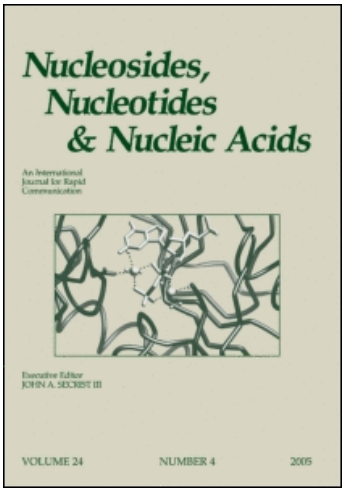

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SYNTHESIS OF 2',3'-DIDEOXYRIBAVIRIN

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ABSTRACT: A synthesis of 1-(2,3-dideoxy-β-D-ribofuranosyl)-1,2,4-triazole-3-carboxamide (2',3'-dideoxyribavirin, ddR) is described. Glycosylation of the sodium salt of 1,2,4-triazole-3-carbonitrile (5) with 1-chloro-2-deoxy-3,5-di-O-p-toluoyl-α-D-erythro-pentofuranose (1) gave exclusively the corresponding N-1 glycosyl derivative with β-anomeric configuration (6), which on ammonolysis provided a convenient synthesis of 2'-deoxyribavirin (7). Similar glycosylation of the sodium salt of methyl 1,2,4-triazole-3-carboxylate (2) with 1 gave a mixture of corresponding N-1 and N-2 glycosyl derivatives (3) and (4), respectively. Ammonolysis of 3 furnished yet another route to 7. A four-step deoxygenation procedure using imidazolylthiocarbonylation of the 3'-hydroxy group of 5'-O-toluoyl derivative (9a) gave ddR (11). The structure of 11 was proven by single crystal X-ray studies. In a preliminary *in vitro* study ddR was found to be inactive against HIV retrovirus.

Recent studies of a number of 2',3'-dideoxynucleosides (ddNs) have demonstrated that these nucleosides inhibit the *in vitro* replication and cytopathic effect of HIV retrovirus[1], the etiologic agent of the Acquired Immune Deficiency Syndrome (AIDS).[2,3] In addition ddNs have shown significant antimicrobial activity.[4] The 5'-triphosphates of ddNs are chain terminators of DNA synthesis[5] and are exploited as reagents for DNA sequencing.[6]

Ribavirin (1-β-D-ribofuranosyl-1,2,4-triazole-3-carboxamide), a broad spectrum antiviral[7,8] nucleoside, has been reported to inhibit the replication of HIV in human adult T lymphocytes at a concentration of 50 μg/mL.[9] The present work describes a synthesis of 2',3'-dideoxyriba-

virin (ddR) utilizing the sodium salt glycosylation procedure developed in our laboratory.[10]

RESULTS AND DISCUSSION: Recently various ddNs have been prepared from 5'-O-acyl-2'-deoxynucleosides, using a new deoxygenation procedure.[11] 2'-Deoxyribavirin (dR, 7) reported from our laboratory[12] seemed to be a viable starting material for our present need, which could be further deoxygenated to the desired ddR. The previously published procedure for the preparation of 7 using methyl 1,2,4-triazole-3-carboxylate (2) furnished an isomeric mixture of α and β-anomers in 20% yield, which required extensive chromatography[12] to obtain desired 7.

In view of this observation we examined glycosylation of 2 using the Na-salt procedure.[10] Thus, the Na-salt of 2 generated in situ by the addition of NaH in CH_3CN was treated with 1-chloro-2-deoxy-3,5-di-O-p-toluoyl-α-D-erythro-pentofuranose (1) to give a mixture of two products. After silica gel column chromatography a high R_f compound (4) in 25% yield and a low R_f compound (3) in 28% yield were obtained. Ammonolysis of 3 and 4 with $MeOH/NH_3$ at ambient temperature gave 7 and 8, respectively (Figure 1). The use of ^1H and ^{13}C NMR provided unequivocal proof for the assignment of structures of 7 and 8 when compared with the NMRs of appropriate triazoles reported from our laboratory.[13] In Table 1, the chemical shift of the base carbons C-3 and C-5, of compounds 7 and 8 are in agreement with reported values, confirming that the above method of glycosylation resulted in stereoselectivity but no regiospecificity.

However, the glycosylation of 1,2,4-triazole-3-carbonitrile (5) has been shown[12] to furnish exclusively the 1-glycosyl isomer and suggested that compound 5 may be employed for site specificity which could be combined with the stereoselectivity of glycosylation using the Na-salt method.[10] The Na-salt of 5 produced in situ by NaH in CH_3CN, was treated with 1 at ambient temperature. The reaction product was purified on a silica gel column to give 1-(2-deoxy-3,5-di-O-p-toluoyl-β-D-erythro-pentofuranosyl)-1,2,4-triazole-3-carbonitrile (6) in 35% yield. Attempts to isolate minor products, presumably the positional isomers, were unsuccessful during chromatography. When 6 was treated with aq. NH_4OH at 100°C for 3 h, deprotection of the sugar and amination of carbonitrile

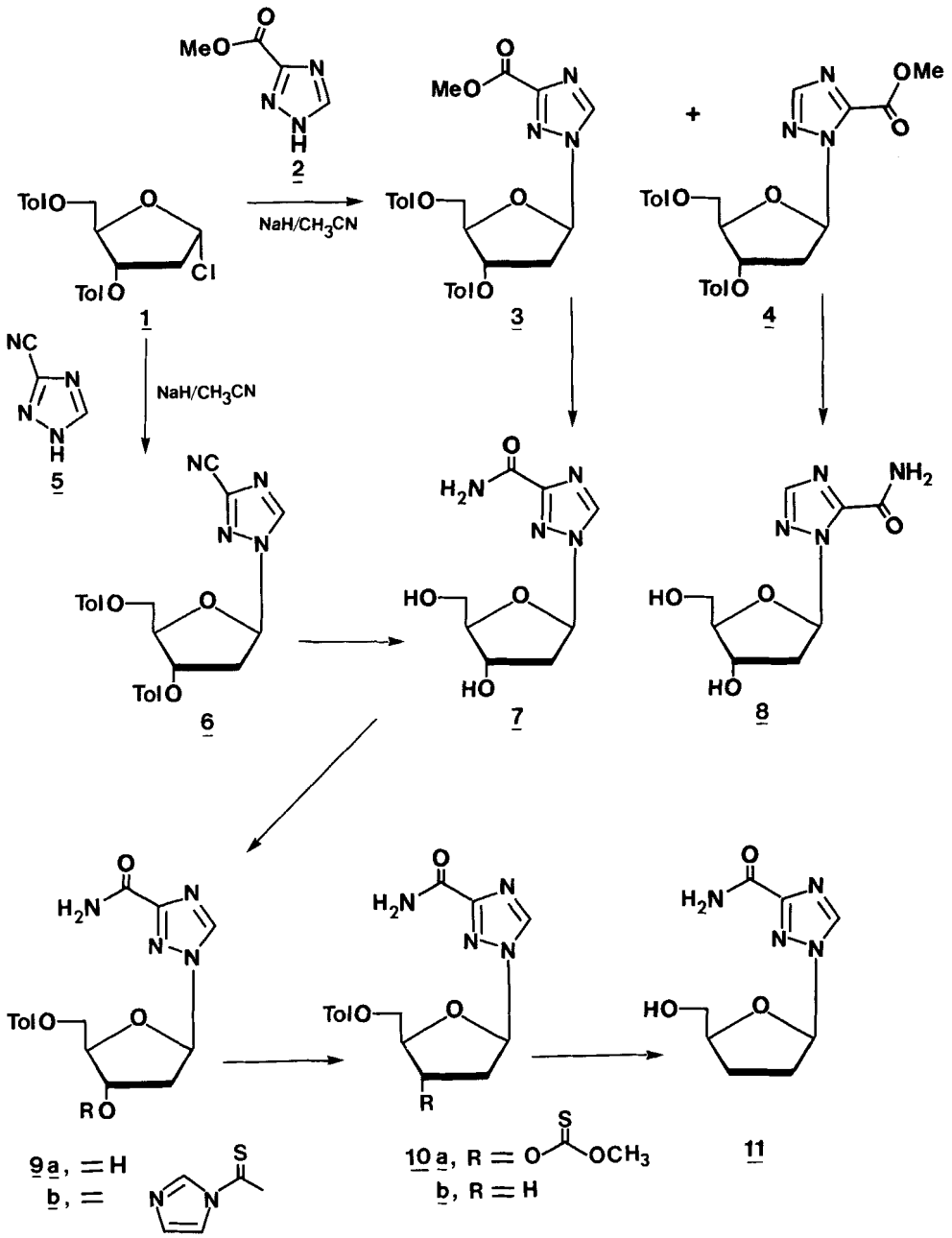

FIGURE-1

TABLE 1

	Compound	^{13}C Chemical Shift, δ ppm	
		C-3	C-5
1.	1-β-D-Ribofuranosyl-1,2,4-triazole-3-carboxamide	158.40	146.30
2.	7	157.19	144.83
3.	1-β-D-Ribofuranosyl-1,2,4-triazole-5-carboxamide	148.80	151.50
4.	8	147.25	150.21

group occurred to give a nucleoside in 84% yield; this material, upon comparison to an authentic sample,[12] was found to be 2'-deoxyribavirin.

Before the final deoxygenation step, the 5'-OH group must be protected with a base labile group, because of well known acid lability[14] of 2',3'-dideoxynucleosides. Treatment of 7 with p-toluoylchloride in pyridine gave 5'-O-p-toluoyl-2'-deoxyribavirin (9a) in 84% yield. The treatment of 9a with excess N,N'-thiocarbonyldiimidazole in DMF gave the intermediate imidazolide (9b), which upon reaction with anhydrous MeOH at 60°C for 2 h yielded a 73% of crystalline methyl thiocarbonate (10a) after column chromatography. The reduction of thionoester 10a with tri-n-butylstannane in toluene containing α,α-azobisisobutyronitrile (AIBN)[15] gave crystalline 10b. Ammonolysis of 10b furnished 2',3'-dideoxyribavirin (11), which crystallized as colorless needles. The structure of 11 was confirmed by single crystal X-ray studies.

X-RAY CRYSTALLOGRAPHY: A crystal of 11 (diameter ~0.065 mm) was cut to approximately 3 mm in length and mounted on an Enraf-Nonius CAD4 diffractometer equipped with Ni filtered Cu K_α radiation. The crystal height was adjusted to give the best agreement in the 2θ values of centered Friedel pairs. Compound 11 crystallizes with two molecules per asymmetric unit (Z=8) in space group $P2_12_12_1$ (No. 19) of the orthorhom-

bic system. Cell parameters, based on the setting angles for 25 measured reflections ($40.88° \leq 2\theta \leq 57.18°$), are $\underline{a}$ = 7.911(3), $\underline{b}$ = 14.974(9), $\underline{c}$ = 17.237(11) A, $\underline{V}$ = 2042(2) A^3. A total of 2426 reflections for $2\theta \leq 152°$ were measured by ω-2θ scans at variable scan speeds with scan width determined by 1.20 + 0.15tanθ (in degrees). The data were corrected for stability (factor range: 1.000-1.016), absorption (μ = 8.768 cm^{-1}; factor range: 1.087-1.121; based on 1 mm crystal length), Lorentz and polarization effects. Cell parameters and data were collected at 295 K.

MULTAN82[16] gave initial positions for 28 of the 30 non-hydrogen atoms; the remainder were found in an electron density difference map. Hydrogen atoms were found in difference maps as well. All atomic positional parameters were refined; non-hydrogen atoms were refined anisotropically and hydrogens were refined isotropically. The structure was refined by full-matrix least-squares (SHELX76[17]). After the final cycle, maximum shift/error was 0.02, R = 0.0429, wR = 0.0514 and S = 1.58 for 368 parameters and 1961 reflections having $F \geq 4\sigma_F$. The largest peak in the final difference map was 0.23 e/A^3. The extinction parameter refined to 1.1(1) x 10^{-6}. The function minimized was $\Sigma w(|F_o|-|F_c|)^2$ where $w = 1/(\sigma^2 + 0.00040F^2)$. Data were reduced to structure factors using SDP-Plus.[18] Scattering factors and anomalous dispersion corrections were taken from the International Tables.[19]

Atomic parameters for non-hydrogen atoms are listed in Table 2;[20] bond lengths and bond angles are in Table 3. Figure 2 is an illustration (ORTEPII[21]) of molecule B (the two molecules are virtually identical). The dideoxy-sugars are of type N, C_2, exo-C_3, endo ($^3T_2$ form) with pseudorotational parameters, P = 4.5° and τ_m = 34./° for A and 3.1° and 36.8° for B.[22] The side chains are gauche-gauche. The glycosidic torsion angles (O1'-C1'-N1-C5) are 13.4° and -4.5° for A and B, respectively, corresponding to an anti configuration. The dihedral angle between the mean planes of the triazole rings and the carboxamide groups are 4.4(2)° and 1.2(2)° for A and B, respectively. The six intermolecular hydrogen bonds are detailed in Table 4. The carboxamide groups, which link through hydrogen bonds, have a dihedral angle of 17.0(1)°. To our knowledge, this is the first reported crystal structure of a 2',3'-dideoxynucleoside.

TABLE 2. Atomic positions in fractional coordinates and U_{eq} for non-hydrogen atoms in molecules A and B of 11.

Atom	x/a	y/b	z/c	Ueq
N(1)	.6707(4)	.1440(2)	.8000(2)	.0407(8)
N(2)	.8310(3)	.1641(2)	.7789(2)	.0437(9)
C(3)	.8086(4)	.2149(2)	.7174(2)	.0352(8)
N(4)	.6454(3)	.2286(2)	.6964(2)	.0424(8)
C(5)	.5616(5)	.1822(3)	.7500(2)	.0452(10)
C(6)	.9531(4)	.2574(2)	.6762(2)	.0392(9)
O(7)	1.0988(3)	.2473(2)	.7029(2)	.0531(8)
N(8)	.9167(4)	.3051(2)	.6150(2)	.0485(10)
C(1')	.6389(5)	.0881(3)	.8696(2)	.0523(12)
C(2')	.6650(5)	.1388(3)	.9435(2)	.0558(13)
C(3')	.4902(5)	.1775(3)	.9594(2)	.0531(12)
C(4')	.3742(5)	.1049(3)	.9297(2)	.0495(11)
C(5')	.2039(6)	.1354(4)	.9000(3)	.072(2)
O(1')	.4677(4)	.0623(2)	.8670(2)	.0573(9)
O(5')	.2207(5)	.2134(3)	.8538(2)	.0910(15)
N(1)B	.6159(3)	.4341(2)	.4014(2)	.0384(8)
N(2)B	.4554(3)	.4316(2)	.4296(2)	.0419(8)
C(3)B	.4750(4)	.3869(2)	.4947(2)	.0372(9)
N(4)B	.6363(3)	.3599(2)	.5101(2)	.0441(9)
C(5)B	.7204(5)	.3905(3)	.4494(2)	.0453(10)
C(6)B	.3313(4)	.3665(2)	.5474(2)	.0450(10)
O(7)B	.1873(3)	.3936(2)	.5312(2)	.0633(10)
N(8)B	.3679(4)	.3194(3)	.6093(2)	.0549(11)
C(1')B	.6495(5)	.4742(3)	.3240(2)	.0464(11)
C(2')B	.6113(5)	.5721(3)	.3231(3)	.0533(12)
C(3')B	.7794(5)	.6117(3)	.3516(2)	.0485(11)
C(4')B	.9080(5)	.5502(3)	.3142(2)	.0488(11)
C(5')B	1.0733(6)	.5405(4)	.3575(3)	.071(2)
O(1')B	.8247(3)	.4642(2)	.3103(2)	.0491(8)
O(5')B	1.0434(5)	.5221(3)	.4364(2)	.0813(13)

$U_{eq} = 1/3\ \Sigma_i \Sigma_j\ U_{ij}\ a_i^*\ a_j^*\ A_{ij}$, where A_{ij} is the dot product of the i^{th} and j^{th} direct-space unit-cell vectors.

ANTIVIRAL TESTING: The inhibition of the cytopathic effect of HIV by 2',3'-dideoxyribavirin (11) against ATH8 cells[1] failed to show significant antiviral activity compared to 2',3'-dideoxycytidine and 2',3'-dideoxyadenosine under the same conditions.[23] 2',3'-Dideoxyribavirin also failed to inhibit the cytopathic effect of herpes, adeno, visna,

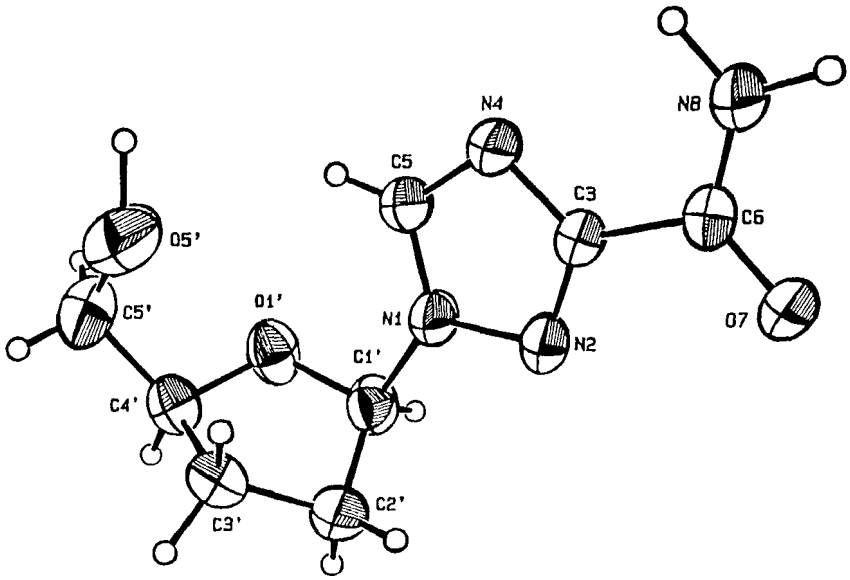

FIGURE 2

Computer drawing of molecule B showing atom labeling.
Thermal ellipsoids are at 50% probability.

parainfluenza, rhino and influenza viruses in cell culture at $\leq$ 1 mM concentration.[24] Perhaps the "dideoxy" form of ribavirin, like 2'-deoxyribavirin (7) is not significantly phosphorylated by cellular adenosine kinase and therefore fails to exhibit antiviral activity.

EXPERIMENTAL SECTION

General Methods: Melting points were taken on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Nuclear magnetic resonance (^{1}H NMR) and (^{13}C NMR) spectra were determined at 300.135 MHz and at 75.469 MHz, respectively, with an IBM NR 300AF spectrometer. The chemical shift values are expressed in δ values (parts per million) relative to tetramethylsilane as an internal standard. The presence of solvent as indicated by elemental analysis was verified by ^{1}H NMR. Infrared spectra (IR in KBr) were obtained on a Perkin-Elmer 1420 spectro-

TABLE 3. Bond lengths (Å) and bond angles (°) in molecules A and B of 11.

1	2	3	A 1 - 2	B 1 - 2	A 1-2-3	B 1-2-3
N(2)	N(1)	C(5)	1.353(4)	1.360(4)	109.5(3)	110.0(3)
C(5)	N(1)	C(1')	1.348(5)	1.340(5)	130.4(3)	129.9(3)
C(1')	N(1)	N(2)	1.484(5)	1.486(5)	120.1(3)	119.9(3)
C(3)	N(2)	N(1)	1.317(4)	1.316(4)	102.7(3)	102.1(2)
N(4)	C(3)	C(6)	1.357(4)	1.365(4)	122.6(3)	122.3(3)
N(4)	C(3)	N(2)			115.4(3)	115.3(3)
C(6)	C(3)	N(2)	1.489(4)	1.487(5)	121.9(3)	122.4(3)
C(5)	N(4)	C(3)	1.332(5)	1.323(5)	102.1(3)	102.3(3)
N(1)	C(5)	N(4)			110.3(3)	110.4(3)
O(7)	C(6)	N(8)	1.251(4)	1.241(4)	124.6(3)	124.2(3)
O(7)	C(6)	C(3)			118.7(3)	119.8(3)
N(8)	C(6)	C(3)	1.306(5)	1.310(5)	116.8(3)	116.0(3)
C(2')	C(1')	O(1')	1.496(6)	1.497(6)	107.4(3)	107.4(3)
C(2')	C(1')	N(1)			112.2(3)	111.7(3)
O(1')	C(1')	N(1)	1.410(5)	1.415(5)	107.0(3)	106.4(3)
C(3')	C(2')	C(1')	1.524(6)	1.537(6)	102.8(3)	101.5(3)
C(4')	C(3')	C(2')	1.512(6)	1.517(5)	102.4(3)	102.1(3)
C(5')	C(4')	O(1')	1.512(6)	1.513(6)	109.5(3)	109.3(3)
C(5')	C(4')	C(3')			116.0(4)	115.3(4)
O(1')	C(4')	C(3')	1.457(5)	1.448(5)	105.0(3)	104.8(3)
O(5')	C(5')	C(4')	1.421(7)	1.407(7)	110.8(4)	110.5(4)
C(1')	O(1')	C(4')			110.1(3)	110.1(3)

TABLE 4. Hydrogen bonding for 11.

D——H·····A			Symmetry of A relative to D	d(D··A) (Å)	d(H··A) (Å)	∠(D-H··A) (°)
N(8)	H(8)1	O(7)B	1+x,y,z	2.902(4)	2.06(5)	167(5)
N(8)	H(8)2	N(4)B	x,y,z	2.977(4)	1.97(7)	139(5)
O(5')	H(5'O)	O(7)	x-1,y,z	2.820(5)	2.01(7)	157(7)
N(8)B	H(8)1B	O(7)	x-1,y,z	2.882(4)	1.94(5)	166(4)
N(8)B	H(8)2B	N(4)	x,y,z	2.988(4)	2.04(6)	151(5)
O(5')B	H(5'O)B	O(7)B	1+x,y,z	2.770(5)	1.68(8)	171(7)

photometer and ultraviolet spectra (UV; sh = shoulder) were recorded on a Beckman DU-50 spectrophotometer. Elemental analyses were performed by Robertson Laboratory, Florham Park, N.J. Thin-layer chromatography (TLC) was run on silica gel 60 F-254 plates (EM Reagents). E. Merck silica gel (230-400 mesh) was used for column chromatography. All solvents were reagent grade. Detection of nucleoside components on TLC was by UV light and with 10% H_2SO_4 in MeOH spray followed by heating. Evaporations were carried out under reduced pressure with the bath temperature below 30°C.

1-(2-Deoxy-3,5-di-O-p-toluoyl-β-D-erythro-pentofuranosyl)-1,2,4-triazole-3-carbonitrile (6). A mixture of 1,2,4-triazole-3-carbonitrile[25] (5, 6.58 g, 70 mmol) and sodium hydride (60% in oil; 3.5 g, 87.5 mmol) in anhydrous CH_3CN (600 mL) was stirred for 30 min. at room temperature under a nitrogen atmosphere. Dry, powdered 1-chloro-2-deoxy-3,5-di-O-p-toluoyl-α-D-erythro-pentofuranose[26] (1, 27.2 g, 70 mmol) was added portionwise with stirring during 20 min. and stirring continued for an additional 20 h. A small amount of insoluble material was removed by filtration. Evaporation of the filtrate gave an oily residue, which was purified on a silica gel column (5 x 60 cm) using hexanes:$CHCl_3$ (3:7, v/v) as the eluent to afford 10.9 g (35%) of the desired product 6: m.p. 90-92°C (Lit.[12] m.p. 85-87°C), which was identical[27] in all respect with an authentic sample.[12]

Methyl 1-(2-deoxy-3,5-di-O-p-toluoyl-β-D-erythro-pentofuranosyl)-1,2,4-triazole-3-carboxylate (3) and Methyl 1-(2-deoxy-3,5-di-O-p-toluoyl-β-D-erythro-pentofuranosyl)-1,2,4-triazole-5-carboxylate (4). A mixture of methyl 1,2,4-triazole-3-carboxylate[28] (2, 1.27 g, 10 mmol) and NaH (60% in oil, 0.5 g, 12.5 mmol) in anhydrous CH_3CN (50 mL) was stirred at room temperature for 30 min. under nitrogen atmosphere. Dry, powdered 1 (3.88 g, 10 mmol) was added in small portions over a period of 30 min. and stirring continued for 15 h. A small amount of insoluble material was removed by filtration. Evaporation of filtrate gave an oily residue, which was loaded onto a silica gel column (4 x 40 cm) and on elution with $CHCl_3$:MeOH (98:2, v/v) two major nucleosides were isolated in the order listed. The compound 4 was isolated on evaporation of desired fractions to give 1.2 g (25%), which was characterized after ammonoly-

sis. The compound 3 was isolated after evaporation of desired fractions to furnish 1.32 g (28%), which was identical[25] in all respects with an authentic sample[12].

1-(2-Deoxy-β-D-erythro-pentofuranosyl)-1,2,4-triazole-3-carboxamide (2'-Deoxyribavirin, 7). Method 1: A mixture of 6 (5.45 g, 12 mmol), MeOH (40 mL) and concentrated NH_4OH (80 mL) was heated with stirring for 3 h in a steel bomb at 100°C. After cooling, the yellow solution was evaporated to dryness. Residue dissolved in MeOH (50 mL) and adsorbed on silica gel (5 g). The silica gel was loaded onto the top of a flash silica gel column and eluted with $CHCl_3$:MeOH (8:2; 7:3, v/v). Fractions containing the pure material were pooled and evaporated to dryness. Crystallization of the residue from warm ethanol gave 2.3 g (84%) of 7; m.p. 113-115°C (Lit[12] m.p. 112-113°C); ^{1}H NMR (Me_2SO-d_6): δ 6.23 (t, 1, $C_{1'}\underline{H}$, $J_{1'2'}$ = 5.97 Hz), 7.62, 7.83 (br s, 2, $N\underline{H}_2$), 8.81 (s, 1, $C_5\underline{H}$) and other sugar protons; ^{13}C NMR (Me_2SO-d_6): δ 144.83 ($\underline{C}$-5), 157.19 ($\underline{C}$-3), 160.6 ($\underline{C}$=O) and other sugar carbons; Anal. Calcd for $C_8H_{12}N_4O_4$: C, 42.10; H, 5.30; N, 24.55. Found: C, 42.14; H, 5.40; N, 24.61.

Method 2: Compound 7 was obtained in 75% yield by treatment of 3 with $MeOH/NH_3$ at room temperature for 3 days in a pressure bottle and isolating the product as described in Method 1 above.

1-(2-Deoxy-β-D-erythro-pentofuranosyl)-1,2,4-triazole-5-carboxamide (8). A solution of 4 (0.68 g, 1.42 mmol) and $MeOH/NH_3$ (80 mL) in a pressure bottle was stirred for 3 days at room temperature. The product was isolated as described in Method 1 above and crystallized from EtOH to obtain 0.26 g (82%); m.p. 98-100°C; ^{1}H NMR (Me_2SO-d_6): δ 7.12 (t, 1, $C_{1'}\underline{H}$, $J_{1'2'}$ = 6.0 Hz), 8.06, 8.27 (br s, 2, $N\underline{H}_2$), 8.19 (s, 1, $C_3\underline{H}$) and other sugar protons; ^{13}C NMR (Me_2SO-d_6): 147.25 ($\underline{C}$-3), 150.21 ($\underline{C}$-5), 158.83 ($\underline{C}$=O) and other sugar carbons; Anal. Calcd for $C_8H_{12}N_4O_4$: C, 42.10; H, 5.30; N, 24.55. Found: C, 41.96; H, 5.35; N, 24.49.

5'-O-p-Toluoyl-2'-deoxyribavirin (9a). A solution of p-toluoylchloride (0.134 mL, 1 mmol) in $ClCH_2CH_2Cl$ (2 mL) was added dropwise to a stirred solution of 7 (0.22 g, 1 mmol) in dry pyridine (2 mL) at -5°C. Stirring was continued for 3 h at 0°C. The reaction mixture was poured into ice

cold water (25 mL) and extracted with $CHCl_3$ (3 x 25 mL). The combined extracts were washed with sat. aqueous $NaHCO_3$ (2 x 25 mL), dried over Na_2SO_4 and evaporated to dryness. The residue was purified by silica gel column chromatography. Elution with $CHCl_3$:MeOH (8:2, v/v) furnished the desired material which, upon crystallization from EtOH gave 0.29 g (83.8%) of 9a; m.p. 175°C; IR: ν 1670, 1680, 1690 (C=O), 3150, 3330, 3430 (OH, NH_2)cm^{-1}; UV λ_{max} (MeOH) 238 nm; ^1H NMR (Me_2SO-d_6): δ 2.37 (s, 3, CH_3), 2.39, 2.67 (m, 2, C_2,H), 4.1, 4.32, 4.40, 4.63 (m, 4, C_3,, C_4,,C_5,H), 5.56 (m, 1, C_3,OH), 6.31 (m, 1, C_1,H), 7.3-7.83 (m, 6, ArH and NH_2), 8.8 (s, 1, C_5H). Anal. Calcd for $C_{16}H_{18}N_4O_5$: C, 55.48; H, 5.23; N, 16.17. Found: C, 55.28; H, 5.15; N, 16.00.

5'-O-p-Toluoyl-3'-O-methoxythiocarbonyl-2'-deoxyribavirin (10a). A solution of 9a (0.22 g, 0.63 mmol) and N,N'-thiocarbonyldiimidazole (0.17 g, 0.96 mmol) in dry DMF (5 mL) was heated at 80°C under an argon atmosphere for 3 h and then evaporated. The residue (9b) was treated with anhydrous MeOH (5 mL) and heated at 60°C for 2 h. The solvent was evaporated and the residue was extracted with $CHCl_3$ (2 x 25 mL), washed with water (2 x 25 mL), dried over Na_2SO_4 and solvent evaporated to dryness. The residue was placed on a silica gel column and elution with $CHCl_3$:MeOH (9:1, v/v) furnished 10a which, upon crystallization from EtOAc gave 0.196 g (73.4%); m.p. 168°C; ^1H NMR (Me_2SO-d_6): δ 2.37 (s, 3, CH_3), 2.70 (m, 1, C_2,αH), 3.15 (m, 1, C_2,βH), 4.03 (s, 3, OCH_3), 4.46 (m, 2, C_5,CH_2), 4.58 (m, 1, C_4,H), 5.94 (m, 1, C_3,H), 6.46 (t, 1, C_1,H, J = 6.6 Hz), 7.32-7.89 (m, 6, ArH, NH_2), 8.85 (s, 1, C_5H). Anal. Calcd for $C_{18}H_{20}N_4O_6S$: C, 51.41; H, 4.79; N, 13.33; S, 7.62. Found: C, 51.29; H, 4.71; N, 13.08; S, 7.43.

5'-O-p-Toluoyl-2',3'-dideoxyribavirin (10b). A solution of 10a (0.18 g, 0.42 mmol), AIBN (10 mg), tri-n-butylstannane (1.2 mL, 4.6 mmol) in toluene (20 mL) was heated at reflux under argon atmosphere for 2 h. Toluene was evaporated under reduced pressure and the residue washed with hexanes (~ 200 mL) until the odor of stannane was removed. The residue, on crystallization from EtOH, furnished fine needles of 10b; 0.124 g (85%); m.p. 169°C; ^1H NMR (Me_2SO-d_6): δ 2.11-2.83 (m, 4, C_2, and C_3,H), 4.45 (m, 1, C_4,H), 4.6 (m, 2, C_5,H), 5.78 (br s, 1, NH_2), 6.13 (d, 1, C_1,H, J = 5.4 Hz), 7.6 (br s, 1, NH_2), 7.24-7.88 (m, 4,

ArH), 8.42 (s, 1, C_5H). Anal. Calcd for $C_{16}H_{18}N_4O_4 \cdot 1\frac{1}{4}H_2O$: C, 54.42; H, 5.78; N, 15.86. Found: C, 54.40; H, 5.42; N, 15.60.

2',3'-Dideoxyribavirin (11). A solution of 10b (0.10 g, 0.3 mmol) in saturated MeOH/NH_3 (5 mL) was stirred at room temperature for 48 h. Evaporation of the solvent followed by purification of the residue by silica gel column chromatography ($CHCl_3$:MeOH, 9:1, v/v) furnished the desired compound which, upon crystallization from water, gave long needles of 11; 0.035 g (50%); m.p. 154°C; ^{1}H NMR (Me_2SO-d_6): δ 1.98 (m, 2, C_3,H), 2.49 (m, 2, C_2,H), 3.55 (m, 2, C_5,H), 4.14 (m, 1, C_4,H), 4.90 (t, 1, C_5,OH, J = 5.5 Hz), 6.35 (d, 1, C_1,H, J = 6.0 Hz), 7.59, 7.8 (br s, 2, NH_2), 8.80 (s, 1, C_5H). Anal. Calcd for $C_8H_{12}N_4O_3$: C, 45.27; H, 5.70; N, 26.40. Found: C, 45.03; H, 5.80; N, 26.38.

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