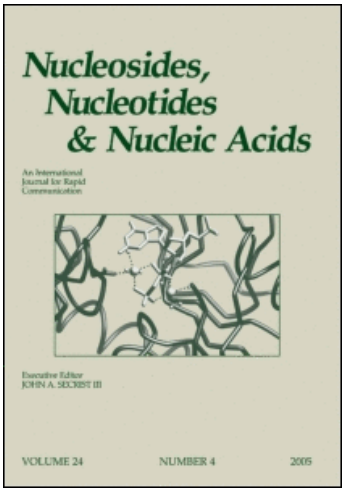

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Synthesis of 2-(3′-Azido- and 3′-Amino-3′-deoxy-β-D-ribofuranosyl)thiazole-4-carboxamide

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ABSTRACT

In view of biological activities of tiazofurin and azido or aminosugar nucleosides, novel azido- and amino-substituted tiazofurin derivatives (**1** and **2**) were efficiently synthesized starting from 1,2;5,6-di-*O*-isopropylidene-D-glucose.

Key Words: IMPDH inhibitor; Amino sugar; Anticancer nucleosides.

INTRODUCTION

Inosine 5′-monophosphate dehydrogenase (IMPDH) is a critical enzyme in the regulation of cell proliferation and differentiation. This enzyme catalyzes the NAD^+-dependent oxidation of inosine 5′-monophosphate (IMP) to xanthine 5′-monophosphate (XMP), the rate limiting step in de novo biosynthesis of guanine nucleotides. Therefore, the biochemical effect of IMPDH inhibition in sensitive cell types is decrease in intracellular guanine nucleotide levels,[1] and the decrease in cellular GTP and deoxy GTP pool levels blocks DNA and RNA synthesis in rapidly

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proliferating tumor cells. Because of its critical role in purine biosynthesis, IMPDH is a drug design target for anticancer, antiviral, immunosuppressive and antimicrobial chemotherapy.[2]

Several compounds have been described as IMPDH inhibitors and among them, tiazofurin, 2-β-D-ribofuranosylthiazole-4-carboxamide, is a C-nucleoside with potent inhibitory activity against IMPDH[3] currently undergoing clinical trials as an antitumor agent.[4] This oncolytic C-nucleoside is converted to the nicotinamide adenine dinucleotide (NAD) analogue, thiazole-4-carboxamide adenine dinucleotide (TAD), which binds to the NAD cofactor-binding site of the enzyme and inhibits IMPDH activity.[5] Recently, several analogues of tiazofurin have been synthesized and are shown in Fig. 1.

It was reported that aminosugar nucleosides possess antiviral and anticancer activities[6,7] and 3′-azido-3′-deoxythymidine was converted to 3′-amino-3′-deoxythymidine in some cells.[8] One of the most important examples is puromycin,[9] a derivative of 3′-amino-3′-deoxyadenosine.

Based upon these findings, it was of interest to put an azido or amino group at the C-3′ position of tiazofurin in order to compare biological activities with the normal ribonucleoside. An amino group serves as a bioisostere of a hydroxyl group and 2′-hydroxyl substituted 3′-aminonucleosides apparently have a higher population of N-type nucleoside conformations.[10] Here, we report the synthesis of the azido- and amino-substituted tiazofurin derivatives (**1** and **2**), starting from 1,2;5,6-di-*O*-isopropylidene-D-glucose.

RESULTS AND DISCUSSION

Our synthetic strategy to the target nucleosides is to synthesize ribofuranosyl cyanide as a key intermediate from 1,2;5,6-di-*O*-isopropylidene-D-glucose (**3**) then to cyclocondense with L-cysteine ethyl ester hydrochloride.

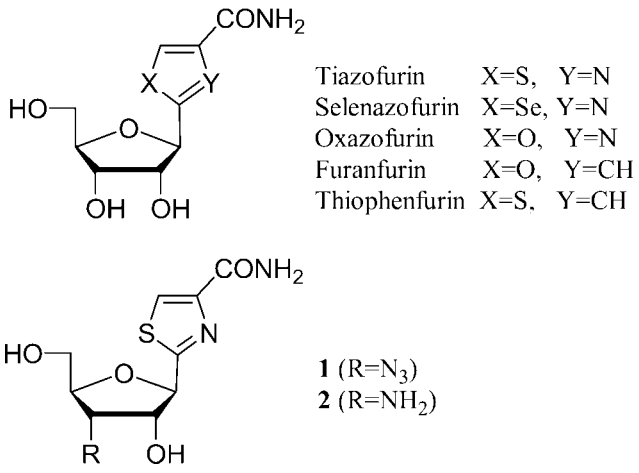

Figure 1. Rationale to the design of the target nucleosides.

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Starting from commercially available diacetone-D-glucose (**3**), the hydroxyl group of **3** was converted to a triflate using trifluoromethanesulfonic anhydride. Triflate **4** was used in next step without purification and reacted with sodium azide in DMF to afford the desired azido sugar **5a** (44%) and the eliminated enose derivative **5b** (32%), respectively. The ratio of **5a** and **5b** was dependent on the reagent, the reaction temperature and the solvent used.[11] The reaction mixture could not be heated due to an undesired elimination reaction and when the tosylate of **3** was reacted with sodium azide in presence of 18-crown-6 in DMF, the yield was very poor. The 5,6-*O*-isopropylidene of **5a** was selectively removed using 75% acetic acid to give the diol **6**. Oxidative cleavage of **6** with sodium periodate followed by reduction of the resulting aldehyde with sodium borohydride yielded the ribofuranose **7**, which was treated with benzoyl chloride to afford the benzoate **8**. It was reported that the reaction of 1,2,3,5-tetra-*O*-acetyl-β-D-ribofuranose with cyanotrimethylsilane in the presence of BF_3 OEt_2 gave 3,5-di-*O*-acetyl-1,2-*O*-(1-endo-cyanoethylidene)-α-D-ribofuranose.[12] Therefore, to synthesize 1-*O*-acetyl-2-*O*-benzoyl derivative, methylglycoside **9** was prepared from the benzoate **8** by acid-catalyzed methanolysis[13] of **8**. Benzoylation of **9** afforded the dibenzoate **10**, which was treated with $Ac_2O/AcOH/H_2SO_4$ to give 1-*O*-acetyl-3-azido-2,5-di-*O*-benzoylribofuranose (**11**). 3-Azido-2,5-di-*O*-benzoyl-β-D-ribofuranosyl cyanide (**12**), a key intermediate, was prepared by reaction of the corresponding acetate **11** with cyanotrimethylsilane and stannic chloride in dichloromethane[14] (Sch. 1).

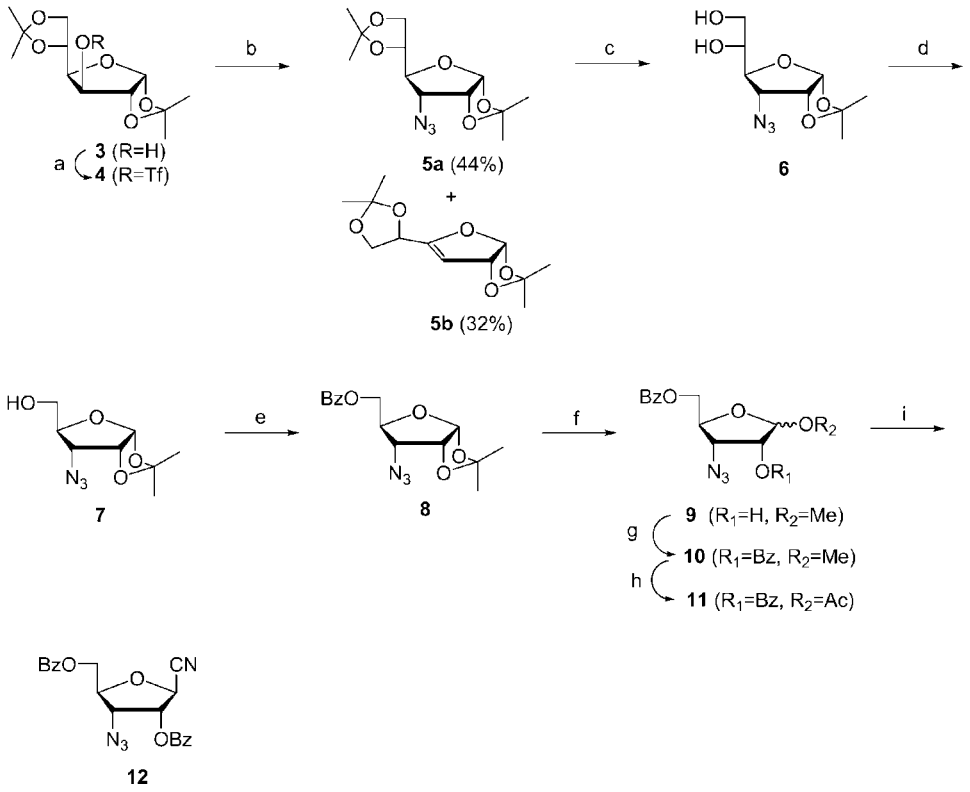
Thiazoline **13** was obtained from cyanide **12** by treatment with L-cysteine ethyl ester hydrochloride in presence of triethylamine according to a previous report[15] and dehydrogenated by treatment with bromotrichloromethane in combination with DBU[16] at 0°C to give the thiazole **14**. ^{1}H NMR spectrum of **14** showed the presence of vinyl proton of the thiazole ring. Ester aminolysis and debenzoylation using methanolic ammonia[17] afforded 3′-azido-substituted tiazofurin derivative **1** in high yield. Catalytic hydrogenation of **1** gave 3′-amino-3′-deoxytiazofurin (**2**) (Sch. 2).

The final nucleosides **1** and **2** were assayed against several viruses such as HIV-1, HSV-1, HSV-2 and HBV. These compounds were found to be inactive against all viruses tested up to 100 μg/Mℓ. Compound **1** and **2** have been evaluated in vitro for their ability to inhibit the growth of Human 143B Osteosarcoma tumor cells, but found to be completely inactive.

In summary, we have successively synthesized the novel 3′-azido- and 3′-amino-3′-deoxytiazofurin (**1** and **2**) by cyclocondensation of glycosyl cyanide and L-cysteine ethyl ester hydrochloride, followed by dehydrogenation, but the final nucleosides did not exhibit any significant biological activity.

EXPERIMENTAL

General Methods. NMR spectra were recorded in a 300 MHz apparatus using tetramethylsilane (TMS) as an internal standard, and the chemical shifts are reported in ppm (δ). Coupling constants are reported in hertz (Hz). Infrared spectra were recorded in a Perkin-Elmer 1710 FTIR spectrophotometer. Mass spectra recorded by FAB (Fast atom bombardment) on a VG Tro-2, GC-MS. TLC were carried



Scheme 1. *Reagents and conditions*: (a) Tf_2O, pyridine, CH_2Cl_2, 0°C, 1 h; (b) NaN_3, DMF, RT, 16 h, 5a(44%), 5b(32%); (c) 75% AcOH, 55°C, 1.5 h, 90%; (d) 1: $NaIO_4$, EtOH, 0°C, 0.5 h; 2: $NaBH_4$, 0°C, 2 h, 84%; (e) BzCl, pyridine, RT, 3 h, 95%; (f) 1% HCl in MeOH, RT, 2 h, 80%; (g) BzCl, pyridine, RT, 3 h, 97%; (h) AcOH, Ac_2O, c-H_2SO_4, RT, 30 min, 98%; (i) TMSCN, $SnCl_4$, CH_2Cl_2, 70°C, 3 h, 63%.

out on Merck silica gel 60 F_{254} precoated plates, and silica gel column chromatography was performed on silica gel 60, 230 ~ 400 mesh, Merck. All anhydrous solvents were distilled over CaH_2 or Na/benzophenone prior to use.

3-Azido-3-deoxy-1,2;5,6-di-*O*-isopropylidene-α-D-allofuranose (5a) and 3-Deoxy-1,2;5,6-di-*O*-isopropylidene-α-D-erythro-hex-3-enofuranose (5b). Trifluoro-methanesulfonic anhydride (2.9 mL, 17.24 mmol) was added dropwise to a solution of 1,2;5,6-di-*O*-isopropylidene-α-D-glucose (3 g, 11.53 mmol) and pyridine (2.8 mL, 34.62 mmol) in dichloromethane (30 mL) at 0°C. The reaction mixture was stirred for 1 h at 0°C and extracted with dichloromethane and water. The organic layer was washed with brine, dried ($MgSO_4$), filtered and concentrated to give **4**.

The triflate **4** was dissolved in anhydrous DMF (20 mL) and treated with sodium azide (2.25 g, 34.61 mmol). The reaction mixture was stirred for 16 h at room temperature. Ethyl acetate and water were added and aqueous phase was extracted with

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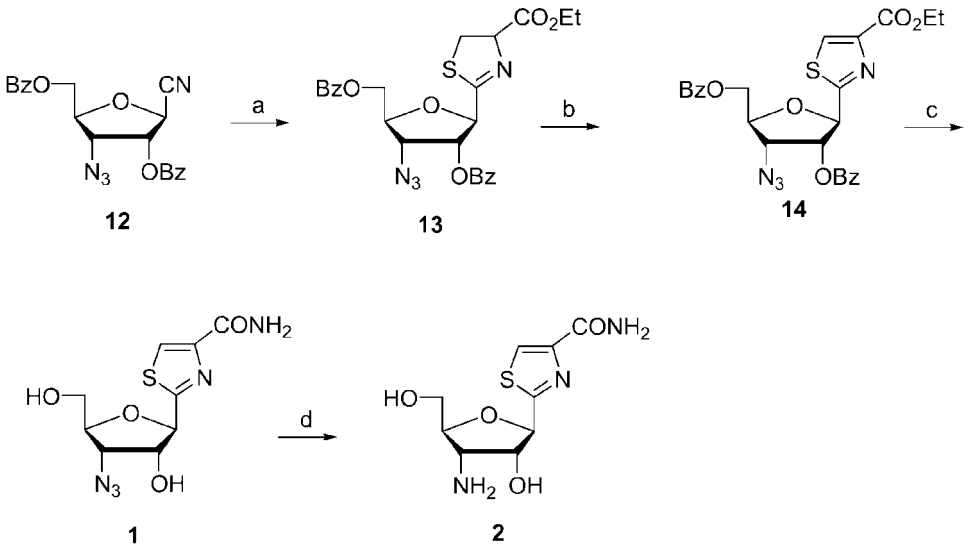

Scheme 2. *Reagents and conditions*: (a) L-cysteine ethyl ester hydrochloride, Et_3N, MeOH, RT, 2 h, 75%; (b) DBU, $BrCCl_3$, CH_2Cl_2, 0°C, 16 h, 88%; (c) NH_3/MeOH, RT, 24 h, 92%; (d) H_2.Pd/C, EtOH, RT, 14 h, 90%.

ethyl acetate (×3). The combined organic layers were washed with brine, dried ($MgSO_4$), filtered and evaporated to dryness. The residue was purified by silica gel flash column chromatography (hexane/EtOAc = 4/1) to give **5a** (1.45 g, 5.08 mmol, 44%) as an oil and **5b** (0.89 g, 3.67 mmol, 32%) as a solid.

5a: R_f 0.33 (hexane/EtOAc = 4/1); IR (KBr): 2987, 2109, 1377, 1259, 1214, 1164, 1065, 1024 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.76 (d, 1H, J = 3.7 Hz, H-1), 4.70 (t, 1H, J = 4.1 Hz, H-2), 3.95–4.21 (m, 4H, H-4, H-5, H-6), 3.48 (dd, 1H, J = 4.9, 9.0 Hz, H-3), 1.56, 1.46, 1.36, 1.34 (4 s, 12H, 4 × CH_3); FAB-MS m/z: 286 $(M + H)^+$.

5b: R_f 0.52 (hexane/EtOAc = 4/1); IR(KBr): 2988, 2938, 1667, 1376, 1321, 1214, 1157, 1073 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 6.05 (d, 1H, J = 5.1 Hz, H-1), 5.26 (m, 1H, H-3), 5.21 (m, 1H, H-2), 4.54 (dd, 1H, J = 5.9, 6.6 Hz, H-5), 4.10 (dd, 1H, J = 6.8, 8.3 Hz, H-6a), 3.92 (dd, 1H, J = 5.9, 8.5 Hz, H-6b), 1.44, 1.42, 1.37 (3 s, 12H, 4 × CH_3); FAB-MS m/z: 243 $(M + H)^+$.

3-Azido-3-deoxy-1,2-*O*-isopropylidene-α-D-allofuranose (6). **5a** (2.15 g, 7.54 mmol) was dissolved in 75% acetic acid (30 mL). The reaction mixture was stirred for 2 h at 55°C, evaporated to dryness and coevaporated with toluene. The residue was purified by silica gel flash column chromatography (hexane/EtOAc = 1/2) to give **6** (1.66 g, 6.77 mmol, 90%) as an oil. ^1H NMR (300 MHz, $CDCl_3$): δ 5.81 (d, 1H, J = 3.7 Hz, H-1), 4.75 (dd, 1H, J = 3.7, 4.8 Hz, H-2), 4.07 (dd, 1H, J = 4.2, 9.3 Hz, H-4), 3.75–4.01 (m, 3H, H-5, H-6), 3.59 (dd, 1H, J = 4.9, 9.4 Hz, H-3), 2.94 (brs, 1H, OH),

2.51 (brs, 1H, OH), 1.59, 1.38 (2 s, 6H, $2 \times CH_3$); FAB-MS m/z: 268 $(M + Na)^+$, 246 $(M + H)^+$.

3-Azido-3-deoxy-1,2-*O*-isopropylidene-α-D-ribofuranose (7). A solution of sodium periodate (1.57 g, 7.34 mmol) in water (15 mL) was added dropwise to a stirred solution of **6** (1.66 g, 6.77 mmol) in EtOH (30 mL) at 0°C. After 30 min, sodium borohydride (597 mg, 15.8 mmol) was added. The reaction mixture was stirred for 2 h at 0°C, filtered and evaporated to dryness. The residue was purified by silica gel flash column chromatography (hexane/EtOAc = 1/1) to give **7** (1.217 g, 5.65 mmol, 84%) as an oil. IR (KBr): 3437, 2988, 2108, 1258, 1110, 1020 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.79 (d, 1H, J = 3.4 Hz, H-1), 4.72 (t, 1H, J = 4.0 Hz, H-2), 4.09 (m, 1H, H-4), 3.96 (dd, 1H, J = 2.4, 12.5 Hz, H-5a), 3.66 (dd, 1H, J = 2.9, 12.6 Hz, H-5b), 3.56 (dd, 1H, J = 4.6, 9.5 Hz, H-3), 1.56, 1.35 (2 s, 6H, $2 \times CH_3$); FAB-MS m/z: 238 $(M + Na)^+$, 216 $(M + H)^+$.

3-Azido-5-*O*-benzoyl-3-deoxy-1,2-*O*-isopropylidene-α-D-ribofuranose (8). To a stirred solution of **7** (1.217 g, 5.65 mmol) in pyridine (20 mL) was added benzoyl chloride (0.98 mL, 8.44 mmol) at 0°C. The mixture was stirred for 3 h at room temperature and evaporated to dryness. The residue was dissolved in EtOAc and extracted with water. The organic layer was washed with saturated $NaHCO_3$ and brine, dried (MgSO4), filtered and evaporated to dryness. The residue was purified by silica gel flash column chromatography (hexane/EtOAc = 4/1) to give **8** (1.72 g, 5.39 mmol, 95%) as an oil. IR (KBr): 2108, 1724, 1275, 1213, 1111, 1021, 710 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.60–8.03 (m, 5H, Ph), 5.85 (d, 1H, J = 3,7 Hz, H-1), 4.78 (dd, 1H, J = 3.7, 4.6 Hz, H-2), 4.66 (dd, 1H, J = 3.1, 12.3 Hz, H-5a), 4.46 (dd, 1H, J = 4.6, 12.2 Hz, H-5b), 4.37 (m, 1H, H-4), 3.43 (dd, 1H, J = 4.7, 9.7 Hz, H-3), 1.52, 1.38 (2 s, 6H, $2 \times CH_3$); FAB-MS m/z: 342 $(M + Na)^+$.

3-Azido-5-*O*-benzoyl-1-*O*-methyl-3-deoxy-D-ribofuranose (9). To a stirred solution of **8** (1.72 g, 5.39 mmol) in MeOH (15 mL) was added acetyl chloride (0.2 mL) at room temperature. After stirring for 3 h at room temperature, the reaction mixture was neutralized with pyridine and evaporated to dryness. The residue was purified by silica gel flash column chromatography (hexane/EtOAc = 2/1) to give **9** (1.257 g, 4.3 mmol, 80%) as an oil. IR (KBr): 3462, 2938, 2109, 1722, 1274, 1120, 1070, 713 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.43–8.10 (m, 5H, Ph), 4.95 (d, 1H, J = 4.4 Hz, α isomer H-1), 4.89 (s, 1H, β isomer H-1), 4.33–4.61 (m, 6H, α and β isomer H-2, H-4, H-5a), 4.13–4.28 (m, 2H, H-5b, β isomer H-3), 3.95 (dd, 1H, J = 4.0, 7.6 Hz, α isomer H-3), 3.45 (s, 3H, α isomer OCH_3), 3.33 (s, 3H, β isomer OCH_3); FAB-MS m/z: 294 $(M + H)^+$, 262 $(M\text{-}OCH_3)^+$.

3-Azido-2,5-di-*O*-benzoyl-1-*O*-methyl-3-deoxy-D-ribofuranose (10). To a stirred solution of **9** (1.257 g, 4.3 mmol) in pyridine (10 mL) was added benzoyl chloride (0.75 mL, 6.46 mmol) dropwise at room temperature and the reaction mixture was stirred for 3 h at room temperature. The reaction mixture was evaporated and the residue was partitioned between ethyl acetate and water. The organic layer was washed with brine, dried ($MgSO_4$), filtered and evaporated to dryness. The residue was purified by silica gel flash column chromatography (hexane/EtOAc = 4/1) to

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give **10** (1.645 g, 4.14 mmol, 97%) as an oil. IR (KBr): 2111, 1725, 1268, 1111, 1070, 710 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.45–8.18 (m, 10H, 2 × Ph), 5.51 (d, 1H, J = 4.6 Hz, H-2), 5.05 (s, 1H, H-1), 4.63 (m, 1H, H-4), 4.45–4.51 (m, 2H, H-5), 4.32 (dd, 1H, J = 4.6, 7.8 Hz, H-3), 3.38 (s, 3H, OCH_3); FAB-MS *m/z*: 398 $(M + H)^+$, 366 $(M\text{-}OCH_3)^+$.

1-*O*-Acetyl-3-azido-2,5-di-*O*-benzoyl-3-deoxy-D-ribofuranose (11). To a stirred solution of **10** (1.645 g, 4.14 mmol) in acetic acid (16 mL) were added acetic anhydride (4 mL) and c-H_2SO_4 (1.12 mL) at room temperature. The reaction mixture was stirred for 30 min at room temperature and poured into saturated $NaHCO_3$ solution. The mixture was extracted with dichloromethane (×3). The combined organic layers were washed with brine, dried ($MgSO_4$), filtered and evaporated to dryness. The residue was purified by silica gel flash column chromatography (hexane/EtOAc = 3/1) to give **11** (1.73 g, 4.07 mmol, 98%) as an oil. IR (KBr): 2952, 2113, 1726, 1268, 1111, 1022, 7111 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.35–8.02 (m, 10H, 2 × Ph), 6.52 (d, 1H, J = 4.4 Hz, α isomer H-1), 6.22 (s, 1H, β isomer H-1), 5.52 (d, 1H, J = 4.6 Hz, β isomer H-2), 5.39 (dd, 1H, J = 4.4, 7.5 Hz, α isomer H-2), 4.37–4.78 (m, 6H, α and β isomer H-4, H-5), 4.26 (dd, 1H, J = 4.6, 7.9 Hz, β isomer H-3), 4.20 (dd, 1H, J = 3.6, 7.5 Hz, α isomer H-3), 2.05 (s, 3H, α isomer OAc), 1.91 (s, 3H, β isomer OAc); FAB-MS *m/z*: 448 $(M + Na)^+$, 366 $(M\text{-}OAc)^+$.

3-Azido-2,5-di-*O*-benzoyl-1-cyano-3-deoxy-β-D-ribofuranose (12). To a stirred solution of **11** (1.73 g, 4.07 mmol) and TMSCN (2.17 mL, 16.27 mmol) in anhydrous dichloromethane (20 mL) was added 1M solution $SnCl_4$ in dichloromethane (0.8 mL) dropwise at room temperature. The reaction mixture was refluxed for 3 h and poured into saturated $NaHCO_3$ solution. The mixture was extracted with dichloromethane (×3). The combined organic layers were washed with brine, dried ($MgSO_4$), filtered and evaporated to dryness. The residue was purified by silica gel flash column chromatography (hexane/EtOAc = 3/1) to give **12** (1 g, 2.55 mmol, 63%) as an oil. IR (KBr): 2116, 1725, 1601, 1452, 1267, 1093, 711 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.46–8.15 (m, 10H, 2 × Ph), 5.85 (dd, 1H, J = 2.9, 4.6 Hz, H-2), 4.88 (d, 1H, J = 3.0 Hz, H-1), 4.65 (dd, 1H, J = 3.2, 12.7 Hz, H-5a), 4.54 (dd, 1H, J = 3.4, 12.4 Hz, H-5b), 4.39–4.49 (m, 2H, H-3, H-4); FAB-MS *m/z*: 415 $(M + Na)^+$, 393 $(M + H)^+$.

Ethyl 2-(3-Azido-2,5-di-*O*-benzoyl-3-deoxy-β-D-ribofuranosyl)-thiazoline-4-carboxylate (13). To a stirred solution of 3-azido-2,5-di-*O*-benzoyl-1-cyano-β-D-ribofuranose **12** (763 mg, 1.94 mmol) in dry MeOH (25 mL) was added L-cysteine ethyl ester hydrochloride (542 mg, 2.92 mmol) followed by TEA (0.4 mL, 2.88 mmol) at room temperature. The reaction mixture was stirred for 2 h and evaporated to dryness. The residue was dissolved in CH_2Cl_2 and washed with water, saturated $NaHCO_3$ solution and brine. The organic layer was dried ($MgSO_4$), filtered and evaporated to dryness. The residue was purified by silica gel flash column chromatography (hexane/EtOAc = 3/1) to give **13** (758 mg, 1.45 mmol, 75%) as an oil IR (KBr): 2984, 2098, 1724, 1272, 1122, 1064, 1025, 713 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.44–8.13 (m, 10H, 2 × Ph), 5.84 (m, 1H, H-2′), 5.03 (m, 2H, H-1′, $CHCO_2Et$), 4.69 (m, 1H, H-4′), 4.51 (m, 1H, H-5′a), 4.13 (m, 4H, H-3′, H-5′b, SCH_2), 3.37

(m, 2H, OCH_2CH_3), 1.24 (m, 3H, OCH_2CH_3); FAB-MS m/z: 419 $(M\text{-}OBz)^+$; Anal. calcd for $C_{25}H_{24}N_4O_7S$: C, 57.24; H, 4.61; N, 10.68; S, 6.11. Found: C, 57.02; H, 4.51; N, 10.58; S, 6.21.

Ethyl 2-(3-Azido-2,5-di-*O*-benzoyl-3-deoxy-β-D-ribofuranosyl)-thiazole-4-carboxylate (14). To a stirred solution of **13** (758 mg, 1.45 mmol) in anhydrous dichloromethane was added 1,8-diazabicyclo[5.4.0]-undec-7-ene (0.43 mL, 2.88 mmol). The solution was cooled to 0°C and $BrCCl_3$ (0.17 mL, 1.73 mmol) was added dropwise. The reaction mixture was stirred for 16 h at 0°C and evaporated to dryness. The residue was dissolved in EtOAc and washed with saturated aqueous NH_4Cl (×3). The organic layer was dried ($MgSO_4$), filtered and evaporated to dryness. The residue was purified by silica gel flash column chromatography (hexane/EtOAc = 3/1) to give **14** (666 mg, 1.27 mmol, 88%) as an oil. IR (KBr): 2983, 2113, 1725, 1267, 1096, 711 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.42–8.24 (m, 11H, SCH, 2 × Ph), 5.96 (dd, 1H, $J = 2.9$, 4.9 Hz, H-2′), 5.58 (d, 1H, $J = 2.9$ Hz, H-1′), 4.80 (dd, 1H, $J = 3.0$, 12.3 Hz, H-5′a), 4.36 (m, 5H, H-3′, H-4′, H-5′b, OCH_2CH_3), 1.37 (t, 3H, $J = 7.06$ Hz, OCH_2CH_3); FAB-MS m/z: 545 $(M + Na)^+$, 523 $(M + H)^+$; Anal. calcd for $C_{25}H_{22}N_4O_7S$: C, 57.46; H, 4.24; N, 10.72; S, 6.14. Found: C, 57.66; H, 4.20; N, 10.62; S, 6.24.

2-(3-Azido-2,5-di-*O*-benzoyl-3-deoxy-β-D-ribofuranosyl)thiazole-4-carboxamide (1). A mixture of **14** (666 mg, 1.27 mmol) in saturated NH_3 in MeOH (20 mL) was stirred for 24 h at room temperature and evaporated to dryness. The residue was purified by silica gel flash column chromatography (CH_2Cl_2/MeOH = 7/1) to give 1 (334 mg, 1.17 mmol, 92%) as a white foam. IR (KBr): 3427, 2925, 2109, 1660, 1260, 1047 cm^{-1}; ^1H NMR (300 MHz, CD_3OD): δ 8.19 (s, 1H, SCH), 5.00 (d, 1H, $J = 5.4$ Hz, H-1′), 4.45 (t, 1H, $J = 5.5$ Hz, H-2′), 4.02 (d″d″, 1H, J = 3.9, 4.1, 5.4 Hz, H-4′), 3.92 (dd, 1H, J = 5.4, 5.6 Hz, H-3′), 3.71 (dd, 1H, J = 3.9, 12.2 Hz, H-5′a), 3.64 (dd, 1H, J = 4.4, 12.2 Hz, H-5′b); additional signals in ^1H NMR (300 MHz, DMSO-d_6): δ 7.71 (brs, 1H, NH_2), 7.57 (brs, 1H, NH_2), 6.15 (d, 1H, $J = 5.6$ Hz, OH), 5.01 (t, 1H, $J = 5.3$ Hz, OH); FAB-MS m/z: 308 $(M + Na)^+$, 286 $(M + H)^+$; Anal. calcd for $C_9H_{11}N_5O_4S$: C, 37.89; H, 3.89; N, 24.55; S, 11.24. Found: C, 37.54; H, 4.08; N, 24.25; S, 11.42.

2-(3-Amino-2,5-di-*O*-benzoyl-3-deoxy-β-D-ribofuranosyl)thiazole-4-carboxamide (2). To a solution of **1** (280 mg, 0.98 mmol) in EtOH (20 mL) was added 5% Pd/C (100 mg) and the reaction mixture was degassed and stirred at one atmosphere of hydrogen for 14 h at room temperature. The catalyst was removed by filtration and the filtrate was evaporated to dryness. The residue was recrystalized from MeOH/EtOAc to give **2** (230 mg, 0.89 mmol, 90%) as a white solid. IR (KBr): 3433, 2918, 1658, 1381, 1043 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 8.18 (s, 1H, SCH), 7.64 (br s, 1H, NH_2), 7.55 (br s, 1H, NH_2), 4.99 (d, 1H, $J = 1.95$ Hz, H-1′), 4.01 (dd, 1H, $J = 1.95$, 9.72 Hz, H-2′), 3.63 (m, 2H, H-4′, H-3′), 3.55 (m, 1H, H-5′a), 2.96 (dd, 1H, J = 4.9, 8.5 Hz, H-5′b), 1.41 (brs, 2H, NH_2); FAB-MS m/z: 260 $[M + H]^+$; Anal. calcd for $C_9H_{13}N_3O_4S$: C, 41.69; H, 5.05; N, 16.21; S, 12.37. Found: C, 41.52; H, 5.15; N, 16.01; S, 12.29.

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