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## Short Communication

# A practical and benign synthesis of amines through $Pd@mpg-C_3N_4$ catalyzed reduction of nitriles

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## ABSTRACT

Liquid phase hydrogenation of nitriles is an important method for the production of amines, which find a variety of applications as intermediates in chemical and pharmaceutical industry. In the present work, a highly efficient Pd@mpg-C<sub>3</sub>N<sub>4</sub> catalytic system has been developed for chemoselective reduction of nitriles providing good to excellent conversion with remarkable chemoselectivity (up to 99%) without additives. Compared with homogeneous catalyst systems, the developed protocol is more advantageous due to the use of ambient hydrogen, solvent free and effective catalyst recyclability.

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#### 1. Introduction

Amines are very important industrial organic compounds in a widespread range of applications, including intermediates for pharmaceuticals, raw materials for resins and plastics, reagents for organic synthesis, and textile additives [1,2]. During the recent decades, several novel catalytic methods have been established for the synthesis of amines, such as the reductive amination of carbonyl compounds [3–5], hydroaminomethylation or hydroamination of olefins and alkynes [6,7], and palladium catalyzed amination of aryl halides [8,9]. Among the different methods used, hydrogenation of nitriles is one of the most common methods to prepare amines due to the high atom efficiency [2,10–14].

In organic synthesis, nitriles are commonly reduced with stoichiometric amounts of metal hydrides, which is expensive and not environmentally benign [15]. Raney Ni, Raney Co, Pd@C, Pt@C, Ru@C, and Rh@C are suitable catalysts and rank among the most commonly used for this process [16–19]. The same metals but supported on SiO<sub>2</sub> or Al<sub>2</sub>O<sub>3</sub> are often employed as well [20,21]. Notably, all these catalysts reveal the formation of side products, which lower the selectivity. In additon, excess of base is usually needed for high chemoselectivity [22]. Recently, homogeneous reduction of nitriles in the presence of ruthenium complexes has been reported [11–13,23]. Although these catalytic systems are effective, the critical process for the synthesis of the catalyst and the use of large amount of base such as *t*BuOK, NaOH and KOH strongly limit the usefulness of these catalysts. Separation of the products from solvents and the catalysts is usually diffcult, which is also a typical problem associated with homogeneous catalysts.

Due to the high reactivity of the reaction intermediates (generally imine), the liquid hydrogenation of nitriles occur as a set of consecutive and parallel reactions (Scheme 1), resulting in a mixture of primary, secondary and tertiary amines [10]. Separation of the reaction products is usually difficult, due to small differences in boiling point. For this reason, one of the most important issues in the hydrogenation of nitriles is the control of the selectivity.

Although there are many factors that affect the selectivity to some degree, the nature of the catalyst is the most important parameter to control the selectivity, therefore, developing of new catalyst for the efficient and selective hydrogenation of nitriles continues to be a challenging goal.

Our group and others have recently shown that an abundant and easily accessible polymeric semiconductor, polymeric mesoporous graphitic carbon nitride (mpg-C<sub>3</sub>N<sub>4</sub>), exhibits extreme chemical and thermal stability, can be chemically shaped to a variety of nanostructures, and can be directly used in heterogeneous catalysis or as catalyst support [24–33]. As part of our ongoing effort to develop new strategies for chemoselective hydrogenation, we report the results of our preliminary investigation of chemoselective hydrogenation of nitriles with  $H_2$  under mild reaction conditions.

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**Scheme 1.** Formation of primary, secondary, and tertiary amines in the catalytic hydrogenation of nitriles.

#### 2. Experimental

#### 2.1. Catalyst preparation

All reagents were obtained from Sigma-Aldrich, Acros, or Merck and were used as received. The catalyst Pd@mpg-C<sub>3</sub>N<sub>4</sub> was synthesized according to our previous published literature procedure [27]. Typically, to synthesize the catalyst, PdCl<sub>2</sub> and mpg-C<sub>3</sub>N<sub>4</sub> were dissolved in distilled water and the mixture was heated to 80 °C and stirred for 12 h. 1 M NaOH was added to adjust the pH of the solution to about 10. Then NaBH<sub>4</sub> solution was added to this suspension. Finally, Pd@mpg-C<sub>3</sub>N<sub>4</sub> was separated by filtration, washed with distilled water for five times and then dried at 80 °C overnight in a vacuum oven. Pd@C was obtained from ThalesNano. Pd@TiO<sub>2</sub>, Pd@CeO<sub>2</sub>, and Pd@ $\gamma$ -Al<sub>2</sub>O<sub>3</sub> were synthesized according to the literatures [34].

#### 2.2. Hydrogenation of nitriles

The reaction was conducted in a Schlenk flask (20 ml) with a graham condenser. A typical procedure was as follows: nitriles (10 mmol), catalyst Pd@mpg-C<sub>3</sub>N<sub>4</sub> (0.02 mmol of Pd, 0.2% mol relative to nitriles) were placed in a flask. The flask was purged with H<sub>2</sub> to remove the air for 3 times, the reaction was then stirred at 800 rpm under H<sub>2</sub> atmosphere (connected to a hydrogen balloon). For the reaction conducted in compressed hydrogen pressure, the hydrogenation was carried out in a Teflon-lined stainless stell batch reactor (50 ml total volume) with a magnetic stirrer. In a typical experiment, nitriles and catalyst were loaded into the reactor. The reactor was sealed and purged with H<sub>2</sub> to remove the air for 3 times, then increased to the desired hydrogen pressure. The stirring was started after the desired temperature was reached. After the reaction the reactor was placed in ice water to quench the reaction and the products were analyzed on GC-MS (Agilent Technologies, GC6890N, MS5970) using nitrobenzene as internal standard. The GC-MS conditions for the product analysis were: Injector Port Temperature: 250 °C; Column Temperature: Initial temperature: 50 °C (1 min); Gradient Rate: 20 °C/min (10 min); Final Temperature: 250 °C (3 min); Flow Rate: 80 ml/min.

The reusability of  $Pd@mpg-C_3N_4$  was tested for butyronitrile hydrogenation. The reaction was conducted at 100 °C for 10 h. After reaction, the reaction mixture was centrifuged and the liquid layer was siphoned out. The residual solid was washed with anhydrous ethanol and acetone and then centrifuged twice. The recycled catalyst

was finally dried in a vacuum oven at 80  $^\circ$ C for 6 h. The catalyst was then reused under the same reaction conditions.

#### 3. Results and discussion

In the present work, hydrogenation of butyronitrile (BTN) was choosed as a model reaction. Various reaction parameters such as effect of time, temperature, hydrogen pressure were studied in detail. In general, the hydrogenation of BTN yields primary amine, mono-nbutylamine (MBA), secondary amine, di-n-butylamine (DBA), and tertiary amine, tri-n-butylamine (TBA), respectively. According to von Braun's mechanism for the hydrogenation of nitriles, as shown in Scheme 1, primary amine (C) is formed via hydrogenation of BTN, passing through the intermediate butylidenimine. The formation of secondary amines (E) is caused by the reaction of the primary amine with the imine intermediate. Subsequent elimination of ammonia yields but-1-envl-dibutylamine as the condensation products to be finally hydrogenated to the tertiary amines (F). The conversion of BTN (at 100 °C, ambient hydrogen pressure) and selectivities toward TBA and MBA as a function of time is presented in Fig. 1. As shown in Fig. 1, the hydrogenation of BTN over the Pd@mpg-C<sub>3</sub>N<sub>4</sub> catalyst vielded TBA as the majority product, as well as minor amounts of MBA at the initial state. In solvent free conditionds, the reaction gave 100% conversion of BTN and 99% selectivity of TBA after 9 h. Nitriles must adsorb weakly on an electron-enriched carbon nitride surface, inhibiting the catalytic activity of the catalyst. Therefore the reaction can only be conducted well under solvent free conditions, if solvents such as water, ethanol or acetone were used, no products have been detected. Once the BTA was reduced to MBA or DBA, depending on the nature of the catalyst's active site, MBA or DBA must adsorb strongly on the carbon nitride surface via the formation of N-H...N strong hydrogen bonds, which favoring the catalytic activity of the Pd@mpg-C<sub>3</sub>N<sub>4</sub> catalyst, hence the as produced MBA and DBA were converted to TBA on the surface of the catalyst immediately, which leads to the high selectivity toward TBA.

In order to examine the effect of temperature on reaction outcome, reactions were carried out at different temperatures ranging from 25 to 120 °C (Fig. 2). With increasing temperature the conversion of BTN increased while the selectivity toward TBA kept at high level (up to 99%). It was observed that at 25 °C the conversion of BTN was 11% whereas with the increase in temperature up to 120 °C, 99% conversion of the desired product was obtained within 5 h (Fig. 2). In general, the hydrogenation of BTN does not occur significantly at normal temperature over the traditional catalyst [12]. However, the hydrogenation of BTN proceeded well using Pd@mpg-C<sub>3</sub>N<sub>4</sub> catalyst even at normal temperature and ambient hydrogen pressure (hydrogen balloon). As shown in Fig. 2, a conversion of 49% and selectivity above 99% was yielded in 5 h at a mild reaction temperature of 40 °C.

 $H_2$  pressure influenced BTN conversion as shown in Fig. 3. The conversion of BTN increased from 70 to 99% by increasing the pressure from 0.1 MPa to 3 MPa at 70 °C for 2 h. Notably, no side product was observed even under high temperature and high hydrogen pressure.

To test the reusability of the catalyst system, the used Pd@mpg-C<sub>3</sub>N<sub>4</sub> was washed with acetone and ethanol, dried at 80 °C, and then reemployed with a new reactant mixture. As shown in Fig. 4, the catalyst exhibited remarkable activity for the first two consecutive recycles while slight decrease in conversion was observed during third and fourth recycle. It is important to highlight that no changes regarding the selectivity to TBA were observed respect to the fresh catalyst. The decrease in yield for third and forth cycle may be caused by the minor leaching of the Pd nano-particles as revealed in our previous work [27].

Furthermore, the applicability of  $Pd@mpg-C_3N_4$  catalyst on different nitriles was also investigated. The acetonitrile furnished 99% conversion with 99% selectivity toward triethylamine (Table 1, entry 1) at 70 °C in 6 h, whereas aromatic benzontrile provided 89% conversion with 99% selectivity (Table 1, entry 3). The hydroxyl-



Fig. 1. Effect of reaction time on the reduction of butyronitrile. Reactions were carried out at 100 °C with 10 mmol butyronitrile and Pd@mpg-C<sub>3</sub>N<sub>4</sub> (0.2% mol Pd relative to butyonitrile) under hydrogen (hydrogen balloon).

substituted 3-hydroxypropionitrile gave a moderate conversion (40%) and selectivity (73%). However, no product was detected in the case of the chloro-substituted 4-chlorobutyronitrile. Moreover, the catalyt Pd@mpg-C<sub>3</sub>N<sub>4</sub> was compared with the commercially available Pd@C, and the home made Pd@TiO<sub>2</sub>, Pd@CeO<sub>2</sub>, and Pd@ $\gamma$ -Al<sub>2</sub>O<sub>3</sub>, for the hydrogenation of benzontrile at 0.1 MPa of hydrogen and 80 °C for 12 h, and the results obtained are shown in Table 1. Results from Table 1 clearly show that the Pd@mpg-C<sub>3</sub>N<sub>4</sub> catalyst synthesized here gives better activity and selectivity than the commercially prepared Pd on carbon and other Pd@ support catalysts.

#### 4. Conclusions

In conclusion, the present study reports a development of highly efficient protocol for chemoselective reduction of nitriles in mild reaction conditions using Pd@mpg-C<sub>3</sub>N<sub>4</sub> as a heterogeneous recyclable catalyst. The catalyst system was optimized with respect to various parameters and affording good to excellent conversion with appreciable selectivity (up to 99%) of the desired products. The catalyst can be easily recycled by simple filtration process up to four consecutive recycles. The developed protocol with solvent free reaction condition, ambient hydrogen pressure and recyclable catalytic system introduces a success towards green approach in organic synthesis. However, it



**Fig. 3.** Effect of pressure on the reduction of butyronitrile. Reactions were carried out at 70 °C for 2 h with 10 mmol butyronitrile and Pd@mpg-C<sub>3</sub>N<sub>4</sub> (0.2% mol Pd relative to butyonitrile) under specified hydrogen pressure.

should be noted that the solvent free method may only be suitable for the substrates with a low melt point and in most cases the reduction of nitriles to primary amines is preferred. Work to improve the selectivity toward primary amines is still ongoing, and we believe that adding



**Fig. 2.** Effect of temperature on the reduction of butyronitrile. Reactions were carried out at the specified temperature for 5 h with 10 mmol butyronitrile and Pd@mpg-C<sub>3</sub>N<sub>4</sub> (0.2% mol Pd relative to butyonitrile) under hydrogen (hydrogen balloon).



**Fig. 4.** Reusing of the Pd@mpg-C<sub>3</sub>N<sub>4</sub> in hydrogenation of butyronitrile. Reactions were carried out at 100 °C for 9 h with 10 mmol butyronitrile and Pd@mpg-C<sub>3</sub>N<sub>4</sub> (0.2% mol Pd relative to butyonitrile) under ambient hydrogen pressure.

#### Table 1

Scope and limitations of Pd@mpg-C<sub>3</sub>N<sub>4</sub> and comparative catalytic performance of different palladium catalysts.<sup>a</sup>

Entry	Substrate	T (°C)	Conv. (%)	Product	Sel. (%)
1	CN	70	99	$\rightarrow$	>99
2	✓ <sup>CN</sup>	70	99		>99
3		100	70		>99
4 <sup>b</sup>	HOCN	80	40	Ностори	73
5 <sup>c</sup>	CICN	80	-	о́н —	_
6		80	89		>99
7 <sup>d</sup>		80	35	0^^0	>99
8 <sup>e</sup>		80	25	0000	85
9 <sup>f</sup>		80	32	000	94
10 <sup>g</sup>		80	16	000	88
11 <sup>h</sup>		80	15		93

<sup>a</sup> 10 mmol substrate, Pd@mpg-C3N4 (0.2% mol Pd relative to substrate), 1.0 MPa H<sub>2</sub>, reaction time 6 h.

<sup>b</sup> 10 mmol 3-hydroxypropionitrile, Pd@mpg-C3N4 (0.2% mol Pd relative to substrate), 0.1 MPa H<sub>2</sub>, reaction time 12 h.

<sup>c</sup> 10 mmol 4-chlorobutyronitrile, other reaction conditions as in entry 4.

- <sup>d</sup> 10 mmol benzonitrile, other reaction conditions as in entry 4.
- <sup>e</sup> commercial Pd/C as catalyt, other reaction conditions as in entry 4.
- <sup>f</sup> Pd/TiO<sub>2</sub> as catalyt, other reaction conditions as in entry 4.

<sup>g</sup> Pd/CeO<sub>2</sub> as catalyt, other reaction conditions as in entry 4.

 $^{\rm h}~Pd/\gamma\text{-Al}_2O_3$  as catalyt, other reaction conditions as in entry 4.

bases or modification of the catalyst support [24,25] (mpg-C<sub>3</sub>N<sub>4</sub>) might offer further potentialities.

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#### Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.catcom.2012.08.005.

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