

4*H*,8*H*-Bis[1,2,5]oxadiazolo[3,4-*b*:3',4'-*e*]pyrazines [1]

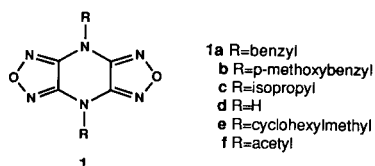
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The dilithio anion of 3,4-*N,N'*-disubstituted diamino[1,2,5]oxadiazole (**4a** R = benzyl, **4b** R = *p*-methoxybenzyl, **4c** R = isopropyl) and cyanogen oxide gave 4,7-disubstituted 5,6-dioximino[1,2,5]oxadiazolo[3,4-*b*]pyrazines **5a,b,c**. Ring closure to the title compound **1** was accomplished upon heating **5** with sodium hydroxide in ethylene glycol at 150°.

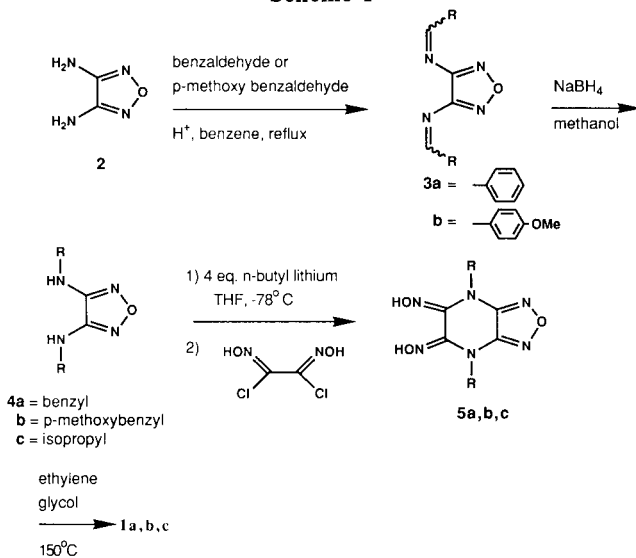
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Our interest [2] in small ring high nitrogen heterocycles prompted us to explore the synthesis of 4,8-disubstituted 4*H*,8*H*-bis[1,2,5]oxadiazolo[3,4-*b*:3',4'-*e*]pyrazines **1**.



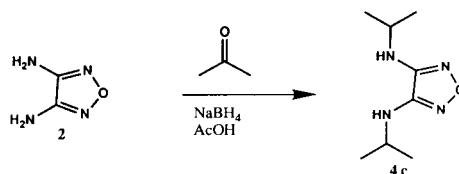
Preparation of 4,8-dibenzyl bis[1,2,5]oxadiazolo[3,4-*b*:3',4'-*e*]pyrazine (**1a**) and 4,8-di(*p*-methoxybenzyl) bis[1,2,5]oxadiazolo[3,4-*b*:3',4'-*e*]pyrazine (**1b**) were accomplished as shown in Scheme 1. Treatment of 3,4-diamino-1,2,5-oxadiazole (**2**) with benzaldehyde or *p*-methoxybenzaldehyde containing a catalytic amount of *p*-toluenesulphonic acid in refluxing benzene [3], gave *N,N'*-3,4-diphenylimino-1,2,5-oxadiazole (**3**) as a mixture of isomers. Compound **3** was unstable on standing and was reduced immediately upon isolation using sodium borohydride in methanol [4]. *N,N'*-3,4-di(benzylamino)-1,2,5-oxadiazole (**4a**) and *N,N'*-3,4-di(*p*-methoxybenzyl)-1,2,5-oxadiazole (**4b**) were isolated as crystalline solids.

Scheme 1



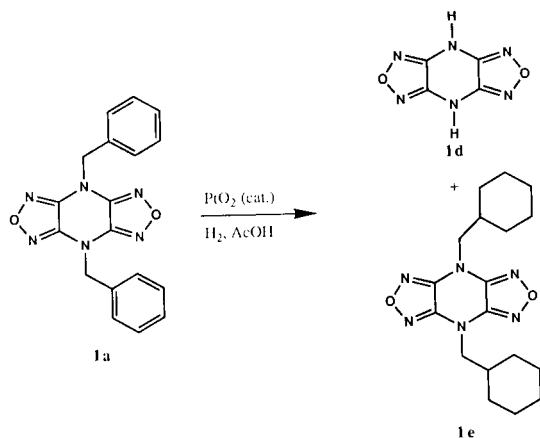
Oxadiazoles **4a** and **4b** were treated with *n*-butyllithium in THF at -78° to form the dilithio anion. Cyanogen oxide was generated *in situ* by adding dichloroglyoxime directly to the dianion containing a two-fold excess of *n*-butyllithium. After warming to ambient temperature and mild aqueous work-up, 4,7-dibenzyl-5,6-dioximino[1,2,5]oxadiazolo[3,4-*b*]pyrazine (**5a**) and 4,7-di(*p*-methoxybenzyl)-5,6-dioximino[1,2,5]oxadiazolo[3,4-*b*]pyrazine (**5b**) were isolated in moderate yields. *n*-Butyllithium was found to give the best results. Sodium hydride, sodium methoxide, potassium hydride, LDA, potassium hexamethyl disilazide, sodium bicarbonate, triethyl amine, and diisopropyl ethyl amine were tried with much reduced yields of **5a** and **5b**. Ring closure of **5** to **1** was accomplished using sodium hydroxide in ethylene glycol at 150°.

Condensation of **4a** with cyanogen oxide worked well and the reaction was reproducible. However, condensation of cyanogen oxide with **4b** usually gave low yields of **5b** and was not reproducible in every attempt. We could determine no reason for this result. The inability to consistently reproduce the condensation with cyanogen oxide was also found with *N,N'*-3,4-di(isopropylamino)-1,2,5-oxadiazole (**4c**) to give 4,7-diisopropyl-5,6-dioximino[1,2,5]oxadiazolo[3,4-*b*]pyrazine (**5c**). Oxadiazole **4c** was made by reaction of **2** with acetone and sodium borohydride in glacial acetic acid [5]. Dioxime **5c** was made as shown in Scheme 1.



With the **1a** readily available, we next attempted various methods of debenylation to arrive at 4*H*,8*H*-bis[1,2,5]oxadiazolo[3,4-*b*:3',4'-*e*]pyrazine (**1d**). Compound **1a** proved to be especially resistant to catalytic hydrogenolysis. Employing palladium on carbon in ethyl acetate, methanol, or acetic acid at 50 psi hydrogen, led to quantitative recovery of starting material. Results using platinum

oxide in acetic acid were more encouraging. After 1 or 2 weeks at 50 psi of hydrogen, the amine **1d** may have formed as evidenced by a broad singlet in the proton nmr spectrum at 7.0 ppm (acetone d-6). Also in the reaction mixture was a significant amount of 4,8-di(cyclohexylmethyl)bis[1,2,5]oxadiazolo[3,4-*b*:3',4'-*e*]pyrazine (**1e**). There was a competition between the desired hydrogenolysis of the benzyl groups and hydrogenation of the aromatic benzene rings. Attempts to separate and purify the mixture resulted in isolation of **1e** and loss of **1d**. If indeed **1d** was formed, it may have been labile, and decomposed during purification.



Because of the competing reduction of the benzene rings, the catalyst was changed to palladium hydroxide in acetic acid. As before, the hydrogenolysis required a lengthy reaction period of at least two weeks at 50 psi of hydrogen. The reaction yielded a mixture of a least two different compounds which we believed to be the amine **1d** and the 4,8-diacetylbis[1,2,5]oxadiazolo[3,4-*b*:3',4'-*e*]pyrazine (**1f**).

The proton nmr (acetone-d-6) showed a broad singlet at 7.0 ppm possibly for the amine and a sharp singlet at 2.0 ppm for the diacetyl methyl hydrogens. Further evidence

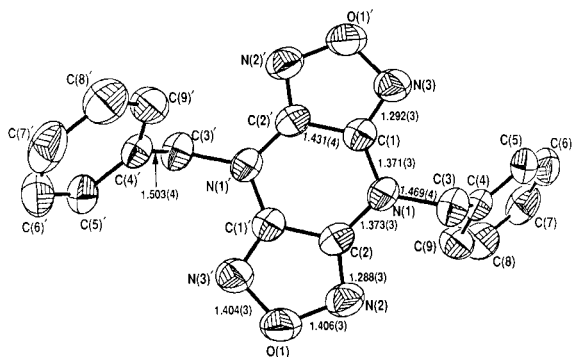
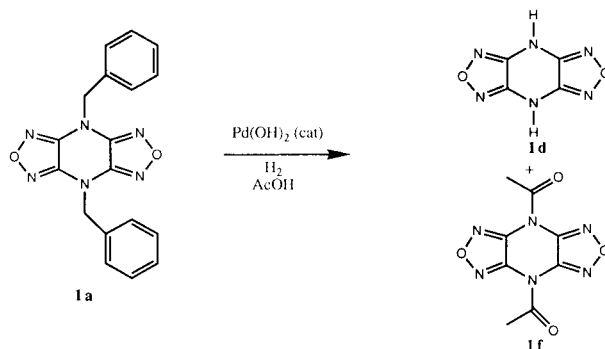


Figure 1. X-Ray Crystal Structure of Compound **1a**. Hydrogen atoms have omitted for clarity.



for **1f** was the infrared (ir) spectrum which showed a carbonyl absorption at 1700 cm^{-1} (potassium bromide) and an M^+ at 250 in the mass spectrum (electron ionization, molecular weight of **1f** is 250). The crude reaction mixture once again was difficult to separate. We were unable to purify the individual components. Similar results were obtained with the *p*-methoxy substituted benzyl compound **1b**. We were never able to isolate and purify diacetate **1f** or amine **1d**.

The resistance of **1a** and **1b** to hydrogenolysis was perplexing. In an effort to gain a better understanding of this problem, an X-ray crystal structure was obtained of **1a**. Suitable crystals for analysis were grown from ethyl acetate. Figure 1 shows the result (see experimental section for X-ray data, atom coordinates, Table 1, bond lengths, Table 2, and bond angles, Table 3). With the exception of the benzene rings, the molecule is entirely planar. Clearly, the strong electron withdrawing effects of the oxadiazole rings delocalizes the electron pairs of the pyrazine nitrogens. These amide like nitrogens no longer retain sp^3 hybridization, but rather sp^2 hybridization is approached. This may account for the lack of reactivity [6]. Although the bisoxadiazolopyrazine moiety is planar suggesting possible electron delocalization, the N(1)-C(1), C(2) bonds are not as short as would be expected if the entire moiety was aromatic. For heterocyclic aromatics, such as pyridine or pyrazine, N-C bond lengths are approximately 1.336 \AA [7]. The observed N(1)-C bond length in **1a** is 1.371 \AA which is more nearly similar to the same bond in 1*H*-pyrrole with a mean value of 1.372 \AA . Interestingly, the observed N(1)-C bond length in **1a** is the same as observed in 4*H*,7*H*-[1,2,5]oxadiazolo[3,4-*e*]pyrazines [8] in which an aromatic ring system would not be expected.

A new class of high nitrogen heterocycles, 4,8-disubstituted 4*H*,8*H*-bis[1,2,5]oxadiazolo[3,4-*b*:3',4'-*e*]pyrazines have been prepared. Although a number of 1,4-disubstituted derivatives were made, the parent amine **1d** was never isolated and fully characterized. We believe this amine and the diacetate derivative **1f** were unstable and readily decomposed especially under strongly acidic conditions.

Table 1

Atom coordinates ($\times 10^4$) and thermal parameters ($\text{\AA}^2 \times 10^3$) of **1a**

atom	x	y	z	U
C(1)	5272	-1252	692	47 [a]
C(2)	4003	2026	-95	47 [a]
C(3)	3555	1583	1234	57 [a]
C(4)	2531	-601	1392	47 [a]
C(5)	2658	-1870	2093	61 [a]
C(6)	1694	-3786	2251	75 [a]
C(7)	590	-4452	1780	79 [a]
C(8)	456	-3218	1009	74 [a]
C(9)	1418	-1304	848	60 [a]
N(1)	4267	791	609	49 [a]
N(2)	3124	4000	-320	61 [a]
N(3)	5710	-2741	1290	62 [a]
O(1)	3275	4504	-1075	72 [a]

[a] Equivalent isotropic U defined as one third of the trace of the orthogonalised U_{ij} tensor.

Table 2

Bond Lengths (\AA) of **1a**

C(1)-N(1)	1.371(3)	C(1)-N(3)	1.292(3)
C(1)-C(2a)	1.431(4)	C(2)-N(1)	1.373(3)
C(2)-N(2)	1.288(3)	C(2)-C(1a)	1.431(4)
C(3)-C(4)	1.503(4)	C(3)-N(1)	1.469(4)
C(4)-C(5)	1.378(4)	C(4)-C(9)	1.381(3)
C(5)-C(6)	1.375(5)	C(6)-C(7)	1.371(5)
C(7)-C(8)	1.366(5)	C(8)-C(9)	1.376(4)
N(2)-O(1)	1.406(3)	N(3)-O(1a)	1.404(3)
O(1)-N(3a)	1.404(3)		

Table 3

Bond angles (degrees) of **1a**. All esd's are 0.2-0.3°

N(1)-C(1)-N(3)	127.3	N(1)-C(1)-C(2a)	122.8
N(3)-C(1)-C(2a)	109.9	N(1)-C(1)-N(2)	127.2
N(1)-C(2)-C(1a)	122.5	N(2)-C(2)-C(1a)	110.3
C(4)-C(3)-N(1)	113.3	C(3)-C(4)-C(5)	120.5
C(3)-C(4)-C(9)	120.8	C(5)-C(4)-C(9)	118.6
C(4)-C(5)-C(6)	120.8	C(5)-C(6)-C(7)	120.0
C(6)-C(7)-C(8)	119.7	C(7)-C(8)-C(9)	120.5
C(4)-C(9)-C(8)	120.3	C(1)-N(1)-C(2)	114.7
C(1)-N(1)-C(3)	121.8	C(2)-N(1)-C(3)	123.5
C(2)-N(2)-O(1)	104.3	C(1)-N(3)-O(1a)	104.4
N(2)-O(1)-N(3a)	111.2		

EXPERIMENTAL

X-ray Crystallography of **1a**.

$\text{C}_{18}\text{H}_{14}\text{N}_6\text{O}_2$, $M = 346.35$, monoclinic, $P2_1/c$, $a = 9.887(5)$, $b = 4.703(2)$, $c = 17.918 \text{ \AA}$, $\beta = 99.74(4)^\circ$, $V = 821.3(8) \text{ \AA}^3$, $Z = 2$, $D_x = 1.40 \text{ g/cm}^3$, $\lambda(\text{Mo K}\alpha) = 0.71069 \text{ \AA}$, $m = 0.91 \text{ cm}^{-1}$, room temperature, $R = 0.060$ for 1179 reflections with $|F_o| > 4\sigma(F)$.

Crystals of **1a** suitable for structure determination were obtained from ethyl acetate. Unit cell parameters for **1a** were obtained by a symmetry-constrained least-squares fit of 25 reflections with 2θ values ranging from 4° to 28° ($\text{Mo K}\alpha$). Intensity data were collected on a Nicolet R3 with graphite monochromated $\text{Mo K}\alpha$ radiation using $2\theta/\theta$ scans. Intensity data collection parameters were: scan range $1^\circ \geq \text{K}\alpha$; to $1^\circ < \text{K}\alpha$; fixed scan speed of $4^\circ/\text{min}$; ratio background to scan time of 1.0; data collected over 4° to 55° (2θ) for octants hkl , hkl , hkl , hkl (h , -13 to +13; k , 0 to 7; l , -24 to +24). Two check reflections (112) and (2,0-12) were monitored every 46 reflections. The intensity data were corrected for Lorentz and polarization effects, but not for absorption. Systematic absences ($h0\ell$, $\ell = 2n+1$; $0k0$, $k = 2n+1$) indicated space group $P2_1/c$.

The first E-maps calculated with default parameters for the multiresolution direct methods in SHELXTL indicated the positions of all the non-hydrogen atoms of **1a**. As $Z = 2$ the molecule must contain a center of symmetry. Refinement was by SHELXTL's blocked-cascade least-squares minimization of $[\sum w(|F_o| - k|F_c|)^2]$ with $w = 1/[\sigma F^2 + gF^2]$ for $g = 0.0007$. All non-hydrogen atoms were refined anisotropically. The hydrogen atoms were observed on the first difference Fourier map and were subsequently constrained to "ride" on their adjacent carbon atoms during refinement, but without constraints on their thermal parameters. The maximum shifts to esd ratios for the final two cycles were less than 0.03; the final difference Fourier map had peak and troughs ranging from +0.18 to -0.28 $e^{-}/\text{\AA}$. Hydrogen atom coordinates, anisotropic thermal parameters, and lists of observed and calculated structure factors are given in the supplementary material.

Melting points were determined in capillary tubes with a Buchi 510 melting point apparatus. Infrared spectra were recorded with a Perkin-Elmer 137, 1330, or a Nicolet 7199 Fourier transform instrument. Proton and carbon magnetic resonance spectra were recorded on Nicolet NT-200 WB or IBM NR80 instruments. High pressure liquid chromatography (hplc) analyses were done on a Perkin-Elmer Series 400 liquid chromatograph using C-18 reverse phase columns. Elemental analyses were performed by Galbraith Laboratories of Knoxville, Tenn. Mass spectra were recorded on a Hewlett-Packard Model 5985 instrument. Exact mass spectra analyses were done by the University of California, Riverside Mass Spectroscopy Center.

Preparation of *N,N*-3,4-Di(benzylamino)-1,2,5-oxadiazole (**4a**).

3,4-diamino-1,2,5-oxadiazole (**2**) [9], (2 g, 20 mmoles), benzaldehyde (4.1 ml, 40 mmoles), and *p*-toluenesulphonic acid (10 mg) were mixed in benzene and heated at reflux under nitrogen in a Dean-Stark apparatus for 18 hours. The yellow solution was then cooled to ambient temperature and solvent was removed under reduced pressure. The oily yellow solid was dissolved in THF (100 ml) and methanol (30 ml); sodium borohydride (6 g) was carefully added over a period of 20 minutes to the stirring solution at room temperature. Once the addition was complete, the resulting mixture was stirred for 18 hours then quenched with 1M hydrochloric acid (100 ml) and extracted with ethyl acetate (3 x 50 ml). The organic layers were combined and washed with water (100 ml), saturated sodium chloride (50 ml), and dried (magnesium sulfate). The solvent was removed under reduced pressure to yield a white oily solid which was recrystallized from ethyl acetate/hexane to afford 4.1 g of the desired material as white needles (mp 109 to 111°, 73% yield); ^1H nmr (deuteriochloro-

form): 7.28 (s, 10 H), 4.31 (d, $J = 5.1$ Hz, 4 H), 4.13 (br s, 2 H); ^{13}C nmr (deuteriochloroform): 149.8, 137.5, 128.6, 127.9, 127.7, 48.7; ir (potassium bromide): cm^{-1} 3370, 3300, 3027, 2921, 1620, 1594, 1495, 1253, 742, 700.

Anal. Calcd. for $\text{C}_{16}\text{H}_{16}\text{N}_4\text{O}$: C, 68.55; H, 5.75; N, 19.99. Found: C, 68.64; H, 5.78; N, 19.95.

Preparation of *N,N'*-3,4-Di(*p*-methoxybenzylamino)-1,2,5-oxadiazole (**4b**).

Preparation of **4b** was the same as for **4a** (22% yield); ^1H nmr (acetone *d*-6): 7.29 (d, $J_A = 8.5$, 4 H), 6.85 (d, $J_B = 8.5$, 4 H), ($J_{AB} = 87.6$), 4.6 (br s, 2 H), 4.32 (d, $J = 8.5$, 4 H), 3.75 (s, 6 H); ^{13}C nmr (acetone *d*-6): 160.0, 150.6, 131.5, 130.1, 114.6, 55.2, 48.4; ir (potassium bromide): cm^{-1} 3420, 3000, 2920, 1620, 1560, 1500, 1260, 1060, 810; mp 149 to 151°.

Anal. Calcd. for $\text{C}_{18}\text{H}_{20}\text{N}_4\text{O}_2$: C, 63.50; H, 5.93; N, 16.46. Found: C, 63.43; H, 6.04; N, 16.46.

Preparation of *N,N'*-3,4-Di(isopropylamino)-1,2,5-oxadiazole (**4c**).

Sodium borohydride (15.2 g, 400 mmoles) was added in portions over ½ hour to a stirring solution of 3,4-diamino-1,2,5-oxadiazole (**2**) (2.0 g, 20 mmoles) in acetone (40 ml) and glacial acetic acid (120 ml) at 0°. The resulting thick white slurry was slowly allowed to warm to ambient temperature and stirred a total of 18 hours. Water (250 ml) was added, and the clear solution was extracted with ethyl acetate (3 x 100 ml). The combined organic layers were neutralized with solid sodium bicarbonate, washed with water (100 ml), brine (100 ml), and dried (magnesium sulfate). Solvent was removed under reduced pressure to afford crude **4c** as an oily white solid which was recrystallized from ethyl acetate/hexane (2.17 g as white needles, mp 83 to 85°, 59% yield); ^1H nmr (acetone *d*-6): 5.1 (br s, 2 H), 3.61 (m, 2 H), 1.19 (d, $J = 6.4$ Hz) 12 H; ^{13}C nmr (acetone *d*-6): 149.1, 45.8, 21.8; ir (potassium bromide): cm^{-1} 3300, 2950, 1600, 1575, 1370, 1175, 820.

Anal. Calcd. for $\text{C}_8\text{H}_{16}\text{N}_4\text{O}$: C, 52.14; H, 8.77; N, 30.41. Found: C, 51.90; H, 8.72; N, 30.28.

Preparation of 4,7-Dibenzyl-5,6-dioximino[1,2,5]oxadiazolo[3,4-*b*]pyrazine (**5a**).

n-Butyllithium (1.6 *M* in hexane, 21.6 ml, 35 mmoles) was added dropwise to a stirring solution of **4a** (2.42 g, 8.6 mmoles), in THF (100 ml) at -78° under nitrogen. After 1 hour, dichloroglyoxime (1.35 g, 8.6 mmoles) in THF (25 ml) was added rapidly in one portion, also at -78°. The solution immediately turned dark red orange in color. After stirring 1 hour at -78° and 2 hours at room temperature, the dark red solution was carefully quenched with 1*M* sodium hydrogen phosphate (monobasic) (100 ml) and extracted into ethyl acetate (3 x 50 ml). The combined organic layers were washed with water (100 ml), brine (100 ml), and dried (magnesium sulfate). Solvent was removed under reduced pressure to afford **5a** as a light yellow solid which was recrystallized from warm benzene (1.3 g, 42% yield, mp 185 to 186°); ^1H nmr (dimethyl sulfoxide *d*-6): mixture of conformers, 11.93 (s), 11.82 (s), 11.78 (s (very small)), 7.31 (br s), 5.29 (s), 4.98 (s); ir (potassium bromide): cm^{-1} 3200 br, 1650, 1600, 1490, 1440, 1360, 1060, 950, 840; ms: (electron ionization) (*m/e*) 364 (M^+), 347 (-OH), 346 (- H_2O), 91 (100%).

Anal. Calcd. for $\text{C}_{18}\text{H}_{16}\text{N}_6\text{O}_3$: C, 59.33; H, 4.43; N, 23.07. Found: C, 59.35; H, 4.42; N, 23.10.

Preparation of 4,7-Di(*p*-methoxybenzyl)-5,6-dioximino[1,2,5]oxadiazolo[3,4-*b*]pyrazine (**5b**).

Preparation of **5b** is the same as for **5a**; ^1H nmr (acetone *d*-6): (2 conformers seen), 12.0 (br s, 2 H), 7.25 (m), 6.75 (m), 5.38 (s), 4.87 (s, benzyl -CH₂-), 3.67 (s, -OCH₃); ir (potassium bromide): cm^{-1} 3200, 3005, 2950, 1595, 1510, 1380, 1260; mp 195 to 197°; ms: (exact mass, chemical ionization using isobutane) Calcd. *m/e*, 425.1573. Found: 425.1567.

Preparation of 4,7-Diisopropyl-5,6-dioximino[1,2,5]oxadiazolo[3,4-*b*]pyrazine (**5c**).

n-Butyllithium (1.6 *M* in hexane, 20.3 ml, 32.6 mmoles) was added dropwise to a stirring solution of *N,N'*-3,4-di(isopropylamino)-1,2,5-oxadiazole (**4c**) (1.50 g, 8.2 mmoles) in THF (75 ml) at -78° under nitrogen. After 1 hour, dichloroglyoxime (1.27 g, 8.2 mmoles) in THF (15 ml) was added rapidly in one portion. The solution immediately turned dark red in color. After stirring 1 hour at -78° and 2 hours at ambient temperature, the dark red-brown solution was carefully quenched with 1*M* sodium hydrogen sulfate (monobasic) (100 ml) and extracted into ethyl acetate (3 x 50 ml). The combined organic extracts were washed with water (100 ml), brine (100 ml), and dried (magnesium sulfate). Solvent was removed under reduced pressure to give **5c** as a dark yellow solid which was recrystallized from warm benzene (0.45 g, 20% yield, mp 151 to 153°); ^1H nmr (acetone *d*-6): 12.0 (br s, 2 H), 4.6 (septet, $J = 6.4$ Hz, 2 H), 1.41 (d, $J = 6.4$ Hz, 12 H); ir (potassium bromide): cm^{-1} 3200 (broad), 2900, 1650, 1600, 1560, 1450, 1370, 1040, 930, 910; ms: (exact mass, electron ionization) Calcd. *m/e*, 268.1284. Found: 268.1277.

Preparation of 4,8-Dibenzylbis[1,2,5]oxadiazolo[3,4-*b*:3',4'-*e*]pyrazine (**1a**).

Dioxime **5a** (1.14 g, 3.1 mmoles) was added in one portion to a stirring solution of sodium hydroxide (0.12 g, 3.1 mmoles) in ethylene glycol (10 ml) at 150°. After 2 hours, the solution was cooled to ambient temperature and water (20 ml) was added. There was an immediate formation of a precipitate. After cooling at 0° for 1 hour, **1a** was collected by vacuum filtration as an off-white solid (0.60 g, 56% yield, 93% yield based on recovered starting material mp 170-175° dec). After the mother liquor stood for 3 days, a white solid (0.46 g), starting material **5a**, was recovered; ^1H nmr (acetone *d*-6): 7.5 (m, 10 H), 5.02 (s, 4 H); ^{13}C nmr (acetone *d*-6): 148.7, 135.3, 129.6, 129.5, 129.2, 52.5; ir (potassium bromide): cm^{-1} 3000, 2990, 1640, 1600, 1390, 1350, 960; ms: (electron ionization, *m/e*) 346 (M^+), 91 (100%).

Anal. Calcd. for $\text{C}_{18}\text{H}_{14}\text{N}_6\text{O}_2$: C, 62.41; H, 4.08; N, 24.27. Found: C, 62.29; H, 4.11; N, 24.12.

Preparation of 4,8-Di(*p*-methoxybenzyl)bis[1,2,5]oxadiazolo[3,4-*b*:3',4'-*e*]pyrazine (**1b**).

The preparation of **1b** was the same as for **1a** (70% yield); ^1H nmr (dimethyl sulfoxide *d*-6): 7.55 (d, $J = 10$, 4 H), 6.95 (d, $J = 10$, 4 H), 4.90 (s, 4 H), 3.70 (s, 6 H); ^{13}C nmr (dimethyl sulfoxide *d*-6): 159.0, 147.2, 129.3, 125.6, 113.8, 54.8, 50.6; ir (potassium bromide): cm^{-1} 3020, 2910, 1580, 1505, 1250, 1175, 1030, 810; mp 187 to 188°; ms (exact mass, electron ionization, *m/e*) Calcd. 406.1389; Found: C, 406.1382.

Preparation of 4,8-Diisopropylbis[1,2,5]oxadiazolo[3,4-*b*:3',4'-*e*]pyrazine (**1c**).

Dioxime **5c** (0.28 g, 1.04 mmoles) was added in one portion to a

stirring solution of sodium hydroxide (42 mg, 1.04 mmoles) in ethylene glycol (5 ml) at 150°. After 2 hours at 150°, the solution was cooled to ambient temperature, water (10 ml) was added, and the resulting slurry cooled to 0° for 1 hour. Compound **1c** was collected by vacuum filtration as an off-white solid (190 mg, 73% yield, mp 159 to 161°); ¹H nmr (acetone d-6): 4.45 (septet J = 6.4 Hz, 2 H), 1.40 (d, J = 6.4 Hz, 12 H); ¹³C nmr (acetone d-6): 147.8, 53.2, 18.4; ir (potassium bromide): cm⁻¹ 2900, 1625, 1590, 1370, 1050, 820; ms: (electron ionization, m/e) 250 (M⁺), 166 (100%); Exact mass: (electron ionization, m/e) Calcd. 250.1178; Found: 250.1188.

Preparation of 4,8-Di(cyclohexylmethyl)bis[1,2,5]oxadiazolo[3,4-*b*:3',4'-*e*]pyrazine (**1e**).

Compound **1a** (230 mg, 0.7 mmole) was dissolved in glacial acetic acid (10 ml). Platinum oxide (10 mg) was added and the mixture was placed on a Parr hydrogenation apparatus at room temperature, 50 psi hydrogen pressure for 7 days. The mixture was celite filtered and partitioned between chloroform (100 ml) and water (30 ml). The chloroform layer was neutralized with aqueous sodium bicarbonate, washed with saturated sodium chloride (25 ml), and dried (magnesium sulfate). Solvent was removed under reduced pressure yielding an off white solid (175 mg) which was purified by silica gel chromatography (eluted with 30% ethyl acetate-hexane). Compound **1e** was isolated as a white solid (50 mg, 20%), ¹H nmr (deuteriochloroform): 3.71 (d, J = 7.2, 4 H), 2.2 (m, 2 H), 1.75 (m, 10 H), 1.2 (m, 10 H); ¹³C nmr (deuteriochloroform): 147.1, 54.6, 35.1, 30.5, 26.1, 25.5; ir

(methylene chloride): cm⁻¹ 2920, 2850, 1670, 1580, 1320, 915, 870, 835; mp 222 to 223°.

Anal. Calcd. for C₁₈H₂₆N₆O₂: C, 60.30; H, 7.32; N, 23.45. Found: C, 60.30; H, 7.38; N, 23.28.

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