Tetrahedron 69 (2013) 816–825

Contents lists available at SciVerse ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Synthesis of 3,3′-neotrehalosadiamine and related 1,1′-aminodisaccharides using disarmed, armed, and superarmed building blocks

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ARTICLE INFO

Article history:
Received 26 July 2012
Received in revised form 19 October 2012
Accepted 19 October 2012
Available online 7 November 2012

Keywords:
1,1′-Disaccharide
Neotrehalosadiamine
Trehalosadiamine
Stereoselective synthesis
Electronic effects
Antimicrobial activities

ABSTRACT

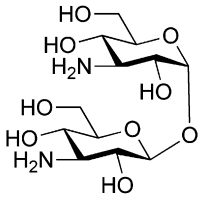
Here we report a high yielding, stereoselective synthesis of the naturally occurring 1,1′-disaccharide neotrehalosadiamine (NTD) and some related analogs. Following an eleven-step sequence, seven of which did not require chromatographic separation, NTD was generated in 60% overall yield from the inexpensive, commercially available precursor 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose. The key α,β-linkage of NTD was formed in a highly stereoselective manner by taking advantage of the participating effect of the acyl group at *O*-2 of the donor glycoside. The influence of electronic effects of disarmed, armed, and superarmed glycosyl donors and acceptors on the outcome of 1,1′-glycosidation was also observed. Antibacterial studies using NTD and its analogs show detectable but weak anti-staphylococcal activity.

1. Introduction

1,1′-Linked non-reducing glycosides are found in plants, fungi, yeasts, red alga, lichens, and insects.[1–3] Several methods of 1,1′-disaccharide synthesis have been reported in the literature since Lemieux became the first to synthesize sucrose in the laboratory.[4] Methods in modern use include adaptations of classical Koenigs–Knorr reactions,[5–8] perchloric acid catalyzed coupling of perbenzylated pyranosides with their halides,[9] TMSOTf-promoted coupling of *manno*- and *galacto*-analogs with their corresponding Schmidt glycosyl donors,[10–12] glycosylation of perbenzylated pyranosides with their 1-*O*-trimethylsilylated derivative,[13] and diphenyldichlorosilane-silver triflate,[14] and a triflic anhydride induced coupling.[15] These methods are not stereoselective, yielding α,α-, α,β-, and β,β-linkages in varying ratios depending upon the stereochemistry and the bulk of substituent at the C-2 position. Additionally, synthetic methods for the production of 1,1′-linked non-reducing glycosides have not been described for amino-sugars, despite the reported antibiotic activity of 3,3′-neotrehalosadiamine (NTD, **1**),[16] trehalosamine,[17] 3-trehalosamine,[18] 4-trehalosamine,[19] and mannosyl glucosaminide.[20]

Bacillus pumilis and *Bacillus circulans* isolates produce NTD, which is a 1,1′-linked aminodisaccharide (Fig. 1). Inaoka et al. demonstrated that introducing a specific Rif^r mutation in the gene encoding the RNA polymerase *rpoB* induced NTD production in the normally non-producing *Bacillus subtilis*.[21] Disruption of the polycistronic operon *ntdABC* (formerly *yhjLKJ*) disrupted NTD biosynthesis.[22] Previous studies have shown NTD to have activity against *Staphylococcus aureus* and *Klebsiella pneumonia*.[16] The emergence of multi-drug resistant *S. aureus* spurred us to synthesize NTD.

Here we describe the synthesis of the 1,1′-linked disaccharide NTD and closely related analogs. The varying electronic effects of protecting groups from disarmed to armed and armed to



NTD, **1**

Fig. 1. Structure of 3,3'-neotrehalosadiamine.

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http://dx.doi.org/10.1016/j.tet.2012.10.058

superarmed glycosyl donors/acceptors have also been studied on azido-sugars for the first time.

2. Results & discussion

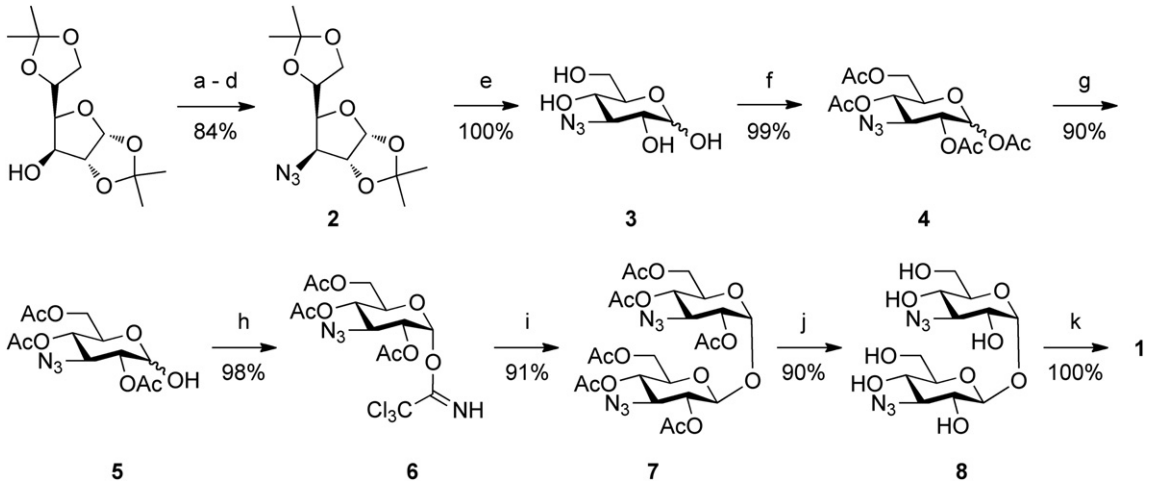
2.1. Synthesis of NTD

We chose to build NTD via construction of a 1,1′-glycosidic linkage between two units equivalent to a protected 3-amino-3-deoxy-D-glucose, which has the trivial name kanosamine. We therefore began by following Frost's reported synthesis of kanosamine,[23] which involves the conversion of commercially available diacetone-D-glucose to the corresponding 3-azido derivative **2** by inversion of configuration at position 3 by oxidation and reduction, then formation of the 3-*O*-triflate, and displacement of the leaving group by azide (Scheme 1). In our hands, this set of reactions could be carried out in 84% overall yield.

−80 °C, a 91% yield of protected neotrehalosadiamine **7** was achieved, accompanied by a mixture of unidentified products. Subsequent deacetylation to form **8** followed by hydrogenation furnished our desired disaccharide NTD (**1**) in good yield. Overall, NTD was synthesized from diacetone-D-glucose in 11 steps with 60% yield.

2.2. Armed and disarmed glycosyl donors and acceptors

Fraser-Reid et al.[24–26] and Bols et al.[27,28] described the vast difference in the reactivity among glycosyl donors and acceptors having acyl-, benzyl-, and *tert*-butyldimethylsilyl-protecting groups as the disarmed–armed–superarmed concept. Therefore, the effect of various protecting groups ranging from disarmed to armed and armed to superarmed glycosyl donor and acceptors on the 1,1′-glycosidation outcome of 3-azido-2-deoxy glucoside was investigated as a means of generating all stereoisomers of NTD optimally. The armed–disarmed–superarmed glycosyl donor/acceptor model has been studied thoroughly and reviewed by Demchenko.[29]



Scheme 1. Reagents: (a) PDC, Ac_2O, CH_2Cl_2, 4 h; (b) $NaBH_4$, EtOH:H_2O (9:1), 0 °C, 2 h; (c) $(CF_3SO_2)_2O$, pyridine, −30 °C; (d) NaN_3, DMF, 50 °C, 24 h; (e) 2 N HCl, 14 h, rt; (e) DOWEX, 80 °C, o/n; (f) Ac_2O, H^+, 2 h, 0 °C–rt; (g) $CH_3COO^-NH_4^+$, DMF, 18 h; (h) CCl_3CN, Cs_2CO_3, CH_2Cl_2, 4 h; (i) **5**, TMSOTf, DCM, −80 °C, 1 h; (j) NaOMe, MeOH; (k) Pd/C, H_2, MeOH:H_2O (1:1).

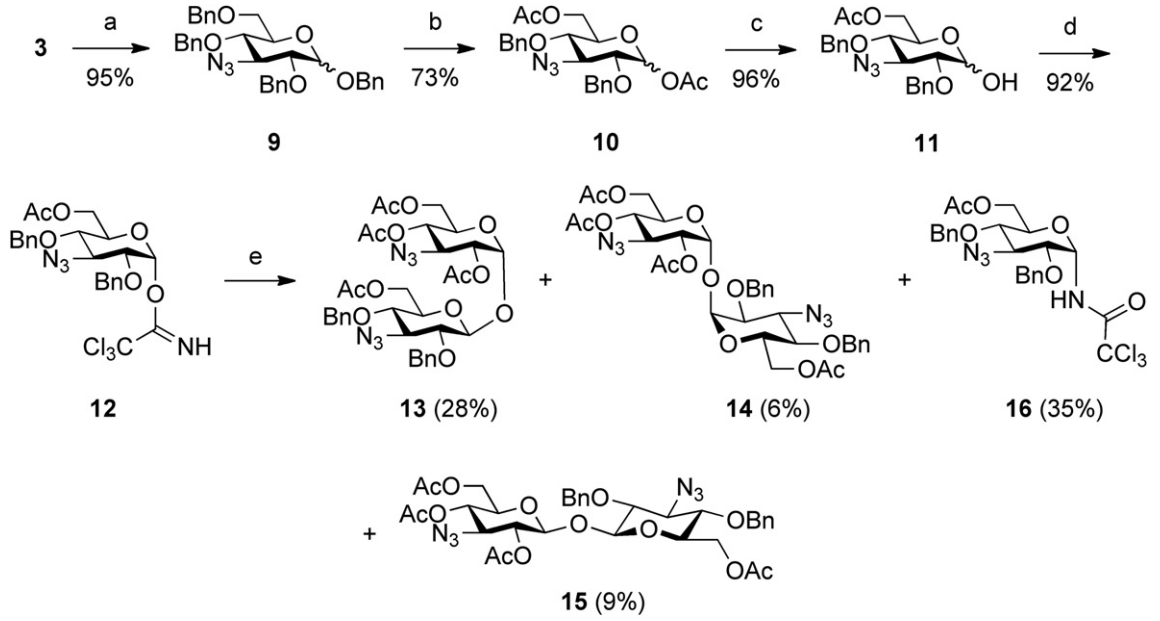
We generated an acetyl-protected glycosyl donor so that the well-known anchimeric assistance of the 2-*O*-acyl group would result in attack of the acceptor from only one side of the molecule. In such reactions, an activated donor in the presence of an appropriate promoter, such as TMSOTf or AgOTf, results in an oxocarbenium ion. The anticipated participation of the adjacent cis acetyl group is expected to stabilize the resulting cation by nucleophilic addition, and the resulting acetoxonium (or acetoxonium-like) species can be attacked only from the 'top' or β-face, forming a β-glycosidic bond. Without some means of controlling the stereochemistry of the forming bond, a mixture of anomers would result. While other anomers might be desirable, the separation of these can be time consuming, and result in loss of material. In order to form the required α,β-1,1′-glycosidic linkage, the acceptor in this case needs to react as the α-anomer.

For the synthesis of neotrehalosadiamine **1**, glycosyl acceptor **5** was obtained after deacetalation of azide **2**, and subsequent acetylation to render peracetylated glycoside **4** in quantitative yields. The regioselective deprotection of the anomeric acetyl group with ammonium acetate yielded glycoside **5**. Trichloroacetimidate synthesis of glycoside **5** furnished glycosyl donor **6** in 98% yield. To build the key glycosidic linkage, varying quantities (0.01–1.5 equiv) of activators (Lewis acids, i.e., $ZnCl_2$, AgOTf, and $BF_3 \cdot Et_2O$, TMSOTf), temperatures ranging from room temperature to −80 °C, and solvents of varying polarity (DCM, DCM/hexane, propionitrile) were investigated. By using only 0.01 equiv of TMSOTf in dry DCM at

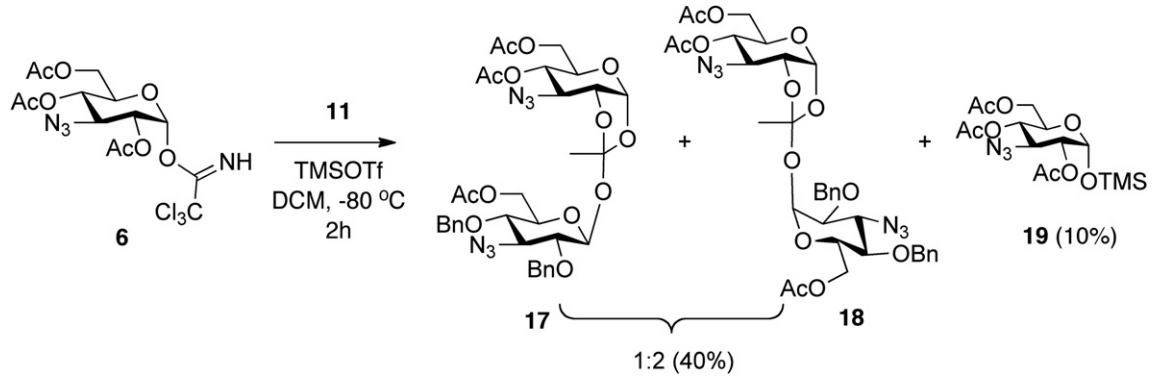
2.2.1. Armed donor, disarmed acceptor. The armed glycosyl donor **12** was synthesized from azide **3** after its benzylation, an acid-mediated simultaneous debenzylation–acetolysis,[30] deacetylation of the anomeric acetyl group[31] and subsequent chloroacetimidate formation using Cs_2CO_3 catalysis[32] (Scheme 2). The reaction of armed glycosyl donor **12** with the disarmed glycosyl acceptor **5** resulted in an inseparable mixture of **13** (α,β-; 28% yield by NMR), **14** (α,α-; 6%), and **15** (β, β-; 9%) along with the amide **16**, a side product of trichloroacetimidate glycosylation reactions.

2.2.2. Disarmed donor, armed acceptor. The reaction of disarmed glycosyl donor **6** with the armed glycosyl acceptor **11** resulted in formation of orthoesters **17** (α,β-) and **18** (α,α-) in 40% yield, along with the trimethylsilyl glycoside **19** as a side product (Scheme 3). Coupling reactions with acylated glycosyl trichloroacetimidates as the donors are known to give orthoesters as intermediates, especially when the coupling is accomplished at slower rates.[33]

2.2.3. Armed donor, armed acceptor. The reaction of armed glycosyl donor **12** with the armed glycosyl acceptor **11** gave the neotrehalose derivative **20** (45%) and the trehalose derivative **21** (22%), again with the amide **16**. Each product was purified and fully characterized through NMR spectroscopic data. The protected azide



Scheme 2. Reagents: (a) BnBr, NaH, DMF, 2 h, 0 °C–rt; (b) H_2SO_4/Ac_2O, rt, 5 min; (c) $CH_3COO^-NH_4^+$, DMF, rt o/n; (d) CCl_3CN, Cs_2CO_3, CH_2Cl_2, 4 h; (e) **5**, TMSOTf, DCM, −80 °C, 1 h.



Scheme 3.

21 was deacetylated to **22** in quantitative yields. Simultaneous reduction of the azide and benzyl protecting groups by hydrogenolysis formed complex product mixtures, therefore **22** was reduced using hydrazine and Pearlman catalyst. The resulting aminoglycoside was subjected to hydrogenolysis with Pearlman catalyst on carbon under an H_2 atmosphere in a methanol:water:-acetic acid mixture, providing 3,3′-trehalosadiamine **23** in quantitative yields (Scheme 4).

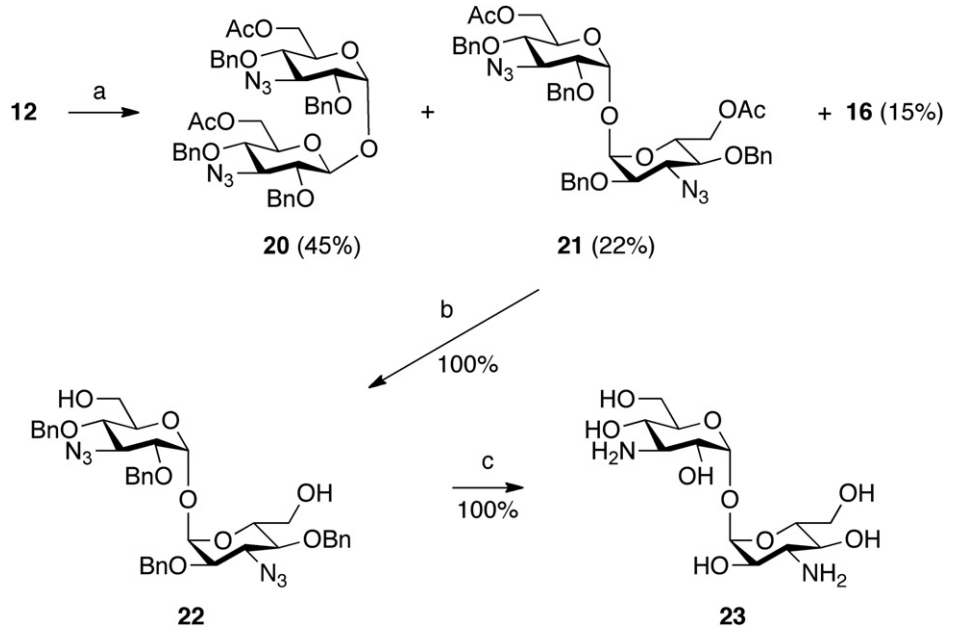
2.2.4. Superarmed donor, superarmed acceptor. Based on existing literature,[34–41] we synthesized superarmed donor and acceptor by introducing TBS protecting groups. The introduction of bulky silyl groups is proposed to induce a ring flip from the $^4C_1$ to the $^1C_4$ conformation. Bols studied the reactivity of carbohydrates by varying the electronic effects on the hydroxyl groups,[27,28] and proposed that an axial polar substituent stabilizes the positive charge to a higher degree than the corresponding equatorial hydroxyl group due to differences in the charge–dipole interactions between a positive charge in the ring and an axial/equatorial C–O dipole. These effects can therefore lead to higher yield in α,α-disaccharide formation.

The 6-*O*-hydroxyl group was protected by benzylation to prevent a stable 1,6-anhydro formation as previously reported.[28] The peracetylated glucoside **4** was treated with thiophenol to produce a mixture of thiophenyl glucoside anomers **24** in 79% yield, which upon deacetylation and benzylidene protection using *p*-anisaldehyde furnished compound **26** in 98% yield. The reductive opening of the benzylidene ring of thioglucoside **26** with $NaCNBH_3$ and 2,4-*O*-protection with TBSOTf gave us our desired compound **28** (Scheme 5). The benzylidene protection with simple benzaldehyde gives reduced yields relative to *p*-anisaldehyde upon reductive cleavage with $NaCNBH_3$, TESH, and TFA.

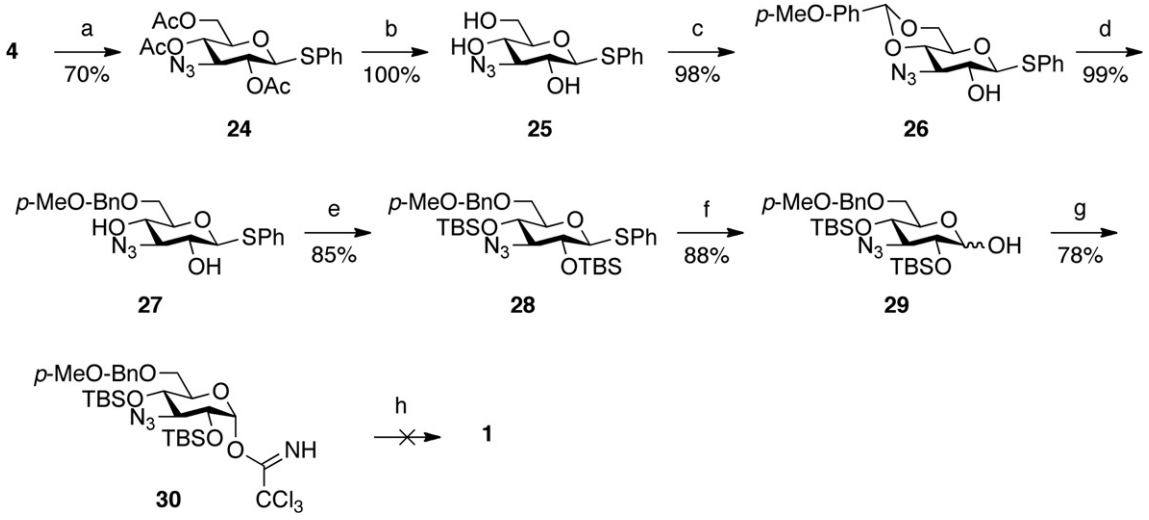
NMR spectra indicated that the TBS-protected 3-azido glycosyl donor **30** did not adopt an altered chair, but remained in the $^4C_1$ conformation. This likely accounts for no disaccharide formation in the reaction of the superarmed donor **30** and acceptor **29**. Extended reaction times resulted in degradation of the donor.

2.3. Other disaccharides

Disarmed donor and acceptor coupling works well with our 3-azido-3-deoxy sugar to get an α,β-linkage in our disaccharides, therefore we extended this methodology to synthesize analogs of NTD, i.e., 3′-neotrehalosamine (**34**) and 3-neotrehalosamine (**38**). The coupling of disarmed donor **6** with disarmed acceptor **31**



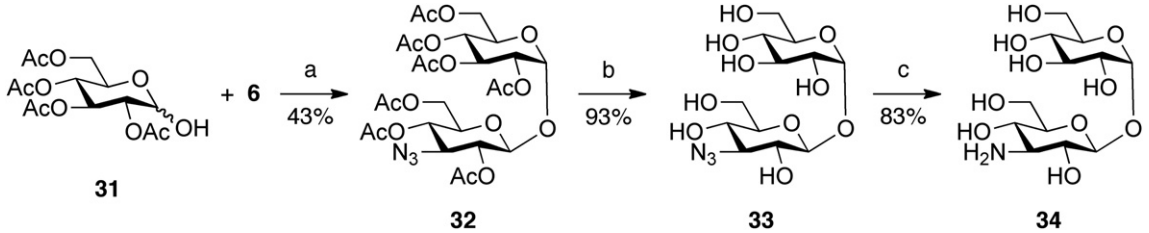
Scheme 4. Reagents: (a) **11**, TMSOTf, DCM, −80 °C, 1 h; (b) NaOMe, MeOH; (c) i- $NH_2NH_2.H_2O$, $Pd(OH)_2$, MeOH, reflux, 15 h; ii- H_2, $Pd(OH)_2$, MeOH:H_2O:AcOH(4:2:1), rt, 24 h.



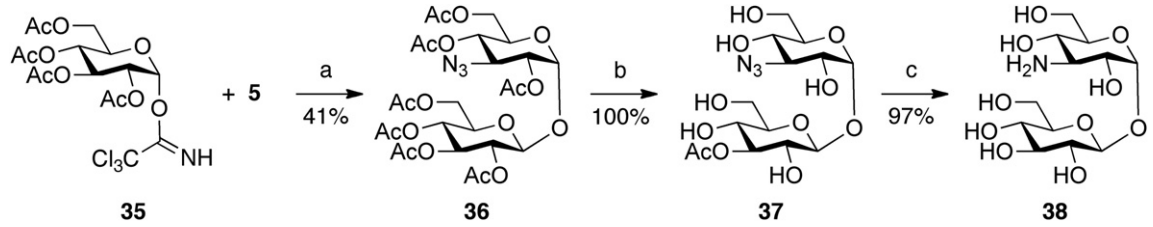
Scheme 5. Reagents: (a) $BF_3{\cdot}Et_2O$, PhSH, DCM, rt, 48 h; (b) NaOMe, MeOH, rt, 4 h; (c) *p*-anisaldehyde, PTSA, DMF, 60 °C, 20 h; (d) $NaCNBH_3$, THF, HCl, 3 Å molecular sieves, 12 h; (e) TBSOTf, DMAP, pyridine, 0 °C—60 °C, 6.5 h; (f) NBS, acetone:H_2O (9:1), rt, 15 min; (g) CCl_3CN, Cs_2CO_3, CH_2Cl_2, 4 h; (h) **29**, TMSOTf, DCM, −40 °C, 1 h.

gave peracetylated 3′-neotrehalosamine **32** as the major product in 43% yield along with some other unidentified products (Scheme 6), which upon deprotection resulted in the desired α-D-glucopyranosyl-(1→1′)-3′-amino-3′-deoxy-β-D-glucopyranoside (**34**).

The glycosylation of disarmed glycoside donor **35** with disarmed 3-azido-glycoside acceptor **5** resulted in peracetylated 3-neotrehalosamine **36** in 41% yield along with some other unidentified products (Scheme 7). Subsequent deacetylation and azide



Scheme 6. Reagents: (a) TMSOTf, DCM, −80 °C, 2 h; (b) NaOMe, MeOH; (c) Pd/C, H_2, MeOH:H_2O (1:1).



Scheme 7. Reagents: (a) TMSOTf, DCM, −80 °C, 2 h; (b) NaOMe, MeOH; (c) Pd/C, H_2, MeOH:H_2O (1:1).

deprotection of **36** resulted in the desired compound, α-D-glucopyranosyl-(1→1′)-3′-amino-3′-deoxy-β-D-glucopyranoside (**38**).

2.4. Antistaphylococcal activity

The antimicrobial activity of NTD was assessed using two methods: disc diffusion and broth dilution. All testing was done according to CLSI guidelines.[42,43] *Escherichia coli* ATCC 25922, *Enterococcus faecalis* ATCC 29212, and *S. aureus* ATCC 29213, commonly used quality control organisms in antimicrobial susceptibility testing, as well as two clinical methicillin-resistant and two methicillin-susceptible strains of *S. aureus* were tested using the disk diffusion technique. Isolates were selected to represent a wide range of aminoglycoside susceptibilities. *S. aureus* ATCC 29213 was also tested using the broth dilution method. Briefly, 20 μl of a 256 μg/ml solution of **1** or 3,3′-trehalosadiamine **23** was applied to sterile commercially prepared filter paper discs (Becton Dickinson and Company, Sparks, MD). For testing, a single disc was applied to a Mueller Hinton agar plate with a standard McFarland 0.5 lawn of bacteria. For the broth dilution test, doubling dilutions of **1** and **23** from 1 μg/ml to1024 μg/ml, were prepared in Mueller Hinton broth. Broths were inoculated with bacteria to a final concentration of 5×10^5 colony forming units/ml. All media was evaluated for bacterial growth/inhibition after incubation at 35 °C for 18–24 h.

An antibacterial effect was not observed for **1** or **23** for any of the seven organisms tested using the disc diffusion test. In addition to failing to produce an inhibitory zone, bacterial growth on NTD containing discs was noted. Using the broth dilution method, inhibition of *S. aureus* ATCC 29213 was achieved at high concentrations of **1** (512 μg/ml) and **23** (1024 μg/ml).

The weak antimicrobial activity of NTD against *S. aureus* was previously reported.[21] However, as the susceptibility of the previously reported *S. aureus* to other aminoglycosides was not reported, this isolate may have been less susceptible to NTD than other *S. aureus* isolates. Despite a wide range of susceptibilities to gentamicin (0.12–≥32), neomycin (≤4–≥32) among the isolates included in disc diffusion testing, none were inhibited by NTD. Interestingly, inhibition of *S. aureus* ATCC 29213 at 512 μg/ml of 3,3′-neotrehalosadiamine **1** is consistent with a previous study, which documented inhibition at 1000 μg/ml NTD but not at 100 μg/ml. These results suggest that the compounds tested are not likely good candidates for development of anti-staphylococcal therapy. Future studies to test the activity of **1** and **23** against different organisms, and other NTD analogs against *S. aureus* are required to fully define the antibacterial activity of NTD and its derivatives.

3. Conclusion

In summary, we have completed the syntheses of naturally occurring of 3,3′-neotrehalosadiamine (**1**), and its other structural analogs, such as 3,3′-trehalosadiamine **23**, 3′-neotrehalosamine **34**, and 3-neotrehalosaamine **38**. Neighboring group participation of the 2-*O*-acetyl group provided high stereoselectivity in the glycosylation reaction. The route employed in our synthesis was highly efficient and provided desired stereoisomer in its optically pure form, thus providing facile access to the NTD analogs **34** and **38** from a common starting material. Our exploration of varying protected groups did not lead to a better yield of **1**, but manipulation of the electronic participating properties of these groups did affect the product distribution, and only through the use of the relatively armed donor and acceptor was an appreciable yield of the α,α-product obtained. The presence of the small and electron-withdrawing azido-group in position-3 of the donor and acceptor apparently allows the $^4C_1$ conformation to be retained even when bulky *tert*-butyldimethylsilyl ether groups are present, so that the superarming effect is not observed.

Although many novel aminoglycosides have shown promise as candidate antibiotics, the quantitative susceptibility studies reported here using clinically-important strains of *S. aureus* suggest that NTD is not a promising candidate.

4. Experimental

4.1. General experimental procedures

Chemicals were obtained from Sigma–Aldrich Canada, Ltd (Oakville, ON) or Alfa Aesar (Ward Hill, MA). Syntheses that required anhydrous conditions were performed under an inert atmosphere of dried argon. Glassware was dried overnight in an oven set at 120 °C and assembled under a stream of inert gas. DCM was freshly distilled from calcium hydride. Analytical thin layer chromatography was performed using silica gel 60 F254 precoated glass plates (Merck); compound spots were visualized by ultraviolet light at 254 nm and/or by charring after treatment with cerium molybdophosphate. Flash chromatography was performed with Merck silica gel 60 (230–400 mesh). NMR spectra were recorded on a Bruker 500 MHz spectrometer. Chemical shifts are reported in parts per million downfield from tetramethylsilane, with the solvent signal as reference. Mass spectrometric characterization of organic compounds was performed on an API Qstar XL pulsar hybrid LC/MS/MS. NMR, and mass spectrometry facilities are a part of the Saskatchewan Structural Sciences Centre.

4.1.1. General procedure for the regioselective anomeric deacetylation. To a solution of peracetylated sugar in DMF, CH_3COONH_4 (2.0 equiv) was added, and the reaction mixture was stirred at room temperature for 20 h. The solvent was evaporated and the product isolated by flash chromatography by elution with 40–50% EtOAc in hexane.

4.1.2. General procedure for the deacetylation. To a solution of peracetylated sugars (0.931 mmol) in MeOH (10 mL), 0.5 M NaOMe (0.2 mL) was added and the reaction mixture stirred at room temperature for 4 h, monitored by TLC. The reaction was neutralized by stirring with DOWEX 50W-X8, filtered, and evaporated to get the desired product.

4.1.3. General procedure for the trichloroacetimidate formation. To a solution of protected glucopyranose (e.g., **5**) (3 mmol) in DCM

(30 mL), Cs_2CO_3 (0.1 equiv), and trichloroacetonitrile (10 equiv) were added, and the reaction mixture was stirred at room temperature for 5 h. The reaction mixture was directly poured onto a silica gel flash column and eluted with 20–30% EtOAc in hexane to get the desired trichloroacetimidate.

4.1.4. General procedure for glycosidation. A mixture of glycosyl donor (trichloroacetimidate) (1.2–1.5 equiv) and acceptor, e.g., **5** (1.0 equiv), in dry DCM (20 mL) was stirred and co-evaporated, then re-dissolved in 40 mL of dry DCM, and freshly activated 4 Å molecular sieves (1.5 g) were added. The reaction mixture was stirred at room temperature for 30 min, then cooled to −80 °C, and treated with TMSOTf (0.1 equiv). The reaction mixture was stirred at −40 °C for 1–2 h, then quenched by the addition of saturated $NaHCO_3$ solution (50 mL). The organic phase was separated and successively washed with water (3×40 mL), dried, and concentrated to a colorless gum that was further purified by flash chromatography eluted with a gradient of EtOAc in hexane.

4.1.5. General procedure for azide reduction. To a solution of azidosugar (0.28 mmol) in MeOH:H_2O (1:1, 10 mL) Pd/C (55 mg) was added, and reaction mixture was degassed and purged with argon three times. The reaction was stirred under H_2 atmosphere and the reaction monitored by TLC until complete (typically 48 h). The catalyst was removed by filtering the reaction mixture through a Celite column, and the solvent evaporated.

4.2. 3-Azido-3-deoxy-α/β-D-glucopyranose (3)

To a suspension of 3-azido-1,2:5,6-di-*O*-isopropylidene-3-deoxy-α-D-glucofuranose (**2**) (1.4 g, 4.9 mmol) in water (30 mL), DOWEX 50W-X8 (500 mg) was added the reaction mixture was stirred overnight at 80 °C. The resin was removed by filtration, and the filtrate concentrated to dryness. The product was obtained in quantitative yield and it was sufficiently pure to set up next reaction. Characterization matched previously reported data.[44] ^{1}H NMR (D_2O, α/β ratio 1.0:1.0): δ 5.09 (d, *J*=3.5 Hz, $1H_{1\alpha}$), 4.59 (d, *J*=8.0 Hz, $1H_{1\beta}$), 3.78–3.69 (m, 3H), 3.64–3.56 (m, 3H), 3.42–3.32 (m, 5H), 3.16–3.11 (m, 1H). HRFABMS *m*/*z* 206.0791 [M+H$^+$] (calcd for $C_6H_{11}N_3O_5$, 206.0777).

4.3. 1,2,4,6-Tetra-*O*-acetyl 3-azido-3-deoxy-α/β-D-glucopyranose (4)

3-Azido-3-deoxy-α/β-D-glucopyranose (**3**) was suspended in acetic anhydride (10 mL) and cooled in an ice bath before addition of concd H_2SO_4 (0.02 mL). The reaction mixture was stirred at room temperature for 3 h, then water (30 mL) was added to quench the reaction, before extracting with ethyl acetate (40 mL). The organic phase was separated and successively washed with water (3×40 mL), then saturated $NaHCO_3$ (3×50 mL), and dried with Na_2SO_4 and concentrated to a colorless oil (2.52 g, 99%). ^{1}H NMR ($CDCl_3$, α/β ratio 1.0:0.2): δ 6.32 (d, *J*=3.5 Hz, $1H_{1\alpha}$), 5.69 (d, *J*=8.2 Hz, $0.2H_{1\beta}$), 5.08 (m, 1.4H), 4.98 (dd, *J*=10.5, 3.5 Hz, 1H), 4.26 (dd, *J*=12.5, 4.5 Hz, 1.2H), 4.12 (m, 2.2H), 4.00 (t, *J*=10.5 Hz, 1H), 3.81 (m, 0.2H), 3.71 (t, *J*=10.1 Hz, 0.2H), 2.21 (s, 3H), 2.16 (s, 3H), 2.15 (s, 0.6H), 2.14 (s, 0.6H), 2.13 (s, 0.6H), 2.12 (s, 6.6H). HRFABMS *m*/*z* 374.1195 [M+H$^+$] (calcd for $C_{14}H_{19}N_3O_9$, 374.1200).

4.4. 2,4,6-Tri-*O*-acetyl 3-azido-3-deoxy-α-D-glucopyranose (5)

The general procedure for anomeric deacetylation was followed, using a solution of **4** (390 mg, 1.05 mmol) in DMF (3.0 mL) and CH_3COONH_4 (161 mg, 2.09 mmol). Flash chromatography yielded 2,4,6-tri-*O*-acetyl 3-azido-α-D-glucopyranose (**5**) (310 mg, 90%) as a light yellow gum. ^{1}H NMR ($CDCl_3$): δ 5.46 (br t, 1H), 4.97 (m, 1H), 4.80 (dd, *J*=11.0, 3.5 Hz, 1H), 4.22–4.05 (m, 4H), 3.58 (br d, $1H_{OH}$), 2.19 (s, 3H), 2.15 (s, 3H), 2.11 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 170.9, 170.0, 169.4, 89.7, 71.8, 68.4, 67.5, 62.0, 60.6, 20.8, 20.8, 20.7. HRFABMS *m*/*z* 332.1088 [M+H$^+$] (calcd for $C_{12}H_{17}N_3O_8$, 332.1094).

4.5. 2,4,6-Tri-*O*-acetyl-3-azido-3-deoxy-α-D-glucopyranosyl trichloroacetimidate (6)

Following the general procedure for trichloroacetimidate synthesis 2,4,6-tri-*O*-acetyl-3-azido-α-D-glucopyranose (**5**) (1.0 g, 3.0 mmol) in DCM (30.0 mL), with Cs_2CO_3 (0.098 g, 0.302 mmol) and trichloroacetonitrile (3.03 mL, 30.2 mmol) resulted in 2,4,6-tri-*O*-acetyl-3-azido-α-D-glucopyranosyl trichloroacetimidate (**6**) (1.16 g, 98%) as a white amorphous solid. ^{1}H NMR ($CDCl_3$): δ 8.75 (s, $1H_{NH}$), 6.54 (d, *J*=3.5 Hz, 1H), 5.09 (t, *J*=10.0 Hz, 1H), 5.01 (dd, *J*=10.5, 4.5 Hz, 1H), 4.29 (dd, *J*=12.5, 3.5 Hz, 1H), 4.16 (m, 3H), 2.17 (s, 3H), 2.12 (s, 3H), 2.09 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 170.7, 169.6, 169.4, 160.9, 92.7, 90.9, 70.6, 70.5, 67.7, 61.4, 60.8, 20.7, 20.6, 20.5. HRFABMS *m*/*z* 475.0200 [M+H$^+$] (calcd for $C_{14}H_{17}Cl_3N_4O_8$, 475.0190).

4.6. 2,4,6-Tri-*O*-acetyl-3-azido-3-deoxy-α-D-glucopyranosyl-(1→1′)-2′,4′,6′-tri-*O*-acetyl-3′-azido-3′-deoxy-β-D-glucopyranoside (7)

Following the general glycosidation procedure, trichloroacetimidate **6** (465 mg, 0.978 mmol) and acceptor **5** (265 mg, 0.8 mmol) in dry DCM (20.0 mL) were converted to **7** as a colorless gum (469 mg, 91% yield). ^{1}H NMR ($CDCl_3$): δ 5.48 (br s, 1H), 4.92 (m, 2H), 4.75 (m, 2H), 4.14 (m, 3H), 3.98 (m, 4H), 3.70 (m, 2H), 2.11 (s, 3H), 2.10 (s, 3H), 2.08 (s, 3H), 2.07 (s, 3H), 2.03 (s, 3H), 2.02 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 171.2, 171.0, 170.2, 169.6, 169.5, 169.4, 95.5, 89.4, 71.9, 69.6, 68.5, 67.9, 67.1, 67.0, 63.7, 62.1, 61.7, 60.5, 20.9, 20.7, 20.7, 20.6, 20.6, 20.5. HRFABMS *m*/*z* 645.2016 [M+H$^+$] (calcd for $C_{24}H_{32}N_6O_{15}$, 645.2004).

4.7. 3-Azido-3-deoxy-α-D-glucopyranosyl-(1→1′)-3-azido-3′-deoxy-β-D-glucopyranoside (8)

Following the general procedure for deacetylation, **7** (600 mg, 0.931 mmol) in MeOH (10 mL) was reacted with 0.5 M NaOMe (0.2 mL), resulting in **8** as a brown gum (329 mg, 90% yield). ^{1}H NMR (CD_3OD+D_2O): δ 5.08 (d, *J*=3.6 Hz, 1H), 4.57 (d, *J*=7.9 Hz, 1H), 3.82–3.58 (m, 6H), 3.43–3.27 (m, 5H), 3.15–3.12 (m, 1H). ^{13}C NMR (CD_3OD+D_2O): δ 95.9, 91.5, 76.5, 72.8, 71.2, 70.3, 68.6, 68.6, 68.4, 65.9, 60.5, 60.3.

4.8. 3-Amino-3-deoxy-α-D-glucopyranosyl-(1→1′)-3′-amino-3′-deoxy-β-D-glucopyranoside (NTD, 1)

The general procedure for azide reduction was followed, using **8** (330 mg, 0.841 mmol) in AcOH:H_2O (10:1, 22 mL) and Pd/C (100 mg), resulting in a brown gum. This product was dissolved in 2 N HCl (20 mL) and solvent was evaporated; then re-dissolved in water (25 mL) and decolorized by stirring at 60 °C using 250 mg of charcoal. The mixture was quickly filtered through Celite while hot, then lyophilized to obtain desired compound **1** as a white amorphous solid (285 mg, quantitative yield). ^{1}H NMR (D_2O): δ 5.11 (d, *J*=3.4 Hz, 1H), 4.58 (d, *J*=7.7 Hz, 1H), 3.74–3.58 (m, 6H), 3.54–3.50 (m, 2 H), 3.41–3.38 (m, 1H), 3.29–3.20 (m, 2 H), 3.11 (t, *J*=10.4 Hz, 1H). ^{13}C NMR (D_2O): δ 96.0, 91.1, 76.5, 71.2, 70.5, 68.1, 65.9, 65.8, 60.1, 59.9, 57.8, 55.0. HRFABMS *m*/*z* 341.1549 [M+H$^+$] (calcd for $C_{12}H_{25}N_2O_9$, 341.1560).

4.9. 3-Azido-1,2,4,6-tetra-*O*-benzyl-3-deoxy-α/β-D-glucopyranose (9)

A solution of 3-azido-3-deoxy-α/β-D-glucopyranose (**3**) (200 mg, 0.975 mmol) in DMF (5 mL) was cooled to 0 °C and NaH (60% dispersion, 215 mg, 5.36 mmol) was added in five portions with stirring at the same temperature. After 10 min, benzyl bromide (0.695 mL, 5.36 mmol) was added dropwise, and the reaction was stirred a further 2 h. The reaction was quenched with MeOH (3 mL), followed by addition of water (50 mL). The solution was extracted with DCM (50 mL×3), dried over anhydrous Na_2SO_4, and concentrated to a colorless oil. Flash chromatography eluting with 25% EtOAc in hexane resulted in isolation of **9** as a colorless gum (522 mg, 95% yield). ^{1}H NMR ($CDCl_3$, α/β ratio 1.0:1.0): δ 7.38 (m, 40H), 5.00 (d, *J*=12 Hz, $1H_{1\beta}$), 4.95 (d, *J*=11 Hz, $1H_{1\alpha}$), 4.83 (m, 2H), 4.76 (d, *J*=11 Hz, 2H), 4.67 (m, 5H), 4.60–4.45 (m, 7H), 4.0 (t, *J*=10 Hz, 1H), 3.80–3.70 (m, 4H), 3.58 (m, 2H), 3.48 (m, 3H), 3.39 (m, 2H). ^{13}C NMR ($CDCl_3$): δ 138.0, 137.8, 137.7, 137.7, 137.6, 137.6, 137.3, 137.0, 129.0–125.0 (40C), 102.6, 94.9, 80.0, 77.8, 76.4, 76.3, 75.5, 74.9, 74.8, 74.7, 74.6, 73.6, 72.8, 71.2, 70.1, 69.3, 68.6, 68.5, 68.1, 65.5. HRFABMS *m*/*z* 565.2648 [M+H$^+$] (calcd for $C_{34}H_{35}N_3O_5$, 565.2655).

4.10. 1,6-Di-*O*-acetyl-3-azido-2,4-di-*O*-benzyl-3-deoxy-α/β-D-glucopyranose (10)

A suspension of 3-azido-1,2,4,6-tetra-*O*-benzyl-3-deoxy-α/β-D-glucopyranose (**9**) (0.5 g, 0.884 mmol) in acetic anhydride (2.0 mL) was added in one portion to a 2% solution of sulfuric acid in acetic anhydride (2.6 mL). The reaction mixture was stirred for 5 min at room temperature then poured into 50 mL ice water. The aqueous phase was extracted successively with EtOAc, and the organic extracts washed with saturated $NaHCO_3$ and brine; dried over anhydrous Na_2SO_4, and concentrated in vacuo. The resulting colorless gum was purified via flash chromatography, eluted with 25–30% EtOAc:hexane to isolate **10** (304.4 mg, 70%). ^{1}H NMR ($CDCl_3$, α/β ratio is 1.0:0.2): δ 7.45–7.30 (m, 12H), 6.35 (d, *J*=3.5 Hz, $1H_{1\alpha}$), 5.65 (d, *J*=8.2 Hz, $0.2H_{1\beta}$), 4.93 (d, *J*=10.7 Hz, 1.2H), 4.77–4.65 (m, 2.4H), 4.62 (d, *J*=10.7 Hz, 1.4 H), 4.29 (d, *J*=3.2 Hz, 2.4H), 3.96 (m, 2.2H), 3.56 (dd, *J*=10.1, 3.5 Hz, 1H), 3.45–3.30 (m, 1.4H), 2.18 (s, 3H), 2.11 (s, 0.6H), 2.09 (s, 0.6H), 2.08 (s, 3H). ^{13}C NMR (DEPT, $CDCl_3$): δ 129.0–128.0 (20C), 93.9, 88.7, 79.0, 76.8, 75.9, 75.2, 75.1, 74.9, 74.3, 73.1, 72.8, 70.8, 65.3, 65.2, 62.8, 62.4, 21.0, 20.9, 20.8, 20.7.

4.11. 6-*O*-Acetyl-3-azido-2,4-di-*O*-benzyl-3-deoxy-α/β-D-glucopyranose (11)

1,6-Di-*O*-acetyl-3-azido-2,4-di-*O*-benzyl-3-deoxy-α/β-D-glucopyranose (**10**) (2.35 g, 5.01 mmol) was deacetylated at the anomeric position following the general procedure in DMF (5.0 mL) and CH_3COONH_4 (0.772 g, 10.02 mmol) stirred for 8 h. Flash chromatography gave **11** (0.892 g, 96% with respect to recovered starting material) as a colorless gum, along with unreacted starting material (1.33 g). ^{1}H NMR ($CDCl_3$, α/β ratio is 1.0:0.4): δ 7.41 (m, 14H), 5.19 (d, *J*=3.5 Hz, $1H_{1\alpha}$), 4.97 (d, *J*=11.0 Hz, $0.4H_{1\beta}$), 4.88 (d, *J*=10.7 Hz, 1.4H), 4.81 (m, 1.4H), 4.73 (m, 1.4H), 4.59 (d, *J*=11 Hz, 1.4H), 4.38 (dd, *J*=12.0, 2.2 Hz, 0.4H), 4.29 (dd, *J*=12.0, 2.2 Hz, 1H), 4.25 (dd, *J*=12.3, 4.1 Hz, 1H), 4.18 (dd, *J*=12.0, 5.0 Hz, 0.4H), 4.10 (m, 1H), 3.96 (t, *J*=9.8 Hz, 1H), 3.60 (t, *J*=9.5 Hz, 0.4H), 3.56 (m, 0.4H), 3.42 (dd, *J*=10.0, 3.5 Hz, 1H), 3.30 (m, 1.8H), 2.07 (s, 4.2H). ^{13}C NMR ($CDCl_3$): δ 170.8, 170.7, 137.6, 137.2, 137.2, 137.1, 128.8–128.0 (20C), 97.5, 90.3, 80.7, 78.1, 75.9, 75.8, 75.0, 74.9, 74.6, 73.6, 73.2, 68.5, 68.3, 65.1, 62.9, 62.8, 20.9, 20.9.

4.12. 6-*O*-Acetyl-3-azido-2,4-di-*O*-benzyl-3-deoxy-α/β-D-glucopyranosyl trichloroacetimidate (12)

Following the general procedure for trichloroacetimidation, **11** (1.29 g, 3.04 mmol) in DCM (20.0 mL), trichloroacetonitrile (3.05 mL, 30.4 mmol) and Cs_2CO_3 (0.099 g, 0.304 mmol) were reacted for 3 h. Purification by flash chromatography with 15–20% EtOAc in hexane gave **12** as a colorless gum (1.6 g, 92%). ^{1}H NMR ($CDCl_3$, α/β 0.8:1.0): δ 8.77 (s, $1H_{NH\beta}$), 8.66 (s, $0.8H_{NH\alpha}$), 7.41–7.28 (m, 18H), 6.44 (d, *J*=3.5 Hz, $0.8H_{1\alpha}$), 5.79 (d, *J*=8.0 Hz, $1H_{1\beta}$), 4.96 (d, *J*=11.0 Hz, 1H), 4.89 (t, *J*=11.0 Hz, 1.8H), 4.79 (d, *J*=11 Hz, 1H), 4.73 (m, 1.8H), 4.60 (dd, *J*=11.0, 6.5 Hz, 1.8H), 4.32 (m, 1H), 4.28 (m, 2.4H), 4.05 (m, 1.8H), 3.68 (m, 1.8H), 3.60 (m, 1.8H), 3.43 (m, 1.8H), 2.06 (m, 5.4H). ^{13}C NMR ($CDCl_3$): δ 170.8, 170.7, 163.4, 163.3, 137.5, 137.2, 137.1, 137.0, 128.8–128.0 (20C), 97.5, 90.3, 80.7, 78.1, 75.8, 75.8, 75.0, 74.9, 74.6, 73.7, 73.2, 68.6, 68.3, 65.1, 62.8, 62.8, 20.9, 20.8. HRFABMS *m*/*z* 571.0911 [M+H$^+$] (calcd for $C_{24}H_{25}Cl_3N_4O_6$, 571.0918).

4.13. 6-*O*-Acetyl-3-azido-2,4-di-*O*-benzyl-3-deoxy-α-D-glucopyranosyl-(1→1′)-2′,4′,6′-tri-*O*-acetyl-3′-azido-3′-deoxy-β-D-glucopyranoside (13), 6-*O*-acetyl-3-azido-2,4-di-*O*-benzyl-3-deoxy-α-D-glucopyranosyl-(1→1′)-2′,4′,6′-tri-*O*-acetyl-3′-azido-3′-deoxy−α-D-glucopyranoside (14), 6-*O*-acetyl-3-azido-2,4-di-*O*-benzyl-3-deoxy-β-D-glucopyranosyl-(1→1′)-2′,4′,6′-tri-*O*-acetyl-3′-azido-3′-deoxy-β-D-glucopyranoside (15), 6-*O*-acetyl-3-azido-2,4-di-*O*-benzyl-3-deoxy-α-D-glucopyranosyl trichloroacetamide (16)

The general glycosylation procedure was followed using **12** (418 mg, 0.664 mmol) and **5** (220 mg, 0.731 mmol), with TMSOTf (24 μL/1 mL of dry DCM, 0.113 mmol), except using 25 mL dry DCM for both steps. Repeated flash column chromatography resulted in **13** as well as **14**, **15**, and **16** as purified compounds in few of the fractions; the percent yield of each product was determined by comparing the NMR of the crude reaction mixture to their corresponding pure compounds. **13**: ^{1}H NMR ($CDCl_3$): δ 7.36–7.29 (m, 10H), 5.41 (d, *J*=3.4 Hz, 1H), 4.96–4.87 (m, 3H), 4.82 (d, *J*=10.8 Hz, 1H), 4.75–4.70 (m, 2H), 4.60 (d, *J*=12.0 Hz, 1H), 4.53 (m, 1H), 4.20–4.15 (m, 2H), 4.11–3.99 (m, 3H), 3.88 (t, *J*=9.9 Hz, 1H), 3.63–3.55 (m, 2H), 3.33–3.28 (m, 1H), 2.14 (s, 3H), 2.11 (s, 3H), 2.10 (s, 3H), 2.07 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 171.1, 170.7, 170.1, 169.5, 137.4, 137.3, 128.7, 128.6, 128.4, 128.3, 128.2, 127.8, 101.7, 89.6, 74.7, 73.2, 71.9, 70.7, 69.5, 68.4, 68.2, 67.3, 64.0, 62.3, 62.0, 60.6, 20.9, 20.8, 20.8, 20.7. HRFABMS *m*/*z* 741.2739 [M+H$^+$] (calcd for $C_{34}H_{40}N_6O_{13}$, 741.2732). **14**: ^{1}H NMR ($CDCl_3$): δ 7.40–7.30 (m, 10H), 5.33 (d, *J*=3.5 Hz, 1H), 5.07 (t, *J*=10.1 Hz, 1H), 4.95 (d, *J*=11.0 Hz, 1H), 4.89–4.86 (m, 1H), 4.84 (d, *J*=10.7, 1H), 4.78 (d, *J*=11.3 Hz, 1H), 4.60–4.56 (m, 2H), 4.41 (dd, *J*=12.3, 1.9 Hz, 1H), 4.26–4.21 (m, 2H), 4.16–4.12 (m, 1H), 4.04–3.97 (m, 2H), 3.57 (t, *J*=9.8 Hz, 1H), 3.54 (m, 1H), 3.30 (dd, *J*=9.8, 8.0 Hz, 1H), 3.23 (t, *J*=9.7 Hz, 1H), 2.13 (s, 3H), 2.09 (s, 3H), 2.06 (s, 3H), 2.04 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 170.9, 170.6, 169.9, 169.2, 137.4, 137.0, 128.8, 128.7, 128.5, 128.3, 127.8, 127.7, 103.7, 97.9, 79.2, 75.8, 75.1, 74.4, 74.4, 71.2, 68.6, 68.4, 67.9, 62.8, 61.3, 61.2, 21.0, 20.8, 20.7, 20.5. HRFABMS *m*/*z* 741.2728 [M+H$^+$] (calcd for $C_{34}H_{40}N_6O_{13}$, 741.2732). **15**: ^{1}H NMR ($CDCl_3$): δ 7.45–7.30 (m, 10H), 5.03 (t, *J*=9.8 Hz, 1H), 4.98 (dd, *J*=10.1, 7.9 Hz, 1H), 4.93 (d, *J*=10.4 Hz, 1H), 4.85 (d, *J*=11.0 Hz, 1H), 4.78 (d, *J*=8.2 Hz, 1H), 4.71 (d, *J*=7.6 Hz, 1H), 4.64 (d, *J*=11.0 Hz, 1H), 4.56 (d, *J*=10.7 Hz, 1H), 4.32 (dd, *J*=12.0, 2.2 Hz, 1H), 4.26 (dd, *J*=12.3, 4.7 Hz, 1H), 4.18 (dd, *J*=11.7, 4.1 Hz, 1H), 4.10 (dd, *J*=12.6, 2.2 Hz, 1H), 4.02–3.92 (m, 1H), 3.69 (t, *J*=10.1 Hz, 1H), 3.56 (t, *J*=9.5 Hz, 1H), 3.47 (m, 1H), 3.31 (t, *J*=9.5 Hz, 1H), 3.28 (dd, *J*=9.8, 7.6 Hz, 1H), 2.13 (s, 3H), 2.11 (s, 3H), 2.06 (s, 3H), 2.03 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 170.8, 170.5, 169.3, 169.2, 137.5, 137.1, 128.9, 128.7, 128.6, 128.5, 128.4, 128.4, 100.3, 98.0, 79.1, 75.3, 74.9, 74.7, 73.6, 73.0, 71.1, 68.3, 68.1, 64.1, 62.6, 62.0, 20.9, 20.8, 20.7, 20.7. HRFABMS *m*/*z* 741.2735 [M+H$^+$] (calcd for

$C_{34}H_{40}N_6O_{13}$, 741.2732). **16**: ^{1}H NMR ($CDCl_3$): δ 7.38–7.30 (m, 10H), 5.49 (t, J=5.4 Hz, 1H), 4.85 (d, J=10.5 Hz, 1H), 4.69 (d, J=11.6 Hz, 1H), 4.62 (d, J=11.7 Hz, 1H), 4.56 (d, J=10.5 Hz, 1H), 4.29–4.22 (m, 2H), 3.75–3.64 (m, 3H), 3.36 (t, J=9.6 Hz, 1H), 2.04 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 170.6, 162.2, 136.8, 136.1, 128.9, 128.8, 128.7, 128.6, 128.5, 128.4, 92.2, 76.4, 75.6, 75.3, 75.2, 73.2, 69.8, 65.9, 62.4, 20.8. HRFABMS m/z 571.0925 [M+H$^+$] (calcd for $C_{24}H_{25}Cl_3N_4O_6$, 571.0918).

4.14. Orthoesters 17 and 18, 2,4,6-tri-*O*-acetyl-3-azido-3-deoxy-α-D-glucopyranosyl trimethylsilyl triflate (19)

The general glycosylation procedure was followed using donor **6** (402 mg, 0.845 mmol) and acceptor **11** (330 mg, 0.772 mmol) with TMSOTf (14 μL/1 mL of dry DCM, 0.113 mmol), except using 25 mL dry DCM for both steps. Flash chromatography gave **17** (85 mg), **18** (24.5 mg), an inseparable mixture of **17** & **18** (200 mg), and **19** (10%) all as colorless gums. **17**: ^{1}H NMR ($CDCl_3$): δ 7.41–7.35 (m, 10H), 5.65 (d, J=5.5 Hz, 1H), 4.97–4.89 (m, 2H), 4.81 (s, 2H), 4.68 (d, J=8.0 Hz, 1H), 4.59 (d, J=11.0 Hz, 1H), 4.40 (dd, J=2.0, 12 Hz, 1H), 4.33 (t, J=4.5 Hz, 1H), 4.22 (d, J=4.0 Hz, 2H), 4.08 (dd, J=5.5, 11.5 Hz, 1H), 4.07–3.97 (m, 1H), 3.86 (t, J=9.5 Hz, 1H), 3.59 (t, J=9.5 Hz, 1H), 3.56–3.44 (m, 1H), 3.30–3.26 (m, 2H), 2.16 (s, 3H), 2.14 (s, 3H), 2.08 (s, 3H), 1.74 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 170.6, 170.4, 169.8, 137.1, 136.6, 128.7, 128.6, 128.5, 128.4, 128.2, 128.0, 121.0, 97.1, 96.9, 79.7, 76.1, 75.1, 75.0, 73.9, 73.6, 68.8, 67.8, 67.2, 63.1, 62.9, 60.1, 22.8, 20.9, 20.8, 20.7. HRFABMS m/z 741.2730 [M+H$^+$] (calcd for $C_{34}H_{40}N_6O_{13}$, 741.2732). **18**: ^{1}H NMR ($CDCl_3$): δ 7.43–7.36 (m, 10H), 5.69 (d, J=5.0 Hz, 1H), 5.14 (d, J=3.0 Hz, 1H), 4.91–4.85 (m, 2H), 4.77 (d, J=11.5 Hz, 1H), 4.65 (d, J=11.5 Hz, 1H), 4.58 (d, J=11.0 Hz, 1H), 4.27–4.20 (m, 5H), 4.05–4.00 (m, 1H), 3.96–3.92 (m, 2H), 3.68 (t, J=3.0 Hz, 1H), 3.39 (dd, J=3.5, 10.0, Hz, 1H), 3.29–3.26 (m, 1H), 2.16 (s, 3H), 2.14 (s, 3H), 2.07 (s, 3H), 1.75 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 170.7, 170.4, 169.8, 140.2, 139.5, 128.7, 128.6, 128.4, 128.3, 128.2, 127.9, 121.9, 97.1, 90.4, 77.8, 76.1, 74.9, 73.4, 72.4, 69.2, 67.9, 67.2, 65.2, 63.1, 62.8, 59.5, 22.1, 20.9, 20.8, 20.7. HRFABMS m/z 741.2744 [M+H$^+$] (calcd for $C_{34}H_{40}N_6O_{13}$, 741.2732). **19**: ^{1}H NMR ($CDCl_3$): δ 5.38 (d, J=3.0 Hz, 1H), 4.92 (t, J=3.5 Hz, 1H), 4.68 (dd, J=10.5, 3.5 Hz, 1H), 4.20 (dd, J=12.0, 4.5 Hz, 1H), 4.23–3.79 (m, 3H), 2.15 (s, 3H), 2.14 (s, 3H), 2.12 (s, 3H), 0.19 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 170.7, 169.8, 169.3, 89.8, 72.6, 68.5, 67.3, 62.12, 60.7, 20.7, 20.7, 20.7, −0.3. HRFABMS m/z 404.1476 [M+H$^+$] (calcd for $C_{15}H_{25}N_3O_8Si$, 404.1489).

4.15. 6-*O*-Acetyl-3-azido-2,4-di-*O*-benzyl-3-deoxy-α-D-glucopyranosyl-(1→1′)-6-*O*-acetyl-3′-azido-2′,4′-di-*O*-benzyl-3′-deoxy-β-D-glucopyranoside (20), 6-*O*-acetyl-3-azido-2,4-di-*O*-benzyl-3-deoxy-α-D-glucopyranosyl-(1→1′)-6-*O*-acetyl-3′-azido-2′,4′-di-*O*-benzyl-3′-deoxy-α-D-glucopyranoside (21)

The general glycosylation procedure was followed using donor **12** (514 mg, 0.898 mmol) and acceptor **11** (320 mg, 0.749 mmol) with TMSOTf (14 μL/1 mL of dry DCM, 0.075 mmol), except using 25 mL dry DCM for the first step and 12 mL for the second. Flash chromatography gave **20** (266 mg, 45%), **21** (138 mg, 22%), and **16** (64 mg, 15%) as colorless gums. **20**: ^{1}H NMR ($CDCl_3$): δ 7.45–7.25 (m, 20H), 5.08 (d, J=3.5 Hz, 1H), 5.02 (d, J=11.5 Hz, 1H), 4.89 (t, J=11.0 Hz, 2H), 4.80 (d, J=11.5 Hz, 1H), 4.73 (d, J=12.5 Hz, 1H), 4.67 (d, J=12.5 Hz, 1H), 4.61–4.55 (m, 3H), 4.39 (dd, J=12.0, 2.0 Hz, 1H), 4.31 (dd, J=13.0, 3.0 Hz, 1H), 4.22–4.18 (m, 2H), 4.06–4.03 (m, 2H), 3.57 (t, J=10.0 Hz, 1H), 3.56–3.51 (m, 1H), 3.44–3.42 (m, 2H), 3.29 (dd, J=10.0, 3.0 Hz, 1H), 3.24 (t, J=10.0 Hz, 1H), 2.07 (s, 3H), 2.06 (s, 3H). ^{13}C NMR (DEPT, $CDCl_3$): δ 128.7, 128.6, 128.6, 128.5, 128.4, 128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 127.8, 104.2, 98.7, 78.9, 77.6, 75.8, 75.6, 75.0, 74.9, 74.4, 74.0, 73.2, 69.3, 68.5, 65.7, 62.8, 62.4, 20.9, 20.8. HRFABMS m/z 837.3467 [M+H$^+$] (calcd for $C_{44}H_{48}N_6O_{11}$, 837.3459). **21**: ^{1}H NMR ($CDCl_3$): δ 7.44–7.24 (m, 20H), 5.13 (d, J=3.5 Hz, 2H), 4.86 (d, J=10.5 Hz, 2H), 4.72 (d, J=14.5 Hz, 2H), 4.67 (d, J=10.0 Hz, 2H), 4.53 (d, J=11.0 Hz, 2H), 4.17–4.15 (m, 2H), 4.09–4.07 (m, 4H), 3.97–3.95 (m, 2H), 3.39 (dd, J=10.5, 3.5 Hz, 2H), 3.24 (t, J=9.5 Hz, 2H), 2.03 (s, 6H). ^{13}C NMR (DEPT, $CDCl_3$): δ 128.6, 128.5, 128.4, 128.2, 128.1, 127.7, 93.2, 77.1, 75.8, 74.9, 72.8, 68.9, 65.1, 62.5, 20.9. HRFABMS m/z 837.3451 [M+H$^+$] (calcd for $C_{44}H_{48}N_6O_{11}$, 837.3459).

4.16. 3-Azido-2,4-di-*O*-benzyl-3-deoxy-α-D-glucopyranosyl-(1→1′)-3′-azido-2′,4′-di-*O*-benzyl-3′-deoxy-α-D-glucopyranoside (22)

The general procedure for deacetylation was followed using **21** (0.3 g, 0.339 mmol) in dry MeOH (10 mL) and Na metal (0.004 g), except that the reaction mixture was refluxed for 5 min, then cooled and neutralized with DOWEX 50W-X8. Filtration and concentration gave **22** (0.286 g) as a white solid. ^{1}H NMR ($CDCl_3$): δ 7.43–7.24 (m, 20H), 5.15 (d, J=3.5 Hz, 2H), 4.85 (d, J=10.5 Hz, 2H), 4.70 (d, J=14.5 Hz, 2H), 4.67 (d, J=8.2 Hz, 2H), 4.65 (d, J=7.2 Hz, 2H), 4.08–3.97 (m, 4H), 3.56 (d, J=2.5 Hz, 4H), 3.45–3.38 (m, 4H). ^{13}C NMR ($CDCl_3$): δ 128.6, 128.5, 128.4, 128.2, 128.1, 128.0, 127.7, 127.4, 93.2, 77.1, 75.8, 74.9, 72.8, 68.9, 65.1, 62.5. HRFABMS m/z 753.3255 [M+H$^+$] (calcd for $C_{40}H_{44}N_6O_9$, 753.3248).

4.17. 3-Amino-3-deoxy-α-D-glucopyranosyl-(1→1′)-3′-amino-3′-deoxy-α-D-glucopyranoside (23)

A solution of **22** (140 mg, 0.186 mmol) in methanol (6 mL) was degassed by evacuating the flask and backfilling with argon three times. Hydrazine (0.07 mL, 1.35 mmol) was added, followed immediately by 20% $Pd(OH)_2$ on carbon (~10 mg, Degussa type), and the reaction mixture was heated at reflux for 16 h. The solution was cooled to room temperature, filtered through Celite, and concentrated to afford a colorless gum (88 mg). This material was dissolved in a 1:1:1 mixture of acetic acid, water, and methanol (7.5 mL) and the solution was degassed as above. Next, 20% $Pd(OH)_2$ on carbon (~10 mg, Degussa type) was added, and the solution was purged with hydrogen. The reaction mixture was stirred at room temperature under hydrogen gas (1 atm, balloon) for 22 h. The solution was filtered through Celite and concentrated under reduced pressure. The residue was purified by anion exchange chromatography (BioRad AG1-X8, 200–400 mesh, acetate form) with a gradient of 0–200 mM aqueous acetic acid. Lyophilization of the fractions gave **23** as a white fluffy solid (62.8 mg, 98% yield). ^{1}H NMR (D_2O): δ 5.23 (d, J=3.2 Hz, 2H), 3.88 (dd, J=10.7, 3.5 Hz, 2H), 3.81 (m, 4H), 3.74 (dd, J=12.0, 4.4 Hz, 2H), 3.66 (t, J=9.8 Hz, 2H), 3.54 (t, J=10.7 Hz, 2H). ^{13}C NMR (D_2O): δ 92.4, 72.1, 67.7, 65.9, 59.9, 54.7. HRFABMS m/z 341.1571 [M+H$^+$] (calcd for $C_{12}H_{25}N_2O_9$, 341.1560).

4.18. Phenyl 2,4,6-tri-*O*-acetyl-3-azido-3-deoxy-1-thio-β-D-glucopyranoside (24)

To a solution of **4** (1.44 g, 3.86 mmol) in DCM (40 mL), thiophenol (0.473 mL, 4.63 mmol) was added, followed by addition of $BF_3{\cdot}Et_2O$ (2.422 mL, 19.29 mmol) in a dropwise manner at room temperature. The reaction mixture was stirred at the same temperature for 48 h, then quenched by adding saturated $NaHCO_3$, extracted with DCM, washed with H_2O, and dried over anhydrous Na_2SO_4. Final purification by flash column chromatography (30% EtOAc:hexane) afforded a white crystalline solid **24** (927.3 mg; 79% yield with respect to recovered staring material). ^{1}H NMR ($CDCl_3$): δ 7.52–7.49 (m, 2H), 7.33–7.31 (m, 3H), 4.93 (q, J=10.0 Hz, 2H), 4.67 (d, J=10.0 Hz, 1H), 4.19 (m, 2H), 3.69 (m, 2H), 2.19 (s, 3H), 2.12 (s, 3H), 2.08 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 170.6, 169.2, 169.1, 132.9, 131.9,

129.0, 128.4, 86.3, 76.4, 70.0, 68.3, 65.8, 62.2, 20.9, 20.8, 20.7. HRFABMS *m/z* 424.1169 [M+H$^+$] (calcd for $C_{18}H_{21}N_3O_7S$, 424.1178).

4.19. Phenyl 3-azido-3-deoxy-1-thio-β-D-glucopyranoside (25)

The general procedure for deacetylation was followed using **24** (1.05 g, 0.931 mmol) in MeOH (20 mL) added 0.5 M NaOMe (2.0 mL). The product **25** was isolated as a white solid in quantitative yield (737 mg). ^{1}H NMR (CD_3OD): δ 7.58 (d, J=7.0 Hz, 2H), 7.36–7.30 (m, 3H), 4.65 (d, J=10.5 Hz, 1H), 3.88 (dd, J=11.0, 2.0 Hz, 1H), 3.67 (dd, J=11.5, 5.5 Hz, 1H), 3.38–3.26 (m, 3H), 3.24 (t, J=9.5 Hz, 1H). ^{13}C NMR (CD_3OD): δ 133.5, 131.5, 128.5, 127.1, 88.2, 81.0, 71.7, 71.4, 68.6, 61.1. HRFABMS *m/z* 298.0870 [M+H$^+$] (calcd for $C_{12}H_{15}N_3O_4S$, 298.0862).

4.20. Phenyl 3-azido-3-deoxy-4,6-*p*-methoxybenzylidene-1-thio-β-D-glucopyranoside (26)

To a solution of thioglycoside **25** (737 mg, 2.479 mmol) in DMF (10 mL), a catalytic amount of *p*-TsOH was added, followed by the addition of *p*-anisaldehyde (0.6 mL, 4.96 mmol). The reaction mixture was stirred at 60 °C for 20 h under argon. The solvent was evaporated, and **26** was isolated flash column chromatography (30–40% EtOAc:Hexane) as a white amorphous solid (618 mg, 98% yield with respect to recovered starting material). ^{1}H NMR ($CDCl_3$): δ 7.57–7.55 (m, 2H), 7.42 (d, J=9.0 Hz, 2H), 7.39–7.37 (m, 3H), 6.92 (d, J=9.0 Hz, 2H), 5.54 (s, 1H), 4.64 (d, J=9.5 Hz, 1H), 4.38 (dd, J=5.0, 10.5 Hz, 1H), 3.80 (s, 3H), 3.76 (t, J=10.0 Hz, 1H), 3.74 (t, J=9.5 Hz, 1H), 3.56 (ddd, J=18.5, 9.5, 4.5 Hz, 1H), 3.52 (t, J=9.5 Hz, 1H), 3.39 (dt, J=9.5, 1.5 Hz, 1H). ^{13}C NMR ($CDCl_3$): δ 160.2, 133.3, 130.8, 129.3, 129.1, 128.7, 127.4, 113.7, 101.6, 89.1, 79.1, 71.7, 71.5, 68.5, 65.9, 55.3. HRFABMS *m/z* 417.1353 [M+H$^+$] (calcd for $C_{20}H_{22}N_3O_5S$, 417.1358).

4.21. Phenyl 3-azido-3-deoxy-6-*O*-*p*-methoxybenzyl-1-thio-β-D-glucopyranoside (27)

To a solution of thioglycoside **26** (1.29 g, 3.10 mmol) in dry THF (40 mL), 3 Å molecular sieves (1.5 g) and $NaCNBH_3$ (1.171 g, 18.63 mmol) were added at room temperature. A solution of 1 M HCl in diethyl ether was added until the pH was between 1 and 2 (~18.6 mL), and the reaction stirred at room temperature for 3 h. The reaction mixture was quenched with Et_3N (8 mL), diluted with DCM and filtered through Celite. Flash column chromatography (30% EtOAc:hexane) gave **27** in quantitative yield (1.3 g) as a white solid. ^{1}H NMR (CD_3OD): δ 7.58–7.56 (m, 2H), 7.30–7.22 (m, 5H), 6.87 (d, J=8.5 Hz, 2H), 4.65 (d, J=12.5 Hz, 1H), 4.49 (s, 2H), 3.82 (s, 3H), 3.61 (dd, J=11.0, 6.0 Hz, 1H), 3.53–3.51 (m, 1H), 3.38–3.26 (m, 4H). ^{13}C NMR ($CDCl_3$): δ 159.4, 133.2, 131.7, 129.3, 129.1, 128.5, 127.1, 113.3, 87.9, 79.9, 72.7, 71.7, 71.4, 68.9, 68.0, 54.3. HRFABMS *m/z* 418.1430 [M+H$^+$] (calcd for $C_{20}H_{23}N_3O_5S$, 418.1437).

4.22. Phenyl 3-azido-2,4-di-*O*-*tert*-butyldimethylsilyl-3-deoxy-6-*O*-*p*-methoxybenzyl-1-thio-β-D-glucopyranoside (28)

Thioglycoside **27** (1.5 g, 3.6 mmol) and one drop of DMAP were dissolved in pyridine (20 mL) and solution was cooled to 0 °C. *tert*-Butyldimethylsilyl triflate (4.13 mL, 18.0 mmol) was added and reaction mixture was heated to 60 °C and stirred 20 h. The reaction was quenched with MeOH (1.0 mL); diluted with EtOAc, extracted with H_2O (30 mL), 1 M HCl (30 mL) and finally with brine (30 mL); dried over anhydrous Na_2SO_4, concentrated, and isolated by flash column chromatography (10% EtOAc in hexane) to yield **28** (2.0 g, 85% yield) as a colorless oil. ^{1}H NMR ($CDCl_3$): δ 7.56–7.54 (m, 2H), 7.29–7.24 (m, 5H), 6.89 (d, J=8.5 Hz, 2H), 4.62 (d, J=9.5 Hz, 1H), 4.56 (d, J=11.5 Hz, 1H), 4.45 (d, J=11.0 Hz, 1H), 3.84 (s, 3H), 3.77 (d, J=10.0 Hz, 1H), 3.56 (dd, J=16.0, 5.8 Hz, 1H), 3.49–3.42 (m, 3H), 3.23 (t, J=9.0 Hz, 1H), 1.00 (s, 9H), 0.91 (s, 9H), 0.29 (s, 3H), 0.26 (s, 3H), 0.24 (s, 3H), 0.10 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 159.3, 134.8, 131.0, 130.4, 129.2, 129.1, 127.1, 113.7, 89.8, 80.6, 74.7, 73.1, 72.8, 70.1, 68.9, 55.3, 26.1, 25.8, 18.8, 17.9, −3.8, −4.3, −4.5, −4.7. HRFABMS *m/z* 646.3126 [M+H$^+$] (calcd for $C_{32}H_{51}N_3O_5SSi_2$, 646.3166).

4.23. 3-Azido-2,4-di-*O*-*tert*-butyldimethylsilyl-3-deoxy-6-*O*-*p*-methoxybenzyl-α/β-D-glucopyranose (29)

To a solution of **28** (0.84 g, 1.3 mmol) in a mixture of acetone:-water (9:1, 20 mL), *N*-bromosuccinimde (0.463 g, 2.6 mmol) was added and reaction mixture was stirred for 30 min. The reaction was quenched by adding 0.5 g of solid $NaHCO_3$, and the solvent evaporated in vacuo at room temperature. The residue was suspended in EtOAc (70 mL) and extracted with water until the pH of the aqueous layer was neutral. The organic phase was dried by washing with brine and evaporated to dryness. Flash column chromatography (20% EtOAc:Hexane) gave **29** (0.634 g, 88% yield) as a colorless gum. ^{1}H NMR ($CDCl_3$, α/β ratio 1.0:0.6): δ 7.26 (d, J=5.0 Hz, 3.2H), 6.89 (d, J=5.0 Hz, 3.2H), 5.14 (br s, 1H), 4.56 (m, 2.2H), 4.43 (m, 1.6H), 3.98–3.96 (m, 1H), 3.83 (s, 4.8H), 3.68 (m, 0.6H), 3.64 (dd, J=11.0, 3.5 Hz, 1H), 3.60–3.54 (m, 2.6H), 3.47–3.42 (m, 2.2H), 3.33 (m, 1H), 3.30–3.26 (dd, J=9.8, 7.9 Hz, 0.6H), 3.17 (t, J=9.5 Hz, 0.6H), 0.96 (s, 9H), 0.95 (s, 5.4H), 0.88 (s, 9H), 0.86 (s, 5.4H), 0.21 (s, 3H), 0.20 (m, 6.6H), 0.17 (s, 1.8H), 0.15 (s, 3H), 0.06 (s, 3H), 0.02 (s, 1.8H). ^{13}C NMR ($CDCl_3$): δ 159.3, 159.2, 130.0, 129.8, 129.5, 129.4, 113.9, 113.8, 97.5, 92.5, 74.9, 73.2, 73.1, 72.7, 72.4, 71.3, 69.9, 69.1, 69.1, 68.8, 68.6, 68.3, 55.3, 55.2, 25.9, 25.8, 25.8, 25.7, 18.2, 18.1, 18.0, 17.9, −4.1, −4.3, −4.4, −4.7, −4.8, −4.8, −4.9, −5.0. HRFABMS *m/z* 554.3071 [M+H$^+$] (calcd for $C_{26}H_{47}N_3O_6Si_2$, 554.3082).

4.24. 3-Azido-2,4-di-*O*-*tert*-butyldimethylsilyl-3-deoxy-6-*O*-*p*-methoxybenzyl-α-D-glucopyranosyl trichloroacetimidate (30)

Following the general procedure for trichloroacetimidation, **29** (1.0 g, 1.8 mmol) in DCM (20.0 mL), Cs_2CO_3 (59 mg, 0.18 mmol) and trichloroacetonitrile (1.81 mL, 18.1 mmol) were added, and reaction mixture was stirred at room temperature for 5 h. Flash chromatography gave **30** (0.55 g, 78%, yield with respect to recovered starting material) as a white amorphous solid. ^{1}H NMR ($CDCl_3$): δ 8.62 (s, 1H$_{NH}$), 7.26 (d, J=8.5 Hz, 2H), 6.89 (d, J=8.5 Hz, 2H), 6.31 (d, J=3.5 Hz, 1H), 4.51 (d, J=11.5 Hz, 1H), 4.44 (d, J=11.5 Hz, 1H), 3.85 (m, 1H), 3.82 (s, 3H), 3.74 (m, 1H), 3.69 (dd, J=11.0, 3.5 Hz, 1H), 3.63 (m, 3H), 0.91 (s, 9H), 0.90 (s, 9H), 0.22 (s, 3H), 0.20 (s, 3H), 0.13 (s, 3H), 0.10 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 163.6, 159.3, 129.7, 129.5, 113.8, 92.4, 91.8, 73.1, 72.8, 71.3, 69.2, 68.5, 68.5, 55.3, 25.9, 25.7, 18.1, 17.9, −4.3, −4.7, −4.8, −5.0. HRFABMS *m/z* 697.2169 [M+H$^+$] (calcd for $C_{28}H_{47}Cl_3N_4O_6Si_2$, 697.2178).

4.25. 2,3,4,6-Tetra-*O*-acetyl-α-D-glucopyranosyl-(1→1′)-2′,4′,6′-tri-*O*-acetyl-3′-azido-3′-deoxy-β-D-glucopyranoside (32)

The general glycosidation procedure was followed using **6** (463 mg, 0.974 mmol), acceptor **31** (234 mg, 0.974 mmol), and TMSOTf (24 μL/1 mL of dry DCM, 0.134 mmol). Flash chromatography gave **32** as a colorless gum (205 mg, 43% yield) along with other unidentified products. ^{1}H NMR ($CDCl_3$): δ 5.48 (t, J=10.0 Hz, 1H), 5.40 (t, J=3.5 Hz, 1H), 5.25–2.16 (m, 1H), 5.00 (t, J=9.5 Hz, 2H), 4.90–4.86 (m, 1H), 4.79 (dd, J=10.0, 3.5 Hz, 1H), 4.75–4.70 (m, 1H), 4.42 (d, J=4.0 Hz, 1H), 4.26–4.15 (m, 2H), 4.12–4.03 (m, 2H), 3.70 (m, 1H), 2.03 (s, 6H), 2.02 (s, 3H), 1.98 (s, 6H), 1.95 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 171.3, 170.9, 170.5, 170.3, 170.3, 169.7, 169.6, 95.3, 89.9, 73.0, 72.4, 71.9, 69.9, 68.5, 68.4, 67.5, 67.0, 62.0, 60.5, 20.7, 20.7, 20.6, 20.6, 20.6, 20.5, 20.5. HRFABMS *m/z* 662.2049 [M+H$^+$] (calcd for $C_{26}H_{35}N_3O_{17}$, 662.2045).

4.26. α-D-Glucopyranosyl-(1→1′)-3′-azido-3′-deoxy-β-D-glucopyranoside (33)

Following the general procedure for deacetylation, **32** (200 mg, 0.302 mmol) was treated in MeOH (5 mL) added 0.03 M NaOMe (0.4 mL). Neutralization and evaporation have **33** (103 mg, 93% yield) as a brown gum. ^{1}H NMR (CD_3OD+D_2O): δ 5.05 (br s, 1H), 4.47 (d, J=8.0 Hz, 1H), 3.81–3.65 (m, 4H), 3.56–3.52 (m, 3H), 3.35–3.27 (m, 2H), 3.24–3.22 (m, 2H), 3.06 (t, J=9.0 Hz, 1H). ^{13}C NMR (CD_3OD+D_2O): δ 95.8, 92.0, 75.9, 75.7, 74.1, 72.7, 71.5, 71.4, 69.6, 69.5, 60.7, 60.5. HRFABMS m/z 368.1315 [M+H$^+$] (calcd for $C_{12}H_{21}N_3O_{10}$, 368.1305).

4.27. α-D-Glucopyranosyl-(1→1′)-3′-amino-3′-deoxy-β-D-glucopyranoside (34)

The general procedure for azide reduction was followed using **33** (103 mg, 0.28 mmol) and Pd/C (55 mg), giving **34** (79.5 mg, 83% yield) as a white amorphous powder. ^{1}H NMR (D_2O): δ 5.11 (d, J=3.0 Hz, 1H), 4.51 (d, J=8.0 Hz, 1H), 3.72 (d, J=10.5, Hz, 1H), 3.70–3.65 (m, 2H), 3.61–3.57 (m, 4H), 3.45–3.25 (m, 4H), 3.09 (t, J=8.5 Hz, 1H). ^{13}C NMR (D_2O): δ 95.9, 92.0, 75.9, 75.7, 74.1, 72.7, 71.4, 71.3, 69.6, 69.5, 60.7, 60.5. HRFABMS m/z 342.1407[M+H$^+$] (calcd for $C_{12}H_{23}NO_{10}$, 342.1400).

4.28. 2,4,6-Tri-*O*-acetyl-3-azido-3-deoxy-α-D-glucopyranosyl-(1→1′)-2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranoside (36)

According to the general glycosidation method, **35** (392 mg, 0.796 mmol) and acceptor **5** (215 mg, 0.8 mmol) were reacted in dry DCM (40.0 L), but after 1 h the reaction was not complete, therefore another 0.1 equiv of TMSOTf was added, and the reaction stirred another 2 h. The reaction was quenched by addition of saturated $NaHCO_3$ solution (40 mL). The organic phase was separated and successively washed with water (3×40 mL), dried, and concentrated in vacuo to get colorless gum that was further purified by flash chromatography eluting with a gradient of EtOAc/hexane to obtain **36** (180 mg, 41% yield) as a colorless gum, along with some other unidentified products. ^{1}H NMR ($CDCl_3$): δ 5.44 (t, J=10.0 Hz, 1H), 5.37 (t, J=3.5 Hz, 1H), 5.15 (t, J=10.0 Hz, 1H), 5.00 (t, J=9.5 Hz, 1H), 4.79 (dd, J=10.0, 3.5 Hz, 1H), 4.72–4.68 (m, 1H), 4.57 (d, J=4.0 Hz, 1H), 4.22–4.18 (m, 2H), 4.16 (d, J=4.0 Hz, 1H), 4.09–4.03 (m, 3H), 3.72–3.70 (m, 1H), 2.03 (m, 6H), 2.02 (s, 3H), 1.98 (s, 6H), 1.96 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 171.1, 170.9, 170.4, 170.3, 170.3, 169.8, 169.6, 95.2, 89.9, 72.9, 72.5, 71.8, 71.2, 69.9, 68.5, 68.4, 66.9, 61.9, 60.6, 20.7, 20.6, 20.6, 20.6, 20.6, 20.5, 20.4. HRFABMS m/z 662.2037 [M+H$^+$] (calcd for $C_{26}H_{35}N_3O_{17}$, 662.2045).

4.29. 3-Azido-3-deoxy-α-D-glucopyranosyl-(1→1′)-β-D-glucopyranoside (37)

The general procedure for deacetylation was followed using **36** (170 mg, 0.257 mmol) in MeOH (10 mL) and 0.03 M NaOMe (0.4 mL). Neutralization and evaporation gave **37** in quantitative yield (94 mg) as a brown gum. ^{1}H NMR (CD_3OD+D_2O): δ 5.15 (d, J=3.5 Hz, 1H), 4.55 (d, J=8.0 Hz, 1H), 3.87 (dd, J=13.5, 1.5 Hz, 1H), 3.84–3.81 (m, 2H), 3.74–3.65 (m, 3H), 3.45–3.40 (m, 2H), 3.39–3.32 (m, 3H), 3.17 (t, J=9.0 Hz, 1H). ^{13}C NMR (CD_3OD+D_2O): δ 96.4, 92.3, 76.4, 76.3, 74.6, 73.2, 72.1, 71.6, 70.2, 70.0, 61.2, 61.1. HRFABMS m/z 368.1311 [M+H$^+$] (calcd for $C_{12}H_{21}N_3O_{10}$, 368.1305).

4.30. 3-Amino-3-deoxy-α-D-glucopyranosyl-(1→1′)-β-D-glucopyranoside (38)

The general procedure for azide reduction was followed using **37** (94 mg, 0.256 mmol) in MeOH (8 mL) and Pd/C (50 mg), giving **38** (85 mg, 97% yield) as a white amorphous powder. ^{1}H NMR (D_2O): δ 5.10 (d, J=3.5 Hz, 1H), 4.51 (d, J=7.5 Hz, 1H), 3.78 (dd, J=7.5, 2.0 Hz, 1H), 3.73–3.68 (m, 2H), 3.65–3.56 (m, 3H), 3.42–3.32 (m, 3H), 3.29–3.23 (m, 2H), 3.09 (d, J=9.5 Hz, 1H). ^{13}C NMR (D_2O): δ 95.9, 92.0, 75.9, 75.7, 74.1, 72.7, 71.4, 71.3, 69.6, 69.5, 60.7, 60.5. HRFABMS m/z 342.1391 [M+H$^+$] (calcd for $C_{12}H_{23}NO_{10}$, 342.1400).

Acknowledgements

This work was supported by a Saskatchewan Health Research Fund Team Grant to the Molecular Design Research Group. We thank Dr. Manuel Chirino-Trejo (Western College of Veterinary Medicine, University of Saskatchewan) for providing the laboratory supplies and facilities required for antimicrobial susceptibility testing, Dr. David Sanders (University of Saskatchewan) and David M. Langill for helpful discussions, and the staff of the Saskatchewan Structural Sciences Centre for many technical contributions.

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