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Synthesis of Some Novel Condensed Pyridine-2(1*H*)-thiones and Related Glycosides

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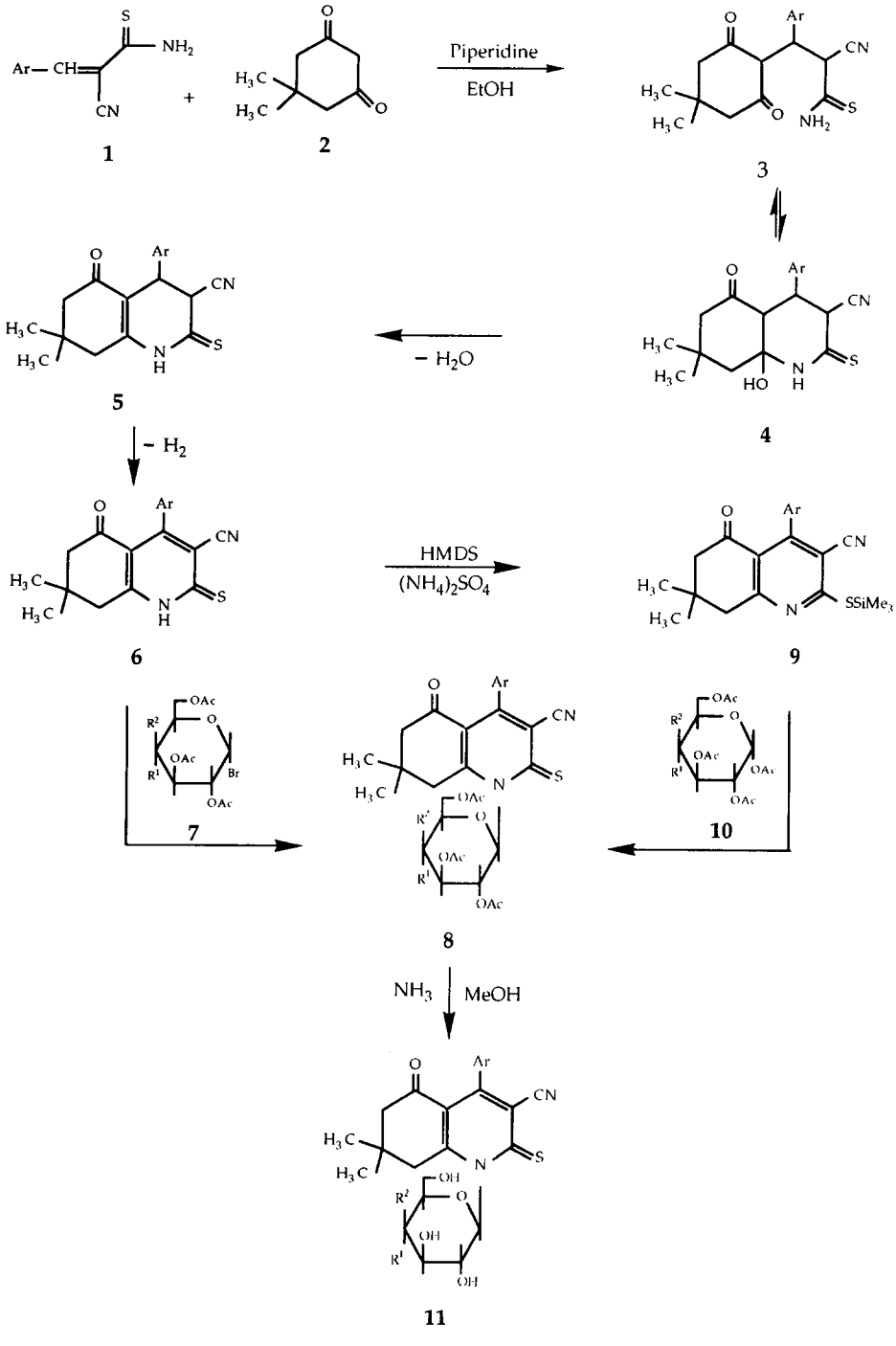
Abstract: A novel synthesis of condensed pyridine-2(1*H*)-thiones and 3-deazapyrimidine glycosides is described utilizing arylmethylenecyanothioacetamides and dimedone as starting components.

We have recently reported approaches for the synthesis of 2-oxo- and 2-thio-pyridines *via* reaction of α,β-unsaturated nitriles with active methylene reagents.[1-4] The importance of such compounds, as intermediates for the synthesis of the biologically active deazafolic acid and 3-deazapyrimidine nucleosides ring systems [5-7] prompted our interest in the synthesis and chemistry of this class of compounds. We now report the novel reaction of 5,5-dimethyl-1,3-cyclohexadione **1** with arylmethylenecyanothioacetamides **2** in refluxing ethanol containing a catalytic amount of piperidine for 3 h to produce the condensed 3-cyano-pyridine-2(1*H*)-thiones **6**. The structure of **6** could be established for the reaction products on the basis of their elemental analysis and spectral data. The formation of **6** from **1** and **2** is assumed to proceed *via* addition of an active methylene group of dimedone **2** to the double bond of **1** to give an intermediate **3**. This Michael adduct then cyclizes to give the intermediate dihydropyridine derivatives **5** which is oxidised under the reaction conditions to yield **6**. Compounds **6** were found useful for the synthesis of 3-deazapyrimidine glycosides. Thus, **6** reacted with tetra-*O*-acetyl-α -D-gluco- and galacto-pyranosyl bromides in the presence of aqueous potassium hydroxide to give the corresponding condensed pyridinethione glycosides **8**. Although the coupling of **6** with glycosyl halides could also give the corresponding thioglycosides, the formation of **8** was proved chemically. Reaction of **6** with hexamethyldisilazane (HMDS) in the presence of ammonium sulfate[8] gave the corresponding 2-trimethylsilylthiopyridines **7**, which were subsequently treated with peracetylated sugars in the presence of $SnCl_4$ according to the method of Vorbruggen *et al* [9-12] to afford the corresponding *N*-glycosides **8**. The chemical formula and molecular structure of the glycosides **8** were identified using elemental analyses and spectral data.The ^{1}H-NMR spectrum of **8a** showed a doublet at δ 5.98 ppm (*J* 8.39 Hz)


Piperidine
EtOH
1
2
3
4
5
6
7
8
9
10
11
HMDS
$(NH_4)_2SO_4$
$- H_2O$
$- H_2$
NH_3
MeOH

	Ar
6 a	4-ClC_6H_4
b	4-$CH_3C_6H_4$
c	4-$CH_3OC_6H_4$
d	2-furanyl
e	2-thienyl
f	1-naphthyl

	Ar	R^1	R^2
8 a	4-ClC_6H_4	OAc	H
b	4-$CH_3C_6H_4$	OAc	H
c	4-$CH_3OC_6H_4$	OAc	H
d	2-furanyl	OAc	H
e	2-thienyl	OAc	H
f	1-naphthyl	OAc	H
g	4-ClC_6H_4	H	OAc
h	4-$CH_3C_6H_4$	H	OAc
i	4-$CH_3OC_6H_4$	H	OAc
j	2-furanyl	H	OAc
k	2-thienyl	H	OAc
l	1-naphthyl	H	OAc

	Ar	R^1	R^2
11 a	4-ClC_6H_4	OH	H
b	4-$CH_3C_6H_4$	OH	H
c	4-$CH_3OC_6H_4$	OH	H
d	2-furanyl	OH	H
e	2-thienyl	OH	H
f	1-naphthyl	OH	H
g	4-ClC_6H_4	H	OH
h	4-$CH_3C_6H_4$	H	OH
i	4-$CH_3OC_6H_4$	H	OH
j	2-furanyl	H	OH
k	2-thienyl	H	OH
l	1-naphthyl	H	OH

assigned to the anomeric proton of the glucose moiety with a diaxial orientation of H-1' and H-2' indicating the β-configuration and $^4C_1$(D) conformation. The other protons of the glucopyranose ring resonate at 4.11-4.95 ppm, while the four acetoxy groups appear as four singlets in the 1.95-2.02 ppm 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. The UV spectrum of **8c** proved that the reaction had led selectively to the formation of *N*-glucosyl derivatives and excluded substitution at the sulfur atom. Thus whereas the *S*-methyl derivative of **6c** showed two maxima at 295 and 342 nm, its *N*-glucosyl derivative exhibited three maxima at 285, 334 and 362 nm. Preparation of highly crystalline 1-(β-D-glycopyranosyl)-3-cyanopyridine-2-thiones **11** was achieved by removal of the acetyl groups on treatment with methanolic ammonia at 0 °C. TLC of the free glycsides **11** showed that a single compound was produced, and their structures were further confirmed by elemental analyses and spectral data. The ^{1}H-NMR spectrum of **11h** showed the anomeric proton as a doublet at δ 5.68 ppm (*J* 8.96 Hz), indicating the presence of only the β-D-galactopyranose.

The compounds described in this manuscript showed no activity against Human Immunodeficiency Virus (HIV) in MT-4 cells. They were also devoid of any activity against different types of tumor virus.

EXPERIMENTAL

Melting points are uncorrected. Aluminum-coated silica gel 60 F_{254} (Merck) sheets were used for thin layer chromatography. IR spectra were collected in the transmission mode on a Pye Unicam Spectra-1000 spectrometer. ^{1}H- and ^{13}C-NMR spectra were measured in $(CD_3)_2SO$ using $SiMe_4$ as internal reference on a Varian 400 MHz spectrometer. Mass spectra were recorded by EI on a Varian Mat 311A spectrometer and FAB on a Kratos MS 50 spectrometer.

Condensed 4-aryl-3-cyanopyridine-2(1*H*)-thiones 6. General procedure:

A mixture of **1** (0.01 Mol) and **2** (0.01 Mol) was dissolved in ethanol (30 mL), a few drops of piperidine were then added. The mixture was heated under reflux for 8 h, and then allowed to stand overnight. The resulting solid product was collected by filtration and crystallized from EtOH-DMF to afford yellow crystals.

6a: Yield 61 %, mp 294 °C; IR(KBr) 3254(NH), 2222(CN), 1645(CO) cm^{-1}; ^1H NMR(DMSO-d_6) 1.03(s,2H,CH_2), 1.12(s,2H,CH_2), 2.16(s,3H,CH_3), 2.30(s,3H,CH_3), 7.33(m,4H,Ar-H), 14.46(s,br,1H,NH) ppm; ^{13}C NMR(DMSO-d_6) 27.3(CH_3), 27.9(CH_3), 32.2(C7), 50.5(CH_2), 52.1(CH_2), 95.8(C9), 108.3(C3), 116.9(CN), 122.4-136.1(Ar-C), 150.6(C10), 155.1(C4), 160.2(CO), 192.6(CS) ppm; m/z 342(Found: C,63.31; H,4.43; N,8.29 $C_{18}H_{15}ClN_2SO$ requires C,63.06; H,4.38; N,8.17 %).

6b: Yield 60 %, mp 298 °C; IR(KBr) 3250(NH), 2228(CN), 1642(CO) cm^{-1}; ^1H NMR(DMSO-d_6) 1.02(s,2H,CH_2), 1.15(s,2H,CH_2), 2.24(s,3H,CH_3), 2.32(s,3H,CH_3), 2.38(s,3H,CH_3), 7.12(m,4H,Ar-H), 14.39(s,br,1H,NH) ppm; ^{13}C NMR(DMSO-d_6) 21.4(CH_3), 27.9(CH_3), 28.1(CH_3), 32.2(C7), 50.9(CH_2), 52.2(CH_2), 96.9(C9), 108.3(C3), 115.9(CN), 126.4-138.3(Ar-C), 150.1(C10), 156.5(C4), 159.8(CO), 192.4(CS) ppm; m/z 322(Found: C,70.92; H,5.67; N,8.86 $C_{19}H_{18}N_2SO$ requires C,70.80; H,5.59; N,8.69 %).

6c: Yield 62 %, mp 289 °C; IR(KBr) 3254(NH), 2225(CN), 1645(CO) cm^{-1}; ^1H NMR(DMSO-d_6) 1.03(s,2H,CH_2), 1.08(s,2H,CH_2), 2.17(s,3H,CH_3), 2.34(s,3H,CH_3), 3.84(s,3H,OCH_3), 7.09(m,4H,Ar-H), 14.33(s,br,1H,NH) ppm; ^{13}C NMR(DMSO-d_6) 27.4(CH_3), 28.2 (CH_3), 32.4(C7), 50.8(CH_2), 52.1(CH_2), 55.4(OCH_3), 96.8(C9), 107.6(C3), 114.9 (CN), 121.9-138.0(Ar-C), 150.7(C10), 156.4(C4), 159.9(CO), 193.6(CS) ppm; m/z 338(Found: C,67.71; H,5.49; N,8.50 $C_{19}H_{18}N_2SO_2$ requires C,67.45; H,5.32; N,8.28 %).

6d: Yield 59 %, mp 261 °C; IR(KBr) 3250(NH), 2226(CN), 1640(CO) cm^{-1}; ^1H NMR(DMSO-d_6) 1.06(s,2H,CH_2), 1.16(s,2H,CH_2), 2.30(s,3H,CH_3), 2.42(s,3H,CH_3), 6.82(d,1H,furan H-4), 7.08(d,1H,furan H-3), 8.08(d,1H,furan H-5), 14.05(s,br,1H,NH) ppm; m/z 298(Found: C,64.62; H,4.76; N,9.58 $C_{16}H_{14}N_2SO_2$ requires C,64.43; H,4.69; N,9.39 %).

6e: Yield 63 %, mp 249 °C; IR(KBr) 3260(NH), 2220(CN), 1648(CO) cm^{-1}; m/z 314(Found: C,61.33; H,4.56; N,9.08 $C_{16}H_{14}N_2S_2O$ requires C,61.14; H,4.45; N,8.91 %).

6f: Yield 60 %, mp 306 °C; IR(KBr) 3428(NH), 2220(CN), 1620(CO) cm^{-1}; ^1H NMR(DMSO-d_6) 1.02(s,2H,CH_2), 1.13(s,2H,CH_2), 2.25(s,3H,CH_3), 2.40(s,3H,CH_3), 7.56(m,7H,Ar-H), 14.12(s,br,1H,NH) ppm; ^{13}C NMR(DMSO-d_6) 27.9(CH_3), 29.3(CH_3), 32.2(C7), 50.8(CH_2), 51.8(CH_2), 94.9(C9), 108.3(C3), 117.8(CN), 125.7-140.3(Ar-C), 151.1(C10), 155.1(C4), 160.3(CO), 193.9(CS) ppm; m/z 358(Found: C,73.96; H,5.23; N,7.97 $C_{22}H_{18}N_2SO$ requires C,73.74; H,5.02; N,7.82 %).

3-Cyano-1-(2',3',4',6'-tetra-*O*-acetyl-β-D-glycopyranosyl)-pyridine-2-thiones 8.

General coupling procedures. Method A: To a solution of 3-cyanopyridine-2(1*H*)-thiones **6** (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-α-D-gluco- or galacto-pyranosyl bromide **7** (0.011 Mol) in 30 mL acetone was added. The reaction mixture was stirred at room temperature until the reaction was judged complete by TLC (30 min to 2 h), using chloroform : ether 4:1, v/v (Rf 0.70-0.76 region), then evaporated under reduced pressure at 40 °C 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-Cyanopyridine-2(1*H*)-thiones **6** (0.01 Mol) were refluxed by stirring under anhydrous condition for 24 h with hexamethyldisilazane 60 mL and $(NH_4)_2SO_4$ (0.02g). The clear solution obtained was cooled and the solvent was removed *in vacuo*. The resulting trimethylsilylated pyridine **9** was dissolved in anhydrous 1,2-dichloroethane 40 mL, and a solution of α-D-glycopyranose pentaacetate **10** (0.011 Mol) in dry 1,2-dichloroethane 20 mL was then added with stirring. The mixture was cooled to - 10 °C and a solution of $SnCl_4$ 1.6 mL in anhydrous 1,2-dichloroethane 5 mL was added dropwise and the mixture was stirred until the reaction was judged complete by TLC (2-3 h), then poured into saturated $NaHCO_3$ solution and extracted with $CHCl_3$. The organic layer was dried over $MgSO_4$, filtered and concentrated to give the crude nucleosides that were purified by recrystallization from EtOH to afford pale yellow needle crystals.

8a: Yield 71 %, mp 176 °C; IR(KBr) 2220(CN), 1754(CO ester), 1630(CO) cm^{-1}; ^1H NMR (DMSO-d_6), 1.03(m,4H,2CH_2), 1.95-2.02(4s,12H,4CH_3CO), 2.22(s,3H,CH_3), 2.38(s,3H,CH_3), 4.11(m,2H,H-6' and 1H,H-5'), 4.52(s,1H,H-4'), 4.94(m,2H,H-3' and H-2'), 5.98(d,$J_{1'\text{-}2'}$ 8.39 Hz,1H,H-1'), 7.36(m,4H,Ar-H) ppm; ^{13}C NMR(DMSO-d_6) 20.1-20.5(4CH_3CO), 26.6(CH_3), 28.5(CH_3), 32.2(C7), 49.9(CH_2), 50.0(CH_2), 61.9(C6'), 67.7(C4'), 69.5(C2'), 72.7((C3'), 74.8(C5'), 83.3(C1'), 94.9(C9), 107.8(C3), 118.1(CN), 127.8-139.7(Ar-C), 143.3(C10), 149.6(C4), 169.0(CO), 169.2-169.8(4$COCH_3$), 194.5(CS) ppm; m/z 672(Found: C,57.32; H,5.07; N,4.29 $C_{32}H_{33}ClN_2SO_{10}$ requires C,57.10; H,4.90; N,4.16 %).

8b: Yield 73 %, mp 141 °C; IR(KBr) 2218(CN), 1752(CO ester), 1634(CO) cm^{-1}; ^1H NMR(DMSO-d_6) 1.14(m,4H,2CH_2), 2.01-2.16(4s,12H,4CH_3CO), 2.22(s,3H,CH_3), 2.26(s,3H,CH_3), 2.38(s,3H,CH_3), 4.21(m,2H,H-6' and 1H,H-5'), 4.64(t,1H,H-4'), 5.08(m,2H,H-3' and H-2'), 6.06(d,$J_{1'\text{-}2'}$ 8.96 Hz,1H,H-1'), 7.17(m,4H,Ar-H) ppm; ^{13}C NMR(DMSO-d_6) 20.1-20.5(4CH_3CO), 26.4(CH_3), 27.9(CH_3), 28.5(CH_3), 32.2(C7), 50.0(CH_2), 50.4(CH_2), 61.8(C6'), 67.7(C4'), 70.2(C2'), 72.8(C3'), 74.8(C5'), 83.6(C1'), 95.7(C9), 108.1(C3), 118.3(CN), 126.9-139.3(Ar-C), 141.6(C10), 149.3(C4), 167.3(CO), 169.0-169.8(4$COCH_3$), 194.4 (CS) ppm; m/z 652(Found: C,60.82; H, 5.61; N,4.44 $C_{33}H_{36}N_2SO_{10}$ requires C,60.73; H,5.52; N,4.29 %).

8c: Yield 72 %, mp 168 °C; IR(KBr) 2215(CN), 1744(CO ester), 1620(CO) cm^{-1}; ^1H NMR(DMSO-d_6) 1.05(s,2H,CH_2), 1.14(s,2H,CH_2), 2.02-2.10(4s,12H,4CH_3CO), 2.27(s,3H,CH_3), 2.36(s,3H,CH_3), 3.82(s,3H,OCH_3), 4.07(s,2H,H-6'), 4.25(s,1H,H-5'), 4.64(m,2H,H-4' and H-3'), 4.98(t,1H,H-2'), 5.82(d,$J_{1'\text{-}2'}$ 8.79 Hz, 1H,H-1'), 7.15(m,4H,Ar-H) ppm; m/z 668(Found: C,59.51; H,5.44; N,4.30 $C_{33}H_{36}N_2SO_{11}$ requires C,59.28; H,5.38; N,4.19 %).

8d: Yield 70 %, mp 136 °C; IR(KBr) 2218(CN), 1756(CO ester), 1640(CO) cm^{-1}; m/z 628(Found: C,57.46; H,5.18; N,4.63 $C_{30}H_{32}N_2SO_{11}$ requires C,57.32; H,5.09; N,4.54 %).

8e: Yield 72 %, mp 143 °C; IR(KBr) 2225(CN), 1752(CO ester), 1638(CO) cm^{-1}; m/z 644(Found: C,56.11; H,5.05; N,4.58 $C_{30}H_{32}N_2S_2O_{10}$ requires C,55.90; H,4.96; N,4.34 %).

8f: Yield 74 %, mp 159 °C; IR(KBr) 2216(CN), 1755(CO ester), 1640(CO) cm^{-1}; ^1H NMR(DMSO-d_6) 1.04(s,2H,CH_2), 1.18(s,2H,CH_2), 1.94-2.06(4s,12H,4CH_3CO), 2.22(s,3H,CH_3), 2.28(s,3H,CH_3), 4.19 (m,2H,H-6' and 1H,H-5'), 4.70(t,1H,H-4'), 4.93(m,2H,H-3' and H-2'), 5.86(d,$J_{1'\text{-}2'}$ 9.56 Hz,1H,H-1'), 7.88 (m,7H,Ar-H) ppm; ^{13}C NMR(DMSO-d_6) 20.1-21.9(4CH_3CO), 28.5(CH_3), 30.5(CH_3), 33.8(C7),49.8(CH_2),

50.9(CH_2), 62.8(C6'), 68.6(C4'), 70.4(C2'), 74.7(C3'), 76.7(C5'), 84.0(C1'), 96.2(C9), 108.8(C3), 117.7(CN), 126.3-142.6(Ar-C), 150.6(C10), 154.2(C4), 157.4(CO), 169.9-170.8 (4$COCH_3$), 195.5(CS) ppm; m/z 688(Found: C, 62.94; H, 5.48; N, 4.21 $C_{36}H_{36}N_2SO_{10}$ requires C,62.79; H,5.23; N,4.06 %).

8g: Yield 73 % , mp 137 °C; IR(KBr) 2228(CN), 1752(CO ester), 1638(CO) cm^{-1}; ^1H NMR(DMSO-d_6) 1.44(s,2H,CH_2), 1.52(s,2H,CH_2), 1.91-2.02(4s,12H,4CH_3CO), 2.23(s,3H,CH_3), 2.38(s,3H,CH_3), 4.05(m,2H,H-6' and 1H, H-5'), 4.93(d,1H,H-4'), 5.37(m,2H,H-3' and H-2'), 6.14(d,$J_{1'-2'}$ 10.25 Hz,1H,H-1'), 7.35(m,4H,Ar-H) ppm; ^{13}C NMR(DMSO-d_6) 20.2-20.4(4CH_3CO), 26.5(CH_3), 28.8(CH_3), 31.9(C7), 49.9(CH_2), 52.3(CH_2), 61.1(C6'), 66.2(C4'), 67.6(C2'), 70.9(C3'), 74.3(C5'), 84.2(C1'), 95.2(C9), 107.8(C3), 113.8(CN), 122.3-143.8(Ar-C), 149.8(C10), 153.6(C4), 161.5(CO), 169.3-169.9 (4$COCH_3$), 195.3(CS) ppm; m/z 672(Found: C,57.34; H,5.02; N,4.37 $C_{32}H_{33}ClN_2SO_{10}$ requires C,57.10; H,4.90; N,4.16 %).

8h: Yield 71 %, mp 117 °C; IR(KBr) 2216(CN), 1750(CO ester), 1635(CO) cm^{-1}; ^1H NMR(DMSO-d_6) 1.08(s,2H,CH_2), 1.58(s,2H,CH_2), 1.94-2.12(4s,12H,4CH_3CO), 2.25(s,3H,CH_3), 2.30(s,3H,CH_3), 2.42(s,3H,CH_3), 4.14(m,2H,H-6' and 1H,H-5'), 4.83(d,1H,H-4'), 5.28(m,2H,H-3' and H-2'), 5.88(d,$J_{1'-2'}$ 8.39 Hz,1H,H-1'), 7.53(m,4H,Ar-H) ppm; ^{13}C NMR(DMSO-d_6) 20.2-20.5(4CH_3CO), 26.2(CH_3), 26.4(CH_3), 28.9(CH_3), 31.9(C7), 50.0(CH_2), 50.9(CH_2), 61.5(C6'), 67.6(C4'), 70.6(C2'), 73.8(C3'), 74.3(C5'), 84.2 (C1'), 94.8(C9), 118.3(CN), 126.8-139.7(Ar-C), 141.8(C10), 149.5(C4), 166.2(CO), 169.3-169.8(4$COCH_3$), 194.5 (CS) ppm; m/z 652(Found: C,60.91; H, 5.58; N,4.40 $C_{33}H_{36}N_2SO_{10}$ requires C,60.73; H,5.52; N,4.29 %).

8i: Yield 72 %, mp 128 °C; IR(KBr) 2214(CN), 1752(CO ester), 1638(CO) cm^{-1}; ^1H NMR(DMSO-d_6) 1.12(s,2H,CH_2), 1.62(s,2H,CH_2), 1.98-2.12(4s,12H,4CH_3CO), 2.22(s,3H,CH_3), 2.38(s,3H,CH_3), 3.86(s,3H,OCH_3), 4.17(m,2H,H-6' and 1H,H-5'), 4.92(t,1H,H-4'), 5.24(m,2H,H-3' and H-2'), 6.05(d,$J_{1'-2'}$ 8.76 Hz,1H,H-1'), 7.18(d,2H,Ar-H),7.64(d,2H,Ar-H) ppm; m/z 668(Found: C,59.47; H,5.50; N,4.36 $C_{33}H_{36}N_2SO_{11}$ requires C,59.28; H,5.38; N,4.19 %).

8j: Yield 70 %, mp 116 °C; IR(KBr) 2220(CN), 1752(CO ester), 1644(CO) cm^{-1}; ^1H NMR(DMSO-d_6) 1.18(m,4H,2CH_2), 1.96-2.10(4s,12H,4CH_3CO), 2.25(s,3H,CH_3), 2.34(s,3H,CH_3), 4.06(m,2H,H-6' and 1H,H-5'), 4.68(t,1H,H-4'), 5.02(t,1H,H-3'), 5.38(m,1H,H-2'), 6.08(d,$J_{1'-2'}$ 10.51 Hz,1H,H-1'), 6.72(q,1H,furan H-4), 6.98(dd,1H,furan H-3), 7.88(m,1H,furan H-5) ppm; ^{13}C NMR(DMSO-d_6) 20.2-20.4(4CH_3CO), 26.1(CH_3), 28.9(CH_3), 32.3(C7), 50.0(CH_2), 52.3(CH_2), 61.4(6'), 66.2(C4'), 67.6(C2'), 70.9(C3'), 74.3(C5'), 84.5(C1'), 94.9(C9), 107.6(C3), 114.0(CN), 118.1(furan C4), 122.4 (furan C3), 142.1(C10), 146.0(C4), 150.4(furan C5), 155.5 (furan C2), 166.1(CO),169.3-169.9(4$COCH_3$), 194.8(CS) ppm; m/z 628(Found: C,57.57; H,5.13; N,4.61 $C_{30}H_{32}N_2SO_{11}$ requires C,57.32; H,5.09; N,4.45 %).

8k: Yield 70 %, mp 126 °C; IR(KBr) 2224(CN), 1748(CO ester), 1642(CO) cm^{-1}; ^1H NMR(DMSO-d_6) 1.26(m,4H,2CH_2), 1.92-2.08(4s,12H,4CH_3CO), 2.15(s,3H,CH_3), 2.24(s,3H,CH_3), 4.05(m,2H,H-6' and 1H,H-5'), 4.48(t,1H,H-4'), 5.12(m,1H,H-3'), 5.36(m,1H,H-2'), 6.14(d,$J_{1'-2'}$ 10.51 Hz,1H,H-1'), 6.94(m,1H,thiophene H-4), 7.16(m,1H,thiophene H-3), 7.78(d,1H,thiophene H-5) ppm; ^{13}C NMR(DMSO-d_6) 20.3-20.8(4CH_3CO), 26.2(CH_3), 27.8(CH_3), 31.9(C7), 49.9(CH_2), 52.5(CH_2), 61.5(C6'), 66.2(C4'), 67.3(C2'), 70.6(C3'), 74.3(C5'), 84.2(C1'), 94.4(C9), 108.5(C3), 113.7(CN), 118.2(thiophene C4), 122.7(thiophene C3), 147.7(C10), 148.0(C4), 149.6(thiophene C5), 161.6(thiophene C2), 166.0(CO), 169.3-169.7(4$COCH_3$), 195.0(CS) ppm; m/z 644(Found: C,56.21; H,5.07; N,4.58 $C_{30}H_{32}N_2S_2O_{10}$ requires C,55.90; H,4.96; N,4.34 %).

8l: Yield 73 %, 136 °C; IR(KBr) 2222(CN), 1755(CO ester), 1648(CO) cm^{-1}; ^1H NMR(DMSO-d_6) 1.12(m,4H,2CH_2), 1.93-2.12(4s,12H,4CH_3CO), 2.17(s,3H,CH_3), 2.31(s,3H,CH_3), 4.06(m,2H,H-6' and 1H,H-5'), 4.38(t,1H,H-4'), 4.72(d,1H,H-3'), 5.06(t,1H,H-2'), 5.88(d,$J_{1'-2'}$ 7.98 Hz,1H,H-1'), 7.33-7.90 (m,7H,Ar-H) ppm; m/z 688(Found: C,62.96; H,5.32; N,4.23 $C_{36}H_{36}N_2SO_{10}$ requires C,62.79; H,5.23; N,4.06 %).

3-Cyano-1-(β-D-glycopyranosyl)-pyridine-2-thiones 11. General Procedure for Nucleoside Deacylation:

Dry ammonia gas was passed into a solution of protected nucleosides **8** (0.5 g) in 20 mL of dry MeOH at 0 °C for 0.5 h. The reaction mixture was stirred until completion as shown by TLC (8-12 h), using chloroform :Methanol 9:1, v:v, (Rf 0.62-0.64 region). The resulting mixture was then concentrated under reduced pressure at 40 °C to afford a solid residue that was crystallized from MeOH to furnish colorless crystals.

11a: Yield 80 %, mp 207 °C; IR(KBr) 3620-3280(OH), 2222(CN), 1656(CO) cm^{-1}; m/z 504(Found: C,57.22; H,5.08; N,5.71 $C_{24}H_{25}N_2ClSO_6$ requires C,57.08; H,4.95;N, 5.55 %).

11b: Yield 81 %, mp 223 °C; IR(KBr) 3680-3210(OH), 2218(CN), 1632(CO) cm^{-1}; ^1H NMR(DMSO-d_6) 1.16(m,4H,2CH_2), 2.22(s,3H,CH_3), 2.30(s,3H,CH_3), 2.38(s,3H,CH_3), 3.12-3.56(m,6H,2H-6',H-5',H-4',H-3' and H-2'), 4.42(d,2H,2'-OH and 3'-OH), 4.82(s,1H,4'-OH), 5.23(s,1H,6'-OH), 5.69(d,$J_{1'-2'}$ 8.84 Hz, 1H,H-1'), 7.38(m,4H,Ar-H) ppm; m/z 484(Found: C,62.17; H,5.88; N,5.90 $C_{25}H_{28}N_2SO_6$ requires C,61.98; H,5.78; N,5.78 %).

11c: Yield 82 %, mp 215 °C; IR(KBr) 3640-3260(OH), 2214(CN), 1636(CO) cm^{-1}; m/z 500(Found: C,60.21; H,5.68; N,5.76 $C_{25}H_{28}N_2SO_7$ requires C,60.00; H,5.60; N,5.60 %).

11d: Yield 79 %, mp 191 °C; IR(KBr) 3580-3190(OH), 2218(CN), 1640(CO) cm^{-1}; m/z 460(Found: C,57.61; H,5.30; N,6.17 $C_{22}H_{24}N_2SO_7$ requires C,57.39; H,5.22; N,6.08 %).

11e: Yield 81 %, mp 196 °C; IR(KBr) 3610-3280(OH), 2223(CN), 1648(CO) cm^{-1}; m/z 476(Found: C,55.65; H,5.15; N,5.99 $C_{22}H_{24}N_2S_2O_6$ requires C,55.46; H,5.04; N,5.88 %).

11f: Yield 83 %, mp 186 °C; IR(KBr) 3640-3200(OH), 2216(CN), 1635(CO) cm^{-1}; ^1H NMR(DMSO-d_6) 1.18(m,4H,2CH_2), 2.20(s,3H,CH_3), 2.34(s,3H,CH_3), 3.12-3.82(m,6H,2H-6',H-5',H-4',H-3' and H-2'), 4.66(d,2H,2'-OH and 3'-OH), 5.05(s,1H,4'-OH), 5.28(s,1H,6'-OH), 5.70(d,$J_{1'-2'}$ 8.92 Hz,1H,H-1'), 7.56(m,7H,Ar-H) ppm; m/z 520(Found: C, 64.80; H,5.46; N,5.52 $C_{28}H_{28}N_2SO_6$ requires C,64.61; H,5.38; N,5.38 %).

11g: Yield 82 %, mp 218 °C; IR(KBr) 3580-3345(OH), 2225(CN), 1660(CO) cm^{-1}; ^1H NMR (DMSO-d_6) 1.15(m,4H,2CH_2), 2.24(s,3H,CH_3), 2.38(s,3H,CH_3), 3.35-3.74(m,6H,2H-6', H-5',H-4',H-3' and H-2'), 4.42(d,1H,2'-OH), 4.82(t,2H,3'-OH and 4'-OH), 4.94(d,1H,6'-OH), 5.78(d,$J_{1'-2'}$ 9.56 Hz,1H,H-1'), 7.36(m,4H,Ar-H) ppm; ^{13}C NMR(DMSO-d_6) 26.5(CH_3), 28.8(CH_3), 31.9(C7), 50.0(CH_2), 52.3(CH_2), 60.4(C6'), 68.1(C4'), 69.7 (C2'), 74.2(C3'), 79.9(C5'), 85.4(C1'), 96.7(C9), 107.6(C3), 113.6(CN),121.2-144.2(Ar-C), 149.5(C10), 156.3(C4), 167.1(CO), 194.4(CS) ppm; m/z 504(Found: C,57.21; H,5.08; N,5.76 $C_{24}H_{25}N_2ClSO_6$ requires C,57.08; H,4.95; N,5.55 %).

11h: Yield 80 %, mp 201 °C; IR(KBr), 3640-3310(OH), 2214(CN), 1654(CO) cm^{-1}; ^1H NMR(DMSO-d_6) 1.14(s,2H,CH_2), 1.21(s,2H,CH_2), 2.18(s,3H,CH_3), 2.26(s,3H,CH_3), 2.34(s,3H,CH_3), 3.12-3.88(m,6H,2H-6',H-

5',H-4',H-3' and H-2'), 4.40(d,1H,2'-OH), 4.82(m,2H,3'-OH and 4'-OH), 5.04(d,1H,6'-OH), 5.68(d,$J_{1'-2'}$ 8.96 Hz,1H,H-1'), 7.16(m,4H,Ar-H) ppm; ^{13}C NMR(DMSO-d_6) 26.4(CH_3), 27.5(CH_3), 28.8(CH_3), 31.9(C7), 50.0(CH_2), 50.1(CH_2), 60.4(C6'), 68.1(C4'), 69.8(C2'), 74.3(C3'), 79.9(C5'), 85.3(C1'), 93.8(C9), 108.2(C3), 118.6(CN), 126.8-141.8(Ar-C), 143.5(C10), 149.3(C4),166.3(CO), 194.4(CS) ppm; m/z 484(Found: C,62.13; H,5.84; N,5.95 $C_{25}H_{28}N_2SO_6$ requires C,61.98; H,5.78; N,5.78 %).

11i: Yield 80 %, mp 198 °C; IR(KBr) 3620-3210(OH), 2217(CN), 1640(CO) cm^{-1}; m/z 500(Found: C,60.17; H,5.69; N,5.78 $C_{25}H_{28}N_2SO_7$ requires C,60.00; H,5.60; N,5.60 %).

11j: Yield 81 %, mp 188 °C; IR(KBr) 3600-3290(OH), 2220(CN), 1645(CO) cm^{-1}; m/z 460 (Found: C,57.50; H,5.33; N,6.26 $C_{22}H_{24}N_2SO_7$ requires C,57.39; H,5.22; N,6.08 %).

11k: Yield 80 %, mp 205 °C; IR(KBr) 3650-3340(OH), 2219(CN), 1644(CO) cm^{-1}; m/z 476(Found: C,55.62; H,5.18; N,6.01 $C_{22}H_{24}N_2S_2O_6$ requires C,55.46; H,5.04; N,5.88 %).

11l: Yield 82 %, mp 220 °C; IR(KBr) 3610-3280(OH), 2220(CN), 1654(CO) cm^{-1}; ^{1}H NMR(DMSO-d_6) 1.10(s,2H,CH_2), 1.16(s,2H,CH_2), 2.25(s,3H,CH_3), 2.36(s,3H,CH_3), 3.22-3.80(m,6H ,2H-6',H-5',H-4',H-3' and H-2'), 4.62(s,1H,2'-OH), 4.80(t,1H,3'-OH), 4.97(d,1H,4'-OH), 5.08(s,1H,6'-OH), 5.68(d,$J_{1'-2'}$ 9.58 Hz,1H,H-1'), 7.48(m,7H,Ar-H) ppm; m/z 520(Found: C,64.85; H,5.43; N,5.54 $C_{28}H_{28}N_2SO_6$ requires C,64.61; H,5.38; N,5.38 %).

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REFERENCES

1. Attia, A. M.; Elgemeie, G. H.; *Carbohyd. Res.*, **1995**, 268, 295.
2. Attia, A. M.; Elgemeie, G. H.; *Nucleosides and Nucleotides*, **1995**, 14, 1211.
3. Elgemeie, G. H.; Fathy, N. M.; Attia, A. M.; *J. Chem. Res.(S)*, **1995**, 292.
4. Elgemeie, G. H.; Attia, A. M.; Fathy, N. M.; *J. Chem. Res.(S)*, **1997**, 112.
5. Watanabe, K. A.; Reichman, U.; Greenberg, N.; Lopez, C.; Fox, J.; *J. Med.Chem.*, **1984**, 27, 91.
6. Degraw, J. I.; Christine, P. H.; Kisliuk, R. L.; Gaumont, Y.; Sirotnak, F. M.; *J. Med. Chem.*, **1990**, 33, 673.
7. Copp, R. R.; Marquez, V. E.; *J. Med. Chem.*, **1991**, 34, 208.
8. Wittenburg, E.; *Z. Chem.*, **1964**, 4, 303.
9. Vorbruggen, H.; Krolikiewicz, K.; Bennua, B.; *Chem. Ber.*, **1981**, 114, 1234.
10. Niedballa, U.; Vorbruggen, H.; *J. Org. Chem.*, **1974**, 39, 3654.
11. Vorbruggen, H.; Hofle, G.; *Chem. Ber.*, **1981**, 114, 1256.
12. Lichtenthaler, F. W.; Voss, P.; Heerd, A.; *Tetrahedron Lett.*, **1974**, 2141.

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