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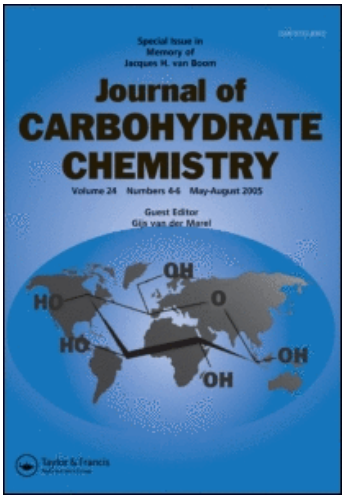

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J. CARBOHYDRATE CHEMISTRY, 4(1), 99-112 (1985)

SYNTHETIC APPROACH TOWARD ANTIBIOTIC TUNICAMYCINS --- VII

SYNTHESIS OF TUNICAMINE AND TUNICAMINYL URACIL DERIVATIVE

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ABSTRACT

A higher carbon carbohydrate moiety of antibiotic tunicamycins named tunicamine has been synthesized in a protected form. The key reaction step of the synthesis is a potassium fluoride catalyzed Henry reaction of a 5-nitroribose derivative and a dialdo-galactosamine derivative. The tunicamine derivative has been converted to a tunicaminyl uracil derivative by condenation with bis(trimethylsilyl)uracil.

INTRODUCTION

Nucleoside antibiotic tunicamycins have been discovered in a fermentation broth of Streptomyces lysosuperficus.[1] The antibiotics inhibit a lipid-mediated protein glycosylation in chick embryo selectively and a multiplication of enveloped viruses at any stage of the proliferation.[2]

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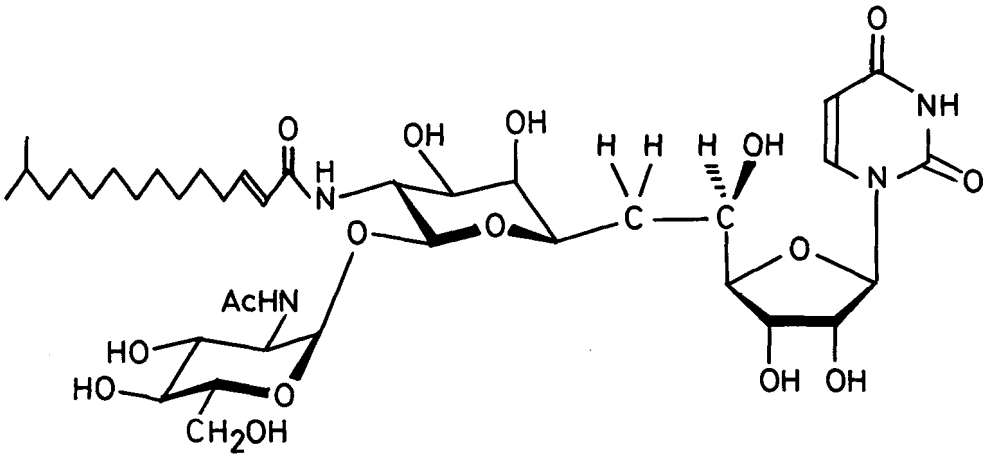

Tunicamycin V

Tunicamycin complex which contains at least 16 homologs,[3] is isolated from the fermentation broths by a solvent extraction, followed by chromatography. Tunicamycins consist of heterocyclic uracil, N-acetyl-D-glucosamine, an eleven carbon carbohydrate named tunicamine,[4] and a fatty acid which may vary in chain length and arrangement. The nucleoside residue which contains uracil and tunicamine is designated as tunicaminyl uracil. Tunicaminyl uracil is also found in other antibiotics, streptovirudins[5] and corynetoxins,[6] as a general component.

In a preceding paper,[7] a versatile synthesis of a higher-carbon carbohydrate has been developed by the Henry reaction of a nitro sugar and a sugar aldehyde in the presence of KF as a catalyst. In the present paper, we wish to report the successful synthesis of a tunicamine derivative as well as a tunicaminyl uracil derivative, the letter being a key intermediate for a consecutive total synthesis of tunicamycin.

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RESULTS AND DISCUSSION

The nitro sugar, 3-O-acetyl-6-deoxy-1,2-O-isopropylidene-6-nitro-α-D-ribofuranose (5) has been prepared in four steps from 3-O-acetyl-1,2:5,6-di-O-isopropylidene-α-D-allofuranose (1)[8] in 23% over-all yield (Scheme 1).

Treatment of 1 with aqueous acetic acid resulted in a preferential hydrolysis of the 5,6-O-isopropylidene group, giving 3-O-acetyl-1,2-O-isopropylidene-α-D-allofuranose (2) in 88% yield. Sodium metaperiodate oxidation of 2 and successive reduction with $NaBH_4$, followed by tosylation afforded 3-O-acetyl-1,2-O-isopropylidene-5-O-(p-toluenesulfonyl)-α-D-ribofuranose (3) in 62% yield. To avoid acetyl migration during the reduction step, the reaction mixture should be kept below 10 °C. Tosylate displacement from 3 with NaI gave 3-O-acetyl-5-deoxy-5-iodo-1,2-O-isopropylidene-α-D-ribofuranose (4) in 98% yield as a syrup. Displacement of iodide from 4 with nitrite was accomplished with sodium nitrite in a mixture of dimethylformamide and dimethylsulfoxide containing phloroglucinol [7] to give the 5-nitroribofuranose derivative 5 in 43% yield. The sugar aldehyde methyl 2-(benzyloxycarbonyl)amino-2-deoxy-3,4-O-isopropylidene-α-D-galactodialdopyranoside-(1,5)[9] (7) was obtained by the Pfitzner-Moffatt oxidation of methyl 2-(benzyloxycarbonyl)amino-2-deoxy-3,4-O-isopropylidene-α-D-galactopyranoside (6).[9]

The reaction of 5 with 7 in the presence of KF in acetonitrile for 2 h at room temperature afforded methyl 9-O-acetyl-2-(benzyloxycarbonyl)amino-2,7-dideoxy-3,4:10,11-di-O-isopropylidene-7-nitro-β-L-undecodialdo-(11R)-furanose-(11,8)-pyranoside-(1,5) (8) as a single diastereomer in 51% yield. Prolonged reaction time resulted in formation of a more complex product mixture.

Dehydration of 8 with acetic anhydride and base (pyridine and 4-dimethylaminopyridine), followed by hydrogenation with

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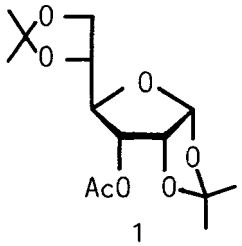
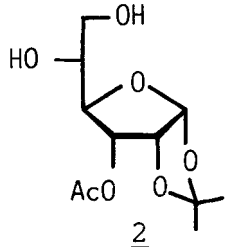


1



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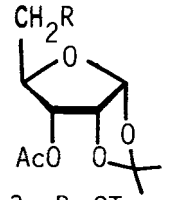
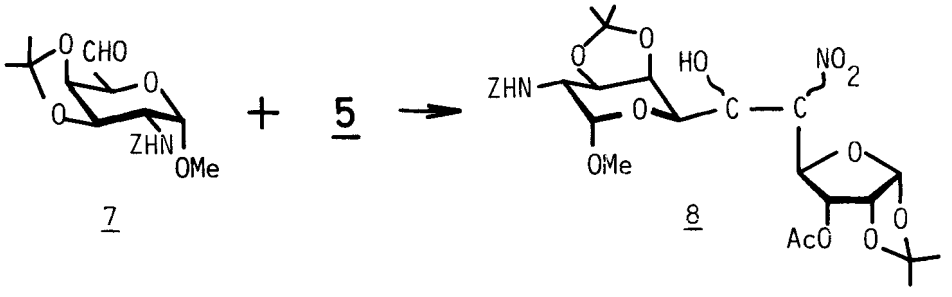
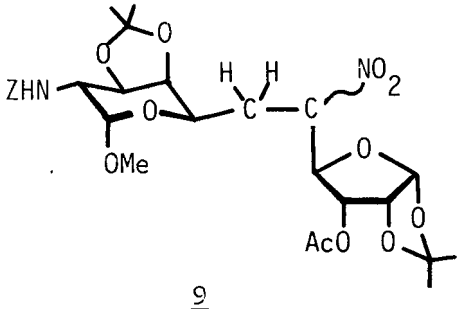


3: R= OTs
4: R= I
5: R= NO_2

Scheme 1



7 8



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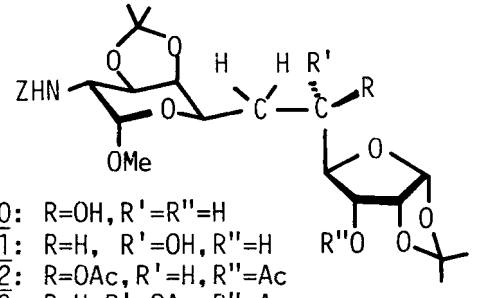
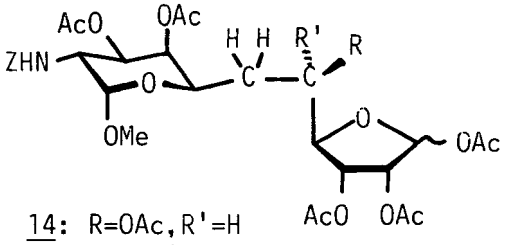
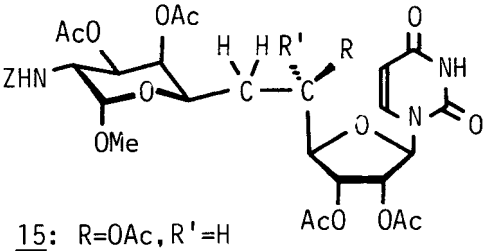


10: R=OH, R'=R"=H
11: R=H, R'=OH, R"=H
12: R=OAc, R'=H, R"=Ac
13: R=H, R'=OAc, R"=Ac



14: R=OAc, R'=H
16: R=H, R'=OAc



15: R=OAc, R'=H
17: R=H, R'=OAc

Scheme 2

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$NaBH_4$ gave methyl 2-(benzyloxycarbonyl)amino-2,6,7-trideoxy-3,4:10,11-di-O-isopropylidene-7-nitro-β-L-undecodialdofuranose-(11,7)-pyranoside-(1,4) (9) in 36% yield.

Oxidation of the nitro group of 9 to the corresponding ketone with potassium permanganate and sodium tert-butoxide, followed by reduction with $NaBH_4$ gave a mixture of two epimeric alcohols. O-Deacetylation of the mixture in methanolic sodium methoxide and successive chromatographic fractionation of the diols gave methyl 2-(benzyloxycarbonyl)amino-2,6-dideoxy-3,4:10,11-di-O-isopropylidene-β-L-undecodialdo-(11R)-furanose-(11,8)-pyranoside-(1,5) (10) mp 155 °C, in 25% yield and its epimer (11) in 42% yield as a syrup. It has been revealed that 10 is a tunicamine derivative since successive reactions lead to a tunicaminyl uracil derivative (10 -> 12 -> 14 -> 15). The 5'-epimer of 15, compound 17, was derived from 11 by an analogous reaction sequence (11 -> 13 -> 16 -> 17). Conventional acetylation of 10 yielded the diacetate (12), mp 187 °C, in 87% yield, and that of 11 gave another diacetate (13), mp 87 °C, in a quantitative yield. Acid hydrolysis of 12 in aqueous acetic acid, followed by acetylation gave a hexaacetate (14) in 71% yield as an anomeric mixture (11S:11R = 1:1).

Condensation of 14 with bis(trimethylsilyl)uracil in 1,2-dichloroethane in the presence of $SnCl_4$ yielded 1-[methyl 2',3',5',9'-penta-O-acetyl-10'-(benzyloxycarbonyl)amino-6',10'-dideoxy-α-L-galacto-D-allo-undecodialdo-(11'S)-pyranoside-(11',7')-furanosyl-(1',4')]-uracil (15), mp 115 °C in 75% yield as an amorphous powder. Compound 15 was identical with an authentic sample prepared from natural tunicamycins as evidenced by ^1H NMR, IR, and specific optical rotation data.

EXPERIMENTAL

General Procedures. Melting points were determined in capillary tubes and are uncorrected. Solutions were con-

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centrated under reduced pressure below 40 °C. Optical rotations were measured with a Japan Spectroscopic DIP-4 polarimeter. ^{1}H NMR spectra were recorded with a Varian EM-390 spectrometer (90 MHz) or a JEOL FX-200 spectrometer (200 MHz), using tetramethylsilane as an internal standard. IR spectra were recorded with a Hitachi 225 spectrophotometer. Chromatography was performed on a column of silica gel (Wakogel C-200 and/or C-300, Wako Pure Chemical Co., Ltd.). TLC was performed on Merck silica gel 60 F_{254} Art. 5715.

3-O-Acetyl-1,2-O-isopropylidene-α-D-allofuranose (2). A solution of 3-O-acetyl-1,2:5,6-di-O-isopropylidene-α-D-allofuranose[8] (1) (28.1 g) in 60% acetic acid (500 mL) was stirred for 14 h at room temperature. The solution was concentrated and the oily residue was chromatographed (C-200, 250g, 3:1 to 1:2 toluene-ethyl acetate) to give 21.5 g (88.0%) of 2: R_f 0.38 on TLC (1.5 ethanol-toluene); $[\alpha]_D^{18}$ + 113.7° (c 8.7, chloroform); ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.33, 1.53 (2s,6H, CMe_2), 2.11 (s, 3H, OAc), 5.82 (d, 1H, $J_{1,2}$=3.6 Hz, H-1); IR (chloroform solution) 1740 (C=O), 3570 cm^{-1}(OH).

Anal. Calcd for $C_{11}H_{18}O_7$: C, 50.38; H, 6.92. Found: C, 50.63; H, 6.96.

3-O-Acetyl-1,2-O-isopropylidene-5-O-p-tolunesulfonyl-α-D-ribofuranose (3). To a solution of 2 (21.2 g) in water (300 mL), a solution of sodium metaperiodate (24.2 g) in water (300 mL) was added under ice cooling. After the reaction mixture was stirred for 30 min below 10°C, a solution of sodium borohydride (4.28 g) in water (200 mL) was added and stirring in the cold continued for an additional 30 min. The solution was extracted with chloroform (400 mL), and the chloroform layer was dried over Na_2SO_4 and concentrated. To a stirred solution of the residue in pyridine (400 mL), tosyl chloride (27.2 g) was added under ice cooling. After 14 h at room temperature, the reaction mixture was poured into ice cold-water (3000 mL),

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and after decantation, a precipitate was dissolved in ethyl acetate (400 mL). The organic solvent layer was washed with water, dried over Na_2SO_4, and evaporated. The residue was recrystallized from cyclohexane to give 19.4 g (62.0%) of 3: R_f 0.54 on TLC (1:5 ethyl acetate-toluene); mp 95-96 °C;$[\alpha]_D^{19}$ +89.0° (c 1.0, chloroform):^{1}H NMR (90 MHz, $CDCl_3$) δ 1.27, 1.47 (2s, 6H, CMe_2), 2.07(s, 3H, OAc), 2.37 (s, 3H, C_6H_4Me, 5.62 (d, 1H,$J_{1,2}$=3 Hz, H-1), 7.28, 7.78 (2d, 4H, J=9 Hz C_6H_4); IR (KBr) 1190 (SO_2), 1740 cm^{-1} (C=O).

Anal. Calcd for $C_{17}H_{22}O_8S$: C, 52.84; H, 5.74; S, 8.30. Found: C, 53.12; H, 5.87; S, 8.04.

3-O-Acetyl-5-deoxy-5-iodo-1,2-O-isopropylidene-α-D-ribofuranose (4). A suspension of 3 (0.47 g) and sodium iodide (0.55 g) in 2-butanone (10 mL) was heated under reflux for 1 h with stirring. After cooling to room temperature, the solvent was evaporated and the residue was dissolved in ethyl acetate (100 mL). The organic layer was washed with water (50 mL), dried over Na_2SO_4, and concentrated. The oily residue was chromatographed on a silica gel column (C-200, 10 g, 1:15-1:5 ethyl acetate-toluene) to give 0.41 g (98%) of oily 4: R_f 0.52 on TLC (1:5 ethyl acetate-toluene): $[\alpha]_D^{15}$ +95.8° (c 1.1, chloroform); ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.37, 1.57 (2s, 6H, CMe_2), 2.17 (s, 3H, OAc), 5.97 (d, 1H, $J_{1,2}$=4 Hz, H-1).

Anal. Calcd for $C_{10}H_{15}O_5I$: C, 35.11; H, 4.42; I, 37.09. Found: C, 35.35; H, 4.40; I, 37.38.

3-O-Acetyl-5-deoxy-1,2-O-isopropyliden-5-nitro-α-D-ribofuranose (5). To a stirred solution of 4 (1.60 g) in dimethyl sulfoxide (18 mL) and dimethyl formamide (4 mL), sodium nitrite (0.80 g) and phloroglucinol (1.6 g) were added and the mixture was stirred for 3 days at room temperature. Water (50 mL) was added to the reaction mixture and the mixture was extracted with ethyl acetate (40 mL). The organic layer was dried over Na_2SO_4 and concentrated. The residue was chromatographed

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(C-200:C-300, 40g, 1:10-1:5 ethyl acetate-toluene). Fractions homogeneous on TLC (R_f 0.5) in 1:5 ethyl acetate-toluene were combined and concentrated. The residue was recrystallized from a mixture of cyclohexane and toluene to give 0.53 g (43.4%) of 5 as needles: mp 104-106 °C; $[\alpha]_D^{19}$ +90.5° (c 1.0, chloroform); ^{1}H NMR (90 MHz, $CDCl_3$) δ 1.34, 1.57 (2s, 6H, CMe_2), 2.13(s, 3H, OAc), 5.83 (d, 1H, $J_{1,2}$=3.8 Hz, H-1): IR (KBr) 1375, 1555 (NO_2), 1750 cm^{-1} (C=O).

Anal. Calcd for $C_{10}H_{15}O_7N$: C, 45.98; H, 5.79; N, 5.36. Found: C, 46.09; H, 5.69; N, 5.25.

Methyl 9-O-acetyl-2-(benzyloxycarbonyl)amino-2,7-dideoxy-3,4:10,11-di-O-isopropylidene-7-nitro- β -L-undecodialdo-(11R)-furanose-(11,8)-pyranoside-(1,5) (8). To a stirred solution of crude 7, which was prepared from methyl 2-(benzyloxycarbonyl)-amino-2-deoxy-3,4-O-isopropylidene- α -D-galactopyranoside[9] (6) (1.0 g), in acetonitrile, 5 (1.43 g) and KF (159 mg) were added under ice cooling. After 2 h, water (50 mL) and ethyl acetate (70 mL) were added to the reaction mixture. The organic layer was separated, dried over Na_2SO_4, and concentrated. The oily residue was chromatographed on a silica gel column (C-200:C-300 1:1, 80 g, 1:4 ethyl acetate-toluene) to give 869 mg (50.7% from 6) of oily 8 and 940 mg of 5 was recovered: R_f 0.20 on TLC (1:3 ethyl acetate-toluene): $[\alpha]_D^{22}$ + 123° (c 1.0, chloroform); ^{1}H NMR (90 Mhz, $CDCl_3$) δ 1.34, 1.57 (2s, 12H, $2CMe_2$), 2.08 (s, 3H, OAc), 3.34 (s, 3H, OMe), 4.62 (d, 1H, $J_{1,2}$=3 Hz, H-1), 5.09 (d, 2H, J=1 Hz, $PhCH_2$), 5.83 (d, 1H, $J_{10,11}$ = 3 Hz, H-11), 7.33 (s, 5H, C_6H_5): IR (chloroform solution) 1378, 1552 (NO_2), 1725 (C=O), 3440 (NH), 3550 cm^{-1} (OH).

Anal. Calcd for $C_{28}H_{38}O_{14}N_2$: C, 53.67; H, 6.11; N, 4.47. Found: C, 53.40; H, 6,13; N, 4.22.

Methyl 9-O-acetyl-2-(benzyloxycarbonyl)amino-2,6,7-trideoxy-3,4:10,11-di-O-isopropylidene-7-nitro-β-L-undecodialdo-(11R)-furanose(11,8)-pyranoside-(1,5) (9). To a

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stirred solution of 8 (152 mg) in chloroform (5 mL), acetic anhydride (0.46 mL), pyridine (0.2 mL) and 4(dimethylamino)-pyridine (12 mg) were added under ice cooling. After 2 h, chloroform (20 mL) was added to the solution and the organic solvent layer was washed successively with water, a saturated $NaHCO_3$ solution, and water. To the organic layer was added toluene (10 mL), and the organic layer was dried over Na_2SO_4, and concentrated to about 10 mL. To the solution was added a solution of sodium borohydride (4 mg) in methanol (2 mL) under ice cooling and stirring continued in the cold for 30 min. Ethyl acetate (20 mL) was added to the solution and the organic layer was washed with water (10 mL), dried (Na_2SO_4) and concentrated. The oily residue was chromatographed on a silica gel column (C-200:C-300 1:1, 10 g, 1:6 ethyl acetate-toluene) to give 54 mg (36%) of 9. Compound 9 was crystallized from methanol: R_f 0.40 on TLC (1:3 ethyl acetate-toluene): mp 167-168 °C; $[\alpha]_D^{23}$+139° (c 0.9, chloroform): ^1H NMR (90 NMz, $CDCl_3$) δ 1.33, 1.53 (2s, 12H, $2CMe_2$), 2.10 (s, 3H, OAc), 2.36 (m, 2H, H-6), 3.29 (s, 3H, OMe), 4.62 (d, 1H, $J_{1,2}$=3.0 Hz, H-1), 5.09 (s, 2H, $PhCH_2$), 6.78 (d, 1H, $J_{10,11}$=3.5 Hz, H-11), 7.35 (s, 5H, C_6H_5); IR (KBr) 1378, 1552 (NO_2), 1725, 1742 (C=O, 3395 cm^{-1} (NH).

Anal. Calcd for $C_{28}H_{38}O_{13}N_2$: C, 55.08; H, 6.27; N, 4.59. Found: C, 54.99; H, 6.21; N, 4.54.

Methyl 2-(benzyloxycarbonyl)amino-2,6-dideoxy-3,4:10,11-di-O-isopropylidene-β-L-undecodialdo-(11R)-furanose-(11,8)-pyranoside-(1,5) (10) and (11). To a stirred solution of 9 (168 mg) in tert-butanol (23 mL), 0.1 N tert-butanolic sodium tert-butoxide (5.5 mL) was added under an argon atmosphere. After 10 min a solution of potassium permanganate (55.7 mg) in water (3 mL) was added to the mixture with stirring. After 15 min acetic acid (0.1 mL) and chloroform (20 mL) were added to the reaction mixture. The insoluble matter was filtered off

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and to the filtrate, chloroform (20 mL) was added. The organic solvent layer was washed with water, dried over Na_2SO_4, and concentrated. To the solution of the residue in ethanol (6 mL), a suspension of sodium borohydride (20 mg) in ethanol (6 mL) was added under ice cooling. After 10 min the reaction mixture was neutralized with Amberlite IR-120B (H^+) resin, the resin was filtered off. The filtrate was concentrated and the oily residue was dissolved in methanol (20 mL). The solution was treated with 1M methanolic sodium methoxide (0.3 mL) for 1 h under ice cooling. The reaction mixture was neutralized with Amberlite IR-120B (H^+) resin, the resin was filtered off and the filtrate was concentrated. The oily residue was chromatographed on a silica gel column (C-200:C-300 1:1, 12 g, 2:3 toluene-ethyl acetate) to give 37.6 mg (25.3%) of 10, 61.9 mg (41.6%) of 11, and 12.5 mg (8.4%) of a mixture of 10 and 11; total yield, 112.0 mg (75.4%). Compound 10 was crystallized from ethanol: 10 R_f 0.19 on TLC (3:2 ethyl acetate-toluene); mp 154-155 °C; $[\alpha]_D^{18}$ +107° (c 0.9 chloroform) ^1H NMR (200 MHz, $CDCl_3$) δ 1.33, 1.37, 1.57 (3s, 12H, $2CMe_2$), 1.97 (m, 2H, H-6), 3.35 (s, 3H, OMe) 5.79 (d, 1H, $J_{10,11}$=3 Hz, H-11), 7.35 (s, 5H,C_6H_5); IR (chloroform solution) 1720 (C=O), 3440 (NH), 3550 cm^{-1} (OH).

Anal. Calcd for $C_{26}H_{37}O_{11}N$: C, 57.88; H, 6.91; N, 2.60. Found: C, 57.92; H, 6,84, N, 2.57.

11: R_f 0.15 on TLC (3:2 ethyl acetate-toluene); $[\alpha]_D^{19}$ +94° (c 1.9, chloroform; ^1H NMR (200 MHz, $CDCl_3$) δ 1.33, 1.37, 1.56 (3s, 12H, $2CMe_2$), 2.12 (m, 2H, H-6), 3.36 (s, 3H, OMe), 5.82 (d, 1H, $J_{10,11}$ = 3.8 HZ, H-11), 7.35 (s, 5H, C_6H_5); IR (chloroform solution) 1720 (C=O), 3440 (NH), 3550 cm^{-1} (OH).

Anal. Calcd for $C_{26}H_{37}O_{11}N$: C, 57.88, H, 6.91; N, 2.60. Found: C, 57.63; H, 6.96; N, 2.39.

Methyl 7,9-di-O-acetyl-2-(benzyloxycarbonyl)amino-2,6-dideoxy-3,4:10,11-di-O-isopropylidene- β -L-undecodialdo-(11R)-

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furanose-(11,8)-pyranoside-(1,5) (12) and (13). To a stirred solution of 11 (53.6 mg) in pyridine (2.0 mL), acetic anhydride (0.1 mL) was added. After 18 h the solution was concentrated to dryness. The oily residue was chromatographed on a silica gel column (C-200:C-300 5:3, 8 g, 1:2 ethyl acetate-toluene) to give 53.1 mg (86.5%) of 13 as an amorphous powder.

Compound 12 was obtained in almost quantitative yield from 10 by an analogous method as described above for 13. 12 was crystallized from ethanol: 12 R_f 0.30 on TLC (1:2 ethyl acetate-toluene); mp 186-187 °C; $[\alpha]_D^{18}$ + 197° (c 0.3, chloroform); ^1H NMR (90 MHz, $CDCl_3$) δ 1.32, 1.53 (2s, 12H, $2CMe_2$), 2.06, 2.12 (2s, 6H, 2OAc), 3.29 (s, 3H, OMe), 5.78 (d, 1H, $J_{10,11}$=3.8Hz, H-11), 7.35 (s, 5H, C_6H_5); IR(KBr) 1740 (C=O), 3440 cm^{-1} (NH).

Anal. Calcd for $C_{40}H_{41}O_{13}N$: C, 57.78; H, 6.63; N, 2.25. Found: C, 57.72; H, 6.55; N, 2.28.

13: R_f 0.30 on TLC (1:2 ethyl acetate-toluene): mp 85-87 °C; $[\alpha]_D^{18}$ +124°(c 0.3, chloroform), ^1H NMR (90 MHz, $CDCl_3$) δ 1.33, 1.53 (2s, 12H, $2CMe_2$), 2.07, 2.10 (2s, 6H, 2OAc), 3.35 (s, 3H, OMe), 5.79 (d, 1H, $J_{10,11}$=3.8 Hz, H-11), 7.35 (s, 5H, C_6H_5); IR (KBr) 1740 (C=O), 3440 cm^{-1} (NH).

Anal. Calcd for $C_{40}H_{41}O_{13}N$: C, 57.78; H, 6.63; N, 2.25. Found: C, 57.72; H, 6.54; N, 2.08.

Methyl 3,4,7,9,10,11-hexa-O-acetyl-2-(benzyloxycarbonyl)-amino-2,6-dideoxy-β-L-undecodialdo-furanose-(11,8)-pyranoside-(1,5) (14) and (16). A solution of 12 (113.8 mg) in 60% acetic acid (14 mL) was heated under reflux for 40 min with stirring. The reaction mixture was concentrated to dryness and the residue was chromatographed on a silica gel column (C-200:C-300, 1:1, 11 g, 1:5 ethanol-toluene). To the mixture of oily product (70 mg), Rf 0.25 and 0.18 on TLC (1:5 ethanol-toluene), pyridine (5.0 mL) and acetic anhydride (0.5 mL) were added under ice cooling. After stirring for 1 day, toluene (ca. 10

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mL) was added, and the reaction mixture was concentrated. The residue was chromatographed on a silica gel column (C-300, 8 g, 1:2 ethyl acetate-toluene) to give 91.7 mg (71%) of oily 14 as an anomeric mixture. By an analogous method as described above compound 16 was obtained from 13.

14: Rf 0.41 and 0.36 on TLC (1:1 ethyl acetate-toluene).

16: Rf 0.39 and 0.33 on TLC (1:1 ethyl acetate-toluene).

1-[Methyl 2',3',5',8',9'-penta-O-acetyl-10'(benzyloxycarbonyl)amino-6',10'-dideoxy-α-L-galacto-D-allo-undecodialdo-(11'S)-pyranoside-(11',7')-furanosyl-(1',4')]-uracil (15) and 1-[Methyl 2'3',5',8',9'-penta-O-acetyl-10'-(benzyloxycarbonyl)-amino-6',10'-dideoxy-α-L-galacto-D-talo-undecodialdo-(11'S)-pyranoside-(11',7')-furanosyl-(1',4')]-uracil (17). To a stirred solution of 14 (24.5 mg) in 1,2-dichloroethane (0.1 mL), bis-(trimethylsilyl)uracil (12.8 mg) prepared by a conventional method, and a solution of stannic chloride (16.7 mg) in 1,2-dichloroethane (0.1 mL) were added below 10 °C under an argon atmosphere. After 2 h at room temperature, chloroform (10 mL) and water (10 mL) were added to the reaction mixture and the insoluble matter was filtered off. To the filtrate, chloroform (10 mL) was added and the organic layer was washed successively with saturated $NaHCO_3$ solution (10 mL) and brine (10 mL). The organic layer was dried over Na_2SO_4 and concentrated. The oily residue was chromatographed on a silica gel column (C-300, 2 g, 1:2 toluene-ethyl acetate) to give 19.6 mg (74.5%) of 15 as an amorphous solid.

By an analogous method as described above compound 17 was obtained as an amorphous powder from 16.

15: R_f 0.45 on TLC (1:5 ethanol-toluene); mp 114-115 °C, $[\alpha]_D^{10}$ +90.8° (c 0.6, chloroform), ^1H NMR (200 MHz, $CDCl_3$) δ 1.70, 1.91, 2.09, 2.13, 2.19 (5s, 18H, Ac), 3.36 (s, 3H, OMe_2), 4.73 (d, 1H, $J_{10',11'}$=3.9 Hz, H-11'), 5.77 (dd, 1H, $J_{5,6}$=8.1 Hz, $J_{3,5}$=2.0 Hz, H-5), 5,83 (d, 1H, $J_{1',2'}$= 5.1 Hz, H-1') 7.17

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(d, 1H, $J_{5,6}$=8.1 Hz, H-6) 7.34 (s, 5H, C_6H_5), 8.72 (bs, 1H, H-3); IR (KBr) 1740 (C=O), 3400 cm^{-1} (NH).

Anal. Calcd for $C_{34}H_{41}O_{17}N_3$: C, 53.47; H, 5.41; N, 5.50. Found: C, 53.69; H, 5.40, N, 5.54.

17: R_f 0.46 on TLC (1:5 ethanol-toluene); mp 118-120 °C; $[\alpha]_D^{10}$ +56.1° (c 0.85, chloroform); ^1H NMR (200 MHz, $CDCl_3$) δ 1.64, 1.89, 2.09, 2.10, 2.15, 2.18 (5s, 18H, Ac), 3.37 (s, 3H, OMe), 4.76 (d, 1H, $J_{10',11'}$=3,9 Hz, H-11'), 5.82 (dd, 1H, $J_{5,6}$=8.1 Hz, $J_{3,5}$=2.0 Hz, H-5), 6.13 (d, 1H, $J_{1'2'}$=5.1 Hz, H-1'), 7.33(s, 5H, C_6H_5), 7.46 (d, 1H, $J_{5,6}$=8.1 Hz, H-6), 8.66 (bs, 1H, H-3); IR (KBr) 1740 (C=O), 3340 cm^{-1} (NH).

Anal. Calcd for $C_{34}H_{41}O_{17}N_3$: C, 53.47; H, 5.41; N, 5.50. Found: C, 53.62; H, 5.43, N, 5.37.

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