

## RESEARCH PAPER

## SPION-A-Pd(EDTA) (superparamagnetic iron oxide nanoparticles-A-ethylendiamine tetraacetic acid) as a robust nanocatalyst for Buchwald-Hartwig C-N Coupling Reaction

Marzieh Ghotbinejad\*, Ahmad R. Khosropour, Iraj Mohammadpoor-Baltork, Majid Moghadam, Valiollah Mirkhani, Shahram Tangestaninejad

Department of Chemistry, Catalysis Division, University of Isfahan, Isfahan, Iran

### ARTICLE INFO

#### Article History:

Received 14 March 2017

Accepted 30 April 2017

Published 1 July 2017

#### Keywords:

Buchwald-Hartwig Reaction

EDTA

Magnetite Nanoparticles

Pd

### ABSTRACT

During the last 20-30 years, palladium-catalyzed reactions have witnessed tremendous advances in the industrial and organic reactions such as hydrogenation, coupling, cyanation and amination. Despite the wide utility of Pd-catalysts in these reactions, they suffer from a number of drawbacks such as recovery, reuse of catalyst and remain as a contaminant in the products at the end of the reaction. A powerful and convenient reaction procedure for the C-N coupling reaction (the Buchwald-Hartwig reaction), yielding products of N-arylanilines and N-arylamines in conventional heating has been reported. The protocol utilized an high stable Pd(EDTA)<sup>2-</sup> salt by counter cation of N-methylimidazolium bounded to 1,3,5-triazine-tethered SPIONs (superparamagnetic iron oxide nanoparticles). The reaction products were produced under conventional heating at extremely low catalyst loading (as low as 0.003 mol% Pd). Finally, we also examined the reusability of the catalyst. It was found that the catalyst could be recovered by external magnetic field and be reused for five times without obvious loss in catalytic activity.

### How to cite this article

Ghotbinejad M, Khosropour AR, Mohammadpoor-Baltork I, Moghadam M, Mirkhani V, Tangestaninejad S. SPION-A-Pd(EDTA) (superparamagnetic iron oxide nanoparticles-A-ethylendiamine tetraacetic acid) as a robust nanocatalyst for Buchwald-Hartwig C-N Coupling Reaction. *Nanochem Res*, 2017; 2(2):230-236. DOI: 10.22036/nrcr.2017.02.010

### INTRODUCTION

Palladium-catalyzed reactions have emerged as powerful and selective tools for synthetic organic chemistry [1-3] such as carbonylation [4-8], cyanation [9,10], hydrogenation [11-13], coupling reactions [14-16], and amination [17].

Despite the wide utility of Pd-catalysts in these reactions, they suffer from a number of drawbacks such as recovery, reuse of catalyst and remain as a contaminant in the products at the end of the reaction.

Magnetic nanoparticles (MNPs) serve as an effective support for the metals in various organic transformations [18-20].

Buchwald-Hartwig type C-N coupling reaction is one of the most efficient tools to prepare nitrogen-containing arylamines [21,22]. This reaction involves the coupling of amines and aryl halides, using palladium as the catalyst.

The formation of the C-N bond has wide applications in biology, biochemistry, pharmaceuticals, pigments, conducting polymers, electronic materials, and other organic synthesis [23-32].

In this work, we hope to report a powerful and efficient nanocatalyst for the N-arylation of various amines. This catalyst could be satisfactory recovered by a simple external magnet, and reused without loss of its reactivity.

\* Corresponding Author Email: [ghotbi\\_mar36@yahoo.com](mailto:ghotbi_mar36@yahoo.com)

## EXPERIMENTALS

### Materials and methods

All chemicals purchased from Merck chemical company.  $\text{Fe}_3\text{O}_4$  nanocomposite and silica-coated magnetite nanoparticles ( $\text{SiO}_2@\text{Fe}_3\text{O}_4$ ) were synthesized according to the literature respectively [33].  $\text{Na}_2\text{Pd}(\text{EDTA})$  complex was prepared by dissolution of  $\text{Pd}(\text{OAc})_2$  (Aldrich),  $\text{Na}_2\text{CO}_3$  and  $\text{Na}_2\text{H}_2\text{EDTA}$  (MERCK) in water (pH 9) as found in the literature [34]. All known organic products were identified by comparison of their physical and spectral data with those of authentic samples. Thin layer chromatography (TLC) was performed on UV-active aluminum-backed plates of silica gel (TLC Silica gel 60 F254).  $^1\text{H}$ , and  $^{13}\text{C}$  NMR spectra were measured on a Bruker DPX 400 MHz spectrometer in  $\text{CDCl}_3$  with chemical shift (d) given in ppm. Coupling constants are given in Hz. The FT-IR spectra were taken on a Nicolet-Impact 400D spectrophotometer in KBr pellets and reported in  $\text{cm}^{-1}$ .

### Synthesis of SPION-A-Pd(EDTA)

$\text{Na}_2\text{CO}_3$  (0.2 mmol, 0.021 g) was added to a mixture of  $\text{Na}_2\text{EDTA}$  (0.1 mmol, 0.037 g) and  $\text{PdCl}_2$  (0.1 mmol, 0.018 g) in water (5 ml) at 25 °C, and was stirred magnetically for 5 h. In an argon atmosphere, SPION- $\text{AlCl}_2$  (0.53 g) in EtOH (5 ml) was added dropwise to the solution and the resulting mixture was stirred for a further 12 h at room temperature. Finally, the catalyst was collected by external permanent magnet and washed with  $\text{CH}_2\text{Cl}_2$  ( $3 \times 10$  ml) and  $\text{H}_2\text{O}$ , and dried under vacuum.

### General Procedure for Buchwald-Hartwig Reaction under Thermal Conditions

A round-bottom flask was charged under argon with aryl halide (2 mmol, 1 equiv), amine (1 mmol, 1 equiv), DMSO (1 mL),  $\text{tBuO}^-\text{Na}^+$  (2 mmol, 2 equiv) and SPION-A-Pd(EDTA) (0.094g, 0.003mol % of Pd). The reaction mixture was stirred and heated at

120 °C for several hours (thin layer chromatography monitoring). After completion of the reaction, the reaction mixture was cooled to room temperature; the mixture was diluted with  $\text{Et}_2\text{O}$ , filtered and concentrated under reduced pressure. The residue was purified by column chromatography on silicagel.

## RESULT AND DISCUSSION

The SPION-A-Pd(EDTA) was successfully prepared (scheme 1) and characterized by means of Fourier transform infrared spectroscopy (FT-IR), inductively coupled plasma atomic emission spectroscopy (ICP), thermal gravimetric analysis (TG), and high resolution transmission electron microscopy (HR-TEM).

Fig. 1 illustrates the FT-IR spectrums of  $\text{Fe}_3\text{O}_4$  (a), silica-encapsulated  $\text{Fe}_3\text{O}_4$  (b), and nanocatalyst SPION-A-Pd(EDTA) (c) respectively.

The FT-IR spectrum of SPION-A-Pd(EDTA) (Fig.1, c) showed absorption bands at  $3421 \text{ cm}^{-1}$  (N-H stretching vibration),  $2930 \text{ cm}^{-1}$  (C-H),  $1622 \text{ cm}^{-1}$  (C=N) and  $635\text{-}587 \text{ cm}^{-1}$  (Fe-O) SPIONs.

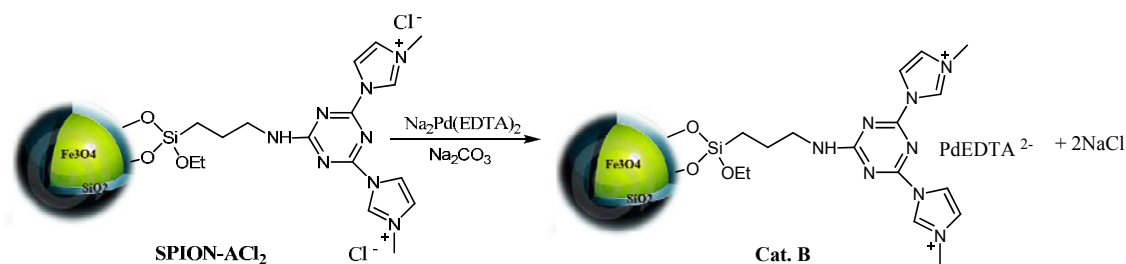
The thermal stability of SPION-A-Pd(EDTA) was also evaluated by TGA-DTG. According to these curves, the weight loss below 600 °C was approximately 8.87%. So, these results approved that SPION-A-Pd(EDTA) has almost high thermal stability below 600 °C (Fig. 2).

For studying the morphology characteristics of SPION-A-Pd(EDTA), HR-TEM image was also investigated (Fig. 3).

HR-TEM images of SPION-A-Pd(EDTA) revealed that it appears to have almost a spherical structure with the average size about 10-13 nm (Fig. 3, b). Then, enormous active sites of this nanoparticle may present excellent activity in organic transformations.

Inductively coupled plasma atomic emission spectroscopy (ICP) determined the amount of palladium in SPION-A-Pd(EDTA) as 3.41wt%.

In continue, catalytic activity of this complex was investigated in Buchwald-Hartwig reaction.



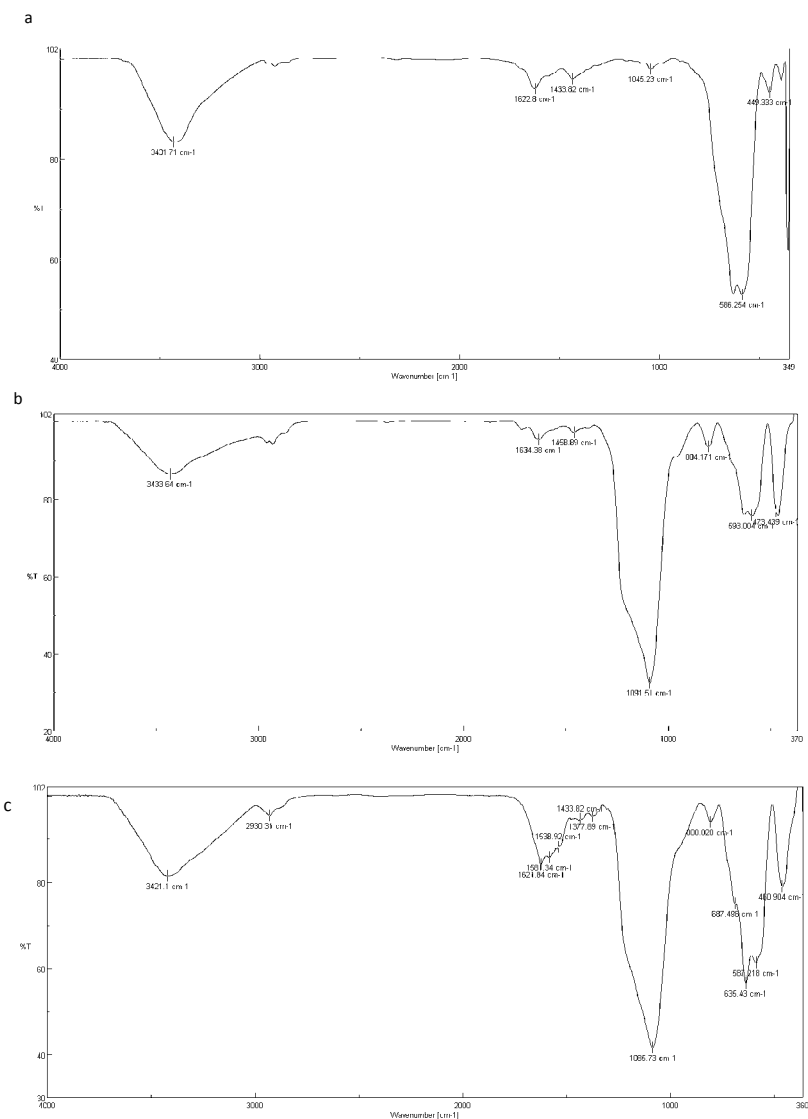


Fig. 1: Comparison of the the FT-IR spectra of (a) Fe<sub>3</sub>O<sub>4</sub>; (b) silica-encapsulated Fe<sub>3</sub>O<sub>4</sub>; (c) SPION-A-Pd(EDTA)

Table 1: Effect of solvent on the synthesis of 4-phenylmorpholine as a model reaction.

Entry	Solvent	Yield (%) <sup>a</sup>
1	Dioxan	43
2	Toluene	50
3	DMF	75
4	DMSO	90

<sup>a</sup> Isolated yield.

Hence, we initially examined reaction between morpholine and bromobenzene as model substrate to optimize the reaction conditions such as solvents, bases, temperature, and catalyst source.

In order to investigate the best solvent for this reaction, a series of solvents such as Dioxan, Toluene, DMF, and DMSO were selected (Table 1).

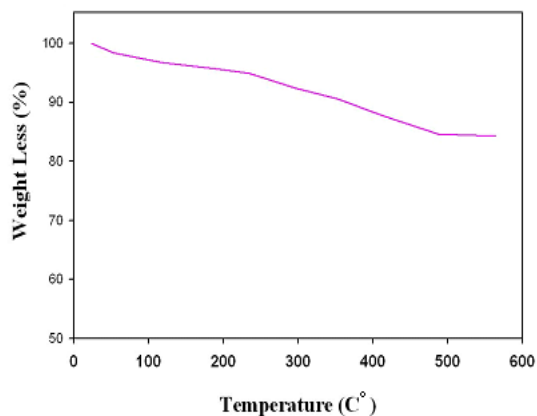


Fig. 2: TG-DTG analysis of SPION-A-Pd(EDTA)

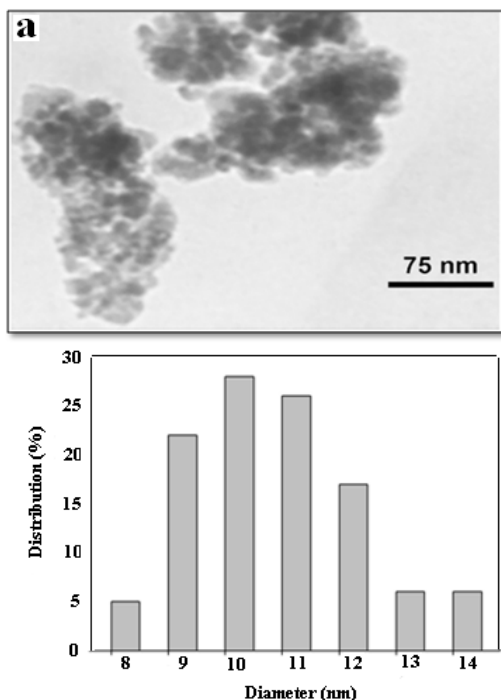


Fig. 3: (a) HR-TEM image of SPION-A-Pd(EDTA) and (b) SPION-A-Pd(EDTA) particle size distribution histogram.

Table 2: Effect of base on the synthesis of 4-phenylmorpholine as a model reaction.

Entry	Base	Yield (%) <sup>a</sup>
1	NEt <sub>3</sub>	30
2	K <sub>2</sub> CO <sub>3</sub>	45
3	K <sub>3</sub> PO <sub>4</sub>	50
4	CS <sub>2</sub> CO <sub>3</sub>	60
5	NaOtBu	90

<sup>a</sup> Isolated yield.

Table 3: Comparison with different catalysts

Entry	Catalyst	Yield (%) <sup>a</sup>
1	-	-
2	Pd(OAc) <sub>2</sub>	5
3	Pd(OAc) <sub>2</sub> @nano-Fe <sub>3</sub> O <sub>4</sub>	16
4	Pd(OAc) <sub>2</sub> @nano-SiO <sub>2</sub>	10
5	SPION-A-Pd(EDTA)	90

<sup>a</sup> Isolated yield.

Table 4: Effect of temperature on the synthesis of 4-phenylmorpholine as a model reaction.

Entry	Temperature	Yield (%) <sup>a</sup>
1	90	50
2	100	70
3	120	90
4	140	90

<sup>a</sup> Isolated yield.

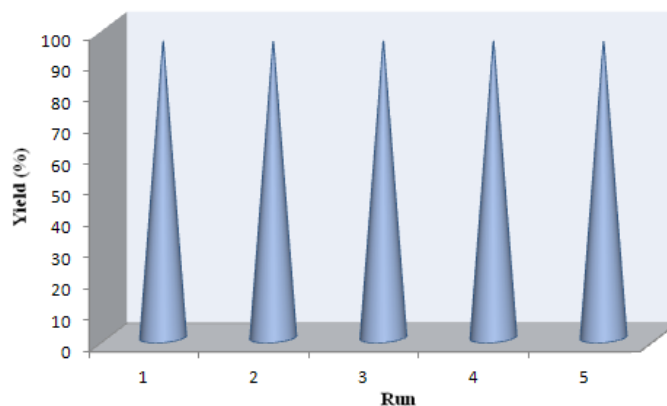


Fig. 4: Reuse of SPION-A-Pd(EDTA) examined on the model reactions of Buchwald-Hartwig reaction.

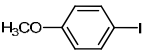
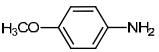
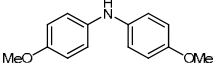
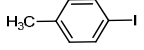
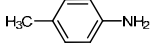
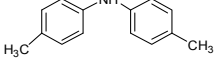


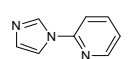
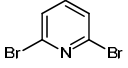

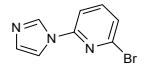
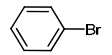

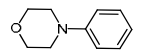
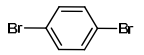

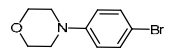
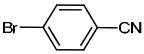

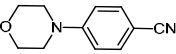
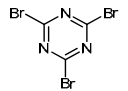

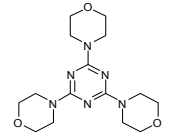
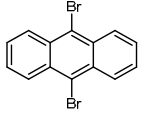

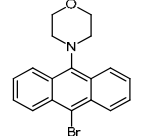
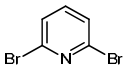

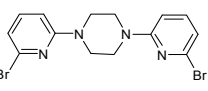
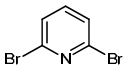
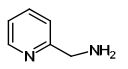
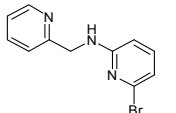
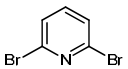
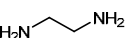
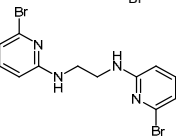
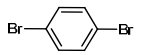
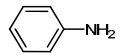
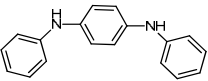
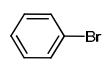

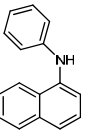
We observed that more polar solvents such as DMSO, and DMF (Table 1, entries 3, 4) were favorable for the reaction. On the contrary, less polar solvents such as Dioxan, and Toluene (Table 1, entries 1, 2) provided slightly lower yields. Therefore, among the solvents tested, DMSO was the best choice.

Next, various bases were investigated. We found that using tBuONa as base in DMSO gives the N-arylated product with an excellent yield (Table 2, entry 5). The other inorganic bases such as K<sub>2</sub>CO<sub>3</sub>,

K<sub>3</sub>PO<sub>4</sub>, and CS<sub>2</sub>CO<sub>3</sub> and organic bases like NEt<sub>3</sub> only afford moderate to low yields of N-arylated products (Table 2, entries 1-4). No product was achieved in the absence of any bases.

Among the four Pd-sources used as a catalyst, SPION-A-Pd(EDTA) gave the highest yield (Table 3, entry 5). Use of Pd(OAc)<sub>2</sub>, nanoSiO<sub>2</sub>@Pd(OAc)<sub>2</sub>, and nanoFe<sub>3</sub>O<sub>4</sub>@Pd(OAc)<sub>2</sub> as catalyst gave low yield of product (Table 3, entries 2-4). The reaction in the absence of any catalyst did not give any product at all (Table 3, entry 1).

Table 5. Amination of aryl and hetero aryl bromides catalyzed by the SPION-A-Pd(EDTA) system <sup>a</sup>

Entry	ArX	Nucleophile	Product <sup>b</sup>	Time/h	Yield % <sup>c</sup>
1				17	78
2				18	73
3				11	82
4				10	85
5				5	90
6				9	85
7				11	84
8				11	83
9				15	82
10				13	89
11				15	80
12				12	81
13				32	80
14				29	81

<sup>a</sup>Reaction conditions: aryl halide (2 mmol), amine (1 mmol), tBuO<sup>-</sup>Na<sup>+</sup> (2 mmol), DMSO (1 mL) in the presence of the catalyst containing 0.003 mol% Pd.

<sup>b</sup>Temperature for entry 1 and 2 was 130 °C

<sup>c</sup>Isolated yield.

We also found that this reaction is sensitive to the reaction temperature. A temperature 120 °C was found to be the best temperature for the model reaction (Table 4, entry 3). A further increase in temperature could not enhance the product yield (Table 4, entry 4). Decrease in the temperature to 90 °C led to a decrease in yield (Table 4, entry 1).

When bromobenzene was reacted with morpholine under air atmosphere, no coupling reaction was observed to take place. Whereas, in the presence of inert atmosphere, products were obtained with an excellent yield. With the optimized conditions in hand, the Buchwald-Hartwig cross-coupling reactions were examined by varying both the amines including aromatic, aliphatic, and cyclic and a variety of aryl bromides. The results are summarized in Table 5.

In general, the presence of electron donating groups on N-nucleophiles and electron withdrawing groups on aryl halides enhanced the N-arylated product yield. Aniline substituted with electron donating group, such as 4-methoxy aniline, gave the product with a good yield (Table 5, entry 1). The reaction of aryl halides with heterocyclic amines such as morpholine, piperidine (Table 5, entries 5-10) resulted in a desired product in an excellent yield. The high nucleophilicity of these heterocyclic amines can be due to their reactivities.

The recyclability of the SPION-A-Pd(EDTA) system was also investigated. Catalyst recovered by a simple external magnet and reused for five times. Results are represented in Fig. 4.

## CONCLUSION

In summary, we have developed a novel, air-moisture, easily recoverable Pd-complexe.

We believe that this catalyst can catalyze amination of aryl halides in the presence of inorganic bases with an excellent recycling efficiency.

## ACKNOWLEDGMENT

The authors are grateful to the Center of Excellence of Chemistry of University of Isfahan (CECUI) and also the Research Council of the University of Isfahan for financial support of this work.

## CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this manuscript.

## REFERENCES

1. Ferré-Filmon K, Delaude L, Demonceau A, Noels AF. Catalytic methods for the synthesis of stilbenes with an

- emphasis on their phytoalexins. *Coordination Chemistry Reviews*. 2004;248(21):2323-36.
2. Fihri A, Meunier P, Hierro J-C. Performances of symmetrical achiral ferrocenylphosphine ligands in palladium-catalyzed cross-coupling reactions: A review of syntheses, catalytic applications and structural properties. *Coordination Chemistry Reviews*. 2007;251(15):2017-55.
3. Polshettiwar V, Len C, Fihri A. Silica-supported palladium: Sustainable catalysts for cross-coupling reactions. *Coordination Chemistry Reviews*. 2009;253(21):2599-626.
4. Jacobi von Wangelin A, Neumann H, Beller M. Carbonylations of Aldehydes. In: Beller M, editor. *Catalytic Carbonylation Reactions*. Berlin, Heidelberg: Springer Berlin Heidelberg; 2006. p. 207-21.
5. Koll'ar L. *Modern Carbonylation Methods*. Germany: Wiley-VCH; 2008.
6. Brennführer A, Neumann H, Beller M. Palladium-Catalyzed Carbonylation Reactions of Aryl Halides and Related Compounds. *Angewandte Chemie International Edition*. 2009;48(23):4114-33.
7. Vizer SA, Yerzhanov KB, Al Quntar AAA, Dembitsky VM. Synthesis of heterocycles by carbonylation of acetylenic compounds. *Tetrahedron*. 2004;60(26):5499-538.
8. Gabriele B, Salerno G, Costa M, Chiusoli GP. Recent Advances in the Synthesis of Carbonyl Compounds by Palladium-Catalyzed Oxidative Carbonylation Reactions of Unsaturated Substrates. *Current Organic Chemistry*. 2004;8(10):919-46.
9. Ramnauth J, Bhardwaj N, Renton P, Rakhit S, Maddaford SP. The Room-Temperature Palladium-Catalyzed Cyanation of Aryl Bromides and Iodides with Tri-*t*-butylphosphine as Ligand. *Synlett*. 2003;2003(14):2237-9.
10. Sundermeier M, Zapf A, Beller M, Sans J. A new palladium catalyst system for the cyanation of aryl chlorides. *Tetrahedron Letters*. 2001;42(38):6707-10.
11. Sangeetha P, Shanthi K, Rao KSR, Viswanathan B, Selvam P. Hydrogenation of nitrobenzene over palladium-supported catalysts—Effect of support. *Applied Catalysis A: General*. 2009;353(2):160-5.
12. Xing Y, Chen J-S, Dong Z-R, Li Y-Y, Gao J-X. Highly efficient chiral PNNP ligand for asymmetric transfer hydrogenation of aromatic ketones in water. *Tetrahedron Letters*. 2006;47(26):4501-3.
13. Kirm I, Medina F, Rodriguez X, Cesteros Y, Salagre P, Sueiras JE. Preparation of 2-phenylethanol by catalytic selective hydrogenation of styrene oxide using palladium catalysts. *Journal of Molecular Catalysis A: Chemical*. 2005;239(1):215-21.
14. Aydemir M, Baysal A, Öztürk G, Gümgüm B. Synthesis and characterizations of N,N'-bis(diphenylphosphino)-2-(aminomethyl)aniline derivatives: application of a palladium(II) complex as pre-catalyst in Heck and Suzuki cross-coupling reactions. *Applied Organometallic Chemistry*. 2009;23(3):108-13.
15. Akba O, Durap F, Aydemir M, Baysal A, Gümgüm B, Özkar S. Synthesis and characterizations of N,N,N',N'-tetrakis(diphenylphosphino)ethylenediamine derivatives: Use of palladium(II) complex as pre-catalyst in Suzuki coupling and Heck reactions. *Journal of Organometallic Chemistry*. 2009;694(5):731-6.
16. Mondal J, Modak A, Bhaumik A. One-pot efficient Heck coupling in water catalyzed by palladium nanoparticles tethered into mesoporous organic polymer. *Journal of Molecular Catalysis A: Chemical*. 2011;350(1):40-8.
17. Islam SM, Salam N, Mondal P, Roy AS. Highly efficient

- recyclable polymer anchored palladium catalyst for CC and CN coupling reactions. *Journal of Molecular Catalysis A: Chemical*. 2013;366(Supplement C):321-32.
18. Senapati KK, Roy S, Borgohain C, Phukan P. Palladium nanoparticle supported on cobalt ferrite: An efficient magnetically separable catalyst for ligand free Suzuki coupling. *Journal of Molecular Catalysis A: Chemical*. 2012;352(Supplement C):128-34.
  19. Li P, Wang L, Zhang L, Wang G-W. Magnetic Nanoparticles-Supported Palladium: A Highly Efficient and Reusable Catalyst for the Suzuki, Sonogashira, and Heck Reactions. *Advanced Synthesis & Catalysis*. 2012;354(7):1307-18.
  20. Maleki A, Ghalavand R, Firouzi Haji R. Synthesis and characterization of the novel diamine-functionalized Fe<sub>3</sub>O<sub>4</sub>@SiO<sub>2</sub> nanocatalyst and its application for one-pot three-component synthesis of chromenes. *Applied Organometallic Chemistry*. e3916-n/a.
  21. Broumidis E, Koutentis PA. A one-pot, two-step synthesis of 3-deazacanthin-4-ones via sequential Pd-catalyzed Suzuki-Miyaura and Cu-catalyzed Buchwald-Hartwig reactions. *Tetrahedron Letters*. 2017;58(27):2661-4.
  22. Avila-Sorrosa A, Estudiante-Negrete F, Hernández-Ortega S, Toscano RA, Morales-Morales D. Buchwald-Hartwig C-N cross coupling reactions catalyzed by a pseudo-pincer Pd(II) compound. *Inorganica Chimica Acta*. 2010;363(6):1262-8.
  23. Kunz K, Scholz U, Ganzer D. Renaissance of Ullmann and Goldberg Reactions - Progress in Copper Catalyzed C-N-, C-O- and C-S-Coupling. *Synlett*. 2003;2003(15):2428-39.
  24. Lawrence SA. *Amines: Synthesis Properties and Applications* UK: Cambridge University Press: Cambridge; 2004.
  25. Weissermel K, Arpe H-J. *Oxidation Products of Xylene and Naphthalene*. *Industrial Organic Chemistry*: Wiley-VCH Verlag GmbH; 2007. p. 385-423.
  26. Corbet J-P, Mignani G. Selected Patented Cross-Coupling Reaction Technologies. *Chemical Reviews*. 2006;106(7):2651-710.
  27. Evano G, Blanchard N, Toumi M. Copper-Mediated Coupling Reactions and Their Applications in Natural Products and Designed Biomolecules Synthesis. *Chemical Reviews*. 2008;108(8):3054-131.
  28. Ley SV, Thomas AW. Modern Synthetic Methods for Copper-Mediated C(aryl)O, C(aryl)N, and C(aryl)S Bond Formation. *Angewandte Chemie International Edition*. 2003;42(44):5400-49.
  29. Lam PYS, Vincent G, Clark CG, Deudon S, Jadhav PK. Copper-catalyzed general CN and CO bond cross-coupling with arylboronic acid. *Tetrahedron Letters*. 2001;42(20):3415-8.
  30. Schlummer B, Scholz U. Palladium-Catalyzed CN and CO Coupling—A Practical Guide from an Industrial Vantage Point†. *Advanced Synthesis & Catalysis*. 2004;346(13-15):1599-626.
  31. Muci AR, Buchwald SL. Practical Palladium Catalysts for C-N and C-O Bond Formation. In: Miyaura N, editor. *Cross-Coupling Reactions: A Practical Guide*. Berlin, Heidelberg: Springer Berlin Heidelberg; 2002. p. 131-209.
  32. D'Aprano G, Leclerc M, Zotti G, Schiavon G. Synthesis and Characterization of Polyaniline Derivatives: Poly(2-alkoxyanilines) and Poly(2,5-dialkoxyanilines). *Chemistry of Materials*. 1995;7(1):33-42.
  33. Schätz A, Hager M, Reiser O. Cu(II)-Azabis(oxazoline)-Complexes Immobilized on Superparamagnetic Magnetite@Silica-Nanoparticles: A Highly Selective and Recyclable Catalyst for the Kinetic Resolution of 1,2-Diols. *Advanced Functional Materials*. 2009;19(13):2109-15.
  34. Wei J-F, Jiao J, Feng J-J, Lv J, Zhang X-R, Shi X-Y, et al. PdEDTA Held in an Ionic Liquid Brush as a Highly Efficient and Reusable Catalyst for Suzuki Reactions in Water. *The Journal of Organic Chemistry*. 2009;74(16):6283-6.