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STUDIES ON THE KOENIGS–KNORR REACTION

PART IV: THE EFFECT OF PARTICIPATING GROUPS ON THE STEREOCHEMISTRY OF DISACCHARIDE FORMATION

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ABSTRACT

Partial benzylation of methyl 2-*O*-benzyl-α-L-fucopyranoside afforded a mixture of methyl 2,3-, and 2,4-di-*O*-benzyl-α-L-fucopyranoside which were separated by means of their monoacetates. Partial benzylation of methyl α-L-fucopyranoside gave the 2,4-, and 3,4-dibenzyl ethers in the ratio of 3:2, and no 2,3-isomer could be detected in the reaction mixture. The structures of the three dibenzyl ethers were established: (a) by analysis of the n.m.r. spectra of their acetates, and (b) by methylation, removal of benzyl groups by hydrogenolysis, and characterization of the methyl ethers of the methyl glycosides. Acid hydrolysis of these compounds gave the monomethyl ethers of L-fucose, two of which were identical with known compounds, whereas the third, 4-*O*-methyl-L-fucose, was a new compound. Selective *p*-nitrobenzoylation of 2,3-, 2,4-, and 3,4-di-*O*-benzyl-L-fucose, followed by acetylation and treatment with hydrogen bromide in dichloromethane, gave the three possible mono-*O*-acetyl-di-*O*-benzyl-α-L-fucopyranosyl bromides, which were condensed with benzyl 2-acetamido-3,4-di-*O*-acetyl-2-deoxy-α-D-glucopyranoside. The disaccharide derived from the 2-*O*-acetyl substituted bromide was enriched in β-L-fucopyranoside, whereas the other two bromides gave mainly the α-L-linked anomer. The α-directing influence of the 3- and 4-*O*-acetyl substituents is not less than the β-directing influence of the 2-*O*-acetyl group in similar bromides; participation of acyl groups and electronic–steric influences are discussed as possible explanations for the steric course of the reaction.

INTRODUCTION

It has been shown that glycosides and disaccharides may be synthesized from glycopyranosyl bromides bearing a nonparticipating group at C-2, and that their anomeric configuration is affected by the nature of the other substituents present in the bromides[1–4]. Thus, although 2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl bromide reacts with a low degree of stereoselectivity[3], replacement of both O-3 and O-4 benzyl ether groups with *p*-nitrobenzoyl esters leads almost to complete stereospecificity in the Koenigs–Knorr reaction and production of an α-L-linked disaccharide in good yield[4]. A hypothesis was developed of the possible participation of the 4-*O*-acyl substituent in

the bromide, thus determining the stereochemistry of the products. It was considered of interest to investigate this hypothesis further and to compare the effects of O-4 and O-3 acyl groups on the production of α-linked disaccharides. The reaction conditions employed have generally led to the isolation of optically pure 1,2-*trans* disaccharides from 2-*O*-acyl substituted bromides[5], but careful analysis of the anomeric configuration of the products before purification was not undertaken. Such an analysis will enable an estimate to be made of the relative β-directing effect of the 2-*O*-acyl substituent and a comparison with the strength of the α-directing effect of a 4-*O*-acyl substituent.

RESULTS AND DISCUSSION

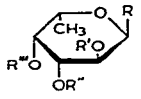
Three different dibenzyl ethers were required as intermediates: 2,3-, 2,4-, and 3,4-di-*O*-benzyl-L-fucose (**18**, **10**, and **17** respectively). The lower reactivity of the *ax*-4-hydroxyl group to acylation conditions in α-D-galactopyranosides[6] and α-L-fucopyranosides[7] is well documented, and partial methylation of methyl α-L-fucopyranoside (**1**) afforded[8] 2,3-di-*O*-methyl-L-fucose (27.5%), the 2,4-ether (11.5%), and only trace amounts of the 3,4-ether (2.5%). Thus, it was predicted that benzylation would proceed analogously and afford a suitable route to the 2,3- and 2,4-dibenzyl ethers, a different approach being required for the 3,4-ether. However, study of a variety of conditions for the benzylation of **1** led to production of the 2,4- and 3,4-ethers while no trace of the 2,3-ether could be detected in the reaction mixture. The conditions selected enabled the partial benzylation of **1** and the isolation, after column chromatography, of methyl 2,4-di-*O*-benzyl-α-L-fucopyranoside (**2**) and methyl 3,4-di-*O*-benzyl-α-L-fucopyranoside (**3**) in yields of 9 and 5.5%, respectively. Some methyl 2,3,4-tri-*O*-benzyl-α-L-fucopyranoside[3] (7.5%) was also obtained, and the low yield of desired dibenzyl ethers was partially compensated for by the considerable recovery of unchanged **1** (58%) which could be recycled. Syrupy **2** and crystalline **3** gave distinct, syrupy monoacetates, each of which possessing one *eq*-acetate group (n.m.r.).

For proof of structure, **2** and **3** were methylated[9] and the syrupy products characterized. Catalytical hydrogenolysis afforded crystalline methyl 3-*O*-methyl-α-L-fucopyranoside (**4**) from **2** in excellent overall yield (79%). Its m.p. and optical rotation were different from those of the crystalline glycoside described by Conchie and Percival[10], to which structure **4** had been assigned; unfortunately, we were unable to obtain a sample of this material for comparison purposes. Gardiner and Percival[8] were unable to crystallize the sample of **4** that they obtained. Our product was not oxidized by periodate, in agreement with the proposed formulation. On acetylation, a crystalline diacetate was obtained, the n.m.r. spectrum of which agrees with the structure of methyl 2,4-di-*O*-acetyl-3-*O*-methyl-α-L-fucopyranoside, showing one *eq* and one *ax* acetate group. Acid hydrolysis of **4** afforded 3-*O*-methyl-L-fucose (**15**), identical with an authentic specimen[8] and clearly distinguished from the other three possible monomethyl ethers of L-fucose. Our product has m.p. 116–118° which

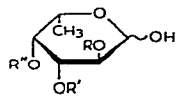
is slightly higher than that reported by Gardiner and Percival[8] (110°). Proof of the structure of **4** confirms that of **2** as methyl 2,4-di-*O*-benzyl-α-L-fucopyranoside.

Methylation of **3**, followed by catalytic hydrogenolysis, gave (in 75% overall yield) methyl 2-*O*-methyl-α-L-fucopyranoside (**5**) which was identical with an authentic specimen prepared by methanolysis of methyl 3,4-*O*-isopropylidene-2-*O*-methyl-α-L-fucopyranoside[11]. The product consumed *ca.* 1 mole of periodate per mole, in agreement with the postulated structure, and afforded a syrupy diacetate containing one *eq* and one *ax* acetate group. On acid hydrolysis, it gave crystalline 2-*O*-methyl-L-fucose (**14**), identical with an authentic specimen[11].

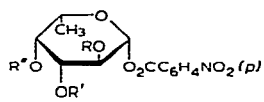
Crystalline methyl 2-*O*-benzyl-α-L-fucopyranoside (**6**) was prepared by methanolysis of methyl 2-*O*-benzyl-3,4-*O*-isopropylidene-α-L-fucopyranoside[4] and gave a syrupy diacetate having one *eq* and one *ax* acetate group. Selective benzylation of **6** in 1:1 *p*-dioxane–toluene afforded methyl 2,3,4-tri-*O*-benzyl-α-L-fucopyranoside (18%), unchanged **6** (15%), and a syrupy dibenzyl ether fraction (55%) which was apparently homogeneous (t.l.c.). However, examination of the n.m.r. spectrum of the acetylation product of this fraction showed the presence of approximately equimolar amounts of *ax* and *eq* acetate groups, and *C*-methyl peaks also consistent with the presence of two different constituents. Attempts to separate these constituents by t.l.c. on silica gel with a variety of solvents were unsuccessful. However, t.l.c. on aluminum oxide showed the presence of two components, which were separated by column



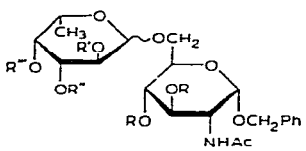
1 R = OMe, R′ = R″ = R‴ = H
2 R = OMe, R′ = R‴ = CH_2Ph, R″ = H
3 R = OMe, R′ = H, R″ = R‴ = CH_2Ph
4 R = OMe, R′ = R‴ = H, R″ = Me
5 R = OMe, R′ = Me, R″ = R‴ = H
6 R = OMe, R′ = CH_2Ph, R″ = R‴ = H
7 R = OMe, R′ = R″ = CH_2Ph, R‴ = Ac
8 R = OMe, R′ = R″ = CH_2Ph, R‴ = H
9 R = OMe, R′ = R″ = H, R‴ = Me
10 R = OH, R″ = H, R′ = R‴ = CH_2Ph
11 R = Br, R′ = R‴ = CH_2Ph, R″ = Ac
12 R = Br, R′ = Ac, R″ = R‴ = CH_2Ph
13 R = Br, R′ = R‴ = CH_2Ph, R″ = Ac



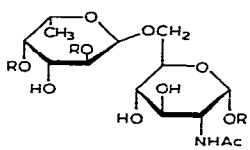
14 R = Me, R′ = R‴ = H
15 R = R‴ = H, R′ = Me
16 R = R′ = H, R‴ = Me
17 R = H, R′ = R‴ = CH_2Ph
18 R = R′ = CH_2Ph, R‴ = H



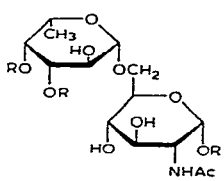
19 R = R‴ = CH_2Ph, R′ = H
20 R = R‴ = CH_2Ph, R′ = Ac
21 R = Ac, R′ = R‴ = CH_2Ph
22 R = R′ = CH_2Ph, R‴ = Ac
23 R = R′ = CH_2Ph, R‴ = H



24 R = R″ = Ac, R′ = R‴ = CH_2Ph
25 R = R′ = Ac, R″ = R‴ = CH_2Ph
26 R = R‴ = H, R′ = R″ = CH_2Ph



27 R = CH_2Ph
28 R = H



29 R = CH_2Ph
30 R = H

chromatography on acid-washed alumina; the faster-migrating acetate was shown to be a new compound (**7**), and the second component proved to be indistinguishable from the acetate of **2**.

Catalytic deacetylation of **7** afforded a new, crystalline dibenzyl ether (**8**), for which a structure of methyl 2,3-di-*O*-benzyl-α-L-fucopyranoside is proposed on the basis of (a) being different from the 2,4- and 3,4-substituted isomers, and (b) having an *ax* acetate group. This structure was confirmed by methylation followed by catalytic hydrogenolysis to give a crystalline methyl glycoside monomethyl ether (**9**), different from **4** and **5**, which consumed *ca.* 1 mole of periodate per mole and was acetylated into a compound having two *eq* acetate groups. It has been reported[12] that the methyl ethers of methyl α-D-glucopyranoside can be distinguished on the basis of their chemical shifts in 6:1 benzene–chloroform-*d*. We could not find any significant differences between the chemical shifts of the methoxy groups at C-2 or C-3 of the derivatives of **1** in this solvent. However, the chemical shift of the *ax* methoxyl group at C-4 was *ca.* 0.2 p.p.m. downfield from that of the equatorial methoxyl groups at C-2 and C-3, and it was possible to identify the peak due to the methoxyl group at C-1. Hydrolysis of **9** gave 4-*O*-methyl-L-fucose (**16**), indistinguishable, on t.l.c. and paper chromatography, from an authentic specimen of 4-*O*-methyl-D-fucose[13,14] and having the same optical rotation but of opposite sign. Although the D-enantiomer has been synthesized[14] and its properties compared with tkose of curacose isolated from natural sources[13], 4-*O*-methyl-L-fucose has not been previously described.

The proportions of dibenzyl ethers produced by partial benzylation of **6** are somewhat surprising; the expected lower reactivity at O-4 should lead to a lower proportion of the 2,4-dibenzyl ether. Even more surprising is the considerable proportion of 2,4-ether obtained by benzylation of methyl α-L-fucopyranoside. The unexpected reactivity at O-4, relative to that at O-2 and O-3, may possibly be explained by (a) examination of the structures of monobenzyl ethers resulting from partial benzylation of **1**, and (b) comparison of the results of selective benzylation of **6** with those of selective benzylation of methyl 3-*O*- and 4-*O*-benzyl-α-L-fucopyranoside, compounds which have not as yet been described.

Acid hydrolysis of the methyl glycosides **2**. **3**, and **8** was accompanied by some undesired degradation and did not go to completion. After purification by column chromatography, 2,4-di-*O*-benzyl-L-fucose (**10**) was obtained in 43% yield, the 3,4-isomer (**17**) in 49% yield, and the 2,3-isomer (**18**) in 68.5% yield; compound **10** crystallized as the α-L anomer.

Partial *p*-nitrobenzoylation of the products, followed by acetylation, afforded crystalline 3-*O*-acetyl-2,4-di-*O*-benzyl-1-*O*-*p*-nitrobenzoyl-β-L-fucopyranose (**20**) and 2-*O*-acetyl-3,4-di-*O*-benzyl-1-*O*-*p*-nitrobenzoyl-β-L-fucopyranose (**21**), and syrupy 4-*O*-acetyl-2,3-di-*O*-benzyl-1-*O*-*p*-nitrobenzoyl-L-fucopyranose (**22**).

Treatment of these compounds with hydrogen bromide in dichloromethane afforded syrupy α-L bromides (**11**, **12**, and **13**, respectively), which were not purified, but condensed directly with benzyl 2-acetamido-3,4-di-*O*-acetyl-2-deoxy-α-D-glucopyranoside (**31**) in the presence of mercuric cyanide. After 48 h, the resulting di-

saccharides were isolated chromatographically in *ca.* 60% yield under conditions which did not separate α-L from β-L anomers.

Two of the products were obtained optically pure after catalytic deacetylation, followed by crystallization: benzyl 2-acetamido-2-deoxy-6-*O*-(2,4-di-*O*-benzyl-α-L-fucopyranosyl)-α-D-glucopyranoside (**27**) and benzyl 2-acetamido-2-deoxy-6-*O*-(3,4-di-*O*-benzyl-β-L-fucopyranosyl)-α-D-glucopyranoside (**29**). Hydrogenolysis of **27** and **29**, followed by reduction to the sugar alcohols and g.l.c. of the per(trimethylsilyl) ethers, ascertained the uniformity of the configuration of the interglycosidic linkage.

Removal of protecting groups from the crude products of the Koenigs–Knorr reaction and g.l.c. of the per(trimethylsilyl) ethers of their derived sugar alcohols gave the proportions of anomers shown in Table I. The results show that each acyl group substituted in the three possible positions of the bromide has some stereochemical effect on the product formed. There is a very marked α-directing influence of the O-4 acetyl substituent, but the effect is less than that previously found for 3,4-di-*O*-acyl substituents[4] (95% α). Although the 2-*O*-acyl group favors the formation of the β anomer, as might be expected from the majority of results of employment of 2-*O*-acyl bromides[5], a stereospecific effect is again not apparent. The stereoselectivity shown by compound **13** (85% α) shows that participation of the O-4 acyl group may occur and be as effective as, if not more so, than that at C-2 (75% β).

TABLE I

PROPORTIONS OF α AND β ANOMERS IN THE SYNTHESIS OF DISACCHARIDES

Bromide	*Anomer* (%) *in disaccharide formed*	
	α	β
11	80	20
12	25	75
13	85	15

However, the relatively high stereoselectivity shown by bromide **11**, in which it is not possible to invoke participation of the acyl group from the β side of the molecule to direct the incoming nucleophile α, shows that the directing effect of the 3-*O*-acetyl group requires a different explanation. Frechet and Schuerch[16] have proposed an electronic influence of the O-6 acyl group, the magnitude of which is dependent on its electron-attracting power. According to their hypothesis, a *p*-nitrobenzoate group at C-6 should favor α-glycoside formation. Although, however, the results with bromide **13** may be in accordance with this explanation, it is difficult to predict from it how an acyl group at O-3, in a very different steric arrangement, would influence the reaction; in fact, the steric effects of participating groups and *p*-orbitals should be similar.

Alternatively, Ishikawa and Fletcher[1] have proposed the intermediate formation of the more reactive β halide by the halide ion formed during the course of the reaction. The proportion of anomers formed will then be affected by the location of

the substituents which hinder the approach of the nucleophile, from the α side of the molecule, to attack the β ion-pair thus formed. Acyl groups substituted at different positions on the ring could, presumably, have different effects on the formation and reactivity of this β ion-pair.

It should also be pointed out that the previous studies discussed[1,16] concerned methanolyses in the presence of a large excess of the nucleophile, whereas the results described in the present paper were obtained from Koenigs–Knorr type reactions in the presence of mercuric salts. Further investigation will be necessary before it is possible to decide whether the steric course of the reaction is, indeed, determined by participation of acyl groups or by electronic or steric effects of the types discussed in references 1 and 16.

EXPERIMENTAL

For general methods, see Ref. 2. In addition, some n.m.r. spectra (90 MHz) were recorded with a Bruker HFX-10 high resolution n.m.r. spectrometer, and the optical rotations were measured on a Bendix–Ericsson (U.K. Ltd.) ETL-NPL Polarimeter, Type 143A.

Methyl 2,4-di-O-benzyl-α-L-fucopyranoside (**2**) *and methyl 3,4-di-O-benzyl-α-L-fucopyranoside* (**3**). — Various conditions were studied in order to ascertain the most satisfactory method for conversion of methyl α-L-fucopyranoside[8] (**1**) into dibenzyl ethers. The procedure described was preferred for large-scale preparation owing to the minimal formation of tribenzyl ether and to the recovery of a large proportion of unchanged **1** which could be recycled to afford a further yield of desired products. A mixture of **1** (10 g), benzyl chloride (80 ml), and powdered potassium hydroxide (30 g) in 1:1 dioxane–toluene (100 ml) was stirred for 6 h at 65–70°. The mixture was cooled and diluted with toluene, and the organic layer was washed several times with water and evaporated; a large amount of water was added to the residue and evaporated. The residual syrup contained three major components having R_F 0.28, 0.35, and 0.70 (t.l.c., 4:1 benzene–ether). It was dissolved in benzene and passed through a column of silica gel. Benzene–ether (9:1) eluted the component having R_F 0.70, identical with methyl 2,3,4-tri-*O*-benzyl-α-L-fucopyranoside[3] (t.l.c., optical rotation, and n.m.r.); yield 1.88 g (7.5%). Benzene–ether (4:1) eluted two homogeneous fractions: The fraction having R_F 0.35 was a syrup (**2**, 1.8 g, 9%), $[\alpha]_D^{23}$ −61.7° (*c* 2.31, chloroform); n.m.r. data: τ 2.68 (10 H, 2 Ph), 6.69 (3 H, OMe), and 8.84 (d, *J* 6.5 Hz, 3 H, CH-Me).

Anal. Calc. for $C_{21}H_{26}O_5$: C, 70.37; H, 7.31. Found: C, 70.58; H, 7.15.

The second fraction gave an amorphous solid (1.1 g, 5.5%). Crystallization from ether afforded needles (**3**), m.p. 92–94°, $[\alpha]^{26}$ −57° (*c* 1.10, chloroform); n.m.r. data: τ 2.62 (10 H, 2 Ph), 6.58 (3 H, OMe), 8.84 (d, *J* 6.5 Hz, 3 H, CH-Me).

Anal. Calc. for $C_{21}H_{26}O_5$: C, 70.37; H, 7.31. Found: C, 70.21; H, 7.23.

A portion of **2** (100 mg) was acetylated with acetic anhydride (1 ml) in pyridine (1 ml) overnight at room temperature. Methanol was added with cooling, the solution

was concentrated *in vacuo*, toluene was added, and the solution concentrated again to a syrup (105 mg, 95%), $[\alpha]_D^{22}$ −96° (*c* 1.15, chloroform); n.m.r. data: τ 2.72 (10 H, 2 Ph), 6.66 (3 H, OMe), 8.05 (3 H, *eq* OAc), 8.87 (doublet, *J* 6.5 Hz, 3 H, CH-Me).

Acetylation of a portion of **3** in a similar way gave a syrup, $[\alpha]_D^{22}$ −85° (*c* 1.06, chloroform); n.m.r. data: τ 2.62 (10 H, 2 Ph), 6.64 (3 H, OMe), 7.93 (3 H, *eq* OAc), 8.81 (doublet, *J* 6.5 Hz, 3 H, CH-Me).

Methyl 3-O-methyl-α-L-fucopyranoside (**4**). — Sodium hydride (0.28 g) was added to a solution of **2** (1.3 g) in dimethyl sulfoxide (25 ml), and the reaction mixture stirred for 2 h under a nitrogen stream[9]. Methyl iodide (20 ml) was added and stirring prolonged for another 30 min. The solution was diluted with water and extracted with chloroform, and the organic layer was washed several times with water, dried with calcium chloride, and evaporated to syrupy methyl 2,4-di-*O*-benzyl-3-*O*-methyl-α-L-fucopyranoside (1.2 g, 90%), $[\alpha]_D^{25}$ −25.5° (*c* 1.05, chloroform); n.m.r. data: τ 2.74 (10 H, 2 Ph), 6.45 (3 H, OMe, ether), 6.67 (3 H, OMe, glycoside), 8.88 (d, *J* 6.5 Hz, 3 H, CH-Me).

This material was dissolved in 90% ethanol (100 ml) and 10% palladium-on-charcoal (200 mg) was added. The suspension was shaken with hydrogen at 3 atm for 24 h at room temperature, the catalyst removed by filtration, and the solution evaporated *in vacuo* to an amorphous solid (0.54 g, 87%), which crystallized from acetone–ether–hexane, m.p. 74–76°. Recrystallization from ethyl acetate gave **4**, m.p. 76–78°, $[\alpha]_D^{26}$ −200° (*c* 1.10, water); n.m.r. data (90 MHz, 6:1 benzene–chloroform-*d*): τ 5.30 (d, *J* 3.5 Hz, H-1), 6.74 (3 H, OMe ether), 6.83 (3 H, OMe, glycoside), 8.70 (d, *J* 6.5 Hz, 3 H, CH-Me); no consumption of periodate was observed during 24 h at 25°; lit.[10]: m.p. 130–132°, $[\alpha]_D^{14}$ −173° (*c* 0.4, water).

Anal. Calc. for $C_8H_{16}O_5$: C, 49.99; H, 8.39. Found: C, 49.73; H, 8.50.

Acetylation of **4** (100 mg) with acetic anhydride in pyridine in the usual way gave a syrup (130 mg, 90%) which crystallized from ether, m.p. 115–117°, $[\alpha]_D^{23}$ −177° (*c* 1.47, chloroform); n.m.r. data: τ 6.62 and 6.64 (6 H, 2 OMe), 7.84 (3 H, *ax* OAc), 7.90 (3 H, *eq* OAc), 8.85 (d, *J* 6.5 Hz, 3 H, CH-Me).

Anal. Calc. for $C_{12}H_{20}O_7$: C, 52.16; H, 7.30. Found: C, 52.34; H, 7.25.

3-O-Methyl-L-fucose (**15**). — Compound **4** (200 mg), dissolved in M hydrochloric acid (20 ml), was kept for 2 h at 95–100°. After being cooled, the solution was neutralized with Amberlite IR 45(OH^-), and, after filtration, evaporated to a syrup (178 mg, 96%) identical with an authentic specimen of 3-*O*-methyl-L-fucose[8] on t.l.c. in 65:15:2 chloroform–methanol–water, and on paper chromatography in 4:1:5 butanol–ethanol–water and 1:5:3:3 benzene–butanol–pyridine–water. Crystallization from ethanol–ether afforded microscopic needles, m.p. 116–118°, $[\alpha]_D^{21}$ −62° (*c* 1.42, ethanol), $[\alpha]_D^{23}$ −93° (*c* 1.40, water); lit.[8]: m.p. 110°, $[\alpha]_D$ −60.8° (*c* 3.8, ethanol), −97° (*c* 4.2, water).

Anal. Calc. for $C_7H_{14}O_5$: C, 47.18; H, 7.92. Found: C, 46.69; H, 8.13.

Methyl 2-O-methyl-α-L-fucopyranoside (**5**). — *A.* A solution of methyl 3,4-*O*-isopropylidene-2-*O*-methyl-α-L-fucopyranoside[11] (0.5 g) in M methanolic hydrogen chloride (50 ml) was kept for 2 h at room temperature. After treatment with excess

silver carbonate, the clear filtrate was evaporated to a syrup (0.36 g, 87%), $[\alpha]_D^{25}$ −196° (*c* 1.20, water); n.m.r. data (90 MHz, 6:1 benzene–chloroform-*d*): τ 5.25 (d, *J* 3.5 Hz, H-1), 6.76 (3 H, OMe, ether), 6.83 (3 H, OMe, glycoside), 8.72 (d, *J* 6.5 Hz, 3 H, CH-Me); lit.[8]: $[\alpha]_D$ −57.7° (*c* 0.52, water).

Anal. Calc. for $C_8H_{16}O_5$: C, 49.99; H, 8.39. Found: C, 50.15; H, 8.20.

B. Methylation of compound 3 (1.0 g) was performed as described for **2** to give a syrupy methyl 3,4-di-*O*-benzyl-2-*O*-methyl-α-L-fucopyranoside (0.90 g, 87%), $[\alpha]_D^{24}$ −21.5° (*c* 1.05, chloroform); n.m.r. data: τ 2.62 (10 H, 2 Ph), 6.42 (3 H, OMe, ether), 6.60 (3 H, OMe, glycoside); 8.86 (d, *J* 6.5 Hz, 3 H, CH-Me). After hydrogenolysis of this material (0.8 g) and processing, a syrup was obtained (0.35 g, 85%) which was identical with **5** (t.l.c., n.m.r., optical rotation). The product consumed 0.99 mole of periodate per mole during 1 h at 25°. No additional periodate was consumed during a further 24 h.

Acetylation of **5** (100 mg) with acetic anhydride–pyridine afforded a syrup (130 mg), $[\alpha]_D^{20}$ −133° (*c* 1.41, chloroform); n.m.r. data: τ 6.52 and 6.56 (6 H, 2 OMe), 7.84 (3 H, *ax* OAc); 7.90 (3 H, *eq* OAc), 8.86 (d, *J* 6.5 Hz, 3 H, CH-Me).

2-O-Methyl-L-fucose (**14**). — Compound **5** (obtained as described under method B) was hydrolyzed with M hydrochloric acid, as described for **15**. The amorphous solid obtained was crystallized from 2-propanol, m.p. 150–152°; $[\alpha]_D^{23}$ −88° (*c* 1.02, water). The product was indistinguishable from an authentic sample of 2-*O*-methyl-L-fucose on t.l.c. in 65:15:2 chloroform–methanol–water and paper chromatography in 4:1:5 butanol–ethanol–water and 1:5:3:3 benzene–butanol–pyridine-water; lit.[8]: m.p. 150–152°; $[\alpha]_D^{18}$ −87° (*c* 1.0, water).

Anal. Calc. for $C_7H_{14}O_5$: C, 47.18; H, 7.92. Found: C, 47.14; H, 7.73.

Methyl 2-O-benzyl-α-L-fucopyranoside (**6**). — A solution of methyl 2-*O*-benzyl-3,4-*O*-isopropylidene-α-L-fucopyranoside[4] (8 g) in M methanolic hydrogen chloride (250 ml) was kept at room temperature for 2 h, and then treated with excess silver carbonate. The clear filtrate was evaporated to a syrup (6.8 g, 95%) which crystallized from chloroform–petroleum ether, m.p. 79–81°; $[\alpha]_D^{25}$ −118° (*c* 1.50, chloroform); n.m.r. data: τ 2.68 (5 H, Ph), 6.68 (3 H, OMe), 8.76 (d, *J* 6.5 Hz, 3 H, CH-Me).

Anal. Calc. for $C_{14}H_{20}O_5$: C, 62.67; H, 7.51. Found: C, 62.82; H, 7.69.

Acetylation of **6** in the usual manner gave a syrup, $[\alpha]_D^{23}$ −77° (*c* 0.91, chloroform); n.m.r. data: τ 2.69 (5 H, Ph), 6.61 (3 H, OMe), 7.87 (3 H, *ax* OAc), 8.04 (3 H, *eq* OAc), 8.89 (d, *J* 6.5 Hz, 3 H, CH-Me).

Compound **6** consumed 1.11 moles of periodate per mole during 1 h at 25°, and continuation of the oxidation for 22 h gave no additional periodate consumption.

Methyl 2,3-di-O-benzyl-α-L-fucopyranoside (**8**). — A mixture of **6** (6.9 g), benzyl chloride (60 ml), toluene (50 ml), *p*-dioxane (50 ml), and powdered potassium hydroxide (14 g) was stirred for 2 h at 65–70°. After the usual processing, a syrup was obtained on evaporation of the organic layer. T.l.c. in 4:1 benzene–ether showed that most of the original **6** had been converted into material having R_F 0.35. A weaker spot also appeared which migrated faster. The mixture was purified by chromatography on silica gel. Benzene–ether (9:1) eluted material (2.1 g, 18%) which was shown to be

methyl 2,3,4-tri-*O*-benzyl-α-L-fucopyranoside (t.l.c., n.m.r., and optical rotation)[3]. Benzene–ether (4:1) eluted a material having R_F 0.35 (5.7 g, 55%) which was shown to be a mixture of **2** and methyl 2,3-di-*O*-benzyl-α-L-fucopyranoside (see next paragraph); n.m.r. data: τ 2.70 (10 H, 2 Ph), 6.66 and 6.70 (3 H, OMe), 8.7, 8.8, and 8.9 (3 H, CH-Me). Unchanged **6** (1.03 g, 15%) was recovered from the aqueous layer.

Acetylation of the material having R_F 0.35 (5 g) with acetic anhydride (50 ml) and pyridine (50 ml) gave a syrup (5.1 g, 92%); n.m.r. data: τ 2.72 (10 H, 2 Ph), 6.66 (3 H, OMe), 7.88 (1.5 H, *ax* OAc), 8.04 (1.5 H, *eq* OAc), 8.86 and 8.89 (2 d, *J* 6.5 Hz, 3 H, CH-Me). T.l.c. on aluminum oxide (DC-Karten Al F) in 100:1 benzene–ether showed the presence of two components which were separated by column chromatography on acid-washed alumina (Merck). Benzene–ether (19:1) eluted methyl 4-*O*-acetyl-2,3-di-*O*-benzyl-α-L-fucopyranoside (**7**, 2.5 g, 49.1%) which could not be crystallized, $[\alpha]_D^{24}$ −46° (*c* 1.06, chloroform); n.m.r. data: τ 2.71 (10 H, 2 Ph), 6.64 (3 H, OMe), 7.87 (3 H, *ax* OAc), 8.88 (d, *J* 6.5 Hz, 3 H, CH-Me). Benzene–ether (9:1) eluted a homogeneous fraction (2.4 g, 47.2%) which was indistinguishable (t.l.c., n.m.r., and optical rotation) from the acetylation product of **2**, methyl 3-*O*-acetyl-2,4-di-*O*-benzyl-α-L-fucopyranoside.

Compound **7** (2 g) was catalytically deacetylated with methanolic sodium methoxide. The solution was neutralized with a few drops of acetic acid and evaporated *in vacuo*. The residue was dissolved in chloroform, and the chloroform solution was washed several times with water, dried with calcium chloride, and evaporated *in vacuo* to a solid (1.74 g, 97%) which crystallized from ether–petroleum ether, m.p. 78–80°, $[\alpha]_D^{25}$ −57.8° (*c* 1.12, chloroform); n.m.r. data: τ 2.67 (10 H, 2 Ph), 6.64 (3 H, OMe), 8.74 (d, *J* 6.5 Hz, 3 H, CH-Me).

Anal. Calc. for $C_{21}H_{26}O_5$: C, 70.37; H, 7.31. Found: C, 70.35; H, 7.20.

Methyl 4-O-methyl-α-L-fucopyranoside (**9**). — Compound **8** (1 g), dissolved in dimethyl sulfoxide (25 ml), was methylated as described previously for **4** with sodium hydride (0.21 g) and methyl iodide (15 ml). After the usual processing, a syrup was obtained; n.m.r. data: ratio of protons due to phenyl (τ 2.68) to methyl ether (τ 6.40) to methyl glycoside (τ 6.68) groups: 10:3:3. This material was hydrogenolyzed and an amorphous solid was obtained (0.52 g, 94%), which was crystallized from acetone–ether, m.p. 134–136°; $[\alpha]_D^{24}$ −192° (*c* 0.9, water); n.m.r. data (90 MHz, 6:1 benzene–chloroform-*d*): τ 5.28 (d, *J* 3.5 Hz, H-1), 6.56 (3 H, OMe, ether), 6.87 (3 H, OMe, glycoside), 8.85 (d, *J* 6.5 Hz, 3 H, CH-Me). The product consumed 1.05 moles of periodate per mole during 3 h at 25°.

Anal. Calc. for $C_8H_{16}O_5$: C, 49.99; H, 8.39. Found: C, 49.97; H, 8.12.

Acetylation of **9** (100 mg) in the usual fashion gave a solid (140 mg, 97%), which crystallized from ether as needles, m.p. 93–95°; $[\alpha]_D^{22}$ −138° (*c* 1.00, chloroform); n.m.r. data: τ 6.48 (3 H, OMe, ether), 6.64 (3 H, OMe, glycoside), 7.91 (6 H, 2 *eq* OAc), 8.74 (d, *J* 6.5 Hz, 3 H, CH-Me).

Anal. Calc. for $C_{12}H_{20}O_7$: C, 52.16; H, 7.30. Found: C, 52.48; H, 7.20.

4-O-Methyl-L-fucose (**16**). — A solution of **9** (0.40 g) in M hydrochloric acid (40 ml) was kept for 2 h at 95–100°. After being processed in the usual fashion, it gave

a syrup (0.33 g, 89%) that was indistinguishable from an authentic sample of 4-*O*-methyl-D-fucose[13,14] on paper chromatography in 4:1:5 butanol–ethanol–water and 1:5:3:3 benzene–butanol–pyridine–water. The product was extremely hygroscopic and, although the corresponding D-isomer has been crystallized, we were unable to obtain **16** in a crystalline state; $[\alpha]_D^{23}$ −76.0° (*c* 1.12, water).

Anal. Calc. for $C_7H_{14}O_5 \cdot H_2O$: C, 42.85; H, 8.22. Found: C, 43.33; H, 8.19.

2,4-Di-O-benzyl-α-L-fucopyranose (**10**). — A suspension of **2** (10 g) in 1.5M sulfuric acid (250 ml) was stirred for 3 h at 100°. After being cooled, the reaction mixture was extracted with chloroform, the chloroform solution was washed with a cold, saturated solution of sodium hydrogen carbonate and water, dried with calcium chloride, and evaporated *in vacuo*. The residue was dissolved in benzene and chromatographed on silica gel. Benzene–ether (4:1) eluted unchanged **2** (2.5 g, 25%) and a further homogeneous fraction, eluted with 1:1 benzene–ether, afforded an amorphous solid (4.1 g, 43%) which crystallized from acetone–ether in needles, m.p. 133–135°; $[\alpha]_D^{25}$ −75.5° (*c* 1.16, chloroform); n.m.r. data: τ 2.68 (10 H, 2 Ph), 4.75 (d, *J* 3 Hz, H-1), 8.84 (d, *J* 6.5 Hz, 3 H, CH-Me).

Anal. Calc. for $C_{20}H_{24}O_5$: C, 69.75, H, 7.02. Found: C, 69.84, H, 6.83.

2,4-Di-O-benzyl-1-O-p-nitrobenzoyl-β-L-fucopyranose (**19**). — Pyridine (10 ml) and *p*-nitrobenzoyl chloride (3.24 g, 1.72 mmoles) were added to a cooled solution of **10** (5 g, 1.45 mmoles) in dichloromethane (100 ml). The reaction mixture was kept overnight at room temperature, washed successively with cold hydrochloric acid, water, a cold saturated solution of sodium hydrogen carbonate and water, dried with calcium chloride, and evaporated *in vacuo*. T.l.c. in 9:1 benzene–ether showed that most of the original **10** had been converted into a material having R_F 0.56. A weaker spot also appeared which migrated faster. The mixture was purified by chromatography on silica gel. Benzene–ether (9:1) eluted a homogeneous fraction as a syrup (1.2 g, 13%) which was shown to be the di-*O*-*p*-nitrobenzoyl derivative, $[\alpha]_D^{25}$ −73.6° (*c* 0.85, chloroform); n.m.r. data: ratio of protons due to *p*-nitrobenzoyl to phenyl to *C*-methyl groups: 8:10:3. A further homogeneous fraction (3.8 g, 54%) was eluted with 4:1 benzene–ether and crystallized from methanol, m.p. 56–58°; $[\alpha]_D^{25}$ +22.6° (*c* 1.19, chloroform); n.m.r. data: τ 1.88 (4 H, 1 *p*-nitrobenzoyl), 2.77 and 2.87 (10 H, 2 Ph), 4.35 (d, *J* 8 Hz, H-1), 8.79 (d, *J* 6.5 Hz, 3 H, CH-Me).

Anal. Calc. for $C_{27}H_{27}NO_8$: C, 65.66; H, 5.49. Found: C, 65.13; H, 5.44.

3-O-Acetyl-2,4-di-O-benzyl-1-O-p-nitrobenzoyl-β-L-fucopyranose (**20**). — A portion of **19** (3.5 g) was acetylated with acetic anhydride (50 ml) in pyridine (50 ml) overnight at room temperature, in the usual fashion. The product (3.4 g, 90%) crystallized from methanol, m.p. 146–147°; $[\alpha]_D^{25}$ +19.1° (*c* 1.05, chloroform); n.m.r. data: τ 1.78 (4 H, 1 *p*-nitrobenzoyl), 2.64 and 2.78 (10 H, 2 Ph), 4.13 (d, *J* 8 Hz, H-1), 8.03 (3 H, *eq* OAc), 8.75 (d, *J* 6.5 Hz, 3 H, CH-Me).

Anal. Calc. for $C_{29}H_{29}NO_9$: C, 65.04; H, 5.46. Found: C, 65.19; H, 5.49.

Benzyl 2-acetamido-6-O-(3-O-acetyl-2,4-di-O-benzyl-L-fucopyranosyl)-3,4-di-O-acetyl-2-deoxy-α-D-glucopyranoside (**24**). — A saturated solution of hydrogen bromide in dichloromethane (20 ml) was added to a solution of **20** (3.4 g) in dichloromethane

(50 ml). After 1 h at room temperature, the precipitated *p*-nitrobenzoic acid was removed by filtration, and the solution was washed with a cold saturated solution of sodium hydrogen carbonate and cold water until neutral and dried with calcium chloride. Evaporation of the solvent *in vacuo* afforded 3-*O*-acetyl-2,4-di-*O*-benzyl-α-L-fucopyranosyl bromide (**11**, 2.7 g, 95%) as a syrup, $[\alpha]_D^{24}$ −184° (*c* 1.50, chloroform); n.m.r. data: τ 2.68 (10 H, 2 Ph), 3.50 (d, *J* 3.5 Hz, H-1), 8.03 (3 H, *eq* OAc), 8.79 (d, *J* 6.5 Hz, 3 H, CH-Me).

Approximately 20 ml of solvent was evaporated from a solution of benzyl 2-acetamido-3,4-di-*O*-acetyl-2-deoxy-α-D-glucopyranoside[3] (**31**) (1.6 g, 4 mmoles) in 1:1 nitromethane–benzene (60 ml) and the remaining solution cooled to room temperature. Mercuric cyanide (1.0 g, 4 mmoles) and **11** (1.8 g, 4 mmoles) were added and the reaction mixture was stirred for 48 h, a further addition of **11** (0.9 g, 2 mmoles) being made after 24 h. The mixture was diluted with benzene, washed sucessively with sodium hydrogen carbonate solution, and water, dried (calcium chloride), and concentrated *in vacuo*. The residue was dissolved in benzene and chromatographed on a column of silica gel. A homogeneous fraction (t.l.c.), eluted with 14:14:1 benzene–ether–methanol was collected. Evaporation of the solvent *in vacuo* afforded a syrup (2.0 g, 65%) which crystallized from ether, m.p. 118–120°; $[\alpha]_D^{26}$ +9.1° (*c* 1.05, chloroform); n.m.r. data: ratio of protons due to benzyl to acetyl to *C*-methyl groups 5:4:1.

Anal. Calc. for $C_{41}H_{49}NO_{13}\cdot H_2O$: C, 62.92; H, 6.31. Found: C, 63.06; H, 6.35.

*Benzyl 2-acetamido-2-deoxy-6-*O*-(2,4-di-*O*-benzyl-α-L-fucopyranosyl)-α-D-glucopyranoside* (**27**). — Crude **24** (1.5 g) was dissolved in anhydrous methanol (50 ml) containing a catalytic amount of sodium methoxide, and the solution was kept overnight at room temperature, neutralized with acetic acid, and evaporated *in vacuo*. The residue was dissolved in chloroform and the chloroform solution extracted several times with water and dried with calcium chloride. Evaporation *in vacuo* afforded 1.1 g (90%) of a syrup, $[\alpha]_D^{26}$ +14.7° (*c* 1.09, chloroform), which crystallized from abs. ethanol (0.5 g, 45.5%), m.p. 196–198°; $[\alpha]_D^{26}$ +4.2° (*c* 1.01, chloroform); n.m.r. data: τ 2.64 (15 H, 3 Ph), 8.14 (3 H, NAc), 8.94 (d, *J* 6.5 Hz, 3 H, CH-Me).

Anal. Calc. for $C_{35}H_{43}NO_{10}$: C, 65.92; H, 6.80. Found: C, 65.75; H, 6.67.

*2-Acetamido-2-deoxy-6-*O*-α-L-fucopyranosyl-D-glucose* (**28**). — Compound **27** (200 mg) was dissolved in 90% ethanol (100 ml), 10% palladium-on-charcoal (50 mg) added, and the suspension shaken with hydrogen at 3.3 atm. for 48 h at room temperature. The catalyst was removed by filtration and the solvent evaporated *in vacuo*. The residue was dissolved in 13:6:1 chloroform–methanol–water and chromatographed on silica gel. An earlier fraction contained apparently incompletely hydrogenolyzed material and was not investigated further. A later fraction eluted from the column gave 100 mg (87%) of **28**, homogeneous on t.l.c. in 3:3:2 2-propanol–ethyl acetate–water and 13:6:1 chloroform–methanol–water. The amorphous product obtained could not be crystallized. It was identical with a disaccharide described in a previous publication[3] (t.l.c., paper chromatography, and optical rotation). The per(trimethylsilyl) ether of the sugar alcohol derived from **28** showed, on g.l.c., a single peak having T_S 1.96 (Ref. 3).

3,4-Di-O-benzyl-L-fucose (**17**). — A suspension of **3** (5 g) in 1.5M sulfuric acid (100 ml) was stirred for 4 h at 100°. After the usual processing, a syrup was obtained on evaporation of the organic layer. The mixture was purified by chromatography on silica gel. Benzene–ether (4:1) eluted unchanged **3** (1.6 g, 30%). Benzene–ether (1:1) eluted **17** (2.4 g, 49%) as a syrup, $[\alpha]_D^{25}$ −72° (*c* 1.41, chloroform); n.m.r. data: τ 2.78 (10 H, 2 Ph), 8.89 (d, *J* 6.5 Hz, 3 H, CH-Me).

Anal. Calc. for $C_{20}H_{24}O_5$: C, 69.75; H, 7.02. Found: C, 69.89; H, 7.07.

2-O-Acetyl-3,4-di-O-benzyl-1-O-p-nitrobenzoyl-β-L-fucopyranose (**21**). — Compound **17** (2 g, 0.58 mmole) was selectively *p*-nitrobenzoylated as described for **19**, and a syrup was obtained which was chromatographed on silica gel. Benzene–ether (4:1) eluted a homogeneous fraction (1.95 g, 68%) which could not by crystallized, $[\alpha]_D^{23}$ −36.9° (*c* 1.03, chloroform); n.m.r. data: τ 1.79 (4 H, 1-*p*-nitrobenzoyl), 2.66 (10 H, 2 Ph), 4.23 (d, *J* 8 Hz, H-1), 8.75 (d, *J* 6.5 Hz, 3 H, CH-Me). Acetylation of the product with acetic anhydride (25 ml) in pyridine (50 ml) in the usual way gave **21** (1.9 g, 90%) which crystallized from methanol, m.p. 145–148°; $[\alpha]_D^{25}$ +19.1° (*c* 1.05, chloroform); n.m.r. data: τ 1.71 (4 H, 1-*p*-nitrobenzoyl), 2.61 (10 H, 2 Ph), 8.03 (3 H, *eq* OAc), 8.73 (d, *J* 6.5 Hz, 3 H, CH-Me).

Anal. Calc. for $C_{29}H_{29}NO_9$: C, 65.04; H, 5.46. Found: C, 65.20; H, 5.20.

Benzyl 2-acetamido-6-O-(2-O-acetyl-3,4-di-O-benzyl-L-fucopyranosyl)-3,4-di-O-acetyl-2-deoxy-α-D-glucopyranoside (**25**). — A saturated solution of hydrogen bromide (11 ml) was added to a solution of **21** (1.9 g) in dichloromethane (25 ml). The reaction mixture was kept for 2 h at room temperature and, after the customary processing, 2-*O*-acetyl-3,4-di-*O*-benzyl-α-L-fucopyranosyl bromide (**12**, 1.47 g, 92%) was obtained as a syrup, $[\alpha]_D^{26}$ −154° (*c* 1.20, chloroform); n.m.r. data: τ 2.66 and 2.71 (10 H, 2 Ph), 3.25 (d, *J* 3 Hz, H-1), 7.92 (3 H, *eq* OAc), 8.78 (d, *J* 6.5 Hz, 3 H, CH-Me).

Treatment of compound **31** (0.8 g, 2 mmoles) with **12** (1.4 g, 3 mmoles) in the presence of mercuric cyanide (0.50 g, 2 mmoles), as described for **24**, afforded a syrup which was dissolved in benzene and chromatographed on silica gel. The fractions that were eluted with 14:14:1 benzene–ether–methanol and were identical and homogeneous on t.l.c. were combined to give a syrup (0.92 g, 59%) which crystallized from ether, m.p. 157–160°, $[\alpha]_D^{25}$ +49° (*c* 1.04, chloroform); n.m.r. data: τ 2.70 (15 H, 3 Ph), 7.96 and 8.02 (9 H, 3 *eq* OAc), 8.13 (3 H, NAc), 8.77 (d, *J* 6.5 Hz, 3 H, CH-Me).

Anal. Calc. for $C_{41}H_{49}NO_{13}$: C, 64.47; H, 6.47. Found: C, 64.42; H, 6.30.

Benzyl 2-acetamido-2-deoxy-6-O-(3,4-di-O-benzyl-β-L-fucopyranosyl)-α-D-glucopyranoside (**29**). — Catalytic deacetylation of crude **25** (0.7 g) as described for **27** afforded an amorphous solid (0.54 g, 92%) which crystallized from methanol, m.p. 185–187°; $[\alpha]_D^{25}$ +67.2° (*c* 0.91, pyridine); n.m.r. data: ratio of protons due to benzyl to *N*-acetyl to *C*-methyl groups: 15:3:3.

Anal. Calc. for $C_{35}H_{43}NO_{10}$: C, 65.92; H, 6.80. Found: C, 65.81; H, 6.80.

2-Acetamido-2-deoxy-6-O-β-L-fucopyranosyl-D-glucose (**30**). — Compound **29** (200 mg) was hydrogenolyzed as described for **28**, and, after the usual processing and purification by column chromatography, **30** (90 mg, 78%) was obtained, which was homogeneous on t.l.c. in 3:3:2 2-propanol–ethyl acetate–water and 13:6:1 chloroform–

methanol–water; $[\alpha]_D^{25}$ +33.3° (*c* 0.60, water); lit.[17]: $[\alpha]_D^{20}$ +31→29° (*c* 0.87, ethanol). The per(trimethylsilyl) ether of the sugar alcohol showed a single peak on g.l.c. with T_S 2.4 (Ref. 3).

2,3-Di-O-benzyl-L-fucose (**18**). — Compound **8** (5 g) was hydrolyzed with 1.5M sulfuric acid for 4 h as described for **10**, and the syrup obtained was dissolved in benzene and chromatographed on silica gel. Benzene–ether (1:1) eluted a homogenous fraction as a syrup (3.3 g, 68.5%), $[\alpha]_D^{23}$ +12.0° (*c* 1.86, chloroform); n.m.r. data: ratio of protons due to benzyl to *C*-methyl groups: 10:3.

Anal. Calc. for $C_{20}H_{24}O_5$: C, 69.75; H, 7.02. Found: C, 69.85; H, 6.80.

2,3-Di-O-benzyl-1-O-p-nitrobenzoyl-β-L-fucopyranose (**23**). — Treatment of **18** (3 g) with *p*-nitrobenzoyl chloride (1.95 g) in pyridine as described for **19** afforded a syrup which was dissolved in benzene and chromatographed on silica gel. Earlier fractions eluted from the column apparently contained the di-*O*-*p*-nitrobenzoyl derivative and were not investigated further. Benzene–ether (4:1) eluted a homogeneous fraction (2.3 g, 55%) which crystallized from ether, m.p. 118–120°; $[\alpha]_D^{25}$ +63.5° (*c* 0.80, chloroform); n.m.r. data: τ 1.80 (4 H, 1-*p*-nitrobenzoyl), 2.68 and 2.81 (10 H, 2 Ph), 4.20 (d, *J* 8 Hz, H-1), 8.72 (d, *J* 6.5 Hz, 3 H, CH-Me).

Anal. Calc. for $C_{27}H_{27}NO_8$: C, 65.75; H, 5.52. Found: C, 65.65; H, 5.45.

A further homogeneous fraction eluted from the column was shown to be unchanged **18**.

Benzyl 2-acetamido-2-deoxy-6-O-(2,3-di-O-benzyl-L-fucopyranosyl)-α-D-glucopyranoside (**26**). — Acetylation of **23** (2 g) as described for **21** afforded 4-*O*-acetyl-2,3-di-*O*-benzyl-1-*O*-*p*-nitrobenzoyl-L-fucopyranose as a syrup (1.9 g, 87%), $[\alpha]_D^{25}$ −4.7° (*c* 1.07, chloroform); n.m.r. data: τ 1.84 (4 H, 1-*p*-nitrobenzoyl), 2.68 and 2.82 (10 H, 2 Ph), 7.80 (3 H, *ax* OAc), 8.79 (d, *J* 6.5 Hz, 3 H, CH-Me). Treatment of this compound with a saturated solution of hydrogen bromide, as described for **24**, afforded 4-*O*-acetyl-2,3-di-*O*-benzyl-α-L-fucopyranosyl bromide (**13**, 1.4 g, 88%), $[\alpha]_D^{25}$ −90° (*c* 1.12, chloroform); n.m.r. data: τ 2.67 (10 H, 2 Ph), 3.51 (d, *J* 3 Hz, H-1), 7.86 (3 H, *ax* OAc), 8.80 (d, *J* 6.5 Hz, 3 H, CH-Me).

Reaction of **31** (0.8 g, 2 mmoles) with bromide **13** (1.4 g, 3 mmoles) in the presence of mercuric cyanide as described for **24**, afforded a syrup which was dissolved in benzene and chromatographed on silica gel. Benzene–ether–methanol (14:14:1) eluted a homogeneous fraction (t.l.c.). Evaporation of the solvent *in vacuo* afforded a syrup (0.94 g, 60%), $[\alpha]_D^{25}$ +24° (*c* 1.25, chloroform); n.m.r. data: τ 2.68 (15 H, 3 Ph), 7.86 (3 H, *ax* OAc), 8.00 and 8.04 (6 H, 2 *eq* OAc), 8.13 (3 H, NAc), 8.88 (d, *J* 6.5 Hz, 3 H, CH-Me). Deacetylation of a portion of this product (0.8 g), as described for **27**, afforded an amorphous solid (0.58 g, 88%), $[\alpha]_D^{24}$ +10.5° (*c* 2.20, chloroform); n.m.r. data; τ 2.67 (15 H, 3 Ph), 8.09 (3 H, NAc), 8.74 (d, *J* 6.5 Hz, 3 H, CH-Me).

Anal. Calc. for $C_{35}H_{43}NO_{10}\cdot H_2O$: C, 64.11; H, 6.92. Found: C, 64.29; H, 7.18.

2-Acetamido-2-deoxy-6-O-α,β-L-fucopyranosyl-D-glucose. — Aliquots of crude **27**, **29**, and **26** (taken directly after deacetylation without additional purification) were hydrogenolyzed, and each one of the disaccharides was isolated by chromatography. The per(trimethylsilyl) ethers of the sugar alcohols of the disaccharides were analyzed

by g.l.c. In each case, two peaks (T_S 1.96 and 2.40) were obtained which correspond to the α- and β-L anomers. The ratio of α:β anomers is presented in Table 1.

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