THE 3-DEAZA AND 7-DEAZA DERIVATIVES OF 5′-AMINO-5′-DEOXY-5′-NORARISTEROMYCIN

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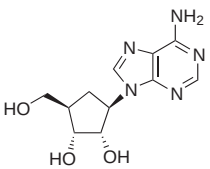
Dedicated to Professor Antonín Holý on the occasion of his 70th birthday in recognition of his outstanding contributions to the area of nucleosides and nucleic acid chemistry.

The 3-deaza and 7-deaza derivatives of 5′-amino-5′-deoxy-5′-noraristeromycin (**6** and **7**, respectively) have been prepared from the common starting material (+)-(1*R*,4*S*)-4-hydroxycyclopent-2-en-1-yl acetate (**8**). Two Pd(0)-catalyzed allylic substitution reactions afforded the desired azide intermediates, **12** and **16**, which were transformed to target compounds by standard procedures. These compounds were evaluated against a large number of viruses and found to be inactive except for weak effect against hepatitis B virus: **6**, EC_{50} 4.7 μM (3TC EC_{50} 0.056 μM); **7**, EC_{50} 4.8 μM (3TC EC_{50} 0.063 μM).

Keywords: Deazapurines; Carbanucleosides; Imidazo[4,5-*c*]pyridines; Allylic substitution; Pyrrolo[2,3-*d*]pyrimidines; Carbocyclic nucleosides; Antivirals.

From a decades long study in our laboratory to improve upon the antiviral potential of aristeromycin[1] (**1**), 5′-noraristeromycin (**2**) continues to be one of the analogs with the most promise[2]. It acts by inhibiting *S*-adenosylhomocysteine hydrolase, consistent with the parent **1**. To build upon this observation, we have considered various 4′-analogs (for example, **3** [3], **4** [4], and **5** [5]; Chart 1); this study is now being extended to varying the hetero-



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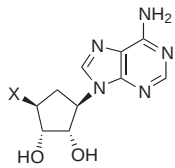
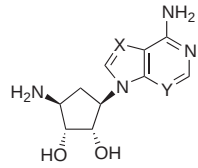


2; X=OH
3a; X=NH_2
3b; X=NHR
4; X=SH
5; X=F



6; X=N,Y=CH
7; X=CH,Y=N

CHART 1

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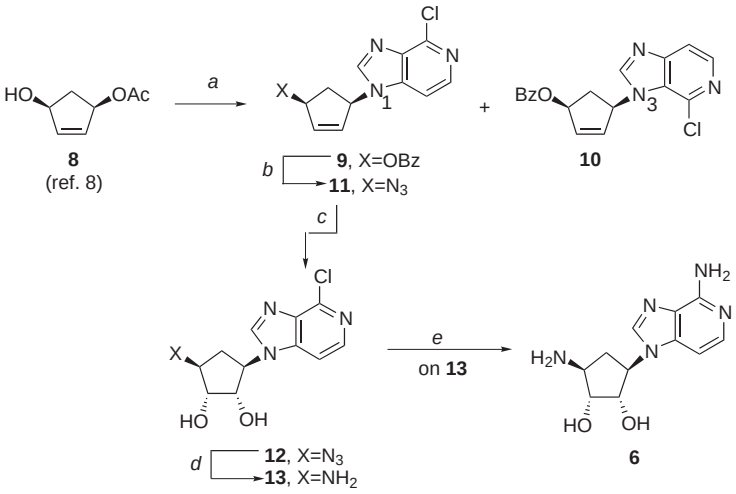
cyclic base of these C-4′ altered agents. For this purpose, the 3-deaza- and 7-deazaadenine bases were selected because of their presence in related compounds that have demonstrated inhibitory effects on the aforementioned hydrolase[6,7]. This manuscript presents the results for the 4′-amino representatives (**6** and **7**).

Chemistry

Synthesis of 5′-amino-5′-deoxy-5′-nor-3-deazaaristeromycin (**6**) commenced with the palladium (0)-catalyzed allylic substitution reaction of (+)-(1*R*,4*S*)-4-hydroxycyclopent-2-en-1-yl acetate[8] (**8**) with 4-chloro-1*H*-imidazo[4,5-*c*]-pyridine (6-chloro-3-deazapurine)[9] to afford an inseparable mixture of N-1 and N-3 coupled isomers (Scheme 1). This mixture was treated with benzoic anhydride. The desired benzoate **9** was easily separated from the N-3 compound **10** by column chromatography. The isomers were distinguished by the characteristic ^{13}C NMR peak at δ 105.8 ppm for the N-1 product (**9**) and the peak at δ 114.8 ppm for the N-3 isomer[10].

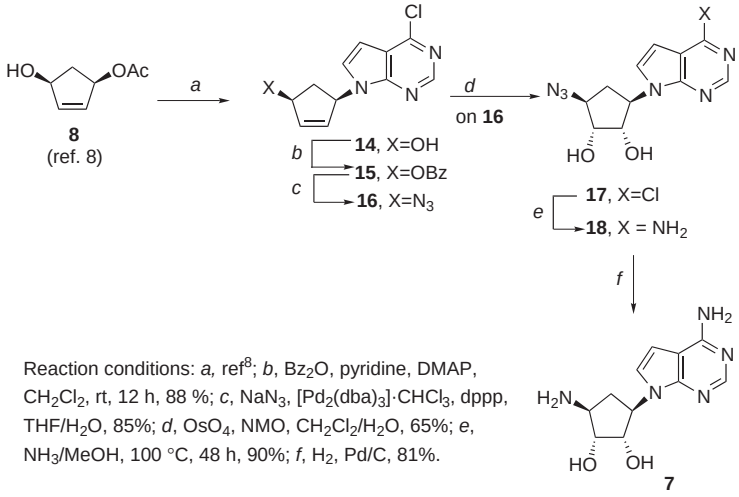


Reaction conditions: *a*, (i) 4-chloro-1*H*-imidazo[4,5-*c*]pyridine[9], [Pd(Ph$_3$P)$_4$], PPh NaH, DMF/THF; (ii) Bz$_2$O, DMAP, pyridine, CH$_2$Cl$_2$, **9** (31%, 2 steps), **10** (15% 2 steps); *b*, NaN$_3$, [Pd$_2$(dba)$_3$]·CHCl$_3$, dppp, THF/H$_2$O, 90%; *c*, OsO$_4$, NMO, CH$_2$Cl$_2$/H$_2$O, 78%; *d*, Ph$_3$P, THF/H$_2$O, 85%; *e*, (i) NH$_2$NH$_2$; (ii) Ra-Ni, H$_2$O, 70%

SCHEME 1

Subjecting **9** to another Pd(0)-catalyzed allylic substitution with sodium azide (to **11**) was followed by dihydroxylation with osmium tetroxide to provide **12** in good yield. A Staudinger reaction of **12** with triphenylphosphine cleanly provided the amino compound **13**. Conversion of **13** into **6** was accomplished by, first, reaction with hydrazine to displace the heterocyclic chloro substituent followed by Raney nickel reduction.

The synthesis of 5′-amino-5′-deoxy-5′-nor-7-deazaaristeromycin (**7**) began with **14**, which is available from **8** by our previous procedure[8] but with improved yields, by changing the solvent from DMF to THF (Scheme 2). Benzoylation of **14** with benzoic anhydride afforded **15**, which was subjected to a Pd(0)-catalyzed allylic azidation with sodium azide to give **16**. Dihydroxylation of **16** to **17** followed by standard ammonolysis (to **18**) and hydrolysis gave the desired **7**.



Reaction conditions: *a,* ref[8]; *b*, Bz_2O, pyridine, DMAP, CH_2Cl_2, rt, 12 h, 88 %; *c*, NaN_3, $[Pd_2(dba)_3]\cdot CHCl_3$, dppp, THF/$H_2O$, 85%; *d*, OsO_4, NMO, CH_2Cl_2/H_2O, 65%; *e*, NH_3/MeOH, 100 °C, 48 h, 90%; *f*, H_2, Pd/C, 81%.

SCHEME 2

Antiviral Analysis[11]

Viruses subjected to **6** and **7** were respiratory syncytial virus, herpes simplex virus 1 and 2, herpes simplex 1 TK^-, human cytomegalovirus, varicella zoster virus, vaccinia virus, cowpox virus, adenovirus type 1, Punta Toro virus, human coronavirus, yellow fever, measles, parainfluenza-3, influenza A (H1N1 and H3N2), influenza B, Venezuelan equine encephalitis, hepatitis B and C, rhinovirus type 2 and West Nile. In addition, **6** was evaluated towards vesicular stomatitis, reo, Dengue, and Coxsackie B4 viruses while **7** was screened versus monkeypox, Ebola, and pichinde viruses. The only ac-

tivity found was against hepatitis B in 2.2.15 cells and that was weak: for **6**, EC_{50} 4.7 μM (3TC EC_{50} 0.056 μM) and for **7**, EC_{50} 4.8 μM (3TC EC_{50} 0.063 μM). The parent amino derivative **3a** was devoid of effects versus HBV [3a].

Among the host cells for the assays, only weak to moderate cytotoxicity was seen for **6** towards CV-1, HeLa Ohio-1, HEL and Huh 7 cells and for **7** towards MA-104. No other cytotoxicity was observed.

EXPERIMENTAL

General Methods

Melting points were recorded on a Meltemp II melting point apparatus and the values were uncorrected. The combustion analysis was performed at Atlantic Microlab, Norcross, GA. ^{1}H and ^{13}C NMR spectra (δ, ppm; *J*, Hz) were recorded on either a Bruker AC 250 spectrometer (250 MHz for ^{1}H and 62.9 MHz for ^{13}C) or Bruker AV 400 spectrometer (400 MHz for ^{1}H and 100 MHz for ^{13}C), all referenced to internal tetramethylsilane (TMS) at 0.0 ppm. The reactions were monitored by thin-layer chromatography (TLC) using 0.25 mm Whatman Diamond silica gel 60-F_{254} precoated plates with visualization by irradiation with a Mineralight UVGL-25 lamp. Column chromatography was performed on Whatman silica, 230–400 mesh, 60 Å and elution with the indicated solvent system. Yields refer to chromatographically and spectroscopically (^{1}H and ^{13}C NMR) homogeneous materials.

(1*S*,4*R*)-4-(4-Chloro-1*H*-imidazo[4,5-*c*]pyridin-1-yl)cyclopent-2-en-1-yl Benzoate (**9**) and (1*S*,4*R*)-4-(4-Chloro-1*H*-imidazo[4,5-*c*]pyridin-3-yl)cyclopent-2-en-1-yl Benzoate (**10**)

To a solution of 4-chloro-1*H*-imidazo[4,5-*c*]pyridine (6-chloro-3-deazapurine)[9] (10.0 g, 64.0 mmol) in dry DMF (90 ml) was added NaH (1.75 g, 69.0 mmol). The reaction mixture was stirred at room temperature for 3 h, followed by the addition of tetrakis(triphenylphosphine)palladium (3.70 g, 3.20 mmol), triphenylphosphine (2.50 g, 9.50 mmol) and a solution of (+)-(1*R*,4*S*)-4-hydroxycyclopent-2-en-1-yl acetate[8] (**8**; 11.0 g, 77.5 mmol) in dry THF (90 ml). This mixture was stirred at 55 °C for 24 h. The solvent was removed and the residue purified by column chromatography (CH_2Cl_2/EtOAc, 3:1) to afford a mixture (14.01 g) of 4-chloro-1*H*-imidazo[4,5-*c*]pyridine and N-1 and N-3 coupled products as indicated by NMR analysis[10]. This mixture was used directly in the next step.

The above mixture was dissolved in CH_2Cl_2 (200 ml) containing pyridine (7.0 ml, 89 mmol) and 4-(dimethylamino)pyridine (200 mg, 1.65 mmol). To this solution was added Bz_2O (13.50 g, 59.73 mmol), and this mixture was stirred at room temperature overnight. The solvent was removed and the residue purified by column chromatography (CH_2Cl_2/EtOAc, 3:1) to afford **9** (6.70 g, 31%) and **10** (3.26 g, 15%) in yields based on 4-chloro-1*H*-imidazo[4,5-*c*]-pyridine (6-chloro-3-deazapurine).

Compound **9** (white solid); m.p. 140–141 °C. ^{1}H NMR (250 MHz, $CDCl_3$): 8.17 (s, 1 H); 8.15 (d, *J* = 5.5, 1 H); 8.00 (m, 2 H); 7.55 (m, 4 H); 6.53 (m, 1 H); 6.31 (m, 1 H); 6.00 (m, 1 H); 5.57 (m, 1 H); 3.29 (ddd, *J* = 15.3, 8.1, 8.1, 1 H); 2.17 (dt, *J* = 15.2, 3.7, 1 H). ^{13}C NMR (62.9 MHz, $CDCl_3$): 165.7, 143.2, 142.8, 141.2, 139.1, 138.1, 136.1, 133.5, 133.3, 129.4,

128.5, 105.8[10], 76.7, 60.2, 59.8, 38.1. For $C_{18}H_{14}ClN_3O_2$ (339.8) calculated: 63.63% C, 4.15% H, 12.37% N; found: 63.63% C, 4.14% H, 12.45% N.

Compound **10** (colorless oil). ^{1}H NMR (250 MHz, $CDCl_3$): 8.21 (s, 1 H); 8.20 (d, *J* = 5.6, 1 H); 7.93 (m, 2 H); 7.65 (d, *J* = 5.6, 1 H); 7.57 (m, 1 H); 7.51 (m, 2 H); 6.57 (ddd, *J* = 7.5, 2.0, 2.0, 1 H); 6.39 (dd, *J* = 5.6, 2.2, 1 H); 6.23 (dd, *J* = 5.6, 2.3, 1.0, 1 H); 6.00 (ddd, *J* = 9.8, 2.5, 2.5, 1 H); 3.29 (ddd, *J* = 15.4, 8.3, 7.8, 7.8, 1 H); 2.09 (dt, *J* = 15.3, 3.1, 1 H). ^{13}C NMR (62.9 MHz, $CDCl_3$): 165.7, 151.2, 150.5, 144.4, 140.9, 136.3, 133.3, 133.2, 133.0, 129.2, 128.2, 127.6, 114.8[10], 76.5, 59.6, 40.1. For $C_{18}H_{14}ClN_3O_2$ (339.8) calculated: 63.63% C, 4.15% H, 12.37% N; found: 63.26% C, 4.34% H, 11.98% N.

1-[(1*R*,4*S*)-4-Azidocyclopent-2-en-1-yl]-4-chloro-1*H*-imidazo[4,5-*c*]pyridine (**11**)

To a solution of benzoate **9** (0.65 g, 1.91 mmol) in THF (15 ml) was added $[Pd_2(dba)_3]\cdot CHCl_3$ (80 mg, 0.078 mmol) and 1,3-diphenylphosphinepropane (dppp) (0.13 g, 0.32 mmol). After the mixture was stirred for 30 min (color changed from deep-red to yellow), a solution of NaN_3 (0.32 g, 4.9 mmol) in H_2O (4 ml) was added. The reaction was stirred at room temperature under N_2 for 4 h. The resulting solid was removed by filtration and the filtrate was separated. The aqueous layer was extracted with CH_2Cl_2 (2 × 30 ml). The combined organic phases were dried (anhydrous $MgSO_4$) and concentrated. The residue was purified by column chromatography (EtOAc/hexanes, 1:2) to afford **11** (0.45 g, 85%) as a foam; m.p. 68–70 °C. ^{1}H NMR (250 MHz, $CDCl_3$): 8.15 (d, *J* = 5.6, 1 H); 8.06 (s, 1 H); 7.41 (d, *J* = 5.6, 1 H); 6.35 (m, 1 H); 6.20 (m, 1 H); 5.51 (m, 1 H); 4.70 (m, 1 H); 3.15 (ddd, *J* = 14.9, 8.1, 8.1, 1 H); 2.00 (ddd, *J* = 14.8, 3.8, 3.8, 1 H). ^{13}C NMR (62.9 MHz, $CDCl_3$): 143.2, 142.8, 141.3, 139.1, 138.2, 135.9, 132.4, 105.9, 65.0, 60.3, 38.0. For $C_{11}H_9ClN_6\cdot 0.18$EtOAc (276.6) calculated: 50.90% C, 3.77% H, 30.81% N; found: 51.29% C, 3.55% H, 30.81% N.

(1*S*,2*R*,3*S*,5*R*)-3-Azido-5-(4-chloro-1*H*-imidazo[4,5-*c*]pyridin-1-yl)-cyclopentane-1,2-diol (**12**)

N-Methylmorpholine oxide (2.13 g, 18.2 mmol) was added to a solution of **11** (2.53 g, 9.15 mmol) in CH_2Cl_2 (50 ml) containing a small amount of H_2O (0.8 ml). After the solution was cooled to 0 °C, a catalytic amount of solid osmium tetroxide (90 mg, 0.36 mmol) was added and the solution stirred at room temperature for 12 h. The reaction mixture was quenched by addition of $NaHSO_3$. The solvent was removed and the residue purified by flash column chromatography (EtOAc) to afford **12** as a white solid (2.22 g, 78%); m.p. 95–96 °C. ^{1}H NMR (400 MHz, DMSO-d_6): 8.54 (s, 1 H); 8.10 (d, *J* = 5.5, 1 H); 7.70 (d, *J* = 5.5, 1 H); 5.43 (d, *J* = 4.8, 1 H, OH); 5.31 (d, *J* = 6.4, 1 H, OH); 4.69 (q, *J* = 8.3, 1 H); 4.20 (q, *J* = 7.3, 1 H); 3.95 (m, 2 H); 2.63 (m, 1 H); 1.90 (m, 1 H). ^{13}C NMR (100 MHz, DMSO-d_6): 145.0, 141.1, 140.8, 140.0, 137.3, 107.1, 74.5, 74.3, 63.9, 60.0, 31.7. For $C_{11}H_{11}ClN_6O_2\cdot 0.2H_2O$ (298.3) calculated: 44.25% C, 3.82% H, 28.16% N; found: 44.33% C, 3.82% H, 27.90% N.

(1*S*,2*R*,3*S*,5*R*)-3-Amino-5-(4-chloro-1*H*-imidazo[4,5-*c*]pyridin-1-yl)-cyclopentane-1,2-diol (**13**)

Triphenylphosphine (1.50 g, 5.72 mmol) was added to a solution of **12** (1.47 g, 4.99 mmol) in THF (10 ml) and H_2O (10 ml). After the reaction mixture was brought to reflux for 6 h, the volatiles were removed under reduced pressure. The residue was purified by column chromatography (EtOAc/MeOH/NH_4OH, 9:3:1) to afford **13** as a pale yellow foam (1.14 g,

85%). ^{1}H NMR (250 MHz, DMSO-d_6): 8.59 (s, 1 H); 8.15 (d, *J* = 5.6, 1 H); 7.98 (d, *J* = 5.6, 1 H); 4.71 (dd, *J* = 8.6, 17.7, 1 H); 4.47 (dd, *J* = 4.8, 8.4, 1 H); 3.68 (m, 1 H); 3.23 (m, 1 H); 2.57 (m, 1 H); 1.73 (m, 1 H). ^{13}C NMR (62.9 MHz, DMSO-d_6): 145.5, 141.0, 140.4, 139.9, 137.5, 107.5, 77.2, 75.6, 60.9, 55.3, 35.2. For $C_{11}H_{13}ClN_4O_2$ (284.7) calculated: 49.17% C, 4.88% H, 20.85% N; found: 49.12% C, 4.80% H, 20.52% N.

(1*S*,2*R*,3*S*,5*R*)-3-Amino-5-(4-amino-1*H*-imidazo[4,5-*c*]pyridin-1-yl)-cyclopentane-1,2-diol (**6**)

A solution of **13** (0.54 g, 2.0 mmol) in hydrazine (20 ml) was brought to reflux for 4 h. After cooling to room temperature, the solution was concentrated. The residue was dissolved in distilled H_2O (40 ml) and freshly prepared Raney Ni W2 (prepared from 30 g of alloy) was added. The reaction mixture was heated to reflux for 1 h. The hot reaction mixture was filtered and washed with hot H_2O (3 × 10 ml). The combined filtrates were evaporated to dryness. The residue was purified via column chromatography (EtOAc/MeOH/NH_4OH, 7:3:1) to afford **6** as white solid (0.35 g, 70%); m.p. 221–222 °C. ^{1}H NMR (250 MHz, DMSO-d_6): 8.21 (s, 1 H); 7.65 (d, *J* = 5.8, 1 H); 6.97 (d, *J* = 5.8, 1 H); 6.17 (br, 2 H); 4.60 (dd, *J* = 8.9, 17.6, 1 H); 4.46 (dd, *J* = 5.3, 8.0, 1 H); 3.87 (m, 1 H); 3.32 (m, 1 H); 2.57 (m, 1 H); 1.88 (m, 1 H). ^{13}C NMR (62.9 MHz, DMSO-d_6): 152.4, 140.6, 140.0, 138.0, 127.0, 97.3, 74.8, 74.2, 59.7, 54.3, 32.8. For $C_{11}H_{15}N_5O_2 \cdot 0.8H_2O$ (263.67) calculated: 50.11% C, 6.30% H, 26.58% N; found: 50.13% C, 6.42% H, 26.29% N.

(1*S*,4*R*)-4-(4-Chloro-7*H*-pyrrolo[2,3-*d*]pyrimidin-7-yl)cyclopent-2-en-1-yl Benzoate (**15**)

To a solution of **14**[8] (1.59 g, 6.77 mmol), pyridine (0.82 ml, 10 mmol) and DMAP (40 mg, 0.33 mmol) in CH_2Cl_2 (50 ml) was added benzoic anhydride (1.55 g, 6.86 mmol). After the reaction mixture was stirred at room temperature for 12 h, the solvent was removed under reduced pressure and the residue purified by column chromatography (EtOAc/hexanes, 1:3) to afford **15** (2.02 g, 88%) as a white solid; m.p. 74–75 °C. ^{1}H NMR (400 MHz, $CDCl_3$): 8.66 (s, 1 H); 8.05 (m, 2 H); 7.60 (m, 1 H); 7.47 (m, 2 H); 7.39 (d, *J* = 3.8, 1 H); 6.65 (d, *J* = 3.8, 1 H); 6.44 (dt, *J* = 5.6, 2.0, 1 H); 6.19 (ddd, *J* = 5.6, 2.3, 1.0, 1 H); 6.06 (m, 1 H); 5.99 (m, 1 H); 3.21 (ddd, *J* = 15.9, 8.3, 7.6, 1 H); 2.02 (dt, *J* =15.3, 3.3, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): 166.4, 152.6, 151.1, 151.1, 135.6, 135.4, 133.7, 130.2, 130.0, 128.9, 126.8, 118.2, 100.8, 78.2, 57.7, 39.0. For $C_{18}H_{14}ClN_3O_2$ (339.8) calculated: 63.63% C, 4.15% H, 12.37% N; found: 63.45% C, 4.09% H, 12.37% N.

7-[(1*R*,4*S*)-(4-Azidocyclopent-2-en-1-yl)]-4-chloro-7*H*-pyrrolo[2,3-*d*]pyrimidine (**16**)

To a solution of **15** (1.70 g, 5.00 mmol) in THF (40 ml) was added $[Pd_2(dba)_3] \cdot CHCl_3$ (0.20 g, 0.19 mmol) and dppp (0.32 g, 0.78 mmol). After the mixture was stirred for 30 min (color changed from deep-red to yellow), a solution of NaN_3 (0.90 g, 15 mmol) in H_2O (12 ml) was added. The reaction mixture was stirred at room temperature under N_2 for 8 h. The resulting solid was removed by filtration and the filtrate recovered and extracted with EtOAc (2 × 50 ml). The combined organic phases were dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (EtOAc) to give **16** as a colorless oil (1.10 g, 85%). ^{1}H NMR (400 MHz, $CDCl_3$): 8.67 (s, 1 H); 7.35 (d, *J* = 3.7, 1 H); 6.67 (d, *J* = 3.7, 1 H); 6.27 (m, 1 H); 6.13 (m, 1 H); 5.01 (m, 1 H); 4.63 (m, 1 H); 3.12 (ddd, *J* = 15.7, 8.2, 7.7, 1 H); 1.88 (dt, *J* = 15.2, 3.2, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$): 152.4, 150.8, 150.1, 134.8, 134.2, 126.6,

118.0, 100.6, 65.2, 57.9, 38.5. For $C_{11}H_9ClN_6$ (260.7) calculated: 50.68% C, 3.48% H, 32.24% N; found: 50.78% C, 3.56% H, 32.02% N.

(1*S*,2*R*,3*S*,5*R*)-3-Azido-5-(4-chloro-7*H*-pyrrolo[2,3-*d*]pyrimidin-7-yl)-cyclopentane-1,2-diol (**17**)

N-Methylmorpholine oxide (0.99 g, 8.5 mmol) was added to a solution of **16** (1.10 g, 4.23 mmol) in CH_2Cl_2 (20 ml) containing a small amount of H_2O (0.8 ml). After the solution was cooled to 0 °C, a catalytic amount of solid osmium tetroxide (40 mg, 0.16 mmol) was added and the solution stirred at room temperature for 8 h. The reaction was quenched by addition of $NaHSO_3$. The solvent was removed and the residue purified by flash column chromatography (EtOAc/hexanes, 3:1) to afford **17** as a white solid (0.81 g, 65%); m.p. 73–74 °C. ^{1}H NMR (400 MHz, DMSO-d_6): 8.63 (s, 1 H); 7.89 (d, *J* = 3.7, 1 H); 7.70 (d, *J* = 3.7, 1 H); 5.37 (d, *J* = 5.2, 1 H); 5.20 (d, *J* = 6.1, 1 H); 4.99 (dq, *J* = 1.8, 9.0, 1 H); 4.28 (q, *J* = 6.9, 1 H); 3.97 (m, 2 H); 2.57 (m, 1 H); 1.90 (m, 1 H). ^{13}C NMR (100 MHz, DMSO-d_6): 150.8, 150.6, 150.1, 129.7, 117.1, 99.0, 74.6, 74.3, 63.8, 59.0, 32.1. For $C_{11}H_{11}ClN_6O_2 \cdot 0.1$EtOAc (303.5) calculated: 45.07% C, 3.89% H, 27.68% N; found: 45.39% C, 3.87% H, 27.51% N.

(1*R*,2*S*,3*R*,5*S*)-3-(4-Amino-7*H*-pyrrolo[2,3-*d*]pyrimidin-7-yl)-5-azidocyclopentane-1,2-diol (**18**)

Compound **17** (0.80 g, 2.7 mmol) was dissolved in saturated methanolic ammonia solution (40 ml) in a stainless steel pressure vessel and this sealed and heated at 100 °C for 48 h. After cooling to 0 °C, the reaction vessel was opened and NH_3 and MeOH removed to dryness. Column chromatography (EtOAc/MeOH, 6:1) of the residue afforded **18** as a white solid (0.68 g, 90%); m.p. 149–151 °C. ^{1}H NMR (400 MHz, DMSO-d_6): 8.04 (s, 1 H); 7.23 (d, *J* = 3.5, 1 H); 6.98 (br, 2 H); 6.56 (d, *J* = 3.5, 1 H); 5.28 (d, *J* = 5.3, 1 H); 5.13 (br, 1 H); 4.81 (dq, *J* = 2.5, 8.9, 1 H); 4.19 (m, 1 H); 4.00 (q, *J* = 5.1, 1 H); 3.91 (dq, *J* = 2.2, 7.6, 1 H); 2.48 (m, 1 H); 1.79 (m, 1 H). ^{13}C NMR (100 MHz, DMSO-d_6): 158.2, 152.1, 150.6, 123.2, 103.6, 99.9, 75.8, 75.3, 64.8, 59.2, 33.3. For $C_{11}H_{13}N_7O_2 \cdot 0.7H_2O$ (287.9) calculated: 45.85% C, 5.00% H, 34.04% N; found: 45.91% C, 4.84% H, 33.97% N.

(1*S*,2*R*,3*S*,5*R*)-3-Amino-5-(4-amino-7*H*-pyrrolo[2,3-*d*]pyrimidin-7-yl)-cyclopentane-1,2-diol (**7**)

To a solution of **18** (0.68 g, 2.5 mmol) in MeOH (50 ml) was added Pd/C (0.21 g), and the mixture placed under 40 psi of H_2 and shaken for 12 h. The mixture was filtered through a Celite pad and the filtrate was evaporated under reduced pressure. The residue was then purified via column chromatography (EtOAc/MeOH/NH_4OH, 7:3:1) to afford **7** as a white solid (0.56 g, 90%); m.p. > 184 °C (dec). ^{1}H NMR (400 MHz, DMSO-d_6): 8.03 (s, 1 H); 7.28 (d, *J* = 3.3, 1 H); 6.93 (br, 2 H); 6.55 (d, *J* = 3.3, 1 H); 4.83 (dd, *J* = 16.9, 8.3, 1 H); 4.36 (dd, *J* = 7.1, 5.3, 1 H); 3.67 (t, *J* = 4.0, 1 H); 3.13 (m, 1 H); 2.42 (dt, *J* = 8.1, 13.1, 1 H); 1.50 (ddd, *J* = 6.1, 8.3, 14.1, 1 H). ^{13}C NMR (100 MHz, DMSO-d_6): 158.3, 152.1, 150.7, 123.2, 103.6, 99.5, 78.6, 76.2, 59.4, 56.2, 37.4. For $C_{11}H_{15}N_5O_2 \cdot 0.3H_2O$ (254.7) calculated: 51.83% C, 6.13% H, 27.49% N; found: 51.96% C, 6.09% H, 27.31% N.

Antiviral Assays

The antiviral and toxicity analyses were performed following standard procedures reported previously by us[11].

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