Syntheses of D-Arabinofuranosyl and 2′-Deoxy-D-ribofuranosyl 1,2,3-Triazolecarboxamides

Osamu MAKABE,* Hiroshi SUZUKI, and Sumio UMEZAWA**

Department of Applied Chemistry, Faculty of Engineering, Keio University, Hiyoshi, Kohoku-ku, Yokohama, Kanagawa 223

(Received February 14, 1977)

Several D-arabino- and 2′-deoxy-D-ribonucleosides of 1,2,3-triazolecarboxamides were synthesized by two methods, one involving acid-catalyzed fusion reactions of 1-*O*-acetyl derivatives (**3**, **5**) of the corresponding sugars and 1,2,3-triazole-4-carboxylate (**1**), and the other by glycosylation of the trimethylsilyl derivative (**2**) of **1** with glycosyl halides (**4**, **6**). Evidence for the *N*-glycosylation sites and anomeric configurations of the resulting nucleosides is presented.

Because of antiviral activity, some azole-carboxamides such as pyrazomycin[1,2] and virazole[3] have attracted attention. The synthesis of 1-(β-D-ribofuranosyl)-1,2,3-triazole-4-carboxamide, which is active *in vitro* against vaccinia viruses, has been reported.[4,5] Modifications of the glycosyl moiety of these nucleosides were of interest for the determination of structure-activity relationships. A report was given on the syntheses of D-arabinofuranosyl and 2′-deoxy-D-ribofuranosyl pyrazolecarboxamides.[6] The present paper deals with an extention of the work;[4] *i.e.* the synthesis of some 1,2,3-triazole nucleosides with modifications of the glycosyl moiety, including the arabinofuranosyl and 2-deoxyribofuranosyl derivatives of 1,2,3-triazole-4-carboxamide. Two methods have been employed to prepare these *N*-glycosyl-1,2,3-triazoles. One method (method A) is the acid-catalyzed fusion reaction of 1-*O*-acetyl derivatives of *O*-blocked sugars and ethyl 1,2,3-triazole-4-carboxylate (**1**), and the other (method B) is the glycosylation of the trimethylsilyl derivative (**2**) of ethyl 1,2,3-triazole-4-carboxylate with *O*-blocked glycosyl halides.

Results and Discussion

Since D-arabinosylation of purine and pyrimidine bases has often been successful in yielding antiviral and cytotoxic activities as exemplified[7] by 9-(β-D-arabinofuranosyl)adenine and 1-(β-D-arabinofuranosyl)cytosine, we performed the synthesis of 1-*N*-(β-D-arabinofuranosyl)-1,2,3-triazole-4-carboxamide (**13β**). Synthesis of the 1′,2′-*cis* nucleoside was first performed by use of 1-*O*-acetyl-2,3,5-tri-*O*-benzyl-D-arabinofuranose[4] (**3**) in which the hydroxyl group at C-2 is blocked with benzyl group (a nonparticipating group). However, fusion of **3** with ethyl 1,2,3-triazole-4-carboxylate[8] in the presence of bis(*p*-nitrophenyl) hydrogenphosphate[9] gave a mixture of isomeric products (total yield 95.8%), *viz.*, ethyl 1-*N*-(2,3,5-tri-*O*-benzyl-β-D-arabinofuranosyl)-1,2,3-triazole-4-carboxylate (**7β**), its α-anomer (**7α**), ethyl 2-*N*-(2,3,5-tri-*O*-benzyl-β-D-arabinofuranosyl)-1,2,3-triazole-4-carboxylate (**8β**) and its α-anomer (**8α**) in a ratio of 1: 5: 7: 13.5, which were separated by chromatography. An improved yield of **7β** (16.7%) was obtained by application of the Lewis acid-catalyzed silyl Hilbert-Johonson reaction.[10] The trimethylsilyl derivative (**2**) of ethyl 1,2,3-triazole-4-carboxylate was treated with 2,3,5-tri-*O*-benzyl-D-arabinofuranosyl chloride[11] (**4**) in the presence of stannic chloride in 1,2-dichloroethane to give a mixture of **7β**, **7α**, **8β**, **8α**, and ethyl 1-*N*-(2,3,5-tri-*O*-benzyl-α-D-arabinofuranosyl)-1,2,3-triazole-5-carboxylate (**9α**) (total yield 83%) in a ratio of 1: 1.5: 1: 1.5: 1.2, which were readily separated by chromatography. The products (**7β**, **7α**, **8β**, **8α**, and **9α**) were converted into the corresponding carboxamides (**10β**, **10α**, **11β**, **11α**, and **12α**) by treatment with methanolic ammonia. The benzyl groups were readily removed by catalytic hydrogenolysis on palladium black to give 1-*N*-(β-D-arabinofuranosyl)-1,2,3-triazole-4-carboxamide (**13β**), its α-anomer (**13α**), 2-*N*-(β-D-arabinofuranosyl)-1,2,3-triazole-4-carboxamide (**14β**), its α-anomer (**14α**), and 1-*N*-(α-D-arabinofuranosyl)-1,2,3-triazole-5-carboxamide (**15α**), respectively.

The structures of these arabinonucleosides were assigned on the basis of their PMR (Table 1) and UV spectra (Table 2). The anomeric proton of **15α** (δ 6.81) appears at lower field than those of **13α** and **13β** (δ 6.16 and 6.40, respectively) and **14α** and **14β** (δ 6.00 and 6.29, respectively). The downfield shift of H-1′ of nucleosides having a carbamoyl group adjacent to the site of glycosylation has been attributed to the anisotropic effect of the carbonyl group.[12,13] The signals for the H-5 of **13α** and **13β** (δ 8.86 and 8.70, respectively) appear at lower field than those of the isomeric **14α** and **14β** (δ 8.39 and 8.31, respectively), indicating[6,14] that **13α** and **13β** are 1-*N*-glycosides and **14α** and **14β** are

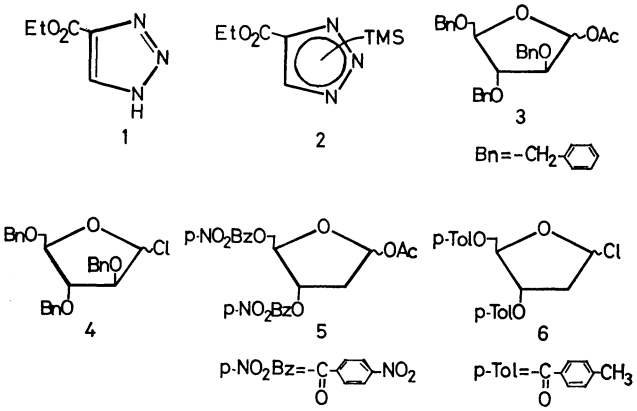


Chart 1.

* Present address: Research Laboratories, Meiji Seika Kaisha, Morooka-cho, Kohoku-ku, Yokohama, Kanagawa 222.

** Present address: Institute of Bio-organic Chemistry, Nakahara, Kawasaki, Kanagawa 211.

Table 1. PMR spectral data in DMSO-d_6

Arabino-nucleosides	Anomeric proton	$J_{1',2'}$	H-5	2'-Deoxyribo-nucleosides	Anomeric proton	$J_{1',2'}$ $J_{1',2''}$	H-5
13α	δ 6.16	3.8 Hz	δ 8.86	**20α**	δ 6.43	2.5, 7.0 Hz	δ 8.72
13β	6.40	5.2	8.70	**20β**	6.40	6.0, 6.0	8.78
14α	6.00	5.3	8.39	**21α**	6.30	5.5, 6.5	8.20
14β	6.29	6.4	8.31	**21β**	6.31	5.0, 6.0	8.13
15α	6.81	4.6	8.35(H-4)				

2-*N*-glycosides. Comparison of **13β** and **14β** with their α-anomers (**13α** and **14α**, respectively) shows downfield shifts for the anomeric protons of the β-anomers as expected for 1',2'-*cis* nucleosides.[15] The coupling constants for the anomeric protons of **13α**, **13β**, **14α**, and **14β** also support their α- and β-configurations. The

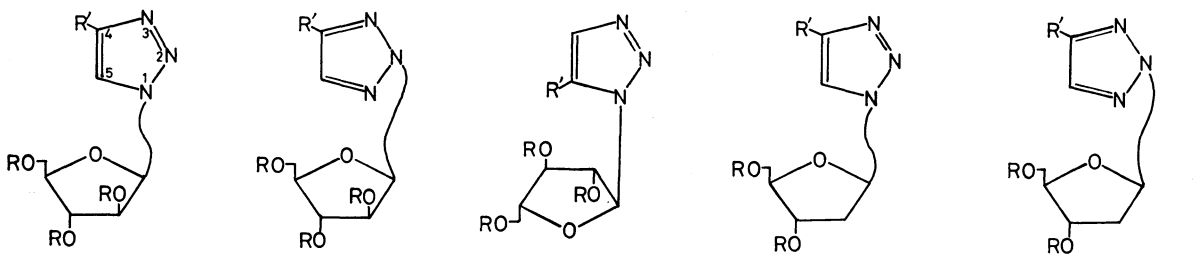
Table 2. Ultraviolet absorption data

Compound No.	Solvents λ_{max} nm and ε: pH 7 (H_2O) λ_{max}	ε	pH 1 (HCl) λ_{max}	ε	pH 13 (NaOH) λ_{max}	ε
13α	212	11200	211	10800	224	8600
13β	211	12000	211	12200	223	9800
14α	229	11900	230	12000	230	10500
14β	229	11600	229	12700	230	11500
15α	218	9700	217	10200	225	6150
20α	213	11100	212	11800	225	8000
20β	213	11900	213	12200	224	11000
21α	228	11400	227	10900	228	11500
21β	228	11600	228	12000	230	11300

anomeric configuration of **15α** was deduced by its specific rotation.

The synthesis of 2'-deoxyribofuranosyl nucleosides was also performed by the two methods. The fusion reaction of 1-*O*-acetyl-2-deoxy-3,5-di-*O*-(*p*-nitrobenzoyl)-D-*erythro*-pentofuranose[6] (**5**) and **1** gave ethyl 1-*N*-[2-deoxy-3,5-di-*O*-(*p*-nitrobenzoyl)-β-D-*erythro*-pentofuranosyl]-1,2,3-triazole-4-carboxylate (**18β**), its α-anomer (**18α**), ethyl 2-*N*-[2-deoxy-3,5-di-*O*-(*p*-nitrobenzoyl)-β-D-*erythro*-pentofuranosyl]-1,2,3-triazole-4-carboxylate (**19β**) and its α-anomer (**19α**) in a ratio of 1.25: 1: 2.5: 1.75 (total yield 78.9%). Protection of hydroxy-groups with substituted benzoyl groups facilitates separation of the anomers usually formed in the synthesis of 2'-deoxyribonucleosides.[6,16] Glycosylation of the trimethylsilyl derivative (**2**) with 2-deoxy-3,5-di-*O*-(*p*-toluoyl)-D-*erythro*-pentofuranosyl chloride[17] in the presence of stannic chloride in 1,2-dichloroethane gave ethyl 1-*N*-[2-deoxy-3,5-di-*O*-(*p*-toluoyl)-β-D-*erythro*-pentofuranosyl]-1,2,3-triazole-4-carboxylate (**16β**), its α-anomer (**16α**), ethyl 2-*N*-[2-deoxy-3,5-di-*O*-(*p*-toluoyl)-β-D-*erythro*-pentofuranosyl]-1,2,3-triazole-4-carboxylate (**17β**), and its α-anomer (**17α**) in a ratio of 1.77: 2.4: 1: 1.1 (total yield 90.5%). Their treatment with methanolic ammonia afforded the corresponding carboxamides, **20β**, **20α**, **21β**, and **21α**, respectively. It should be noted that in the synthesis of the 2'-deoxyribonucleosides by method B, no formation of isomeric 5-carboxylate was detected as compared with a 14.7% yield of **9α** in the synthesis of arabinonucleosides. The H-5 protons of **20α** and **20β** appear at significantly lower field than those of **21α** and **21β**, indicating that the former are 1-*N*-glycosyl derivatives and the latter 2-*N*-glycosyl derivatives. Their UV spectra also show a characteristic difference[4] (Table 2). The anomeric proton of **20β** appears as a pseudotriplet with a peak width of 12 Hz which is in line with the β-configuration.[18,19] The anomeric proton of **20α** appears as a quartet whose *J*-values indicate the α-configuration. The anomeric configuration of **21α** and **21β** was deduced by their specific rotation, though their PMR spectra provided no definite assignments.

Of the nucleosides prepared, 1-*N*-(β-D-arabinofuranosyl)-1,2,3-triazole-4-carboxamide (**13β**) and 1-*N*-(2-deoxy-β-D-*erythro*-pentofuranosyl)-1,2,3-triazole-4-carboxamide (**20β**) were found to have antiviral and cytotoxic activities.[5]



7α, R'=CO_2Et, R=Bn
7β, R'=CO_2Et, R=Bn
10α, R'=$CONH_2$, R=Bn
10β, R'=$CONH_2$, R=Bn
13α, R'=$CONH_2$, R=H
13β, R'=$CONH_2$, R=H

8α, R'=CO_2Et, R=Bn
8β, R'=CO_2Et, R=Bn
11α, R'=$CONH_2$, R=Bn
11β, R'=$CONH_2$, R=Bn
14α, R'=$CONH_2$, R=H
14β, R'=$CONH_2$, R=H

9α, R'=CO_2Et, R=Bn

12α, R'=$CONH_2$, R=Bn

15α, R'=$CONH_2$, R=H

16α, R'=CO_2Et, R=p-NO_2Bz
16β, R'=CO_2Et, R=p-NO_2Bz
18α, R'=CO_2Et, R=p-Tol
18β, R'=CO_2Et, R=p-Tol
20α, R'=$CONH_2$, R=H
20β, R'=$CONH_2$, R=H

17α, R'=CO_2Et, R=p-NO_2Bz
17β, R'=CO_2Et, R=p-NO_2Bz
19α, R'=CO_2Et, R=p-Tol
19β, R'=CO_2Et, R=p-Tol
21α, R'=$CONH_2$, R=H
21β, R'=$CONH_2$, R=H

Chart 2.

Experimental

Melting points were determined on a micro hot stage and are uncorrected. Thin layer chromatography (TLC) was carried out with Wakogel B-5, silica gel column chromatography with Wakogel C-200. UV spectra were taken with a Hitachi Perkin-Elmer UV-VIS spectrometer 139 and PMR spectra with a Varian A-60D spectrometer with TMS as an internal standard.

Silylation of Ethyl 1,2,3-Triazole-4-carboxylate. To a solution of ethyl 1,2,3-triazole-4-carboxylate[8] (**1**, 5.0 g, 35.5 mmol) and chlorotrimethylsilane (7.45 g, 67.5 mmol) in dried 1,4-dioxane (48 ml) was added dropwise, with stirring, a solution of triethylamine (6.9 g) in dried 1,4-dioxane (3 ml). The reaction mixture was stirred for 12 h at room temperature. The precipitated triethylamine hydrochloride was filtered off and washed with two 5 ml portions of dried 1,4-dioxane. The filtrate and washings were combined and evaporated under reduced pressure. The resulting oil was distilled at 114 °C/1 mmHg, to give 6.86 g (91%) of a colorless oil (**2**).

Ethyl 1-N-(2,3,5-Tri-O-benzyl-β-D-arabinofuranosyl)-1,2,3-triazole-4-carboxylate (7β), Its α-Anomer (7α) and Ethyl 2-N-(2,3,5-Tri-O-benzyl-β-D-arabinofuranosyl)-1,2,3-triazole-4-carboxylate (8β), Its α-Anomer (8α) and Ethyl 1-N-(2,3,5-Tri-O-benzyl-α-D-arabinofuranosyl)-1,2,3-triazole-5-carboxylate (9α). *Method A*: A mixture of ethyl 1,2,3-triazole-4-carboxylate (**1**, 890 mg, 6.30 mmol) and 1-*O*-acetyl-2,3,5-tri-*O*-benzyl-D-arabinofuranose[4] (**3**, 2.19 g, 6.30 mmol) was heated at 143°C. To the melt was added bis(*p*-nitrophenyl) hydrogenphosphate (4 mg), and the mixture was heated at 143°C under reduced pressure for *ca.* 20 min until the evolution of acetic acid ceased. The resulting mixture was dissolved in a minimum amount of ethyl acetate and was placed on a column of silica gel (180 g, 2.8×70 cm, packed with 2:1 hexane–diisopropyl ether) and successively eluted with 2:1- (120 ml) and 1:1 hexane–diisopropyl ether. The effluent was fractionated into 12 ml-fractions.

Fractions 37—53 gave **8α**, colorless syrup, 1.38 g (40.2%). Fractions 54—63 gave a mixture of **8α** and **8β**, 820 mg (23.9 %), α:β=2:3 (from PMR). Fractions 64—69 gave **8β**, colorless syrup, 390 mg (11.4%). Fractions 81—91 gave **7α**, colorless syrup, 530 mg (15.4%). Fractions 92—98 gave a mixture of **7α** and **7β**, 90 mg (2.6%), α:β=1:1 (from PMR). Fractions 99—105 gave **7β**, colorless syrup, 80 mg (2.3%).

Method B: To a solution of 2,3,5-tri-*O*-benzyl-D-arabinofuranosyl chloride[11] (**4**, 2.00 g, 4.6 mmol) and silylated ethy-1,2,3-triazole-4-carboxylate (**2**, 1.00 g, 4.8 mmol) in 1,2-dichloroethane (50 ml) was added a solution of redistilled $SnCl_4$ (1.2 ml, 2.0 mmol) in 1,2-dichloroethane (3 ml) at 0 °C under stirring. The reaction mixture was stirred at room temperature for 12 h. After dilution with 1,2-dichloroethane (20 ml), the reaction mixture was washed with saturated aqueous $NaHCO_3$ solution. The organic layer separated by centrifugation was dried (Na_2SO_4), and evaporated under reduced pressure. The resulting mixture was dissolved in a minimum amount of ethyl acetate and chromatographed on a column of silica gel (140 g, 2.8×60 cm, packed with 1:1 hexane–diisopropyl ether) and eluted with the same solvent system. The effluent was fractionated into 11 ml-fractions.

Fractions 40—44 gave **8α**, colorless syrup, 396 mg (17.3%); $[\alpha]_D^{20}$ +58.4° (*c* 1.0, $CHCl_3$). PMR ($CDCl_3$): δ 8.25 (s, 1H, H-5), 7.40 (d, 15H, Ar), 6.39 (d, 1H, $J_{1',2'}$=3.7 Hz, H-1'), 5.05 (dq, 1H, H-2'), 4.70—4.30 (m, 10H, CH_2-ester, CH_2-Ar, H-3', H-4'), 3.75 (d, 2H, H-5',5''), 1.45 (t, 3H, CH_3-ester). Found: C, 68.14; H, 6.16; N, 7.53%. Calcd for $C_{31}H_{33}O_6N_3$: C, 68.49; H, 6.12; N, 7.73%.

Fractions 45—48 gave a mixture of **8α** and **8β**, 85 mg (3.7 %), α:β=1:1 (from PMR).

Fractions 49—52 gave **8β**, colorless crystal, 236 mg (10.3%); mp 101—102 °C. $[\alpha]_D^{20}$ −54.5° (*c* 1.0, $CHCl_3$). PMR ($CDCl_3$): δ 8.35 (s, 1H, H-5), 7.45 (d, 15H, Ar), 6.67 (d, 1H, $J_{1',2'}$= 4.8 Hz, H-1'), 4.50 (m, 11H, H-2', CH_2-Ar, CH_2-ester, H-3', H-4'), 3.75 (d, 2H, H-5',5''), 1.41 (t, 3H, CH_3-ester). Found: C, 68.63; H, 6.11; N, 7.86%. Calcd for $C_{31}H_{33}O_6N_3$: C, 68.49; H, 6.12; N, 7.73%.

Fractions 63—66 gave **9α**, colorless syrup, 358 mg (14.7%); $[\alpha]_D^{20}$ +55.0° (*c* 1.0, $CHCl_3$). PMR ($CDCl_3$): δ 8.12 (s, 1H, H-4), 7.30 (d, 15H, Ar), 6.85 (d, 1H, $J_{1',2'}$=3.3 Hz, H-1'), 5.20 (dq, 1H, H-2'), 4.70—4.20 (m, 10H, CH_2-Ar, CH_2-ester, H-3', H-4'), 3.69 (d, 2H, H-5',5''), 1.39 (t, 3H, CH_3-ester). Found: C, 68.58; H, 6.18; N, 7.51%. Calcd for $C_{31}H_{33}O_6N_3$: C, 68.49; H, 6.12; N, 7.73%.

Fractions 75—83 gave **7α**, colorless syrup, 465 mg (20.3%); $[\alpha]_D^{20}$ +61.0° (*c* 1.0, $CHCl_3$). PMR ($CDCl_3$): δ 8.44 (s, 1H, H-5), 7.45 (d, 15H, Ar), 6.42 (d, 1H, $J_{1',2'}$=1.5 Hz, H-1'), 4.75—4.20 (m, 11H, CH_2-Ar, CH_2-ester, H-2', H-3', H-4'), 3.73 (d, 2H, H-5',5''), 1.40 (t, 3H, CH_3-ester). Found: C, 68.26; H, 6.12; N, 7.55%. Calcd for $C_{31}H_{33}O_6N_3$: C, 68.49; H, 6.12; N, 7.73%.

Fractions 85—91 gave **7β**, colorless syrup, 380 mg (16.7%); $[\alpha]_D^{20}$ −30.2° (*c* 1.0, $CHCl_3$). PMR ($CDCl_3$): δ 8.65 (s, 1H, H-5), 7.45 (d, 15H, Ar), 6.65 (d, 1H, $J_{1',2'}$=4.0 Hz, H-1'), 4.70—4.10 (m, 11H, CH_2-Ar, CH_2-ester, H-2', H-3', H-4'), 3.75 (d, 2H, H-5',5''), 1.40 (t, 3H, CH_3-ester). Found: C, 68.69; H, 6.25; N, 7.63%. Calcd for $C_{31}H_{33}O_6N_3$: C, 68.49; H, 6.12; N, 7.73%.

1-N-(2,3,5-Tri-O-benzyl-α-D-arabinofuranosyl)-1,2,3-triazole-4-carboxamide (10α). A sample of **7α** (400 mg, 0.74 mmol) in absolute methanol (40 ml) saturated with ammonia at 0 °C was kept at room temperature for 12 h and evaporated under reduced pressure at 40 °C. The residual syrup was washed with hexane and the resulting gum was crystallized from ethyl acetate and diisopropyl ether to give **10α**, 315 mg (85%); mp 135—136 °C. $[\alpha]_D^{20}$ +67.2° (*c* 1.0, $CHCl_3$). PMR ($CDCl_3$): δ 8.48 (s, 1H, H-5), 7.40 (m, 15H, Ar), 6.40 (d, 1H, $J_{1',2'}$= 1.9 Hz, H-1'), 6.30 (br d, 2H, $CONH_2$), 4.65 (m, 8H, CH_2-Ar, H-2', H-3'), 4.30 (m, 1H, H-4'), 3.73 (d, 2H, H-5',5''). Found: C, 67.54; H, 5.81; N, 10.70%. Calcd for $C_{29}H_{30}O_5N_4$: C, 67.69; H, 5.88; N, 10.89%.

1-N-(2,3,5-Tri-O-benzyl-β-D-arabinofuranosyl)-1,2,3-triazole-4-carboxamide (10β). By a procedure similar to that for **10α**, **7β** (153 mg, 0.28 mmol) gave **10β**. Recrystallization from benzene–diisopropyl ether gave a pure sample, 110 mg (76%); mp 122—123 °C. $[\alpha]_D^{20}$ −47.5° (*c* 0.61, $CHCl_3$). PMR($CDCl_3$): δ 8.62 (s, 1H, H-5), 7.40 (m, 15H, Ar), 6.60 (d, 1H, $J_{1',2'}$= 4.3 Hz, H-1'), 5.85 (br d, 2H, $CONH_2$), 4.85—4.20 (m, 9H, CH_2-Ar, H-2', H-3', H-4'), 3.75 (d, 2H, H-5',5''). Found: C, 67.69; H, 5.97; N, 10.70%. Calcd for $C_{29}H_{30}O_5N_4$: C, 67.69; H, 5.88; N, 10.89%.

2-N-(2,3,5-Tri-O-benzyl-α-D-arabinofuranosyl)-1,2,3-triazole-4-carboxamide (11α). By a procedure similar to that for **10α**, **8α** (883 mg, 1.62 mmol) gave **11α**. Recrystallization from ethyl acetate and diisopropyl ether gave 701 mg (84%); mp 89.5°C. $[\alpha]_D^{20}$ +67.6° (*c* 1.4, $CHCl_3$). PMR ($CDCl_3$): δ 8.30 (s, 1H, H-5), 7.40 (m, 15H, Ar), 6.50 (br d, 2H, $CONH_2$), 6.30 (d, 1H, $J_{1',2'}$=3.5 Hz, H-1'), 5.00 (t, 1H, H-2'), 4.75—4.25 (m, 8H, CH_2-Ar, H-3', H-4'), 3.72 (d, 2H, H-5',5''). Found: C, 67.64; H, 6.05; N, 10.66%. Calcd for $C_{29}H_{30}O_5N_4$: C, 67.69; H, 5.88; N, 10.89%.

2-N-(2,3,5-Tri-O-benzyl-β-D-arabinofuranosyl)-1,2,3-triazole-4-carboxamide (11β). By a procedure similar to that for **10α**, **8β** (706 mg, 1.3 mmol) gave **11β**. Recrystallization from benzene–diisopropyl ether gave 535 mg (80%). mp 131—132 °C.

$[\alpha]_D^{20}$ −57.5° (*c* 1.2, $CHCl_3$). PMR ($CDCl_3$): δ 8.31 (s, 1H, H-5), 7.40 (m, 15H, Ar), 6.48 (d, 1H, $J_{1',2'}$=5.5 Hz, H-1'), 6.30 (br d, 2H, $CONH_2$), 4.80—4.20 (m, 9H, CH_2-Ar, H-2', H-3', H-4'), 3.90 (d, 2H, H-5',5''). Found: C, 67.82; H, 5.91; N, 10.82%. Calcd for $C_{29}H_{30}O_5N_4$: C, 67.69; H, 5.88; N, 10.89%.

*1-N-(2,3,5-Tri-O-benzyl-α-D-arabinofuranosyl)-1,2,3-triazole-5-carboxamide (**12α**).* By a procedure similar to that **10α**, **9α** (200 mg, 0.37 mmol) gave **12α**. Recrystallization from benzene-diisopropyl ether gave 153 mg (81%); mp 122—123 °C. $[\alpha]_D^{20}$ +65.5° (*c* 1.0, $CHCl_3$). PMR ($CDCl_3$): δ 8.00 (s, 1H, H-4), 7.30 (d, 15H, Ar), 6.92 (d, 1H, $J_{1',2'}$=3.1 Hz, H-1'), 6.60 (br s, 2H, $CONH_2$), 5.20 (dq, 1H, H-2'), 4.70—4.20 (m, 8H, CH_2-Ar, H-3', H-4'), 3.73 (d, 2H, H-5',5''). Found: C, 68.00; H, 6.10; N, 11.07%. Calcd for $C_{29}H_{30}O_5N_4$: C, 67.69; H, 5.88; N, 10.89%.

*1-N-(α-D-Arabinofuranosyl)-1,2,3-triazole-4-carboxamide (**13α**).* A sample of **10α** (300 mg, 0.583 mmol) in 6 ml methanol was hydrogenated over palladium black catalyst at 3.5 atm for 24h. After removal of the catalyst, the methanol layer was evaporated and the residue was crystalilzed from methanol and benzene to give **13α**, 101 mg (78%); mp 185—185.5 °C. $[\alpha]_D^{20}$ +89.1° (*c* 0.73, H_2O). PMR (DMSO-d_6): δ 8.86 (s, 1H, H-5), 7.80 (br d, 2H, $CONH_2$), 6.16 (d, 1H, $J_{1',2'}$=3.8 Hz, H-1'), 6.06 (d, 1H, OH), 5.67 (d, 1H, OH), 5.00 (t, 1H, OH), 4.60 (t, 1H, H-2'), 4.20 (m, 2H, H-3', H-4'), 3.69 (m, 2H, H-5,5''). Found: C, 39.37; H, 5.03; N, 23.22%. Calcd for $C_8H_{12}O_5N_4$: C, 39.34; H, 4.95; N, 22.94%.

*1-N-(β-D-Arabinofuranosyl)-1,2,3-triazole-4-carboxamide (**13β**).* A sample of **10β** (100 mg, 0.19 mmol) was hydrogenated and worked up in a similar manner to that described above. Recrystallization from methanol gave **13β**, 42 mg (84%); mp 163—164 °C. $[\alpha]_D^{20}$ −31.0° (*c* 1.0, H_2O). PMR (DMSO-d_6): δ 8.70 (s, 1H, H-5), 7.75 (br d, 2H, $CONH_2$), 6.40 (d, 1H, $J_{1',2'}$=5.2 Hz, H-1'), 5.70 (m, 2H, OH), 5.18 (d, 1H, OH), 4.40—3.90 (m, 3H, H-2', H-3', H-4'), 3.75 (m, 2H, H-5',5''). Found: C, 39.00; H, 4.88; N, 22.65%. Calcd for $C_8H_{12}O_5N_4$: C, 39.34; H, 4.95; N, 22.94%.

*2-N-(α-D-Arabinofuranosyl)-1,2,3-triazole-4-carboxamide (**14α**).* Similar hydrogenation of **11α** (515 mg, 1.0 mmol) followed by recrystallization from methanol gave **14α**, 181 mg (74%); mp 188—189 °C. $[\alpha]_D^{20}$ +89.0° (*c* 0.87, H_2O). PMR (DMSO-d_6): δ 8.39 (s, 1H, H-5), 7.89 (br d, 2H, $CONH_2$), 6.00 (d, 1H, $J_{1',2'}$=5.3 Hz, H-1'), 5.95 (d, 1H, OH), 5.61(d, 1H, OH), 4.90 (m, 2H, OH, H-2'), 4.15 (m, 2H, H-3', H-4'), 3.68 (m, 2H, H-5',5''). Found: C, 39.10; H, 4.94; N, 23.19%. Calcd for $C_8H_{12}O_5N_4$: C, 39.34; H, 4.95; N, 22.94%.

*2-N-(β-D-Arabinofuranosyl)-1,2,3-triazole-4-carboxamide (**14β**).* Similar hydrogenation of **11β** (118 mg, 0.23 mmol), followed by recrystallization from isopropyl alcohol, gave amorphos **14β**, 35.4 mg (63%); $[\alpha]_D^{20}$ −44.6° (*c* 0.42, H_2O). PMR (DMSO-d_6): δ 8.31 (s, 1H, H-5), 7.80 (br d, 2H, $CONH_2$), 6.29 (d, 1H, $J_{1',2'}$=6.4 Hz, H-1'), 5.60 (d, 1H, OH), 5.47 (d, 1H, OH), 4.78 (t, 1H, OH), 4.45 (m, 2H, H-2', H-3'), 3.80 (m, 3H, H-4', H-5',5''). Found: C, 39.35; H, 5.15; N, 22.65%. Calcd for $C_8H_{12}O_5N_4$: C, 39.34; H,4.95; N, 22.94%.

*1-N-(α-D-Arabinofuranosyl)-1,2,3-triazole-5-carboxamide (**15α**).* A sample of **12α** (80 mg, 0.16 mmol) in 5 ml methanol was hydrogenated over palladium black catalyst at 3.5 atm for 72 h. After removal of the catalyst, the methanol layer was evaporated and the residue was crystallized from methanol to give **15α**, 12 mg (31.6%); mp 189—190 °C. $[\alpha]_D^{20}$ +85.5° (*c* 0.5, H_2O). PMR (DMSO-d_6): δ 8.35 (s, 1H, H-4), 7.80 (br d, 2H, $CONH_2$), 6.81 (d, 1H, $J_{1',2'}$=4.6 Hz, H-1'), 6.00 (d, 1H, OH), 5.65 (d, 1H, OH), 4.80 (m, 2H, OH, H-2'), 4.18 (m, 2H, H-3', H-4'), 3.68 (d, 2H, H-5',5''). Found: C, 39.08; H, 4.97; N, 22.69%. Calcd for $C_8H_{12}O_5N_4$: C, 39.34; H, 4.95; N, 22.94%.

*Ethyl 1-N-[2-Deoxy-3,5-di-O-(p-nitrobenzoyl)-β-D-erythro-pentofuranosyl]-1,2,3-triazole-4-carboxylate (**16β**), Its α-Anomer (**16α**) and Ethyl 2-N-[2-Deoxy-3,5-di-O-(p-nitrobenzoyl)-β-D-erythro-pentofuranosyl]-1,2,3-triazole-4-carboxylate (**17β**), Its α-Anomer (**17α**).* Ethyl 1,2,3-triazole-4-carboxylate (**1**, 560 mg, 3.59 mmol) and 1-*O*-acetyl-3,5-di-*O*-(*p*-nitrobenzoyl)-D-2-deoxyribofuranose (**2**, 1.70 g, 3.59 mmol) were heated at 143 °C. To the melt was added bis(*p*-nitrophenyl) hydrogenphosphate (4 mg) and the mixture was heated at 143 °C under reduced pressure for *ca.* 20 min until the evolution of acetic acid cessed. The resulting gum was dissolved in ethyl acetate (5 ml). Silica gel (2.5 g) was added and the suspension was evaporated to dryness. The residue was placed on a column of silica gel (170 g, 3.2×70 cm, packed with benzene) and eluted with 10:1 benzene–ethyl acetate. The effluent was fractionated into 9.2 ml-fractions.

Fractions 47—53 gave colorless crystals. Recrystallization from benzene gave **17β**, 430 mg (21.6%); mp 178.5—179 °C. $[\alpha]_D^{20}$ −37.5° (*c* 1.0, $CHCl_3$). PMR ($CDCl_3$): δ 8.43 (s, 8H, Ar), 8.25 (s, 1H, H-5), 6.79 (t, 1H, H-1'), 6.10 (m, 1H, H-3'), 4.75 (br s, 3H, H-4', H-5',5''), 4.53 (q, 2H, CH_2-ester), 3.60—2.75 (m, 2H, H-2',2''), 1.41 (t, 3H, CH_3-ester). Found: C, 51.89; H, 3.88; N, 12.82%. Calcd for $C_{24}H_{21}O_{11}N_5$: C, 51.90; H, 3.81; N, 12.82%.

Fractions 54—60 gave a mixture of **17β** and **17α**, 388 mg (19.6%).

Fractions 61—68 gave colorless crystals. Recrystallization from acetone gave **17α**, 212 mg (10.7%); mp 128—129°C. $[\alpha]_D^{20}$ +33.5° (*c* 1.0, $CHCl_3$). PMR ($CDCl_3$): δ 8.45 (d, 8H, Ar), 8.26 (s, 1H, H-5), 6.85 (t, 1H, H-1'), 5.90 (m, 1H, H-3'), 5.10 (m, 1H, H-4'), 4.83 (d, 2H, H-5',5''), 4.58 (q, 2H, CH_2-ester), 3.28 (t, 2H, H-2',2''), 1.47 (t, 3H, CH_3-ester). Found: C, 51.93; H, 3.90; N, 12.58%. Calcd for $C_{24}H_{21}O_{11}N_5$: C, 51.90; H, 3.81; N, 12.61%.

Fractions 76—96 gave a mixture of **16α** and **16β**, 566 mg. The crude gum of the mixture was crystallized from ethyl acetate giving **16β**, 256 mg (12%); mp 204.5—205.0 °C. $[\alpha]_D^{20}$ −33.0° (*c* 1.0, DMSO). PMR (DMSO-d_6): δ 9.18 (s, 1H, H-5), 8.50 (m, 8H, Ar), 6.87 (t, 1H, H-1'), 6.08 (m, 1H, H-3'), 4.80 (m, 3H, H-4', H-5',5''), 4.45 (q, 2H, CH_2-ester), 3.10 (m, 2H, H-2',2''), 1.35 (t, 3H, CH_3-ester). Found: C, 51.80; H, 3.97; N, 12.52%. Calcd for $C_{24}H_{21}O_{11}N_5$: C, 51.90; H, 3.81; N, 12.61%.

The mother liquor contains **16β** and **16α** (about 1:4 from PMR). **16α** could not be isolated by recrystallization or chromatography with silica gel.

*Ethyl 1-N-[2-Deoxy-3,5-di-O-(p-toluoyl)-β-D-erythro-pentofuranosyl]-1,2,3-triazole-4-carboxylate (**18β**), Its α-Anomer (**18α**) and Ethyl 2-N-[2-Deoxy-3,5-di-O-(p-toluoyl)-β-D-erythro-pentofuranosyl]-1,2,3-triazole-4-carboxylate (**19β**), Its α-Anomer (**19α**).*
To a solution of 3,5-di-*O*-(*p*-toluoyl)-D-2-deoxyribofuranosyl chloride[17] (**6**, 3.99 g, 10.3 mmol) and silylated ethyl 1,2,3-triazole-4-carboxylate (**2**, 2.72 g, 12.7 mmol) in 1,2-dichloroethane (70 ml) was added a solution of redistilled $SnCl_4$ (1.73 ml, 14.1 mmol) in 1,2-dichloroethane (40 ml) at 0 °C under stirring. The reaction mixture was stirred at room temperature for 12 h. After dilution with 1,2-dichloroethane (60 ml), the reaction mixture was washed with saturated $NaHCO_3$ solution and the resulting emulsion was separated by centrifugation. The organic layer was dried (Na_2SO_4) and evaporated under reduced pressure. The resulting syrup was triturated with benzene and the insoluble product obtained by filtration was recrystallized from benzene to give **18β**, 1.13 g (22.3%); mp 157—158°C. $[\alpha]_D^{20}$ −64.5° (*c* 1.0, $CHCl_3$). PMR ($CDCl_3$): δ 8.32 (s, 1H, H-5), 7.90 (m, 4H, Ar), 7.30 (m, 4H, Ar), 6.58 (t, 1H, H-1'), 5.80 (m, 1H, H-3'), 4.70

(m, 3H, H-4′, H-5′,5″), 4.40 (q, 2H, CH_2-ester), 3.10 (m 2H, H-2′,2″), 2.40 (d, 6H, CH_3-Ar), 1.40 (t, 3H, CH_3-ester). Found: C, 63.03; H, 5.42; N, 8.70%. Calcd for $C_{26}H_{27}O_7N_3$: C, 63.27; H, 5.51; N, 8.52%. The filtrates were combined and evaporated. The resulting syrup was dissolved in ethyl acetate and was placed on a column of silica gel (150 g, 3.2 ×60 cm, packed with benzene) and eluted with 10: 1 benzene–ethyl acetate. The effluent was fractionated into 10 ml-fractions.

Fractions 52—57 gave colorless crystals. Recrystallization from ethanol gave **19β**, 761 mg (15.0%); mp 121—122 °C, $[\alpha]_D^{20}$ −33.0° (*c* 1.0, $CHCl_3$). PMR ($CDCl_3$): δ 8.15 (s, 1H, H-5), 8.00 (m, 4H, Ar), 7.28 (m, 4H, Ar), 6.65 (dt, 1H, H-1′), 5.98 (m, 1H, H-3′), 4.68 (m, 3H, H-4′, H-5′,5″), 4.37 (q, 2H. CH_2-ester), 3.6—2.4 (m, 2H, H-2′,2″), 2.43 (d, 6H, CH_3-Ar), 1.40 (t, 3H, CH_3-ester). Found: C, 63.40; H, 5.64; N, 8.51%. Calcd for $C_{26}H_{27}O_7N_3$: C, 63.27; H, 5.51; N, 8.52%.

Fractions 59—64 gave **19α**, colorless syrup, 780 mg (15.4%); $[\alpha]_D^{20}$ +35.0° (*c* 1.0, $CHCl_3$). PMR ($CDCl_3$): δ 8.12 (s, 1H, H-5), 7.90 (m, 4H, Ar), 7.25 (m, 4H, Ar), 6.58 (t, 1H, H-1′), 5.63 (m, 1H, H-3′), 4.94 (m, 1H, H-4′), 4.60 (d, 2H, H-5′,5″), 4.40 (q, 2H, CH_2-ester), 3.10 (m, 2H, H-2′,2″), 2.40 (d, 6H, CH_3-Ar), 1.37 (t, 3H, CH_3-ester). Found: C, 63.14; H, 5.59; N, 8.50%. Calcd for $C_{26}H_{27}O_7N_3$: C, 63.27; H, 5.51; N, 8.52%.

Fractions 77—88 gave **18α**, colorless syrup, 1.70 g (33.5%); $[\alpha]_D^{20}$ +72.0° (*c* 1.0, $CHCl_3$). PMR ($CDCl_3$): δ 8.35 (s, 1H, H-5), 7.80 (m, 4H, Ar), 7.20 (m, 4H, Ar), 6.55 (q, 1H, H-1′), 5.65 (m, 1H, H-3′), 4.80 (m, 1H, H-4′), 4.62 (d, 2H, H-5′5″), 4.40 (q, 2H, CH_2-ester), 3.08 (m, 2H, H-2′,2″), 2.38 (d, 6H, CH_3-Ar), 1.37 (t, 3H, CH_3-ester). Found: C, 63.00; H, 5.58; N, 8.61%. Calcd for $C_{26}H_{27}O_7N_3$: C, 63.27; H, 5.51; N, 8.52%.

Fractions 90—96 gave **18β**, colorless crystal, 218 mg (4.3%).

*1-N-(2-Deoxy-β-*D*-*erythro*-pentofuranosyl)-1,2,3-triazole-4-carboxamide (20β).* A sample of **18β** (600 mg, 1.45 mmol) in absolute methanol (60 ml) saturated with ammonia at 0 °C was kept at room temperature for 2 days and evaporated under reduced pressure below 40 °C. The residual syrup was dissolved in water (30 ml) and washed with ethyl acetate (10 ml ×3). The aqueous layer was evaporated to dryness. The crude syrup was crystallized from methanol and benzene to give **20β**, 264 mg (80%); 156—157 °C. $[\alpha]_D^{20}$ −32.2° (*c* 1.0, CH_3OH). PMR (DMSO-d_6): δ 8.78 (s, 1H, H-5), 7.60 (br d, 2H, $CONH_2$), 6.40 (t, 1H, H-1′), 5.30 (d, 1H, OH), 4.88 (t, 1H, OH), 4.45 (m, 1H, H-3′), 3.95 (m, 1H, H-4′), 3.55 (m, 2H, H-5′,5″), 2.90—1.90 (m, 2H, H-2′,2″). Found: C, 41.89; H, 5.16; N, 24.61%. Calcd for $C_8H_{12}O_4N_4$: C, 42.11; H, 5.30; N, 24.55%.

*1-N-(2-Deoxy-α-*D*-erythro-pentofuranosyl)-1,2,3-triazole-4-carboxamide (20α).* A sample of **18α** (1.00 g, 2.03 mmol) was subjected to ammonolysis and worked up in a similar manner to that described for **20β**. The crude syrup was crystallized from ethanol and benzene to give **20α**, 364 mg (78.5%); mp 161—162 °C. $[\alpha]_D^{20}$ +85.0° (*c* 1.0, CH_3OH). PMR (DMSO-d_6): δ 8.72 (s, 1H, H-5), 7.60 (br d, 2H, $CONH_2$), 6.43 (q, 1H, H-1′), 5.42 (d, 1H, OH), 4.80 (t, 1H, OH), 4.28 (m, 2H, H-3′, H-4′), 3.50 (m, 2H, H-5′,5″), 3.01—2.11 (m, 2H, H-2′, 2″). Found: C, 41.79; H, 5.22; N, 24.52%. Calcd for $C_8H_{12}O_4N_4$: C, 42.11; H, 5.30; N, 24.55%.

*2-N-(2-Deoxy-β-*D*-eyythro-pentofuranosyl)-1,2,3-triazole-4-carboxamide (21β).* Ammonolysis of **19β** (600 mg, 1.22 mmol) in a similar manner to that described above gave crude syrup which was crystallized from methanol and benzene to give **21β**, 233 mg, (84%); mp 139 °C. $[\alpha]_D^{20}$ −45.5° (*c* 1.0. CH_3OH). PMR (DMSO-d_6): δ 8.13 (s, 1H, H-5), 7.67 (br d, 2H, $CONH_2$), 6.31 (dt, 1H, H-1′), 5.30 (d, 1H, OH), 4.60 (m, 2H, OH, H-3′), 3.90 (m, 1H, H-4′), 3.40 (m, 2H, H-5′,5″), 3.05—2.10 (m, 2H, H-2′,2″). Found: C, 41.88; H, 5.20; H, 24.10%. Calcd for $C_8H_{12}O_4N_4$: C, 42.11; H, 5.30; N, 24.55 %.

*2-N-(2-Deoxy-α-*D*-erythro-pentofuranosyl)-1,2,3-triazole-4-carboxamide (21α).* Ammonolysis of **19α** (600 mg, 1.22 mmol) was subjected to and worked up in a similar manner to that described for the preparation of **20β**. The residual syrup was crystallized from ethanol and benzene to give **21α**, 210 mg (76 %); mp 125—126 °C. $[\alpha]_D^{20}$ +74.5° (*c* 1.0, CH_3OH). PMR (DMSO-d_6): δ 8.20 (s, 1H, H-5), 7.70 (br d, 2H, $CONH_2$), 6.30 (q, 1H, H-1′), 5.22 (d, 1H, OH), 4.75 (t, 1H, OH), 4.20 (m, 2H, H-3′ H-4′), 3.55 (m, 2H, H-5′, 5″), 2.90—2.20 (m, 2H, H-2′, 2″). Found; C, 41.88; H, 5.20; N, 24.80%. Calcd for $C_8H_{12}O_4N_4$: C, 42.11; H, 5.30; N, 24.55%.

The authors wish to thank Mr. Saburo Nakada, Department of Chemistry, Keio University, for the microanalysis. The research was supported in part by a grant for cancer research, Ministry of Education, Science and Culture.

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