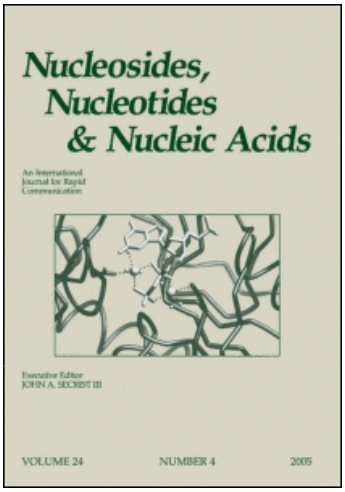

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SYNTHESIS AND BIOLOGICAL EVALUATION OF *S*-GLYCOSYLATED PYRIDINES

Adel M. E. Attia[a]
[a] Department of Chemistry, Faculty of Education, University of Tanta (Kafr El-Sheikh Branch), Kafr El-Sheikh, Egypt

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SYNTHESIS AND BIOLOGICAL EVALUATION OF *S*-GLYCOSYLATED PYRIDINES

Adel M. E. Attia

Department of Chemistry, Faculty of Education, University of Tanta (Kafr El-Sheikh Branch), Egypt

ABSTRACT

The formation of thioglycosides **7a-j** and **10a-j** via the reaction of sodium salts of thiopyridines **3a-e** with glycosyl bromides **6a,b** has been studied. Comparison with the products obtained from silylated thiopyridines **8a-e** and peracetylated sugars **9a,b** is made. ^{13}C NMR was utilized to elucidate the proposed structures of the products.

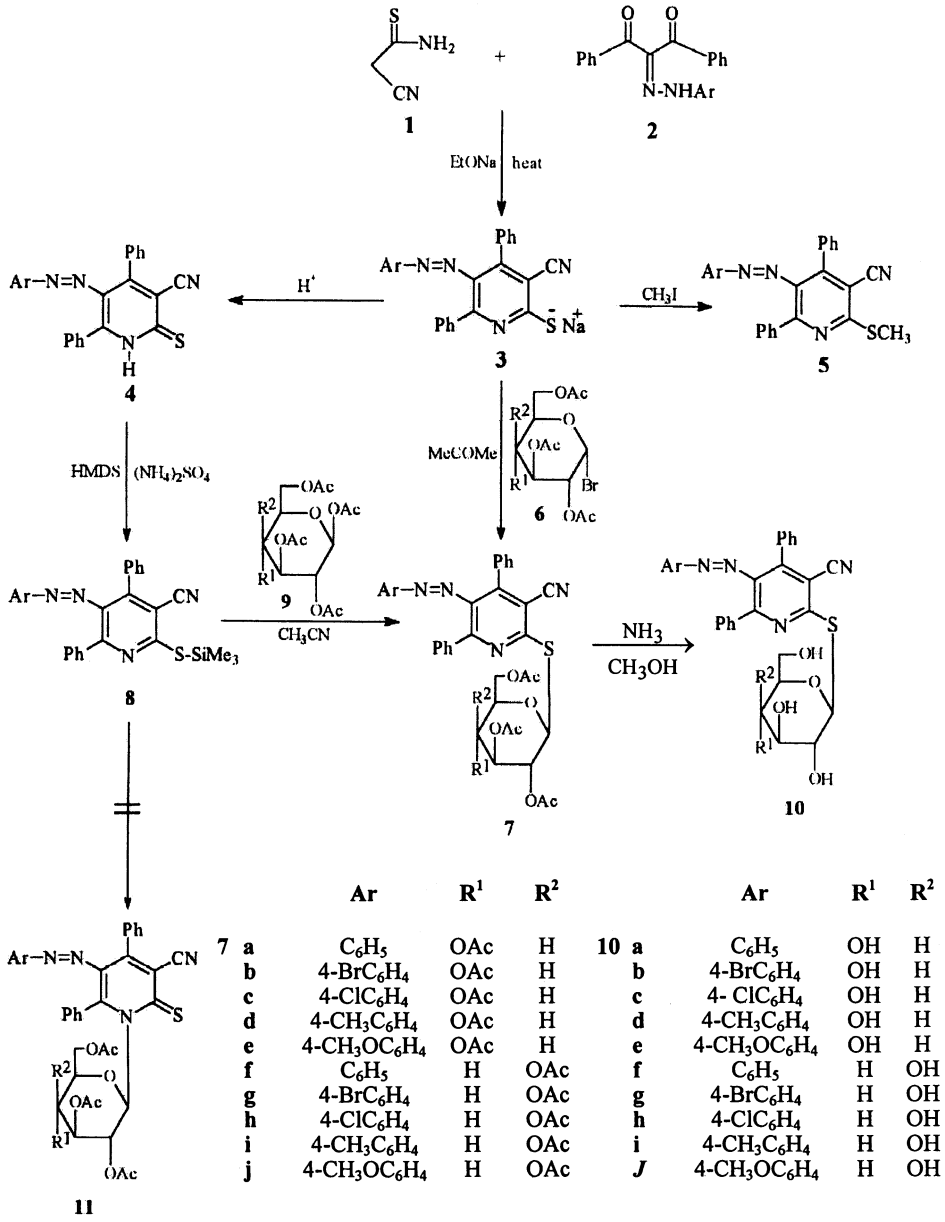
INTRODUCTION

Various nucleoside analogues are well-known as important agents in the field of chemotherapy of cancer and viral diseases. Among them, 1-β-D-arabinosylcytosine[1] for the treatment of acute myeloblastic leukemia and 3′-deoxy-3′-azidothymidine[2], dideoxycytidine[3] and dideoxy inosine[4] for the treatment of acquired immunodeficiency syndrome (AIDS). A new class of anti-HIV agents including 1-[(2-hydroxyethoxy)-methyl]-6-(phenylthio)thymine (HEPT) and 1-(benzoyloxymethyl)-5-ethyl-6-(phenylthio)uracil (BEPU), has been identified[5–7]. Such compounds show a high selectivity for the HIV-1 reverse transcriptase. Other active nucleosides related to HEPT and BEPU, like pyridine and pyrimidine glycosides were recently reported, and some of these compounds look promising as anti-HIV agents[8–11]. As an extension of our work on thiopyridine glycosides, we report herein a synthesis of a new class of unnatural nucleosides, 2-(β-D-glycopyranosylthio)pyridines. In addition, we have tested these glycosides against HIV.

CHEMISTRY

5-Arylazo-3-cyanopyridine-2(1*H*)-thiones (**4**) were prepared in high yields in two steps from the reaction of cyanothioacetamide (**1**) with 2-arylhydrazono-1,3-diphenylpropane-1,3-dione (**2**) according to reported procedures[12]. The sodium salts **3** could be isolated from the reaction whose acidification gave **4**. A model study on the alkylation of **3** and/or **4** was carried out using iodomethane by the reaction of one mole of alkylating agent directly with the sodium salts of 5-arylazo-3-cyanopyridine-2(1*H*)-thiones **3** or the reaction with **4** in the presence of sodium hydroxide in dry DMF whereby the same products **5** were obtained in each case (Chart 1). The structures of compounds **5** were confirmed by their elemental analyses and spectral data. The ^{1}H NMR spectrum of **5a** showed a band at δ 2.62 assigned to S-CH_3 group, and its ^{13}C NMR showed signals at δ 24 (S-CH_3) and 163 (C-2). These data as well as the mode of the reaction indicated that the site of alkylation was the sulphur rather than the nitrogen. Compounds **4** bearing a latent functional substituent were found useful for the synthesis of interesting *S*-glycoside derivatives. Thus, it has been found that compounds **3** react with 2, 3, 4, 6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide or its α-D-galactopyranosyl isomer **6** in acetone to give *S*-glycosylated pyridines **7**a-j (Chart 1). Compound **7** could also be obtained in good yields by the reaction of **4** with glycosyl bromides **6** in the presence of aqueous potassium hydroxide. The structures of the reaction products **7a-j** were established and confirmed by their elemental analyses and spectral data (MS, IR, ^{1}H NMR, ^{13}C NMR). The analytical data for **7e** revealed a molecular ion corresponding to (M^+ 752). The ^{1}H NMR spectrum showed a doublet at δ 6.20 (J = 10.63 Hz) assigned to the anomeric proton of the glucose moiety with a diaxial orientation of H-1′ and H-2′ indicating the β-configuration and $^4C_1$ conformation.

The other protons of the glucopyranose ring resonate at δ 4.02-5.68, while the four acetoxy groups appear as four singlets in the 1.76-2.05 region providing further verification of the $^4C_1$ (D) conformation with β-configuration, since these signals lie within the range expected for equatorial secondary acetoxy groups. Although the coupling of **3** with **6** could also give the corresponding *N*-glycosides **11**, the formation of **7e** was proven using ^{13}C NMR which revealed the absence of the thione carbon at δ 178 and appearance of C-2 carbon at δ 162.8 of the same value of the corresponding *S*-methyl derivative **5e**. Ammonolysis of mononucleosides **7a-j** furnished the corresponding 2-(β-D-glycopyranosylthio)pyridines **10a-j** in yields of 84–87%. TLC of the free thioglycosides **10** showed that single compounds were produced, and their structures were further confirmed by elemental analyses and spectral data. The analytical data for **10f** reveal the molecular ion corresponding to (M^+ 554). The ^{1}H NMR spectrum of **10f** showed the anomeric proton as a doublet at δ 5.64 (J = 10.27 Hz), indicating the presence of only the β-D-galactopyranose, while the signals of the four hydroxy groups of the galactose moiety resonated



		Ar	R^1	R^2
7	a	C_6H_5	OAc	H
	b	4-BrC_6H_4	OAc	H
	c	4-ClC_6H_4	OAc	H
	d	4-$CH_3C_6H_4$	OAc	H
	e	4-$CH_3OC_6H_4$	OAc	H
	f	C_6H_5	H	OAc
	g	4-BrC_6H_4	H	OAc
	h	4-ClC_6H_4	H	OAc
	i	4-$CH_3C_6H_4$	H	OAc
	j	4-$CH_3OC_6H_4$	H	OAc

		Ar	R^1	R^2
10	a	C_6H_5	OH	H
	b	4-BrC_6H_4	OH	H
	c	4- ClC_6H_4	OH	H
	d	4-$CH_3C_6H_4$	OH	H
	e	4-$CH_3OC_6H_4$	OH	H
	f	C_6H_5	H	OH
	g	4-BrC_6H_4	H	OH
	h	4-ClC_6H_4	H	OH
	i	4-$CH_3C_6H_4$	H	OH
	J	4-$CH_3OC_6H_4$	H	OH

Chart 1.

at δ 4.62-5.40 (exchangeable by D_2O). The ^{13}C NMR spectrum of **10**f was characterized by a signal at δ 84.3 corresponding to the C-1′ atom of β-D-galactopyranose. Another five signals at δ 60.8, 63.7, 68.6, 74.8 and 80.1 were assigned to C-6′, C-4′, C-2′, C-3′ and C-5′ respectively, while the C-2 of aglycone appear at δ 161.9. With this pyridine thioglycosides as model, it was

decided to synthesize these compounds with the silylation method and comparing the products for stereochemical consideration. Thus, in a simple experimental procedure, silylation of thiopyridines **4** followed by a Lewis acid-catalyzed reaction of the resultant silylthiopyridines **8** with pentaacetyl-β-D-glycopyranose **9** afforded the *S*-glycosyl compounds **7**, which were shown to be the same as those obtained from the reaction of **3** with **6** by their melting points and spectral data. A suggested mechanism for the formation of the *S*-glycosides **7** by the silylation method is illustrated in chart 2. In summary, the glycosides obtained by these syntheses seem promising as potential substrates for the preparation of other carbohydrate derivatives as deoxy, amino and azido nucleosides.

Cytotoxicity of thioglycosides **7** and **10** against different types of tumor viruses and Human Immunodeficiency virus HIV-1 in MT-4 cells in vitro was examined[13]. None of these nucleosides showed any significant cytotoxicity up to 100 μg/mL. None of these nucleosides showed substantial anti-HIV activity.

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 spectra were recorded by EI on a Varian Mat 311A spectrometer and FAB on a Kratos MS 50 spectrometer. Analytical data were obtained from the Microanalytical Center at Qatar University.

Sodium salts of 5-arylazo-3-cyanopyridine-2(1*H*)-thiones (3). A mixture of cyanothioacetamide (**1**) (0.01 mol) and 2-arylhydrazono-1, 3-diphenyl-propane-1,3-dione (**2**) (0.01 mol) was dissolved in ethanol (30 mL) containing sodium ethoxide (0.68 g, 0.01 mol). The mixture was refluxed for 6 h, and then allowed to stand overnight. The resultant precipitate was isolated by filtration and crystallized from the appropriate solvent to give the solid products **3**.

5-Arylazo-3-cyanopyridine-2(1*H*)-thiones (4). The sodium salt **3** was dissolved in water at 80°C, filtered and neutralized with cold dilute hydrochloric acid. The resulting solid product was collected by filtration and washed with distilled water to remove sodium chloride. The product was dried prior to crystallization from EtOH-DMF to afford the products **4**[12].

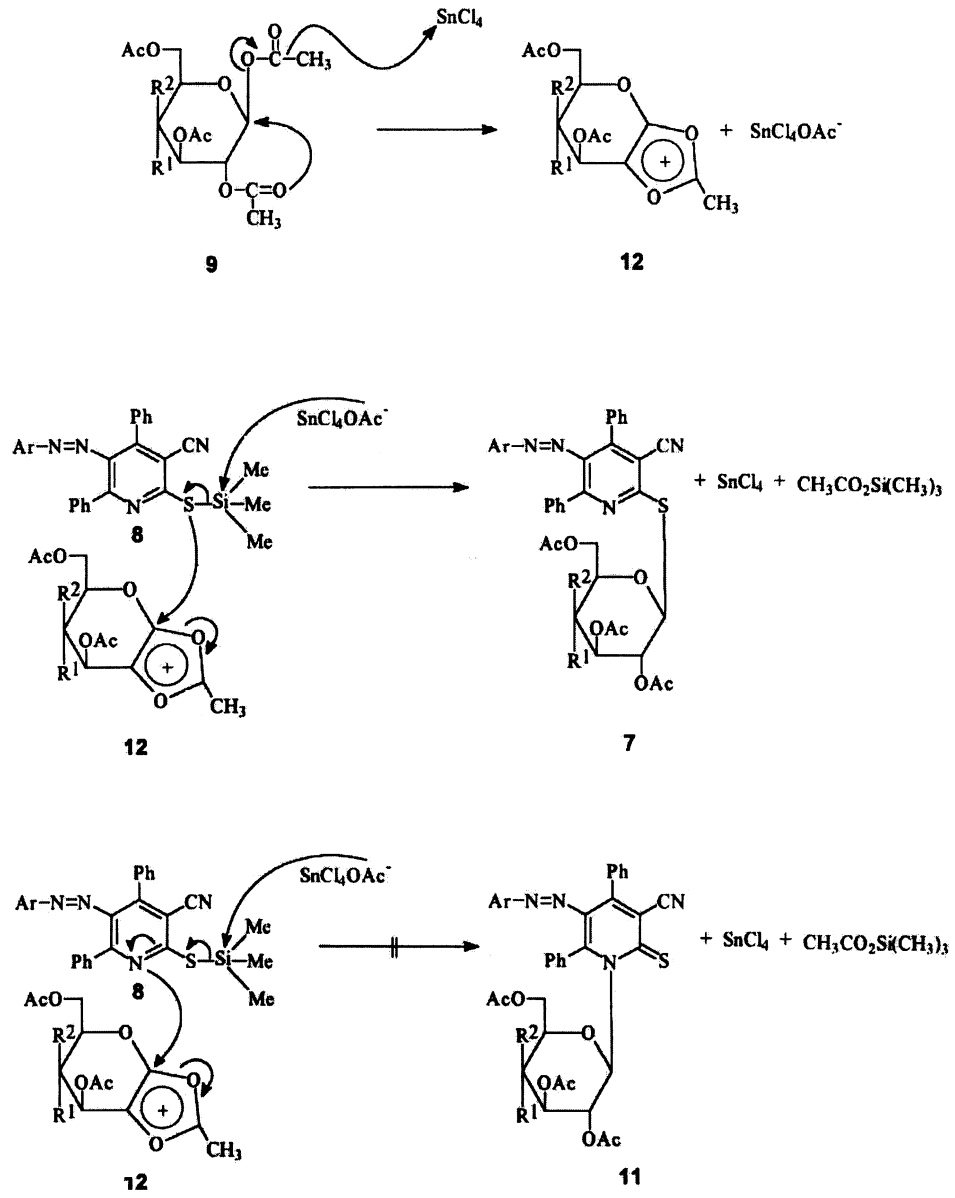


Chart 2.

5-Arylazo-3-cyano-2-methylthiopyridines (5).

Method A: The sodium salt **3** (0.01 mol) was suspended in ethanol (30 mL). An excess of methyl iodide (0.015 mol) was then added dropwise to the resulting suspension. The precipitate obtained after 4 h of stirring at room temperature was filtered off and crystallized from ethanol to afford the products **5**.

Method B: A mixture of **4** (0.01 mol), NaOH (0.4 g, 0.01 mol) and methyl iodide (0.015 mol) in dry DMF (30 mL) was stirred at room temperature for 12 h and then diluted with cold water (100 mL). The resulting solid product was collected by filtration and crystallized from ethanol to give the products **5**.

5a: Yield 53%, mp 138°C; IR 2212(CN) cm^{-1}; ^1H NMR δ 2.62(s, SCH_3), 7.40-7.98(m, Ar-H); ^{13}C NMR δ 24.0(SCH_3), 106.8-158.2(Ar-C), 163.0(C-2); MS (ionization method): m/z 406(M^+); Anal. Calcd for $C_{25}H_{18}N_4S$: C, 73.89; H, 4.43; N, 13.79. Found: C, 74.11; H, 4.60; N, 13.98.

5b: Yield 51%, mp 131°C; IR 2210(CN) cm^{-1}; MS (ionization method): m/z 485 (M^+); Anal. Calcd for $C_{25}H_{17}N_4SBr$: C, 61.85; H, 3.50; N, 11.55. Found: C, 62.14; H, 3.12; N, 11.70.

5c: Yield 50%, mp 122°C; IR 2214(CN) cm^{-1}; MS (ionization method): m/z 440 (M^+); Anal. Calcd for $C_{25}H_{17}N_4SCl$: C, 68.10; H, 3.86; N, 12.71. Found: C, 68.27; H, 4.04; N, 12.96.

5d: Yield 52%, mp 142°C; IR 2218(CN) cm^{-1} MS (ionization method): m/z 420 (M^+); Anal. Calcd for $C_{26}H_{20}N_4S$: C, 74.28; H, 4.76; N, 13.33. Found: C, 74.52; H, 4.89; N, 13.48.

5e: Yield 54%, mp 129°C; IR 2215(CN) cm^{-1}; ^1H NMR δ 2.58(s, SCH_3), 3.88(s, OCH_3), 7.62-8.00(m, Ar-H);^{13}C NMR δ 23.8(SCH_3), 55.6 (OCH_3), 107.0–157.5(Ar-C), 162.9(C-2); MS (ionization method): m/z 436 (M^+); Anal. Calcd for $C_{26}H_{20}N_4SO$: C, 71.56; H, 4.59; N, 12.84. Found: C, 71.68; H, 4.71; N, 12.95.

3-Cyano-2-(2,3,4,6-Tetra-*O*-acetyl-β-D-glycopyranosylthio)-pyridines (7).

General coupling procedures: Method A: To a solution of pyridinethione sodium salts **3a-e** (0.01 mol) in acetone (10 mL), a solution of 2,3,4,6-tetra-*O*-acetyl-α-D-glycopyranosyl bromide **6** (0.011 mol) in acetone (20 mL) was added. The reaction mixture was stirred at room temperature until judged to be complete by TLC (1 to 2 h), using chloroform:ether 4:1, v/v (Rf 0.70–0.74 region). The mixture was evaporated under reduced pressure at 40°C and the crude glycoside was washed with distilled water to remove the formed sodium bromide. The product was dried prior to crystallization from ethanol to afford the products **7a-j**.

Method B: To a solution of 2(1*H*)-pyridinethiones **4** (0.01 mol) in aqueous potassium hydroxide (0.56 g, 0.01 mol, in 6 mL of distilled water) was added a solution of 2, 3, 4, 6-tetra-*O*-acetyl-α-D-glycopyranosyl bromide **6** (0.011 mol) in acetone (30 mL). The reaction mixture was stirred at room temperature until judged to be complete by TLC (1 to 2 h) then processed as described above.

Method C: 3-Cyano-2(1*H*)-pyridinethiones **4** (0.01 mol) were heated under reflux, with stirring, under anhydrous conditions for 48 hours with

hexamethyldisilazane (25 mL) and $(NH_4)_2SO_4$ (0.02 g). The excess of HMDS was removed under diminished pressure, providing the silylated bases **8** as colourless oils. To a solution of silylated base in dry MeCN (30 mL) was added a solution of β-D-glucose- or β-D-galactose-pentaacetate (0.011 mol) in dry MeCN (10 mL), followed by $SnCl_4$ (1.6 mL). The reaction mixture was stirred at room temperature until reaction was judged complete by TLC, then poured into saturated $NAHCO_3$ solution and extracted with $CHCl_3$. The organic layers were dried over $MgSO_4$, filtered and concentrated to give the crude nucleosides which were purified by recrystallization from ethanol to afford the products **7a-j**.

7a: Yield 73%, mp 116°C; IR 2210(CN), 1750 (CO) cm^{-1}; ^1H NMR δ 1.91-2.16(4s, $4CH_3CO$), 4.09(m, 2H-6′), 4.63(m, H-5′), 5.03(t, H-4′), 5.26(t, H-3′), 5.68(t, H-2′), 6.22(d, $J = 10.26$ Hz, H-1′), 7.20-8.01(m, Ar-H); MS (ionization method): m/z 722(M^+); Anal. Calcd for $C_{38}H_{34}N_4SO_9$: C, 63.16; H, 4.71; N, 7.76. Found: C, 63.33; H, 4.89; N, 7.92.

7b: Yield 67%, mp 127°C; IR 2210(CN), 1750(CO) cm^{-1}; ^1H NMR δ 1.75-2.03(4s, $4CH_3CO$), 4.09(m, 2H-6′ and H-5′), 5.06(t, H-4′), 5.26(t, H-3′), 5.68(t, H-2′), 6.21(d, $J = 9.73$ Hz, H-1′), 7.32-7.74(m, Ar-H); MS (ionization method): m/z 801 (M^+); Anal. Calcd for $C_{38}H_{33}N_4BrSO_9$: C, 56.93; H, 4.12; N, 6.99. Found: C, 57.17; H, 4.28; N, 7.21.

7c: Yield 69%, mp 143°C; IR (2223), 1754(CO) cm^{-1}; MS (ionization method): m/z 756 (M^+); Anal. Calcd for $C_{38}H_{33}N_4ClSO_9$: C, 60.28; H, 4.36; N, 7.40. Found: C, 60.44; H, 4.51; N, 7.63.

7d: Yield 72%, mp 130°C; IR 2222(CN), 1753(CO) cm^{-1}; ^1H NMR δ 1.76-2.08(4s, $4CH_3CO$), 2.31(s, CH_3), 4.12(m, 2H-6′ and H-5′), 5.01(t, H-4′), 5.25(t, H-3′), 5.66(t, H-2′), 6.18(d, $J = 10.62$ Hz, H-1′), 7.24-7.87(m, Ar-H); ^{13}C NMR δ 20.2-20.6($4CH_3CO$), 21.2(CH_3), 62.0(C-6′), 68.8(C-4′), 71.4(C-2′), 72.9(C-3′), 75.0(C-5′), 80.3(C-1′), 107.1(C-3), 114.4(CN), 122.2-156.8(Ar-C), 161.6(C-2), 169.4-169.9(4CO); MS (ionization method): m/z 736(M^+); Anal. Calcd for $C_{39}H_{36}N_4SO_9$: C, 63.59; H, 4.89; N, 7.61. Found: C, 63.81; H, 4.97; N, 7.80.

7e: Yield 74%, mp 118°C; IR 2222(CN), 1755(CO) cm^{-1}; ^1H NMR δ 1.76-2.05(4s, $4CH_3CO$), 3.84(s, OCH_3), 4.02(m, 2H-6′ and H-5′), 4.99(t, H-4′), 5.26(t, H-3′) 5.68(t, H-2′), 6.20(d, $J = 10.63$ Hz, H-1′), 7.18-7.72(m, Ar-H); ^{13}C NMR δ 20.2-20.4($4CH_3CO$), 55.7(OCH_3), 63.7(C-6′), 68.8(C-4′), 72.9(C-2′), 73.5(C-3′), 75.0(C-5′), 81.6(C-1′), 107.1(C-3), 114.6(CN), 124.4-156.5(Ar-C), 162.8(C-2), 169.4-169.9(4CO); MS (ionization method): m/z 752 (M^+); Anal. Calcd for $C_{39}H_{36}N_4SO_{10}$: C, 62.23; H, 4.79; N, 7.45. Found: C, 62.48; H, 4.95; N, 7.73.

7f: Yield 71%, mp 128°C; IR 2222(CN), 1751(CO) cm^{-1}; ^1H NMR δ 1.77-2.09(4s, $4CH_3CO$), 4.08(m, 2H-6′), 4.56(m, H-5′), 5.30(t, H-4′), 5.44(d, H-3′), 5.64(d, H-2′) 6.21(d, $J = 10.84$ Hz, H-1′), 7.24-8.03(m, Ar-H); ^{13}C NMR δ 20.3-20.5($4CH_3CO$), 61.9(C-6′), 66.7(C-4′), 67.8(C-2′), 70.8(C-3′), 74.4(C-5′), 80.7(C-1′), 107.4(C-3), 115.1(CN), 131.9-157.0(Ar-C), 161.9(C-2), 169.4-170.0(4CO); MS (ionization method): m/z 722 (M^+); Anal. Calcd

for $C_{38}H_{34}N_4SO_9$: C, 63.16; H, 4.71; N, 7.76. Found: C, 63.38; H, 4.93; N, 7.99.

7g: Yield 68%, mp 150°C; IR 2210(CN), 1748(CO) cm^{-1}; MS (ionization method): m/z 801 (M^+); Anal. Calcd for $C_{38}H_{33}N_4BrSO_9$: C, 56.93; H, 4.12; N, 6.99. Found: C, 57.11; H, 4.30; N, 7.19.

7h: Yield 70%, mp 138°C; IR 2220(CN), 1746(CO) cm^{-1}; MS (ionization method): m/z 756 (M^+); Anal. Calcd for $C_{38}H_{33}N_4ClSO_9$: C, 60.28; H, 4.36; N, 7.40. Found: C, 60.51; H, 4.48; N, 7.66.

7i: Yield 73%, mp 112°C; IR 2222(CN), 1748(CO) cm^{-1}; ^1H NMR δ 1.74-2.12(4s, $4CH_3CO$), 2.28(s, CH_3), 4.05(m, 2H-6′), 4.37(m, H-5′), 5.28(t, H-4′), 5.40(d, H-3′), 5.62(d, H-2′), 6.18(d, $J = 10.81$ Hz, H-1′), 7.16-8.12(m, Ar-H); ^{13}C NMR δ 20.2-20.5($4CH_3CO$), 21.1(CH_3), 61.2(C-6′), 68.4(C-4′), 69.8(C-2′), 70.8(C-3′), 74.3(C-5′), 80.7(C-1′), 107.3(C-3), 115.2(CN), 122.0-156.2(Ar-C), 162.4(C-2), 169.4-170.0(4CO); MS (ionization method): m/z 736 (M^+); Anal. Calcd for $C_{39}H_{36}N_4SO_9$: C, 63.59; H, 4.89; N, 7.61. Found: C, 63.84; H, 5.00; N, 7.77.

7j: Yield 72%, mp 120°C; IR 2224(CN), 1749(CO) cm^{-1}; ^1H NMR δ 1.90-2.05(4s, $4CH_3CO$), 3.82(s, OCH_3), 4.04(m, 2H-6′), 4.28(m, H-5′), 5.26(t, H-4′), 5.56(d, H-3′), 5.68(d, H-2′), 6.16(d, $J = 10.34$ Hz, H-1′), 7.20-7.79(m, Ar-H); ^{13}C NMR δ 20.2-20.6($4CH_3CO$), 55.5(OCH_3), 62.8(C-6′), 68.2(C-4′), 70.8(C-2′), 78.9(C-3′), 79.4(C-5′), 81.8(C-1′), 107.5(C-3), 114.9 (CN), 124.2-158.6(Ar-C), 162.8(C-2), 169.2-169.9(4CO); MS (ionization method): m/z 752 (M^+); Anal. Calcd for $C_{39}H_{36}N_4SO_{10}$: C, 62.23; H, 4.79; N, 7.45. Found: C, 62.56; H, 4.92; N, 7.60.

3-Cyano-2-(β-D-glycopyranosylthio)pyridines (10).

General procedure for nucleoside deacylation: Dry ammonia gas was passed into a solution of protected nucleosides **7** (0.5 g) in 20 mL of dry methanol at 0°C for 0.5 h. The reaction mixture was stirred until completion as shown by TLC (10–12 h), using chloroform:Methanol 19:1, v:v, (Rf 0.60-62 region). The resulting mixture was then concentrated under reduced pressure at 40°C to afford a solid residue that was crystallized from methanol to furnish the products **10**a-j.

10a: Yield 84%, mp 203°C; IR 3370(OH), 2222(CN) cm^{-1}; ^1H NMR δ 3.15-3.82(m, 2H-6′, H-5′, H-4′, H-3′ and H-2′), 4.62(d, 2′-OH), 4.75(s, 3′-OH), 5.14(d, 4′-OH), 5.29(d, 6′-OH), 5.63(d, $J = 9.34$ Hz, H-1′), 7.25-7.64(m, Ar-H); ^{13}C NMR δ 61.0(C-6′), 69.8(C-4′), 71.5(C-2′), 78.5(C-3′), 82.0(C-5′), 83.8(C-1′), 106.7(C-3), 114.6(CN), 121.9-153.8(Ar-C), 159.6(C-2); MS (ionization method): m/z 554 (M^+); Anal. Calcd for $C_{30}H_{26}N_4SO_5$: C, 64.98; H, 4.69; N, 10.11. Found: C, 65.33; H, 4.82; N, 10.40.

10b: Yield 83%, mp 196°C; IR 3380(OH), 2215(CN) cm^{-1}; MS (ionization method): m/z 633 (M^+); Anal. Calcd for $C_{30}H_{25}N_4BrSO_5$: C, 56.87; H, 3.95; N, 8.85. Found: C, 57.19; H, 4.14; N, 9.09.

10c: Yield 80%, mp 204°C; IR 3370(OH), 2220(CN) cm^{-1}; ^1H NMR δ 3.18-3.76(m, 2H-6′, H-5′, H-4′, H-3′ and H-2′), 4.64(d, 2′-OH), 5.15(d, 3′-OH), 5.30(d, 4′-OH), 5.52(d, 6′-OH), 5.96(d, $J = 8.98$ Hz, H-1′), 7.26-8.00(m, Ar-H); ^{13}C NMR δ 61.6(C-6′), 69.9(C-4′), 72.0(C-2′), 78.2(C-3′), 81.8(C-5′), 83.4(C-1′), 106.8(C-3), 116.6(CN), 123.2-153.9(Ar-C), 159.9(C-2); MS (ionization method): m/z 588 (M^+); Anal. Calcd for $C_{30}H_{25}N_4ClSO_5$: C, 61.17; H, 4.25; N, 9.51. Found: C, 61.50; H, 4.41; N, 9.77.

10d: Yield 85%, mp 193°C; IR 3370(OH), 2222(CN) cm^{-1}; ^1H NMR δ 2.30(s, CH_3), 3.32-3.78(m, 2H-6′, H-5′, H-4′, H-3′ and H-2′), 4.64(d, 2′-OH), 5.06(d, 3′-OH), 5.14(d, 4′-OH), 5.28(d, 6′-OH), 5.62(d, $J = 8.83$ Hz, H-1′), 7.12-7.90(m, Ar-H); ^{13}C NMR δ 21.0(CH_3), 61.9(C-6′), 69.8(C-4′), 71.5(C-2′), 78.5(C-3′), 81.9(C-5′), 83.8(C-1′), 106.6(C-3), 115.2(CN), 122.0-153.6(Ar-C), 159.8(C-2); MS (ionization method): m/z 568 (M^+); Anal. Calcd for $C_{31}H_{28}N_4SO_5$: C, 65.49; H, 4.93; N, 9.86. Found: C, 65.68; H, 5.12; N, 10.09.

10e: Yield 86%, mp 180°C; IR 3360(OH), 2210(CN) cm^{-1}; ^1H NMR δ 3.20-3.84(m, 2H-6′, H-5′, H-4′, H-3′ and H-2′), 3.84(s, OCH_3), 4.63(d, 2′-OH), 4.78(s, 3′-OH), 5.13(d, 4′-OH), 5.27(d, 6′-OH), 5.68(d, $J = 9.70$ Hz, H-1′), 7.20-7.79(m, Ar-H); ^{13}C NMR δ 55.6(OCH_3), 61.0(C-6′), 69.8(C-4′), 71.5(C-2′), 78.5(C-3′), 81.9(C-5′), 83.8(C-1′), 106.6(C-3), 114.6(CN), 124.3-158.0(Ar-C), 162.7(C-2); MS (ionization method): m/z 584 (M^+); Anal. Calcd for $C_{31}H_{28}N_4SO_6$: C, 63.70; H, 4.79; N, 9.59. Found: C, 64.07; H, 4.93; N, 9.81.

10f: Yield 85%, mp 189°C; IR 3360(OH), 2222(CN) cm^{-1}; ^1H NMR δ 3.36-3.84(m, 2H-6′, H-5′, H-4′, H-3′ and H-2′), 4.62(d, 2′-OH), 4.78(s, 3′-OH), 5.06(s, 2′-OH), 5.40(d, 6′-OH), 5.64(d, $J = 10.27$ Hz, H-1′), 7.12-8.14(m, Ar-H); ^{13}C NMR δ 60.8(C-6′), 63.7(C-4′), 68.6(C-2′), 74.8(C-3′), 80.1(C-5′), 84.3(C-1′), 106.7(C-3), 115.1(CN), 121.9-158.3(Ar-C), 161.9(C-2); MS (ionization method): m/z 554 (M^+); Anal. Calcd for $C_{30}H_{26}N_4SO_5$: C, 64.98; H, 4.69; N, 10.11. Found: C, 65.30; H, 4.86; N, 10.29.

10g: Yield 81%, mp 205°C; IR 3360(OH), 2210(CN) cm^{-1}; MS (ionization method): m/z 633 (M^+); Anal. Calcd for $C_{30}H_{25}N_4BrSO_5$: C, 56.87; H, 3.95; N, 8.85. Found: C, 57.10; H, 4.13; N, 8.99.

10h: Yield 83%, mp 200°C; IR 3370(OH), 2218(CN) cm^{-1}; MS (ionization method): m/z 588 (M^+); Anal. Calcd for $C_{30}H_{25}N_4ClSO_5$ C, 61.17; H, 4.25; N, 9.51. Found: C, 61.39; H, 4.36; N, 9.69.

10i: Yield 82%, mp 208°C; IR 3360(OH), 2220 (CN) cm^{-1}; ^1H NMR δ 2.31(s, CH_3), 3.32-3.83(m, 2H-6′, H-5′, H-4′, H-3′ and H-2′), 4.61(d, 2′-OH), 4.79(s, 3′-OH), 5.06(s, 4′-OH), 5.45(d, 6′-OH), 5.63(d, $J = 10.45$ Hz, H-1′), 7.19-8.10(m, Ar-H); ^{13}C NMR δ 21.0(CH_3), 60.8(C-6′), 68.5(C-4′), 68.7(C-2′), 74.9(C-3′), 80.2(C-5′), 84.3(C-1′), 106.6(C-3), 115.2(CN), 122.0-158.5(Ar-C), 161.8(C-2); MS (ionization method): m/z 568 (M^+); Anal. Calcd for $C_{31}H_{28}N_4SO_5$: C, 65.49; H, 4.93; N, 9.86. Found: C, 65.70; H, 5.05; N, 10.03.

10j: Yield 84%, mp 198°C; IR 3350(OH), 2222(CN) cm^{-1}; MS (ionization method): m/z 584 (M^+); Anal. Calcd for $C_{31}H_{28}N_4SO_6$: C, 63.70; H, 4.79; N, 9.59. Found: C, 63.95; H, 4.88; N, 9.73.

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