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Synthesis of a 1,3 β-glucan hexasaccharide designed to target vaccines to the dendritic cell receptor, Dectin-1

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ABSTRACT

Transformation of 3-O-benzyl-1,2:5,6-di-O-isopropylidene-α-D-glucofuranose into 2,4,6-tri-O-benzoyl-3-O-benzyl glucopyranosyl imidate proceeded efficiently via crystalline benzyl and per-benzoylated derivatives. This imidate glycosylated di-O-isopropylidene-α-D-glucofuranose in high yield and glycosylation of the disaccharide after removal of the 3′-O-benzyl ether afforded the β1,3 linked trisaccharide in excellent yield. Di- and trisaccharides imidates were readily prepared from the furanose terminated glycosylation products but both were unreactive in glycosylation reaction with the debenzylated di- and trisaccharide alcohols. The 3′-O-benzyl perbenzoylated disaccharide pyranose derivative could be selectively debenzoylated and converted to the corresponding perbenzoylated 4,6:4′,6′-di-O-benzylidene derivative. Lewis acid catalyzed glycosidation gave the selectively protected disaccharide ethyl-thioglycoside in good overall yield. Glycosidation of this thioglycoside donor with 5-methoxycarbonylpentanol gave the disaccharide tether glycoside and after catalytic removal of benzyl ether the resulting disaccharide alcohol was glycosylated by the thioglycoside in a 2+2 reaction to yield a tetrasaccharide. Repetition of selective deprotection of the terminal 3-O-benzyl ether followed by glycosylation by the disaccharide thioglycoside gave a protected hexasaccharide. Hydrogenolysis of this hexasaccharide followed by transesterification and second hydrogenolysis to remove a residual benzyl group gave the target hexasaccharide glycoside **1** as a Dectin-1 ligand functionalized to permit covalent attachment to glycoconjugate vaccines and thereby facilitate improved antigen processing by dendritic cells.

1. Introduction

Conjugate vaccines containing 1,3 linked β-glucans as B-cell epitopes can afford protection against fungal pathogens.[1–3] The same glycans are ligands for Dectin-1, a C-type lectin receptor present on the surface of dendritic cells (DCs).[4–11] The 2011 Nobel prize for Medicine recognized the concept of targeting antigens to dendritic cells for uptake and processing by these cells of the innate immune system leading to improved immune responses against tumor antigens.[12–15] The possibility of targeting vaccines to DCs by attaching carbohydrate ligands for one of the several C-type lectin receptors that occur on DCs has provoked considerable interest. Since Dectin-1 binds β-glucan this property was used to direct an otherwise poorly immunogenic β-mannotriose epitope conjugated to tetanus toxoid for DC uptake and processing.[16] The simple trimannoside-tetanus toxoid vaccine was a potent immunogen in rabbits[17] but not mice and became an effective immunogen in mice when laminarin was conjugated to it.[16] Five-fold higher antibody titers to the mannan were observed and shown to be attributable to DC processing of the antigen, whereas uptake of conjugates lacking laminarin was so poor it could not be detected by uptake of fluorescently labeled antigen. We also showed that Dectin-1 mediated uptake of this tri-component vaccine resulted in stimulation of innate immune cells to produce cytokines, mainly interleukin-6 (IL-6) and tumor-necrosis factor (TNFα), which induce differentiation of CD4 positive T helper lymphocytes (T_H cells) into T_H1 cells and IL-17 producing T_H-17 cells [16]. IL-17 is a potent recruitment factor for neutrophils while T_H1 cells are involved in B cell stimulation and antibody class switching. Both are desirable attributes of an anti-fungal immune response.

These findings promoted us to consider using a synthetic β1,3-glucan that lacks the 1,6 side chains present in laminarin to target

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vaccines to DCs. The size of the β1,3-glucan ligand recognized by Dectin-1 has been cited to range between hexasaccharide up to oligosaccharide as large as 15–25 mers.[8–11] It is rare for the binding sites of either lectins or antibodies to make crucial contacts with oligosaccharides larger than a hexasaccharide and we envisaged a hexasaccharide presented in multivalent format to be a suitable ligand to evoke strong uptake of a conjugate by DCs. Unpublished data in our laboratory confirms that presentation of β-1,3-glucan in multivalent format leads to enhanced activation of DCs. We have therefore envisioned a hexasaccharide **1** derivatized for attachment to a dendrimer that could in turn be conjugated to a protein carrier bearing an epitope of interest. This required a robust synthesis of β-1,3-glucan attached to a tether for conjugation to terminal amino groups of a dendrimer. 5-Methoxycarbonyl-pentanol[18,19] was chosen as the linker because of its compatibility with deprotection of the assembled oligosaccharide and its compatibility with different conjugation reactions[18,20] (Fig. 1).

Employing different glycosylation methods several groups have achieved the synthesis of β-glucans; linear tetra-,[21] penta-,[22] hexa-,[23–25] dodeca-[26] and hexadecasaccharides,[8] and a branched heptadeca-oligosaccharide.[8] Some difficulties were reported in obtaining high yield glycosylation reactions accompanied in one case by the unusual conformation of an internal glucose residue, which adopted a twist boat conformation, despite the presence of a 4,6-O-benzylidene group.[25] We report here our attempts to synthesize a hexasaccharide β-1,3-linked glucan attached to a tether.

2. Results and discussion

We initially envisioned a convergent synthesis of β(1→3) hexasaccharide starting from D-glucose diacetonide as it allows facile selective protection at C-3. Benzylation of diisopropylidene glucofuranose using benzyl chloride and sodium hydride in DMF afforded **2** in almost quantitative yield.[27] Subsequent acid-catalyzed hydrolysis of compound **2** afforded crystalline tetraol **3**,[28] which was then benzoylated using benzoyl chloride in pyridine furnishing crystalline perbenzoate **4**. Selective removal of anomeric benzoate was achieved via treatment with methylamine[3] and the resulting alcohol was converted into imidate **5** upon treatment with trichloroacetonitrile and DBU.[29] Synthesis of building block **5** could be performed efficiently on a large scale since column chromatography was only required for compound **5** (Scheme 1).

2.1. Disaccharide and trisaccharide synthesis

Glycosylation of diisopropylidene-D-glucofuranose by imidate **5** gave disaccharide **6** in high yield after crystallization. Disaccharide alcohol **7** was obtained by hydrogenolysis of the benzyl ether. Formation of trisaccharide **8** was accomplished in high yield from glycosyl acceptor **7** and imidate donor **5** by employing a catalytic amount of TMSOTf in DCM for 45 min.[29] The trisaccharide alcohol **9** was obtained by hydrogenolysis using the same procedure as compound **7**. The stereoselectivity of the two glycosylation reactions was controlled by neighboring group participation of the O-2-benzoyl group and was confirmed by measuring heteronuclear $^{1}J_{C\text{-}1,H\text{-}1}$ coupling constants of 160–161.4 Hz (Scheme 2).[30]

2.2. Attempted glycosylation with a trisaccharide imidate donor *10*

Our initial plan was to synthesize the β(1→3) hexaglucan via a 3+3 approach. With trisaccharide glycosyl acceptor **9** in hand, trisaccharide imidate **10** was synthesized in good yield by acid-catalyzed hydrolysis[28] of **8** followed by perbenzoylation of the resulting tetraol using BzCl and pyridine, removal of the anomeric ester using methylamine[3] and treatment of the resulting trisaccharide pyranose derivative with trichloroacetonitrile and DBU in DCM.[29] Attempts to glycosylate acceptor **7** or **9** using imidate donor **10** employing a catalytic amount of TMSOTf at room temperature for two days failed to yield any hexasaccharide. Increasing the amount of TMSOTf to as high as two equivalents also with a reaction time for two days failed to provide the anticipated product (Scheme 3). Other variables examined included increasing the equivalence of both donor and acceptor (for glycosylations of **7** and **9** three equivalents of donor were used), performing glycosylation reactions at reflux in DCM and also with toluene as solvent at 100 °C. All of these modifications were without effect. Different activators were not tried. Since unreacted imidate was not recovered we assumed the failure to obtain glycosylation products was due to low reactivity of the acceptors.

2.3. Attempted glycosylation with a disaccharide imidate donor *12*

We examined the possibility of coupling a disaccharide imidate donor to either di or trisaccharide glycosyl acceptor. Hydrolysis of the acetal groups of disaccharide **6** followed by perbenzoylation of the resulting tetraol gave the perbenzoylated disaccharide **11**. Selective removal of the anomeric benzoate of **11** using methylamine[3] followed by treatment with trichloroacetonitrile and DBU gave imidate **12**.[3] Glycosylation of either acceptor **7** or **9** was again attempted but in this case disaccharide donor **12** was tried using first a catalytic amount and then up to two equivalent of TMSOTf for two days. No glycosylation product was obtained in either case (Scheme 4).

2.4. Attempted tetrasaccharide synthesis with monosaccharide imidate donor *5*

Unsuccessful attempts to execute donor–acceptor glycosylation reactions consisting of the following combinations, 3+3, 3+2, 2+3 or 2+2 prompted us to examine the possibility of using the monosaccharide imidate donor **5** to extend trisaccharide **9** to form the corresponding tetrasaccharide under similar conditions to those previously tried.

However, after two days no glycosylation product was observed (Scheme 5). Although synthesis with imidate **5** did not provide the intended larger oligosaccharides, it did provide an optimized route for large-scale synthesis of β(1→3)–linked trisaccharide **8** via a series of transformations that required only limited column chromatography for purification.

2.5. Synthesis of disaccharide thioglycoside donor *15*

An alternative approach was investigated using a thioglycoside donor. Treatment of disaccharide **11** with 0.5 equiv of freshly

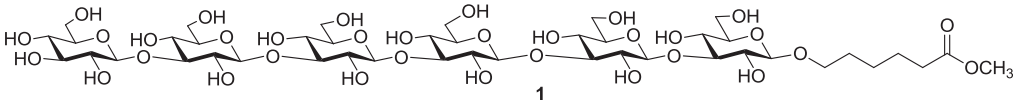

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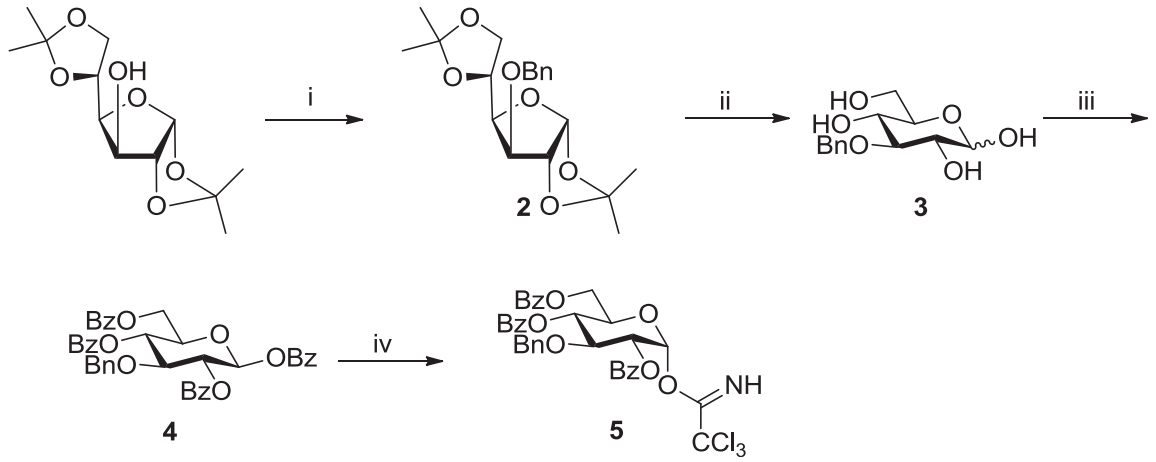
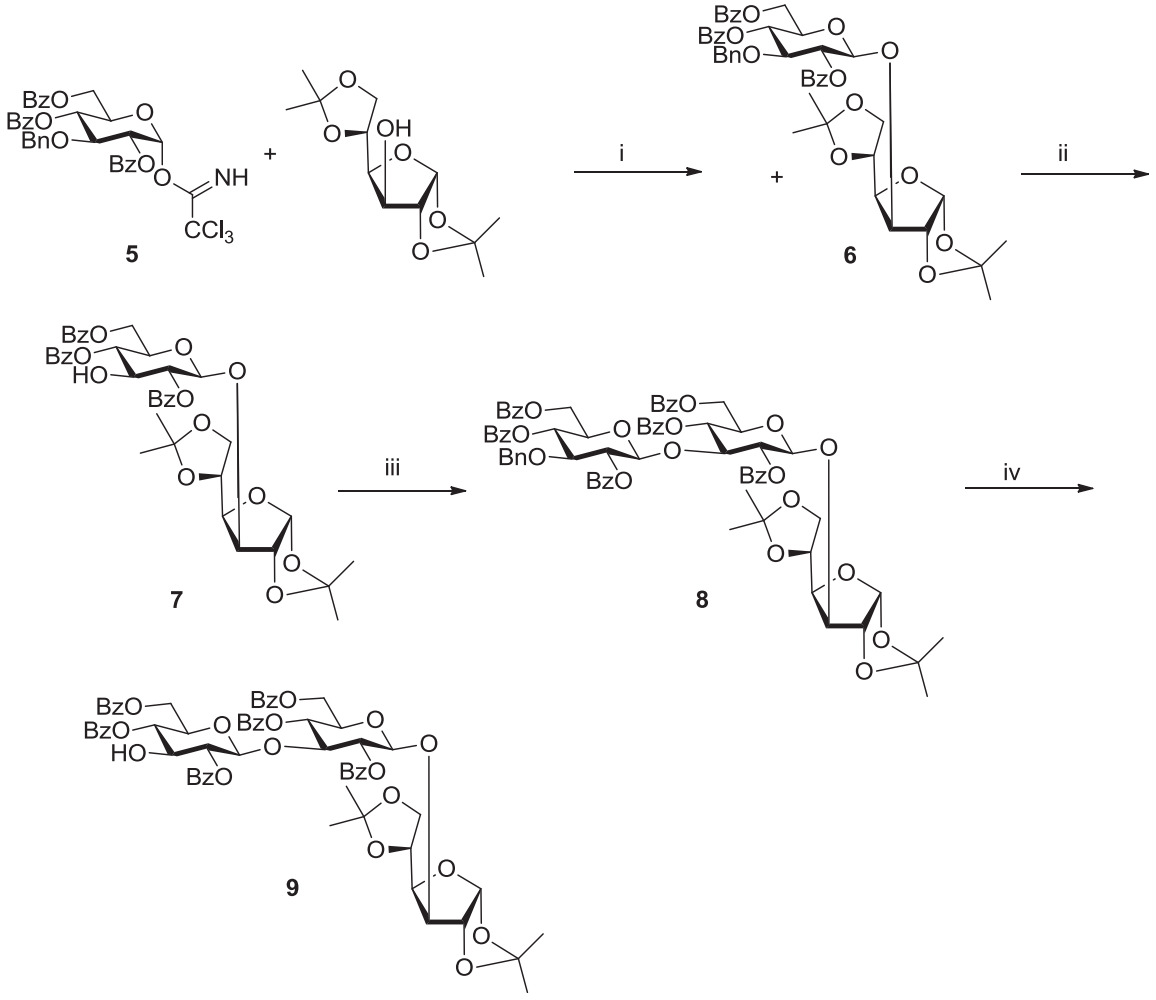
Fig. 1. Structure of the β1,3-glucan tether glycoside **1** designed to serve as a dendritic cell targeting ligand. After conjugation to a glycoconjugate vaccine the resulting vaccine construct can be more effectively processed by these antigen presenting cells.

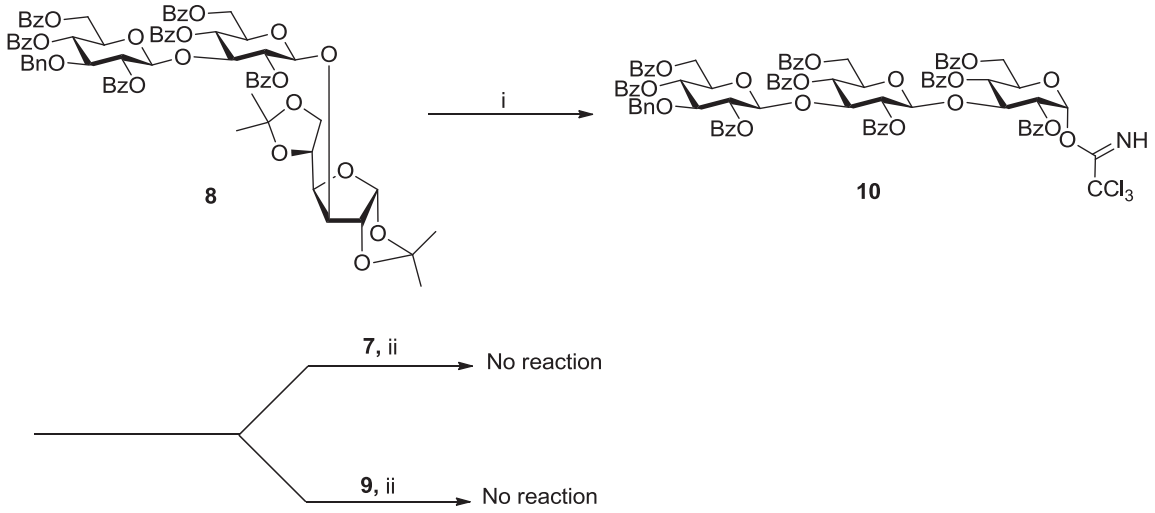


Scheme 1. (i) BnCl, NaH, DMF, 97%; (ii) Dioxane/6 M HCl (4:1), overnight, 93.5%; (iii) BzCl, pyridine, 0 °C, 92%; (iv) CH_3NH_2, DCM/THF, 4 h; CCl_3CN, DCM, DBU, 30 min, 84%.

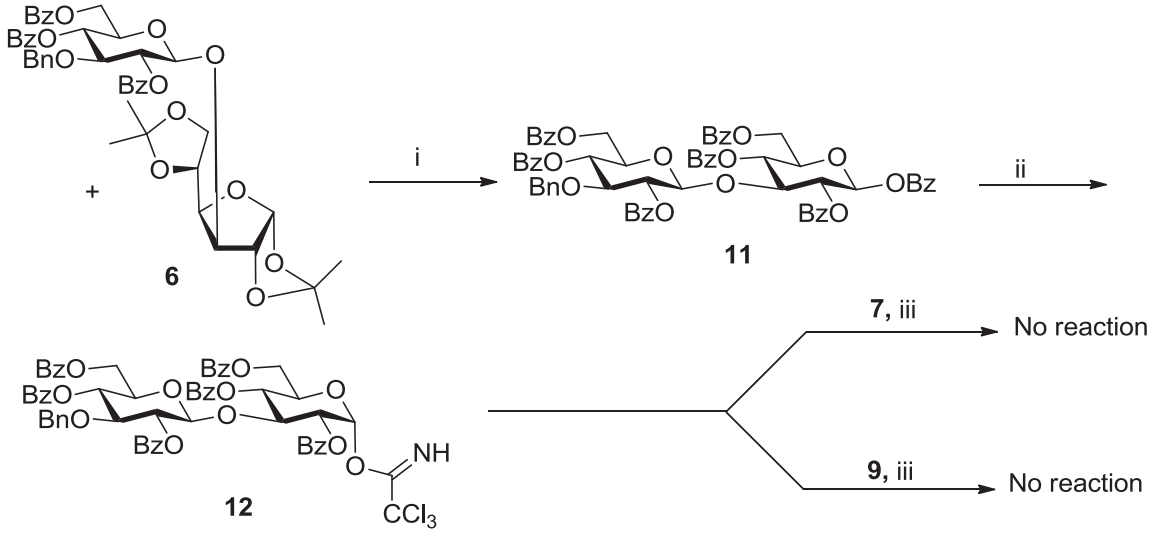
prepared $NaOCH_3$ for one hour conveniently transesterified only those benzoate groups at C-4, C-6, C-4′ and C-6′ affording tetraol **13** in 72% yield. Longer reaction time resulted in removal of other benzoate groups. Tetraol **13** reacted with benzaldehyde dimethylacetal and a catalytic amount of *p*-toluenesulfonic acid to give the diacetal **14** in a good yield.[31] Then glycosidation[32] of **14** by thioethanol using $BF_3 \cdot Et_2O$ promotor in DCM gave a 83% yield of thioglycoside **15** (Scheme 6).



Scheme 2. (i) DCM, TMSOTf, 45 min, 89%; (ii) Pd/C, H_2, DCM/CH_3OH (1:4), overnight, 93%; (iii) **5**, DCM, TMSOTf, 4 h, 91%; (iv) Pd/C, H_2, DCM/CH_3OH (1:4), overnight, 89%.



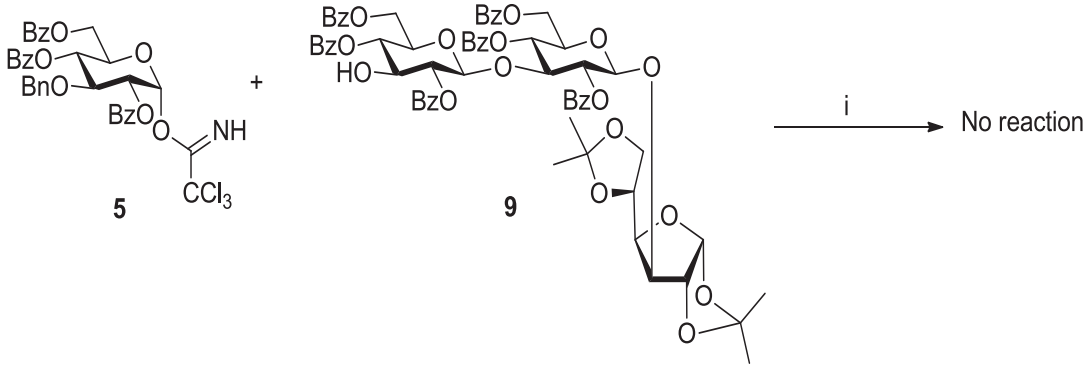
Scheme 3. (i) 6 M HCl/Dioxane, 17 h; BzCl, pyridine, 2 h; CH_3NH_2, DCM/THF (1:10), 3 h; CCl_3CN, DCM, DBU, 30 min, 78% over four steps; (ii) TMSOTf, DCM, rt, 2 days.



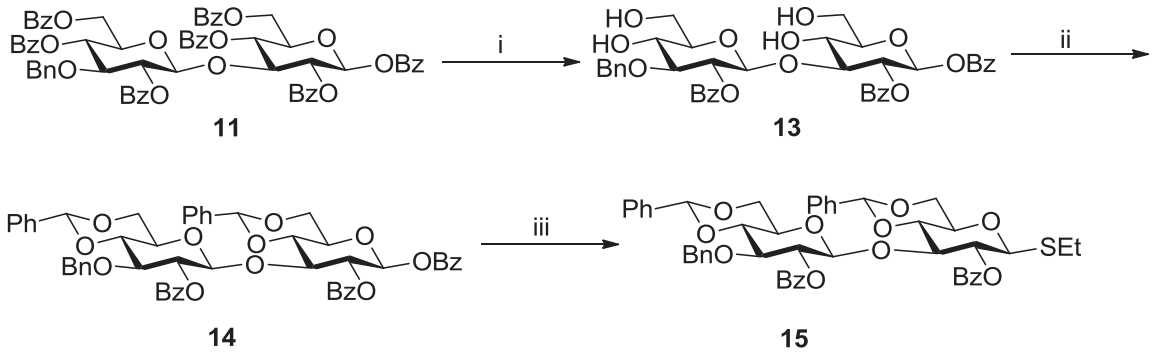
Scheme 4. (i) 6 M HCl/Dioxane, 17 h; BzCl, pyridine, 2 h, 82%; (ii) CH_3NH_2, DCM, 3 h; CCl_3CN, DCM, DBU, 30 min, 81% over two steps; (iii) TMSOTf, DCM, rt, 2 days.

*2.6. Hexasaccharide synthesis utilizing the disaccharide thioglycoside donor **15***

5-Methoxycarbonylpentanol was efficiently glycosylated by disaccharide donor **15** using NIS–AgOTf[32] activation to give disaccharide glycoside **16** in 89% yield. Debenzylation of compound **16** using Pd/C under hydrogen atmosphere for three hours furnished alcohol **17** with minimal hydrogenolysis of benzylidene acetals. Glycosylation of disaccharide alcohol **17** by donor **15** using the same procedures as for **16** gave **18**, which was in turn converted



Scheme 5. (i) TMSOTf, DCM, rt, 2 days.



Scheme 6. (i) DCM/CH_3OH (1:2), $NaOCH_3$, 1 h, 72%; (ii) $PhCH(OCH_3)_2$, acetonitrile, *p*-TsOH, 1 h, 94%; (iii) DCM, EtSH, $BF_3 \cdot Et_2O$, overnight, 83%.

to tetrasaccharide alcohol **19** by controlled hydrogenolysis. Finally NIS–AgOTf[32] mediated glycosylation of **19** by donor **15** furnished the protected hexasaccharide **20** in 87% yield. A coupled HSQC experiment was used to confirm the stereochemistry of all newly formed glycosidic linkages after each glycosylation cycle. The values of $^1J_{C\text{-}1,H\text{-}1}$ were found to be 160.4–161.2 Hz, which confirms the β-configuration.[30]

An acetic acid solution of hexasaccharide **20** was subjected to hydrogenolysis using Pd/C under hydrogen atmosphere followed by methanolysis of benzoate groups and a further hydrogenolysis step in the presence of $Pd(OH)_2$ on carbon was used to remove small amounts of residual of benzyl ether to furnish hexasaccharide **1**, (Scheme 7).

Imidates are recognized to be highly effective glycosylating derivatives. However, here we experienced success with a thioglycoside donor when glycosylations with mono-, di- and trisaccharide imidate donors failed. A similar experience was reported during synthesis of Neisseria lipopolysaccharide inner core oligosaccharides.[33]

3. Conclusion

3-O-Benzyl-1,2:5,6-di-O-isoopropylidene-α-D-glucofuranose **2** provides convenient access to selectively protected β1,3 linked di and trisaccharides **6** and **9** as well as the corresponding imidates **10** and **12**. The trisaccharide and disaccharide imidates were unable to glycosylate the selectively protected di or trisaccharide alcohols **7** and **9**. However, the target hexasaccharide **1** could be synthesized by a 2+2 and 2+4 glycosylation sequence. This involved conversion of 3′-O-benzyl perbenzoylated disaccharide **11** to the 4,6:4′,6′-di-O-benzylidene derivative **14** followed by Lewis acid catalyzed reaction to yield the selectively protected disaccharide ethylthioglycoside **15**. Glycosidation of **15** with 5-methoxycarbonylpentanol followed by a repetitive cycle involving removal of benzyl ether and glycosylation by **15** in 2+2 and 2+4 reactions provided a route to glycoside **1**.

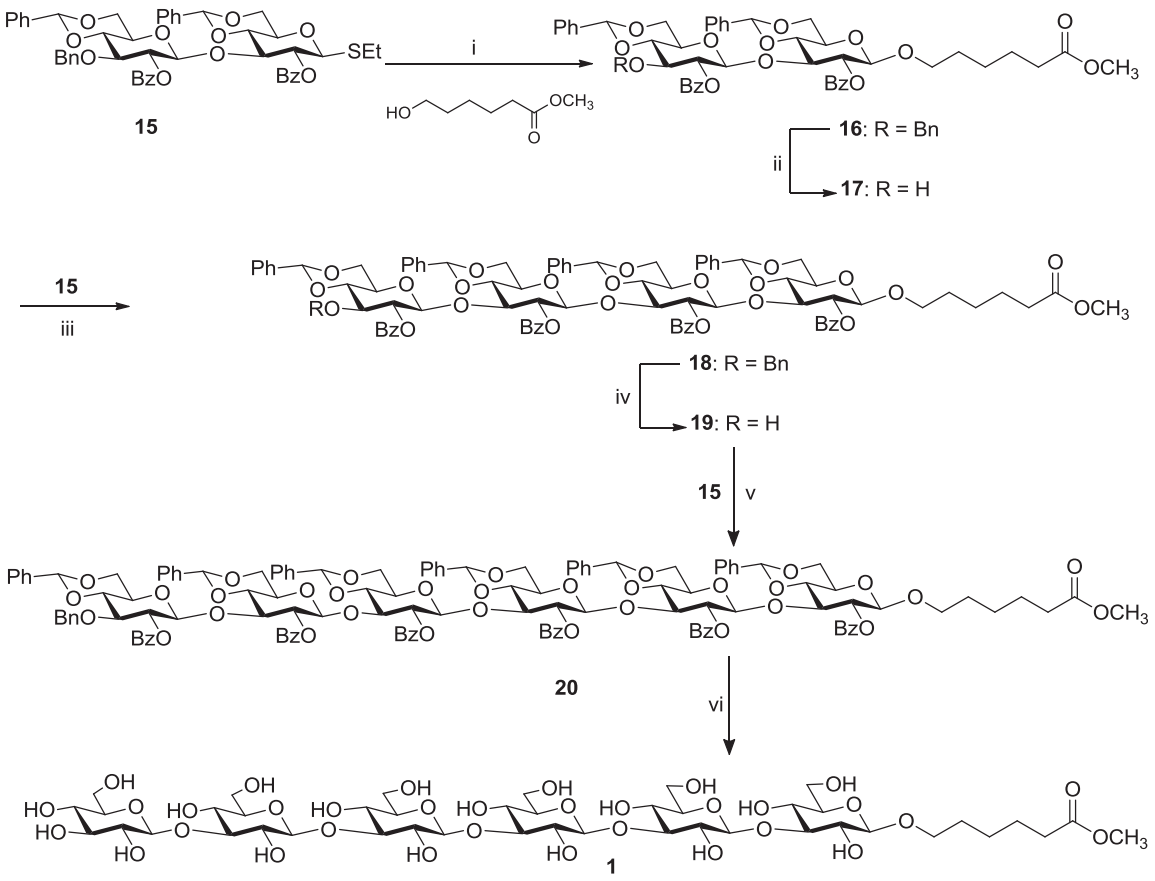
4. Experimental data

4.1. General methods

Solvents used in reactions were purified by successive passage through columns of alumina and copper under an argon atmosphere. Analytical thin-layer chromatography (TLC) was performed on silica gel 60-F254 (Merck). TLC detection was achieved by charring with 5% sulfuric acid in ethanol. All commercial reagents were used as supplied. Column chromatography used silica gel (SiliCycle, 230–400 mesh, 60 Å). ^1H NMR spectra were recorded at either 500, 600, or 700 MHz, and are referenced to internal standards of the residual protonated solvent peaks; δ H 7.24 ppm for solutions in $CDCl_3$, and to 0.1% external acetone (δ H 2.225 ppm) for solutions in D_2O. Assignments were made with the aid of GCOSY, TOCSY, and TROESY experiments. ^{13}C NMR spectra were referenced to internal $CDCl_3$ (δ C 77.0 ppm) or to external acetone (δ C 31.07 ppm). Optical rotations were measured with a Perkin–Elmer 241 polarimeter at 22 °C. Mass spectrometric analysis was performed by positive-mode electrospray ionization on a Micromass ZabSpec Hybrid Sector-TOF mass spectrometer.

4.2. 5-Methoxycarbonylpentyl β-D-glucopyranosyl-(1→3)-β-D-glucopyranosyl-(1→3)-β-D-glucopyranosyl-(1→3)-β-D-glucopyranosyl-(1→3)-β-D-glucopyranoside (*1*)

To a solution of **20** (400 mg, 0.17 mmol) in DCM/CH_3OH (1:3) (30 mL) was added Pd/C (40 mg, 10% w/w). The reaction mixture was stirred for two days under hydrogen atmosphere before it was filtered, concentrated under reduced pressure. The crude product was dissolved in CH_3OH (10 mL) and freshly prepared $NaOCH_3$ was added until the pH=12 and the reaction was allowed overnight at rt. The solution was neutralized with Amberlite IR-120 H^+ resin, filtered and concentrated under reduced pressure and the resulting crude product was purified with column chromatography (DCM/methanol 5:1) to give the product as white solid. NMR and MS spectra of it indicated that it was a mixture with the main component as O-benzyl derivative of expected hexasaccharide **1** so it was subjected to further deprotection. This product (172 mg) and $Pd(OH)_2$ (20% wt on carbon, 159 mg) were suspended in glacial acetic acid (5.5 mL) and left stirred under H_2 atmosphere overnight. After 24 h TLC of the reaction mixture (DCM/MeOH/H_2O/AcOH 12:6:1:0.1) indicated the reaction was complete. The catalyst was filtered off using syringe filter (Milipore PVDF 0.45 mm) and rinsed with water. The combined filtrate was concentrated and purified on RP-HPLC [Phenomex Luna C18(2), water/acetonitrile 99:1→50:50, 50 min, t_R=24.9 min. After lyophilization, compound **1** was obtained as white fluffy solid (45 mg, 24%); R_f 0.24 (DCM/MeOH/H_2O/AcOH 12:6:1:0.1); $[\alpha]_D$ −18.6° (*c* 1.0, H_2O); ^1H NMR (700 MHz, D_2O, 35 °C): δ 4.73–4.76 (m, 3H), 4.73 (d, *J*=7.9 Hz, 1H), 4.70 (d, *J*=7.9 Hz, 1H), 4.43 (d, *J*=8.2 Hz, 1H), 3.84–3.90 (m, 7H), 3.71–3.76 (m, 4H), 3.66–3.71 (m, 7H), 3.65 (s, 3H), 3.61–3.64 (m, 1H), 3.39–3.53 (m, 17H), 3.34–3.38 (m, 1H), 3.31 (dd, *J*=9.3, 8.1 Hz, 1H), 2.36 (t, *J*=7.4 Hz, 2H), 1.56–1.62 (m, 4H), 1.31–1.36 ppm (m, 2H). ^{13}C NMR (125 MHz, D_2O): δ 178.6 (C=O), 103.8,103.5, 102.9, 85.4, 85.2, 85.0, 76.9 76.7, 76.5, 74.4, 74.3, 73.9, 71.3, 70.6, 69.2, 69.1, 61.7, 53.1, 34.6, 29.3, 25.6, 25.0 ppm. HRMS (ESI) calcd $(M+Na)^+$ $C_{43}H_{74}O_{33}Na$: 1141.4005. Found: 1141.3991.



Scheme 7. (i) NIS, AgOTf, DCM, −10 °C, 30 min, 89%; (ii) Pd/C, H_2, THF-CH_3OH (1:1), 3 h, 87%; (iii) NIS, AgOTf, DCM, −20 °C, 2 h, 91%; (iv) Pd/C, H_2, THF-CH_3OH (1:1), 3 h, 73%; (v) NIS, AgOTf, DCM, −20 °C, 4 h, 87%; (vi) Pd/C, H_2, acetic acid, overnight; $NaOCH_3$, CH_3OH, overnight, $Pd(OH)_2$/C, H_2, acetic acid, overnight, 24%.

4.3. 1,2:5,6-Di-O-isopropylidene-3-O-benzyl-α-D-glucofuranose (**2**)

To a solution of 1,2:5,6-di-O-isopropylidene-α-D-glucofuranose, (100 g, 0.38 mol) and benzyl chloride (50.024 g, 45.47 mL, 0.395 mol) in DMF (300 mL), NaH (14.59 g, 0.608 mol) was added portion-wise over 10 min at 0 °C. The reaction mixture was stirred at rt for 30 min before water (500 mL) was added. The solution was diluted with EtOAc (2×200 mL) and washed with water (2×200 mL). The organic layer was dried (Na_2SO_4), filtered, concentrated, and the resulting crude product was pure enough to give **2** (130.6 g, 97%) as a yellowish oil, which was carried to the next step without further purification: R_f 0.56 (5:1 hexane–EtOAc); $[\alpha]_D$ −24.3° (*c* 6.8, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$): δ 7.38–7.25 (m, 5H, Ar–H), 5.89 (d, 1H, *J*=3.7 Hz, H-1), 4.69–4.62 (m, 2H, Ar–CH_2), 4.58 (d, 1H, *J*=3.7 Hz, H-2), 4.37 (dt, 1H, *J*=7.7, 6.0 Hz, H-3), 4.17–4.08 (m, 2H, H-5, H-6), 4.03–3.98 (m, 2H, H-4, H-6), 1.49 (s, 3H, CH_3), 1.42 (s, 3H, CH_3), 1.37 (s, 3H, CH_3), 1.30 (s, 3H, CH_3)); ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.7, 128.4, 127.9, 127.7, 111.8 ((CH_3)$_2C$), 109.0 ((CH_3)$_2C$), 105.3, 82.7, 81.7, 81.4, 72.6, 72.4, 67.4, 26.9, 26.3, 26.3, 25.5. HRMS (ESI) calcd $(M+Na)^+$ $C_{19}H_{26}O_6Na$: 373.1622. Found: 373.1614.

4.4. 3-O-Benzyl-α/β-D-glucopyranose (**3**)

A solution of 6 M HCl (25 mL) was added to a solution of compound **2** (50 g, 0.143 mol) in dioxane (100 mL) and stirred overnight at room temperature. Dichloromethane (DCM) (50 mL) was added to the reaction mixture and the yellowish organic layer was separated and discarded. The aqueous layer was neutralized by adding a solution of satd Na_2CO_3 and then extracted with EtOAc (3×75 mL). After the organic solvent was removed under reduced pressure, a white pasty material was obtained, which was then dissolved in a small amount of EtOAc and was kept in fridge. Compound **3** (36 g, 93.5%) crystalized out as a white crystalline solid: mp 132–134 °C; R_f 0.25 (EtOAc); $[\alpha]_D$ +21.6° (*c* 1.3, H_2O); ^1H NMR (700 MHz, D_2O) δ 7.45–7.34 (m, 10H, Ar–H), 5.17 (d, 1H, *J*=3.7 Hz, H-1$_\beta$), 4.82 (d, 2H, *J*=6.2 Hz, Ar–CH_2), 4.60 (d, 1H, *J*=8.0 Hz, H-1$_\alpha$), 3.84 (dd, 1H, *J*=12.3, 2.2 Hz, H-5$_\beta$), 3.82–3.75 (m, 2H, H-3$_\beta$, H-5$_\alpha$), 3.73–3.64 (m, 4H, H-6$_{(a,b)\alpha}$, H-6$_{(a,b)\beta}$), 3.57 (dd, 1H, *J*=9.8, 3.7 Hz, H-2$_\beta$), 3.49–3.44 (m, 2H, H-3$_\alpha$, H-4$_\alpha$), 3.41 (ddd, 1H, *J*=10.0, 5.7, 2.0 Hz, H-4$_\beta$), 3.29 (td, 1H, *J*=8.0, 1.5 Hz, H-2$_\alpha$); ^{13}C NMR (125 MHz, $CDCl_3$): δ 137.7, 137.6, 128.8, 128.7, 128.4, 128.3, 96.0 (C-1$_\alpha$), 92.3 (C-1$_\beta$), 84.0 (C-3$_\alpha$), 81.4 (C-3$_\beta$), 75.9 (C-4$_\beta$), 75.1 (Ar–CH_2), 74.9 (Ar–CH_2), 74.0 (C-2$_\beta$), 71.6 (C-4$_\alpha$), 71.4 (C-2$_\alpha$), 69.40 (C-5$_{\alpha,\ \beta}$), 60.71 (C-6 $_\beta$), 60.55 (C-6$_\alpha$). HRMS (ESI) calcd $(M+Na)^+$ $C_{13}H_{18}O_6Na$: 293.0996. Found: 293.0988.

4.5. 1,2,4,6-Tetra-O-benzoyl-3-O-benzyl-β-D-glucopyranose (**4**)

To a solution of **3** (30 g, 111 mmol) in pyridine (300 mL) was added BzCl (103.2 mL, 0.9 mol) dropwise at 0 °C over 1 h. The reaction mixture was stirred for additional 2 h at room temperature before it was quenched with ice/H_2O (500 g) and stirring was continued for another 1 h. The formed precipitate was filtered, washed with H_2O and then recrystallized from EtOAc/Hexane to give **4** (70 g, 92%) as a white crystalline solid: mp=131.50 °C; R_f 0.38 (EtOAc/hexane 1:3); $[\alpha]_D$ +1.3° (*c* 1.33, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 8.07–8.03 (m, 7H, Ar–H), 7.63–7.55 (m, 4H, Ar–H), 7.50–7.39 (m, 9H, Ar–H), 7.14–7.03 (m, 5H, Ar–H), 6.23 (d, 1H,

J=7.7 Hz, H-1), 5.80–5.74 (m, 2H, H-2, H-3), 4.70–4.65 (m, 3H, Ar–CH_2, H-6$_a$), 4.49 (dd, 1H, *J*=12.2, 5.1 Hz, H-6$_b$), 4.31 (ddd, 1H, *J*=9.6, 5.1, 3.1 Hz, H-5), 4.25 (t, 1H, *J*=8.7 Hz, H-4); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.2, 165.0, 164.8, 137.0, 133.7, 133.5, 133.4, 133.0, 130.2, 129.9, 129.8, 129.6, 129.2, 129.2, 128.6, 128.5, 128.5, 128.3, 128.2, 128.1, 127.8, 92.6, 79.2, 77.3, 77.1, 76.8, 74.3, 73.1, 72.1, 70.3, 62.9. HRMS (ESI) calcd (M+Na)$^+$ $C_{41}H_{34}O_{10}Na$: 709.2044. Found: 709.2048.

*4.6. 2,4,6-Tri-O-benzoyl-3-O-benzyl-α-D-glucopyranosyl trichloroacetimidate (**5**)*

To a solution of **4** (30 g, 43.7 mmol) in DCM/THF (1:10) (200 mL) was added CH_3NH_2 (30 mL, 33 wt% in absolute EtOH) and the reaction mixture was stirred for 4 h at room temperature. The reaction was quenched with 1 M HCl (100 mL), diluted with DCM (100 mL) and the organic layer was separated and the solvent was removed under reduced pressure. The resulting crude mass (25.5 g) was dissolved in dry DCM (100 mL), trichloroacetonitrile (87.6 mL) and DBU (0.5 mL) were added and the reaction mixture was stirred for 30 min. The mixture was concentrated under reduced pressure and the resulting crude product was purified with column chromatography (EtOAc/hexane 1:3) to give **5** (26.7 g, 84%) as an amorphous solid: R_f 0.54 (EtOAc/hexane 3:1); $[\alpha]_D$ +113.3° (*c* 1.20, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.61 (s, 1H, NH), 8.06 (q, 6H, *J*=7.3 Hz, Ar–H), 7.68–7.60 (m, 3H, Ar–H), 7.60–7.55 (m, 6H, Ar–H), 7.53–6.99 (m, 5H, Ar–H), 6.76 (d, 1H, *J*=3.7 Hz, H-1), 5.72 (t, 1H, *J*=9.7 Hz, H-4), 5.55 (dd, 1H, *J*=9.7, 3.7 Hz, H-2), 4.72 (ABq, 2H, *J*=11.4 Hz, BnCH_2), 4.64 (dd, 1H, *J*=12.2, 2.5 Hz, H-6$_a$), 4.54–4.51 (m, 1H, H-5), 4.48 (t, 1H, *J*=9.7 Hz, H-3), 4.43 (dd, 1H, *J*=12.2, 5.0 Hz, H-6$_b$); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.1 (CO), 165.3 (CO), 165.0 (CO), 160.4 (C=NH), 137.2, 133.5, 133.5, 133.1, 129.9, 129.8, 129.8, 129.7, 129.2, 129.2, 128.5, 128.5, 128.4, 128.2, 128.1, 127.8, 93.5, 90.9, 76.6, 74.9, 72.47, 70.8, 70.2, 62.7. HRMS (ESI) calcd (M+Na)$^+$ $C_{36}H_{30}O_9NCl_3Na$: 748.0878. Found: 748.0885.

*4.7. 2′,4′,6′-Tri-O-benzoyl-3′-O-benzyl-β-D-glucopyranosyl-(1→3)-1,2:5,6-di-O-isopropylidene-α-D-glucofuranose (**6**)*

To a solution of **5** (20 g, 27.5 mmol) and 1,2:5,6-di-O-isopropylidene-α-D-glucofuranose (7.9 g, 30.3 mmol) in DCM (100 mL) was added molecular sieves 4 Å (10 g). After the solution was stirred for 30 min, TMSOTf (250 μL, 1.4 mmol) was added and the reaction mixture was stirred for 45 min at room temperature. After neutralization with Et_3N, the solution was concentrated under reduced pressure and the crude mass was recrystallized from EtOAc/hexane to afford **6** (20.2 g, 89%) as a crystalline white solid: mp 197–199 °C; R_f 0.42 (EtOAc/hexane 1:2); $[\alpha]_D$ −3.6° (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.06–7.99 (m, 6H, Ar–H), 1.26–1.23 (m, 3H), 7.64–7.57 (m, 2H, Ar–H), 7.54 (ddt, 1H, *J*=8.8, 7.4, 1.3 Hz, Ar–H), 7.51–7.47 (m, 2H, Ar–H), 7.46–7.42 (m, 2H, Ar–H), 7.41–7.37 (m, 2H, Ar–H), 7.08–7.04 (m, 1H, Ar–H), 7.01 (d, 4H, *J*=5.0 Hz, Ar–H), 5.60 (dd, 1H, *J*=9.9, 9.0 Hz, C-4′), 5.46 (d, 1H, *J*=3.7 Hz, H-1), 5.38 (dd, 1H, *J*=9.1, 7.7 Hz, H-2′), 4.81 (d, 1H, *J*=7.7 Hz, H-1′), 4.61 (dd, 1H, *J*=12.0, 3.4 Hz, H-6′$_a$), 4.59 (d, 2H, *J*=1.0 Hz, Ar–CH_2), 4.45 (dd, 1H, *J*=12.0, 5.3 Hz, H-6′$_b$), 4.36 (dt, 1H, *J*=6.5, 5.6 Hz, H-5), 4.31 (d, 1H, *J*=3.7 Hz, H-2), 4.28 (d, 1H, *J*=3.2 Hz, H-3), 4.23 (dd, 1H, *J*=5.4, 3.1 Hz, H-4), 4.08 (t, 1H, *J*=9.1 Hz, H-3′), 4.04–3.99 (m, 2H, H-5′, H-6$_a$), 3.96 (dd, 1H, *J*=8.7, 5.8 Hz, H-6$_b$), 1.42 (s, 3H, CH_3), 1.37 (s, 3H, CH_3), 1.24 (s, 3H, CH_3)1.12 (s, 3H, CH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.2, 165.0, 164.6, 137.1, 133.5, 133.5, 133.01, 129.9, 129.7, 129.7, 129.6, 129.4, 129.2, 128.6, 128.5, 128.4, 128.2, 128.0, 127.7, 111.8, 108.6, 104.9, 99.8, 82.7, 81.1, 80.4, 79.1, 77.2, 77.0, 76.8, 73.8, 73.33, 73.02, 72.48, 70.92, 66.11, 63.20, 26.67, 26.57, 25.97, 25.07. HRMS (ESI) calcd (M+Na)$^+$ $C_{39}H_{42}O_{14}Na$: 757.2467. Found: 757.2457.

*4.8. 2′,4′,6′-Tri-O-benzoyl-β-D-glucopyranosyl-(1→3)-1,2:5,6-di-O-isopropylidene-α-D-glucofuranose (**7**)*

To a solution of **6** (20 g, 24.2 mmol) in CH_3OH/DCM (4:1) (100 mL) was added Pd/C (1 g, 5% w/w). The reaction mixture was stirred overnight under hydrogen atmosphere before it was filtered, concentrated under reduced pressure and the crude mass was recrystallized from EtOAc/hexane to give **7** (16.6 g, 93%) as a crystalline white solid: mp 241–243 °C; R_f 0.29 (EtOAc/hexane 1:2); $[\alpha]_D$ −4.8° (*c* 1.4, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.10–7.99 (m, 6H, Ar–H), 7.63–7.53 (m, 3H, Ar–H), 7.51–7.37 (m, 6H, Ar–H), 5.55 (d, 1H, *J*=3.7 Hz, H-1), 5.44 (t, 1H, *J*=9.6 Hz, H-4′), 5.22 (dd, 1H, *J*=9.1, 7.7 Hz, H-2′), 4.88 (d, 1H, *J*=7.7 Hz, H-1′), 4.66 (dd, 1H, *J*=12.1, 3.1 Hz, H-6′$_a$), 4.48 (dd, 1H, *J*=12.1, 5.3 Hz, H-6′$_b$), 4.41 (d, 1H, *J*=3.7 Hz, H-2), 4.36 (q, 1H, *J*=5.9 Hz, H-5), 4.34 (d, 1H, *J*=3.2 Hz, H-3), 4.24 (dd, 1H, *J*=5.9, 3.2 Hz, H-4), 4.14 (t, 1H, *J*=8.9 Hz, H-3′), 4.05 (ddd, 1H, *J*=9.9, 5.2, 3.1 Hz, H-5′), 4.01 (dd, 1H, *J*=8.7, 6.5 Hz, H-6$_a$), 3.96 (dd, 1H, *J*=8.7, 5.6 Hz, H-6$_b$), 1.44 (s, 3H, CH_3), 1.37 (s, 3H, CH_3), 1.21 (s, 3H, CH_3), 1.17 (s, 3H, CH_3); ^{13}C NMR (150.86 MHz, $CDCl_3$, δ_C) 166.2 (C=O), 166.1 (C=O), 165.8 (C=O), 133.6, 133.2, 129.9, 129.8, 129.7, 129.5, 129.3, 129.0, 128.6, 128.5, 128.4, 111.9, 108.7, 105.0, 99.5, 82.9, 81.0, 80.4, 74.6, 73.9, 73.0, 72.3, 72.2, 66.2, 63.2, 26.7, 26.6, 26.1, 25.1. HRMS (ESI) calcd (M+Na)$^+$ $C_{36}H_{30}O_9NCl_3Na$: 748.0878. Found: 748.0885.

*4.9. 2″,4″,6″-Tri-O-benzoyl-3″-O-benzyl-β-D-glucopyranosyl-(1→3)-2′,4′,6′-tri-O-benzoyl-β-D-glucopyranosyl-(1→3)-1,2:5,6-di-O-isopropylidene-α-D-glucofuranose (**8**)*

To a solution of **5** (8.9 g, 12.25 mmol) and **7** (10 g, 13.6 mmol) in DCM (100 mL) was added molecular sieves 4 Å (10 g). After the solution was stirred for 30 min at rt, the reaction was cooled to 0 °C, TMSOTf (100 μL, 0.56 mmol) was added and the reaction mixture was stirred for 4 h. After neutralization with Et_3N, the solution was concentrated under reduced pressure and the crude mass was recrystallized from EtOAc/hexane to afford **8** (14.5 g, 91%) as an amorphous white powder: R_f 0.35 (EtOAc/hexane 1:2); $[\alpha]_D$ −29.0° (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08–8.02 (m, 3H, Ar–H), 7.98–7.95 (m, 2H, Ar–H), 7.92–7.87 (m, 2H, Ar–H), 7.81–7.76 (m, 2H, Ar–H), 7.75–7.65 (m, 1H, Ar–H), 7.63–7.49 (m, 7H, Ar–H), 7.49–7.44 (m, 1H, Ar–H), 7.44–7.24 (m, 12H, Ar–H), 7.05–6.98 (m, 1H, Ar–H), 6.92 (t, *J*=7.6 Hz, 2H, Ar–H), 6.87–6.77 (m, 2H, Ar–H), 5.50 (t, *J*=9.4 Hz, 1H), 5.34–5.27 (m, 1H), 5.27–5.21 (m, 1H), 4.95 (d, *J*=7.8 Hz, 1H), 4.71 (d, *J*=7.4 Hz, 1H), 4.64 (dd, *J*=12.1, 3.6 Hz, 1H), 4.45 (ddd, *J*=11.2, 9.7, 5.2 Hz, 4H), 4.41 (d, *J*=5.1 Hz, 1H), 4.30 (q, *J*=5.9 Hz, 1H), 4.23 (d, *J*=3.2 Hz, 1H), 4.18 (ddt, *J*=9.7, 5.9, 3.4 Hz, 3H), 4.11–3.96 (m, 4H), 3.90 (td, *J*=8.9, 4.8 Hz, 3H), 1.42 (s, 3H), 1.38 (s, 3H), 1.26 (s, 3H), 1.10 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.2 (C=O), 166.0 (C=O), 165.0 (C=O), 164.9 (C=O), 164.8 (C=O), 163.9 (C=O), 137.0, 133.6, 133.4, 133.3, 133.2, 133.1, 133.0, 129.9, 129.8, 129.76, 129.71, 129.68, 129.63, 129.57, 129.53, 129.50, 129.3, 129.2, 111.8, 108.5, 104.8, 100.8, 99.44, 82.5, 80.9, 80.5, 79.6, 77.7, 73.8, 73.5, 72.9, 72.4, 72.1, 71.2, 70.0, 66.1, 63.6, 63.4, 26.7, 26.6, 25.9, 25.0. HRMS (ESI) calcd (M+Na)$^+$ $C_{73}H_{70}O_{22}Na$: 1321.4251. Found: 1321.4238.

*4.10. 2″,4″,6″-Tri-O-benzoyl-β-D-glucopyranosyl-(1→3)-2′,4′,6′-tri-O-benzoyl-β-D-glucopyranosyl-(1→3)-1,2:5,6-di-O-isopropylidene-α-D-glucofuranose (**9**)*

To a solution of **8** (1 g, 0.8 mmol) in CH_3OH/DCM (2:1) (30 mL) was added Pd/C (50 mg, 5% w/w). The reaction mixture was stirred

overnight under hydrogen atmosphere before it was filtered, concentrated under reduced pressure and the crude mass was recrystallized from EtOAc/hexane to give **9** (0.83 g, 89%) as amorphous white powder: R_f 0.3 (EtOAc/hexane 1:2); $[\alpha]_D$ −39.7° (*c* 1.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09–8.05 (m, 2H, Ar–H), 8.05–7.92 (m, 8H, Ar–H), 7.88–7.82 (m, 2H, Ar–H), 7.73–7.67 (m, 1H, Ar–H), 7.62–7.51 (m, 7H, Ar–H), 7.40 (td, *J*=7.7, 1.9 Hz, 8H, Ar–H), 7.36–7.31 (m, 2H, Ar–H), 5.49 (t, *J*=9.4 Hz, 1H), 5.36 (dd, *J*=8.9, 7.5 Hz, 1H), 5.27 (d, *J*=3.7 Hz, 1H), 5.11–5.00 (m, 2H), 4.93 (d, *J*=7.7 Hz, 1H), 4.71 (d, *J*=7.9 Hz, 1H), 4.63 (dd, *J*=12.1, 3.4 Hz, 1H), 4.46 (dd, *J*=10.2, 7.5 Hz, 2H), 4.31 (q, *J*=5.8 Hz, 1H), 4.27–4.17 (m, 4H), 4.07 (dt, *J*=11.8, 6.2 Hz, 3H), 4.00 (dd, *J*=8.7, 6.6 Hz, 1H), 3.91 (dd, *J*=9.0, 5.9 Hz, 3H), 1.42 (s, 3H), 1.38 (s, 3H), 1.26 (s, 3H), 1.11 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.4 (C=O), 166.1 (C=O), 165.9 (C=O), 165.8 (C=O), 164.9 (C=O), 164.0 (C=O), 133.8, 133.5, 133.4, 133.3, 133.2, 133.1, 130.0, 129.8, 129.8, 129.7, 129.6, 129.6, 129.5, 129.4, 129.3, 129.2, 129.1, 128.9, 128.8, 128.6, 128.5, 128.4, 128.3, 128.2, 111.8, 108.6, 104.8, 100.4, 99.5, 82.6, 81.0, 80.4, 77.6, 74.8, 74.0, 73.5, 72.9, 72.5, 72.4, 71.8, 69.8, 66.1, 63.6, 63.3, 26.7, 26.6, 25.9, 25.0. HRMS (ESI) calcd $(M+Na)^+$ $C_{66}H_{64}O_{22}Na$: 1231.3781. Found: 1231.3762.

4.11. 2″,4″,6″-Tri-O-benzoyl-3″-O-benzyl-β-D-glucopyranosyl-(1→3)-2′,4′,6′-tri-O-benzoyl-β-D-glucopyranosyl-(1→3)-2,4,6-tri-O-benzoyl-β-D-glucopyranosyl trichloroacetimidate (**10**)

A solution of **8** (5 g, 3.84 mmol) in dioxane/6 M HCl (4:1) (100 mL) was stirred at room temperature for 17 h before the solution with diluted with H_2O (100 mL). DCM (100 mL) was added to the mixture and the organic layer was separated, washed with satd Na_2CO_3 (100 mL), satd NaCl (100 mL), dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure to give amorphous solid (3.5 g). The crude solid was dissolved in pyridine (20 mL) and BzCl (3.6 mL, 30.8 mmol) was added dropwise at 0 °C over 10 min. The reaction mixture was stirred for additional 2 h at room temperature before it was quenched with ice/H_2O (100 g) and stirring was continued for another 1 h. The formed precipitate was filtered, washed with H_2O, dissolved in DCM (50 mL) and washed with satd NaCl (50 mL) before was dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. The formed white solid was dissolved in THF/DCM (4:1) (50 mL) and CH_3NH_2 (7.5 mL, 33 wt% in absolute ethanol) was added and the reaction mixture was stirred for 3 h before it was neutralized with 1 M HCl (25 mL), diluted with DCM (100 mL), the organic layer was separated, dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. The resulting crude mass was dissolved in dry DCM (40 mL), trichloroacetonitrile (7 mL) and DBU (100 μL) were added and the reaction mixture was stirred for 30 min. The mixture was concentrated under reduced pressure and the resulting crude product was purified with column chromatography (EtOAc/hexane 1:1) to give **10** (5 g, 78%) as an amorphous solid: R_f 0.39 (EtOAc/hexane 1:1); $[\alpha]_D$ −20.3° (*c* 1.2, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.55 (s, 1H, NH), 8.12 (d, *J*=7.7 Hz, 2H, Ar–H), 8.04 (t, *J*=7.0 Hz, 6H, Ar–H), 7.97 (d, *J*=7.7 Hz, 2H, Ar–H), 7.91–7.83 (m, 4H, Ar–H), 7.69 (d, *J*=7.7 Hz, 2H, Ar–H), 7.64–7.18 (m, 28H, Ar–H), 6.99 (t, *J*=7.4 Hz, 1H, Ar–H), 6.89 (t, *J*=7.6 Hz, 2H, Ar–H), 6.77 (d, *J*=7.5 Hz, 2H, Ar–H), 6.69 (d, *J*=3.7 Hz, 1H, Ar–H), 5.57 (t, *J*=9.8 Hz, 1H), 5.28 (t, *J*=8.7 Hz, 1H), 5.21 (ddt, *J*=24.7, 11.2, 5.0 Hz, 4H), 5.01 (d, *J*=8.0 Hz, 1H), 4.69 (dd, *J*=8.8, 4.1 Hz, 1H), 4.65 (d, *J*=4.3 Hz, 1H), 4.63 (d, *J*=2.8 Hz, 1H), 4.56 (dt, *J*=10.4, 4.0 Hz, 21H), 4.43 (dd, *J*=12.0, 5.2 Hz, 2H), 4.34 (dd, *J*=11.8, 6.5 Hz, 4H), 4.13 (ddd, *J*=25.2, 11.3, 5.4 Hz, 2H), 4.01 (dd, *J*=11.9, 5.6 Hz, 1H), 3.92 (dd, *J*=12.0, 6.7 Hz, 1H), 3.74 (dt, *J*=9.7, 4.8 Hz, 1H), 3.68 (t, *J*=9.1 Hz, 1H);^{13}C NMR (126 MHz, $CDCl_3$) δ 166.1 (C=O), 166.0 (C=O), 165.9 (C=O), 165.0 (C=O), 164.9 (C=O), 164.8 (C=O), 164.7 (C=O), 164.5 (C=O), 163.8 (C=O), 160.2 (C=O), 136.9, 133.7, 133.5, 133.4, 133.3, 133.2, 133.1, 133.0, 132.9, 130.0, 129.9, 129.8, 129.76, 129.73, 129.68, 129.66, 129.59, 129.56, 129.47, 129.38, 129.36, 129.13, 128.9, 128.7, 128.5, 128.4, 128.3, 128.3, 128.2, 128.0, 127.8, 127.5, 101.8, 101.0, 93.0, 90.8, 79.4, 77.9, 76.4, 73.7, 73.6, 73.1, 72.9, 72.3, 71.9, 71.2, 70.7, 68.5, 63.8, 63.6, 62.8. HRMS (ESI) calcd $(M+Na)^+$ $C_{90}H_{74}O_{25}NCl_3Na$: 1696.3508. Found: 1696.3527.

4.12. 2′,4′,6′-Tri-O-benzoyl-3′-O-benzyl-β-D-glucopyranosyl-(1→3)-2,4,6-tri-O-benzoyl-β-D-glucopyranosyl benzoate (**11**)

A solution of **6** (5 g, 6.1 mmol) in dioxane/6 M HCl (4:1) (50 mL) was stirred at room temperature for 17 h before the solution was diluted with H_2O (50 mL). DCM (100 mL) was added to the mixture and the organic layer was separated, washed with satd Na_2CO_3 (50 mL), satd NaCl (50 mL), dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure to give sticky white mass. The crude solid was dissolved in pyridine (40 mL) and BzCl (5.6 mL, 48.5 mmol) was added dropwise at 0 °C over 10 min. The reaction mixture was stirred for additional 2 h at room temperature before it was quenched with ice/H_2O (100 g) and stirring was continued for another 1 h. The formed precipitate was filtered, washed with H_2O, dissolved in DCM (50 mL) and washed with satd NaCl (50 mL) before was dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure to give **11** as white solid (5.8, 82%): R_f 0.38 (EtOAc/hexane 1:3); $[\alpha]_D$ −48.6° (*c* 1.5, $CHCl_3$); mp 62.0–64.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 (d, *J*=1.3 Hz, 1H, Ar–H), 8.14 (d, *J*=1.3 Hz, 1H, Ar–H), 8.12 (d, *J*=1.2 Hz, 1H, Ar–H), 8.11 (d, *J*=1.4 Hz, 1H, Ar–H), 8.03 (dd, *J*=2.8, 1.2 Hz, 2H, Ar–H), 8.02–8.01 (m, 3H, Ar–H), 8.00 (d, *J*=1.3 Hz, 1H, Ar–H), 7.95–7.93 (m, 1H, Ar–H), 7.93 (t, *J*=1.4 Hz, 2H, Ar–H), 7.91 (d, *J*=1.5 Hz, 1H, Ar–H), 7.61–7.29 (m, 18H, Ar–H), 7.20 (dd, *J*=8.3, 7.5 Hz, 2H, Ar–H), 7.04–6.98 (m, 1H, Ar–H), 6.92 (t, *J*=7.6 Hz, 2H, Ar–H), 6.85–6.80 (m, 2H, Ar–H), 6.76 (d, *J*=3.8 Hz, 1H, Ar–H), 5.64 (t, *J*=9.7 Hz, 1H), 5.43 (dd, *J*=9.9, 3.8 Hz, 1H), 5.35 (dd, *J*=9.3, 7.9 Hz, 1H), 5.29 (dd, *J*=9.8, 9.0 Hz, 1H), 5.07 (d, *J*=7.9 Hz, 1H), 4.79 (t, *J*=9.6 Hz, 1H), 4.68–4.60 (m, 1H), 4.49–4.37 (m, 2H), 4.29 (dd, *J*=11.8, 3.6 Hz, 4H), 4.08 (ddd, *J*=9.8, 6.2, 3.6 Hz, 1H), 3.97 (dd, *J*=11.9, 6.3 Hz, 1H), 3.93 (t, *J*=9.1 Hz, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.2 (C=O), 166.1 (C=O), 163.0 (2C=O), 164.7 (C=O), 164.6 (C=O), 164.3 (C=O), 136.9, 133.7, 133.6, 133.5, 133.4, 133.3, 133.2, 133.1, 133.0, 130.1, 129.8, 129.8, 129.8, 129.7, 129.6, 129.5, 129.4, 129.2, 129.2, 129.1, 128.9, 128.7, 128.6, 128.5, 128.4, 128.4, 128.3, 128.2, 128.1, 127.9, 127.6, 101.4, 90.0, 79.4, 76.0, 73.7, 73.2, 72.7, 72.1, 71.16, 70.4, 69.1, 63.6, 62.9. HRMS (ESI) calcd $(M+Na)^+$ $C_{68}H_{56}O_{18}Na$: 1183.3359. Found: 1183.3345.

4.13. 2′,4′,6′-Tri-O-benzoyl-3′-O-benzyl-β-D-glucopyranosyl-(1→3)-2,4,6-tri-O-benzoyl-β-D-glucopyranosyl trichloroacetimidate (**12**)

To a solution of **11** (2.5 g, 2.2 mmol) in THF/DCM (4:1) (25 mL) CH_3NH_2 (10 mL, 33 wt% in absolute ethanol) was added. The reaction was stirred for 3 h before it was neutralized with 1 M HCl (25 mL), diluted with DCM (50 mL), the organic layer was separated, dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. The resulting crude mass was dissolved in dry DCM (30 mL), trichloroacetonitrile (5 mL) and DBU (100 μL) were added and the reaction solution was stirred for 30 min. The mixture was concentrated under reduced pressure and the resulting crude product was purified with column chromatography (EtOAc/hexane 1:1) to give **12** (2.1 g, 81%) as an amorphous solid: R_f 0.4 (EtOAc/hexane 1:1); $[\alpha]_D$ +4.82° (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.53 (s, 1H, NH), 8.15–8.10 (m, 2H, Ar–H), 8.06–8.01 (m, 4H, Ar–H), 7.96 (ddd, *J*=10.0, 8.2, 1.5 Hz, 4H, Ar–H),

7.74–7.67 (m, 1H, Ar–H), 7.62–7.39 (m, 15H, Ar–H), 7.34 (t, *J*=7.7 Hz, 2H, Ar–H), 7.19 (t, *J*=7.7 Hz, 2H, Ar–H), 7.01 (t, *J*=7.4 Hz, 1H, Ar–H), 6.92 (t, *J*=7.6 Hz, 2H, Ar–H), 6.82 (d, *J*=7.2 Hz, 2H, Ar–H), 6.69 (d, *J*=3.6 Hz, 1H), 5.61 (t, *J*=9.8 Hz, 1H), 5.36–5.29 (m, 2H), 5.24 (t, *J*=9.4 Hz, 1H), 5.04 (d, *J*=8.0 Hz, 1H), 4.70 (t, *J*=9.6 Hz, 1H), 4.63 (dd, *J*=12.3, 2.7 Hz, 1H), 4.54 (ddd, *J*=10.5, 5.1, 2.8 Hz, 1H), 4.46–4.37 (m, 3H), 4.33 (dd, *J*=12.0, 3.0 Hz, 1H), 4.06 (ddd, *J*=9.9, 6.9, 3.0 Hz, 1H), 3.94–3.86 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.2 (C=O), 166.1 (C=O), 165.0 (C=O), 164.9 (C=O), 164.7 (C=O), 164.6 (C=O), 160.2 (*C*=NH), 136.9, 133.6, 133.5, 133.4, 133.3, 133.1, 132.9, 130.0, 129.9, 129.8, 129.7, 129.6, 129.5, 129.4, 129.3, 129.2, 128.9, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.5, 101.5, 93.1, 90.7, 79.3, 76.0, 73.5, 73.1, 72.9, 72.3, 71.0, 70.7, 68.5, 63.7, 62.8. HRMS (ESI) calcd $(M+Na)^+$ $C_{63}H_{52}O_{17}NCl_3Na$: 1222.2193. Found: 1222.2192.

*4.14. 3′-O-Benzyl-β-D-glucopyranosyl-(1→3)-2-O-benzoyl-β-D-glucopyranosyl benzoate (**13**)*

To a solution of **11** (2 g, 1.72 mmol) in DCM/CH_3OH (1:2) (30 mL) was added freshly prepared $NaOCH_3$ (46.5 mg, 0.86 mmol) and the reaction mixture was stirred for 1 h and then was neutralized with Amberlite IR-120 H^+ resin, filtered and concentrated under reduced pressure. Column chromatography in (EtOAc/hexane 2:1) gave the title compound, **13**, as waxy white solid (0.92 g, 72%): R_f 0.19 (EtOAc/hexane 2:1); $[\alpha]_D$ +36.8° (*c* 1.3, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00 (dd, *J*=8.3, 1.3 Hz, 2H, Ar–H), 7.66 (dd, *J*=8.4, 1.4 Hz, 2H, Ar–H), 7.61–7.55 (m, 3H, Ar–H), 7.50–7.42 (m, 3H, Ar–H), 7.38 (tt, *J*=7.4, 1.3 Hz, 1H, Ar–H), 7.24 (dd, *J*=8.3, 7.4 Hz, 2H, Ar–H), 7.14–7.04 (m, 7H, Ar–H), 6.59 (d, *J*=3.8 Hz, 1H), 5.28 (dd, *J*=9.3, 7.8 Hz, 1H), 5.24 (dd, *J*=9.8, 3.8 Hz, 1H), 4.91 (d, *J*=7.8 Hz, 1H), 4.61 (d, *J*=11.5 Hz, 2H), 4.29 (dd, *J*=9.8, 8.2 Hz, 1H), 4.07 (dd, *J*=12.1, 2.6 Hz, 1H), 4.01–3.83 (m, 7H), 3.66 (t, *J*=9.1 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.4 (C=O), 164.9 (C=O), 164.6 (C=O), 137.7, 133.7, 133.5, 133.1, 132.9, 130.2, 129.9, 129.6, 129.5, 129.2, 129.0, 128.8, 128.6, 128.4, 128.3, 128.2, 128.1, 128.0, 127.7, 101.3, 90.2, 82.1, 80.9, 76.2, 74.7, 73.9, 73.6, 71.5, 70.0, 68.5, 61.7, 61.5. HRMS (ESI) calcd $(M+Na)^+$ $C_{40}H_{40}O_{14}Na$: 767.2310. Found: 767.2298.

*4.15. 2′-O-Benzoyl-3′-O-benzyl-4′,6′-O-benzylidene-β-D-glucopyranosyl-(1→3)-2-O-benzoyl-4,6-O-benzylidene-β-D-glucopyranosyl benzoate (**14**)*

To a solution of **13** (3 g, 4.02 mmol) in acetonitrile (40 mL) was added benzaldehyde dimethylacetal (1.5 mL, 9.7 mmol) followed by *p*-toluenesulfonic acid (100 mg). The solution was stirred for 1 h and then was quenched with pyridine (1 mL) and concentrated to a yellow oil under vacuum. The oil was chromatographed on silica gel in (EtOAc/hexane 1:3) to yield **14** as a white waxy solid (3.5 g, 94%) after concentration: R_f 0.3 (EtOAc/hexane 1:3); $[\alpha]_D$ −65.3° (*c* 1.4, $CHCl_3$); ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.02 (d, *J*=7.7 Hz, 2H, Ar–H), 7.75 (d, *J*=7.8 Hz, 2H, Ar–H), 7.64–7.58 (m, 4H, Ar–H), 7.57–7.34 (m, 11H, Ar–H), 7.29 (dd, *J*=15.8, 8.0 Hz, 2H, Ar–H), 7.21 (t, *J*=7.7 Hz, 2H, Ar–H), 7.11 (ddt, *J*=21.5, 14.7, 7.1 Hz, 7H, Ar–H), 5.67 (s, 1H), 5.40 (s, 1H), 5.38 (dd, *J*=9.5, 4.0 Hz, 1H), 5.33 (t, *J*=7.3 Hz, 1H), 5.06 (d, *J*=6.8 Hz, 1H), 4.75 (d, *J*=12.1 Hz, 1H), 4.66 (d, *J*=12.1 Hz, 1H), 4.56 (t, *J*=9.5 Hz, 1H), 4.36 (ddd, *J*=15.1, 10.4, 5.0 Hz, 2H), 4.17 (td, *J*=10.0, 5.0 Hz, 1H), 3.99 (t, *J*=9.3 Hz, 1H), 3.94 (t, *J*=9.6 Hz, 1H), 3.85 (t, *J*=10.3 Hz, 2H), 3.81–3.76 (m, 2H), 3.59 (td, *J*=9.8, 4.9 Hz, 1H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 164.9 (C=O), 164.8 (C=O), 164.4 (C=O), 137.8, 137.3, 137.0, 133.8, 133.2, 132.9, 129.9, 129.7, 129.6, 129.3, 129.2, 129.1, 129.0, 128.8, 128.6, 128.5, 128.4, 128.3, 128.2, 128.11, 127.9, 127.5, 126.12, 126.0, 101.5, 101.1, 101.0, 90.4, 80.9, 79.0, 78.2, 75.3, 73.7, 73.5, 72.4, 68.8, 68.6, 66.2, 65.3. HRMS (ESI) calcd $(M+Na)^+$ $C_{54}H_{48}O_{14}Na$: 943.2936. Found: 943.2935.

*4.16. Ethylthio 2′-O-benzoyl-3′-O-benzyl-4′,6′-O-benzylidene-β-D-glucopyranosyl-(1→3)-2-O-benzoyl-4,6-O-benzylidene-β-D-glucopyranoside (**15**)*

To a solution of **14** (3 g, 3.3 mmol) in DCM (30 mL) and crushed 4 Å molecular sieves (3 g) was added EtSH (0.4 mL, 4.9 mmol). The reaction mixture was stirred for 30 min at room temperature and then cooled to 0 °C before $BF_3 \cdot Et_2O$ (1.6 mL, 13.2 mmol) was added dropwise over 10 min. The reaction mixture was stirred overnight before it was quenched with satd aq $NaHCO_3$ soln (30 mL), the organic layer was separated and concentrated to a yellow syrup under reduced pressure. Column chromatography in (EtOAc/hexane 1:3) gave **15** (2.3 g, 82%) as a white powder after concentration: R_f 0.39 (EtOAc/hexane 1:3); $[\alpha]_D$ +0.7° (*c* 1.0, $CHCl_3$); mp 192.0–194.0 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.17 (d, *J*=7.0 Hz, 2H, Ar–H), 7.86–7.83 (m, 2H, Ar–H), 7.64 (dd, *J*=9.0, 7.1 Hz, 4H, Ar–H), 7.60–7.48 (m, 5H, Ar–H), 7.48–7.34 (m, 6H, Ar–H), 7.30 (t, *J*=7.7 Hz, 1H, Ar–H), 7.15–7.12 (m, 1H, Ar–H), 7.11–7.05 (m, 4H, Ar–H), 5.61 (s, 1H), 5.37 (t, *J*=9.5 Hz, 1H), 5.35 (s, 1H), 5.31 (t, *J*=6.9 Hz, 1H), 4.94 (d, *J*=6.9 Hz, 1H), 4.74, 4.62 (dd, *J*=12.0 Hz, 2H), 4.61 (d, *J*=9.5 Hz, 1H), 4.43 (dd, *J*=10.5, 4.8 Hz, 1H), 4.28–4.22 (m, 2H), 3.94 (t, *J*=9.3 Hz, 1H), 3.85 (dt, *J*=14.0, 9.8 Hz, 1H), 3.78–3.70 (m, 1H), 3.62 (td, *J*=9.7, 4.9 Hz, 1H), 3.46 (td, *J*=9.8, 4.9 Hz, 1H), 2.69 (tp, *J*=15.0, 7.5 Hz, 2H, SCH_2), 1.20 (t, *J*=7.5 Hz, 3H, SCH_2CH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.8 (C=O), 164.7 (C=O), 137.8, 137.3, 137.2, 133.8, 133.0, 132.7, 130.2, 129.8, 129.7, 129.5, 129.4, 129.3, 128.9, 128.5, 128.3, 128.2, 128.1, 128.1, 127.8, 127.4, 126.2, 126.0, 101.6, 101.0, 100.6, 84.3, 80.7, 79.4, 79.0, 78.5, 73.8, 73.5, 72.1, 71.1, 68.7, 68.6, 66.0, 23.9, 14.7. HRMS (ESI) calcd $(M+Na)^+$ $C_{49}H_{48}O_{12}SNa$: 860.2866. Found: 860.2857.

*4.17. 5-Methoxycarbonylpentyl 2′-O-benzoyl-3′-O-benzyl-4′,6′-O-benzylidene-β-D-glucopyranosyl-(1→3)-2-O-benzoyl-4,6-O-benzylidene-β-D-glucopyranoside (**16**)*

To a solution of **15** (3 g, 3.5 mmol) and methyl 6-hydroxyhexanoate (600 mg, 4.2 mmol) in dry DCM (30 mL) was added crushed 4 Å molecular sieves (3 g) and the mixture was stirred for 30 min at rt. NIS (94 mg, 4.2 mmol) and AgOTf (51 mg, 0.2 mmol) were added to the mixture after it was cooled to −10 °C and was stirred for additional 30 min at the same temperature. The reaction mixture was neutralized with Et_3N (0.5 mL), filtered and concentrated to a colorless syrup under reduced pressure. Column chromatography in (EtOAc/hexane 2:1) yielded **16** (2.9 g, 89%) as amorphous white solid: R_f 0.33 (EtOAc/hexane 1:2); $[\alpha]_D$ −14.8° (*c* 1.3, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19–8.09 (m, 1H, Ar–H), 7.87–7.80 (m, 2H, Ar–H), 7.67 (d, *J*=6.8 Hz, 2H, Ar–H), 7.60–7.49 (m, 2H, Ar–H), 7.49–7.34 (m, 6H, Ar–H), 7.30 (t, *J*=7.8 Hz, 2H, Ar–H), 7.19–6.93 (m, 5H, Ar–H), 5.60 (s, 1H), 5.39 (s, 1H), 4.94 (d, *J*=7.1 Hz, 1H), 4.74 (d, *J*=12.0 Hz, 1H), 4.63 (d, *J*=12.1 Hz, 1H), 4.58 (d, *J*=7.6 Hz, 1H), 4.40 (dd, *J*=10.6, 4.9 Hz, 1H), 4.28–4.14 (m, 2H), 3.92 (t, *J*=9.4 Hz, 1H), 3.86 (td, *J*=10.2, 9.8, 7.6 Hz, 2H), 3.83–3.79 (m, 1H), 3.80–3.71 (m, 3H), 3.63 (s, 3H), 3.57 (td, *J*=9.7, 4.8 Hz, 1H), 3.44 (td, *J*=9.8, 5.0 Hz, 1H), 3.40–3.33 (m, 1H), 3.20 (q, *J*=7.3 Hz, 1H), 2.10–1.91 (m, 2H), 1.50–1.28 (m, 4H), 1.12 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 174.0 ($COCH_3$), 164.7 (C=O), 164.5 (C=O), 137.9, 137.3, 137.2, 132.9, 132.7, 130.0, 129.9, 129.8, 129.7, 129.6, 129.2, 128.9, 128.4, 128.3, 128.2, 128.1, 128.0, 127.8, 127.4, 126.2, 126.0, 101.6, 101.5, 101.0, 100.7, 80.9, 79.4, 78.4, 78.1, 73.8, 73.6, 73.6, 69.7, 68.8, 68.7, 66.5, 66.1, 51.4, 33.7, 29.0, 25.3, 24.4. HRMS (ESI) calcd $(M+Na)^+$ $C_{54}H_{56}O_{15}Na$: 967.3517. Found: 967.3513.

*4.18. 5-Methoxycarbonylpentyl 2′-O-benzoyl-4′,6′-O-benzylidene-β-D-glucopyranosyl-(1→3)-2-O-benzoyl-4,6-O-benzylidene-β-D-glucopyranoside (**17**)*

To a solution of **16** (2.5 g, 2.6 mmol) in THF/CH_3OH (1:1) (60 mL) was added Pd/C (125 mg, 5% w/w). The reaction mixture was stirred for 3 h under hydrogen atmosphere before it was filtered, concentrated under reduced pressure to a colorless syrup. Column chromatography of the crude product in (EtOAc/hexane 1:2) gave **17** (2 g, 87%) as amorphous white solid: R_f 0.29 (EtOAc/hexane 1:2); $[\alpha]_D$ −9.06° (*c* 1.0, $CHCl_3$); mp 81.0–83 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.82 (dd, *J*=8.2, 1.4 Hz, 2H, Ar–H), 7.76–7.71 (m, 2H, Ar–H), 7.57–7.49 (m, 4H, Ar–H), 7.46–7.33 (m, 10H, Ar–H), 7.30 (dd, *J*=8.3, 7.3 Hz, 2H, Ar–H), 5.57 (s, 1H), 5.38 (s, 1H), 5.26 (dd, *J*=8.6, 7.5 Hz, 1H), 5.13 (dd, *J*=8.3, 7.1 Hz, 1H), 4.95 (d, *J*=7.2 Hz, 1H), 4.57 (d, *J*=7.6 Hz, 1H), 4.38 (dd, *J*=10.5, 4.9 Hz, 1H), 4.24–4.14 (m, 2H), 3.87 (dd, *J*=9.2, 8.2 Hz, 1H), 3.83 (td, *J*=10.3, 9.8, 5.4 Hz, 2H), 3.79 (dt, *J*=9.7, 6.0 Hz, 1H), 3.71 (t, *J*=10.3 Hz, 1H), 3.70–3.66 (m, 1H), 3.61 (s, 3H), 3.56 (td, *J*=9.8, 4.9 Hz, 1H), 3.40 (td, *J*=9.8, 5.0 Hz, 1H), 3.35 (ddd, *J*=9.7, 7.2, 5.8 Hz, 1H), 2.03 (ddd, *J*=15.5, 8.8, 6.7 Hz, 1H), 1.96 (ddd, *J*=15.6, 8.6, 6.6 Hz, 1H), 1.47–1.33 (m, 4H), 1.11 (m, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 173.9 (*C*OCH_3), 165.5 (C═O), 164.5 (C═O), 137.2, 136.9, 133.0, 132.9, 129.8, 129.6, 129.5, 129.3, 129.2, 129.1, 128.3, 128.2, 128.1, 126.3, 126.1, 101.7, 101.5, 101.4, 100.3, 80.5, 79.3, 78.0, 75.3, 73.6, 72.6, 69.6, 68.76, 68.6, 66.4, 66.1, 51.4, 33.6, 28.9, 25.2, 24.4. HRMS (ESI) calcd $(M+Na)^+$ $C_{47}H_{50}O_{15}Na$: 877.3042 Found: 877.3026.

*4.19. 5-Methoxycarbonylpentyl 2‴-O-benzoyl-3‴-O-benzyl-4‴,6‴-O-benzylidene-β-D-glucopyranosyl-(1→3)-2″-O-benzoyl-4″,6″-O-benzylidene-β-D-glucopyranosyl-(1→3)-2′-O-benzoyl-4′,6′-O-benzylidene-β-D-glucopyranosyl-(1→3)-2-O-benzoyl-4,6-O-benzylidene-β-D-glucopyranoside (**18**)*

To a solution of donor **15** (2 g, 2.3 mmol) and acceptor **17** (1.7 g, 2 mmol) in dry DCM (30 mL) was added crushed 4 Å molecular sieves (3 g) and the mixture was stirred for 30 min at rt. NIS (620 mg, 2.76 mmol) and AgOTf (26 mg, 0.1 mmol) were added to the mixture after it was cooled to −10 °C and was stirred for additional 2 h at the same temperature. The reaction mixture was neutralized with Et_3N (0.5 mL), filtered and concentrated to a colorless syrup under reduced pressure. Column chromatography in (EtOAc/hexane 1:2) yielded **18** (3 g, 91%) as amorphous white solid: R_f 0.33 (EtOAc/hexane 1:2); $[\alpha]_D$ +8.4° (*c* 3.0, $CHCl_3$); mp 98.0–100.0 °C; ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.88–7.81 (m, 4H, Ar–H), 7.79–7.75 (m, 2H, Ar–H), 7.66–7.61 (m, 2H, Ar–H), 7.57–7.55 (m, 2H, Ar–H), 7.55–7.50 (m, 4H, Ar–H), 7.48–7.45 (m, 2H, Ar–H), 7.44–7.22 (m, 23H, Ar–H), 7.19 (dd, *J*=8.5, 6.5 Hz, 1H, Ar–H), 7.14–7.10 (m, 3H, Ar–H), 7.07 (t, *J*=7.6 Hz, 2H, Ar–H), 5.56 (s, 1H), 5.44 (s, 1H), 5.31 (t, *J*=7.9 Hz, 1H), 5.13 (t, *J*=5.0 Hz, 1H), 5.01 (d, *J*=7.5 Hz, 1H), 4.95 (d, *J*=5.5 Hz, 2H), 4.84–4.75 (m, 5H), 4.65 (d, *J*=12.1 Hz, 1H), 4.47 (d, *J*=7.8 Hz, 1H), 4.35 (dd, *J*=10.5, 4.7 Hz, 1H), 4.21 (dd, *J*=10.4, 5.0 Hz, 1H), 4.17–4.07 (m, 3H), 4.03 (dd, *J*=8.3, 4.9 Hz, 1H), 3.99 (t, *J*=9.0 Hz, 1H), 3.93 (dd, *J*=8.5, 5.6 Hz, 1H), 3.87 (t, *J*=9.3 Hz, 1H), 3.85–3.67 (m, 5H), 3.63 (s, 3H), 3.58 (td, *J*=9.8, 4.4 Hz, 1H), 3.53 (t, *J*=10.0 Hz, 1H), 3.51–3.43 (m, 4H), 3.43–3.38 (m, 2H), 3.37–3.32 (m, 1H), 2.11–1.89 (m, 2H), 1.48–1.34 (m, 4H), 1.13 (m, 2H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 173.9 (*C*OCH_3), 165.0 (C═O), 164.6 (C═O), 164.5 (C═O), 164.4 (C═O), 137.9, 137.3, 137.2, 137.1, 133.4, 133.2, 133.0, 132.9, 129.8, 129.7, 129.6, 129.3, 129.1, 129.0, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 128.03, 127.9, 127.8, 127.4, 126.4, 126.3, 126.1, 126.0, 101.8, 101.5, 101.2, 101.1, 100.7, 98.9, 98.6, 96.9, 81.2, 78.9, 78.3, 78.2, 77.5, 76.7 75.3, 74.1, 74.0, 73.7, 73.6, 73.4, 72.5, 69.6, 68.7, 68.6, 66.4, 66.0, 65.6, 65.4, 51.3, 33.6, 29.0, 25.3, 24.3. HRMS (ESI) calcd $(M+Na)^+$ $C_{94}H_{92}O_{27}Na$: 1675.5718. Found: 1675.5694.

*4.20. 5-Methoxycarbonylpentyl 2‴′-O-benzoyl-4‴′,6‴′-O-benzylidene-β-D-glucopyranosyl-(1→3)-2‴-O-benzoyl-4‴,6‴-O-benzylidene-β-D-glucopyranosyl-(1→3)-2″-O-benzoyl-4″,6″-O-benzylidene-β-D-glucopyranosyl-(1→3)-2′-O-benzoyl-4′,6′-O-benzylidene-β-D-glucopyranosyl-(1→3)-2-O-benzoyl-4,6-O-benzylidene-β-D-glucopyranoside (**19**)*

To a solution of **18** (1 g, 0.6 mmol) in THF/CH_3OH (1:1) (60 mL) was added Pd/C (50 mg, 5% w/w). The reaction mixture was stirred for 3 h under hydrogen atmosphere before it was filtered, concentrated under reduced pressure to a colorless syrup. Column chromatography of the crude product in (EtOAc/hexane 1:2) gave **19** (690 mg, 73%) as amorphous white solid: R_f 0.30 (EtOAc/hexane 1:2); $[\alpha]_D$ +12.5° (*c* 2.4, $CHCl_3$); ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.95 (dd, *J*=8.3, 1.4 Hz, 2H, Ar–H), 7.85 (dd, *J*=8.3, 1.4 Hz, 2H, Ar–H), 7.79 (dd, *J*=8.3, 1.4 Hz, 2H, Ar–H), 7.66 (dd, *J*=8.3, 1.4 Hz, 2H, Ar–H), 7.58–7.50 (m, 8H, Ar–H), 7.47 (dd, *J*=7.7, 1.9 Hz, 2H, Ar–H), 7.45–7.31 (m, 16H, Ar–H), 7.30–7.23 (m, 5H, Ar–H), 7.22–7.17 (m, 1H, Ar–H), 5.55 (s, 1H), 5.44 (s, 1H), 5.19 (dd, *J*=8.5, 7.4 Hz, 1H), 5.16 (t, *J*=5.0 Hz, 1H), 5.08 (d, *J*=7.4 Hz, 1H), 4.98 (d, *J*=5.1 Hz, 1H), 4.95 (dd, *J*=8.8, 7.8 Hz, 1H), 4.86–4.80 (m, 4H), 4.47 (d, *J*=7.8 Hz, 1H), 4.34 (dd, *J*=10.5, 4.8 Hz, 1H), 4.21 (dd, *J*=10.5, 5.0 Hz, 1H), 4.16–4.09 (m, 3H), 4.07 (dd, *J*=8.4, 4.9 Hz, 1H), 4.02–3.97 (m, 2H), 3.97–3.92 (m, 1H), 3.78 (dt, *J*=9.9, 6.1 Hz, 1H), 3.75 (t, *J*=10.2 Hz, 1H), 3.73–3.67 (m, 2H), 3.63 (s, 3H), 3.59 (td, *J*=9.9, 4.2 Hz, 1H), 3.53 (t, *J*=10.1 Hz, 1H), 3.50–3.44 (m, 4H), 3.41 (tt, *J*=9.9, 2.8 Hz, 2H), 3.35 (ddd, *J*=9.7, 7.2, 5.8 Hz, 1H), 2.10–2.01 (m, 1H), 1.98 (ddd, *J*=15.7, 8.6, 6.6 Hz, 1H), 1.48–1.34 (m, 4H), 1.20–1.06 (m, 2H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 173.9 (*C*OCH_3), 165.8 (C═O), 164.6 (C═O), 164.5 (2C═O), 137.3, 137.2, 137.1, 137.0, 133.6, 133.3, 133.1, 133.0, 129.9, 129.8, 129.7, 129.6, 129.5, 129.4, 129.3, 129.24, 129.2, 129.1, 129.0, 128.9, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 126.4, 126.3, 126.2, 126.0, 101.8, 101.8, 101.5, 101.2, 100.7, 98.7, 98.6, 97.0, 80.8, 78.9, 78.1, 77.5, 76.8, 76.8, 75.4, 74.8, 74.3, 74.0, 73.6, 72.6, 72.5, 69.6, 68.7, 68.6, 66.4, 66.0, 65.6, 65.5, 51.4, 33.7, 29.0, 25.3, 24.3. HRMS (ESI) calcd $(M+Na)^+$ $C_{87}H_{86}O_{27}Na$: 1585.5249. Found: 1585.5243.

*4.21. 5-Methoxycarbonylpentyl 2⁗′-O-benzoyl-4⁗′,6⁗′-O-benzylidene-β-D-glucopyranosyl-(1→3)-2⁗-O-benzoyl-4⁗,6⁗-O-benzylidene-β-D-glucopyranosyl-(1→3)-2‴-O-benzoyl-4‴,6‴-O-benzylidene-β-D-glucopyranosyl-(1→3)-2″-O-benzoyl-4″,6″-O-benzylidene-β-D-glucopyranosyl-(1→3)-2′-O-benzoyl-4′,6′-O-benzylidene-β-D-glucopyranosyl-(1→3)-2-O-benzoyl-4,6-O-benzylidene-β-D-glucopyranoside (**20**)*

To a solution of donor **15** (500 mg, 0.54 mmol) and acceptor **19** (700 mg, 0.45 mmol) in dry DCM (20 mL) was added crushed 4 Å molecular sieves (1 g) and the mixture was stirred for 30 min at rt. NIS (146 mg, 0.65 mmol) and AgOTf (26 mg, 0.1 mmol) were added to the mixture after it was cooled to −10 °C and was stirred for additional 4 h at the same temperature. The reaction mixture was neutralized with Et_3N (0.2 mL), filtered and concentrated to a colorless syrup under reduced pressure. Column chromatography in (EtOAc/hexane 1:2) yielded **20** (925 mg, 87%) as amorphous white solid: R_f 0.38 (EtOAc/hexane 1:2); $[\alpha]_D$ +18.0° (*c* 1.4, $CHCl_3$); ^{1}H NMR (700 MHz, $CDCl_3$) δ 7.91–7.88 (m, 12H, Ar–H), 7.88–7.84 (m, 12H, Ar–H), 7.83–7.77 (m, 6H, Ar–H), 7.67–7.64 (m, 2H, Ar–H), 7.63–7.58 (m, 2H, Ar–H), 7.53 (t, *J*=7.4 Hz, 2H, Ar–H), 7.51–7.21 (m, 43H, Ar–H), 7.21–7.17 (m, 1H, Ar–H), 7.17–7.12 (m, 3H, Ar–H), 7.09 (t, *J*=7.3 Hz, 2H, Ar–H), 5.55 (s, 1H), 5.47 (s, 1H), 5.35 (t, *J*=7.9 Hz, 1H), 5.19 (t, *J*=4.9 Hz, 1H), 5.08 (d, *J*=7.5 Hz, 1H), 5.00 (d, *J*=5.1 Hz, 1H), 4.96 (t, *J*=8.3 Hz, 1H), 4.92–4.85 (m, 7H), 4.83–4.77 (m, 4H),

4.68 (d, J=12.1 Hz, 1H), 4.48 (d, J=7.8 Hz, 1H), 4.35 (dd, J=10.5, 4.9 Hz, 1H), 4.25 (dd, J=10.4, 4.9 Hz, 1H), 4.21–4.10 (m, 6H), 4.08 (dd, J=8.3, 4.7 Hz, 1H), 4.06–4.01 (m, 2H), 3.98 (dd, J=8.3, 5.4 Hz, 1H), 3.96–3.93 (m, 1H), 3.90 (t, J=9.3 Hz, 1H), 3.85 (t, J=8.7 Hz, 1H), 3.79 (dt, J=9.8, 6.1 Hz, 1H), 3.74 (td, J=10.2, 7.0 Hz, 2H), 3.64 (s, 3H), 3.62–3.42 (m, 11H), 3.36 (ddd, J=15.1, 11.8, 7.2 Hz, 3H), 2.10–1.93 (m, 2H), 1.51–1.37 (m, 4H), 1.20–1.08 (m, 2H); ^{13}C NMR (176 MHz, $CDCl_3$) δ 173.9 ($COCH_3$), 165.0 (C═O), 164.8 (C═O), 164.6 (2C═O), 164.6 (C═O), 164.5 (C═O), 138.0, 137.5, 137.4, 137.3, 137.2, 137.1, 133.8, 133.7, 133.6, 133.5, 133.4, 133.3, 130.0, 129.9, 129.8, 129.7, 129.6, 129.5, 129.4, 129.3, 129.2, 129.18, 129.17, 129.13, 129.08, 129.02, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 128.3, 128.2, 128.14, 128.10, 127.9, 127.8, 127.4, 126.4, 126.3, 126.2, 126.1, 126.0, 101.9, 101.4, 101.30, 101.2, 101.1, 100.7, 98.7, 98.6, 97.1, 97.1, 96.9, 81.2, 78.9, 78.4, 78.1, 77.9, 77.6, 76.6, 75.4, 74.6, 74.3, 74.1, 74.0, 73.7, 73.4, 73.4, 73.3, 72.9, 72.4, 69.6, 68.9, 68.8, 68.7, 68.6, 68.5, 66.4, 66.1, 65.6, 65.5, 65.4, 51.4, 33.6, 29.5, 25.3, 24.3. HRMS (ESI) calcd $(M+Na)^+$ $C_{134}H_{128}O_{39}Na$: 2383.7925. Found: 2383.7908.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.carres.2015.03.007. These data include MOL files and InChiKeys of the most important compounds described in this article.

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