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## ARTICLE

# Nanocrystalline Magnesium Oxide-Stabilized Palladium(0): An Efficient and Reusable Catalyst for Synthesis of *N*-(2-pyridyl)Indoles

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A selective and efficient catalytic process has been developed for the oxidative coupling between *N*-aryl-2-aminopyridines and alkynes using nanocrystalline magnesium oxide (NAP-MgO)-supported palladium nanoparticles [NAP-Mg-Pd(0)] catalyst and CuCl<sub>2</sub> as an oxidant. The process involves the ortho C-H activation of *N*-aryl-2-aminopyridines to give *N*-pyridyl indoles in excellent yields and the true heterogeneity of the catalyst is verified by studying the recoverability and reusability for four cycles without significant loss of catalytic activity.

## Introduction

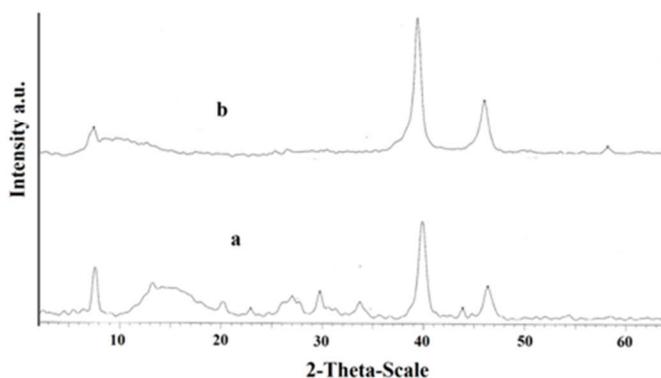
Carbon-carbon and carbon-heteroatom bond formation via transition metal-catalyzed C-H activation of aromatics has received great attention because it represents the atom-economic strategy to construct complex structures.<sup>1</sup> Recently, various methods with C-H bond activation of arenes and the oxidative coupling with unsaturated molecules have been reported with high efficiency.<sup>2</sup> These methods revealed that the C-H bond activation of arenes requires the directing group in order to direct the C-H functionalization to the *ortho*-position.<sup>3</sup> Very recently, Li and co-workers reported Rh(III) and Pd(II)-catalyzed C-H activation of *N*-aryl-2-aminopyridines, with the pyridine moiety as a directing group,<sup>4,5</sup> and the oxidative coupling with alkynes to give substituted indole derivatives which are widely present in natural products and pharmaceuticals.<sup>6</sup> In spite of success, the development of environmentally benign and economical synthetic methods is still a challenging task.<sup>7</sup> Therefore, it is essential to develop a recoverable and reusable catalytic system for oxidative C-H functionalization of arenes from industrial and environmental point of view.

In recent years, nanocrystalline metal oxides have received much attention because of their usefulness as materials<sup>8</sup> and more importantly as catalyst for organic transformations.<sup>9</sup> The presence of edge-corner and other defect sites allows the nanostructured MgO materials to possess a high concentration

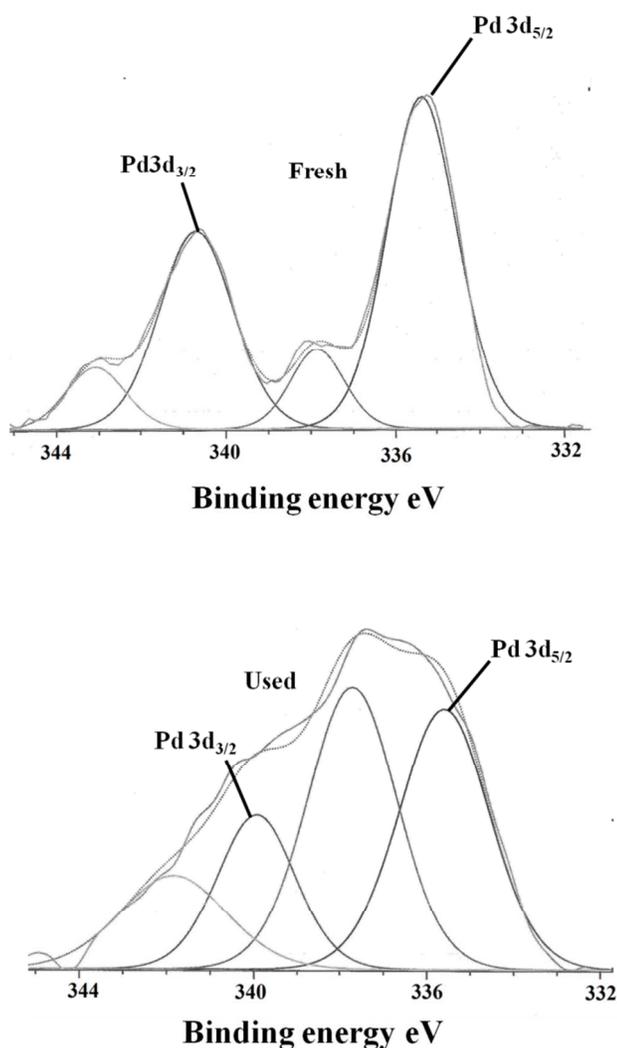
of reactive surface ions, such as Lewis acid Mg<sup>2+</sup> and Lewis base O<sup>2-</sup>, lattice bound and isolated hydroxyl groups and anionic and cationic vacancies. Nanocrystalline magnesium oxide, with its three-dimensional structure and well-defined shape, acts as an excellent support for different metals.<sup>10</sup> Our previous work showed that nanocrystalline magnesium oxide (NAP-MgO)-supported palladium nanoparticles [NAP-Mg-Pd(0)] is an active and efficient heterogeneous catalyst for different C-C coupling reactions,<sup>11</sup> reduction of nitro compounds<sup>12</sup> and oxidation of alcohols.<sup>13</sup> Very recently, our group has reported the NAP-Mg-Pd(0) catalyzed Heck reaction of heteroaryl halides in the absence of ligand and base free conditions.<sup>14</sup> In this direction, herein we wish to communicate an efficient and reusable heterogeneous NAP-Mg-Pd(0) catalyst for oxidative ortho C-H activation of *N*-aryl-2-aminopyridines with alkynes using CuCl<sub>2</sub> as an oxidant.

## Results and discussion

XRD patterns of the fresh and used Pd supported on NAP-MgO catalysts are reported in Fig. 1. The fresh and used catalysts displayed diffraction lines due to metallic Pd phase (PCPDF # 88-2335) appeared at 2θ = 40.0, 46.5° and their corresponding 'd' values are 0.225, 0.195 nm. Both fresh and used catalysts exhibited metallic Pd phase only. Absence of peaks due to Pd-halides either may be due to lower amounts or below the X-ray detection limit.



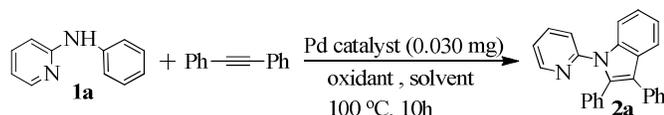
**Fig. 1** XRD patterns of the fresh (a) and used (b) NAP-Mg-Pd(0) catalysts.



**Fig. 2** X-ray photoelectron spectra of fresh and used NAP-Mg-Pd(0) catalysts.

The X-ray photoelectron spectra analysis of NAP-Mg-Pd(0) fresh and used catalysts are represented in Fig. 2. The binding energy (B.E) values of Pd  $3d_{5/2}$  and Pd  $3d_{3/2}$  in the NAP-Mg-Pd(0) fresh and used catalysts are 335.3, 340.4 and 335.5, 340.3 eV respectively. These values clearly indicate the existence of Pd in metallic form.<sup>15</sup> However, the reduction of NAP-Mg-PdCl<sub>4</sub> was not complete during the in-situ reduction as there was a trace amount of Pd in the form of a halide at BE=337.6 eV as observed in both fresh and used catalyst.<sup>16</sup> From these observations, it indicates that Pd (0) species are intact after the reaction.

For optimization of the reaction conditions, we initiated our study in the coupling of *N*-phenyl-2-aminopyridine (**1a**) with diphenylacetylene using NAP-Mg-Pd(0) as a catalyst in the presence of an oxidant. In a typical experiment, 0.5 mmol of *N*-phenyl-2-aminopyridine, 0.7 mmol of diphenylacetylene, 8.9 wt% (0.030 g) of NAP-Mg-Pd(0) and CuCl<sub>2</sub> (2 equiv) were taken in 3 mL of DMA and the reaction mixture was stirred at 100 °C for 10 h. Interestingly, the product **2a** was obtained in 36% yield (Table 1, entry 1). Encouraged by this result, various solvents, catalysts and oxidants were used for further optimization and the results are summarized in Table 1. Among the oxidants studied (entries 1-6), the best result was obtained with CuCl<sub>2</sub> (Table 1, entry 1). On the other hand, no coupled product was observed with other oxidants such as Ag<sub>2</sub>O, Ag<sub>2</sub>CO<sub>3</sub>, O<sub>2</sub> and TBHP (Table 1, entries 3-6). With the above results, it was observed that the oxidant has a pronounced effect on the yields of the reaction. Next, we examined the different solvents such as DMF, DMSO, NMP and toluene (Table 1, entries 7-10), wherein DMF afforded excellent yield of the product **2a** in 86% (entry 7) and other solvents afforded 0% yield of the product (entries 8-10). Similarly, the catalyst screening was performed with other different heterogeneous palladium catalysts such as Pd/C, LDH-Pd(0) and Mg-La-Pd(0) (Table 1, entries 11-13). No coupled product was observed in case of Pd/C and LDH-Pd(0) (entries 11 & 12) and a significant decrease in the product yield was observed when the reaction was carried out with Mg-La-Pd(0) (entry 13) clearly showing that the nano metal oxide supported palladium contribute significantly for the reaction to proceed with ease. Decrease in yields of the product was observed when the reaction was performed at 75 °C and 60 °C (Table 1, entry 14 & 15). The reaction was also carried out at the same optimum condition with low catalyst loading (0.015 g), however, the corresponding product was obtained in 20% yield (Table 1, entry 16). From the above study, we eventually concluded the optimized reaction conditions: NAP-Mg-Pd(0) (0.030 g) as catalyst in the presence of (2 equiv) CuCl<sub>2</sub> as oxidant in 3 mL of DMF as solvent at 100 °C for 10 h.

**Table 1** Optimization of reaction condition.<sup>a</sup>

Entry	Catalyst	Oxidant	Solvent	Yield(%) <sup>b</sup>
1	NAP-Mg-Pd(0)	CuCl <sub>2</sub>	DMA	36
2	NAP-Mg-Pd(0)	Cu(OAc) <sub>2</sub>	DMA	15
3	NAP-Mg-Pd(0)	Ag <sub>2</sub> CO <sub>3</sub>	DMA	0
4	NAP-Mg-Pd(0)	Ag <sub>2</sub> O	DMA	0
5	NAP-Mg-Pd(0)	O <sub>2</sub> atm	DMA	0
6	NAP-Mg-Pd(0)	TBHP	DMA	0
7	<b>NAP-Mg-Pd(0)</b>	<b>CuCl<sub>2</sub></b>	<b>DMF</b>	<b>86</b>
8	NAP-Mg-Pd(0)	CuCl <sub>2</sub>	DMSO	0
9	NAP-Mg-Pd(0)	CuCl <sub>2</sub>	NMP	0
10	NAP-Mg-Pd(0)	CuCl <sub>2</sub>	Toluene	0
11	Pd-C	CuCl <sub>2</sub>	DMF	0
12	LDH-Pd(0)	CuCl <sub>2</sub>	DMF	0
13	Mg-La-Pd(0)	CuCl <sub>2</sub>	DMF	25
14	NAP-Mg-Pd(0)	CuCl <sub>2</sub>	DMF	60 <sup>c</sup>
15	NAP-Mg-Pd(0)	CuCl <sub>2</sub>	DMF	50 <sup>d</sup>
16	NAP-Mg-Pd(0)	CuCl <sub>2</sub>	DMF	20 <sup>e</sup>

<sup>a</sup> Reaction conditions. 1a (0.5 mmol), 2a (0.7 mmol), catalyst (0.030 mg), oxidant (2 equiv), and 3 mL of solvent at 100 °C for 10h. <sup>b</sup> Isolated yields. <sup>c</sup> Reaction at 70 °C. <sup>d</sup> Reaction at 60 °C. <sup>e</sup> Reaction with (0.015 mg) of NAP-Mg-Pd(0).

Next, we turned our attentions to explore the scope and limitations of NAP-Mg-Pd(0) catalyst in the oxidative coupling reaction of various aminopyridines with alkynes under optimized conditions and the results are summarized in Table 2. Initially, we studied the coupling reaction of *N*-phenyl-2-aminopyridine (**1a**) with various symmetrical and unsymmetrical internal alkynes. As it can be seen from Table 2, this protocol is rather general in nature for the reactions of electron-rich and electron-deficient symmetrical alkynes (Table 2, entries 1-4). In contrast, the unsymmetrically substituted alkyne such as methyl phenyl acetylene was coupled with **1a** to afford **2e** relatively in lower yield but as a single regioisomer, in which phenyl group of alkyne unit was disposed adjacent to the nitrogen atom (Table 2, entry 5). The electronic properties of the *N*-aryl group appears to have a minor effect on the yield of the coupled products. The *N*-aryl-2-aminopyridines having electron donating substituents at *para*-position of *N*-aryl ring such as Me, OMe, Et and <sup>t</sup>Bu groups were coupled with diphenylacetylene to give the substituted indoles in good yields (Table 2, entries 6-9). Whereas, the *N*-aryl-2-aminopyridines having electron withdrawing substituents, such as Cl and F atoms at *para*-position of *N*-aryl ring gave excellent yields of corresponding products. (Table 2, entries 10 & 11). Slightly high yield of the coupled product was obtained with **1h** bearing

OMe at 3-position when compared to **1c** bearing OMe at 4-position, but the C-H activation occurs exclusively at the less hindered position (Table 2, entry 12). The catalytic efficiency of NAP-Mg-Pd(0) was also studied in the oxidative coupling reactions using other amino-heterocycles such as *N*-aryl-2-aminoquinoline and *N*-aryl-2-aminopyrimidine.

**Table 2** NAP-Mg-Pd(0) catalyzed oxidative coupling of *N*-aryl-2-aminopyridines with alkynes.<sup>a</sup>

entry	1	Alkyne	product	yield (%) <sup>b</sup>
1		R <sub>1</sub> = R <sub>2</sub> = C <sub>6</sub> H <sub>5</sub>	<b>2a</b>	86
2	<b>1a</b>	R <sub>1</sub> = R <sub>2</sub> = 4-(OMe)-C <sub>6</sub> H <sub>4</sub>	<b>2b</b>	83
3	<b>1a</b>	R <sub>1</sub> = R <sub>2</sub> = 4-(Me)-C <sub>6</sub> H <sub>4</sub>	<b>2c</b>	81
4	<b>1a</b>	R <sub>1</sub> = R <sub>2</sub> = 4-(F)-C <sub>6</sub> H <sub>4</sub>	<b>2d</b>	85
5	<b>1a</b>	R <sub>1</sub> = C <sub>6</sub> H <sub>5</sub> , R <sub>2</sub> = Me	<b>2e</b>	69
6		R <sub>1</sub> = R <sub>2</sub> = C <sub>6</sub> H <sub>5</sub>	<b>2f</b>	81
7		R <sub>1</sub> = R <sub>2</sub> = C <sub>6</sub> H <sub>5</sub>	<b>2g</b>	52
8		R <sub>1</sub> = R <sub>2</sub> = C <sub>6</sub> H <sub>5</sub>	<b>2h</b>	79
9		R <sub>1</sub> = R <sub>2</sub> = C <sub>6</sub> H <sub>5</sub>	<b>2i</b>	75
10		R <sub>1</sub> = R <sub>2</sub> = C <sub>6</sub> H <sub>5</sub>	<b>2j</b>	85
11		R <sub>1</sub> = R <sub>2</sub> = C <sub>6</sub> H <sub>5</sub>	<b>2k</b>	87
12		R <sub>1</sub> = R <sub>2</sub> = C <sub>6</sub> H <sub>5</sub>	<b>2l</b>	76
13		R <sub>1</sub> = R <sub>2</sub> = C <sub>6</sub> H <sub>5</sub>	<b>2m</b>	24
14		R <sub>1</sub> = R <sub>2</sub> = C <sub>6</sub> H <sub>5</sub>	<b>2n</b>	77

<sup>a</sup> Reaction conditions. 1 (0.5 mmol), 2 (0.7 mmol), NAP-Mg-Pd(0) (0.030 mg), CuCl<sub>2</sub> (2 equiv) and 3 mL of solvent at 100 °C for 10 h. <sup>b</sup> Isolated yields

From the above results, it indicates that the yields and selectivity of products in NAP-Mg-Pd(0) catalyzed oxidative coupling reactions depend on various factors such as steric, electronic and also the position of substituents (directing groups).

The spent catalyst was recovered from the reaction mixture by simple centrifugation after the completion of the reaction. The catalyst was washed with water and followed by diethyl ether to remove any organic materials. It was dried at room temperature and used for reusability study. The spent catalyst was examined for the oxidative coupling reaction of *N*-phenyl-2-aminopyridine with  $\text{PhC}\equiv\text{CPh}$  using same reaction condition. The catalyst showed consistent activity up to four cycles (Fig. 3). No trace of leached Pd was detected in the spent catalyst as determined by atomic absorption spectrometry (AAS) studies of both fresh and spent catalyst.

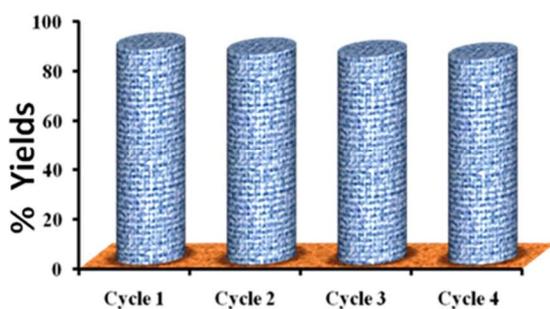


Fig. 3 Recyclability test.

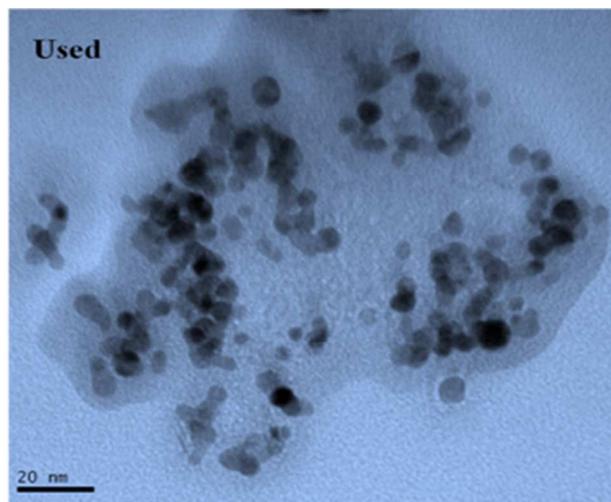
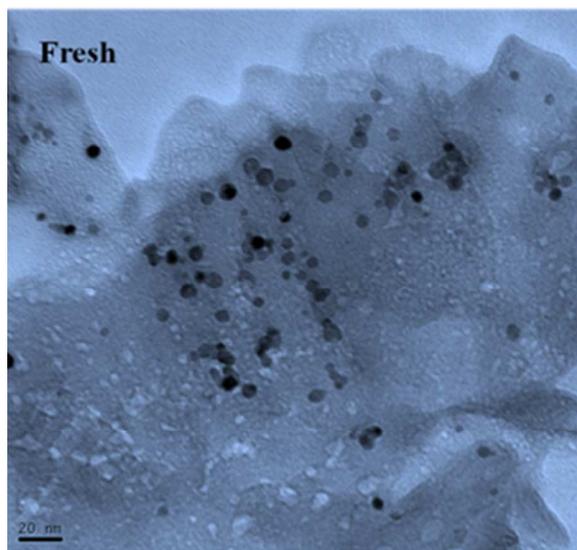


Fig. 4 Transmission electron micrographs of fresh NAP-Mg-Pd(0) and used (after 4<sup>th</sup> cycle) catalyst.

The TEM images of the fresh and used NAP-Mg-Pd(0) catalysts are shown in Fig. 4. It appears that there is not much change in the shape and size of the Pd particles in both fresh and used catalysts. TEM analysis indicated that the nano Pd particles had a mean diameter of 8 and 10 nm for fresh and used catalysts. The morphology of the catalyst remains the same even after 4 recycles.

## Conclusions

In summary, we have developed a first heterogeneous catalytic protocol for the selective oxidative coupling between *N*-aryl-2-aminopyridines and alkynes to give *N*-pyridyl indoles in excellent yields using nanocrystalline magnesium oxide (NAP-MgO)-supported palladium nanoparticles [NAP-Mg-Pd(0)] catalyst and  $\text{CuCl}_2$  as an oxidant. The catalyst works equally well in the ortho C-H activation of *N*-aryl-2-aminopyridines as reported previously by homogeneous catalysts. The recovery and reusability study of the catalyst showed consistent catalytic activity up to four cycles.

## Experimental section

NAP-MgO (commercial name: Nano Active™ Magnesium Oxide Plus) was purchased from Nano Scale Materials, Inc. (Manhattan, USA). All chemicals were purchased commercially and were used as received. All solvents used for experiments were dried using standard procedures and distilled prior to use. Pd-C was purchased from commercial sources and has 10%Pd on carbon.

The X-ray diffraction (XRD) patterns of the fresh and used samples were obtained on a Rigaku Miniflex X-ray diffractometer using Ni filtered  $\text{Cu K}\alpha$  radiation ( $\lambda = 0.15406$  nm), at a scan rate of  $2^\circ \text{ min}^{-1}$ , with the beam voltage and beam current of 30 kV and 15 mA respectively. The X-ray photoelectron spectroscopic (XPS) analysis of the fresh and

used NAP-Mg-Pd(0) sample was recorded using a Kratos Axis Ultra Imaging X-ray photoelectron spectrometer equipped with Mg anode and a multichannel detector. Charge referencing was done against adventitious carbon (C 1s, 284.8 eV). Shirley-type background was subtracted from the signals. The recorded spectra were always fitted using Gauss-Lorentz curves to determine the binding energies of the different elements. For the transmission electron microscope (TEM) analysis, samples were dispersed in methanol solution and dropped on a 200-mesh Cu grid, and images were taken using JEOL JEM 2100F high-resolution transmission electron microscope at an acceleration voltage of 200 kV. The  $^1\text{H}$  and  $^{13}\text{C}$  spectra were recorded on Inova 500 and Avance 300 (300 MHz  $^1\text{H}$  and  $^{13}\text{C}$ ) spectrometer in  $\text{CDCl}_3$  using TMS as internal standard. ACME silica gel (60-120 mesh) was used for column chromatography purposes and thin layer chromatography was performed on Merck pre coated silica gel 60-F254 plates.

### Preparation of catalyst

NAP-MgO was purchased from NanoScale Materials, Inc. (Manhattan, USA). NAP-Mg-Pd(0) was synthesized following the procedure reported earlier by our group<sup>12</sup>. NAP-Mg-PdCl<sub>4</sub>: NAP-MgO was calcined in air at 450 °C for 4 h (1.0g; BET-surface area = 147 m<sup>2</sup>g<sup>-1</sup>), treated with Na<sub>2</sub>PdCl<sub>4</sub> (0.294 g, 1 mmol), dissolved in 100 mL decarbonated water with vigorous stirring for 12 h at room temperature under nitrogen atmosphere to afford the brown coloured NAP-Mg-PdCl<sub>4</sub>. Then, the catalyst was filtered and washed with deionized water and acetone and dried under vacuum. NAP-Mg-Pd(0): NAP-Mg-PdCl<sub>4</sub> (1.0g) was reduced with sodium borohydride (1.5g, 39.6 mmol) in 20 mL of dry ethanol with vigorous stirring for 3 h under a nitrogen atmosphere at room temperature. Then, the reduced catalyst was filtered through a G-3 sintered glass funnel and washed with deionized water and acetone then dried under vacuum to get the black-coloured, air stable NAP-Mg-Pd(0) (0.9 mmol of Pd/g, BET – surface area = 116 m<sup>2</sup>g<sup>-1</sup>). The catalyst was used for the oxidative coupling reaction between N-aryl-2-aminopyridines with alkynes.

### General producer for the synthesis of N-(2-pyridyl)indoles

A reaction vessel was equipped with a magnetic bar and charged with compound **1a** (0.5 mmol), diphenylacetylene (0.7 mmol), anhydrous CuCl<sub>2</sub> (2 equiv), NAP-Mg-Pd(0) (0.030 g), and 3 mL of DMF was added via syringe at room temperature. The reaction mixture was heated at 100 °C for 10 h and then cooled to room temperature. The catalyst was separated from the reaction mixture by simple centrifugation. The catalyst was washed with water followed by diethyl ether. It was then dried at room temperature and used as it for next cycle of reaction. The reaction mixture was diluted with water and then extracted with ethyl acetate (20 mL). The combined organic layer was washed with brine solution (10 mL) and then dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. After removal of the solvent, the crude product was purified by flash chromatography over silica gel

(60-120 mesh) column using hexane/ethyl acetate as an eluent to afford the pure product.

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### Notes and references

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- (a) L. Wang, J. Huang, S. Peng, H. Liu, X. Jiang, J. Wang, *Angew. Chem. Int. Ed.* 2013, **52**, 1768; (b) P. Villuendas E. P. Urriolabeitia, *J. Org. Chem.* 2013, **78**, 5254; (c) C. Zhu, R. Wang, J. R. Falck, *Chem. Asian J.* 2012, **7**, 1502; (d) L. Ackermann, *Chem. Rev.* 2011, **111**, 1315; (e) D. A. Colby, R. G. Bergman, J. A. Ellman, *Chem. Rev.* 2010, **110**, 625; (f) O. Baudoin, R. Jazzar, J. Hitce, A. Renaudat, J. S-Kreutzer, O. Baudoin, *Chem. Eur. J.* 2010, **16**, 2654; (g) C-L. Sun, B-J. Li, Z-J. Shi *Chem. Commun.* 2010, **46**, 667; (i) T. Satoh, M. Miura, *Chem. Eur. J.* 2010, **16**, 11212; (j) L. Ackermann, R. Vicente, A. R. Kapdi, *Angew. Chem. Int. Ed.* 2009, **48**, 9792; (k) J. C. Lewis, R.G. Bergman, J. A. Ellman, *Acc. Chem. Res.* 2008, **41**, 1013; (l) I. V. Seregin, V. Gevorgyan, *Chem. Soc. Rev.* 2007, **36**, 1173; (m) D. Alberico, M. E. Scott, M. Lautens, *Chem. Rev.* 2007, **107**, 175; (n) V. Ritleng, C. Sirlin, M. Pfeffer, *Chem. Rev.* 2002, **102**, 1731.
- (a) J. Wencel-Delord, F. Glorius *Nature Chem.* 2013, **5**, 369–375; (b) G. Song, F. Wang, X. Li, *Chem. Soc. Rev.* 2012, **41**, 3651; (c) W-D. Joanna, T. Droge, F. Liu, F. Glorius, *Chem. Soc. Rev.* 2011, **40**, 4740; (d) F. Wang, G. Song, Z. Du, J. Li, *J. Org. Chem.* 2011, **76**, 2926; (e) S. Rakshit, F. W. Patureau, F. Glorius, *J. Am. Chem. Soc.* 2010, **132**, 9585; (f) T. K. Hyster T. Rovis, *J. Am. Chem. Soc.* 2010, **132**, 10565; (g) F. Wang, G. Song, X. Li, *Org. Lett.* 2010, **12**, 5430; (h) Y. Su, M. Zhao, K. Han, G. Song, X. Li, *Org. Lett.* 2010, **12**, 5462; (i) S. Ding, Z. Shi, N. Jiao, *Org. Lett.* 2010, **12**, 1540; (j) N. Guimond, K. Fangou, *J. Am. Chem. Soc.* 2009, **131**, 12050.
- (a) G. Li, D. Leow, L. man, J-Q. Yu, *Angew. Chem. Int. Ed.* 2013, **52**, 1245; (b) S. Chen, J. Yu, Y. Jiang, F. Chen, J. Cheng, *Org. Lett.* 2013, **15**, 4754; (c) W. Song, L. Ackermann, *Chem. Commun.* 2013, **49**, 6638; (d) L. Ackermann, A.V. Lygin, N. Hofmaan, *Angew. Chem. Int. Ed.* 2011, **50**, 6397; (e) D. R. Stuart, P. Alsabeh, M. Kuhn, K. Fangou, *J. Am. Chem. Soc.* 2010, **132**, 18326; (f) G. Song, D. Chen, C-L. Pan, R. H. Crabtree, X. Li, *Org. Chem.* 2010, **75**, 7487; (g) Z. Shi, C. Zhang, S. Li, D. Pan, S. Ding, Y. Cui, N. Jiao, *Angew. Chem. Int. Ed.* 2009, **48**, 4572; (h) M. Yamashita, H. Horiguchi, K. Hirano, T. Satoh, M. Miura, *Org. Chem.* 2009, **74**, 7481; (i) S. Wurtz, S. Rakshit, J. Neumann, T. droge, F. Glorius. *Angew. Chem. Int. Ed.* 2008, **47**, 7230; (j) Y-T. Wu, K-H. Huang, C-C. Shin, T-C. Wu. *Chem. Eur. J.* 2008, **14**, 6697; (k) K. Ueura, T. Satoh, M. miura, *Org. Lett.* 2007, **9**, 1409.
- J. Chen, G. Song, C-L. Pan, X. Li, *Org. Lett.* 2010, **12**, 5426.
- J. Chen, Q. Pang, Y. Sun, X. Li, *J. Org. Chem.* 2011, **76**, 3523.
- (a) A Beilstein search for indoles with biological activity yielded>45 000 results; (b) J. M Richter, Y. Ishihara, T. Masuda, B. W

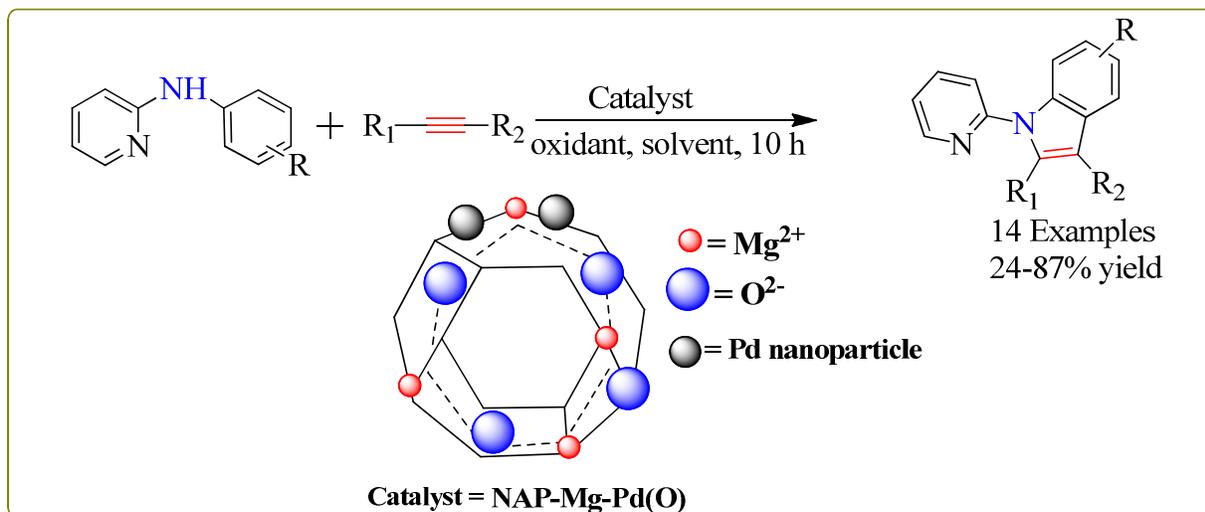
- Whitefield, T. Llamas, A. Pohjakallio, P. S. Baran, *J. Am. Chem. Soc.* 2008, **130**, 17938, and references therein; (c) K. Kruger, A. Tillack, M. Beller, *Adv. Synth. Catal.* 2008, **350**, 2153.
7. (a) K. D. Collins, R. Honeker, S. Vasquez, D. D. Tang and F. Glorius, *Chem. Sci.*, 2014, DOI: 10.1039/C4SC03051F; (b) D.-T. D. Tang, K. D. Collins, J. B. Ernst, F. Glorius, *Angew. Chem. Int. Ed.* 2014, **53**, 1809-1813; (c) D.-T. D. Tang, K. Collins, F. Glorius, *J. Am. Chem. Soc.* 2013, **135**, 7450–7453.
8. (a) E. Lucas, S. Decker, A. Khaleel, A. Seitz, S. Fultz, A. Ponce, W. Li, C. Carnes, K. J. Klabunde, *Chem. Eur. J.* 2001, **7**, 2505; (b) R. Schlogl, S. B. Abd Hamid, *Angew. Chem., Int. Ed.* 2004, **43**, 1628; (c) A. T. Bell, *Science* 2003, **299**, 1688; (d) B. M. Choudary, K. V. S. Ranganath, J. Yadav, M. L. Kantam, *Tetrahedron Lett.* 2005, **46**, 1369; (e) C. L. Carnes, K. J. Klabunde, *Langmuir* 2000, **16**, 3764; (f) Y. Jiang, S. Decker, C. Mohs, K. J. Klabunde, *J. Catal.* 1998, **180**, 24; (g) L. Vayssieres, K. Keis, A. Hagfeldt, S. E. Lindquist, *Chem. Mater.* 2001, **13**, 4395; (h) Z. W. Pan, Z. R. Dai, Z. L. Wang, *Science* 2001, **291**, 1947; (i) C. X. Xu, X. W. Sub, B. J. Chen, P. Shum, S. Lu, X. Hu, *J. Appl. Phys.* 2004, **95**, 661.
9. (a) B. M. Choudary, M. L. Kantam, K. V. S. Ranganath, K. Mahendar, B. Sreedhar *J. Am. Chem. Soc.* 2004, **126**, 3396; (b) M. L. Kantam, K. B. ShivaKumar, Ch. Sridhar, *Adv. Synth. Catal.* 2005, **347**, 1212; (c) B. M. Choudary, K. V. S. Ranganath, U. Pal, M. L. Kantam, B. Sreedhar, *J. Am. Chem. Soc.* 2005, **127**, 13167; (d) M. L. Kantam, S. Laha, J. Yadav, B. M. Choudary, B. Sreedhar *Adv. Synth. Catal.* 2006, **348**, 867; (e) M. L. Kantam, S. Laha, J. Yadav, B. Sreedhar, *Tetrahedron Lett.* 2006, **47**, 6213; (f) B. M. Choudary, K. Mahendar, M. L. Kantam, K. V. S. Ranganath, T. Athar, *Adv. Synth. Catal.* 2006, **348**, 1977; (g) A. Monopoli, A. Nacci, V. Calò, F. Ciminale, P. Cotugno, A. Mangone, L. C. Giannossa, P. Azzone, N. Cioffi, *Molecules*, 2010, **15**, 4511; (h) L. Yin, J. Liesbscher, *Chem. Rev.* 2007, **107**, 133; (i) Ch. Venkat Reddy, M. L. Kantam, *Catal. Surv. Asia*. 2011, **15**:89, 110.
10. (a) M. L. Kantam, S. Roy, M. Roy, B. Sreedhar, B. M. Choudary, *Adv. Synth. Catal.* 2005, **347**, 2002; (b) M. L. Kantam, S. Roy, M. Roy, M. S. Subhas, P. R. Likhari, B. Sreedhar, B. M. Choudary, *Synlett* **2006**, 17, 2747.
11. M. L. Kantam, R. Chakravarthi, U. Pal, B. Sreedhar, *Adv. Synth. Catal.* 2008, **350**, 8222.
12. M. L. Kantam, R. Chakravarthi, Ch. Venkat Reddy, B. Sreedhar, S. Bhargava, *Adv. Synth. Catal.* 2008, **350**, 2554.
13. K. Layek, H. Maheswaran, R. Arundhati, M. L. Kantam, S. Bhargava, *Adv. Synth. Catal.* 2011, **353**, 606.
14. M. L. Kantam, P. Vishnuvardhan Reddy, P. Srinivas, A. Venugopal, Y. Nishina, S. Bhargava, *Catal. Sci. Technol.* 2013, **3**, 2550.
15. A. H. Padmasri, A. Venugopal, J. Krishnamurthy, K. S. Rama Rao, P. Kanta Rao, *J. Phys. Chem. B.* 2002, **106**, 1024-1031.
16. Y. Shen, S. Wang, K. Huang, *Appl. Catal. A: Gen.* 1990, **55**, 57-57.

# Nanocrystalline Magnesium Oxide-Stabilized Palladium(0): An Efficient and Reusable Catalyst for the Synthesis of *N*-(2-pyridyl)indoles

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The synthesis of *N*-(2-pyridyl)indoles by NAP-Mg-Pd(0) catalyzed oxidative coupling between *N*-aryl-2-aminopyridines with alkynes.