

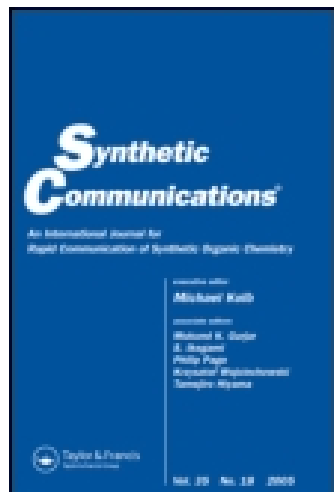
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Facile Deoxygenation of Amine-*N*-oxides With $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ –Indium System

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Abstract: $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}/\text{In}$ system was found to be a new reagent for deoxygenation of various amine-*N*-oxides to the corresponding amines in good to excellent yields under sonication.

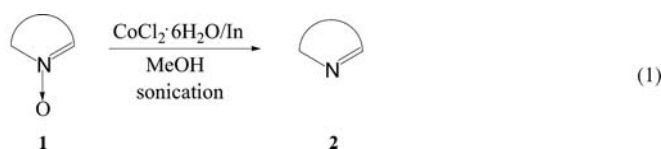
Keywords: Amine-*N*-oxides, cobalt, deoxygenation, indium

The deoxygenation of amine-*N*-oxides to amines is an important transformation in the synthesis of nitrogenous aromatic heterocycles.^[1] A number of methods have been described for the reduction of amine-*N*-oxides, including agents such as low-valent titanium,^[2] $\text{Zn}/\text{HCOONH}_4$,^[3] InCl_3 ,^[4] tributyltinhydride,^[5] Pd/C ,^[6] SmI_2 ,^[7] tetrathiomolybdate,^[8] and indium/ NH_4Cl .^[9] However, these deoxygenations often require prolonged reaction times and severe reaction conditions. Some of these are associated with limitations regarding selectivity and compatibility with other functional groups, are

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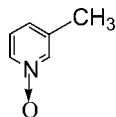
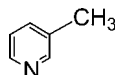
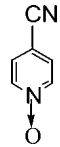
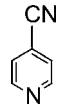
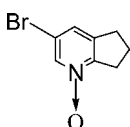
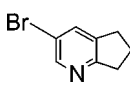
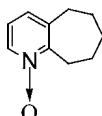
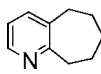
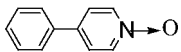
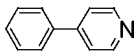
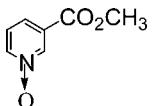
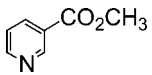
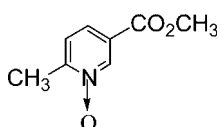
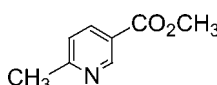
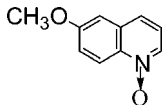
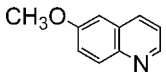
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hazardous, and are sensitive to both air and moisture. Consequently, there is still a need for introducing selective, mild, and cheap reagents for the deoxygenation of amine-*N*-oxides to amines. The reduction of CoCl_2 to low-valent cobalt species and the synthetic utility of such species are well documented in the literature.^[10] In continuation of our efforts to find low-valent metal reagents for organic transformations,^[11] we observed that a combination of CoCl_2 with indium could bring about the deoxygenation of amine-*N*-oxides



under mild conditions. To the best of our knowledge, to date there are no reports of the use of the $\text{CoCl}_2 \cdot 6\text{H}_2\text{O/In}$ system for the deoxygenation of amine-*N*-oxides in the literature. The new reducing system was generated by the addition of indium powder to a stirred solution of cobalt(II) chloride hexahydrate in MeOH under sonication. We herein report a mild and efficient method for the deoxygenation of amine-*N*-oxides using a $\text{CoCl}_2 \cdot 6\text{H}_2\text{O/In}$ system in MeOH. A variety of amine *N*-oxides were treated with the $\text{CoCl}_2 \cdot 6\text{H}_2\text{O/In}$ system, and the corresponding amines were obtained in high yields. The results are summarized in Table 1. The reactions proceed readily in all cases with substrates reacting completely within 2 h at room temperature. The optimum ratio of reagents was found to be 1:2:4 (substrate– CoCl_2 –indium). Some control experiments revealed that amine-*N*-oxides could not be deoxygenated by indium alone under the present reaction conditions, and starting materials were recovered unchanged. To explore the scope and limitation of this reagent system we have tested its applicability for selective deoxygenation of amine-*N*-oxides bearing other potentially sensitive functional groups in the heteroaromatic ring. The functional group tolerance of this deoxygenation system is evident from the table, which shows that cyano, bromo, ester, and methoxy substituents remain unchanged under the reaction conditions. However, the application of this procedure to aliphatic amine-*N*-oxide proved unsuccessful, and only the recovered starting material was isolated. We have been able to demonstrate the utility of an easily accessible $\text{CoCl}_2 \cdot 6\text{H}_2\text{O/In}$ system as a convenient reagent for effecting chemoselective deoxygenation of amine-*N*-oxides. All the compounds obtained showed IR, NMR, and mass spectral data compatible with the structure. Although the reaction mechanism is still unclear, it can be rationalized as the result of a two-stage process. In the first step, cobalt(II) chloride is probably reduced by indium to form low-valent cobalt species, which, in the subsequent step, would reductively deoxygenate amine-*N*-oxides **1** to give the corresponding amines **2**. The notable advantages of the present procedure are the mild reaction conditions,

Table 1. Deoxygenation of amine-*N*-oxides with $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}/\text{In}$ system

Entry	Substrate	Product	Reaction time (h)	Yield (%) ^a
1	Quinnoline- <i>N</i> -oxide	Quinnoline	2.0	92
2	Isoquinnoline- <i>N</i> -oxide	Isoquinnoline	2.0	90
3	4- <i>t</i> -Butylpyridine- <i>N</i> -oxide	4- <i>t</i> -Butylpyridine	2.0	85
4			2.0	90
5			1.5	95
6			2.0	90
7			2.0	85
8			1.5	91
9			0.5	88
10			2.0	80
11			1.0	82

^aIsolated yields.

the short reaction times, the excellent yields, and the tolerance of some labile functional groups.

In conclusion, we believe that the use of the $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}/\text{In}$ system offers an attractive alternative to the existing methods available for the

reduction of amine-*N*-oxides to the corresponding amines. Further investigations of the $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}/\text{In}$ system as a reducing agent in organic synthesis are currently in progress.

EXPERIMENTAL

The ^1H NMR spectra were recorded on an FT-Bruker AF-300 (300 MHz for ^1H NMR) using TMS as an internal standard. Infrared spectra were obtained on a Perkin Elmer 16F PC FT-IR Shimadzu. TLC analysis was performed on silica-gel plates (Merck, 60 F-254). All products were purified by flash column chromatography using silica gel 60 (79–230 mesh, Merck).

General Procedure for the Reaction

A typical procedure for the deoxygenation of amine-*N*-oxide is as follows: Indium powder (230 mg, 2.0 mmol), cobalt(II) chloride hexahydrate (238 mg, 1.0 mmol), and MeOH (1 mL) were mixed under sonication. The resulting mixture was stirred at room temperature for 1 h, and a solution of the low-valent cobalt–indium complex was obtained. 4-*tert*-Butylpyridine-*N*-oxide (76 mg, 0.5 mmol) was added dropwise to this solution. The reaction mixture was stirred for 2 h at room temperature under sonication. The solvent was evaporated under reduced pressure, and the residue was extracted with ether, washed with brine, and dried over anhydrous MgSO_4 . The crude product was purified by silica-gel column chromatography (hexane–ethyl acetate = 1:1) to afford 4-*tert*-butylpyridine (65 mg, 85%).

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