The Photochemistry of Carbohydrate Derivatives. Part 6.[1] Synthesis of 3-(Methoxycarbonyl)propyl Pyranosides of 2,3-Di-*O*-(β-D-galactopyranosyl)-α-D-galactose and 3-*O*-(α-D-Galactopyranosyl)-2-*O*-(β-D-galactopyranosyl)-α-D-galactose using Photolabile *O*-(2-Nitrobenzylidene) Acetals as Temporary Blocking Groups

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The branched trisaccharide glycosides (7) and (8) named in the title have been prepared from 3-(methoxycarbonyl)propyl 3,4-*O*-(2-nitrobenzylidene)-6-*O*-pivaloyl-α-D-galactopyranoside (2). Galactosylation of compound (2) afforded the fully protected β-galactosyl-α-galactoside derivative (3) which upon sequential photolysis and oxidation was regioselectively converted into the partially blocked 4-*O*-(2-nitrobenzoyl)disaccharide (4). Further galactosylation of compound (4) gave a mixture of equal amounts of the di-(β-galactosyl)-α-galactoside derivative (5) and the β-galactosyl-α-galactosyl-α-galactoside derivative (6) which were separated, and these yielded the title compounds upon subsequent deacylation.

Branched polysaccharides occur in many biological systems and consequently there is a great deal of interest in their synthesis.[2-4] As has already been pointed out,[3] one of the problems in all the approaches to their synthesis is the development of a partial blocking–deblocking sequence for the central monosaccharide, which permits orderly glycosylations for the construction of the branched oligomer.

We have previously shown [1] that the photolabile *O*-(2-nitrobenzylidene) residue can be used as a temporary blocking group in the synthesis of trisaccharides branched at the 2,3-positions of fucose. We now report the value of this temporary protecting group in the synthesis of model trisaccharides branched at the 2,3-positions of D-galactose since 2,3-di-*O*-glycosylgalactoses are common in biological systems and many have been synthesised.[5]

In contrast to the fucose system studied earlier, galactose has one additional hydroxy-group to be blocked. Since we have found [6] that esters are compatible with the formation and photorearrangement of the *O*-(2-nitrobenzylidene) residue, the 6-*O*-pivaloyl derivative was used. This particular ester group was chosen owing to its good ^{1}H n.m.r. characteristics and its ease of preparation by selective acylation of the 6-OH group.[7]

We also extended the usefulness of this temporary protecting group by determining its compatibility with a more elaborate aglycone than the methyl group usually employed and, by introducing a spacer arm,[8] extended its value in synthesis.

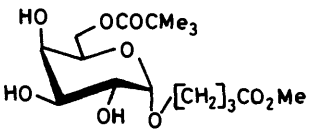
The 3-(methoxycarbonyl)propyl pyranoside of α-D-galactose 6-pivalate, compound (1), was selected as the model and its preparation will be described elsewhere.[9]

The partially blocked galactoside (1) was heated for 3 h at 45 °C with dimethoxy-(2-nitrophenyl)methane in dioxan containing a catalytic amount of sulphuric acid to give, after chromatography, the analytically pure 3,4-*O*-(2-nitrobenzylidene)galactoside 6-pivalate (2) in 70% yield. The two equally intense singlets at δ_H 6.58 and 6.88 arising from the nitrobenzylidene acetal hydrogen indicated that a 1 : 1 *endo–exo* mixture had been formed.[10] This made complete analysis of the ^{1}H- and ^{13}C-n.m.r. spectra difficult, but they were both in accord with structure (2).

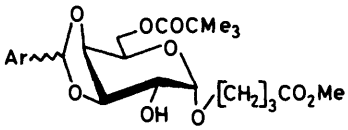
The partially protected galactoside (2) was condensed with tetra-*O*-acetyl-α-D-galactopyranosyl bromide as described by Flowers,[11] using the Helferich [12] mercury(II) cyanide catalyst to give, after chromatography, an almost quantitative yield of the fully blocked galactosyl galactoside (3). Although the material gave a satisfactory C, H, and N analysis it showed a complex ^{1}H n.m.r. spectrum because, as expected, equal amounts of the *endo* and *exo* isomers were present as indicated by the signals at δ_H 6.63 and 6.85 for the nitrobenzylidene acetal hydrogen. The spectrum was, however, fully consistent with the gross structure of (3) but it gave no information about the anomeric configuration at the newly formed glycosidic centre. The ^{13}C n.m.r. spectrum was much more informative, showing *inter alia* resonances for both anomeric carbons with the α C-1 appearing at δ_C 98.1 as a signal of full strength and the C-1′ atom appearing as two equally intense signals, each of half intensity, at δ_C 101.9 and 102.1 p.p.m. The last two resonances are similar to those found for the galactose ring in methyl 3,4-*O*-*endo*- and 3,4-*O*-*exo*-(2-nitrobenzylidene)-2-*O*-(tetra-*O*-acetyl-β-D-galactopyranosyl)-α-L-fucopyranoside [1] and thus they indicate that, as anticipated from the method of glycosylation, a β-galactoside linkage had been formed. The C-1′ anomeric carbon of the peracetylated galactose ring is probably more influenced by the stereochemistry of the nitrobenzylidene residue because of its closer proximity to the aromatic ring than the C-1 atom.

The key step in our synthetic sequence is the partial deblocking of compound (3) and this was carried out on a methanolic solution of the *endo–exo* mixture. An advantage with this method is that the photochemical opening of the dioxolan ring is not sensitive to the stereochemistry at the acetal carbon.[1,6] The solution was irradiated for 45 min with u.v. light from a 450-W medium-pressure mercury lamp in a conventional Pyrex photoreactor. The nitrosobenzoate obtained was oxidized with a solution of trifluoroperacetic acid, and t.l.c. (thin-layer chromatography) of the crude material showed that the 4-(nitrobenzoate) was the preponderant isomer.

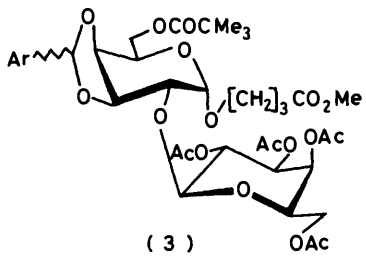
Chromatography of the product removed some unchanged (3) and a small quantity of impure product (4); further elution gave the pure, partially protected disaccharide 4-(nitrobenzoate) (4) in 73% yield. The 200-MHz ^{1}H n.m.r. spectrum of this material clearly showed that it was a single isomer. In particular the most deshielded glycose proton gave a doublet of doublets at δ_H 5.64 coupled by 3.2 and *ca.* 1.0 Hz and this unequivocally places the nitrobenzoate at C-4. The two anomeric proton doublets were well resolved. The 1-H atom of the α-galactopyranoside gave a signal at δ_H 4.95 (*J* 3.5 Hz) and 1′-H gave one at δ_H 4.74 (*J* 7.5 Hz) which supports the earlier conclusion that a β-disaccharide linkage



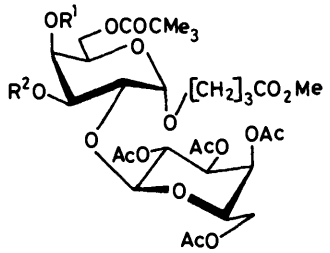
(1)



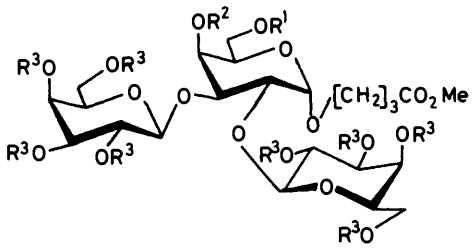
(2)



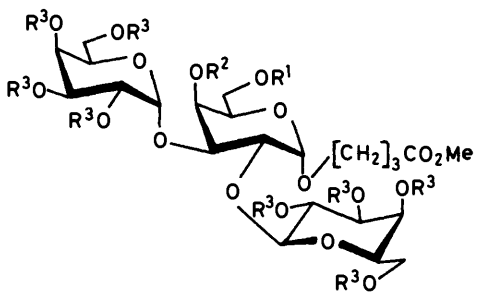
(3)



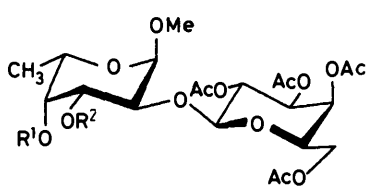
(4) R^1 = ArCO, R^2 = H
(9) R^1 = H, R^2 = ArCO



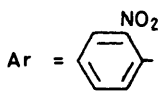
(5) R^1 = Me_3CCO, R^2 = ArCO, R^3 = Ac
(7) R^1 = R^2 = R^3 = H



(6) R^1 = Me_3CCO, R^2 = ArCO, R^3 = Ac
(8) R^1 = R^2 = R^3 = H



(10) R^1 = ArCO, R^2 = H
(11) R^1 = H, R^2 = ArCO



had been formed during the glycosylation reaction. The ^{13}C n.m.r. spectrum verified that the material was a pure isomer and the signals at δ_C 98.7 and 102.6 p.p.m. indicate that α- and β-galactosidic linkages were present.[13]

The 200-MHz ^1H n.m.r. spectrum of the small quantity of impure product (4) revealed that its composition was roughly 8 parts (4), 2 parts uncharacterised impurities, and 3 parts 3-*O*-nitrobenzoyl isomer (9). The last compound was identified by its 1′-, 4′-, and 1-H signals which resonated in 'windows' in the spectrum of the major isomer (4). They could be assigned because of their close similarity to the analogous signals of methyl 3-*O*-(2-nitrobenzoyl)-2-*O*-(tetra-*O*-acetyl-β-D-galactopyranosyl)-α-L-fucopyranoside (11).[1] A quantitative estimation of the two position isomers was made by comparing the intensities of the 1′-, 4′-, and 1-H signals of the 3-(nitrobenzoate) (9) and the 4-(nitrobenzoate) (4).

Thus we estimated that the nitrophenyldioxolan ring moiety in compound (3) was opened regioselectively to form the 4- and 3-nitrobenzoate (4) and (9) in 91% yield in the ratio 18 : 1.

The disaccharide (4) was condensed with tetra-*O*-acetyl-α-D-galactosyl bromide under Helferich [12] conditions but the reaction was very slow and even though a four-fold excess of bromo-sugar was added in portions and the reaction was allowed to proceed for 46 h some disaccharide still remained unchanged.

A trisaccharide component was isolated from the crude product by column chromatography and this was fractionated into equal amounts of two pure compounds by preparative layer chromatography (p.l.c.). The less polar of these was the fully blocked αβ-trisaccharide α-glycoside (6). Its structure follows from its elemental composition and n.m.r. spectra. Salient features in the correctly integrating ^1H n.m.r. spectrum were eight singlets for the acetyl groups, an intense singlet for the pivaloyl ester, four aromatic protons, and signals for the CH_3OCOCH_2 and OCH_2 parts of the aglycone. There were also resonances for all the carbon atoms of the protecting groups. Seven glycose hydrogen signals were well resolved. Three of these, at δ_H 5.67, 5.50, and 5.42, were due to 4-H protons and two, which were doublets at δ_H 5.02 (J 3.5 Hz) and 4.85 (J 7.8 Hz), arose from the α- and β-anomeric protons. The third anomeric proton resonated in an unresolved multiplet at δ_H 5.26—5.40. The chemical shift of the 4-H proton at δ_H 5.67 clearly indicated that the nitrobenzoyl residue had remained attached to O-4 during the galactosylation reaction. The ^{13}C n.m.r. spectrum was in accord with the structure proposed, exhibiting the required eighteen resonances for the glycose carbon atoms. In particular it exhibited resonances at δ_C 93.8 and 98.7 p.p.m. for two anomeric carbons with the α-configuration and one at δ_C 101.3 p.p.m. for an anomeric carbon with the β-configuration. Shin and Perlin [13] report δ_C 97.0 and 101.5 p.p.m. for similar carbon atoms.

The structure of the more polar fraction, which was a little less pure than compound (6), was similarly determined and was found to be that of the anticipated peracylated ββ-trisaccharide α-glycoside (5). The ^1H n.m.r. spectrum showed ten singlets for the acetyl, pivaloyl, and methoxycarbonyl

groups and a multiplet for the aromatic protons. Three doublets for the anomeric protons resonated at δ_H 4.58, 4.65, and 4.97 with splittings of 8.0, 8.0, and 3.5 Hz, respectively; this established that both the intersaccharide linkages were β, and this point was corroborated by the three resonances in the ^{13}C n.m.r. spectrum at δ_C 101.9, 101.1, and 99.0 p.p.m. In this isomer the only 4-H resonance to be resolved was the most deshielded one at δ_H 5.67 and this established the compound to be a 4-(nitrobenzoate). The other two 4-H protons (from the peracetylated galactose rings) were more shielded than in isomer (6) and contributed to a multiplet in the region δ_H 3.4—4.5.

The sluggish non-stereoselective glycosylation of compound (4) contrasts with the smooth β-glycosylation of the related methyl 4-*O*-(2-nitrobenzoyl)-2-*O*-(tetra-*O*-acetyl-β-D-galactopyranosyl)-α-L-fucopyranoside (10).[1] Thus the 4-*O*-nitrobenzoyl group is not solely responsible for the decreased nucleophilicity of the 3-hydroxy-group in the disaccharide (4); the substitution of an electron-withdrawing pivaloyloxy-group at C-6 in compound (4) in place of the hydrogen in compound (10) [1] could account for the decreased reactivity of the former compound.

Factors affecting the rates of glycosylations and the anomeric purity of the products formed are now more fully understood.[4] Consequently, efforts to improve the glycosylation of compound (4) using these guidelines are now underway.[14]

Zemplen deacylations of the fully protected trisaccharides (5) and (6) were straightforward. The deblocked trisaccharide glycosides (7) and (8) were both isolated in high yield as crystalline trihydrates. Their 400-MHz ^1H n.m.r. spectra exhibited signals for thirty carbon-bound hydrogen atoms, which included three doublets for the anomeric protons and singlets and multiplets arising from the methoxy-group and two methylene groups of the $CH_3OCOCH_2CH_2$ component of the aglycones.

Their ^{13}C n.m.r. spectra showed 23 carbon resonances, eight of which were individually assigned; five to the $CH_3OCOCH_2CH_2CH_2$ aglycone and three to the anomeric carbons. The remaining signals arose from the other fifteen glycose carbon atoms.

The anomeric configurations of the two isomers were readily determined from these n.m.r. spectra. The ββ-trisaccharide α-glycoside (7) showed a pair of doublets at relatively high field (δ_H 4.61 and 4.55) both coupled by 7.8 Hz, and a pair of carbon signals at relatively low field (δ_C 104.9 and 105.0 p.p.m.) for the anomeric protons and carbons of two β-linked galactosides.[15] The anomeric proton and carbon of the α-galactoside appeared as a relatively deshielded narrow doublet (δ_H 5.09, *J* 3.5 Hz), and a relatively shielded resonance at δ_C 98.7 p.p.m. (see ref. 15).

The n.m.r. signals for the anomeric hydrogens and carbons of the αβα-isomer (8) were, as expected, grouped differently. There were two narrow doublets (*J* 3.5 Hz) at relatively low field (δ_H 5.11 and 5.13) and two carbon signals at δ_C 98.8 and 94.3 p.p.m. for the anomeric protons and carbons of the two α-linked galactose units. The anomeric proton and carbon of the β-galactopyranose ring resonated, respectively, as a relatively shielded doublet at δ_H 4.50, *J* 8.0 Hz, and a relatively deshielded signal at δ_C 104.9 p.p.m.

Experimental *

^1H N.m.r. spectra were usually measured in $CDCl_3$ with tetramethylsilane (TMS) as internal standard, either with a Jeol M100 CW instrument or a Jeol FX200 FT instrument, and some were measured with a Brucker WH-400 spectrometer. Natural abundance ^{13}C n.m.r. spectra were determined with a Jeol FX60 FT instrument operating at 15 MHz; spectra were determined for $CDCl_3$ solutions (TMS as internal standard) or for D_2O solutions with dioxan as standard. All δ_C values were recorded with reference to TMS. Optical rotations were measured with an Optical Activity polarimeter model A100.

T.l.c. was carried out on silica gel GF_{254} (Merck) and materials were located either visually under u.v. light or with a sulphuric acid–ethanol spray reagent. Column chromatography was carried out on silica gel 70—230 mesh (Merck 7734) at atmospheric pressure. Organic solutions were dried with molecular sieves 4 A.

3-(*Methoxycarbonyl*)*propyl* 3,4-O-endo- *and* 3,4-O-exo-(2-*Nitrobenzylidene*)-6-O-*pivaloyl*-α-D-*galactopyranoside* (2).—To a stirred solution of 3-(methoxycarbonyl)propyl 6-*O*-pivaloyl-α-D-galactopyranoside (1) (2.78 g, 7.6 mmol) and dimethoxy-(2-nitrophenyl)methane (4.51 g, 22.9 mmol) in dioxan (16 ml) at 0 °C was added concentrated sulphuric acid (0.66 ml). The solution was heated to 44 °C for 3 h and was then cooled and poured into rapidly stirred aqueous sodium hydrogen carbonate (100 ml) at 0 °C. The product was extracted into diethyl ether (3 × 60 ml) and the organic phase was washed sequentially with water, aqueous sodium hydrogen carbonate, and water. The dried ethereal solution was evaporated to dryness to give a crude residue (4.52 g) which was purified by column chromatography [diethyl ether–benzene (9 : 1) as eluant] to give the pure, syrupy *endo–exo* nitrobenzylidenated galactoside (2) (2.65 g, 70%), R_F 0.49; $[\alpha]_D^{27}$ +63.8° (*c*, 2.1 in $CHCl_3$); $\nu_{max.}$ 3 480 cm^{-1} (OH) (Found: C, 55.6; H, 6.3; N, 2.9. $C_{23}H_{31}NO_{11}$ requires C, 55.5; H, 6.3; N, 2.8%); δ_H (100 MHz) 7.45—8.2 (4 H, m, ArH), 6.58 and 6.88 (total 1 H, 2 × s, intensity ratio 1 : 1, ArC*H* of the *endo* and *exo* isomers), 5.0 and 4.88 (each 0.5 H, 2 × d, $J_{1,2}$ 4.0 Hz, 1-H of the two isomers), 2.84 and 2.94 (each 0.5 H, s × d, D_2O exchangeable, $J_{OH,2}$ 7.0 Hz, OH of two isomers), 1.20 and 1.24 (each 4.5 H, 2 × s, Me_3C of two isomers), 3.72 (3 H, s, OMe), 1.88—2.04 (2 H, m, CH_2), 2.08—2.60 (2 H, m, CH_2), and 3.48—4.60 (total 8 *H*, m, aglycone OCH_2, plus the glycose 2-, 3-, 4-, 5-, 6-, and 6′-H); δ_C 26.8, 38.5, and 178.1 [$(CH_3)_3CCO$], 51.5, 173.9, 30.8, 24.5, and 67.1 [$CH_3OCOCH_2CH_2CH_2O$], 127.8 148.5, 124.6, 132.2, 133.5, 130.0, and 99.8 [Aryl C-1 to C-6 and acetal carbon (all *endo*-form)], 127.3, 148.6, 124.4, 132.8, 133.3, 129.6, and 99.3 [Aryl C-1 to C-6 and acetal carbon (all *exo*-form)], 96.8 and 97.1 (C-1 *endo* and *exo*), and 76.1, 73.3, 68.3, 66.2, 63.0 p.p.m. (glycose carbons).

3-(*Methoxycarbonyl*)*propyl* 3,4-O-endo- *and* 3,4-O-exo-(2-*Nitrobenzylidene*)-6-O-*pivaloyl*-2-O-(2,3,4,6-*tetra*-O-*acetyl*-β-D-*galactopyranosyl*)-α-D-*galactopyranoside* (3).—A solution of the partially protected galactoside (2) (1.0 g, 2 mmol) in a mixture of nitromethane (0.8 ml) and benzene (0.8 ml) was stirred at room temperature with mercury(II) cyanide (0.76 g, 3 mmol) and tetra-*O*-acetyl-α-D-galactopyranosyl bromide (1.24 g, 3 mmol) for 4.5 h whence t.l.c. [Et_2O–C_6H_6 (3 : 1) as developer] indicated complete reaction. The reaction mixture was then diluted with benzene (100 ml), filtered, and the filtrate was washed sequentially with aqueous sodium hydrogen carbonate, water, 10% aqueous potassium iodide, and water. The dried organic solution was evaporated to dryness and the residue was purified by column chromatography [Et_2O–C_6H_6 (1 : 1) as eluant] which gave the title compound (3) (1.64 g, 99%) as a foam, R_F 0.45; $[\alpha]_D^{21}$ +45.3° (*c*, 1.06 in $CHCl_3$) (Found: C, 53.4; H, 5.9; N, 1.7. $C_{37}H_{49}NO_{20}$ requires C, 53.7; H, 6.0; N, 1.7%); δ_H 7.5—8.1 (4 H, m, ArH), 6.63 and 6.85 (total 1 H, 2 × s, ratio 1 : 1, *endo*- and *exo*-ArC*H*],

* Non-systematic (glycoside-type) nomenclature used for compounds (1)—(8).

1.24 and 1.27 (total 9 H, 2 × s, ratio 1 : 1, CMe_3), 3.76 (3 H, s, OMe), 1.8—2.3 (total 14 H, m, 4 × Ac and CH_2), 2.35—2.60 (2 H, m, CH_2), 3.4—4.6 (total 11 H, m, 9 × glycose protons and OCH_2), and 4.8—5.6 (total 5 H, m, 1'-, 2'-, 3'-, 4'-, and 1-H); δ_C 27.1, 38.9, and 178.4 [$(CH_3)_3CCO$], 51.6, 174.1, 30.6, and 24.6 ($CH_3OCOCH_2CH_2$), 67.3 and 67.6 (CH_2O, *endo* and *exo*), 20.6, 170.6, 170.4, 170.1, and 170.0 (4 × CH_3CO), 126.9, 148.8,* 124.8, 133.8, 130.3, and 128.6 (Aryl C-1 to C-6 of *endo*-form), 127.1, 149.0,* 125.1, 133.5, 130.0, and 128.6 (Aryl C-1 to C-6 of *exo*-form), 99.8 and 99.3 (ArCH, *endo* and *exo* forms), 98.1 (C-1), 101.9 and 102.1 (C-1', *endo* and *exo*), and 60.9, 61.4, 61.6, 63.1, 65.4, 66.2, 66.9, 68.7, 68.9, 70.6, 71.0, 74.0, 75.6, 76.3, 76.7, and 78.5 p.p.m. [10 C (glycose), some of which give coincident resonances]. The assignment of carbon resonances marked with an asterisk could be interchanged.

3-(Methoxycarbonyl)propyl 4-O-(2-Nitrobenzoyl)-6-O-pivaloyl-2-O-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-α-D-galactopyranoside (4).—A deoxygenated solution of the nitrobenzylidenated disaccharide (3) (1.0 g, 1.2 mmol) in methanol (80 ml) was irradiated, with a 450-W medium-pressure lamp, in the annular space around a Pyrex water-cooled photolysis probe. T.l.c. [C_6H_6–Et_2O (1 : 1) as developer] indicated that the photorearrangement was complete after 45 min. The methanol was then evaporated under reduced pressure and the nitrosobenzoate product was dissolved in dichloromethane (50 ml). The green solution was cooled to 0 °C and a solution of trifluoroperacetic acid (1.8 mmol) in dichloromethane (1.5 ml) added. The mixture was stirred at 0 °C for 1.5 h, poured into dichloromethane (150 ml), and the solution was washed sequentially with water, aqueous sodium hydrogen carbonate, and water. Evaporation of the dried organic solution gave material which was fractionated by column chromatography [C_6H_6–Et_2O–EtOAc (2 : 1 : 1) as eluant] to give unchanged disaccharide (3) (154 mg), R_F 0.54; an impure sample of compound (4) (185 mg), R_F 0.28—0.35; and the pure *dissacharide nitrobenzoate* (4) [629 mg, 73% after allowance for unchanged (3)], R_F 0.29; $[\alpha]_D^{26}$ +4.3° (*c*, 1.36 in $CHCl_3$) (Found: C, 53.1; H, 5.9; N, 1.8. $C_{37}H_{43}NO_{21}$ requires C, 52.7; H, 5.9; N, 1.7%); δ_H (200 MHz; $CDCl_3$) 4.74 (d, $J_{1',2'}$ 7.5 Hz, 1'-H), 5.20 (dd, $J_{2',3'}$ 10.5 Hz, 2'-H), 5.04 (dd, $J_{3',4'}$ 3.2 Hz, 3'-H), 5.38br (d, $J_{4',5'}$ *ca.* 1.0 Hz, 4'-H), 1.98, 2.05, 2.06, and 2.15 (12 H, 4 × s, 4 × Ac), 1.21 (9 H, s, CMe_3), 4.95 (d, $J_{1,2}$ 3.5 Hz, 1-H), 5.64 (dd, $J_{4,3}$ 3.2, $J_{4,5}$ *ca.* 1.0 Hz, 4-H), 2.56 (d, $J_{OH,2}$ 4.5 Hz, D_2O-exchangeable, OH), 7.64—7.92 (4 H, m, ArH), 3.68 (3 H, s, OMe), 2.38—2.54 (2 H, m, CH_2CO_2Me), 1.84—2.05 (2 H, m, $CH_2CH_2CH_2$), 3.38—3.55 (1 H, m) and 3.68—3.78 (1 H, m) (together OCH_2), and 3.92—4.36 (total 8 H, m, remaining glycose protons); δ_C 102.6 and 98.7 (C-1' and C-1, respectively), 61.9 and 61.5 (2 × C-6), 67.0, 67.5, 67.9, 69.3, 71.0, 71.1, 72.9, and 78.9 (8 C, remaining unassigned glycose carbons), 51.6, 174.0, 30.7, 24.8, and 67.2 ($CH_3OCOCH_2CH_2CH_2O$), 20.6, 170.2, 170.4, 170.6, and 170.7 (4 × CH_3CO), 27.2, 38.8, and 178.3 [$(CH_3)_3CCO$], and 126.7, 148.7, 123.9, 133.1, and 132.6, 131.1, and 164.7 p.p.m. (Aryl C-1 to C-6 and ArCO, respectively).

The impure sample of compound (4) (185 mg) was shown to have the composition 62% (4), 23% 3-(methoxycarbonyl)-propyl 3-*O*-(2-nitrobenzoyl)-6-*O*-pivaloyl-2-*O*-(tetra-*O*-acetyl-β-D-galactopyranosyl)-α-D-galactopyranoside (9), and *ca.* 15% unidentified materials since the presence of the 3-(2-nitrobenzoate) was indicated by the 200-MHz ^1H n.m.r. spectrum, which showed signals at δ_H 4.56 (d, $J_{1',2'}$ 7.5 Hz), 4.48 (d, $J_{1,2}$ 3.5 Hz), and 5.30br (d, $J_{4',3'}$ 3.2, $J_{4',5'}$ *ca.* 1.0 Hz). These signals had half the intensity of the resonances from the corresponding protons of the 4-*O*-(2-nitrobenzoate) (4).

The 2,3-Di-O-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl) and 3-O-(2,3,4,6-Tetra-O-acetyl-α-D-galactopyranosyl)-2-O-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl) Derivatives of 3-(Methoxycarbonyl)propyl 4-O-(2-Nitrobenzoyl)-6-O-pivaloyl-α-D-galactopyranoside, Compounds (5) *and* (6).—A solution of the partially deblocked disaccharide (4) (396 mg, 0.47 mmol) in a mixture of benzene (0.1 ml) and nitromethane (0.1 ml) was stirred with acetobromogalactose (290 mg, 0.71 mmol) and mercury(II) cyanide (178 mg, 0.71 mmol) at room temperature. T.l.c. [Et_2O–C_6H_6 (5 : 1) as developer] showed that, after 5 h, all the bromo-sugar had reacted but also that some unchanged disaccharide (4) remained [shown by t.l.c. (Et_2O, 4 developments)]. More bromo-sugar (290 mg), mercury(II) cyanide (178 mg), benzene (0.2 ml) and nitromethane (0.2 ml) were added and the mixture was stirred and monitored by t.l.c. After 15 h similar quantities of the reagents and solvents were again added and the reaction was allowed to proceed for a further 26 h; the mixture was then worked up. The crude residue (1.42 g) was partially fractionated by column chromatography [EtOAc–light petroleum b.p. 40—60 °C (3 : 2) as eluant] to give a solid which we believed was tetra-*O*-acetylgalactopyranosyl cyanide (0.44 g) (R_F 0.63), and a fraction containing trisaccharide derivatives (565 mg). P.l.c. (four developments with Et_2O) of this fraction gave two bands of pure material (153 mg) and (162 mg) (R_F 0.47 and 0.40, respectively) and a mixture of these (90 mg) which was refractionated into further crops (31 mg) and (23 mg) of pure isomers.

The *peracyl-ββ-trisaccharide α-glycoside* (5) (184 mg, 34%) had R_F 0.4; m.p. 80—83 °C; $[\alpha]_D^{26}$ −5.3° (*c*, 1.0 in $CHCl_3$) (Found: C, 52.8; H, 6.0; N, 1.5. $C_{51}H_{67}NO_{30}$ requires C, 52.2; H, 5.8; N, 1.2%); δ_H (200 MHz) 1.95, 1.98, 2.02, 2.05, 2.06, 2.13, 2.14, and 2.17 (24 H, 8 × s, 8 × Ac), 1.20 (9 H, s, Me_3C), 7.5—8.0 (4 H, m, ArH), 3.64 (3 H, s, OMe), 4.58 (d, *J* 8.0 Hz), 4.65 (d, *J* 8.0 Hz), and 4.97 (d, *J* 3.5 Hz) (together 3 × 1-H), 5.67br (d, $J_{4,3}$ 3.5, $J_{4,5}$ 1.0 Hz, 4-H), 4.8—5.5 (6 H, m, 6 × AcOC*H*), 3.4—4.5 (total 13 H, m, 11 glycose protons plus OCH_2), and 1.90—2.65 (4 H, m, CH_2CH_2CO), plus some weak signals from impurities in the region δ_H 0.7—1.7; δ_C 27.2, 38.8, and 178.3 [$(CH_3)_3CCO$], 20.5, 169.4, 169.6, 170.3, 170.5, and 170.6 (8 × Ac), 51.6, 174.1, 30.7, 24.8, and 67.1 ($CH_3OCOCH_2CH_2CH_2O$), 127.2, 148.6, 123.8, 133.0, 132.1, 131.3, and 164.1 (Aryl C-1 to C-6 and Ar*C*O, respectively), 101.9, 101.1, and 99.0 [2 × C-1 (β) and C-1 (α)], and 61.1, 61.2, 62.3, 67.0, 67.2, 67.6, 69.5, 69.7, 70.7, 70.8, 71.0, 71.1, 73.1, 73.4, and 76.1 p.p.m. (15 glycose carbons).

The *peracyl-αβ-trisaccharide α-glycoside* (6) (185 mg, 34%) had R_F 0.47; m.p. 76—79 °C; $[\alpha]_D^{26}$ +20.7° (*c*, 1.3 in $CHCl_3$) (Found: C, 52.8; H, 6.0; N, 1.4. $C_{51}H_{67}NO_{30}$ requires C, 52.2; H, 5.8; N, 1.2%); δ_H (200 MHz) 1.64, 1.94, 1.98, 2.04, 2.12, 2.14, 2.15, and 2.16 (24 H, 8 × s, 8 × Ac), 1.20 (9 H, s, Me_3C), 7.5—8.0 (4 H, m, ArH), 3.68 (3 H, s, OMe), 2.1—2.3 (2 H, m) and 3.4—3.6 (2 H, m) (together CH_2CH_2CO), 4.85 (d, $J_{1,2}$ 7.8 Hz, 1'-H), 5.21 (dd, $J_{2,3}$ 10.0 Hz, 2'-H), 5.07 (dd, $J_{4,3}$ 3.5 Hz, 3'-H), 5.50br (d, $J_{4,5}$ 1.0 Hz, 4'- or 4''-H), 5.26—5.40 (total 3 H, m, 1- or 1'', 2- or 2'', and 3- or 3''-H), 5.42br (d, $J_{4,3}$ 3.0, $J_{4,5}$ 1.0 Hz, 4''- or 4'-H) 5.02 (d, $J_{1,2}$ 3.5 Hz, 1''- or 1-H), 5.67br (d, $J_{4,3}$ 2.5, $J_{4,5}$ 1.0 Hz, 4-H), and 3.94—4.48 (total 13 H, m, 11 glycose protons plus OCH_2); δ_C 27.2, 38.8, and 178.3 [$(CH_3)_3CCO$], 20.7, 170.1, 170.3, 170.5, 170.6, and 170.8 (8 × Ac), 51.6, 173.8, 30.7, 24.9, and 67.1 ($CH_3OCOCH_2CH_2CH_2O$), 126.9, 148.4, 124.0, 133.2, 132.6, 130.9, and 164.5 (Aryl C-1 to C-6 and Ar*C*O, respectively), 101.3, 98.7, and 93.8 [C-1 (β) and 2 × C-1 (α)], and 71.2, 71.3, 71.6, 69.5, 69.3, 69.0, 62.3, 61.9, 61.3, 67.3, 67.4, 67.6, 67.9, 67.7, and 67.8 p.p.m. (15 glycose carbons).

3-(*Methoxycarbonyl*)*propyl* 2,3-*Di*-O-(β-D-*galactopyranosyl*)-α-D-*galactopyranoside* (7) *and* 3-(*Methoxycarbonyl*)*propyl* 3-O-(α-D-*Galactopyranosyl*)-2-O-(β-D-*galactopyranosyl*)-α-D-*galactopyranoside* (8).—The two fully protected trisaccharide derivatives (5) (150 mg, 0.13 mmol) and (6) (140 mg, 0.12 mmol) were separately dissolved in methanol (10 ml) and 0.1M methanolic sodium methoxide (0.9 ml) was added to each solution. The reactions were monitored by t.l.c. [Bu^{n}OH–MeOH–H_2O (3 : 1 : 1)] which showed that compound (6) was deacylated in 27 h whereas compound (5) required 48 h. The chromatograms revealed that the nitrobenzoyl moiety was the last ester function to be removed.

Neutralisation of the solutions with Amberlite IR-120H$^+$ resin gave, after the usual work-up, residues which were triturated with diethyl ether and were then dissolved in a minimum quantity of methanol. A large volume of diethyl ether was added and the solutions were filtered through Celite to remove the precipitated methyl 2-nitrobenzoate.

The trisaccharides were thus obtained as their deblocked glycosides. The ββ-*trisaccharide* α-*glycoside* (7) (73 mg, 93%) showed R_F 0.4; m.p. 128—130 °C; $[\alpha]_D^{26}$ +57.9° (*c*, 0.71 in MeOH) (Found: C, 42.1; H, 7.4. $C_{23}H_{40}O_{18}\cdot 3H_2O$ requires C, 41.9; H, 7.05%); δ_H (400 MHz; D_2O) 5.09 (d, $J_{1,2}$ 3.5 Hz, 1-H), 4.61 (d, $J_{1,2}$ 7.8 Hz, 1′- or 1″-H), 4.55 (d, $J_{1,2}$ 7.8 Hz, 1″- or 1′-H), 4.06 and 4.01 (1 H, dd, $J_{2,3}$ 10.0, $J_{2,1}$ 3.5 Hz, 2-, 2′-, or 2″-H) and (1 H, dd, $J_{3,2}$ 10.0, $J_{3,4}$ 3.0 Hz, 3-, 3′-, or 3″-H), 4.17br (d, $J_{4,3}$ 3.0, $H_{4,5}$ 1.0 Hz, 4-, 4′-, or 4″-H), 3.92 (3 H, m, 3 glycose protons), 3.47—3.75 (total 14 H, m, 12 glycose protons plus OCH_2 of aglycone), 3.65 (3 H, s, OMe), and 1.82—1.99 (2 H, m) and 2.45 (2 H, t, *J* 7.5 and 7.5 Hz) (together CH_2CH_2). The signal at δ_H 5.09 is the only one that can be assigned to a specific ring; δ_C (D_2O) 53.0, 177.7, 31.6, 24.6, and 67.8 ($CH_3OCOCH_2CH_2CH_2O$), 98.7 (α C-1), 104.9 and 105.0 (2 × β C-1), and 61.7, 61.8, 61.9, 69.5, 69.6, 70.2, 71.3, 71.9, 72.1, 73.6, 73.7, 75.8, 75.9, 77.3, and 78.5 p.p.m. (15 glycose carbons).

The αβ-*trisaccharide* α-*glycoside* (8) (68 mg, 94%) showed R_F 0.46; m.p. 108—I12 °C; $[\alpha]_D^{26}$ +131° (*c* 0.88 in MeOH) (Found: C, 42.4; H, 7.4. $C_{23}H_{40}O_{18}\cdot 3H_2O$ requires C, 41.9; H, 7.05%); δ_H (400 MHz; D_2O) 5.11 (d, $J_{1,2}$ 3.5 Hz), 5.13 (d, $J_{1,2}$ 3.5 Hz), and 4.50 (d, $J_{1,2}$ 8.0 Hz) (3 anomeric protons), 4.04 (dd, $J_{2,1}$ 3.5, $J_{2,3}$ 10.0 Hz, 2- or 2″-H), 4.08 (dd, $J_{3,2}$ 10.0, $J_{3,4}$ 2.8 Hz, 3-, 3′-, or 3″-H), 4.24br (d, $J_{4,3}$ 2.8, $J_{4,5}$ 1.0 Hz, 4-, 4′-, or 4″-H), 4.27br (dt, $J_{5,6}$ 6.4, 6.4, $J_{5,4}$ 1.0 Hz, 5-, 5′-, or 5″-H), 3.47—3.59 (4 H, m, 4 glycose protons), 3.64—3.75 (total 7 H, m, 5 glycose protons and aglycone OCH_2), 3.76—3.94 (5 H, m, 5 glycose protons), 3.64 (3 H, s, OMe), and 1.89 (2 H, m) and 2.45 (2 H, m) (together CH_2-CH_2CO). The signal at δ_H 4.50 is the only one that can be assigned to a proton in a specific ring, *i.e.* 1′-H or 2-*O*-galactosyl ring; δ_C (D_2O) 53.0, 177.6, 31.4, 24.8, and 67.4 ($CH_3OCOCH_2CH_2CH_2O$), 98.8 and 94.3 (2 × α C-1), 104.9 (β C-1), and 61.7, 62.0, 62.2, 65.6, 69.0, 69.5, 70.2, 70.3, 71.7, 71.8, 72.0, 73.9, 75.7, and 75.8 p.p.m. (15 glycose carbons).

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