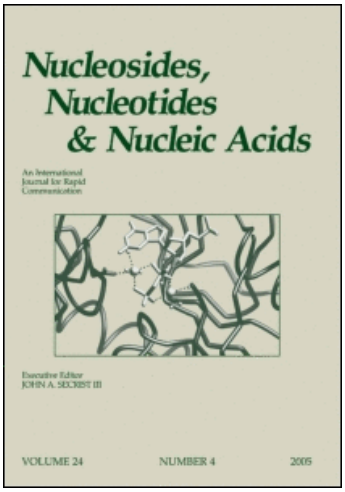

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Synthesis of *N*-Glycosylated Pyridines as New Antiviral Agents

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SYNTHESIS OF *N*-GLYCOSYLATED PYRIDINES AS NEW ANTIVIRAL AGENTS

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Abstract: A series of 3-cyanopyridine glycosides have been synthesized and evaluated for their inhibitory activity against human immunodeficiency virus (HIV) replication in MT-4 cells. Among the 3-cyanopyridine glycosides 6-(p-methylphenyl) and 6-(p-aminophenyl) were the most selective inhibitors of HIV replication.

3-Deazauridine and 3-deazacytidine were found to exert marked inhibitory effects on the growth of neoplastic and bacterial culture[1] and also have antiviral activity against RNA viruses[2]. Also 3-deazauridine apparently blocks the action of an enzyme which catalyzes overall amination of UTP to CTP[3]. The 3-deazapyrimidine nucleosides constitute another logical class of analogues with potential biological activity[4,5]. As a part of our program directed for development of new, simple and efficient procedures for the synthesis of antimetabolites[6-11], we report in this paper a novel synthesis of 3-deazapyrimidine glycosides **5** utilizing our previously reported pyridine-2(1*H*)-ones **3**[12] as starting materials. Compounds **3** can be prepared by the reaction of α, ß-unsaturated nitriles **1** with acetophenones **2** in boiling ethanol containing ammonium acetate. Compounds **3** reacted with 2,3,4,6-tetra-*O*-acetyl-α-D-gluco- and galactopyranosyl bromides **4** in the presence of aqueous potassium hydroxide to give the corresponding *N*-glucosides **5a-h** and *N*-galactosides **5i-p**, respectively. The structures of the reaction products **5** were established and confirmed on the basis of their elemental analyses and spectral data (MS, IR, ^{1}H NMR, ^{13}C NMR). Thus the analytical data for **5n** revealed a molecular formula $C_{31}H_{30}N_2O_{11}$ (m/z 606). The ^{1}H NMR spectrum showed a doublet at δ 6.6 ppm assigned to the anomeric proton of the galactose moiety with a spin-spin

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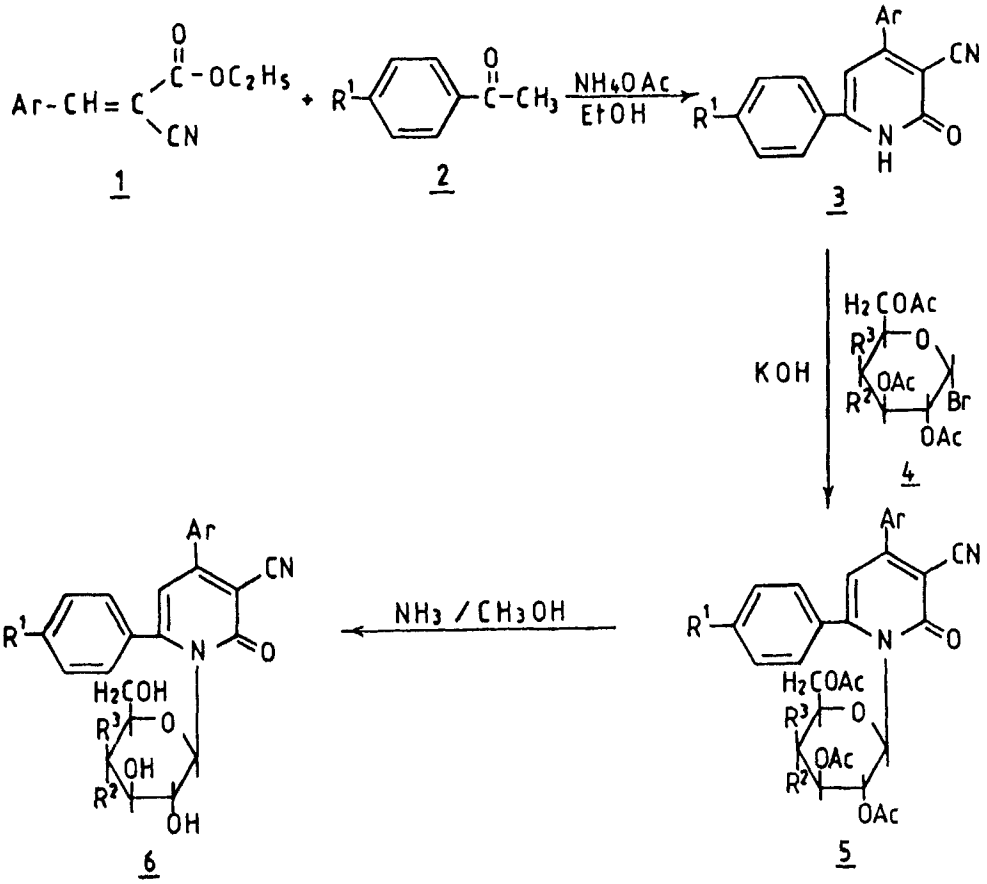

	Ar	R^1	R^2	R^3
5a	Phenyl	H	OAc	H
b	Phenyl	CH_3	OAc	H
c	Phenyl	OCH_3	OAc	H
d	Phenyl	NH_2	OAc	H
e	2-Furyl	H	OAc	H
f	2-Furyl	CH_3	OAc	H
g	2-Furyl	OCH_3	OAc	H
h	2-Furyl	NH_2	OAc	H
i	Phenyl	H	H	OAc
j	Phenyl	CH_3	H	OAc
k	Phenyl	OCH_3	H	OAc
l	Phenyl	NH_2	H	OAc
m	2-Furyl	H	H	OAc
n	2-Furyl	CH_3	H	OAc
o	2-Furyl	OCH_3	H	OAc
p	2-Furyl	NH_2	H	OAc

	Ar	R^1	R^2	R^3
6a	Phenyl	H	OH	H
b	Phenyl	CH_3	OH	H
c	Phenyl	OCH_3	OH	H
d	Phenyl	NH_2	OH	H
e	2-Furyl	H	OH	H
f	2-Furyl	CH_3	OH	H
g	2-Furyl	OCH_3	OH	H
h	2-Furyl	NH_2	OH	H
i	Phenyl	H	H	OH
j	Phenyl	CH_3	H	OH
k	Phenyl	OCH_3	H	OH
l	Phenyl	NH_2	H	OH
m	2-Furyl	H	H	OH
n	2-Furyl	CH_3	H	OH
o	2-Furyl	OCH_3	H	OH
p	2-Furyl	NH_2	H	OH

Table 1: Comparative potency and selectivity of 3-cyanopyridine-2-one glucosides and galactosides analogues as inhibitors of HIV replication in MT-4 cells.

Compd	EC_{50}[a] μM	IC_{50}[b] μM	TI[c] (ratio IC_{50}/EC_{50})
5a		>16.5	
5b		>11.7	
5c		>15.8	
5d		>11.6	
5e		>16.8	
5f		>8.6	
5g		>11.6	
5h	11.7	>11.8	>1
5j		>16.5	
5k		>11.4	
5m		>11.9	
5n		>16.4	
5o		>11.6	
6a		>21.4	
6f	8.03	>82.1	>10.2
6i		>59.9	
6j	18.6	>22.3	>1.2
6k		>21.5	

a. Approximate values for 50% effective concentration of MT-4 cells against the cytopathic effect of HIV (EC_{50})

b. Inhibitor concentration for 50% (IC_{50}).

c. Therapeutic index TI (IC_{50}/EC_{50}).

coupling constant equal to 8.9 Hz which corresponds to a diaxial orientation for the H-1' and H-2' protons indicating the presence of only ß-configuration. The other six protons of the galactopyranosyl ring resonate in the δ 4.12-5.64 ppm region. The remaining four acetoxy groups appeared as four singlets at δ 1.78-2.18 ppm region, while the methyl group of the aglycone resonated at δ 2.41 ppm. The ^{13}C NMR spectrum of **5n** was characterized by a signal at δ 87.1 ppm corresponding to the C-1' atom of the ß-D-galactopyranose. Four signals appeared at δ 170.5-169.4 ppm due to the four acetoxy carbonyl carbon atoms of galactose, while a signal appearing at δ 20.33-20.26 ppm was attributed to the galactose methyl carbons. Another five

Table 2: Physical and analytical data for compounds **5a-p** and **6a-p**.

Compd.	MP °C	Yield %	Mol.formula	Found/Calcd. (%)			m/z
				C	H	N	
5a	180	74	$C_{32}H_{30}N_2O_{10}$	63.9	5.1	4.6	602
			(602)	63.8	5.0	4.7	
5b	196	76	$C_{33}H_{32}N_2O_{10}$	64.6	5.1	4.7	616
			(616)	64.3	5.2	4.5	
5c	192	73	$C_{33}H_{32}N_2O_{11}$	62.9	5.3	4.5	632
			(632)	62.7	5.1	4.4	
5d	177	70	$C_{32}H_{31}N_3O_{10}$	62.5	5.2	6.9	617
			(617)	62.2	5.0	6.8	
5e	222	71	$C_{30}H_{28}N_2O_{11}$	61.0	4.8	4.9	592
			(592)	60.8	4.7	4.7	
5f	206	75	$C_{31}H_{30}N_2O_{11}$	61.5	4.9	4.8	606
			(606)	61.4	5.0	4.6	
5g	190	70	$C_{31}H_{30}N_2O_{12}$	60.0	4.8	4.7	622
			(622)	59.8	4.8	4.5	
5h	226	67	$C_{30}H_{29}N_3O_{11}$	59.4	4.9	7.1	607
			(607)	59.3	4.8	6.9	
5i	146	72	$C_{32}H_{30}N_2O_{10}$	64.0	4.8	4.5	
			(602)	63.8	5.0	4.7	
5j	183	74	$C_{33}H_{32}N_2O_{10}$	64.1	5.2	4.4	616
			(616)	64.3	5.2	4.5	
5k	168	71	$C_{33}H_{32}N_2O_{11}$	62.9	5.2	4.1	632
			(632)	62.7	5.1	4.4	
5l	105	68	$C_{32}H_{31}N_3O_{10}$	62.1	5.1	7.0	
			(617)	62.2	5.0	6.8	
5m	180	70	$C_{30}H_{28}N_2O_{11}$	60.9	4.6	4.5	592
			(592)	60.8	4.7	4.7	
5n	220	73	$C_{31}H_{30}N_2O_{11}$	61.6	5.0	4.6	606
			(606)	61.4	5.0	4.6	
5o	210	69	$C_{31}H_{30}N_2O_{12}$	59.9	4.9	4.6	
			(622)	59.8	4.8	4.5	
5p	170	65	$C_{30}H_{29}N_3O_{11}$	59.6	5.0	6.9	
			(607)	59.3	4.8	6.9	
6a	296	83	$C_{24}H_{22}N_2O_6$	66.6	5.0	6.7	434
			(434)	66.4	5.1	6.5	

Table 2. (Continued)

6b	263	85	$C_{25}H_{24}N_2O_6$	67.2	5.4	6.5	448
			(448)	67.0	5.4	6.3	
6c	256	84	$C_{25}H_{24}N_2O_7$	64.5	5.3	6.3	464
			(464)	64.7	5.2	6.0	
6d	180	83	$C_{24}H_{23}N_3O_6$	64.3	5.1	9.2	
			(449)	64.1	5.1	9.4	
6e	295	84	$C_{22}H_{20}N_2O_7$	62.4	4.5	6.8	424
			(424)	62.3	4.7	6.6	
6f	297	85	$C_{23}H_{22}N_2O_7$	63.1	5.0	6.3	438
			(438)	63.0	5.0	6.4	
6g	285	81	$C_{23}H_{22}N_2O_8$	60.6	4.9	6.5	
			(454)	60.8	4.8	6.2	
6h	190	83	$C_{22}H_{21}N_3O_7$	60.0	4.8	9.7	439
			(439)	60.1	4.8	9.6	
6i	287	84	$C_{24}H_{22}N_2O_6$	66.5	5.3	6.6	
			(434)	66.4	5.1	6.5	
6j	261	85	$C_{25}H_{24}N_2O_6$	66.9	5.4	6.5	448
			(448)	67.0	5.4	6.3	
6k	264	82	$C_{25}H_{24}N_2O_7$	64.6	5.4	6.1	
			(464)	64.7	5.2	6.0	
6l	173	84	$C_{24}H_{23}N_3O_6$	64.2	5.3	9.5	449
			(449)	64.1	5.1	9.4	
6m	288	83	$C_{22}H_{20}N_2O_7$	62.5	4.6	6.8	424
			(424)	62.3	4.7	6.6	
6n	285	84	$C_{23}H_{22}N_2O_7$	63.2	5.2	6.6	438
			(438)	63.0	5.0	6.4	
6o	290	82	$C_{23}H_{22}N_2O_8$	60.9	4.9	6.4	454
			(454)	60.8	4.8	6.2	
6p	288	84	$C_{22}H_{21}N_3O_7$	60.3	5.0	9.5	
			(439)	60.1	4.8	9.6	

Table 3: Spectral data for selected compounds listed in Table 2.

Compd.	IR(KBr)/cm^{-1}	^{1}H NMR (DMSO) δ/ppm
5a	2220 (CN), 1752 (CO ester), 1648 (CO pyridone)	1.82-2.08 (4s, 12H, 4CH_3CO), 4.21 (m, 2H, H-6',6"), 4.60 (m, 1H, H-5'), 5.32 (m, 2H, H-4' and H-3'), 5.78 (m, 1H, H-2'), 6.80 (d, J_{1-2} = 8.38 Hz, 1H, H-1'), 7.73 (s, 1H, Pyridine H-5), 7.90 (s, 5H, Ar-H), 8.13 (s, 5H, Ar-H).
5b	2222 (CN), 1750 (CO ester), 1636 (CO pyridone)	1.76-2.10 (4s, 12H, 4CH_3CO), 2.40 (s, 3H, CH_3), 4.16 (m, 2H, H-6', 6"), 4.53 (m, 1H, H-5'), 5.21 (m, 2H, H-4' and H-3'), 5.70 (t, 1H, H-2'), 6.76 (d, J_{1-2} = 8.63 Hz, 1H, H-1'), 7.39 (d, 2H, Ar-H), 7.65 (s, 3H, Ar-H), 7.76 (s, 1H, pyridine H-5), 7.96 (s, 2H, Ar-H), 8.30 (d, 2H, Ar-H)
5c	2218 (CN), 1755 (CO ester), 1640 (CO pyridone)	1.85-2.12 (4s, 12H, 4CH_3CO), 3.90 (s, 3H, OCH_3), 4.19 (m, 2H, H-6', 6"), 4.56 (t, 1H, H-5'), 5.18 (m, 2H, H-4' and H-3'), 5.70 (d, 1H, H-2'), 6.65 (d, J_{1-2} = 8.55 Hz, 1H, H-1'), 7.11 (d, 2H, Ar-H), 7.66 (s, 3H, Ar-H), 7.77 (s, 1H, pyridine H-5), 7.95 (s, 2H, Ar-H), 8.30 (d, 2H, Ar-H).
5d	3460, 3380 (NH_2), 2220 (CN), 1750(CO ester), 1642(CO pyridone)	1.88-2.09 (4s, 12H, 4CH_3CO), 4.25 (m, 2H, H-6',6"), 4.60 (m, 1H, H-5'), 5.28 (m, 2H, H-4' and H-3'), 5.80 (t, 1H, H-2'), 6.00 (s, 2H, NH_2), 6.70 (d, J_{1-2} = 8.35 Hz, 1H, H-1'), 7.64 (s, 5H, Ar-H), 7.71 (s, 1H, pyridine H-5), 8.23 (d, 4H, Ar-H).
5e	2220 (CN), 1756 (CO ester), 1610 (CO pyridone)	1.67-2.11 (4s, 12H, 4CH_3CO), 4.12 (d, 2H, H-6',6"), 4.31 (m, 1H, H-5'), 5.32 (m, 2H, H-4' and H-3'), 5.51 (m, 1H, H-2'), 6.38 (d, J_{1-2} = 8.46 Hz, 1H, H-1'), 6.72 (s, 1H, furan H-4), 7.58 (s, 5H, Ar-H), 7.71 (s, 1H, pyridine H-5), 8.03 (s, 1H, furan H-3), 8.18 (s, 1H, furan H-5).
5f	2222 (CN), 1750 (CO ester), 1600 (CO pyridone)	1.64-2.05 (4s, 12H, 4CH_3CO), 2.46 (s,3H, CH_3), 4.08 (m, 2H, H-6',6" and 1H, H-5'), 4.36 (m, 1H, H-4'), 5.34 (m, 2H, H-3' and H-2'), 6.32 (d, J_{1-2} = 8.64 Hz, 1H, H-1'), 6.70 (s, 1H, furan H-4), 7.41 (d, 4H, Ar-H), 7.69 (s, 1H, pyridine H-5), 7.80 (s, 1H, furan H-3), 8.00 (d, 1H, furan H-5).
5g	2218 (CN), 1752 (CO ester), 1610 (CO pyridone)	1.62-2.10 (4s, 12H, 4CH_3CO), 3.88 (s, 3H, OCH_3), 4.05 (m, 2H, H-6',6" and 1H, H-5'), 4.34 (m, 1H, H-4'), 5.30 (t, 1H, H-3'), 5.48 (m, 1H, H-2'), 6.31 (d, J_{1-2} = 8.66 Hz, 1H, H-1'), 6.62 (s, 1H, furan H-4), 7.10 (d, 4H, Ar-H), 7.67 (s, 1H, pyridine H-5), 7.94 (s, 1H, furan H-3), 8.16 (d, 1H, furan H-5)
5h	3460, 3360 (NH_2), 2220 (CN), 1760 (CO ester), 1610 (CO pyridone)	1.94-2.16 (4s, 12H, 4CH_3CO), 4.23 (m, 2H, H-6', 6"), 4.51 (s, 1H, H-5'), 5.22 (m, 2H, H-4' and H-3'), 5.72 (t, 1H, H-2'), 6.00 (s, 2H, NH_2), 6.70 (d, J_{1-2} = 8.56 Hz, 1H, H-1'), 6.85 (s, 1H, furan H-4), 7.80 (d, 4H, Ar-H), 7.73 (s, 1H, pyridine H-5), 7.91 (s, 1H, furan H-3), 8.10 (s, 1H, furan H-5).
5i	2220 (CN), 1760 (CO ester), 1650 (CO pyridone)	1.86-2.12 (4s, 12H, 4CH_3CO), 4.21 (m, 2H, H-6', 6"), 4.63 (m, 1H, H-5'), 5.44 (m, 2H, H-4' and H-3'), 5.60 (t, 1H, H-2'), 6.61 (d, J_{1-2} = 8.38 Hz, 1H, H-1'), 6.90 (s, 1H, furan H-4), 7.65 (s, 5H, Ar-H), 7.78 (s, 1H, pyridine H-5), 8.20 (d, 1H, furan H-3), 8.41 (s, 1H, furan H-5)
5j	2222 (CN), 1758 (CO ester), 1650 (CO pyridone)	1.75-2.15 (4s, 12H, 4CH_3CO), 2.40 (s, 3H, CH_3), 4.15 (m, 2H, H-6',6" and 1H, H-5'), 4.65 (t, 1H, H-4'), 5.57 (m, 2H, H-3' and H-2'), 6.65 (d, J_{1-2} = 8.71 Hz, 1H, H-1'), 6.85 (s, 1H, furan H-4), 7.35 (d, 4H, Ar-H), 7.75 (d, 1H, furan H-3), 8.10 (s, 1H, pyridine H-5), 8.34 (d, 1H, furan H-5).
5m	2218 (CN), 1754 (CO ester), 1650 (CO pyridone)	1.86-2.16 (4s, 12H, 4CH_3CO), 4.22 (m, 2H, H-6',6"), 4.64 (m, 1H, H-5'), 5.41 (m, 2H, H-4' and H-3'), 5.60 (t, 1H, H-2'), 6.58 (d, J_{1-2} = 8.68 Hz, 1H, H-1'), 6.88 (s, 1H, furan H-4), 7.65 (s, 5H, Ar-H), 7.76 (s, 1H, pyridine H-5), 8.20 (d, 1H, furan H-3), 8.34 (s, 1H, furan H-5).

Table 3: (Continued)

5n	2220 (CN), 1760 (CO ester), 1650 (CO pyridone)	1.78-2.18 (4s, 12H, $4CH_3CO$), 2.41 (s, 3H, CH_3), 4.12 (m, 2H, H-6',6" and 1H, H-5'), 4.65 (t, 1H, H-4'), 5.51 (m, 2H, H-3' and H-2'), 6.60 (d, J_{1-2} = 8.90 Hz, 1H, H-1') 6.85 9s, 1H, furan H-4), 7.32 (d, 4H, Ar-H), 7.78 (s, 1H, pyridine H-5), 8.10 (d, 1H, furan H-3), 8.33 (d, 1H, furan H-5).
6c	3600-3150 (OH), 2220 (CN), 1630 (CO pyridone)	3.25-3.78 (m, 6H, H-6',6", H-5', H-4', H-3' and H-2'), 3.88 (s, 3H, OCH_3), 4.67 (t, 1H, 2'-OH), 5.18 (d, 1H, 3'-OH), 5.24 (s, 1H, 4'-OH), 5.50 (d, 1H, 6'-OH), 6.20 (d, J_{1-2} = 8.64 Hz, 1H, H-1'), 7.12 (d, 2H, Ar-H), 7.63 (m, 3H, Ar-H), 7.74 (m, 2H, Ar-H), 7.81 (s, 1H, pyridine H-5), 8.25 (d, 2H, Ar-H)
6d	3650-3200 (OH), 2222 (CN), 1635 (CO pyridone)	3.21-3.74 (m, 6H, H-6', 6", H-5', H-4', H-3' and H-2'), 4.65 (t, 1H, 2'-OH), 5.15 (d, 1H, 3'-OH), 5.21 (s, 1H, 4'-OH), 4.45 (d, 1H, 6'-OH), 5.88 (s, 2H, NH_2), 6.18 (d, J_{1-2} = 8.55 Hz, 1H, H-1'), 6.68 (d, 2H, Ar-H), 7.56 (m, 3H, Ar-H), 7.62 (s, 1H, pyridine H-5), 7.72 (m, 2H, Ar-H), 8.00 (d, 2H, Ar-H).
6e	3600-3180 (OH) 2218 (CN) 1610 (CO Pyridone)	3.18-3.65 (m, 6H, H-6',6", H-5', H-4', H-3' and H-2'), 4.61 (t, 1H, 2'-OH), 5.18 (d, 2H, 3'-OH and 4'-OH), 5.46 (s, 1H, 6'-OH), 6.14 (d, J_{1-2} = 8.63 Hz, 1H, H-1'), 6.85 (dd, 1H, furan H-4), 7.54 (t, 3H, Ar-H), 7.72 (d, 1H, furan H-3), 8.08 (s, 1H, pyridine H-5), 8.11 (d, 2H, Ar-H), 8.24 (dd, 1H, furan H-5).
6f	3650-3150 (OH) 2220 (CN), 1610 (CO pyridone)	2.32 (s, 3H, CH_3), 3.26-3.85 (m, 6H, H-6',6", H-5', H-4', H-3' and H-2'), 4.65 (t, 1H, 2'-OH), 5.15 (d, 2H, 3'-OH and 4'-OH), 5.45 (s, 1H, 6'-OH), 6.15 (d, J_{1-2} = 8.52 Hz, 1H, H-1'), 6.85 (m, 1H, furan H-4), 7.35 (d, 4H, Ar-H), 7.71 (d, 1H, furan H-3), 8.05 (s, 1H, pyridine H-5), 8.15 (d, 1H, furan H-5).
6g	3600-3200 (OH) 2222 (CN), 1600 (CO pyridone)	3.21-3.77 (m, 6H, H-6',6", H-5', H-4', H-3' and H-2'), 3.86 (s, 3H, OCH_3), 4.65 (s, 1H, 2'-OH), 5.20 (s, 2H, 3'-OH and 4'-OH), 5.54 s, 1H, 6'-OH), 6.18 (d, J_{1-2} = 8.38 Hz, 1H, H-1'), 6.88 (dd, 1H, furan H-4), 7.18 (d, 2H, Ar-H), 7.65 (d, 1H, furan H-3), 8.00 (s, 1H, pyridine H-5), 8.13 (m, 1H, furan H-5), 8.21 (d, 2H, Ar-H).
6j	3640-3180 (OH), 2220 (CN), 1630 (CO pyridone)	2.28 (s, 3H, CH_3), 3.21-3.78 (m, 6H, H-6',6", H-5', H-4', H-3' and H-2'), 4.63 (t, 1H, 2'-OH), 5.16 (d, 1H, 3'-OH), 5.21 (s, 1H, 4'-OH), 5.42 (d, 1H, 6'-OH), 6.18 (d, J_{1-2} = 9.30 Hz, 1H, H-1'), 7.38 (d, 2H, Ar-H), 7.60 (m, 3H, Ar-H), 7.78 (m, 2H, Ar-H), 7.84 (s, 1H, pyridine H-5), 8.18 (d, 2H, Ar-H).
6k	3660-3200 (OH), 2220 (CN), 1620 (CO pyridone)	3.31-3.78 (m, 6H, H-6',6", H-5', H-4', H-3' and H-2'), 3.86 (s, 3H, OCH_3), 4.61 (t, 1H, 2'-OH), 5.18 (d, 1H, 3'-OH), 5.25 (s, 1H, 4'-OH), 5.50 (d, 1H, 6'-OH), 6.20 (d, J_{1-2} = 8.58 Hz, 1H, H-1'), 7.11 (d, 2H, Ar-H), 7.60 (m, 3H, Ar-H), 7.70 (s, 1H, pyridine H-5), 7.81 (d, 2H, Ar-H), 8.05 (d, 2H, Ar-H).
6l	3650-3180 (OH, NH_2), 2220 (CN), 1620 (CO pyridone)	3.28-3.87 (m, 6H, H-6', 6", H-5', H-4', H-3' and H-2'), 4.65 (t, 1H, 2'-OH), 5.12 (d, 1H, 3'-OH), 5.24 (s, 1H, 4'-OH), 5.48 (d, 1H, 6'-OH), 5.96 (s, 2H, NH_2), 6.21 (d, J_{1-2} = 8.66 Hz, 1H, H-1'), 6.68 (d, 2H, Ar-H), 7.58 (m, 3H, Ar-H), 7.68 (s, 1H, pyridine H-5) 7.85 (m, 2H, Ar-H), 8.05 (d, 2H, Ar-H).
6m	3660-3200 (OH), 2222 (CN), 1625 (CO pyridone)	2.40 (s, 3H, CH_3), 3.18-3.66 (m, 6H, H-6',6", H-5', H-4', H-3' and H-2'), 4.62 (t, 1H, 2'-OH), 5.18 (d, 2H, 3'-OH and 4'-OH), 5.45 (s, 1H, 6'-OH), 6.15 (d, J_{1-2} = 8.48 Hz, 1H, H-1'), 6.88 (m, 1H, furan H-4), 7.40 (d, 4H, Ar-H), 7.69 (d, 1H, furan H-3), 8.05 (s, 1H, pyridine H-5), 8.15 (d, 1H, furan H-5).
6p	3600-3200 (OH, NH_2), 2220 (CN), 1600 (CO pyridone)	3.22-3.68 (m, 6H, H-6', 6", H-5', H-4', H-3' and H-2'), 4.58 (t, 1H, 2'-OH), 5.08 (d, 1H, 3'-OH), 5.17 (s, 1H, 4'-OH), 5.49 (d, 1H, 6'-OH), 5.90 (s, 2H, NH_2), 6.16 (d, J_{1-2} = 8.55 Hz, 1H, H-1'), 6.74 (d, 2H, Ar-H), 6.88 (dd, 1H, furan H-4), 7.60 (d, 1H, furan H-3), 7.78 (s, 1H, pyridine H-5), 8.00 (d, 2H, Ar-H), 8.14 (d, 1H, furan H-5).

signals at δ 61.7, 67.7, 67.9, 70.3 and 71.3 ppm were assigned to C-6', C-4', C-2', C-3' and C-5', respectively. On the other hand, the signal of the carbonyl carbon atom of aglycone appeared at δ 162.7 ppm and the nitrile carbon atom appeared at δ 115.1 ppm. The preparation of crystalline 1-(ß-D-glycopyranosyl)3-cyanopyridine-2-ones **6a-p** was achieved by removing the blocking acetyl groups on treatment with methanolic ammonia at 0°C. The structures of compounds **6** were established on the basis of elemental analyses and spectral data. Thus, the analytical data for **6f** revealed a molecular formula $C_{23}H_{22}N_2O_7$ (m/z 438). The ^{1}HNMR spectra showed the anomeric proton as a doublet at δ 6.18 ppm ($J_{1\text{-}2}$ = 9.3 Hz) indicating the presence of only the ß-configuration. The other six glucose protons appeared as a multiplet at δ 3.21-3.78 ppm, while the four hydroxy groups of the glucose moiety resonated at δ 4.63-5.48 ppm (exchangeable by D_2O). The ^{13}C NMR spectra was characterized by a signal at δ 96.8 ppm corresponding to the C-1' atom of ß-D-glucopyranose. Another five signals at δ 60.6, 69.7, 72.9, 77.1 and 78.2 ppm were assigned to C-6', C-4', C-2', C-3' and C-5' of the glucose moiety, respectively.

In summary, we have achieved a regiospecific synthesis of interesting 3-deazapyrimidine nucleosides by the reaction of pyridine-2(1*H*)-ones with α-halomonosugars. These nucleosides can be utilized as an excellent starting materials for the synthesis of other carbohydrate derivatives.

Antiviral Activity:

The anti-HIV activity and cytotoxicity of some 3-cyano-4 and 6-disubstituted-2-pyridone glucosides and galactosides are shown in Table 1. Among these types of glycosides the 4-furyl-6(p-methylphenyl) glucoside **6f** turned out to be the most selective anti-HIV agent, followed by 4-phenyl-6(p-methylphenyl) galactosides **6j** and 4-furyl-6 (p-aminophenyl) glucose tetraacetate **5h.**, while; 4-furyl-6-phenyl- and 4, 6-diphenyl-, 4-furyl-6 (p-methylphenyl)-, and 4-phenyl-6(p-methylphenyl) glucosides or galactosides were devoid any theraputic index at the indicated concentration.

EXPERIMENTAL:

1-(2,3,4,6-Tetra-*O*-acetyl-ß-D-gluco-and D-galactopyranosyl)3-cyanopyridine-2-ones; 5

General Coupling Procedure:

To a solution of 2(1*H*)-pyridineones **3a-h** (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-gluco- or galactopyranosyl bromide **4** (4.521 g, 0.011 mol) in acetone (30 mL). The reaction mixture was stirred at room temperature until judged complete by TLC (8-12h), then evaporated under reduced pressure at 40°C and the residue washed with distilled water to remove the formed potassium bromide. The product was dried and crystallized from ethanol to afford colourless crystals (cf. Table 2).

1-(ß-D-Gluco- and D-galactopyranosyl)3-cyanopyridine-2-ones; 6

General Procedure for Nucleoside Deacylation:

Dry gaseous ammonia was passed through a solution of protected nucleosides **5** (0.5 gm) in dry methanol (20 mL) at 0°C for about 0.5 hour. The reaction mixture was then stirred at 0°C until judged complete by

TLC (20-24 h). The mixture was evaporated under reduced pressure at 40°C giving a solid residue which was crystallized from methanol to afford colourless crystals (cf. Table 2).

Biological Procedure

The compounds **5a-p** and **6a-p** were dissolved in dimethyl sulfoxide then diluted 1:100 in cell culture medium before preparing serial half-Log_{10} dilutions. T_4 Lymphocytes were added and after a brief interval HIV-1 is added, resulting in 1:200 final dilution of the compound. Uninfected cells with the compound serve as a toxicity control, and infected and uninfected cells without the compound serve as basic controls. Cultures are incubated at 37° in a 5% carbon dioxide atmosphere for 6 days. The tetrazolium salt, XTT, is added to all wells, and cultures are incubated to allow formazan color development by viable cells. Individual wells are analyzed spectrophotometrically to quantitate formazan production, and in addition are viewed microscopically for detection of viable cells and confirmation of protective activity.

Drug-treated virus-infected cells are compared with drug-treated noninfected cells and with other appropriate controls on the same plate. Data are reviewed in comparison with other tests done at the same time and a determination about activity is made.

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