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A facile and efficient deoxygenation of amine-*N*-oxides with $Mo(CO)_6$

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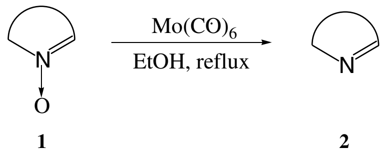
Abstract—A variety of amine-*N*-oxides have been found to be selectively deoxygenated to the corresponding amines in high yields with $Mo(CO)_6$ in ethanol under mild conditions.

The deoxygenation of amine-*N*-oxides to amines has received much attention, being an important step in the synthesis of heterocycles in many procedures.[1] A number of methods have been developed for the reduction of amine-*N*-oxides, including agents such as low-valent titanium,[2] phosphorous compounds,[3] Zn/$HCOONH_4$,[4] $InCl_3$,[5] tributyltinhydride,[6] Pd/C,[7] SmI_2,[8] tetrathiomolybdate,[9] indium/NH_4Cl.[10] However, many are associated with limitations regarding incompatibility with other functional groups, low yields, harsh reaction conditions and intricate procedures. In certain cases, the reagents required are expensive. Therefore, there is still a need for introducing selective, simple and cheap reagents for the deoxygenation of amine-*N*-oxides to amines. We herein wish to report a simple and efficient deoxygenation method for amine-*N*-oxides using the cheap metal carbonyl, molybdenum hexacarbonyl [$Mo(CO)_6$] under mild conditions. The chemistry of $Mo(CO)_6$ is one of the current interests in organic synthesis due to the ease of handling, mild reaction conditions and availability (it is commercially available as a stable crystalline solid).[11] Particularly, $Mo(CO)_6$ has been used to reduce the N–O bonds of isoxazoles,[12] isoxazolines,[13] isoxazolidines[14] and 1,2-oxazines.[15] The selective reduction of azides, nitro compounds and deoxygenation of epoxides have also been accomplished.[16] To the best of our knowledge, there have been no previous studies on the deoxygenation of amine-*N*-oxides with $Mo(CO)_6$. We envisaged that $Mo(CO)_6$ could bring about the deoxygenation of amine-*N*-oxides under mild conditions. A variety of amine *N*-oxides are selectively deoxygenated to the corresponding amines in high yields (80–96%) by simply heating the substrate in the presence of stoichiometric quantity of $Mo(CO)_6$ (Eq. 1) in ethanol.[17] The results are presented in Table 1. The reactions proceed readily in all cases with substrates reacting completely within 4 h in refluxing ethanol. In order to explore the scope and limitation of this reagent, 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 reagent is evident from the table, which shows that nitrile, bromo, chloro, hydroxy, ester and amide substituents remain unchanged under the reaction conditions. We have been able to demonstrate the utility of easily accessible $Mo(CO)_6$ as a convenient reagent for effecting chemoselective deoxygenation of various amine-*N*-oxides. All the compounds obtained showed IR, NMR and mass spectral data compatible with the structure. Although the mechanism of the reaction is not yet clarified, it can be rationalized as the result of a two-stage process. A plausible mechanism for the reductive N–O bond



(1)

Keywords: Deoxygenation; Amine-*N*-oxides; Amine; $Mo(CO)_6$.

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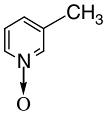
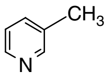
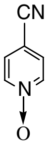
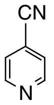
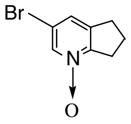
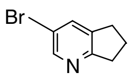
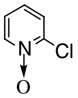
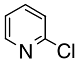
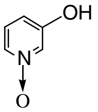
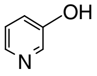
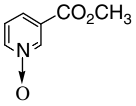
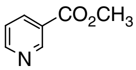
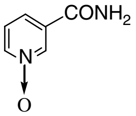
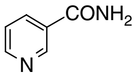
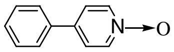
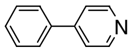
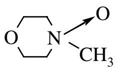
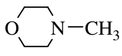
Table 1. Deoxygenation of amine-*N*-oxides with $Mo(CO)_6$

Entry	Substrate	Product	Time (h)	Yields (%)[a]
1	Pyridine-*N*-oxide	Pyridine	1.0	96
2	Quinoline-*N*-oxide	Quinoline	3.0	92
3	Isoquinoline-*N*-oxide	Isoquinoline	4.0	85
4			1.0	90
5			2.0	95
6			2.0	92
7			1.0	85
8			2.0	83
9			1.0	82
10			2.0	80
11			4.0	93
12			2.0	88

[a] Isolated yields.

cleavage of amine-*N*-oxide is outlined in Scheme 1, using pyridine-*N*-oxide as the substrate. In the first step, the reaction was assumed to proceed by loss of CO. Then the oxygen of the amine-*N*-oxide coordinates to $Mo(CO)_6$ to give complex **3** and facilitate the N–O bond cleavage. In a subsequent step, cleavage of the N–O bond leads to the formation of the corresponding amine. The notable advantages of the present procedure are the ease of manipulation, the high yields, the mild reaction conditions and the tolerance of several labile functional groups.

In conclusion, we believe that the use of $Mo(CO)_6$ offers an attractive alternative to the currently available methods for the deoxygenation of amine-*N*-oxides to the corresponding amines. Further studies to develop other new reactions using $Mo(CO)_6$ are currently in progress.

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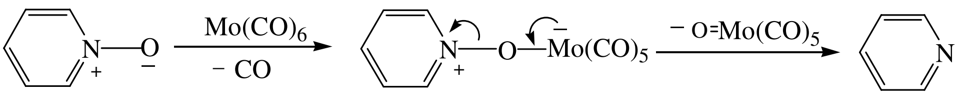
17. A typical procedure for the deoxygenation of amine-*N*-oxide is as follows: To a solution of 4-cyanopyridine-*N*-oxide (120 mg, 1.0 mmol) in ethanol (10 mL) is added $Mo(CO)_6$ (264 mg, 1.0 mmol). The mixture was refluxed for 2 h and monitored by TLC. After completion of the reaction, the resulting mixture was concentrated under reduced pressure, extracted with ether, concentrated and the residue was purified by silica gel column chromatography (hexane/ethyl acetate = 1:1) to afford 4-cyanopyridine (99 mg, 95%).



3

Scheme 1.