Carbohydrate Research, 117 (1983) 101–111
Elsevier Science Publishers B.V., Amsterdam – Printed in The Netherlands

A FACILE SYNTHESIS OF 2-ACETAMIDO-2-DEOXY-4-*O*-α-L-FUCOPYRANOSYL-3-*O*-β-D-GALACTOPYRANOSYL-D-GLUCOPYRANOSE, THE LEWIS a BLOOD-GROUP ANTIGENIC DETERMINANT, AND RELATED COMPOUNDS*

SURJIT S. RANA AND KHUSHI L. MATTA**

Department of Gynecologic Oncology, Roswell Park Memorial Institute, New York State Department of Health, Buffalo, New York 14263 (U.S.A.)

(Received December 17th, 1982; accepted for publication, January 7th, 1983)

ABSTRACT

A simple strategy was developed for the procurement of benzyl 2-acetamido-6-*O*-benzyl-2-deoxy-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-β-D-glucopyranoside (**8**). Reductive opening of the acetal ring of benzyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-β-D-gluco-pyranoside gave, exclusively, the desired, key intermediate **8**. Fucosylation of **8** with 2,3,4,-tri-*O*-benzyl-α-L-fucopyranosyl bromide, under catalysis by bromide ion, afforded the trisaccharide derivative which, on *O*-deacetylation, followed by hydrogenolysis, produced the title trisaccharide. Starting from methyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galacto-pyranosyl)-α-D-glucopyranoside, the synthesis of methyl 2-acetamido-2-deoxy-4-*O*-α-L-fucopyranosyl-3-*O*-β-D-galactopyranosyl-α-D-glucopyranoside was accomplished by a similar reaction-sequence. The synthesis of 2-acetamido-2-deoxy-4-*O*-α-L-fucopyranosyl-D-glucopyranose is also described. The structures of the final saccharides, and of various other intermediates, were established by ^{1}H- and ^{13}C-n.m.r. spectroscopy.

INTRODUCTION

During the past decade, there has been an extraordinary burst of activity in studies related to the chemical synthesis of oligosaccharides[2]. There is no doubt that the appropriately protected glycosylating reagents and new catalysts now available have proved to be excellent tools for successful synthesis of such compounds. However, another key factor that plays an important role in the achievement of these synthetic ventures is the availability of different, new protecting groups introduced into the field of carbohydrate chemistry[3]. Moreover, efficient

*Synthetic Studies in Carbohydrates, Part XXXIII. For Part XXXII, see ref. 1.
**To whom correspondence should be addressed.

0008-6215/83/$ 03.00

and attractive methodologies for the removal of such protecting groups have been developed[3]. For example, partial alkylation of polyhydroxy compounds through the (trialkylstannyl)ation procedure is very efficient[4]. Use of organotin derivatives of a pair of vicinal, axial and equatorial, hydroxyl groups for selective acylation and alkylation has proved successful[5]. In another approach, monoalkylation of a diol by the phase-transfer-catalysis method[6] has been found to be an excellent method. Interestingly, the trityl group, which has frequently been used for selective protection of the primary hydroxyl group of polyhydroxy compounds, can now also be successfully employed for protection of certain secondary hydroxyl groups[7]. Thus, different methods have been developed for the preparation of appropriately protected sugars having free hydroxyl groups which can be further employed for glycosylation.

Recently, Garegg and co-workers[8] reported a novel method of reductive ring-opening of carbohydrate benzylidene acetals with sodium cyanoborohydride in HCl–ether. Thus, under these conditions, the 4,6-benzylidene acetal of a given sugar affords the 6-*O*-benzyl derivative exclusively. We have made successful use of these reaction conditions to procure suitable aglycon hydroxides needed for the synthesis of oligosaccharides[1,9], and applied[1] this reaction in the synthesis of 2-acetamido-2-deoxy-3,4-di-*O*-β-D-galactopyranosyl-D-galactopyranose.

We have now extended the use of this key reaction for the synthesis of 2-acetamido-2-deoxy-4-*O*-α-L-fucopyranosyl-3-*O*-β-D-galactopyranosyl-D-glucopyranose[10,11] (**16**) and methyl 2-acetamido-2-deoxy-4-*O*-α-L-fucopyranosyl-3-*O*-β-D-galactopyranosyl-α-D-glucopyranoside (**17**). The disaccharide **5** and the trisaccharides **16** and **17** are needed in our laboratory for studies of L-fucosidase[12] and L-fucosyltransferase[13].

RESULTS AND DISCUSSION

Treatment of benzyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside[14] (**1**) in anhydrous oxolane with sodium cyanoborohydride in the presence of HCl–ether[8] gave, exclusively, benzyl 2-acetamido-6-*O*-benzyl-2-deoxy-β-D-glucopyranoside (**2**) in 72% yield. The ^{13}C-n.m.r. spectrum of **2** showed the complete absence of a C-6 signal in the region of 60–63 p.p.m., confirming thereby that reductive cleavage of the 4,6-benzylidene acetal **1** yields only the 6-*O*-benzyl derivative (**2**). Exposure of benzyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-β-D-glucopyranoside[15] (**6**) to sodium cyanoborohydride under identical conditions afforded benzyl 2-acetamido-6-*O*-benzyl-2-deoxy-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-β-D-glucopyranoside (**8**) in 55.4% yield. Its ^{1}H-n.m.r. spectrum showed the presence of four *O*-acetyl and two benzyl groups. To prove the structure of **8** unambiguously, a portion of **8** was *O*-deacetylated[16] to give **9**. The ^{13}C-n.m.r. data for **9**, along with those for **2**, are reported in Table I. Data cited in Table I, clearly supported the structure assigned to compound **9**. Similarly, reductive cleavage[8] of methyl 2-acetamido-4,6-*O*-

benzylidene-2-deoxy-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-α-D-glucopyranoside[17] (**7**) gave only the 6-*O*-benzyl derivative **10**, which, on *O*-deacetylation[16], afforded methyl 2-acetamido-6-*O*-benzyl-2-deoxy-3-*O*-β-D-galactopyranosyl-α-D-glucopyranoside (**11**). The structure of the latter compound was also supported by its ^{13}C-n.m.r. spectrum (see Table I).

TABLE I

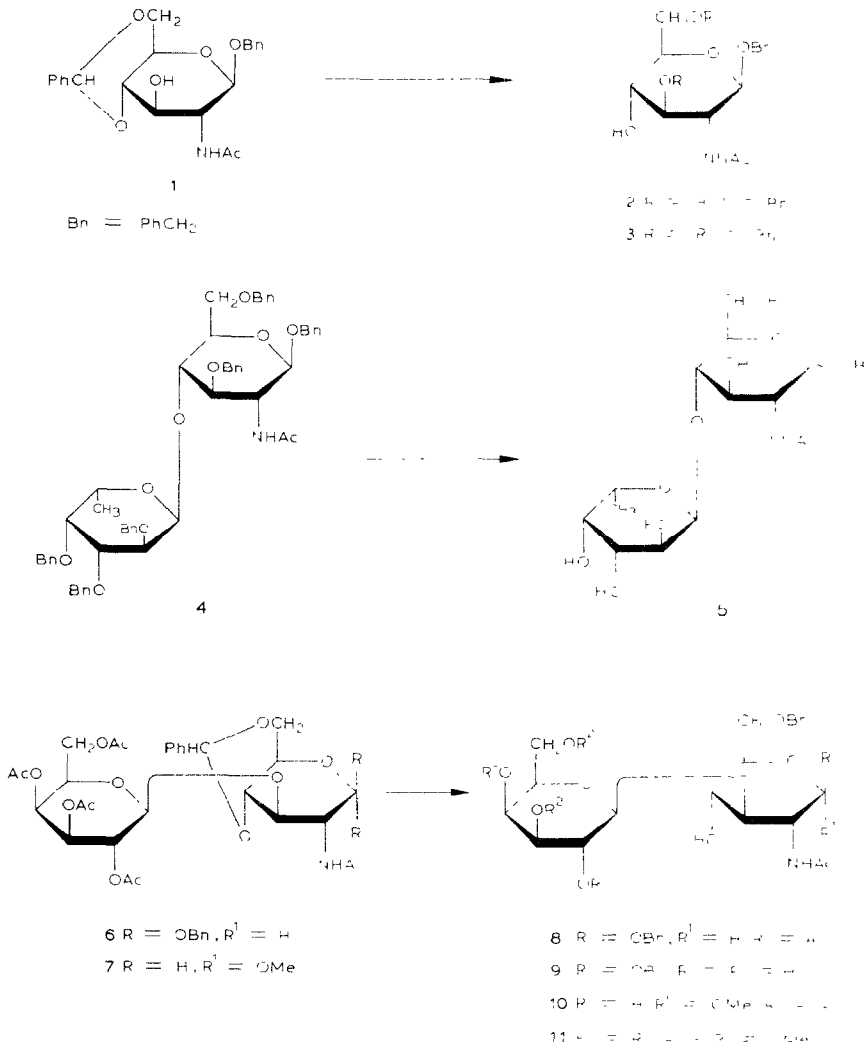
25.2-MHz, ^{13}C-N M.R. CHEMICAL SHIFTS[a] IN Me_2SO-d_6

Atom	*Compound*			
	β-GlcNAc-1→OCH$_2$Ph	**2**	**9**	**11**
C-1	100.53	100.59	100.10	97.74
C-2	55.32	55.33	54.12	52.18
C-3	74.05	74.02	84.08	79.98
C-4	70.57	70.61	68.80	68.84
C-5	76.90	75.62	75.04	70.34
C-6	61.01	72.24	72.27	72.27
$NCOCH_3$	23.01	22.99	22.99	22.67
C=O	168.82	168.88	169.70	169.75
OCH_3				54.36
C-1′			103.73	103.05
C-2′			70.46	70.98
C-3′			72.91	73.17
C-4′			68.17	68.27
C-5′			75.69	75.80
C-6′			60.54	60.57

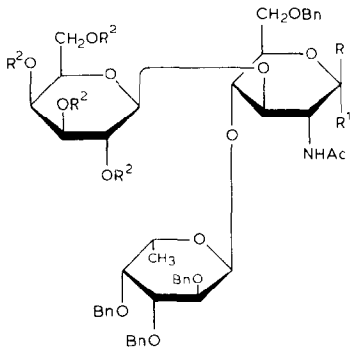
[a]In p.p.m. downfield from internal Me_4Si.

L-Fucosylation[18] of **8** with 2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl bromide under bromide-ion-catalyzed reaction-conditions gave crystalline **12** in excellent yield. The ^{1}H-n.m.r. spectrum of the trisaccharide derivative **12** exhibited a clear doublet at δ 5.4 (d, 1 H, $J_{1'',2''}$ 3 Hz, H-1), supporting the presence of an α-linked L-fucosyl group in **12**. Subjected to L-fucosylation[18] under identical conditions, compound **10** produced **13** in 86% yield.

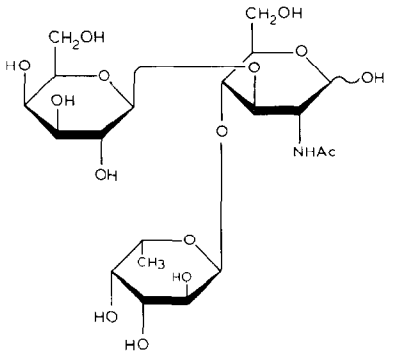
Interestingly, *O*-deacetylation[16] of both of the trisaccharide derivatives, **12** and **13**, proceeded satisfactorily to give **14** and **15**, respectively. The ^{1}H-n.m.r. spectrum clearly showed the complete absence of *O*-acetyl groups in these two derivatives, which were readily isolated in pure form. It should be mentioned that, in a previous investigation[13], on the synthesis of phenyl 2-acetamido-2-deoxy-4-*O*-α-L-fucopyranosyl-3-*O*-β-D-galactopyranosyl-β-D-glucopyranoside, phenyl 2-acetamido-6-*O*-acetyl-2-deoxy-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-β-D-glucopyranoside reacted with 2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl bromide under similar conditions to give phenyl 2-acetamido-6-*O*-acetyl-2-deoxy-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-4-*O*-(2,3,4-tri*O*-benzyl-α-L-fucopy-



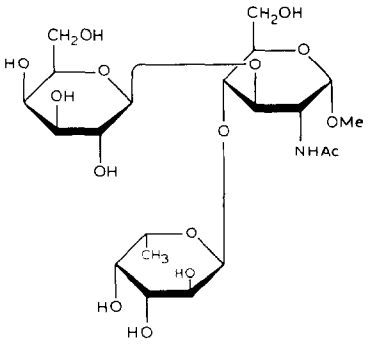
ranosyl)-β-D-glucopyranoside. However, t.l.c. of the product obtained by *O*-deacetylation of the latter product revealed the presence of two components, and the ^{1}H-n.m.r. spectrum showed the presence of an *O*-acetyl group. As also reported by Lemieux and co-workers[19], *O*-deacetylation of 8-ethoxycarbonyloctyl 2-acetamido-6-*O*-acetyl-2-deoxy-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-4-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-β-D-glucopyranoside with sodium methoxide in methanol gave a product that still possessed an *O*-acetyl group. In the investigation by Lemieux and co-workers[19] as well as in our own previous studies[13], it was tentatively assumed that the acetyl group on O-6 of the 2-acetamido-2-deoxy-D-glucoside residue remains intact on saponification. However, in the present studies, we found no difficulty in the saponification of derivatives **12**



12 R = OBn, R^1 = H, R^2 = Ac
13 R = H, R^1 = OMe, R^2 = Ac
14 R = OBn, R^1 = R^2 = H
15 R = R^2 = H, R^1 = OMe



16



17

and **13** which possess a benzyl group at O-6 of the 2-acetamido-2-deoxy-D-glucoside residue. The structures of the deacetylated products **14** and **15** were also supported by their ^{13}C-n.m.r. spectra. Catalytic hydrogenolysis of **14** and **15** in 95% ethanol, in the presence of 10% Pd–C, respectively, gave the title trisaccharide **16** and methyl 2-acetamido-2-deoxy-4-*O*-α-L-fucopyranosyl-3-*O*-β-D-galactopyranosyl-α-D-glucopyranoside (**17**). The structures of **16** and **17** were confirmed by ^{1}H- and ^{13}C-n.m.r. spectroscopy.

For the synthesis of 2-acetamido-2-deoxy-4-*O*-α-L-fucopyranosyl-D-glucopyranose[20] (**5**), benzyl 2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside[9] (**3**) was treated with 2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl bromide under bromide-ion-catalyzed reaction-conditions[18]. Compound **4** was isolated from the reaction mixture as an amorphous material after chromatography in a column of silica gel. Hydrogenolysis of **4** in 95% ethanol in the presence of 10% Pd–C provided the

known disaccharide **5**; its structure was confirmed by ^{1}H- and ^{13}C-n.m.r. spectroscopy (see Table II)

TABLE II

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

Atom	*Compound*		
	5α	**5β**	**17**
C-1	91.67	95.81	99.24
C-2	55.45	58.24	54.69
C-3	70.46	73.67	75.80
C-4	78.63	78.38	75.47
C-5	71.84	76.35	72.51
C-6	60.98	60.98	60.76
C=O	175.36	175.36	175.16
$NCOCH_3$	23.01	23.27	23.22
OCH_3			56.25
C-1′			103.98
C-2′			71.54
C-3′			73.47
C-4′			68.91
C-5′			73.57
C-6′			62.71
C-1″	100.56		99.24
C-2″	69.14		69.45
C-3″	70.46		70.25
C-4″	72.93		73.07
C-5″	68.03		67.92
C-6″	16.34		16.57

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

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% sulfuric acid in ethanol and heating. Descending p.c. was performed on Whatman No. 3MM paper, and spots were detected with periodate, followed by the silver nitrate reagent[21]. Elemental analyses were performed by Robertson Laboratory, Florham Park, New Jersey, U.S.A. N.m.r. spectra were recorded with Varian EM-390 and XL-100 instruments; ^{1}H-n.m.r. spectra (100 MHz) and ^{13}C-n.m.r. spectra (25.2 MHz) were determined by use of the Fourier-transform (F.t.) mode; the positions of the peaks are expressed in δ from the signal for tetramethylsilane

Benzyl 2-acetamido-6-O-benzyl-2-deoxy-β-D-glucopyranoside (**2**). — A solution of **1** (3.99 g, 10 mmol) and sodium cyanoborohydride (5.656 g, 90 mmol) in dry oxolane (150 mL) containing 3A molecular sieves (15 g) was cooled to 0°. Hydrogen chloride in diethyl ether was added until the solution was acidic (pH paper, gas evolution). After the mixture had been stirred for 40 min at 0°, t.l.c. in 3:2 (v/v) chloroform–acetone indicated complete reaction; the mixture was poured into ice–water, and extracted with dichloromethane (4 × 100 mL), and the extracts were combined, washed successively with water, saturated sodium hydrogencarbonate solution, and water, dried (sodium sulfate), and evaporated *in vacuo*, to give a solid residue which was purified by chromatography on a column of silica gel, eluting with 9:1 (v/v) chloroform–methanol, to give **2** in 72% yield (2.9 g); m.p. 176–178° (from hot ethyl acetate), $[\alpha]_D$ −41.8° (*c* 1.6, Me_2SO); t.l.c. (9:1 chloroform–methanol): R_F 0.46; ^{1}H-n.m.r. data (Me_2SO-d_6): δ 1.82 (s, 3 H, NAc), 7.3–7.45 (m, 10 H, aromatic), and 7.73 (d, 1 H, $J_{NH,2}$ 9 Hz, NH).

Anal. Calc. for $C_{22}H_{27}NO_6$: C, 65.82; H, 6.78; N, 3.49. Found: C, 65.53; H, 6.97; N, 3.24.

Benzyl 2-acetamido-3,6-di-O-benzyl-2-deoxy-4-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-β-D-glucopyranoside (**4**). — Compound **3** (0.653 g, 1.33 mmol) was dissolved in a mixture of dichloromethane (15 mL), *N*,*N*-dimethylformamide (3 mL), tetraethylammonium bromide (0.55 g, 2.65 mmol), and diisopropylethylamine (0.5 mL). A solution of freshly prepared 2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl bromide (1.32 g, 2.65 mmol) in dichloromethane (5 mL) and dry $HCONMe_2$ (1 mL) was added, and the mixture was stirred for 3 days at room temperature. Dichloromethane (200 mL) was added, and the solution was washed with water (3 × 50 mL), dried, and evaporated. The residue was purified by chromatography on a column of silica gel, eluting first with 9:1 (v/v) hexane–ethyl acetate, then with 5:1 (v/v) hexane–ethyl acetate (to remove the 2,3,4-tri-*O*-benzyl-L-fucose), and finally with 2:1 (v/v) hexane–ethyl acetate, giving amorphous **4** in 79% yield (950 mg); $[\alpha]_D$ −83.4° (*c* 2, chloroform); t.l.c. (3:2 hexane–ethyl acetate): R_F 0.35; ^{1}H-n.m.r. data ($CDCl_3$): δ 0.98 (d, 3 H, *J* 6 Hz, CMe), 1.6 (s, 3 H, NAc), 5.27 (d, 1 H, $J_{1',2'}$ 3.5 Hz, H-1′), 6.50 (d, 1 H, $J_{NH,2}$ 9 Hz, NH), and 7.20–7.50 (m, 30 H, aromatic); ^{13}C-n.m.r. data ($CDCl_3$): δ 16.54 (C-6′), 22.90 (NAc), 51.12 (C-2), 66.92 (C-5′), 77.41 (C-4), 79.35 (C-3), 94.27 (C-1′), 99.03 (C-1), and 169.67 (C=O).

Anal. Calc. for $C_{56}H_{61}NO_{10}$: C, 74.07; H, 6.77; N, 1.54. Found: C, 73.99; H, 6.96; N, 1.39.

2-Acetamido-2-deoxy-4-O-α-L-fucopyranosyl-D-glucopyranose (**5**). — A solution of **4** (500 mg) in 95% ethanol (50 mL) was hydrogenolyzed in the presence of 10% Pd–C (500 mg) for 2 days, the suspension filtered, and the filtrate evaporated to dryness. The residue was purified by chromatography on a column of silica gel, with elution with 65:35:8 (v/v) chloroform–methanol–water, to give amorphous **5** (175 mg, 87%); $[\alpha]_D$ −93.8° (*c* 1.3, water) {lit.[20] $[\alpha]_D$ −99° [*c* 0.8, 1:1 (v/v)

methanol–H_2O]}; ^{1}H-n.m.r. data (D_2O): δ 1.57 (d, 3 H, J 6.5 Hz, CMe) and 2.46 (s, 3 H, NAc); for ^{13}C-n.m.r. data, see Table II.

Benzyl 2-acetamido-6-O-benzyl-2-deoxy-3-O-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-β-D-glucopyranoside (**8**). — Compound **8** was prepared from **6** (1.458 g, 2 mmol) as described for **2**. After purification by chromatography on a column of silica gel, with elution with 6:1 (v/v) chloroform–acetone, crystalline compound **8** was obtained in a yield of 55.4% (810 mg); m.p. 145–146° (acetone–ether–hexane), $[\alpha]_D$ −12.6° (*c* 1, chloroform); t.l.c. (3:2 chloroform–acetone), R_F 0.76; ^{1}H-n.m.r. ($CDCl_3$): δ 1.94, 1.98, 2.02, 2.08, and 2.16 (s each, 15 H, 4 AcO + 1 NAc), 6.08 (d, 1 H, $J_{NH,2}$ 9 Hz, NH), and 7.25–7.45 (m, 10 H, aromatic); ^{13}C-n.m.r. data ($CDCl_3$): δ 20.48, 20.55, 20.72 (AcO), 23.66 (NAc), 57.48 (C-2), 61.47 (C-6'), 83.36 (C-3), 98.41 (C-1), 101.23 (C-1'), and 168.89, 169.88 and 170.43 (C=O).

Anal. Calc. for $C_{36}H_{45}NO_{15}$: C, 59.09; H, 6.20; N, 1.91. Found: C, 58.88; H, 6.14; N, 1.85.

Benzyl 2-acetamido-6-O-benzyl-2-deoxy-3-O-β-D-galactopyranosyl-β-D-glucopyranoside (**9**). — A solution of compound **8** (150 mg) in dry methanol (15 mL) was stirred overnight in the presence of a catalytic amount of the macroreticular Amberlyst A-26 (OH^-) resin. The disaccharide which precipitated out was redissolved by addition of a few drops of water. The resin was removed by filtration, and the filtrate was evaporated, to give amorphous **9** (105 mg) in 91% yield; $[\alpha]_D$ −24.1° (*c* 0.9, Me_2SO); ^{1}H-n.m.r. (Me_2SO-d_6): δ 1.80 (s, 3 H, NAc), 7.3–7.45 (m, 10 H, aromatic), and 7.81 (d, 1 H, $J_{NH,2}$ 9 Hz, NH).

Anal. Calc. for $C_{28}H_{37}NO_{11}$: C, 59.67; H, 6.62; N, 2.49. Found: C, 59.57; H, 6.76; N, 2.40.

Methyl 2-acetamido-6-O-benzyl-2-deoxy-3-O-(2,3,4,6-tetra-O-acetyl)-β-D-galactopyranosyl)-α-D-glucopyranoside (**10**). — Compound **10** was prepared from **7** (3.918 g, 6 mmol) as described for **2**. After being stirred for 6 h at 10–15°, the mixture was processed, and the residue was purified by chromatography on a column of silica gel, eluting with 9:1 (v/v) chloroform–acetone, to give **10** in a yield of 68.7% (2.7 g); m.p. 119–120° (from ethyl acetate–hexane), $[\alpha]_D$ +42.9° (*c* 1.3, chloroform); t.l.c. (4:1 chloroform–acetone): R_F 0.31; ^{1}H-n.m.r. data ($CDCl_3$): δ 1.93, 1.98, 2.0, 2.07 and 2.12 (s each, 15 H, 4 AcO + 1 NAc), 3.35 (s, 3 H, OMe), 4.97 (d, 1 H, $J_{1,2}$ 3 Hz, H-1), 5.12 (d, 1 H, $J_{1',2'}$ 7 Hz, H-1'), 5.33 (d, 1 H, $J_{3',4'}$ 3, $J_{4',5'}$ <1 Hz, H-4'), 5.57 (d, 1 H, $J_{NH,2}$ 9 Hz, NH), and 7.25 (m, 5 H, aromatic); ^{13}C-n.m.r. data ($CDCl_3$): δ 20.57 (OAc), 23.44 (NAc), 51.38 (C-2), 54.96 (OMe), 61.16 (C-6'), 83.08 (C-3), 98.31 (C-1), 101.49 (C-1'), and 169.10, 169.24, 169.90 and 170.19 (C=O).

Anal. Calc. for $C_{30}H_{41}NO_{15}$: C, 54.95; H, 6.30; N, 2.14. Found: C, 54.72, H, 6.41; N, 2.09.

Methyl 2-acetamido-6-O-benzyl-2-deoxy-3-O-β-D-galactopyranosyl-α-D-glucopyranoside (**11**). — *O*-Deacetylation of **10** (150 mg) as described for **9** gave crystalline **11** (90 mg, 80.7%); m.p. 215–217° (from methanol), $[\alpha]_D$ +68.5° (*c* 0.7,

Me_2SO); t.l.c. (5:1 chloroform–methanol): R_F 0.35; ^{1}H-n.m.r. data (Me_2SO-d_6): δ 1.81 (s, 3 H, NAc), 3.30 (s, 3 H, OMe), 7.30 (m, 5 H, aromatic), and 7.60 (d, 1 H, $J_{NH,2}$ 7.5 Hz, NH).

Anal. Calc. for $C_{22}H_{33}NO_{11}$: C, 54.20; H, 6.82; N, 2.87. Found: C, 53.99; H, 7.08; N, 2.70.

*Benzyl-2-acetamido-6-*O*-benzyl-2-deoxy-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-*D*-galactopyranosyl)-4-*O*-(2,3,4-tri-*O*-benzyl-α-*L*-fucopyranosyl)-β-*D*-glucopyranoside* (**12**). — Glycosylation of compound **8** (1.462 g) as described for **4** gave **12** (1.9 g, 82.7%); m.p. 112–114° (ethyl acetate–ether–hexane), $[\alpha]_D$ −74.9° (*c* 1, chloroform); t.l.c. (4:1 chloroform–acetone): R_F 0.69; ^{1}H-n.m.r. data ($CDCl_3$): δ 1.23 (d, 3 H, *J* 6.5 Hz, CMe), 1.68, 1.86, 1.96, 1.98 and 2.0 (s each, 15 H, 4 AcO + 1 NAc), 5.40 (d, 1 H, $J_{1'',2''}$ 3 Hz, H-1''), 6.36 (d, 1 H, $J_{NH,2}$ 9 Hz, NH), and 7.20–7.45 (m, 25 H, aromatic); ^{13}C-n.m.r. data ($CDCl_3$): δ 16.72 (C-6''), 20.52 (AcO), 22.89 (NAc), 51.56 (C-2), 60.48 (C-6'), 76.94 (C-4), 79.96 (C-3), 94.10 (C-1''), 98.17 (C-1), 99.22 (C-1'), and 169.15, 169.45, 169.75 and 169.95 (C=O).

Anal. Calc. for $C_{63}H_{73}NO_{19}$: C, 65.90; H, 6.41; N, 1.22. Found: C, 65.85; H, 6.47; N, 1.21.

*Methyl 2-acetamido-6-*O*-benzyl-2-deoxy-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-*D*-galactopyranosyl)-4-*O*-(2,3,4-tri-*O*-benzyl-α-*L*-fucopyranosyl)-α-*D*-glucopyranoside* (**13**). — Glycosylation of compound **10** (1.31 g, 2 mmol) as described for **4** gave amorphous **13** (1.85 g, 86%); $[\alpha]_D$ +3.2° (*c* 0.8, chloroform); t.l.c. (4:1 chloroform–acetone): R_F 0.53; ^{1}H-n.m.r. data ($CDCl_3$): δ 1.32 (d, 3 H, *J* 6.5 Hz, CMe), 1.81 (s, 3 H, NAc), 1.96, 2.0, 2.04 and 2.10 (4 s, 4 × 3 H, 4 OAc), 3.32 (s, 3 H, OMe), 5.36 (d, 1 H, $J_{1'',2''}$ 3.5 Hz, H-1''), 5.60 (d, 1 H, $J_{NH,2}$ 9.5 Hz, NH), and 7.32 (m, 20 H, aromatic).

Anal. Calc. for $C_{57}H_{69}NO_{19}$: C, 63.85; H, 6.49; N, 1.31. Found: C, 63.62; H, 6.38; N, 1.37.

*Benzyl 2-acetamido-6-*O*-benzyl-2-deoxy-3-*O*-β-*D*-galactopyranosyl-4-*O*-(2,3,4-tri-*O*-benzyl-α-*L*-fucopyranosyl)-β-*D*-glucopyranoside* (**14**). — *O*-Deacetylation of **12** (2.0 g) as described for **9** gave amorphous **14** (1.4 g, 82%); $[\alpha]_D$ −81.6° (*c* 1.6, methanol); t.l.c. (9:1 chloroform–methanol): R_F 0.37; ^{1}H-n.m.r. data (CD_3OD): δ 1.22 (d, 3 H, *J* 6.5 Hz, CMe), 1.94 (s, 3 H, NAc), 4.95 (d, 1 H, $J_{1,2}$ 6.5 Hz, H-1), 5.1 (d, 1 H, $J_{1'',2''}$ 3 Hz, H-1''), and 7.2–7.45 (m, 25 H, aromatic); ^{13}C-n.m.r. data (CD_3OD): δ 17.06 (C-6''), 23.13 (NAc), 57.05 (C-2), 63.23 (C-6'), 79.53 (C-4), 80.89 (C-3), 98.37 (C-1''), 101.44 (C-1), 104.67 (C-1'), and 173.62 (C=O).

Anal. Calc. for $C_{55}H_{65}NO_{15} \cdot H_2O$: C, 66.18; H, 6.77; N, 1.40. Found: C, 66.43; H, 6.76; N, 1.33.

*Methyl 2-acetamido-6-*O*-benzyl-2-deoxy-3-*O*-β-*D*-galactopyranosyl-4-*O*-(2,3,4-tri-*O*-benzyl-α-*L*-fucopyranosyl)-α-*D*-glucopyranoside* (**15**). — *O*-Deacetylation of **13** (1.2 g) as described for **9** gave crystalline **15** (900 mg, 89%); m.p. 220–222° (from ethyl acetate), $[\alpha]_D$ −35.8° (*c* 1.9, methanol), t.l.c. (9:1 chloroform–methanol): R_F 0.33; ^{1}H-n.m.r. data (Me_2SO-d_6): δ 1.09 (d, 3 H, *J* 6 Hz, CMe),

1.86 (s, 3 H, NAc), 3.30 (s, 3 H, OMe), 4.90 (d, 2 H, J 3 Hz, H-1,1''), 7.3–7.45 (m, 20 H, aromatic), and 8.02 (d, 1 H, $J_{NH,2}$ 9 Hz, NH); ^{13}C-n.m.r. data (Me_2SO-d_6): δ 16.41 (C-6''), 22.61 (NAc), 53.02 (C-2), 54.18 (OMe), 60.33 (C-6'), 65.82 (C-5''), 75.56 (C-5'), 78.27 (C-4), 78.81 (C-3), 96.68 (C-1''), 98.25 (C-1), 102.49 (C-1'), and 169.69 (C=O).

Anal. Calc. for $C_{49}H_{61}NO_{15}$: C, 65.10; H, 6.80; N, 1.55. Found: C, 65.05; H, 6.74; N, 1.48.

*2-Acetamido-2-deoxy-4-*O*-α-*L*-fucopyranosyl-3-*O*-β-*D*-galactopyranosyl-*D*-glucopyranose* (**16**). — A solution of **14** (300 mg) in 95% ethanol (30 mL) was hydrogenolyzed in the presence of 10% Pd–C for 40 h. The suspension was filtered, and the filtrate evaporated to dryness. The residue was purified by paper chromatography (Whatman No. 3MM) using 10:4:3 (v/v) ethyl acetate–pyridine–water, to give amorphous **16** (100 mg, 62%); $[\alpha]_D$ −44.5° (*c* 1, water) {lit.[10] $[\alpha]_D^{25}$ −45.1° (*c* 1, water), lit.[22] $[\alpha]_D$ −44 ±3° (*c* 0.3, water)}; its ^{1}H- and ^{13}C-n.m.r. data were comparable to those reported by Lemieux and Driguez[10].

*Methyl 2-acetamido-2-deoxy-4-*O*-α-*L*-fucopyranosyl-3-*O*-β-*D*-galactopyranosyl-α-*D*-glucopyranoside* (**17**). — Compound **15** (200 mg) was hydrogenolyzed as described for **5**, to give amorphous **17** (95 mg, 79%); $[\alpha]_D$ −17.4° (*c* 0.8, water); t.l.c. (11:9:2 chloroform–methanol–water): R_F 0.44; ^{1}H-n.m.r. data (D_2O): δ 1.64 (d, 3 H, J 6.5 Hz, CMe), 2.50 (s, 3 H, NAc), and 3.86 (s, 3 H, OMe); for ^{13}C-n.m.r. data, see Table II.

Anal. Calc. for $C_{21}H_{37}NO_{15} \cdot 2\ H_2O$: C, 43.52; H, 7.13; N, 2.42. Found: C, 43.64; H, 6.89; N, 2.60.

ACKNOWLEDGMENTS

We thank C. F. Piskorz for his excellent technical assistance, and Mrs. Onda Simmons for recording the n.m.r. spectra. We also thank Miss Maria Fox for kindly typing the manuscript. The n.m.r. studies were supported by National Cancer Institute Core Grant CA-16056. This investigation was supported by Grant No. CA-24051, awarded by the National Institutes of Health.

REFERENCES

1 S. S. RANA AND K. L. MATTA, *Carbohydr. Res.*, 116 (1983) 71–81
2 H. PAULSEN, *Angew. Chem., Int. Ed. Engl.*, 21 (1982) 155–173.
3 A. H. HAINES, *Adv. Carbohydr. Chem. Biochem.*, 33 (1976) 11–109; 39 (1981) 13–70
4 T. OGAWA, T. NUKADA, AND M. MATSUI, *Carbohydr. Res.*, 101 (1982) 263–270; T. OGAWA AND M. MATSUI, *ibid.*, 62 (1978) c1–c4.
5 D. WAGNER, J. P. H. VERHEYDEN, AND J. G. MOFFATT, *J. Org. Chem.*, 39 (1974) 24–30; M. A. NASHED AND L. ANDERSON, *Tetrahedron Lett.*, (1976) 3503–3506.
6 P. J. GAREGG, T. IVERSON, AND S. OSCARSON, *Carbohydr. Res.*, 50 (1976) c12–c14.
7 S. S. RANA, C. F. PISKORZ, J. J. BARLOW AND K. L. MATTA, *Carbohydr. Res.*, 83 (1980) 170–174.
8 P. J. GAREGG AND H. HULTBERG, *Carbohydr. Res.*, 93 (1981) c10–c11; P. J. GAREGG, H. HULTBERG, AND S. WALLIN, *ibid.*, 108 (1982) 92–101

9 S. S. RANA, R. VIG, AND K. L MATTA, *J. Carbohydr. Chem.*, in press.
10 R. U. LEMIEUX AND H. DRIGUEZ, *J. Am Chem. Soc.*, 97 (1975) 4063–4069.
11 N. V. BOVIN, S. E. ZURABYAN, AND A. YA KHORLIN, *Bioorg. Khim.*, 6 (1980) 789–790
12 R. A. DICIOCCIO, J. J. BARLOW, AND K. L. MATTA, *J. Biol. Chem.*, 257 (1982) 714–718.
13 D. E. SYKES, S. S. RANA, J. J. BARLOW, AND K. L. MATTA, *Carbohydr. Res.*, 112 (1983) 221–232.
14 M. PARQUET AND P. SINAY, *Carbohydr. Res.*, 18 (1971) 195–202; P. H. GROSS AND R. W. JEANLOZ, *J. Org. Chem.*, 32 (1967) 2759–2763.
15 C. AUGÉ AND A. VEYRIÈRES, *Carbohydr. Res.*, 46 (1976) 293–298.
16 L A. REED, III, P. A. RISBOOD, AND L. GOODMAN, *J. Chem. Soc., Chem. Commun.*, (1981) 760–761.
17 K. L. MATTA AND J. J. BARLOW, *Carbohydr. Res.*, 53 (1977) 47–56.
18 R. U. LEMIEUX, K. B. HENDRICKS, R. V. STICK, AND K. JAMES, *J. Am. Chem. Soc.*, 97 (1975) 4056–4062.
19 R. U. LEMIFUX, D. R. BUNDLE, AND D. A. BAKER, *J. Am. Chem. Soc.*, 97 (1975) 4076–4083.
20 J.-C. JACQUINET AND P. SINAY, *Carbohydr Res* , 42 (1975) 251–258.
21 L. HOUGH AND J. K. N. JONES, *Methods Carbohydr. Chem* , 1 (1962) 21–31.
22 V. P. REGE, T. J. PAINTER, W. M. WATKINS, AND W. T. J. MORGAN, *Nature (London)*, 204 (1964) 740–742