

A NEW METHOD FOR DEOXYGENATION OF TERTIARY AMINE
N-OXIDES WITH ACETIC FORMIC ANHYDRIDE

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Trialkylamine N-oxides and N,N-dialkylarylamine N-oxides were readily deoxygenated with acetic formic anhydride in dichloromethane at room temperature to give the corresponding tertiary amines in high yields, while heteroaromatic N-oxide and sulfoxides were not affected.

Although many methods for deoxygenation of amine N-oxides have been reported such as trivalent phosphorus compounds, sulfur compounds, metal hydrides, dissolving metals,¹⁾ photochemical deoxygenation,²⁾ in situ generated sulfur monoxide,³⁾ a combination of sulfur dioxide and trialkylamine,⁴⁾ phosphorus tetraiodide,⁵⁾ chlorotrimethylsilane/sodium iodide/zinc,⁶⁾ and carbon disulfide,⁷⁾ most of them have disadvantages due to their rather severe reaction conditions and/or intricate procedure. Furthermore their application has been mostly limited to the reduction of heteroaromatic N-oxides and very few examples have been reported on aliphatic and aromatic amine N-oxides.

We now wish to report here a new and simple deoxygenation method for tertiary amine N-oxides via their formyloxylammonium salts under very mild reaction conditions.⁸⁾ Thus, trialkylamine N-oxides or N,N-dialkylarylamine N-oxides **1** reacted with acetic formic anhydride (AFA), which is known as a good formylating reagent,⁹⁾ in dichloromethane to give the corresponding tertiary amines **3** in excellent yields.

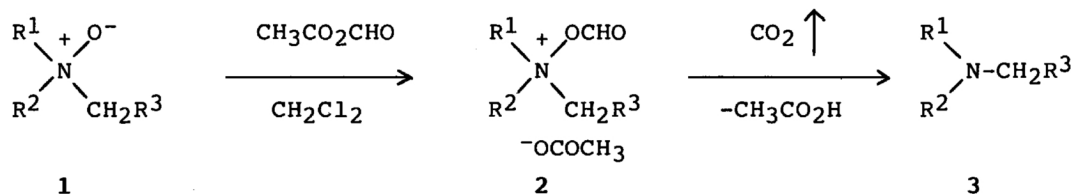
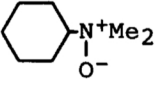
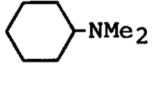
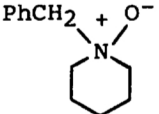
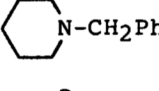
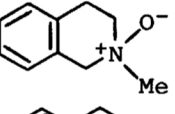
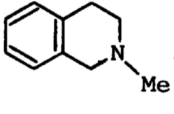
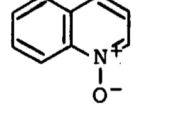
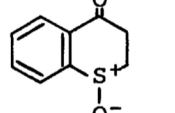


Table 1. Deoxygenation of Amine N-Oxides with Acetic Formic Anhydride (AFA)

Entry	N-Oxide	AFA equiv.	Solv.	Temp/°C	Products	Yield/% ^{a)}
1	$(\text{PhCH}_2)_3\text{N}^+\text{O}^-$ 1a	2.5	CH_2Cl_2	0 — r.t.	$(\text{PhCH}_2)_3\text{N}$ 3a	93
2	 1b	2.5	CH_2Cl_2	0 — r.t.	 3b	100
3	 1c	2.5	CH_2Cl_2	0 — r.t.	 3c	95
4	$\text{Ph-N}^+\text{Me}_2\text{O}^-$ 1d	2.5	CH_2Cl_2	0 — r.t.	Ph-NMe_2 3d	97 ^{b)}
5	$\text{PhCH}_2\text{-N}^+\text{Me}_2\text{O}^-$ 1e	2.5	CH_2Cl_2	0 — r.t.	$\text{PhCH}_2\text{-NMe}_2$ 3e	88 ^{c)}
6	 1f	2.5	CH_2Cl_2	0 — r.t.	 3f	69 ^{c)}
7	 1g	5.0	$(\text{CH}_2\text{Cl})_2$	0 — reflux	no reaction	
8	 4	3.0	$(\text{CH}_2\text{Cl})_2$	0 — reflux	no reaction	
9	$\text{Bu}^n\text{-S}^+\text{-Bu}^n\text{O}^-$ 5	3.0	$(\text{CH}_2\text{Cl})_2$	0 — reflux	no reaction ^{d)}	
10	$\left. \begin{array}{l} \text{1a} \\ \text{5} \end{array} \right\} \text{mixture}$	3.0	CH_2Cl_2	0 — r.t.	$\left\{ \begin{array}{l} \text{3a} \\ \text{5} \end{array} \right.$	$\left\{ \begin{array}{l} 97 \\ 97 \end{array} \right.$
11	$\text{Ph-CH=N}^+\text{-MeO}^-$ 6	3.0	CH_2Cl_2	reflux	Ph-CH=N-Me	100 ^{e)}

a) Isolated yield after Al_2O_3 short column chromatography. b) See Ref. 10. c) See Ref. 11. d) 93% of dibutyl sulfoxide (5) was recovered. e) See Ref. 12.

A typical example is as follows: To a solution of tribenzylamine N-oxide (**1a**, 303 mg, 1 mmol) in 15 ml of dichloromethane was added AFA (220 mg, 2.5 mmol) by means of a syringe at 0 °C. After stirring for 2 h at room temperature, the mixture was condensed by rotary evaporator and the residue was directly subjected to a short column chromatography on alumina with hexane-ether (3:1) as an eluent to give 267 mg (93%) of pure tribenzylamine (**3a**), the spectral data of which were identical with those of the authentic sample. The results obtained from the reactions of other amine N-oxides and related compounds are summarized in Table 1.¹³⁾ In all cases the corresponding tertiary amines were obtained in high yields except for the case of quinoline N-oxide (**1g**), a typical heteroaromatic N-oxide.

This deoxygenation reaction is considered to proceed via initially formed formyloxyammonium salts **2** which lead to the amines **3** by the subsequent decarboxylative fragmentation. The evolution of a gas was confirmed upon the addition of AFA. The instability of **2** leading to the facile conversion into **3** is in a sharp contrast to the stability of the acetyloxyammonium salts in the Polonovski reaction¹⁴⁾ which enables the base-promoted rearrangement into α -acetyloxyamines and subsequent dealkylation.

Of particular note on this deoxygenation reaction is its high chemoselectivity toward tertiary amine N-oxides. Although some kinds of heteroaromatic N-oxide and sulfoxides were treated with AFA, they were not affected even in refluxing 1,2-dichloroethane as shown in the Table (entries 7-9). Furthermore, when a mixture of tribenzylamine N-oxide (**1a**) and dibutyl sulfoxide (**5**) was treated with AFA in dichloromethane at room temperature, the former was deoxygenated to tribenzylamine (**3a**) almost quantitatively while the latter was recovered unchanged (entry 10).

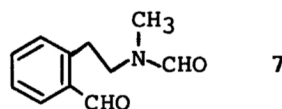
In conclusion, a new and convenient method for deoxygenation of tertiary amine N-oxides has been established. We believe that this new reduction of amine N-oxides will be useful for the synthesis of nitrogen-containing natural products because of its experimental simplicity, mild reaction conditions, and high chemoselectivity toward tertiary amine N-oxides.

References

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- 8) Although some examples of oxidative decarboxylation of acid anhydrides using pyridine N-oxide derivatives have been reported, they were limited to the investigation of the oxidizing ability of heteroaromatic N-oxides and can not

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- 10) Although in the case of N,N-dimethylaniline N-oxide (**1d**) the Polonovski reaction using acetic anhydride gives mainly o-acetyl rearrangement product, the reduction of **1d** by AFA proceeded quantitatively.
- 11) In the case of **1e** and **1f**, the formyl Polonovski-type reaction products such as benzaldehyde and **7** were obtained as by-products in 10 and 30% yields, respectively.



- 12) While an N-alkylnitrone such as **6** was reduced by AFA in refluxing dichloromethane almost quantitatively, N-arylnitrones gave a complex mixture under similar reaction conditions.
- 13) All the products described here showed satisfactory spectral data ($^1\text{H-NMR}$, $^{13}\text{C-NMR}$, and MS spectra) which were identical with those of the authentic samples.
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