Deoxygenation of Quinoxaline and Phenazine *N*-Oxides by Catalytic Transfer Reduction and by Iodide in the Presence of Pyridine/Sulfur Trioxide Complex

S. H. Demirdji, M. J. Haddadin, and C. H. Issidorides*

Chemistry Department, American University of Beirut,
Beirut, Lebanon

Received June 30, 1983.

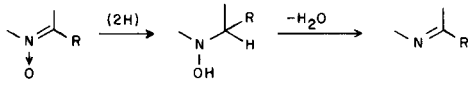
Quinoxaline and phenazine di-*N*-oxides are deoxygenated under mild conditions by catalytic transfer reduction or by treatment with sodium iodide in the presence of pyridine/sulfur trioxide complex.

J. Heterocyclic Chem., **20**, 1735 (1983).

In a previous paper [1] we described the deoxygenation of quinoxaline di-*N*-oxides by derivatives of silane and disilane as well as by the combination of titanium IV chloride and zinc. We now report two useful additions to the existing methods for deoxygenating quinoxaline and phenazine di-*N*-oxides: (i) catalytic transfer reduction and (ii) reduction by sodium iodide in the presence of pyridine/-sulfur trioxide complex.

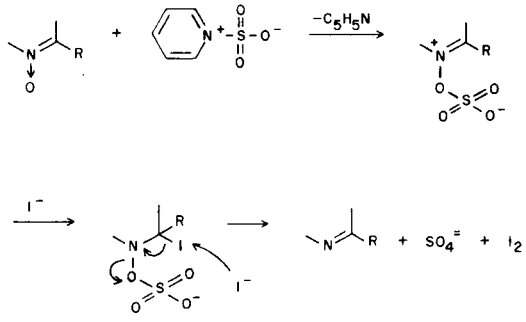
In 1978 Entwistle, Gilkerson, Johnstone, and Telford [2] showed that aromatic nitro compounds are rapidly converted to *N*-substituted hydroxylamines by catalytic transfer reduction using sodium hypophosphite as the hydrogen donor and palladium-charcoal as the catalyst. In the present paper we describe a novel application of catalytic transfer reduction for deoxygenating quinoxaline and phenazine di-*N*-oxides. The method consists in simply adding palladium-charcoal catalyst to a stirred solution of the *N*-oxide in tetrahydrofuran [3] containing an aqueous solution of sodium hypophosphite. Deoxygenation is complete within a period of twenty minutes to two hours (Table). The reaction, which probably proceeds *via* hydroxylamino intermediates (Scheme 1; partial structures), gives good yields of products under mild conditions; furthermore it utilizes readily available reagents which can be easily handled and stored.

Scheme 1



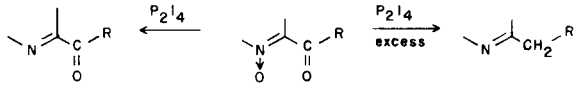
Recently Olah, Vankar, and Arvanaghi [4] found that sodium iodide along with pyridine/sulfur trioxide complex deoxygenates aliphatic and aromatic sulfoxides at room temperature in high yields. We now report that the same reagent effects facile deoxygenation of quinoxaline and phenazine di-*N*-oxides in acetonitrile solution (see Table). Yields are good, and the by-products (molecular iodine and sodium sulfate) are easily removed from the deoxygenated products. A plausible mechanism is outlined in Scheme 2 (partial structures), which depicts iodide's dual role as nucleophile and reducing agent.

Scheme 2



The deoxygenations described in this paper may be conveniently carried out also with diphorphorus tetraiodide, a reagent recently introduced for pyridine *N*-oxides by Suzuki and coworkers [5]. The reagent is commercially available and can be stored without considerable deterioration. We have found, however, that excess diphosphorus tetraiodide in chloroform solution may effect over-reduction of quinoxaline di-*N*-oxides carrying acyl substituents at position 2 (Scheme 3; partial structures).

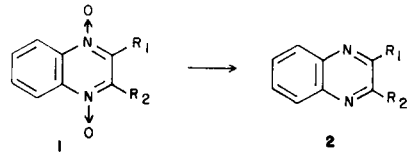
Scheme 3



EXPERIMENTAL

Melting points were taken on a Fisher-Johns apparatus and are uncorrected. Proton magnetic resonance spectra were taken on a Varian EM 360L spectrometer in deuteriochloroform with tetramethylsilane as internal reference. Infrared spectra were recorded on a Perkin-Elmer 398 spectrophotometer using potassium bromide disks. Thick layer chromatography was carried out on freshly prepared Merck GF_{254} type (60) silica gel plates. Some typical experimental procedures are given below.

Table



1 2

1	R_1	R_2	Method [a] A	Method [a] B	Method [a] C	2	Yield § [b] A	Yield § [b] B	Yield § [b] C	Mp (°C)	Mp [lit] (°C)
1a	CH_2Ph	Ph	30 minutes	1 hour (reflux)	24 hours (1:2.5)	**2a**	61	56	80	91-97 [c]	97 [6]
1b	COPh	Ph	30 minutes	1 hour	30 minutes (1:1)	**2b**	71	84	58	150-152 [c]	150-151 [7]
1c	$COCH_3$	CH_3	20 minutes	30 minutes	3 hours (2:1)	**2c**	50	66	47	84-86 [c]	87-88 [6]
1d	$CO_2C_2H_5$	CH_3	30 minutes	3 hours	3 hours	**2d**	71	78	74	72-73 [d]	73-74 [1]
1e	CH_3	Ph	25 minutes	1 hour (reflux)	6 hours (1:2.5)	**2e**	75	54	50	47-49 [d]	53-54 [1]
1f	Ph	H	45 minutes	1 hour (reflux)	2 hours	**2f**	60	70	78	74-75 [c]	78 [6]
1b	COPh	Ph			1 hour (1:2.5)	**2a**			67	96-97 [c]	97 [6]
1c	$COCH_3$	CH_3			5 hours	[e]			70	46-48 [c]	
1g			30 minutes	20 minutes (reflux)	30 minutes (reflux, 1:3)	**2g**	60	53	56	140-142 [c]	142 [8]
1h			2 hours			**2h**	41			265 dec [f]	275 [9]
1i			2 hours			**2i**	73			250 dec [f]	250-260 dec [10]

[a] Method A: Sodium hypophosphite, 5% Palladium on carbon; Method B: sodium iodide/pyridine-sulfur trioxide; Method C: diphosporus tetraiodide. Unless specified otherwise, the reactions were carried out at room temperature. Reagent ratios for A and B were di-*N*-oxide: sodium hypophosphite:5% Palladium on carbon = $1 : 2 : 4 \times 10^{-2}$, and di-*N*-oxide: sodium iodide:pyridine-sulfur trioxide = 1 : 32 : 16; unless specified otherwise, reagent ratio for C was di-*N*-oxide:diphosporus tetraiodide = 1 : 2. [b] Yields refer to pure products obtained by thick layer chromatography. The products were identical with authentic samples. [c] Recrystallized from methanol-water. [d] Recrystallized from water. [e] The product is 2-ethyl-3-methylquinoxaline identified by nmr: δ 1.40 (triplet, 3H), δ 2.75 (singlet, 3H), δ 3.05 (quartet, 2H), δ 7.70 (multiplet, 2H), and δ 8.00 (multiplet, 2H). No carbonyl absorption was observed in the ir. [f] Recrystallized from methanol-trifluoroacetic acid.

2-Phenylquinoxaline (**2f**) by Method A.

A stirred solution of 2-phenylquinoxaline di-*N*-oxide (**1f**, 0.120 g) in tetrahydrofuran (20 ml) was treated with an aqueous solution (2 ml) of sodium hypophosphite (0.106 g). To the resulting mixture was added 5% palladium-charcoal (0.050 g) [11]. The reaction was carried out at room temperature and monitored by tlc. After 45 minutes, the mixture was extracted with ether (3 × 20 ml) and the organic layer was washed with water and dried over magnesium sulfate. The solvent was removed and the crude product was purified by thick layer chromatography (toluene). The purified product (0.062 g, 60% yield) was identical with an authentic sample (tlc, ir) and melted at 74-75° (methanol-water).

2-Benzoyl-3-phenylquinoxaline (**2b**) by Method B.

To a stirred solution of freshly prepared pyridine-sulfur trioxide complex (1.3 g) [12] in acetonitrile (50 ml) was added a solution of 2-benzoyl-3-phenylquinoxaline di-*N*-oxide (**1b**, 0.170 g) in acetonitrile (5 ml), followed by a solution of sodium iodide (2.40 g) in acetonitrile (50 ml). The reaction was carried out at room temperature and monitored by tlc. After one hour, the brown mixture was diluted with water, decolorized with 10% aqueous sodium thiosulfate solution (2 × 15 ml), and extracted with ether (3 × 20 ml). The ether extract was washed with aqueous sodium chloride and dried over anhydrous magnesium sulfate. Evaporation of the solvent gave a crude product which was purified by thick layer chromatography (toluene). The pure product (0.130 g, 84% yield) was identical with an authentic sample (tlc, ir). After recrystallization from methanol-water it melted at 150-152°.

2-Ethoxycarbonyl-3-methylquinoxaline (**2d**) by Method C.

To a stirred solution of 2-ethoxycarbonyl-3-methylquinoxaline di-*N*-oxide (**1d**, 0.250 g) in chloroform (3 ml) was added in one portion a suspension of diphosphorus tetraiodide (1.140 g) [13] in chloroform (10 ml).

The reaction was carried out at room temperature and monitored by tlc. After 3 hours, the mixture was diluted with water and washed with aqueous sodium thiosulfate. The organic layer was washed with dilute sodium hydroxide (10 ml) and dried over anhydrous magnesium sulfate. The crude product, obtained by evaporation of the solvent, was purified by thick layer chromatography (toluene). The purified product (0.160 g, 74% yield) was identical with and authentic sample (tlc, ir) and melted at 72-73° (water).

2-Benzyl-3-phenylquinoxaline (**2a**) from **1b** by Method C (excess reagent).

To a stirred solution of 2-benzoyl-3-phenylquinoxaline di-*N*-oxide (**1b**, 0.170 g) in chloroform (3 ml) was added in one portion a suspension of diphosphorus tetraiodide (0.700 g) in chloroform (10 ml). The reaction was carried out at room temperature and monitored by tlc. After one hour, the reaction mixture was worked up as in the previous example. The purified product (**2a**, obtained by thick layer chromatography) weighed 0.100 g (67% yield), was identical with an authentic sample (tlc, ir), and melted at 96-97°(methanol-water).

Acknowledgment.

We are greatly indebted to Professor Mary Kasparian for helpful suggestions and discussions during the course of the work, and to Mr. Rudolph Jabbur for the preparation of the manuscript.

REFERENCES AND NOTES

[1] F. R. Homaidan and C. H. Issidorides, *Heterocycles*, **16**, 411 (1981).

[2] I. D. Entwistle, T. Gilkerson, R. A. W. Johnstone, and R. P. Telford, *Tetrahedron*, **34**, 213 (1978).

[3] Phenazine *N*-oxides such as **1h** and **1i**, which are sparingly soluble in tetrahydrofuran, are readily deoxygenated by this method within one hour at room temperature with trifluoroacetic acid as the solvent.

[4] G. A. Olah, Y. D. Vankar, and M. Arvanaghi, *Synthesis*, 984 (1979).

[5] H. Suzuki, N. Sato, and A. Osuka, *Chemistry Letters* (Chem. Soc. Japan), 459 (1980).

[6] J. C. E. Simpson, in "The Chemistry of Heterocyclic Compounds", Vol 5, A. Weissberger, ed, Interscience Publishers Inc., New York, NY, 1953, p 206.

[7] F. R. Homaidan, M. S. Thesis, American University of Beirut, Beirut, Lebanon, 1980.

[8] T. N. Rawdah, M. S. Thesis, American University of Beirut, Beirut, Lebanon, 1972.

[9] G. A. Swan and D. G. I. Felton, in "The Chemistry of Heterocyclic Compounds", Vol 11, A. Weissberger, ed, Interscience Publishers Inc., New York, NY, 1957, p 89.

[10] G. R. Clemo and H. McIlwain, *J. Chem. Soc.*, 479 (1938).

[11] The catalyst (5% Pd-C) was purchased from Matheson, Coleman and Bell, Norwood, Ohio, 45212, U.S.A.

[12] H. H. Sisler and L. F. Audrieth, in "Inorganic Syntheses", Vol 2, W. C. Fernelius, ed, McGraw-Hill Book Company, Inc., New York, NY, 1946, p 173.

[13] Diphosphorus tetraiodide was purchased from Aldrich Chemical Company, Inc., Milwaukee, Wis. 53233, U.S.A.