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Preparation of a set of selectively protected disaccharides for modular synthesis of heparan sulfate fragments: toward the synthesis of several *O*-sulfonated [β-D-GlcUA-(1→4)-β-D-GlcNAc]OPr types

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Abstract: A concise method for a stereocontrolled synthesis of a set of selectively protected disaccharides is reported. Coupling of the donor **11** onto acceptors **23** and **24,** promoted by trimethylsilyl triflate-*N*-iodosuccinimide (TMSOTf-NIS), generated the disaccharides **25** and **26**. Under typical conditions, condensation of the fully protected donor **12** onto acceptors **23** and **24** produced the disaccharides **27** and **28**. The building blocks **25-28** were prepared in moderate yields having exclusive β-stereoselectivity. A unique pattern of protecting groups distinguished clearly between positions to be sulfated and functional groups remaining as free hydroxyl groups. Acetyl and/or levulinoyl esters temporarily protected the positions to be sulfated, while benzyl ethers were used for permanent protection. The anomeric positions were protected as allyl ethers, whereas the 4'-positions were masked as *p*-methoxybenzyl (PMB) ethers. The orthogonality of the PMB and allyl groups can then be used for further elongation of the chain by recurrent deprotection and activation steps. The hydroxyl group, OH-6, of glucosamine moieties was protected as a TBDPS ether to avoid oxidation. A five-step deprotection/sulfonation sequence was applied to the disaccharide **27** to generate the corresponding sulfated [β-D-GlcUA-2-OSO_3Na-(1→4)-β-D-Glc*p*NAc]-(1→O-Pro) **34**.

Keywords: Heparin, Glucal, Glycosylation, β-stereoselectivity, protecting groups, sulfated disaccharide

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1 Introduction

The proteoglycan family (PGs) is one of the most abundant natural types of glycoproteins that occur in all tissues, on cell surfaces, and in the extracellular matrix (ECM) [1]. Glycosaminoglycans (GAGs) represent the saccharide moieties of PGs that perform a myriad of physiological functions. GAG polymers are extensively sulfated, repeating disaccharide units of pyranosyl uronic acid, and either 2-amino-2-deoxy D-glucopyranose (glucosamine) or 2-amino-2-deoxy D-galactopyranose [2]. Heparin (HP) and heparan sulfate (HS) are members of the GAG family that are involved in many important biological functions such as blood coagulation, cell growth differentiation, and angiogenesis [3]. HP and HS are linear sulfated polysaccharides having a basic disaccharide unit composed of a uronic acid (1→4) linked to a 2-amino-2-deoxy-D-glucopyranose. The uronic acid may be either D-glucuronic or L-iduronic acid, while *O*-sulfation may occur on position 2 of the uronic acid and on positions 3 and/or 6 of the amino sugar. The glucosamine nitrogen may be sulfated, acetylated or, less frequently, unmodified, thus resulting in 48 possible disaccharides [4]. The diversity grows exponentially with the polymer length, giving 2304 possible tetrasaccharides, 110,592 hexasaccharides, and more than 5×10^6 octasaccharides. All of the theoretical structures resulting from HP and HS biosynthesis cannot be expressed; however, 23 compounds are characterized in the literature [2a]. The polymer, typically composed of 50-200 disaccharide units (25-100 kD), is not fully heterogeneous. Fairly regular *N*-acetylated regions, mainly composed of glucuronic acid and *N*-acetylated glucosamine, separate heavily variable *N*-sulfated regions. The latter are typically three to eight disaccharides long, while the former are more regular approximately 15 disaccharides in length [5]. The *N*-sulfated regions are expressed dynamically and specifically at the cell surface and are responsible for specific interactions with various proteins [6]. The isolation of *N*-acetylated and *N*-sulfated fragments by enzymatic or chemical degradation of the polymer is impeded by a low level of occurrence. Moreover, HP and HS fragments purified by size exclusion and ion-exchange chromatography after de-polymerization are often found to be non-homogeneous [7]. The primary interaction between HP or HS and a protein is an attraction between the highly negatively charged *N*-sulfated regions and clusters of basic residues at the protein surface, mainly arginines and lysines. In some cases, for example, with antithrombin III (AT-III) [8], fibroblast growth factors (FGFs) [6], or stromal cell-derived factor (SDF-1) [9], the cellular receptors are activated by ligand-induced dimerisation requiring HP or HS proteoglycans (HSPGs). The general consensus is that highly sulfated oligosaccharides containing at least six saccharide units comprised of iduronic acid are required to promote signaling. Interestingly, a paper by van Boeckel et al [10] demonstrated that a pentasaccharide in the HP chain with a precise uronic acid content and sulfation patterns was bound with high affinity and specificity to AT III and was responsible for the anti Xa properties of HP. However, for proteins other than antithrombin, such as platelet factor 4 (PF-4), regulated-on-activation normally T-cell expressed and secreted proteins (RANTES) (9-68) [11], or macrophage inflammatory protein (MIP) 1α [12], the epimerization and sulfation patterns responsible for selective

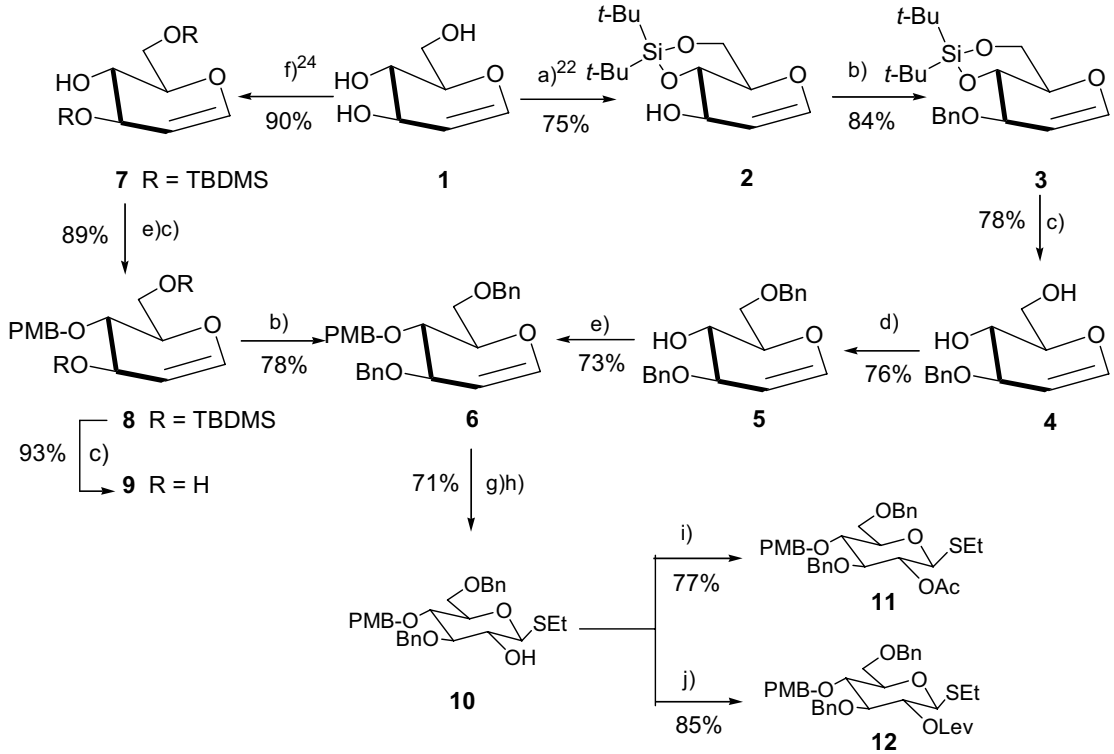
binding of a given protein are generally unknown.

The oligosaccharide sequence and sulfation pattern of the HP or HS fragment required for activation or deactivation of a given protein is often difficult to determine [13]. For this reason, it is desirable to develop effective syntheses of heparin-like oligosaccharide chains with defined size, sequence, and charge distribution to be used in interaction studies. Impressive advances in the synthesis of HS fragments were made in the last decade. HS fragments having diverse structures were synthesized [14-16]. In this paper, a brief method is reported for the preparation of a set of disaccharide building blocks that form the basis of a combinatorial approach for synthesis of several HS fragments. In order to avoid tedious deprotection schemes, a protective group pattern was selected that distinguished clearly between positions to be sulfated and positions remaining as free hydroxyl groups. Acetyl and/or levulinoyl esters protected the positions to be sulfated, while benzyl ethers were used for permanent protection. A *p*-methoxybenzyl group (PMB) at the 4-position avoided the need to prepare a special building block for masking the nonreducing end of the molecule. The PMB group should be removed either together with the benzyl ethers, by hydrogenolysis at the last step of the synthesis, or selectively, by oxidation or acidic treatment. The anomeric positions were protected by an allyl group that was removed to give a disaccharide donor after activation of the anomeric position. The orthogonality of the PMB and allyl groups were used for further elongation of the chain by recurrent deprotection and activation steps [15c]. The hydroxyl group, OH-6, of glucosamine moieties were protected as TBDPS ethers to avoid oxidation and selectively removed by treatment with HF in pyridine. The disaccharide building blocks were central to the strategy for preparation of longer GlcUA-containing GAG fragments. A 2+2 strategy is under investigation for the preparation of tetrasaccharides and will be discussed elsewhere. The tetrasaccharides thus formed will utilize the same protecting group pattern at the anomeric and 4'-positions, allowing further iterative chain elongation using sequential addition of disaccharides to be performed.

2 Results and discussion

Two attractive routes for preparing thioglycosyl donors **11** and **12** from the commercial glucal **1** were established (Scheme 1). The known 4,6-di-*O*-(*tert*-butyl)silanediyl-D-glucal (**2**) [17] was obtained in 75 % yield by reaction of **1** with di-*tert*-butyl-silylditriflate (*t*-$Bu_2Si(OTf)_2$) in DMF. Benzylation of the free hydroxyl group of **2** produced **3** (84 %). Reaction of glucal **3** with tetrabutylammonium fluoride (TBAF) in THF yielded diol **4** (78 %). Regioselective benzylation of the OH-6 position of glucal **4** produced **5** (76 %) by reaction with dibutyltin dimethoxide ($Bu_2Sn(OCH_3)_2$) to produce the corresponding 4,6-tin acetal followed by reaction with BnBr and tetrabutylammonium iodide (Bu4NI) [18]. Reaction of **5** with PMB chloride, sodium hydride and a catalytic amount of Bu_4NI in DMF gave glucal **6** (73 %). The key intermediate **6** was prepared by a alternative route from glucal **1**. Thus, reaction of **1** with *tert*-butyldimethylsilyl chloride (TBDMSCl) (2 equiv) and imidazole in DMF yielded the known glucal **7** [19] as a waxy white solid (90

%). The OH-4 functional group of **7** was protected as the PMB ether using standard methods to generate **8** (89 %) as a clear oil. Desilylation of **8** with TBAF in THF at 0 °C produced **9** (93 %); thereby, protection of the OH-3 and OH-6 groups of glucal **9** was achieved by treatment with benzyl bromide (3 equiv) and sodium hydride in DMF to generate the key glucal **6** (78 %) as a waxy white solid. Reaction of **6** with dimethyldioxirane (DMDO) in CH_2Cl_2 [20], generated *in situ* the expected epoxide derivative, Addition of ethanethiol and a catalytic amount of trifluoroacetic anhydride generated the β-thioethylglucoside **10** (71 %). Analysis of the ^{1}H-NMR (chloroform-*d*) spectrum of the crude intermediate **10** indicated a (10:1β:α) stereoselectivity. The isomers were separated chromatographically. The β-anomer of 3,4,6-tri-*O*-benzyl glucal was reportedly the sole stereoisomer isolated [21]. The observed stereoselectivity of thioglycosylation of the epoxy-**6** generated *in situ* may be attributed to the nature of the protecting groups. The donor **10** was an attractive agent in terms of the overall design of the synthesis. The OH-2 functional group of compound **10** was thus protected by an acetate, by allowing **10** to react with Ac_2O-Py-4,4'-dimethylamino pyridine (DMAP) yielding compound **11** (77 %), or as a levulinoyl ester, by allowing **10** to react with a mixture of levulinic acid, 1,3-dicyclohexylcarbodiimide (DCC), and DMAP in CH_2Cl_2 to produce compound **12** (85 %).

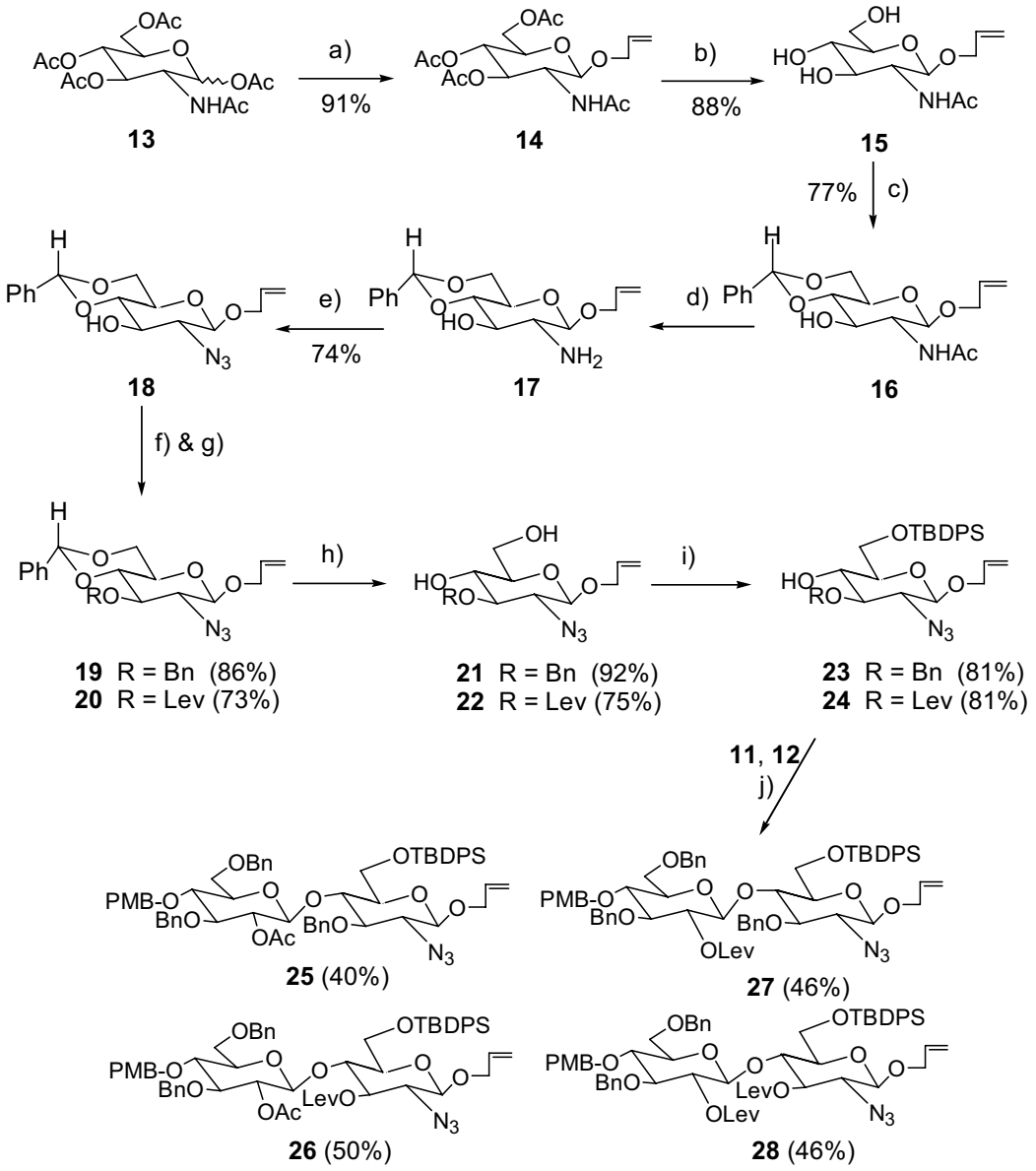


a) ^{t}Bu$_2$Si(OTf)$_2$, DMF; b) BnBr, NaH, Bu$_4$NI, DMF; c) TBAF, THF, -10°C; d) BnBr, Bu$_4$NI Bu$_2$Sn(OCH$_3$)$_2$, PhCH$_3$; e) *p*-methoxybenzyl chloride, Bu$_4$NI, NaH, DMF; f) TBDMSCl, imidazole, DMF, 0°C; g) dimethyldioxirane, CH_2Cl_2; h) EtSH, trifluoroacetic anhydride; i) acetic anhydride, pyridine; j) levulinic acid, DCC, DMAP, CH_2Cl_2.

Scheme 1

Two differentially protected glycosyl acceptors (Scheme 2), based on a modified procedure developed by the *Boons* group [22], were synthesized. The known β-allyl glycoside **14** was isolated in 91 % yield from the readily available *N*-acetylglucosamine pentaacetate (**13**) by reaction with allyl alcohol and TMSOTf. De-*O*-acetylation of **14** by treatment with NaOMe in MeOH produced **15** (88 %) that was not isolated but was directly converted into the 4,6-di-*O*-benzylidene derivative **16** (77 %) by reaction with benzaldehyde dimethylacetal and a catalytic amount of camphorsulfonic acid (CSA) in CH_3CN. The *N*-acetyl functionality of compound **16** was removed by heating with aqueous $Ba(OH)_2$ [23] to yield the amino sugar **17** after neutralization with aqueous sulfuric acid (1N). Treatment of **17** with triflic azide and $CuSO_4$ in MeOH [24] produced the azido sugar **18** in 74 % yield. The OH-3 functional group of compound **18** was protected as the benzyl ether, by reaction with benzyl bromide and sodium hydride in DMF yielding compound **19** (86 %) and as the levulinoyl ester, by reaction of **18** with a mixture of levulinic acid, DCC, and DMAP in CH_2Cl_2 to produce compound **20** (73 %). The benzylidene acetal protecting group of compounds **19** and **20** were removed by heating at 90 °C with 85 % AcOH yielding diols **21** (92 %) and **22** (75 %), respectively. The primary OH-6 groups of the diols **21** and **22** were selectively protected as TBDPS ethers by reaction with TBDPSCl and imidazole in DMF to synthesize the glycosyl acceptors **23** and **24** in 81 % yields, respectively.

The monosaccharide building blocks **11**, **12** and **23**, **24** contained all needed protecting groups in the correct positions. Synthesis of a series of stereoselective glycosidation reactions was attempted (Scheme 2). Coupling of the donor **11** onto acceptors **23** and **24**in CH_2Cl_2-Et_2O (4:1) at - 5 °C → 0 °C in the presence of a mixture of TMSOTf-NIS to promote reaction produced the disaccharides **25** and **26** that were isolated in 40 % and 50 % yields, respectively. Under typical conditions, condensation of the fully protected donor **12** onto acceptors **23** and **24** generated the targeted disaccharides **27** and **28** in moderate and equal yield (46 %). ^{1}H NMR analysis of the crude disaccharides **25**-**28** revealed, as expected, that the β-stereoisomer was formed in all reactions as a sole reaction product. The stereoselectivity observed is attributed to the participation of the acetyl or levulinoyl neighboring groups on the C-2 positions of the donors **11** and **12**, respectively. The coupling constant J 1',2' of the disaccharides **25**-**28** was 8.2 Hz while the four C'-1 carbons resonated at δ 100.6, 100.5, 100.6 and 100.7 ppm, and the four C-1 carbons appeared at δ 100.4, 100.6, 100.3 and 100.4 ppm, respectively, confirming β-stereochemistry. Changing solvents, by performing the reaction in CH_3CN, or varying the promoter, by using only a catalytic amount of TMSOTf, or reaction temperature did not improve the yields. To investigate whether the donor/acceptor ratio had any effect on glycosidation, an increased ratio of the donor to acceptor was examined. Again, coupling of **11** and **23** (2.5:1 ratio), under the conditions mentioned previously, produced the disaccharide **25** (40 %) together with some unreacted donor that was recovered by chromatography. Increasing the acceptor/donor ratio was unsuccessful but the excess of the acceptor was recovered quantitatively. The moderate yield of the glycosidation step may have resulted from the bulky 6-*O*-*tert*-butyldiphenylsilyl in conjunction with



key: a) TMSOTf, CH_2Cl_2, 60°C, 20h, then allyl alcohol, MS 4 Å; b) NaOMe, MeOH, pH = 10; c) benzaldehyde dimethylacetal, CH_3CN, CSA, pH = 3, 18h; d) $Ba(OH)_2.8H_2O$, H_2O/MeOH (2:1), reflux, 15h; e) TfN_3, K_2CO_3, $CuSO_4.5H_2O$, H_2O/MeOH; f) BnBr, NaH, Bu_4NI, DMF, g) levulinic acid, DCC, DMAP, CH_2Cl_2; h) 85% AcOH, 90°C, 15h; i) TBDPSCl, imidazole, DMF; j) NIS, CH_2Cl_2/Et_2O (5:1), 0°C.

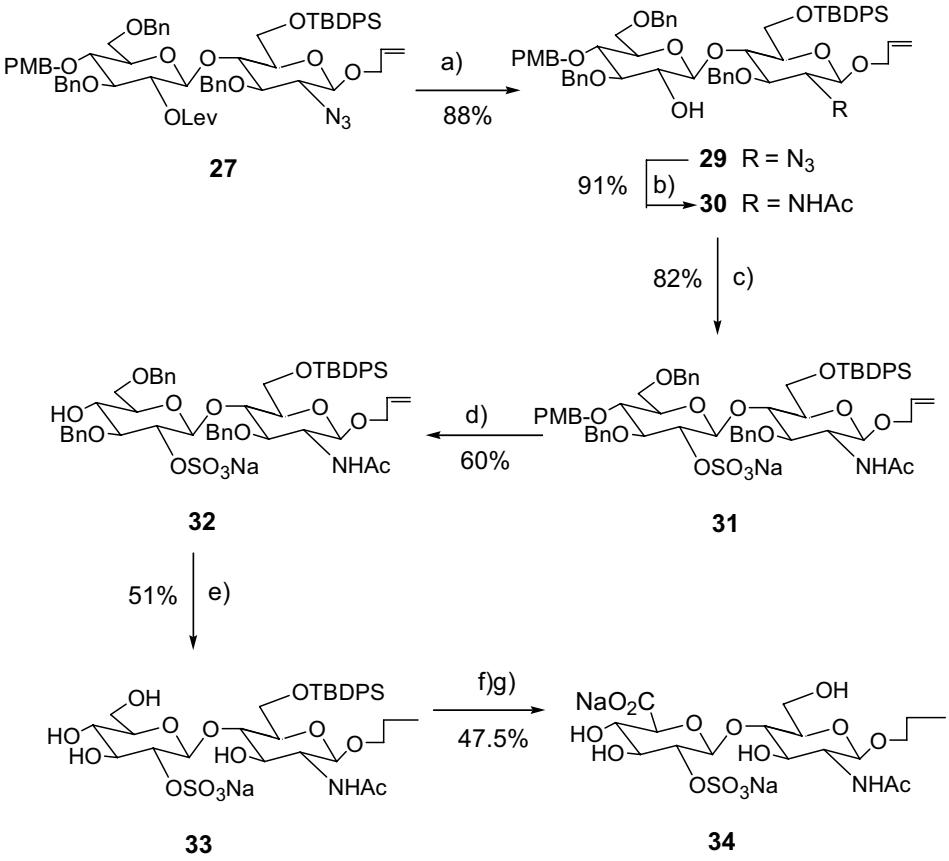
Scheme 2

the OH-3 protecting group covering the top sides (3,5-*cis*) in acceptors **23** and **24** and blocking the glycosyl donors from approaching the OH-4 functional group.

To test the present protecting group strategy for regioselective sulfonation and deprotection steps, the preparation of a sulfated disaccharide fragment was investigated. As shown in Scheme 3, the levulinoyl group of the disaccharide **27** was removed by simple treatment with NaOMe in MeOH for 2 h to produce **29** in 88 % yield. Reduction and

concomitant acetylation of the azide **29** using thioacetic acid [25] generated the corresponding acetamido derivative **30** in 91 % yield. Analysis of the ^{1}H NMR (chloroform-*d*) spectrum of compound **30** revealed that 1-H (d, $J_{1,2}$ 8.2 Hz) and 2-H (ddd, $J_{2,1}$ 8.2 Hz,$J_{2,NH}$ 7.7 Hz, $J_{2,3}$ 10.2 Hz) were deshielded and appeared, at 4.98 and 4.30 ppm, respectively, whereas 1'-H (d, J1',2' 7.9 Hz) and 2'-H appeared at 4.47 and 4.17 ppm, respectively. The ^{13}C-NMR spectrum of compound **30** indicated that C-1, C-2, C-1' and C-2' appeared at 98.9, 51.2, 102.5, 72.6 ppm, respectively. *O*-Sulfonation of OH-2 of **30** with a sulfur trioxide-trimethylamine complex (SO_3. NMe_3) in DMF at 55 °C overnight, followed by purification on Sephadex LH-20, led to the sulfated disaccharide **31**, as its sodium salt, in 82 % yield. The ^{1}H NMR (chloroform-*d*) spectrum of compound **31** revealed that 1-H (d, $J_{1,2}$ 8.4 Hz) and 2-H (m) resonated at 4.95 and 4.39 ppm, respectively, whereas 1'-H (d, $J_{1',2'}$ 8.3 Hz) and 2'-H (m) appeared at 4.70 and 5.10 ppm, respectively. The ^{13}C-NMR spectrum of compound **31** indicated that C-1, C-2, C-1' and C-2' appeared at 98.7, 46.2, 99.6 and 79.6 ppm, respectively. The expected downfield shift of the 2'-H signal of **31** relative to its non-sulfated precursor **30** were found to be in good agreement with the literature [26] and clearly indicated the sulfation of O-2'. Hydrogenation of the *O*-sulfated disaccharide **31** with 10 % Pd/C was troublesome and required prolonged reaction time. Reduction of **31** with 10 % Pd/C and H_2 in EtOH solution (4 bar) produced the sub-target disaccharide **33** after 7 days in 29 % yield. Obviously, the yield was very low. Some materials were isolated without the corresponding sulfate ester probably due to the instability of the sulfate group under the reaction conditions. In a trial to alleviate this problem, the PMB group of the *O*-sulfated disaccharide **31** was selectively cleaved with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in wet CH_2Cl_2 and the reaction was buffered with di-*tert*-butyl pyridine to minimize the decomposition of sulfate ester, resulting in the disaccharide **32** in 60 % yield. The *O*-benzyl groups were removed by 10 % Pd/C and H_2 giving the disaccharide **33** (51 %) after about 72 h of reaction. The primary OH-6' was selectively oxidized with catalytic 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) and sodium hypochloride as co-oxidant [27]. The pH of the solution was carefully monitored below pH = 10 to avoid cleavage of the sulfate group. Finally, the silyl ether (TBDPS group) of OH-6 was successfully cleaved with HF/Py to produce the *O*-sulfated disaccharide **34** in 47 % overall yield.

In conclusion, we demonstrated a simple method for the assembly of a number of well-defined disaccharides containing all the protecting groups in the required positions. The unique pattern of protecting groups made clear distinction between the positions needed to be sulfated and those remaining as free hydroxyl groups. The important features of the reported approach are: a) Acetyl and/or levulinoyl esters protect temporary the positions to be sulfated, while benzyl ethers are used for permanent protection. b) The anomeric positions are protected as allyl ethers, whereas the 4'-positions are masked as PMB ethers. The orthogonality of the PMB and allyl groups can then be used for further elongation of the chain by recurrent deprotection and activation steps. c) The hydroxyl group OH-6 of glucosamine moieties is protected as TBDPS ether to avoid oxidation. d) The primary OH-6' of the sulfated disaccharide was selectively oxidized to a carboxylic acid using



a) NaOMe, MeOH; b) CH_3COSH, Py, 15h, rt.; c) $SO_3.Et_3N$, DMF, 55°C, 15h; d) DDQ,di-*tert*-butyl-pyridine, CH_2Cl_2, H_2O (20:1); e) Pd/C, H_2, EtOH; f) TEMPO, NaBr, NaOCl, H_2O, 0°C; g) HF.Py / Py.

Scheme 3

TEMPO / NaOCl mixture. As exemplified by the synthesis of **34**, the present pattern of the protecting groups proved to be compatible with the oxidation and sulfonation steps and could be used for the preparation of several *O*-sulfonated fragments.

3 Experimental

3.1 General methods

All solvents were distilled from the appropriate drying agents prior to use; dichloromethane, toluene, benzene were distilled from P_2O_5 and stored over molecular sieves (4 Å). DMF and CH_3CN were distilled from CaH_2 and stored over molecular sieves (4 Å). Et_2O, THF and 1,4-dioxane were distilled from $LiAlH_4$. Molecular sieves were crushed and activated in *vacuo* at 390 °C for 4 hours prior to use.TLC analysis was conducted on silica gel plates (EM Science; Kieselgel 60 F254) and the products were detected by UV light after charring with 5 % sulfuric acid in methanol. Column chromatography was performed on silica gel 60 (EM Science, 70-230 mesh). Size exclusion column chromatography was performed on Sephadex LH-20 (methanol/dichloromethane 1:1 v/v, Pharmacia Biotech

AB) or Sephadex G-25 (water elution). 1D ^{1}H-NMR, 2D correlated spectroscopy (^{1}H-^{1}H COSY, ^{1}H-^{13}C correlation) and ^{13}C-NMR were recorded on *Varian* 300 MHz and 500 MHz spectrometers equipped with a SUN_off-line editing workstation. Matrix-assisted Laser Desorption Ionization-Time-of-Flight (MALDI-TOF) mass spectrometry was performed using a HP MALDI-TOF spectrometer using gentisic acid as the matrix. Optical rotations were measured using a JASCO P-1020 polarimeter and $[\alpha]_D$-values are given in units of deg cm^2 mg^{-1}.

1,5-Anhydro-3-*O*-benzyl-4,6-di-*O*-(*tert*-butyl)silanediyl-2-deoxy-D-arabino-hex-1-enitol (3)

A solution of D-glucal **2** (1g, 3.49 mmol) dissolved in 6.0 mL of DMF was treated with benzyl bromide (900 μL, 5.58 mmol) and Bu_4NI (30 mg) at 0 °C. NaH (100 mg) was added incrementally over 30 min. The mixture was allowed to stir 1 h. The reaction mixture was quenched with 2.0 ml H_2O. The mixture was poured into H_2O and extracted with $CHCl_3$ (3 × 20 mL). The organic phase was separated, dried ($MgSO_4$) and evaporated to dryness. Purification of the crude material on silica gel column using EtOAc-hexane (1:10, R_f 0.25) produced **3** (1.1 g, 84 %) as a colorless oil. $[\alpha]_D$ -16.1 (c0.53 CH_2Cl_2). ^{1}H-NMR (300 MHz, $CDCl_3$): 7.40-7.25 (m, 5H, arom), 6.28 (dd, 1H, $J_{1,2}$ 6.0, 1.6 Hz, 1-H), 4.90 (d, 1H, J_{AB} 12.3 Hz, $PhCH_2$), 4.78 (dd, 1H, J6.0, 2.8 Hz, 2-H), 4.76 (d, 1H, J_{AB} 12.3 Hz, $PhCH_2$), 4.59-4.55 (m, 1H, 5-H), 4.23-4.16 (m, 2H, 2x 6-H,), 3.99 (dd, 1H, $J_{4,3}$ 9.0, $J_{4,5}$ 9.0 Hz, 4-H), 3.87-3.83 (m, 1H, 3-H), 1.09 (s, 9H, 3x CH_3), 0.99 (s, 9H, 3x CH_3). ^{13}C-NMR (75 MHz, $CDCl_3$): 144.2 (1-C), 128.6, 127.9, 127.7, 102.6 (2-C), 79.7 (5-C), 76.6 (4-C), 72.9 (3-C), 72.3 (CH$_2$-Ph), 66.2 (6-C), 27.7, 27.2. MS: M^+ 376; Found: 399, M$^+$ + Na and 415, M$^+$ + K. Calculated for $C_{21}H_{32}O_4Si$: C, 67.02; H, 8.51. Found: C, 67.00; H, 8.30.

1,5-anhydro-3-*O*-benzyl-2-deoxy-D-arabino-hex-1-enitol (4)

To a stirred solution of glucal **3** (610 mg, 1.62 mmol) dissolved in 5 mL of THF at -10 °C was added 2.0 mL (1M solution in THF) of TBAF. The mixture was stirred for 3 h at the same temperature; 10 mL of H_2O was added and the mixture was extracted with $CDCl_3$ (3 × 20 mL). The organic layer was dried ($MgSO_4$) and evaporated to dryness. Purification on silica gel using EtOAc-toluene (1:1, R_f 0.19) gave (300 mg, 78 %) of pure **4** as a colorless oil. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.36-7.22 (m, 5H, arom), 6.35 (d, 1H, $J_{1,2}$ 6.3 Hz, 1-H), 4.85 (dd, $J_{2,1}$ 6.3, 2.6 Hz, 1H, 2-H), 4.71 (d, 1H, J_{AB} 11.4 Hz, $PhCH_2$), 4.56 (d, 1H, J_{AB} 11.4 Hz, $PhCH_2$), 4.11-4.08 (m, 1H, 5-H), 3.93-3.86 (m, 2H, 2x 6-H), 3.39-3.34 (m, 1H, 3-H), 2.48 (s br, 1H, OH), 2.09 (s br, 1H, OH). ^{13}C-NMR (75 MHz, $CDCl_3$): 144.9 (1-C), 128.8, 128.1, 128.0, 100.2 (2-C), 76.9 (5-C), 74.9 (4-C), 72.6 (CH2-Ph), 69.8 (3-C), 62.3 (6-C). MS: M$^+$ 236; Found: 259, M$^+$ + Na and 275 M$^+$ + K. Calculated for $C_{13}H_{16}O_4$: C, 66.10; H, 6.77. Found: C, 65.88; H,6.46.

1,5-Anhydro-3,6-di-*O*-benzyl-2-deoxy-D-arabino-hex-1-enitol (5)

Dibutyltin dimethoxide (94 mg, 0.319 mmol) was added to a stirred solution of glucal **4** (70 mg, 0.29 mmol) dissolved in 20 mL of dry toluene. The mixture was refluxed for 1 h, after which the solvent was reduced into half of its volume under vacuum. Benzyl

bromide (50 μL, 0.319 mmol) and Bu_4NI (160 mg, 0.435 mmol) was subsequently added and the mixture was stirred at 50 °C for 16 h. H_2O (10 mL) was added and the content of the flask was partitioned between EtOAc-H_2O (cold) 50 mL (1:1 v/v). The organic phase was separated and dried ($MgSO_4$). Pure glucal **5** was obtained in (76 %, 72 mg) after purification of the crude product on silica gel column using toluene-EtOAc mixture (5:1, R_f 0.2). ^{1}H-NMR (300 MHz, $CDCl_3$): 7.28-7.18 (m, 10 H, arom), 6.31 (dd, 1H, $J_{1,2}$ 6.1, 1.7 Hz, 1-H), 4.77 (dd, 1H, $J_{2,1}$ 6.1, 2.4 Hz, 2-H), 4.62 (d, 1H, J_{A1B1} 11.8 Hz, $PhCH_2$), 4.60 (d, 1H, $J_{A1'B1'}$ 11.8 Hz, $PhCH_2$), 4.58 (d, 1H, J_{A2B2}11.8 Hz, $PhCH_2$), 4.55 (d, 1H, $J_{A2'B2'}$ 11.8 Hz, $PhCH_2$), 4.44-4.40 (m, 1H, 5-H), 3.92-3.89 (m, 1H, 4-H), 3.73-3.70 (m, 2H, 2x 6-H), 3.37-3.33 (m, 1H, H-3), 2.36 (s br, 1H, OH). ^{13}C-NMR (75 MHz, $CDCl_3$): 144.7 (1-C), 138.4, 137.8, 128.5, 128.4, 127.8, 109.8, 100.1 (2-C), 77.6 (5-C), 76.6 (4-C), 76.3 (CH_2-Ph), 73.7 (CH_2-Ph), 70.8 (3-C), 69.2 (6-C). MS: M^+ 326; Found: 349, M^+ + Na and 365, M^+ + K. Anal. Calcd for $C_{20}H_{22}O_4$: C, 73.61; H, 6.74. Found: C, 73.33; H, 6.50.

1,5-Anhydro-1,3-di-*O*-(*t*ert-butyldimethylsilyl)-2-deoxy-D-arabino-hex-1- enitol (7)[24]

Commercial D-glucal **1** (1 g, 6.74 mmol) dissolved in 5 mL of DMF was cooled to 0 °C and treated subsequently with TBDMS chloride (2 g, 13.48 mmol) and imidazole (2 g, 29.37 mmol). The reaction was allowed to stir at constant temperature. After 6 h the solvent was evaporated to dryness under high vacuum (temperature of the bath should not exceed 35 °C). The residue was mixed with 100 mL EtOAc-H_2O (1:1 v/v). The organic phase was separated, dried ($MgSO_4$) and evaporated. The pure glucal **7** (90 %, 2.3 g) was obtained by silica gel column chromatography purification using hexane-EtOAc (6:1, R_f0.2). The product, recovered as colorless oil, crystallized to a white waxy solid. Spectral data were identical as previously reported [24]; however, more details are recorded as follows: $[\alpha]_D$ -22.0 (c0.68 CH_2Cl_2). ^{1}H-NMR (300 MHz, $CDCl_3$): 6.18 (dd, 1H, J6.1, 1.3 Hz, 1-H), 4.53 (dd, 1H, J6.1, 2.2 Hz, 2-H), 4.14-4.12 (m, 1H, 4-H), 3.88 (dd, 1H, J_{gem} 11.9, 4.4 Hz, 6a-H), 3.79 (dd, 1H, J_{gem} 11.9, 4.4 Hz, 6b-H), 3.75-3.71 (m, 1H, 5-H), 3.69-3.63 (m, 1H, 3-H), 2.51 (s br, 1H, OH), 0.82 (s, 9H, 3x CH_3), 0.80 (s, 9H, 3x CH_3), 0.03 (s, 6H, 2x CH_3), 0.00 (s, 6H, 2x CH_3). ^{13}C-NMR (75 MHz, $CDCl_3$): 143.2 (1-C), 103.4 (2-C), 77.9 (4-C), 76.9 (5-C), 69.8 (3-C), 63.1 (6-C), 25.9, 25.8, 18.4, 18.1, -4.4, -4.5, -5.3, -5.4. MS: M^+ 374; Found: 397, M^+ + Na, 413, M^+ +K. Anal. Calcd for $C_{18}H_{38}O_4Si_2$: C, 57.75; H, 10.16. Found: C, 57.55; H, 10.10.

1,5-Anhydro-1,3-di-*O*-(*tert*-butyldimethylsilyl)-4-*O*-(4-methoxybenzyl)-2-deoxy-D-arabino-hex-1- enitol (8)

To a stirred solution of glucal **7** (1 g, 2.67 mmol), *p*-methoxybenzyl chloride (667 mg, 4.01 mmol), and Bu_4NI (30 mg) dissolved in 3 mL of DMF, 100 mg of NaH were added over 10 min. in three equal portions at 0 °C. The reaction was allowed to stir for 1h at the same temperature and for 30 min at rt. The reaction mixture was combined with EtOAc-H_2O (100 mL, 1:1 v/v). The organic phase was separated, washed once with brine, dried ($MgSO_4$), evaporated to dryness and the residue was purified on silica gel column (EtOAc-hexane 1:4, R_f 0.23) to produce pure glucal **8** (1.17 g, 89 %) as a

colorless oil. $[\alpha]_D$ 45.71 (*c*0.42 CH_2Cl_2). ^{1}H-NMR (300 MHz, $CDCl_3$): 7.20 (d, 2H, *J*8.4 Hz, *p*-OMe-*Ph*), 6.80 (d, 2H, *J*8.4 Hz, *p*-OMe-*Ph*), 6.22 (d, 1H, *J* 1,2 6.1 Hz, 1-H), 4.67 (d, 1H, J_{AB} 11.9 Hz, $PhCH_2$), 4.57 (d, 1H, J_{AB} 11.9 Hz, $PhCH_2$), 4.55 (dd, 1H, $J_{2,1}$ 6.1, 2.6 Hz, 2-H), 4.25 (dd, 1H, $J_{5,6a}$ 5.5 Hz, $J_{4,5}$ 8.5 Hz, 5-H), 3.86 (dd, 1H, $J_{6a,6b}$ 11.5 Hz, $J_{6a,5}$ 5.5 Hz, 6_a-H), 3.83 (dd, 1H, , $J_{6b,6a}$ 11.5 Hz, $J_{6b,5}$ 1.9 Hz, 6_b-H), 3.81-3.78 (m, 1H, 4-H), 3.73 (s, 3H, OCH_3), 3.58-3.54 (m, 1H, 3-H), 0.85 (s, 9H, 3x CH_3), 0.83 (s, 9H, 3x CH_3), 0.03 (s, 6H, 2x CH_3), 0.00 (s, 6H, 2x CH_3). ^{13}C-NMR (75 MHz, $CDCl_3$): 159.2, 143.4 (1-C), 130.6, 129.5, 113.8, 103.3 (2-C), 78.1 (4-C), 76.2 (5-C), 73.6 (CH_2-Ph), 68.9 (3-C), 61.9 (6-C), 55.3 (OCH_3), 25.9, 25.8, 18.4, 18.1, -4.4, -4.6, -5.1, -5.3. MS: M^+ 494; Found: 517; M^+ + Na and 533, M^+ + K. Anal. Calcd for $C_{26}H_{46}O_5Si_2$: C, 63.15; H, 9.31. Found: C, 63.23; H, 9.11.

1,5-Anhydro-4-*O*-(4-methoxybenzyl)-2-deoxy-D-arabino-hex-1-enitol (9)

Glucal **8** (1 g, 2.02 mmol), dissolved in 5 mL of THF at -10 °C, was treated with 2.5 mL (2.50 mmol) of TBAF solution (1M) in THF. The mixture was stirred continuously for 3 h. H_2O (5 mL) was added and the solution was extracted with CH_2Cl_2 (3 × 10 mL). The organic extracts was dried and evaporated to dryness. The residue was purified on silica gel column using toluene-EtOAc (2:1, R_f 0.20) to furnish 500 mg (93 %) of pure **9**. $[\alpha]_D$ 64.8 (*c* 0.97 CH_2Cl_2). ^{1}H-NMR (300 MHz, $CDCl_3$): 7.29 (d, 2H, *J* 8.8 Hz, arom), 6.88 (d, 2H, *J* 8.8 Hz, arom), 6.33 (dd, 1H, *J*1,2 6.1, 1.3 Hz, 1-H), 4.73 (d, 1H, J_{AB} 11.8 Hz, PhCH2), 4.71 (d, 1H, J_{AB} 11.8 Hz, $PhCH_2$), 4.66 (dd, 1H, $J_{2,1}$ 6.1, 2.4 Hz H-2), 4.36-4.33 (m, 1H, 5-H), 3.92-3.82 (m, 3H, 2x 6-H, 4-H), 3.79 (s, 3H, OCH_3), 3.60-3.56 (m, 1H, 3-H), 2.10 (s br, 2H, 2x OH). ^{13}C-NMR (75 MHz, $CDCl_3$): 159.4, 144.1 (1-C), 130.2, 129.7, 114.0, 103.3 (2-C), 80.1 (4-C), 77.3 (5-C), 73.5 (CH_2-Ph), 69.2 (3-C), 61.8 (6-C), 55.2 (OCH_3). MS: M^+ 266; Found: 289, M^+ + Na and 305, M^+ + K. Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.15; H, 6.76. Found: C, 63.23; H, 6.61.

1,5-Anhydro-3,6-di-*O*-benzyl-4-*O*-(4-methoxybenzyl)-2-deoxy-D-*arabino*-hex-1-enitol (6)

Method 1: A solution of glucal **5** (100 mg, 0.30 mmol) in DMF (3 mL) was treated with *p*-methoxybenzyl chloride (94 mg, 0.6 mmol) at 0 °C. Bu_4NI (10 mg) was added followed by NaH (30 mg). The reaction was stirred for 30 min at the same temperature after which an additional 30 mg of NaH were added. After stirring continuously for 2 h at rt, the mixture was partitioned between EtOAc-H_2O (100 mL, 1:1 *v*/*v*). The organic phase was separated, dried ($MgSO_4$), and the solvent was evaporated to dryness. Purification on silica gel column using hexane-EtOAc (9:1, R_f 0.19) produced pure **6** (100 mg, 73 %).

Method 2: A solution of glucal **9** (1 g, 3.75 mmol) dissolved in 10 mL of DMF was treated with benzyl bromide (1.76 mL, 11.27 mmol) at 0 °C. Bu_4NI (10 mg) was added followed by NaH (100 mg). The reaction mixture was stirred for 30 min. An additional 100 mg of NaH were added. Stirring continued for 2 h at rt. The mixture was partitioned between EtOAc-H_2O (100 mL, 1:1 *v*/*v*). The organic phase was separated, dried ($MgSO_4$), and the solvent was evaporated to dryness. Pure **6** (1.3 g, 78 %) was recovered after purification on silica gel column using hexane-EtOAc (9:1, R_f 0.19) $[\alpha]_D$ -2.78 (*c*0.86 CH_2Cl_2). ^{1}H-

NMR (300 MHz, $CDCl_3$): 7.34-7.28 (m, 10H, arom), 7.16 (d, 2H, *J*8.1 Hz, *p*-OMe-*Ph*), 6.83 (d, 2H, *J*8.1 Hz, *p*-OMe-*Ph*), 6.42 (d, 1H, $J_{1,2}$ 6.2 Hz, 1-H), 4.87 (dd, 1H, $J_{2,1}$ 6.2, 2.2 Hz, 2-H), 4.75 (d, 1H, J_{A1B1} 11.8 Hz, $PhCH_2$), 4.64 (d, 1H, $J_{A1'B1'}$ 11.8 Hz, $PhCH_2$), 4.60 (d, 1H, J_{A2B2} 11.8 Hz, $PhCH_2$), 4.58 (d, 1H, $J_{A2'B2'}$ 11.8 Hz, $PhCH_2$), 4.56 (d, 1H, J_{A3B3} 11.8 Hz, $PhCH_2$), 4.53 (d, 1H, $J_{A3'B3'}$ 11.8 Hz, $PhCH_2$), 4.19-4.08 (m, 1H, 4-H), 3.86-3.77 (m, 4H, H-3, H-5, 2x 6-H), 3.79 (s, 3H, OCH_3). ^{13}C-NMR (75 MHz, $CDCl_3$): 159.3, 144.7 (1-C), 138.4, 138.0, 130.3, 129.6, 128.4, 128.3, 127.7, 127.6, 127.5, 113.8, 99.9 (2-C), 76.6 (4-C), 75.8 (5-C), 74.0 (CH_2-Ph), 73.5 (CH_2-Ph), 73.4 (CH_2-Ph), 70.4 (3-C), 68.6 (6-C), 55.2 (OCH_3). MS: M^+ 446; Found: 469, M^+ + Na and 485, M^+ + K. Anal. Calcd for $C_{28}H_{30}O_5$: C, 75.33; H, 6.72. Found: C, 75.30; H, 6.58.

Ethyl 3,6-di-*O*-benzyl-2-hydroxy-4-*O*-(4-methoxybenzyl)-1-thio-β-D-glucopyranoside (10)

Glucal **6** (1 g, 2.24 mmol) was dissolved in CH_2Cl_2 (10 mL) and cooled to 0 °C. DMDO (31.25 mL, 1M solution in acetone [20b], 2.5 mmol) was added and stirred for 30 min. The solvent was evaporated in a stream of nitrogen gas. After drying for 1 h under high vacuum, the epoxide was dissolved in 10 mL of CH_2Cl_2. EtSH (1.48 mL, 20.0 mmol) was added. The mixture was cooled to –78 °C and trifluoroacetic anhydride (100 μL) was added dropwise. Stirring was continued at –78 °C for 30 min, after which the reaction mixture was allowed to warm to rt. The solvent was removed under a stream of nitrogen gas and the residue was purified on silica gel column using EtOAc-hexane (1:4, R_f 0.2) resulting in pure **10** (830 mg, 71 %). (α/β 1:10, separable). $[\alpha]_D$ -9.43 (*c*0.68 CH_2Cl_2). ^{1}H-NMR (300 MHz, $CDCl_3$): 7.40-7.27 (m, 12H, arom), 7.09 (d, 2H, *J*8.7 Hz, *p*-OMe-*Ph*), 6.81 (d, 2H, *J*8.7 Hz, *p*-OMe-*Ph*), 4.94 (d, 1H, J_{A1B1} 11.4 Hz, $PhCH_2$), 4.87 (d, 1H, $J_{A1'B1'}$ 11.4 Hz, $PhCH_2$), 4.76 (d, 1H, J_{A2B2} 11.4 Hz, $PhCH_2$), 4.60 (d, 1H, J_{A3B3} 12.3 Hz, $PhCH_2$), 4.54 (d, 1H, $J_{A3'B3'}$ 12.3 Hz, $PhCH_2$), 4.49 (d, 1H, $J_{A2'B2'}$ 11.4 Hz, $PhCH_2$), 4.29 (d, 1H, $J_{1,2}$ 8.8 Hz, 1-H, β-anomer), 3.78 (s, 3H, OCH_3), 3.77-3.72 (m, 2H, 2-H, 4-H), 3.67 (dd, 1H, $J_{6a,6b} = J_{6a,5} = 10.5$ Hz, 6_a-H), 3.60 (dd, 1H, $J_{6b,6a}$ 10.5, $J_{6b,5}$ 4.5 Hz, 6_b-H), 3.46 (m, 2H, 5-H, 3-H), 2.73 (q, 2H, *J*6.0, 1.2 Hz, CH_2), 2.36 (s br, 1H, OH), 1.30 (t, 3H, *J*6.0 Hz, CH_3). ^{13}C-NMR (75 MHz, $CDCl_3$): 140.6, 130.3, 129.7, 128.5, 128.3, 127.9, 127.7, 127.6, 113.8, 86.0 (1-C), 79.5 (CH_2-Ph), 77.8 (CH_2-Ph), 75.2 (CH_2-Ph), 74.7 (3-C), 73.4 (2-C), 73.3 (5-C), 69.1 (6-C), 68.2 (4-C), 55.3 (OCH_3), 24.3 (CH_2), 15.4 (CH_3). MS: M^+ 524; Found: 547, M^+ + Na and 563, M^+ + K.

Ethyl 2-*O*-acetyl-3,6-di-*O*-benzyl-4-*O*-(4-methoxybenzyl)-1-thio-β-D-glucopyranoside (11)

A solution of thioglycoside **10** (500 mg, 0.95 mmol) dissolved in 5.0 mL of pyridine was treated with 3.0 mL of Ac_2O and 20 mg of DMAP. Stirring was continued at rt for 2 h after which the solvent was evaporated to dryness. The crude material was purified using silica gel column chromatography. Pure **11** (420 mg, 77 %) was recovered as a colorless oil that crystallized as a white solid. $[\alpha]_D$ 25.6 (*c*0.86 CH_2Cl_2). ^{1}H-NMR (300 MHz, $CDCl_3$): 7.34-7.58 (m, 10H, arom), 7.09 (d, 2H, *J*8.4 Hz, *p*-OMe-*Ph*), 6.80 (d, 2H, *J*8.4 Hz, *p*-OMe-*Ph*), 5.01 (d, 1H, *J*1,2 9.7 Hz, 1-H), 4.81 (d, 1H, J_{A1B1} 11.4 Hz, $PhCH_2$), 4.70 (d, 1H, J_{A2B2} 11.8 Hz, $PhCH_2$), 4.69 (d, 1H, $J_{A1'B1'}$ 11.4 Hz, $PhCH_2$), 4.66 (dd, 1H, $J_{2,1}$

9.7 Hz, $J_{2,3}$ 9.7 Hz, 2-H), 4.61 (d, 1H, $J_{A2'B2}$, 11.8 Hz, $PhCH_2$), 4.54 (d, 1H, J_{A3B3} 11.4 Hz, $PhCH_2$), 4.52 (d, 1H, $J_{A3'B3'}$ 11.4 Hz, $PhCH_2$), 4.46 (dd, 1H, $J_{5,4}$ 8.4 Hz, $J_{5,6a}$ 4.8 Hz, 5-H), 3.78 (s, 3H, OCH_3), 3.76 (dd, 1H, $J_{3,2}$ 9.7, $J_{3,4}$ 8.4 Hz, 3-H), 3.69 (dd, 1H, $J_{6a,5}$ 5.7, $J_{6a,6b}$ 12.4 Hz, 6_a-H), 3.68 (dd, 1H, $J_{6b,5}$ 2.4, $J_{6b,6a}$ 12.4 Hz, 6_b-H), 3.47 (dd, 1H, $J_{4,3}$ 8.4, $J_{4,5}$ 8.4 Hz, 4-H), 2.76-2.63 (q, 2H, *J*2.3, 1.1 Hz, CH_2), 1.97 (s, 3H, CH_3), 1.20 (t, 3H, *J*2.3 Hz, CH_3). ^{13}C-NMR (75 MHz, $CDCl_3$): 171.0 (*C*O), 138.2, 129.7, 128.4, 128.3, 127.7, 127.6, 113.8, 84.4 (1-C), 83.4 (2-C), 79.5 (CH_2-Ph), 75.2 (CH_2-Ph), 74.7 (CH_2-Ph), 73.5 (5-C), 71.8 (3-C), 68.9 (6-C), 68.0 (4-C), 55.3 (O*C*H_3), 23.8 (S*C*H_2), 20.9 (CO*C*H_3), 14.9 (CH_3). MS: M^+ 566; Found: 589, M^+ + Na and 605, M^+ + K. Anal. Calcd for $C_{32}H_{38}O_7S$: C, 67.84; H, 6.71; S, 5.66. Found: C, 67.67; H, 6.52; S, 5.36.

Ethyl 3,6-di-*O*-benzyl-4-*O*-(4-methoxybenzyl)-2-*O*-levulinoyl-1-thio-β-D-glucopyranoside (12).

A solution of thioglycoside **10** (892 mg, 1.70 mmol) dissolved in 15 mL of CH_2Cl_2 at –20 °C was subsequently treated with 300 mg (2.50 mmol) of levulinic acid, 520 mg (4.48 mmol) DCC and 50 mg of DMAP. Stirring was continued at -20 °C for 1 h followed by stirring at rt for additional 12 h. The mixture was diluted with 30 mL of CH_2Cl_2, washed with sat. $NaHCO_3$, brine, dried ($MgSO_4$) and the solvent was evaporated to dryness. The crude material was purified using silica gel column with hexane-EtOAc (4:1, R_f 0.2) yielding pure **12** (900 mg, 85 %) as a colorless oil that crystallized as a white solid. $[\alpha]_D$ = -14.2 (c = 0.88 in CH_2Cl_2). ^{1}H-NMR (300 MHz, $CDCl_3$): 7.33-7.30 (m, 10H, arom), 7.08 (d, 2H, *J*8.4 Hz, *p*-OMe-*Ph*), 6.80 (d, 2H, *J*8.4 Hz, *p*-OMe-*Ph*), 5.01 (d, 1H, *J*1,2 9.2 Hz, 1-H), 4.79 (d, 1H, J_{A1B1} 11.4 Hz, PhCH_2), 4.72 (d, 1H, $J_{A1'B1}$, 11.4 Hz, PhCH_2), 4.70 (d, 1H, J_{A2B2} 11.5 Hz, PhCH_2), 4.68 (d, 1H, $J_{A2'B2'}$ 11.5 Hz, PhCH_2), 4.66 (dd, 1H, $J_{2,1}$ 9.2 Hz, $J_{2,3}$ 9.2 Hz, 2-H), 4.60 (d, 1H, J_{A3B3} 11.4 Hz, PhCH_2), 4.54 (d, 1H, $J_{A3'B3}$, 11.4 Hz, PhCH_2), 4.49 (dd, 1H, $J_{5,4}$ 8.0 Hz, $J_{5,6a}$ 2.5 Hz, 5-H), 4.34 (dd, 1H, $J_{3,2}$ =$J_{3,4}$ = 9.2 Hz, 3-H), 3.78 (s, 3H, OCH_3), 3.70 (dd, 1H, $J_{6a,6b}$ 12.3 Hz, $J_{6a,5}$ 2.5 Hz, 6_a-H), 3.64 (dd, 1H, $J_{6b,6a}$ 12.3 Hz, $J_{6b,5}$ 4.6 Hz, 6_b-H), 3.47 (dd, 1H, $J_{4,3}$ 9.2 Hz, $J_{4,5}$ 8.0 Hz, 4-H), 2.75-2.66 (m, 2H, CH_2CO), 2.65-2.57 (m, 2H, COCH_2), 2.53-2.43 (m, 2H, SCH_2), 2.15 (s, 3H, COCH_3), 1.25 (t, 3H, *J*7.5 Hz, CH_3). ^{13}C-NMR (75 MHz, $CDCl_3$): 207.0 (*C*O), 171.5 (O*C*O), 159.3, 138.2, 130.1, 129.7, 128.3, 127.8, 127.7, 127.6, 127.5, 113.8, 84.3 (1-C), 83.4 (2-C), 79.5, 75.1 (*C*H_2-Ph), 74.7 (*C*H_2-Ph), 73.5 (*C*H_2-Ph), 72.2 (5-C), 72.0 (3-C), 68.9 (6-C), 67.5 (4-C), 55.3 (O*C*H_3), 37.9 (*C*H_2CO), 29.8 (OCO*C*H_2), 28.1 (CO*C*H_3), 23.8 (S*C*H_2), 14.9 (CH_3). MS: M^+ 622; Found: 645, M^+ + Na and 661, M^+ + K. Anal. Calcd for $C_{35}H_{42}O_8S$: C, 67.52; H, 6.75; S, 5.14. Found: C, 67.44; H, 6.55; S, 5.10.

Allyl 2-*N*-acetyl-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranoside (14)

To a stirred solution of 1,3,4,6-tetra-*O*-acetyl-2-acetamido-2-deoxy-α-D-glucopyranoside (**13**) (6.2 g, 16.35 mmol) in CH_2Cl_2 (100 mL), TMSOTf (4.2 mL, 23.2 mmol) was added dropwise. After the mixture was heated at 60 °C for 20 h, it was allowed to cool to rt. Activated powdered molecular sieves (4 Å, 5 g) were added and the solution was stirred for 2 h at rt After addition of 6.0 mL of allyl alcohol, the mixture was stirred at rt for 20 h. The reaction mixture was quenched with Et_3N (1.0 mL). The mixture was filtered

over *Celite* (5 g) and washed thoroughly with 10 % MeOH-CH_2Cl_2. The combined filtrate and washings were evaporated to dryness. Purification on silica gel column using 5 % MeOH-CH_2Cl_2 (R_f0.25) produced pure **14** (6.7 g, 91 %). ^{1}H-NMR ($CDCl_3$, 300 MHz): 5.81 (dddd, *J*17.0, *J*10.5, 6.0 Hz, 5.0 Hz, 1 H, CH_2-C*H*=CH_2), 5.72 (d, $J_{NH,2}$ 8.8 Hz, 1H, NH), 5.26 (dq, *J* 10.5, 1.5 Hz, 1H, 1H, CH_2-CH=CHH_a), 5.19 (dq, *J* 10.5, 1.5 Hz, 1H, 1H, CH_2-CH=CHH_b), 5.11 (dd, $J_{1,2}$ 8.3 Hz, 1-H), 4.97 (dd, $J_{3,4}$ 9.2 Hz, $J_{3,2}$ 9.6 Hz, 1H, 3-H), 4.63 (dd, $J_{5,4}$ 9.6 Hz, $J_{5,6}$ 6.8 Hz, 1H, 5-H), 4.22 (dd, $J_{4,3}$ 9.2 Hz, $J_{4,5}$ 9.6 Hz, 1H, 4-H), 4.11 (ddt, J_{gem} 13.0, J_{vic} 5.0, J_{all}1.5 Hz, 1 H, CH_2-CH=CH_2), 3.99 (ddt, J_{gem} 13.0, J_{vic} 6.0, J_{all} 1.5 Hz, 1 H, CH_2-CH=CH_2), 3.84-3.75 (m, 1H, 2-H), 3.68-3.59 (m, 2H, 2x 6-H), 1.99 (s, NHCOCH_3), 1.93 (s, COCH_3), 1.92 (s, COCH_3), 1.85 (s, COCH_3). ^{13}C-NMR ($CDCl_3$, 75Hz): 170.8 (O*C*OCH$_3$), 170.6 (O*C*OCH$_3$), 170.2 (O*C*OCH$_3$), 169.3 (NH*C*O), 133.5 (*C*H=CH_2), 117.6 (CH=*C*H$_2$), 99.6 (C-1), 72.3 (C-3), 71.7 (C-4), 70.6 , 69.9 (C-5), 68.7 (*C*H$_2$CH=CH_2), 62.1 (C-6), 54.6 (C-2), 23.2 (NHCOCH_3), 20.7, 20.6, 20.4 (3x CH_3). MS: M+387; Found: 410, M^+ + Na.

Allyl 2-*N*-acetyl-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (16)

Allyl glycoside **14** (6.7 g, 17.31 mmol) dissolved in 25 mL of MeOH was treated at 0 °C with NaOMe (1M) added dropwise till the pH reached 10. The solution was stirred for 3 h and neutralized by addition of H^+-type resin. The resin was removed by filtration, washed thoroughly with MeOH (200 mL) and the solvent was removed under vacuum to yield 4 g (88 %) of de-*O*-acetylated reaction product **15.** The crude product was dried under high vacuum overnight and utilized for the next step without further purification.

Crude **15** was dissolved in 80 mL CH_3CN and 5.35 g (35.24 mmol) of benzylidene dimethylacetal was added. The reaction mixture was acidified by camphor sulfonic acid to pH = 3 and it was stirred overnight (18 h) at rt. The solvent was removed under high vacuum and the crude product was purified using silica gel column using CH_2Cl_2-MeOH (95:5, R_f 0.4, to furnish (4.1 g, 77 %) of pure **16** as a white solid. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.51-7.47 (m, 2H, arom), 7.36-7.34 (m, 3H, arom), 5.89 (dddd, *J*17.0, 10.5, 6.0, 5.0 Hz, 1 H, CH_2-CH=CH_2), 5.66 (d, $J_{NH,2}$ 8.8 Hz, 1H, N*H*), 5.56 (s, 1H, C*H*-Ph), 5.25 (dq, *J*17.0, 1.5 Hz, 1 H, CH_2-CH=CH_2), 5.18 (dq, *J* 10.5, 1.5 Hz, 1 H, CH_2-CH=CH_2), 4.77 (d, $J_{1,2}$ 8.5 Hz, 1H, 1-H), 4.39-4.32 (m, 1H, H-2), 4.19 (ddd, $J_{3,4}$ 9.3, $J_{3,2}$ 9.3, $J_{2,NH}$ 8.8 Hz, 1H, H-3), 4.11 (ddt, J_{gem} 13.0, J_{vic} 5.0, J_{all} 1.5 Hz, 1 H, CH_2-CH=CH_2), 3.99 (ddt, J_{gem} 13.0, J_{vic} 6.0, J_{all} 1.5 Hz, 1 H, CH_2-CH=CH_2)., 3.80 ((dt $J_{3,4}$ 9.3, $J_{5,6}$ 7.3, 1H, H-5), 3.57 (dd, $J_{4,3}$ 9.6, $J_{4,5}$ 8.5 Hz, 1H, 4-H), 3.54 (dd, $J_{6a,6b}$ 11.9 Hz, $J_{6a,5}$ 4.5 Hz, 1H, H-6$_a$), 3.49 (dd, $J_{6b,6a}$ 11.9 Hz, $J_{6b,5}$ 2.8 Hz, 1H, H-6$_b$), 2.05 (s, 3H, CH_3). ^{13}C-NMR (75 MHz, $CDCl_3$): 172.2 (NH*C*O), 136.3, 134.4 (*C*H=CH_2), 133.4, 129.7, 128.3, 126.3, 118.3 (CH=*C*H$_2$), 101.9 (PHC*H*), 99.6 (C-1), 81.7 (C-5), 76.6 (C-4), 71.2 (C-3), 70.2, 68.6 (C-6), 66.3 (*C*H$_2$-CH=CH_2), 59.3 (C-2), 23.68 (COCH_3). MS: M^+ 349; Found: 372, M^+ + Na.

Allyl 2-azido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranoside (18)

Compound **16** (2.5 g, 7.16 mmol) was dissolved in 30 mL of H2O/MeOH (2:1 *v*/*v*), treated with 6.0 g of $Ba(OH)_2.8H_2O$, and stirred overnight (15 h) at 90 °C. The mixture was cooled to r.t. H_2SO_4 (1N) was added dropwise until no additional precipitation of

$BaSO_4$ (pH = 3) was observed. The white precipitate was filtered after centrifugation. The filtrate was evaporated under high vacuum to give crude **17** as a white solid (2 g, 91 %) that was used in the next procedure without further purification.

Crude **17** was dissolved in 10 mL of H_2O/MeOH (5:1 v/v) and treated with 400 mg of K_2CO_3, 3 mg of $CuSO_4.5H_2O$ and Tf_3N solution. The Tf_3N solution was prepared by reaction of 1 g of NaN_3 and 1 g of Tf_2O in 5 mL of CH_2Cl_2 MeOH (6 mL) was added to ensure formation of a homogenous mixture. The mixture was allowed to stir at rt for 16 h. The mixture was filtered and the filtrate was evaporated under vacuum. The crude product was purified on silica gel column using CH_2Cl_2-MeOH (20:1, R_f 0.5) to yield pure **18** (1.6 g, 74 %). ^{1}H-NMR (300 MHz, $CDCl_3$): 7.47-7.36 (m, 5H, arom), 5.87 (dddd, *J* 17.0, 10.5, 6.0, 5.0 Hz, 1 H, CH_2-C*H*=CH_2), 5.53 (s, 1H, Ph-C*H*), 5.29 (dq, *J* 17.0, 1.5 Hz, 1 H, CH_2-CH=CHH_b), 5.18 (dq, *J* 10.5, 1.5 Hz, 1 H, CH_2-CH=CHH_b), 4.47 (d, *J*7.9 Hz, 1H, 1-H), 4.43 (dd, $J_{5,4}$ 9.2 Hz, $J_{5,6}$ 5.1 Hz, 1H, H-5), 4.31 (dd, $J_{4,5}$ 9.2, $J_{4,3}$ 9.2 Hz, 1H, H-4), 4.11 (ddt, J_{gem} 13.0, J_{vic} 5.0, J_{all}1.5 Hz, 1 H, CHH_a-CH=CH_2), 3.99 (ddt, J_{gem} 13.0, J_{vic} 6.0, J_{all} 1.5 Hz, 1 H, CHH_b-CH=CH_2), 3.78 (dd, $J_{6a,6b}$ 12.1 Hz, $J_{6a,5}$ 4.8 Hz, 1H, H-6$_a$), 3.67 (dd, $J_{6b,6a}$ 12.1 Hz, $J_{6b,5}$ 2.3 Hz, 1H, H-6$_b$), 3.55 (m, 1H, H-3), 3.43 (dd, $J_{2,1}$ 7.9 Hz, $J_{2,3}$ 9.0 Hz, 1H, 2-H). ^{13}C-NMR (75 MHz, $CDCl_3$): 136.2, 133.2 (*C*H=CH_2), 128.4, 126.3, 118.2 (CH=*C*H_2), 102.0 (PhC*H*O(O)), 101.5 (C-1), 80.6 (C-6), 72.1 (C-5), 70.8 (C-4), 68.5 (C-3), 66.5 (*C*H_2CH=CH_2), 64.2 (C-2). MS: M^+ 333; Found: 356, M^+ + Na. Anal. Calcd for $C_{16}H_{19}O_5N_3$: C, 57.65; H, 5.70; N, 12.61. Found: C, 57.50; H, 5.73; N, 12.44.

Allyl 2-azido-4,6-*O*-benzylidene-3-*O*-benzyl-2-deoxy-β-D-glucopyranoside (19) Allyl glycoside **18** (1 g, 3.0 mmol) was dissolved in 10 mL of DMF and treated subsequently with benzyl bromide (937 mg, 5.48 mmol) and Bu_4NI (20 mg). The mixture was cooled to 0 °C. NaH (100 mg, 4.11 mmol) was added incrementally (25 mg every 10 min.) The reaction mixture was allowed to stir for 1 h at rt, The reaction was quenched by pouring into a mixture of 200 g ice / 200 mL EtOAc. The phases were separated, and the organic phase was washed once with water and evaporated until dryness. The crude material was purified using silica gel column (CH_2Cl_2, R_f = 0.63) to yield pure **19** (1.1 g, 86 %) as a waxy white solid. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.49-7.28 (m, 10H, arom), 5.87 (dddd, *J*17.0, 10.5, 6.0, 5.0 Hz, 1 H, CH_2-C*H*=CH_2), 5.57 (s, 1H, PhC*H*), 5.24 (dq, *J* 17.0, 1.5 Hz, 1 H, CH_2-CH=CHH_a), 5.18 (dq, *J* 10.5, 1.5 Hz, 1 H, CH_2-CH=CHH_b), 4.91 (d, $J_{A,B}$ 11.4 Hz, 1H, PhCH_2), 4.79 (d, $J_{A,B}$ 11.4 Hz, 1H, PhCH_2), 4.41 (d, *J*7.5 Hz, 1H, 1-H), 4.34 (dd, $J_{5,4}$ 9.6, $J_{5,6}$ 5.8 Hz, 1H, H-5), 4.11 (ddt, J_{gem} 13.0, J_{vic} 5.0, J_{all} 1.5 Hz, 1 H, CHH_a-CH=CH_2), 3.99 (ddt, J_{gem} 13.0, J_{vic} 6.0, J_{all} 1.5 Hz, 1 H, CHH_b-CH=CH_2), 3.80 (dd, $J_{6a,6b}$ 11.3, $J_{6a,5}$ 4.2 Hz, 1H, H-6$_a$), 3.71 (dd, $J_{6b,6a}$ 11.3, $J_{6b,5}$ 3.8 Hz, 1H, H-6$_b$), 3.56 (dd, $J_{4,3}$ 9.4, $J_{4,5}$8.4 Hz, 1H, H-4), 3.47 (dd, $J_{3,4}$ 9.4, $J_{3,2}$9.4 Hz, 1H, H-3), 3.36 (dd, $J_{2,3}$ 9.4, $J_{2,1}$ 7.5 Hz, 1H, H-2). ^{13}C-NMR (75 MHz, $CDCl_3$): 136.2, 133.2 (*C*H=CH_2), 129.1, 128.4, 128.3, 128.2, 127.9, 125.9, 118.1 (CH=*C*H_2), 101.4 (PhC*H*O(O)), 101.3 (C-1), 81.6 (C-6), 79.1 (*C*H_2-Ph), 74.9 (C-5), 70.7 (C-3), 68.6 (C-4), 66.2 (*C*H_2-CH=CH_2), 64.4 (C-2). MS: M^+ 423; Found: 446, M^+ + Na. Anal. Calcd for $C_{23}H_{25}O_5N_3$: C, 65.24; H, 5.91; N, 9.92. Found: C, 65.15; H, 5.90; N, 9.69.

Allyl 2-azido-4,6-*O*-benzylidene-3-*O*-levulinoyl-2-deoxy-β-D-glucopyranoside (20)

Glycoside **18** (1.5 g, 4.50 mmol) was dissolved in 40 mL of CH_2Cl_2 and cooled to -20 °C. Levulinic acid (750 mg, 6.25 mmol), DCC (1.3 g, 6.25 mmol) and DMAP (35 mg) were subsequently added. The mixture was stirred for 1h at –20 °C followed by stirring overnight at r.t. The mixture was diluted with CH_2Cl_2 (40 mL), washed with $NaHCO_3$, brine, dried ($MgSO_4$) and evaporated under vacuum. Purification using silica gel column (CH_2Cl_2-MeOH 20:1) yielded pure **20** (1.4 g, 73 %) as a clear syrup. ^{1}H-NMR ($CDCl_3$, 300 MHz): 7.44-7.37 (m, 2H, arom), 7.35-7.28 (m, 3H, arom), 5.85 (dddd, *J* 17.0, 10.5, 6.0, 5.0 Hz, 1 H, $CH_2 - CH{=}CH_2$), 5.49 (s, 1H, CH-Ph), 5.25 (dq, *J* 17.0, 1.5 Hz, 1 H, CH_2-CH=CHH_a), 5.18 (dq, *J*10.5, 1.5 Hz, 1 H, CH_2-CH=CHH_b), 5.12 (dd, $J_{3,2}$ 10.1, $J_{3,4}$ 9.3 Hz, 1H, H-3), 4.53 (d, $J_{1,2}$ 8.4 Hz, 1H, 1-H), 4.40 (dd, $J_{4,3}$ 9.3, $J_{4,5}$ 9.3 Hz, 1H, H-4), 4.34 (dd, $J_{5,4}$ 9.3, $J_{5,6}$ 6.0 Hz, 1H, H-5), 4.11 (ddt, J_{gem} 13.0, J_{vic} 5.0, J_{all} 1.5 Hz, 1 H, CHH_a-CH=CH_2), 3.99 (ddt, J_{gem} 13.0, J_{vic} 6.0, J_{all} 1.5 Hz, 1 H, CHH_b-CH=CH_2), 3.63 (dd, $J_{6a,6b}$ 12.1, $J_{6a,5}$ 6.2 Hz, 1H, H-6$_a$), 3.50 (dd, $J_{6b,6a}$ 12.1, $J_{6b,5}$ 3.2 Hz, 1H, H-6$_b$), 3.40 (dd, $J_{2,1}$ 8.4 Hz, $J_{2,3}$ 9.7 Hz, 1H, 2-H), 2.90-2.83, 2.82-2.77 (2m, 2H, CH_2CH_2CO), 2.70-2.60, 2.60-2.53 (2m, 2H,$OCOCH_2$), 2.14 (s, 3H, $COCH_3$). ^{13}C-NMR ($CDCl_3$, 75 MHz): 207.1 ($COCH_3$), 171.6 ($OCOCH_2$), 136.7, 132.9 ($CH{=}CH_2$), 129.0, 128.2, 126.0, 118.3 ($CH{=}CH_2$), 101.5 (PhCHO(O)), 101.2 (C-H), 78.6 (C-6), 71.4 (C-5), 70.9 (C-3), 68.4 (C-4), 66.4 ($CH_2CH{=}CH_2$), 64.7 (C-2), 37.9 ($OCOCH_2CH_2CO$), 29.8 ($OCOCH_2CH_2$), 27.9 ($COCH_3$). MS: M^+ 431; Found: 454, M^+ + Na. Anal. Calcd for $C_{21}H_{25}O_7N_3$: C, 58.46; H, 5.80; N, 9.74. Found: C, 58.23; H, 5.77; N, 9.47.

Allyl 2-azido-3-*O*-benzyl-2-deoxy-β-D-glucopyranoside (21)

A solution of compound **19** (1.1 g, 2.60 mmol) in 50 mL of 85 % AcOH/H_2O was heated at 90 °C for 15 h after which the solvent and volatiles were removed under vacuum. The residue was purified using column chromatography with 5 % CH_2Cl_2-MeOH (R_f 0.3) to yield **21** (800 mg, 92 %) as a clear heavy oil. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.38-730 (m, 5H, arom), 5.89 (dddd, *J* 17.0, 10.5, 6.0, 5.0 Hz, 1 H, CH_2-CH=CH_2), 5.25 (dq, *J* 17.0, 1.5 Hz, 1 H, CH_2-CH=CHH_a), 5.18 (dq, *J* 10.5, 1.5 Hz, 1 H, CH_2-CH=CHH_b), 4.97 (d, $J_{A,B}$ 11.5 Hz, 1H, PhCH_2), 4.70 (d, $J_{A,B}$ 11.5 Hz, 1H, PhCH_2), 4.39 (d, $J_{1,2}$ 7.9 Hz, 1H, 1-H), 4.11 (ddt, J_{gem} 13.0, J_{vic} 5.0, J_{all}1.5 Hz, 1 H, CHH_a-CH=CH_2), 3.99 (ddt, J_{gem} 13.0, J_{vic} 6.0, J_{all} 1.5 Hz, 1 H, CHH_b-CH=CH_2), 3.87 (dd, $J_{6a,6b}$ 11.8, $J_{6a,5}$ 3.3 Hz, 1H, H-6$_a$), 3.77 (dd, $J_{6b,6a}$ 11.8, $J_{6b,5}$ 4.7 Hz, 1H, H-6$_b$), 3.59 (dd, $J_{3,4}$ 9.3, $J_{3,2}$ 9.3 Hz, 1H, H-3), 3.43 (dt $J_{5,4}$ 9.0, $J_{5,6}$ 4.4 Hz, 1H, H-5), 3.30 (m, 1H, 4-H), 3.27 (dd, $J_{3,2}$ 9.3, $J_{2,1}$ 7.9 Hz, 1H, 2-H), 2.32 (s br, 1H, OH), 2.16 (s br, 1H, OH). ^{13}C-NMR (75 MHz, $CDCl_3$): 137.6, 133.4 ($CH{=}CH_2$), 128.7, 128.2, 128.1, 127.6, 117.9 ($CH{=}CH_2$), 101.3 (C-1), 82.6 (C-3), 75.1 (C-5), 74.1 (CH_2Ph), 70.5 (C-4), 65.9 ($OCH_2CH{=}CH_2$), 62.4 (C-6), 54.4 (C-2). MS: M^+ 335; Found: 358, M^+ + Na.

Allyl 2-azido-3-*O*-levulinoyl-2-deoxy-β-D-glucopyranoside (22)

A solution of compound **20** (1 g, 2.32 mmol) in 50 mL of 85 % AcOH-H2O was heated and prepared according to the method given for **21**. The residue was purified by column chromatography using 5 % CH_2Cl_2-MeOH (R_f 0.2) to yield **22** (600 mg, 75 %) as a

clear oil. ^{1}H-NMR (300 MHz, $CDCl_3$): 5.87 (dddd, *J* 17.0, 10.5, 6.0, 5.0 Hz, 1 H, CH_2-C*H*=CH_2), 5.29 (dq, *J* 17.0, 1.5 Hz, 1 H, CH_2-CH=CHH_a), 5.18 (dq, *J* 10.5, 1.5 Hz, 1 H, CH_2- CH=CHH_b), 4.87 (dd, $J_{3,2}$ 10.1 Hz, $J_{3,4}$ 9.2 Hz, 1H, H-3), 4.46 (d, $J_{1,2}$ 7.8 Hz, 1H, 1-H), 4.23 (m, 1H, H-4), 4.11 (ddt, J_{gem} 13.0, J_{vic} 5.0, J_{all}1.5 Hz, 1 H, CHH_a-CH=CH_2), 3.99 (ddt, J_{gem} 13.0, J_{vic}6.0, J_{all} 1.5 Hz, 1 H, CHH_b-CH=CH_2), 3.92 (dd, $J_{6a,6b}$ 11.8, $J_{6a,5}$ 3.5 Hz, 1H, 6$_a$-H), 3.82 (dd, $J_{6b,6a}$ 11.8, $J_{6b,5}$ 4.8 Hz, 1H, 6$_b$-H), 3.77 (dd, $J_{5,4}$ 9.0 Hz, $J_{5,6}$ 5.2 Hz, 1H, 5-H), 3.46 (dd, $J_{2,3}$ 10.3, $J_{2,1}$ 7.8 Hz, 1H, H-2), 3.06 (s br, 1H, OH), 2.97-2.83, 2.82-2.77 (2m, 2H, CH_2CH_2CO), 2.70-2.60, 2.60-2.50 (2m, 2H,OCOCH_2), 2.19 (s, 3H, COCH_3). ^{13}C-NMR (75 MHz, $CDCl_3$): 207.1 (*C*OCH$_3$), 171.2 (O*C*OCH$_2$), 133.2 (*C*H=CH_2), 118.1 (CH=*C*H$_2$), 101.0 (C-1), 76.1 (C-3), 75.3 (C-5), 70.7 (*C*H$_2$CH=CH_2), 69.8 (C-4), 63.5 (C-6), 62.3 (C-2), 38.6 (OCOCH$_2$*C*H$_2$CO), 29.75 (OCO*C*H$_2$CH$_2$), 28.3 (CO*C*H$_3$). MS: M$^+$ 343: Found: 366, M$^+$ + Na.

Allyl 2-azido-3-*O*-benzyl-6-*O*-(*tert*-butyldiphenylsilyl)-2-deoxy-β-D-glucopyranoside (23)

Diol **21** (790 mg, 2.35 mmol) was dissolved in 5.0 mL of DMF and treated with 911 mg (3.53 mmol) of TBDPSCl and 500 mg (7.5 mmol) of imidazole. After stirring continuously for 15 h at rt, the solvent was removed under high vacuum. The residue was dissolved in 25 mL of EtOAc and washed with sat. $NaHCO_3$, brine, dried ($MgSO_4$) and concentrated. The crude product was purified by silica gel column using EtOAc-toluene (20:1, R_f 0.4) to generate **23** (1.1 g, 81 %) as a clear thick oil. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.74-7.60 (m, 4H, arom), 7.41-7.29 (m, 11 H, arom), 5.87 (dddd, *J* 17.0, 10.5, 6.0, 5.0 Hz, 1 H, CH_2-C*H*=CH_2), 5.29 (dq, *J* 17.0, 1.5 Hz, 1 H, CH_2-CH=CH$_a$H), 5.18 (dq, *J* 10.5, 1.5 Hz, 1 H, CH_2-CH=C*H*H$_b$), 4.92 (d, *J*11.4 Hz, 1H, PhCH_2), 4.83 (d, *J*11.4 Hz, 1H, PhCH_2), 4.34 (d, *J*7.9 Hz, 1H, 1-H), 4.16 (dd, $J_{6a,6b}$ 11.9, $J_{6a,5}$ 4.8 Hz, 1H, H-6$_a$), 4.13 (dd, $J_{6b,6a}$ 11.9, $J_{6b,5}$ 2.2 Hz, 1H, H-6$_b$), 4.11 (ddt, J_{gem} 13.0, J_{vic} 5.0, J_{all} 1.5 Hz, 1 H, CH_2-CH=CH_2), 3.99 (ddt, J_{gem} 13.0, J_{vic} 6.0, J_{all} 1.5 Hz, 1 H, CH_2-CH=CH_2), 3.88 (dd, $J_{5,6}$ 4.8 Hz, $J_{5,4}$ 10.1 Hz, 1H, 5-H), 3.85-3.77 (m, 1H, H-4), 3.42 (dd, $J_{3,2}$ 8.9 Hz, $J_{3,4}$ 9.3 Hz, 1H, 3-H), 3.30 (dd, $J_{2,1}$ 7.9 Hz, $J_{2,3}$ 8.8 Hz, 1H, 2-H), 2.85 (s br, 1H, OH), 1.07 (s, 9H, 3x CH_3). ^{13}C-NMR (75 MHz, $CDCl_3$): 135.9, 135.8, 135.5, 135.4, 135.0 (*C*H=CH_2), 133.8, 130.1, 129.9, 128.8, 128.4, 128.3, 128.0, 127.9, 117.9 (CH=*C*H$_2$), 101.1 (C-1), 83.0 (C-3), 75.4 (C-5), 75.1 (*C*H$_2$-Ph), 72.2 (C-4), 70.3 (*C*H$_2$-CH=CH_2), 65.9 (C-6), 64.6 (C-2), 19.6 (CH_3). MS: M$^+$ 573; Found: 596, M$^+$ + Na. Anal. Calcd for $C_{32}H_{39}O_5N_3Si$: C; 67.01, H; 6.80, N; 7.32. Found: C, 67.22; H, 6.84; N, 7.00.

Allyl 2-azido-6-*O*-(*tert*-butyldiphenylsilyl)-3-*O*-levulinoyl-2-deoxy-β-D-glucopyranoside (24)

Diol **22** (651 mg, 1.89 mmol) was dissolved in 5.0 mL of DMF and treated with 634 mg (3.53 mmol) of TBDPSCl and 490 mg (7.38 mmol) of imidazole. The crude product was processed as described for **23** and purified on silica gel column using EtOAc-toluene (20:1, R_f 0.4) to produce **24** (1.1 g, 81 %) as a clear thick oil. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.71-7.69 (m, 4H, arom), 7.46-7.35 (m, 6H, arom), 5.85 (dddd, *J* 17.0, 10.5, 6.0, 5.0 Hz, 1 H, CH_2-C*H*=CH_2), 5.28 (dq, *J* 17.0, 1.5 Hz, 1 H, CH_2-CH=C*H*$_a$H), 5.18 (dq, *J* 10.5, 1.5 Hz, 1 H, CH_2-CH=CHH_b), 4.88 (dd, $J_{3,2}$ 9.0, $J_{3,4}$ 10.2 Hz, 1H, 3-H), 4.43 (d, *J*7.9 Hz, 1H,

1-H), 4.11 (ddt, J_{gem} 13.0, J_{vic} 5.0, J_{all} 1.5 Hz, 1 H, CH_aHCH=CH_2), 3.99 (ddt, J_{gem} 13.0, J_{vic} 6.0, J_{all} 1.5 Hz, 1 H, CHH_b-CH=CH_2), 3.97 (dd, $J_{6a,6b}$ 11.0, $J_{6a,5}$ 3.7 Hz, 1H, 6_a-H), 3.92 (dd, $J_{6b,6a}$ 11.0, $J_{6b,5}$ 4.1 Hz, 1H, 6_b-H), 3.72 (dd, $J_{5,4}$ 9.0 Hz, $J_{5,6}$ 5.2 Hz, 1H, 5-H), 3.22 (dd, $J_{2,1}$ 7.9 Hz, $J_{2,3}$ 9.0 Hz, 1H, 2-H), 2.96-2.85, 2.85-2.78 (2m, 2H, CH_2-CH_2CO), 2.70-2.60, 2.60-2.50 (2m, 2H,OCOCH_2), 2.19 (s, 3H, CH_3), 1.06 (s, 9H, 3x CH_3). ^{13}C-NMR (75 MHz, $CDCl_3$): 207.5 (COCH$_3$), 172.8 (OCOCH$_2$), 135.7, 135.6 (CH=CH_2), 133.3, 133.2, 133.1, 129.8, 127.7, 127.6, 117.9 (CH=CH$_2$), 100.7 (C-1), 76.1 (C-3), 75.6 (C-5), 70.1 (C-4), 70.0 (CH$_2$CH=CH_2), 68.3 (C-6), 63.6 (C-2), 38.4 (OCOCH$_2$$CH_2$CO), 28.2 (OCO$CH_2CH_2$), 26.8 (CO$CH_3$), 19.3 ($CH_3$). MS: M^+ 581; Found: 604, M^+ + Na. Anal. Calcd for $C_{30}H_{39}O_7N_3Si$: C, 61.96; H, 6.71; N, 7.22. Found: C, 61.84; H, 6.78; N, 7.18.

Allyl (2-*O*-acetyl-3,6-di-*O*-benzyl-4-*O*-(4-methoxybenzyl)-β-D-glucopyranosyl)-(1→4)-2-azido-3- *O*-benzyl-6-*O*-(*tert*-butyldiphenylsilyl)-2-deoxy-β-D-glucopyranoside (25)

Thioglycoside **11** (300 mg, 0.53 mmol) and the acceptor **23** (233 mg, 0.40 mmol) were co-evaporated twice with 10 mL of toluene and dried under vacuum for 3 h. The mixture was dissolved in 4 mL of CH_2Cl_2 containing 0.5 ml Et_2O and stirred with 300 mg of molecular sieves (4 Å) for 1 h at rt. The mixture was cooled to -5 °C. *N*-iodosuccinimide (113 mg, 0.5 mmol) and 8 μL of TMSOTf were subsequently added. The mixture was stirred for 15 min. and thin layer chromatography demonstrated the consumption of the donor. The reaction mixture was quenched with pyridine. The insoluble residue and molecular sieves were removed by filtration, washed thoroughly with 10 % MeOH-CH_2Cl_2 (30 ml), and the combined filtrate and the washing were evaporated to dryness. The residue was purified on silica gel column using 5 % toluene-EtOAc (R_f0.23) to produce pure **25** (230 mg, 40 %) as a colorless oil. ^{1}H-NMR (500 MHz, $CDCl_3$): 7.75-7.64 (m, 5 H, arom), 7.44-7.27 (m, 20 H, arom), 7.15 (d, *J*8.5 Hz, 2H, *p*-OMe-*Ph*), 6.80 (d, *J*8.5 Hz, 2H, *p*-OMe-*Ph*), 5.89 (dddd, *J* 17.0, 10.5, 6.0, 5.0 Hz, 1 H, CH_2-CH=CH_2), 5.29 (dq, *J* 17.0, 1.5 Hz, 1 H, CH_2-CH=CH_aH), 5.21 (dq, *J* 10.5, 1.5 Hz, 1 H, CH=CHH_b), 5.13 (d, $J_{A1,B}$1 11.5 Hz, 1H, PhCH$_2$), 5.11 (d, $J_{A2,B2}$ 11.3 Hz, 1H, PhCH$_2$), 5.05 (d, $J_{1',2'}$, 8.2 Hz, 1H, 1'-H), 4.93 (d, $J_{A2',B2}$, 11.3 Hz, 1H, PhCH$_2$), 4.89 (d, $J_{A3,B3}$ 11.3 Hz, 1H, PhCH$_2$), 4.86 (dd, $J_{2',1'}$, 8.2 Hz, $J_{2',3'}$, 9.3 Hz, 1H, 2'-H), 4.72 (d, $J_{A3',B3}$, 11.3 Hz, 1H, PhCH$_2$), 4.67 (d, $J_{A1',B1}$, 11.5 Hz, 1H, PhCH$_2$), 4.51 (dd, $J_{4,3}$ 10.7, $J_{4,5}$ 10.7 Hz, 1H, 4-H), 4.40 (d, $J_{1,2}$ 8.8 Hz, 1H, 1-H), 4.38 (dd, 1H, $J_{6a,6b}$ 12.0 Hz, $J_{6a,5}$ 3.6 Hz, 6_a-H), 4.36-4.33 (m, 2H, 3'-H, 6_b-H), 4.11 (ddt, J_{gem} 13.0, J_{vic} 5.0, J_{all} 1.5 Hz, 1 H, CH_aH-CH=CH_2), 3.99 (ddt, J_{gem} 13.0, J_{vic} 6.0, J_{all} 1.5 Hz, 1 H, CHH_b-CH=CH_2), 3.89 (dd, $J_{3',2'}$, 9.3, $J_{3',4'}$, 9.6 Hz, 1H, 3'-H), 3.80 (dt, $J_{5,4}$ 10.7 Hz, $J_{5,6a}$ 2.2 Hz, 1H, 5-H), 3.78 (dd, $J_{3,2}$ 9.6, $J_{3,4}$ 10.7 Hz, 1H, 3-H), 3.75 (s, 3H, OCH$_3$), 3.58-3.53 (m, 2H, 2x 6'-H), 3.42 (dd, $J_{4',3'}$, 9.6, $J_{4',5'}$, 9.6 Hz, 1H, 4'-H), 3.29 (dt, $J_{5',4'}$, 9.6, $J_{5',6'}$, 3.3 Hz, 1H, 5'-H), 3.22 (dd, $J_{2,1}$ 8.8 Hz, $J_{2,3}$ 9.6 Hz, 1H, 2-H), 1.89 (s, 3H,OCOCH_3), 1.06 (s, 9H, 3x CH$_3$). ^{13}C-NMR (125 MHz, $CDCl_3$): 171.2 (CO), 161.4, 140.5, 140.4, 137.9, 137.7, 137.6, 137.4, 137.2, 136.8, 135.7 (-CH=CH_2),132.4, 132.0, 129.4, 117.6 (CH=CH$_2$), 113.8, 100.6 (1-C), 100.4 (1'-C), 83.4, 80.9 (2'-C), 77.9 (CH$_2$-Ph), 76.1 (CH$_2$-Ph), 75.5 (CH$_2$-Ph), 75.4 (5-C), 75.2 (6-C), 74.9

(6'-C), 74.7 (4-C), 73.8 (5'-C), 73.3 (3'-C), 70.6 (3-C), 69.5 (4'-C), 68.8 (-CH_2-CH=CH_2), 65.9 (2-C), 55.3 (OCOCH_3), 20.8 (CH_3), 19.3 (CH_3), 14.8 (CMe_3). MS: M^+ 1077; Found: 1101, M^+ + Na. Anal. Calcd for $C_{62}H_{71}O_{12}N_3Si$: C, 69.06; H, 6.64; N, 3.90. Found: C, 68.88; H, 6.60; N, 3.79.

The reaction between thioglycoside **11** (300 mg, 0.53 mmol) and the acceptor **24** (203 mg, 0.35 mmol) was conducted as described previously for compound **25**. The residue was purified on silica gel column using 10 % toluene-EtOAc (R_f 0.20) to produce pure **26** (287 mg, 50 %) as a colorless oil. ^{1}H-NMR (500 MHz, $CDCl_3$): 7.76-7.69 (m, 4 H, arom), 7.43-7.30 (m, 16 H, arom), 7.06 (d, *J*8.5 Hz, 2H, *p*-OMe-*Ph*), 6.79 (d, *J*8.5 Hz, 2H, *p*-OMe-*Ph*), 5.88 (dddd, *J* 17.0, 10.5, 6.0, 5.0 Hz, 1 H, CH_2-C*H*=CH_2), 5.32 (d, $J_{1',2'}$, 8.2 Hz, 1H, 1'-H), 5.29 (dq, *J* 17.0, 1.5 Hz, 1 H, CH_2-CH=CH_aH), 5.18 (dq, *J* 10.5, 1.5 Hz, 1 H, CH_2-CH=CHH_b), 4.90 (dd, $J_{3,2}$ 9.6 Hz, $J_{3,4}$ 9.6 Hz, 1H, 3-H), 4.84 (dd, $J_{2',1'}$, 8.2 Hz, $J_{2',3'}$, 9.3 Hz, 1H, 2'-H), 4.78 (d, $J_{A1,B1}$ 12.6 Hz, 1H, $PhCH_2$), 4.72 (d, $J_{A1',B1'}$, 12.6 Hz, 1H, $PhCH_2$), 4.68 (dd, $J_{4',3'}$ 9.3, $J_{4',5'}$ 9.3 Hz, 1H, 4'-H), 4.65 (d, $J_{A2,B2}$ 12.1 Hz, 1H, $PhCH_2$), 4.59 (d, $J_{A2',B2'}$, 12.1 Hz, 1H, $PhCH_2$), 4.55 (d, $J_{A3,,B3}$ 12.1 Hz, 1H, $PhCH_2$), 4.51 (d, $J_{A3',B3'}$, 12.1 Hz, 1H, $PhCH_2$), 4.39 (d, $J_{1,2}$ 7.9 Hz, 1H, 1-H), 4.22 (dd, J_{gem} 12.9 Hz, $J_{6a,5}$ 2.3 Hz, 1H, H-6$_a$), 4.18-4.11 (m, 2H, H-5, H-6$_b$), 4.11 (ddt, J_{gem} 13.0, J_{vic} 5.0, J_{all} 1.5 Hz, 1 H, CH_aH-CH=CH_2), 3.99 (ddt, J_{gem} 13.0, J_{vic} 6.0, J_{all} 1.5 Hz, 1H, CHH_b-CH=CH_2), 3.82 (dd, $J_{3',4'}$9.3, $J_{3',2'}$, 9.3 Hz, 1H, 3'-H), 3.75 (s, 3H, OCH_3), 3.64 (dd, J_{gem} 13.0 Hz, $J_{6'a,5'}$ 2.3 Hz, 1H, H-6'$_a$), 3.59-3.53 (m, 2H, H-4, H-6'$_b$), 3.34 (dt, $J_{5',4'}$ 9.3, $J_{5',6'}$ 4.8 Hz, 1H, 5'-H), 3.25 (dd, $J_{2,1}$ 7.9 Hz, $J_{2,3}$ 9.6 Hz, 1H, 2-H), 2.90-2.80 (m, 2H, CH_2CH_2CO), 2.55-2.45 (m, 2H, COCH_2CH_2), 2.19 (s, 3H, -CH_2COCH_3), 2.04 (s, 3H, -OCOCH_3), 1.06 (s, 9H, 3x CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$): 205.9 (-CH_2*C*OCH_3), 171.8 (O*C*OCH_2-), 170.0 (O*C*OCH_3), 141.1, 138.6, 135.9, 135.6 (*C*H=CH_2), 133.7, 133.4, 133.2, 130.3, 129.8, 129.7, 129.5, 129.0, 128.4, 128.2, 127.8, 127.7, 127.6, 127.5, 117.8 (CH=*C*H_2), 113.8, 100.6 (C-1'), 100.5 (C-1), 83.4 (C-2'), 81.9 (C-3), 80.9 (C-3'), 79.5 (C-4), 75.5 (*C*H_2-Ph), 74.7 (*C*H_2-Ph), 73.6 (*C*H_2-Ph), 73.5 (C-5'), 71.8 (C-5), 70.7 (C-4'), 69.9 (C-6), 68.9 (*C*H_2-CH=CH_2), 64.4 (C-6'), 62.7 (C-2), 55.3 (OCH_3), 37.8 (OCOCH_2*C*H_2CO), 28.2 (OCO*C*$H_2$$CH_2$CO), 24.1 ($CH_2$CO*C*$H_3$), 23.7, 20.9 (*C*$H_3$), 19.3 (*C*$H_3$), 16.6 (OCO*C*$H_3$), 14.8 (*C*$Me_3$). MS: M^+ 1085; Found: 1109, M^+ + Na and 1125, M^+ + K. Anal. Calcd for $C_{60}H_{71}O_{14}N_3Si$: C, 66.35; H, 6.54; N, 3.87. Found: C, 66.23; H, 6.44; N, 3.49.

Allyl (3,6-di-*O*-benzyl-2-*O*-levulinoyl-4-*O*-(4-methoxybenzyl)-β-D-glucopyranosyl)-(1→4)-2-azido-3-*O*-benzyl-6-*O*-(*tert*-butyldiphenylsilyl)-2-deoxy-β-D-glucopyranoside (27)

The reaction between thioglycoside **12** (311 mg, 0.5 mmol) and the acceptor **23** (268 mg, 0.46 mmol) was conducted as described previously for compound **25**. The residue was purified on silica gel column using 5 % toluene-EtOAc (R_f 0.26) to generate pure **27** (244 mg, 46 %) as a colorless oil. ^{1}H-NMR (500 MHz, $CDCl_3$): 7.74 (m, 4H, arom), 7.73-7.21 (m, 25H, arom), 7.06 (d, *J*8.4 Hz, 2H, *p*-OMe-*Ph*), 6.78 (d, *J*8.4 Hz, 2H, *p*-OMe-*Ph*), 5.87 (dddd, *J* 17.0, 10.5, 6.0, 5.0 Hz, 1 H, CH_2-C*H*=CH_2), 5.29 (dq, *J* 17.0, 1.5 Hz, 1 H, CH_2-CH=CH_aH), 5.23 (d, $J_{1',2'}$, 8.2 Hz, 1H, 1'-H), 5.18 (dq, *J* 10.5, 1.5

Hz, 1 H, CH_2-CH=CHH_b), 5.12 (d, J_{A1B1} 11.0 Hz, 1H, PhCH_2), 5.04 (dd, $J_{2',1'}$, 8.2 Hz, $J_{2',3'}$, 9.0 Hz, 1H, 2'-H), 4.89 (d, J_{A1B1} 11.0 Hz, 1H, PhCH_2), 4.83 (d, $J_{A2,B2}$ 11.3 Hz, 1H, PhCH_2), 4.67 (d,$J_{A2',B2'}$ 11.3 Hz, 1H, PhCH_2), 4.65 (d, $J_{A3,B3}$ 11.9 Hz, 1H, PhCH_2), 4.63 (d, $J_{A3',B3'}$ 11.9 Hz, 1H, PhCH_2), 4.36 (d, $J_{1,2}$ 7.9 Hz, 1H, 1-H), 4.26 (d, $J_{A4,B4}$ 11.9 Hz, 1H, PhCH_2), 4.20-4.15 (m, 2H, 4'-H, PhCH_2),4.15 (dd, $J_{4,3}$ 9.2 Hz, $J_{4,5}$ 9.2 Hz, 1H, 4-H), 4.11 (ddt, J_{gem} 13.0, J_{vic} 5.0, J_{all} 1.5 Hz, 1 H, CH_aHCH=CH_2), 3.99 (ddt, J_{gem} 13.0, J_{vic} 6.0, J_{all} 1.5 Hz, 1 H, CHH_b-CH=CH_2), 3.93 (dd, $J_{6a,6b}$ 12.9 Hz,$J_{6a,5}$ 3.4 Hz, 1H, H-6$_a$), 3.88 (dd, $J_{6b,6a}$ 12.9 Hz, $J_{6b,5}$ 5.6 Hz, 1H, H-6$_b$), 3.78 (s, 3H, OCH_3), 3.75 (dd, $J_{3',2'}$, 9.0 Hz, $J_{3',4'}$, 10.2 Hz, 1H, 3'-H), 3.72 (dd, $J_{3,2}$ 9.2 Hz, $J_{3,4}$ 9.2 Hz, 1H, 3-H), 3.73 (d, $J_{6a',6b'}$, 13.0 Hz, $J_{6a',5'}$, 2.6 Hz, 1H, 6'$_a$-H), 3.57 (d, $J_{6a',6b'}$, 13.0 Hz, $J_{6a',5'}$, 2.6 Hz, 1H, 6'$_b$-H), 3.55-3.48 (m, 2H, 5-H, 5'-H), 3.22 (dd, $J_{2,1}$ 7.9 Hz, $J_{2,3}$ 9.2 Hz, 1H, 2-H), 2.90-2.77 (m, 2H, CH_2CH_2CO), 2.53-2.41 (m, 2H, COC$H_2$$CH_2$), 2.08 (s, 3H, COC$H_3$), 1.04 (s, 9H, 3x CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$): 205.8 (-CH_2COCH_3), 171.2 (OCOCH_2), 159.3, 138.7, 138.4, 136.4, 136.0, 135.5 (CH=CH_2), 135.2, 134.8, 133.8, 133.5, 132.5, 130.0, 127.3, 117.8 (CH=CH_2), 113.8, 100.6 (C-1'), 100.3 (C-1), 83.4 (C-2'), 81.0 (C-3), 77.1 (CH_2-Ph), 75.4 (C-5), 75.3 (CH_2-Ph), 75.1 (CH_2-Ph), 74.1 (CH_2-Ph), 73.3 (C-6'), 69.7 (C-4'), 68.8 (C-3'), 68.6 (CH_2-CH=CH_2), 68.5 (C-6), 68.3 (C-5'), 65.9 (C-4), 61.3 (C-2), 55.3 (OCH_3), 37.6 (OCOC$H_2$$CH_2$CO), 29.7 (OCOCH$_2CH_2$CO), 27.7 ($CH_2COCH_3$), 26.8 ($CH_3$), 26.6 ($CH_3$), 19.4 ($CH_3$), 14.8 (CMe$_3$). MS: M^+ 1133; Found: 1156, M^+ + Na. Anal. Calcd for $C_{65}H_{75}O_{13}N_3Si$: C, 68.84; H, 6.61; N, 3.71. Found: C, 68.70; H, 6.64; N, 3.47.

Allyl (3,6-di-*O*-benzyl-2-*O*-levulinoyl-4-*O*-(4-methoxybenzyl)-β-D-glucopyranosyl)-(1→4)-2-azido-6-*O*-(*tert*-butyldiphenylsilyl)-3-*O*-levulinoyl-2-deoxy-β-D-glucopyranoside (28)

The reaction between thioglycoside **12** (300 mg, 0.45 mmol) and the acceptor **24** (203 mg, 0.35 mmol) was conducted as described previously for compound **25**. The residue was purified on silica gel column using 10 % toluene-EtOAc (R_f 0.20) to produce **28** (244 mg, 46 %) as a colorless oil. ^{1}H-NMR (500 MHz, $CDCl_3$): 7.76-7.69 (m, 4 H, arom), 7.43-7.30 (m, 16 H, arom), 7.06 (d, *J*8.5 Hz, 2H, *p*-OMe-*Ph*), 6.79 (d, *J*8.5 Hz, 2H, *p*-OMe-*Ph*), 5.88 (dddd, *J* 17.0, 10.5, 6.0, 5.0 Hz, 1 H, CH_2-C*H*=CH_2), 5.32 (d, $J_{1',2'}$, 8.2 Hz, 1H, 1'-H), 5.29 (dq, *J* 17.0, 1.5 Hz, 1 H, CH_2-CH=CH_aH), 5.18 (dq, *J* 10.5, 1.5 Hz, 1 H, CH_2-CH=CHH_b), 4.90 (dd, $J_{3,2}$ 9.6 Hz, $J_{3,4}$ 9.6 Hz, 1H, 3-H), 4.84 (dd, $J_{2',1'}$, 8.2 Hz, $J_{2',3'}$, 9.3 Hz, 1H, 2'-H), 4.78 (d, $J_{A1,B1}$ 11.8 Hz, 1H, PhCH_2), 4.72 (d, $J_{A1',B1'}$, 11.8 Hz, 1H, PhCH_2), 4.68 (dd, $J_{4',3'}$ 9.3, $J_{4',5'}$ 9.3 Hz, 1H, 4'-H), 4.65 (d, $J_{A2,B2}$ 12.1 Hz, 1H, PhCH_2), 4.59 (d, $J_{A2',B2'}$, 12.1 Hz, 1H, PhCH_2), 4.55 (d, $J_{A3,,B3}$ 12.1 Hz, 1H, PhCH_2), 4.51 (d, $J_{A3',B3'}$, 12.1 Hz, 1H, PhCH_2), 4.39 (d, $J_{1,2}$ 8.0 Hz, 1H, 1-H), 4.22 (dd, J_{gem} 12.9 Hz, $J_{6a,5}$ 2.3 Hz, 1H, H-6$_a$), 4.18-4.11 (m, 2H, H-5, H-6$_b$), 4.11 (ddt, J_{gem} 13.0, J_{vic} 5.0, J_{all} 1.5 Hz, 1 H, CH_aH-CH=CH_2), 3.99 (ddt, J_{gem} 13.0, J_{vic} 6.0, J_{all} 1.5 Hz, 1H, CHH_b-CH=CH_2), 3.82 (dd, $J_{3',4'}$, 9.3, $J_{3',2'}$, 9.3 Hz, 1H, 3'-H), 3.76 (s, 3H, OCH_3), 3.64 (dd, J_{gem} 13.0 Hz, $J_{6'a,5'}$ 2.3 Hz, 1H, H-6'$_a$), 3.59-3.53 (m, 2H, H-4, H-6'$_b$), 3.34 (dt, $J_{5',4'}$ 9.3, $J_{5',6'}$ 5.3 Hz, 1H, 5'-H), 3.20 (dd, $J_{2,1}$ 8.0 Hz, $J_{2,3}$ 9.6 Hz, 1H, 2-H), 2.90-2.76 (m, 4H, CH_2CH_2CO), 2.60-2.44 (m, 4H, OCOC$H_2$$CH_2$), 2.10 (s, 3H, -$CH_2COCH_3$),

2.08 (s, 3H, -CH_2COCH_3), 1.06 (s, 9H, 3x CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$): 206.6 (CH_2COCH_3), 205.9 (CH_2COCH_3), 172.0 ($OCOCH_2$), 170.7 ($OCOCH_2$), 159.4, 138.4, 138.0, 135.9, 135.8, 135.6, 135.4 ($CH{=}CH_2$), 133.7, 133.5, 133.3, 132.4, 129.9, 129.8, 129.7, 128.4, 127.8, 127.7, 127.6, 127.3, 117.8 ($CH{=}CH_2$), 113.8, 100.6 (C-1'), 100.4 (C-1), 83.5 (C-2'), 76.1 (CH2-Ph), 75.5 (C-3), 74.1 (CH_2-Ph), 73.7 (CH_2-Ph), 72.8 (C-4), 72.3 (6'-C), 70.1 (C-5), 69.9 (C-5'), 68.7 (CH_2-$CH{=}CH_2$), 67.6 (C-3'), 64.3 (C-4'), 63.8 (C-6), 61.2 (2-C), 55.2 (OCH_3), 38.4 ($OCOCH_2CH_2CO$), 37.7 ($OCOCH_2CH_2CO$), 29.7 ($OCOCH_2CH_2CO$), 29.6 ($OCOCH_2CH_2CO$), 27.5 (CH_3), 26.8 (CH_3), 19.4 (CH_3), 14.7 (CMe_3). MS: M^+ 1141; Found: 1164, M^+ + Na. Anal. Calcd for $C_{63}H_{75}O_{15}N_3Si$: C, 66.25; H, 6.57; N, 3.68. Found: C, 66.39; H, 6.50; N, 3.42.

Allyl (3,6-di-*O*-benzyl-2-*O*-hydroxyl-4-*O*-(4-methoxybenzyl)-β-D-glucopyranosyl)-(1→4)-2-azido-3-*O*-benzyl-6-*O*-(*tert*-butyldiphenylsilyl)-2-deoxy-β-D-glucopyranoside (29)

A solution of the disaccharide **27** (50 mg, 0.043 mmol), dissolved in MeOH (3 mL), was treated with $NaOCH_3$ (1 mL, 1M in MeOH) and allowed to stir for 3 h. The mixture was neutralized by addition of H^+-type resin. The resin was recovered by filtration, washed thoroughly with MeOH, and the solvent was removed under vacuum. The residue was purified on silica gel column using 5 % toluene-EtOAc (R_f 0.25) to produce **29** (40 mg, 88 %) as a clear thick oil. ^{1}H-NMR (500 MHz, $CDCl_3$): 7.73-7.71 (m, 5 H, arom), 7.40-7.24 (m, 20 H, arom), 7.07 (d, *J*8.4 Hz, 2H, *p*-OMe-*Ph*), 6.78 (d, *J*8.4 Hz, 2H, *p*-OMe-*Ph*), 5.87 (dddd, *J* 17.0, 10.5, 6.0, 5.0 Hz, 1 H, CH_2-$CH{=}CH_2$), 5.29 (dq, *J* 17.0, 1.5 Hz, 1 H, CH_2-$CH{=}CH_2$), 5.18 (dq, *J* 10.5, 1.5 Hz, 1 H, CH_2-$CH{=}CH_2$), 5.07 (d, $J_{1',2}$, 8.3 Hz, 1H, 1'-H), 5.02 (d, $J_{A1,B1}$ 11.3 Hz, 1H, $PhCH_2$), 5.00 (d, $J_{A1',B1}$, 11.3 Hz, 1H, $PhCH_2$), 4.74 (d, $J_{A2,B2}$ 11.9 Hz, 1H, $PhCH_2$), 4.64 (d, $J_{A2',B2'}$ 11.9 Hz, 1H, $PhCH_2$), 4.62 (d, $J_{A3,B3}$ 11.3 Hz, 1H, $PhCH_2$, 4.54 (d, $J_{A3',B3'}$ 11.3 Hz, 1H, $PhCH_2$), 4.52 (d, $J_{A4,B4}$ 11.9 Hz, 1H, $PhCH_2$), 4.48 (d, $J_{A4',B4'}$ 11.9 Hz, 1H, $PhCH_2$), 4.40 (d, $J_{1,2}$ 8.3 Hz, 1H, 1-H), 4.26 (dd, $J_{4',3'}$ 9.2 Hz, $J_{4',5'}$ 9.2 Hz, 1H, 4'-H), 4.11 (ddt, J_{gem} 13.0, J_{vic} 5.0, J_{all} 1.5 Hz, 1 H, CH_2-$CH{=}CH_2$), 4.07 (dd, $J_{4,3}$ 9.0 Hz, $J_{4,5}$ 9.0 Hz, 1H, 4-H), 3.99 (ddt, J_{gem} 13.0, J_{vic} 6.0, J_{all} 1.5 Hz, 1 H, CH_2-$CH{=}CH_2$), 3.96 (dd, J_{gem} 13.0 Hz, $J_{6a,5}$ 3.3 Hz, 1H, H-6_a), 3.90-3.80 (m, 2H, H-2', H-6_b), 3.78 (s, 3H, OCH_3), 3.73 (dd, $J_{3,2}$ 9.6 Hz, $J_{3,4}$ 9.6 Hz, 1H, 3-H), 3.57 (dd, J_{gem}11.0 Hz, $J_{6a,5}$ 2.3 Hz, 1H, H-6'$_a$), 3.55-3.47 (m, 2H, H-3', H-6'$_b$), 3.44 (dd, $J_{5,4}$ 9.0 Hz, $J_{5,6}$ 5.5 Hz, 1H, 5-H), 3.41 (dd, $J_{5',4'}$ 9.2 Hz, $J_{5',6'}$ 4.8 Hz, 1H, 5'-H), 3.30 (dd, $J_{2,1}$ 8.3 Hz, $J_{2,3}$ 9.6 Hz, 1H, 2-H), 2.95 (s br,1H, OH), 1.06 (s, 9H, 3x CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$): 159.3, 138.7, 138.5, 138.3, 136.0, 135.5, 135.2 ($CH{=}CH_2$), 134.8, 133.6, 132.7, 130.3, 129.7, 129.6, 128.5, 128.3, 128.2, 127.9, 127.8, 127.7, 127.7, 127.6, 127.5, 127.4, 117.5 ($CH{=}CH_2$), 113.8, 102.6 (C-1'), 100.7 (C-1), 84.7 (2'-C), 81.6 (C-3), 76.3 (CH_2-Ph), 75.5 (CH_2-Ph), 75.3 (CH_2-Ph), 74.5 (CH_2-Ph), 73.3 (6'-C), 72.4 (C-4), 72.3 (C-5), 70.1 (C-4'), 69.9 (C-3'), 69.8 (6-C), 68.7 (5'-C), 66.2 (CH_2-$CH{=}CH_2$), 62.2 2 (C-2), 55.3 (OCH_3), 19.4 (CH_3), 14.6 (CMe_3). MS: M^+ 1035; Found: 1058, M^+ + Na.

Allyl (3,6-di-*O*-benzyl-2-*O*-hydroxyl-4-*O*-*(*4-methoxybenzyl)-β-D-glucopyranosyl)-(1→4)-2-acetamido-3-*O*-benzyl-6-*O*-(*tert*-butyldiphenylsilyl)-2-deoxy-β-D-glucopyranoside (30)

To a stirred solution of **29** (40 mg, 0.038 mmol) dissolved in 1 mL of dry pyridine, thiolacetic acid (30 μL, 0.38 mmol) was added. The mixture was stirred at rt for 18 h and the solvent was evaporated and the residue was purified by silica gel column (10 % EtOAc in toluene + 8 to 10 drops of CH_3OH) to yield pure **30** (37 mg, 91 %) as a white solid. ^{1}H-NMR (500 MHz, $CDCl_3$): 7.73-7.71 (m, 5 H, arom), 7.37-7.24 (m, 20 H, arom), 7.09 (d, *J*8.4 Hz, 2H, *p*-OMe-*Ph*), 6.80 (d, *J*8.4 Hz, 2H, *p*-OMe-*Ph*), 5.87 (dddd, *J* 17.0, 10.5, 6.0, 5.0 Hz, 1 H, CH_2-C*H*=CH_2), 5.48 (br d, $J_{NH,2}$ 7.7 Hz, 1H, N*H*), 5.25 (dq, *J* 17.0, 1.5 Hz, 1 H, CH_2-CH=CH_2), 5.20 (dq, *J* 10.5, 1.5 Hz, 1 H, CH_2-CH=CH_2, 4.98 (d, $J_{1,2}$ 8.2 Hz, 1 H, H-1), 4.88 (d, $J_{A1,B1}$ 11.8 Hz, 1H, PhCH_2), 4.86-4.75 (m, 2H, PhCH_2), 4.66 (d, $J_{A2,B2}$ 12.0 Hz, 1H, $PhCH_2$), 4.64 (d, $J_{A1'},_{B1'}$ 11.8 Hz, 1H, $PhCH_2$), 4.58 (d, $J_{A3,B3}$ 11.8 Hz, 1H, $PhCH_2$), 4.56 (d, $J_{A3',B3'}$ 11.8 Hz, 1H, $PhCH_2$), 4.50 (d, $J_{A2',B2'}$ 12.0 Hz, 1H, $PhCH_2$), 4.47 (d, $J_{1',2'}$ 7.9 Hz, 1H, 1'-H), 4.30 (ddd, $J_{2,1}$ 8.2 Hz, $J_{2,NH}$ 7.7 Hz, $J_{2,3}$ 10.2 Hz, 1H, 2-H), 4.21-4.14 (m, 2H, 2'-H, 4'-H), 4.11 (ddt, J_{gem} 13.0, J_{vic} 5.0, J_{all} 1.5 Hz, 1 H, CH_2-CH=CH_2), 3.99 (ddt, J_{gem} 13.0, J_{vic} 6.0, J_{all} 1.5 Hz, 1 H, CH_2-CH=CH_2), 4.04 (dd, $J_{4,3}$ 10.2, $J_{4,5}$ 9.3 Hz,, 1H, H-4), 3.98-3.90 (m, 3H, H-3, 2x H-6), 3.78 (s, 3H, OCH_3), 3.74-3.61 (m, 3H, H-3', 2x H-6'), 3.33-3.25 (m, 2H, 5-H, 5'-H), 1.79 (s, 3H, NHCOCH_3), 1.05 (s, 9H, 3x CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$): 170.2 (NH*C*OCH_3), 159.3, 139.1, 138.7 138.2, 135.9, 135.5 (*C*H=CH_2), 134.1, 133.7, 132.9, 130.3, 129.6, 128.5, 128.3, 127.9, 127.8, 127.7, 127.6, 127.5, 127.4, 117.1 5 (CH=*C*H_2), 113.8, 102.5 (C-1'), 98.9 (C-1), 78.7 (*C*H_2-Ph), 76.6 (*C*H_2-Ph), 75.4 (*C*H_2-Ph), 75.2 (*C*H_2-Ph), 74.5 (C-3), 73.9 (C-6'), 72.6 (C-2'), 72.4 (C-5), 71.5 (C-3'), 71.1 (C-4'), 69.2 (C-4), 68.7 (C-6), 68.3 (C-5'), 66.1 (*C*H_2-CH=CH_2), 55.9 (OCH_3), 51.2 (C-2), 22.8 (CH3), 19.4 ($COCH_3$). MS: M^+ 1051; Found: 1074, M^+ + Na. Anal. Calcd for $C_{62}H_{73}O_{12}NSi$ (1051): C, 70.78; H, 6.94. Found: C, 70.62; H, 6.76.

Allyl (3,6-di-*O*-benzyl-4-*O*-*(*4-methoxybenzyl)-2-*O*-sulfonato.β-D-glucopyranosyl)-(1→4)-2-acetamido-3-*O*-benzyl-6-*O*-(*tert* -butyldiphenylsilyl)-2-deoxy-β-D-glucopyranoside sodium salt (31)

A solution of **30** (40 mg, 0.038 mmol), dissolved in dry DMF (1 mL), was heated to 55 ^{o}C and a complex of SO_3.NMe_3 (68.8 mg, 0.38 mmol) was added. The mixture was stirred for 18 h (overnight). Sodium acetate (200 mg) dissolved in water (20 mL) was added and the mixture was stirred continuously at rt for an additional 1 h. The solvent was evaporated in vacuo. The residue was co-evaporated with water (3x 10 mL) and purified by passing it through a column containing Sephadex LH-20 using 50 % MeOH in CH_2Cl_2 as eluent to produce pure **31** (30 mg, 82 %) as a white solid. ^{1}H-NMR (500 MHz, $CDCl_3$): 7.65-7.53 (m, 5 H, arom), 7.39-7.13 (m, 20 H, arom), 6.94 (d, *J*8.7 Hz, 2H, *p*-OMe-*Ph*), 6.68 (d, *J*8.7 Hz, 2H, *p*-OMe-*Ph*), 5.87 (dddd, *J* 17.0, 10.5, 6.0, 5.0 Hz, 1 H, CH_2-CH=CH_2), 5.48 (br d, $J_{NH,2}$ 8.8 Hz, 1H, N*H*), 5.26 (dq, *J* 17.0, 1.5 Hz, 1 H, CH_2-CH=CH_2), 5.18 (dq, *J* 10.5, 1.5 Hz, 1 H, CH_2-CH=CH_2), 5.16-5.10 (m, 1H, 2'-H), 5.09 (d, $J_{A1,B1}$ 11.9 Hz, 1H, $PhCH_2$), 4.95 (d, $J_{1,2}$ 8.4 Hz, 1 H, H-1), 4.84-4.78 (m, 1H,

CH_2Ph), 4.72 (d, $J_{A1',B1'}$ 11.9 Hz, 1H, PhCH_2), 4.70 (d, $J_{1',2'}$ 8.3 Hz, 1H, 1'-H), 4.66 (d, $J_{A2,B2}$ 12.1 Hz, 1H, PhCH_2), 4.57 (d, $J_{A2',B2'}$ 12.1 Hz, 1H, PhCH_2), 4.53 (d, $J_{A3,B3}$ 11.8 Hz, 1H, PhCH_2), 4.47 (d, $J_{A3',B3'}$ 11.8 Hz, 1H, PhCH_2), 4.39-4.35 (m, 1H, 2-H), 4.37 (d,$J_{A4,B4}$ 12.4 Hz, 1H, PhCH_2), 4.33 (dd, $J_{4',3'}$ 10.2, $J_{4',5'}$ 9.8 Hz, 1H, 4'-H), 4.29 (m, 1H, CH_2Ph), 4.11 (ddt, J_{gem} 13.0, J_{vic}5.0, J_{all} 1.5 Hz, 1 H, CH_2-CH=CH_2), 4.03 (dd, $J_{4,3}$ 10.2, $J_{4,5}$ 9.8 Hz, 1H, 4-H), 3.99 (ddt, J_{gem} 13.0, J_{vic} 6.0, J_{all} 1.5 Hz, 1 H, CH_2-CH=CH_2), 3.98-3.90 (m, 3H, H-3, 2x H-6), 3.69 (s, 3H, OCH_3), 3.64-3.56 (m, 3H, H-3', 2x H-6'), 3.40-3.27 (m, 2H, 5-H, 5'-H), 1.87 (s, 3H, COCH_3), 0.95 (s, 9H, 3x CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$): 170.2 (NH*C*OCH_3), 159.2, 139.2, 138.8, 138.1, 135.9, 135.6, 135.5 (*C*H=CH_2), 134.6, 133.5, 133.3, 130.4, 129.6, 129.5, 128.3, 128.0, 127.9, 127.7, 127.6, 127.5, 127.2, 127.0, 116.1 (CH=*C*H_2), 113.8, 99.6 (C-1'), 98.7 (C-1), 79.6 (C-2'), 76.1 (*C*H_2-Ph), 74.7 (*C*H_2-Ph), 74.5 (*C*H_2-Ph), 73.5 (*C*H_2-Ph), 72.9 (C-3), 72.4 (C-6'), 71.4 (C-5), 69.4 (C-4'), 68.4 (C-6), 67.7 (C-5'), 67.3 (C-3'), 63.7 (C-4), 55.2 (OCH_3), 46.2 (C-2), 22.9 (CH_3), 19.2 (CO*C*H_3), 14.5 (*C*Me_3). MS: M^+ 1153.5; Found: 1177, M^+ + Na. Anal. Calcd for $C_{62}H_{72}O_{15}NSSiNa$: C, 64.49; H, 6.24. Found: C, 64.18; H, 6.38.

Allyl (3,6-di-*O*-benzyl-2-*O*-sulfonato4-hydroxylβ-D-glucopyranosyl)-(1→4)-2-acetamido-3-*O*-benzyl- 6-*O*-(*tert*-butyldiphenylsilyl)-2-deoxy-β-D-glucopyranoside (32)

A solution of **31** (30 mg, 0.026 mmol) dissolved in 5 mL CH_2Cl_2 / H_2O (4:1 *v*/*v*) was treated with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (12 mg, 0.052 mmol) in the presence of a catalytic amount of di-*tert*-butylpyridine. The mixture was stirred vigorously at rt overnight (15 h). The solvent was evaporated in *vacuo* and the residue was purified by passing it through a column containing Sephadex LH-20 using 50 % MeOH in CH_2Cl_2 as eluent to produce pure **32** (16 mg, 60 %) as a white solid. ^{1}H-NMR (500 MHz, $CDCl_3$): 7.65-7.53 (m, 5 H, arom), 7.39-7.13 (m, 20 H, arom), 5.87 (dddd, *J* 17.0, 10.5, 6.0, 5.0 Hz, 1 H, CH_2-CH=CH_2), 5.48 (br d, $J_{NH,2}$ 8.8 Hz, 1H, N*H*), 5.25 (dq, *J* 17.0, 1.5 Hz, 1 H, CH_2-CH=CH_2), 5.18 (dq, *J* 10.5, 1.5 Hz, 1 H, CH_2-CH=CH_2), 5.16-5.10 (m, 1H, 2'-H), 5.08 (d, $J_{A1,B1}$ 11.8 Hz, 1H, PhCH_2), 4.95 (d, $J_{1,2}$ 8.0 Hz, 1H, H-1), 4.80 (d, $J_{A1',B1'}$ 11.8 Hz, 1H, PhCH_2), 4.72 (d, J_{A2B2} 12.1 Hz, 1H, PhCH_2), 4.70 (d, $J_{1',2'}$ 8.3 Hz, 1H, 1'-H), 4.66 (d, $J_{A2',B2'}$ 12.1 Hz, 1H, PhCH_2), 4.55 (d, $J_{A3,B3}$ 11.8 Hz, 1H, PhCH_2), 4.47 (d, $J_{A3,B3}$ 11.8 Hz, 1H, PhCH_2), 4.18 (dd, $J_{6a,6b}$ 12.9 Hz, $J_{6a,5}$ 3.2 Hz, 1H, H-6$_a$), 4.17 (dd, $J_{6b,6a}$ 12.9 Hz, $J_{6b,5}$ 5.1 Hz, 1H, H-6$_b$), 4.11 (ddt, J_{gem} 13.0, J_{vic} 5.0, J_{all} 1.5 Hz, 1 H, CH_2-CH=CH_2), 4.07-4.00 (m, 2H, H-5', H-4), 3.99 (ddt, J_{gem} 13.0, J_{vic} 6.0, J_{all} 1.5 Hz, 1 H, CH_2-CH=CH_2), 3.90 (dd, $J_{3,4}$ 10.2, $J_{3,2}$ 9.8 Hz, 1H, 3-H), 3.64-3.60 (m, 1H, H-4'), 3.56-3.52 (m, 2H, 2x H-6'), 3.29-3.17 (m, 2H, H-3', H-5), 2.6 (s br 1H, OH), 1.80 (s, 3H, NHCOCH_3), 1.02 (s, 9H, 3x CH_3). ^{13}C-NMR (125 MHz, $CDCl_3$): 170.2 (NH*C*OCH_3), 159.2, 139.2, 138.8, 138.1, 135.9, 135.5, 135.3 (*C*H=CH_2), 134.8, 133.5, 133.3, 130.4, 129.6, 129.5, 128.3, 128.0, 127.9, 127.7, 127.6, 127.5, 127.2, 127.0, 116.1 (CH=*C*H_2), 99.9 (C-1'), 98.7 (C-1), 83.7 (C-3), 79.6 (C-2'), 79.2 (C-5), 76.2 (*C*H_2-Ph), 74.7 (*C*H_2-Ph), 74.5 (*C*H_2-Ph), 73.5 (C-5') , 72.3 (C-6'), 71.4 (C-3'), 69.5 (C-6), 68.0 (*C*H_2-CH=CH_2), 63.9 (C-4), 51.0 (C-4'), 46.2 (C-2), 22.9 (CH_3), 19.3 (NHCO*C*H_3), 14.5 (*C*Me_3). MS: Calculated for $C_{54}H_{64}O_{14}NSSiNa$; M^+1033.5. Found: 1057, M^+ + Na.

_n_-Propyl (2-_O_-sulfonato.β-D-glucopyranosyl)-(1→4)-2-acetamido-6-_O_-(_tert_-butyldiphenylsilyl)-2-deoxy-β-D- glucopyranoside sodium salt (33)

To a solution of **32** (29 mg, 0.028 mmol) dissolved in EtOH (15 mL), $Pd(OAc)_2$ (100 mg) was added and the mixture was stirred at rt under a H_2 atmosphere for 72 h. The reaction was monitored by TLC. After 48 h, the solution was filtered and $Pd(OAc)_2$ (100 mg) was added a second time. The filtrate was concentrated under reduced pressure to yield **33** as a colorless glass. The crude product was used as such for the subsequent procedure without further purification. ^{1}H-NMR (300 MHz, CD_3OD): δ 7.68-7.65 (m, 4H, arom), 7.38-7.32 (m, 6H, arom), 5.27-5.22 (m, 1H, 2'-H), 5.18-5.10 (m, 2H, H-1, H-1'), 4.30-4.26 (m, 1H, H-3), 4.10-3.90 (m, 4H, 2x H-6, H-4, H-2), 3.74-3.60 (m, 3H, 2x H-6', H-5'), 3.52-3.40 (m, O-CH_2, 3'-H, 4'-H, 5-H), 1.94-0.94 (m, 17H, NHCOCH_3, $OCH_2CH_2CH_3$, 3x CH_3). ^{13}C-NMR (75 MHz, CD_3OD): δ 174.3 (CO), 135.2-126.5 (arom.Cs), 101.2 (C-1), 100.1 (C-1'), 80.5 (C-2'), 76.3 (C-5'), 74.9 (C-5), 74.1 (C-3), 73.8 (C-4), 73.4 (C-4'), 72.6 (C-3'), 70.1 (C-6), 64.8 ($OCH_2CH_2CH_3$), 63.5 (C-6'), 47.2 (C-2), 26.3 (OCH_2CH_2), 20.3 (CH_3), 19.3 ($NHCOCH_3$), 16.6 (CH_3). MS: Calculated for $C_{33}H_{48}O_{14}NSSiNa$; M^+ 765.5. Found: 790, M^+ + Na.

_n_-Propyl (2-_O_-sulfonato.β-D-glucuronicacid)-(1→4)-2-acetamido-2-deoxy-β-D-glucopyranoside disodium salt (34)

2,2,6,6-Tetramethyl-1-piperidinyloxy (TEMPO) (0.28 mg, 2 μmol), and a solution of NaBr (0.71 mg, 7 μmol) in H_2O (100 μL) were added to a cooled (0 °C) solution of **33** (17 mg, 0.022 mmol) in H_2O (0.5 mL). The mixture was stirred vigorously at 0 °C and the pH adjusted to 8.5 by dropwise addition of aqueous NaOH (1 M) solution. NaOCl solution, adjusted to pH 8.5 prior to use, was added dropwise (about 100 μL were consumed) and the progress of the reaction was carefully monitored by TLC. The reaction was determined to be complete after 30 min. The mixture was purified by passing it through a column containing Sephadex LH-20 using 0-90 % MeOH in H_2O to generate pure *(n-Propyl)-6-O-(tertbutyldiphenylsilyl)-2-deoxy-2-acetamido-4-O-(2'-O-sulfo-$\beta-D$-glucuronic acid)-$\beta-D$-glucopyranoside disodium salt* (9 mg, 51 %) as a white solid. MS: M^+ 802 calculated for $C_{33}H_{45}O_{15}NSSiNa_2$. Found: 827, M^+ + Na. A solution of the oxidation product (6 mg, 0.007 mmol) in pyridine (300 μL) was carefully treated with a solution of 70 % HF-Pyridine (10 μL) at -5 °C. The mixture was stirred for 1h at the same temperature, followed by stirring overnight at rt. The solvent and volatiles were evacuated under reduced pressure and the remaining residue was passed through a column containing Sephadex LH-20 using 0-20 % MeOH in H_2O to produce pure **34** (1.9 mg, 47.5 %) as a white solid. ^{1}H-NMR (500 MHz, D_2O): δ 5.42 (s br, 1H, 1'-H), 4.92-4.80 (m, 2H, H-1, H-2'), 4.40-4.35 (m, 1H, 5'-H), 4.27-4.0 (m, 4 H, H-4', H-2, H-3, H-4), 3.70-3.63 (m, 3H, 5-H, 2x 6-H), 3.55-3.00 (m, 3H, OCH_2, H-3'), 2.01 (s, 3H, $NHCOCH_3$), 1.72-1.62, 1.53-0.94 (2 m, 5H, $OCH_2CH_2CH_3$). ^{13}C-NMR (125 MHz, D_2O): δ 99.8 (C-1), 97.1 (C-1'), 82.6 (C-5'), 81.4 (C-2'), 73.3 (C-5), 71.5 (C-3), 70.3 (C-4), 67.3 (OCH_2), 61.2 (C-3'), 60.9 (C-4'), 60.6 (C-6), 53.5 (C-2), 26.2 (OCH_2CH_2), 19.4 ($NHCOCH_3$), 16.8 (CH_3). MALDI-TOFMS: Calculated for $C_{17}H_{27}O_{15}NSNa_2$; M^+ 564. Found: 589, M^+ + Na.

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References

[1] H.V. Patel, A.A. Vyas, K.A. Vyas, Y.S. Liu, C.M. Chiang, L.M. Chi and W. Wu: "Heparin and Heparan Sulfate Bind to Snake Cardiotoxin. Sulfated oligosaccharides as a potential target for cardiotoxin action", *J. Biol. Chem.*, Vol. 272, (1997), pp. 1484–1492.

[2] a) J.D. Esko and S.B. Selleck: "Order out of chaos: Assembly of Ligand Binding Sites in Heparan Sulfate", *Annu. Rev. Biochem.*, Vol. 71, (2002), pp. 435–471.

b) H.E. Conrad: *Heparin-Binding Proteins*, Academic Press, San Diego, USA, 1998.

c) R.L. Jackson, S.J. Busch and A.D. Cardin: "Glycosaminoglycans: molecular properties, protein interactions, and role in physiological processes", *Physiol. Rev.*, Vol. 71, (1991), pp. 481–539.

[3] R.J. Linhardt and Y. Toida: "Heparin Analogs-Development and Applications", In: Z. Witczak and K. Nieforth (Eds.): *Carbohydrates in Drug Design*, Marcel Dekker, New York, 1997, p 277–341.

[4] a) F. Chevalier, R. Lucas, J. Angulo, M.M. Lomas and P.M. Nieto: "The heparin–Ca2+ interaction: the influence of the O-sulfation pattern on binding", *Carbohydr. Res.*, Vol. 339, (2004), pp. 975–983.

b) J.D. Esko and U. Lindhal: "Molecular diversity of heparan sulfate", *J. Clin. Invest.*, Vol. 108, (2001), pp. 169–173.

c) A.M. Clement, K. Sugahara and A. Faissner: "Chondroitin sulfate E promotes neurite outgrowth of rat embryonic day 18 hippocampal neurons", *Neurosci. Lett.*, Vol. 269, (1999), pp. 125–128.

[5] J.E. Turnbull and J. T. Gallagher: "Distribution of iduronate 2-sulphate residues in heparan sulphate. Evidence for an ordered polymeric structure", *Biochem. J.*, Vol. 273, (1991), pp. 553–559.

[6] I. Capila and R.J. Linhardt: "Heparin-Protein-Wechselwirkungen", *Angew. Chem.*, Vol. 114, (2002), pp. 426–450; *Angew. Chem. Int. Ed.*, Vol. 41, (2002), pp. 390–412.

[7] R. Vive's, S. Goodger and D.A. Pye: "Combined strong anion-exchange HPLC and PAGE approach for the purification of heparan sulphate oligosaccharides", *Biochem. J.*, Vol. 354, (2001), pp. 141–147.

[8] a) U. Lindahl, G. Bäckström, L. Thunberg and I.G. Leder: "Evidence for a 3-*O*-sulfated D-glucosamine Residue in the Antithrombin-Binding Sequence of Heparin", *Proc. Natl. Acad. Sci. USA*, Vol. 77, (1980), pp. 6551–6555.

b) B. Casu, P. Oreste, G. Torri, G. Zoppetti, J. Choay, J.C. Lormeau, M. Petitou and P. Sinaÿ: "The structure of heparin oligosaccharide fragments with high anti-(factor Xa) activity containing the minimal antithrombin III-binding sequence. Chemical and ^{13}C nuclear-magnetic-resonanc studies", *Biochem. J.*, Vol. 197, (1981), pp. 599–609.

[9] R. Sadir, F. Baleux, A. Grosdidier, A. Imberty and H.L. Jacob: "Characterization of the Stromal Cell-derived Factor-1 -Heparin Complex", *J. Biol. Chem.*, Vol. 276, (2001), pp. 8288–8296.

[10] C.A.A. van Boeckel and M. Petitou: "The Unique Antithrombin III Binding Domain of Heparin: A Lead to New Synthetic Antithrombotics", *Angew. Chem. Int. Ed. Engl.*, Vol. 32, (1993), pp. 1671–1690.

[11] R.R. Vivos, R. Sadir, A. Imberty, A. Rencurosi and J. H. Jacob: "A Kinetics and Modeling Study of RANTES(9-68) Binding to Heparin Reveals a Mechanism of Cooperative Oligomerization", *Biochemistry*, Vol. 41, (2002), pp. 14779–14789.

[12] S.E. Stringer, M.J. Forster, B. Mulloy, C.R. Bishop, G.J. Graham and J.T. Gallagher: "Characterization of the binding site on heparan sulfate for macrophage inflammatory protein 1α", *Blood*, Vol. 100, (2002), pp. 1543–1550.

[13] R.R. Vives, D.A. Pye, M. Salmivirta, J.J. Hopwood, U. Lindahl and J.T. Gallagher: "Sequence analysis of heparan sulphate and heparin oligosaccharides", *Biochem. J.*, Vol. 339, (1999), pp. 767–773.

[14] a) H.N. Yu, J.I. Furukawa, T. Ikeda and C.H. Wong: "Novel Efficient Routes to Heparin Monosaccharides and Disaccharides Achieved via Regio- and Stereoselective Glycosidation", *Org. Lett.*, Vol. 6, (2004), pp. 723–726.

b) A. Lubineau, H.L. Jacob, O. Gavard, S. Sarrazin and D. Bonnaffé: "Synthesis of Tailor-Made Glycoconjugate Mimetics of Heparan Sulfate That Bind IFN-g in the Nanomolar Range", *Chem. Eur. J.*, Vol. 10, (2004), pp. 4265–4282.

c) A. Prabhu, A. Venot and G.J. Boons: "New Set of Orthogonal Protecting Groups for the Modular Synthesis of Heparan Sulfate Fragments", *Org. Lett.*, Vol. 5, (2003), pp. 4975–4978.

d) M. Haller and G.J. Boons: "Selectively protected disaccharide building blocks for modular synthesis of heparin fragments (Part 2)", *Eur. J. Org. Chem.*, Vol. 13, (2002), pp. 2033–2038.

e) M. Haller and G.J. Boons: "Toward a modular approach for heparin synthesis", *J. Chem. Soc., Perkin Trans. 1*, (2001), pp. 814–822.

f) P.G. Wang and C.R. Bertozzi (Eds.): *Glycochemistry*, Marcel Dekker, New York, 2001, pp. 425–492.

[15] a) H.A. Orgueira, A. Bartolozzi, P. Schell, R.E.J.N. Litjens, E.R. Palmacci and P.H. Seeberger: "Modular Synthesis of Heparin Oligosaccharides", *Chem. Eur. J.*, Vol. 9, (2003), pp. 140–169.

b) L. Poletti and L. Lay: "Chemical Contributions to Understanding Heparin Activity: Synthesis of Related Sulfated Oligosaccharides", *Eur. J. Org. Chem.*, (2003), pp. 2999–3024.

c) O. Gavard, Y. Hersant, J. Alais, V. Duverger, A. Dilhas, A. Bascou and D. Bonnaffé: "Efficient Preparation of Three Building Blocks for the Synthesis of Heparan Sulfate Fragments: Towards the Combinatorial Synthesis of Oligosaccharidesfrom Hypervariable Regions", *Eur. J. Org. Chem.*, (2003), pp. 3603–3620.

d) N. Karst and J.C. Jacquinet: "Stereocontrolled Total Syntheses of Shark Cartilage Chondroitin Sulfate and Related Tetra- and Hexasaccharide Methyl Glycosides", *Eur. J. Org. Chem.*, (2002), pp. 815–825.

e) L. Chan and F. Kong: "A practical synthesis of β-D-GlcA-(1→3)-β-D-Gal-(1→3)-β-D-Gal-(1→4)-D-Xyl, a part of the common linkage region of a glycosaminoglycan", *Carbohydr. Res.*, Vol. 337, (2002), pp. 1373–1380.

[16] a) A. O'Brien, C. Lynch, K.M. O'Boyle and P.V. Murphy: "Synthesis of disaccharides derived from heparin and evaluation of effects on endothelial cell growth and on binding of heparin to FGF-2", *Carbohydr. Res.*, Vol. 339, (2004), pp. 2343–2354.

b) W. Ke, D.M. Whitfield, J.R. Brisson, G. Enright, H.C. Jarrell and W.G. Wu: "Development of specific inhibitors for heparin-binding proteins based on the cobra cardiotoxin structure: an effective synthetic strategy for rationally modified heparin-like disaccharides and a trisaccharide", *Carbohydr. Res.*, Vol. 340, (2005), pp. 355–372.

[17] J.O. Hoberg: "Synthesis and Chemistry of 4,6-*O*-di-(tert-butyl)silanediyl-D-glucal", *Carbohydr. Res.*, Vol. 300, (1997), pp. 365–367.

[18] G.J. Boons, G.H. Castle, J.A. Clase, P. Grice, S.V. Ley and C. Pinel: "Selective Acylation and Alkylation Reactions of Diols Using Dibutyltin Dimethoxide", *Synlett*, (1993), pp. 913–914.

[19] W. Kinzy and R.R. Schmidt: "Direct 3,6-di-*O*-protection of glucal and galactal", *Tetrahedron Lett.*, Vol. 28, (1987), pp. 1981–1983.

[20] a) R.L. Halcomb and S.L. Danishefsky: "On the direct epoxidation of glycals: application of a reiterative strategy for the synthesis of .beta.-linked oligosaccharides", *J. Am. Chem. Soc.*, Vol. 111, (1989), pp. 6661–6666.

b) R.W. Murray and R.J. Jeyaramen: "Dioxiranes: synthesis and reactions of methyldioxiranes", *J. Org. Chem.*, Vol. 50, (1985), pp. 2847–2853.

[21] S.L. Danishefsky, S. Hu, P.F. Cirillo, M. Eckhardt and P.H. Seeberger: "Highly Convergent Synthetic Route to Glycopeptides Carrying a High Mannose Core Pentasaccharide Domain N-linked to a Natural Peptide Motif", *Chem. Eur. J.*, Vol. 3, (1997), pp. 1617–1628.

[22] Y. Bai, G.J. Boons, A. Burton, M. Johnson and M. Haller: "Vinyl glycosides in oligosaccharide synthesis: 3 buten-2-yl 2-azido-2-deoxy glycosides and 3-buten-2-yl-phthalimido-2-deoxy glycosides as novel glycosyl Donors", *J. Carbohydr. Chem.*, Vol. 19, (2000), pp. 939–958 and references cited therein.

[23] F.I. Auzanneau, M. Mondange, D. Charon and L. Szabo: "Synthesis of allyl 6-*O*-(3-deoxy-α- and - β-D-*manno*-oct-2-ulopyranosylonicacid)-(1→6)-2-deoxy-2-[(3*R*)-3-hydroxytetradecanamido]-β-D-glucopyranoside-4phosphate and of the copolymer of the α-anomer with acrylamide", *Carbohydr. Res.*, Vol. 228, (1992), pp. 37–45.

[24] P.B. Alper, S.C. Hung and C.H. Wong: "Metal catalyzed diazo transfer for the synthesis of azides from amines", *Tetrahedron Lett.*, Vol. 37, (1996), pp. 6029–6032.

[25] T. Rosen, I.M. Lico and D.T.W. Chu: "A Convenient and Highly Chemoselective Method for the Reductive Acetylation of Azides", *J. Org. Chem.*, Vol. 53, (1988), pp. 1580–1582.

[26] J. Kovensky, P. Duchaussoy, M. Petitou and P. Sinaÿ: "Binding of heparan sulfate to fibroblast growth factor-2 total synthesis of a putative pentasaccharide binding site", *Tetrahedron: Asymmetry*, Vol. 7, (1996), pp. 3119–3128.

[27] a) N.J. Davis and S.L. Flitsch: "Selective oxidation of monosaccharide derivatives to uronic acids", *Tetrahedron Lett.*, Vol. 34, (1993), pp. 1181–1184.

b) A.E.J. de Nooy, A.C. Besemer and H. van Bekkum: "Highly selective nitroxyl radical-mediated oxidation of primary alcohol groups in water-soluble glucans", *Carbohydr. Res.*, Vol. 269, (1995), pp. 89–98.