

## Efficient and Selective Reduction of Aromatic Nitro Compounds to Aromatic Amines by NbCl<sub>5</sub>/Indium System

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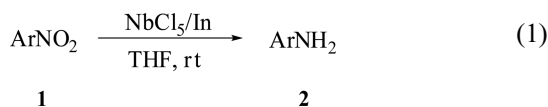
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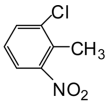
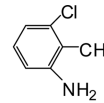
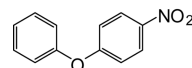
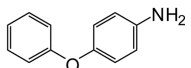
Aromatic amines find applicability in diverse fields including dyes, pharmaceuticals, agrochemicals, and photographic materials.<sup>1</sup> To date, there are a variety of methods, which can be used to convert aromatic nitro compounds to their corresponding amines. Some of them include Cp<sub>2</sub>TiCl<sub>2</sub>/In,<sup>2</sup> Al/NH<sub>4</sub>Cl,<sup>3</sup> (NH<sub>4</sub>)<sub>2</sub>SO<sub>4</sub>/NaBH<sub>4</sub>,<sup>4</sup> NiCl<sub>2</sub>·6H<sub>2</sub>O/In,<sup>5</sup> HI,<sup>6</sup> Sm/I<sub>2</sub>,<sup>7</sup> In/NH<sub>4</sub>Cl,<sup>8</sup> B<sub>4</sub>H<sub>10</sub>/Pd/C,<sup>9</sup> Co<sub>2</sub>(CO)<sub>8</sub>/H<sub>2</sub>O<sup>10</sup> and In/HCl.<sup>11</sup> However, most methods still lack the desired chemoselectivity when other reducible functional groups are present in the nitroarene and often require long reaction times, or harsh reaction conditions. Consequently, efficient and selective methods for the reduction of aromatic nitro compounds continue to be developed. It has been reported that NbCl<sub>5</sub>/Zn system is used as a reagent for reducing sulfoxides, epoxides, and amine *N*-oxides.<sup>12</sup> Because of the close resemblance of indium to zinc in several respects, including first ionization potential, we considered that NbCl<sub>5</sub>/In system can be an efficient reducing agent for the conversion of aromatic nitro compounds to the corresponding amines. Recently, indium metal has attracted much attention for its unique properties such as low toxicity and high stability in water and air compared with other metals.<sup>13</sup> In continuation of our interest in exploring the utility of metal-metal salt system in organic synthesis,<sup>14</sup> we would like to report an efficient and chemoselective method for the reduction of various aromatic nitro compounds to the corresponding amines by treatment with NbCl<sub>5</sub>/In system (eq. 1). The new reduction system was generated by the addition of indium powder to a stirred



solution of niobium(V) chloride in THF under sonication.<sup>15</sup> The generation of low-valent niobium species was examined at room temperature with an excess of indium metal. The appearance of a black color was judged as the formation of low-valent niobium complexes. Encouraged by the convenient generation of low-valent niobium complexes from reduction of NbCl<sub>5</sub> with indium metal, we have investigated the reactions of NbCl<sub>5</sub>/In system with various aromatic nitro compounds and found that the reductions generally proceeded with high yields and showed selectivity

over other labile substituents. The high yields of the reduction products and selectivity over other labile substituents demonstrate the efficiency of this new method. Some control experiments confirmed that the reaction was not initiated at all using niobium(V) chloride in the absence of indium metal and was also not very effective with indium metal without niobium(V) chloride. Thus, a combination of indium and niobium(V) chloride is essential to carry out the reduction. The scope of the reaction was examined using various substituted aromatic nitro compounds and the results were summarized in Table 1. In the course of this process, several sensitive functional groups such as -OH, -Br, -Cl, -COOCH<sub>3</sub>, -COCH<sub>3</sub>, -COOH, -OCH<sub>3</sub>, and -NH<sub>2</sub> groups remained unaffected. In the case of carbonyl substituted aromatic nitro compound, the corresponding aniline was obtained in high yield without any further reduction of carbonyl group (entry 7). Furthermore, haloaromatic nitro compounds (entries 4, 5, and 11) showed remarkable

**Table 1.** Reduction of various aromatic nitro compounds by NbCl<sub>5</sub>/In system

Entry	Substrate	Product <sup>a</sup>	Time (h) (Yield %) for NbCl <sub>5</sub> /In	Time (h) (Yield %) for NbCl <sub>5</sub> /Zn
1	C <sub>6</sub> H <sub>5</sub> NO <sub>2</sub>	C <sub>6</sub> H <sub>5</sub> NH <sub>2</sub>	1.5(95)	2.5(90)
2	<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> NO <sub>2</sub>	<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> NH <sub>2</sub>	3.0(88)	3.5(81)
3	<i>p</i> -HOC <sub>6</sub> H <sub>4</sub> NO <sub>2</sub>	<i>p</i> -HOC <sub>6</sub> H <sub>4</sub> NH <sub>2</sub>	4.0(81)	4.5(78)
4	<i>p</i> -BrC <sub>6</sub> H <sub>4</sub> NO <sub>2</sub>	<i>p</i> -BrC <sub>6</sub> H <sub>4</sub> NH <sub>2</sub>	2.0(92)	3.0(88)
5	<i>p</i> -ClC <sub>6</sub> H <sub>4</sub> NO <sub>2</sub>	<i>p</i> -ClC <sub>6</sub> H <sub>4</sub> NH <sub>2</sub>	0.5(94)	1.5(90)
6	<i>p</i> -CH <sub>3</sub> COCC <sub>6</sub> H <sub>4</sub> NO <sub>2</sub>	<i>p</i> -CH <sub>3</sub> COCC <sub>6</sub> H <sub>4</sub> NH <sub>2</sub>	1.5(92)	2.0(89)
7	<i>o</i> -CH <sub>3</sub> COC <sub>6</sub> H <sub>4</sub> NO <sub>2</sub>	<i>o</i> -CH <sub>3</sub> COC <sub>6</sub> H <sub>4</sub> NH <sub>2</sub>	1.5(93)	3.0(91)
8	<i>p</i> -HOCC <sub>6</sub> H <sub>4</sub> NO <sub>2</sub>	<i>p</i> -HOCC <sub>6</sub> H <sub>4</sub> NH <sub>2</sub>	0.5(90)	1.0(90)
9	<i>p</i> -CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> NO <sub>2</sub>	<i>p</i> -CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> NH <sub>2</sub>	3.5(82)	4.5(76)
10	<i>p</i> -NH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> NO <sub>2</sub>	<i>p</i> -NH <sub>2</sub> C <sub>6</sub> H <sub>4</sub> NH <sub>2</sub>	4.0(80)	4.0(79)
11			0.5(93)	0.5(90)
12			2.5(87)	3.0(80)

<sup>a</sup>All isolated amines were fully characterized by spectral analysis.

<sup>b</sup>Isolated yield.

selectivity to give the corresponding anilines without any dehalogenation, which was often encountered with several procedures such as hydrogenation.<sup>1</sup> These observations suggest that this procedure can be applied for the chemoselective reduction of aromatic nitro compounds in the presence of the above-mentioned functional groups. After screening the reaction conditions, THF has been found to be the most suitable solvent for the reaction in terms of reaction time and yield. We investigated that the use of NbCl<sub>5</sub>/Zn in place of NbCl<sub>5</sub>/In is also equally effective but require slight longer reaction time and lower yield as compared to NbCl<sub>5</sub>/In (Table 1). Thus, we have been able to demonstrate the utility of easily accessible NbCl<sub>5</sub>/In system as a convenient reagent for effecting chemoselective reduction of aromatic nitro compounds. Although the role of niobium(V) chloride is still not clarified, it is assumed that reduction of niobium(V) chloride with indium provides low-valent niobium species, which are involved in complexation with the substrates. The reduction probably proceeds by a reductive cleavage of polarized N–O bonds through a single electron transfer from indium metal to the niobium-substrate complex due to the high oxophilic nature of the niobium species. The reducing property exhibited by metal-metal salt combinations proceeds through transfer of one electron from the metal surface to the substrate. We believe that the present procedure using NbCl<sub>5</sub>/In system proceeds through a SET (single electron transfer) process. The notable advantages of this methodology are mild reaction condition, simple manipulation, high yield, and tolerance of various functional groups.

In conclusion, we have demonstrated that the NbCl<sub>5</sub>/In system mediates an efficient and mild reduction of aromatic nitro compounds to the corresponding amines. Although the scope and limitations were not fully established, the present method could be a practical alternative to the conventional method. Further work on the application of the NbCl<sub>5</sub>/In system is currently in progress.

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15. Typical procedure: Niobium(V) chloride (270 mg, 1.0 mmol), indium powder (460 mg, 4.0 mmol) and THF (3 mL) were mixed and the resulting mixture was sonicated for 30 min. A black solution of the complex was obtained. To this solution, nitrobenzene (62 mg, 0.5 mmol) was added. The reaction mixture was stirred for 1.5 h at room temperature. After the reaction was over, as indicated by TLC, water was added and then it was extracted with ether. The combined organic extract was washed with brine, dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, and concentrated under reduced pressure. The crude product was purified by silica gel column chromatography (hexane:ethyl acetate = 2:1) to yield aniline (44 mg, 95%).