The Photochemistry of Carbohydrate Derivatives. Part 5.[1] Synthesis of Methyl 2,3-Di-*O*-(β-D-glucopyranosyl)-α-L-fucopyranoside and Methyl 2,3-Di-*O*-(β-D-galactopyranosyl)-α-L-fucopyranoside using Photolabile *O*-(2-Nitrobenzylidene) Acetals as Temporary Blocking Groups

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The branched trisaccharide derivatives (6) and (12) named in the title have been synthesised from methyl 3,4-*O*-(2-nitrobenzylidene)-α-L-fucopyranoside (1) using the 2-nitrobenzylidene residue as a temporary blocking group.

Glucosylation and galactosylation of compound (1) afforded the blocked disaccharides (2) and (7), respectively, and upon sequential photolysis and oxidation these were regioselectively transformed into the partially blocked 4-*O*-(2-nitrobenzoyl)disaccharides (4) and (9), the 3-*O*-(2-nitrobenzoyl) positional isomers being formed in <5 and 3% yield, respectively.

Further glycosylations of compounds (4) and (9) gave the fully protected trisaccharide derivatives (5) and (11), respectively, which were converted into the title compounds (6) and (12) upon deacylation.

The synthesis of branched oligosaccharides requires that partially blocked sugars serve as potential 'aglycones' protected with groups (which are compatible with glycosylation) that can be subsequently selectively removed to expose one hydroxy-group for further glycosylation.[2,3]

Several blocking–deblocking methods using temporary and persistent hydroxy-protecting groups [4] have been employed to overcome this far from trivial problem. Some of these methods include selective acylation,[5,6] often combined with benzylation [7] or allylation,[8] which affords blocked derivatives that can be subsequently deblocked. Selective glycosylation,[5,9] sometimes assisted by stannylation,[9,10] has on occasions proved convenient. Diglycosylations of a dihydroxy-sugar derivative have been used [11] in cases where branching to identical sugars is involved.

In a highly novel approach [12] to the problem, a butadienyl ether residue has been used for protection during the initial glycosylation; the butadienyl ether was then elaborated into a pyranose ring *via* a Diels–Alder reaction to give a branched trisaccharide.

Methods for simultaneous protection of two hydroxy-groups with cyclic derivatives and subsequent exposure of one hydroxy-group have also proved successful. For example, orthoesters which can be partially hydrolysed to hydroxy-*O*-acyl derivatives have been used by two major groups working in this area,[13] and *exo*-*O*-benzylidene derivatives have also proved useful, since they can be converted by hydrogenolysis into hydroxybenzylated sugars.[14]

In this paper we report an approach to this problem which utilises the photolabile *O*-2-nitrobenzylidene group. We have shown that *O*-(2-nitrobenzylidenated) sugars can be sequentially photolysed and oxidized to give hydroxy-*O*-2-nitrobenzoyl derivatives which are useful partially protected sugars. Working with the 2-*O*-acetyl derivative of methyl 3,4-*O*-(2-nitrobenzylidene)-α-L-fucopyranoside (1) we found that the reaction was highly regioselective, affording methyl 2-*O*-acetyl-4-*O*-(2-nitrobenzoyl)-α-L-fucoside.[15] We now report the use of compound (1) in the synthesis of trisaccharides branched at the 2- and 3-positions of fucose.[16]

An *endo*–*exo* mixture of methyl 3,4-*O*-(2-nitrobenzylidene)-α-L-fucopyranoside (1) [17] was glycosylated by Flowers' method using the Helferich mercury(II) cyanide catalyst [18] to give, after chromatography, a 2 : 1 *endo*–*exo* mixture [19] of the disaccharide derivative (2) in 80% yield.

The *endo*-isomer of compound (2) could be crystallised from the mixture but this was unnecessary since the stereochemical outcome of the subsequent photochemical ring-opening reaction does not depend upon the configuration at the nitrobenzylidene acetal centre. This contrasts markedly with the regioselective hydrogenolysis of *O*-benzylidene derivatives which *is* dependent upon the configuration at the acetal carbon.[20]

Although the anomeric configuration and the anomeric purity of the disaccharide were readily determined at later stages in the synthesis, *e.g.* with compounds (3) and (4) when n.m.r. spectra were not complicated by the *endo* and *exo* forms, the indications from the 200-MHz ^{1}H n.m.r. spectrum

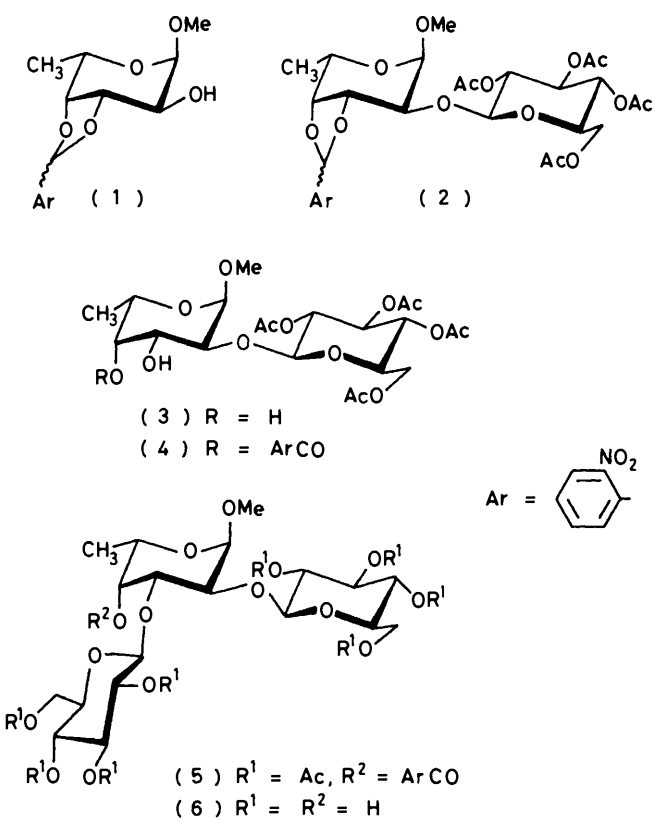
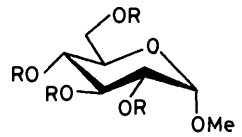
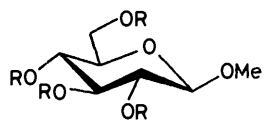


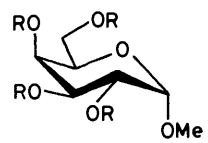
Table 1. δ_C Values from proton-decoupled 15-MHz ^{13}C n.m.r. spectra for some glycosylfucose and diglycosylfucose derivatives measured in $CDCl_3$ or D_2O



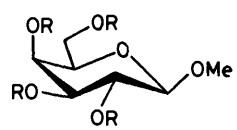
(13) R = H
(14) R = Ac



(15) R = H
(16) R = Ac



(17) R = H
(18) R = Ac



(19) R = H
(20) R = Ac

	Glucose/Galactose						Fucose							
Carbons	1	2	3	4	5	6	1	2	3	4	5	6	MeO	
Compd.														References
(16) [a]	101.6	71.3	73.0	68.6	71.8	62.1								21, 22, 23
(14) [a]	96.3	70.4	69.7	68.2	66.8	61.6								22, 24
(3)	101.4	71.2	72.4	68.6 [b]	72.4	61.7	98.4	79.9	71.2 [c]	68.4 [b,c]	65.5	16.1	55.6	
(4)	101.7	71.2	72.4	68.6	72.1	61.7	98.6	80.6	75.4 [b]	66.9 [b]	64.8	16.1	55.9	
(5) [d]	98.9	71.3	73.0	68.2	71.8	61.8	98.2	74.1 [b]	73.3 [b]	73.0 [b]	64.6	16.0	55.6	
	99.4	71.3	73.0	68.3	71.9	61.9								
(15) [a,e]	104.3	74.2	76.9	70.8	76.9	61.9								23, 25, 26
(13) [a,e]	100.0	72.2	74.1	70.6	72.5	61.6								23, 24, 26
(6) [d]	101.4	73.2	77.4	70.3	76.4	61.6	98.3	74.9 [b]	72.6 [b]	70.3 [b]	67.0	16.1	55.8	
	100.4	73.2	77.4	70.3	76.4	61.6								
(20) [a]	101.5	68.5 [b]	70.2 [b]	66.8 [b]	70.6 [b]	61.0								23, 27
(18) [a]	96.5	67.0 [b]	67.6 [b]	65.7 [b]	67.6 [b]	61.2								23, 27
(8)	102.4	68.9 [b]	70.8 [b]	67.2 [b]	71.5 [b]	61.8	98.7	80.7	71.5 [b]	68.7 [b]	65.5	16.1	55.8	
(9)	102.4	68.9 [b]	70.7 [b]	67.2 [b]	71.2 [b]	61.5	98.8	81.0	75.1 [c]	67.1 [c]	64.8	16.1	55.9	
(11) [d]	100.4	69.3	71.1	66.8	70.8	60.6	98.4	74.1 [b]	73.7 [b]	72.5 [b]	64.6	16.0	55.8	
	99.0	68.9	71.0	66.6	70.7	60.4								
(19) [a,e]	104.5	71.7	73.8	69.7	76.0	62.0								23, 26
(17) [a,e]	100.1	69.2	70.5	70.2	71.6	62.2								23, 26
(12) [d]	102.1	71.0	73.5	69.5	76.5	62.1	98.6	74.8 [b]	72.5 [b]	70.9	67.0	16.1	55.9	
	101.1	71.0	73.5	69.5	76.5	62.1								

[a] The α and β anomers of methyl D-glucopyranoside (13) and (15) and their tetra-acetates (14) and (16). The α and β anomers of methyl D-galactopyranoside (17) and (19) and their tetra-acetates (18) and (20). [b,c] Assignments for these signals may be interchanged. [d] When two identical substituent rings are present, assignment of a set of resonances to a particular ring is not possible. Thus some signals are interchangeable. [e] Dioxan used as internal standard in D_2O solutions and taken to have δ_C 67.4 p.p.m. relative to TMS.

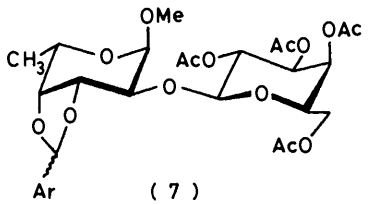
The signals for acetyl groups and the 2-nitrobenzoyl group exhibited by compound (4) at 169.1, 169.5, 170.2, 170.3, 20.5 (intense); 126.1 and 148.9 (both weak), 123.5 132.3, 132.4, 131.1, and 164.4 p.p.m. are typical. The oligosaccharide carbon signals have been assigned by reference to the spectra of the monosaccharide models.

of compound (2) were that only the β-linked disaccharide had been produced. The anomeric proton doublets (J 3.5 Hz) at δ_H 4.64 and 4.76 with 2 : 1 intensities arising from the α-fucopyranoside were accompanied by another pair of doublets, each split by 8.0 Hz, at δ_H 4.58 and 4.80 also with intensities 2 : 1; this indicated that the glucopyranose is β-linked to fucose in both the *endo*- and *exo*-form of the disaccharide (2).

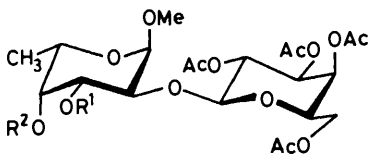
The dihydroxy-disaccharide (3), obtained from compound (2) by mild hydrolysis of the nitrobenzylidene residue, exhibited only two anomeric carbon signals, at δ_C 98.4 and 101.4 p.p.m. (Table 1) for the fucose and glucose rings, respectively, which confirms that the disaccharide sample contained only β-linked glucose.[21-23]

The fully protected disaccharide (2) was then partially deblocked. A methanolic solution of the *endo–exo*-nitrobenzylidenated disaccharide mixture (2) was irradiated through Pyrex with a 450-W medium-pressure mercury lamp for 45 min. The nitrosobenzoate obtained was oxidised with trifluoroperacetic acid in dichloromethane at 0 °C to afford the disaccharide nitrobenzoate (4) in 95% yield. The ^{13}C n.m.r. spectrum (Table 1) reaffirmed that the earlier glycosylation had occurred stereospecifically, since there were only two anomeric signals, at δ_C 98.6 and 101.7 p.p.m. for the fucopyranose and glucopyranose rings, respectively. A comparison of the chemical shift of the latter signal with that of the anomeric carbon signals for α- and β-methyl D-glucopyranoside tetra-acetates (14) and (16) indicated that a β-disaccharide linkage had been formed and this was confirmed by the ^1H n.m.r. spectrum of compound (4) which showed a signal for glucose 1-H at δ 4.26 ($J_{1,2}$ 7.5 Hz).

More importantly, the ^1H n.m.r. spectrum showed that the nitrobenzylidene ring had opened to give *ca.* 95% of the 4-(2-nitrobenzoate). The hydrogen attached to the carbon carrying the nitrobenzoyloxy-group would be expected to be the most deshielded glycoside proton. A doublet of doublets split by 3.0 and 1.0 Hz and integrating for one proton could be seen at δ_H (5.36, just resolved from the neighbouring signals at

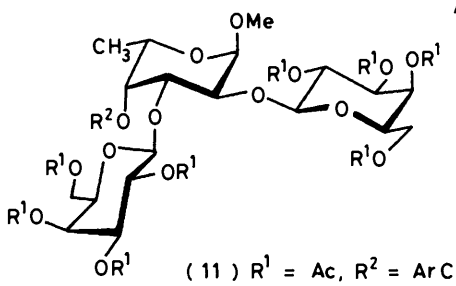


(7)



(8) $R^1 = R^2 = H$
(9) $R^1 = H, R^2 = ArCO$
(10) $R^1 = ArCO, R^2 = H$

Ar = 



(11) $R^1 = Ac, R^2 = ArCO$
(12) $R^1 = R^2 = H$

higher field.* These coupling constants are in the range expected for J_{ax-eq}, J_{ax-eq}, thus indicating 4-H of fucose. They are not satisfactorily in the range of J_{ax-ax}, J_{ax-eq} couplings which 3-H of this sugar would exhibit. The ^{13}C n.m.r. spectrum supports the view that essentially one ring-opened product was formed since only twelve hexose carbons were observed (Table 1).

The *endo*-nitrobenzylidene disaccharide (2) behaved identically to the *endo–exo* mixture when sequentially photolysed and oxidised. Thus the *endo* and *exo* forms of the nitrobenzylidene moiety in compound (2) are photochemically opened in the same direction so that the nitrobenzoyl group is attached to the axial 4-hydroxy-group and the equatorial 3-hydroxy-group is unblocked, just as we observed with the simpler derivatives studied earlier.[15] This is fortunate since, in consequence, the tedious and wasteful separation of the *endo* and *exo* forms of compound (2) is avoided.

The monohydroxy-product (4) was condensed, without prior chromatographic purification, with acetobromoglucose as described for the preparation of the disaccharide (2). Chromatography gave a trisaccharide mixture in 75% yield from which 60% of the ββ-linked compound (5), m.p. 92—94 °C, was isolated by preparative layer chromatography (p.l.c.). The ^{13}C n.m.r. spectrum (Table 1) indicated that the material was anomerically pure since it showed only three discrete signals at δ_C 98.2, 98.9, and 99.4 p.p.m. in the anomeric carbon spectral region,[28] and the three anomeric protons showed up as doublets in the ^1H n.m.r. spectrum with couplings of 7.4, 7.6, and 4.0 Hz, indicating that both glucose units were β-linked to the methyl α-fucoside. Since the lowest field non-aromatic proton signal at δ_H 5.48 was a doublet of doublets coupled by 3.4 and 1.0 Hz it must be the 4-H resonance of the fucose ring. Thus the nitrobenzoyl residue had not migrated from O-4 during the glucosylation reaction. Consequently the intersaccharide links are, as anticipated, at the 2,3-positions of fucose.

The fully protected trisaccharide (5) was deacylated to give the crystalline methyl glycoside (6) of the free trisaccharide, the ^{13}C n.m.r. spectrum of which was very clean, showing the expected nineteen carbon resonances (Table 1), and the ^1H n.m.r. spectrum exhibited three anomeric proton doublets at δ 5.08, 4.75, and 4.72 with 2.4, 7.9, and 7.3 Hz splittings, respectively, again indicating the presence of an α-fucoside and two β-linked glucose units.

The fucoside (1) was next condensed with acetobromogalactose to give, after chromatography, the fully protected *O*-nitrobenzylidene disaccharide (7) as a 1 : 1 *endo–exo* mixture in 77% yield in which the β-linkage of galactose to fucose was indicated by two doublets ($J_{1,2}$ 8.0 Hz) at δ_H 4.54 and 4.73 for the anomeric proton of the galactose moiety in the two isomers. The dihydroxy-disaccharide (8), obtained upon mild hydrolysis of compound (7), gave simpler ^{13}C n.m.r. and ^1H n.m.r. spectra which also confirmed the presence of a β-linked galactose.

The disaccharide (7) was partially deblocked by photolysis and subsequent oxidation to give a compound in 93% yield whose ^1H n.m.r. (Table 2) and ^{13}C n.m.r. spectra showed it to be the 3-hydroxy-4-*O*-nitrobenzoyl disaccharide (9). The position of the nitrobenzoyl group was ascertained from the multiplicity of the most deshielded glycoside proton signal at δ 5.55. The couplings measured from this doublet of doublets were 3.2 and 1.0 Hz which showed that it was the 4-H resonance of the fucose ring. The 4-H of the galactose ring also gave a similarly shaped resonance at δ_H 5.42 (*J* 3.5 and 0.7 Hz). Consequently the analysis of this spectrum was more complex than that of disaccharide (4) but was readily achieved with the spectrum measured at 200 MHz. The anomeric carbon and proton signals at δ_C 98.8 and 102.4 p.p.m. and δ_H 4.69 (d, *J* 3.6 Hz) and 4.59 (d, *J* 7.8 Hz) for fucose and galactose, respectively, in these spectra also confirmed that the galactose was β-linked to the α-methyl fucoside.

A critical assessment of the regioselectivity of the opening of the nitrobenzylidene ring is not easy when only traces of the alternative ring-opened product are present in the oxidised photolysate, as we also found with the reaction product from compound (2). However with a 400-MHz spectrum of the reaction product from compound (7) the regioselectivity could be evaluated with ease. The determination was facilitated by the spectrum of the pure 3-nitrobenzoate (10), which was prepared as the major product by nitrobenzoylation of the dihydroxy-disaccharide (8).

A comparison of the spectra of compounds (9) and (10) (Table 2) showed that signals for 1-H, 3-H and OMe of the fucose ring and for 1-H of the galactose ring of the 3-nitrobenzoate (10) occurred at chemical shifts for which there were no resonances in the spectrum of the 4-nitrobenzoate (9). These signals had relative intensities of *ca.* 3.0% in the 400-MHz spectrum of the oxidised photolysate from compound (7), which showed that the 3,4-*O*-(2-nitrobenzylidene) residue had cleaved to give the 4- and 3-(2-nitrobenzoate) in a ratio of *ca.* 32 : 1.

The deblocked 3-OH group in the partially protected disaccharide (9) was condensed with another molecule of acetobromogalactose to give, after chromatography, the crystalline trisaccharide (11) in 80% yield. The anomeric region of the ^{13}C n.m.r. spectrum showed three clear signals, indicating that the product was a single isomer, and the ^1H n.m.r. spectrum supported this conclusion. In particular the

* These signals arise from 2-, 3-, and 4-H of the acetylated glucose ring. Because they are all strongly J_{ax-ax},J_{ax-ax} coupled, confusion with the fucose protons is unlikely, K. Izumi, *J. Biochem.*, 1974, **76**, 535.

Table 2. ^{1}H N.m.r. parameters [δ; (multiplicity) *J* in Hz] for the 3- and 4-*O*-(2-nitrobenzoyl) disaccharide derivatives (10) and (9), respectively in $CDCl_3$

	Fucose ring								Galactose ring						
Carbons	1	2	3	4	5	6	MeO	Ar	1	2	3	4	5	6	Ac
Compound															
(9) [a]	4.69 (d) $J_{1,2}$ 3.6	3.76 (dd) $J_{2,3}$ 10.5	*c*	5.55 (dd) $J_{4,3}$ 3.2, $J_{4,5}$ 1.0	*c*	1.24 (d) $J_{6,5}$ 6.5	3.40 (s)	7.6—8.0 (m)	4.59 (d) $J_{1,2}$ 7.8	5.33 (dd) $J_{2,3}$ 10.5	5.08 (dd) $J_{3,4}$ 3.5	5.42 (dd) $J_{4,5}$ 0.7	*c*	*c*	1.95, 2.01, 2.09, and 2.15 (4 × s)
(10) [b]	4.78 (d) $J_{1,2}$ 3.8	4.26 (dd) $J_{2,3}$ 10.5	5.46 (dd) $J_{3,4}$ 3.0	4.17br (d) $J_{4,5}$ 0.7	4.10br (t) $J_{5,6}$ 6.5	1.34 (d) $J_{5,6}$ 6.5	3.42 (s)	7.5—8.0 (m)	4.50 (d) $J_{1,2}$ 7.5	5.16 (dd) $J_{2,3}$ 10.5	5.00 (dd) $J_{3,4}$ 3.2	5.32br (d) $J_{4,5}$ 0.7	*d*	*e*	2.00, 2.02, 2.08, and 2.13 (4 × s)

[a] Measured at 400 MHz. [b] Measured at 200 MHz. [c] Complex m in region δ 3.95—4.25. [d] m in region δ 3.50—3.68. [e] m in region δ 3.72—3.92.

two anomeric proton signals with couplings of 8.5 Hz in addition to the one coupled by 3.8 Hz confirmed that both galactoses were β-linked to the fucoside. Furthermore the spectrum shows that migration of the 4-*O*-nitrobenzoyl group had not occurred during the galactosylation reaction since the glycoside proton resonance at lowest field was a doublet of doublets (δ_H 5.49, *J* 1.0 and 3.0 Hz) that was assigned to 4-H.

The methyl glycoside of the free trisaccharide, compound (12), was obtained in crystalline form after deacylation of compound (11). It was characterized by its ^{13}C and ^{1}H n.m.r. spectra and by its positive ion FAB mass spectrum, which showed peaks for $[M + H]^+$ and $[M + Na]^+$ ions, the sodium presumably being carried through from the deacylation.

Thus the synthesis of the two trisaccharides (6) and (12) show that methyl 3,4-*O*-(2-nitrobenzylidene)-α-L-fucopyranoside (1) is a good synthon for preparing trisaccharides branched at the 2- and 3-positions of fucose. The *O*-2-nitrobenzylidene residue proved to be a good blocking group since it functions well during glycosylations and is photochemically cleaved with high regioselectivity. Also, the hydroxy-nitrobenzoyl disaccharides obtained on mild oxidation of the photoproducts glycosylate satisfactorily.

Experimental

^{1}H N.m.r. spectra were measured in $CDCl_3$ (unless otherwise stated), either with a Jeol M100 CW instrument, a Jeol FX200 FT instrument, or a Brucker WH-400 spectrometer, with tetramethylsilane (TMS) as internal standard. Natural-abundance ^{13}C n.m.r. spectra were determined with a Jeol FX60 FT instrument operating at 15 MHz for solutions in reference to TMS. Low-resolution mass spectra were obtained with a VG Micromass ZAB-1F double focusing spectrometer. Optical rotations were measured with an Optical Activity polarimeter model A100. Column chromatography was carried out on silica gel, 70—230 mesh (Merck Kieselgel 7734) and for t.l.c. 0.25 mm films of silica gel (Merck Kieselgel 60 F_{254}) were used. The eluting solvents were dried over molecular sieves 4 A.

Methyl 3,4-O-endo- *and* 3,4-O-exo-(2-*Nitrobenzylidene*)-2-O-(*tetra*-O-*acetyl*-β-D-*glucopyranosyl*)-α-L-*fucopyranoside* (2).—An *endo–exo* mixture of methyl 3,4-*O*-(2-nitrobenzylidene)-α-L-fucopyranoside (1) [17] (1.0 g), acetobromoglucose (2.0 g), and mercury(II) cyanide (0.8 g) were stirred together at 25 °C in an anhydrous mixture of nitromethane (4 ml) and benzene (4 ml).[18] The reaction was monitored by t.l.c. [SiO_2; light petroleum–diethyl ether (1 : 2) as developer] which showed, after two developments, compound (1), R_F 0.27, and the derived product, R_F 0.17. After the mixture had been stirred for 24 h benzene (50 ml) was added and the mixture was washed successively with aqueous sodium hydrogen carbonate and water. The dried organic phase was evaporated to dryness and the crude product was purified by column chromatography on silica gel [light petroleum–diethyl ether (1 : 2) as eluant] to give the title compound (2) as a 2 : 1 mixture of *endo*- and *exo*-isomers (1.64 g, 80%), m.p. 100—104 °C; $[\alpha]_D^{23}$ −70° (*c*, 0.85 in $CHCl_3$). The major (*endo*) isomer was crystallised from diethyl ether, m.p. 107—109 °C; $[\alpha]_D^{20}$ −62° (*c*, 1.0 in $CHCl_3$).

The *endo–exo* mixture of compound (2) showed δ_H (200 MHz) (fucose ring) 6.52 and 6.80 (2 : 1 intensity) (total 1 H, 2 × s, Ar*CH*O_2, *endo*- and *exo*-form), 8.1—7.5 (4 H, ArH), 4.64 and 4.76 (2 : 1 intensity) (total 1 H, 2 × d, $J_{1,2}$ 3.5 Hz, 1-H, *endo* and *exo*), 1.39 (3 H, d, $J_{6,5}$ 6.5 Hz, 6-H_3), 3.40 and 3.42 (2 : 1 intensity) (total 3 H, 2 × s, OMe); (glucose ring) 4.58 and 4.80 (2 : 1 intensity) (total 1 H, 2 × d, $J_{1,2}$ 8.0 Hz, 1-H, *endo* and *exo*), and 2.0—2.1 (12 H m, 4 × Ac). The remaining protons gave rise to complex signals. These assignments were facilitated by an analysis of the ^{1}H n.m.r. spectra of the *endo*-isomer of compound (2) and of methyl 2-*O*-methyl-3,4-*O*-*endo*- and *exo*-(2-nitrobenzylidene)-α-L-fucopyranoside which showed the following significant signals: δ_H (200 MHz) 6.53 and 6.78 (total 1 H, 2 × s, Ar*CH*O_2, *endo*- and *exo*-form), 4.70 and 4.84 (total 1 H, 2 × d, $J_{1,2}$ 3.8 Hz, 1-H, *endo* and *exo*), and 1.44 (3 H, d, $J_{6,5}$ 6.5 Hz, 6-H_3) Compound (2) also has δ_C 97.3 and 97.9 (2 : 1 intensity) (*endo* and *exo*, C-1), 16.2 (C-6 of fucose), 99.3 and 100.3 (C-1′), 20.0 ($COCH_3$), and 99.2 p.p.m. (ArCHO_2, *endo* and *exo*); the other glycose carbons were difficult to assign [Found: $(M - OMe)^{\cdot+}$, 611: $C_{27}H_{32}NO_{15}$ requires *m/z*, 611].

The fully blocked disaccharide (2) (150 mg) was hydrolysed with 10% aqueous trifluoroacetic acid (5 ml) at 23 °C during 30 min. The solution was evaporated to dryness and benzene was added to, and then evaporated from, the residue to give the dihydroxy-tetra-*O*-acetyldisaccharide (3), contaminated with a trace of 2-nitrobenzaldehyde; the δ_C values are given in Table 1.

Methyl 4-O-(2-*Nitrobenzoyl*)-2-O-(*tetra*-O-*acetyl*-β-D-*glucopyranosyl*)-α-L-*fucopyranoside* (4).—A pale-yellow solution of the *endo–exo*-nitrobenzylidene disaccharide mixture (2)

(0.71 g, 1.1 mmol) in methanol (250 ml) was irradiated with a 450-W medium-pressure mercury arc lamp in the annular space surrounding a Hanovia Pyrex immersion well. After 45 min irradiation, t.l.c. [SiO_2; light petroleum–diethyl ether (1 : 2)] revealed that photolysis was complete. The pale-green solution was evaporated, the residue was dissolved in dichloromethane (50 ml), trifluoroperacetic acid (2.2 mmol) was then added, and the solution was then stirred at 0 °C for 1.5 h. The oxidised solution was diluted with dichloromethane (150 ml) and was then washed sequentially with water, aqueous sodium hydrogen carbonate, and water. After being dried the organic phase was evaporated to give a gum (0.69 g, 95%), $[\alpha]_D^{22}$ +7° (*c*, 1.4 in $CHCl_3$), which was shown by ^{13}C n.m.r. spectroscopy (Table 1), t.l.c. [R_F 0.62 (SiO_2; C_6H_6–EtOAc (2 : 1), 2 developments], and ^1H n.m.r. spectroscopy to be a single compound δ_H (C_6D_6) (fucose ring) 4.56 (d, $J_{1,2}$ 3.0 Hz, 1-H), 5.36 (dd, $J_{4,3}$ 3.0, $J_{4,5}$ 1.0 Hz, 4-H), 1.20 (3 H, d, $J_{6,5}$ 6.5 Hz, 6-H_3), 3.2 (3 H, s, OMe), and 6.4—7.6 (4 H, m, ArH); (glucose ring) 4.26 ($J_{1,2}$ 7.5 Hz, 1-H), 4.7—5.26 (total 3 H, m, 2-, 3-, and 4-H), and 1.62, 1.66, 1.68, and 1.72 (12 H, 4 × s, 4 × Ac); the other signals were not resolved, δ_H ($CDCl_3$) (fucose) 5.29 (dd, *J* 3.0 and 1.0 Hz, 4-H) [Found: $(M - OMe)^{+\cdot}$ 627. $C_{27}H_{32}NO_{16}$ requires *m/z*, 627].

Methyl 4-O-(2-*Nitrobenzoyl*)-2,3-*di*-O-(*tetra*-O-*acetyl*-β-D-*glucopyranosyl*)-α-L-*fucopyranoside* (5).—The disaccharide nitrobenzoate (4) (0.5 g) was glycosylated, without prior chromatographic purification, with acetobromoglucose (0.31 g) and mercury(II) cyanide (0.19 g) as catalyst in a mixture of anhydrous nitromethane (1.5 ml) and benzene (1.5 ml). The mixture was stirred at 25 °C for 24 h whence t.l.c. (SiO_2; Et_2O, two developments) revealed the presence of unchanged compound (4). Another portion of acetobromoglucose (0.15 g) was added and after the mixture had been stirred for a further 6 h, the usual work-up yielded a crude product which gave, after column chromatography, Et_2O as eluant, unchanged disaccharide (4) (0.04 g) and a trisaccharide [0.52 g, 75% based on the amount of compound (4) consumed]. The trisaccharide was further purified by p.l.c. on SiO_2 with two developments with diethyl ether. Two bands were separated. The more polar band was the *title trisaccharide* (5) [0.41 g, 60% based on (4) consumed], m.p. 92—94 °C; $[\alpha]_D^{23}$ −12° (*c*, 1.95 in $CHCl_3$); δ_H (200 MHz) (fucose ring) 4.79 (d, $J_{1,2}$ 4.0 Hz, 1-H), 5.48 (dd, $J_{4,3}$ 3.4, $J_{4,5}$ 1.0 Hz, 4-H), 1.27 (d, $J_{6,5}$ 6.5 Hz, 6-H_3), 7.6—7.95 (4 H, m, ArH), and 3.39 (3 H, s, OMe); (glucose rings) 4.70 (d, $J_{1,2}$ 7.4 Hz, 1-H), 4.69 (d, $J_{1,2}$ 7.6 Hz, 1-H), 1.68, 1.92, 1.99, 2.00, 2.02, 2.08, 2.10, and 2.13 (24 H, 8 × 6, 8 × Ac), and 4.85—5.30 (total 6 H, m, 2-, 3-, and 4-H in both rings); the remaining signals at δ 3.6—3.85 (2 H, m) and 3.95—4.55 (7 H, m) were not assigned; the δ_C values are given in Table 1 [Found: $(M - OMe)^{+\cdot}$, 957. $C_{41}H_{50}NO_{25}$ requires *m/z* 957].

Methyl 2,3-*Di*-O-(β-D-*glucopyranosyl*)-α-L-*fucopyranoside* (6).—A solution of the octa-acetyltrisaccharide nitrobenzoate (5) (0.15 g) in anhydrous methanol (5 ml) was treated with sodium methoxide at 25 °C for 1.5 h. Neutralisation with Amberlite IR 120H resin, followed by the usual work-up, gave a syrup which was crystallised from diethyl ether to afford compound (6) (0.071 g, 95%), m.p. 143—145 °C; $[\alpha]_D^{23}$ −57.1° (*c*, 0.2 in MeOH); δ_H 200 MHz (D_2O) (glucose rings) 4.72 (d, $J_{1,2}$ 7.3 Hz, 1-H) and 4.75 (d, $J_{1,2}$ 7.9 Hz, 1-H); (fucose ring) 5.08 (d, $J_{1,2}$ 2.4 Hz, 1-H), 1.40 (3 H, d, $J_{6,5}$ 6.5 Hz, 6-H_3), and 3.54 (3 H, s, OMe); the δ_C values are given in Table 1.

Methyl 3,4-O-endo- and 3,4-O-exo-(2-*Nitrobenzylidene*)-2-O-(*tetra*-O-*acetyl*-β-D-*galactopyranosyl*)-α-L-*fucopyranoside* (7).—A 1 : 1 *endo–exo* mixture of the nitrobenzylidene fucoside (1) (1.7 g) was condensed, in similar manner to the preparation of compound (2), with tetra-*O*-acetyl-α-D-galactopyranosyl bromide (3.4 g) for a period of 24 h whence t.l.c. showed nearly complete reaction: R_F (7) 0.63 and R_F (1) 0.48 [SiO_2; CH_2Cl_2–EtOAc (4 : 1), two developments] column. Column chromatography with the same eluant gave a 1 : 1 *endo–exo* mixture of the nitrobenzylidene disaccharide (7) (2.7 g, 77%), m.p. 73—77 °C; $[\alpha]_D^{23}$ −70° (*c*, 2.2 in $CHCl_3$); δ_H (200 MHz) (Signals are in pairs for *endo*- and *exo*-forms, but often they remain unassigned because they are of *ca.* equal intensity) (galactose ring) 4.54 and 4.73 (total 1 H, 2 × d, $J_{1,2}$ 8.0 Hz, 1-H), 5.24 and 5.18 (total 1 H, 2 × dd, $J_{2,3}$ 9.8 Hz, 2-H), 5.10 and 5.00 (total 1 H, 2 × dd, $J_{3,4}$ 3.5 Hz, 3-H), 5.42 and 5.38 (total 1 H, 2 × dd, $J_{4,5}$ 1.5 Hz, 4-H), and 1.96, 1.99, 2.00, 2.02, 2.04, 2.08, 2.14, and 2.16 (24 H, 8 × s, 8 × Ac); (fucose ring) 4.74 and 4.64 (total 1 H, 2 × d, $J_{1,2}$ 3.5 Hz, 1-H), 1.38 and 1.40 (total 3 H, s × d, $J_{6,5}$ 6.5 Hz, 6-H_3), 3.40 and 3.42 (total 3 H, s × s, OMe), and 6.48 and 6.78 (total 1 H, 2 × s, Ar*CH*O_2, *endo*- and *exo*-form); δ_C (galactose ring) 101.4 and 100.3 (C-1, *exo*- and *endo*-form), 69.0, 71.0, 67.3 and 67.1, 71.0 61.2 (C-2 to C-6, respectively), and 20.7, 169.5, and 170.4 (4 × Ac); (fucose ring) 98.1 and 97.8 (C-1, *exo* and *endo*), 63.4 and 16.2 (C-5 and C-6, respectively), 78.1 * and 76.1,* 75.2 ** and 74.7,** and 76.6 (C-2, -3, and -4), 99.4 p.p.m. (Ar*C*HO_2 *endo* and *exo*), plus aromatic signals (Found: $(M - OMe)^{+\cdot}$, 611. $C_{27}H_{32}NO_{15}$ requires *m/z*, 611).

A sample of compound (7) (0.14 g) was hydrolysed with 10% aqueous trifluoroacetic acid (1.5 ml) during 20 min at 21 °C. The solution was then evaporated to dryness to give a material which was chromatographed on silica gel with EtOAc as eluant to yield unchanged (7) (0.15 g) R_F 0.9 and methyl 2-*O*-(tetra-*O*-acetyl-β-D-galactopyranosyl)-α-L-fucopyranoside (8) (0.09 g, 91%) R_F 0.5, $[\alpha]_D^{22}$ −32° (*c*, 0.68 in $CHCl_3$); δ_H (200 MHz) (galactose ring) 5.59 (1 H, d, $J_{1,2}$ 8.0 Hz, 1-H), 5.39 (1 H, dd, $J_{2,3}$ 10.5 Hz, 2-H), 5.03 (1 H, dd, $J_{3,4}$ 3.0 Hz, 3-H), 5.42 (1 H, dd, $J_{4,5}$ 0.7 Hz, 4-H), and 2.01, 2.07, 2.09, and 2.15 (12 H, 4 × s, 4 × Ac); (fucose ring) 4.66 (1 H, d, $J_{1,2}$ 3.0 Hz, 1-H), 1.31 (3 H, d, $J_{6,5}$ 6.5 Hz, 6-H_3), and 3.39 (3 H, s, OMe). Signals for the remaining protons are in region δ 3.8—4.3. The δ_C values are given in Table 1.

Methyl 4-O-(2-*Nitrobenzoyl*)-2-O-(*tetra*-O-*acetyl*-β-D-*galactopyranosyl*)-α-L-*fucopyranoside* (9).—A solution of the fully protected disaccharide (7) (1.1 g) in methanol (570 ml) was photolysed for 1.25 h in a Hanovia Pyrex immersion well as described above for the preparation of compound (4); the product was subsequently oxidised in the usual way with trifluoroperacetic acid to give, after work-up, *compound* (9) as a glass (1.02 g, 93%), R_F 0.28 [R_F (7) 0.56] (t.l.c., SiO_2; Et_2O); $[\alpha]_D^{21}$ +29° (*c* 1.03 in $CHCl_3$) [Found: $(M - OMe)^{+\cdot}$, 627. $C_{27}H_{32}NO_{16}$ requires *m/z* 627]; the δ_C values are given in Table 1; δ_H values are given in Table 2. Very weak signals in the 400-MHz spectrum, additional to those for compound (9) and the 3% of compound (10) recorded in Table 1, appeared at δ 1.25, 1.53, 1.97, 2.05, 2.10, 2.15, 2.17, 3.47, 3.50, 3.51, 3.52, 3.56, 4.63, 4.65, 5.43, 5.47, 5.48, 5.49, and 5.52.

A small sample of compound (7) (0.07 g) was also photolysed in methanol (40 ml) containing acetic acid (1.6 ml) and the product was then oxidised and worked up in the usual way to give a product (0.06 g) which was again essentially

* (**) Signals assigned to C-2(C-3) of *endo*- and *exo*-isomers (definitive assignment not achieved).

pure nitrobenzoate (9) with an identical 200-MHz ^{1}H n.m.r. spectrum with that of the product obtained in the original photolysis.

Methyl 3-O-(2-*Nitrobenzoyl*)-2-O-(*tetra*-O-*acetyl*-β-D-*galactopyranosyl*)-α-L-*fucopyranoside* (10).—A solution of the dihydroxy-disaccharide (8) (0.08 g, 0.16 mmol) in anhydrous pyridine (1.5 ml) was treated with freshly prepared 2-nitrobenzoyl chloride (0.2 mmol) at 20 °C for 2 h. The usual work-up gave a gum which comprised four compounds with R_F 0.54 [compound (8)], 0.77 [compound (10)], 0.85 [compound (9)], and 0.98 [presumably the 3,4-bis(nitrobenzoate)] [t.l.c., SiO_2; $CHCl_3$–MeOH (9 : 1)]. Compound (10) was freed from the other materials by p.l.c. and its ^{1}H n.m.r. spectrum was measured. The δ_H values are given in Table 2.

Methyl 4-O-(2-*Nitrobenzoyl*)-2,3-*di*-O-(*tetra*-O-*acetyl*-β-D-*galactopyranosyl*)-α-L-*fucopyranoside* (11).—The disaccharide nitrobenzoate (9) (0.14 g) was condensed, as described for the preparation of compound (5), with acetobromogalactose (0.2 g) in the presence of mercury(II) cyanide (0.13 g) in a mixture of nitromethane (0.5 ml) and benzene (0.5 ml). After 24 h at room temperature, t.l.c. (SiO_2; diethyl ether) of the reaction mixture indicated that compound (9), R_F 0.35, had been transformed into the derived product (11), R_F 0.12, which was worked up and isolated by column chromatography on silica gel with Et_2O as eluant. The pure *trisaccharide* (11) (0.17 g, 80%) had m.p. 95—96 °C; $[\alpha]_D^{23}$ −8.5° (*c*, 0.94 in $CHCl_3$); the δ_C values are recorded in Table 1; δ_H (220 MHz) (fucose ring) 4.80 (1 H, d, $J_{1,2}$ 3.8 Hz, 1-H), 5.49 (1 H, dd, $J_{4,5}$ 1.0, $J_{4,3}$ 3.0 Hz, 4-H), 1.25 (3 H, d, $J_{6,5}$ 6.0 Hz, 6-H_3), 3.41 (3 H, s, OMe), and 7.6—8.1 (4 H, m, ArH); (galactose rings) 4.68 and 4.92 (together 2 H, 2 × d, $J_{1,2}$ 8.5 Hz, 1-H), 5.0—5.35 (total 4 H, complex m, 2-H and 3-H), 5.39—5.41 (2 H, m, 4-H), and 1.68, 1.92, 1.98, 2.00, 2.02, 2.11, 2.13, and 2.14 (24 H, 8 × s, 8 × Ac); together with unassigned signals at 3.9—4.5 (total 9 H, complex m) [Found: C, 50.7; H, 5.5; N, 1.3. $C_{42}H_{53}NO_{26}$ requires C, 51.1; H, 5.4; N, 1.4%].

Methyl 2,3-*Di*-O-(β-D-*galactopyranosyl*)-α-L-*fucopyranoside* (12).—The fully protected trisaccharide (11) (0.1 g) was treated with sodium methoxide and worked up, as described for the preparation of compound (6), to give, after crystallisation from diethyl ether, the trisaccharide methyl glycoside (12) (0.072 g, 95%), m.p. 145—147 °C; $[\alpha]_D^{24}$ −26.6° (*c*, 1.0 in MeOH); δ_C values are given in Table 1; δ_H (400 MHz) (D_2O) (fucose ring) 5.16 (1 H, d, $J_{1,2}$ 3.0 Hz, 1-H), 4.39 (1 H, dd, $J_{2,3}$ 10.0 Hz, 2-H), 4.45 (1 H, dd, $J_{3,4}$ 2.5 Hz, 3-H), 4.25br (1 H, d, $J_{4,5}$ *ca.* 1.0 Hz, 4-H), 4.29br (1 H, t, $J_{5,6}$ 6.5 Hz, 5-H), 1.47 (3 H, d, $J_{6,5}$ 6.5 Hz, 6-H_3) and 3.61 (3 H, s, OMe); (galactose rings) 4.76 (d, $J_{1,2}$ 7.0 Hz, 1-H), 4.73 (d, $J_{1,2}$ 7.0 Hz, 1-H), and 3.79—4.15 (complex m). The positive ion FAB mass spectrum showed for compound (12) in glycerol $(M + Na)^+$ 525 and $(M + K)^+$ 541; for compound (12) in glycerol plus a trace of AcOH additional peaks were observed at $(M + H)^+$ 503 and $(M - OMe)^+$ 471, $C_{19}H_{34}O_{15}$ requires *m/z* 502 for $(M)^+$. The sodium was introduced during the deacetylation and the potassium originates from the KI used to set up the spectrometer.

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