

Accepted Manuscript

An Efficient Heterogeneous Ligand Free C-N Coupling Reaction Catalyzed by Palladium Supported on Magnetic Nanoparticles

Ezzat Rafiee, Ali Ataei, Mohammad Joshaghani

PII: S0040-4039(15)30439-1

DOI: <http://dx.doi.org/10.1016/j.tetlet.2015.12.020>

Reference: TETL 47067

To appear in: *Tetrahedron Letters*

Received Date: 25 April 2015

Revised Date: 19 October 2015

Accepted Date: 3 December 2015

Please cite this article as: Rafiee, E., Ataei, A., Joshaghani, M., An Efficient Heterogeneous Ligand Free C-N Coupling Reaction Catalyzed by Palladium Supported on Magnetic Nanoparticles, *Tetrahedron Letters* (2015), doi: <http://dx.doi.org/10.1016/j.tetlet.2015.12.020>

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

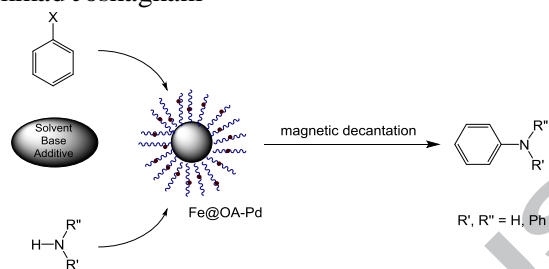


Graphical Abstract

An Efficient Heterogeneous Ligand Free C-N Coupling Reaction Catalyzed by Palladium Supported on Magnetic Nanoparticles

Ezzat Rafiee *, Ali Ataei, Mohammad Joshaghani

Leave this area blank for abstract info.





An Efficient Heterogeneous Ligand Free C-N Coupling Reaction Catalyzed by Palladium Supported on Magnetic Nanoparticles

Ezzat Rafiee^{a, b, *}, Ali Ataei^a, Mohammad Joshaghani^{a, b}

^a Faculty of Chemistry, Razi University, Kermanshah 67149, Iran

^b Institute of Nano Science and Nano Technology, Razi University, Kermanshah, 67149, Iran

ARTICLE INFO

Article history:

Received

Received in revised form

Accepted

Available online

Keywords:

Palladium

Magnetic nanoparticle

Amination coupling

Triphenylamine

Catalyst

ABSTRACT

The catalytic activity of palladium supported on magnetic nanoparticles in the amination coupling reaction of different nitrogen containing substrates with aryl halides was investigated. C–N bond formation was achieved in moderate to excellent yields and the catalyst could be separated by magnetic decantation.

2009 Elsevier Ltd. All rights reserved.

1. Introduction

The palladium-catalyzed amination coupling reaction of aryl halides with nitrogen containing substrates is an important reaction with major roles in various areas of chemistry, including, agrochemicals, dyes, pigments, rubber and pharmaceuticals.^{1,2} Since the discovery of the catalytic amination method,³⁻⁷ increased efforts have been undertaken in order to determine the best conditions for this transformation.⁸⁻¹⁰ Despite considerable advances,¹¹⁻¹⁵ drawbacks such as the use of expensive, air and moisture sensitive ligands,¹⁶ low yields using non-aromatic amines, long reaction times, harsh reaction conditions,^{17, 18} tedious work-up, poor ligand stability, and the formation of toxic side products are features of some methods. Thus, improved methods for this reaction are still of interest. Palladium nanoparticles, particularly those smaller than 10 nm, have been found to exhibit unexpectedly high catalytic activities toward different types of reactions when compared to bulk palladium.¹⁹⁻²¹ Recently, many attempts have been made to immobilize palladium nanoparticles on diverse solid supports such as polymers,^{22,23} carbon,²⁴ and metal oxides²⁵⁻²⁸ in order to construct heterogeneous palladium catalysts with high catalytic activity for various coupling reactions such as the amination of aryl halides.

Recovery of the catalyst from the reaction mixture is not only useful for catalyst reusability but also simplifies the work-up procedure. To overcome problems with separation, magnetic nanoparticles, such as Fe₃O₄ nanoparticles, have been used as support materials due to their unique physical properties and easy separation from the reaction mixture using an external

magnet.^{28,29} Recently we reported results concerning the utility of palladium supported on magnetic nanoparticles coated by oleic acid (Fe@OA-Pd) in the ligand-free Heck coupling of various aryl halides in various media.^{28,29} Considering the importance of the ligand-free Buchwald–Hartwig type amination reaction in organic synthesis, and in continuation of our studies on Pd-catalyzed carbon–carbon coupling reactions,³⁰⁻³⁴ herein, we report the carbon–nitrogen coupling reaction using Fe@OA-Pd.

Initially, attempts to couple bromobenzene with aniline using catalytic Fe@OA-Pd and K₂CO₃ as base in *N,N*-dimethylformamide (DMF) were unsatisfactory,³⁵ (Table 1, entry 1) giving only 21% diphenylamine (DPA) as the main product after 24 hours. Use of additives such as water to increase the nucleophilic strength of the base gave only 35% of the desired product after 20 h (Table 1, entry 2). Increasing the catalyst loading had no effect on the yield (Table 1, entry 3). Use of *t*-BuONa as base, significantly reduced the reaction time, however the extended reaction time led to trace amounts of triphenylamine (TPA) as a by-product (Table 1, entry 4). Because diarylamine derivatives (Ar₂NH) are expensive, the double arylation of aniline with haloarenes should offer a practical synthetic route to produce various triarylamines. Thus, the arylation of aniline with bromobenzene was carried out with Fe@OA-Pd as catalyst in DMF in the presence of H₂O as an additive; the arylation took place twice on the aniline nitrogen to give the corresponding triarylamines. Increasing the catalyst loading to 3 mol% of Pd in the presence of *t*-BuONa markedly improved the yield and reduced the reaction time, however the selectivity was low (Table 1, entry 5). Next, we screened nonpolar solvents such as toluene in order to reduce the amount of triphenylamine (Table 1, entry

* Corresponding author: Tel/Fax: +98 83-34274559; E-mail: e.rafiei@razi.ac.ir, ezzat_rafiee@yahoo.com

6). Attempts to promote coupling by inclusion of halide additives such as aluminum chloride (AlCl_3) or tetrabutylammonium bromide (TBAB) were also unsatisfactory (Table 1, entries 7 and 8). Using a secondary amine such as *N*-

methylaniline gave a low yield compared with aniline under similar reaction conditions (Table 1, entries 6 and 9), but in the case of piperidine, excellent yields were obtained (>99%) without by-product formation (Table 1, entry 10).

Table 1. Optimization of the amination coupling reaction ^a

Entry	Amine	Catalyst loading (mol%)	Base	Additive	Temp. (°C)	Yield (%) ^b		Time (h)
						DPA	TPA	
1 ^c	Aniline	0.3	K_2CO_3	–	120	21	0	24
2 ^c	Aniline	0.3	K_2CO_3	H_2O	120	35	0	20
3 ^c	Aniline	1.5	K_2CO_3	H_2O	120	43	0	20
4 ^c	Aniline	0.3	<i>t</i> -BuONa	H_2O	120	42	7	5
5 ^c	Aniline	3	<i>t</i> -BuONa	H_2O	120	60	40	3
6 ^d	Aniline	1.5	<i>t</i> -BuONa	H_2O	105	62	~5	5
7 ^d	Aniline	3	<i>t</i> -BuONa	TBAB	105	67	~5	7
8 ^d	Aniline	3	<i>t</i> -BuONa	AlCl_3	105	64	~5	10
9 ^d	<i>N</i> -methyl aniline	1.5	<i>t</i> -BuONa	H_2O	105	35	0	20
10 ^{de}	Piperidine	1.5	<i>t</i> -BuONa	H_2O	105	>99 (98, 98, 96)	–	1

^a Reaction conditions: bromobenzene (2 mmol), amine (2.5 mmol), base (3 mmol), solvent (5 mL), additives (H_2O , 1 mL; TBAB or AlCl_3 , 3 mmol).

^b Isolated yield.

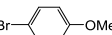
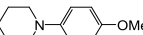
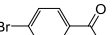
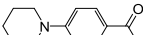
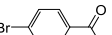
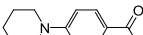
^c DMF.

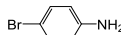
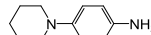
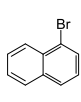
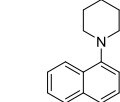
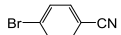
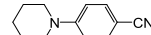
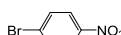
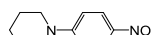
^d Toluene.

^e Results in parenthesis are related to successive runs.

The scope of the heterogeneous catalytic amination was then investigated under the optimized reaction conditions: Table 1 entry 10. Various aryl bromides were reacted with piperidine and converted into the corresponding coupling products (Table 2, entries 1-8). For example, the reaction of 1-bromo-4-methylbenzene with piperidine gave the corresponding amine in 90% yield (Table 2, entry 1). The reactions of 4-bromoanisole, 4-bromobenzaldehyde and 4-bromoacetophenone proceeded in good to excellent yields to give the corresponding coupling products (Table 2, entries 2-4). Next, 4-bromoaniline was reacted with piperidine in moderate yield without any Ullman by-products (Table 2, entry 5). Amination of 1-bromonaphthalene was complete within 2 h in 95% yield. However, the reaction of piperidine with 1-bromo-4-nitrobenzene gave only 41% yield and the reaction with 4-bromobenzonitrile did not proceed after 20 h, probably due to a competitive dehalogenation reaction which has been reported in the literature to occur when using aryl halides bearing electron-withdrawing substituents (Table 2, entries 7 and 8).^{36,37}

Table 2. Palladium-catalyzed amination of aryl bromides ^a

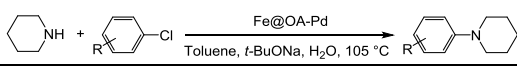
Entry	Aryl halide	Product	Yield (%) ^b	Time (h)
2			86	4
3			92	4
4			94	6

5			70	5
6			95	2
7			No reaction	20
8			41	20

^a Reaction conditions: aryl bromide (2 mmol), piperidine (2.5 mmol), *t*-BuONa (3 mmol), Fe@OA-Pd (1.5 mol%), toluene (5 mL), H_2O (1 mL), 105 °C.

^b Isolated yield.

Because of the high reactivity of this catalyst system, we were encouraged to explore aryl chlorides under the optimum reaction conditions. Various aryl chlorides were reacted with piperidine and converted into the corresponding coupling products (Table 3, entries 1-8). However, in the cases of 4-chlorobenzonitrile and 1-chloro-4-nitrobenzene the yields of the corresponding products decreased dramatically to 42% and 63%, respectively presumably due to a competitive dehalogenation reaction (Table 3, entries 7 and 8). As reported in Table 3, 1-chloro-4-methylbenzene and 4-chloroanisole reacted with piperidine in good to excellent yield, (entries 1 and 2). No significant difference in yield was observed using aryl chloride substrates with electron-donating or electron-withdrawing groups (Table 3, entries 3-5). 4-Chloroaniline reacted with piperidine with complete selectivity (> 97:3) for amination coupling over Ullman coupling (entry 5). The amination of sterically hindered 1-chloronaphthalene also afforded the coupled product in high yield (Table 3, entry 6).

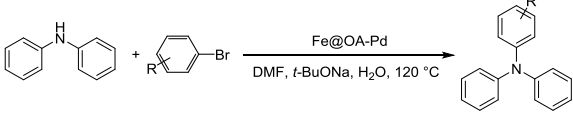
Table 3. Palladium-catalyzed amination of aryl chlorides ^a


Entry	Aryl halide	Product	Yield (%) ^b	Time (h)
1			71	9
2			82	6
3			83	5
4			80	8
5			76	9
6			90	3
7			42	20
8			63	20

^a Reaction conditions: aryl chloride (2 mmol), piperidine (2.5 mmol), *t*-BuONa (3 mmol), Fe@OA-Pd (1.5 mol%), toluene (5 mL), H₂O (1 mL), 105 °C.

^b Isolated yield.

Considering the utility of the triarylamine motif as optoelectroactive materials,^{37, 38} we decided to study the catalytic aromatic amination of diarylamines (Table 4). In the initial optimization, the coupling of bromobenzene with aniline was carried out in DMF at reflux using *t*-BuONa as base for 24 h in the presence of 3.0 mol% Fe@OA-Pd (Table 1, entry 5). This gave the desired Ph₃N in 40% yield (conversion = 100%). Next, we examined the amination reaction of bromobenzenes with diphenylamine under the following reaction conditions: aryl bromide (2 mmol), diphenylamine (2.5 mmol), *t*-BuONa (3 mmol), Fe@OA-Pd (1.5 mol%), DMF (5 mL), H₂O (1 mL) at 120 °C (Table 4). The catalytic efficiency was strongly affected by substituents at the *ortho* position of the bromoarenes. Thus, amination of diphenylamine with 1-bromo-2-methylbenzene gave only 43% yield (Table 4, entry 1), whereas in the case of *meta*- and *para*-tolyl bromides, the corresponding product was obtained in 65% and 70% yield, respectively (Table 4, entries 2 and 3). 4-Bromobenzonitrile did not give any product and in the case of 1-bromo-4-nitrobenzene the yield of corresponding product dramatically decreased to 28% possibly due to competitive dehalogenation (Table 4, entries 4 and 5). Use of 4-bromoaniline in this reaction gave 4-amino *N,N*-diphenylaniline in moderate yield (55%) but with a longer reaction time (Table 4, entry 6).

Table 4. Palladium-catalyzed amination of diphenylamine ^a


Entry	Aryl halide	Product	Yield (%) ^b	Time (h)
1			43	4

2			65	4
3			70	3
4			No reaction	24
5			28	2
6			55	10

^a Reaction conditions: aryl bromide (2 mmol), diphenylamine (2.5 mmol), *t*-BuONa (3 mmol), Fe@OA-Pd (1.5 mol%), DMF (5 mL), H₂O (1 mL), 120 °C.

^b Isolated yield.

To test the reusability of the catalyst, recycling experiments were carried out for the coupling of piperidine with bromobenzene (entry 10, Table 1). Upon reaction completion, the catalyst was removed from the reaction vessel with the aid of an external magnet. The Pd content in the Fe@OA-Pd catalyst after the first and fourth runs was determined as 8.4 wt.% and 7.6 wt.%, respectively, using atomic absorption spectroscopic analysis. This shows that the palladium content of the catalyst does not significantly change after reaction or recycling processes, indicating that no significant leaching of palladium occurs.

In summary, the use of a ligand free heterogeneous palladium supported on magnetic nanoparticle has been shown to be a simple and highly efficient system for the C-N coupling of different nitrogen containing substrates with aryl halides. Good to high yields of products with excellent functional group tolerance was found. Increasing the electron withdrawing nature of the substituted group dramatically decreased the yield of the reaction probably due to a competitive dehalogenation reaction.

Acknowledgment

The authors thank Razi University Research Council for support of this work.

References and notes

1. Ward, J.; Wohlgemuth, R. *Curr. Org. Chem.* **2010**, *14*, 1914.
2. D'Aproano, G.; Schiavon, G.; Zotti, G.; Leclerc, M. *Chem. Mater.* **1995**, *7*, 33.
3. Driver, M. S.; Hartwig, J. F. *Tetrahedron Lett.* **1995**, *36*, 3609.
4. Guram, A. S.; Rennels, R., A; Buchwald, S. L. *Angew. Chem., Int. Ed.* **1995**, *34*, 1348.
5. Kosugi, M.; Kameyama, M.; Migita, T. *Chem. Lett.* **1983**, 927.
6. Louie, J.; Hartwig, J. F. *Tetrahedron Lett.* **1995**, *36*, 3609.
7. Kosugi, M.; Kameyama, M.; H. Sano; Migita, T. *Nippon Kagaku Kaishi.* **1985**, *3*, 547.
8. Hartwig, J. F.; Negishi, i. E. *Handbook of Organopalladium Chemistry for Organic Synthesis*; Wiley-Interscience: New York, 2002.
9. Marion, N.; Nolan, S. P. *Acc. Chem. Res.* **2008**, *41*, 1440.

10. Hartwig, J. F. *Acc. Chem. Res.* **2008**, *41*, 1534.
11. Martin, R.; Buchwald, S. L. *Acc. Chem. Res.* **2008**, *41*, 1461.
12. Wolfe, J.; Wagaw, S.; Buchwald, S. *J. Am. Chem. Soc.* **1996**, *118*, 7215.
13. Driver, M.; Hartwig, J. *J. Am. Chem. Soc.* **1996**, *118*, 7217.
14. Reddy, C. V.; Kingston, J. V.; Verkade, J. G. *J. Org. Chem.* **2008**, *73*, 3047.
15. Surry, D. S.; Buchwald, S. L. *Chem. Sci.* **2011**, *2*, 27.
16. Old, D. W.; Wolfe, J. P.; Buchwald, S. L. *J. Am. Chem. Soc.* **1998**, *120*, 9722.
17. Lindley, J. *Tetrahedron.* **1984**, *40*, 1433
18. Bunnett, J. F. *Acc. Chem. Res.* **1978**, *11*, 413.
19. Jansat, S.; M. Gomez; Philippot, K.; G. Muller; Guiu, E.; Claver, C.; Castillon, S.; Chaudret, B. *J. Am. Chem. Soc.* **2004**, *126*, 1592.
20. Kidambi, S.; Dai, J.; Li, J.; Bruening, M. L. *J. Am. Chem. Soc.* **2004**, *126*, 2658.
21. Kobayashi, H.; Yamauchi, M.; Kitagawa, H.; Kubota, Y.; Kato, K.; Takata, M. *J. Am. Chem. Soc.* **2008**, *130*, 1828.
22. Sreedhar, B.; Reddy, P. S.; Devi, D. K. *J. Org. Chem.* **2009**, *74*, 8806.
23. Dell'Anna, M. M.; Mastroilli, P.; Rizzuti, A.; Leonelli, C. *Appl. Catal. A.* **2011**, *401*, 134.
24. Byun, E.; B. Hong; Castro, K. A. D.; Lim, M.; Rhee, H. *J. Org. Chem.* **2007**, *72*, 9815.
25. Zhu, J.; Zhou, J. H.; Zhao, T. J.; Zhou, X. G.; Chen, D.; Yuan, W. K. *Appl. Catal. A.* **2009**, *352*, 243.
26. Corma, A.; Ródenas, T.; Sabater, M. J. *Chem.-Eur. J.* **2010**, *16*, 254.
27. Corma, A.; Ródenas, T.; Sabater, M. J. *J. Catal.* **2011**, *279*, 319.
28. Rafiee, E.; Ataei, A.; Nadri, Sh.; Joshaghani, M.; Eavani, S. *Inorg. Chim. Acta.* **2014**, *409*, 302–309.
29. Mori, K.; Yoshioka, N.; Kondo, Y.; Takeuchi, T.; Yamashita, H. *Green Chemistry.* **2009**, *11*, 1337.
30. Köhler, K.; Wagner, M.; Djakovitch, L. *Catal. Today.* **2001**, *66*, 105.
31. Ataei, A.; Nadri, Sh.; Rafiee, E.; Jamali, S.; Joshaghani, M. *J. Mol. Catal. A: Chem.* **2013**, *366*, 30–35.
32. Nadri, Sh.; Joshaghani, M.; Rafiee, E. *Organometallics.* **2009**, *28*, 6281–6287.
33. Nadri, Sh.; Joshaghani, M.; Rafiee, E. *Appl. Catal. A: Gen.* **2009**, *362*, 163–168.
34. Nadri, Sh.; Azadi, E.; Ataei, A.; Joshaghani, M.; Rafiee, E. *J. Organomet. Chem.* **2011**, *696*, 2966–297
35. An oven-dried Schlenk tube was charged with the aryl halide (2 mmol) and amine (2.5 mmol), Fe@OA-Pd (0.05 g, 0.04 mmol, 1.5 mol%), base (3 mmol), solvent (5 mL) and additive. The resulting mixture was stirred for the appropriate time and temperature. After reaction completion the reaction mixture was then cooled to room temperature and the catalyst separated using a magnet, taken up in Et₂O (4 mL), and washed with brine (5 mL). The resulting solution was dried over anhydrous MgSO₄, filtered and concentrated. The crude product was purified by flash chromatography on silica gel.
36. Kleist, W.; Pröckl, S. S.; Drees, M.; Köhler, K.; Djakovitch, L. *J. Mol. Catal. A: Chem.* **2009**, *303*, 15.
37. Shirota, Y. *J. Mater. Chem.* **2000**, *10*, 1.
38. Shirota, Y. *J. Mater. Chem.* **2005**, *15*, 75.