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Supplementary Material Available: ^{13}C NMR spectra (^1H broad-band decoupled) of new compounds **1**, **2**, **5b**, **6**, **7**, **8**, and **9** (8 pages). Ordering information is given on any current masthead page.

Nucleic Acid Related Compounds. 64. Synthesis of 2',3'-Diazido-2',3'-dideoxyadenosine and 2',3'-Diamino-2',3'-dideoxyadenosine from 9-(β-D-Arabinofuranosyl)adenine[1]

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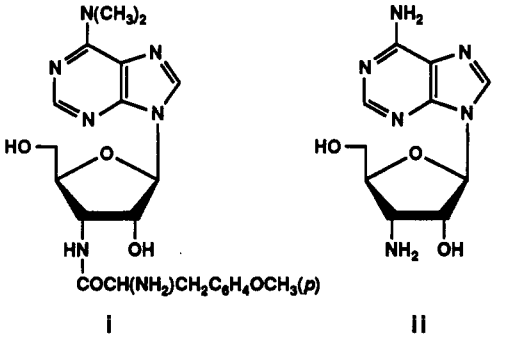
Treatment of 9-(β-D-arabinofuranosyl)adenine (**1**) with triphenylphosphine and diethyl azodicarboxylate gave 9-(2,3-anhydro-β-D-lyxofuranosyl)adenine (**2**). Treatment of **2** with lithium azide and protection of the major product gave 9-[3-azido-5-*O*-(*tert*-butyldimethylsilyl)-3-deoxy-β-D-arabinofuranosyl]adenine (**4**). Trifluoromethanesulfonylation of **4** and treatment of the resulting triflate **5** with lithium azide gave 9-(5-*O*-TBDMS-2,3-diazido-2,3-dideoxy-β-D-ribofuranosyl)adenine (**6**). Deprotection of **6** gave 2',3'-diazido-2',3'-dideoxyadenosine (**7**), which was hydrogenated to give the secondary diamino nucleoside analogue, 2',3'-diamino-2',3'-dideoxyadenosine (**8**). Biological rationale for the synthesis of nucleoside analogues **7** and **8** is discussed.

There has been a strong resurgence of interest recently in the chemistry of nucleosides.[4] Marked attention to the synthesis and properties of 2',3'-dideoxynucleosides and their sugar-substituted azido derivatives has been spurred by the efficacy of 3'-azido-3'-deoxythymidine (AZT) as a potent inhibitor of the human immunodeficiency virus (HIV) in the treatment of AIDS[5,6] and the parallel biological activity of several 2',3'-dideoxynucleosides.[6] At present, 2',3'-dideoxyadenosine,[7] 2',3'-dideoxycytidine,[8] and 2',3'-dideoxyinosine[9] are undergoing clinical trials in patients suffering from AIDS and AIDS-related complex.[10] It was recently noted that 2'-azido-2',3'-dideoxyadenosine has little inhibitory effect on HIV replication,[11] whereas 3'-azido-2',3'-dideoxyadenosine is active, but cytotoxic.[11,12]

Examples of 2'-amino-2'-deoxy- and 3'-amino-3'-deoxyribonucleosides are known to possess antibacterial, anticancer, and biosynthetic inhibitory activities.[13,14] Puromycin (i) is the well-known inhibitor of peptide biosynthesis.[13b,14b] Its core nucleoside component, 3'-amino-3'-deoxyadenosine (ii), has antitumor activity, and the 5'-triphosphate of ii has been observed to block RNA synthesis.[13c,14c] The 5'-triphosphate of 2'-amino-2'-deoxyadenosine and 2'-amino-2'-deoxyuridine are weak competitive inhibitors of DNA-dependent RNA polymerases from *E. coli*,[15] and both 2'-amino-2'-deoxy-



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adenosine[16] and 2′-amino-2′-deoxyguanosine[14d] are naturally occurring nucleoside antibiotics. Thus, a sizable number of syntheses and biological studies involving the singly substituted 2′(or 3′)-azido- and 2′(or 3′)-amino-2′(or 3′)-deoxynucleosides have been reported. However, no studies on doubly secondary-substituted 2′,3′-diazido-2′,3′-dideoxy- or 2′,3′-diamino-2′,3′-dideoxyribonucleosides have appeared since our preliminary report.[17] Such molecules might function as RNA chain terminators and/or as inhibitors of RNA polymerases. Furthermore, the incorporation of 2′-3′-diamino-2′,3′-dideoxyadenosine at the 5′-CCA-3′ termini of tRNA molecules would provide tools to identify the initial position of aminoacylation during charging of tRNA's by their cognate tRNA synthetases.[18]

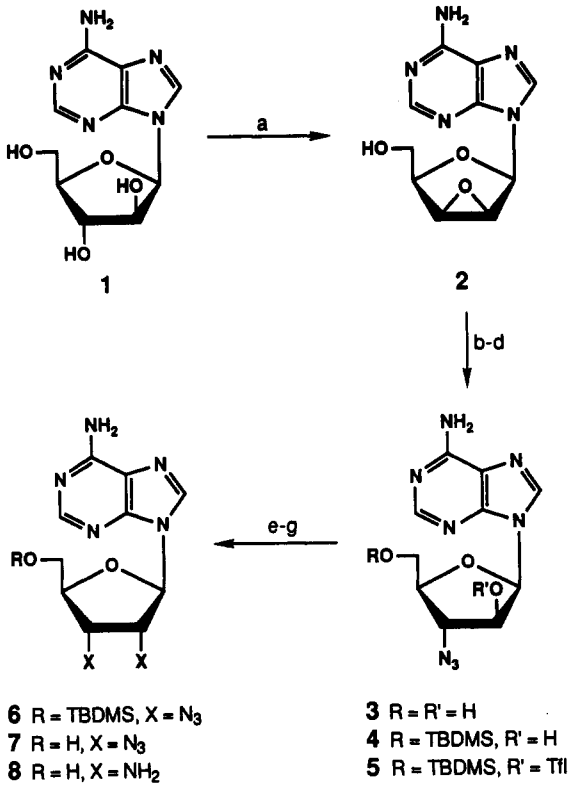
Two principle strategies for the synthesis of such doubly-substituted sugar nucleosides exist. The first involves coupling of preformed, derivatized sugars with appropriate purine or pyrimidine bases.[4] Disadvantages of this approach include possible formation of regioisomers and/or anomers and subsequent requirements for their separation. Difficult separations result in lower yields from chromatographic losses as well as the amounts lost as unwanted isomers. The second strategy involves transformations of the sugar moieties of parent nucleosides into target structures. This approach has been used to synthesize a wide variety of 2′- and 3′-substituted nucleosides.[4,17,19,20] For example, treatment of uridine with diphenyl carbonate efficiently generated 2,2′-anhydro-1-(β-D-arabinofuranosyl)uracil,[21] which underwent cyclonucleoside ring opening at C2′ with lithium azide to yield 2′-azido-2′-deoxyuridine.[22] Reduction of the azido function generated 2′-amino-2′-deoxyuridine.

We have developed synthetic transformation routes to 2′,3′-diamino-2′,3′-dideoxynucleosides that are independent of the functionality on the nucleoside base.[17] Such routes do not require extensive protection/deprotection strategies and allow access to a wide range of nucleosides, particularly those in which activation of the 2′-position by cyclonucleoside formation is precluded.

Treatment of 9-(β-D-arabinofuranosyl)adenine (1) with triphenylphosphine and diethyl azodicarboxylate in 1,4-dioxane/*N*,*N*-dimethylformamide (DMF) at 70 °C gave 9-(2,3-anhydro-β-D-lyxofuranosyl)adenine[23] (2) in 91% yield after column chromatography. This procedure[23b] affords the strained epoxide directly under mild neutral conditions. ^{1}H NMR analysis of the product revealed the absence of starting material or significant impurities, so this material was used in the next step without further purification.

Treatment of 2 with lithium azide in warm DMF gave 9-(3-azido-3-deoxy-β-D-arabinofuranosyl)adenine (3) and its 2′-azido-2′-deoxy-*xylo* isomer in ratios ranging from

Scheme I[a]



6 R = TBDMS, X = N_3
7 R = H, X = N_3
8 R = H, X = NH_2

3 R = R′ = H
4 R = TBDMS, R′ = H
5 R = TBDMS, R′ = Tfl

[a] Key: (a) $Ph_3P/EtO_2CN{=}NCO_2Et/DMF/1,4$-dioxane, 70 °C; (b) LiN_3/DMF, 80 °C; (c) $(CH_3)_3CSi(CH_3)_2Cl$/imidazole/DMF; (d) $CF_3SO_2Cl/DMAP/CH_2Cl_2$, 0 °C; (e) LiN_3/DMF; (f) $Bu_4N^+F^-$/THF; (g) $H_2/Pd/C/MeOH/HCl/H_2O$.

10–15:1 as previously described[24] with no attempts made to further enhance the 3′-regioisomer (Scheme I). Isomer 3 was recovered in 85% yield by recrystallization from water without observed contamination by the 2′-azido compound. Selective protection of the primary alcohol function (5′-OH) with *tert*-butyldimethylsilyl[25] or *tert*-butyldiphenylsilyl[26] groups gave 4 (TBDMS, 87%), which was activated by trifluoromethanesulfonylation of the 2′-hydroxyl group to give 9-(3-azido-5-*O*-TBDMS-3-deoxy-2-*O*-triflyl-β-D-arabinofuranosyl)adenine (5). Displacement of the triflate group from 5 with lithium azide in DMF at ambient temperature gave 6 (93%), which was deprotected with tetrabutylammonium fluoride[25a] (TBAF) to yield 2′,3′-diazido-2′,3′-dideoxyadenosine (7, 87%). The 2′-hydroxyl group can also be activated by conversion to its mesyl ester. However, this mesylate is significantly less reactive than the triflate and the subsequent azide displacement must be performed at elevated temperatures. This increases the formation of byproducts, and also raises concern for the **potential of explosions** if larger quantities of 7 (high nitrogen ratio) were to be prepared. We also observed that the use of more than 1 equiv of TBAF in the deprotection of 6 to 7 results in formation of a second product (tentatively identified as a monoazido unsaturated nucleoside). Catalytic hydrogenation of 7 in weakly acidic aqueous methanol followed by passage through an anion exchange column[27] and lyophilization gave 2′,3′-diamino-2′,3′-dideoxyadenosine (8, 57%) that was

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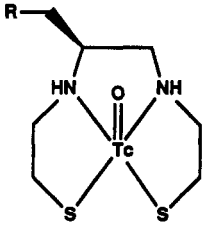
crystallized by the diffusion method.[28]

This mild seven-stage sequence gave 8 in 30% yield overall from 9-(β-D-arabinofuranosyl)adenine (1). All of the reactions proceeded smoothly in good to high yields except the final reduction of 2',3'-diazido-2',3'-dideoxyadenosine (7, 53% overall from 1) to 2',3'-diamino-2',3'-dideoxyadenosine (8). Although this reaction was not examined in detail, it appeared that hydrogenation over other catalysts or Staudinger reduction with triphenylphosphine in aqueous ammoniacal 1,4-dioxane[29] did not provide significantly enhanced yields.

Compounds 7 and 8 are under investigation as potential inhibitors of HIV and lipophilic and hydrophilic probes of partitioning and nucleoside transport across cell membranes. They also are unique precursors for model transition-state analogues of enzymatic reactions. Phosphoryl transfers are believed to take place through a pentacoordinate intermediate. However, there are no examples of hydrolytically stable pentacoordinate phosphorus compounds, and few examples of appropriately stable pentacoordinate metal complexes exist. For example, vanadate ribonucleotide esters are used as general inhibitors of ribonucleases.[30] However, they are unstable and exist as an equilibrium mixture of monomers and dimers,[31] which makes quantitative studies of their efficacy as inhibitors difficult. Complexes of the general structure 9 have been synthesized and are known to be stable.[32] Studies of new models in which the ethylenediamine group of 9 has been substituted by the 2',3'-diamino moiety of compound 8 will be reported separately.



9

Experimental Section

Uncorrected melting points were determined on a hot-stage apparatus. ^{1}H NMR spectra were obtained at 300 or 400 MHz in Me_2SO-d_6 or $CDCl_3$ with chemical shifts relative to internal Me_4Si (or the δ 2.49 resonance of residual dimethylsulfoxide). Ultraviolet (UV) spectra were recorded on a diode array spectrophotometer. Low-resolution fast atom bombardment (FAB) mass spectra (MS m/z (relative intensity, ion)) were obtained by direct probe techniques by the Midwest Mass Spectrometry Facility. Thin-layer chromatography (TLC) was performed with use of Merck silica gel 60 F 256 plates. THF was freshly distilled from sodium benzophenone ketyl, and methylene chloride was distilled from calcium hydride. 9-(β-D-Arabinofuranosyl)adenine was obtained from Sigma. Lithium azide was purchased from Pfaltz & Bauer. All other chemicals were obtained from Aldrich and were used without further purification. All reactions were performed in oven- or flame-dried glassware in a dry nitrogen atmosphere. Solid reagents were dried in vacuo at 50 °C overnight prior to use.

9-(2,3-Anhydro-β-D-lyxofuranosyl)adenine (2). 9-(β-D-Arabinofuranosyl)adenine (1; 1.44 g, 5.4 mmol) and triphenylphosphine (2.12 g, 8.1 mmol) were suspended in a mixture of 1,4-dioxane/DMF (80 mL, 1:1, v/v) and warmed at 70 °C for 15 min. A solution of diethyl azodicarboxylate (1.27 mL, 1.41 g, 8.1 mmol) in 1,4-dioxane was added dropwise to the solution. The reaction mixture slowly became clear and then turned yellow during the course of the addition. After 40 min, solvent was removed in vacuo and the resulting yellow residue was diluted with methanol. Silica gel (10 g) was added and the mixture evaporated to dryness. The dry powder was added to a silica gel column (190 g, 5 × 24 cm) packed in ethyl acetate. The column was washed with ethyl acetate (900 mL) and developed with MeOH/EtOAc (1:4). Appropriate fractions were combined and evaporated to give 1.22 g (4.9 mmol, 91%) of 2 as a white powder: mp 203–205 °C (lit.[23a] mp 205–206 °C dec); ^{1}H NMR (Me_2SO-d_6) δ 3.62 (m, 2, H5',5''), 4.15 (m, 2, H3',4'), 4.28 (d, $J_{2'-3'}$ = 3 Hz, 1, H2'), 5.03 (t, $J_{OH-5',5''}$ = 5.7 Hz, 1, 5'-OH), 6.26 (s, 1, H1'), 7.37 (s, 2, 6-NH_2), 8.14, 8.17 (s, s, 1, 1, H2,8). Anal. Calcd for $C_{10}H_{11}N_5O_3$ (249.2): C, 48.19; H, 4.45; N, 28.10. Found: C, 48.17; H, 4.44; N, 28.05.

9-(3-Azido-3-deoxy-β-D-arabinofuranosyl)adenosine (3). Lithium azide (1.24 g, 25.3 mmol) and 2 (1.22 g, 4.9 mmol) were dissolved in DMF (60 mL) and heated at 80 °C. The reaction was monitored by TLC (MeOH/EtOAc (1:4)) and stopped when all starting material had disappeared (~1 h). DMF was removed in vacuo and the residue taken up in boiling water (150 mL). The solution was allowed to cool and stored at 4 °C overnight. The resulting precipitate was collected and dried in vacuo over P_2O_5 to give 1.13 g (3.9 mmol, 85%) of 3 as a white powder. Recrystallization from water afforded transparent needles that were dried in vacuo over P_2O_5 at 100 °C: mp crystals darkened from 180–190 °C with no melting below 300 °C (lit.[24a] mp >340 °C); ^{1}H NMR (Me_2SO-d_6) δ 3.68 (m, 2, H5',5''), 3.78 (m, 1, H4'), 4.34 (dd, $J_{3'-2'}$ = 7.5 Hz, $J_{3'-4'}$ = 7.8 Hz, 1, H3'), 4.55 (dd, $J_{2'-1'}$ = 6 Hz, 1, H2'), 5.28 (t, $J_{OH-5',5''}$ = 5.7 Hz, 1, 5'-OH), 6.05 (d, $J_{OH-2'}$ = 5.4 Hz, 1, 2'-OH), 6.23 (d, 1, H1'), 7.28 (br s, 2, 6-NH_2), 8.13, 8.27 (s, s, 1,1, H2,8). Anal. Calcd for $C_{10}H_{12}N_8O_3$ (292.3): C, 41.10; H, 4.14; N, 38.34. Found: C, 40.98; H, 4.12; N, 38.41.

9-[3-Azido-5-*O*-(*tert*-butyldimethylsilyl)-3-deoxy-β-D-arabinofuranosyl]adenine (4). Imidazole (491 mg, 7.2 mmol) and 3 (806 mg, 2.76 mmol) were dissolved in DMF. The suspension was stirred for 5 min, after which *tert*-butyldimethylsilyl chloride (542 mg, 3.6 mmol) was added. The mixture became homogeneous after 20 min and was stirred for an additional 2.5 h. DMF was removed in vacuo and the residue taken up in 5% MeOH/$CHCl_3$ and applied to a silica gel column (160 g, 5 × 22 cm, packed in the same solvent system). The column was eluted with the same solvent system, and appropriate fractions (R_f ~0.31) were combined and evaporated to yield yellowish residue (1.03 g, 2.54 mmol, 92%). This residue was recrystallized from $CHCl_3$/hexanes to afford 4 as a fluffy, white solid (983 mg, 2.42 mmol, 87%): mp 180–182 °C; UV (MeOH) λ_{max} 212 (ε 15 000), 260 nm (ε 12 000); ^{1}H NMR ($CDCl_3$) δ 0.12, 0.13 (s, s; 3, 3, $SiCH_3$'s), 0.92 (s, 9, *tert*-butyl), 3.82 (dd, $J_{5'-4'} \cong$ 2.2 Hz, $J_{5'-5''} \cong$ 11.4 Hz, 1, H5'), 3.97 (dd, $J_{5''-4'} \cong$ 2.8 Hz, 1, H5''), 4.02 (m, 1, H4'), 4.35 (t, $J \cong$ 4.5 Hz, 1, H3'), 4.46 (m, 1, H2'), 5.08 (d, $J_{OH-2'} \cong$ 9.5 Hz, 1, 2'-OH), 5.61 (br s, 2, 6-NH_2), 6.23 (d, $J_{1-2'} \cong$ 4.2 Hz, 1, H1'), 8.18, 8.34 (s, s, 1, 1, H2,8); MS m/z 407 (43, M + H), 349 (4, M − $C(CH_3)_3$), 178 (11), 136 (100, B + 2 H). Anal. Calcd for $C_{16}H_{26}N_8O_3Si$ (406.5): C, 47.27; H, 6.45; N, 27.56. Found: C, 47.12; H, 6.49; N, 27.18.

9-[3-Azido-5-*O*-(*tert*-butyldimethylsilyl)-3-deoxy-2-*O*-(trifluoromethanesulfonyl)-β-D-arabinofuranosyl]adenine (5). A solution of 4 (966 mg, 2.35 mmol) and 4-(dimethylamino)pyridine (876 mg, 7.17 mmol) in CH_2Cl_2 (12 mL) was cooled to 0 °C. Trifluoromethanesulfonyl chloride (300 μL, 474 mg, 2.81 mmol) was added and the stirring continued for 10 min. The solution was poured into 360 mL ice-cold 1% AcOH/H_2O and extracted with CH_2Cl_2 (5 × 75 mL). The combined organic extracts were washed with saturated $NaHCO_3$/H_2O and NaCl/H_2O, and dried (Na_2SO_4). Evaporation of solvent yielded 1.26 g of a white residue (2.35 mmol, 99%). Its crystallization from $CHCl_3$/hexanes afforded 1.25 g (2.32 mmol, 97%) of 5 as a white, fluffy solid: mp 174–175 °C dec; UV (MeOH) λmax 210 (ε 17 300), 260 nm (ε 14 800); ^{1}H NMR ($CDCl_3$) δ 0.15 (s, 6, $SiCH_3$'s), 0.96 (s, 9, *tert*-butyl), 3.98 (m, 3, H4',5',5''), 4.86 (t, $J \cong$ 5.9 Hz, 1, H3'), 5.36 (t, $J \cong$ 5.4 Hz, 1, H2'), 5.62 (br s, 2, 6-NH_2), 6.46 (d, $J_{1'-2'}$

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≅ 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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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

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