.Y. Mou, F.Y. Tsai, Molecules 15 (2010) 9157-9173.

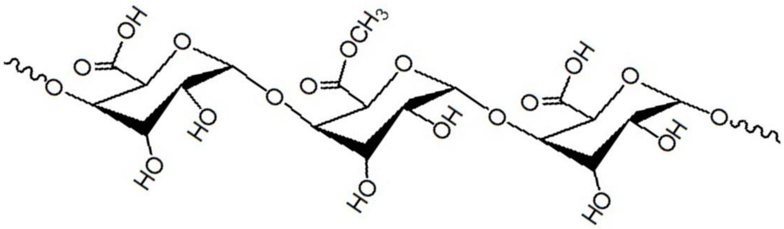


**Fig. 1** Chemical structure of pectin

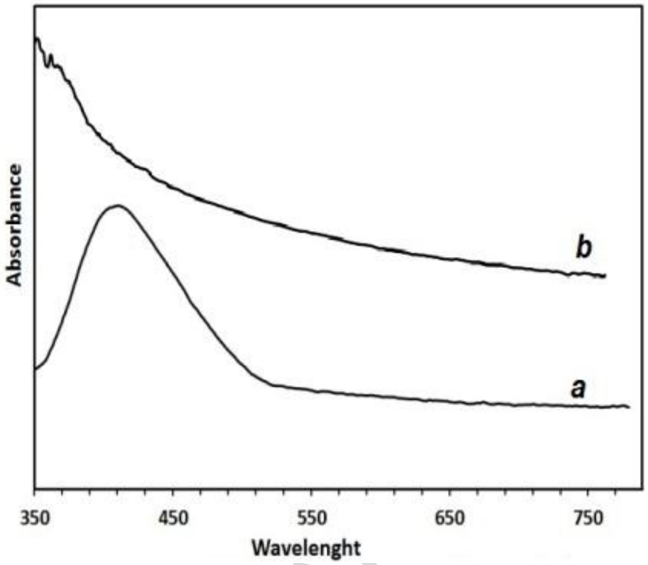


**Fig. 2** UV–Vis spectra of (a)Pd(II) before reduction and (b) Pd(0) after reduction with pectin

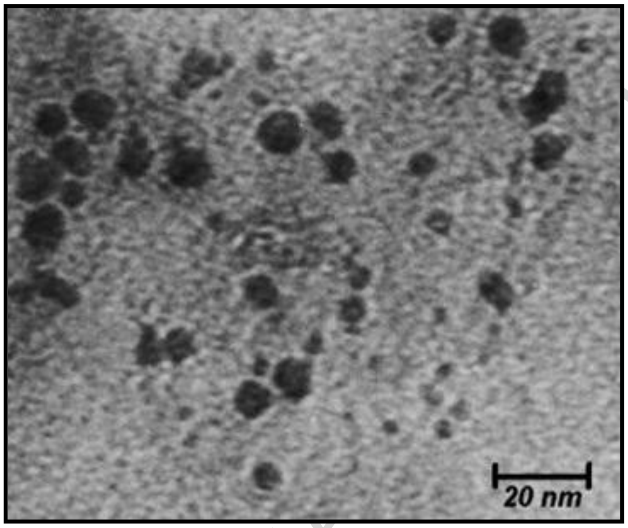
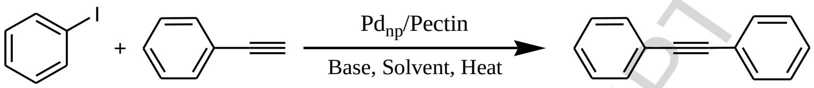


**Fig. 3** TEM image of palladium nanoparticles supported on pectin

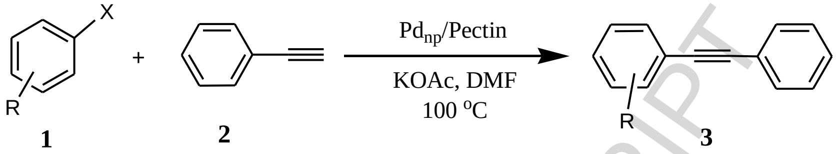
**Table 1**
Optimization conditions in Sonogashira reaction between iodobenzene and phenylacetylene in the presence of $Pd_{np}$/Pectin

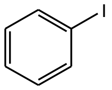
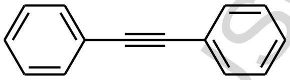
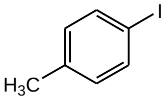
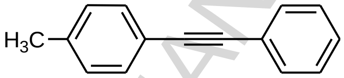
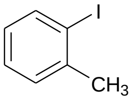
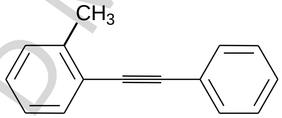
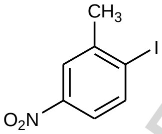
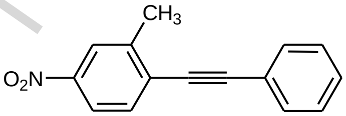
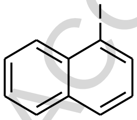
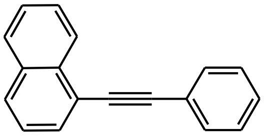
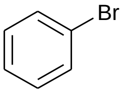
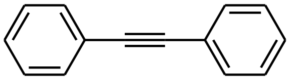
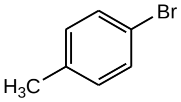
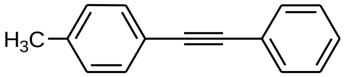
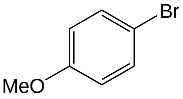
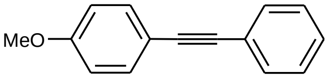


| Entry | Solvent | Base | Temperature (˚C) | Time | Conversion (%) |
|---|---|---|---|---|---|
| 1 | $H_2O$ | KOAc | 100 | 5 h | Trace |
| 2 | $H_2O$/TBAB | KOAc | 100 | 3 h | 20 |
| 3 | TBAB | KOAc | 100 | 50 min | 91 |
| 4 | TBAB | NaOAc | 100 | 2 h | 73 |
| 5 | PEG | KOAc | 100 | 70 min | 82 |
| 6 | DMF | KOAc | 60 | 4 h | Trace |
| 7 | DMF | KOAc | 80 | 4 h | 78 |
| 8 | **DMF** | **KOAc** | **100** | **25 min** | **100** |
| 9 | DMF | NaOAc | 100 | 65 min | 60 |
| 10 | DMF | DABCO | 100 | 55 min | 81 |
| 11 | DMF | $K_2CO_3$ | 100 | 85 min | 52 |
| 12 | DMF | $Et_3N$ | 100 | 3 h | Trace |
| 13 | DMF | n-$Pr_3N$ | 100 | 3h | 15 |

**Table 2**

Reaction of aryl halides with phenylacetylene catalyzed by $Pd_{np}$/Pectin[a]



| Entry | Aryl halide | Product | Time | Yield (%)[b] |
|---|---|---|---|---|
| 1 |  1a |  3a | 25 min | 91 |
| 2 |  1b |  3b | 45 min | 93 |
| 3 |  1c |  3c | 2.5 h | 90 |
| 4 |  1d |  3d | 70 min | 79 |
| 5 |  1e |  3e | 2.5 h | 82 |
| 6 |  1f |  3a | 3 h | 82 |
| 7 |  1g |  3b | 4 h | 76 |
| 8 |  1h |  3h | 5.5 h | 73 |

| | | | | |
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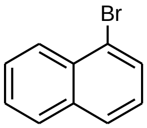
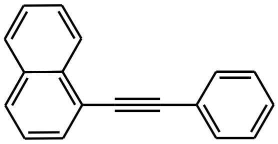
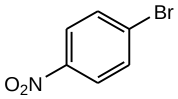
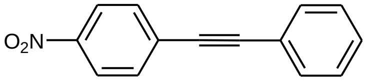
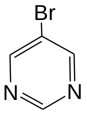
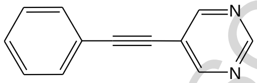
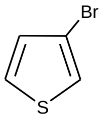
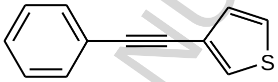
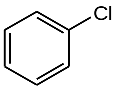
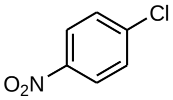
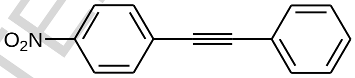
| 9 |  1i |  3e | 4 h | 53 |
| 10 |  1j |  3j | 70 min | 80 |
| 11 |  1k |  3k | 90 min | 79 |
| 12 |  1l |  3l | 7.5 h | 82 |
| 13 |  1m |  3a | 9 h | 68 |
| 14 |  1n |  3j | 8 h | 76 |

[a]Reaction conditions: Aryl halide (1 mmol), Phenylacetylene (2 mmol), $Pd_{np}$/Pectin (0.05 g, 0.0028 mmol of Pd), KOAc (1.5 mmol), DMF (2 mL) at 100 °C.

[b]Isolated yield.

**Table 3**

Recycling of Palladium nanoparticles supported on pectin for the reaction of iodobenzene with phenylacetylene.

| Run | 1 | 2 | 3 |
|---|---|---|---|
| Time for completion of the reaction (min) | 25 | 50 | 130 |

## Graphical Abstract

### An efficient ligand- and copper-free Sonogashira reaction catalyzed by palladium nanoparticles supported on pectin

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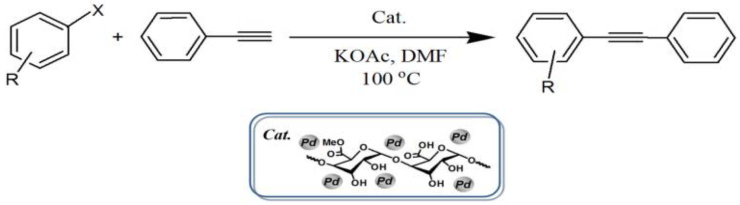

## Highlights

- Green and *in situ* formation of palladium nanoparticles in water.
- $Pd_{np}$/Pectin system shows the good catalytic activity for Sonogashira reaction in short times and aerobic conditions.
- $Pd_{np}$/Pectin could be recycled and reused.