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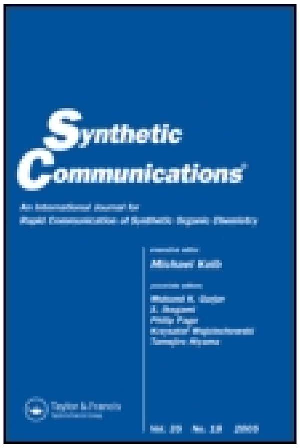

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An Efficient Deoxygenation of Heteroaromatic *N*-Oxides Using Zinc Dust/Ammonium Formate Reagent System

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ABSTRACT

Heteroaromatic *N*-oxides were readily and selectively deoxygenated to the corresponding bases with zinc/ammonium formate reagent system.

Key Words: Deoxygenation; *N*-Oxide; Ammonium formate.

Selective, mild, and cheap deoxygenation of amine *N*-oxides is still area of considerable interest, particularly when a molecule has other reducible and labile groups. A survey of the literature reveals that many methods have been reported for reduction of hetroaromatic *N*-oxides,

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including agents such as: trivalent phosphorus compounds,[1,2] sulphur or selenium compounds,[3,4] metals in acids,[5] aluminium iodide,[6] and catalytic hydrogenation.[7] In general, these traditional procedures often require severe reaction conditions and prolonged reaction times, and afford products of insufficient purity in moderate or low yield. Previously, we reported that amine *N*-oxides may be easily and efficiently reduced to the corresponding bases with low-valent titanium, generated through the reaction $TiCl_4$ with lithium aluminium hydride[8] or stannous chloride[9] in tetrahydrofuran.

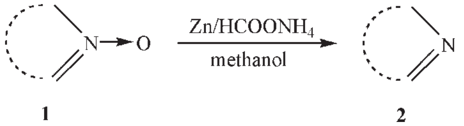
Excellent results were obtained when the deoxygenation of amine *N*-oxides was performed in neutral medium using some hydrogen transfer agents in the presence of palladium on carbon as catalyst.[10,11] However, our last methods appear to be inappropriate for large-scale preparation due to necessity of using $LiAlH_4$ or expensive palladium.

In this communication we report a new and efficient method for deoxygenation of the N–O function to the corresponding bases using zinc dust/ammonium formate reagent system. The application of this cheap and simple agent was till now limited to the reduction of nitro group[12] and reductive cleavage of azo compounds.[13] A variety of amine *N*-oxides were treated with zinc dust/ammonium formate system, and the corresponding bases were obtained in high yields; the results are summarized in Table 1. The reaction proceeds readily upon addition of anhydrous ammonium formate to a suspention of *N*-oxide and activated zinc dust in boiling methanol within 2–7 h. The optimum ratio reagent was found to be 1:3:2 (substrate **1**/ammonium formate/ zinc dust) for monooxides (**1a–l**) or 1:6:4 for dioxides (**1m**,**n**). Acetic acid is also acceptable solvent in some cases, but the reaction was slower in this medium. Among the metals tested, zinc appear to be the most effective, while magnesium and iron powder gave much lower yields. The selectivity of our method is demonstrated by several examples. Substituents, like halogen (**1b**,**d**), methoxy (**1g**), cyano (**1h**), acetyl (**1f**) or esters (**1i**,**j**) remained unchanged; however nitro group (**1e**) was easily reduced under the reaction conditions to 4-aminopyridine.

The progress of the reaction was monitored by TLC, and the corresponding products **2** were isolated by the usual work-up and identified by IR, MS, and TLC.

We believe that the present procedure offers an attractive alternative for other method available for the reduction of *N*-oxides. Its principal advantages are: the ease of manipulation, mild reaction conditions, selectivity, cheap reagents, and good yields for a wide variety of heteroaromatic *N*-oxides.

Table 1. Deoxygenation of heteroaromatic *N*-oxides using zinc dust/ammonium formate reagent system.



1 **2**

Substrate		Reaction time (h)	Product[a]		Yield[b] (%)
1a	4-*t*-Butylpyridine *N*-oxide	4	**2a**	4-*t*-Butylpyridine	81
1b	4-Chloropyridine *N*-oxide	3	**2b**	4-Chloropyridine	85
1c	3-Picoline *N*-oxide	5	**2c**	3-Picoline	77
1d	3,5-Dibromopyridine *N*-oxide	3	**2d**	3,5-Dibromopyridine	72
1e	4-Nitropyridine *N*-oxide	5	**2e**	4-Aminopyridine	70
1f	3-Acetylpyridine *N*-oxide	6	**2f**	3-Acetylpyridine	65
1g	3-Methoxypyridine *N*-oxide	6	**2g**	3-Methoxypyridine	68
1h	4-Pyridinecarbonitrile *N*-oxide	5	**2h**	4-Pyridinecarbonitrile	54
1i	Methyl isonicotinate *N*-oxide	3	**2i**	4-Carbomethoxypyridine	78
1j	Methyl nicotinate *N*-oxide	4	**2j**	3-Carbomethoxypyridine	76
1k	Quinoline *N*-oxide	3	**2k**	Quinoline	81
1l	Isoquinoline *N*-oxide	4	**2l**	Isoquinoline	76
1m	Phenazine *N*,*N*-dioxide	7	**2m**	Phenazine	62
1n	2,2′-Bipyridine *N*,*N*′-dioxide	6	**2n**	2,2′-Bipyridine	69

[a] All products are commercially available and were identified by comparison of their IR and MS spectra as well as their R_r values (TLC) with those of authentic samples.

[b] Yield of isolated product based on a single experiment and not optimized.

EXPERIMENTAL

Infrared spectra were obtained on a Beckman 4240 spectrophotometer and MS spectra was recorded on a LKB-9000A instrument.

Deoxygenation of *N*-Oxides (General Procedure)

To a magnetically stirred suspension of the appropriate amine *N*-oxides **1** (2 mmol for monooxides or 1 mmol for dioxides) and freshly activated zinc dust (4 mmol) in methanol (8 mL) was introduced anhydrous ammonium formate (6 mmol). The resulting reaction mixture was refluxed for 2–6 h. The catalyst was then removed by filtration through celite and washed with methanol (2 mL). The residue obtained by evaporation of solvent was purified by flash column chromatography on silica gel (eluent:hexane/AcOEt, 8:1) or crystallized to give pure product **2**. The results are summarized in Table 1.

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