Indium Mediated Reduction of Nitro and Azide Groups in the Presence of HCl in Aqueous Media

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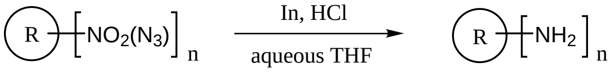
Abstract: Indium mediated reduction of azide and nitro groups in the presence of HCl (1.5 equiv based on indium) at room temperature in aqueous THF successfully provided the corresponding amine in high to quantitative yields. Under the same reaction conditions, selective reduction of azide and nitro group in the presence of vinyl group could be accomplished.

Key words: nitro compounds, azides, reductions, indium, amines



n = 1, 2

R = aliphatic or aromatic

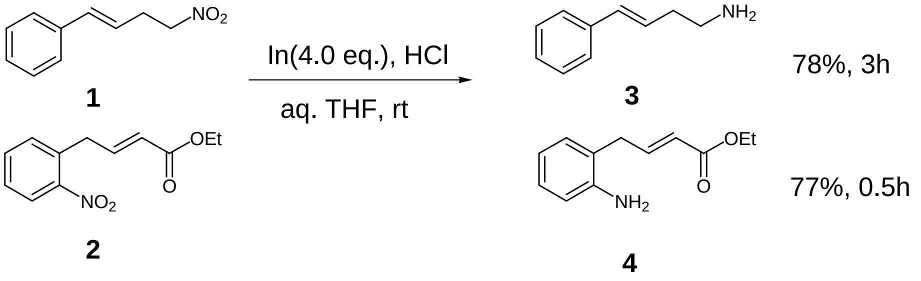
Scheme 1

A number of reduction reactions of nitro groups and azides have been studied since they provide ways to the useful amino functional group.[1] Reduction of nitro groups generally depends on the nature of the carbon atom to which it is bonded. Especially aliphatic nitro groups are easily reduced to various groups, e.g. aldoximes, ketoximes, hydroxyamines, ketones, and aldehydes according to the reaction conditions.[2] Besides, nitro compounds bearing carbon-carbon double bond lead to saturated nitro compounds, saturated amines or oximes by numerous methods.[3] Recently, Moody et al.[4] and Reddy et al.[5] independently reported reduction of nitro and azide groups using indium in the presence of NH_4Cl in aqueous EtOH and EtOH reflux conditions, respectively.

In this paper we report more efficient, simple, practical, and milder reduction of nitro and azide groups using indium at room temperature in acidic aqueous media. As shown in Scheme 1, we found that aliphatic or aromatic nitro and azide groups were easily reduced to the corresponding amine in the presence of HCl at room temperature in aqueous THF (H_2O/THF, 3:1 v/v) in high to quantitative yields.

Table 1 summarizes the results of reduction of azide groups. Aromatic as well as aliphatic azides reacted with indium (2.0 equiv) in the presence of HCl (1.5 equiv based on indium) to provide the corresponding amine at room temperature in aqueous THF in 68–98% yield. Especially the allylamine (Table 1, Entry 4) and α-amino ester (Table 1, Entry 10) could be obtained from the corresponding azides leaving the vinyl and ester group intact, respectively. Next, we turned our attention to the reduction of nitro groups. Aromatic and aliphatic nitro groups were treated with indium (4.0 equiv) in the presence of HCl (1.5 equiv based on indium) in aqueous THF at r.t. to give the corresponding amine in excellent yields as shown in Table 2. Reaction times were mostly short compared to azide groups. It is noteworthy that (4-nitrobut-1-enyl)benzene (**1**) and ethyl 4-(2-nitrophenyl)but-2-enoate (**2**) were converted to the corresponding amine without reduction of double bond in 78% and 77% yield, respectively (Scheme 2). Finally, we investigated the reduction of compounds bearing two nitro groups, two azides, and mixed azide-nitro groups, respectively. As shown in Table 3, those groups reacted with indium (6.0 equiv in nitro-azide, 8.0 equiv in nitro-nitro, and 4.0 equiv in azide-azide) in the presence of HCl at r.t. to yield the corresponding diamine in 60–99% yield.

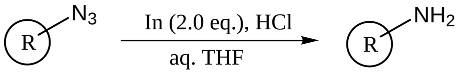
In summary, we have demonstrated an efficient, mild and novel reduction methodology of azide and nitro groups



Scheme 2

Synthesis 2001, No. 1, 81–84 ISSN 0039-7881 © Thieme Stuttgart · New York

Table 1 Indium Mediated Reduction of Azide Groups[a]



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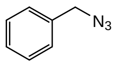
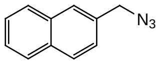
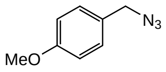
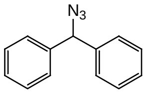
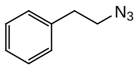
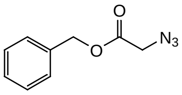
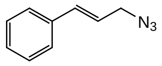
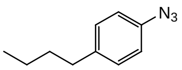
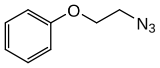
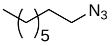
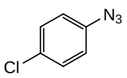
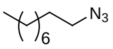
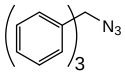
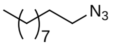
1		2	85	8		2.5	91
2		3	95	9		8.5	96
3		1.5	85	10		3	85
4		3	92	11		3	95
5		3	98	12		2.5	80
6		4	68	13		2	88
7		8	90	14		2	92

[a] All reactions were carried out in 0.2–0.4 mmol scale at r.t.

[b] Isolated yields. All compounds displayed satisfactory spectroscopic data (NMR, IR, Mass).

using indium in the presence of HCl at room temperature in aqueous media. Our method is distinguished from other analogous reactions[4,5] by shorter reaction time, mild reaction condition and good yields for both aromatic and aliphatic compounds. In particular, it provides an excellent synthetic pathway to the selective reduction of azide and nitro groups in the presence of unsaturated carbon-carbon bonds.

^{1}H NMR spectra were obtained on a Varian Gemini 300 and Bruker Avance 300 spectrometers. Chemical shifts were reported in ppm. Infrared spectra were obtained on a Perkin Elmer 16FPC FT-IR spectromter. MS spectra were obtained on a HP G1034C spectrometer. Analytical TLC were carried out on precoated silica gel plates (Merk Kieselgel 60F254, layer thickness 0.25 mm).

Ethyl 4-(2-Aminophenyl)but-2-enoate; Typical Procedure

To a solution of (4-nitrobut-1-enyl)benzene (**1**; 100 mg, 0.56 mmol) in aq THF (3 mL) was added indium powder (260 mg, 2.26 mmol) and concd HCl (300 μL). After stirring for 3 h at r.t., the pH of the reaction mixture was adjusted to 7 with solid $NaHCO_3$, diluted with H_2O and extracted with EtOAc, and the organic layer was dried ($MgSO_4$) and concentrated in vacuo. The crude product was purified by a short column chromatography on neutral alumina (Scheme 2).

^{1}H NMR ($CDCl_3$): δ = 7.17 (m, 1 H), 6.99 (m, 1 H), 6.59 (m, 1 H), 6.45 (d, 1 H, *J* = 15.7 Hz), 6.13–6.04 (m, 1 H), 4.10 (m, 2 H), 4.70 (br s, 2 H), 3.17 (m, 2 H), 1.45 (m, 3 H).

^{13}C NMR ($CDCl_3$): δ = 172.0, 143.9, 129.6, 128.9, 128.0, 124.2, 119.3, 116.4, 61.2, 39.2, 14.6.

IR (KBr): ν = 3450, 1720, 1632, 1461, 1267, 1156, 1033, 748 cm^{-1}.

MS(70eV): *m*/*z* (%) = 205 (M$^+$), 132, 117 (100), 103, 77, 65, 51.

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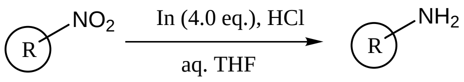
References

(1) (a) Hudlický, M. *Reductions in Organic Chemistry*, 2nd ed.; ACS Monograph.
(b) Scriven, E. F. V. *Chem. Rev.* **1988**, *88*, 297.
(2) (a) Calder, A.; Hepburn, S. P. *Org. Synth.* **1972**, *52*, 77.
(b) Kende, A. S.; Mendoza, J. S. *Tetrahedron Lett.* **1991**, *32*, 1699.
(c) Hanson, J. R.; Premuzic, E. *Tetrahedron* **1967**, *23*, 4105.
(d) Grundmann, C. *Angew. Chem.* **1950**, *62*, 558.
(e) McMurry, J. E.; Melton, J. *J. Org. Chem.* **1973**, *38*, 4367.

Table 2 Indium Mediated Reduction of Nitro Groups[a]



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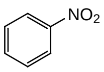
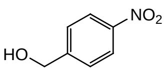
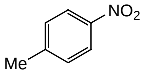
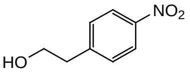
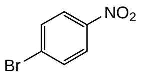
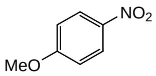
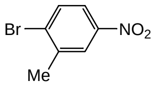
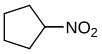
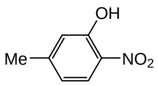
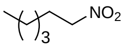
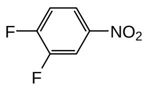
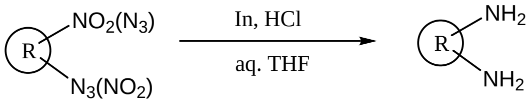
1		0.5	84	7		1	94
2		0.5	96	8		1.5	98
3		0.5	98	9		0.5	89
4		1	84	10		0.5	78
5		1	73	11		0.5	90
6		0.5	75				

[a,b] See the corresponding footnotes in Table 1.

Table 3 Indium Mediated Reduction of Azide and Nitro Groups[a]



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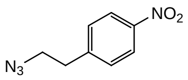
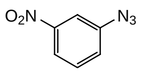
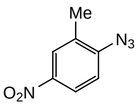
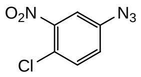
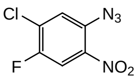
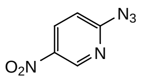
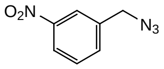
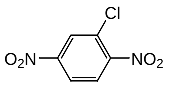
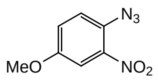
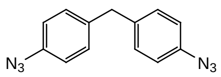
1		7	63	6		8	76
2		12	83	7		6	84
3		8	85	8		5	84
4		5	73	9		2	94
5		6	99	10		24	60

[a,b] See the corresponding footnotes in Table 1.

(3) (a)Varma, R. S.; Kabalka, G. W. *Synth. Commun*. **1984**, *14*, 1093.
(b) Sinhababu, A. K.; Borchardt, R. T. *Tetrahedron Lett*. **1983**, *24*, 227.
(c) Ranu, B. C.; Chakraborty, R. *Tetrahedron* **1992**, *48*, 5317.
(d) Aizpurna, J. M.; Oiarbide, M.; Palomo, C. *Tetrahedron Lett*. **1987**, *28*, 5365.
(e) Mourad, M. S.; varma, R. S.; Kabalka, G. W. *J. Org. Chem*. **1985**, *50*, 133.
(4) Moody, C. J.; Pitts, M. R. *Synlett* **1998**, 1028.
(5) Reddy, G. V.; Rao, G. V.; Iyengar, D. S. *Tetrahedron Lett*. **1999**, *40*, 3937.

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