

**SYNTHESIS OF 1-( $\beta$ -D-GLYCOPYRANOSYL)-3-DEAZAPYRIMIDINES  
FROM 2-HYDROXY AND 2-MERCAPTOPYRIDINES**

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**Abstract:** The synthesis of new 4- and 5-substituted-3-cyanopyridine nucleosides has been performed by reacting the silylated pyridines and penta-*O*-acetyl- $\alpha$ -D-glycopyranose in dichloroethane in the presence of SnCl<sub>4</sub>. The free nucleosides were tested for their potential activity against HIV and different types of tumor.

3-Deazauridine (4-hydroxy-1-( $\beta$ -D-ribofuranosyl)-2-pyridone), a synthetic analogue of uridine<sup>1</sup> is cytotoxic to tumor cells *in vitro* and *in vivo*, and its activity in tumor bearing animals has led to phase I clinical trials to determine its toxic effects in humans.<sup>2</sup> 3-Deazapyrimidine nucleoside analogues have been of interest because of their antiviral activity.<sup>3,4</sup> As a part of our program directed for the development of new, simple and efficient procedures for the synthesis of nucleosides and nucleotides,<sup>5-10</sup> we report in this work the results of our investigation on the utility of the reaction of 2-pyridones and their thione derivatives **3** with  $\alpha$ -halogenosugars for the synthesis of 3-deaza-pyrimidine glycosides. Compounds **3**<sup>11</sup> were prepared by reacting ethoxymethylenes of acetylacetone, benzoylacetone, ethyl acetoacetate and ethyl benzoylacetate **1** with both cyanoacetamide and cyano-thioacetamide **2** in boiling ethanol containing piperidine as a catalyst. Compounds **3** were reacted with 2,3,4,6-tetra-*O*-acetyl- $\alpha$ -D-gluco- and galactopyranosyl bromides **4** in the presence of aqueous KOH to give the corresponding *N*-glycosyl **5**. It may be argued that the coupling reaction of **3c-f** with **4** occurs on the sulfur atom to give the corresponding *S*-glycosides **6**. However, the formation of **5** was verified by treating

the compounds **3** with hexamethyldisilazane (HMDS) in the presence of  $(\text{NH}_4)_2\text{SO}_4$  to give the corresponding 2-trimethylsilylthiopyridines **7**. Treatment of the latter compounds with peracetylated sugars **8** in dry 1,2-dichloroethane and in the presence of redistilled  $\text{SnCl}_4$  gave the corresponding *N*-glycosides. All the previous literature report that Lewis acid-induced coupling of *S*-silylated heterocyclic bases with peracylated sugars gave the corresponding *N*-nucleosides as the sole product.<sup>12-14</sup> The chemical formula and molecular structure of the formed compounds **5** were identified using elemental analyses, IR,  $^1\text{H}$ -,  $^{13}\text{C}$ -NMR and mass spectroscopies. The protons in the NMR spectra were assigned by the  $^1\text{H}$ - $^1\text{H}$ - homonuclear shift-correlated (COSY) 2D-NMR. The  $^1\text{H}$ -NMR spectrum

	X	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>		X	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>	R <sup>4</sup>
<b>5 a</b>	O	CH <sub>3</sub>	COCH <sub>3</sub>	OAc	H	<b>9 a</b>	O	CH <sub>3</sub>	COCH <sub>3</sub>	OH	H
<b>b</b>	O	CH <sub>3</sub>	COC <sub>6</sub> H <sub>5</sub>	OAc	H	<b>b</b>	O	CH <sub>3</sub>	COC <sub>6</sub> H <sub>5</sub>	OH	H
<b>c</b>	S	CH <sub>3</sub>	COCH <sub>3</sub>	OAc	H	<b>c</b>	S	CH <sub>3</sub>	COCH <sub>3</sub>	OH	H
<b>d</b>	S	CH <sub>3</sub>	COC <sub>6</sub> H <sub>5</sub>	OAc	H	<b>d</b>	S	CH <sub>3</sub>	COC <sub>6</sub> H <sub>5</sub>	OH	H
<b>e</b>	S	CH <sub>3</sub>	CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	OAc	H	<b>e</b>	S	CH <sub>3</sub>	CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	OH	H
<b>f</b>	S	C <sub>6</sub> H <sub>5</sub>	CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	OAc	H	<b>f</b>	S	C <sub>6</sub> H <sub>5</sub>	CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	OH	H
<b>g</b>	O	CH <sub>3</sub>	COCH <sub>3</sub>	H	OAc	<b>g</b>	O	CH <sub>3</sub>	COCH <sub>3</sub>	H	OH
<b>h</b>	O	CH <sub>3</sub>	COC <sub>6</sub> H <sub>5</sub>	H	OAc	<b>h</b>	O	CH <sub>3</sub>	COC <sub>6</sub> H <sub>5</sub>	H	OH
<b>i</b>	S	CH <sub>3</sub>	COCH <sub>3</sub>	H	OAc	<b>i</b>	S	CH <sub>3</sub>	COCH <sub>3</sub>	H	OH
<b>j</b>	S	CH <sub>3</sub>	COC <sub>6</sub> H <sub>5</sub>	H	OAc	<b>j</b>	S	CH <sub>3</sub>	COC <sub>6</sub> H <sub>5</sub>	H	OH
<b>k</b>	S	CH <sub>3</sub>	CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	H	OAc	<b>k</b>	S	CH <sub>3</sub>	CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	H	OH
<b>l</b>	S	C <sub>6</sub> H <sub>5</sub>	CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	H	OAc	<b>l</b>	S	C <sub>6</sub> H <sub>5</sub>	CO <sub>2</sub> C <sub>2</sub> H <sub>5</sub>	H	OH

of **5c** showed the anomeric proton as a doublet at 6.08 ppm with spin-spin coupling constant equal to 10.77 Hz that corresponds to the diaxial orientation of H-1' and H-2' protons, which indicates the presence of only  $\beta$ -configuration and  $^4\text{C}_1$  conformation. The

other six protons of the glucopyranosyl ring appear in the range 3.96-5.53 ppm. The remaining four acetoxy groups appear as four singlets in the 1.92-2.08 ppm region. On the other hand, the two methyl groups of aglycone are shown at 2.34 and 2.40 ppm. The  $^{13}\text{C}$ -NMR spectrum was characterized by a signal at 80.2 ppm identifying C-1' atom of the  $\beta$ -D glucopyranose. Four signals appear at 169.1, 169.2, 169.4 and 169.8 ppm for the four acetoxy carbonyls of the sugar moiety. Other four signals are observed in the range 20.2-24.2 ppm due to the acetoxy methyl groups. The methyl groups of aglycone appear at 19.6 and 30.5 ppm. In addition, five signals at 61.7, 68.1, 68.9, 73.1 and 74.9 ppm appear to associate with the glucose C-6', C-4', C-2', C-3' and C-5', respectively. The UV spectrum of **5c-f** and **5i-l** confirms that the reaction proceeds selectively towards the formation of *N*-glycosyl derivatives and excluded substitution at the sulfur atom. Thus, while the *S*-methyl derivative of **3d** showed two maxima at 269 and 334 nm, its *N*-glucosyl derivative **5d** exhibited three maxima at 266, 303 and 328 nm.

Removal of the protecting acetyl groups from the glycone moiety with methanolic ammonia gave the free glycosides **9** after chromatographic purification. The structures of compounds **9** were confirmed by elemental and spectral analyses. The  $^1\text{H}$ -NMR spectrum of **9j** showed the anomeric proton as a doublet at 5.64 ppm ( $J_{1,2}=9.98$  Hz) indicating the presence of only  $\beta$ -configuration. The other six protons of the galactose ring appear as a multiplet in the range 3.18-3.82 ppm, while the four hydroxyls are shown at 4.55, 4.61, 4.97 and 5.36 ppm as confirmed by the deuteration-induced shifts. The  $^{13}\text{C}$ -NMR spectrum was characterized by a signal at 84.3 ppm for the C-1' of  $\beta$ -D-galactopyranose. The five signals at 60.4, 68.4, 68.6, 74.9 and 79.2 ppm are respectively assigned to C-6', C-4', C-2', C-3' and C-5' of the galactose moiety.

The glycosides **5** and **9** did not show any significant activity against Human Immunodeficiency Virus (HIV) in MT-4 cells. They were devoid of any activity against different types of tumor virus.

## EXPERIMENTAL

All evaporation were carried out under reduced pressure at 40 °C. Melting points are uncorrected. Aluminum-coated Silica Gel 60 F<sub>254</sub> (Merck) sheets were used for thin layer chromatography. Detection was performed using short wavelength UV-lamp. IR spectra

were collected in the transmission mode using the KBr disk technique on a Pye Unicam Spectra-1000 spectrometer.  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR spectra were measured in  $(\text{CD}_3)_2\text{SO}$  using  $\text{SiMe}_4$  as internal reference on a Varian 400 MHz spectrometer. Mass spectra were recorded by EI on a Varian Mat 311 A spectrometer and FAB on a Kratos MS 50 spectrometer.

### 3-Cyano-1-(2,3,4,6-tetra-*O*-acetyl- $\beta$ -D-glycopyranosyl)-pyridines 5.

**General coupling procedures: Method A:** To a solution of 3-cyano-2-pyridones or their thione derivatives **3** (0.01 mol) in aqueous KOH [0.56 g (0.01 mol) in 6 mL of distilled water], a solution of 2,3,4,6-tetra-*O*-acetyl- $\alpha$ -D-gluco- or galactopyranosyl bromide **4** (0.011 mol) in 30 mL of acetone was added. The reaction mixture was stirred at room temperature until the reaction was judged complete by TLC (30 min to 4 h), using chloroform : petroleum ether 4:1, v/v ( $R_f$  0.70-0.74 region), then evaporated under reduced pressure and the residue was washed with distilled water to remove KBr. The product was dried prior to crystallization from EtOH to afford pale yellow needle crystals.

**Method B:** 3-Cyano-2-pyridones and their corresponding thiones **3** (0.01 mol) were refluxed with stirring, under anhydrous conditions for 30 h with hexamethyldisilazane (HMDS) 60 mL and  $(\text{NH}_4)_2\text{SO}_4$  (0.02g). The clear solution obtained was cooled and the solvent was removed *in vacuo*. The resulting trimethylsilylated derivative **7** was dissolved in anhydrous 1,2-dichloroethane 40 mL, and a solution of  $\alpha$ -D-glycopyranose pentaacetate (0.011 mol) in dry 1,2-dichloroethane 20 mL was then added with stirring. The mixture was cooled to  $-10\text{ }^\circ\text{C}$  and a solution of 1.6 mL of  $\text{SnCl}_4$  in 5 mL of 1,2-dichloroethane was added dropwise with continued stirring until the reaction was judged to be complete by TLC (1-3 h), the contents of the flask were then poured into saturated  $\text{NaHCO}_3$  solution and extracted with  $\text{CHCl}_3$ . The organic layer was dried over  $\text{MgSO}_4$ , filtered and concentrated to give the crude nucleosides that were purified by recrystallization from EtOH to afford pale yellow crystals.

**5a:** yield 60 %, mp  $130\text{ }^\circ\text{C}$ ; IR 2210(CN), 1754(CO ester), 1657(CO pyridine)  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR 1.94-2.08(4s, 12H, 4CH<sub>3</sub>CO), 2.22(s, 3H, CH<sub>3</sub>CO), 2.42(s, 3H, CH<sub>3</sub>), 4.18(m, 2H, H-6' and 1H, H-5'), 5.09(m, 2H, H-4' and H-3'), 5.51(t, 1H, H-2'), 6.11(d,  $J_{1-2}=7.99\text{ Hz}$ , 1H, H-1'), 7.11(s, 1H, pyridine H-6);  $^{13}\text{C}$  NMR 18.8(CH<sub>3</sub>), 19.5-20.5(4CH<sub>3</sub>), 24.0(CH<sub>3</sub>), 61.4(C6'), 67.8(C4'), 70.4(C2'), 71.3(C3'), 71.8 (C5'), 93.2 (C1'), 107.3(C3), 115.9(CN),

136.2(C6), 151.1(C4), 155.3(C5), 160.8(C2), 168.7-169.8 (4CO); m/z 506 (Found: C,54.61; H,5.20; N,5.64.  $C_{23}H_{26}N_2O_{11}$  requires C,54.55; H,5.14; N,5.53 %).

**5b:** yield 61 %, mp 121 °C; IR 2222(CN), 1750(CO ester), 1660(CO pyridine)  $cm^{-1}$ ; m/z 568 (Found: C,59.30; H,5.11; N,5.18.  $C_{28}H_{28}N_2O_{11}$  requires C,59.15; H,4.93; N,4.93 %).

**5c:** Yield 65 %, mp 175 °C; IR 2220(CN), 1748(CO)  $cm^{-1}$ ;  $^1H$  NMR 1.92-2.08(4s,12H,4CH<sub>3</sub>CO), 2.34(s,3H,CH<sub>3</sub>CO), 2.40(s,3H,CH<sub>3</sub>), 4.12(m,2H,H-6' and 1H,H-5'), 5.13(m,2H,H-4' and H-3'), 5.50(t,1H,H-2'), 6.08(d, $J_{1-2}$ =10.77 Hz,1H,H-1'), 7.20(s,1H,pyridine H-6);  $^{13}C$  NMR 19.6(CH<sub>3</sub>), 20.2-24.2 (4CH<sub>3</sub>), 30.5(CH<sub>3</sub>), 61.7(C6'), 68.1(C4'), 68.9(C2'), 73.1(C3'), 74.9(C5'), 80.2(C1'), 105.1(C3), 114.6(CN), 133.9(C6), 138.9(C4), 144.4(C5), 152.7(CO), 161.8(C2), 169.1-169.8(4CO); m/z 522 (Found: C,53.14; H,5.16; N,5.71  $C_{23}H_{26}N_2SO_{10}$  requires C,52.87; H,4.98; N,5.36 %).

**5d:** Yield 67 %, mp 202 °C; IR 2218(CN), 1754(CO)  $cm^{-1}$ ;  $^1H$  NMR 1.80- 2.16(4s,12H, 4CH<sub>3</sub>CO), 2.36(s,3H,CH<sub>3</sub>), 4.15(m,2H,H-6' and 1H,H-5'), 5.16(t,1H,H-4'), 5.37(m,2H,H-3' and H-2'), 6.02(d, $J_{1-2}$ = 9.99 Hz,1H,H-1'), 7.46(s,1H,pyridine H-6), 7.54(m,3H,Ar-H), 8.02(m,2H,Ar-H); m/z 584 (Found: C,57.82; H,4.85; N,5.07  $C_{28}H_{28}N_2SO_{10}$  requires C,57.53; H,4.79; N,4.79 %).

**5e:** Yield 66 %, mp 136 °C; IR 2223(CN), 1750(CO ester), 1660(CO pyridine)  $cm^{-1}$ ;  $^1H$  NMR 1.34(t,3H,CH<sub>3</sub>), 1.90-2.15(4s,12H,4CH<sub>3</sub>CO), 2.34(s,3H,CH<sub>3</sub>), 4.02(q,2H,CH<sub>2</sub>), 4.31(m,2H,H-6' and 1H,H-5'), 5.39(m,3H,H-4',H-3' and H-2'), 6.11(d, $J_{1-2}$ =10.39 Hz,1H,H-1'), 8.30 (s,1H,pyridine H-6); m/z 552 (Found: C,52.53; H,5.15; N,5.35  $C_{24}H_{28}N_2SO_{11}$  requires C,52.17; H,5.07; N,5.07 %).

**5f:** Yield 68 %, mp 165 °C; IR 2224(CN), 1743(CO ester), 1666(CO pyridine)  $cm^{-1}$ ;  $^1H$  NMR 1.09(t,3H,CH<sub>3</sub>), 1.72-2.03(4s,12H,4CH<sub>3</sub>CO), 4.15 (q,2H,CH<sub>2</sub>), 4.19(m,2H,H-6' and 1H,H-5'), 5.01(t,1H,H-4'), 5.25(t,1H,H-3'), 5.66 (t,1H,H-2'), 6.15(d, $J_{1-2}$ = 9.19 Hz,1H,H-1'), 7.74(m, 5H,Ar-H), 8.60(s,1H,pyridine H-6);  $^{13}C$  NMR 13.4(CH<sub>3</sub>), 20.1-20.3(4CH<sub>3</sub>), 20.4(CH<sub>3</sub>), 61.7(CH<sub>2</sub>), 61.9 (C6'), 68.1(C4'), 68.7(C2'), 72.8(C3'), 75.0(C5'), 80.1(C1'), 105.2(C3), 114.5(CN), 123.6-130.3(Ar-C), 137.3(C6), 143.4(C4), 159.6(C5), 160.0(CO), 165.8(C2), 169.3- 169.8(4CO); m/z 614 (Found: C,57.01; H,5.04; N,5.83  $C_{29}H_{30}N_2SO_{11}$  requires C,56.68; H,4.88; N,4.56 %).

**5g:** Yield 60 %, mp 152 °C; IR 2215(CN), 1746(CO ester), 1650(CO pyridine)  $cm^{-1}$ ;  $^1H$  NMR 1.95-2.12(4s,12H,4CH<sub>3</sub>CO), 2.22(s,3H,CH<sub>3</sub>), 2.40(s,3H,CH<sub>3</sub>), 4.06(m,2H,H-6'),

4.46(m, 1H, H-5'), 5.35(m,3H,H-4',H-3' and H-2'), 6.15(d, $J_{1-2}=7.99$  Hz,1H,H-1'), 7.11(s,1H,pyridine H-6); m/z 506 (Found: C,54.72; H,5.20; N,5.77  $C_{23}H_{26}N_2O_{11}$  requires C,54.55; H,5.14; N,5.53 %).

**5h:** Yield 62 %, mp 148 °C; IR 2225(CN), 1749(CO ester), 1665(CO pyridine)  $cm^{-1}$ ;  $^1H$  NMR 1.97-2.15(4s,12H,4CH<sub>3</sub>CO), 2.37(s,3H,CH<sub>3</sub>), 4.06(m,2H,H-6'), 4.51(m,1H,H-5'), 5.38(m,3H,H-4',H-3' and H-2'), 6.17(d, $J_{1-2}=8.39$  Hz,1H,H-1'), 7.25(s,1H,pyridine H-6), 7.74(m,5H,Ar-H); m/z 568 (Found: C,59.47; H,4.98; N,5.13  $C_{28}H_{28}N_2O_{11}$  requires C,59.15; H,4.93; N,4.93 %).

**5i:** Yield 66 %, mp 164 °C, IR 2217(CN), 1751(CO)  $cm^{-1}$ ;  $^1H$  NMR 1.90- 2.14(4s,12H, 4CH<sub>3</sub>CO), 2.34(s,3H,CH<sub>3</sub>CO), 2.41(s,3H,CH<sub>3</sub>), 4.01(m,2H,H-6'), 4.37(m, 1H,H-5'), 5.43(m,3H,H-4',H-3' and H-2'), 6.05(d, $J_{1-2}=10.39$  Hz,1H,H-1'), 7.20(s, 1H,pyridine H-6);  $^{13}C$  NMR 19.7(CH<sub>3</sub>), 20.3-20.4(4CH<sub>3</sub>CO), 24.3(CH<sub>3</sub>), 61.4(C6'), 66.4(C4'), 67.6(C2'), 70.9(C3'), 74.1(C5'), 80.6(C1'), 105.2(C3), 116.2(CN), 135.3(C6), 152.8(C4), 156.8(C5), 157.1(CO), 161.8(C2), 169.5-169.9 (4CO); m/z 522 (Found: C,53.14; H,5.19; N,5.72  $C_{23}H_{26}N_2SO_{10}$  requires C,52.87; H,4.98; N,5.36 %).

**5j:** Yield 65 %, mp 180 °C, IR 2217(CN), 1757(CO)  $cm^{-1}$ ;  $^1H$  NMR 1.77- 2.06(4s,12H, 4CH<sub>3</sub>CO), 2.57(s,3H,CH<sub>3</sub>), 4.16(m,2H,H-6'and 1H,H-5'), 5.22(t,1H,H-4'), 5.51(m,2H,H-3'and H-2'), 6.04(d, $J_{1-2}=10.39$  Hz,1H,H-1'), 7.46(s,1H, pyridine H- 6), 7.54(m,3H,Ar-H), 8.03(m,2H,Ar-H);  $^{13}C$  NMR 20.4-20.6(4CH<sub>3</sub>), 20.8 (CH<sub>3</sub>), 61.9(C6'), 66.2(C4'), 67.6(C2'), 72.2(C3'), 75.1(C5'), 81.6(C1'), 106.9 (C3), 117.7(CN), 127.2-130.7(Ar-C), 137.2(C6), 153.1(C4), 158.7(C5), 159.2(CO), 169.3-170.3(4CO); m/z 584 (Found: C,57.78; H,4.85; N,4.94  $C_{28}H_{28}N_2SO_{10}$  requires C,57.53; H,4.79; N,4.79 %).

**5k:** Yield 64 %, mp 147 °C, IR 2224(CN), 1751(CO)  $cm^{-1}$ ;  $^1H$  NMR 1.32 (t,3H,CH<sub>3</sub>), 1.91-2.00(4s,12H,4CH<sub>3</sub>CO), 2.34(s,3H,CH<sub>3</sub>), 4.08(q,2H,CH<sub>2</sub>), 4.28(m,2H, H-6' and 1H,H-5'), 5.00(t,1H, H-4'), 5.17(t,1H,H-3'), 5.55(t,1H,H-2'), 6.16(d, $J_{1-2}=10.79$  Hz,1H,H-1'), 8.56(s,1H,pyridine H-6); m/z 552 (Found: C,52.52; H,5.33; N,5.41  $C_{24}H_{28}N_2SO_{11}$  requires C,52.17; H,5.07; N,5.07 %).

**5l:** Yield 68 %, mp 151 °C, IR 2224(CN), 1747(CO)  $cm^{-1}$ ;  $^1H$  NMR 1.66(t,3H, CH<sub>3</sub>), 1.95-2.13(4s,12H,4CH<sub>3</sub>CO), 4.01(q,2H,CH<sub>2</sub>), 4.17(m,2H,H-6'), 4.46(m,1H, H-5'), 5.24(t,1H,H-4'), 5.39(t, 1H,H-3'), 5.57(t,1H,H-2'), 6.10(d, $J_{1-2}=10.39$  Hz, 1H,H-1'), 7.53(m,3H,Ar-H), 7.73(m,2H,Ar-H), 8.61 (s,1H,pyridine H-6);  $^{13}C$  NMR 13.4(CH<sub>3</sub>),

20.1-20.3(4CH<sub>3</sub>), 30.6(CH<sub>2</sub>), 61.7(C6'), 66.2(C4'), 67.7 (C2'), 70.7(C3'), 74.3(C5'), 80.4(C1'), 105.3(C3), 114.5(CN), 123.7-130.3(Ar-C), 137.2(C6), 143.4(C4), 159.5(CO), 165.7(C2), 169.3-169.9(4CO); m/z 614 (Found: C,56.95; H,5.06; N,4.81 C<sub>29</sub>H<sub>30</sub>N<sub>2</sub>SO<sub>11</sub> requires C,56.68; H,4.88; N,4.56 %).

### 3-Cyano-1-( $\beta$ -D-glycopyranosyl)-pyridines 9. General Procedure for Nucleoside Deacylation:

Dry ammonia gas was passed into a solution of protected nucleosides **5a-l** (0.5 g) in 20 mL of MeOH at 0 °C for 0.5 h. The reaction mixture was stirred till complete as shown by TLC (8-12 h), using CHCl<sub>3</sub> : MeOH 9:1, v:v, (Rf 0.62-0.64 region). The resulting mixture was then concentrated under reduced pressure to afford a solid residue that was crystallized from MeOH to furnish colorless crystals.

**9a:** Yield 79 %, mp 217 °C, IR 3434(OH), 2217(CN), 1661(CO) cm<sup>-1</sup>; <sup>1</sup>H NMR 2.22(s,3H,CH<sub>3</sub>CO), 2.29(s,3H,CH<sub>3</sub>), 3.14-3.68(m,6H,2H-6',H-5',H-4',H-3' and H-2'), 4.12(m,1H,2'-OH), 4.51(d,1H,3'-OH), 4.70(m,2H,4'-OH and 6'-OH), 5.98 (d,J<sub>1'-2'</sub>=10.31 Hz,1H,H-1'), 7.21(s,1H,pyridine H-6); m/z 338 (Found:C,53.61; H,5.50; N,8.55 C<sub>15</sub>H<sub>18</sub>N<sub>2</sub>O<sub>7</sub> requires C,53.25; H,5.32; N,8.28 %).

**9b:** Yield 78 %, mp 197 °C, IR 3460(OH), 2220(CN), 1663(CO) cm<sup>-1</sup>; m/z 400 (Found: C,60.43; H,5.21; N,7.38 C<sub>20</sub>H<sub>20</sub>N<sub>2</sub>O<sub>7</sub> requires C,60.00; H,5.00; N,7.00 %).

**9c:** Yield 80 %, mp 206 °C, IR 3436(OH), 2216(CN), 1662(CO) cm<sup>-1</sup>; m/z 354 (Found: C,51.19; H,5.14; N,8.23 C<sub>15</sub>H<sub>18</sub>N<sub>2</sub>SO<sub>6</sub> requires C,50.85; H,5.08; N,7.90 %).

**9d:** Yield 81 %, mp 270 °C; IR 3420(OH), 2224(CN), 1663(CO) cm<sup>-1</sup>; <sup>1</sup>H NMR 2.18(s,3H,CH<sub>3</sub>), 3.18-3.74(m,6H,2H-6',H-5',H-4',H-3' and H-2'), 4.31 (t,1H,2'-OH), 5.00(t,1H,3'-OH), 5.21(t,1H,4'-OH), 5.70 (t,1H,6'-OH), 6.12(d,J<sub>1'-2'</sub>=9.54Hz,1H,H-1'), 7.56(m,3H,Ar-H), 7.98(s,1H,pyridine H-6), 8.31(m,2H,Ar-H); m/z 416 (Found: C,57.95; H,4.89; N,6.86 C<sub>20</sub>H<sub>20</sub>N<sub>2</sub>SO<sub>6</sub> requires C,57.69; H,4.80; N,6.73 %).

**9e:** Yield 80 %, mp 213 °C, IR 3462(OH), 2225(CN), 1648(CO) cm<sup>-1</sup>; m/z 384 (Found: C,50.39; H,5.30; N,7.57 C<sub>16</sub>H<sub>20</sub>N<sub>2</sub>SO<sub>7</sub> requires C,50.00; H,5.21; N,7.29 %).

**9f:** Yield 82 %, mp 209 °C, IR 3462(OH), 2222(CN), 1655(CO) cm<sup>-1</sup>; m/z 446 (Found: C,56.84; H,5.08; N,6.49 C<sub>21</sub>H<sub>22</sub>N<sub>2</sub>SO<sub>7</sub> requires C,56.50; H,4.93; N,6.28 %).

**9g:** Yield 77 %, mp 233 °C, IR 3434(OH), 2224(CN), 1666(CO) cm<sup>-1</sup>; <sup>1</sup>H NMR 2.22(s,3H,CH<sub>3</sub>), 2.40(s,3H,CH<sub>3</sub>), 3.17-3.71(m,6H,2H-6',H-5',H-4',H-3' and H-2'),

4.57(m,1H,2'-OH), 4.81(m,2H,3'-OH and 4'-OH), 5.13(m,1H,6'-OH), 5.92(d,  $J_{1'-2'} = 10.37$  Hz,1H,H-1'), 7.03(s, 1H,pyridine H-6); m/z 338 (Found: C,53.62; H,5.54; N,8.39  $C_{15}H_{18}N_2O_7$  requires C,53.25; H,5.32; N,8.28 %).

**9h:** Yield 78 %, mp 220 °C; IR 3490(OH), 2225(CN), 1665(CO)  $cm^{-1}$ ; m/z 400 (Found: C,60.41; H,5.19; N,7.37  $C_{20}H_{20}N_2O_7$  requires C,60.00; H,5.00; N,7.00 %).

**9i:** Yield 81 %, mp 206 °C; IR 3428(OH), 2217(CN), 1680(CO)  $cm^{-1}$ ;  $^1H$  NMR 2.30(s,3H,CH<sub>3</sub>), 2.42(s,3H,CH<sub>3</sub>), 3.18-3.75(6H,2H-6',H-5',H-4',H-3' and H-2'), 4.49(m,2H,2'-OH and 3'-OH), 4.92(s, 1H,4'-OH), 5.31(s,1H,6'-OH), 5.52(d, $J_{1'-2'} = 10.39$  Hz,1H,H-1'), 7.10(s,1H,pyridine H-6);  $^{13}C$  NMR 19.7 (CH<sub>3</sub>), 24.5 (CH<sub>3</sub>), 60.2(C6'), 68.3(C4'), 68.7(C2'), 74.9(C3'), 79.7(C5'), 84.1(C1'), 104.6 (C3), 115.0(CN), 120.7(C6), 152.4(C4), 159.7(C5), 161.5(C2), 169.3(CO); m/z 354 (Found: C,51.13; H, 5.11; N,8.26  $C_{15}H_{18}N_2SO_6$  requires C,50.85; H,5.08; N,7.90 %).

**9j:** Yield 82 %, mp 236 °C, IR 3434(OH), 2224(CN), 1645(CO)  $cm^{-1}$ ;  $^1H$  NMR 2.32(s,3H,CH<sub>3</sub>), 3.18-3.82(m,6H,2H-6',H-5',H-4',H-3' and H-2'), 4.55(s,1H,2'-OH), 4.61(s,1H,3'-OH), 4.97(s,1H,4'-OH), 5.36 (s,1H,6'-OH), 5.64(d, $J_{1'-2'} = 9.98$  Hz,1H,H-1'), 7.55(m,3H,Ar-H), 7.86(s,1H, pyridine H-6), 8.19 (m,2H,Ar-H);  $^{13}C$  NMR 19.9(CH<sub>3</sub>), 60.4(C6'), 68.4(C4'), 68.6(C2') , 74.9(C3'), 79.2 (C5'), 84.3(C1'), 105.4(C3), 114.9(CN), 127.3-130.5(Ar-C), 136.7(C6), 153.4(C5), 157.7 (CO), 160.4(C2); m/z 416 (Found: C,58.02; H,4.89; N,6.98  $C_{20}H_{20}N_2SO_6$  requires C,57.69; H,4.80; N,6.73 %).

**9k:** Yield 81 %, mp 204 °C, IR 3390(OH), 2225(CN), 1648(CO)  $cm^{-1}$ ; m/z 384 (Found: C,50.32; H,5.28; N,7.68  $C_{16}H_{20}N_2SO_7$  requires C,50.00; H,5.21; N,7.29 %).

**9l:** Yield 80 %, mp 217 °C; IR 3476(OH), 2224(CN), 1662(CO)  $cm^{-1}$ ; m/z 446 (Found: C, 56.65; H,4.98; N,6.50  $C_{21}H_{22}N_2SO_7$  requires C,56.50; H,4.93; N,6.28 %).

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### REFERENCES

1. Robins, M. J.; Currie, B. L.; *Chem. Commun.*, **1968**, 1547.
2. Creaven, P. J.; Priore, R. L.; Mittelman, A.; Bruno, S.; Henderson, E. S.; Rustum, Y. M.; Solomon, K.; *Cancer Treat. Rep.*, **1982**, *66*, 81.

3. Watanabe, K. A.; Reichman, U.; Greenberg, N.; Lopez C.; Fox, J.; *J. Med. Chem.*, **1984**, *27*, 91.
4. Copp, R. R.; Marquez, V. E.; *J. Med. Chem.*, **1991**, *34*, 208.
5. Elgemeie, G. H.; Attia, A. M.; *Phosphorus, Sulfur, and Silicon*, **1994**, *92*, 95.
6. Elgemeie, G. H.; Attia, A. M.; Farag, D. S.; Sherif, S. M.; *J. Chem. Soc. Perkin Trans. 1*, **1994**, 1285.
7. Elgemeie, G. H.; Attia, A. M.; Elzanate, A. M.; Mansour, A. K.; *Bull. Chem. Soc. Jpn.*, **1994**, *67*, 1627.
8. Attia, A. M.; Elgemeie, G. H.; *Carbohydr. Res.*, **1995**, *268*, 295.
9. Attia, A. M.; Elgemeie, G. H.; *Nucleosides & Nucleotides*, **1995**, *14*(6), 1211.
10. Elgemeie, G. H.; Attia, A. M.; Fathy, N. M.; *J. Chem. Res.(S)*, **1997**, 112.
11. Elgemeie, G. H.; Ramiz, M. M.; *Phosphorus, Sulfur, and Silicon*, **1989**, *46*, 95.
12. Niedballa, U.; Vorbruggen, H.; *J. Org. Chem.*, **1974**, *39*, 3654, 3660.
13. Vorbruggen, H.; Hofle, G.; *Chem. Ber.*, **1981**, *114*, 1256.
14. Lichtenthaler, F. W.; Voss, P.; Heerd, A.; *Tetrahedron Lett.*, **1974**, 2141.

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