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SYNTHESIS OF PHENYL 2-ACETAMIDO-2-DEOXY-3-*O*-α-L-FUCOPYRANOSYL-β-D-GLUCOPYRANOSIDE AND RELATED COMPOUNDS*

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ABSTRACT

The reaction of phenyl 2-acetamido-2-deoxy-4,6-*O*-(*p*-methoxybenzylidene)-β-D-glucopyranoside with 2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl bromide under halide ion-catalyzed conditions proceeded readily, to give phenyl 2-acetamido-2-deoxy-4,6-*O*-(*p*-methoxybenzylidene)-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-β-D-glucopyranoside (**8**). Mild treatment of **8** with acid, followed by hydrogenolysis, provided the disaccharide phenyl 2-acetamido-2-deoxy-3-*O*-α-L-fucopyranosyl-β-D-glucopyranoside. Starting from 6-(trifluoroacetamido)hexyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranoside, the synthesis of 6-(trifluoroacetamido)hexyl 2-acetamido-2-deoxy-3-*O*-α-L-fucopyranosyl-β-D-glucopyranoside has been accomplished by a similar reaction-sequence. On acetolysis, methyl 2-acetamido-2-deoxy-3-*O*-α-L-fucopyranosyl-α-D-glucopyranoside gave 2-methyl-[4,6-di-*O*-acetyl-1,2-dideoxy-3-*O*-(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-α-D-glucopyrano]-[2,1-*d*]-2-oxazoline as the major product.

INTRODUCTION

The substrate specificity of α-L-fucosidases has been found to vary according to the origin of the enzyme. Thus, the enzymes from marine gastropods[2] and rat epididymis[3] possess broad specificity, and nitrophenyl α-L-fucosides can be effectively used as substrates for their detection. However, the α-L-fucosidases from *Clostridium perfringens*[4], *Bacillus fulminans*[5], and *Aspergillus niger*[6] cleave only α-Fuc-(1→2)-Gal linkages. Various methods have been devised for assaying these substrate-specific α-L-fucosidases[6–9]. Recently, we have made use of the synthetic substrate α-Fuc-(1→2)-β-Gal-(1→$OC_6H_4NO_2$-*p* for rapid assay of α-(1→2)-L-fucosidase[10]. Our strategy was based on the sequential action of α-L-fucosidase and exogenously added exo-β-D-galactosidase, and the technique was successfully applied for the detection of α-L-fucosidase from *Clostridium perfringens*, *Aspergillus niger*, and almond emulsin[7]. The last source of the enzyme is also known to contain another α-L-fucosidase, which hydrolyzes α-L-Fuc-(1→3)-GlcNAc and α-L-Fuc-(1→4)-GlcNAc in milk

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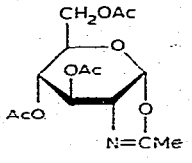
oligosaccharides[7]. In order to facilitate the detection of such specific enzymes, we aimed at the preparation of phenyl 2-acetamido-2-deoxy-3- and -4-*O*-α-L-fucopyranosyl-β-D-glucopyranoside. It is apparent that, if the enzyme acts on a simple saccharide, addition of exo-2-acetamido-2-deoxy-β-D-glucosidase should release (readily measurable) phenol.

We now describe the synthesis of α-Fuc-(1→3)-β-GlcNAc-1→OR [R = Ph, $C_6H_4NH_2$-*p*, and $(CH_2)_6NHCOCF_3$] and α-Fuc-(1→3)-α-GlcNAc-1→OMe.

RESULTS AND DISCUSSION

Benzyl 2-acetamido-2-deoxy-4,6-*O*-(*p*-methoxybenzylidene)-α-D-glucopyranoside has been used for the synthesis of the corresponding 3-*O*-α-L-fucopyranosyl derivatives[11]. As mentioned earlier, we preferred the use of *p*-methoxybenzylidene as a protecting group over the widely used benzylidene group. Thus, for the present studies, phenyl 2-acetamido-2-deoxy-β-D-glucopyranoside was treated with *p*-methoxybenzaldehyde in the presence of anhydrous zinc chloride, to give the desired "aglycon" **4** in 76% yield. Condensation of **4** with 2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl bromide under halide ion-catalyzed reaction-conditions[12] gave compound **8** which, on mild treatment with acid, provided phenyl 2-acetamido-2-deoxy-3-*O*-



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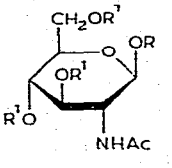
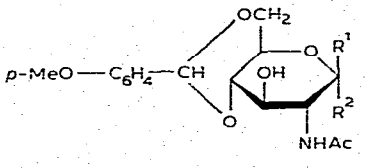
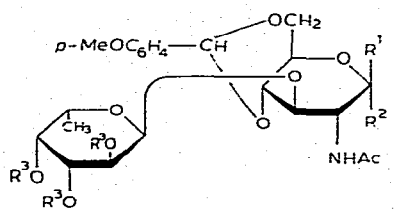


2 R = $-(CH_2)_6NHCOCF_3$, R^1 = Ac
3 R = $-(CH_2)_6NHCOCF_3$, R^1 = H

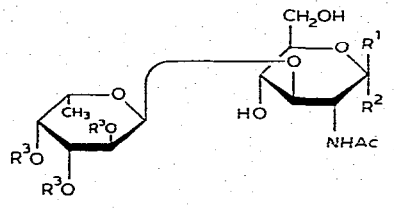


4 R^1 = OPh, R^2 = H
5 R^1 = $O(CH_2)_6NHCOCF_3$ R^2 = H
6 R^1 = $OC_6H_4NO_2$-*p*, R^2 = H
7 R^1 = H, R^2 = OMe

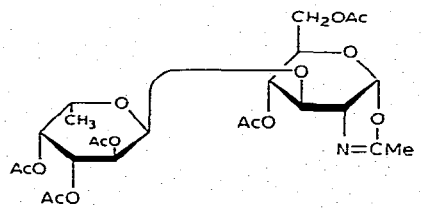
(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-β-D-glucopyranoside (**12**) in crystalline form. The n.m.r. spectrum clearly supported the presence of an α-L-fucopyranosyl linkage (d, 1 H, *J* 3.0 Hz, H-1′) in compound **12**. Catalytic hydrogenolysis of **12** produced the desired phenyl 2-acetamido-2-deoxy-3-*O*-α-L-fucopyranosyl-β-D-glucopyranoside



8 R^1 = OPh, R^2 = H, R^3 = CH_2Ph
9 R^1 = $O(CH_2)_6NHCOCF_3$, R^2 = H, R^3 = CH_2Ph
10 R^1 = $OC_6H_4NO_2$-*p*, R^2 = H, R^3 = CH_2Ph
11 R^1 = H, R^2 = OMe, R^3 = CH_2Ph



12 R^1 = OPh, R^2 = H, R^3 = CH_2Ph
13 R^1 = $O(CH_2)_6NHCOCF_3$, R^2 = H, R^3 = CH_2Ph
14 R^1 = $OC_6H_4NO_2$-*p*, R^2 = H, R^3 = CH_2Ph
15 R^1 = H, R^2 = OMe, R^3 = CH_2Ph
16 R^1 = OPh, R^2 = R^3 = H
17 R^1 = $O(CH_2)_6NHCOCF_3$, R^2 = R^3 = H
18 R^1 = $OC_6H_4NH_2 \cdot HCl$, R^2 = R^3 = H
19 R^1 = R^3 = H, R^2 = OMe



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(**16**). The optical rotation and n.m.r. spectrum of the crystalline compound supported the anomeric configuration assigned.

The affinity-chromatography technique has been successfully applied for the purification of one of the almond emulsin α-L-fucosidases[13], and a derivative of lacto-*N*-fucopentaose, namely, 6-aminohexanoyl-lacto-*N*-fucopentaosylamine coupled to Sepharose, was used as the ligand. In one of the approaches used in the present studies for the preparation of an appropriate ligand, we chose 6-(trifluoroacetamido)-hexyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranoside[14,15] (**2**) as a suitable starting-material. Our strategy for the attachment of an α-L-fucopyranosyl

group at O-3 of **5** was similar to the one described for the preparation of disaccharide **16**.

Treatment of 6-(trifluoroacetamido)-1-hexanol with the oxazoline[16] **1** produced crystalline **2** which, on Zemplén deacetylation, gave 6-(trifluoroacetamido)hexyl 2-acetamido-2-deoxy-β-D-glucopyranoside (**3**) in 85% yield. On reaction with 2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl bromide as described for **8**, the aglycon **5**, obtained from **3**, gave **9** which, on mild treatment with acid, produced **13** in an overall yield of 81%. Catalytic hydrogenolysis of **13** gave crystalline disaccharide **17** in 84% yield; its structure was supported by the i.r. and n.m.r. data.

In another approach to the preparation of a suitable ligand for α-(1→3)-L-fucosidase, the readily accessible aglycon **6** was condensed with 2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl bromide under similar conditions, giving **10**. On treatment with 70% acetic acid, disaccharide **10** gave **14** which, on hydrogenolysis in the presence of hydrochloric acid, afforded the crystalline disaccharide **18**.

The disaccharide sequence α-Fuc-(1→3)-β-GlcNAc has been found to be a part of the carbohydrate moiety of the A, B, H, and Le blood-group substances[17,18]. The sequence is also found to occur in certain glycoproteins, in which this unit is further linked to a D-mannosyl residue[19,20]. Our continued interest in the preparation of 2-methylglyco[2,1-*d*]-2-oxazolines as suitable glycosylating agents for the synthesis of 1,2-*trans*-2-acetamido-2-deoxy-β-D-glucopyranosides prompted us to synthesize the disaccharide oxazoline **20**. As reported earlier, use of the acetolysis procedure[21] for the 3-*O*-methyl-substituted 2-acetamido-2-deoxy-D-glucopyranosyl derivative of such an oxazoline was found to be simple. Based upon these findings, we prepared methyl 2-acetamido-2-deoxy-3-*O*-α-L-fucopyranosyl-α-D-glucopyranoside (**19**), starting from the aglycon **7**, by a reaction sequence similar to that already described herein. Acetolysis[21] of disaccharide **19** provided the oxazoline **20** in almost quantitative yield, and its i.r. and n.m.r. spectra supported the structure assigned.

EXPERIMENTAL

General methods. — Melting points were determined with a Fisher–Johns apparatus and are uncorrected. Optical rotations were measured with a Perkin–Elmer 241 polarimeter at room temperature. Ascending t.l.c. was conducted on plates coated with a 0.25-mm layer of silica gel CC-7 (Mallinckrodt); the components were located by exposure to u.v. light, or by spraying the plate with 5% sulfuric acid in ethanol and heating. Organic solutions were generally dried over anhydrous magnesium sulfate. Elemental analyses were performed by Robertson Laboratory, Florham Park, New Jersey, U.S.A. I.r. spectra were recorded with a Perkin–Elmer 297 spectrophotometer, and n.m.r. spectra, with a Varian XL-100 instrument at 100 MHz, with Me_4Si as the internal standard.

Phenyl 2-acetamido-2-deoxy-4,6-O-(p-methoxybenzylidene)-β-D-glucopyranoside (**4**). — A mixture of phenyl 2-acetamido-2-deoxy-β-D-glucopyranoside (5.0 g), anhydrous zinc chloride (5.0 g), and *p*-methoxybenzaldehyde (50 mL) was stirred

for three days at room temperature, and then poured into cold water with stirring. The solid was filtered off, washed with hexane and water, dissolved in *N,N*-dimethylformamide, and precipitated by addition of water, to afford pure compound **4** as a white powder in 76% yield; m.p. 282°, $[\alpha]_D$ −32.2° (*c* 1, $HCONMe_2$); n.m.r. data (Me_2SO-d_6): δ 1.84 (s, 3 H, Ac), 3.71 (s, 3 H, OMe), 5.24 (d, 1 H, *J* 8.0 Hz, H-1), 5.60 (s, 1 H, benzylic proton), and 6.9–7.5 (m, 9 H, aromatic).

*Phenyl 2-acetamido-2-deoxy-4,6-*O*-(*p*-methoxybenzylidene)-3-*O*-(2,3,4-tri-*O*-benzyl-α-*L*-fucopyranosyl)-β-*D*-glucopyranoside* (**8**). — A suspension of compound **4** (1.1 g, 2.65 mmol) in dichloromethane (40 mL) was stirred for 2 h at room temperature in the presence of tetraethylammonium bromide (1.11 g, 5.30 mmol) and 4A molecular sieves (10 g). A solution of freshly prepared 2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl bromide (2.64 g, 5.31 mmol) in dichloromethane (50 mL) and dry $HCONMe_2$ (60 mL) was added, and the mixture was stirred under dry nitrogen for 5 days at room temperature. Methanol (20 mL) was added, the mixture was stirred for 3 h, solids were removed by filtration, and the filtrate was evaporated. A solution of the solid residue in dichloromethane (150 mL) was successively washed with $NaHCO_3$ solution and water, dried, and evaporated. The residue was used, as such, for the next operation, as we were unable to separate compound **8** from 2,3,4-tri-*O*-benzyl-L-fucose.

*Phenyl 2-acetamido-2-deoxy-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-β-D-glucopyranoside* (**12**). — A mixture of **8** (1.5 g) and 80% acetic acid (50 mL) was stirred for 20 min at 100°, cooled, and evaporated. Several additions and evaporations of water, and then of toluene, gave a solid mass which was dissolved in chloroform (200 mL), and the solution washed with water, dried, and evaporated. The residue was purified by chromatography on a column of silica gel, eluting first with chloroform, then with 19:1 (v/v) chloroform–acetone (to remove the 2,3,4-tri-*O*-benzyl-L-fucose), and finally with 5:1 (v/v) chloroform–acetone, giving **12** in an overall yield of 77%; m.p. 205–206°, $[\alpha]_D$ −72.9° (*c* 1, Me_2SO); ν_{max}^{KBr} 3400 cm^{-1} (OH); n.m.r. data (Me_2SO-d_6): δ 1.10 (d, 3 H, *J* 6.5 Hz, CMe), 1.82 (s, 3 H, Ac), 5.03 (d, 1 H, *J* 7.5 Hz, H-1), 5.32 (d, 1 H, *J* 3.0 Hz, H-1′), and 6.90–7.54 (m, 20 H, aromatic).

Anal. Calc. for $C_{41}H_{47}NO_{10}$: C, 68.98; H, 6.64; N, 1.96. Found: C, 68.73; H, 6.50; N, 1.83.

*Phenyl 2-acetamido-2-deoxy-3-*O*-α-L-fucopyranosyl-β-D-glucopyranoside* (**16**). — A solution of **12** (500 mg) in acetic acid (50 mL) was hydrogenolyzed in the presence of 10% Pd–C for 2 days, the suspension filtered, and the filtrate evaporated to dryness. The residue crystallized from methanol–ether to give disaccharide **16** in 90% yield (280 mg), m.p. 250–251°, $[\alpha]_D$ −90.2° (*c* 0.5, MeOH): n.m.r. data (CD_3OD and Me_2SO-d_6): δ 1.16 (d, 3 H, *J* 6.5 Hz, CMe), 1.92 (s, 3 H, Ac), 4.92 (1 H, H-1′), 5.14 (d, 1 H, *J* 8.0 Hz, H-1), and 6.94–7.45 (m, 5 H, Ph).

Anal. Calc. for $C_{20}H_{29}NO_{10} \cdot 1.5\ H_2O$: C, 51.05; H, 6.86; N, 2.98. Found: C, 51.28; H, 6.70; N, 2.98.

*6-(Trifluoroacetamido)hexyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-gluco-*

pyranoside (**2**). — To a solution of oxazoline **1** (14.0 g) in 1:1 (v/v) nitromethane–toluene (140 mL) were added 6-(trifluoroacetamido)-1-hexanol (7.0 g) and *p*-toluenesulfonic acid (150 mg). The solution was boiled under reflux for 2 h, with stirring, cooled, made neutral with pyridine (2 mL), and evaporated to dryness. A solution of the solid residue in chloroform (200 mL) was washed with water (3 × 50 mL) and dried. To this, activated charcoal (5.0 g) was added, and the suspension was stirred for 30 min, filtered through a Celite pad, and the filtrate evaporated to dryness, giving **2** in 60% yield (14.6 g), m.p. 162–163° (lit.[14] m.p. 165.5–166.5°), $[\alpha]_D$ −14.4° (*c* 1, chloroform) (lit.[14] $[\alpha]_D$ +3.0 ±1.0°); n.m.r. data ($CDCl_3$): δ 1.20–1.72 [m, 8 H, $C(CH_2)_4C$], 1.96 (s, 3 H, NHAc), 2.04 (s, 6 H, 2 Ac), 2.10 (s, 3 H, Ac), 4.64 (d, 1 H, *J* 8 Hz, H-1), 5.08 (t, 1 H, *J* 9 Hz, H-4), 5.30 (t, 1 H, *J* 9 Hz, H-3), 5.88 (d, 1 H, *J* 8 Hz, NHAc), and 7.16 (m, 1 H, $NHCOCF_3$).

*6-(Trifluoroacetamido)hexyl 2-acetamido-2-deoxy-β-*D*-glucopyranoside* (**3**). — A molar solution of sodium methoxide (0.3 mL) was added to a solution of **2** (3.5 g) in anhydrous methanol (35 mL), and the mixture was stirred for ~3 h at room temperature, made neutral with acetic acid, and evaporated, followed by a few additions and evaporations of dry toluene. The residue crystallized from hot ethanol, to give **3** (2.2 g) in 85% yield, m.p. 185–187° (lit.[15] m.p. 189–192°), $[\alpha]_D$ −19.4° (*c* 1, MeOH); ν_{max}^{KBr} 3450 (OH), 3280 (NH), 1700 ($NHCOCF_3$), and 1650 cm^{-1} (NHAc); n.m.r. data (CD_3OD): δ 1.22–1.70 [m, 8 H, $C(CH_2)_4C$], 1.98 (s, 3 H, NHAc), and 4.40 (d, 1 H, *J* 8 Hz, H-1).

*6-(Trifluoroacetamido)hexyl 2-acetamido-2-deoxy-4,6-*O*-(*p*-methoxybenzylidene)-β-*D*-glucopyranoside* (**5**). — A mixture of compound **3** (2.5 g), anhydrous zinc chloride (2.5 g), and *p*-methoxybenzaldehyde (25 mL) was stirred for 2 days at room temperature, and then poured into cold water with stirring. The solid residue was filtered off, washed with hexane and water, and recrystallized from $HCONMe_2$–water, to afford crystalline compound **3** in 78% yield (2.58 g). A sample for analysis was purified by chromatography on a column of silica gel, with elution with 1:1 (v/v) chloroform–acetone, to give **5**, m.p. 228–229°, $[\alpha]_D$ −52.9° (*c* 1, $HCONMe_2$); t.l.c. (1:1 chloroform–acetone): R_F 0.67; n.m.r. data (Me_2SO-d_6): δ 1.12–1.64 [m, 8 H, $C(CH_2)_4C$], 1.82 (s, 3 H, NHAc), 3.76 (s, 3 H, OMe), 4.48 (d, 1 H, *J* 8 Hz, H-1), 5.56 (s, 1 H, benzylic proton), 6.94 and 7.40 (2 d, 2 × 2 H, *J* 8 Hz, aromatic protons), 7.82 (d, 1 H, *J* 8 Hz, NHAc), and 9.40 (m, 1 H, $NHCOCF_3$).

*6-(Trifluoroacetamido)hexyl 2-acetamido-2-deoxy-4,6-*O*-(p-methoxybenzylidene)-3-*O*-(2,3,4-tri-*O*-benzyl-α-*L*-fucopyranosyl)-β-*D*-glucopyranoside* (**9**). — Compound **9** was obtained from **5** (1.378 g, 2.65 mmol) as described for **8**, and was used as such for the next reaction.

*6-(Trifluoroacetamido)hexyl 2-acetamido-2-deoxy-3-*O*-(2,3,4-tri-*O*-benzyl-α-*L*-fucopyranosyl)-β-*D*-glucopyranoside* (**13**). — The *p*-methoxybenzylidene group of compound **9** was removed as described for the preparation of **12**, to give a solid residue which was purified by chromatography on a column of silica gel, eluting first with chloroform, then with 19:1 chloroform–acetone (to remove the 2,3,4-tri-*O*-benzyl-L-fucose), and, finally, with 19:1 chloroform–ethanol, to give **13** in 81%

yield; m.p. 200–201°, $[\alpha]_D$ −75.0° (*c* 0.5, Me_2SO); ν_{max}^{KBr} 3400 (OH), 3300 (NH), 1700 ($NHCOCF_3$), 1650 (NHAc), and 730 and 700 cm^{-1} (aromatic); n.m.r. data (Me_2SO-d_6): δ 1.07 (d, 3 H, *J* 6.0 Hz, CMe), 1.20–1.62 [m, 8 H, $C(CH_2)_4C$], 1.80 (s, 3 H, NHAc), 5.26 (d, 1 H, *J* 3 Hz, H-1′), and 7.20–7.50 (m, 15 H, aromatic).

Anal. Calc. for $C_{43}H_{55}F_3N_2O_{11}$: C, 62.00; H, 6.66; N, 3.36. Found: C, 61.77; H, 6.57; N, 3.11.

*6-(Trifluoroacetamido)hexyl 2-acetamido-2-deoxy-3-*O*-α-*L*-fucopyranosyl-β-*D*-glucopyranoside* (**17**). — A solution of **13** (300 mg) in acetic acid (30 mL) was hydrogenolyzed in the presence of 10% Pd–C for 2 days. The suspension was filtered, the filtrate evaporated to dryness, and the residue purified by chromatography on a column of silica gel, with elution with 65:35:8 (v/v) chloroform–methanol–water, to give **17** (170 mg, 84%), m.p. 218–220°, $[\alpha]_D$ −80.1° (*c* 1, methanol); n.m.r. data (CD_3OD): δ 1.18 (d, 3 H, *J* 6.5 Hz, CMe), 1.26–1.80 [m, 8 H, $C(CH_2)_4C$], 1.96 (s, 3 H, NHAc), 4.28 (q, 1 H, *J* 6.5 Hz, H-5′), 4.48 (d, 1 H, *J* 8 Hz, H-1), and 5.12 (d, 1 H, *J* 3.5 Hz, H-1′).

Anal. Calc. for $C_{22}H_{37}F_3N_2O_{11} \cdot H_2O$: C, 45.51; H, 6.77; N, 4.83. Found: C, 45.37; H, 6.80; N, 4.76.

p-*Nitrophenyl 2-acetamido-2-deoxy-4,6-*O*-(p-methoxybenzylidene)-3-*O*-(2,3,4-tri-*O*-benzyl-α-*L*-fucopyranosyl)-β-*D*-glucopyranoside* (**10**). — Compound **10** was prepared from *p*-nitrophenyl 2-acetamido-2-deoxy-4,6-*O*-(*p*-methoxybenzylidene)-β-D-glucopyranoside (**6**; 5.0 g), as described for **8**, and was used as such for the next operation.

p-*Nitrophenyl 2-acetamido-2-deoxy-3-*O*-(2,3,4-tri-*O*-benzyl-α-*L*-fucopyranosyl)-β-*D*-glucopyranoside* (**14**). — The *p*-methoxybenzylidene group of compound **10** was removed, as described for **12**, to give compound **14**. After purification by column chromatography, a white solid was obtained in a yield of 74%; m.p. 210–211°, $[\alpha]_D$ −70.4° (*c* 0.5, Me_2SO); the i.r. spectrum showed the presence of hydroxyl group; n.m.r. data (Me_2SO-d_6): δ 1.10 (d, 3 H, *J* 6.5 Hz, CMe), 1.81 (s, 3 H, NHAc), 5.22 (d, 1 H, *J* 8 Hz, H-1), 5.30 (d, 1 H, *J* 3.5 Hz, H-1′), and 7.10–8.34 (m, 19 H, aromatic).

Anal. Calc. for $C_{41}H_{46}N_2O_{12}$: C, 64.89; H, 6.11; N, 3.69. Found: C, 65.06; H, 6.10; N, 3.80.

Hydrochloride of p-*Aminophenyl 2-acetamido-2-deoxy-3-*O*-α-*L*-fucopyranosyl-β-*D*-glucopyranoside* (**18**). — A solution of **14** (150 mg) in methanol (50 mL) was hydrogenolyzed in the presence of 0.05M HCl (3.5 mL) and 10% Pd–C (150 mg) for 2 days, the suspension was filtered, and the filtrate evaporated to dryness. The residue was dissolved in water, the solution passed through silica gel, and the eluate lyophilized, to give **18** (70 mg, 72%), m.p. 192–193°, $[\alpha]_D$ −69.0° (*c* 0.5, MeOH); n.m.r. data (CD_3OD): δ 1.20 (d, 3 H, *J* 6.0 Hz, CMe), 1.98 (s, 3 H, Ac), 4.32 (q, 1 H, *J* 6.0 Hz, H-5′), 5.22 (d, 1 H, *J* 8.0 Hz, H-1), and 7.12–7.46 (m, 4 H, aromatic).

*Methyl 2-acetamido-2-deoxy-4,6-*O*-(p-methoxybenzylidene)-3-*O*-(2,3,4-tri-*O*-benzyl-α-*L*-fucopyranosyl)-α-*D*-glucopyranoside* (**11**). — Glycosylation of methyl 2-acetamido-2-deoxy-4,6-*O*-(*p*-methoxybenzylidene)-α-D-glucopyranoside (**7**; 0.94 g),

as described for **8**, gave compound **11**, which was used as such for the next reaction.

*Methyl 2-acetamido-2-deoxy-3-*O*-(2,3,4-tri-*O*-benzyl-α-*L*-fucopyranosyl)-α-*D*-glucopyranoside* (**15**). — Removal of the *p*-methoxybenzylidene group of compound **11**, as described for **12**, gave compound **15** in an overall yield of 70%; m.p. 195–196°, $[\alpha]_D$ −39.2° (*c* 1, Me_2SO); n.m.r. data (CD_3OD and C_6D_6): δ 1.19 (d, 3 H, *J* 6.5 Hz, CMe), 1.62 (s, 3 H, NHAc), 3.34 (s, 3 H, OMe), 4.90 (d, 1 H, *J* 3 Hz, H-1), 5.21 (d, 1 H, *J* 3.5 Hz, H-1′), and 7.26–7.54 (m, 15 H, aromatic).

Anal. Calc. for $C_{36}H_{45}NO_{10}$: C, 66.43; H, 6.96; N, 2.15. Found: C, 66.54; H, 7.03; N, 1.97.

*Methyl 2-acetamido-2-deoxy-3-*O*-α-*L*-fucopyranosyl-α-*D*-glucopyranoside* (**19**).— Compound **15** (200 mg) was hydrogenolyzed as described for **16**, to give compound **19** (105 mg, 90%), m.p. 276–277°, $[\alpha]_D$ −19.8° (*c* 0.5, MeOH); n.m.r. data (CD_3OD): δ 1.20 (d, 3 H, *J* 6.5 Hz, CMe), 1.98 (s, 3 H, NHAc), 3.41 (s, 3 H, OMe), 4.30 (q, 1 H, *J* 6.5 Hz, H-5′), 4.69 (d, 1 H, *J* 3.5 Hz, H-1), and 4.96 (1 H, H-1′).

Anal. Calc. for $C_{15}H_{27}NO_{10}$: C, 47.24; H, 7.14; N, 3.67. Found: C, 47.12; H, 7.36; N, 3.51.

*2-Methyl-[4,6-di-*O*-acetyl-1,2-dideoxy-3-*O*-(2,3,4-tri-*O*-acetyl-α-*L*-fucopyranosyl)-α-*D*-glucopyrano]-[2,1-d]-2-oxazoline* (**20**). — A solution of compound **19** (50 mg) in a mixture of acetic anhydride (1.0 mL), acetic acid (1.0 mL), and sulfuric acid (0.01 mL) was stirred for 2 days at room temperature. It was then diluted with cold dichloromethane (50 mL), washed successively with ice-cold, saturated sodium hydrogencarbonate solution and ice-cold water (2 × 10 mL), dried (anhydrous sodium sulfate), and evaporated, to give a syrup (64 mg, 87%); t.l.c. (10:10:1 chloroform–ethyl ether–methanol) R_F 0.74; $[\alpha]_D$ −57.6° (*c* 0.5, dichloromethane); ν_{max}^{neat} 1750 (OAc) and 1675 cm^{-1} (C=N); n.m.r. data ($CDCl_3$): δ 1.14 (d, 3 H, *J* 6.0 Hz, CMe of fucose), 1.96–2.20 (cluster of singlets, 18 H, 5 Ac + 1 Me of oxazoline), 4.34 (q, 1 H, *J* 6.0, H-5′), 5.91 (d, 1 H, *J* 7.0 Hz, H-1), and 6.19 (d, 1 H, *J* 3 Hz, H-1′).

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