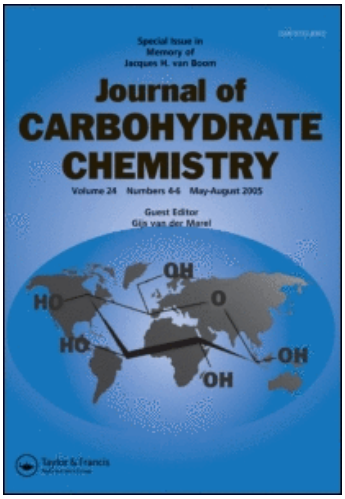

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LAMINARIBIOSE AS THE STARTING MATERIAL : FACILE SYNTHESIS OF β-(1→3)-LINKED Gal-Gal DISACCHARIDE DERIVATIVES AND RELATED COMPOUNDS

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ABSTRACT

The synthesis of β-(1→3)-linked galactobiose octaacetate (14) was achieved in a 6-step reaction sequence in more than 30% overall yield, starting from the readily available laminaribiose octaacetate (2). The key steps in this synthesis involved the efficient transformation of 4,6:4',6'-di-*O*-benzylidene derivative (5) into the diol (6) through regioselective reductive ring opening of the two benzylidene acetals, the preparation of the corresponding ditriflate (12) and dimesylate (8), and thier subsequent S_N2 displacement by benzoate and/or thiolacetate anion to give the β-(1→3)-linked Gal-Gal disacharide derivative (10) and related thio compounds 11 and 13. The big difference of the reactivities between the two mesyloxyl groups of 8 enabled their replacement with different nucleophiles.

INTRODUCTION

In the course of our studies on utilization of oligosaccharides as key starting materials for syntheses of biologically important compounds, we have reported successful conversions of several α- or β-(1→4)-linked di- and trisaccharides, such as maltose, cellobiose, chitobiose, and maltotriose.[1-10] Recently, the range of the utilizable oligosaccharides has been extended to β-(1→3)-linked disaccharide, 3-*O*-β-D-glucopyranosyl-D-glucopyranose

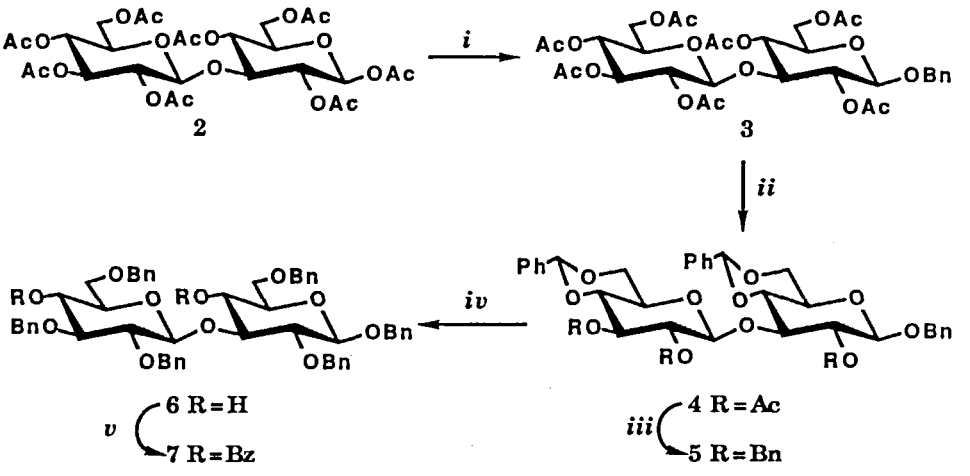
(laminaribiose, 1). Thus, we described, in the preceding paper of this series, an efficient preparation of laminaribiose octaacetate (2) through specific degradation of curdlan, a microbial polysaccharide, and its conversion into *N*-acetyl hyalobiuronic acid.[11]

This paper presents another example about chemical conversion of 2, i.e., preparation of β-(1→3)-linked Gal-Gal disaccharide derivatives and related compounds. This type of disaccharide sequence has been found as one of the key components in variety of natural sugar chains. For example, most of glycosaminoglycans are assumed to be bound to the protein cores through the specific linkage, -GlcAβ1→3**Gal**β1→3**Gal**β1→4Xylβ1-.[12] The related sequence like Galβ1→3GalNAc also forms the core structure of many tumour-associated antigens.[13]

RESULTS AND DISCUSSION

Benzyl β-laminaribioside peracetate (3) was prepared from 2 in the conventional way and converted into the 4,6:4',6'-di-*O*-benzylidene derivative, which was isolated as peracetate (4). The overall yield was 83% through Zemplen deacetylation, benzylidenation with α,α-dimethoxytoluene in DMF, and reacetylation. After de-*O*-acetylation of 4, the resulting three hydroxyl groups were benzylated, giving 5 in almost quantitative yield. Regioselective reductive ring opening of the two benzylidene acetals was achieved by treatment of 5 with borane trimethylamine and aluminium chloride in tetrahydrofuran, according to the procedure of Garegg,[14] to give the diol 6 (84%) with hydroxy groups at C-4 and 4' positions (Scheme I). The structure of 6 was elucidated through its transformation into the corresponding dibenzoate 7.

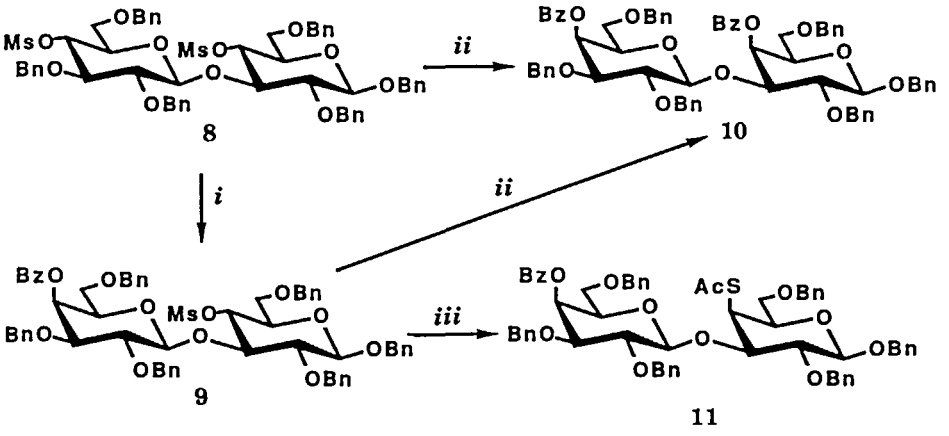
For preparation of the Gal-Gal sequence expected, the configurations of both hydroxyl groups at C-4 and C-4' of 6 should be inverted. Therefore, S_N2 type reactions of the 4,4'-di-*O*-sulfonyl compounds derived from 6 were examined. Firstly, compound 6 was methanesulfonated to give the dimesylate 8. Attempts to replace the mesyloxyl groups with benzoate anion disclosed that one of the sulfates resisted replacement. Thus, when 8 was treated with sodium benzoate in hexamethylphosphoramide (HMPA) at 100 °C for 5 h, one mesyloxyl group was displaced by benzoate, giving benzyl 3-*O*-(4-*O*-benzoyl-2,3,6-tri-*O*-benzyl-β-D-galactopyranosyl)-2,6-di-*O*-benzyl-4-*O*-methanesulfonyl-β-D-glucopyranoside (9) in 80% yield. Apparently, the



i : (a) 25% HBr in HOAc, $(CH_2Cl)_2$; (b) BnOH, Ag_2CO_3, $(CH_2Cl)_2$.
ii : (a) MeONa, MeOH; (b) $PhCH(OMe)_2$, *cat.* TsOH, DMF; (c) Ac_2O, Pyridine.
iii : (a) MeONa, MeOH; (b) BnBr, NaH, DMF.
iv : BH_3-Me_3N, $AlCl_3$, THF, MS4A. *v*. BzCl, pyridine.

Scheme I

mesyloxyl group at C-4 remained unaffected. Under more drastic reaction conditions (120 °C, 48 h), **9** yielded benzyl 4-*O*-benzoyl-3-*O*-(4-*O*-benzoyl-2,3,6-tri-*O*-benzyl-β-D-galactopyranosyl)-2,6-di-*O*-benzyl-β-D-galactopyranoside (**10**) in 81% yield. In a one-pot manner, **8** was directly converted into the dibenzoate **10** (51%) under similar conditions (sodium benzoate in HMPA, 120 °C, 48 h). The big difference in the reactivities between the two mesyloxyl groups in compound **8** also enabled their replacement with different nucleophiles. Thus, treatment of **9** with potassium thiolacetate in HMPA at 100 °C for 30 h gave the benzyl 4-*S*-acetyl-3-*O*-(4-*O*-benzoyl-2,3,6-tri-*O*-benzyl-β–D-galactopyranosyl)-2,6-di-*O*-benzyl-4-thio-β-D-galactopyranoside (**11**) in 60% yield (Scheme II). Structure elucidation of these products was achieved mainly on the basis of ^1H NMR analyses. All ring protons of compounds **9**, **10**, and **11** were unambiguously assigned using the decoupling technique, and the configurations of C-4 and C-4' were easily determined from the coupling constants, $J_{3,4}$, $J_{4,5}$, $J_{3',4'}$, and $J_{4',5'}$, respectively (see Experimental).

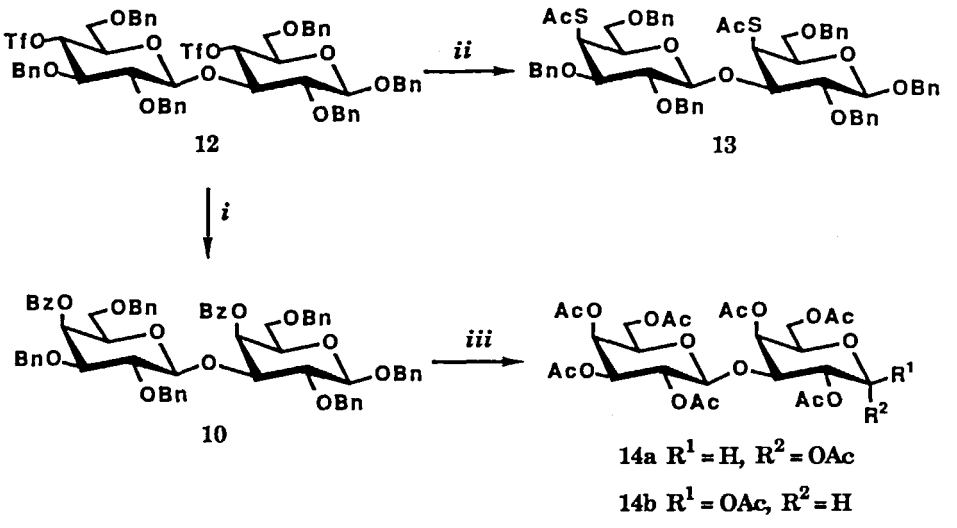


i : BzONa, HMPA, 100 °C, 5 *h*. *ii* : BzONa, HMPA, 120 °C, 48 *h*.
iii : KSAc, HMPA, 100 °C, 30 *h*.

HMPA : hexamethylphosphoramide; Ms : methanesulfonyl.

Scheme II

Low reactivity of the 4-mesyloxyl group of **8** prompted us to use a more efficient leaving group like triflate.[15] Benzyl 2,6-di-*O*-benzyl-3-*O*-(2,3,6-tri-*O*-benzyl-4-*O*-trifluoromethanesulfonyl-β-D-glucopyranosyl)-4-*O*-trifluoromethanesulfonyl-β-D-glucopyranoside (**12**) was prepared by treating the diol **6** with trifluoromethanesulfonic anhydride at -10 °C in pyridine, and its S_N2 reaction was examined. As expected, nucleophilic substitutions with benzoate anion proceeded smoothly on both carbons (C-4 and C-4') of **12** at room temperature in HMPA, giving the galactobioside **10** as the sole product (72% yield based on **6**, not optimized). In a similar manner, the reaction of **12** with potassium thiolacetate in HMPA at room temperature for 1 h afforded benzyl 4-*S*-acetyl-3-*O*-(4-*S*-acetyl-2,3,6-tri-*O*-benzyl-4-thio-β-D-galactopyranosyl)-2,6-di-*O*-benzyl-4-thio-β-D-galactopyranoside (**13**) in 67% yield. De-*O*-benzoylation of **10** followed by hydrogenolysis and acetylation gave known 1,2,4,6-tetra-*O*-acetyl-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-α- (**14a**) and -β-D-galactopyranose (**14b**) in 76% total, overall yield (**14a** :**14b** = 1:2).



i : BzONa, HMPA, 20 °C, 3 *h*. *ii* : KSAc, HMPA, 20 °C, 1 *h*.
iii : (a) MeONa, MeOH; (b) H_2, 10% Pd/C, EtOH-H_2O;
(c) Ac_2O, Pyridine.

HMPA : hexamethylphosphoramide; Tf : trifluoromethanesulfonyl.

Scheme III

In conclusion, the biologically important β-(1→3)-linked Gal-Gal sequence became readily accessible without using glycosylation reactions. The overall yield of 6 steps for conversion of **2** into **14** reached more than 30%. This efficiency seemed to be superior to that of the conventional stepwise preparations so far reported.[16-19]

EXPERIMENTAL

General Procedures. Melting points were determined with a Yamato micro melting point apparatus and are uncorrected. Optical rotations were determined with a Perkin-Elmer Model 241 MC polarimeter. IR spectra were recorded with Shimadzu IR-27 spectrophotometer, using KBr disks for solid samples and KRS (thallium bromide-iodide) for liquid samples. ^1H NMR spectra were recorded at 400 MHz with a JEOL JNM-GX 400

spectrometer, using tetramethylsilane as the internal standard for solutions in $CDCl_3$. Ring-proton assignments in NMR were made by first-order analysis of the spectra, and were supported by homonuclear decoupling experiments. Reactions were monitored by TLC on precoated plates of silica gel $60F_{254}$ (layer thickniss, 0.25 mm, E. Merck, Darmstadt, Germany), spots were detected by charring with a solution of methanol-concd sulfuric acid-*p*-anisaldehyde (85:10:5, v:v). R_F values were measured on HPTLC precoated plates of silica gel $60F_{254}$ (layer thickness, 0.25 mm, E. Merck, Darmstadt, Germany). Column chromatography was performed on silica gel 60 (230-400 mesh, E. Merck, Darmstadt, Germany). All extractions were concentrated below 45 °C under diminished pressure.

Benzyl 2,4,6-Tri-*O*-acetyl-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-β-D-glucopyranoside (3). - To a solution of β-laminaribiose octaacetate (2) (20.5 g, 30 mmol) in a mixture of acetic acid (100 mL) and 1,2-dichloroethane (50 mL) was added a solution of hydrogen bromide in acetic acid (25% solution, 30 mL). The resulting mixture was stirred at room temperature (r.t.) for 6 h, poured into ice-water, and extracted with chloroform (3 x 120 mL). The extracts were combined, washed with aqueous sodium hydrogen carbonate (aq. $NaHCO_3$) and water, dried (Na_2SO_4), and concentrated, giving the glycosyl bromide as a white solid. Without purification, the glycosyl bromide was dissolved in dry 1,2-dichloroethane (150 mL) containing Drierite (40 g). To the mixture were added benzyl alcohol (35 mL) and silver carbonate (24.8 g, 90 mmol). The resulting mixture was stirred at r.t. for 18 h in the dark, then filtered through a celite pad, and washed with $CHCl_3$. The filtrate and washings were combined and concentrated. The residue was put on a silica gel column. The column was first eluted with 10:1 toluene-ethyl acetate to remove excess benzyl alcohol, then eluted with 3:1 toluene-ethyl acetate to give crystalline **3** (18.6 g, 85%), R_F 0.58 (1:1 benzene-ethyl acetate), mp 188-189 °C, $[\alpha]_D^{22}$ -64.8 ° (*c* 0.5, $CHCl_3$); lit.[20] mp 190 °C, $[\alpha]_D^{20}$ -66.0 ° (*c* 0.5, $CHCl_3$).

Benzyl 2-*O*-Acetyl-3-*O*-(2,3-di-*O*-acetyl-4,6-*O*-benzylidene-β-D-glucopyranosyl)-4,6-*O*-benzylidene-β-D-glucopyranoside (4). - To a solution of **3** (11.0 g, 15 mmol) in tetrahydrofuran-methanol (3:7, 100 mL) was added a solution of sodium methoxide in methanol (5.2 M, 1 mL), the mixture was stirred at r.t. for 2 h, then neutralized with Dowex 50w-x8 (H^+), filtered, and concentrated to dryness. The residue was dissolved in *N,N*-

dimethylformamide (DMF) (120 mL). To the solution were added α,α-dimethoxytoluene (5.71 mL, 37.5 mmol) and *p*-toluenesulfonic acid (100 mg). The resulting mixture was evacuated by a water pump with stirring at 50-60 °C. After 3 h, TLC showed complete reaction to form a major component. To the reaction mixture cooled to r.t. were added pyridine (60 mL) and acetic anhydride (35 mL), and then the mixture was stirred at r.t. for 10 h. Usual work-up followed by column chromatography with 9:1 toluene-ethyl acetate gave **4** (9.2 g, 83.5%) as white crystals, R_F 0.32 (9:1 benzene-ethyl acetate), mp 192-194 °C, $[\alpha]_D^{22}$ -101.3 ° (*c* 1.0, $CHCl_3$); lit.[20] mp 197 °C, $[\alpha]_D^{20}$ -102.5 ° (*c* 0.48, CH_2Cl_2).

Benzyl 2-*O*-Benzyl-3-*O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-glucopyranosyl)-4,6-*O*-benzylidene-β-D-glucopyranoside (5). - To a solution of **4** (7.34 g, 10 mmol) in tetrahydrofuran-methanol (3:7, 100 mL) was added a solution of sodium methoxide in methanol (5.2 M, 0.5 mL). The mixture was stirred at r.t. for 40 min, and the white precipitate formed was filtered and dried. The precipitate was dissolved in DMF (150 mL), and to this solution was added sodium hydride (55% dispersion in oil, 3.90 g, 90 mmol). After stirred at r.t. for 30 min, the mixture was cooled to 0 °C, benzyl bromide (11 mL, 90 mmol) was added, and the resulting mixture was stirred at r.t. overnight. With cooling, methanol (15 mL) was added dropwise to decompose excess sodium hydride. The mixture was partitioned between water and $CHCl_3$, the organic layer was separated, washed with brine and water, dried (Na_2SO_4), and concentrated. The residue was subjected to column chromatography. The column was first eluted with toluene containing 3% triethylamine (Et_3N) to remove benzyl bromide; eluted next with 30:1 toluene-ethyl acetate containing 1% Et_3N to give **5** (8.5 g, 96.7%) as a white solid, R_F 0.44 (15:1 benzene-ethyl acetate) , $[\alpha]_D^{22}$ -31.0 ° (*c* 0.7, $CHCl_3$); ^1H NMR: δ 5.55 (s, 1 H, PhCH), 5.35 (s, 1 H, PhCH), 4.99 (d, 1 H, H-1', $J_{1',2'}$ = 7.3 Hz), 4.63 (d, 1 H, H-1, $J_{1,2}$ = 7.1 Hz), 4.37 (dd, 1 H, H-6a, $J_{5,6a}$ = 4.9 Hz, $J_{6a,6b}$ = 10.5 Hz), 4.17 (dd, 1 H, H-6'a, $J_{5',6'a}$ = 4.90 Hz, $J_{6'a,6'b}$ = 10.4 Hz), 4.07 (t, 1 H, H-3, $J_{2,3} = J_{3,4}$ = 9.0 Hz), 3.82 (t, 1 H, H-6b, $J_{5,6b}$ = 10.3 Hz), 3.76 (t, 1 H, H-4', $J_{3',4'} = J_{4',5'}$ = 9.2 Hz), 3.72-3.63 (m, 3 H, H-3',4,6'b), 3.57 (dd, 1 H, H-2, $J_{2,3}$ = 8.5 Hz), 3.51 (t, 1 H, H-2', $J_{2',3'}$ = 7.8 Hz), 3.45 (dt, 1 H, H-5, $J_{4,5}$ = 9.0 Hz), 3.25 (dt, 1H, H-5').

Anal. Calcd for $C_{54}H_{54}O_{11}$: C, 73.77; H, 6.20. Found: C, 73.55; H, 6.19.

Benzyl 2,6-Di-*O*-benzyl-3-*O*-(2,3,6-tri-*O*-benzyl-β-D-glucopyranosyl)-β-D-glucopyranoside (6). - A mixture of **5** (3.96 g, 4.5 mmol), borane trimethylamine (2.63 g, 36 mmol), and 4A molecular sieves (12 g) in tetrahydrofuran (100 mL) was stirred at r.t. for 30 min, then cooled to 0 °C, and aluminium chloride (4.80 g, 36 mmol) was added. After stirring at r.t. for 6 h, TLC showed complete reaction. The mixture was filtered through a celite pad, and the filtrate was concentrated. The residue was diluted with dichloromethane, washed with dilute hydrochloric acid and water, dried (Na_2SO_4), and concentrated. Column chromatography of the residue with 10:1 toluene-ethyl acetate gave **6** (3.35 g, 84.2%) as a white solid, R_F 0.18 (9:1 benzene-ethyl acetate), $[\alpha]_D^{22}$ -22.0 ° (*c* 0.3, $CHCl_3$); IR: ν_{max}^{KBr} 3450 cm^{-1} (OH); ^1H NMR, δ 4.75 (d, 1 H, H-1', $J_{1',2'}$ = 7.95 Hz), 4.54 (d, 1 H, H-1, $J_{1,2}$ = 7.80 Hz), 3.92-3.43 (m, 12 H, sugar ring protons).

Anal. Calcd for $C_{54}H_{58}O_{11}$: C, 73.44; H, 6.62. Found: C, 73.21; H, 6.65.

Benzyl 4-*O*-Benzoyl-3-*O*-(4-*O*-benzoyl-2,3,6-tri-*O*-benzyl-β-D-glucopyranosyl)-2,6-di-*O*-benzyl-β-D-glucopyranoside (7). -To a solution of **6** (270 mg, 0.3 mmol) in dichloromethane-pyridine (3:1, 4 mL) was added benzoyl chloride (0.215 mL, 1.83 mmol), the mixture was stirred at r.t. for 10 h. Usual work-up and chromatography gave **7** (340 mg, quantitative) as a white solid, R_F 0.50 (15:1 benzene-ethyl acetate), $[\alpha]_D^{22}$ -40.2 ° (*c* 1, $CHCl_3$); IR: ν_{max}^{KBr} 1715 cm^{-1} (OBz); ^1H NMR: δ 5.23 (t, 1 H, H-4, $J_{3,4} = J_{4,5}$ = 9.30 Hz), 4.89 (t, 1 H, H-4', $J_{3',4'} = J_{4',5'}$ = 9.53 Hz), 4.88 (d, 1 H, H-1', $J_{1',2'}$ = 8.05 Hz), 4.57 (d, 1 H, H-1, $J_{1,2}$ = 7.80 Hz), 4.13 (t, 1 H, H-3, $J_{2,3}$ = 9.28 Hz), 3.74 (m, 1 H, H-5), 3.70-3.65 (m, 1 H, H-6a), 3.60 (dd, 1 H, H-2), 3,57-3.53 (m, 2 H, H-3',6b), 3.45 (m, 1 H, H-5'), 3.36 (dd, 1 H, H-2', $J_{2',3'}$ = 9.20 Hz), 3.22 (dd, 1 H, H-6'a, $J_{5',6'a}$ = 3.66 Hz, $J_{6'a,6'b}$ = 10.6 Hz), 3.14 (dd, 1 H, H-6'b, $J_{5',6'b}$ = 6.20 Hz).

Anal. Calcd for $C_{68}H_{66}O_{13}$: C, 74.84; H, 6.10. Found: C, 74.91; H, 6.12.

Benzyl 2,6-Di-*O*-benzyl-3-*O*-(2,3,6-tri-*O*-benzyl-4-*O*-methanesulfonyl-β-D-glucopyranosyl)-4-*O*-methanesulfonyl-β-D-glucopyranoside (8). -To a solution of **6** (500 mg, 0.566 mmol) in dichloromethane-pyridine (4:1, 5 mL) was added methanesulfonyl chloride (0.35 mL, 4.45 mmol). The mixture was stirred at r.t. for 12 h, then poured into ice-water, extracted with dichloromethane. The extract was washed with dilute hydrochloric acid and water, dried (Na_2SO_4), and concentrated. The residue was chromatographed with 15:1 toluene-ethyl acetate to give **8** (520 mg, 88.4%) as

a syrup, R_F 0.36 (15:1 benzene-ethyl acetate), $[\alpha]_D^{22}$ +10.5 ° (*c* 0.2, $CHCl_3$); IR ν_{max}^{film} 1350 and 1170 cm^{-1} (OMs); ^1H NMR: δ 4.96 (d, 1 H, H-1', $J_{1',2'}$ = 8.0 Hz), 4.69 (t, 1 H, H-4', $J_{3',4'} = J_{4',5'}$ = 9.5 Hz), 4.52 (d, 1 H, H-1, $J_{1,2}$ = 7.9 Hz), 3.95 (t, 1 H, H-3, $J_{2,3} = J_{3,4}$ = 9.3 Hz), 3.91 (dd, 1 H, H-6a, $J_{5,6a}$ = 2.0 Hz, $J_{6a,6b}$ = 11.0 Hz), 3.73-3.69 (m, 2 H, H-6'a,6b), 3.62 (dd, 1 H, H-6'b, $J_{5',6'b}$ = 3.3 Hz, $J_{6'a,6'b}$ = 11.0Hz), 3.55 (m, 1 H, H-5), 3.51 (dd, 1 H, H-2), 3.50 (t, 1 H, H-3', $J_{2',3'}$ = 9.3 Hz), 3.35 (m, 1 H, H-5'), 3.31 (dd, 1 H, H-2'), 2.91 (s, 3 H, CH_3SO_2), 2.77 (s, 3 H, CH_3SO_2).

Anal. Calcd for $C_{56}H_{62}O_{15}S_2$: C, 64.72; H, 6.01; S, 6.18. Found: C, 64.86; H, 6.05; S, 6.02.

Benzyl 3-*O*-(4-*O*-Benzoyl-2,3,6-tri-*O*-benzyl-β-D-galactopyranosyl)-2,6-di-*O*-benzyl-4-*O*-methanesulfonyl-β-D-glucopyranoside (9) - To a solution of **8** (310 mg, 0.30 mmol) in HMPA (4 mL) was added sodium benzoate (200 mg). The mixture was stirred at 100 °C for 5 h, then cooled, poured into water, and extracted with ethyl acetate. The extracts were washed with water, dried (Na_2SO_4), and concentrated. Column chromatography of the residue with 20:1 toluene-ethyl acetate gave **9** (255 mg, 80.2%) as a syrup, R_F 0.50 (15:1 benzene-ethyl acetate), $[\alpha]_D^{22}$ -14.4 ° (*c* 0.2, $CHCl_3$); IR: ν_{max}^{film} 1720 (OBz), 1350 and 1100 cm^{-1} (OMs); ^1H NMR: δ 5.74 (bs, 1 H, H-4', $J_{3',4'} < 1$ Hz, $J_{4',5'} < 1$ Hz), 5.02 (m, 1 H, H-1'), 4.53 (t, 1 H, H-4, $J_{3,4} = J_{4,5}$ = 9.6 Hz), 4.44 (d, 1 H, H-1, $J_{1,2}$ = 7.81 Hz), 3.98 (t, 1 H, H-3, $J_{2,3}$ = 9.2 Hz), 3.90 (dd, 1 H, H-6a, $J_{5,6a}$ = 2.45 Hz, $J_{6a,6b}$ = 11.0 Hz), 3.71 (dd, 1 H, H-6b, $J_{5,6b}$ = 5.90 Hz), 3.60-3.42 (m, 7 H, H-2,2',3',5,5',6'a,6'b), 3.05 (s, 3 H, CH_3SO_2).

Anal. Calcd for $C_{62}H_{64}O_{14}S$: C, 69.90; H, 6.06; S, 3.01. Found: C, 69.85; H, 6.05; S, 3.08.

Benzyl 4-*O*-Benzoyl-3-*O*-(4-*O*-benzoyl-2,3,6-tri-*O*-benzyl-β-D-galactopyranosyl)-2,6-di-*O*-benzyl-β-D-galactopyranoside (10).

(a) From Compound 9. - A mixture of **9** (106.5 mg, 0.1 mmol) and sodium benzoate (100 mg) in HMPA (3 mL) was stirred at 120 °C for 48 h. Work-up as described for the preparation of **9** and column chromatography with 20:1 toluene-ethyl acetate afforded **10** (92.8 mg, 81%) as a syrup which, on staying, became a solid, R_F 0.37 (15:1 benzene-ethyl acetate), $[\alpha]_D^{22}$ +52.6 ° (*c* 0.4, $CHCl_3$); IR: ν_{max}^{KBr} 1710 cm^{-1} (OBz); ^1H NMR: δ 5.79 (bd, 1 H, H-4, $J_{3,4}$ = 3.40 Hz, $J_{4,5} < 1.0$ Hz), 5.77 (bd, 1 H, H-4', $J_{3',4'}$ = 3.20 Hz, $J_{4',5'} < 1$ Hz), 4.89 (d, 1 H, H-1', $J_{1',2'}$ = 7.80 Hz), 4.58 (d, 1 H, H-1, $J_{1,2}$ = 8.10 Hz), 4.11 (dd, 1 H, H-3,

$J_{2,3}$ = 9.60 Hz), 3.92-3.83 (m, 2 H, H-2,5), 3.75-3.63 (m, 3 H, H-6a,6b,6'a), 3.58-3.45 (m, 4 H, H-2',3',5',6'b).

Anal. Calcd for $C_{68}H_{66}O_{13}$: C, 74.84; H, 6.10. Found: C, 74.68; H, 6.13.

(b) Directly From Compound 8. - To a solution of **8** (65 mg, 0.0625 mmol) in HMPA (2 mL) was added sodium benzoate (80 mg), then the mixture was heated at 120 °C for 48 h. Work-up in the usual way gave **10** (35 mg, 51%), which was identical with the product obtained in procedure (**a**).

(c) From Ditriflate (12). - To a solution of **6** (620 mg, 0.70 mmol) in dichloromethane-pyridine (5:1, 12 mL) cooled to -10 °C was added trifluoromethanesulfonic anhydride (0.71 mL, 4.2 mmol). The mixture was then stirred at that temperature for 3 h, TLC showed the complete conversion of **6** into a mobile product. The reaction mixture was diluted with dichloromethane (100 mL), and successively washed with cold 10% aqueous solution of potassium hydrogen sulphate (30 mL) and cold water (2 x 30 mL), dried (Na_2SO_4), and concentrated, to give the yellow syrupy triflate **12.** Without further purification, the syrup was dissolved in HMPA (5 mL), sodium benzoate (500 mg) was added, and the mixture was stirred at r.t. for 2 h, TLC showed complete reaction of **12.** Work-up in the usual way afforded compound **10** (560 mg, 72%), which was identical with the product obtained in procedures (**a**) and (**b**).

Benzyl 4-*S*-Acetyl-3-*O*-(4-*O*-benzoyl-2,3,6-tri-*O*-benzyl-β-D-galactopyranosyl)-2,6-di-*O*-benzyl-4-thio-β-D-galactopyranoside (11) - To a solution of **9** (106.5 mg, 0.1 mmol) in HMPA (3 mL) was added potassium thiolacetate (91.3 mg, 0.8 mmol). After being stirred at 100 °C for 30 h, the reaction mixture was diluted with dichloromethane and washed with brine and water, dried (Na_2SO_4), and concentrated. The residue was chromatographed with 30:1 benzene-ethyl acetate to give **11** (62.7 mg, 60%) as a pale yellow syrup, R_F 0.36 (15:1 benzene-ethyl acetate), $[\alpha]_D^{22}$ +33.3 ° (*c* 0.04, $CHCl_3$); IR: ν_{max}^{film} 1700 (SAc) and 1715 cm^{-1} (OBz); ^1H NMR: δ 5.76 (bs, 1 H, H-4', $J_{3',4'} < 1$ Hz, $J_{4',5'} < 1$ Hz), 4.90 (d, 1 H, H-1', $J_{1',2'}$ = 7.25 Hz), 4.43 (d, 1 H, H-1, $J_{1,2}$ = 7.56 Hz), 4.39 (bd, 1 H, H-4, $J_{3,4}$ = 4.68 Hz, $J_{4,5} < 1$ Hz), 4.19 (dd, 1 H, H-3, $J_{2,3}$ = 9.60 Hz), 3.84 (m, 1 H, H-5), 3.71-3.59 (m, 3 H, H-3',6a,6b), 3.58-3.49 (m, 4 H, H-2',5,6'a,6'b), 3.42 (dd, 1 H, H-2), 2.34 (s, 3 H, SAc).

Anal. Calcd for $C_{63}H_{64}O_{12}S$: C, 72.39; H, 6.17; S, 3.07. Found: C, 72.20; H, 6.25; S, 2.87.

Benzyl 4-*S*-Acetyl-3-*O*-(4-*S*-acetyl-2,3,6-tri-*O*-benzyl-4-thio-β-D-galactopyranosyl)-2,6-di-*O*-benzyl-4-thio-β-D-galactopyranoside (13). - The syrupy triflate **12** , prepared from **6** (442 mg, 0.5 mmol) according to the procedure described above, was dissolved in HMPA (3 mL), and potassium thiolacetate (343 mg, 3 mmol) was added. The mixture was kept at r.t. for 1 h, TLC showed the complete reaction of **12** , to give one major component. Usual work-up followed by column chromatography with 30:1 benzene-ethyl acetate afforded **13** (336 mg, 67.2%) as a pale yellow solid, R_F 0.32 (15:1 benzene-ethyl acetate), $[\alpha]_D^{22}$ +8.63 (*c* 0.4, $CHCl_3$); IR: ν_{max}^{KBr} 1695 cm^{-1} (SAc); ^1H NMR: δ 4.75 (d, 1 H, H-1', $J_{1',2'}$ = 7.56 Hz), 4.45 (bd, 1 H, H-4', $J_{3',4'}$ = 4.64 Hz, $J_{4',5'}$ < 1 Hz), 4.40 (d, 1 H, H-1, $J_{1,2}$ = 7.81 Hz), 4.29 (dd, 1 H, H-4, $J_{3,4}$ = 4.89 Hz, $J_{4,5}$ = 1.20 Hz), 4.11 (dd, 1 H, H-3, $J_{2,3}$ = 9.77 Hz), 3.80 (m, 1 H, H-5), 3.69 (dd, 1 H, H-3', $J_{2',3'}$ = 9.76 Hz), 3.69-3.64 (m, 2 H, H-5',6a), 3.60-3.55 (m, 3 H, H-6b,6'a,6'b), 3.36 (dd, 1 H, H-2), 3.16 (dd, 1 H, H-2'), 2.35 and 2.32 (s each, 3 H each, 2 x SAc).

Anal. Calcd for $C_{58}H_{62}O_{11}S_2$: C, 69.71; H, 6.25; S, 6.42. Found: C, 69.62; H, 6.25; S, 6.32.

1,2,4,6-Tetra-*O*-acetyl-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-α-(14a) and -β-D-galactopyranose (14b). - To a solution of **10** (200 mg, 0.183 mmol) in tetrahydrofuran-methanol (1:1, 5 mL) was added a solution of sodium methoxide in methanol (28%, 0.06 mL). After being kept at 40 °C for 2 h, the reaction mixture was made neutral with Dowex 50w-x8 (H^+), filtered, and concentrated to dryness to give white crystals. A mixture of the crystal and 10% Pd-C (200 mg) in tetrahydrofuran (4 mL), ethanol (8 mL), and water (3 mL) was shaken under a hydrogen atmosphere for 10 h at r.t., filtered and the filtrate was concentrated. The residue was dissolved in pyridine (4 mL), and acetic anhydride (1 mL) was added. The resulting mixture was stirred at r.t. overnight. Usual work-up and column chromatography with 2:1 toluene-ethyl acetate gave first the β-isomer **14b** (63 mg, 51%), ^1H NMR spectrum of which showed the trace contamination of its α-isomer (**14a**), R_F 0.40 (1:1 benzene-ethyl acetate); ^1H NMR: δ 5.64 (d, 1 H, H-1, $J_{1,2}$ = 8.31 Hz), 5.45 (bd, 1 H, H-4, $J_{3,4}$ = 3.45 Hz, $J_{4,5}$ < 1 Hz), 5.37 (bd, 1 H, H-4', $J_{3',4'}$ = 3.42 Hz, $J_{4',5'}$ < 1 Hz), 5.33 (dd, 1 H, H-2, $J_{2,3}$ = 10.0 Hz), 5.11 (dd, 1 H, H-2', $J_{1',2'}$ = 7.81 Hz, $J_{2',3'}$ = 10.5 Hz), 4.96 (dd, 1 H, H-3'), 4.59 (d, 1 H, H-1'), 4.22-4.11 (m, 3 H, H-6a,6'a,6'b), 4.05 (dd, 1 H, H-6b, $J_{5,6b}$ = 7.20 Hz, $J_{6a,6b}$ =

11.4 Hz), 3.98 (m, 1 H, H-5), 3.94 (dd, 1 H, H-3), 3.88 (bt, 1 H, H-5'), 2.18, 2.16, 2.12, 2.10, 2.09, 2.085, 2.082, 2.04, 1.98 (s each, 3 H each, 8 x OAc).

Eluted next was the crystalline α-isomer **14a** (31 mg, 25%), R_F 0.36 (1:1 benzene-ethyl acetate), mp 189-190 °C (ethanol), $[\alpha]_D^{22}$ +53.8 ° (*c* 0.1, $CHCl_3$); lit.[21] mp 185 °C (ethanol), $[\alpha]_D^{25}$ +54 ° (*c* 1.5, $CHCl_3$); ^1H NMR: δ 6.30 (d, 1 H, H-1, $J_{1,2}$ = 3.35 Hz), 5.51 (bd, 1 H, H-4, $J_{3,4}$ = 3.36 Hz, $J_{4,5}$ < 1 Hz), 5.35 (bd, 1 H, H-4', $J_{3',4'}$ = 3.60 Hz, $J_{4',5'}$ < 1 Hz), 5.30 (dd, 1 H, H-2, $J_{2,3}$ = 9.80 Hz), 5.10 (dd, 1 H, H-2', $J_{1',2'}$ = 7.90 Hz, $J_{2',3'}$ = 10.5 Hz), 4.95 (dd, 1 H, H-3'), 4.63 (d, 1 H, H-1'), 4.27-4.23 (m, 2 H, H-6a,6b), 4.15 (d, 1 H, H-3), 4.14-4.09 (m, 2 H, H-5,6'b), 4.02 (dd, 1 H, H-6b, $J_{5,6b}$ = 7.02 Hz, $J_{6a,6b}$ = 11.6 Hz), 3.92 (bt, 1 H, H-5'), 2.17, 2.16, 2.13, 2.06, 2.058 (2), 1.98, 1.96 (s each, 3 H each, 8 x OAc).

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