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

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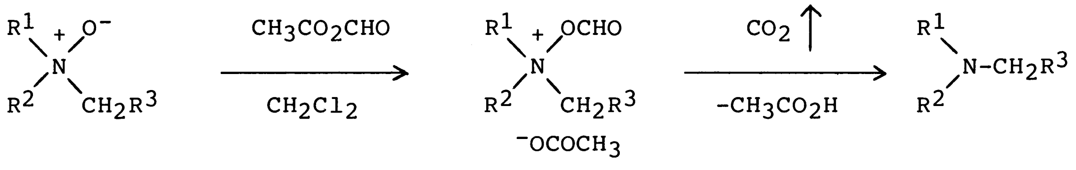
Trialkylamine N-oxides and N,N-dialkylarylamine N-oxides were readily deoxygenated with acetic formic anhydride in dichloromethane at room temperature to give the corresponding tertiary amines in high yields, while heteroaromatic N-oxide and sulfoxides were not affected.

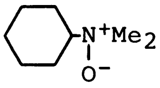
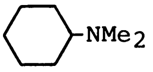
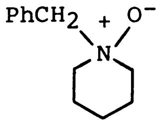
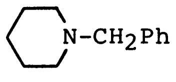
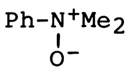
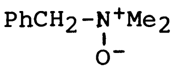
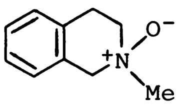
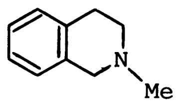
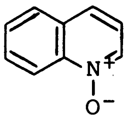
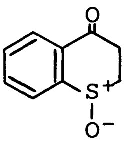
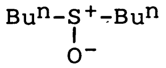
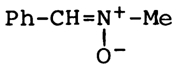
Although many methods for deoxygenation of amine N-oxides have been reported such as trivalent phosphorus compounds, sulfur compounds, metal hydrides, dissolving metals,1) photochemical deoxygenation,2) in situ generated sulfur monoxide,3) a combination of sulfur dioxide and trialkylamine,4) phosphorus 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 formyloxyammonium 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.



1 **2** **3**

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

Entry	N-Oxide	AFA equiv.	Solv.	Temp/°C	Products	Yield/%[a]
1	$(PhCH_2)_3N^+\text{-}O^-$ **1a**	2.5	CH_2Cl_2	0 — r.t.	$(PhCH_2)_3N$ **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	 $\mathrm{Ph{-}}\underset{\mathrm{O^-}}{\underset{\vert}{\mathrm{N}}}{}^{+}\mathrm{Me_2}$ **1d**	2.5	CH_2Cl_2	0 — r.t.	$Ph\text{-}NMe_2$ **3d**	97[b]
5	 $\mathrm{PhCH_2{-}}\underset{\mathrm{O^-}}{\underset{\vert}{\mathrm{N}}}{}^{+}\mathrm{Me_2}$ **1e**	2.5	CH_2Cl_2	0 — r.t.	$PhCH_2\text{-}NMe_2$ **3e**	88[c]
6	 **1f**	2.5	CH_2Cl_2	0 — r.t.	 **3f**	69[c]
7	 **1g**	5.0	$(CH_2Cl)_2$	0 — reflux	no reaction	
8	 **4**	3.0	$(CH_2Cl)_2$	0 — reflux	no reaction	
9	 $\mathrm{Bu^n{-}}\underset{\mathrm{O^-}}{\underset{\vert}{\mathrm{S}}}{}^{+}\mathrm{{-}Bu^n}$ **5**	3.0	$(CH_2Cl)_2$	0 — reflux	no reaction[d]	
10	**1a** **5** } mixture	3.0	CH_2Cl_2	0 — r.t.	**3a** **5**	97 97
11	 $\mathrm{Ph{-}CH{=}}\underset{\mathrm{O^-}}{\underset{\vert}{\mathrm{N}}}{}^{+}\mathrm{{-}Me}$ **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 reaction[14) 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.

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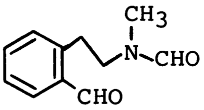
6) T. Morita, K. Kuroda, Y. Okamoto, and H. Sakurai, Chem. Lett., 1981, 921.
7) T. Yoshimura, K. Asada, and S. Oae, Bull. Chem. Soc. Jpn., 55, 3000 (1982).
8) Although some examples of oxidative decarboxylation of acid anhydrides using pyridine N-oxide derivatives have been reported, they were limited to the investigation of the oxidizing ability of heteroaromatic N-oxides and can not

be practically used for deoxygenation of amine N-oxides. C. Rüchardt, S. Eichler, and O. Krätz, Tetrahedron Lett., 1965, 233; T. Cohen, I. H. Song, and J. H. Frager, ibid., 1965, 237.

9) I. Muramatsu, M. Murakami, T. Yoneda, and A. Hagitani, Bull. Chem. Soc. Jpn., 38, 244 (1965).

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.



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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}H-NMR, ^{13}C-NMR, and MS spectra) which were identical with those of the authentic samples.

14) M. Polonovski and M. Polonovski, Bull. Chim. Soc. Fr., 41, 1190 (1927); For reviews, see G. A. Russell and J. G. Mikol, "Mechanism of Molecular Migrations," ed by B. S. Tyagarajan, Interscience, New York (1968), Vol. 1, p. 176; A. R. Katritzky and J. N. Lagowski, "Chemistry of Heterocyclic N-Oxides," Academic Press, New York (1971), pp. 279 and 362.

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