

## Indium-mediated deoxygenation of amine-*N*-oxides in aqueous media<sup>†</sup>

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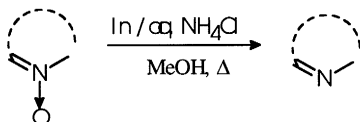
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### Abstract

Several aromatic and aliphatic amine-*N*-oxides were deoxygenated to the corresponding amines in good to quantitative yield using indium metal in neutral aqueous media. Other functional groups such as alkenes, halides, esters, ethers, nitriles, amides and sulfones are unaffected under the present reaction conditions. © 2000 Elsevier Science Ltd. All rights reserved.

**Keywords:** indium; amine-*N*-oxides; deoxygenation; aqueous media.

The deoxygenation of amine *N*-oxides is an important transformation in the synthesis of nitrogen containing heterocycles.<sup>1</sup> Many reagents<sup>2</sup> such as Pd, Ni, sulfurous acid, phosphorous compounds, iron and zinc have been employed for the deoxygenation of aromatic *N*-oxides to give aromatic amines. In addition, selective deoxygenating agents<sup>3</sup> like trialkylamine–SO<sub>2</sub> complex, aluminium iodide, ammonium formate–Pd/C and tin reagents have also been utilised. Recently low valent titanium,<sup>4</sup> chromium<sup>5</sup> and SmI<sub>2</sub><sup>6</sup> mediated deoxygenations of aromatic *N*-oxides have been reported, although most are associated with limitations<sup>7</sup> regarding selectivity and incompatibility with other functional groups. Some of the reagents employed for this transformation are expensive, hazardous and sensitive to both air and moisture. The difficulties associated with these reagents can be overcome by the use of indium metal as a reducing agent because of its special properties in water<sup>8</sup> and its close resemblance to magnesium and zinc in several aspects.

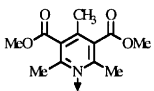
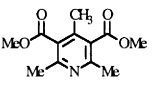
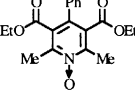
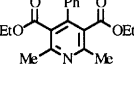
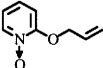
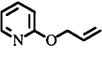
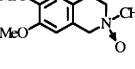
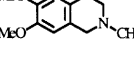
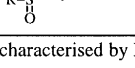
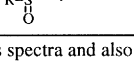


Scheme 1.

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Table 1  
Reduction of *N*-oxides with indium in aqueous ammonium chloride

| Entry | Substrate<br>(1)                                                                    | Product <sup>a</sup><br>(2)                                                         | Reaction<br>(h.) | Yield <sup>b</sup><br>(%) |
|-------|-------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|------------------|---------------------------|
| a     |    |    | 4                | 93                        |
| b     |    |    | 5                | 91                        |
| c     |    |    | 5                | 94                        |
| d     |    |    | 4                | 90                        |
| e     |    |    | 4                | 89                        |
| f     |    |    | 5                | 92                        |
| g     |  |  | 5                | 95                        |
| h     |  |  | 4                | 90                        |
| i     |  |  | 4                | 88                        |
| j     |  |  | 4                | 85                        |
| k     |  |  | 4                | 87                        |
| l     |  |  | 3                | 96                        |
| m     |  |  | 3                | 94                        |
| n     |  |  | 3                | 95                        |
| o     |  |  | 4                | 91                        |

a) All the products were characterised by IR, <sup>1</sup>H NMR and mass spectra and also compared with literature data.<sup>2,3</sup>

b) Isolated yields are reported

In continuation of our work on applications of indium,<sup>9</sup> we report a mild and efficient method for the deoxygenation of amine-*N*-oxides using indium metal in aqueous methanolic ammonium chloride (Scheme 1). Furthermore, deoxygenations of pyridine-*N*-oxides with chlorine containing dehydrating reagents such as PCl<sub>5</sub>, POCl<sub>3</sub>, SO<sub>2</sub>Cl<sub>2</sub> and SOCl<sub>3</sub> etc. suffer serious drawbacks such as chlorination of the pyridine nucleus.<sup>7</sup> Several amine-*N*-oxides are selectively deoxygenated to the corresponding amines by simply heating the substrate with indium powder in aqueous methanolic ammonium chloride;<sup>10</sup> the results are summarised in the Table 1. In general, the reactions were very clean, high-yielding and complete within 3–5 h and gave the corresponding amines in good to quantitative yields. The reaction conditions are compatible with other functional groups such as halides, carboxylic acids, nitriles, ethers and sulphones.

In conclusion, we have described a mild and efficient method for the selective reduction of amine-*N*-oxides to amines using metallic indium in neutral aqueous media. Because of the mild reaction conditions, our method is compatible with other functional groups present in the molecule, and may find application in organic synthesis.

## Acknowledgements

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10. Experimental procedure: A mixture of the amine-*N*-oxide (5 mmol), indium powder (6 mmol) and saturated ammonium chloride (10 ml) in ethanol (15 ml) was refluxed for an appropriate time (Table 1). After complete conversion, as indicated by TLC, the reaction mass was filtered through Celite and washed with ether (2×30 ml). The organic layer was washed with water and dried over Na<sub>2</sub>SO<sub>4</sub>. Evaporation of the solvent in vacuo gave the corresponding amine in pure form. Representative data for compound **2f**: (solid) m.p. 62–63°C, <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 0.8 (t, 6H, J=8.1 Hz), 2.6 (s, 6H), 3.95 (q, 4H, J=8.1 Hz), 7.1–7.35 (m, 5H). <sup>13</sup>C: δ 13.27 (-CH<sub>2</sub>-CH<sub>3</sub>), 22.62 (-CH<sub>3</sub>), 61.04 (-CH<sub>2</sub>-CH<sub>3</sub>), 126.52, 126.66, 127.53, 127.69, 127.86, 128.19, 136.20, 136.21, 145.90, 155.10, 155.27, 168.15, 168.10 (aromatic, pyridine and carbonyl carbons). EI-MS: *m/z* (%) 327 (M<sup>+</sup>) (100) 282 (70), 254 (50), 236 (60), 209 (30), 180 (15), 139 (40), 105 (15), 83 (80), 77 (5), 47 (40). Compound **1f**: <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 0.75 (t, 6H, J=8.1 Hz), 2.52 (s, 6H), 3.85 (q, 4H, J=8.1 Hz), 6.9–7.2 (m, 5H). EI-MS: *m/z* 343 (M<sup>+</sup>), 327 (M–16), 282, 254, 236, 209, 105, 77. Compound **2l**: m.p. 78–80°C. <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 2.42 (s, 3H, -N-CH<sub>3</sub>), 2.65 (t, 2H, Ar-C<sub>2</sub>-CH<sub>2</sub>-N-), 2.85 (t, 2H, Ar-CH<sub>2</sub>-CH<sub>2</sub>-N-), 3.5 (s, 2H, Ar-CH<sub>2</sub>-N-), 3.85 (s, 6H, OCH<sub>3</sub>), 6.45 (s, 1H, aromatic), 6.55 (s, 1H, aromatic). EI-MS: *m/z* 207 (M<sup>+</sup>), 165 (M–43). Compound **1l**: <sup>1</sup>H NMR (DMSO): δ 2.35 (s, 3H, N-CH<sub>3</sub>), 2.55 (t, 2H, Ar-CH<sub>2</sub>-CH<sub>2</sub>-N-), 2.75 (t, 2H, Ar-CH<sub>2</sub>-CH<sub>2</sub>-N-), 3.36 (s, 2H, Ar-CH<sub>2</sub>-N-), 3.8 (s, 6H, -OCH<sub>3</sub>), 6.35 (s, 1H, Ar-H), 6.45 (s, 1H, aromatic). EI-MS: *m/z* 223 (M<sup>+</sup>), 207, (M–16).