A Re-Examination of the Reaction of 3,4-Diamino[1,2,5]oxadiazole with Glyoxal

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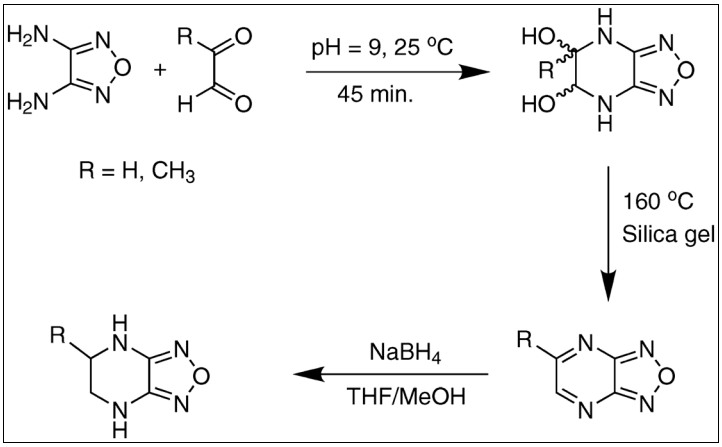
Received April 19, 2011
DOI 10.1002/jhet.1054
View this article online at wileyonlinelibrary.com.



Reaction coordinate mapping was used to study the reaction of 3,4-diamino[1,2,5]oxadiazole (3,4-diaminofurazan) and 3,4-diamino[1,2,5]thiadiazole with glyoxal. The thiadiazole was known to give a good yield of [1,2,5]thiadiazolo[3,4-*b*]pyrazine, whereas the oxadiazole had not yielded, until now, [1,2,5]oxadiazolo[3,4-*b*]pyrazine (or furazano[2,3-*b*]pyrazine). The calculations suggested that the diols, 5,6-dihydroxy-4,5,6,7-tetrahydro[1,2,5]oxadiazolo[3,4-*b*]pyrazine and 5,6-dihydroxy-4,5,6,7-tetrahydro [1,2,5]thiadiazolo[3,4-*b*]pyrazine should be stable intermediates, and once formed, should provide a pathway to the target compounds *via* two dehydration steps, under forcing conditions. With this information in mind, the reactions of 3,4-diamino[1,2,5]oxadiazole with glyoxal and pyruvic aldehyde were re-examined. The reaction of 3,4-diamino[1,2,5]oxadiazole with glyoxal and pyruvic aldehyde produced, under slightly basic conditions, a near quantitative yield of the expected initial products, 5,6-dihydroxy-4,5,6,7-tetrahydro[1,2,5]oxadiazolo[3,4-*b*]pyrazine and the 5-methyl analog, respectively. The diols were easily isolated by lyophilizing the aqueous reaction mixture. The diols were pyrolized on silica gel at 160°C to give the desired [1,2,5]oxadiazolo[3,4-*b*]pyrazine and the 5-methyl analog. Both compounds were easily reduced to the corresponding 4,5,6,7-tetrahydro-derivative using sodium borohydride in THF/methanol. The [1,2,5]oxadiazolo[3,4-*b*]pyrazine also displayed other interesting chemistry.

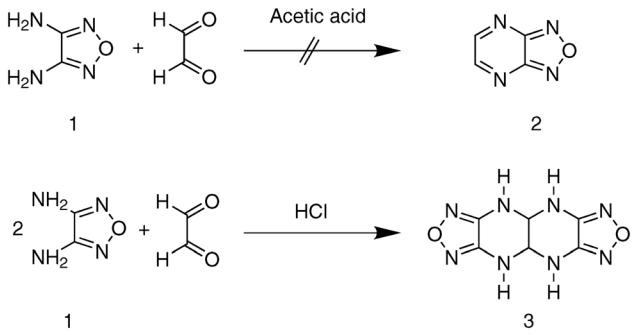
J. Heterocyclic Chem., **49**, 919 (2012).

INTRODUCTION

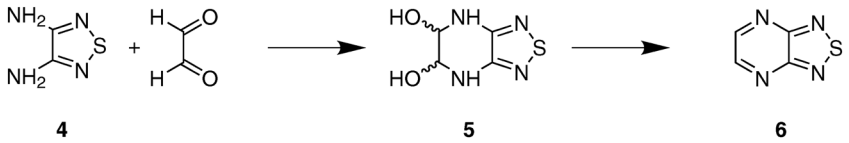
The reaction of 3,4-diamino[1,2,5]oxadiazole (3,4-diaminofurazan), **1**, with glyoxal has been examined several times in the past (see Scheme 1). In 1978, Sato and Adachi investigated the reaction of **1** and aqueous glyoxal at a 1:1 stoichiometry utilizing acetic acid as the catalyst with the hopes of synthesizing [1,2,5] oxadiazolo[3,4-*b*]pyrazine (or furazano[3,4-*b*]pyrazine), **2** [1]. They reported that the reaction produced no product. In 1985, Willer and Moore re-examined the reaction of **1** with glyoxal using hydrochloric acid as the catalyst and found that when using a 2:1 stoichiometry of **1** to glyoxal they could isolate an almost quantitative yield of the tetracyclo-compound **3** [2].

These results stand in stark contrast to the results of the reaction of the related 3,4-diamino[1,2,5]thiadiazole, **4**, with glyoxal. In 1976, Komin and Carmack reported on the reaction of **4** with glyoxal and biacetyl [3]. They found that **4** initially reacted with aqueous glyoxal at 100°C to produce a chloroform insoluble precipitate that appeared to be the diol adduct, **5** (see Scheme 2).

Scheme 1. Reported reactions of 3,4-diamino[1,2,5]oxadiazole with glyoxal [1,2].



Scheme 2. Reaction of 3,4-diamino[1,2,5]thiadiazole with glyoxal [3].



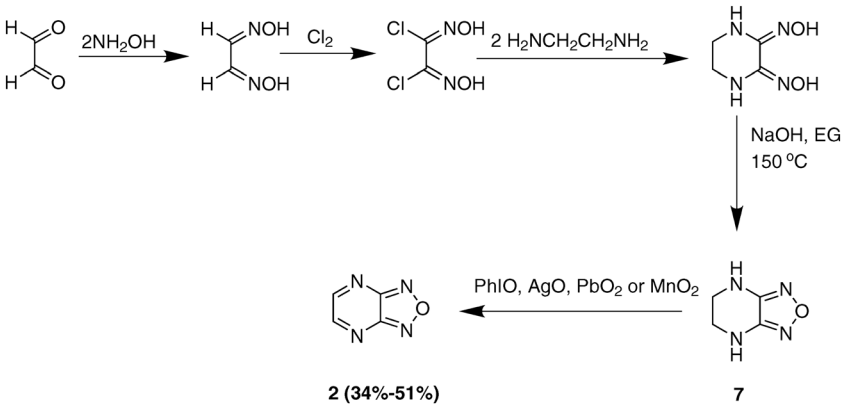
Continued heating dissolved some of the precipitate. Extraction of the reaction mixture with chloroform gave the desired [1,2,5]thiadiazolo[3,4-*b*]pyrazine, **6**. Reheating the aqueous layer and re-extracting with chloroform gave a total yield of **6** of 81.5%.

An important question arises from an examination of this literature. Is the failure to form [1,2,5]oxadiazolo [3,4-*b*]pyrazine from the reaction of **1** with glyoxal simply a result of not using the proper reaction conditions or is it the result of the 1,2,5]oxadiazolo[3,4-*b*]pyrazine being unstable relative to the diol intermediate? It should be noted that in a review in 2003, Sheremetev and Yudin mentioned that the synthesis of **2** had been accomplished by the dehydrogenation of 4,5,6,7-tetrahydro [1,2,5]oxadiazolo[3,4-*b*]pyrazine, **7**, but no experimental details or properties of the compound were reported [4]. Compound **7** had been synthesized by the four-step procedure of Willer and Moore [2]. This overall very low yield, five-step synthesis of **2** is summarized in Scheme 3. These results are important in that they show that **2** is a stable molecule but they shed no light on why **2** could not be directly synthesized from **1** and glyoxal.

RESULTS AND DISCUSSION

To understand why attempts to make **2** directly from **1** and glyoxal have been unsuccessful, reaction coordinate mapping was used to examine the reaction of both **1** and **4** with glyoxal [5–7]. The results are shown in Figures 1 and 2.

Scheme 3. Literature synthesis of **2** [2,4].



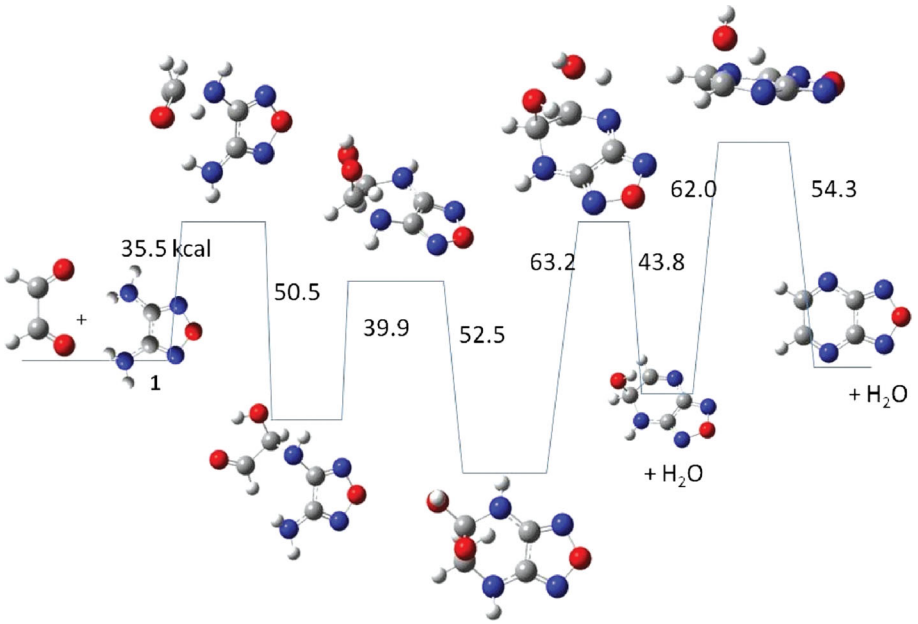


Figure 1. Reaction coordinate mapping of the reaction of **1** with glyoxal. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

First, both reactions appear to be exothermic, with the thiadiazole reaction being the more exothermic of the two. Second, both reactions occur *via* a similar mechanism, namely, a carbonyl carbon on glyoxal is attacked by an amine group on **1** or **4** followed by a similar attack on the other glyoxal carbon by the remaining amine nitrogen on **1** or **4**, resulting in a diol intermediate, **5** or **8**. The reaction then proceeds to product *via* two dehydration steps. Third, the energetics of the two reactions are qualitatively similar. Fourth, the diol intermediates (**5** and **8**) appear to be significantly more stable than the reactants, increasing the chances that they could be isolated.

Given that the calculations on both reactions result in the same qualitative picture, coupled with the fact that Komin and Carmack produced [1,2,5]thiadiazolo[3,4-*b*]pyrazine, **6**, *via* the reaction of **4** with glyoxal, we believe that the failure of the analogous reaction of **1** with glyoxal to give [1,2,5]oxadiazolo[3,4-*b*]pyrazine, **2**, is most plausibly ascribed to the use of improper reaction conditions rather than instability of **2** relative to the diol intermediate. This

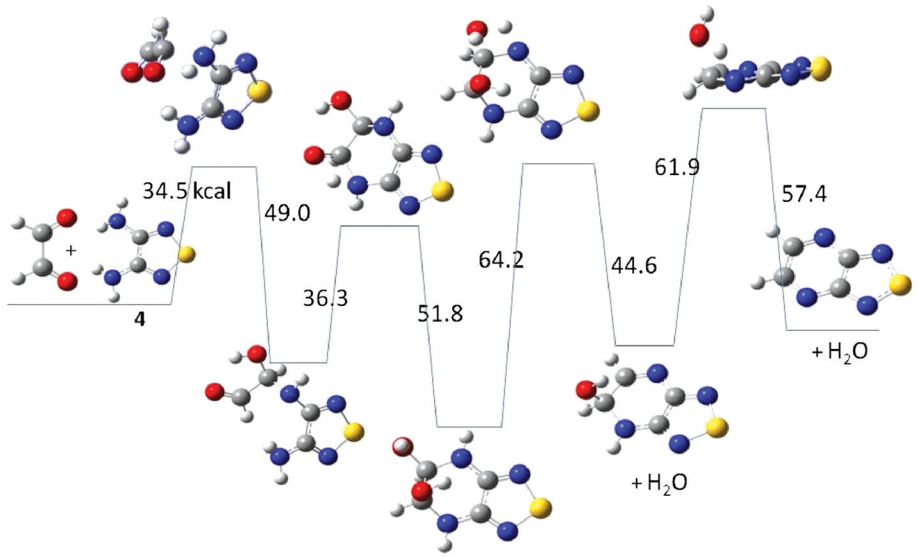


Figure 2. Reaction coordinate mapping of the reaction of **4** with glyoxal. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

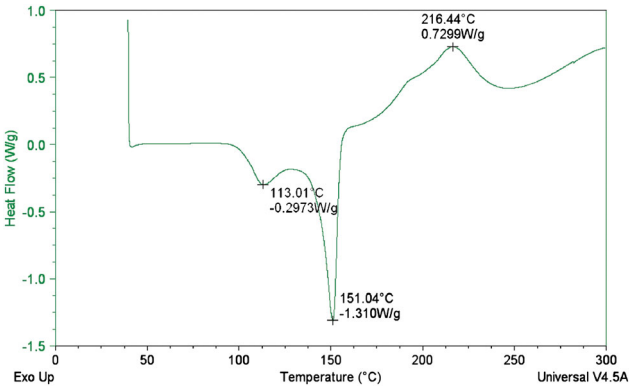


Figure 3. DSC thermogram of 5,6-dihydroxy-4,5,6,7-tetrahydro[1,2,5]oxadiazolo[3,4-*b*]pyrazine, **8**. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

conclusion is further supported by the fact that Sato and Adachi, rather than observing the diol intermediate, were unable to isolate any product, whatsoever.

The prediction that the diol was a stable compound prompted a search for better conditions for its synthesis and isolation. An article by Vail etal. stressed the importance of keeping the reaction slightly basic and the reaction temperature low in the reaction of amides with glyoxal to give *N*,*N*′-dihydroxylethylenebisamides [8]. The reaction of **1** with glyoxal at 45°C under these conditions produced a clear solution that, when examined by ^{13}C NMR, clearly contained a single product. To isolate this product under very mild conditions, the solution was frozen and the water removed by lyophilization. The resulting white powder was identified as the expected 5,6-dihydroxy-4,5,6,7-tetrahydro[1,2,5]oxadiazolo[3,4-*b*]pyrazine, **8**, based on spectroscopic data, although we have yet been unable to establish its stereochemistry. It was later found that if the reaction temperature was lowered to 20°C, the product would actually crystallize from the reaction mixture.

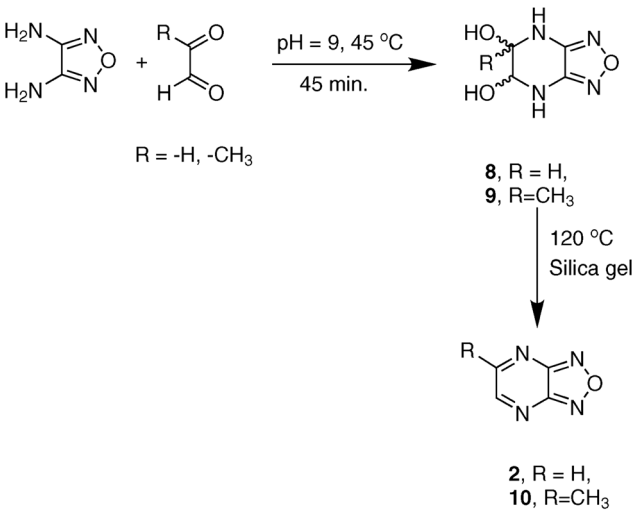
The differential scanning calorimetry (DSC) and high resolution mass spectrometry (HRMS) analyses of **8** were extremely enlightening. The DSC thermogram is shown in Figure 3. The two endotherms at 113 and 151°C were very suggestive of a stepwise dehydration process leading to the desired [1,2,5]oxadiazolo[3,4-*b*]pyrazine, **2**, which is consistent with the theoretical prediction. In the mass spectrum of **8**, the molecular ion (158.0431) was relatively weak. A peak of almost equal intensity was observed at 140.0334 Da (M-H_2O), and a very strong peak was observed at 122.0265 Da (M-2H_2O).

Both of these facts were very suggestive that pyrolysis of **8** might be a viable route to the desired [1,2,5]oxadiazolo[3,4-*b*]pyrazine, **2**. Komin and Carmack had used pyrolysis of 1,2,3,4-tetrahydro-2,3-dihydroxypyrazano[2,3-*b*]quinoxaline to give pyrazano[2,3-*b*]quinoxaline [3]. Pyrolysis of **8** at 130°C and 2 torr for 2 h produced a small amount of a light-yellow, crystalline material on the cold finger and a substantial amount of a brown residue. The light-yellow, crystalline material was easily identified as the desired [1,2,5]oxadiazolo[3,4-*b*]pyrazine, **2**, based on spectroscopic data. The brown residue was very impure **8** based on standard spectroscopic data. Repeating the pyrolysis at 160°C and 0.5 torr produced similar results. It was theorized that the low yield of **2** might be due to the molecules of **8** reacting with each other in the "melt" phase. A significant improvement to the yield was obtained, when the diol was deposited on silica gel in a 1:10 ratio, and this material was pyrolyzed at 160°C. The product was isolated in ≈30% yield by extracting the material on the silica gel with hot anhydrous chloroform. The product could be purified by sublimation or column chromatography ($CHCl_3$, silica gel, R_f = 0.7).

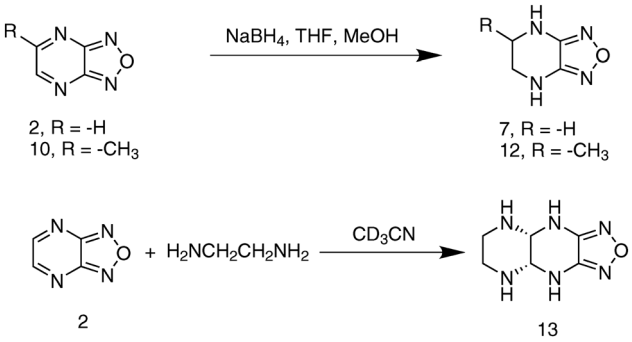
Similar results were obtained when pyruvic aldehyde was substituted for glyoxal. The diol, **9**, was much less stable and could not be characterized except by NMR and IR. Pyrolysis of the material on silica gel gave only a 10% yield of 5-methyl[1,2,5]oxadiazolo[3,4-*b*]pyrazine, **10**, which is stable and was completely characterized (see Experimental section). These results are summarized in Scheme 4.

The principal reason for the great interest in the synthesis of **2** is that it might offer a shorter synthetic route to 4,5,6,7-tetrahydro[1,2,5]oxadiazolo[3,4-*b*]pyrazine, **7**. Sato and Adachi had shown that more highly substituted [1,2,5]oxadiazolo[3,4-*b*]pyrazines could be reduced to the tetrahydro-analogs using sodium borohydride or lithium aluminum hydride [1]. Compound **7** is of interest, because it is the precursor to 4,7-dinitro-4,5,6,7-tetrahydro[1,2,5]oxadiazolo[3,4-*b*]pyrazine, **11**, a well-known energetic material [2]. It has also shown interesting electronic properties [9–11]. The original four-step synthesis of **7** is shown in Scheme 3 [2]. We have indeed established that

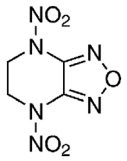
Scheme 4. Synthesis of [1,2,5]oxadiazolo[3,4-*b*]pyrazine, **2**, and its 5-methyl analog.



Scheme 5. Chemistry of [1,2,5]oxadiazolo[3,4-b]pyrazine and its 5-methyl analog.



both **2** and **10** can be reduced to **7** and **12** in very high yields using sodium borohydride in methanol/THF (see Scheme 5).



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Reaction coordinate mapping calculations showed that tetraaminoethane compounds, obtained by addition of amines to **2**, are significantly more stable than **2**. This suggested that **2** would readily react with amines. As an example, the reaction of **2** with ethylene diamine was studied. A vigorous reaction occurred, yielding **13** as the sole product. The stereochemistry of the ring juncture appears to be *cis*, based on the ^{1}H NMR data. This assignment was made on the following basis: the ethylene group protons appear as two multiplets typical of a conformationally mobile AA′ BB′ system [12], and the ^{13}C satellites for the bridgehead protons show that there is a small coupling of 4.2 Hz between them which is consistent with the *cis*-stereochemistry.

Compound **2** also reacts vigorously with other primary amines and, at slightly elevated temperatures, primary alcohols. These reactions can produce very interesting [1,2,5]oxadiazole containing polymers, if difunctional or trifunctional amines and alcohols are used. These results will be reported separately.

The X-ray crystal structure of **2** was determined and is shown in Figure 4; crystallographic data are listed in Table 1. The experimental density (1.536 g cm^{-3}) is very close to that calculated by the "Energy" program (1.55 g cm^{-3}) [13]. The ^{1}H NMR chemical shifts in both **2** and the sulfur analog, **6**, are very close (8.97 *vs.* 9.06 [3]) and are shifted ~0.5 ppm downfield from the ^{1}H NMR chemical shifts in pyrazine. The ^{13}C NMR chemical shifts for **2** are 152.03 and 153.04 ppm. They are easily assigned because of the lack of a nuclear Overhauser effect (NOE) enhancement for the oxadiazole carbons (152.03). The

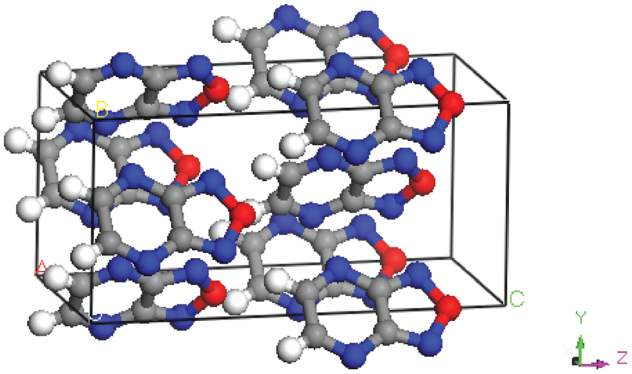

Figure 4. X-ray structure of [1,2,5]oxadiazolo[3,4-b]pyrazine, **2**. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

pyrazine type carbons are shifted downfield from pyrazine (145.7 ppm) by over 7 ppm. Unfortunately, the ^{13}C NMR chemical shifts for **6** were not reported.

In conclusion, a direct synthesis of [1,2,5]oxadiazolo [3,4-*b*]pyrazine, **2**, from 3,4-diamino[1,2,5]oxadiazole has been developed. The compound exhibits interesting and useful chemistry and studies to improve the yield and explore its chemistry continue.

Table 1

Crystal data and structure refinement for [1,2,5]oxadiazolo[3,4-*b*]pyrazine, **2**.

Empirical formula	$C_4H_2N_4O$
Formula weight	122.10
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	*Aba*2
Unit cell dimensions	a = 6.395(8) Å, α = 90° b = 6.179(8) Å, β = 90° c = 12.669(16) Å, γ = 90°
Volume	500.6(11) Å^3
Z	4
Density (−173°C)	1.620 mg m^{-3}
Density (20°C)	1.536 mg m^{-3}
Absorption coefficient	0.126 mm^{-1}
F(0 0 0)	248
Crystal size	0.18 × 0.15 × 0.14 mm^3
Theta range for data collection	4.86–26.52°
Index ranges	$-8 \le h \le 7, -7 \le k \le 7, -15 \le l \le 13$
Reflections collected	1606
Independent reflections	469 [R_{int} = 0.0413]
Completeness to theta = 26.52°	97.8%
Absorption correction	Semiempirical from equivalents
Max. and min. transmission	0.9825 and 0.9776
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	469/1/42
Goodness-of-fit on F^2	1.158
Final R indices [$I > 2\sigma(I)$]	R_1 = 0.0570, wR_2 = 0.1707
R indices (all data)	R_1 = 0.0597, wR_2 = 0.1751
Largest diff. peak and hole	0.493 and −0.788 e Å^{-3}

EXPERIMENTAL

Reaction coordinate mapping. All calculations describing the potential energy surface (PES) were performed using the Gaussian 09x quantum chemistry suite [14]. Critical points on the PES were determined using the BHandHLYP functional and the 6-311++G(2df,2p) basis set. The gradients for all geometry optimizations were converged to the default settings. Each critical point on the PES was characterized through normal-mode analysis. All transition states reported here had one imaginary frequency, and all minima had no imaginary frequencies. The transition states were subjected to intrinsic reaction coordinate (IRC) calculations (using the default step size) to facilitate connection with minima along the reaction path. Each IRC terminated upon reaching a minimum as defined by the default criteria provided in G09. For those points that did not terminate in this fashion, the last converged point on the reaction path was used as the initial structure for a full geometry optimization. For each instance in which such an optimization was attempted, a local minimum was found. It is assumed that this is the minimum to which the IRC would have converged, if convergence problems had not been encountered.

3,4-Diamino[1,2,5]oxadiazole (3,4-diaminofurazan), 1. This compound was made by the procedure of Visalok and Ostrovskoya [15]. The melting point was 179–180°C (lit. [15] 180°C).

5,6-Dihydroxy-4,5,6,7-tetrahydro[1,2,5]oxadiazolo[3,4-b]pyrazine, 8. Finely ground (≈105–177 μm) 3,4-diamino[1,2,5]oxadiazole (2.0 g, 20 mmol), 40% aqueous glyoxal (3.0 g, 21 mmol) and sodium bicarbonate (25 mg) are placed in a 20-mL scintillation vial equipped with a magnetic stirring bar. The mixture is stirred at 20°C for 1 h. The clear solution is frozen in liquid nitrogen, and the water is removed by lyophilization. The white product is slurried with acetonitrile and collected. The yield is 3.05 g (19.2 mmol, 96%). The compound does not melt, but it exhibits two decomposition endotherms at 113°C and 151°C. ^{1}H NMR(DMSO-d_6): δ = 4.65 (s, 1H), 5.92 (bs, 1H), 7.79 (s, 1H) ppm. ^{13}C NMR(DMSO-d_6): δ = 75.45, 146.52 ppm.

FT-IR(KBr) = 3143 (vs), 1720 (sh), 1709 (vs), 1599 (m), 1532 (m), 1385 (vs), 1061 (s), 945 (m), 828 (w), 770 (w), 765 (w), 715 (w), 601 (m) cm^{-1}. HRMS (EI); $C_4H_6N_4O_3$; $[M]^+$: calcd. 158.0440; found 158.0431 amu.

[1,2,5]Oxadiazolo[3,4-b]pyrazine, 2 (method 1). 5,6-Dihydroxy-4,5,6,7-tetrahydro[1,2,5]oxadiazolo[3,4-*b*]pyrazine (0.79 g, 5 mmol) is placed in a sublimation apparatus, which is then heated at 160°C for 2 h at 0.5 mm. A yellow crystalline material deposits on the cold finger. The apparatus is cooled, dried, and kept under vacuum. It is transferred to a dry box and opened. The light yellow crystals are collected and stored under nitrogen. The yield is 0.06 g (0.1 mmol, 10%). DSC shows that the compound melts at 89°C and undergoes a very exothermic decomposition starting at 240°C with a maximum at 266°C.

[1,2,5]Oxadiazole [3,4-b]pyrazine, 2 (method 2). 5,6-Dihydroxy-4,5,6,7-tetrahydro[1,2,5]oxadiazolo[3,4-*b*]pyrazine (0.79 g, 5 mmol) is dissolved in 10 mL of acetone, and the resulting solution is added to a slurry of 8 g of silica gel and 30–40 mL of acetone in a 100 mL round-bottom flask. This mixture is stirred for 1 h; then, most of the acetone is removed at reduced pressure. A tall condenser is attached, and the mixture is stirred at room temperature under high vacuum until frothing ceases. The mixture is slowly heated to 160°C under high vacuum and held for 2 h. Yellow crystals deposit near the top of the flask. The flask is allowed to cool, and the crystals apparently are reabsorbed onto the silica gel. The silica gel is extracted with two 70-mL portions of chloroform. The chloroform extracts are combined and stripped at reduced pressure. The yield of slightly impure product was 0.20 g (1.6 mmol, 33%). ^{1}H NMR($CDCl_3$): δ = 8.97 (s) ppm. ^{13}C NMR($CDCl_3$): δ = 152.03, 153.04 ppm. FT-IR(KBr) = 1984 (w), 1957 (w), 1716 (w), 1558 (m), 1524 (m), 1447 (m), 1390 (w), 1358 (m), 1344 (sh), 1270 (w), 1237 (m), 1024 (m), 980 (m), 946 (m), 882 (m), 868 (m), 750 (m), 638 (w), 603 (m) cm^{-1}.

5-Methyl[1,2,5]oxadiazolo[3,4-b]pyrazine, 10. Finely ground (≈105–177 μm) 3,4-diamino[1,2,5]oxadiazole (1.0 g, 10 mmol), 40% pyruvic aldehyde (1.85 g, 10.5 mmol), and sodium bicarbonate (100 mg) are placed in a 20-mL scintillation vial equipped with a magnetic stirring bar. The mixture is stirred at 25°C for 1 h. The 3,4-diamino[1,2,5]oxadiazole slowly dissolves. The crude product is diluted with 10 mL of dry acetonitrile, and the resulting solution is slowly added to a mixture of 50 mL of acetone and 12 g of silica gel. The solvents are then evaporated under reduced pressure. A reflux condenser is attached to reduce the loss of the silica gel when a vacuum is applied, and the mixture is placed under high vacuum at room temperature to remove the remaining acetone and any water. The apparatus is placed in a 50°C oil bath, and the contents are stirred. After 20 min, the temperature is raised first to 120°C and then to 160°C. The mixture darkens considerably, and the 5-methyl[1,2,5]oxadiazolo[3,4-*b*]pyrazine starts to collect at the top of the flask and in the condenser. After 1 h, the apparatus is removed from the oil bath and allowed to cool. The product that had sublimed is readsorbed onto the silica gel. Methylene chloride (300 mL) is poured down the condenser, and the mixture is stirred for 30 min. The silica gel is removed by filtration and extracted with two 50-mL portions of methylene chloride. The methylene chloride extracts are combined and stripped to give the crude product that is slightly red in color. The yield of slightly impure product is 0.14 g (0.1 mmol, 10%). The melting point is 57–58°C. ^{1}H NMR($CDCl_3$): δ = 2.88 (s, 3H), 7.79 (s, 1H) ppm. ^{13}C NMR($CDCl_3$): δ = 23.06, 149.97, 150.71, 154.51, 162.88 ppm. FT-IR(KBr) = 3143 (vs), 1720 (sh), 1709 (vs), 1599 (m), 1532 (m), 1385 (vs), 1061 (s), 945 (m), 828 (w), 770 (w), 765 (w), 715 (w), 601 (m) cm^{-1}. HRMS (EI); $C_4H_6N_4O_3$; $[M]^+$: calcd. 136.0385; found 136.0382 amu.

1,4,5,6-Tetrahydro[1,2,5]oxadiazolo[3,4-b]pyrazine, 7. [1,2,5]Oxadiazolo[3,4-*b*]pyrazine (122 mg, 1.0 mmol) is placed in a 50-mL round-bottom flask equipped with a magnetic stirring bar. Anhydrous THF (10 mL) is added. Sodium borohydride (80 mg, 2.1 mmol) is added as a solid. A dark solution is obtained. The mixture is stirred for 1 h without apparent reaction. Approximately 1 mL of methanol is added, and the reaction becomes quite vigorous. It is stirred for an additional 1 h. Two milliliters of water is added, and the solution is stirred for 1 h. The solution is stripped to give a solid. The crude product is taken up in 3 mL of acetonitrile, and the solution is syringe filtered to give a clear solution. The solution is evaporated under a stream of nitrogen to give 116 mg (0.92 mmol, 92%) of 1,4,5,6-tetrahydro[1,2,5]oxadiazolo [3,4-*b*]pyrazine, **7**, as colorless crystals. The melting point is 153–155°C (lit [2] 153–155°C).

5-Methyl-1,4,5,6-tetrahydro[1,2,5]oxadiazolo[3,4-b]pyrazine, 12. 5-Methyl[1,2,5]oxadiazolo[3,4-*b*]pyrazine (68 mg, 0.5 mmol) is placed in a 25 mL round-bottom flask equipped with a magnetic stirring bar. Anhydrous THF (5 mL) is added. Sodium borohydride (38 mg, 1.0 mmol) is added as a solid. A dark solution is obtained. The mixture is stirred for 1 h without apparent reaction. Approximately 0.5 mL of methanol is added, and the reaction becomes quite vigorous. It is stirred

for an additional 1 h. Two milliliters of water is added, and the solution is stirred for 1 h. The solution is stripped to give a solid. The crude product is taken up in 3 mL of acetonitrile, and the solution is syringe filtered to give a clear solution. The solution is evaporated under a stream of nitrogen to give 65 mg (0.46 mmol, 92%) of 5-methyl-1,4,5,6-tetrahydro[1,2,5] oxadiazolo[3,4-*b*]pyrazine as colorless crystals, melting point 97–99°C. ^{1}H NMR(CD_3CN): δ = 1.90 (d, *J* = 6.3 Hz, 3H), 2.98 (d × d, *J* = 11.7 and 8.1 Hz, 1H), 3.33 (d × m, *J* = 11.7 Hz, 1H), 3.56 (m, 1H), 5.45 (bs, 2H) ppm. ^{13}C NMR(CD_3CN): δ = 18.38, 46.76, 47.07, 148.41, 148.93 ppm. FT-IR(KBr) = 3274 (vs), 2972 (m), 2930 (m), 2871 (m), 1646 (sh), 1598 (vs), 1343 (m), 1284 (w), 1170 (m), 1071 (m), 996 (m), 813 (m) cm^{-1}. HRMS (EI); $C_4H_6N_4O_3$; [M]+: calcd. 140.0698; found 140.0698 amu.

1,4,4a,5,6,7,8,8a-Octahydro[1,2,5]oxadiazolo[3,4-b]pyrazino [2,3-e]pyrazine, 13. [1,2,5]Oxadiazolo[3,4-*b*]pyrazine (61 mg, 0.5 mmol) is dissolved in 0.5 mL of CD_3CN in a small test tube equipped with a small magnetic stirring bar. The solution is stirred, and ethylene diamine (30 mg, 0.05 mmol) is added *via* a microliter syringe. The solution gets very warm, and a white precipitate forms almost immediately. The CD_3CN is evaporated under a stream of nitrogen to give the product. The yield of **13** is 91 mg (0.5mmol, 100%). ^{1}H NMR(DMSO-d_6): δ = 2.53 (m,1H), 2.82 (m,1H), 2.93 (bs, 1H), 4.12 (s, 1H), 7.01 (bs, 1H) ppm. ^{13}C NMR(DMSO-d_6): δ = 41.85, 63.18, 148.07 ppm. FT-IR(KBr) = 3377 (vs), 3316 (vs), 3001 (m), 2982 (m), 2934 (m), 2886 (m), 1640 (sh), 1598 (vs), 720 (sh), 1463 (m), 1428 (m), 1404 (m), 1331 (s), 1290 (m), 1222 (m), 1214 (m), 1140 (m), 1029 (s), 988 (m), 945 (m), 824 (m), 767 (m), 740 (sh) cm^{-1}. HRMS (EI); $C_6H_{10}N_6O$; $[M]^+$: calcd. 182.0916; found 182.0910 amu.

Single-crystal X-ray diffraction analysis of [1,2,5]oxadiazolo [3,4-*b*]pyrazine, 2. $C_4H_2N_4O$, FW = 122.10, orthorhombic, *Aba*2, *a* = 6.395(8) Å, *b* = 6.179(8) Å, *c* = 12.669(16) Å, α = 90°, β = 90°, γ = 90°, *V* = 500.6(11) Å^3, *Z* = 4, d_{calc} = 1.620 mg m^{-3}, μ = 0.126 mm^{-1}, *F*(0 0 0) = 248, R_1 = 0.0570 for 451 observed [$I > 2\sigma(I)$] reflections and 0.0597 for all 1606 reflections, Goodness-of-fit = 1.158, 42 parameters.

A yellow crystal of dimensions 0.18 × 0.15 × 0.14 mm^3 was mounted on a MiteGen MicroMesh using a small amount of Cargille Immersion Oil. Data were collected on a Bruker three-circle platform diffractometer equipped with a SMART APEX II CCD detector. The crystals were irradiated using graphite monochromated MoK_α radiation (λ = 0.71073). An Oxford Cobra low temperature device was used to keep the crystals at a constant 100(2) K during data collection.

Data collection was performed, and the unit cell was initially refined using "APEX2" (v2010.3-0; ref. 16). Data reduction was performed using "SAINT" (v7.60A]; ref. 17) and "XPREP" (v2008/2; ref. 18). Corrections were applied for Lorentz, polarization, and absorption effects using "SADABS" (v2008/1; ref. 19). The structure was solved and refined with the aid of the programs in the "SHELXTL-plus" [v2008/4] system of programs [20]. The full-matrix least-squares refinement on F^2 included atomic coordinates and anisotropic thermal parameters for all non-H atoms. The H atoms were included using a riding model. The molecule lies on a special position, with only half the molecule being crystallographically unique.

Acknowledgments. This work was funded by grants N00014-081006 (USM), N00014-11-AF-0-0002 (NRL), and N0001411MP20002 (ARL) from the Office of Naval Research (Dr. Clifford Bedford). The 3,4-diamino[1,2,5]oxadiazole used was kindly supplied by Dr. Stephen Palopoli and Robert Day of Alliant Tech Systems-Elkton, MD. All calculations were performed at the ARL DoD Supercomputing Resource Center of the Department of Defense High Performance Computing Modernization Program.

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