Chemical synthesis of selectively protected tetrasaccharides of the type "Glcp-β-D-(1→4)GlcpN₃-α-D-(1→4)Glcp-β-D-(1→4)GlcpN₃"

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Received: 14th February, 2007 ; Accepted: 19th February, 2007

ABSTRACT

We describe here the chemical synthesis of two tetrasaccharides (18) and (19) contained all different protecting groups in the correct positions for further manipulation using the 2+2 coupling strategy.
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INTRODUCTION

Heparan sulfate(HS) is a member of the glycosaminoglycan(GAG) family and close in structure to heparin(HP), which is clinically used for its antithrombotic activity. It is a linear sulfated polysaccharide and its basic disaccharide unit composed of a uronic acid 1,4-linked to a 2-deoxy-2-aminoglucose. HS chains, either at the cell surface or in the extracellular matrix, interact and regulate the activity of numerous proteins, such as growth factors, cytokines, chemokines, viral proteins or coagulation factors[1]. HS is one of the most heterogeneous biopolymers since the uronic acid may have either the D-*gluco* or L-*ido* configuration and various sulfation patterns (sulfoforms) may occur along the chain[2,3]. There is growing evidence that the formation of different HS structures is tightly controlled during biosynthesis, with the presumed goal of generating sequences with biological specificity[4]. It has often

been difficult to determine the oligosaccharide sequence and sulfation pattern of HP or HS fragment required for activation or deactivation of a given protein[5]. For this reason it is highly desirable to develop effective syntheses of this heparin-like oligosaccharide chains with defined size, sequence, and charge distribution to be used in the interaction studies. Impressive improvements in the synthesis of HS fragments have been made in the last decade and have allowed HS fragments with a large structural variety to be synthesized[6,7].

In continuation of our effort to synthesize HS fragments for biological studies, we reported previously the synthesis of sulfated disaccharides that contain glucoside moieties[8]. The important features of that primary approach were: **(a)** Avoids problems caused by uronic acids such as epimerization of the C-5 position, by selective TEMPO oxidation of the primary hydroxyl group in a latter step. **(b)** OH-C(**6**) of glucosamine moieties were protected as TBDPS ethers to avoid oxidation

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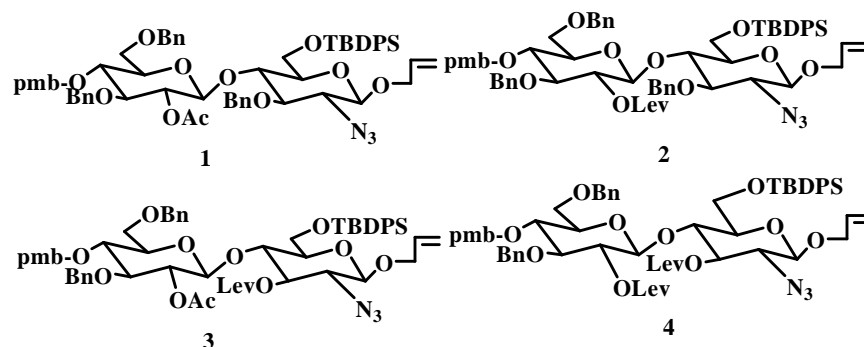
SCHEME 1

and it cleanly deblocked by treatment with HF in pyridine. **(c)** Acetyl and/or levulinoyl esters protect the positions to be sulfated, while benzyl ethers are used for permanent protection. **(d)** The 2-Azido-2-deoxyglycoside was used as a glycosyl acceptor where the anomeric OH group was masked as allyl ether and the OH-C-(4) is free. **(e)** The glucosyl moiety was employed as thioglycosyl donor and the hydroxyl group at C-4 was protected as *p*-methoxybenzyl (PMB) ether. The use of this anomeric functionality in glucosamine derivative in combination with a set of other protecting groups allows one common building block that could be elongated at either the reducing or non-reducing end for the synthesis of larger saccharide libraries. In this paper, we report the preparation of two tetrasaccharide building blocks using 2+2 strategy which relies upon either glycosyl fluoride or a Schmidt trichloroacetimidate-mediated coupling between the 2-azido disaccharide donors **(11), (12), (13)** and the disaccharide acceptor **(15)**. The key point in this approach is to obtain good a- stereoselectivity in the glycosylation reaction between acceptors and donors. The non-participating azide at the 2-position of the donors should allow for a 1,2-cis glycosylation. A quick survey of the literature revealed that, although reactions between donors containing a non-participating azido[9], and glycosyl acceptors may lead to some unwanted b-anomer, this is not the general trend. Indeed, in many cases, the reported a-anomer was formed as the sole isolated stereoisomer[10]. We thus felt rather confident that we would be able to find highly a-diastereoselective glycosylation conditions between **(11-13)** and **(15)**. The tetrasaccharide thus formed will comprise the same protecting group pattern at the anomeric and 4_d-positions,

allowing us to perform further iterative chain elongation using sequential addition of disaccharides.

RESULTS AND DISCUSSION

We recently reported a concise method for a stereocontrolled synthesis of a set of selectively protected disaccharide **(1-4)** (SCHEME 1)[8]. A unique pattern of protecting groups made clear distinction between the positions to be sulfated and those remaining as free hydroxyl groups. In addition, 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. Therefore, the next issue to be addressed towards the disaccharide donors was deallylation of the disaccharides **(1-4)** to get the free reducing end carbohydrates.
(SCHEME 1).

Preparation of disaccharide donors (11-14)

O-Allyl ethers are usually "*clipped off*" by a two-step process, isomerisation[11] of the double bond to get 1-propenyl ether and conversion into the corresponding free OH using either acid or $HgCl_2/HgO$. Despite the procedure involves mild reaction condition it could not be applied to the substrates containing acid labile protecting groups such as PMB group. On the other hand, 'clip off' allyl group under $DDQ/CH_2Cl_2/H_2O$ method was not the optimum choice because not only the PMB could be cleaved[12] under this condition but also anomeric allyl ethers proved to be resistant to DDQ[13]. The deallylation method using $PdCl_2$ in
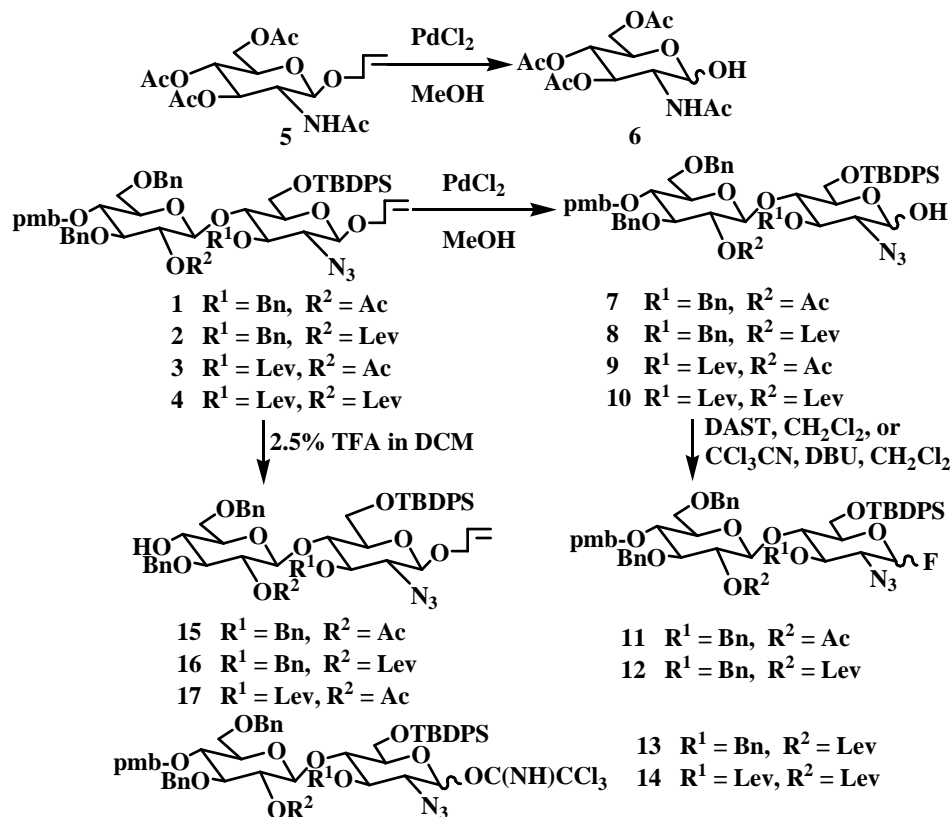
SCHEME 2

MeOH[14] is dealing with substrates containing non-anomeric allyl ethers while anomeric allyl ethers were removed using $PdCl_2/NaOAc/AcOH$ mixture[15], a conditions that is not suitable for substrates such as(**1-4**). As a model reaction, deallylation of (**5**)[8] with $PdCl_2$ (SCHEME 2) in MeOH furnished the lactol (**6**)(67%) after 2h reaction time. The deallylation reaction had to be monitored carefully by TLC and worked up immediately, because prolonged reaction times resulted in complete decomposition of (**6**). ^{1}H-NMR spectra of (**6**) in $CDCl_3$ clearly demonstrated the disappearance of the allyl protons and proved that (**6**) is a mixture of 1:3 α/β anomers, respectively. The β-H-1 proton appeared at $\delta 5.19$ppm as double t($J_{1,2}=8.3$Hz), while α-H-1 proton appeared as doublet ($J_{1,2}=3.6$Hz) at $\delta 5.22$ppm. The mass spectroscopy (MALDI-TOF) showed fragments at 347 (M^+), 370(M^++Na) and 386(M^++K). Under similar conditions, allyl glycosides (**1-4**) were transformed into the corresponding hemiacetal intermediates (**7-10**), respectively, by treatment with $PdCl_2/MeOH$ mixture. It is noteworthy to mention

that solutions of lactols (**7-10**) in $CDCl_3$ proved to be unstable carbohydrates and therefore they were passed immediately to the next step. The fluoride donors(**11**) and (**12**) were next prepared: reaction of (**7-8**) with (diethylamino) sulfur trifluoride (DAST; Et_2NSF_3) in CH_2Cl_2 at -30^0C gave (**11**) (70%) and (**12**)(64%) respectively as a mixture of 1:1 α/β anomers. Interestingly, the levulinoyl group in compound (**8**) proved to be stable and thus glycosyl fluoride (**12**) was separated as a single reaction product. The expected gem-difluorides derivative by reaction of levulinoyl CO group in compound (**8**) with DAST was not formed under this condition. The structures of(**11**) and(**12**) were evident from their ^{1}H-NMR spectra. The H-1 proton of compounds(**11**) appeared at $\delta 5.60$ppm(d, $J_{1,F}=53.0$Hz), H-1' proton resonated at $\delta 4.75$ppm as doublet of doublets and the coupling constant $J_{1',2'}=8.4$Hz confirming the β-stereochemistry. ^{1}H-NMR spectrum of(**12**)revealed that H-1 proton appeared at $\delta=5.53$ ppm(dd, $J_{1,F}=55.4$Hz, $J_{1,2}=3.0$Hz, a-anomer), H-1' proton at $\delta=4.10$ppm(d, $J_{1',2'}=7.9$Hz) and ^{13}C-NMR

SCHEME 3
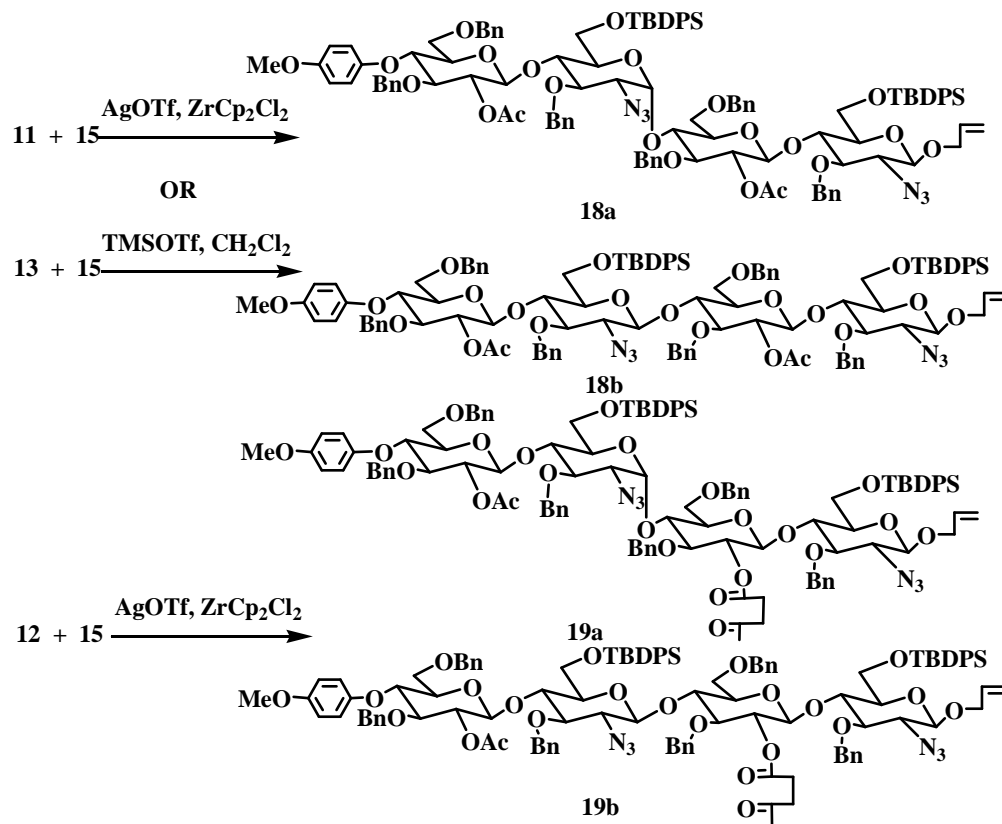
spectrum showed that C-1 and C-1' are resonated at 106.89ppm and 100.22ppm, respectively. Table 1 compiles selected ^{1}H- and ^{13}C-nmr data of the carbohydrate portions in glycosyl donors (**11**-**14**).

Preparation of disaccharide acceptor (15-17)

The cleavage of the p-methoxybenzyl groups in disaccharides(**1-3**) was then achieved with 2.5% trifluoroacetic acid (TFA) in dichloromethane (DCM)[16] to give the desired disaccharide acceptors (**15**)(97%), (**16**)(92%) and (**17**)(91%), respectively, (Scheme 2). We found that this method for the cleavage of the p methoxybenzyl group gave higher yields to the use of DDQ. Table 2 compiles selected ^{1}H-NMR and ^{13}C-NMR data of the carbohydrate portions in acceptors (**15-17**).

Glycosylation reactions of disaccharide donors 11-13 with disaccharide acceptor (15)

With the disaccharide building blocks (**11-14**) and (**15-17**) in hand containing protecting groups in the correct positions, we initially investigated the glycosylation

reaction between donor(**11**) and acceptor (**15**)under standard conditions, using CH_2Cl_2-Et_2O (4:1v/) as solvent and in the presence of Cp_2ZrCl_2-AgOTf as the promoter system at -5^0C® 0^0C gave the desired tetrasaccharides(**18**) in only 10% yield and an α/β ratio of 50:50, together with several side reaction products as evidenced by mass spectrometry. The typical course of the reaction involved the slow hydrolysis of the donor (**11**) upon addition of further quantities of promoter. In addition, after treatment of the reaction mixture, the acceptor (**15**) could be partly recovered together with some partially unprotected derivatives. We then looked at the effects of changing the promoter to $BF_3.OEt_2$ or TMSOTf as well as the presence or absence of molecular sieves; in all cases the reactions were unsuccessful. We reasoned that, in compound(**15**), the nucleophilicity of the OH-C(4)$_b$ may be reduced by the presence of acetyl that would be the cause of the low glycosylation yield. A literature survey shows that the 4-OH nucleophilicity is variable and linked to the protecting groups used. In the case of glycosylation reactions with bromide donors, an acetyl group at the 3-

TABLE 1 : Selected NMR chemical shifts (dppm) of carbohydrate ring in glycosyl donors (11-14)

	H-1a (H-1b)	H-2a (H-2b)	H-3a (H-3b)	H-4a (H-4b)	H-5a (H-5b)	H-6a (H-6b)	C-1a (C-1b)	C-2a (C-2b)	C-3a (C-3b)	C-4a (C-4b)	C-5a (C-5b)	C-6a (C-6b)
11	5.60α 4.75β (5.04)	3.47 (4.86)	3.69 (3.85)	4.45 (4.22)	3.96 (3.49)	4.45 (3.96)						
12	5.53α 4.83β (4.78)	3.28 - (4.17)	3.78 - (3.68)	4.07 - (4.03)	3.85 - (3.59)	3.87 - (3.43)	- 106.89 (83.29)	61.07 60.84 (100.22)	77.78 - (77.41)	69.70 70.12 (73.35)	70.91 - (70.55)	66.48 67.75 (68.78)
13	5.05α 4.66β (4.80)	- 3.48 (4.48)	- 3.70 (3.92)	- 4.45 (4.41)	- 4.36 (4.23)	- 4.33 (4.09)	94.73 100.36 (100.53)	62.73 60.98 (83.37)	77.66 77.42 (77.89)	73.30 - (75.48)	75.16 74.60 (74.18)	65.28 68.51 (68.82)
14	5.04α 4.76β (4.87)	3.37 3.33 (4.72)	- 3.99 (4.08)	- 4.43 (4.68)	- 4.05 (3.96)	- 4.45 (3.90)						

TABLE 2 : Selected NMR chemical shifts (d ppm) of carbohydrate ring in acceptors (15-17)

	H-1a (H-b)	H-2a (H-2b)	H-3a (H-3b)	H-4a (H-4b)	H-5a (H-5b)	H-6a (H-6b)	C-1a (C-1b)	C-2a (C-2b)	C-3a (C-3b)	C-4a (C-4b)	C-5a (C-5b)	C-6a (C-6b)
15	4.40 (5.05)	3.34 (4.86)	3.78 (3.89)	4.51 (4.34)	3.80 (3.35)	4.38 (3.55)	100.58 (100.29)	61.19 (82.50)	----- -----	----- (80.91)	74.22 (73.71)	71.24 (72.91)
16	4.36 (5.23)	3.22 (5.04)	3.72 (3.75)	4.15 -----	3.52 (3.52)	3.93 (3.73)	100.62 (100.29)	61.31 (83.43)	81.00 (73.34)	69.70 (74.14)	74.62 (76.06)	65.99 (68.27)
17	4.39 (5.32)	3.25 (4.84)	3.78 (3.82)	4.55 (4.68)	4.15 (3.34)	4.15 (3.55)	100.60 (100.53)	62.67 (84.45)	83.38 (73.46)	71.79 (70.74)	74.22 (73.71)	64.36 (69.96)

position, for instance, gives low glycosylation yields, while allyl or benzyl groups allow efficient couplings[17]. We have already reported the moderate yield of glycosylation reaction at the OH-4 of a 2-azido glucose acceptor containing an ester group[8]. We could not test this hypothesis by changing the acetyl protecting group that present at its correct 2-position and we, therefore, looked for alterative explanation for the low glycosylation yield.

It is well known that the solvent used in a glycosylation has an impact on reactions yields[18]. In the first experiment for the preparation of (18) in CH_2Cl_2 and Et_2O as co-solvent, we faced a dual reactivity and diastereoselectivity problem. Under S_N^1 conditions the effect of ethers on the oxycarbenium intermediate generally results in the formation of the thermodynamically more stable glycoside anomer, due to stabilisation of the epimeric oxonium anomer by the reverse anomeric effect[19]. By conducting the condensation between donor (12) and acceptor (15) in Et_2O in the presence of Cp_2ZrCl_2-AgOTf as the promoter system at -$5^0C \rightarrow 0^0C$, quite surprisingly, the tetrasaccharides (19) obtained in a similar low yield(10%) and the a/b ratio remained unchanged(50:50). It is important to note that the donor consumed more slowly in Et_2O (30 to 45min) than in CH_2Cl_2(15min), in accordance with the change in solvent polarity.

For the moment, we anticipated that the low yield obtained during the current glycosylation step could be attributed to the inadequate reactivity of the glycosyl fluorides as donors in comparison to the side reactions occurred under such reaction conditions, such as the instability of the PMB group. It was necessary to device more activated glycosyl donors such as glycosyl trichloroacetimidates. Compounds(13) and (14) were obtained by treatment of the lactols(8)and (10) respectively, with trichloroacetonitrile (CCl_3CN) in the presence of 1,8-diazabicyclo-[5.4.0] undec-7-ene(DBU). As revealed by NMR spectroscopy (TABLE 1), the glycosyl imidates(18)and(14) were found to be a mixture of anomers(α/β 1:3 ratio). H-1a and H-1b protons of (13)were appeared in the ¹H-NMR spectrum δ 5.05ppm (d, $J_{1a,2a}$=3.8Hz, a-anomer), δ 4.66ppm (d, $J_{1a,2a}$=8.3Hz, β-anomer), δ 4.80(d, $J_{1b,2b}$=8.5Hz) whereas the NH proton resonated at δ 8.64ppm as a broad singlet signal. ¹³C-NMR of anomeric mixture (13)showed C-1a and C-1b at(δ100.53, δ 00.36, β-anomer), and (δ 100.14, δ 94.73, α-anomer) ppm respectively. Based on the presence of an appreciable ratio of β-imidate donor, we were anticipated much higher α-stereoselectivity during the course of glycosylation step, therefore, (13) were immediately subjected to the next glycosylation step to avoid anomerization which is likely taken place in favor of the more stable a- imidate anomer. Coupling

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reaction of imidate**(13)** and acceptor **(15)** catalyzed by TMSOTf in CH_2Cl_2-Et_2O(4:1 ν/ν) as solvent yielded a mixture of tetrasaccharide **(18)** which was contaminated with some other side reaction products. Purification on silica gel and Sephadex LH-20 using CH_2Cl_2/MeOH(1:1 ν/ν) yielded the desired tetrasaccharide **(18)** (20% yield), a derivative of tetrasaccharide **(18)**(without PMB group; 20% as evidenced by mass spectrometry; probably formed after the coupling step) and some partially unprotected derivative of acceptor**(15)**. Interestingly, the diastereo selectivity was improved leading to a 3:1α/β ratio as judged by careful ^{1}H-NMR analysis of the crude product (TABLE 3). A rational explanation for the observed diastereoselectivity of the glycosylation reaction using fluoride donors **(13)** and/or**(12)** with the acceptor**(15)** could be attributed to the reverse anomeric effect. The observed α/β ratio of product may support this assumption. On the other hand, formation of**(18)** from the imidate**(13)**and acceptor **(15)** could occurred *via* the systematic oxycarbenium intermediate($S_N{}^1$ pathway) and the presence of the non-participating azide at the 2-position of the donor allows a 1,2-cis glycosylation, nevertheless, considering the higher β-anomer ratio of the imidate **(13)**, we should not exclude the possibility of $S_N{}^2$ pathway as well.

In conclusion we demonstrated that imidate**(13)** as a diasaccharide donor gave a moderate yield and good stereoselectivity during coupling reaction with the diasaccharide acceptor **(15)** than its flouro analogue**(11)**. The low reactivity of the fluoride as donor and/or the OH-4$_b$ in acceptor were perceived to be obstacles to obtain good yield during such glycosylation step. In our study, we found that changing solvent mixture(CH_2Cl_2-Et_2O; 4:1 ν/ν) to Et_2O did not show any improvement in either reaction yield or diastereoselectivity. Imidate disaccharide donor**(14)** and acceptors**(16,17)** that have not been used in this study could be considered as novel synthetic subtargets for oligosaccharide synthesis.

EXPERIMENTAL

General methods

All solvents were dried over standard drying agents and freshly distilled prior to use. All moisture-sensitive reactions were performed under an argon atmosphere

TABLE 3: Selected NMR Chemical shifts (δppm) of carbohydrate ring in tetrasaccharides (18-19)

	18α	18β	19α	19β
H-1$_a$	5.03	4.86	4.71	4.59
H-1$_b$	4.42	4.29	4.92	4.70
H-1$_c$	5.53	5.00	5.45	5.02
H-1$_d$	4.95	4.39	4.93	-----
H-2$_a$	3.29	3.22	3.25	3.22
H-2$_b$	3.85-3.74(m)	3.33	4.63	4.40-4.30(m)
H-2$_c$	3.24	3.26	3.03	3.03
H-2$_d$	3.39-3.32(m)	4.54	4.65	4.40-4.30(m)
H-3$_a$	3.27	3.44	4.24-4.19(m)	4.40-4.30(m)
H-3$_b$	3.46	3.30	3.38-3.33(m)	4.50-4.45 (m)
H-3$_c$	3.30	3.73-3.71(m)	4.24-4.19(m)	4.40-4.30(m)
H-3$_d$	3.39-3.32 (m)	4.40	3.38-3.33(m)	4.55
H-4$_a$	3.85-3.74 (m)	3.81	4.24-4.19(m)	4.40-4.30(m)
H-4$_b$	3.65-3.54 (m)	3.85	3.38-3.33(m)	4.50-4.45(m)
H-4$_c$	3.85-3.74 (m)	3.90	3.38-3.33 (m)	3.33
H-4$_d$	3.85-3.74(m)	3.73-3.71(m)	4.24-4.19 (m)	4.40-4.30(m)
H-5$_a$	3.65-3.54(m)	3.66-3.63(m)	3.52	4.0-3.33(m)
H-5$_b$	3.65-3.54(m)	3.36	4.05	4.50-4.45(m)
H-5$_c$	3.65-3.54(m)	3.53-3.49(m)	4.03	4.0-3.33(m)
H-5$_d$	3.65-3.54(m)	3.61-3.53(m)	4.14-4.10(m)	4.0-3.33(m)
C-1$_a$	100.33		100.19	
C-1$_b$	100.16		100.04	
C-1$_c$	96.00		94.77	
C-1$_d$	103.88		103.00	
C-2$_a$	62.93		62.44	
C-2$_b$	80.60		82.36	
C-2$_c$	62.40		62.96	
C-2$_d$	83.11		83.36	
C-3$_a$	77.92		77.70	
C-3$_b$	-		77.34	
C-3$_c$	77.39		77.30	
C-3$_d$	84.84		83.59	
C-4$_a$	76.94		75.80	
C-4$_b$	83.92		79.87	
C-4$_c$	76.50		78.71	
C-4$_d$	80.35		78.23	
C-5$_a$	69.73		70.01	
C-5$_b$	73.46		74.00	
C-5$_c$	72.03		74.34	
C-5$_d$	73.12		74.30	
C-6$_a$	65.76		66.52	
C-6$_b$	-		66.70	
C-6$_c$	68.56		69.12	
C-6$_d$	-		69.46	

using oven-dried glassware. Evaporation was performed under vacuum with a water bath temperature below 40°C. Molecular sieves were crushed and activated in *vacuo* at 390°C for 4 hours prior to use. Reactions were monitored by TLC on glass Silica Gel 60 F$_{254}$ plates with detection by UV at 254nm and by charring with 5% ethanolic H_2SO_4. Column chromatography was performed on silica gel 60 (EM Science, 70-230 mesh), size exclusion column chromatography was performed on Sephadex LH-20 (methanol/dichlorometh ane 1:1 ν/ν, Pharmacia Biotech AB) or Sephadex G-25 (wa-

ter elution). 1D ^{1}H-NMR, 2D correlated spectroscopy (^{1}H-^{1}H COSY, ^{1}H-^{13}C HSQC) and ^{13}C-NMR were recorded on *Varian* 300MHz and 500MHz spectrometers equipped with Sun off-line editing workstation. Me$_4$Si or solvent signals were used for δ calibration (CDCl$_3$: ^{1}H δ=7.26; ^{13}C δ=77.0ppm). Matrix-assisted laser desorption ionization-Time-of-Flight (MALDI-TOF)mass spectroscopy was performed using a HP MALDI-TOF spectrometer using gentisic acid as matrix. For the determination of the a/b ratio for tetrasaccharides**(18)** and**(19)** size-exclusion chromatography was first performed followed by careful NMR analysis of the product.

2-N-acetyl-3,4,6-tri-O-acetyl-2-deoxy-α/β-D-glucopyranoside (6)

To a solution of Allyl 2-N-acetyl-3,4,6-tri-O-acetyl-2-deoxy-β-d-glucopyranoside **(5)**[12](100mg, 0.243mmol) dissolved in 5.0ml MeOH was added Palladium(II) chloride(20mg). The mixture was stirred at rt for 2h(TLC) and then filtered through a short column (2cm) of Celite. The solvent was evaporated to dryness and the oil residue was purified on silica gel column using 5% MeOH-CH$_2$Cl$_2$ (R$_f$ 0.19) afforded(60mg, 67%) of pure**(6)** as clear oil. The ratio of α/β anomers was 1:3 as judged by ^{1}H-NMR spectra. The following data were recorded: ^{1}H-NMR(CDCl$_3$, 300MHz): β-anomer: 5.90(d, $J_{NH,2}$=8.8Hz, 1H, NH), 5.19(dd, $J_{1,2}$=8.3Hz, 1-H), 5.10(dd, $J_{3,4}$=9.6Hz, $J_{3,2}$=9.6Hz, 1H, 3-H), 4.61(dd, $J_{5,4}$=9.6Hz, $J_{5,6}$=6.6Hz, 1H, 5-H), 4.44(dd, $J_{4,3}$= 9.2Hz, $J_{4,5}$=9.6Hz, 1H, 4-H), 3.82 (ddd, 1H, $J_{2,3}$=9.6, $J_{2,1}$=8.3, $J_{2,NH}$=8.8 Hz, H-2), 3.70-3.65(m, 1H), 3.59-3.54(m, 1H), 2.14(s, NHCOCH$_3$), 2.06 (s, COCH$_3$), 1.99(s, COCH$_3$), 1.92 (s, COCH$_3$). MS: M$^+$ 347; Found: 347 (M$^+$), 370 (M$^+$+Na), 386 (M$^+$+K). α-anomer: 5.22(dd, $J_{1,2}$=3.6 Hz, 1-H), 5.10(dd, $J_{3,4}$=9.6 Hz, $J_{3,2}$=9.6Hz, 1H, 3-H), 4.61(dd, $J_{5,4}$=9.6Hz, $J_{5,6}$=6.6Hz, 1H, 5-H), 4.44 (dd, $J_{4,3}$=9.2 Hz, $J_{4,5}$=9.6Hz, 1H, 4-H), 3.89 (ddd, 1H, $J_{2,3}$=9.6, $J_{2,1}$=3.6, $J_{2,NH}$=8.8Hz, H-2), 3.80-3.70 (m, 1H), 3.33-3.24(m, 1H), 2.12(s, NHCOCH$_3$), 2.00 (s, COCH$_3$), 1.95(s, COCH$_3$), 1.93(s, COCH$_3$).

2-O-acetyl-3,6-di-O-benzyl-4-O-(4-methoxy benzyl)-β-D-glucopyranosyl-(1→4)-2-azido-3-O-benzyl-6-O-(tert-butyldiphenylsilyl)-2-deoxy-α/β-D-glucopyranosyl fluoride(11)

To a solution of disaccharide **(1)**(100mg, 0.092 mmol) in MeOH(10ml) was added PdCl$_2$(20mg). The mixture was stirred at rt and the progress of the reaction was monitored by TLC until the starting material was consumed(2h). The mixture was filtered through Celite, and the filtrate was concentrated and purified by a column chromatography(EtOAc-hexane 1:4, R$_f$ 0.2) to give(2-O-acetyl-3,6-di-O-benzyl-4-O-(4-methoxybenzyl)-β-D-glucopyranosyl)-(14)-2-azido-3-O-benzyl-6-O-(tert-butyldiphenylsilyl)-2-deoxy-α/β-D-glucopyranose **(7)** as colorless oil and passed immediately to the next step. The following data were recorded: ^{1}H-NMR(500MHz, CDCl$_3$): 7.72-7.67(m, 5 H, arom), 7.43-7.25(m, 20H, arom), 7.08(d, J_{ortho}=8.4 Hz, 2H, MeO-Ph), 6.80(d, J_{ortho}=8.4Hz, 2 H, MeO-Ph), 5.237(d, J_{gem}=10.9Hz, 1H, PhCH$_2$), 5.07(d, J_{gem}=10.5Hz, 1H, PhCH$_2$), 5.05 (dd, $J_{2b,1b}$=8.3Hz, $J_{2b,3b}$=8.8Hz, 1H, H-2$_b$),4.84(d, $J_{1a,2a}$=3.5Hz, 1H, H-1$_a$ (α-anomer), 4.86(d, $J_{1b,2b}$=8.8Hz, 1H, H-1$_b$), 4.83(d, J_{gem}=12.3Hz, 1H, PhCH$_2$), 4.71(d, J_{gem}=10.9Hz, 1H, PhCH$_2$), 4.64(d, J_{gem}= 10.9Hz, 1H, PhCH$_2$), 4.94 (d, J_{gem}=10.5Hz, 1H, PhCH$_2$), 4.51(dd, $J_{4b,3b}$=$J_{4b,5b}$=10.7Hz, 1H, H-4$_b$), 4.43-4.33(m, 2H, H-5, H-6$_a$), 4.25-4.22(m, 1H, H-6$_a$), 4.16(d, $J_{1a,2a}$=8.8Hz, 1H, H-1$_a$, β-anomer), 3.89 (m, 1H, H-6$_b$), 3.78(dd, $J_{3b,2b}$=8.8Hz, $J_{3b,4b}$=9.6Hz, 1H, H-3$_b$), 3.76(dd, $J_{3a,2a}$=9.3Hz, $J_{3a,4a}$=10.7Hz, 1H, H-3$_a$), 3.75(s, 3H, OCH$_3$), 3.58 (m, 1H, H-6$_b$), 3.42 (dd, $J_{4b,3b}$=9.6, $J_{4b,5b}$=9.9Hz, 1H, H-4$_b$), 3.3(dd, $J_{5b,4b}$= 9.9, $J_{5b,6b}$=6.3Hz, 1H, H-5$_b$), 3.22(dd, $J_{2a,1a}$=8.3Hz, $J_{2a,3a}$=9.3Hz, 1H, H-2), 1.79 (s, 3H, COCH$_3$), 1.05 (s, 9H, 3×CH$_3$). MS: M$^+$ 1037; Found: 1060, M$^+$+Na and 1076, M$^+$+K.

The solution of the lactol **(7)** dissolved in 1.0 ml of CH$_2$Cl$_2$ was cooled to -30^{0}C and 28μl(0.23mmol) of DAST was added. After 30min stirring TLC showed complete conversion of the starting material. The mixture was quenched with 100μl of MeOH and then the solvents were concentrated in vacu. The residue was dissolved in MeOH (50 ml) and washed thoroughly with saturated aqueous NaHCO$_3$(20ml), brine(20ml), dried(MgSO$_4$), filtered and the filtrate was concentrated in vacu. The residue was purified on silica gel column chromatography (EtOAc-hexane 1:4, R$_f$=0.16) to give fluoride **(11)**(70mg, 70%) as a colorless oil. ^{1}H-NMR

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(500MHz, CDCl$_3$): 7.70(d, J=6.6Hz, 2H, arom), 7.64(d, J=6.6Hz, 2H, arom), 7.43-7.30(m, 21H, arom), 7.09(d, J=8.4Hz, 2 H, MeO-Ph), 6.81 (d, J=8.4Hz, 2H, MeO-Ph), 5.60 (dd, J$_{1,F}$=53.0Hz, J$_{1a,2a}$=3.6Hz, 1H, H-1; a-anomer)), 5.18(d, J$_{gem}$= 10.9Hz, 1H, PhCH$_2$), 5.04(dd, J$_{2b,1b}$=8.4Hz, J$_{2b,3b}$=9.2Hz, 1 H, H-2$_b$), 4.82 (d, J$_{gem}$=11.4 Hz, 1H, PhCH$_2$), 4.78(d, J$_{1a,2a}$=9.2Hz, 1H, H-1$_a$), 4.75 (d, J$_{1b,2b}$=8.4Hz, 1H, H-1$_b$(βanomer), 4.72(d, J$_{gem}$=11.4Hz, 1H, PhCH$_2$), 4.67(d, J$_{gem}$=12.3Hz, 1 H, PhCH$_2$), 4.64(d, J$_{gem}$=11.4 Hz, 1H, PhCH$_2$), 4.50-4.34(m, 2H, 2×H-6$_a$), 4.40(d, J$_{gem}$=10.9Hz, 1H, PhCH$_2$), 4.36 (d, J$_{gem}$=12.3 Hz, 1H, PhCH$_2$), 4.22 (dd, J$_{3b,2b}$=9.2, J$_{3b,4b}$=9.7Hz, 1H, H-3'), 4.00-3.92 (m, 2H, H-5$_b$, H-6$_b$), 3.85 (dd, J$_{4b,3b}$=9.7, J$_{4b,5b}$=9.2 Hz, 1H, H-4$_b$), 3.80(d, J$_{gem}$=11.4 Hz, 1H, PhCH$_2$), 3.78(s, 3H, OCH$_3$), 3.69 (dd, J$_{4a,3a}$=9.2, J$_{4a,5a}$=9.2 Hz, 1H, H-4$_a$), 3.53-3.44(m, 1H, H-5$_a$), 3.51(dd, J$_{3a,2a}$=9.2 Hz, J$_{3a,4a}$=9.2Hz, 1H, H-3$_a$), 3.47(dd, J$_{2a,1a}$=9.2Hz, J$_{2a,3a}$= 9.2Hz, 1H, H-2$_a$), 2.16(s, 3H, COCH$_3$), 1.06 (s, 9H, 3×CH$_3$). MS: M$^+$ 1038; Found 1061, M$^+$+Na and 1077, M$^+$+K.

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-α/β-D-glucopyranosyl fluoride (12)

The disaccharide(**2**)(100mg, 0.088mmol) dissolved in MeOH(10ml) was treated with PdCl$_2$(20 mg) and work up following the same method described above to prepare the lactol(**7**). The filtrate was concentrated and purified by a short column chromatography (EtOAc-hexane 1:2, R$_f$ 0.2) to give(3,6-di-O-Benzyl-2-O-levulinoyl-4-O-(4-methoxybenzyl)-b-D-glucopyranosyl)-(1→4)-2-azido-3-O-benzyl-6-O-(tert-butyldiphenylsilyl)-2-deoxy-α/β-D-glucopyranose (**8**) as colorless oil. The following data were recorded: ^{1}H-NMR (500 MHz, CDCl$_3$): 7.73-7.68(m, 5 H, arom), 7.42-7.22(m, 21 H, arom), 7.09(d, J$_{ortho}$=8.4Hz, 2H, MeO-Ph), 6.81(d, J$_{ortho}$=8.4Hz, 2 H, MeO-Ph), 5.26(d, J$_{1a,2a}$= 3.3Hz, 1H, H-1$_a$; α-anomer), 5.19(d, J$_{gem}$=11.0Hz, 1H, PhCH$_2$), 5.07((d, J$_{1a,2a}$=8.0Hz, 1H, H-1$_a$; β-anomer), 5.05(dd, J$_{2b,1b}$=7.7Hz, J$_{2b,3b}$=8.8Hz, 1H, H-2$_b$), 4.89(d, J$_{gem}$=12.4Hz, 1H, PhCH$_2$), 4.70 (dd, J$_{3b,2b}$=8.8, J$_{3b,4b}$=9.6Hz, 1H, H-3$_b$), 4.79(d, J$_{gem}$=11.3Hz, 1H, PhCH$_2$), 4.65(dd, J$_{4b,3b}$=9.6, J$_{4b,5b}$= 9.6 Hz, 1H, H-4$_b$), 4.57(d, J$_{gem}$=12.4 Hz, 1H, PhCH$_2$), 4.52(d, J$_{1b,2b}$=7.7Hz, 1H, H-1$_b$), 4.45(d, J$_{gem}$=11.3Hz, 1H,

PhCH$_2$),4.48-4.44(m, 1H, H-6$_a$), 4.43-4.40(m, 1H, H-6$_a$), 4.20 (d, J$_{gem}$=12.4Hz, 1H, PhCH$_2$), 4.13(d, J$_{gem}$= 12.4Hz, 1H, PhCH$_2$), 3.95(dd, J$_{5b,4b}$=9.6, J$_{5b,6b}$=7.4 Hz, 1H, H-5$_b$), 3.79-3.71(m, 2H, 2x H-6$_b$), 3.75(s, 3H, OCH$_3$), 3.58(dd, J$_{3a,2a}$=9.3, J$_{3a,4a}$=8.8Hz, 1H, H-3$_a$), 3.69(dd, J$_{5a,4a}$=9.4, J$_{5a,6a}$=7.2Hz, 1H, H-5$_a$), 3.61 (dd, J$_{4a,3a}$=8.8, J$_{4a,5a}$=9.4Hz, 1H, H-4$_a$), 3.49 (dd, J$_{2a,1a}$=8.0Hz, J$_{2a,3a}$=9.6Hz, 1H, H-2$_a$), 2.73-2.62(m, 2H, CH$_2$CH$_2$CO), 2.30-2.13(m, 2H, COCH$_2$CH$_2$), 2.09(s, 3H, COCH$_3$), 1.05(s, 9H, 3×CH$_3$). MS: M$^+$ 1093; Found: 1116, M$^+$+Na and 1132, M$^+$+K.

The lactol (**8**)dissolved in 1.0ml of CH$_2$Cl$_2$ was cooled to -30^{0}C and treated with 28μl (0.23mmol) of DAST and worked up as the method mentioned above for(**11**). The residue was purified on silica gel column chromatography (EtOAc-hexane 1:2, R$_f$ 0.2) to give fluoride(**12**) (64mg, 64% overall yield from **2**) as colorless oil. ^{1}H-NMR (500MHz, CDCl$_3$): 7.66(d, J=6.6Hz, 2H, arom), 7.50(d, J =6.6Hz, 2H, arom), 7.35-7.14(m, 20H, arom), 7.00(d, J=8.4Hz, 2 H, MeO-Ph), 6.73(d, J=8.4Hz, 2 H, MeO-Ph), 5.53(dd, J$_{1,F}$=55.4Hz, J$_{1,2}$=3.0Hz, 1H; H-1$_a$, α-anomer), 5.11(d, J$_{gem}$= 11.4Hz, 1H, PhCH$_2$), 4.96(dd, J$_{2b,1b}$=7.9Hz, J$_{2b,3b}$=9.7Hz, 1H, H-2$_b$), 4.83(d, J$_{1a,2a}$=8.4 Hz, 1H, H-1$_a$ (banomer), 4.78(d, J$_{1b,2b}$=9.2Hz, 1H, H-1$_b$), 4.64(d, J$_{gem}$=11.4Hz, 1H, PhCH$_2$), 4.60 (d, J$_{gem}$=11.8Hz, 1H, PhCH$_2$), 4.36(d, J$_{gem}$=12.3Hz, 1H, PhCH$_2$), 4.32(d, J$_{gem}$=12.3Hz, 1H, PhCH$_2$), 4.28(d, J$_{gem}$= 12.3 Hz, 1H, PhCH$_2$), 4.17(dd, J$_{3b,2b}$=9.7Hz, J$_{3b,4b}$=9.2Hz, 1H, H-3$_b$), 4.10-4.05 (m, 1H, H-3$_a$), 4.06-4.00(m, 1H, H-6$_a$), 3.92-3.85(m, 1H, H-6$_a$), 3.85(dd, J$_{4a,3a}$=10.1, J$_{4a,5a}$=10.1 Hz, 1H, H-4$_a$), 3.78(dd, J$_{5a,4a}$=10.1, J$_{5a,6a}$=8.8Hz, 1H, H-5$_a$), 3.71(s, 3H, OCH$_3$), 3.70-3.65(m, 1H, H-5$_b$), 3.59(dd, J$_{4b,5b}$=9.2Hz, J$_{4b,5b}$=9.2 Hz, 1H, H-4$_b$), 3.43 (dd, J$_{2a,1a}$=3.0, J$_{2a,3a}$=9.2Hz, 1H, H-2$_a$; α-anomer), 3.40(dd, J$_{2a,1a}$=8.2, J$_{2a,3a}$=10.1 Hz, 1H, H-2$_a$; β-anomer), 3.30-3.26(m, 2H, 2×H-6$_b$), 2.63-2.47(m, 2H, CH$_2$CH$_2$CO), 2.28-2.09 (m, 2H, COCH$_2$CH$_2$), 2.02(s, 3H, COCH$_3$), 0.981(s, 9H, 3×CH$_3$). ^{13}C-NMR(125MHz, CDCl$_3$): 205.50(-CH$_2$COCH$_3$), 170.99 (OCOCH$_2$), 159.22(C-OMe), 138.28, 135.72, 135.37, 132.09, 129.96, 129.74, 129.62, 129.00, 128.50, 128.30, 128.17, 128.06, 127.76, 127.69, 127.58, 127.43, 127.27, 127.19, 122.75, 121.43, 121.30, 121.20, 120.89, 120.70, 120.58, 120.40, 113.76(MeO-Ph), 106.89(C-1$_a$), 100.22(C-1$_b$), 83.29

(C-2$_b$), 77.78(C-3$_b$), 77.41(C-3$_a$), 75.34(CH$_2$Ph), 75.13(CH$_2$Ph), 74.62, (CH$_2$Ph); 74.03 (C-4$_b$), 73.35 (C-4$_a$), 70.91(C-5$_a$), 70.55(C-5$_b$), 70.12, 69.70, 68.78 (C-6$_a$; anomer-1), 68.25(C-6$_a$; anomer-2), 67.75(C-6$_b$; anomer-1), 66.48 (C-6$_b$; anomer-2), 61.07 (C-2$_a$; anomer-1), 60.84 (C-2$_a$; anomer-2), 55.30 (OCH$_3$-Ph), 48.43, 37.64(OCOCH$_2$CH$_2$CO; anomer-1), 37.55 (OCOCH$_2$CH$_2$CO; anomer-2), 29.77 (OCO CH$_2$CH$_2$ CO), 27.78, 26.92(CH$_3$), 22.91(CH$_3$), 20.05(CH$_3$), 19.46(CH$_3$). MS: M$^+$ 1095; Found 1118, M$^+$+Na and 1134, M$^+$+K. Calculated for C$_{62}$H$_{70}$ O$_{12}$N$_3$SiF: C, 67.94; H, 6.39; N, 3.83. Found; C, 67.78.

3,6-Di-O-benzyl-2-O-levulinoyl-4-O-(4-metho xybenzyl)-β-D-glucopyranosyl-(1→4)-2-azido-3-O-benzyl-6-O-(tert-butyldiphenylsilyl)-2-deoxy-α/β-D-glucopyranosyl trichloroacetimi date(13)

The lactol**(8)**((crude product out of (100mg, 0.088mmol) of disaccharide **2**)) dissolved in 2.0ml of CH$_2$Cl$_2$ was cooled to -10^{0}C and treated with 90µl (0.90mmol) of trichloroacetonitrile. DBU(8.6µl, 0.06mmol) was added dropwise and stirring was continued for 1h. then the mixture was quenched with 100µl of MeOH and the solvents were concentrated in vacu. The residue was purified on silica gel column chromatography(EtOAc-hexane 1:3, R$_f$ 0.2) to give **(13)** (55mg, 51%) as colorless oil. The ratio of α/β**(13)** anomers was 1:2 as judged from ^{1}H-NMR data. The following data were recorded: ^{1}H-NMR(500MHz, CDCl$_3$, selected data for the β anomer): δ 8.64(brs, 1H, NH), 7.74-7.62(m, 5H, arom),7.43-7.21(m, 20H, arom), 7.08(d, J$_{ortho}$=8.4Hz, 2H, MeO-Ph), 6.80(d, J$_{ortho}$=8.4Hz, 2H, MeO-Ph), 5.57(d, J$_{1a,2a}$=8.3Hz, 1H, H-1), 5.23(d, J$_{gem}$=11.0Hz, 1H, PhCH$_2$), 5.20 (d, J$_{gem}$=11.0Hz, 1H, PhCH$_2$), 5.11 (d, J$_{gem}$=11.0Hz, 1H, PhCH$_2$), 5.11(d, J$_{gem}$ =11.0Hz, 1H, PhCH$_2$), 5.05(dd, J$_{2b,1b}$=8.5Hz, J$_{2b,3b}$=10.1Hz, 1H, H-2$_b$), 4.81(J$_{gem}$ = 11.4Hz, 1H, PhCH$_2$), 4.77(J$_{gem}$=11.0Hz, 1H, PhCH$_2$), 4.73(d, J$_{gem}$=11.4Hz, 1H, PhCH$_2$), 4.66(d, J$_{1b,2b}$= 8.5Hz, 1H, H-1$_b$), 4.58(J$_{gem}$=11.0Hz, 1H, PhCH$_2$), 4.48(dd, J$_{4b,3b}$=J$_{4b,5b}$ 10.1Hz, 1H, H-4$_b$), 4.45(dd, J$_{4a,3a}$ =J$_{4a,5a}$=9.2Hz, 1H, H-4$_a$), 4.41(dd, J$_{3a,2a}$=10.1Hz, J$_{3a,4a}$ =10.1 Hz,1H, H-3$_a$), 4.36 (dd, J$_{6b,6b}$=12.1, J$_{6b,5b}$ =3.7Hz, 1H, H-6$_b$), 4.33 (dd, J$_{6b,6b}$=12.1, J$_{6b,5b}$=4.0Hz, 1H, H-6$_b$), 4.23(dd, J$_{3a,2a}$= 9.0, J$_{3a,4a}$=9.2Hz, 1H, H-3$_a$), 4.09 (m, 1H, H-5$_b$), 4.00-3.84(m, 2H, 2×H-6$_a$),

3.78(s, 3H, OCH$_3$), 3.70 (dd, J$_{5a,4a}$=9.2, J$_{5a,6a}$=3.8Hz, 1H, H-5$_a$), 3.48(dd, J$_{2a,1a}$ =8.3, J$_{2a,3a}$=9.0Hz, 1H, H-2$_a$), 2.70-2.62(m, 2H, CH$_2$CH$_2$CO), 2.50-2.35(m, 2H, COCH$_2$CH$_2$), 2.05 (s, 3H, COCH$_3$), 1.05(s, 9H, 3×CH$_3$). ^{13}C-NMR (125MHz, CDCl$_3$, selected data for the b anomer): d100.53(C-1$_b$), 94.73(C-1$_a$), 83.37(C-2$_b$), 77.89(C-3$_b$), 77.66(C-3$_a$), 76.18(C-4$_b$), 75.48(C-4$_a$), 75.16(C-5$_b$), 74.60(C-5$_a$), 68.82(C-6$_b$), 68.51(C-6$_a$), 62.73(C-2$_a$). Recorded data for the α anomer: δ 100.36 (C-1$_b$), 90.98(C-1$_a$), 77.42, 74.18, 65.28(C-6$_b$), 60.98(C-6$_a$), 62.64(C-2$_a$). Other ^{13}C-NMR signals: δ205.50(-CH$_2$COCH$_3$), 171.69 (OCOCH$_2$), 171.23(C=O), 160.80(C=NH), 159.97(C-OMe), 138.48, 138.37, 138.28, 138.21, 135.93, 135.87, 135.34, 132.42, 130.05, 129.80, 129.73, 129.58, 129.49, 128.44, 128.41, 128.35, 128.26, 128.13, 128.11, 127.89, 127.84, 127.70, 127.66, 127.58, 127.48, 127.41, 127.33, 127.29, 127.19, 113.83(MeO-Ph), 76.43 (CH$_2$Ph), 75.16(CH$_2$Ph), 74.02(CH$_2$Ph), 73.35 (CH$_2$Ph), 55.26(OCH$_3$-Ph), 48.06, 37.48 (OCOCH$_2$CH$_2$CO), 31.27, 29.61 (OCOCH$_2$ CH$_2$CO), 29.34, 27.67, 27.7(CH$_2$COCH$_3$), 26.85 (CH$_3$),26.70(CH$_3$), 20.80 (CH$_3$), 19.37(CH$_3$). MS: M$^+$1237.5; Found: 1261, M$^+$+Na and 1277, M$^+$+K.

3,6-Di-O-benzyl-2-O-levulinoyl-4-O-(4-methox ybenzyl)-β-D-glucopyranosyl-(1→4)-2-azido-6-O-(tert-butyldiphenylsilyl)-3-O-levulinoyl-2-deoxy-α/β-D-glucopyranosyl trichloroace timidate (14)

The disaccharide **(4)**(100mg, 0.088mmol) dissolved in MeOH(10ml) was treated with PdCl$_2$(20 mg) and work up following the same method described above to prepare the lactol **(7)**.The mixture was filtered through Celite, and the filtrate was concentrated and purified by a short column chromatography (EtOAc-hexane 2:3, R$_f$ 0.19) gave a mixture of(3,6-di-O-Benzyl-2-O-levulinoyl-4-O-(4-methoxybenzyl)-β-D-glucopy ranosyl)-(1→4)-2-azido-6-O-(tert-butyl diphenylsilyl)-3-O-levulinoyl-2-deoxy-α/β-D-glucopyranose**(10)** as colorless oil. The following data were recorded: ^{1}H-NMR(500MHz, CDCl$_3$): 7.76-7.64(m, 5H, arom), 7.45-7.21(m, 15H, arom), 7.06 (dd, J$_{ortho}$=8.4Hz, 2H, MeO-Ph), 6.79(dd, J$_{ortho}$ = 8.4Hz, 2H, MeO-Ph), 5.48 (dd, J$_{2b,1b}$=8.3Hz, J$_{2b,3b}$=10.3Hz, 1H, H-2$_b$), 4.97(d, J$_{1b,2b}$=8.3Hz, 1H, H-1$_b$), 4.92 (dd, J$_{3a,2a}$=8.8Hz,

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$J_{3a,4a}$=9.3Hz, 1H, H-3$_a$, α-anomer), 4.80(d, J_{gem}=11.2Hz, 1H, PhCH$_2$), 4.79(d, J_{gem}=11.2 Hz, 1H, PhCH$_2$), 4.76(d, J=8.3Hz, 1H), 4.69(d, $J_{1a,2a}$=2.4Hz, 1H, H-1$_a$, a-anomer), 4.68(dd, $J_{3b,2b}$=10.3, $J_{3',4'}$=10.3Hz, 1H, H-3$_b$), 4.60(d, J_{gem}=12.2Hz, 1H, PhCH$_2$), 4.57(d, J_{gem}=12.2Hz, 1H, PhCH$_2$), 4.51(d, J_{gem}=12.2Hz, 1H, PhCH$_2$), 4.43(dd, $J_{4b,3b}$=10.3, $J_{4b,5b}$=9.7Hz, 1H, H-4$_b$), 4.16 (d, J_{gem} = 12.2 Hz, 1H, PhCH$_2$), 4.06 (dd, $J_{4a,3a}$=9.7, $J_{4a,5a}$=9.7 Hz, 1H, H-4$_a$), 4.05(dm, $J_{5a,4a}$=9.7Hz, 1H, H-5$_a$), 3.99 (dd, $J_{3a,2a}$=10.3, $J_{3a,4a}$=9.7Hz, 1H, H-3$_a$), 3.96 (dm, $J_{5b,4b}$=9.7Hz, 1H, H-5$_b$), 3.92(d, $J_{1a,2a}$=7.3Hz, 1H, H-1$_a$), 3.92-3.89 (m, 2H, 2×H-6$_b$), 3.83-3.78 (m, 2H, 2×H-6$_a$), 3.77(s, 3H, OCH$_3$), 3.37(dd, $J_{2a,3a}$=8.8, $J_{2a,1a}$=2.4Hz, 1H, H-2$_a$, α-anomer), 3.33(dd, $J_{2a,3a}$=10.3, $J_{2a,1a}$=7.3Hz, 1H, H-2$_a$), 2.90-2.50(m, 4H, 2´OCOCH$_2$CH$_2$), 2.48-2.15(m, 4H, 2×OCOCH$_2$CH$_2$), 2.08 (s, 3H, CH$_2$COCH$_3$), 2.01(s, 3H, CH$_2$COCH$_3$), 1.07(s, 9H, 3×CH$_3$). ^{13}C-NMR (125MHz, CDCl$_3$): 205.98(CH$_2$COCH$_3$), 172.06(OCOCH$_2$), 170.82(OCOCH$_2$), 138.72, 138.39, 138.04, 136.01, 135.65, 135.59, 135.46, 130.01, 129.80, 129.66, 128.35, 127.84, 127.69, 127.60, 127.53, 127.28, 113.84(MeO-Ph), 100.66(C-1$_a$), 100.44(C-1$_b$), 87.38 (C-2$_b$), 84.83(C-5$_b$), 83.44(C-4$_a$), 74.67(PhCH$_2$), 74.59(PhCH$_2$), 73.68 (PhCH$_2$), 72.83(C-3$_a$), 72.26(C-5$_a$), 71.23, 70.14(C-3$_b$), 70.01 (C-4$_b$), 68.68(C-6$_b$), 65.50(C-6$_a$), 61.45(C-2$_a$), 55.23(OCH$_3$), 38.36 (OCOCH$_2$CH$_2$CO), 37.75 (OCOCH$_2$CH$_2$CO), 37.50(OCOCH$_2$CH$_2$CO), 34.37(OCOCH$_2$CH$_2$CO), 29.72(OCOCH$_2$CH$_2$CO), 29.61 (OCOCH$_2$CH$_2$CO), 28.21 (OCOCH$_2$CH$_2$CO), 27.62(CH$_3$), 26.87(CH$_3$), 19.38(CH$_3$). MS: M$^+$ 1101; Found: 1125, M$^+$+Na and 1141, M$^+$+K.

The lactol (10) was treated with trichloroace tonitrile and DBU and worked up as described for lactol (8). The residue was purified on silica gel column chromatography (EtOAc-hexane 1:2, R$_f$ 0.2) to give(14) (44mg, 40% overall yield from(4)) as colorless oil. The ratio of α/β(14) anomers was 1:2 as judged from ^{1}H-nmr data. ^{1}H-NMR (500 MHz, CDCl$_3$, data recorded for β-anomer).

δ8.76(s br, 1H, NH), 7.73-7.68(m, 5H, arom), 7.38-7.25(m, 15H, arom), 7.05(dd, J_{ortho}=8.2Hz, 2 H, MeO-Ph), 6.79(dd, J_{ortho}=8.2Hz, 2 H, MeO-Ph), 5.48(dd, $J_{2b,1b}$=8.3Hz, $J_{2b,3b}$=10.3Hz, 1H, H-2$_b$), 4.97(d, $J_{1b,2b}$=8.3Hz, 1H, H-1$_b$), 4.80(d, J_{gem}=11.5 Hz, 1H,

PhCH$_2$), 4.79(d, J_{gem}=11.5Hz, 1H, PhCH$_2$), 4.76(d, $J_{1a,2a}$=8.3Hz, 1H, H-1$_a$), 4.68(dd, $J_{3b,2b}$=10.3, $J_{3b,4b}$=10.3Hz, 1H, H-3$_b$), 4.60(d, J_{gem}=12.6Hz, 1H, PhCH$_2$), 4.57(d, J_{gem}=12.6Hz, 1H, PhCH$_2$), 4.51(d, J_{gem}=12.2Hz, 1H, PhCH$_2$), 4.43 (dd, $J_{4b,3b}$=10.3, $J_{4b,5b}$=9.7Hz, 1H, H-4$_b$), 4.16(d, J_{gem}=12.2Hz, 1H, PhCH$_2$), 4.08(dd, $J_{4a,3a}$=9.7, $J_{4a,5a}$=9.7Hz, 1H, H-4$_a$), 4.05(dm, $J_{5a,4a}$=9.7Hz, 1H, H-5$_a$), 3.99(dd, $J_{3a,2a}$=10.3, $J_{3a,4a}$=9.7Hz, 1H, H-3$_a$), 3.96 (dm, $J_{5b,4b}$=9.7Hz, 1H, H-5$_b$), 3.92-3.89 (m, 2H, 2×H-6$_b$), 3.83-3.78(m, 2H, 2×H-6$_a$), 3.76(s, 3H, OCH$_3$), 3.33(dd, $J_{2a,3a}$=10.3, $J_{2a,1a}$=8.3Hz, 1H, H-2$_a$), 2.90-2.50(m, 4H, 2× OCOCH$_2$CH$_2$), 2.48-2.15 (m, 4H, 2×OCOCH$_2$CH$_2$), 2.08 (s, 3H, CH$_2$COCH$_3$), 2.01(s, 3H, CH$_2$COCH$_3$), 1.07(s, 9H, 3×CH$_3$). MS: M$^+$ 1247; Found: 1270, M$^+$+Na, 1286; M$^+$+K.

Selected ^{1}H-NMR data for (14)a-anomer: d 4.92(dd, $J_{3a,2a}$=8.8Hz, $J_{3a,4a}$=9.3Hz, 1H, H-3$_a$), 4.87 (d, $J_{1a,2a}$=4.0 Hz, 1H, H-1$_a$), 4.72(dd, $J_{4a,5a}$=9.3, $J_{4a,3a}$=9.3Hz, 1H, H-4$_a$), 3.47(dd, $J_{5a,4a}$=9.3, $J_{5a,6a}$=4.8Hz, 1H, H-5$_a$), 3.37(dd, $J_{2a,3a}$=8.8, $J_{2a,1a}$=4.0Hz, 1H, H-2$_a$).

Allyl(2-O-acetyl-3,6-di-O-benzyl-4-hydroxy-β-D-glucopyranosyl)-(1→4)-2-azido-3-O-benzyl-6-O-(tert-butyldiphenylsilyl)-2-deoxy-β-D-glucopy ranoside (15)

Disaccharide (1)(300mg, 0.278mmol) was dissolved in CH$_2$Cl$_2$(25ml) and TFA(500ml) containing water (10µl) was added. After 10min the solution changed into a purple color and stirring was continued for additional 1h at rt. The reaction mixture was diluted with toluene(30ml) and concentrated to dryness. The residue was purified by silica gel column chromatography (10% EtOAc in toluene, R$_f$ 0.2) to give(260mg, 97%), of compound (15)as a clear oil. ^{1}H-NMR (500MHz, CDCl$_3$): δ7.75-7.70 (m, 4 H, arom), 7.44-7.27(m, 21H, arom), 5.96(dddd, J=17.0, 10.5, 6.0, 5.0Hz, 1H, CH$_2$-CH=CH$_2$), 5.34 (dq, J=1 7.0, 1.5Hz, 1H, CH$_2$-CH=CH$_a$H), 5.24 (dq, J=10.5, 1.5Hz, 1 H, CH=CHH$_b$), 5.03 (d, J_{gem}=11.3Hz, 1H, PhCH$_2$), 5.11(d, J_{gem}=11.5Hz, 1H, PhCH$_2$), 5.05(d, $J_{1b,2b}$=8.0 Hz, 1H, H-1$_b$), 4.93(d, J_{gem}=11.5Hz, 1H, PhCH$_2$), 4.89(d, J_{gem}=11.5Hz, 1H, PhCH$_2$), 4.86 (dd, $J_{2b,1b}$=8.0Hz, $J_{2b,3b}$=9.3Hz, 1H, H-2$_b$), 4.72(d, J_{gem}=11.5 Hz, 1H, PhCH$_2$), 4.67 (d, J_{gem}=11.3Hz, 1H, PhCH$_2$), 4.51(dd, $J_{4a,3a}$ =$J_{4a,5a}$=10.7 Hz, 1H, H-4$_a$), 4.40 (d,

$J_{1a,2a}$=8.8Hz, 1H, H-1a), 4.38(dd, 1H, $J_{6a,6a}$=12.0 Hz, $J_{6a,5a}$=3.6Hz, H-6$_a$), 4.36-4.33(m, 2H, H-3$_b$, H-6$_a$), 4.11(ddt, J_{gem}=13.0, J_{vic}=5.0, J_{all}=1.5 Hz, 1 H, CH$_a$H-CH=CH$_2$), 3.99(ddt, J_{gem}=13.0, J_{vic}=6.0, J_{all} 1.5Hz, 1 H, CHH$_b$-CH=CH$_2$), 3.89(dd, $J_{3b,2b}$=9.3, $J_{3b,4b}$=9.6Hz, 1H, H-3$_b$), 3.80(dt, $J_{5a,4a}$=10.7Hz, $J_{5a,6a}$=2.2Hz, 1H, H-5$_a$), 3.78(dd, $J_{3a,2a}$=9.6, $J_{3a,4a}$=10.7Hz, 1H, H-3$_a$), 3.58-3.53(m, 2H, 2×H-6$_b$), 3.42(dd, $J_{4b,3b}$=9.6, $J_{4b,5b}$=9.6Hz, 1H, H-4$_b$), 3.35 (dt, $J_{5b,4b}$=9.6, $J_{5b,6b}$=3.3Hz, 1H, H-5$_b$), 3.34(dd, $J_{2a,1a}$=8.8Hz, $J_{2a,3a}$=9.6Hz, 1H, H-2$_a$), 1.81(s, 3H, OCOCH$_3$), 1.06(s, 9H, 3×CH$_3$). ^{13}C-NMR(125MHz, CDCl$_3$): 169.13(CO), 138.50, 138.35, 137.46, 135.97, 135.43, 133.61(-CH=CH$_2$), 132.36, 129.84, 128.49, 128.44, 128.28, 128.12, 127.87, 127.80, 127.66, 127.59, 127.55, 117.62(CH=CH$_2$), 100.58 100.6(1-C), 100.29(C-1$_b$), 82.50(C-4$_b$), 80.91(C-2$_b$), 75.97(CH$_2$-Ph), 75.40(CH$_2$-Ph), 74.44(CH$_2$-Ph), 74.22(C-5$_a$), 73.71(C-5$_b$), 73.03, 72.91, 71.24(C-6$_a$), 65.87(-CH$_2$-CH=CH$_2$), 61.19(C-2$_a$), 34.38, 26.77 (CH$_3$), 20.76(CH$_3$), 19.34(CH$_3$). MS: M$^+$ 957; Found: 980, M$^+$+Na and 996, M$^+$+K. Calculated for C$_{54}$H$_{63}$O$_{11}$N$_3$Si: C, 67.71; H, 6.58; N, 4.38. Found: C, 67.50; H, 6.55; N, 4.12.

Allyl (3,6-di-O-benzyl-2-O-levulinoyl-4-hydroxy-β-D-glucopyranosyl)-(14)-2-azido-3-O-benzyl-6-O-(tert-butyldiphenylsilyl)-2-deoxy-β-D-glucopyranoside (16)

Disaccharide **(2)**(300mg, 0.264mmol) dissolved in CH$_2$Cl$_2$(25ml) was treated with TFA and worked up following the method described for **(15)**. The residue was purified by silica gel column chromatography (20% EtOAc in toluene, R$_f$ 0.2) to give (248mg, 92%) of compound**(16)** as a thick clear oil. ^{1}H-NMR (500MHz, CDCl$_3$): δ 7.76-7.71(m, 4 H, arom), 7.43-7.29(m, 21H, arom), 5.96(d, J=17.0, 10.5, 6.0, 5.0Hz, 1H, CH$_2$-CH=CH$_2$), 5.35(dq, J=17.0, 1.5Hz, 1H, CH$_2$-CH=CH$_a$H), 5.23 (d, $J_{1b,2b}$=8.2Hz, 1H, H-1$_b$), 5.18(dq, J=10.5, 1.5Hz, 1H, CH$_2$-CH=CHH$_b$), 5.12(d, J_{gem} 11.0Hz, 1H, PhCH$_2$), 5.04(dd, $J_{2b,1b}$=8.2Hz, $J_{2b,3b}$=9.0Hz, 1H, H-2$_b$), 4.89(d, J_{gem}=11.0Hz, 1H, PhCH$_2$), 4.83 (d, J_{gem}=11.3Hz, 1H, PhCH$_2$), 4.67(d, J_{gem}=11.3Hz, 1H, PhCH$_2$), 4.65(d, J_{gem}=11.9Hz, 1H, PhCH$_2$), 4.63 (d, J_{gem}=11.9Hz, 1H, PhCH$_2$), 4.36(d, $J_{1a,2a}$=7.9Hz, 1H, H-1$_a$), 4.26 (d, J_{gem}

=11.9Hz, 1H, PhCH$_2$), 4.20-4.15(m, 2H, H-4$_b$, PhCH$_2$), 4.15(dd, $J_{4a,3a}$=9.2Hz, $J_{4a,5a}$=9.2Hz, 1H, H-4$_a$), 4.11(ddt, J_{gem}=13.0, J_{vic}=5.0, J_{all}=1.5Hz, 1 H, CH$_a$H-CH=CH$_2$), 3.99 (ddt, J_{gem}=13.0, J_{vic}=6.0, J_{all} 1.5Hz, 1 H, CHH$_b$-CH=CH$_2$), 3.93(dd, $J_{6a,6a}$=12.9Hz, $J_{6a,5a}$=3.4Hz, 1H, H-6$_a$), 3.88(dd, J_{6a6a}=12.9 Hz, $J_{6a,5a}$=5.6 Hz, 1H, H-6$_a$), 3.75(dd, $J_{3b,2b}$=9.0Hz, $J_{3b,4b}$=10.2Hz, 1H, H-3$_b$), 3.72(dd, $J_{3a,2a}$=9.2Hz, $J_{3a,4a}$=9.2Hz, 1H, H-3$_a$), 3.73(d, $J_{6b,6b}$=13.0Hz, $J_{6b,5a}$=2.6Hz, 1H, H-6$_b$), 3.57(d, $J_{6b,6b}$=13.0Hz, $J_{6b,5b}$=2.6Hz, 1H, H-6$_b$), 3.55-3.48(m, 2H, H-5$_a$, H-5$_b$), 3.22(dd, $J_{2a,1a}$=7.9Hz, $J_{2a,3a}$=9.2Hz, 1H, H-2$_a$), 2.53-2.43(m, 2H, CH$_2$CH$_2$CO), 2.35-2.24(m, 2H, COCH$_2$CH$_2$), 2.08(s, 3H, COCH$_3$), 1.06(s, 9H, 3× CH$_3$). ^{13}C-NMR (125 MHz, CDCl$_3$): 205.83 (-CH$_2$COCH$_3$), 171.18(OCOCH$_2$), 136.01, 135.45 (CH=CH$_2$), 134.78, 133.87, 133.72, 130.09, 129.74, 129.63, 129.02, 128.39, 128.31,128.25, 128.07, 127.79, 127.70,127.54, 127.40, 127.34, 127.28, 118.40 (CH=CH$_2$), 100.62(C-1$_b$), 100.29(C-1$_a$), 83.43 (C-2$_b$), 81.00 (C-3$_a$), 76.57(CH$_2$-Ph),76.06(C-5$_b$), 75.37 (CH$_2$-Ph), 75.24(CH$_2$-Ph), 75.12(CH$_2$-Ph), 74.62(C-5$_a$), 74.14(C-4$_b$), 73.34(C-3$_b$), 69.70(C-6$_b$), 68.79 (CH$_2$-CH=CH$_2$), 68.27(C-4$_a$), 65.99(C-6$_a$), 61.31(C-2$_a$), 37.50 (OCOCH$_2$CH$_2$CO), 29.73 (OCOCH$_2$CH$_2$CO), 27.71(CH$_2$COCH$_3$), 26.83 (CH$_3$), 26.55(CH$_3$), 19.35 (CH$_3$) MS: M$^+$ 1013; Found: 1036, M$^+$+Na and 1052, M$^+$+K. Calculated for C$_{57}$H$_{67}$O$_{12}$N$_3$Si: C, 67.52; H, 6.61; N, 4.14. Found; C, 67.33; H, 6.60; N, 3.76.

Allyl(2-O-acetyl-3,6-di-O-benzyl-4-hydroxy-β-D-glucopyranosyl)-(1→4)-2-azido-6-O-(tert-butyl-diphenylsilyl)-3-O-levulinoyl-2-deoxy-β-D-glucopyranoside (17)

Disaccharide **(3)** (160mg, 0.147mmol) dissolved in 25ml of CH$_2$Cl$_2$ was treated with TFA(500µl) and water (10µl) and worked up as the method described for preparation of **(15)**. The residue was purified by silica gel column chromatography (25% EtOAc in toluene, R$_f$ 0.2) to give(130mg, 91%) of compound **(17)** as clear oil. ^{1}H-NMR (500 MHz, CDCl$_3$): δ7.76-7.72 (m, 4 H, arom), 7.53-7.27(m, 16 H, arom), 5.91 (d, J=17.0, 10.5, 6.0, 5.0Hz, 1H, CH$_2$-CH= CH$_2$), 5.32 (d, $J_{1b,2b}$=8.2Hz, 1H, H-1$_b$), 5.30(dq, J=17.0, 1.5Hz, 1H, CH$_2$-CH=CH$_a$H), 5.21(dq, J=10.5, 1.5Hz, 1H,

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CH_2 $CH=CHH_b$**),** 4.90 (dd, $J_{3a,2a}$=9.6Hz, $J_{3a,4a}$= 9.6Hz, 1H, H-3$_a$), 4.84 (dd, $J_{2b,1b}$=8.2Hz, $J_{2b,3b}$=9.3Hz, 1H, H-2$_b$), 4.78 (d, J_{gem}=12.1Hz, 1H, PhCH$_2$), 4.72(d, J_{gem}=12.1Hz, 1H, PhCH$_2$), 4.68 (dd, $J_{4b,3b}$=9.3, $J_{4b,5b}$=9.3Hz, 1H, H-4$_b$), 4.65(d, J_{gem}=12.1Hz, 1H, PhCH$_2$), 4.59(d, J_{gem}=12.1Hz, 1H, PhCH$_2$), 4.55 (d, J_{gem}=12.1Hz, 1H, PhCH$_2$), 4.52(d, J_{gem}=12.1Hz, 1H, PhCH$_2$), 4.39(d, $J_{1a,2a}$=7.9Hz, 1H, H-1$_a$), 4.22(dd, J_{gem}=12.9Hz, $J_{6a,5a}$=2.3Hz, 1H, H-6$_a$), 4.18-4.11(m, 2H, H-5a, H-6$_a$), 4.11(ddt, J_{gem}=13.0, J_{vic}=5.0, J_{all}=1.5Hz, 1H, CH$_a$H-CH=CH$_2$), 3.99(ddt, J_{gem}=13.0, J_{vic}=6.0, J_{all} 1.5Hz, 1H, CHH$_b$-CH=CH$_2$), 3.82 (dd, $J_{3b,4b}$=9.3, $J_{3b,2b}$=9.3Hz, 1H, H-3$_b$), 3.64(dd, J_{gem}=13.0Hz, $J_{6b,5b}$=2.3Hz, 1H, H-6$_b$), 3.59-3.53(m, 2H, H-4$_a$, H-6$_b$), 3.34(dt, $J_{5b,4b}$=9.3, $J_{5b,6b}$=4.8Hz, 1H, H-5$_b$), 3.25(dd, $J_{2a,1a}$=7.9Hz, $J_{2a,3a}$=9.6Hz, 1H, H-2$_a$), 2.90-2.80(m, 2H, CH$_2$CH$_2$CO), 2.55-2.45(m, 2H, COCH$_2$CH$_2$), 2.21(s, 3H, -CH$_2$COCH$_3$), 2.08 (s, 3H, -OCOCH$_3$), 1.09 (s, 9H, 3×CH$_3$). ^{13}C-NMR(125 MHz, CDCl$_3$): 205.90(-CH$_2$COCH$_3$), 171.82 (OCOCH$_2$-), 170.04 (OCOCH$_3$), 138.57, 135.93, 135.60(CH=CH$_2$), 133.68, 133.42, 133.16 130.31, 129.74, 129.67, 129.56, 129.02, 128.42 128.21, 127.80, 127.72, 127.62, 127.54, 117.79 (CH=CH$_2$), 100.60(C-1$_b$), 100.53(C-1$_a$), 84.45(C-2$_b$), 83.38(C-3$_a$), 81.91(C-3$_b$), 75.46(CH$_2$-Ph), 75.17(CH$_2$-Ph), 74.72 (CH$_2$-Ph), 73.55(C-4$_a$), 73.46(C-5$_b$), 71.79(C-5$_a$), 70.74(C-4$_b$), 69.96(C-6$_a$), 68.91(CH$_2$-CH=CH$_2$), 64.36(C-6$_b$), 62.67(C-2$_a$), 37.84(OCOCH$_2$CH$_2$CO), 28.20(OCOCH$_2$CH$_2$CO), 24.10(CH$_2$COCH$_3$), 23.74 (CH$_3$), 20.92(CH$_3$), 19.28(CH$_3$), 16.59 (OCOCH$_3$). MS: M$^+$ 965; Found: 988, M$^+$+Na and 1004, M$^+$+K. Calculated for C$_{52}$H$_{63}$O$_{13}$N$_3$Si: C, 64.66; H, 6.52; N, 4.35. Found: C, 64.58; H, 6.33; N, 4.16.

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-α/β-D-glucopyranosyl-(1→4)-O-(2-O-acetyl-3,6-di-O-benzyl-β-D-glucopyranosyl)-(1→4)-2-azido-3-O-benzyl-6-O-(tert-butyl diphenylsilyl)-2-deoxy-β-D-glucopyranoside (18)

Method 1

The disaccharide donor **(11)**(30mg, 0.028mmol) and the disaccharide acceptor **(15)**(18mg, 0.019 mmol) were co-evaporated twice with dry toluene and acti-

vated molecular sieves (100mg) and 3ml (CH$_2$Cl$_2$-Et$_2$O 4:1v/v) were subsequently added. The mixture was stirred at rt for 2h, then the temperature was cooled to -5^{0}C and ZrCp$_2$Cl$_2$(22mg, 0.055mmol) and AgOTf (10mg, 0.03mmol) were added. The mixture was allowed to warm to rt and stirring was continued for additional 18h (overnight). The solution was filtered and the insoluble residue was washed with CH$_2$Cl$_2$ and the combined filtrate was removed in vacuo and the residue was purified on silica gel column chromatography using 5% EtOAc in toluene(R$_f$ 0.3) to give (6mg, 10%, 1:1 α/β) of pure **(18)** as a clear thick oil.

Method 2

A solution of TMSOTf(20mL in 100 mL CH$_2$Cl$_2$) was added to a cooled solution (-30^{0}C) of **(13)** (30mg, 0.024mmol) and **(15)**(18mg, 0.019mmol, 1.27equiv.) in(CH$_2$Cl$_2$-Et$_2$O 4:1v/v)(500μL). The solution was stirred for 2h at this temperature, and then neutralised with Et$_3$N. The solvent was evaporated and the crude reaction mixture was passed through a short gel-filtration chromatography column (LH-20, 2g) with CH$_2$Cl$_2$/MeOH, 1:1 as eluent to afford a 3:1 α/β mixture of the corresponding tetrasaccharides. Flash column chromatography (toluene/EtOAc, 9:1 to 6:1) afforded 20mg **(18a)** and **(18b)** (41.7%) as clear oil.

Data for(18α)

TLC(toluene/EtOAc, 6:1): R$_f$=0.66, ^{1}H-NMR(500MHz, CDCl$_3$): δ=7.55-7.50(m, 4 H, Ph), 7.34-7.12(m, 46H, Ph), 7.07(d, J$_{ortho}$=8.4Hz, 2 H, CH$_3$O-Ph), 6.76 (d, J$_{ortho}$=8.4Hz, 2 H, CH$_3$O-Ph), 5.90(dddd, J=17.0, 10.5, 6.0, 5.0 Hz, 1 H, CH$_2$-CH=CH$_2$), 5.53 (d, J$_{1c,2c}$=4.0 Hz, 1H, H-1c), 5.25(dq, J =17.0, 1.5Hz, 1H, CH$_2$ CH=CH$_2$), 5.15(br. d, J=10.5Hz, 1H, CH$_2$-CH=CH$_2$), 5.09 (d, J$_{gem}$=11.3 Hz, 1H, CH$_2$Ph), 5.03(d, J$_{gem}$=11.3Hz, 1 H, CH$_2$Ph), 4.92(d, J$_{gem}$=11.3Hz, 1 H, CH$_2$Ph), 4.86(d, J$_{1a,2a}$=7.4 Hz, 1 H, H-1$_a$), 4.79-4.71(m, 6H, CH$_2$Ph), 4.70-4.53(m, 7 H, CH$_2$Ph), 4.48 (d, J$_{gem}$=12.1 Hz, 1H, CH$_2$Ph), 4.45(d, J$_{gem}$=12.1Hz, 1H, CH$_2$Ph), 4.39(d, J$_{1d,2d}$=7.2Hz, 1H, H-1$_d$), 4.35 (d, J$_{gem}$=12.1Hz, 1 H, CH$_2$Ph), 4.32(d, J$_{gem}$=12.1Hz, 1H, CH$_2$Ph), 4.29 (d, J$_{1b,2b}$=7.2Hz, 1 H, H-1$_b$), 4.20(dd, J$_{6b,5b}$=1.6, J$_{6b,6b}$=10.0Hz, 1H, H-6$_b$), 4.10(br. dd, J$_{gem}$=13.0, J= 5.0Hz, 1H, CH$_2$-CH=CH$_2$), 4.03-3.94(m, 3 H, H-4$_c$, H-4$_a$,

CH_2-CH=CH_2), 3.85-3.74(m, 6 H, H-6$_a$, H-6$_b$, H-6$_c$, H-4$_d$, H-3$_a$, H-3$_c$), 3.71(s, 3H, Ph-OCH$_3$), 3.65-3.54(m, 4H, H-5$_d$, H-5$_c$, H-5$_a$, H-4$_b$), 3.46(t, $J_{3b,2b}$=$J_{3b,4b}$=9.0Hz, 1H, H-3$_b$), 3.39-3.32(m, 4H, H-3$_d$, H-6$_c$, H-2$_d$, H-6$_a$), 3.30(dd, $J_{2c,1c}$=4.0, $J_{2c,3c}$=10.0Hz, 1H, H-2$_c$), 3.29(dd, $J_{2b,1b}$=7.2, $J_{2b,3b}$=9.0Hz, 1 H, H-2$_b$), 3.24 (dd, $J_{2c,1c}$=4.0, $J_{2c,3c}$=10.5Hz, 1H, H-2$_c$), 3.27-3.21(m, 1 H, H-5$_b$), 2.09(s, 3H, OCOCH$_3$), 1.81(s, 3H, OCOCH$_3$), 0.980(s, 9H, 3×CH$_3$), 0.935 (s, 9H, 3×CH$_3$). ^{13}C-NMR(125 MHz, CDCl$_3$): δ169.14 (C=O), 159.13(C-OCH$_3$), 138.05, 137.45, 135.91, 135.83, 135.67, 135.40, 135.30, 133.37(CH$_2$-CH=CH$_2$), 132.06, 129.77, 129.58, 128.50, 128.41, 128.30, 128.19, 128.07, 128.02, 127.91, 127.78, 127.64, 127.56, 127.50, 127.40, 127.20, 127.09, 126.87, 117.71 (CH$_2$-CH=CH$_2$), 113.69(CH$_3$O-Ph), 103.88(C-1$_d$), 100.33(C-1$_a$), 100.16(C-1$_b$), 96.00(C-1$_c$), 84.84(C-3$_d$), 83.92(C-3$_b$), 83.11(C-2$_d$), 80.60(C-2$_b$), 80.35(C-4$_d$), 77.92(C-3$_a$), 77.39(C-3$_c$), 76.94(C-4$_a$), 76.50(C-4$_c$), 75.22(CH$_2$Ph), 74.94 (CH$_2$Ph), 74.65(CH$_2$Ph), 74.50(CH$_2$Ph), 73.46(C-5$_b$), 73.12 (C-5$_d$), 72.03 (C-5$_c$), 69.73(C-5$_a$), 68.56(C-6$_c$), 68.25 (CH$_2$-CH=CH$_2$), 65.76(C-6$_a$), 62.93(C-2$_c$), 62.40(C-5$_b$), 55.26(OCH$_3$), 31.09, 29.76, 26.84 (CH$_3$), 26.64 (CH$_3$), 20.87(CH$_3$), 19.37(CH$_3$), 19.31 (CH$_3$), 19.23 (CH$_3$), 8.19 (CMe$_3$). MS: M$^+$ 1976.86; Found: 1976.00 and 2003.00, M$^+$+Na.

^1H-NMR(500MHz, CDCl$_3$ for 18β)

δ 7.70-7.50(m, 4H, Ph, CH$_3$O-Ph), 7.34-7.11(m, 46 H, Ph), 7.04(d, J_{ortho}=8.8Hz, 2 H, CH$_3$O-Ph), 6.76 (d, J_{ortho}=8.8Hz, 2 H, CH$_3$O-Ph), 5.90(dddd, J=17.0, 10.5, 6.0, 5.0Hz, 1H, CH$_2$-CH=CH$_2$), 5.25 (dq, J=17.0, 1.5Hz, 1H, CH$_2$-CH=CH$_2$), 5.15(dq, J=10.5, 1.5Hz, 1H, CH$_2$-CH=CH$_2$), 5.11(d, J_{gem}=12.1Hz, 1H, PhCH$_2$), 5.09(d, J_{gem}=12.1Hz, 1H, PhCH$_2$), 5.03(d, $J_{1a,2a}$=8.3Hz, 1H, H-1$_a$), 5.00(d, $J_{1d,2d}$=8.5Hz, 1H, H-1$_d$), 4.95(d, $J_{1c,2c}$=7.4Hz, 1H, H-1$_c$), 4.92(d, J_{gem}=11.3Hz, 1H, PhCH$_2$), 4.86(d, J_{gem}=11.3Hz, 1H, PhCH$_2$), 4.84(d, J_{gem}=11.3Hz, 1H, PhCH$_2$), 4.78(d, J_{gem}=11.3Hz, 1H, PhCH$_2$), 4.74 (d, J_{gem}=12.1Hz, 1H, PhCH$_2$), 4.72(d, J_{gem}=11.3 Hz, 1H, PhCH$_2$), 4.68(d, J_{gem}=12.1Hz, 1H, PhCH$_2$), 4.60(d, J_{gem}=11.6Hz, 1H, PhCH$_2$), 4.54 (dd, $J_{2a,3a}$=9.0, $J_{2a,1a}$=7.4Hz, 1H, H-2$_a$), 4.50 (d, J_{gem} = 11.6 Hz, 1H, PhCH$_2$), 4.47(d, J_{gem}=12.1 Hz, 1H, PhCH$_2$), 4.44(d, J_{gem}=11.6Hz, 1H, PhCH$_2$),

4.42 (d, J=8.0Hz, 1H, H-1$_b$), 4.40(dd, $J_{2d,3d}$=9.0, $J_{2d,1d}$=8.0Hz, 1H, H-3$_d$), 4.34(d, J_{gem}=12.1Hz, 1H, PhCH$_2$), 4.07(ddt, J_{gem}=13.0, J=5.0, J=1.5Hz, 1 H, CH$_2$-CH=CH$_2$), 4.01(m, 3H, H-4$_b$, H-4$_a$, CH$_2$-CH= CH$_2$), 3.90(dd, $J_{4c,5c}$=9.6, $J_{4c,3c}$=8.8 Hz, 1 H, H-4$_c$), 3.85 (dd, J=9.3, 6.8Hz, 1H), 3.82(dd, $J_{6,6}$=12.8, $J_{6a,5a}$= 3.8 Hz, 1H, H-6$_a$), 3.813(dd, $J_{4,5}$=9.6, $J_{4,3}$=8.8Hz, 1 H, H-4c), 3.73-3.71(m, 5 H, H-3$_c$, H-4$_d$, Ph-OCH$_3$), 3.66-3.63(m, 2 H, H-5$_a$, H-6$_a$), 3.61-3.53 (m, 4 H, H-6$_d$, H-6$_b$, H-6$_c$, H-5$_d$), 3.53-3.49 (m, 1H, H-5$_c$), 3.44(dd, $J_{3a,4a}$=8.5, $J_{3a,4a}$=10.0Hz, 1 H, H-3$_a$), 3.33-3.28(m, 5 H, H-2$_c$, H-2$_d$, H-5$_c$, H-3$_b$, H-2$_b$), 3.00 (ddd, $J_{5,6}$=1.5, $J_{5,6}$=3.0, $J_{5,4}$=10.0, 1 H, H-5$_b$), 2.09(s, 3H, OCOCH$_3$), 1.81(s, 3H, OCOCH$_3$), 0.98(s, 9H, 3×CH$_3$), 0.93(s, 9H, 3×CH$_3$).

Allyl (2-O-acetyl-3,6-di-O-benzyl-4-O-(4-methoxy benzyl)-β-D-glucopyranosyl)-(1→4)-2-azido-3-O-benzyl-6-O-(tert-butyldiphenylsilyl)-2-deoxy-α-D-glucopyranosyl-(1→4)-O-(2-O-levulinoyl-3,6-di-O-benzyl-β-D-glucopyranosyl)-(1→4)-2-azido-3-O-benzyl-6-O-(tert-butyldiphenylsilyl)-2-deoxy-β-D-glucopyranoside(19)

The disaccharide donor **(12)**(30mg, 0.028mmol) and the disaccharide acceptor **(15)**(19mg, 0.019 mmol) were treated together following method 1 as described above for **(18)** to furnish(5mg, 10%, 1:1 α/β) of pure **(19)** as clear oil. ^1H-NMR(500MHz, CDCl$_3$, **(19α)**-anomer): δ7.69-7.52(m, 4 H, Ph), 7.39-7.11(m, 46 H, Ph), 6.91(d, J_{ortho}=8.8Hz, 2H, CH$_3$O-Ph), 6.72(d, J_{ortho}=8.8Hz, 2H, CH$_3$O-Ph), 5.87(dddd, J=17.0, 10.5, 6.0, 5.0Hz, 1H, CH$_2$-CH=CH$_2$), 5.45 (d, $J_{1c,2c}$=4.4Hz, 1 H, H-1c), 5.25 (dq, J=17.0, 1.5Hz, 1H, CH$_2$CH=CH$_2$), 5.15 (br. d, J=10.5Hz, 1H, CH$_2$-CH=CH$_2$), 5.16(d, J_{gem}=11.2Hz, 1H, PhCH$_2$), 5.10(d, J_{gem}=11.2Hz, 1H, PhCH$_2$), 4.93 (dd, $J_{2d,1d}$=7.8Hz, $J_{2d,3d}$=9.8Hz, 1H, H-2$_d$), 4.92(dd, $J_{2b,1b}$=7.8Hz, $J_{2b,3b}$=9.8Hz, 1H, H-2$_b$), 4.90(d, J_{gem}=11.2Hz, 1H, PhCH$_2$), 4.87(d, J_{gem}=11.0Hz, 1H, PhCH$_2$), 4.83-4.76 (m, 6H, CH$_2$Ph), 4.71(d, $J_{1a,2a}$=8.3 Hz, 1H, H-1$_a$), 4.68 (d, J_{gem}=11.2 Hz, 1H, PhCH$_2$), 4.65(d, $J_{1b,2b}$=7.8Hz, 1H, H-1$_b$), 4.63(d, $J_{1d,2d}$=8.0Hz, 1H, H-1$_d$), 4.62 (d, J_{gem}=11.0 Hz, 1H, PhCH$_2$), 4.33 (d, J_{gem}=12.2Hz, 1H, PhCH$_2$), 4.30(d, J_{gem}=11.2Hz, 1H, PhCH$_2$), 4.24-4.19(m, 7H, H-6$_a$, 2× H-6$_b$, H-6$_c$, H-4$_d$, H-3$_a$, H-3$_c$), 4.16(br. dd, J_{gem}=13.0, J=5.0Hz, 1H, CH$_2$-CH=CH$_2$), 4.14-4.10(m, 1H, H-

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5_d), 4.05 (dd, $J_{5b,6b}=4.7$, $J_{5b,4b}=9.3$Hz, 1H, H-5_b), 4.03(dd, $J_{5c,4c}=8.8$Hz, $J_{5c,6c}$3.3Hz, 1H, H-5_c), 3.52(m, 1H, H-5_a), 3.38-3.33(m, 7H, $2\times$H-6_d, H-6_a, H-4_b, H-6_c, H-4_a, H-3_b, H-3_d), 3.25 (dd, $J_{2a,1a}=8.3$Hz, $J_{2a,3a}=9.2$Hz, 1H, H-2_a), 3.03(dd, $J_{2c,1c}=4.4$Hz, $J_{2c,3c}=10.1$Hz, 1H, H-2_c), 2.52-2.40(m, 2H, CH_2CH_2CO), 2.33-2.21(m, 2H, $COCH_2CH_2$), 2.10(s, 3H, $COCH_3$), 1.18(s, 9H, $3\times CH_3$). ^{13}C-NMR (125MHz, CDCl$_3$): 205.76(-CH_2COCH_3), 171.80 ($OCOCH_2$-), δ169.59($OCOCH_3$), 159.13(C-OCH_3), 138.05, 137.45, 135.91, 135.83, 135.67, 135.40, 135.30, 133.37(CH_2-CH=CH_2), 132.06, 129.77, 129.58, 128.50, 128.41, 128.30, 128.19, 128.07, 128.02, 127.91, 127.78, 127.64, 127.56, 127.50, 127.40, 127.20, 127.09, 126.87, 117.71(CH_2-CH=CH_2), 113.69(CH_3O-Ph), 103.00 (C-1_d), 100.19 (C-1_a), 100.04(C-1_b), 94.77(C-1_c), 83.59(C-3_d), 79.87(C-4_b), 77.34 (C-3_b), 83.36 (C-2_d), 82.36(C-2_b), 78.23(C-4_d), 77.70(C-3_a), 77.30 (C-3_c), 75.80(C-4_a), 78.71(C-4_c), 75.22(CH_2Ph), 74.94 (CH_2Ph), 74.65 (CH_2Ph), 74.50(CH_2Ph), 74.00(C-5_b), 74.30(C-5_d), 74.34 (C-5_c), 70.01(C-5_a), 69.46 (C-6_d), 69.12(C-6_c), 68.25(CH_2-CH=CH_2), 66.70 (C-6_b), 66.52 (C-6_a), 62.96(C-2_c), 62.44(C-2_a), 55.26 (OCH_3), 31.09, 29.76, 26.84(CH_3), 26.64(CH_3), 20.87(CH_3), 19.37 (CH_3), 19.31 (CH_3), 19.23(CH_3), 8.19 (CMe_3). MS: M$^+$ 2034.49; Found: 2059, M$^+$+Na and 2074, M$^+$+K.

Selected ^{1}H-NMR data for **(19)**β anomer: δ 5.02(d, $J_{1c,2c}=8.0$Hz, 1H, H-1_c), 4.70(d, $J_{1b,2b}=7.9$Hz, 1H, H-1_b), 4.59(d, $J_{1a,2a}=8.8$Hz, 1H, H-1_a), 4.55 (dd, $J_{3d,2d}=9.8$Hz, $J_{3d,4d}=9.3$Hz, 1H, H-3_d), 4.50-4.45 (m, 3H, H-3_b, H-4_b, H-5_b), 4.42-4.40(m, 1H, H-6c), 4.40-4.30(m, 6H, H-2_b, H-2_d, H-3_a, H-3_c, H-4_a, H-4_d), 4.0-3.33(m, 5H, H-5_a, H-5_c, H-5_d, H-6_a,H-6_b), 3.33(dd, $J_{4c,3c}=9.3$Hz, $J_{4c,5c}=9.3$Hz, 1H, H-4_c), 3.22(dd, $J_{2a,1a}=7.9$Hz, $J_{2a,3a}=8.8$Hz, 1H, H-2_a), 3.03(dd, $J_{2c,1c}=8.0$Hz, $J_{2c,3c}=10.1$Hz, 1H, H-2_c), 1.73 (s, 3H, $COCH_3$).

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