Mild and Efficient Deoxygenation of Amine-*N*-Oxides with Bis(cyclopentadienyl)titanium(IV) Dichloride-Indium System

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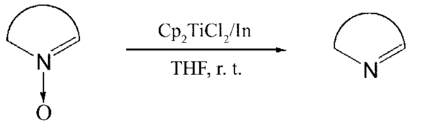
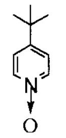
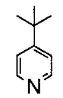
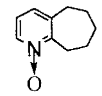
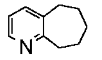
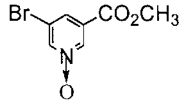
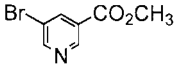
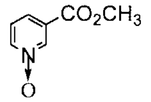
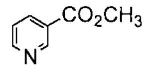
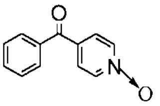
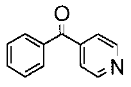
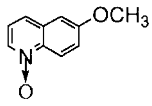
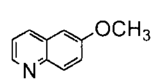
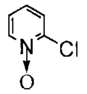
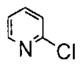
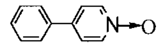
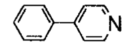
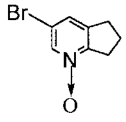
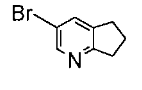
The deoxygenation of amine-*N*-oxides to amines in the presence of other functional groups is an important transformation in the synthesis of nitrogenous aromatic heterocycles.[1] Many reagents have been employed for the deoxygenation of amine-*N*-oxides, including agents such as: low-valent titanium,[2] phosphorous[3] and sulphur[4] compounds, tributyltin hydride,[5] Pd/C,[6] tetrathiomolybdate,[7] SmI_2,[8] indium/NH_4Cl.[9] The chemical reactivity of Cp_2TiCl_2/M system (M = Na, Zn, Al, Mg, Sm) has been the subject of considerable interest and the reducing ability of these systems has been extensively studied.[10] The reduction of Cp_2TiCl_2 to lower valent titanium species and the synthetic utility of such species are well documented in the literature.[11] Recently we reported that Cp_2TiCl_2/In system could be used for the debromination of various dibromides.[12] It is expected that Cp_2TiCl_2/In system can also be an efficient reagent for the deoxygenation of amine-*N*-oxides to amines. We have found that various amine-*N*-oxides **1** on treatment with Cp_2TiCl_2/In system in THF are smoothly converted into the corresponding amines **2** in good to excellent yields. The new reducing system was generated by the addition of indium powder to a stirred solution of bis(cyclopentadienyl)titanium(IV) dichloride in THF under nitrogen. The reactions can be generalized as in eq. (1). Some control experiments revealed that amine-*N*-oxides could not be deoxygenated by Cp_2TiCl_2 or indium alone and were recovered unchanged.



1 **2** (1)

In general, the reactions were fast in all cases with substrates reacting completely in less than 5 min at room temperature and excellent yields of the corresponding amines were realized. It was observed that 1 : 2 ratio of indium and Cp_2TiCl_2 was found to be the best ratio in terms of yield and reaction time.[13] In order to explore the scope and limitations of this reagent system we have tested its applicability for selective deoxygenation of aromatic-*N*-oxides bearing other potentially sensitive functional groups in the heteroaromatic ring. Extension of this method to aliphatic-*N*-oxides did not succeed. Neither longer reaction time nor more elevated temperature had any effect on the reaction. The results are outlined in Table 1. All the com-

Table 1. Deoxygenation of amine-*N*-oxides with Cp_2TiCl_2/In system

Entry	Substrate	Product	Reaction time (min)	Yield (%)[a]
1	3-Picoline-*N*-oxide	3-Picoline	5	93
2	Quinoline-*N*-oxide	Quinoline	5	92
3	Isoquinoline-*N*-oxide	Isoquinoline	5	86
4			5	95
5			5	85
6			5	87
7			5	91
8			5	88
9			5	95
10			5	85
11			5	90
12			5	95

[a]Isolated yields.

pounds obtained showed IR, NMR and mass spectral data compatible with the structure. We have been able to demonstrate the utility of easily accessible Cp_2TiCl_2/In system as a convenient reagent for effecting deoxygenation of amine-*N*-oxides. The functional group tolerance of this deoxygenation reaction is evident from entries 6-10 which show that bromo, ester, ketone, methoxy, and chloro remain unchanged under the reaction conditions. Although the reaction mechanism is still unclear, the reaction can be envisaged to proceed in two stages. In the first, bis(cyclopentadienyl)titanium(IV) dichloride is probably reduced by indium to form low-valent titanium species, which, in the subsequent step, would deoxygenate amine-*N*-oxides **1** to give the corresponding amines **2**. The notable advantages of the present methodology are the mild reaction conditions, the short reaction times, the excellent yields, the experimental simplicity, and the tolerance of some functional groups.

In conclusion, we have demonstrated that the deoxygenation of amine-*N*-oxides with Cp_2TiCl_2/In system provided various amines in good to excellent yields under the mild conditions. We believe that the mild, efficient method described here will present an attractive alternative to the existing methods available for the reduction of amine-*N*-oxides to the corresponding amines.

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13. A typical procedure for the deoxygenation of amine-*N*-oxide is as follows: Indium powder (115 mg, 1.0 mmol), bis(cyclopentadienyl)titanium(IV) dichloride (498 mg, 2.0 mmol) and THF (10 mL) were mixed under nitrogen atmosphere and the resulting mixture was stirred at reflux for 1 hr. A dark-red solution of the low-valent titanium-indium complex was obtained and cooled to room temperature. To this solution, 4-*tert*-butylpyridine-*N*-oxide (75 mg, 0.5 mmol) was added. The reaction mixture turned dark purple almost immediately and was stirred for 5 min at room temperature under nitrogen. The reaction solution was quenched with dilute HCl and the residue was extracted with ether, washed with water, dried over anhydrous $MgSO_4$. The crude product was purified by column chromatography on silica gel (hexane : ethylacetate = 1 : 1) to afford 4-*tert*-butylpyridine (64 mg, 95%).