51% yield: mp 159–161 °C; H^1 NMR ($CDCl_3$) 9.3 (s, 1 H, H-6), 8.0–7.0 (m, 20 H, CH_2S) 6.0–5.7 (m, 3 H, H-2′, H-3′, H-4′), 4.6 (s, 2 H, CH_2O), 3.8 (s, 2 H, CH_2S); IR (KBr) Anal. Calcd for $C_{37}H_{30}N_2O_9S$: C, 65.47; H, 4.46; N, 4.13. Found: C, 65.50; H, 4.21; N, 4.21.

N^1-(β-D-Ribofuranosyl)-5-(benzylthio)uracil (15a). Deblocking of **15** to **15a** was done in the same manner and scale as in the preparation of **11a** from **11**. The product formed in 72% yield: mp °C; H^1 NMR (D_2O) δ 7.5 (s, 1 H, H-6), 7.3–7.0 (m, 5 H, C_6H_5), 5.9 (d, 1 H, J = 6 Hz, H-1′), 3.7 (s, 2 H, SCH_2); IR (KBr) Anal. Calcd for $C_{16}H_{18}N_2O_6S$: C, 52.45; H, 4.95; N, 7.65. Found: C, 52.51; H, 4.85; N, 7.69.

1-(2′,3′,5′-Tri-*O*-benzoyl-β-D-ribofuranosyl)-2*H*,3*H*,6(8)*H*-1,4-oxathiino[2,3-*d*]pyrimidin-7-one (16). This material was prepared in the same scale and manner as used in the preparation of **11**; the bicyclic pyrimidine **9** was the starting material. The product formed in 28% yield: mp 214–220 °C dec; ^1H NMR (Me_2SO-d_6) δ 8.8 (s, 1 H, H-6), 8.1–7.2 (m, 15 H, COC_6H_5), 6.1–5.6 (m, 3 H, H-2′, H-3′, H-4′), 4.3 (d, 2 H, J = 5 Hz, CH_2O, 2.9 (d, 2 H, J = 5 Hz, CH_2S); IR (KBr) 2920 (CH_2 str), 1570 cm^{-1} (C=O). Anal. Calcd for $C_{32}H_{26}N_2O_9$: C, 62.54; H, 4.25; N, 4.56. Found: C, 62.40; H, 4.31; N, 4.50.

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Registry No. 1, 14020-53-2; 2, 80822-27-1; 4, 73236-43-8; (*E*)-5, 80822-28-2; (*Z*)-5, 80822-29-3; 6, 73236-44-9; 7, 16350-59-7; 8, 21736-44-7; 9, 80822-30-6; 11, 80822-31-7; 11a, 71106-92-8; (*E*)-12, 80822-32-8; (*Z*)-12, 80822-33-9; (*E*)-12a, 80822-34-0; (*Z*)-12a, 80822-35-1; 13, 80845-38-1; 13a, 80822-36-2; 14, 29979-89-3; 14a, 71106-89-3; 15, 80845-39-2; 15a, 58367-10-5; 16, 80822-37-3; 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-D-ribofuranose, 14215-97-5; 2-bromoethanol, 540-51-2.

Some Addition Reactions of 2-Substituted Quinoxaline 1,4-Dioxides

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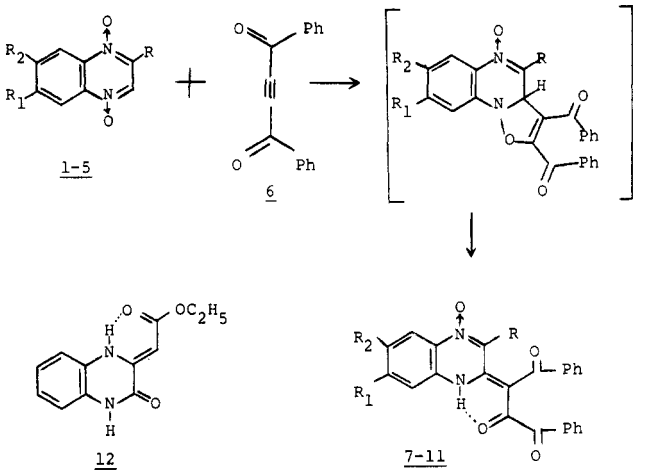
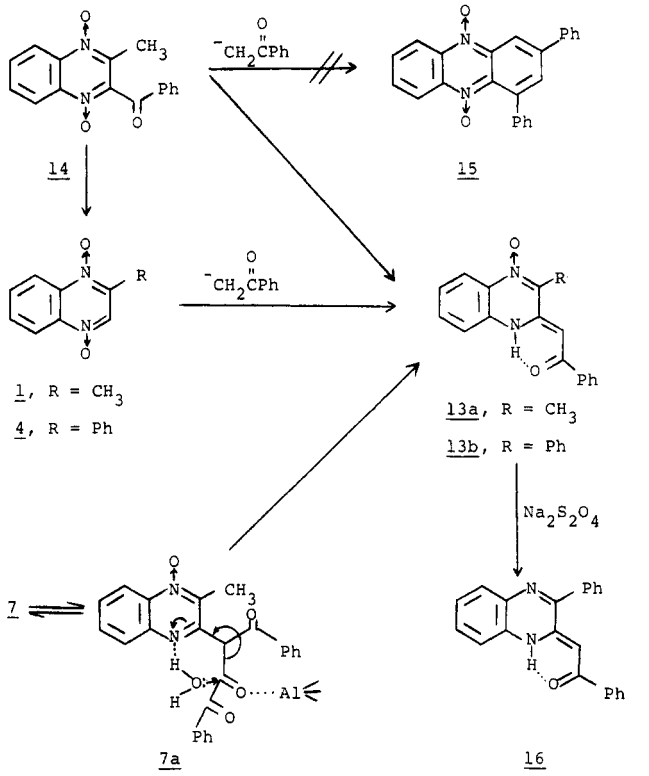
Our interest in the chemistry of quinoxaline 1,4-dioxides and phenazine 5,10-dioxides stems from their properties as antibacterial agents. Indeed, a 2-substituted quinoxaline 1,4-dioxide, methyl 3-[(2-quinoxalinyl)methylene]carbazate 1,4-dioxide, known commercially as Mecadox,[1] has proven to be an effective antibacterial agent. In an earlier paper,[2] we reported the easy conversion of 2,3-dimethylquinoxaline 1,4-dioxides into phenazine 5,10-dioxides. In this work we describe the syntheses of a number of 2,3-disubstituted quinoxaline monoxides from 2-substituted quinoxaline 1,4-dioxides.

Although various cycloaddition reactions of alkynes to heteroaromatic *N*-oxides have been reported,[3] no examples of such reactions that involve quinoxaline 1,4-dioxides are known. We found that treatment of quinoxaline 1,4-dioxides **1–5**, which hold a substituent at position 2 and none at position 3, with dibenzoylacetylene (**6**) in benzene or ethanol at room temperature resulted in the immediate development of a red color and the gradual precipitation of products **7–10** as red solids from the reaction mixture (see Scheme I and Table I). Product **11** was yellow in the crystalline form and red in solution. The progress of the reaction was monitored by TLC, and the reaction was found to be complete in 2–4 days. The yields ranged between 60% and 85% and were improved when the total residue of the reaction mixture was separated by thick-layer chromatography. Comparable yields were obtained when the reactions were carried out in boiling benzene or ethanol.

Scheme I



Scheme II



The infrared spectra of each of products **7–11** showed a broad band at 3300–3100 (hydrogen bonded OH or NH), 1685–1675 (α,β-unsaturated C=O), and 1345–1340 cm^{-1} (N→O). Products **7–11** can exist in tautomeric equilibria; from the intense colors of these adducts, the structure of what is believed to be the predominant tautomer is as shown in Scheme I. Such tautomerism is not without precedent, as quinoxalinones **12** have been reported to possess three tautomeric structures.[4]

Furthermore, in an attempt to purify product **7** by column chromatography on alumina (Merck activity II),

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0022-3263/82/1947-1772$01.25/0

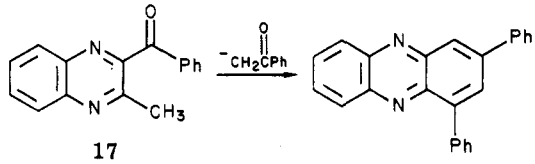
Table I

reactants	substituents R	R_1	R_2	products	% yield	mp, °C	color
1	CH_3	H	H	7	60	177-179	red
2	CH_3	CH_3O	H	8	80	229-231	dark red
3	CH_3	CH_3	CH_3	9	85	191-193	red
4	Ph	H	H	10	70	194-196	violet
5	styryl	H	H	11	65	216-218	yellow

elution with a benzene/methanol mixture (19:1) gave a new orange solid instead of the expected red **7**. The new product was identified as 2-phenacylidinyl-3-methyl-1*H*-quinoxaline 4-oxide (**13a**) which resulted from the cleavage of a C(O)C(O)Ph group as proposed in Scheme II.

Product **13a** showed a weak broad OH (NH) absorption in the 3300-cm^{-1} region, and an extensively conjugated carbonyl broad band at 1580 and 1330 cm^{-1} (N→O). The orange color of **13a** suggests that tautomer **13a** is the predominant tautomer. The NMR spectrum of **13a** is consistent with such a structure. The structure of **13a** was confirmed by an independent, though serendipitous, preparation of **13a**. In an attempt to prepare 1,3-diphenylphenazine 5,10-dioxide (**15**) via the condensation of 2-benzoyl-3-methylquinoxaline 1,4-dioxide (**14**) with acetophenone in base, the reaction took a different course and yielded quinoxaline **13a** instead of phenazine **15** (Scheme II). The proposed mechanism for the formation of **13a** from **14** postulates the intermediacy of 2-methylquinoxaline 1,4-dioxide (**1**). Treatment of authentic **1** with acetophenone in base gave **13a** although in 4% yield. The low yield of **13a** is due to the extensive decomposition of **1** in base. Furthermore, the nucleophilic attack at the 3-position of a 2-substituted quinoxaline 1,4-dioxide was demonstrated further by the reaction of 2-phenylquinoxaline 1,4-dioxide (**4**) with acetophenone to give 2-phenacylidinyl-3-phenyl-1*H*-quinoxaline 4-oxide (**13b**) in 45% yield. The structure of the latter was established by its reduction with sodium dithionite to give quinoxaline **16**. The identity of **16** was confirmed by comparison with an authentic sample of **16** which was prepared from the reaction of *o*-phenylenediamine and dibenzoylacetylene.[5] It is of particular interest to note that the stretching vibration bands of OH (NH) in the infrared spectra of **13** and **16** (KBr disks) were broad and weak, which could be due to extensive hydrogen bonding. Moreover, quinoxaline **16** showed the same pattern of an extensively conjugated carbonyl group (1580 cm^{-1}).

Benzoyl groups at the 2- or 3-positions of quinoxaline 1,4-dioxides are known to be cleaved by base.[6] This tendency for cleavage is diminished considerably upon deoxygenation of the N→O function. Thus, 2-benzoyl-3-methylquinoxaline[7] (**17**) underwent double condensation



17 18

in base to afford 1,3-diphenylphenazine (**18**) in 15% yield. The reaction is accompanied by considerable decomposition.

Experimental Section

All melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected. IR spectra were taken of KBr pellets on a Perkin-Elmer infrared spectrophotometer, Model 257 or 621. Proton NMR spectra were recorded on a Varian T60 or EM 360L spectrometer in $CDCl_3$ or $(CD_3)_2SO$ with tetramethylsilane as an internal reference. Thick-layer chromatography was run by using silica gel Merck 60 PF_{254}. Elemental analyses were performed by E. Pascher, Bonn, Germany.

2-Phenylquinoxaline 1,4-dioxide, 2-styrylquinoxaline 1,4-dioxide, and dibenzoylacetylene were prepared according to literature methods.[2,8,9] 2-Methylquinoxaline 1,4-dioxide (58%, mp 183–184 °C) and 2-methyl-6(7)-methoxyquinoxaline 1,4-dioxide (47%, mp 207–208 °C) were prepared by the following general procedure:[8] the specific benzofurazan oxide (0.05 mol) was dissolved in acetone (20–30 mL) and acetonitrile (20–30 mL). Pyrrolidine (1–2 mL) was added, and the solution was heated at reflux temperature for 20 min and allowed to stand overnight at room temperature. The precipitated yellow solid was collected by suction filtration, washed, and recrystallized from methanol.

General Procedure for the Cycloaddition Reaction of Quinoxaline 1,4-Dioxides with Dibenzoylacetylene To Give 7–11. The specific 2-substituted quinoxaline 1,4-dioxide (0.5 mmol) was dissolved in warm benzene (15 mL). Dibenzoylacetylene (120 mg, 0.5 mmol) was added to the warm solution. The reaction mixture was allowed to stand at room temperature for 2–4 days. The product precipitated out and was collected by suction filtration.

2-[α-(Phenylglyoxyloyl)phenacylidene]-3-methyl-1*H*-quinoxaline 4-Oxides (7). 2-Methylquinoxaline 1,4-dioxide (**1**, 90 mg) was used. Product **7** could not be recrystallized: 130 mg (60%); mp 177–179 °C; IR 3300 (br), 1680, 1590, 1470, 1380, 760, 730 cm^{-1}; NMR ($CDCl_3$) δ 8.5 (m, 1 H), 7.6 (m, 14 H), 2.3 (d, 3 H); mass spectrum, *m/e* (relative intensity) 432 (1), 406 (11), 122 (29), 105 (100), 77 (59). Anal. Calcd for $C_{25}H_{18}N_2O_4$: C, 73.16; H, 4.42; N, 6.83. Found: C, 72.87; H, 4.39; N, 6.98.

2-[α-(Phenylglyoxyloyl)phenacylidene]-3-methyl-7-methoxy-1*H*-quinoxaline 4-Oxide (8). 2-Methyl-6(7)-methoxyquinoxaline 1,4-dioxide (**2**, 100 mg) was used. Two crops were collected and recrystallized from methanol–benzene: 180 mg (80%); mp 229–231 °C; IR 3100 (br), 1680, 1620, 1380, 830 cm^{-1}; NMR (CF_3COOH) δ 8.6 (d, 1 H), 7.6 (m, 13 H), 4.1 (s, 3 H), 2.4 (s, 3 H). Anal. Calcd for $C_{26}H_{20}N_2O_5$: C, 70.90; H, 4.58; N, 6.36. Found: C, 70.68; H, 4.62; N, 6.33.

2-[α-(Phenylglyoxyloyl)phenacylidene]-3,6,7-trimethylquinoxaline 4-Oxide (9). 2,6,7-Trimethylquinoxaline 1,4-dioxide (**3**, 100 mg) was used. The title product was isolated: 85% yield (190 mg); mp 191–193 °C; IR 3060 (br), 1680, 1590, 1470, 1380, 1160, 700 cm^{-1}; NMR ($CDCl_3$) δ 8.3 (br s, 1 H), 7.5 (m, 11 H), 2.3 (3 s, 3 H each). Anal. Calcd for $C_{27}H_{22}N_2O_4$: C, 73.96; H, 5.06; N, 6.39. Found: C, 73.83; H, 5.01; N, 6.50.

2-[α-(Phenylglyoxyloyl)phenacylidene]-3-phenylquinoxaline 4-Oxide (10). 2-Phenylquinoxaline 1,4-dioxide (**4**, 120 mg) was used. The title compound (**10**) was obtained: 70% yield (165 mg); mp 194–196 °C; IR 3240 (br), 1685, 1590, 1370, 1345, 755, 700 cm^{-1}; NMR $(CD_3)_2SO$ δ 7.8 (m). Anal. Calcd for $C_{30}H_{20}N_2O_4$: C, 76.26; H, 4.27; N 5.93. Found: C, 76.47; H, 4.55; N, 5.82.

2-[α-(Phenylglyoxyloyl)phenacylidene]-3-styrylquinoxaline 4-Oxide (11). 2-Styrylquinoxaline 1,4-dioxide (**5**,

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132 mg) was used. The title product (11) was recrystallized from methanol: 65% yield (165 mg); mp 216–218 °C; IR 3250 (br), 1700, 1365, 895, 750, 680 cm^{-1}; NMR (CF_3COOH) δ 7.8 (m). Anal. Calcd for $C_{32}H_{22}N_2O_4$: C, 77.09; H, 4.45; N, 5.62. Found: C, 76.79; H, 4.41; N, 5.82.

2-Phenacylidene-3-methyl-1*H*-quinoxaline 4-Oxide (13a). 2-Benzoyl-3-methylquinoxaline 4-oxide (14, 1.12 g) was dissolved in ethanol (40 mL). Acetophenone (0.6 g) was added, and the mixture was brought to boiling on a steam bath. Methanolic potassium hydroxide (10%, 5 mL) was added, and the mixture was allowed to cool to room temperature. After dilution with water and extraction with chloroform, the concentrated solution was subjected to thick-layer chromatography. Repeated chromatography (benzene) gave the title product (13a) as an orange-yellow solid which was recrystallized from benzene–methanol: 20% yield (0.22 g); mp 167–169 °C; IR (KBr) 1580, 1335, 745 cm^{-1}; NMR ($CDCl_3$) δ 15.9 (br s 1 H), 8.4 (m, 1 H), 7.9 (m, 2 H), 7.5 (m, 6 H), 6.3 (s, 1 H), 2.7 (s, 3 H). Anal. Calcd for $C_{17}H_{14}N_2O_2$: C, 73.36; H, 5.07; N, 10.07. Found: C, 73.04; H, 5.21; N, 9.96.

Product **13a** was obtained in 4% yield from the reaction of 2-methylquinoxaline 1,4-dioxide (1; 176 mg, 1 mmol) and acetophenone (145 mg, 1.2 mmol) in methanolic KOH solution (10 mL of 5% KOH solution). After the solution was heated on a steam bath for 5 min, the solution was cooled, acidified with HCl, and extracted with C_6H_6. The product was isolated by TLC (silica gel, C_6H_6–CH_3OH, 25:1). The product (10 mg) was recrystallized from CH_3OH–H_2O and found to be identical with **13a** (mixture melting point, IR, and NMR).

Cleavage of 7 to 13a. The application of 7 (210 mg) on an alumina (Merck, grade II) column and elution with C_6H_6–CH_3OH (98:2) gave product **13a** (40 mg, 60%). A similar result was obtained when a benzene–methanol (95:5) solution of 7 was stirred in a slurry of alumina in benzene. The reaction is accompanied by a color change from red to yellow-orange.

2-Phenacylidene-3-phenyl-1*H*-quinoxaline 4-Oxide (13b) and 2-Phenacylidene-3-phenyl-1*H*-quinoxaline (16). 2-Phenylquinoxaline 1,4-dioxide (4; 120 mg, 0.5 mmol) and acetophenone (100 mg, 0.8 mmol) were dissolved in methanol (10 mL). Methanol potassium hydroxide (10%, 3 mL) was added. The dark red mixture was heated at the reflux temperature of methanol for a few minutes. Water was added to the mixture until incipient crystallization. Product **13b** was collected and recrystallized from methanol: red needles; 75 mg (45%); mp 184–185 °C; IR 3400 (vw), 3050, 1580 (br), 1485, 1350 (s), 1300, 1100, 1070, 1020, 760, 690 cm^{-1}; NMR ($CDCl_3$) δ 15.9 (br s, 1 H), 8.5 (m, 1 H), 7.6 (m, 13 H), 5.9 (s, 1 H).

Product **13b** (75 mg, 0.2 mmol) was dissolved in hot methanol (20 mL). Sodium dithionite (200 mg in 3 mL of water) was added dropwise. The reaction mixture turned yellow and was heated for an additional 5 min. Thereafter it was diluted with water and extracted with $CHCl_3$. Evaporation of $CHCl_3$ and recrystallization of the residue from methanol gave orange crystals of **16**: 40 mg (70%); mp 161–163 °C. A mixture melting point determination with a sample prepared from *o*-phenylenediamine and dibenzoylacetylene showed no depression: IR 3040, 1570 (br), 1540, 1350, 1275, 740, 685 cm^{-1}.

1,3-Diphenylphenazine (18). 2-Benzoyl-3-methylquinoxaline (17; 0.5 g, 2 mmol) was dissolved in methanol (20 mL). Acetophenone (0.3 g, 2.5 mmol) was added. Potassium hydroxide (0.5 g) was added, and the mixture was heated at reflux temperature for 0.5 h. Upon concentration of the mixture and cooling, the yellowish orange product crystallized out (140 mg). Recrystallization from $CHCl_3$–CH_3OH gave purified product: 100 mg (15%); mp 167–168 °C; IR 3050, 1395, 1130, 750, 690 cm^{-1}; NMR ($CDCl_3$) δ 8.5 (d, 1 H), 8.3 (m, 3 H), 7.5–7.9 (m, 14 H). Anal. Calcd for $C_{24}H_{16}N_2$: C, 86.72; H, 4.85; N, 8.43. Found: C, 86.84; H, 4.89; N, 8.46.

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Registry No. 1, 6639-86-7; 2, 18080-49-4; 3, 65896-77-7; 4, 5023-53-0; 5, 6449-86-1; 6, 1087-09-8; 7, 80765-45-3; 8, 80780-61-6; 9, 80765-46-4; 10, 80765-47-5; 11, 80765-48-6; 13a, 80765-49-7; 13b, 80765-50-0; 14, 19803-53-3; 16, 57436-88-1; 17, 22239-97-0; 18, 80765-51-1.

Chemistry of Oxaziridines. 2.[1] Improved Synthesis of 2-Sulfonyloxaziridines

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2-Sulfonyloxaziridines **2** are a new class of stable, aprotic, and neutral oxidizing reagents of considerable synthetic and mechanistic versatility.[1] These reagents oxidize sulfides and disulfides to sulfoxides and thiosulfinates, respectively,[2] epoxidize olefins in a syn-stereospecific manner,[3] and hydroxylate carbanions.[4,5] Chiral 2-sulfonyloxaziridines afford optically active sulfoxides[6] and have been used in the chiral synthesis of (+)-kjellmanianone.[5] Recently the application of these reagents to the preparation and study of sulfenic acids (RSOH), a biologically important functional group, has been reported.[7-9] In this paper we describe an improved method for the preparation of these oxidizing reagents using phase-transfer catalysts.

The general preparation of 2-sulfonyloxaziridines **2** as developed in our laboratories is outlined in Scheme I.[1] An alkane- or arenesulfonamide (RSO_2NH_2) is heated with the diethyl acetal of an aromatic aldehyde to give sulfonimine **1**.[1] Oxidation of **1** to **2** utilizes biphasic conditions and involves the addition of a 2.2-fold excess of *m*-chloroperbenzoic acid (MCPBA) in chloroform to a rapidly stirring solution of **1** in chloroform–water–10% sodium bicarbonate at 0 °C.[1] After a reaction time of 4–5 h the yields of **2** were in the range of 43–70%, depending on substituents.

A Baeyer–Villiger-type mechanism has been proposed for the oxidation of **1** to **2** involving attack of the peroxy acid anion (RCO_3^-) on the electron-deficient C–N bond of the sulfonimine **1**.[1] The principal limitation of the oxidation procedure outlined in Scheme I appears to be in bringing the hydrophobic sulfonimine, dissolved in the organic phase, together efficiently with the hydrophilic peroxy acid anion, dissolved in the aqueous phase. Competing with this reaction is hydrolysis of **1** to the sulfonamide and aldehyde.

It was thought that a lipophilic phase-transfer catalyst (PTC) such as benzyltriethylammonium chloride (BTEAC) might increase the efficiency of the oxidation reaction while minimizing hydrolysis. Indeed, the yield of **2** dramatically increased when 0.1 molar equiv of BTEAC was used in the oxidation (Scheme I). The yields of **2** increased from 43–64% to 80–92%, and the reaction time was lowered from 4–5 h to a maximum of 1 h. Furthermore, only a slight excess, 1.1 equiv, of MCPBA was necessary for

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