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Synthesis and Antiviral Activity of Some *N*-Pentopyranosyl-2-Pyridinethiones

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Synthesis and Antiviral Activity of Some *N*-Pentopyranosyl-2-Pyridinethiones

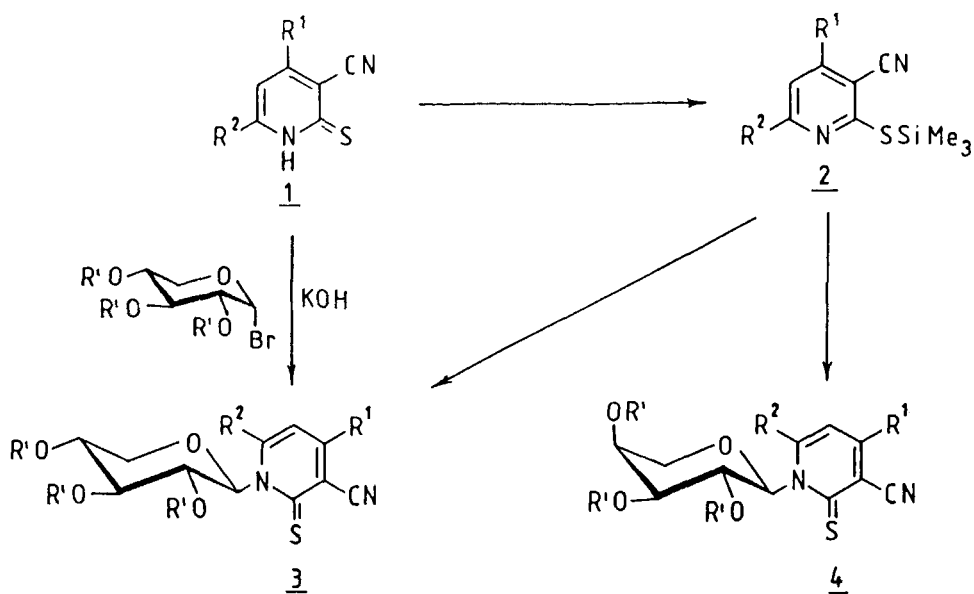
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Abstract: A novel synthesis of 1-(β -D-pentopyranosyl)pyridinethione nucleosides utilizing pyridine-2(1*H*)-thiones and α -bromoxylose or β -bromoarabinose triacetate as starting components is described. The free nucleosides were tested for their potential activity against HIV and different types of tumor virus.

3-Deazauridine, a pyrimidine nucleoside analogue that is an effective antitumor agent, must be activated to the di- and triphosphates (deazaUDP and deazaUTP) in order to exert its cytotoxic effects. 3-Deazauridine-5'-triphosphate, an active form of this antime-tabolite, is a potent inhibitor of CTP synthetase. DeazaUTP is a competitive inhibitor of this enzyme with respect to UTP. DeazaUDP is an inhibitor of ribonucleotide reductase activity. The net result of the inhibition of these enzymes is that the cells become deficient in cytidine and deoxycytidine nucleotides, causing inhibition of both RNA and DNA synthesis¹. The 3-deazapyrimidine nucleosides constitute another logical class of analogues with potential biological activity^{2,3}. As a part of our program directed toward the development of new, simple and efficient procedures for the synthesis of

nucleosides and nucleotides⁴⁻⁸, we report here the results of our investigation into the utility of the reaction of our previously reported pyridine-2(1*H*)-thiones **1**^{9,10} with acylated pentopyranosyl halides for the synthesis of 3-deazapyrimidine nucleosides. Compounds **1** were prepared by the reaction of α -cyanothioacetamide with chalcones in boiling ethanol containing catalytic amounts of piperidine. Compounds **1** reacted with 2,3,4-tri-*O*-acetyl- α -D-xylo- and β -L-arabinopyranosyl bromides in the presence of aqueous potassium hydroxide to give the corresponding *N*-xylosides **3a-g** and *N*-arabinosides **4a-d**. Although the coupling of **1** with the pentopyranosyl bromides could also give the corresponding *S*-nucleosides, the formation of **3a-g** and **4a-d** was proved chemically. Reaction of **1** with 1,1,1,3,3,3-hexamethyldisilazane (HMDS) in the presence of a catalytic amount of ammonium sulfate gave the corresponding 2-trimethylsilylthiopyridines **2**, which were subsequently treated with peracetylated sugars in the presence of redistilled SnCl₄ to afford the corresponding *N*-glycosyl compounds. All previous literature reports that Lewis acid-induced coupling reactions of *S*-silylated nitrogen bases with peracetylated sugars gave the corresponding *N*-nucleosides as the sole product.^{11,12} The structures of the reaction products **3** and **4** were established and confirmed by the correct analytical and spectral data (MS, IR, UV, ¹H NMR, ¹³C NMR). Thus, the mass spectrum of **3a** was compatible with the molecular formula C₂₉H₂₆N₂SO₇ (*m/z* 546). The ¹H NMR spectrum showed a doublet at 6.32 ppm assigned to the anomeric proton of the xylose moiety with a spin-spin coupling constant equal to 8.80 Hz corresponding to a diaxial orientation of H1' and H2' protons indicating the β -configuration and ⁴C₁(D) conformation for this xyloside. The other protons of the xylopyranosyl ring over in the δ 3.76-5.60 ppm region, while the three acetoxy groups appear as three singlets at δ 1.96-2.08 ppm. The ¹³C NMR spectrum of **3a** contained a signal at δ 87.6 corresponding to the C1' atom of the β -configuration. Three signals appeared at δ 168.8-169.6 due to the ester carbonyl carbon atoms, while signals appearing at δ 19.0-19.9 were attributed to the acetoxy methyl carbons. Another four signals at δ 64.4, 68.3, 75.8 and 80.0 were assigned to C5', C4', C2' and C3', respectively. The UV spectrum of **3a** proved that the reaction had led selectively to the formation of *N*-xyloside derivatives and excluded substitution at the sulfur atom. Thus



	R ¹	R ²	R'		R ¹	R ²	R'
3 a	C ₆ H ₅	C ₆ H ₅	Ac	4 a	C ₆ H ₅	C ₆ H ₅	Ac
b	C ₆ H ₅	p-ClC ₆ H ₄	Ac	b	p-CH ₃ OC ₆ H ₄	p-CH ₃ C ₆ H ₄	Ac
c	C ₆ H ₅	p-CH ₃ C ₆ H ₄	Ac	c	2-furyl	p-CH ₃ C ₆ H ₄	Ac
d	p-CH ₃ OC ₆ H ₄	C ₆ H ₅	Ac	d	2-furyl	p-CH ₃ OC ₆ H ₄	Ac
e	p-CH ₃ OC ₆ H ₄	p-CH ₃ C ₆ H ₄	Ac	e	C ₆ H ₅	C ₆ H ₅	H
f	2-furyl	p-CH ₃ C ₆ H ₄	Ac	f	p-CH ₃ OC ₆ H ₄	p-CH ₃ C ₆ H ₄	H
g	2-furyl	p-CH ₃ OC ₆ H ₄	Ac	g	2-furyl	p-CH ₃ C ₆ H ₄	H
h	C ₆ H ₅	C ₆ H ₅	H	h	2-furyl	p-CH ₃ OC ₆ H ₄	H
i	C ₆ H ₅	p-CH ₃ C ₆ H ₄	H				
j	p-CH ₃ OC ₆ H ₄	C ₆ H ₅	H				
k	2-furyl	p-CH ₃ C ₆ H ₄	H				
l	2-furyl	p-CH ₃ OC ₆ H ₄	H				

whereas the *S*-methyl derivative of **1a** showed one maximum at 280 nm, its *N*-xyloside derivative exhibited two maxima at 271 and 329 nm. Removal of the protecting acetyl groups from the glycon moiety of **3a-g** and **4a-d** with saturated methanolic ammonia at room temperature gave the free nucleosides **3h-l** and **4e-h** after chromatographic purification. The structures of compounds **3** and **4** were confirmed by their elemental analyses and spectral data. Thus, the analytical data for **4g** revealed a molecular formula C₂₂H₂₀N₂SO₅ (*m/z* 424). The ¹H NMR spectrum showed the anomeric proton as a

doublet at δ 6.30 ppm ($J_{1',2'} = 3.30$ Hz) indicating the presence of only the β -configuration. The other five arabinose protons appeared as a multiplet at δ 3.22–3.78 ppm, while the three hydroxy groups resonated at δ 4.62–5.68 ppm (exchangeable by D_2O). The ^{13}C NMR spectrum of **4g** was characterized by a signal at δ 81.8 ppm corresponding to the C1' atom of β -L-arabinopyranose. Another four signals at δ 62.8, 64.2, 70.0 and 71.3 ppm were assigned to C5', C4', C2' and C3' of the arabinose moiety, respectively. The nucleosides obtained through these results constitute an important and versatile class of compounds for potential application in the synthesis of other carbohydrate derivatives.

The nucleosides **3** and **4** did not show any significant activity against Human Immunodeficiency Virus (HIV) in MT-4 cells. They were also devoid of any activity against different types of tumor virus.

Experimental

All evaporations were carried out under reduced pressure at 40°C. Melting points are uncorrected. TLC aluminium sheets silica gel 60 F₂₅₄ (Merck) was used for thin layer chromatography; detection by short-wavelength UV light. IR spectra were obtained (KBr disc) with a Pye Unicam Spectra-1000. 1H NMR and ^{13}C NMR spectra were measured with a Wilmad 270 MHz or a Varian 400 MHz spectrometer for solutions in $(CD_3)_2SO$ using $SiMe_4$ as internal standard. Mass spectra were recorded with a Varian MAT 112 spectrometer. Analytical data were obtained from the Microanalytical Data Center at Cairo University.

3-Cyano-1-(2,3,4-tri-*O*-acetyl- β -D-xylo- and β -L-arabinopyranosyl)-2-pyridinethiones **3a-g** and **4a-d**.

General Coupling Procedure.

Method A. To a solution of 3-cyanopyridine-2(1*H*)-thiones **1** (0.01 mol) in aqueous potassium hydroxide [0.56 gm (0.01 mol) in 6 ml of distilled water], a solution of 2,3,4-tri-*O*-acetyl- α -D-xylo- or β -L-arabinopyranosyl bromide (0.011 mol) in acetone (30 ml) was added. The mixture was stirred at room temperature until the reaction was

judged complete by TLC (30 min to 2 h), then evaporated under reduced pressure at 40°C and the residue washed with distilled water to remove KBr. The product was dried and crystallized from ethanol to afford pale yellow crystals.

Method B. 3-Cyanopyridine-2(1*H*)-thiones **1** (0.01 mol) were boiled under reflux, with stirring, under anhydrous conditions for 48 hours with 1,1,1,3,3,3-hexamethyldisilazane (25 ml) and ammonium sulfate (0.02 gm). The clear solution obtained was cooled and the solvent was evaporated in vacuo to give the silylated compounds **2** as pale yellow oils. To a solution of silylated base in anhydrous acetonitrile (20 ml) was added a solution of α -D-xylose- or β -L-arabinosetetraacetate (0.011 mol) in anhydrous acetonitrile (10 ml) followed by SnCl₄ (1.6 ml). The mixture was stirred at room temperature until reaction was judged complete by TLC (6 to 12 h), then poured into saturated NaHCO₃ solution and extracted with CHCl₃. The organic layers were dried over Na₂SO₄, filtered and concentrated in vacuo to give the crude nucleosides which were purified by recrystallization from ethanol to afford pale yellow crystals.

Compound 3a: Yield 73 %, mp 177°C; IR (KBr) 2215 (CN), 1748 (CO) cm⁻¹; UVmax 271, 329 nm; ¹H NMR (DMSO-d₆) δ 1.96-2.08 (3s, 9H, 3CH₃CO), 3.76-4.18 (m, 2H, H5', 5"), 4.96 (m, 1H, H4'), 5.21 (t, 1H, H2'), 5.58 (t, 1H, H3'), 6.32 (d, J_{1'-2'} = 8.80 Hz, 1H, H1'), 7.58 (m, 5H, Ar-H), 7.74 (m, 3H, Ar-H), 8.01 (s, 1H, pyridine 5-H), 8.35 (, m, 2H, Ar-H); ¹³C NMR (DMSO-d₆) δ 19.0-19.9 (3CH₃), 64.4 (C5'), 68.3 (C4'), 75.8 (C2'), 80.0 (C3'), 87.6 (C1'), 108.0 (C3), 116.2 (CN), 122.4-130.4 (Ar-C), 135.7 (C5), 154.4 (C4), 158.1 (C6), 168.8-169.6 (3CO), 194.2 (C2); m/z 546 (Found: C, 63.89; H, 4.84; N, 5.20. C₂₉H₂₆N₂SO₇ requires C, 63.73; H, 4.76; N, 5.12 %).

Compound 3b: Yield 76 %, mp 207°C; IR (KBr) 2217 (CN), 1760 (CO) cm⁻¹; ¹H NMR (DMSO-d₆) δ 1.98-2.08 (3s, 9H, 3CH₃CO), 3.77-4.17 (m, 2H, H5', 5"), 5.00 (m, 1H, H4'), 5.20 (t, 1H, H2'), 5.56 (t, 1H, H3'), 6.30 (d, J_{1'-2'} = 8.80 Hz, 1H, H1'), 7.62 (m, 5H, Ar-H), 7.75 (d, 2H, Ar-H), 8.05 (s, 1H, pyridine 5-H), 8.39 (d, 2H, Ar-H); m/z 581 (Found: C, 60.13; H, 4.42; N, 4.54. C₂₉H₂₅ClN₂SO₇ requires C, 59.94; H, 4.30; N, 4.82 %).

Compound 3c: yield 74 %, mp 182°C; IR (KBr) 2214 (CN), 1756 (CO) cm^{-1} ; ^1H NMR (DMSO- d_6) δ 1.98-2.12 (3s, 9H, 3CH₃CO), 2.36 (s, 3H, CH₃), 4.03 (m, 2H, H5', 5"), 4.90 (m, 1H, H4'), 5.08 (t, 1H, H2'), 5.46 (t, 1H, H3'), 6.26 (d, $J_{1',2'} = 8.30$ Hz, 1H, H1'), 7.34 (d, 2H, Ar-H), 7.68 (m, 5H, Ar-H), 7.98 (s, 1H, pyridine 5-H), 8.21 (d, 2H, Ar-H); m/z 560 (Found: C, 64.41; H, 5.13; N, 5.22. C₃₀H₂₈N₂SO₇ requires C, 64.28; H, 5.00; N, 5.00 %).

Compound 3d: Yield 71 %, mp 188°C; IR (KBr) 2215 (CN), 1759 (CO) cm^{-1} ; ^1H NMR (DMSO- d_6) δ 1.99-2.06 (3s, 9H, 3CH₃CO), 3.87 (s, 3H, OCH₃), 4.12 (m, 2H, H5', 5"), 5.00 (m, 1H, H4'), 5.23 (t, 1H, H2'), 5.55 (t, 1H, H3'), 6.31 (d, $J_{1',2'} = 9.20$ Hz, 1H, H1'), 7.16 (d, 2H, Ar-H), 7.60 (m, 3H, Ar-H), 7.78 (d, 2H, Ar-H), 7.99 (s, 1H, pyridine 5-H), 8.37 (m, 2H, Ar-H); m/z 576 (Found: C, 62.34; H, 4.80; N, 4.93. C₃₀H₂₈N₂SO₈ requires C, 62.50; H, 4.86; N, 4.86 %).

Compound 3e: Yield 73 %, mp 150°C; IR (KBr) 2208 (CN), 1746 (CO) cm^{-1} ; ^1H NMR (DMSO- d_6) δ 1.98-2.06 (3s, 9H, 3CH₃CO), 2.40 (s, 3H, CH₃), 3.85 (s, 3H, OCH₃), 4.12 (m, 2H, H5', 5"), 4.96 (m, 1H, H4'), 5.28 (t, 1H, H2'), 5.56 (t, 1H, H3'), 6.32 (d, $J_{1',2'} = 8.84$ Hz, 1H, H1'), 7.16 (d, 2H, Ar-H), 7.40 (d, 2H, Ar-H), 7.75 (d, 2H, Ar-H), 7.92 (s, 1H, pyridine 5-H), 8.26 (d, 2H, Ar-H); m/z 590 (Found: C, 63.40; H, 5.14; N, 4.93. C₃₁H₃₀N₂SO₈ requires C, 63.05; H, 5.08; N, 4.74 %).

Compound 3f: Yield 75 %, mp 207°C; IR (KBr) 2215 (CN), 1758 (CO) cm^{-1} ; m/z 550 (Found: C, 61.31; H, 4.82; N, 5.01. C₂₈H₂₆N₂SO₈ requires C, 61.09; H, 4.72; N, 5.09 %).

Compound 3g: Yield 76 %, mp 210°C; IR (KBr) 2214 (CN), 1756 (CO) cm^{-1} ; ^1H NMR (DMSO- d_6) δ 1.98-2.03 (3s, 9H, 3CH₃CO), 3.85 (s, 3H, OCH₃), 4.08 (m, 2H, H5', 5"), 4.96 (m, 1H, H4'), 5.16 (t, 1H, H2'), 5.52 (t, 1H, H3'), 6.26 (d, $J_{1',2'} = 9.16$ Hz, 1H, H1'), 6.88 (d, 1H, furan 4-H), 7.12 (d, 2H, Ar-H), 7.69 (d, 1H, furan 3-H), 8.12 (m, 1H, furan 5-H and 1H, pyridine 5-H), 8.30 (d, 2H, Ar-H); m/z 566 (Found: C, 59.60; H, 4.74; N, 5.11. C₂₈H₂₆N₂SO₉ requires C, 59.36; H, 4.59; N, 4.94 %).

Compound 4a: Yield 70 %, mp 185°C; IR (KBr) 2221 (CN), 1748 (CO) cm^{-1} ; ^1H NMR (DMSO- d_6) δ 2.02, 2.08 and 2.09 (3s, 9H, 3CH₃CO), 4.12 (m, 2H, H5', 5"),

5.28 (m, 2H, H4' and H2'), 5.56 (q, 1H, H3'), 6.28 (d, $J_{1',2'} = 8.80$ Hz, 1H, H1'), 7.59 (m, 5H, Ar-H), 7.76 (m, 3H, Ar-H), 8.01 (s, 1H, pyridine 5-H), 8.35 (m, 2H, Ar-H); m/z 546 (Found: C, 63.53; H, 4.90; N, 5.34. $C_{29}H_{26}N_2SO_7$ requires C, 63.73; H, 4.76; N, 5.12 %).

Compound 4b: Yield 76 %, mp 196°C; IR (KBr) 2218 (CN), 1749 (CO) cm^{-1} ; 1H NMR (DMSO- d_6) δ 2.02, 2.07 and 2.09 (3s, 9H, 3CH₃CO), 2.39 (s, 3H, CH₃), 3.84 (s, 3H, OCH₃), 4.06 (m, 2H, H5', 5"), 5.29 (t, 2H, H4' and H2'), 5.45 (q, 1H, H3'), 6.26 (d, $J_{1',2'} = 9.08$ Hz, 1H, H1'), 7.16 (d, 2H, Ar-H), 7.39 (d, 2H, Ar-H), 7.74 (d, 2H, Ar-H), 7.91 (s, 1H, pyridine 5-H), 8.21 (d, 2H, Ar-H); m/z 590 (Found: C, 63.40; H, 5.02; N, 4.84. $C_{31}H_{30}N_2SO_8$ requires C, 63.05; H, 5.08; N, 4.74 %).

Compound 4c: Yield 74 %, mp 165°C; IR (KBr) 2215 (CN), 1746 (CO) cm^{-1} ; 1H NMR (DMSO- d_6) δ 2.01, 2.06 and 2.09 (3s, 9H, 3CH₃CO); 2.39 (s, 3H, CH₃), 4.04 (m, 2H, H5', 5"), 5.26 (m, 2H, H4' and H2'), 5.53 (q, 1H, H3'), 6.19 (d, $J_{1',2'} = 9.00$ Hz, 1H, H1'), 6.84 (m, 1H, furan 4-H), 7.39 (d, 2H, Ar-H), 7.69 (d, 1H, furan 3-H), 8.08 (d, 1H, furan 5-H), 8.13 (s, 1H, pyridine 5-H), 8.23 (d, 2H, Ar-H); m/z 550 (Found: C, 61.31; H, 4.94; N, 5.40. $C_{28}H_{26}N_2SO_8$ requires C, 61.09; H, 4.72; N, 5.09 %).

Compound 4d: Yield 75 %, mp 210°C; IR (KBr) 2213 (CN), 1743 (CO) cm^{-1} ; UV max 276, 338 nm; 1H NMR (DMSO- d_6) δ 2.01, 2.06 and 2.09 (3s, 9H, 3CH₃CO), 3.85 (s, 3H, OCH₃), 4.08 (m, 2H, H5', 5"), 5.26 (m, 2H, H4' and H2'), 5.51 (q, 1H, H3'), 6.22 (d, $J_{1',2'} = 9.08$ Hz, 1H, H1'), 6.82 (m, 1H, furan 4-H), 7.12 (d, 2H, Ar-H), 7.66 (d, 1H, furan 3-H), 8.07 (s, 1H, pyridine 5-H), 8.10 (d, 1H, furan 5-H), 8.27 (d, 2H, Ar-H); m/z 566 (Found: C, 59.53, 4.72; N, 5.10. $C_{28}H_{26}N_2SO_9$ requires C, 59.36; H, 4.59; N, 4.94 %).

3-Cyano-1-(β -D-Xylo- and β -L-arabinopyranosyl)-2-pyridinethiones 3h-l and 4e-h.

General procedure for nucleoside deacylation.

Dry gaseous ammonia was passed through a solution of protected nucleoside **3a-g** and **4a-d** (0.5 gm) in dry methanol (20 ml) at 0°C for about 0.5 h, then the mixture was stirred at room temperature until reaction was judged to be complete by TLC (8-12 h).

The mixture was evaporated under reduced pressure at 40°C to give a solid residue, which was crystallized from methanol to afford colourless crystals.

Compound 3h: Yield 86 %, mp 210°C; IR (KBr) 3600-3180 (OH), 2216 (CN) cm^{-1} ; UV max 271, 329 nm; ^1H NMR (DMSO- d_6) δ 3.28-3.77 (m, 5H, H5', 5'', H4', H3' and H2'), 5.19 (q, 1H, 4'-OH), 5.38 (t, 1H, 3'-OH), 5.65 (d, 1H, 2'-OH), 5.87 (d, $J_{1'-2'} = 8.80$ Hz, 1H, H1'), 7.60 (m, 5H, Ar-H), 7.94 (s, 1H, pyridine 5-H), 8.05 (m, 3H, Ar-H), 8.28 (m, 2H, Ar-H); m/z 420 (Found: C, 65.54; H, 4.83; N, 6.90. $\text{C}_{23}\text{H}_{20}\text{N}_2\text{SO}_4$ requires C, 65.71; H, 4.76; N, 6.66 %).

Compound 3i: Yield 84 %, mp 216°C; IR (KBr) 3600-3200 (OH), 2215 (CN) cm^{-1} ; ^1H NMR (DMSO- d_6) δ 2.38 (s, 3H, CH_3), 3.21-3.78 (m, 5H, H5', 5'', H4', H-3' and H2'), 5.20 (q, 1H, 4'-OH), 5.38 (d, 1H, 3'-OH), 5.64 (t, 1H, 2'-OH), 5.81 (d, $J_{1'-2'} = 8.30$ Hz, 1H, H1'), 7.36 (d, 2H, Ar-H), 7.73 (m, 5H, Ar-H), 7.90 (s, 1H, pyridine 5-H), 8.15 (d, 2H, Ar-H); m/z 434 (Found: C, 66.70; H, 5.14; N, 6.40. $\text{C}_{24}\text{H}_{22}\text{N}_2\text{SO}_4$ requires C, 66.35; H, 5.06; N, 6.45 %).

Compound 3j: Yield 87 %, mp 212°C; IR (KBr) 3660-3200 (OH), 2213 (CN) cm^{-1} ; m/z 450 (Found: C, 64.31; H, 5.04; N, 6.33. $\text{C}_{24}\text{H}_{22}\text{N}_2\text{SO}_5$ requires C, 64.00; H, 4.88; N, 6.22 %).

Compound 3k: Yield 85 %, mp 230°C; IR (KBr) 3640-3180 (OH), 2214 (CN) cm^{-1} ; ^1H NMR (DMSO- d_6) δ 2.40 (s, 3H, CH_3), 3.18-3.60 (m, 5H, H5', 5'', H4', H3' and H2'), 5.11 (d, 1H, 4'-OH), 5.32 (t, 1H, 3'-OH), 5.58 (d, 1H, 2'-OH), 5.79 (d, $J_{1'-2'} = 8.64$ Hz, 1H, H1'), 6.88 (m, 1H, furan 4-H), 7.18 (d, 1H, furan 3-H), 7.41 (d, 2H, Ar-H), 7.68 (d, 1H, furan 5-H), 8.12 (m, 1H, pyridine 5-H and 2H, Ar-H); m/z 424 (Found: C, 62.20; H, 4.93; N, 6.54. $\text{C}_{22}\text{H}_{20}\text{N}_2\text{SO}_5$ requires C, 62.26; H, 4.71; N, 6.60 %).

Compound 3l: Yield 84 %, mp 220°C, IR (KBr) 3680-3190 (OH), 2215 (CN) cm^{-1} ; m/z 440 (Found: C, 60.22; H, 4.42; N, 6.70. $\text{C}_{22}\text{H}_{20}\text{N}_2\text{SO}_6$ requires C, 60.00; H, 4.54; N, 6.36 %).

Compound 4e: Yield 86 %, mp 210°C; IR (KBr) 3600-3200 (OH), 2213 (CN) cm^{-1} ; ^1H NMR (DMSO- d_6) δ 3.26-3.80 (m, 5H, H5', 5'', H4', H3' and H2'), 4.72 (d, 1H, 4'-OH), 5.21 (d, 1H, 3'-OH), 5.68 (d, 1H, 2'-OH), 6.41 (d, $J_{1'-2'} = 3.12$ Hz, 1H,

H1'), 7.58 (m, 5H, Ar-H), 7.72 (m, 3H, Ar-H), 7.92 (s, 1H, pyridine 5-H), 8.28 (m, 2H, Ar-H); ^{13}C NMR (DMSO- d_6) δ 62.6 (C5'), 64.1 (C4'), 69.9 (C2'), 71.4 (C3'), 81.9 (C1'), 103.1 (C3), 115.9 (CN), 127.0-136.1 (Ar-C), 143.8 (C5), 154.0 (C4), 157.2 (C6), 191.6 (C2); m/z 420 (Found: C, 65.64; H, 4.90; N, 6.92. $\text{C}_{23}\text{H}_{20}\text{N}_2\text{SO}_4$ requires C, 65.71; H, 4.76; N, 6.66 %).

Compound 4f: Yield 84 %, mp 215°C; IR (KBr) 3680-3200 (OH), 2210 (CN) cm^{-1} ; ^1H NMR (DMSO- d_6) δ 2.36 (s, 3H, CH₃), 3.32-3.78 (m, 5H, H5', 5'', H4', H3' and H2'), 3.87 (s, 3H, OCH₃), 3.77 (d, 1H, 4'-OH), 4.21 (d, 1H, 3'-OH), 5.67 (t, 1H, 2'-OH), 6.34 (d, $J_{1',2'} = 3.20$ Hz, 1H, H1'), 7.13 (d, 2H, Ar-H), 7.35 (d, 2H, Ar-H), 7.71 (d, 2H, Ar-H), 7.79 (s, 1H, pyridine 5-H), 8.12 (d, 2H, Ar-H); m/z 464 (Found: C, 64.91; H, 5.14; N, 6.30. $\text{C}_{25}\text{H}_{24}\text{N}_2\text{SO}_5$ requires C, 64.65; H, 5.17; N, 6.03 %).

Compound 4g: Yield 87 %, mp 240°C; IR (KBr) 3660-3180 (OH), 2212 (CN) cm^{-1} ; ^1H NMR (DMSO- d_6) δ 2.38 (s, 3H, CH₃), 3.22-3.78 (m, 5H, H5', 5'', H4', H3' and H2'), 4.61 (t, 1H, 4'-OH), 5.20 (d, 1H, 3'-OH), 5.64 (d, 1H, 2'-OH), 6.30 (d, $J_{1',2'} = 3.32$ Hz, 1H, H1'), 6.82 (m, 1H, furan 4-H), 7.35 (d, 2H, Ar-H), 7.66 (d, 1H, furan 3-H), 8.08 (s, 1H, pyridine 5-H), 8.12 (d, 1H, furan 5-H), 8.20 (d, 2H, Ar-H); ^{13}C NMR (DMSO- d_6) δ 20.4 (CH₃), 62.8 (C5'), 64.2 (C4'), 70.0 (C2'), 71.3 (C3'), 81.8 (C1'), 110.2 (C3), 115.4 (CN), 126.7-140.3 (Ar-C), 145.8 (C5), 147.2 (C4), 157.1 (C6), 192.3 (C2); m/z 424 (Found: C, 62.53; H, 4.80; N, 6.90. $\text{C}_{22}\text{H}_{20}\text{N}_2\text{SO}_5$ requires C, 62.26; H, 4.71, N, 6.60 %).

Compound 4h: Yield 86 %, mp 248°C; IR (KBr) 3640-3160 (OH), 2210 (CN) cm^{-1} ; UV max 276, 338 nm; ^1H NMR (DMSO- d_6) δ 3.24-3.78 (m, 5H, H5', 5'', H4', H3' and H2'), 3.88 (s, 3H, OCH₃), 4.72 (d, 1H, 4'-OH), 5.20 (d, 1H, 3'-OH), 5.63 (d, 1H, 2'-OH), 6.30 (d, $J_{1',2'} = 3.01$ Hz, 1H, H1'), 6.82 (m, 1H, furan 4-H), 7.11 (d, 2H, Ar-H), 7.63 (d, 1H, furan 3-H), 8.00 (s, 1H, pyridine 5-H), 8.06 (d, 1H, furan 5-H), 8.23 (d, 2H, Ar-H); m/z 440 (Found: C, 60.31; H, 4.52; N, 6.60. $\text{C}_{22}\text{H}_{20}\text{N}_2\text{SO}_6$ requires C, 60.00; H, 4.54; N, 6.36 %).

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