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ARTICLE

Synthesis of building blocks for an iterative approach towards oligomers of the *Streptococcus pneumoniae* type 1 zwitterionic capsular polysaccharide repeating unit

Aisling Ní Cheallaigh and Stefan Oscarson

Abstract: Zwitterionic capsular polysaccharide extracts, ~8 kDa in mass, from *Streptococcus pneumoniae* type 1 (*Spt*1) have shown unique T-cell activating properties. Oligomers of the trisaccharide repeating unit of the *Spt*1 capsular polysaccharide [→3)-4-NH_2-α-D-Qui*p*NAc-(1→4)-α-D-Gal*p*A-(1→3)-α-D-Gal*p*A-(1-]$_n$ of defined length are needed to further investigate this response. An approach towards iteratively extendable trisaccharide building blocks of the zwitterionic capsular polysaccharides of *Spt*1 is described. Key elements include the comparison of pre-glycosylation oxidation and post-glycosylation oxidation approaches using thioglycoside donors to the target trisaccharide, the optimisation of the post-glycosylation oxidation approach, and the conversion of the trisaccharide to building blocks tailored for iterative glycosylation. The construction and evaluation of stereotunable 2-*N*-3-*O*-oxazolidinone donors for the common bacterial 2-acetamido-4-amino-2,4,6-trideoxy-α-D-galactopyranoside motif is also described, as is a key intermediate for their efficient synthesis.

Key words: Streptococcus pneumoniae type 1, glycosylation, uronic acids, zwitterionic.

Résumé : On a découvert que des extraits de polysaccarides capsulaires amphotères, de poids moléculaire avoisinant les 8 kDa, issus de l'espèce *Streptococcus pneumoniae* de type 1 (*Spt*1) présentaient des propriétés exceptionnelles d'activation des lymphocytes T. Afin d'étudier cette réponse de façon plus poussée, on doit pouvoir fabriquer des oligomères d'une longueur déterminée par répétition d'une unité trisaccaridique pour former des polysaccarides capsulaires de *Spt*1 de formule [→3)-4-NH_2-α-D-Qui*p*NAc-(1→4)-α-D-Gal*p*A-(1→3)-α-D-Gal*p*A-(1-]$_n$. Dans le présent article, nous décrivons une approche itérative visant à construire des synthons par allongement de la chaîne de trisaccarides afin d'accéder à des polysaccarides capsulaires amphotères de *Spt*1. Parmi les principaux éléments de la synthèse, notons la comparaison entre les méthodes d'oxydation avant et après la glycosylation, dans lesquelles interviennent des donneurs à base de thioglycosides pour former le trisaccharide cible; l'optimisation de la méthode d'oxydation post-glycosylation et la transformation du trisaccharide en synthons adaptés aux étapes successives de glycosylation. En outre, nous décrivons et évaluons la synthèse de donneurs à base de 2-*N*-3-*O*-oxazolidinone stéréoréglables permettant la formation du groupement 2-acétamido-4-amino-2,4,6-tridésoxy-α-D-galactopyranoside, communément présent chez la bactérie, car celui-ci constitue un intermédiaire clé dans le cadre d'une synthèse à haut rendement de ces composés. [Traduit par la Rédaction]

Mots-clés : Streptococcus pneumoniae de type 1, glycosylation, acides uroniques, amphotère.

Introduction

Bacterial capsular polysaccharides (CPS) are the outermost layer of bacterial cells and interact with the human immune system.[1] CPS are processed by antigen presenting cells but not presented by MHC class II proteins and so are not presented to T-cells.[2] This inhibits the interleukin release necessary to produce antibody maturation that gives the desired long-term protective immunoglobulin G. The CPS is commonly used in vaccine formulations, in which case, it is often conjugated to a carrier protein (glycoconjugate).[3] The presence of this protein allows for MHC II presentation and stimulation of CD4+ T-cell proliferation, giving long-term immunogenic protection. A notable exception is the unique class of polysaccharides that bear a zwitterionic repeating motif, zwitterionic polysaccharides. This is the only known class of carbohydrates capable of initiating T-cell proliferation in the absence of any protein.[4] To fully elucidate the pathway by which these charged polysaccharides interact with the immune cells, structures of a well-defined nature are necessary.

The CPS of *Streptococcus pneumoniae* type 1 (*Spt*1) and *Bacteroides fragilis* were used to identify this response and the nitric oxide-mediated degradation of the polymers in the MHC II pathway.[5] *Spt*1 is a virulent bacterium and a causative agent in meningitis, pneumonia, septicaemia, and otitis media.[6] It is currently included in multivalent glycoconjugate vaccines (Prevnar (Pfizer) and Synflorix (GSK)), which are implemented in mass vaccination schemes for the prevention of bacterial meningitis.[7] There is evidence to suggest that repeat exposure to a recurring carrier protein can lead to a suppressed immune response against the epitope. With most humans being exposed multiple times to specific carrier proteins, this may have an effect on future vaccine efficiency.[8] Therefore, the possibility of removing the need for protein conjugation in the case of zwitterionic polysaccharide serotypes could be advantageous.

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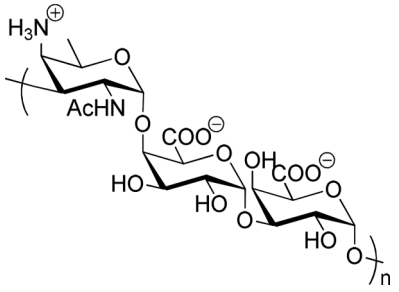
This article is part of a Special Issue dedicated to Professor David Bundle in recognition of his seminal contributions and lifetime achievements in the fields of carbohydrate chemistry and glycobiology.

Fig. 1. Chemical structure of the zwitterionic capsular polysaccharide repeating unit of *Streptococcus pneumoniae* type 1.



The *Spt*1 CPS contains a nonbranched, trisaccharide repeating unit [→3)-4-NH_2-α-D-Qui*p*NAc-(1→4)-α-D-Gal*p*A-(1→3)-α-D-Gal*p*A-(1-]$_n$ (Fig. 1).[9] The first total synthesis of this trisaccharide and also a hexasaccharide dimer as their methyl glycosides was achieved by Bundle and co-workers employing galactose donors and a late-stage oxidation to galacturonic acid esters.[10] This was followed by the preparation by Christina et al. of all three possible frame shifts of the trisaccharide repeating unit using conformationally locked galacturonic acid donors.[11] More recently, Bundle and co-workers reported a subsequent synthesis adopting their previous approach but with an alternative frame shift[12] and Seeberger and co-workers produced a trisaccharide repeating unit disulfide synthesised from galacturonic acid donors.[13]

However, none of these synthetic targets when biologically tested have so far been able to activate the desired immune response. Molecular modelling studies have shown that a 6-mer (six repeats of the trisaccharide unit) is required to form secondary helical structure, which is thought to be necessary to activate the response.[14] The previously reported syntheses lacked the ability for iterative glycosylations, which would allow access to these larger structures.

We here report the investigation of both a pre-glycosylation oxidation and post-glycosylation oxidation approach to the *Spt1* trisaccharide repeating unit and the synthesis of a trisaccharide building block suitable for iterative glycosylation to access spacer-equipped oligomers of the repeating unit.

Results and discussion

The trisaccharide motif is a challenging target containing exclusively 1,2-*cis* linkages[15] as well as the unusual 2-acetamido-4-amino-2,4,6-trideoxy-α-D-galactopyranoside (AAT) motif.[16] Furthermore, galacturonic acids are generally regarded as both poor glycosyl donors and poor glycosyl acceptors due to the electron-withdrawing effect of the carboxylic acid ester at C5.[17,18] Also, the targeted iterative approach adds additional complexity to the protecting group pattern and often requires orthogonal glycosylations. In light of this, both a pre-glycosylation oxidation approach and a post-glycosylation oxidation approach were investigated to identify the optimum route for production of the trisaccharide unit. Also, the synthesis and glycosylation properties of a number of AAT donors with variant protecting group pattern were investigated.

Synthesis of AAT intermediate

Multiple groups have been working towards the synthesis of AAT moieties and there are many published routes towards the target. Using glucosamine as a precursor, introduction of the amino group to the 4-position with inversion of stereochemistry and deoxygenation of the 6-position needs to be achieved. Axial amino group introduction is generally accomplished via S_N2 displacement of an equatorial leaving group (mesylate, tosylate, triflate) with a nucleophile such as azide or phthalimide. Deoxygenation has been carried out by introduction of a leaving group such as mesylate, tosylate, or bromine, which is either reduced directly or displaced by iodine before reduction. These methodologies was adopted by Sharon,[19] Lonngren,[20] Pozsgay,[21] Schmidt,[22] Grindley,[23] van der Marel,[24] and their respective co-workers. Synthetic efforts have also been made from D-glucal by Bundle[25] and D-mannose by van Boom[26] and Kulkarni[27] and also, a de novo strategy from Cbz-protected L-threonine has been derived.[28]

A versatile thioglycoside intermediate **6** to ATT donors, allowing flexible 2,3-protection, was designed and synthesized from D-glucosamine (Scheme 1).

Phthalimido protection and acetylation of D-glucosamine hydrochloride followed by thioglycoside formation was carried out under standard conditions.[29] The Garegg–Samuelsson reaction[30] was employed for iodination followed by in situ acetylation to give **2**. The iodine was reduced with tributyltin hydride and AIBN (→**3**, 99%) and following deacetylation, a regioselective 3-*O*-benzoylation was carried out at –30 °C to give **4** in a 91% yield.[22,23] The 4-position was subjected to an S_N2 displacement of a triflate with sodium azide to give **5** in 86% yield.[31] Treatment with ethylene diamine in ethanol deprotected the 2-*N* and 3-*O* positions giving the target intermediate **6** (82%).[32] This route was repeated on a large scale to give multigram quantities of the intermediate **6** in nine steps with an overall yield of 32%.

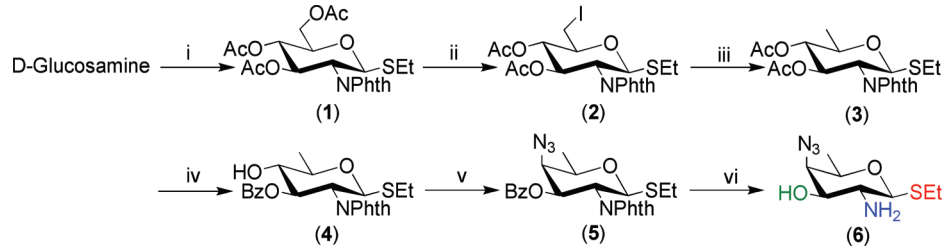
The pre-glycosylation oxidation approach

To investigate the extent of potential problems using galacturonic acid as donors and acceptors in the synthesis of the trisaccharide, a pre-glycosylation oxidation approach was performed involving use of ATT donor **7**, a derivative of **6** bearing a nonparticipating imine group in the 2*N*-position, and galacturonic acid ester building blocks **10** and **16** (Schemes 2 and 3). Initial attempts to build up a thioglycoside trisaccharide repeating unit using trichloracetimidate donors and a galacturonic ester thioglycoside acceptor met with severe problems mainly due to aglycon transfer side reactions. Thus, an alternative approach using a trimethylsilyl ethyl (TMSE) glycoside acceptor and thioglycoside donors was developed.[33] The selection of the imine-protecting group in **7** was initially based on reports from Nguyen et al. showing excellent yields and α-selectivity in nickel-catalysed formation of 1,2-*cis* 2-aminoglycosides using this type of imine trichloroacetimidate donors.[34] In our case, the approach failed, and recently, Nguyen et al. have also reported on problems with the use of these donors in orthogonal glycosylations to thioglycoside acceptors.[35] However, as shown below, the imine thioglycoside **7** was found to be an excellent donor although not very stereoselective.

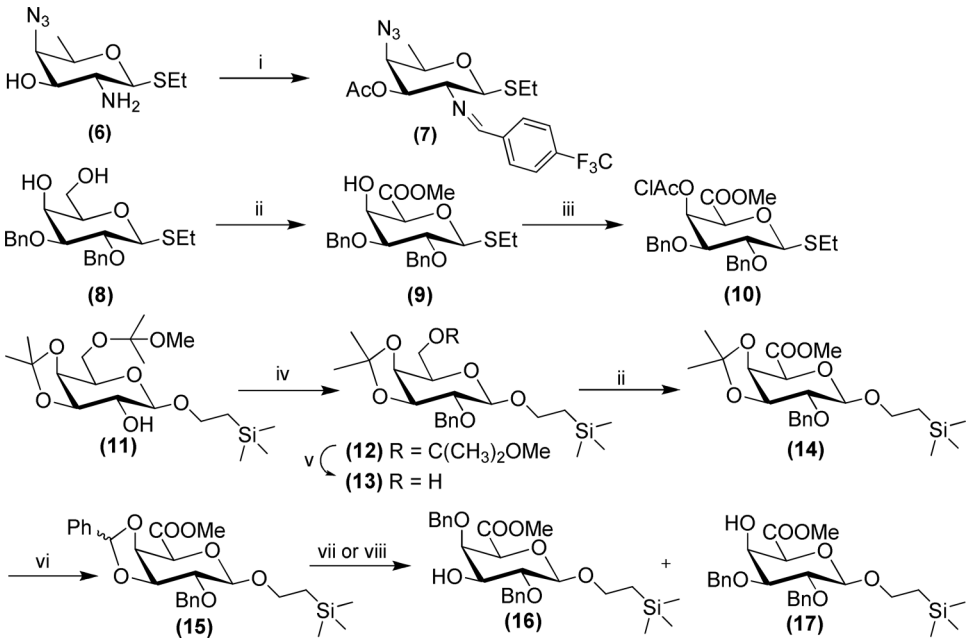
Donor **7** was readily synthesised from **6** by treatment with *p*-trifluoromethyl benzaldehyde with trimethylorthoformate as a dehydrating solvent followed by acetylation (93%). TEMPO/BAIB oxidation[36] of compound **8**[37] followed by esterification afforded galacturonic acid ester **9**[13] (Scheme 2, 67%). Subsequent protection with an orthogonal chloroacetate group gave **10** (92%). Benzylation of TMSE glycoside **11**[38] followed by mild acidic hydrolysis yielded **13** (87%), which was oxidized with the TEMPO/BAIB reagent and the crude carboxylic acid was then esterified to give methyl ester **14** (56%). An exchange of the isopropylidene acetal for a benzylidene acetal was then performed to prepare for subsequent reductive opening of the benzylidene acetal to afford the 4-*O*-benzyl-protected acceptor **16**. Formation of the 3,4-*O*-benzylidene acetal using benzaldehyde dimethylacetal on the corresponding ethyl thioglycoside compound gave an *endo*:*exo* ratio of ~10:1 (which is what is normally found); however and surprisingly, the TMSE glycoside gave an *endo*:*exo* ratio of only 2.2:1.

In most cases, the regioselectivity in the reductive opening of eq,ax-dioxolane acetals has been found to be dependent on the configuration of the acetal and not on the reagent or solvent used (in contrast with dioxane 4,6-acetals), *endo* giving the axial benzyl ether and *exo* the equatorial. However, Tanaka et al. showed that opening of mannose *exo*-2,3-*O*-benzylidene acetals could show solvent (and reagent) dependence, CH_2Cl_2 affording the axial 2-*O*-

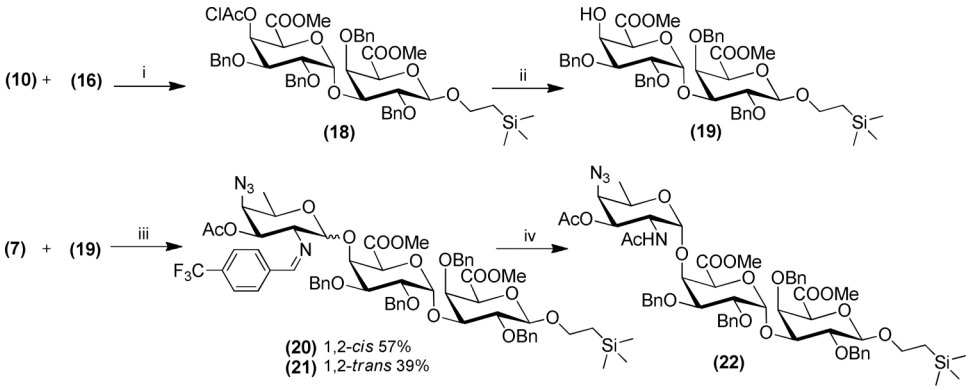
Scheme 1. Synthesis of common intermediate **6**. Reagents: (*i*) (*a*) NaOMe, Et_3N, phthalic anhydride, MeOH; (*b*) Ac_2O, pyridine; (*c*) EtSH, $BF_3{\cdot}Et_2O$, CH_2Cl_2; (*ii*) (*a*) NaOMe, MeOH; (*b*) Ph_3P, I_2, imidazole, toluene, reflux; (*c*) Ac_2O, 92% over three steps; (*iii*) AIBN, Bu_3SnH, toluene, reflux, 99%; (*iv*) (*a*) NaOMe, MeOH; (*b*) BzCl, pyridine, –30 °C, 91%; (*v*) (*a*) Tf_2O, pyridine, CH_2Cl_2, –20 °C; (*b*) NaN_3, DMF, 86%; (*vi*) ethylenediamine, EtOH, 70 °C, 82%.



Scheme 2. Synthesis of ATT donor **7** and of galacturonic acid donor **10** and acceptor **16**. Reagents: (*i*) (*a*) trifluoromethylbenzaldehyde, trimethylorthoformate, DMF; (*b*) Ac_2O, pyridine; (*ii*) (*a*) TEMPO, BAIB, CH_2Cl_2–H_2O; (*b*) MeI, K_2CO_3, DMF, 67%; (*iii*) ClAcCl, pyridine, CH_2Cl_2, 92%; (*iv*) (*a*) BnBr, NaH, DMF; (*b*) 4/1 AcOH–H_2O, 88%; (*v*) (*a*) TEMPO, BAIB, CH_2Cl_2–H_2O; (*b*) MeI, K_2CO_3, DMF, 56%; (*vi*) (*a*) 4/1 AcOH–H_2O, 80 °C; (*b*) $PhCH(OMe)_2$, CSA, DMF, 76%; (*vii*) *endo*: $BH_3{\cdot}NMe_3$, $AlCl_3$, THF, H_2O, 68%; (*viii*) *exo*: 1 M BH_3 in THF, 1 M Bu_2BOTf in toluene, 81%, 3/2 4OBn–3OBn.



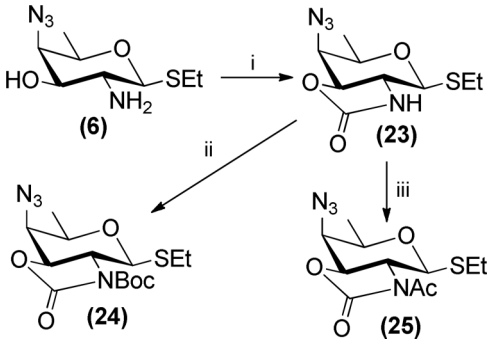
Scheme 3. Synthesis of the trisaccharide repeating unit as its TMSE glycoside. Reagents: (*i*) Me_2S_2–Tf_2O, 3/2 Et_2O–CH_2Cl_2, 0 °C, 74%; (*ii*) thiourea, $NaHCO_3$, TBAI, THF, 60 °C, 84%; (*iii*) Me_2S_2–Tf_2O, 3/2 Et_2O–CH_2Cl_2, 0 °C, 96%, 3α:2β; (*iv*) (*a*) CSA, MeOH; (*b*) Ac_2O, MeOH, 64%.



benzyl and toluene the equatorial 3-*O*-benzyl product.[39] In light of this, *endo* **15** was subjected to trimethylaminoborane and aluminum chloride to give the wanted and expected 4-*O*Bn product **16** in a 68% yield. However, when *exo* **15** was subjected to the "Tanaka" conditions for 4-OBn selectivity, it resulted in an unselective opening with a 3:2 ratio of **16** and **17**, respectively, in an 80% yield (48% being the desired 4-*O*-benzylated product).

The glycosylation of acceptor **16** with donor **10** employing the dimethyl disulphide/triflic anhydride promoter system[40] worked smoothly to give the α-linked disaccharide **18** in a 78% yield with no 1,2-*trans* product observed and showing none of the anticipated problems with galacturonic acid donors and acceptors (Scheme 3). Removal of the chloroacetate group and subsequent glycosylation with donor **7** gave a separable mixture of 1,2-*cis* **20** and 1,2-*trans* **21**

Scheme 4. Synthesis of oxazolidinone donors **24** and **25**. Reagents: (*i*) triphosgene, sat. aq. $NaHCO_3$, MeCN, 78%; (*ii*) Boc_2O, 4-dimethylaminopyridine, THF, 60 °C, 91%; (*iii*) AcCl, DIPEA, CH_2Cl_2, 99%.



products in a 96% yield with a 3:2 ratio. The imine group was then removed by mild acidic cleavage with camphorsulfonic acid in methanol and the resulting amine was acetylated with acetic anhydride in methanol to give the target trisaccharide **22** in a 35% overall yield from the building blocks **7**, **10**, and **16**.

The post-glycosylation oxidation approach

In the post-glycosylation oxidation approach, stereotunable AAT moiety donors **24** and **25** were investigated together with galactose building blocks **35** and **39**, with a temporary 6-*O*-Nap protecting group to allow later oxidations.

Glucosamine 2-*N*-acetyl-2,3-*N*,*O*-oxazolidinone donors are known to possess an innate stereoselective tunability in glycosylations; 0.1 equiv. of silver triflate and 1 equiv. of *N*-iodosuccinimide (NIS) as promoter system results in the 1,2-*trans* product, whilst 0.4 equiv. of silver triflate and 1 equiv. of NIS yields the 1,2-*cis* product through an efficient anomerisation of the initially formed *trans*-product via an *endo*-cyclic opening mechanism.[41] Since the AAT motif is found both 1,2-*cis* and 1,2-*trans* linked in a number of different bacterial structures,[42] a single donor that could be used to create both types of linkages is of interest.

Treatment of intermediate **6** with triphosgene and saturated aqueous sodium bicarbonate in acetonitrile produced the 2,3-*N*,*O*-oxazolidinone **23**, treatment of which with a strong base and either Boc anhydride or acetyl chloride gave the corresponding product **24** or **25**, respectively (Scheme 4).

The 2-*N*-acetyl-2,3-*N*,*O*-oxazolidinone-protected donor **25** was initially tested in glycosylations with known galactose acceptors **26** and **29** (Scheme 5).[43] Using silver triflate (0.1 equiv.) and NIS in dichloromethane with a short reaction time of 10 min gave a 65% yield of disaccharide as a 6:1 α/β mixture (**27**/**28**). Using silver triflate (0.4 equiv.) and NIS in dichloromethane with a longer reaction time of 40 min gave exclusively the 1,2-*cis* product **27** in a 59% yield, in accordance with what has been found earlier for glucosamine compounds. Although the acetylated 2,3-oxazolidinones have been shown to be efficient and stereotunable donors, a drawback of their use are problems found in the removal of the cyclic carbamate to give the target acetamide, which is often not selective and thus low yielding. Benzylated 2,3-oxazolinones have been introduced to address this problem[44] and here, a Boc-protected version **24** was investigated.

Donor **24** was coupled to acceptor **29** using 0.1 equiv. of silver triflate; this led to the formation of the β product with a small trace of α as observed by thin-layer chromatography (TLC). After complete consumption of the donor, a further 0.3 equiv. of silver triflate was added to the reaction. The previously observed β product anomerised over half an hour to give exclusively the 1,2-*cis* product **31** in a 52% yield, showing that the Boc derivative also allowed efficient anomerisation. As expected, the 2,3-*N*,*O*-oxazolidinone in Boc-protected **31** could selectively be removed by sodium methoxide treatment to give **32** in a 92% yield.

The synthesis of the galactose derivatives **35** and **39** started from the earlier used galactose precursors **8** and **13** (Scheme 6). Naphthylmethylidene acetal, introduced to **8,** was subjected to reductive ring opening conditions of $NaCNBH_3$ and HCl to give the 6-*O*-methylnaphthyl-protected **34** (76%), which was acetylated to give **35**. **13** was alkylated using NapBr to afford **36**. The exchange of the isopropylidene group for a benzylidene acetal again resulted in an unusually low 1:1 *endo*:*exo* ratio, similar to that observed for **15**. The *endo* product was subjected to reductive ring opening conditions of $BH_3{\cdot}NMe_3$ and $AlCl_3$, while the *exo* was subjected to 1 M BH_3 in THF with 1 M Bu_2BOTf in toluene. As observed before, the *endo* opened to the desired 4-*O*Bn, whilst the *exo* opening was unselective with a 4-*O*Bn:3-*O*Bn ratio of 1:1.2 being observed.

Acceptor **39** and donor **35** were coupled using the Me_2S_2/Tf_2O promoter system in diethyl ether and dichloromethane (Scheme 7). This gave α-linked disaccharide **41** in an excellent yield of 92% with no 1,2-*trans* product observed. The acetate group was removed by treatment with sodium methoxide and the resulting acceptor **42** was glycosylated with Boc-donor **24** to give **43** in a 51% yield. An inverse glycosylation procedure[45] was then applied to the reaction that increased the yield to 65%; however, prolonged reaction times resulted in partial loss of 6-*O*-Nap and (or) 6′-*O*-Nap protecting groups by acidic cleavage.

Glycosylation attempts were also made using the acetylated donor **25**. Using the inverse glycosylation approach, trisaccharide **44** was formed in a 74% yield with little loss of the 6-*O*-Nap groups. Trisaccharide **44** was treated with sodium methoxide and the 2,3-*N*,*O*-oxazolidinone was removed in a 92% yield. The removal of the Nap ether was achieved by oxidative cleavage with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) in dichloromethane and methanol. This reaction provided a complex mixture, as partial benzyl group removal was also observed. Triol **46** was isolated in a 65% yield but the removal issues in combination with the complex mixture obtained during glycosylation highlighted that Nap ethers are not the optimum protecting group for the 6- and 6′-positions.

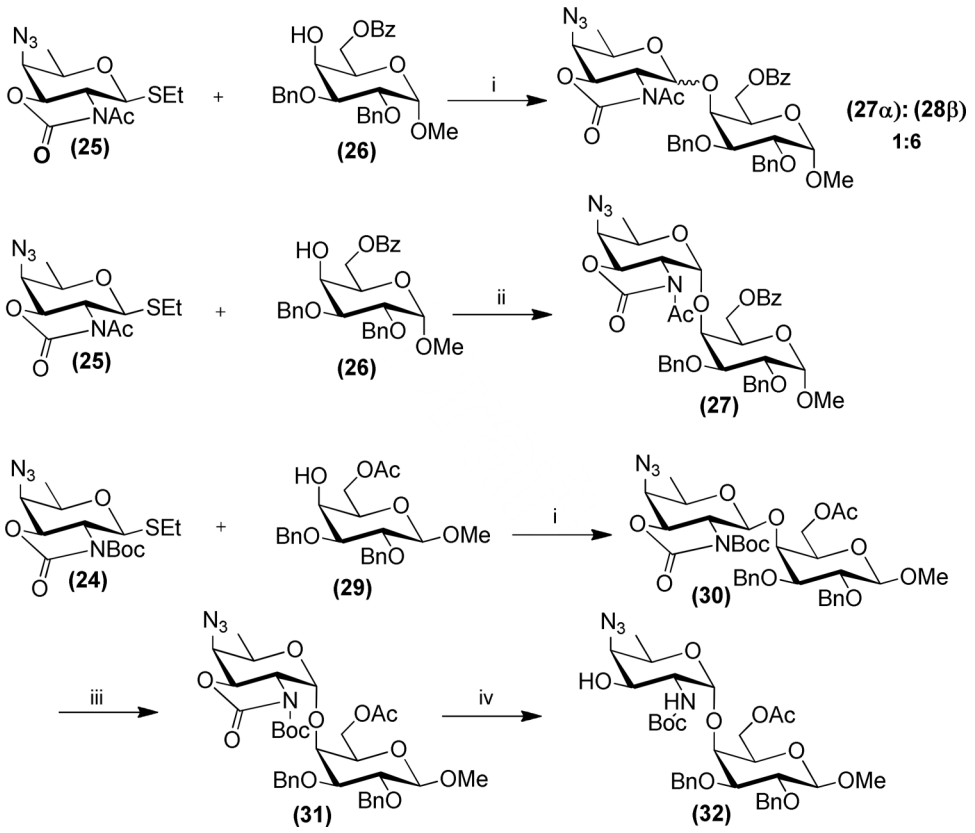
Selective oxidation of the primary 6 and 6′ hydroxyl groups was achieved using TEMPO and BAIB and the acids were esterified with cesium fluoride and benzyl bromide to give the benzyl ester **47** with a 57% yield over the two steps. From building blocks **24**, **35**, and **39**, trisaccharide **47** was achieved in a 20% yield over six steps.

Optimised postglycosylation oxidation approach

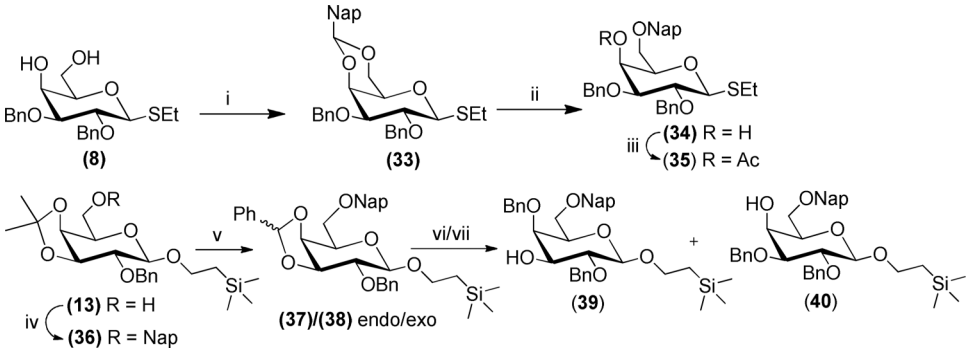
An optimised route for the post-glycosylation oxidation approach was then carried out using the *N*-acetyl oxazolidinone AAT donor **25** together with galactose building blocks **49** and **56** in which the 6-*O*-NAP ether had been changed to a benzoyl ester (Scheme 8). Using low temperatures of –30 °C and a stoichiometric quantity of benzoyl chloride, the intermediate **46** was obtained from **8** in a 73% yield.[46] The chloroacetyl group was introduced to the 4-position to give donor **49** in an 82% yield. The acetal and mixed acetal were removed from **12** by acid hydrolysis to give the triol, to which a 4,6-*O*-benzylidene acetal was introduced.[47] The reductive ring opening of **51** gave low selectivity for the 4-OBn over the 6-OBn with a 2:1 ratio observed. It has been empirically found that the selectivity of reductive ring openings is reduced with the number of free hydroxyl groups on the substrate.[48] To increase the selectivity, the 3-position of **51** was acetylated and the resulting product **54** was subjected to the reductive ring opening reagents. This gave **55** in a 70% yield with no 6-*O*-benzyl product observed. The acetate group was subsequently removed with Zemplén conditions in a 97% yield. A benzoyl group was introduced selectively to the 6-position as described for compound **48** to give acceptor **56** in a 70% yield.

Glycosylation of acceptor **56** with donor **49** was achieved in a 94% yield with only the desired 1,2-*cis* product **57** observed using Me_2S_2/Tf_2O as the promoter (Scheme 9). The chloroacetate group

Scheme 5. Glycosylations with donors **24** and **25**. Reagents: (*i*) AgOTf (0.1 equiv.), NIS, CH_2Cl_2, 0 °C, 10 min, 65%, 1α:6β; (*ii*) AgOTf (0.4 equiv.), NIS, CH_2Cl_2, 0 °C, 40 min, 59%; (*iii*) AgOTf (0.1 equiv.), NIS, CH_2Cl_2, 0 °C, 10 min; (*iv*) AgOTf (0.3 equiv.), 0 °C, 30 min, 52%; (*v*) NaOMe, MeOH, 92%.



Scheme 6. Synthesis of galactose donor **35** and acceptor **39**. Reagents: (*i*) $NapCH(OMe)_2$, CSA, DMF, 83%; (*ii*) $NaCNBH_3$, HCl, THF, 77%; (*iii*) Ac_2O, pyridine, 99%; (*iv*) 2-NapBr, NaH, DMF, 92%; (*v*) (*a*) $AcOH/H_2O$, 80 °C, 99%; (*b*) $PhCH(OMe)_2$, CSA, DMF, 77%; (*v*) **37** *endo*: BH_3NMe_3, $AlCl_3$, THF, 76%; (*vi*) **38** *exo*: BH_3 in THF, Bu_2BOTf in toluene, 88%, 1.2/1 4OBn–3OBn.



was then removed and the resulting 3′-*O*-acceptor **58** glycosylated with **25** using the inverse addition procedure. The desired 1,2-*cis*-linked trisaccharide (60%) and the 1,2-*trans* product (12%) were isolated and the 1,2-*trans* product was anomerised by treatment with silver triflate in dichloromethane, giving a total of 71% yield of the α-trisaccharide **59** from the glycosylation.

Compound **59** was treated with barium hydroxide for complete removal of the 2-*N*-acetyl–2,3-*N*,*O*-oxazolidinone functionality and the primary benzoyl esters.[49] After heating for 16 h, acetic anhydride was added, leading to acetamide formation giving the desired **60** in an 80% yield. The triol was selectively oxidized at the primary positions using the previously employed biphasic TEMPO and BAIB method to give the corresponding uronic acid. The crude was esterified with methyl iodide and potassium carbonate to give the methyl ester **61** in a 70% yield.

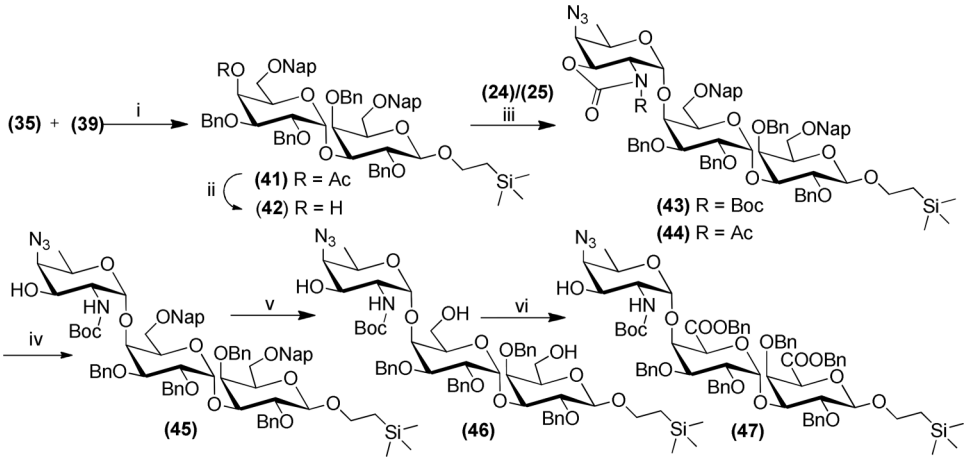
With the new protecting group pattern employed, the trisaccharide **61** was obtained from building blocks **25**, **49**, and **56** in five steps with a yield of 35%.

Although the overall yield from the building blocks to the target trisaccharide is the same, 35%, in the pre- and post-glycosylation approach, the much simpler preparation of the building blocks in the post-glycosylation approach makes this the preferred route to the target trisaccharide, which now was converted to a donor and subsequently to a spacer-equipped acceptor (Scheme 10).

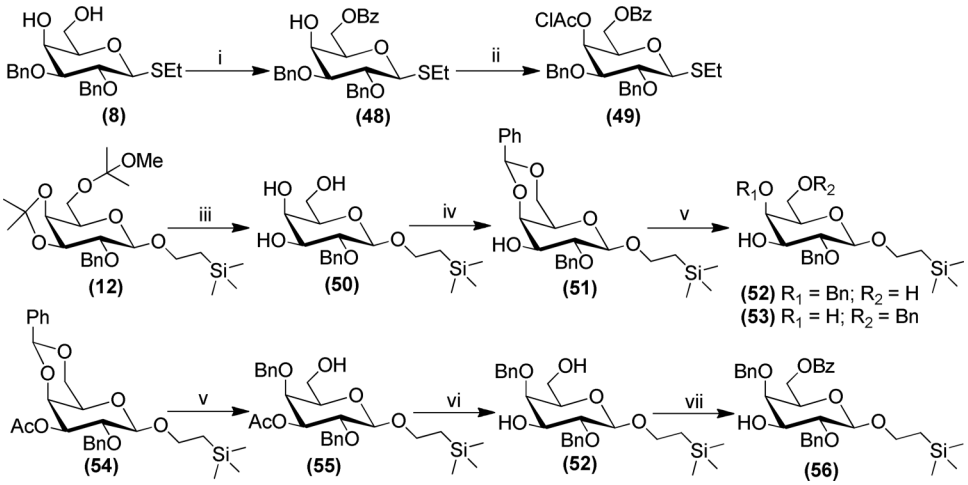
Building blocks for the iterative approach

A chloroacetyl group was introduced to **61** using standard conditions to give **62** in an 84% yield. The TMSE glycoside was then hydrolyzed with trifluoroacetic acid and water to give the hemiacetal product **63** (80%) from which the trichloroacetimidate (TCA)

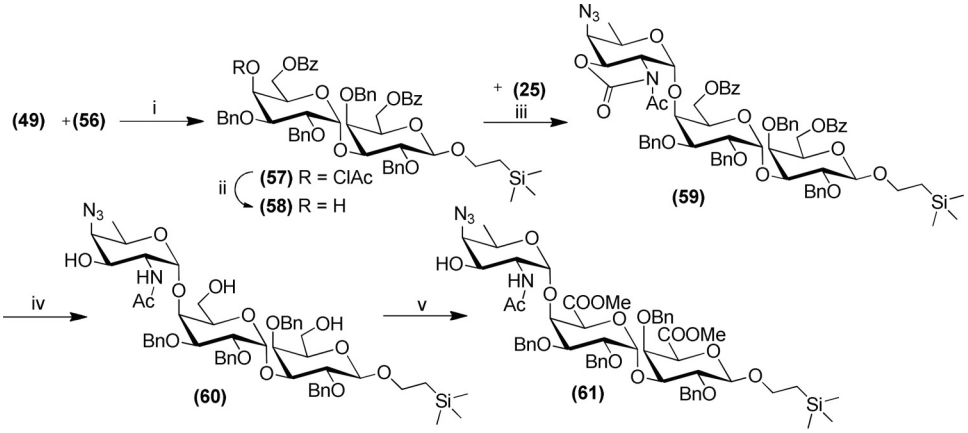
Scheme 7. Synthesis of the trisaccharide repeating unit. Reagents: (*i*) Me_2S_2–Tf_2O (1.2 equiv.); 3/2 Et_2O–CH_2Cl_2, 0 °C, 92%; (*ii*) NaOMe, MeOH, 99%; (*iii*) (*a*) **24**, NIS, AgOTf (0.4 equiv.), CH_2Cl_2, 51%; (*b*) **24**, NIS, AgOTf (0.4 equiv.), CH_2Cl_2, inverse addition, 65%; (*c*) **25**, NIS, AgOTf (0.4 equiv.), CH_2Cl_2, inverse addition, 74%; (*iv*) **43**, NaOMe, MeOH, 92%; (*v*) DDQ, MeOH, CH_2Cl_2, 62%; (*vi*) (*a*) TEMPO, BAIB, CH_2Cl_2, H_2O; (*b*) BnBr, CsF, DMF, 57%.



Scheme 8. Synthesis of donors **49** and **56** for optimized route. Reagents: (*i*) BzCl, pyridine, –30 °C, 73%; (*ii*) ClAcCl, pyridine, CH_2Cl_2, 0 °C, 82%; (*iii*) 4/1 AcOH–H_2O, 80 °C; (*iv*) $PhCH(OMe)_2$, CSA, DMF 70% over two steps; (*v*) 1 M BH_3 in THF, 1 M Bu_2BOTf in toluene, 2/1 **52–53**, 68%; **55**, 70%; (*vi*) NaOMe, MeOH, 99%; (*vii*) BzCl, pyridine, CH_2Cl_2, 70%.



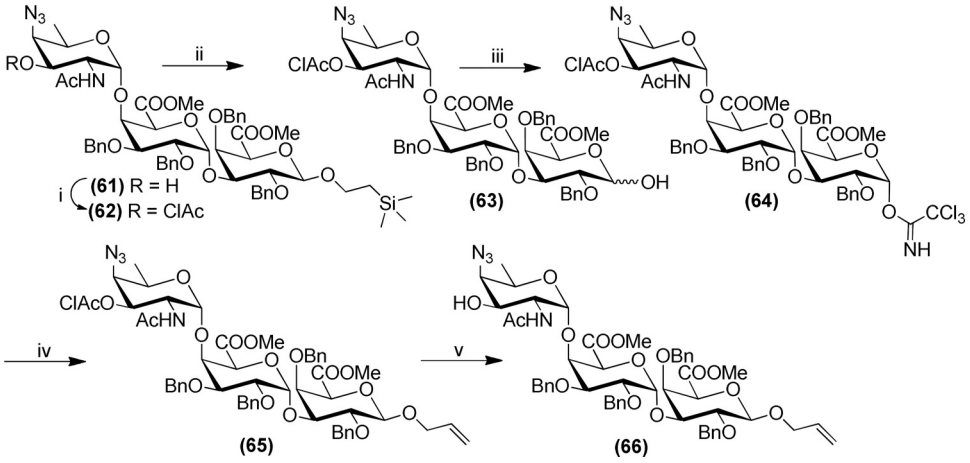
Scheme 9. Optimized synthesis of the trisaccharide repeating unit. Reagents: (*i*) Me_2S_2–Tf_2O, 3/2 Et_2O–CH_2Cl_2, 95%; (*ii*) thiourea, $NaHCO_3$, TBAI, THF, 96%; (*iii*) NIS, AgOTf, CH_2Cl_2, 71%; (*iv*) (*a*) $Ba(OH)_2{\cdot}8H_2O$, EtOH–H_2O; (*b*) Ac_2O, 80%; (*v*) (a) TEMPO, BAIB, 2/1 CH_2Cl_2–H_2O; (*b*) MeI, K_2CO_3, DMF, 70%.



donor **64** was formed. Prolonged reaction times resulted in only the α TCA being produced in a 98% yield.

Choosing a suitable linker for the *Spt*1 repeating unit was complicated by the high functionality in the structure (amino, acetamido, carboxylic acid, and alcohol groups). After much consideration, an allyl linker was decided upon. Compound **64** was glycosylated with an excess of allyl alcohol acceptor to give **65** in an 82% yield (Scheme 10). Despite the use of a combination of

Scheme 10. Synthesis of the trisaccharide trichloroacetimidate donor **64** and trisaccharide OAll acceptor **66**. Reagents: (*i*) ClAcCl, pyridine, CH_2Cl_2, 0 °C, 84%; (*ii*) 9/1 TFA–H_2O, 80%; (*iii*) Cl_3CCN, K_2CO_3, CH_2Cl_2, 84%; (*iv*) allyl alcohol, TMSOTf, CH_2Cl_2, Et_2O, 0 °C, 82%; (*v*) thiourea, $NaHCO_3$, TBAI, THF, 60 °C, 86%.



ethereal solvent, high temperatures, and TMSOTf as a promotor, the trisaccharide isolated was exclusively β at the new anomeric linkage. The chloroacetate group was removed using standard conditions to provide trisaccharide **66** in an 86% yield ready for use as the reducing end acceptor.

With the repeating unit acceptor and donor available, formation of a dimer was attempted. Glycosylation of donor **64** and acceptor **66** with TMSOTf as the promoter and diethyl ether as a participating solvent resulted in a hexasaccharide in a high 83% yield, but again the β-linked product was formed exclusively (Scheme 11). Interestingly, all of the α-linkages in the *Spt*1 CPS structure could possibly be obtained through anomerisation of the corresponding β-linkages, for the ATT motif using oxazolidinone donors as discussed above and for the galacturonic acid moieties through $TiCl_4$-assisted anomerisation again via an endocyclic cleavage mechanism facilitated by complexation of the titanium to the carboxylic acid part as shown and developed by Murphy and co-workers.[49] In this project, we have had success with the anomerisation of β-galacturonic acid glycosidic linkages on the mono- and disaccharide level utilising the $TiCl_4$ methodology, and so an anomerisation was also attempted on the hexasaccharide. This successfully anomerised the aglycon β-linkage but unfortunately not the internal β-linkage (Scheme 11). This can clearly be observed from the HSQC experiments shown in Fig. 2 that illustrate the movement of the C1 signal from 103 ppm in **67** to 97 pmm in **68** but no movement of the C1‴ signal in the spectra.

Throughout this work, it has been noted that the glycosylation outcome with galacturonic acid TCA donors has been exclusively 1,2-*trans*, despite the use of alpha directing solvents and higher temperatures. However, when exploiting thioglycosides as the galacturonic acid donor, the outcome has been consistently 1,2-*cis*.[32] With this in mind, it is envisioned that by converting TCA donor **64** to a thioglycoside donor, the glycosylation with trisaccharide **66** should form a 1,2-*cis* hexasaccharide.

Conclusions

We have described the synthesis of the zwitterionic trisaccharide repeating unit of the CPS of *Spt*1 via both a pre-glycosylation oxidation and a post-glycosylation oxidation approach. In most cases, excellent yields and selectivity were observed during glycosylation, in particular with the implementation of the Me_2S_2/Tf_2O methodology. The post-glycosylation oxidation approach was optimised and scaled up for the synthesis of the iterative glycosylation building blocks. Iterative building block donor and acceptor were constructed from the trisaccharide **62** in high yields. A multigram-scale synthesis was also carried out of a key AAT intermediate **6**, from which many building blocks can be derived utilising the native chemoselectivity of the amide, hydroxyl, and thio functionalities. Two stereotunable AAT donors **24** and **25** are also described that can be used to give either the 1,2-*cis* or the 1,2-*trans* product by varying the reaction conditions. The *N*-Boc-*N*,*O*-oxazolidinone derivative also provides an alternative to the previously seen *N*-acetyl and *N*-benzyl oxazolidinone donors while retaining the tunability of the reaction. No issues were observed when glycosylating the O-4s of the galacturonic acid. This position is notorious for being less reactive as a nucleophile.[50] The use of galacturonic acid donors provided only slightly lower yields than the comparable galactose donors. In this case, we have found that the classification of galacturonic acids as poor glysosyl donors and acceptors is lacking in its justification, making the pre- and post-glycosylation approaches similar in efficiency of providing the trisaccharide building blocks.

Experimental

General materials and methods

All chemicals were purchased from commercial suppliers and used without purification. Anhydrous dichloromethane, tetrahydrofuran (THF), diethyl ether, and toluene were obtained from PureSolv-EN™ solvent purification system. All other anhydrous solvents were purchased from Sigma-Aldrich in AcroSeal® bottles. Reactions were monitored by TLC using Merck aluminum foil coated TLC plates carrying silica gel 60 F254 with a 0.2 mm thickness. Ultraviolet light, sulphuric acid (8% H_2SO_4 in ethanol) and (or) ninhydrin (3 g of ninhydrin and 3 mL of acetic acid in 100 mL of ethanol) were used to detect compounds. Purification of compounds was carried out using column chromatography (Grace Davidsil chromatographic silica LC60A 40–60 μm particle size) or flash chromatography using a Biotage system (SNAP KP-Sil) or Grace Reveleris system (Silica 40 μm particle size). All compounds were analysed by nuclear magnetic resonance (NMR) spectroscopy with ^{1}H NMR spectra recorded at 400 or 500 MHz and ^{13}C NMR recorded at 106 or 125 MHz on Varian spectrometers at 20 °C. Additional experiments were frequently performed for novel compounds to aid complete characterisation including ^{1}H–^{1}H homonuclear correlation spectroscopy (COSY), total correlation spectroscopy (TOCSY), ^{1}H–^{13}C heteronuclear single quantum coherence spectroscopy (HSQC), and heteronuclear multiple bond correlation spectroscopy (HMBC). Spectra were recorded in deuterated solvents and were standardised against the deuterated solvent peak and the internal tetramethylsilane (TMS) standard ($CDCl_3$ δ = 7.26 ppm, CH_3OD δ = 3.31 ppm, TMS δ = 0.00 ppm).

Scheme 11. Glycosylation of **64** and **66** to hexasaccharide **67** and subsequent anomerisation to **68**. Reagents: (*i*) CH_2Cl_2, Et_2O, TMSOTf, 0 °C, 83%; (*ii*) $TiCl_4$, CH_2Cl_2, 0 °C, 65%.

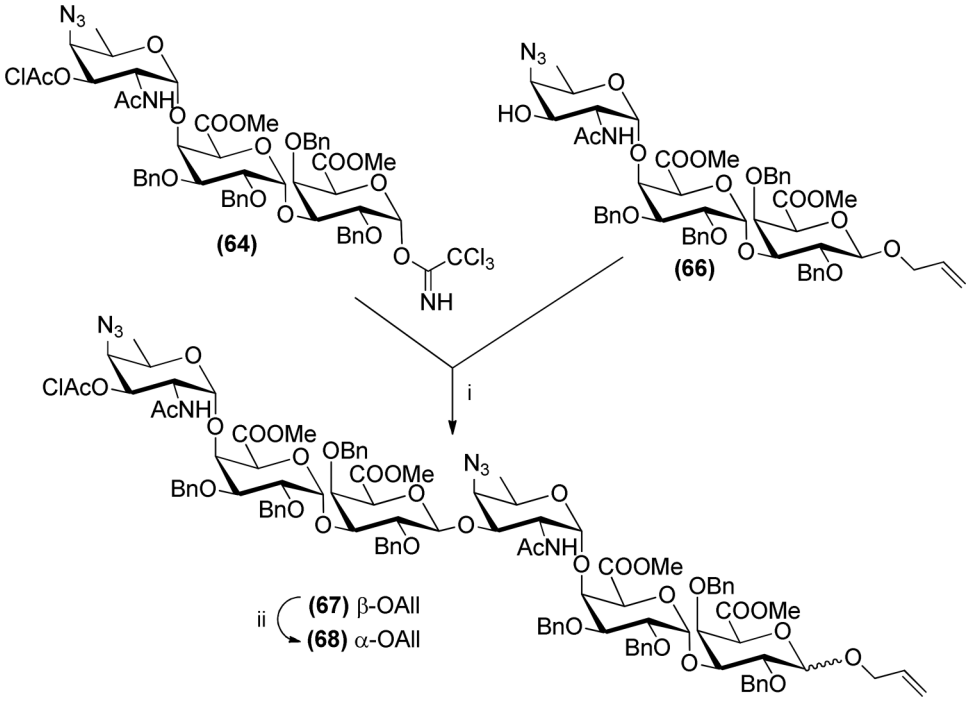
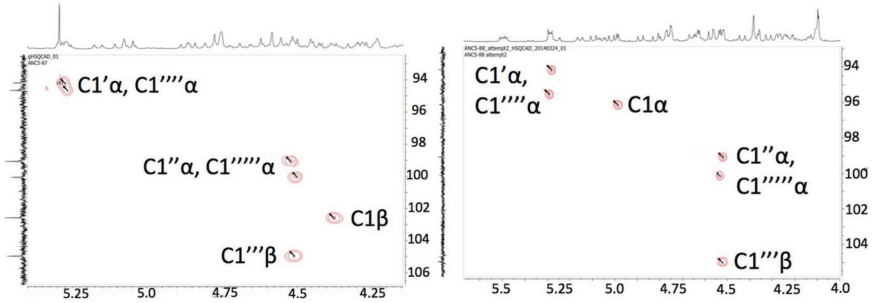


Fig. 2. HSQC showing the anomeric region of **67** (left) and **68** (right).



Coupling constants (*J* values) are expressed in Hz and were calculated using MestraNova processing software. Low-resolution mass spectrometry (LRMS) was often used for monitoring reactions (micromass *Quattro micro*™ LC-MS/MS instrument). High-resolution mass spectrometry (HRMS) was carried out using Waters micromass LCT LC-TOF instrument with ESI detection in positive or negative mode. Optical rotation was recorded at 20 °C in a 1 cm^3 cell at a g/100 mL concentration in the indicated solvent using a Perkin-Elmer polarimeter.

Ethyl 3,4-di-O-acetyl-2,6-dideoxy-6-iodo-2-N-phthalimido-1-thio-β-D-glucopyranoside (2)

A solution of triphenylphosphine (12.6 g, 48.1 mmol) and imidazole (6.54 g, 96.2 mmol) in dry toluene (252 mL, 0.112 M) was prepared and heated to 60 °C under a flow of nitrogen. To this, deacetylated **1** (10.0 g, 28.3 mmol) was added portion wise to promote dissolution. Iodine pellets (17.2 g, 67.9 mmol) were then added to the reaction, which was stirred vigorously at 90 °C for 2 h. The reaction was cooled to 0 °C and acetic anhydride (80.0 mL) was added and stirred until acetylation was complete. The iodine was quenched by washing with 10% $Na_2S_2O_3$ and the organic phase was dried over Na_2SO_4 and reduced by rotary evaporation. The compound **2** was isolated from a mixture of product and acetylated starting material by column chromatography (cyclohexane – ethyl acetate, 2/1 *v*/*v*). The product was isolated (8.21 g) as a white foam with a 92% recovered yield (starting material 5.40 g). $[\alpha]_D$ = +38.9 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.86–7.73 (m, 4H, Ar*H*), 5.82 (dd, 1H, H-3, *J* = 10.2, 9.1 Hz), 5.53–5.51 (d, 1H, H-1, *J* = 10.6 Hz), 4.98 (t, 1H, H-4, *J* = 9.4 Hz), 4.38 (t, 1H, H-2, *J* = 10.4 Hz), 3.70 (m, 1H, H-5), 3.33–3.20 (m, 2H, H-6a, H-6b), 2.83–2.63 (m, 2H, SCH_2CH_3), 2.06 (s, 3H, $COCH_3$), 1.85 (s, 3H, $COCH_3$), 1.26 (t, 3H, SCH_2CH_3, *J* = 7.4 Hz). ^{13}C NMR (500 MHz, $CDCl_3$) δ: 170.1–167.4 (2 × *N*C=O, 2 × C=O) 123.7 (2 × Ar*C*H), 80.9 (C1), 77.5 (C5), 72.9 (C4), 71.2 (C3), 54.1 (C2), 24.6 (SCH_2CH_3), 20.9, 20.5 ($COCH_3$), 15.2 (SCH_2CH_3), 3.5 (C6) HRMS $C_{20}H_{22}NO_7SINa$ [M + Na^+] calculated: 570.0059; found: 570.0048.

Ethyl 3,4-di-O-acetyl-2,6-dideoxy-2-N-phthalimido-1-thio-β-D-glucopyranoside (3)

Compound **2** (8.00 g, 14.6 mmol) and triphenyltin hydride (20.5 g, 58.5 mmol) were added in a round-bottom flask, covered in tin foil, and dried under reduced pressure overnight. Toluene (96.0 mL), degassed by freeze–thaw methods, was then added. The solution was heated to reflux and AIBN (178 mg, 0.73 mmol) was added under a strict flow of nitrogen. After 30 min, the reaction was complete as indicated by LRMS. The solvent was removed and the product was purified by column chromatography (cyclohexane – ethyl acetate, 4/1 *v*/*v*) to yield **3** (6.60 g, 99%) as a white foam.

$[\alpha]_D$ = +57.2 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.86–7.75 (m, 4H, Ar*H*), 5.79 (dd, 1H, H-3, *J* = 10.2, 9.3 Hz), 5.46–5.44 (d, 1H, H-1, *J* = 10.6 Hz), 4.92 (t, 1H, H-4, *J* = 9.5 Hz), 4.38 (t, 1H, H-2, *J* = 10.4 Hz), 3.80–3.74 (m, 1H, H-5), 2.75–2.60 (m, 2H, SCH_2CH$_3$), 2.05 (s, 3H, COCH_3), 1.86 (s, 3H, COCH_3), 1.31–1.29 (d, 3H, H-6a, H-6b, H-6c, *J* = 6.2 Hz) 1.20 (t, 1H, SCH$_2$CH_3, *J* = 7.4 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 170.3–167.4 (2 × *C*=O, 2 × N*C*O), 134.5, 134.3, 123.8, 123.7 (Ar*C*, Ar*C*H), 80.7 (C1), 74.5 (C5), 74.1 (C4), 71.7 (C3), 54.1 (C2), 24.1 (S*C*H$_2$CH$_3$), 20.9 (CO*C*H$_3$), 20.6 (CO*C*H$_3$), 17.9 (C6), 14.9 (SCH$_2$*C*H$_3$). HRMS $C_{20}H_{23}NO_6SNa$ [M + Na$^+$] calculated: 444.1093; found: 444.1080.

*Ethyl 3-O-benzoyl-2,6-dideoxy-2-*N*-phthalimido-1-thio-β-D-glucopyranoside (4)*

Compound **3** (6.60 mg, 15.7 mmol) was deacetylated by addition of NaOMe in MeOH (200 mL, 0.10 M). After 2 h, the solution was acidified to pH 7 using IR-120 H$^+$ resin. The resin was filtered off and the solvent was removed. The crude was dissolved in pyridine (97.0 mL, 0.16 M) and cooled to –30 °C. A diluted solution of benzoyl chloride (1.05 equiv.) in pyridine (20.5 mL, 0.81 M) was then added dropwise over 10 min. The reaction was stirred for 1 h and quenched with water. The solution was diluted with EtOAc (200 mL) and washed with 2 M HCl (50 mL × 2), saturated $NaHCO_3$ (50 mL), and brine (50 mL) and then concentrated under vacuum. The crude was purified by column chromatography (cyclohexane – ethyl acetate, 4/1 *v*/*v*) to yield **4** (6.29 mg, 91%) as a white foam. $[\alpha]_D$ = +118.8 (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.88–7.33 (m, 8H, Ar*H*), 5.85 (dd, 1H, H-3, *J* = 10.2, 8.9 Hz), 5.52–5.50 (d, 1H, H-1, *J* = 10.5 Hz), 4.52 (t, 1H, H-2, *J* = 10.4 Hz), 3.76–3.71 (m, 1H, H-5), 3.56 (t, 1H, H-4, *J* = 9.3 Hz), 2.94 (s, 1H, O*H*), 2.77–2.63 (m, 2H, SCH_2CH$_3$), 1.46–1.45 (d, 3H, CH_3, *J* = 6.1 Hz) 1.22 (t, 3H, SCH$_2$CH_3, *J* = 7.3 Hz). ^{13}C NMR (500 MHz, $CDCl_3$) δ: 168.0–167.4 (N*C*O, *C*=O) 134.3, 134.2, 133.6 (Ar*C*), 129.9, 128.8, 128.6, 123.7, 123.6 (Ar*C*H), 80.7 (C1), 76.7 (C5), 75.8 (C3), 75.7 (C4), 54.0 (C2), 24.4 (S*C*H$_2$CH$_3$), 18.1 (C6), 15.0 (SCH$_2$*C*H$_3$). HRMS $C_{23}H_{23}NO_6SNa$ [M + Na$^+$] calculated: 464.1144; found: 464.1149.

*Ethyl 4-azido-3-O-benzoyl-2,4,6-trideoxy-2-*N*-phthalimido-1-thio-β-D-glucopyranoside (5)*

Compound **4** (6.00 g, 13.6 mmol) was dissolved in dry CH_2Cl_2 (97.0 mL, 0.14 M) under a flow of nitrogen and, to this, pyridine (1.43 mL, 17.7 mmol) was added. The solution was cooled to –20 °C and a solution of triflic anhydride (2.70 mL, 16.3 mmol) in CH_2Cl_2 (30.0 mL) was added over 30 min. The solution was stirred for a further 30 min at –20 °C and then diluted with CH_2Cl_2 and washed with water (2 × 100 mL), saturated $NaHCO_3$ (2 × 100 mL), and brine (1 × 100 mL). The organic layer was dried over Na_2SO_4, filtered through a silica plug, and concentrated to give the triflate intermediate. This was then redissolved in dimethylformamide (DMF) (85 mL, 0.16 M) under a flow of nitrogen and NaN_3 (2.21 g, 40.8 mmol) was added. After stirring at room temperature for 1 h, the solvent was removed and the product **5** (5.40 g, 86%) was isolated by column chromatography (cyclohexane – ethyl acetate, 4/1 *v*/*v*) as a white foam. $[\alpha]_D$ = –30.4 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.95–7.93 (m, 2H, Bz*H*), 7.80(m, 2H NPhth*H*) 7.68 (m, 2H, NPhth*H*), 7.53–7.50 (m, 1H, Bz*H*) 7.39–7.36 (m, 2H, Bz*H*), 6.08 (dd, 1 H, H-3, *J* = 10.8, 3.7 Hz), 5.44 (d, 1H, H-1, *J* = 10.5 Hz), 4.83 (t, 1H, H-2, *J* = 10.6 Hz), 4.12 (dd, 1H, H-4, *J* = 3.7, 0.8 Hz), 4.03 (qd, 1H, H-5), 2.83–2.59 (m, 2H, SCH_2CH$_3$), 1.43 (s, 3H, CH_3), 1.22 (t, 3H, SCH$_2$CH_3). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 168.1, 167.4 (2 × N*C*O), 165.4 (*C*=O), 134.2–123.4 (Ar*C*, Ar*C*H), 80.6 (C1), 73.5 (C5), 71.8 (C3), 63.8 (C4), 50.0 (C2), 23.7 (S*C*H$_2$CH$_3$), 17.8 (C6), 14.8 (SCH$_2$*C*H$_3$) HRMS $C_{23}H_{22}N_4O_5SNa$ [M + Na$^+$] calculated: 489.1209; found: 489.1205.

Ethyl 2-amino-4-azido-2,4,6-trideoxy-1-thio-β-D-glucopyranoside (6)

A solution of compound **5** (5.40 g, 11.7 mmol) and ethylene diamine (2.63 mL, 39.3 mmol) in ethanol (120 mL, 0.10 M) was prepared and heated to 70 °C for 1.5 h. The solvent was then removed by rotary evaporation and the crude was coevaporated to dryness with acetonitrile. The residue was purified by column chromatography (ethyl acetate – methanol – water, 7/2/1 *v*/*v*) to yield compound **6** (2.23 g, 82%) as a white solid. On a large scale, the crude was dry loaded onto silica gel due to solubility issues when loading the column. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 4.13 (d, 1 H, H-1, *J* = 9.8 Hz), 3.72–3.62 (m, 2H, H-4, H-5), 3.58 (dd, 1 H, H-3, *J* = 10.8, 3.7 Hz), 2.87 (t, 1H, H-2, *J* = 9.8 Hz), 2.75–2.66 (m, 2H, SCH_2CH$_3$), 2.18 (s, 3H NH_2, O*H*), 1.34 (d, 3H, CH_3, *J* = 6.1 Hz) 1.29 (t, 3H, SCH$_2$CH_3, *J* = 7.3 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 87.6 (C1), 75.8 (C3), 73.8 (C4/5), 65.3 (C4/5), 53.2 (C2), 24.1 (S*C*H$_2$CH$_3$), 18.1 (C6), 15.3 (SCH$_2$*C*H$_3$). ^{1}H NMR data recorded were in accordance with those found in the literature.[31]

*Ethyl 3-O-acetyl-4-azido-2-*N*-(4-trifluoromethylbenzylidene)-2,4,6-trideoxy-1-thio-β-D-galactopyranoside (7)*

Compound **6** (35.1 mg, 0.15 mmol) was suspended in trimethylorthoformate (0.30 mL), and to this, 4-(trifluoromethyl) benzaldehyde (21.0 μL, 0.15 mmol) was added. After 2 h, the trimethylorthoformate was removed under reduced pressure and the crude product was dissolved in pyridine (2.00 mL), cooled to 0 °C, and acetic anhydride (1.00 mL) added. The reaction was stirred at room temperature until there was no starting material observed. The solvent was removed and the product was coevaporated with toluene and then purified by column chromatography (cyclohexane – ethyl acetate, 5/1 *v*/*v*) to give **7** as a 93% yield as a white foam. $[\alpha]_D$ = –92.4 (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.34 (s, 1H, N*H*), 7.86–7.84 (d, 2H, Ar*H*), 7.68–7.66 (d, 2H, ArH_A), 5.27–5.25 (dd, 1H, H-3 *J* = 9.7, 3.6 Hz), 4.77–4.75 (d, 1H, H-1, *J* = 9.7 Hz), 3.91 (dd, 1H, H-4, *J* = 3.5, 0.9 Hz), 3.88 (m, 1H, H-5), 3.62 (t, 1H, H-2, *J* = 9.7 Hz), 2.68 (m, 2H, SCH_2CH$_3$), 1.98 (s, 3H, CH_3), 1.40–1.39 (d, 3H, H-6a-c, *J* = 6.3 Hz), 1.23 (t, 3H, SCH$_2$CH_3, *J* = 7.4 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 170.0 (C=O), 163.4 (C=N), 138.7 (Ar*C*), 133.3–132.5 (q, *C*CF$_3$, $^2J_{CF3}$ = 32.5 Hz), 128.8 (ArC_X), 125.8–125.7 (q, ArC_A, $^3J_{CF3}$ = 3.8 Hz), 127.2–120.7 (q, *C*F$_3$, $^1J_{CF3}$ = 274 Hz), 84.2 (C1), 75.1 (C3), 73.4 (C5), 69.6 (C2), 62.7 (C4), 24.6 (S*C*H$_2$CH$_3$), 20.6 (*C*H$_3$) 18.0 (C6), 15.0 (SCH$_2$*C*H$_3$). HRMS $C_{18}H_{21}F_3N_4O_3SNa$ [M + Na$^+$] calculated: 453.1184; found: 453.1203.

Methyl (ethyl 2,3-di-O-benzyl-1-thio-β-D-galactopyranoside) uronate (9)

Diol **8** (1.00 g, 2.47 mmol) was dissolved in a biphasic mixture of CH_2Cl_2 and water (12 mL, 2/1 *v*/*v*) and cooled to 0 °C. BAIB (2.00 g, 6.18 mmol) was added followed by TEMPO (77.0 mg, 0.49 mmol) and the reaction was vigorously stirred for 20 min. The reaction was quenched by addition of $Na_2S_2O_3$ (5 mL, 10% *w*/*v* aqueous solution). The solution was diluted with CH_2Cl_2 and the organic layer was separated. The aqueous phase was acidified to pH 1 with 1 M HCl and extracted with ethyl acetate (3 × 50 mL). The organic layers were dried over Na_2SO_4, combined, and the solvent removed under reduced pressure. The crude was dried under vacuum and then dissolved in DMF (12.0 mL). To this, K_2CO_3 (1.02 g, 7.41 mmol) and MeI (0.46 mL, 7.41 mmol) were added and the reaction was stirred overnight. The reaction was diluted with ethyl acetate (100 mL) and the organic phase was washed with water (3 × 100 mL) and dried over Na_2SO_4. The solvent was removed and the product was isolated by column chromatography (cyclohexane – ethyl acetate, 4/1 *v*/*v*) to give **9** (715 mg, 67%) as a white foam. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.40–7.26 (m, 10H, Ar*H*), 4.90–4.69 (dd × 2, 4H, CH_2Ph), 4.44–4.41 (d, 1H, H-1, *J* = 9.8 Hz), 4.39 (s, 1H), 4.06 (s, 1H), 3.82 (s, 3H, COOCH_3), 3.70 (t, 1H, H-2, *J* = 9.4 Hz), 3.62–3.59 (dd, 1H, H-3, *J* = 9.2, 3.4 Hz), 2.84–2.72 (m, 2H, SCH_2CH$_3$), 1.32 (t, 3H, SCH$_2$CH_3, *J* = 7.3 Hz). Data recorded were in accordance with those found in the literature.[13]

Methyl (ethyl 4-O-chloroacetyl-2,3-di-O-benzyl-1-thio-β-D-galactopyranoside) uronate (10)

Compound **9** (163 mg, 0.37 mmol) was dissolved in anhydrous CH_2Cl_2 (2.50 mL). Dry pyridine (0.17 mL) was added to the solution and the temperature was reduced to 0 °C. Chloroacetyl chloride (0.06 mL, 0.75 mmol) was added and the reaction was stirred for 1 h. The solvent was removed under reduced pressure and the residue was coevaporated with toluene. Purification by column chromatography (toluene – ethyl acetate, 6/1 *v*/*v*) gave **10** (176 mg, 92%) as a pale yellow oil. $[\alpha]_D$ = +14.9 (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.38–7.30 (m, 10H, Ar*H*), 5.90–5.89 (dd, 1H, H-4, *J* = 3.3, 1.1 Hz), 4.84–4.54 (m × 2, 4H, 2 × C*H*$_2$Ph), 4.51 – 4.49 (d, 1H, H-1, *J* = 11.2 Hz), 4.19 (d, 1H, H-5, *J* = 9.7 Hz), 3.77 (s, 3H, COOC*H*$_3$), 3.71–3.69 (dd, 1H, H-3, *J* = 9.1, 3.4 Hz), 3.62–3.58 (t, 1H, H-2, *J* = 9.4 Hz), 2.84–2.73 (m, 2H, SC*H*$_2$CH$_3$), 1.33 (t, 3H, SCH$_2$C*H*$_3$, *J* = 7.4 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 167.0, 166.8 (C=O × 2), 137.9, 137.3 (Ar*C*), 128.6–128.1 (Ar*C*H), 85.6 (C1), 80.3 (C3), 77.2 (C2), 76.1 (*C*H$_2$Ph), 75.6 (C5), 72.5 (*C*H$_2$Ph), 69.9 (C4), 53.0 (COO*C*H$_3$), 40.9 (*C*H$_2$Cl), 25.3 (S*C*H$_2$CH$_3$), 15.1 (SCH$_2$*C*H$_3$). HRMS $C_{25}H_{29}O_7SClNa$ [M + Na$^+$] calculated: 531.1220; found: 531.1234.

2-(Trimethylsilyl)ethyl 2-O-benzyl-3,4-O-isopropylidene-β-D-galactopyranoside (13)

Compound **11** (3.91 g, 9.98 mmol) was dissolved in DMF (100 mL) and cooled to 0 °C before addition of sodium hydride (60% dispersion, 798 mg, 20.0 mmol). The reaction was stirred at 0 °C for 30 min following which benzyl bromide (2.44 mL, 20.0 mmol) was added. The reaction was stirred at room temperature for 1 h and then cooled to 0 °C and quenched by slow addition of MeOH. The solvent was removed and a solution of acetic acid – water (4/1, 50.0 mL) was added to the crude (9.98 mmol) at room temperature. The solution was stirred for 30 min and then quenched by pouring onto ice-cold saturated $NaHCO_3$ (200 mL). The product was extracted with CH_2Cl_2 (150 mL) and washed with saturated $NaHCO_3$ (2 × 100 mL) and water (2 × 100 mL). The organic layer was dried over Na_2SO_4 and the product was purified by column chromatography (cyclohexane – ethyl acetate, 5/1 *v*/*v*). The solvent was removed to give **13** (3.6 g, 88%) as a clear oil. $[\alpha]_D$ = +30.8 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.3–7.22 (m, 5H, Ar*H*), 4.85–4.77 (dd, 2H, C*H*$_2$Ph), 4.33–4.31 (d, 1H, H-1, *J* = 8 Hz), 4.16 (m, 1H, H-4), 4.11 (dd, 1H, H-3, *J* = 5.6, 1.9 Hz), 3.99 (m, 2H, H-6a, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 3.80 (m, 2H, H-5, H-6b), 3.58 (m, 1H, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 3.36 (dd, 1H, H-2, *J* = 8.0, 7.0 Hz), 2.15 (s, 1H, H6-O*H*), 1.03 (m, 2H, OCH$_2$C*H*$_2$Si(CH$_3$)$_3$), 0.01 (s, 9H, OCH$_2$CH$_2$Si(C*H*$_3$)$_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 138.5 (Ar*C*), 128.3, 127.7 (Ar*C*H), 110.3 (q*C*), 102.6 (C1), 79.7 (C2), 79.4 (C3), 74.2 (C4), 73.7 (*C*H$_2$Ph), 73.2 (C5), 67.5 (O*C*H$_2$CH$_2$Si(CH$_3$)$_3$), 62.7 (C6), 27.9, 26.5 (C(*C*H$_3$)$_2$), 18.6 (OCH$_2$*C*H$_2$Si(CH$_3$)$_3$), –1.3 (OCH$_2$CH$_2$Si(*C*H$_3$)$_3$). HRMS $C_{21}H_{34}O_6SiNa$ [M + Na$^+$] calculated: 433.2022; found: 433.2042.

Methyl (2-(trimethylsilyl)ethyl 2-O-benzyl-3,4-O-isopropylidene-β-D-galactopyranoside) uronate (14)

Bis(acetoxyiodo)benzene (3.26 g, 10.1 mmol) was added to a biphasic solution of CH_2Cl_2 and water (20.0 mL, 2/1 *v*/*v*) containing **13** (1.66 g, 4.05 mmol). The solution was cooled to 0 °C and TEMPO (120 mg, 0.81 mmol) was added. The reaction was stirred vigorously for 1 h and then quenched by addition of 10% sodium thiosulfate solution (20 mL). The mixture was diluted with CH_2Cl_2 and the organic phase was washed with saturated $NaHCO_3$ (2 × 50 mL) and water (2 × 50 mL). After drying over sodium sulphate and filtration, the solvent was removed from the organic layer. The crude material and K_2CO_3 (1.12 g, 8.10 mmol) were dried under reduced pressure overnight before dissolving in DMF (40 mL). The solution was cooled to 0 °C and MeI (0.50 mL, 8.10 mmol) was added dropwise. The solution was stirred at room temperature overnight. The solvents were removed and the product was isolated by column chromatography (cyclohexane – ethyl acetate, 3/1 *v*/*v*) to give **14** (992 mg, 56%) as a clear oil. $[\alpha]_D$ = +8.4 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.37–7.24 (m, 5H, Ar*H*), 4.83–4.75 (dd, 2H, C*H*$_2$Ph), 4.43–4.42 (dd, 1H, H-4), 4.35–4.33 (m, 2H, H-1, H-5), 4.20 (dd, 1H, H-3, *J* = 6.4, 6.0 Hz), 4.09–4.02 (m, 1H, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 3.81 (s, 3H, OC*H*$_3$), 3.57–3.50 (m, 1H, OCH$_2$C*H*$_2$Si(CH$_3$)$_3$), 3.44 (dd, 1H, H-2, *J* = 7.6, 6.8 Hz), 1.32 (s, 3H C*H*$_3$), 1.31 (s, 3H, C*H*$_3$), 1.03 (m, 2H, OCH$_2$C*H*$_2$Si(CH$_3$)$_3$), 0.00 (s, 9H, Si(C*H*$_3$)$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 168.0 (C=O), 138.3 (Ar*C*), 128.4, 127.7 (Ar*C*H), 110.6 (q*C*), 102.5 (C1), 78.8 (C2), 78.8 (C3), 74.1 (C4), 73.7 (*C*H$_2$Ph), 72.2 (C5), 67.6 (O*C*H$_2$CH$_2$Si(CH$_3$)$_3$), 52.6 (O*C*H$_3$), 27.7 (*C*H$_3$), 26.5 (*C*H$_3$), 18.5 (OCH$_2$*C*H$_2$Si(CH$_3$)$_3$), –1.3 (Si(*C*H$_3$)$_3$). HRMS $C_{22}H_{34}O_7SiNa$ [M + Na$^+$] calculated: 461.1972; found: 461.1977.

Methyl (2-(trimethylsilyl)ethyl 2-O-benzyl-endo-3,4-O-benzylidene-β-D-galactopyranoside) uronate (15* endo*) and methyl (2-(trimethylsilyl)ethyl 2-O-benzyl-exo-3,4-O-benzylidene-β-D-galactopyranoside) uronate (15* exo*)

A solution of acetic acid and water (25.0 mL, 4/1 *v*/*v*) was added to compound **14** (890 mg, 2.02 mmol) and the reaction was heated to 80 °C for 1 h. Upon completion, the reaction was cooled to room temperature and poured onto excess ice-cold saturated $NaHCO_3$. The product was extracted with CH_2Cl_2 (50.0 mL) and washed with saturated $NaHCO_3$ (2 × 100 mL) and water (2 × 100 mL). The organic layer was dried over Na_2SO_4 and the product was purified by filtration through a silica plug. The solvent was removed to give the diol (735 mg, 91%) as a clear oil. HRMS $C_{19}H_{30}O_7SiNa$ [M + Na$^+$] calculated: 421.1659; found: 421.1674. Camphorsulfonic acid (21.0 mg, 0.09 mmol) was added to a stirred solution of the crude diol (735 mg, 1.84 mmol) and benzaldehyde dimethyl acetal (0.55 mL, 3.68 mmol) in DMF (13.0 mL) at 0 °C. The reaction was stirred at 60 °C for 24 h and quenched by addition of Et_3N at 0 °C. The solvent was removed and the diastereomers were isolated by column chromatography (cyclohexane – ethyl acetate, 4/1 *v*/*v*) to give **15** *endo* and **15** *exo* as clear oils with a ratio of 2.2/1 (693 mg, 76%). Analysis for (**15** *endo*): $[\alpha]_D$ = –1.8 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.41–7.22 (m, 10H, Ar*H*), 5.90 (s, 1H, C*H*Ph), 4.75–4.66 (dd, 2H, C*H*$_2$Ph), 4.55–4.53 (dd, 1H H-3, *J* = 6.3, 2.5 Hz), 4.46–4.45 (m, 1H, H-5), 4.44–4.42 (d, 1H, H-1, *J* = 7.5 Hz), 4.37 (t, 1H, H-2, *J* = 6.2 Hz), 4.10–4.03 (m, 1H, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 3.81 (s, 3H, COOC*H*$_3$), 3.59–3.49 (m, 2H, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 1.04–1.00 (m, 2H, H-4, OCH$_2$C*H*$_2$Si(CH$_3$)$_3$), 0.00 (s, 9H, OCH$_2$CH$_2$Si(C*H*$_3$)$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 167.7 (C=O), 138.2, 137.0 (Ar*C*), 129.4–127.0 (Ar*C*H), 104.9 (*C*HPh), 102.6 (C1), 79.3 (C4), 78.5 (C2), 756.0 (C3), 73.7 (*C*H$_2$Ph), 72.2 (C5), 67.6 (O*C*H$_2$CH$_2$Si(CH$_3$)$_3$), 52.7 (COO*C*H$_3$), 18.5 (OCH$_2$*C*H$_2$Si(CH$_3$)$_3$), –1.3 (OCH$_2$CH$_2$Si(CH$_3$)$_3$). HRMS $C_{26}H_{34}O_7SiNa$ [M + Na$^+$] calculated: 509.1972; found: 509.1987. Analysis for (**15** exo): $[\alpha]_D$ = +8.3 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.40–7.24 (m, 10H, Ar*H*), 5.93 (s, 1H, C*H*Ph), 4.89–4.80 (dd, 2H, C*H*$_2$Ph), 4.55 (t, 1H, H-2, *J* = 6.0 Hz), 4.52–4.50 (dd, 1H, H-4, *J* = 5.72, 2.09 Hz), 4.45–4.43 (d, 1H, H-1, *J* = 7.8), 4.34 (d, 1H, H-5, *J* = 2.1 Hz), 4.12–4.06 (m, 1H, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 3.63–3.56 (m, 2H, H-3, OCH$_2$C*H*$_2$Si(CH$_3$)$_3$), 1.05 (t, 2H, OCH$_2$C*H*$_2$Si(CH$_3$)$_3$, *J* = 8.5 Hz), 0.03 (s, 9H, OCH$_2$CH$_2$Si(C*H*$_3$)$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 167.9 (*C*OOMe), 138.1 (Ar*C*), 129.4–126.5 (Ar*C*H), 103.8 (*C*HPh), 102.3 (C1), 79.7 (C2), 76.5 (C3), 74.3 (C4), 73.8 (*C*H$_2$Ph), 72.7 (C5), 67.7 (O*C*H$_2$CH$_2$Si(CH$_3$)$_3$), 18.5 (OCH$_2$*C*H$_2$Si(CH$_3$)$_3$), –1.3 (OCH$_2$CH$_2$Si(*C*H$_3$)$_3$). HRMS $C_{26}H_{34}O_7SiNa$ [M + Na$^+$] calculated: 509.1972; found: 509.1964.

Methyl (2-(trimethylsilyl)ethyl 2,4-di-O-benzyl-β-D-galactopyranoside) uronate (16)

Method 1

Compound **15** *endo* (200 mg, 0.41 mmol) was dissolved in anhydrous THF (10.0 mL) and borane timethyl amine was added (124 mg, 1.74 mmol) to the solution. The reaction was cooled to 0 °C and aluminum chloride (348 mg, 2.62 mmol) was added. The reaction was stirred for 30 min before water (16 μL, 0.82 mmol) was added. The product was taken up in CH_2Cl_2 and washed with 1 M hydrochloric acid solution (2 × 100 mL), saturated $NaHCO_3$ (2 ×

100 mL), and water (2 × 100 mL). The organic layer was then dried over Na_2SO_4 and the product was isolated by column chromatography (cyclohexane – ethyl acetate, 4/1 *v*/*v*) to give **16** (136 mg, 68%) as a clear oil.

Method 2

Compound **15** *exo* (50 mg, 0.10 mmol) was dissolved in 1 M, BH_3 in THF (1.00 mL) at 0 °C; to this, 1 M Bu_2BOTf in toluene (0.10 mL) was added and the solution was stirred for 2 h. The reaction was quenched with Et_3N followed by slow addition of MeOH until H_2 evolution ceased. The solvents were removed and the two products were separated by column chromatography using a gradient elution (dichloromethane–methanol, 1/0 to 5/1 *v*/*v*) to give an 81% yield (40 mg) with a 3/2 ratio of 4OBn (24 mg) to 3OBn (16 mg) as clear oils.

$[\alpha]_D$ = +1.2 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.35–7.24 (m, 10H, Ar*H*), 4.99–4.60 (dd × 2, 4H, C*H*$_2$Ph), 4.36–4.34 (d, 1H, H-1, *J* = 7.4 Hz), 4.18–4.17 (m, 1H), 4.12–4.05 (m, 2H), 3.70–3.65 (m, 4H), 3.60–3.51 (m, 2H), 1.33–1.31 (d, 1H, O*H*) 1.10–0.99 (m, 2H, $OCH_2CH_2Si(CH_3)_3$), 0.01 (s, 9H, $OCH_2CH_2Si(CH_3)_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 168.8 (C=O), 138.6, 138.2 (Ar*C*), 128.6–127.8 (Ar*C*H), 103.1 (C1), 78.9, 76.9, 75.0, 74.8, 74.1, 73.9 (C2, C3, C4, C5, 2 × *C*H$_2$Ph), 67.8 ($OCH_2CH_2Si(CH_3)_3$), 52.4 ($COOCH_3$), 18.6 ($OCH_2CH_2Si(CH_3)_3$), –1.3 ($OCH_2CH_2Si(CH_3)_3$). HRMS $C_{26}H_{36}O_7SiNa$ [M + Na$^+$] calculated: 511.2128; found: 511.2131.

2-(Trimethylsilyl)ethyl (methyl (4-O-chloroacetyl-2,3-di-O-benzyl-D-galactopyranosyl) uronate-α(1→3)-methyl (2,4-di-O-benzyl-β-D-galactopyranoside) uronate) (18)

Donor **10** (150 mg, 0.22 mmol), acceptor **16** (90.0 mg, 0.18 mmol), and 4 Å molecular sieves were dried under reduced pressure. To this, a solution of Et_2O and CH_2Cl_2 (3/2, 2.52 mL) was added and stirred at room temperature under nitrogen for 30 min and then cooled to 0 °C. Meanwhile, a 1 M solution of promoter was prepared by adding dimethyl disulfide (0.10 mL, 1.10 mmol) and triflic anhydride (0.17 mL, 1.00 mmol) to anhydrous dichloromethane (0.75 mL) at 0 °C. The solution of promoter was stirred for 30 min before adding the promoter (0.33 mL, 0.33 mmol) to the glycosylation reaction. The glycosylation was allowed to come to room temperature and after 30 min was quenched by the addition of excess Et_3N. The reaction was diluted with CH_2Cl_2 and washed with 1 M hydrochloric acid (2 × 50 mL), saturated $NaHCO_3$ solution (2 × 50 mL), and water (2 × 50 mL) and the organic layer was then dried over Na_2SO_4 and the solvent was removed. The α-disaccharide product **18** (128 mg, 74%) was isolated by column chromatography (toluene – ethyl acetate, 6/1 *v*/*v*) as a clear oil with no β-disaccharide observed. $[\alpha]_D$ = +64.5 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.33–7.04 (m, 20H, Ar*H*), 5.48 (dd, 1H, H-4′, *J* = 3.2, 1.8 Hz), 5.22 (d, 1H, H-1′, *J* = 3.3), 5.01–4.96 (dd, 2H, C*H*$_2$Ph), 4.95 (d, 1H, H-5′, *J* = 1.6 Hz), 4.79–4.37 (m, 6H, C*H*$_2$Ph), 4.36 (d, 1H, H-1, *J* = 6..9), 4.21 (m, 1H, H-5), 4.1 (m, 1H, $OCH_2CH_2Si(CH_3)_3$)1, 4.05 (m, 1H, H-4), 3.95–3.91 (dd, 1H, H-3, *J* = 10.1, 3.3 Hz), 3.82 (m, 3H, H-2, H-2′, H-3′), 3.61 (s, 3H, CH_3), 3.55 (m, 4H, C*H*$_3$, $OCH_2CH_2Si(CH_3)_3$), 1.00 (m, 2H, $OCH_2CH_2Si(CH_3)_3$), −0.01 (s, 9H, $OCH_2CH_2Si(CH_3)_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 168.6, 168.0, 166.5 (3 × C=O), 138.5, 138.4, 137.7, 137.6 (4 × Ar*C*), 128.6–127.4 (Ar*C*H), 103.5 (C1), 95.3 (C1′), 77.5, 76.7 (C2, C2′), 75.8 (C3), 75.3, 75.0, 74.8 (3 × *C*H$_2$Ph), 74.4 (C3′), 74.3 (C5), 74.0 (C4), 72.5 (CH_2Ph), 70.9 (C4′), 68.8 (C5′), 67.9 ($OCH_2CH_2Si(CH_3)_3$), 52.5, 52.4 (2 × $COOCH_3$), 40.7 (CH_2Cl), 18.6 ($OCH_2CH_2Si(CH_3)_3$), –1.3 ($OCH_2CH_2Si(CH_3)_3$). HRMS $C_{49}H_{59}O_{14}SiClNa$ [M + Na$^+$] calculated: 957.3260; found: 957.3242.

2-(Trimethylsilyl)ethyl (methyl 2,3-di-O-benzyl-D-galactopyranosyl uronate-α(1→3)-methyl 2,4-di-O-benzyl-β-D-galactopyranoside uronate) (19)

Disaccharide **18** (144 mg, 0.15 mmol) was dissolved in THF (1.70 mL), and to this solution, thiourea (37.0 mg, 0.51 mmol), tetrabutylammonium iodide (11.0 mg, 0.03 mmol), and sodium bicarbonate (39.0 mg, 0.46 mmol) were added. The suspension was heated to 60 °C for 16 h. The reaction was then diluted with CH_2Cl_2 and filtered through a Celite plug. The solvent was removed and the crude was purified by column chromatography (toluene – ethyl acetate, 3/1 *v*/*v*) to give **19** (112 mg, 84%) as a clear oil. $[\alpha]_D$ = +32.8 (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.36–7.06 (m, 20 H, Ar*H*), 5.26–5.25 (d, 1H, H-1′, *J* = 3.3 Hz), 5.03–4.37 (m × 4, 8H, C*H*$_2$Ph), 4.37–4.36 (d, 1H, H-1, *J* = 7.5 Hz), 4.24 (m, 1H, H-5′), 4.12–4.07 (m, 2H, $OCH_2CH_2Si(CH_3)_3$), 4.05 (m, 1H, H-4′), 4.03 (m, 1H, H-5), 3.98–3.95 (dd, 1H, H-3, *J* = 9.9, 3.3 Hz), 3.89–3.86 (dd, 1H, H-2′, *J* = 9.9, 3.3 Hz), 3.85–3.84 (m, 2H, H-2, H-3′), 3.66 (s, 3H, $COOCH_3$), 3.62 (s, 3H, $COOCH_3$), 3.58 – 3.52 (m, 1H, $OCH_2CH_2Si(CH_3)_3$), 1.0 (m, 2H, $OCH_2CH_2Si(CH_3)_3$), 0.00 (s, 9H, $OCH_2CH_2Si(CH_3)_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 169.2, 168.7 (2 × C=O), 138.6, 138.6, 137.9, 137.8 (4 × Ar*C*), 128.8–127.3 (Ar*C*H), 103.5 (C1), 95.1 (C1′), 77.5, 77.2 (C2, C2′), 76.5 (C3), 75.3, 75.0, 74.8 (3 × *C*H$_2$Ph), 74.7 (C3′), 74.4 (C5), 74.0 (C4), 72.5 (*C*H$_2$Ph), 69.9 (C4′), 68.4 (C5′), 67.9 ($OCH_2CH_2Si(CH_3)_3$), 52.5 ($COOCH_3$), 52.3 ($COOCH_3$), 18.7 ($OCH_2CH_2Si(CH_3)_3$), –1.31 ($OCH_2CH_2Si(CH_3)_3$). HRMS $C_{47}H_{58}O_{13}SiNa$ [M + Na$^+$] calculated: 881.3544; found: 881.3558.

2-(Trimethylsilyl)ethyl (3-O-acetyl-4-azido-2-N-(4-trifluoromethylbenzylidene)-2,4,6-trideoxy-D-galactopyranosyl-α(1→4)-methyl (2,3-di-O-benzyl-D-galactopyranosyl) uronate-α(1→3)-methyl (2,4-di-O-benzyl-β-D-galactopyranoside) uronate) (20) and 2-(trimethylsilyl)ethyl (3-O-acetyl-4-azido-2-N-(4-trifluoromethylbenzylidene)-2,4,6-trideoxy-D-galactopyranosyl-β(1→4)-methyl (2,3-di-O-benzyl-D-galactopyranosyl) uronate-α(1→3)-methyl (2,4-di-O-benzyl-β-D-galactopyranoside) uronate) (21)

Donor **7** (38.0 mg, 0.08 mmol), disaccharide acceptor **19** (64.0 mg, 0.07 mmol), and 4 Å molecular sieves were dried under reduced pressure. To this, a solution of Et_2O and CH_2Cl_2 (3/2, 1.00 mL) was added and stirred at room temperature under nitrogen for 30 min and then cooled to 0 °C. Meanwhile, a 1 M solution of promoter was prepared by adding dimethyldisulfide (0.10 mL, 1.10 mmol) and triflic anhydride (0.17 mL, 1.00 mmol) to anhydrous CH_2Cl_2 (0.75 mL) at 0 °C. The solution was stirred for 30 min before adding the promoter (126 μL, 0.13 mmol) to the glycosylation reaction. The glycosylation was allowed come to room temperature and after 30 min was quenched by the addition of excess triethylamine. The reaction was diluted with CH_2Cl_2 and washed with 1 M hydrochloric acid (2 × 50 mL), saturated $NaHCO_3$ (2 × 50 mL), and water (2 × 50 mL) and the organic layer was then dried over Na_2SO_4 and the solvent was removed. The trisaccharide was obtained in a 96% yield as a 3α/2β mixture, which was separable by column chromatography to give the α-trisaccharide product **20** (49.0 mg, 57%) and the β-trisaccharide **21** (34.0 mg, 39%) both as clear oils.

Analysis **20**: $[\alpha]_D$ = +69.2 (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.32 (s, 1H, N*H*), 7.91–7.02 (m, 24H, Ar*H*), 5.40–5.37 (dd, 1H H-3″), 5.33 (d, 1H, H-1′, *J* = 3.3 Hz), 5.08 (d, 1H, C*H*$_2$Ph), 4.88–4.84 (m, 2H, CH_2Ph, H-1″, *J* = 3.3 Hz), 4.82–4.70 (m, 4H C*H*$_2$Ph), 4.59 (s, 1H, H-4′), 4.47–4.43 (m, 4H, C*H*$_2$Ph, H-2″, H-1, *J* = 7.8 Hz), 4.25 (s, 1H, H-5), 4.13 (m, 2H, H-3′, H-2/H-2′), 4.03 (m, 2H, H-4, $OCH_2CH_2Si(CH_3)_3$), 3.89–3.85 (m, 3H, H-3, H-4″, H-5″), 3.78–3.75 (m, 2H, H-2/H-2″, H-5′), 3.64 (s, 3H, $COOCH_3$), 3.56–3.49 (m, 1H, $OCH_2CH_2Si(CH_3)_3$), 3.03 (s, 3H, $COOCH_3$), 1.94 (s, 3H, $COOCH_3$), 1.04–1.03 (d, 3H, H-6a-c), 1.01–0.94 (m, 2H, $OCH_2CH_2Si(CH_3)_3$), −0.02 (s, 9H, $OCH_2CH_2Si(CH_3)_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 170.1, 168.7, 168.3 (3 × C=O), 163.5 (N=*C*), 138.7, 138.5, 137.8 (Ar*C*), 137.8–133.7 (q, *C*CF_3, $^2J_{CF3}$ = 32.5 Hz), 129.5–127.4 (Ar*C*H), 103.5 (C1), 101.1 (C1″), 94.8 (C1′), 75.1, 75.0, 74.3, 73.0 (4 × C*H*$_2$Ph) 77.6, 77.4, 76.5, 76.4, 74.7, 74.5, 74.0, 71.3, 70.3, 68.6, 65.4, 63.9 (C2, C2′, C2″, C3, C3′, C3″, C4, C4′, C4″, C5, C5′, C5″), 67.9 ($OCH_2CH_2Si(CH_3)_3$), 52.5 ($COOCH_3$), 51.7 ($COOCH_3$), 20.6 ($COCH_3$), 18.6 (C6), 17.4 ($OCH_2CH_2Si(CH_3)_3$), –1.3 ($OCH_2CH_2Si(CH_3)_3$). HRMS $C_{63}H_{73}N_4O_{16}SiF_3Na$ [M + Na$^+$] calculated: 1249.4641; found: 1249.4618.

Analysis **21**: $[\alpha]_D$ = +36.6 (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.41 (s, 1H, N*H*), 7.82–6.75 (m, 24H, Ar*H*), 5.23–5.20 (dd, 1H, H-3″, *J* = 10.2, 3.7 Hz), 5.11 (d, 1H, H-1′, *J* = 3.3 Hz), 4.99–4.98 (d, 1H, H-1″, *J* = 7.6 Hz), 4.96–4.83 (dd, 2H, CH_2Ph), 4.80 (m, 1H, *H*-4′), 4.68–4.55 (dd, 3H, CH_2Ph), 4.32 (d, 1H, *H*-1, *J* = 7.2 Hz), 4.24 (m, 2H, *H*-2″), 4.22–4.15 (m, 2H, CH_2Ph), 4.11 (s, 1H, H-5′), 4.03 (m, 1H, OCH_2CH$_2$Si(CH$_3$)$_3$), 3.96 (m, 1H, H-3″), 3.82–3.77 (m, 5H, CH_2Ph, H-4, H-3, H-4″, H-2′), 3.68–3.66 (m, H-5′, H-5″), 3.61 (s, 3H, COOCH_3), 3.57 (s, 3H, COOCH_3), 3.54–3.50 (m, 2H, *H*-2, OCH_2CH$_2$Si(CH$_3$)$_3$), 1.99 (s, 3H, COCH_3), 1.34–1.33 (d, 3H, H-6a-c‴, *J* = 6.3 Hz), 1.04–0.96 (m, 2H, OCH$_2$CH_2Si(CH$_3$)$_3$), −0.02 (s, 9H, OCH$_2$CH$_2$Si(CH_3)$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 170.3 168.6, 168.6 (3 × C=O), 163.3 (C=N), 139.2, 139.2, 138.7, 138.6, 138.5, 137.7 (6 × Ar*C*), 137.8–133.7 (q, CCF_3, $^2J_{CF3}$ = 32.5 Hz), 128.8–125.6 (Ar*C*H), 103.5 (C1), 100.9 (C1″), 95.4 (C1′), 75.0, 74.9, 74.8 (3 × CH_2Ph), 70.8 (CH_2Ph), 78.0, 77.3, 76.7, 76.5, 74.6, 74.5, 74.0, 73. 5, 72.9, 70.2, 69.1, 62.2 (C2, C2′, C2″, C3, C3′, C3″, C4, C4′, C4″, C5, C5′, C5″), 67.9 (OCH_2CH$_2$Si(CH$_3$)$_3$), 52.4, 52.2 (2 × COO*C*H$_3$), 20.6 (CO*C*H$_3$), 18.6 (OCH$_2$*C*H$_2$Si(CH$_3$)$_3$), 17.7 (C6″), −1.3 (OCH$_2$CH$_2$Si(*C*H$_3$)$_3$). HRMS $C_{63}H_{73}N_4O_{16}SiF_3Na$ [M + Na$^+$] calculated: 1249.4641; found: 1249.4642.

*2-(Trimethylsilyl)ethyl (2-*N*-acetamido-3-*O*-acetyl-4-azido-2,4,6-trideoxy-*D*-galactopyranosyl-α(1→4)-methyl (2,3-di-*O*-benzyl-*D*-galactopyranosyl) uronate-α(1→3)-methyl (2,4-di-*O*-benzyl-β-*D*-galactopyranoside) uronate) (22)*

Methanol (2.00 mL) was added to trisaccharide **20** (49.0 mg, 0.04 mmol) and a couple of drops of CH_2Cl_2 were added to help solubility. A catalytic quantity of camphor sulfonic acid was then added and the reaction was stirred for 6 h. The reaction was quenched by addition of Et_3N and the solvent was removed. The crude was dried under reduced pressure and then taken up in methanol (2.00 mL) and acetic anhydride was added (0.40 mL) and the reaction was stirred overnight. The solvent was then removed and the crude was coevaporated with toluene before being purified by column chromatography (dichloromethane–methanol, 9/1 *v*/*v*) to give **22** (28.0 mg, 64%) as a clear oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.59–7.00 (m, 20H, Ar*H*), 5.54–5.52 (d, 1H), 5.26–5.26 (d, 1H, H-1′, *J* = 3.1 Hz) 5.04–4.97 (m, 2H), 4.87–4.84 (d, 1H), 4.76–4.65 (m, 3H), 4.60–4.48 (m, 3H), 4.42–4.39 (d, 1H), 4.32–4.27 (dd, 2H), 4.20–4.16 (m, 2H), 4.07–3.98 (m, 3H), 3.93–3.90 (dd, 1H), 3.85–3.82 (dd, 1H), 3.80–3.71 (dd, 1H), 3.75–3.71 (m, 1H), 3.62 (s, 3H, COOCH_3), 3.56–3.47 (m, 1H, OCH_2CH$_2$Si(CH$_3$)$_3$), 3.30 (s, 3H, COOCH_3), 2.08 (s, 3H, COCH_3), 1.97 (s, 3H, COCH_3), 1.74–1.70 (m, 2H, OCH$_2$CH_2Si(CH$_3$)$_3$), 0.96–0.95 (d, 3H, H-6a-c″, *J* = 6.3 Hz), −0.04 (s, 9H, OCH$_2$CH$_2$Si(CH_3)$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 171.0, 170.9, 168.9, 168.6 (4 × C=O), 138.5, 138.2, 138.2, 137.4 (Ar*C*), 128.8–127.8 (Ar*C*H), 103.4, (C1), 99.4 (C1″), 94.6 (C1′), 77.3, 77.29, 76.6, 75.3, 75.2, 75.0, 74.5, 74.4, 74.2, 73.9, 73.2, 71.0, 70.2, 67.9, 65.6, 64.4 (C2, C2′, C3, C3′, C3″, C4, C4′, C4″, C5, C5′, C5″, CH_2Ph × 4, OCH_2CH$_2$Si(CH$_3$)$_3$), 52.8, 52.5 (COO*C*H$_3$), 52.0 (C2″), 23.4 (CO*C*H$_3$), 20.8 (CO*C*H$_3$), 18.6 (OCH$_2$*C*H$_2$Si(CH$_3$)$_3$), 17.2 (C6″), −1.4 (OCH$_2$CH$_2$Si(*C*H$_3$)$_3$).

*Ethyl 4-azido-2,3-*N,O*-oxazolidinone-2,4,6-trideoxy-1-thio-β-D-glucopyranoside (23)*

Compound **6** (1.02 g, 4.40 mmol) was dissolved in mixture of acetonitrile (40.0 mL) and saturated $NaHCO_3$ (20.0 mL) and stirred for 30 min. The reaction was cooled to 0 °C and triphosgene (781 mg, 2.64 mmol) was added. The reaction was stirred for 30 min and monitored by TLC (methanol – ethyl acetate – water, 7/2/1 *v*/*v*). A solution of ethylenediamine (10.0 mL) in ethyl acetate (60.0 mL) was added to the reaction and stirred for a further 30 min. The organic layer was then separated, washed with water, dried over Na_2SO_4, filtered, and reduced to dryness. The crude was purified by column chromatography (cyclohexane – ethyl acetate, 1/1 *v*/*v*) to give **23** (885 mg, 78%) as a white foam. $[\alpha]_D$ = −116.7 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.20 (s, 1H, N*H*), 4.51 (d, 1H, H-1, *J* = 9.7 Hz), 4.31–4.28 (dd, 1H, H-3, *J* = 11.2, 3.9 Hz), 4.00 (m, 1H, H-4), 3.89–3.86 (m, 2H, H-2, H-5), 2.78–2.70 (m, 1H, SCH_2CH$_3$), 1.40–1.39 (d, 3H, CH_3, *J* = 6.4 Hz), 1.32–1.29 (t, 3H, SCH$_2$CH_3, *J* = 7.4 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 158.0 (C=O), 83.5 (C1), 82.2 (C3), 75.1 (C2), 61.0 (C4), 55.0 (C5), 24.7 (SCH_2CH$_3$), 17.9 (C6), 15.4 (SCH$_2$CH_3). HRMS $C_9H_{14}N_4O_3SNa$ [M + Na$^+$] calculated: 281.0684; found: 281.0691.

*Ethyl 4-azido-2-*N*-tert-butyloxycarbonyl-2,3-*N,O*-oxazolidinone-2,4,6-trideoxy-1-thio-β-D-glucopyranoside (24)*

To a stirred solution of **23** (3.50 mg, 0.14 mmol) in THF (1.00 mL), Boc_2O (147 mg, 0.68 mg) and 4-dimethylaminopyridine (2.00 mg, 0.01 mmol) were added. The solution was heated to 60 °C and monitored by TLC (cyclohexane – ethyl acetate, 2/1 *v*/*v*). After 1 h, the solvent was removed and the product **24** (44.0 mg, 91%) was isolated as a white foam by column chromatography (cyclohexane – ethyl acetate, 2/1 *v*/*v*). $[\alpha]_D$ = −66.8 (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 4.60 (d, 2H, H-1, *J* = 8.4 Hz), 4.28–4.20 (m, 2H, H-2, H-3), 4.06 (m, 1H, H-4), 3.90–3.86 (m, 1H, H-5), 2.67 (m, 2H, SCH_2CH$_3$), 1.57 (s, 9H, 3 × CH_3), 1.40 (d, 3H, CH_3, *J* = 6.3 Hz), 1.25 (t, 3H, SCH$_2$CH_3, *J* = 7.4 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 153.1, 150.7 (2 × C=O), 85.7 (q*C*), 85.3 (C1), 79.7 (C3), 75.0 (C5) 61.1 (C4), 56.5 (C2), 27.9 (C(CH_3)$_3$), 25.0 (SCH_2CH$_3$), 17.6 (C6), 14.6 (SCH$_2$CH_3). HRMS $C_{14}H_{22}N_4O_5SNa$ [M + Na$^+$] calculated: 381.1209; found 381.1214.

*Ethyl 2-*N*-acetyl-4-azido-2,3-*N,O*-oxazolidinone-2,4,6-trideoxy-1-thio-β-D-glucopyranoside (25)*

Compound **23** (172 mg, 0.67 mmol) was dissolved in anhydrous dichloromethane and cooled to 0 °C. *N*,*N*-diisopropylethylamine (0.59 mL, 3.37 mmol) and acetyl chloride (0.24 mL, 3.37 mmol) were added and the reaction was stirred for 1 h. TLC (cyclohexane – ethyl acetate, 1/1 *v*/*v*) indicated that the reaction was complete and the reaction was diluted with CH_2Cl_2, washed with saturated $NaHCO_3$, water, and 1 M HCl and dried over Na_2SO_4. Column chromatography (cyclohexane – ethyl acetate, 1/1 *v*/*v*) gave the product **25** in a quantitative yield as a white foam. $[\alpha]_D$ = −64.5 (*c* = 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 4.63–4.61 (d, 1H, H-1, *J* = 8.1 Hz), 4.33–4.30 (m, 2H, H-3, H-2), 4.08 (m, 1H, H-4), 3.90–3.86 (m, 1H, H-5), 2.65–2.59 (m, 2H, SCH_2CH$_3$), 2.51 (s, 3H, COCH_3), 1.40–1.39 (d, 3H, H-6a-c, *J* = 6.3 Hz), 1.23 (t, 3H SCH$_2$CH_3, *J* = 7.4 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 172.9 (C=O), 153.6 (C=O), 85.4 (C1), 79.8 (C3), 74.9 (C5), 61.1 (C4), 56.3 (C2), 25.1 (SCH_2CH$_3$), 25.0 (CO*C*H$_3$), 17.5 (C6), 14.2 (SCH$_2$*C*H$_3$). HRMS $C_{11}H_{16}N_4O_4SNa$ [M + Na$^+$] calculated: 323.0790; found: 323.0778.

*Methyl (2-*N*-acetyl-4-azido-2,3-*N,O*-carbonyl-2,4,6-trideoxy-D-galactopyranosyl-α(1→4)-6-*O*-benzoyl-2,3-di-*O*-benzyl-α-D-galactopyranoside (27)*

Donor **25** (20.0 mg, 0.07 mmol) and acceptor **26** (27.0 mg, 0.06 mmol) were dissolved in CH_2Cl_2 (1.00 mL) and cooled to 0 °C. NIS (25.0 mg, 0.11 mmol) was added followed by AgOTf (5.60 mg, 0.02 mmol). The reaction was stirred for 30 min and then quenched with Et_3N. The crude was loaded directly onto a column for purification (toluene – ethyl acetate, 6/1 *v*/*v*). This gave exclusively the α-disaccharide **27** in a 59% yield (23.0 mg) as a white foam. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.02–7.29 (m, 15H, Ar*H*), 5.67–5.66 (d, 1H, H-1′, *J* = 2.5 Hz), 4.84–4.77 (m, 4H, H-1), 4.73–4.64 (m, 3H), 4.57–4.48 (m, 1H), 4.45–4.41 (dd, 1H), 4.22–4.17 (m, 2H), 4.10–4.10 (d, 1H), 4.07–3.98 (m, 3H), 3.92–3.85 (m, 2H), 3.80–3.77 (m, 2H), 3.37 (s, 3H, OCH_3), 2.54 (s, 3H, COCH_3), 0.98–0.96 (d, 3H, H-6a-c′, *J* = 6.4 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 172.6, 165.0, 153.0 (C=O), 138.4–133.3 (Ar*C*), 129.8–128.0 (Ar*C*H), 98.2 (C1), 97.4 (C1′), 77.6, 76.7, 76.3, 75.2, 73.8, 73.3, 73.1, 68.3, 67.5, 62.9, 62.3, 56.3, 55.5 (OCH_3), 24.0 (COCH_3), 17.0 (C6′). HRMS $C_{37}H_{40}N_4O_{11}Na$ [M + Na$^+$] calculated: 739.2591; found: 739.2615.

Methyl (2-N-acetyl-4-azido-2,3-N,O-carbonyl-2,4,6-trideoxy-D-galactopyranosyl-β(1→4)-6-O-benzoyl-2,3-di-O-benzyl-α-D-galactopyranoside (28)

Donor **25** (20.0 mg, 0.07 mmol) and acceptor **26** (27.0 mg, 0.06 mmol) were dissolved in CH_2Cl_2 (1.00 mL) and cooled to 0 °C. NIS (25.0 mg, 0.11 mmol) was added followed by AgOTf (1.40 mg, 5.50 μmol). The reaction was stirred for 10 min and then quenched with Et_3N. The crude was loaded directly onto a column for purification (toluene – ethyl acetate, 6/1 *v*/*v*). This gave a 1α:6β ratio of disaccharide in a 65% yield (25 mg) as a white foam. Analysis for major product: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.02–7.27 (m, 15H, Ar*H*), 4.88–4.81 (dd, 2H, C*H*$_2$Ph), 4.67–4.57 (m, 5H, C*H*$_2$Ph, H-1, H-1′, H-6a), 4.41–4.37 (dd, 1H, H-6b), 4.25–4.20 (m, 2H), 4.05–4.02 (m, 2H), 3.90–3.86 (m, 3H), 3.69–3.64 (m, 1H), 3.32 (s, 3H, OC*H*$_3$), 2.30 (s, 3H, COC*H*$_3$), 1.29–1.28 (m, 3H, H-6a-c′). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 171.3 (C=O), 153.8 (C=O), 138.9–133.2 (Ar*C*), 129.7–127.8 (Ar*C*H), 103.8 (C1′), 99.0 (C1), 78.1, 77.8, 74.0, 71.8, 67.8, 60.4, 56.6 (C2, C2′, C3, C3′, C4, C4′, C5, C5′), 77.0 (*C*H$_2$Ph), 76.7 (*C*H$_2$Ph), 64.7 (C6), 55.5 (O*C*H$_3$), 25.0 (CO*C*H$_3$), 17.3 (C6′). HRMS $C_{37}H_{40}N_4O_{11}Na$ [M + Na$^+$] calculated: 739.2591; found: 739.2605.

Methyl (2-N-tert-butyloxycarbonyl-4-azido-2,3-N,O-carbonyl-2,4,6-trideoxy-D-galactopyranosyl-α(1→4)-6-O-acetyl-2,3-di-O-benzyl-β-D-galactopyranoside (31)

Donor **24** (40.0 mg, 0.11 mmol) and acceptor **29** (19.0 mg, 0.05 mmol) were dissolved in CH_2Cl_2 (1.00 mL) and cooled to 0 °C. NIS (25.0 mg, 0.11 mmol) was added followed by AgOTf (4.60 mg, 0.01 mmol). The reaction was stirred for 30 min, the formation of the β-disaccharide **30** was observed by TLC, another 0.3 equiv. of AgOTf was added, and the anomerisation to the α-disaccharide was observed. The reaction was then quenched by addition of Et_3N. The crude was loaded directly onto a column for purification (toluene – ethyl acetate, 6/1 *v*/*v*). This gave exclusively the α-disaccharide **31** in a 52% yield (17.0 mg). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.40–7.29 (m, 10H, Ar*H*), 5.48–5.47 (d, 1H, H-1′, *J* = 2.6 Hz), 4.92–4.90 (d, 1H, C*H*$_2$Ph), 4.78–4.74 (m, 2H, C*H*$_2$Ph), 4.70–4.67 (d, 1H, C*H*$_2$Ph), 4.66–4.63 (dd, 1H), 4.32–4.28 (m, 1H, H-6a), 4.26–4.23 (m, 2H, H-1, *J* = 7.5 Hz), 4.16–4.13 (dd, 1H), 4.03–3.99 (m, 2H), 3.78 (s, 1H), 3.57 (m, 1H), 3.53 (s, 3H, OC*H*$_3$), 3.48 (t, 1H), 3.41–3.38 (dd, 1H), 2.06 (s, 3H, COC*H*$_3$), 1.53 (s, 9H, C(C*H*$_3$)$_3$), 0.96–0.94 (d, 3H, H-6a-c′, *J* = 6.4 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 170.6 (C=O), 151.2, 151.0 (C=O), 138.4, 138.1 (Ar*C*), 128.6–127.8 (Ar*C*H), 105.1 (C1), 97.0 (C1′), 84.9 (qC), 74.8 (*C*H$_2$Ph), 73.6 (*C*H$_2$Ph), 79.8, 78.3, 74.1, 72.7, 71.9, 67.4, 62.2 (C2, C3, C3′, C4, C4′, C5, C5′), 61.9 (C6), 57.1, 56.3 (C2′), 28.1 (C(*C*H$_3$)$_3$), 21.0 (CO*C*H$_3$), 17.0 (C6′). HRMS $C_{37}H_{40}N_4O_{11}Na$ [M + Na$^+$] calculated: 735.2853; found: 735.2841.

Methyl (2-N-tert-butyloxycarbonyl-4-azido-2,4,6-trideoxy-D-galactopyranosyl-α(1→4)-2,3-di-O-benzyl-β-D-galactopyranoside (32)

Disaccharide **31** (8.00 mg, 0.01 mmol) was dissolved in MeOH (1.00 mL) and a couple of drops of CH_2Cl_2 were added to increase solubility. The solution was cooled to 0 °C and added to a freshly prepared solution of NaOMe in MeOH until a pH 11 was achieved. After 30 min, the reaction was quenched by addition of IR-120 H$^+$ resin until pH 7 was reached. The resin was filtered off and the solvent was removed. The product was isolated after column chromatography (toluene – ethyl acetate, 6/1 *v*/*v*) to give **32** (6.60 mg, 92%). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.39–7.28 (m, 10H, Ar*H*), 5.35 (s, 1H, N*H*), 4.90–4.88 (d, 2H, C*H*$_2$Ph), 4.78–4.68 (m, 4H, H-1, H-1′, C*H*$_2$Ph), 4.34–4.29 (m, 2H), 4.07–4.06 (d, 1H), 3.97–3.91 (m, 2H), 3.85–3.82 (dd, 1H, H-6a), 3.72–3.66 (m, 1H, H-6b), 3.60–3.54 (m, 2H), 3.57 (s, 3H, OC*H*$_3$), 3.45–3.40 (m, 2H), 1.47 (s, 9H, C(C*H*$_3$)$_3$), 1.43 (d, 1H, O*H*), 1.01 – 1.00 (d, 3H, H-6a-c′, *J* = 6.3 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 138.4, 138.0 (Ar*C*), 128.4–127.4 (Ar*C*H), 105.2 (C1), 98.3 (C1′), 79.7, 74.9, 78.9, 74.9, 74.6, 72.8, 72.7, 71.1, 66.7, 65.7 (C2, C3, C3′, C4, C4′, C5, C5′), 61.0 (C6), 57.2 (O*C*H$_3$), 51.9 (C2′), 28.3 (C(*C*H$_3$)$_3$), 17.3 (C6′).

Ethyl 2,3-di-O-benzyl-4,6-O-naphtylmethylidene-1-thio-β-D-galactopyranoside (33)

A solution of **8** (3.20 g, 14.3 mmol) in DMF (90.0 mL) was added with dimethyl naphthaldehyde (8.70 g, 42.9 mmol) and camphor sulfonic acid (660 mg, 2.86 mmol). The mixture was heated up to 60 °C and stirred overnight. The reaction was then cooled down to 0 °C and added with Et_3N until pH 7 was reached. The solvent was removed under reduced pressure and the crude was taken up with CH_2Cl_2 and washed with water. The crude was purified by flash column chromatography (ethyl acetate – cyclohexane, 9/1 *v*/*v*) to give **33** (4.30 g, 83% yield) as a white foam. $[\alpha]_D$ = +26.7 (*c* 0.88, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.03–7.19 (m, 17H, Ar*H*), 5.63 (s, 1H, C*H*Nap), 4.90 (d, 1H, H-1, *J* = 10.2), 4.84 (d, 1H, C*H*$_2$Ph), 4.81–4.72 (m, 2H, C*H*$_2$Ph), 4.46 (d, 1H, C*H*$_2$Ph), 4.36 (dd, 1H, H-6a), 4.23–4.21 (m, 1H, H-4), 4.01 (dd, 1H, H-6b), 3.92 (t, 1H, H-2, *J* = 6.4 Hz), 3.62 (dd, 1H, H-3, *J* = 4.6, 1.2 Hz), 3.41–3.37 (m, 1H, H-5), 2.93–2.72 (m, 2H, SC*H*$_2$CH$_3$), 1.34 (t, 3H, SCH$_2$C*H*$_3$, *J* = 7.4 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 138.7–133.2 (Ar*C*), 128.6–124.4 (Ar*C*H), 101.8 (Nap*C*H), 84.7 (C1), 81.4 (C3), 77.1 (C2), 75.9 (*C*H$_2$Ph), 74.3 (C4), 72.0 (*C*H$_2$Ph), 70.1 (C5), 69.7 (C6), 24.1 (S*C*H$_2$CH$_3$), 15.3 (SCH$_2$*C*H$_3$). HRMS $C_{33}H_{34}O_5SNa$ [M + Na$^+$] calculated: 565.2025; found: 565.2031.

Ethyl-2,3-di-O-benzyl-6-O-2-naphtylmethyl-1-thio-β-D-galactopyranoside (34)

A solution of **33** (200 mg, 0.37 mmol) in anhydrous THF containing activated crushed 3 Å molecular sieves (200 mg) was added with $NaCNBH_3$ (136 mg, 2.16 mmol). The solution was then added with HCl·Et_2O until pH 1–2 was reached and was stirred for 1 h. The reaction was then cooled down to 0 °C and added with Et_3N until pH 7 was reached. The sieves were filtered off and the solvent was removed under reduced pressure. The crude was purified by flash column chromatography (cyclohexane –)ethyl acetate, 4/1 *v*/*v*) to give **34** (156 mg, 77% yield) as a colourless syrup. $[\alpha]_D$ = −4.2 (*c* 1.1, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.91–7.16 (m, 15H, Ar*H*), 4.87–4.76 (dd, 2H, C*H*$_2$Ph, *J* = 58.0, 10.3 Hz), 4.73 (s, 2H, C*H*$_2$Ph), 4.70–4.67 (m, 2H, C*H*$_2$Ph), 4.42 (d, 1H, H-1, *J* = 9.7), 4.10–4.08 (s, 1H, H-4), 3.81 (dd, 1H, H-6a, *J* = 10.0, 5.9 Hz), 3.77 (dd, 1H, H-6b, *J* = 9.9, 5.9 Hz), 3.67 (t, 1H, H-2, *J* = 9.3 Hz), 3.58 (t, 1H, H-5, *J* = 5.8 Hz), 3.54 (dd, 1H, H-3, *J* = 9.0, 3.2 Hz), 2.82–2.66 (m, 2H, SC*H*$_2$CH$_3$), 1.30 (t, 3H, SCH$_2$C*H*$_3$, *J* = 7.4 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 138.4–133.2 (Ar*C*), 128.7–125.9 (Ar*C*H), 85.3 (C1), 82.6 (C3), 78.1 (C2), 77.2 (C6), 76.0 (*C*H$_2$Ph), 74.0 (*C*H$_2$Ph), 72.3 (*C*H$_2$Nap), 69.6 (C5), 67.1 (C4), 24.9 (S*C*H$_2$CH$_3$), 15.3 (SCH$_2$*C*H$_3$). HRMS $C_{33}H_{36}O_5SNa$ [M + Na$^+$] calculated: 567.2182; found: 567.2205.

Ethyl-4-O-acetyl-2,3-di-O-benzyl-6-O-2-naphtylmethyl-1-thio-β-D-galactopyranoside (35)

Compound **34** (150 mg, 0.28 mmol) was dissolved in pyridine (1.90 mL, 0.14 M), cooled to 0 °C, and acetic anhydride (56.0 μL, 0.55 mmol) was added. The solution was stirred for 4 h and the solvent was then removed under reduced pressure and the product was isolated by column chromatography (cyclohexane – ethyl acetate, 4/1 *v*/*v*) to give **35** (159 mg, 99%) as a white foam. $[\alpha]_D$ = +2.1 (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.84–7.26 (m, 17 H, Ar*H*), 5.66 (m, 1H, H-4), 4.81–4.47 (dd × 3, d, 7H, CH_2Ph × 2, CH_2Nap, H-1), 3.75 (t, 1H, H-2, *J* = 6.4 Hz), 3.62–3.55 (m, 4H, H-3, H-5, H-6a, H-6b), 2.75 (m, 2H, SC*H*$_2$CH$_3$), 2.04 (s, 3H, COC*H*$_3$), 1.31 (t, 3H, SCH$_2$CH$_3$, *J* = 7.4 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 170.5 (C=O), 138.3, 137.9, 135.2, 133.4, 133.2 (Ar*C*), 128.5, 128.5, 128.4, 128.4, 128.3, 128.1, 127.9, 127.8, 127.0, 126.3, 126.1, 126.1 (Ar*C*H), 85.6 (C1), 81.2 (C3), 78.0 (C5), 76.0 (C2, *C*H$_2$Ar), 74.0, 72.0 (*C*H$_2$Ar), 68.4 (C6), 67.1(C4), 25.2 (S*C*H$_2$CH$_3$), 21.1 (CO*C*H$_3$), 15.2 (SCH$_2$*C*H$_3$). HRMS $C_{35}H_{38}O_6SNa$ [M + Na$^+$] calculated: 609.2287; found: 609.2294.

2-(Trimethylsilyl)ethyl 2-O-benzyl-3,4-O-isopropylidene-6-O-naphthylmethyl-β-D-galactopyranoside (36)

Compound **13** (1.93 g, 4.70 mmol) was dissolved in DMF (50.0 mL) and cooled to 0 °C under a nitrogen atmosphere. To this

solution, sodium hydride (60% dispersion, 377 mg, 9.41 mmol) was added and the reaction was stirred for 30 min before 2-(bromomethyl)naphthalene (2.08 g, 9.41 mmol) was added. The reaction was stirred at room temperature for 30 min and returned to 0 °C before quenching by addition of MeOH. The solvent was removed and the product was isolated by column chromatography (cyclohexane – ethyl acetate, 4/1 *v*/*v*) to give **36** (2.38 g, 92%) as a clear oil. $[\alpha]_D$ = +15.2 (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.81–7.23 (m, 13H, Ar*H*), 4.84–4.69 (m, 4H, C*H*$_2$Ph, C*H*$_2$Nap), 4.32–4.30 (d, 2H, H-1, *J* = 8.2 Hz), 4.14 (m, 2H, H-3, H-4), 4.06–4.00 (m, 1H, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 3.93 (m, 1H, H-5) 3.82 (m, 2H, H-6a, H-6b) 3.58 (m, 1H, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 3.36 (dd, 1H, H-2, *J* = 8.0, 6.3 Hz), 1.33 (s, 3H, C*H*$_3$), 1.31 (s, 3H, C*H*$_3$), 1.03 (t, 2H, OCH$_2$C*H*$_2$Si(CH$_3$)$_3$, *J* = 8.6 Hz), 0.00 (s, 9H, OCH$_2$CH$_2$Si(C*H*$_3$)$_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 138.6–133.1 (Ar*C*), 128.3–125.8 (Ar*C*H), 110.0 (q*C*), 102.6 (C1), 79.9 (C2), 79.3 (C4), 74.0, 73.9, 73.7 (C3, *C*H$_2$Ph, *C*H$_2$Nap), 72.4 (C5), 69.8 (C6), 67.4 (O*C*H$_2$CH$_2$Si(CH$_3$)$_3$), 27.9 (CH$_3$), 26.6 (CH$_3$), 18.6 (OCH$_2$*C*H$_2$Si(CH$_3$)$_3$), –1.3 (OCH$_2$CH$_2$Si(*C*H$_3$)$_3$). HRMS $C_{32}H_{42}O_6SiNa$ [M + Na$^+$] calculated: 573.2648; found: 573.2649.

2-(Trimethylsilyl)ethyl 2-O-benzyl-endo-3,4-O-benzylidene-6-O-naphthylmethyl-β-D-galactopyranoside (37 **endo***) and 2-(trimethylsilyl)ethyl 2-O-benzyl-exo-3,4-O-benzylidene-6-O-naphthylmethyl-β-D-galactopyranoside (38* **exo***)*

A solution of acetic acid and water (4/1, 200 mL) was added to compound **36** (2.38 g, 4.32 mmol) and the reaction was heated to 80 °C for 2 h. Upon completion, the reaction was cooled to room temperature and poured on to excess ice-cold saturated $NaHCO_3$. The product was extracted with CH_2Cl_2 and washed with saturated $NaHCO_3$ (2 × 100 mL) and water (2 × 100 mL). The organic layer was dried over Na_2SO_4 and the product was purified by filtration through a silica plug. The solvent was removed to give the diol (2.20 g, 99%) as a clear oil. $[\alpha]_D$ = +4.6 (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.81–7.26 (m, 12 H, Ar*H*), 4.96–4.65 (m, 2H, C*H*$_2$Nap), 4.72 (s, 2H, C*H*$_2$Ph), 4.37–4.35 (d, 1H, H-1, *J* = 7.7 Hz), 4.05 (m, 1H, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 3.99 (m, 1H, H-5), 3.83–3.74 (m, 2H, H-6a, H-6b), 3.63–3.54 (m, 3H, H-3, H-4, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 3.47,(dd, 1H, H-2, *J* = 7.9, 6.5 Hz), 2.53, 2.47 (s, 2H, 3-O*H*, 4-O*H*), 1.02 (t, 2H, OCH$_2$C*H*$_2$Si(CH$_3$)$_3$, *J* = 8.6 Hz), –0.00 (s, 9H, OCH$_2$CH$_2$Si(C*H*$_3$)$_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 138.7–135.5 (Ar*C*), 133.2–125.8 (Ar*C*H), 103.3 (C1), 79.4 (C2), 74.7 (*C*H$_2$Nap), 74.0 (*C*H$_2$Ph), 73.4, 73.4 (C3, C4), 69.5 (C6), 69.1 (C5), 67.5 (O*C*H$_2$CH$_2$Si(CH$_3$)$_3$), 18.7 (OCH$_2$*C*H$_2$Si(CH$_3$)$_3$), –1.3 (OCH$_2$CH$_2$Si(*C*H$_3$)$_3$). HRMS $C_{29}H_{38}O_6SiNa$ [M + Na$^+$] calculated: 533.2335; found: 533.2325.

Camphor sulfonic acid (50.0 mg, 0.22 mmol) was added to a stirred solution of the diol (2.20 g, 4.32 mmol) and benzaldehyde dimethyl acetal (1.84 mL, 13.0 mmol) in DMF (30.0 mL) at 0 °C. The reaction was stirred at room temperature for 16 h and quenched by addition of triethylamine at 0 °C. The solvent was removed and the diastereomers were isolated by column chromatography (cyclohexane – ethyl acetate, 6/1 *v*/*v*) to give **37** *endo* and **38** *exo* as clear oils with a ratio of 1:1 (1.99 g, 77%). Analysis for **37** *endo*: $[\alpha]_D$ = +9.2 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.84–7.29 (m, 17H, ArH), 5.95 (s, 1H, C*H*Ph), 4.96–4.86, 4.82–4.70 (2 × dd, 4H, 2 × C*H*$_2$Ar), 4.53 (m, 1H, H-3), 4.44 (d, 1H, H-1, *J* = 7.8 Hz), 4.23 (dd, 1H, H-4, *J* = 6.2, 2.2 Hz), 4.11–4.09 (m, 1H, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 3.94–3.88 (m, 3H, H-5, H-6a, H-6b), 3.70–3.63 (m, 1H OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 3.56 (t, 1H, H-2, *J* = 8.6 Hz), 1.10 (m, 2H, OCH$_2$C*H*$_2$Si(CH$_3$)$_3$), 0.06 (s, 9H, OCH$_2$CH$_2$Si(C*H*$_3$)$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 138.7–133.1 (Ar*C*), 129.3–125.8 (Ar*C*H), 103.5 (Ph*C*H), 102.4 (C1), 80.3 (C3), 77.4 (C2), 74.2 (C4), 73.9, 73.8 (*C*H$_2$Ph, *C*H$_2$Nap), 72.7 (C5), 69.7 (C6), 67.4 (O*C*H$_2$CH$_2$Si(CH$_3$)$_3$), 18.6 (OCH$_2$*C*H$_2$Si(CH$_3$)$_3$), –1.2 (OCH$_2$CH$_2$Si(*C*H$_3$)$_3$). Analysis for **38** exo: $[\alpha]_D$ = +13.6 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.85–7.24 (m, 17H, Ar*H*), 5.91 (s, 1H, C*H*Ph), 4.84–4.73 (m, 4H, C*H*$_2$Ar × 2), 4.44–4.42 (d, 1H, H-1, *J* = 8.0 Hz) 4.35 (t, 1H, H-3, *J* = 6.3 Hz), 4.28–4.26 (dd, 1H, H-4, *J* = 6.2, 2.2 Hz), 4.06 (m, 2H, H-5, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 3.98–3.87 (m, 2H, H-6a, H-6b), 3.66–3.59 (m, 1H, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$) 3.52–3.48 (dd, 1H, H-2, *J* = 7.9, 6.5 Hz), 1.07 (m, 2H OCH$_2$C*H*$_2$Si(CH$_3$)$_3$) 0.04 (s, 9H, OCH$_2$CH$_2$Si(C*H*$_3$)$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 138.5–133.1 (Ar*C*), 129.3–125.8 (Ar*C*H), 104.7 (*C*HPh), 102.6 (C1), 80.5 (C2), 78.9 (C3), 76.3 (C4), 73.9, 73.6 (2 × *C*H$_2$Ar), 72.2 (C5), 69.5 (C6), 67.4 (O*C*H$_2$CH$_2$Si(CH$_3$)$_3$), 18.5 (OCH$_2$*C*H$_2$Si(CH$_3$)$_3$), –1.3(OCH$_2$CH$_2$Si(*C*H$_3$)$_3$). HRMS $C_{38}H_{41}O_6SiNa$ [M + Na$^+$] calculated: 621.2672; found: 621.2672.

2-(Trimethylsilyl)ethyl 2,4-di-O-benzyl-6-O-naphthylmethyl-β-D-galactopyranoside (39)

Method 1

Compound **37** *endo* (940 mg, 1.57 mmol) was dissolved in anhydrous THF (32.0 mL) and Me_3NBH_3 was added (458 mg, 6.28 mmol) to the solution. The reaction was cooled to 0 °C and aluminum chloride (1.26 g, 9.43 mmol) was added. The reaction was stirred for 30 min before water (56.0 μL, 3.14 mmol) was added. The reaction was monitored by TLC and quenched by the addition of excess water. The product was taken up in CH_2Cl_2 and washed with 1 M hydrochloric acid solution (2 × 100 mL), saturated $NaHCO_3$ (2 × 100 mL), and water (2 × 100 mL). The organic layer was then dried over Na_2SO_4 and the product was isolated by column chromatography (cyclohexane – ethyl acetate, 4/1 *v*/*v*) to give **39** (824 mg, 88%) as a clear oil.

Method 2

Compound **38** *exo* (60 mg, 0.10 mmol) was dissolved in 1 M BH_3 in THF (1.00 mL) at 0 °C. To this, 1 M Bu_2BOTf in toluene (0.10 mL) was added. The reaction was stirred for 2 h until the reaction had completed as indicated by TLC (cyclohexane – ethyl acetate, 4/1 *v*/*v*). The reaction was quenched with Et_3N followed by slow addition of MeOH until H_2 evolution ceased. The solvents were removed and the two products were separated by column chromatography using a gradient elution (dichloromethane–methanol, 1/0–5/1 *v*/*v*) to give a 76% yield (45.0 mg) with a 1.2:1 ratio of **39** (24.0 mg) to **40** (20.0 mg).

$[\alpha]_D$ = –8.0 (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.83–7.25 (m, 17H, Ar*H*), 5.01–4.61 (dd × 3, 6H, C*H*$_2$Ph × 2, C*H*$_2$Nap), 4.39–4.37 (d, 1H, H-1, *J* = 7.6 Hz), 4.06–4.00 (m, 1H, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 3.90–3.89 (d, 1H, H-5), 3.70–3.66 (m, 3H, H-4, H-6a, H-6b), 3.60–3.54 (m, 2H, H-2, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 2.67 (s, 1H, H-3), 2.28 (s, 1H, 3-O*H*), 1.04 (m, 2H, OCH$_2$C*H*$_2$Si(CH$_3$)$_3$), 0.02 (s, 9H, OCH$_2$CH$_2$Si(C*H*$_3$)$_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 138.8–133.1 (Ar*C*), 128.6–125.9 (Ar*C*H), 103.4 (C1), 79.9 (C2), 75.7 (C5), 75.1, 74.7, 73.7 (*C*H$_2$Ph × 2, *C*H$_2$Nap), 74.2 (C4), 68.9 (C6), 67.4 (OCH$_2$CH$_2$Si(CH$_3$)$_3$), 54.3 (C3), 18.6 (OCH$_2$CH$_2$Si(CH$_3$)$_3$), –1.3 (OCH$_2$CH$_2$Si(*C*H$_3$)$_3$). HRMS $C_{36}H_{44}O_6SiNa$ [M + Na$^+$] calculated: 623.2805; found: 623.2814.

2-(Trimethylsilyl)ethyl (4-O-acetyl-2,3-di-O-benzyl-6-O-napthylmethyl-D-galactopyranosyl-α(1→3)-2,4-di-O-benzyl-6-O-naphthylmethyl-β-D-galactopyranoside) (41)

Donor **35** (542 mg, 0.93 mmol), acceptor **39** (645 mg, 1.08 mmol), and 4 Å molecular sieves were dried under reduced pressure. To this a solution of Et_2O and CH_2Cl_2 (3/2, 12.0 mL) was added and stirred at room temperature under nitrogen for 30 min and then cooled to 0 °C before adding to the Me_2S_2/Tf_2O promoter (1.35 mL, 1.35 mmol) to the glycosylation reaction. The glycosylation was allowed come to room temperature and after 30 min was quenched by the addition of excess Et_3N. The reaction was diluted with CH_2Cl_2 and washed with 1 M hydrochloric acid (2 × 50 mL), saturated $NaHCO_3$ (2 × 50 mL), and water (2 × 50 mL) and the organic layer was then dried over Na_2SO_4 and the solvent was removed. The α-disaccharide product **41** (966 mg, 92%) was isolated by column chromatography (toluene – ethyl acetate, 6/1 *v*/*v*) as a clear oil with no β-disaccharide observed. $[\alpha]_D$ = +35.4 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.84–7.07 (m, 34H, Ar*H*), 5.36–5.35 (d, 1H, H-4′, *J* = 3.40 Hz), 5.20–5.19 (d, 1H, H-1′, *J* = 3.4 Hz), 5.01–4.37 (6 × dd, 12H, C*H*$_2$Ar), 4.46 (m, 1H, H-5), 4.28–4.26 (d, 1H, H-1, *J* = 7.8 Hz), 3.99–3.90 (m, 3H, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$, H-3′, H-5),

3.88–3.84 (dd, 1H, H-2′, *J* = 10.0, 3.4 Hz), 3.79–3.78 (m, 2H, H-2, H-4), 3.57–3.56 (m, 2H, H-3, H-6a), 3.51–3.44 (m, 1H, H-6b, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 3.41–3.37 (dd, 1H, H-6a′, *J* = 10.0, 6.5 Hz), 3.28–3.25 (dd, 1H, H-6b′, *J* = 10.1 5.7 Hz), 1.01 (m, 2H, OCH$_2$C*H*$_2$Si(CH$_3$)$_3$), 0.95 (s, 9H, OCH$_2$CH$_2$Si(C*H*$_3$)$_3$). ^{13}C NMR (101 MHz, CDCl$_3$) δ: 170.5 (C=O), 139.0, 138.9, 138.4, 138.3, 138.0, 135.8, 135.7, 133.4, 133.38, 133.1, 133.0 (Ar*C*), 129.2–125.4 (Ar*C*H), 103.9 (C1), 95.8 (C1′), 78.5, 77.9, 76.6, 75.7, 73.4, 72.7, 67.4, 68.5 (C2, C2′, C3, C3′, C4, C4′, C5, C5′), 75.21, 74.6, 74.57, 73.7, 73.1, 71.8 (6 × *C*H$_2$Ar), 68.9, 68.8 (C6, C6′), 67.5 (OCH$_2$CH$_2$Si(CH$_3$)$_3$), 21.1 (CO*C*H$_3$), 18.7 (OCH$_2$CH$_2$Si(CH$_3$)$_3$), –1.3 (OC*H*$_2$CH$_2$Si(*C*H$_3$)$_3$). HRMS C$_{69}$H$_{76}$O$_{12}$SiNa [M + Na$^+$] calculated: 1147.5004; found: 1147.4982.

2-(Trimethylsilyl)ethyl (2,3-di-O-benzyl-6-O-napthylmethyl-D-galactopyranosyl-α(1→3)-2,4-di-O-benzyl-6-O-naphthylmethyl-β-D-galactopyranoside) (42)

Disaccharide **41** (920 mg, 0.82 mmol) was dissolved in a solution of MeOH–CH$_2$Cl$_2$ (9/1 *v*/*v*, 20.0 mL), cooled to 0 °C, and a catalytic quantity of NaOMe (4.50 mg, 0.08 mmol) was added. The reaction was stirred for 3 h and Amberlite IR-150 H$^+$ resin was added until pH 7 was achieved. The resin was filtered off and the solvent was removed. The product was purified by column chromatography (toluene – ethyl acetate, 6/1 *v*/*v*) to give **42** (877 mg, 99%) as a clear oil. [α]$_D$ = +16.7 (*c* 1.0, CHCl$_3$). ^{1}H NMR (400 MHz, CDCl$_3$) δ: 7.80–7.10 (m, 34H, Ar*H*), 5.21–5.20 (d, 1H, H-1′, *J* = 3.4 Hz), 5.04–4.37 (6 × dd, 12H, C*H*$_2$Ar), 4.28 (m, 2H, H-1, H-5) 4.02–3.86 (m, 4H, H-2′, H-3′, H-5′, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 3.81–3.77 (m, 3H, H-4′, H-2, H-4), 3.58–3.57 (m, 2H, H-6a, H-6b), 3.53–3.45 (m, 4H, H-6a′, H6-b′, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$, H-3), 0.98 (m, 2H, OCH$_2$C*H*$_2$Si(CH$_3$)$_3$), 0.00 (s, 9H, OCH$_2$CH$_2$Si(C*H*$_3$)$_3$). ^{13}C NMR (101 MHz, CDCl$_3$) δ: 139.1, 139.0, 138.4, 135.7, 135. 7, 133.4, 133.1, 133.06 (Ar*C*), 129.2–125.7 (Ar*C*H), 103.9 (C1), 95.4 (C1′), 78.6, 77.9, 77.6, 75.9, 73.3, 72.7, 68.6, 67.9 (C2, C2′, C3, C3′, C4, C4′, C5, C5′), 75.2, 74.6, 74.6, 73.6, 73.4, 72.1 (6 × *C*H$_2$Ar), 70.3, 68.9 (C6, C6′), 67.5 (OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 18.7 (OCH$_2$C*H*$_2$Si(CH$_3$)$_3$), –1.3 (OCH$_2$CH$_2$Si(*C*H$_3$)$_3$). HRMS C$_{67}$H$_{74}$O$_{11}$SiNa [M + Na$^+$] calculated: 1105.4898; found: 1105.4854.

2-(Trimethylsilyl)ethyl (4-azido-2-N-Boc-2,3-N,O-carbonyl-2,4,6-trideoxy-D-galactopyranosyl-α(1→4)-2,3-di-O-benzyl-6-O-napthylmethyl-D-galactopyranosyl-α(1→3)-2,4-di-O-benzyl-6-O-naphthylmethyl-β-D-galactopyranoside) (43)

Donor **24** (144 mg, 0.40 mmol), disaccharide acceptor **42** (299 mg, 0.28 mmol), and 4 Å molecular sieves were dried under reduced pressure. CH$_2$Cl$_2$ (4.20 mL) was then added and the reaction was cooled to 0 °C. *N*-iodosuccinimde (180 mg, 0.80 mmol) was added to the reaction followed by silver triflate (41.3 mg, 0.16 mmol). The reaction was quenched after 1 h by addition of 10% sodium thiosulfate solution (5.00 mL). The reaction was diluted with CH$_2$Cl$_2$ and the organic layer was washed with saturated NaHCO$_3$ (3 × 25 mL) and water (2 × 25 mL) before being dried over Na$_2$SO$_4$. The solvent was filtered off and then removed. The unreacted acceptor (110 mg) was recovered and the product was isolated by column chromatography (toluene – ethyl acetate, 16/1 *v*/*v*) to give **43** (193 mg, 51%) as a clear oil. [α]$_D$ = +79.7 (*c* 1.0, CHCl$_3$). ^{1}H NMR (500 MHz, CDCl$_3$) δ: 7.83–7.14 (m, 34H, Ar*H*), 5.53–5.52 (d, 1H, H-1″, *J* = 2.8 Hz), 5.25–5.24(d, 1H, H-1′, *J* = 3.0 Hz), 5.02–4.54 (m, 11 H, 5 × C*H*$_2$Ar, H-3″) 4.42–4.29 (m, C*H*$_2$Ar, H-5′, H-4′), 4.26–4.24 (d, 1H, H-1, *J* = 7.0 Hz), 4.20–4.17 (dd, 1H, H-2″, *J* = 12.0, 2.6 Hz), 4.11(m, 1H, H-3′), 3.97–3.90 (m, 4H, H-5″, H-2′, H-3, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 3.79–3.72 (m, 3H, H-4″, H-5, H-2), 3.61–3.57 (m, 2H, H-6a,b′), 3.52–3.36 (m, 3H, H-4, H-6a,b, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 1.55 (s, 9H, C(C*H*$_3$)$_3$), 1.02–0.90 (m, 5H, H6a,b,c″, OCH$_2$C*H*$_2$Si(CH3)$_3$), –0.00 (s, 9H, OCH$_2$CH$_2$Si(C*H*$_3$)$_3$). ^{13}C NMR (126 MHz, CDCl$_3$) δ: 151.6, 151.0 (2 × C=O), 139.03, 139.0, 138.4, 138.0, 136.0, 135.6, 133.39, 133.37, 133.2, 133.0 (10 × Ar*C*), 129.2–125.4 (Ar*C*H), 103.9 (C1), 96.2 (C1″), 95.2 (C1′), 84.8 (*C*(CH$_3$)$_3$), 75.0, 74.6, 73.9, 73.7, 73.2, 72.4 (6 × C*H*$_2$Ar), 78.5, 78.1, 76.9, 76.0, 74.0, 73.3, 68.8, 73.0, 67.1 (C2, C2′, C3, C3′, C3″, C4, C4′, C5, C5′, C5″), 72.7 (C6′), 68.6, 67.5 (C6), 67.4 (OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 62.4 (H4″), 56.3 (C2″), 28.2 (C(*C*H$_3$)$_3$), 18.6 (OCH$_2$*C*H$_2$Si(CH$_3$)$_3$), 17.0 (C6″), –1.3 (OCH$_2$CH$_2$Si(*C*H$_3$)$_3$). HRMS C$_{79}$H$_{90}$N$_4$O$_{16}$SiNa [M + Na$^+$] calculated: 1401.6019; found: 1401.6027.

2-(Trimethylsilyl)ethyl (2-N-acetyl-4-azido-2,3-N,O-carbonyl-2,4,6-trideoxy-D-galactopyranosyl-α(1→4)-2,3-di-O-benzyl-6-O-napthylmethyl-D-galactopyranosyl-α(1→3)-2,4-di-O-benzyl-6-O-naphthylmethyl-β-D-galactopyranoside) (44)

Donor **25** (42.0 mg, 0.07 mmol) was dissolved in CH$_2$Cl$_2$ (1.50 mL) and added dropwise to a stirred solution of acceptor **42** (53.0 mg, 0.05 mmol), NIS (33.0 mg, 0.15 mmol), and AgOTf (7.00 mg, 0.03 mmol) in CH$_2$Cl$_2$ at 0 °C. The addition was carried out over 2 h and the reaction was subsequently quenched with Et$_3$N. The reaction was then diluted in CH$_2$Cl$_2$ and washed with Na$_2$S$_2$O$_3$ (2 × 5 mL, 10% aqueous solution). The organic layer was dried over Na$_2$SO$_4$, filtered, and the solvent was removed. The crude was purified by column chromatography using a gradient elution (toluene – ethyl acetate, 16/1–8/1 *v*/*v*) to give trisaccharide **44** (48.0 mg, 76%). [α]$_D$ = +72.0 (*c* 1.0, CHCl$_3$). ^{1}H NMR (500 MHz, CDCl$_3$) δ: 7.83–7.15 (m, 34H, Ar*H*), 5.64–5.63 (d, 1H, H-1″, *J* = 2.6 Hz), 5.25 (d, 1H, H-1′, *J* = 2.7 Hz), 5.04–4.41 (6 × dd, 16H, C*H*$_2$Ar), 4.71–4.69 (dd, 1H, H-3″, *J* = 12.0, 2.8 Hz), 4.35–4.31 (m, 2H, H-5″, H-4′), 4.28–4.27 (d, 1H, H-1, *J* = 7.6 Hz), 4.21–4.18 (dd, 1H, H-2″, *J* = 12.1, 2.6 Hz), 4.04 (m, 1H, H-3′), 3.97–3.92 (m, 2H, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$, H-3), 3.91–3.90 (m, 2H, H-2′, H-5′), 3.82–3.81 (t, 1H, H-4″, *J* = 8.3 Hz), 3.79–3.78 (m, 2H, H-2, H-5), 3.62–3.60 (m, 2H, H-6′a/b), 3.54–3.46 (m, 2H, H-4, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 3.43–3.27 (m, 2H, H-6a/b), 2.50 (s, 3H, CH$_3$), 1.03–0.90 (m, 3H, OCH$_2$C*H*$_2$Si(CH$_3$)$_3$, H-6″a-c), 0.00 (s, 8H, OCH$_2$CH$_2$Si(C*H*$_3$)$_3$). ^{13}C NMR (126 MHz, CDCl$_3$) δ: 172.1 (*C*OOCH$_3$), 153.2 (C=O), 139.1, 138.9, 138.4, 138.0, 136.0, 135.6, 133.4, 133.4, 133.1, 133.0 (10 × Ar*C*), 128.6–125.8 (Ar*C*H), 103.9 (C1), 96.3 (C1″), 95.0 (C1′), 78.4 (C2), 77.9 (C5), 77.0 (C2′), 75.7 (C5′), 75.0 (*C*H$_2$Ar), 74.6 (*C*H$_2$Ar), 74.3 (C3′), 73.8 (*C*H$_2$Ar), 73.7 (*C*H$_2$Ar), 73.3 (C3″), 73.3 (C4), 73.1 (*C*H$_2$Ar), 72.9 (C3), 72.6 (*C*H$_2$Ar), 68.8 (C4′, C6′), 67.9 (C6), 67.5 (OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 67.1 (C5″), 62.4 (C4″), 56.2 (C2″), 24.0 (*C*H$_3$), 18.6 (OCH$_2$*C*H$_2$Si(CH$_3$)$_3$), 17.0 (C6″), –1.3 (OCH$_2$CH$_2$Si(*C*H$_3$)$_3$). HRMS C$_{76}$H$_{84}$N$_4$O$_{15}$SiNa [M + Na$^+$] calculated: 1343.5600; found: 1343.5660.

2-(Trimethylsilyl)ethyl (4-azido-2-N-Boc-2,4,6-trideoxy-D-galactopyranosyl-α(1→4)-2,3-di-O-benzyl-6-O-napthylmethyl-D-galactopyranosyl-α(1→3)–2,4-di-O-benzyl-6-O-naphthylmethyl-β-D-galactopyranoside) (45)

Trisaccharide **43** (30.0 mg, 0.02 mmol) was dissolved in methanol–dichloromethane (10/1, 3.00 mL) and a catalytic quantity of NaOMe was added. The reaction was stirred for 1 h and Amberlite IR-150 H$^+$ resin was added until pH 7 was achieved. The resin was filtered off and the solvent was removed. The product was purified by column chromatography (toluene – ethyl acetate, 6/1 *v*/*v*) to give **45** (27.0 g, 92%) as a clear oil. [α]$_D$ = +19.5 (*c* 1.0, CHCl$_3$). ^{1}H NMR (500 MHz, CDCl$_3$) δ: 7.83–7.16 (m, 34H, Ar*H*), 5.22–5.21 (d, 1H, H-1′, *J* = 3.3 Hz), 5.03 – 4.49 (m, 13H, 6 × C*H*$_2$Ar, H-1″), 4.40–4.37 (m, 3H, C*H*$_2$Ar, H-4′), 4.29–4.28 (d, 1H, H-1, *J* = 7.0 Hz), 4.20 (m, 1H, H-5′), 4.01–3.70 (m, 8H, H-2, H-2′, H-3, H-3′, H-3″, H5, H5″, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 3.61 (m, 3H, H-4″, H-6a,b′), 3.53–3.47 (m, 2 H, H-4, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 3.34–3.24 (m, 2H, H-6a,b), 1.44 (s, 9H, C(C*H*$_3$)$_3$), 0.95 (m, OCH$_2$C*H*$_2$Si(CH$_3$)$_3$, H-6a-c″), 0.00 (s, 9H, OCH$_2$CH$_2$Si(C*H*$_3$)$_3$). ^{13}C NMR (126 MHz, CDCl$_3$) δ: 158.0 (C=O), 139.0, 138.9, 138.5, 138.0, 135.6, 135.1, 133.4, 133.3, 133.1 (Ar*C*), 128.5–125.8 (Ar*C*H), 103.9 (C1), 98.0 (C1″), 95.6 (C1′), 80.7 (*C*(CH$_3$)$_3$), 75.1, 74.7, 74.3, 73.7, 73.2, 72.7 (C*H*$_2$Ar), 78.4, 78.2, 77.0, 76.0, 74.5, 73.3, 73.0, 68.7, 67.0, 65.6 (C2, C2′, C3, C3′, C4, C4′, C4″, C5, C5′, C5″), 72.0 (C3″), 68.8 (C6′), 68.0 (C6), 67.5 (OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 52.1 (C2″), 28.5 (C(*C*H$_3$)$_3$), 18.6 (OCH$_2$*C*H$_2$Si(CH$_3$)$_3$), 17.5 (C6″), –1.3 (OCH$_2$CH$_2$Si(*C*H$_3$)$_3$). HRMS C$_{78}$H$_{92}$N$_4$O$_{15}$SiNa [M + Na$^+$] calculated: 1375.6226; found: 1375.6210.

2-(Trimethylsilyl)ethyl (4-azido-2-N-Boc-2,4,6-trideoxy-D-galactopyranosyl-α(1→4)-2,3-di-O-benzyl-D-galactopyranosyl-α(1→3)-2,4-di-O-benzyl-β-D-galactopyranoside) (46)

Trisaccharide **45** (51.0 mg, 0.04 mmol) was dissolved in dichloromethane–methanol (1 mL, 10/1 *v*/*v*) and to this, DDQ (33.0 mg, 0.11 mmol) was added. The reaction was stirred for 7 h at room temperature and monitored by TLC (toluene – ethyl acetate, 1/1 *v*/*v*). The reaction was diluted with CH_2Cl_2 and washed with $NaHCO_3$ (2 × 10 mL) and $Na_2S_2O_3$ (2 × 10 mL, 10% aqueous solution). The organic phase was dried over Na_2SO_4, filtered, and the solvent was removed. The product was isolated by column chromatography (toluene – ethyl acetate, 1/1 *v*/*v*) to give **46** as a clear oil (25.0 mg, 62%). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.42–7.16 (m, 20H, Ar*H*), 5.12–5.11 (d, 1H, H-1″, *J* = 3.5 Hz), 5.00–4.70 (m, 6H, C*H*$_2$Ph, H-1′), 4.47–4.32 (m, 4 H, C*H*$_2$Ph, H-1, H-3″), 4.00–3.73 (m, 11H, H-2, H-2′, H-2″, H-3, H-3′, H-4, H-4′, H-4″, H-5″, H-6b′, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 3.59–3.45(m, 3H, H-6a′, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$, H-5′), 3.37 (m, 1H, H-5), 3.26–3.06 (m, 2H, H-6ab), 1.44 (s, 9H, C(C*H*$_3$)$_3$), 1.08 (d, 3H, H-6a-c″, *J* = 6.3 Hz), 1.00 (m, 2H, OCH$_2$C*H*$_2$Si(CH$_3$)$_3$), 0.00 (s, 9H, OCH$_2$CH$_2$Si(C*H*$_3$)$_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 138.7–137.9 (Ar*C*), 129.2–125.4 (Ar*C*H), 104.0 (C1), 98.3 (C1″), 95.6 (C1′), 74.7, 74.5, 74.47, 72.7 (*C*H$_2$Ph), 78.6, 78.2, 76.9, 76.1, 75.5, 74.4, 72.7, 71.8, 70.4, 67.7, 66.9 (C2, C2′, C3, C3′, C3″, C4, C4′, C4″, C5, C5′, C5″), 65.7 (C6′), 62.1 (C6), 54.9 (C2″), 28.5 (C(*C*H$_3$)$_3$), 18.8 (OCH$_2$*C*H$_2$Si(CH$_3$)$_3$), 17.5 (C6″), –1.3 (OCH$_2$CH$_2$Si(*C*H$_3$)$_3$) HRMS $C_{56}H_{72}N_4O_{15}SiNa$ [M + Na$^+$] calculated: 1095.4974; found: 1095.4969.

2-(Trimethylsilyl)ethyl (4-azido-2-N-Boc-2,4,6-trideoxy-D-galactopyranosyl-α(1→4)-benzyl (2,3-di-O-benzyl-D-galactopyranosyl) uronate-α(1→3)-benzyl (2,4-di-O-benzyl-β-D-galactopyranoside) uronate) (47)

Bisacetoxyiodo benzene (18.0 mg, 0.06 mmol) was added to a biphasic solution of CH_2Cl_2 and water (0.50 mL, 2/1 *v*/*v*) containing **46** (24.0 mg, 0.02 mmol). The solution was cooled to 0 °C and TEMPO (1 mg, 4.40 μmol) was added. The reaction was stirred vigorously for 4 hand then quenched by addition of 10% sodium thiosulfate solution (20.0 mL). The mixture was diluted with CH_2Cl_2 and the organic phase was washed with saturated sodium bicarbonate solution (2 × 50.0 mL) and water (2 × 50.0 mL). After drying over sodium sulphate and filtration, the solvent was removed from the organic layer. The crude material was dried under reduced pressure before dissolving in DMF (1.0 mL). The solution was cooled to 0 °C and benzyl bromide (7.00 μL, 0.06 mmol) and cesium fluoride (8.80 mg, 0.06 mmol) were added. The reaction was stirred for 48 h following which the solvents were removed and the crude was purified by column chromatography (toluene – ethyl acetate, 6/1 *v*/*v*) to give **47** (16.0 mg, 57%) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.07–7.05 (m, 30H, Ar*H*), 5.26–5.25 (d, 1H, H-1″), 5.17–4.98 (m, 4H, C*H*$_2$Ph), 4.84 – 4.68 (m, 6H), 4.59–4.56 (d, 1H, C*H*$_2$Ph), 4.42–4.40 (d, 1H), 4.33–4.31 (d, 2H), 4.26 (s, 1H), 4.23 (s, 1H), 4.10–4.04 (m, 2H), 4.02 (s, 1H), 3.93 (s, 1H), 3.85–3.82 (dd, 1H), 3.80–3.79 (m, 2H), 3.77–3.70 (m, 3H), 3.60–3.50 (m, 2H), 1.48 (s, 9H, C(C*H*$_3$)$_3$), 1.03–0.95 (m, 5H, H-6a-c″, OCH$_2$C*H*$_2$Si(CH$_3$)$_3$), –0.01 (OCH$_2$CH$_2$Si(C*H*$_3$)$_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 129.9–127.3 (Ar*C*, Ar*C*H), 103.3 (C1), 99.2 (C1″), 94.5 (C1′), 75.0, 74.6, 74.0, 72.8 (4 × *C*H$_2$Ph), 77.3, 76.7, 76.5, 75.9, 74.3, 74.2, 73.7, 72.1, 70.1, 66.7, 65.7 (C2, C2′, C3, C3′, C3″, C4, C4′, C4″, C5, C5′, C5″), 67.2, 66.9 (COOC*H*$_2$Ph), 67.7 (O*C*H$_2$CH$_2$Si(CH$_3$)$_3$), 51.5 (C2″), 28.3 (C(*C*H$_3$)$_3$), 18.3 (OCH$_2$*C*H$_2$Si(CH$_3$)$_3$), 17.1 (C6″), –1.2 (OCH$_2$CH$_2$Si(*C*H$_3$)$_3$). HRMS $C_{70}H_{84}N_4O_{17}SiNa$ [M + Na$^+$] calculated: 1303.5498; found: 1303.5540.

Ethyl 6-O-benzoyl-2,3-di-O-benzyl-1-thio-β-D-galactopyranoside (48)

Compound **8** (4.71 g, 11.6 mmol) was dissolved in pyridine (82.0 mL) and cooled to –20 °C. A dilute solution of benzoyl chloride (1.42 mL, 12.2 mmol in 10 mL pyridine) was added dropwise over 30 min. The reaction was stirred for 1 h and monitored by TLC (cyclohexane – ethyl acetate, 2/2 *v*/*v*). Upon completion, the reaction was poured onto ice water and extracted with ethyl acetate. The organic layer was washed with aqueous 1 M HCl (3 × 200 mL), saturated $NaHCO_3$ (2 × 200 mL), and water (1 × 200 mL). It was then dried over Na_2SO_4, filtered, and the solvent was removed. The crude was then purified by column chromatography (cyclohexane – ethyl acetate, 4/1 *v*/*v*) to give **48** (4.317 g, 73%) as a clear oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.02–7.27 (m, 15H, Ar*H*), 4.88–4.73 (m, 2H, C*H*$_2$Ph), 4.75–4.68 (m, 2H, C*H*$_2$Ph), 4.61–4.51 (m, 2H, H-6a, H-6b), 4.45–4.43 (d, 1H, H-1, *J* = 9.6 Hz), 4.02 (s, 1H, H-4), 3.75–3.72 (t, 1H, H-5), 3.69–3.64 (t, 1H, H-2), 3.58–3.55 (dd, 1H, H-3), 2.81–2.64 (m, 2H, SC*H*$_2$CH$_3$), 2.48 (s, 1H, O*H*), 1.27 (t, 3H SCH$_2$C*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 166.3 (C=O), 138.0, 137.6, 133.1 (Ar*C*), 129.7, 128.6, 128.4, 128.1, 127.9 (Ar*C*H), 85.1 (C1), 82.2 (C3), 77.8 (C2), 75.8 (*C*H$_2$Ph), 75.6 (C5), 72.5 (*C*H$_2$Ph), 66.8 (C4), 63.6 (C6), 24.9 (S*C*H$_2$CH$_3$), 15.1 (SCH$_2$*C*H$_3$). Data recorded were in accordance with those that were found in the literature[42].

Ethyl 4-O-chloroacetyl-2,3-di-O-benzyl-6-O-2-naphtylmethyl-1-thio-β-D-galactopyranoside (49)

Chloroacetyl chloride (1.35 mL, 17.0 mmol) was added dropwise to a stirred solution of **48** (4.32 g, 8.49 mmol) and pyridine (4.00 mL) in CH_2Cl_2 (60.0 mL). The solution was stirred for 1.5 h and monitored by TLC (cyclohexane – ethyl acetate, 4/1 *v*/*v*). The reaction was diluted with dichloromethane and poured onto ice water. The organic layer was then washed with saturated $NaHCO_3$ and brine and then dried over Na_2SO_3. The solvent was removed and the product was isolated by column chromatography (cyclohexane – ethyl acetate, 4/1 *v*/*v*) to give **49** (4.17 g, 82%) as a white foam. $[\alpha]_D$ = –1.1 (c 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.04–7.26 (m, 15H, ArH), 5.69–5.68 (d, 1H, H-4, *J* = 3.2 Hz), 4.84–4.74 (m, 3H, C*H*$_2$Ph), 4.56–4.52 (m, 3H, C*H*$_2$Ph, H-1, H-6a), 4.34–4.31 (m, 1H, H-6b), 4.24–4.17 (m, 2H, C*H*$_2$Cl), 3.95 (td, 1H, H-5, *J* = 6.8, 0.7 Hz), 3.70–3.67 (dd, 1H, H-3, *J* = 9.2, 3.3 Hz), 3.61 (t, 1H, H-2, *J* = 9.7 Hz), 2.82–2.69 (m, 2H, SC*H*$_2$CH$_3$), 1.31 (t, 3H, SCH$_2$C*H*$_3$, *J* = 7.4 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 167.2, 166.2 (C=O), 138.0, 137.4, 133.5 (Ar*C*), 129.9–128.0 (Ar*C*H), 85.6 (C1), 80.8 (C3), 77.7 (C2), 76.1 (*C*H$_2$Ph), 74.2 (*C*H$_2$Ph), 72.6 (C5), 69.1 (C4), 62.2 (C6), 41.0 (*C*H$_2$Cl), 25.2 (S*C*H$_2$CH$_3$), 15.3 (SCH$_2$*C*H$_3$) HRMS $C_{31}H_{33}O_7SClNa$ [M + Na$^+$] calculated: 607.1533; found: 607.1212.

2-(Trimethylsilyl)ethyl 2-O-benzyl-4,6-O-benzylidene-β-D-galactopyranoside (50, 51)

Compound **12** (5.20 g, 12.7 mmol) was dissolved in a solution of acetic acid and water (90.0 mL, 4/1 *v*/*v*) and heated to 80 °C for 4 h. The reaction was monitored by TLC and upon complete hydrolysis of the acetal, the reaction was diluted with ethyl acetate and washed with water and $NaHCO_3$. The organic layer was dried over Na_2SO_4, filtered and the solvent was removed to give the crude triol. Triol **50** (4.69 g, 12.7 mmol) was dissolved in DMF (90.0 mL) and PhCH(OMe)$_2$ (3.80 mL, 25.4 mmol) was added. The solution was cooled to 0 °C and CSA (60.0 mg, 0.25 mmol) was added. The reaction was stirred at room temperature for 3 days and then quenched by addition of triethylamine. The solution was poured onto ice water (500 mL) and extracted with ethyl acetate (3 × 200 mL). The organic phase was dried over Na_2SO_3, the solvent was removed, and the crude was purified by column chromatography (cyclohexane – ethyl acetate, 4/1 *v*/*v*) to yield **51** (3.98 g, 70%) as a clear oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.53–7.28 (m, 10H, Ar*H*), 5.56 (s, 1H, C*H*Ph), 5.01–4.72 (dd, 2H, C*H*$_2$Ph), 4.42–4.40 (d, 1H, H-1), 4.36–4.32 (d, 1H, H-6a), 4.22–4.21 (d, 1H, H-4), 4.11–4.04 (m, 2H, H-6b, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 3.76–3.71 (m, 1H, H-3), 3.64–3.55 (m, 2H, H2, OCH$_2$C*H*$_2$Si(CH$_3$)$_3$), 3.44 (s, 1H, H-5), 2.49–2.47 (d, 1H, OH), 1.08–1.03 (m, 2H, OCH$_2$C*H*$_2$Si(CH$_3$)$_3$), 0.04 (t, 9H, OCH$_2$CH$_2$Si(C*H*$_3$)$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 138.9, 137.8 (2 × Ar*C*), 129.3–126.7 (Ar*C*H), 103.3 (C1), 101.6 (*C*HPh), 79.5 (C2), 75.7 (C4), 75.0 (*C*H$_2$Ph), 72.7 (C3), 69.4 (C6), 67.6 (O*C*H$_2$CH$_2$Si(CH$_3$)$_3$), 66.6 (C5), 18.6 (OCH$_2$*C*H$_2$Si(CH$_3$)$_3$), –1.3 (OCH$_2$CH$_2$Si(*C*H$_3$)$_3$). Data recorded were in accordance with those that were found in the literature[43].

2-(Trimethylsilyl)ethyl 2,4-di-O-benzyl-β-D-galactopyranoside (52)

Method 1

Benzylidene protected **51** was dissolved in a solution of 1 M BH_3 in THF (5.30 mL) at 0 °C and to this, 1 M Bu_2OTf in toluene (0.75 mL) was added. The solution was quenched with Et_3N after 30 min and MeOH was added dropwise. Once liberation of H_2 had ceased, the solvent was removed with coevaporation of MeOH. Column chromatography gave a mixture of the 4-OBn and 6-OBn product in a 2:1 ratio, 68% yield.

Method 2

Compound **55** (2.04 g, 4.06 mmol) was dissolved in MeOH (30.0 mL) cooled to 0 °C and NaOMe was added until pH 9 was reached. Upon completion of the reaction, Amberlite IR-150H$^+$ resin was added until pH 7 was achieved and the solution was filtered from the resin. The solvent was removed and the crude was purified by column chromatography (cyclohexane – ethyl acetate, 2/1 *v*/*v*) to give **52** (1.80 g, 97%) as a clear oil.

$[\alpha]_D$ = –3.1 (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.39–7.30 (m, 10H, Ar*H*), 5.02–5.00 (d, 1H, C*H*$_2$Ph), 4.85–4.83 (d, 1H, C*H*$_2$Ph), 4.71–4.65 (m, 2H, C*H*$_2$Ph), 4.39–4.37 (d, 1H, H-1, *J* = 7.8 Hz), 4.04–3.98 (m, 1H, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 3.83–3.78 (m, 2H, H-6a, H-5), 3.69–3.65 (m, 1H, H-3), 3.63–3.55 (m, 3H, H-2, H-6b, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 3.48–3.46 (m, 1H, H-4), 2.37 (d, 1H, C3-O*H*, *J* = 4.0 Hz), 1.66–1.64 (dd, 1H, C6-O*H*, *J* = 8.7, 4.0 Hz), 1.03 (m, 2H, OCH$_2$C*H*$_2$Si(CH$_3$)$_3$), 0.02 (s, 9H, OCH$_2$CH$_2$Si(C*H*$_3$)$_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 138.7, 138.3 (Ar*C*), 128.7–128.0 (Ar*C*H), 103.5 (C1), 79.7 (C2), 74.9, 74.9, 74.8, 74.76 (C4, C5, *C*H$_2$Ph, *C*H$_2$Ph), 74.4 (C3), 67.6 (O*C*H$_2$CH$_2$Si(CH$_3$)$_3$), 62.2 (C6), 18.7 (OCH$_2$*C*H$_2$Si(CH$_3$)$_3$), –1.3 (OCH$_2$CH$_2$Si(*C*H$_3$)$_3$). HRMS $C_{25}H_{36}O_6SiNa$ [M + Na$^+$] calculated: 483.2179; found: 483.2172.

2-(Trimethylsilyl)ethyl 3-O-acetyl-2-O-benzyl-4,6-O-benzylidene-β-D-galactopyranoside (54)

Compound **51** (3.48 g, 7.59 mmol) was dissolved in pyridine (55.0 mL), cooled to 0 °C, and acetic anhydride (10.0 mL) was added. The reaction was stirred at room temperature for 2 h. The solvent was removed under reduced pressure and the product was isolated by column chromatography (cyclohexane – ethyl acetate, 4/1 *v*/*v*) to yield **54** (3.11 g, 82%) as a clear oil. $[\alpha]_D$ = +71.8 (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.47–7.20 (m, 10H, Ar*H*), 5.44 (s, 1H, C*H*Ph), 4.89–4.85 (m, 2H, C*H*$_2$Ph, H-3), 4.62–4.59 (d, 1H, C*H*$_2$Ph), 4.44–4.42 (d, 1H, H-1, *J* = 7.7 Hz), 4.30 – 4.26 (m, 2H, H-4, H-6a) 4.05–3.98 (m, 2H, H-6b, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 3.79–3.76 (dd, 1H, H-2, *J* = 10.2, 7.4 Hz), 3.57–3.52 (m, 1H, OCH$_2$C*H*$_2$Si(CH$_3$)$_3$), 3.42 (s, 1H, H-5), 2.00 (s, 3H, COC*H*$_3$), 1.02–0.98 (m, 2H, OCH$_2$C*H*$_2$Si(CH$_3$)$_3$), –0.02 (s, 9H, OCH$_2$CH$_2$Si(C*H*$_3$)$_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 171.0 (C=O), 138.9, 137.9 (Ar*C*), 129.1–126.5 (Ar*C*H), 103.3 (C1), 101.2 (*C*HPh), 76.6 (C2), 75.0 (*C*H$_2$Ph), 74.0 (C4), 73.7 (C3), 69.2 (C6), 67.7 (O*C*H$_2$CH$_2$Si(CH$_3$)$_3$), 66.2 (C5), 21.2 (COCH$_3$), 18.6 (OCH$_2$*C*H$_2$Si(CH$_3$)$_3$), –1.3 (OCH$_2$CH$_2$Si(*C*H$_3$)$_3$). HRMS $C_{27}H_{36}O_7SiNa$ [M + Na$^+$] calculated: 523.2128; found: 523.2134.

2-(Trimethylsilyl)ethyl 3-O-acetyl–2,4-di-O-benzyl-β-D-galactopyranoside (55)

Benzylidene protected **54** (2.85 g, 5.69 mmol) was dissolved in a cold solution of 1 M BH_3 in THF (20.0 mL). The reaction was cooled to 0 °C and a 1 M Bu_2BOTf in toluene (5.70 mL) was added and the reaction was stirred for 1 h. The reaction was quenched by addition of triethylamine and MeOH was added dropwise until the evolution of H_2 ceased. The solvent was removed under reduced pressure and coevaporated three times with MeOH. Column chromatography was carried out using a gradient elution (cyclohexane – ethyl acetate, 10/1–3/1 *v*/*v*) to give **55** (2.04 g, 70%) as an opaque oil. $[\alpha]_D$ = +67.2 (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.34–7.27 (m, 10H, Ar*H*), 4.90–4.87 (m, 2H, C*H*$_2$Ph, H-3), 4.67–4.64 (q, 2H, C*H*$_2$Ph), 4.50–4.47 (d, 1H, C*H*$_2$Ph), 4.43–4.42 (d, 1H, H-1, *J* = 7.7 Hz), 4.03–3.97 (m, 1H, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 3.86 (d, 1H, H-4, *J* = 3.0 Hz), 3.79–3.74 (m, 2H, H-6a, H-2), 3.60–3.50 (m, 3H, H-5, H-6b, OCH$_2$C*H*$_2$Si(CH$_3$)$_3$), 2.34 (s, 1H, O*H*), 1.95 (s, 3H, COC*H*$_3$), 1.04–1.00 (m, 2H, OCH$_2$C*H*$_2$Si(CH$_3$)$_3$), 0.00 (t, 9H, OCH$_2$CH$_2$Si(C*H*$_3$)$_3$, *J* = 8.7 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 170.6 (C=O), 138.8, 137.8 (2 × Ar*C*), 129.2–127.7 (Ar*C*H), 103.6 (C1), 77.1 (C2), 75.4 (C3), 74.9 (*C*H$_2$Ph), 74.9 (*C*H$_2$Ph), 74.5 (C5), 74.0 (C4), 67.8 (O*C*H$_2$CH$_2$Si(CH$_3$)$_3$), 62.0 (C6), 21.1 (CO*C*H$_3$), 18.7 (OCH$_2$*C*H$_2$Si(CH$_3$)$_3$), –1.3 (OCH$_2$CH$_2$Si(*C*H$_3$)$_3$). HRMS $C_{27}H_{38}O_7SiNa$ [M + Na$^+$] calculated: 525.2285; found: 525.2277.

2-(Trimethylsilyl)ethyl 6-O-benzoyl-2,4-di-O-benzyl-β-D-galactopyranoside (56)

Diol **52** (1.59 g, 3.45 mmol) was dissolved in pyridine (30.0 mL) and cooled to 0 °C. A dilute solution of benzoyl chloride (0.43 mL, 3.62 mmol) in pyridine (5.00 mL) was added dropwise over 15 min. The reaction was stirred for 4 h and then poured onto excess ice water and extracted with ethyl acetate. The organic layer was washed with 1 M HCl (3 × 100 mL), saturated $NaHCO_3$ (2 × 100 mL), and brine (1 × 100 mL) and then dried over Na_2SO_3. The solvent was removed and the crude was purified by column chromatography (cyclohexane – ethyl acetate, 4/1 *v*/*v*) to isolate the product **56** (1.51 g, 70%), remaining starting material, and 3-O-benzoylated and dibenzoylated products. The 3-O-benzoylated and dibenzoylated products were recovered, combined, and treated with NaOMe to recover the starting material. $[\alpha]_D$ = –15.6 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.13–7.17 (m, 15H, Ar*H*), 5.03- 4.69 (dd × 2, 4H, 2 × C*H*$_2$Ph), 4.56–4.52 (dd, 1H, H-6a, *J* = 11.5, 6.9 Hz), 4.41–4.39 (d, 1H, H-1, *J* = 7.2 Hz), 4.40–4.35 (m, 1H, H-6b), 4.05–3.98 (m, 1H, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 3.89 (d, 1H, H-5, *J* = 2.6 Hz), 3.77 (t, 1H, H-3, *J* = 6.7 Hz), 3.73–3.69 (m, 1H, H-4), 3.68–3.63 (m, 1H, H-2), 3.61–3.55 (m, 1H, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 2.36 (s, 1H, OH), 1.06–1.02 (m, 2H, OCH$_2$C*H*$_2$Si(CH$_3$)$_3$), 0.01(m, 1H, OCH$_2$CH$_2$Si(C*H*$_3$)$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 166.2 (C=O), 138.6, 138.3, 133.9, 133.3, 130.3, 129.8, 128.7, 128.6, 128.5, 128.5, 128.4, 128.3, 128.0, 127.9 (Ar*C*, Ar*C*H), 103.4 (C1), 79.5 (C2), 75.1 (*C*H$_2$Ph), 74.9 (C5), 74.8 (*C*H$_2$Ph), 74.4 (C4), 72.3 (C3), 67.4 (O*C*H$_2$CH$_2$Si(CH$_3$)$_3$), 63.2 (C6), 18.6 (OCH$_2$*C*H$_2$Si(CH$_3$)$_3$), –1.3 (OCH$_2$CH$_2$Si(*C*H$_3$)$_3$). HRMS $C_{32}H_{40}O_7SiNa$ [M + Na$^+$] calculated: 587.2441; found: 587.2424.

2-(Trimethylsilyl)ethyl (4-chloroacetyl-6-O-benzoyl-2,3-di-O-benzyl-D-galactopyranosyl-α(1→3)-6-O-benzoyl-2,4-di-O-benzyl-β-D-galactopyranoside) (57)

Donor **49** (1.50 g, 2.56 mmol) and acceptor **55** (1.44 g, 2.54 mmol) were dissolved in Et_2O–CH_2Cl_2 (3/2, 18.5 mL, 0.16 M), 4 Å molecular sieves were added, and the solution was stirred for 1 h before cooling to 0 °C. Once the solution had reached 0 °C, Me_2S_2/Tf_2O promoter (4.00 mL, 1 M solution in CH_2Cl_2) was added and the reaction was stirred for 10 min. The reaction was quenched with Et_3N and diluted with CH_2Cl_2. The molecular sieves were removed by filtration and the organic phase was washed with 2 M aqueous HCl, saturated $NaHCO_3$, and water. The organic phase was dried over Na_2SO_4, filtered, and the solvent was removed. The disaccharide was isolated by column chromatography using a gradient elution (toluene – ethyl acetate, 16/1–8/1 *v*/*v*) to give **57** (2.62 g, 94%) as a clear oil. $[\alpha]_D$ = +49.1 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.07–7.17 (m, 30H, Ar*H*) 5.17 (s, 2H, H-1′, H-4′), 5.07–4.47 (4 × dd, 8H, C*H*$_2$Ph), 4.56 (s, 1H, H-5), 4.42–4.34 (m 2H, H-6a, H-6b), 4.21–4.00 (m, 2H, H-6a, H-6b), 4.17 (m, 1H, H-1), 4.10 (d, 2H, C*H*$_2$Cl), 3.98–3.50 (m, 2H, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 3.89–3.78 (m, 5H, H-2, H-2′, H-3′, H-4, H-5′), 3.56 (t, 1H, H-3), 1.01 (m, 2H, OCH$_2$C*H*$_2$Si(CH$_3$)$_3$), 0.02 (s, 9H, OCH$_2$CH$_2$Si(C*H*$_3$)$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 166.9, 166.1, 165.9 (3 × C=O), 138.8, 138.4, 138.0, 137.8, 133.3, 133.2 (6 × Ar*C*), 130.0–127.6 (Ar*C*H), 103.9 (C1), 94.9 (C1′), 78.3, 77.0, 76.4, 75.0, 72.1, 71.6, 70.4, 63.0 (C2, C2′, C3, C3′, C4, C4′, C5, C5′), 75.4, 74.8, 74.5, 72.2 (4 × *C*H$_2$Ph), 67.5 (O*C*H$_2$CH$_2$Si(CH$_3$)$_3$), 66.8, 63.3 (C6, C6′), 40.9 (*C*H$_2$Cl), 18.6 (OCH$_2$*C*H$_2$Si(CH$_3$)$_3$), –1.3 (OCH$_2$CH$_2$Si(*C*H$_3$)$_3$). HRMS $C_{61}H_{67}O_{14}SiClNa$ [M + Na$^+$] calculated: 1109.3886; found: 1109.3921.

2-(Trimethylsilyl)ethyl (6-O-benzoyl-2,3-di-O-benzyl-D-galactopyranosyl-α(1→3)-6-O-benzoyl-2,4-di-O-benzyl-β-D-galactopyranoside) (58)

Disaccharide **57** (1.80 g, 1.66 mmol) was dissolved in THF (18.0 mL) and to this, $NaHCO_3$ (460 mg, 5.47 mg), thiourea (378 mg, 4.97 mmol), and TBAI (122 mg, 0.33 mmol) were added. The reaction was heated to 60 °C for 4 h. The reaction was diluted with CH_2Cl_2, washed with water, and dried over Na_2SO_4. Column chromatography (cyclohexane – ethyl acetate, 5/1 *v*/*v*) of the crude gave the pure product **58** (1.56 g, 93%) as a white foam. $[\alpha]_D$ = +34.0 (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.07–7.17 (m, 30H, Ar*H*), 5.19 (d, 1H, H-1′, *J* = 3.5 Hz), 5.07–4.48 (4 × dd, 8H, C*H*$_2$Ph), 4.44–4.27 (m, 5H, H-5, H-6a, H-6b, H-6a′, H-6b′), 4.09 (m, 1H, H-1), 3.96 (dd, 1H, H-2′, *J* = 9.7, 3.3 Hz), 3.90–3.41 (m, 2H, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 3.86 (s,1H, H-5′), 3.82–3.79 (m, 3H, H-2, H-3′, H-4), 3.63 (s, 1H, H-4′), 3.53 (t, 1H, H-3, *J* = 6.5 Hz), 2.39 (s, 1H, OH), 1.01–0.93 (m, 2H, OCH$_2$C*H*$_2$Si(CH$_3$)$_3$), −0.00 (s, 9H, OCH$_2$CH$_2$Si(C*H*$_3$)$_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 166.1, 166.1 (C=O), 139.0, 138.5, 138.1, 138.0, 133.3, 133.0 (Ar*C*), 130.5–127.6 (Ar*C*H), 103.9 (C1), 94.7 (C1′), 78.2, 78.0, 76.7, 75.5, 72.1, 71.7, 68.0, 67.9 (C2, C2′, C3, C3′, C4, C4′, C5, C5′), 75.1, 74.7, 74.5, 72.4 (4 × *C*H$_2$Ph), 67.5 (O*C*H$_2$CH$_2$Si(CH$_3$)$_3$), 64.5, 63.4 (C6, C6′), 18.5 (OCH$_2$*C*H$_2$Si(CH$_3$)$_3$), −1.3 (OCH$_2$CH$_2$Si(*C*H$_3$)$_3$), HRMS $C_{59}H_{66}O_{13}SiNa$ [M + Na$^+$] calculated: 1033.4170; found: 1033.4202.

2-(Trimethylsilyl)ethyl (2-N-acetyl-4-azido-2,3-N,O-carbonyl-2,4,6-trideoxy-D-galactopyranosyl-α(1→4)-6-O-benzoyl-2,3-di-O-benzyl-D-galactopyranosyl-α(1→3)-6-O-benzoyl-2,4-di-O-benzyl-β-D-galactopyranoside) (59)

Donor **25** (554 mg, 1.84 mmol) as a solution in CH_2Cl_2 (12.0 mL) was added dropwise to a stirred solution of acceptor **58** (1.56 mL, 1.54 mmol), NIS (689 mg, 3.08 mmol), AgOTf (197 mg, 0.77 mmol), and 4 Å molecular sieves in CH_2Cl_2 (12.0 mL) at 0 °C for 1 h. The reaction was quenched with Et_3N and diluted with CH_2Cl_2. The organic phase was washed with 10% aqueous $Na_2S_2O_3$ and water and then dried over Na_2SO_4. The solvent was removed and the crude was purified by column chromatography (toluene – ethyl acetate, 12/1 *v*/*v*) to isolate the desired α-trisaccharide (1.15 g, 60%), the β-trisaccharide (230 mg, 12%), and unreacted acceptor (217 mg, 14%) to give the reaction a recovered yield of 84%. Following anomerisation of the β-trisaccharide (207 mg, 90%), a total of 1.309 g (71%) of trisaccharide **59** was obtained. $[\alpha]_D$ = +73.8 (*c* 1.0, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.06–7.18 (m, 30 H, Ar*H*), 5.54–5.53 (d, 1H, H-1″, *J* = 2.6 Hz), 5.20–5.19 (d, 1H, H-1′, *J* = 3.3 Hz), 5.10–4.47 (m, 9H, 4 × C*H*$_2$Ph, H-3″), 4.43–4.40 (dd, 1H, H-6a/H6-a′) 4.34–4.29 (m, 2H, H-2″, H-6b/H-6b′), 4.25–4.21 (dd, 1H, H-6a/H-6a′), 4.17–4.14 (m, 2H, H-5, H-5″), 4.08–4.06 (d, 1H, H-1, *J* = 7.2 Hz), 3.95–3.89 (m, 1H, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 3.87–3.73 (m, 7H, H-2, H-3, H-3′, H-4, H-4″, H-5′, H-6b/H-6b′), 3.69 (m, 1H, H-2), 3.47–3.42 (m, 2H, H-4′, OC*H*$_2$CH$_2$Si(CH$_3$)$_3$), 2.55 (s, 3H, COC*H*$_3$), 1.01–0.93 (m, 5H, H-6a,b,c″, OCH$_2$C*H*$_2$Si(CH$_3$)$_3$), 0.01 (s, 9H, OCH$_2$CH$_2$Si(C*H*$_3$)$_3$). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 172.5, 166.1, 165.7, 152.9 (C=O), 138.9, 138.4, 138.3, 137.8, 133.3, 133.1 (Ar*C*), 130.3–125.4 (Ar*C*H), 103.8 (C1), 97.4 (C1″), 94.1 (C1′), 75.1, 74.5, 74.0, 73.0 (4 × *C*H$_2$Ph), 78.1, 77.0, 76.6, 76.6, 74.9, 73.3, 72.1, 71.7, 68.9, 67.4, 62.3 (C2, C2′, C3, C3′, C3″, C4, C4′, C4″, C5, C5′, C5″), 67.5 (O*C*H$_2$CH$_2$Si(CH$_3$)$_3$), 63.4, 63.3 (C6, C6′), 56.3 (C2″), 24.0 (COC*H*$_3$), 18.6 (OCH$_2$*C*H$_2$Si(CH$_3$)$_3$), 17.0 (C6″), −1.4 (OCH$_2$CH$_2$Si(*C*H$_3$)$_3$). HRMS $C_{69}H_{76}N_4O_{17}SiNa$ [M + Na$^+$] calculated: 1271.4872; found: 1271.4935.

2-(Trimethylsilyl)ethyl (2-N-acetyl-4-azido-2,4,6-trideoxy-D-galactopyranosyl-α(1→4)-2,3-di-O-benzyl-D-galactopyranosyl-α(1→3)-2,4-di-O-benzyl-β-D-galactopyranoside) (60)

$Ba(OH)_2.8H_2O$ (2.46 g, 7.80 mmol) was added to a suspension of trisaccharide **59** (650 mg, 0.52 mmol) in ethanol (20 mL) and water (10 mL). The solution was heated at 70 °C for 16 h and then cooled to room temperature. Ac_2O (344 μL, 3.64 mmol) was added and the reaction was stirred for 3 h. The aqueous phase was acidified to pH 1 and extracted with ethyl acetate (3 × 50 mL). The organic layers were combined, dried over Na_2SO_4, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (100% ethyl acetate to ethyl acetate – methanol, 95/5 *v*/*v*) to give **60** (415 mg, 80%) as an opaque oil. $[\alpha]_D$ = +78.4 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.44–7.09 (m, 20 H, Ar*H*), 5.11–5.11 (d, 1H, H-1′, *J* = 3.1 Hz), 5.01 (m, 2H, C*H*$_2$Ph), 4.87–4.84 (d, 1H, C*H*$_2$Ph), 4.76–4.69 (m, 4H, C*H*$_2$Ph, H-1″), 4.50–4.47 (d, 1H, C*H*$_2$Ph), 4.37–4.34 (m, 2H, C*H*$_2$Ph, H-1), 4.27–4.19 (m, 2H), 4.03–3.96 (m, 2H), 3.91–3.84 (m, 4H), 3.79–3.73 (m, 4H), 3.70–3.67 (dd, 1H, *J* = 10.0, 2.5 Hz), 3.65 (d, 1H, *J* = 1.6 Hz), 3.61- 3.52 (m, 3H), 3.38 (t, 1H, *J* = 6.21 Hz), 3.17–3.08 (m, 2H, H-6ab/H-6ab′), 1.97 (s, 3H, COC*H*$_3$), 1.10–1.09 (d, 3H, H-6abc″, *J* = 6.3 Hz), 1.03–0.98 (m, 2H, OCH$_2$C*H*$_2$Si(CH$_3$)$_3$), 0.00 (s, 9H, OCH$_2$CH$_2$Si(C*H*$_3$)$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 173.7 (N*C*O), 138.7, 138.7, 138.4, 137.8 (Ar*C*), 128.7–127.7 (Ar*C*H), 103.9 (C1), 99.0 (C1″), 95.9 (C1′), 75.5, 74.7, 74.5, 72.7 (4 × *C*H$_2$Ph), 78.7, 78.4, 76.7 (2) 75.8, 74.45 72.7, 72.5, 69.3, 66.8, 65.8 (C2, C2′, C3, C3′, C3″, C4, C4′, C4″, C5, C5′, C5″), 67.7 (O*C*H$_2$CH$_2$Si(CH$_3$)$_3$), 62.0, 61.1 (C6, C6′), 51.3 (C2″), 22.9 (COC*H*$_3$), 18.8 (OCH$_2$*C*H$_2$Si(CH$_3$)$_3$), 17.5 (C6″), −1.3 (OCH$_2$CH$_2$Si(*C*H$_3$)$_3$). HRMS $C_{53}H_{70}N_4O_{14}SiNa$ [M + Na$^+$] calculated: 1037.4556; found: 1037.4602.

2-(Trimethylsilyl)ethyl (2-N-acetamido-4-azido-2,4,6-trideoxy-D-galactopyranosyl-α(1→4)-methyl (2,3-di-O-benzyl-D-galactopyranosyl) uronate-α(1→3)-methyl (2,4-di-O-benzyl-β-D-galactopyranoside) uronate) (61)

Trisaccharide **60** (415 mg, 0.41 mmol) was dissolved in CH_2Cl_2 and water (3.00 mL, 2/1 *v*/*v*) and cooled to 0 °C. To this, BAIB (789 mg, 2.45 mmol) was added followed by TEMPO (63.0 mg, 0.41 mmol) and the reaction was vigorously stirred for 2 h. Once only the desired product was observed by LRMS, the reaction was diluted with CH_2Cl_2 and quenched by addition of $Na_2S_2O_3$ (1.00 mL, 10% aqueous solution). The organic layer was separated and the aqueous phase was acidified to pH 1 and extracted with ethyl acetate (3 × 3 mL). The organic layers were combined and dried over Na_2SO_4, filtered, and the solvent was removed under reduced pressure. The crude was redispersed in DMF (4.00 mL), cooled to 0 °C, and added with K_2CO_3 (225 mg, 1.64 mmol) and MeI (76.0 μL, 1.23 mmol). The reaction was allowed to come to room temperature where it was stirred for 16 h. The reaction was diluted with ethyl acetate (20 mL) and washed with water (3 × 20 mL) and brine (20 mL). The organic layers were dried over Na_SO_4 and the solvent was removed. The product **61** was isolated (304 mg, 70%) as a white foam following purification by column chromatography using a gradient elution (ethyl acetate – methanol, 1/0–5/1 *v*/*v*). $[\alpha]_D$ = +89.8 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.44–7.05 (m, 20H, Ar*H*), 6.10–6.08 (d, 1H, N*H*), 5.29 (s, 1H, H-1′), 5.05–5.02 (d, 1H, C*H*$_2$Ph), 4.91–4.89 (d, 1H, C*H*$_2$Ph), 4.80–4.70 (m, 4H, C*H*$_2$Ph), 4.68 (s, 1H), 4.49–4.48 (d, 1H, H-1″, *J* = 3.8 Hz), 4.44–4.41 (d, 1H, C*H*$_2$Ph), 4.37–4.33 (m, 2H, H-1, C*H*$_2$Ph), 4.23–4.16 (m, 3H), 4.11–4.01 (m, 4H), 3.89 (s, 2H), 3.82–3.75 (m, 3H), 3.66 (s, 3H, COOC*H*$_3$), 3.57–3.50 (m, 2H), 3.43 (s, 3H, COOC*H*$_3$), 2.09 (s, 3H, COC*H*$_3$), 1.08–0.94 (m, 5H, H-6a-c″, OCH$_2$C*H*$_2$Si(CH$_3$)$_3$), −0.01 (s, 9H, OCH$_2$CH$_2$Si(C*H*$_3$)$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 173.7 (NCO), 169.8, 168.5 (C=O), 138.4, 138.2, 138.0, 137.4 (Ar*C*), 128.6–127.4 (Ar*C*H), 103.4 (C1), 98.6 (C1″), 94.8 (C1′), 77.2, 76.8, 76.6, 75.4, 75.0, 75.0, 74.6, 74.6, 74.2, 73.9, 73.0, 72.1, 69.9, 66.7, 66.0, (C2, C2′, C3, C3′, C3″, C4, C4′, C4″, C5, C5′, C5″, C*H*$_2$Ph × 4) 67.9 (O*C*H$_2$CH$_2$Si(CH$_3$)$_3$), 52.4 (COO*C*H$_3$), 52.0 (COO*C*H$_3$), 50.8 (C2″), 22.9 (COC*H*$_3$), 18.6 (OCH$_2$*C*H$_2$Si(CH$_3$)$_3$), 17.3 (C6″), −1.4 (OCH$_2$CH$_2$Si(*C*H$_3$)$_3$). HRMS $C_{55}H_{70}N_4O_{16}SiNa$ [M + Na$^+$] calculated: 1093.4454; found: 1093.4501.

2-(Trimethylsilyl)ethyl (2-N-acetamido-4-azido-3-O-chloroacetyl-2,4,6-trideoxy-D-galactopyranosyl-α(1→4)-methyl (2,3-di-O-benzyl-D-galactopyranosyl) uronate-α(1→3)-methyl (2,4-di-O-benzyl-β-D-galactopyranoside) uronate) (62)

Trisaccharide **61** (300 mg, 0.28 mmol) was dissolved in anhydrous CH_2Cl_2 (2.00 mL) and cooled to 0 °C. To the solution, pyridine (0.20 mL) was added followed by a dropwise addition of chloroacetyl chloride (44.0 μL, 0.56 mmol). The reaction was stirred at 0 °C for 40 min and monitored by TLC (cyclohexane – ethyl acetate, 1/1 *v*/*v*). The reaction was then quenched with Et_3N and the material was loaded directly onto a column. Chromatography purification was carried out using a gradient elution (cyclohexane – ethyl acetate, 2/1–1/3 *v*/*v*) to give **62** (270 mg, 84%) as a white foam. $[\alpha]_D$ = +49.1 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.44–7.01 (m, 20H, Ar*H*), 5.53–5.50 (d, 1H, N*H*), 5.30–5.29 (d, 1H, H-1′, *J* = 2.6 Hz), 5.09–5.05 (dd, 2H, CH_2Ph, H-3″), 4.90–4.88 (d, 1H, CH_2Ph), 4.78–4.72 (m, 4H, CH_2Ph), 4.69–4.64 (m, 1H), 4.55 (m, 2H, H-1′, H-2″), 4.46–4.44 (d, 1H CH_2Ph) 4.35–4.30 (dd, 2H, CH_2Ph, H-1), 4.24–4.17 (m, 2H), 4.14–4.01 (m, 5H, H_x, H_x, CH_2Cl, OCH_2CH$_2$Si(CH$_3$)$_3$), 3.95–3.92 (dd, 1H, *J* = 10.4, 3.1 Hz), 3.88–3.85 (dd, 1H, *J* = 10.4, 3.6 Hz), 3.83–3.80 (dd, 1H, *J* = 10.1, 3.5 Hz), 3.79–3.74 (m, 1H), 3.65 (s, 3H, COOCH_3), 3.57–3.50 (m, 1H, OCH_2CH$_2$Si(CH$_3$)$_3$), 3.38 (s, 3H, COOCH_3), 1.99 (s, 3H, COCH_3), 1.07–0.93 (m, 2H, OCH$_2$CH_2Si(CH$_3$)$_3$), 1.00–0.98 (d, 3H, H-6a-c″, *J* = 6.2 Hz), −0.01 (s, 9H, OCH$_2$CH$_2$Si(CH_3)$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 170.8, 169.0, 168.6, 167.5 (C=O), 138.5, 138.3, 138.1, 137.4 (Ar*C*), 129.2–127.5 (Ar*C*H), 103.4 (C1), 99.3 (C1″), 94.6 (C1′), 75.2, 75.1, 74.2, 73.3 (*C*H$_2$Ph), 77.4, 77.3, 76.6, 75.2, 74.6, 74.4, 73.9, 70.1, 65.7, 64.3 (C2, C2′, C3, C3′, C4, C4′, C4″, C5, C5′, C5″), 73.2 (C3″), 67.9 (O*C*H$_2$CH$_2$Si(CH$_3$)$_3$), 52.5, 52.0 (COO*C*H$_3$), 47.2 (C2″), 40.6 (*C*H$_2$Cl), 23.5 (CO*C*H$_3$), 18.7 (OCH$_2$*C*H$_2$Si(CH$_3$)$_3$), 17.1 (C6″), −1.3 (OCH$_2$CH$_2$Si(*C*H$_3$)$_3$). HRMS showed a fragmented structure of the molecule where the chloroacetate group was not present. HRMS $C_{55}H_{70}N_4O_{16}SiNa$ [M + Na$^+$] calculated: 1093.4448; found: 1093.2372.

2-N-acetamido-4-azido-3-O-chloroacetyl-2,4,6-trideoxy-D-galactopyranoside-α(1→4)-methyl (2,3-di-O-benzyl-D-galactopyranosyl) uronate-α(1→3)-methyl (2,4-di-O-benzyl-D-galactopyranosyl) uronate (63)

Trisaccharide **62** (300 mg, 0.26 mmol) was dissolved in CH_2Cl_2 (1.20 mL) and cooled to 0 °C. Trifluoroacetic acid (2.40 mL) was added and the reaction was stirred at 0 °C for 3 h. Upon complete consumption of the starting material, the reaction was diluted in CH_2Cl_2 and quenched by pouring onto excess saturated $NaHCO_3$. The organic phase was washed with saturated $NaHCO_3$ (3 × 20 mL) and brine (2 × 20 mL) before drying over Na_2SO_4. The solvent was removed under reduced pressure and the product was isolated by column chromatography (100% ethyl acetate) to give **63** (219 mg, 80%) with a 2.5:1 α to β ratio. NMR data for major anomer: ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.46–7.05 (m, 20H, Ar*H*), 5.62–5.60 (m, 1H, N*H*), 5.43–5.42 (d, 1H, H-1, *J* = 3.4 Hz), 5.34 (d, 1H, H-1′, *J* = 3.2 Hz), 5.12–5.09 (dd, 1H, H-3″, *J* = 10.7, 3.5 Hz), 5.06–5.04 (d, 1H, CH_2Ph), 4.80–4.75 (m, 4H, CH_2Ph), 4.63–4.57 (m, 4H), 4.51–4.38 (m, 3H, CH_2Ph), 4.33 (s, 1H), 4.25–4.20 (m, 2H), 4.15 (s, 1H), 4.11 (m, 2H, CH_2Cl), 4.02–3.99 (dd, 1H, *J* = 10.1, 3.5 Hz), 3.98–3.95 (dd, 1H, *J* = 10.4, 3.2 Hz), 3.92–3.90 (dd, 1H, *J* = 10.3, 2.9 Hz), 3.69–3.68 (m, 1H), 3.67 (s, 3H, COOCH_3), 3.46 (s, 3H, COOCH_3), 2.01 (s, 3H, COCH_3), 1.02–1.01 (d, 3H, H-6a′c‴, *J* = 6.3 Hz). ^{13}C NMR (126 MHz, $CDCl_3$) δ: 170.9 (NCO), 169.2, 168.8, 167.5 (C=O), 138.6, 138.1, 137.4, 137.3 (Ar*C*), 128.9–127.5 (Ar*C*H), 99.3 (C1″), 95.3 (C1′), 91.3 (C1), 75.2, 74.1, 73.1, 73.0 (4 × *C*H$_2$Ph), 77.2, 75.8, 75.2, 75.1, 74.6, 74.0, 73.1, 70.8, 70.2, 65.7, 64.2 (C2, C2′, C3, C3′, C3″, C4, C4′, C4″, C5, C5′, C5″), 52.5 (COO*C*H$_3$), 52.1 (COO*C*H$_3$), 47.3 (C2″), 40.6 (*C*H$_2$Cl), 23.4 (CO*C*H$_3$), 17.2 (C6″). LRMS $C_{52}H_{59}ClN_4O_{17}Na$ [M + Na$^+$] calculated: 1069.34; found 1069.46. HRMS showed a fragmented structure of the molecule where the chloroacetate group was not present. HRMS $C_{50}H_{58}N_4O_{16}Na$ [M + Na$^+$] calculated: 993.3746; found: 993.3765.

2-N-acetamido-4-azido-3-O-chloroacetyl-2,4,6-trideoxy-D-galactopyranoside-α(1→4)-methyl (2,3-di-O-benzyl-D-galactopyranosyl) uronate-α(1→3)-methyl (2,4-di-O-benzyl-D-galactopyranosyl trichloroacetimidate) uronate (64)

Hemiacetal **63** (165 mg, 0.16 mmol) was dissolved in DCE (1.20 mL) and cooled to 0 °C. To this solution, trichloroacetonitrile (31.0 μL, 0.31 mmol) and K_2CO_3 (43.0 mg, 0.31 mmol) were added and the solution was stirred for 24 h. The reaction mixture was loaded directly onto a silica gel column for chromatography (ethyl acetate – cyclohexane, 4/1 *v*/*v*) where the product **64** (143 mg, 84%) was isolated and the unreacted hemiacetal was recovered. The major isomer was found to be alpha trichloroacetimidate, the spectra of which is given herein: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.58 (s, 1H, N*H*), 7.43–7.10 (m, 18H, Ar*H*), 6.99–6.97 (m, 2H, Ar*H*), 6.80 (d, 1H, H-1, *J* = 3.2 Hz), 5.50–5.48 (d, 1H, N*H*), 5.34–5.34 (d, 1H, H-1′, *J* = 3.2 Hz), 5.12–5.05 (m, 2H, H_x, CH_2Ph), 4.83–4.75 (m, 3H, CH_2Ph), 4.71–4.58 (m, 5H, CH_2Ph, H_x, H_x), 4.55–4.53 (m, 2H, H-3″, H-1″), 4.46–4.43 (d, 1H, CH_2Ph), 4.43–4.39 (m, 2H), 4.30 – 4.27 (d, 1H, CH_2Ph), 4.24–4.20 (m, 2H), 4.15–4.09 (d, 2H, CH_2Cl), 4.09–4.08 (d, 1H, *J* = 1.4 Hz), 4.00 (s, 1H), 3.96–3.93 (dd, 1H, *J* = 10.4, 3.2 Hz), 3.88–3.85 (dd, 1H, *J* = 10.4, 2.6 Hz), 3.67 (s, 3H, COOCH_3), 3.64 (s, 1H), 3.36 (S, 3H, COOCH_3), 2.04 (s, 3H, COCH_3), 1.98 (s, 3H, COCH_3), 0.99–0.97 (d, 3H, H-6a-c″, *J* = 6.3 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 170.7, 168.7, 168.1, 167.2 (C=O), 160.6 (C=N), 138.1, 137.9, 137.2, 137.1 (Ar*C*), 128.7–127.5 (Ar*C*H), 99.3 (C1″), 94.1 (C1′), 93.9 (C1), 90.9 (*C*Cl$_3$), 75.3, 74.2, 73.1, 73.0 (*C*H$_2$Ph), 77.1, 75.3, 75.0, 74.3, 74.2, 73.2, 72.9, 72.3, 69.9, 65.6, 64.2 (C2, C2′, C3, C3′, C3″, C4, C4′, C4″, C5, C5′, C5″), 52.6, 51.9 (COO*C*H$_3$), 47.2 (C2″), 40.4 (*C*H$_2$Cl), 26.9, 23.3 (CO*C*H$_3$), 17.0 (C6″).

Allyl (2-N-acetamido-4-azido-3-O-chloroacetyl-2,4,6-trideoxy-D-galactopyranoside-α(1→4)-methyl (2,3-di-O-benzyl-D-galactopyranosyl) uronate-α(1→3)-methyl (2,4-di-O-benzyl-β-D-galactopyranoside) uronate) (65)

Donor **64** (50.0 mg, 41.9 μmol) and allyl alcohol (2.00 μL, 83.9 μmol) were dissolved in CH_2Cl_2 (200 μL) and Et_2O (300 μL) and stirred with 4 Å molecular sieves for 3 h. The solution was cooled to 0 °C and a TMSOTf (20.0 μL, 10% *v*/*v* solution of TMSOTf in Et_2O, ~8.00 μmol) was added. The reaction was quenched with Et_3N after 15 min. The reaction mixture was loaded directly onto a silica gel column for chromatography (ethyl acetate – toluene, 3/1 *v*/*v*). The isolated product **65** (37.0 mg, 82%) was exclusively the β-anomer. $[\alpha]_D$ = +79.0 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.45–7.00 (m, 20H, Ar*H*), 5.95–5.85 (m, 1H, C*H*CH$_2$), 5.52–5.50 (d, 1H, N*H*) 5.31–5.26 (m, 2H, H-1′, CHCH_2), 5.19–5.16 (dd, 1H, CHCH_2, *J* = 10.4, 1.4 Hz), 5.08–5.01 (m, 2H, H-3″, CH_2Ph), 4.89–4.87 (d, 1H, CH_2Ph), 4.79–4.69 (m, 4H, CH_2Ph), 4.62 (s, 1H), 4.59–4.54 (m, 2H, H-1″, H_x), 4.50–4.44 (m, 2H, CH_2Ph, OCH_2), 4.40–4.38 (d, 1H, *H*-1, *J* = 7.7 Hz), 4.31–4.29 (d, 1H, CH_2Ph), 4.25 (s, 1H), 4.22–4.17 (q, 1H, *J* = 6.6 Hz), 4.14–4.08 (m, 3H, OCH_2, CH_2Cl), 4.02–4.01 (m, 2H), 3.95–3.92 (dd, 1H, *J* = 10.4, 3.1 Hz), 3.89–3.86 (dd, 1H, *J* = 10.4, 2.6 Hz), 3.82–3.81 (m, 2H), 3.66 (s, 4H, H_x, COOCH_3), 3.38 (s, 3H, COOCH_3), 2.36 (s, 3H, COCH_3), 1.99 (s, 3H, COCH_3), 1.01–0.99 (d, 3H, H6a-c″, *J* = 6.3 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 170.8, 168.9, 168.5, 167.5 (C=O), 138.5, 138.1, 138.1, 137.4 (Ar*C*), 133.9 (*C*HCH$_2$), 129.2–125.4 (Ar*C*H), 117.7 (CH*C*H$_2$), 102.7 (C1), 99.3 (C1″), 94.6 (C1′), 75.3, 75.1, 74.2, 73.3 (*C*H$_2$Ph), 77.4, 77.2, 76.6, 75.1, 74.5, 74.4, 74.0, 73.2, 70.2, 65.7, 64.3 (C2, C2′, C3, C3′, C3″, C4, C4′, C4″, C5, C5′, C5″), 70.5 (OCH_2), 52.6, 52.0 (COO*C*H$_3$), 47.3 (C2″), 40.6 (*C*H$_2$Cl), 23.4, 21.6 (CO*C*H$_3$), 17.1 (C6″). HRMS showed a fragmented structure of the molecule where the chloroacetate group was not present. HRMS $C_{53}H_{62}N_4O_{16}Na$ [M + Na$^+$] calculated: 1033.4059; found: 1033.2223.

Allyl (2-N-acetamido-4-azido-2,4,6-trideoxy-D-galactopyranoside-α(1→4)-methyl (2,3-di-O-benzyl-D-galactopyranosyl) uronate-α(1→3)-methyl (2,4-di-O-benzyl-β-D-galactopyranoside) uronate) (66)

Trisaccharide **65** (35.0 mg, 32.2 μmol) was dissolved in THF (0.40 mL). $NaHCO_3$ (9.00 mg, 106 μmol), thiourea (7.00 mg,

96.0 μmol), and TBAI (2.00 mg, 6.40 μmol) were added and the reaction was heated at 60 °C for 16 h. The reaction was placed directly onto a silica gel column for chromatography (ethyl acetate – cyclohexane, 4/1 *v*/*v* to 100% ethyl acetate) to give **66** (28.0 mg, 86%). $[\alpha]_D$ = +84.4 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.44–7.03 (m, 20H, Ar*H*), 6.09 – 6.07 (d, 1H, N*H*), 5.95–5.85 (m, 1H, C*H*CH$_2$), 5.31–5.26 (m, 2H, H-1′, CHC*H*$_2$), 5.18–5.15 (dd, 1H, CHC*H*$_2$), 5.05–4.87 (dd, 2H, C*H*$_2$Ph), 4.80–4.70 (m, 4H, 2 × C*H*$_2$Ph), 4.66 (s, 1H), 4.49–4.46 (m, 2H, H-1′, OC*H*$_2$), 4.44–4.41 (d, 1H, C*H*2Ph), 4.39–4.37 (m, 1H, H-1), 4.35–4.32 (d, 1H, C*H*$_2$Ph), 4.23 (s, 1H), 4.21–4.17 (m, 2H), 4.13–4.08 (m, 1H, OC*H*$_2$), 4.03 (s, 1H), 4.00 (d, 1H), 3.89 (s, 2H), 3.81–3.80 (m, 2H), 3.65 (s, 3H, COOC*H*$_3$), 3.57–3.56 (m, 1H), 3.42 (s, 3H, COOC*H*$_3$), 2.09 (s, 3H, COC*H*$_3$), 1.04–1.02 (d, 3H, H-6a-c″, *J* = 6.3 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 173.8 (NC=O), 169.9, 168.5 (C=O), 138.5, 138.1, 138.1, 137.5 (Ar*C*), 133.9 (*C*HCH$_2$), 128.7–127.5 (Ar*C*H), 117.7 (CH*C*H$_2$), 102.8 (C1), 98.7 (C1″), 94.9 (C1′), 77.2, 76.7, 75.4, 74.6 (2), 74.0, 72.2, 70.1, 66.7, 66.1, 60.5 (C2, C2′, C3, C3′, C3″, C4, C4′, C4″, C5, C5′, C5″), 70.6 (O*C*H$_2$), 75.3, 75.1, 74.3, 73.1 (*C*H$_2$Ph), 52.6, 52.1 (COO*C*H$_3$), 50.9 (C2″), 23.0 (CO*C*H$_3$), 17.4 (C6″). HRMS $C_{53}H_{62}N_4O_{16}Na$ [M + Na$^+$] calculated: 1033.4059; found: 1033.4097.

Allyl (2-N-acetamido-4-azido-3-O-chloroacetyl-2,4,6-trideoxy-D-galactopyranoside-α(1→4)-methyl (2,3-di-O-benzyl-D-galactopyranosyl) uronate-α(1→3)-methyl (2,4-di-O-benzyl-D-galactopyranosyl) uronate-β(1→3)-2-N-acetamido-4-azido-2,4,6-trideoxy-D-galactopyranoside-α(1→4)-methyl (2,3-di-O-benzyl-D-galactopyranosyl) uronate-α(1→3)-methyl (2,4-di-O-benzyl-β-D-galactopyranoside) uronate) (67)

Donor **64** (26.0 mg, 21.8 μmol) and acceptor **66** (21.0 mg, 20.0 μmol) were dissolved in CH_2Cl_2 (120 μL) and Et_2O (180 μL). The reaction was stirred with 4 Å molecular sieves at room temperature for 2 h before cooling to 0 °C and adding TMSOTf (1 μL, 4 μmol, added 10 μL of a 10% *v*/*v* solution TMSOTf/Et_2O). The reaction was stirred for 3 h until at which point it was quenched with Et_3N. The solution was added directly onto a column for chromatography and a gradient elution (toluene – ethyl acetate, 1/1–0/1 *v*/*v*) was preformed to isolate the hexasaccharide **67** (25.0 mg, 83% considering recovery) and recover the unreacted acceptor (6.00 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.46–6.97 (m, 40H, Ar*H*), 5.91–5.84 (m, 1H, C*H*CH$_2$), 5.50–5.47 (d, 1H, N*H*), 5.43–5.40 (d, 1H, N*H*), 5.28–5.25 (m, 3H, H-1″, H-1‴″, CHC*H*$_2$), 5.18–5.15 (dd, 1H, CHC*H*$_2$), 5.11–5.04 (m, 3 H, C*H*$_2$Ph, H-3‴″), 4.89–4.27 (m, 24H, 7 × C*H*$_2$Ph, OC*H*$_2$, H1′, H1″, H1″″, H1‴″, H2″, H2‴″, 3 × H$_x$), 4.23 (s, 2H), 4.17–4.05 (m, 5H, C*H*$_2$Cl, OC*H*$_2$, H$_x$, H$_x$), 3.99 (s, 2H), 3.91–3.75 (m, 10H), 3.70–3.61 (m, 2H), 3.66 (s, 3H, COOC*H*$_3$), 3.62 (s, 3H, COOC*H*$_3$), 3.49 (s, 3H, COOC*H*$_3$), 3.32 (s, 3H, COOC*H*$_3$), 2.00 (s, 3H, COC*H*$_3$), 1.64 (s, 3H, COC*H*$_3$), 1.06 – 1.04 (d, 3H, H-6a-c″, *J* = 6.4 Hz), 0.91–0.90 (d, 3H, H-6a-c‴″, *J* = 6.3 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 170.7, 170.5 (2 × NCO), 169.1, 169.0, 168.6, 168.0, 167.5 (5 × C=O), 138.7, 138.4, 138.4, 138.1, 138.06, 138.0, 137.6, 137.4 (8 × ArC), 133.9 (*C*HCH$_2$), 129.2–127.2 (Ar*C*H), 117.7 (CH*C*H$_2$), 105.1 (C1‴), 102.7 (C1), 100.2, 99.2 (C1″, C1‴″), 94.8, 94.4 (C1′, C1‴′), 77.4, 77.3, 77.0, 76.7, 76.1, 75.5, 75.45, 75.4, 75.3, 75.1, 74.7, 74.6, 74.3, 74.2, 74.09, 74.03, 74.02, 73.8, 73.2, 73.1, 73.0, 70.6, 70.3, 70.1, 66.0, 65.7, 65.7, 64.3 (C2, C2′, C2‴, C2‴″, C3, C3′, C3″, C3‴, C3‴″, C3‴″, C4, C4′, C4″, C4‴, C4‴″, C4‴″, C5, C5′, C5″, C5‴, C5‴″, C5‴″, 8 × *C*H$_2$Ph, O*C*H$_2$), 52.6, 52.5, 52.1, 51.9 (4 × COO*C*H$_3$), 48.2, 47.3 (C2″, C2‴″), 40.6 (*C*H$_2$Cl), 23.5, 23.4 (2 × CO*C*H$_3$), 17.5, 17.0 (C6″, C6‴″).

Anomerisation attempt (68)

Hexasaccharide **67** (20.0 mg) was dissolved in CH_2Cl_2 and cooled to 0 °C, $TiCl_4$ (18.0 μL, 1 M solution in toluene) was added, and the reaction was stirred at room temperature overnight. TLC analysis showed a new spot and no presence of the starting material. The reaction was quenched by addition of Et_3N and the new spot was isolated by column chromatography (ethyl acetate – toluene, 4/1 *v*/*v*) to give the α-OAll hexasaccharide **67** (13.0 mg, 65%) with the remaining anomeric positions retaining their original configuration. **67**: ^{13}C NMR (101 MHz, $CDCl_3$) δ: 105.0, 102.61, 100.0, 99.1, 94.7, 94.2 (anomeric carbons before anomerisation). **68**: ^{13}C NMR (101 MHz, $CDCl_3$) δ: 105.0, 100.1, 99.1, 96.2, 95.5, 94.2 (anomeric carbons after anomerisation).

Supplementary material

Supplementary material is available with the article through the journal Web site at http://nrcresearchpress.com/doi/suppl/10.1139/cjc-2016-0006.

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