The Photochemistry of Carbohydrate Derivatives. Part 7.[1] The Synthesis of Methyl 3,4-Di-*O*-(β-D-glucopyranosyl)-α-L-rhamnopyranoside from Photolabile Methyl 2,3-*O*-(2-Nitrobenzylidene)-α-L-rhamnopyranoside

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Methyl *endo/exo*-2,3-*O*-(2-nitrobenzylidene)-α-L-rhamnopyranoside (1) was glucosylated to give the fully protected β-(1 → 4)-linked disaccharide derivative (5) as an *endo/exo* mixture which, upon photolysis and oxidation gave, after chromatography, the partially protected disaccharide (15) with an unprotected 3-hydroxy group. Further glucosylation at this position gave the fully blocked trisaccharide (17) which was de-esterified to give methyl 3,4-di-*O*-(β-D-glucopyranosyl)-α-L-rhamnopyranoside (18).

Branched oligosaccharides occur in several biologically important systems.[2-4] Consequently their synthesis is of interest. Success in this type of chemistry requires a blocking–deblocking sequence which can be applied to the sugar unit at which the branch is to be formed.[3]

We have shown that 2-*O*-acetyl-[5] and 2-*O*-glycosyl-[1,6] 3,4-*O*-(2-nitrobenzylidene)pyranosides with the D-*galacto*-configuration, and 4-*O*-acetyl-2,3-*O*-(2-nitrobenzylidene)-α-L-rhamnoside,[5] can be deblocked regioselectively to give products with the equatorially orientated 3-hydroxy group unprotected.

Herein we report our findings with methyl 2,3-*O*-(2-nitrobenzylidene)-α-L-rhamnopyranoside (1) as a precursor for trisaccharides branched at the 3 and 4 positions of rhamnopyranose.[7] Other workers[8] have shown the value of analogous 2,3-*O*-benzylidene derivatives as precursors for trisaccharides branched at the 2 and 4 positions of this sugar.

Polysaccharides branched at the 3 and 4 positions of rhamnose have been found in the *O*-specific side-chain of the lipopolysaccharide of *Shigella flexneri* serotype 4b-Stammes[9] and in the capsular polysaccharides of *Klebsiella* type 9,[10] type 47,[11] and type 55.[12]

The compatibility of a 2-nitrobenzoyl group in a glucosylation reaction was ascertained with methyl 4-*O*-acetyl-2-*O*-(2-nitrobenzoyl)-α-L-rhamnopyranoside (3) which was prepared in high yield by sequential photolysis and oxidation of an *endo/exo* mixture of methyl 2,3-*O*-(2-nitrobenzylidene)-rhamnopyranoside 4-acetate (2). The 3-OH group in the rhamnoside (3) was glucosylated with acetobromoglucose as described by Flowers and Jeanloz[13] in almost quantitative yield to give preponderantly the β-linked disaccharide (4) as expected for this method. The stereochemistry was ascertained by the 8.0 Hz splitting of the anomeric proton doublet at δ_H 4.65, and a signal at δ_C 101.2 p.p.m. arising from the anomeric carbon of the glucose moiety, which the values in the Table[14-16] show are in close agreement with the spectra of methyl β-D-glucopyranoside tetra-acetate. A doublet of doublets (J 1.5 and 4.5 Hz) at δ_H 5.48 and a signal at δ_C 98.0 p.p.m. arising from 2-H and C-1, respectively, of the rhamnose unit were also present, and these were virtually identical with the corresponding signals of compounds (3), which indicates that the ester function is unchanged at C-2 of rhamnose and thus deshields 2-H, and also shields C-1 by the β-ester effect.[19]

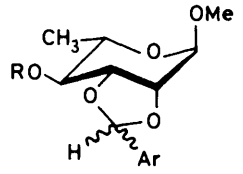
Therefore compound (1) was considered to be a satisfactory starting material for the synthesis of trisaccharides linked at the 3 and 4 positions of rhamnose. The *endo/exo*-nitrobenzylidene rhamnoside (1) was condensed with acetobromoglucose to give a crystalline disaccharide (5) as an *endo/exo* mixture. The ^{1}H and ^{13}C n.m.r. spectra clearly indicated that the gross structure of the material was as anticipated. However, the former spectrum gave no information on the anomeric configuration of the disaccharide linkage. On the other hand the ^{13}C n.m.r. spectrum was more informative. The anomeric carbon of the rhamnopyranoside unit resonated at δ_C 97.6 p.p.m. which is consistent with the C-1 resonance of compound (1). The acetylated glycopyranose C-1 signal at δ_C 99.6 p.p.m. was in closer agreement with the anomeric carbon resonance of methyl tetra-*O*-acetyl-β-D-glucopyranoside than with that of its anomer [see compounds (19) and (20) in the Table] and the nitrobenzylidene acetal carbon signals for the *endo*- and *exo*-isomer were at δ_C 99.4 and 99.0 p.p.m., in similar relative positions to the acetal carbon signals of the benzylidene analogues,[20] but shielded by the *ortho*-nitro substituent.[21] In consequence the anomeric region of the ^{13}C n.m.r. spectrum of compound (5) was rather complex and the presence of traces of the α-anomer could not, at this stage, be completely ruled out.

Mild hydrolysis of compound (5) removed the nitrobenzylidene group and gave the dihydroxydisaccharide tetra-acetate (6) which possessed a very clean ^{13}C n.m.r. spectrum (Table). It exhibited only two anomeric carbon signals, at δ_C 100.7 and 101.1 p.p.m., thus confirming the anomeric purity of the disaccharide, and it further indicated, when compared with the spectra of the β-glucoside tetra-acetate (19) and 4-*O*-methyl-α-rhamnopyranoside (21),[17] the presence of both a β-glucosidic and an α-rhamnosidic linkage.

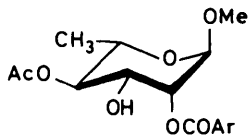
The anomeric proton signals of compound (5) were obscured by the acetoxymethine proton signals. Consequently, compound (5) was deacetylated to give the crystalline *endo/exo*-nitrobenzylidene disaccharide (7) which exhibited two pairs of anomeric doublets with $J_{1,2}$ values of 7.5 and 1.0 Hz indicating that the glucose had a β-linkage to the α-rhamnoside ring. Thus our original assumption that only disaccharide (5) with a β-linkage had been formed is supported by these spectroscopic observations.

The *endo/exo O*-nitrobenzylidene disaccharide tetra-acetate (5) was partially deblocked by irradiating it as a methanol solution and oxidizing the crude nitrosobenzoate formed with trifluoroperacetic acid at 0 °C in dichloromethane as described in our earlier work.[1] This gave two nitrobenzoates which t.l.c. suggested were present in a 1 : 1 ratio, a conclusion supported by the equal intensities of two methoxy group signals in the ^{1}H n.m.r. spectrum of the crude product.

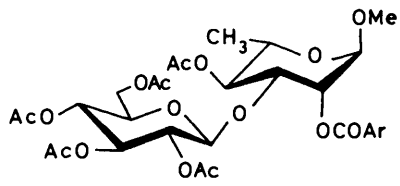
An attempt to increase the proportion of one product was made by changing the conditions of irradiation, while keeping the oxidation method constant. It is known that the conditions used for oxidation do not cause isomerisation (see



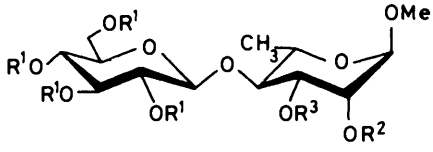
(1) R = H
(2) R = Ac



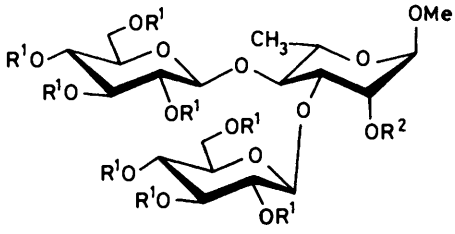
(3)



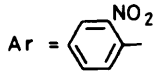
(4)



(5) R^1 = Ac, R^2R^3 = CHAr
(6) R^1 = Ac, R^2 = R^3 = H
(7) R^1 = H, R^2R^3 = CHAr
(8) R^1 = Me, R^2R^3 = CHAr
(9) R^1 = Ac, R^2R^3 = CMe_2
(10) R^1 = H, R^2R^3 = CMe_2
(11) R^1 = Me, R^2R^3 = CMe_2
(12) R^1 = Me, R^2 = R^3 = H
(13) R^1 = Me, R^2 = COAr, R^3 = H
(14) R^1 = Me, R^2 = H, R^3 = COAr
(15) R^1 = Ac, R^2 = COAr, R^3 = H
(16) R^1 = Ac, R^2 = H, R^3 = COAr



(17) R^1 = Ac, R^2 = COAr
(18) R^1 = R^2 = H



below). Irradiation of the disaccharide (5) in methanol at −70 °C and in dimethyl sulphoxide (DMSO) at 25 °C had little effect upon the composition of the product. Irradiation of a methanol solution to which 4% triethylamine had been added caused extensive degradation of compound (5). However, with 4% acetic acid added to the methanol, compound (5) gave, upon irradiation and sequential oxidation, the same two nitrobenzoates, which were estimated to be present in the ratio 4 : 1. Consequently, the disaccharide (5) was irradiated on a preparative scale under these conditions and the nitrosobenzoates so formed were oxidized to give, upon work-up, the two nitrobenzoyl disaccharides (15) and (16) in 80% yield which were separated chromatographically into crystalline forms in 60 and 14% yield, respectively.

The ^1H and ^{13}C n.m.r. spectra of the preponderant isomer indicated that it was the pure 2-nitrobenzoate (15). Six carbon resonances could be assigned to the C-1 to -6 atoms of a tetra-*O*-acetyl-β-D-glucopyranoside unit (see Table) which indicated that this moiety had remained intact. The rhamnose anomeric carbon resonance at δ_C 97.7 p.p.m., which was shielded compared with the corresponding carbon signal in the disaccharide diol (6), indicated [19] that an ester group was at C-2 in the rhamnose ring. The lowest field glycose proton signal at δ_H 5.32 could be assigned to the hydrogen attached to the carbon carrying the nitrobenzoyloxy group and since it was a narrow doublet of doublets with splittings of $J_{1,2}$ 1.0 and $J_{2,3}$ 3.5 Hz it was identified as 2-H of the rhamnose ring. Thus the major product was the partially protected disaccharide (15) in which the axial hydroxy group of the rhamnose ring was esterified, as was expected to occur in the photochemical rearrangement.[1,5,6]

The ^{13}C n.m.r. spectrum for the minor isomer (see Table) indicated that it had structure (16). The site of isomerisation was shown not to be in the glucopyranosyl ring since the C-1 to -6 resonances for this moiety were readily identified with those of the corresponding carbons in compounds (15) and (19) (Table). The rhamnose anomeric carbon signal at δ_C 100.6 p.p.m. was deshielded compared with that of the 2-*O*-nitrobenzoyl derivatives (3), (4), and (15), which indicated that the ester function was not at C-2.[19] Thus the nitrobenzoyloxy group must be at C-3, which is borne out by the ^1H n.m.r. spectrum. This clearly shows a doublet of doublets of one-proton intensity at δ_H 5.41, downfield from all the other glycose protons. The splittings of 3.5 and 8.5 Hz measured for this signal would be expected for $J_{3,2}$ and $J_{3,4}$ of 3-H in rhamnose.

The non-regiospecific photochemical opening of the nitrophenyl dioxolan ring had not been anticipated from our earlier work.[1,5,6] Migration of the aroyl group during oxidation with peracid was not expected [5] to be responsible for the lack of stereospecificity, a point verified when it was shown that pure samples of the compounds (15) and (16) were stable under the oxidation conditions.

Migration of an acetyl group from the glucopyranose to the rhamnose ring appeared improbable from the ^{13}C n.m.r. evidence, and this point was further substantiated by the reaction of the tetra-*O*-methyl nitrobenzylidene disaccharide (8) which had non-migrating methyl groups in the glucopyranosyl ring. It also afforded two products when subjected to the photolysis–oxidation sequence and the ^1H n.m.r. spectrum clearly showed them to be the isomeric 2- and 3-nitrobenzoyl disaccharide (13) and (14), respectively.

Thus the opening of the 2,3-*O*-nitrobenzylidene ring in methyl L-rhamnopyranoside derivatives appears to be sensitive to the substituent present at O-4. An acetyl group at O-4, as we have shown, gives only the 2-nitrobenzoyl ester,

Table. ^{13}C Chemical shifts of some glucosylrhamnose derivatives measured at 15 MHz in $CDCl_3$ relative to TMS

Compound	Carbon atom	Glucose 1	2	3	4	5	6	(MeO) *Me*CO	Rhamnose 1	2	3	4	5	6	MeO (*Me*CO)
β-D-Glc*p*Ac$_4$-(1 → 4)-α-L-Rha*p*1Me	(6)	101.1	71.5 [c]	72.9	68.9	71.7 [c]	62.2	20.7	100.7	71.2 [c]	71.0 [c]	81.2	66.1	17.7	54.7
β-D-Glc*p*Ac$_4$-(1 → 4)-α-L-Rha*p*2COAr1Me	(15)	101.4	71.6 [c]	73.0	68.7	71.8 [c]	62.1	20.7	97.7	74.9	69.9	81.3	66.7	17.5	55.1
β-D-Glc*p*Ac$_4$-(1 → 4)-α-L-Rha*p*3COAr1Me	(16)	100.6	71.2 [c]	72.7	68.6	71.9 [c]	62.1	20.6	100.6	68. 6	76.6	76.6	66.6	17.6	55.1
β-D-Glc*p*Ac$_4$-(1 → 3)-α-L-Rha*p*4Ac2COAr1Me	(4)	101.2	71.2 [c]	72.8	68.5	71.7 [c]	61.6	20.7	98.0	69.9 [c]	75.0 [c]	72.5 [c]	66.0	17.3	55.1 (20.7)
β-D-Glc*p*Ac$_4$-(1 → 4)-α-L-Rha2COAr1Me	(17) [a]	101.6	72.1	73.4	68.9	72.2	62.1	20.6	97.7	74.2	75.8	78.5	66.9	17.8	55.0
β-D-Glc*p*Ac$_4$-(1 → 3)-α-L-Rha2COAr1Me	(17) [a]	99.9	71.6	73.2	68.5	72.2	62.0								
α-L-Rha*p*4Ac2COAr1Me	(3)								97.9	74.6 [c]	68.5 [d]	74.2 [c]	65.9 [d]	17.3	55.2 (20.9)
β-D-Glc*p*Ac$_4$1Me	(19) [14,15]	101.7	71.6	73.1	68.8	72.1	62.2	20.5 (56.9)							
α-D-Glc*p*Ac$_4$1Me	(20) [14,16]	97.0	71.0	70.3	68.9	67.5	62.2	20.6 (55.6)							
α-L-Rha*p*1,4Me$_2$	(21) [17,b]								101.0	71.4	71.3	83.4	67.4	18.0	60.5, 54.8
β-D-Glc*p*1Me	(22) [18,b]	104.3	74.2	76.9	70.8	76.9	61.9	(58.3)							
α-D-Glc*p*1Me	(23) [18,b]	100.3	72.5	74.2	70.6	72.7	61.7	(56.2)							
α-L-Rha*p*1Me	(24) [18,b]								101.9	71.0	71.3	73.1	69.4	17.7	55.8
β-D-Glc*p*-(1 → 4)-α-L-Rha*p*1Me	(18) [a,b]	104.4	74.5	77.0	70.7	76.7	61.4		101.3	70.2	78.9	81.4	67.9	17.8	55.6
β-D-Glcp-(1 → 3)-α-L-Rha*p*1Me	(18) [a,b]	103.4	74.2	76.8	70.5	76.7	61.3								

Ar = 2-Nitrophenyl

Compounds: methyl 2,3,4,6-tetra-*O*-acetyl-D-glucopyranoside, α-form (20), β-form (19); methyl 4-*O*-methyl-α-L-rhamnopyranoside (21); methyl D-glucopyranoside, α-form (23), β-form (22); methyl α-L-rhamnopyranoside (24).

[a] When two identical glycoses are present, assignment of a set of resonances to a particular ring is not possible; thus some signals are interchangeable. [b] Measurements made in D_2O with dioxan as internal standard taken to have δ_C 67.4 p.p.m. relative to TMS. [c,d] Signals could be interchanged.

whereas disaccharides which form an ether linkage at O-4 give both 2- and 3-esters. This neighbouring group effect, which has not been observed [1,6] with various 2-*O*-substituted 3,4-*O*-nitrobenzylidene fucopyranosides, is currently under investigation.

β-Glucosylation of the 3-hydroxy group in the disaccharide (15) was readily achieved as anticipated from the preliminary experiment. The fully protected 3,4-di-*O*-(β-D-glucosyl)-rhamnoside (17) was isolated, after chromatography, in 70% yield. The ^{13}C n.m.r. spectrum (Table) showed three signals at δ_C 101.6, 99.9, and 97.7 p.p.m., respectively for the anomeric carbons of two β-linked tetra-*O*-acetylglucopyranoside rings and a 2-*O*-nitrobenzoyl-α-rhamnopyranoside. These were assigned by comparison with the signals recorded in the Table from the corresponding carbons of compounds (19), (20), and (3). A pair of anomeric proton doublets in the ^1H n.m.r. spectrum of (17), coupled by 7.5 Hz, at δ_H 4.55 and 4.78 confirm that the glucopyranoses are β-linked to rhamnose and the low-field signal at δ_H 5.79 ($J_{2,1}$ 1.0, $J_{2,3}$ 3.5 Hz) substantiates our assumption that the nitrobenzoyl group is at O-2 and in consequence that the saccharides are linked to O-3 and O-4.

A crystalline trisaccharide methyl glycoside was obtained in 95% yield upon de-esterification of the fully blocked trisaccharide (17). It was shown to be methyl 3,4-di-*O*-(β-D-glucopyranosyl)-α-L-rhamnopyranoside (18). The ^1H n.m.r. spectrum exhibited two anomeric proton signals for the β-glucose rings at δ_H 4.89 and 5.03, with $J_{1,2}$ 7.3 and 7.8 Hz, and one for the α-rhamnose ring at δ_H 4.91, with $J_{1,2}$ 1.9 Hz. The ^{13}C n.m.r. spectrum showed the related carbons at δ_C 104.4, 103.4, and 101.3 p.p.m. There were ten resonances for the remaining glucose carbons and five for the rhamnose ring carbons, the C-6 signal at δ_C 17.8 p.p.m. being very diagnostic and readily confirmed by the δ_H 1.57 doublet, $J_{6,5}$ 6.0 Hz. The methyl aglycone gave prominent signals at δ_C 55.6 p.p.m. and δ_H 3.49.

Experimental

^1H N.m.r. spectra were usually measured in $CDCl_3$ with Jeol M100 or Varian HA200 CW instruments or a Jeol FX200 FT instrument. Natural-abundance ^{13}C n.m.r. spectra were determined with a Jeol FX60 FT instrument operating at 15 MHz, usually for $CDCl_3$ solutions, with tetramethylsilane (TMS) as internal standard, or in D_2O with dioxan as standard. All δ_C values were recorded with reference to TMS. The low-resolution mass spectra were measured by the PCMU, Harwell with a VG Micromass ZAB IF spectrometer. Optical rotations were measured with an Optical Activity polarimeter model A100.

Methyl 4-O-*Acetyl*-2-O-(2-*nitrobenzoyl*)-3-O-(2,3,4,6-*tetra*-O-*acetyl*-β-D-*glucopyranosyl*)-α-L-*rhamnopyranoside* (4).—Methyl 4-*O*-acetyl-*endo*/*exo*-2,3-*O*-(2-nitrobenzylidene)-α-L-rhamnopyranoside (2) (0.2 g) [δ_C ($CDCl_3$) 97.7 (C-1), 99.9 and 99.3 p.p.m. (ArCH, *endo* and *exo* isomers)] was irradiated and sequentially oxidized to give the 3-hydroxy-2-nitrobenzoate (3) [5] (0.2 g, 0.54 mmol), δ_H (200 MHz FT) 4.81 (d, $J_{1,2}$ 1.5 Hz, 1-H), 5.34 (dd, $J_{2,3}$ 4.3 Hz, 2-H), 4.1 (dd, $J_{3,4}$ 9.5 Hz, 3-H), 4.78 (t, $J_{4,5}$ 9.5 Hz, 4-H), 3.81 (dt, $J_{5,6}$ 5.6 Hz, 5-H), 1.21 (d, $J_{6,5}$ 5.6 Hz, 6-H_3), 2.10 (3 H, s, AcO), 3.40 (3 H, s, OMe), and 7.6—7.9 (4 H, m, Ar); δ_C, see Table.

The 3-ol (3) was glycosylated [13] with acetobromoglucose (0.2 g, 0.58 mmol) in a stirred, anhydrous mixture of nitromethane (1.5 ml) and benzene (1.5 ml) containing mercury(II) cyanide (0.14 g, 0.56 mmol) at 25 °C. After 24 h, t.l.c. revealed the presence of unchanged compound (3). Consequently, a further portion of acetobromoglucose (0.24 g) was added and after a further period of 24 h the mixture was worked up to give a crude product which was fractionated by column chromatography on silica gel with Et_2O–light petroleum (40—60 °C) (9 : 1) as eluant. This gave unchanged (3) (0.05 g recovery) and a disaccharide mixture (0.26 g, 91%) which was separated by preparative layer chromatography (p.l.c.) into two components, ratio 1 : 3, with R_F 0.3 and 0.26 respectively, after two developments with the usual solvent. The major component was the β-disaccharide (4), $[\alpha]_D^{23}$ −35° (*c*, 0.98 in $CHCl_3$); δ_H (220 MHz CW; $CDCl_3$) (rhamnose ring) 4.83 (d, $J_{1,2}$ 1.5 Hz, 1-H), 5.48 (dd, $J_{2,1}$ 1.5, $J_{2,3}$ 4.5 Hz, 2-H), 1.17 (d, $J_{6,5}$ 6.0 Hz, 6-H_3), 3.43 (3 H, s, OMe), 7.55—8.0 (4 H, m, Ar); (glucose ring) 4.65 (d, $J_{1,2}$ 8.0 Hz, 1-H), 5.2—4.9 (4 H, m, unassigned), 4.4—3.6 (5 H, unassigned) and 1.98, 2.01, 2.02, 2.06, and 2.10 (each 3 H, s, AcO); δ_C, see Table [Found: *m*/*z* 669 (*M* −OMe). $C_{29}H_{34}NO_{17}$ requires *m*/*z* 669].

The minor component, $[\alpha]_D$ +16.6° (*c*, 1.1 in $CHCl_3$), which was not pure was believed to be mainly the α-glucosyl anomer of (4) as determined from the ^{13}C n.m.r. spectrum which showed two anomeric carbons at δ_C 97.9 and 94.6 p.p.m.

Methyl endo/exo-2,3-O-(2-*Nitrobenzylidene*)-4-O-(2,3,4,6-*tetra*-O-*acetyl*-β-D-*glucopyranosyl*)-α-L-*rhamnopyranoside* (5).—Methyl *endo*/*exo*-2,3-*O*-(2-nitrobenzylidene)-α-L-rhamnopyranoside (1) [δ_C 97.7 (C-1), 99.4 and 99.2 p.p.m. (ArCH, *endo* and *exo* isomers)] (5.0 g, 16 mmol) was condensed with acetobromoglucose (10.0 g, 24 mmol) in a mixture of anhydrous nitromethane (10 ml) and benzene (10 ml) containing mercury(II) cyanide (4.1 g, 16 mmol) at 23 °C. After 24 h, t.l.c. [light petroleum (40—60 °C)–EtOAc (2 : 1)] indicated that compound (1), R_F 0.5, had reacted to give a product with R_F 0.4. The mixture was worked up in the usual fashion to produce material which crystallised slowly from diethyl ether to give a 2 : 3 mixture of the endo/exo *nitrobenzylidene disaccharide* (5) (8.8 g, 85%), m.p. 58—60 °C; $[\alpha]_D^{23}$ −7.4° (*c*, 3.0 in $CHCl_3$); δ_C ($CDCl_3$) 99.6, (71.3 and 71.5), (73.2 and 72.9), 68.6, 71.7, and (62.0 and 61.6) p.p.m., (respectively C-1 to -6 of glucose ring); 97.6, 76.9, 74.9, 79.1, 63.5, and 17.4 p.p.m. (C-1 to -6 of rhamnose ring); 99.0 and 99.4 (Ar*C*H of two isomers), and 20.5 p.p.m. (*C*H_3CO), plus signals for aromatic and carbonyl carbons. Most carbons of the *endo* and *exo* isomers give coincident signals; δ_H ($CDCl_3$) 1.32 and 1.18 (total 3 H, 2 × d, 6-H_3 *exo* and *endo*), 2.00 and 2.30 (total 12 H, 4 × AcO), 3.26 and 3.28 (total 3 H, 2 × s, OMe *exo* and *endo*), 3.4—5.3 (12 H, m), 6.38 and 6.56 (total 1 H, 2 × s, Ar*CH endo* and *exo*), and 7.4—7.9 (4 H, m, Ar) [Found: C, 52.3; H, 5.4; N, 2.1%; *m*/*z*, 611 (*M* − OMe). $C_{28}H_{35}NO_{16}$ requires C, 52.4; H, 5.5; N, 2.2%; $C_{27}H_{32}NO_{15}$ requires *m*/*z* 611].

The disaccharide (5) was also prepared by the Hanessian method.[22] The partially protected rhamnoside (1) (1.2 g, 4 mmol) was condensed under nitrogen with acetobromoglucose (1.9 g, 4.7 mmol) in dichloromethane (23.5 ml) containing silver trifluoromethanesulphonate (1.2 g, 4.7 mmol) and tetramethylurea (1.3 ml, 11.8 mmol) at 23 °C for 4 h. The mixture was then worked up in the usual way to give, after chromatography, unchanged (1) (0.16 g) and the disaccharide (5) (1.41 g, 65% conversion).

Methyl 4-O-(2,3,4,6-*Tetra*-O-*acetyl*-β-D-*glucopyranosyl*)-α-L-*rhamnopyranoside* (6).—The fully blocked disaccharide (5) (0.5 g) was hydrolysed with 10% aqueous trifluoroacetic acid (5 ml) at 23 °C during 15 min. The solution was evaporated and then benzene was added and re-evaporated to give the dihydroxy tetra-acetate (6) (0.36 g, 90%), $[\alpha]_D^{23}$ −31.4° (*c*, 2.4 in $CHCl_3$); δ_C, see Table; δ_H ($CDCl_3$) 1.28 (3 H, d, *J* 6.0 Hz, 6-H_3), 1.96, 2.00, 2.04, and 2.05 (total 12 H, 4 × s,

4 × AcO), 3.30 (3 H, s, OMe), 4.60 (1 H, d, $J_{1,2}$ 1.0 Hz, Rha 1-H), 3.35—4.25 (9 H), and 4.65—5.25 (4 H).

Methyl 4-O-(β-D-*Glucopyranosyl*)-endo/exo-2,3-O-(2-*nitrobenzylidene*)-α-L-*rhamnopyranoside* (7).—The fully protected disaccharide (5) (0.5 g) was treated in methanol with a catalytic amount of sodium methoxide for 1.5 h at 23 °C. The usual work-up gave the endo/exo-*nitrobenzylidenated disaccharide* (7) (0.33 g, 90%), m.p. 87 °C; $[\alpha]_D^{23}$ −41.2° (*c*, 1.85 in $CHCl_3$); δ_H (DMSO–D_2O) 1.10 and 1.20 (total 3 H, 2 × d, $J_{6,5}$ 5.5 Hz, 6-H_3, *endo* and *exo*), 3.2 (3 H, s, OMe), 4.82 and 4.86 (total 1 H, 2 × d, $J_{1,2}$ 1.0 Hz, Rha 1-H, *endo* and *exo*), 4.42 and 4.52 (total 1 H, 2 × d, $J_{1,2}$ 7.5 Hz, Glc 1-H, *endo* and *exo*), and 6.24 and 6.44 [total 1 H, 2 × s (2 : 3), ArC*H*, *endo* and *exo*] (Found: C, 48.7; H, 5.7; N, 2.6. $C_{20}H_{27}NO_{12}$, H_2O requires C, 48.9; H, 5.9; N, 2.9%).

Irradiation and *Subsequent Oxidation* of *Methyl* endo/exo-2,3-O-(2-*Nitrobenzylidene*)-4-O-(2,3,4,6-*tetra*-O-*acetyl*-β-D-*glucopyranosyl*)-α-L-*rhamnopyranoside* (5).—A solution of the nitrobenzylidenated disaccharide (5) (0.5 g) in methanol (200 ml) containing acetic acid (8 ml) was agitated by the passage of nitrogen and irradiated through Pyrex with a 450-W medium-pressure mercury lamp in the annular space of a conventional photochemical well. After 45 min, t.l.c. indicated that all compound (5) had reacted and the solution was evaporated to give a residue which was dissolved in dichloromethane (35 ml) and oxidized with trifluoroperacetic acid at 0 °C during 1.5 h. The solution was washed in turn with water, aqueous sodium hydrogen carbonate, and water, and dried. Evaporation gave a solid (0.41 g, 80%), comprising two components with R_F 0.45 and 0.36 [CH_2Cl_2–EtOAc (4 : 1)] which were separated by chromatography. The more mobile component was the 2-nitrobenzoate (15) (0.31 g, 60%), m.p. 185 °C (from diethyl ether); $[\alpha]_D^{23}$ −49.9° (*c*, 1.8 in $CHCl_3$) [Found: N, 1.8%; *m/z* 627 (*M* − OMe). $C_{28}H_{35}NO_{17}$ requires N, 2.1%; $C_{27}H_{32}NO_{16}$ requires *m/z* 627]; δ_H (220-MHz CW; $CDCl_3$) (glucose ring) 4.88 (1 H, d, $J_{1,2}$ 7.8 Hz, 1-H), 5.22 and 4.92—5.15 (1 H t and 2 H m, respectively 2-H and 3- and 4-H), 2.00, 2.02, 2.06, and 2.07 (total 12 H, 4 × s, 4 × AcO); (rhamnose ring) 4.70 (1 H, d, $J_{1,2}$ 1.0 Hz, 1-H), 5.32 (1 H, dd, $J_{2,1}$ 1.0 and $J_{2,3}$ 3.5 Hz, 2-H), 1.29 (3 H, d, $J_{6,5}$ 6.0 Hz, 6-H_3), 3.38 (3 H, s, OMe), 7.65—7.95 (4 H, m, ArH), and 2.3 (1 H, br s, OH); (unassigned) 3.4—3.5 (1 H, m), 3.6—3.9 (2 H, m), 4.0—4.15 (1 H, m), and 4.15—4.3 (2 H, m); δ_C, see Table.

The minor component was the 3-nitrobenzoate (16) (0.07 g, 14%), m.p. 188 °C (from diethyl ether); $[\alpha]_D^{23}$ +17.5° (*c*, 2.0 in $CHCl_3$) [Found: N, 1.8%; *m/z* 627 (*M* − OMe). $C_{28}H_{35}NO_{17}$ requires N, 2.1%; $C_{27}H_{32}NO_{16}$ requires *m/z*, 627]; δ_H (220 MHz CW; $CDCl_3$) (glucose ring) 4.62 (1 H, d, $J_{1,2}$ 7.5 Hz, 1-H), 4.8—5.2 (3 H, m, 2-, 3-, and 4-H), 2.00, 2.01, 2.03, and 2.06 (total 12 H, 4 × s, 4 × AcO); (rhamnose ring) 4.72 (1 H, d, $J_{1,2}$ 1.0 Hz, 1-H), 5.41 (1 H, dd, $J_{3,2}$ 3.5 and $J_{3,4}$ 8.5 Hz, 3-H), 1.33 (3 H, d, $J_{6,5}$ 6.5 Hz, 6-H_3), 3.42 (3 H, s, OMe), 2.45 (1 H, br s, OH); (unassigned) 3.52—3.95 (3 H, m), and 4.05—4.40 (3 H, m); δ_C, see Table.

Preparation and Sequential Irradiation–Oxidation of Methyl endo/exo-2,3-O-(2-*Nitrobenzylidene*)-4-O-(2,3,4,6-*tetra*-O-*methyl*-β-D-*glycopyranosyl*)-α-L-*rhamnopyranoside* (8).—Methyl 2,3-*O*-isopropylidene-α-L-rhamnopyranoside (5.0 g, 22 mmol) was condensed with acetobromoglucose (9.9 g, 24 mmol) as described for the 2,3-*O*-nitrobenzylidenated compound to give the β-*linked disaccharide* (9) (10.6 g, 85%), m.p. 156 °C; δ_H 1.29, and 1.46 (total 6 H, 2 × s, Me_2C), 1.9—2.0 (total 12 H, m, 4 × AcO), and 3.29 (3 H, s, OMe); δ_C 99.5, and 97.7 p.p.m. (anomeric carbons) (Found: C, 52.6; H, 6.6. $C_{24}H_{36}O_{14}$ requires C, 52.6; H, 6.6%).

Compound (9) (2 g) was deacetylated by the Zemplen method and the tetraol (10) (1.3 g, 93%) thus obtained was treated with iodomethane (7 ml) and sodium hydride (0.7 g) in tetrahydrofuran (25 ml) at 80 °C for 8 h to give, in 88% yield, the tetramethyl ether of the isopropylidenated disaccharide, compound (11), δ_C 101.4 and 98.1 (anomeric carbons), 109.2, 27.8, and 26.4 (isopropylidene), and 54.7, 59.5, 60.2, 60.4, and 60.6 p.p.m. (5 × MeO).

Deisopropylidenation of compound (11) (1.0 g) with aqueous trifluoroacetic acid gave the diol (12) (0.9 g, 99%), δ_C 103.7, 86.9, 84.5, 79.8, 74.7, and 71.5 (6 C for Glc), 100.8, 72.0, 71.0, 82.8, 66.8, and 17.5 (6 C for Rha), and 60.9, 60.7, 60.3, 59.4, and 54.8 p.p.m. (5 × OMe), which was condensed with 2-nitrobenzaldehyde to give the *exo* and *endo* isomers of the fully protected disaccharide (8), δ_H 4.80 and 4.74 (total 1 H, 2 × d, $J_{1,2}$ 1.0 Hz, Rha 1-H, both isomers), 4.58 and 4.34 (total 1 H, 2 × d, $J_{1,2}$ 7.5 Hz, Glc 1-H, both isomers), 1.2 and 1.3 (total 3 H, 2 × s, $J_{6,5}$ 6.0 Hz, 6-H_3, both isomers), 6.50 and 6.26 (total 1 H, 2 × s ArC*H*, ratio 1 : 4 *exo* : *endo*), plus multiplets for other protons; δ_C (*endo*-form) 101.1 and 97.7 (C-1 of glucose and rhamnose, respectively), 99.4 (ArCH); (*exo*-form) 101.6 and 97.7 (C-1 glucose and rhamnose), and 98.9 p.p.m. (ArCH).

A solution of methyl *endo/exo*-2,3-*O*-(2-nitrobenzylidene)-4-*O*-(2,3,4,6-tetra-*O*-methyl-β-D-glucopyranosyl)-α-L-rhamnopyranoside (8) (0.11 g) in methanol (40 ml) was irradiated for 45 min and then oxidized as described above. This gave a product which was shown by t.l.c. [C_6H_6–EtOAc (2.7 : 1.0)] to contain two components in a *ca.* 1 : 1 ratio: δ_H (C_6D_6) 5.50 (0.44 H, dd, $J_{2,1}$ 1.0 and $J_{2,3}$ 2.5 Hz, 2-H, Rha) and 5.80 (0.56 H, dd $J_{3,2}$ 2.5 and $J_{3,4}$ 8.0 Hz, 3-H, Rha) for signals arising from the 2- and 3-nitrobenzoyl disaccharides (13) and (14), respectively, 2.79—3.20 (total 15 H, 10 × s, 5 × MeO from each isomer), 4.27 (*ca.* 0.5 H, d, $J_{1,2}$ 1.0 Hz), 4.60 (*ca.* 0.5 H, d, $J_{1,2}$ 1.0 Hz) (Rha 1-H from each isomer), and 1.5 (3 H, d, $J_{6,5}$ 6.0 Hz, 6-H_3).

Methyl 2-O-(2-*Nitrobenzoyl*)-3,4-*di*-O-(2,3,4,6-*tetra*-O-*acetyl*-β-D-*glucopyranosyl*)-α-L-*rhamnopyranoside* (17).—The disaccharide (15) (0.2 g) was stirred with acetobromoglucose (0.13 g) and mercury(II) cyanide (0.08 g) in a mixture of nitromethane (1.5 ml) and benzene (1.5 ml) under anhydrous conditions. After 24 h, t.l.c. showed unchanged (15), therefore a further portion of acetobromoglucose (0.06 g) was added. After a further 10 h the mixture was worked up in the usual way and chromatographed to give compound (15) (0.03 g recovery) and a mixture of trisaccharides (0.23 g, 88%).

The crude trisaccharide was fractionated by p.l.c. [Et_2O–light petroleum (40—60 °C) (9 : 1) as eluant] to give, as the more mobile component, the ββ-*linked trisaccharide* (17) (0.18 g, 70%), m.p. 85—87 °C; $[\alpha]_D^{24}$ −28.7° (*c*, 1.0 in $CHCl_3$); δ_H (220-MHz CW; C_6D_6), 1.52 (3 H, d, $J_{6,5}$ 6.5 Hz, 6-H_3), 1.60, 1.63, 1.64, 1.68, 1.69, 1.70, 1.75, and 1.90 (total 24 H, 8 × s, 8 × AcO), 2.98 (3 H, s, OMe), 4.55 4.98 (total 2 H, 2 × d, $J_{1,2}$, 7.5 Hz, 1-H of each Glc), 5.02 (1 H, d, $J_{1,2}$ 1.5 Hz, Rha 1-H), and 5.79 (1 H, dd, $J_{2,1}$ 1.0 and $J_{2,3}$ 3.5 Hz, Rha 2-H); δ_C, see Table [Found: C, 51.4; H, 5.6; N, 1.4%; *m/z* 957 (*M* − OMe). $C_{42}H_{53}NO_{26}$ requires C, 51.1; H, 5.4; N, 1.4%; $C_{41}H_{50}NO_{25}$ requires *m/z*, 957].

The less mobile component from p.l.c. was a by-product of the reaction, believed to be the β,α-linked trisaccharide (0.03 g, 12%).

Methyl 3,4-*Di*-O-(β-D-*glucopyranosyl*)-α-D-*rhamnopyranoside* (18).—The fully esterified trisaccharide (17) (0.15 g) was treated with sodium methoxide in methanol for 1.5 h at 25 °C. The solution was filtered, neutralised with Amberlite IR 120H$^+$ resin, filtered, and evaporated to give a syrup

which was triturated with chloroform to remove the methyl nitrobenzoate. The residue was crystallised from diethyl ether to give the hygroscopic methyl glycoside of the deblocked trisaccharide, compound (18) (0.072 g, 95%), m.p. 145—147 °C; $[\alpha]_D^{24}$ −26.6° (*c*, 1.0 in MeOH); δ_H (200-MHz FT; D_2O; at 50 °C to shift the interfering HOD signal) (rhamnose ring) 1.57 (3 H, d, $J_{6,5}$ 6.0 Hz, 6-H_3), 4.91 (1 H, d, $J_{1,2}$ 1.9 Hz, 1-H), 3.49 (3 H, s, OMe); (glucose rings) 4.89 (1 H, d, $J_{1,2}$ 7.3 Hz, 1-H) and 5.03 (1 H, d, $J_{1,2}$ 7.8 Hz, 1-H); δ_C, see Table.

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