

# Catalytic transfer hydrogenation of imines to secondary amines using inexpensive commercial zinc dust and ammonium formate

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A simple protocol for the chemo-selective reduction of imines to the corresponding secondary amines in good yield using inexpensive commercial zinc dust and ammonium formate in methanol at ambient temperature and pressure is described.

**Keywords:** imines, secondary amines, ammonium formate, zinc dust

The conversion of carbonyl derivatives to secondary amines *via* imines is a useful synthetic transformation. Although addition to the C=N bonds of imines, hydrazones and oximes is well known,<sup>1</sup> exploitation of these reactions is often limited by the poor electrophilicity of the C=N carbon. Numerous reagents have been developed for the reduction of imines to amines such as NaBH<sub>4</sub>,<sup>2,3</sup> LiAlH<sub>4</sub>,<sup>4,5</sup> NH<sub>3</sub>/Ra-Ni,<sup>6</sup> NH<sub>4</sub>Cl/PtO<sub>2</sub>,<sup>7</sup> isopropyl alcohol/aluminum isopropoxide/Ra-Ni,<sup>8</sup> CH<sub>3</sub>COONH<sub>4</sub>/Ra-Ni.<sup>9</sup> Although some of these systems are widely used, they have limitations based on chemo-selectivity, low yield and economic considerations. Catalytic hydrogenation is also commonly used,<sup>10,11</sup> but, the success of reaction depends on the catalyst, solvent and substrate. Catalytic hydrogenation employs highly diffusible, low molecular weight and flammable hydrogen gas and may require pressure equipment. Electrolytic reduction of imines to amines, in acid solution has also been reported,<sup>12</sup> but this system proceeds in very low yield.

Catalytic transfer hydrogenation (CTH) using a stable hydrogen donor in conjunction with a metal catalyst is emerging as a viable tool for the reductive functional group transformation in organic synthesis.<sup>13–16</sup> Several CTH systems have been reported for the reduction of imines.<sup>17–20</sup> However, these systems requires long reaction time at reflux and expensive pyrophoric catalysts such as Pd/C, Ra-Ni and Pd(OAc)<sub>2</sub>. Recently, zinc has been successfully utilised as safe and low cost alternative to Pd/C and/or Ra-Ni for the reduction of nitro compounds, azo compounds, azides and also for the synthesis of biaryls.<sup>21–24</sup> In this communication, we report the zinc catalysed rapid and selective transfer hydrogenation of imines to corresponding secondary amines using ammonium formate at room temperature in methanol (Scheme 1).

The results given in Table 1 reveal the viability of using Zn and ammonium formate system for the reduction of imines. The course of reaction was monitored by TLC and IR spectra. The work-up and isolation of the products were easy. Thus, the imines reduced by this system were obtained in good yields and most of the reactions were completed within 30 minutes. The products were characterised by comparison of their boiling points or melting points, TLC, IR and <sup>1</sup>H NMR spectra with authentic samples. The disappearance of strong absorption bands between 1690 and 1640 cm<sup>-1</sup> due to C=N stretching and

the appearance of a strong absorption bands between 3500 and 3200 cm<sup>-1</sup> for the -NH group clearly shows that the imines were reduced to corresponding secondary amines. In the case of nitro imines, the aryl nitro group and the imine group both undergo reduction to yield primary and secondary amines respectively at room temperature. A controlled experiment carried out using imines with ammonium formate without zinc powder did not yield the desired product.

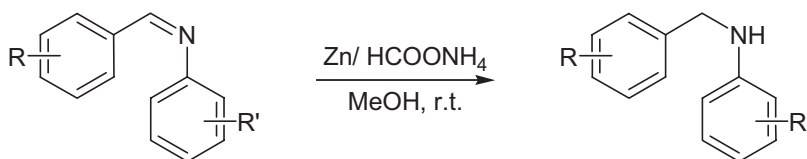
In conclusion, we have developed a facile system for the reduction of imines to corresponding secondary amines. The use of zinc dust instead of Pd/C or Raney Ni not only reduces the cost and risk containments but also enhances the chemo-selectivity particularly with halogens which are not compatible under Pd/C or Raney Ni catalysed transfer hydrogenation conditions.<sup>25,26</sup> The yields are virtually quantitative and the compounds obtained were analytically pure. In addition, the easy availability of the reagents, operational simplicity, mild reaction condition and rapid reduction make this procedure extremely attractive.

## Experimental

To a solution of the substrate (1 mmole) in methanol or in any other suitable solvent (10 ml) was added ammonium formate (2 mmole) and zinc dust powder (1 mmole; Loba Chemie Pvt. Ltd. Mumbai, India). The mixture was stirred under nitrogen atmosphere at room temperature. The reaction was exothermic and effervescent. After the completion of reaction (monitored by TLC), the reaction mixture was filtered through Celite. The organic layer was evaporated, the residue was dissolved in chloroform, dichloromethane or ether and washed with saturated sodium chloride solution to remove excess of ammonium formate. The organic layer was dried over anhydrous sodium sulfate and the solvent was evaporated under vacuum. The products were purified either by preparative TLC or by column chromatography. Column chromatography was performed by using 60–120 mesh silica gel and a suitable eluting system (90:10 chloroform: hexane, 80:20 chloroform: methanol, 85:15 chloroform: methanol, 90:10 chloroform: methanol, 95:5 chloroform: methanol).

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Scheme 1

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**Table 1** Zinc-catalysed reduction of imines to secondary amines using ammonium formate.

Entry	Substrate		Product <sup>a,b,c</sup>		Time/min	Yield/%	M.p./°C (lit.)	
	R	R'	R	R'			Found	Literature
1	-H	-H	-H	-H	25	85	36–37	37–38 <sup>27</sup>
2	-H	4'-Cl	-H	4'-Cl	28	80	45–46	46–48 <sup>27</sup>
3	-H	4'-Me	-H	4'-Me	30	80	Liquid	19–20 <sup>28</sup>
4	3-NO <sub>2</sub>	-H	3-NH <sub>2</sub>	-H	25	75	83–84	84–85 <sup>29</sup>
5	-H	4'-OMe	-H	4'-OMe	25	78	48–50 <sup>d</sup>	–
6	4-Cl	4'-OMe	4-Cl	4'-OMe	30	80	68–69	69–70 <sup>29</sup>
7	4-Cl	4'-Cl	4-Cl	4'-Cl	20	84	68–70	70–71 <sup>27</sup>
8	4-Me	4'-Me	4-Me	4'-Me	30	76	55–56	60–61 <sup>28</sup>
9	-H	2'-Cl	-H	2'-Cl	25	78	35–37 <sup>e</sup>	36–38 <sup>30</sup>
10	-H	2'-OMe	-H	2'-OMe	25	75	Oily <sup>f</sup>	–
11	4-Cl	3'-Me	4-Cl	3'-Me	30	80	34–36 <sup>g</sup>	–

<sup>a</sup><sup>1</sup>H NMR spectra were obtained on an AMX-400 MHz spectrometer in CDCl<sub>3</sub> as the solvent and TMS as internal standard.

<sup>b</sup>Isolated products gave IR spectra in agreement with their structures.

<sup>c</sup>Isolated yields are based on single experiment and the yields were not optimised.

<sup>d</sup>Benzyl-(4-methoxyphenyl)-amine: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz, SiMe<sub>4</sub>) δ 7.18 (m, 2H, CH), 7.10 (m, 3H, CH), 6.55 (m, 2H, CH), 6.30 (m, 2H, CH), 4.32 (s, 2H, CH<sub>2</sub>), 3.92 (s, 1H, NH), 3.70 (s, 3H, OCH<sub>3</sub>); Anal. Calcd for C<sub>14</sub>H<sub>15</sub>NO: C, 78.84; H, 7.09; N, 6.57; Found: C, 77.96; H, 6.88; N, 6.62.

<sup>e</sup>Benzyl-(2-chlorophenyl)-amine: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz, SiMe<sub>4</sub>) δ 7.14 (m, 2H, CH), 7.06 (m, 4H, CH), 6.92 (m, 1H, CH), 6.52 (m, 1H, CH), 6.37 (m, 1H, CH), 4.32 (s, 2H, CH<sub>2</sub>), 3.80 (s, 1H, NH); Anal. Calcd for C<sub>13</sub>H<sub>12</sub>ClN: C, 71.72; H, 5.56; N, 6.43; Found: C, 71.55; H, 5.66; N, 6.40.

<sup>f</sup>Benzyl-(2-methoxyphenyl)-amine: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz, SiMe<sub>4</sub>) δ 7.14 (m, 2H, CH), 7.06 (m, 3H, CH), 6.60 (m, 1H, CH), 6.55 (m, 1H, CH), 6.47 (m, 1H, CH), 6.32 (m, 1H, CH), 4.12 (s, 2H, CH<sub>2</sub>), 3.85 (s, 1H, NH), 3.75 (s, 3H, OCH<sub>3</sub>); Anal. Calcd for C<sub>14</sub>H<sub>15</sub>NO: C, 78.84; H, 7.09; N, 6.57; Found: C, 77.86; H, 6.93; N, 6.49.

<sup>g</sup>4-chlorobenzyl-(3-methylphenyl)-amine: <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz, SiMe<sub>4</sub>) δ 7.35 (m, 2H, CH), 7.18 (m, 2H, CH), 6.90–7.12 (m, 4H, CH), 4.21 (s, 2H, CH<sub>2</sub>), 3.78 (s, 1H, NH), 2.42 (s, 3H, CH<sub>3</sub>); Anal. Calcd for C<sub>14</sub>H<sub>14</sub>ClN: C, 72.57; H, 6.09; N, 6.04; Found: C, 72.25; H, 6.13; N, 5.98.

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