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OLIGOSACCHARIDES FROM "STANDARDIZED INTERMEDIATES". SYNTHESIS OF A BRANCHED TETRASACCHARIDE GLYCOSIDE ISOMERIC WITH THE BLOOD-GROUP B, TYPE 2 DETERMINANT

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ABSTRACT

Building-block derivatives of the component monosaccharides were used to construct the tetrasaccharide glycoside **15**, in which an α-D-Gal*p*-(1→4)-D-Gal linkage replaces the α-(1→3) linkage of the human blood-group B, type 2, determinant structure. The initial coupling of 2-*O*-benzoyl-3,6-di-*O*-benzyl-4-*O*-(tetrahydropyran-2-yl)-α-D-galactopyranosyl chloride to allyl 2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside was followed by selective deprotection of the disaccharide product, either at O-4′ (to give **8**) or O-2′ (to give **3**). The conversion of **8** into **15** involved successive coupling with tetra-*O*-benzyl-α-D-galactopyranosyl bromide (**8** → **11**), *O*-debenzoylation at O-2′ (**11** → **12**), coupling with tri-*O*-benzyl-α-L-fucopyranosyl bromide (**12** → **14**), and *O*-debenzylation by hydrogenolysis (**14** → **15**). Alternatively, **3** was α-L-fucosylated to give **6**, and **6** was selectively deprotected at O-4′ to give **7**. However, attempts to α-D-galactosylate **7** were unsuccessful. The unsubstituted forms of the intermediate disaccharide (**8**) and trisaccharide (**12**) glycosides were obtained by appropriate deblocking procedures.

INTRODUCTION

The preparation of differentially substituted sugars designed as "standardized building-blocks" for oligosaccharide synthesis has been the subject of a series of papers from this laboratory[1–4]. In the work cited, emphasis was given to derivatives of 2-acetamido-2-deoxy-D-glucose ("*N*-acetyl-D-glucosamine") and D-galactose. A novel synthesis of oxazolines related to *N*-acetyl-D-glucosamine was devised[2], and the coupling of the *O*-acetyl-di-*O*-benzyloxazolines to partially protected sugar acceptors was demonstrated[5]. Among the D-galactose derivatives prepared were the chloride **1** and its 4-*O*-allyl analog, to serve as precursors of β-linked, interior residues having chain extension at O-4, with branching at O-2 if desired[3]. Recently, we

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described the use of these chlorides in the facile assembly of the branched tetrasaccharide glycoside[6] α-L-Fuc*p*(1→2)[α-D-Gal*p*(1→4)]β-D-Gal*p*(1→3)β-D-Glc*p*NAc-(1→OPr. This tetrasaccharide derivative, having a 1→3 linkage between its β-D-galactosyl and *N*-acetyl-D-glucosaminyl residues, is an isomer of the type 1 terminal structure of the human blood-group B substances[7].

We now report the synthesis of propyl *O*-α-L-fucopyranosyl-(1→2)-[*O*-α-D-galactopyranosyl-(1→4)]-*O*-β-D-galactopyranosyl-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranoside (**15**), which is distinguished by having an *N*-acetyllactosamine unit as its reducing-terminal structure. The compound is thus related to the type 2 chains found in the ABO antigens[7].

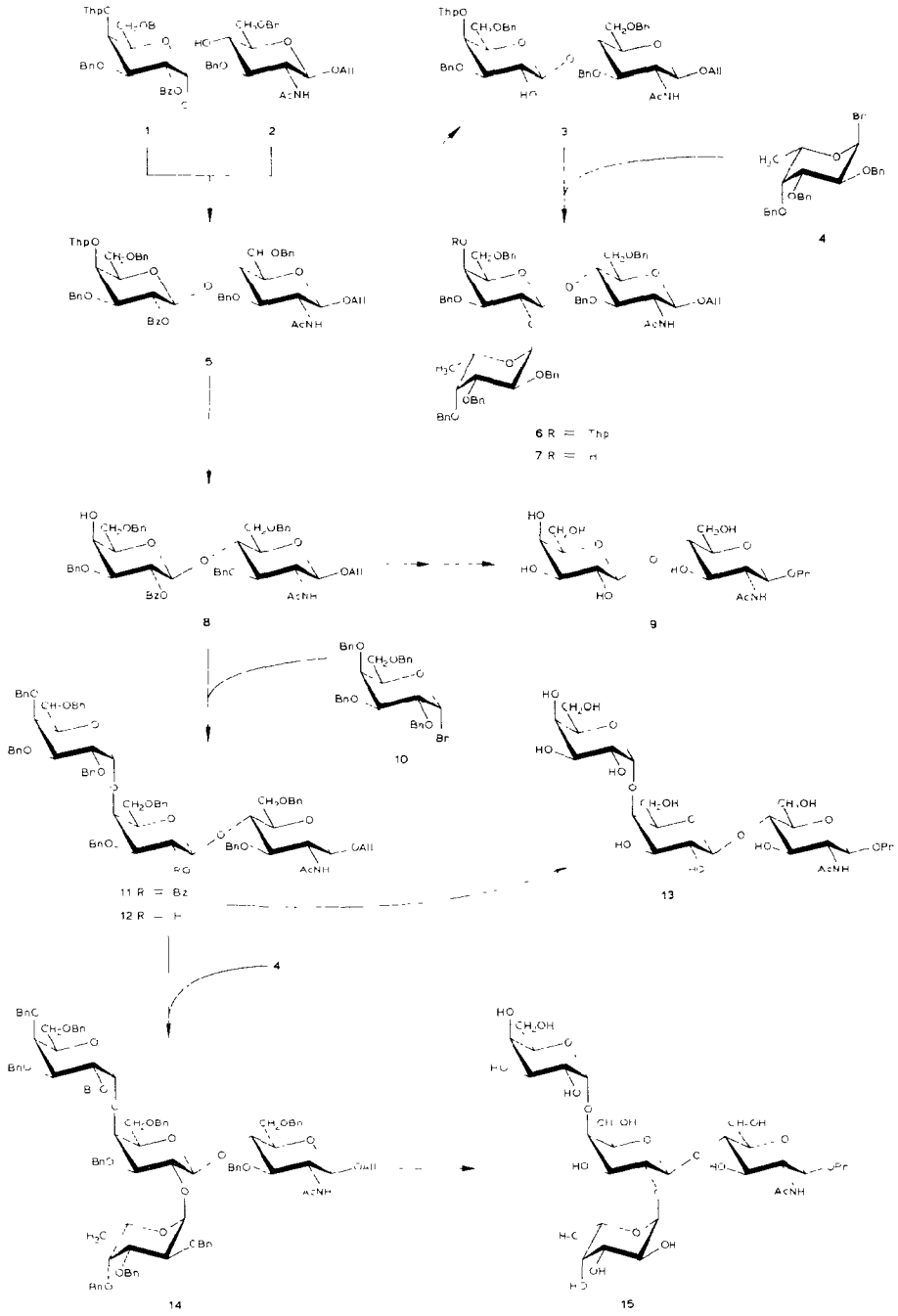
RESULTS AND DISCUSSION

The overall scheme for the preparation of the tetrasaccharide glycoside **15** is shown in Scheme 1. The strategy of synthesis followed is that discussed previously[6]. The compound was sequentially assembled from the four building-blocks **2**, **1**, **10**, and **4**, by alternate coupling and partial-deblocking reactions, with complete deblocking as the final step. Because the end product has three inter-sugar linkages, three coupling–deblocking cycles (six steps in all) were required.

Allyl 2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside (**2**), chosen as the precursor of the reducing-end residue in **15**, is an intermediate in the synthesis of the 4-*O*-acetyl-3,6-di-*O*-benzyl oxazoline derivative of *N*-acetyl-D-glucosamine[2]. After the final coupling-reaction, the allyl group could have been removed prior to *O*-debenzylation of the tetrasaccharide product **14**. We elected to bypass this operation, and hence obtained a propyl β-glycoside when **14** was subjected to hydrogenolysis. As the corresponding *N*-acetyl-D-glucosaminyl residue in the blood-group substances is coupled to the succeeding sugar by a β-linkage, this glycoside mimics the natural structure. If the free tetrasaccharide were desired, the benzyl α- or β-glycoside corresponding to **2** would be preferable as a reducing-end building-block.

The β-D-galactosylation of **2** was accomplished by treating it with **1** in the presence of silver trifluoromethanesulfonate ("triflate") and 1,1,3,3-tetramethylurea, according to Hanessian and Banoub[8]. Because compound **1** contains an acid-labile substituent (tetrahydropyran-2-yl), 2,6-dimethylpyridine was included in the reaction mixture[6]. The coupling proceeded readily in the two-armed reaction-vessel previously described[6], to give a homogeneous, fully substituted disaccharide (**5**). Although only a modest excess (1.2 molar proportions) of **1** was employed, the yield of **5** was 70%. Given the difficulties frequently encountered in glycosylating the 4-hydroxyl group of protected hexoses, this is an excellent result.

Cleavage of the tetrahydropyran-2-yl group from **5**, by brief treatment with aqueous methanolic acetic acid, furnished the 4′-hydroxy compound **8**. On *O*-debenzoylation and hydrogenolysis, a sample of **8** gave the completely deprotected glycoside **9**, which was characterized by n.m.r. spectroscopy; as the data (see Table I) clearly indicate the presence of two β-anomeric centers, the intersugar linkage in **5**



Ac = MeCO, All = H_2C=CHCH, Bn = PhCH, Bz = PhCO, Pr = MeCH$_2$CH$_2$, Thp = tetrahydropyran-2-yl

Scheme 1

TABLE I

N.M.R. PARAMETERS OF THE OLIGOSACCHARIDE PRODUCTS

Product	*^{1}H-Chemical shifts, δ (coupling constants, Hz)*[a]		*^{13}C-Chemical shifts, δ*[b]			
	Anomeric protons	*Other protons*	*C-1‴*	*C-1″*	*C-1′*	*C-1*
βGal→4*β*GlcNAc→OPr (**9**)	4.54 (8.0) (*β*) 4.47 (7.7) (*β*)	2.05 (s) ($COCH_3$) 1.56 (m) ($CH_2CH_2CH_3$) 0.87 (t, 7.5) ($CH_2CH_2CH_3$)			104.2	102.3
*α*Gal→4*β*Gal→4*β*GlcNAc→OPr (**13**)	4.94 (3.6) (Gal) 4.53 (7.4) (*β*) 4.53 (7.4) (*β*)	2.04 (s) 1.56 (m) 0.87 (t)		101.6	104.4	102.4
*α*Gal→4*β*Gal→4*β*GlcNAc→OPr 2 ↑ 1 *α*Fuc (**15**)	5.31 (~3) (*α*Fuc) 4.95 (3.3) (*α*Gal) 4.59 (7.7) (*β*) 4.52 (7.8) (*β*)	2.04 (s) 1.56 (m) 1.23 (d, 7.0) ($CHCH_3$) 0.86 (t)	101.8[c]	101.0[c]	102.3[d]	102.2[d]

[a]Determined in D_2O, with sodium 2,2,3,3-tetradeuterio-4,4-dimethyl-4-silapentanoate (TSP) as the internal standard. [b]From Me_4Si. Determined in D_2O, with 1,4-dioxane (δ 67.85) as the internal standard. [c,d]These assignments may be transposed.

and its derivatives (**8** and **9**) must have the β configuration. Hence, **9** is the propyl glycoside of *O*-β-D-galactopyranosyl-(1→4)-2-acetamido-2-deoxy-D-glucose ("*N*-acetyllactosamine"). We saw no evidence of α-linked anomer, or orthoester, among the products of the coupling reaction. However, when the 4-*O*-(*tert*-butyldimethylsilyl) analog[3] of **1** was used as the glycosyl donor, under the same conditions as for **1**, the product was an α,β mixture, with the α anomer preponderant. This result provides a second, and surprising, example of the subtle effects of the nature of the 4-substituent on the steric course of coupling reactions involving the chlorides of the "4(2)-Gal-β" series[4,6].

For the next stage of the synthesis, namely, the α-D-galactosylation of **8** at O-4′, tetra-*O*-benzyl-α-D-galactopyranosyl bromide (**10**) was used as the D-galactosyl donor under modified Koenigs–Knorr conditions (silver triflate and silver carbonate as catalysts[9]). This method had given superior results in our previous work with the (1→3)-linked analog of **8**. In the present case, it furnished the fully substituted trisaccharide glycoside **11** in 60–65% yield. *O*-Debenzoylation of **11** at O-2′ gave **12**, the intermediate needed for the final coupling-reaction, and, on hydrogenolysis, **12** afforded the deprotected propyl glycoside **13**. Evidence for the α-anomeric configuration of the newly added D-galactosyl group was provided by the n.m.r. data for **13** (see Table I).

The L-fucosylation of **12** by tri-*O*-benzyl-α-L-fucopyranosyl bromide (**4**) in the presence of tetraethylammonium bromide ("common-ion method"[10]) proceeded readily, as expected from our previous results[6], and many others recorded in the literature; the coupling product, **14**, was obtained in 58% yield. Except at the anomeric position, **14** carried only *O*-benzyl protecting groups; hence, as already discussed, only hydrogenolysis was needed in order to produce the tetrasaccharide glycoside **15**. The n.m.r. data established the α configuration of the L-fucosyl group.

Because each of the temporary protecting-groups in the initial, disaccharide coupling-product **5** (2′-*O*-benzoyl, 4′-*O*-tetrahydropyran-2-yl) can be removed independently of the other, we expected that the synthesis of **15** could be completed by first adding the L-fucosyl group, and then the α-D-galactosyl group. Indeed, *O*-debenzoylation of **5** furnished the partially deprotected glycoside **3**, and compound **3** was readily L-fucosylated by the procedure used for **12**. Cleavage of the tetrahydropyran-2-yl group from the product (**6**) gave a selectively deprotected trisaccharide glycoside formulated as **7** on the basis of its ^{1}H-n.m.r. spectrum (d for H-1″ at δ 5.61, J 3.3 Hz). Using the same procedure as for **8**, we attempted the α-D-galactosylation of **7**, and, to our surprise, found it completely resistant. In some fashion, the glycosyl group attached to O-2′ blocked the coupling reaction at O-4′, even though the converse does not occur (*cf.*, **12** → **14**). We can offer no rationalization of this effect, but similar results have occasionally been reported by others.

The relationship of the final product **15** to the blood-group antigens of the ABO series was noted in the introduction. Neglecting the glycosidic propyl group, compound **15** may be described as an isomer of the terminal tetrasaccharide portion of the blood-group B substance, type 2 chains[7]. In the natural materials, the α-D-

galactosyl group is attached to O-3 of the β-D-galactosyl residue, rather than to O-4, giving the terminal segment the structure α-L-Fuc*p*(1→2)[α-D-Gal*p*(1→3)]β-D-Gal*p*-(1→4)β-D-Glc*p*NAc. Syntheses of this tetrasaccharide have been reported by Paulsen and Kolář[9], and by Milat and Sinay[11], and the linear trisaccharide α-D-Gal*p*(1→3)-β-D-Gal*p*(1→4)D-GlcNAc has been prepared in Sinay's laboratory[12]. Compound **13** is an isomer (as the propyl glycoside) of the latter structure. All of the syntheses mentioned were preceded by the work of Lemieux and Driguez[13] on the construction of the terminal, branched trisaccharide α-L-Fuc*p*(1→2)[α-D-Gal*p*(1→3)]D-Gal, common to both the type 1 and type 2, group B antigens. An alternative synthesis of this branched trisaccharide and related compounds has been described by David *et al.*[14]. It should also be mentioned that **6** is a fully substituted form of the blood-group O(H), type 2 determinant. This trisaccharide was synthesized chemically by Jacquinet and Sinay[15] in 1976, and an enzymic synthesis has recently been reported by Rosevear *et al.*[16].

In the preparation of **15** and the linear trisaccharide glycoside **13**, described here, the key intermediate is the differentially substituted D-galactosyl chloride **1**. Our results provide a second demonstration of the excellent characteristics of this compound as a synthon for β-linked, interior D-galactosyl residues, in particular for facile construction of the *N*-acetyllactosamine derivatives **3** and **8**. In view of the wide occurrence of the *N*-acetyllactosamine structure in glycoproteins and glycolipids, these compounds should be generally valuable intermediates.

EXPERIMENTAL

General methods. — The instrumental and chromatographic procedures employed were those previously listed[2]. ^{1}H-N.m.r. spectra were recorded at 270 MHz, with decoupling as required for the identification of signals that could not be assigned unambiguously by inspection. ^{13}C-N.m.r. spectra were recorded with a Bruker HX90E instrument operated at 22.63 MHz, with 1,4-dioxane as the internal standard. Chromatography on silica gel was accomplished with ethyl acetate–hexane, acetone–chloroform, or methanol–chloroform. Elemental analyses were performed at Galbraith Laboratories, Inc., Knoxville, TN.

Coupling reactions were conducted by our standard procedure. The two-armed vessels used, and the manipulations involved, were described in detail in a previous paper[6].

Allyl O-[*2-O-benzoyl-3,6-di-O-benzyl-4-O-(tetrahydropyran-2-yl)-β-D-galacto-pyranosyl*]-(*1→4*)-*2-acetamido-3,6-di-O-benzyl-2-deoxy-β-D-glucopyranoside* (**5**). — A reactor was charged with allyl 2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-gluco-pyranoside[2] (**2**; 260 mg, 0.59 mmol) and silver trifluoromethanesulfonate (302 mg, 1.18 mmol) (in the flat-bottomed arm), and 2-*O*-benzoyl-3,6-di-*O*-benzyl-4-*O*-(tetra-hydropyran-2-yl)-β-D-galactopyranosyl chloride[3] (**1**; 400 mg, 0.71 mmol) (in the conical arm). After the reactants had been dried, the following further additions were made: dichloromethane (1 mL), 1,1,3,3-tetramethylurea (0.21 mL, 1.76 mmol), and

2,6-dimethylpyridine (0.1 mL, 0.86 mmol) (in the flat-bottomed arm), and dichloromethane (3 mL) (in the conical arm). The solutions were mixed, the mixture was stirred overnight at room temperature, and processed to give a crude syrup. Chromatography of the syrup on a column of silica gel furnished 398 mg (70%) of pure compound **5** as a glass: $[\alpha]_D^{25}$ +17.9°, $[\alpha]_{436}^{25}$ +36.9° (*c* 0.62, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 8.12–7.15 (m, Ph-H), 6.08–5.95 (2 d, 1 H, $J_{NH,2}$ 7.8 Hz, D_2O-exchangeable, N*H*), 5.80–5.38 (m, -C*H*= and H-2′), 5.25–4.95 (m, CH=CH_2), 4.92–3.33 (m, PhCH_2, sugar C*H* and CH_2, OCH_2CH=, and tetrahydropyranyl H), 2.03 and 2.00 (2 s, 3 H, CH_3CO), and 1.92–1.23 (m, tetrahydropyranyl H). The duplication or broadening of the signals in the ranges 6.08–4.95 and 2.03–2.00 is evidently due to the stereoisomerism of the tetrahydropyranyl group (see n.m.r. data for **8**).

Anal. Calc. for $C_{57}H_{65}NO_{13}$ (972.14): C, 70.42; H, 6.74; N, 1.44. Found: C, 70.10; H, 6.71; N, 1.31.

O-*Debenzoylation and* L-*fucosylation of compound* **5**. — The coupling product **5** was treated with methanolic sodium methoxide as described for the conversion of **8** into **9**, to give *allyl* O-(*3,6-di*-O-*benzyl-4*-O-(*tetrahydropyran-2-yl*)-β-D-*galactopyranosyl*)-(*1*→*4*)-*2-acetamido-3,6-di*-O-*benzyl*-β-D-*glucopyranoside* (**3**). Compound **3** (260 mg, 0.30 mmol) plus tetraethylammonium bromide (105 mg, 0.50 mmol) and powdered 4A molecular sieves (1 g), and 2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl bromide[17] (**4**) freshly prepared from the crystalline 1-acetate[6] (244 mg, 0.51 mmol), were separately dried on the liquid nitrogen-cooled Dewar[6]. Then, disaccharide **3** was dissolved in dry dichloromethane (6 mL), and the bromide was dissolved in dichloromethane (4 mL) and *N,N*-dimethylformamide (4 mL). The mixtures were combined, and the whole was stirred under dry nitrogen for 4 days at room temperature. Conventional extractive processing, after dilution with chloroform, gave a crude syrup containing the coupling product *allyl* O-(*2,3,4-tri*-O-*benzyl*-α-L-*fucopyranosyl*)-(*1*→*2*)-O-(*3,6-di*-O-*benzyl-4*-O-(*tetrahydropyran-2-yl*)-β-D-*galactopyranosyl*)-(*1*→*4*)-*2-acetamido-3,6-di*-O-*benzyl-2-deoxy*-β-D-*glucopyranoside* (**6**). After treatment with aqueous methanolic acetic acid, as described for the conversion of **5** into **8**, the material was fractionated on a column of silica gel, to give 325 mg (90% overall yield from **3**) of the depyranylated compound; amorphous; $[\alpha]_D^{25}$ −28.2°, $[\alpha]_{436}^{25}$ −58.8° (*c* 0.33, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 7.42–7.30 (m, Ph-H), 5.98–5.79 (m, -C*H*=), 5.74 (d, $J_{NH,2}$ 7.5 Hz, D_2O-exchangeable, N*H*), 5.61 (d, $J_{1'',2''}$ 3.3 Hz, H-1″), 5.31–5.09 (m, -CH=CH_2), 5.00–3.30 (m, PhCH_2, sugar C*H* and CH_2, and OCH_2CH=), 2.33 (bs, D_2O-exchangeable, O*H*), 1.88 (s, CH_3CO), and 1.20 (d, *J* 6.0 Hz, CHCH_3). These data characterize the product as *allyl* O-(*2,3,4-tri*-O-*benzyl*-α-L-*fucopyranosyl*)-(*1*→*2*)-O-(*3,6-di*-O-*benzyl*-β-D-*galactopyranosyl*)-(*1*→*4*)-*2-acetamido-3,6-di*-O-*benzyl-2-deoxy*-β-D-*glucopyranoside* (**7**). According to its elemental analysis the preparation was not quite pure (Calc. for $C_{72}H_{81}NO_{15}$: C, 72.04; H, 6.80; N, 1.17. Found: C, 73.10; H, 7.08; N, 1.02).

Allyl O-(*2*-O-*benzoyl-3,6-di*-O-*benzyl*-β-D-*galactopyranosyl*)-(*1*→*4*)-*2-acetamido-3,6-di*-O-*benzyl-2-deoxy*-β-D-*glucopyranoside* (**8**). — To a stirred solution of

compound **5** (200 mg) in methanol (2 mL) was added 80% aqueous acetic acid (5 mL), and the mixture was boiled for 1 h under reflux, cooled, and evaporated under diminished pressure, and residual acetic acid was removed by coevaporation with toluene. The residue was purified on a column of silica gel, to afford 160 mg (88%) of glassy **8**; $[\alpha]_D^{25}$ +6.3°, $[\alpha]_{436}^{25}$ +14.8° (*c* 1.1, chloroform); ^{1}H-n.m.r. ($CDCl_3$): δ 8.03–7.05 (m, Ph-H), 6.03 (d, $J_{NH,2}$ 8.8 Hz, D_2O-exchangeable, N*H*), 5.76–5.60 (m, -C*H*=), 5.45 (t, *J* 9.0 Hz, H-2′), 5.11–4.91 (m, -CH=CH_2), 4.73–3.34 (m, PhCH_2, sugar C*H* and CH_2, and OCH_2CH=), and 2.01 (s, CH_3CO). It may be noted that N*H*, H-2′, the olefinic protons of the allyl group (δ 6.03–4.91), and the acetyl methyl protons (δ 2.01) now gave the single, sharp signals characteristic of a pure isomer.

Anal. Calc. for $C_{52}H_{57}NO_{12}$ (888.02): C, 70.33; H, 6.47; N, 1.58. Found: C, 70.23; H, 6.69; N, 1.47.

Propyl O-*β*-D-*galactopyranosyl*-(*1*→*4*)-*2-acetamido-2-deoxy*-*β*-D-*glucopyranoside* (**9**). — Compound **8** (200 mg) in anhydrous methanol (5 mL) was treated with 0.5M sodium methoxide (0.5 mL), and the mixture was boiled for 30 min under reflux. The solution was cooled, de-ionized with Rexyn 101 (H^+) resin, the suspension filtered, and the filtrate stirred overnight with 10% palladium-on-charcoal under hydrogen at room temperature and atmospheric pressure. The catalyst was removed by filtration through Celite, and the filtrate and washings were combined, and evaporated to dryness. Crystallization, and recrystallization, of the residue from methanol–ether furnished 92 mg (94%) of **9** as needles, m.p. 240–242° (dec.), $[\alpha]_D^{25}$ −5.7° (*c* 0.97, methanol). The n.m.r. data are given in Table I.

Anal. Calc. for $C_{17}H_{31}NO_{11} \cdot 0.5\ H_2O$ (434.44): C, 47.00; H, 7.42; N, 3.22. Found: C, 47.07; H, 7.19; N, 3.22.

Allyl O-(*2,3,4,6-tetra*-O-*benzyl*-*α*-D-*galactopyranosyl*)-(*1*→*4*)-O-(*2*-O-*benzoyl*-*3,6-di*-O-*benzyl*-*β*-D-*galactopyranosyl*)-(*1*→*4*)-*2-acetamido-3,6-di*-O-*benzyl*-*2-deoxy*-*β*-D-*glucopyranoside* (**11**). — A coupling reactor was charged with compound **8** (100 mg, 0.11 mmol), silver carbonate (85 mg, 0.31 mmol), and silver triflate (80 mg, 0.31 mmol) (in the flat-bottomed arm), and tetra-*O*-benzyl-α-D-galactopyranosyl bromide (**10**) freshly prepared[6] from the 1-acetate (175 mg, 0.30 mmol) (in the conical arm). These components were dried (liquid-nitrogen-cooled trap) for 4 h, and then dry dichloromethane (3 mL) was added to each arm, the flat-bottomed arm was cooled to −25°, and the galactosyl bromide solution was tipped in, portionwise. The mixture was stirred for 3 h at −25°, and kept overnight at 5°; then, methanol (0.2 mL) was added, and stirring was continued for 1 h at 25°. The suspension was filtered through a bed of Celite, the solids were washed with dichloromethane, and the filtrate and washings were combined, and washed with 5% sodium hydrogencarbonate solution. Further processing gave a crude syrup, which was purified on a column of silica gel, to yield 102 mg (64%) of compound **11**, a syrup: $[\alpha]_D^{25}$ +38.6° (*c* 0.85, chloroform); ^{1}H-n.m.r. ($CDCl_3$): similar to that of **8**, with additional signal intensity at δ 8.0–7.15 (Ph-H) and 5.2–3.5 (PhCH_2, OCH_2CH=CH_2, sugar C*H* and CH_2), and loss of the O*H* signal.

Anal. Calc. for $C_{86}H_{91}NO_{17}$ (1410.66): C, 73.22; H, 6.50; N, 0.99. Found: C, 73.08; H, 6.67; N, 1.00.

Allyl O-(*2,3,4,6-tetra*-O-*benzyl*-α-D-*galactopyranosyl*)-(*1→4*)-O-(*3,6-di*-O-*benzyl*-β-D-*galactopyranosyl*)-(*1→4*)-*2-acetamido-4,6-di*-O-*benzyl-2-deoxy*-β-D-*glucopyranoside* (**12**). — Zemplén *O*-debenzoylation of compound **11** (80 mg), as in the first step of the conversion of **8** into **9**, yielded 66 mg (89%) of compound **12** as an amorphous solid; $[\alpha]_D^{25}$ +42.7° (*c* 0.3, chloroform); ^{1}H-n.m.r. ($CDCl_3$): similar to that of **11**, except for an upfield shift of the N*H* signal to δ 5.47, disappearance (upfield shift) of the triplet for H-2′ (was δ 5.53), and appearance of a signal at δ 2.77 (s, 1 H, D_2O-exchangeable, O*H*). The signal for H-1″ was well resolved, at δ 5.01 (d, *J* 2.3 Hz).

Anal. Calc. for $C_{79}H_{87}NO_{16}$ (1306.56): C, 72.62; H, 6.71; N, 1.07. Found: C, 72.27; H, 6.75; N, 0.97.

Propyl O-α-D-*galactopyranosyl*-(*1→4*)-O-β-D-*galactopyranosyl*-(*1→4*)-*2-acetamido-2-deoxy*-β-D-*glucopyranoside* (**13**). — The hydrogenolysis of compound **12** (70 mg) in methanol (10 mL) was conducted in the presence of 10% palladium-on-charcoal (50 mg), as described for the conversion of **8** into **9**. The yield of compound **13** was 30 mg (95%), amorphous solid; $[\alpha]_D^{25}$ +18.8° (*c* 0.25, methanol). The n.m.r. data are given in Table I.

Anal. Calc. for $C_{23}H_{41}NO_{16}$ (587.57): N, 2.38. Found: N, 2.00.

Allyl O-(*2,3,4-tri*-O-*benzyl*-α-L-*fucopyranosyl*)-(*1→2*)-[O-(*2,3,4,6-tetra*-O-*benzyl*-α-D-*galactopyranosyl*)-(*1→4*)]-O-(*3,6-di*-O-*benzyl*-β-D-*galactopyranosyl*)-(*1→4*)-*2-acetamido-3,6-di*-O-*benzyl-2-deoxy*-β-D-*glucopyranoside* (**14**). — The L-fucosylation of **12** was conducted as already described for conversion of **3** into **6**. The materials used were **12** (125 mg, 96 μmol), tetraethylammonium bromide (56 mg, 0.26 mmol), and powdered 4A molecular sieves (0.5 g) in dichloromethane (3 mL), and the tri-*O*-benzyl-α-L-fucopyranosyl bromide (**4**) from 125 mg (0.26 mmol) of the 1-acetate, in dichloromethane (3 mL) plus *N,N*-dimethylformamide (3 mL). Chromatography of the products on a column of silica gel furnished 95 mg (58%) of pure compound **14**; amorphous; $[\alpha]_D^{25}$ −2.8° (*c* 0.5, chloroform); ^{1}H-n.m.r. similar to that of **12**, with additional signals at δ 5.77 (d, *J* 3.1 Hz, H-1 of fucose) and 1.28 (d, *J* 6.0 Hz, CH_3 of fucose), additional signal intensity at δ 7.5–7.0 (Ph-H) and 5.0–3.3 (PhCH_2, $OCH_2CH=$, and sugar C*H* and CH_2), and loss of the O*H* signal.

Anal. Calc. for $C_{106}H_{115}NO_{20}$ (1723.07): C, 73.89; H, 6.73; N, 0.81. Found: C, 73.53; H, 6.91, N, 0.66.

Propyl O-α-L-*fucopyranosyl*-(*1→2*)-[O-α-D-*galactopyranosyl*-(*1→4*)]-O-β-D-*galactopyranosyl*-(*1→4*)-*2-acetamido-2-deoxy*-β-D-*glucopyranoside* (**15**). — Compound **14** (50 mg) was hydrogenolyzed as described for the conversion of **8** into **9**. The yield of **15** was 20 mg (94%) of amorphous solid; $[\alpha]_D^{25}$ −19.1° (*c* 0.23, methanol). The n.m.r. data are recorded in Table I.

Anal. Calc. for $C_{29}H_{51}NO_{20}$ (733.71): N, 1.91. Found: N, 1.61.

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