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THE CHEMICAL SYNTHESIS OF *O*-α-L-FUCOPYRANOSYL-(1→2)-*O*-β-D-GALACTOPYRANOSYL-(1→3)-*O*-[α-L-FUCOPYRANOSYL-(1→4)]-2-ACETAMIDO-2-DEOXY-D-GLUCOPYRANOSE, THE LEWIS b BLOOD-GROUP ANTIGENIC DETERMINANT*

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ABSTRACT

An approach has been developed for the rapid synthesis of benzyl 2-acetamido-2-deoxy-3-*O*-β-D-galactopyranosyl-β-D-glucopyranoside (**5**). Disaccharide **5** was per(trimethylsilyl)ated, to provide the fully protected trimethylsilyl (Me_3Si) derivative which, on treatment with pyridine–acetic anhydride–acetic acid for 2 days, gave the disaccharide derivative having *O*-acetyl groups selectively at the primary positions and Me_3Si groups at the secondary positions. The latter groups were readily cleaved by treatment with aqueous acetic acid in methanol, to afford benzyl 2-acetamido-6-*O*-acetyl-3-*O*-(6-*O*-acetyl-β-D-galactopyranosyl)-2-deoxy-β-D-glucopyranoside, which, on isopropylidenation, gave the desired, key intermediate **9**, having two hydroxyl groups free. Condensation of **9** with 2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl bromide, under catalysis by halide ion, afforded the tetrasaccharide derivative, from which the title tetrasaccharide was obtained by systematic removal of the protecting groups. The structure of the final product, and of various other intermediates, was established by ^1H- and ^{13}C-n.m.r. spectroscopy.

INTRODUCTION

In recent years, there has been considerable success in the chemical synthesis of complex oligosaccharides containing a variety of linkages. Such chemical reactions as glycosidation catalyzed by halide ion[2], those involved in the oxazoline method[3,4], and those catalyzed by silver triflate[5] have been widely used in the synthesis of such sugar molecules, which are of great biological interest. In fact, recent progress made in the field of carbohydrate chemistry has provided a unique approach toward the chemical synthesis of synthetic antigens[6,7]. As a result, considerable effort has been devoted to synthesis of oligosaccharides that occur as a part of blood-group sub-

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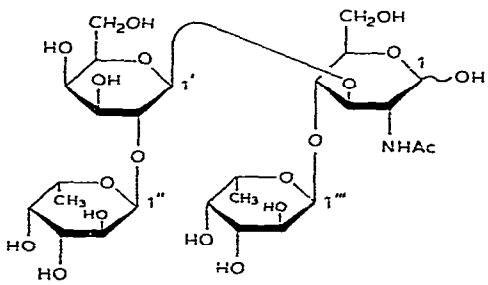

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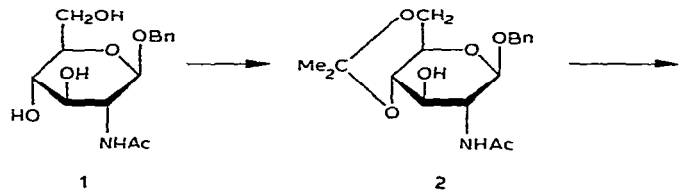
stances[8,9]. In the present studies, we describe a rapid, chemical synthesis of the tetrasaccharide (**13**) that had been isolated by alkaline degradation of human, blood-group H, Le^b substance, and considered to be a Le^b-active determinant[10].

RESULTS AND DISCUSSION

Isopropylidenation[11] of benzyl 2-acetamido-2-deoxy-β-D-glucopyranoside (**1**) with 2,2-dimethoxypropane in *N*,*N*-dimethylformamide in the presence of *p*-toluenesulfonic acid afforded the 4,6-acetal **2** in 68% yield. The ^{13}C-n.m.r. data for **2** exhibited a resonance for the acetal carbon atom at 98.6 p.p.m., and the chemical shifts for the methyl groups were separated by 10 p.p.m., supporting thereby the presence of a second, six-membered ring in **2**. The reaction of **2** with 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide in freshly distilled, anhydrous acetonitrile in the presence of mercuric cyanide for 5 h at room temperature proceeded readily, to give the disaccharide derivative **3** in 73% yield. The ^{13}C-n.m.r. spectrum of crystalline compound **3** clearly showed the presence of the 4,6-*O*-isopropylidene group, confirming thereby that the 4,6-*O*-isopropylidene ring did not migrate during the *O*-glycosylation.

Acetal migrations have frequently been reported in other oligosaccharide syntheses[12–14]. Moreover, in our laboratory, we recently observed that reaction of benzyl 2-*O*-benzoyl-4,6-*O*-isopropylidene-β-D-galactopyranoside with tetra-*O*-acetyl-α-D-galactosyl bromide under the usual conditions gave the 6-*O*-glycosylated disaccharide derivative, not the 3-*O*-substituted compound expected, due to acetal migration[15]. It may also be mentioned that, for glycosylation of O-3 of 2-acetamido-2-deoxy-D-glucopyranose, use of the corresponding, protected sugar alcohol, such as the 4,6-*O*-benzylidene or -*p*-methoxybenzylidene acetal of benzyl 2-acetamido-2-deoxy-D-glucopyranoside has frequently been made[16,17]. With such sugar derivatives, the reaction with a glycosyl halide has been conducted in 1 : 1 nitromethane–benzene in the presence of mercuric cyanide for 2 to 3 days. As the condensation of a glycosyl halide with a free alcohol group of a sugar, in anhydrous acetonitrile in the presence of mercuric cyanide, is not time-consuming, we preferred the use of "aglycon" **2**, which is quite soluble in acetonitrile, for the preparation of disaccharide derivative **3**. Removal of the 4,6-*O*-isopropylidene group from **3** provided **4** which, on *O*-de-



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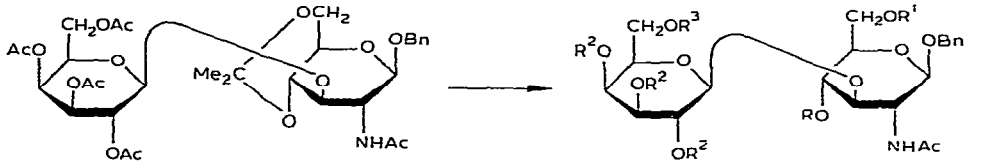

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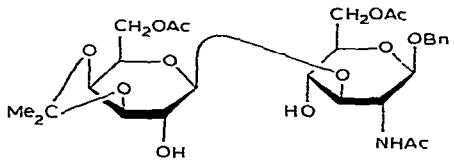
4 R = R^1 = H, R^2 = R^3 = Ac
5 R = R^1 = R^2 = R^3 = H
6 R = R^1 = R^2 = R^3 = $SiMe_3$
7 R = R^2 = $SiMe_3$, R^1 = R^3 = Ac
8 R = R^2 = H, R^1 = R^3 = Ac



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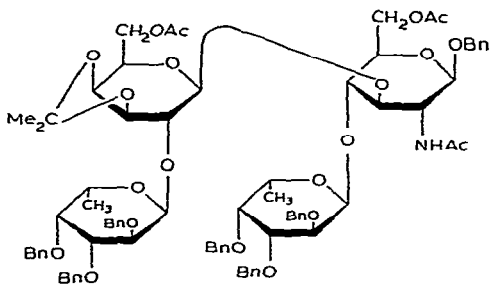

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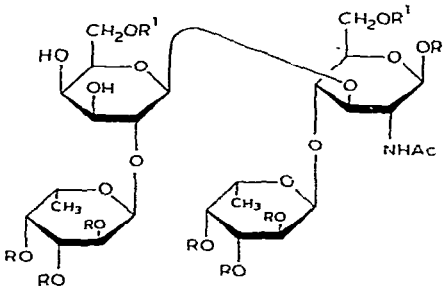
Bn = benzyl



11 R = Bn, R^1 = Ac
12 R = Bn, R^1 = H

acetylation, gave crystalline compound **5** in 83% yield. The ^{13}C-n.m.r. spectrum of **5** was in excellent agreement with the structure assigned.

After developing this rapid synthesis of disaccharide **5**, we desired a facile preparation of benzyl 2-acetamido-6-*O*-acetyl-3-*O*-(6-*O*-acetyl-3,4-*O*-isopropylidene-β-D-galactopyranosyl)-2-deoxy-β-D-glucopyranoside (**9**), the key intermediate for the synthesis of the title tetrasaccharide. Our main strategy for the preparation of compound **9** from **5** was based on the observation that per(trimethylsilyl)ated derivatives can be selectively acetylated at the primary hydroxyl group by using a

mixture of pyridine, acetic anhydride, and a small proportion of acetic acid[18,19]. Consequently, the disaccharide derivative **5** was per(trimethylsilyl)ated[20], to yield the fully protected derivative **6**, the i.r. spectrum of which showed complete absence of hydroxyl groups. Compound **6** was treated with acetic anhydride, glacial acetic acid, and pyridine for 2 days at room temperature[18], to give the desired compound **7**, having an acetyl group on both primary hydroxyl groups; the course of the reaction was monitored by t.l.c., as prolonged treatment may cause acetylation at the secondary positions[19]. The removal of the remaining trimethylsilyl groups from **7**, by means of aqueous acetic acid in methanol[18], gave **8**, which was isolated crystalline. The downfield shifts of 2.5 p.p.m. exhibited by C-6 and C-6′ on acetylation, and the upfield shifts of C-5 (3.4 p.p.m.) and C-5′ (3.3 p.p.m.) confirmed the positions of substitution in **8**. Isopropylidenation[11] of compound **8** with 2,2-dimethoxypropane in *N*,*N*-dimethylformamide, in the presence of *p*-toluenesulfonic acid, gave a product whose ^{1}H-n.m.r. spectrum clearly showed the presence of an isopropylidene group. The ^{13}C-n.m.r. spectrum of the compound confirmed the presence of the five-membered ring of the acetal group. Based on these observations, we assigned structure **9** to the compound.

L-Fucosylation of **9** with 2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl bromide, under catalysis by bromide ion[2], for 5 days, followed by the usual processing, afforded **10** in 78% yield; it was purified by chromatography on a column of silica gel, and the ^{1}H- and ^{13}C-n.m.r. spectra confirmed the structure assigned. Treatment of **10** with 65% acetic acid for 1 h at 60° gave **11** in 82% yield. Zemplén deacetylation of **11** afforded **12**, which, on catalytic hydrogenolysis in glacial acetic acid in the presence of 10% Pd–C, gave the title tetrasaccharide **13** as an amorphous material whose purity was established by paper chromatography.

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 60 PF-254 (E. Merck, Darmstadt, Germany); the components were located by exposure to u.v. light, or by spraying the plate with 5% of sulfuric acid in ethanol and heating. Elemental analyses were performed by Robertson Laboratory, Florham Park, New Jersey, U.S.A. N.m.r. spectra were recorded with a Varian XL-100 instrument; ^{1}H-n.m.r. spectra at 100 MHz and ^{13}C-n.m.r. spectra at 25.2 MHz were determined in the Fourier-transform (F.t.) mode; the positions of the peaks are expressed in δ from the signal of tetramethylsilane.

Benzyl 2-acetamido-2-deoxy-4,6-O-isopropylidene-β-D-glucopyranoside (**2**). — A solution of benzyl 2-acetamido-2-deoxy-β-D-glucopyranoside (**1**; 10 g) and 2,2-dimethoxypropane (50 mL) in *N*,*N*-dimethylformamide (150 mL) was stirred for 4 h at room temperature in the presence of *p*-toluenesulfonic acid (250 mg). The mixture was made neutral with triethylamine, and evaporated to dryness, affording

TABLE I

^{13}C-N.M.R. CHEMICAL SHIFTS[a] (25.2 MHz, Me_2SO-d_6) FOR ISOPROPYLIDENE ACETALS

Compound	*Acetal carbon atom*	*Methyl groups*	*Ring size*
2	98.6	19.0, 29.0	6[b]
9	108.8	26.1, 27.7	5[b]

[a]In p.p.m. downfield from Me_4Si (internal). [b]For values, see ref. 21.

TABLE II

^{13}C-N.M.R. CHEMICAL SHIFTS[a] (25.2 MHz, Me_2SO-d_6)

Compound	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*C-1'*	*C-2'*	*C-3'*	*C-4'*	*C-5'*	*C-6'*	*OCOCH$_3$*	*CH$_2$*	*C=O*
1	100.5	55.3	74.0	70.6	76.9	61.0							23.0	69.3	168.8
5	100.0	54.0	84.2	68.5	76.4	60.5	103.6	70.4	72.8	68.1	75.6	60.7,	22.9	69.4	169.6
8	99.9	54.1	84.1	68.8	73.0	63.0	104.1	70.0	72.5	68.0	72.3	63.2,	20.4, 20.5, 22.9	69.6	169.5, 170.0

[a]In p.p.m. downfield from Me_4Si (internal).

a solid residue which crystallized from ethanol, to give acetal **2** in 68% yield (7.68 g), m.p. 186–187°, $[\alpha]_D$ −110.2° (*c* 1, chloroform); ^{1}H-n.m.r. (Me_2SO-d_6): δ 1.32, 1.44 (2 s, 2 × 3 H, isopropylidene methyls), 1.82 (s, 3 H, NAc), 4.54 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 7.32 (m, 5 H, Ph), and 7.83 (d, 1 H, $J_{NH,2}$ 8 Hz, NH).

Anal. Calc. for $C_{18}H_{25}NO_6$: C, 61.52; H, 7.17; N, 3.99. Found: C, 61.79; H, 7.35; N, 4.03.

Benzyl 2-acetamido-2-deoxy-4,6-O-isopropylidene-3-O-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-β-D-glucopyranoside (**3**). — A mixture of compound **2** (3.51 g, 10 mmol), 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide (6.37 g, 15 mmol), mercuric cyanide (2.53 g, 10 mmol), and dry acetonitrile (100 mL) was stirred for 8 h at room temperature, and then evaporated to dryness. A solution of the solid residue in chloroform (150 mL) was successively washed with water, a saturated solution of potassium bromide, sodium hydrogencarbonate solution, and water, dried (anhydrous magnesium sulfate), and evaporated. The solid mass was recrystallized from acetone–hexane to give compound **3** in 73% yield (4.97 g), m.p. 209–210°, $[\alpha]_D$ −20.5° (*c* 1, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 1.42, 1.54 (2 s, 2 × 3 H, isopropylidene methyls), 1.90, 1.98, 2.02, 2.06, 2.15 (s each, 15 H, 5 Ac), 5.37 (dd, 1 H, $J_{3',4'}$ 3, $J_{4',5'}$ < 1 Hz, H-4'), 5.71 (d, 1 H, $J_{NH,2}$ 7 Hz, NH), and 7.32 (m, 5 H, Ph).

Anal. Calc. for $C_{32}H_{43}NO_{15}$: C, 56.38; H, 6.36; N, 2.06. Found: C, 56.23; H, 6.63; N, 2.07.

*Benzyl 2-acetamido-2-deoxy-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-*D*-galactopyranosyl)-β-*D*-glucopyranoside* (**4**). — A mixture of **3** (5.0 g) and 80% acetic acid (250 mL) was stirred for 30 min at 100°, cooled, and evaporated. Several additions and evaporations of water, and then of toluene, gave a solid mass which was recrystallized from hot ethanol, to give **4** (3.72 g) in 79% yield, m.p. 175–176°, $[\alpha]_D$ −36.5° (*c* 1.1, Me_2SO), {lit.[17] m.p. 176–177°, $[\alpha]_D$ −14° (*c* 3.39, chloroform)}; ^{1}H-n.m.r. (Me_2SO-d_6): δ 1.84, 1.92, 2.01, 2.03, 2.14 (s each, 15 H, 5 Ac), 5.30 (dd, 1 H, $J_{3',4'}$ 3, $J_{4',5'}$ <1 Hz, H-4'), 7.35 (m, 5 H, Ph), and 7.84 (d, 1 H, $J_{NH,2}$ 8 Hz, NH).

*Benzyl 2-acetamido-2-deoxy-3-*O*-β-*D*-galactopyranosyl-β-*D*-glucopyranoside* (**5**). — A molar solution of sodium methoxide in methanol (5 mL) was added to a solution of compound **4** (5 g) in methanol (50 mL), and the mixture was kept overnight at room temperature, made neutral with acetic acid, and evaporated; this was followed by a few additions and evaporations of dry toluene. The residue crystallized from methanol–ether, to give **5** (3.06 g) in 83% yield, m.p. 225–226°, $[\alpha]_D$ −31.4° (*c* 0.5, Me_2SO); ^{1}H-n.m.r. (Me_2SO-d_6 + MeOH-d_4): δ 1.90 (s, 3 H, NAc) and 7.36 (m, 5 H, Ph).

Anal. Calc. for $C_{21}H_{31}NO_{11}$: C, 53.27; H, 6.60; N, 2.96. Found: C, 53.01; H, 6.64; N, 2.91.

*Benzyl 2-acetamido-2-deoxy-3-*O*-[2,3,4,6-tetra-*O*-(trimethylsilyl)-β-*D*-galactopyranosyl]-4,6-di-*O*-(trimethylsilyl)-β-*D*-glucopyranoside* (**6**). — A solution of compound **5** (2 g) in absolute pyridine (60 mL) was treated with hexamethyldisilazane (24 mL), warmed to dissolve the suspension, and cooled to 5°; then chlorotrimethylsilane (10 mL) was added from a syringe. The mixture was stirred for 24 h at 60°, cooled, and filtered to remove a white precipitate. The filtrate was evaporated, and the residue was subjected to a few additions and evaporations of dry toluene, taken up in hexane, and the suspension filtered to remove a trace of precipitate. The filtrate was evaporated to dryness, to afford amorphous **6** (3.64 g) in 95% yield; $[\alpha]_D$ −4.5° (*c* 1, chloroform); the i.r. spectrum showed the absence of hydroxyl group.

*Benzyl 2-acetamido-6-*O*-acetyl-3-*O*-[6-*O*-acetyl-2,3,4-tri-*O*-(trimethylsilyl)-β-*D*-galactopyranosyl]-2-deoxy-4-*O*-(trimethylsilyl)-β-*D*-glucopyranoside* (**7**). — A solution of compound **6** (4.345 g, 5 mmol) in absolute pyridine (10 mL) and acetic anhydride (7.5 mL) was stirred at room temperature in the presence of glacial acetic acid (1.2 g, 20 mmol), and the reaction was monitored by t.l.c. in 4:1 (v/v) ether–hexane. After 2 days, the solution was evaporated under diminished pressure. A solution of the solid residue in chloroform(200 mL) was washed with water, dried (anhydrous magnesium sulfate), and evaporated. The solid mass was purified by chromatography on a column of silica gel, with elution with 4:1 (v/v) ether–hexane, to afford amorphous **7** (3.325 g, 82%), $[\alpha]_D$ −2.1° (*c* 1.1, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 0.1–0.16 (cluster of singlets, 36 H, 4 $SiMe_3$), 1.93 (s, 3 H, NAc), 2.08, 2.12 (2 s, 2 × 3 H, 2 Ac), and 7.36 (m, 5 H, aromatic).

Anal. Calc. for $C_{37}H_{67}NO_{13}Si_4$: C, 52.51; H, 7.98; N, 1.66. Found: C, 52.75; H, 8.22; N, 1.47.

*Benzyl 2-acetamido-6-*O*-acetyl-3-*O*-(6-*O*-acetyl-β-*D*-galactopyranosyl)-2-deoxy-*

β-D-glucopyranoside (**8**). — A mixture of compound **7** (4.5 g, 5 mmol), methanol (25 mL), and 30% acetic acid (30 mL) was stirred for 6 h at room temperature, and then poured into cold water, with stirring. The solid residue was filtered off, washed with water, and recrystallized from methanol–ether, to give **8** in 78% yield (2.31 g), m.p. 241–242°, $[\alpha]_D$ −25.2° (*c* 1, Me_2SO); ^{1}H-n.m.r. (Me_2SO-d_6): δ 1.92 (s, 3 H, NAc), 2.02, 2.08 (s each, 2 × 3 H, Ac), 7.37 (m, 5 H, aromatic), and 7.82 (d, 1 H, $J_{NH,2}$ 8 Hz, NH).

Anal. Calc. for $C_{25}H_{35}NO_{13}$: C, 53.85; H, 6.33; N, 2.51. Found: C, 53.82; H, 6.58; N, 2.52.

Benzyl 2-acetamido-6-O-acetyl-3-O-(6-O-acetyl-3,4-O-isopropylidene-β-D-galactopyranosyl)-2-deoxy-β-D-glucopyranoside (**9**). — A solution of crystalline **8** (2 g) and 2,2-dimethoxypropane (4 mL) in dry *N*,*N*-dimethylformamide (30 mL) containing *p*-toluenesulfonic acid (30 mg) was stirred for 1 h at 60°, made neutral with triethylamine, and evaporated. A solution of the solid residue in chloroform (100 mL) was washed with water (2 × 25 mL), dried (anhydrous sodium sulfate), and evaporated to dryness. The solid mass was purified by chromatography on a column of silica gel, with elution with 15:1 (v/v) chloroform–ethanol, to give **9** in 69% yield (1.48 g), m.p. 92–94° (ethyl acetate–hexane), $[\alpha]_D$ −15.6° (*c* 0.5, Me_2SO); t.l.c. (15:1 chloroform–ethanol): R_F 0.38; ^{1}H-n.m.r. (Me_2SO-d_6): δ 1.27, 1.42 (2 s, 2 × 3 H, isopropylidene methyls), 1.81 (s, 3 H, NAc), 2.02, 2.06 (2 s, 2 × 3 H, Ac), 7.34 (m, 5 H, Ph), and 7.83 (d, 1 H, $J_{NH,2}$ 7.5 Hz, NH).

Anal. Calc. for $C_{28}H_{39}NO_{13}$: C, 56.27; H, 6.58; N, 2.34. Found: C, 56.00; H, 6.78; N, 2.52.

Benzyl 2-acetamido-6-O-acetyl-3-O-[6-O-acetyl-3,4-O-isopropylidene-2-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-β-D-galactopyranosyl]-2-deoxy-4-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-β-D-glucopyranoside (**10**). — A suspension of acetal **9** (1.194 g, 2 mmol) in dry dichloromethane (60 mL) was stirred for 3 h at room temperature in the presence of tetraethylammonium bromide (1.675 g, 8 mmol) and molecular sieves 4 A (15 g). A solution of freshly prepared 2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl bromide (3.977 g, 8 mmol) in dichloromethane (75 mL) and dry $HCONMe_2$ (90 mL) was added, and the mixture was stirred under dry nitrogen for 5 days at room temperature. Methanol (25 mL) was added, the mixture was stirred for 4 h, the solids were removed by filtration, and the filtrate was evaporated. A solution of the solid residue in dichloromethane (200 mL) was successively washed with sodium hydrogencarbonate solution and water, dried (anhydrous sodium sulfate), and evaporated. The residue was purified by chromatography on a column of silica gel, eluting first with chloroform, and then with 15:1 chloroform–acetone, to give **10** in 78% yield (2.23 g), amorphous, $[\alpha]_D$ −60.4° (*c* 0.5, chloroform); t.l.c. (15:1 chloroform–acetone) R_F 0.32; ^{1}H-n.m.r. ($CDCl_3$): δ 1.06, 1.13 (d each 2 × 3 H, $J_{5'',6''} = J_{5''',6'''} = 6.5$ Hz, 2 C-Me), 1.32, 1.44 (s each, 2 × 3 H, isopropylidene methyls), 1.75 (s, 3 H, NAc), 2.04, 2.06 (s each, 2 × 3 H, Ac), 5.54 (d, 1 H, $J_{1'',2''}$ 3 Hz, H-1''), 6.38 (d, 1 H, $J_{NH,2}$ 7.5 Hz, NH), and 7.2–7.5 (m, 35 H, aromatic); ^{13}C-n.m.r. ($CDCl_3$): δ 16.5, 16.8 (C-6'',C-6'''), 20.9, 21.0 ($OCOCH_3$), 22.8 ($NHCOCH_3$), 26.4, 27.8

(>C(CH_3)$_2$), 57.3 (C-2), 94.9 (C-1‴), 96.9 (C-1″), 97.9 (C-1), 100.3 (C-1′), and 110.2 (>CMe_2).

Anal. Calc. for $C_{82}H_{95}NO_{21}$: C, 68.84; H, 6.69; N, 0.98. Found: C, 68.97; H, 6.83; N, 1.01.

Benzyl 2-acetamido-6-O-acetyl-3-O-[6-O-acetyl-2-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-β-D-galactopyranosyl]-2-deoxy-4-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-β-D-glucopyranoside (**11**). — The isopropylidene group of compound **10** was removed, as described for **4**, to give compound **11**. After purification by column chromatography, amorphous material was obtained in a yield of 82%; $[\alpha]_D$ −52.5° (*c* 1, chloroform); t.l.c. (5:1 chloroform–acetone) R_F 0.71; ^{1}H-n.m.r. ($CDCl_3$): δ 1.14, 1.21 (2 d, 2 × 3 H, $J_{5'',6''} = J_{5''',6'''}$ = 6.5 Hz, 2 C-Me), 1.79 (s, 3 H, NAc), 2.04, 2.07 (s each, 2 × 3 H, Ac), 5.27 (d, 1 H, *J* 3.5 Hz, H-1″), 6.34 (d, 1 H, $J_{NH,2}$ 7.5 Hz, NH), and 7.2–7.5 (m, 35 H, aromatic).

Anal. Calc. for $C_{79}H_{91}NO_{21}$: C, 68.23; H, 6.60; N, 1.01. Found: C, 68.50; H, 6.81; N, 1.21.

Benzyl 2-acetamido-2-deoxy-4-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-3-O-[2-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-β-D-galactopyranosyl]-β-D-glucopyranoside (**12**). — A solution of compound **11** (500 mg) in absolute methanol (20 mL) containing M sodium methoxide solution (0.5 mL) was kept at room temperature until the reaction was complete, as judged by t.l.c. The solution was then de-ionized, and evaporated to dryness, to afford amorphous **12** in 92% yield (430 mg), $[\alpha]_D$ −110.2° (*c* 0.5, Me_2SO); ^{1}H-n.m.r. (Me_2SO-d_6): δ 1.06–1.21 (6 H, 2 C-Me), 1.79 (s, 3 H, NAc), 5.11 (d, 1 H, $J_{1''',2'''}$ 3 Hz, H-1‴), 5.30 (d, 1 H, $J_{1'',2''}$ 3.5 Hz, H-1″), 7.2–7.5 (m, 35 H, aromatic), and 8.02 (d, 1 H, $J_{NH,2}$ 7.5 Hz, NH).

Anal. Calc. for $C_{75}H_{87}NO_{19}$: C, 68.95; H, 6.71; N, 1.07. Found: C, 68.77; H, 6.66; N, 1.08.

O-α-L-*Fucopyranosyl*-(1→2)-O-β-D-*galactopyranosyl*-(1→3)-O-[α-L-*fucopyrano-*

TABLE III

^{13}C-N.M.R. CHEMICAL SHIFTS[a] (25.2 MHz, D_2O)

Compound[b]	*C-1*	*C-1′*	*C-1″*	*C-1‴*	*C-2*	*C-6″*	*C-6‴*	*COCH*$_3$	*C=O*
13α	91.7	101.5	100.5	98.8	55.6	16.5	16.5	23.1	174.4
13β	96.6				57.7			23.4	174.6

[a]In p.p.m. downfield from Me_4Si (external).

[b]For values for β-D-Gal-(1→3)-GlcNAc, see Ref. 22;

4
↑
1
α-L-Fuc

for α-L-Fuc-(1→2)-β-D-Gal-(1→3)-GlcNAc, see Ref. 23.

syl-(1→4)]-*2-acetamido-2-deoxy*-D-*glucopyranose* (**13**). — A solution of **12** (400 mg) in glacial acetic acid (40 mL) was hydrogenolyzed with hydrogen in the presence of 10% Pd–C for 3 days. The suspension was filtered, and the filtrate evaporated to dryness. The residue was purified by chromatography on a column of coconut charcoal, eluting first with water, then with 19:1 (v/v) water–ethanol, and finally, with 4:1 (v/v) water–ethanol, to give the title saccharide in 87% yield (180 mg), amorphous, $[\alpha]_D$ −75.7° (*c* 1, water), [lit.[10] $[\alpha]_D$ −62° (*c* 1, water)]. The purity of compound **13** was established by paper chromatography (Whatman No. 1) using 3:2:1 (v/v) butyl acetate–acetic acid–water, and it showed R_{Fuc} 0.38 (silver nitrate reagent); ^{1}H-n.m.r. (CD_3OD): δ 1.27 (d, 6 H, $J_{5'',6''} = J_{5''',6'''}$ = 6 Hz, 2 C-Me), 2.02 (s, 3 H, NAc), 4.42 (d, 1 H, $J_{1',2'}$ 8 Hz, H-1′), 5.02 (d, 1 H, $J_{1''',2'''}$ 3 Hz, H-1‴), and 5.08 (d, 1 H, $J_{1'',2''}$ 3.5 Hz, H-1″); for ^{13}C-n.m.r. data, see Table III.

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