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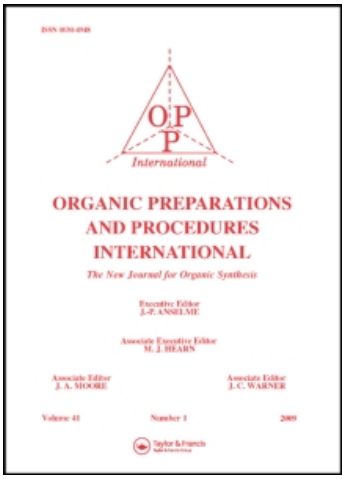

Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

DEOXYGENATION OF QUINOXALINE 1,4-DIOXIDES WITH TITANIUM TRICHLORIDE

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To cite this Article Cue Jr., Berkeley W. , Dirlam, John P. and Glaser, Edward A.(1977) 'DEOXYGENATION OF QUINOXALINE 1,4-DIOXIDES WITH TITANIUM TRICHLORIDE', Organic Preparations and Procedures International, 9: 6, 263 — 266
To link to this Article: DOI: 10.1080/00304947709356085
URL: http://dx.doi.org/10.1080/00304947709356085

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ORGANIC PREPARATIONS AND PROCEDURES INT. 9(6), 263-266 (1977)

DEOXYGENATION OF QUINOXALINE 1,4-DIOXIDES WITH TITANIUM TRICHLORIDE

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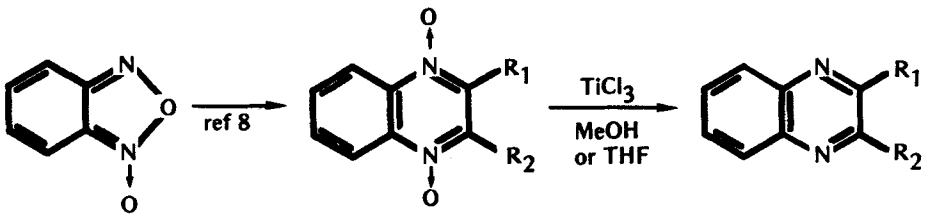
We recently reported that reduction of certain 2,3-disubstituted quinoxaline 1,4-dioxides (QNO's) with trimethyl phosphite in refluxing alcohol solvent furnished the corresponding monooxides selectively in good yield.[1] In a similar study of the dideoxygenation of QNO's to quinoxalines using reducing agents such as phosphorus trichloride[2,3] and sodium dithionite,[4,5] we found that side reaction products sometimes accompanied the desired quinoxaline.[6] We now report that aqueous titanium trichloride is a convenient, synthetically useful alternative to available reagents for the reduction of QNO's.[7]



BFO (1) (2)

a) R_1 = CHO; R_2 = H
b) R_1 = $COCH_3$; R_2 = CH_3
c) R_1 = COPh; R_2 = CH_3
d) R_1 = CO_2CH_3; R_2 = CH_3
e) R_1 = R_2 = H
f) R_1 = CH_3; R_2 = H
g) R_1 = CH_2COCH_3; R_2 = CH_3

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The results of this investigation are summarized in Table 1. The QNO's (1a-d) were conveniently prepared by the elegant Beirut reaction[8] from benzofurazan 1-oxide (BFO). They were rapidly reduced by dropwise addition of a 20% aqueous titanium trichloride solution[9] to a solution of the compound in either methanol or tetrahydrofuran. Analysis of the crude products (2a-d) by TLC indicated no monooxides were present. The quinoxaline products (2a-d) were identified by comparison of their spectral properties and physical constants with those of known compounds. The reported yields are for isolated, pure products. No attempts were made to optimize the yields.

Table 1. Reduction of Quinoxaline 1,4-Dioxides with Titanium Trichloride

Cmpd.	Yield (%)	MP °C	Lit. MP °C
2a	30[a]	105-107	107-108[b]
2b	39	84-86	87-88[c]
2c	34	85-86	-[d]
2d	35	83-85	83-85[e]

[a]THF was used as solvent. The use of MeOH gave a 1:1 mixture of 2a and the dimethylacetal of 2a based on NMR analysis. [b]Reference 10. [c]Reference 11. [d]Calcd. for $C_{16}H_{12}N_2O$: C, 77.39; H, 4.87; N, 11.28. Found: C, 77.38; H, 4.95; N, 11.33. [e]Reference 1.

Attempts to extend this reaction to some other QNO's, e.g. 1e-g, led to complex mixtures that included isomeric quinoxaline monooxides in addition to the desired quinoxalines. The use of more vigorous reaction conditions (i.e., 70° for 17 hrs) still gave complex mixtures. Thus, the reduction of QNO's to quinoxalines using titanium trichloride appears to be facilitated by the presence of at least one electron-withdrawing group adjacent to one of the N-oxide functions, which presumably increases the oxidation potential of the QNO.

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EXPERIMENTAL

The starting materials were prepared by published procedures: quinoxaline-2-carboxaldehyde 1,4-dioxide,[12] 2-acetyl-3-methylquinoxaline 1,4-dioxide,[1] 2-benzoyl-3-methylquinoxaline 1,4-dioxide,[13] methyl 3-methylquinoxaline-2-carboxylate 1,4-dioxide,[1] quinoxaline 1,4-dioxide,[12] 2-methylquinoxaline 1,4-dioxide,[14] and 2-acetonyl-3-methylquinoxaline 1,4-dioxide.[15]

General Procedure for the Preparation of Quinoxalines.- A vigorously stirred solution of 2-acetyl-3-methylquinoxaline-1,4-dioxide (7.00 g, 32 mmol) in methanol (300 ml) was treated dropwise with 20% aqueous titanium trichloride (75 ml) at such a rate that the purple color barely persisted in the reaction mixture. When the addition was complete the dark solution was stirred at room temperature for 30 min, then the solvent was removed in vacuo. The residue was treated with saturated aqueous sodium bicarbonate solution (foaming) until the solution was basic to litmus paper. Chloroform (250 ml) was added and the two phases vigorously agitated for 30 min. The liquids were decanted, an additional 250-ml portion of chloroform was added and the process was repeated. The solutions were combined, and the aqueous layer was separated. The organic layer was washed with water, dried over anhydrous potassium carbonate, and evaporated to dryness in vacuo. The residue was chromatographed on a silica gel column. Elution with chloroform gave 2b, 2.30 g (39%); mp. 84-86° (from methanol); lit.[11] mp. 87-88°. Anal. Calcd. for $C_{11}H_{10}N_2O$: C, 70.95; H, 5.41; N, 15.05. Found: C, 70.94; H, 5.39; N, 15.34.

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(Received July 18, 1977)

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