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Palladium nanoparticles supported on agarose-catalyzed Heck–Matsuda and Suzuki–Miyaura coupling reactions using aryl diazonium salts

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In this article, palladium nanoparticles supported on agarose were used as an efficient catalyst for Heck–Matsuda and Suzuki–Miyaura coupling reactions of structurally different aryldiazonium tetrafluoroborate substrates in aqueous media. Heck–Matsuda reactions proceeded at 40°C whereas Suzuki-Miyaura reactions were carried out at room temperature. Both reactions required low catalyst loading. The catalyst was also recycled for the model reaction for three runs. Copyright © 2012 John Wiley & Sons, Ltd.

Supporting information may be found in the online version of this article.

Keywords: agarose; palladium; aryl diazonium salts; Heck; Suzuki

Introduction

Palladium-catalyzed cross-coupling reactions are recognized as essential tools for the generation of carbon–carbon or carbon–heteroatom bonds for the preparation of fundamental precursors used for the synthesis of pharmaceuticals, agrochemicals etc.[1,2]

Among vast number of reactions catalyzed by palladium, the Heck–Mizoroki reaction, which occurs between aryl or vinyl halides and olefins,[3] and the Suzuki–Miyaura reaction, which takes place between aryl halides and arylboronic acids, could be considered important reactions with very wide applications. These important reactions have placed considerable impact upon the preparation of aryl-olefin and biaryl compounds, which are found in the building blocks of a wide range of pharmaceuticals and natural products.[4–6]

In many palladium-catalyzed reactions leading to carbon–carbon and carbon–heteroatom bond formation, use of phosphane ligands is a common practice. However, many phosphane ligands are expensive, poisonous and air sensitive, with poor thermal stability.[7]

Arenediazonium salts[8] are a potential alternative to aryl halides or triflates, which are commonly used in Heck–Mizoroki and Suzuki–Miyaura reactions. The diazonium salts show higher reactivity and tolerance to many different reaction conditions. Moreover, they are easily prepared from inexpensive anilines, which makes them suitable surrogates for the aryl halides or triflates used in these coupling reactions. Using aryl diazonium salts[9] in Heck,[10] Suzuki,[11] Sonogashira[12] and Hiyama[13] reactions has attracted attention in recent years. The reactions can be performed in the presence of *N*-heterocyclic carbene ligands, palladacycle systems or under ligand-free conditions.[9,14] A Pd/charcoal catalytic system has been recently used as a heterogeneous catalyst in the Heck–Matsuda coupling reaction of aryl diazonium salts.

The high surface area-to-volume ratio of noble metal nanoparticles makes them highly attractive tools for catalysis. Along this line, palladium nanoparticles have been widely used as the catalysts in different palladium-catalyzed coupling reactions.[15] Very recently, the Suzuki-Miyaura cross-coupling of aryl diazonium salts catalyzed by alginate/gellan-stabilized palladium nanoparticles[16] and the aluminium hydroxide-supported palladium nanoparticles[17] were reported in the literature.

Herein we report a new catalytic application of palladium nanoparticles supported on agarose[18] for the Heck–Matsuda and Suzuki–Miyaura coupling reactions using aryl diazonium salts in aqueous media.

Experimental

General

Solvents and other reagents were used either as received from commercial suppliers or, when necessary, purified. Using a Bruker Avance III-400 instrument, ^{1}H NMR spectra were recorded at 400 MHz and ^{13}C NMR spectra at 100 MHz. NMR acquisitions were performed at 295 K and $CDCl_3$ was used as solvent. Chemical shifts are reported in ppm with solvent resonance as the internal standard (1H; $CHCl_3$: δ 7.29 ppm and 13C, δ 77.0 ppm). For scanning electron microscopy (SEM) a Philips XL-30 FEG instrument, operating at 20 kV, was used. Inductively coupled plasma (ICP) technique (Varian, Vista-pro) was employed for determination of the amount of palladium nanoparticles supported on agarose.

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† *This paper is dedicated to my mentor Professor Habib Firouzabadi on the occasion of his 70th birthday.*

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Gram-Scale Preparation of Palladium Nanoparticles Supported on Agarose Hydrogel

A solution of the agarose (1 g) in water (100 ml) was added with stirring to an acidic solution (100 ml water with pH adjusted to 4 by HCl) of $Pd(OAc)_2$ (0.022 g, 1 mmol) at 80°C. To the solution obtained, an aqueous solution of citric acid (4 mmol in 20 ml H_2O) was added dropwise. The mixture was refluxed for 1 h then cooled to room temperature to produce a gray-brown mass of hydrogel. Drying of the resulting hydrogel mass under a flow of air overnight and under vacuum for 24 h gave a black powder of agarose-supported palladium nanoparticles of size 20–30 nm.

General Procedure for Heck–Matsuda Coupling Reaction

Aryldiazonium tetrafluoroborate (1 mmol) and alkene (1.5 mmol) were added to a flask containing Pd catalyst (0.025 g, 0.0026 mmol% Pd as determined by ICP analysis) and water (3 ml) at 40°C. The resulting mixture was stirred in air for 5 h. The reaction mixture was then cooled to room temperature and washed with Et_2O (3 × 5 ml) to extract the desired product. Further purification was performed using silica gel column chromatography eluted with *n*-hexane–EtOAc to yield the desired aryl alkene products in high yield (Table 2) (See supporting information for ^1H and ^{13}C NMR of the products).

General Procedure for Suzuki–Miyaura Coupling Reaction

Aryldiazonium tetrafluoroborate (1 mmol) and arylboranic acid (1.5 mmol) were added to a flask containing Pd catalyst (0.025 g, 0.0026 mmol% Pd) and a mixture of water–methanol (1:1, 5 ml) at room temperature. The mixture was stirred in air for 10 h and extracted with Et_2O (3 × 5 ml). The ethereal solution was evaporated and the resulting residue was purified by silica gel column chromatography eluted with *n*-hexane–EtOAc to obtain the pure biphenyl products in high yield (Table 4) (See supporting information for ^1H and ^{13}C NMR of the products).

Typical Procedure for Recycling of the Catalyst for the Reaction of 4-Methoxyphenyl Diazonium Tetrafluoroborate with Ethyl Acrylate

After completion of the reaction, the resulting mixture was cooled to room temperature, upon which a gelatinous mass was formed. Product and organic substrates were extracted by Et_2O (3 × 5 ml) and the obtained dark gelatinous residue was reused for another batch of the similar reaction. The catalyst was recycled for three runs, giving 90%, 87% and 87% isolated yields respectively.

Results and Discussion

Agarose, as an eco-friendly degradable polysaccharide and abundant in nature (Fig. 1), has the potential for use as a support and ligand for the stabilization and entrapment of palladium nanoparticles generated in its presence.[18a,b] Along this line, in our previous studies we demonstrated the use of agarose-supported Pd nanoparticles as an effective catalyst for Suzuki–Miyaura,[18a] Mizoriki–Heck and Sonogashira–Hagihara[18b] coupling reactions under green conditions.

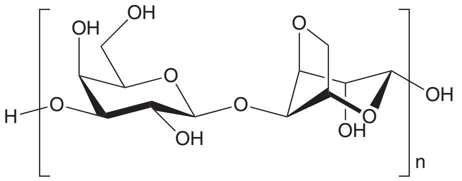


Figure 1. Agarose molecule.

In this study we present another important application of the agarose-supported Pd nanoparticles for the Heck–Matsuda and Suzuki–Myiaura coupling reactions using aryl diazonium tetrafluoroborate instead of aryl halides with low loading of palladium catalyst at 25–40°C in more friendly solvents.

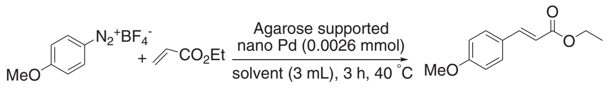
The optimized conditions for Heck–Matsuda coupling reaction were obtained using the reaction of 4-methoxyphenyl diazonium tetrafluoroborate (1 mmol) with ethyl acrylate (1.5 mmol) in different solvents such as toluene, methanol–water (1:1), acetonitrile, methanol and water, in the presence or absence of Et_3N using 0.25 g agarose supported palladium nanoparticles containing 0.0026 mmol Pd as determined by ICP analysis (Table 1).

As the results in Table 1 show, H_2O is the most suitable solvent for the reaction and the addition or elimination of Et_3N does not indicate any significant effect on the yield or progress of the reaction. The resulting optimized conditions were then applied to the reactions of various aryl diazonium tetrafluoroborates with styrene and ethyl acrylate (Table 2).

The results shown in Table 2 indicate that the reaction of aryl diazonium tetrafluoroborates bearing electron-donating as well as electron-withdrawing groups proceeded well and in excellent isolated yields.

In continuation of this study, we have also applied the catalyst to the Suzuki–Miyaura coupling reaction, using aryl diazonium tetrafluoroborate. Initially, the effect of different solvents on the reaction of 4-methoxyphenyl diazonium tetrafluoroborate (1 mmol) with phenylboronic acid (1.5 mmol) as a model reaction at room temperature was investigated. The reaction proceeded well in the mixture of methanol–water (1:1, 5 ml) to give the desired biphenyl compound in an excellent isolated yield. The results of this investigation are shown in Table 3. The optimized conditions were then applied to structurally different substrates, with excellent yields. The results are presented in Table 4.

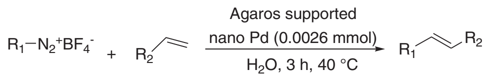
Table 1. Screening of different solvents for the reaction of 4-methoxyphenyl diazonium tetrafluoroborate with butyl acrylate in the presence of the catalyst



Entry	Solvent	Isolated yield (%)
1	Toluene	30
2	**H_2O**	**85**
3	$MeOH-H_2O$	73
4	CH_3CN	25
5	MeOH	60
6	H_2O	86[a]

[a]Reaction in the presence of Et_3N as a base.

Table 2. Reaction of different diazonium tetrafluoroborates with styrene and butyl acrylate in the presence of the catalyst in water



Entry	R_1	R_2	Isolated yield (%)
1	Ph	Ph	81
2	Ph	COOEt	83
3	4-MeC_6H_4	Ph	80
4	4-MeC_6H_4	COOEt	86
5	4-$MeOC_6H_4$	Ph	85
6	4-$MeOC_6H_4$	COOEt	85
7	4-$NO_2C_6H_4$	Ph	84
8	4-$NO_2C_6H_4$	COOEt	90
9	4-CNC_6H_4	Ph	80
19	4-CNC_6H_4	COOEt	84

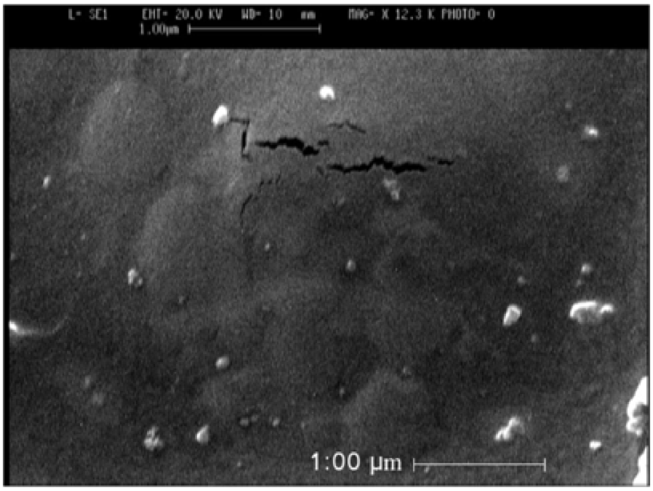
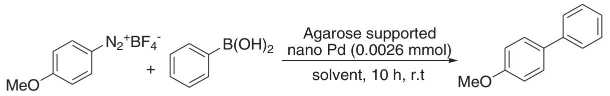


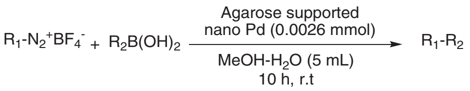
Figure 2. SEM picture of the catalyst after the third reaction cycle (scale bar: 1 μm).

Table 3. The effect of different solvents on the reaction of 4-methoxyphenyl diazonium tetrafluoroborate with phenylboronic acid in the presence of the catalyst



Entry	Solvent	Isolated yield
1	Toluene	15
2	H_2O	60
3	$MeOH–H_2O$	90
4	CH_3CN	20
5	MeOH	72

Table 4. Reaction of structurally different diazonium tetrafluoroborates with various aryl boronic acids in the presence of catalyst



Entry	R_1	R_2	Isolated yield (%)
1	Ph	Ph	80
2	Ph	2-Me–C_6H_4	83
3	Ph	4-OMe–C_6H_4	84
4	4-MeC_6H_4	4-OMe–C_6H_4	88
5	4-MeC_6H_4	4-Me–C_6H_4	90
6	4-MeC_6H_4	Ph	90
7	4-MeC_6H_4	4-Me–C_6H_4	80
8	4-MeC_6H_4	4-OMe–C_6H_4	90
9	4-$NO_2C_6H_4$	4-OMe–C_6H_4	84
10	4-$NO_2C_6H_4$	Ph	87
11	4-$NO_2C_6H_4$	2-Me–C_6H_4	90
12	4-CNC_6H_4	Ph	83
13	4-CNC_6H_4	4-Me–C_6H_4	85

In order to ascertain the major role of agarose-supported palladium nanoparticles as a catalyst in the Heck–Matsuda reaction, the reaction of 4-methoxyphenyl diazonium tetrafluoroborate with ethyl acrylate was studied in the absence of the catalyst and also in the presence of the same amount of unsupported bulk Pd (0.0026 mmol) using $Pd(OAc)_2$. In the absence of catalyst, in the appropriate reaction time, the reaction did not proceed at all. However, in the presence of bulk palladium as the catalyst the reaction was performed with only 15% isolated yield.

Finally, recycling of catalyst was studied for the reaction of 4-methoxyphenyl diazonium tetrafluoroborate (5 mmol) with ethyl acrylate (7.5 mmol) using 0.125 g of the catalyst. After completion of reaction, the reaction mixture was washed with ethyl acetate (3 × 10 ml) and decanted. The resulting mass was reused for another batch with a similar reaction. This process was repeated for three consecutive runs with 90%, 87% and 87% isolated yield respectively. The SEM picture of the recovered catalyst after the third run did not show any observable agglomeration of the nanoparticles of Pd catalyst (Fig. 2).

Conclusion

Heck-Matsuda and Suzuki-Miyaura coupling reactions of aryl diazonium salts were studied using Pd nanoparticles supported on agarose at 40°C by the low loading of Pd nanoparticle supported on agarose in neat water. In the presence of this catalyst, Suzuki–Miyaura coupling reactions were performed at room temperature in methanol–water mixture as a solvent. This air-stable catalyst was recycled for three consecutive runs with preservation of the catalytic activity in a Heck–Matsuda reaction. The SEM image of the catalyst, after the third recycle, shows preservation of the nanoparticles of Pd in the agarose network without noticeable particle aggregation.

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References

[1] a) D. S. Surry, S. L. Buchwald, *Angew. Chem.* **2008**, *120*, 6438; *Angew. Chem. Int. Ed.* **2008**, *47*, 6338; b) H. Doucet, J.-C. Hierso, *Angew. Chem.* **2007**, *119*, 850–888; *Angew. Chem. Int. Ed.* **2007**, *46*, 834; c) P. Rollet, W. Kleist, V. Dufaud, L. Djakovitch, *J. Mol. Catal. A Chem.* **2005**, *241*, 39; d) A. Zapf, M. Beller, *Chem. Commun.* **2005**, 431; e) A. Frisch, M. Beller, *Angew. Chem.* **2005**, *117*, 680; *Angew. Chem. Int. Ed.* **2005**, *44*, 674; f) I. P. Beletskaya, A. V. Cheprakov, *Coord. Chem. Rev.* **2004**, *248*, 2337; g) R. B. Bedford, C. S. J. Cazin, D. Holder, *Coord. Chem. Rev.* **2004**, *248*, 2283.

[2] a) C. Torborg, M. Beller, *Adv. Synth. Catal.* **2009**, *351*, 3027; b) A. Zapf, M. Beller, *Top. Catal.* **2002**, *19*, 101; c) C. E. Tucker, J. G. de Vries, *Top. Catal.* **2002**, *19*, 111; d) J. G. de Vries, *Can. J. Chem.* **2001**, *79*, 1086.

[3] a) A. M. Trzeciak, J. J. Ziołkowski, *Coord. Chem. Rev.* **2007**, *251*, 1281; b) L. Huang, W. P. Kwan, *Curr. Org. Chem.* **2010**, *7*, 599; c) V. Farina, *Adv. Synth. Catal.* **2004**, *346*, 1553; d) B. Karimi, H. Behzadnia, E. Farhangi, E. Jafari, A. Zamani, *Curr. Org. Synth.* **2010**, *7*, 543; e) B. Karimi, H. Behzadnia, D. Elhamifar, P. F. Akhavan, F. K. Esfahani, A. Zamani, *Synthesis* **2010**, 1399.

[4] a) A. Suzuki, *J. Organomet. Chem.* **1999**, *576*, 147; b) N. Miyaura, A. Suzuki, *Chem. Rev.* **1995**, *95*, 2457; c) F. Alonso, I. P. Beletskaya, M. Yus, *Tetrahedron* **2008**, *64*, 3047; d) N. Miyaura, A. Suzuki, *Chem. Rev.* **1995**, *95*, 2457; e) E. Giralt, P. Lloyd-Williams, *Chem. Soc. Rev.* **2001**, *30*, 145; f) J. Hassan, M. Sevignon, C. Gozzi, E. Schultz, M. Lemaire, *Chem. Rev.* **2002**, *102*, 1359; g) H. Firouzabadi, N. Iranpoor, M. Gholinejad, *J. Organomet. Chem.* **2010**, *695*, 2093.

[5] K. C. Nicolaou, P. G. Bulger, D. Sarlah, *Angew. Chem. Int. Ed.* **2005**, *44*, 4442.

[6] a) S. Kotha, K. Lahiri, D. Kashinath, *Tetrahedron* **2002**, *58*, 9633; b) B. Karimi, P. F. Akhavan, *Inorg. Chem.* **2011**, *50*, 6063; c) B. Karimi, P. F. Akhavan, *Chem. Commun.* **2011**, *47*, 7686.

[7] B. Punji, J. T. Mague, M. S. Balakrishna, *Dalton Trans.* **2006**, 1322.

[8] M. P. Doyle, B. Siegfried, R. C. Elliott, J. F. Dellaria Jr., *J. Org. Chem.* **1977**, *42*, 2431.

[9] A. Roglans, A. Pla-Quintana, M. Moreno-Manas, *Chem. Rev.* **2006**, *106*, 4622.

[10] a) F. L. Callonnec, E. Fouquet, F.-X. Felpin, *Org. Lett.* **2002**, *4*, 2079; b) F.-X. Felpin, K. Miqueu, J.-M. Sotiropoulos, E. Fouquet, O. Ibarguren, J. Laudien, *Chem. Eur. J.* **2010**, *16*, 5191; c) A. A. Sabino, A. H. L. Machado, C. R. D. Correia, M. N. Eberlin, *Angew. Chem.* **2004**, *116*, 2568; d) A. V. Moro, F. S. P. Cardoso, C. R. D. Correia, *Org. Lett.* **2009**, *11*, 3642; e) R. P. D. Veronese, F. Coelhob, O. A. C. Antunes, *Tetrahedron Lett.* **2006**, *47*, 1325; f) A. V. Moro, F. S. P. Cardoso, C. R. D. Correia, *Tetrahedron Lett.* **2008**, *49*, 5668; g) A. H. L. Machado, M. A. de Sousa, D. C. S. Patto, L. F. S. Azevedo, F. I. Bombonato, C. R. D. Correia, *Tetrahedron Lett.* **2009**, *50*, 1222; h) J. G. Taylor, A. V. Moro, C. R. D. Correia, *Eur. J. Org. Chem.* **2011**, 1403; i) S. Darses, G. Michaud, J.-P. Genêt, *Tetrahedron Lett.* **1998**, *39*, 5045.

[11] a) H. Bonin, E. Fouquet, F.-X. Felpin, *Adv. Synth. Catal.* **2011**, *353*, 3063; b) A. Zarei, L. Khazdooz, A. R. Hajipour, F. Rafiee, G. Azizi, F. Abrishami, *Tetrahedron Lett.* **2012**, *53*, 406; c) M. B. Andrus, C. Song, *Org. Lett.* **2001**, *3*, 3761; d) H. Bonin, D. Delbrayelle, P. Demonchaux, E. Gras, *Chem. Commun.* **2010**, *46*, 2677; e) S. Darses, T. Jeffery; J.-P. Genet, J.-L. Brayer, J.-P. Demoute, *Tetrahedron Lett.* **1996**, *37*, 3857; f) S. Darses, T. Jeffery, J.-P. Genet, J.-L. Brayer, J.-P. Demoute, *Tetrahedron Lett.* **1997**, *38*, 4393; g) S. Darses, G. Michaud, J.-P. Genêt, *E. J. Org. Chem.* **1999**, *8*, 1875; h) S. Darses, T. Jeffery, B. Jean-Louis, J.-P. Demoute, J.-P. Genêt, *Bull. Soc. Chim. Fr.* **1996**, *133*, 1095.

[12] a) G. Fabrizi, A. Goggiamani, A. Sferrazza, S. Cacchi, *Angew. Chem. Int. Ed.* **2010**, *49*, 4067; b) B. Panda, T. K. Sarkar, *Chem. Commun.* **2010**, *46*, 3131; c) X.-F. Wu, H. Neumann, M. Beller, *Chem. Commun.* **2011**, *47*, 7959.

[13] K. Cheng, C. Wang, Y. Ding, Q. Song, C. Qi, X.-M. Zhang, *J. Org. Chem.* **2011**, *76*, 9261.

[14] I. Peñafiel, I. M. Pastor, M. Yus, *Eur. J. Org. Chem.* **2012**, 3151.

[15] D. A. Alonso, C. Najera, *Chem. Soc. Rev.* **2010**, *39*, 2891.

[16] S. Cacchi, E. Caponetti, M. A. Casadei, A. Di Giulio, G. Fabrizi, G. Forte, A. Goggiamani, S. Moreno, P. Paolicelli, F. Petrucci, A. Prastaro, M. L. Saladino, *Green Chem.* **2012**, *14*, 317.

[17] X. Li, X.-Y. Yan, H.-H. Chang, L.-C. Wang, Y. Zhang, W.-W. Chen, Y.-W. Li, W.-L. Wei, *Org. Biomol. Chem.* **2012**, *10*, 495.

[18] a) H. Firouzabadi, N. Iranpoor, M. Gholinejad, F. Kazemi, *RSC Advances* **2011**, *1*, 1013; b) H. Firouzabadi, N. Iranpoor, F. Kazemi, M. Gholinejad, *J. Mol. Catal. A: Chem.* **2012**, *357*, 154.