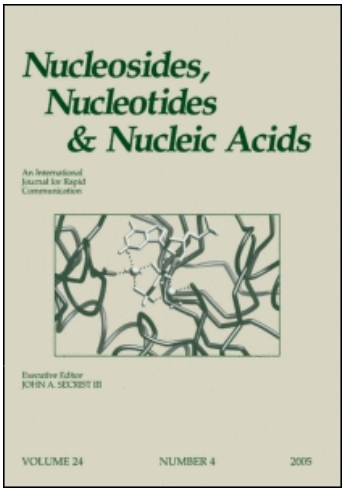

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A Convenient Method for the Synthesis of 2-(β-D-Glycopyranosylthio) Pyridines

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A Convenient Method for the Synthesis of 2-(β-D-Glycopyranosylthio) Pyridines

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ABSTRACT

Treatment of piperidinium salts of dihydropyridinethiolates **3** with glycosyl bromides **4** in dry acetone provides a convenient and high yielding synthesis of 1,4-dihydro-3-cyanopyridine thioglycosides **5**. The structures of **5** were confirmed by oxidation as well as by ^{1}H NMR and ^{13}C NMR spectral analysis.

Key Words: Piperidinium salts; Glycosyl bromides; Dihydropyridine thioglycosides; Medicinal cavity.

The bioisosteric replacement of nitrogen by carbon in pyrimidine heterocycle of the naturally occurring pyrimidine nucleosides cytidine and uridine has generated effective inhibitors of cell growth.[1,2] 3-Deazauridine and 3-deazacytidine produced significant growth inhibition against L-1210 leukemia cells in vitro[3] and have also shown antiviral activity against RNA viruses.[4] The 3-deazapyrimidine nucleosides, substituted analogously to naturally occurring pyrimidines, constitute another logical class of analogous with potential biological activity.[5–7] As a part of our program of research on the synthesis of new pyridine and pyrimidine nucleosides[8–13] with considerable biological and medicinal activity, we report here

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a convenient method for the synthesis of a new class of non-natural nucleosides, 2-(β-D-glycopyranosylthio)-1,4-dihydropyridines. In addition, we have tested these glycosides against HIV. Thus, 3-aryl-2-cyano(thioacrylamides) **1** have been found to react with aliphatic ketones **2** in ethanol containing equivalent amounts of piperidine at room temperature to give the corresponding piperidinium salts of 1,4-dihydropyridinethiones **3**. Compounds **3** reacted with tetra-*O*-acetyl-α-D-glucopyranosyl bromide or its α-D-galactopyranosyl isomer **4** in dry acetone at 0°C to give the corresponding dihydrothioglycosides **5** in high yields. The structures of the reaction products **5** were established and confirmed by the correct analytical and spectral data. The ^{1}H NMR spectrum of **5b** showed a doublet at δ 6.10 ($J = 10.5$ Hz) assigned to the anomeric proton of the glucose moiety with a diaxial orientation of H-1′ and H-2′ indicating the presence of only β-configuration and $^4C_1$ (D) conformation for this glucoside. Ammonolysis of protected glycosides **5** with methanolic ammonia at 0°C furnished the free glycosides 2-(β-D-glycopyranosylthio)-1,4-dihydro-3-cyanopyridines 7 in 85–88% yields. The ^{1}H NMR spectrum of **7g** showed the anomeric proton as a doublet at δ 5.60 ($J = 10.1$ Hz) indicating the presence of only the β-D-galactopyranoside. In another experiment, the dihydrothioglycosides **5a-h** were heated at reflux in dry ethanol for three minutes, the corresponding aromatized pyridine thioglycosides **10a-h** were obtained. In order to investigate the scope of the formation of these glycosides further we studied the coupling of 3-aryl-2-cyano(thioacrylamide) potassium salts **8** with tetra-*O*-acetyl-α-D-glycopyranosyl bromides **4** in aqueous acetone at room temperature to give the corresponding 3-aryl-2-cyanoacrylamide thioglycosides **9**. Compounds **9** reacted with aliphatic ketones **2** in dry ethanol containing catalytic amounts of piperidine at 60°C to afford the pyridine thioglycosides **10a-h.**

Although the coupling of piperidinium salts **3** with the glycosyl bromides **4** could also give the corresponding *N*-glycosides **6**, the formation *S*-glycosides **5** were proved using the ^{13}C NMR spectroscopy which revealed the absence of a C-2 thione carbon at δ 162 of the same value of the corresponding S-methyl derivatives.[13] Removal of the protecting acetyl groups from the glycon moiety of 10 with ammonia in methanol at room temperature furnished 2-(β-D-glycopyranosylthio) pyridiness **11**.

In conclusion, we have synthesized dihydropyridine thioglycosides and their aromatized derivatives, via piperidinium salts. The high yields, high purity of products and experimental simplicity make this method particular attractive. The glycosides **5a-h** and **7a-h** did not show any significant activity against Human Immunodeficiency Virus HIV in MT-4 cells at a concentration of 100 μg/mL. None of the free glycosides showed cytotoxicity at this concentration.

EXPERIMENTAL

Melting points are uncorrected. TLC was carried out on aluminum sheet silica gel 60 F_{254} (Merck) detected by short UV light. IR Spectra were obtained (kBr) using a Pye Unicam spectra 1000. ^{1}H NMR and ^{13}C NMR spectra were measured on a Varian 400 MHz spectrometer in DMSO-d_6 using $SiMe_4$ as internal standard. Mass

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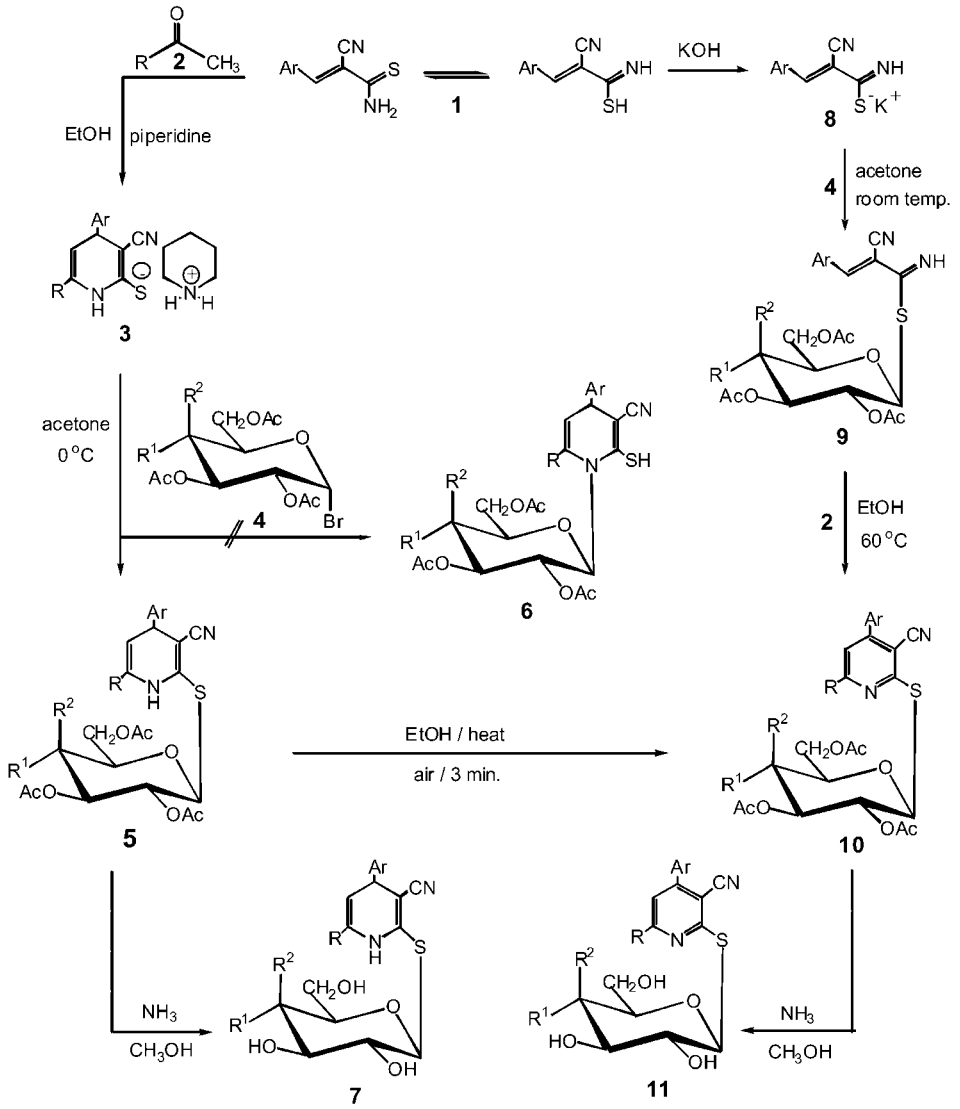

	Ar	R	R^1	R^2		Ar	R	R^1	R^2
5,10 a	4-CH_3O-C_6H_4	CH_3	OAc	H	**7,11 a**	4-CH_3O-C_6H_4	CH_3	OH	H
b	2-furyl	CH_3	OAc	H	**b**	2-furyl	CH_3	OH	H
c	4-CH_3O-C_6H_4	C_2H_5	OAc	H	**c**	4-CH_3O-C_6H_4	C_2H_5	OH	H
d	2-furyl	C_2H_5	OAc	H	**d**	2-furyl	C_2H_5	OH	H
e	4-CH_3O-C_6H_4	CH_3	H	OAc	**e**	4-CH_3O-C_6H_4	CH_3	H	OH
f	2-furyl	CH_3	H	OAc	**f**	2-furyl	CH_3	H	OH
g	4-CH_3O-C_6H_4	C_2H_5	H	OAc	**g**	4-CH_3O-C_6H_4	C_2H_5	H	OH
h	2-furyl	C_2H_5	H	OAc	**h**	2-furyl	C_2H_5	H	OH

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spectra were recorded by EI on a Varian Mat 311 A spectrometer and by FAB on a Kratos MS spectrometer.

3-Cyano-2-(2,3,4,6-tetra-*O*-acetyl-β-D-glycopyranosylthio)-1,4-dihydrophridines (5a-h)

General Coupling Procedures. To a mixture of 3-aryl-2-cyano(thioarylamides) **1** (0.01 mol) and **2** (0.01 mol) in dry ethanol (5 mL), was added piperidine (0.01 mol). The reaction mixture was stirred at room temperature for one hour, then evaporated under reduced pressure and the resulting piperidinium salt **3** was dissolved in dry acetone (5 mL) and a solution of glycosyl bromide **4** (0.001 mol) in dry acetone (20 mL) was then added to 0°C. The mixture was stirred until the reaction was judged complete by TLC (4–6 h), using chloroform-ether (9:1 v/v) (Rf 0.70–0.74 region), then evaporated under reduced pressure for 15 min. The residue was crystallized from chloroform-petroleum ether 40–60 at 0°C to give the title compounds **5.**

5a. Yield 78%, mp 139°C; IR 3390 (NH), 2218 (CN), 1748 (CO) CM^{-1}; ^{1}H NMR δ 1.95-2.07 (4s, 12H, $4CH_3CO$), 2.40 (s, 3H, CH_3), 3.88 (s, 3H OCH_3), 4.13 (m, 2H, 2H-6′), 4.28 (m, 2H, H-5′ and pyridine H-4), 5.03 (m, 3H, H-4′, H-3′ and H-2′), 6.12 (d, $J_{1'-2'} = 10.3$ Hz, 1H, H-1′), 7.60 (m, 4H, Ar-H and 1H, pyridine H-5), 8.19 (s, 1H, NH); ^{13}C NMR δ 18.9 (CH_3), 20.2–24.3 ($4CH_3CO$), 55.3 (OCH_3), 61.7 (C6′), 67.8 (C4′), 68.9 (C2′), 73.2 (C3′), 75.0 (C5′), 80.3 (C1′), 102.5 (C4), 110.6 (C3), 115.5 (CN), 125.0–142.9 (Ar-C), 152.9 (C5), 155.9 (C6), 162.1 (C2), 169.2–170.0 ($4COCH_3$); MS m/z 588; Anal. Calcd for $C_{28}H_{32}N_2SO_{10}$: C, 57.14; H, 5.44; N, 4.76. Found: C, 57.30; H, 5.59; N, 4.91.

5b. Yield 80%, mp 144°C; IR 3360 (NH), 2216 (CN), 1750 (CO) cm^{-1}; ^{1}H NMR δ 1.94–2.02 (4s, 12H, $4CH_3CO$), 2.38 (s, 3H, CH_3), 4.02 (m, 2H, 2H-6′), 4.15 (m, 2H, H-5′ and pyridine H-4), 5.02 (t, $J = 9.2$ Hz, 1H, H-4′), 5.17(t, $J = 8.9$ Hz, 1H, H-3′), 5.53 (t, $J = 9.1$ Hz, 1H, H-2′), 6.10 (d, $J_{1'-2'} = 10.5$ Hz, 1H, H-1′), 6.83 (m, 1H, furan H-4), 7.07 (S, 1H, pyridine H-5), 7.60 (m, 1H furan H-3), 8.08 (dd, 1H furan H-5), 8.28 (s, br, 1H NH); ^{13}C NMR δ 19.0 (CH_3), 20.2–24.4 ($4CH_3CO$), 61.7 (C6′), 68.1 (C4′), 72.4 (C2′), 73.1 (C3′), 74.9 (C5′), 80.2 (C1′), 97.9 (C4), 113.0 (C3), 115.4 (CN), 119.9 (furan C4), 139.8 (furan C3), 146.0 (C5), 147.1 (C6), 152.9 (furan C5), 159.2 (furan C2), 162.2 (C2), 169.2–169.8 ($4COCH_3$); MS m/z 548; Anal. Calcd for $C_{25}H_{28}N_2SO_{10}$: C, 54.74; H, 5.11; N, 5.11. Found: C, 55.05; H, 5.30; N, 5.38.

5c. Yield 76%, mp 126°C; IR 3380 (NH), 2220 (CN), 1746 (CO) cm^{-1}; ^{1}H NMR δ 1.35 (t, $J = 6.6$ Hz, 3H, CH_3), 1.96–2.07 (4s, 12H, $4CH_3CO$), 2.71 (q, 2H, CH_2), 3.83 (s, 3H, OCH_3), 4.05 (m, 2H, 2H-6′), 4.20 (m, 2H, H-5′ and pyridine H-4), 5.09 (m, 2H, H-4′ and H-3′), 5.57 (t, $J = 9.3$ Hz, 1H, H-2′), 6.15 (d, $J_{1'-2'} = 10.5$ Hz, 1H, H-1′), 7.38 (m, 4H, Ar-H and 1H, pyridine H-5), 8.30 (s, 1H, NH); ^{13}C NMR δ 15.4 (CH_3), 20.2–23.7 ($4CH_3CO$), 24.8 (CH_2), 55.0 (OCH_3), 61.7 (C6′), 68.1 (C4′), 68.9 (C2′), 73.2 (C3′), 75.0 (C5′), 80.3 (C1′), 105.7 (C4), 113.6 (C3), 115.1 (CN), 124.9–142.8 (Ar-C), 153.0 (C5), 158.3 (C6), 162.0 (C2), 169.2–169.8

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($4COCH_3$); MS m/z 602; Anal. Calcd for $C_{29}H_{34}N_2SO_{10}$: C, 57.81; H, 5.65; N, 4.65. Found: C, 58.08; H, 5.79; N, 4.88.

5d. Yield 77%, mp 150°C; IR 3330 (NH), 2213 (CN), 1755 (CO) cm^{-1}; ^1H NMR δ 1.33 (t, $J = 7.0$ Hz, 3H, CH_3), 1.92–2.03 (4s, 12H, $4CH_3CO$), 2.88 (q, 2H, CH_2), 4.08 (m, 2H, 2H-6′), 4.24 (m, 2H, H-5′ and pyridine H-4), 5.16 (m, 2H, H-4′ and H-3′), 5.56 (t, $J = 9.2$ Hz, 1H, H-2′), 6.12 (d, $J_{1'-2'} = 10.5$ Hz, 1H, H-1′), 6.78 (m, 1H, furan H-4), 7.03 (s, 1H, pyridine H-5), 7.58 (m, 1H, furan H-3), 8.05 (dd, 1H, furan H-5), 8.24 (s, 1H, NH): ^{13}C NMR δ 15.8 (CH_3), 20.2–23.8 ($4CH_3CO$), 30.6 (CH_2), 61.7 (C6′), 67.2 (C4′), 68.8 (C2′), 73.0 (C3′), 74.9 (C5′), 80.3 (C1′), 97.3 (C4), 112.9 (C3), 115.4 (CN), 127.0 (furan C4), 140.1 (furan C3), 145.8 (C5), 147.2 (C6), 154.9 (furan C5), 159.4 (furan C2), 162.4 (C2), 169.2–169.8 ($4COCH_3$); MS m/z 562; Anal. Calcd for $C_{26}H_{30}N_2SO_{10}$: C, 55.52; H, 5.34; N, 4.98. Found: C, 55.81; H, 5.47; N, 5.19.

5e. Yield 76%, mp 130°C; IR 3320 (NH), 2214 (CN), 1751 (CO) cm^{-1}; ^1H NMR δ 1.95–2.07 (4s, 12H, $4CH_3CO$), 2.34 (s, 3H, CH_3), 3.84 (s, 3H, OCH_3), 4.03 (m, 2H, 2H-6′), 4.19 (m, 2H, H-5′ and pyridine H-4), 5.03 (m, 3H, H-4′, H-3′ and H-2′), 6.08 (d, $J_{1'-2'} = 10.5$ Hz, 1H, H-1′), 77.63 (m, 4H, Ar-H and pyridine H-5), 8.18 (s, 1H, NH); ^{13}C NMR δ 18.2 (CH_3), 20.3–27.4 ($4CH_3CO$), 54.9 (OCH_3), 61.3 (C6′), 67.5 (C4′), 70.8 (C2′), 73.9 (C3′), 74.5 (C5′), 83.3 (C1′), 105.7 (C4), 113.4 (C3), 116.9 (CN), 126.4–146.7 (Ar-C), 152.0 (C5), 155.1 (C6), 160.8 (C2), 169.2–169.8 (4 $COCH_3$); MS m/z 588; Anal. Calcd for $C_{28}H_{32}N_2SO_{10}$: C, 57.14; H, 5.44; N, 4.76. Found: C, 57.40; H, 5.63; N, 4.99.

5f. Yield 79%, mp 149°C; IR 3365 (NH), 2222 (CN), 1750 (CO) cm^{-1}; MS m/z 548; Anal. Calcd for $C_{25}H_{28}N_2SO_{10}$: C, 54.74; H, 5.11; N, 5.11. Found: C, 55.07; H, 5.29; N, 5.35.

5g. Yield 75% mp 137°C; IR 3340 (NH), 2210 (CN), 1754 (CO) cm^{-1}; ^1H NMR δ 1.37 (t, $J = 6.6$ Hz, 3H, CH_3), 1.92–2.15 (4s, 12H $4CH_3CO$), 2.88 (q, 2H, CH_2), 3.85 (s, 3H, OCH_3), 4.06 (m, 2H, 2H-6′), 4.42 (m, 2H, H-5′ and pyridine H-4), 5.41 (m, 3H, H-4′, H-3′ and H-2′), 6.13 (d, $J_{1'-2'} = 10.4$ Hz, 1H, H-1′), 7.48 (m, 4H, Ar-H and 1H, pyridine H-5), 8.13 (s, 1H, NH); ^{13}C NMR δ 15.4 (CH_3), 20.3–23.7 ($4CH_3CO$), 27.2 (CH_2), 55.1 (OCH_3), 61.3 (C6′), 66.3 (C4′), 67.6 (C2′), 71.0 (C3′), 74.1 (C5′), 80.7 (C1′), 105.7 (C4), 114.0 (C3), 115.1 (CN), 127.3–138.0 (Ar-C), 152.3 (C5), 159.6 (C6), 161.7 (C2), 169.3–169.9 (4 $COCH_3$); MS m/z 602; Anal. Calcd for $C_{29}H_{34}N_2SO_{10}$: C, 57.81; H, 5.65; N, 4.65. Found: C, 58.20; H, 5.81; N, 4.93.

5h. Yield 78% mp 167°C; IR 3370 (NH), 2208 (CN), 1746 (CO) cm^{-1}; ^1H NMR δ 1.34 (t, $J = 6.4$ Hz, 3H, CH_3), 1.93–2.16 (4s, 12H $4CH_3CO$), 2.90 (q, 2H, CH_2), 4.04 (m, 2H, 2H-6′), 4.42 (m, 2H, H-5′ and pyridine H-4), 5.26 (t, $J = 9.7$ Hz, 1H, H-4′), 5.52 (m, 2H, H-3′ and H-2′), 6.14 (d, $J_{1'-2'} = 10.6$ Hz, 1H, H-1′), 6.76 (m, 1H, furan H-4), 7.12 (s, 1H, pyridine H-5), 7.59 (m, 1H, furan H-3), 8.01 (dd, 1H, furan H-5), 8.34 (s, 1H, NH); ^{13}C NMR δ 15.8 (CH_3), 20.6–23.8 ($4CH_3CO$), 30.7 (CH_2), 61.5 (C6′), 66.9 (C4′), 67.6 (C2′), 70.9 (C3′), 74.1 (C5′), 80.7 (C1′), 103.5

(C4), 113.0 (C3), 115.0 (CN), 123.4 (furan C4), 140.8 (furan C3), 146.1 (C5), 150.0 (C6), 154.9 (furan C5), 159.3 (furan C2), 162.6 (C2), 169.3–169.9 (4 $COCH_3$); MS m/z 562; Anal. Calcd for $C_{26}H_{30}N_2SO_{10}$: C, 55.52; H, 5.34; N, 4.98. Found: C, 55.77; H, 5.50; N, 5.29.

3-Cyano-2-(β-D-glycopyranosylthio)-1,4-dihydropyridines (7a-h)

General Procedure for Nucleoside Deacylation. Dry gaseous ammonia was passed through a solution of acetylated glycosides **5** (0.5 gm) in dry methanol (10 mL) at 0°C for about 0.5 h. The reaction mixture was stirred at 0°C until complete as shown by TLC (10 to 12 h), using chloroform-methanol (19 : 1 v/v) (Rf 0.68–0.70 region). The resulting mixture was then concentrated under reduced pressure to afford a solid residue that was crystallized from methanol-ether at 0°C to furnish the title compounds **7.**

7a. Yield 87%, mp 189°C; IR 3620–3180 (OH and NH), 2215 (CN) cm^{-1}; ^1H NMR δ 2.39 (s, 3H, CH_3), 3.24–3.98 (m, 6H, 2H-6′, H-5′-H-4′, H-3′, H-2′ and 1H, pyridine H-4), 4.52 (m, 2H, 2′-OH and 3′-OH), 5.08 (m, 2H, 4′-OH and 6′-OH), 5.68 (d, $J_{1'-2'} = 9.9$ Hz, 1H, H-1′), 7.39 (m, 4H, Ar-H and 1H, pyridine H-5), 8.14 (s, 1H, NH); MS m/z 420; Anal. Calcd for $C_{20}H_{24}N_2SO_6$: C, 57.14; H, 5.71; N, 6.67. Found: C, 57.40; H, 5.89; N, 6.93.

7b. Yield 86%, mp 196°C IR 3630–3200 (OH and NH), 2218 (CN) cm^{-1}; ^1H NMR δ 2.39 (s, 3H, CH_3), 3.36–3.96 (m, 6H, 2H-6′, H-5′-H-4′, H-3′, H-2′ and 1H, pyridine H-4), 4.60 (m, 2H, 2′-OH and 3′-OH), 5.18 (m, 2H, 4′-OH and 6′-OH), 5.70 (d, $J_{1'-2'} = 9.7$ Hz, 1H, H-1′), 6.81 (m, 1H, furan H-4), 7.05 (s, 1H, pyridine H-5), 7.53 (m, 1H, furan H-3), 8.07 (dd, 1H, furan H-5), 8.44 (s, 1H, NH); ^{13}C NMR δ 19.1 (CH_3), 60.7 (C6′), 69.7 (C4′), 71.7 (C2′), 78.6 (C3′), 81.6 (C5′), 83.6 (C1′), 104.8 (C4), 113.0 (C3), 115.8 (CN), 120.1 (furan C4), 139.8 (furan C3), 141.8 (C5), 146.7 (C6), 147.9 (furan C5), 153.0 (furan C2), 162.1 (C2); MS m/z 380; Anal. Calcd for $C_{17}H_{20}N_2SO_6$: C, 53.68; H, 5.26; N, 7.37. Found: C, 54.05; H, 5.49; N, 7.60.

7c. Yield 88%, mp 200°C; IR 3660–3240 (OH and NH), 2213 (CN) cm^{-1}; ^1H NMR δ 1.29 (t, $J = 6.5$ Hz, 3H, CH_3), 2.86 (q, 2H, CH_2), 3.25–4.07 (m, 6H, 2H-6′, H-5′, H-4′, H-3′, H-2′ and 3H, OCH_3 and 1H, pyridine H-4), 4.47 (s, 1H, 2′-OH), 5.18 (m, 3H, 3′-OH, 4′-OH and 6′-OH), 5.64 (d, $J_{1'-2'} = 9.5$ Hz, 1H, H-1′), 7.36 (m, 4H, Ar-H and 1H, pyridine H-5), 8.20 (s, 1H, NH); ^{13}C NMR δ 15.8 (CH_3), 24.9 (CH_2), 55.2 (OCH_3), 60.7 (C6′), 69.7 (C4′), 71.8 (C2′), 78.6 (C3′), 81.5 (C5′), 83.6 (C1′), 105.1 (C4), 114.0 (C3), 115.9 (CN), 126.5–152.8 (Ar-C), 156.3 (C5), 159.6 161.8 (C2); MS m/z 434; Anal. Calcd for $C_{21}H_{26}N_2SO_6$: C, 58.06; H, 5.99; N, 6.45. Found: C, 58.33; H, 6.16; N, 6.69.

7d. Yield 85%, mp 205°C IR 3680–3210 (OH and NH), 2212 (CN) cm^{-1}; ^1H NMR δ 1.28 (t, $J = 6.6$ Hz, 3H, CH_3), 2.86 (q, 2H, CH_2), 3.22–4.06 (m, 6H, 2H-6′, H-5′, H-4′, H-3′, H-2′ and 1H, pyridine H-4), 4.45 (t, $J = 7.2$ Hz, 1H, 2′-OH), 5.04 (d, $J = 6.9$ Hz, 1H, 3′-OH), 5.22 (d, $J = 9.0$ Hz, 1H, 4′-OH), 5.43 (d, $J = 7.6$

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Hz, 1H, 6′-OH), 5.62 (d, $J_{1'-2'} = 9.9$ Hz, 1H, H-1′), 6.80 (m, 1H, furan H-4), 7.01 (s, 1H, pyridine H-5), 7.52 (d, 1H, furan H-3), 8.04 (m, 1H, furan H-5), 8.36 (s, 1H, NH); ^{13}C NMR δ 15.6 (CH_3), 24.0 (CH_2), 60.6 (C6′), 69.6 (C4′), 71.7 (C2′), 72.4 (C3′), 78.5 (C5′), 83.6 (C1′), 102.9 (C4), 111.8 (C3), 115.3 (CN), 126.1 (furan C4), 140.5 (C5), 146.4 (C6), 147.8 (furan C5), 157.2 (furan C2), 162.5 (C2); MS m/z 394; Anal. Calcd for $C_{18}H_{22}N_2SO_6$: C, 54.82; H, 5.58; N, 7.11. Found: C, 55.17; H, 5.80; N, 7.43.

7e. Yield 86%, mp 194°C; IR 3630–3190 (OH and NH), 2210 (CN) cm^{-1}; ^{1}H NMR δ 2.41 (s, 3H CH_3), 3.40–4.02 (m, 6H, 2H-6′, H-5′, H-4′, H-3′, H-2′ and 3H, OCH_3 and 1H, pyridine H-4), 4.82 (M, 3H, 2′-OH, 3′-OH and 4′-OH), 5.06 (s, 1H, 6′-OH), 5.60 (d, $J_{1'-2'} = 10.1$ Hz, 1H, H-1′), 7.35 (m, 4H, Ar-H and 1H, pyridine H-5), 8.08 (s, 1H, NH); ^{13}C NMR δ 19.0 (CH_3), 55.4 (OCH_3), 60.5 (C6′), 68.3 (C4′), 70.2 (C2′), 74.9 (C3′), 79.9 (C5′), 84.7 (C1′), 102.0 (C4), 113.6 (C3), 115.9 (CN), 125.8-152.9 (Ar-C), 156.9 (C5), 158.1 (C6), 161.9 (C2); MS m/z 420; Anal. Calcd for $C_{20}H_{24}N_2SO_6$: C, 57.14; H, 5.71; N, 6.67. Found: C, 57.53; H, 5.90; N, 6.94.

7f. Yield 85%, mp 190°C; IR 3700-3260 (OH and NH), 2220 (CN) cm^{-1}; MS m/z 380; Anal. Calcd for $C_{17}H_{20}N_2SO_6$: C, 53.68; H, 5.26; N, 7.37. Found: C, 54.11; H, 5.43; N, 7.75.

7g. Yield 88%, mp 188°C; IR 3600–3200 (OH and NH), 2214 (CN) cm^{-1}; ^{1}H NMR δ 1.28 (t, $J = 6.2$ Hz, 3H, CH_3), 2.86 (q, 2H, CH_2), 3.42–3.98 (m, 6H, 2H-6′, H-5′, H-4′, H-3′, H-2′ and 3H, OCH_3 and 1H, pyridine H-4), 4.50 (d, $J = 8.8$ Hz, 2H, 2′-OH and 3′-OH), 5.60 (d, $J_{1'-2'} = 10.1$ Hz, 1H, H-1′), 7.40 (m, 4H, Ar-H and 1H, pyridine H-5), 8.17 (s, 1H, NH); ^{13}C NMR δ 17.9 (CH_3), 24.5 (CH_2), 55.2 (OCH_3), 60.2 (C6′), 68.3 (C4′), 68.7 (C2′), 75.0 (C3′), 79.6 (C5′), 84.1 (C1′), 105.1 (C4), 114.0 (C3), 115.9 (CN), 126.4-152.8 (Ar-C), 156.4 (C5), 159.6 (C6), 162.0 (C2); MS m/z 434; Anal. Calcd for $C_{21}H_{26}N_2SO_6$: C, 58.06; H, 5.99; N, 6.45. Found: C, 58.44; H, 6.26; N, 6.78.

7h. Yield 86%, mp 218°C; IR 3680–3200 (OH and NH), 2215 (CN) cm^{-1}; MS m/z 394; Anal. Calcd for $C_{18}H_{22}N_2SO_6$: C, 54.82; H, 5.58; N, 7.11. Found: C, 55.17; H, 5.69; N, 7.38.

(2,3,4,6-Tetra-*O*-acetyl-β-D-glycopyranosylthio)-3-aryl-2-cyanoacryl imidates (9)

To a solution of 3-aryl-2-cyano(thioacrylamides) 1 (0.01 mol) in aqueous KOH [0.56 gm (0.01 mol) in 6 mL of distilled water], a solution of 2,3,4,6-tetra-*O*-acetyl-α-D-glycopyranosyl bromide 4 (0.011 mol) in 30 mL of acetone was added. The reaction mixture was stirred at room temperature until complete (TLC, one hour), then evaporated under reduced pressure and the residue was washed with distilled water to remove KBr. The resulting product was dried and crystallized from chloroform-petroleum ether 40-60 to give the title compounds **9**.

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9a. Yield 82%, mp 178°C; IR 2224 (CN), 1752 (CO ester of glucose) cm^{-1}; ^1H NMR δ 1.82–2.08 (4s, 12H, $4CH_3CO$), 3.90 (s, 3H, OCH_3), 4.12 (m, 3H, 2H-6′ and H-5′), 4.94 (m, 3H, H-4′, H-3′ and H-2′), 5.48 (d, $J_{1'-2'} = 9.0$ Hz, 1H, H-1′), 6.96 (s, 1H, CH), 7.18 (d, 2H, Ar-H), 8.12 (d, 2H, Ar-H), 10.02 (s, 1H, NH); MS m/z 548; Anal. Calcd for $C_{25}H_{28}N_2SO_{10}$: C, 54.74; H, 5.11; N, 5.11. Found: C, 55.08; H, 5.26; N, 5.34.

9e. Yield 81%, mp 164°C; IR 2228 (CN), 1756 (CO ester of galactose) cm^{-1}; ^1H NMR δ 1.90–2.12 (4s, 12H $4CH_3CO$), 3.88 (s, 3H, OCH_3), 4.08 (m, 3H, 2H-6′ and H-5′), 4.58 (m, 1H, H-4′), 5.14 (m, 2H, H-3′ and H-2′), 5.40 (d, $J_{1'.2'} = 9.2$ Hz, 1H, H-1′), 7.68 (m, 1H, CH and 4H, Ar-H), 9.98 (s, 1H, NH); MS m/z 548; Anal. Calcd for $C_{25}H_{28}N_2SO_{10}$: C, 54.74; H, 5.11; N, 5.11. Found: C, 54.91; H, 5.28; N, 5.35.

3-Cyano-2-(2,3,4,6-tetra-*O*-acetyl-β-D-glycopyranosylthio) pyridines (10)

Method A. 3-Cyano-1,4-dihydropyridine-2-thioglycosides **5** (0.01 mol) were heated at reflux in dry ethanol (30 mL) with stirring under anhydrous condition for three minutes, and then allowed to stand overnight. The resulting solid product was collected by filtration and crystallized from ethanol to afford the title compounds **10**.

Method B. A mixture of **9** (0.01 mol) and **2** (0.01 mol) was dissolved in dry ethanol (30 mL), a few drops of piperidine were then added. The mixture was heated at 60°C for 3 h, and then allowed to stand overnight. The resulting solid product was collected by filtration and crystallized from ethanol.

10a. Yield 78%, mp 166°C; IR 2215 (CN), 1755 (CO) cm^{-1}; ^1H NMR δ 1.94–2.04 (4s, 12H, $4CH_3CO$), 2.60 (s, 3H, CH_3), 3.85 (s, 3H,OCH_3), 4.02 (m, 2H, 2H-6′), 4.18 (m, 1H, H-5′), 5.05 (t, $J = 9.6$ Hz, 1H, H-4′), 5.20 (t, $J = 9.3$ Hz, 1H, H-3′), 5.55 (t, $J = 9.7$ Hz, 1H, H-2′), 6.15 (d, $J_{1'-2'} = 10.4$ Hz, 1H, H-1′), 7.14 (d, 2H, Ar-H), 7.32 (s, 1H, pyridine H-5), 7.68 (d, 2H, Ar-H); MS m/z 586; Anal. Calcd for $C_{28}H_{30}N_2SO_{10}$: C, 57.33; H, 5.12; N, 4.78 Found: C, 57.58; H, 5.26; N, 4.99.

10e. Yield 77%, mp 162°C; IR 2218 (CN), 1752 (CO) cm^{-1}; ^1H NMR δ 1.96–2.08 (4s, 12H, $4CH_3CO$), 2.62 (s, 3H, CH_3), 3.90 (s, 3H, OCH_3), 4.05 (m, 2H, 2H-6′), 4.28 (t, $J = 8.5$ Hz, 1H, H-5′), 5.21 (m, 1H, H-4′), 5.39 (d, $J = 8.9$ Hz, 1H, H-3′), 5.54 (m, 1H, H-2′), 6.14 (d, $J_{1'-2'} = 10.5$ Hz, 1H, H-1′), 77.12 (d, 2H, Ar-H), 7.26 (s, 1H, pyridine H-5), 7.69 (d, 2H, Ar-H); ^{13}C NMR δ 15.4 (CH_3), 20.2-23.7 ($4CH_3CO$), 55.3 (OCH_3), 61.3 (C6′), 66.2 (C4′), 67.5 (C2′), 70.9 (C3′), 74.0 (C5′), 80.6 (C1′), 114.0 (C3), 115.5 (CN), 127.3-133.2 (Ar-C), 151.5 (C5), 153.7 (C4), 159.6 (C6), 161.7 (C2), 169.3–169.9 ($4COCH_3$); MS m/z 586; Anal. Calcd for $C_{28}H_{30}N_2SO_{10}$: C, 57.33; H, 5.12; N, 4.78. Found: C, 57.60; H, 5.35; N, 5.07.

3-Cyano-2-(β-D-glycopyranosylthio) pyridines (11)

Dry gaseous ammonia was passed through a solution of protected glycosides **10** (0.5 gm) in dry methanol (20 mL) at 0°C for about 0.5 h, then the reaction mixture

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was stirred at room temperature until TLC indicated complete conversion (4 to 6 h). The resulting reaction mixture was subsequently concentrated under reduced pressure at 40°C to afford a solid residue which was crystallized from methanol to furnish the title compounds **11**.

11a. Yield 89%, mp 200°C; IR 3650–3200 (OH), 2216 (CN) cm^{-1}; MS m/z 418; Anal. Calcd for $C_{20}H_{22}N_2SO_6$: C, 57.42; H, 5.26; N, 6.70. Found: C, 57.69; H, 5.51; N, 6.94.

11e. Yield 87%, mp 212°C; IR 3600–3160 (OH), 2218 (CN) $cm^{-1;}$ ^{1}H NMR δ 2.56 (s, 3H, CH_3), 3.34–3.80 (m, 6H, 2H-6′, H-5′, H-4′, H-3′ and H-2′), 3.84 (s, 3H, OCH_3), 4.52 (m, 2H, 2′-OH and 3′-OH), 4.96 (d, $J = 9.4$ Hz, 1H, 4′-OH), 5.36 (d, $J = 9.7$ Hz, 1H, 6′-OH), 5.56 (d, $J_{1'-2'} = 10.3$ Hz, 1H, H-1′), 7.08 (d, 2H, Ar-H), 7.25 (s, 1H, pyridine H-5), 7.60 (d, 2H, Ar-H); MS m/z 418; Anal. Calcd for $C_{20}H_{22}N_2SO_6$: C, 57.42; H, 5.26; N, 6.70. Found: C, 57.74; H, 5.48; N, 6.98.

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