

Efficient Deoxygenation of Heteroaromatic *N*-Oxides with Ammonium Formate as a Catalytic Hydrogen Transfer Agent

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Ammonium formate catalytic transfer hydrogenation in the presence of 10% palladium on carbon has shown utility for mild and excellent deoxygenation of heteroaromatic *N*-oxides in neutral medium.

Since early seventies it is known¹⁻⁴ that formic acid and their salts can be utilized as active hydrogen donors for transfer hydrogenation in the presence of palladium on carbon as catalyst. This way, azides,⁵ aromatic^{3,4,6} and aliphatic⁶ nitro compounds as well as carbonyl groups⁷ have been successfully reduced to the corresponding amines or hydrocarbons, respectively.⁸ In connection with other work, we have required a satisfactory route for mild deoxygenation of the *N*-oxide function on the pyridine ring. We therefore tested several hydrogen transfer agents to achieve this goal.

A large number of methods have been described for the reduction of amine *N*-oxides, including agents such as: trivalent phosphorus compounds,^{9,10} various sulfur and selenium compounds,¹¹⁻¹³ iron in acid,¹⁴ titanium trichloride in aqueous solution,¹⁵ titanium tetrachloride in the presence of magnesium,¹⁶ sodium borohydride,¹⁷ lithium aluminum hydride,¹⁸ stannous chloride,¹⁹ and catalytic hydrogenation.²⁰

Many of these methods are deficient in some respects, such as: low yields, expensive or not readily available reagents, severe reaction conditions, or difficulties with isolation of the product.

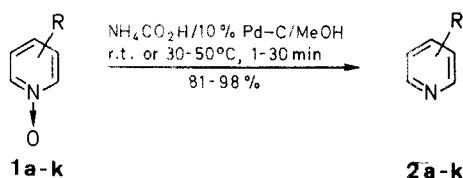


Table. Deoxygenation of Heteroaromatic *N*-Oxides with Ammonium Formate

Substrate ^a	R	Reaction Conditions		Product ^b	Yield ^c
		Temp. (°C)	Time (min)		
1a	4-CH ₃	r. t.	10	2a	94
1b	2-CH ₃	r. t.	15	2b	90
1c ²¹	4- <i>t</i> -Bu	r. t.	10	2c	97
1d ²²	4-CO ₂ Me	r. t.	< 1	2d	98
1e ²³	3-CO ₂ Me	r. t.	< 1	2e	98
1f ²⁴	4-CN	40	20	2f	85
1g ²⁵	4-CO ₂ H	30	15	2g	90
1h ²⁶	3-OMe	40	20	2h	81
1i	^d	40	20	2i	88
1j	^e	40	15	2j	96
1k ²⁷	^f	50	30	2k	85

^a *N*-Oxides listed without indication to a reference are commercially available.

^b All products are commercially available and were characterized by comparison of their TLC, IR, and mass spectra with authentic samples.

^c Yield of isolated product.

^d Quinoline *N*-oxide.

^e Isoquinoline *N*-oxide.

^f Acridine *N*-oxide.

In this communication we report a facile and efficient deoxygenation of heteroaromatic *N*-oxides into the respective bases using catalytic transfer hydrogenation with ammonium formate as the hydrogen source, in the presence of palladium on carbon.

The reaction is carried out in methanolic solution and in most cases the reaction is over within 1 to 20 min at room temperature. In the case of *N*-oxides containing ester groups, an exothermic reaction takes place, and the products were formed immediately.

The selectivity of our method is demonstrated by several examples. Such reducible substituents as methoxycarbonyl, methoxy, carboxyl, and cyano remain unchanged, however, nitro or halo groups are readily reduced or eliminated under the reaction conditions.

We believe that the present procedure offers an attractive alternative for other methods available for the reduction of *N*-oxides. Its principal advantages are: the avoidance of strong acid media and harsh reagents, the ease of manipulation, very mild conditions of the reaction, and excellent yields for a wide variety of *N*-oxides.

IR spectra were obtained on a Beckman 4240 spectrophotometer and mass spectra were recorded on a LKB-9000 A instrument.

Reduction of *N*-Oxides 1 a–k; General Procedure:

To a stirred suspension of the appropriate *N*-oxide **1** (0.002 mol) and 10% Pd–C (0.08–0.09 g) in MeOH (5 mL) is introduced anhydrous ammonium formate (0.01 mol). The resulting reaction mixture (slightly exothermic) is stirred at r.t. (**1 a–e**) or at 30–50°C (**1 f–k**), for 1–30 min. The catalyst is then removed by filtration through celite and washed with MeOH (4 mL). The residue obtained by evaporation of solvent is purified by flash column chromatography on silica gel (eluent: hexane/EtOAc, 8:1) or crystallized to give pure product **2**.

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