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Synthesis of a trisaccharide repeat of the zwitterionic Sp1 capsular polysaccharide utilizing 2-azido-4-benzylamino-4*N*,3-*O*-carbonyl-2,4,6-trideoxy-D-galactopyranosyl trichloroacetimidate

Ithayavani Iynkkaran, David R. Bundle *

Alberta Ingenuity Centre for Carbohydrate Science and Department of Chemistry, The University of Alberta, Gunning-Lemieux Chemistry Centre, Edmonton, AB, Canada T6G 2G2

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This paper is dedicated to the memory of Dr. Malcolm Perry and Professor Lennart Kenne.

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Cyclic carbamate hydrolysis by lithium hydroxide
Uronic acid via post assembly oxidation

ABSTRACT

2-Azido-4-benzylamino-4*N*,3-*O*-carbonyl-2,4,6-trideoxy-D-galactopyranosyl trichloroacetimidate **2** conveniently prepared in six steps from 6-deoxy-D-glucal glycosylated a selectively protected α1,3 linked methyl galabioside to afford the trisaccharide skeleton of a repeating unit of the Sp1 zwitterionic capsular polysaccharide. Lithium hydroxide hydrolysis of the 3,4-cyclic carbamate permitted the creation of a 2-acetamido-4-amino-2,4,6-trideoxygalactose residue. Selective cleavage of *p*-methoxybenzyl ethers by trifluoroacetic acid gave a selectively deprotected trisaccharide with two hydroxymethyl groups that were oxidized by the TEMPO reagent to afford access to trisaccharide glycoside **1** containing 2-acetamido-4-amino-2,4,6-trideoxygalactose and two galacturonic acid residues.

1. Introduction

Protein antigens are processed and presented to T-cells after intracellular degradation into T-cell peptides that are bound in the grove of a major histocompatibility protein (MHC I or MHC II).[1] Following recognition of the peptide complex with MHC by the T-cell receptor, T-cells are triggered to release cytokines that allow those B-cells with Ig receptors that bind the antigen to produce protein specific antibodies.[1a] Pure carbohydrate antigens are T-cell independent antigens and do not produce a secondary immune response that is augmented by T-cell help.[1b] A notable exception to this generality are zwitterionic polysaccharides which are degraded into ~10 kDa fragments that can be presented by T-cells.[2] In fact processing of polysaccharide conjugate vaccines employs a combination of this degradative pathway with that of proteins.[2c,3] The ability of zwitterionic polysaccharides to be taken up and presented to T-cells has attracted considerable attention and stimulated a number of synthetic efforts to construct the repeating units of these polymers.[4] Zwitterionic polysaccharides have also been used as non-protein carriers of oligosaccharide haptens.[5]

The type I pneumococcal polysaccharide (Sp1) has the structure shown (Fig. 1) and like the polysaccharide of *Bacteroides fragilis* utilizes the major histocompatibility complex (MHC) class II pathway in antigen-presenting cells (APCs) for processing and presentation.[2a,d] We have reported the synthesis of a mono- and dimeric repeating units of the zwitterionic Sp1 capsular polysaccharide.[4a] Christina et al. have prepared all three of the frame shifted monomeric repeating units of the same polysaccharide.[4b] Our work avoids the use of uronic acid glycosyl donors by performing oxidation of selectively protected hexose residues after oligosaccharide assembly.[4a] The Dutch group of Marel and Codée demonstrated an alternative approach by effective use of uronic acid building blocks.[4b]

We recently reported a novel and concise synthesis of a glycosyl donor that is well suited for introduction of 2-acetamido-4-amino-2,4,6-trideoxy-α-D-galactopyranosyl repeating unit that contains this sugar as a terminal residue.[6] The synthesis of the trisaccharide methyl glycoside **1** containing the diaminohexose as a terminal

* Corresponding author. Tel.: +1 780 492 8808; fax: +1 780 492 7705.
E-mail address: dave.bundle@ualberta.ca (D.R. Bundle).

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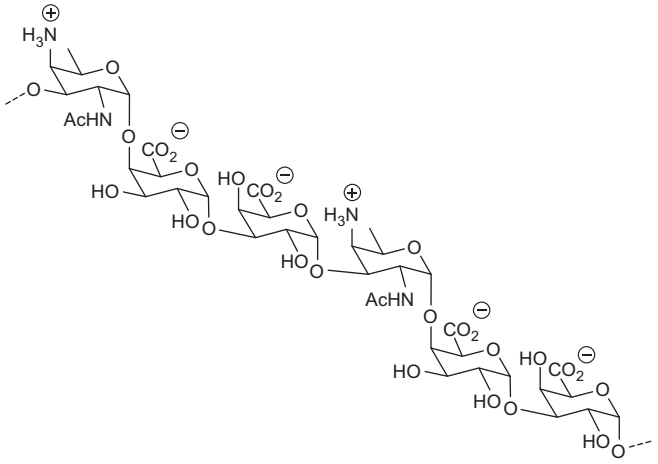


Figure 1. The structure of the type I *Streptococcus pneumoniae* capsular polysaccharide.

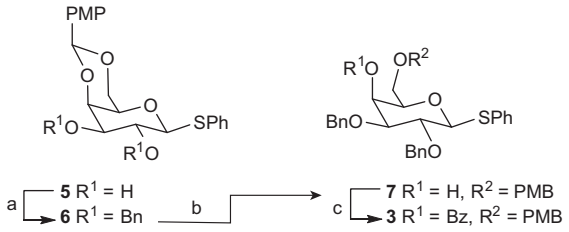
residue is reported utilizing this glycosyl donor **2** and monosaccharide building blocks **3** and **4** (Fig. 2).

2. Results and discussion

2.1. Monosaccharide building blocks

2-Azido-4-benzylamino-4*N*,3-*O*-carbonyl-2,4,6-trideoxy-D-galactopyranosyl trichloroacetimidate **2** was prepared from D-glucal in seven steps as previously described.[6] Assembly of the target molecule was envisaged to proceed via the glycosidation of phenylthiogalactoside **3** by methyl galactoside **4** followed by glycosylation of the resulting galabioside by imidate **2**. This approach requires the oxidation of a selectively deprotected trisaccharide to create two uronic acid residues. As we have shown before this avoids the challenges associated with glycosylation reactions between relatively unreactive uronic acid acceptors and donors.

The most direct route to **3** from phenyl thiogalactopyranoside involved the formation of the 4,6-*O*-*p*-methoxybenzylidene acetal **5**, (although this compound has been previously reported its characterization in several papers is rather sketchy).[7] Benzylation of **5** gave **6** and regioselective opening of the acetal provided the 6-*O*-*p*-methoxybenzyl derivative **7**, which was benzoylated to give **3** (Scheme 1).



Scheme 1. Reagents and conditions: (a) BnBr, NaH, DMF, 85%; (b) $NaCNBH_3$, TFA, DCM, 75% (c) BzCl, Py, 92%.

Methyl galactopyranoside was converted to the TBDPS derivative **8**[8] in 92% yield on a 20 g scale. Dibutyltin oxide was used to effect selective introduction of a 3-*O*-allyl ether to afford the diol **9**. Benzylation of **9** gave the fully protected galactopyranoside **10** and after removal of the silyl ether, compound **11** was converted to the *p*-methoxybenzyl ether **12**. Selective removal of the allyl ether gave the glycosyl acceptor **4** (Scheme 2).

2.2. Oligosaccharide assembly

The glycosidation of **3** by **4** was attempted under a variety of conditions. Activation of **3** by Ph_2SO–Tf_2O gave disaccharide glycoside **13** in yields of 30% or less. NIS–TfOH at −30 °C gave a 57% yield of disaccharide **13**. The best yield 70% of **13** was obtained with NIS–AgOTf. The disaccharide alcohol **14** was obtained by transesterification of **13** (Scheme 3).

Glycosylation of disaccharide **14** by imidate **2**[6] was most effectively carried out with a donor:acceptor molar ratio of 1.5:1.0 using TMSOTf as the Lewis acid promotor. The reaction was initiated at 0 °C and allowed to warm to room temperature (Scheme 4). Trisaccharide **15** was obtained in 70% yield exclusively as its α-anomer ($^3J_{1,2}$ homonuclear coupling constant).

2.3. Deprotection of trisaccharide 15

Deprotection of trisaccharide **15** to give the target compound **1** required a series of carefully controlled steps to cleave the oxazolidinone to afford the 2-acetamido-4-amino-2,4,6-tridoxyhexose residue with the correct *N*-acyl protection pattern while also

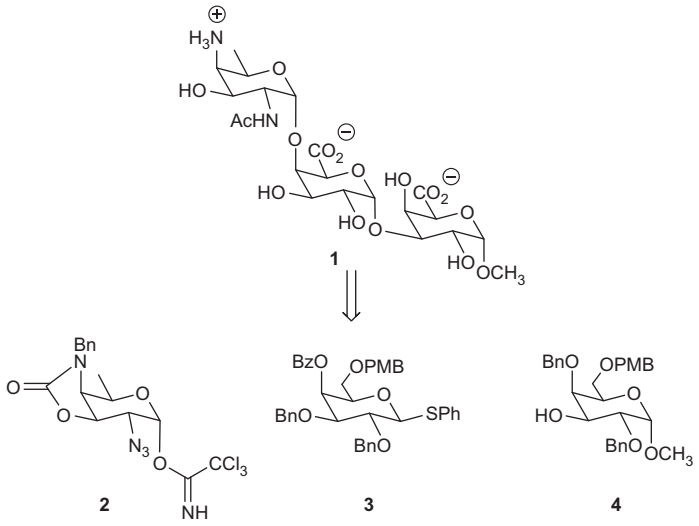
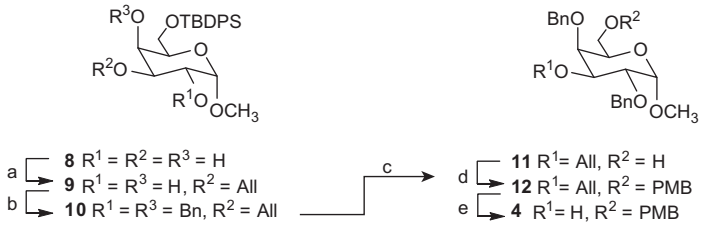
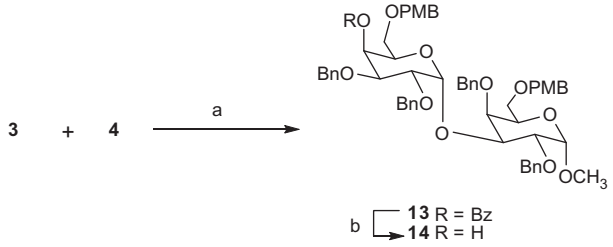


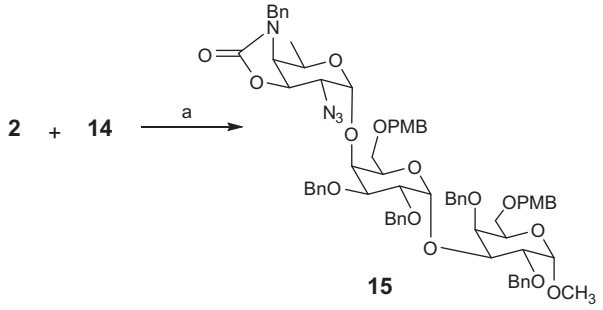
Figure 2. Trisaccharide target **1** and monosaccharide synthons **2**–**4**.



Scheme 2. Reagents and conditions: (a) Bn_2SnO, AllBr, TBAI, $PhCH_3$, 60 °C, 60%; (b) BnBr, NaH, DMF, 87%; (c) TBAF, THF, 92%; (d) PMBBr, NaH, 89%; (e) $PdCl_2$, HOAc, H_2O, NaOAc, 87%.



Scheme 3. Reagents and conditions: (a) NIS, AgOTf, DCM 4 Å MS, −30 °C, 70%; (b) MeONa, MeOH, DCM 45 °C 10 h, 94%.



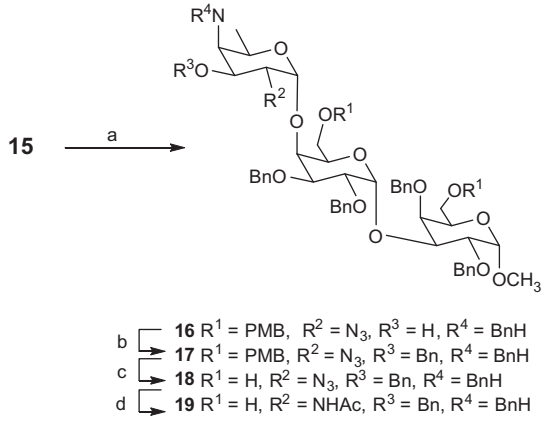
Scheme 4. Reagents and conditions: (a) TMSOTf, DCM, 4 Å MS, 70%.

permitting selective deprotection of the hydroxymethyl groups of the two galactopyranoside residues as a prelude to their oxidation to provide the galacturonic acid residues.

Of the several methods available in the literature for the cleavage of the oxazolidinone ring we elected to use base hydrolysis.[9] After screening a series of reaction conditions, varying the inorganic base, solvent system, temperature and reaction time, we found that the cleavage of oxazolidinone could be achieved by choosing a small and strongly Lewis acid; lithium cation. Treatment of **15** with LiOH and a catalytic amount of LiI in a mixture of THF and ethanol under reflux for 4 days gave the 4*N*-benzylgalatosamine derivative **16** in excellent yield (Table 1, entry 8). As can

Table 1
Conditions for controlled hydrolysis of the oxazolidinone **16** to provide access to a 2-acetamido-4-amino-2,4,6-tridoxyhexose residue

Entry	Reaction condition	Temperature (°C)	Yield (%)
1	Cs_2CO_3–THF	rt	—
2	Cs_2CO_3–THF	Varying from 40 to 80	—
3	1 M NaOH–THF	rt	—
4	1 M NaOH–THF	Varying from 40 to 80	—
5	1 M NaOH–THF–EtOH	80	50
6	KOTMS–THF	80	—
7	2 M LiOH–THF–EtOH	80	80
8	2 M LiOH–LiI–THF–EtOH	80	95

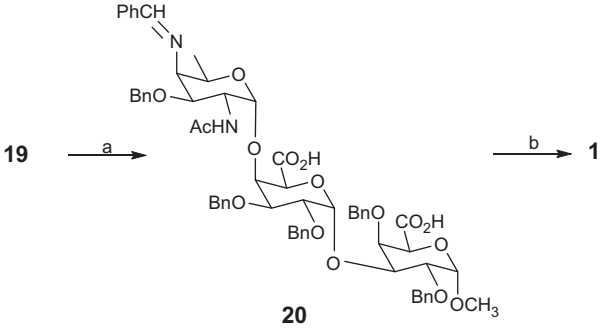


Scheme 5. Reagents and conditions: (a) 2 M LiOH, LiI, THF/EtOH (2:1) reflux 2 days 95%; (b) BnBr, NaH, DMF, 80%; (c) TFA, DCM, 20 min, 75%; (d) (i) H_2S, Py/H_2O/Et_3N, 20 h rt, (ii) Ac_2O, MeOH, 72%.

be seen neither Cs_2CO_3–THF nor KOTMS–THF afforded product and 1 M NaOH–THF–EtOH gave only moderate yield (Scheme 5).

In order to protect the newly revealed hydroxyl group, **16** was initially benzylated with excess benzyl bromide to give a dibenzylated tertiary amine. Although reduction of the azide and acetylation of the resulting amine proceeded in excellent yield subsequent attempts to selectively remove the two PMB ethers using DDQ and CAN resulted in a mixture of products that included incompletely hydrolysed PMB ethers and a series of partially N-debenzylated products. We reasoned that a dibenzylamine created an electron rich environment that was prone to oxidation and we sought to avoid N-benzylation of **16**. By employing a limited amount of benzyl bromide regioselective benzylation at the 3″ OH group was achieved in 80% yield to afford **17**.

Attempts to oxidatively cleave the PMB groups using DDQ/CAN gave only a trace amount of the desired diol **18**. However mild acid



Scheme 6. Reagents and conditions: (a) TEMPO/NaOCl, Me_2CO, $NaHCO_3$/KBr/H_2O, 10 min; (b) H_2, $Pd(OH)_2$/C, H_2O/AcOH, 53% over two steps from **19**.

hydrolysis of **17** using 5% TFA in DCM gave **18** in excellent yield. Selective reduction of the azide and acetylation of the resulting amine gave the N-acetylated diol **19**. This diol was oxidized by TEMPO-NaOCl-KBr[10] to give the di-acid **20** in which the secondary amine group had been oxidized to an imine Scheme 6. Global deprotection to afford **1** was then accomplished by hydrogenolysis. Gel permeation chromatography on Bio-gel P2 was used to purify the highly polar zwitterionic target molecule **1**. The three bond proton homonuclear coupling constants establish the α-anomeric configuration of each pyranose ring of **1** and it is note worthy that ^{1}H and ^{13}C NMR chemical shifts were similar to those reported for a related oligosaccharide synthesized as its glycerol glycoside.[4b]

Although glycosyl donor **2** was previously shown to be effective in yielding α-glycosides with model acceptors,[6] the application here demonstrates its utility for the synthesis of oligosaccharide sequences that require C2 and C4 amino groups that can be readily differentiated.

2.4. Biological evaluation

Trisaccharide glycoside **1** was tested for its ability to stimulate interleukin 10 (IL-10) and Interferon-gamma (IFN-γ) (unpublished results, Kasper and co-workers at Harvard Medical School). Each of these responses is representative of the T-cell activating ability of zwitterionic antigens.[11] Unfortunately, this trisaccharide, as well as a previously frame-shifted trisaccharide and its corresponding hexasaccharide were not active.[4a] Published data describing the molecular weight required for activity[2d] that appeared after synthetic work was initiated is consistent with this result. Based on this data, it appears that at least six repeating units are required for activity.

3. Experimental

3.1. General methods

All chemical reagents were of analytical grade and used as obtained from commercial sources unless otherwise indicated. Solvents used in water-sensitive reactions were purified by successive passage through columns of alumina and copper under nitrogen, except for DMSO, which was distilled under vacuum and collected over 4 Å molecular sieves. Unless otherwise noted, reactions were carried out at room temperature, and water-sensitive reactions were performed under an atmosphere of argon. Molecular sieves were flame dried and then allowed to cool to room temperature under argon before use. Reactions were monitored by analytical thin-layer chromatography (TLC) performed on Silica Gel 60-F254 (E. Merck). Plates were visualized under UV light, and/or by treatment with 5% sulphuric acid in ethanol followed by heating. Organic solvents were removed under vacuum at <40 °C. Medium-pressure chromatography was conducted using silica gel (230–400 mesh, Silicycle, Montreal) at flow rates between 5 and 10 mL min^{-1}. Following deprotection, final compounds were purified by HPLC (Flow rate = 3.0 mL/min, Diameter = 7.8 mm) with 70% CH_3CN–30% H_2O as eluent on a TSK-GEL Amide-80 column, concentrated under reduced pressure to remove acetonitrile, and then lyophilized. ^{1}H NMR spectra were recorded at 498 or 600 MHz, and chemical shifts, reported in δ (ppm), were referenced to internal residual protonated solvent signals or to external acetone (0.1% ext. acetone δ 2.225 ppm) in the case of D_2O. ^{13}C NMR spectra were recorded at 125 MHz, and chemical shifts are referenced to internal $CDCl_3$ (δ 77.23) or external acetone (δ 31.07). First order chemical shifts of ^{1}H and ^{13}C are reported to the second and first decimal place, respectively. High resolution mass spectra were obtained on a Micromass Zabspec TOF-mass spectrometer by analytical services in the department. Optical rotations were determined with a Perkin-Elmer, model 241, polarimeter at room temperature using the sodium D-line and are reported in units of deg mL g^{-1} dm^{-1}. Elemental analysis was performed by analytical services of this department.

3.2. Methyl 2-acetamido-4-amino-2,4,6-trideoxy-α-D-galactopyranosyl-(1→4)-α-D-galactopyranosiduronate-(1→3)-α-D-galactopyranosiduronate (1)

Crude **20** was dissolved in a mixture of H_2O–AcOH (4:1, 3 mL) and 20% $Pd(OH)_2/C$ (0.015 g) was added to the resulting solution. The reaction mixture was shaken under a hydrogen atmosphere at 60 psi for 2 days. The catalyst was filtered off through cotton wool and then through a microfilter. The filtrate was concentrated (1 mL) under reduced pressure. Purification was performed on a Bio-gel P2 column (1.6 × 35 cm) using NH_4OH (1 mL/L) in water as eluent and with monitoring by a Waters R403 refractive index detector. Subsequent lyophilization of the purified fractions afforded the final trisaccharide **1** (0.004 g, 53%) as a white solid. $[\alpha]_D$ +49.1 (*c* 0.2, H_2O); ^{1}H NMR of the NH_4^+ salt form (600 MHz, D_2O) δ 5.22 (d, 1H, $J_{1',2'}$ = 3.7 Hz, H-1′), 4.92 (d, 1H, $J_{1'',2''}$ = 3.3 Hz, H-1″), 4.86 (d, 1H, $J_{1,2}$ = 3.8 Hz, H-1), 4.64 (qd, 1H, $J_{4'',5''}$ = 1.6 Hz, $J_{5'',6''}$ = 6.5 Hz, H-5″), 4.55 (app s, 1H, H-5′), 4.49 (d, 1H, $J_{3,4}$ = 3.1 Hz, $J_{4,5}$ = 1.2 Hz, H-4), 4.33 (d, 1H, $J_{3',4'}$ = 3.1 Hz, $J_{4',5'}$ = 0.9 Hz, H-4′), 4.22 (d, 1H, $J_{4,5}$ = 1.1 Hz, H-5), 4.10 (dd, 1H, $J_{2',3'}$ = 10.9 Hz, $J_{3',4'}$ = 3.3 Hz, H-3′), 4.08 (dd, 1H, $J_{2'',3''}$ = 9.0 Hz, $J_{3'',4''}$ = 3.7 Hz, H-3″), 4.06 (dd, 1H, $J_{1'',2''}$ = 3.5 Hz, $J_{2'',3''}$ = 11.2 Hz, H-2″), 4.00 (dd, 1H, $J_{2,3}$ = 10.3 Hz, $J_{3,4}$ = 3.2 Hz, H-3), 3.94 (dd, 1H, $J_{1,2}$ = 3.8 Hz, $J_{2,3}$ = 10.2 Hz, H-2), 3.89 (dd, 1H, $J_{1',2'}$ = 3.9 Hz, $J_{2',3'}$ = 10.7 Hz, H-2′), 3.41 (s, 3H, OCH_3), 3.37 (dd, 1H, $J_{3'',4''}$ = 4.1 Hz, $J_{4'',5''}$ = 1.5 Hz, H-4″), 2.09 (s, 3H, $COCH_3$), 1.24 (d, 3H, $J_{5'',6''}$ = 6.7 Hz, H-6″ CH_3). ^{13}C NMR of the NH_4^+ salt form (125 MHz, D_2O) δ 176.4, 175.9, 175.5, 100.3, 99.8, 96.7, 81.0, 76.2, 72.1, 71.9, 69.6, 68.9, 68.4, 67.3, 67.0, 65.7, 56.1, 55.6, 50.1, 23.2, 16.5. ESI HRMS calcd for $C_{21}H_{33}N_2O_{16}$ (M−H): 569.1837, found 569.1839.

3.3. Phenyl 4-*O*-benzoyl-2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-1-thio-β-D-galactopyranoside (3)

Compound **7** (1.71 g, 2.98 mmol) was dissolved in dry pyridine (25 mL) under an argon atmosphere. Benzoyl chloride (0.50 mL, 3.58 mmol, 1.2 equiv) was added at room temperature and after 7 h the reaction mixture was quenched by addition of MeOH. After stirring for 25 min the solution was concentrated under reduced pressure. The residue was dissolved in DCM, washed with saturated $NaHCO_3$ solution and brine. Then, the DCM solution was dried over Na_2SO_4, filtered and concentrated to dryness. Chromatography of the residue using hexanes–EtOAc (17:3) afforded the benzoylated galactoside **3** (1.86 g, 92%). $[\alpha]_D$ +7.2 (*c* 1.3, CH_2Cl_2); ^{1}H NMR (498 MHz, $CDCl_3$) δ 8.11 (d, 1H, *J* = 7.4 Hz, ArH), 8.02–7.96 (m, 2H, ArH), 7.67–7.55 (m, 3H, ArH), 7.53–7.41 (m, 3H, ArH), 7.41–7.18 (m, 13H, ArH), 6.81–6.75 (m, 2H, ArH), 5.89 (dd, 1H, $J_{3,4}$ = 2.1 Hz, $J_{4,5}$ = 0.4 Hz, H-4), 4.85 (d, 1H, J_{gem} = 11.2 Hz, PhCH_2), 4.73 (s, 2H, PhCH_2), 4.70 (d, 1H, $J_{1,2}$ = 9.5 Hz, H-1), 4.52 (d, 1H, J_{gem} = 11.2 Hz, PhCH_2), 4.45 (d, 1H, J_{gem} = 11.4 Hz, PhCH_2), 4.37 (d, 1H, J_{gem} = 11.4 Hz, PhCH_2), 3.88 (app t, 1H, $J_{5,6a}$ = 6.3 Hz, $J_{5,6b}$ = 6.3 Hz, H-5), 3.78–3.73 (dd, H, $J_{2,3}$ = 9.0 Hz, $J_{3,4}$ = 3.2 Hz, H-3), 3.74 (s, 3H, $OCH_2C_6H_4OCH_3$), 3.71 (app t, 1H, $J_{1,2}$ = 9.3 Hz, $J_{2,3}$ = 9.3 Hz, H-2), 3.68–3.63 (dd, 1H, $J_{5,6a}$ = 5.9 Hz, $J_{6a,6b}$ = 9.5 Hz, H-6a), 3.55 (dd, 1H, $J_{5,6b}$ = 5.9 Hz, $J_{6a,6b}$ = 9.3 Hz, H-6b). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.6, 159.3, 138.3, 137.6, 133.1, 132.9, 132.8, 130.0, 129.8, 129.7, 129.6, 128.8, 128.3, 128.2, 128.1, 127.7, 127.6, 113.8, 87.2, 81.5, 76.5, 76.2, 75.7, 73.3, 71.8, 67.9, 67.3, 55.2. ESI HRMS calcd for $C_{41}H_{40}O_7SNa$ (M+Na): 699.2387,

found 699.2394. Anal. Calcd for $C_{41}H_{40}O_7S$: C, 72.76; H, 5.96; O, 16.55, S, 4.74. Found: C, 73.10; H, 6.12; O, 16.87, S, 3.91.

3.4. Methyl 2,4-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-α-D-galactopyranoside (4)

To a solution of **12** (0.48 g, 0.91 mmol) in acetic acid (10 mL) and water (10 drops) were added $PdCl_2$ (0.32 g, 1.82 mmol, 2 equiv) and NaOAc (0.32 g, 3.91 mmol, 4.3 equiv) at room temperature with stirring. After 7 h the reaction mixture was filtered through Celite. The filtrate was diluted with EtOAc (15 mL) and then washed with an equal volume of saturated aqueous $NaHCO_3$ solution, brine and water. The organic phase was dried over Na_2SO_4, filtered and then concentrated to dryness. The residue was chromatographed using hexanes–EtOAc (7:3) as eluent to give **4** (0.39 g, 87%) as a syrup. $[\alpha]_D$ +63.7 (*c* 1.3, CH_2Cl_2); ^1H NMR (600 MHz, $CDCl_3$) δ 7.39–7.25 (m, 11H, ArH), 7.24–7.18 (m, 2H, ArH), 6.88–6.83 (m, 2H, ArH), 4.80 (d, 1H, J_{gem} = 11.6 Hz, PhCH_2), 4.70 (d, 1H, J_{gem} = 9.1 Hz, PhCH_2), 4.69 (s, 1H, H-1), 4.66 (d, 1H, J_{gem} = 12.0 Hz, PhCH_2), 4.61 (d, 1H, J_{gem} = 11.6 Hz, PhCH_2), 4.46 (d, 1H, J_{gem} = 11.4 Hz, PhCH_2), 4.37 (d, 1H, J_{gem} = 11.4 Hz, PhCH_2), 4.04 (ddd, 1H, $J_{2,3}$ = 10.0 Hz, $J_{3,3OH}$ = 4.8 Hz, $J_{3,4}$ = 3.3 Hz, H-3), 3.92.

3.5. Phenyl 4,6-*O*-*p*-methoxybenzylidene-1-thio-β-D-galactopyranoside (5)

Phenyl-1-thio-β-D-glucopyranoside (4.97 g, 18.4 mmol) was dissolved in dry CH_3CN (30 mL). *p*-Anisaldehyde dimethyl acetal (4.10 mL, 22.08 mmol, 1.2 equiv) and a catalytic amount of camphorsulphonic acid were added. The reaction was stirred at room temperature for 3 h. Then the reaction mixture was quenched by addition of TEA and concentrated under reduced pressure. The yellow residue was purified by column chromatography (5% MeOH in DCM) to afford **5** (6.61 g, 92%) as a white crystalline solid. NMR chemical shifts and coupling constants were in excellent agreement with the literature.[7] $[\alpha]_D$ −7.5 (*c* 1.5, $CHCl_3$) (lit. $[\alpha]_D$ −7.5).

3.6. Phenyl 2,3-di-*O*-benzyl-4,6-*O*-*p*-methoxybenzylidene-1-thio-β-D-galactopyranoside (6)

To a solution of diol **5**[7] (6.34 g, 16.25 mmol) in dry DMF (25 mL) at 0 °C was added NaH (dispersion in mineral oil; 60% by mass; 1.18 g, 16.25 mmol, 3 equiv) in portions under an inert argon atmosphere. After 1 h, BnBr (8.45 mL, 16.25 mmol, 3 equiv) was slowly added to the above mixture, which was then warmed to room temperature and stirred for a further 5 h. The reaction mixture was then quenched by careful addition of MeOH. The solution was diluted with DCM (100 mL) and washed with an equal volume of water and brine. The organic extract was dried over Na_2SO_4, filtered and the filtrate was concentrated. Chromatography on silica gel with toluene–EtOAc (13:1) as eluent gave **6** (7.95 g, 85%). $[\alpha]_D$ +3.2 (*c* 0.6, CH_2Cl_2); ^1H NMR (498 MHz, $CDCl_3$) δ 7.77–7.71 (m, 2H, ArH), 7.51–7.41 (m, 4H, ArH), 7.41–7.19 (m, 11H, ArH), 6.94 (t, 2H, *J* = 5.6 Hz, ArH), 5.47 (s, 1H, C*H*PhOCH_3), 4.78–4.67 (m, 4H, PhCH_2), 4.64 (d, 1H, $J_{1,2}$ = 9.6 Hz, H-1), 4.37 (d, 1H, $J_{6a,6b}$ = 12.2 Hz, H-6a), 4.16 (d, 1H, $J_{3,4}$ = 3.3 Hz, H-4), 4.00–3.96 (d, 1H, $J_{6a,6b}$ = 3.3 Hz, H-6b), 3.93 (app t, 1H, $J_{1,2}$ = 9.4 Hz, $J_{2,3}$ = 9.4 Hz, H-2), 3.86 (s, 3H, CHPhOCH_3), 3.64 (dd, 1H, $J_{2,3}$ = 9.2 Hz, $J_{3,4}$ = 3.4 Hz, H-3), 3.40 (s, 1H, H-5). ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.2, 138.6, 138.2, 132.9, 132.7, 130.6, 128.9, 128.4, 128.3, 128.2, 127.9, 127.9, 127.8, 127.8, 127.7, 127.5, 113.5, 101.3, 86.6, 81.4, 73.7, 71.8, 69.9, 69.4, 55.4. ESI HRMS calcd for $C_{34}H_{34}O_6SNa$ (M+Na): 593.1968, found 593.1970.

3.7. Phenyl 2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-1-thio-β-D-galactopyranoside (7)

TFA (0.78 mL, 7.01 mmol, 5 equiv) was added dropwise to a cooled (0 °C) solution of **6** (0.8 g, 1.40 mmol) and $NaCNBH_3$ (0.44 g, 7.01 mmol, 5 equiv) in dry THF (10 mL) containing activated 4 Å molecular sieves (0.20 g). The solution was then stirred at room temperature until TLC showed complete consumption of starting material. The reaction was quenched with TEA and then it was diluted with EtOAc (20 mL). Molecular sieves were removed by filtering through Celite. The filtrate was washed with an equal volume of saturated aqueous $NaHCO_3$ solution and brine. The combined organic phase was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexanes–EtOAc, 8:2) to give **7** (0.60 g, 75%) as a white solid. $[\alpha]_D$ +0.5 (*c* 1.5, CH_2Cl_2); ^1H NMR (600 MHz, $CDCl_3$) δ 7.61–7.56 (m, 2H, ArH), 7.44–7.39 (m, 2H, ArH), 7.38–7.22 (m, 13H, ArH), 6.91–6.85 (m, 2H, ArH), 4.84 (d, 1H, J_{gem} = 10.3 Hz, PhCH_2), 4.76 (d, 1H, J_{gem} = 10.3 Hz, PhCH_2), 4.73 (d, 1H, J_{gem} = 11.6 Hz, PhCH_2), 4.69 (d, 1H, J_{gem} = 10.3 Hz, PhCH_2), 4.64 (d, 1H, $J_{1,2}$ = 9.8 Hz, H-1), 4.51 (s, 2H, PhCH_2), 4.11 (d, 1H, *J* = 3.2 Hz, H-4), 3.81 (s, 3H, $OCH_2C_6H_4OCH_3$), 3.81–3.73 (m, 3H, H-2, H-6), 3.58 (m, 2H, H-5, H-3). ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.3, 138.2, 137.7, 133.9, 131.8, 130.0, 129.5, 128.9, 128.5, 128.4, 128.3, 128.0, 127.9, 127.8, 127.3, 113.8, 87.7, 82.6, 77.3, 75.8, 73.4, 72.1, 69.1, 66.9, 55.3. ESI HRMS calcd for $C_{34}H_{36}O_6SNa$ (M+Na): 595.2125, found 595.2123. Anal. Calcd for $C_{34}H_{36}O_6S$: C, 71.30; H, 6.34. Found: C, 70.85; H, 6.34.

3.8. Methyl 6-*O*-*tert*-butyldiphenylsilyl-α-D-galactopyranoside (8)

Methyl α-D-galactopyranoside (20.00 g, 103.1 mmol) was dissolved in DMF (50 mL) with stirring under argon. Imidazole (8.41 g, 123.72 mmol, 1.2 equiv) and then by *tert*-butylchlorodiphenylsilane (31.16 mL, 113.53 mmol, 1.1 equiv) were added to the solution. After 5 h the reaction was quenched by adding MeOH. Then the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel using a mixture of hexanes/EtOAc (7:3) as eluent to afford **8** (41.00 g, 92%) as a syrup. NMR chemical shifts and coupling constants were in general agreement with the literature.[8] Our observed values are reported since there are some differences; $[\alpha]_D$ +75.7 (*c* 0.3, $CHCl_3$); ^1H NMR (498 MHz, $CDCl_3$) δ 7.70 (m, 4H, ArH), 7.48–7.35 (m, 6H, ArH), 4.79 (d, 1H, $J_{1,2}$ = 3.9 Hz, H-1), 4.11 (s, 1H, H-4), 3.93 (dd, 1H, $J_{5,6a}$ = 6.1 Hz, $J_{6a,6b}$ = 10.6 Hz, H-6a), 3.90–3.85 (dd, 1H, $J_{5,6b}$ = 5.3 Hz, $J_{6a,6b}$ = 10.6 Hz, H-6b), 3.85–3.81 (dd, 1H, $J_{1,2}$ = 3.9 Hz, $J_{2,3}$ = 9.4 Hz, H-2), 3.77 (t, 1H, $J_{5,6}$ = 5.7 Hz, H-5), 3.74 (dd, 1H, $J_{2,3}$ = 9.4 Hz, $J_{3,4}$ = 3.3 Hz, H-3), 3.37 (s, 3H, OCH_3), 2.52 (s, 4H, OH), 1.07 (s, 9H, C(CH_3)$_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.6, 135.6, 133.3, 133.2, 129.7, 127.7, 99.6, 71.0, 70.4, 69.6, 69.4, 63.4, 55.1, 26.8, 19.2. ESI HRMS calcd for $C_{23}H_{32}O_6SiNa$ (M+Na): 455.1860, found 455.1853. Anal. Calcd for $C_{23}H_{32}O_6Si$: C, 63.86; H, 7.46. Found: C, 63.56; H, 7.45.

3.9. Methyl 3-*O*-allyl-6-*O*-*tert*-butyldiphenylsilyl-α-D-galactopyranoside (9)

A mixture of **8** (0.51 g, 1.18 mmol) and dibutyltin oxide (0.32 g, 1.30 mmol, 1.1 equiv) in toluene (15 mL) was heated at reflux for 3 h with azeotropic removal of water. The solution was concentrated to 10 mL by continued evaporation and was cooled to 60 °C. TBAI (0.47 g, 1.30 mmol, 1.1 equiv) and allyl bromide (0.16 mL, 1.30 mmol, 1.1 equiv) were added to the solution. The reaction mixture was heated at 60 °C overnight and the solution was then evaporated under reduced pressure. The residue was

purified by silica gel column chromatography using a stepped gradient (20–30% EtOAc in hexanes) to give compound **9** (0.33 g, 60%). $[\alpha]_D$ +88.8 (*c* 0.4, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.73–7.67 (m, 4H, ArH), 7.46–7.36 (m, 6H, ArH), 5.97 (m, 1H, $OCH_2CH{=}CH_2$), 5.37–5.28 (ddd, 1H, J_{trans} = 17.2 Hz, J_{gem} = 3.1 Hz, ^4J = 1.5 Hz, $OCH_2CH = CH$), 5.26–5.19 (ddd, 1H, J_{cis} = 10.3 Hz, J_{gem} = 2.8 Hz, ^4J = 1.2 Hz, $OCH_2CH = CH$), 4.81 (d, 1H, $J_{1,2}$ = 4.0 Hz, H-1), 4.20 (m, 2H, $OCH_2CH = CH_2$), 4.15–4.12 (m, 1H, H-4), 3.99–3.92 (m, 2H, H-2, H-6), 3.87 (dd, 1H, $J_{5,6b}$ = 5.8 Hz, $J_{6a,6b}$ = 10.4 Hz, H-6b), 3.77 (app t, 1H, $J_{4,5}$ = 5.9 Hz, $J_{5,6b}$ = 5.9 Hz, H-5), 3.54 (dd, 1H, $J_{2,3}$ = 9.7 Hz, $J_{3,4}$ = 3.2 Hz, H-3), 3.39 (s, 3H, OCH_3), 2.48–2.45 (s, 1H, 4-OH), 2.07 (s, 1H, 2-OH), 1.10–1.05 (s, 9H, $C(CH_3)_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.6, 135.6, 134.6, 133.3, 133.2, 129.7, 129.7, 127.8, 117.8, 99.4, 78.2, 70.9, 70.1, 68.5, 66.8, 63.3, 55.2, 26.8, 19.2. ESI HRMS calcd for $C_{26}H_{36}O_6SiNa$ (M+Na): 495.2173, found 495.2176.

3.10. Methyl 3-*O*-allyl-2,4-di-*O*-benzyl-6-*O*-*tert*-butyldiphenylsilyl-α-D-galactopyranoside (10)

To a stirred solution of **9** (0.40 g, 0.85 mmol) in dry DMF (7 mL), NaH (dispersion in mineral oil; 60% by mass; 0.073 g, 1.78 mmol, 2.1 equiv) was added in portions at 0 °C and stirring was continued until the evolution of gas had ceased. After 1 h, BnBr (0.30 mL, 1.78 mmol, 2.1 equiv) was slowly added to the above mixture, which was then warmed to room temperature and stirred for 4 h. The reaction mixture was then quenched with MeOH. The solution was diluted with DCM (20 mL) and washed with an equal volume of water and brine. The organic extract was dried over Na_2SO_4, filtered and concentrated to a light yellow residue. Chromatography on silica gel with hexanes–EtOAc (4:1) as eluent gave **10** (0.48 g, 87%) as a white solid. $[\alpha]_D$ +76.2 (*c* 0.4, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.66–7.60 (m, 4H, ArH), 7.47–7.20 (m, 16H, ArH), 6.03–5.95 (m, 1H, $OCH_2CH{=}CH_2$), 5.37 (ddd, 1H, J_{trans} = 17.2 Hz, J_{gem} = 3.5 Hz, ^4J = 1.7 Hz, $OCH_2CH = CH$), 5.20 (ddd, 1H, J_{cis} = 10.6 Hz, J_{gem} = 3.2 Hz, ^4J = 1.4 Hz, $OCH_2CH{=}CH$), 4.95 (d, 1H, J_{gem} = 11.4 Hz, $PhCH_2$), 4.82 (d, 1H, J_{gem} = 12.1 Hz, $PhCH_2$), 4.67 (d, 1H, J_{gem} = 12.1 Hz, $PhCH_2$), 4.63 (d, 1H, $J_{1,2}$ = 3.7 Hz, H-1), 4.61 (d, 1H, J_{gem} = 11.4 Hz, $PhCH_2$), 4.31 (ddt, 1H, J_{gem} = 13.0 Hz, J_{vic} = 5.1 Hz, ^4J = 1.5 Hz, $OCH_2CH{=}CH_2$), 4.23 (ddt, 1H, J_{gem} = 13.0 Hz, J_{vic} = 5.5 Hz, ^4J = 1.4 Hz, $OCH_2CH{=}CH_2$), 3.97 (d, 1H, $J_{3,4}$ = 2.9 Hz, H-4), 3.95 (dd, 1H, $J_{1,2}$ = 3.7 Hz, $J_{2,3}$ = 10.1 Hz, H-2), 3.80 (dd, 1H, $J_{2,3}$ = 10.1 Hz, $J_{3,4}$ = 2.9 Hz, H-3), 3.75–3.68 (m, 3H, H-6, H-5), 3.28 (s, 3H, OCH_3), 1.10–1.03 (m, 9H, $C(CH_3)_3$). ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.7, 138.6, 135.5, 135.3, 133.4, 129.7, 129.68, 128.3, 128.1, 128.0, 127.7, 127.68, 127.6, 127.4, 116.3, 98.7, 78.8, 76.3, 74.8, 74.7, 73.5, 71.8, 70.7, 62.7, 55.0, 26.9, 19.2. ESI HRMS calcd for $C_{40}H_{48}O_6SiNa$ (M+Na): 675.3112, found 675.3113.

3.11. Methyl 3-*O*-allyl-2,4-di-*O*-benzyl-α-D-galactopyranoside (11)

A solution of silyl ether **10** (0.48 g, 0.73 mmol) in dry THF (10 mL) was reacted with TBAF (1.0 M in THF; 0.23 mL, 0.88 mmol, 1.2 equiv) under stirring at room temperature for 6 h. The solution was then diluted with EtOAc (15 mL), washed with water, brine and the organic phase was dried over sodium sulphate, filtered and the filtrate concentrated in vacuo. The residue was purified by silica gel column chromatography to give compound **11** (0.28 g, 92%) as a colourless oil. $[\alpha]_D$ +71.1 (*c* 2.3, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.42–7.25 (m, 10H, ArH), 6.00 (m, 1H, $OCH_2CH{=}CH_2$), 5.37 (ddd, 1H, J_{trans} = 17.2 Hz, J_{gem} = 3.3 Hz, ^4J = 1.6 Hz, $OCH_2CH{=}CH$), 5.21 (ddd, 1H, J_{cis} = 10.6 Hz, J_{gem} = 3.3 Hz, ^4J = 1.4 Hz, $OCH_2CH{=}CH$), 4.98 (d, 1H, J_{gem} = 11.2 Hz, $PhCH_2$), 4.84 (d, 1H, J_{gem} = 12.1 Hz, $PhCH_2$), 4.70 (s, 1H, H-1), 4.67 (d, 1H, J_{gem} = 12.1 Hz, $PhCH_2$), 4.61 (d, 1H, J_{gem} = 11.2 Hz, $PhCH_2$), 4.33 (ddt, 1H, J_{gem} = 13.0 Hz, J_{vic} = 5.6 Hz, ^4J = 1.4 Hz, $OCH_2CH{=}CH_2$), 4.23 (ddt, 1H, J_{gem} = 13.0 Hz, J_{vic} = 5.6 Hz, ^4J = 1.4 Hz, $OCH_2CH{=}CH_2$), 4.00 (dd, 1H, $J_{1,2}$ = 3.7 Hz, $J_{2,3}$ = 10.1 Hz, H-2), 3.89 (d, 1H $J_{4,5}$ = 2.7 Hz, H-5), 3.83 (dd, 1H, $J_{2,3}$ = 10.1 Hz, $J_{3,4}$ = 2.9 Hz, H-3), 3.77–3.69 (m, 2H, H-4, H-6a), 3.55–3.46 (m, 1H, H-6b), 3.37 (s, 3H, OCH_3), 1.68 (dd, 1H, $J_{6a,6OH}$ = 9.0 Hz, $J_{6b,6OH}$ = 2.8 Hz, 2-OH). ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.5, 138.2, 135.1, 128.6, 128.5, 128.3, 128.1, 128.0, 127.7, 116.6, 98.9, 78.7, 76.2, 74.8, 74.4, 73.6, 72.1, 70.2, 62.5, 55.3. ESI HRMS calcd for $C_{24}H_{30}O_6Na$ (M+Na): 437.1935, found 437.1935.

3.12. Methyl 3-*O*-allyl-2,4-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-α-D-galactopyranoside (12)

Alcohol **11** (0.28 g, 0.68 mmol) was dissolved in DMF (5 mL) and treated with NaH (dispersion in mineral oil; 60% by mass; 0.03 g, 0.75 mmol, 1.1 equiv) in portions at 0 °C. The reaction was stirred at room temperature for 1 h and then PMBBr (0.15 mL, 0.75 mmol, 1.1 equiv) was added drop wise and stirring was continued at room temperature for a further 5 h. Unreacted NaH was quenched by slow addition of MeOH at 0 °C. The reaction mixture was diluted with DCM (10 mL), and the organic phase was washed with water, brine, and the organic phase was dried over $MgSO_4$. The filtrate was concentrated under reduced pressure and the residue was purified by column chromatography (hexanes–EtOAc, 9:1) to give **12** (0.31 g, 89%) as a colourless syrup. $[\alpha]_D$ +38.3 (*c* 2.2, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40–7.27 (m, 8H, ArH), 7.27–7.00 (m, 5H, ArH), 6.93–6.82 (m, 2H, ArH), 5.96 (m, 1H, $OCH_2CH = CH_2$), 5.35 (ddd, 1H, J_{trans} = 17.2 Hz, J_{gem} = 3.5 Hz, ^4J = 1.7 Hz, $OCH_2CH{=}CH$), 5.18 (ddd, 1H, J_{cis} = 10.4 Hz, J_{gem} = 3.2 Hz, ^4J = 1.4 Hz, $OCH_2CH{=}CH$), 4.93 (d, 1H, J_{gem} = 11.4 Hz, $PhCH_2$), 4.83 (d, 1H, J_{gem} = 12.1 Hz, $PhCH_2$), 4.69 (d, 1H, J_{gem} = 15.2 Hz, $PhCH_2$), 4.67 (s, 1H, H-1), 4.56 (d, 1H, J_{gem} = 11.4 Hz, $PhCH_2$), 4.43 (d, 1H, J_{gem} = 11.4 Hz, $PhCH_2$), 4.34 (d, 1H, J_{gem} = 11.4 Hz, $PhCH_2$), 4.28 (ddt, 1H, J_{gem} = 13.0 Hz, J_{vic} = 5.1 Hz, ^4J = 1.6 Hz, $OCH_2CH{=}CH_2$), 4.20 (ddt, 1H, J_{gem} = 13.0 Hz, J_{vic} = 5.5 Hz, ^4J = 1.5 Hz, $OCH_2CH{=}CH_2$), 3.97 (dd, 1H, $J_{1,2}$ = 3.7 Hz, $J_{2,3}$ = 10.1 Hz, H-2), 3.94–3.90 (dd, 1H, $J_{3,4}$ = 3.0 Hz, $J_{4,5}$ = 1.1 Hz, H-4), 3.88 (ddd, 1H, $J_{4,5}$ = 1.1 Hz, $J_{5,6a}$ = 6.5 Hz, $J_{5,6b}$ = 6.5 Hz, H-5), 3.81 (dd, H, $J_{2,3}$ = 10.1 Hz, $J_{3,4}$ = 2.9 Hz, H-3), 3.80 (s, 3H, $OCH_2C_6H_4OCH_3$), 3.53 (dd, 1H, $J_{5,6a}$ = 7.0 Hz, $J_{6a,6b}$ = 9.3 Hz, H-6a), 3.49 (dd, 1H, $J_{5,6b}$ = 5.9 Hz, $J_{6a,6b}$ = 9.3 Hz, H-6b), 3.39–3.31 (m, 3H, OCH_3). ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.3, 138.8, 138.6, 135.1, 130.1, 129.5, 128.3, 128.2, 128.2, 128.0, 127.6, 127.5, 116.3, 113.8, 98.9, 78.6, 76.2, 75.0, 74.78, 73.6, 73.2, 71.8, 69.2, 68.7, 55.3, 55.3. ESI HRMS calcd for $C_{32}H_{38}O_7Na$ (M+Na): 557.2510, found 557.2510.

3.13. Methyl 4-*O*-benzoyl-2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-α-D-galactopyranosyl-(1→3)-2,4-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-α-D-galactopyranoside (13)

Acceptor **4** (0.44 g, 0.88 mmol) and phenyl thiogalactoside **3** (0.77 g, 1.15 mmol, 1.3 equiv) were combined and concentrated from a toluene solution and the residue was then dried in vacuo overnight. The residue was dissolved in freshly distilled DCM (25 mL) and the mixture was stirred under argon at room temperature in the presence of powdered 4 Å molecular sieves for 30 min before being cooled to −30 °C. NIS (0.28 g, 1.01 mmol, 1.2 equiv) was then added and stirring was continued for 30 min. After addition of AgOTf (0.02 g, 0.09 mmol, 0.1 equiv) the reaction mixture turned deep purple, and the reaction mixture was then stirred for a further 1 h at −30 °C at which point the reaction was complete. The mixture was made basic by addition of TEA and stirred for an additional 20 min. The mixture was diluted, filtered through Celite and washed with 5% $Na_2S_2O_3$ solution and dried over

anhydrous $MgSO_4$. The filtrate was concentrated to a residue that was subjected to silica gel column chromatography using 8% EtOAc in toluene as eluent to obtain the disaccharide **13** as a white crystalline solid (exclusively α, 0.7 g, 70%). $[\alpha]_D$ +202.7 (*c* 0.4, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.15–7.99 (m, 3H, ArH), 7.65–7.10 (m, 27H, ArH), 6.94–6.64 (m, 5H, ArH), 5.77 (d, 1H, *J* = 2.0 Hz, H-4′), 5.26 (d, 1H, $J_{1',2'}$ = 3.3 Hz, H-1′), 4.99 (d, 1H, J_{gem} = 11.5 Hz, PhCH_2), 4.83 (d, 2H, *J* = 11.6 Hz, PhCH_2), 4.72 (d, 1H, J_{gem} = 12.0 Hz, PhCH_2), 4.69–4.62 (m, 2H, PhCH_2), 4.61–4.50 (m, 3H, H-5′, H-1, PhCH_2), 4.43 (d, 1H, J_{gem} = 11.5 Hz, PhCH_2), 4.37 (d, 1H, J_{gem} = 11.5 Hz, PhCH_2), 4.33 (d, 1H, J_{gem} = 11.5 Hz, PhCH_2), 4.30 (d, 1H, J_{gem} = 11.5 Hz, PhCH_2), 4.27 (d, 1H, J_{gem} = 11.5 Hz, PhCH_2), 4.18 (dd, 1H, $J_{2,3}$ = 10.2 Hz, $J_{3,4}$ = 2.5 Hz, H-3), 4.14 (dd, 1H, $J_{2',3'}$ = 10.0 Hz, $J_{3',4'}$ = 3.1 Hz, H-3′), 4.01 (dd, 1H, $J_{1,2}$ = 3.6 Hz, $J_{2,3}$ = 10.0 Hz, H-2), 3.99 (dd, 1H, $J_{1',2'}$ = 3.3 Hz, $J_{2',3'}$ = 8.8 Hz, H-2′), 3.95 (d, 1H, $J_{3,4}$ = 1.4 Hz, H-4), 3.85 (t, 1H, *J* = 6.8 Hz, H-5), 3.81 (s, 3H, $OCH_2C_6H_4OCH_3$), 3.72 (s, 3H, $OCH_2C_6H_4OCH_3$), 3.50 (dd, $J_{5',6a'}$ = 6.1 Hz, 1H, $J_{6a',6b'}$ = 9.8 Hz, H-6a′), 3.47 (d, 2H, *J* = 6.3 Hz, H-6), 3.39 (dd, $J_{5',6a'}$ = 6.8 Hz, 1H, $J_{6a',6b'}$ = 9.6 Hz, H-6b′), 3.31 (s, 3H, OCH_3). ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.8, 159.2, 159.0, 139.0, 138.6, 138.2, 138.2, 132.9, 130.2, 130.2, 130.1, 129.9, 129.8, 129.4, 129.4, 128.5, 128.4, 128.3, 128.3, 128.2, 128.2, 128.1, 128.1, 128.0, 128.0, 127.9, 127.8, 127.8, 127.7, 127.6, 127.4, 127.2, 113.8, 113.5, 98.5, 96.9, 76.4, 76.0, 75.8, 75.6, 74.8, 74.8, 74.3, 73.2, 73.0, 72.7, 71.3, 69.2, 68.7, 68.7, 67.9, 67.8, 55.3, 55.2, 55.1. ESI HRMS calcd for $C_{64}H_{68}O_{14}Na$ (M+Na): 1083.4501, found 1083.4503.

3.14. Methyl 2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-α-D-galactopyranosyl-(1→3)-2,4-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-α-D-galactopyranoside (14)

Disaccharide **13** (0.90 g, 0.85 mmol) was dissolved in a mixture of freshly distilled DCM and MeOH (4:1; v/v, 15 mL). Then 1.5 M MeO-Na/MeOH (0.3 mL) was added drop wise. The solution was heated at 45 °C for 10 h then it was neutralized with Amberlite resin IR-120 (H^+), filtered and concentrated under reduced pressure. Chromatography over silica gel using a gradient eluent (25–35% EtOAc in hexanes) gave **14** (0.76 g, 94%) as a colourless syrup. $[\alpha]_D$ +64.1 (*c* 0.8, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.38–7.33 (m, 2H, ArH), 7.33–7.14 (m, 22H, ArH), 7.12 (m, 2H, ArH), 6.88–6.81 (m, 4H, ArH), 5.21 (d, 1H, $J_{1',2'}$ = 3.5 Hz, H-1′), 4.99 (d, 1H, J_{gem} = 11.4 Hz, PhCH_2), 4.83 (d, 1H, J_{gem} = 11.5 Hz, PhCH_2), 4.71–4.66 (m, 3H, PhCH_2), 4.64 (s, 1H, H-1), 4.63 (d, 1H, J_{gem} = 8.7 Hz, PhCH_2), 4.53 (d, 1H, J_{gem} = 11.9 Hz, PhCH_2), 4.46 (d, 1H, J_{gem} = 11.6 Hz, PhCH_2), 4.41 (d, 1H, J_{gem} = 11.5 Hz, PhCH_2), 4.33 (m, 3H, PhCH_2), 4.24 (t, 1H, *J* = 5.2 Hz, H-5′), 4.14 (dd, 1H, $J_{2,3}$ = 10.2 Hz, $J_{3,4}$ = 2.7 Hz, H-3), 4.01 (m, 2H, H-4′, H-2′), 3.97 (dd, 1H, $J_{1,2}$ = 3.6 Hz, $J_{2,3}$ = 10.2 Hz, H-2), 3.92 (app s, 1H, H-4), 3.90 (dd, 1H, $J_{2',3'}$ = 9.9 Hz, $J_{3',4'}$ = 3.2 Hz, H-3′), 3.84 (t, 1H, *J* = 6.8 Hz, H-5), 3.80 (s, 3H, $OCH_2C_6H_4OCH_3$), 3.78 (s, 3H, $OCH_2C_6H_4OCH_3$), 3.60 (dd, 1H, $J_{5',6a'}$ = 5.4 Hz, $J_{6a',6b'}$ = 10.3 Hz, H-6a′), 3.52 (dd, 1H, $J_{5',6b'}$ = 5.2 Hz, $J_{6a',6b'}$ = 10.3 Hz, H-6b′), 3.46 (dd, 2H, *J* = 6.7, *J* = 1.4 Hz, H-6), 3.30 (s, 3H, OCH_3), 2.90 (s, 1H, 4′-OH). ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.0, 138.5, 138.3, 138.2, 130.1, 129.4, 129.3, 128.4, 128.3,, 128.1, 128.0, 127.9, 127.7, 127.6, 127.6, 127.2, 113.8, 113.7, 98.4, 96.5, 77.7, 76.0, 75.8, 75.7, 74.8, 74.7, 74.2, 73.1, 73.0, 72.9, 71.8, 69.5, 69.2, 68.6, 68.3, 68.1, 55.3, 55.2, 55.2. ESI HRMS calcd for $C_{57}H_{64}O_{13}Na$ (M+Na): 979.4239, found 979.4239.

3.15. Methyl 2-azido-4-benzylamino-4-*N*,3-*O*-carbonyl-2,4,6-trideoxy-α-D-galactopyranosyl-(1→4)-2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-α-D-galactopyranosyl-(1→3)-2,4-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-α-D-galactopyranoside (15)

The acceptor **14** (0.44 g, 0.46 mmol) and imidate **2**[6] (0.31 g, 0.69 mmol, 1.5 equiv) were combined and concentrated from dry toluene and dried in vacuo overnight. The residue was dissolved in freshly distilled DCM (15 mL) and the mixture was stirred under argon at room temperature in the presence of powdered 4 Å molecular sieves for 30 min before being cooled to 0 °C. TMSOTf (5.0 μL, 0.09 mmol, 0.05 equiv) was added and the reaction mixture was stirred for 1 h at 0 °C and then it was allowed to warm to room temperature. The reaction mixture was quenched by addition of TEA and stirred for an additional 20 min, the mixture was diluted, filtered through Celite and the filtrate was concentrated. The residue was subjected to silica gel column chromatography using a stepped gradient eluent (20–30% EtOAc in hexanes) to obtain the trisaccharide **15** as a colourless syrup (exclusively α, 0.40 g, 70%). $[\alpha]_D$ +90.8 (*c* 1.0, CH_2Cl_2); ^{1}H NMR (498 MHz, $CDCl_3$) δ 7.38–7.09 (m, 31H, ArH), 7.09 (s, 1H, ArH), 6.92–6.76 (m, 4H, ArH), 5.13 (s, 1H, H-1′), 5.03 (d, 1H, $J_{1'',2''}$ = 4.2 Hz, H-1″), 4.93 (d, 1H, J_{gem} = 11.7 Hz, PhCH_2) 4.91 (d, 2H, J_{gem} = 15.5 Hz, PhCH_2), 4.75 (d, 1H, J_{gem} = 8.0 Hz, PhCH_2), 4.72 (d, 1H, J_{gem} = 7.0 Hz, PhCH_2), 4.64–4.57 (m, 4H, H-1, PhCH_2), 4.53 (dd, 1H, $J_{2'',3''}$ = 6.3 Hz, $J_{3'',4''}$ = 7.8 Hz, H-3″), 4.46 (d, 1H, J_{gem} = 12.2 Hz, PhCH_2), 4.41 (d, 1H, J_{gem} = 11.5 Hz, PhCH_2), 4.36–4.17 (m, 7H, H-5″, H-4′, H-5′, H-3′, 3 × PhCH_2), 4.07 (dd, 1H, $J_{2,3}$ = 10.0 Hz, $J_{3,4}$ = 2.8 Hz, H-3), 4.05 (d, 1H, J_{gem} = 15.0 Hz, PhCH_2), 3.92 (dd, 1H, $J_{1,2}$ = 3.7 Hz, $J_{2,3}$ = 10.2 Hz, H-2), 3.91–3.88 (m, 2H, PhCH_2, H-2′), 3.87 (d, 1H, $J_{4,5}$ = 2.3 Hz, H-4), 3.81–3.77 (m, 7H, H-5, 2 OCH_3), 3.76 (dd, 1H, $J_{1'',2''}$ = 3.9 Hz, $J_{2'',3''}$ = 6.2 Hz, H-2″), 3.66 (dd, 1H, $J_{3'',4''}$ = 8.0 Hz, $J_{4'',5''}$ = 3.0 Hz, H-4″), 3.50 (t, 1H, $J_{6a',6b'}$ = 9.0 Hz, H-6a′), 3.47–3.41 (m, 3H, 2 H-6, H-6b′), 3.28 (s, 3H, OCH_3), 1.03 (d, 3H, $J_{5'',6''}$ = 6.8 Hz, H-6″ CH_3). ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.3, 159.2, 158.7, 139.0, 138.6, 138.5, 138.1, 135.7, 130.1, 130.0, 129.6, 129.3, 129.0, 128.4–127.1 (m), 113.9, 113.8, 98.5, 96.5, 96.5, 76.6, 76.1, 75.8, 75.5, 74.9, 74.7, 73.9, 73.7, 73.1, 73.0, 72.9, 72.5, 72.0, 69.2, 68.6, 68.6, 66.7, 64.9, 58.4, 55.3, 55.2, 48.7, 17.4. ESI HRMS calcd for $C_{71}H_{78}O_{16}N_4Na$ (M+Na): 1265.5305, found 1265.5305.

3.16. Methyl 2-azido-4-benzylamino-2,4,6-trideoxy-α-D-galactopyranosyl-(1→4)-2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-α-D-galactopyranosyl-(1→3)-2,4-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-α-D-galactopyranoside (16)

To a solution of oxazolidinone derivative **15** (0.32 g, 0.26 mmol) in a mixture of THF and EtOH (2:1, v/v, 12 mL) were added 2 M LiOH (4 mL), and a catalytic amount of LiI. The mixture was heated under reflux for 4 days. It was then concentrated to dryness under reduced pressure. The residue was dissolved in DCM (15 mL) and washed with an equal volume of water and brine. The extract was dried over Na_2SO_4, filtered and the filtrate was concentrated. Column chromatography on silica gel using hexanes and EtOAc (3:1) afforded the title compound **16** (0.30 g, 95%) as a colourless syrup. $[\alpha]_D$ +150.1 (*c* 0.5, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.49–7.05 (m, 31H, ArH), 6.88–6.79 (m, 4H, ArH), 5.22 (d, 1H, $J_{1',2'}$ = 3.3 Hz, H-1′), 4.95 (d, 1H, J_{gem} = 11.3 Hz, PhCH_2), 4.86–4.79 (m, 2H, H-1″, PhCH_2), 4.74 (d, 1H, J_{gem} = 12.5 Hz, PhCH_2), 4.70 (d, 1H, J_{gem} = 11.5 Hz, PhCH_2), 4.67 (d, 1H, J_{gem} = 11.5 Hz, PhCH_2), 4.63 (d, 1H, J_{gem} = 12.3 Hz, PhCH_2), 4.56 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-1), 4.53 (q, 1H, $J_{5'',6''}$ = 6.5 Hz, H-5″), 4.46 (d, 1H, J_{gem} = 12.3 Hz, PhCH_2), 4.41 (d, 1H, J_{gem} = 11.5 Hz, PhCH_2), 4.35–4.26 (m, 4H, PhCH_2), 4.23 (dd, 1H, $J_{5',6a'}$ = 5.8 Hz, $J_{5',6b'}$ = 9.1 Hz, H-5′), 4.15 (app s, 1H, H-4′), 4.10 (dd, 1H, $J_{2,3}$ = 9.1 Hz, $J_{3,4}$ = 5.7 Hz, H-3), 4.03 (d, 1H, J_{gem} = 12.6 Hz, PhCH_2), 3.99 (dd, 1H, $J_{1',2'}$ = 3.3 Hz, $J_{2',3'}$ = 10.3 Hz, H-2′), 3.95–3.85 (m, 4H, H-3′, H-4, H-2, H-3″), 3.82 (m, 1H, H-5), 3.80 (s, 3H, $OCH_2C_6H_4OCH_3$), 3.78–3.68 (m, 5H, $OCH_2C_6H_4OCH_3$, PhCH_2, H-6a′), 3.50 (dd, 1H, $J_{5',6b'}$ = 5.7 Hz, $J_{6a',6b'}$ = 9.0 Hz, H-6b′), 3.43 (d, 2H, *J* = 7.5 Hz, H-6), 3.27 (s, 3H, OCH_3), 2.90 (dd, 1H, $J_{1'',2''}$ = 3.7 Hz, $J_{2'',3''}$ = 10.0 Hz, H-2″), 2.78 (dd, 1H, *J* = 4.3, 1.0 Hz, H-4″), 1.00 (d, 3H, $J_{5'',6''}$ = 6.5 Hz, H-6″ CH_3). ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.2, 140.0, 139.0, 138.6, 138.1, 130.2, 130.0, 129.7,

129.3, 128.7, 128.3, 128.0, 127.9, 127.6, 127.5, 127.4, 127.2, 127.2, 113.8, 113.7, 98.5, 98.3, 96.4, 76.9, 76.2, 76.0, 75.5, 74.9, 74.7, 73.9, 73.8, 73.1, 73.0, 72.5, 72.3, 69.2, 68.9, 68.6, 67.4, 66.5, 66.5, 62.4, 61.5, 55.5, 55.3, 55.2, 55.1, 17.3. ESI HRMS calcd for $C_{70}H_{81}N_4O_{15}$ (M+H): 1217.5693, found 1217.5687.

3.17. Methyl 2-azido-3-benzyl-4-benzylamino-2,4,6-trideoxy-α-D-galactopyranosyl-(1→4)-2,3-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-α-D-galactopyranosyl-(1→3)-2,4-di-*O*-benzyl-6-*O*-*p*-methoxybenzyl-α-D-galactopyranoside (17)

To a solution of **16** (0.125 g, 0.123 mmol) in dry DMF (4 mL) at 0 °C was added NaH (dispersion in mineral oil; 60% by mass; 0.006 g, 0.18 mmol, 1.5 equiv) in portions under an atmosphere of argon. After 1 h, BnBr (26.34 μL, 0.18 mmol, 1.5 equiv) was slowly added to the above mixture, which was then warmed to room temperature and stirred for 5 h. The reaction was then quenched by careful addition of MeOH. The solution was diluted with DCM (6 mL) and washed with an equal volume of water and brine. The organic extract was dried over Na_2SO_4, filtered and the filtrate was concentrated. Chromatography of the residue on silica gel with hexanes–EtOAc (17:3) as eluent gave **17** (0.107 g, 80%). $[\alpha]_D$ +47.0 (*c* 0.3, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.42–6.96 (m, 36H, ArH), 6.88–6.81 (m, 4H, ArH), 5.23 (d, 1H, $J_{1',2'}$ = 3.2 Hz, H-1′), 4.95 (s, 1H, H-1″), 4.93 (s, 1H, PhCH_2), 4.80 (d, 1H, J_{gem} = 11.7 Hz, PhCH_2), 4.77 (d, 1H, J_{gem} = 12.7 Hz, PhCH_2), 4.71 (d, 1H, J_{gem} = 11.6 Hz, PhCH_2), 4.67 (d, 1H, J_{gem} = 12.7 Hz, PhCH_2), 4.64 (d, 1H, J_{gem} = 12.3 Hz, PhCH_2), 4.56 (d, 1H, $J_{1,2}$ = 3.5 Hz, H-1), 4.49–4.40 (m, 4H, PhCH_2), 4.35 (q, 1H, $J_{5'',6''}$ = 6.4 Hz, H-5″), 4.33–4.28 (m, 4H, H-4′, PhCH_2), 4.22 (dd, 1H, $J_{5',6a'}$ = 6.0 Hz, $J_{5',6b'}$ = 6.1 Hz, H-5′), 4.18 (s, 1H, PhCH_2), 4.11 (dd, 1H, $J_{2,3}$ = 10.1 Hz, $J_{3,4}$ = 2.5 Hz, H-3), 3.97 (dd, 1H, $J_{1',2'}$ = 3.3 Hz, $J_{2',3'}$ = 10.3 Hz, H-2′), 3.92 (m, 5H, H-2, H-4, H-3′, H-3″, PhCH_2), 3.84–3.74 (m, 9H, H-5, H-6a′, PhCH_2, 2 × $OCH_2C_6H_4OCH_3$), 3.56 (dd, 1H, $J_{1'',2''}$ = 3.7 Hz, $J_{2'',3''}$ = 10.8 Hz, H-2″), 3.51 (dd, 1H, $J_{5',6b'}$ = 5.8 Hz, $J_{6a',6b'}$ = 9.1 Hz, H-6b′), 3.44 (dd, 2H, *J* = 6.7, 1.8 Hz, H-6), 3.28 (s, 3H, OCH_3), 3.01 (d, 1H, *J* = 3.4 Hz, H-4″), 1.06 (d, 3H, $J_{5'',6''}$ = 6.6 Hz, H-6″ CH_3). ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.2, 139.0, 138.6, 138.3, 137.6, 130.2, 130.0, 129.6, 129.3, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.6, 127.4, 127.3, 127.2, 127.1, 113.8, 113.7, 98.6, 98.4, 96.5, 77.0, 76.6, 76.1, 76.1, 75.5, 74.9, 74.7, 73.8, 73.6, 73.2, 73.0, 72.6, 71.1, 69.2, 68.6, 67.0, 66.7, 59.8, 57.6, 55.3, 55.2, 55.2, 55.0, 17.8. ESI HRMS calcd for $C_{77}H_{87}N_4O_{15}$ (M+H): 1307.6162, found 1307.6161.

3.18. Methyl 2-azido-3-benzyl-4-benzylamino-2,4,6-trideoxy-α-D-galactopyranosyl-(1→4)-2,3-di-*O*-benzyl-α-D-galactopyranosyl-(1→3)-2,4-di-*O*-benzyl-α-D-galactopyranoside (18)

Trisaccharide **17** (0.125 g, 0.0.096 mmol) was dissolved in DCM (5 mL) stirring at room temperature. To the resulting solution 5% TFA (0.25 mL) was added drop wise and the reaction was monitored by TLC (5% MeOH in DCM). After 20 min the reaction was quenched by adding saturated $NaHCO_3$ solution (10 mL). The reaction mixture was diluted with DCM (10 mL), and the DCM solution was washed with water and brine. The organic phase was dried over $MgSO_4$, filtered and the filtrate was concentrated under reduced pressure. Purification of the residue via column chromatography (3% MeOH in DCM) gave the titled compound **18** (0.08 g, 75%) as a colourless syrup. $[\alpha]_D$ +91.5 (*c* 0.2, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40–7.09 (m, 30H, ArH), 5.19 (d, 1H, $J_{1',2'}$ = 3.3 Hz, H-1′), 5.00 (d, 1H, J_{gem} = 11.5 Hz, PhCH_2), 4.94 (d, 1H, $J_{1'',2''}$ = 3.1 Hz, H-1″), 4.80 (d, 1H, J_{gem} = 11.5 Hz, PhCH_2), 4.75 (d, 1H, J_{gem} = 12.8 Hz, PhCH_2), 4.74 (s, 1H, H-1), 4.73 (d, 1H, J_{gem} = 11.3 Hz, PhCH_2), 4.69 (d, 1H, J_{gem} = 11.5 Hz, PhCH_2), 4.54 (s, 2H, PhCH_2), 4.40 (d, 1H, J_{gem} = 11.5 Hz, PhCH_2), 4.38–4.20 (m, 4H, PhCH_2, H-5″), 4.15 (dd, 1H, $J_{2,3}$ = 10.2 Hz, $J_{3,4}$ = 2.5 Hz, H-3), 4.04 (app t, 1H, $J_{5',6'}$ = 6.6 Hz, H-5′), 3.98 (dd, 1H, $J_{1,2}$ = 3.5 Hz, $J_{2,3}$ = 10.2 Hz, H-2), 3.96–3.70 (m, 6H, H-4, H-2′, H-3′, H-4′, H-3″, PhCH_2) 3.76 (d, 1H, $J_{2'',3''}$ = 10.3 Hz, H-2″), 3.72–3.66 (m, 2H, H-5, H-6a), 3.60 (dd, 1H, $J_{5',6a'}$ = 6.9 Hz, $J_{6a',\ 6b'}$ = 10.7 Hz, H-6a′), 3.52 (dd, 1H, $J_{5,6b}$ = 4.6 Hz, $J_{6a,6b}$ = 10.8 Hz, H-6b), 3.47 (dd, 1H, $J_{5',6a'}$ = 6.8 Hz, $J_{6a',6b'}$ = 10.8 Hz, H-6b′), 3.34 (s, 3H, OCH_3), 3.13 (d, 1H, *J* = 2.8 Hz, H-4″), 1.11 (d, 3H, $J_{5'',6''}$ = 5.6 Hz, H-6″ CH_3). ^{13}C NMR (125 MHz, $CDCl_3$) δ 138.5, 138.3, 138.0, 138.0, 136.7, 129.5, 129.0, 128.5, 128.4, 128.3, 128.1, 128.1, 127.7, 127.4, 98.3, 98.2, 96.0, 76.3, 75.6, 75.4, 75.1, 75.0, 74.6, 74.1, 73.0, 72.5, 71.8, 70.7, 70.3, 62.4, 60.7, 59.7, 59.5, 57.2, 55.3, 38.1, 31.2, 29.7, 17.5. ESI HRMS calcd for $C_{61}H_{71}N_4O_{13}$ (M+H): 1067.5012, found 1067.5015.

3.19. Methyl 2-acetamido-3-benzyl-4-benzylamino-2,4,6-trideoxy-α-D-galactopyranosyl-(1→4)-2,3-di-*O*-benzyl-α-D-galactopyranosyl-(1→3)-2,4-di-*O*-benzyl-α-D-galactopyranoside (19)

Trisaccharide **18** (0.09 g, 0.086 mmol) was dissolved in a solution of pyridine, water and TEA (10:1:0.3, 11.3 mL). The solution was saturated with H_2S by bubbling gas into the solution for 1 h at 0 °C, followed by stirring at room temperature for 20 h. Solvent was evaporated under reduced pressure and the residue was further dried in vacuo for 5 h. The crude amine was dissolved in dry MeOH and acetic anhydride (0.1 mL) was added to the resulting mixture. After 30 min at room temperature the reaction mixture was concentrated. The residue was subjected to silica gel column chromatography using a stepped gradient eluent (DCM–MeOH 1→3) to obtain the acetamide derivative **19** (0.067 g, 72%). $[\alpha]_D$ +89.4 (*c* 0.1, CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.41–7.07 (m, 30H, ArH), 5.13 (d, 1H, $J_{1',2'}$ = 3.3 Hz, H-1′), 4.98 (d, 1H, J_{gem} = 12.8 Hz, PhCH_2), 4.89 (d, 1H, $J_{1'',2''}$ = 3.0 Hz, H-1″), 4.87 (d, 1H, J_{gem} = 11.5 Hz, PhCH_2), 4.79 (d, 1H, J_{gem} = 12.5 Hz, PhCH_2), 4.74 (d, 1H, $J_{1,2}$ = 3.4 Hz, H-1), 4.70 (d, 1H, J_{gem} = 11.5 Hz, PhCH_2), 4.67 (d, 1H, J_{gem} = 12.5 Hz, PhCH_2), 4.53 (app s, 2H, PhCH_2), 4.39 (m, 3H, PhCH_2, H-2″, H-4), 4.26 (q, 1H, $J_{5'',6''}$ = 6.4 Hz, H-5″), 4.10 (dd, 1H, $J_{2,3}$ = 10.2 Hz, $J_{3,4}$ = 2.8 Hz, H-3), 4.02 (app t, 1H, *J* = 6.5 Hz, H-5′), 3.98 (dd, 1H, $J_{1,2}$ = 3.5 Hz, $J_{2,3}$ = 10.3 Hz, H-2), 3.91–3.82 (m, 5H, H-2′, H-3′, H-4′, PhCH_2), 3.73–3.64 (m, 3H, H-6, PhCH_2), 3.56 (dd, 1H, $J_{2'',3''}$ = 10.4 Hz, $J_{3'',4''}$ = 2.9 Hz, H-3″), 3.49 (d, 1H, *J* = 9.7 Hz, H-5), 3.37–3.29 (m, 4H, OCH_3, H-6a′), 3.20 (dd, 1H, $J_{5',6a'}$ = 6.4 Hz, $J_{6a',6b'}$ = 10.7 Hz, H-6b′), 3.01 (app s, 1H, H-4″), 1.90 (s, 3H, COCH_3), 1.17 (d, 3H, $J_{5'',6''}$ = 5.6 Hz, H-6″ CH_3). ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.8, 138.5, 138.2, 138.1, 138.0, 128.7, 128.5, 128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 127.9, 127.6, 127.6, 98.2, 96.8, 76.2, 76.1, 75.8, 75.1, 74.6, 74.3, 73.0, 72.2, 70.9, 70.3, 62.3, 60.6, 59.5, 55.3, 53.6, 49.1, 38.1, 31.2, 29.7, 23.3, 17.5. ESI HRMS calcd for $C_{63}H_{75}N_2O_{14}Na$ (M+Na): 1083.5213, found 1083.5211.

3.20. Methyl 2-acetamido-3-benzyl-4-benzylideneamino-2,4,6-trideoxy-α-D-galactopyranosyl-(1→4)-2,3-di-*O*-benzyl-α-D-galactopyranosiduronate-(1→3)-2,4-di-*O*-benzyl-α-D-galactopyranosiduronate (20)

To a stirred solution of 6,6′ diol **19** (0.015 g, 13.8 μmol) in acetone (1 mL) at 0 °C was added 5% $NaHCO_3$ aqueous solution (0.5 mL) followed by KBr (0.003 g, 0.03 mmol, 2 equiv) and TEMPO (0.003 g, 0.004 mmol, 3 equiv) at 0 °C. After 10 min, NaOCl (0.027 mL, 0.055 mmol, 4 equiv) was slowly added to the above mixture at the same temperature and it was stirred for further 10 min. The solution was concentrated under reduced pressure.

The crude product was carried to the next step without purification. A small portion of crude **20** was purified by Sephadex G-10 column using H_2O–NH_4OH as eluent monitored by Pharmacia UV detector. Subsequent lyophilization of the purified fractions afforded **20** as a white solid. ^{1}H NMR of the NH_4^+ salt form (600 MHz, D_2O) δ 7.49–7.27 (m, 27H, ArH, PhCH_2), 7.19 (m, 2H, ArH), 5.50 (d, 1H, $J_{1',2'}$ = 3.4 Hz, H-1′), 4.93 (d, 1H, $J_{1'',2''}$ = 3.4 Hz, H-1″), 4.89 (d, 1H, J_{gem} = 10.7 Hz, PhCH_2), 4.81–4.63 (m, 7H, H-1, H-5, PhCH_2), 4.58–4.49 (m, 4H, H-4, H-4′, H-5′, PhCH_2), 4.45 (m, 3H, PhCH_2), 4.22–4.17 (m, 3H, H-3, H-5″, PhCH_2), 4.15 (dd, 1H, $J_{1'',2''}$ = 3.7 Hz, $J_{2'',3''}$ = 10.8 Hz, H-2″), 3.93 (dd, 1H, $J_{1',2'}$ = 3.6 Hz, $J_{2',3'}$ = 11.3 Hz, H-2′) 3.88 (dd, 1H, $J_{1,2}$ = 3.7 Hz, $J_{2,3}$ = 10.3 Hz, H-2), 3.81 (dd, 1H, $J_{2',3'}$ = 10.5 Hz, $J_{3',4'}$ = 2.4 Hz, H-3′), 3.63 (dd, 1H, $J_{2'',3''}$ = 10.9 Hz, $J_{3'',4''}$ = 3.7 Hz, H-3″), 3.32 (s, 3H, OCH_3), 3.11 (app s, 1H, H-4″), 2.04 (s, 3H, COCH_3), 0.99 (d, 3H, $J_{5'',6''}$ = 7.2 Hz, H-6″ CH_3). ESI HRMS calcd for $C_{63}H_{66}O_{16}N_2Na_3$ (M+Na): 1175.4100, found 1175.4100.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.carres.2013.05.005.

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