415 (8), 400 (13), 211 (17), 196 (11), 135 (100); exact mass for $C_{26}H_{29}NO_2Si$ calcd m/e 415.1967, found m/e 415.1962. Anal. Calcd for $C_{26}H_{29}NO_2Si$: C, 75.14; H, 7.03. Found: C, 75.12; H, 7.18.

***rel*-(1′*R*,3*R*,4*R*)-3-[1′-(Dimethylphenylsilyl)ethyl]-4-phenyl-2-azetidinone (4b)**: IR ($CHCl_3$) 3400, 1750 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.20 (s, 3 H, CH_3Si), 0.30 (s, 3 H, CH_3Si), 0.80 (d, J = 7.4, 3 H, CH_3CH), 1.01 (dq, J = 4.5, 7.4, 1 H, CH_3CH), 3.62 (ddd, J = 5.6, 4.5, 2.1, 1 H, CHC=O), 4.65 (d, J = 5.6, 1 H, CHN), 6.11 (s, 1 H, NH), 7.13–7.45 (m, 10 H, ArH); ^{13}C NMR ($CDCl_3$) δ −4.80 (q), −4.58 (q), 11.44 (q), 16.20 (d), 55.56 (d), 57.64 (d), 126.96 (d), 127.73 (d), 127.89 (d), 128.44 (d), 129.10 (d), 134.02 (d), 137.79 (s), 137.95 (s), 170.48 (s); mass spectrum m/e (relative intensity) 309 (2), 294 (43), 216 (22), 189 (9), 135 (100), 91 (12), 85 (23); exact mass for $C_{19}H_{23}NOSi$ calcd m/e 309.1549, found m/e 309.1529.

***rel*-(1′*R*,3*S*,4*R*)-3-[1′-(Dimethylphenylsilyl)ethyl]-4-phenyl-2-azetidinone (5b)**: mp 116.5–118.0 °C; IR ($CHCl_3$) 3400, 1750 cm^{-1}; NMR (200 MHz, $CDCl_3$) δ 0.22 (s, 3 H, CH_3Si), 0.30 (s, 3 H, CH_3Si), 1.13 (d, J = 7.4, 3 H, $CHCH_3$), 1.55 (dq, J = 5.1, 7.4, 1 H, CH_3CH), 3.18 (ddd, J = 5.1, 2.4, 0.9, 1 H, CHC=O), 4.35 (d, J = 2.4, 1 H, CHN), 6.03 (s, 1 H, NH), 7.16–7.44 (m, 10 H, ArH); mass spectrum m/e (relative intensity) 309 (2), 294 (30), 216 (17), 189 (9), 135 (100); exact mass for $C_{19}H_{23}NOSi$ calcd m/e 309.1549, found m/e 309.1545.

***rel*-(1′*R*,3*R*,4*S*)-3-[1′-(Dimethylphenylsilyl)ethyl]-4-phenyl-2-azetidinone (6b)**: mp 97.5–98.5 °C; IR ($CHCl_3$) 3400, 1750 cm^{-1}; NMR (200 MHz, $CDCl_3$) δ 0.27 (s, 3 H, CH_3Si), 0.33 (s, 3 H, CH_3Si), 1.21 (d, J = 7.3, 3 H, $CHCH_3$), 1.48 (q, J = 7.3, 1 H, CH_3CH), 3.11 (ddd, J = 6.8, 2.2, 0.7, 1 H, CHC=O), 4.32 (d, J = 2.2, 1 H, CHN), 6.02 (s, 1 H, NH), 7.15–7.48 (m, 10 H, ArH); mass spectrum, m/e (relative intensity) 309 (2), 294 (34), 216 (17), 189 (10), 135 (100); exact mass for $C_{19}H_{23}NOSi$ calcd m/e 309.1549, found m/e 309.1548.

***rel*-(1′*R*,3*R*,4*R*)-3-(1′-Hydroxyethyl)-4-phenyl-2-azetidinone (8)**: mp 94.5–96.0 °C; IR ($CHCl_3$) 3500, 3400, 1755 cm^{-1}; NMR (200 MHz, $CDCl_3$) δ 1.39 (d, J = 6.4, 3 H, CH_3), 2.14 (br s, 1 H, OH), 3.09 (dd, J = 5.9, 2.3, 1 H, CHC=O), 4.19–4.26 (m, 1 H, $CHCH_3$), 4.60 (d, J = 2.3, 1 H, CHN), 6.13 (br s, 1 H, NH), 7.31–7.55 (m, 5 H, ArH); mass spectrum, m/e (relative intensity) 191 (2), 173 (10), 148 (62), 130 (12), 106 (100), 105 (85), 91 (34), 77 (35), 68 (49); exact mass for $C_{11}H_{13}NO_2$ calcd m/e 191.0946, found m/e 191.0904.

***rel*-(1′*R*,3*S*,4*S*)-3-[1′-(Dimethylphenylsilyl)ethyl]-4-(2-furyl)-2-azetidinone (12)**: mp 80.5–81.5 °C; IR ($CHCl_3$) 3400, 1760 cm^{-1}; NMR (200 MHz, $CDCl_3$) δ 0.37 (s, 3 H, CH_3Si), 0.45 (s, 3 H, CH_3Si), 0.53 (d, J = 7.2, 3 H, $CHCH_3$), 1.10–1.20 (m, 1 H, $CHCH_3$), 3.31 (ddd, J = 12.1, 5.0, 1.1, 1 H, CHC=O), 4.76 (d, J = 5.0, 1 H, CHN), 5.84 (br s, 1 H, NH), 6.34 (d, J = 3.0, 1 H, CH=CROR), 6.39 (dd, J = 3.0, 1.8, 1 H, CH=CHOR), 7.31–7.35 (m, 3 H, ArH), 7.41 (d, J = 1.8, 1 H, CHOR), 7.52–7.59 (m, 2 H, ArH); mass spectrum, m/e (relative intensity) 299 (7), 284 (37), 206 (32), 135 (100); exact mass for $C_{17}H_{21}NO_2Si$ calcd m/e 299.1342, found m/e 299.1350.

Acknowledgment. We thank the National Institutes of Health for their generous support (Grant AI-21074).

Supplementary Material Available: Crystallographic information, final positional and thermal parameters, structure factor tables, bond lengths and angles, and an ORTEP for compounds **3** and **7** (10 pages). Ordering information is given on any current masthead page.

Synthesis and Chemistry of Some Furazano- and Furoxano[3,4-*b*]piperazines[1]

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Received April 2, 1985

A series of N,N′-disubstituted furazano- and furoxano[3,4-*b*]piperazines **1a–d** and **2b–d** have been synthesized from N,N′-disubstituted 2,3-piperazinedione dioximes **5a–d** by base-promoted dehydration and by basic potassium ferricyanide oxidation, respectively. The N,N′-disubstituted 2,3-piperazinedione dioximes were synthesized by reacting the appropriate N,N′-disubstituted ethylenediamine with dichloroglyoxime. Also studied was the reaction of 3,4-diaminofurazan with glyoxal and formaldehyde. The compounds have been studied by ^1H and ^{13}C NMR spectroscopy.

There have been numerous studies[2] of compounds with furazan ([1,2,5]oxadiazolo-) and furoxan ([1,2,5]oxadiazolo 1-oxide) rings fused to aromatic rings and saturated carbocyclic rings, but few studies of compounds with furazan or furoxan rings fused to saturated heterocyclic rings have been reported in the open literature.[2] We became interested in compounds with furazan and furoxan rings fused to saturated nitrogen heterocycles because calculations[3,4] predict that nitrated derivatives of some of these compounds would be quite dense and energetic. In this paper, we report on the synthesis, chemistry, and spectroscopy of some furazano[3,4-*b*]piperazines **1a–d**, furoxano[3,4-*b*]piperazines **2b–d**, and some related compounds. These

(1) The accepted IUPAC nomenclature for these compounds is 4,5,6,7-tetrahydro-1,2,5-oxadiazolo[3,4-*b*]pyrazines and 1-oxides.

(2) (a) Boyer, J. H. In "Heterocyclic Compounds"; Elderfield, R. C., Ed.; John Wiley & Sons: New York, 1961; Vol. 7, pp 462–540. (b) Khmel'nitskiy, L. I.; Novekov, S. S.; Godovikova, T. I. "The Chemistry of Furoxanes"; Nauka: Moscow, USSR, 1981. (c) Katritzky, A. R.; Lagowski, J. M. "Chemistry of Heterocyclic *N*-Oxides"; Academic Press: New York, 1971; pp 113–118.

(3) Cichra, D. A.; Holden, J. R.; Dickinson, C.; NSWC Report TR79-273, Naval Surface Weapons Center, Silver Spring, MD, 1980, pp 39.

(4) (a) Rothstein, L. R. Petersen, R. *Prop. Explo.* **1979**, *4*, 56–60. (b) Rothstein, L. R. *Prop. Explo.* **1981**, *6*, 91–93.

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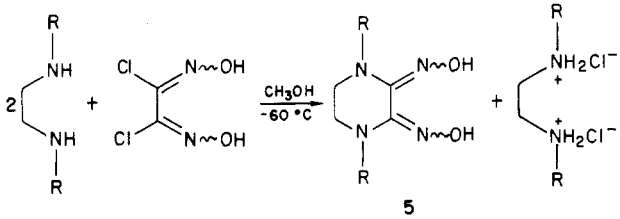
Table I. Synthesis and Properties of 2,3-Piperazinedione Dioximes 5a-d[a]

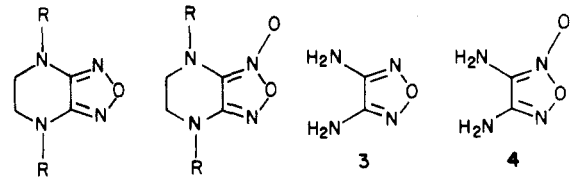


5

	R	yield (%)	mp (°C)	solvent
a	H	50	215–216[b]	H_2O
b	CH_3	66	158–160	$EtOH/H_2O$
c	$CH(CH_3)_2$	75	170–171	$EtOH/H_2O$
d	$CH(CH_3)_3$	92	180–182	EtOH

[a] All new compounds gave satisfactory C, H, and N analysis (±0.3%). [b] Lit.[6] mp 205–206 °C.

compounds can be considered to be derivatives of the known 3,4-diaminofurazan, **3**,[5] and the unknown 3,4-diaminofuroxan, **4**.



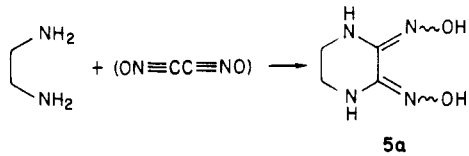
1 2 3 4

a, R = H;
b, R = CH_3;
c, R = $CH(CH_3)_2$;
d, R = $CH(CH_3)_3$

Results

Synthesis. Furazans are normally made by either dehydration of an α-dioxime or by reduction of a furoxan. Furoxans are normally made either by oxidation of a α-dioxime or by generating a vinyl nitro nitrene. Since α-dioximes are precursors to both furazans and furoxans, we chose to explore this route for the synthesis of the desired furazano[3,4-*b*]piperazines and furoxano[3,4-*b*]piperazines.

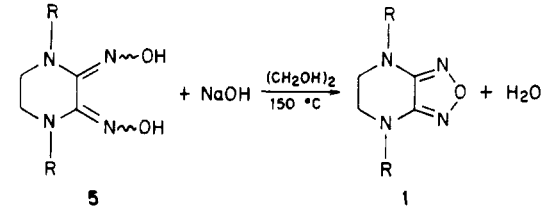
The parent compound 2,3-piperazinedione dioxime, **5a**, is a known compound[6] made by reacting ethylenediamine with in situ generated cyanogen di-*N*-oxide (eq 1). This



5a (1)

synthesis of **5a** proved to be difficult to reproduce and impossible to scale up. We then examined the direct reaction of N,N′-disubstituted ethylenediamines with dichloroglyoxime for the synthesis of the desired 2,3-piperazinedione dioximes. This reaction gave good yields of the desired 2,3-piperazinedione dioximes when a second mole of the diamine was used as the base to scavenge the hydrochloric acid produced. Attempts to use sodium hydroxide or triethylamine as the base led to lower yields. The main difficulty encountered was the separation of the products from the diamine dihydrochloride byproducts

Table II. Synthesis and Properties of Furazano[3,4-*b*]piperazines 1a-d[a]

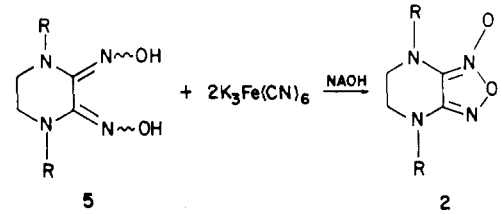


5 1

	R	yield (%)	mp (°C)	solvent
a	H	50	153–155	H_2O
b	CH_3	52	79–80	$EtOH/H_2O$
c	$CH(CH_3)_2$	60	59–60	EtOH
d	$C(CH_3)_3$	75	135–137	EtOH

[a] All new compounds gave satisfactory C, H, and N analysis (±0.3%).

Table III. Synthesis and Properties of Furoxano[3,4-*b*]piperazines 2a-d[a]



5 2

	R	yield (%)	mp (°C)	solvent
a	H	0		
b	CH_3	72	88–90	H_2O
c	$CH(CH_3)_2$	90	98–100 dec	EtOH
d	$C(CH_3)_3$	98		EtOH

[a] All new compounds gave satisfactory C, H, and N analysis (±0.3%).

which have similar solubilities in the unsubstituted and methyl substituted cases. These results are summarized in Table I.

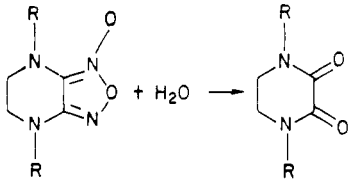
Several procedures have been developed for dehydrating α-dioximes to furazans.[2] We used the sodium hydroxide in ethylene glycol procedure developed by Visalok and Ostrovskoya[7] for dehydrating the 2,3-piperazinedione dioximes to furazano[3,4-*b*]piperazines. These results are summarized in Table II.

Various oxidizing agents such as sodium hypochlorite, bromine, and potassium ferricyanide have been used to convert α-dioximes to furoxans.[2] We found the procedure of Walstra, Trompen, and Hackmann utilizing basic potassium ferricyanide to be convenient.[8] Using this procedure, good yields of all the furoxano[3,4-*b*]piperazines, except the NH compound **2a**, could be obtained. In this latter case, the compound apparently undergoes further oxidation as observed for some acyclic analogues.[8] These results are summarized in Table III.

These compounds proved to be rather unstable. Attempts to recrystallize either the isopropyl or *tert*-butyl compounds from water resulted in complete conversion of the compounds to the corresponding 2,3-diketopiperazines (eq 2). The methyl compound also undergoes this reaction but more slowly.

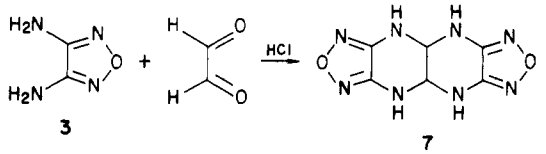
Reaction of 3,4-Diaminofurazan, 3, with Glyoxal and Formaldehyde. Previous workers, who examined the reaction of **3** with glyoxal, reported that no reaction oc-

(5) (a) Colburn, M. D. *J. Heterocycl. Chem.* **1968**, *5*, 83–87. (b) Komin, A. P.; Street, R. W.; Carmack, M. *J. Org. Chem.* **1975**, *40*, 2749–2752.
(6) Grundmann, C.; Mini, V.; Dean, J. M.; Frommeld, H.-D. *Jusutus Liebigs Ann. Chem.* **1965**, *687*, 191–214.
(7) Visalok, I. V.; Ostrovskoya, A. V. *Khim. Tekhnol. Elementoorg. Soedin Polim.* **1978**, *78*, 48–49.
(8) Walstra, P.; Trompen, W. P.; Hackmann, J. T. *Recl. Trav. Chim. Pays-Bas* **1968**, *87*, 452–460.



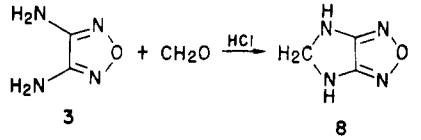
(2)

curred.[9] We found that **3** and glyoxal react in warm HCl solution to give the 2:1 condensation product **7** in essentially quantitative yield (see eq 3). This compound has been fully characterized spectroscopically. However, we have been unable to establish the stereochemistry of the ring junction.



(3)

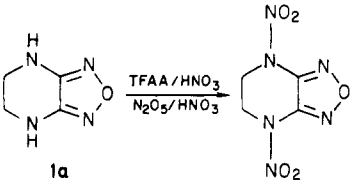
The reaction of **3** with formaldehyde under similar conditions was examined in hope of synthesizing the related furazano[3,4-*b*]imidazolidine, **8** (see eq 4). A nearly



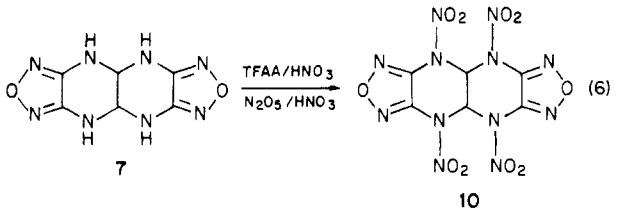
(4)

quantitative yield of a product which gave a correct analysis for $C_3H_4N_4O$ was obtained. However, from the physical and chemical properties of the compound it is clear that this compound is not **8** but a polymer or oligomer. In particular, the product showed no definite melting point, and it is only very slightly soluble in hot water; whereas the furazano[3,4-*b*]piperazine, **1a**, is quite soluble. An X-ray powder pattern of the material indicates it has a low degree of crystallinity. Similar observations have been made with a butylated analogue of **3**.[10]

Nitration of 1a and 7. Both **1a** and **7** undergo smooth, direct nitration to give the corresponding nitro derivatives **9** and **10** (eq 5 and 6) using either mixtures of trifluoro-



(5)

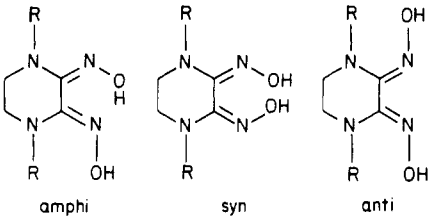


(6)

acetic anhydride (TFAA) and 100% nitric acid or a solution of N_2O_5 in 100% nitric acid.[11] Compound **9** shows reasonable thermal stability, melting with decomposition

(9) Sato, N.; Adachi, J. *J. Org. Chem.* 1978, *43*, 341–343.
(10) Ostrovskoya, A. V.; Vigalok, I. V.; Svetlakov, N. V. *Chem. Abstr.* 1981, *94*, 85092v.
(11) Harrar, J. E.; Pearson, R. K. *J. Electrochem. Soc.* 1982, 129.

Scheme I. Possible Rotamers of 2,3-Piperazinedione Dioximes



Scheme II. Ring Isomerization in Furoxano[3,4-*b*]piperazines 2b-d

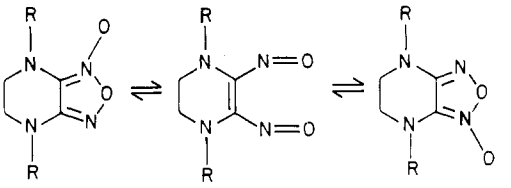
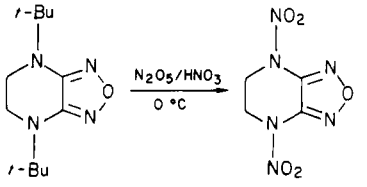


Table VI. Rotamer Distribution in 2,3-Piperazinedione Dioximes

compd	R	rotamer concn, % amphi	anti	syn
5a	H	0	100	0
5b	CH_3	76	16	8
5c	$CH(CH_3)_2$	68	17	15
5d	$C(CH_3)_3$	12	20	68

at 132–134 °C. However, compound **10** is unstable and undergoes slow decomposition even at room temperature. It can, however, be stored at −20 °C for months without decomposition.

Compound **9** can also be made by treatment of the 1,4-di-*tert*-butylfurazano[3,4-*b*]piperazine, **1d**, with N_2O_5/HNO_3 solutions (eq 7). The nitrolysis of *tert*-butyl groups has been used previously by Cichra and Adolph to synthesize nitramines.[12]



(7)

NMR Spectra. The ^1H and ^{13}C NMR chemical shift data for most of the compounds synthesized in this study are summarized in Tables IV and V which can be found in the supplementary section.

Although proton NMR spectra of **5a–d** did not reveal rotational isomerism as shown in Scheme I, ^{13}C spectra did show unambiguous evidence for the existence of all three possible oxime configurations. The distribution of isomers is markedly dependent upon the nitrogen substituent, as summarized below in Table VI.

The preference for the anti form in the parent compound is doubtless due to hydrogen bonding between the hydrogen on the secondary nitrogen and the oxime oxygen. With N-alkyl substitution, the isomer distribution is evidently determined by steric effects and the possibility of hydrogen bonding between the oxime groups. Structural models suggest that these molecules probably exist as chair or twist-boat conformers and that the oxime groups will not be coplanar unless they are linked by a hydrogen bond.

(12) Cichra, D. A.; Adolph, H. G. *J. Org. Chem.* 1982, *47*, 2474–2476.

The relative importance of steric repulsion between the alkyl substituent and oxime group is seen in the increase of the syn rotamer population with increasing bulk of the alkyl group.

Ring Isomerization in Furoxano[3,4-*b*]piperazines. It is well established that furoxan rings undergo an isomerization through a vinyl dinitroso intermediate (see Scheme II).[13] If the substituents on the furoxan ring are identical, then this is a degenerate isomerization, but if they are different, it allows the two isomers to reach thermodynamic equilibrium. The barrier for this isomerization ranges from 14.0 kcal/mol in benzofuroxan[14] to 34.0 kcal/mol in dimethylfuroxane.[15] All attempts to measure this for **2b–d** by variable temperature NMR have failed because the compounds decompose when heated. However, the barrier must be greater than 14 kcal/mol since separate resonances are seen for the methyl groups in **2b** and isopropyl groups in **2c**.

Experimental Section

Warning! Compounds **9** and **10** are explosives of moderate sensitivity and should be handled accordingly.

Routine ^1H NMR spectra were recorded on a Varian EM-360 spectrometer. The ^{13}C NMR spectra were recorded on a Nicolet WB-200 spectrometer. Both the ^1H and ^{13}C spectra were referenced to internal Me_4Si and are reported on the δ scale. IR spectra were recorded on a Nicolet 7000 FT IR spectrometer. Elemental analyses were carried out by Galbraith Laboratories, Inc., Knoxville, TN.

2,3-Piperazinedione Dioximes 5a–d. Dichloroglyoxime (15.7 g, 0.10 mol) and 400 mL of methanol were placed in a 1-L, round-bottomed flask. This solution was cooled to −40 °C and stirred vigorously while a solution of 0.2 mol of the appropriate diamine in 100 mL of methanol was added to one portion. The slurry was allowed to come to room temperature, and the methanol was then removed at reduced pressure. The solid was slurried with 20 mL of water to dissolve the diamine dihydrochloride and the crude product was collected by vacuum filtration. The results are summarized in Table I.

Furazano[3,4-*b*]piperazines 1a–d. Sodium hydroxide (4.0 g, 0.10 mol) was added to 10 mL of well stirred ethylene glycol maintained at 150 °C. When the sodium hydroxide had dissolved, 0.1 mol of the appropriate 2,3-dioximinopiperazine were added over 5 min. The solution was stirred for 20 additional minutes and then cooled to room temperature. The mixture was diluted with 20 mL of water and cooled to 0 °C. The crude product was collected by vacuum filtration and recrystallized from the appropriate solvent. The results are summarized in Table II.

Furoxano[3,4-*b*]piperazines 2b–d. To a solution (or suspension) of 0.02 mol of the appropriate 2,3-dioxaminopiperazine in 30 mL of 4 M sodium hydroxide was added 40 mL of a 1.0 M potassium ferricyanide solution. The furoxan precipitated and was collected by vacuum filtration and recrystallized from the solvent indicated in Table III. The results are summarized in Table III.

Diaminoglyoxime. The procedure of E. Fisher was used to prepare this compound. The product was recrystallized from H_2O to give crystals with mp 200–201 °C (lit.[16] mp 200 °C).

3,4-Diaminofurazan (3). The procedure of Carmack and co-workers[5b] was used to prepare this compound from diaminoglyoxime. After recrystallization from water it melted at 179–180 °C (lit.[5a] mp 180 °C).

1,4-Dialkyl-2,3-diketopiperazines 6b–d. The appropriate amount of 1,4-dialkylfuroxano[3,4-*b*]piperazine **2b–d** (0.01 mol) was dissolved in 5 mL of 50% ethanol, and this solution was refluxed for 5 min. The solvent was removed at reduced pressure to give the crude product which was recrystallized from ethanol water.

6b: mp 175–177 °C (lit.[17] mp 176–177 °C).

6c: mp 200–202 °C. Anal. Calcd for $C_{10}H_{18}N_2O_2$: C, 60.57; H, 9.15; N, 14.13. Found: C, 60.38; H, 9.00; N, 14.36.

6d: mp 275–280 °C. Anal. Calcd for $C_{12}H_{22}N_2O_2$: C, 63.68; H, 9.80; N, 12.38. Found: C, 63.82; H, 9.79; N, 12.42.

4a,5,9a,10-Tetrahydro-4*H*,9*H*-[1,2,5]oxadiazolo[3,4-*b*]-[1,2,5]oxadiazolo[3′,4′:5,6]pyrazino[2,3-*c*]pyrazine (7). A 10-g portion (0.1 mol) of 3,4-diaminofurazan was added to a solution of 10 g of 37% hydrochloric acid in 20 mL of distilled water. This slurry was stirred at 60 °C while 7.25 g of 40% aqueous glyoxal was added. The mixture was stirred for one additional hour and then cooled. The product was collected and washed well with water. After drying, it weighed 10.86 g (0.049 mol, 98%). The material could be recrystallized from 50:50 DMF/H_2O to give plates with mp 230–231 °C: ^1H NMR (Me_2SO-d_6) 5.02 (br s, 2H, CH), 7.92 (br s, 4H, NH) ppm. Anal. Calcd for $C_6N_6N_8O_2$: C, 32.43; H, 2.72; N, 50.44. Found: C, 32.26; H, 2.74; N, 50.19.

Reaction of 3,4-Diaminofurazan and Formaldehyde. A 1.0-g portion (0.01 mol) of 3,4-diaminofurazan was added to a solution of 1.0 g of 37% hydrochloric acid in 25 mL of H_2O. This was heated to 60 °C and stirred until the diaminofurazan dissolved; then 1.0 g of 37% aqueous formaldehyde was added. The product preciptiated immediately. The mixture was cooled and the product was collected by vacuum filtration and washed well with water. After drying, it weighed 1.06 g (8.5 mol 95%). The product showed no definite melting point. Anal. Calcd for $(C_3H_4N_4O)_n$: C, 32.14; H, 3.60; N, 49.99. Found: C, 32.23; H, 3.68; N, 49.86.

1,4-Dinitrofurazano[3,4-*b*]piperazine (9). Method A. Fourteen milliliters of trifluoroacetic anhydride and a magnetic stirring bar were placed in a 100-mL round-bottomed flask. The anhydride was cooled to −30 °C (dichloroethane, dry ice), and 6 mL of 100% nitric acid were added dropwise over a 2-min period. The cooling bath was removed and the mixture allowed to warm to 0 °C. The mixture was recooled to −30 °C, and 2.52 g (0.02 mol) of **1a** were added in small portions over a 5-min period. The cooling bath was removed and the mixture allowed to come to room temperature over 5 min. The reaction mixture was poured onto a mixture of 20 g of ice and 50 mL of water. The product precipitated out and was collected by vacuum filtration. The yield of crude product is 2.87–3.12 g (66–75%). The product was recrystallized from acetone–water to yield platelets with a melting point of 132–134 °C dec.

Method B. A solution of 12 mL of 24% N_2O_5 in 100% nitric acid was placed in a 50-mL Erlenmeyer flask. This was cooled to 0 °C and stirred while 2.52 g of **1a** were added in small portions over 5 min. The cooling batch was removed and the mixture stirred for 5 min; then the reaction mixture was poured onto a mixture of 20 g of ice and 50 mL of water. The product precipitated and was collected by vacuum filtration. The crude product was recrystallized from acetone water. Anal. Calcd for $C_4H_4N_6O_5$: C, 22.23; H, 1.87; N, 38.89. Found: C, 22.40; H, 2.00; N, 38.80.

4,5,9,10-Tetranitro-4a,5,9a,10-tetrahydro-4*H*,9*H*-[1,2,5]oxadiazolo[3,4-*b*][1,2,5]oxadiazolo[3′,4′:5,6]pyrazino[2,3-*e*]pyrazine (10). Fourteen milliliters of trifluoroacetic anhydride and a magnetic stirring bar were placed in a 100-mL round-bottomed flask. The solution was cooled to −5 °C (salt–ice bath) and 6.0 mL of 100% nitric acid were added dropwise, with stirring, over a period of 20 min. This mixture was allowed to briefly warm to room temperature; then it was recooled and 2.22 g of **7** were added in small portions over a period of 10 min. The mixture was allowed to come slowly to room temperature over 4 h. The product was collected by vacuum filtration under a blanket of nitrogen and washed well with methylene chloride. The last traces of solvent were removed under vacuum. ^1H NMR (Me_2SO-D_6) 8.32 ppm.

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Registry No. **1a**, 98778-06-4; **1b**, 98778-07-5; **1c**, 98778-08-6; **1d**, 98778-09-7; **2b**, 98778-10-0; **2c**, 98778-11-1; **2d**, 98778-12-2; **3**, 17220-38-1; (**3a**-CH_2O)$_x$, 76643-24-8; *anti*-**5a**, 98778-03-1; *amphi*-**5b**, 98778-16-6; *anti*-**5b**, 98799-23-6; *syn*-**5b**, 98778-17-7; *amphi*-**5c**, 98778-18-8; *anti*-**5c**, 98778-04-2; *syn*-**5c**, 98778-19-9; *amphi*-**5d**, 98778-20-2; *anti*-**5d**, 98778-05-3; *syn*-**5d**, 98778-21-3; **6b**, 59417-06-0; **6c**, 98778-13-3; **6d**, 98778-14-4; **7**, 97288-72-7; **9**, 98778-15-5; **10**, 97288-73-8; HON=C(Cl)C(Cl)=NOH, 2038-44-0; $H_2NCH_2CH_2NH_2$, 107-15-3; $H_3CNHCH_2CH_2NHCH_3$, 110-70-3; $(CH_3)_2CHNHCH_2CH_2NHCH(CH_3)_2$, 4013-94-9; $(CH_3)_3CNHCH_2CH_2NHC(CH_3)_3$, 4062-60-6; OHCCHO, 107-22-2.

Supplementary Material Available: Tables of the ^1H and ^{13}C NMR data for most of the compounds in this paper (2 pages). Ordering information is given on any current masthead page.

Synthesis and Properties of 7-Alkoxyfurazano[3,4-*d*]pyrimidines and Their Use in the Preparation of 4-Alkoxypteridines and N^3-Substituted Pterins[1]

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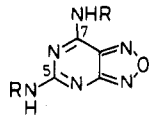
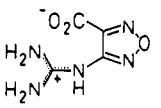
Reaction of 5-amino-7-(methylthio)furazano[3,4-*d*]pyrimidine (**4**) with a range of alcohols in the presence of bromine leads to the formation of the corresponding 5-amino-7-alkoxyfurazano[3,4-*d*]pyrimidines (**5–10**). These on hydrogenolysis afford 6-alkoxy-2,4,5-triaminopyrimidines, which can be condensed with benzil to give 2-amino-4-alkoxypteridines (**17–21**). The product from hydrogenolysis of 5-amino-7-(2-chloroethoxy)furazano-[3,4-*d*]pyrimidine (**7**), however, undergoes intramolecular cyclization to a 2,3-dihydrooxazolo[3,2-*c*]pyrimidinium compound (**23**), which behaves as a heteronuclear resonance stabilized ambident cation. Reaction of it with nucleophiles followed by condensation with benzil leads to N^3-substituted pteridines.

The pyrimidine ring of furazano[3,4-*d*]pyrimidines is highly π-deficient,[2] and this electron deficiency is particularly marked at position 7. As a result, nitrogen substituents at position 7 of furazanopyrimidines such as **1** or **2** have been found to undergo ready replacement by



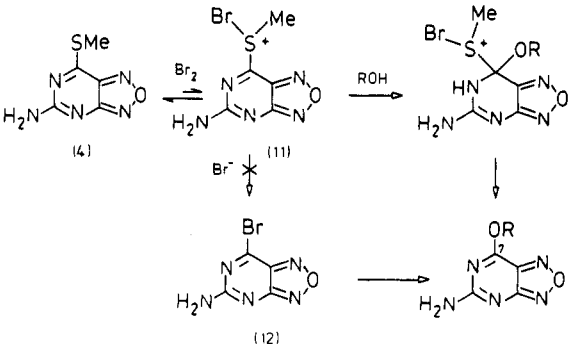
(1) R = H
(2) R = COC_6H_5



(3)

both nitrogen nucleophiles such as amines,[3,4] and carbon nucleophiles such as enolate anions.[5] Analogous replacement by alkoxide nucleophiles cannot be achieved, however. 7-Alkoxyfurazano[3,4-*d*]pyrimidines have not so far been reported, and 7(6*H*)-oxo compounds are rare.[6] For example, treatment of either **1** or **2** with ethanolic sodium ethoxide led to extensive decomposition, and no useful product could be isolated, while treatment of the same compounds with aqueous base gave 4-guanidino-3-furazancarboxylic acid (**3**), formed by hydrolytic cleavage of the pyrimidine ring.[6] In contrast, we now report that 5-amino-7-(methylthio)furazano[3,4-*d*]pyrimidine (**4**) serves as an excellent substrate for the introduction of a range of alkoxy groups into the 7 position of the furazano[3,4-*d*]pyrimidine ring system, and the resulting 7-alkoxy-5-aminofurazano[3,4-*d*]pyrimidines may be used as

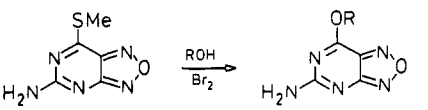
Scheme I



precursors in a convenient synthesis of 4-alkoxypteridines. These latter are potentially very useful due to their increased solubility, but have not hitherto been readily available.

Results and Discussion

5-Amino-7-(methylthio)furazano[3,4-*d*]pyrimidine[6] (**4**), which may be prepared by the lead tetraacetate oxidation[3] of 2,4-diamino-6-(methylthio)-5-nitrosopyrimidine, is quite stable when warmed in an alcohol. If bromine (or chlorine) is added to the solution, however, a smooth reaction ensues and the corresponding 7-alkoxyfurazanopyrimidine may be isolated in yields of up to 90% (eq 1). A wide range



(1)

(4)

(5) R = CH_3
(6) R = C_2H_5
(7) R = CH_2CH_2Cl
(8) R = CH_2CH_2OH
(9) R = $CH_2(CH_2)_3CH_2OH$
(10) R = CH_2·CHOH·CH_2OH

of alcohols may be used in this reaction and products **5–10**

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