

Communications

A Facile and Efficient Reduction of Nitroarenes with NiCl₂·6H₂O/Indium System

Jung Hwa Han, Jin Woo Choi, Kyung Il Choi,[†] Joong Hyup Kim,[†] and Byung Woo Yoo^{*}

Department of Advanced Materials Chemistry, Korea University, Jochiwon, Chungnam 339-700, Korea

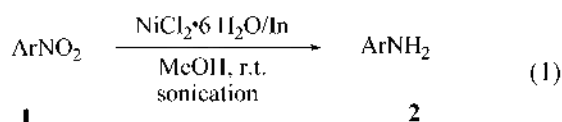
^{*}E-mail: bwyoo@korea.ac.kr

[†]Biochemicals Research Center, Korea Institute of Science and Technology, Seoul 130-650, Korea

Received May 25, 2006

Key Words : Nitroarene, Aniline, Nickel chloride, Indium

Aromatic amines are versatile synthetic intermediates for the synthesis of dyes, photographic materials, pharmaceutical and agricultural chemicals.¹ There are a wide variety of methods, which can be used to convert aromatic nitro groups to their corresponding anilines. Some of them include Cp₂TiCl₂/In,² Al/NH₄Cl,³ (NH₄)₂SO₄/NaBH₄,⁴ *N,N*-dimethyl hydrazine/ferric chloride,⁵ HI,⁶ Sm/I₂,⁷ In/NH₄Cl,⁸ B₃H₁₀/Pd/C⁹ and Co₂(CO)₈/H₂O.¹⁰ However, most methods still lack the desired chemoselectivity when other reducible functional groups are present in the nitroarene and often require prolonged reaction times, or harsh reaction conditions. Recently, indium metal has drawn an increasing attention for its unique properties such as low toxicity and high stability in water and air compared with other metals.¹¹ In continuation of our interest on the applications of indium reagents for various transformations,¹² we wish to report here an efficient and chemoselective method for the reduction of various aromatic nitro compounds to the corresponding amines by treatment with NiCl₂·6H₂O/In (eq. 1). We have investigated the reactions of NiCl₂·6H₂O/indium system with various nitroarenes and found that the reductions generally proceeded with high yields and showed selectivity over other labile substituents.



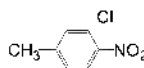
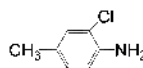
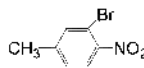
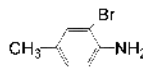
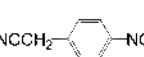
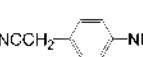
The high yields of the reduction products and selectivity over other labile substituents demonstrated the efficiency of this new method. The new reduction system was generated by the addition of indium powder to a stirred solution of nickel chloride hexahydrate in methanol under sonication.¹² The effect of the relative amounts of nickel chloride hexahydrate to indium on the reaction was significant as can be seen in Table 1. Some control experiments revealed that nitroarenes could not be reduced by nickel chloride hexahydrate or indium alone under the reaction condition. Table 2 illustrates the generality and the scope of this reagent system. From the Table 2, we could see that this method was

highly chemoselective and many sensitive functional groups, such as -Br, -Cl, -OH, -COCH₃, -CN, -OCH₃, and -COOC₂H₅ are unaffected under the reaction conditions. It was worth commenting that the sensitive carbonyl group remains intact without any further reduction under the reaction condition (entry 7). In addition, 4-nitrophenol

Table 1. The effect of the molar ratio of NiCl₂·6H₂O and indium to the substrates on the reduction reaction

Nitrobenzene	NiCl ₂ ·6H ₂ O	Indium	Aniline yield (%)
1	1	1	45
1	1	2	56
1	1	4	95
1	1.5	3	64
1	2	4	70

Table 2. Reduction of nitroarenes to aromatic amines with NiCl₂·6H₂O/In^a

Entry	Substrate	Product ^b	Reaction time (hrs)	Yield (%) ^c
1	C ₆ H ₅ NO ₂	C ₆ H ₅ NH ₂	1.5	95
2	<i>p</i> -CH ₃ C ₆ H ₄ NO ₂	<i>p</i> -CH ₃ C ₆ H ₄ NH ₂	3.0	88
3	<i>p</i> -HOC ₃ H ₇ NO ₂	<i>p</i> -HOC ₃ H ₇ NH ₂	2.0	85
4	<i>p</i> -BrC ₆ H ₄ NO ₂	<i>p</i> -BrC ₆ H ₄ NH ₂	2.0	92
5	<i>m</i> -BrC ₆ H ₄ NO ₂	<i>m</i> -BrC ₆ H ₄ NH ₂	2.0	90
6	<i>p</i> -ClC ₆ H ₄ NO ₂	<i>p</i> -ClC ₆ H ₄ NH ₂	1.5	94
7	<i>o</i> -CH ₃ COC ₆ H ₄ NO ₂	<i>o</i> -CH ₃ COC ₆ H ₄ NH ₂	3.0	95
8	<i>p</i> -EtOCC ₆ H ₄ NO ₂	<i>p</i> -EtOCC ₆ H ₄ NH ₂	1.5	86
9	<i>o</i> -CH ₃ OC ₆ H ₄ NO ₂	<i>o</i> -CH ₃ OC ₆ H ₄ NH ₂	3.0	82
10			2.0	84
11			2.0	92
12			1.5	91

^aAll the reactions were carried out under sonication. ^bAll isolated amines were fully characterized by spectral analysis. ^cIsolated yield.

proceeded successfully with this reduction system (entry 3). Furthermore, this procedure showed remarkable selectivity to give the anilines without any further dehalogenation (entry 4, 5, 6, 10 and 11). The wide chemoselectivity of the reaction and the mild reaction conditions should be synthetically useful. After screening the reaction conditions, methanol has been found to be the most suitable solvent for the reaction in terms of reaction time and yield.¹³ All the compounds obtained showed IR, NMR and mass spectral data compatible with the structure. Thus, we have been able to demonstrate the utility of easily accessible $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}/\text{In}$ system as a convenient reagent for effecting chemoselective reduction of nitroarenes. Although the role of nickel (II) chloride hexahydrate is still not clarified, it was assumed that reduction of nickel (II) chloride with indium provided low-valent nickel, which might be reducing the nitroarenes **1** to give the corresponding amines **2**. The reducing property exhibited by metal-metal salt combinations proceeds through transfer of one electron from the metal surface to the substrate. In such combinations elementary metal part needs to be more electropositive than the metal part of the salt.¹⁴ Another important aspect of metal-metal salt combinations is the reduction potential difference of Ni^{+2}/Ni ($E^\circ = -0.236$ V), In^{+3}/In ($E^\circ = -0.338$ V) on which activity as well as reactivity of these reagents depend. We believe that the present procedure using $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}/\text{In}$ system proceeds through a single electron transfer (SET) process. The notable advantages of this methodology are mild reaction condition, readily available and inexpensive reagents, high yield, and tolerance of various functional groups.

In conclusion, we have demonstrated that this procedure using $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}/\text{In}$ system provides a useful alternative to the other presently used procedures since the reduction of aromatic nitro compounds proceeds expeditiously and in high yields under mild conditions. Further investigations of $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}/\text{In}$ system as reducing agent in organic synthesis are currently in progress.

Acknowledgements. This work was financially supported by Korea Institute of Science and Technology and partially by Korea University.

References

1. (a) For a review, see Tafesh, A. M.; Weiguny, J. *Chem. Rev.* **1996**, *96*, 2035. (b) Mestoni, G.; Camus, A.; Zassinovich, G. In *Aspects of Homogeneous Catalysis*; Ugo, R., Ed.; Reidel: Dordrecht, 1981; Vol. 4, pp 71-80.
2. Yoo, B. W.; Lee, S. J.; Yoo, B. S.; Choi, K. I.; Kim, J. H. *Synth. Commun.* **2002**, *32*, 2489.
3. Nagaraja, D.; Pasha, M. A. *Tetrahedron Lett.* **1980**, *40*, 7855.
4. Gohain, S.; Prajapati, D.; Sandhu, J. *Chem. Lett.* **1995**, 725.
5. Boothroyd, S.; Michael, A. *Tetrahedron Lett.* **1995**, *36*, 2411.
6. Kumar, J. S.; Ho, M. M.; Toyokuni, T. *Tetrahedron Lett.* **2001**, *42*, 5601.
7. Banik, B. K.; Mukhopadhyay, C.; Venkatraman, M. S.; Becker, F. *Tetrahedron Lett.* **1998**, *39*, 7243.
8. Moody, C. J.; Pitts, M. R. *Synlett.* **1998**, 1028.
9. Bae, J. W.; Cho, Y. J.; Lee, S. H.; Yoon, C. M. *Tetrahedron Lett.* **2000**, *41*, 175.
10. Lee, H. Y.; An, M. *Bull. Korean Chem. Soc.* **2004**, *25*, 1717.
11. For review: (a) Nair, V.; Ros, S.; Jayan, C. N.; Pillia, B. S. *Tetrahedron* **2004**, *60*, 1959. (b) Podlech, J.; Maier, T. C. *Synlett.* **2003**, 633. (c) Li, C.-J.; Chan, T.-H. *Tetrahedron* **1999**, *55*, 11149.
12. (a) Yoo, B. W.; Choi, K. H.; Lee, S. J.; Yoon, C. M.; Kim, S. H.; Kim, J. H. *Synth. Commun.* **2002**, *32*, 63. (b) Yoo, B. W.; Lee, S. J.; Yoo, B. S.; Choi, K. I.; Kim, J. H. *Synth. Commun.* **2002**, *32*, 2489. (c) Yoo, B. W.; Choi, K. H.; Kim, D. Y.; Choi, K. I.; Kim, J. H. *Synth. Commun.* **2003**, *33*, 53. (d) Yoo, B. W.; Hwang, S. K.; Kim, D. Y.; Choi, J. W.; Kang, S. O.; Yoo, B. S.; Choi, K. I.; Kim, J. H. *Bull. Korean Chem. Soc.* **2004**, *25*, 1633. (e) Choi, K. H.; Choi, K. I.; Kim, J. H.; Yoon, C. M.; Yoo, B. W. *Bull. Korean Chem. Soc.* **2005**, *26*, 1495. (f) Han, J. H.; Choi, J. W.; Choi, K. I.; Kim, J. H.; Yoo, B. W. *Bull. Korean Chem. Soc.* **2005**, *26*, 1921.
13. Sonication were carried out in a BRANSONIC ultrasonic cleaner bath, which delivered a 47 kHz wave, with a fixed electrical power of 125 Watts.
14. A typical procedure for the reaction: Nickel(II) chloride hexahydrate (238 mg, 1.0 mmol), indium powder (512 mg, 4.0 mmol) and MeOH (4 mL) were mixed and the resulting mixture was stirred at room temperature under sonication for 30 min. A dark-yellow solution of the complex was obtained. Nitrobenzene (123 mg, 1.0 mmol) was added to this solution and the reaction mixture was stirred for 1.5 hr at room temperature. The solvent was evaporated under reduced pressure and the residue was extracted with ether. The extract was washed with brine, dried over anhydrous MgSO_4 . The crude product was purified by silica gel column chromatography (hexane : ethyl acetate = 6 : 1) to afford aniline (88 mg, 95%).
15. Mourad, M. S.; Verma, R. S.; Kabalka, G. W. *J. Org. Chem.* **1985**, *50*, 133.