

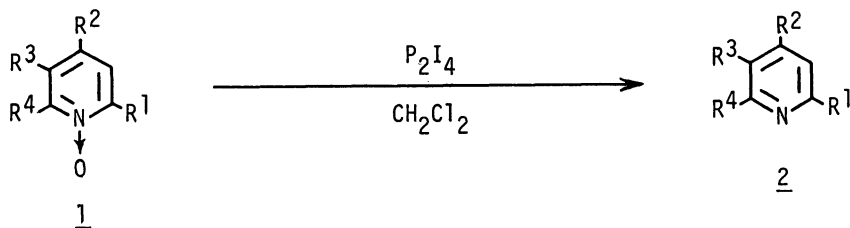
A MILD DEOXYGENATION OF HETEROAROMATIC N-OXIDES
WITH DIPHOSPHORUS TETRAIODIDE

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When treated with diphosphorus tetraiodide in dichloromethane under gentle reflux, the title N-oxides are easily deoxygenated to the parent bases in good yields.

Reductive removal of the N-oxide oxygen atom constitutes one of the important processes for the synthesis of heteroaromatic compounds. The commonly used methods involve reduction with alkali metal hydrides or dissolving metals, catalytic hydrogenation, and treatment with trivalent phosphorus compounds.¹ However, these methods have certain drawbacks; reduction or reductive cleavage of heterocycles, concurrent displacement of labile groups such as nitro and halogens, reduction of unsaturated groupings, and/or forcing conditions.

In previous communications,^{2,3} we have described an efficient procedure for the deoxygenation of epoxides and sulfoxides with diphosphorus tetraiodide (P_2I_4), which is easily accessible by the disproportionation of phosphorus triiodide in dry ether.⁴ We now wish to report an extension of that work as applied to the deoxygenation of heteroaromatic N-oxides.



Thus, P_2I_4 was added in one portion to a stirred solution of N-oxide 1 in dichloromethane and the mixture was heated under gentle reflux. The reaction occurred immediately and the oxygen-containing phosphorus compound precipitated as a pasty solid. The reduction of the N-oxide function was complete within 10-30 min. The product 2 was easily obtained by quenching the reaction mixture with aqueous sodium sulfite, making the solution weakly alkaline with 30% sodium hydroxide, separating the organic phase, and evaporating the solvent. The yields exceeded 80% in most cases examined (Table). The major advantages of the present method are

Table. Reduction of Heteroaromatic N-Oxides with Diphosphorus Tetraiodide

Substrate	Product	R ¹	R ²	R ³	R ⁴	Yield (%) ^a
1a	2a	H	H	H	H	95 ^b
1b	2b	CH ₃	H	H	H	95
1c	2c	CH ₃	H	H	CH ₃	84
1d	2d	CH ₃	CH ₃	H	CH ₃	97
1e	2e	H	Cl	H	H	80
1f	2f	H	NO ₂	H	H	25 ^c
1g	2g	H	H	-(CH=CH) ₂ -		80

a Isolated products are in all respects identical to the authentic specimens.

b Determined by GLC.

c 2f was obtained by extracting a crude product with light petroleum; a significant part of the product was a dark brown crystalline solid unidentified yet.

less laborious work-up, absence of substituent exchange and further reduction, high purity and satisfactory yield of the product, short reaction time, and mild conditions.

Typical Procedure: Freshly prepared P₂I₄ (0.57 g; 1.0 mmol) was added in one portion to a stirred solution of 4-chloropyridine 1-oxide 1e (0.13 g; 1.0 mmol) in dry dichloromethane (6 ml). A bright orange reagent immediately changed to dark brown and the oxygen-containing phosphorus compound precipitated on the wall of the reaction vessel. The brown turbid mixture was heated under gentle reflux and the progress of the amine formation was monitored by GLC. The deoxygenation was complete within 10-20 min. The supernatant liquid was decanted and a pasty insoluble residue was decomposed with aqueous sodium sulfite. Both solutions were combined and made weakly alkaline by the addition of 30% sodium hydroxide solution. The organic layer was separated and aqueous layer extracted several times with dichloromethane. The combined extracts were dried over anhydrous sodium sulfate and evaporated to give amine 2e as a pale yellow oil. Yield, 0.09 g (80%).

REFERENCES

1. See: A.R. Katritzky and J.M. Lagowski, "Chemistry of the Heterocyclic N-Oxides", Academic Press, London (1971).
2. H. Suzuki, T. Fuchita, A. Iwasa, and T. Mishina, *Synthesis*, 1978, 905; *Nippon Kagaku Kaishi*, 1979, 91.
3. H. Suzuki, N. Sato, and A. Osuka, *Chem. Lett.*, 1980, 143.
4. See ref. 2. Now commercially available from Aldrich.

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