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Chemical Modification of Lactose. XVII.[1] Syntheses of *O*-α- and *O*-β-L-Fucopyranosyl-(1→4)- or -(1→6)-*O*-β-D-galactopyranosyl-(1→4)-D-glucopyranoses (4′- or 6′-*O*-α- and -*O*-β-L-Fucopyranosyllactoses)[2]

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1,6-Anhydro-2,2′,3,3′,6′- and -2,2′,3,3′,4′-penta-*O*-benzyl-β-lactoses (**4** and **7**) were synthesized from 1,6-anhydro-2,2′,3,3′-tetra-*O*-benzyl-4′,6′-*O*-benzylidene-β-lactose (**1**). Condensation of **4** with 2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl bromide (acetobromofucose) in the conventional Koenigs–Knorr reaction, followed by deacetylation, gave 4′-*O*-linked trisaccharide derivatives bearing α- and β-L-fucopyranosyl linkages (**10** and **15**) in 13.4 and 25.6% yields, respectively. Analogous condensation of **7** with acetobromofucose gave a 6′-*O*-linked, fully protected trisaccharide bearing a β-L-fucopyranosyl linkage (**20**) in 64% yield. Halide ion-catalyzed condensation of **7** with 2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl bromide gave a trisaccharide derivative bearing an α-L-fucopyranosyl linkage (**26**) in 51.8% yield. Removal of the protecting groups of **10**, **15**, **20**, and **26** provided the title trisaccharides (**14**, **19**, **25**, and **30**). ^{1}H- and ^{13}C-NMR spectral data of **14**, **19**, **25**, **30**, and synthetic intermediates are also presented.

Keywords——synthesis; 4′-*O*-α-L-fucopyranosyllactose; 4′-*O*-β-L-fucopyranosyllactose; 6′-*O*-α-L-fucopyranosyllactose; 6′-*O*-β-L-fucopyranosyllactose; human milk oligosaccharide; 1,6-anhydro-trisaccharide; ^{1}H-NMR; ^{13}C-NMR

Syntheses of oligosaccharides bearing an α- or a β-L-fucosyl linkage have been carried out during the last ten years,[3] because the occurrence of α-L-fucopyranose-containing oligosaccharides in natural products of biological interest has often been reported.[4] Human milk also contains fucosyl-oligosaccharides with various structures, among which 2′-*O*- or 3-*O*-α-L-fucopyranosyllactose has the simplest structure.[5] Baer and Abbas reported the syntheses of 3′-*O*-α-, 3′-*O*-β,[6a,b] and 6′-*O*-α-L-fucopyranosyllactoses,[6c] positional isomers of fucosyllactose in human milk. Recently, Abbas *et al.* reported the synthesis of 2′-*O*-α-L-fucosyllactose[7] having the same structure as a fucosyllactose in human milk.

In Part XV of this series,[8] 3′-*O*-α- and 3′-*O*-β-L-fucopyranosyllactoses were synthesized. Subsequent biological studies of these compounds yielded interesting results. Namely, the antiserum induced by an artificial antigen prepared by coupling the former with bovine serum albumin reacts with human colon adenocarcinoma and murine teratocarcinoma cells, but scarcely reacts in normal cells.[9] This finding is of interest from the viewpoints of carcinogenesis, cancer diagnosis, and also cancer immunotherapy. As an extension of our synthetic studies of oligosaccharides in human milk and their analogs, and because of the biological significance of these compounds as haptens of artificial antigens, we now report the syntheses of the title compounds in the four subdivisions.

Syntheses of 1,6-Anhydro-2,2′,3,3′,6′- and 1,6-Anhydro-2,2′,3,3′,4′-penta-*O*-benzyl-β-lactoses (4 and 7)

Benzylation of 2,2′,3,3′-tetra-*O*-acetyl-1,6-anhydro-4′,6′-*O*-benzylidene-β-lactose[10] afforded crystalline 2,2′,3,3′-tetrabenzylether (**1**). Debenzylidenation of **1** gave 1,6-anhydro-2,2′,3,3′-tetra-*O*-benzyl-β-lactose (**2**). Subsequent selective benzylation of **2** with 1.04 molar

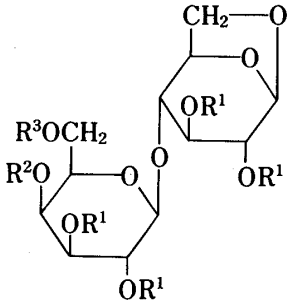
equivalents of benzyl bromide and excess alkali in *N,N*-dimethylformamide (DMF) gave three products, which were detected by thin-layer chromatography (TLC). Each product was isolated by column chromatography and designated **3**, **4**, and **7** in order of decreasing *Rf* value: **4** predominated.

Compound **3** was obtained in 9.2% yield and identified as 1,6-anhydro-2,2′,3,3′,4′,6′-hexa-*O*-benzyl-β-lactose by comparison with an authentic sample prepared by benzylation of 2,2′,3,3′,4′,6′-hexa-*O*-acetyl-1,6-anhydro-β-lactose[11] with excess benzyl chloride and alkali.

Compound **4**, the major product in this selective benzylation, was isolated in 34% yield. The infrared (IR) spectrum showed a signal due to the hydroxyl group. The proton nuclear magnetic resonance (^{1}H-NMR) spectrum showed resonances due to the corresponding pentabenzylether bearing one unprotected hydroxyl group. Further structural assignment was carried out by methylation analysis. Thus, methylation of **4** gave the pentabenzylmonomethylether (**5**), and subsequent debenzylation provided the monomethylether (**6**). The carbon-13 nuclear magnetic resonance (^{13}C-NMR) spectrum of **6** was measured in deuterium oxide (D_2O). The results are shown in Table I. The assignments of anomeric and methoxyl carbons were carried out by selective proton decoupling of the corresponding protons, and other carbons were assigned by comparison with the observed values for 1,6-anhydro-β-lactose.[12] The C-4′ resonance appeared at 80.2 ppm, deshielded by 10.3 ppm as compared to the chemical shift of C-4′ of 1,6-anhydro-β-lactose (69.9 ppm). Therefore, the methoxyl group of **6** is located in the C-4′ position and the structure of **4** was thus assigned as 1,6-anhydro-2,2′,3,3′,6′-penta-*O*-benzyl-β-lactose.

Compound **7** was isolated in 2.8% yield. The structure was assigned as 1,6-anhydro-2,2′,3,3′,4′-penta-*O*-benzyl-β-lactose by comparison of **7** with an authentic sample.[13] Methylation of **7**, followed by debenzylation, provided the monomethylether (**9**). In the ^{13}C-NMR spectrum, the C-6′ resonance, assigned by proton off-resonance decoupling, was deshielded as compared to the chemical shift of C-6′ of 1,6-anhydro-β-lactose (Table I). This result provides unequivocal proof of the position of the newly introduced substituent in **7**.

On the other hand, selective cleavage of the benzylidene acetal in **1** with the lithium aluminum hydride–aluminum chloride reagent[14] gave **7** as the major product (70.9%) with a small amount of **4** (6.3%).



2: R^1=Bn, R^2=R^3=H
3: R^1=R^2=R^3=Bn
4: R^1=R^3=Bn, R^2=H
5: R^1=R^3=Bn, R^2=Me
6: R^1=R^3=H, R^2=Me
7: R^1=R^2=Bn, R^3=H
8: R^1=R^2=Bn, R^3=Me
9: R^1=R^2=H, R^3=Me

Bn=benzyl, Me=methyl

Chart 1

Syntheses of *O*-α- and *O*-β-Fucopyranosyl-(1→4)-*O*-β-D-galactopyranosyl-(1→4)-D-glucopyranoses (4′-*O*-α- and 4′-*O*-β-L-Fucopyranosyllactoses) (14 and 19)

Reaction of **4** (1 mol) and 2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl bromide (acetobromofucose)[15] (2.61 mol) with mercuric cyanide in benzene–nitromethane was carried out by stirring the mixture at room temperature for 72 h. The ^{1}H-NMR spectroscopy of the product ioslated by column chromatography indicated that it is a mixture of α- and β-isomers. Thus, in order to isolate each isomer, the mixture was deacetylated and the deacetylated product was

chromatographed on a column. Trisaccharide derivative bearing an α-L- or a β-L-fucopyranosyl linkage (**10** or **15**) was isolated from the earlier or the later fraction in 13.4 or 25.6% yield, respectively. Hydrogenolytic debenzylation of **10** and **15** provided the 1,6-anhydro-trisaccharides (**11** and **16**).

In order to determine the position and configuration of the fucopyranosyl linkage, the ^{1}H- and ^{13}C-NMR spectra were measured in D_2O. The signals due to the anomeric protons were assigned by comparison with those of methyl α- or β-L-fucopyranoside, and 1,6-anhydro-β-lactose. In **11** and **16**, the newly introduced anomeric protons (H-1″) appeared as doublets with reasonable coupling constants (J=3 and 7 Hz, respectively) for the assigned configurations. In the ^{13}C-NMR spectra (Table I), the signals were assigned by comparison with the literature values for methyl α- or β-L-fucopyranoside[8] and with the observed values for 1,6-anhydro-β-lactose. The resonances due to the anomeric carbons of the fucopyranosyl linkage (C-1″) appeared at 102.4 and 104.2 ppm. The resonance for C-4′ was deshielded as compared to the chemical shift for that of 1,6-anhydro-β-lactose.

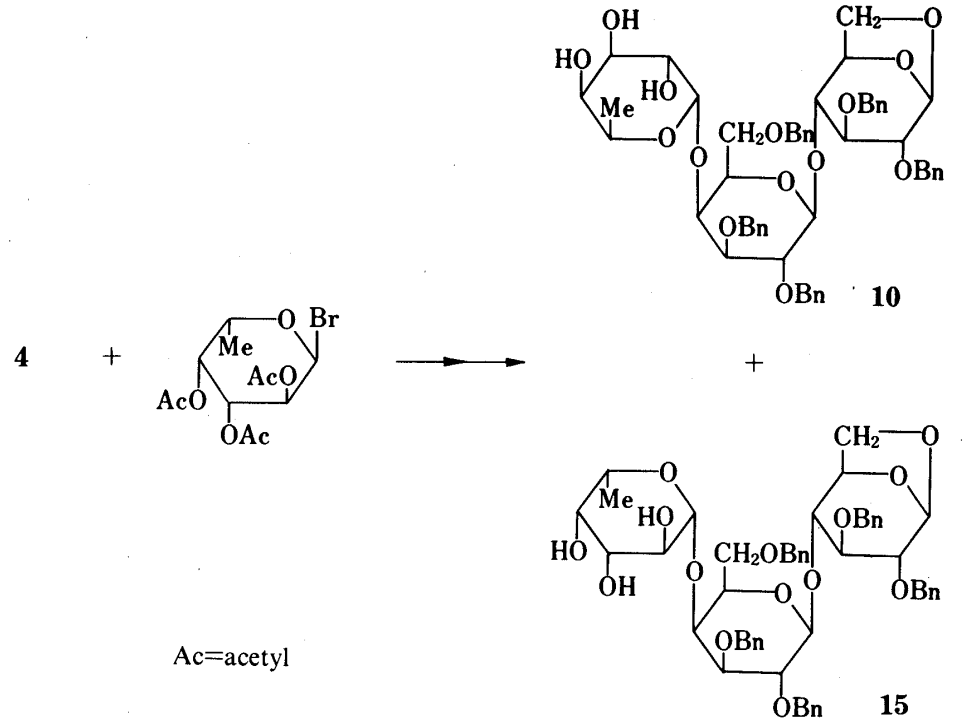


Chart 2

Acetylation of **11** and **16** gave the corresponding octaacetates (**12** and **17**). Subsequent treatment of **12** and **17** with titanium tetrabromide in boiling chloroform resulted in selective cleavage of the 1,6-anhydro-ring to give the bromide with a free hydroxyl group at the C-6 position. Without purification, the bromide was quickly converted into the corresponding β-nonaacetate (**13** or **18**) by the conventional Koenigs–Knorr reaction. The β-configurations of **13** and **18** were confirmed by the values of coupling constants in the ^{1}H-NMR spectra.

Deacetylaion of **13** or **18** provided 4′-*O*-α- or 4′-*O*-β-L-fucopyranosyllactose (**14** or **19**) as a hygroscopic amorphous powder. The ^{13}C-NMR spectra of **14** and **19** were measured in D_2O (Table II). The signals were assigned by comparison with literature values for methyl α- and β-L-fucopyranosides,[8] and α- and β-lactoses.[16] The data support the validity of the assigned position and configuration of the newly introduced fucopyranosyl group in each product.

TABLE I. ^{13}C Chemical Shifts, δ (ppm) from TMS

Compound	Carbon																		
	C-1	C-2	C-3	C-4	C-5	C-6	C-1′	C-2′	C-3′	C-4′	C-5′	C-6′	C-1″	C-2″	C-3″	C-4″	C-5″	C-6″	OMe
6[a]	102.7	71.1	72.7	78.8	75.2	66.3	103.1	72.2	74.1	80.2	76.7	61.9							62.6
9[b]	102.6	71.1	72.7	78.9	75.2	66.3	103.1	71.8	73.5	70.1	74.6	72.9							59.7
11[c]	102.7	71.2	72.7	78.9	75.1	66.3	103.0	72.5	74.6	79.4	76.5	62.5	102.4	73.0	69.9	70.8	68.8	16.5	
16[d]	102.6	71.1	72.5	78.7	75.1	66.2	103.1	72.1	73.0	78.7	76.4	61.5	104.2	72.5	73.8	72.5	72.1	16.6	
22[e]	102.7	71.2	72.7	79.1	75.3	66.4	103.2	71.8	73.7	69.8	74.4	69.8	103.9	72.5	74.2	72.2	71.7	16.7	
27[f]	102.6	71.1	72.6	79.0	75.2	66.2	103.3	71.8	73.7	69.9	74.9	68.3	100.2	72.9	69.2	70.8	67.9	16.5	
1,6-Anhydro-β-lactose[g]	102.7	71.2	72.7	78.9	75.3	66.3	103.3	71.9	73.7	69.9	76.5	62.3							
Methyl α-L-fucopyranoside[8]													100.7	73.0	69.1	70.8	67.6	16.5	56.3
Methyl β-L-fucopyranoside[8]													104.9	72.6	74.2	72.1	71.7	16.6	58.4

a) 1,6-Anhydro-4′-*O*-methyl-β-lactose.
b) 1,6-Anhydro-6′-*O*-methyl-β-lactose.
c) *O*-α-L-Fucopyranosyl-(1→4)-*O*-β-D-galactopyranosyl-(1→4)-1,6-anhydro-β-D-glucopyranose.
d) *O*-β-L-Fucopyranosyl-(1→4)-*O*-β-D-galactopyranosyl-(1→4)-1,6-anhydro-β-D-glucopyranose.
e) *O*-β-L-Fucopyranosyl-(1→6)-*O*-β-D-galactopyranosyl-(1→4)-1,6-anhydro-β-D-glucopyranose.
f) *O*-β-L-Fucopyranosyl-(1→6)-*O*-β-D-galactopyranosyl-(1→4)-1,6-anhydro-β-D-glucopyranose.
g) The observed values.

TABLE II. ^{13}C Chemical Shifts, δ (ppm) from TMS

Compound	Carbon																	
	C-1	C-2	C-3	C-4	C-5	C-6	C-1′	C-2′	C-3′	C-4′	C-5′	C-6′	C-1″	C-2″	C-3″	C-4″	C-5″	C-6″
14 (α)[a]	93.0	72.3	72.6	80.0	71.2	61.1	104.1	72.6	74.5	79.2	76.5	62.4	102.4	72.9	69.8	70.7	68.8	16.5
14 (β)[a]	96.9	75.0	75.6	79.9	76.0	61.3												
19 (α)[b]	93.0	72.4	72.6	79.8	71.3	61.2	104.2	72.4	72.9[e]	78.9	76.4	61.5	104.2	73.0[e]	73.9	72.1	72.0	16.6
19 (β)[b]	96.9	75.0	75.6	79.7	76.0	61.3												
25 (α)[c]	93.0	72.0	72.1	80.9	71.1	61.3	103.7	72.0[f]	73.7	69.7	74.4	69.5	104.5	72.5	74.0	72.1[f]	71.6	16.6
25 (β)[c]	96.9	74.9	75.7	80.7	75.8	61.4												
30 (α)[d]	93.0	72.4	72.7	80.7	71.1	61.2	104.4	71.9	73.8	69.8[g]	74.9	68.6	100.5	73.0	69.4[g]	70.7	68.0	16.6
30 (β)[d]	96.8	75.0	75.6	80.5	75.8	61.3												
Lactose (α)[16]	92.7	72.2	72.4	79.3	71.0	61.0	103.6	72.0	73.5	69.5	76.2	62.0						
Lactose (β)[16]	96.6	74.8	75.3	79.2	75.6	61.1	103.7	72.0	73.5	69.5	76.2	62.0						

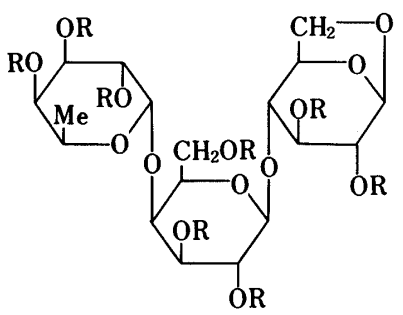
a) *O*-α-L-Fucopyranosyl-(1→4)-*O*-β-D-galactopyranosyl-(1→4)-glucopyranose.
b) *O*-β-L-Fucopyranosyl-(1→4)-*O*-β-D-galactopyranosyl-(1→4)-glucopyranose.
c) *O*-β-L-Fucopyranosyl-(1→6)-*O*-β-D-galactopyranosyl-(1→4)-glucopyranose.
d) *O*-α-L-Fucopyranosyl-(1→6)-*O*-β-D-galactopyranosyl-(1→4)-glucopyranose.
e, f, g) Assignments may be reversed.

Synthesis of *O*-β-L-Fucopyranosyl-(1→6)-*O*-β-D-galactopyranosyl-(1→4)-D-glucopyranose (6′-*O*-β-L-Fucopyranosyllactose) (25)

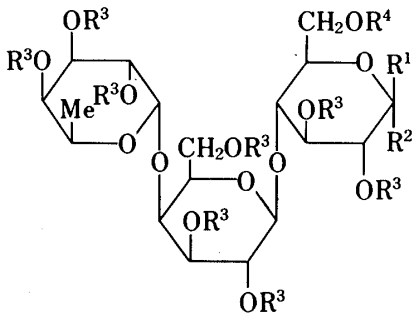
Condensation of acetobromofucose[15] (1.22 mol) at the C-6′ position of **7** (1 mol) was carried out as described for the C-4′ isomer (**4**) but with a shorter reaction time (48 h). TLC indicated the formation of one main product with a trace of by-products. On column chromatographic purification, the fully protected trisaccharide bearing a β-L-fucopyranosyl linkage (**20**) was isolated in 64% yield. The ^1H-NMR spectrum of **20** was consistent with the proposed structure.

Deacetylation of **20** gave an amorphous powder (**21**), which was debenzylidenated to provide the crystalline 1,6-anhydro-trisaccharide (**22**) in 93% overall yield. In the ^1H-NMR spectrum of **22**, the resonance due to the anomeric proton of the fucopyranosyl linkage (H-1″) appeared as a doublet with a coupling constant $J=7$ Hz This value is consistent with β-L-configuration. The ^{13}C-NMR spectral data are summarized in Table I. The resonance due to the anomeric carbon of the fucopyranosyl linkage (C-1″) appeared at 103.9 ppm and that for C-6′ appeared at 69.8 ppm. The latter was deshielded by 7.5 ppm as compared to the chemical shift of C-6′ of 1,6-anhydro-β-lactose.

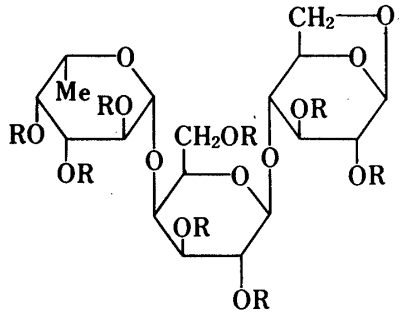
In the L-fucosidation of **7** mentioned above, stereospecific β-L-fucosidation proceeded to give only one main product, and the formation of a trisaccharide bearing an α-L-fucopyranosyl linkage could not be detected. However, in the formation of trisaccharides branched at the C-4′ position, as described in the earlier part of this paper, both α- and β-L-fucosyl linkages



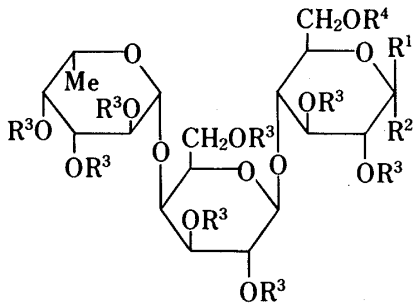
11 : R=H
12 : R=Ac



13 : R^1=OAc, R^2=R^4=H, R^3=Ac
14 : R^1, R^2=H, OH, R^3=R^4=H



16 : R=H
17 : R=Ac



18 : R^1=OAc, R^2=R^4=H, R^3=Ac
19 : R^1, R^2=H, OH, R^3=R^4=H

Chart 3

were formed in a yield ratio of *ca.* 1 : 2. This difference may be attributed to the difference of reactivity at the primary and the secondary hydroxyl groups.

The 1,6-anhydro-ring of **22** was similarly cleaved *via* three steps as described for the C-4′ isomer (**15**) to give the trisaccharide β-nonaacetate (**24**). In the ^{1}H-NMR spectrum of **24,** the signal of the anomeric proton of the terminal glucose appeared as a doublet with a coupling constant J=8 Hz.

Deacetylation of **24** gave 6′-*O*-β-L-fucopyranosyllactose (**25**) as a hygroscopic amorphous powder. In the ^{1}H-NMR spectrum of **25**, the resonances due to anomeric protons appeared at 5.65 (α-Glc, d, J=3.5 Hz) and 5.10 (β-Glc, d, J=7.8 Hz) ppm, but those due to H-1′ and H-1″ overlapped with other ring protons and could not be assigned. The ^{13}C-NMR spectral for **25** are summarized in Table II. The C-1 and C-1′, and C-1″ resonances appeared at 93.0 (α-Glc), 96.9 (β-Glc), 103.7 (β-Gal), and 104.5 (β-Fuc) ppm, respectively. The C-6′ resonance (69.5 ppm) was distinguished from that for C-4′ (69.7 ppm) by proton off-resonance decoupling, and was deshielded by 7.5 ppm as compared to the chemical shift for C-6′ of lactose (62.0 ppm).

Synthesis of *O*-α-L-Fucopyranosyl-(1→6)-*O*-β-D-galactopyranosyl-(1→4)-D-glucopyranose (6′-*O*-α-L-Fucopyranosyllactose) (30)

α-L-Fucosidation of **7** was carried out by means of the halide ion catalyzed reaction established by Lemieux and co-workers.[17] A mixture of **7** and 2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl bromid[18] in DMF-1,2-dichloroethane containing tetraethylammonium bromide, diisopropylethylamine, and molecular sieve was stirred at room temperature under a nitrogen atmosphere: TLC indicated the formation of one main product with a trace of by-products. On column chromatographic purification, fully benzylated 1,6-anhydro-trisaccharide bearing an α-L-fucopyranosyl linkage (**26**) was isolated in 51.8% yield. Hydrogenolytic debenzylation of **26** afforded *O*-α-L-fucopyranosyl-(1→6)-*O*-β-D-galactopyranosyl-(1→4)-1,6-anhydro-β-D-glucopyranose (**27**). In the ^{1}H-NMR spectrum of **27**, the

resonance due to the anomeric proton of the fucopyranosyl linkage (H-1″) appeared as a doublet with a coupling constant $J=3$ Hz, which is consistent with α-L-fucopyranosyl configuration. The ^{13}C-NMR spectral data are summarized in Table I. The resonance due to the anomeric carbon of the fucopyranosyl linkage (C-1″) appeared at 100.2 ppm. The C-6′ and C-5″ resonances were assigned as 68.3 and 67.9 ppm, respectively, by proton off-resonance decoupling. The C-6′ resonance was deshielded by 6.0 ppm as compared to the chemical shift for C-6′ of 1,6-anhydro-β-lactose (62.3 ppm).

Conversion of **27** to the trisaccharide β-nonaacetate (**29**) was carried out by a method similar to that used for the corresponding β-isomer (**22**). In the ^{1}H-NMR spectrum of **29**, the anomeric proton due to the terminus glucose appeared as a doublet with a coupling constant $J=8$ Hz. Deacetylation of **29** gave 6′-*O*-L-fucopyranosyllactose (**30**) as a hygroscopic amorphous powder, $[\alpha]_D^{22}$ −27.8° (no mutarotation, H_2O). Baer and Abbas[6c] obtained 6′-*O*-α-L-fucopyranosyllactose as a white hygroscopic solid, $[\alpha]_D^{25}$ −28.3° in methanol, $[\alpha]_D^{22}$ −23° (initial) → −21° (22 h, H_2O). In the ^{1}H-NMR spectrum of **30**, the resonances due to the anomeric protons H-1 (α and β), H-1′, and H-1″ appeared at 5.67 (α-Glc, d, $J=3.5$ Hz), 5.12 (β-Glc, d, $J=7$ Hz), 4.89 (β-Gal, d, $J=6$ Hz), and 5.39 (α-Fuc, d, $J=3.5$ Hz) ppm, respectively. The ^{13}C-NMR spectral data of **30** are summarized in Table II. The resonances due to the anomeric carbons C-1 (α and β), C-1′, and C-1″ appeared at 93.0 (α-Glc), 96.8 (β-Glc), 104.4 (β-Gal), and 100.5 (α-Fuc) ppm, respectively. The C-6′ resonance of **30**, assigned by proton off-resonance decoupling, appeared at 68.6 ppm, and was deshielded by 6.6 ppm as compared to the chemical shift for C-6′ of lactose (62.0 ppm).

Experimental

Melting points were determined with a Yanagimoto MP-S2 micro melting point apparatus and are uncorrected. Solutions were concentrated in a rotary evaporator below 40°C under a vacuum. Optical rotations were measured with a Union Giken PM-201 automatic digital polarimeter in a 0.5 dm tube. IR spectra were recorded with a JASCO IRA-2 or A-102 spectrometer. ^{1}H-NMR spectra were recorded at 100 MHz with a JEOL JNM-MH-100 or JNM-FX-100 spectrometer. ^{13}C-NMR spectra were recorded at 25 MHz with a JEOL JNM-FX-100 spectrometer. Tetramethylsilane was used as an internal (in $CDCl_3$) or external (in D_2O) standard. Chemical shifts are given on the δ scale. TLC was performed on pre-coated silica gel plates 0.25 mm thick (Kieselgel $60F_{254}$, Merck) with the following solvent combinations (v/v): (A), $CHCl_3$–EtOH (93:7); (B), $CHCl_3$–acetone (3:1); (C), benzene–ether (1:1); (D), 70% aq. 2-PrOH–AcOEt (2:1). Detection was effected with H_2SO_4 or by UV irradiation at 254 nm. Column chromatography was performed on either Wakogel C-200 (Wako Pure Chemical Industries, Ltd., Osaka), Silica Gel BW-80 or BW-820-H (Fuji-Davison Chemical Ltd., Nagoya). Solvent combinations for elution are given as v/v.

1,6-Anhydro-2,2′-3,3′-tetra-*O*-benzyl-4′,6′-*O*-benzylidene-β-lactose (1)——A mixture of 2,2′,3,3′-tetra-*O*-acetyl-1,6-anhydro-4′,6′-*O*-benzylidene-β-lactose[10] (20 g), powdered KOH (70 g), and benzyl chloride (120 ml) was heated at 130—135°C for 3 h under stirring. The mixture was diluted with H_2O, stirred overnight, and then extracted with CH_2Cl_2 (3×50 ml). The combined extracts were washed with H_2O, dried (Na_2SO_4), and concentrated (finally at 110—120°C) under a vacuum to remove benzyl alcohol. The residue was chromatographed on a column first with benzene and then successively with 20:1, 10:1, 5:1, and 1:1 benzene–ether. Removal of the solvent from the benzene–ether fractions gave a residue, which was crystallized from EtOH. Recrystallization from EtOH gave pure **1** (22.73 g, 85.4%), mp 116—117°C $[\alpha]_D^{24}$ −16.6° ($c=1.05$, $CHCl_3$), as fine needles. ^{1}H-NMR ($CDCl_3$): 5.45 (2H, s, H-1, β-Glc and $C_6H_5C\underline{H}$), 7.00—7.60 (25H, m, aromatic protons). TLC: *Rf* 0.73 (solvent A), 0.60 (B), 0.44 (C). *Anal.* Calcd for $C_{47}H_{48}O_{10}$: C, 73.04; H, 6.26. Found: C, 73.12; H, 6.20.

1,6-Anhydro-2,2′,3,3′-tetra-*O*-benzyl-β-lactose (2)——A solution of **1** (10 g) in EtOH (30 ml) and 60% (v/v) aq. AcOH (100 ml) was refluxed for 15 min to carry out debenzylidenation. The mixture was concentrated to a syrup, which was chromatographed on a column with $CHCl_3$–acetone (20:1) to yield **2** (8.01 g, 90.4%), $[\alpha]_D^{20}$ −25.3° ($c=1.41$, $CHCl_3$), as a syrup. IR ν_{max}^{Nujol} cm^{-1}: 3600—3150 (br OH). ^{1}H-NMR ($CDCl_3$): 2.72 (2H, br s, exchangeable with D_2O, OH×2), 5.46 (1H, s, H-1, β-Glc), 7.10—7.50 (20H, m, aromatic protons). TLC: *Rf* 0.44 (solvent A), 0.18 (B), 0.10 (C). *Anal.* Calcd for $C_{40}H_{44}O_{10}$: C, 70.16; H, 6.48. Found: C, 70.16; H, 6.50.

1,6-Anhydro-2,2′,3,3′,4′,6′-hexa-*O*-benzyl-β-lactose (3)——Benzylation of 2,2′,3,3′,4′,6′-hexa-*O*-acetyl-1,6-anhydro-β-lactose[11] (1 g) with powdered KOH (3.5 g) and benzyl chloride (6 ml) was carried out as described for the preparation of **1**. On column chromatography with benzene–ether (10:1), **3** (1.45 g, 96.7%),

$[\alpha]_D^{22}$ −27.2° (c=1.02, $CHCl_3$), was isolated as a syrup. ^{1}H-NMR ($CDCl_3$): 5.41 (1H, s, H-1, β-Glc), 7.00—7.60 (30H, m, aromatic protons). TLC: *Rf* 0.73 (solvent A), 0.65 (B), 0.65 (C). *Anal.* Calcd for $C_{54}H_{56}O_{10}$: C, 74.98; H, 6.53. Found: C, 74.59; H, 6.55.

1,6-Anhydro-2,2′,3,3′,6′-penta-*O*-benzyl-β-lactose (4) and 1,6-Anhydro-2,2′,3,3′,4′-penta-*O*-benzyl-β-lactoses (7)——1) Selective Benzylation of **2**: Benzyl bromide (1.80 ml, 15.2 mmol) was added dropwise with stirring at 0°C to a suspension of **2** (10 g, 14.6 mmol), BaO (5.50 g, 35.9 mmol), and $Ba(OH)_2 \cdot 8H_2O$ (2.16 g, 6.85 mmol) in dry DMF (100 ml). After being stirred for 2 d at room temperaure, the mixture was poured into ice-H_2O, stirred for a further 24 h, and then filtered. The residue was washed with CH_2Cl_2. The organic layers from the filtrate and washings were separated and the aqueous layer was extracted with CH_2Cl_2 (3×50 ml). The combined organic layers were successively washed with H_2O, 10% HCl, H_2O, aq. $NaHCO_3$, and H_2O, then dried ($MgSO_4$), and concentrated to a syrup, which showed four spots, *Rf* 0.65, 0.50 (major), 0.16, and 0.10 on TLC with solvent C. On column chromatography, successive elutions with 20:1, 10:1, 6:1, 3:1, and 1:1 $CHCl_3$–acetone gave the following products.

The component having *Rf* 0.65 was a syrup (1.04 g, 9.2%), which was indistinguishable (IR, ^{1}H-NMR, and TLC) from **3**.

The component having *Rf* 0.50 gave **4** (3.84 g, 34%), $[\alpha]_D^{21}$ −25.1° (c=1, $CHCl_3$), as a syrup. IR ν_{max}^{Nujol} cm^{-1}: 3430 (OH). ^{1}H-NMR ($CDCl_3$): 2.24 (1H, br s, exchangeable with D_2O, OH), 5.48 (1H, s, H-1, β-Glc), 7.00—7.50 (25H, m, aromatic protons). TLC: *Rf* 0.69 (solvent A), 0.56 (B), 0.50 (C). *Anal.* Calcd for $C_{47}H_{50}O_{10}$: C, 72.85; H, 6.50. Found: C, 73.01; H, 6.49.

The component having *Rf* 0.16 crystallized from EtOH. Recrystallization from EtOH gave pure **7** (0.32 g, 2.8%), mp 121—122°C, $[\alpha]_D^{24}$ −40.5° (c=1.04, $CHCl_3$, as fine needles. [lit.[13] mp 122—123°C, $[\alpha]_D^{18}$ −42.9°, (c=1.05, $CHCl_3$)]. *IR* ν_{max}^{Nujol} cm^{-1}: 3520 (OH). ^{1}H-NMR ($CDCl_3$): 5.44 (1H, s, H-1, β-Glc), 7.00—7.60 (25H, m, aromatic protons). TLC: *Rf* 0.55 (solvent A), 0.29 (B), 0.16 (C). *Anal.* Calcd for $C_{47}H_{50}O_{10}$: C, 72.85; H, 6.50. Found: C, 72.58; H, 6.42.

The component having *Rf* 0.10 was the starting material (**2**, 4.28 g, 42.8%), which was recycled.

2) Selective Cleavage of **1** with $LiAlH_4$–$AlCl_3$ Reagent[14]: $LiAlH_4$ (3.40 g, 89.6 mmol) was added in three portions under stirring to a solution of **1** (10 g, 10.3 mmol) in ether–CH_2Cl_2 (300 ml, 1:1, v/v), and the mixture was gradually heated to the boiling point. A solution of $AlCl_3$ (10 g, 75 mmol) in ether (100 ml) was then added to the hot solution over a period of 30 min under stirring. After being refluxed for 2 h, the mixture was cooled to room temperature. Ethyl acetate and H_2O were successively added in small portions to decompose excess reagent. The whole was filtered and the residue was washed with ether. The combined filtrate and washings were washed with H_2O, dried (Na_2SO_4), and concentrated to a syrup, which showed two spots, *Rf* 0.50 (minor) and 0.16 (major), on TLC with solvent C. On column chromatography with $CHCl_3$–acetone (20:1), the minor product was eluted first and isolated as a syrup (0.63 g, 6.3%), which was indistinguishable (IR, ^{1}H-NMR, and TLC) from **4**.

Removal of the solvent from the subsequent fractions gave an amorphous powder, which was crystallized from EtOH. Recrystallization from EtOH yielded fine needles (7.11 g, 70.9%), which were indistinguishable (mixed mp, IR, ^{1}H-NMR, and TLC) from **7**.

1,6-Anhydro-2,2′,3,3′,6′-penta-*O*-benzyl-4′-*O*-methyl-β-lactose (5)——A suspension of **4** (610 mg, 0.79 mmol) and Ag_2O (1.22 g, 5.26 mmol) in CH_3I (24 ml) was refluxed under stirring, with exclusion of light and moisture. After 7, 14, and 21 h, further portions of Ag_2O (each 1.22 g) were added, and refluxing was continued for a further 7 h under stirring. The mixture was diluted with CH_2Cl_2 (30 ml) and filtered. The residue was washed with CH_2Cl_2 and the combined CH_2Cl_2 solutions were concentrated to a syrup, which was re-dissolved in CH_2Cl_2 (50 ml). The CH_2Cl_2 solution was washed with H_2O, 10% $Na_2S_2O_3$, and H_2O, then dried ($CaCl_2$), and concentrated to a syrup. On column chromatography with $CHCl_3$–acetone (20:1), pure **5** (494 mg, 79.5% $[\alpha]_D^{24}$ −34° (c=1, $CHCl_3$), was isolated as a syrup. ^{1}H-NMR ($CDCl_3$): 3.56 (3H, s, $OC\underline{H}_3$), 7.10—7.50 (25H, m, aromatic protons). TLC: *Rf* 0.75 (solvent A), 0.63 (B), 0.64 (C). *Anal.* Calcd for $C_{48}H_{52}O_{10}$: C, 73.08; H, 6.64. Found: C, 72.91; H, 6.88.

1,6-Anhydro-4′-*O*-methyl-β-lactose (6)——A solution of **5** (340 mg) in dry MeOH (20 ml) was hydrogenated at room temperature under atmospheric pressure with a Pd catalyst freshly prepared[19] from $PdCl_2$ (300 mg). The mixture was filtered and the filtrate was concentrated to a syrup, which was dissolved in H_2O. After removal of insoluble material by filtration, the filtrate was concentrated to provide pure **6** (145 mg, 99.9%), $[\alpha]_D^{20}$ −46.2° (c=0.88, H_2O), as a hygroscopic glass. ^{1}H-NMR (D_2O): 3.99 (3H, s, $OC\underline{H}_3$), 5.23 (1H, d, $J_{1',2'}$=6 Hz, H-1′, β-Gal), 5.91 (1H, s, H-1, β-Gal). ^{13}C-NMR: see Table I. TLC: *Rf* 0.39 (solvent D). *Anal.* Calcd for $C_{13}H_{22}O_{10} \cdot H_2O$: C, 43.82; H, 6.79. Found: C, 44.16; H, 6.94.

1,6-Anhydro-2,2′,3,3′,4′-penta-*O*-benzyl-6′-*O*-methyl-β-lactose (8)——Methylation of **7** (0.88 g) with Ag_2O (1.76 g) and CH_3I (35 ml) was carried out as described for the methylation of **5** to afford **8** (740 mg, 82.6%), $[\alpha]_D^{23}$ −25.3° (c=1.07, $CHCl_3$), as a syrup. ^{1}H-NMR ($CDCl_3$): 3.20 (3H, s, OCH_3), 7.10—7.50 (25H, m, aromatic protons). TLC: *Rf* 0.72 (solvent A), 0.56 (B), 0.46 (C). *Anal.* Calcd for $C_{48}H_{52}O_{10}$: C, 73.08; H, 6.64. Found: C, 72.77; H. 6.80.

1,6-Anhydo-6′-*O*-methyl-β-lactose (9)——Debenzylation of **8** (0.45 g) in dry MeOH (30 ml) was carried out as described for **6** to provide **9** (183 mg, 94.8%), $[\alpha]_D^{21}$ −50.5° (c=1.06, H2O), as a hygroscopic solid. ^{1}H-

NMR (D_2O): 3.85 (3H, s, OCH_3), 5.22 (1H, d, $J_{1',2'}$=6 Hz, H-1', β-Gal), 5.90 (1H, s, H-1, β-Glc). ^{13}C-NMR: see Table I. TLC: *Rf* 0.36 (solvent D). *Anal.* Calcd for $C_{13}H_{22}O_{10}\cdot H_2O$: C, 43.82; H, 6.79. Found: C, 43.77; H, 6.85.

O-α- and O-β-L-Fucopyranosyl-(1→4)-O-(2,3,6-tri-O-benzyl-β-D-galactopyranosyl)-(1→4)-1,6-anhydro-2,3-di-O-benzyl-β-D-glucopyranoses (10 and 15)——2,3,4-Tri-*O*-acetyl-α-L-fucopyranosyl bromide[15] (3.63 g, 10.3 mmol) and mercuric cyanide (3.32 g, 13.1 mmol) were added to a solution of **4** (3.06 g, 3.95 mmol) in dry benzene–nitromethane (60 ml, 1:1, v/v). The mixture was stirred at room temperature for 72 h, diluted with benzene (50 ml), and then filtered to remove mercuric salts. The residue was washed with benzene, and the combined filtrate and washings were successively washed with H_2O, aq. $NaHCO_3$, and H_2O, then dried ($MgSO_4$), and concentrated to a syrup (5.52 g). The syrup was stored overnight in a vacuum desiccator to effect complete desiccation. A 0.5 M methanolic solution of MeONa (3 ml) was added to a solution of the syrup in dry MeOH (55 ml) to carry out deacetylation. After being stirred for 4 h at room temperature, the mixture was neutralized with Amberlite IR-120 (H^+) resin, filtered, and concentrated to an amorphous powder (4.03 g), which showed two spots, *Rf* 0.55 (minor) and 0.30 (major), on TLC with $CHCl_3$–acetone (1:1). On column chromatography, successive elutions with 10:1, 3:1, and 1:1 $CHCl_3$–acetone, afforded **10** (487 mg, 13.4%), $[\alpha]_D^{24}$ −52.5° (*c*=0.99, $CHCl_3$), as a syrup. ^{1}H-NMR ($CDCl_3$): 1.21 (3H, d, $J_{5'',6''}$=6.5 Hz, CH_3), 5.45 (1H, s, H-1, β-Glc), 7.10—7.50 (25H, m, aromatic protons). TLC: *Rf* 0.43 (solvent A), 0.14 (B), 0.06 (C). *Anal.* Calcd for $C_{53}H_{60}O_{14}\cdot 1/2H_2O$: C, 68.45; H, 6.61. Found:, 68.54; H, 6.24.

From the subsequent fractions after **10** had emerged, **15** (931 mg, 25.6%), $[\alpha]_D^{26}$ −10.4° (*c*=1.08, $CHCl_3$), was isolated as a syrup. ^{1}H-NMR ($CDCl_3$): 1.25 (3H, d, $J_{5'',6''}$=6.5 Hz, CH_3), 5.45 (1H, s, H-1, β-Glc), 7.10—7.50 (25H, m, aromatic protons). TLC: *Rf* 0.35 (solvent A), 0.06 (B), 0.03 (C). *Anal.* Calcd for $C_{53}H_{60}O_{14}\cdot 1/2H_2O$: C, 68.45; H, 6.61. Found: C, 68.40; H, 6.65.

O-α-L-Fucopyranosyl-(1→4)-O-β-D-galactopyranosyl-(1→4)-1,6-anhydro-β-D-glucopyranose (11)——Hydrogenolytic debenzylation of **10** (1.10 g) in dry MeOH (50 ml) with a Pd catalyst was carried out as described for **6** to provide **11** (560 mg 99.6%) $[\alpha]_D^{20}$ −105.8° (*c*=0.82, H_2O), as an amorphous powder. ^{1}H-NMR (D_2O): 5.03 (1H, d, $J_{1',2'}$=7 Hz, H-1', β-Gal), 5.63 (1H, d, $J_{1'',2''}$=3 Hz, H-1'', α-Fuc), 5.91 (1H, s, H-1, β-Glc). ^{13}C-NMR: see Table I. TLC: *Rf* 0.33 (solvent D). *Anal.* Calcd for $C_{18}H_{30}O_{14}\cdot 1/2H_2O$: C, 45.09; H, 6.52. Found: C, 44.85; H, 6.72.

O-(2,3,4-Tri-O-acetyl-α-L-fucopyranosyl)-(1→4)-O-(2,3,6-tri-O-acetyl-β-D-galactopyranosyl)-(1→4)-2,3-di-O-acetyl-1,6-anhydro-β-D-glucopyranose (12)——Compound **11** (290 mg) was acetylated with Ac_2O (5 ml) and pyridine (5 ml) overnight at room temperature. The mixture was treated in the usual way to provide crude acetate. On column chromatography with $CHCl_3$–acetone (6:1), pure **12** (454 mg, 91.3%), $[\alpha]_D^{21}$ −104.6° (*c*=0.7, $CHCl_3$), was isolated as an amorphous powder. ^{1}H-NMR ($CDCl_3$): 1.13 (3H, d, $J_{5'',6''}$=6.5 Hz, CH_3), 2.02, 2.04, 2.08, 2.12, 2.16, 2.17, 2.22 (24H, each s, OAc×8). TLC: *Rf* 0.55 (solvent A), 0.27 (B), 0.06 (C). *Anal.* Calcd for $C_{34}H_{46}O_{22}$: C, 50.62; H, 5.75. Found: C, 50.56; H, 5.98.

O-(2,3,4-Tri-O-acetyl-α-L-fucopyranosyl-(1→4)-O-(2,3,6-tri-O-acetyl-β-D-galactopyranosyl)-(1→4)-1,2,3-tri-O-acetyl-β-D-glucopyranose (13)——Crystalline titanium tetrabromide (*ca.* 1 g) was added to a solution of **12** (268 mg) in dry $CHCl_3$ (8 ml). The mixture was refluxed under stirring for 5 h, with exclusion of moisture. After cooling, the mixture was diluted with $CHCl_3$ (30 ml) and poured into ice-H_2O (50 ml) with stirring. The separated organic layer was washed with chilled H_2O (2×30 ml), dried ($MgSO_4$), and concentrated to yield an amorphous powder, which was treated with mercuric acetate (0.27 g) and AcOH (20 ml) overnight at room temperature. The mixture was poured into ice-H_2O (60 ml), and the whole was extracted with CH_2Cl_2 (4×20 ml). The combined extracts were washed with H_2O, aq. $NaHCO_3$, and H_2O, then dried ($MgSO_4$), and concentrated to an amorphous powder. On column chromatography with 10:1, 6:1, and 3:1 $CHCl_3$–acetone, **13** (171 mg, 59.4%), $[\alpha]_D^{20}$ −72.2° (*c*=0.63, $CHCl_3$), was isolated as an amorphous powder. IR ν_{max}^{Nujol} cm^{-1}: 3600—3200 (br OH), 1735 (OAc). ^{1}H-NMR ($CDCl_3$): 1.13 (3H, d, $J_{5'',6''}$=6.5 Hz, CH_3), 1.86, 2.00, 2.03, 2.10, 2.12, 2.16, 2.22 (27H, each s, OAc×9), 5.70 (1H, d, $J_{1,2}$=8 Hz, H-1, β-Glc). TLC: *Rf* 0.48 (solvent A), 0.15 (B), 0.06 (C). *Anal.* Calcd for $C_{36}H_{50}O_{24}$: C, 49.89; H, 5.81. Found: C, 50.16; H, 5.77.

O-α-L-Fucopyranosyl-(1→4)-O-β-D-galactopyranosyl-(1→4)-D-glucopyranose (14)——Deacetylation of **13** (130 mg) in dry MeOH (15 ml) with a 0.5 M methanolic solution of MeONa (0.1 ml) was carried out as described for **10** to provide **14** (71 mg, 96.9%), $[\alpha]_D^{17}$ −37.2° (no mutarotation, *c*=0.39, H_2O), as a hygroscopic amorphous powder. ^{1}H-NMR (D_2O): 1.69 (3H, d, $J_{5'',6''}$=6.5 Hz, CH_3), 4.93 (1H, d, $J_{1',2'}$=7.3 Hz, H-1', β-Gal), 5.10 (<1H, d, $J_{1,2}$=7.8 Hz, H-1(β), β-Glc), 5.46 (<2H, br s, H-1(α) and H-1'', α-Glc and α-Fuc). ^{13}C-NMR: see Table II. TLC: *Rf* 0.20 (solvent D). *Anal.* Calcd for $C_{18}H_{32}O_{15}\cdot 1/2H_2O$: C, 43.46; H, 6.69. Found: C, 43.22; H, 6.40.

O-β-L-Fucopyranosyl-(1→4)-O-β-D-galactopyranosyl-(1→4)-1,6-anhydro-β-D-glucopyranose (16)——Hydrogenolytic debenzylation of **15** (2.07 g) in dry MeOH (30 ml) as described for **11** provided crude **16.** Pure **16** (791 mg, 74.8%), mp 257—260°C, $[\alpha]_D^{21}$ −32.5° (*c*=0.57, H_2O), was isolated as white needles by addition of MeOH to an aqueous solution of the crude product. ^{1}H-NMR (D_2O): 4.40 (1H, d, $J_{1'',2''}$=7 Hz, H-1'', β-Fuc), 4.65 (1H, d, $J_{1',2'}$=7 Hz, H-1', β-Gal), 5.52 (1H, s, H-1, β-Glc). ^{13}C-NMR: see Table I. TLC: *Rf* 0.25 (solvent D). *Anal.* Calcd for $C_{18}H_{30}O_{14}$: C, 45.96; H, 6.43. Found: C, 45.73; H, 6.47.

***O*-(2,3,4-Tri-*O*-acetyl-β-L-fucopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3-di-*O*-acetyl-1,6-anhydro-β-D-glucopyranose (17)**———Acetylation of **16** (790 mg) with Ac_2O (10 ml) and pyridine (10 ml) gave a crude acetate. Pure **17** (1.10 g, 81.2%), mp 246—247°C, $[\alpha]_D^{25}$ +4.4° (c=1.1, $CHCl_3$), was obtained as fine needles by addition of MeOH to a solution of the crude product in AcOEt. ^{1}H-NMR ($CDCl_3$): 1.18 (3H, d, $J_{5'',6''}$=6.5 Hz, C$\underline{H}_3$), 1.98, 2.06, 2.12, 2.15, 2.23 (24H, each s, OAc×8). TLC: *Rf* 0.54 (solvent A), 0.19 (B), 0.04 (C). *Anal.* Calcd for $C_{34}H_{46}O_{22}$: C, 50.62; H, 5.75. Found: C, 50.47; H, 5.51.

***O*-(2,3,4-Tri-*O*-acetyl-β-L-fucopyranosyl-(1→4)-*O*-(2,3,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-1,2,3-tri-*O*-acetyl-β-D-glucopyranose (18)**———Conversion of **17** (500 mg) to **18** was carried out as described for the preparation of **13**: in the column chromatographic purification, **18** (318 mg, 59.2%), $[\alpha]_D^{20}$ +11.7° (c=1.04, $CHCl_3$), was isolated as an amorphous powder after unreacted **17** (35 mg, 7%) had emerged. IR ν_{max}^{Nujol} cm^{-1}: 3600—3200 (br OH), 1728 (OAc). ^{1}H-NMR ($CDCl_3$): 1.18 (3H, d, $J_{5'',6''}$=6.5 Hz, C$\underline{H}_3$), 1.98, 2.02, 2.04, 2.08, 2.12, 2.16, 2.20 (27H, each s, OAc×9), 5.68 (1H, d, $J_{1,2}$=8 Hz, H-1, β-Glc). TLC: *Rf* 0.46 (solvent A), 0.10 (B), 0.03 (C). *Anal.* Calcd for $C_{36}H_{50}O_{24}$: C, 49.89; H, 5.81. Found: C, 49.69; H, 5.86.

***O*-β-L-Fucopyranosyl-(1→4)-*O*-β-D-galactopyranosyl-(1→4)-D-glucopyranose (19)**———Deacetylation of **18** (224 mg) was carried out as described for the preparation of **14** to give **19** (125 mg, 99%), $[\alpha]_D^{22}$ +36.8° (no mutarotation, c=0.84, H_2O), as a hygroscopic amorphous powder. ^{1}H-NMR (D_2O): 1.72 (3H, d, $J_{5'',6''}$= 6.5 Hz, C$\underline{H}_3$), 4.80 (1H, d, $J_{1'',2''}$=6.8 Hz, H-1″, β-Fuc), 4.96 (1H, d, $J_{1',2'}$=6.8 Hz, H-1′, β-Gal), 5.13 (<1H, d, $J_{1,2}$=7.8 Hz, H-1(β), β-Glc), 5.68 (<1H, d, $J_{1,2}$=3.4 Hz, H-1(α), α-Glc). ^{13}C-NMR: see Table II. TLC: *Rf* 0.17 (solvent D). *Anal.* Calcd for $C_{18}H_{32}O_{15}\cdot H_2O$: C, 42.69; H, 6.77. Found: C, 42.48; H, 6.58.

***O*-(2,3,4-Tri-*O*-acetyl-β-L-fucopyranosyl)-(1→6)-*O*-(2,3,4-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-1,6-anhydro-2,3-di-*O*-benzyl-β-D-glucopyranose (20)**———Condensation of **7** (2.60 g, 3.36 mmol) in dry benzene–nitromethane (60 ml, 1:1, v/v) with acetobromofucose[15] (1.45 g, 4.11 mmol) in the presence of mercuric cyanide (0.90 g, 3.56 mmol) was carried out by stirring the mixture at room temperature for 2 d. The mixture was diluted with benzene (50 ml), then filtered, and the residue was washed with benzene. The combined filtrate and washings were washed with H_2O, aq. $NaHCO_3$, and H_2O, dried ($MgSO_4$), and concentrated to an amorphous powder, which was dissolved in CH_2Cl_2. On column chromatography with benzene–ether (5:1), **20** (2.25 g, 64%), $[\alpha]_D^{21}$ −15.8° (c=1.06, $CHCl_3$), was isolated as an amorphous powder. The unreacted **7** (0.78 g, 30%) was recovered from the subsequent fractions after **20** had emerged. ^{1}H-NMR ($CDCl_3$): 1.14 (3H, d, $J_{5'',6''}$=6.5 Hz, C$\underline{H}_3$), 1.92, 1.96, 2.11 (9H, each s, OAc×3), 5.45 (1H, s, H-1, β-Glc), 7.00—7.50 (25H, m, aromatic protons). TLC: *Rf* 0.74 (solvent A), 0.60 (B), 0.51 (C). *Anal.* Calcd for $C_{59}H_{66}O_{17}$: C, 67.67; H, 6.35. Found: C, 67.80; H, 6.42.

***O*-β-L-Fucopyranosyl-(1→6)-*O*-(2,3,4-tri-*O*-benzyl-β-D-galactopyranosyl-(1→4)-1,6-anhydro-2,3-di-*O*-benzyl-β-D-glucopyranose (21)**———Deacetylation of **20** (1.41 g) was carried out as described for the preparation of **14** to provide **21** (1.20 g, 96.8%), $[\alpha]_D^{22}$ −23.1° (c=1.23, $CHCl_3$), as an amorphous powder after column chromatography with $CHCl_3$–EtOH (100:3). ^{1}H-NMR ($CDCl_3$): 1.19 (3H, d, $J_{5'',6''}$=6.5 Hz, C$\underline{H}_3$), 5.47 (1H, s, H-1, β-Glc), 7.00—7.60 (25H, m, aromatic protons). TLC: *Rf* 0.25 (solvent A), 0.04 (B), 0.03 (C). *Anal.* Calcd for $C_{53}H_{60}O_{14}\cdot 1/2H_2O$: C, 68.45; H, 6.61. Found: C, 68.24; H, 6.60.

***O*-β-L-Fucopyranosyl-(1→6)-*O*-β-D-galactopyranosyl-(1→4)-1,6-anhydro-β-D-glucopyranose (22)**——— Hydrogenolytic debenzylation of **21** (1.17 g) was carried out as described for the preparation of **11** to give an amorphous powder, which was crystallized from aq. EtOH. Recrystallization from aq. EtOH provided pure **22** (556 mg, 93%), mp 244—245°C, $[\alpha]_D^{22}$ −28.4° (c=1.03, H_2O), as hygroscopic white needles. ^{1}H-NMR (D_2O): 4.84 (1H, d, $J_{1'',2''}$=7 Hz, H-1″, β-Fuc), 5.21 (1H, d, $J_{1',2'}$=6 Hz, H-1′, β-Gal), 5.89 (1H, s, H-1, β-Glc). ^{13}C-NMR: see Table I. TLC: *Rf* 0.22 (solvent D). *Anal.* Calcd for $C_{18}H_{30}O_{14}$: C, 45.96; H, 6.43. Found: C, 45.75; H, 6.58.

***O*-(2,3,4-Tri-*O*-acetyl-β-L-fucopyranosyl-(1→6)-*O*-(2,3,4-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3-di-*O*-acetyl-1,6-anhydro-β-D-glucopyranose (23)**———Compound **22** (440 mg) was acetylated with Ac_2O (10 ml) and pyridine (10 ml). On column chromatography with $CHCl_3$–acetone (10:1), **23** (675 mg, 89.5%), $[\alpha]_D^{24}$ −32.2° (c=1.12, $CHCl_3$), was isolated as an amorphous powder. ^{1}H-NMR ($CDCl_3$): 1.23 (3H, d, $J_{5'',6''}$=6.5 Hz, C$\underline{H}_3$), 1.99, 2.07, 2.13, 2.17, 2.20 (24H, each s, OAc×8). TLC: *Rf* 0.58 (solvent A), 0.28 (B), 0.10 (C). *Anal.* Calcd for $C_{34}H_{46}O_{22}$: C, 50.62; H, 5.75. Found: C, 50.35; H, 5.79.

***O*-(2,3,4-Tri-*O*-acetyl-β-L-fucopyranosyl)-(1→6)-*O*-(2,3,4-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-1,2,3-tri-*O*-acetyl-β-D-glucopyranose (24)**———Conversion of **23** (231 mg) to **24** was carried out as described for the preparation of **13** from **12**. On column chromatography with $CHCl_3$–acetone (10:1), **24** (135 mg, 54.4%), $[\alpha]_D^{21}$ −5.4° (c=0.62, $CHCl_3$), was isolated as an amorphous powder. IR ν_{max}^{Nujol} cm^{-1}: 3600—3200 (br OH), 1725 (OAc). ^{1}H-NMR ($CDCl_3$): 1.22 (3H, d, $J_{5'',6''}$=6.5 Hz, C$\underline{H}_3$), 1.95, 1.97, 2.06, 2.10, 2.15, 2.19 (27H, each s, OAc×9), 5.70 (1H, d, $J_{1,2}$=8 Hz, H-1, β-Glc). TLC: *Rf* 0.51 (solvent A), 0.16 (B), 0.06 (C). *Anal.* Calcd for $C_{36}H_{50}O_{24}$: C, 49.89; H, 5.81. Found: C, 49.73; H, 6.01.

***O*-β-L-Fucopyranosyl-(1→6)-*O*-β-D-galactopyranosyl-(1→4)-D-glucopyranose (25)**———Deacetylation of **24** (72 mg) was carried out as described for the preparation of **14** to give **25** (38 mg, 93.6%), $[\alpha]_D^{20}$ +48.4° (no mutarotation, c=1.59, H_2O), as a hygroscopic amorphous powder. ^{1}H-NMR (D_2O): 1.70 (3H, d, $J_{5'',6''}$=6.5 Hz, C$\underline{H}_3$), 5.10 (<1H, d, $J_{1,2}$=7.8 Hz, H-1(β), β-Glc), 5.65 (<1H, d, $J_{1,2}$=3.5 Hz, H-1(α), α-Glc),

H-1′, and H-1″ signals overlapped with other ring protons. ^{13}C-NMR: see Table II. TLC: *Rf* 0.14 (solvent D). *Anal.* Calcd for $C_{18}H_{32}O_{15}\cdot H_2O$: C, 42.69; H, 6.77. Found: C, 43.00; H, 6.84.

***O*-(2,3,4-Tri-*O*-benzyl-α-L-fucopyranosyl-(1→6)-*O*-(2,3,4-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-1,6-anhydro-2,3-di-*O*-benzyl-β-D-glucopyranose (26)**———A solution of freshly prepared 2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl bromide[18] (2.56 g, 5.15 mmol) and diisopropylethyl amine (1.60 ml, 5.60 mmol) in dry 1,2-dichloroethane (20 ml) was added to a mixture of **7** (3 g, 3.88 mmol), tetraethylammonium bromide (4.20 g, 20 mmol), and molecular sieve 4Å (3 g) in dry DMF (30 ml). After being stirred at room temperature for 48 h under a dry nitrogen atmosphere, the mixture was diluted with CH_2Cl_2 (60 ml), then filtered, and the residue was washed with CH_2Cl_2. The combined filtrate and washings were successively washed with H_2O, 10% H_2SO_4, H_2O, aq. $NaHCO_3$, and H_2O, then dried ($MgSO_4$), and concentrated to a syrup. On column chromatography with benzene–ether (10:1), **26** (2.39 g, 51.8%), $[\alpha]_D^{21}$ −49.7° (c=1.03, $CHCl_3$), was isolated as a syrup. ^{1}H-NMR ($CDCl_3$): 0.93 (3H, d, $J_{5'',6''}$=6.5 Hz, C$\underline{H}_3$), 5.44 (1H, s, H-1, β-Glc), 7.10—7.50 (40H, m, aromatic protons). TLC: *Rf* 0.79 (solvent A), 0.69 (B), 0.76 (C). *Anal.* Calcd for $C_{74}H_{78}O_{14}$: C, 74.60; H, 6.60. Found: C, 74.70; H, 6.78.

***O*-α-L-Fucopyranosyl-(1→6)-*O*-β-D-galactopyranosyl-(1→4)-1,6-anhydro-β-D-glucopyranose (27)**——Hydrogenolytic debenzylation of **26** (850 mg) was carried out as described for the preparation of **11** to give **27** (330 mg, 98.3%), $[\alpha]_D^{20}$ −59.3° (c=0.32, H_2O), as a hygroscopic amorphous powder. ^{1}H-NMR (D_2O): 5.23 (1H, d, $J_{1',2'}$=6 Hz, H-1′, β-Gal), 5.39 (1H d, $J_{1'',2''}$=3 Hz, H-1″, α-Fuc), 5.90 (1H, s, H-1, β-Glc). ^{13}C-NMR: see Table I. TLC: *Rf* 0.26 (solvent D). *Anal.* Calcd for $C_{18}H_{30}O_{14}\cdot 1/2H_2O$: C, 45.09; H, 6.52. Found: C, 45.32; H, 6.45.

***O*-(2,3,4-Tri-*O*-acetyl-α-L-fucopyranosyl-(1→6)-*O*-(2,3,4-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3-di-*O*-acetyl-1,6-anhydro-β-D-glucopyranose (28)**———Compound **27** (320 mg) was acetylated with Ac_2O (5 ml) and pyridine (5 ml). On column chromatography of the mixture with $CHCl_3$–acetone (10:1), **28** (396 mg 72.2%), $[\alpha]_D^{20}$ −88.3° (c=1.16, $CHCl_3$), was isolated as an amorphous powder. ^{1}H-NMR ($CDCl_3$): 1.11 (3H, d, $J_{5'',6''}$=6.5 Hz, C$\underline{H}_3$), 1.97, 2.04, 2.06, 2.09, 2.14 (24H, each s, OAc×8). TLC: *Rf* 0.58 (solvent A), 0.29 (B), 0.12 (C). *Anal.* Calcd for $C_{34}H_{46}O_{22}$: C, 50.62; H, 5.75. Found: C, 50.26; H, 5.96.

***O*-(2,3,4-Tri-*O*-acetyl-α-L-fucopyranosyl)-(1→6)-*O*-(2,3,4-tri-*O*-acetyl-β-D-galactopyranosyl)-1,2,3-tri-*O*-acetyl-β-D-glucopyranose (29)**———Conversion of **28** (309 mg) was carried out as described for that of **12** to **13**. On column chromatography with $CHCl_3$–acetone (10:1), **29** (189 mg, 56.9%), $[\alpha]_D^{20}$ −71.6° (c=0.7, $CHCl_3$), was isolated as an amorphous powder. IR ν_{max}^{Nujol} cm^{-1}: 3600—3200 (br OH), 1735 (OAc). ^{1}H-NMR ($CDCl_3$): 1.11 (3H, d, $J_{5'',6''}$=6.5 Hz, C$\underline{H}_3$), 1.97, 1.98, 2.02, 2.04, 2.05, 2.10, 2.17 (27H, each s, OAc×9), 5.68 (1H, d, $J_{1,2}$=8 Hz, H-1, β-Glc). TLC: *Rf* 0.53 (solvent A), 0.16 (B), 0.06 (C). *Anal.* Calcd for $C_{36}H_{50}O_{24}$: C, 49.89; H, 5.81. Found: C, 49.67; H, 5.96.

***O*-α-L-Fucopyranosyl-(1→6)-*O*-β-D-galactopyranosyl-(1→4)-D-glucopyranose (30)**———Deacetylation of **29** (165 mg) was carried out as described for that of **14** to provide **30** (90 mg, 96.8%), $[\alpha]_D^{22}$ −27.8° (no mutarotation, c=0.58, H_2O), as a hygroscopic glass. [lit.[6c] $[\alpha]_D^{25}$ −28.3° (c=0.24, MeOH) and $[\alpha]_D^{25}$ −23° (initial)→ −21° (22 h, c=0.3, H_2O)]. ^{1}H-NMR (D_2O): 1.69 (3H, d, $J_{5'',6''}$=6.5 Hz, C$\underline{H}_3$), 4.89 (1H, d, $J_{1',2'}$=6 Hz, H-1′, β-Gal), 5.12 (<1H, d, $J_{1,2}$=7 Hz, H-1(β), β-Glc), 5.39 (1H, d, $J_{1'',2''}$=3.5 Hz, H-1″, α-Fuc), 5.67 (<1H, d, $J_{1,2}$=3.5 Hz, H-1(α), α-Glc). ^{13}C-NMR: see Table II. TLC: *Rf* 0.19, (solvent D). *Anal.* Calcd for $C_{18}H_{32}O_{15}\cdot H_2O$: C, 42.69; H, 6.77. Found: C, 42.59; H, 7.06.

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References and Notes

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