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Note

Synthesis of 3-β-D-ribofuranosyl-1*H*-pyrazole-4-carboxamide

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Abstract

The synthesis of 3-β-D-ribofuranosyl-1*H*-pyrazole-4-carboxamide (**11**) is described. Treatment of enaminone glycoside **1** with trimethyl orthoformate afforded the aldehyde **2**. The aldehyde **2** was oximated with hydroxylamine. Oxime **3** was cyclized with hydrazine to afford the pyrazole **8**. The pyrazole **8** was dehydrated with acetic anhydride, and the nitrile **9** was treated with nickel acetate in acetic acid. The resulting carboxamide **10** was deblocked by aq ammonia gave **11**. © 1997 Published by Elsevier Science Ltd.

Keywords: Synthesis; *C*-Nucleoside; Pyrazole-4-carboxamide; Glycosyl enaminone

We have recently reported the synthesis of glycosyl enaminone **1** and the use of this intermediate in the preparation of the *C*-nucleoside derivatives of isoxazole [1], quinoline [2], pyrazolo[1,5-*a*]pyrimidine [3], and pyrido[2,3-*d*]pyrimidine [4]. In the present paper we further extend those studies and describe route for the synthesis of 3-β-D-ribofuranosyl-1*H*-pyrazole-4-carboxamide (**11**). In view of the known biological activities of several nucleosides bearing carboxamido substituents on the heterocyclic ring [5], it was of interest to prepare the carboxamide **11**. Previously pyrazoles substituted at C-3 by ribofuranose have been described via reactions of acetylenes with either diazo- [6] or nitrilimino sugars [7].

Treatment of glycosyl enaminone **1** with trimethyl orthoformate in the presence of $BF_3 \cdot$ diethyl etherate at room temperature for 30 min afforded (*E*)- and (*Z*)-1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl) -3-(4-hydroxy)anilino-1-oxo-2-propene-2-carbaldehyde (**2**) in 92% yield as a 1:1 inseparable mixture of two geometrical isomers. This assumption was supported by the ^{1}H NMR spectrum, which showed chemical shifts for the aldehyde protons at δ 9.60 (singlet) for the *Z* isomer and at δ 9.99 (doublet, $J_{CHO,3}$ 3.3 Hz) for the *E* isomer. The aldehyde **2** was treated with hydroxylamine hydrochloride in methanol at room temperature for 2 h to give three products, 1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-2-hydroxyiminomethyl-3-(4-hydroxy)anilino-1-oxo-2-propene (**3**) in 61% yield as the major product and (*Z*)- and (*E*)-4-hydroxyiminomethyl-5-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl) isoxazole (**4a**) and (**4b**) in 7% and 5% yields, respectively. The ^{1}H NMR spectrum of **3** was well resolved and clearly indicated the presence of only a single geometrical isomer. In the absence of the other isomer, it is difficult to make a direct assignment of configuration. Treatment of **3** with hydroxylamine hydrochloride afforded a mixture of

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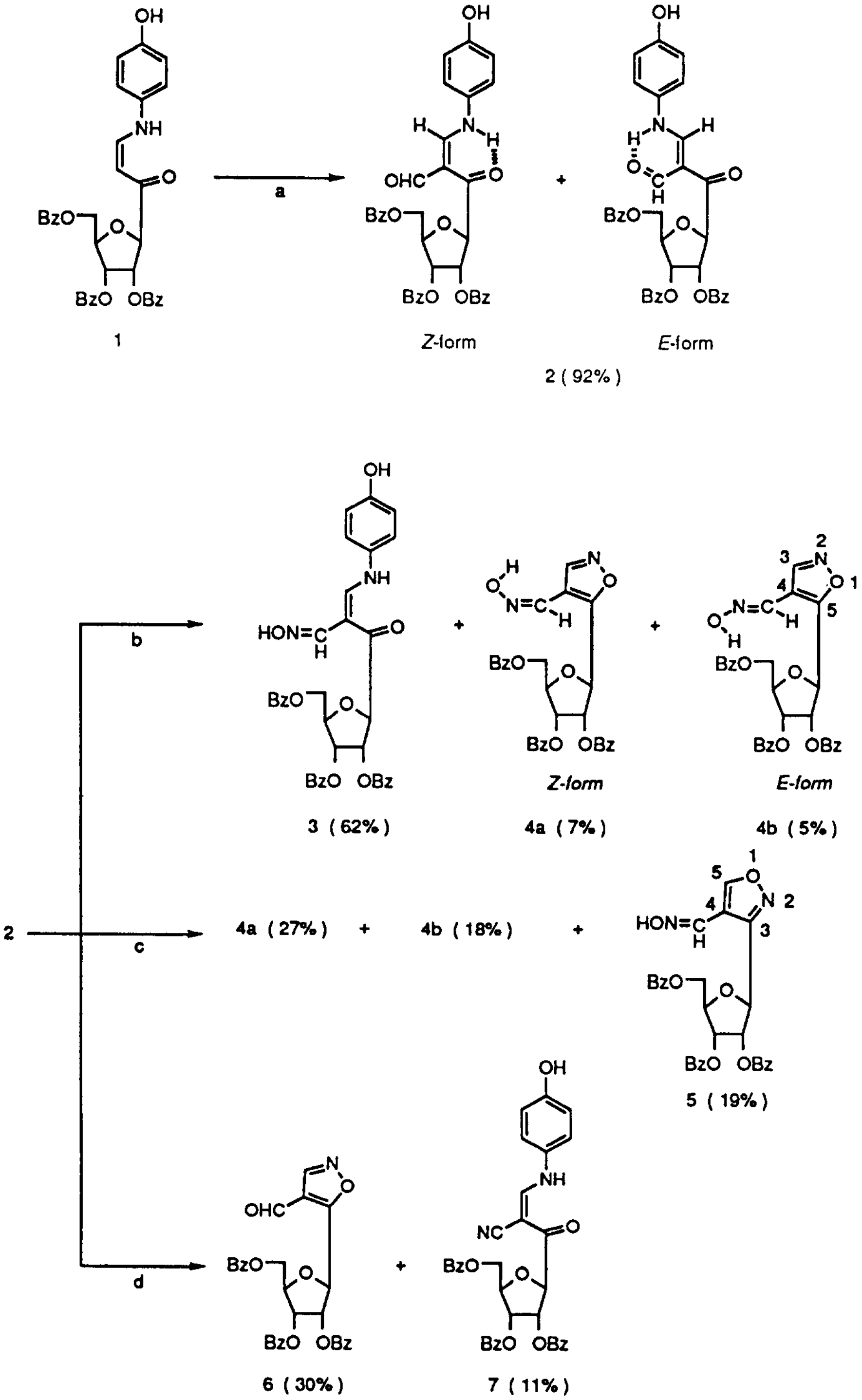
diastereoisomers **4a** and **4b**. Isomerization was observed during the cyclization experiment. On the other hand, configurational assignment of the two isomers **4a** and **4b** was made on the basis of their ^{1}H NMR spectra. The isoxazole ring proton signal of compound **4a** at δ 8.19 occurs at lower field than that of its isomer **4b** (δ 7.66). This chemical-shift difference can be attributed to the deshielding effect of the hydroxyl *syn* to the isoxazole ring [8]. However, reaction of **2** with hydroxylamine in refluxing methanol afforded three products, **4a**, **4b**, and 3-(2,3,5-tri-*O*-benzoyl-β-D-ribofurariosyl)-4-hydroxy-



Scheme 1. Reagents and conditions: a. $CH(OCH_3)_3$, BF_3–Et_2O, r.t.; b. $NH_2OH \cdot HCl$, MeOH, r.t.; c. $NH_2OH \cdot HCl$, MeOH, reflux; d. H_2NOSO_3H, MeOH, −10 °C.

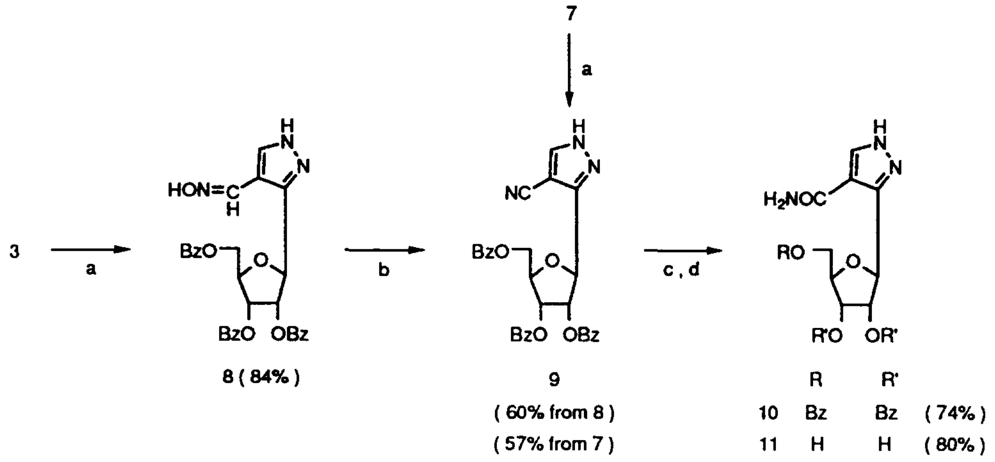
iminomethylisoxazole (**5**) in 27%, 18%, and 19% yield, respectively. To ascertain the structure, the position of the ribofuranosyl groups in isoxazoles **4a**, **4b**, and **5** was confirmed by ^{13}C NMR spectroscopy. In the ^{13}C NMR spectrum of compound **5**, the chemical shift of the isoxazole C-5 was found to be 160 ppm, whilst the chemical shift of C-3 in compounds **4a** and **4b** was observed at 140 and 136 ppm, respectively. These values are consistent with the observation that the carbon bonded to the oxygen atom is deshielded relative to the carbon bonded to nitrogen. When the reaction of **2** with hydroxylamine-*O*-sulfonic acid (HOSA) in methanol at −10 °C 5-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)isoxazole-4-carbaldehyde (**6**) and 1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-3-(4-hydroxy)anilino-1-oxo-2-prop- ene-2-carbonitrile (**7**) were isolated in yields of 30% and 11%, respectively. See Scheme 1.

Cyclocondensation of **3** with anhydrous hydrazine in dioxane gave (*E*)- and (*Z*)-3-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-4-hydroxyiminomethylpyrazole (**8**) in 79% yield as a roughly 5:2 inseparable mixture of two isomers by ^{1}H NMR spectroscopy. Compound **8** was then treated with acetic anhydride at 130 °C to give 3-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-4-cyanopyrazole (**9**) in 60% yield. The IR spectrum of **9** contains an absorption band at 2237 cm^{-1} due to the nitrile group of the pyrazole ring. Cyclocondensation of **7** with anhydrous hydrazine in dioxane gave **9** in 57% yield. It was then necessary to convert the nitrile group of **9** into a carboxamide. Hydrolysis of **9** was completed at reflux in glacial acetic acid in the presence of nickel acetate tetrahydrate, pyrazole carboxamide **10** being isolated in 84% yield after PLC. The removal of the sugar protecting groups in compound **10** was readily accomplished with aq ammonia to produce carboxamide **11** in 80% yield. The stereochemistry of **11** was determined by a nuclear Overhauser effect experiment. Irradiation of the H-1′ signal (δ 5.21) in **11** gave a 3.7% enhancement of the signal at δ 3.81 assignable to H-4′. Examination of the biological activities of **11** is now in progress. See Scheme 2.

1. Experimental

Mass spectra were taken on a Hitachi M-80 instrument by direct insertion at 70 eV; fast-atom bombardment (FAB) mass spectra were run on a JMS-HX 110 spectrometer. The ^{1}H and ^{13}C NMR spectra were measured with a JNM-GX-270 or an A-600 (Jeol) spectrometer, with tetramethylsilane as the internal standard. The IR spectrum was measured with a FT/IR-230 (Jasco) spectrometer. UV spectra were recorded with a Shimadzu UV-3100PC spectrophotometer. Optical rotations were measured with a Jasco DIP-370 polarimeter (10-cm cell) at 25 °C. Elemental analyses were carried out by the microanalysis service of the University of Meijo. Analytical TLC was performed on glass plates coated with a 0.5-mm layer of Silica Gel GF$_{254}$ (E. Merck). The compounds were detected by UV light (254 nm).

(E)- and (Z)-1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-3-(4-hydroxy)anilino-1-oxo-2-propene-2-carbaldehyde (**2**).—To a solution of **1** (220 mg, 0.362 mmol) in methyl orthoformate (15 mL) at 0 °C was added 1 mL of $BF_3 \cdot Et_2O$. The mixture was stirred at room temperature for 30 min. Water was added, and the mixture was neutralized with satd aq



Scheme 2. Reagents and conditions: a. NH_2NH_2, dioxane, r.t.; b. $(CH_3CO)_2O$, 130 °C; c. $(CH_3COO)_2Ni \cdot 4H_2O$, CH_3COOH, reflux; d. MeOH, aq NH_4OH, r.t.

$\mathrm{NaHCO_3}$ and extracted with $\mathrm{CHCl_3}$ (3 × 10 mL). The extracts were combined, washed with water, and dried over $\mathrm{MgSO_4}$. On evaporation, the extracts afforded a yellow oil that was chromatographed on a column of silica gel with $\mathrm{CHCl_3}$ as eluent. This afforded 212 mg (92%) of **2** as a yellow foam: ^{1}H NMR ($\mathrm{CDCl_3}$): δ 4.56 (dd, 0.5 H, $J_{5'a,4'}$ 4.4, $J_{5'a,5'b}$ 11.7 Hz, H-5'a), 4.65 (dd, 0.5 H, $J_{5'a,4'}$ 4.8, $J_{5'a,5'b}$ 11.7 Hz, H-5'a), 4.47–4.87 (m, 2 H, H-4', 5'b), 5.31 (d, 0.5 H, $J_{1',2'}$ 3.3 Hz, H-1'), 5.39–5.83 (m, 1.5 H, H-1', 3'), 6.06 (dd, 0.5 H, $J_{1',2'}$ 2.4, $J_{2',3'}$ 5.0 Hz, H-2'), 6.18 (dd, 0.5 H, $J_{1',2'}$ 5.1 Hz, H-2'), 6.85–7.07 (m, 4 H, Ph), 7.29–8.07 (m, 15.5 H, *Z*-H-3, Ph), 8.42 (dd, 0.5 H, $J_{\mathrm{CHO},3}$ 3.3, $J_{3,\mathrm{NH}}$ 14 Hz, *E*-H-3 became a doublet when the aldehyde proton was irradiated), 9.60 (s, 0.5 H, *Z*-CHO), 9.99 (d, 0.5 H, $J_{\mathrm{CHO},3}$ 3.3 Hz, *E*-CHO), 12.56 (br d, 0.5 H, $J_{3,\mathrm{NH}}$ 13.6 Hz, NH, exchanged with $\mathrm{D_2O}$), 12.76 (br d, 0.5 H, $J_{3,\mathrm{NH}}$ 14.0 Hz, NH, exchanged with $\mathrm{D_2O}$); ^{13}C NMR ($\mathrm{CDCl_3}$): δ 63.7, 64.1 (C-5'), 72.5, 72.6, 73.8, 73.9, 79.1, 79.9, 82.9, 83.3 (C-1', 2', 3', 4'), 109.9, 110.4 (C-2), 116.7, 116.8, 120.0, 120.1, 128.3–133.6, 152.5, 155.1, 155.3 (C-3, Ph), 165.4, 165.5, 165.6, 166.2, 166.4 (C=O), 187.4 (C-1), 190.7, 190.8 (CHO), 194.2 (C-1). FABMS (nitrobenzyl alcohol as matrix). Found: [M + N]$^+$ *m/z* 636.1864. Calcd for $\mathrm{C_{36}H_{30}NO_{10}}$: [M + H] 636.1870.

1-(2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl)-2-hydroxyiminomethyl-3-(4-hydroxy)anilino-1-oxo-2-propene (**3**)*, (Z)- and (E)-4-Hydroxyiminomethyl-5-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)isoxazole* (**4a**) and (**4b**).—To a solution of **2** (150 mg, 0.236 mmol) in MeOH (15 mL) was added 33 mg (0.48 mmol) of hydroxylamine hydrochloride. The mixture was stirred at room temperature for 2 h. After this time, three new compounds were detected (TLC) in the reaction mixture which had R_f values of 0.14, 0.37, 0.44 (3:2, hexane–EtOAc), respectively. Water was added, and the mixture was neutralized with satd aq $\mathrm{NaHCO_3}$ and then extracted with $\mathrm{CHCl_3}$ (3 × 10 mL). The extracts were combined, washed with water and dried over $\mathrm{MgSO_4}$. The extracts, on evaporation, afforded a yellow oil which was separated by preparative TLC with 3:1 hexane–EtOAc as eluent after two elutions.

Compound **3**: R_f 0.14; yellow foam (61%); ^{1}H NMR ($\mathrm{CDCl_3}$): δ 4.63 (dd, 1 H, $J_{5'a,4'}$ 4.4, $J_{5'a,5'b}$ 11.2 Hz, H-5'a), 4.79 (m, 2 H, H-4', 5'b), 5.28 (d, 1 H, $J_{1',2'}$ 2.6 Hz, H-1'), 5.77 (dd, 1 H, $J_{2',3'} = J_{3',4'} =$ 5.0 Hz, H-3'), 6.07 (dd, 1 H, $J_{1',2'}$ 2.6, $J_{2',3'}$ 5.0 Hz, H-2'), 6.77, 6.91 (each d, 2 H each, J 8.8 Hz, Ph), 7.30–8.09 (m, 15 H, Ph), 8.31 (d,1 H, $J_{3,\mathrm{NH}}$ 12.8 Hz, H-3), 8.49 (s, 1 H, –C*H*=NOH), 10.76 (br d, 1 H, $J_{3,\mathrm{NH}}$ 12.8 Hz, NH, exchanged with $\mathrm{D_2O}$); ^{13}C NMR ($\mathrm{CDCl_3}$): δ 64.2 (C-5'), 72.9, 74.5, 79.6, 82.5 (C-1', 2', 3', 4'), 116.5, 119.2, 128.4–133.8 (C-2, Ph), 146.2,149.6 (C-3, –CH=NOH), 153.7 (Ph), 165.5, 165.7, 166.5 (C=O), 189.5 (C-1). FABMS (nitrobenzyl alcohol as matrix). Found: [M + H]$^+$ *m/z* 651.1982. Calcd for $\mathrm{C_{36}H_{31}N_2O_{10}}$: [M + H] 651.1979.

Compound **4a**: R_f 0.44; colorless foam (7%); ^{1}H NMR ($\mathrm{CDCl_3}$): and 4.66 (dd, 1 H, $J_{4',5'a}$ 11.7 Hz, H-5'a), 4.79 (m, 2 H, H-4', 5'b), 5.60 (d, 1 H, $J_{1',2'}$ 4.8 Hz, H-1'), 5.91 (m, 2 H, H-2', 3'), 7.36–8.09 (m, 15 H, Ph), 8.19 (s, 1 H, H-3), 8.48 (s, 1 H –C*H*=NOH); ^{13}C NMR ($\mathrm{CDCl_3}$): δ 63.6 (C-5'), 72.3, 74.6, 75.6, 80.8 (C-1', 2', 3', 4'), 112.3 (C-4), 128.5–133.7 (Ph), 139.6 (C-3), 148.5 (–CH=NOH), 164.4, 165.1, 165.3, 166.3 (C-5, C=O). FABMS (nitrobenzyl alcohol as matrix). Found: [M + H]$^+$ *m/z* 557.1567. Calcd for $\mathrm{C_{30}H_{25}N_2O_9}$: [M + H] 557.1560.

Compound **4b**: R_f 0.37; colorless foam (5%); ^{1}H NMR ($\mathrm{CDCl_3}$): δ 4.68 (m, 1 H, H-5'a), 4.81 (m, 2 H, H-4', 5'b), 5.61 (d, 1 H, $J_{1',2'}$ 4.8 Hz, H-1'), 5.89 (m, 2 H, H-2', 3'), 7.36–8.08 (m, 15 H, Ph), 7.66 (s, 1 H, H-3), 9.02 (s, 1 H, –C*H*=NOH); ^{13}C NMR ($\mathrm{CDCl_3}$): δ 63.6 (C-5'), 72.2, 74.8, 75.6, 81.1 (C-1', 2', 3', 4'), 109.9 (C-4), 128.5–133.7 (Ph), 135.5 (C-3), 151.9 (–CH=NOH), 165.1, 165.3, 165.8, 166.2 (C-5, C=O). FABMS (nitrobenzyl alcohol as matrix). Found: [M + H]$^+$ *m/z* 557.1561. Calcd for $\mathrm{C_{30}H_{25}N_2O_9}$: [M + H] 557.1560.

3-(2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl)-4-hydroxyiminomethylisoxazole (**5**) and (**4a,b**).—To a solution of **2** (155 mg, 0.244 mmol) in MeOH (15 mL) was added 33 mg (0.48 mmol) of hydroxylamine hydrochloride. The mixture was stirred at reflux for 1 h. Workup as above gave **4a,b** and **5** in 27%, 18%, and 19% yield, respectively.

Compound **5**: R_f 0.47 (3:1, hexane–EtOAc); colorless foam (19%); ^{1}H NMR ($\mathrm{CDCl_3}$): δ 4.54 (dd, 1 H $J_{4',5'a}$ 4.7 $J_{5'a,5'b}$ 12.9 Hz, H-5'a) 4.74 (m, 2H, H-4', 5'b), 5.18 (d, 1 H, $J_{1',2'}$ 5.1 Hz, H-1'), 5.56 (dd, 1 H, $J_{2',3'} = J_{3',4'} =$ 5.1 Hz, H-3'), 6.19 (dd, 1 H, H-2'), 7.34–8.00 (m, 15 H, Ph), 8.79 (s, 1 H, H-5), 9.18 (s, 1 H, –C*H*=NOH) ^{13}C NMR ($\mathrm{CDCl_3}$): δ 63.5 (C-5'), 72.3, 72.9, 80.3, 81.4 (C-1', 2', 3', 4'), 110.1 (C-4), 128.4–133.5 (Ph), 144.1 (C-3), 148.9 (–CH=NOH), 160.4 (C-5), 165.3, 165.4, 166.1 (C=O). FABMS (nitrobenzyl alcohol as matrix). Found: [M + H]$^+$ *m/z* 557.1556. Calcd for $\mathrm{C_{30}H_{25}N_2O_9}$: [M + H] 557.1560.

5-(2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl)isoxazole-4-carbaldehyde (**6**) *and 1-(2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl)-3-(4-hydroxy)anilino-1-oxo-2-propene-2-carbonitrile* (**7**).—To a solution of **2** (33.6 mg, 0.053 mmol) in MeOH (4 mL) was added 7.2 mg (0.06 mmol) of hydroxylamine-*O*-sulfonic acid. The mixture was stirred at − 10 °C for 1.5 h. Water was added, and the mixture was neutralized with saturated $NaHCO_3$ solution and then extracted with $CHCl_3$ (3 × 10 mL). The extracts were combined, washed with water and dried $MgSO_4$. The extracts, on evaporation, afforded a yellow oil which was separated by preparative TLC with 3:1 hexane–EtOAc as eluent.

Compound **6**: R_f 0.70; colorless foam (30%); ^1H NMR ($CDCl_3$): δ 4.67 (dd, 1 H, $J_{5'a,4'}$ 4.8, $J_{5'a,5'b}$ 13.2 Hz, H-5′a), 4.84 (m, 2 H, H-4′, 5′b), 5.80 (d, 1 H, $J_{1',2'}$ 5.1 Hz, H-1′), 5.92 (m, 2 H, H-2′, 3′), 7.34–8.07 (m, 15 H, Ph), 8.60 (s, 1 H, H-3), 10.13 (s, 1 H, CHO); ^{13}C NMR ($CDCl_3$): δ 63.4 (C-5′), 72.2, 74.7, 76.0, 81.3 (C-1′, 2′, 3′, 4′), 119.6 (C-4), 128.4–133.8 (Ph), 148.6 (C-3), 165.1, 165.2, 166.1 (C=O), 171.7 (C-5), 182.9 (CHO). FABMS (nitrobenzyl alcohol as matrix). Found: $[M + H]^+$ *m/z* 542.1454. Calcd for $C_{30}H_{24}NO_9$: [M + H] 542.1451.

Compound **7**: R_f 0.15; yellow foam (11%); ^1H NMR ($CDCl_3$): δ 4.63 (dd, 1 H, $J_{5'a,4'}$ 4.4, $J_{5'a,5'b}$ 11.7 Hz, H-5′a), 4.76 (m, 1 H, m, H-4′), 4.81 (dd, 1 H, $J_{5'a,4'}$ 3.7, $J_{5'a,5'b}$ 11.7 Hz, H-5′b), 5.31 (d, 1 H, $J_{1',2'}$ 4.0 Hz, H-1′), 5.46 (br, 1 H, OH exchanged with D_2O), 5.83 (dd, 1 H, $J_{2',3'} = J_{3',4'} = 5.6$ Hz, H-3′), 5.96 (dd, 1 H, $J_{1',2'}$ 4.0, $J_{2',3'}$ 5.6 Hz, H-2′), 6.89, 7.00 (each d, 2 H each, $J = 8.8$ Hz, Ph), 7.34–8.09 (m, 15 H, Ph), 7.76 (d, 1 H, $J_{3,NH}$ 13.2 Hz, H-3), 12.40 (br d, 1 H, $J_{3,NH}$ 13.2 Hz, NH exchanged with D_2O); ^{13}C NMR ($CDCl_3$): δ 64.0 (C-5′), 72.8, 73.7, 80.2, 82.7 (C-1′, 2′, 3′, 4′), 116.9, 119.8 (Ph), 118.5 (CN), 128.3–133.6 (C-2, 5, Ph), 153.5 (C-3), 155.3 (C-8), 165.5,166.3 (C=O), 192.8 (C-1). FABMS (nitrobenzyl alcohol as matrix). Found: $[M + H]^+$ *m/z* 633.1863. Calcd for $C_{36}H_{29}N_2O_9$: [M + H] 633.1873.

3-(2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl)-4-hydroxyiminomethylpyrazole (**8**).—To a solution of **3** (279 mg, 0.429 mmol) in dioxane (10 mL) at 0 °C was added 20.6 mg (0.643 mmol) of anhydrous hydrazine. The mixture was stirred at room temperature for 1 h. Water was added, and the mixture was neutralized with AcOH and extracted with $CHCl_3$ (3 × 10 mL). The extracts were combined, washed with water, and dried over $MgSO_4$. The extracts, on evaporation, afforded an oil that was chromatographed on a column of silica gel with $CHCl_3$ as eluent to give 200 mg (84%) of **8** as a colorless foam; ^1H NMR ($CDCl_3$): δ 4.63–4.77 (m, 3 H, H-4′, 5′a,b), 5.59 (d, 0.7 H, $J_{1',2'}$ 5.1 Hz, H-1′), 5.66 (d, 0.3 H, $J_{1',2'}$ 4.0 Hz, H-1′), 5.90 (m, 1 H, H-3′), 6.10 (m, 1 H, H-2′), 7.31–8.02 (m, 15 H, Ph), 7.71 (s, 0.7 H, H-5), 7.79 (s, 0.3 H, H-5), 8.21 (s, 0.3 H, –C*H*=NOH), 8.44 (s, 0.7 H, –C*H*=NOH); ^{13}C NMR ($CDCl_3$): δ 64.2 (C-5′), 72.5, 72.6, 75.2, 76.9, 77.2, 77.5, 79.7, 80.3 (C-1′, 2′, 3′, 4′), 110.2, 112.5 (C-4), 128.4-133.5 (Ph), 136.0, 138.4 (C-5), 142.6, 146.6 (–CH=NOH) 165.3, 165.4, 165.5, 166.4, 166.6 (C-3, C=O): FABMS (nitrobenzyl alcohol as matrix). Found: $[M + H]^+$ *m/z* 556.1723. Calcd for $C_{30}H_{26}N_3O_8$: [M + H] 556.1720.

3-(2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl)-4-cyanopyrazole (**9**).—A solution of **8** (112 mg, 0.201 mmol) in acetic anhydride (3 mL) was heated at 130 °C for 3 h. Water was added, and the mixture was neutralized with satd aq $NaHCO_3$ and extracted with $CHCl_3$ (3 × 10 mL). The extracts were combined, washed with water, and dried over $MgSO_4$. The extracts, on evaporation, afforded a colorless oil that was chromatographed on a column of silica gel with $CHCl_3$ as eluent to give 65.4 mg (60%) of **9** as a colorless foam: IR (KBr) 3268, 2237, 1725, 1452, 1268, 1124, 713 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.79 (m, 3 H, H-4′, 5′a,b), 5.58 (d, 1 H, $J_{1',2'}$ 4.9 Hz, H-1′), 5.75 (dd, 1 H, $J_{2',3'} = J_{3',4'} = 4.9$ Hz, H-3′), 5.84 (dd, 1 H, H-2′), 7.37–8.08 (m, 15 H, Ph), 7.91 (s, 1 H, H-5), 11.26 (br, 1 H, NH, exchanged with D_2O); ^{13}C NMR ($CDCl_3$): δ 64.1 (C-5′), 72.6, 75.5, 75.9, 81.3 (C-1′, 2′, 3′, 4′), 112.7 (C-4), 128.5–133.8 (CN, Ph), 165.4, 165.5, 167.0 (C-3, C=O). FABMS (nitrobenzyl alcohol as matrix). Found: $[M + H]^+$ *m/z* 538.1599. Calcd for $C_{30}H_{24}N_3O_7$: [M + H] 538.1614.

Treatment of compound 7 with hydrazine.—The same procedure was used as for the reaction of compound **3** with anhydrous hydrazine. This afforded compound **9** (57%) as a colorless foam. Identity was confirmed by comparing the ^1H NMR spectra.

3-(2,3,5-Tri-O-benzoyl-β-D-ribofuranosyl)pyrazole-4-carboxamide (**10**).—To a solution of **9** (66.1 mg, 0.123 mmol) in AcOH (15 mL) was added 340 mg of nickel acetate tetrahydrate. The mixture was stirred at reflux for 30 min and then was allowed to cool to room temperature. EDTA was added and then extracted with $CHCl_3$ (3 × 10 mL). The extract were combined, washed with water and dried over $MgSO_4$. The extracts, on evaporation, the residue was purified by PLC with 4:1 $CHCl_3$–MeOH as the eluent to give 50.8 mg (74%) of **10** as a colorless oil: ^1H NMR

($CDCl_3$): δ 4.64 (dd, 1 H, $J_{4',5'a}$ 5.1, $J_{5'a,5'b}$ 12.8 Hz, H-5'a), 4.8 (m, 2 H, H-4', 5'b), 5.54 (br, 1 H, NH, exchanged with D_2O), 5.71 (d, 1 H, $J_{1',2'}$ 4.6 Hz, H-1'), 5.96 (dd, 1 H, $J_{2',3'} = J_{3',4'} = 4.6$ Hz, H-3'), 6.42 (dd, 1 H, H-2'), 7.06 (br, 1 H, NH, exchanged with D_2O), 7.33–8.05 (m, 16 H, H-5, Ph); ^{13}C NMR ($CDCl_3$): δ 63.3 (C-5'), 72.3, 74.4, 77.5, 80.2 (C-1', 2', 3', 4'), 105.4 (C-4), 128.4–133.6 (Ph), 135.4 (C-5), 164.5,165.3, 165.6, 166.0, 166.3 (C-3, C=O). FABMS (nitrobenzyl alcohol as matrix). Found: $[M + H]^+$ m/z 556.1706. Calcd for $C_{30}H_{26}N_3O_8$: [M + H] 556.1720.

3-(β-D-Ribofuranosyl)pyrazole-4-carboxamide (**11**).—To a solution of **10** (39 mg, 0.07 mmol) in MeOH (4 mL) was added 28% aq NH_4OH (0.2 mL) at room temperature for 7 days, and then the reaction mixture was evaporated. The solid was recrystallized from MeOH to give colorless needles of **11** ,13.6 mg (80%): mp 235–237 °C. $[\alpha]_D$ +31.2° (c 0.1, Me_2SO); λ_{max}^{MeOH} 217 nm(log ε 2.4); ^1H NMR [$(CD_3)_2SO$]: δ 3.51 (dd, 1 H $J_{4',5'a}$ 3.1, $J_{5'a,5'b}$ 10.7 Hz, H-5'a), 3.64 (dd, 1 H, $J_{4',5'b}$ 3.1, $J_{5'a,5'b}$ 10.7 Hz, H-5'b), 3.81 (m, 1 H, H-4'), 3.96 (m, 2 H, H-2', 3'), 4.8–5.8 (br, 3 H, OH, exchanged with D_2O), 5.21 (d, 1 H, $J_{1',2'}$ 4.1 Hz, H-1'), 7.10. 7.57 (each s, 1 H each, $CONH_2$, exchanged with D_2O), 7.99 (s, 1 H, H-3), 12.74 (s, 1 H, NH, exchanged with D_2O). Anal. Calcd for $C_9H_{13}N_3O_5$: C, 44.45; H, 5.39; N, 17.28. Found: C, 44.41, H, 5.34; N, 17.10.

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