Synthesis of some blocked di- and trisaccharide derivatives related to the repeating unit of the O-antigen from *Shigella dysenteriae* type 3 in the form of their glycosides

Sujit Kumar Sarkar & Nirmolendu Roy

Department of Biological Chemistry, Indian Association for the Cultivation of Science, Jadavpur, Kolkata 700 032, India.

Email: nirmolendu@yahoo.com

Received 1 September 2003; accepted (revised) 10 February 2004

We have already reported\(^1\) the synthesis of blocked pentasaccharide related to the repeating unit\(^2\) of *Shigella dysenteriae* type 3, a gram-negative pathogen responsible for many intestinal diseases including dysentery. There are possibilities of the successful use of protein conjugates of synthetic oligosaccharides as vaccines against many bacterial infections.\(^3\) Since β-D-galactofuranosyl and 2-acetamido-β-D-galactopyranosyl fragments in combination with other sugar moieties in the repeating unit may play vital role in immunodominancy, it is relevant to synthesize oligosaccharides containing these sugar moieties. In this communication, we report the synthesis of two disaccharides ED and DA and two trisaccharides EDA and BA(D) related to the repeating unit I of the O-antigen from *Shigella dysenteriae* type 3 in their blocked form. The oligomers EDA and DA are in the form of their 2-(trimethylsilyl)ethyl glycosides while ED is in the form of its thiophenyl glycoside and BA(D) is in the form of its p-methoxyphenyl glycoside.

The known 2-(trimethylsilyl)ethyl 2,6-di-O-benzyl-β-D-galactopyranoside\(^4\) 1 with two free OH groups was selectively acetylated via orthoester\(^5\) intermediate. The 4-O-acetate 2 was allowed to react with the phenyl 3,4,6-tri-O-acetyl-2-deoxy-2-phthalimido-1-thio-β-D-galactopyranosyl 3 in the presence of N-iodosuccinimide (NIS) and trifluoromethanesulfonic acid\(^6\) (TfOH) to afford the disaccharide, 2-(trimethylsilyl)ethyl 3,4,6-tri-O-acetyl-2-deoxy-2-phthalimido-β-D-galactopyranosyl-(1→3)-4-O-acetyl-2,6-di-O-benzyl-β-D-galactopyranoside 6 (Scheme 1), which was characterized by its \(^1\)H NMR spectrum. The anomeric configuration of the newly formed glycosidic linkage in 6 was established from the coupling (J\(_{1,2} = 8.3\) Hz) of the doublet at \(\delta 5.49\) in the \(^1\)H NMR spectrum. The disaccharide 6 was deacetylated under mild condition and the product was dissolved in the same pot in pyridine and treated with tert-butyldiphenylsilyl chloride\(^7\) (TBDPSCI) to afford the 6-O-TBDPS derivative 7 which has one acetyl group intact at the 4\(^\beta\)-position. The position of the acetyl group in 7 was confirmed from its \(^1\)H and \(^13\)C NMR spectra and resulted most probably because of the steric difficulty in approaching of the C-4\(^\beta\) hydroxyl group towards acetic anhydride molecule. Treatment of 7 with 2,2-dimethoxypropane\(^8\) afforded the 3\(^\delta\), 4\(^\delta\)-isopropylidene derivative 8. Formation of isopropylidene derivative clearly demonstrated the
presence of acetate at the C-4\(^\alpha\) position and also the location of TBDPS at the C-6\(^\beta\) position. The disaccharide 7 was also characterized by its signals at \(\delta 5.30\) (H-1\(^\beta\)), 5.23 (H-4\(^\alpha\)), 4.16 (H-1\(^\beta\)), and 1.95 (COC\(_3\)) in the \(^1\)H NMR spectrum and at \(\delta 171.1\) (CO\(_\text{CH}_3\)), 168.5, 168.4 [N(CO\(_3\))\(_2\)C\(_6\)H\(_4\)], 103.1 (C-1\(^\beta\)), 98.6 (C-1\(^\beta\)), 26.9 [\(\text{Ph}_2\)Si\(_3\text{CCCH}_3\)], 20.9 (CO\(_\text{CH}_3\)), 19.2 [\(\text{Ph}_2\)Si\(_2\text{CCCH}_3\)], 18.5 [OCH\(_2\)\(_2\)\(_2\)\(_2\)] and -1.5 [OCH\(_2\)\(_2\)\(_2\)\(_2\)] in the \(^13\)C NMR spectrum.

The disaccharide acceptor 7 was then allowed to react with the known trichloroacetimidate donor\(^9\) in the presence of trimethylsilyl trifluoromethanesulfonate (TESOTf)\(^{10}\) to afford the trisaccharide, 2-(trimethylsilyl)ethyl 6-O-acetyl-2,3,5-tri-O-benzoyl-\(\beta\)-D-galactofuranosyl-(1→3)-6-O-tert-butylidene-2-deoxy-2-phthalimido-\(\beta\)-D-galactopyranosyl-(1→3)-4-O-acetyl-2,6-di-O-benzyl-\(\beta\)-D-galactopyranoside 10 in 77\% yield. The formation of the \(\beta\)-D-galactofuranosidic linkage was confirmed from low coupling constant for H-1\(^E\) (\(<1\) Hz) in the \(^1\)H NMR spectrum and characteristic C-1\(^E\) signal\(^{11,12}\) at \(\delta 108.9\) in the \(^13\)C NMR spectrum. Formation of the (1→3)-linked trisaccharide was confirmed by acetylation of 10, which showed a downfield shift of H-4\(^\beta\) proton from \(\delta 4.07\) to 5.34 ppm. No (1→4)-linked condensation product was detected in this reaction. Treatment of 10 with ethylenediamine and butanol\(^{13}\) afforded the free amine which upon acetylation with acetic anhydride and pyridine afforded the desired blocked trisaccharide, namely 2-(trimethylsilyl)ethyl 2,3,5,6-tetra-O-acetyl-\(\beta\)-D-galactofuranosyl-(1→3)-2-acetamido-4,O-acetyl-6-O-tert-butylidene-2-deoxy-\(\beta\)-D-galactopyranosyl-(1→3)-4-O-acetyl-2,6-di-O-benzyl-\(\beta\)-D-galactopyranoside 11 in 95\% yield (Scheme I).

In another experiment, phenyl 3,4,6-tri-O-acetyl-2-deoxy-2-phthalimido-1-thio-\(\beta\)-D-galactopyranoside 3 prepared from D-galactosamine hydrochloride was deacetylated and the product on benzylideneation\(^{14}\) followed by acetylation gave 5 (Scheme II).
Scheme II—(a) (i) NaOMe, MeOH, 15 min; (ii) PhCH(OCH)₂, CH₂CN, CSA, 88.7%; (b) Ac₂O, Pyr, 2 hr; (c) NIS, TIOH, CH₂Cl₂, -20°C, 20 min, 89%; (d) (i) H₂NCH₂CH₂NH₂, 1-BuOH, 90°C, 20 hr; (ii) Ac₂O, Pyr, 12 hr, 90%; (e) NaOMe, MeOH, 1 hr.

compound 5 was characterized from its signals for acetyl, benzylidene, H-2, C-2 and anomeric proton and carbon in its ¹H and ¹³C NMR spectra. While we wanted to synthesize the trisaccharide 11 with reduced number of reaction steps, we prepared disaccharide acceptors 13 and 15 with a 3°-OH and containing the 4,6-benzylidene group and 2-phthalimido NHAc respectively in the galactose moiety. The thiophenyl glycoside donor 5 was allowed to react with the acceptor 2 in the presence of NIS and TIOH to give the disaccharide, 12 in 88% yield (Scheme II). The formation of the β-linkage was established from the chemical shift and large coupling (J₁₂=8.4 Hz) of H-1 in its ¹H NMR spectrum. Removal of the acetyl group of 12 afforded the acceptor 13 in quantitative yield. Treatment of 12 with ethylenediamine and butanol afforded the free amine, which upon acetylation gave the 2-acetamido compound 14 in 90% yield. Deacetylation of 14 afforded 2-(trimethylsilyl)ethyl 2-acetamido-2-deoxy-4,6-O-benzylidene-β-D-galactopyranosyl-(1→3)-2,6-di-O-benzyl-β-D-galactopyranoside 15.

It was observed that, the formation of the trisaccharide did not proceed when the 4,6-benzylidene disaccharide acceptors (13 or 15) were attempted to react either with the trichloroacetimidate donor 9 or the thioglycoside donor 16. However the donor 16 did react with the monosaccharide acceptor 5 to give the disaccharide, phenyl 6-O-acetyl-2,3,5-tri-O-benzoyl-β-D-galactofuranosyl-(1→3)-4,6-O-benzylidene-2-deoxy-2-phthalimido-β-D-galactopyranoside 17 in low yield (25%), although the reaction proceeded chemoselectively. These observations in the unsuccessful attempts were probably due to the steric hindrance of the bulky NPhth group at the 2-position and the orientation of the 4,6-benzylidene ring in the D-galactosamine moiety. This type of inhibition in the glycosidation at the 3-position of the galactosamine moiety was also reported previously.

In a separate experiment, the known 4-methoxyphenyl 2,3,4,6-tetra-O-acetyl-β-D-galactopyranoside 18 on deacetylation followed by acetonation afforded 4-methoxyphenyl 3,4-O-isopropylidene-β-D-galactopyranoside 19 which was benzylated to give 20. Removal of isopropylidene group from 20 gave 21, which has two hydroxyl groups. Compound 21 was then allowed to react with the known trichloroacetimidate donor, 3,4,6-tri-O-acetyl-2-deoxy-2-phthalimido-β-D-galactopyranosyl trichloroacetimidate 22 in the presence of TESOTf to afford the disaccharide 23 in 76% yield (Scheme III). Formation of the β-glycosidic linkage was confirmed from the high
coupling constant of H-1D ($J_{1,2}=8.2$ Hz). Again, the formation of the 1→3 linked product was confirmed by acetylation of 23, which showed downfield shift of H-4 signal from δ 4.02 to 5.34. The disaccharide 23 was then allowed to react with the known thiglycoside donor, ethyl 2,3-di-O-benzyl-4,6-O-benzylidene-$\beta$-D-glucopyranoside$^{20}$ 24 in the presence of MeOTf$^{21}$ to afford the trisaccharide, 4-methoxyphenyl 2,3-di-O-benzyl-4,6-O-benzylidene-$\alpha$-$\beta$-D-glucopyranosyl-(1→4)-2,6-di-O-benzyl-3-O-(3,4,6-tri-O-acetyl-2-deoxy-2-phthalimido-$\beta$-$\beta$-galactopyranosyl)-$\beta$-$\beta$-D-galactopyranoside 25 in 86% yield (Scheme III). The anomeric configuration of the newly formed glyco-sidic linkage was confirmed from the signals at δ 5.15 ($J_{1,2}=3.5$ Hz) in the $^1$H NMR and at δ 99.4 in $^{13}$C NMR spectrum.

In summary, we have synthesized some blocked oligosaccharides related to the repeating unit of Shigella dysenteriae type 3. These blocked oligosaccharides can be utilized for the synthesis of glyco-conjugates as synthetic vaccines.

**Experimental Section**

**General.** All reactions were monitored by TLC on Silica Gel G (SRL, India). Column chromatography was performed on 100-200 mesh Silica Gel (SRL,
India) using 10-20 times (by weight) of the crude product. The organic extracts were dried over anhydrous Na₂SO₄. All solvents were distilled and/or dried before use and all evaporation were conducted at or below 40°C under reduced pressure unless stated otherwise. Optical rotations were measured at 24°C with a Perkin-Elmer 241 MC polarimeter. The ¹H and ¹³C NMR spectra were recorded with a Bruker DPX 300 spectrometer using CDCl₃ as solvent and tetramethylsilane as internal standard unless otherwise stated.

**2-(Trimethylsilyl)ethylethyl 4-O-acetyl-2,6-di-O-benzyl-β-D-galactopyranoside 2.** To a solution of compound 1 (9.9 mg, 1.95 mmol) in acetonitrile (10 mL) was added trimethyl orthoacetate (503 μL, 2.93 mmol) and CSA (20 mg). The reaction mixture was stirred for 30 min at room temperature when TLC showed complete formation of the orthoester. The reaction was quenched with Et₃N, concentrated under reduced pressure maintaining the temperature below 20°C. The syrupy residue was dissolved in AcOH (10 mL) and stirred vigorously at 25°C for 10 min. The reaction mixture was concentrated and traces of AcOH were removed by co-evaporation with toluene. Column chromatography with toluene-EtOAc (5:1) gave 2 (875 mg, 89%); [α]DA⁻⁶⁺ = 3.3° (c 2.5, CHCl₃); ¹H NMR: δ 7.25-7.11 (m, 10H, aromatic protons), 5.17 (d, 1H, J₆,₆₅ = 3.2 Hz, H-4), 4.80, 4.51 (2 d, 2H, J = 11.3 Hz, CH₂Ph), 4.38, 4.28 (2 d, 2H, J = 11.8 Hz, CH₂Ph), 4.26 (d, 1H, J₆,₆₅ = 7.7 Hz, H-I), 3.89 (dd, 1H, J₆,₆₅ = 7.8 Hz, J₆,₆₅ = 11.0 Hz, H-2), 3.59 (m, 2H, OCH₂CH₂Si(CH₃)₃), 3.51-3.32 (m, 4H, H-3, H-5, H-6), 1.91 (s, 3H, COCH₃), 0.92 (m, 2H, OCH₂CH₂Si(CH₃)₃), -0.15 [s, 9H, OCH₂CH₂Si(CH₃)₃]; ¹³C NMR: δ 171.4 (COCH₃), 139.0-128.2 (aromatic carbons), 103.6 (C-1), 79.4, 75.2, 74.0, 72.8, 72.3, 70.3, 69.8, 68.1 (C-6), 21.3 (COCH₃), 19.0 [OCH₂CH₂Si(CH₃)₃], -1.0 [OCH₂CH₂Si(CH₃)₃]. Anal. Calcd for C₈₁H₇₇O₃Si: C, 80.95; H, 6.45; Found: C, 81.05; H, 6.34.

**Phenyl 3,4,6-tri-O-acetyl-2-deoxy-2-phthalimido-1-thio-β-D-galactopyranoside 3.** 1,3,4,6-Tetra-O-acetyl-2-thiophenyl glycosides 3 (1.9 g, 85.9%) by conventional method; [α]DA⁺⁵⁺ = 31.4° (c 0.5, CHCl₃); ¹H NMR: δ 7.91-7.76 [m, 4H, N(CO₂)₂C₆H₄], 7.46-7.27 (m, 5H, aromatic protons), 5.84 (dd, 1H, J₆,₆₅ = 10.9 Hz, J₆,₆₅ = 3.4 Hz, H-3), 5.72 (d, 1H, J₆,₆₅ = 10.7 Hz, H-4), 5.52 (d, 1H, J₆,₆₅ = 10.7 Hz, H-2), 2.20, 2.07, 1.85 (3 COOCH₃); ¹³C NMR: δ 170.8, 170.7, 170.2 (3 COCH₃), 134.6-124.1 (aromatic carbons), 84.4 (C-1), 75.0, 69.2, 67.3, 62.1 (C-6), 50.5 (C-2), 21.1, 21.1, 20.9 (3 COCH₃). Anal. Calcd for C₃₅H₃₉O₈S: C, 59.19; H, 4.78; N, 2.66. Found: C, 59.30; H, 4.67; N, 2.56%.

**Phenyl 4,6-O-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-galactopyranoside 4.** The acetyl groups of 3 (500 mg, 0.94 mmole) were removed with NaOMe to give the solid residue (380 mg, quantitative); [α]DA⁺⁵⁺ = 34±6° (c 1.7, CHCl₃). The crude de-O-acetylated product (350 mg, 0.86 mmole) was conventionally converted to corresponding benzylidene derivative 4 (378 mg, 88.7%); [α]DA⁺⁵⁺ = 15±3° (c 0.8, CHCl₃); ¹H NMR: δ 7.83-7.71 (m, 4H, Phth), 7.54-7.26 (m, 10H, aromatic protons), 5.67 (d, 1H, J₆,₆₅ = 10.1 Hz, H-1), 5.58 (s, 1H, CH₂Ph), 4.49 (m, 1H, H-3), 4.46 (t, 1H, J₆,₆₅ = 10.4 Hz, H-2), 4.43 (dd, 1H, J₆,₆₅ = 1.3 Hz, J₆,₆₅ = 12.5 Hz, H-6), 4.30 (d, 1H, J₆,₆₅ = 1.8 Hz, H-4), 4.08 (dd, 1H, J₆,₆₅ = 1.5 Hz, J₆,₆₅ = 12.5 Hz, H-6), 7.67 (bs, 1H, H-5), 2.55 (bs, 1H, OH). Anal. Calcd for C₃₅H₃₉O₈S: C, 66.24; H, 4.73; N, 2.86. Found: C, 66.38; H, 4.54; N, 2.90%.

**Phenyl 3-O-acetyl-4,6-O-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-galactopyranoside 5.** Conventional acetylation of 4 gave the corresponding acetate derivative 5 in quantitative yield; [α]DA⁺⁵⁺ = 12° (c 1.7, CHCl₃); ¹H NMR: δ 7.86-7.73 (m, 4H, Phth), 7.54-7.23 (m, 10H, aromatic protons), 5.75 (d, 1H, J₆,₆₅ = 10.7 Hz, H-1), 5.74 (dd, 1H, J₆,₆₅ = 11.0 Hz, J₆,₆₅ = 2.0 Hz, H-3), 5.54 (s, 1H, CH₂Ph), 4.81 (t, 1H, J₆,₆₅ = 10.7 Hz, H-2), 4.49 (m, 1H, H-3), 4.54 (m, 1H, H-4), 4.41 (dd, 1H, J₆,₆₅ = 1.3 Hz, J₆,₆₅ = 12.6 Hz, H-6), 4.07 (dd, 1H, J₆,₆₅ = 1.3 Hz, J₆,₆₅ = 12.4 Hz, H-6), 3.75 (bs, 1H, H-5), 1.87 (s, 3H, COCH₃), 2.55 (bs, 1H, OH). ¹³C NMR: δ 170.4 (COCH₃), 168.3, 166.9 [N(CO₂)₂C₆H₄], 137.6-123.5 (aromatic carbons), 101.0 (CH₂OH), 82.6 (C-1), 73.0, 70.0, 69.9, 69.3 (C-6), 49.5 (C-2), 20.8 (COCH₃). Anal. Calcd for C₃₅H₃₉O₈S: C, 67.56; H, 4.89; N, 2.72. Found: C, 67.49; H, 4.82; N, 2.68%.

**2-(Trimethylsilyl)ethyl 3,4,6-tri-O-acetyl-2-deoxy-2-phthalimido-1-thio-β-D-galactopyranosyl-(1→3)-4-O-acetyl-2,6-di-O-benzylidene-β-D-galactopyranoside 6.** A solution of the donor 3 (250 mg, 0.47 mmole) and the acceptor 2 (203.9 mg, 0.39 mmole) in CH₂Cl₂ containing 4 Å MS (200 mg) was stirred at r.t. for 1 hr under N₂. The reaction mixture was cooled to -20°C and NIS (116.3 mg, 0.52 mmole) and TIOH (5.5 μL, 0.05 mmole) were added and stirred for another 30
min at this temperature. The reaction mixture was diluted with 
CH₂Cl₂ (30 mL), washed repeatedly with water, 5% Na₂SO₄, saturated NaHCO₃, and water. The
organic layer was dried (Na₂SO₄), concentrated, and the syrupy residue was column chromatographed
with toluene-EtOAc (3:1) to give 6 (302 mg, 82%) as a glassy syrup; [α]D²⁵ +2.2° (c 0.9, CHCl₃); ¹H NMR: δ 
7.56-7.48 (m, 4H, Phth), 7.27-6.99 (m, 10H, aromatic protons), 5.71 (dd, 1H, J₁₂=8.3 Hz, H⁻⁴²), 5.49 (d, 1H, 
J₃₂=3.2 Hz, H⁻⁴), 5.32 (d, 1H, J₃₂=3.4 Hz, H⁻⁴⁰), 4.58-4.38 (m, 4H, 2CH₂C₆H₄), 4.22 (d, 1H, J₁₂=7.5 
Hz, H⁻¹), 4.08 (d, 2H, J=6.5 Hz, H⁻⁶), 3.99-3.80 [m, 2H, OCH₂CH₂Si(CH₃)₂], 3.71 (dd, 1H, J₃₂=9.5 
Hz, H⁻³), 3.66-3.56 (m, 2H, H⁻⁶), 3.50-3.32 (m, 4H, H⁻⁵, H⁻⁴²), 2.11, 1.97, 1.95, 1.74 (4 COCH₃), 0.77 [m, 2H, 
OCH₂CH₂Si(CH₃)₂], 0.15 [m, 2H, OCH₂CH₂Si(CH₃)₂]. ¹³C NMR: δ 170.5, 
170.4, 170.2, 169.9 (4 COCH₃), 168.3, 167.5 [N(CO)₂C₆H₄], 138.7-123.4 (aromatic carbons), 103.2 
(C⁻¹), 98.3 (C⁻²), 78.8, 78.4, 74.8, 74.3, 73.6, 73.6, 
72.8, 70.9, 69.6, 69.2, 67.9, 67.8, 66.6, 66.1, 61.2 (C⁻⁶), 
51.7 (C⁻²), 20.8, 20.8, 20.7, 20.6 (4 COCH₃), 18.4 
[OCH₂CH₂Si(CH₃)₂], -1.5 [OCH₂CH₂Si(CH₃)₂]. Anal. Calcd for 
C₄₇H₇₂O₁₆NSi: C, 61.36; H, 6.24; N, 1.52. Found: C, 61.42; H, 6.19; N, 1.49%.

2-(Trimethylsilyl)ethyl 6-O-tert-butyldiphenyl-
-silyl-3,4-O-isopropylidene-2-deoxy-2-phthalimido-
β-D-galactopyranosyl-(1→3)-4-O-acetyl-2,6-di-O-
benzyl-β-D-galactopyranoside 8. Compound 7 was 
acetoned conventionally using DMP and p-TsOH in 
DMF to give 8 as amorphous solid in 85.8% yield; 
[α]D²⁵ +14.6° (c 1.7, CHCl₃); ¹H NMR: δ 7.65-7.53 
(m, 4H, Phth), 7.33-7.14 (m, 20H, aromatic protons), 
5.28 (d, 1H, J₁₂=8.6 Hz, H⁻¹), 5.23 (d, 1H, J₃₂=3.5 
Hz, H⁻⁴), 4.74 (dd, 1d, J₃₂=9.2 Hz, J₁₂=5.0 Hz, H⁻²), 
4.53, 4.14 (2 d, 2H, J=10.9 Hz, CH₂CH₂), 4.38, 4.32 
(2 d, 2H, J=11.8 Hz, CH₂CH₂), 4.24 (d, 1H, J₁₂=2.2 
Hz, H⁻⁴), 4.19 (d, 1H, J₁₂=7.2 Hz, H⁻¹), 3.86 (m, 2H, 
OCH₂CH₂SiMe₂), 3.74 (dd, 1H, J₁₂=3.6 Hz, J₃₂=9.5 
Hz, H⁻³), 3.50 (m, 1H, H⁻⁵), 1.79 (s, 3H, COCH₃), 1.53, 1.22 [2s, 6H, (CH₂)₃], 0.97 [s, 9H, 
Ph₂Si(CH₂)₃], 0.81 [s, 2H, OCH₂CH₂SiMe₃], -1.5 [s, 
9H, OCH₂CH₂Si(CH₃)₂]. ¹³C NMR: δ 170.0 (COCH₃), 
138.8-127.3 (aromatic carbons), 110.3 [C(CH₃)], 103.2 
(C⁻¹), 97.5 (C⁻²), 79.3, 76.1, 74.3, 73.7, 73.6, 
73.6, 73.5, 73.1, 72.9, 69.8, 69.3 (C⁻⁶), 67.7, 62.4 
(C⁻⁶), 55.8 (C⁻²), 26.8 [Ph₂Si(CH₂)₃], 28.1, 26.5 
[CH₂CH₃], 20.6 (COCH₃), 19.3 [Ph₂Si(CH₂)₃], 18.5 
[OCH₂CH₂Si(CH₃)₂], -1.5 [OCH₂CH₂Si(CH₃)₂]. Anal. Calcd 
for C₆₀H₁₁₀O₂₃Si₃N: C, 67.20; H, 6.86; N, 1.31. 
Found: C, 67.09; H, 6.68; N, 1.34%.

2-(Trimethylsilyl)ethyl 6-O-acetyl-2,3,5-tri-O-
benzoyl-β-D-galactofuranosyl-(1→3)-6-O-tert-butyldi-
phehylsilyl-2-deoxy-2-phthalimido-β-D-galactopy-
ranosyl-(1→3)-4-O-acetyl-2,6-di-O-benzyl-β-D-galac-
topyranoside 10. The donor 9 (130 mg, 
0.19 mmole) was glycosylated with the acceptor 7 
(152 mg, 0.15 mmole) to afford the trisaccharide 
10 (176 mg, 77.2%), [α]D²⁵ +15° (c 0.5, CHCl₃); 
¹H NMR: δ 7.93-7.05 (m, 35H, aromatic protons), 
5.65-5.56 (m, 1H, H⁻⁻⁴), 5.58 (d, 1H, J₁₂=1.9 Hz, 
H⁻⁻⁴), 5.56 (bs, 1H, H⁻²), 5.34 (d, 1H, J₃₂=3.5 Hz, 
H⁻⁻⁴), 5.28 (d, 1H, J₁₂=8.3 Hz, H⁻¹), 5.15 (bs, 1H, 
H⁻¹), 5.09 (d, 1H, J=2.1 Hz, H⁻⁴), 4.65-4.60 
(m, 2H, H⁻⁶), 4.16 (d, 1H, J₁₂=7.7 Hz, H⁻¹), 
4.12 (d, 1H, J₃₂=2.3 Hz, H⁻⁴), 4.05 (dd, 1H, 
H⁻⁶).
2-(Trimethylsilyl)ethyl 2,3,5,6-tetra-O-acetyl-\(\beta\)-D-galactofuranosyl-(1→3)-2-acetamido-4-O-acetyl-6-O-tert-butylphenylsilyl-2-deoxy-\(\beta\)-D-galactopyranoside 11. The compound 10 (120 mg, 0.077 mmole) was converted to corresponding acamido derivative 11 (96.9 mg, 95%) with ethylenediamine,\(\textsuperscript{13}\) \([\alpha]_D^{25}+33.8^\circ\) (c 1.0, CHCl\(_3\)). \(^1\)H NMR: \(\delta 7.50-7.10\) (m, 20H, aromatic protons), 5.33 (d, 1H, J\(_{3,4}=3.0\) Hz, H\(_5\)), 4.47 (d, 1H, J\(_{3,4}=7.9\) Hz, H\(_6\)), 4.13 (d, 1H, J\(_{3,4}=7.7\) Hz, J\(_{3,4}=1.9\) Hz, H\(_5\)), 3.86 (dd, 1H, J\(_{1,2}=7.3\) Hz, J\(_{1,2}=11.0\) Hz, H\(_2\)), 3.64 (dd, 1H, J\(_{1,2}=9.7\) Hz, J\(_{1,2}=3.6\) Hz, H\(_3\)), 3.14 (m, 1H, H\(_5\)), 1.94, 1.91, 1.85, 1.83 (7 s, 21H, 7 COCH\(_3\)), 0.88 [s, 9H, PhSi(CH\(_3\))] , 0.84 [m, 2H, OCH\(_2\)CH\(_2\)Si(CH\(_3\))] , -0.15 [s, 9H, OCH\(_2\)CH\(_2\)Si(CH\(_3\))] ; \(^1\)C NMR: \(\delta 171.2\) (2COCH\(_3\)), 170.5, 170.2, 170.0, 169.6, 169.9, 139.1-127.5 (aromatic carbons), 107.3 (C-1\(_1\)), 103.2 (C-1\(_2\)), 98.9 (C-1\(_3\)), 81.8, 80.4, 79.6, 76.5, 74.8, 73.6, 72.8, 69.5, 69.4, 69.1, 67.7, 63.0, 61.1, 55.3 (C-2\(_3\)), 26.7 [PhSi(CH\(_3\))] , 23.2 (NCH\(_3\)) , 20.8, 20.8, 20.7, 20.7 (5 COCH\(_3\)) , 19.0 [PhSi(CH\(_3\))] , 18.5 [OCH\(_2\)CH\(_2\)Si(CH\(_3\))] , -1.5 [OCH\(_2\)CH\(_2\)Si(CH\(_3\))] . Analyzed for C\(_{65}H_{102}O_{32}Si_N: C: 66.12; H: 6.81; N: 1.06.

Found: C: 66.15; H: 6.74; N: 1.09%.

2-(Trimethylsilyl)ethyl 3-O-acetyl-4,6-O-benzylidene-2-deoxy-2-phthalimido-\(\beta\)-D-galactopyranosyl-(1→3)-4-O-acetyl-2,6-di-O-benzyl-\(\beta\)-D-galactopyranoside 12. The donor 5 (253.8 mg, 0.48 mmole) was allowed to condense with the acceptor 2 (200 mg, 0.40 mmole) in the same manner as in case of 6 to give the disaccharide 12 (323.6 mg, 88%) as an amorphous solid. \([\alpha]_D^{25}+33.8^\circ\) (c 1.0, CHCl\(_3\)). \(^1\)H NMR: \(\delta 7.60-7.46\) (m, 4H, Phth), 7.34-6.97 (m, 15H, aromatic protons), 5.58 (dd, 1H, J\(_{2,3}=11.4\) Hz, J\(_{2,3}=3.6\) Hz, H\(_3\)), 5.49 (d, 1H, J\(_{2,3}=8.4\) Hz, H\(_1\)), 5.44 (s, 1H, CHC\(_6\)H\(_4\) ), 5.30 (d, 1H, J\(_{2,3}=3.6\) Hz, H\(_4\)), 4.68 (dd, 1H, J\(_{2,3}=8.4\) Hz, J\(_{2,3}=11.5\) Hz, H\(_2\)), 4.68, 4.29 (2d, 2H, J=11.5 Hz, CH\(_2\)C\(_6\)H\(_5\)), 4.44 (s, 2H, CH\(_3\)C\(_6\)H\(_5\)), 4.35 (d, 1H, J\(_{2,3}=3.6\) Hz, H\(_4\)), 4.21 (d, 1H, J\(_{2,3}=7.7\) Hz, H\(_1\)), 3.93-3.81 [m, 2H, OCH\(_2\)CH\(_2\)Si(CH\(_3\))] , 3.70 (dd, 1H, J\(_{2,3}=9.6\) Hz, J\(_{2,3}=3.7\) Hz, H\(_3\)), 3.62-3.52 (m, 3H, H-6\(_1\), H-6\(_2\), H-6\(_3\)), 3.47-3.33 (m, 4H, H-2\(_1\), H-2\(_2\), H-2\(_3\), H-2\(_4\)), 1.98, 1.82 (2 s, 6H, COCH\(_3\)), 0.80 [m, 2H, OCH\(_2\)CH\(_2\)Si(CH\(_3\))] , -0.15 [m, 9H, OCH\(_2\)CH\(_2\)Si(CH\(_3\))] . Analyzed for C\(_{76}H_{114}O_{36}S_{14}N: C: 64.99; H: 6.22; N: 1.52.

Found: C: 64.85; H: 6.10; N: 1.46%.
Phenyl 6-O-acetyl-2, 3, 5-tri-O-benzoyl-β-D-galactofuranosyl-(1→3)-4,6-O-benzylidene-2-deoxy-2-phthalimido-β-D-galactopyranoside 17. The donor 16 (384 mg, 0.66 mmole) was allowed to condense with the acceptor 4 (250 mg, 0.51 mmole) in the same manner as in case of 6 to give the disaccharide 17 (128 mg, 25%) as a solid residue; [α]D25 +26.6° (c 3.2, CHCl3); 1H NMR: δ 7.99-7.09 (m, 29H, aromatic protons), 5.72 (m, 1H, H-5α), 5.62 (bs, 1H, H-2β), 5.61 (d, 1H, J1,2=10.2 Hz, H-1β), 5.48 (d, 1H, J=5.7 Hz, H-3β), 5.25 (s, 1H, CHPh), 5.06 (bs, 1H, H-1′β), 4.91 (t, 1H, J=10.5 Hz, H-4β), 4.77 (m, 2H, H-6β), 4.00 (d, 1H, J=12.5 Hz, H-5β), 3.68 (bs, 1H, H-2α), 1.85 (s, 3H, COOCH3); 13C NMR: δ 170.9 (COCH3), 165.9, 165.9, 165.3 (3 COCH2), 138.0-126.6 (aromatic carbons), 107.8 (C-I′β), 101.1 (CHPh), 83.9 (C-β′), 82.9, 81.9, 76.5, 75.8, 70.7, 70.4, 69.8, 50.8 (C-2β′), 20.9 (COCH3). Anal. Calcd for C36H33O17SN: C, 71.02; H, 6.70%. Found: C, 70.9; H, 6.70%.

4-Methoxyphenyl 3,4,6-tri-O-acetyl-2-deoxy-2-phthalimido-β-D-galactopyranoside 21. Compound 20 (3.5 g, 7.50 mmole) was de-acetonated with 80% acetic acid to give pure 21 (2.96 g, 92%); [α]D25 +9.3° (c 2.1, CHCl3); 1H NMR: δ 7.36-7.21 (m, 10H, aromatic protons), 7.02, 6.78 (2 d, 4H, J=12.5 Hz, CH3OC6H4), 5.02, 4.64 (2d, 2H, J=11.3 Hz, CH2Ph), 4.82 (d, 1H, J=7.6 Hz, H-1), 4.52 (s, 2H, CH2Ph), 3.95 (bs, 1H, H-4), 3.77-3.70 (m, 3H, H-2, H-6), 3.73 (s, 3H, COOCH3), 3.67-3.60 (m, 2H, H-3, H-5), 2.86, 2.80 (2s, 2H, 3-OH, 4-OH); 13C NMR: δ 155.7, 151.8, 138.7-115.0 (aromatic carbons), 103.3 (C-1′), 79.4, 75.3, 74.1, 74.1, 73.6, 69.8, 69.3 (C-6), 56.1 (COOCH3). Anal. Calcd for C37H33O16SN: C, 69.51; H, 6.48. Found: C, 69.43; H, 6.42%.

Phenyl 6-O-benzyl-3,4,6-tri-O-isopropylidene-β-D-galactopyranoside 23. The donor 22 (445 mg, 0.77 mmole) was glycosylated with the acceptor 21 (200 mg, 0.5 mmole) to give 23 (292 mg, 76%); [α]D25 +15.4° (c 0.6, CHCl3); 1H NMR: δ 7.63-7.54 (m, 4H, Phth), 7.32-6.95 (m, 10H, aromatic protons), 6.86, 6.69 (2d, 4H, J=9 Hz, CH3OC6H4), 5.79 (dd, 1H, J3=3.3 Hz, J2=11.4 Hz, H-3′β), 5.61 (d, 1H, J1,2=8.5 Hz, H-1′β), 5.49 (d, 1H, J3=3.2 Hz, H-4′β), 4.73 (d, 1H, J1,2=7.4 Hz, H-1′β), 4.67 (dd, 1H, J1,2=8.6 Hz, J2=11.6 Hz, H-2′β), 4.64, 4.34 (2d, 2H, J=11.4 Hz, CH2Ph), 4.59, 4.53 (2d, 2H, J=11.9 Hz, CH2Ph), 4.11 (bs, 1H, H-4′β), 4.19-4.12 (m, 2H, H-6′β), 3.85-3.63 (m, 4H, H-6′β, H-5′α, H-5′β), 3.71 (s, 3H, CH3OC6H4), 2.24, 2.01, 1.84 (3s, 9H, 3 COCH3); 13C NMR: δ 170.8, 170.7, 170.1 (3 COCH3), 155.6, 151.7, 138.6-115.0 (aromatic carbons), 103.0 (C-1′β), 99.2 (C-1′β), 83.6, 77.6, 75.0, 74.1, 74.0, 73.6, 71.7, 69.7, 68.3, 68.3, 67.1 (C-6′β), 62.1 (C-6′β), 56.0 (COOCH3), 51.8 (C-2′β), 21.1, 21.0, 20.9 (COCH3). DEPT-135 NMR: δ 134.0-114.5 (aromatic carbons), 102.7 (C-1′β), 99.0 (C-1′β), 83.3, 77.3 (2 CH), 74.7, 73.8 (2 CH), 73.4, 71.4 (2 CH), 69.4 (C-6′β), 68.0, 68.0, 66.8 (3 CH), 61.8 (C-6′β), 55.7 (COOCH3), 51.5 (C-2′β), 20.9, 20.7, 20.6 (3 COCH3). Anal. Calcd for C42H40O13SN: C, 63.86; H, 5.58; N, 1.58. Found: C, 63.64; H, 5.47; N, 1.54%.
Ethyl 2,3-di-O-benzyl-4,6-O-benzylidene-1-thio-
β-D-glucopyranoside 24. Ethyl 4,6-O-benzylidene-1-thio-
β-D-glucopyranoside (1 g, 2.1 mmole) was
benzylated conventionally to afford pure 24 (1.85 g,
95%); \( \alpha \). 25°-21° (c 1.4, CHCl3); \( \delta \) H NMR: δ 7.47-
7.26 (m, 15H, aromatic protons), 5.57 (s, 1H, CHPh),
4.56 (d, 1H, J=9.8 Hz, H-1), 3.81 (m, 2H, H-6), 3.46
(m, 1H, H-5), 2.75 (m, 2H, SCH2CH3), 1.32 (t, 3H,
J=7.3 Hz, SCH2CH3); \( \delta \) C NMR: δ 138.4-126.4
( aromatic carbons), 101.7 (CHPh), 86.3 (C-1), 83.2,
82.0, 81.7, 76.4, 75.6, 70.7, 69.1 (C-1), 25.6 (SCH2CH3),
15.5 (SCH2CH3). Anal. Calcd for C29H32O8S5:
C 74.0, 73.9, 73.7, 71.9, 70.2, 70.1, 69.3, 68.2, 67.2 (C-6\(^{d}\)),
63.1 (C-6\(^{b}\)), 61.7, 57.2 (COOCH3), 52.1 (C-2\(^{b}\)),
21.1, 21.1, 20.9 (COCH3). DEPT-135 NMR spectra showed
16 CH and CH3 signals, and 7CH2 signals in between
50-105. Anal. Calcd for C29H32O8N: C, 67.62; H,
5.75; N, 1.06. Found: C, 67.57; H, 5.65; N, 1.02%.

Acknowledgement

Financial support from the Department of Science and Technology, New Delhi, India (Project No.
SP/S1/G14/95) is thankfully acknowledged.

References

2 Dmitriev B A, L'vov V L & Kochetkov N K, Carbohydr Res,
56, 1977, 207.
6 Veeneman G H, van Leeuwen S H & van Boom J H,
8 Pozsgay V, Coxon B & Yeh H, Bioorg Med Chem, 1, 1993,
237.
11 Sarkar S K, Choudhury A K, Mukhopadhyay B & Roy N, J
13 Kanie O, Crawley S C, Palcic M M & Hindsauge O,
14 Evans M E, In Methods in Carbohydrate Chemistry; Vol. 8,
edited by R L Whistler and J N BeMiller, (Academic Press,
16 Wengart R & Schmidt R R, Tetrahedron Lett, 41, 2000,
8753.
18 Brancazio J S, In Methods in Carbohydrate Chemistry;
edited by R L Whistler and J N BeMiller, (Academic Press,
20 Bochkov A F & Jain A Ch, Izv Akad Nauk USSR, Ser Khim,
1968, 179.