≅ 5.4 Hz, 1, H1'), 8.04, 8.37 (s, s, 1, 1, H2,8); MS m/z 539 (68, M + H), 481 (13, M - $C(CH_3)_3$, 177 (10), 136 (100, B + 2 H). Anal. Calcd for $C_{17}H_{25}F_3N_8O_5SSi$ (538.6): C, 37.91; H, 4.68; N, 20.81. Found: C, 37.93; H, 4.61; N, 20.80.

9-[5-*O*-(*tert*-Butyldimethylsilyl)-2,3-diazido-2,3-dideoxy-β-D-ribofuranosyl]adenine (6). To a solution of **5** (1.59 g, 2.96 mmol) in DMF (20 mL) was added lithium azide (725 mg, 14.8 mmol), and the mixture was stirred for 45 min. DMF was removed in vacuo and the residue taken up in $CHCl_3$ and applied to a silica gel column (48 g, 2.5 × 30 cm, packed in $CHCl_3$). The column was washed with $CHCl_3$ (250 mL) and developed with 2% MeOH/$CHCl_3$. The chloroform wash and appropriate fractions were combined and evaporated to yield a white residue that was recrystallized from $CHCl_3$/hexanes to afford 1.19 g (2.77 mmol, 93%) of **6** as a fluffy, white solid: mp 120-121 °C; UV (MeOH) λmax 210 (ε 14 000), 260 nm (ε 10 600); ^{1}H NMR ($CDCl_3$) δ 0.107, 0.111 (s, s, 3, 3, $SiCH_3$'s), 0.92 (s, 9, *tert*-butyl), 3.84 (dd, $J_{5'-4'} \cong$ 2.8 Hz, $J_{5'-5''} \cong$ 11.8 Hz, 1, H5'), 4.04 (dd, $J_{5''-4'} \cong$ 3.3 Hz, 1, H5''), 4.17 (m, 1, H4') 4.56 (t, $J_{3'-2'} \cong$ 5.5 Hz, 1, H3'), 4.95 (dd, $J_{2'-1'} \cong$ 3.7 Hz, 1, H2'), 5.52 (br s, 2, 6-NH_2), 6.00 (d, 1, H1'), 8.08, 8.36 (s, s, 1, 1, H2,8); MS m/z 432 (62, M + H), 374 (8, M - $C(CH_3)_3$), 164 (14, sugar), 136 (100, B + 2 H). Anal. Calcd for $C_{16}H_{25}N_{11}O_2Si$ (431.5): C, 44.53; H, 5.84; N, 35.70. Found: C, 44.33; H, 5.74; N, 35.51.

9-(2,3-Diazido-2,3-dideoxy-β-D-ribofuranosyl)adenine (7). To a solution of **6** (429 mg, 1 mmol) in 10 mL of THF was added 1 mL of a solution of tetrabutylammonium fluoride (1 M in THF). After 1 h, the reaction mixture was diluted with MeOH, and silica gel (1.8 g) was added. The mixture was concentrated and added to a silica gel column (120 g, 5 × 15 cm) packed in $CHCl_3$. The column was washed successively with $CHCl_3$, 1% MeOH/$CHCl_3$, 3% MeOH/$CHCl_3$ (250 mL each), and 5% MeOH/$CHCl_3$. Appropriate fractions were combined and evaporated to yield a white residue that was recrystallized from MeOH to yield 273 mg (0.86 mmol, 87%) of **7** as a granular, white solid: mp 171-172 °C dec; UV (MeOH) λmax 210 (ε 14 500), 260 nm (ε 11 300); ^{1}H NMR (Me_2SO-d_6) δ 3.55-3.70 (m, 2, H5',5''), 4.03 (m, 1, H4'), 4.85 (dd, $J_{3'-2'}$ = 5.06 Hz, $J_{3'-4'}$ = 5.01 Hz, 1, H3'), 5.27 (t, $J_{2'-1'}$ = 5.6 Hz, 1 H2'), 5.49 (dd, $J_{OH-5'}$ = 5.5 Hz, $J_{OH-5''}$ = 6.0 Hz, 1, 5'-OH), 6.00 (d, 1, H1'), 7.42 (br s, 2, 6-NH_2), 8.18, 8.40 (s, s, 1, 1; H2,8); MS m/z 318 (53, M + H), 154 (44), 136 (100, B + 2 H). Anal. Calcd for $C_{10}H_{11}N_{11}O_2$ (317.3): C, 37.86; H, 3.49; N, 48.56. Found: C, 37.78; H, 3.52; N, 48.51.

9-(2,3-Diamino-2,3-dideoxy-β-D-ribofuranosyl)adenine (8). A mixture of **7** (51 mg, 161 μmol) and 10% Pd/C (21 mg) in MeOH (25 mL) containing 2% of 1 N HCl was hydrogenated at 30 psi for 21 h. The catalyst was filtered with a pad of Celite, and the pad was washed well with MeOH. Solvent was removed in vacuo to yield a yellowish, solid residue that was dissolved in a minimum of water and applied to a Dowex 1X4 (OH^-) column. The column was washed with water, and appropriate fractions were combined and lyophilized to yield **8** as a white powder (24.5 mg, 92.3 μmol, 57%). An analytical sample was obtained by recrystallization from methanol (with diffusion of ether[28] to afford colorless needles: mp softened at ~155 °C and melted by ~175 °C; ^{1}H NMR (Me_2SO-d_6) δ 1.74 (br s, 4, 2',3'-NH_2's), 3.48-3.84 (m, 4, H2',3',5',5''), 5.27 (dd, $J_{OH-5'}$ = 5.5 Hz, $J_{OH-5''}$ = 6.5 Hz, 1, 5'-OH), 5.74 (d, $J_{1'-2'}$ = 6 Hz, 1, H1'), 7.29 (br s, 2, 6-NH_2), 8.12, 8.32 (s, s, 1, 1, H2,8); MS m/z 266 (27, M + H), 154 (80), 136 (100, B + 2 H). Anal. Calcd for $C_{10}H_{15}N_7O_2$ (265.3): C, 45.28; H, 5.70; N, 36.96. Found: C, 45.32; H, 5.66; N, 36.84.

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Registry No. **1**, 5536-17-4; **2**, 40110-98-3; **3**, 29411-70-9; **4**, 132980-95-1; **5**, 132980-96-2; **6**, 132980-97-3; **7**, 119644-21-2; **8**, 90362-10-0.

Facile Synthesis and Nitration of *cis-syn-cis*-2,6-Dioxodecahydro-1*H*,5*H*-diimidazo[4,5-*b*:4',5'-*e*]pyrazine

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The title ring system was synthesized for the first time by acid-promoted condensation of ureas with 1,4-diformyl-2,3,5,6-tetrahydroxypiperazine. Nitrosation and nitration of the polycycle occurs first at the piperazine nitrogens. Successive further nitration leads to tetra-, penta-, and hexanitro derivatives. X-ray crystallographic analysis of the tetra- and hexanitro derivatives established the cis-syn-cis configuration and an all-axial conformation for this ring system. Possible reasons for the stereoselectivity of the condensation reaction are discussed.

The condensation of glyoxal with ureas is a well-established route to tetraazabicyclo[3.3.0]octanediones.[2] Related condensation reactions of ureas with 4,5-dihydroxyimidazolidines[3] and 2,3-dihydroxypiperazines[4] lead to the same ring system and to tetraazabicyclo[3.4.0]nonanes, respectively. In many cases the condensation

(1) Work performed while a visiting scientist at the Naval Surface Warfare Center.

(2) Petersen, H. *Synthesis* **1973**, 243.

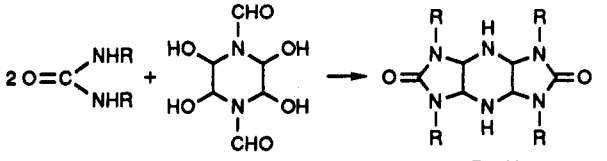
(3) (a) Li, W.; Hua, G.; Chen, M. *Proceedings of the Symposium on Pyrotechnics and Explosives*, October 1987, Beijing, China; China Academic Publishers: Beijing, 1987. (b) Suvorava, L. I.; Epishina, L. V.; Lebedev, D. V.; Khmelnitskii, L. I.; Novikov, S. S. *Bull. Acad. Sci. USSR, Div. Chem. Sci. (Engl. Transl.)* **1979**, 2108 and references cited therein.

(4) Adolph, H. G., unpublished results.

0022-3263/91/1956-3413$02.50/0

products were shown to have the cis configuration by X-ray crystallography.[5] The analogous condensation of 1,4-diformyl-2,3,5,6-tetrahydroxypiperazine with ureas, which would be expected to lead to the title ring system, has not been reported and is the subject of this paper.

The reaction conditions used in the condensation of urea with 1,3-diformyl-4,5-dihydroxyimidazolidine[3a] proved to be successful for the condensation of urea and *N,N'*-dimethylurea with diformyltetrahydroxypiperazine as well, except that longer reaction times were required. The initial products formed are believed to be dihydrochlorides of **1** (hydrated in the case of **1a**) on the basis of the elemental analysis and NMR spectral data. The ^{1}H NMR spectrum

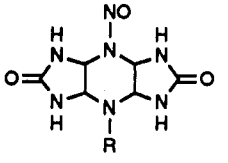


1a: R = H
1b: R = CH_3

of **1a** in DMSO shows a singlet at δ 4.87 for the methine protons and a broad singlet at δ 7.80 for the remaining protons, which are exchangeable with D_2O. The crude salt obtained from the condensation reaction can be purified by precipitation from its aqueous solution with methanol or acetone. The ^{1}H NMR spectrum now shows two broad NH absorptions, one for the piperazine NH's at δ 3.67 and one for the urea NH's at δ 7.20. The singlet for the methine protons appears at δ 4.73. On the basis of the elemental analysis, this compound is a monohydrochloride of **1a**. The simplicity of the ^{1}H NMR spectrum of this monohydrochloride implies that it has a symmetrical structure or that, in solution, a proton is exchanged rapidly between the two piperazine nitrogens.

The IR spectrum of the dihydrochloride salt showed a carbonyl absorption at 1738 cm^{-1} (amide 1) whereas the monohydrochloride salt showed two absorptions at 1722 and 1692 cm^{-1}. In the latter, intermolecular hydrogen bonding between the free secondary amine and a carbonyl group may give rise to the second amide 1 band at the lower frequency.

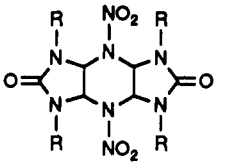
The two hydrochlorides of **1a** can be distinguished further by their behavior toward aqueous sodium nitrite solution. The dihydrochloride gives a product that appears to be an approximately equimolar mixture of the *syn*- and *anti*-dinitroso derivatives **2** (elemental analysis, ^{1}H NMR spectrum). The monohydrochloride gives the mononitroso



2: R = NO
3: R = H

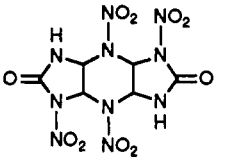
derivative **3**, which can be converted to **2** by treatment with aqueous $NaNO_2$/HCl. **2** can also be obtained from the monohydrochloride directly by addition of 1 equiv of HCl to the reaction mixture with excess aqueous $NaNO_2$. It was not possible to obtain X-ray quality crystals of **3** because of its poor solubility. The ^{1}H NMR spectrum in D_2O (obtained with a Bruker 300-MHz spectrometer) showed four nonequivalent protons with vicinal HH coupling, as would be expected for **3**, assuming slow rotation about the N–N bond.

Low-temperature nitration of **1a** and **1b** mono- and dihydrochlorides, respectively, in 100% HNO_3 gave nitration at the piperazine ring nitrogens only. The dinitro derivatives **4a** and **4b** were isolated in 28 and 55% yields, respectively. The ^{1}H NMR spectra showed only one signal for the methine protons, and **4a** showed only one CH peak in the ^{13}C NMR spectrum. This rules out isomeric dinitro structures for **4a**, which would be expected to show two or more C*H* signals as well as two or more C*H* signals.

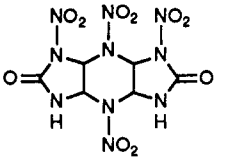


4a: R = H
4b: R = CH_3

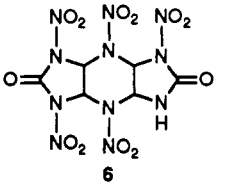
Well-defined derivatives of **1a** were also obtained by nitration of the monohydrochloride with HNO_3/Ac_2O, which produced a mixture of the tetranitro derivatives **5a** and **5b**. Surprisingly, **5b** was the major product of nitration (**a**:**b** $\simeq$ 1:3, estimated from the ^{1}H NMR spectrum of the crude nitration product). Compounds **5a** and **5b** were separated by column chromatography and fractional crystallization.



5a



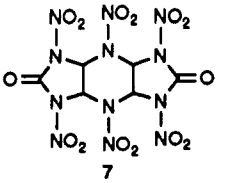
5b



6

Prolonged nitration with HNO_3/Ac_2O or nitration with $HNO_3/(CF_3CO)_2O$ gave the pentanitro compound **6**, which was identified by its ^{1}H and ^{13}C NMR spectra and elemental analysis.

Further nitration of the mixture of **5a** and **5b**, or of **6**, with NO_2BF_4 in MeCN produced the hexanitro compound **7**. Compounds **5b**, **6**, and **7** show increasing reactivity toward alcohols and water, while **5a** is quite stable and only decomposes very slowly in boiling methanol. This is



7

reminiscent of the properties of the nitro derivatives of glycoluril (2,4,6,8-tetraazabicyclo[3.3.0]octane-3,7-dione), whose 2,4,6,8-tetranitro derivative hydrolyzes easily,[6] while mixtures of the 2,4- and 2,6-dinitro derivatives can be freed of the 2,4 component by boiling with water.[7]

(5) (a) Koppes, W. M.; Chaykovsky, M.; Adolph, H. G.; Gilardi, R.; George, C. *J. Org. Chem.* **1987**, *52*, 1113. (b) Boileau, J.; Wimmer, E.; Gilardi, R.; Stinecipher, M.; Gallo, R.; Pierrot, M. *Acta Crystallogr.* **1988**, *C44*, 696. (c) Flippen-Anderson, J. L.; George, C.; Gilardi, C. *Acta Crystallogr.* **1990**, *C46*, 1122.

(6) Ross, D. L.; Coon, C. L.; McGuire, R. R. Lawrence Livermore National Laboratory, Livermore, CA, personal communication.

Table I. ^{1}H NMR Spectral Data for Compounds 4–7

compound (solvent)	ppm[a] (multiplicity; J_{HH}, Hz; integration) C–H	N–H
4a (Me_2SO-d_6)	6.60 (s; –; 4)	7.80 (s; –; 4)
4b (Me_2SO-d_6)	2.96 (s; –; 12), 6.18 (s; –; 4)	
5a (Me_2CO-d_6)	7.00 (br d; 9; 2), 8.20 (dd; 9, 2; 2)	8.97 (br s; –; 2)
5b (Me_2CO-d_6)	7.12 (d; 9; 2), 8.33 (d; 10; 2)	8.80 (br s; –; 2)
6 (Me_2CO-d_6)	7.11 (br d; 10; 1), 8.17–8.60 (m; –; 3)	9.05 (br s; –; 1)
7 (Me_2CO-d_6)	8.41 (s; –; –)[b]	

[a] TMS internal standard. [b] Obtained with a Bruker 300-MHz spectrometer.

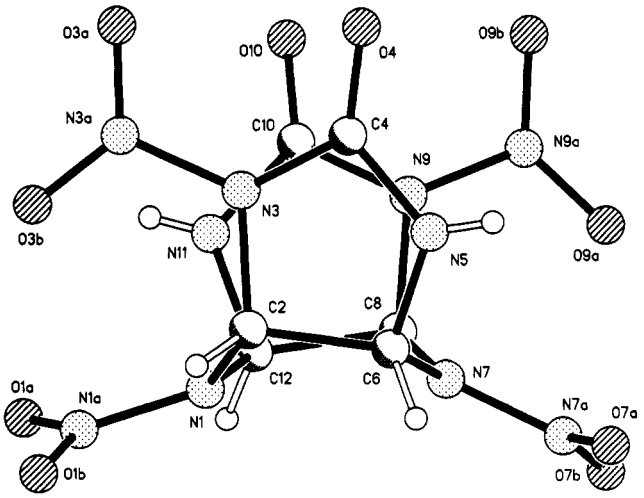
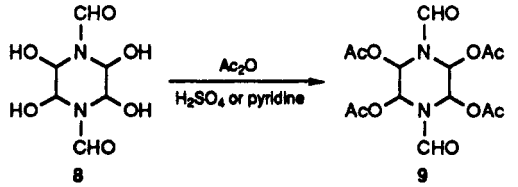


Figure 1. X-ray molecular structure and numbering scheme for **5a**.

Compound **7** was also prepared in one step in 74% yield from the monohydrochloride of **1a** by nitration with HNO_3/P_2O_5. In this reaction, partial nitration at low temperature was followed by more forcing conditions to complete nitration.

The structures of compounds **4–7** are supported by the ^{1}H NMR data compiled in Table I. In addition, X-ray molecular structures were determined for **5a** and **5b** and are shown in Figures 1 and 2. The structure of the hexanitro compound **7** was also determined by X-ray diffraction.[8] These establish the cis-syn-cis configuration for these compounds and probably also for **1a**, since it is unlikely that an isomerization would have occurred under the conditions of nitration.

The stereochemistry of compounds **1–7** was expected to be related to that of the starting material, **8**. Attempts to grow crystals of **8** were unsuccessful, but the configuration of the tetraacetyl derivative **9**, prepared under several different conditions with acetic anhydride, was resolved by X-ray crystallographic analysis. The crystal structure



8 **9**

of **9** (Figure 3 and Experimental Section) shows a single meso isomer with a somewhat flattened chair conformation

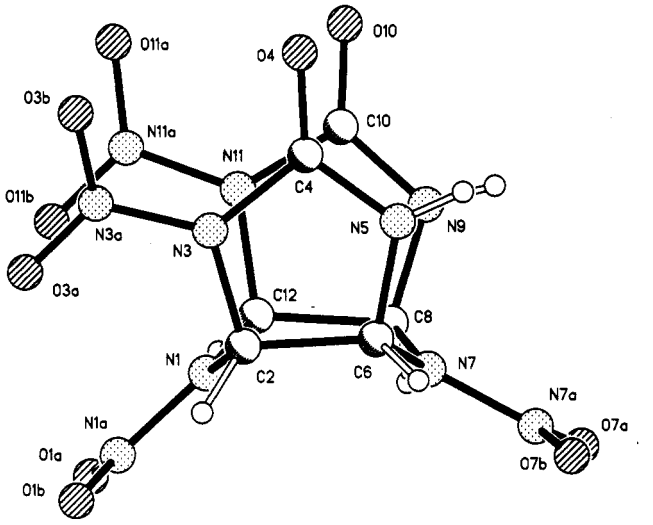


Figure 2. X-ray molecular structure and numbering scheme for **5b**.

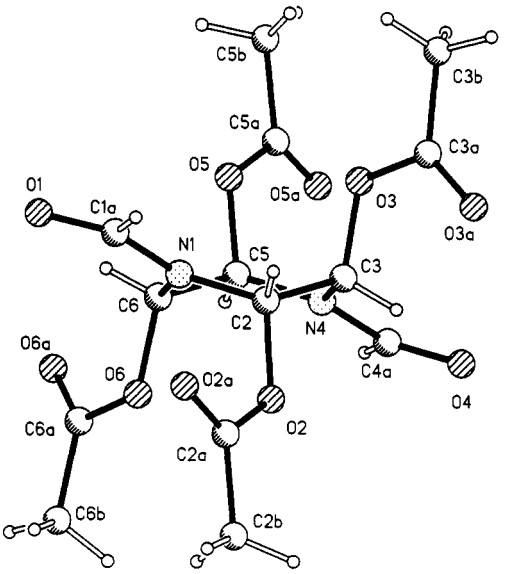


Figure 3. X-ray molecular structure and numbering scheme for **9**.

with all acetoxy groups in axial positions. The smaller than normal ring torsion angles (±45° rather than 60°) are due to the partial sp^2 character of the nitrogens, which increases the C–N–C angle from the normal tetrahedral angle. It has been shown for *N*-acylpiperidines that the relatively planar configuration would cause severe steric interactions (A strain) between the acyl group and equatorial substituents on the adjacent carbon atoms 2 and 6. This results in a strong preference for axial orientation of these substituents.[9,10] The same effect and additional steric interactions between adjacent equatorial substituents are likely to account for the observed structure of **9**. In **8** the substituents on carbon are smaller; intramolecular hydrogen bonding between OH and C=O would require equatorial hydroxy groups, whereas A strain and anomeric interaction between the lone pair on nitrogen and the

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(9) Palasz, P. D.; Utley, J. H. P.; Hardstone, J. D. *J. Chem. Soc., Perkin Trans. 2* **1984**, 807.
(10) Chow, Y. L.; Colon, C. J.; Tam, J. N. S. *Can. J. Chem.* **1968**, *46*, 2821.
(11) Szarek, S. A., Horton, D., Eds. *Anomeric Effect, Origin and Consequences*; ACS Symposium Series 87; American Chemical Society: Washington, DC, 1979.

Table II. Selected X-ray Structural Data for 5a and 5b

compound	piperazine lone-pair torsion,[a] deg	bend,[b] deg	axial C–N bond length, Å	piperazine C–N bond length, Å
5a	lp–N1–C2–N3, 159.5	28.9	1.478 (10)	1.446 (9)
	lp–N1–C12–N11, 179.6	28.9	1.426 (9)	1.451 (9)
	lp–N7–C6–N5, 179.9	11.3	1.424 (12)	1.454 (9)
	lp–N7–C8–N9, 161.6	11.3	1.458 (9)	1.449 (9)
5b first molecule	lp–N1–C2–N3, 159.5	1.5	1.453 (11)	1.440 (11)
	lp–N1–C12–N11, –151.3	1.5	1.469 (11)	1.443 (11)
	lp–N7–C6–N5, –166.2	4.1	1.422 (12)	1.445 (11)
	lp–N7–C8–N9, 172.8	4.1	1.448 (12)	1.450 (11)
5b second molecule	lp–N21–C22–N23, 163.3	4.4	1.443 (12)	1.435 (11)
	lp–N21–C32–N31, –146.0	4.4	1.479 (12)	1.458 (11)
	lp–N27–C26–N25, 179.1	24.0	1.443 (13)	1.452 (11)
	lp–N27–C28–N29, –165.3	24.0	1.441 (12)	1.476 (12)

[a] The lone pairs were not directly found by the crystallographic analysis. The nitrogen atoms are all at least slightly pyramidal; it is assumed that the major lobe of the nitrogen lone-pair orbital is directed outward from the apex of this pyramid on a line that makes equal angles with each of the three bonds to the N atom. This major lobe is called the "lone pair" for the purposes of this calculation. [b] The bend reported here is the angle between the N–N bond and the adjacent three-atom segment of the ring. It is a measure of the hybridization and is expected to be 0° for sp^2 and 54.5° for sp^3 hybridizations.

substituents on carbon (see below) favor axial substituents. The ^1H NMR spectra of 8 and 9 are similar and indicate that both compounds are meso isomers. Both spectra show two singlets of equal intensity for the methine protons on the piperazine ring, resulting from slow rotation of the *N*-acyl groups. The separations of the signals (0.47 and 0.75 ppm, respectively) fall in between those reported for the axial and equatorial protons in an *N*-acylpiperidine[9] and do not permit an unequivocal conformational assignment for 8. Thus, 8 and 9 have the same configuration, but the preferred conformation of both molecules in solution, and of 8 in the solid, cannot be unequivocally assigned at this time.

In an attempt to investigate the mechanism of the formation of **1a**, the solids present in the reaction mixture were analyzed at various intervals. They were found to consist of a mixture of the tetrahydroxypiperazine starting material and **1a**. No intermediates were present, and none could be isolated from the filtrate. It is known that the tetrahydroxypiperazine slowly hydrolyzes in concd HCl to the dihydrochloride of $H_2NCH(OH)CH(OH)NH_2$.[12] Hydrolysis of a formyl group may be the slow step in this decomposition and in the reaction sequence leading to 1. The reaction may then proceed, after hydrolysis of one formyl group, by mechanisms analogous to those discussed by Butler[13] for the condensation of methylurea with a 4,5-dihydroxy-2-imidazolidinone, involving the intermediacy of an iminium ion, and by Palasz[9] for the anodic methoxylation of *N*-acylpiperidines. Conversely, both *N*-formyl groups may be removed in the last step. In either case the presence of a partial double bond and planarity of adjacent equatorial substituents on the piperazine ring could give rise to steric interactions affecting the stereochemistry of ring formation.

The X-ray molecular structures of **5a** and **5b** show that in these molecules the piperazine rings assume a twist-boat conformation. The two five-membered rings are attached via axial bonds, which gives rise to the observed cis-syn-cis stereochemistry. This conformation is also indicated for **5a** in solution, by the ^4J coupling of 2 Hz in the ^1H NMR spectrum (Table I; referee's suggestion). The preference for the boat conformer with axial substitution does not appear to be related to steric effects. Inspection of molecular models of the all-axial and all-equatorial conformations of **1a** and its nitro derivatives, with the piperazine rings in boat conformations, does not indicate substantial differences in steric interactions. The torsion angles (Figure 4) listed in Table II show that the alignment of the N–C–N segments in **5a** and **5b** (and presumably also in **1a**) permit overlap between the lone-pair orbital on each piperazine nitrogen and the antibonding orbital of the axial C–N bonds (anomeric effect).[11] The X-ray crystallographically determined C–N bond lengths in **5a** and **5b** (Table II) lend some support to the invocation of an anomeric effect in these compounds. Examination of the data in Table II reveals shortened axial C–N bonds to the unsubstituted nitrogens in **5a** coinciding with torsion angles between the piperazine nitrogen lone pairs and these axial bonds of 179–180°. In the more highly strained **5b** only one such correlation (C_6–N_5) is found in the two independent molecules. Thus, some kind of stereoelectronic interaction involving the anomeric carbons C_6 and C_{12} in **5a**, and C_6 in **5b**, is indicated.

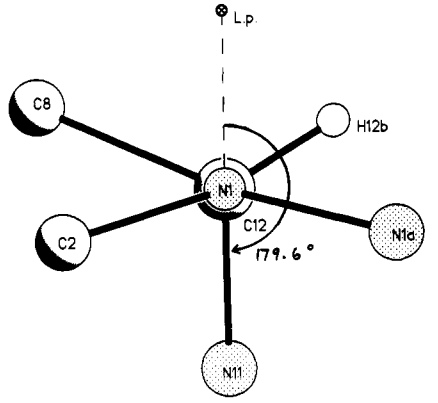

Figure 4. Torsion angle lone pair–N1–C12–N11 in **5a**.

Experimental Section

CAUTION! Compounds 5–7 are sensitive explosives and should be handled with appropriate precautions.

Melting points were determined in open capillary tubes on a Thomas-Hoover capillary apparatus and are uncorrected, unless noted otherwise. Infrared spectra were recorded on a Perkin-Elmer Model 283 grating spectrophotometer. ^1H NMR spectra were obtained at 60 and 90 MHz on Varian Model EM-360 and EM-390 and JEOL FX90Q NMR spectrometers (Me_4Si internal standard). ^{13}C NMR spectra were recorded on a JEOL FX90Q NMR spectrometer (Me_4Si internal standard). Mass spectra were recorded on a Hewlett-Packard 5985 (70 eV) spectrometer; *m/z* is reported for selected peaks of relative intensity >1. Micro-

(12) Nurgatin, V. V.; Ginzburg, B. M.; Kovalenko, V. I.; Marchenko, G. A. *Khim. Geterotsikl. Soedin.* **1985**, 1265; *Chem. Abstr.* **1986**, *105*, 78908*h*.

(13) Butler, A. R.; Hussain, I. *J. Chem. Soc., Perkin Trans. 2* **1981**, 310.

analyses were performed by Galbraith Laboratories, Inc., Knoxville, TN, and by National Analytical Laboratories, Pty Ltd., Victoria, Australia.

1,4-Diformyl-2,3,5,6-tetrahydroxypiperazine. The literature method[14] was modified as follows: Formamide (135 g, 119 mL, 3.0 mol) was added to stirred aqueous glyoxal (40% w/w, 435 g, 3.0 mol), and the pH was adjusted to 8.5 by using aqueous sodium hydroxide solution (10 M). The temperature rose slowly to 30 °C over the first 30 min, and the solution developed a yellow tinge. The exotherm subsided, and after 4 h of stirring, the mixture was left to stand for 3 days. A first crop of the product (93 g) was collected by filtration, and a second crop was obtained by adjusting the pH of the filtrate to 9, the temperature of the mixture being controlled at 25 °C with ice/water and the additional product being collected after 5 h. Both crops were washed well with water, dried, and purified by digesting the solid twice in a hot mixture of dimethylformamide/water (80:20). This involved using 70 mL of this mixture for each 30 g of solid, maintaining the stirred slurry at 75 °C for 30 min, then cooling it to 30 °C, collecting the solid, and washing it well with water. The product was dried over a desiccant to give a white solid (204 g, 66%), which darkened substantially above 190 °C and decomposed above 210 °C (lit.[15] mp ca. 225 °C dec): IR (KBr) 3350 (br), 1680 (s), 1475, 1440, 1410, 1358, 1330, 1300, 1200, 1078, 1060, 942, 800, 658 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 8.39 (s, 2, CHO), 6.05 (br s, 4, OH, exchanged with D_2O), 5.57 (s, 2, CH), 5.10 (s, 2, 2 CH). Anal. Calcd for $C_6H_{10}N_2O_6$: C, 34.94; H, 4.89; N, 13.59. Found: C, 34.96; H, 4.86; N, 13.60.

***cis*-*syn*-*cis*-2,6-Dioxodecahydro-1*H*,5*H*-diimidazo[4,5-*b*:4′,5′-*e*]pyrazine (1a).** Finely ground 1,4-diformyl-2,3,5,6-tetrahydroxypiperazine (24 g, 0.115 mol) was added to a stirred solution of urea (21 g, 0.35 mol) in concentrated hydrochloric acid (37% w/w, 100 mL) over 15 min. The mixture was stirred for 90 h, after which time the ^1H NMR spectrum of a sample showed that all starting material had been consumed. The solid was collected by filtration, washed with methanol (300 mL), and dried at aspirator vacuum and then at 75 °C (1 mm) to give the crude product (28.2 g, 80.2%) as a hydrate of the dihydrochloride salt. This was dissolved in chilled water (22.5 mL/g) and precipitated by the addition of cold methanol (100 mL/g) to give the monohydrochloride salt (10.3 g, 38%), which darkens above 170 °C: mp 183–185 °C dec (corrected); IR (KBr) 3340 (s), 3210 (s), 2930, 1722 (C=O), 1692 (C=O), 1532 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 7.20 (br s, 4, NH), 4.73 (s, 4 H, CH), 3.67 (br s, 3 H, NH, NH_2). Anal. Calcd for $C_6H_{10}N_6O_2$·HCl: C, 30.71; H, 4.73; Cl, 15.11; N, 35.82. Found: C, 30.54; H, 4.81; Cl, 15.33; N, 35.80.

Alternatively, the crude salt may be converted to the monohydrochloride by precipitation from an aqueous solution (1 g/10 mL) by the addition of acetone (3 mL/mL of solution); the yield was 32% based on piperazine starting material.

A pure sample of the monohydrated dihydrochloride salt was obtained by twice adding a concentrated aqueous solution of the monohydrochloride salt to 6 times the volume of concentrated hydrochloric acid (37% w/w). The collected dihydrochloride salt (78% recovery) was dried at 40 °C (0.1 mm) for 20 h over silica gel to give the monohydrate, which darkens above 150 °C: mp 168–170 °C (corrected); IR (KBr) 3160 (s), 2800 (br), 1738 (C=O) cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 7.80 (br s, 10, NH, NH_2^+, H_2O), 4.87 (s, 4 H, CH). Anal. Calcd for $C_6H_{10}N_6O_2$·2HCl·H_2O: C, 24.93; H, 4.88; Cl, 24.52; N, 29.07; O, 16.60. Found: C, 24.76; H, 4.93; Cl, 24.74; N, 28.78; O, 16.54.

2,6-Dioxo-1,3,5,7-tetramethyldecahydro-1*H*,5*H*-diimidazo[4,5-*b*:4′,5′-*e*]pyrazine (1b). To a stirred solution of 1,3-dimethylurea (11.0 g, 0.12 mol) in concentrated hydrochloric acid (40 mL) was added 1,4-diformyl-2,3,5,6-tetrahydroxypiperazine (5.5 g, 0.03 mol) in portions over a period of 10 min. Stirring was continued at 25 °C for 2 days. A precipitate was isolated and triturated with absolute alcohol (3 × 20 mL) and methanol (5 × 40 mL); the combined extracts were evaporated to give the tetramethyl derivative **1b** as a dihydrochloride (2.5 g, 29%): mp 208–211 °C dec; ^1H NMR (DMSO-d_6) δ 9.25 (br s, 4, NH_2^+), 5.76 (s, 4 H, CH), 2.87 (s, 12 H, CH_3); EI-MS, m/z (relative intensity) 127 (21), 57 (15), and 36 (100). Anal. Calcd for $C_{10}H_{20}N_6O_2Cl_2$: C, 36.70; H, 6.16; N, 25.68; Cl, 21.66. Found: C, 36.67; H, 5.78; N, 26.02; Cl, 21.70.

***cis*-*syn*-*cis*-2,6-Dioxo-4,8-dinitrosodecahydro-1*H*,5*H*-diimidazo[4,5-*b*:4′,5′-*e*]pyrazine (2).** Crude **1a**·2HCl, 2.7 g (10 mmol), was added gradually with stirring and cooling (ice bath) to a solution of 2.1 g (30 mmol) of sodium nitrite in 25 mL of water. The resulting mixture was stirred for 1 h while slowly warming to room temperature. The precipitate was filtered, washed with water, and dried. The ^1H NMR spectrum was consistent with an approximately 1:1 mixture of *syn*- and *anti*-dinitroso isomers (1.45 g, 56.9%). An analytical sample was obtained, as a DMSO solvate, by crystallization from DMSO/water (8:2): dec 175–180 °C; ^1H NMR (DMSO-d_6) δ 8.00, 7.93, 7.80, 7.63 (4 s, NH), 7.12, 7.04, 6.93, 6.5, 6.45, 6.40 (2 d, 2 s all CH of syn and anti isomers; individual assignments not made). Anal. Calcd for $C_6H_8N_8O_4$·C_2H_6SO: C, 28.74; H, 4.22; N, 33.52. Found: C, 28.54; H, 4.22; N, 33.56.

Preparation of 2 from the Monohydrochloride of 1a. To 0.1 N HCl (2.5 mL) at 0 °C was added sodium nitrite (0.21 g, 3.0 mol) followed immediately by addition of the monohydrochloride (0.27 g, 1.0 mmol). The resulting mixture was stirred at 0 °C for 30 min and then at room temperature for another 30 min. The precipitate was filtered, washed with water, and dried in vacuo to afford the product as a white solid (0.22 g, 0.87 mmol, 88%).

Preparation of 2 from 3. To 0.1 N HCl (2.5 mL) at 0 °C was added sodium nitrite (0.083 g, 1.2 mmol) followed immediately by **3** (0.23 g, 1.0 mmol). The resulting mixture was stirred at 0 °C for 30 min and then at room temperature for another 30 min. The precipitate was filtered, washed with water, and dried in vacuo to give the product (0.2 g, 0.79 mmol, 80%) as a slightly tan solid. This material had the same ^1H NMR spectrum as **2** prepared from **1a** hydrochlorides.

***cis*-*syn*-*cis*-2,6-Dioxo-4-nitrosodecahydro-1*H*,5*H*-diimidazo[4,5-*b*:4′,5′-*e*]pyrazine (3).** To a stirred solution of sodium nitrite (0.28 g, 4.1 mmol) in water (3.4 mL) at 0 °C was slowly added the monohydrochloride of **1a** (0.37 g, 1.4 mmol). The stirred mixture was allowed to warm slowly to room temperature over a period of 1 h. The product was then filtered, washed with water, and dried over P_2O_5 in vacuo to give a white solid (0.29 g, 1.3 mmol, 94%). An analytical sample was obtained by recrystallization from water: mp >290 °C, darkens >250 °C; ^1H NMR (D_2O, 3-(trimethylsilyl)-1-propanesulfonic acid, sodium salt, external standard) δ 6.69 (d, 1, J_{HH} = 9.7 Hz), 6.04 (d, 1, J_{HH} = 8.8 Hz), 5.39 (d, 1, J_{HH} = 9.7 Hz), 5.25 (d, 1, J_{HH} = 8.8 Hz). Anal. Calcd for $C_6H_8N_7O_3$: C, 31.72; H, 3.99; N, 43.16. Found: C, 31.72; H, 3.95; N, 43.24.

***cis*-*syn*-*cis*-2,6-Dioxo-4,8-dinitrodecahydro-1*H*,5*H*-diimidazo[4,5-*b*:4′,5′-*e*]pyrazine (4a).** The monohydrochloride of **1a** (1.0 g, 4.3 mmol) was added in portions to nitric acid (100%, 10 mL, 0.24 mol) at −40 °C, and the mixture was stirred for 30 min before it was poured onto ice. After the mixture was allowed to stand at 25 °C for 20 h, a precipitate was isolated, washed with water, and dried to give 2,6-dioxo-4,8-dinitrodecahydro-1*H*,5*H*-diimidazo[4,5-*b*:4′,5′-*e*]pyrazine as a light yellow solid (0.35 g, 28%), mp 302 °C **explosive dec**. It was purified by reprecipitation (dimethyl sulfoxide/acetone): IR (KBr) 3350–3100, 1740, 1580, 1285, 1250, 1140, 1090, 1065, 910, 865 cm^{-1}; ^{13}C NMR (DMSO-d_6) δ 159.03 (CO) and 63.17 (CH). Anal. Calcd for $C_6H_8N_8O_6$: C, 25.00; H, 2.78; N, 38.89; O, 33.33. Found: C, 25.09; H, 2.88; N, 38.71; O, 33.12.

2,6-Dioxo-4,8-dinitro-1,3,5,7-tetramethyldecahydro-1*H*,5*H*-diimidazo[4,5-*b*:4′,5′-*e*]pyrazine (4b). The dihydrochloride (4.0 g, 0.01 mol) of **1b** was added in portions to a solution of nitric acid (100%, 40 mL, 0.98 mol) at −40 °C over a period of 10 min with stirring. Stirring was continued for 1 h at the same temperature, and the mixture was poured onto crushed ice and stored for 1 h. A colorless precipitate was isolated, washed with ice-cold water (3 × 15 mL), and dried to give **4b**, 2.3 g (55%): mp 295–298 °C dec (from dimethyl sulfoxide/chloroform); EI-MS, m/z (relative intensity) 345 $(M + 1)^+$ (1) and 126 (100). Anal. Calcd for $C_{10}H_{16}N_8O_6$: C, 34.88; H, 4.65; N, 32.56. Found: C, 35.10; H, 4.62; N, 32.54.

***cis*-*syn*-*cis*-2,6-Dioxotetranitrodecahydrodiimidazo[4,5-*b*:4′,5′-*e*]pyrazines 5a and 5b.** To stirred acetic anhydride (100 mL) cooled in an ice/water bath was added, in small portions,

(14) Currie, A. C.; Dinwoodie, A. H.; Fort, G.; Thompson, J. M. C. *J. Chem. Soc. C* **1967**, 491.

(15) Vail, S. L.; Moran, C. M.; Barker, R. H. *J. Org. Chem.* **1965**, *30*, 1195.

2,6-dioxodecahydro-1*H*,5*H*-diimidazo[4,5-*b*:4′,5′-*e*]pyrazine monohydrochloride (20.0 g, 85.2 mmol). With stirring, 100% HNO_3 (90 mL, 2.2 mol) was added dropwise at such a rate that the temperature of the reaction mixture remained below 7 °C. Then the mixture was stirred for another 4 h at 4 °C. It was poured slowly onto 600 g of crushed ice and extracted five times with ethyl acetate. The combined extracts were washed with saturated aqueous sodium chloride, dried ($MgSO_4$), filtered, and concentrated in vacuo to give the crude product as a white, brittle foam. The crude product was dissolved in ethanol (95%, 280 mL) and heated at gentle reflux for 15 min. A white precipitate developed and was collected by filtration, washed with 95% ethanol, and air-dried to give 7.42 g (19.6 mmol, 23%) of isomer **5b**, contaminated with a small amount of isomer **5a**. The filtrate was concentrated in vacuo and the residue triturated with dichloromethane/acetone/hexanes (2:2:3, 50 mL). The solid isomer **5a** was filtered off. The filtrate was applied to a column of 200 g of silica gel 60 (EM Science). Elution with the same solvent mixture afforded additional **5a**. The combined batches of **5a** were washed with acetone/hexanes (1:2) to give 4.46 g (11.8 mmol, 14%) as a colorless solid.

The crude isomer **5b** above was purified further by chromatography on silica gel 60 (EM Science), eluting with 1:1:2 dichloromethane/acetone/hexanes, and was then crystallized from acetonitrile, mp 220–225 °C dec. Anal. Calcd for $C_6H_6N_{10}O_{10}$: C, 19.06; H, 1.60; N, 37.04. Found: C, 19.16; H, 1.60; N, 36.95.

Isomer **5a** obtained as above was also crystallized from acetonitrile: mp 238 °C dec. Anal. Calcd for $C_6H_6N_{10}O_{10}$: C, 19.06; H, 1.60; N, 37.04. Found: C, 19.48; H, 1.64; N, 36.69.

***cis*-*syn*-*cis*-2,6-Dioxo-1,3,4,5,8-pentanitrodecahydro-1*H*,5*H*-diimidazo[4,5-*b*:4′,5′-*e*]pyrazine (6). A. With HNO_3/Ac_2O.** To a well-stirred suspension of the monohydrochloride of **1a** (1.37 g, 5.84 mmol, dried in vacuo) in acetic anhydride (7.5 mL) at 0 °C was added HNO_3 (100%, 6.2 mL, 9.7 g, 150 mmol) at such a rate that the temperature of the reaction solution did not rise above 10 °C. After 26 h at 0 °C the reaction mixture was poured slowly onto 150 g of crushed ice and extracted with ethyl acetate (3 × 30 mL). The combined extracts were washed with saturated aqueous sodium bicarbonate (3 × 30 mL) and brine (3 × 30 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo to give the crude product mixture as a pale yellow, brittle foam. Column chromatography on silica gel 40 (EM Science, 200 g), eluting with 40% ethyl acetate/hexanes, afforded **6** (0.70 g, 1.65 mmol, 28%), **5a** (0.35 g, 0.93 mmol, 16%), and **5b** (0.50 g, 1.32 mmol, 23%) as pale yellow, brittle foams. The crude **6** contained an impurity that could be washed out with warm toluene. Further purification involved crystallization from benzene/acetone: **6** was dissolved in acetone, benzene (0.5 volume) was added, and the solvents were allowed to evaporate until most of the material had crystallized; mp 212 °C **violent dec.**

B. With $HNO_3/(CF_3CO)_2O$. The monohydrochloride of **1a** (1.0 g, 4.3 mmol) was added in portions with stirring to nitric acid (100%, 25 mL, 0.6 mol) at 0 °C. After 15 min, trifluoroacetic anhydride (20 mL) was added dropwise, and stirring was continued at 10 °C for 1 h and at 25 °C for 17 h. The precipitate was collected by filtration, washed with ice water, and dried to give the pentanitro derivative **6** as a colorless solid (0.85 g, 47%): mp 225 °C **explosive dec** (from acetone/hexane; ^1H NMR spectrum identical with that of **6** synthesized with HNO_3/Ac_2O); ^{13}C NMR (Me_2CO-d_6) δ 147.47, 139.87, 65.47, 62.48, 61.90, 58.48. Anal. Calcd for $C_6H_5N_{11}O_{12}$: C, 17.02; H, 1.18. Found: C, 16.98; H, 1.18.

***cis*-*syn*-*cis*-2,6-Dioxo-1,3,4,5,7,8-hexanitrodecahydro-1*H*,5*H*-diimidazo[4,5-*b*:4′,5′-*e*]pyrazine (7). A. From 5 or 6 with NO_2BF_4 in Acetonitrile.** To a solution of 2,6-dioxotetranitrodecahydro-1*H*,5*H*-diimidazo[4,5-*b*:4′,5′-*e*]pyrazines **5a** and **5b** (2.0 g, 5.3 mmol) in dry acetonitrile (75 mL) was added nitronium tetrafluoroborate (2.2 g, 16.5 mmol), and the mixture was heated at 65–70 °C for 3 h, as the initial clear solution gradually turned yellow. The reaction mixture was stirred at room temperature for 17 h and concentrated in a rotary evaporator (below 40 °C) to one-fourth the volume, and ice-cold water (20 mL) was added to the residue. A light brown solid was obtained, which was filtered, washed with water, and dried to give the hexanitro compound **7**, 1.8 g (73%): mp 205 °C **explosive dec.** Recrystallization from an acetonitrile/chloroform mixture furnished the hexanitro compound as a colorless solid **decomposing explosively** at 210 °C: IR (KBr) 3000, 1810 (s), 1590 (vs), 1340 (sh), 1300 (sh), 1270 (sh), 1245 (vs), 1180 (s), 1090 (s), 980, 935, 830, 715 cm^{-1}; ^{13}C NMR (acetone-d_6) δ 141.39 and 63.03. Anal. Calcd for $C_6H_4N_{12}O_{14}$: C, 15.38; H, 0.85; N, 35.90; O, 47.86. Found: C, 15.66; H, 0.89; N, 35.30; O, 46.72.

Treatment of 2,6-dioxo-1,3,4,7,8-pentanitrodecahydro-1*H*,5*H*-diimadazo[4,5-*b*:4′,5′-*e*]pyrazine (0.4 g, 0.95 mmol) with nitronium tetrafluoroborate (1.33 g, 10 mmol) in dry acetonitrile (75 mL) at 80 °C for 3 h followed by stirring at 24 °C for 17 h resulted in a dark brown mixture. Isolation as above furnished the hexanitro compound **7**, 0.25 g (56%).

Treatment of the pentanitro derivative **6** with trifluoromethanesulfonic anhydride and nitric acid (100%) at room temperature for 16 h or at 55 °C for 3 h followed by stirring at room temperature for 40 h did not give the hexanitro compound; only the starting material **6** (50% recovery) was identified by NMR.

B. From 1a with HNO_3/P_2O_5. Phosphorus pentoxide (15.6 g, 10.0 mmol) was slowly added to absolute (100%) nitric acid (30 mL, 750 mmol) which was stirred under nitrogen and cooled in ice/water to keep the temperature of the acid below 30 °C. The mixture was then maintained at 30 °C for 40 min to give a clear yellow solution. The stirred solution was cooled to −15 °C and kept below −10 °C as the monohydrochloride of **1a** (1.2 g, 0.5 mmol) was added in portions over 30 min. The mixture was allowed to warm to 25 °C over 1.5 h and was maintained at this temperature for 30 min, then at 35 °C for 1 h, and at 45 °C for 2 h. The cooled mixture was stirred into ice/water (300 mL). The precipitated solid was quickly collected by filtration, washed with cold water and dichloromethane, and then dried to give the crude product (1.78 g, 74%): mp 210 °C **explosive dec.** Recrystallization from dry acetone/dry benzene under nitrogen gave white plates which contained residual solvent. When fine crystals were dried at 100 °C (0.01 mm) for 35 h, they contained less than 0.2% w/w acetone as determined from the ^1H NMR spectrum in CD_3CN. These crystals **decomposed explosively** at 215 °C: IR (KBr) 1822 (C=O), 1612, 1592 cm^{-1} (NO_2). Anal. Calcd for $C_6H_4N_{12}O_{14}$: C, 15.39; H, 0.86; N, 35.90. Found: C, 15.74; H, 0.92; N, 35.70.

1,4-Diformyl-2,3,5,6-tetraacetoxypiperazine (9). Method A. A mixture of 1,4-diformyl-2,3,5,6-tetrahydroxypiperazine (**8**, 10.3 g, 0.05 mol), acetic anhydride (108 g, 1.06 mol), and sulfuric acid (96.5% w/w, 0.55 g, 5.63 mmol) was heated at 100 °C for 1 h. The mixture was cooled in ice and the collected solid washed with ether to give the crude product (15.7 g, 83.9%). Recrystallizations from acetonitrile gave crystals, mp 262–263 °C dec (lit.[9] mp 262–263 °C), used for X-ray crystallographic analysis: ^1H NMR (CD_2Cl_2) δ 8.58 (s, 2, CHO), 6.88 (s, 2, CH), 6.13 (s, 2, CH), 2.12 (s, 12, CH_3). An identical sample (mp, mmp, IR, ^1H NMR) was prepared at room temperature (2 days) by using a 1:1 (v/v) mixture of acetic anhydride/acetic acid and H_2SO_4 as catalyst.

Method B. A mixture of finely ground **8** (1.0 g, 4.85 mmol), acetic anhydride (10.8 g, 106 mmol), and pyridine (5 g, 63.29 mmol) was stirred at room temperature for 5 days. The mixture was cooled in ice and filtered and the collected solid washed with ice water to give the product (1.7 g, 94%). Recrystallizations from acetonitrile gave crystals identical (mp, mmp, IR, ^1H NMR) with the compound prepared by method A.

Single-Crystal X-ray Diffraction. Diffraction experiments were performed at the Naval Research Laboratory on one of two automated Siemans diffractometers equipped with incident-beam graphite monochromators. All structures were solved and refined with the aid of the SHELXTL system of programs.[16]

***cis*-*syn*-*cis*-2,6-Dioxo-1,4,5,8-tetranitrodecahydro-1*H*,5*H*-diimidazo[4,5-*b*:4′,5′-*e*]pyrazine (5a):** $C_6H_6N_{10}O_{10}$, FW = 378.2, orthorhombic space group *F*2*dd*, a = 15.5895 (15) Å, b = 16.754 (2) Å, c = 19.524 (2) Å, V = 5099.6 (9) Å^3, Z = 16, ρ_{calcd} = 1.970 mg mm^{-3}, λ(Mo Kα) = 0.71073 Å, μ = 0.175 mm^{-1}, $F(000)$ = 3072, T = 293 K.

A clear, colorless 0.24 × 0.22 × 0.32 mm crystal, in the shape of a prism, was used for data collection. Lattice parameters were

(16) Sheldrick, G. M. *SHELXTL80. An Integrated System for Solving, Refining, and Displaying Crystal Structures from Diffraction Data*; University of Gottingen: Gottingen, Federal Republic of Germany, 1980.

determined from 27 centered reflections within 17.9° ≤ 2θ ≤ 22.5°. The data collection range of *hkl* was 0 ≤ *h* < 18, 0 ≤ *k* ≤ 19, 0 ≤ *l* ≤ 23, with $[(\sin\theta)/\lambda]_{max}$ = 0.595. Three standards, monitored after every 97 reflections, exhibited random variations with deviations up to ±1.5% during the data collection. A set of 1280 reflections was collected in the θ/2θ scan mode, with scan width [2θ(Kα$_1$) − 0.4]° to [2θ(Kα$_2$) + 0.4]° and a constant ω scan rate of 15.63 deg/min. There were 1167 unique reflections, and 923 were observed with $F_o > 3\sigma(F_o)$. The full-matrix least-squares refinement varied 241 parameters: atom coordinates and anisotropic thermal parameters for all non-H atoms and atom coordinates for the two amino hydrogen atoms. All CH hydrogen atoms were included by using a riding model (coordinate shifts of C applied to attached H atoms, C–H distances set to 0.96 Å, H angles idealized). The U_{iso}(H) were set to 1.1 × U_{eq}(neighboring atom). The final residuals were *R* = 0.051 and *wR* = 0.043 with final difference Fourier excursions of 0.36 and −0.36 e Å^{-3}.

***cis-syn-cis*-2,6-Dioxo-1,4,7,8-tetranitrodecahydro-1*H*,5*H*-diimidazo[4,5-*b*:4′,5′-*e*]pyrazine (5b)**: $C_6H_6N_{10}O_{10}$, FW = 378.2, monoclinic space group $P2_1/n$, *a* = 8.5114 (14) Å, *b* = 12.259 (3) Å, *c* = 24.952 (7) Å, β = 97.30 (2)°, *V* = 2582.4 (1.1) Å^3, *Z* = 8, ρ_{calcd} = 1.945 mg mm^{-3} at −50 °C (1.930 at 20 °C), λ(Cu Kα) = 1.541 84 Å, μ = 1.579 mm^{-1}, *F*(000) = 1536, *T* = 223 K.

A translucent, colorless 0.04 × 0.08 × 0.25 mm crystal, in the shape of a lath, was used for data collection. Lattice parameters were determined from 25 centered reflections within 36.3° ≤ 2θ ≤ 93.9°. The data collection range of *hkl* was −9 ≤ *h* ≤ 8, 0 ≤ *k* ≤ 13, 0 ≤ *l* ≤ 26, with $[(\sin\theta)/\lambda]_{max}$ = 0.531. Three standards, monitored after every 97 reflections, exhibited random variations with deviations up to ±2.5% during the data collection. A set of 3985 reflections was collected in the θ/2θ scan mode, with scan width [2θ(Kα$_1$) − 0.5]° to [2θ(Kα$_2$) + 0.5]° and ω scan rate (a function of count rate) from 12.0 to 30.0 deg/min. There were 3230 unique reflections, and 2342 were observed with $F_o > 3\sigma(F_o)$. The full-matrix least-squares refinement varied 506 parameters: atom coordinates and anisotropic thermal parameters for all non-H atoms and atomic coordinates for the hydrogen atoms (the U_{iso}(H) were set to 0.05 Å^2). The final residuals were *R* = 0.081 and *wR* = 0.080 with final difference Fourier excursions of 0.52 and −0.47 e Å^{-3}.

1,4-Diformyl-2,3,5,6-tetraacetoxypiperazine (9): $C_{14}H_{18}N_2O_{10}$, FW = 374.3, monoclinic space group $P2_1/n$, *a* = 7.905 (2) Å, *b* = 25.691 (4) Å, *c* = 13.536 (2) Å, β = 98.69 (1)°, *V* = 2717.2 (7) Å^3, *Z* = 6 (1.5 mol/asymmetric unit), ρ_{calcd} = 1.372 mg mm^{-3}, λ(Cu Kα) = 1.541 84 Å, μ = 0.983 mm^{-1}, *F*(000) = 1176, *T* = 293 K.

A clear, colorless 0.12 × 0.14 × 0.27 mm crystal, in the shape of a prism, was used for data collection. Lattice parameters were determined from 25 centered reflections within 40° ≤ 2θ ≤ 57°. The data collection range of *hkl* was 0 ≤ *h* ≤ 8, 0 ≤ *k* ≤ 28, −14 ≤ *l* ≤ 14, with $[(\sin\theta)/\lambda]_{max}$ = 0.547. Three standards, monitored after every 97 reflections, exhibited random variations with deviations up to ±2.5% during the data collection. A set of 4327 reflections was collected in the θ/2θ scan mode, with scan width [2θ(Kα$_1$) − 0.5]° to [2θ(Kα$_2$) + 0.5]° and ω scan rate (a function of count rate) from 8.0 to 29.3 deg/min. There were 3738 unique reflections, and 2606 were observed with $F_0 > 3\sigma(F_o)$. The full-matrix least-squares refinement varied 398 parameters: atom coordinates and anisotropic thermal parameters for all non-H atoms and atomic coordinates for all (nine) non-methyl hydrogen atoms. Eighteen methyl H atoms were included as rigid rotatable groups (C–H distances set to 0.96 Å, H angles idealized). The U_{iso}(H) were set to 0.050 or, if methyl, 0.075 Å^2. The final residuals were *R* = 0.066 and *wR* = 0.059 with final difference Fourier excursions of 0.31 and −0.26 e Å^{-3}.

There are two independent molecules in the asymmetric unit of this crystal, one sitting on a crystallographic center of symmetry and the other in a general position. The conformations of both are identical (to within experimental error); the molecules are somewhat flattened chair forms (alternating ring torsions of ca. ±45° rather than ±60°), and each has four axial acetoxy substituents.

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Supplementary Material Available: Tables of atomic coordinates and equivalent isotropic displacement coefficients, bond lengths and angles, anisotropic displacement coefficients, and H-atom coordinates and isotropic displacement coefficients for compounds **5a**, **5b**, and **9**, Supplementary Figure 5 showing the numbering scheme for the second molecule of **5b**, and Supplementary Figure 6 showing the numbering scheme for the second molecule of **9** (13 pages). Ordering information is given on any current masthead page.

Novel Heterocycles by Bis Heteroannulation of Oxazoles[1]

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We report the first examples of intramolecular Diels–Alder addition of heterodienophiles N=N, C=N, C=O, C=S to oxazoles. The required 5-ethoxy- and 5-phenyloxazoles were synthesized bearing a side chain of variable length on C-2 to which the different heterodienophiles are attached. The products of the thermal bis heteroannulation are 3-triazolines, imidazolines, oxazolines, or thiazolines fused to a five- to six-membered ring. Relative reactivities were established and the mechanism is discussed.

Introduction

In a previous paper[2] we reported the results of intermolecular cycloaddition of different oxazoles with heterodienophiles (Scheme I). These reactions were HOMO diene controlled since they required the normally electron poor azadiene to bear electron-donating groups (OEt, $OSiMe_3$) at C-2 or C-5. The heterodienophiles **2** were electron poor: PTAD, DEAD, dehydrohydantoin, and diethyl ketomalonate. The thermal reactions (in the dehydrohydantoin and diethyl ketomalonate cases, BF_3·etherate was needed to facilitate the reaction) led to 3-triazolines (**3**; X, Y = N), imidazolines (**3**; X = C, Y =

(1) Cycloadditions 48. For paper 47, see: Hassner, A.; Dehaen, W. *Chem. Ber.*, in press.
(2) Hassner, A.; Fischer, B. *Tetrahedron* **1989**, *45*, 3535.

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