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A highly α-selective glycosylation for the convenient synthesis of repeating α-(1→4)-linked *N*-acetyl-galactosamine units

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ABSTRACT

The repeating Gal*p*NAc-α-(1→4)-Gal*p*NAc unit is part of a series of essential structures that can be found in many important biomolecules such as the glycoproteins and the O-antigenic polysaccharides of clinically important bacterial strains. In this paper, we describe an exclusive α-selective glycosylation reaction, using a 4,6-di-*O*-*tert*-butyldimethylsilyl-*N*-acetyloxazolidinone-protected thioglycoside as the glycosyl donor, under pre-activation conditions, with only half amount of the promoter, providing the product Gal*p*NAc-α-(1→4)-Gal*p*NAc in high isolated yield. This reaction can be also applied to increasing the length of the repeating structure, which is of significant use in further synthesis of branched or linear oligosaccharides.

1. Introduction

The repeating Gal*p*NAc-α-(1→4)-Gal*p*NAc unit constitutes essential structures incorporated in a range of oligosaccharides and glycoconjugates with biologically important roles. For instance, *Campylobacter jejuni*, a pathogenic Gram negative bacterium causing gastroenteric disorder and neuromuscular paralysis, has an antigenic asparagine (Asn)-linked (N-linked) glycoprotein which contains pentameric α-(1→4)-linked 2-acetamido-2-deoxy-D-galactopyranose residues (Fig. 1A).[1,2] In addition, the repeating unit of the O-antigen moiety of the lipopolysaccharide (LPS) from *Acinetobacter baumannii* strain 9,[3] *Escherichia coli* O142,[4] *E. coli* O121,[5] *Providencia alcalifaciens* O21[6] and the sheath polysaccharide (SPS) of *Sphaerotilus natans* (Fig. 1B),[7] all contain the important Gal*p*NAc-α-(1→4)-Gal*p*NAc motif.

The synthesis of such glycans can lead the way to synthetic neoglycoconjugate vaccines. Obviously, the construction of repeating α-(1→4)-linked *N*-acetylgalactosamine residues is one of the most significant parts of the synthetic work in the preparation of these glycans. In previous studies, several efforts have been made to synthesize the N-linked glycan of *C. jejuni*. Imperiali and co-workers have reported the chemoenzymatic synthesis of this glycan.[8–10] However, the enzymatic approach called for strict control of reaction conditions and could not be performed to provide the target molecule in large quantity. Ito and co-workers developed a chemical route for the stereoselective construction of the α-(1→4)-Gal*p*NAc repeat, utilizing a pentafluoropropionyl (PFP) group as a temporary protective group of the C-4 OH group in the Gal*p*NAc glycosyl donor.[11–13] Although the ratio of anomeric isomers (α/β) was high, the use of 2-azido-D-pyranosides required several functional group transformations, which decreased the synthetic efficiency. Here, we report a convenient and highly α-selective glycosylation for the preparation of the repeating Gal*p*NAc-α-(1→4)-Gal*p*NAc unit.

2. Results and discussion

Since oxazolidinone-protected glucosamine was first described by the Kerns group to be an α-selective glycosyl donor,[14] several studies had been made subsequently on its *N*-acetyl analogues,[15,16] confirming that the ring-fused oxazolidinone moiety is an effective non-participating group for the stereoselective synthesis of α-linked glycosides of 2-amino-2-deoxy-D-hexopyranoses. This protective group had been also introduced into acceptors to enhance the reactivity of the 4-hydroxy group during the glycosylation.[17,18] The 'tied-back' nature of the oxazolidinone can reduce the hindrance around the nucleophilic oxygen.[19] Moreover, the *N*-acetyloxazolidinone functionality also decreases the tendency for amide glycosylation,[20] and removes the possibility of problematic hydrogen bonding networks.[21]

Considering that *N*-acetyloxazolidinone can serve as a stereoselective donor and an effective glycosyl acceptor, and can be easily removed by chemoselective deprotection,[17,18,22] we decided to

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A α-Gal*p*NAc-(1→4)-α-Gal*p*NAc-(1→4)-[β-Glc*p*-(1→3)]-α-Gal*p*NAc-(1→4)-α-Gal*p*NAc-(1→4)-α-Gal*p*NAc-(1→)-β-Bacp-Asn-

B →4)-β-D-Gal*p*NAc-(1→4)-β-D-Glc*p*-(1→3)-β-D-Gal*p*NAc-(1→4)-α-D-Gal*p*NAc-(1→4)-α-D-Gal*p*NAc-(1→

Figure 1. Structures of glycans: (A) the structure of the Asn-linked heptasaccharide glycan of *Campylobacter jejuni*; (B) the structure of the repeating unit from the sheath polysaccharide of *Sphaerotilus natans*.

introduce this protecting group into the galactosamine moiety. Thus, 4,6-protected *N*-acetyloxazolidinone thioglycosides were chosen as building blocks to construct α-(1→4)-linked Gal*p*NAc fragments. Three glycosyl donors and one acceptor were chosen (Fig. 2).

The oxazolidinone-containing glycosyl donors and acceptor can be readily prepared from commercially available D-galactosamine (**5**) on large scale, in high yield (Scheme 1). Acetylation of **5** gave galactosamine pentaacetate (**6**), which was then treated with *p*-toluenethiol and $SnCl_4$ to produce thioglycoside **7**. By sequential deacetylation and oxazolidinone formation, the key synthetic intermediate **8** was obtained. Following well-established procedure, donors **1**, **2** and **3** were prepared smoothly from the common intermediate **8** under different conditions. The reductive cleavage of the benzylidene acetal in **2** using Et_3SiH and TfOH[23] provided acceptor **4** with a hydroxyl group exposed at the 4-position. Interestingly, the anomeric configuration was changed from β to α under acidic conditions.[16,18,24,25]

The 'pre-activation' protocol described a method in which a glycosyl donor is completely activated and consumed (by TLC detection) prior to the addition of a glycosyl acceptor.[26–31] We adopted this protocol with the belief that a pre-activation protocol might influence the stereochemistry outcome of the glycosylations.[32] Under the pre-activation conditions, we first coupled acceptor **4** with donor **1** employing different promoter systems. The combination of benzenesulfinyl morpholine (BSM)[33] and triflic anhydride (Tf_2O) gave similar low yield (around 10%) of the coupling product to the 1-benzenesulfinyl piperidine (BSP)–Tf_2O[34] system. The combination of *p*-toluenesulfenyl chloride (*p*-TolSCl) and silver triflate (AgOTf) gave no separable coupling product. The best result was obtained by using diphenyl sulfoxide (Ph_2SO)–Tf_2O combination[35,36] in 20% isolated yield.

We then took the best promoter system, Ph_2SO–Tf_2O, to test the glycosylation of **4** with the two other donors, **2** and **3** (Table 1). However, the glycosylation of **4** with **2** gave no disaccharide and the glycosylation of **4** with **3** provided a low yield of disaccharide with exclusive α-anomeric selectivity. The major problem of this glycosylation was the low reactivity of acceptor **4**. Compound **4** always remained in large quantity while donors decomposed. This difficulty is common to most pyranose acceptors with a 4-OH free, especially in galactosamine acceptors with the much lower reactivity of this hydroxyl group.

In the consideration of acceptors, we tried other types of protecting groups on 6-OH. However, the benzyl-protected acceptor **4** was the only one that reacted, owing to its electron-donating ability which enhances the nucleophilicity of 4-OH. In the consideration of donors, the lack of reaction of **2** might be attributed to the three-ring structure of the oxocarbenium intermediate, which could be quite unstable because of the great ring tension. Acetylated donor **1** also had low reactivity due to the electron-withdrawing substituents. Therefore, more attention was paid to donor **3**, which should theoretically have higher reactivity (Scheme 2).

To optimize the coupling yield, we focused on the amount of the promoter and donor used in the glycosylation (Table 2). As shown in Table 2, the combination of Ph_2SO–Tf_2O without the hindered base 2,4,6-tri-*tert*-butylpyrimidine (TTBP)[37,38] in the pre-activation protocol gave no disaccharide product (entry 1) but instead decomposed donor and intact acceptor. The mechanism of this reaction is unclear. One possible reason is that the indispensable TTBP might act as a stabilizing agent to protect the highly active oxocarbenium intermediate after the pre-activation of donor in this glycosylation case.

By reducing the amount of Ph_2SO–Tf_2O to nearly half that of the donor (entry 3), it was surprisingly found that not only could donor **3** be pre-activated readily and completely, but also the yield of disaccharide **9** was increased greatly from 17.4% to 59.0%. Nonetheless, when the amount of promoter was raised to 0.8 equiv the yield was decreased (entry 4). Thus, we presumed that the optimum number of equivalents of Ph_2SO–Tf_2O was half that of the donor. Under these conditions we then raised the amount of donor **3**, trying to reduce the remaining amount of acceptor **4** (entries 5, 6 and 7). The outcomes were good and the best yield, 74.1%, was obtained by only using 1.5 equiv of donor **3** and almost half the amount of promoter (entry 6).

In addition, an obvious distinction was found between the pre-activation protocol and the traditional non-preactivation procedure by comparing entry 3 with 8 and entry 6 with 9, indicating the obvious advantage of pre-activation. In all conditions, the number of equivalents of TTBP needed was twice as much as that of the donor or the yield declined dramatically. Donors **1** and **2** were also checked again with half amount of promoter. However, donor **1** was too inactive to be pre-activated completely, leading to much lower yield than the previous method; donor **2** still gave no coupling product although it was able to be entirely pre-activated.

As Wong and co-workers has proposed,[39] one possible rationalization for this outcome may be that the reaction pathway involves sulfonium intermediates that can further promote glycosylations

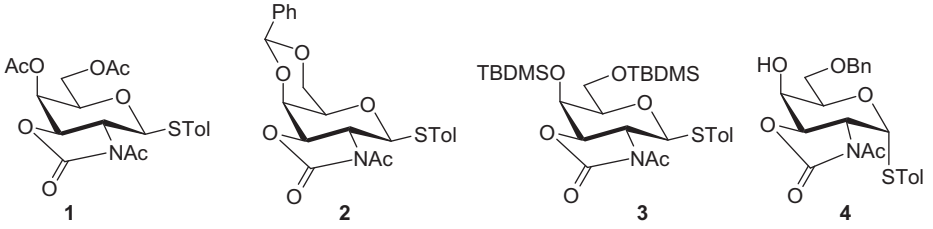
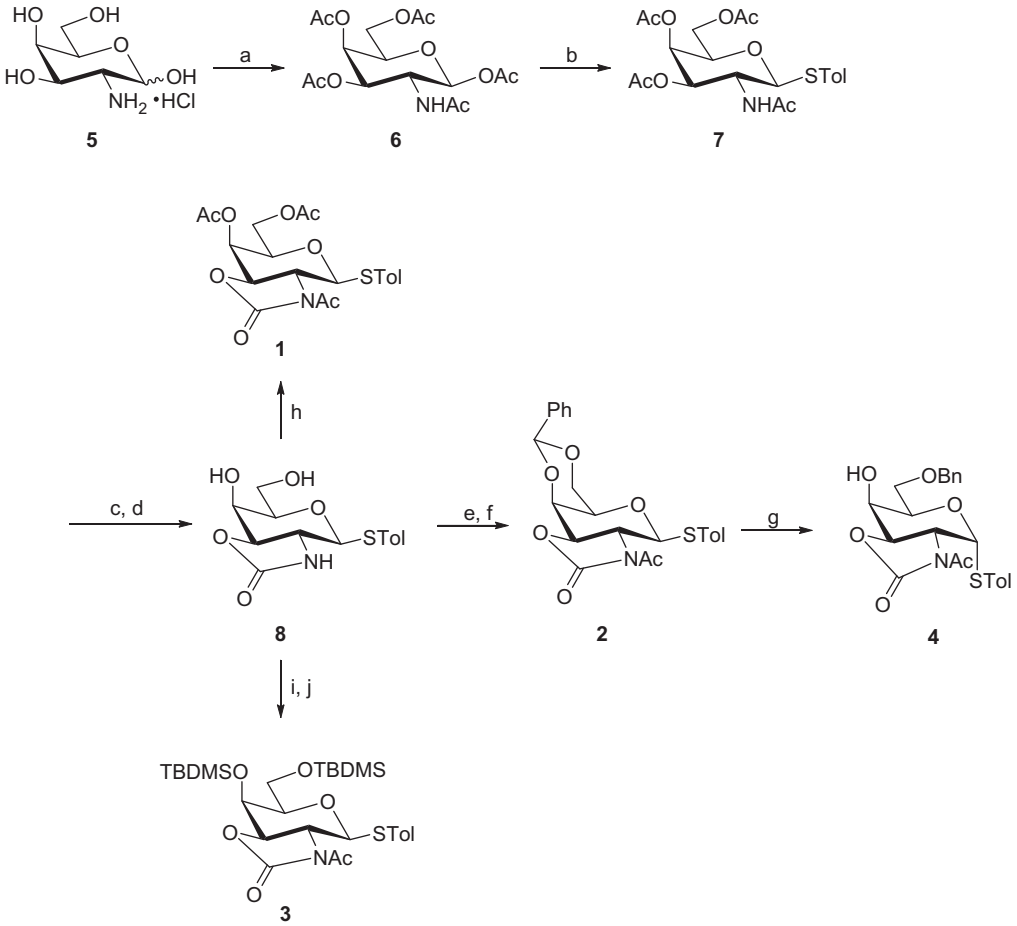


Figure 2. Glycosyl building blocks.



Scheme 1. Synthesis of monosaccharide blocks. Reagents and conditions: (a) NaOAc, Ac_2O, 140 °C. 3 h, 91%; (b) $SnCl_4$, TolSH, CH_2Cl_2, reflux, overnight, 93%; (c) NaOH, H_2O, reflux, 12 h; (d) triphosgene, $NaHCO_3$, CH_3CN/H_2O = 2:1, 30 min, 81% for two steps; (e) $PhCH(OMe)_2$, CSA, CH_3CN, rt, 10 min; (f) Ac_2O, pyridine, DMAP, 12 h, 90% for two steps. (g) Et_3SiH, TfOH, CH_2Cl_2, −72 °C, 1 h, 73%; (h) Ac_2O, pyridine, DMAP, 3 h, 88%; (i) TBDMSCl, imidazole, DMF, 70 °C, 26 h; (j) Ac_2O, pyridine, DMAP, 12 h, 77% for two steps.

Table 1
Glycosylation of **4** with **1**, **2** and **3**

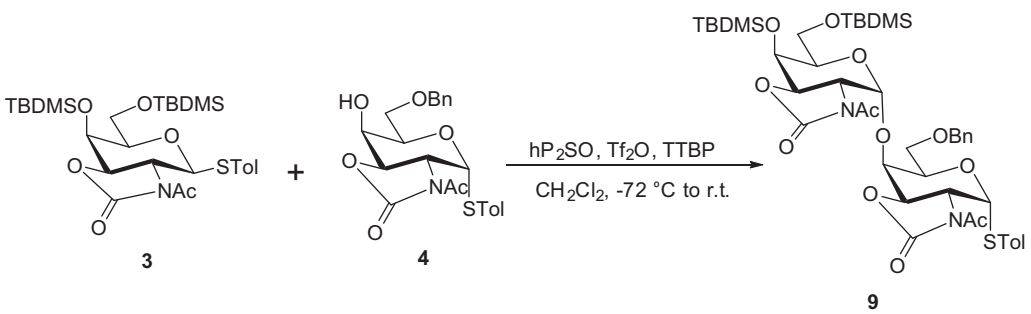
Donor	Acceptor	Yield of disaccharide (%)	α/β
1	4	20	α only
2	4	No reaction	
3	4	17	α only

Reagents and conditions: Ph_2SO, Tf_2O, TTBP, CH_2Cl_2, −72 °C to r.t.

(Fig. 3). If a full equivalent of promoter was provided, half was enough to activate the donor and the other half would remain to activate the subsequently added acceptor or even the newly formed disaccharide and destroy them.

Subsequently, disaccharide **9** was transformed to acceptor **11** in order to lengthen the repeating α-(1→4)-linked Gal*p*NAc unit. With the method used in the synthesis of monosaccharide building blocks, compound **9** was readily changed into **11** in high yield (Scheme 3A). Trisaccharide **12** was obtained as a single α-anomer by the coupling of **3** and **11** (Scheme 3B). As was done for the disaccharide, the glycosylation could be greatly improved by changing the amount of promoter (Table 3).

The relationship between the amount of promoter and the yield was similar to the disaccharide case. It seemed that using a little more than half amount of promoter was better (Table 3, entry 3 vs 2 and entry 8 vs 7). Due to the larger sugar fragment and much lower 4-OH reactivity, the best yield of **12** was 68% using 2.0 equiv



Scheme 2. The coupling reaction of **4** and **3**.

Table 2
Glycosylation of **4** with **3** under different conditions

Entry	Donor (equiv)	Acceptor (equiv)	Promoter system (equiv)	Yield of **9** (%)	α/β
Pre-activation					
1	1.1	1.0	Ph_2SO (1.1)/Tf_2O (1.1)	Trace	
2	1.1	1.0	Ph_2SO (1.1)/Tf_2O (1.1)/TTBP(2.2)	17.4	α only
3	1.1	1.0	Ph_2SO (0.6)/Tf_2O (0.7)/TTBP (2.2)	59.0	α only
4	1.1	1.0	Ph_2SO (0.8)/Tf_2O (0.9)/TTBP (2.2)	45.0	α only
5	1.3	1.0	Ph_2SO (0.7)/Tf_2O (0.8)/TTBP (2.6)	64.3	α only
6	1.5	1.0	Ph_2SO (0.8)/Tf_2O (0.9)/TTBP (3.0)	74.1	α only
7	2.0	1.0	Ph_2SO (1.0)/Tf_2O (1.1)/TTBP (4.0)	72.9	α only
Non-pre-activation					
8	1.1	1.0	Ph_2SO (0.6)/Tf_2O (0.7)/TTBP (2.2)	48.0	α only
9	1.5	1.0	Ph_2SO (0.8)/Tf_2O (0.9)/TTBP (3.0)	54.2	α only

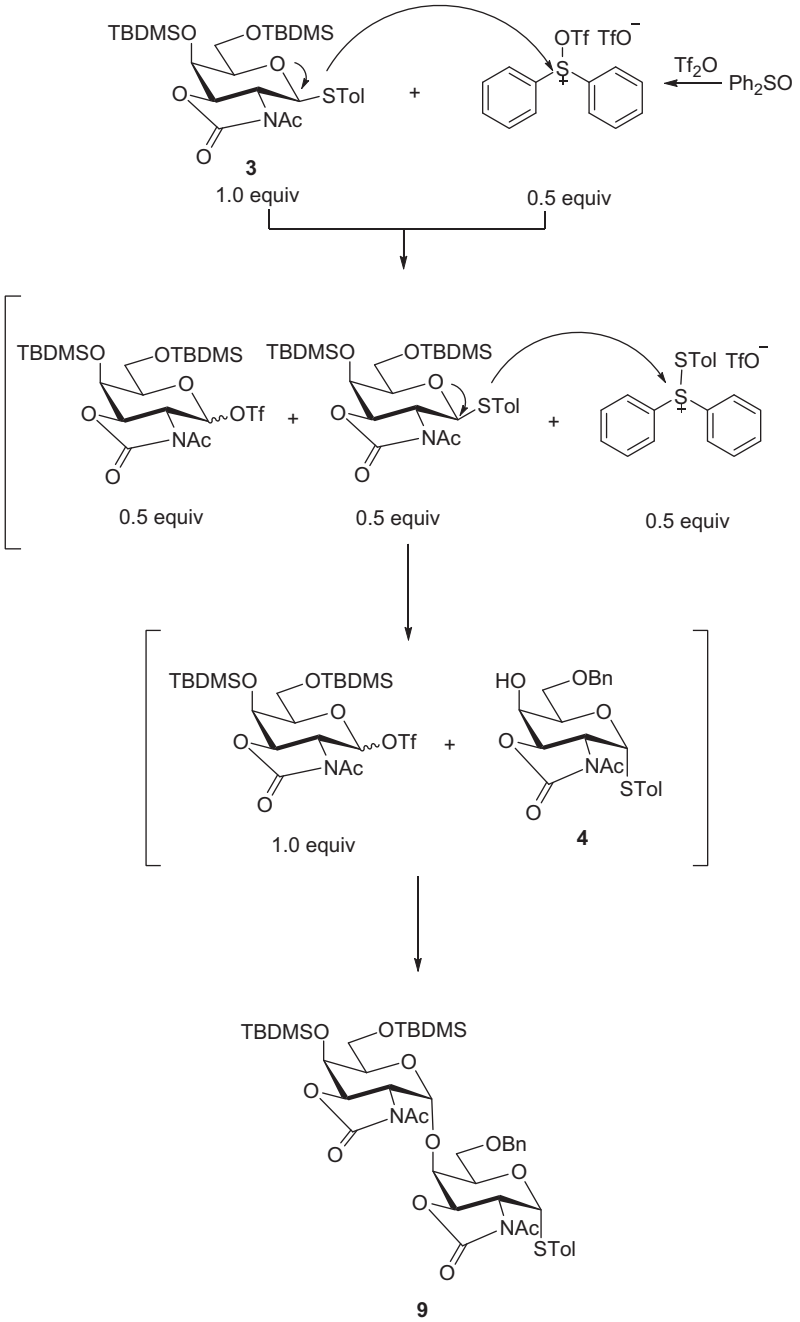
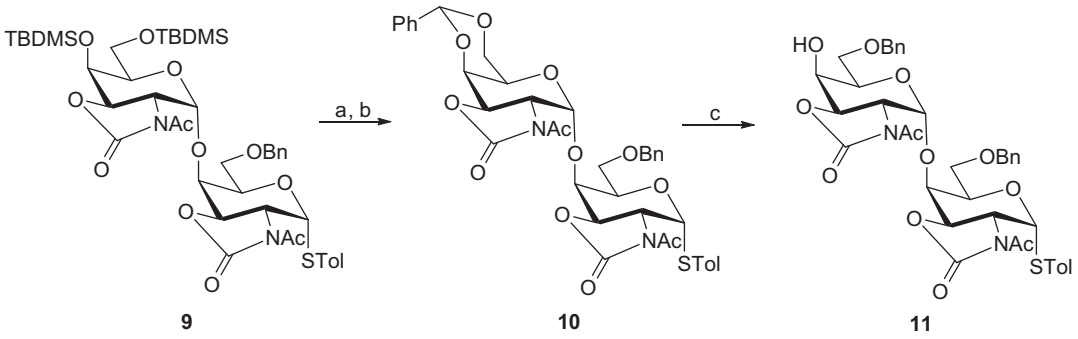
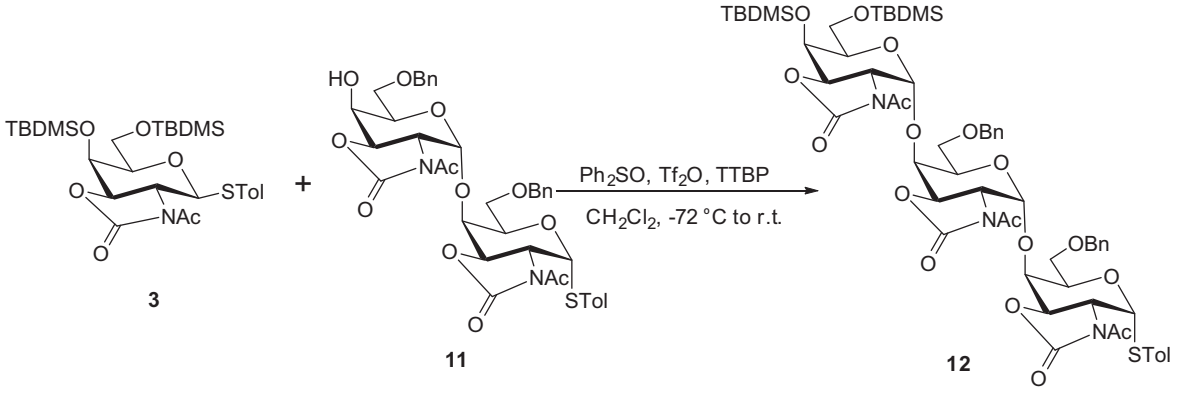


Figure 3. Proposed reaction pathway for disaccharide formation with substoichiometric amount of Ph_2SO–Tf_2O.



(A) Synthesis of disaccharide blocks. Reagents and conditions: (a) TBAF/THF, r.t., 10 min; (b) $PhCH(OMe)_2$, CSA, CH_3CN, r.t., 10 min, 88% for two steps. (c) Et_3SiH, TfOH, CH_2Cl_2, -72 °C, 50 min, 80%.



(B) Synthesis of trisaccharide

Scheme 3. The synthesis of trisaccharide as an example of increasing the α-(1→4)-linked Gal*p*NAc-repeating unit.

Table 3
Glycosylation of **11** with **3** under different conditions

Entry 1	Donor (equiv)	Acceptor (equiv)	Promoter system (equiv)	Yield of **12** (%)	α/β
Pre-activation					
1	1.1	1.0	Ph_2SO (1.1)/Tf_2O (1.1)/TTBP (2.2)	22.7	α only
2	1.1	1.0	Ph_2SO (0.6)/Tf_2O (0.7)/TTBP (2.2)	26.0	α only
3	1.1	1.0	Ph_2SO (0.8)/Tf_2O (0.9)/TTBP (2.2)	33.3	α only
4	1.5	1.0	Ph_2SO (0.8)/Tf_2O (0.9)/TTBP (3.0)	41.0	α only
5	1.5	1.0	Ph_2SO (1.2)/Tf_2O (1.2)/TTBP (3.0)	20.8	α only
6[a]	2.0	1.0	Ph_2SO (0.8)/Tf_2O (0.9)/TTBP (4.0)	38.2	α only
7	2.0	1.0	Ph_2SO (1.0)/Tf_2O (1.1)/TTBP (4.0)	43.8	α only
8	2.0	1.0	Ph_2SO (1.2)/Tf_2O (1.3)/TTBP (4.0)	68.0	α only
9	2.0	1.0	Ph_2SO (1.5)/Tf_2O (1.6)/TTBP (4.0)	20.0	α only
Non-preactivation					
10	1.1	1.0	Ph_2SO (0.8)/Tf_2O (0.9)/TTBP (2.2)	20.8	α only

[a] The donor was not activated completely.

of donor **3** and 1.2 equiv of Ph_2SO. Nevertheless, the pre-activation protocol showed a higher yield than the ordinary non-preactivation procedure (entry 3 vs 10).

As donor **3** and acceptor **4** could be easily synthesized on a large scale, this simple but effective method might be a more convenient way to construct the repeating Gal*p*NAc-α-(1→4)-Gal*p*NAc unit for the synthesis of bioactive oligosaccharides. Meanwhile, the disaccharide (**9**), acceptor (**11**) and trisaccharide (**12**) products could be further used as building blocks in the synthesis of branched and linear glycans with diverse bioactivities. Furthermore, as both the donor and acceptor are thioglycosides, this 'thioglycoside-to-thioglycoside' glycosylation reaction could be applied to the iterative one-pot oligosaccharide assembly.

In conclusion, an examination of glycosylation reactions for the construction of the repeating Gal*p*NAc-α-(1→4)-Gal*p*NAc unit was performed. The use of the *N*-acetyloxazolidinone-protected thioglycosides as the glycosyl donor and acceptor was effective in providing the exclusive α-stereoselective glycosylation. The greatly increased yield of disaccharide and trisaccharide in the coupling reaction was achieved by reducing the amount of Ph_2SO–Tf_2O promoter. This method may find applications in the chemical synthesis of various complex oligosaccharides with

biological importance. Further extension of this protocol is now under investigation.

3. Experimental

3.1. General methods

All chemicals were purchased as reagent grade and used without further purification, unless otherwise noted. Dichloromethane (CH_2Cl_2), pyridine and acetonitrile (CH_3CN) were distilled over calcium hydride (CaH_2). MeOH was distilled from magnesium. DMF was stirred with CaH_2 and distilled under reduced pressure. All glycosylation reactions were carried out under anhydrous conditions with freshly distilled solvents, unless otherwise noted. Reactions were monitored by analytical thin-layer chromatography on Silica Gel 60 F_{254} precoated on aluminium plates (E. Merck). Spots were detected under UV (254 nm) and/or by staining with acidic ceric ammonium molybdate. Solvents were evaporated under reduced pressure and below 40 °C (bath). Organic solutions of crude products were dried over anhydrous Na_2SO_4. Column chromatography was performed on silica gel (200–300 mesh). ^{1}H NMR spectra were recorded on a JEOL AL-300, Varian INOVA-500 or Advance DRX Bruker-400 spectrometers at 25 °C. Chemical shifts (in ppm) were referenced to tetramethylsilane (δ = 0 ppm) in deuterated chloroform. ^{13}C NMR spectra were obtained by using the same NMR spectrometers and were calibrated with $CDCl_3$ (δ = 77.00 ppm). Mass spectra were recorded using a PE SCLEX QSTAR spectrometer. Elemental analysis data were recorded on a Vario EL-III elemental analyzer.

3.2. *p*-Tolyl 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-1-thio-β-D-galactopyranoside (7)

$SnCl_4$ (6.0 g, 2.7 mL, 23.1 mmol, 0.9 equiv) was added to a stirred solution of D-galactosamine pentaacetate (**6**)[40,41] (10.0 g, 25.7 mmol, 1.0 equiv) and *p*-toluenethiol (3.8 g, 30.8 mmol, 1.2 equiv) in dry CH_2Cl_2 (200 mL). The reaction mixture was heated at reflux overnight, then cooled to room temperature and the reaction was quenched by the addition of satd aq $NaHCO_3$ (250 mL). The aqueous layer was separated and extracted with CH_2Cl_2 (2 × 250 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and evaporated. The residue obtained was recrystallized from hexane–EtOAc to give **7** (10.8 g, 93%) as a white amorphous solid. R_f = 0.5 (EtOAc): $[\alpha]_D^{27}$ −9.4 (*c* 1.0, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, 2H, *J* = 8.0 Hz Ar), 7.11 (d, 2H, *J* = 8.0 Hz, Ar), 5.68 (d, 1H, *J* = 9.2 Hz, NH), 5.37 (d, 1H, *J* = 2.8 Hz, H-4), 5.20 (dd, 1H, $J_{3,2}$ = 10.8 Hz, $J_{3,4}$ = 3.2 Hz, H-3), 4.86 (d, 1H, $J_{1,2}$ = 10.4 Hz, H-1), 4.21–4.08 (m, 3H, H-2, H-6a, H-6b), 3.92 (t, 1H, *J* = 6.4 Hz, H-5), 2.33 (s, 3H, CH_3), 2.12 (s, 3H, CH_3), 2.02 (s, 3H, CH_3), 1.98 (s, 6H, CH_3 × 2); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.52, 170.39, 170.25, 138.03, 132.59, 129.57, 129.19, 87.42, 74.26, 71.08, 66.90, 61.78, 49.65, 23.38, 21.07, 20.64. HRMS (ESI) calcd for $C_{21}H_{31}N_2O_8S$ $[M+NH_4]^+$: 471.1796. Found: 471.1794.

3.3. *p*-Tolyl 2-amino-2,3-*N*,*O*-carbonyl-2-deoxy-1-thio-β-D-galactopyranoside (8)

Compound **7** (5.0 g, 11.0 mmol, 1.0 equiv) was dissolved in 2 N NaOH (100 mL), and heated at reflux for 24 h, cooled to room temperature and the reaction was quenched by the addition of 2 N HCl (100 mL). The mixture was evaporated to give the crude product, which was then dissolved in MeCN (100 mL) and added with satd aq $NaHCO_3$ (50 mL). The mixture was cooled to 0 °C, and triphosgene (1.3 g, 4.4 mmol, 0.4 equiv) was added to the vigorously stirred mixture. After 30 min, EtOAc (150 mL) containing ethylenediamine (2.1 mL, 30.9 mmol) was added and the stirring was continued for 15 min. The aqueous layer was separated and extracted with EtOAc (2 × 75 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and evaporated. The residue obtained was purified by column chromatography on silica gel (1:5 hexane–EtOAc) to give **8** (2.8 g, 81%) as a white amorphous solid. R_f = 0.1 (1:3 hexane–EtOAc): $[\alpha]_D^{27}$ −51.1 (*c* 1.0, MeOH); ^{1}H NMR (400 MHz, CD_3COCD_3) δ 7.50–7.47 (m, 2H, Ar), 7.16 (d, 2H, *J* = 8.0 Hz, Ar), 6.73 (s, 1H, NH), 4.87 (d, 1H, $J_{1,2}$ = 9.6 Hz, H-1), 4.57 (d, 1H, *J* = 4.4 Hz, 4-OH), 4.37 (d, 1H, *J* = 4.0 Hz, 6-OH), 4.32 (dd, 1H, $J_{3,2}$ = 11.2 Hz, $J_{3,4}$ = 2.0, H-3), 3.94–3.89 (m, 2H, H-2, H-6a), 3.82–3.78 (m, 3H, H-4, H-5, H-6b), 2.32 (s, 3H, CH_3); ^{13}C NMR (100 MHz, CD_3COCD_3) δ 159.49, 138.79, 133.59, 130.43, 129.47, 86.59, 83.50, 81.06, 65.63, 62.20, 54.70, 21.02. HRMS (ESI) calcd for $C_{28}H_{35}N_2O_{10}S_2$ $[2M+H]^+$: 623.1728. Found: 623.1729.

3.4. *p*-Tolyl 2-acetamino-4,6-*O*-diacetyl-2,3-*N*,*O*-carbonyl-2-deoxy-1-thio-β-D-galactopyranoside (1)

4-(Dimethylamino)pyridine (9.8 mg, 0.08 mmol, 0.05 equiv) was added to a stirred solution of compound **8** (500 mg, 1.61 mmol, 1.0 equiv) in 8 mL of pyridine. The mixture was cooled to 0 °C and acetic anhydride (Ac_2O) (1.64 g, 1.52 mL, 16.1 mmol) was added dropwise. The resulting solution was gradually warmed to room temperature and stirred for further 3 h. The crude product was concentrated and the residue was purified by column chromatography on silica gel (2:1 hexane–EtOAc) to give **1** as a white amorphous solid (618 mg, 88%): R_f = 0.25 (1.5:1 hexane–EtOAc); $[\alpha]_D^{27}$ −67.4 (*c* 1.0, MeOH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 (d, 2H, *J* = 7.8 Hz, Ar), 7.11 (d, 2H, *J* = 7.8 Hz, Ar), 5.66 (s, 1H, H-4), 4.81 (d, 1H, $J_{1,2}$ = 8.7 Hz, H-1), 4.50 (dd, 1H, $J_{2,1}$ = 8.7 Hz, $J_{2,3}$ = 11.7 Hz, H-2), 4.27 (dd, 1H, $J_{3,2}$ = 11.7 Hz, $J_{3,4}$ = 2.1 Hz, H-3), 4.20 (dd, 1H, *J* = 5.7, 11.4 Hz, H-6a), 4.10 (dd, 1H, *J* = 7.2, 11.4 Hz, H-6b), 3.95–3.91 (m, 1H, H-5), 2.59 (s, 3H, CH_3), 2.34 (s, 3H, CH_3), 2.17 (s, 3H, CH_3), 2.00 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.07, 170.21, 169.34, 153.19, 138.34, 133.26, 129.70, 129.52, 88.69, 78.06, 75.60, 64.96, 61.70, 56.40, 24.76, 21.05, 20.54, 20.51. HRMS (ESI) calcd for $C_{20}H_{23}NO_8SNa$ $[M+Na]^+$: 460.1037. Found: 460.1049.

3.5. *p*-Tolyl 2-acetamido-4,6-*O*-benzylidene-2,3-*N*,*O*-carbonyl-2-deoxy-1-thio-β-D-galactopyranoside (2)

Benzaldehyde dimethyl acetal (1.76 g, 1.74 mL, 11.58 mmol, 2.0 equiv) was added dropwise to a stirred solution of compound **8** (1.80 g, 5.79 mmol, 1.0 equiv) and camphorsulfonic acid (134.40 mg, 0.58 mmol, 0.1 equiv) in dry CH_3CN (18 mL) at room temperature. The pH was about 2–3. The solution was then stirred for 10 min, at which time TLC showed complete disappearance of **8**. The reaction was quenched by the addition of Et_3N to pH around 7 and concentrated in vacuo. After the addition of DMAP (35.3 mg, 0.29 mmol, 0.05 equiv), the mixture was dissolved in 18 mL of pyridine. The solution was cooled to 0 °C and Ac_2O (5.91 g, 5.5 mL, 57.9 mmol, 10 equiv) was added dropwise. The resulting mixture was gradually warmed to room temperature and stirred for further 12 h. The crude product was concentrated and the residue was purified by column chromatography on silica gel (2:1 hexane–EtOAc) to give **2** as a white amorphous solid (2.29 g, 90%): R_f = 0.4 (1:1 hexane–EtOAc); $[\alpha]_D^{27}$ −119.8 (*c* 1.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.53–7.47 (m, 4H, Ar), 7.39–7.37 (m, 3H, Ar), 7.10 (d, 2H, *J* = 8.0 Hz, Ar), 5.60 (s, 1H, PhC*H*), 4.84 (d, 1H, $J_{1,2}$ = 8.8 Hz, H-1), 4.73 (dd, 1H, $J_{2,1}$ = 8.8 Hz, $J_{2,3}$ = 11.2 Hz, H-2), 4.60 (s, 1H, H-4), 4,34 (dd, 1H, *J* = 0.8, 12.8 Hz, H-6a), 4.22 (dd, 1H, $J_{3,2}$ = 11.2 Hz, $J_{3,4}$ = 2.0 Hz, H-3), 4.08 (dd, 1H, *J* = 2.0, 12.8 Hz,

H-6b), 3.48 (s, 1H, H-5), 2.56 (s, 3H, CH_3), 2.33 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.94, 153.61, 138.24, 136.85, 133.51, 130.04, 129.53, 129.39, 128.29, 126.38, 100.54, 88.61, 79.26, 70.98, 69.83, 69.64, 55.43, 24.90, 21.15. HRMS (ESI) calcd for $C_{23}H_{23}NO_6SK$ $[M+K]^+$: 480.0872. Found: 480.0867. Anal. Calcd for $C_{23}H_{23}NO_6S$: C, 62.57; H, 5.25; N, 3.17. Found: C, 62.81; H, 5.49; N, 2.98.

3.6. *p*-Tolyl 2-acetamido-4,6-di-*O*-*tert*-butyldimethylsilyl-2,3-*N*,*O*-carbonyl-2-deoxy-1-thio-β-D-galactopyranoside (3)

A mixture of compound **8** (1.5 g, 4.82 mmol, 1.0 equiv), *tert*-butyldimethylsilyl chloride (4.4 g, 29.1 mmol, 6.0 equiv) and imidazole (1.3 g, 19.11 mmol, 4.0 equiv) in dry DMF (8.8 mL, 0.5 g *tert*-butyldimethylsilyl chloride per mL) was heated at 70 °C for 26 h. After the TLC showed complete disappearance of **8**, the reaction mixture was extracted with EtOAc (90 mL) and the organic layer was washed with satd aq NH_4Cl (30 mL × 2) and water (30 mL). The washed organic layer was dried over Na_2SO_4 and concentrated in vacuo. After the addition of DMAP (29.4 mg, 0.24 mmol, 0.05 equiv), the mixture was dissolved in 15 mL of pyridine. The solution was cooled to 0 °C and Ac_2O (4.92 g, 4.5 mL, 48.23 mmol, 10 equiv) was added dropwise. The resulting solution was gradually warmed to room temperature and stirred for further 12 h. The crude product was concentrated and the residue was purified by column chromatography on silica gel (10:1 hexane–EtOAc) to give **3** as a white amorphous solid (2.16 g, 77%): R_f = 0.7 (3:1 hexane–EtOAc); $[\alpha]_D^{27}$ −58.9 (*c* 1.0, MeOH); ^1H NMR ($CDCl_3$, 400 MHz): δ 7.40 (d, 2H, *J* = 8.0 Hz Ar), 7.08 (d, 2H, *J* = 8.0 Hz Ar), 4.77 (d, 1H, $J_{1,2}$ = 8.7 Hz, H-1), 4.55 (dd, 1H, $J_{2,1}$ = 8.7 Hz, $J_{2,3}$ = 11.3 Hz, H-2), 4.39 (s, 1H, H-4), 4,14 (dd, 1H, $J_{3,2}$ = 11.3 Hz, $J_{3,4}$ = 1.9 Hz, H-3), 3.78 (dd, 1H, *J* = 7.1, 10.2 Hz, H-6a), 3.70 (dd, 1H, *J* = 5.7, 10.2 Hz, H-6b), 3.54–3.50 (m, 1H, H-5), 2.57 (s, 3H, CH_3), 2.32 (s, 3H, CH_3), 0.90 (s, 9H, *t*-Bu), 0.88 (s, 9H, *t*-Bu), 0.12 (s, 3H, CH_3), 0.09 (s, 3H, CH_3), 0.05 (s, 3H, CH_3), 0.03 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 173.22, 153.85, 137.61, 131.99, 130.93, 129.47, 88.57, 81.21, 80.68, 65.72, 61.42, 55.23, 25.84, 24.95, 21.08, 18.21, −4.44, −5.02, −5.43. MS (ESI) 582 $[M+H]^+$, 604 $[M+Na]^+$, 620 $[M+K]^+$. Anal. Calcd for $C_{28}H_{47}NO_6SSi_2$: C, 57.79; H, 8.14; N, 2.41. Found: C, 57.68; H, 7.95; N, 2.26.

3.7. *p*-Tolyl 2-acetamido-6-*O*-benzyl-2,3-*N*,*O*-carbonyl-2-deoxy-1-thio-α-D-galactopyranoside (4)

Et_3SiH (1.19 g, 1.63 mL, 10.23 mmol, 3.0 equiv) and TfOH (1.02 g, 0.60 mL, 6.80 mmol, 2.0 equiv) were added to a stirred mixture of **2** (1.5 g, 3.40 mmol, 1.0 equiv) and activated 4 Å molecular sieves (2.0 g, powder) in CH_2Cl_2 (60 mL, 25 mg of **2** per mL) at −72 °C under nitrogen atmosphere. After being stirred for 1 h at −72 °C, Et_3N (1 mL) and MeOH (1 mL) were added successively. The mixture was filtered and the filtrate was concentrated. The residue was purified by column chromatography on silica gel (4:1 hexane–EtOAc) to give white amorphous solids (1.1 g, 73%): R_f = 0.5 (1:1 hexane–EtOAc); $[\alpha]_D^{27}$ +227.4 (*c* 1.0, MeOH); ^1H NMR ($CDCl_3$, 300 MHz): δ 7.36–7.31 (m, 7H, Ar), 7.09 (d, 2H, *J* = 8.1 Hz, Ar), 6.17 (d, 1H, $J_{1,2}$ = 4.5 Hz, H-1), 4.74 (dd, 1H, $J_{2,1}$ = 4.5 Hz, $J_{2,3}$ = 12.3 Hz, H-2), 4.61 (d, 1H, *J* = 11.4 Hz, PhCH_2), 4.55 (d, 1H, *J* = 11.1 Hz, PhCH_2), 4.53 (s, 1H, H-4), 4,40 (dd, 1H, $J_{3,2}$ = 12.3 Hz, $J_{3,4}$ = 1.8 Hz, H-3), 4.33 (t, 1H, *J* = 5.1 Hz, H-5), 3.82 (d, 2H, *J* = 5.1 Hz, H-6a, H-6b), 3.29 (s, 1H, 4-OH), 2.54 (s, 3H, CH_3), 2.33 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 171.50, 153.00, 138.36, 137.12, 133.02, 129.94, 128.60, 128.12, 127.83, 87.71, 76.54, 73.96, 70.08, 69.91, 66.97, 54.86, 23.93, 21.14. MS (ESI) 444 $[M+H]^+$, 466 $[M+Na]^+$, 482 $[M+K]^+$. Anal. Calcd for $C_{23}H_{25}NO_6S$: C, 62.29; H, 5.68; N, 3.16. Found: C, 62.44; H, 5.72; N, 3.10.

3.8. *p*-Tolyl (2-acetamido-4,6-di-*O*-*tert*-butyldimethylsilyl-2,3-*N*,*O*-carbonyl-2-deoxy-α-D-galactopyranosyl)-(1→4)-2-acetamido-6-*O*-benzyl-2,3-*N*,*O*-carbonyl-2-deoxy-1-thio-α-D-galactopyranoside (9)

Tf_2O (8.7 mg, 5.1 μL, 0.031 mmol, 0.9 equiv) was added to a stirred mixture of **3** (29.6 mg, 0.051 mmol, 1.5 equiv), Ph_2SO (5.5 mg, 0.027 mmol, 0.8 equiv), TTBP (26 mg, 0.11 mmol, 3.0 equiv) and activated 4 Å molecular sieves (500 mg, powder) in CH_2Cl_2 (5 mL) at −72 °C under nitrogen atmosphere. The reaction mixture was stirred for 5 min, after loss of **3** detected by TLC, a solution of the acceptor **4** (15.0 mg, 0.034 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) was added dropwise to the mixture. The mixture was stirred and warmed up to room temperature slowly and stirred for further 2 h, and the reaction was quenched by the addition of Et_3N (0.1 mL). The precipitate was filtered off and the filtrate was concentrated. The residue was purified by column chromatography on silica gel (10:1 hexane–EtOAc) to give **9** as a syrup (22.6 mg, 74%): R_f = 0.7 (3:1 hexane–EtOAc); $[\alpha]_D^{27}$ +172.8 (*c* 2.5, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ 7.37–7.31 (m, 7H, Ar), 7.05 (d, 2H, *J* = 8.0 Hz, Ar), 6.06 (d, 1H, $J_{1,2}$ = 4.0 Hz, H-1), 5.81 (d, 1H, $J_{1',2'}$ = 2.8 Hz, H-1′), 4.73 (d, 1H, *J* = 11.6 Hz, PhCH_2), 4.61 (dd, 1H, $J_{3,2}$ = 12.0 Hz, $J_{3,4}$ = 2.0 Hz, H-3), 4.59 (s, 1H, H-4), 4.52 (d, 1H, *J* = 11.6 Hz, PhCH_2), 4.50 (dd, 1H, $J_{2,1}$ = 4.0 Hz, $J_{2,3}$ = 12.0 Hz, H-2), 4.45 (dd, 1H, $J_{3',2'}$ = 9.6 Hz, $J_{3',4'}$ = 2.0 Hz, H-3′), 4.44 (s, 1H, H-4′), 4.39 (t, 1H, *J* = 8.0 Hz, H-5′), 4.37 (dd, 1H, $J_{2',1'}$ = 2.8 Hz, $J_{2',3'}$ = 9.6 Hz, H-2′), 3.89 (dd, 1H, *J* = 6.0, 8.0 Hz, H-6a′), 3.74 (t, 1H, *J* = 9.6 Hz, H-5), 3.63–3.59 (m, 2H, H-6b′, H-6a), 3.50 (dd, 1H, *J* = 6.0, 9.6 Hz, H-6b), 2.54 (s, 3H, CH_3), 2.47 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 0.90 (s, 18H, *t*-Bu × 2), 0.13 (s, 3H, CH_3), 0.10 (s, 3H, CH_3), 0.09 (s, 3H, CH_3), 0.08 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.07, 171.37, 152.98, 152.37, 138.53, 137.78, 133.41, 129.90, 128.37, 128.13, 127.69, 96.11, 87.29, 75.29, 74.83, 73.02, 72.96, 70.40, 69.31, 66.81, 65.70, 60.25, 55.64, 54.92, 25.84, 23.88, 21.11, 18.22, −4.57, −5.13, −5.47. HRMS (ESI) Calcd for $C_{44}H_{65}N_2O_{12}SSi_2$ $[M + H]^+$: 901.3791. Found: 901.3786.

3.9. *p*-Tolyl (2-acetamido-4,6-*O*-benzylidene-2,3-*N*,*O*-carbonyl-2-deoxy-α-D-galactopyranosyl)-(1→4)-2-acetamido-6-*O*-benzyl-2,3-*N*,*O*-carbonyl-2-deoxy-1-thio-α-D-galactopyranoside (10)

The disaccharide **9** (378 mg, 0.42 mmol, 1.0 equiv) was dissolved in 4 mL of 1 M TBAF in THF solvent at room temperature by stirring for about 10 min. The mixture was then extracted with EtOAc (50 mL) and the organic layer was washed with satd aq NH_4Cl (15 mL × 2) and water (10 mL). The washed organic layer was dried over Na_2SO_4 and concentrated in vacuo. Purification using a short chromatography column, from which the crude product was readily flushed out by EtOAc, was necessary to remove the large amount of inorganic salts. The crude product, along with camphorsulfonic acid (9.75 mg, 0.04 mmol, 0.1 equiv), was then dissolved in dry CH_3CN (4 mL) at room temperature. The pH was about 2–3. Benzaldehyde dimethyl acetal (127 mg, 125.7 μL, 0.84 mmol, 2.0 equiv) was added dropwise to this stirred solution. The reaction was finished rapidly in about 10 min and was quenched by the addition of Et_3N to pH of around 7 and concentrated in vacuo. The residue was purified by column chromatography on silica gel (2:1 hexane–EtOAc) to give white amorphous solids **10** (280 mg, 88%): R_f = 0.5 (1:1 hexane–EtOAc); $[\alpha]_D^{27}$ +306.0 (*c* 0.7, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ 7.51 (d, 2H, *J* = 4.8 Hz, Ar), 7.38–7.31 (m, 10H, Ar), 7.06 (d, 2H, *J* = 8.0 Hz, Ar), 6.07 (d, 1H, $J_{1,2}$ = 4.0 Hz, H-1), 6.00 (s, 1H, H-1′), 5.62 (s, 1H, PhC*H*), 4.76 (d, 1H, *J* = 11.6 Hz, PhCH_2), 4.71–4.46 (m, 7H, PhCH_2, H-2, H-2′, H-3, H-3′, H-4, H-4′), 4.41 (t, 1H, *J* = 6.8 Hz, H-5), 4.35 (d, 1H, *J* = 12.8 Hz, H-6a′), 4.15 (d, 1H, *J* = 12.8 Hz, H-6b′), 3.90 (s, 1H, H-5′), 3.59 (t, 1H, *J* = 8.8 Hz, H-6a), 3.49 (dd, 1H, *J* = 6.4, 9.6 Hz, H-

6b), 2.56 (s, 3H, CH_3), 2.47 (s, 3H, CH_3), 2.31 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 171.90, 171.30, 152.76, 152.69, 138.66, 137.75, 136.89, 133.39, 129.98, 129.32, 128.45, 128.28, 128.04, 127.86, 127.79, 126.17, 100.27, 96.94, 87.20, 75.40, 73.06, 72.38, 71.46, 70.33, 69.82, 69.65, 66.67, 63.70, 55.94, 54.87, 23.96, 23.85, 21.13. HRMS (ESI) calcd for $C_{39}H_{40}N_2O_{12}SK$ $[M+K]^+$: 799.1928. Found: 799.1923.

3.10. *p*-Tolyl (2-acetamido-6-*O*-benzyl-2,3-*N*,*O*-carbonyl-2-deoxy-α-D-galactopyranosyl)-(1→4)-2-acetamido-6-*O*-benzyl-2,3-*N*,*O*-carbonyl-2-deoxy-1-thio-α-D-galactopyranoside (11)

Et_3SiH (83.8 mg, 115 μL, 0.72 mmol, 6 equiv) and TfOH (71.7 mg, 42 μL, 0.48 mmol, 4 equiv) were added to a stirred mixture of **10** (91.3 mg, 0.12 mmol, 1.0 equiv) and activated 4 Å molecular sieves (400 mg, powder) in CH_2Cl_2 (7.3 mL, 12.5 mg of **10** per mL) at −72 °C under nitrogen atmosphere. After being stirred for 1 h at −72 °C, Et_3N (1 mL) and MeOH (1 mL) were added successively. The mixture was filtered and the filtrate was concentrated. The residue was purified by column chromatography on silica gel (2:1 hexane–EtOAc) to give white amorphous solids (73.2 mg, 80%): R_f = 0.4 (1:1 hexane–EtOAc); $[\alpha]_D^{27}$ +223.5 (*c* 1.4, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz): δ 7.38–7.32 (m, 12H, Ar), 7.05 (d, 2H, *J* = 8.0 Hz, Ar), 6.07 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-1), 5.90 (s, 1H, H-1′), 4.72 (d, 1H, *J* = 11.6 Hz, PhCH_2), 4.62 (d, 1H, *J* = 12.0 Hz, PhCH_2), 4.58–4.51 (m, 8H, PhCH_2 × 2, H-2, H-2′, H-3, H-3',H-4, H-4′), 4.41 (t, 1H, *J* = 7.2 Hz, H-5), 4.03 (t, 1H, *J* = 4.0 Hz, H-5′), 3.81 (d, 2H, *J* = 4.0 Hz, H-6a′, H-6b′), 3.59 (dd, 1H, *J* = 7.2, 11.2 Hz, H-6a), 3.50–3.46 (m, 2H, H-6b, 4-OH), 2.53 (s, 3H, CH_3), 2.46 (s, 3H, CH_3), 2.31 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 172.06, 171.32, 152.98, 152.58, 138.60, 137.79, 137.07, 133.38, 129.94, 128.60, 128.41, 128.07, 127.81, 96.95, 87.24, 75.42, 74.28, 73.89, 73.05, 70.58, 70.43, 69.97, 69.79, 67.09, 67.00, 55.87, 54.56, 23.91, 23.83, 21.12. HRMS (ESI) calcd for $C_{39}H_{46}N_3O_{12}S$ $[M+NH_4]^+$: 780.2797. Found: 780.2812.

3.11. *p*-Tolyl (2-acetamido-4,6-di-*O*-*tert*-butyldimethylsilyl-2,3-*N*,*O*-carbonyl-2-deoxy-α-D-galactopyranosyl)-(1→4)-(2-acetamido-6-*O*-benzyl-2,3-*N*,*O*-carbonyl-2-deoxy-α-D-galactopyranosyl)-(1→4)-2-acetamido-6-*O*-benzyl-2,3-*N*,*O*-carbonyl-2-deoxy-1-thio-α-D-galactopyranoside (12)

Tf_2O (27.2 mg, 16 μL, 0.096 mmol, 1.3 equiv) was added to a stirred mixture of **3** (85.7 mg, 0.15 mmol, 2.0 equiv), Ph_2SO (17.9 mg, 0.089 mmol, 1.2 equiv), TTBP (75.3 mg, 0.29 mmol, 4.0 equiv) and activated 4 Å molecular sieves (1.5 g, powder) in CH_2Cl_2 (15 mL) at −72 °C under a nitrogen atmosphere. The reaction mixture was stirred for 5 min, after loss of **3** detected by TLC, a solution of the acceptor **11** (56.2 mg, 0.074 mmol, 1.0 equiv) in CH_2Cl_2 (3 mL) was added dropwise to the mixture. The mixture was stirred and warmed up to room temperature slowly and stirred for further 2 h, and the reaction was quenched by the addition of Et_3N (0.1 mL). The precipitate was filtered and the filtrate was concentrated. The residue was purified by column chromatography on silica gel (5:1 hexane–EtOAc) to give **12** as a syrup (61.1 mg, 68%): R_f = 0.4 (3:1 hexane–EtOAc); $[\alpha]_D^{27}$ +147.1 (*c* 1.2, $CHCl_3$); ^1H NMR ($CDCl_3$, 500 MHz): δ 7.39–7.28 (m, 12H, Ar), 7.05 (d, 2H, *J* = 9.0 Hz, Ar), 6.06 (d, 1H, $J_{1,2}$ = 3.5 Hz, H-1), 5,83 (d, 1H, $J_{1',2'}$ = 3.0 Hz, H-1′), 5.81 (d, 1H, $J_{1'',2''}$ = 2.5 Hz, H-1″), 4.70 (d, 1H, *J* = 12.5 Hz, PhCH_2), 4.68 (d, 1H, *J* = 12.0 Hz, PhCH_2), 4.62 (dd, 1H, $J_{3,2}$ = 12.0 Hz, $J_{3,4}$ = 2.0 Hz, H-3), 4.59–4.55 (m, 3H, H-3′, PhCH_2 × 2), 4.51(s, 1H, H-4), 4.50–4.46 (m, 3H, H-2, H-3″, H-4′), 4.44 (s, 1H, H-4″), 4.41 (t, 1H, *J* = 7.0 Hz, H-5), 4.36 (dd, 1H, $J_{2'',1''}$ = 2.5 Hz, $J_{2'',3''}$ = 12.0 Hz, H-2″), 4.24 (dd, 1H, $J_{2',1'}$ = 3.0 Hz, $J_{2',3'}$ = 12.5 Hz, H-2′), 4.12 (t, 1H, *J* = 7.0 Hz, H-5′), 3.86 (dd, 1H, *J* = 5.5, 8.5 Hz, H-6a″), 3.72 (t, 1H, *J* = 9.0 Hz, H-5″), 5.7–3.45 (m, 5H, H-6a, H-6b, H-6a′, H-6b′, H-6b″), 2.53 (s, 3H, CH_3), 2.47 (s, 3H, CH_3), 2.45 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 0.90 (s, 9H, *t*-Bu), 0.89 (s, 9H, *t*-Bu), 0.12 (s, 3H, CH_3), 0.10 (s, 3H, CH_3), 0.08 (s, 3H, CH_3), 0.07 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz): δ 172.03, 171.89, 171.35, 153.07, 152.37, 138.59, 137.93, 137.83, 133.42, 131.00, 129.94, 129.29, 128.40, 128.12, 127.75, 127.67, 127.62, 127.58, 124.77, 96.49, 96.06, 87.35, 75.36, 74.89, 73.13, 73.04, 72.97, 72.83, 71.00, 70.44, 70.35, 69.05, 67.21, 66.22, 65.70, 60.14, 55.82, 55.50, 54.98, 25.88, 23.86, 23.80, 21.11, 18.25. 18.21, −4.53, −5.07, −5.41, −5.49. HRMS (ESI) calcd for $C_{60}H_{81}N_3O_{18}SSi_2K$ $[M+K]^+$: 1258.4400. Found: 1258.4398.

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Supplementary data

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References

1. Wacker, M.; Linton, D.; Hitchen, P. G.; Nita-Lazar, M.; Haslam, S. M.; North, S. J.; Panico, M.; Morris, H. R.; Dell, A.; Wren, B. W.; Aebi, M. *Science* **2002**, *298*, 1790–1793.
2. Young, N. M.; Brisson, J.-R.; Kelly, J.; Watson, D. C.; Tessier, L.; Lanthier, P. H.; Jarrell, H. C.; Cadotte, N.; Michael, F. St.; Aberg, E.; Szymanski, C. M. *J. Biol. Chem.* **2002**, *227*, 42530–42539.
3. Haselety, S. R.; Holst, O.; Brande, H. *Eur. J. Biochem.* **1998**, *251*, 189–194.
4. Landersjö, C.; Widmalm, G. *Biopolymers* **2002**, *64*, 283–291.
5. Parolis, H.; Parolis, L. A. S.; Olivieri, G. *Carbohydr. Res.* **1997**, *303*, 319–325.
6. Kocharova, N. A.; Maszewska, A.; Zatonsky, G. V.; Bystrova, O. V.; Ziolkowski, A.; Torzewska, A.; Shashkov, A. S.; Knirel, Y. A.; Rozalski, A. *Carbohydr. Res.* **2003**, *338*, 1425–1430.
7. Takeda, M.; Nakamori, T.; Hatta, M.; Yamada, H.; Koizumi, J.-I. *Int. J. Biol. Macromol.* **2003**, *33*, 245–250.
8. Glover, K. J.; Weerapana, E.; Numao, S.; Imperiali, B. *Chem. Biol.* **2005**, *12*, 1311–1316.
9. Weerapana, E.; Glover, K. J.; Chen, M. M.; Imperiali, B. *J. Am. Chem. Soc.* **2005**, *127*, 13766–13767.
10. Glover, K. J.; Weerapana, E.; Imperiali, B. *Proc. Natl. Acad. Sci. U.S.A.* **2005**, *102*, 14255–14259.
11. Ishiwata, A.; Ohta, S.; Ito, Y. *Carbohydr. Res.* **2006**, *341*, 1557–1573.
12. Amin, M. N.; Ishiwata, A.; Ito, Y. *Tetrahedron* **2007**, *63*, 8181–8198.
13. Lee, Y. J.; Ishiwata, A.; Ito, Y. *Tetrahedron* **2009**, *65*, 6310–6319.
14. Benakli, K.; Zha, C.; Kerns, R. J. *J. Am. Chem. Soc.* **2001**, *123*, 9461–9462.
15. Wei, P.; Kerns, R. J. *J. Org. Chem.* **2005**, *70*, 4195–4198.
16. Boysen, M.; Gemma, E.; Lahmann, M.; Oscarson, S. *Chem. Commun.* **2005**, 3044–3046.
17. Crich, D.; Vinod, A. U. *Org. Lett.* **2003**, *5*, 1297–1300.
18. Crich, D.; Vinod, A. U. *J. Org. Chem.* **2005**, *70*, 1291–1296.
19. Paulsen, H. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 155–173.
20. Kerns, R. J.; Zha, C.; Benakli, K.; Liang, Y.-Z. *Tetrahedron Lett.* **2003**, *44*, 8069–8072.
21. Crich, D.; Dudkin, V. *J. Am. Chem. Soc.* **2001**, *123*, 6819–6825.
22. Wei, P.; Kerns, R. J. *Tetrahedron Lett.* **2005**, *46*, 6901–6905.
23. Sakagami, M.; Hamana, H. *Tetrahedron Lett.* **2000**, *41*, 5547–5551.
24. Olsson, J. D. M.; Eriksson, L.; Lahmann, M.; Oscarson, S. *J. Org. Chem.* **2008**, *73*, 7181–7188.
25. Satoh, H.; Hutter, J.; Lüthi, H. P.; Manabe, S.; Ishii, K.; Ito, Y. *Eur. J. Org. Chem.* **2009**, *2009*, 1127–1131.
26. Huang, X.; Huang, L.; Wang, H.; Ye, X.-S. *Angew. Chem., Int. Ed.* **2004**, *43*, 5221–5224.
27. Wang, Y.; Ye, X.-S.; Zhang, L.-H. *Org. Biomol. Chem.* **2007**, *5*, 2189–2200.
28. Crich, D.; Sun, S. *J. Org. Chem.* **1996**, *61*, 4506–4507.
29. Codée, J. D. C.; van den Bos, L. J.; Litjens, R. E. J. N.; Overkleeft, H. S.; van Boom, J. H.; van der Marel, G. A. *Org. Lett.* **2003**, *5*, 1947–1950.
30. Yamago, S.; Yamada, T.; Maruyama, T.; Yoshida, J.-I. *Angew. Chem., Int. Ed.* **2004**, *43*, 2145–2148.
31. Nguyen, H. M.; Poole, J. L.; Gin, D. Y. *Angew. Chem., Int. Ed.* **2001**, *40*, 414–417.
32. Geng, Y.-Q.; Zhang, L.-H.; Ye, X.-S. *Chem. Commun.* **2008**, 597–599.
33. Wang, C.-N.; Wang, H.-S.; Huang, X.-F.; Zhang, L.-H.; Ye, X.-S. *Synlett* **2006**, 2846–2850.
34. Crich, D.; Smith, M. *J. Am. Chem. Soc.* **2001**, *123*, 9015–9020.

35. Garcia, B. A.; Gin, D. Y. *J. Am. Chem. Soc.* **2000**, *122*, 4269–4279.
36. Codée, J. D. C.; Litjens, R. E. J. N.; den Heeten, R.; Overkleeft, H. S.; van Boom, J. H.; van der Marel, G. A. *Org. Lett.* **2003**, *5*, 1519–1522.
37. van der Plas, H. C.; Koudijs, A. *Recl. Trav. Chim. Pays-Bas* **1978**, *97*, 159–161.
38. Crich, D.; Smith, M.; Yao, Q.; Picione, J. *Synthesis* **2001**, *2*, 323–326.
39. Mong, T. K.-K.; Lee, H.-K.; Durón, S. G.; Wong, C.-H. *Proc. Natl. Acad. Sci. U.S.A.* **2003**, *100*, 797–802.
40. Tarasiejska, Z.; Jeanloz, R. W. *J. Am. Chem. Soc.* **1958**, *80*, 6325–6327.
41. Deng, S.; Gangadharmath, U.; Chang, C-W. T. *J. Org. Chem.* **2006**, *71*, 5179–5185.