

Communications

A Facile and Efficient Deoxygenation of Amine-*N*-oxides with WCl_6/NaI System

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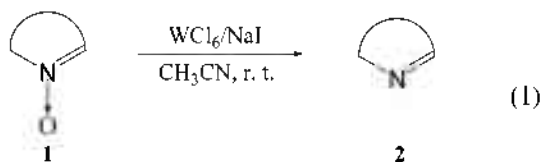
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The deoxygenation of amine-*N*-oxides to amines is an important transformation in the synthesis of nitrogenous aromatic heterocycles and an area of considerable interest, particularly when a molecule has other reducible or labile moieties.¹ A number of methods have been described for the reduction of amine-*N*-oxides, including agents such as low-valent titanium,² Zn/HCOONH₄,³ InCl₃,⁴ tributyltin-hydride,⁵ Pd/C,⁶ SmI₂,⁷ tetrathiomolybdate,⁸ indium/NH₄Cl,⁹ Mo(CO)₆.¹⁰ However, many of these methods are deficient in some respects such as relatively severe reaction conditions, low yields, poor selectivity or occurrence of side reactions. Consequently, there is still a need for introducing selective and mild reagents for the deoxygenation of amine-*N*-oxides to amines. In continuation of our efforts towards the development of the low-valent metal reagents for organic transformations,¹¹ we observed that a combination of WCl_6 with sodium iodide could bring about the deoxygenation of amine-*N*-oxides under mild conditions. The new reducing system was generated by the addition of sodium iodide to a stirred solution of tungsten hexachloride in acetonitrile under nitrogen atmosphere. In this communication, we wish to report an efficient and chemoselective method for the deoxygenation of various amine-*N*-oxides to the corresponding amines by treatment with WCl_6/NaI system in aceto-



nitrile. Some control experiments revealed that amine-*N*-oxides could not be deoxygenated by WCl_6 alone under the present reaction conditions and starting materials were recovered unchanged. The reactions proceeded smoothly in all cases with substrates reacting completely within 1-3 hrs at room temperature. Thin-layer chromatography of the crude reaction mixture showed the conversion to be almost quantitative. The optimum ratio of reagents was found to be 1:2:4 (WCl_6 :substrate:NaI).¹² In order to explore the scope and limitation of this reagent system we have tested its applicability for selective deoxygenation of amine-*N*-oxides

Table 1. Deoxygenation of amine-*N*-oxides with WCl_6/NaI system

Entry	Substrate	Product	Reaction Time (hr)	Yield (%) ^a
1	3-Picoline- <i>N</i> -oxide	3-Picoline	1.0	94
2	Quinoline- <i>N</i> -oxide	Quinoline	1.5	91
3	Isoquinoline- <i>N</i> -oxide	Isoquinoline	2.0	88
4	4- <i>t</i> -Butylpyridine- <i>N</i> -oxide	4- <i>t</i> -Butylpyridine	1.0	95
5			2.0	89
6			3.0	86
7			1.5	90
8			2.0	87
9			1.0	94
10			2.5	86
11			2.0	90
12			2.0	85
13			1.0	92

^aIsolated yields.

bearing other potentially sensitive functional groups in the heteroaromatic ring. The functional group tolerance of this deoxygenation system is evident from entries 5-12 which show that cyano, bromo, ester, amide, methoxy, and chloro substituents remain unchanged under the reaction conditions. The generality of the reaction with various amine-*N*-oxides is illustrated in Table 1. However, the application of

this procedure to aliphatic amine-*N*-oxide proved unsuccessful and only recovered starting material was isolated. We have been able to demonstrate the utility of easily accessible WCl_6/NaI 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 mechanism of this reaction is still unclear, it can be rationalized as the result of a two-stage process. In the first step, tungsten(VI) chloride is probably reduced by sodium iodide to form low-valent tungsten species, which, in the subsequent step, would reductively deoxygenate amine-*N*-oxides **1** to give the corresponding amines **2**.¹³ The notable advantages of the present methodology are the mild reaction conditions, the high yields, the experimental simplicity, and the tolerance of some functional groups.

In conclusion, we have demonstrated that the procedure using WCl_6/NaI system described here provides a useful alternative to the other presently used procedures since the deoxygenation of amine-*N*-oxides proceeds selectively and in high yields under mild conditions. Further investigations of WCl_6/NaI system as reducing agent in organic synthesis are currently in progress.

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- A typical procedure for the deoxygenation of amine-*N*-oxide is as follows: Sodium iodide (300 mg, 2.0 mmol), tungsten hexachloride (136 mg, 0.5 mmol) and CH_3CN (10 mL) were mixed under nitrogen atmosphere and the resulting mixture was stirred at room temperature for 30 min. To this solution, 4-*tert*-butylpyridine-*N*-oxide (151 mg, 1.0 mmol) was added. The reaction mixture was stirred for 1 hr at room temperature under nitrogen. The reaction solution was quenched with water 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 (129 mg, 95%).
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