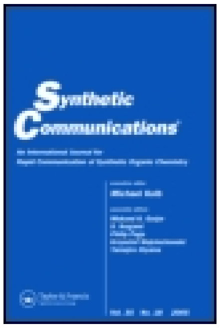
This article was downloaded by: [Moskow State Univ Bibliote]
On: 17 December 2013, At: 09:36
Publisher: Taylor & Francis
Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Reductive Amination of Aldehydes and Amines with an Efficient Pd/NiO Catalyst

Huimin Yang [a] [b] , Xinjiang Cui [a] , Youquan Deng [a] & Feng Shi [a]
[a] Centre for Green Chemistry and Catalysis , Lanzhou Institute of Chemical Physics, Chinese Academy of Sciences, No.18, Tianshui Middle Road , Lanzhou , 730000 , China
[b] University of the Chinese Academy of Sciences , Beijing , 100049 , China
Accepted author version posted online: 02 Dec 2013.Published online: 02 Dec 2013.

To cite this article: Synthetic Communications (2013): Reductive Amination of Aldehydes and Amines with an Efficient Pd/NiO Catalyst, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, DOI: 10.1080/00397911.2013.857690

To link to this article: http://dx.doi.org/10.1080/00397911.2013.857690

Disclaimer: This is a version of an unedited manuscript that has been accepted for publication. As a service to authors and researchers we are providing this version of the accepted manuscript (AM). Copyediting, typesetting, and review of the resulting proof will be undertaken on this manuscript before final publication of the Version of Record (VoR). During production and pre-press, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal relate to this version also.

PLEASE SCROLL DOWN FOR ARTICLE

Taylor & Francis makes every effort to ensure the accuracy of all the information (the “Content”) contained in the publications on our platform. However, Taylor & Francis, our agents, and our licensors make no representations or warranties whatsoever as to the accuracy, completeness, or suitability for any purpose of the Content. Any opinions and views expressed in this publication are the opinions and views of the authors, and are not the views of or endorsed by Taylor & Francis. The accuracy of the Content should not be relied upon and should be independently verified with primary sources of information. Taylor and Francis shall not be liable for any losses, actions, claims, proceedings, demands, costs, expenses, damages, and other liabilities whatsoever or howsoever caused arising directly or indirectly in connection with, in relation to or arising out of the use of the Content.

This article may be used for research, teaching, and private study purposes. Any substantial or systematic reproduction, redistribution, reselling, loan, sub-licensing, systematic supply, or distribution in any form to anyone is expressly forbidden. Terms & Conditions of access and use can be found at http://www.tandfonline.com/page/terms-and-conditions

Reductive Amination of Aldehydes and Amines with an Efficient Pd/NiO Catalyst

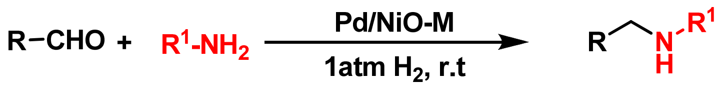
Huimin Yang[1,2], Xinjiang Cui[1], Youquan Deng[1], Feng Shi[1,]

[1]*Centre for Green Chemistry and Catalysis, Lanzhou Institute of Chemical Physics, Chinese Academy of Sciences, No.18, Tianshui Middle Road, Lanzhou, 730000, China,*

[2]*University of the Chinese Academy of Sciences. Beijing, 100049, China*

Address correspondence to Feng Shi E-mail: fshi@licp.cas.cn

GRAPHICAL ABSTRACT



24 examples, up to 98% yield

Abstract

By applying a simple Pd/NiO catalyst, the reductive amination of amines and aldehydes can be progressed efficiently under mild reaction conditions. 24 substituted amines with different structures were synthesized with up to 98% isolated yields.

KEYWORDS: Amination; aldehydes; amines; palladium

INTRODUCTION

The formation of N-alkyl amines is one of the most important transformations in organic chemistry[1-2]. In particular, N-alkyl amines are important building blocks for natural products, pharmaceuticals and agrochemicals. The reaction of amines and alkyl halides with the addition of stoichiometric amounts of inorganic bases is the most effective and universal method[3-5]. However, this method often suffers from drawbacks such as usage of toxic substrates and generation of inorganic salt waste. Moreover, various methods have been developed for the synthesis of N-alkyl amines such as amination of alcohols[6-9], the reaction of amines with amines, hydroaminations[10-16], and hydroaminomethylation[17-21]. Reductive amination is a general and attractive reaction for the synthesis of N-alkyl amines which includes two synthetic steps: C=N double-bond formation and hydrogenation of the imine derivatives. The traditional protocol for reductive amination is based on the use of stoichiometric amount of boron hydrides [22-27]. In order to develop clean and economic way for the reductive amination reaction, the applying of molecular hydrogen as reducing agent in the presence of homogeneous Pd or Ru catalysts was developed successfully[28-30]. However, the using of homogeneous catalyst system faces problem in catalyst-product separation and catalyst recycling. Heterogeneous catalysts have innate advantages, such as ligand-free, easy isolation and catalyst reuse[31-34]. If taking these advantages into account, the exploration of reductive amination reaction with heterogeneous catalyst is highly desirable [35-40].

Although good results were obtained, the known heterogeneous catalyst system is limited by the relatively poor generality or rigorous reaction conditions. Here, we report an effective Pd/NiO, which was an active catalyst for nitrobenzene hydrogenation[41], for the reductive amination reaction under hydrogen atmosphere and at room temperature.

RESULTS AND DISCUSSION

The structure of the catalysts were characterized by TEM and HR-TEM (Figure 1), which suggested that the palladium particles were well dispersed and the average size of the palladium particles in Pd/NiO was about 5 nm (Figure 1a). The Pd (111) crystal lattice can be clearly observed from the HR-TEM picture (Figure 1b). The XRD diffraction patterns of NiO suggested that it was a better-crystallized structure and obvious Ni (111), (200), and (220) peaks were observed (PDF-87-0712). The introduction of palladium didn't change the crystal structure of NiO. Moreover, there was no observable diffraction peak of palladium which suggested that the palladium species were highly dispersed over the NiO support. XPS analysis showed that typical binding energies of NiO (854.3 eV) and Pd (335.4 eV). According to ICP-AES analysis, the palladium loading is 1.1 wt%.

Initially, the reductive amination of benzaldehyde and aniline was used as the model reaction for reaction conditions optimization under 1 atm hydrogen using Pd/NiO as catalyst[42]. The solvents were optimized first (Table 1). Clearly, benzotrifluoride, acetonitrile and dichloromethane are suitable solvents for the reaction (Entries 1-3). The yields to N-benzyl aniline were 33-69% with >90% aniline conversions. The major byproduct is the imine without being hydrogenated. Possibly, these solvents are unfavorable for the imine hydrogenation. In reverse, lower conversions were obtained with high N-benzyl aniline selectivities if acetone, THF and methanol were used as the solvents (Entries 4-6). The selectivities in these reactions were >90% but the aniline conversions were 41-89%. According to GC-MS analysis, it was found that large amount of toluene was generated via benzaldehyde hydrogenation, which resulted in the lower conversion of aniline. Better results were obtained if toluene, xylene, isopropanol and ethanol were used as the solvents (Entries 7-10). Although trace amount of imine and toluene are detectable in these cases, the yields to N-benzyl aniline reached 89-91%. If the reaction time was prolonged, relatively lower yield was obtained, which suggested that the reaction was reversible and small amount of N-benzyl aniline was dehydrogenated (Entry 11). Similarly, higher reaction temperature or catalyst loadings resulted in lower yields, too, due to the hydrogenation of benzaldehyde to toluene (Entries 12-14). Although good result was also gained with lower catalyst loadings in the reductive amination of aniline and benzaldehyde, (Entries 15-16), the applying of lower catalyst loadings caused poor generality in the reductive amination of other compounds. Therefore, 20 mg catalyst was used for the next exploration.

According to the above discussions, the optimized reaction conditions, i.e. 1 mmol amine, 1 mmol aldehyde, 20 mg catalyst, 2 mL ethanol, r.t. and 12 h, were used in the generality testing. As shown in Table 2, the reductive amination of benzaldehyde with aniline and 1-naphthylamine can obtain desired products in good yield of 84% and 88% (Entries 1 and 2). Benzylamines with electron-withdrawing and electron-donating groups can also be converted into the desired products in good to excellent yields (Entries 3-6). Interestingly, the reductive amination reactions of benzaldehyde with primary amines containing different heterocyclic ring structures, i.e. pyridin-2-amine, furan-2-ylmethanamine and 2-(piperazin-1-yl)ethanamine, can progress well with up to 98% isolated yields (Entries 6-8). Excellent results were also obtained if aliphatic amines such as butan-1-amine, heptan-1-amine dodecan-1-amine were used as the starting materials (Entries 9-11). The yields to the aim products all reached 98% in the reactions of benzaldehyde with typical secondary amines 1-phenylethanamine and cyclohexanamine (Entries 12-13).

Next, aldehydes with different structures can react with aniline to give the desired products, too (Table 3). Irrespective of the structure and position of the substituting groups, good to excellent yields, i.e. 87-98%, of the corresponding products were obtained (Entries 1–9). Thus there were no remarkable steric and electronic effects on the reactivity of the aromatic aldehydes. Noteworthy, 95% of the corresponding product was obtained when furan-2-carbaldehyde was used (Entry 10). Typical aliphatic aldehyde, i.e. butaldehyde, can also be converted into the desired N-benzyl butyl amine successfully with 98 % yield under this reaction conditions (Entry 11).

Moreover, in order to see if the dissolved catalytic species from Pd/NiO catalyzed the reaction or not, after the first run, 1.0 mmol aniline and 1.0 mmol benzaldehyde were added into the reaction solution again after removing the catalyst. However, there is no any observable N-benzyl aniline formation by GC-FID after it was reacted for another 12 h. These results excluded the possible contribution of homogeneous catalytic species leached from Pd/NiO catalyst. Finally, the reusability of the Pd/NiO catalyst was tested. The catalyst can be easily separated from the mixture solution by centrifugation. Then the catalyst was washed by ethanol for two times and reused directly without other treatment. Clearly, the catalyst showed high catalytic activity on the reductive amination of benzaldehyde and aniline even if the catalyst was reused at the fifth run (Table 4). It suggests that the catalyst is reusable potentially.

EXPERIMENTAL

Preparation Of The Nio Nanoparticles

The catalyst samples were prepared starting from sol-gel polymerization of resorcinol and formaldehyde with Na_2CO_3 as a catalyst with 50%Ni-doped monolithic carbon aerogels. Typically, resorcinol (2.20 g, 20 mmol), formaldehyde (3.25 g, 40 mmol, 36.5% in water, methanol stabilized) and 6 mL distilled water were added into a 100 mL PTFE autoclave and the mixture was stirred for 0.5 h. Subsequently, an aqueous solution of 5.8 g $Ni(NO_3)_2 \cdot 6H_2O$ was added dropwise and a 0.9M solution of Na_2CO_3 (4 mL)were added into the mixture. After vigorous stirring for 1 h, the autoclave was sealed and kept at 80 ^oC for 1 day. Then the autoclave was cooled to room temperature. The wet gels were placed into a round-bottomed flask and vacuum dried at 130 ^oC for 3 h. After being pyrolyzed at 800 ^oC for 5 h in nitrogen flow (20 mL/min), about 7 g black solid was obtained. Then the black solid was treated at 500 ^oC for 5 h in a flow of oxygen (20 mL/min) to afford the NiO nanoparticles (about 4.1 g).

Preparation Of Pd/Nio Catalysts

Pd that was supported on NiO was prepared according to a solimmobilization method. For the 1.1 wt% Pd/NiO catalyst, the detailed preparation procedure employed is described below. 0.067 ml an aqueous solution of H_2PdCl_4 (0.067 mL, 35 mg mL^{-1}) was added to distilled water (5 mL). Then, an aqueous solution of PVA (1.2 mL, $5mgmL^{-1}$) was added. After 30 min, a freshly prepared 0.1 M solution of $NaBH_4$ ($NaBH_4$ /Pd, 4:1 mol/mol) was then added to form a dark-brown sol. After 30 min of sol generation, the colloid was immobilized by adding NiO powder (100 mg). The solution was acidified to pH 1 by sulfuric acid under string conditions and was stirred for another 2 h finally. The resulting solid was washed with distilled water (3×40 m L) and was dried in air at 80 ^{o}C for 2 h to afford the Pd/NiO catalyst.

Reductive Reaction Of Aldehydes And Amines

1.0 mmol amine, 1.0 mmol aldehyde, 2 mL solvent and 20 mg catalyst were added in a 40 mL reaction tube. The above mixture were reacted at 25 ^{o}C and under hydrogen atmosphere for 12 h. After the reaction, the reaction mixture was detected by GC-MS. The aimed product was obtained by TLC and analysis by NMR.

CONCLUSION

In conclusion, we have developed a simple Pd/NiO catalyst system for the reductive amination reaction under mild reaction conditions. The Pd/NiO catalyst exhibited excellent activity and selectivity in the reductive amination reaction using various amines and aldehydes as the substrates. In addition, the Pd/NiO catalyst can be easily recycled for several runs without deactivation.

SUPPLEMENTAL MATERIAL

Supplemental data for this article can be accessed on the publisher's website. the publisher's website will be a live link

ACKNOWLEDGMENTS

We thank the National Natural Science Foundation of China (21073208) and Chinese Academy of Sciences for financial support

REFERENCES

1. Buchwald, S. L.; Mauger, C.; Mignani, G.; Scholz, U. *Adv. Synth. Catal.* **2006**, *348*, 23.
2. Navarro, O.; Marion, N.; Mei, J.; Nolan, S. P. *Chem. Eur. J.* **2006**, *12*, 5142.
3. Salvatore, R. N.; Yoon, C. H.; Jung, K. W. *Tetrahedron.* **2001**, 57, 7785.
4. Alsabeh, P. G.; Lundgren, R. J.; McDonald, R.; Seechurn, C. C. C. J.; Colacot, T. J.; Stradiotto, M. *Chem. Eur. J.* **2013**, *19*, 2131.
5. Guo, D.; Huang, H.; Zhou, Y.; Xu, J.; Jiang, H.; Chen, K.; Liu, H. *Green Chem.* **2010**, *12*, 276.
6. He, L.; Lou, X.-B.; Ni, J.; Liu, Y.-M.; Cao, Y.; He, H.-Y.; Fan, K.-N. *Chem. Eur. J.* **2010**, *16*, 13965.
7. Zhang, Y.; Qi, X.; Cui, X.; Shi, F.; Deng, Y. *Tetrahedron Lett.* **2011**, *52*, 1334.
8. Cui, X.; Zhang, Y.; Shi, F.; Deng, Y. *Chem. Eur. J.* **2011**, *17*, 1021.
9. Cui, X.; Shi, F.; Tse, M. K.; Goerdes, D.; Thurow, K.; Beller, M.; Deng, Y. *Adv. Synth. Catal.* **2009**, *351*, 2949.

10. MacDonald, M. J.; Schipper, D. J.; Ng, P. J.; Moran, J.; Beauchemin, A. M. *J. Am. Chem. Soc.* **2011**, *133*, 20100.

11. Werkmeister, S.; Fleischer, S.; Zhou, S.; Junge, K.; Beller, M. *Chemsuschem.* **2012**, *5*, 777.

12. Li, H.; Wen, M.; Lu, G.; Wang, Z.-X. *Dalton T* **2012**, *41*, 9091.

13. Liu, G.; Huang, K.; Cao, B.; Chang, M.; Li, S.; Yu, S.; Zhou, L.; Wu, W.; Zhang, X. *Org. Lett.* **2012**, *14*, 102.

14. Shen, X.; Buchwald, S. L. *Angew. Chem. Int. Ed.* **2010**, *49*, 564.

15. Wood, M. C.; Leitch, D. C.; Yeung, C. S.; Kozak, J. A.; Schafer, L. L. *Angew. Chem. Int. Ed.* **2009**, *48*, 6937.

16. Perl, N. R.; Ide, N. D.; Prajapati, S.; Perfect, H. H.; Durón, S. G.; Gin, D. Y. *J. Am. Chem. Soc.* **2010**, *132*, 1802.

17. Ahmed, M.; Seayad, A. M.; Jackstell, R.; Beller, M. *J. Am. Chem. Soc.* **2003**, *125*, 10311.

18. Ahmed, M.; Buch, C.; Routaboul, L.; Jackstell, R.; Klein, H.; Spannenberg, A.; Beller, M. *Chem. Eur. J.* **2007**, *13*, 1594.

19. Sudheesh, N.; Shukla, R. S. *Appl. Catal., A: Chem.* **2013**, *453*, 159.

20. Wu, L.; Fleischer, I.; Jackstell, R.; Beller, M. *J. Am. Chem. Soc.* **2013**, *135*, 3989.

21. Crozet, D.; Gual, A.; McKay, D.; Dinoi, C.; Godard, C.; Urrutigoity, M.; Daran, J.-C.; Maron, L.; Claver, C.; Kalck, P. *Chem. Eur. J.* **2012**, *18*, 7128.

22. Tarasevich, V. A.; Kozlov, N. G. *Usp. Khim.* **1999**, *68*, 61.

23. Mattson, R. J.; Pham, K. M.; Leuck, D. J.; Cowen, K. A. *J. Org. Chem.* **1990**, *55*, 2552.

24. Abdel-Magid, A. F.; Carson, K. G.; Harris, B. D.; Maryanoff, C. A.; Shah, R. D. *J. Org. Chem.* **1996**, *61*, 3849.

25. Bomann, M. D.; Guch, I. C.; DiMare, M. *J. Org. Chem.* **1995**, *60*, 5995.

26. Suwa, T.; Sugiyama, E.; Shibata, I.; Baba, A. *Synlett.* **2000**, *556*.

27. Sato, S.; Sakamoto, T.; Miyazawa, E.; Kikugawa, Y. *Tetrahedron.* **2004**, *60*, 7899.

28. Pagnoux-Ozherelyeva, A.; Pannetier, N.; Mbaye, M. D.; Gaillard, S.; Renaud, J.-L. *Angew. Chem. Int. Ed.* **2012**, *51*, 4976.

29. Zhang, M.; Yang, H.; Zhang, Y.; Zhu, C.; Li, W.; Cheng, Y.; Hu, H. *Chem. Commun.* **2011**, *47*, 6605.

30. Werkmeister, S.; Junge, K.; Beller, M. *Green Chem.* **2012**, *14*, 2371.

31. Wei, S.; Dong, Z.; Ma, Z.; Sun, J.; Ma, J. *Catal. Commun.* **2013**, *30*, 40.

32. Li, L.; Niu, Z.; Cai, S.; Zhi, Y.; Li, H.; Rong, H.; Liu, L.; Liu, L.; He, W.; Li, Y. *Chem. Commun.* **2013**, *49*, 6843.

33. Domine, M. E.; Hernández-Soto, M. C.; Navarro, M. T.; Pérez, Y. *Catal. Today* **2011**, *172*, 13.

34. Dell'Anna, M. M.; Mastrorilli, P.; Rizzuti, A.; Leonelli, C. *Appl. Catal., A: Chem.* **2011**, *401*, 134.

35. Bagal, D. B.; Watile, R. A.; Khedkar, M. V.; Dhake, K. P.; Bhanage, B. M. *Catal. Sci. Tech.* **2012**, *2*, 354.

36. Das, B. G.; Ghorai, P. *Chem. Commun.* **2012**, *48*, 8276.

37. Gomez, S.; Peters, J. A.; van der Waal, J. C.; Zhou, W. Z.; Maschmeyer, T. *Catal. Lett.* **2002**, *84*, 1.

38. Sreedhar, B.; Reddy, P. S.; Devi, D. K. *J. Org. Chem.* **2009**, *74*, 8806.

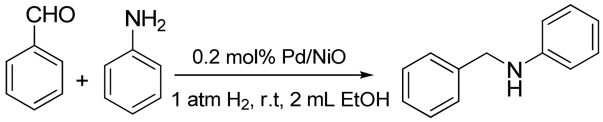
39. Domine, M. E.; Consuelo Hernandez-Soto, M.; Navarro, M. T.; Perez, Y. Catal. Today 2011, *172*, 13.

40. Pintado-Sierra, M.; Rasero-Almansa, A. M.; Corma, A.; Iglesias, M.; Sánchez, F. *J. Catal.* **2013**, *299*, 137.

41. Yang, H.; Cui, X.; Deng, Y.; Shi, F. *ChemCatChem* **2013**, *5*, 1739.

42. **Representative procedure for the reductive amination reactions of aldehydes and amines:** 1.0 mmol amine, 1.0 mmol aldehyde, 2 mL solvent and 20 mg catalyst were added into a 40 mL reaction tube. The above mixture was reacted at 25 ^{o}C and under hydrogen atmosphere for 12 h. Then, the reaction mixture was filtrated to remove the catalyst. Pure products can be obtained simply after removing the solvent and other impurities using rotary evaporator and vacuum drying. All the products were analyzed by GC-MS and ^{1}H NMR.

Table 1. Optimization of reaction conditions[a]



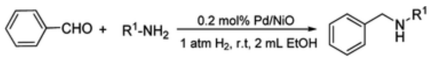
Entry	Solvent	T/°C	Cat./ mg	t/h	Conv./ %[b]	Sel./ %[b]	Y./ %[c]
1	Benzotrifluoride	25	20	10	94	73	69
2	Acetonitrile	25	20	10	90	64	58
3	Dichloromethane	25	20	10	95	35	33
4	Acetone	25	20	10	89	96	85
5	THF	25	20	10	80	96	77
6	MeOH	25	20	10	41	92	38
7	Toluene	25	20	10	94	95	89
8	Xylene	25	20	10	93	96	89
9	Isopropanol	25	20	10	95	96	91
10	EtOH	25	20	10	95	95	90
11	EtOH	25	20	12	91	95	86
12	EtOH	50	20	12	77	95	71
13	EtOH	75	20	12	65	94	61
14	EtOH	25	5	12	91	96	87
15	EtOH	25	10	12	97	96	93
16	EtOH	25	30	12	80	95	76

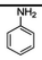
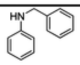
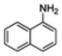
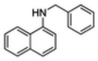
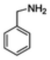
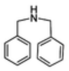
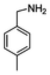
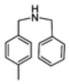
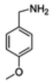
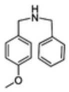
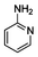
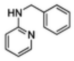
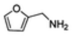
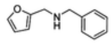
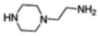
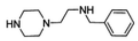
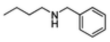
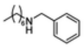
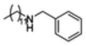
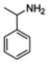
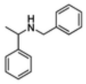
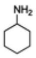
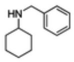
[a] Reaction conditions: benzaldehyde (1.0 mmol), aniline (1.0 mmol), Pd/NiO (20 mg, 0.2 mol% Pd to aniline), under hydrogen atmosphere, solvent (2 mL).

[b] Conversion of aniline. Selectivity to N-benzyl aniline.

[c] GC yield determined by GC-FID using biphenyl as external standard material.

Table 2. Reductive amination of benzaldehyde with various amines[a]

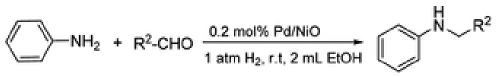


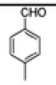
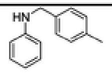
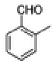
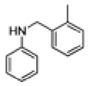
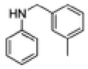
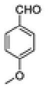
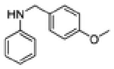
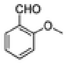
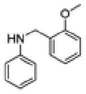
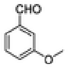
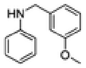
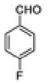
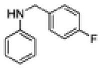
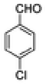
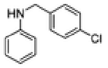
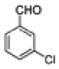
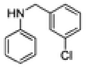
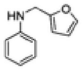
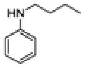
Entry	R^1-NH_2	R^1-NH_2	Yield/%[b]
1			88[c]
2			84
3			97
4			92
5			90
6			84
7			92
8			98
9			98[c]
10			98
11			96
12			98
13			98

[a] Reaction conditions: benzaldehyde (1.0 mmol), amine (1.0 mmol), Pd/NiO (20 mg), under hydrogen atmosphere, EtOH (2 mL), 25 °C, 12 h.

[b] Isolated yield.

Table 3. Reductive amination of aniline with various aldehydes[a].



Entry	R^2-CHO	R^2-CHO	Yield/%[b]
1			96
2			98
3			96
4			93
5			97
6			93
7			97
8			87
9			94
10			95
11			98

---

[a] Reaction conditions: benzaldehyde (1 mmol), amine (1 mmol), Pd/NiO (20 mg), under

hydrogen atmosphere, EtOH (2 mL) at 25 °C for 12 h..

[b] Isolated yield.

Table 4. Recycling exploration of Pd/NiO[a].

$$\mathrm{PhCHO + PhNH_2 \xrightarrow[\text{1atm H2, r.t, 2mlEtOH}]{\text{0.2mol\%Pd/NiO-M}} PhCH_2NHPh}$$

Run	1st	2nd	3rd	4th	5th
Yield[%][b]	88	90	89	87	91

[a] Reaction conditions: benzaldehyde(1.0 mmol), aniline(1.0 mmol),

Pd/NiO (20 mg) and solvent (2 mL), under hydrogen atmosphere, 12 h, 25 °C.

[b] GC yield.

Figure 1. TEM and HR-TEM pictures of Pd/NiO (scale bar: a. 20 nm; b. 5 nm).