Total synthesis of alginate and zwitterionic SP1 oligosaccharides

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On the Reactivity of Gulose and Guluronic Acid Building Blocks in the Context of Alginate Assembly

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3.1 Introduction

Gulose (Figure 3.1) is a rare monosaccharide that can be found in bacteria, archaea and algae. It can be considered to be the C-3 epimer of galactose or the C-5 epimer of mannose. L-guluronic acid and D-mannuronic acid are the two constituting monomers of alginate (see Figure 3.1), an important cell-wall polysaccharide of brown algae that is used in the pharmaceutical industry and food industry because of its gelating properties.[1]

Alginate also represents the exopolysaccharide of *Pseudomonas aeruginosa*, an opportunistic pathogen that is responsible for, amongst others, urinary tract, kidney, lung and burn wound infections.[2] *P. aeruginosa* uses alginate to create a protective biofilm, which makes it difficult to combat the bacterium by the host immune system and antibiotic therapies. Short alginate fragments can interact with the innate part of our immune system through interactions with Toll like receptors (TLRs)[3] and poly-mannuronic acid alginates have been used as an carbohydrate antigen in protein conjugate vaccine modalities to generate a potential *Pseudomonas aeruginosa* vaccine.[4] Well-defined synthetic fragments of the alginate polysaccharide are very valuable tools to unravel the mode of action of alginate at the molecular level.[5] Therefore several synthetic strategies to assemble different stretches of the alginate polymer have been developed,[6] and efficient routes towards the assembly of oligo-mannuronates,[7] and short oligo-guluronates[8] have been reported so far. The assembly of mixed sequence alginated has not been described so far.[9]

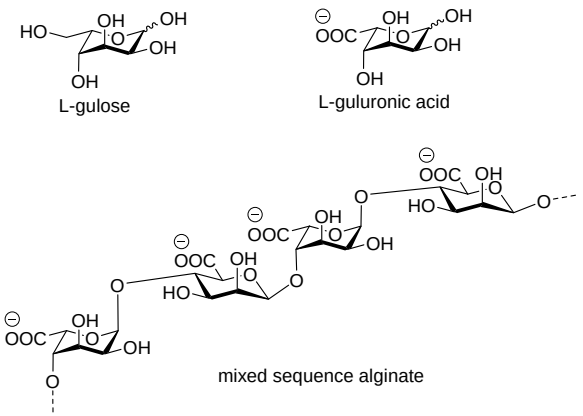


Figure 3.1 Structure of L-gulose, L-guluronic acid and mixed sequence alginate.

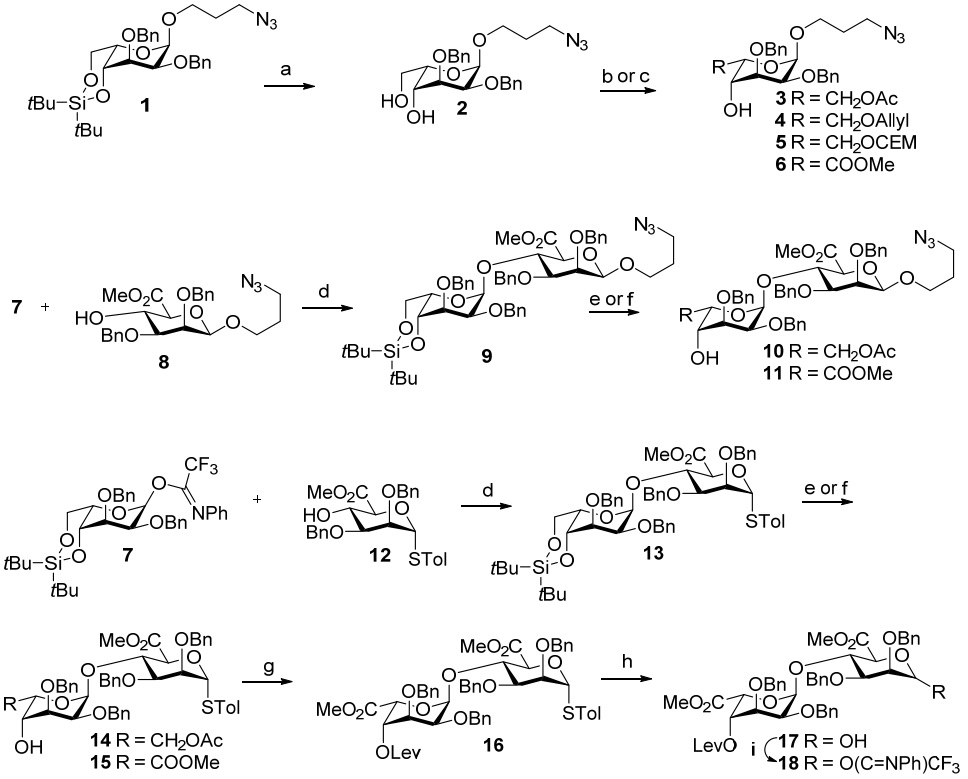
During the assembly of guluronic acid containing alginate fragments, it has become apparent that gulosyl donor building blocks have the tendency to provide 1,2-*cis*-glycosidic linkages with unusual selectivity.[10] This behaviour has been rationalized by taking into account the reactivity of the intermediate oxocarbenium ion (-like) intermediates. An L-gulose oxocarbenium ion can adopt a $^4H_3$-half chair conformation, in which all substituents occupy an orientation considered favourable for the stability of the cation.[11] Attack on this ion by the incoming nucleophile occurs from the diasterotopic face that leads, *via* a chair-like transition state, to the 1,2-*cis*-product. Thus, the stereoselective introduction of the α-gulosyl linkage can be effected with relative ease. The use fo guluronic acid and gulose acceptor building blocks however, represents a challenge, as the gulosyl C-4-OH is a relatively poor nucleophile. To circumvent this problematic reactivity, Hung and co-workers have reported on the use of 1,6-anhydrogulose synthons, in which the steric and electronic surroundings of the alcohol are changed for the better.[6] Functional groups on a carbohydrate not only influence the reactivity of a carbohydrate donor building block but also the nucleophilicity of carbohydrate acceptors, and it is often surmised that uronic acid acceptors are relatively poor nucleophiles because of the electron withdrawing effect of the C-5-carboxylate.[12] To find an effective gulose / guluronic acid acceptor building block for the assembly of mixed alginate sequences and to shed light on the influence of the neighbouring C-5-functionality on the reactivity of the gulose acceptors this Chapter reports a study of a panel of gulose and guluronic acid acceptors in a variety of glycosylation reactions.

3.2 Results and Discussion

A set of glycosylation reactions was investigated using gulosyl acceptors, varying in the nature of their C-5 functionality and using coupling partners of varying size. Both monomeric and dimeric donors and acceptors were combined and both guluronic acid acceptors and gulose acceptors were examined. Also, the nature of the C-6-*O*-protecting group in the gulose acceptors was varied to see whether this has any influence on the efficiency of the condensation reactions.

The synthesis of the new gulosyl acceptors (**3**-**6**, **10**-**11**, **14**-**15**) and disaccharide donors (**16** and **18**) is shown in Scheme 3.1. Starting from silylidene protected α-azidopropyl L-guloside **1**, the synthesis of which was reported previously by Dinkelaar *et al.*,[8] monomeric acceptors **3**-**6** were obtained. Thus, the silylidene functionality was removed to provide diol **2**, of which the primary alcohol was protected with an acetyl group (in **3**), as an allyl ether (in **4**) or masked with a cyanoethoxymethyl (CEM) group (in **5**). The latter group has not been employed in oligosaccharide synthesis before, but has found applications in RNA assembly and serves as a minimally intrusive base labile alcohol protecting group.[13] All these regioselective protections were achieved using Taylor's 2-aminoethyl diphenylborinic acid catalyst in conjunction with the appropriate electrophiles (acetyl chloride, allylbromide, cyanoethoxymethylchloride).[14] Guluronic ester acceptor **6** was obtained from **2** by a regioselective oxidation using the combination of tetramethylpiperidinyloxy free radical (TEMPO) and bisacetoxy iodobenzene (BAIB) and ensuing ester formation as described before.[9] The assembly of the disaccharide acceptors is also depicted in Scheme 3.1. A set of four disaccharide alcohols (**10**-**11** and **14**-**15**) was generated, having either a guluronic ester or a gulose acceptor at the non-reducing end end with either an anomeric α-thiocresol (STol) or an β-azidopropyl group attached to the

Scheme 3.1 Synthesis of building blocks.



Reagents and conditions: (a) HF/Pyridine, Pyridine, THF, 0 °C to room temperature, yield: 81%. (b) 2-aminoethyl diphenylborinic acid, MeCN, AcCl for **3**: 90%; 2-aminoethyl diphenylborinic acid, MeCN, K_2CO_3, KI, AllBr for **4**: 83%; 2-aminoethyl diphenylborinic acid, MeCN, cyanoethoxymethylchloride for **5**: 97%. (c) i) TEMPO, BAIB, DCM/*t*BuOH/H_2O (4/4/1,v/v/v); ii) MeI, K_2CO_3, DMF, 87%. (d) TMSOTf (cat.), CH_2Cl_2, -78 °C - -20 °C, **9**: 58%; **13**: 91%. (e) for **10** and **14**: i. HF.pyridine, pyridine, THF; ii. 2-aminoethyl diphenylborinic acid, MeCN, AcCl, **10**: 98%; **14**: 87%. (f) for **11** and **15**: i. HF.pyridine, pyridine, THF; ii. TEMPO, BAIB, *t*BuOH, THF, H_2O, iii. MeI, K_2CO_3, DMF, **11**: 84% (3 steps); **15**: 83% (3 steps). (g) LevOH, EDCI, DMAP, CH_2Cl_2, 92%; (h) NIS, TFA, CH_2Cl_2, 91%; (i) $F_3CC(=NPh)Cl$, K_2CO_3, acetone, 98%.

mannuronic acid side. The disaccharide acceptors were obtained from the fully protected gulose-mannuronic acid disaccharides **9** and **12**, which are synthesized from gulose donor

7 and mannouronic acid acceptors **8** and **12**, respectively. Unmasking of the silylidene as described above and ensuing regioselective acetylation of the C-6-OH, again using Taylor's borinic acid catalyst and acetyl chloride, gave the gulose-mannuronic acid coupling partners **10** and **14**. Oxidation of the liberated primary alcohol functionalities and methyl ester formation gave the guluronic acid-mannuronic acid acceptors **11** and **15**. To generate donors **16**-**18**, the C-4-OH of disaccharide **15** was protected with a Lev group to form **16**. Hydrolysis of of the thioacetal using NIS/TFA produced lactol **17**, which was then transfomred into imidate donor **18**.

With the set of donors (**16**-**19**) [7d] and acceptors (**3**-**6**, **10** and **11**) in hand the series of glycosylation reactions tabularized in Table 3.1 was performed. First, the mannuronic acid monosaccharide donor **19** was combined with the three differentially protected monomeric gulose acceptors **3**-**5** (Table 3.1, Entries 1-3). The three condensation reactions proceeded under TMSOTf catalysis and gave the disaccharides **22**-**24** with excellent stereoselectivity but in relatively poor yields. Where it could be reasoned that a more electron rich protecting group at C-6 would lead to a more nucleophilic C-4-OH, this was not apparent from the obtained results: the C-6-OAc gulose acceptor outperformed the acceptors protected with the allyl ether or cyanoethoxymethyl protecting groups (Table 3.1, Entries 1-3). In the next set of optimizations, it was found that the efficiency of the condensation of mannuronic acid donor **13** and the C-6-OAc gulose acceptor **3** could be improved by the use of TBSOTf, but not TfOH, in stead of TMSOTf under otherwise unchanged conditions (Table 3.1, Entries 4 and 5). When TBSOTf was used as a promotor in the condensation of guluronic acid acceptor **6** and donor **19**, disaccharide **25** was obtained in 55% yield (Table 3.1, entry 6). Notably the stereoselectivity of this coupling

reaction was significantly worse than the other glycosylations of mannuronic acid donor **19**, for which there currently is no adequate explanation.

Next, glycosylations of disaccharide imidate donor **18** were investigated. In the first instance, **18** was reacted with either C-6-OAc gulose acceptor **3** or guluronic ester acceptor **6**, under the agency of a catalytic amount of TBSOTf (Table 3.1, entry 7 and 8). Strikingly, these condensations proceeded with higher yields than the glycosylations of the monomeric donors and the guluronic acid acceptor gave the most productive glycosylation reaction (84% *vs* 69% for the C-6-OAc acceptor). Trisaccharide **27** was obtained as a single anomer, in contrast to the condensation of **6** with monosaccharide donor **19** (Table 3.1, entry 6). Next, the disaccharide acceptors **10**, **11**, **14** and **15** were probed. When the azidopropyl-functionalized dimers **10** and **11** were condensed with dimer donor **18**, tetrasaccharides **28** and **29** were obtained in low yields (33% and 26%, respectively, Table 3.1, entry 9 and 10). Increasing the amount of activator and prolonged reaction time gave **29** in 45% yield (Table 3.1, entry 11). The use of other donor types (**16** or **17**) and a pre-activation strategy to generate a higher concentration of the reactive intermediate anomeric triflate did not lead to a better outcome (Table 3.1, entries 12-14). Apparently, the larger size of the disaccharide nucleophiles (**10** *vs* **3** and **11** *vs* **6**) has a large impact on the reactivity of the gulosyl and guluronic acid C-4-OH.

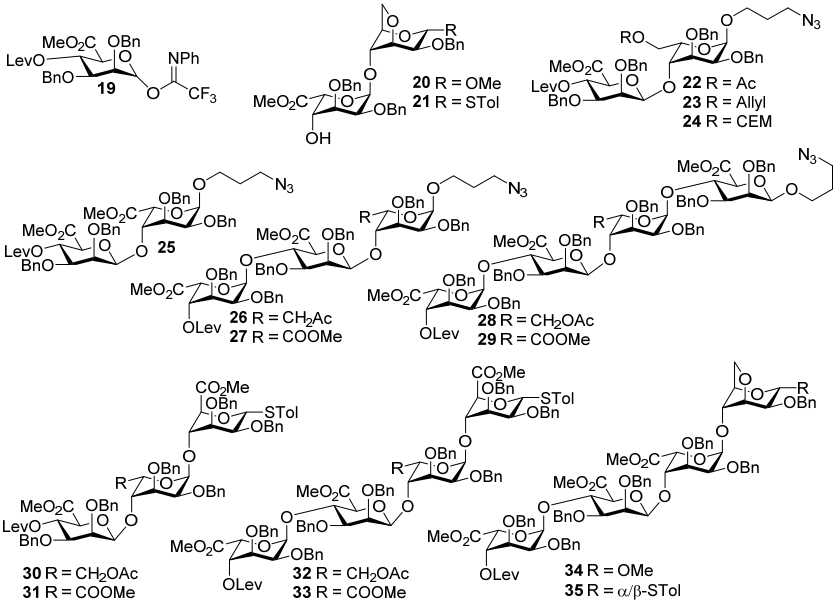
Switching to the acceptor disaccharides with the anomeric α-thiocresol moiety gave a significant increase in yield both for the C-6-OAc gulose acceptor **14** and the guluronic acid acceptor **15**. Tetrasaccharides **32** and **33** were obtained in 80% and 91% yield, respectively (Table 3.1, entry 15 and 16). When the two disaccharide acceptors **14** and **15** were condensed with monosaccharide donor **19** (Table 3.1, Entries 17 and 18) the two

trisaccharides **30** and **31** were also obtained in good yield and excellent stereoselectivity.

Remarkably, the large difference in yield for the glycosylations between disaccharide acceptors **10**, **11** and **14**, **15**, is caused by the difference in the anomeric functionality - a thiocresol (**14**, **15**) or azidopropanol group (**10**, **11**) - at the reducing end of the disaccharide acceptor, rather far removed from the reacting C4'-OH. To identify the underlying cause for the difference in reactivity of **10**-**11** and **14**-**15** a set of model couplings was performed. Thioether additives have previously been reported to modulate glycosylation reactions and anomeric sulfonium ions can serve as glycosylating species.[15] To probe whether the anomeric thio function was at the basis of the improved reactivity of acceptor **15** we added thiophene[15b] to the condensation of **18** and **11**, to find that this external sulphide had no notable effect on the reaction (Table 3.1, entry 19). Having established that the presence of a sulfur containing molecule in the mixture is not the main contributing factor at play, it was reasoned that the conformational flexibility of the acceptor could be the cause for the difference in reactivity between **10**-**11** and **14**-**15**. Where the α-mannuronic acid moiety in **10**-**11** occupies a 'normal' $^4C_1$ chair conformation, the α-mannuronic acid in **14**-**15** takes up either a $^4C_1$ or the 'inverted' $^1C_4$ conformation, with a strong preference for the latter chair.[16]

Table 3.1 Glycosylation reactions using different gulosyl acceptors with mannuronic acid donors.

donors: **16-19** acceptors: **3-6**, **10-11**, **14-15** and **20-21** products: **22-35**



Entry	Donor	Acceptor	Conditions[a]	Product	Yield (α : β)[b]
1	**19**	**3**	TMSOTf	**22**	49% (0 : 1)
2	**19**	**4**	TMSOTf	**23**	23% (0 : 1)
3	**19**	**5**	TMSOTf	**24**	35% (0 : 1)
4	**19**	**3**	TfOH	**22**	30% (0 : 1)
5	**19**	**3**	TBSOTf	**22**	65% (0 : 1)
6	**19**	**6**	TBSOTf	**25**	55% (1 : 3)
7	**18**	**3**	TBSOTf	**26**	69% (0 : 1)
8	**18**	**6**	TBSOTf	**27**	84% (0 : 1)
9	**18**	**10**	TBSOTf	**28**	33% (0 : 1)
10	**18**	**11**	TBSOTf	**29**	26% (0 : 1)
11	**18**	**11**	TBSOTf	**29**	45% (0 : 1)
12	**17**	**11**	Ph_2SO/TTBP/Tf_2O	**29**	21% (0 : 1)
13	**17**	**11**	BSP/TTBP/Tf_2O	**29**	32% (0 : 1)
14	**16**	**11**	BSP/TTBP/Tf_2O	**29**	20% (0 : 1)
15	**18**	**14**	TBSOTf	**32**	80% (0 : 1)
16	**18**	**15**	TBSOTf	**33**	91% (0 : 1)
17	**19**	**14**	TBSOTf	**30**	77% (0 : 1)
18	**19**	**15**	TBSOTf	**31**	100% (0 : 1)
19	**18**	**11**	TBSOTf, thiophene	**29**	32% (0 : 1)
20	**18**	**20**	TBSOTf	**34**	95% (0 : 1)
21	**18**	**21**	TBSOTf	**35**	71% (0 : 1)

The conformational flexibility of **14** and **15** is reflected in their ^{1}H NMR and ^{13}C NMR spectra; the signals of the mannuronic acid ring appear as broad and poorly resolved resonances at room temperature. Figure 3.2 displays the ^{1}H NMR spectra of acceptor **15** recorded at different temperatures. At low temperature (-60 °C), two resonance sets are apparent that coalesce with increasing temperature. The two resonance sets belong to the disaccharides with the mannuronic acid in a "normal" $^{4}C_{1}$ chair conformation or taking up a $^{1}C_{4}$ chair conformation. It becomes clear from the spectra that the $^{1}C_{4}$ chair conformer is the most prevalent acceptor species present in the mixture. The ring flipping of the reducing end mannuronic acid to a $^{1}C_{4}$ chair, changes the overall structure of the disaccharide and may make the C4' hydroxy group more accessible and, therefore, more reactive. To further test this hypothesis, two model acceptors were generated having a reducing end mannoside, locked in a $^{1}C_{4}$ chair conformation: disaccharide **20** having an anomeric *α-O*-methyl group and disaccharide **21** with an anomeric thiocresol moiety (Table 3.1, Entries 20 and 21). The acceptors could be condensed with donor **18** in good to excellent yield. In the latter condensation, the only notable side reaction that took place was the epimerisation of the anomeric thioacetal. From these experiments, it can be concluded that the overall three dimensional structure of the acceptor is of decisive influence and that the "open" shape of disaccharide **14** and **15** is at the basis of the apt nucleophilicity of the C-4'-OH.

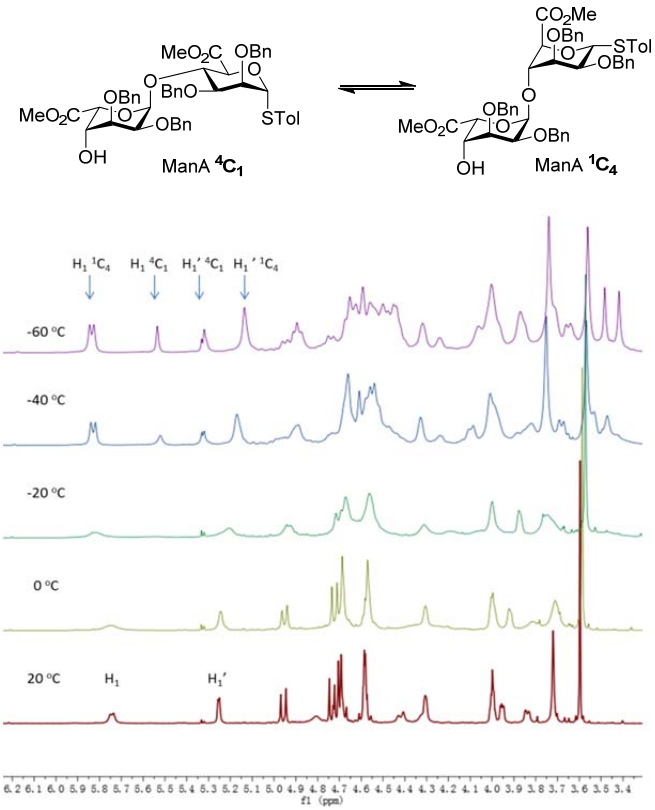


Figure 3.2 variable-temerature NMR spectra showing the converging resonance sets belonging to $^{4}C_{1}$ and $^{1}C_{4}$ mannuronic acid conformers.

3.3 Conclusions

In conclusion, a set of glycosylation reactions has been described to produce fully protected mixed sequence alginate oligomers up to the tetrasaccharide level. It was found that the gulosyl C-4 hydroxyl is a relatively poor nucleophile that can be hard to glycosylate. From the results presented in Table 3.1, it can be concluded that the functional group close to the acceptor alcohol group has little influence on its reactivity and at least in the set of glycosylations studied here no important disarming effect of the

C-5 carboxylate on the reactivity of the C-4-OH was found. In fact, C-5 carboxylic acid ester acceptors can outperform their non-oxidized counterparts (see Table 3.1, Entry 7 *vs* 8, 9 *vs* 10, 15 *vs* 16). An all-important factor, influencing the effectivity of the glycosylations, turned out to be the conformational flexibility of the acceptors at hand. Where the presence of a rigid β-mannuronic acid *O*-glycoside reducing end in the disaccharide acceptors led to poor glycosylation reactions the flexible α-*S*-tolyl mannuronic acid reducing ends endowed the acceptors with excellent nucleophilicity. Further studies are required to provide detailed insight into how the conformational behaviour of mannuronic acid reducing ends influences the steric and electronic surroundings of the gulose-C-4'-alcohol. Conformational flexibilty may prove to be important in many other glycosylations, since glycosylation reactions involving secondary alcohol acceptors generally proceed through a very crowded transition state.

3.4 Experimental Section

General experimental procedures

All reagents were of commercial grade and used as received. All moisture sensitive reactions were performed under an argon atmosphere. DCM used in the glycosylation was distilled over P_2O_5 and stored on activated 5Å molecular sieves before being used. Reactions were monitored by TLC analysis with detection by UV (254 nm) and where applicable by spraying with 20% sulfuric acid in EtOH or with a solution of $(NH_4)_6Mo_7O_{24}{\cdot}4H_2O$ (25 g/L) and $(NH_4)_4Ce(SO_4)_4{\cdot}2H_2O$ (10 g/L) in 10% sulfuric acid (aq.) followed by charring at ~150 °C. Flash column chromatography was performed on silica gel (40-63µm). ^{1}H and ^{13}C spectra were recorded on a Bruker AV 400, in $CDCl_3$. Chemical shifts (δ) are given in ppm relative to tetramethylsilane as internal standard (^{1}H NMR in $CDCl_3$) or the residual signal of the deuterated solvent. Coupling constants (*J*) are given in Hz. All ^{13}C spectra are proton decoupled. NMR peak assignments were made using COSY and HSQC experiments. Where applicable NOESY, HMBC and HMBCipvGATED experiments were used to further elucidate the structure. The anomeric product ratio's were analysed through integration of proton NMR signals.

General procedure for deprotecting of the di-*tert*-butyl silylidene ketal

A solution of HF/Pyridine solution (0.5 mmol, 5.0 eq) was added to a solution of starting material in a mixture of THF and pyridine (1/1, v/v, 2 ml) at 0 °C. The reaction was allowed to stir overnight at room temperature. Sat. aq. $NaHCO_3$ was added to neutralize the mixture, which was then diluted with EtOAc and washed with sat. aq. NaCl. The organic phase was dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatograpy yielded the deprotected product.

General procedure for selective acetylation of the gulosyl C-6-OH

2-Aminoethyl diphenylborinate (20 mol %) and the diol substrate (1 mmol) were transferred to a 25-mL round-bottomed flask containing a magnetic stir bar. The flask was then sealed with a septum and purged with a balloon of argon. Anhydrous acetonitrile (5 mL) was added to the flask, followed by *N*,*N*-diisopropylethylamine (1.5 mmol) and acetyl chloride (1.3-1.5 mmol). The resulting mixture was stirred at room temperature for 4 hours. The mixture was then transferred to a separatory funnel containing water and ethyl acetate. The organic layer was separated, and the aqueous layer was extracted two more times with ethyl acetate. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting crude material was purified by silica gel chromatography.

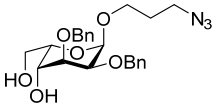
General Procedure for selective alkylation of the gulosyl C-6-OH

2-Aminoethyl diphenylborinate (20 mol %), the diol substrate (0.20 mmol), potassium iodide (0.20 mmol) and potassium carbonate (0.22 mmol) were transferred to a round-bottomed flask containing a magnetic stir bar. The vial was then sealed with a septum and purged with a balloon of argon. Anhydrous acetonitrile (1 mL) was added to the flask, followed by allyl bromide (0.30 mmol). The resulting mixture was stirred at 60 °C for 24 hours. The mixture was then transferred to a separatory funnel containing water and ethyl acetate. The organic layer was separated, and the aqueous layer was extracted two more times with ethyl acetate. The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting crude material was purified by silica gel chromatography.

General procedure for glycosylation reactions

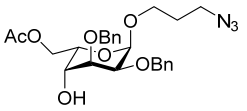
Imidate donor (1.5-3.0 eq) and acceptor (1.0 eq) were co-evaporated with toluene (three times). The residue was dissolved in dry DCM (0.1 M acceptor in DCM). The solution was cooled to -78 °C, followed by the addition of TBSOTf or TMSOTf (0.2-0.6 eq) and the reaction was allowed to stir for 12h-48h at -78 °C to -20 °C. The reaction was quenched with Et_3N and diluted with EtOAc, washed with sat. aq. NaCl. The organic phase was dried over Na_2SO_4 and concentrated in vacuo. Purification by column chromatograpy yielded the product.

3-Azidopropyl 2,3-*O*-benzyl-α-L-gulopyranoside (2): This product was prepared following the general procedure for deprotecting of the di-*tert*-butyl silylidene ketal. 590 mg (1.33 mmol), yield: 81%. 1H

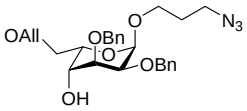


NMR (CDCl3, 400 MHz, HH-COSY, HSQC): δ 7.32-7.24 (m, 10H, CHarom), 4.94-4.79 (m, 2H, H-1, C*H*H Bn), 4.71-4.44 (m, 3H, C*H*H Bn), 4.07 (dd, *J* = 3.7, 1.3 Hz, 1H, H-4), 3.99 (dd, *J* = 3.8, 1.3 Hz, 1H, H-5), 3.93-3.73 (m, 5H, H-2, H-3, H-6, -OC*H*2CH2CH2N3), 3.45 (dt, *J* = 9.8, 5.5 Hz, 1H, -OC*H*2CH2CH2N3), 3.37 (t, *J* = 6.6 Hz, 2H, OCH2CH2C*H*2N3), 1.99-1.71 (m, 2H, -OCH2C*H*2CH2N3); 13C-APT NMR (CDCl3, 100 MHz, HSQC): δ 138.9, 138.2(Cq), 128.5, 128.3, 127.9, 127.7, 127.7, 127.6(CHarom), 98.0(C-1), 75.6(C-3), 73.4(C-2), 73.2 (CH2 Bn), 71.6(CH2 Bn), 71.3(C-5), 65.6(C-4), 64.8(-O*C*H2CH2CH2N3), 64.4(C-6), 48.4(-OCH2CH2*C*H2N3), 29.0(-OCH2*C*H2CH2N3).

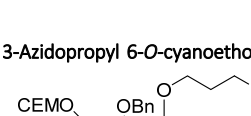
3-Azidopropyl 6-*O*-acetyl-2,3-*O*-benzyl-α-L-gulopyranoside (3): This product was prepared following the general procedure for selective acetylation of the gulosyl C-6-OH. Yield: 346 mg (0.71 mmol), 90%. TLC: R_f = 0.69 (pentane:ethyl acetate = 1:1). ^{1}H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.45 – 7.16 (m,10H, CH_{arom}), 4.69 – 4.52 (m, 5H, CH_2 Bn, H-1), 4.37 – 4.06 (m, 3H, H-5, H-6), 3.92 – 3.69 (m, 4H, H-3,H-2, H-4, -OCH_2CH$_2$CH$_2$N$_3$), 3.50-3,36 (m, 3H, -OCH_2CH$_2$CH_2N$_3$), 2.60 (bs, 1H, 4-OH), 2.05 (s, 3H, CH_3CO), 2.01 – 1.72 (m, 2H, -OCH$_2$CH_2CH$_2$N$_3$); ^{13}C –APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 171.2(C=O Ac), 138.8, 138.1($C_{q\ arom}$), 128.5, 128.3, 127.9, 127.7, 127.7, 127.6(CH_{arom}), 97.6(C-1), 75.9(C-3), 73.2(C-2), 73.2, 71.7(CH_2Bn), 68.7(C-4), 64.9(C-5), 64.9(-OCH$_2$CH$_2$CH$_2$N$_3$), 63.5(C-6), 48.4(-OCH$_2$CH$_2$CH$_2$N$_3$), 29.0(CH_3CO), 20.9(-OCH$_2$CH$_2$ CH$_2$N$_3$). $[\alpha]^{20}_D$ = -113° (c = 1.0, $CHCl_3$). IR (neat): 606, 652, 696, 734, 817, 908, 955, 1026, 1069, 1115, 1140, 1234, 1302, 1369, 1454, 1717, 1738, 2093, 2875, 2924. HR-MS: [M+Na$^+$] Calculated for $C_{25}H_{31}N_3O_7$: 508.20542; found: 508.20518.



3-Azidopropyl 6-*O*-allyl-2,3-*O*-benzyl-α-L-gulopyranoside (4): This product was prepared following the general procedure for selective alkylation of the gulosyl C-6-OH. Yield: 160 mg, (0.33 mmol), 83%. TLC: R_f = 0.64 (pentane:ethyl acetate = 2:1). ^{1}H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.44 – 7.14 (m, 10H, CH_{arom}), 5.87 (m, 1H, CH All), 5.32 – 5.10 (m, 2H, CH_2 All), 4.95 – 4.81 (m, 2H, C*H*H Bn, H-1), 4.71 – 4.49 (m, 3H, CH_2 Bn), 4.23 – 4.11 (m, 1H, H-5), 4.10 – 3.61 (m, 8H, CH_2 All, H-4, H-2, H-3, H-6, -OCH_2CH$_2$CH$_2$N$_3$), 3.46 (dt, *J* = 9.9, 5.5 Hz, 1H, -OCH_2CH$_2$CH$_2$N$_3$), 3.36 (t, *J* = 6.7 Hz, 2H, -OCH$_2$CH$_2$CH_2N$_3$), 2.00 – 1.76 (m, 2H, -OCH$_2$CH_2CH$_2$N$_3$); ^{13}C –APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 139.1, 138.3($C_{q\ arom}$), 133.8(CH All), 128.4, 128.2, 127.8, 127.7, 127.6, 127.5(CH_{arom}), 118.0(CH_2=*C*H All), 98.2(C-1), 75.5(C-3), 73.4(C-2), 73.1(CH_2Bn), 72.8(CH_2 All), 72.0(C-6), 71.5(CH_2Bn), 71.2(C-4), 64.8(C-5), 64.7(-OCH$_2$CH$_2$CH$_2$N$_3$), 48.4(-OCH$_2$CH$_2$CH$_2$N$_3$), 29.0(-OCH$_2$CH$_2$CH$_2$N$_3$). $[\alpha]^{20}_D$ = -45° (c = 1.0, $CHCl_3$). IR (neat): 633, 696, 731, 822, 910, 1026, 1067, 1088, 1207, 1265, 1306, 1339, 1456, 2095, 2870, 2920. HR-MS: [M+Na$^+$] Calculated for $C_{26}H_{33}N_3O_6$: 506.22616; found: 506.22587.

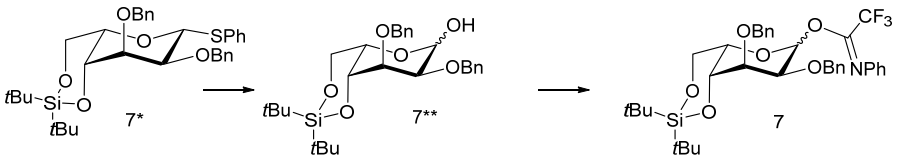


3-Azidopropyl 6-*O*-cyanoethoxyl methyl-2,3-*O*-benzyl-α-L-gulopyranoside (5): This product was prepared following the general procedure for selective acetylation of the gulosyl C-6-OH. Yield: 206 mg, (0.39 mmol), 97%. TLC: R_f = 0.39 (pentane:ethyl acetate = 1:1). ^{1}H NMR

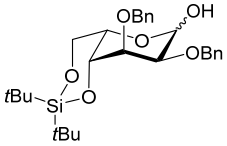


($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.40 – 7.20 (m, 10H, CH_{arom}), 4.97 – 4.83 (m, 2H, C*H*H Bn, H-1), 4.73 (d, *J* = 1.3 Hz, 2H, CH_2OCH$_2$CH$_2$CN), 4.70 – 4.51 (m, 3H, CH_2Bn), 4.25 (t, *J* = 4.1, 1H, H-5), 3.97 (bs, 1H, H-3), 3.93 – 3.79 (m, 5H, H-2, H-4, H-6, -OCH_2CH$_2$CH$_2$N$_3$), 3.79 – 3.70 (m, 2H, CH$_2$OCH_2CH$_2$CN), 3.48 (dt, *J* = 9.8, 5.5 Hz, 1H, OCH_2CH$_2$CH$_2$N$_3$), 3.39 (t, *J* = 6.7 Hz, 2H, OCH$_2$CH$_2$CH_2N$_3$), 2.97 (s, 1H, 4-OH), 2.61 (t, *J* = 6.2 Hz, 2H, CH$_2$OCH$_2$CH_2CN), 2.06 – 1.76 (m, 2H, OCH$_2$CH_2CH$_2$N$_3$); ^{13}C –APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 138.9, 138.2($C_{q\ arom}$), 128.4, 128.2, 127.8, 127.7, 127.5 CH_{arom}, 117.8 (CH$_2$OCH$_2$CH$_2$*C*N), 98.0(C-1), 95.7(*C*H$_2$OCH$_2$CH$_2$CN), 75.5(C-2), 73.2(C-4), 73.1, 71.5(CH_2Bn), 70.5(C-3), 69.1(C-6), 64.9(O*C*H$_2$CH$_2$CH$_2$N$_3$), 64.8(C-5), 62.8(CH$_2$O*C*H$_2$CH$_2$CN), 48.3(OCH$_2$CH$_2$*C*H$_2$N$_3$), 29.0(CH$_2$OCH$_2$*C*H$_2$CN), 19.0(OCH$_2$*C*H$_2$CH$_2$N$_3$). $[\alpha]^{20}_D$ = -43° (c = 0.42, $CHCl_3$). IR (neat): 698, 735, 820, 910, 1028, 1080, 1117, 1165, 1263, 1456, 1263, 1454, 1735, 2095, 2853, 2924. HR-MS: [M+Na$^+$] Calculated for $C_{27}H_{34}N_4O_7$: 549.23197; found: 549.23166.

Synthesis of gulose donor (7)

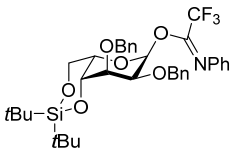


2,3-Di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylidene-α/β-L-gulopyranoside (7**)



NIS (1.12 g, 5.0 mmol) and TFA (385 ul, 5.0 mmol) were added to a solution of **7*** (2.95 g, 5.0 mmol) in CH_2Cl_2 (40 ml) at 0 °C. After analysis by TLC showed complete consumption of the starting material, the reaction was quenched with Et_3N. Saturated $Na_2S_2O_3$ (aq) was added to the reaction mixture, which was then stirred for 30 min. The aqueous layer was extracted twice with CH_2Cl_2, and concentrated *in vacuo*. Purification by column chromatography yielded **7**** as a colourless oil (2.2 g, 88%). Spectroscopic data were in accord with those reported previously.[8]

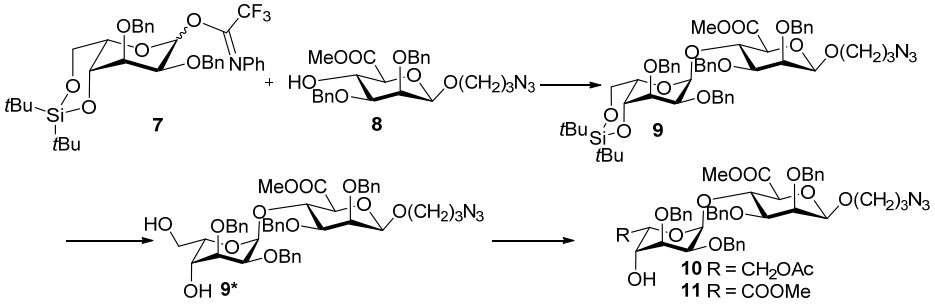
2,3-Di-*O*-benzyl-4,6-*O*-di-*tert*-butylsilylidene-1-O-(*N*-phenyl-trifluoroacetimidoyl)-α,β-L-gulopyranoside (7):



Compound **3**** (4.16 g, 8.3 mmol) was dissolved in acetone (75 ml) and the solution was cooled to 0 °C. *N*-phenyl-trifluoroacetimidoyl chloride (2.27 g, 10.9 mmol) and cesium carbonate (4.06 g, 12.5 mmol) were added and the resulting suspension was stirred overnight at room temperature. Then Et_3N was added to the reaction mixture, after which it was filtered and the filtrate was concentrated *in vacuo*. Purification by column

chromatography (silica gel, pentane/EtOAc/Et_3N, 20/1/trace, v/v/trace) yielded **3** as a slightly yellow solid (5.57 g, quantitative). Analytical data are reported for the major isomer (α). TLC: R_f = 0.86 (pentane/EtOAc, 10/1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz, 50°C, HH-COSY, HSQC): δ 7.48 – 7.15 (m, 12H, CH_{arom}), 7.14 – 6.96 (m, 1H, CH_{arom}), 6.92 – 6.76 (m, 2H, CH_{arom}), 5.94 (s, 1H, H-1) , 4.85 (d, *J* = 11.8 Hz, 1H, C*H*H Bn), 4.77 (d, *J* = 12.0 Hz, 1H, C*H*H Bn), 4.65 (d, *J* = 12.0 Hz, 1H, C*H*H Bn), 4.57 (d, *J* = 12.0 Hz, 1H, C*H*H Bn), 4.21 – 4.00 (m, 3H, H-4, H-6), 3.95 – 3.80 (m, 2H, H-3, H-2), 3.61 (bs, 1H, H-5), 1.00 (s, 18H, 6XCH_3); ^{13}C–APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 144.0, 138.4, 138.0($C_{q\ arom}$), 128.5, 128.4, 128.3, 128.1, 127.8, 127.7, 127.7($C_{q\ arom}$), 124.0, 119.6(CH NPh), 96.1(C-1), 77.9(C-2), 74.6(C-3), 73.9, 73.2(CH_2Bn), 71.8(C-4), 70.9(C-5), 66.7(C-6), 27.6, 27.3(CH_3 *tert*-Bu), 23.2(C_q *tert*-Bu), 20.5(C_q *tert*-Bu). HR-MS: [M+Na$^+$] Calculated for $C_{36}H_{44}F_3NO_6Si$: 694.27822; found: 694.27827.

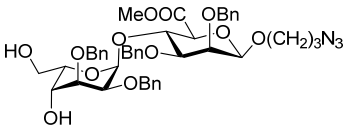
Synthesis of dissacharide 12



Methyl (3-Azidopropyl 2,3-di-*O*-benzyl-4-*O*-[2,3-di-*O*-benzyl-4,6-di-*tert*-Butylsilylidene-α-L-gulopyranosyl]- α-D-mannopyranosyl uronate) (9): Imidate donor **7** (492 mg, 0.733 mmol) and acceptor **8**[7a] (230 mg, 0.488 mmol) were co-evaporated with toluene (three times). The residue was dissolved in dry DCM (5 ml). The solution was cooled to -78 °C and TBSOTf (23 ul, 0.1 mmol) was added, after which the reaction was allowed to stir for 2 days during which is was gradually warmed from -78°C to -20°C. The reaction was quenched with Et_3N and diluted with EtOAc, washed with sat. aq. NaCl and the organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. Purification by column chromatography (silica gel, pentane/EtOAc, 4/1, v/v) yielded **11** as a colourless syrup (270 mg, 58%). TLC: R_f = 0.14 (pentane/ EtOAc, 6/1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.49 – 7.05 (m, 20H, CH_{arom}), 5.12 – 5.00 (m, 1H, H-1_{Gul}), 4.97 (d, *J* = 11.8 Hz, 1H, CH_2Bn), 4.83 (d, *J* = 12.3 Hz, 1H, CH_2Bn), 4.73 – 4.48 (m, 6H, CH_2Bn, H-1_{Mann}, H-4_{Mann}), 4.45 (d, *J* = 10.9 Hz, 1H, CH_2Bn), 4.27 (d, *J* = 10.9 Hz, 1H, CH_2Bn), 4.13 – 4.01 (m, 3H, H-6_{Gul}, H-4_{Gul}, H-5_{Gul}), 3.98 (dd, *J* = 3.6, 1.2 Hz, 1H, H-3_{Gul}), 3.90 (dd, *J* = 2.8, 1.3 Hz, 1H, H-3_{Mann}), 3.79 – 3.71 (m, 3H, H-2_{Gul}, H-5_{Mann}, -OC*H*$_2$CH$_2$CH$_2$N$_3$), 3.59 (s, 3H,), 3.57 – 3.43 (m, 2H, H-6_{Gul}, H-2_{Mann}), 3.43 – 3.26 (m, 3H, OC*H*$_2$CH$_2$C*H*$_2$N$_3$), 2.02 – 1.76 (m, 2H, OCH$_2$C*H*$_2$CH$_2$N$_3$), 0.92(s, 9H, 3xCH_3 *tert*-Bu), 0.84(s, 9H, 3xCH_3 *tert*-Bu); ^{13}C–

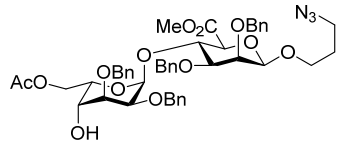
APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 169.1(-$COOCH_3$), 139.3, 138.7, 138.1, 137.9($C_{q\ arom}$), 128.4, 128.2, 128.2, 128.1, 128.0, 127.7, 127.7, 127.5, 127.5, 127.4(CH_{arom}), 101.5(C-1_{Mann}), 96.9(C-1_{Gul}), 79.9(C-2_{Mann}), 75.8(C-2_{Gul}, C-4_{Gul}), 73.8(C-3_{Mann}), 73.8(CH_2Bn), 73.1(CH_2Bn), 72.9(C-5_{Mann}), 72.6(C-3_{Gul}), 72.4(C-4_{Mann}), 71.8, 71.1(CH_2Bn), 66.7(O$CH_2CH_2CH_2N_3$, C-6_{Gul}), 64.0(C-5_{Gul}), 52.2(-$COOCH_3$), 48.4($OCH_2CH_2CH_2N_3$), 29.1($OCH_2CH_2CH_2N_3$), 27.6, 27.2(CH_3 *tert*-Bu), 23.2, 20.3(C_q *tert*-Bu). $[\alpha]^{20}_D$ = -65° (c = 0.24, $CHCl_3$). IR (neat): 650, 698, 737, 826, 860, 1084, 1138, 1362, 1456, 1558, 1684, 1749, 2857, 2932. HR-MS: [M+Na^+] Calculated for $C_{52}H_{67}O_{12}SiN_3$: 976.43862; found: 976.43980.

Methyl (3-Azidopropyl 2,3-di-*O*-benzyl-4-*O*-[2,3-di-*O*-benzyl-4,6-di-hydroxyl-α-L-gulopyranosyl]-α-D-mannopyranosyl uronate) (9*):



A HF/Pyridine solution (146 ul) was added to a solution of compound **11** (300 mg, 0.315 mmol) in a mixture of THF (2 ml) and pyridine(2 ml) at 0 °C. The reaction was allowed to stir overnight at room temperature. Then, a sat. aq. $NaHCO_3$ was added to neutralize the mixture, which was diluted with EtOAc, washed with sat. aq. NaCl. The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. Purification by column chromatography (silica gel, pentane/EtOAc, 1/1, v/v) yielded **9*** as a colourless oil (220 mg, 86%). TLC: R_f = 0.36 (pentane/ EtOAc, 6/1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.46 – 7.00 (m, 20H, CH_{arom}), 5.08 (d, *J* = 4.0 Hz, 1H, H-1_{Gul}), 4.88 (dd, *J* = 12.2, 8.5 Hz, 2H, CH_2Bn), 4.70 (d, *J* = 12.4 Hz, 1H, CH_2Bn), 4.66 – 4.45 (m, 5H, H-1_{Mann}, H-4_{Mann}, CH_2Bn), 4.41 (d, *J* = 11.0 Hz, 1H, CH_2Bn), 4.25 (d, *J* = 11.0 Hz, 2H, H-5_{Gul}, CH_2Bn), 4.13 – 3.97 (m, 2H, H-5_{Mann}, -O$CH_2CH_2CH_2N_3$), 3.90 (d, *J* = 3.1 Hz, 1H, H-3_{Mann}), 3.80 (dt, *J* = 7.8, 3.3 Hz, 3H, H-2_{Gul}, H-4_{Gul}, H-3_{Gul}), 3.59 (s, 3H, CH_3 $COOCH_3$), 3.58 – 3.40 (m, 3H, -O$CH_2CH_2CH_2N_3$, H-6_{Gul}, H-2_{Mann}), 3.37 (t, *J* = 6.6 Hz, 2H, -$OCH_2CH_2CH_2N_3$), 3.23 (dd, *J* = 12.0, 3.8 Hz, 1H, H-6_{Gul}), 1.88 (m, 2H, -$OCH_2CH_2CH_2N_3$). ^{13}C–APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 169.1(-COO-), 139.1, 138.7, 137.6($C_{q\ arom}$), 128.4, 128.3, 128.3, 128.2, 128.0, 127.8, 127.6, 127.6, 127.6, 127.5(CH_{arom}), 101.7(C-1_{Mann}), 96.8(C-1_{Gul}), 79.9(C-2_{Mann}), 75.8(C-5_{Mann}), 75.3(C-3_{Gul}), 74.1(C-3_{Mann}), 74.1(CH_2Bn), 73.5(C-2_{Gul}), 73.0(CH_2Bn), 72.3 C-4_{Mann}), 72.0, 71.4(CH_2Bn), 71.3(C-4_{Gul}), 66.8(O$CH_2CH_2CH_2N_3$), 65.5(C-5_{Gul}), 64.0(C-6_{Gul}), 52.4(-$COOCH_3$), 48.4($OCH_2CH_2CH_2N_3$), 29.2($OCH_2CH_2CH_2N_3$). $[\alpha]^{20}_D$ = -83° (c = 0.3, $CHCl_3$). HR-MS: [M+Na^+] Calculated for $C_{44}H_{51}O_{12}N_3$: 836.33650; found: 836.33755.

Methyl (3-Azidopropyl 2,3-di-*O*-benzyl-4-*O*-[6-*O*-acetyl-2,3-di-*O*-benzyl-4-di-hydroxyl-α-L-gulopyranosyl]- α-D-mannopyranosyl uronate) (10):

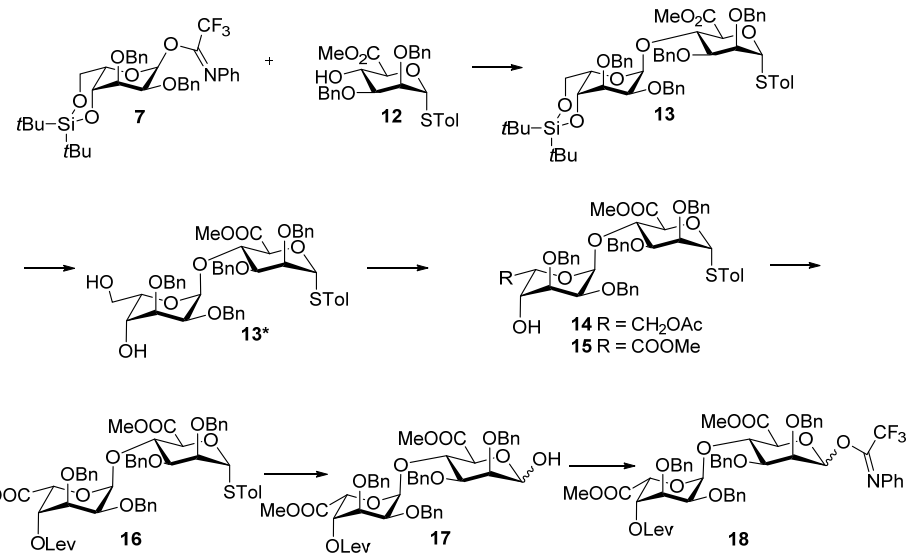


This product was prepared following the general procedure for selective acetylation of the gulosyl C-6-OH. TLC: R_f = 0.50 (pentane:ethyl acetate = 7:5). Yield: 68 mg, (0.08 mmol), 79%. ^{1}H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.45 – 7.05 (m, 20H, CH_{arom}), 5.08 (d, *J* = 4.0 Hz, 1H, H-1_{Gul}), 4.86 (dd, *J* = 18.4, 12.2 Hz, 2H, CH_2Bn), 4.74 – 4.34 (m, 8H, H-1_{Mann}, H-4_{Mann}, CH_2Bn), 4.20 – 3.97 (m, 3H, H-6_{Gul}, H-5_{Mann}, -O$CH_2CH_2CH_2N_3$), 3.94 – 3.72 (m, 4H, H-3_{Mann}, H-3_{Gul}, H-2_{Gul}, H-6_{Gul}), 3.68 – 3.43 (m, 5H, H-4_{Gul}, CH_3 $COOCH_3$, H-2_{Mann}, -$OCH_2CH_2CH_2N_3$), 3.36 (t, *J* = 6.8 Hz, 2H, -$OCH_2CH_2CH_2N_3$),

2.58 (t, *J* = 4.1 Hz, 1H, G_4-OH), 1.94 (s, 3H, CH_3 Ac), 1.92 – 1.77 (m, 2H, -$OCH_2CH_2CH_2N_3$); ^{13}C –APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 171.1, 169.2(-COO-), 139.0, 138.1($C_{q\ arom}$), 128.5, 128.3, 128.3, 128.2, 128.2, 128.1, 127.9, 127.8, 127.7, 127.7, 127.6, 127.6, 127.5(CH_{arom}), 101.4(C-1_{Mann}), 96.7(C-1_{Gul}), 79.4(C-2_{Mann}), 75.6(C-5_{Mann}), 75.5(C-3_{Mann}), 74.3(C-3_{Gul}), 73.9(CH_2Bn), 73.4(C-2_{Gul}), 73.2(CH_2Bn), 73.0(C-4_{Mann}), 72.1, 71.6(CH_2Bn), 69.2(C-4_{Gul}), 66.8(O$CH_2CH_2CH_2N_3$), 64.6(C-5_{Gul}), 63.6(C-6_{Gul}), 52.4(-$COOCH_3$), 48.4($OCH_2CH_2CH_2N_3$), 29.2($OCH_2CH_2CH_2N_3$), 20.9(CH_3 Ac); ^{13}C –HMBC ($CDCl_3$, 100 MHz): 101.4($J_{C1,H1}$ = 157Hz, C-1_{Mann}), 96.7($J_{C1,H1}$ = 168Hz, C-1_{Gul}). $[\alpha]^{20}_D$ = -81° (c = 0.28, $CHCl_3$). HR-MS: [M+NH_4^+] Calculated for $C_{46}H_{53}N_3O_{13}$: 873.39166; found: 873.39255.

Methyl (3-Azidopropyl 2,3-di-*O*-benzyl-4-*O*-[methyl 2,3-di-*O*-benzyl-4-hydroxyl-α-L-gulopyranosyl uronate]-β-D-mannopyranosyl uronate) (11): Compound **9*** (260 mg, 0.319 mmol) was dissolved in DCM/*tert*-BuOH/H_2O (4.5 ml, 4/4/1,v/v/v). The mixture was cooled to 0 °C and treated with TEMPO (10 mg, 0.064 mmol) and BAIB (267 mg, 0.829 mmol). After stirring overnight at 4 0°C, $Na_2S_2O_3$ was added, the mixture was diluted with EtOAc, washed with sat. aq. NaCl and the organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. The crude residue was dissolved in DMF (3 ml), followed by addition of K_2CO_3 (45 mg, 0.326 mmol) and MeI (60 ul) at 0°C. The mixture was allowed to stir overnight at 4 °C, and then diluted with EtOAc, washed with sat. aq. NaCl. The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. Purification by column chromatography (silica gel, pentane/DCm/EtOAc, 2/1/1, v/v/v) yielded **12** as a colourless oil (234 mg, 87%). TLC: R_f = 0.53 (pentane/ DCM/EtOAc, 1/1/1, v/v/v); ^{1}H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.47 – 7.07 (m, 20H, CH_{arom}), 5.24 (d, *J* = 3.9 Hz, 1H, H-1_{Gul}), 5.05 (d, *J* = 2.0 Hz, 1H, H-5_{Gul}), 4.82 (dd, *J* = 25.5, 12.1 Hz, 2H, CH_2Bn), 4.67 – 4.35 (m, 8H, H-1_{Mann}, H-4_{Mann}, CH_2Bn), 4.15 – 3.98 (m, 3H, H-4_{Gul}, H-5_{Mann}, -O$CH_2CH_2CH_2N_3$), 3.91 – 3.70 (m, 3H, H-3_{Mann}, H-3_{Gul}, H-2_{Gul}), 3.68 – 3.40 (m, 7H, 2xCH_3 $COOCH_3$, H-2_{Mann}), 3.35 (t, *J* = 6.9 Hz, 2H, -$OCH_2CH_2CH_2N_3$), 1.98 – 1.68 (m, 2H, -$OCH_2CH_2CH_2N_3$); ^{13}C–APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 170.6, 168.9(-COO-), 138.9, 138.1($C_{q\ arom}$), 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 128.2, 128.0, 127.9, 127.9, 127.8, 127.7, 127.7, 127.6, 127.5, 127.4(CH_{arom}), 101.5(C-1_{Mann}), 97.3(C-1_{Gul}), 79.3(C-2_{Mann}), 75.7(C-5_{Mann}), 75.3(C-3_{Gul}), 74.0(C-3_{Mann}), 73.9(C-4_{Gul}), 73.1(CH_2Bn), 73.1(C-2_{Gul}), 73.0, 71.8, 71.6(CH_2Bn), 70.0(C-4_{Gul}), 68.3(C-5_{Gul}), 66.8(O$CH_2CH_2CH_2N_3$), 52.4(-$COOCH_3$), 52.2(-$COOCH_3$), 48.5($OCH_2CH_2CH_2N_3$), 29.2($OCH_2CH_2CH_2N_3$); ^{13}C -HMBCipvGATED ($CDCl_3$, 100 MHz): 101.5($J_{C1,H1}$ = 156Hz, C-1_{Mann}), 97.3($J_{C1,H1}$ = 170Hz, C-1_{Gul}). $[\alpha]^{20}_D$ = -80° (c = 1, $CHCl_3$). HR-MS: [M+Na^+] Calculated for $C_{45}H_{51}O_{13}N_3$: 864.33141; found: 864.33247.

Synthesis of disaccharide acceptor 14-15 and disaccharide donors 16-18



Methyl (*p*-methyphenyl 2,3-di-*O*-benzyl-4-*O*-[2,3-di-*O*-benzyl-4,6-di-*tert*-butyl-silylidene-α-L-gulopyranosyl]- 1-thio-α-D-mannopyranosyl uronate) (13): Imidate donor **7** (2.24 g, 3.34 mmol) and acceptor **12** (1.1 g, 2.23 mmol) were co-evaporated with toluene (three times). The residue was dissolved in dry DCM (22 mL). The solution was cooled to -78 °C and TBSOTf (102 ul, 0.45 mmol) was added, after which the reaction was allowed to stir overnight and slowly warm to -20 °C. The reaction was quenched with Et_3N and diluted with EtOAc, washed with sat. aq. NaCl. The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. Purification by column chromatography (silica gel, pentane/EtOAc, 15/1, v/v) yielded **5** as a colourless oil (2.02 g, 93%). TLC: R_f = 0.43 (pentane/EtOAc, 10/1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.53 (d, *J* = 8.2 Hz, 2H, CH_{arom}), 7.48 – 7.10 (m, 20H, CH_{arom}), 7.05 (d, *J* = 8.2 Hz, 2H, CH_{arom}), 5.70 (d, *J* = 7.9 Hz, 1H, H-1_{Mann}), 5.04 – 4.91 (m, 2H, H-1_{Gul}, C*H*H Bn), 4.69 – 4.52 (m, 4H, H-5_{Mann}, CH_2Bn), 4.52 – 4.32 (m, 4H, H-4_{Mann}, CH_2Bn), 4.23 – 4.06 (m, 2H, H-3_{Gul}, C*H*H Bn), 3.97 – 3.65 (m, 7H, H-2_{Gul}, H-4_{Gul} , H-6_{Gul}, H-2_{Mann}, H-5_{Gul}, H-3_{Mann}), 3.55 (s, 3H, CH_3O), 2.26 (s, 3H, CH_3CO), 1.00 (s, 9H, 3xCH_3 *tert*-Bu), 0.93 (s, 9H, 3xCH_3 *tert*-Bu). ^{13}C–APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 169.8(-$COOCH_3$), 139.3, 138.3, 137.8, 136.9($C_{q\ arom}$), 131.7, 129.6(CH_{arom}), 129.4($C_{q\ arom}$),128.5, 128.4, 128.3, 128.2, 128.0, 127.9, 127.8, 127.8, 127.7, 127.5, 127.5(CH_{arom}), 97.6(C-1_{Gul}), 83.3 (C-1_{Mann}, the chemical shift of this carbon is determined from the HSQC spectrum because it is not apparent in the APT spectrum), 75.8(C-3_{Mann}, C-2_{Gul}), 75.0(C-2_{Mann}), 74.2(C-4_{Mann}), 73.3(C-4_{Gul}), 73.0(C-3_{Gul}), 73.3, 72.6, 72.4, 71.5(CH_2Bn), 66.9(C-6_{Gul}), 64.7(C-5_{Gul}), 52.0(-$COOCH_3$), 27.6, 27.3(CH_3 *tert*-Bu), 23.3, (C_q *tert*-Bu), 21.1(CH_3CO), 20.5(C_q *tert*-Bu). $[\alpha]^{20}_D$ = -25° (c = 0.44, $CHCl_3$). IR (neat): 698, 737, 799, 1016, 1086, 1117, 1140,

1749, 2859, 2891, 2932. HR-MS: [M+H$^+$] Calculated for $C_{56}H_{68}O_{11}SSi$: 977.43244; found: 977.43354.

Methyl (*p*-methyphenyl 2,3-di-*O*-benzyl-4-*O*-[2,3-di-*O*-benzyl-4,6-di-hydroxyl-α-L-gulopyranosyl]- 1-thio-α-D-mannopyranosyl uronate) (13*): A HF/Pyridine solution (675 ul) was added to a solution of compound **13** (0.9 g, 0.92 mmol) in a mixture of THF (5 ml) and pyridine (5 ml) at 0 °C. The reaction was allowed to stir overnight at room temperature. Then sat. aq. $NaHCO_3$ was added to neutralize the mixture, which was subsequently diluted with EtOAc, washed with sat. aq. NaCl. The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. Purification by column chromatography (silica gel, pentane/EtOAc, 2/1, v/v) yielded **13*** as a colourless oil (0.65 g, 85%). TLC: R_f = 0.52 (pentane/EtOAc, 1/1, v/v). ^{1}H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.64 – 6.88 (m, 24H, CH_{arom}), 5.66 (d, *J* = 7.2 Hz, 1H, H-1_{Mann}), 5.09 (d, *J* = 4.0 Hz, 1H, H-1_{Gul}), 4.86 (d, *J* = 11.7 Hz, 1H, CH_2Bn), 4.73 – 4.34 (m, 8H, H-5_{Mann}, H-4_{Mann}, CH_2Bn), 4.31 – 4.12 (m, 1H, CH_2Bn), 4.06 – 3.67 (m, 6H, H-5_{Gul}, H-4_{Gul}, H-2_{Gul}, H-3_{Gul}, H-2_{Mann}, H-3_{Mann}), 3.51 (bs, 5H, H-6_{Gul}, CH_3 $COOCH_3$), 2.24 (s, 3H, CH_3 STol); ^{13}C–APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 169.9(-COO-), 139.0($C_{q\ arom}$), 138.3, 138.0, 137.6, 137.1($C_{q\ arom}$), 131.8(CH_{arom}), 130.3($C_{q\ arom}$), 129.6, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 127.9, 127.9, 127.8, 127.7, 127.7, 127.7, 127.6, 127.6, 127.5, 127.5, 127.4(CH_{arom}), 97.0(C-1_{Gul}), 85.7(C-1_{Mann}, the chemical shift of this carbon is determined from the HSQC spectrum because it is not apparent in the APT spectrum), 75.6(C-3_{Mann}), 75.0(C-3_{Gul}, C-2_{Mann}), 73.8(C-2_{Gul}, C-4_{Mann}), 73.6(C-5_{Mann}), 73.0, 72.4, 71.6(CH_2Bn), 71.5(C-4_{Gul}), 66.3(C-5_{Gul}), 63.8(C-6_{Gul}), 52.1(-$COOCH_3$), 21.1(CH_3CO). $[\alpha]^{20}_D$ = -40° (c = 0.88, $CHCl_3$). IR (neat): 696, 733, 808, 891, 910, 947, 1018, 1026, 1072, 1105, 1207, 1242, 1281, 1362, 1395, 1454, 1495, 1734, 1749, 2857, 2922, 3450. HR-MS: [M+Na$^+$] Calculated for $C_{48}H_{52}O_{11}S$: 859.31225; found: 859.31366.

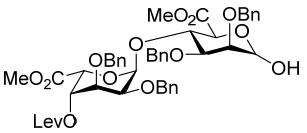
Methyl (*p*-methyphenyl 2,3-di-*O*-benzyl-4-*O*-[6-*O*-acetyl-2,3-di-*O*-benzyl-4-hydroxyl-α-L-gulopyranosyl]- 1-thio-α-D-mannopyranosyl uronate) (14): This product was prepared following the general procedure for selective acetylation of the gulosyl C-6-OH. Yield: 153 mg, (0.17 mmol), 87%. TLC: R_f = 0.26 (pentane:ethyl acetate = 2:1). ^{1}H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.66 – 6.87 (m, 20H, CH_{arom}), 5.71 (d, *J* = 8.5 Hz, 1H, H-1_{Mann}), 5.15 – 4.97 (m, 1H, H-1_{Gul}), 4.86 (d, *J* = 11.8 Hz, 1H, CH_2Bn), 4.71 – 4.35 (m, 8H, H-5_{Mann}, H-4_{Mann}, CH_2Bn), 4.31 – 4.03 (m, 3H, H-5_{Gul}, CH_2Bn, H-6_{Gul}), 3.98 (dd, *J* = 11.4, 6.6 Hz, 1H, H-6_{Gul}), 3.92 – 3.72 (m, 5H, H-3_{Gul}, H-2_{Gul}, H-4_{Gul}, H-3_{Mann}, H-2_{Mann}), 3.51 (s, 3H, CH_3 $COOCH_3$), 2.67 (d, *J* = 5.4 Hz, 1H, G_4-OH), 2.25 (s, 3H, CH_3 STol), 1.98 (s, 3H, CH_3CO); ^{13}C –APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 171.1, 169.7(-COO-), 138.9, 138.1, 137.8($C_{q\ arom}$), 131.6(CH_{arom}), 130.5($C_{q\ arom}$), 129.6, 128.5, 128.5, 128.4, 128.3, 128.3, 128.1, 128.0, 128.0, 127.9, 127.8, 127.8, 127.7, 127.6, 127.6(CH_{arom}), 96.7(C-1_{Gul}), 82.8(C-1_{Mann}), 75.7(C-3_{Gul}, C-3_{Mann}), 75.1(C-2_{Mann}), 74.0(C-4_{Mann}), 73.7(C-5_{Mann}), 73.7(C-2_{Gul}), 73.2, 72.7, 72.6, 71.8(CH_2Bn), 69.4(C-4_{Gul}), 65.6(C-5_{Gul}), 63.4(C-6_{Gul}), 52.1(-$COOCH_3$), 29.8(CH_3CO), 21.1(CH_3 STol). $[\alpha]^{20}_D$ = -27° (c = 0.94, $CHCl_3$). HR-MS: [M+Na$^+$] Calculated for $C_{50}H_{54}O_{12}S$: 901.32282; found: 901.32365.

Methyl (*p*-methyphenyl 2,3-di-*O*-benzyl-4-*O*-[methyl 2,3-di-*O*-benzyl-4-hydroxyl-α-L-gulopyranosyl uronate]-1-thio-α-D-mannopyranosyl uronate) (15): Compound **13*** (1.86 g, 2.61 mmol) was dissolved in DCM/*tert*-BuOH/H_2O (22.5 ml, 4/4/1, v/v/v) and the mixture was cooled to 0 °C and treated with TEMPO (72 mg, 0.46 mmol) and BAIB (1.92 g, 5.96 mmol). After stirring overnight at 4 °C, $Na_2S_2O_3$ was added, the mixture diluted with EtOAc, washed with sat. aq. NaCl and the organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. The crude residue was dissolved in DMF (15 ml), followed by the addition of K_2CO_3 (580 mg, 4.2 mmol) and MeI (250 ul) at 0 °C. The mixture was allowed to stir overnight at 4 °C, after which it was diluted with EtOAc, washed with sat. aq. NaCl. The organic phase was dried over Na_2SO_4 and concentrated *in vacuo.* Purification by column chromatography (silica gel, pentane/EtOAc, 2/1, v/v) yielded **6** as a colourless oil (1.9 g, two steps: 98%). TLC: R_f = 0.50 (pentane/EtOAc, 1/1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.52 (d, *J* = 8.1 Hz, 2H, CH_{arom}), 7.47 – 7.11 (m, 20H, CH_{arom}), 7.04 (d, *J* = 8.2 Hz, 2H, CH_{arom}), 5.69 (d, *J* = 8.0 Hz, 1H, H-1_{Mann}), 5.15 (d, *J* = 3.8 Hz, 1H, H-1_{Gul}), 4.85 (d, *J* = 11.8 Hz, 1H, CH_2Bn), 4.71 – 4.30 (m, 7H, H-5_{Gul}, CH_2Bn, H-5_{Mann}, H-4_{Mann}), 4.19 (m, 2H, H-4_{Gul}, CH_2Bn), 3.91 – 3.59 (m, 7H, H-3_{Gul}, H-2_{Gul}, H-3_{Mann}, H-2_{Mann}, CH_3 $COOCH_3$), 3.51 (s, 3H, CH_3 $COOCH_3$), 2.46 (d, *J* = 6.1 Hz, 1H, C-4_{Glu}-OH), 2.26 (s, 3H, CH_3 STol); ^{13}C–APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 170.4, 169.6(-COO-), 138.7, 138.2($C_{q\ arom}$), 131.9(CH_{arom}), 130.2($C_{q\ arom}$), 129.6, 128.6, 128.5, 128.3, 128.0, 127.9, 127.8(CH_{arom}), 97.8(C-1_{Gul}), 82.8(C-1_{Mann}, the chemical shift of this carbon is according to HSQC because it can not seen from carbon spectrum), 75.4(C-3_{Mann}), 75.2(C-3_{Gul}), 74.8(C-4_{Mann}, C-2_{Mann}), 74.0(C-5_{Mann}), 73.4(C-2_{Gul}), 73.2, 72.5, 72.5, 72.2(CH_2Bn), 70.2(C-4_{Gul}), 68.9(C-5_{Gul}), 52.4(-$COOCH_3$), 52.2(-$COOCH_3$), 21.2(CH_3 STol). $[\alpha]^{20}_D$ = -16° (c = 0.42, $CHCl_3$). IR (neat): 698, 737, 810, 947, 1028, 1072, 1088, 1121, 1209, 1304, 1456, 1749, 2311, 2349, 2378, 2922, 3030, 3450. HR-MS: [M+Na^+] Calculated for $C_{49}H_{52}O_{12}S$: 887.30717; found: 887.30827.

Methyl (*p*-methyphenyl 2,3-di-*O*-benzyl-4-*O*-[methyl 2,3-di-*O*-benzyl-4-levulinoyl-α-L-gulopyranosyl uronate]-1-thio-α-D-mannopyranosyl uronate) (16): EDCI (0.29 g, 0.151 mmol) and DIPEA (0.25 ml, 0.144 mmol) were added to a solution of compound **15** (0.83 g, 0.096 mmol), levulinic acid (178 mg, 0.153 mmol) and DMAP (180 mg, 0.148 mmol) in DCM (4 ml) at 0 °C. The mixture was allowed to stir overnight at room temperature, and then diluted with EtOAc, washed with sat. aq. NaCl. The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. Purification by column chromatography (silica gel, pentane/DCM/EtOAc, 3/1/1, v/v/v) yielded **16** as a colourless oil (821 mg, 92%). TLC: R_f = 0.74 (pentane/DCM/EtOAc, 1/1/1, v/v/v); ^{1}H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.58 – 6.83 (m, 24H, CH_{arom}), 5.66 (d, *J* = 7.7 Hz, 1H, H-1_{Mann}), 5.29 (m, 1H, H-4_{Gul}), 5.16 (d, *J* = 4.0 Hz, 1H, H-1_{Gul}), 4.87 (d, *J* = 11.7 Hz, 1H, CH_2Bn), 4.80 (bs, 1H, H-5_{Gul}), 4.78 – 4.29 (m, 8H, CH_2Bn, H-5_{Mann}, H-4_{Mann}), 4.20 (d, *J* = 11.7 Hz, 1H, CH_2Bn), 3.95 (t, *J* = 3.6 Hz, 1H, H-3_{Gul}), 3.74(m, 3H, H-2_{Gul}, H-3_{Mann}, H-2_{Mann}), 3.63 (s, 3H, CH_3 $COOCH_3$), 3.52 (s, 3H, CH_3 $COOCH_3$), 2.86 – 2.57 (m, 2H, CH_2 Lev), 2.58 – 2.35 (m, 2H, CH_2 Lev), 2.28 (s, 3H, CH_3 STol), 2.17 (s, 3H, CH_3CO); ^{13}C–APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 206.2(C=O Lev), 171.5,

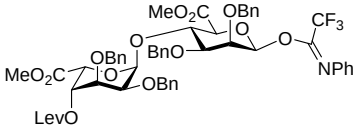
169.5, 168.9(-COO-), 138.5, 137.9, 137.8($C_{q\ arom}$), 131.9(CH_{arom}), 130.3($C_{q\ arom}$), 129.6, 128.5, 128.5, 128.4, 128.3, 128.0, 127.9, 127.9, 127.9, 127.8, 127.7, 127.6, 127.6(CH_{arom}), 97.6(C-1_{Gul}), 83.1(C-1_{Mann}, the chemical shift of this carbon is according to HSQC because it can not seen from carbon spectrum), 75.2(C-3_{Mann}, C-4_{Mann}), 74.8(C-2_{Mann}, 74.0(C-5_{Mann}), 73.4(CH_2Bn), 73.0(C-2_{Gul}), 72.6(C-3_{Gul}), 72.5, 71.7(CH_2Bn), 71.2(C-4_{Gul}), 66.9(C-5_{Gul}), 52.3($COOCH_3$), 52.1($COOCH_3$), 37.9(CH_2 Lev), 29.8(CH_3CO), 28.0(CH_2 Lev), 21.2(CH_3 STol). $[\alpha]^{20}_D$ = -23° (c = 0.5, $CHCl_3$). IR (neat): 698, 739, 1028, 1038, 1076, 1123, 1209, 1242, 1364, 1454, 1717, 1748, 2922. HR-MS: [M+H^+] Calculated for $C_{54}H_{58}O_{14}S$: 963.36200; found: 963.36433.

Methyl (2,3-di-*O*-benzyl-4-*O*- [methyl 2,3-di-*O*-benzyl-4-levulinoyl-α-L-gulopyranosyl uronate]-α-D-mannopyranosyl uronate) (17): NIS (170 mg, 0.756 mmol) and TFA (59 ul) were added to a solution of **16** (724 mg, 0.752 mmol) in



CH_2Cl_2 (8 ml) at 0 °C. After analysis by TLC showed complete consumption of the starting material, the reaction was quenched with Et_3N. Saturated $Na_2S_2O_3$ (aq) was added to the reaction mixture, which was then stirred for 30 min. The aqueous layer was extracted twice with CH_2Cl_2, and concentrated *in vacuo*. Purification by column chromatography (silica gel, pentane/DCM/EtOAc, 3/1/1, v/v/v) yielded **17** as a colourless oil (587 mg, 91%). TLC: R_f = 0.36 (pentane/DCM/EtOAc, 3/2/2, v/v/v); ^{1}H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.48 – 7.08 (m, 20H, CH_{arom}), 5.48 (d, *J* = 6.0 Hz, 1H, H-1_{Mann}), 5.28 (dt, *J* = 4.3, 2.2 Hz, 1H, H-4_{Gul}), 5.18 (d, *J* = 3.8 Hz, 1H, H-1_{Gul}), 4.86 – 4.81 (m, 2H, H-5_{Gul}, CH_2Bn), 4.72 – 4.41 (m, 8H, H-5_{Gul}, CH_2Bn, H-5_{Mann}, H-4_{Mann}), 4.32 (d, *J* = 12.0 Hz, 1H, CH_2Bn), 3.93 (q, *J* = 3.3 Hz, 1H, H-3_{Gul}), 3.84 (dd, *J* = 5.8, 2.8 Hz, 1H, H-3_{Mann}), 3.78 – 3.68 (m, 1H, H-2_{Gul}), 3.62 (s, 3H, CH_3 $COOCH_3$), 3.60 – 3.53 (m, 1H, H-2_{Mann}), 3.52 (s, 3H, CH_3 $COOCH_3$), 2.69 (m, 2H, CH_2 Lev), 2.51 – 2.42 (m, 2H, CH_2 Lev), 2.16 (s, 3H, CH_3CO); ^{13}C–APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 206.3(C=O Lev), 171.5, 169.9, 168.8(-COO-), 138.5, 137.8 $C_{q\ arom}$), 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 127.4(CH_{arom}), 97.7(C-1_{Gul}),, 92.7(C-1_{Mann}), 76.6(C-3_{Mann}), 76.4(C-2_{Mann}), 75.2(C-4_{Mann}), 73.6(C-5_{Mann}), 73.2, 72.9(CH_2Bn), 72.7(C-2_{Gul}), 72.5(C-3_{Gul}), 72.3, 71.6(CH_2Bn), 70.9(C-4_{Gul}), 66.7(C-5_{Gul}), 52.3($COOCH_3$), 52.2($COOCH_3$), 37.9(CH_2 Lev), 29.8(CH_3CO), 28.0(CH_2 Lev); ^{13}C -HMBCipvGATED ($CDCl_3$, 100 MHz): 97.7($J_{C1,H1}$ = 170Hz, C-1_{Gul}), 92.7($J_{C1,H1}$ = 170Hz, C-1_{Mann}). IR (neat): 677, 698, 735, 814, 908, 926, 957, 1026, 1074, 1088, 1121, 1207, 1240, 1304, 1362, 1454, 1717, 1744, 2924, 2951. HR-MS: [M+H^+] Calculated for $C_{47}H_{52}O_{15}$: 857.33790; found: 857.33937.

Methyl (2,3-di-*O*-benzyl-4-*O*-[methyl 2,3-di-*O*-benzyl-4-levulinoyl-α-L-gulopyranosyl uronate]-1-O-(*N*-phenyl trifluoroacetimidoyl)-α/β-D-mannopyranosyl uronate) (18): Compound

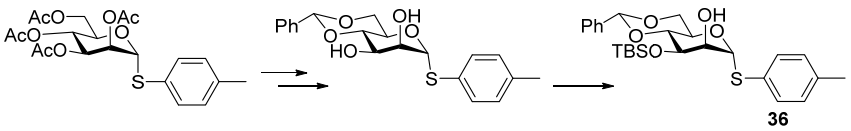


17 (580 mg, 0.677 mmol) was dissolved in acetone (6 ml) and the solution was cooled to 0 °C. *N*-phenyl trifluoroacetimidoyl chloride (211 mg, 1.02 mmol) and potassium carbonate (112 mg, 0.812 mmol) were added and the resulting suspension was stirred overnight at

room temperature. Then, Et_3N was added to the reaction mixture, which was filtered and the resulting filtrate was concentrated *in vacuo*. Purification by column chromatography (silica gel, pentane/DCM/EtOAc, 3/1/1, v/v/v) yielded **18** as a colourless syrup (680 mg, 98%, α:β = 3.9:1). TLC: R_f = 0.43 (pentane/DCM/EtOAc, 2/1/1, v/v/v); ^{1}H NMR (CD_3COCD_3, 400 MHz,HH-COSY, HSQC): δ 7.60 – 7.13 (m, 22H, CH_{arom}), 7.08 (t, *J* = 7.5 Hz, 1H, CH_{arom}), 6.88 – 6.74 (m, 2H, CH_{arom}), 6.44 (bs, 1H, H-1_{Mann}), 5.37 – 5.14 (m, 2H, H-1_{Gul}, H-4_{Gul}), 4.97 (bs, 1H, H-5_{Gul}), 4.88 (d, *J* = 11.5 Hz, 1H, CH_2Bn), 4.75 – 4.28 (m, 9H, CH_2Bn, H-5_{Mann}, H-4_{Mann}), 4.12 – 3.85 (m, 3H, H-3_{Gul}, H-3_{Mann}, H-2_{Mann}), 3.81 (t, *J* = 3.6 Hz, 1H, H-2_{Gul}), 3.60(s, 3H, CH_3 $COOCH_3$), 3.58 (s, 3H, CH_3 $COOCH_3$), 2.70 (m, 2H, CH_2 Lev), 2.42 (m, 2H, CH_2 Lev), 2.08 (s, 3H, CH_3CO); ^{13}C–APT NMR (CD_3COCD_3, 100 MHz, HSQC): δ 206.7(C=O Lev), 172.1, 169.5, 169.1(-COO-), 140.0, 139.5, 139.2, 138.8 $C_{q\ arom}$), 129.7, 129.6, 129.2, 129.1, 129.1, 129.0, 128.9, 128.7, 128.6, 128.6, 128.5, 128.4, 128.4, 128.3, 128.3, 128.1, 128.0, 125.2, 124.8, 120.3(CH_{arom}), 97.8(C-1_{Gul}), 95.5(C-1_{Mann}), 77.2(C-3_{Mann}), 75.4(C-2_{Mann}), 75.3(C-4_{Mann}), 74.5(C-2_{Gul}), 74.2(C-5_{Mann}), 74.0(C-2_{Gul}), 73.8(C-3_{Gul}), 73.7, 73.1, 72.2, 71.8(CH_2Bn), 71.7(C-4_{Gul}), 67.6(C-5_{Gul}), 52.6($COOCH_3$), 52.3($COOCH_3$), 38.3(CH_2 Lev), 28.7 (CH_2 Lev). HR-MS: [M+Na^+] Calculated for $C_{55}H_{56}O_{15}F_3N$: 1050.34943; found: 1050.35019.

The synthesis of disaccharide acceptor (20)

***p*-methoxyl benzyl 4,6-*O*-benzylidene-3-*O*-(*tert*-butyl-di-methyl)-silyl-1-thio-α-D-mannopyranoside (36)**

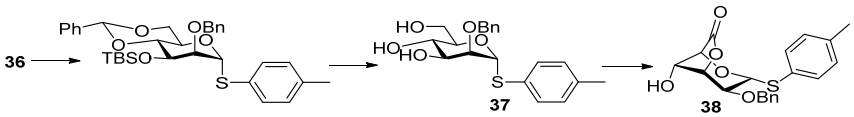


36

The starting material *p*-methyl phenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-α-D-mannopyranoside (4.81 g, 10.58 mmol) was dissolved in MeOH (100 ml) and then the catalytic amount NaOMe was added. The reaction was allowed to stir for overnight at room temperature. The mixture was neutralized with Amberlite IR120 (H^+) resin, filtered, and concentrated under reduced pressure. The residue was dried over in vacuo, which was used in the next step without further purification. To a solution of *p*-methyl phenyl 1-thio-α-D-mannopyranoside in anhydrous DMF (20 mL) were added, successively with stirring under argon at 0 °C, α,α-dimethoxytoluene (2.38 mL, 15.9 mmol) and tetrafluoroboric acid diethyl ether complex (1.81 mL, 13.3 mmol). The mixture was stirred at room temperature overnight, neutralized with Et_3N (20 mL), and concentrated under reduced pressure. The residue, a yellow-orange solid, diluted with EtOAc, washed with sat. aq. NaCl, the organic phase was dried over Na_2SO_4 and concentrated in vacuo. Which was used in the next step without further purification.[4] After *p*-methoxyl benzyl 4,6-*O*-benzylidene-1-thio-α-D-mannopyranoside was dissolved in anhydrous DMF (14 ml), imidazole (1.44 g, 21.16 mmol) and TBSCl (1.44 g, 9.52 mmol) were added to the mixture at 0 °C. Then the mixture was stirred at room temperature overnight, quenched with MeOH (10 mL), and concentrated under reduced pressure. The residue was diluted with EtOAc, washed with sat. aq. NaCl, the organic phase was dried over Na_2SO_4 and concentrated in vacuo. Purification

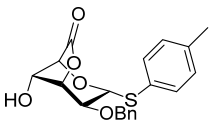
by column chromatograpy (silica gel, pentane/EtOAc, 20/1, v/v) yielded **36** as a colourless foam (1.72 g, four steps yield: 33%). TLC: R_f = 0.52 (pentane/EtOAc, 8/1, v/v); $[\alpha]^{20}_D$ = +167° (c = 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.59 – 7.43 (m, 2H, CH STol), 7.43 – 7.29 (m, 5H, CH_{arom}), 7.14 (d, *J* = 8.2 Hz, 2H, CH STol), 5.58 (s, 1H, H-1), 5.56 (s, 1H, CH benzylidene), 4.34 (m, 1H, H-5), 4.26 – 4.06 (m, 3H, H-2, H-3, H-6), 4.03 – 3.72 (m, 2H, H-4, H-6), 2.34 (s, 3H, CH_3 STol), 0.91 (d, *J* = 3.0 Hz, 9H, TBS), 0.14 (s, 3H, TBS), 0.09 (s, 3H, TBS). ^{13}C –APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 138.1, 137.5($C_{q\ arom}$), 132.5, 130.1(CH_{arom}), 129.6($C_{q\ arom}$), 129.0, 128.3, 126.2(CH_{arom}), 102.0(CH benzylidene), 88.0(C-1), 79.3(C-4), 73.4(C-2), 70.2(C-3), 68.6(C-6), 64.5(C-5), 25.9(CH_3 *tert*-Bu), 21.3(CH_3 STol), 18.3(C_q *tert*-Bu), -4.2(CH_3 TBS), -4.9(CH_3 TBS). IR (neat): 610, 675, 696, 748, 777, 808, 835, 851, 966, 1005, 1084, 1211, 1252, 1379, 1462, 1493, 2857, 2893, 2927, 2951. HR-MS: [M+H$^+$] Calculated for $C_{26}H_{36}O_5SSi$: 489.21255; found: 489.21238.

The synthesis of monosaccharide acceptor *p*-methyl phenyl 2-*O*-benzyl-1-thio- α-D-mannopyranosidurone-6,3-lactone (38)

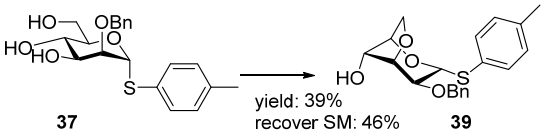


BnBr (380 ul, 3.0 mmol) and NaH 60% dispersion in mineral oil (120 mg, 3.0 mmol) were added to the mixture of *p*-methyl phenyl 4,6-*O*-benzylidene-3-*O*-(*tert*-butyl-di-methyl)-silyl-1-thio-α-D-mannopyranoside **36** (733 mg, 1.5 mmol) in DMF (10 ml) at 0 °C. And then the mixture was stirred at room temperature overnight, quenched with H_2O, diluted with EtOAc, washed with sat. aq. NaCl, the organic phase was dried over Na_2SO_4 and concentrated in vacuo. Which was used in the next step without further purification. The residue was dissolved in MeOH (20 ml), and then TsOH/H_2O was added to the mixture until the PH = 2. Then the mixture was stirred at room temperature overnight, quenched with Et_3N (0.5 mL), and concentrated under reduced pressure. The residue was diluted with EtOAc, washed with sat. aq. NaCl, the organic phase was dried over Na_2SO_4 and concentrated in vacuo. Purification by column chromatograpy (silica gel, pentane/EtOAc, 1/1, v/v) yielded **37** as a white solid (350 mg, two steps yield: 62%). TLC: R_f = 0.26 (pentane/EtOAc, 1/1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz, HH-COSY, HSQC): δ 7.31-7.12 (m, 9H, CH_{arom}), 5.49 (d, *J* = 7.5 Hz, 1H, H-1), 4.85 – 4.61 (m, 1H, CH_2 Bn), 4.52 (dd, *J* = 11.7, 3.3 Hz, 1H, CH_2 Bn), 4.18 –3.82 (m, 6H, H-2, H-3, H-4, H-5, H-6), 2.33 (s, 3H, CH_3 STol). ^{13}C –APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 138.2, 137.3($C_{q\ arom}$), 132.7, 130.1, 128.8, 128.2(CH_{arom}), 85.9(C-1), 79.5(C-2), 72.7(CH_2 Bn), 73.0, 72.0, 69.0(C-3, C-4, C-5), 62.3(C-6), 21.3(CH_3 STol). $[\alpha]^{20}_D$ = +100° (c = 0.42, $CHCl_3$). IR (neat): 665, 698, 737, 764, 791, 845, 914, 1018, 1040, 1069, 1099, 1207, 1352, 1398, 1454, 1493, 2920, 3298, 3366. HR-MS: [M+Na$^+$] Calculated for $C_{20}H_{24}O_5S$: 399.12367; found: 399.12361.

***p*-methyl phenyl 2-*O*-benzyl-1-thio-α-D-mannopyranosidurone-6,3-lactone (38)**: *p*-methoxyl phenyl 2-*O*-benzyl-1-

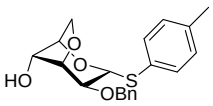


thio-α-D-mannopyranoside **37** (75 mg, 0.2mmol) was dissolved in DCM/*tert*-Buol/H_2O (3 ml, 1/1/1,v/v/v), the mixture was cooled to 0 °C and treated with TEMPO (8 mg, 0.051 mmol) and BAIB (161 mg, 0.5 mmol). After stirring for overnight at 4 °C, $Na_2S_2O_3$ was added, diluted with EtOAc, washed with sat. aq. NaCl, the organic phase was dried over Na_2SO_4 and concentrated in vacuo. The crude residue was dissolved in DCM (7 ml), followed by the addition of DIPEA (45 ul, 0.25 mmol) and ethyl chloroformate (24 ul, 0.25 mmol) at 0 °C. The mixture was allowed to stir for 3 h at room temperature, and then diluted with EtOAc, washed with sat. aq. NaCl, the organic phase was dried over Na_2SO_4 and concentrated in vacuo. Purification by column chromatograpy (silica gel, pentane /EtOAc, 2/1, v/v) yielded **38** as a colourless form (28 mg, 38%).[5] TLC: R_f = 0.22 (pentane/ EtOAc, 2/1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.48 – 7.27 (m, 7H, CH_{arom}), 7.12 (d, *J* = 8.1 Hz, 2H, CH_{arom}), 4.94 – 4.57 (m, 4H, H-1, H-3, CH_2 Bn), 4.34 – 4.00 (m, 2H, H-4, H-5), 3.78 (dd, *J* = 8.9, 1.7 Hz, 1H, H-2), 2.33 (s, 3H, CH_3 STol); ^{13}C –APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 169.8(-COO-), 139.2, 137.2($C_{q\ arom}$), 133.8, 130.1, 128.6, 128.2, 128.2, 127.8(CH_{arom}), 84.6(C-1), 78.6(C-3), 73.9(C-5), 73.4(C-2), 73.1(CH_2 Bn), 69.4(C-4), 21.3(CH_3 STol). $[\alpha]^{20}_D$ = +42° (c = 1, $CHCl_3$). IR (neat): 698, 737, 810, 876, 930, 1002, 1016, 1038, 1074, 1090, 1157, 1209, 1258, 1360, 1398, 1454, 1748, 1797, 2922. HR-MS: [M+Na^+] Calculated for $C_{20}H_{20}O_5S$: 373.11042; found: 373.11040.



37 **39**

synthesis of 39: *p*-methyl phenyl 2-*O*-benzyl-1-thio-α-D-mannopyranoside **37** (347 mg, 0.923 mmol) was dissolved

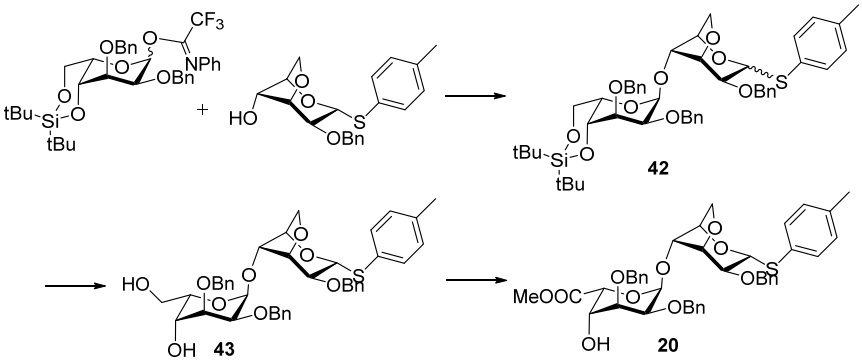


in DCM (4 ml), the mixture was cooled to -10 °C and treated with lutidine (161 ul, 1.385 mmol), DIPEA (241 mg, 1.385 mmol) and then Tf_2O (186 ul, 1.11 mmol). After stirring for overnight at 0 °C, diluted with EtOAc, washed with sat. aq. NaCl, the organic phase was dried over Na_2SO_4 and concentrated in vacuo. Purification by column chromatograpy (silica gel, pentane/EtOAc, 3/2, v/v) yielded **39** as a colourless form (130 mg, 39%) and recover starting material SI-2 (159 mg). TLC: R_f = 0.22 (pentane/ EtOAc, 2/1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.51 – 7.26 (m, 7H, CH_{arom}), 7.12 (d, *J* = 8.1 Hz, 2H, CH_{arom}), 5.00 (d, *J* = 8.7 Hz, 1H, H-1), 4.68 (q, *J* = 11.7 Hz, 2H, CH_2 Bn), 4.34 – 4.02 (m, 4H, H-3, H-5, H-4, H-6), 3.93 (dd, *J* = 10.9, 3.0 Hz, 1H, H-6), 3.55 (dd, *J* = 8.7, 1.6 Hz, 1H, H-2), 2.33 (s, 3H, CH_3 STol); ^{13}C –APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 138.7, 137.8($C_{q\ arom}$), 133.9, 129.9(CH_{arom}), 128.4($C_{q\ arom}$), 128.4, 128.2, 127.9(CH_{arom}), 83.2(C-1), 76.7(C-5), 75.6(C-3), 74.6(C-2), 72.5(CH_2 Bn), 71.4(C-4), 68.5(C-6), 21.2(CH_3 STol). $[\alpha]^{20}_D$ = +76° (c = 1, $CHCl_3$). IR (neat): 633, 696, 733, 808, 853, 924, 943, 962, 995, 1018, 1058, 1092, 1101, 1263, 1317, 1454, 1493, 2922, 3372. HR-MS: [M+Na^+] Calculated for $C_{20}H_{22}O_4S$: 359.13116; found: 359.13114.

The glycosylation of the imidate donor 3 with the locked $^1C_4$ conformational acceptor 38

Imidate donor **7** (162 mg, 0.242 mmol) and acceptor **38** (60 mg, 0.161 mmol) were together co-evaporated with toluene (three times). The residue was dissolved in dry DCM (1.6 ml). The solution was cooled to -78 °C and followed by adding TBSOTf (7.4 ul, 0.032 mmol) and the reaction was allowed to stir for overnight at -78°C to -20 °C. The reaction was quenched with Et_3N and diluted with EtOAc, washed with sat. aq. NaCl, the organic phase was dried over Na_2SO_4 and concentrated in vacuo. Purification by column chromatograpy (silica gel, pentane/EtOAc, 2/1, v/v to DCM/MeOH, 10/1, v/v) yielded **41** as a colourless syrum (89 mg, 58%). TLC: R_f = 0.39 (DCM/MeOH, 10/1, v/v). For this reaction, the glycosylation product **40** was not stable in basic condition, the lactone ring was opened and yield the salt of Et_3N **41**. ^{1}H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.68 – 6.84 (m, 19H, CH_{arom}), 5.72 – 5.44 (m, 1H, H-1_{Mann}), 5.22 (s, 1H, H-1_{Gul}), 4.90 (d, *J* = 11.9 Hz, 1H, CH_2Bn), 4.77 – 4.49 (m, 5H, CH_2Bn), 4.40 – 3.74 (m, 9H), 3.16 – 2.85 (m, 6H, NEt_3), 2.26 (s, 3H(CH_3 STol), 1.13 (t, *J* = 7.4 Hz, 9H, NEt_3), 0.98 (s, 9H, 3xCH_3 *tert*-Bu), 0.86 (s, 9H, 3xCH_3 *tert*-Bu); ^{13}C NMR (101 MHz, $CDCl_3$): δ 138.6, 137.9, 137.7($C_{q\ arom}$), 130.3(CH_{arom}), 128.5($C_{q\ arom}$), 128.4, 128.4, 128.3, 128.2, 128.0, 127.8(CH_{arom}), 114.1, 97.1(C-1_{Gul}), 85.0(C-1_{Mann}), 77.7, 77.5, 76.4, 75.9, 73.4, 72.7, 72.3, 71.7, 71.6, 71.2, 70.8, 69.6, 67.0, 45.4(CH_2 NEt_3), 27.6(CH_3 *tert*-Bu), 27.2(CH_3 *tert*-Bu), 23.3(C_q *tert*-Bu), 21.2(CH_3 STol), 20.4(C_q *tert*-Bu), 8.4(CH_3 NEt_3). IR (neat): 602, 638, 650, 696, 735, 797, 825, 860, 885, 935, 1018, 1028, 1083, 1138, 1209, 1242, 1362, 1454, 1472, 1602, 1743, 2857, 2930. HR-MS: [M+H$^+$] Calculated for $C_{48}H_{60}O_{11}SSi$: 873.36984; found: 873.37065.

The synthesis of disaccharide acceptor (20)



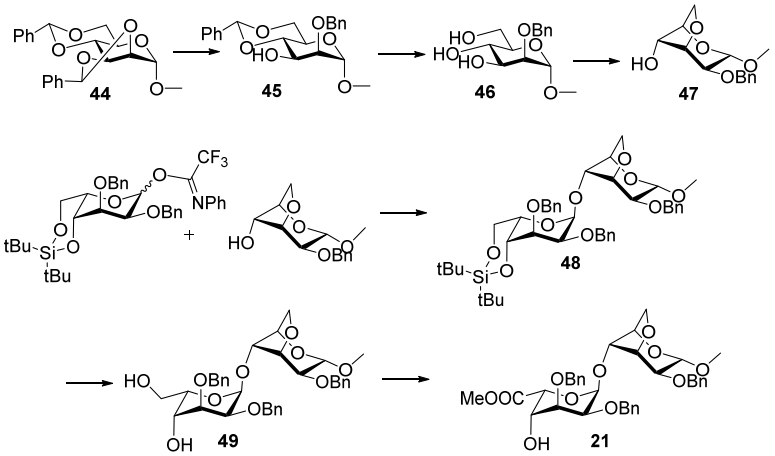
As described for the synthesis of **13** using **7** and **12**. The **42**, the 1-thio-α-D-mannopyranoside was epimerided in glycosylation condition (α/β = 5/1), was obtained (152 mg, 81%). TLC: R_f = 0.20 (PhMe/EtOAc, 4/3, v/v). $[\alpha]^{20}_D$ = -22° (c = 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.65 – 7.54 (m, 2H, CH_{arom}), 7.53 – 7.24 (m, 15H, CH_{arom}), 7.15 (d, *J* = 8.1 Hz, 2H, CH_{arom}), 5.44 (d, *J* = 2.1 Hz, 0.2H), 5.33 – 5.14 (m, 4H), 5.00 (d, *J* = 12.1 Hz, 1H), 4.88 – 4.67 (m, 3H), 4.64 – 4.49 (m, 3H), 4.46 – 4.31 (m, 5H), 4.31 – 3.95 (m, 8H), 3.88 (dd, *J* = 8.9, 1.5 Hz, 1H), 3.66 – 3.60 (m, 0.2H), 2.38 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 139.5, 138.3, 138.2, 137.1, 131.7, 131.6, 129.7, 128.5, 128.3, 128.2, 128.0, 128.0, 127.6, 127.5, 127.4, 97.9, 95.6, 85.4, 83.0, 78.0, 77.1, 76.3, 75.9, 74.0, 73.3, 73.0, 72.9,

72.8, 72.6, 72.0, 71.5, 71.2, 69.7, 67.0, 65.0, 27.7, 27.2, 23.3, 21.2, 20.5. IR (neat): 650, 696, 737, 799, 826, 862, 937, 1001, 1028, 1067, 1086, 1105, 1118, 1141, 1454, 1472, 1495, 2857, 2889, 2932. HR-MS: [M+Na^+] Calculated for $C_{48}H_{60}O_9SSi$: 863.36195; found: 863.36157.

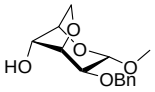
As described in the general procedure for deprotecting of di-*tert*-butyl silylation. The **43** was obtained (85 mg, 71%). TLC: R_f = 0.20 (DCM/acetone, 5/1, v/v). $[\alpha]^{20}_D$ = -36° (c = 1, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.53 – 7.16 (m, 17H, CH_{arom}), 7.07 (d, *J* = 8.3 Hz, 2H, CH_{arom}), 5.19 (d, *J* = 3.8 Hz, 1H, H-1_{Gul}), 5.13 (d, *J* = 8.9 Hz, 1H, H-1_{Mann}), 4.96 (d, *J* = 12.2 Hz, 1H, CH_2Bn), 4.87 (d, *J* = 12.2 Hz, 1H, CH_2Bn), 4.62 (dd, *J* = 20.5, 12.1 Hz, 2H, CH_2Bn), 4.50 (d, *J* = 11.5 Hz, 1H, CH_2Bn), 4.45 (t, *J* = 2.8 Hz, 1H, H-5_{Mann}), 4.41 – 4.28 (m, 2H, H-3_{Mann}, CH_2Bn), 4.22 (dd, *J* = 6.3, 2.6 Hz, 1H, H-4_{Mann}), 4.09 (d, *J* = 10.7 Hz, 1H, H-6_{Mann}), 4.06 – 3.71 (m, 8H, H-5_{Gul}, H-4_{Gul} , H-2_{Gul}, H-6_{Mann}, H-3_{Gul}, H-2_{Mann}, H-6_{Gul}), 3.61 (bs, 1H, -OH), 2.29 (s, 3H, CH_3 STol). ^{13}C –APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 139.1, 138.5, 138.1, 137.3($C_{q\ arom}$), 131.7(CH_{arom}), 131.7($C_{q\ arom}$), 129.7, 128.4, 128.4, 128.3, 128.3, 127.7, 127.7, 127.6, 127.5, 127.5(CH_{arom}), 95.9(C-1_{Gul}), 85.4(C-1_{Mann}), 76.6, 76.1, 75.8(C-2_{Mann}, C-3_{Mann}, C-3_{Gul}), 74.2(C-4_{Mann}), 73.6(C-2_{Gul}), 73.0(CH_2Bn), 72.9(C-5_{Mann}), 71.8(CH_2Bn), 71.7(C-5_{Gul}), 69.7(C-6_{Mann}), 67.1(C-4_{Gul}), 63.8(C-6_{Gul}), 21.2(CH_3 STol).IR (neat): 696, 735, 810, 930, 943, 966, 999, 1026, 1058, 1101, 1209, 1265, 1312, 1354, 1454, 1493, 2889, 2920, 3433. HR-MS: [M+Na^+] Calculated for $C_{40}H_{44}O_9S$: 723.25982; found: 723.25911.

Disaccharide acceptor **20,** as described in the general procedure for oxidition and subsequent methylation. The disaccharide acceptor **20** was obtained (81 mg, 97%). TLC: R_f = 0.23 (DCM/acetone, 15/1, v/v). $[\alpha]^{20}_D$ = -38° (c = 0.58, $CHCl_3$). ^1H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.54 – 6.98 (m, 19H, CH_{arom}), 5.31 (d, *J* = 3.4 Hz, 1H, H-1_{Gul}), 5.13 (d, *J* = 8.9 Hz, 1H, H-1_{Mann}), 4.89 (dd, *J* = 12.1, 2.2 Hz, 2H, CH_2Bn), 4.76 (d, *J* = 2.8 Hz, 1H, H-5_{Gul}), 4.71 – 4.19 (m, 7H, H-5_{Mann}, H-3_{Gul} , H-4_{Gul}, H-4_{Mann}, CH_2Bn), 4.13 (d, *J* = 10.8 Hz, 1H, H-6_{Mann}), 4.02 – 3.68 (m, 7H, H-6_{Mann}, H-2_{Gul}, H-3_{Mann}, H-2_{Mann}, CH_3OCO), 2.49 (d, *J* = 5.8 Hz, 1H, -OH), 2.30 (s, 3H, CH_3 STol); ^{13}C –APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 170.4(-$COOCH_3$), 138.8, 138.4, 138.1, 137.4($C_{q\ arom}$), 131.9(CH_{arom}), 131.5($C_{q\ arom}$), 129.8, 128.5, 128.4, 128.4, 128.2, 128.0, 127.7, 127.7, 127.6(CH_{arom}), 96.3(C-1_{Gul}), 85.3(C-1_{Mann}), 76.4(C-3_{Mann}), 76.1(C-2_{Mann}), 75.6(C-3_{Gul}), 74.7(C-4_{Mann}), 73.3(C-2_{Gul}), 73.0(CH_2Bn), 72.9(C-5_{Mann}), 72.5(CH_2Bn), 70.0(C-4_{Gul}), 69.7(C-6_{Mann}), 69.6(C-5_{Gul}), 52.6(-$COOCH_3$), 21.2(CH_3 STol). IR (neat): 696, 735, 810, 856, 928, 1001, 1026, 1062, 1115, 1146, 1209, 1308, 1358, 1439, 1454, 2924, 2953, 3412. HR-MS: [M+Na^+] Calculated for $C_{41}H_{44}O_{10}S$: 751.25474; found: 751.25436.

The synthesis of disaccharide acceptor (21)



Methyl 2,3,4,6-*O*-di-benzylidene-1-thio-α-D-mannopyranoside **44** (200 mg, 0.54 mmol) was dissolved in toluene (11 ml) and cooled to -40 ^{o}C, then DIBAL-H (1 M, 1.62 ml, 1.62 mmol) was added to the mixture. The mixture was allowed to stir 2 h at room temperature, diluted with EtOAc, washed with sat. aq. NaCl, the organic phase was dried over Na_2SO_4 and concentrated in vacuo. Which was used in the next step without further purification. The residue was dissolved in MeOH (10 ml), and then TsOH/H_2O was added to the mixture until the PH = 2. Then the mixture was stirred at room temperature overnight, quenched with Et_3N (0.5 mL), and concentrated under reduced pressure. The residue was diluted with EtOAc, washed with sat. aq. NaCl, the organic phase was dried over Na_2SO_4 and concentrated in vacuo. Purification by column chromatograpy (silica gel, pentane/EtOAc, 1/2, v/v) yielded **46** [6]as a white solid (134 mg, two steps yield: 62%). TLC: R_f = 0.11 (pentane/EtOAc, 5/7, v/v);



As described for the synthesis of **39** using **37**. The compound **47** was obtained (65 mg, 53%). TLC: R_f = 0.20 (pentane/EtOAc, 5/7, v/v); $[\alpha]^{20}_{D}$ = +43° (c = 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.42 – 7.22 (m, 5H, CH_{arom}), 4.82 (d, *J* = 6.5 Hz, 1H, H-1), 4.73 (d, *J* = 12.0 Hz, 1H, CH_2Bn), 4.62 (d, *J* = 12.2 Hz, 1H, CH_2Bn), 4.29 – 4.13 (m, 3H, H-3, H-5, H-4), 4.07 (d, *J* = 10.6 Hz, 1H, H-6), 3.94 (dd, *J* = 10.7, 2.9 Hz, 1H, H-6), 3.60 (dd, *J* = 6.7, 1.6 Hz, 1H, H-2), 3.55 (s, 3H, -OCH_3); ^{13}C –APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 138.2($C_{q\ arom}$), 128.4, 127.9(CH_{arom}), 103.13(C-1), 76.4(C-2), 76.3(C-3), 75.4(C-5), 72.7(CH_2Bn), 71.4(C-4), 69.1(C-6), 57.4(OMe).IR (neat): 638, 698, 741, 804, 854, 878, 907, 939, 964, 1005, 1026, 1042, 1069, 1105, 1201, 1244, 1313, 1393, 1454, 2924, 2953, 3412. HR-MS: [M+Na^+] Calculated for $C_{14}H_{18}O_5$: 289.10464; found: 289.10500.

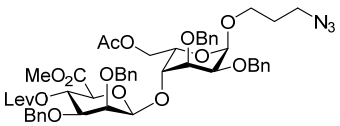
Compound **48**, as described for the synthesis of **13** using **7**. The **48** was obtained (158 mg, 91%). TLC: R_f = 0.37 (Pentane/EtOAc, 1/1, v/v). $[\alpha]^{20}_D$ = -51° (c = 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.50 – 7.04 (m, 15H), 5.19 (d, *J* = 3.9 Hz, 1H, H-1_{Gul}), 5.00 (d, *J* = 12.2 Hz, 1H, C*H*H Bn), 4.93 – 4.74 (m, 2H, H-1_{Mann}, C*H*H Bn), 4.71 – 4.43 (m, 4H, H-5_{Mann}, C*H*H Bn), 4.36 – 3.69 (m, 11H, C*H*H Bn, H-3_{Mann}, H-4_{Gul}, H-4_{Mann}, H-6_{Gul}, H-6_{Mann}, H-2_{Gul} , H-3_{Gul}, H-5_{Gul}, H-2_{Mann}), 3.46 (s, 3H), 1.02 (s, 9H, 3xCH_3 *tert*-Bu), 0.93 (s, 9H, 3xCH_3 *tert*-Bu); ^{13}C –APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 139.5, 138.6, 138.4($C_{q\ arom}$), 128.3, 127.5(CH_{arom}), 103.0(C-1_{Mann}), 95.8(C-1_{Gul}), 76.4(C-3_{Mann}), 76.1(C-2_{Mann}), 76.0(C-3_{Gul}), 74.3(C-4_{Mann}), 73.2(C-4_{Gul}), 73.1(C-2_{Gul}), 73.0, 72.6(CH_2Bn), 71.8(C-5_{Mann}), 71.1(CH_2Bn), 70.0(C-6_{Mann}), 67.1(C-6_{Gul}), 64.9(C-5_{Gul}), 56.3(OMe), 27.7(CH_3 *tert*-Bu), 27.3(CH_3 *tert*-Bu), 23.4(C_q *tert*-Bu), 20.5(C_q *tert*-Bu). IR (neat): 650, 696, 735, 797, 825, 862, 881, 939, 1008, 1028, 1083, 1041, 1074, 1126, 1140, 1204, 1364, 1387, 1454, 1474, 1497, 2856, 2887, 2932. HR-MS: [M+Na^+] Calculated for $C_{42}H_{56}O_{10}Si$: 771.35350; found: 771.5294.

Compound **49**, as described of the general procedure for deprotecting of di-*tert*-butyl silylation. The **49** was obtained (102 mg, 81%). TLC: R_f = 0.18 (DCM/acetone, 4/1, v/v). $[\alpha]^{20}_D$ = -60° (c = 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.46 – 7.04 (m, 15H, CH_{arom}), 5.22 (d, *J* = 3.8 Hz, 1H, H-1_{Gul}), 4.99 – 4.69 (m, 4H, H-1_{Mann}, C*H*H Bn), 4.72 – 4.42 (m, 4H, H-5_{Mann}, C*H*H Bn), 4.42 – 3.55 (m, 14H), 3.46 (s, 3H, OMe); ^{13}C –APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 139.2, 138.5($C_{q\ arom}$), 128.3, 128.2, 127.9, 127.6, 127.4(CH_{arom}), 103.0(C-1_{Mann}), 96.0(C-1_{Gul}), 76.3(C-3_{Gul}), 76.0(C-2_{Mann}), 76.0(C-3_{Mann}), 74.5(C-4_{Mann}), 73.6(C-2_{Gul}), 72.9(CH_2Bn), 72.6(CH_2Bn), 71.8(C-5_{Mann}), 71.8(C-4_{Gul}), 71.4(CH_2Bn), 70.0(C-6_{Mann}), 66.7(C-5_{Gul}), 64.0(C-6_{Gul}), 56.4(OMe). IR (neat): 698, 735, 881, 908, 941, 968, 1026, 1070, 1117, 1206, 1454, 2926, 3420. HR-MS: [M+Na^+] Calculated for $C_{34}H_{40}O_{10}$: 631.25137; found: 631.25042.

Disaccharide acceptor **21**, As described in the general procedure for oxidation and subsequent methylation. The disaccharide acceptor **21** was obtained (92 mg, 90%). TLC: R_f = 0.57 (DCM/acetone, 5/1, v/v). $[\alpha]^{20}_D$ = -55° (c = 0.8, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.48 – 7.06 (m, 15H, CH_{arom}), 5.33 (d, *J* = 3.5 Hz, 1H, H-1_{Gul}), 5.02 – 4.68 (m, 4H, H-1_{Mann}, C*H*H Bn, H-5_{Gul}), 4.66 – 4.45 (m, 4H, H-5_{Mann}, C*H*H Bn), 4.37 (d, *J* = 11.9 Hz, 1H, C*H*H Bn), 4.32 – 4.22 (m, 3H, H-3_{Mann}, H-4_{Gul}, H-4_{Mann}), 4.12 (d, *J* = 10.5 Hz, 1H, H-6_{Mann}), 4.04 – 3.83 (m, 3H, H-6_{Mann}, H-2_{Gul}, H-3_{Gul}), 3.77 (s, 4H, H-2_{Mann}, -OCH_3), 3.47 (s, 3H, -$COOCH_3$); ^{13}C –APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 170.4(-$COOCH_3$), 138.8, 138.5, 138.3($C_{q\ arom}$), 128.4, 128.3(CH_{arom}), 103.0(C-1_{Mann}), 96.0(C-1_{Gul}), 76.2(C-2_{Mann}), 76.1(C-3_{Mann}), 75.8(C-3_{Gul}), 74.7(C-4_{Mann}), 73.1(C-2_{Gul}), 72.9, 72.7, 71.9(CH_2Bn), 71.7(C-5_{Mann}), 70.0(C-4_{Gul}), 70.0(C-6_{Mann}), 69.0(C-5_{Gul}), 56.5(-OCH_3), 52.5(-$COOCH_3$). IR (neat): 698, 735, 881, 908, 941, 968, 1008, 1026, 1042, 1072, 1119, 1148, 1206, 1310, 1362, 1454, 1497, 1738,

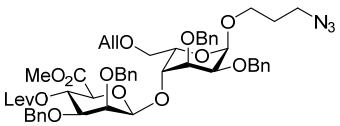
1758, 2895, 3468. HR-MS: [M+Na$^+$] Calculated for $C_{35}H_{40}O_{11}$: 659.24268; found: 659.24554.

6-*O*-acetyl-2,3-di-*O*-benzyl-4-*O*-[methyl 2,3-di-*O*-benzyl-4-*O*-levulinoyl-β-D-mannouronate]-α-L-gulopyranoside (22):



This product was prepared following the general procedure for glycosylation (0.2eq TBSOTf, -78 °C, overnight). Yield: 61 mg, (0.064 mmol), 65%, recovered acceptor **2** 7 mg, 14%. TLC: R_f = 0.42 (pentane:DCM:ethyl acetate = 2:1:1). ^{1}H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.47 – 7.13 (m, 20H, CH_{arom}), 5.49 (t, *J* = 9.7 Hz, 1H, H-4_{Mann}), 4.94 (d, *J* = 12.2 Hz, 1H, CH_2Bn), 4.79 – 4.70 (m, 2H, H-1_{Gul}, CH_2Bn), 4.69 – 4.59 (m, 2H, CH_2Bn), 4.56 – 4.43 (m, 3H, CH_2Bn), 4.40 (t, *J* = 3.5 Hz, 1H, H-3_{Gul}), 4.37 – 4.23 (m, 3H, H-5_{Gul}, H-1_{Mann}, CH_2Bn), 4.16 – 4.01 (m, 2H, H-3_{Gul}), 3.90 – 3.66 (m, 7H, H-2_{Gul}, H-2_{Mann}, H-$5_{Mann,}$ CH_3OCO-, -OC*H*$_2$$CH_2CH_2N_3$), 3.55 – 3.31 (m, 5H, H-4_{Gul}, H-3_{Mann}, -OC*H*$_2$$CH_2CH_2N_3$, -$OCH_2CH_2$C*H*$_2$$N_3$), 2.72 (q, *J* = 6.5 Hz, 2H, CH_2 Lev), 2.63 – 2.46 (m, 2H, CH_2 Lev), 2.18 (s, 3H, CH_3CO-), 2.04 (s, 3H, CH_3CO-), 1.98 (ddd, *J* = 13.6, 8.2, 5.3 Hz, 1H, -OCH_2C*H*$_2$$CH_2N_3$), 1.87 (tdd, *J* = 7.0, 5.5, 2.1 Hz, 1H, -OCH_2C*H*$_2$$CH_2N_3$); ^{13}C –APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 206.3(C=O Lev), 171.7, 170.8, 167.8(-COO-), 139.4, 138.3, 138.1, 137.7($C_{q\ arom}$), 128.5, 128.3, 128.3, 128.3, 128.0, 127.9, 127.8, 127.7, 127.6(CH_{arom}), 103.3(C-1_{Mann}), 98.0(C-1_{Gul}), 78.2, 78.1(C-3_{Mann}, C-4_{Gul}), 74.5(C-3_{Gul}), 74.0, 73.9(CH_2Bn), 73.3, 73.0, 72.8(C-2_{Mann} , C-5_{Mann}, C-2_{Gul}), 71.5, 71.2(CH_2Bn), 68.8(C-4_{Mann}), 65.0(-O$CH_2CH_2CH_2N_3$), 64.3(C-5_{Gul}), 63.4(C-6_{Gul}), 52.8(-$COOCH_3$), 48.6(-OCH_2CH_2CH_2N_3), 37.9(CH_2 Lev), 30.0(CH_3CO), 29.1(-$OCH_2CH_2CH_2N_3$), 28.0(CH_2 Lev), 21.0(CH_3CO). ^{13}C –HMBC ($CDCl_3$, 100 MHz): 103.3($J_{C1,H1}$ = 157Hz, C-1_{Mann}), 98.3($J_{C1,H1}$ = 168Hz, C-1_{Gul}). $[\alpha]^{20}_D$ = -74° (c = 1.0, $CHCl_3$). IR (neat): 602, 696, 735, 822, 843, 883, 910, 1026, 1044, 1099, 1150, 1175, 1207, 1234, 1362, 1456, 1717, 1742, 2095, 2877, 2918. HR-MS: [M+Na$^+$] Calculated for $C_{51}H_{59}N_3O_{15}$: 976.38384; found: 976.38532.

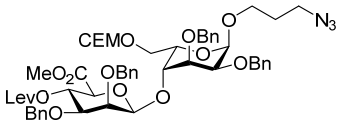
6-*O*-allyl-2,3-di-*O*-benzyl-4-*O*-[methyl 2,3-di-*O*-benzyl-4-*O*-levulinoyl-β-D-mannouronate]-α-L-gulopyranoside (23):



This product was prepared following the general procedure for glycosylation reactions (0.2eq TMSOTf, -78 °C, overnight). Yield: 22 mg, (0.023 mmol), 23% (recovered acceptor 33 mg, 68%). TLC: R_f = 0.30 (pentane:DCM:ethyl acetate = 3:1:1). ^{1}H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): 7.45 – 7.16 (m, 20H, CH_{arom}), 5.78 (m, 1H, CH All), 5.49 (t, *J* = 9.8 Hz, 1H, H-4_{Mann}), 5.24 – 5.03 (m, 2H, C*H*$_2$=CH All), 4.90 (d, *J* = 12.2 Hz, 1H, CH_2Bn), 4.83 – 4.70 (m, 2H, H-1_{Gul}, CH_2Bn), 4.70 – 4.41 (m, 5H, CH_2Bn), 4.41 – 4.20 (m, 4H, CH_2Bn, H-1_{Mann}, H-3_{Gul}, H-5_{Gul}), 3.95 (m, 1H, CH_2 All), 3.88 – 3.64 (m, 8H, CH_2 All, H-2_{Mann}, H-5_{Mann}, H-4_{Gul}, CH_3 $COOCH_3$, -OC*H*$_2$$CH_2CH_2N_3$), 3.57 – 3.29 (m, 5H, -OC*H*$_2$$CH_2CH_2N_3$, H-$4_{Gul}$, H-$3_{Mann}$, -$OCH_2CH_2$C*H*$_2$$N_3$), 2.80 – 2.64 (m, 2H, CH_2 Lev), 2.67 – 2.46 (m, 2H, CH_2 Lev), 2.18 (s, 3H, CH_3CO), 2.08 – 1.74 (m, 2H, -OCH_2C*H*$_2$$CH_2N_3$); ^{13}C – APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 206.4(C=O Lev), 171.7, 167.9(-COO-), 139.4, 138.3, 137.8($C_{q\ arom}$), 134.5, 128.5, 128.5, 128.4, 128.3, 128.2, 127.9, 127.9, 127.8, 127.7, 127.6, 127.6, 124.9(CH_{arom}), 117.2(CH_2=*C*H All), 103.3(C-1_{Mann}), 97.9(C-1_{Gul}), 78.3(C-3_{Mann}), 77.4(C-4_{Gul}), 74.5(C-3_{Gul}), 73.9, 73.6(CH_2Bn), 73.4, 73.2, 73.1(C-2_{Mann} , C-5_{Mann}, C-2_{Gul}), 72.2, 71.7, 71.2 (CH_2Bn, CH_2 All), 69.0(C-4_{Mann}), 68.4(C-6_{Gul}), 65.0(-O$CH_2CH_2CH_2N_3$), 64.3(C-5_{Gul}), 52.8(-

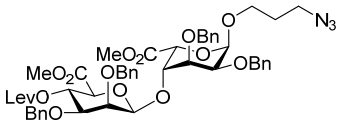
$COOCH_3$), 48.6(-$OCH_2CH_2CH_2N_3$), 37.9(CH_2 Lev), 30.0(CH_3CO), 29.2(-$OCH_2CH_2CH_2N_3$), 28.0(CH_2 Lev). $[\alpha]^{20}_D$ = -59° (c = 0.20, $CHCl_3$). HR-MS: [M+Na^+] Calculated for $C_{52}H_{61}N_3O_{14}$: 974.40457; found: 974.40601.

6-*O*-(2-cyanoethoxyl methyl)-2,3-di-*O*-benzyl-4-*O*-[methyl 2,3-di-*O*-benzyl-4-*O*-levulinoyl-β-D-mannouronate] -α-L-gulopyranoside (24): This product was prepared following the general procedure for glycosylation reactions (0.2eq



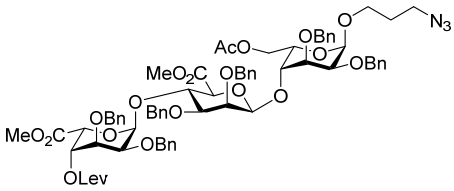
TBSOTf, -78 °C, overnight). Yield: 34 mg, (0.034 mmol), 35% (recovered acceptor 30 mg, 56%). TLC: R_f = 0.70 (pentane:DCM:ethyl acetate = 1:1:1). ^{1}H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.46 – 7.07 (m, 20H), 5.49 (t, *J* = 9.7 Hz, 1H), 4.91 (d, *J* = 12.2 Hz, 1H), 4.83 – 4.32 (m, 11H), 4.31 – 4.24 (m, 1H), 3.92 – 3.29 (m, 11H), 2.77 – 2.39 (m, 5H), 2.17 (s, 3H), 2.03 – 1.80 (m, 2H); ^{13}C –APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 206.3, 171.7, 167.8, 139.4, 138.4, 137.9, 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.2, 128.2, 128.1, 127.9, 127.8, 127.7, 127.7, 127.7, 127.6, 127.5, 117.9, 103.1, 97.9, 95.6, 78.3, 78.0, 74.4, 73.9, 73.6, 73.3, 73.3, 73.2, 71.7, 71.2, 68.9, 67.4, 65.0, 64.9, 62.5, 52.7, 48.5, 37.9, 30.0, 29.1, 28.0, 19.1. ^{13}C -HMBC ($CDCl_3$, 100 MHz): 103.1($J_{C1,H1}$ = 157Hz, C-1_{Mann}), 97.9($J_{C1,H1}$ = 166Hz, C-1_{Gul}). $[\alpha]^{20}_D$ = -74° (c = 1.0, $CHCl_3$). IR (neat): 696, 735, 793, 822, 866, 887, 910, 1026, 1080, 1111, 1152, 1207, 1238, 1263, 1294, 1341, 1362, 1454, 1717, 1748, 2095, 2854, 2924. HR-MS: [M+Na^+] Calculated for $C_{53}H_{62}N_4O_{15}$: 1017.41039; found: 1017.41149.

Methyl (3-Azidopropyl 2,3-di-*O*-benzyl-4-*O*-[methyl 2,3-di-*O*-benzyl-4-*O*-levulinoyl-β-D-mannopyranosyl uronate]-α-L-gulopyranosyl uronate) (25): This product was prepared following the general procedure for glycosylation



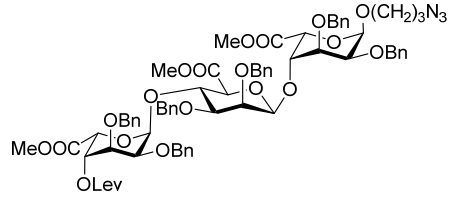
reactions (0.2eq TBSOTf, -78 °C, 1d, -78 °C - -45 °C, 1d). Yield: 52 mg, (0.055 mmol), 55% (β:α = 3:1). TLC: R_f = 0.63 (toluene:acetone = 3:1). ^{1}H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.43 – 7.12 (m, 20H, CH_{arom}), 5.46 (t, *J* = 9.7 Hz, 1H, H-4_{Mann}), 4.93 – 4.84 (m, 2H, H-1_{Gul}, CH_2Bn), 4.80 (d, *J* = 1.8 Hz, 1H, H-5_{Gul}), 4.75 (d, *J* = 12.4 Hz, 1H, CH_2Bn), 4.65 – 4.52 (m, 3H, CH_2Bn), 4.44 (d, *J* = 12.0 Hz, 1H, CH_2Bn), 4.41 – 4.26 (m, 4H, CH_2Bn, H-1_{Mann}, H-3_{Gul}), 4.09 (dd, *J* = 3.8, 1.8 Hz, 1H, H-4_{Gul}), 3.83 (t, *J* = 3.6 Hz, 2H, H-2_{Gul}, -O$CH_2CH_2CH_2N_3$), 3.77 (d, *J* = 9.7 Hz, 1H, H-5_{Mann}), 3.71 (6H, 2xCH_3 $COOCH_3$), 3.67 (d, *J* = 3.0 Hz, 1H, H-2_{Mann}), 3.50 (dt, *J* = 9.9, 5.5 Hz, 1H, -O$CH_2CH_2CH_2N_3$), 3.42 – 3.31 (m, 3H, H-3_{Mann}, -$OCH_2CH_2CH_2N_3$), 2.79 – 2.65 (m, 2H, CH_2 Lev), 2.62 – 2.45 (m, 2H, CH_2 Lev), 2.17 (s, 3H, CH_3CO), 2.00 – 1.76 (m, 2H, -$OCH_2CH_2CH_2N_3$); ^{13}C –APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 206.3(C=O Lev), 171.7, 170.4, 167.7(-COO-), 139.1, 138.4, 138.0, 137.8v, 128.5, 128.5, 128.4, 128.2, 127.9, 127.7, 127.5(CH_{arom}), 103.3(C-1_{Mann}), 98.3(C-1_{Gul}), 78.7(C-4_{Gul}), 78.1(C-3_{Mann}), 74.4(C-3_{Gul}), 74.2(CH_2Bn), 73.6(C-2_{Mann}), 73.4(C-5_{Mann}), 72.8(C-2_{Gul}), 71.7, 71.5(CH_2Bn), 68.9(C-4_{Mann}), 67.1(C-5_{Gul}), 65.5(-O$CH_2CH_2CH_2N_3$), 52.8, 52.5(-$COOCH_3$), 48.4(-$OCH_2CH_2CH_2N_3$), 37.9(CH_2 Lev), 30.0(CH_3CO), 29.0(-$OCH_2CH_2CH_2N_3$), 28.0(CH_2 Lev); ^{13}C –HMBC ($CDCl_3$, 100 MHz): 103.3($J_{C1,H1}$ = 157Hz, C-1_{Mann}), 98.3($J_{C1,H1}$ = 168Hz, C-1_{Gul}). $[\alpha]^{20}_D$ = -36° (c = 0.88, $CHCl_3$). IR (neat): 698, 737, 910, 1026, 1053, 1082, 1092, 1105, 1150, 1177, 1207, 1236, 1304, 1362, 1456, 1717, 1749, 2095, 2852, 2922, 2953. HR-MS: [M+Na^+] Calculated for $C_{50}H_{57}N_3O_{15}$: 962.36819; found: 962.36937.

3-Azidopropyl 6-*O*-acetyl-2,3-*O*-benzyl-4-*O*-[methyl 2,3-di-*O*-benzyl-4-*O*-{methyl 2,3-di-*O*-benzyl-4-*O*- levulinoyl-α-L-gulopyranosyl urinate}-β-D-mannopyranosyl uronate]-α-L-gulopyranoside (26): This product was prepared following



the general procedure for glycosylation reactions (0.2eq TBSOTf, -78 °C,1d, -78°C - -20 °C, 1d). Yield: 46 mg, (0.035 mmol), 69%. TLC: R_f = 0.50 (pentane:DCM:ethyl acetate = 3:2:2). ^{1}H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.48 – 7.08 (m, 30H, CH_{arom}), 5.33 (d, *J* = 3.9 Hz, 1H, H-$1_{Gul'}$), 5.22 (dd, *J* = 3.8, 1.9 Hz, 1H, H-$4_{Gul'}$), 5.17 (d, *J* = 1.9 Hz, 1H, H-$5_{Gul'}$), 4.88 (dd, *J* = 13.6, 11.9 Hz, 2H, CH_2Bn), 4.76 – 4.64 (m, 3H, H-1_{Gul}, CH_2Bn), 4.62 – 4.22 (m, 12H, H-4_{Mann}, CH_2Bn, H-5_{Gul}, H-1_{Mann}, H-3_{Gul}), 4.06 (m, 2H, H-6_{Gul}), 4.01 (d, *J* = 8.5 Hz, 1H, H-5_{Mann}), 3.89 (t, *J* = 3.5 Hz, 1H, H-$3_{Gul'}$), 3.84 – 3.74 (m, 3H, H-2_{Gul}, H-4_{Gul}, -OC*H*$_2$CH$_2$CH$_2$N$_3$), 3.66 (t, *J* = 3.7 Hz, 1H, H-$2_{Gul'}$), 3.56 (s, 4H, H-5_{Mann}, CH_3 $COOCH_3$), 3.47 (dt, *J* = 10.4, 5.3 Hz, 1H, -OC*H*$_2$CH$_2$CH$_2$N$_3$), 3.44 – 3.35 (m, 6H, H-5_{Mann}, CH_3 $COOCH_3$, -OCH$_2$CH$_2$C*H*$_2$N$_3$), 2.76 – 2.55 (m, 2H, CH_2 Lev), 2.49 – 2.38 (m, 2H, CH_2 Lev), 2.15 (s, 3H, CH_3CO), 2.04 (s, 3H, CH_3CO), 2.02 – 1.71 (m, 2H, -OCH$_2$C*H*$_2$CH$_2$N$_3$); ^{13}C –APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 206.3(C=O Lev), 171.6, 170.8, 169.0, 168.7(-COO-), 139.4, 138.6, 138.1, 138.0, 137.7, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.8, 127.7, 127.7, 127.4, 127.4, 127.4(CH_{arom}), 103.6(C-1_{Mann}), 97.8(C-1_{Gul}), 96.7(C-$1_{Gul'}$), 79.6(C-3_{Mann}), 77.8(C-2_{Mann}), 76.1(C-5_{Mann}), 75.1(C-3_{Gul}), 74.0, 73.9(CH_2Bn), 73.4, 73.1, 73.0(C-2_{Mann}, C-4_{Gul}, C-2_{Gul}), 73.0(CH_2Bn), 72.5, 72.3(C-$3_{Gul'}$, C-$2_{Gul'}$), 71.3, 71.1(CH_2Bn), 71.0(C-$4_{Gul'}$), 66.3(C-$5_{Gul'}$), 64.9(-O*C*H$_2$CH$_2$CH$_2$N$_3$), 64.2(C-5_{Gul}), 63.3(C-6_{Gul}), 52.4, 52.2(-$COOCH_3$), 48.6(-OCH$_2$CH$_2$*C*H$_2$N$_3$), 38.0(CH_2 Lev), 29.8(CH_3CO), 29.1(-OCH$_2$*C*H$_2$CH$_2$N$_3$), 28.1(CH_2 Lev), 21.0(CH_3CO); ^{13}C -HMBCipvGATED ($CDCl_3$, 100 MHz): 103.6($J_{C1,H1}$ = 157Hz, C-1_{Mann}), 97.8($J_{C1,H1}$ = 168Hz, C-1_{Gul}) , 96.7($J_{C1,H1}$ = 170Hz, C-$1_{Gul'}$). $[\alpha]^{20}_D$ = -83° (c = 0.84, $CHCl_3$). IR (neat): 601, 675, 698, 737, 824, 847,912, 1026, 1092, 1119, 1140, 1177, 1207, 1236, 1304, 1364, 1402, 1437, 1454, 1497, 1719, 1742, 2095, 2916, 3030. HR-MS: [M+Na$^+$] Calculated for $C_{72}H_{81}N_3O_{21}$: 1346.52528; found: 1346.52759.

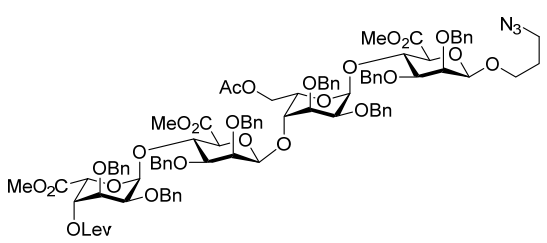
Methyl (3-Azidopropyl 2,3-di-*O*-benzyl-4-*O*-[methyl 2,3-di-*O*-benzyl-4-*O*-{methyl 2,3-di-*O*-benzyl-4-levulinoyl-α-L-gulopyranosyl urinate}-β-D-mannopyranosyl uronate]-α-L-gulopyranosyl uronate) (27): The disaccharide imidate



donor **18** (103 mg, 0.1 mmol) and acceptor **6** (24 mg, 0.05mmol) were together co-evaporated with toluene (three times). The residue was dissolved in dry DCM (1 ml). The solution was cooled to -78 °C and followed by adding TBSOTf (5 ul, 0.022 mmol) and the reaction was allowed to stir for 1 day at -78 °C and then -78°C to -30 °C for 12 h. The reaction was quenched with Et_3N and diluted with EtOAc, washed with sat. aq. NaCl, the organic phase was dried over Na_2SO_4 and concentrated in vacuo. Purification by column chromatograpy (silica gel, pentane/DCM/EtOAc, 3/1/1, v/v/v) yielded **27** as a colourless syrup (55 mg, 84%). TLC: R_f = 0.42 (pentane/DCM/EtOAc, 2/1/1, v/v/v); $[\alpha]^{20}_D$ = -82° (c = 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.49 – 7.00 (m, 30H, CH_{arom}), 5.31 (d, *J* =

3.9 Hz, 1H, H-$1_{Gul'}$), 5.24 (dd, *J* = 3.7, 1.8 Hz, 1H, H-$4_{Gul'}$), 5.20 (d, *J* = 1.9 Hz, 1H, H-$5_{Gul'}$), 4.91 – 4.80 (m, 3H, H-1_{Gul}, CH_2Bn), 4.76 (d, *J* = 1.8 Hz, 1H, H-5_{Gul}), 4.73 (s, 1H, CH_2Bn), 4.70 (d, *J* = 1.4 Hz, 1H, CH_2Bn), 4.65 – 4.48 (m, 5H, H-4_{Mann}, 2xCH_2Bn), 4.46 – 4.32 (m, 3H, H-1_{Mann}, CH_2Bn), 4.34 – 4.21 (m, 2H, H-3_{Gul}, CH_2Bn), 4.13 (dd, *J* = 3.8, 1.8 Hz, 1H, H-4_{Gul}), 4.01 (d, *J* = 8.4 Hz, 1H, H-5_{Mann}), 3.89 (t, *J* = 3.6 Hz, 1H, H-$3_{Gul'}$), 3.81 (m, 2H, H-2_{Gul}, -OC*H*$_2$CH_2C$H_2$$N_3$), 3.68 (m, 4H, H-$2_{Gul'}$, CH_3 $COOCH_3$), 3.59 (d, *J* = 3.4 Hz, 1H, H-2_{Mann}), 3.54 (s, 3H, CH_3 $COOCH_3$), 3.46 (m, 4H, -OC*H*$_2$CH_2C$H_2$$N_3$, CH_3 $COOCH_3$), 3.35 (t, *J* = 6.7 Hz, 1H, H-3_{Mann}), 2.66 (m, 2H, CH_2 Lev), 2.50 – 2.36 (m, 2H, CH_2 Lev), 2.15 (s, 3H, $COCH_3$), 1.98 – 1.70 (m, 2H, -OCH_2C*H*$_2$C$H_2$$N_3$). ^{13}C–APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 206.3(-CO-Lev), 171.6, 170.3, 169.1, 168.6(-COO-), 139.0, 138.7, 138.6, 138.1, 138.0, 137.7($C_{q\ arom}$), 128.4, 128.3, 128.3, 128.3, 128.1, 128.0, 128.0, 127.9, 127.8, 127.8, 127.8, 127.7, 127.7, 127.7, 127.5(CH_{arom}), 103.4(C-1_{Mann}), 98.2(C-1_{Gul}), 96.7(C-$1_{Gul'}$), 79.3(C-3_{Mann}), 78.3(C-4_{Gul}), 76.2(C-5_{Mann}), 74.9(C-3_{Gul}), 74.2(CH_2Bn), 74.2(C-2_{Mann}), 73.5(CH_2Bn), 73.2(C-4_{Mann}), 73.0(CH_2Bn), 72.8, 72.6, 72.4(C-2_{Gul}, C-$2_{Gul'}$, C-$3_{Gul'}$), 71.5, 71.3, 71.2(CH_2Bn), 71.0(C-$4_{Gul'}$), 67.1(C-5_{Gul}), 66.3(C-$5_{Gul'}$), 65.4(-OCH_2CH_2C$H_2$$N_3$), 52.4, 52.4, 52.2(-$COOCH_3$), 48.4(-O$CH_2CH_2CH_2$$N_3$), 37.9($CH_2$ Lev), 29.8($COCH_3$), 29.0(-OCH_2CH_2C$H_2$$N_3$), 28.1($CH_2$ Lev); ^{13}C -HMBCipvGATED ($CDCl_3$, 100 MHz): 103.4($J_{C1,H1}$ = 157Hz, C-1_{Mann}), 98.2($J_{C1,H1}$ = 168Hz, C-1_{Gul}), 96.7($J_{C1,H1}$ = 171Hz, C-$1_{Gul'}$). HR-MS: [M+H^+] Calculated for $C_{71}H_{79}O_{21}N_3$: 1310.52788; found: 1310.55688.

Tetrasaccharide (28): This product was prepared following the general procedure for glycosylation reactions (0.2eq



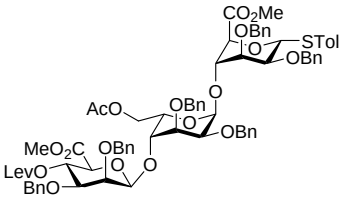
TBSOTf, -78 °C,1d, -78 °C - -20 °C, 1d). Yield: 28 mg, (0.017 mmol), 33%. TLC: R_f = 0.65 (pentane:DCM:ethyl acetate = 3:2:2). ^{1}H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.48 – 7.39 (m, 2H, CH_{arom}), 7.39 – 7.08 (m, 38H, CH_{arom}), 5.30 (d, *J* = 4.0 Hz, 1H, H-$1_{Gul'}$), 5.22 (dd, *J* = 3.8, 1.9 Hz, 1H, H-$4_{Gul'}$), 5.18 (d, *J* = 2.0 Hz, 1H, H-$5_{Gul'}$), 4.99 (d, *J* = 4.0 Hz, 1H, H-1_{Gul}), 4.94 – 4.82 (m, 2H, CH_2Bn), 4.77 (d, *J* = 12.3 Hz, 1H, CH_2Bn), 4.70 (d, *J* = 12.5 Hz, 2H, CH_2Bn), 4.62 – 4.37 (m, 12H, H-1_{Mann}, CH_2Bn), 4.33 (s, 2H, CH_2Bn), 4.28 (t, *J* = 3.6 Hz, 1H, H-3_{Gul}), 4.24 (s, 1H, H-$1_{Mann'}$), 4.13 – 3.94 (m, 4H, -OC*H*$_2$CH_2C$H_2$$N_3$, H-$6_{Gul}$, H-$5_{Mann}$, H-$5_{Mann'}$), 3.95 – 3.84 (m, 2H, H-6_{Gul}, H-$3_{Gul'}$), 3.82 – 3.72 (m, 3H, H-3_{Mann}, H-2_{Gul}, H-$2_{Mann'}$), 3.65 (t, *J* = 3.7 Hz, 1H, H-$2_{Gul'}$), 3.59 (dd, *J* = 8.3, 2.7 Hz, 1H, H-2_{Mann}), 3.54 (d, *J* = 1.5 Hz, 6H, 2xCH_3 $COOCH_3$), 3.52 – 3.44 (m, 2H, H-4_{Gul}, -OC*H*$_2$CH_2C$H_2$$N_3$), 3.42 (s, 3H, CH_3 $COOCH_3$), 3.40 – 3.29 (m, 3H, H-$3_{Mann'}$, -OCH_2CH_2C*H*$_2$$N_3$), 2.75 – 2.56 (m, 2H, CH_2 Lev), 2.48 – 2.38 (m, 2H, CH_2 Lev), 2.15 (s, 3H, CH_3CO), 1.94 – 1.79 (m, 5H, CH_3CO, -OCH_2C*H*$_2$C$H_2$$N_3$); ^{13}C –APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 206.3(C=O Lev), 171.6, 170.7, 169.3, 169.1, 168.7(-COO-), 139.4, 138.8, 138.7, 138.6, 138.6, 138.2, 138.0, 137.7, 128.5, 128.4, 128.4, 128.3, 128.2, 128.2, 128.0, 127.9, 127.8, 127.8, 127.5, 127.5, 127.4(CH_{arom}), 103.6(C-$1_{Mann'}$), 101.2(C-1_{Mann}), 96.8, 96.7(C-$1_{Gul'}$, C-1_{Gul}), 79.6(C-$3_{Mann'}$), 79.1(C-2_{Mann}), 77.8(C-4_{Gul}), 76.1(C-$5_{Mann'}$), 75.5(C-5_{Mann}), 74.6(C-3_{Gul}), 74.4(C-3_{Mann}), 74.1, 73.9, 73.7(CH_2Bn), 73.6, 73.4, 73.2, 73.1, 73.0(CH_2Bn), 72.5, 72.4, 72.1, 71.3, 71.1, 71.1, 71.0(C-$4_{Gul'}$), 66.7(-OCH_2CH_2C$H_2$$N_3$), 66.3(C-$5_{Gul'}$), 64.2(C-$5_{Gul}$), 62.8(C-$6_{Gul}$), 52.4,

52.4, 52.2(-$COOCH_3$), 48.5(-$OCH_2CH_2CH_2N_3$), 38.0(CH_2 Lev), 29.9(CH_3CO), 29.2(-$OCH_2CH_2CH_2N_3$), 28.1(CH_2 Lev), 21.0(CH_3CO); ^{13}C -HMBCipvGATED ($CDCl_3$, 100 MHz): 103.6($J_{C1,H1}$ = 157Hz, C-$1_{Mann'}$), 101.2($J_{C1,H1}$ = 157Hz, C-1_{Mann}),96.8, 96.7($J_{C1,H1}$ = 169Hz, C-1_{Gul}, $J_{C1,H1}$ = 170Hz, C-$1_{Gul'}$). $[\alpha]^{20}_D$ = -71° (c = 0.64, $CHCl_3$). IR (neat): 698, 737, 910, 1028, 1051, 1098, 1142, 1177, 1206, 1237, 1302, 1362, 1456, 1744, 2097, 2878, 2924. HR-MS: [M+Na^+] Calculated for $C_{93}H_{103}N_3O_{27}$: 1716.66712; found: 1716.66739.

Methyl (3-Azidopropyl 2,3-di-*O*-benzyl-4-*O*-[methyl 2,3-di-*O*-benzyl-4-*O*-{methyl 2,3-di-*O*-benzyl-4-*O*-(methyl 2,3-di-*O*-benzyl 4-levulinoyl)-α-L-gulopyranosyl urinate-β-D-mannopyranosyl urinate}-α-L-gulopyranosyl urinate]-β-D-mannopyranosyl uronate) (29): The disaccharide imidate donor **18** (154 mg, 0.15 mmol) and acceptor **11** (42 mg, 0.05 mmol) were together co-evaporated with toluene (three times). The residue was dissolved in dry DCM (0.5 ml). The solution was cooled to -78 °C and followed by adding TBSOTf (7 ul, 0.03 mmol) and the reaction was allowed to stir for 1 day at -78 °C and then -78 °C to -45 °C for 2 days. The reaction was quenched with Et_3N and diluted with EtOAc, washed with sat. aq. NaCl, the organic phase was dried over Na_2SO_4 and concentrated in vacuo. Purification by size exclusion and column chromatograpy (silica gel, pentane/DCM/EtOAc, 3/1/1, v/v/v) yielded product 15 (38 mg, 45%). TLC: R_f = 0.50 (toluene/acetone, 3/1, v/v); ^{1}H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.52 – 6.99 (m, 40H, CH_{arom}), 5.28 (d, *J* = 4.0 Hz, 1H, H-$1_{Gul'}$), 5.22 (dd, *J* = 3.7, 1.9 Hz, 1H, H-$4_{Gul'}$), 5.21 – 5.16 (m, 2H, H-1_{Gul}, H-$5_{Gul'}$), 5.02 (d, *J* = 1.8 Hz, 1H, H-5_{Gul}), 4.87 (d, *J* = 3.4 Hz, 1H, CH_2 Bn), 4.84 (d, *J* = 3.4 Hz, 1H, CH_2 Bn), 4.79 (d, *J* = 12.4 Hz, 1H, CH_2 Bn), 4.75 – 4.17 (m, 18H, 2xH-$1_{Mann'}$, 2xH-$4_{Mann'}$, H-3_{Gul}, CH_2 Bn), 4.07 – 4.00 (m, 3H, -O$CH_2CH_2CH_2N_3$, H-4_{Gul}, H-5_{Mann}), 3.97 (d, *J* = 8.4 Hz, 1H, H-$5_{Mann'}$), 3.88 (t, *J* = 3.5 Hz, 1H, H-$3_{Gul'}$), 3.84 – 3.79 (m, 1H, H-2_{Mann}), 3.76 (t, *J* = 3.6 Hz, 1H, H-2_{Gul}), 3.65 (t, *J* = 3.8 Hz, 1H, H-$2_{Gul'}$), 3.58 – 3.24 (m, 15H, H-$2_{Mann'}$, H-$3_{Mann'}$, H-3_{Mann}, -O$CH_2CH_2CH_2N_3$, 3xCH_3 $COOCH_3$, -$OCH_2CH_2CH_2N_3$), 2.66 (dt, *J* = 14.9, 6.1 Hz, 1H, CH_2 Lev), 2.50 – 2.37 (m, 2H, CH_2 Lev), 2.14 (s, 3H, $COCH_3$), 1.87-1.70 (m, 2H, -$OCH_2CH_2CH_2N_3$); ^{13}C–APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 206.3(C=O Lev), 177.1, 171.6, 170.2, 169.1, 168.8, 168.6(-COO-), 139.3, 138.8, 138.7, 138.6, 138.2, 138.0, 137.7($C_{q\ arom}$), 128.4, 128.4, 128.4, 128.3, 128.3, 128.3, 128.1, 128.1, 128.1, 128.1, 128.1, 127.9, 127.9, 127.9, 127.8, 127.8, 127.8, 127.8, 127.7, 127.7, 127.7, 127.6, 127.6, 127.5, 127.4, 127.3, 127.2(CH_{arom}), 103.3(C-$1_{Mann'}$), 101.5(C-1_{Mann}), 97.3(C-1_{Gul}), 96.7(C-$1_{Gul'}$), 79.5(C-$3_{Mann'}$), 79.4(C-3_{Mann}), 78.5(C-4_{Gul}), 76.8(C-5_{Mann}), 76.1(C-$5_{Mann'}$), 75.7(C-3_{Gul}), 74.4(C-$2_{Mann'}$), 74.3, 73.9(2xCH_2Bn), 73.8(C-2_{Mann}), 73.5(C-$4_{Mann'}$), 73.3, 73.0(2xCH_2Bn), 73.4, 73.2, 72.5, 72.4(C-2_{Gul} ,C-4_{Mann}, C-$2_{Gul'}$, C-$3_{Gul'}$), 71.3, 71.3, 71.2, 71.1(4xCH_2Bn), 71.0(C-$4_{Gul'}$), 67.5(C-5_{Gul}), 66.8(C-$5_{Gul'}$), 66.3(-O$CH_2CH_2CH_2N_3$), 52.4(-$COOCH_3$), 52.2(-$COOCH_3$), 52.0(-$COOCH_3$), 48.5(-$OCH_2CH_2CH_2N_3$), 38.0(CH_2 Lev), 29.9($COCH_3$), 29.2(CH_2 Lev), 28.1(-$OCH_2CH_2CH_2N_3$); ^{13}C-HMBCipvGATED ($CDCl_3$, 100 MHz): 103.3($J_{C1,H1}$ = 157Hz, C-$1_{Mann'}$), 101.5($J_{C1,H1}$ = 157Hz, C-1_{Mann}), 97.3($J_{C1,H1}$ = 170Hz, C-1_{Gul}), 96.7($J_{C1,H1}$ = 170Hz, C-$1_{Gul'}$). $[\alpha]^{20}_D$ = -104° (c = 0.36, $CHCl_3$). IR (neat): 698, 739,

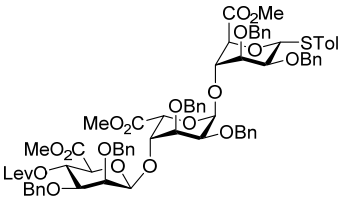
968, 1028, 1038, 1080, 1121, 1209, 1236, 1362, 1456, 1748, 2099, 2853, 2922, 2953. HR-MS: [M+Na^+] Calculated for $C_{92}H_{101}O_{27}N_3$: 1702.65147; found: 1702.65155.

Methyl (*p*-methyphenyl 2,3-di-*O*-benzyl-4-*O*-[6-*O*-acetyl-2,3-di-*O*-benzyl-4-*O*-{ methyl 2,3-di-*O*-benzyl-4-*O*-levulinoyl-β-D-mannopyranosyl uronate }-α-L-gulopyranosyl]-1-thio-α-D-mannopyranosyl uronate) (30): This product was



prepared following the general procedure for glycosylation reactions (0.2eq TBSOTf, -78 °C, 1d, -78 °C - -45 °C, 1d). Yield: 51 mg, (0.038 mmol), 77%. TLC: R_f = 0.55 (pentane:DCM:ethyl acetate = 2:1:1). ^{1}H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.58 – 7.20 (m, 30H, CH_{arom}), 7.05 (d, *J* = 8.3 Hz, 2H, CH_{arom}), 5.70 (d, *J* = 8.4 Hz, 1H, H-1_{Mann}), 5.50 (t, *J* = 9.7 Hz, 1H, H-$4_{Mann'}$), 5.02 (d, *J* = 3.9 Hz, 1H, H-1_{Gul}), 4.91 (d, *J* = 12.0 Hz, 1H, CH_2Bn), 4.80 (d, *J* = 12.4 Hz, 1H, CH_2Bn), 4.69 (d, *J* = 12.4 Hz, 1H, CH_2Bn), 4.64 – 4.26 (m, 13H, H-5_{Mann}, H-4_{Mann}, CH_2Bn, H-$1_{Mann'}$, H-3_{Gul}, H-5_{Gul}), 4.21 (d, *J* = 11.8 Hz, 1H, CH_2Bn), 4.13 – 3.73 (m, 7H, H-6_{Gul}, H-2_{Gul}, H-$5_{Mann'}$, H-2_{Mann}, H-3_{Mann}, H-$2_{Mann'}$), 3.70 (s, 3H, CH_3 $COOCH_3$), 3.65 – 3.54 (m, 1H, H-4_{Gul}), 3.49 (s, 3H, CH_3 $COOCH_3$), 3.43 (dd, *J* = 9.7, 2.9 Hz, 1H, H-$3_{Mann'}$), 2.73 (td, *J* = 6.5, 3.3 Hz, 2H, CH_2 Lev), 2.61 – 2.47 (m, 2H, CH_2 Lev), 2.26 (s, 3H, CH_3 STol), 2.18 (s, 3H, CH_3CO), 1.92 (s, 3H, CH_3CO); ^{13}C –APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 206.4(C=O Lev), 171.7, 170.7, 169.9, 167.7(-COO-), 139.4, 138.4, 138.2, 137.7($C_{q\ arom}$), 131.6(CH_{arom}), 130.6($C_{q\ arom}$), 129.6, 128.5, 128.4, 128.3, 128.3, 128.0, 127.9, 127.9, 127.7, 127.7, 127.6, 127.6(CH_{arom}), 103.2(C-$1_{Mann'}$), 97.1(C-1_{Gul}), 83.0(C-1_{Mann}), 78.6(C-4_{Gul}), 78.2(C-$3_{Mann'}$), 76.4(C-3_{Mann}), 75.3(C-2_{Mann}), 74.1(CH_2Bn), 74.0(C-3_{Gul} ,C-4_{Mann}), 73.9(C-5_{Mann}), 73.7(CH_2Bn), 73.5(C-2_{Gul}), 73.4(C-$5_{Mann'}$), 73.2(C-$2_{Mann'}$), 72.8, 72.6, 71.5, 71.2(CH_2Bn), 68.8(C-$4_{Mann'}$), 64.8(C-5_{Gul}), 63.4(C-6_{Gul}), 52.8(-$COOCH_3$), 52.1(-$COOCH_3$), 37.9(CH_2 Lev), 30.0(CH_3CO), 28.0(CH_2 Lev), 21.2(CH_3 STol), 21.0(CH_3 Ac). $[\alpha]^{20}_D$ = -72° (c = 1.0, $CHCl_3$). IR (neat): 601, 696, 733, 810, 864, 893, 910, 951, 1026, 1047, 1072, 1103, 1118, 1152, 1177, 1207, 1236, 1263, 1362, 1454, 1717, 1744, 2855, 2922, 2951. HR-MS: [M+Na^+] Calculated for $C_{76}H_{82}O_{20}S$: 1369.50124; found: 1369.50226.

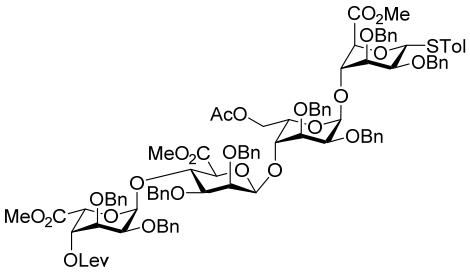
Methyl (*p*-methyphenyl 2,3-di-*O*-benzyl-4-*O*-[methyl 2,3-di-*O*-benzyl-4-*O*-{ methyl 2,3-di-*O*-benzyl-4-*O*-levulinoyl-β-D-mannopyranosyl uronate }-α-L-gulopyranosyl uronate]-1-thio-α-D-mannopyranosyl uronate) (31): This product was



prepared following the general procedure for glycosylation reactions (0.2eq TBSOTf, -78 °C, 3d, -78 °C - -45 °C, 1d). Yield: 59 mg, (0.044 mmol), quantitative yield. TLC: R_f = 0.70 (pentane:DCM:ethyl acetate = 2:1:1). ^{1}H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.65 – 6.93 (m, 34H, CH_{arom}), 5.67 (d, *J* = 7.2 Hz, 1H, H-1_{Mann}), 5.47 (t, *J* = 9.7 Hz, 1H, H-$4_{Mann'}$), 5.17 – 4.99 (m, 1H, H-1_{Gul}), 4.90 (d, *J* = 12.1 Hz, 1H, CH_2Bn), 4.79 (d, *J* = 12.4 Hz, 1H, CH_2Bn), 4.76(bs, 1H, H-5_{Gul}), 4.69 – 4.24 (m, 13H, H-5_{Mann}, H-4_{Mann}, CH_2Bn, H-$1_{Mann'}$, H-3_{Gul}), 4.20 (d, *J* = 10.9 Hz, 1H, CH_2Bn), 4.10 (d, *J* = 3.2 Hz, 1H, H-4_{Gul}), 3.92 – 3.64 (m, 8H, H-2_{Gul}, H-$5_{Mann'}$, H-2_{Mann}, H-3_{Mann}, CH_3

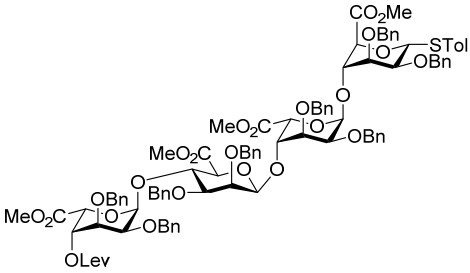
$COOCH_3$, H-$2_{Mann'}$), 3.59 (s, 3H, CH_3 $COOCH_3$), 3.49 (s, 3H, CH_3 $COOCH_3$), 3.39 (dd, *J* = 9.8, 3.0 Hz, 1H, H-$3_{Mann'}$), 2.72 (td, *J* = 6.5, 3.8 Hz, 2H, CH_2 Lev), 2.66 – 2.43 (m, 2H, CH_2 Lev), 2.27 (s, 3H, CH_3 STol), 2.17 (s, 3H, CH_3CO); ^{13}C –APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 206.4(C=O Lev), 171.7, 170.1, 169.6, 167.7(-COO-), 139.1, 138.4, 137.9($C_{q\ arom}$), 131.9(CH_{arom}), 130.4($C_{q\ arom}$), 129.6, 128.5, 128.5, 128.4, 128.3, 128.3, 128.2, 128.0, 127.9, 127.9, 127.9, 127.7, 127.7, 127.6, 127.6, 127.6, 127.5(CH_{arom}), 103.2(C-$1_{Mann'}$), 98.0(C-1_{Gul}) , 83.1(C-1_{Mann}), 79.1(C-4_{Gul}), 78.0(C-$3_{Mann'}$), 75.8(C-3_{Mann}), 74.9(C-4_{Mann} , C-2_{Mann}), 74.2(CH_2Bn), 74.0(C-5_{Mann}), 73.8(C-3_{Gul}), 73.7(C-$2_{Mann'}$), 73.5(CH_2Bn), 73.4(C-$5_{Mann'}$), 73.3(C-2_{Gul}), 72.5, 72.4, 71.7, 71.4(CH_2Bn), 68.9(C-$4_{Mann'}$), 67.8(C-5_{Gul}), 52.8(-$COOCH_3$), 52.2(-$COOCH_3$), 52.1(-$COOCH_3$), 37.9(CH_2 Lev), 30.0(CH_3CO), 27.9(CH_2 Lev), 21.2(CH_3 STol). $[\alpha]^{20}_D$ = -30° (c = 1.0, $CHCl_3$). IR (neat): 696, 733, 808, 864, 908, 947, 1026, 1057, 1082, 1105, 1117, 1150, 1177, 1207, 1240, 1265, 1302, 1362, 1456, 1717, 1749, 2853, 2922, 2951. HR-MS: [M+Na^+] Calculated for $C_{75}H_{80}O_{20}S$: 1355.48559; found: 1355.48641.

Tetrasaccharide (32): This product was prepared following the general procedure for glycosylation reactions (0.6eq



TBSOTf, -78 °C, 1d, -78 °C - -45 °C, 12h). Yield: 69 mg, (0.04 mmol), 80%. TLC: R_f = 0.52 (toluene:ethyl acetate = 4:3). ^{1}H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.53 (d, *J* = 7.8 Hz, 2H), 7.48 – 7.40 (m, 2H), 7.41 – 7.10 (m, 34H), 7.05 (d, *J* = 8.3 Hz, 2H), 5.71 (d, *J* = 8.3 Hz, 1H), 5.32 (d, *J* = 4.0 Hz, 1H), 5.23 (dd, *J* = 3.6, 1.9 Hz, 1H), 5.18 (d, *J* = 1.9 Hz, 1H), 4.98 (d, *J* = 4.0 Hz, 1H), 4.87 (dd, *J* = 11.9, 9.2 Hz, 2H), 4.78 – 4.67 (m, 2H), 4.65 – 4.24 (m, 15H), 4.19 (d, *J* = 12.9 Hz, 1H), 4.10 – 3.92 (m, 3H), 3.93 – 3.74 (m, 5H), 3.66 (dt, *J* = 6.1, 3.6 Hz, 2H), 3.54 (s, 3H), 3.47 (s, 3H), 3.43 (s, 3H), 2.75 – 2.54 (m, 2H), 2.50 – 2.35 (m, 2H), 2.26 (s, 3H), 2.15 (s, 3H), 1.92 (s, 3H); ^{13}C –APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 206.2, 171.5, 170.6, 169.7, 169.0, 168.6, 139.3, 138.5, 138.3, 138.2, 138.0, 137.9, 137.6, 131.4, 129.5, 128.4, 127.7, 103.4(C-$1_{Mann'}$), 97.0, 96.6(C-1_{Gul}, C-$1_{Gul'}$), 82.8(C-1_{Mann}), 79.5, 78.2, 76.0, 75.3, 74.5, 74.2, 74.1, 73.8, 73.8, 73.5, 73.2, 72.9, 72.8, 72.6, 72.4, 72.3, 71.3, 71.1, 70.9, 66.2, 63.2, 52.1, 37.9, 29.7, 28.0, 20.9; ^{13}C –HMBC ($CDCl_3$, 100 MHz): 103.4($J_{C1,H1}$ = 157Hz, C-$1_{Mann'}$), 82.8(C-1_{Mann}),97.0, 96.6($J_{C1,H1}$ = 169Hz, $J_{C1,H1}$ = 170Hz, C-1_{Gul}, C-$1_{Gul'}$). $[\alpha]^{20}_D$ = -42° (c = 1.0, $CHCl_3$). HR-MS: [M+Na^+] Calculated for $C_{97}H_{104}O_{26}S$: 1739.64287; found: 1739.64349.

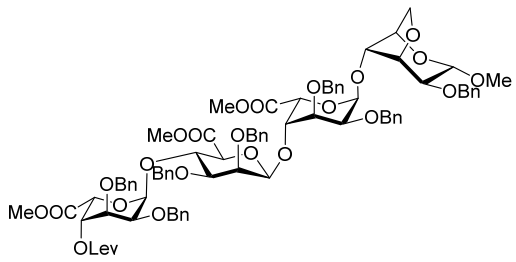
Tetrasaccaride 33: As General procedure for glycosylation reactions, purification by column chromatograpy (silica



gel, pentane/DCM/EtOAc, 3/1/1, v/v/v) yielded **33** as a colourless form (164 mg, 91%, β:α > 20:1). TLC: R_f = 0.54 (toluene/EtOAc, 4/3, v/v); $[\alpha]^{20}_D$ = -61° (c = 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.60 – 6.92 (m, 44H, CH_{arom}), 5.68 (d, *J* = 7.8 Hz, 1H, H-1_{Mann}), 5.41 – 5.12 (m, 3H, H-$1_{Gul'}$, H-$4_{Gul'}$, H-$5_{Gul'}$), 5.13 – 4.97 (m, 1H, H-1_{Gul}),

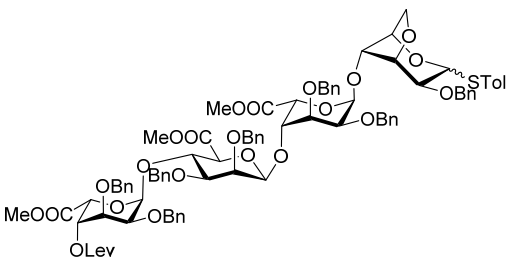
4.98 – 4.20 (m, 19H), 4.23 – 3.98 (m, 2H, H-4_{Gul}, H-$5_{Mann'}$), 3.95 – 3.25 (m, 19H), 2.86 – 2.33 (m, 4H, Lev), 2.27 (s, 3H, CH_3 STol), 2.13 (s, 3H, $COCH_3$); ^{13}C –APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 206.2(C=O Lev), 171.5, 169.8, 169.5, 169.0, 168.6(-$COOCH_3$), 139.0, 138.6, 138.5, 138.1, 138.1, 137.9, 137.8, 137.6($C_{q\ arom}$), 131.7(CH_{arom}), 130.3($C_{q\ arom}$), 129.5, 128.4, 128.4, 128.2, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.7, 127.6, 127.5, 127.2(CH_{arom}), 103.3(C-$1_{Mann'}$), 97.9(C-1_{Gul}), 96.6(C-$1_{Gul'}$), 82.5(C-1_{Mann}, the chemical shift of this carbon is according to HSQC because it can not seen from carbon spectrum), 79.3(C-$3_{Mann'}$), 78.6(C-4_{Gul}), 77.2(C-$5_{Mann'}$), 76.1, 74.8, 74.3, 74.2, 74.1, 74.0, 73.5, 73.2, 72.9, 72.4, 72.4, 72.3, 72.3, 71.4, 71.2, 71.2, 70.9(C-$4_{Gul'}$), 67.7(C-5_{Gul}), 66.2(C-$5_{Gul'}$), 52.3, 52.1, 52.1(-$COOCH_3$), 37.8(CH_2 Lev), 29.7(CH_3CO), 28.0(CH_2 Lev), 21.1(CH_3 STol). IR (neat): 698, 737, 810, 910, 930, 953, 1028, 1063, 1090, 1121, 1177, 1207, 1240, 1285, 1302, 1329, 1362, 1437, 1454, 1497, 1746, 2870, 2922, 3030. HR-MS: [M+Na^+] Calculated for $C_{96}H_{102}O_{26}S$: 1725.62722; found: 1725.62820.

Tetrasaccaride 34: As General procedure for glycosylation reactions, purification by column chromatograpy (silica



gel, pentane/DCM/EtOAc, 3/1/1, v/v/v) yielded **34** as a colourless syrup (110 mg, 95%, β:α > 20:1). TLC: R_f = 0.20 (toluene/EtOAc, 4/3, v/v); $[\alpha]^{20}_D$ = -71° (c = 1, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.54 – 6.98 (m, 35H), 5.32 – 5.14 (m, 6H), 4.91 – 4.80 (m, 4H, H-$1_{Gul'}$, H-1_{Gul}, H-$4_{Gul'}$, H-$5_{Gul'}$), 4.77 (d, *J* = 1.6 Hz, 2H), 4.69 (d, *J* = 3.6 Hz, 1H, H-5_{Gul}), 4.65 (s, 1H), 4.62 – 4.39 (m, 11H), 4.38 – 4.16 (m, 9H), 4.12 (d, *J* = 10.5 Hz, 1H), 4.01 (d, *J* = 8.4 Hz, 1H), 3.92 (m, 4H), 3.74 (dd, *J* = 6.7, 1.3 Hz, 1H), 3.68 (s, 3H), 3.66 (s, 1H), 3.63 – 3.55 (m, 1H), 3.52 (s, 3H), 3.46 (s, 3H), 3.43 (s, 3H), 3.36 (dd, *J* = 9.2, 2.6 Hz, 1H), 2.74 – 2.56 (m, 2H), 2.50 – 2.34 (m, 2H), 2.14 (s, 3H). ^{13}C –APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 206.2, 171.6, 169.9, 169.1, 168.6, 139.3, 138.6, 138.6, 138.6, 138.4, 138.0, 137.7, 128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.7, 127.6, 127.5, 127.3, 103.3(C-$1_{Mann'}$), 102.7(C-1_{Mann}), 96.7(C-$1_{Gul'}$), 95.9(C-1_{Gul}), 79.3, 78.7, 77.5, 77.2, 76.8, 76.2, 76.0, 74.9, 74.5, 74.2, 74.2, 73.3, 73.3, 73.0, 72.7, 72.5, 72.4, 71.5, 71.3, 71.2, 71.0, 70.1, 67.6(C-5_{Gul}), 66.3(C-$5_{Gul'}$), 56.1, 52.4, 52.2, 37.9, 29.8, 28.1; ^{13}C-HMBCipvGATED ($CDCl_3$, 100 MHz): 103.3($J_{C1,H1}$ = 157Hz, C-$1_{Mann'}$), 102.7($J_{C1,H1}$ = 164Hz, C-1_{Mann}), 96.7, 95.9 ($J_{C1,H1}$ = 171Hz, 168Hz). IR (neat): 698, 737, 941, 968, 1026, 1070, 1121, 1206, 1238, 1306, 1362, 1437, 1454, 1497, 1744, 2922. HR-MS: [M+Na^+] Calculated for $C_{82}H_{90}O_{25}$: 1497.56634; found: 1497.56672.

Tetrasaccaride 35: As General procedure for glycosylation reactions, purification by column chromatograpy (silica



gel, pentane/DCM/EtOAc, 3/1/1, v/v/v) yielded **35**, the 1-thio-α-D-mannopyranoside was epimerided in glycosylation condition (α/β = 5/1), as a colourless syrup (76 mg, 71%, β:α > 20:1). TLC: R_f = 0.36

(toluene/EtOAc, 4/3, v/v). ^{1}H NMR ($CDCl_3$, 400 MHz,HH-COSY, HSQC): δ 7.56 – 7.01 (m, 34H), 5.30 (d, *J* = 3.9 Hz, 1H), 5.26 – 5.18 (m, 3H), 5.12 (d, *J* = 8.9 Hz, 1H), 4.99 (d, *J* = 12.2 Hz, 1H), 4.87 (d, *J* = 12.0 Hz, 1H), 4.82 – 4.65 (m, 5H), 4.61 – 4.20 (m, 15H), 4.15 – 4.07 (m, 1H), 4.04 (d, *J* = 8.3 Hz, 1H), 3.98 – 3.84 (m, 3H), 3.73 (dd, *J* = 8.9, 1.3 Hz, 1H), 3.67 (m, 4H), 3.63 – 3.55 (m, 1H), 3.53 (s, 3H), 3.46 (s, 3H), 3.37 (dd, *J* = 9.2, 2.8 Hz, 1H), 2.85 – 2.38 (m, 4H), 2.30 (s, 3H), 2.15 (s, 3H); ^{13}C –APT NMR ($CDCl_3$, 100 MHz, HSQC): δ 206.2, 171.6, 169.9, 169.1, 168.6, 139.3, 138.6, 138.6, 138.4, 138.2, 138.0, 137.7, 137.2, 131.8, 131.7, 129.7, 128.4, 128.4, 128.3, 128.3, 128.1, 128.0, 128.0, 127.9, 127.8, 127.7, 127.7, 127.7, 127.6, 127.6, 127.5, 127.5, 127.5, 127.4, 127.3, 103.3, 96.7, 96.2, 85.3, 79.4, 78.8, 77.5, 77.2, 76.8, 76.3, 76.3, 75.6, 75.2, 74.5, 74.2, 73.5, 73.3, 73.1, 73.0, 72.7, 72.5, 72.4, 71.5, 71.3, 71.0, 69.7, 67.8, 66.3, 52.4, 52.2, 37.9, 29.8, 28.1, 21.2. IR (neat): 698, 734, 810, 1026, 1061, 1094, 1117, 1207, 1238, 1306, 1360, 1437, 1454, 1495, 1744, 2920, 3030. HR-MS: [M+Na^{+}] Calculated for $C_{88}H_{94}O_{24}S$: 1589.57480; found: 1589.57607.

3.5 References

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