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Note

Synthesis of pyrrolo[2,1-*f*][1,2,4]triazine *C*-nucleosides. Isosteres of sangivamycin, tubercidin, and toyocamycin

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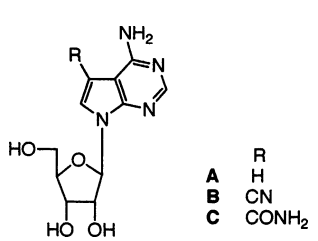
Abstract

Syntheses of pyrrolo[2,1-*f*][1,2,4]triazine *C*-nucleosides are reported. Treatment of pyranulose glycoside with aminoguanidine in acetic acid gave the corresponding semicarbazone in 96% yield. The ring transformation of the semicarbazone in dioxane afforded a 51% yield of 2-amino-7-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)pyrrolo[2,1-*f*]-[1,2,4]triazine. Vilsmeier formylation of the pyrrolotriazine gave the major product, 5-formylpyrrolo[2,1-*f*]-[1,2,4]triazine, in 69% yield. The aldehyde was treated with hydroxylamine hydrochloride in methanol to give aldoximes. Dehydration of aldoxime with trifluoromethanesulfonic anhydride and triethylamine in dichloromethane afforded 5-cyanopyrrolo[2,1-*f*][1,2,4]triazine in 44% yield. Conversion of the nitrile to the deprotected amide, 2-amino-7-(β-D-ribofuranosyl)pyrrolo[2,1-*f*][1,2,4]triazine-5-carboxamide, was accomplished in 96% yield on treatment with 30% H_2O_2 in ethanol for 1 day at room temperature. Debenzoylation with sodium hydroxide solution produced deprotected *C*-nucleosides.

Keywords: Synthesis; *C*-nucleoside; Pyranulose glycoside; Pyrrolo[2,1-*f*][1,2,4]triazine; Pyrrolo[2,1-*f*][1,2,4]triazine *C*-nucleosides; Isostere

The pyrrolo[2,3-*d*]pyrimidine (7-deazapurine) nucleoside antibiotics, tubercidin (**A**), toyocamycin (**B**), and sangivamycin (**C**), have stimulated considerable research because of their action against bacteria, mammalian cells in culture, RNA and DNA viruses, and the treatment of cutaneous neoplasms in humans.[1,2] In particular, sangivamycin (**C**) is one of the few nucleosides that has been selected for clinical studies. These findings prompted us to synthesize pyrrolo[2,1-*f*][1,2,4]triazine *C*-nucleosides **7**, **8**, and **9**, which are structurally related to **A**, **B**, and **C**. During efforts to develop a general synthetic method for *C*-nucleosides, we have prepared an extremely useful intermediate, 6-hydroxy-6-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)pyran-3(2*H*,6*H*)-one (**1**),[3] from which some ring transformations with a variety of amines have been reported.[4] We report herein, the synthesis of pyrrolo[2,1-*f*][1,2,4]triazine *C*-nucleosides from **1** (Scheme 1).



	R
A	H
B	CN
C	$CONH_2$

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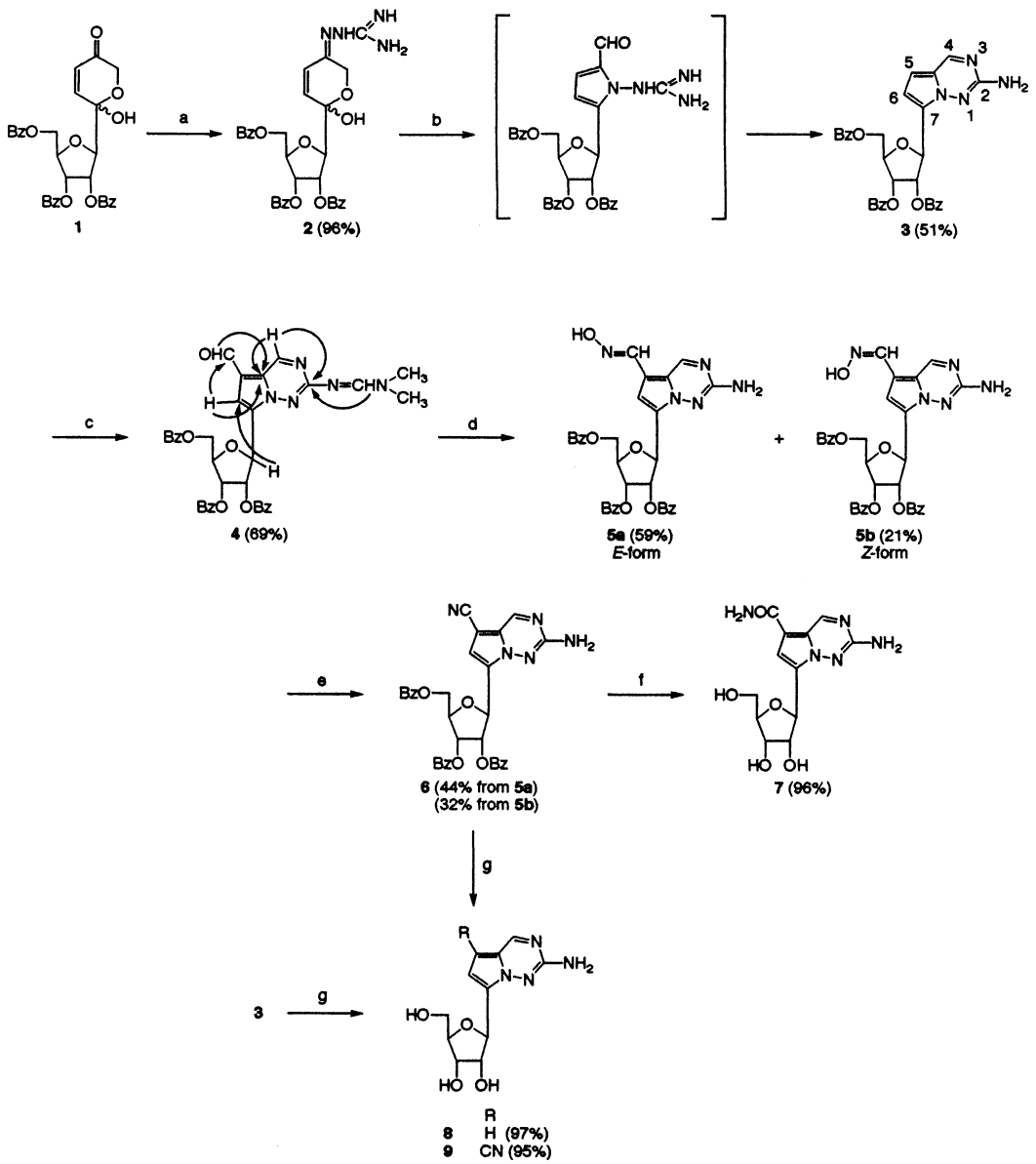
Treatment of pyranulose glycoside **1** with aminoguanidine in acetic acid at room temperature afforded the corresponding semicarbazone **2** in 96% yield. Semicarbazone **2** is an inseparable mixture of diastereoisomers (differing in configuration only at C-6). The semicarbazone **2** in dioxane was treated with concentrated hydrochloric acid at 60 °C to give a 51% yield of 2-amino-7-(2,3,5-tri-*O*-benzoyl - β - D - ribofuranosyl)pyrrolo[2,1-*f*][1,2,4]triazine (**3**) without isolation of the pyrrole - 2 - carboxaldehyde intermediate. Vilsmeier formylation of the aromatic nucleus was carried out by the dropwise addition of **3** to a solution of $POCl_3$ in *N*,*N*-dimethylformamide (DMF) at 0 °C. After the addition of **3**, the mixture was kept at 80 °C for 40 min. The major product, 2-(*N*,*N*-dimethylaminomethyleneamino)-5-formyl-7-(2,3,5-tri-*O*-benzoyl - β - D - ribofuranosyl)pyrrolo[2,1-*f*][1,2,4]triazine (**4**), was isolated by preparative thin-layer chromatography (PTLC) in 69% yield. The position of the formyl group in compound **4** was determined by a $^{1}H-^{13}C$ long-range COSY experiment. A correlation was observed between H-1′ at δ 5.95 and C-6 at δ



Scheme 1. Reagents and conditions: (a) aminoguanidine bicarbonate, AcOH, rt. (b) HCl, dioxane, 60 °C. (c) Vilsmeier reagent, DMF, 80 °C. (d) $NH_2OH{\cdot}HCl$, MeOH, reflux. (e) $(CF_3SO_2)_2O$, Et_3N, CH_2Cl_2, rt. (f) aq NH_4OH, aq H_2O_2, aq NaOH, EtOH, rt. (g) Aq NaOH. MeOH, 0 °C.

116.3. Other long-range correlations for it are shown by arrows Scheme 1. These data indicated that the formyl group was located at the 5-position.

Aldehyde **4** was treated with hydroxylamine hydrochloride in methanol at reflux for 3 h to give (*E*)- and (*Z*)-2-amino-5-hydroxyiminomethyl-7-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)pyrrolo[2,1-*f*][1,2,4]triazine (**5a**) and (**5b**) in 59 and 21% yields, respectively. The configurational assignment of the two isomers **5a** and **5b** was made based on their ^{1}H NMR spectra. The pyrrole ring proton signal of compound **5b** at δ 7.13 occurs at a lower field than that of its isomer **5a** (δ 6.80). This chemical shift difference can be attributed to the deshielding effect of the hydroxyl syn pyrrole ring.[5] Dehydration of aldoxime **5a** with trifluoromethanesulfonic anhydride[6] and triethylamine in dichloromethane at room temperature afforded 2-amino-5-cyano-7-(2,3,5-tri-*O*-benzoyl - β - D - ribofuranosyl)pyrrolo[2,1-*f*]-[1,2,4]triazine (**6**) in 44% yield. Dehydration of **5b** by the same procedure gave **6** in 32% yield. The IR spectrum of **6** contains an absorption band at 2227 cm^{-1} due to the nitrile group on the pyrrole ring. Conversion of the nitrile **6** to the deprotected amide, 2-amino-7-(β-D-ribofuranosyl)pyrrolo[2,1-*f*][1,2,4]triazine - 5 - carboxamide (**7**) was accomplished in 96% yield on treatment of **6** with basic hydrogen peroxide[7] in ethanol for 1 day at room temperature. The removal of the sugar protecting groups in compounds **3** and **6** was readily accomplished with 5% aq sodium hydroxide to afford compounds **8** and **9**. The stereochemistry of the C-1′ position in compounds **7**, **8**, and **9** was confirmed as to be β by the observation of an NOE between the C-1′ and C-4′ protons. Examination of the biological activities of compounds **7**, **8**, and **9** is now in progress.

1. Experimental

General.—Fast-atom bombardment mass spectra (FABMS) were run on a JMS-HX 110 spectrometer. The ^{1}H and ^{13}C NMR spectra were measured with a JNM-A-400 or an A-600 (JEOL) spectrometer, with tetramethylsilane as an internal standard. The IR spectrum was measured with an FTIR-230 (JASCO) spectrometer. Optical rotations were measured with a JASCO DIP-370 polarimeter (10-cm cell) at 25 °C. Analytical TLC was performed on glass plates coated with a 0.2-mm layer of Silica Gel GF_{254} (E. Merck). The compounds were detected by UV light (254 nm).

*(6*S*)- and (6*R*)-6-hydroxy-6-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)pyran-3-(2*H*,6*H*)-iminosemicarbazone* (**2**).—To a solution of **1** (1.20 g, 2.16 mmol) in AcOH (12 mL) was added aminoguanidine bicarbonate (293.8 mg, 2.159 mmol). The mixture was stirred at rt for 2 h, and then the reaction mixture was evaporated. The residue was chromatographed on a column of silica gel with 9:1 $CHCl_3$–MeOH as eluent to give 1.27 g (96%) of **2** as a pale-yellow foam. ^{1}H NMR ($CDCl_3$): δ 4.34 (d, 0.5 H, $J_{1',2'}$ 1.5 Hz, H-1′), 4.41 (d, 0.5 H, $J_{1',2'}$ 2.9 Hz, H-1′), 4.43–4.93 (m, 5 H, H-2,4′,5′), 5.63–5.91 (m, 2 H, H-2′,3′), 6.23–6.48 (m, 2 H, H-4,5), 7.27–8.02 (m, 15 H, Ph). ^{13}C NMR ($CDCl_3$): δ 64.7 (C-5′), 67.0 (C-2), 72.4, 73.0, 73.3, 79.0, 87.4 (C-1′,2′,3′,4′), 92.7 (C-6), 127.1–133.2 (C-4,5, Ph), 147.8 (C-3), 159.7 (C=NH), 165.3, 165.6, 166.3, 166.5 (C=O). FABMS (nitrobenzyl alcohol as matrix): Anal. Calcd for $C_{32}H_{31}N_4O_9$: 615.2087 [MH]. Found: *m*/*z* 615.2091 [MH]$^+$.

*2-Amino-7-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)pyrrolo[2,1-*f*][1,2,4]triazine* (**3**).—A solution of **2** (906.2 mg, 1.459 mmol) in dioxane (90 mL) containing 0.6 mL of concd HCl was heated at 60 °C for 40 min. After this time, water was added, and the reaction mixture was neutralized with satd aq $NaHCO_3$ and then extracted with $CHCl_3$ (3 × 150 mL). The extracts were combined, washed with water, dried over $MgSO_4$, and concentrated to dryness. The residual syrup was chromatographed on a column of silica gel with $CHCl_3$ as eluent. This afforded 434.4 mg (51%) of **3** as a yellow foam. ^{1}H NMR ($CDCl_3$): δ 4.63 (dd, 1 H, $J_{4',5'a}$ 4.2, $J_{5'a,5'b}$ 11.8 Hz, H-5′a), 4.70 (s, 2 H, NH_2, exchanged with D_2O), 4.76 (m, 1 H, H-4′), 4.81 (dd, 1 H, $J_{4',5'b}$ 3.7, $J_{5'a,5'b}$ 11.8 Hz, H-5′b), 5.77 (d, 1 H, $J_{1',2'}$ 5.5 Hz, H-1′), 6.12 (dd, 1 H, $J_{2',3'}$ 5.5 Hz, H-3′), 6.23 (dd, 1 H, $J_{1',2'} = J_{2',3'}$ 5.5 Hz, H-2′),

6.66 (d, 1 H, $J_{5,6}$ 4.6 Hz, H-5), 6.76 (d, 1 H, $J_{5,6}$ 4.6 Hz, H-6), 7.2–8.07 (m, 15 H, Ph), 8.63 (s, 1 H, H-4). ^{13}C NMR ($CDCl_3$): δ 64.1 (C-5′), 72.7, 73.7, 75.5, 79.4 (C-1′,2′,3′,4′), 104.7, 112.4 (C-5,6), 122.1, 126.2 (C-4a,7), 128.4–133.4 (Ph), 152.2 (C-4), 155.9 (C-2), 165.3, 165.5, 166.3 (C=O). FABMS (nitrobenzyl alcohol as matrix): Anal. Calcd for $C_{32}H_{27}N_4O_7$: 579.1895 [MH]. Found: m/z 579.1880 $[MH]^+$.

*2-(*N,N-*Dimethylaminomethyleneamino)-5-formyl-7-(2,3,5-tri-*O-*benzoyl-β-*D-*ribofuranosyl)pyrrolo[2,1-*f*][1,2,4]triazine* (**4**).—To a mixture of 0.5 mL of DMF and 1 mL of phosphorus oxychloride, which was kept at 0–5 °C for 20 min, was added 101.9 mg (0.176 mmol) of **2** in 0.8 mL of DMF under stirring at such a rate that the temperature of reaction mixture did not rise above 20 °C. After the addition of **2**, the mixture was kept at 80 °C for 40 min. The reaction mixture was poured into 30 mL of cracked ice and water and neutralized with satd aq $NaHCO_3$, and the mixture was extracted with EtOAc (3×50 mL). The extracts were combined, washed with water, dried over $MgSO_4$, and evaporated in vacuo to a brown syrup. The residue was purified by PTLC with 98.5:1.5 $CHCl_3$–MeOH as eluent. This afforded 80.2 mg (69%) of **4** as a yellow oil. ^{1}H NMR ($CDCl_3$): δ 3.13, 3.14 (each s, each 3 H, CH_3), 4.61 (dd, 1 H, $J_{4',5'a}$ 3.8, $J_{5'a,5'b}$ 12.3 Hz, H-5′a), 4.77 (m, 1 H, H-4′), 4.87 (dd, 1 H, $J_{4',5'b}$ 3.1, $J_{5'a,5'b}$ 12.3 Hz, H-5′b), 5.95 (m, 2 H, H-1′,3′), 6.21 (dd, 1 H, $J_{1',2'} = J_{2',3'}$ 5.3 Hz, H-2′), 7.25 (s, 1 H, H-6), 735–8.08 (m, 15 H, Ph), 8.65 (s, 1 H, –N=C*H*), 9.46 (s, 1 H, H-4), 9.78 (s, 1 H, C*H*O). ^{13}C NMR ($CDCl_3$): δ 35.0, 40.9 (–N–CH_3), 63.3, (C-5′), 72.0, 73.6, 74.8, 79.3 (C-1′,2′,3′,4′), 115.9 (C-5), 1163 (C-6), 122.5 (C-4a), 127.9–133.3 (C-7, Ph), 152.4 (–N=*C*H–N), 158.0 (C-4), 160.8 (C-2), 165.1, 165.3, 165.9 (C=O), 184.5 (*C*HO). FABMS (nitrobenzyl alcohol as matrix): Anal Calcd for $C_{36}H_{32}N_5O_8$: 662.2256 [MH]. Found: m/z 662.2251 $[MH]^+$.

*(*E*)- and (Z)-2-amino-5-hydroxyiminomethyl-7-(2,3,5-tri-*O-*benzoyl-β-*D-*ribofuranosyl)pyrrolo[2,1-*f*][1,2,4]triazine* (**5a**) *and* (**5b**).—To a solution of **4** (117.7 mg, 0.178 mmol) in MeOH (10 mL) was added 29.7 mg (0.427 mmol) of hydroxylamine hydrochloride. The mixture was stirred at reflux for 3 h. After this time, TLC (97:3 $CHCl_3$–MeOH) showed that the reaction mixture contained two major components (R_f 0.23 and 0.16). The mixture was allowed to cool to rt, and the solvent was evaporated. The residue was separated by PTLC with 49:1 $CHCl_3$–MeOH as eluent after two elutions.

Compound **5a**. Yellow oil; yield 65.3 mg (59%); R_f 0.23. ^{1}H NMR ($CDCl_3$): δ 4.61 (dd, 1 H, $J_{4',5'a}$ 4.0, $J_{5'a,5'b}$ 12.1 Hz, H-5′a), 4.76 (m, 1 H, H-4′), 4.79 (br, 2 H, NH_2, exchanged with D_2O), 4.86 (dd, 1 H, $J_{4',5'b}$ 3.3, $J_{5'a,5'b}$ 12.1 Hz, H-5′b), 5.72 (d, 1 H, $J_{1',2'}$ 5.4 Hz, H-1′), 6.08 (dd, 1 H, $J_{2',3'} = J_{3',4'}$ 5.4 Hz, H-3′), 6.20 (dd, 1 H, $J_{1',2'} = J_{2',3'}$ 5.4 Hz, H-2′), 6.80 (s, 1 H, H-6), 7.34–8.14 (m, 16 H, C*H*=NOH, Ph), 9.26 (s, 1 H, H-4). ^{13}C NMR ($CDCl_3$): δ 63.6 (C-5′), 72.4, 73.6, 75.4, 79.3 (C-1′,2′,3′,4′), 112.7 (C-5), 113.3 (C-6), 119.1, 126.8 (C-4a, 7), 128.4–133.4 (Ph), 143.9 (*C*H=NOH), 153.5 (C-4), 155.8 (C-2), 165.2, 165.5, 166.2 (C=O). FABMS (nitrobenzyl alcohol as matrix): Anal. Calcd for $C_{33}H_{28}N_5O_8$: 622.1934 [MH]. Found: m/z 622.1938 $[MH]^+$.

Compound **5b**. Yellow oil; yield 22.7 mg (21%); R_f 0.16. ^{1}H NMR ($CDCl_3$): δ 4.63 (dd, 1 H, $J_{4',5'a}$ 4.0, $J_{5'a,5'b}$ 12.1 Hz, H-5′a), 4.79 (m, 1 H, H-4′), 4.87 (dd, 1 H, $J_{4',5'b}$ 3.7, $J_{5'a,5'b}$ 12.1 Hz, H-5′b), 5.53 (br, 2 H, NH_2, exchanged with D2O), 5.75 (d, 1 H, $J_{1',2'}$ 53 Hz, H-1′), 6.13 (dd, 1 H, $J_{2',3'} = J_{3',4'}$ 5.3 Hz, H-3′), 6.23 (dd, 1 H, $J_{1',2'} = J_{2',3'}$ 5.3 Hz, H-2′), 7.13 (s, 1 H, H-6), 7.34–8.07 (m, 16 H, C*H*=NOH, Ph), 9.51 (s, 1 H, H-4). ^{13}C NMR ($CDCl_3$): δ 63.7 (C-5′), 72.5 (C-3′), 73.7 (C-2′), 75.7 (C-1′), 79.3 (C-4′), 110.2 (C-5), 116.0 (C-6), 120.2, 127.0 (C-4a,7), 128.4–133.4 (Ph), 138.9 (*C*H=NOH), 154.4 (C-4), 155.7 (C-2), 165.2, 165.5, 1663 (C=O). FABMS (nitrobenzyl alcohol as matrix): Anal. Calcd for $C_{33}H_{28}N_5O_8$: 622.1938 [MH]. Found: m/z 622.1938 $[MH]^+$.

*2-Amino-5-cyano-7-(2,3,5-tri-*O-*benzoyl-β-*D-*ribofuranosyl)pyrrolo[2,1-*f*][1,2,4]triazine* (**6**).—To a solution of **5a** (122.1 mg, 0.197 mmol) and triethylamine (45.2 mg, 0.447 mmol) in CH_2Cl_2 (12 mL) at 0 °C was added CH_2Cl_2 (3 mL) containing trifluoromethanesulfonic anhydride (56.4 mg, 0.200 mmol). The mixture was stirred at rt for 1 h. Water was added,

and the mixture was neutralized with satd aq $NaHCO_3$ and extracted with $CHCl_3$ (3×30 mL). The extracts were combined, washed with water, dried over $MgSO_4$, and concentrated in vacuo to a yellow oil. The residue was purified by PTLC (99:1 $CHCl_3$–MeOH) as eluent. This afforded 51.9 mg (44%) of **6** as a pale-yellow oil. IR (KBr) 2227 (CN) cm^{-1}. ^1H NMR ($CDCl_3$): δ 4.62 (dd, 1 H, $J_{4',5'a}$ 4.8, $J_{5'a,5'b}$ 12.1 Hz, H-5′a), 4.77 (m, 1 H, H-4′), 4.87 (dd, 1 H, $J_{4',5'b}$ 3.7, $J_{5'a,5'b}$ 12.1 Hz, H-5′b), 4.92 (s, 2 H, NH_2, exchanged with D_2O), 5.65 (d, 1 H, $J_{1',2'}$ 5.6 Hz, H-1′), 6.05 (dd, 1 H, $J_{2',3'} = J_{3',4'}$ 5.6 Hz, H-3′), 6.18 (dd, 1 H, $J_{1',2'} = J_{2',3'}$ 5.6 Hz, H-2′), 7.06 (s, 1 H, H-6), 7.37–8.06 (m, 15 H, Ph), 8.88 (s, 1 H, H-4). ^{13}C NMR ($CDCl_3$): δ 63.5 (C-5′), 72.3 (C-3′), 73.1 (C-2′), 75.4 (C-1′), 79.6 (C-4′), 86.5 (C-5), 113.9 (CN), 116.7 (C-6), 124.3 (C-4a), 127.2 (C-7), 128.5–133.6 (Ph), 151.4 (C-4), 156.8 (C-2), 165.1, 165.5, 166.2 (C=O). FABMS (nitrobenzyl alcohol as matrix): Anal. Calcd for $C_{33}H_{26}N_5O_7$: 604.1832 [MH]. Found: m/z 604.1824 $[MH]^+$.

*2-Amino-7-(β-*D*-ribofuranosyl)pyrrolo[2,1-*f*]-[1,2,4]triazine-5-carboxamide* (**7**).—To a solution of **6** (79.3 mg, 0.132 mmol) and 28% aq NH_4OH (2.6 mL) in EtOH (17 mL) was added dropwise 30% aq H_2O_2 (0.7 mL). The mixture was stirred at rt for 1 day, then 5% aq NaOH (1.2 mL) was added at 0 °C, and the mixture was stirred at rt for 3 h. After this time, the reaction mixture was neutralized with AcOH, and the solvents were evaporated under reduced pressure. The residue was chromatographed on a column of silica gel with 4:1 $CHCl_3$–MeOH as eluent to afford 39.2 mg (96%) of **7** as a yellow oil. The oil was recrystallized from 2-propanol–hexane to give a pale-yellow solid; mp 209–211 °C. $[\alpha]_D^{25}$ −66.5° (*c* 0.6, CH_3OH). ^1H NMR [$(CD_3)_2$SO]: δ 3.46 (dd, 1 H, $J_{4',5'a}$ 5.1, $J_{5'a,5'b}$ 11.5 Hz, H-5′a), 3.52 (dd, 1 H, $J_{4',5'a}$ 11.5 Hz, H-5′b), 3.79 (m, 1 H, H-4′), 3.95 (dd,1 H, $J_{2',3'} = J_{3',4'}$ 5.7 Hz, H-3′), 4.17 (dd, 1 H, $J_{1',2'} = J_{2',3'}$ 5.7 Hz, H-2′), 5.12 (d, 1 H, $J_{1',2'}$ 5.7 Hz, H-1′), 6.57 (s, 2 H, NH_2, exchanged with D_2O), 7.10, 7.73 (br, 1 H × 2, CONH_2, exchanged with D_2O), 7.29 (s, 1 H, H-6), 9.23 (s, 1 H, H-4). ^{13}C NMR [$(CD_3)_2$SO]: δ 62.1 (C-5′), 71.2 (C-3′), 73.8, 73.9 (C-1′,2′), 84.7 (C-4′), 110.9 (C-6), 111.8 (C-5), 120.7 (C-4a), 128.3 (C-7), 152.7 (C-4), 156.9 (C-2), 164.6 (*C*ONH_2). FABMS (nitrobenzyl alcohol as matrix): Anal. Calcd for $C_{12}H_{16}N_5O_5$: 310.1151 [MH]. Found: m/z 310.1147 $[MH]^+$. Anal. Calcd for $C_{12}H_{15}N_5O_5$: C, 46.60; H, 4.89; N, 22.64. Found: C, 46.45; H, 4.95; N, 22.40.

*2-Amino-7-(β-*D*-ribofuranosyl)pyrrolo[2,1-*f*]-[1,2,4]triazine* (**8**).—To a solution of **3** (18.0 mg, 0.031 mmol) in MeOH (2 mL) at 0 °C was added 5% aq NaOH (0.35 mL). The mixture was kept at 0 °C for 2 h. After this time, the mixture was neutralized with AcOH, and the solvent was evaporated under reduced pressure. The residue was purified by PTLC (3:1 $CHCl_3$–MeOH) as eluent to afford 8.0 mg (97%) of **8** as a yellow solid. The yellow solid was recrystallized from MeOH to a give pale-yellow solid; mp 110–112 °C. $[\alpha]_D^{25}$ −7.3° (*c* 1.8, CH_3OH). ^1H NMR (CD_3OD): δ 3.69 (dd, 1 H, $J_{4',5'a}$ 4.0, $J_{5'a,5'b}$ 11.8 Hz, H-5′a), 3.81 (dd, 1 H, $J_{4',5'b}$ 3.4, $J_{5'a,5'b}$ 11.8 Hz, H-5′b), 4.02 (m, 1 H, H-4′), 4.17 (dd, 1 H, $J_{2',3'} = J_{3',4'}$ 5.6 Hz, H-3′), 4.46 (dd, 1 H, $J_{1',2'} = J_{2',3'}$ 5.6 Hz, H-2′), 5.26 (d, 1 H, $J_{1',2'}$ 5.6 Hz, H-1′), 6.77 (s, 2 H, H-5,6), 8.65 (s, 1 H, H-4). ^{13}C NMR (CD_3OD): δ 63.7 (C-5′), 73.2, 74.9, 78.3, 86.1 (C-1′,2′,3′,4′), 106.2, 113.5 (C-5,6), 123.1, 130.2 (C-4a,7), 153.0 (C-4), 157.6 (C-2). FABMS (glycerol as matrix): Anal. Calcd for $C_{11}H_{15}N_4O_4$; 267.1093 [MH]. Found: m/z 267.1093 $[MH]^+$. Anal. Calcd for $C_{11}H_{14}N_4O_4 \cdot 0.2\ H_2O$: C, 48.96; H, 5.38; N, 20.76. Found: C, 48.86; H, 5.42; N, 20.56.

*2-Amino-5-cyano-7-(β-*D*-ribofuranosyl)-pyrrolo[2,1-*f*][1,2,4]triazine* (**9**).—The same procedure was used as for the debenzoylation of **3** with 5% aq NaOH.

Compound **9**. Yield: 95%; pale yellow solid (2-propanol–hexane); mp 196–198 °C. $[\alpha]_D^{25}$ 3.0° (*c* 0.7, CH_3OH). ^1H NMR [$(CD_3)_2$SO]: δ 3.45 (dd, 1 H, $J_{4',5'a}$ 4.4, $J_{5'a,5'b}$ 12.2 Hz, H-5′a), 3.54 (dd, 1 H, $J_{4',5'}$ 3.9, $J_{5'a,5'b}$ 12.2 Hz, H-5′b), 3.78 (m, 1 H, H-4′), 3.97, 4.19 (each dd, each 1 H, $J_{1',2'} = J_{2',3'} = J_{3',4'}$ 5.3 Hz, H-2′,3′),4.85 (br, 1 H, OH, exchanged with D_2O), 5.12 (d, 1 H, $J_{1',2'}$ 5.3 Hz, H-1′), 5.34 (br, 2 H, OH, exchanged with D_2O), 6.89 (s, 2 H, NH_2, exchanged with D_2O), 7.34 (s, 1 H, H-6), 9.06 (s, 1 H, H-4). ^{13}C NMR [$(CD_3)_2$SO]: δ 61.6 (C-5′), 70.9, 73.9, 74.0, 84.6 (C-1′,2′,3′,4′), 84.1

(C-5), 114.9 (CN), 115.6 (C-6), 123.0 (C-4a), 130.4 (C-7), 151.4 (C-4), 157.6 (C-2). FABMS (nitrobenzyl alcohol as matrix): Anal. Calcd for $C_{12}H_{14}N_5O_4$: 292.1046 [MH]. Found: m/z 292.1045 $[MH]^+$. Anal. Calcd for $C_{12}H_{13}N_5O_4$: C, 49.48; H, 4.50; N, 24.04. Found: C, 49.31; H, 4.53; N, 23.84.

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