

Article ID: 1001-3555(2013)05-0393-07

Direct Hydrogenation of Nitroarenes and One-Pot Amidation using Formic Acid Over Heterogeneous Palladium Catalysts

LI Ze-long^{1,2}, LIU Jian-hua¹, LI Jin-lei^{1,2}, XIA Chun-gu^{1*}, LI Fu-wei^{1*}

(1. State Key Laboratory for Oxo Synthesis and Selective Oxidation, Lanzhou Institute of Chemical Physics, Chinese Academy of Sciences, Lanzhou 730000, China;

2. University of the Chinese Academy of Sciences, Beijing 100049, China)

Abstract: A highly chemoselective reduction of a wide diversity of aromatic nitro compounds to the corresponding amines have been achieved by a combination of Pd catalysts and HCOOH in ethanol under mild conditions. Moreover, a direct route to formanilides and benzimidazole derivatives from aromatic nitro compound bearing different functional groups has been established by using Pd/C catalyst and HCOOH.

Key words: Pd/C; hydrogenation; formic acid; heterogeneous catalysis; amidation

CLC number: O643.32 **Document code:** A

The reduction of nitro compounds is a key step in the preparation of many pharmaceutical agents and fine chemicals^[1-3]. Aromatic amines as important products can be prepared from the reduction of nitrobenzene and its derivatives. However, traditional synthetic methods for the reduction of aromatic nitro compounds involve hazardous systems^[4-7]. Recently, the catalytic transfer hydrogenation (CTH) using cheap and easily accessible hydrogen donor is simpler, safer, highly selective, and eco-friendly^[5,8]. HCOOH, which is one of the major products formed in biomass processing, can be as good hydrogen source, simultaneously, the using of formic acid as hydrogen source can meet the requirement of a sustainable chemistry^[9]. Amide and benzimidazole derivatives are also used widely as functional groups in both small and complex synthetic and naturally occurring molecules by medicinal chemists^[4-5, 10-11]. The commonly used synthetic procedures of amide often involve the reaction of amines with pre-activated carboxylic acid derivatives. The synthesis of benzimidazole and their derivatives were realized using 1, 2-diaminoarenes as starting materials by coupling of

carboxylic acids or condensation of aldehydes, however, both syntheses result in side products.

The direct reductive synthesis of amide and benzimidazole derivatives from nitroaromatics is also one of the most powerful transformations using HCOOH as hydrogen and carboxylic acid sources. Such one-pot reactions have been developed as economical, environmentally friendly, and efficient synthetic processes in organic chemistry. In 2011, Gu groups reported the synthesis of amidation with carboxylic acids over Pt nanowires, however, H₂ was used as hydrogen donor for the reduction of nitroaromatics and then to couple with the carboxylic acids in this system, and benzamide was not reported^[4]. Cao and co-workers accomplished the direct conversion of aromatic nitro compounds to the corresponding N-formanilides by using the HCOONH₄ and Au/TiO₂ system, the HCOONH₄^[4] serves as hydrogen source for nitro reduction and as a formylating agent, however, HCOOH as renewable reactants was not active^[5].

Herein, we develop a highly effective system for the hydrogenation of nitro compounds to corresponding

Received date: 2013-09-25; **Revised date:** 2013-10-13.

Foundation: This work was supported by the Chinese Academy of Sciences and the National Natural Science Foundation of China (21002106, 21133011 and 21373246).

First author: LI Ze-long (1984-), male, PhD. E-mail: lzl_0918@126.com.

* **Corresponding author:** Tel: +86-931-4968129; Fax: +86-931-4968129; E-mail: fuweili@licp.cas.cn, cgxia@licp.cas.cn

anilines using HCOOH as hydrogen source, and report a one-pot amidation of nitroaromatics with HCOOH under mild reaction condition, simultaneously, benzimidazole derivatives also can be synthesized through this method. This system shows the high catalytic performance for both hydrogenation of nitroaromatics and one-pot amidation reactions under mild conditions.

1 Experimental

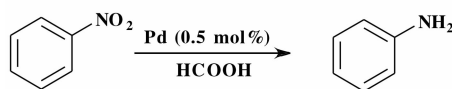
5% Pd/C was purchased from Alfa-Aesar. Catalytic tests were conducted in a 50 mL Schlenk glass tube with a magnetic bar; heterogeneous Pd catalyst, substrate, formic acid and solvent were introduced into the glass tube, and then it was vacuumed and purged with Ar three times before it was finally pressurized with 0.1 MPa of Ar gas. Subsequently, the reaction mixture was stirred at targeted temperature. After the reaction, excess Ar was carefully released, and the internal standard (toluene) was added. The resultant product mixtures were analyzed by an Agilent gas chromatograph.

2 Results and discussion

In the course of our recent findings on the suppor-

ted palladium nanoparticles catalysts^[12-13], we have discovered that Pd@C acted as an effective and recyclable heterogeneous catalyst for the title reaction. Initially, nitrobenzene was chosen as a model substrate for optimization of the reaction conditions. Table 1 shows the hydrogenation of nitrobenzene in different solvents. In heterogeneous catalytic system, the solvation of reacting species and its impact on the overall reaction mechanism are not clearly understood^[14]. However, it has been stated that hydrogenation of less polar substrate in more polar solvents is preferred^[15-16]. In our reaction systems, the solvent have a strong influence on the catalytic efficiency. Table 1 shows the conversion of the nitrobenzene in different solvents. Pd/C catalyst is highly active for the hydrogenation of nitrobenzene to aniline at room temperature in ethanol, and the full conversion with 97% yield is obtained within 1 hour (Table 1, entry 1). Other solvents, such as methanol, tetrahydrofuran, n-hexane, water and CH₂Cl₂ are less effective solvents, the xylene and acetonitrile as solvent are almost not active for the transformation (Table 1, entries 2-8). Moreover, H₂ as hydrogen source is tested for comparison, only 32% yield was obtained (Table 1, entry 9). The hydrogenation of nitrobenzene

Table 1 Evaluation of different solvents for the reduction of nitrobenzene^a



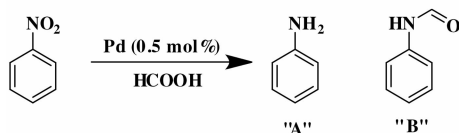
Entry	Catalyst ^c	Solvent	Conv./Selec/%	Yield ^b /%
1	Pd/C	Ethanol	>99/97	97
2	Pd/C	Methanol	74/95	70
3	Pd/C	n-hexane	>99/57	57
4	Pd/C	Tetrahydrofuran	12/82	10
5	Pd/C	Water	20/96	19
6	Pd/C	Xylene	trace	trace
7	Pd/C	Acetonitrile	trace	trace
8	Pd/C	CH ₂ Cl ₂	19/73	14
9 ^d	Pd/C	Ethanol	32/99	32
10 ^e	Pd/C	Ethanol	trace	trace

a. Reaction conditions; All reaction were carried out using nitrobenzene (1 mmol), Pd (0.5 mol%, based on nitrobenzene), solvent (2 mL), HCOOH (5 mmol), Ar protection at room temperature for 1 hour unless otherwise indicated; b. yields based on nitrobenzene, determined by GC and GC-MS analysis using toluene as internal standard; c. 5% Pd/C purchased from Alfa-Aesar was used in all reactions; d. 0.1 MPa H₂ as hydrogen source; e. this reaction was performed without the protection of Ar.

was also performed without Ar protection, only trace yield was obtained (Table 1, entry 10). Therefore, formic acid as hydrogen source showed high active for the hydrogenation of nitrobenzene to the aniline. Based on above experiments, ethanol was selected as the solvent. Table 2 shows the hydrogenation of nitrobenzene in different temperature. It is found that the reaction temperature is critical with higher temperature favoring

the one-pot amidation of nitrobenzene. A reaction temperature of 80 °C results in a yield of 88% formamidobenzene (Table 2, entry 4). Both at 0 and 30 °C, aniline is obtained as main product, with increasing temperature to 50 °C, the yield of formamidobenzene increases to 64% (Table 2, entries 1-3). Therefore, temperature thus mainly influences the later amidation step rather than the former hydrogenation step.

Table 2 Optimization of reaction temperature ^a



Entry	T / °C	Conv. / %	Selectivity / %	
			A	B
1	0	>99	>99	0
2	30	>99	94	6
3	50	>99	36	64
4	80	>99	12	88

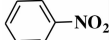
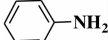
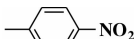
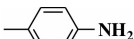
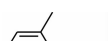
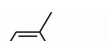
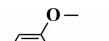
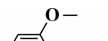
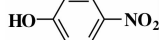
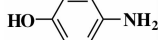
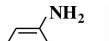
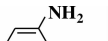
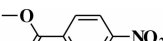
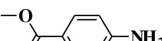
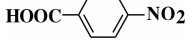
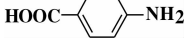




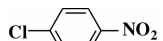
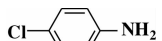


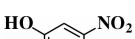
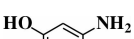
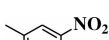
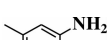
a. Reaction conditions: nitrobenzene (1 mmol), HCOOH (5.0 mmol), ethanol (2 mL), Pd (0.5 mol%, based on nitrobenzene), 1 h, Ar protection

On the basis of above experimental data, ethanol as solvent, and the temperature of 30 °C were selected as the reaction condition to investigate the effect of substrate type to establish the scope of the CTH reaction with the HCOOH-Pd/C system. Table 3 summarizes the main products and yields under these conditions. Various structurally diverse aryl nitro compounds, regardless of the presence of electron-withdrawing or electron-donating functions, can be selectively reduced to the corresponding amine compounds. High yields from *o*-, *p*-methyl nitrobenzene (Table 3, entries 2-3) show the good regioselectivity and the yields of the corresponding anilines are high to 92%. Good chemoselectivity is observed for substrates containing electron-donating or electron-withdrawing groups (Table 3, entries 4-9), the functional groups do not influence the reduction of the nitroaromatics significantly. In the case of 2-nitronaphthalene and 2,4-dinitro-toluene,

Pd/C showed the high catalytic performance, the hydrogenation yield of 2-nitronaphthalene is 85% and the hydrogenation yield of 2,4-dinitro-toluene is only 63% because the by-products (2-methyl-5-nitroaniline and 4-methyl-3-nitroaniline) are formed (Table 3, entries 9 and 10). In the transformation of chloronitroaromatics, it shows the lower yield of the products because the substrate is reduced to the corresponding anilines with hydrodechlorination over Pd/C (Table 3, entries 11 and 12). Hydrogenation of 2-Nitroaniline derivatives also give good yields and produce corresponding dianilines with yields of 88% and 86% (Table 3, entries 13 and 14).

It has been reported that HCOONH₄ could be as a formylating agent,^[5] we envisioned that HCOOH as a inexpensive and easily available agent could afford a green and efficient protocol for the direct synthesis of formanilides from nitro compounds. Using of the Pd/C

Table 3 Reduction of nitroarenes to anilines^a

Entry	Substrate	Product	t / h	Yield ^b /%
1			1	94
2			2	96
3			3	92
4			2	99
5			2	97
6			2	92
7			5	86
8			5	82
9			5	85
10			5	63
11			5	56 ^c
12			5	53 ^c
13			5	88
14			5	86

a. Reaction conditions: All reaction were carried out using substrate (1 mmol), Pd (0.5 mol%, based on nitroarenes), Ethanol (2 mL) at room temperature unless otherwise indicated; b. Determined by GC and GC-MS analysis, yields based on nitroarenes, determined by GC using toluene as internal standard; c. the aniline was produced as by-product.

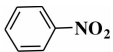
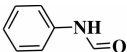
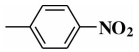
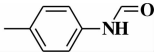
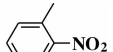
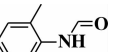
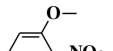
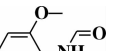
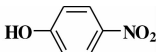
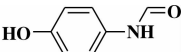
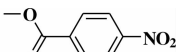
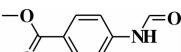
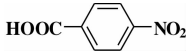
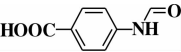
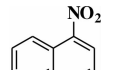
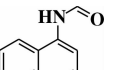
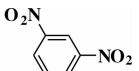
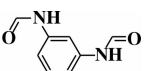
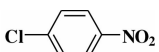
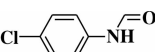
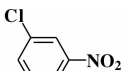
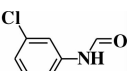
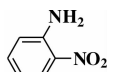
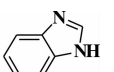
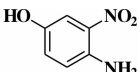
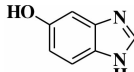
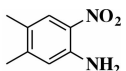
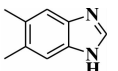
show good regioselectivity in the one-pot amidation, and the yield of the corresponding amide is high. Nitroaromatics containing both electron-donating (Table 4, entries 1-5) or electron-withdrawing (Table 4, entries 6 and 7) groups are efficient converted into corre-

sponding amides with high yields following the procedure as depicted in Table 4. In the case of 2-nitronaphthalene and 2,4-dinitro-toluene, the amidation yield of 2-nitronaphthalene is 89% and the 2,4-dinitro-toluene is only 66% because the by-products

(N-(5-amino-2-methylphenyl)formamide and N-(3-amino-4-methylphenyl)formamide) were formed (Table 4, entries 8 and 9). For chloronitroaromatics, the rel-

ative lower yields could be attributed to the hydrodechlorination in this system (Table 4, entries 10 and 11).

Table 4 One-pot amidation of nitroarenes^a

Entry	Substrate	Product	t / h	Yield ^b / %
1			5	99
2			5	99
3			5	92
4			5	89
5			8	92
6			16	88
7			24	88
8			16	89
9			24	66
10			24	69
11			24	62
12			16	85
13			16	78
14			16	86

a. Reaction conditions: nitro compounds (1 mmol), HCOOH (10 mmol), ethanol (2 mL), catalyst (Pd; 0.5 mol%, based on nitroarenes), 50 °C, Ar protection; b. Determined by GC and GC-MS analysis using toluene as internal standard. Yields based on nitroarenes, determined by GC using toluene as internal standard.

The benzimidazole scaffold is a useful structural motif for displaying chemical functionality in biologically active molecules, and the synthesis of benzimidazole and their derivatives are realized using 1,2-diaminoarenes as starting materials by coupling of carboxylic acids. On the basis of the above experimental results, we conceived that the HCOOH could be as both the hydrogen and carboxylic acid source to realize the one-pot synthesis of benzimidazole and their derivatives. In our HCOOH-Pd system, 2-nitroaniline, 4-amino-3-nitrophenol, 4,5-dimethyl-2-nitroaniline substrates can efficiently convert to the corresponding benzimidazole and their derivatives with high yields (Table 4, entries 12-14). Recently, it reported that the synthesis of benzimidazole and their derivatives with the carbon dioxide, however, the toxic silane as hydrogen source limited the scope of the method.¹⁷In contrast, the present HCOOH-Pd system has the following significant advantages: 1) the reaction is much more efficient even at lower temperature; 2) the HCOOH is a major products formed in biomass processing and the only 10 equivalents is employed.

3 Conclusions

We have developed an efficient and highly chemo- and regioselective Pd-catalyzed, HCOOH-mediated CTH method for the hydrogenation of nitroaromatics and direct amide, benzimidazole and their derivatives synthesis from nitroaromatics in a one-pot reaction. Most of reported synthesis of amide, benzimidazole and their derivatives require harsh conditions, such as high temperature. It is worth noting that these products can be efficiently synthesized using this new approach under very mild conditions. In this process, HCOOH serve as two distinct functions: as hydrogen source and as reagent. The mild reaction conditions and the using of HCOOH, which major produce in biomass processing, can greatly facilitate the synthesis of anilines, amide, and benzimidazole and their derivatives in both laboratory and industrial production.

Acknowledgements

This work was supported by the Chinese Academy

of Sciences and the National Natural Science Foundation of China (21002106, 21133011 and 21373246).

References:

- [1] Gunanathan C, Milstein D. Selective synthesis of primary amines directly from alcohols and ammonia[J]. *Angew Chem Int Ed*, 2008, **47**: 8661-8664.
- [2] Wienhöfer G, Sorribes I, Boddien A, et al. General and selective iron-catalyzed transfer hydrogenation of nitroarenes without base [J]. *J Am Chem Soc*, 2011, **133**: 12875-12879.
- [3] Wu W M, Lin R, Shen L J, et al. Highly efficient visible-light-induced photocatalytic hydrogenation of nitrobenzene to aniline in water[J]. *Rsc Adv*, 2013, **3**: 10894-10899.
- [4] Li M, Hu L, Cao X, et al. Direct hydrogenation of nitroaromatics and one-pot amidation with carboxylic acids over platinum nanowires [J]. *Chem Eur J*, 2011, **17**: 2763-2768.
- [5] Lou X B, He L, Qian Y, et al. Highly chemo- and regioselective transfer reduction of aromatic nitro compounds using ammonium formate catalyzed by supported gold nanoparticles[J]. *Adv Synth Catal*, 2011, **353**: 281-286.
- [6] Bae J W, Cho Y J, Lee S H, et al. A one-pot synthesis of -alkylaminobenzenes from nitroaromatics; reduction followed by reductive amination using BH[J]. *Chem Commun*, 2000, 1857-1858.
- [7] Junge K, Wendt B, Shaikh N, et al. Iron-catalyzed selective reduction of nitroarenes to anilines using organosilanes[J]. *Chem Commun*, 2010, **46**: 1769-1771.
- [8] Ikariya T, Blacker A J. Asymmetric transfer hydrogenation of ketones with bifunctional transition metal-based molecular catalysts[J]. *Acc Chem Res*, 2007, **40**: 1300-1308.
- [9] Boddien A, Loges B, Gärtner F, et al. Iron-catalyzed hydrogen production from formic acid [J]. *J American Chem Soc*, 2010, **132**: 8924-8934.
- [10] Yu B, Zhang H Y, Zhao Y F, et al. Cyclization of o-phenylenediamines by CO₂ in the presence of H-2 for the synthesis of benzimidazoles[J]. *Green Chem*, 2013, **15**: 95-99.
- [11] Climent M J, Corma A, Hernández J C, et al. Biomass into chemicals: One-pot two- and three-step synthesis of quinoxalines from biomass-derived glycols and 1,2-dinitrobenzene derivatives using supported gold nanoparticles as catalysts[J]. *J Catal*, 2012, **292**: 118-129.
- [12] Li Z, Liu J, Huang Z, et al. One-pot synthesis of pd

- nanoparticle catalysts supported on N-doped carbon and application in the domino carbonylation[J]. *ACS Catal*, 2013, 839–845.
- [13] Li Z, Liu J, Xia C, *et al.* Nitrogen-functionalized ordered mesoporous carbons as multifunctional supports of ultrasmall Pd nanoparticles for hydrogenation of phenol [J]. *ACS Catal*, 2013, 2440–2448.
- [14] Akpa B S, Agostino C D, Gladden L F, *et al.* Solvent effects in the hydrogenation of 2-butanone[J]. *J Catal*, 2012, **289**: 30–41.
- [15] Mukherjee S, Vannice M A. Solvent effects in liquid-phase reactions; I. Activity and selectivity during citral hydrogenation on Pt/SiO₂ and evaluation of mass transfer effects[J]. *J Catal*, 2006, **243**: 108–130.
- [16] Rajadhyaksha R A, Karwa S L. Solvent effects in catalytic hydrogenation[J]. *Chem Eng Sci*, 1986, **41**: 1765–1770.
- [17] Jacquet O, Das Neves Gomes C, Ephritikhine M, *et al.* Complete catalytic deoxygenation of CO₂ into formamide derivatives[J]. *Chem Cat Chem*, 2013, **5**: 117–120.

钯催化甲酸为氢源的芳硝基化合物直接加氢和一锅法酰胺化

李泽龙^{1,2}, 刘建华¹, 李金磊^{1,2}, 夏春谷^{1*}, 李福伟^{1*}

(1. 中国科学院兰州化学物理研究所 羰基合成与选择氧化国家重点实验室, 甘肃 兰州 730000;

2. 中国科学院大学, 北京 100049)

摘要: Pd/C 催化剂实现了甲酸为氢源的芳硝基化合物的直接加氢及甲酸为氢源和羰基源的一锅法芳硝基化合物的酰胺化. 在芳硝基化合物的直接加氢过程中, 该体系体现了很好的催化活性, 实现了对同时带有其它可还原官能团的芳硝基化合物的选择性加氢, 得到较高收率的胺类化合物. 同时, 通过提高反应温度和增加甲酸的量, 实现了芳硝基化合物的加氢和甲酰化的串联反应, 该体系体现了较高的催化活性.

关键词: Pd/C; 加氢; 甲酸; 多相催化; 酰胺化