crystallization from methanol and filtration on a column of silica, khellin, identical with **9**, was obtained.

Registry No.—**1**, 525-82-6; **2**, 22115-89-5; **7**, 491-38-3; **8**, 61348-46-7; **9**, 82-02-0; **10**, 61348-47-8; **11**, 61348-48-9; **12**, 30992-84-8; **14**, 61348-49-0; **15**, 61348-50-3; **15'**, 61348-51-4; **16**, 61348-52-5; **17**, 61348-53-6; hydroxylamine hydrochloride, 5470-11-1.

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(43) We believe that under our conditions the chromone behaves like a 4-hydroxypyrilium derivative and the nucleophilic attack occurs at position 4 as has been observed on other pyrylium compounds bearing a leaving group in position 4 [see J. Farkas, B. Costisella, M. Rabosi, H. Gross, and R. Bognar, *Chem. Ber.*, **102**, 1333 (1969); S. Yoneda, T. Sugimoto, O. Tanaka, Y. Moriya, and Z. Yoshida, *Tetrahedron*, **31**, 2669 (1975)].
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(45) **Notes Added in Proof.** (i) W. Basinski and Z. Jerzmanovska, *Rocz. Chem.*, **50**, 1067 (1976), report that flavone **1** heated with hydroxylamine hydrochloride in pyridine yields oxime **2** and a coproduct previously assigned structure **3** (**5**) but now reassigned as the isomeric 3-phenyl-5-*o*-hydroxyphenylisoxazole. (ii) Recently a number of pryones and flavones ^{13}C studies relevant to our work have appeared: M. J. Looks, L. R. Weingarten, and R. Levin, *J. Am. Chem. Soc.*, **98**, 4571 (1976); C. A. Kingsbury, M. Clifton, and J. H. Looker, *J. Org. Chem.*, **41**, 2777 (1976); A. Pelter, R. S. Ward, and T. I. Gray, *J. Chem. Soc., Perkin Trans. 1*, 2475 (1976). (iii) We have been able to improve the yield of oxime formation by passing dry gaseous hydrogen chloride in anhydrous methanol until pH 1 is reached; thus khellin oxime (**17**) is obtained in >95% yield.

Selective Monodeoxygenation of Certain Quinoxaline 1,4-Dioxides with Trimethyl Phosphite

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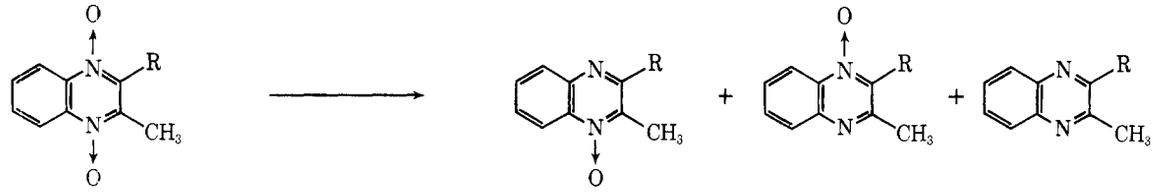
The reduction of some 2,3-disubstituted quinoxaline 1,4-dioxides with trimethyl phosphite in refluxing alcohol solvent furnished the corresponding monooxides selectively in good yield. Deoxygenation occurred exclusively at the nitrogen adjacent to carbon bearing an electron-withdrawing group. These results are quite remarkable when compared with the reduction of the same quinoxaline 1,4-dioxides with other commonly used reducing agents such as phosphorus trichloride and sodium dithionite which afforded a mixture of isomeric monooxides and dideoxygenated product. The scope and limitations of this reaction are discussed.

Recent interest in the preparation and reactions of quinoxaline 1,4-dioxides (QNO's) has remained at a high level[1] owing in part to the commercial importance of this class of compounds. For example, the QNO carbadox[2] is highly effective as a growth promotant for swine.[3] Quinoxaline monooxides have been isolated as QNO metabolites in several different experimental animals.[4] We desired to prepare a number of quinoxaline 1-oxides for biological study, and have discovered that trimethyl phosphite is a superior reducing agent for the selective monodeoxygenation of certain QNO's.

Although trialkyl phosphites have been used in several instances for the deoxygenation of heterocyclic *N*-oxides, to our knowledge their application in the QNO series has not been reported. Emerson and Rees[5] were able to reduce pyridine 1-oxides with triethyl phosphite in diethylene glycol diethyl

Table I. Reduction of Quinoxaline 1,4-Dioxides



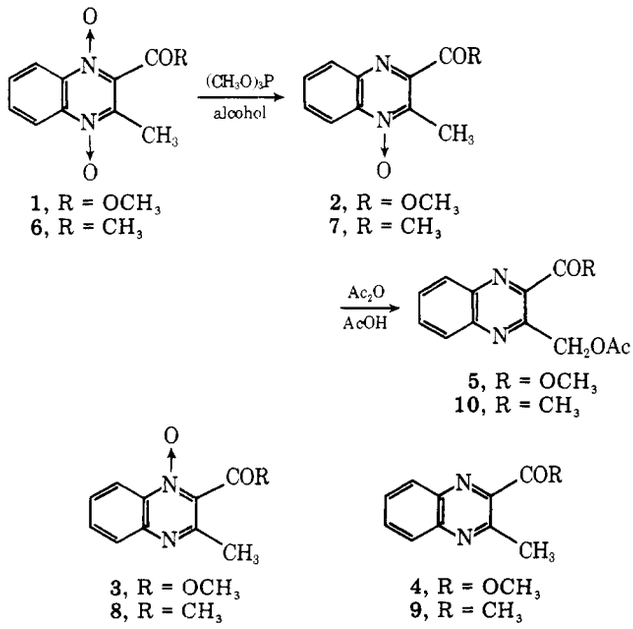
Compd	R	Reagent	Products[a] (%)		
1	CO_2CH_3	$(CH_3O)_3P$	2 (>95)	3 (<5)	4 (<5)
		PCl_3	(16)	(57)	(27)
		$Na_2S_2O_4$	(66)	(20)	(14)
6	$COCH_3$	$(CH_3O)_3P$	7 (>99.5)[b]	8 (<0.5)[b]	9 (<0.5)[b]
		PCl_3	(30)	(50)	(20)
		$Na_2S_2O_4$	(63)	(11)	(26)

[a] Determined by NMR as described in the Experimental Section, unless otherwise noted. [b] Determined by HPLC as described in the Experimental Section.

ether if both oxygen and peroxide, formed adventitiously from the solvent, were present. However, these reductions did not go to completion even with triethyl phosphite in a 100-fold excess. A free-radical chain mechanism was proposed to explain their kinetic results. 5-Chlorobenzofurazan 1-oxide was reduced to 5-chlorobenzofurazan in 60% yield with trimethyl phosphite in refluxing ethanol by Boulton, Gray, and Katritzky.[6] Recently, Boulton and co-workers[7] deoxygenated some furazan 1-oxides using both trimethyl and triethyl phosphite. The convenient and selective synthesis of several quinoxaline monooxides by the use of trimethyl phosphite is the topic of this paper.

Results and Discussion

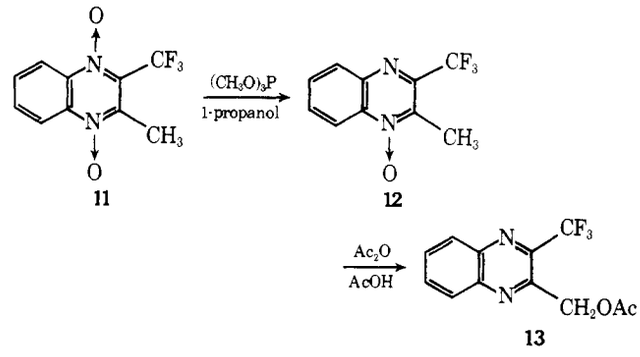
Methyl 3-methylquinoxaline-2-carboxylate 1,4-dioxide (**1**) was allowed to react with excess trimethyl phosphite in refluxing 1-propanol. NMR analysis of the crude product mixture indicated the sole formation of the monooxide **2**. None of isomeric monooxide **3** was detected (<5%), nor was any of the totally deoxygenated quinoxaline **4** observed (<5%). Upon



purification, monooxide **2** was obtained in 81% yield.[8] The present structural assignment for **2**, in which the *N*-oxide is adjacent to the 3-methyl group, was confirmed by acetic anhydride–acetic acid rearrangement[9] of **2** to the corresponding 3-acetoxymethylquinoxaline derivative **5**. The monooxide **3**, prepared in the manner described below, does not react with acetic anhydride–acetic acid under the same conditions.

The selective monodeoxygenation of **1** observed with trimethyl phosphite is quite remarkable when this result is compared with the reduction of **1** with two other commonly used QNO reducing agents such as phosphorus trichloride[1f,10] and sodium dithionite.[1e,11] Indeed, a mixture of all three possible products (**2**, **3**, and **4**) was found upon reduction of **1** with these two reagents (Table I). In the reduction of **1** with phosphorus trichloride, the monooxide **3** was formed as the major product and isolated in 20% yield. The outcome was similar when other 2,3-disubstituted QNO's, wherein R-2 was an electron-withdrawing group and R-3 was methyl, were reduced with trimethyl phosphite, phosphorus trichloride, or sodium dithionite. For example, in the case where R-2 is acetyl (**6**), trimethyl phosphite gave selective monodeoxygenation to form the monooxide **7**; neither the monooxide **8** nor the deoxide **9** was detected by NMR analysis (<5%). A more sensitive analysis of the product mixture by HPLC indicated the sole formation of the monooxide **7** (>99.5%). Treatment of **7** with acetic anhydride–acetic acid gave rise to 2-acetoxymethyl-3-acetylquinoxaline (**10**), whereas the monooxide **8** failed to react with acetic anhydride–acetic acid under conditions that rearrange **7**. As summarized in Table I, phosphorus trichloride and sodium dithionite reduction of **6** gave a mixture of isomeric monooxides (**7** and **8**) and the deoxide (**9**).

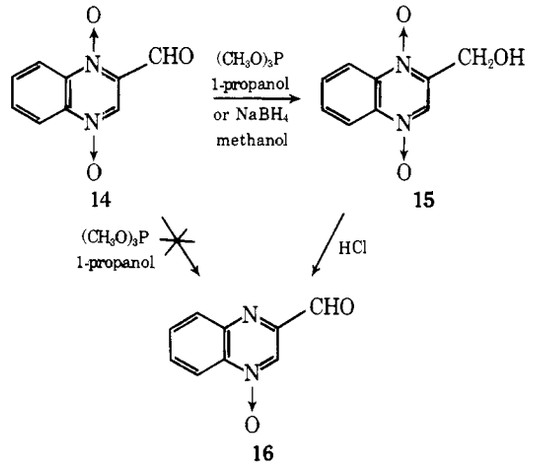
Trimethyl phosphite reduction of 2-methyl-3-trifluoromethylquinoxaline 1,4-dioxide (**11**) also gave selective monodeoxygenation to afford **12**. Rearrangement of **12** with acetic anhydride–acetic acid yielded **13**, which confirmed that



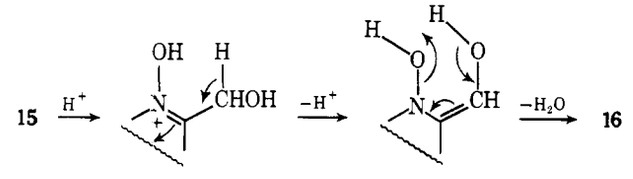
the *N*-oxide was adjacent to the methyl group prior to rearrangement. In contrast, treatment of a quinoxaline 1,4-dioxide without an electron-withdrawing group adjacent to an *N*-oxide, such as 2-methylquinoxaline 1,4-dioxide,[12] with tri-

methyl phosphite in refluxing 1-propanol resulted in no detectable reduction products; starting material was recovered unchanged.

Based on the above results with trimethyl phosphite, a one-step reduction leading to **16** was envisioned, i.e., monodeoxygenation of quinoxaline-2-carboxaldehyde 1,4-dioxide (**14**). Unexpectedly, **14** was instead selectively reduced with trimethyl phosphite to afford the carbinol **15**. This result is

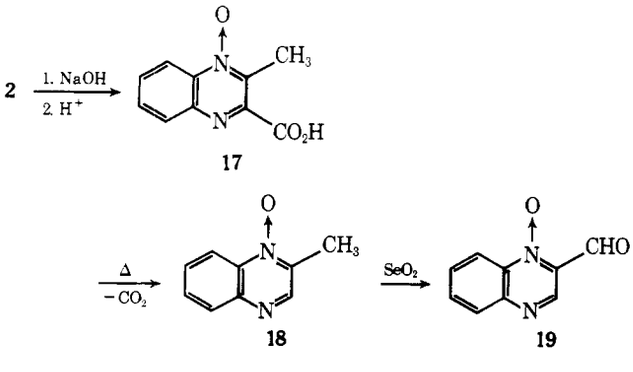


unique in that in previous cases reduction of a functional group on a QNO has resulted in concomitant reduction of one or both *N*-oxides.[13] The use of 0.25 molar equiv of sodium borohydride gave identical results with those found with trimethyl phosphite, and **15** was obtained in 78% yield.[14] The desired quinoxaline-3-carboxaldehyde 1-oxide (**16**) was obtained from 2-hydroxymethyl-QNO (**15**) by rearrangement of this alcohol with concentrated hydrochloric acid. A plausible mechanism is depicted with partial structures shown below. Aldehyde formation from enolamine intermediates has



been suggested previously by Chilton and Butler in the base-catalyzed conversion of 2-hydroxymethylpyridine 1-oxide into pyridine-2-carboxaldehyde.[15]

In order to confirm the structure of **16** the corresponding isomer, quinoxaline-2-carboxaldehyde 1-oxide (**19**), was synthesized by a four-step sequence outlined below. The first step involved selective monodeoxygenation of **1** with trimethyl phosphite as described above to afford **2**. Decarboxylation of **17** proceeded efficiently at 100 °C in toluene and the resulting 2-methylquinoxaline 1-oxide (**18**) was oxidized with selenium oxide to yield **19**.



The present study offers little insight into the mode of action of phosphorus(III) compounds with QNO's. However, trimethyl phosphite in refluxing alcohol appears to be uniquely suitable for selective deoxygenation at the nitrogen adjacent to carbon bearing an electron-withdrawing group in certain QNO's.

Experimental Section

General. Melting points (uncorrected) were taken with a Thomas-Hoover capillary apparatus. NMR spectra were recorded on Varian A-60 and T-60 spectrometers with Me_4Si as internal standard. IR spectra were determined with a Perkin-Elmer Model 21 spectrophotometer. UV spectra were recorded on a Cary Model 14 spectrophotometer. Mass spectra were obtained with a Perkin-Elmer RMU-6E mass spectrometer. Analytical HPLC was performed using a Chromatronix Model 3510 instrument equipped with an Altex LiChrosorb 5-μ column (25 cm × 3.2 mm) and a 254-nm UV detector. Microanalyses were performed by the Pfizer Analytical Department. All evaporations were conducted in vacuo using either a water aspirator or a vacuum pump.

Methyl 3-methyl-2-quinoxalinecarboxylate 1,4-dioxide (1) was prepared in 78% yield according to a published procedure[16] by condensing methyl acetoacetate with benzofurazan 1-oxide in 2-propanol at 65 °C using a catalytic amount of calcium hydroxide: mp 167–169 °C (from methanol); NMR ($CDCl_3$) δ 2.50 (3, s, CH_3), 4.03 (3, s, OCH_3), 7.80 (2, m, H-6, H-7), 8.52 (2, m, H-5, H-8); IR (KBr) 1754 cm^{-1} (C=O); UV λ_{max} (MeOH) 234 nm (ϵ 21 800), 264 (26 700), 383 (12 500); mass spectrum *m/e* 234 $(M)^+$. Anal. Calcd for $C_{11}H_{10}N_2O_4$: C, 56.46; H, 4.31; N, 11.97. Found: C, 56.27; H, 4.24; N, 11.93.

Methyl 2-Methyl-3-quinoxalinecarboxylate 1-Oxide (2). Methyl 3-methyl-2-quinoxalinecarboxylate 1,4-dioxide (200 g, 0.86 mol) was dissolved in 1-propanol (2 L) containing trimethyl phosphite (118 g, 0.95 mol). The reaction mixture was heated under reflux for 2.5 h and then cooled to 15 °C to afford a crystalline precipitate. The tan solid was collected by filtration and recrystallized from methanol to give 152 g (81%) of **2**: mp 109–111 °C; NMR ($CDCl_3$) δ 2.70 (3, s, CH_3), 3.97 (3, s, OCH_3), 7.73 (2, m, H-6, H-7), 8.13 (1, m, H-8), 8.48 (1, m, H-5); IR (KBr) 1739 cm^{-1} (C=O); UV λ_{max} (MeOH) 246 nm (ϵ 33 800), 325 (8500); mass spectrum *m/e* 218 $(M)^+$. Anal. Calcd for $C_{11}H_{10}N_2O_3$: C, 60.61; H, 4.62; N, 12.85. Found: C, 60.70, H, 4.69; N, 13.07.

Methyl 3-Methyl-2-quinoxalinecarboxylate 1-Oxide (3). Phosphorus trichloride (10 mL) was added to a stirred solution of methyl 3-methyl-2-quinoxalinecarboxylate 1,4-dioxide (3.00 g) in chloroform (30 mL). After stirring overnight at room temperature the reaction mixture was diluted with ice–water and excess aqueous sodium hydroxide was added. The chloroform layer was separated and the aqueous phase was extracted with chloroform. The combined chloroform extracts were dried with anhydrous magnesium sulfate and evaporated to give a solid (2.47 g, ca. 85%). NMR analysis of the crude product mixture indicated the presence of three compounds: **3** (57%), **2** (16%), and **4** (27%). Compounds **2** and **4** were removed from the crude product by washing with ether, which left behind **3** (0.56 g, 20%): mp 108–110 °C; NMR ($CDCl_3$) δ 2.60 (3, s, CH_3), 4.00 (3, s, CO_2CH_3), 7.5–8.2 (3, m, H-5, H-6, H-7), 8.47 (1, m, H-8); IR (KBr) 1755 cm^{-1} (C=O); UV λ_{max} (MeOH) 243 nm (ϵ 37 200), 320 (6900); mass spectrum *m/e* 218 $(M)^+$. Anal. Calcd for $C_{11}H_{10}N_2O_3$: C, 60.61; H, 4.62; N, 12.85. Found: 60.44; H, 4.59; N, 12.87.

Methyl 3-Methyl-2-quinoxalinecarboxylate (4). To a stirred, heated solution of methyl 3-methyl-2-quinoxalinecarboxylate 1,4-dioxide (1.00 g, 4.27 mmol) in 60% EtOH (20 mL) was added sodium dithionite (3.27 g, 18.8 mmol) in portions over 30 min. The mixture was heated under reflux for 3 h, diluted with cold water, and extracted with chloroform (2 × 50 mL). The chloroform extract was dried ($MgSO_4$), filtered, and evaporated to dryness. The residue was recrystallized from ether–hexane to yield 0.44 g (50%) of **4**: mp 83–85 °C; NMR ($CDCl_3$) δ 2.90 (3, s, CH_3), 4.00 (3, s, OCH_3), 7.7–8.3 (4, m, H-5, H-6, H-7, H-8); IR (KBr) 1740 cm^{-1} (C=O); UV λ_{max} (MeOH) 241 nm (ϵ 30 200), 315 (5600); mass spectrum *m/e* 202 $(M)^+$. Anal. Calcd for $C_{11}H_{10}N_2O_2$: C, 65.41; H, 4.99; N, 13.87. Found: C, 65.61; H, 5.26; N, 14.08.

When the above procedure was repeated using 0.37 g (2.10 mmol) of sodium dithionite, NMR analysis ($CDCl_3$) of total crude product mixture (0.79 g, ca. 85%) indicated the presence of **3**, **2**, and **4** in the ratio 20:66:14, respectively. The methyl resonances for these three compounds were observed at different chemical shifts, and thus integration of the methyl region allowed relative molar percentages to be readily ascertained.

Methyl 3-Acetoxymethyl-2-quinoxalinecarboxylate (5). A solution of methyl 2-methyl-3-quinoxalinecarboxylate 1-oxide (1.0 g) in acetic anhydride (20 mL) and glacial acetic acid (5 mL) was heated under reflux for 48 h. The solution was cooled and poured onto ice, and the aqueous layer was extracted with chloroform. The chloroform extract was dried ($MgSO_4$), filtered, and evaporated, leaving 1.03 g of **5**, mp 90–92 °C. Recrystallization from ethyl acetate afforded 0.75 g (63%): mp 100–101 °C; NMR ($CDCl_3$) δ 2.43 (3, s, $OCOCH_3$), 4.30 (3, s, OCH_3), 6.23 (2, s, CH_2), 8.50 (4, m, H-5, H-6, H-7, H-8); IR (KBr) 1755, 1725 cm^{-1} (ester C=O's); UV λ_{max} (MeOH) 243 nm (ε 35 400), 317 (5710); mass spectrum *m/e* 260 $(M)^+$. Anal. Calcd for $C_{13}H_{12}N_2O_4$: C, 60.06; H, 4.65; N, 10.77. Found: C, 60.01; H, 4.69; N, 10.92.

2-Acetyl-3-methylquinoxaline 1,4-Dioxide (6) was prepared according to the general procedure of Issidorides et al.,[17] by condensing pentane-2,4-dione (180 g, 1.80 mol) with benzofurazan 1-oxide (204 g, 1.50 mol) in ethanol (1 L) using a catalytic amount of sodium hydroxide (6.0 g, 0.15 mol). The reaction was exothermic and was maintained at 55 °C with ice-bath cooling for 30 min, and was then stirred overnight at room temperature. A thick, yellow precipitate was collected, washed with ethanol, and dried to afford 176 g (54%) of **6**: mp 154–155 °C; NMR ($CDCl_3$) δ 2.50 (3, s, CH_3 or $COCH_3$), 2.72 (3, s, $COCH_3$ or CH_3), 7.85 (2, m, H-6, H-7), 8.52 (2, m, H-5, H-8); IR (KBr) 1725 cm^{-1} (C=O); UV λ_{max} (MeOH) 235 nm (ε 20 600), 263 (19 700), 384 (10 860); mass spectrum *m/e* 218 $(M)^+$. NMR and IR values are in agreement with values previously reported[18] in the literature. Anal. Calcd for $C_{11}H_{10}N_2O_3$: C, 60.61; H, 4.62; N, 12.85. Found: C, 60.45; H, 4.67; N, 12.87.

3-Acetyl-2-methylquinoxaline 1-Oxide (7). 2-Acetyl-3-methylquinoxaline 1,4-dioxide (20.0 g, 0.092 mol) was dissolved in 1-propanol (200 mL) containing trimethyl phosphite (12.5 g, 0.10 mol). The reaction mixture was heated under reflux for 4 h and then concentrated in vacuo causing a crystalline solid to form. The solid was collected by suction filtration and was washed with ether leaving pale yellow crystals: 4.91 g; mp 93–94 °C. Additional material was collected from a second crop: 6.51 g (total yield of **7** was 63%); mp 91–93 °C; NMR ($CDCl_3$) δ 2.80 (6, s, CH_3, $COCH_3$), 7.82 (2, m, H-6, H-7), 8.15 (1, m, H-8), 8.60 (1, m, H-5); IR (KBr) 1710 cm^{-1} (C=O); UV λ_{max} (MeOH) 253 nm (ε 29 200), 325 (7600); mass spectrum *m/e* 202 $(M)^+$. Anal. Calcd for $C_{11}H_{10}N_2O_2$: C, 65.41, H, 4.99; N, 13.87. Found: C, 65.14; H, 5.02; N, 13.94.

The above reaction was repeated with 1.0 g of the quinoxaline 1,4-dioxide and the reaction solution then concentrated in vacuo leaving a pale yellow solid. HPLC analysis of the total product mixture using a flow rate of 0.4 mL/min and a hexane–chloroform–methanol (57.5/41.8/0.7 by volume) solvent system indicated the presence of **7** (retention time 9.6 min). Compounds **8** (retention time 11.6 min), **9** (retention time 8.4 min), and **6** (retention time 21.0 min) were not detected (<0.5%).

2-Acetyl-3-methylquinoxaline 1-Oxide (8). Following a procedure analogous to the preparation of **3**, 1.0 g of 2-acetyl-3-methylquinoxaline 1,4-dioxide was reduced with phosphorus trichloride to furnish 0.72 g (ca. 77%) of material after workup. NMR analysis of the crude product mixture indicated the presence of three compounds: **8** (50%), **7** (30%), and **9** (20%). Compounds **7** and **9** were selectively removed by washing the crude product with hexane, which left behind **8** (0.28 g, 30%): mp 78–81 °C; NMR ($CDCl_3$) δ 2.53 (3, s, CH_3 or $COCH_3$), 2.60 (3, s, $COCH_3$ or CH_3), 7.5–8.2 (3, m, H-5, H-6, H-7), 8.44 (1, m, H-8); IR (KBr) 1725 cm^{-1} (C=O); UV λ_{max} (MeOH) 243 nm (ε 30 100), 320 (6800); mass spectrum *m/e* 202 $(M)^+$. Anal. Calcd for $C_{11}H_{10}N_2O_2$: C, 65.41; H, 4.99; N, 13.87. Found: C, 65.16; H, 4.97; N, 13.86.

2-Acetyl-3-methylquinoxaline (9). To a stirred, refluxing solution of 2-acetyl-3-methylquinoxaline 1,4-dioxide (2.00 g, 9.17 mmol) in 60% EtOH (30 mL) was added sodium dithionite (6.28 g, 36.1 mmol) in portions over 20 min. The mixture was heated under reflux for 3 h, cooled to room temperature, and filtered to remove an undesired solid. The aqueous filtrate was extracted with chloroform (5 × 20 mL). The chloroform extract was dried ($MgSO_4$), filtered, and evaporated to dryness to yield an oil (1.26 g, 74%). NMR analysis ($CDCl_3$) of the oil indicated the presence of desired product and 2-methylquinoxaline in a 60:40 ratio, respectively. The oil was crystallized from methanol to afford 0.14 g (8%) of **9**: mp 85–86 °C (lit.[1e] mp 85–86 °C); NMR ($CDCl_3$) δ 2.80 (3, s, CH_3 or $COCH_3$), 2.90 (3, s, $COCH_3$ or CH_3), 7.90 (4, m, H-5, H-6, H-7, H-8); IR 1695 cm^{-1} (C=O); UV λ_{max} (MeOH) 244 nm (ε 29 900), 310 (5750); mass spectrum *m/e* 186 $(M)^+$.

To a stirred, heated solution of the quinoxaline 1,4-dioxide **6** (10.0 g, 0.046 mol) in 60% EtOH (150 ml) was added dropwise aqueous sodium dithionite (183 mL, 1 M) over 1 h. The mixture was heated at 90 °C for 2 h, diluted with cold water, and extracted with ether. The ether extract was dried, filtered, and evaporated to dryness: 8.42 g (98%) of material, mp 65–72 °C. NMR analysis of the product mixture indicated the presence of three compounds: **8** (11%), **7** (63%), and **9** (26%). No deacetylated product (i.e., 2-methylquinoxaline) was detected in this experiment, which was carried out at a lower temperature than the one described above.

2-Acetoxymethyl-3-acetylquinoxaline (10). A solution of 3-acetyl-2-methylquinoxaline 1-oxide (4.0 g), acetic anhydride (16 mL), and glacial acetic acid (4 mL) was heated under reflux for 2 h. The solution was cooled and poured onto ice, and the aqueous layer was extracted with chloroform. The chloroform extract was dried, filtered, and evaporated, leaving a brown oil, 2.80 g (58%) of **10**: NMR ($CDCl_3$) δ 2.23 (3, s, $OCOCH_3$), 2.84 (3, s, $COCH_3$), 5.72 (2, s, CH_2), 7.6–8.2 (4, m, H-5, H-6, H-7, H-8). An analytical sample was obtained by thick layer chromatography purification using plates coated with silica gel (95% chloroform–5% methanol solvent system): mp 80–82 °C; IR (KBr) 1755 cm^{-1}; UV λ_{max} (MeOH) 247 nm (ε 28 000), 320 (5200); mass spectrum *m/e* 244 $(M)^+$. Anal. Calcd for $C_{13}H_{12}N_2O_3$: C, 63.99; H, 4.96; N, 11.48. Found: C, 63.98; H, 4.91; N, 11.46.

2-Methyl-3-trifluromethylquinoxaline 1,4-dioxide (11) was prepared according to the procedure of Abushanab:[11] mp 122–125 °C (lit.[11] mp 126–128 °C); NMR ($CDCl_3$) δ 2.77 (3, q, CH_3, J_{HF} = 2.8 Hz), 7.87 (2, m, H-6, H-7), 8.58 (2, m, H-5, H-8); mass spectrum *m/e* 244 $(M)^+$. The IR and UV spectra were identical with those reported[11] for **11**.

2-Methyl-3-trifluormethylquinoxaline 1-Oxide (12). 2-Methyl-3-trifluoromethylquinoxaline 1,4-dioxide (300 mg, 1.23 mmol) was dissolved in 1-propanol (10 mL) containing trimethyl phosphite (170 mg, 1.37 mmol). The reaction mixture was heated under reflux for 1.5 h and then concentrated under vacuum. Ether–hexane was added and the product precipitated to yield 101 mg (36%) of **12**, mp 112–115 °C. NMR, IR, UV, and mass spectra were identical with those previously reported[11] in the literature for **12**.

2-Acetoxymethyl-3-trifluoromethylquinoxaline (13). A solution of 2-methyl-3-trifluoromethylquinoxaline 1-oxide (150 mg, 0.66 mmol) in 13 mL of acetic anhydride–glacial acetic acid (4:1) was heated under reflux for 3 h. The workup procedure was the same as that described above for the preparation of **5**. The crude product was crystallized from hexane to give 61 mg (34%) of **13**: mp 76–77 °C; NMR ($CDCl_3$) δ 2.23 (3, s, CH_3), 5.60 (2, m, CH_2), 7.8–8.4 (4, m, H-5, H-6, H-7, H-8); IR (KBr) 1770 cm^{-1} (C=O); UV λ_{max} (MeOH) 237 nm (ε 37 800), 320 (4860); mass spectrum *m/e* 270 $(M)^+$. Anal. Calcd for $C_{12}H_9F_3N_2O_2$: C, 53.38; H, 3.36; N, 10.38. Found: C, 52.85; H, 3.45; N, 10.24.

2-Hydroxymethylquinoxaline 1,4-Dioxide (15). A. Quinoxalinecarboxaldehyde 1,4-dioxide[12] (1.90 g, 10 mmol) was dissolved in 1-propanol (30 mL) containing trimethyl phosphite (1.24 g, 10 mmol). The reaction mixture was heated under reflux for 30 min and then cooled to 15 °C to afford a precipitate. The yellow solid was collected by suction filtration and washed with methanol to yield 0.64 g, (33%) of **15**: mp 176–178 °C; NMR (CF_3CO_2D) δ 5.47 (2, s, CH_2), 8.28 (2, m, H-6, H-7), 8.85 (2, m, H-5, H-8), 9.37 (1, s, H-3); IR (KBr) 3220 cm^{-1} (OH); UV λ_{max} (MeOH) 232 nm (ε 18 270), 259 (22 880), 379 (12 980); mass spectrum *m/e* 192 $(M)^+$.

B. 2-Quinoxalinecarboxaldehyde 1,4-dioxide[12] (1.90 g, 10 mmol) was suspended in 100 mL of methanol. Sodium borohydride (0.095 g, 2.5 mmol) was added in small portions over 20 s, causing starting material to dissolve. The reaction mixture was stirred for 30 min, during which time solid precipitated. The yellow solid was collected by suction filtration and was washed with ether to yield 1.50 g (78%) of **15**, mp 180–182 °C. The NMR, IR, UV, and mass spectra were identical with those obtained from material prepared by using procedure A. An analytical sample was obtained by recrystallization from methanol, mp 214–215 °C (lit.[19] mp 191–192 °C). Anal. Calcd for $C_9H_8N_2O_3$: C, 56.30; H, 4.20; N, 14.59. Found: C, 56.28; H, 4.26; N, 14.89.

Quinoxaline-3-carboxaldehyde 1-Oxide (16). 2-Hydroxymethylquinoxaline 1,4-dioxide (1.00 g, 5.20 mmol) was added to concentrated hydrochloric acid (3 mL) and the reaction mixture was heated at 100 °C with stirring for 1 h. A tan solid precipitated that was collected by suction filtration and recrystallized from acetone to afford 0.57 g (63%): mp 175–176 °C; NMR (CF_3CO_2D) δ 7.6–8.4 (4, m, H-5, H-6, H-7, H-8), 8.87 (1, s, H-3), 9.60 (1, s, CHO); mass spectrum *m/e* 174 $(M)^+$. The IR spectrum (KBr) indicated that this material was most likely hydrated to some extent [3080 (OH) and 1725 cm^{-1} (w, C=O)]. An analytical sample of the aldehyde was obtained by heating 2-acetoxymethylquinoxaline 1,4-dioxide[19] (50.0 g, 0.21 mol) and concentrated hydrochloric acid (150 mL) under reflux for 15 min. Workup as above followed by recrystallization from acetone yielded 16.7 g (45%) of **16**: mp 175–176 °C; NMR same as above; IR (KBr)

1725 cm^{-1} (s, C=O); UV λ_{max} (MeOH) 240 nm (ϵ 41 000), 322 (9500); mixture melting point with material from above was 175–176 °C. Anal. Calcd for $C_9H_6N_2O_2$: C, 62.07; H, 3.47; N, 16.09. Found: C, 62.05; H, 3.73; N, 16.21.

2-Methylquinoxaline-3-carboxylic Acid 1-Oxide (17). Methyl 2-methyl-3-quinoxalinecarboxylate 1-oxide (5.00 g, 23.0 mmol) was suspended in aqueous 0.5 M sodium hydroxide solution (50 mL). All starting material went into solution within 10 min, and a white precipitate formed upon addition of aqueous 0.5 M hydrochloric acid solution (50 mL). The solid was collected and recrystallized from water to give 4.00 g (81%) of **17**:[4b] mp 150–151 °C; NMR (CF_3CO_2D) δ 3.10 (3, s, CH_3), 8.20–8.90 (4, m, H-5, H-6, H-7, H-8); IR (KBr) 1735 cm^{-1} (C=O); UV λ_{max} (MeOH) 244 nm (ϵ 23 800), 330 (7450); mass spectrum *m/e* 204 $(M)^+$. Several attempts to obtain an analytical sample of **17** were unsuccessful apparently owing to the thermal instability of this compound (vide infra).

2-Methylquinoxaline 1-Oxide (18). 2-Methylquinoxaline-3-carboxylic acid 1-oxide (1.00 g, 4.9 mmol) was added to toluene (10 mL). The resulting suspension was heated at 100 °C for 1.5 h, during which time all the starting material went into solution and a gas was evolved. The reaction mixture was cooled to room temperature and the toluene was removed under vacuum, leaving a colorless solid. The crude product was recrystallized from ether to afford 0.66 g (83%) of pure **18**: mp 85–87 °C; NMR ($CDCl_3$) δ 2.69 (3, s, CH_3), 7.77 (2, m, H-6, H-7), 8.16 (1, m, H-5), 8.58 (1, m, H-8), 8.71 (1, s, H-3); UV λ_{max} (MeOH) 240 nm (ϵ 43 300), 320 (10 500); mass spectrum *m/e* 160 $(M)^+$. Anal. Calcd for $C_9H_8N_2O$: C, 67.56; H, 5.04; N, 17.51. Found: C, 67.60; H, 5.15; N, 17.48.

Quinoxaline-2-carboxaldehyde 1-Oxide (19). 2-Methylquinoxaline 1-oxide (0.90 g, 5.6 mmol) was dissolved in ethyl acetate (15 mL). Selenium dioxide (0.75 g, 6.7 mmol) was added and the reaction mixture was refluxed for 5 h, during which time a black precipitate formed. The reaction mixture was filtered through Super-Cel and the filtrate was treated with activated carbon and evaporated, leaving a tan solid. The solid was recrystallized from acetone to give 0.39 g (39%) of **19**: mp 131–132 °C; NMR (CF_3CO_2D) δ 7.3–8.0 (3, m, H-5, H-6, H-7), 8.25 (1, m, H-8), 8.90 (1, s, H-3), 10.00 (1, s, CHO); IR (KBr) 1680 cm^{-1} (C=O); UV λ_{max} (MeOH) 242 nm (ϵ 38 700), 323 (8900); mass spectrum *m/e* 174 $(M)^+$. Anal. Calcd for $C_9H_6N_2O_2$: C, 62.07; H, 3.47; N, 16.09. Found: C, 62.01; H, 3.36; N, 16.03.

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Synthesis with Pyridine *N*-Oxides. 3.[1] Synthesis of 2-Arylisoxazolo[2,3-*a*]pyridinium Bromides via Acid-Catalyzed Rearrangements of 1-Aryl-2-(2-pyridinyl)ethanone *N*-Oxides

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Reaction of 1-aryl-2-(2-pyridinyl)ethanone *N*-oxides with hydrobromic acid in acetic acid gave 2-arylisoxazolo[2,3-*a*]pyridinium bromides. Cyclization of methoxy-substituted compounds (**21**, **23**, and **31**) gave 2-(2-methoxyaryl)-isoxazolo[2,3-*a*]pyridinium bromides (**22**, **24**, and **32**), which were surprisingly refractory to demethylation. Reaction of 1-phenyl-2-pyridineethanol *N*-oxide with hydrobromic acid in acetic acid gave 2-(2-phenylethenyl)pyridine *N*-oxide hydrobromide and not 2-phenyl-2,3-dihydroisoxazolo[2,3-*a*]pyridinium bromide.

The acid-catalyzed cyclization of **1** to **3** via intramolecular nucleophilic attack on the Pummerer intermediate (**2**) was described previously.[2] 1-(2-Hydroxyphenyl)-2-(2-pyridinyl)ethanone *N*-oxide (**4**) was prepared[3] as an intermediate for the synthesis of various heterocyclic systems.[1] As 2-picoline *N*-oxide is known to undergo a rearrangement[4-6] similar to the Pummerer rearrangement, it was expected that *N*-oxide **4** may cyclize in a manner analogous to sulfoxide **1** to give benzofuranone (**7**).

Treatment of **4** under conditions (trifluoroacetic acid in refluxing benzene) which generate **3** from **1** gave no reaction. Prolonged refluxing (24 h) also failed to give any reaction. A product with the composition expected for the HBr salt of **7** was isolated when **4** was refluxed with hydrobromic acid in acetic acid. Isoxazolo[2,3-*a*]pyridinium bromide (**10**) and 11-hydroxypyrido[1,2-*b*][1,2]benzoazepinium bromide (**11**) are other possible products arising from cyclizations of enolic intermediates **8** and **9**, respectively. The infrared spectrum