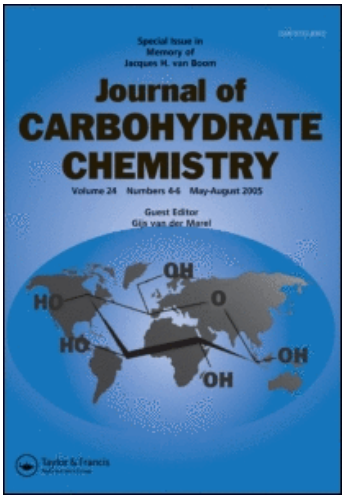

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A CONVENIENT SYNTHESIS OF TYPE IV GLYCOSYL DONORS FROM TYPE I DISACCHARIDES

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ABSTRACT

The synthesis of 4,6-di-*O*-acetyl-3-*O*-(tetra-*O*-acetyl-ß-D-galactopyranosyl)-2-deoxy-2-phthalimido-α,ß-D-galactopyranosyl chloride **14** and its 6-*O* -benzyl derivative **12** was achieved in a 5-step sequence starting from the readily available type I disaccharide derivative **3**. The key step in the synthesis involved the preparation of trifluoromethanesulfonate (triflate) derivatives **7** and **9** and their subsequent SN_2 displacement by acetate ion for conversion of 2-deoxy-2-phthalimido-ß-D-glucopyranosyl moiety to the corresponding *galacto* configuration.

INTRODUCTION

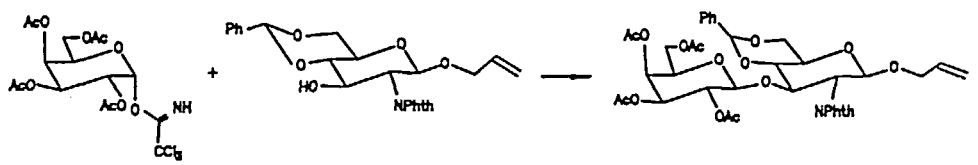
The sequences ß-D-Gal (1-3) ß-D-GlcNAc (Type I) and ß-D-Gal(1-3)ß-D-GalNAc (Type IV) are the core structures present in many tumor-associated antigens.[1] We have previously reported the synthesis of sialyl Le^a, sialyl Le^x and their biological properties.[2] The ongoing program was to design a convenient synthesis of type I disaccharide which could be utilized as the building unit for different oligosaccharides, as well as for the transformation into type IV analogues. The previous synthesis reported in the literature involved the use of the relatively expensive 2-azido-2-deoxy galactose derivatives for the construction of the ß-D-Gal (1-3) ß-D-GalNAc sequence.[3,4]

In recent years, use of triflates and mesylates as leaving groups in carbohydrate synthesis has opened new domains.[5] Hindsgaul *et al.* [6] have utilized the triflate for the

conversion of glucosamine to galactosamine derivatives and Lubineau *et al.* [7] have also utilized the triflate displacement reaction for the synthesis of Tα hapten. Our work deals with the one step conversion of type 1 glocosides to their type IV analogues by Walden inversion of the mono- and ditriflates by acetate ion in an aprotic medium. This method allows an alternative route for the synthesis of asialo GM_1.[8]

RESULTS AND DISCUSSION

The monosaccharide acceptor **2** was synthesized in four steps from the commercially available glucosamine hydrochloride. Several attempts for the glycosidation of the alcohol **1** with acetobromogalactose under a variety of conditions gave varying mixtures of α and ß disaccharides. However, the use of 2, 3, 4, 6-tetra- *O*-acetyl-galactopyranosyl α-trichloroacetimidate as the donor[9] and trimethylsilyl triflate as the promoter proved to be an efficient method for obtaining exclusively ß-linked disaccharide **3** in good yields (~ 70%). This disaccharide **3** serves as an important intermediate, which after a series of chemical manipulations, leads to the synthesis of different oligosaccharides.[10] The present work deals with an efficient method for converting the Type I structure to yet another important class, i.e., the Type IV structure. The debenzylidenation of **3** in aqueous acetic acid did not give us good yields of the diol **5**, however, the use of ethylene glycol in acetonitrile and catalytic amounts of p-toluenesulfonic acid gave the desired diol in excellent yields. This mild method could be applied to other complex carbohydrates having acid-sensitive functionalities. The inversion at C-4 of glucosamine moiety should in principle give us the desired Type IV structures. The 6-OBn **4** and 6-OAc **6** were synthesized as precursors to the target compounds **8** and **10**. Reductive opening of compound **3** in the presence of sodium cyanoborohydride and ethereal hydrogen chloride gave **4** in 85% yield and selective acetylation of **5** with acetyl chloride and pyridine at -30°C gave **6** in 90% yield. In order to invert the configuration at C-4 position, the compounds **4** and **5** were treated with



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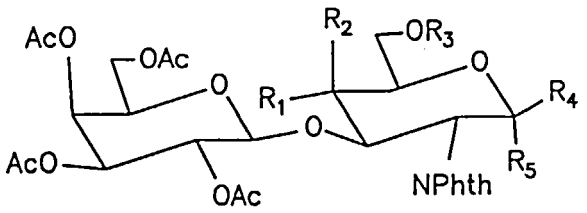
trifluoromethanesulfonic anhydride and pyridine in dichloromethane to give the trifluoromethanesulfonates **7** and **9**. The 4-*O*-trifluoromethanesulfonate **7** was characterized by ^1H NMR spectroscopy which showed a downfield shift for the signal of H-4



No.	R_1	R_2	R_3	R_4	R_5
4	OH	H	Bn	O-allyl	H
5	OH	H	H	O-allyl	H
6	OH	H	Ac	O-allyl	H
7	OTf	H	Bn	O-allyl	H
8	H	OAc	Bn	O-allyl	H
9	OTf	H	Tf	O-allyl	H
10	H	OAc	Ac	O-allyl	H
11	H	OAc	Bn	H(OH)	OH(H)
12	H	OAc	Bn	H(Cl)	Cl(H)
13	H	OAc	Ac	H(OH)	OH(H)
14	H	OAc	Ac	H(Cl)	Cl(H)

(δ 4.88) and H-3 (δ 4.95). The triflate **7** is stable on silica gel column and is easily converted to the *galacto* derivative **8** on treatment with tetraethylammonium acetate in N,N-dimethylformamide (DMF). Similarly, the configuration at C-4 of the trifluoromethanesulfonate **9** was also inverted to give the *galacto* derivative **10**. The successful inversions of the C-4 configurations of compounds **4** and **6** prompted us to attempt the epimerization of the diol **5**, via its 4',6' di-*O* -trifluoromethanesulfonate **9**. Compound **9** was subsequently inverted at C-4 to the already synthesized *galacto* derivative **10**. However, the di-*O*-triflation reaction of the diol was slow and needed longer completion time; whereas inversion followed the same kinetics as for **7**. The removal of the allyl group from these allyl glycosides gave the corresponding reducing sugar. Finally, the

treatment of the reducing sugar **1** **2** and **1** **3** with Vilsmeir reagent gave the glycosyl donors in excellent yields.

EXPERIMENTAL

General Procedures. Melting points were determined with a Gallenkamp melting point apparatus and are uncorrected. Optical rotations were recorded on 1% solutions in chloroform using an AA-100 Polarimeter (Optical Activity Limited). NMR spectra were recorded at 25°C for solutions in $CDCl_3$ unless otherwise stated using Bruker AM 300 and AM400 instruments. The following reference signals were used: $CDCl_3$ 77.2 ppm (^{13}C NMR in $CDCl_3$); internal Me_4Si 0.00 ppm (^1H NMR in $CDCl_3$). All TLC was performed on silica gel F_{254} (Merck, Darmstadt, W. Germany) with detection by charring with 5% sulfuric acid in ethanol or by quenching of UV light when applicable. Column chromatography was performed on silica gel 60 (230-400 mesh ASTM) Merck, Darmstadt, W. Germany. Solvents were dried by distilling from P_2O_5 and storing over 4Å molecular sieves.

Allyl 3-O-(Tetra-O-acetyl-ß-D-galactopyranosyl)-4,6-O-benzylidene-2-deoxy-2-phthalimido-ß-D-glucopyranoside (3). To a stirred mixture of the alcohol **2** (2.18g, 7.5mmol), 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl α-trichloroacetimidate **1** (3.68g, 7.5mmol) in dry dichloromethane (50mL) was added, dropwise, a solution of trimethylsilylmethyl triflate (20µL) in dichloromethane (10mL) at 0°C. The mixture was stirred for 16 h. The solid was filtered and the filtrate washed with a saturated bicarbonate solution, then water. Solvent evaporation left a foam which was applied to a column of silica gel. On elution with 20:10:1 hexane-ethyl acetate-acetonitrile, pure ß-linked disaccharide was obtained (2.65g, 69.4% yield). An analytical sample was prepared by crystallization from ethyl acetate-isopropanol-hexane; mp149-153 °C, $[\alpha]_D^{20}$ + 8.5 (*c*1, chloroform); ^1H NMR ($CDCl_3$): δ 8.00-7.75 (m,4H, phthalimido, protons), 7.60-7.35 (m, 5H,benzylidene aromatic protons), 5.78-5.60 (m,1H,allyl proton), 5.60 (s, 1H, benzylidene CH), 5.22 (d,1H,H-1,$J_{1,2}$ = 8.5Hz), 5.22 (d,1H,H-4'), 5.24-5.00 (m,2H,allyl protons), 5.02 (dd,1H,H-2',$J_{1',2'}$ = 8.0Hz,$J_{2',3'}$ = 10.5Hz), 4.77 (dd,1H,H-3,$J_{2,3}$ = 11.0 Hz,$J_{3,4}$ = 8.0Hz),4.77 (dd,1H,H-3'), 4.55 (d,1H,H-1',$J_{1',2'}$ = 8.0 Hz), 4.12-4.04 (m,2H,H-6a and H-2 overlapping), 4.00 (m,1H,allyl proton), 3.95-3.78 (m,5H,H-6a',H-6b',H-6b,H-4 and allyl proton overlapping), 3.65 (m,H-5,$J_{5,6a}$ = 4.5Hz,$J_{4,5}$=$J_{5,6b}$=10.0Hz), 3.50 (dd,1H,H-5',$J_{5',6a'}$ = 6.0Hz,$J_{5',6b'}$ = 8.0 Hz), 2.10, 1.93, 1.88, 1.58 (4s,12H,acetyl CH_3); ^{13}C NMR ($CDCl_3$): δ 168.8, 170.0, 170.2 (C=O), 137.2, 129.3, 128.4, 126.1 (benzylidene carbons), 134.2, 133.3, 123.58 (phthalimido carbon), 131.8, 117.6 (allyl carbons), 101.5 (C-1'), 100.5

(benzylidene CH), 97.9 (C-1), 81.1 (C-3), 75.7, 71.1, 70.4, 70.0 (allyl carbon), 69.3, 68.8 (C-6), 66.8, 66.4, 60.9 (C-6'), 55.4 (C-2), 20.1, 20.4, 20.5, 20.6 (acetyl CH_3).
Anal. Calcd for $C_{38}H_{41}NO_{16}$: C, 59.45; H, 5.38; N, 1.82 Found: C.59.39; H,5.26; N,1.82

Allyl 3-O-(Tetra-O-acetyl-ß-D-galactopyranosyl)-6-O-benzyl-2-deoxy-2-phthalimido-ß-D-galactopyranoside (4). A solution of **3** (3.0g, 3.91mmol) and sodium cyanoborohydride (1.5 g, 23.87 mmol) in dry tetrahydrofuran (30mL) containing 3Å molecular sieves and a crystal of methyl orange was cooled at 0°C. Diethyl ether saturated with hydrogen chloride was added dropwise to the stirred yellow solution until the pink color persisted. The mixture was warmed to room temperature and stirring was continued for 6 hours. The mixture was diluted with dichloromethane (50mL) and washed successively with a saturated sodium bicarbonate solution and water. The syrup obtained after evaporation of solvent was taken up in chloroform and applied to a column of silica gel. The column was eluted with 3:2 hexane-ethyl acetate. A pure fraction (2.55g, 3.31 mmol, 85%) was obtained as a foam; $[\alpha]_D^{20}$ 3.0 (*c* 1.0, chloroform); R_F 0.23 in 1:1 ethyl acetate-hexane; ^1H NMR ($CDCl_3$) δ 7.00-7.76 (m, 4H, phthalimido protons), 7.50-7.30 (m, 5H, benzyl protons), 5.70 (m, 1H, allyl proton), 5.32 (dd, 1H, H-4', $J_{3',4'}$ = 3.5 Hz), 5.18 (dd, 1H, H-2', $J_{1',2'}$ = 8.0 Hz, $J_{2',3'}$ = 10.5 Hz), 5.08 (d, 1H, H-1, $J_{1,2}$ = 8.5Hz) 5.14-5.00 (m, 2H, allyl protons), 4.84 (dd, 1H, H-3'), 4.66 (t, 2H, benzyl CH_2), 4.52 (dd, 1H, H-3, $J_{2,3}$ = 11.0 Hz, $J_{3,4}$ = 7.5 Hz), 4.43 (d, 1H, H-1'), 4.32 (m,2H,H-2 and allyl proton overlapping), 4.20-3.60 (m,9H,other protons), 2.16,2.06,1.91,1.48 (4s,12H,acetyl CH_3); ^{13}C NMR ($CDCl_3$) δ 168.7, 169.9, 170.0, 170.3 (C=O), 138.5,128.3,127.5 (benzyl), 134.4, 133.6,123.6 (phthalimido), 131.7,117.3 (allyl), 101.2 (C-1'), 97.3 (C-1), 82.2 (C-3), 75.7,73.6 (benzyl CH_2), 71.3,70.9,70.0,69.7,69.6 (allyl carbon and C-6), 68.7,66.9,61.52(C-6'), 54.96 (C-2), 19.77,20.33,20.51 (acetyl CH_3). Anal. Calcd for $C_{38}H_{43}NO_{16}$: C,59.29; H,5.63; N,1.82 Found: C,59.30; H.5.44; N,1.81.

Allyl 3-O-(tetra-O-acetyl-ß-D-galactopyranosyl)-2-deoxy-2-phthalimido-β-D-glucopyranoside (5). The benzylidene compound **3** (1.5 g, 1.95 mmol) was treated with ethylene glycol (2.5 g, 40 mmol) in dry acetonitrile containing catalytic amount of p-toluenesulfonic acid monohydrate (approx. 5 mg) for 36 h at room temperature. Neutralization with triethylamine and solvent removal left a foam which was applied to a silica gel column. After the column had been eluted with 3:2 ethyl acetate-hexane, the title compound **5** (1.04 g, 1.53 mmol, 78%) was obtained by concentration; $[\alpha]_D^{20}$ + 2.2 (*c* 1.0,chloroform); ^1H NMR ($CDCl_3$) δ 7.95-7.76 (m, 4H, phthalimido protons), 5.68 (m, 1H, allyl proton), 5.34 (dd, 1H, H-4', $J_{3',4'}$ = 3.5 Hz), 5.25 (d, 1H, H-1, $J_{1,2}$ = 8.5 Hz), δ 5.22 (m, 2H, allyl protons), δ

5.20 (dd, 1H, $J_{1',2'}$ = 8.0 Hz, $J_{2',3'}$ = 10.5 Hz), 4.85 (dd, 1H, H-3'), 4.52 (dd, 1H, H-3, $J_{2,3}$ = 11.0 Hz, $J_{3,4}$ = 8.0 Hz), 4.45 (d, 1H, H-1',$J_{1',2'}$ = 8.0 Hz), 4.26 (m, 2H, H-2 and allyl proton overlapping), 4.25-3.50 (m, 10H, other protons), 2.16, 2.11, 1.92, 1.46,(4s, 12H, acetyl CH_3); ^{13}C NMR ($CDCl_3$) δ 168.7,169.9,170.1, 170.3 (C=O),134.5,133.5,123.7 (phthalimido carbons), 131.7,117.5 (allyl carbons), 101.2 (C-1'), 97.6 (C-1),82.1 (C-3), 75.6, 71.4, 70.9, 70.7, 70.0 (allyl carbon), 68.7, 7.0, 63.0(C-6), 61.6,(C-6'), 54.9,(C-2),19.8, 20.4, 20.52(acetyl CH_3).

Allyl 6-O-Acetyl-3-O-(Tetra-O-acetyl-ß-D-galactopyranosyl)-2-deoxy-2-phthalimido-ß-D-glucopyranoside (6). Acetyl chloride (50 mg, 0.6 mmol) was added to a solution of the diol **5** (340 mg, 0.5 mmol) in dry dichloromethane (10 mL) containing pyridine (60 mg, 0.75 mmol) cooled at -60°C. The reaction mixture was slowly warmed to 30°C and kept for 2 h. Solvent removal left a foam which was applied to a column of silica gel. The column was eluted with 40:1 $CHCl_3$-CH_3OH and the appropriate fractions concentrated to give **6** (325mg, mmol, 90%); H NMR ($CDCl_3$) δ 7.95-7.72 (m, 4H, phthalimido protons), 5.65 (m, 1H, allyl proton), 5.25 (bd, 1H, H-4', $J_{3',4'}$ = 3.0Hz), 5.18-4.95 (m, 4H, H-2', H-1 and allyl protons overlapping), 4.80 (dd, 1H, H-3', $J_{2',3'}$ = 10.0 Hz, $J_{3',4'}$ = 3.0 Hz), 4.52-3.55 (m, 13H, other protons), 2.12, 2.11, 2.05, 1.85, 1.44 (5s,15H, acetyl CH_3).

Allyl 4-O-Acetyl-3-O-(tetra-O-acetyl-ß-D-galactopyranosyl)-6-O-benzyl-2-deoxy-2-phthalimido-ß-D-galactopyranoside (8). Compound **4** (500mg, 0.65 mmol) was dissolved in dry dichloromethane (8 mL) containing dry pyridine (0.25mL, 3.09 mmol) and cooled to -5°C before a solution of trifluoromethanesulfonic anhydride (0.22mL, 1.31 mmol) in dichloromethane (1mL) was added. The reaction mixture was stirred between -5°C to+10°C for 4 h until TLC showed complete conversion of starting material (R_F 0.23 in 1:1 ethyl acetate-hexane) to a faster-moving material (R_F 0.37). The mixture was diluted with dichloromethane (10mL) and washed with cold 2M HCl and cold water. The solution was dried with sodium sulfate and concentrated at room temperature to give a yellow foam identified as the triflate **7**; ^1H NMR ($CDCl_3$) δ 7.98-7.80 (m, 4H, phthalimido protons), 7.44-7.28 (m, 5H, benzyl protons), 5.66 (m, 1H, allyl proton), 5.22 (bd, 1H, H-4', $J_{3',4'}$ = 3.0Hz), 5.12 (d, 1H, H-1,$J_{1,2}$ = 9.0Hz), 5.14-5.00 (m, 3H, H-2' and allyl protons overlapping), 4.95 (t, 1H, H-3, $J_{2,3} = J_{3,4}$ = 10Hz,) 4.88 (t, 1H, H-4), 4.62 (q, 2H, benzyl CH_2), 4.58 (dd, 1H, H-3'), 4.32 (dd, 1H, H-2), 4.24 (m, 1H, allyl protons), 4.18 (d, 1H, H-1', $J_{1',2'}$ = 8.0Hz), 4.12 (d, 2H, H-6a' and H-6b'), 4.04-3.94 (m, 1H, allyl protons), 3.94-3.58 (m, 4H, H-6a, H-6b, H-5 and H-5'), 2.10, 2.06, 1.99, 1.90 (4s, 12H, acetyl CH_3).

The yellow triflate **7** thus obtained was taken up in a solution of tetraethylammonium acetate (1.27 g) in dry DMF (15 mL). TLC showed that reaction was complete in about 15 min (product R_F 0.24, 1:1 ethyl acetate-hexane). Solvent was evaporated and the residue was

redissolved in dichloromethane and washed twice with water. The solution was concentrated and the residue was purified by chromatography on silica gel column using 1:1 ethyl acetate-hexane as eluant to give the desired compound, **8** (0.42 g, 0.52 mmol, 80%); $[\alpha]_D^{20}$ +9.5 (c 1.0, chloroform); ^{1}H NMR ($CDCl_3$) δ 7.95-7.70 (m, 4H, phthalimido protons), 7.42-7.25 (m, 5H, benzyl aromatic protons), 5.77-5.60 (m, 1H, allyl protons), 5.50 (d, 1H, H-4, $J_{3,4}$ = 3.0 Hz), 5.25 (d, 1H, H-4', $J_{3',4'}$ = 3.5 Hz), 5.13 (d, 1H, H-1, $J_{1,2}$ = 8.8 Hz), 5.13-4.95 (m, 3H, allyl protons overlapping with H-2'), 4.78 (dd, 1H, H-3', $J_{2',3'}$ = 10.1 Hz), 4.72 (dd, 1H, H-3, $J_{2,3}$ = 11.0 Hz), 4.55 (dd, 1H, H-2), 4.54 (q, 2H, benzyl CH_2), 4.42 (d, 1H, H-1', $J_{1',2'}$ = 8.0 Hz), 4.28 (m, 1H, allyl proton), 4.11-3.98 (m, 3H, allyl protons, H-6a and H-6b overlapping), 3.93 (t,1 H, H-5, J = 7 Hz), 3.77 (t, 1H, H-5', J = 7 Hz), 3.60 (m, 2H, H-6a' and H-b'), 2.14, 2.10, 2.00,1 .86, 1.52 (5s, 15H, acetyl CH_3); ^{13}C NMR ($CDCl_3$): δ 170.3,170.0,169.7,169.0, (C=O), 138.1,128.4,127.8 (benzyl), 134.3,133.6,123.7,123.3 (phthalimido), 131.8,117.5 (allyl), 100.8 (C-1), 73.9, 73.7 (benzyl CH_2), 73.9, 71.0, 70.9, 69.9. (allyl), 69.3, 69.2 (C-6), 68.8, 66.8, 60.9 (C-6'), 52.8 (C-2),20.0, 20.4, 20.6, 20.9 (acetyl methyl).

Anal. Calcd for $C_{40}H_{45}NO_{17}$: C, 59.18; H, 5.59; N, 1.73. Found: C, 58.80; H, 5.48; N, 1.71.

Allyl 4,6-Di-O-acetyl-3-O-(tetra-O-acetyl-ß-D-galactopyranosyl)-2-deoxy-2-phthalimido-β-D-galactopyranoside (10). A. Epimerization of the diol **5:** Compound **5** (500 mg, 0.74 mmol) was dissolved in dry dichloromethane (10 mL) containing dry pyridine (0.5 mL, 6.18 mmol) then cooled to -5°C before a solution of trifluoromethanesulfonic anhydride (0.5 mL, 2.97 mmol) in dichloromethane (4 mL) was added. The mixture was stirred for 6 h at 5°C-10°C. An additional batch of trifluoromethanesulfonic anhydride (0.25 mL) was added and the mixture was stirred at room temperature for 2 h until TLC showed a single spot (R_F 0.4 in 1:1 ethyl acetate-hexane). The mixture was diluted with dichloromethane (10 mL), then washed with cold 2M HCl and cold water. Drying with sodium sulfate and solvent removal at room temperature gave crude ditriflate **9**; ^{1}H NMR ($CDCl_3$) δ 8.10-7.86 (m, 4H, phthalimido protons), 5.68 (m, 1H, allyl proton), 5.26 (dd, 1H, H-4' overlapping with H-1), 5.22 (d, 1H, H-1, $J_{1,2}$ = 8.5 Hz), 5.18-5.04 (m, 3H ,H-2' overlapping with allyl protons) 4.98 (dd, 1H, H-3, $J_{2,3}$ = 11.0 Hz, $J_{3,4}$ = 9.0 Hz), 4.83 (dd, 1H, H-6a,$J_{6a,6b}$ = 12 Hz,$J_{6a,5}$ = 3.0 Hz), 4.78-4.58 (m, 3H, H-4, H-6b and H-3' overlapping), 4.36 (dd, 1H, H-2,$J_{1,2}$ = 8.5 Hz,$J_{2,3}$ = 11.0 Hz), 4.20 (d,1H,H-1',$J_{1',2'}$ = 8.0 Hz), 4.32-4.00 (m,5H,other protons), 3.68 (t,1H,H-5'), 2.10,2.06,2.00,1.90 (4s,12H,acetyl CH_3).

The ditriflate **9** thus obtained was treated with a solution of tetraethylammonium acetate (2 g) in dry DMF for 15 min before the solution was concentrated, the residue was redissolved in dichloromethane and washed twice with water. The residue obtained after

solvent evaporation was purified by silica gel column using 1:1 ethyl acetate-hexane as eluant to give a white solid (412 mg, 0.54 mmol, 73%); $[\alpha]_D^{20}$ +15.4 (*c* 1.0, chloroform). The ^{1}H NMR spectrum of **9** was identical with that in the literature.[3]

B. Epimerization of compound **6:** The triflation of **6** and its subsequent inversion with tetraethylammonium acetate DMF was performed as for compound **10**.

4-O-Acetyl-3-O-(tetra-O-acetyl-ß-D-galactopyranosyl)-6-O-benzyl-2-deoxy-2-phthalimido-D-galactopyranose (11). A solution of **8** (300 mg, 0.37 mmol), tris(triphenylphosphine)rhodium (I) chloride (50 mg, 0.054 mmol), and 1,4-diazabicyclo [2.2.2] octane (18 mg, 0.16 mmol), in 7:3:1 ethanol-benzene-water (15 mL) was refluxed for 2 days. Solvent removal left a residue which was dissolved in 9:1 acetone-water (10 mL) containing mercuric chloride (502 mg) and mercuric oxide (2 mg) and stirred overnight. Evaporation of solvent left a dark residue which was taken up in 1:1 ethyl acetate-hexane. The solution was washed with 30% KBr, then water. Evaporation of solvent left a residue which was purified on a column of silica gel using 3:2 ethyl acetate-hexane as eluant to give the desired reducing sugar **11** (214 mg, 0.277 mmol, 75%). A sample of the material was dissolved in 1:1 ethyl acetate-hexane to which was added pentane to incipient turbidity. Crystallization occurred on storage at 4°C, mp 167-170°C; ^{1}H NMR ($CDCl_3$) δ 7.90-7.70 (m, 4H, phthalimido protons), 7.40-7.26 (m, 5H, benzyl aromatic protons), 5.60 and 5.50 (d, 1H, H-4αß, $J_{3,4}$ = 3.0 Hz), 5.42-3.30 (m, 16H, other protons), 2.15, 2.12, 2.11, 2.10, 2.00, 1.99,1 .86, 1.48, 1.31, (9s, 15H, αß acetyl CH_3).

Anal. Calcd for $C_{37}H_{41}NO_{17}$: C, 57.59; H, 5.35; N, 1.81Found: C,57.15; H,5.50; N,1.81

4-O-Acetyl-3-O-(tetra-O-acetyl-ß-D-galactopyranosyl)-6-O-benzyl-2-deoxy-2-phthalimido-α-ß-D-galactopyranosyl Chloride (12). A solution of oxalyl chloride (50 mg, 0.39 mmol) in dichloromethane (0.5 mL) was added slowly at room temperature to a stirred solution of compound **11** (100 mg, 0.13 mmol) in dichloromethane (1 mL) containing DMF (7.5 mg, 0.10 mmol). Stirring was continued for 3 h before dichlorormethane (10 mL) was added. The solution was washed three times with cold water, dried with sodium sulfate, and then concentrated to a yellowish oily residue which was applied to a short silica gel column. The column was eluted with 1:1 ethyl acetate-hexane. A colourless powder (88 mg, 0.11 mmol, 85%) was obtained by lyophilization of the main fraction from benzene. Part of the powder was dissolved in 1:1 ethyl acetate-hexane to which was added pentane until incipient turbidity. When the mixture was stored at 4°C, crystals of **12** were deposited; mp 85-115°C(α, β mixture) ^{1}H NMR ($CDCl_3$) δ 8.00-7.80 (m, 4H, phthalimido protons), 7.50-7.25 (m, 5H, benzyl aromatic protons), 6.35 (d, H-1α, $J_{1,2}$ = 4.2 Hz), 6.00 (d, 8.0 Hz, H-1ß, splitting pattern showing second-order effect), 5.78 (dd,

0.2H, H-4α, $J_{3,4}$ = 3.0 Hz), 5.60 (dd, 0.8H, H-4ß), 5.52 (dd, 0.2H, H-3α,$J_{2,3}$ = 11.0 Hz), 5.36 (dd, 0.2H, H-4α', J = 3.0 Hz), 5.28 (dd, 0.8H, H-4ß'), 5.05 (dd, 1H, H-2',$J_{1',2'}$ = 8.0 Hz,$J_{2',3'}$ = 10.5 Hz), 4.42 (d, 1H, H-1'), 5.00-3.55 (m, 10H, other protons), 2.21, 2.16, 2.15, 2.02, 1.92, 1.91, 1.60, (7s, 15H, αß acetyl CH_3)

Anal. Calcd $C_{37}H_{40}NO_{16}Cl$: C,56.24;H,5.10; N,1.77; Cl,4.49 Found: C,55.91; H,5.17;N,1.86;Cl,4.16

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REFERENCES

1. S. Hakomori, Ann. Rev. Immunol., 103 (1982).

2. a) S.Z. Abbas, S. Sugiyama, J. Diakur and P. Rudnew in: *Proceedings of the Japanese - German Symposium on Sialic Acids*, R. Schauer and T. Yamakawa, Eds.; Kier Verlag, Berlin, 1988, p 22.
b) S.Z. Abbas, J. Diakur, S. Sugiyama and D. Fleming in: *Proceedings of the Japanese - German Symposium on Sialic Acids*, R. Schauer and T. Yamakawa, Eds.; Kier Verlag, Berlin, 1988, p 20.
c) A. van Heel, D. Jette, C.J. Turner, B.A. Skoczenski, S. Sugiyama, J. Diakur, S.A. Abbas, and M.R. Suresh in: *Proceedings of the Japanese - German Symposium on Sialic Acids*, R. Schauer and T. Yamakawa, Eds.; Kier Verlag, Berlin, 1988, p 274.

3. S. Sabesan and R.U. Lemieux, *Can. J. Chem.*, **62**, 644, (1984).

4. J.C. Jacquinet and H. Paulsen, *Tetrahedron Lett.*, **22**, 15, 1387 (1981).

5. R.W. Brinkley and M.G. Ambrose, *J. Carbohydr. Chem.*, **3**, 1, (1984).

6. Vandana and O. Hindsgaul, *Can. J. Chem.*, **65**, 1645 (1987).

7. A. Lubineau and H. Bienayme *XIVth International Carbohydrate Symposium* (1988), Stockholm, Sweden.

8. M. Sugimoto, T. Horisaki and T. Ogawa, *J. Glycoconjugate*, **2**, 11 (1988).

9. P.H.A. Zollo and P. Sinay, *Carbohydr. Res.*, **150**, 199 (1986).

10. A. A. Noujaim et al., personal communication.