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# A Mild Deoxygenation of Heteroaromatic N-Oxides by Formamidinesulfinic Acid

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**Summary.** Various heteroaromatic N-oxides were efficiently deoxygenated to the corresponding bases under mild conditions using formamidinesulfinic acid (thiourea S,S-dioxide).

**Keywords.** Deoxygenations; Amine N-oxides; Thiourea S,S-dioxide.

## Introduction

Many reports on the deoxygenation of heteroaromatic N-oxides, which are important in the synthesis of nitrogen containing heterocyclic compounds, exist in literature [1]. For example, metals in acids [2–3], various selenium and sulfur compounds [4–5], trivalent phosphorous compounds [6–7], zinc in sodium hydroxide [8], low-valent titanium reagents [9], aluminum iodide [10], and catalytic hydrogenation [11] have been utilized for the deoxygenation of amine N-oxides. Many of these methods are deficient with respect to costs, availability of reagents, reaction conditions, yields, or reaction time.

In connection with another investigation we have required a satisfactory route for the simple reduction of the N-oxide function of an N-heteroaromatic ring. Exellent results have been previously obtained when the deoxygenation was carried out in a neutral medium using hydrogen transfer agents in the presence of palladium on carbon [12]. However, the methodology described has appeared to be inappropriate for large-scale preparations due to the necessity of using the expensive palladium catalyst.

In this communication, we report a new and efficient method for the deoxygenation of amine N-oxides to the corresponding bases using formamidinesulfinic acid [13, 14]. This agent, which is easily prepared by the oxidation of thiourea with hydrogen peroxide, is known to be a strong reducing compound for inorganic metal ions [15]. However, its application in organic synthesis is rather limited to the reduction of nitro groups [16], sulfoxides [17], or carbonyl compounds [18].

## Results and Discussion

A variety of heteroaromatic N-oxides were treated with thiourea dioxide, and the corresponding amines were obtained in high to excellent yields; the results are

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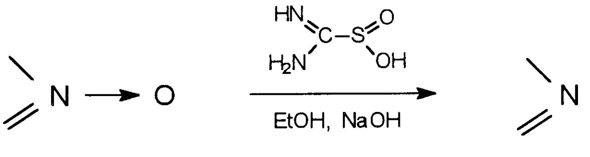
**Table 1.** Deoxygenation of heteroaromatic N-oxides by formamidinesulfinic acid (thiourea dioxide)



1 2

| Substrate | | Reaction time/h | Product[a] | | Yield[b]/% |
|---|---|---|---|---|---|
| **1a** | 4-*t*-butylpyridine N-oxide | 1,0 | **2a** | 4-*t*-butylpyridine | 84 |
| **1b** | 2,6-dimethylpyridine N-oxide | 1,5 | **2b** | 2,6-dimethylpyridine | 85 |
| **1c** | 4-acetylpyridine N-oxide | 3,5 | **2c** | 4-acetylpyridine | 52 |
| **1d** | 4-pyridinecarbonitrile N-oxide | 3,5 | **2d** | 4-pyridinecarbonitrile | 66 |
| **1e** | 4-chloropyridine N-oxide | 1,5 | **2e** | 4-chloropyridine | 80 |
| **1f** | 3,5-dibromopyridine N-oxide | 2,0 | **2f** | 3,5-dibromopyridine | 81 |
| **1g** | 3-methoxypyridine N-oxide | 2,5 | **2g** | 3-methoxypyridine | 82 |
| **1h** | 4-nitropyridine N-oxide | 4,0 | **2h** | 4-aminopyridine | 63 |
| **1i** | quinoline N-oxide | 2,0 | **2i** | quinoline | 90 |
| **1j** | isoquinoline N-oxide | 2,5 | **2j** | isoquinoline | 86 |
| **1k** | acridine N-oxide | 3,0 | **2k** | acridine | 74 |
| **1l** | 2,2′-bipyridine N,N-dioxide | 1,5 | **2l** | 2,2′-bipyridine | 80 |
| **1m** | 4,4′-bipyridine N,N-dioxide | 1,5 | **2m** | 4,4′-bipyridine | 81 |
| **1n** | phenazine N,N-dioxide | 3,0 | **2n** | phenazine | 76 |

[a] All products are commercially available and were characterized by comparison of their IR and MS spectra as well as their $R_f$ values (TLC) with those of authentic samples; [b] yield of isolated product based on a single experiment and not optimized

summarized in Table 1. The reaction is very simple and proceeds upon addition of thiourea dioxide to a suspension of N-oxide and 3 *N* sodium hydroxide in ethanol at 80–85°C. The optimum ratio of reagents was found to be 1:2 (substrate **1** to thiourea dioxide) or 1:4 when the substrate **1** contained two N→O moieties (**1l**,**n**). Acetonitrile is also an acceptable solvent in some cases, but the reaction was slower in this medium. Among the alkali tested, NaOH was the most effective, although KOH gave also good results. The selectivity of our method is demonstrated by several examples. Substituents like halogen (**1e**,**f**), methoxy (**1g**), cyano (**1d**), or acetyl (**1c**) remained unaffected; however, the nitro group (**1h**) was reduced under the reaction conditions giving 4-aminopyridine contaminated by side-products. After completion of the reaction the corresponding amines were isolated by the usual work-up and identified by IR, MS, and TLC.

In conclusion, we believe that the present procedure offers an attractive alternative to other methods available for the reduction of N-oxides. Its principal advantages are ease of manipulation, relatively smooth reaction conditions, selectivity, mild reagents, and high yields for a wide variety of heteroaromatic N-oxides.

## Experimental

IR spectra were obtained on a Beckman 4240 spectrophotometer, mass spectra were recorded on a LKB-9000A instrument. Formamidinesulfinic acid (thiourea dioxide) is commercially available.

*Deoxygenation of N-oxides (general procedure)*

A mixture of N-oxide **1** (4 mmol for monooxides or 2 mmol for dioxides), 10 $cm^3$ 3 *N* sodium hydroxide, and 12 $cm^3$ ethanol was stirred at 80–85°C. Thiourea dioxide (0.864 g, 8 mmol) was then added portionwise over 5 min, and the mixture was stirred for 1–4 h before being poured into $H_2O$. The aqueous solution was extracted continuously with $CH_2Cl_2$ or $CHCl_3$. The combined organic layers were washed with $H_2O$, the solvent was removed, and the residue was purified by flash chromatography on silica gel (eluent:hexane/ethyl acetate = 9:1) to give the pure base **2**. The results are summarized in Table 1.

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