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Rapid and Efficient Reduction of Nitroarenes to Their Corresponding Amines with Promotion of $NaBH_4/NiCl_2·6H_2O$ System in Aqueous CH_3CN

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$NaBH_4$ in the presence of catalytic amounts of $NiCl_2·6H_2O$ reduces varieties of nitroarenes to their corresponding amines. Reduction reactions were carried out in a mixture of CH_3CN and H_2O (3.0:0.3 mL) at room temperature with high to excellent yields of products.

Key Words: Amines, $NiCl_2·6H_2O$, $NaBH_4$, Nitroarenes, Reduction.

INTRODUCTION

Reduction of nitroarenes is one of the important methods for the preparation of aryl amines. Nitro compounds have traditionally been reduced by high-pressure hydrogenation[1]. The application of $NaBH_4$ as a mild reducing agent has brought about fundamental changes in the reduction of functional groups in modern organic synthesis. It is known that solely sodium borohydride does not reduce nitro compounds under ordinary conditions[2]. However, the reducing power of this reagent or its polymeric analogue *i.e.*, borohydride exchange resin (BER) undergoes a drastic change toward reduction of nitro groups by the combination with transition metal halides or salts such as $NaBH_4/CoCl_2$[3], $NaBH_4/FeCl_2$[4], $NaBH_4/CuSO_4$[5], $NaBH_4/Ni(OAc)_2$[6], $NaBH_4$/Co(pyridyl)[7], $NaBH_4/Cu(acac)_2$[8], borohydride exchange resin (BER); BER/$Ni(OAc)_2$, $CoCl_2$, $PdCl_2$, $Cu(OAc)_2$[9] are effective for the reduction of aliphatic or aromatic nitro compounds. It was reported that by the combination of transition metal halides or salts with $NaBH_4$ in protic or aqueous solvent systems[3,8,10] the formation of transition metal borides which are actively catalyzes-resulting from the decomposition of borohydride-with the evolving of hydrogen gas and in conjunction with the hydride attack reduce nitro compounds to their corresponding amines. Osby *et al.*[10a] reported that the combination of $NaBH_4$ with catalytic quantities of $NiCl_2·6H_2O$ smoothly reduces aliphatic nitro compounds to their amines at room temperature. The method is successful for reduction of aliphatic nitro compounds, however the literature survey could find no published example of nitroarenes reduction by this system ($NaBH_4/NiCl_2·6H_2O/CH_3OH$). Our preliminary experiments revealed that nitroarenes could reduce to corresponding aryl amines by this protocol but the amount of $NaBH_4$ and moderated yields of products (Table-1) in the best optimized reaction conditions (Table-1, entry 4) are of disadvantages. It is worthwhile to investigate one of the more highly reactive systems for reduction of nitro aromatic compounds to their corresponding aryl amines. To expand the above mentioned strategy in the reduction of nitroarenes by the $NaBH_4$/transation metal halide system and our continuous efforts to develop modified borohydride agents in organic synthesis[11], here we report that the combination of $NiCl_2 \cdot 6H_2O$ as a more efficient promoter for rapid and convenient reduction of nitroarenes with sodium borohydride in aqueous CH_3CN at room temperature.

TABLE-1
REDUCTION OF NITROBENZENE TO ANILINE WITH
$NaBH_4/NiCl_2 \cdot 6H_2O$ SYSTGEM IN CH_3OH

Entry	Molar ratio Subs/$NaBH_4/NiCl_2 \cdot 6H_2O$	Condition	Time (h)	Yield (%)[a]
1	1:4:0.2	RT	1	5
2	1:4:0.2	Reflux	1	25
3	1:8:0.2	Reflux	1	37
4	1:8:0.5	Reflux	1	48

[a]Yield refer to isolated pure products.
RT = Room temperature.

EXPERIMENTAL

All reagents and substrates were purchased from commercial sources with the best quality and were used without further purification. IR and ^1H NMR spectra were recorded on Thermo Nicolet Nexus 670 FT-IR and 300 MHz Bruker Avance spectrometers, respectively. The products were characterized by a comparison with authentic samples (melting or boiling points) and their ^1H NMR or IR spectra. All yields refer to isolated pure products. TLC was applied for the purity determination of substrates, products and reaction monitoring over silica gel 60 F_{254} aluminum sheet.

Reduction of nitrobenzene to aniline with $NaBH_4/NiCl_2 \cdot 6H_2O$ system; typical procedure: In a round-bottomed flask (15 mL) equipped with a magnetic stirrer, a solution of nitrobenzene (0.123 g, 1 mmol) in $CH_3CN:H_2O$ (3.0:0.3 mL) was prepared. To the resulting solution, $NiCl_2 \cdot 6H_2O$ (0.047 g, 0.2 mmol) was added and the mixture was then stirred for 3 min. Afterwards, $NaBH_4$ (0.151 g, 4 mmol) as a fine powder was added to the reaction mixture and a fine black precipitate was immediately deposited. The mixture continued to be stirred for 5 min and the progress of the reaction was monitored by TLC (eluent; CCl_4/Et_2O: 5/2). At the end of reaction, distilled water (5 mL) was added to the reaction mixture and the mixture stirred for 10 min. The mixture was extracted with CH_2Cl_2 (3 × 8 mL) and dried over anhydrous sodium sulfate. Evaporation of the solvent and short column chromatography of the resulting crude material over silica gel (eluent; CCl_4/Et_2O: 5/3) gave the pure liquid aniline (0.088 g, 95 %, entry 1, Table-3).

RESULTS AND DISCUSSION

Our preliminary experiments showed that the reduction of nitrobenzene with 4 molar equivalents of $NaBH_4$ and catalytic amounts of $NiCl_2{\cdot}6H_2O$ (0.2 mol) in CH_3CN (as an efficient aprotic solvent) without deposition of any precipitate was completed within 3 h under reflux conditions (Table-2, entry 4). However, a mixture of products with a 35 % yield of aniline was obtained from the reduction. In another attempt, it is found that by adding a small amount of water to the reaction mixture, when there was an immediate deposition of a fine black precipitate, the rate of reduction was dramatically increased and the reaction was completed within 5 min at room temperature (Table-2, entry 6). In the latter case, aniline was the sole product of reduction. The optimization reactions showed that using 4 molar equivalents of $NaBH_4$ and 0.2 molar equivalents of $NiCl_2{\cdot}6H_2O$ in a mixture of $CH_3CN:H_2O$ (3.0:0.3 mL) are the best conditions for the complete conversion of nitrobenzene into aniline (Fig. 1).

TABLE-2
OPTIMIZATION REACTION CONDITIONS OF REDUCTION OF NITROBENZENE TO ANILINE WITH $NaBH_4/NiCl_2{\cdot}6H_2O$ SYSTEM IN WET CH_3CN

Entry	Molar ratio Subs/$NaBH_4$/$NiCl_2{\cdot}6H_2O$	Solvent	Condition	Time (min)	Yield (%)[a]
1	1:4:0.2	THF	RT	60	0
2	1:4:0.2	THF	Reflux	60	10
3	1:4:0.2	CH_3CN	RT	60	20
4	1:4:0.2	CH_3CN	Reflux	180	35
5	1:4:0.2	$CH_3CN:H_2O$ (3.0:0.5 mL)	Reflux	10	90
6	1:4:0.2	$CH_3CN:H_2O$ (3.0:0.3 mL)	Reflux	5	95
7	1:4:0.2	$CH_3CN:H_2O$ (3.0:0.15 mL)	Reflux	30	80

[a]Yield refer to isolated pure products; RT = Room temperature.

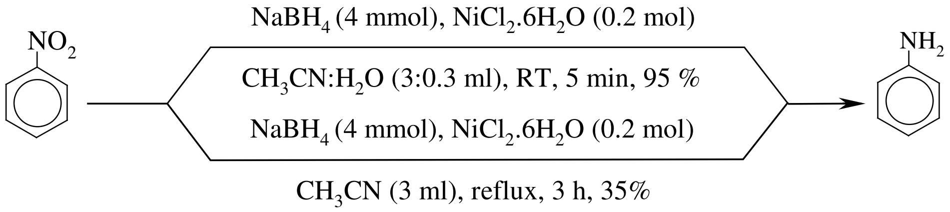
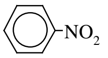
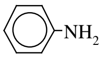
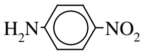
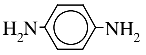
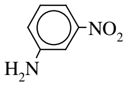
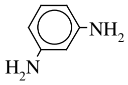
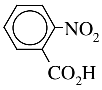
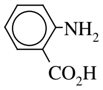
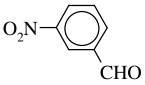
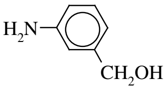
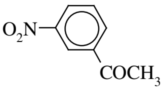
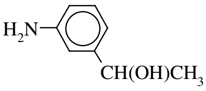
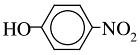
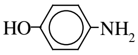
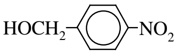
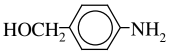
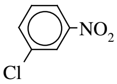
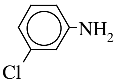
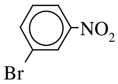
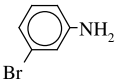
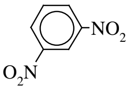
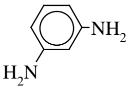
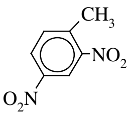
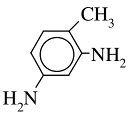
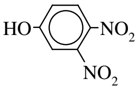
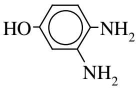
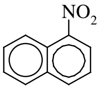
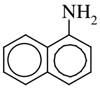


Fig. 1.

We applied the optimal conditions for the reduction of a variety of nitroarenes to their corresponding amines. As shown in Table-3. The product amines were obtained in high to excellent yields within 5-20 min. The chemoselective reduction of nitro group in the presence of carboxylic acid was proven with the reduction of 2-nitro benzoic acid to anthranilic acid in 94 % yield (Table-3, entry 4). Our attempts

TABLE-3

REDUCTION OF NITRO ARENES WITH $NaBH_4/NiCl_2·6H_2O$ SYSTEM IN WET CH_3CN^a

Entry	Substrate	Product	Molar ratio Subs./$NaBH_4/NiCl_2.6H_2O$	Time/min	Yield/%[b)]
1			1:4:0.2	5	95
2			1:4:0.2	10	96
3			1:4:0.2	6	93
4			1:4:0.2	6	94
5			1:5:0.2	7	93
6			1:5:0.2	10	92
7			1:4:0.2	8	95
8			1:4:0.2	5	94
9			1:4:0.2	5	95
10			1:4:0.2	5	95
11			1:8:0.2	15	95
12			1:8:0.2	20	94
13			1:8:0.2	20	96
14			1:4:0.2	5	92

a) All reactions were performed in CH_3CN-H_2O (3:0.5 ml) at room temperature.

b)Yields refer to isolated pure products.

to reduce C=O over nitro group in 3-nitro benzaldehyde and 3'-nitro acetophenone were unsatisfactory and under the different conditions both of the functional groups were reduced (Table-3, entries 5,6). The complete reduction of nitroarenes with two nitro groups was also achieved perfectly by this protocol: using 8 molar equivalents of $NaBH_4$ in the presence of 0.2 molar equivalents of $NiCl_2·6H_2O$ were the requirements for these transformations (Table-3, entries 11,12, 13). All attempts to perform chemoselective reduction of one nitro group in the presence of the other one were unsuccessful and the mixture of products was identified from the reaction mixture. The exact mechanism of this protocol is not clear. However, in present experiments, some results are noteworthy. In all reductions, by the combination of $NaBH_4$ with $NiCl_2·6H_2O$ in aqueous CH_3CN, the immediate deposition of a fine black precipitate and the subsequent evolution of hydrogen gas were observed. We think that reduction of nitro compounds is probably due to formation of the black precipitate which catalyzes the decomposition of $NaBH_4$, strongly adsorbs nitro compounds and activates them towards reduction by $NaBH_4$. This black precipitate may be boride, zerovalent metal or a mixture of these.

Conclusion

It is shown that a variety of nitroarenes were reduced efficiently to their corresponding amines by the combination of $NaBH_4$ with catalytic amounts of $NiCl_2·6H_2O$ in aqueous CH_3CN. The reductions were completed within 5-20 min at room temperature. We think that in the view points of molar equivalents of, $NaBH_4$ and catalyst, high efficiency, shorter reaction times, easy work-up procedure and presentation of $NiCl_2·6H_2O$ as a more efficient catalyst for the probable boride-catalyzed reduction of aromatic nitro compounds. This protocol is a synthetically useful addition to the present methodologies.

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REFERENCES

1. (a) M. Stiles and H.L. Finkbeiner, *J. Am. Chem. Soc.*, **81**, 505 (1959); (b) H.L. Finkbeiner and M. Stiles, *J. Am. Chem. Soc.*, **85**, 616 (1963).
2. (a) S.D. Burke and R.L. Danheiser, Handbook of Reagents for Organic Synthesis, Oxidising and Reducing Agents, Wiley-VCH, New York (1999); (b) J. Seyden-Penne, Reductions by the Alumino and Borohydrides in Organic Synthesis, Wiley-VCH, New York, edn. 2 (1997); (c) M. Hudlicky, Reductions in Organic Chemistry, Ellis Horwood, Chichester (1984).
3. T. Satoh, S. Suzuki, Y. Suzuki, Y. Miyaji and Z. Imai, *Tetrahedron Lett.*, **10**, 4555 (1969).
4. A. Ono, H. Sasaki and F. Yaginuma, *Chem. Ind. (London)*, 480 (1983).
5. S.E. Yoo and S.H. Lee, *Synlett*, 419 (1990).
6. A.A. Vlcek and A. Rusina, *Chem. Soc. (London)*, 161 (1961).
7. K. Hanaya, T. Muramatsu, H. Kudo and Y.L. Chow, *J. Chem. Soc. Perkin Trans. I*, 2409 (1979).
8. (a) J.W. Chem and C.Q. Qin, *React. Polym.*, **16**, 287 (1992); (b) N.M. Yoon and J. Choi, *Synlett*, 135 (1993) and the references cited therein.

9. B. Ganem and J.O. Osbey, *Chem. Rev.*, **86**, 763 (1986).
10. (a) J.O. Osby and B. Ganem, *Tetrahedron Lett.*, **26**, 6413 (1985); (b) A. Nose and T. Kudo, *Chem. Pharm. Bull.*, **29**, 1159 (1981); (c) J.C. Sarma, M. Borbaruah and R.P. Sharma, *Tetrahedron Lett.*, **26**, 4657 (1985); (d) D.N. Sharma and R.D. Sharma, *Tetrahedron Lett.*, **26**, 2581 (1985).
11. (a) D. Setamdideh and B. Zeynizadeh, *Z. Naturforsch.*, **61b**, 1275 (2006); (b) B. Zeynizadeh and D. Setamdideh, *Synth. Commun.*, **36**, 2699 (2006); (c) B. Zeynizadeh and D. Setamdideh, *J. Chin. Chem. Soc.*, **52**, 1179 (2005); (d) B. Zeynizadeh and D. Setamdideh, *Asian J. Chem.*, **21**, 3588 (2009); (e) B. Zeynizadeh and D. Setamdideh, *Asian J. Chem.*, **21**, 3603 (2009).

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