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Synthesis of tri- and pentasaccharide fragments corresponding to the O-antigen of *Shigella boydii* type 6

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ABSTRACT

A convenient synthetic strategy for the synthesis of the acidic pentasaccharide repeating unit and its trisaccharide fragment corresponding to the O-antigen of *Shigella boydii* type 6 has been successfully developed. A stereoselective sequential glycosylation method has been exploited to obtain the target tri- and pentasaccharide derivatives. Most of the synthetic intermediates were solid and prepared in high yields from commercially available reducing sugars following a series of protection–deprotection reactions. A late-stage TEMPO mediated selective oxidation reaction finally resulted in the pentasaccharide containing a glucuronic acid unit. A 2-(4-methoxyphenoxy) ethyl group has been chosen as the anomeric protecting group to provide trisaccharide and pentasaccharide derivatives linked to an ethylene glycol linker.

1. Introduction

Shigella is a well-documented human pathogen responsible for diarrheal disease and bacilliary dysentery (shigellosis). *Shigella dysenteriae* is the most virulent bacilli among the genus *Shigella* and has the potential for causing devastating health problems in developing countries.[1] *Shigella* strains are divided into four species: *Shigella boydii*, *S. dysenteriae*, *Shigella flexneri,* and *Shigella sonnei*, which are also known as *Shigella* subgroups A, B, C, and D, respectively.[2] The first three species are typed into multiple serotypes, based on the antigenic variation in their O-antigens.[3] All *Shigella* O-antigens, except for a few, are acidic due to the presence of either a sugar acid (uronic or pseudaminic acid) or a noncarbohydrate acidic component, such as lactic acid ethers, pyruvic acid acetals, or alanine.[4] Recently Senchenkova et al. reported a revised structure of the D-glucuronic acid containing pentasaccharide repeating unit of the O-antigen of *S. boydii* type 6 (Fig. 1).[5] Long back, Dmitriev et al.[6] had initially reported the structure of this O-antigen, which was partially incorrect.

→3)-α-D-Gal*p*-(1→6)-α-D-Man*p*-(1→2)-α-D-Man*p*-(1→3)-β-D-Gal*p*NAc-(1→
4
↑
1
β-D-Glc*p*A

Figure 1. Pentasaccharide repeating unit of the O-antigen of *Shigella boydii* type 6.

Although, a number of effective therapeutics have appeared in the past to control *Shigella* infections, the emergence of drug resistant bacterial strains demands the development of alternative methods toward the development of anti-shigellosis agents.[7] Since, O-antigenic polysaccharides are highly immunogenic and important virulence factors, antibodies against the O-specific polysaccharide of a particular *Shigella* strain could have the potential to protect the host from *shigella* infections.[8] A number of reports have already appeared in the literature for the development of glycoconjugate based therapy against *Shigella* infections.[9] For detailed biological studies with the glycoconjugates derived from the pentasaccharide O-antigen of *S. boydii* type 6, a large quantity of pentasaccharide is required, which is not accessible from a natural source. Hence, chemical synthesis is the only option to obtain large quantities of the particular oligosaccharide and its smaller fragments. The synthesis of smaller fragments of the oligosaccharide repeating unit is useful for determining the immunodominant fragment of the whole oligosaccharide repeating unit. In this context, we herein report a convenient synthesis of a trisaccharide and a pentasaccharide as their 2-(4-methoxyphenoxy) ethyl glycoside (**1** and **2**) corresponding to the O-antigen of *S. boydii* type 6 using a sequential glycosylation strategy (Fig. 2). The 4-methoxyphenyl (PMP) group can be easily removed under oxidative conditions to give trisaccharide and pentasaccharide derivatives linked to an ethylene glycol linker useful for the preparation of glycoconjugate derivatives.

2. Results and discussion

The synthesis of trisaccharide **1** and pentasaccharide **2** as their 2-(4-methoxyphenoxy) ethyl glycoside (Fig. 2) was achieved using a sequential glycosylation strategy via stereoselective glycosylation of monosaccharide intermediates. For this purpose, a series

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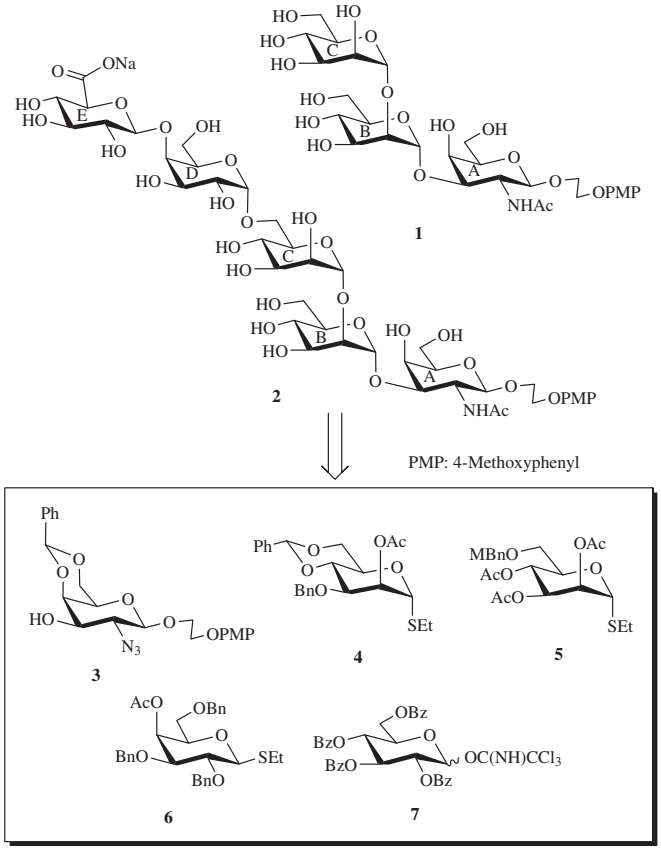
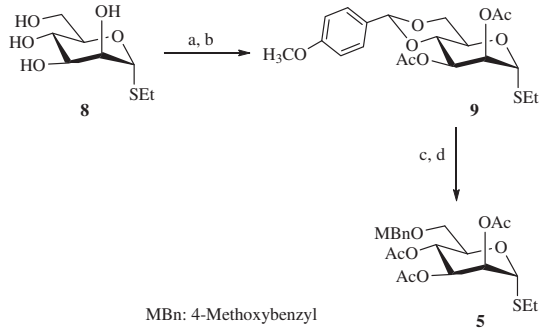


Figure 2. Structure of the synthesized trisaccharide **1** and pentasaccharide **2** as their 2-(4-methoxyphenoxy) ethyl glycoside.

of monosaccharide intermediates **3**,[10] **4**,[11] **5**, **6**,[12] and **7**[13] were prepared from the commercially available reducing sugars using a series of protection and deprotection reaction methodologies. A late-stage TEMPO mediated selective oxidation of a primary hydroxyl group in the presence of secondary hydroxyl groups under a biphasic reaction condition has been applied to achieve the target pentasaccharide **2** containing a D-glucuronic acid moiety. Stereoselective glycosylation reactions were carried out using either thioglycoside or glycosyl trichloroacetimidate derivatives under different glycosylation conditions.

Ethyl 1-thio-α-D-mannopyranoside **8**[14] was subjected to a sequence of functional group transformations involving 4-methoxybenzylidene acetal formation[15] and acetylation to give compound **9** in 79% yield. Compound **9** was converted into ethyl 2,3,4-tri-*O*-acetyl-6-*O*-(4-methoxybenzyl)-1-thio-α-D-mannopyranoside **5** in 73% yield after reductive ring opening[15] of the benzylidene acetal of compound **9** followed by acetylation (Scheme 1).

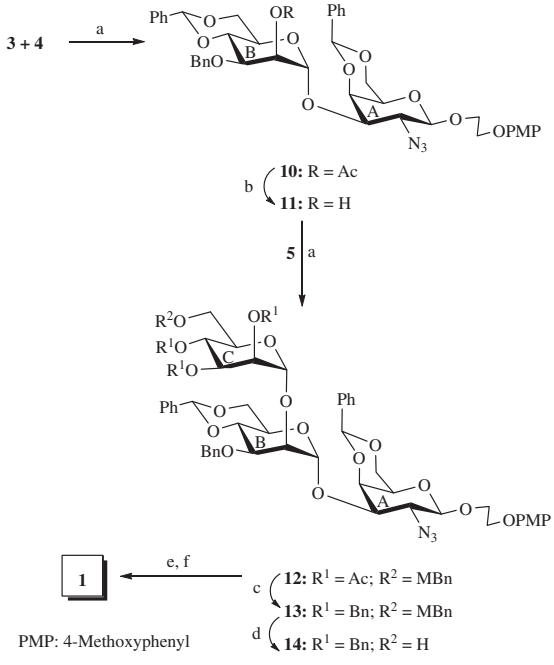
The stereoselective glycosylation of compound **3** with thioglycoside derivative **4** in the presence of an *N*-iodosuccinimide (NIS) and trifluoromethane sulfonic acid (TfOH) combination[16] furnished disaccharide derivative **10** in 75% yield, which was deacetylated to give the disaccharide acceptor **11** in 97% yield. The presence of an *O*-acetyl group at the C-2 position of compound **4** favored the formation of 1,2-*trans*-glycoside **10**, which was confirmed from its NMR spectra [signals at δ 5.61 (s, PhC*H*), 5.57 (s, PhC*H*), 5.02 (br s, H-1_B), 4.43 (d, J = 8.0 Hz, H-1_A) in the ^{1}H NMR and δ 102.8 (PhC*H*), 102.1 (*C*OCH$_3$), 101.3 (C-1_A), 95.5 (C-1_B) in the ^{13}C NMR spectra]. The iodonium ion mediated stereoselective coupling of compound **11** with the thioglycoside donor **5** in the presence of NIS-TfOH[16] furnished trisaccharide derivative **12** in 72% yield. The formation of trisaccharide **12** was influenced by the presence



Scheme 1. Reagents and conditions: (a) *p*-anisaldehyde dimethyl acetal, *p*-TsOH, CH_3CN, room temperature, 12 h; (b) acetic anhydride, pyridine, room temperature, 2 h, overall yield 79%; (c) $NaBH_3CN$, TFA, DMF, room temperature, 10 h; (d) acetic anhydride, pyridine, room temperature, 1 h, over all 73%.

of an *O*-acetyl group at the C-2 position of compound **5**, which directs the formation of an α-mannosidic linkage through neighboring group participation. The presence of signals in the NMR spectra confirmed the formation of compound **12** [signals at δ 5.68 (s, PhC*H*), 5.39 (s, PhC*H*), 5.17 (br s, H-1_C), 4.95 (br s, H-1_B), 4.27 (d, J = 8.0 Hz, H-1_A) in the ^{1}H NMR and δ 102.7 (PhC*H*), 102.0 (PhC*H*), 101.0 (C-1_A), 100.6 (C-1_B), 96.5 (C-1_C) in the ^{13}C NMR spectra]. The removal of functional groups from compound **12** involving hydrogenolysis[17] followed by N-acetylation and O-deacetylation furnished trisaccharide derivative **1** as its 2-(4-methoxyphenoxy) ethyl glycoside in 66% yield, which was supported by its spectroscopic analysis [Signals at δ 5.16 (br s, H-1_C), 4.85 (br s, H-1_B), 4.43 (d, J = 8.4 Hz, H-1_A) in the ^{1}H NMR and δ 103.2 (C-1_B), 102.1 (C-1_A), 94.9 (C-1_C) in the ^{13}C NMR spectra] (Scheme 2).

In a separate experiment, the *O*-acetoxy groups of compound **12** were converted into *O*-benzyl ethers under one-pot deacetylation–

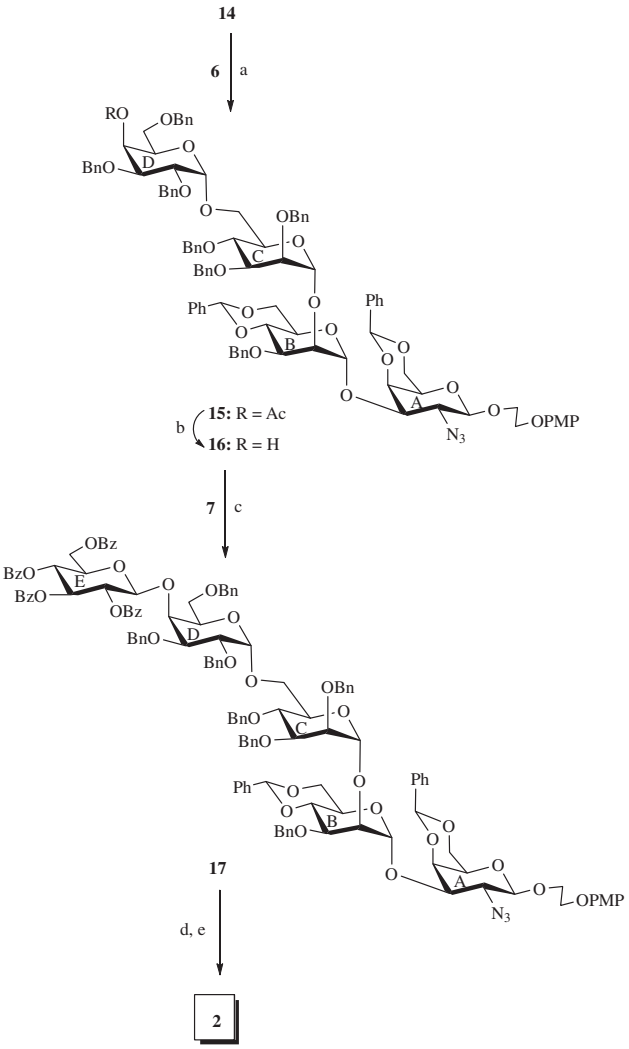


Scheme 2. Reagents and conditions: (a) *N*-iodosuccinimide (NIS), TfOH, CH_2Cl_2, MS 4 Å, −40 °C, 1 h, 75% for **10** and 72% for **12**; (b) 0.1 M CH_3ONa, CH_3OH, room temperature, 1 h, 97%; (c) benzyl bromide, NaOH, DMF, TBAB, room temperature, 5 h, 76%; (d) DDQ, CH_2Cl_2, H_2O, room temperature, 2 h, 72%; (e) H_2, 20% $Pd(OH)_2$–C, CH_3OH, room temperature, 24 h; (f) (i) acetic anhydride, pyridine, room temperature, 2 h; (ii) 0.1 M CH_3ONa, CH_3OH, room temperature, 1 h, overall yield 6%.

benzylation conditions[18] to give compound **13** in 76% yield. Oxidative removal[19] of 4-methoxybenzyl group from compound **13** using DDQ furnished trisaccharide acceptor **14** in 72% yield. Iodonium ion mediated 1,2-*cis* glycosylation of compound **14** with thioglycoside derivative **6** in the presence of NIS-TfOH[16] furnished tetrasaccharide derivative **15** in 76% yield, which was quantitatively deacetylated to give tetrasaccharide acceptor **16**. Due to the presence of an *O*-benzyl group at the C-2 position of compound **6**, desired α-linked glycosylation product **15** was obtained as a major product together with a minor quantity of its 1,2-*trans* glycosylation product (~12%), which was separated by flash column chromatography. The formation of compound **15** was confirmed from its 1D and 2D NMR spectroscopic analysis [signals at δ 5.52 (s, PhC*H*), 5.42 (s, PhC*H*), 5.11 (br s, H-1_C), 4.95 (br s, H-1_B), 4.32 (br s, H-1_D), 4.26 (d, J = 7.9 Hz, H-1_A) in the ^{1}H NMR and δ 170.3 (*C*OCH$_3$), 154.2–114.7 (Ar-C), 104.4 ($J_{C\text{-}1/H\text{-}1}$ = 155 Hz, C-1_A), 102.4 ($J_{C\text{-}1/H\text{-}1}$ = 172.8 Hz, C-1_D), 101.6 (Ph*C*H), 101.0 (Ph*C*H), 100.3 ($J_{C\text{-}1/H\text{-}1}$ = 170.5 Hz, C-1_B), 96.1 ($J_{C\text{-}1/H\text{-}1}$ = 171.3 Hz, C-1_C), in the ^{13}C NMR spectra]. Unambiguous assignment of the stereochemistry of the glycosyl linkages in compound **15** was achieved using gated ^{1}H coupled ^{13}C NMR, 2D HMBC, and HMQC NMR spectra.[20] The appearance of anomeric carbon atoms with $J_{C\text{-}1/H\text{-}1}$ = 155 Hz (β-D-GalpN), $J_{C\text{-}1/H\text{-}1}$ = 171.3 Hz (α-D-Manp), $J_{C\text{-}1/H\text{-}1}$ = 170.5 Hz (α-D-Manp) and $J_{C\text{-}1/H\text{-}1}$ = 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 glycosylyl linkages. Gated ^{1}H coupled ^{13}C NMR spectrum of compound **15** also confirmed the achievement of the desired stereochemical outcome of previous glycosylation reactions. The stereoselective coupling of compound **16** with trichloroacetimidate derivative **7** under Schmidt's glycosylation conditions[21] furnished pentasaccharide derivative **17** in 72% yield. The presence of signals in the NMR spectra [δ 5.60 (s, PhC*H*), 5.58 (s, PhC*H*), 5.20 (d, J = 7.9 Hz, H-1_E), 5.11 (br s, H-1_C), 5.07 (br s, H-1_B), 4.46 (br s, H-1_D), 4.14 (d, J = 7.8 Hz, H-1_A) in the ^{1}H NMR and δ 105.1 (C-1_A), 102.6 (C-1_E), 102.3 (Ph*C*H), 101.8 (Ph*C*H), 101.4 (C-1_D), 101.0 (C-1_B), 97.2 (C-1_C) in the ^{13}C NMR spectra] confirmed its formation. The presence of a neighboring group participating 2-*O*-benzoyl group in the trichloroacetimidate donor **7** directed the exclusive formation of 1,2-*trans* glycosyl product **17**. It is worth mentioning that use of thioglycoside derivatives as a glycosyl donor was unsuccessful in furnishing the glycosylation product. Compound **17** was converted into the target pentasaccharide derivative **2** following a series of reactions involving saponification using sodium methoxide, chemoselective TEMPO mediated oxidation[22] of the primary hydroxyl group to a carboxylic group under phase transfer reaction condition, hydrogenolysis over Pearlman's catalyst, and N-acetylation followed by O-deacetylation in 64% over all yield. Spectroscopic analysis of compound **2** supported its formation [signals at δ 5.19 (s, H-1_C), 4.77 (br s, H-1_B), 4.62 (d, J = 8.1 Hz, H-1_E), 4.40 (d, J = 7.8 Hz, H-1_A), 4.17 (br s, H-1_D) in the ^{1}H NMR and δ 174.6 (*C*OONa), 105.4 (C-1_A), 105.0 (C-1_D), 103.8 (C-1_B), 101.6 (C-1_E), 101.0 (C-1_C)] (Scheme 3).

3. Conclusion

In conclusion, a convenient synthetic strategy for the preparation of tri- and pentasaccharide fragments corresponding to the O-specific polysaccharide of *S. boydii* type 6 has been successfully developed. Stereoselective sequential glycosylation reactions allowed us to obtain the target tri- and pentasaccharides in minimum number of steps. All intermediate steps were reasonably high yielding and reproducible for a scale-up preparation. Oligosaccharides as their 2-(4-methoxyphenoxy) ethyl glycoside provide access to an ethylene glycol linked tri- and pentasaccharide derivatives for their further use.



Scheme 3. Reagents and conditions: (a) *N*-iodosuccinimide (NIS), TfOH, CH_2Cl_2, MS 4 Å, −25 °C, 45 min, 76%; (b) 0.1 M CH_3ONa, CH_3OH, room temperature, 1 h, quantitative; (c) TMSOTf, CH_2Cl_2, −10 °C, 1 h, 72%; (d) (i) 0.1 M CH_3ONa, CH_3OH, room temperature, 3 h; (ii) NaBr, CH_2Cl_2, H_2O, TBAB, TEMPO, $NaHCO_3$, NaOCl, 0–5 °C, 3 h; (iii) *tert*-butanol, 2-methyl-but-2-ene, $NaClO_2$, NaH_2PO_4, room temperature, 3 h; (e) (i) H_2, 20% $Pd(OH)_2$–C, room temperature, 24 h; (ii) acetic anhydride, pyridine, room temperature, 4 h; (iii) 0.1 M CH_3ONa, CH_3OH, room temperature, 2 h, overall yield 64%.

4. Experimental

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% $Ce(SO_4)_2$ in 2 N H_2SO_4]-sprayed plates on a hot plate. Silica gel 230–400 mesh was used for column chromatography. ^{1}H and ^{13}C NMR, DEPT 135, 2D COSY, HMQC, HMBC, and gated ^{1}H coupled ^{13}C NMR spectra were recorded on Brucker Avance DRX 300 and 500 MHz spectrometers using $CDCl_3$ and CD_3OD as solvents and TMS as internal reference unless stated otherwise. Chemical shift values are expressed in δ ppm. ESI-MS were recorded on a Micromass Quttro II mass spectrometer. Elementary analysis was carried out on Carlo Erba-1108 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.

4.1.1. Ethyl 2,3-di-*O*-acetyl-4,6-*O*-(4-methoxy)benzylidene-1-thio-α-D-mannopyranoside 9

To a solution of compound **8** (3.0 g, 13.37 mmol) in dry CH_3CN (15 mL) were added 4-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 Et_3N (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 SiO_2 using toluene–EtOAc (3:1) as eluant to give pure **9** (4.5 g, 79%). White solid; mp 82–84 °C; $[\alpha]_D^{25} = +95.3$ (*c* 1.2, $CHCl_3$); ν_{max} (KBr): 3462, 2930, 1740, 1519, 1254, 1224, 1095, 1025, 834, 753 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.38 (d, *J* = 8.7 Hz, 2H, Ar-H), 6.88 (d, *J* = 8.7 Hz, 2H, Ar-H), 5.53 (s, 1H, PhC*H*), 5.44–5.43 (m, 1H, H-2), 5.33 (dd, *J* = 10.3, 3.4 Hz, 1H, H-3), 5.23 (br s, 1H, H-1), 4.35–4.31 (m, 1H, H-5), 4.23 (dd, *J* = 10.3, 4.9 Hz, 1H, H-6_a), 4.06 (t, *J* = 10.0 Hz each, 1H, H-4), 3.86 (t, *J* = 10.3 Hz each, 1H, H-6_b), 3.79 (s, 3H, OC*H*$_3$), 2.68–2.60 (m, 2H, SC*H*$_2$CH$_3$), 2.16 (s, 3H, COC*H*$_3$), 2.00 (s, 3H, COC*H*$_3$), 1.29 (t, *J* = 7.4 Hz each, 3H, SCH$_2$C*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.2 (*C*OCH$_3$), 170.2 (*C*OCH$_3$), 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 (O*C*H$_3$), 25.8 (S*C*H$_2$CH$_3$), 21.3 (CO*C*H$_3$), 21.2 (CO*C*H$_3$), 15.2 (SCH$_2$*C*H$_3$); ESI-MS: 449.1 $[M+Na]^+$; Anal. Calcd for $C_{20}H_{26}O_8S$ (426.13): C, 56.32; H, 6.14. Found: C, 56.10; H, 6.40.

4.1.2. Ethyl 2,3,4-tri-*O*-acetyl-6-*O*-(4-methoxybenzyl)-1-thio-α-D-mannopyranoside 5

To an ice-cooled solution of **9** (4.0 g, 9.38 mmol) in dry DMF (10 mL) were added MS 3 Å (3 g) and $NaBH_3CN$ (3.0 g, 47.74 mmol) followed by TFA (3.0 mL, 40.38 mmol) and the reaction mixture was allowed to stir at room temperature for 10 h. The reaction mixture was diluted with water and extracted with CH_2Cl_2 (100 mL). The organic layer was successively washed with satd. $NaHCO_3$ and water, dried (Na_2SO_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 **5** (3.2 g, 73%). Yellow oil; $[\alpha]_D^{25} = +65.8$ (*c* 1.2, $CHCl_3$); ν_{max} (neat): 3442, 3016, 2963, 2934, 1749, 1613, 1514, 1370, 1244, 1223, 1095, 1047, 756 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.26 (d, *J* = 8.6 Hz, 2H, Ar-H), 6.85 (d, *J* = 8.6 Hz, 2H, Ar-H), 5.35 (t, *J* = 9.9 Hz each, 1H, H-4), 5.32–5.31 (m, 1H, H-2), 5.29 (br s, 1H, H-1), 5.24 (dd, *J* = 9.8, 3.4 Hz, 1H, H-3), 4.52 (d, *J* = 11.6 Hz, 1H, PhC*H*$_2$), 4. 39 (d, *J* = 11.6 Hz, 1H, PhC*H*$_2$), 4.33–4.29 (m, 1H, H-5), 3.78 (s, 3H, OC*H*$_3$), 3.57–3.49 (m, 2H, H-6_{ab}), 2.66–2.60 (m, 2H, SC*H*$_2$CH$_3$), 2.14 (s, 1H, COC*H*$_3$), 1.98 (s, 1H, COC*H*$_3$), 1.90 (s, 1H, COC*H*$_3$), 1.28 (t, *J* = 7.4 Hz each, 3H, SCH$_2$C*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.5 (*C*OCH$_3$), 170.3 (*C*OCH$_3$), 170.2 (*C*OCH$_3$), 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 (COCH$_3$), 21.1 (COCH$_3$), 21.0 (COCH$_3$), 15.1 (SCH$_2$CH$_3$); ESI-MS: 493.1 $[M+Na]^+$; Anal. Calcd for $C_{22}H_{30}O_9S$ (470.16): C, 56.16; H, 6.43. Found: C, 55.92; H, 6.66.

4.1.3. 2-(4-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 10

To a solution of compound **3** (2.0 g, 4.51 mmol) and compound **4** (2.4 g, 5.40 mmol) in anhydrous CH_2Cl_2 (10 mL) were 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 CH_2Cl_2 (100 mL). The combined organic layer was washed with 5% $Na_2S_2O_3$, satd. $NaHCO_3$, and water in succession, dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified over SiO_2 using hexane–EtOAc (7:1) as eluant to give pure **10** (2.8 g, 75%). White solid; mp 152–154 °C; $[\alpha]_D^{25} = +21.8$ (*c* 1.2, $CHCl_3$); ν_{max} (KBr): 3336, 2926, 2111, 1735, 1711, 1509, 1457, 1230, 1172, 1060, 753, 697 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.53–7.25 (m, 15H, Ar-H), 6.86–6.79 (m, 4H, Ar-H), 5.61 (s, 1H, PhC*H*), 5.57 (s, 1H, PhC*H*), 5.37–5.36 (m, 1H, H-2_B), 5.02 (br s, 1H, H-1_B), 4.61 (br s, 2H, PhC*H*$_2$), 4.43 (d, *J* = 8.0 Hz, 1H, H-1_A), 4.32–4.27 (m, 2H, OC*H*$_2$), 4.23 (d, *J* = 3.2 Hz, 1H, H-4_A), 4.21–4.18 (m, 1H, H-3_A), 4.15–4.13 (m, 2H, OC*H*$_2$), 4.07–4.03 (m, 4H, H-4_B, H-5_B, H-6_{abB}), 3.98–3.94 (m, 1H, H-6_{aA}), 3.83–3.78 (m, 2H, H-2_A, H-6_{bA}), 3.75 (s, 3H, OC*H*$_3$), 3.60 (dd, *J* = 10.4, 3.6 Hz, 1H, H-3_B), 3.37 (br s, 1H, H-5_A), 2.15 (s, 3H, COC*H*$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.5 (*C*OCH$_3$), 154.4–115.0 (Ar-C), 102.8 (PhCH), 102.1 (*C*OCH$_3$), 101.3 (C-1_A), 95.5 (C-1_B), 78.6 (C-4_B), 74.8 (C-3_B), 74.2 (C-5_B), 73.0 (PhCH$_2$), 71.1 (C-3_A), 70.7 (C-2_B), 69.5 (C-6_A), 68.9 (C-6_B), 68.6 (OCH$_2$), 68.4 (OCH$_2$), 66.8 (C-5_A), 65.0 (C-4_A), 61.4 (C-2_A), 56.0 (OCH$_3$), 21.4 (COCH$_3$); ESI-MS: 848.3 $[M+Na]^+$; Anal. Calcd for $C_{44}H_{47}N_3O_{13}$ (825.31): C, 63.99; H, 5.74. Found: C, 63.78; H, 5.96.

4.1.4. 2-(4-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 11

A solution of compound **10** (2.5 g, 3.03 mmol) in 0.1 M CH_3ONa (25 mL) was allowed to 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 the crude product, which was purified over SiO_2 using hexane–EtOAc (5:1) as eluant to give pure **11** (2.3 g, 97%). White solid; mp 158–159 °C; $[\alpha]_D^{25} = +33.7$ (*c* 1.2, $CHCl_3$); ν_{max} (KBr): 3540, 2926, 2111, 1711, 1509, 1458, 1327, 1231, 1172, 1060, 823, 753, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.44–7.17 (m, 15H, Ar-H), 6.81–6.74 (m, 4H, Ar-H), 5.54 (s, 1H, PhC*H*), 5.45 (s, 1H, PhC*H*), 5.04 (br s, 1H, H-1_B), 4.78 (d, *J* = 11.5 Hz, 1H, PhC*H*$_2$), 4.62 (d, *J* = 11.5 Hz, 1H, PhC*H*$_2$), 4.39 (d, *J* = 8.0 Hz, 1H, H-1_A), 4.24–4.21 (m, 2H, OC*H*$_2$), 4.19 (d, *J* = 3.2 Hz, 1H, H-4_A), 4.18–4.13 (m, 1H, H-3_A), 4.09–4.02 (m, 4H, H-2_B, H-4_B, OC*H*$_2$), 3.99–3.94 (m, H-5_B, H-6_{abB}), 3.92–3.89 (m, 1H, H-6_{aA}), 3.79–3.74 (m, H-2_A, H-6_{bA}), 3.68 (s, 3H, OC*H*$_3$), 3.59 (dd, *J* = 10.4, 3.3 Hz, 1H, H-3_B), 3.33 (br s, 1H, H-5_A); ^{13}C NMR (125 MHz, $CDCl_3$): δ 154.4–115.0 (Ar-C), 102.9 (PhCH), 102.1 (PhCH), 101.4 (C-1_A), 96.0 (C-1_B), 79.0 (C-4_B), 76.0 (C-3_B), 73.8 (PhCH$_2$), 73.4 (C-5_B), 70.7 (C-3_A), 70.4 (C-2_B), 69.6 (C-6_A), 69.1 (C-6_B), 68.7 (OCH$_2$), 68.4 (OCH$_2$), 66.8 (C-5_A), 64.3 (C-4_A), 61.6 (C-2_A), 56.1 (OCH$_3$); ESI-MS: 806.3 $[M+Na]^+$; Anal. Calcd for $C_{42}H_{45}N_3O_{12}$ (783.30): C, 64.36; H, 5.79. Found: C, 64.15; H, 5.97.

4.1.5. 2-(4-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 12

To a solution of compound **11** (2.2 g, 2.81 mmol) and compound **5** (1.5 g, 3.19 mmol) in anhydrous CH_2Cl_2 (10 mL) were 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_2Cl_2 (100 mL). The combined organic layer was washed with 5% $Na_2S_2O_3$, satd $NaHCO_3$, and water in succession, dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified over SiO_2 using hexane–EtOAc (6:1) as eluant to give pure **12** (2.4 g, 72%). White solid; mp 78–81 °C;

$[\alpha]_D^{25} = +23.5$ (*c* 1.2, $CHCl_3$); ν_{max} (KBr): 3476, 2928, 2870, 2115, 1753, 1507, 1371, 1248, 1221, 1104, 1079, 1050, 822, 750, 737, 699 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.37–7.19 (m, 17H, Ar-H), 6.89–6.83 (m, 6H, Ar-H), 5.68 (s, 1H, PhC*H*), 4.43–4.40 (m, 2H, H-2_C, H-3_C), 5.39 (s, 1H, PhC*H*), 5.20 (t, *J* = 9.8 Hz each, 1H, H-4_C), 5.17 (br s, 1H, H-1_C), 4.95 (br s, 1H, H-1_B), 4.80 (d, *J* = 11.9 Hz, 1H, PhCH_2), 4.55 (d, *J* = 11.9 Hz, 1H, PhCH_2), 4.42 (d, *J* = 11.9 Hz, 1H, PhCH_2), 4.33–4.30 (m, 1H, H-3_A), 4.27 (d, *J* = 8.0 Hz, 1H, H-1_A), 4.21 (d, *J* = 11.6 Hz, 1H, PhCH_2), 4.19–4.10 (m, 6H, H-2_B, H-4_B, H-6_{abB}, OCH_2), 4.06–4.00 (m, 3H, H-5_C, OCH_2), 3.99 (br s, 1H, H-4_A), 3.95–3.91 (m, 2H, H-5_B, H-6_{aA}), 3.82–3.79 (m, 1H, H-6_{bA}), 3.79 (s, 3H, OCH_3), 3.75 (s, 3H, OCH_3), 3.72 (dd, *J* = 8.0 Hz each, 1H, H-2_A), 3.52–3.49 (m, 1H, H-6_{aC}), 3.44 (dd, *J* = 10.4, 3.3 Hz, 1H, H-3_B), 3.33–3.31 (m, I H, H-6_{bC}), 2.88 (br s, 1H, H-5_A), 2.09 (s, 3H, COCH_3), 1.99 (s, 3H, COCH_3), 1.95 (s, 3H, COCH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.4 (*C*OCH$_3$), 170.2 (*C*OCH$_3$), 170.1 (*C*OCH$_3$), 159.7–114.2 (Ar-C), 102.7 (PhCH), 102.0 (PhCH), 101.0 (C-1_A), 100.6 (C-1_B), 96.5 (C-1_C), 79.0 (C-4_B), 78.5 (C-4_A), 75.9 (C-3_A), 74.1 (C-3_B), 73.7 (PhCH$_2$), 73.4 (PhCH$_2$), 70.8 (C-2_B), 70.7 (C-5_B), 69.8 (C-2_C), 69.7 (C-6_A), 69.5 (C-3_C), 69.4 (C-6_B), 69.0 (C-6_C), 68.7 (OCH$_2$), 68.8 (OCH$_2$), 67.4 (C-4_C), 66.7 (C-5_A), 61.6 (C-2_A), 56.1 (OCH$_3$), 55.7 (OCH$_3$), 21.3 (COCH$_3$), 21.2 (COCH$_3$), 21.1 (COCH$_3$); ESI-MS: 1214.4 $[M+Na]^+$; Anal. Calcd for $C_{62}H_{69}N_3O_{21}$ (1191.44): C, 62.46; H, 5.83. Found: C, 62.24; H, 6.05.

4.1.6. 2-(4-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 13

To a solution of **12** (2.0 g, 1.67 mmol) in dry DMF (15 mL) were added benzyl bromide (1.2 mL, 10.08 mmol), crushed 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 H_2O (100 mL) and extracted with CH_2Cl_2 (100 mL). The organic layer was washed with H_2O, dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified over SiO_2 using hexane–EtOAc (9:1) as eluant to give pure **13** (1.7 g, 76%). White solid; mp 86–88 °C; $[\alpha]_D^{25} = +49.2$ (*c* 1.2, $CHCl_3$); ν_{max} (KBr): 3488, 3034, 2920, 2871, 2113, 1611, 1509, 1457, 1370, 1288, 1239, 1073, 914, 824, 744, 697 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.51–6.80 (m, 38H, Ar-H), 5.60 (s, 1H, PhC*H*), 5.43 (s, 1H, PhC*H*), 5.18 (br s, 1H, H-1_C), 4.96 (br s, 1H, H-1_B), 4.88 (d, *J* = 10.7 Hz, 1H, PhCH_2), 4.69 (d, *J* = 11.6 Hz, 1H, PhCH_2), 4.62–4.45 (m, 7H, PhCH_2), 4.33–4.28 (m, 1H, H-3_A), 4.23 (d, *J* = 11.2 Hz, 1H, PhCH_2), 4.18–4.02 (m, 6H, H-1_A, H-2_B, H-4_B, H-5_C, OCH_2), 3.99–3.91 (m, 4H, H-6_{abB}, OCH_2), 3.90–3.88 (m, 3H, H-5_B, H-6_{abA}), 3.88 (br s, 1H, H-4_A), 3.85–3.79 (m, 2H, H-2_A, H-2_C), 3.76 (s, 3H, OCH_3), 3.74 (s, 3H, OCH_3), 3.78–3.63 (m, 3H, H-3_C, H-4_C, H-6_{aC}), 3.56–3.53 (m, 1H, H-6_{bC}), 3.34 (dd, *J* = 10.4, 3.3 Hz, 1H, H-3_B), 2.70 (br s, 1H, H-5_A); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.7–114.2 (Ar-C), 102.6 (PhCH), 101.9 (PhCH), 101.5 (C-1_A), 101.1 (C-1_B), 91.5 (C-1_C), 79.9 (C-4_B), 79.2 (C-4_A), 78.7 (C-3_A), 75.9 (C-3_B), 75.7 (PhCH$_2$), 75.4 (C-2_B), 75.0 (C-5_B), 74.5 (C-2_C), 73.5 (PhCH$_2$), 73.4 (PhCH$_2$), 72.8 (PhCH$_2$), 72.7 (C-3_C), 72.3 (PhCH$_2$), 70.8 (C-4_C), 70.7 (C-6_A), 69.4 (C-6_B), 69.1 (C-6_C), 68.5 (OCH$_2$), 68.2 (OCH$_2$), 66.6 (C-5_A), 65.0 (C-5_C), 61.5 (C-2_A), 56.0 (OCH$_3$), 55.6 (OCH$_3$); ESI-MS: 1358.5 $[M+Na]^+$; Anal. Calcd for $C_{77}H_{81}N_3O_{18}$ (1335.55): C, 69.20; H, 6.11. Found: C, 69.00; H, 6.35.

4.1.7. 2-(4-Methoxyphenoxy)ethyl (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 14

To a solution of **13** (1.5 g, 1.12 mmol) in CH_2Cl_2 (20 mL) was added a solution of 2,3-dicholoro-5,6-dicyano-*p*-benzoquinone (DDQ, 500 mg, 2.20 mmol) in H_2O (10 mL) and the biphasic reaction mixture was allowed to stir at room temperature for 2 h. The reaction mixture was diluted with H_2O and extracted with CH_2Cl_2 (100 mL). The organic layer was successively washed with satd $NaHCO_3$ and water, dried (Na_2SO_4), and concentrated. The crude product was purified over SiO_2 using hexane–EtOAc (6:1) as eluant to give pure **14** (980 mg, 72%). White solid; mp 91–94 °C; $[\alpha]_D^{25} = +10.2$ (*c* 1.2, $CHCl_3$); ν_{max} (KBr): 3470, 3064, 3031, 2926, 2872, 2114, 1509, 1454, 1311, 1233, 1176, 1105, 1075, 1028, 1002, 914, 823, 741, 698 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.43–7.13 (m, 30H, Ar-H), 6.79–6.72 (m, 4H, Ar-H), 5.53 (s, 1H, PhC*H*), 5.46 (s, 1H, PhC*H*), 5.05 (br s, 1H, H-1_C), 4.94 (br s, 1H, H-1_B), 4.83 (d, *J* = 10.7 Hz, 1H, PhCH_2), 4.75 (d, *J* = 11.4 Hz, 1H, PhCH_2), 4.55–4.47 (m, 7H, PhCH_2), 4.38 (d, *J* = 8.0 Hz, 1H, H-1_A), 4.37–4.34 (m, 2H, PhCH_2), 4.16–4.11 (m, 4H, H-3_A, H-4_B, OCH_2), 4.08–4.05 (m, 2H, OCH_2), 3.99–3.85 (m, 6H, H-2_B, H-4_A, H-5_B, H-5_C, H-6_{abB}), 3.82–3.63 (m, 5H, H-2_A, H-2_B, H-2_C, H-3_C, H-6_{abA}), 3.65 (s, 3H, OCH_3), 3.63–3.49 (m, 2H, H-4_C, H-6_{aC}), 3.48–3.44 (m, 2H, H-3_B, H-6_{bC}), 3.25 (br s, 1H, H-5_A); ^{13}C NMR (125 MHz, $CDCl_3$): δ 154.5–115.0 (Ar-C), 102.8 (PhCH), 101.7 (PhCH), 101.3 (C-1_A), 100.4 (C-1_B), 95.4 (C-1_C), 79.7 (C-4_B), 79.5 (C-4_A), 76.6 (C-3_A), 76.3 (C-3_B), 75.8 (PhCH$_2$), 75.6 (C-2_B), 75.2 (C-5_B), 74.3 (PhCH$_2$), 73.5 (C-2_C), 73.3 (C-3_C), 72.8 (PhCH$_2$), 72.3 (PhCH$_2$), 70.5 (C-4_C), 69.4 (C-6_A), 69.0 (C-6_B), 68.6 (OCH$_2$), 68.3 (OCH$_2$), 66.8 (C-5_A), 64.8 (C-5_C), 62.9 (C-6_C), 61.5 (C-2_A), 56.0 (OCH$_3$); ESI-MS: 1238.4 $[M+Na]^+$; Anal. Calcd for $C_{69}H_{73}N_3O_{17}$ (1215.49): C, 68.13; H, 6.05. Found: C, 67.90.; H, 6.30.

4.1.8. 2-(4-Methoxyphenoxy)ethyl (4-*O*-acetyl-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 15

To a solution of compound **14** (900 mg, 0.74 mmol) and compound **6** (475 mg, 0.88 mmol) in anhydrous CH_2Cl_2 (5 mL) were 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 CH_2Cl_2 (50 mL). The combined organic layer was washed with 5% $Na_2S_2O_3$, satd $NaHCO_3$, water in succession, dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified over SiO_2 using hexane–EtOAc (6:1) as eluant to give pure **15** (950 mg, 76%). White solid; mp 71–74 °C; $[\alpha]_D^{25} = +9.2$ (*c* 1.2, $CHCl_3$); ν_{max} (KBr): 3345, 3031, 2926, 2113, 1730, 1507, 1659, 1375, 1284, 1228, 1064, 920, 824, 745, 699 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 7.46–7.05 (m, 45H, Ar-H), 6.79–6.71 (m, 4H, Ar-H), 5.52 (s, 1H, PhC*H*), 5.45 (br s, 1H, H-4_D), 5.42 (s, 1H, PhC*H*), 5.11 (br s, 1H, H-1_C), 4.95 (br s, 1H, H-1_B), 5.74–4.66 (m, 3H, PhCH_2), 4.60–4.35 (m, 9H, PhCH_2), 4.34–4.27 (m, 3H, H-1_D, PhCH_2), 4.26 (d, *J* = 7.9 Hz, 1H, H-1_A), 4.21–4.12 (m, 1H, H-6_{aB}), 4.11–3.95 (m, 8H, H-3_A, H-4_A, H-5_D, H-6_{bB}, H-6_{abA}, OCH_2), 3.94–3.75 (m, 8H, H-2_B, H-4_B, H-5_B, H-5_C, H-6_{abD}, OCH_2), 3.74–3.55 (m, 3H, H-2_A, H-3_D, H-6_{aC}), 3.66 (s, 3H, OCH_3), 3.54–3.50 (m, 1H, H-6_{bC}), 3.49–3.37 (m, 2H, H-2_C, H-3_C), 3.36–3.30 (m, 2H, H-3_B, H-4_C), 3.28–3.26 (m, 1H, H-2_D), 3.08 (br s, 1H, H-5_A), 1.91 (s, 3H, COCH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.3 (*C*OCH$_3$), 154.2–114.7 (Ar-C), 104.4 ($J_{C\text{-}1/H\text{-}1}$ = 155 Hz, C-1_A), 102.4 ($J_{C\text{-}1/H\text{-}1}$ = 172.8 Hz, C-1_D), 101.6 (PhCH), 101.0 (PhCH), 100.3 ($J_{C\text{-}1/H\text{-}1}$ = 170.5 Hz, C-1_B), 96.1 ($J_{C\text{-}1/H\text{-}1}$ = 171.3 Hz, C-1_C), 79.4 (2 C, C-2_D, C-4_C), 79.0 (C-4_B), 78.7 (C-4_A), 76.6 (C-3_C), 76.0 (C-3_A), 75.4 (C-3_B), 75.3 (C-2_B), 74.8 (C-5_B), 74.6 (C-3_D), 73.7 (2 C, 2 PhCH$_2$), 73.6 (PhCH$_2$), 72.4 (PhCH$_2$), 72.1 (C-2_C), 72.0 (PhCH$_2$), 71.7 (PhCH$_2$), 70.4 (C-4_D), 69.2 (C-6_A), 69.0 (C-6_C), 68.7 (C-6_D), 68.3 (OCH$_2$), 68.0 (OCH$_2$), 67.8 (C-6_B), 66.7 (C-5_A), 66.4 (C-5_D), 64.6 (C-5_C), 61.1

(C-2_A), 55.7 (OCH_3), 20.9 (COCH_3); ESI-MS: 1712.6 [M+Na]$^+$; Anal. Calcd for $C_{98}H_{103}N_3O_{23}$ (1689.69): C, 69.61; H, 6.14. Found: C, 69.43; H, 6.38.

4.1.9. 2-(4-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 16

A solution of compound **15** (900 g, 0.53 mmol) in 0.1 M CH_3ONa (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 the crude product, which was purified over SiO_2 using hexane–EtOAc (3:1) as eluant to give pure **16** (875 mg, quantitative). White solid; mp 77–79 °C; $[\alpha]_D^{25} = +15.4$ (*c* 1.2, $CHCl_3$); ν_{max} (KBr): 3452, 3033, 2924, 2920, 2114, 1507, 1457, 1369, 1287, 1232, 1067, 915, 824, 742, 697 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35–7.17 (m, 41H, Ar-H), 6.87–6.80 (m, 4H, Ar-H), 5.59 (s, 1H, PhC*H*), 5.57 (s, 1H, PhC*H*), 5.10 (br s, 1H, H-1_C), 5.08 (br s, 1H, H-1_B), 4.82 (d, *J* = 11.0 Hz, 1H, PhCH_2), 4.75 (d, *J* = 10.8 Hz, 1H, PhCH_2), 4.73–4.34 (m, 11H, PhCH_2), 4.32–4.28 (m, 2H, H-1_D, PhCH_2), 4.24–4.16 (m, 1H, H-6_{aB}), 4.20 (d, *J* = 7.8 Hz, 1H, H-1_A), 4.15–4.10 (m, 3H, H-3_A, OCH_2), 4.06 (br s, 1H, H-4_A), 4.03–3.85 (m, 11H, H-2_B, H-4_B, H-4_D, H-5_B, H-5_C, H-5_D, H-6_{abA}, H-6_{abD}, H-6_{bB}), 3.78–3.69 (m, 4H, H-2_A, H-2_C, H-3_D, H-6_{aC}), 3.73 (s, 3H, OCH_3), 3.64–3.61 (m, 1H, H-6_{bC}), 3.59 (dd, *J* = 10.3, 3.2 Hz, 1H, H-3_C), 3.54 (t, *J* = 7.9 Hz each, 1H, H-4_C), 3.38–3.35 (m, 2H, H-2_D, H-3_B), 3.22 (br s, 1H, H-5_A); ^{13}C NMR (125 MHz, $CDCl_3$): δ 153.3–115.0 (Ar-C), 105.8 (C-1_A), 102.6 (C-1_D), 101.9 (PhCH), 101.3 (PhCH), 100.9 (C-1_B), 96.9 (C-1_C), 81.1 (C-2_D), 79.8 (C-4_C), 79.4 (C-4_B), 79.1 (C-4_A), 76.2 (C-3_A), 75.6 (PhCH$_2$), 75.4 (PhCH$_2$), 75.3 (C-3_B), 75.1 (C-2_B), 74.8 (C-5_B), 73.9 (2 C, PhCH$_2$, C-3_D), 73.4 (C-2_C), 72.9 (C-3_C), 72.7 (PhCH$_2$), 72.6 (PhCH$_2$), 72.0 (PhCH$_2$), 71.9 (PhCH$_2$), 71.1 (C-4_D), 69.3 (C-6_A), 69.1 (2 C, C-6_C, C-6_D), 69.0 (C-6_B), 68.4 (OCH$_2$), 68.3 (OCH$_2$), 66.9 (C-5_D), 66.8 (C-5_A), 64.9 (C-5_C), 61.6 (C-2_A), 56.0 (OCH_3); ESI-MS: 1670.6 [M+Na]$^+$; Anal. Calcd for $C_{96}H_{101}N_3O_{22}$ (1647.68): C, 69.93; H, 6.17. Found: C, 69.72; H, 6.40.

4.1.10. 2-(4-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 17

To a solution of compound **16** (850 mg, 0.51 mmol) and compound **7** (530 mg, 0.71 mmol) in anhydrous CH_2Cl_2 (5 mL) was added TMSOTf (15 μL) at −10 °C under argon and the reaction mixture was allowed to stir at the same temperature for 1 h. The reaction mixture was quenched with Et_3N (0.1 mL) and diluted with CH_2Cl_2 (50 mL). The organic layer was successively washed with satd $NaHCO_3$ and water, dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified over SiO_2 using hexane–EtOAc (4:1) as eluant to give pure compound **17** (820 mg, 72%). White solid; mp 82–84 °C; $[\alpha]_D^{25} = +12.3$ (*c* 1.2, $CHCl_3$); ν_{max} (KBr): 3450, 3034, 2926, 2873, 2114, 1732, 1507, 1455, 1369, 1267, 1099, 916, 826, 741, 703 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.16–6.82 (m, 65H, Ar-H), 5.92 (t, *J* = 9.6 Hz each, 1H, H-3_E), 5.72 (t, *J* = 9.6 Hz each, 1H, H-4_E), 5.60 (s, 1H, PhC*H*), 5.58 (s, 1H, PhC*H*), 5.50 (t, *J* = 8.0 Hz each, 1H, H-2_E), 5.20 (d, *J* = 7.9 Hz, 1H, H-1_E), 5.11 (br s, 1H, H-1_C), 5.07 (br s, 1H, H-1_B), 4.73–4.61 (m, 4H, PhCH_2), 4.58–4.47 (m, 7H, H-6_{abE}, PhCH_2), 4.46 (br s, 1H, H-1_D), 4.44–4.32 (m, 5H, PhCH_2), 4.30–4.18 (m, 3H, H-3_A, OCH_2), 4.16–4.08 (m, 5H, H-2_B, H-4_A, H-6_{abB}), 4.14 (d, *J* = 7.8 Hz, 1H, H-1_A), 4.06–3.94 (m, 8H, H-4_B, H-4_D, H-5_B, H-5_C, H-5_D, H-6_{bB}, OCH_2), 3.91–3.73 (m, 8H, H-2_A, H-2_D, H-5_E, H-6_{abA}, H-6_{abD}, H-6_{aC}), 3.75 (s, 3H, OCH_3), 3.71–3.60 (m, 3H, H-3_C, H-4_C, H-6_{bC}), 3.41–3.27 (m, 4H, H-2_C, H-2_D, H-3_B, H-5_A); ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.3 (*C*OPh), 166.1 (*C*OPh), 166.4 (*C*OPh), 165.3 (*C*OPh), 154.4–115.0 (Ar-C), 105.1 (C-1_A), 102.6 (C-1_E), 102.3 (PhCH), 101.8 (PhCH), 101.4 (C-1_D), 101.0 (C-1_B), 97.2 (C-1_C), 81.6 (C-2_D), 80.2 (C-4_C), 79.6 (C-4_B), 79.2 (C-4_A), 76.1 (C-3_A), 75.5 (2 C, C-2_B, C-3_B), 75.3 (2 C, C-5_B, PhCH$_2$), 75.2 (C-3_D), 75.0 (C-2_C), 74.0 (C-3_C), 73.9 (PhCH$_2$), 73.7 (PhCH$_2$), 73.5 (PhCH$_2$), 73.4 (C-2_D), 73.0 (C-5_E), 72.8 (C-5_D), 72.6 (C-3_E), 72.4 (PhCH$_2$), 71.9 (C-2_E), 71.3 (2 C, 2 PhCH$_2$), 70.1 (C-4_E), 69.4 (3 C, C-6_A, C-6_C, C-6_D), 69.0 (C-6_B), 68.6 (OCH$_2$), 68.4 (OCH$_2$), 66.8 (C-5_A), 65.0 (C-5_C), 63.1 (C-6_E), 61.6 (C-2_A), 56.0 (OCH_3); MALDI-MS: 2248.8 [M+Na]$^+$; Anal. Calcd for $C_{130}H_{127}N_3O_{31}$ (2225.84): C, 70.10; H, 5.75. Found: C, 69.87; H, 6.00.

4.1.11. 2-(4-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 **12** (300 mg, 0.25 mmol) in CH_3OH (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 sodium methoxide (5 mL) was allowed to stir at room temperature for 2 h and neutralized with Dowex 50 W X8 (H^+) resin. The reaction mixture was filtered and evaporated to dryness to give compound **1**, which was purified over Sephadex® LH-20 using CH_3OH (60 mL) as eluant to give pure **1** (115 mg, 66%). White powder; $[\alpha]_D^{25} = +16$ (*c* 1.2, CH_3OH); ν_{max} (KBr): 3434, 2945, 1628, 1378, 1148, 1078, 668 cm^{-1}; ^{1}H NMR (500 MHz, CD_3OD): δ 6.88–6.83 (m, 6H, Ar-H), 5.16 (br s, 1H, H-1_C), 4.85 (br s, 1H, H-1_B), 4.43 (d, *J* = 8.4 Hz, 1H, H-1_A), 4.04–4.00 (m, 3H, H-3_A, OCH_2), 3.97 (m, 2H, OCH_2), 3.88–3.87 (m, 1H, H-2_B), 3.82–3.81 (m, 1H, H-2_C), 3.79–3.75 (m, 3H, H-4_A, H-6_{abC}), 3.70–3.64 (m, 4H, H-3_C, H-4_C, H-6_{abB}), 3.63 (s, 3H, OCH_3), 3.60–3.52 (m, 4H, H-4_B, H-5_C, H-6_{abA}), 3.48–3.39 (m, 3H, H-3_B, H-5_A, H-5_B), 3.25–3.21 (m, 1H, H-2_A), 1.18 (s, 3H, COCH_3); ^{13}C NMR (125 MHz, CD_3OD): δ 172.7 (*C*OCH$_3$), 103.2 (C-1_B), 102.1 (C-1_A), 94.9 (C-1_C), 79.7 (C-2_C), 75.7 (C-5_A), 75.2 (C-5_B), 74.0 (C-3_B), 73.9 (C-2_B), 71.4 (C-5_C), 70.9 (C-4_C), 70.8 (C-4_B), 68.2 (OCH$_2$), 68.1 (OCH$_2$), 68.0 (C-4_A), 67.7 (C-3_C), 63.7 (C-3_A), 62.4 (C-6_B), 62.3 (C-6_A), 61.7 (C-6_C), 55.1 (OCH_3), 53.5 (C-2_A), 22.2 (COCH_3); ESI-MS: 718.2 [M+Na]$^+$; Anal. Calcd for $C_{29}H_{45}NO_{18}$ (695.26): C, 50.07; H, 6.52. Found: C, 49.85; H, 6.77.

4.1.12. 2-(4-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** (700 mg, 0.31 mmol) in 0.1 M CH_3O-Na (20 mL) was allowed 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 CH_2Cl_2 (20 mL) and H_2O (3.5 mL) were added an aq solution of NaBr (1 mL; 1 M), an aq solution of TBAB (2 mL; 1 M), TEMPO (80 mg, 0.5 mmol), a satd aq solution of $NaHCO_3$ (8 mL), and 4% aq NaOCl (10 mL) in succession and the reaction mixture was allowed to stir at 0–5 °C for 3 h. The reaction mixture was neutralized with the addition of 1 N aq HCl solution. To the reaction mixture were added *tert*-butanol (25 mL), 2-methyl-but-2-ene (30 mL; 2 M solution in THF), aq solution of $NaClO_2$ (1 g in

5 mL), and aq solution of NaH_2PO_4 (1 g in 5 mL) and the reaction mixture was allowed to stir at room temperature for 3 h. The reaction mixture was diluted with satd aq NaH_2PO_4 and extracted with CH_2Cl_2 (100 mL). The organic layer was washed with water, dried (Na_2SO_4) and concentrated to dryness. To a solution of the crude product in CH_3OH (30 mL) was added 20% $Pd(OH)_2$–C (200 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. 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 under reduced pressure. A solution of the acetylated product in 0.1 M sodium methoxide (10 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 **2**, which was purified over Sephadex® LH-20 using CH_3OH–H_2O (60 mL; 4:1 v/v) as eluant to give pure **2** (210 mg, 64%). White powder; $[\alpha]_D^{25} = +21$ (*c* 1.2, CH_3OH); ν_{max} (KBr): 3432, 2943, 1607, 1377, 1145, 1089, 665 cm^{-1}; ^1H NMR (500 MHz, CD_3OD): δ 6.79–6.71 (m, 4H, Ar-H), 5.19 (s, 1H, H-1_C), 4.77 (br s, 1H, H-1_B), 4.62 (d, J = 8.1 Hz, 1H, H-1_E), 4.48 (m, 2H, H-3_A, H-2_B), 4.40 (d, J = 7.8 Hz, 1H, H-1_A), 4.17 (br s, 1H, H-1_D), 4.15–4.10 (m, 2H, H-4_A, H-4_D), 4.08–3.93 (m, 4H, H-4_B, H-5_D, OCH_2), 3.88–3.82 (m, 1H, H-5_B), 3.80–3.70 (m, 4H, H-5_C, H-5_E, OCH_2), 3.68–3.57 (m, 6H, H-2_E, H-3_E, H-6_{abB}, H-6_{abD}), 3.63 (br s, 3H, OCH_3), 3.54–3.35 (m, 7H, H-3_C, H-4_C, H-4_E, H-6_{abA}, H-6_{abC}), 3.31–3.23 (m, 2H, H-2_A, H-3_D), 3.21–3.10 (m, 4H, H-2_C, H-2_D, H-3_B, H-5_A); ^{13}C NMR (125 MHz, CD_3OD): δ 174.6 (*C*OONa), 172.4 (*C*OCH$_3$), 105.4 (C-1_A), 105.0 (C-1_D), 103.8 (C-1_B), 101.6 (C-1_E), 101.0 (C-1_C), 80.8 (C-2_E), 78.6 (C-4_B), 77.3 (C-4_A), 77.1 (C-4_C), 75.0 (C-3_A), 74.8 (C-3_B), 74.1 (C-2_B), 73.9 (C-2_D), 73.2 (C-2_C), 72.5 (C-3_D), 71.3 (C-4_D), 71.1 (C-5_E), 70.9 (2 C, C-5_D, C-3_E), 70.6 (2 C, C-3_C, C-4_E), 68.2 (2 C, 2 O*C*H$_2$), 67.6 (2 C, C-5_A, C-5_C), 66.9 (C-5_B), 62.0 (C-6_B), 61.8 (C-6_D), 60.9 (C-6_A), 60.5 (C-6_C), 55.1 (O*C*H$_3$), 53.4 (C-2_A), 22.2 (CO*C*H$_3$); ESI-MS: 1056.3 $[M+1]^+$; Anal. Calcd for $C_{41}H_{62}NNaO_{29}$ (1055.33): C, 46.64; H, 5.92. Found: C, 46.41; H, 6.18.

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