in dry DMF (0.5 mL) at room temperature. After being kept overnight, the reaction mixture was diluted with ether and filtered through SiO_2, and the filtrate was evaporated. The remaining DMF and unreacted 1 were removed by SiO_2 column chromatography to give citronellic acid (31 mg, 0.18 mmol).

(*R*)-(+)-1-(1-Naphthyl)ethylamide of the acid was prepared by the procedure described in ref 1b. HPLC analysis (column: Varian Micro Pak Si5 50 cm × 8 mm; solvent, hexane/Et_2O = 2/1, 2 mL/min; pressure: 54–56 kg/cm^2; detector 270 nm) showed the diastereomer ratio of [*SR* acid amide (t_R 52.9 min)] vs. [*RR* acid amide (t_R 47.4 min)] was 98.3 ± 0.5:1.7 ± 0.5. The optical purity is therefore 96.6 ± 1.0%.

Registry No. 1, 7540-51-4; 2, 93041-00-0; 3, 93041-01-1; 4, 93041-02-2; 5, 93041-03-3; 6, 93041-04-4; pivaloyl chloride, 3282-30-2; tosyl chloride, 98-59-9.

Oxidative Elimination of Nitrous Acid from Nitrate Esters. Preparation of Mecadox

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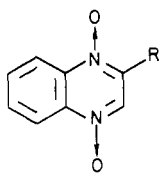
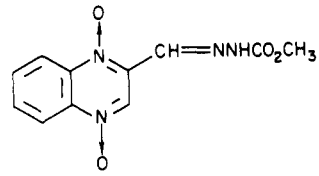
We report a new synthesis of the carbazate derivative of 2-formylquinoxaline 1,4-dioxide (**2**), the highly effective antibacterial and growth-promoting agent[1] marketed under the trade name of Mecadox or Carbadox.



R

1a, CH_3
b CH_2Br
c CH_2ONO_2
d CHO

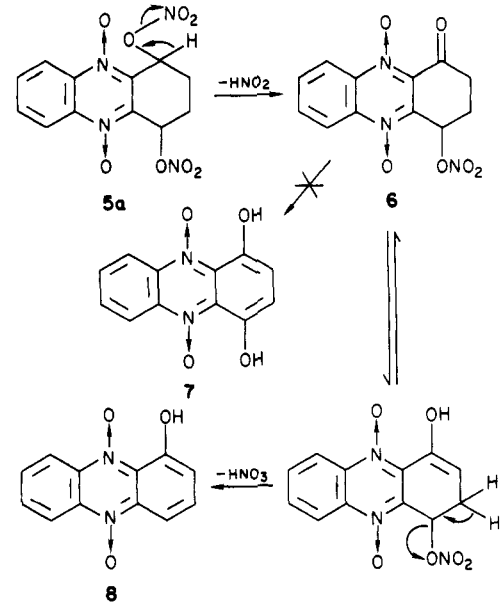


2

Treatment of 2-methylquinoxaline 1,4-dioxide (**1a**) with bromine in ethyl acetate[2] gave the bromomethyl derivative **1b** which reacted with silver nitrate in acetonitrile to give the nitrate ester **1c** (recognizable by the characteristic nitrate ester bands at 1640 and 1285 cm^{-1} and by the NMR singlet at δ 5.9). When a solution of **1c** in dichloromethan e was treated with methyl carbazate and allowed to stand overnight at room temperature, it gave directly Mecadox (**2**, 96% yield from **1c**), presumably via the aldehyde **1d** arising from **1c** by oxidative elimination of nitrous acid.

The transformation of **1a** to **2** entails a two-level increase in oxidation (**1a** to **1b** and **1c** to **1d**). In view of the greatly enhanced antibacterial potency of quinoxaline di-*N*-oxides carrying hydroxymethyl or acyl substituents at positions 2 or 3,[4] we tested the generality of this oxidation on a number of readily available precursors of the type defined by **3a** to **3e**. These were converted to the corresponding nitrate esters (**5a** to **5e**) via the bromo derivatives **4a–e** (Table I).

Scheme I



5a **6** **7** **8**

Attempts to effect elimination of nitrous acid from nitrate esters **5c** and **5e** gave intractable mixtures. Nitrate ester **5b**, which failed to undergo elimination of nitrous acid even in the presence of potassium *tert*-butoxide in refluxing *tert*-butyl alcohol, decomposed when treated with 5% methanolic potassium hydroxide. On the other hand, treatment of **5d** with triethylamine affected smooth oxidative elimination of nitrous acid to give the expected 2-benzoyl-3-phenylquinoxaline 1,4-dioxide (**9**) in 72% yield. Nitrate ester **5a** displayed a remarkable behavior: when treated with triethylamine it gave 1-hydroxyphenazine 9,10-dioxide (**8**) rather than the expected 1,4-dihydroxyphenazine 9,10-dioxide (**7**). Scheme I suggests a plausible pathway for the formation of **8** from **5a** by two successive eliminations: loss of HNO_2 (oxidative) followed by rapid loss of HNO_3 (nonoxidative).

Experimental Section

Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected. Infrared spectra were recorded as potassium bromide disks on a Perkin-Elmer Model 398 grating infrared spectrophotometer. Proton nuclear magnetic resonance spectra were taken on a Varian EM 360L spectrometer in $CDCl_3$ with $(CH_3)_4Si$ as internal reference. Thick layer chromatography was run on silica gel Merck 60_{259}. Elemental analyses were performed by E. Pascher, Bonn, Germany.

All quinoxaline 1,4-dioxides were prepared according to literature methods.[4,5] Bromoketoquinoxaline 1,4-dioxides **4c** and **4e** were prepared according to ref 6.

6,10-Dibromo-7,8,9,10-tetrahydro-6*H*-cyclohepta[*b*]quinoxaline 5,11-Dioxide (4b). A solution of 7,8,9,10-tetrahydro-6*H*-cyclohepta[*b*]quinoxaline 5,11-dioxide (**3b**, 2.3 g) in ethyl acetate (50 mL) was heated at reflux temperature during which a solution of bromine (3.2 g, in 20 mL of ethyl acetate) was added dropwise. The solution was heated for 4 h after which the solvent was evaporated and the product **4b** was collected and recrystallized from $CHCl_3$–CH_3OH: 2.9 g (74%); mp 179–181 °C; IR (cm^{-1}) 2920, 1490, 1450, 1345, 1325, 1310, 1050, 920, 765. The analytical sample was purified by TLC.

2-(Bromomethyl)quinoxaline 1,4-Dioxide (1b). The same procedure as for **4b** was followed, starting with 2-methylquinoxaline 1,4-dioxide (**1a**, 2.64 g, in 50 mL of ethyl acetate) and bromine (2.4 g in 15 mL of ethyl acetate); reaction time 2.5 h. **1b**: 2.10 g (55%); mp 160–162 °C (lit.[7] mp 162–164 °C).

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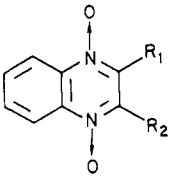
Table I[c]



	R_1	R_2		R_1	R_2	yield, %		R_1	R_2	yield, %
1a	CH_3	H	**1b**	CH_2Br	H	56[b]	**1c**	CH_2NO_3	H	56
3a	$-(CH_2)_4-$		**4a**	$BrCH(CH_2)_2$	CHBr	87[a]	**5a**	$CHNO_3(CH_2)_2$	$CHNO_3$	97
3b	$-(CH_2)_5-$		**4b**	$BrCH(CH_2)_3$	CHBr	70[b]	**5b**	$CHNO_3(CH_2)_3$	$CHNO_3$	70
3c	$COCH_3$	CH_3	**4c**	$COCH_3$	CH_2Br	70[a]	**5c**	$COCH_3$	CH_2NO_3	82
3d	$CH_2C_6H_5$	C_6H_5	**4d**	$CHBrC_6H_5$	C_6H_5	70[b]	**5d**	$CHNO_3C_6H_5$	C_6H_5	90
3e	COC_6H_5	CH_3	**4e**	COC_6H_6	CH_2Br	65[b]	**5e**	COC_6H_5	CH_2NO_3	71

[a] CH_3OH as solvent. [b] $CH_3COOC_2H_5$ as solvent. [c] Satisfactory analyses (±0.3% for C, H, N, and Br if present) were recorded for **4b,d** and **5a,b,d**. Compounds **1c**, **5c**, and **5e** could not be obtained in analytical purity.

2-(Bromobenzyl)-3-phenylquinoxaline 1,4-Dioxide (4d). The same procedure as for **4b** was followed using 2-benzyl-3-phenylquinoxaline 1,4-dioxide[5] (**3d**, 1.29 g, in 75 mL of ethyl acetate) and bromine (0.64 g, in 10 mL of ethyl acetate); reaction time 4 h. **4d**: 1.12 g (70%); mp 178–180 °C; IR (cm^{-1}) 3100, 3020, 1600, 1510, 1490, 1440, 1360, 1335, 1290, 1270, 1085, 1020, 1000, 990, 965, 890, 855, 815, 765, 750, 715, 700, 660.

***trans*-1,4-Dibromo-1,2,3,4-tetrahydrophenazine 5,10-Dioxide (4a).** To a magnetically stirred suspension of 1,2,3,4-tetrahydrophenazine 5,10-dioxide (**3a**, 3.20 g) in methanol (30 mL) was added bromine (5.64 g) dropwise. Stirring was continued in the dark for 5 days at room temperature. The resulting yellow precipitate was collected by suction filtration, washed with cold CH_3OH and ether, and recrystallized from CH_3OH–$CHCl_3$. **4a**: 5.11 g (87%); mp 179–181 °C (lit.[7] mp 171–173 °C).

Preparation of Quinoxaline 1,4-Dioxide Nitrate Esters. General Procedure. A solution of silver nitrate (7.1 mmol) and the specific bromo derivative (**1b**, **4a–e**; 1.3 mmol) in CH_3CN (30 mL) was stirred in the dark at room temperataure for 1.5 h unless otherwise specified. The solution was filtered and the precipitate was washed twice with $CHCl_3$ (30 mL each). The combined filtrates were concentrated. Ethyl acetate (100 mL) was added to the concentrate and any precipitate formed was filtered out. The ethyl acetate solution was washed twice with water (50 mL each), the organic layer was dried, and ethyl acetate was evaprated under reduced pressure to yield products **1c** and **5a–e** which were recrystallized from $CHCl_3$–CH_3OH (Table I).

1c (R_1 = CH_2NO_3, R_2 = H): mp 137–139 °C; yield 56%; IR (cm^{-1}) 3100, 3030, 1660, 1640, 1550, 1510, 1370, 1355, 1285, 1270, 1240, 1160, 1095, 1045, 1000, 975, 945, 860, 850, 785, 755, 710, 660; NMR δ 5.90 (s, 2 H), 8.00 (m, 2 H), 8.63 (m, 3 H).

5a (R_1,R_2 = $-CHNO_3(CH_2)_2CHNO_3-$): mp 205–207 °C dec; yield 97%; reaction time 20 min; IR (cm^{-1}) 3100, 3000, 1650, 1515, 1445, 1370, 1330, 1315, 1275, 1100, 1015, 940, 910, 845, 785, 670; NMR δ 2.3 (br s, 4 H), 6.8 (br s, 2 H), 7.9 (m, 2 H), 8.6 (m, 2 H).

5b (R_1,R_2 = $-CHNO_3(CH_2)_3CHNO_3$): mp 196–198 °C yield 70%; IR (cm^{-1}) 3080, 2940, 1640, 1500, 1445, 1355, 1320, 1275, 1110, 1070, 1045, 980, 955, 915, 855, 800, 770, 660; NMR δ 2.03 (br s, 6 H), 7.2 (m, 2 H), 7.9 (m, 2 H), 8.6 (m, 2 H).

5c (R_1 = $COCH_3$, R_2 = CH_2NO_2): mp 136–138 °C dec; yield 82%; IR (cm^{-1}) 3110, 2960, 2940, 1715, 1665, 1605, 1445, 1430, 1375, 1340, 1290, 1270, 1105, 1055, 980, 955, 855, 790, 760, 700, 690; NMR δ 2.80 (s, 3 H), 5.86 (s, 2 H), 7.93 (m, 2 H), 8.63 (m, 2 H).

5d (R_1 = $CHNO_3C_6H_5$, R_2 = C_6H_5): mp 138–140 °C dec; yield 90%; IR (cm^{-1}) 3060, 1640, 1495, 1455, 1445, 1365, 1325, 1280, 1270, 1090, 1025, 1050, 995, 980, 940, 925, 905, 860, 845, 785, 770, 730, 715, 705, 670.

5e (R_1 = COC_6H_5, R_2 = CH_2NO_3): mp 177–180 °C; yield 71%; IR (cm^{-1}) 3100, 3050, 1655, 1600, 1585, 1510, 1440, 1430, 1330, 1275, 1245, 1185, 1170, 1110, 1065, 1030, 1010, 950, 880, 840, 820, 790, 760, 740, 710, 690, 665; NMR δ 5.86 (s, 2 H), 7.80 (m, 7 H), 8.70 (m, 2 H).

Methyl (Quinoxalinylmethylene)carbazate (Mecadox, 2). A solution of 2-[(nitrooxy)methyl]quinoxaline 1,4-dioxide (**1c**, 1.52 g) and methyl carbazate (3.24 g) in dichloromethane (15 mL) was heated on a steam bath to dissolve the starting materials. The reaction mixture was allowed to stand overnight at room temperature. The product precipitated out and was collected, washed with dichloromethane, and recrystallized from ethanol: 1.60 g (96%); mp 243–245 °C; IR (cm^{-1}) 3220, 1755, 1555, 1535, 1445, 1385, 1335, 1245, 1205, 1160, 1135, 1095, 1055, 995, 845, 795, 775. The product was identical with an authentic sample (mmp, TLC, IR) prepared by an independent method.[8]

1-Hydroxyphenazine 5,10-Dioxide (8). A solution of 1,4-bis(nitrooxy)-1,2,3,4-tetrahydrophenazine 5,10-dioxide (**5a**, 0.17 g) and triethylamine (0.14 mL) in dichloromethane (5 mL) was refluxed for 35 min. The dichloromethane was evaporated and product **8** was isolated by TLC: 0.06 g (55%); mp 187–189 °C (lit.[9] mp 184–185 °C).

2-Benzoyl-3-phenylquinoxaline 1,4-Dioxide (9). The same procedure used in the preparation of **8** was followed with 2-[[(phenyloxy)nitros]oxy]-3-phenylquinoxaline 1,4-dioxide (**5d**, 0.13 g) and triethylamine (0.25 mL) in 5 mL of dichloromethane; reaction time 1.25 h. Product **9** was purified by TLC: 0.08 g (72%); 228–230 °C (lit.[10] mp 234 °C).

Registry No. **1a**, 6639-86-7; **1b**, 18080-66-5; **1c**, 93222-85-6; **2**, 6804-07-5; **3b**, 18965-43-0; **3c**, 13297-17-1; **3d**, 53326-80-0; **3e**, 19803-53-3; **4a**, 93222-83-4; **4b**, 18965-53-2; **4c**, 60949-39-5; **4d**, 93222-84-5; **4e**, 62686-03-7; **5a**, 93222-86-7; **5b**, 93222-87-8; **5c**, 93222-88-9; **5d**, 93222-89-0; **5e**, 93222-90-3; **8**, 18274-55-0; **9**, 13494-38-7; silver nitrate, 7761-88-8; methyl carbazate, 6294-89-9; dichloromethane, 75-09-2.

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Heteroacylsilanes: Synthesis and Synthetic Potentialities of New Nucleophilic Acylation Agents

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As a part of our continuing interest in the chemistry of acylsilanes, we describe here the first synthesis dealing with the hitherto unknown class of heteroacylsilanes and the

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