Chapter 2

Synthesis of Oligosaccharide Fragments
Corresponding to the O-Antigen of Shigella boydii Strains
2.1. Introduction

Diarrhoeal disease is a common cause of death in the tropical countries and it is the second mostly causing infant deaths worldwide. *Shigella* is one of the well-studied human pathogens that cause diarrhoeal disease and dysentery (e.g., shigellosis). Among several types of *Shigella* species, *Shigella dysenteriae* is the most virulent pathogen causing devastating health problems in developing countries. In the 1950's *Shigella* was accepted as a genus and subgrouped into four species: *S. dysenteriae*, *S. fexneri*, *S. boydii*, and *S. sonnei*. Sometimes, these species are also termed as *Shigella* subgroups A, B, C, and D. Based on the O-antigens, the *Shigella* species are divided into multiple serotypes. In general, O-antigens of *Shigella* species are acidic in nature because of the presence of acidic constituents (e.g. uronic acid, pseudaminic acid etc. or lactic acid, pyruvic acid etc.) in their structures.

*S. boydii* inhabits the intestine and rectum of humans and other primates. It can survive in faeces and soil and/or food, water contaminated with faecal matter. For example, in Guadalajara, Mexico, *Salmonella* and *Shigella* species were found in freshly squeezed orange juice, oranges, and wiping cloths found in public markets and street booths. *S. boydii* was specifically found in the oranges and wiping cloths. This may indicate poor sanitary methods of food processing which led to raw sewage exposure.

*Shigella* bacteria are thought to be derived from different strains of *Escherichia coli*. *S. boydii* is the most genetically divergent and some serotypes seem to be more closely related to other species. *S. boydii* type 13, for example, shares sequence similarities with *Vibrio cholerae* for the genes encoding the O-antigen, the polysaccharide part of the lipopolysaccharide (LPS), and therefore these may be more closely related.

*Shigella*'s structural characteristics follow that of Gram-negative bacteria. Most research would agree that *Shigella* is non-motile but some evidence suggests that they do in fact have flagella, although motility is not necessary for infection of intestine. The flagella present on the one pole of the cell and about 10 microns in length and 12-14 nm in diameter. The genes coding for the flagella in *S. dysenteriae*, *S. flexneri*, *S. boydii* and *S. sonnei* were found to be different and confirm the genetic diversity among the species. *S. boydii*, when found in the intestine, go through anaerobic metabolic pathways but can survive outside the body due to its ability to utilize aerobic pathways. More specifically, *S. boydii*, typically does not have oxidase enzymes but rather catalase enzymes (catalyzes the reduction of H$_2$O$_2$ to H$_2$O). The bacteria use a mixed acid fermentation pathway, which has been reflected in the positive methyl red test. *S. Boydii* does not produce H$_2$S and does not hydrolyze urea as well as they are not grown in KCN broth.
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*Shigella* bacteria cause diarrhea and shigellosis (bacillary dysentery) through oral-faecal transmission. In favorable conditions, *Shigella* can infect a host in 12-48 hours. Once ingested, the *Shigella* makes its way through the gastrointestinal tract until it reaches the epithelial cells of the intestinal mucosa, there it infects, causes irritation, inflammation and necrosis (swelling and breaking of infected cells, which spreads infection). General symptoms of shegellosis include stomach cramps, high fever, mucus in feces, and bloody diarrhea due to the ulceration of the intestinal lining and rectum. In most cases these symptoms are mild and can be resolved in about a week but some cases become severe enough to be fatal without proper medical care. The elderly, very young and those weakened by disease are much more sensitive to the bacteria. In very young children very high fever may also be accompanied with seizures. Usually *Shigella* bacteria are found in areas of poor sanitation. Food washed with contaminated water or not cleaned properly may also be considered as potential source of *Shigella*. In 1998, an outbreak of Shigellosis occurred in Chicago due to the infection of *Shigella boydii* type 18 found on the cilantro and parsley in bean salad.

Development of effective therapeutics to control the infections of drug-resistant bacterial strains is the thrust area in medicinal chemistry. Like other bacterial infections, emergence of the drug resistant *Shigella* infections requires development of the newer therapeutics than the earlier used anti-shigellosis agents.\(^5\) Because of the high antigenic nature of the *O*-antigens, antibodies against the *O*-specific polysaccharide of a particular *Shigella* strain have the potential to control *Shigella* infections.\(^6\) A number of reports have been cited earlier to develop glycoconjugate based therapy to control *Shigella* infections.\(^7\) In order to develop a glycoconjugate based therapeutic agent from the repeating unit of the *O*-antigen of *Shigella boydii* strains, it is essential to perform several immunochemical studies with the glycoconjugates derived from these oligosaccharide repeating units. For this purpose large quantities of these oligosaccharides are required, which cannot be accessible from a natural source. Therefore, chemical synthesis is the best option to get access to a large quantity of oligosaccharides and its close analogs. As a first step towards the preparation of glycoconjugates, the oligosaccharide structures of the cell-wall of the following strains have been selected for their chemical synthesis using a number of recently developed synthetic methodologies:

1. A tri- and a pentasaccharide corresponding to the *O*-antigen of *Shigella boydii* type 6.
2. A tetrasaccharide repeating unit of the *O*-antigen of *Shigella boydii* type 9.
3. A common tetrasaccharide repeating unit of the *O*-antigen of *Shigella boydii* type 8 and enteroinvasive *Escherichia coli* O143.
2.2. *Synthesis of Tri- and Pentasaccharide Fragments Corresponding to the O-Antigen of Shigella boydii Type 6*
2.2.1. Introduction

*Shigella* is a well-documented human pathogen responsible for the diarrheal disease and bacillary dysentery (shigellosis). Recently, Senchenkova *et al.* reported a revised structure of the pentasaccharide repeating unit of the *O*-antigen of *S. boydii* type 6 (Figure 1). Long back, Dmitriev *et al.* reported the structure of this *O*-antigen, which was partially incorrect. The repeating unit of the *O*-antigen contains D-galactosamine (D-GalpNAc), D-mannose (D-Manp), D-galactose (D-Galp) and D-glucuronic acid (D-GlcPA). A convenient synthetic strategy for the synthesis of a trisaccharide and a pentasaccharide as their 2-(p-methoxyphenoxy) ethyl glycoside (1 and 2) corresponding to the *O*-antigen of *S. boydii* type 6 is presented using sequential glycosylation strategy (Figure 2). The p-methoxyphenyl (PMP) group can be easily removed under an oxidative condition to give trisaccharide and pentasaccharide derivatives linked to an ethylene glycol linker useful for the preparation of glycoconjugate derivatives.

\[ \rightarrow^{3}\alpha-D-Galp-(1\rightarrow6)\alpha-D-Manp-(1\rightarrow2)\alpha-D-Manp-(1\rightarrow3)\beta-D-GalpNAc-(1\rightarrow4) \]

\[ \uparrow \]

\[ \beta-D-GlpPA \]

**Figure 1:** Structure of the pentasaccharide repeating unit corresponding to the *O*-antigen of *Shigella boydii* type 6.

![Structure of the pentasaccharide repeating unit corresponding to the O-antigen of Shigella boydii type 6.](image)

**Figure 2:** Structure of the synthesized tri- and pentasaccharides corresponding to the *O*-antigen of *Shigella boydii* type 6.

![Structure of the synthesized tri- and pentasaccharides corresponding to the O-antigen of Shigella boydii type 6.](image)
Scheme 1: Retrosynthetic strategy for the synthesis of compound 1 and 2.
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2.2.2. Results and Discussion

The retrosynthetic strategy for the synthesis the trisaccharide (1) and pentasaccharide (2) as their 2-(p-methoxyphenoxy) ethyl glycoside led to a number of differentially protected monosaccharide intermediates, which were prepared from the commercially available monosaccharides using a number of protecting group manipulations (Figure 2). Stereoselective glycosylations of the suitably functionalized monosaccharide units and functional group transformations yielded desired trisaccharide (1) and pentasaccharide (2) as their 2-(p-methoxyphenoxy) ethyl glycoside in excellent yield (Scheme 1).

2.2.2.1. Preparation of 2-(p-methoxyphenoxy) ethyl 2-azido-4,6-O-benzylidene-2-deoxy-β-D-galactopyranoside (8)

3,4,6-Tri-O-acetyl-D-galactal (4) was prepared from D-galactose (3) in 78% yield using a two step reaction sequence involving the formation of acetobromogalactose using 30% HBr-AcOH and reduction using zinc in AcOH. Compound 4 was subjected to a sequence of reactions involving azido-nitration, hydrolysis of anomeric nitrite group, and treatment with CCl₃CN in the presence of potassium carbonate to furnish compound 5. Compound 5 was stereoselectively glycosylated with 2-(p-methoxyphenoxy) ethanol (6) in the presence of TMSOTf in CH₃CN to give compound 7 in 78% over all yield. Exclusive formation of 1,2-trans glycoside was achieved by exploiting the nitrile effect of the solvent. Saponification of compound 7 followed by benzylidene acetal formation furnished compound 8 in 87% yield (Scheme 2).

Scheme 2: Reagents: (a) (i) Ac₂O, 30% HBr-AcOH, r t, 4 h; (ii) NaOAc-3H₂O, Zn dust, AcOH-H₂O, −20 °C, 3 h, 78%; (b) (i) CAN, NaN₃, CH₃CN, −20 °C, 1 h; (ii) NaNO₂, dioxane-H₂O (10:1), 80 °C, 12 h; (iii) K₂CO₃, CCl₃CN, CH₂Cl₂, r t, 24 h; (c) TMSOTf, CH₃CN, −20 °C, 1 h, 78%; (d) (i) 0.1 N CH₃ONa, CH₃OH, r t, 3 h; (ii) PhCH(OCH₃)₂, p-TsOH, CH₃CN, r t, 12 h, 87%.
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2.2.2. Preparation of ethyl 2-O-acetyl-3-O-benzyl-4,6-O-benzylidene-1-thio-\(\alpha\)-D-mannopyranoside (11)\(^{20}\) and ethyl 2,3,4-tri-O-acetyl-6-O-(p-methoxybenzyl)-1-thio-\(\alpha\)-D-mannopyranoside (14)

Ethyl 2,3,4,6-tetra-O-acetyl-1-thio-\(\alpha\)-D-mannopyranoside (10) was prepared from D-mannose (9) by successive treatment with acetic anhydride and ethanethiol in the presence of boron trifluoride diethyl etherate\(^{21}\) in 88% yield. Removal of acetyl groups from compound 10 using sodium methoxide\(^{18}\) followed by 4,6-O-benzylidene acetal formation using benzaldehyde dimethyl acetal\(^{19}\) in the presence of p-toluenesulfonic acid gave ethyl 4,6-O-benzylidene-1-thio-\(\beta\)-D-mannopyranoside (11) in 78% yield. Selective 3-O-benzylation of compound 11 via stannyldiene acetal formation\(^{22}\) followed by acetylation using acetic anhydride and pyridine furnished ethyl 2-O-acetyl-3-O-benzyl-4,6-O-benzylidene-1-thio-\(\alpha\)-D-mannopyranoside (12) in 75% yield. In another experiment, benzylidene acetal formation using anisaldehyde dimethyl acetal\(^{19}\) in the presence of p-toluenesulfonic acid and followed by acetylation using acetic anhydride and pyridine gave ethyl 2,3-di-O-acetyl-4,6-O-(p-methoxy)-benzylidene-1-thio-\(\alpha\)-D-mannopyranoside (13) in 79% yield. Regioselective ring opening of the p-methoxybenzylidene acetal in compound 13 using a combination of sodium cyanoborohydride and trifluoroacetic acid\(^{23}\) followed by acetylation using acetic anhydride and pyridine\(^{24}\) gave ethyl 2,3,4-tri-O-acetyl-6-O-(p-methoxybenzyl)-1-thio-\(\alpha\)-D-mannopyranoside (14) in 73% yield (Scheme 3).

![Scheme 3: Reagents:](image)

**Scheme 3:** Reagents: (a) (i) \(\text{Ac}_2\text{O}, \text{BF}_3\cdot\text{OEt}_2\), r t, 1 h; (ii) \(\text{EtSH}, \text{CH}_2\text{Cl}_2\), 0 °C- r t, 5 h, 88%; (b) (i) \(\text{CH}_3\text{ONa}, \text{MeOH}, \) r t, 4 h; (ii) \(\text{PhCH(OOMe)}_2\), p-TsOH, CH\(_3\)CN, r t, 10 h, 78%; (c) (i) \(\text{Bu}_2\text{SnO}, \) toluene, 110 °C, 4 h, then benzyl bromide, TBAB, 80 °C, 16 h; (ii) \(\text{Ac}_2\text{O}, \) pyridine, r t, 2 h, overall 75%; (d) (i) p-anisaldehyde dimethyl acetal, p-TsOH, CH\(_3\)CN, r t, 12 h; (ii) \(\text{Ac}_2\text{O}, \) pyridine, r t, 2 h, overall yield 79%; (e) (i) \(\text{NaBH}_3\text{CN}, \) TFA, DMF, r t, 10 h; (ii) \(\text{Ac}_2\text{O}, \) pyridine, r t, 1 h, over all 73%.
2.2.2.3. Preparation of ethyl 4-O-acetyl-2,3,6-tri-O-benzylidene-1-thio-β-D-galactopyranoside (17)

Ethyl 2,3,4,6-tetra-O-acetyl-1-thio-β-D-galactopyranoside (15) was prepared from D-galactose (3) by successive treatment with acetic anhydride and ethanethiol in the presence of boron trifluoride diethyl etherate in 85% yield. Compound 15 was subjected to set reactions involving saponification using sodium methoxide, benzylidene acetal formation using benzaldehyde dimethyl acetal in the presence of p-toluenesulfonic acid, benzylolation using benzyl bromide and sodium hydroxide to furnish ethyl 2,3-di-O-benzyl-4,6-O-benzylidene-1-thio-β-D-galactopyranoside (16) in 88% yield. Regioselective ring opening of the benzylidene acetal of compound 16 using a combination of triethylsilane and molecular iodine followed by acetylation using pyridine and acetic anhydride gave ethyl 4-O-acetyl-2,3,6-tri-O-benzyl-1-thio-β-D-galactopyranoside (17) in 82% yield (Scheme 5).

Scheme 5: Reagents: (a) (i) Ac₂O, BF₃-OEt₂, r.t., 1 h; (ii) EtSH, BF₃-OEt₂, CH₂Cl₂, 5 °C, 5 h, 85%; (b) (i) CH₃ONa, MeOH, r.t., 4 h, quant.; (ii) PhCH(OMe)₂, p-TsOH, CH₃CN, r.t., 10 h, 78%; (iii) benzyl bromide, NaOH, TBAB, THF, r.t., 6 h, 88%; (c) Et₃SiH, I₂, CH₂Cl₂, 0-5 °C, 15 min; (d) Ac₂O, pyridine, r.t., 1 h, over all 82%.

2.2.2.4. Preparation of 2,3,4,6-tetra-O-benzoyl-α-D-glucopyranosyl trichloroacetimidate (21)

1,2,3,4,6-Penta-O-benzoyl-α-D-glucopyranose (19) was prepared from D-glucose (18) on treatment with benzoyl chloride in the presence of pyridine in 95% yield. Compound 19 was treated with benzylamine to give the hemiacetal derivative 20 which on treatment with trichloroacetronitrile in the presence of DBU furnished 2,3,4,6-tetra-O-benzoyl-α-D-glucopyranosyl trichloroacetimidate (21) in 91% yield (Scheme 6).
2.2.2.5. Synthesis of 2-(p-methoxyphenoxy)ethyl (α-D-mannopyranosyl)-(1→2)-(α-D-mannopyranosyl)-(1→3)-2-acetamido-2-deoxy-β-D-galactopyranoside (1) and 2-(p-methoxyphenoxy)ethyl (sodium β-D-glucopyranosyluronate)-(1→4)-(α-D-galactopyranosyl)-(1→6)-(α-D-mannopyranosyl)-(1→2)-(α-D-mannopyranosyl)-(1→3)-2-acetamido-2-deoxy-β-D-galactopyranoside (2)

Stereoselective glycosylation of compound 8 with thioglycoside derivative 12 in the presence of N-iodosuccinimide (NIS) and trifluoromethanesulfonic acid (TfOH) combination furnished disaccharide derivative 22 in 75% yield, which was deacetylated to give disaccharide acceptor 23 in 97% yield. Presence of an O-acetyl group at C-2 position of the compound 12 favored the formation of 1,2-trans-glycoside (22), which was confirmed from its NMR spectra [signals at $\delta$ 5.61 (s, PhCH), 5.57 (s, PhCH), 5.02 (br s, H-1B), 4.43 (d, $J = 8.0$ Hz, H-1A) in the $^1$H NMR and $\delta$ 102.8 (PhCH), 102.1 (COCH$_3$), 101.3 (C-1A), 95.5 (C-1B) in the $^{13}$C NMR spectra]. Iodonium ion mediated stereoselective coupling of compound 23 with the thioglycoside donor 14 in the presence of NIS-TfOH furnished trisaccharide derivative 24 in 72% yield. Formation of trisaccharide 24 was influenced by the presence of an O-acetyl group in the C-2 position of compound 14, which directs the formation of α-mannosidic linkage through neighboring group participation. Presence of the signals in the NMR spectra confirmed the formation compound 24 [signals at $\delta$ 5.68 (s, PhCH), 5.39 (s, PhCH), 5.17 (br s, H-1C), 4.95 (br s, H-1B), 4.27 (d, $J = 8.0$ Hz, H-1A) in the $^1$H NMR and $\delta$ 102.7 (PhCH), 102.0 (PhCH), 101.0 (C-1A), 100.6 (C-1B), 96.5 (C-1C) in the $^{13}$C NMR spectra]. Removal of functional groups from compound 25 involving hydrogenolysis followed by N-acetylation and O-deacetylation furnished trisaccharide derivative 1 as its 2-(p-methoxyphenoxy) ethyl glycoside in 66% yield, which was supported by its spectral analysis [Signals at $\delta$ 5.16 (br s, H-1C), 4.85 (br s, H-1B), 4.43 (d, $J = 8.4$ Hz, H-1A) in the $^1$H NMR and $\delta$ 103.2 (C-1B), 102.1 (C-1A), 94.9 (C-1C) in the $^{13}$C NMR spectra] (Scheme 7).
Scheme 7: Reagents: (a) N-iodosuccinimide (NIS), TfOH, CH₂Cl₂, MS 4Å, −40 °C, 1 h, 75% for 22 and 72% for 24; (b) 0.1 M CH₃ONa, CH₃OH, r t, 1 h, 97%; (c) benzyl bromide, NaOH, DMF, TBAB, r t, 5 h, 76%; (d) DDQ, CH₂Cl₂, H₂O, r t, 2 h, 72%; (e) H₂, 20% Pd(OH)₂-C, CH₃OH, r t, 24 h; (f) (i) Ac₂O, pyridine, r t, 2 h; (ii) 0.1 M CH₃ONa, CH₃OH, r t, 1 h, over all 66%.

In a separate experiment, O-acetoxy groups of compound 24 were converted to O-benzyl ethers under a one-pot deacetylation-benzylation⁶ to give compound 25 in 76% yield. Oxidative removal³⁴ of p-methoxybenzyl group from compound 25 using DDQ furnished trisaccharide acceptor 26 in 72% yield. Iodonium ion mediated 1,2-cis glycosylation of compound 26 with thioglycoside derivative 17 in the presence of NIS-TfOH³² furnished tetrasaccharide derivative 27 in 76% yield, which was deacetylated to give tetrasaccharide acceptor 28. Due to the presence of O-benzyl group a the C-2 position of compound 17, desired α-linked glycosylation product 27 was obtained as a major product. Formation of compound 27 was confirmed from its NMR spectral analysis [signals at δ 5.52 (s, PhCH), 5.42 (s, PhCH), 5.11 (br s, H-1c), 4.95 (br s, H-1a), 4.32 (br s, H-1d), 4.26 (d, J = 7.9 Hz, H-1a) in the ¹H NMR and δ 170.3 (COCH₃), 154.2-114.7 (Ar-C), 104.4 (C-1A), 102.4 (C-1D), 101.6 (PhCH), 101.0 (PhCH), 100.3 (C-1B), 96.1 (C-1C) in the ¹³C NMR spectra]. Unambiguous assignment of the stereochemistry of the glycosyl linkages in compound 27 were achieved using gated ¹H coupled ¹³C NMR, 2D HMBC and HSQC NMR spectra. Appearance of anomeric carbon atoms with J_C-1/H-1 = 155 Hz (β-D-GalpN), J_C-1/H-1 = 171.3 Hz (α-D-Manp), J_C-1/H-1 = 170.5 Hz (α-D-Manp) and J_C-1/H-1 = 172.8 Hz (α-D-Galp)
indicates the presence of three axial and one equatorial glycosyl linkages. The three bond correlations in the 2D HMBC spectrum also supported the regioselectivity of the glycosyl linkages. Gated $^1$H coupled $^{13}$C NMR spectrum of compound 27 also confirmed the achievement of desired stereochemical outcome of previous glycosylation reactions. Stereoselective coupling of compound 28 with compound 21 under Schmidt's glycosylation condition furnished pentasaccharide derivative 29 in 72% yield. Presence of signals in the NMR spectra [δ 5.60 (s, PhCH), 5.58 (s, PhCH), 5.20 (d, $J$ = 7.9 Hz, H-1E), 5.11 (br s, H-1C), 5.07 (br s, H-1B), 4.46 (br s, H-1D), 4.14 (d, $J$ = 7.8 Hz, H-1A) in the $^1$H NMR and δ 105.1 (C-1A), 102.6 (C-1E), 102.3 (PhCH), 101.8 (PhCH), 101.4 (C-1D), 101.0 (C-1B), 97.2 (C-1C) in the $^{13}$C NMR spectra] confirmed its formation. Presence of neighboring group participating 2-O-benzoyl group in the compound 21 directed the exclusive formation of 1,2-trans glycosyl product 29. Compound 29 was converted to the target pentasaccharide derivative 2 following a series of reactions involving saponification using sodium methoxide, TEMPO mediated selective oxidation of primary hydroxyl group to a carboxylic group under a phase transfer reaction condition, hydrogenolysis over Pearlman catalyst and $N$-acetylation in 64% over all yield. Spectral analysis of compound 2 supported its formation [signals at δ 5.19 (s, H-1C), 4.77 (br s, H-1B), 4.62 (d, $J$ = 8.1 Hz, H-1E), 4.40 (d, $J$ = 7.8 Hz, H-1A), 4.17 (br s, H-1D) and δ 174.6 (COONa), 105.4 (C-1A), 105.0 (C-1B), 103.8 (C-1B), 101.6 (C-1E), 101.0 (C-1C) in the $^1$H and $^{13}$C NMR spectra respectively] (Scheme 8).

Scheme 8: Reagents: (a) NIS, TfOH, CH$_2$Cl$_2$, MS 4Å, −25 °C, 45 min, 76%; (b) 0.1 M CH$_3$ONa, CH$_3$OH, r t, 1 h, quantitative; (c) TMSOTf, CH$_2$Cl$_2$, −10 °C, 1 h, 72%; (d) (i) 0.1 M CH$_3$ONa, CH$_3$OH, r t, 3 h; (ii) NaBr, CH$_2$Cl$_2$, H$_2$O, TBAB, TEMPO, NaHCO$_3$, NaOCl, 0-5 °C, 3 h; (iii) tert-butanol, 2-methyl-but-2-ene, NaClO$_2$, NaH$_2$PO$_4$, r t, 3 h; (e) (i) H$_2$, 20% Pd(OH)$_2$-C, r t, 24 h; (ii) Ac$_2$O, pyridine, r t, 4 h; (iii) 0.1 M CH$_3$ONa, CH$_3$OH, r t, 2 h, over all 64%.
2.2.3. Conclusion

In summary, a convenient synthetic strategy for the preparation of tri- and pentasaccharide fragments corresponding to the O-specific polysaccharide of *Shigella boydii* type 6 has been developed successfully. Stereoselective sequential glycosylation reactions allowed achieving the target tri- and pentasaccharide in minimum number of steps. All intermediate steps were reasonably high yielding and reproducible for a scale-up preparation.

2.2.4. Experimental section

2.2.4.1. General methods: All reactions were monitored by thin layer chromatography over silica gel-coated TLC plates. The spots on TLC were visualized by warming ceric sulfate (2% Ce(SO₄)₂ in 2 N H₂SO₄)-sprayed plates on a hot plate. Silica gel 230-400 mesh was used for column chromatography. ¹H and ¹³C NMR, DEPT 135, 2D COSY, HSQC, HMBC and gated ¹H coupled ¹³C NMR spectra were recorded on Brucker 300 and 500 MHz spectrometer using CDCl₃ and CD₃OD as solvents and TMS as internal reference unless stated otherwise. Chemical shift values are expressed in δ ppm. ESI-MS and MALDI-MS were recorded on Micromass and Bruker spectrometer respectively. Elementary analysis was carried out on Carlo Erba analyzer. Optical rotations were measured at 25 °C on a Jasco P-2000 polarimeter. Commercially available grades of organic solvents of adequate purity are used in all reactions.

2.2.4.2. Preparation and and spectral data of compounds 1-29

3,4,6-Tri-⁰-acetyl-D-galactal (4): To a suspension of D-galactose (10 g, 55.5 mmol) in acetic anhydride (50 mL) was added 30% HBr-AcOH (5.0 mL), and the reaction mixture was allowed to stir at room temperature for 1 h till the reaction mixture became clear. To the reaction mixture was added another lot of 30% HBr-AcOH (50 mL), and it was allowed to stir for further 3 h. The reaction mixture was poured into ice and extracted with CH₂Cl₂ (300 mL). The organic layer was washed with aq. NaHCO₃ and water in succession, dried (Na₂SO₄) and concentrated to dryness under reduced pressure to furnish acetobromogalactose. To a well stirred solution of NaOAc·H₂O (36 g) in AcOH-H₂O (90 mL, 2:3, v/v) was added zinc dust (20 g). After cooling the reaction mixture to −20 °C, the crude acetobromogalactose was added to it and the reaction mixture was allowed to stir at this temperature for 3 h. The reaction mixture was filtered through a Celite® bed. The filtrate was diluted with CH₂Cl₂ (400 mL), washed with aq. NaHCO₃ and water in succession. The organic layer was dried (Na₂SO₄) and concentrated under reduced
pressure. The crude product was purified over SiO₂ using hexane-EtOAc (6:1) as eluant to furnish pure compound 4 (11.7 g; 78%); ¹H NMR (500 MHz, CDCl₃): δ 6.47 (d, J = 6.2 Hz, 1 H), 5.56 (br s, 1 H), 5.43 (d, J = 4.1 Hz, 1 H), 4.74 (d, J = 6.3 Hz, 1 H), 4.34-4.21 (m, 2 H), 2.14, 2.09, 2.04 (3 s, 9 H, 3 COC₄H₂); ¹³C NMR (CDCl₃, 125 MHz): δ 170.3, 170.0, 169.9, 145.2 (C-1), 98.6 (C-2), 72.6, 63.7, 63.5, 61.7, 20.5 (2 C), 20.4; ESI-MS: 273 [M+H]+; Anal. Calcd. for C₁₂H₁₆O₇ (272): C, 52.94; H, 5.92; found: C, 52.72; H, 6.20.

3,4,6-Tri-O-acetyl-2-azido-2-deoxy-β-D-galactopyranosyl trichloroacetimidate (5): To a solution of compound 4 (4 g, 15.5 mmol) and sodium azide (1.3 g, 20.13 mmol) in dry CH₃CN (30 mL) was added ceric ammonium nitrate (27.2 g, 49.5 mmol) at −20 °C and the reaction mixture was allowed to stir at the same temperature for 1 h under argon atmosphere. The reaction mixture was diluted with EtOAc (30 mL) and the organic layer was washed with water and satd. NaHCO₃ solution successively. The organic layer was dried (Na₂SO₄), filtered and concentrated under reduced pressure. To a solution of the crude product in dioxane-water (22 mL, 10:1 v/v) was added sodium nitrite (1.3 g, 18.6 mmol) and the reaction mixture was heated at 80 °C for 12 h. The reaction mixture was concentrated, diluted with CH₂Cl₂ (30 mL) and washed with water and brine respectively. The organic layer was dried (Na₂SO₄), filtered and concentrated. To the solution of crude material in anhydrous CH₂Cl₂ were added CCl₃CN (7.8 mL, 77.45 mmol) followed by anhydrous K₂CO₃ (2.6 g, 18.6 mmol) and the reaction mixture was allowed to stir at room temperature for 24 h. The reaction mixture was filtered and evaporated under reduced pressure and the crude product was purified over silica using hexane-EtOAc (5:1) as eluant to give pure compound 5 (5.1 g, 78%) as a colorless oil, which was immediately used for the next step without further characterization.

2-(p-Methoxyphenoxy) ethyl 3,4,6-tri-O-acetyl-2-azido-2-deoxy-β-D-galactopyranoside (7): To a solution of compound 5 (4 g, 8.4 mmol) in anhydrous CH₃CN (40 mL) was added 2-(p-methoxyphenoxy) etanol (2.2 g, 13.08 mmol) and the solution was cooled to −20 °C. To the cold reaction mixture was added TMSOTf (60 µL) and the reaction mixture was allowed to stir at same temperature for 1 h. The reaction was quenched by addition of Et₃N (0.1 mL) and diluted with CH₂Cl₂ (200 mL). The organic layer was successively washed with satd. NaHCO₃ and H₂O, dried (Na₂SO₄) and concentrated to dryness. The crude product was purified over SiO₂ using hexane-EtOAc (4:1) as eluant to give pure compound 7 (3.2 g, 78%). Yellow oil; IR (neat): 3020, 2837, 2116, 1794, 1508, 1370, 1229, 1045, 827, 758 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ 6.88-6.81 (m, 4 H, Ar-H), 5.33 (d, J = 3.2 Hz, 1 H, H-4), 4.79 (dd, J = 10.3 and 3.3 Hz, 1 H, H-...
3), 4.52 (d, \( J = 8.1 \text{ Hz} \), 1 H, H-1), 4.20-4.09 (m, 5 H, H-6ab, OCH2ab, and OCH2a), 4.01-3.96 (m, 1 H, OCH2b), 3.88-3.85 (m, 1 H, H-5), 3.76 (s, 3 H, OCH3), 3.71 (dd, \( J = 8.1 \text{ Hz} \), 1 H, H-l), 4.20-4.09 (m, 5 H, H-6ab, OCH2ab, and OCH2a), 4.01-3.96 (m, 1 H, OC\( \text{H}_2\)b), 3.88-3.85 (m, 1 H, H-5), 3.76 (s, 3 H, OCH3), 3.71 (dd, \( J = 10.9 \text{ Hz} \), 1 H, H-1), 2.16, 2.09, 2.03 (3 s, 9 H, 3 COCH3); \(^{13}\text{C} \) NMR (125 MHz, CDCl3): \( \delta \) 170.7, 170.4, 170.2 (3 COCH3), 103.1 (C-1'), 71.4 (C-4'), 71.1 (C-3'), 69.1 (C-5'), 68.2 (OCH2), 66.7 (OCH2), 61.6 (C-2'), 61.1 (C-6'), 56.1 (OCH3), 21.0 (3 C, 3 COCH3); ESI-MS: 504.1 [M+Na]+; Anal. Calcd. for C21H25N3O7 (481.17): C, 52.39; H, 5.65; found: C, 52.20; H, 5.90.

2-(p-Methoxyphenoxy) ethyl 2-azido-4,6-0-benzylidene-2-deoxy-\( \beta \)-D-galactopyranoside (8): A solution of compound 7 (3 g, 6.21 mmol) in 0.1 M CH3ONa in CH3OH (40 mL) was allowed to stir at room temperature for 3 h and neutralized with Amberlite IR 120 (H\(^+\)) resin. The reaction mixture was filtered and concentrated under reduced pressure. To a solution of the deacetylated product in anhydrous CH3CN (25 mL) was added benzaldehyde dimethylacetal (1.4 mL, 9.3 mmol) and p-TsOH (150 mg) and the reaction mixture was allowed to stir at room temperature for 12 h. The reaction was quenched with Et3N (0.3 mL) and the solvents were removed under reduced pressure. The crude product was purified over SiO\(_2\) using toluene-EtOAc (2:1) as eluant to give pure compound 8 (2.6 g, 87%). Yellow oil; \(^1\text{H} \) NMR (500 MHz, CDCl3): \( \delta \) 7.51-7.49 (m, 2 H, Ar-H), 7.37-7.35 (m, 3 H, Ar-H), 6.87 (d, \( J = 9.1 \text{ Hz} \), 2 H, Ar-H), 6.81 (d, \( J = 9.1 \text{ Hz} \), 2 H, Ar-H), 5.53 (s, 1 H, PhCH), 4.42 (d, \( J = 7.9 \text{ Hz} \), 1 H, H-1'), 4.27 (dd, \( J = 12.5 \) and 1.3 Hz, 1 H, H-6A), 4.23-4.19 (m, 1 H, OCH2a), 4.15-4.12 (m, 3 H, OCH2ab and OCH2b), 4.01 (dd, \( J = 12.5 \) and 1.7 Hz, 1 H, H-6b), 3.97-3.93 (m, 1 H, OCH2b), 3.74 (s, 3 H, OCH3), 3.65 (dd, \( J = 10.8 \text{ Hz} \), 1 H, H-2'), 3.53 (dd, \( J = 9.9 \) and 2.9 Hz, 1 H, H-3'), 3.40-3.38 (m, 1 H, H-5'); \(^{13}\text{C} \) NMR (125 MHz, CDCl3): \( \delta \) 154.4-115.0 (Ar-C), 102.8 (PhCH), 101.7 (C-1'), 75.0 (C-5'), 71.7 (C-4'), 69.3 (C-3'), 68.7 (OCH2), 68.4 (OCH2), 66.9 (C-6'), 64.2 (C-2'), 56.1 (OCH3); ESI-MS: 466.1 [M+Na]+; Anal. Calcd. for C22H25N3O7 (443.17): C, 59.59; H, 5.68; found: C, 59.41; H, 5.90.

Ethyl 2,3,4,6-tetra-O-acetyl-1-thio-\( \alpha \)-D-mannopyranoside (10): To a solution of compound 9 (8 g, 44.4 mmol) in CH2Cl2 (100 mL) were added BF3.OEt2 (8.4 mL, 66.6 mmol) and ethanethiol (7.0 mL, 96 mmol) and the reaction mixture was allowed to stir at 5 °C for 5 h. The reaction was quenched by addition of aq. NaHCO\(_3\) and the mixture was extracted with CH2Cl2 (200 mL). The organic layer was washed with water, dried (Na2SO\(_4\)) and concentrated under reduced pressure. Purification of the crude product over SiO\(_2\) using hexane-EtOAc (3:1) as the eluant furnished pure compound 10 (16 g, 85%). White solid; m.p. 105-106 °C (EtOH); [\( \alpha \)]\(_D\)\(^{25}\) + 104 (c 1.3, CHCl3); IR (KBr): 2964, 2891, 1759, 1593, 1379, 1241, 1042, 909, 601 cm\(^{-1}\); \(^1\text{H} \) NMR (500 MHz, CDCl3): \( \delta \) 5.44 (d, \( J = 3.6 \text{ Hz} \), 1 H, H-2'), 5.01 (dd, \( J = 9.9 \), 3.6 Hz, 1 H, H-3'), 4.70 (br s, 1
H, H-l), 4.36-4.32 (m, 2 H, H-l, H-6b), 4.21 (dd, J = 9.9, 3.6 Hz, 1 H, H-4), 3.90 (t, J = 6.6 Hz each, 1 H, H-5), 2.69 (m, 2 H, SCH2CH3), 2.12, 2.03, 2.00, 1.95 (4 s, 12 H, 4 COCH3), 1.25 (t, J = 7.5 Hz each, 3 H, SCH2CH3); 13C NMR (75 MHz, CDCl3): δ 170.8, 170.6, 170.4, 169.9 (4 COCH3), 84.4 (C-1), 74.7, 72.3, 67.7, 67.6, 61.9 (C-6), 24.7 (SCH2CH3), 21.2, 21.1, 21.0, 20.9 (4 COCH3), 15.2 (SCH2CH3); ESI-MS: 415.4 [M+Na]+; Anal. Calcd. for C16H24O9S (392.12): C, 48.99; H, 6.16; found: C, 48.90; H, 6.40.

Ethyl 4,6-O-benzylidene-1-thio-α-D-mannopyranoside (11): A solution of the compound 10 (8 g, 20.6 mmol) in 0.1 M CH3ONa in CH3OH (50 mL) was stirred at room temperature for 4 h. The reaction mixture was neutralized with Amberlite IR-120 (H+) resin, filtered and the filtrate was evaporated to dryness to give an amorphous solid in quantitative yield. The dried mass was dissolved in anhydrous CH3CN (50 mL) and benzaldehyde dimethylacetal (4.6 mL, 30.8 mmol) was added to it followed by p-TsOH (500 mg) to make the solution acidic (pH~2). After stirring the reaction mixture at room temperature for 10 h, Et3N (1 mL) was added to it and evaporated under reduced pressure. The crude mass was purified over SiO2 using hexane-EtOAc (2.5:1) as eluant to give pure compound 11 (5.5 g, 78%). White solid, m.p. 173-174 °C (EtOH), [α]D25 +166 (c 0.9, CHCl3); IR (KBr) 3386, 2977, 2923, 2882, 1496, 1450, 1404, 1365, 1248, 1169, 1100, 1075, 1058, 1027, 1000, 697, 650 cm⁻¹; 1H NMR (400 MHz, CDCl3): δ 7.36-7.49 (m, 5 H, Ar-H), 5.56 (s, 1 H, PhCH), 4.33-4.27 (m, 2 H, H-1, H-6b), 4.25 (d, J = 2.5 Hz, 1 H, H-4), 4.04 (dd, J = 12.5, 2.0 Hz, 1 H, H-6b), 3.70 (dd, J = 9.8, 3.5 Hz, 1 H, H-3), 3.05 (d, , J = 3.6 Hz, 1 H, H-2), 3.52 (m, 1 H, H-5), 2.76-2.87 (m, 2 H, SCH2CH3), 1.34 (t, J = 7.5 Hz each, 3 H, SCH2CH3); 13C NMR (100 MHz, CDCl3): δ 137.6-126.4 (Ar-C), 101.4 (PhCH), 85.2 (C-1), 75.6 (C-4), 73.8 (C-3), 70.0 (C-5), 69.6 (C-2), 69.2 (C-6), 23.4 (SCH2CH3), 15.2 (SCH2CH3); ESI-MS: 335.4 [M+Na]+; Anal. Calcd. for C15H20O5S (312.47): C, 57.67; H, 6.45; found: C, 57.42; H, 6.57.

Ethyl 2-O-acetyl-3-O-benzyl-4,6-O-benzylidene-1-thio-α-D-mannopyranoside (12): To a solution of the compound 11 (5 g, 16.0 mmol) in dry toluene (200 mL) was added dibutyltin oxide (4.8 g, 19.2 mmol) and the reaction mixture was allowed to stir at 110 °C with azotropically removal of water for 4 h. The solvents were reduced to half of the volume and benzyl bromide (2.3 mL, 19.2 mmol) and TBAB (500 mg) was added to it and the reaction mixture was stirred at 80 °C for 16 h. The solvents were removed under reduced pressure and crude product was diluted with CH2Cl2 (150 mL). The organic layer was washed with 1 N aq. HCl, satd. NaHCO3 and water in succession, dried (Na2SO4) and concentrated under reduced pressure. The crude
product was acetylated using acetic anhydride (15 mL) and pyridine (20 mL) at room temperature. The solvents were removed under reduced pressure to give the crude product, which was purified over SiO₂ using hexane-EtOAc (5:1) as eluant to furnish pure compound 12 (3.5 g, 95%). Colorless oil; [α]₂⁰⁺ - 26.7 (c 1.5, CHCl₃); IR (neat): 2926, 2367, 1745, 1649, 1516, 1461, 1378, 1236, 1093, 1031, 757, 693 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 7.50-7.25 (m, 10 H, Ar-H), 5.62 (s, 1 H, PhCH), 5.44 (dd, J = 10.0, 8.6 Hz, 1 H, H-2), 5.24 (br s, 1 H, H-1), 4.68 (d, J = 11.7 Hz, 1 H, PhCH₂), 4.63 (d, J = 11.7 Hz, 1 H, PhCH₂), 4.25-4.19 (m, 2 H, H-5, H-6a), 4.10 (t, J = 9.6 Hz, 1 H, H-4), 3.82-3.66 (m, 1 H, H-6b), 2.71 (dd, J = 9.9, 7.4, 2.5 Hz, 2 H, SCH₂CH₃), 2.0, 1.9 (s, 6 H, 2 COCH₃), 1.27 (t, J = 7.5 Hz each, 3 H, SCH₂CH₃); ¹³C NMR (75 MHz, CDCl₃): δ 170.6, 169.9 (COCH₃), 159.2 (Ar-C), 137.2-127.75 (Ar-C), 96.29 (C-1), 82.3, 79.0, 73.8, 71.1, 70.6, 68.5, 23.6 (SCH₂CH₃), 20.8 (COCH₃), 14.7 (SCH₂CH₃); ESI-MS: 467.2 [M+Na]⁺; Anal. Calcd. for C₂₄H₂₈O₆S (444.17): C, 64.84; H, 6.35; found: C, 63.06; H, 6.60.

Ethyl 2,3-di-O-acetyl-4,6-O-(p-methoxy)benzylidene-1-thio-α-D-mannopyranoside (13): A solution of the compound 10 (8 g, 20.6 mmol) in 0.1 M CH₃ONa in CH₃OH (50 mL) was stirred at room temperature for 4 h. The reaction mixture was neutralized with Amberlite IR-120 (H⁺) resin, filtered and the filtrate was evaporated to dryness to give an amorphous solid in quantitative yield. To a solution of the dried mass in dry CH₃CN (15 mL) were added p-methoxybenzaldehyde dimethylacetal (3.4 mL, 20 mmol) and p-TsOH (400 mg) and the reaction mixture was allowed to stir at room temperature for 12 h. The reaction mixture was neutralized with Et₃N (1.5 mL) and concentrated under reduced pressure. A solution of the crude product in acetic anhydride-pyridine (10 mL, 1:1 v/v) was kept at room temperature for 2 h and the solvents were removed under reduced pressure. The crude product was purified over SiO₂ using toluene-EtOAc (3:1) as eluant to give pure compound 13 (4.5 g, 79%). White solid; m.p. 82-84 °C [EtOH]; [α]₁⁰⁻ + 95 (c 1.2, CHCl₃); IR (KBr): 3462, 2930, 1740, 1519, 1254, 1224, 1095, 1025, 834, 753 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ 7.38 (d, J = 8.7 Hz, 2 H, Ar-H), 6.88 (d, J = 8.7 Hz, 2 H, Ar-H), 5.53 (s, 1 H, PhCH), 5.44-5.43 (m, 1 H, H-2), 5.33 (dd, J = 10.3, 3.4 Hz, 1 H, H-3), 5.23 (br s, 1 H, H-1), 4.35-4.31 (m, 1 H, H-5), 4.23 (dd, J = 10.3, 4.9 Hz, 1 H, H-6a), 4.06 (t, J = 10.0 Hz each, 1 H, H-4), 3.86 (t, J = 10.3 Hz each, 1 H, H-6a), 3.79 (s, 3 H, OCH₃), 2.68-2.60 (m, 2 H, SCH₂CH₃), 2.16, 2.00 (2 s, 6 H, 2 COCH₃), 1.29 (t, J = 7.4 Hz each, 3 H, SCH₂CH₃); ¹³C NMR (125 MHz, CDCl₃): δ 170.2 (2 C, 2 COCH₃), 160.6-114.0 (Ar-C), 102.3 (PhCH), 83.6 (C-1), 76.7 (C-5), 72.1 (C-3), 69.1 (C-2), 68.9 (C-6), 64.9 (C-4), 55.6 (OCH₃), 25.8 (SCH₂CH₃), 21.3, 21.2 (2 COCH₃), 15.2 (SCH₂CH₃); ESI-MS: 449.1 [M+Na]⁺; Anal. Calcd. for C₂₀H₂₆O₈S (426.13): C, 56.32; H, 6.14; found: C, 56.10; H, 6.40.
Ethyl 2,3,4-tri-O-acetyl-6-O-(p-methoxybenzyl)-1-thio-α-D-mannopyranoside (14): To an ice-cooled solution of compound 13 (4 g, 9.38 mmol) in anhydrous DMF (10 mL) were added MS 3Å (3 g) and NaBH\(_{3}\)CN (3 g, 47.74 mmol). TFA (3 mL, 40.38 mmol) was added dropwise to the cold reaction mixture and it was allowed to stir at room temperature for 10 h. The reaction mixture was diluted with water and extracted with CH\(_2\)Cl\(_2\) (100 mL). The organic layer was successively washed with satd. NaHCO\(_3\) and water, dried (Na\(_2\)SO\(_4\)) and concentrated under reduced pressure. A solution of the crude product in acetic anhydride-pyridine (8.0 mL, 1:1 v/v) was kept at room temperature for 1 h and the solvents were removed under reduced pressure. The crude product was purified over SiO\(_2\) using toluene-EtOAc (3:1) as eluant to give pure compound 14 (3.2 g, 73%). Yellow oil; [α]\(_D^25\) = +65.8 (c 1.2, CHCl\(_3\)); IR (neat): 3442, 3016, 2963, 2934, 1749, 1613, 1514, 1370, 1244, 1223, 1095, 1047, 756 cm\(^{-1}\); \(^1\)H NMR (500 MHz, CDCl\(_3\)): δ 7.26 (d, \(J = 8.6\) Hz, 2 H, Ar-H), 6.85 (d, \(J = 8.6\) Hz, 2 H, Ar-H), 5.35 (t, \(J = 9.9\) Hz each, 1 H, H-4), 5.32-5.31 (m, 1 H, H-2), 5.29 (br s, 1 H, H-1), 5.24 (dd, \(J = 9.8, 3.4\) Hz, 1 H, H-3), 4.52 (d, \(J = 11.6\) Hz, 1 H, PhCH\(_2\)), 4.39 (d, \(J = 11.6\) Hz, 1 H, PhCH\(_2\)), 4.33-4.29 (m, 1 H, H-5), 3.78 (s, 3 H, OCH\(_3\)), 3.57-3.49 (m, 2 H, H-6ab), 2.66-2.60 (m, 2 H, SCH\(_2\)CH\(_3\)), 2.14, 1.98, 1.90 (3 s, 9 H, 3 COCH\(_3\)), 1.28 (t, \(J = 7.4\) Hz each, 3 H, SCH\(_2\)CH\(_3\)); \(^1\)C NMR (125 MHz, CDCl\(_3\)): δ 170.5, 170.3, 170.2 (3 COCH\(_3\)), 159.6-114.0 (Ar-C), 82.4 (C-1), 73.5 (PhCH\(_2\)), 71.7 (C-5), 70.4 (C-3), 70.1 (C-2), 68.8 (C-6), 67.4 (C-4), 55.7 (OCH\(_3\)), 25.7 (SCH\(_2\)CH\(_3\)), 21.3, 21.1, 21.0 (3 COCH\(_3\)), 15.1 (SCH\(_2\)CH\(_3\)); ESI-MS: 493.1 [M+Na]\(^+\); Anal. Calcd. for C\(_{22}\)H\(_{30}\)O\(_9\)S (470.16): C, 56.16; H, 6.43; found: C, 55.92; H, 6.66.

Ethyl 2,3,4,6-tetra-O-acetyl-1-thio-β-D-galactopyranoside (15): To a solution of compound 3 (16 g, 88.8 mmol) in CH\(_2\)Cl\(_2\) (200 mL) were added BF\(_3\)-OEt\(_2\) (16.7 mL, 133.2 mmol) and ethanethiol (7 mL, 96 mmol) and the reaction mixture was allowed to stir at 5 °C for 5 h. The reaction was quenched by addition of aq. NaHCO\(_3\) and the mixture was extracted with CH\(_2\)Cl\(_2\) (200 mL). The organic layer was washed with water, dried (Na\(_2\)SO\(_4\)) and concentrated under reduced pressure. Purification of the crude product over SiO\(_2\) using hexane-EtOAc (3:1) as eluant furnished pure compound 15 (27.2 g, 85%). White solid; m.p. 73-74 °C [EtOH]; [α]\(_D^25\) = -7 (c 0.9, CHCl\(_3\)); IR (KBr): 2964, 2891, 1759, 1593, 1379, 1241, 1042, 909, 601 cm\(^{-1}\); \(^1\)H NMR (300 MHz, CDCl\(_3\)): δ 5.39 (d, \(J = 2.8\) Hz, 1 H, H-4), 5.19 (t, \(J = 9.9\) Hz each, 1 H, H-2), 5.01 (dd, \(J = 9.9, 3.4\) Hz, 1 H, H-3), 4.46 (d, \(J = 9.9\) Hz, 1 H, H-1), 4.15-4.04 (m, 2 H, H-6ab), 3.90 (t, \(J = 6.6\) Hz each, 1 H, H-5), 2.69 (m, 2 H, SCH\(_2\)CH\(_3\)), 2.12, 2.03, 2.00, 1.95 (4 s, 12 H, 4 COCH\(_3\)), 1.25 (t, \(J = 7.5\) Hz each, 3 H, SCH\(_2\)CH\(_3\)); \(^1\)C NMR (75 MHz, CDCl\(_3\)): δ 170.8, 170.6, 170.4, 169.9 (4 COCH\(_3\)), 84.4 (C-1), 74.7, 72.3, 67.7, 67.6, 61.9 (C-6), 24.7 (SCH\(_2\)CH\(_3\)), 21.2,
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Ethyl 2,3-di-O-benzyl-4,6-O-benzylidene-1-thio-β-D-galactopyranoside (16): A solution of the compound 15 (8 g, 20.6 mmol) in 0.1 M CH₃ONa in CH₃OH (50 mL) was stirred at room temperature for 4 h. The reaction mixture was neutralized with Amberlite IR-120 (H⁺) resin, filtered and the filtrate was evaporated to dryness to give an amorphous solid in quantitative yield. The dried mass was dissolved in anhydrous CH₃CN (50 mL) and benzaldehyde dimethylacetal (4.6 mL, 30.8 mmol) was added to it followed by p-TsOH (500 mg) to make the solution acidic (pH-2). After stirring the reaction mixture at room temperature for 10 h, the reaction was quenched with Et₃N (1 mL) and evaporated under reduced pressure. To a solution of the crude product in THF (20 mL) were added powdered NaOH (1.6 g, 40.8 mmol), benzyl bromide (2.1 mL, 19.3 mmol) and tetrabutylammonium bromide (50 mg) and it was allowed to stir vigorously at room temperature for 6 h. The reaction mixture was diluted with water (100 mL) and extracted with CH₂Cl₂ (150 mL). The organic layer was washed with water, dried (Na₂SO₄) and concentrated under reduced pressure. The crude product was purified over SiO₂ using hexane-EtOAc (10:1) as eluant to furnish pure compound 11 (2.2 g, 88%). Colorless oil; ¹H NMR (400 MHz; CDCl₃): δ 7.54-7.25 (m, 15 H, Ar-H), 5.47 (s, 1 H, PhCH₃), 4.90-4.82 (q, J = 10.2 Hz each, 2 H, PhCH₂), 4.44 (d, J = 9.6 Hz, 1 H, H-1), 4.32-4.29 (dd, J = 1.5, 12.3 Hz, 1 H, H-6a), 4.15 (d, J = 3.0 Hz, 1 H, H-4), 3.97-3.94 (dd, J = 1.7, 12.3 Hz, 1 H, H-6b), 3.89 (t, J = 4.7 Hz each, 1 H, H-2), 3.60-3.58 (m, 1 H, H-3), 3.35-3.34 (m, 1 H, H-5), 2.85-2.75 (m, 2 H, SCH₂CH₃), 1.33 (t, J = 7.5 Hz each, 3 H, SCH₂CH₃); ESI-MS: 510.4 [M+Na]⁺; Anal. Calcd. for C₂₉H₃₂O₉S (492.42): C, 70.70; H, 6.55; found: C, 70.55; H, 6.69.

Ethyl 4-O-acetyl-2,3,6-tri-O-benzyl-1-thio-β-D-galactopyranoside (17): To a solution of compound 16 (2 g, 4.05 mmol) in CH₂CN (15 mL) were added triethylsilane (1.3 mL, 8.11 mmol) and iodine (0.2 g, 0.78 mmol) and the reaction mixture was allowed to stir at 0-5 °C for 30 min. The reaction mixture was poured into water and extracted with CH₂Cl₂ (100 mL). The organic layer was successively washed with satd. Na₂S₂O₃ and water, dried (Na₂SO₄) and concentrated. The solvents were removed under reduced pressure and a solution of the crude product in acetic anhydride-pyridine (8 mL; 1:1, v/v) was kept at room temperature. The solvents were removed under reduced pressure and the crude product was purified over SiO₂ using hexane-EtOAc (5:1) as eluant to give pure compound 17 (1.65 g, 82%). Yellow oil; ¹H NMR (500 MHz, CDCl₃): δ 7.37-7.25 (m, 15 H, Ar-H), 5.63 (br s, 1 H, H-4), 4.82-4.75 (m, 3 H, PhCH₂), 4.57 (d, J = 12.0 Hz, 1 H, PhCH₂), 4.51-4.67 (m, 2 H, PhCH₂), 4.60 (d, J = 8.5 Hz, 1 H,
2,3,4,6-Tetra-O-benzoyl-α-D-glucopyranose (19): Benzoyl chloride (6.9 mL, 60.0 mmol) was added dropwise to a suspension of D-glucose (1.8 g, 10.0 mmol) in pyridine (50 mL) at 0 °C and the mixture was stirred for 2 h. The reaction was quenched by adding cold water (100 mL) and the product was extracted with EtOAc (100 mL). The organic layer was successively washed with 1 N HCl and brine, dried (Na2SO4) and concentrated. The residue was crystallized from hexane/ethyl acetate to give compound 19 (6.7 g, 95%). White solid; m.p. 177-179 °C [hexane-EtOAc]; [α]D25 +137 (c 1.0, CH2Cl2); 1H NMR (300 MHz, CDCl3): δ 8.15-7.56 (m, 25 H, Ar-H), 6.84 (d, J = 3.9 Hz, 1 H, H-1), 6.31 (t, J = 9.9 Hz, 1 H, H-3), 5.67 (dd, J = 3.3, 9.9 Hz, 1 H, H-2), 5.32 (dd, J = 3.3, 9.9 Hz, 1 H, H-3), 4.67 (dd, J = 3.0, 4.5, 9.9 Hz, 1 H, H-4), 4.44 (dd, J = 4.5, 12.0 Hz, 1 H, H-6a), 3.71 (t, J = 9.5 Hz each, H-3), 3.61-3.50 (m, 3 H, H-5, H-6ab), 3.50-3.46 (m, 1 H, H-2), 2.80-2.70 (2 H, SCH2CH3), 2.09 (s, 3 H, COC3H3); ESI-MS: 559.2 [M+Na]+; Anal. Calcd. for C31H36O6S (536.22): C, 69.38; H, 6.76; found: 69.20; H, 6.95.

2,3,4,6-Tetra-O-benzoyl-α/β-D-glucopyranose (20): To a solution of compound 19 (2.6 g, 3.66 mmol) in THF (20 mL) was added benzylamine (2 mL) and the reaction mixture was stirred at room temperature for 2 h. The reaction mixture was concentrated in vacuo and the residue was purified over SiO2 using hexane-EtOAc (3:1) as eluant to give pure compound 20 (1.8 g, 83%; α/β = 4:1). Colorless oil; 1H NMR (300 MHz, CDCl3): α-anomer: δ 7.83-7.61 (m, 20 H, Ar-H), 6.25 (t, J = 9.9 Hz each, 1 H, H-3), 5.75 (d, J = 3.3 Hz, 1 H, H-1), 5.73 (t, J = 9.9 Hz, 1 H, H-4), 5.32 (dd, J = 3.3, 9.9 Hz, 1 H, H-2), 4.67 (dd, J = 3.0, 4.5, 9.9 Hz, 1 H, H-5), 4.44 (dd, J = 4.5, 12.0 Hz, 1 H, H-6a), 4.19 (dd, J = 3.0, 5.1, 9.7 Hz, 1 H, H-5); β-anomer: δ 7.83-7.61 (m, 20 H, Ar-H), 5.96 (t, J = 9.7 Hz, 1 H, H-3), 5.70 (t, J = 9.7 Hz each, 1 H, H-4), 5.35 (dd, J = 8.1, 9.7 Hz, 1 H, H-2), 5.06 (d, J = 8.1 Hz, 1 H, H-1), 4.67 (dd, J = 3.0, 12.3 Hz, 1 H, H-6a), 4.49 (dd, J = 5.1, 12.3 Hz, 1 H, H-6b); 13C NMR (75 MHz, CDCl3): α-anomer: δ 165.8, 165.4 (2 C), 164.8 (4 PhCO), 133.1-127.9 (Ar-C), 90.2 (C-1), 72.0 (C-2), 69.9 (C-3), 69.2 (C-4), 67.6 (C-5), 62.7 (C-6); ESI-MS: 619.1 [M+Na]+; Anal. Calcd. for C34H28O10 (596.59): C, 68.45; H, 4.73; found C, 68.06; H, 4.73.

O-(2,3,4,6-Tetra-O-benzoyl-α-D-glucopyranosyl) trichloroacetimidate (21): To a solution of compound 20 (1.5 g, 2.51 mmol) and trichloroacetonitrile (2.5 mL, 25.1 mmol) in CH2Cl2 (5
mL) was added DBU (0.3 g, 1.97 mmol) and the mixture was stirred at -5 °C for 30 min. The reaction mixture was concentrated in vacuo and the crude product was purified over SiO₂ using hexane-EtOAc (3:1) to give pure compound 21 (1.3 g, 91%). Colorless oil; ¹H NMR (300 MHz, CDCl₃): δ 8.62 (s, 1 H, N-H), 7.84-7.58 (m, 20 H, Ar-H), 6.83 (d, J = 3.8 Hz, 1 H, H-1), 6.27 (t, J = 10.0 Hz each, 1 H, H-3), 5.81 (t, J = 10.0 Hz each, 1 H, H-4), 5.61 (dd, J = 3.8, 10.0 Hz each, 1 H, H-2), 4.61-4.66 (m, 2 H, H-5, H-6), 4.48 (dd, J = 5.7, 12.9 Hz, 1 H, H-6); ¹³C NMR (75 MHz, CDCl₃): δ 165.5, 165.1, 164.9, 164.7 (4 PhCO), 160.0 (C=NH), 133.2-127.9 (Ar-C), 92.8 (C-1), 70.5 (2 C, C-2, C-5), 70.0 (C-3), 68.5 (C-4), 62.3 (C-6); ESI-MS: 762.1 [M+Na⁺]; Anal. Calcd. for C₃₆H₂₈Cl₃NO₁₀ (740.97): C, 58.35, H, 3.81; found: C, 58.47; H, 3.80.

2-(p-Methoxyphenoxy)ethyl (2-O-acetyl-3-O-benzyl-4,6-O-benzylidene-α-D-mannopyranosyl)-(1→3)-2-azido-4,6-O-benzylidene-2-deoxy-β-D-galactopyranoside (22): To a solution of compound 8 (2 g, 4.51 mmol) and compound 12 (2.4 g, 5.40 mmol) in anhydrous CH₂Cl₂ (10 mL) was added MS 4 Å (2 g) and the reaction mixture was allowed to stir at room temperature for 30 min under argon. The reaction mixture was cooled to -40 °C and N-iodosuccinimide (NIS; 1.4 g, 6.22 mmol) followed by TfOH (25 μL) were added to it. After stirring at the same temperature for 1 h the reaction mixture was filtered through a Celite® bed and washed with CH₂Cl₂ (100 mL). The combined organic layer was washed with 5% Na₂S₂O₃, satd. NaHCO₃, water in succession, dried (Na₂SO₄) and concentrated under reduced pressure. The crude product was purified over SiO₂ using hexane-EtOAc (7:1) as eluant to give pure compound 22 (2.8 g, 75%). White solid; m.p. 152-154 °C [EtOH]; [α]D²⁵ + 22 (c 1.2, CHCl₃); IR (KBr): 3336, 2926, 2111, 1735, 1711, 1509, 1457, 1230, 1172, 1060, 753, 697 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ 7.53-7.25 (m, 15 H, Ar-H), 6.86-6.79 (m, 4 H, Ar-H), 5.61 (s, 1 H, PhCH), 5.57 (s, 1 H, PhCH), 5.37-5.36 (m, 1 H, H-2α), 5.02 (br s, 1 H, H-1α), 4.61 (br s, 2 H, PhCH₂), 4.43 (d, J = 8.0 Hz, 1 H, H-1α), 4.32-4.27 (m, 2 H, OCH₂), 4.23 (d, J = 3.2 Hz, 1 H, H-4α), 4.21-4.18 (m, 1 H, H-3α), 4.15-4.13 (m, 2 H, OCH₂), 4.07-4.03 (m, 4 H, H-4β, H-5B, H-6αβ), 3.98-3.94 (m, 1 H, H-6αβ), 3.83-3.78 (m, 2 H, H-2α, H-6βα), 3.75 (s, 3 H, OCH₃), 3.60 (dd, J = 10.4, 3.6 Hz, 1 H, H-3α), 3.37 (br s, 1 H, H-5α), 2.15 (s, 3 H, COCH₃); ¹³C NMR (125 MHz, CDCl₃): δ 170.5 (COCH₃), 154.4-115.0 (Ar-C), 102.8 (PhCH), 102.1 (COCH₃), 101.3 (C-1α), 95.5 (C-1β), 78.6 (C-4α), 74.8 (C-3β), 74.2 (C-5β), 73.0 (PhCH₂), 71.1 (C-3α), 70.7 (C-2α), 69.5 (C-6α), 68.9 (C-6β), 68.6 (OCH₂), 68.4 (OCH₂), 66.8 (C-5α), 65.0 (C-4α), 61.4 (C-2α), 56.0 (OCH₃), 21.4 (COCH₃); ESI-MS: 848.3 [M+Na⁺]; Anal. Calcd. for C₄₄H₄₇N₃O₁₃ (825.31): C, 63.99; H, 5.74; found: C, 63.78; H, 5.96.
2-(p-Methoxyphenoxy)ethyl (3-O-benzyl-4,6-O-benzylidene-α-D-mannopyranosyl)-(1→3)-2-azido-4,6-O-benzylidene-2-deoxy-β-D-galactopyranoside (23): A solution of compound 22 (2.5 g, 3.03 mmol) in 0.1 M CH$_3$ONa in CH$_3$OH (25 mL) was allowed stir at room temperature for 1 h and neutralized with Amberlite IR 120 (H$^+$) resin. The reaction mixture was filtered and concentrated under reduced pressure to give crude product, which was purified over SiO$_2$ using hexane-EtOAc (5:1) as eluant to give pure compound 23 (2.3 g, 97%). White solid; m.p. 158-159 °C [EtOH]; [α]$^2_{D}$ $^0$ + 34 (c 1.2, CHCl$_3$); IR (KBr): 3540, 2926, 2111, 1711, 1509, 1458, 1327, 1231, 1172, 1060, 823, 753, 698 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$): δ 7.44-7.17 (m, 15 H, Ar-H), 6.81-6.74 (m, 4 H, Ar-H), 5.54 (s, 1 H, PhC=O), 5.45 (s, 1 H, PhC=O), 5.04 (br s, 1 H, H-1B), 4.78 (d, $^J$ = 11.5 Hz, 1 H, PhC=O), 4.62 (d, $^J$ = 11.5 Hz, 1 H, PhC=O), 4.39 (d, $^J$ = 8.0 Hz, 1 H, H-1A), 4.24-4.21 (m, 2 H, OCH$_2$), 4.19 (d, $^J$ = 3.2 Hz, 1 H, H-4A), 4.18-4.13 (m, 1 H, H-3A), 4.09-4.02 (m, 4 H, H-2B, H-4B, OCH$_2$), 3.99-3.94 (m, H-5B, H-6ab), 3.92-3.89 (m, 1 H, H-6a), 3.79-3.74 (m, H-2a, H-6ba), 3.68 (s, 3 H, OCH$_3$), 3.59 (dd, $^J$ = 10.4, 3.3 Hz, 1 H, H-3B), 3.59 (dd, $^J$ = 10.4, 3.3 Hz, 1 H, H-3B), 3.33 (br s, 1 H, H-5A); $^{13}$C NMR (125 MHz, CDCl$_3$): δ 154.4-115.0 (Ar-C), 102.9 (PhCH), 102.1 (PhCH), 101.4 (C-1A), 96.0 (C-1B), 79.0 (C-4B), 76.0 (C-3B), 73.8 (PhC=O), 73.4 (C-5B), 70.7 (C-3A), 70.4 (C-2B), 69.6 (C-6a), 69.1 (C-6b), 68.7 (OCH$_2$), 68.4 (OCH$_2$), 66.8 (C-5a), 64.3 (C-4a), 61.6 (C-2a), 56.1 (OCH$_3$); ESI-MS: 806.3 [M+Na]$^+$; Anal. Calcd. for C$_{42}$H$_{45}$N$_3$O$_7$ (783.30): C, 64.36; H, 5.79; found: C, 64.15; H, 5.97.

2-(p-Methoxyphenoxy)ethyl [2,3,4-tri-O-acetyl-6-O-(p-methoxybenzyl)-α-D-mannopyranosyl]-(1→2)-(3-O-benzyl-4,6-O-benzylidene-α-D-mannopyranosyl)-(1→3)-2-azido-4,6-O-benzylidene-2-deoxy-β-D-galactopyranoside (24): To a solution of compound 23 (2.2 g, 2.81 mmol) and compound 14 (1.5 g, 3.19 mmol) in anhydrous CH$_2$Cl$_2$ (10 mL) was added MS 4 Å (2 g) and the reaction mixture was allowed to stir at room temperature for 30 min under argon. The reaction mixture was cooled to −40 °C and NIS (850 mg, 3.77 mmol) followed by TfOH (10 μL) were added to it. After stirring at the same temperature for 1 h the reaction mixture was filtered through a Celite® bed and washed with CH$_2$Cl$_2$ (100 mL). The combined organic layer was successively washed with 5% Na$_2$SO$_3$, satd. NaHCO$_3$, water, dried (Na$_2$SO$_4$) and concentrated under reduced pressure. The crude product was purified over SiO$_2$ using hexane-EtOAc (6:1) as eluant to give pure compound 24 (2.4 g, 72%). White solid; m.p. 78-81 °C [CH$_2$Cl$_2$-hexane]; [α]$^2_{D}$ $^0$ + 23.5 (c 1.2, CHCl$_3$); IR (KBr): 3476, 2928, 2870, 2115, 1753, 1507, 1371, 1248, 1221, 1104, 1079, 1050, 822, 750, 737, 699 cm$^{-1}$; $^1$H NMR (500 MHz, CDCl$_3$): δ 7.37-7.19 (m, 17 H, Ar-H), 6.89-6.83 (m, 6 H, Ar-H), 5.68 (s, 1 H, PhCH$_2$), 4.43-4.40
(m, 2 H, H-2c, H-3c), 5.39 (s, 1 H, PhCH), 5.20 (t, J = 9.8 Hz each, 1 H, H-4c), 5.17 (br s, 1 H, H-1c), 4.95 (br s, 1 H, H-1b), 4.80 (d, J = 11.9 Hz, 1 H, PhCH2), 4.55 (d, J = 11.9 Hz, 1 H, PhCH2), 4.42 (d, J = 11.9 Hz, 1 H, PhCH2), 4.33-4.30 (m, 1 H, H-3A), 4.27 (d, J = 8.0 Hz, 1 H, H-1A), 4.21 (d, J = 11.6 Hz, 1 H, PhCH2), 4.19-4.10 (m, 6 H, H-2b, H-4b, H-6ab, OCH2), 4.06-4.00 (m, 3 H, H-5C, OCH2), 3.99 (br s, 1 H, H-4A), 3.95-3.91 (m, 2 H, H-5b, H-6ab), 3.82-3.79 (m, 1 H, H-6aa), 3.79 (s, 3 H, OCH3), 3.75 (s, 3 H, OCH3), 3.72 (dd, J = 8.0 Hz each, 1 H, H-2A), 3.52-3.49 (m, 1 H, H-6ac), 3.44 (dd, J = 10.4, 3.3 Hz, 1 H, H-3b), 3.33-3.31 (m, 1 H, H-6bc), 2.88 (br s, 1 H, H-5A), 2.09 (s, 3 H, COCH3), 1.99 (s, 3 H, COCH3), 1.95 (s, 3 H, COCH3); 13C NMR (125 MHz, CDCl3): δ 170.4, 170.2, 170.1 (3 COCH3), 159.7-114.2 (Ar-C), 102.7 (PhCH), 102.0 (PhCH), 101.0 (C-1A), 100.6 (C-1B), 96.5 (C-1C), 79.0 (C-4a), 78.5 (C-4b), 75.9 (C-3a), 74.1 (C-3b), 73.7 (PhCH2), 73.4 (PhCH2), 70.8 (C-2b), 70.7 (C-5b), 69.8 (C-2c), 69.7 (C-6a), 69.5 (C-3c), 69.4 (C-6b), 69.0 (C-6c), 68.7 (OCH2), 68.8 (OCH2), 67.4 (C-4c), 66.7 (C-5a), 61.6 (C-2A), 56.1 (OCH3), 55.7 (OCH3), 21.3, 21.2, 21.1 (3 COCH3); ESI-MS: 1214.4 [M+Na]+; Anal. Calcd. for C62H69N3021 (1191.44): C, 62.46; H, 5.83; found: C, 62.24; H, 6.05.

2-(p-Methoxyphenoxy)ethyl [2,3,4-tri-O-benzyl-6-O-(p-methoxybenzyl)-α-D-mannopyranosyl]-(1→2)-(3-O-benzyl-4,6-0-benzylidene-α-D-mannopyranosyl)-(1→3)-2-azido-4,6-0-benzylidene-2-deoxy-β-D-galactopyranoside (25): To a solution of compound 24 (2 g, 1.67 mmol) in dry DMF (15 mL) were added benzyl bromide (1.2 mL, 10.08 mmol), powdered NaOH (700 mg, 17.5 mmol) and TBAB (300 mg, 0.93 mmol) and the reaction mixture was allowed to stir at room temperature for 5 h. The reaction mixture was diluted with H2O (100 mL) and extracted with CH2Cl2 (100 mL). The organic layer was washed with H2O, dried (Na2SO4) and concentrated under reduced pressure. The crude product was purified over SiO2 using hexane-EtOAc (9:1) as eluant to give pure compound 25 (1.7 g, 76%). White solid; m.p. 86-88 °C [EtOH]; [α]D25 + 49.2 (c 1.2, CHCl3); IR (KBr): 3488, 3034, 2920, 2871, 2113, 1611, 1509, 1457, 1370, 1288, 1239, 1073, 914, 824, 744, 697 cm⁻¹; 1H NMR (500 MHz, CDCl3): δ 7.51-6.80 (m, 38 H, Ar-H), 5.60 (s, 1 H, PhC=H), 5.43 (s, 1 H, PhCH3), 5.18 (br s, 1 H, H-1c), 4.96 (br s, 1 H, H-1b), 4.88 (d, J = 10.7 Hz, 1 H, PhCH2), 4.69 (d, J = 11.6 Hz, 1 H, PhCH2), 4.62-4.45 (m, 7 H, PhCH2), 4.33-4.28 (m, 1 H, H-3A), 4.23 (d, J = 11.2 Hz, 1 H, PhCH2), 4.19-4.02 (m, 6 H, H-1a, H-2b, H-4b, H-5c, OCH2), 3.99-3.91 (m, 4 H, H-6ab, OCH2), 3.90-3.88 (m, 3 H, H-5b, H-6aa), 3.88 (br s, 1 H, H-4A), 3.85-3.79 (m, 2 H, H-2a, H-2c), 3.76 (s, 3 H, OCH3), 3.74 (s, 3 H, OCH3), 3.78-3.63 (m, 3 H, H-3c, H-4c, H-6ac), 3.56-3.53 (m, 1 H, H-6bc), 3.34 (dd, J = 10.4, 3.3 Hz, 1 H, H-3b), 2.70 (br s, 1 H, H-5A); 13C NMR (125 MHz, CDCl3): δ 159.7-114.2 (Ar-C), 102.6 (PhCH3), 101.9 (PhCH3), 101.5 (C-1A), 101.1 (C-1b), 91.5 (C-1c), 79.9 (C-4a), 79.2
(C-4\textsubscript{A}), 78.7 (C-3\textsubscript{A}), 75.9 (C-3\textsubscript{B}), 75.7 (PhCH\textsubscript{2}), 75.4 (C-2\textsubscript{A}), 75.0 (C-5\textsubscript{A}), 74.5 (C-2\textsubscript{C}), 73.5 (PhCH\textsubscript{2}), 73.4 (PhCH\textsubscript{2}), 72.8 (PhCH\textsubscript{2}), 72.7 (C-3\textsubscript{C}), 72.3 (PhCH\textsubscript{2}), 70.8 (C-4\textsubscript{C}), 70.7 (C-6\textsubscript{A}), 69.4 (C-6\textsubscript{B}), 69.1 (C-6\textsubscript{C}), 68.5 (OCH\textsubscript{2}), 68.2 (OCH\textsubscript{2}), 66.6 (C-5\textsubscript{A}), 65.0 (C-5\textsubscript{C}), 61.5 (C-2\textsubscript{A}), 56.0 (OCH\textsubscript{2}), 55.6 (OCH\textsubscript{2}); ESI-MS: 1358.5 [M+Na]+; Anal. Calcd. for C\textsubscript{77}H\textsubscript{81}N\textsubscript{30}I\textsubscript{8} (1335.55): C, 69.20; H, 6.11; found: C, 69.00; H, 6.35.

2-(p-Methoxyphenoxy)ethyl (2,3,4-tri-0-benzyl-\alpha-D-mannopyranosyI)-(1->2)-(3-0-benzyl-4,6-O-benzylidene-\alpha-D-mannopyranosyl)-(1->3)-2-azido-4,6-O-benzylidene-2-deoxy-\beta-D-galactopyranoside (26): To a solution of compound 25 (1.5 g, 1.12 mmol) in CH\textsubscript{2}Cl\textsubscript{2} (20 mL) was added a solution of 2,3-dichloro-5,6-dicyano-p-benzoquinone (DDQ; 500 mg, 2.20 mmol) in H\textsubscript{2}O (10 mL) and the biphasic reaction mixture was allowed to stir at room temperature for 2 h. The reaction mixture was diluted with H\textsubscript{2}O and extracted with CH\textsubscript{2}Cl\textsubscript{2} (100 mL). The organic layer was successively washed with satd. NaHCO\textsubscript{3} and water, dried (Na\textsubscript{2}SO\textsubscript{4}) and concentrated. The crude product was purified over SiO\textsubscript{2} using hexane-EtOAc (6:1) as eluant to give pure compound 26 (980 mg, 72%). White solid; m.p. 91-94 °C [EtOH]; [\alpha]\textsubscript{D}\textsubscript{25} + 10 (c 1.2, CHCl\textsubscript{3}); IR (KBr): 3470, 3064, 3031, 2926, 2872, 2114, 1509, 1454, 1311, 1233, 1176, 1105, 1075, 1028, 1002, 914, 823, 741, 698 cm\textsuperscript{-1}; \textsuperscript{1}H NMR (500 MHz, CDC\textsubscript{13}): \delta 7.43-7.13 (m, 30 H, Ar-H), 6.79-6.72 (m, 4 H, Ar-H), 5.53 (s, 1 H, PhCH\textsubscript{2}), 5.46 (s, 1 H, PhCH\textsubscript{2}), 5.05 (br s, 1 H, H-1\textsubscript{c}), 4.94 (br s, 1 H, H-1\textsubscript{b}), 4.83 (d, \textit{J} = 10.7 Hz, 1 H, PhCH\textsubscript{2}), 4.75 (d, \textit{J} = 11.4 Hz, 1 H, PhCH\textsubscript{2}), 4.55-4.47 (m, 7 H, PhCH\textsubscript{2}), 4.38 (d, \textit{J} = 8.0 Hz, 1 H, H-1\textsubscript{A}), 4.37-4.34 (m, 2 H, PhCH\textsubscript{2}), 4.16-4.11 (m, 4 H, H-3\textsubscript{A}, H-4\textsubscript{B}, OCH\textsubscript{2}), 4.08-4.05 (m, 2 H, OCH\textsubscript{2}), 3.99-3.85 (m, 6 H, H-2\textsubscript{B}, H-4\textsubscript{A}, H-5\textsubscript{B}, H-5\textsubscript{C}, H-6\textsubscript{ab\textsubscript{A}}), 3.82-3.63 (m, 5 H, H-2\textsubscript{A}, H-2\textsubscript{B}, H-2\textsubscript{C}, H-3\textsubscript{C}, H-6\textsubscript{ab\textsubscript{A}}), 3.65 (s, 3 H, OCH\textsubscript{3}), 3.63-3.49 (m, 2 H, H-3\textsubscript{B}, H-3\textsubscript{C}, H-6\textsubscript{BC}), 3.48-3.44 (m, 2 H, H-4\textsubscript{C}, H-6\textsubscript{BC}), 3.25 (bs, 1 H, H-5\textsubscript{A}); \textsuperscript{13}C NMR (125 MHz, CDC\textsubscript{13}): \delta 154.5-115.0 (Ar-C), 102.8 (PhCH), 101.7 (PhCH), 101.3 (C-1\textsubscript{A}), 100.4 (C-1\textsubscript{B}), 95.4 (C-1\textsubscript{C}), 79.7 (C-4\textsubscript{B}), 79.5 (C-4\textsubscript{A}), 76.6 (C-3\textsubscript{A}), 76.3 (C-3\textsubscript{B}), 75.8 (PhCH\textsubscript{2}), 75.6 (C-2\textsubscript{B}), 75.2 (C-5\textsubscript{B}), 74.3 (PhCH\textsubscript{2}), 73.5 (C-2\textsubscript{C}), 73.3 (C-3\textsubscript{C}), 72.8 (PhCH\textsubscript{2}), 72.3 (PhCH\textsubscript{2}), 70.5 (C-4\textsubscript{C}), 69.4 (C-6\textsubscript{A}), 69.0 (C-6\textsubscript{B}), 68.6 (OCH\textsubscript{2}), 68.3 (OCH\textsubscript{2}), 66.8 (C-5\textsubscript{A}), 64.8 (C-5\textsubscript{C}), 62.9 (C-6\textsubscript{C}), 61.5 (C-2\textsubscript{A}), 56.0 (OCH\textsubscript{2}); ESI-MS: 1238.4 [M+Na]+; Anal. Calcd. for C\textsubscript{69}H\textsubscript{73}N\textsubscript{3}O\textsubscript{17} (1215.49): C, 68.13; H, 6.05; found: C, 67.90.; H, 6.30.

2-(p-Methoxyphenoxy)ethyl (4-O-acetyl-2,3,6-tri-0-benzyl-\alpha-D-galactopyranosyI)-(1->6)-(2,3,4-tri-0-benzyl-\alpha-D-mannopyranosyI)-(1->2)-(3-0-benzyl-4,6-O-benzylidene-\alpha-D-mannopyranosyl)-(1->3)-2-azido-4,6-O-benzylidene-2-deoxy-\beta-D-galactopyranoside (27): To a solution of compound 26 (900 mg, 0.74 mmol) and compound 17 (475 mg, 0.88 mmol) in
anhydrous CH2Cl2 (5 mL) was added MS 4 Å (1 g) and the reaction mixture was allowed to stir at room temperature for 30 min under argon. The reaction mixture was cooled to -25 °C and NIS (240 mg, 1.06 mmol) followed by TfOH (3 µL) were added to it. After stirring at the same temperature for 45 min the reaction mixture was filtered through a Celite® bed and washed with CH3Cl2 (50 mL). The combined organic layer was washed with 5% Na2S2O3, satd. NaHCO3, water in succession, dried (Na2SO4) and concentrated under reduced pressure. The crude product was purified over SiO2 using hexane-EtOAc (6:1) as eluant to give pure compound 27 (950 mg, 76%). White solid; m.p. 71-74 °C [EtOH]; [α]D25 + 9 (c 1.2, CHCl3); IR (KBr): 3452, 3033, 2924, 2920, 2114, 1507, 1457, 1369, 1287, 1232, 1067, 915, 824, 749 cm⁻¹; 1H NMR (500 MHz, CDCl3): δ 7.46-7.05 (m, 45 H, Ar-H), 6.79-6.71 (m, 4 H, Ar-H), 5.52 (s, 1 H, PhC//=), 5.45 (br s, 1 H, H-4D), 5.42 (s, 1 H, PhCH3), 5.11 (br s, 1 H, H-1C), 4.95 (br s, 1 H, H-1B), 5.74-4.66 (m, 3 H, PhCH2), 4.60-4.35 (m, 9 H, PhC//=2), 4.34-4.27 (m, 3 H, H-1D, PhCH2), 4.26 (d, J = 7.9 Hz, 1 H, H-1α), 4.21-4.12 (m, 1 H, H-6aB), 4.11-3.95 (m, 8 H, H-3A, H-4A, H-5D, H-6bB, H-6abA, OCH2), 3.74-3.55 (m, 8 H, H-2B, H-4B, H-5B, H-5C, H-6abD, OCH2), 3.66 (s, 3 H, OCH3), 3.54-3.50 (m, 1 H, H-6bC), 3.49-3.37 (m, 2 H, H-2C, H-3C), 3.36-3.30 (m, 2 H, H-3B, H-4C), 3.28-3.26 (m, 1 H, H-2D), 3.08 (br s, 1 H, H-5A), 1.91 (s, 3 H, COCH3); 13C NMR (125 MHz, CDCl3): δ 170.3 (COCH3), 154.2-114.7 (Ar-C), 104.4 (JC-1H-1 = 155 Hz, C-1A), 102.4 (JC-1H-1 = 172.8 Hz, C-1D), 101.6 (PhCH3), 101.0 (PhCH), 100.3 (JC-1H-1 = 170.5 Hz, C-1B), 96.1 (JC-1H-1 = 171.3 Hz, C-1C), 79.4 (2 C, C-2D, C-4C), 79.0 (C-4B), 78.7 (C-4A), 76.6 (C-3C), 76.0 (C-3A), 75.4 (C-3b), 75.3 (C-2B), 74.8 (C-5b), 74.6 (C-3D), 73.7 (2 C, 2 PhCH2), 73.6 (PhCH2), 72.4 (PhCH2), 72.1 (C-2C), 72.0 (PhCH2), 71.7 (PhCH2), 70.4 (C-4b), 69.2 (C-6A), 69.0 (C-6C), 68.7 (C-6D), 68.3 (OCH2), 68.0 (OCH2), 67.8 (C-6B), 66.7 (C-5A), 66.4 (C-5D), 64.6 (C-5C), 51.1 (C-2A), 55.7 (OCH3), 20.9 (COCH3); ESI-MS: 1712.6 [M+Na]+; Anal. Calcd. for C98H133N3O23 (1689.69): C, 69.61; H, 6.14; found: C, 69.43; H, 6.38.

2-(p-Methoxyphenoxy)ethyl (2,3,6-tri-O-benzyl-α-D-galactopyranosyl)-(1→6)-(2,3,4-tri-O-benzyl-α-D-mannopyranosyl)-(1→2)-(3-O-benzyl-4,6-O-benzylidene-α-D-mannopyranosyl)-(1→3)-2-azido-4,6-O-benzylidene-2-deoxy-β-D-galactopyranoside (28): A solution of compound 27 (900 g, 0.53 mmol) in 0.1 M CH3ONa in CH3OH (10 mL) was allowed stir at room temperature for 1 h and neutralized with Amberlite IR 120 (H⁺) resin. The reaction mixture was filtered and concentrated under reduced pressure to give crude product, which was purified over SiO2 using hexane-EtOAc (6:1) as eluant to give pure compound 28 (875 mg, quantitative). White solid; m.p. 77-79 °C [EtOH]; [α]D25 + 15.4 (c 1.2, CHCl3); IR (KBr): 3452, 3033, 2924, 2920, 2114, 1507, 1457, 1369, 1287, 1232, 1067, 895, 824, 749 cm⁻¹; 1H NMR (500 MHz,
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CDC13): δ 7.35-7.17 (m, 41 H, Ar-H), 6.87-6.80 (m, 4 H, Ar-H), 5.59 (s, 1 H, PhCH), 5.57 (s, 1 H, PhCH), 5.10 (br s, 1 H, H-1c), 4.82 (d, J = 11.0 Hz, 1 H, PhCH2), 4.75 (d, J = 10.8 Hz, 1 H, PhCH2), 4.73-4.34 (m, 11 H, PhCH2), 4.32-4.28 (m, 2 H, H-1D, PhCH2), 4.24-4.16 (m, 1 H, H-6ab), 4.20 (d, J = 7.8 Hz, 1 H, H-1A), 4.15-4.10 (m, 3 H, H-3a, OCH2), 4.06 (br s, 1 H, H-4a), 4.03-3.85 (m, 11 H, H-2B, H-4B, H-4D, H-5B, H-5C, H-5D, H-6abA, H-6abB, H-6abD), 3.78-3.69 (m, 4 H, H-2A, H-2C, H-3D, H-6ac), 3.73 (s, 3 H, OCH3), 3.64-3.61 (m, 1 H, H-6bC), 3.59 (dd, J = 10.3, 3.2 Hz, 1 H, H-3C), 3.54 (t, J = 7.9 Hz each, 1 H, H-4D), 3.53-3.35 (m, 2 H, H-2D, H-3b), 3.22 (br s, 1 H, H-5a); 13C NMR (125 MHz, CDC13): δ 153.3-115.0 (Ar-C), 105.8 (C-1A), 102.6 (C-1D), 101.9 (PhCH), 101.3 (PhCH), 100.9 (C-1B), 96.9 (C-1c), 81.1 (C-2b), 79.8 (C-4c), 79.4 (C-4b), 79.1 (C-4a), 76.2 (C-3a), 75.6 (PhCH2), 75.4 (PhCH2), 75.3 (C-3b), 75.1 (C-2a), 74.8 (C-5a), 73.9 (2 C, PhCH2-C-3b), 73.4 (C-2c), 72.9 (C-3c), 72.7 (PhCH2), 72.6 (PhCH2), 72.0 (PhCH2), 71.9 (PhCH2), 71.1 (C-4d), 69.3 (C-6a), 69.1 (2 C, C-6c, C-6b), 69.0 (C-6b), 68.4 (OCH2), 68.3 (OCH2), 66.9 (C-5d), 66.8 (C-5a), 64.9 (C-5c), 61.6 (C-2a), 56.0 (OCH3); ESI-MS: 1670.6 [M+Na]+; Anal. Calcd. for C96H101N3O22 (1647.68): C, 69.93; H, 6.17; found: C, 69.72; H, 6.40.

2-(p-Methoxyphenoxy)ethyl (2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyl)-(1→4)-(2,3,6-tri-O-benzyl-α-D-galactopyranosyl)-(1→6)-(2,3,4-tri-O-benzyl-α-D-mannopyranosyl)-(1→2)-(3-O-benzyl-4,6-O-benzylidene-α-D-mannopyranosyl)-(1→3)-2-azido-4,6-O-benzylidene-2-deoxy-β-D-galactopyranoside (29): To a solution of compound 28 (850 mg, 0.51 mmol) and compound 21 (530 mg, 0.71 mmol) in anhydrous CH2Cl2 (5 mL) was added TMSOTf (15 µL) at -10 °C under argon and the reaction mixture was allowed to stir at same temperature for 1 h. The reaction mixture was quenched with Et3N (0.1 mL) and diluted with CH2Cl2 (50 mL). The organic layer was successively washed with satd. NaHCO3 and water, dried (Na2SO4) and concentrated under reduced pressure. The crude product was purified over SiO2 using hexane-EtOAc (4:1) as eluant to give pure compound 29 (820 mg, 72%). White solid; m.p. 82-84°C [EtOH]; [α]D25 +12.3 (c 1.2, CHCl3); IR (KBr): 3450, 3034, 2926, 2873, 2114, 1732, 1507, 1455, 1369, 1267, 1099, 916, 826, 741, 703 cm⁻¹; 1H NMR (500 MHz, CDC13): δ 8.16-6.82 (m, 65 H, Ar-H), 5.92 (t, J = 9.6 Hz each, 1 H, H-3E), 5.72 (t, J = 9.6 Hz each, 1 H, H-4E), 5.60 (s, 1 H, PhCH), 5.58 (s, 1 H, PhCH), 5.50 (t, J = 8.0 Hz each, 1 H, H-2E), 5.20 (d, J = 7.9 Hz, 1 H, H-1E), 5.11 (br s, 1 H, H-1C), 5.07 (br s, 1 H, H-1B), 4.73-4.61 (m, 4 H, PhCH2), 4.58-4.47 (m, 7 H, H-6ab, PhCH2), 4.46 (br s, 1 H, H-1D), 4.44-4.32 (m, 5 H, PhCH2), 4.30-4.18 (m, 3 H, H-3A, OCH2), 4.16-4.08 (m, 5 H, H-2B, H-4A, H-6abB), 4.14 (d, J = 7.8 Hz, 1 H, H-1A), 4.06-3.94 (m, 8 H, H-4B, H-4D, H-5B, H-5C, H-5D, H-6abB, OCH2), 3.91-3.73 (m, 8 H, H-2A, H-2D, H-5E, H-6abC,
H-6abD, H-6ac), 3.75 (s, 3 H, OCH₃), 3.71-3.60 (m, 3 H, H-3c, H-4c, H-6bc), 3.41-3.27 (m, 4 H, H-2c, H-2d, H-3b, H-5a); ¹³C NMR (125 MHz, CDCl₃): δ 166.3 (COPh), 166.1 (COPh), 166.4 (COPh), 165.3 (COPh), 154.4-115.0 (Ar-C), 105.1 (C-1a), 102.6 (C-1e), 102.3 (PhCH), 101.8 (PhCH), 101.2 (C-1d), 101.2 (C-1b), 97.2 (C-1c), 81.6 (C-2d), 80.2 (C-4c), 79.6 (C-4b), 70.2 (C-4a), 76.1 (C-3a), 75.5 (2 C, C-2b, C-3b), 75.3 (2 C, C-5b, PhCH₂), 75.2 (C-3d), 75.0 (C-2c), 74.0 (C-3c), 73.9 (PhCH₂), 73.7 (PhCH₂), 73.5 (PhCH₂), 73.4 (C-2d), 73.0 (C-5b), 72.8 (C-5d), 72.6 (C-3e), 72.4 (PhCH₂), 71.9 (C-2e), 71.3 (2 C, 2 PhCH₂), 70.1 (C-4e), 69.9 (3 C, C-6a, C-6c, C-6b), 69.0 (C-6b), 68.6 (OCH₂), 68.4 (OCH₂), 68.4 (C-5a), 65.0 (C-5c), 63.1 (C-6e), 61.6 (C-2a), 36.0 (OCH₃); MALDI-MS: 718.2 [M+Na⁺]; Anal. Calcd. for C₂₉H₄₅NO₁₈ (695.26): C, 70.10; H, 5.75; found: C, 69.87; H, 6.00.

2-(p-Methoxyphenoxy)ethyl (α-D-mannopyranosyl)-(1→2)-(α-D-mannopyranosyl)-(1→3)-2-acetamido-2-deoxy-β-D-galactopyranoside (1): To a solution of compound 29 (300 mg, 0.25 mmol) in CH₃OH (10 mL) was added 20% Pd(OH)₂-C (150 mg) and the reaction mixture was allowed to stir at room temperature under a positive pressure of hydrogen for 24 h. The reaction mixture was filtered through a Celite® bed and evaporated to dryness under reduced pressure. A solution of the crude product in acetic anhydride-pyridine (2 mL, 1:1 v/v) was kept at room temperature for 2 h and the solvents were removed under reduced pressure. A solution of the acetylated product in 0.1 M CH₃ONa (5 mL) was allowed to stir at room temperature for 2 h and neutralized with Dowex 50W X8 (H⁺) resin. The reaction mixture was filtered and evaporated to dryness to give compound 1, which was purified over Sephadex® LH-20 using CH₃OH (60 mL) as eluant to give pure compound 1 (115 mg, 66%). White powder; [α]₂⁰ + 16 (c 1.2, CH₃OH); IR (KBr): 3434, 2945, 1628, 1378, 1148, 1078, 668 cm⁻¹; ¹H NMR (500 MHz, CD₃OD): δ 6.88-6.83 (m, 6 H, Ar-H), 5.16 (br s, 1 H, H-1c), 4.85 (br s, 1 H, H-1b), 4.43 (d, J = 8.4 Hz, 1 H, H-1a), 4.04-4.00 (m, 3 H, H-3a, OCH₂), 3.97 (m, 2 H, OCH₂), 3.88-3.87 (m, 1 H, H-2b), 3.82-3.81 (m, 1 H, H-2c), 3.79-3.75 (m, 3 H, H-4a, H-6abc), 3.70-3.64 (m, 4 H, H-3c, H-4c, H-6abbc), 3.63 (s, 3 H, OCH₃), 3.60-3.52 (m, 4 H, H-4b, H-5c, H-6abba), 3.48-3.39 (m, 3 H, H-3b, H-5a, H-5b), 3.25-3.21 (m, 1 H, H-2a), 1.18 (s, 3 H, COCH₃); ¹³C NMR (125 MHz, CD₃OD): δ 172.7 (COCH₃), 103.2 (C-1b), 102.1 (C-1a), 94.9 (C-1c), 79.7 (C-2c), 75.7 (C-5a), 75.2 (C-5b), 74.0 (C-3b), 73.9 (C-2b), 71.4 (C-5c), 70.9 (C-4c), 70.8 (C-4b), 68.2 (OCH₂), 68.1 (OCH₂), 68.0 (C-4a), 67.7 (C-3c), 63.7 (C-3a), 62.4 (C-6b), 62.3 (C-6a), 61.7 (C-6c), 55.1 (OCH₃), 53.5 (C-2a), 22.2 (COCH₃); ESI-MS: 718.2 [M+Na⁺]; Anal. Calcd. for C₂₉H₄₅NO₁₈ (695.26): C, 50.07; H, 6.52; found: C, 49.85; H, 6.77.
2-(p-Methoxyphenoxy)ethyl (sodium β-D-glucopyranosyluronate)-(1→4)-(α-D-galactopyranosyl)-(1→6)-(α-D-mannopyranosyl)-(1→2)-(α-D-mannopyranosyl)-(1→3)-2-acetamido-2-deoxy-β-D-galactopyranoside (2): A solution of compound 17 (0.7 g, 0.31 mmol) in 0.1 M CH₃ONa in CH₃OH (20 mL) was stirred at room temperature for 3 h, neutralized with Dowex 50W X8 (H⁺) resin, filtered and concentrated. To a solution of the crude product in CH₂Cl₂ (20 mL) and H₂O (3.5 mL) were added aq. NaBr (1 mL; 1 M), aq. TBAB (2 mL; 1 M), TEMPO (80 mg, 0.5 mmol), satd. NaHCO₃ (8 mL) and 4% aq. NaOCl (10 mL) and it was stirred at 0-5 °C for 3 h and neutralized with 1 N HCl. To the reaction mixture were added tert-butanol (25 mL), 2-methyl-but-2-ene (30 mL; 2 M solution in THF), aq. NaClO₂ (1 g in 5 mL) and aq. NaH₂PO₄ (1 g in 5 mL) and it was allowed to stir at room temperature for 3 h. The reaction mixture was diluted with satd. aq. NaH₂PO₄ and extracted with CH₂Cl₂ (100 mL). The organic layer was washed with water, dried (Na₂SO₄) and concentrated to dryness. To a solution of the crude product in CH₃OH (30 mL) was added 20% Pd(OH)₂-C (200 mg) and it was allowed to stir at room temperature under a positive pressure of hydrogen for 24 h. The reaction mixture was filtered through a Celite® bed and evaporated to dryness. A solution of the crude product in acetic anhydride-pyridine (3 mL, 1:1 v/v) was kept at room temperature for 4 h and the solvents were removed. A solution of the acetylated product in 0.1 M CH₃ONa (10 mL) was allowed to stir at room temperature for 2 h, neutralized with Dowex 50W X8 (H⁺) resin, filtered and evaporated to give compound 2, which was purified over Sephadex® LH-20 using CH₃OH-H₂O (60 mL; 4:1 v/v) as eluant to give pure compound 2 (210 mg, 64%). White powder; [α]D²⁵ + 21 (c 1.2, CH₃OH); IR (KBr): 3432, 2943, 1607, 1377, 1145, 1089, 665 cm⁻¹; ¹H NMR (500 MHz, CD₃OD): δ 6.79-6.71 (m, 4 H, Ar-H), 5.19 (s, 1 H, H-1c), 4.77 (br s, 1 H, H-1B), 4.62 (d, J = 8.1 Hz, 1 H, H-1E), 4.48 (m, 2 H, H-3A, H-2B), 4.40 (d, J = 7.8 Hz, 1 H, H-1A), 4.17 (br s, 1 H, H-1D), 4.15-4.10 (m, 2 H, H-4A, H-4D), 4.08-3.93 (m, 4 H, H-4B, H-5D, OCH₂), 3.88-3.82 (m, 1 H, H-5B), 3.80-3.70 (m, 4 H, H-5C, H-5E, OCH₂), 3.68-3.57 (m, 6 H, H-2E, H-3E, H-6abB, H-6abD), 3.63 (br s, 3 H, OCH₃), 3.54-3.35 (m, 7 H, H-3C, H-4C, H-4E, H-6abA, H-6abcC), 3.31-3.23 (m, 2 H, H-2A, H-3D), 3.21-3.10 (m, 4 H, H-2C, H-2D, H-3B, H-5A); ¹³C NMR (125 MHz, CD₃OD): δ 174.6 (COONa), 172.4 (COCH₃), 105.4 (C-1A), 105.0 (C-1D), 103.8 (C-1B), 101.6 (C-1E), 101.0 (C-1C), 80.8 (C-2E), 78.6 (C-4A), 77.3 (C-4A), 77.1 (C-4C), 75.0 (C-3A), 74.8 (C-3B), 74.1 (C-2B), 73.9 (C-2D), 73.2 (C-2C), 72.5 (C-3D), 71.3 (C-4D), 71.1 (C-5E), 70.9 (2 C, C-5D, C-3E), 70.6 (2 C, C-3C, C-4E), 68.2 (2 C, 2 OCH₂), 67.6 (2 C, C-5A, C-5C), 66.9 (C-5B), 62.0 (C-6B), 61.8 (C-6D), 60.9 (C-6A), 60.5 (C-6C), 55.1 (OCH₃), 53.4 (C-2A), 22.2 (COCH₃); ESI-MS: 1056.3 [M+1]⁺; Anal. Calcd. for C₄₁H₆₀NNaO₉ (1055.33): C, 46.64; H, 5.92; found: C, 46.41; H, 6.18.
2.2.5. Representative NMR spectra of synthesized compounds

$^1$H and $^{13}$C NMR spectra of ethyl 2,3-di-O-acetyl-4,6-O-(p-methoxy)benzylidene-1-thio-$\alpha$-D-mannopyranoside (13) (CDCl$_3$).
$^1$H and $^{13}$C NMR spectra of ethyl 2,3,4-tri-O-acetyl-6-O-(p-methoxybenzyl)-1-thio-α-D-mannopyranoside (14) (CDCl$_3$).
$^1$H and $^{13}$C NMR spectra of 2-(p-methoxyphenoxy)ethyl (2-O-acetyl-3-O-benzyl-4,6-O-benzylidene-$\alpha$-D-mannopyranosyl)-(1$\rightarrow$3)-2-azido-4,6-O-benzylidene-2-deoxy-$\beta$-D-galactopyranoside (22) (CDCl$_3$-CCl$_4$).
$^{13}$C DEPT 135 and 2D HSQC (selected region) spectra of 2-(p-methoxyphenoxo)ethyl (2-O-acetyl-3-O-benzyl-4,6-O-benzylidene-α-D-mannopyranosyl)-(1→3)-2-azido-4,6-O-benzylidene-2-deoxy-β-D-galactopyranoside (22).
$^1$H, $^{13}$C and 2D HSQC (selected region) NMR spectra of 2-(p-methoxyphenoxy)ethyl (3-O-benzyl-4,6-O-benzylidene-$\alpha$-D-mannopyranosyl)-(1$\rightarrow$3)-2-azido-4,6-O-benzylidene-2-deoxy-$\beta$-D-galactopyranoside (23) (CDCl$_3$).
$^1$H and $^{13}$C NMR spectra of 2-(p-methoxyphenoxy)ethyl [2,3,4-tri-O-acetyl-6-O-(4-methoxybenzyl)-α-D-mannopyranosyl]-(1→2)-(3-O-benzyl-4,6-O-benzylidene-α-D-mannopyranosyl)-(1→3)-2-azido-4,6-O-benzylidene-2-deoxy-β-D-galactopyranoside (24) (CDCl$_3$).
$^{13}$C DEPT 135 and 2D HSQC (selected region) spectra of 2-(p-methoxyphenoxo)ethyl [2,3,4-tri-O-acetyl-6-O-(p-methoxybenzyl)-α-D-mannopyranosyl]-(1→2)-(3-O-benzyl-4,6-O-benzylidene-α-D-mannopyranosyl)-(1→3)-2-azido-4,6-O-benzylidene-2-deoxy-β-D-galactopyranoside (24).
$^1$H and $^{13}$C NMR spectra of 2-(p-methoxyphenoxy)ethyl [2,3,4-tri-O-benzyl-6-O-(4-methoxybenzyl)-α-D-mannopyranosyl]-(1→2)-(3-O-benzyl-4,6-O-benzylidene-α-D-mannopyranosyl)-(1→3)-2-azido-4,6-O-benzylidene-2-deoxy-β-D-galactopyranoside (CDCl$_3$-CCl$_4$).
$^{13}$C DEPT 135 and 2D HSQC (selected region) spectra of 2-(p-methoxyphenoxy)ethyl [2,3,4-tri-$O$-benzyl-6-$O$-(p-methoxybenzyl)-$\alpha$-$D$-mannopyranosyl]+(1→2)-(3-$O$-benzyl-4,6-$O$-benzylidene-$\alpha$-$D$-mannopyranosyl)-(1→3)-2-azido-4,6-$O$-benzylidene-2-deoxy-$\beta$-$D$-galactopyranoside (25).
$^1$H and $^{13}$C NMR spectra of 2-(p-methoxyphenoxy)ethyl (2,3,4-tri-O-benzyl-$\alpha$-D-mannopyranosyl)-(1→2)-(3-O-benzyl-4,6-O-benzylidene-$\alpha$-D-mannopyranosyl)-(1→3)-2-azido-4,6-O-benzylidene-2-deoxy-$\beta$-D-galactopyranoside (26) (CDCl$_3$-CCl$_4$).
$^{1}$H and $^{13}$C NMR spectra of 2-(p-methoxyphenoxy)ethyl (4-0-acetyl-2,3,6-tri-O-benzyl-$\alpha$-D-galactopyranosyl)-(1$\rightarrow$6)-(2,3,4-tri-O-benzyl-$\alpha$-D-mannopyranosyl)-(1$\rightarrow$2)-(3-O-benzyl-4,6-O-benzylidene-$\alpha$-D-mannopyranosyl)-(1$\rightarrow$3)-2-azido-4,6-O-benzylidene-2-deoxy-$\beta$-D-galactopyranoside (27) (CDCl$_3$-CCl$_4$).
$^1$H and $^{13}$C NMR spectra of 2-(p-methoxyphenoxy)ethyl \((2,3,6\text{-tri-}O\text{-benzyl-}\alpha\text{-D-}
galactopyranosyl)-(1\rightarrow6)-(2,3,4\text{-tri-}O\text{-benzyl-}\alpha\text{-D-mannopyranosyl})-(1\rightarrow2)-(3\text{-O-benzyl-}4,6\text{-O-}
benzyldiene-\alpha\text{-D-mannopyranosyl})-(1\rightarrow3)-2\text{-azido-}4,6\text{-O-benzylidene-2-deoxy-}\beta\text{-D-}
galactopyranoside (28) (CDCl$_3$-CCl$_4$).
13C DEPT 135 and 2D HSQC (selected region) spectra of 2-((p-methoxyphenoxy)ethyl (2,3,6-tri-O-benzyl-α-D-galactopyranosyl)-(1→6)-(2,3,4-tri-O-benzyl-α-D-mannopyranosyl)-(1→2)-(3-O-benzyl-4,6-O-benzylidene-α-D-mannopyranosyl)-(1→3)-2-azido-4,6-O-benzylidene-2-deoxy-β-D-galactopyranoside (28).
$^1$H and $^{13}$C NMR spectra of 2-(p-methoxyphenoxy)ethyl (2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyl)-(1→4)-(2,3,6-tri-O-benzyl-α-D-galactopyranosyl)-(1→6)-(2,3,4-tri-O-benzyl-α-D-mannopyranosyl)-(1→2)(3-O-benzyl-4,6-O-benzylidene-α-D-mannopyranosyl)-(1→3)-2-azido-4,6-O-benzylidene-2-deoxy-β-D-galactopyranoside (29) (CDCl$_3$-CCl$_4$).
$^{13}$C DEPT 135 and 2D HSQC (selected region) spectra of 2-(p-methoxyphenoxy)ethyl (2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyl)-(1→4)-(2,3,6-tri-O-benzyl-α-D-galactopyranosyl)-(1→6)-(2,3,4-tri-O-benzyl-α-D-mannopyranosyl)-(1→2)-(3-O-benzyl-4,6-O-benzylidene-α-D-mannopyranosyl)-(1→3)-2-azido-4,6-O-benzylidene-2-deoxy-β-D-galactopyranoside (29).
$^1$H and $^{13}$C NMR spectra of 2-(p-methoxyphenoxy)ethyl (α-D-mannopyranosyl)-(1→2)-(α-D-mannopyranosyl)-(1→3)-2-acetamido-2-deoxy-β-D-galactopyranoside (1) (CD$_3$OD).
13C DEPT 135 and 2D HSQC (selected region) spectra of 2-(p-methoxyphenoxy)ethyl (α-D-mannopyranosyl)-(1→2)-(α-D-mannopyranosyl)-(1→3)-2-acetamido-2-deoxy-β-D-galactopyranoside (1).
1H, 13C and 2D HSQC (selected region) NMR spectra of 2-(p-methoxyphenoxy)ethyl (sodium β-D-glucopyranosyluronate)-(1→4)-(α-D-galactopyranosyl)-(1→6)-(α-D-mannopyranosyl)-(1→2)-(α-D-mannopyranosyl)-(1→3)-2-acetamido-2-deoxy-β-D-galactopyranoside (CD3OD).
2.3. Convergent Synthesis of the
Tetrasaccharide Repeating Unit of the
O-Antigen of Shigella boydii Type 9
2.3.1. Introduction

Diarrhoeal disease is a common cause of death in the tropical countries and it is the second mostly causing infant deaths worldwide. *Shigella* is one of the well-studied human pathogens cause diarrhoeal disease and dysentery, which is termed as shigellosis. *Shigella* strains are classified into four species: *Shigella boydii*, *Shigella dysenteriae*, *Shigella flexneri* and *Shigella sonnei*. Recently, L’vov *et al.* reported the structure of the repeating unit of the O-antigen of *Shigella boydii* type 9, which is a tetrasaccharide containing a D-glucuronic acid moiety (Figure 1).³⁷

\[
\rightarrow 3)-\alpha-D-Glc\alpha-(1\rightarrow 3)-\alpha-L-Rhap-(1\rightarrow 4)-\alpha-D-Glc\beta-(1\rightarrow 4)-\beta-D-Glc\alpha-(1\rightarrow
\]

**Figure 1:** Structure of the tetrasaccharide repeating unit of the cell wall O-antigen of *Shigella boydii* type 9.

The recent thrust in the medicinal chemistry is to develop effective therapeutics to control the infections from the drug-resistant bacterial strains. Emergence of the drug resistant *Shigella* infections requires development of the newer therapeutics than the earlier used anti-shigellosis agents.⁵ Antibodies against the O-specific polysaccharide of a particular *Shigella* strain could be useful in the development of therapeutics to control *Shigella* infections.⁶ A number of reports have been cited earlier to develop glycoconjugate based therapy to control *Shigella* infections.⁷ In order to develop a glycoconjugate based therapeutic agent from the O-antigen, it is essential to perform several immunochemical studies with the glycoconjugates derived from the tetrasaccharide repeating unit. Since a significant quantity of the tetrasaccharide required for this purpose, which can not be accessible from the natural source, chemical synthesis could allow getting access to this molecule. A convergent chemical synthesis of the tetrasaccharide as its *p*-methoxyphenyl glycoside (1) corresponding to the O-antigen of *Shigella boydii* type 9 using [2+2] block glycosylation strategy is presented here (Figure 2).

**Figure 2:** Structure of the synthesized tetrasaccharide corresponding to the O-antigen of *Shigella boydii* type 9.
2.3.2. Results and Discussion

The retrosynthetic strategy for the synthesis of tetrasaccharide fragments corresponding to the O-antigen of *Shigella boydii* type 9 as its p-methoxyphenyl glycoside led to a number of differentially protected monosaccharide intermediates (Scheme-1). A number of notable features are present in the synthetic strategy, which include (a) convergent [2+2] block glycosylation; (b) application of recently developed environmentally benign reaction conditions for protecting group manipulations and glycosylations such as, (i) regioselective ring opening of the benzylidene acetal using a combination of triethylsilane and iodine\(^{27}\) (ii) direct one-pot conversion of *O*-acetyl group to *O*-benzyl group\(^{26}\) (iii) activation of glycosyl trichloroacetimidate and thioglycoside donors by perchloric acid supported over silica (HClO\(_4\)-SiO\(_2\))\(^{38-40}\) and late stage TEMPO mediated selective oxidation\(^{36}\) of the primary hydroxyl group to the carboxylic group under a phase transfer condition without affecting the secondary hydroxyl groups; (c) use of *p*-methoxyphenyl (PMP) group as anomeric protecting group, which can be easily removed under oxidative condition for the preparation of glycoconjugate derivatives.

![Scheme 1: Retrosynthetic strategy for the synthesis of compound 1.](image-url)
2.3.2.1. Preparation of p-methoxyphenyl (2,3-di-O-acetyl-6-O-benzyl-α-D-glucopyranosyl)-(1→4)-2,3,6-tri-O-acetyl-β-D-glucopyranoside (5)

The synthesis of the compound 5 was started from D-maltose octaacetate (2). Treatment of compound 2 with p-methoxyphenol in the presence of borontrifluoride diethyletherate furnished p-methoxyphenyl (2,3,4,6-tetra-O-acetyl-α-D-glucopyranosyl)-(1→4)-2,3,6-tri-O-acetyl-α-D-glucopyranoside (3) in 90% yield. Saponification of compound 3 using sodium methoxide followed by benzylidene acetal formation using benzaldehyde dimethylacetal in the presence of p-toluenesulfonic acid and acetylation using acetic anhydride and pyridine furnished p-methoxyphenyl (2,3-di-O-acetyl-4,6-(9-benzylidene-α-D-glucopyranosyl)-(1→4)-2,3,6-tri-O-acetyl-β-D-glucopyranoside (4) in 91% yield. Regioselective reductive ring opening of the benzylidene acetal in compound 4 using a combination of triethylsilane and iodine furnished p-methoxyphenyl (2,3-di-O-acetyl-6-O-benzyl-α-D-glucopyranosyl)-(1→4)-2,3,6-tri-O-acetyl-β-D-glucopyranoside (5) in 82% yield (Scheme 2).

![Scheme 2: Reagents](image)

**Scheme 2**: Reagents: (a) p-methoxy phenol, CH₂Cl₂, 0 °C- r t, 5 h, 90%; (b) 0.1 M CH₃ONa, CH₃OH, r t, 4 h, quantitative; (c) PhCH(OMe)₂, p-TsOH, CH₃CN, r t, 10 h; (d) Ac₂O, pyridine, r t, 2 h, 91%; (e) Et₃SiH, I₂, 0-5 °C, 30 min, 82%.

2.3.2.2. Preparation of 2,4-di-O-benzyl-1-thio-α-L-rhamnopyranoside (9)

Acetylation of L-rhamnose (6) using acetic anhydride and HClO₄-SiO₂ followed by thioglycosylation using ethanethiol and borontrifluoride diethyletherate gave ethyl 2,3,4-tri-O-acetyl-1-thio-α-L-rhamnopyranoside (7) in 90% overall yield. Compound 7 was subjected to a
reaction sequence involving deacetylation using sodium methoxide, 2,3-O-isopropylidene ketal formation using 2,2-dimethoxypropane and p-toluenesulfonic acid\textsuperscript{44} and benzylation using benzyl bromide and sodium hydroxide\textsuperscript{36} to furnish ethyl 4-O-benzyl-2,3-O-isopropylidene-1-thio-α-L-rhamnopyranoside (8) in 86% overall yield. Removal of isopropylidene ketal\textsuperscript{45} from compound 8 using 80% aq. acetic acid followed by selective benzylation\textsuperscript{46} in a biphasic reaction condition furnished ethyl 2,4-di-O-benzyl-1-thio-α-L-rhamnopyranoside (9) in 73% yield (Scheme 3).

Scheme 3: Reagents: (a) (i) Ac\textsubscript{2}O, HClO\textsubscript{4}-SiO\textsubscript{2}, r t, 10 min; (ii) EtSH, BF\textsubscript{3}·OEt\textsubscript{2}, CH\textsubscript{2}Cl\textsubscript{2}, 5-10 °C, 5 h, 90%; (b) (i) 0.1 M CH\textsubscript{3}ONa, CH\textsubscript{3}OH, r t, 3 h; (ii) 2,2-dimethoxypropane, DMF, p-TsOH, r t, 10 h; (c) benzyl bromide, NaOH, THF, r t, 2 h, 86%; (d) 80% aq. AcOH, 80 °C, 1.5 h; (e) 5% aq. NaOH-CH\textsubscript{2}Cl\textsubscript{2} (1:1), benzyl bromide, TBAHS, r t, 3 h, 73%.

2.3.2.3. Preparation of 2-azido-2-deoxy-3,4,6-tri-O-acetyl-α-D-glucopyranosyl trichloroacetimidate (12)\textsuperscript{47}

Treatment of D-glucosamine hydrochloride (10) with trifluoromethanesulfonic azide (TfN\textsubscript{3})\textsuperscript{48} in the presence of copper (II) sulphate in a biphasic reaction mixture followed by conventional acetylation\textsuperscript{35} furnished 3,4,6-tri-O-acetyl-2-azido-2-deoxy-α,β-D-glucopyranose (11) in 72% yield. Reaction of compound 11 with benzyl amine\textsuperscript{30} furnished hemiacetal derivative, which on treatment with trichloroacetonitrile in the presence of DBU\textsuperscript{31} furnished 3,4,6-tri-O-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl trichloroacetimidate in 74% yield (Scheme 4).

Scheme 4: Reagents: a) TfN\textsubscript{3}, K\textsubscript{2}CO\textsubscript{3}, CuSO\textsubscript{4}, CH\textsubscript{3}OH-H\textsubscript{2}O-CH\textsubscript{2}Cl\textsubscript{2} (6:3:1), r t, 16 h; (b) Ac\textsubscript{2}O, pyridine, r t, 10 h, 72%; (b) (i) benzyl amine, DMF, 50 °C, 45 min; (ii) DBU, CCl\textsubscript{3}CN, CH\textsubscript{2}Cl\textsubscript{2}, 0 °C, 1 h, 74%.
2.2.2.4. Synthesis of \( p \)-methoxyphenyl \((\text{2-acetamido-2-deoxy-}\alpha\text{-D-glucopyranosyl})(1\rightarrow3)(\alpha\text{-L-rhamnopyranosyl})(1\rightarrow4)(\alpha\text{-D-glucopyranosyl})(1\rightarrow4)\)-sodium \( \beta \)-D-glucopyranosiduronate (1)

Compound 12 was allowed to couple stereoselectively with compound 9 under Schmidt's reaction condition\(^{17}\) using \( \text{HClO}_4\cdot \text{SiO}_2\)\(^{38,40}\) as glycosylation activator to give compound 13 in 81\% yield. Stereoselective formation of compound 13 was confirmed from its spectral analysis [presence of signals at \( \delta 5.35 \) (br s, H-1C), 4.95 (d, \( J = 3.6 \) Hz, H-1D) in the \( ^1H \) NMR and signals at \( \delta 92.8 \) (C-1D), 81.0 (C-1C) in the \( ^13C \) NMR spectra]. Compound 13 was transformed into thioglycoside derivative 14 in 91\% yield under a one-pot deacetylation-benzylation reaction\(^{26}\) (Scheme 5). In this case thioethyl group acts as an orthogonal anomic protecting group since it acts as a glycosyl acceptor in the case of compound 9 whereas compound 14 has been used as the glycosyl donor in the next step. Iodonium ion promoted stereoselective glycosylation of the thioglycoside derivative 14 with the disaccharide acceptor 5 in the presence of a combination of \( N \)-iodosuccinimide (NIS) and \( \text{HClO}_4\cdot \text{SiO}_2\)\(^{39,40}\) furnished tetrasaccharide derivative 15 in 82\% yield. Stereoselective formation of new \( \alpha \)-glycosyl linkage in compound 15 was confirmed from the 1D and 2D NMR spectral analysis [signals at \( \delta 5.34 \) (d, \( J = 4.5 \) Hz, H-1B), 4.97 (d, \( J = 3.5 \) Hz, H-1D), 4.95 (d, \( J = 8.0 \) Hz, H-1A), 4.89 (d, \( J = 2.0 \) Hz, H-1C) in the \( ^1H \) NMR and signals at \( \delta 99.7 \) (C-1A), 98.8 (C-1C), 96.0 (C-1B), 93.9 (C-1D) in the \( ^13C \) NMR spectra]. Because of the presence of the non-participating benzyloxy group in the C-2 position of the L-rhamnosyl moiety, involved in the glycosylation reaction, a minor amount of \( \beta \)-glycosyl linked product also formed (\( \sim 6\% \)), which was separated by the column chromatography. Appearance of \( J_{C1-H1} \) 172.0 Hz, 171.6 Hz, 170.5 Hz and 162.0 Hz values in the anomic region of \( ^1H \) coupled \( ^13C \) spectrum unambiguously supported the presence of three \( \alpha \)-linkages and one \( \beta \)-linkage in compound 15. Compound 15 was subjected to a reaction sequence involving (a) deacetylation\(^{18}\) using 0.1 M sodium methoxide in methanol; (b) TEMPO mediated selective oxidation of the primary hydroxy group leaving secondary hydroxy groups unaffected in a phase transfer reaction condition\(^{36}\) and (c) removal of benzyl ethers and reduction of azido group to amine by hydrogenation\(^{33}\) over 20\% \( \text{Pd(OH)}_2\cdot \text{C} \) followed by \( N \)-acetylation in methanol to furnish target tetrasaccharide 1 as its sodium salt and \( p \)-methoxyphenyl glycoside in 64\% yield (Scheme 6). Spectroscopic analysis of compound 1 confirmed its formation [signals at \( \delta 5.20 \) (d, \( J = 3.6 \) Hz, H-1B), 4.93 (br s, H-1D), 4.89 (br s, H-1C), 4.82 (d, \( J = 7.8 \) Hz, H-1A) in the \( ^1H \) NMR and signals at \( \delta 103.3 \) (C-1A), 102.8 (C-1B), 102.4 (C-1C), 96.7 (C-1D) in the \( ^13C \) NMR spectra].
Scheme 5: Reagents: (a) HClO₄-SiO₂, CH₂Cl₂, -15 °C, 1 h, 81%; (b) benzyl bromide, NaOH, TBAB, THF, r.t, 2 h, 91%.

Scheme 5: Reagents: (a) A-iodosuccinimide, HClO₄-SiO₂, -10 °C, 1 h, 82%; (b) 0.1 M CH₃ONa, CH₃OH, r.t, 3 h; (c) (i) NaBr, TBAB, TEMPO, CH₂Cl₂, H₂O, NaOCl, NaHCO₃, 5 °C, 2 h; (ii) tert-butanol, 2-methyl-but-2-ene, NaClO₂, NaH₂PO₄, r.t, 3 h; (d) (i) H₂, 20% Pd(OH)₂-C, CH₃OH-EtOAc, r.t, 10 h; (ii) Ac₂O, CH₃OH, r.t, 30 min, over all 64%.

2.3.3. Conclusion

In conclusion, a convenient synthetic strategy has been developed for the synthesis of the tetrasaccharide repeating unit of the O-antigen of *Shigella boydii* type 9 as its β-methoxyphenyl glycoside sodium salt using a [2+2] block synthetic strategy. Use of a block glycosylation strategy and a late-stage selective oxidation of the primary hydroxy group significantly reduced the number of protection-deprotection steps. A number of modified reaction methodologies have been applied for the preparation of intermediates. HClO₄-SiO₂ has been used as an effective acid catalyst to activate glycosyl trichloroacetimidate derivative and thioglycoside in combination with NIS avoiding the use of moisture sensitive protic acids. All intermediate steps were high yielding and glycosylation steps were stereoselective.


2.3.4. Experimental section

2.3.4.1. General methods: Please see page no. 67.

2.3.4.2. Preparation of $\text{HClO}_4\cdot\text{SiO}_2$: Perchloric acid ($\text{HClO}_4$) (1.8 g, 12.5 mmol, as a 70% aq. solution) was added dropwise to a suspension of $\text{SiO}_2$ (230-400 mesh, 23.7 g) in $\text{Et}_2\text{O}$ (70.0 mL). The mixture was concentrated and the residue was heated at 100 °C for 72 h under vacuum to furnish $\text{HClO}_4\cdot\text{SiO}_2$ (0.5 mmol/g) as a free flowing powder.$^{49,50}$

2.3.4.3. Preparation and spectral data of compounds 1-15

$p$-Methoxyphenyl 2,3,6-tri-$O$-acetyl-$4$-$O$-(2,3,4,6-tetra-$O$-acetyl-$\alpha$-$D$-glucopyranosyl)-$\beta$-$D$-glucopyranoside (3): To a solution of $\beta$-$D$-maltose octaacetate (2; 17.4 g, 25.6 mmol) and $p$-methoxy phenol (4.3 g, 38.4 mmol) in dry $\text{CH}_2\text{Cl}_2$ (100 mL) was added $\text{BF}_3\cdot\text{Et}_2\text{O}$ (6.4 mL, 51.2 mmol) and the mixture was stirred at 0 °C-room temperature for 5 h. The reaction mixture was diluted with $\text{CH}_2\text{Cl}_2$ (150 mL), washed with aq. $\text{NaHC}O_3$ and water in succession. The organic layer was dried (Na$_2$SO$_4$) and concentrated to dryness under reduced pressure. Crystallization of the crude product from diethyl ether gave pure compound 3 (15.6 g, 90%); m.p. 130-132 °C [Et$_2$O]; $[\alpha]_D +49 \ (c\ 1.0, \text{CHCl}_3)$; $^1$H NMR (500 MHz, CDC$_3$): $\delta$ 6.89 (d, $J = 8.5$ Hz, 2 H, Ar-H), 6.78 (d, $J = 8.5$ Hz, 2 H, Ar-H), 5.40 (d, $J = 4.0$ Hz, 1 H, H-1B), 5.31 (t, $J = 10.0$ Hz each, 1 H, H-3B), 5.02 (d, $J = 5.5$ Hz, 1 H, H-2A), 5.02 (d, $J = 7.5$ Hz, 1 H, H-1A), 4.97 (t, $J = 9.5$ Hz each, 1 H, H-4B), 4.82 (dd, $J = 9.0$, 4.0 Hz, 1 H, H-2B), 4.45 (dd, $J = 12.5$, 2.5 Hz, 1 H, H-6aB), 4.25-4.19 (m, 2 H, H-6aA, H-6bB), 4.06-4.00 (m, 2 H, H-4A, H-6bA), 3.93-3.92 (m, 1 H, H-5A), 3.78-3.76 (m, 1 H, H-5B), 3.74 (s, 3 H, OCH$_3$), 2.08, 2.07, 2.02, 2.01, 2.00, 1.97 (7s, 21 H, 7 COCH$_3$); $^{13}$C NMR (125 MHz, CDC$_3$): $\delta$ 170.3, 170.1, 170.0, 169.9 (2 C), 169.7, 168.9 (7 COCH$_3$), 154.6-114.5 (Ar-C), 99.8 (C-1A), 95.7 (C-1B), 75.4, 72.5, 72.2, 72.1, 70.0, 69.2, 68.5, 68.0, 62.7, 61.5, 55.5 (OCH$_3$), 21.1, 21.0, 20.9, 20.8 (2 C), 20.7 (2 C) (7 COCH$_3$); ESI-MS: 765.2 [M+Na]$^+$; Anal. Calcd. for C$_{33}$H$_{42}$O$_{19}$ (742.23): C, 53.37; H, 5.70; found: C, 53.20; H, 5.87.

$p$-Methoxyphenyl (2,3-di-$O$-acetyl-4,6-$O$-benzylidene-$\alpha$-$D$-glucopyranosyl)-(1$\rightarrow$4)-2,3,6-tri-$O$-acetyl-$\beta$-$D$-glucopyranoside (4): A solution of the compound 3 (6 g, 8.07 mmol) in 0.1 M $\text{CH}_3\text{ONa}$ in $\text{CH}_3\text{OH}$ (50 mL) was stirred at room temperature for 4 h. The reaction mixture was neutralized with Amberlite IR-120 (H$^+$) resin, filtered and the filtrate was evaporated to dryness to give an amorphous solid in quantitative yield. The dried mass thus obtained was dissolved in
anhydrous CH$_3$CN (30 mL) and benzaldehyde dimethyl acetal (1.5 mL, 10.0 mmol) was added to it followed by p-TsOH (300 mg) to make the reaction mixture acidic (pH~2). After stirring the reaction mixture at room temperature for 10 h, it was quenched with Et$_3$N (0.5 mL), filtered and evaporated to dryness. A solution of the crude mass in acetic anhydride-pyridine (15 mL, 1:1 v/v) was kept at room temperature for 2 h and concentrated under reduced pressure. The crude mass was purified over SiC$_2$ using hexane-EtOAc (2:1) as eluant to give pure compound 4 (4 g, 91%). White solid; m.p. 114-116 °C [EtOH]; $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.43-7.33 (m, 5 H, Ar-H), 6.94 (d, $J$ = 9.0 Hz, 2 H, Ar-H), 6.82 (d, $J$ = 9.0 Hz, 2 H, Ar-H), 5.48 (s, 1 H, PhCH$_2$), 5.46 (t, $J$ = 10.0 Hz each, 1 H, H-3B), 5.06 (dd, $J$ = 7.4 Hz each, 1 H, H-2A), 4.98 (d, $J$ = 7.8 Hz, 1 H, H-1B), 4.90 (dd, $J$ = 10.2, 4.2 Hz, 1 H, H-3a), 5.04 (t, $J$ = 8.5 Hz each, 1 H, H-2A), 4.96 (d, $J$ = 8.0 Hz, 1 H, H-1B), 4.80 (dd, $J$ = 12.0, 5.0 Hz, 1 H, H-3B), 4.60-4.54 (m, 2 H, PhCH$_2$), 4.50 (d, $J$ = 11.5 Hz, 1 H, H-6a), 4.22 (dd, $J$ = 12.0, 5.0 Hz, 1 H, H-6b), 3.75 (s, 3 H, OCH$_3$), 2.07, 2.03, 2.00, 1.99 (4 s, 15 H, 5 COCH$_3$); $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.42-7.30 (m, 5 H, Ar-H), 6.96 (d, $J$ = 9.0 Hz, 2 H, Ar-H), 6.84 (d, $J$ = 9.0 Hz, 2 H, Ar-H), 5.38 (d, $J$ = 4.0 Hz, 1 H, H-3B), 5.28 (t, $J$ = 9.0 Hz each, 1 H, H-3A), 5.21 (t, $J$ = 9.0 Hz each, 1 H, H-3B), 5.04 (t, $J$ = 8.5 Hz each, 1 H, H-2A), 4.96 (d, $J$ = 8.0 Hz, 1 H, H-1A), 4.80 (dd, $J$ = 12.0, 5.0 Hz, 1 H, H-6a), 4.22 (dd, $J$ = 12.0, 5.0 Hz, 1 H, H-6b), 3.75 (s, 3 H, OCH$_3$), 3.63 (m, 3 H, CH$_2$), 2.07, 2.03, 2.00, 1.99 (4 s, 15 H, 5 COCH$_3$); $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.42-7.30 (m, 5 H, Ar-H), 6.96 (d, $J$ = 9.0 Hz, 2 H, Ar-H), 6.84 (d, $J$ = 9.0 Hz, 2 H, Ar-H), 5.38 (d, $J$ = 4.0 Hz, 1 H, H-3B), 5.28 (t, $J$ = 9.0 Hz each, 1 H, H-3A), 5.21 (t, $J$ = 9.0 Hz each, 1 H, H-3B), 5.04 (t, $J$ = 8.5 Hz each, 1 H, H-2A), 4.96 (d, $J$ = 8.0 Hz, 1 H, H-1A), 4.80 (dd, $J$ = 12.0, 5.0 Hz, 1 H, H-6a), 4.22 (dd, $J$ = 12.0, 5.0 Hz, 1 H, H-6b), 3.75 (s, 3 H, OCH$_3$), 3.63 (m, 3 H, CH$_2$), 2.07, 2.03, 2.00, 1.99 (4 s, 15 H, 5 COCH$_3$); $^1$H NMR (500 MHz, CDCl$_3$): $\delta$ 7.42-7.30 (m, 5 H, Ar-H), 6.96 (d, $J$ = 9.0 Hz, 2 H, Ar-H), 6.84 (d, $J$ = 9.0 Hz, 2 H, Ar-H), 5.38 (d, $J$ = 4.0 Hz, 1 H, H-3B), 5.28 (t, $J$ = 9.0 Hz each, 1 H, H-3A), 5.21 (t, $J$ = 9.0 Hz each, 1 H, H-3B), 5.04 (t, $J$ = 8.5 Hz each, 1 H, H-2A), 4.96 (d, $J$ = 8.0 Hz, 1 H, H-1A), 4.80 (dd, $J$ = 12.0, 5.0 Hz, 1 H, H-6a), 4.22 (dd, $J$ = 12.0, 5.0 Hz, 1 H, H-6b), 3.75 (s, 3 H, OCH$_3$), 3.63 (m, 3 H, CH$_2$), 2.07, 2.03, 2.00, 1.99 (4 s, 15 H, 5 COCH$_3$); $^1$C NMR (125 MHz, CDCl$_3$): $\delta$ 170.1, 170.6, 170.5, 170.2, 169.6 (5 COCH$_3$), 155.6-114.5 (Ar-C), 99.6 (C-1A), 95.7 (C-1B), 75.4 (C-3A), 73.7 (PhCH$_2$), 72.3 (C-4A), 72.1 (C-3B), 72.0 (C-2A), 71.9 (C-5A), 71.5 (C-5B), 70.0 (C-2B), 69.7 (C-4B), 68.8 (C-6B), 62.7 (C-6A), 108
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55.6 (OCH₃), 20.8, 20.7, 20.6, 20.5 (2 C) (5 COCH₃); ESI-MS: 771.2 [M+Na]⁺; Anal. Calcd. for C₃₆H₄₄O₁₇ (748.26): C, 57.75; H, 5.92; found: C, 57.54; H, 6.15.

**Ethyl 2,3,4-tri-O-acetyl-1-thio-α-L-rhamnopyranoside (7):** To a suspension of L-rhamnose monohydrate (10 g, 54.9 mmol) in acetic anhydride (40 mL) was added HClO₄-SiO₂ (2 g) and the mixture was allowed to stir at room temperature for 10 min. The solvents was removed under reduced pressure and co-evaporated with toluene (2×20 mL). To a solution of the crude mass in dry CH₂Cl₂ (100 mL) was added ethanethiol (10.2 mL, 137.3 mmol) under argon. The reaction mixture was cooled to 0 °C and BF₃-OEt₂ (13.9 mL, 109.8 mmol) was added to it and the reaction mixture was allowed to stir at 5-10 °C for 5 h. The reaction mixture was diluted with CH₂Cl₂ (100 mL), washed with aq. NaHCO₃ and water in succession. The organic layer was dried (Na₂SO₄) and concentrated under reduced pressure. The crude product was purified over SiO₂ using hexane-EtOAc (3:1) as eluant to furnish compound 7 (16.5 g, 90%). White solid; m.p. 69-70 °C [EtOH]; [α]D²⁵ = −144 (c 1.0, CHCl₃); IR (KBr): 2361, 1722, 1588, 1352, 1212, 1032, 766 cm⁻¹; ¹H NMR (300 MHz, CDC₁₃): δ 5.30 (dd, J = 3.0, 1.5 Hz, 1 H, H-2), 5.21 (dd, J = 10 Hz, 1 H, H-3), 5.17 (br s, 1 H, H-1), 5.07 (t, J = 10 Hz each, 1 H, H-4), 4.20 (m, 1 H, H-5), 2.60-2.54 (m, 2 H, SCH₂CH₃), 2.09, 2.02, 1.95 (3 s, 9 H, 3 COCH₃), 1.25-1.19 (m, 6 H, CH₂ and SCH₂CH₃); ¹³C NMR (75 MHz, CDC₁₃): 8 169.6, 169.5, 169.3 (3 COCH₃), 81.8 (C-1), 71.4, 71.2, 69.3, 66.8, 25.3 (SCH₂CH₃), 20.7, 20.6, 20.5 (3 COCH₃), 17.3 (CCH₃), 14.8 (SCH₂CH₃); ESI-MS: 357.1 [M+Na]⁺; Anal. Calcd. for C₁₄H₂₂O₇S (334): C, 50.29; H, 6.63; found: C, 50.08; H, 6.85.

**Ethyl 4-O-benzyl-2,3-O-isopropylidene-1-thio-α-L-rhamnopyranoside (8):** A solution of compound 7 (10 g, 29.9 mmol) in 0.1 M CFLONa in CH₃OH (50 mL) was allowed to stir at room temperature for 3 h and neutralized with Dowex-50W X8 (H⁺). The reaction mixture was filtered and evaporated to dryness. To a solution of the crude mass in anhydrous DMF (30 mL) were added 2,2-dimethoxypropane (7.4 mL, 59.8 mmol) and p-TsOH (250 mg) and the reaction mixture was allowed to stir at room temperature for 10 h. The reaction mixture was quenched with Et₃N (0.5 mL) and the solvents were removed under reduced pressure. To a solution of the crude mass in THF (30 mL) were added powdered NaOH (2.4 g, 59.8 mmol) and benzyl bromide (5.3 mL, 44.9 mmol) and the reaction mixture was allowed to stir at room temperature for 2 h. The reaction mixture was concentrated under reduced pressure and diluted with CH₂Cl₂ (50 mL). The organic layer was washed with water, dried (Na₂SO₄) and concentrated under reduced pressure. The crude product was purified over SiO₂ using hexane-EtOAc (4:1) as eluant to furnish pure compound 8 (8.7 g, 86%). Colorless oil; [α]D²⁵ = −143 (c 1.0, CHCl₃); IR (neat):
2981, 2897, 1451, 1383, 1249, 1218, 1163, 1097, 1069, 1007, 742, 695 cm\(^{-1}\); \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 7.38-7.25 (m, 5 H, Ar-H), 5.50 (br s, 1 H, H-1), 4.92 (d, \(J = 11.7\) Hz, 1 H, PhCH\(_2\)), 4.64 (d, \(J = 11.6\) Hz, 1 H, PhCH\(_2\)), 4.24 (t, \(J = 6.0\) Hz each, 1 H, H-3), 3.72 (dd, \(J = 9.7, 7.1\) Hz, 1 H, H-4), 2.71-2.58 (m, 2 H, SCH\(_2\)CH\(_3\)), 1.53 (s, 3 H, C(C\(_\text{H}_3\))\(_2\)), 1.38 (s, 3 H, C(C\(_\text{H}_3\))\(_2\)), 1.32 (t, \(J = 7.3\) Hz each, 3 H, SCH\(_2\)CH\(_3\)), 1-2.9 (d, \(J = 6.0\) Hz, 3 H, CH\(_3\)CH\(_3\)).

Ethyl 2,4-di-O-benzyl-1-thio-L-rhamnopyranoside (9): A solution of compound 8 (2.5 g, 7.38 mmol) in 80% aq. AcOH was allowed to stir at 80 °C for 1.5 h. The solvents were removed under reduced pressure. To a solution of the crude product in CH\(_2\)Cl\(_2\) (15 mL) were added TBAHS (600 mg), benzyl bromide (1.3 mL, 10.9 mmol), and aq 5% NaOH (15 mL) and the mixture was vigorously stirred at room temperature for 3 h. It was then diluted with CH\(_2\)Cl\(_2\) (100 mL) and the organic layer was washed with water, dried, and concentrated. The crude product was purified over SiO\(_2\) using hexane-EtOAc (7:1) as eluant to furnish pure compound 9 (2.1 g, 73%). Colorless oil; [\(\alpha\)]\(_D\)\(^{25}\) - 91 (c 1.2, CHCl\(_3\)); \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta\) 7.30-7.21 (m, 10 H, Ar-H), 5.33 (d, \(J = 1.5\) Hz, 1 H, H-1), 4.90-4.50 (m, 4 H, 2 PhCH\(_2\)), 4.04 (dd, \(J = 10.0, 6.0\) Hz, 1 H, H-5), 3.91 (dd, \(J = 10.0, 4.0\) Hz, 1 H, H-3), 3.82 (dd, \(J = 1.5, 4.0\) Hz, 1 H, H-2), 3.36 (t, \(J = 10.0\) Hz each, 1 H, H-4), 2.57-2.54 (m, 2 H, SCH\(_2\)CH\(_3\)), 1.30-1.24 (m, 6 H, CCH\(_3\), SCH\(_2\)CH\(_3\)); Anal. Calcd. for C\(_{22}\)H\(_{28}\)O\(_4\)S (388.17): C, 68.01; H, 7.26; found: C, 67.85; H, 7.30.

3,4,6-Tri-O-acetyl-2-azido-2-deoxy-\(\alpha,\beta-D-glucopyranose\) (11): To an ice-cooled solution of NaN\(_3\) (29.8 g, 457.5 mmol) in H\(_2\)O (75 mL) was added drop wise a solution of triflic anhydride (26.2 g, 92.50 mmol) in CH\(_2\)Cl\(_2\) (125 mL) over a period of 5 min. To the resulting biphasic reaction mixture was stirred vigorously at 5 °C for 2 h. The organic phase containing triflic azide (Tf\(_3\)N) was separated and washed with satd. NaHCO\(_3\) and used directly for the next step. To a solution of glucosamine hydrochloride (10; 10 g, 46.5 mmol) in H\(_2\)O (150 mL) and CH\(_3\)OH (300 mL) were sequentially added K\(_2\)CO\(_3\) (9.6 g, 69.5 mmol), CuSO\(_4\) hydrate (70 mg, 440 mmol) and Tf\(_3\)N solution. The reaction mixture was allowed to stir at room temperature for 16 h and the solvent was removed under reduced pressure. A solution of the crude product in acetic anhydride (100 mL) and pyridine (100 mL) was stirred at room temperature for 10 h and concentrated under reduced pressure. The crude product was purified over SiO\(_2\) using hexane-EtOAc (3:1) as
eluant to furnish pure compound 11 (12.5 g, 72%). $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 6.30 (d, $J = 3.6$ Hz, 1 H, H-1$_a$), 5.55 (d, $J = 8.7$ Hz, 1 H, H-1$_b$), 5.43 (t, $J = 8.0$ Hz each, 1 H), 5.18-5.04 (m, 3 H), 4.34-4.27 (m, 2 H), 4.11-4.05 (m, 4 H), 3.68-3.64 (m, 2 H), 2.19 (s, 6 H) 2.11 (s, 3 H), 2.10 (s, 3 H), 2.08 (s, 6 H), 2.05 (s, 3 H), 2.02 (s, 3 H). Anal. Calcd. for C$_{14}$H$_{19}$N$_3$O$_9$ (373.11): C, 45.04; H, 5.13; found: C, 44.88; H, 5.30.

3,4,6-Tri-O-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl trichloroacetimidate (12): To a solution of compound 11 (4 g, 10.7 mmol) in DMF (30 mL) was added benzyl amine (1.8 mL, 16.5 mmol) and the reaction mixture was allowed to stir at 50 °C for 45 min. The solvents were removed under reduced pressure and the crude product was passed through a short pad of SiO$_2$ using EtOAc as eluant to give the hemiacetal derivative. To a solution of the hemiacetal derivative (3.2 g, 9.64 mmol) in dry CH$_2$Cl$_2$ (30 ml) were added Cl$_3$CCN (8 ml, 79.8 mmol) and DBU (300 µL, 2 mmol) and the reaction mixture was stirred at 0 °C for 1 h. The reaction mixture was concentrated under reduced pressure and the crude product was purified over SiC$_{2}$ using hexane-EtOAc (1:1) as eluant to give pure compound 12 (3.4 g, 74%), which was used for the next step without detail spectroscopic characterization. Colorless oil; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.81 (s, 1 H, NH), 6.43 (d, $J = 3.6$ Hz, 1 H, H-1), 5.55 (t, $J = 9.6$ Hz each, 1 H, H-3), 5.11 (t, $J = 10.0$ Hz each, 1 H, H-4), 4.24-4.21 (m, 2 H, H-6$_{ab}$), 4.05-4.02 (m, 1 H, H-5), 2.04, 2.01, 1.99 (3 s, 9 H, 3 COCH$_3$); $^{13}$C (CDCl$_3$) $\delta$ 170.6, 170.0, 169.7 (3 COCH$_3$), 94.1 (C-1), 72.8, 70.8, 68.1, 63.4, 61.5 (C-6), 20.8, 20.7 (2 C) (3 COCH$_3$).

Ethyl (3,4,6-tri-O-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl)-(1→3)-2,4-di-O-benzyl-1-thio-α-L-rhamnopyranoside (13): A solution of compound 12 (2.4 g, 5.04 mmol) and compound 9 (1.5 g, 3.86 mmol) in anhydrous CH$_2$Cl$_2$ (10 mL) was cooled to −15 °C under Argon. To the cooled reaction mixture was added HClO$_4$-SiO$_2$ (50 mg) and the reaction mixture was allowed to stir at same temperature for 1 h. The reaction mixture was filtered through a Celite® bed and concentrated under reduced pressure. The crude product was purified over SiO$_2$ using hexane-EtOAc (3:1) as eluant to furnish pure compound 13 (2.2 g, 81%). Yellow oil; $[\alpha]_D^{25} + 63.3$ (c 1.2, CHCl$_3$); IR (neat): 2930, 2110, 1750, 1455, 1368, 1233, 1094, 1039, 755, 699 cm$^{-1}$; $^1$H NMR (600 MHz, CDCl$_3$): $\delta$ 7.43-7.26 (m, 10 H, Ar-H), 5.11 (t, $J = 10.0$ Hz each, 1 H, H-3), 5.05 (t, $J = 10.2$ Hz each, 1 H, H-4), 4.82 (t, $J = 10.2$ Hz each, 1 H, H-1), 4.91 (d, $J = 11.4$ Hz, 1 H, PhCH$_2$), 4.74 (d, $J = 12.0$ Hz, 1 H, PhCH$_2$), 4.70 (d, $J = 11.4$ Hz, 1 H, PhCH$_2$), 4.64 (d, $J = 12.0$ Hz, 1 H, PhCH$_2$), 4.15-4.13 (m, 1 H, H-5$_D$), 4.08-4.03 (m, 2 H, H-5$_C$, H-6$_{ab}$), 4.00 (dd, $J = 9.6, 3.0$ Hz, 1 H, H-3$_C$), 3.93 (br s, 1 H, H-2$_C$), 3.88 (d, $J = 12.0$ Hz, 1 H, H-2$_D$), 3.07 (s, 3 H, NCH$_3$), 3.03 (s, 3 H, NCH$_3$).
Hz, 1 H, H-6bD), 3.69 (t, J = 9.6 Hz each, 1 H, H-4c), 3.31 (dd, J = 10.8, 3.6 Hz, 1 H, H-2d), 2.61-2.56 (m, 2 H, SCH2CH3), 2.08, 2.05, 1.90 (3 s, 9 H, 3 COCH3), 1.36 (d, J = 6.0 Hz, 3 H, CCH3), 1.25 (t, J = 7.2 Hz, 3 H, SCH2CH3); 13C NMR (150 MHz, CDCl3): δ 170.5, 169.8, 169.6 (3 COCH3), 138.0-127.6 (Ar-C), 92.8 (C-1D), 79.4 (C-3c), 75.5 (PhCH2), 74.6 (C-3c), 74.2 (C-2c), 71.8 (PhCH2), 70.4 (C-3d), 68.4 (C-5c), 68.1 (C-4c), 67.3 (C-5d), 61.5 (C-6d), 60.6 (C-2d), 25.4 (SCH2CH3), 20.7, 20.6, 20.5 (3 COCH3), 17.7 (CCH3), 14.9 (SCH2CH3); ESI-MS: 724.2 [M+Na]+; Anal. Calcd. for C34H43N3O11S (701.26): C, 58.19; H, 6.18; found: C, 58.0; H, 6.42.

Ethyl (2-azido-3,4,6-tri-O-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→3)-2,4-di-O-benzyl-1-thio-α-L-rhamnopyranoside (14): To a solution of compound 13 (2 g, 2.85 mmol) in THF (10 mL) were added powdered NaOH (1 g, 25 mmol), benzyl bromide (2.1 mL, 17.6 mmol) and "Bu4NBr (50 mg) and the reaction mixture was allowed to stir at room temperature for 2 h. The reaction mixture was poured into water and extracted with CH2Cl2 (100 mL). The organic layer was washed with water, dried (Na2SO4) and concentrated under reduced pressure. The crude product was purified over SiO2 using hexane-EtOAc (6:1) as eluant to give pure compound 14 (2.2 g, 91%). Yellow oil; [α]D25 +12.0 (c 1.2, CHCl3); IR (neat): 3430, 3031, 2925, 2107, 1642, 1496, 1454, 1361, 1215, 1091, 1051, 1028, 751, 697 cm⁻¹; 1H NMR (600 MHz, CDCl3): δ 7.45-7.07 (m, 25 H, Ar-H), 5.32 (br s, 1 H, H-lc), 4.93 (d, J = 3.6 Hz, 1 H, H-1d), 4.85 (br s, 2 H, PhCH2), 4.83 (d, J = 10.2 Hz, 1 H, PhCH2), 4.77 (d, J = 10.8 Hz, 1 H, PhCH2), 4.74 (d, J = 12.0 Hz, 1 H, PhCH2), 4.69 (d, J = 12.0 Hz, 1 H, PhCH2), 4.60 (d, J = 12.6 Hz, 1 H, PhCH2), 4.55 (d, J = 10.2 Hz, 1 H, PhCH2), 4.48 (d, J = 10.8 Hz, 1 H, PhCH2), 4.35 (d, J = 12.6 Hz, 1 H, PhCH2), 4.07 (t, J = 9.6 Hz each, 1 H, H-3d), 4.04-3.99 (m, 3 H, H-3c, H-5c, H-5d), 3.93 (br s, 1 H, H-2c), 3.79 (t, J = 9.6 Hz each, 1 H, H-4c), 3.66 (t, J = 9.6 Hz each, 1 H, H-4d), 3.60 (dd, J = 10.8, 2.4 Hz, 1 H, H-6d), 3.51 (dd, J = 10.8, 1.2 Hz, 1 H, H-6ad), 3.40 (dd, J = 10.2, 3.6 Hz, 1 H, H-2d), 2.60-2.50 (m, 2 H, SCH2CH3), 1.35 (d, J = 6.0 Hz, 3 H, CCH3), 1.22 (t, J = 7.8 Hz each, 3 H, SCH2CH3); 13C NMR (150 MHz, CDCl3): δ 137.7-127.5 (Ar-C), 93.2 (C-1D), 81.1 (C-1c), 80.2 (C-3d), 79.8 (C-4d), 78.1 (C-4c), 75.9 (PhCH2), 74.8 (PhCH2), 74.5 (C-3c), 74.4 (C-2c), 73.3 (PhCH2), 71.8 (PhCH2), 70.4 (C-5c), 68.3 (C-5d), 67.8 (C-6d), 63.0 (C-2d), 25.4 (SCH2CH3), 17.8 (CCH3), 14.9 (SCH2CH3); ESI-MS: 868.3 [M+Na]+; Anal. Calcd. for C49H55N3O11S (845.37): C, 69.56; H, 6.55; found: C, 69.33; H, 6.80.

p-Methoxyphenyl (2-azido-3,4,6-tri-O-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→3)-(2,4-di-O-benzyl-α-L-rhamnopyranosyl)-(1→4)-(2,3-di-O-acetyl-6-O-benzyl-α-D-glucopyranosyl)-
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(1→4)-2,3,6-tri-O-acetyl-β-D-glucopyranoside (15): To a solution of compound 5 (1.2 g, 1.60 mmol) and compound 14 (1.6 g, 1.89 mmol) in anhydrous CH₂Cl₂ (8 mL) was added MS 4Å (2.0 g) and reaction mixture was cooled to −10 °C. To the cooled reaction mixture were added NIS (500 mg, 2.22 mmol) and HClO₄-SiO₂ (20 mg) and it was allowed to stir at same temperature for 1 h. The reaction mixture was filtered through a Celite® bed and washed with CH₂Cl₂ (100 mL). The organic layer was successively washed with 5% aq. Na₂S₂O₅, NaHCO₃ and water, dried (Na₂SO₄) and concentrated under reduced pressure. The crude product was purified over SiO₂ using hexane-EtOAc (2:1) as eluant to give pure compound 15 (2 g, 82%).

White solid; m. p. 66-68 °C [EtOH]; [α]D²⁵ + 18.2 (c 1.2, CHCl₃); IR (KBr): 3428, 3032, 2932, 2108, 1753, 1508, 1455, 1368, 1230, 1044, 740, 698 cm⁻¹; ¹H NMR (600 MHz, CDCl₃): δ 7.35-7.05 (m, 30 H, Ar-H), 6.91 (d, J = 9.0 Hz, 2 H, Ar-H), 6.80 (J = 9.0 Hz, 2 H, Ar-H), 5.34 (d, J = 4.5 Hz, 1 H, H-1B), 5.29 (t, J = 10.0 Hz each, 1 H, H-3A), 5.27 (t, J = 9.0 Hz each, 1 H, H-3B), 5.04 (dd, J = 8.0 Hz each, 1 H, H-2A), 4.97 (d, J = 3.5 Hz, 1 H, H-1D), 4.95 (d, J = 8.0 Hz, 1 H, H-1A), 4.89 (d, J = 2.0 Hz, 1 H, H-1C), 4.85-4.80 (m, 2 H, PhCH₂), 4.78-4.75 (m, 3 H, H-2B, PhCH₂), 4.65 (d, J = 12.0 Hz, 1 H, PhCH₂), 4.60 (d, J = 12.0 Hz, 1 H, PhCH₂), 4.58-4.44 (m, 5 H, PhCH₂), 4.41 (dd, J = 12.5, 2.5 Hz, 1 H, H-6a₂), 4.35 (d, J = 12.0 Hz, 1 H, PhCH₂), 4.21 (dd, J = 12.5, 2.5 Hz, 1 H, H-6a₂), 4.05-4.01 (2 t, J = 9.5 Hz each, 2 H, H-3d, H-4c), 3.98-3.92 (m, 2 H, H-3c, H-5c), 3.90 (t, J = 10.0 Hz each, 1 H, H-4b), 3.81 (t, J = 8.5 Hz each, 1 H, H-4a), 3.77 (s, 3 H, OCH₃), 3.76-3.74 (m, 1 H, H-4b), 3.72-3.71 (m, 1 H, H-5b), 3.69-3.65 (m, 2 H, H-5a, H-6a₂), 3.63-3.61 (m, 1 H, H-6a₃), 3.58-3.55 (m, 3 H, H-2c, H-5d, H-6b), 3.53-3.51 (m, 1 H, H-6bd), 3.43 (dd, J = 10.0, 3.5 Hz, 1 H, H-2d), 2.04, 2.02, 2.01, 1.99, 1.95 (5 s, 15 H, 5 COCH₃), 1.25 (d, J = 6.2 Hz, 3 H, CCH₃); ¹³C NMR (150 MHz, CDCl₃): δ 170.7, 170.2 (2 C), 169.8, 169.7 (5 COCH₃), 155.7-114.5 (Ar-C), 99.7 (C-1A), 98.8 (C-1C), 96.0 (C-1B), 93.9 (C-1D), 80.2 (C-3B), 79.4 (C-4B), 78.2 (C-5A), 77.2 (C-5B), 75.5 (PhCH₂), 75.4 (C-3A), 75.3 (PhCH₂), 74.8 (PhCH₂), 74.3 (C-2B), 74.2 (C-4c), 73.7 (PhCH₂), 73.3 (PhCH₂), 72.6 (2 C, C-5D, PhCH₃), 72.2 (C-4A), 72.1 (C-2A), 71.3 (C-4B), 70.7 (2 C, C-3C, C-5C), 70.4 (C-3b), 69.0 (C-2C), 67.9 (C-6b), 67.8 (C-6d), 63.3 (C-2d), 62.6 (C-6a), 55.6 (OCH₃), 21.0, 20.9, 20.7, 20.6 (2 C) (5 COCH₃), 17.9 (CCH₃); ESI-MS: 1554.6 [M+Na]⁺; Anal. Calcd. for C₈₃H₆₉N₃O₂₅ (1531.61): C, 65.04; H, 6.12; found: C, 64.82; H, 6.36.

p-Methoxyphenyl (2-acetamido-2-deoxy-α-D-glucopyranosyl)-(1→3)-(α-L-rhamnopyranosyl)-(1→4)-(α-D-glucopyranosyl)-(1→4)-sodium β-D-glucopyranosiduronate (1): A solution of compound 15 (1.3 g, 0.85 mmol) in 0.1 M CH₃ONa in CH₃OH (25 mL) was allowed to stir at room temperature for 3 h and neutralized with Dowex 50W X8 (H⁺) resin. The
reaction mixture was filtered and concentrated under reduced pressure. To a solution of the crude product in CH₂Cl₂ (25 mL) and H₂O (4 mL) were sequentially added aq. NaBr (2 mL; 1 M), aq. TBAB (2.5 mL; 1 M), TEMPO (100.0 mg, 0.64 mmol), satd. NaHCO₃ (10 mL) and 4% aq. NaOCl (15 mL) and the reaction mixture was allowed to stir at 0-5 °C for 2 h. The reaction mixture was neutralized with 1 N aq. HCl solution. To the reaction mixture were added tert-butanol (25 mL), 2-methyl-but-2-ene (20 mL; 2 M solution in THF), aq. NaClO₂ (1.5 g in 5 mL) and aq. Na₂HPO₄ (1.5 g in 5 mL) and the reaction mixture was stirred at room temperature for 3 h. The reaction mixture was diluted with satd. aq. Na₂HPO₄ and extracted with CH₂Cl₂ (150 mL). The organic layer was washed with water, dried (Na₂SO₄) and concentrated to dryness. The crude product was passed through short pad of SiO₂ using EtOAc-toluene (2:1) as eluant. To a solution of the oxidized product (800 mg) in CH₃OH-EtOAc (20 mL; 10:1 v/v) was added 20% Pd(OH)₂-C (150 mg) and the reaction mixture was allowed to stir at room temperature under a positive pressure of hydrogen for 10 h. The reaction mixture was filtered through a Celite® bed and evaporated to dryness. To a solution of the crude product in CH₃OH (10 mL) was added acetic anhydride (2 mL) and the solution was kept at room temperature for 30 min. The solvents were removed under reduced pressure and the product was passed through a column of Sephadex® LH-20 using CH₃OH-H₂O (60 mL; 4:1 v/v) as eluant to give pure compound 1 (450 mg, 64%). White powder; [α]D₂₅ + 14 (c 1.0, CH₃OH); IR (KBr): 3428, 2937, 1621, 1366, 1152, 1087, 669 cm⁻¹; ¹H NMR (600 MHz, CD₃OD): δ 7.04 (d, J = 9.0 Hz, 2 H, Ar-H), 6.84 (d, J = 9.0 Hz, 2 H, Ar-H), 5.26 (d, J = 3.6 Hz, 1 H, H-1B), 4.93 (br s, 1 H, H-1D), 4.89 (br s, 1 H, H-1c), 4.82 (d, J = 7.8 Hz, 1 H, H-1A), 4.03-3.98 (m, 2 H, H-2A, H-5C), 3.97-3.95 (m, 2 H, H-2C, H-2D), 3.88-3.86 (m, 1 H, H-6aB), 3.83-3.75 (m, 5 H, H-3A, H-3b, H-5D, H-6aB, H-6bD), 3.74 (s, 3 H, OCH₃), 3.73-3.71 (m, 1 H, H-4A), 3.70-3.67 (m, 2 H, H-2B, H-6bB), 3.64 (t, J = 9.6 Hz, 1 H, H-3D), 3.56-3.50 (m, 4 H, H-4B, H-4C, H-5A, H-5b), 3.49-3.44 (m, 2 H, H-3C, H-4D), 2.02 (s, 3 H, COCH₃), 1.30 (d, J = 6.1 Hz, 3 H, CCH₃); ¹³C NMR (150 MHz, CDCl₃): δ 175.0 (COONa), 172.6 (NHCOCH₃), 156.7-115.5 (Ar-C), 103.3 (C-1A), 102.8 (C-1B), 102.4 (C-1c), 96.7 (C-1d), 81.2 (C-3D), 79.5 (C-4b), 78.1 (C-3A), 77.7 (C-4A), 76.6 (C-5A), 74.6 (C-3c), 74.2 (C-4c), 73.8 (C-2b), 73.6 (C-2A), 73.0 (C-5D), 72.0 (C-5b), 71.9 (C-4D), 70.8 (C-5c), 69.3 (C-2c), 62.1 (C-6b), 62.0 (C-6d), 56.2 (OCH₃), 55.3 (C-2D), 23.1 (NHCOCH₃), 18.1 (CCH₃); ESI-MS: 834.2 [M+H]⁺; Anal. Calcd. for C₃₅H₄₈NNaO₂₂ (833.26): C, 47.54; H, 5.80; found: C, 47.72; H, 6.07.
2.3.5. Representative NMR spectra of synthesized compounds

$^1$H and $^{13}$C NMR spectra of $p$-methoxyphenyl (2,3-di-O-acetyl-6-O-benzyl-$\alpha$-D-glucopyranosyl)-(1→4)-2,3,6-tri-0-acetyl-$\beta$-D-glucopyranoside (5) (CDCl$_3$).
$^{13}$C DEPT 135 and 2D HSQC (selected region) spectra of $p$-methoxyphenyl (2,3-di-$O$-acetyl-6-$O$-benzyl-$\alpha$-$D$-glucopyranosyl)-(1$\rightarrow$4)-2,3,6-tri-$O$-acetyl-$\beta$-$D$-glucopyranoside (5).
$^1$H and $^{13}$C NMR spectra of ethyl (3,4,6-tri-O-acetyl-2-azido-2-deoxy-α-D-glucopyranosyl)-(1→3)-2,4-di-O-benzyl-1-thio-α-L-rhamnopyranoside (13) (CDCl$_3$).
2D COSY and 2D HSQC (selected region) spectra of ethyl (3,4,6-tri-O-acetyl-2-azido-2-deoxy-\(\alpha\)-D-glucopyranosyl)-(1→3)-2,4-di-O-benzyl-1-thio-\(\alpha\)-L-rhamnopyranoside (13).
$^1$H, $^{13}$C and 2D HSQC (selected region) NMR spectra of ethyl (2-azido-3,4,6-tri-O-benzyl-2-deoxy-$\alpha$-D-glucopyranosyl)-(1$\rightarrow$3)-2,4-di-O-benzyl-1-thio-$\alpha$-L-rhamnopyranoside (14) (CDCl$_3$).
\textsuperscript{1}H and \textsuperscript{13}C NMR spectra of \textit{p}-methoxyphenyl (2-azido-3,4,6-tri-O-benzyl-2-deoxy-\textgreek{d}-glucopyranosyl)-(1→3)-(2,4-di-O-benzyl-\textgreek{l}-rhamnopyranosyl)-(1→4)-(2,3-di-O-acetyl-6-O-benzyl-\textgreek{d}-glucopyranosyl)-(1→4)-2,3,6-tri-O-acetyl-\textgreek{d}-glucopyranoside (15) (CDC\textsubscript{3}).
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2D COSY and 2D HSQC spectra (selected region) of \( p \)-methoxyphenyl (2-azido-3,4,6-tri-\( O \)-benzyl-2-deoxy-\( \alpha \)-D-glucopyranosyl)-(1\( \rightarrow \)3)-(2,4-di-\( O \)-benzyl-\( \alpha \)-L-rhamnopyranosyl)-(1\( \rightarrow \)4)-(2,3-di-\( O \)-acetyl-6-\( O \)-benzyl-\( \alpha \)-D-glucopyranosyl)-(1\( \rightarrow \)4)-2,3,6-tri-\( O \)-acetyl-\( \beta \)-D-glucopyranoside (15).
$^1$H, $^{13}$C and 2D HSQC (selected region) NMR spectra of p-methoxyphenyl (2-acetamido-2-deoxy-α-D-glucopyranosyl)-(1→3)-(α-L-rhamnopyranosyl)-(1→4)-(α-D-glucopyranosyl)-(1→4)-sodium β-D-glucopyranosiduronate (1) (CD$_3$OD).
2.4. Synthesis of a Common Tetrasaccharide Corresponding to the O-Antigen of Enteroinvasive Escherichia coli O143 and Shigella boydii Type 8
2.4.1. Introduction

*Escherichia coli* strains are mostly abundant in the gastrointestinal tract and considered as friendly microorganisms for human. However, certain species of *E. coli* acquired virulence factors and causes severe intestinal and urinary infections in humans and animals. Among several clinically observed *E. coli* infections, diarrhea is most frequent. Diarrhea causing *E. coli* strains are classified in six subgroups, which are (i) enteropathogenic *E. coli* (EPEC), (ii) enteroinvasive *E. coli* (EIEC), (iii) enterohemorrhagic *E. coli* (EHEC), (iv) enterotoxigenic *E. coli* (ETEC), (v) diffusely adherent *E. coli* (DAEC), and (vi) enteroaggregative *E. coli* (EAEC). The EIEC strains are mostly transmitted to humans by contaminated food and water and cause illness similar to that of bacillary dysentery. A number of EIEC strains have been identified and characterized in the past.

The close association of the gene sequences and the pathogenicity of virulent *E. coli* and *Shigella* strains are well documented. The structure of the repeating unit of the *O*-antigenic cell wall polysaccharide of enteroinvasive *Escherichia coli* O143 containing D-glucuronic acid and D-galacturonic acid has been reported by Widmalm *et al.* In another communication, L’vov *et al.* reported the structure of the repeating unit of the *O*-antigen of *Shigella boydii* type 8, which is identical to the repeating unit of the *O*-antigen of enteroinvasive *Escherichia coli* O143 (Figure 1).

\[\rightarrow 3\)-\(\alpha\)-D-GalpNAc-(1\(\rightarrow\)4\)-\(\beta\)-D-GlcpA-(1\(\rightarrow\)3\)-\(\beta\)-D-GlcpNAc-(1\(\rightarrow\)2\)-\(\beta\)-D-GalpA-(1\(\rightarrow\)

**Figure 1:** Structure of the common tetrasaccharide repeating unit corresponding to the *O*-antigen of enteroinvasive *Escherichia coli* O143 and *Shigella dysenteriae* type 8.

In the past, a number of therapeutics has been developed with remarkable efficacy for the treatment of these infections. However, the emergence of the drug resistant strains poses the challenge to the development of newer approaches for controlling these infections. Bacterial cell wall *O*-polysaccharides are highly immunogenic in nature and has significant role on their virulence. *O*-Polysaccharides and their smaller fragments have been used to prepare glycoconjugates for their use as antibacterial vaccine candidates. A large quantities of oligosaccharides related to the *O*-antigens are required for the detailed studies on the biological role of *O*-antigens. Since the natural source can not provide the large quantity oligosaccharides, chemical synthesis of a particular oligosaccharide is essential for the development of glycoconjugates. Because of the fact that both enteroinvasive *Escherichia coli* O143 and *Shigella*
_dysenteriae_ type 8 have common structure of their O-antigens as well as their pathogenic actions, synthesis of this tetrasaccharide was considered for the development of glycoconjugate derivatives. A concise chemical synthesis of the tetrasaccharide as its 2-(p-methoxyphenoxy)ethyl glycoside (1) using a [2+2] block glycosylation and late stage oxidation strategy is presented here (Figure 2). 2-(p-Methoxyphenoxy) ethyl (MPE) group can be easily transformed to an ethylene glycol linked oligosaccharide for its further use.

![Figure 2: Structure of the synthesized tetrasaccharide disodium salt as its 2-(p-methoxyphenoxy) ethyl glycoside.](image)

### 2.4.2. Results and Discussion

The synthesis of the target tetrasaccharide 1 disodium salt as its 2-(p-methoxyphenoxy) ethyl glycoside was achieved following a [2+2] block synthetic strategy. The notable features in the synthetic strategy include (a) application of [2+2] block glycosylations; (b) use of perchloric acid supported over silica (HClO₄-SiO₂) as a general solid acid catalyst for the activation of glycosyl trichloroacetimidate and thioglycoside derivative and in the acetylations of amine and hydroxyl groups; (c) TEMPO mediated late stage oxidation of two primary hydroxyl groups in the presence of secondary hydroxyl groups; (d) use of a 2-(p-methoxyphenoxy) ethyl group as anomeric protecting group. 2-(p-Methoxyphenoxy) ethyl (MPE) group can be easily transformed to an ethylene glycol linked oligosaccharide for its further use. The retrosynthetic strategy for the synthesis of compound 1 led to a number of suitably protected monosaccharide intermediates, which are prepared from the commercially available reducing sugars (Scheme 1).
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Scheme 1: Retrosynthetic strategy for the synthesis of compound 1.

2.4.2.1. Preparation of 2-(p-methoxyphenoxy) ethyl 3,4,6-tri-O-benzyl-\(\beta\)-D-galactopyranoside (8)

3,4,6-Tri-O-acetyl-D-galactal (2) was transformed to 3,4,6-tri-O-benzyl-D-galactal (3) using a one pot two step de-O-acetylation and benzylation\(^\text{26}\) reaction condition in 95% yield. Treatment of compound 3 with Oxone\(^\text{59}\) in acetone-water (5:1, v/v) followed by conventional acetylation\(^\text{24}\) furnished compound 4 in 88% yield. Selective removal of the anomeric acetate from compound 4 using benzyl amine\(^\text{30}\) furnished hemiacetal derivative, which on treatment with trichloroacetonitrile in the presence of DBU\(^\text{31}\) furnished compound 5 in 88% yield. Stereoselective glycosylation of compound 5 with 2-(p-methoxyphenoxy) ethanol (6) in the presence of HClO\(_4\)-SiO\(_2\) furnished\(^\text{18,40}\) compound 7 in 74% yield, which on de-O-acetylation\(^\text{18}\) using sodium methoxide furnished compound 8 in 92% yield (Scheme 2).
**Scheme 2:** Reagents: (a) Benzyl bromide, NaOH, TBAI, THF, r t, 5 h, 95%; (b) (i) Oxone, acetone-H_2O (5:1), r t, 5 h; (ii) Ac_2O, pyridine, r t, 3 h, 88%; (c) (i) benzyl amine, THF, r t, 12 h; (ii) CCl_3CN, DBU, CH_2Cl_2, -10 °C, 1 h, 88%; (d) HClO_4-SiO_2, CH_2Cl_2, -10 °C, 1 h, 74%; (e) 0.01 M CH_3ONa, CH_3OH, r t, 1 h, 92%.

**2.4.2.2. Preparation of ethyl 3-O-acetyl-4,6-O-benzylidene-2-deoxy-2-N-phthalimido-1-thio-β-D-glucopyranoside (13)**

Treatment of D-glucosamine hydrochloride (9) with phthalic anhydride in the presence of NaOH followed by acetylation resulted in 1,3,4,6-tetra-O-acetyl-2-deoxy-2-N-phthalimido-β-D-glucopyranoside (10) in 90% yield. Treatment of compound 10 with ethanethiol in the presence of boron trifluoride diethyletherate furnished ethyl 3,4,6-tri-O-acetyl-2-deoxy-2-N-phthalimido-1-thio-β-D-glucopyranoside (11) in 85% yield. Compound 11 was subjected to a sequence of reactions involving saponification using sodium methoxide, benzylidene acetal formation using benzaldehyde dimethyl acetal and p-toluenesulfonic acid and acetylation using acetic anhydride and pyridine to give compound 13 in 85% yield (Scheme 3).

**Scheme 3:** Reagents: (a) Phthalic anhydride, NaOH, H_2O, r t, 16 h; (b) Ac_2O, NaOAc, reflux, 30 min, 83%; (c) EtSH, BF_3·OEt_2, CH_2Cl_2, 0 °C-r t, 5 h, 85%; (d) (i) 0.05 M MeONa, MeOH, r t, 20 min; (ii) PhCH(OMe)_2, p-TsOH, CH_3CN, r t, 10 h, 76%; (e) Ac_2O, pyridine, r t, 6 h, 85%.
2.4.2.3. Preparation of phenyl 2,3-di-O-benzoyl-6-O-benzyl-1-thio-β-D-glucopyranoside (17)

Phenyl 2,3,4,6-tetra-O-acetyl-1-thio-β-D-glucopyranoside (15) was prepared from D-glucose (14) following a one-pot two-step reaction protocol by successive treatment with acetic anhydride and thiophenol in the presence of boron trifluoride diethyl etherate in 90% yield. Removal of acetyl groups from the compound 15 using sodium methoxide, followed by benzylidene acetal formation using benzaldehyde dimethylacetal and conventional benzoylation furnished phenyl-2,3-di-O-benzoyl-4,6-O-benzylidene-1-thio-β-D-glucopyranoside (16) in 88% overall yield. Regioselective reductive opening of the benzylidene ring of compound 16 with triethylsilane and iodine furnished phenyl 2,3-di-O-benzoyl-6-O-benzyl-1-thio-β-D-glucopyranoside (17) in 80% yield (Scheme 4).

Scheme 4: Reagents: (a) (i) Ac$_2$O, BF$_3$·OEt$_2$, r t, 15 min; (ii) PhSH, BF$_3$·OEt$_2$, CH$_2$Cl$_2$, 5 °C, 5 h, 90%; (b) (i) CH$_3$ONa, MeOH, r t, 4 h; (ii) PhCH(OMe)$_2$, p-TsOH, CH$_3$CN, r t, 10 h; (c) benzyl chloride, pyridine, r t, 4 h, 88%; (d) Et$_3$SiH, I$_2$, CH$_2$Cl$_2$, 0-5 °C, 15 min, 80%.

2.4.2.4. Preparation of 2,3,4-tri-O-acetyl-2-azido-2-deoxy-β-D-galactopyranosyl trichloroacetimidate (18)

Please see page no. 63.

2.4.2.5. Synthesis of 2-(p-methoxyphenoxy) ethyl (4,6-O-benzylidene-2-deoxy-2-N-phthalimido-β-D-glucopyranosyl)-(1→2)-3,4,6-tri-O-benzyl-β-D-galactopyranoside (20)

Stereoselective glycosylation of glycoside acceptor with thioglycoside derivative in the presence of a combination of N-iodosuccinimide (NIS) and HClO$_4$·SiO$_2$ resulted in the formation of 2-(p-methoxyphenoxy) ethyl (3-O-acetyl-4,6-O-benzylidene-2-deoxy-2-N-phthalimido-β-D-glucopyranosyl)-(1→2)-3,4,6-tri-O-benzyl-β-D-galactopyranoside (19) in 76% yield. Appearance of signals in the NMR spectra [δ 5.86 (d, J = 8.4 Hz, H-1B), 5.47 (s, PhCH), 4.33 (d, J = 7.7 Hz, H-1A) in the $^1$H NMR and δ 102.7 (C-1A), 101.6 (PhCH), 99.3 (C-1B) in the
13C NMR spectra confirmed its formation. Saponification of compound 19 using sodium methoxide afforded compound 20 in 87% yield (Scheme 5).

**Scheme 5:** Reagents: (a) NIS, HClO₄-SiO₂, MS 4Å, CH₂Cl₂, -25 °C, 1 h, 76% (b) 0.01 M CH₃ONa, CH₃OH, r t, 1 h, 87%.

### 2.4.2.6. Synthesis of phenyl (3,4,6-tri-0-acetyl-2-azido-2-deoxy-α-D-galactopyranoyl)-(1→4)-2,3-di-0-benzoyl-6-0-benzyl-1-thio-β-D-glucopyranoside (21)

Stereoselective condensation of trichloroacetimidate derivative 18 with thioglycoside derivative 17 as glycosyl acceptor in the presence of HClO₄-SiO₂³⁸,³⁹ furnished phenyl (3,4,6-tri-0-acetyl-2-azido-2-deoxy-α-D-galactopyranoyl)-(1→4)-2,3-di-0-benzoyl-6-0-benzyl-1-thio-β-D-glucopyranoside (21) in 70% yield exploiting the orthogonal property of thiophenyl group⁶⁴ in compound 17. Appearance of signals in the NMR spectra [δ 5.22 (d, J = 3.1 Hz, H-1d), 4.96 (d, J = 9.8 Hz, H-1c)] in the 1H NMR and 89.7 (C-1D), 85.8 (C-1c) in the 13C NMR spectra confirmed its formation (Scheme 6).

**Scheme 6:** Reagents: HClO₄-SiO₂, CH₂Cl₂, -10 °C, 1 h, 70%.

### 2.4.2.7. Synthesis of 2-(p-methoxyphenoxy) ethyl (2-acetamido-2-deoxy-α-D-galactopyranoyl)-(1→4)-(sodium β-D-glucopyranosyluronate)-(1→3)-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→2)-sodium-β-D-galactopyranosiduronate (1)
Stereoselective glycosylation of disaccharide thioglycoside donor 21 with disaccharide acceptor 20 in the presence of NIS and HClO₄-SiO₂ furnished 2-(p-methoxyphenoxy) ethyl (3,4,6-tri-O-acetyl-2-azido-2-deoxy-α-D-galactopyranoyl)-(1→4)-(2,3-di-O-benzoyl-6-O-benzyl-β-D-glucopyranosyl)-(1→3)-(4,6-O-benzylidene-2-deoxy-2-N-phthalimido-β-D-galactopyranosyl)-(1→2)-3,4,6-tri-O-benzyl-β-D-galactopyranoside (22) in 72% yield. Appearance of signals in the NMR spectra [δ 5.60 (d, J = 8.4 Hz, H-1_B), 5.27 (s, PhCH), 5.07 (d, J = 3.6 Hz, H-1_D), 4.80 (d, J = 7.8 Hz, H-1_C), 4.39 (d, J = 8.0 Hz, H-1_A) in the ¹H NMR and δ 102.6 (C-1ₐ), 101.5 (PhCH), 99.9 (C-1_c), 99.1 (C-1_b), 98.2 (C-1_d) in the ¹³C NMR spectra] confirmed its formation. Finally compound 22 was subjected to a sequence of functional group transformations involving (a) conversion of N-phthalimido group to acetamido group, (b) selective removal of benzyl ethers and reduction of azide group, (c) TEMPO mediated oxidation of two primary hydroxyl groups to the carboxylic groups under a phase transfer reaction condition, (d) removal of benzylidene acetal and saponification of O-acetyl groups to furnish target tetrasaccharide 1 as its disodium salt and 2-(p-methoxyphenoxy) ethyl glycoside in overall 50% yield. Spectral analysis of compound 1 unambiguously confirmed its formation [δ 5.01 (br s, H-1_d), 4.84 (br s, H-1_B), 4.30 (d, J = 7.8 Hz, H-1_A), 4.28 (d, J = 7.7 Hz, H-1_C) in the ¹H NMR and δ 100.8 (C-1_c), 100.6 (C-1_d), 99.0 (C-1_b), 98.9 (C-1_d) in the ¹³C NMR spectra]. It is note-worthy that two uronic acid moieties were prepared in one step applying a late stage selective oxidation protocol (Scheme 7).

**Scheme 7:** Reagents: (a) NIS, HClO₄-SiO₂, MS 4Å, CH₂Cl₂, −25 °C, 1 h, 72%; (b) (i) NH₂NH₂·H₂O, C₂H₅OH, 80 °C, 8 h; (ii) Ac₂O, HClO₄-SiO₂, r t, 30 min; (c) (i) H₂, 20% Pd(OH)₂-C, CH₃OH, r t, 6 h; (ii) Ac₂O, CH₃OH, r t, 30 min; (d) (i) NaBr, TBAB, TEMPO, NaHCO₃, NaOCl, CH₂Cl₂, H₂O, 0-5 °C, 5 h; (ii) tert-butanol, 2-methyl-but-2-ene, NaClO₂, NaH₂PO₄, r t, 5 h; (c) (i) H₂, 20% Pd(OH)₂-C, CH₃OH, r t, 24 h; (ii) 0.1 M CH₃ONa, CH₃OH, r t, 6 h, over all 50%.
2.4.3. Conclusion

In conclusion, a concise synthetic strategy has been developed for the synthesis of the common tetrasaccharide repeating unit corresponding to the O-antigen of enteroinvasive *Escherichia coli* O143 and *Shigella dysenteriae* type 8 as its disodium salt and 2-(p-methoxyphenoxy) ethyl glycoside. A [2+2] block synthetic strategy has been applied to achieve the target compound in minimum number of steps. HClO₄-SiO₂ has been used as a moisture tolerant, low cost, environmentally benign solid acid catalyst in all glycosylation steps and functional group transformations. A late stage selective oxidation of primary hydroxyl group has been successfully incorporated in the synthetic strategy.

2.4.4. Experimental section

2.4.4.1. General methods: Please see page no. 67.

2.4.4.2. Preparation of HClO₄-SiO₂⁴⁹,⁵⁰: Please see page no. 107.

2.4.4.3. Preparation and spectral data of compounds 1-22

3,4,6-Tri-O-acetyl-D-galactal (2): Please see page no. 67.

3,4,6-Tri-O-benzyl-D-galactal (3): To a solution of 3,4,6-tri-O-acetyl-D-galactal 2 (2.8 g, 10.3 mmol) in THF (10 mL) were added powdered NaOH (2.5 g, 62.5 mmol), tetrabutylammoniumiodide (TBAI) (100 mg, 0.27 mmol), and benzyl bromide (5.5 mL, 46.2 mmol) and the reaction mixture was allowed to stir briskly at room temperature for 5 h. The reaction mixture was poured into water and extracted with CH₂Cl₂ (150 mL). The organic layer was washed with water, dried (Na₂SO₄), and concentrated to dryness. The crude reaction product was purified over SiO₂ using hexane-EtOAc (8:1) as the eluant to furnish pure compound 3 (4.1 g, 95%). Yellow oil; ¹H NMR (200 MHz, CDCl₃): δ 7.33-7.25 (m, 15 H, Ar-H), 6.36 (d, J = 6.1 Hz, 1 H), 4.90-4.84 (m, 2 H), 4.69-4.60 (m, 3 H), 4.44-4.38 (m, 2 H), 4.18 (br s, 2 H), 3.94 (s, 1 H), 3.78 (dt, J = 7.5, 2.2 Hz, 1 H), 3.64 (q, J = 5.0 Hz each, 1 H); ESI-MS: 439 [M+Na]+; Anal. Calcd. for C₂₇H₂₉O₄ (416): C, 77.86; H, 6.78; found: C, 77.68; H, 6.98.

1,2-Di-O-acetyl-3,4,6-tri-O-benzyl-α/β-D-galactopyranose (4): To a solution of compound 3 (2.5 g, 6.0 mmol) in acetone-water (50 mL, 5:1, v/v) was added Oxone® (11 g, 75 mmol) and NaHCO₃ (3 g, 150 mmol) at 20-25°C in small portions over a period of 30-60 min with continuous stirring. After the completion of the reaction, acetone was evaporated and the
remaining semi-solid mass was filtered and washed with EtOAc (100 mL). The organic layer was successively washed with water and brine, dried (Na\textsubscript{2}SO\textsubscript{4}) and concentrated. A solution of the crude product in acetic anhydride (8 mL) and pyridine (8 mL) was kept at room temperature for 3 h. The solvent were removed under reduced pressure and the crude product was purified over SiO\textsubscript{2} using hexane-EtOAc (3:1) as the eluant to furnish pure compound \textit{4} (2.2 g, 88%; \(\alpha/\beta: 1/1\)). Yellow oil; \([\alpha]\text{D}\)\textsubscript{25} +164.1 (c 1.0, CHCl\textsubscript{3}); IR (neat): 2923, 2341, 1751, 1596, 1355, 1228, 1062, 754 cm\textsuperscript{-1}; \(\text{\textsuperscript{1}H NMR (300 MHz, CDCl}_{3}\text{): \delta 7.33-7.21 (m, 30 H, Ar-H), 6.33 (d, \(J = 3.6 \text{ Hz}, \text{ 1 H, H-1a}\)), 5.59 (d, \(J = 8.1 \text{ Hz}, \text{ 1 H, H-1b}\)), 5.53-5.44 (m, 2 H, H-2a, H-2b), 4.95 (d, \(J = 11.1 \text{ Hz}, \text{ 2 H, PhCH}_{2}\)), 4.73-4.64 (m, 3 H, PhCH\textsubscript{2}), 4.61-4.48 (m, 4 H, PhCH\textsubscript{2}, H-4a), 4.47-4.38 (m, 5 H, PhCH\textsubscript{2}, H-4b), 4.06-3.99 (m, 1 H, H-5a), 3.92-3.88 (dd, \(J = 10.5, 2.4 \text{ Hz}, \text{ 1 H, H-3a}\)), 2.08, 2.05 (2 s, 6 H, 2 COC\textsubscript{6}H\textsubscript{5}), 2.00 (s, 6 H, 2 COCH\textsubscript{3}), 2.13, 2.12 (2 C, 21.0; ESI-MS: 557 [M+Na]+; Anal. Calcd. for C\textsubscript{31}H\textsubscript{34}O\textsubscript{8} (534): C, 69.65; H, 6.41; found C, 69.40; H, 6.67.

\textit{2-O-Acetyl-3,4,6-tri-0-benzyl-\(\alpha\)-d-galactopyranosyl trichloroacetimidate (5)}: To a solution of compound \textit{4} (2.2 g, 4.05 mmol) in THF (30 mL) was added benzyl amine (660 \mu L, 6.07 mmol) and the reaction mixture was stirred at room temperature for 12 h. The reaction mixture was concentrated under reduced pressure and the crude mass was purified over SiO\textsubscript{2} using hexane-EtOAc (1:1) as eluant to give hemiacetal derivative (1.9 g) as colorless oil. To a solution of the hemiacetal derivative (1.9 g, 3.86 mmol) in anhydrous CH\textsubscript{2}CL\textsubscript{2} (25 mL) was added trichloroacetonitrile (1.95 mL, 19.3 mmol) followed by DBU (80 \mu L, 0.52 mmol) at \(-10 \text{ °C}\) and the reaction mixture was allowed to stir at same temperature for 1 h. The reaction mixture was concentrated under reduced pressure and the crude product was purified over SiO\textsubscript{2} using hexane-EtOAc (2:1) as eluant to give pure compound \textit{5} (2.3 mg, 88%) as colorless oil, which has been used immediately for the next reaction.

\textit{2-(p-Methoxyphenoxy) ethyl 2-O-acetyl-3,4,6-tri-0-benzyl-\(\beta\)-d-galactopyranoside (7)}: A solution of compound \textit{5} (2 g, 3.13 mmol) and \(2-(p\text{-methoxyphenoxy})\) ethanol \textit{6} (550 mg, 3.26 mmol) in anhydrous CH\textsubscript{2}Cl\textsubscript{2} (15 mL) was cooled to \(-10 \text{ °C}\). To the cooled reaction mixture was added HClO\textsubscript{4}-SiO\textsubscript{2} (100 mg) and it was allowed to stir at same temperature for 1 h. The reaction
mixture was filtered through a Celite® bed, washed with CH₂Cl₂ (100 mL) and concentrated under reduced pressure. The crude product was purified over SiO₂ using hexane-EtOAc (5:1) as eluant to give pure compound 7 (1.5 g, 74%). Yellow oil; [α]D²⁵ = -4.2 (c 1.2, CHCl₃); IR (neat): 2931, 2873, 1748, 1508, 1455, 1367, 1234, 1066, 826, 738 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ 7.43-7.23 (m, 15 H, Ar-H), 6.80-6.77 (m, 4 H, Ar-H), 5.38 (t, J = 8.4 Hz each, 1 H, H-2), 4.91 (d, J = 11.6 Hz, 1 H, PhCH₂), 4.67 (d, J = 12.1 Hz, 1 H, PhCH₂), 4.67 (d, J = 12.1 Hz, 1 H, PhCH₂), 4.59 (d, J = 12.1 Hz, 1 H, PhCH₂), 4.52 (d, J = 11.6 Hz, 1 H, PhCH₂), 4.48 (d, J = 8.1 Hz, 1 H, H-1), 4.46 (d, J = 11.8 Hz, 1 H, PhCH₂), 4.42 (d, J = 11.8 Hz, 1 H, PhCH₂), 4.06-4.01 (m, 3 H, -C₃H₂-), 3.98 (t, J = 8.0 Hz each, 1 H, H-2), 3.95 (s, 3 H, OCH₃), 3.64-3.55 (m, 3 H, H-5, H-6ab), 3.53 (dd, J = 10.0, 2.3 Hz, 1 H, H-3); ¹³C NMR (125 MHz, CDCl₃): δ 169.6 (COCH₃), 153.9-114.6 (Ar-C), 101.6 (C-1), 80.2 (C-2), 74.5 (PhCH₂), 73.7 (PhCH₂), 73.6 (PhCH₂), 72.6 (C-3), 72.0 (C-5), 71.2 (C-4), 68.6 (C-6), 68.0 (CH₂), 67.5 (CH₂), 55.7 (OCH₃), 20.9 (COCH₃); ESI-MS: 665.2 [M+Na]⁺; Anal. Calcd. for C₃₈H₄₂O₉ (642.28): C, 71.01; H, 6.59; found: C, 70.80; H, 6.82.

2-(p-Methoxyphenoxy) ethyl 3,4,6-tri-O-benzyl-β-D-galactopyranoside (8): A solution of compound 7 (1.4 g, 2.18 mmol) in 0.01 M NaOH in CH₃OH (25 mL) was allowed to stir at room temperature for 1 h. The reaction mixture was neutralized with Dowex 50W X8 (H⁺) resin, filtered and concentrated to give pure compound 8 (1.2 g, 92%). White solid; m.p. 65-67 °C [EtOH]; [α]D²⁵ = -9.2 (c 1.2, CHCl₃); IR (KBr): 3441, 2950, 2882, 1510, 1454, 1367, 1237, 1122, 1054, 821, 734, 696 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ 7.36-7.24 (m, 15 H, Ar-H), 6.84-6.78 (m, 4 H, Ar-H), 4.90 (d, J = 11.5 Hz, 1 H, PhCH₂), 4.71 (s, 2 H, PhCH₂), 4.61 (d, J = 11.5 Hz, 1 H, PhCH₂), 4.44 (d, J = 11.6 Hz, 1 H, PhCH₂), 4.42 (d, J = 11.6 Hz, 1 H, PhCH₂), 4.34 (d, J = 7.6 Hz, 1 H, H-1), 4.20-4.02 (m, 3 H, -CH₂-), 3.98 (t, J = 8.0 Hz each, 1 H, H-2), 3.95-3.80 (m, 2 H, H-4, -CH₂-), 3.74 (s, 3 H, OCH₃), 3.60-3.55 (m, 3 H, H-5, H-6ab), 3.46 (dd, J = 10.0, 2.3 Hz, 1 H, H-3); ¹³C NMR (125 MHz, CDCl₃): δ 154.0-114.6 (Ar-C), 81.8 (C-2), 74.6 (PhCH₂), 73.8 (PhCH₂), 73.6 (PhCH₂), 72.6 (C-3), 72.4 (C-5), 71.4 (C-4), 68.7 (C-6), 68.2 (-CH₂-), 67.8 (-CH₂-), 55.7 (OCH₃); ESI-MS: 623.2 [M+Na]⁺; Anal. Calcd. for C₃₆H₄₀O₈ (600.27): C, 70.71; H, 6.59; found: C, 70.80; H, 6.62.

1,3,4,6-Tetra-O-acetyl-2-deoxy-2-N-phthalimido-β-D-glucopyranose (10): To a solution of D-glucosamine hydrochloride (9; 10 g, 46.5 mmol) in methanol-water (60 mL; 1:2, v/v) was added NaOH (1.9 g, 46.5 mmol) and the reaction mixture was allowed to stir at room temperature for 1 h. The reaction mixture was then cooled to 15 °C and a solution of phthalic anhydride (8 g, 54.0
mmol) in acetone (40 mL) was added to it slowly maintaining the temperature below 15 °C. After stirring at room temperature for 2 h, solid NaHCO₃ (8 g, 95.2 mmol) was added in portions and the reaction mixture was allowed to stir at 50 °C for 30 min. The reaction mixture was then allowed to stir at room temperature for 12 h. The reaction mixture was neutralized with cold HCl maintaining the temperature below 20 °C. On cooling the resulting reaction mixture 2-deoxy-2-N-phthalimido-α/β-d-glucopyranose precipitated out as white solid. The product was collected by filtration, washed with cold water and dried. To a suspension of crude product in acetic anhydride (100 mL), anhydrous sodium acetate (25 g) was added and the reaction mixture was refluxed for 30 min. After cooling, the reaction mixture was diluted with CH₂Cl₂ (300 mL) and successively washed with water and saturated NaHCO₃. The organic layer was dried (Na₂SO₄) and concentrated to a yellow syrup. Column chromatography of the crude product over SiO₂ using hexane-EtOAc (8:1) as eluant gave pure compound 10 (14.5 g, 83%). White solid; m. p. 126-127 °C [EtOH]; [α]D25 + 38 (c 1.5, CHCl₃); ¹H NMR (300 MHz, CDCl₃): δ 7.89-7.83 (m, 2 H, Ar-H), 7.78-7.74 (m, 2 H, Ar-H), 6.51 (d, J = 8.8 Hz, 1 H), 5.89 (t, J = 9.1 Hz each, 1 H), 5.21 (t, J = 9.9 Hz each, 1 H), 4.78 (t, J = 8.9 Hz each, 1 H), 4.39-4.33 (m, 1 H), 4.18-4.11 (m, 2 H), 2.12, 2.04, 2.00, 1.87 (4 s, 12 H, 4 COCH₃); ¹³C NMR (75 MHz, CDCl₃): δ 171.0, 169.8, 167.7 (2 C), 134.8-124.0 (Ar-C), 90.1 (C-1), 73.0, 70.9, 68.7, 61.9, 53.9, 21.3, 21.0, 20.9, 20.7 (4 COCH₃); IR (KBr): 2364, 1754, 1722, 1382, 1220, 771 cm⁻¹; ESI-MS: 500 [M+Na]⁺; Anal. calcd. for C22H23NO7 (477): C, 55.35; H, 4.86; found: C, 55.54; H, 5.03.

Ethyl 3,4,6-tri-O-acetyl-2-deoxy-2-N-phthalimido-1-thio-β-D-glucopyranoside (11): To a solution of compound 10 (12 g, 25.9 mmol) in dried CH₂Cl₂ (40 mL) was added EtSH (7.6 mL, 103.7 mmol) and BF₃·Et₂O (9.8 mL, 77.7 mmol) at 0 °C and the reaction was allowed to stir at 5 °C for 5 h. The reaction mixture was diluted with CH₂Cl₂ (200 mL) and the organic layer was washed with saturated NaHCO₃ and water, dried (Na₂SO₄) and concentrated. Purification of the crude product over SiO₂ using hexane-EtOAc (5:1) as eluant, afforded the pure compound 11 (10.5 g, 85%). Yellow oil; [α]D25 + 81.3 (c 1.5, CHCl₃); IR (neat): 3002, 1740, 1428, 1591, 1384, 1228, 1074, 1037 cm⁻¹; ¹H NMR (300 MHz, CDCl₃): δ 7.81-7.75 (m, 2 H, Ar-H), 7.70 - 7.65 (m, 2 H, Ar-H), 5.76 (t, J = 9.6 Hz each, 1 H), 5.42 (d, J = 10.6 Hz, 1 H), 5.10 (t, J = 9.6 Hz each, 1 H), 4.31 (t, J = 10.4 Hz each, 1 H), 4.26-4.18 (m, 1 H), 4.10 (dd, J = 12.3, 2.2 Hz, 1 H), 3.87-3.79 (m, 1 H), 2.63-2.57 (m, 2 H, SCH₂CH₃), 2.02, 1.95, 1.78 (3 s, 9 H, 3 COCH₃), 1.15 (t, J = 7.5 Hz each, 3 H, SCH₂CH₃); ¹³C NMR (75 MHz, CDCl₃): δ 170.9, 170.3, 169.8, 168.0, 167.5,
**Ethyl 4,6-0-benzylidene-2-deoxy-2-N-phthalimido-1-thio-β-D-glucopyranoside (12):** A solution of compound 11 (7 g, 23.25 mmol) in 0.01 M CH₃ONa in CH₃OH (60 mL) was allowed to stir at room temperature for 30 min and neutralized with Dowex-50W X8 (H⁺) resin. The reaction mixture was filtered and evaporated to dryness. The dried mass was dissolved in anhydrous CH₃CN (20 mL) and benzaldehyde dimethylacetal (5.25 mL, 35 mmol) was added to it followed by p-TsOH (200 mg). After stirring at room temperature for 10 h, the reaction mixture was quenched with Et₃N (0.5 mL) and solvents were removed under reduced pressure and the crude mass was purified over SiO₂ using hexane-EtOAc (2:1) as eluant to furnish pure compound 12 (4.9 g, 76 %). Yellow oil; ¹H NMR (500 MHz, CDCl₃): δ 7.80-7.31 (m, 9 H, Ar-H), 5.51 (s, 1 H, PhCH), 5.28 (d, J = 10.6 Hz, 1 H, H-1), 4.57-4.53 (m, 1 H, H-4), 4.32 (dd, J = 10.5, 4.8 Hz each, 1 H, H-6a), 4.22 (t, J = 10.3, 2.5 Hz each, 1 H, H-6b), 3.73 (t, J = 10.1 Hz each, 1 H, H-3), 3.62-3.57 (m, 1 H, H-5), 3.51 (t, J = 9.2 Hz each, 1 H, H-2), 2.69-2.59 (m, 2 H, SCH₂CH₃), 1.16 (t, J = 7.4 Hz each, 3 H, SCH₂CH₃); ¹³C NMR (125 MHz, CDCl₃): δ 168.5, 167.9 (2 Phth), 137.4-123.7 (Ar-C), 102.1 (PhCH), 82.4 (C-1), 82.1 (C-4), 70.7 (C-3), 69.8 (C-6), 68.9 (C-5), 55.9 (C-2), 24.4 (SCH₂CH₃), 15.2 (SCH₂CH₃); ESI-MS: 463.0 [M+Na]⁺; Anal. Calcd. for C₂₃H₂₃N₀₆S (441.5): C, 62.57; H, 5.25; found: C, 63.12; H, 5.74.

**Ethyl 3-O-acetyl-4,6-0-benzylidene-2-deoxy-2-N-phthalimido-1-thio-β-D-glucopyranoside (13):** To a solution of compound 12 (2 g, 4.5 mmol) in pyridine (15 ml) was added acetic anhydride (10 ml) and the reaction mixture was allowed to stir at room temperature for 6 h. The solvents were removed under reduced pressure to give the crude product, which was purified over SiO₂ using hexane-EtOAc (3:1) as eluant to furnish pure compound 13 (1.9 g, 85%). White solid; m.p. 138 °C [EtOH]; [α]₂⁵⁺ + 35 (c 1.0, CHCl₃); IR (neat): 3020, 2361, 1718, 1508, 1385, 1216, 1099, 758 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ 7.86-7.33 (m, 9 H, Ar-H), 5.88 (t, J = 9.3 Hz each, 1 H, H-3), 5.56 (d, J = 10.6 Hz, 1 H, H-1), 5.52 (s, 1 H, PhCH), 4.39-4.40 (m, 1 H, H-5), 4.34 (t, J = 10.2 Hz each, 1 H, H-2), 3.81-3.75 (m, 3 H, H-4, H-6a), 2.73-2.63 (m, 2 H, SCH₂CH₃), 1.89 (s, 3 H, COCH₃), 1.20 (t, J = 7.4 Hz each, 3 H, SCH₂CH₃); ¹³C NMR (125 MHz, CDCl₃): δ 170.3 (COCH₃), 167.5, 167.6 (2 CO, Phth), 137.3-124.0 (Ar-C), 102.0 (PhCH), 82.0 (C-1), 79.6 (C-4), 70.9 (2 C, C-3, C-5), 69.0 (C-6), 54.6 (C-2), 24.7 (SCH₂CH₃), 20.9 (COCH₃), 15.3 (SCH₂CH₃); ESI-MS: 507.0 [M+Na]⁺; Anal. Calcd. for C₂₅H₂₅N₀₇S (483.5): C, 62.10; H, 5.21; found: C, 62.85; H, 6.82.
Phenyl 2,3,4,6-tetra-O-acetyl-l-thio-β-D-glucopyranoside (15): A suspension of D-glucose (14) (2 g, 11.1 mmol) in acetic anhydride (5.5 mL, 57 mmol) was placed in an ice bath with continuous stirring. To this cold suspension was added BF$_3$·OEt$_2$ (2.1 mL, 16.7 mmol) in one portion. An exothermic reaction started immediately and the mixture was allowed to stir at room temperature for 15 min. After consumption of the starting material, thiophenol (1.8 mL, 17.3 mmol) was added and the reaction mixture was allowed to stir for another 5 h at 5 °C. The reaction was quenched by the addition of aq NaHCO$_3$ and extracted with CH$_2$Cl$_2$ (100 mL). The organic layer was washed with water, dried (Na$_2$SO$_4$), and concentrated under reduced pressure. Column chromatography of the crude product over SiO$_2$ using hexane-EtOAc (3:1) as the eluant furnished pure compound 15, which was crystallized from Et$_2$O-hexane (4.4 g, 90%). White solid, m.p. 117-118 °C [Et$_2$O-hexane]; [α]$_D^{25}$ −15 (c 1.2, CHCl$_3$); IR (KBr): 3024, 1750, 1477, 1436, 1371, 1237, 1067, 763 cm$^{-1}$; $^1$H NMR (300 MHz, CDCl$_3$): δ 7.51-7.29 (m, 5 H, Ar-H), 5.17 (t, $J$ = 9.2 Hz each, 1 H), 5.05 (t, $J$ = 9.7 Hz each, 1 H), 4.97 (t, $J$ = 9.2 Hz each, 1 H), 4.70 (d, $J$ = 9.9 Hz, 1 H), 4.21-4.18 (m, 2 H), 3.80-3.65 (m, 1 H), 2.08, 2.07, 2.01, 1.98 (4 s, 12 H, 4 CO$_2$H$_3$); $^{13}$C NMR (75 MHz, CDCl$_3$): δ 170.3, 170.1, 169.2, 169.0 (4 COCl$_3$), 133.7-128.7 (Ar-C), 85.9, 76.2, 74.4, 70.3, 68.5, 62.3, 20.9 (2 C), 20.8 (2 C) (4 COCH$_3$); ESI-MS: 463 [M+Na]; Anal. Calcd. for C$_{20}$H$_{24}$O$_9$S (440): C, 54.54; H, 5.49; found: C, 54.38; H, 5.65.

Phenyl 2,3-di-O-benzoyl-4,6-O-benzylidene-l-thio-β-D-glucopyranoside (16): A solution of compound 15 (4.4 g, 10 mmol) in 0.05 M CH$_3$ONa in methanol (100 mL) was stirred at room temperature for 4 h. The reaction mixture was neutralized with Amberlite IR-120 (H$^+$) resin, filtered and the filtrate was evaporated to dryness to give an amorphous solid in quantitative yield. The dried mass was dissolved in anhydrous CH$_3$CN (30 mL) and benzaldehyde dimethyl acetal (3.0 mL, 20.0 mmol) was added to it followed by p-TsOH (300 mg) to make the reaction mixture acidic (pH~2). After stirring the reaction mixture at room temperature for 10 h, triethyl amine (0.5 mL) was added to it and concentrated under reduced pressure. To a solution of the crude mass in pyridine (5 mL) was added benzoyl chloride (3 mL) and the reaction mixture was stirred at room temperature for 4 h. The solvents were removed under reduced pressure and the crude mass was purified over SiO$_2$ using hexane-EtOAc (3:1) as eluant to afford pure compound 16 (3 g, 88%). White solid; m.p. 210-211 °C [EtOH]; [α]$_D^{25}$ −43 (c 1.5, CHCl$_3$); IR (KBr): 2930, 1729, 1598, 1453, 1352, 1270, 1094, 1025, 995, 706 cm$^{-1}$; $^1$H NMR (200 MHz, CDCl$_3$): δ 7.95-7.89 (m, 4 H, Ar-H), 7.49-7.25 (m, 16 H, Ar-H), 5.78-5.72 (t, $J$ = 9.3 Hz each, 1 H, H-2), 5.48 (s, 1 H, PhCH$_3$), 5.44-5.38 (t, $J$ = 9.3 Hz each, 1 H, H-3), 4.99 (d, $J$ = 9.9 Hz, 1 H, H-1), 4.44-4.39 (dd, $J$ = 4.5, 9.9 Hz, 1 H, H-4), 3.88-3.74 (m, 2 H, H-6$\alpha$), 3.73-3.67 (m, 1 H, H-5); $^{13}$C
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NMR (50 MHz, CDCl₃): δ 165.3, 164.9 (2 PhCO), 136.7-126.2 (Ar-C), 101.5 (PhCH), 86.9 (C-1), 78.6, 73.3, 71.0, 70.9, 68.5; ESI-MS: 591 [M+Na]⁺; Anal. Calcd. for C₃₃H₂₈O₇S (568): C, 69.70; H, 4.96; found: C, 69.45; H, 5.22.

**Phenyl 2,3-di-O-benzoyl-6-O-benzyl-l-thio-β-D-glucopyranoside (17):** To a solution of the compound 16 (2 g, 3.51 mmol) in CH₃CN (15 mL) were added Et₃SiH (1.1 mL, 6.9 mmol) and iodine (0.2 mg, 0.78 mmol) was added at 0-5 °C and the reaction mixture was allowed to stir at same temperature for 15 min. The reaction mixture was poured into water and extracted with CH₂Cl₂ (100 mL). The organic layer was successively washed with satd. Na₂S₂O₃ and water, dried (Na₂SO₄) and concentrated. The solvents were removed under reduced pressure and the crude product was purified over SiO₂ using hexane-EtOAc (2:1) as eluant to give pure compound 17 (1.6 g, 80%). White solid; m.p. 134-135 °C [EtOH]; ¹H NMR (600 MHz, CDCl₃): δ 7.96-7.90 (m, 4 H, Ar-H), 7.49-7.47 (m, 4 H, Ar-H), 7.46-7.23 (m, 12 H, Ar-H), 5.46 (t, J= 9.0 Hz each, 1 H, H-3), 5.39 (t, J = 9.5 Hz each, 1 H, H-2), 4.93 (d, J = 9.5 Hz, 1 H, H-1), 4.63-4.58 (qt, J = 12.0 Hz each, 2 H, PhCH₂), 3.91-3.85 (m, 3 H, H-4, H-6ab), 3.74-3.71 (m. 1 H, H-5), 3.33 (br s, 1 H, OMe); ESI-MS: 593.1 [M+Na]⁺; Anal. Calcd. for C₃₃H₃₀O₇S (570.17): C, 69.30; H, 5.52; found: C, 69.90; H, 5.52.

**2,3,4-Tri-O-acetyl-2-azido-2-deoxy-β-D-galactopyranosyl trichloroacetimidate (18):** Please see page no. 68.

**2-(p-Methoxyphenoxy) ethyl (3-O-acetyl-4,6-O-benzylidene-2-deoxy-2-N-phthalimido-β-D-glucopyranosyl)-(1→2)-3,4,6-tri-O-benzyl-β-D-galactopyranoside (19):** To a solution of compound 13 (970 mg, 2.0 mmol) and compound 8 (1 g, 1.66 mmol) in anhydrous CH₂Cl₂ (10 mL) was added MS 4Å (1.0 g) and the reaction mixture was cooled to ~25 °C. To the cooled reaction mixture were added N-iodosuccinimide (NIS; 500 mg, 2.22 mmol) and HClO₄-SiO₂ (25 mg) and the reaction mixture was allowed to stir at same temperature for 1 h. The reaction mixture was filtered through a Celite® bed, washed with CH₂Cl₂ (100 mL). The organic layer was successively washed with 5% Na₂S₂O₃, satd. NaHCO₃ and water, dried (Na₂SO₄) and concentrated. The crude product was purified over SiO₂ using hexane-EtOAc (4:1) as eluant to give pure compound 19 (1.3 g, 76%). White solid; m.p. 71-73 °C [EtOH]; [α]D²⁵ = 6.2 (c 1.2, CHCl₃); IR (KBr): 3031, 2930, 2871, 1776, 1744, 1716, 1509, 1455, 1388, 1231, 1085, 1030, 722, 698 cm⁻¹; ¹H NMR (600 MHz, CDCl₃): δ 7.56-7.04 (m, 24 H, Ar-H), 6.95 (d, J = 9.0 Hz, 2 H, Ar-H), 6.84 (d, J = 9.0 Hz, 2 H, Ar-H), 5.86 (d, J = 8.4 Hz, 1 H, H-1B), 5.79 (dd, J = 9.0 Hz,...
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each, 1 H, H-3B), 5.47 (s, 1 H, PhCH), 4.42- 4.36 (m, 5 H, H-5B, 2 PhCH₂), 4.33 (d, \( J = 7.7 \) Hz, 1 H, H-1A), 4.31 (t, \( J = 8.0 \) Hz each, 1 H, H-2b), 4.21-4.17 (m, 3 H, PhCH₂, -CH₂-), 4.13-4.04 (m, 2 H, -CH₂-), 3.95-3.88 (m, 1 H, -CH₂-), 3.83 (dd, \( J = 7.2 \) Hz each, 1 H, H-2A), 3.80-3.76 (m, 1 H, H-4b), 3.75 (s, 3H, OC-3), 3.73-3.70 (m, 2 H, H-6abB), 3.54 (d, \( J = 2.1 \) Hz, 1 H, H-4A), 3.45-3.42 (m, 2 H, H-6abA), 3.38-3.36 (m, 1 H, H-5A), 3.29 (dd, \( J = 10.0, 2.3 \) Hz, 1 H, H-3A), 1.86 (s, 3 H, COCH₃); \[^{13}C\text{NMR} \text{(150MHz, CDCl}_3\text{): \delta} 170.1 \text{ (COCH}_3\text{), 167.9, 167.8 (2 C, Phth), 153.9-114.7 \text{ (Ar-C), 102.7 (C-1A), 101.6 (PhCH), 99.3 (C-1b), 80.1 (C-3A), 79.3 (C-2A), 79.2 (C-4b), 73.8 (PhCH}_2\text{), 73.4 (PhCH}_2\text{), 73.1 (C-5A), 72.8 (C-4A), 72.3 (PhCH}_2\text{), 70.0 (C-3b), 68.7 (C-5b), 68.5 (C-6A), 68.1 (-CH}_2\text{-), 68.0 (-CH}_2\text{-), 66.2 (C-6b), 56.2 (C-2a), 55.7 (OCH}_3\text{), 20.5 (COCH}_3\text{); ESI-MS: 1044.3 [M+N+Na]^+; Anal. Calcd. for C}_{59}H_{59}NO_{14} (1021.39): C, 69.33; H, 5.82; found: C, 69.51; H, 6.05.

2-(p-Methoxyphenoxy) ethyl (4,6-O-benzylidene-2-deoxy-2-N-phthalimido-\( \beta\)-D-glucopyranosyl)-(1->2)-3,4,6-tri-O-benzyl-\( \beta\)-D-galactopyranoside (20): A solution of compound 19 (1.2 g, 1.17 mmol) in 0.01 M CH₃ONa in CH₃OH (20 mL) was allowed to stir at room temperature for 1 h. The reaction mixture was neutralized with Dowex 50W X8 (H⁺) resin, filtered and concentrated to give pure compound 20 (1 g, 87%). White solid; m.p. 69-71 °C [EtOH]; \([\alpha]_D^{25} + 16.4 \text{ (c 1.2, CHCl}_3\text{); IR (KBr): 3466, 2925, 2856, 2113, 1715, 1508, 1390, 1233, 1090, 1027, 739, 699 cm}^{-1}; ^{1}H\text{NMR (500 MHz, CDCl}_3\text{): \delta} 7.61-7.07 \text{ (m, 24 H, Ar-H), 6.97 (d, \( J = 9.0 \) Hz, 2 H, Ar-H), 6.85 (d, \( J = 9.0 \) Hz, 2 H, Ar-H), 5.72 (d, \( J = 8.5 \) Hz, 1 H, H-1b), 5.50 (s, 1 H, PhCH), 4.55 (t, \( J = 9.7 \) Hz each, 1 H, H-3b), 4.45-4.28 (m, 7 H, H-1A, H-2b, H-5b, 2 PhCH₂), 4.25-4.17 (m, 3 H, -CH₂-, PhCH₂), 4.16-4.05 (m, 2 H, -CH₂-), 3.95-3.86 (m, 1 H, -CH₂-), 3.85 (dd, \( J = 7.2 \) Hz each, 1 H, H-2A), 3.75 (s, 3 H, OCH₃), 3.74-3.64 (m, 2 H, H-6abB), 3.58-3.50 (m, 2 H, H-4A, H-6abA), 3.48-3.42 (m, 2 H, H-6abB), 3.40-3.32 (m, 1 H, H-5A), 3.30 (dd, \( J = 10.0, 2.3 \) Hz, 1 H, H-3A); ESI-MS: 1002.3 [M+Na]^+; Anal. Calcd. for C}_{59}H_{59}NO_{14} (979.38): C, 69.85; H, 5.86; found: C, 69.66; H, 6.10.

Phenyl (3,4,6-tri-O-acetyl-2-azido-2-deoxy-\( \alpha\)-D-galactopyranosyl)-(1->4)-2,3-di-O-benzoyl-6-\( \beta\)-benzyl-1-thio-\( \beta\)-D-glucopyranoside (21): A solution of compound 18 (650 mg, 1.36 mmol) and 17 (700 mg, 1.23 mmol) in anhydrous CH₂Cl₂ (5 mL) was cooled to \(-10 \) °C. To the cooled reaction mixture was added HClO₄-SiO₂ (50 mg) and it was allowed to stir at same temperature for 1 h. The reaction mixture was filtered through a Celite® bed, washed with CH₂Cl₂ (50 mL) and concentrated under reduced pressure. The crude product was purified over SiO₂ using hexane-EtOAc (6:1) as eluant to give pure compound 21 (760 mg, 70%). White solid; m.p. 72-74
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°C [EtOH]; [α]D25 + 55.7 (c 1.2, CHCl3); IR (KBr): 3437, 2113, 1740, 1273, 1248, 1130, 1069, 1027, 755, 709 cm⁻¹; ¹H NMR (500 MHz, CDCl₃): δ 7.95-7.22 (m, 20 H, Ar-H), 5.77 (t, J = 9.2 Hz each, 1 H, H-3c), 5.34-5.28 (m, 2 H, H-2c, H-4d), 5.22 (d, J = 3.1 Hz, 1 H, H-1d), 5.14 (dd, J = 11.0, 3.0 Hz each, 1 H, H-3d), 4.96 (d, J = 9.8 Hz, 1 H, H-1c), 4.66 (br s, 2 H, PhCH₂), 4.19-4.14 (m, 2 H, H-4c, H-6ad), 3.93-3.88 (m, 4 H, H-5d, H-6bd, H-6abc), 3.79-3.77 (m, 1 H, H-5c), 3.50-3.47 (dd, J = 11.0, 3.2 Hz, 1 H, H-2d), 2.06, 2.00, 1.97 (3 s, 9 H, 3 COCH₃); ¹³C NMR (125 MHz, CDCl₃): δ 170.1, 169.8, 169.5 (3 COCH₃), 165.4, 165.2 (2 PhCO), 138.0-127.6 (Ar-C), 98.7 (C-1d), 85.8 (C-1c), 78.7 (C-5c), 76.1 (C-3c), 74.9 (C-4c), 73.4 (PhCH₂), 70.8 (C-2c), 68.8 (C-6d), 68.2 (C-3d), 67.3 (C-5d), 67.2 (C-4d), 61.4 (C-6c), 57.3 (C-2d), 20.6, 20.2 (2 C) (3 COCH₃); ESI-MS: 906.2 [M+Na]+; Anal. Calcd. for C₄₅H₄₅N₃O₁₄S (883.26): C, 61.15; H, 5.13; found: C, 61.35; H, 6.35.

2-(p-Methoxyphenoxo) ethyl (3,4,6-tri-O-acetyl-2-azido-2-deoxy-α-D-galactopyranosyl)-(1→4)-(2,3-di-O-benzoyl-6-O-benzyl-β-D-gluco pyranosyl)-(1→3)-(4,6-O-benzylidene-2-deoxy-2-N-phthalimido-β-D-gluco pyranosyl)-(1→2)-3,4,6-tri-O-benzyl-β-D-galactopyranoside (22): To a solution of compound 20 (775 mg, 0.79 mmol) and compound 21 (750 g, 0.85 mmol) in anhydrous CH₂Cl₂ (5 mL) was added MS 4Å (1.0 g) and the reaction mixture was cooled to −25 °C. To the cooled reaction mixture were added NIS (220 mg, 0.97 mmol) and HClO₄-SiO₂ (25 mg) and the reaction mixture was allowed to stir at same temperature for 1 h. The reaction mixture was filtered through a Celite® bed, washed with CH₂Cl₂ (50 mL). The organic layer was successively washed with 5% Na₂S₂O₃, satd. NaHCO₃ and water, dried (Na₂SO₄) and concentrated. The crude product was purified over SiO₂ using hexane-EtOAc (4:1) as eluant to give pure compound 22 (1 g, 72%). White solid; m.p. 77-79 °C [EtOH]; [α]D25 + 45.8 (c 1.2, CHCl₃); IR (KBr): 3455, 2925, 2871, 2113, 1737, 1717, 1509, 1454, 1390, 1272, 1232, 1089, 1070, 1028, 709 cm⁻¹; ¹H NMR (600 MHz, CDCl₃): δ 7.74-6.94 (m, 39 H, Ar-H), 6.92 (d, J = 9.0 Hz, 2 H, Ar-H), 6.80 (d, J = 9.0 Hz, 2 H, Ar-H), 5.60 (d, J = 8.4 Hz, 1 H, H-1b), 5.46 (t, J = 9.0 Hz each, 1 H, H-3c), 5.27 (s, 1 H, PhCH), 5.23 (br s, 1 H, H-4b), 5.09 (t, J = 9.0 Hz each, 1 H, H-2c), 5.07 (d, J = 3.6 Hz, 1 H, H-1d), 5.01 (dd, J = 11.4, 3.0 Hz each, 1 H, H-3d), 4.80 (d, J = 7.8 Hz, 1 H, H-1c), 4.65 (dd, J = 10.2, 8.4 Hz, 1 H, H-3b), 4.56 (d, J = 12.6 Hz, 1 H, PhCH₂), 4.41 (d, J = 12.6 Hz, 1 H, PhCH₂), 4.39 (d, J = 8.0 Hz, 1 H, H-1a), 4.37-4.21 (m, 5 H, H-2b, 2 PhCH₂), 4.16-4.12 (m, 2 H, -CH₂-, PhCH₂), 4.08-4.01 (m, 4 H, H-4c, -CH₂-, PhCH₂), 3.97-3.95 (m, 1 H, H-5d), 3.89-3.78 (m, 5 H, H-4a, H-4b, H-6abc, -CH₂-), 3.74 (s, 3 H, OCH₃), 3.73-3.67 (m, 3 H, H-5b, H-6abc), 3.46-3.35 (m, 6 H, H-2a, H-2d, H-6abc, H-6ab), 3.31-3.29 (m,
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1 H, H-5C), 3.22-3.17 (m, 2 H, H-3A, H-5A), 2.02, 2.00, 1.93 (3 s, 9 H, 3 COCH3); 13C NMR (150 MHz, CDCl3): δ 170.1, 169.8, 169.4 (3 COCH3), 168.0, 167.9 (2 C, Phth), 165.1, 164.5 (2 PhCO), 153.9-114.6 (Ar-C), 102.6 (C-1A), 101.5 (PhCH), 99.9 (C-1C), 99.1 (C-1B), 98.2 (C-1D), 81.3 (C-4A), 80.0 (C-5A), 79.0 (C-2A), 76.2 (C-3B), 74.8 (C-5B), 74.5 (C-3C), 74.0 (C-4C), 73.5 (C-3A), 73.3 (PhCH2), 73.0 (PhCH2), 72.9 (PhCH2), 72.8 (C-4B), 72.6 (PhCH2), 72.4 (C-2C), 68.7 (C-6B), 68.5 (C-3D), 68.3 (C-4D), 68.0 (-CH2-), 67.9 (-CH2-), 67.8 (C-6A), 67.0 (C-5C), 66.9 (C-6C), 61.2 (C-6D), 57.3 (C-2B), 55.8 (C-2B), 55.6 (OCH3), 20.6, 20.5, 20.4 (3 COCH3); MALDI-MS: 1775.6 [M+Na]+; Anal. Calcd. for C96H98N4O28 (1752.62): C, 65.74; H, 5.52; found: C, 65.52; H, 5.75.

2-(p-Methoxyphenoxy) ethyl (2-acetamido-2-deoxy-α-D-galactopyranoyl)-(1→4)-(sodium β-D-glucopyranosyluronate)-(1→3)-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→2)-sodium-β-D-galactopyranosiduronate (1): To a solution of compound 22 (800 mg, 0.45 mmol) in C2H5OH (10 mL) was added hydrazine monohydrate (0.1 mL, 2.0 mmol) and the reaction mixture was allowed to stir at 80 °C for 8 h and the solvents were removed under reduced pressure. To a solution of the crude mass in acetic anhydride (3 mL) was added HClO2-SiO2 (25 mg) and the reaction mixture was stirred at room temperature for 30 min. The reaction mixture was filtered, concentrated and the crude reaction product was passed through a short pad of SiO2 using hexane-EtOAc (1:1) as eluant. To a solution of the acetylated product in CH3OH-EtOAc (10 mL, 1:1 v/v) was added 20% Pd(OH)2-C (150 mg) and the reaction mixture was allowed to stir at room temperature under a positive pressure of hydrogen for 6 h. The reaction mixture was filtered through a Celite® bed, washed with CH3OH (50 mL) and concentrated. To a solution of the hydrogenolyzed product in CH3OH (2 mL) was added acetic anhydride (0.5 mL) and the reaction mixture was kept at room temperature for 30 min. The solvents were removed under reduced pressure. To a solution of the crude product in CH2Cl2 (20 mL) and H2O (3 mL) were successively addedaq. solution of NaBr (4 mL; 1 M),aq. solution of TBAB (4 mL; 1 M), TEMPO (150 mg, 0.96 mmol), satd. aq. NaHCO3 (15 mL) and 4% aq. NaOCl (20 mL) and the reaction mixture was stirred at 0-5 °C for 5 h. The reaction mixture was neutralized with the addition of 1 N aq. HCl solution. To the reaction mixture were added tert-butanol (20 mL), 2-methyl-but-2-ene (20 mL; 2 M solution in THF), aq. solution of NaClO2 (4 g in 15 mL) and aq. solution of NaH2PO4 (4 g in 15 mL) and the reaction mixture was allowed to stir at room temperature for 5 h. The reaction mixture was concentrated under reduced pressure and the crude mass was extracted with CHCl3 (100 mL). The organic layer was washed with water, dried (Na2SO4) and concentrated to dryness. The crude product was passed through a short pad of SiO2.
using CH₂Cl₂-CH₃OH (10:1) as eluant. To a solution of the oxidized product in CH₃OH (10 mL) was added 20% Pd(OH)₂-C (100 mg) and the reaction mixture was allowed to stir at room temperature under a positive pressure of hydrogen for 24 h. The reaction mixture was filtered through a Celite® bed and concentrated under reduced pressure. A solution of the crude product in 0.1 M CH₃ONa in CH₃OH (10 mL) was allowed to stir at room temperature for 6 h and neutralized with Dowex-50W X8 (H⁺) resin. The reaction mixture was filtered and concentrated under reduced pressure. The crude product was passed through a Sephadex® LH-20 column using CH₃OH-H₂O (2:1) as eluant to give pure compound 1 (220 mg, 50%) as disodium salt.

White powder; [α]D²⁵ + 16 (c 1.0, CH₃OH); IR (KBr): 3432, 2943, 1607, 1377, 1145, 1089, 665 cm⁻¹; ¹H NMR (500 MHz, CD₃OD): δ 6.75-6.73 (m, 4 H, Ar-H), 5.01 (br s, 1 H, H-1D), 4.84 (br s, 1 H, H-1b), 4.30 (d, J = 7.8 Hz, 1 H, H-1A), 4.28 (d, J = 7.7 Hz, 1 H, H-1C), 4.26-4.10 (m, 6 H, H-3D, H-4D, H-5C, -CH₂-, H-3C), 3.78-3.70 (m, 3 H, H-2B, -CH₂-), 3.78-3.64 (m, 10 H, H-2A, H-4A, H-6abB, H-6abD, H-2C, H-3B, H-4C, H-5D), 3.72 (s, 3 H, OCH₃), 3.60-3.35 (m, 3 H, H-3A, H-4B, H-5B), 2.02, 1.94 (2 s, 6 H, 2 COCH₃); ¹³C NMR (125 MHz, CD₃OD): δ 174.4 (2 C, 2 COONa), 171.6, 170.8 (2 COCH₃), 153.5-114.8 (Ar-C), 100.8 (C-1c), 100.6 (C-1d), 98.9 (C-1B), 77.6 (C-3B), 76.9 (C-2A), 76.6 (C-5B), 74.1 (C-2C), 73.6 (2 C, C-3A, C-3C), 73.4 (C-4C), 72.3 (C-5C), 71.7 (C-3D), 70.4 (C-4A, C-4B, C-5A, C-5D), 69.7 (C-4D), 62.4 (2 C, 2 CH₂-), 61.6 (C-6D), 56.4 (OCH₃), 54.3 (C-2B), 53.6 (C-2D), 23.6, 23.4 (2 COCH₃); ESI-MS: 970.2 [M]+; Anal. Calcd. for C₃₇H₅₂N₂Na₂O₂₅ (970.27): C, 45.78; H, 5.40; found: C, 46.00; H, 5.66.
2.4.5. Representative NMR spectra of synthesized compounds

$^1$H and $^{13}$C NMR spectra of 2-$(p$-methoxyphenoxy) ethyl 2-$O$-acetyl-3,4,6-tri-$O$-benzyl-β-D-galactopyranoside (7) (CDCl$_3$).
$^1$H and $^{13}$C NMR spectra of 2-(p-methoxyphenoxy) ethyl 3,4,6-tri-O-benzyl-β-D-galactopyranoside (8) (CDCl$_3$).
$^1$H and $^{13}$C NMR spectra of 2-(p-methoxyphenoxy) ethyl (3-O-acetyl-4,6-O-benzylidene-2-deoxy-2-N-phthalimido-β-D-glucopyranosyl)-(1→2)-3,4,6-tri-O-benzyl-β-D-galactopyranoside (19) (CDCl₃).
2D COSY and 2D HSQC (selected region) spectra of 2-(p-methoxyphenoxy) ethyl (3-O-acetyl-4,6-O-benzylidene-2-deoxy-2-N-phthalimido-β-D-glucopyranosyl)-(1→2)-3,4,6-tri-O-benzyl-β-D-galactopyranoside (19).
$^1$H and $^{13}$C NMR spectra of phenyl (3,4,6-tri-0-acetyl-2-azido-2-deoxy-\(\alpha\)-D-galactopyranoyl)-(1\(\rightarrow\)4)-2,3-di-O-benzoyl-6-O-benzyl-1-thio-\(\beta\)-D-glucopyranoside (21) (CDCl$_3$).
\[ ^{13}C \text{ DEPT 135 and 2D HSQC (selected region) spectra of phenyl (3,4,6-tri-}O\text{-acetyl-2-azido-2-deoxy-}\alpha-D\text{-galactopyranoyl)-(1} \rightarrow 4\text{-)}2,3\text{-di-}O\text{-benzoyl-6-}O\text{-benzyl-1-thio-}\beta-D\text{-glucopyranoside (21).} \]
$^1$H and $^{13}$C NMR spectra of 2-(p-methoxyphenoxy) ethyl (3,4,6-tri-O-acetyl-2-azido-2-deoxy-α-D-galactopyranoyl)-(1→4)-(2,3-di-O-benzoyl-6-O-benzyl-β-D-glucopyranosyl)-(1→3)-(4,6-O-benzylidene-2-deoxy-2-N-phthalimido-β-D-glucopyranosyl)-(1→2)-3,4,6-tri-O-benzyl-β-D-galactopyranoside (22) (CDCl$_3$).
2D COSY and 2D HSQC (selected region) spectra of 2-(p-methoxyphenoxy) ethyl (3,4,6-tri-O-acetyl-2-azido-2-deoxy-α-D-galactopyranoyl)-(1→4)-(2,3-di-O-benzoyl-6-O-benzyl-β-D-glucopyranosyl)-(1→3)-(4,6-O-benzylidene-2-deoxy-2-N-phthalimido-β-D-glucopyranosyl)-(1→2)-3,4,6-tri-O-benzyl-β-D-galactopyranoside (22).
$^{1}H$, $^{13}C$ and 2D HSQC (selected region) NMR spectra of 2-(p-methoxyphenoxy) ethyl (2-acetamido-2-deoxy-\(\alpha\)-D-galactopyranoyl)-(1\(\rightarrow\)4)-(sodium \(\beta\)-D-glucopyranosyluronate)-(1\(\rightarrow\)3)-(2-acetamido-2-deoxy-\(\beta\)-D-glucopyranosyl)-(1\(\rightarrow\)2)-sodium-\(\beta\)-D-galactopyranosiduronate (1) (CD$_3$OD).
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