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Glycosylations

Reagent Controlled Stereoselective Assembly of α-(1,3)-Glucans

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Abstract: Pre-activation based glycosylations have become a very powerful tool in the assembly of oligosaccharides and the use of nucleophilic additives allows for the in situ generation of reactive intermediates with tailored reactivity. We here use a glycosylation strategy that is based on the use of per-benzylated imidate building blocks for the fully stereoselective construction of a spacer equipped *Aspergillus fumigatus* α-1,3-octaglucan. We have used the trimethylsilyl iodide (TMSI)-triphenylphosphine oxide ($Ph_3P=O$) for the stereoselective installation of an azidopropanol spacer and triflic acid (TfOH)-dimethyl formamide (DMF) enabled glycosylations for the coupling reactions with the secondary glucosyl C-3-alcohols. An operationally simple in situ activation coupling procedure is introduced and used for the final glycosylation events towards the octasaccharide.

Introduction

The stereoselective construction of 1,2-*cis*-glycosidic bonds continues to be a great challenge in the assembly of oligosaccharides and glycoconjugates and no general solution exists for the construction of these linkages.[1] The large panel of diastereoisomeric monosaccharides in combination with the plethora of different functional and protecting group schemes generates a humongous diversity in carbohydrate building blocks.[1] The structural variation translates to varying reactivity of both the donor glycoside[2] and acceptor glycoside[3] and because of the large differences in the reactivity of both coupling partners it is often difficult to translate a productive glycosylation reaction from one glycosylation couple to another. The introduction of nucleophilic additives to modulate the coupling reaction has been an important step forwards as this opens up the way to match donor and acceptor reactivity.[4] Recently we have reported on the fully stereoselective assembly of a *Mycobacterium tuberculosis* derived α-glucan **1**, built up from a 1,4-linked-hexa-α-glucose backbone, bearing a mono- and disaccharide α-glucose branch.[5] The assembly of this nonasaccharide was accomplished using additive controlled glycosylation reactions and built on the following design parameters: 1) Only a single type of *N*-phenyltrifluoroimidate building block was used, bearing a uniform protecting group pattern, solely relying on the use of benzyl type ethers; 2) A triad of benzyl ethers [namely the benzyl (Bn), *para*-methoxybenzyl (PMB) and 2-methylnaphthyl (Nap) ether] was used to discriminate the alcohol groups that required permanent protection or needed to be removed to introduce the branches or grow the α-1,4-backbone. 3) The intrinsic differences in reactivity between the primary and secondary alcohol acceptors was accommodated for in the coupling reaction using two different activator/additive couples: Trifluoromethanesulfonic acid (TfOH) in conjunction with dimethylformamide (DMF) for the condensation of the secondary alcohols and trimethylsilyliodide (TMSI) in combination with triphenylphosphine oxide for the coupling to the more reactive primary alcohols (See Figure 1). Besides the fact that all building blocks were of nearly identical reactivity, as a result of the chosen protecting group strategy, the use of solely benzyl ether-type protecting groups is beneficial at the stage of building block assembly – the benzyl ethers used are very robust and easily introduced – and at the final stage of the synthesis, as unmasking all groups can be achieved under mild conditions in a single hydrogenation event. The successful assembly of the 1,4-α-glucan nonasaccharide was an incentive to explore the above described synthesis strategy for the assembly of the related α-1,3-glucans. These compounds are prominent components of fungal cell walls[6] and they have been shown to interact with our immunesystem, through as yet undefined receptor(s).[7] Nifantiev and co-workers recently reported the synthesis of an *Aspergillus fumigatus* α-1,3-glucan pentasaccharide, employing a long-range participation approach to ensure the stereoselective construction of the *cis*-glucosidic linkages.[8] The spacer-equipped pentasaccharide was used for the generation of a BSA-conjugate vaccine and the polyclonal mouse serum raised with the conjugate could recognize α-1,3-glucan-expressing *A. fumigatus*.

We here describe the synthesis of the largest synthetic α-1,3-glucan to date, i.e. the assembly of octasaccharide **2** (Figure 1). To streamline the synthesis of large oligosaccharides using a nucleophilic additive glycosylation based approach we have

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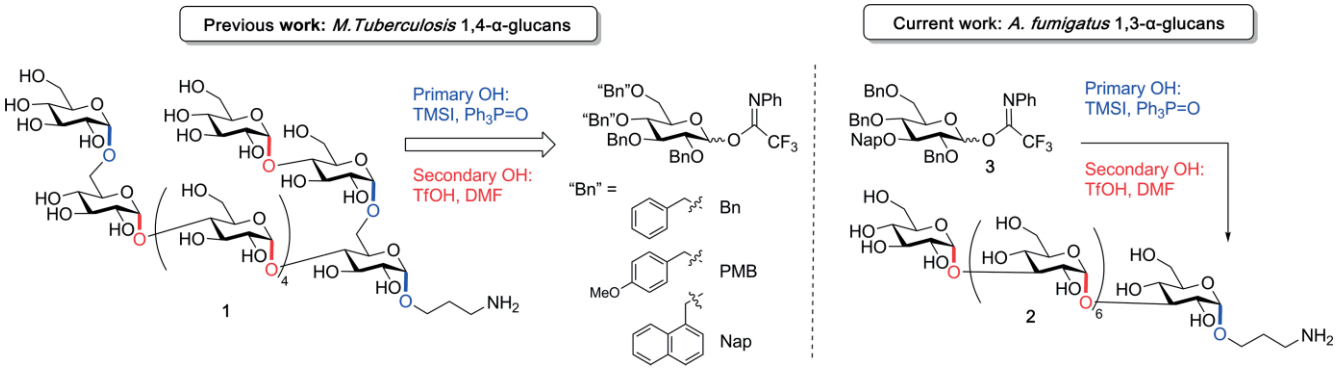


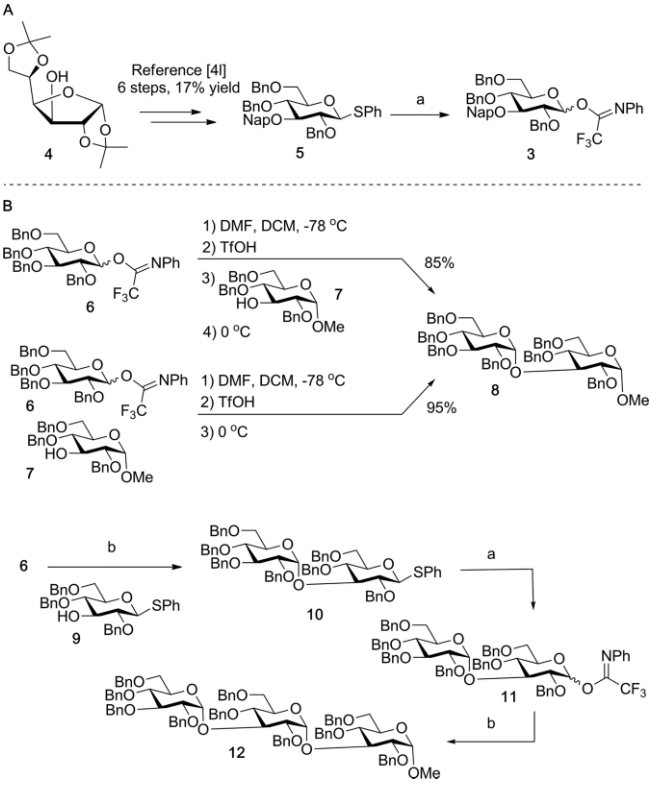
Figure 1. Schematic syntheses of branched 1,4-α-glucans (previously reported) and 1,3-α-glucans. The strategy hinges on the use of building blocks carrying solely benzyl-type protecting groups in combination with different activator/additive systems for glycosylations of primary (more reactive) or secondary (less reactive) alcohols.

further optimized the coupling protocol by showing that pre-activation of the donor glycoside can be omitted allowing for a much-simplified experimental procedure.

Results and Discussion

In line with the strategy outlined above our synthetic approach is built on the use per-benzylated donor and acceptor building blocks. To temporarily mask the C-3-OH a 2-methylnaphthyl (Nap)-ether[9] was used (building block **3**, See Figure 1). The assembly of the required building block for this study is depicted in Scheme 1A. The free alcohol in 1,2;5,6-di-*O*-isopropylidene-α-D-glucofuranose was used to introduce the Nap ether at this position. Acidic hydrolysis of both acetone ketals, ensuing acetylation, introduction of an anomeric thiophenol group and benzylation of the alcohols at C-2, C-4 and C-6 then delivered glucoside **5**. The anomeric thio acetal in this building block was hydrolyzed using *N*-iodosuccinimide in acetone/water to liberate the anomeric hydroxyl group, which could then be turned into the required *N*-phenyltrifluoroimidate **3**.

With the required building block in hand we first performed a series of glycosylations to probe the feasibility of the DMF-mediated glycosylation conditions for the construction of the α-1,3-glucosyl bond (Scheme 1B). We have recently established that the glucosyl C-3-OH is somewhat more nucleophilic than its C-4-OH counterpart, which could impact the stereoselectivity of the projected glycosylation reactions.[3a,3c] Thus, donor **6** was activated at –78 °C using an equimolar amount of TfOH in the presence of 16 equivalents of DMF, as originally prescribed by Mong co-workers.[4k] After 30 minutes C-3-OH acceptor **7** was added and the mixture warmed to 0 °C. This protocol installed the desired α-glucosyl linkage with excellent stereoselectivity and generated diglucoside **8** in 85 % yield. To allow for an operationally simpler protocol we examined whether the donor and acceptor could be premixed. Indeed, addition of TfOH to a mixture containing donor **6**, acceptor **7** and DMF at –78 °C and subsequent warming to 0 °C proved feasible as the yield and stereoselectivity of the condensation remained excellent (See Scheme 1B). Especially in the generation of larger oligomers, using large and expensive acceptor building blocks (vide infra) this simpler protocol represents a

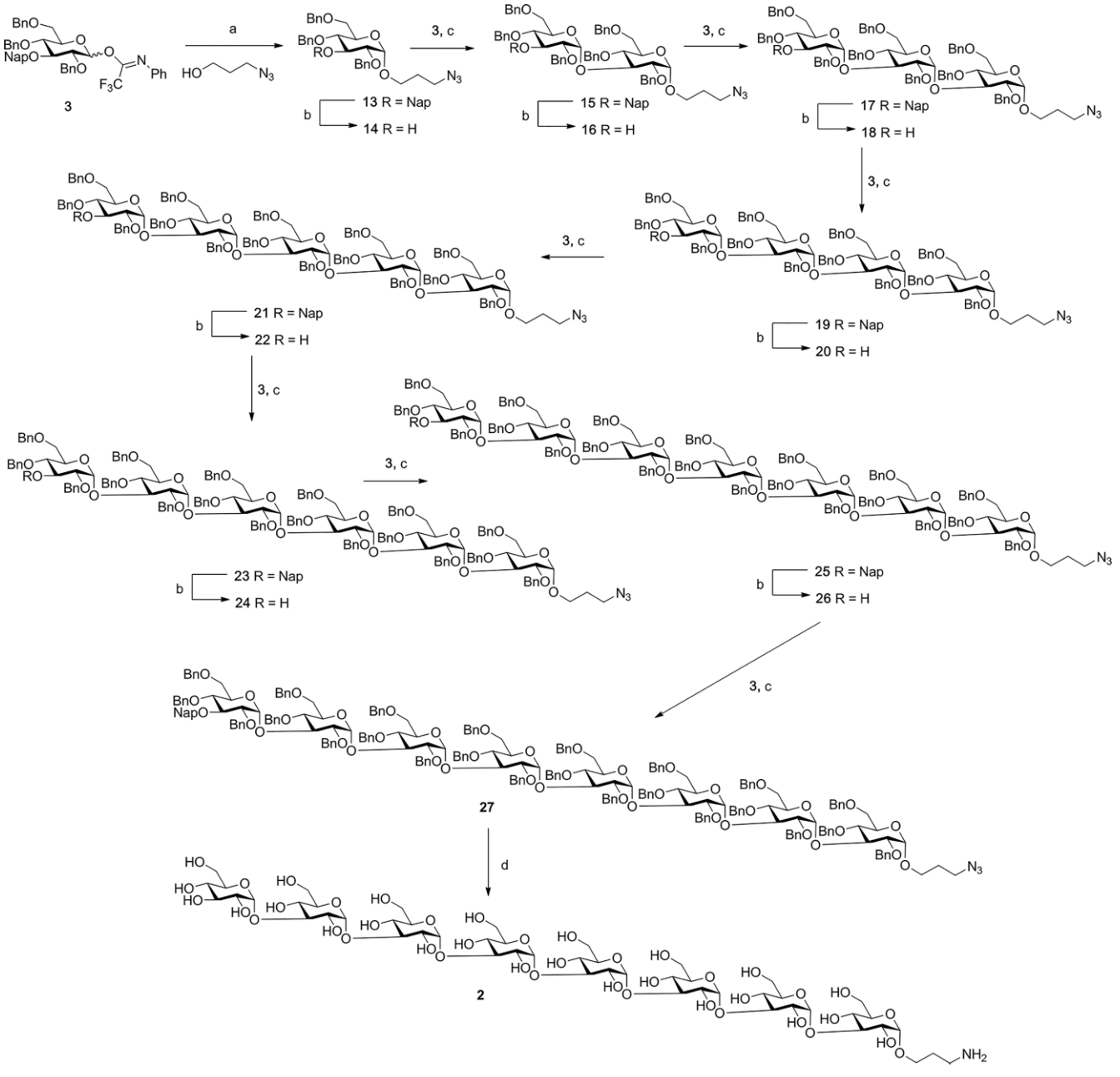


Scheme 1. **A**) Synthesis of building block **3** and **B**) model glycosylations. a) 1) NIS, acetone/H_2O = 10:1; 2) 2,2,2-trifluoro-*N*-phenylacetimidoyl chloride, Cs_2CO_3, acetone, **3**: 90 %; **11**: 80 %. b) DMF, TfOH, DCM, –78–0 °C, **8**: α:β > 20:1; **10**: 91 %, α:β > 20:1; **12**: 63 %, α:β > 20:1.

significant improvement, as less manipulations are required on the side of the acceptor. We also explored whether a chemoselective glycosylation could be achieved under these conditions, and to this end donor **6** and thioglucoside **9**, obtained by removal of the Nap ether in **5**, were coupled using TfOH/DMF to provide diglucoside **10** in 91 %, again with excellent stereoselectivity. The resulting thiodisaccharide could be turned into *N*-phenyltrifluoroimidate donor **11** and used in a subsequent glycosylation event. In the event disaccharide imidate **11** and acceptor **7** were pre-mixed with DMF in dichloromethane (DCM), after which the activator was added and the mixture

warmed to 0 °C. Trisaccharide **12** was obtained as a single anomer in 63 % yield.

Next we turned our attention to the assembly of a longer and spacer-functionalized α-1,3-glucan as depicted in Scheme 2. Firstly, the azidopropanol spacer was introduced. To this end donor **3** was activated using a combination of TMSI and $Ph_3P{=}O$ (6 equivalents). As we have described previously these conditions work well to install the α-glucosidic linkage on reactive primary alcohols and also in this case the desired azidopropyl glucoside **13** was obtained in good yield and stereoselectivity (α/β = 10:1). Deprotection of the C-3-O-Nap ether under oxidative conditions [dichlorodicyanobenzoquinone (DDQ) in DCM/H_2O, 10:1 v/v] proceeded uneventfully and set the stage for elongation of the aziopropyl glucoside which was purified with silica gel column chromatography to get pure α-anomer **14**. Activation of donor **3** with the TfOH/DMF combination and coupling with acceptor **14** delivered the desired disaccharide **15** as the sole anomer. The only side product that was detected was a 1,1′-coupled trehalose. Unfortunately this side product was difficult to remove form the disaccharide product and we therefore continued with the deprotection of **15** to give disaccharide alcohol **16**, which was now readily purified and obtained in 90 % over the two steps. Elongation of the diglucoside proceeded smoothly and gave the trisaccharide **17**



Scheme 2. **A**) Assembly of an *a. fumigatus* α-1,3-octaglucan. a) TMSI, $Ph_3P{=}O$, DCM, room temp., **13**: 80 %, α:β = 10:1. b) DDQ, DCM/H_2O, **14**: 80 %; **16**: 90 % (with two steps); **18**: 95 %; **20**: 80 %; **22**: 75 %; **24**: 70 %; **26**: 51 %. c) DMF, TfOH, DCM, –78–0 °C, **15**: > 90 %, α:β > 20:1; **17**: 81 %, α:β > 20:1; **19**: 84 %, α:β > 20:1; **21**: 81 %, α:β > 20:1; **23**: 90 %, α:β > 20:1; **25**: 90 %, α:β > 20:1; **27**: 98 %, α:β > 20:1. d) $Pd(OH)_2$, H_2 (40 bar), THF/H_2O/tBuOH, 40 %.

in 81 % yield. Oxidative deprotection of the C-3‴-O-Nap ether and subsequent elongation with another copy of donor **3** delivered the tetrasaccharide **19**. Repetition of the deprotection-coupling cycle then generated pentasaccharide **21** and hexasaccharide **23**. Deprotection of the Nap ether again proceeded uneventfully to set the stage for the next glycosylation. From this stage on we employed the donor-acceptor pre-mixing strategy and using the above described protocol heptasaccharide **25** was generated as the sole anomer in 90 % yield. Denaphthylation gave heptasaccharide alcohol **26**, which was elongated in a final glucosylation event, again under the donor-acceptor pre-mixing conditions, to give the *all-cis* octaglucoside **27** in 98 % yield. Deprotection of the octasaccharide was accomplished in a single hydrogenation event to give **2** in 40 % yield and complete the synthesis.

Conclusions

In summary we have presented a synthesis of a spacer-equipped octa-α-1,3-glucan using a strategy that is built on the use of benzyl ether protected building blocks in combination with appropriate activator-additive reagent combinations to install the desired glucosidic linkages. To stereoselectively install the linker on the first building block we relied on the TMSI-Ph_3P=O reagent combination, while all other glycosylations, generating linkages to secondary alcohols, were promoted by the TfOH-DMF reagent system. We have shown that a pre-activation strategy, which encompasses the activation of the donor glycoside in the absence of the acceptor, is not required to achieve high yielding stereoselective glycosylation reactions. This has allowed the development of an effective α-glucosylation protocol that is operationally easier and requires less manipulation of (expensive) acceptor alcohols. Extension of the here reported glycosylation strategy to other *cis*-glycans is currently underway in our laboratory.

Experimental Section

General Experimental Procedures: All reagents were of commercial grade and used as received. All moisture sensitive reactions were performed under an argon atmosphere. DCM used in the glycosylation reactions was dried with flamed 4 Å molecular sieves before being used. Reactions were monitored by TLC analysis with detection by UV (254 nm) and where applicable by spraying with 20 % sulfuric acid in EtOH or with a solution of $(NH_4)_6Mo_7O_{24}{\cdot}4H_2O$ (25 g/L) and $(NH_4)_4Ce(SO_4)_4{\cdot}2H_2O$ (10 g/L) in 10 % sulfuric acid (aq.) followed by charring at ca. 150 °C. Column chromatography was carried out using silica gel (0.040–0.063 mm). Size-exclusion chromatography was carried out using Sephadex LH-20. High resolution mass (HRMS) was performed on a Thermo Finnigan LTQ Orbitrap mass spectrometer equipped with an electrospray ion souce in positive ion mode (source voltage 3.5 kV, sheath gas flow 10, capillary temperature 275 °C) resolution R = 60.000 at *m/z* 400 (mass range of 150–4000) and dioctylphthalate(*m/z* = 391.28428) as lock mass, or on a Waters Spynat G2-Si(OTF) equieped with an electrospary ion souce in positive mode (source voltage 3.5 kV) and LeuEnk (*m/z* = 556.2771). 1 μL of 2,5-dihydroxybenzoic acid (2,5-DHB; Bruker Daltonics) matrix [20 mg/mL in ACN/water; 50:50 (v/v)] was applied on a 384-MTP target plate (Bruker Daltonics, Bremen, Germany) and air-dried. Subsequently, 1 μL of xxx solution was spotted on the plate and the spots were left to dry prior MALDI-TOF analysis. An Ultraflextreme MALDI-TOF (Bruker Daltonics), equipped with Smartbeam-II laser was used to measure the samples in reflectron positive ion mode. The MALDI-TOF was calibrated using a peptide calibration standard prior to measurement. ^1H and ^{13}C spectra were recorded on a Bruker AV 400 and Bruker AV 500 in $CDCl_3$ or D_2O. Chemical shifts (δ) are given in ppm relative to tetramethylsilane as internal standard (^1H NMR in $CDCl_3$) or the residual signal of the deuterated solvent. Coupling constants (*J*) are given in Hz. All ^{13}C spectra are proton decoupled. NMR peak assignments were made using COSY and HSQC experiments, where applicable Clean TOCSY, HMBC and GATED experiments were used to further elucidate the structure. The anomeric product ratios were analyzed through integration of proton NMR signals. IR spectra were recorded on a Shimadzu FTIP-8300 IR spectrometer and are reported in cm Specific rotations were measured on a Propol automatic polarimeter or an Anton-Paar MCP 100 modular circular polarineter at 589 nm unless otherwise stated.

Standard Procedure A for Glycosylation of Secondary Alcohols: The donor (1.0 eq, co-evaporated with toluene) was dissolved in dry DCM under nitrogen and stirred over fresh flame-dried molecular sieves 3A, after which DMF (16 equiv.) was added to the solution. The solution was cooled to –78 °C, after which TfOH (1.0 equiv.) was added. After 30 min, the pre-activation was complete as indicated by TLC-analysis. Acceptor (0.7 equiv.) was added to the solution and the mixture was placed in an ice bath. The reaction was stirred at 0 °C until TLC-analysis showed complete conversion of the acceptor. The reaction was quenched with Et_3N, filtered and concentrated in vacuo. The products were purified by size exclusion and silica gel column chromatography.

Standard Procedure B for Glycosylation of Secondary Alcohols: A mixture of donor (1.0 equiv.), acceptor (0.7 equiv.) (donor and acceptor co-evaporated with toluene three times), DMF (6 equiv.) in dry DCM were stirred over fresh flame-dried molecular sieves 3A under nitrogen. The solution was cooled to –78 °C, after which TfOH (1.0 equiv.) was added. After 30 min, the mixture was placed in an ice bath. The reaction was stirred at 0 °C until TLC-analysis showed complete conversion of the acceptor. The reaction was quenched with Et_3N, filtered and concentrated in vacuo. The products were purified by size exclusion and silica gel column chromatography.

Standard Procedure C for the Glycosylation of Primary Alcohols: A mixture of donor (1.0 equiv.), acceptor (0.7 equiv.) (donor and acceptor co-evaporated with toluene three times), Ph_3P=O (6 equiv.) in dry DCM were stirred over fresh flame-dried molecular sieves 3A under nitrogen. Then TMSI (1.0 equiv.) was added slowly in the mixture. The reaction was stirred at room temperature until TLC-analysis indicated the reaction to be complete. The solution was diluted and the reaction quenched with saturated $Na_2S_2O_3$. The organic phase was washed with water and brine, dried with anhydrous $MgSO_4$, filtered and concentrated in vacuo. The products were purified by size exclusion and silica gel column chromatography.

Standard Procedure D for Deprotection of the Nap Protecting Group: The starting material (1 equiv.) was dissolved in DCM/H_2O (10:1, 0.1 M). DDQ (1.1 equiv.) was added to the mixture. The reaction stirred until TLC-analysis indicated full consumption of the starting material (± 2 h). Then the mixture was diluted with DCM and the reaction quenched with saturated $Na_2S_2O_3$. The organic phase was washed with water and brine, dried with anhydrous $MgSO_4$, filtered and concentrated in vacuo. The product was purified by silica gel column chromatography.

Experimental Procedures and Characterization Data of Products: For the synthesis procedure and data of known compounds **6**, **8** see reference 5. We used "a", "b", "c", "d", "e", "f", "g", and "h" to specify the H-1 and C-13 NMR signals of sugar rings from the "reducing" to the "non-reducing" end and "°" to specify the H-1 and C-13 NMR signals of the spacer.

Phenyl 2,4,6-Tri-*O*-benzyl-3-*O*-(naphthalen-2-ylmethyl)-1-thio-β-D-glucopyranoside (5): $[\alpha]_D^{20}$ = +8.1, *c* = 1, $CHCl_3$. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.81–7.70 (m, 4 H, aromatic *H*), 7.61–7.59 (m, 2 H, aromatic *H*), 7.46–7.16 (m, 21 H, aromatic *H*), 5.05 (d, *J* = 11.2 Hz, 1 H, C*H*H), 4.99 (d, *J* = 11.2 Hz, 1 H, CH*H*), 4.91 (d, *J* = 10.8 Hz, 1 H, CH*H*), 4.85 (d, *J* = 10.8 Hz, 1 H, CH*H*), 4.75 (d, *J* = 10.8 Hz, 1 H, CH*H*), 4.69 (d, *J* = 9.6 Hz, 1 H, 1-H), 4.61 (bd, 2 H, C*H*H), 4.54 (d, *J* = 12.0 Hz, 1 H, C*H*H), 3.81–3.67 (m, 4 H), 3.57–3.51 (m, 2 H) ppm. ^{13}C-APT ($CDCl_3$, 100 MHz,): δ = 137.97, 137.73, 135.56, 133.52, 133.01, 132.65 (aromatic *C*), 131.62, 128.62, 128.14, 128.06, 127.91, 127.88, 127.63, 127.61, 127.57, 127.51, 127.38, 127.28, 127.14, 126.18, 125.78, 125.59, 125.55 (aromatic *C*H), 87.15 (C-1), 86.45, 80.53, 78.79, 77.49, 75.55 (PhCH$_2$), 75.16 (PhCH$_2$), 74.78 (PhCH$_2$), 73.11 (PhCH$_2$), 68.69 (C-6) ppm. HR-MS: Calculated for $C_{44}H_{42}O_5S$ [M + Na]$^+$: 705.2645, found 705.2657.

2,4,6-Tri-*O*-benzyl-3-*O*-(naphthalen-2-ylmethyl)-α/β-D-glucopyranosyl *N*-Phenyltrifluoroacetimidate (3): Compound **5** (9.5 g, 13.9 mmol) was dissolved in acetone/H_2O (10:1, 140 mL). *N*-Iodosuccinimide (NIS) (6.2 g, 27.6 mmol) was added in one portion and the reaction was stirred at room temperature for 2 h. The solution was diluted with DCM and the reaction was quenched with saturated aqueous $Na_2S_2O_3$. Then the organic layer was washed with water and brine. The organic layer was dried with anhydrous $MgSO_4$, filtered and concentrated in vacuo, and the product purified by column chromatography [pentane/ethyl acetate (EA) = 3:1]. The lactol (7.4 g, 90 % yield) was obtained as a white solid. Next, the lactol (7.4 g, 12.5 mmol) was dissolved in acetone (120 mL). Cs_2CO_3 (6.1 g, 18.7 mmol) and 2,2,2-trifluoro-*N*-phenylacetimidoyl chloride (3.0 mL, 18.7 mmol) were added to the solution respectively. The reaction was stirred overnight, then quenched with Et_3N, filtered and concentrated in vacuo. The product was purified by column chromatography (pentane/EA = 40:1–20:1). Compound **3** (9.1 g, 95 % yield, α:β = 1:1.2, pentane/EA = 10:1, R_f = 0.45–0.55) was obtained as yellow syrup. ^1H NMR ($CDCl_3$, 500 MHz, 60 °C): δ = 7.79–6.72 (m, aromatic *H*), 6.47 (br. s, 1 H, H-1α), 5.60 (br. s, 1 H, H-1β), 5.11–4.74 (m, CH*H*), 4.61–4.48 (m, CH*H*), 4.08 (t, *J* = 9.0 Hz, 1 H, H-α), 3.97 (bd, 1 H, H-α), 3.78–3.68 (m), 3.40 (br. s, 1 H). ^{13}C-APT ($CDCl_3$, 125 MHz, 60 °C): δ = 143.97, 143.76, 138.48, 138.39, 138.38, 138.27, 138.65, 138.15, 136.45, 136.20, 133.69, 133.65, 133.29 (aromatic *C*), 129.52, 128.84, 128.63, 128.59, 128.54, 128.51, 128.21, 128.18, 128.12, 128.11, 128.00, 127.95, 127.85, 127.78, 126.69, 126.56, 126.51, 126.19, 126.18, 126.13, 125.99, 125.93, 124.47, 124.32, 120.77, 119.70, 119.63 (aromatic *C*H), 116.50 (q, *C*F$_3$), 97.69, 93.94, 84.77, 81.85, 81.29, 79.76, 77.67, 77.40, 76.09, 75.89, 75.69, 75.34, 75.11, 75.09, 73.78, 73.69, 73.60, 73.56, 68.73, 68.71 ppm.

Phenyl 2,4,6-Tri-*O*-benzyl-1-thio-β-D-glucopyranoside (9): The reaction was carried out according to the general procedure D, using **5** (235 mg, 0.35 mmol, 0.1 M in DCM/H_2O) and DDQ (89 mg, 0.39 mmol). The product was purified by silica gel column chromatography (pentane/EA = 15:1). Compound **9** (168 mg, 87 % yield, pentane/EA = 8:1, R_f = 0.44) was obtained as a colorless syrup. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.60–7.56 (m, 2 H, aromatic *H*), 7.41–7.22 (m, 18 H, aromatic *H*), 4.95 (d, *J* = 11.2 Hz, 1 H, C*H*H), 4.78 (d, *J* = 11.2 Hz, 1 H, CH*H*), 4.68–4.59 (m, 4 H, 3 C*H*H, 1-H), 4.54 (d, *J* = 11.6 Hz, 1 H, C*H*H), 3.81–3.70 (m, 3 H, 6-H, 3-H), 3.56–3.46 (m, 2 H, 4-H, 5-H), 3.37 (dd, J_1 = 8.8, J_2 = 9.6 Hz, 1 H, 2-H), 2.42 (d, *J* = 2.4 Hz, 1 H, O*H*) ppm. ^{13}C-APT ($CDCl_3$, 100 MHz): δ = 138.35, 138.33, 138.19, 133.94 (aromatic *C*), 131.89, 129.05, 128.73, 128.62, 128.48, 128.35, 128.20, 128.08, 128.00, 127.84, 127.72, 127.57 (aromatic *C*H), 87.18 (C-1), 80.70 (C-2), 878.91, 78.75, 77.48 (C-4), 75.25 (PhCH$_2$), 74.77 (PhCH$_2$), 73.55 (PhCH$_2$), 68.17 (C-6) ppm.

Phenyl 2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-1-thio-β-D-glucopyranoside (10): The reaction was carried out according to the standard procedure B, using **6** (330 mg, 0.46 mmol), **9** (168 mg, 0.31 mmol, 0.1 M in DCM), DMF (580 µL, 7.38 mmol) and TfOH (41 µL, 0.46 mmol). The reaction was stirred at −78–0 °C until TLC-analysis showed complete conversion of the acceptor. The reaction was quenched with Et_3N, filtered and concentrated in vacuo. The product was purified by size exclusion chromatography (DCM/MeOH = 1:1). Compound **10** (301 mg, 91 % yield, α:β > 20:1, pentane/EA = 8:1, R_f = 0.46) was obtained as a colorless syrup. $[\alpha]_D^{20}$ = +31.0, *c* = 1, $CHCl_3$. IR (neat): $\tilde{\nu}$ = 696, 745, 1028, 1071, 1090, 1361, 1454, 1497, 2862, 2910, 3030, 3063 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 7.60–7.57 (m, 2 H, aromatic *H*), 7.45 (bd, 2 H, aromatic *H*), 7.37–7.01 (m, 36 H, aromatic *H*), 5.68 (d, *J* = 3.5 Hz, 1 H, 1-Hb), 4.97–4.89 (m, 4 H, 3 C*H*H), 4.81 (d, *J* = 10.5 Hz, 1 H, C*H*H), 4.72–4.48 (m, 8 H, 1-Ha, 7 C*H*H), 4.40 (d, *J* = 10.5 Hz, 1 H, C*H*H), 4.11 (d, *J* = 11.5 Hz, 1 H, C*H*H), 4.14 (bd, 1 H), 4.10–4.04 (m, 2 H), 3.85 (t, *J* = 9.5 Hz, 1 H), 3.75–3.65 (m, 3 H), 3.59–3.56 (m, 2 H, 6-H), 3.50–3.48 (m, 2 H), 3.33–3.27 (m, 2 H) ppm. ^{13}C-APT ($CDCl_3$, 125 MHz): δ = 138.72, 138.58, 138.27, 138.14, 137.95, 137.80, 137.55, 133.81 (aromatic *C*), 131.81, 129.01, 128.87, 128.37, 128.33, 128.28, 128.25, 128.12, 127.94, 127.91, 127.76, 127.72, 127.60, 127.58, 127.53, 127.46, 127.39, 126.77 (aromatic *C*H), 97.30 (C-1b), 87.66 (C-1a), 79.42, 79.25, 78.95, 78.84, 78.20, 75.55, 75.20, 75.12, 73.91, 73.36, 73.31, 70.01, 68.73, 68.01 ppm.

2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-1-thio-β-D-glucopyranosyl *N*-Phenyltrifluoroacetimidate (11): Compound **10** (265 mg, 0.25 mmol) was dissolved in acetone/H_2O (10:1, 3.3 mL). *N*-Iodosuccinimide (NIS) (112 mg, 0.50 mmol) was added in one portion and the reaction was stirred at room temperature for 2 h. The solution was diluted with DCM and the reaction was quenched with saturated aqueous $Na_2S_2O_3$, then the organic layer was washed with water and brine. The organic layer was dried with anhydrous $MgSO_4$, filtered and concentrated in vacuo, and the product purified by column chromatography (pentane/EA = 2:1). Compound Di-glucose alcohol (185 mg, 76 % yield) was obtained as a white solid. Next, compound Di-glucose alcohol (185 mg, 0.19 mmol) was dissolved in acetone (2 mL). Cs_2CO_3 (93 mg, 0.28 mmol) and 2,2,2-trifluoro-*N*-phenylacetimidoyl chloride (50 µL, 0.28 mmol) were added to the solution respectively. The reaction stirred overnight, then quenched with Et_3N, filtered and concentrated in vacuo. The product was purified by column chromatography (pentane/EA = 50:1–20:1). Compound **11** (170 mg, 80 % yield, α:β = 1.1:1) was obtained as yellow syrup. ^1H NMR ($CDCl_3$, 500 MHz, 60 °C): δ = 7.31–7.01 (m, aromatic *H*), 6.77 (d, *J* = 13.0 Hz, 2 H), 6.68 (d, *J* = 13.0 Hz, 2 H), 6.48 (br. s, 1 Hα), 5.65 (br. s, 1 H), 5.55 (d, *J* = 3.5 Hz, 1 H), 5.51 (d, *J* = 3.5 Hz, 1 H), 4.99 (d, *J* = 11.5 Hz, 1 H), 4.92–4.68 (m, CH*H*), 4.61–4.42 (m, CH*H*), 4.36–4.28 (m), 4.18 (bd, 1 H), 4.10–3.43 (m) ppm. ^{13}C-APT ($CDCl_3$, 125 MHz, 60 °C): δ = 143.83, 143.73, 139.16, 139.07, 139.02, 138.91, 138.53, 138.49, 138.48, 138.41, 138.38, 138.37, 138.33, 138.20, 137.88, 137.71 (aromatic *C*), 128.81, 128.77, 128.52, 128.50, 128.46, 128.41, 128.38, 128.37, 128.35, 128.29, 128.22, 128.02, 128.00, 127.94, 127.90, 127.86, 127.83, 127.79, 127.72, 127.64, 127.62, 127.60, 127.58, 127.53, 127.48, 127.24, 127.16, 124.45, 124.31, 119.70, 119.61 (aromatic *C*H), 115.31 (q, *C*F$_3$), 97.78, 97.71, 97.61, 93.35, 82.49, 82.33, 80.31, 80.25, 79.83, 78.57, 78.55, 78.35, 78.20, 78.18, 76.24, 75.66, 75.56, 75.51, 75.10, 74.94, 74.73, 74.04, 73.89, 73.85, 73.77, 73.71,

73.64, 73.60, 73.46, 73.18, 70.90, 70.74, 68.96, 68.87, 68.63, 68.55 ppm.

Methyl 2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,3,6-tri-*O*-benzyl-α-D-glucopyranoside (12): The reaction was carried out according to the standard procedure B, using **11** (78 mg, 0.07 mmol), **7** (33 mg, 0.07 mmol, 0.1 M in DCM), DMF (87 μL, 1.12 mmol) and TfOH (7 μL, 0.07 mmol). The reaction was stirred at –78–0 °C until TLC-analysis showed complete conversion of the acceptor. The reaction was quenched with Et_3N, filtered and concentrated in vacuo. The product was purified by size exclusion chromatography (DCM/MeOH = 1:1). Compound **12** (65 mg, 63 % yield, α:β > 20:1, pentane/EA = 4:1, R_f = 0.50) was obtained as a colorless syrup. $[\alpha]_D^{20}$ = +60.1, *c* = 1 (10 mg), $CHCl_3$. IR (neat): $\tilde{\nu}$ = 696, 735, 1028, 1072, 1157, 1362, 1454, 1497, 2864, 2916, 3031 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.39–6.87 (m, 50 H, aromatic *H*), 5.66 (bd, *J* = 3.6 Hz, 2 H, 2 1-H), 4.90–4.21 (m, 24 H), 4.08 (d, *J* = 12.0 Hz, 1 H, C*H*H), 4.01 (t, *J* = 9.6 Hz, 1 H), 3.85 (t, *J* = 9.6 Hz, 1 H), 3.74–3.48 (m, 10 H), 3.30–3.24 (m, 5 H) ppm. ^{13}C-APT ($CDCl_3$, 100 MHz): δ = 138.90, 138.71, 138.43, 138.18, 138.09, 137.90, 137.86 (aromatic *C*), 128.77, 128.51, 128.49, 128.39, 128.38, 128.32, 128.29, 128.24, 128.22, 128.18, 128.17, 128.11, 128.04, 127.99, 127.91, 127.83, 127.69, 127.62, 127.52, 127.44, 127.32, 127.13, 126.67 (aromatic *C*H), 97.70 (C-1), 97.43 (C-1), 96.21 (C-1), 82.35, 79.55, 79.24, 79.00, 78.90, 78.59, 78.12, 77.05, 75.76, 75.50, 74.71, 73.64, 73.60, 73.52, 73.37, 73.28, 73.09, 70.11 (C-5), 69.98 (C-5), 69.15 (C-a), 68.62 (2 C-6), 68.416 (C-6), 55.16 (CH_3) ppm.

3-Azidopropyl 2,3,4,6-Tetra-*O*-benzyl-α-D-glucopyranoside (13): The reaction was carried out according to the standard procedure C, using **3** (2500 mg, 3.28 mmol, 0.1 M in DCM), 3-aminopropanol (399 μL, 4.27 mmol), $Ph_3P{=}O$ (5.48 g, 19.7 mmol) and TMSI (516 μL, 3.61 mmol). The product was purified by silica gel column chromatography (pentane/EA = 15:1). Compound **13** (1716 mg, 80 % yield, α:β = 10:1, pentane/EA = 4:1, R_f = 0.74) was obtained as a colorless syrup. IR (neat): $\tilde{\nu}$ = 697, 736, 820, 1072, 1085, 1363, 1454, 2095, 2868, 2917, 3030 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.81–7.70 (m, 4 H, aromatic *H*), 7.48–7.39 (m, 3 H, aromatic *H*), 7.36–7.21 (m, 13 H, aromatic *H*), 7.13–7.10 (m, 4 H, aromatic *H*), 5.13 (d, *J* = 11.2 Hz, 1 H, C*H*H), 4.97 (d, *J* = 11.2 Hz, 1 H, CH*H*), 4.85 (d, *J* = 10.4 Hz, 1 H, CH*H*), 4.78 (d, *J* = 8.4 Hz, 1 H, CH*H*), 4.77 (s, 1 H, 1-H), 4.65 (d, *J* = 8.4 Hz, 1 H, C*H*H), 4.60 (d, *J* = 12.0 Hz, 1 H, C*H*H), 4.49 (d, *J* = 10.4 Hz, 1 H, C*H*H), 4.47 (d, *J* = 12.0 Hz, 1 H, C*H*H), 4.03 (t, *J* = 9.2 Hz, 1 H, 3-H), 3.78–3.57 (m, 6 H), 3.48–3.30 (m, 3 H), 1.94–1.79 (m, 2 H, 2°-H) ppm. ^{13}C-APT ($CDCl_3$, 100 MHz): δ = 138.21, 138.15, 137.85, 136.32, 133.34, 132.92 (aromatic *C*), 128.47, 128.37, 128.06, 128.00, 127.92, 127.88, 127.71, 127.66 (aromatic *C*H), 97.18 (C-1), 82.04 (C-3), 80.07 (C-2), 77.65 (C-4), 75.69, 75.11, 73.47, 73.24 (4 PhCH_2), 70.34 (C-5), 68.42 (C-6), 64.72 (C-1°), 48.26 (C-3°), 28.83 (C-2°) ppm. HR-MS: Calculated for $C_{41}H_{43}O_6N_3$ [M + Na^+]: 696.3044, found 696.3059.

3-Azidopropyl 2,4,6-Tri-*O*-benzyl-α-D-glucopyranoside (14): The reaction was carried out according to the general procedure D, using **13** (1.67 g, 2.53 mmol, 0.1 M in DCM/H_2O) and DDQ (632 mg, 2.78 mmol). The product was purified by silica gel column chromatography (pentane/EA = 8:1). Compound **14** (1.08 g, 80 % yield, pentane/EA = 4:1, R_f = 0.33) was obtained as a colorless syrup. $[\alpha]_D^{20}$ = +69.8, *c* = 1 (10 mg), $CHCl_3$. IR (neat): $\tilde{\nu}$ = 697, 734, 1028, 1070, 1154, 1453, 2096, 2869, 2918, 3031 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.31–7.19 (m, 15 H, aromatic *H*), 4.86 (d, *J* = 11.2 Hz, 1 H, C*H*H), 4.74 (s, *J* = 3.6 Hz, 1 H, 1-H), 4.68 (d, *J* = 12.0 Hz, 1 H, C*H*H), 4.60 (d, *J* = 12.0 Hz, 1 H, C*H*H), 4.59 (d, *J* = 12.4 Hz, 1 H, C*H*H), 4.51 (d, *J* = 11.2 Hz, 1 H, C*H*H), 4.46 (d, *J* = 12.4 Hz, 1 H, C*H*H), 4.06 (t, *J* = 9.2 Hz, 1 H, 3-H), 3.72–3.53 (m, 5 H), 3.41–3.28 (m, 4 H), 2.69 (br. s, 1 H, O*H*), 1.86–1.75 (m, 2 H, 2°-H) ppm. ^{13}C-APT ($CDCl_3$, 100 MHz): δ = 138.33, 137.99, 137.86 (aromatic *C*), 128.53, 128.35, 128.01, 127.91, 127.68 (aromatic *C*H), 96.58 (C-1), 79.62 (C-3), 77.35 (C-2), 74.61, 73.43 (2 PhCH_2), 73.42 (C-4), 72.92 (PhCH_2), 69.94 (C-5), 68.41 (C-6), 64.55 (C-1°), 48.17 (C-3°), 28.80 (C-2°) ppm. HR-MS: Calculated for $C_{30}H_{35}O_6N_3$ [M + Na^+]: 556.2418, found 556.2423.

3-Azidopropyl 2,4,6-Tri-*O*-benzyl-3-*O*-(naphthalen-2-ylmethyl)-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranoside (15): The reaction was carried out according to the standard procedure A at –78–0 °C. The donor **3** (2.18 g, 2.86 mmol, co-evaporated with toluene 3 times) was dissolved in dry DCM (24 mL) under nitrogen and stirred over fresh flame-dried molecular sieves 3A, after which DMF (2.50 mL, 31.7 mmol) was added to the solution. The solution was cooled to –78 °C, after which TfOH (173 μL, 1.96 mmol) was added. After 30 min, the pre-activation was complete as indicated by TLC-analysis. Acceptor **14** (910 mg, 1.70 mmol, dissolved in a little DCM and washed 3 times with DCM, totally 10 mL) was added to the solution and the mixture was placed in an ice bath. The reaction was stirred at 0 °C until TLC-analysis showed complete conversion of the acceptor. The reaction was quenched with Et_3N, filtered and concentrated in vacuo. The product was purified by size exclusion chromatography (DCM/MeOH = 1:1). Crude compound **15** (α:β > 20:1, pentane/EA = 4:1, R_f = 0.62) was obtained as a colorless syrup. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.79–7.64 (m, 4 H, aromatic *H*), 7.43–7.01 (m, 34 H, aromatic *H*), 5.62 (d, *J* = 3.6 Hz, 1 H, 1-Hb), 5.07 (d, *J* = 11.2 Hz, 1 H, C*H*H), 5.00 (d, *J* = 11.2 Hz, 1 H, C*H*H), 4.97 (d, *J* = 11.6 Hz, 1 H, C*H*H), 4.84–4.80 (bt, 2 H, 1-Ha, C*H*H), 4.72–4.57 (m, 5 H, 5 C*H*H), 4.51–4.32 (m, 6 H, 5 C*H*H, 5-H), 4.28 (dd, J_1 = 8.4, J_2 = 9.2 Hz, 1 H, 3-Ha), 4.12 (t, *J* = 9.2 Hz, 1 H, 3-Hb), 3.84–3.56 (m, 8 H), 3.50–3.44 (m, 2 H, 6-H), 3.41–3.30 (m, 3 H, 1°-H_a, 3°-H), 1.85–1.79 (m, 2 H, 2°-H) ppm. ^{13}C-APT ($CDCl_3$, 100 MHz): δ = 138.70, 138.36, 138.07, 138.04, 137.96, 137.85, 136.32, 133.33 (aromatic *C*), 128.55, 128.40, 128.30, 128.24, 128.23, 128.11, 128.04, 128.00, 127.95, 127.93, 127.87, 127.76, 127.67, 127.65, 127.61, 127.47, 127.43, 127.29, 126.89, 126.57, 126.52, 126.48, 126.40, 126.12, 126.08, 125.98, 125.95, 125.74 (aromatic *C*H), 97.40 (C-1b), 96.64 (C-1a), 82.33 (C-3b), 79.70 (C-2b), 78.77 (C-2a), 78.57 (C-4a), 78.20 (C-4b), 76.47 (C-3a), 75.51, 74.83, 73.67, 73.63, 73.52, 73.34, 73.01 (7 CH_2), 70.10 (C-5), 69.98 (C-5), 68.43 (C-6), 68.31 (C-6), 64.59 (C-1°), 48.28 (C-3°), 28.85 (C-2°) ppm.

3-Azidopropyl 2,4,6-Tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranoside (16): The reaction was carried out according to the general procedure D, using crude **15** (2 g, 1.81 mmol, 0.1 M in DCM/H_2O) and DDQ (451 mg, 1.99 mmol). The product was purified by silica gel column chromatography (pentane/EA = 8:1–5:1). Compound **15** (1.53 g, 90 % yield with two steps, pentane/EA = 4:1, R_f = 0.32) was obtained as a colorless syrup. $[\alpha]_D^{20}$ = +78.6, *c* = 1, $CHCl_3$. IR (neat): $\tilde{\nu}$ = 696, 734, 1028, 1070, 1089, 1149, 1453, 1497, 2097, 2867, 2918, 3030 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.31–7.07 (m, 30 H, aromatic *H*), 5.59 (d, *J* = 3.6 Hz, 1 H, 1-Hb), 4.91 (d, *J* = 11.6 Hz, 1 H, C*H*H), 4.78 (d, *J* = 3.6 Hz, 1 H, 1-Ha), 4.71 (d, *J* = 11.2 Hz, 1 H, C*H*H), 4.62–4.55 (m, 4 H, 4 C*H*H), 4.48–4.40 (m, 5 H, 5 C*H*H), 4.32 (d, *J* = 12.0 Hz, 1 H, C*H*H), 4.28–4.23 (m, 2 H, 3-Ha, 5-Hb), 4.13 (t, *J* = 11.6 Hz, 1 H, 3-Hb), 3.79–3.51 (m, 7 H), 3.46–3.29 (m, 6 H), 2.34 (d, *J* = 1.6 Hz, 1 H, O*H*), 1.84–1.78 (m, 2 H, 2°-H) ppm. ^{13}C-APT ($CDCl_3$, 100 MHz): δ = 138.67, 138.27, 137.94, 137.84, 137.82 (aromatic *C*), 128.48, 128.34, 128.32, 128.23, 128.20, 128.10, 127.89, 127.85, 127.79, 127.69, 127.67, 127.57, 127.47, 127.25, 126.72 (aromatic *C*H), 96.86 (C-1b), 96.58 (C-1a), 79.14 (C-2b), 78.65 (C-2a), 78.53 (C-4a), 77.90 (C-4b), 76.28 (C-3a), 74.33 (CH_2), 73.68 (C-3b), 73.51, 73.43, 73.27, 73.09, 72.95 (5 CH_2), 69.92 (C-5a), 69.46 (C-5b), 68.32 (C-6), 68.18 (C-6), 64.50 (C-1°), 48.19

(C-3°), 28.77 (C-2°) ppm. HR-MS: Calculated for $C_{57}H_{63}O_{11}N_3$ [M + Na^+]: 988.4355, found 988.4391.

3-Azidopropyl 2,4,6-Tri-*O*-benzyl-3-*O*-(naphthalen-2-ylmethyl)-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranoside (17): The reaction was carried out according to the standard procedure A at –78–0 °C. The donor **3** (1.78 g, 2.34 mmol, co-evaporated with toluene 3 times) was dissolved in dry DCM (20 mL) under nitrogen and stirred over fresh flame-dried molecular sieves 3A, after which DMF (2.94 mL, 37.4 mmol) was added to the solution. The solution was cooled to –78 °C, after which TfOH (210 µL, 2.38 mmol) was added. After 30 min, the pre-activation was complete as indicated by TLC-analysis. Acceptor **16** (1.47 g, 1.52 mmol, dissolved in a little DCM and washed 3 times with DCM, totally 10 mL) was added to the solution and the mixture was placed in an ice bath. The reaction was stirred at 0 °C until TLC-analysis showed complete conversion of the acceptor. The reaction was quenched with Et_3N, filtered and concentrated in vacuo. The product was purified by size exclusion chromatography (DCM/MeOH = 1:1). Compound **17** (1.81 g, 81 %, α:β > 20:1, pentane/EA = 4:1, R_f = 0.58) was obtained as a colorless syrup. $[\alpha]_D^{20}$ = +56.8, *c* = 1, $CHCl_3$. IR (neat): $\tilde{\nu}$ = 697, 750, 1028, 1072, 1088, 1155, 1364, 1454, 2096, 2865, 2927, 3030 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.77–7.62 (m, 4 H, aromatic *H*), 7.47–7.06 (m, 42 H, aromatic *H*), 6.99–6.94 (m, 4 H, aromatic *H*), 6.90–6.88 (m, 2 H, aromatic *H*), 5.69 (d, *J* = 3.6 Hz, 1 H, 1-Hc), 5.65 (d, *J* = 3.6 Hz, 1 H, 1-Hb), 5.01 (d, *J* = 11.2 Hz, 1 H, C*H*H), 4.94 (d, *J* = 11.2 Hz, 1 H, C*H*H), 4.90 (d, *J* = 12.0 Hz, 1 H, C*H*H), 4.81–4.23 (m, 21 H, 1-Ha, 3-Ha, 3-Hb, 2 5-H, 16 C*H*H), 4.12–4.05 (m, 2 H, 1 C*H*H, 3-Hc), 3.85 (t, *J* = 9.6 Hz, 1 H, 4-H), 3.78–3.45 (m, 11 H), 3.39–3.24 (m, 5 H), 1.87–1.77 (m, 2 H, 2°-H) ppm. ^{13}C-APT ($CDCl_3$, 100 MHz): δ = 138.81, 138.61, 138.34, 138.15, 138.08, 138.05, 138.00, 137.83, 137.80, 136.28, 133.30, 132.86 (aromatic *C*), 128.50, 128.42, 128.32, 128.25, 128.21, 128.19, 128.15, 128.11, 128.06, 128.03, 127.96, 127.93, 127.87, 127.82, 127.77, 127.63, 127.55, 127.47, 127.37, 127.34, 127.23, 127.01, 126.60, 126.46, 126.04, 125.90, 125.70 (aromatic *C*H), 97.35 (C-1c), 96.60 (C-1a), 96.25 (C-1b), 82.18 (C-3c), 79.52, 79.21, 78.95, 78.91, 78.47, 78.01, 76.99 (C-3a), 75.75 (C-3b), 75.43, 74.62, 73.55, 73.46, 73.36, 73.23, 73.19, 73.15, 73.07, 69.93 (C-5b), 69.88 (C-5c), 69.54 (C-5a), 68.50 (C-6), 68.46 (C-6), 68.32 (C-6), 64.60 (C-1°), 48.29 (C-3°), 28.83 (C-2°) ppm. HR-MS: Calculated for $C_{95}H_{99}O_{16}N_3$ [M + Na^+]: 1560.6918, found 1560.6923.

3-Azidopropyl 2,4,6-Tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranoside (18): The reaction was carried out according to the general procedure D, using **17** (1.40 g, 0.95 mmol, 0.1 M in DCM/H_2O) and DDQ (238 mg, 1.05 mmol). The product was purified by silica gel column chromatography (pentane/EA = 8:1–5:1). Compound **18** (1.27 g, 95 % yield, pentane/EA = 4:1, R_f = 0.32) was obtained as a colorless syrup. $[\alpha]_D^{20}$ = +80.0, *c* = 1, $CHCl_3$. IR (neat): $\tilde{\nu}$ = 696, 735, 1029, 1071, 1089, 1153, 1454, 1497, 2095, 2868, 2921, 3030 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.33–7.07 (m, 39 H, aromatic *H*), 7.02–7.00 (m, 4 H, aromatic *H*), 6.88–6.86 (m, 2 H, aromatic *H*), 5.67 (d, *J* = 3.6 Hz, 1 H, 1-Hc), 5.62 (d, *J* = 3.6 Hz, 1 H, 1-Hb), 4.84–4.75 (m, 3 H, 2 C*H*H, 1-Ha), 4.68 (d, *J* = 11.2 Hz, 1 H, C*H*H), 4.81–4.05 (m, 20 H, 3-Hc, 3-Ha, 3-Hb, 2 5-H, 15 C*H*H), 3.82–3.18 (m, 17 H), 2.25 (s, 1 H, O*H*), 1.87–1.77 (m, 2 H, 2°-H) ppm. ^{13}C-APT ($CDCl_3$, 100 MHz): δ = 138.79, 138.57, 138.28, 138.03, 137.96, 137.79, 137.76 (aromatic *C*), 128.44, 128.40, 128.36, 128.30, 128.24, 128.18, 128.10, 128.02, 127.86, 127.79, 127.76, 127.73, 127.67, 127.61, 127.59, 127.53, 127.33, 127.30, 127.21, 127.10, 126.88, 126.51 (aromatic *C*H), 96.87 (C-1c), 96.56 (C-1a), 96.23 (C-1b), 79.19, 79.06, 78.87, 78.83, 78.49, 77.83, 76.82, 76.68, 74.18, 73.57, 73.54, 73.38, 73.34, 73.24, 73.09, 73.03, 73.01, 69.82 (C-5), 69.53 (C-5), 69.34 (C-5), 68.48 (C-6), 68.40 (C-6), 68.27 (C-6), 64.58 (C-1°), 48.28 (C-3°), 28.81 (C-2°) ppm. HR-MS: Calculated for $C_{84}H_{91}O_{16}N_3$ [M + Na^+]: 1420.6292, found 1420.6320.

3-Azidopropyl 2,4,6-Tri-*O*-benzyl-3-*O*-(naphthalen-2-ylmethyl)-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranoside (19): The reaction was carried out according to the standard procedure A at –78–0 °C. The donor **3** (1.10 g, 1.45 mmol, co-evaporated with toluene 3 times) was dissolved in dry DCM (10 mL) under nitrogen and stirred over fresh flame-dried molecular sieves 3A, after which DMF (1.83 mL, 23.2 mmol) was added to the solution. The solution was cooled to –78 °C, after which TfOH (128 µL, 1.45 mmol) was added. After 30 min, the pre-activation was complete as indicated by TLC-analysis. Acceptor **18** (1.01 g, 0.73 mmol, dissolved in a little DCM and washed 3 times with DCM, totally 5 mL) was added to the solution and the mixture was placed in an ice bath. The reaction was stirred at 0 °C until TLC-analysis showed complete conversion of the acceptor. The reaction was quenched with Et_3N, filtered and concentrated in vacuo. The product was purified by size exclusion chromatography (DCM/MeOH = 1:1). Compound **19** (1.20 g, 84 %, α:β > 20:1, pentane/EA = 4:1, R_f = 0.46) was obtained as a colorless syrup. $[\alpha]_D^{20}$ = +70.4, *c* = 1, $CHCl_3$. IR (neat): $\tilde{\nu}$ = 697, 734, 1028, 1071, 1087, 1155, 1363, 1454, 1497, 2093, 2867, 2924, 3031 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.62–6.80 (m, 67 H, aromatic *H*), 5.71 (d, *J* = 3.6 Hz, 1 H, 1-H), 5.61 (bd, 2 H, 2 1-H), 4.95 (d, *J* = 11.2 Hz, 1 H, C*H*H), 4.87 (d, *J* = 11.2 Hz, 1 H, C*H*H), 4.80–4.18 (m, 30 H), 4.11 (d, *J* = 12.0 Hz, 1 H, C*H*H), 3.99 (t, *J* = 9.6 Hz, 1 H, 3-H), 3.83–3.22 (m, 21 H), 1.85–1.80 (m, 2 H, 2°-H) ppm. ^{13}C-APT ($CDCl_3$, 100 MHz): δ = 138.91, 138.71, 138.56, 138.32, 138.21, 138.12, 138.07, 138.05, 137.91, 137.89, 137.84, 136.35, 133.34, 132.91 (aromatic *C*), 128.52, 128.50, 128.48, 128.39, 128.32, 128.27, 128.25, 128.22, 128.12, 128.08, 128.04, 127.99, 127.97, 127.95, 127.87, 127.75, 127.68, 127.61, 127.59, 127.41, 127.38, 127.19, 127.13, 127.03, 126.92, 126.50, 126.45, 126.11, 125.92, 125.73 (aromatic *C*H), 97.33 (C-1), 96.63 (C-1), 96.33 (C-1), 96.12 (C-1), 82.21, 79.48, 79.36, 78.98, 78.95, 78.82, 78.72, 78.45, 78.04, 77.01, 75.64, 75.45, 74.56, 73.64, 73.50, 73.46, 73.37, 73.28, 73.13, 72.87, 72.72, 69.85 (C-5), 69.72 (C-5), 69.59 (2 C-5), 68.53 (3 C-6), 68.40 (C-6), 64.66 (C-1°), 48.37 (C-3°), 28.91 (C-2°) ppm. HR-MS: Calculated for $C_{122}H_{127}O_{21}N_3$ [M + Na^+]: 1992.8854, found 1992.8793.

3-Azidopropyl 2,4,6-Tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranoside (20): The reaction was carried out according to the general procedure D, using **19** (1.20 g, 0.61 mmol, 0.1 M in DCM/H_2O) and DDQ (152 mg, 0.67 mmol). The product was purified by silica gel column chromatography (pentane/EA = 5:1). Compound **20** (890 mg, 80 % yield, pentane/EA = 4:1, R_f = 0.21) was obtained as a colorless syrup. $[\alpha]_D^{20}$ = +87.8, *c* = 1, $CHCl_3$. IR (neat): $\tilde{\nu}$ = 697, 735, 1028, 1091, 1154, 1364, 1453, 1497, 2098, 2866, 2924, 3029 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.35–6.78 (m, 60 H, aromatic *H*), 5.68 (d, *J* = 3.6 Hz, 1 H, 1-Hc), 5.61 (d, *J* = 3.6 Hz, 1 H, 1-Hb), 5.60 (d, *J* = 3.6 Hz, 1 H, 1-Hd), 4.79–4.76 (m, 2 H, 1-Ha, C*H*H), 4.72–4.18 (m, 28 H), 4.11 (bd, 2 H, 2 C*H*H), 4.00 (t, *J* = 9.2 Hz, 1 H, 3-Hd), 3.83–3.20 (m, 21 H), 2.19 (s, 1 H, O*H*), 1.86–1.80 (m, 2 H, 2°-H) ppm. ^{13}C-APT ($CDCl_3$, 100 MHz): δ = 138.85, 138.67, 138.49, 138.31, 138.09, 138.01, 137.88, 137.87, 137.82 (aromatic *C*), 128.40, 128.38, 128.23, 128.19, 128.18, 128.04, 127.99, 127.94, 127.84, 127.78, 127.75, 127.70, 127.65, 127.60, 127.48, 127.41, 127.33, 127.30, 127.28, 127.17, 127.08, 127.01, 126.96, 126.56, 126.40, 126.34 (aromatic *C*H), 96.86 (C-1d), 96.60 (C-1a), 96.29 (C-1b), 96.11 (C-1c), 79.35, 79.00, 78.91, 78.72, 78.68, 78.45, 77.85, 76.97, 75.53, 75.35, 74.11, 73.62, 73.56,

73.49, 73.40, 73.25, 73.11, 73.09, 72.95, 72.88, 72.67, 69.69 (C-5), 69.58 (C-5), 69.54 (C-5), 69.23 (C-5), 68.53 (C-6), 68.48 (2 C-6), 68.34 (C-6), 64.65 (C-1°), 48.35 (C-3°), 28.89 (C-2°) ppm. HR-MS: Calculated for $C_{111}H_{119}O_{21}N_3$ [M + Na^+]: 1852.8228, found 1852.8154.

3-Azidopropyl 2,4,6-Tri-*O*-benzyl-3-*O*-(naphthalen-2-ylmethyl)-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranoside (21): The reaction was carried out according to the standard procedure A at –78–0 °C. The donor **3** (587 mg, 0.77 mmol, co-evaporated with toluene 3 times) was dissolved in dry DCM (4 mL) under nitrogen and stirred over fresh flame-dried molecular sieves 3A, after which DMF (970 mL, 12.3 mmol) was added to the solution. The solution was cooled to –78 °C, after which TfOH (68 µL, 0.77 mmol) was added. After 30 min, the pre-activation was complete as indicated by TLC-analysis. Acceptor **20** (705 mg, 0.38 mmol, dissolved in a little DCM and washed 3 times with DCM, totally 4 mL) was added to the solution and the mixture was placed in an ice bath. The reaction was stirred at 0 °C until TLC-analysis showed complete conversion of the acceptor. The reaction was quenched with Et_3N, filtered and concentrated in vacuo. The product was purified by size exclusion chromatography (DCM/MeOH = 1:1). Compound **21** (750 mg, 81 %, α:β > 20:1, pentane/EA = 4:1, R_f = 0.36) was obtained as a colorless syrup. $[\alpha]_D^{20}$ = +77.8, *c* = 1, $CHCl_3$. IR (neat): $\tilde{\nu}$ = 697, 734, 1029, 1071, 1089, 1154, 1364, 1454, 1497, 2097, 2864, 2923, 3030 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.75–6.64 (m, 82 H, aromatic *H*), 5.69 (d, *J* = 3.2 Hz, 1 H, 1-Hc), 5.65 (d, *J* = 3.2 Hz, 1 H, 1-Hd), 5.61 (d, *J* = 3.6 Hz, 1 H, 1-Hb), 5.57 (d, *J* = 3.2 Hz, 1 H, 1-He), 4.95 (d, *J* = 11.2 Hz, 1 H, C*H*H), 4.86 (d, *J* = 11.2 Hz, 1 H, C*H*H), 4.80–4.09 (m, 39 H), 3.97 (t, *J* = 9.6 Hz, 1 H, 3-He), 3.83–3.20 (m, 25 H), 1.88–1.81 (m, 2 H, 2°-H) ppm. ^{13}C-APT ($CDCl_3$, 100 MHz): δ = 139.28, 138.87, 138.68, 138.50, 135.35, 138.26, 138.17, 138.06, 138.03, 137.99, 137.90, 137.84, 137.77, 136.31, 133.29, 132.84 (aromatic *C*), 128.48, 128.44, 128.42, 128.33, 128.27, 128.25, 128.20, 128.14, 128.06, 127.98, 127.95, 127.93, 127.90, 127.80, 127.72, 127.70, 127.63, 127.61 127.55, 127.50, 127.33, 127.29, 127.26, 127.19, 127.10, 127.00, 126.77, 126.51, 126.44, 126.34, 126.22, 126.06, 126.86, 125.66 (aromatic *C*H), 97.21 (C-1e), 96.54 (C-1a), 96.26 (C-1b), 96.11 (C-1c), 95.99 (C-1d), 82.10 (C-3e), 79.40, 79.20, 79.13, 78.91, 78.86, 78.78, 78.56, 78.51, 78.42, 77.98, 76.87, 75.53, 75.36, 75.06, 74.46, 75.58, 73.44, 73.31, 73.09, 72.99, 72.93, 72.70, 72.64, 72.51, 69.73 (C-5), 69.55 (C-5), 69.49 (2 C-5), 69.36 (C-5), 68.48 (2 C-6), 68.43 (2 C-6), 68.33 (C-6), 64.60 (C-1°), 48.29 (C-3°), 28.85 (C-2°) ppm. HR-MS: Calculated for $C_{149}H_{155}O_{26}N_3$ [M + H^+]: 2403.0972, found 2403.0933.

3-Azidopropyl 2,4,6-Tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranoside (22): The reaction was carried out according to the general procedure D, using **21** (520 mg, 0.22 mmol, 0.1 M in DCM/H_2O) and DDQ (54 mg, 0.24 mmol). The product was purified by silica gel column chromatography (Tol/EA = 20:1). Compound **22** (370 mg, 75 % yield, pentane/EA = 4:1, R_f = 0.20) was obtained as a colorless syrup. $[\alpha]_D^{20}$ = +98.6, *c* = 1, $CHCl_3$. IR (neat): $\tilde{\nu}$ = 696, 734, 1028, 1071, 1088, 1153, 1453, 1497, 2092, 2864, 2923, 3031 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.34–6.60 (m, 75 H, aromatic *H*), 5.69 (d, *J* = 3.6 Hz, 1 H, 1-Hc), 5.61 (bt, 2 H, 1-Hb, 1-Hd), 5.54 (d, *J* = 3.6 Hz, 1 H, 1-He), 4.79 (d, *J* = 3.6 Hz, 1 H, 1-Ha), 4.76 (d, *J* = 11.6 Hz, 1 H, C*H*H), 4.69–4.07 (m, 37 H), 3.98 (t, *J* = 9.6 Hz, 1 H, 3-He), 3.83–3.17 (m, 25 H), 2.17 (s, 1 H, O*H*), 1.87–1.80 (m, 2 H, 2°-H) ppm. ^{13}C-APT ($CDCl_3$, 100 MHz): δ = 138.85, 138.67, 138.52, 138.47, 138.28, 138.06, 138.01, 137.91, 137.86, 137.85, 137.79 (aromatic *C*), 128.49, 128.47, 128.45, 128.36, 128.29, 128.23, 128.23, 128.16, 128.11, 128.09, 128.05, 127.99, 127.96, 127.92, 127.82 127.80, 127.73, 127.67, 127.63, 127.57, 127.44, 127.29, 127.20, 127.01, 126.85, 126.79, 126.49, 126.27, 126.15 (aromatic *C*H), 96.79 (C-1e), 96.56 (C-1a), 96.28 (C-1), 96.10 (C-1), 96.01 (C-1), 79.22, 79.15, 78.95, 78.87, 78.77, 78.55, 78.44, 77.81, 76.87, 75.50, 75.02, 74.04, 73.61, 73.49 (C-3e), 73.47, 73.42, 73.38, 73.35, 73.30, 73.09, 73.01, 72.83, 72.69, 72.50, 69.57 (C-5), 69.48 (2 C-5), 69.37 (C-5), 69.14 (C-5), 68.51 (2 C-6), 68.44 (2 C-6), 68.31 (C-6), 64.63 (C-1°), 48.33 (C-3°), 28.88 (C-2°) ppm. HR-MS: Calculated for $C_{138}H_{147}O_{26}N_3$ [M + H^+]: 2263.0346, found 2263.0291.

3-Azidopropyl 2,4,6-Tri-*O*-benzyl-3-*O*-(naphthalen-2-ylmethyl)-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranoside (23): The reaction was carried out according to the standard procedure A at –78–0 °C. The donor **3** (310 mg, 0.41 mmol, co-evaporated with toluene 3 times) was dissolved in dry DCM (1 mL) under nitrogen and stirred over fresh flame-dried molecular sieves 3A, after which DMF (512 µL, 6.56 mmol) was added to the solution. The solution was cooled to –78 °C, after which TfOH (36 µL, 0.41 mmol) was added. After 30 min, the pre-activation was complete as indicated by TLC-analysis. Acceptor **22** (260 mg, 0.12 mmol, dissolved in a little DCM and washed 3 times with DCM, totally 1 mL) was added to the solution and the mixture was placed in an ice bath. The reaction was stirred at 0 °C until TLC-analysis showed complete conversion of the acceptor. The reaction was quenched with Et_3N, filtered and concentrated in vacuo. The product was purified by size exclusion chromatography (DCM/MeOH = 1:1). Compound **23** (293 mg, 90 %, α:β > 20:1, pentane/EA = 4:1, R_f = 0.32) was obtained as a colorless syrup. $[\alpha]_D^{20}$ = +78.7, *c* = 1, $CHCl_3$. IR (neat): $\tilde{\nu}$ = 697, 734, 1029, 1072, 1089, 1154, 1363, 1454, 1497, (m2097), 2863, 2926, 3029 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.75–6.58 (m, 97 H, aromatic *H*), 5.68 (d, *J* = 3.2 Hz, 1 H, 1-H), 5.63–5.60 (m, 3 H, 3 1-H), 5.55 (d, *J* = 3.2 Hz, 1 H, 1-Hf), 4.94 (d, *J* = 11.2 Hz, 1 H, C*H*H), 4.86 (d, *J* = 11.2 Hz, 1 H, C*H*H), 4.79 (d, *J* = 3.6 Hz, 1 H, 1-Ha), 4.76–4.08 (m, 46 H), 3.96 (t, *J* = 9.6 Hz, 1 H, 3-Hf), 3.83–3.18 (m, 29 H), 1.85–1.81 (m, 2 H, 2°-H) ppm. ^{13}C-APT ($CDCl_3$, 100 MHz): δ = 138.87, 138.68, 138.51, 138.48, 135.35, 138.26, 138.17, 138.03, 137.87, 137.84, 137.82, 137.77, 136.31, 133.28, 132.83 (aromatic *C*), 128.48, 128.42, 128.33, 128.28, 128.26, 128.25, 128.21, 128.15, 128.14, 128.07, 128.06, 128.05, 128.01, 128.99, 127.96, 127.92, 127.89, 127.79, 127.75, 127.70, 127.64, 127.61, 127.54, 127.49, 127.32, 127.27, 127.24, 127.02, 126.83, 126.74, 126.69, 126.45, 126.43, 126.31, 126.29, 126.13, 126.05, 125.96, 125.85, 125.66 (aromatic *C*H), 97.19 (C-1f), 96.53 (C-1a), 96.23 (C-1), 96.08 (C-1), 96.02 (C-1), 95.93 (C-1), 82.10 (C-3f), 79.38, 79.20, 79.08, 79.03, 78.87, 78.74, 78.48, 78.39, 77.96, 76.91, 75.52, 75.44, 75.35, 75.13, 75.02, 74.44, 73.58, 73.44, 73.37, 73.30, 73.28, 73.00, 72.83, 72.73, 72.66, 72.52, 72.36, 69.69 (C-5), 69.53 (C-5), 69.46 (C-5), 69.41 (C-5), 69.32 (C-5), 69.15 (C-5), 68.46 (5 C-6), 68.29 (C-6), 64.60 (C-1°), 48.29 (C-3°), 28.84 (C-2°) ppm. MALDI-TOF: Calculated for $C_{16}H_{83}O_3N_3$ [M + H^+]: 2835.3, found 2832.9.

3-Azidopropyl 2,4,6-Tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranoside (24): The reaction was carried out according to the general procedure D, using **21** (480 mg, 0.17 mmol, 0.1 M in DCM/H_2O) and DDQ (46 mg, 0.20 mmol). The product was purified by silica gel column chromatography (Tol/EA = 20:1). Compound **24** (320 mg, 70 % yield, Tol/EA = 9:1, R_f = 0.26) was obtained as a colorless syrup. $[\alpha]_D^{20}$ = +79.4, *c* = 1, $CHCl_3$. IR

(neat): $\tilde{\nu}$ = 697, 735, 1029, 1070, 1089, 1155, 1364, 1453, 1497, 2098, 2868, 2923, 3029 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 7.33–6.56 (m, 90 H, aromatic *H*), 5.68 (d, *J* = 3.5 Hz, 1 H, 1-H), 5.62 (bt, 2 H, 2 1-H), 5.57 (d, *J* = 4.0 Hz, 1 H, 1-H), 5.53 (d, *J* = 3.5 Hz, 1 H, 1-Hf), 4.78 (bt, 2 H, 1-Ha, C*H*H), 4.69–4.06 (m, 45 H), 3.97 (t, *J* = 9.5 Hz, 1 H, 3-Hf), 3.82–3.16 (m, 29 H), 2.16 (br. s, 1 H, O*H*), 1.87–1.78 (m, 2 H, 2°-H) ppm. ^{13}C-APT ($CDCl_3$, 125 MHz): δ = 138.86, 138.68, 138.53, 138.50, 138.29, 138.04, 138.02, 137.90, 137.87, 137.81 (aromatic *C*), 128.46, 128.43, 128.42, 128.33, 128.28, 128.26, 128.20, 128.13, 128.08, 128.03, 128.01, 127.96, 127.89, 127.78, 127.76, 127.69, 127.62, 127.59, 127.53, 127.42, 127.28, 127.22, 127.21, 127.04, 126.84, 126.81, 126.70, 126.49, 126.29, 126.28, 126.10 (aromatic *C*H), 96.75 (C-1f), 96.55 (C-1a), 96.23 (C-1), 96.07 (C-1), 95.99 (C-1), 95.93 (C-1), 79.23, 79.13, 79.07, 78.97, 78.92, 78.52, 78.44, 78.37, 77.82, 75.46, 75.13, 74.99, 74.00, 73.59, 73.48, 73.45, 73.38, 73.35, 73.32, 73.28, 73.01, 72.83, 72.79, 72.66, 72.58, 72.51, 72.37, 69.57 (C-5), 69.49 (C-5), 69.43 (C-5), 69.35 (C-5), 69.18 (C-5), 69.13 (C-5), 68.49 (5 C-6), 68.31 (C-6), 64.63 (C-1°), 48.31 (C-3°), 28.86 (C-2°) ppm. MALDI-TOF: Calculated for $C_{16}H_{83}O_3N_3$ [M + K^+]: 2733.2, found 2732.9.

3-Azidopropyl 2,4,6-Tri-*O*-benzyl-3-*O*-(naphthalen-2-ylmethyl)-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranoside (25): The reaction was carried out according to the standard procedure B, using **3** (275 mg, 0.36 mmol), **24** (330 mg, 0.12 mmol, 0.05 M in DCM), DMF (455 µL, 5.78 mmol) and TfOH (32 µL, 0.36 mmol). The reaction was stirred at –78–0 °C until TLC-analysis showed complete conversion of the acceptor. The reaction was quenched with Et_3N, filtered and concentrated in vacuo. The product was purified by size exclusion chromatography (DCM/MeOH = 1:1). Compound **25** (360 mg, 90 % yield, α:β > 20:1, pentane/EA = 4:1, R_f = 0.24) was obtained as a colorless syrup. $[\alpha]_D^{20}$ = +83.8, *c* = 1, $CHCl_3$. IR (neat): $\tilde{\nu}$ = 697, 734, 1029, 1071, 1089, 1155, 1454, 2096, 2858, 2924, 3031 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 7.74–6.58 (m, 112 H, aromatic *H*), 5.69 (d, *J* = 3.5 Hz, 1 H, 1-H), 5.63–5.55 (m, 5 H, 5 1-H), 4.93 (d, *J* = 11.5 Hz, 1 H, C*H*H), 4.85 (d, *J* = 11.5 Hz, 1 H, C*H*H), 4.79–4.09 (m, 55 H), 3.96 (t, *J* = 9.0 Hz, 1 H, 3-H g), 3.83–3.19 (m, 33 H), 1.85–1.79 (m, 2 H, 2°-H) ppm. ^{13}C-APT ($CDCl_3$, 125 MHz): δ = 138.84, 138.65, 138.49, 138.46, 128.23, 128.15, 138.03, 138.00, 137.84, 137.80, 137.74, 136.29, 133.24, 132.79 (aromatic *C*), 128.39, 128.38, 128.36, 128.27, 128.22, 128.21, 128.19, 128.14, 128.08, 128.03, 127.98, 127.96, 127.90, 127.86, 127.83, 127.72, 127.70, 127.64, 127.55, 127.48, 127.42, 127.32, 127.27, 127.21, 127.17, 127.04, 126.97, 126.78, 126.59, 126.64, 126.45, 126.37, 126.28, 126.24, 126.20, 126.11, 126.00, 125.79, 125.60 (aromatic *C*H), 97.11 (C-1 g), 96.48 (C-1a), 96.17 (C-1), 95.99 (C-1), 95.92 (2 C-1), 95.87 (C-1), 82.03 (C-3 g), 79.40, 79.17, 79.05, 79.00, 78.85, 78.75, 78.47, 78.38, 78.32, 77.95, 76.83, 75.46, 75.42, 75.28, 75.05, 74.94, 74.39, 73.52, 73.38, 73.31, 73.25, 73.22, 72.98, 72.93, 72.75, 72.61, 72.47, 72.35, 72.27, 69.67 (C-5), 69.52 (C-5), 69.43 (C-5), 69.36 (C-5), 69.30 (C-5), 69.11 (C-5), 69.06 (C-5), 68.44 (6 C-6), 68.29 (C-6), 64.56 (C-1°), 48.22 (C-3°), 28.79 (C-2°) ppm. MALDI-TOF: Calculated for $C_{16}H_{83}O_3N_3$ [M + K^+]: 3305.4, found 3306.1.

3-Azidopropyl 2,4,6-Tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranoside (26): The reaction was carried out according to the general procedure D, using **25** (300 mg, 0.09 mmol, 0.05 M in DCM/H_2O) and DDQ (23 mg, 0.10 mmol). The product was purified by silica gel column chromatography (Tol/EA = 20:1). Compound **26** (145 mg, 51 % yield, Tol/EA = 9:1, R_f = 0.25) was obtained as a colorless syrup. $[\alpha]_D^{20}$ = +129.9, *c* = 1, $CHCl_3$. IR (neat): $\tilde{\nu}$ = 696, 733, 1028, 1071, 1089, 1153, 1364, 1454, 1497, 2096, 2863, 2926, 3031 cm^{-1}. ^1H NMR ($CDCl_3$, 500 MHz): δ = 7.33–6.54 (m, 105 H, aromatic *H*), 5.68 (d, *J* = 3.5 Hz, 1 H, 1-H), 5.61 (bt, 2 H, 2 1-H), 5.58 (d, *J* = 3.5 Hz, 1 H, 1-H), 5.55 (d, *J* = 3.5 Hz, 1 H, 1-H), 5.52 (d, *J* = 3.5 Hz, 1 H, 1-H g), 4.78 (bt, 2 H, 1-Ha, C*H*H), 4.69–4.06 (m, 53 H), 3.96 (t, *J* = 9.5 Hz, 1 H, 3-Hg), 3.82–3.15 (m, 33 H), 2.15 (br. s, 1 H, O*H*), 1.84–1.80 (m, 2 H, 2°-H) ppm. ^{13}C-APT ($CDCl_3$, 125 MHz): δ = 138.88, 138.70, 138.55, 138.52, 138.29, 138.07, 138.04, 138.03, 137.96, 137.88, 137.82 (aromatic *C*), 128.47, 128.45, 128.43, 128.34, 128.29, 128.27, 128.21, 128.16, 128.14, 128.10, 128.05, 128.02, 127.97, 127.94, 127.89, 127.80, 127.77, 127.71, 127.63, 127.60, 127.54, 127.43, 127.39, 127.33, 127.30, 127.21, 127.14, 127.12, 127.05, 126.84, 126.81, 126.77, 126.68, 126.61, 126.51, 126.29, 126.28, 126.23, 126.08 (aromatic *C*H), 96.75 (C-1f), 96.56 (C-1a), 96.23 (C-1), 96.05 (C-1), 96.00 (C-1), 95.95 (2 C-1), 79.24, 79.10, 79.06, 78.97, 78.44, 78.41, 78.30, 77.82, 75.48, 75.11, 74.97, 74.01, 73.60, 73.46, 73.39, 73.36, 73.34, 73.29, 73.02, 72.79, 72.74, 72.65, 72.56, 72.51, 72.38, 72.31, 69.58 (C-5), 69.49 (C-5), 69.40 (C-5), 69.36 (C-5), 69.16 (C-5), 69.12 (2 C-5), 68.49 (6 C-6), 68.31 (C-6), 64.64 (C-1°), 48.33 (C-3°), 28.88 (C-2°) ppm. MALDI-TOF: Calculated for $C_{16}H_{83}O_3N_3$ [M + K^+]: 3165.4, found 3165.0.

3-Azidopropyl 2,4,6-Tri-*O*-benzyl-3-*O*-(naphthalen-2-ylmethyl)-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-α-D-glucopyranoside (27): The reaction was carried out according to the standard procedure B, using **3** (110 mg, 0.14 mmol), **24** (120 mg, 0.038 mmol, 0.025 M in DCM), DMF (182 µL, 2.31 mmol) and TfOH (13 µL, 0.15 mmol). The reaction was stirred at –78–0 °C until TLC-analysis showed complete conversion of the acceptor. The reaction was quenched with Et_3N, filtered and concentrated in vacuo. The product was purified by size exclusion chromatography (DCM/MeOH = 1:1). Compound **27** (140 mg, 98 % yield, α:β > 20:1, pentane/EA = 4:1, R_f = 0.17) was obtained as a colorless syrup. $[\alpha]_D^{20}$ = +97.1, *c* = 1, $CHCl_3$. IR (neat): $\tilde{\nu}$ = 697, 734, 1028, 1071, 1154, 1208, 1364, 1455, 1497, 2097, 2864, 2925, 3030 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 7.75–6.56 (m, 127 H, aromatic *H*), 5.69 (d, *J* = 3.5 Hz, 1 H, 1-H), 5.63–5.54 (m, 6 H, 6 1-H), 4.93 (d, *J* = 11.2 Hz, 1 H, C*H*H), 4.85 (d, *J* = 11.2 Hz, 1 H, C*H*H), 4.809–4.08 (m, 63 H), 3.95 (t, *J* = 9.2 Hz, 1 H, 3-Hh), 3.83–3.15 (m, 37 H), 1.84–1.80 (m, 2 H, 2°-H) ppm. ^{13}C-APT ($CDCl_3$, 100 MHz): δ = 139.17, 138.87, 138.67, 138.52, 138.49, 138.48, 138.34, 138.25, 138.17, 138.06, 138.02, 137.86, 137.80, 137.76, 136.32, 133.27, 132.82 (aromatic *C*), 128.47, 128.44, 128.42, 128.33, 128.27, 128.21, 128.17, 128.12, 128.07, 128.06, 128.03, 127.99, 127.95, 127.89, 127.80, 127.74, 127.71, 127.61, 127.53, 127.47, 127.38, 127.31, 127.27, 127.22, 127.16, 127.08, 127.04, 127.01, 126.83, 126.72, 126.46, 126.42, 126.28, 126.25, 126.17, 126.09, 126.05, 125.84, 125.65 (aromatic *C*H), 97.17 (C-1), 96.528 (C-1), 96.22 (C-1), 96.03 (C-1), 95.95 (4 C-1), 82.09 (C-3 h), 79.37, 79.19, 79.02, 78.86, 78.73, 78.44, 78.39, 78.28, 77.95, 76.89, 75.51, 75.43, 75.35, 75.05, 74.97, 74.84, 74.43, 73.58, 73.44, 73.37, 73.30, 73.26, 72.99, 72.77, 72.64, 72.57, 72.46, 72.29, 69.67 (C-5), 69.52 (C-5), 69.45 (C-5), 69.35 (C-5), 69.31 (C-5), 69.10 (C-5), 69.03 (2 C-5), 68.41 (7 C-6), 68.29 (C-6), 64.60 (C-1°), 48.29 (C-3°), 28.84 (C-2°) ppm. MALDI-TOF: Calculated for $C_{16}H_{83}O_3N_3$ [M + K^+]: 3737.6, found 3737.5.

3-Aminopropyl α-D-Glucopyranosyl-(1→3)-α-D-glucopyranosyl-(1→3)-α-D-glucopyranosyl-(1→3)-α-D-glucopyranosyl-(1→3)-α-

D-glucopyranosyl-(1→3)-α-D-glucopyranosyl-(1→3)-α-D-glucopyranosyl-(1→3)-α-D-glucopyranoside (2): Compound **27** (20 mg, 0.0054 mmol) was dissolved in THF/H_2O/*t*BuOH (2 mL/2 mL/1 mL) before a catalytic amount of $Pd(OH)_2$/C was added. The reaction mixture was stirred for 2 d under a H_2 atmosphere (40 bar), filtered and concentrated in vacuo. A white powder was obtained, which was purified by gel filtration (HW-40, 0.15*M* NH_4OAc in H_2O) to yield **2** (2.9 mg, 40 %). ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 5.35 (bd, 7 H, 7 1-H), 4.91 (d, J = 3.5 Hz, 1 H, 1-H), 4.02–3.53 (m, 53 H), 3.41 (t, J = 10.0 Hz, 1 H), 3.14–3.00 (m, 2 H), 1.96–1.91 (m, 2 H) ppm. ^{13}C-APT ($CDCl_3$, 125 MHz): δ = 99.39, 99.23, 98.47, 79.94, 79.89, 79.75, 72.89, 71.84, 71.73, 71.62, 70.39, 69.93, 69.86, 69.74, 69.51, 65.91, 60.51, 60.39, 60.30, 37.88, 27.60 ppm. HR-MS: Calculated for $C_{51}H_{89}O_{41}N_3$ [M + H^+]: 1372.4983, found 1372.5005.

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[1] a) C. S. Bennett, *Selective Glycosylations: Synthetic Methods and Catalysts*, Wiley VCH Verlag GmbH, **2017**; b) S. S. Nigudkar, A. V. Demchenko, *Chem. Sci.* **2015**, *6*, 2687–2704; c) X. Zhu, R. R. Schmidt, *Angew. Chem. Int. Ed.* **2009**, *48*, 1900–1934; *Angew. Chem.* **2009**, *121*, 1932; d) P. Peng, R. R. Schmidt, *Acc. Chem. Res.* **2017**, *50*, 1171–1183.

[2] a) C. W. Andrews, R. Rodebaugh, B. Fraser-Reid, *J. Org. Chem.* **1996**, *61*, 5280–5289; b) N. L. Douglas, S. V. Ley, U. Lucking, S. L. Warriner, *J. Chem. Soc., Perkin Trans. 1* **1998**, 51–66; c) Z. Zhang, I. R. Ollmann, X.-S. Ye, R. Wischnat, T. Baasov, C.-H. Wong, *J. Am. Chem. Soc.* **1999**, *121*, 734–753; d) J. D. C. Codee, R. E. J. N. Litjens, L. J. van den Bos, H. S. Overkleeft, G. A. van der Marel, *Chem. Soc. Rev.* **2005**, *34*, 769–782; e) B. Fraser-Reid, J. C. López in *Armed–Disarmed Effects in Carbohydrate Chemistry: History, Synthetic and Mechanistic Studies, Vol* (Eds.: B. Fraser-Reid, J. Cristóbal López), Springer Berlin Heidelberg, Berlin, Heidelberg, **2011**, pp. 1–29.

[3] a) S. van der Vorm, J. M. A. Van Hengst, M. Bakker, H. S. Overkleeft, G. A. van der Marel, J. D. C. Codée, *Angew. Chem. Int. Ed.* **2018**, *57*, 8240–8244; *Angew. Chem.* **2018**, *130*, 8372–8376; b) B. Hagen, S. Ali, H. S. Overkleeft, G. A. van der Marel, J. D. C. Codée, *J. Org. Chem.* **2017**, *82*, 848–868; c) S. van der Vorm, T. Hansen, H. S. Overkleeft, G. A. van der Marel, J. D. C. Codee, *Chem. Sci.* **2017**, *8*, 1867–1875.

[4] a) B. A. Garcia, D. Y. Gin, *J. Am. Chem. Soc.* **2000**, *122*, 4269–4279; b) S. N. Lam, J. Gervay-Hague, *Org. Lett.* **2002**, *4*, 2039–2042; c) S. N. Lam, J. Gervay-Hague, *Carbohydr. Res.* **2002**, *337*, 1953–1965; d) T. Mukaiyama, Y. Kobashi, *Chem. Lett.* **2004**, *33*, 10–11; e) Y. Kobashi, T. Mukaiyama, *Chem. Lett.* **2004**, *33*, 874–875; f) D. Crich, W. Li, *Org. Lett.* **2006**, *8*, 959–962; g) J. Park, S. Kawatkar, J.-H. Kim, G.-J. Boons, *Org. Lett.* **2007**, *9*, 1959–1962; h) T. Nokami, A. Shibuya, S. Manabe, Y. Ito, J. Yoshida, *Chem. Eur. J.* **2009**, *15*, 2252–2255; i) A.-H. A. Chu, S. H. Nguyen, J. A. Sisel, A. Minciunescu, C. S. Bennett, *Org. Lett.* **2013**, *15*, 2566–2569; j) L. Yang, Q. Qin, X.-S. Ye, *Asian J. Org. Chem.* **2013**, *2*, 30–49; k) S.-R. Lu, Y.-H. Lai, J.-H. Chen, C.-Y. Liu, K.-K. T. Mong, *Angew. Chem. Int. Ed.* **2011**, *50*, 7315–7320; *Angew. Chem.* **2011**, *123*, 7453; l) C.-Y. I. Liu, S. Mulani, K.-K. T. Mong, *Adv. Synth. Catal.* **2012**, *354*, 3299–3310; m) R. U. Lemieux, H. Driguez, *J. Am. Chem. Soc.* **1975**, *97*, 4056–4062; n) R. U. Lemieux, H. Driguez, *J. Am. Chem. Soc.* **1975**, *97*, 4063–4068; o) A. B. Ingle, C.-S. Chao, W.-C. Hung, K.-K. T. Mong, *Org. Lett.* **2013**, *15*, 5290–5293; p) S. K. Mulani, W.-C. Hung, A. B. Ingle, K.-S. Shiau, K.-K. T. Mong, *Org. Biomol. Chem.* **2014**, *12*, 1184–1197.

[5] L. Wang, H. S. Overkleeft, G. A. van der Marel, J. D. C. Codée, *J. Am. Chem. Soc.* **2018**, *140*, 4632–4638.

[6] a) P. Zhang, L. Zhang, S. Cheng, *Biosci. Biotechnol. Biochem.* **1999**, *63*, 1197–1202; b) M. Nishimura, *Physiol. Mol. Plant Pathol.* **2016**, *95*, 14–19.

[7] a) D. Maubon, S. Park, M. Tanguy, M. Huerre, C. Schmitt, M. C. Prévost, D. S. Perlin, J. P. Latgé, A. Beauvais, *Fungal Genet. Biol.* **2006**, *43*, 366–375; b) T. Fontaine, A. Beauvais, C. Loussert, B. Thevenard, C. C. Fulgsang, N. Ohno, C. Clavaud, M.-C. Prevost, J.-P. Latgé, *Fungal Genet. Biol.* **2010**, *47*, 707–712; c) A. Yoshimi, K. Miyazawa, K. Abe, *J. Fungi* **2017**, *3*, 63; d) S. Puanglek, S. Kimura, T. Iwata, *Carbohydr. Polym.* **2017**, *169*, 245–254.

[8] a) B. S. Komarova, M. V. Orekhova, Y. E. Tsvetkov, R. Beau, V. Aimanianda, J.-P. Latge, N. E. Nifantiev, *Chem. Eur. J.* **2015**, *21*, 1029–1035; b) A. A. Karelin, Y. E. Tsvetkov, N. E. Nifantiev, *Russ. Chem. Rev.* **2017**, *86*, 1073–1126.

[9] a) M. J. Gaunt, J. Yu, J. B. Spencer, *J. Org. Chem.* **1998**, *63*, 4172–4173; b) J. Xia, S. A. Abbas, R. D. Locke, C. F. Piskorz, J. L. Alderfer, K. L. Matta, *Tetrahedron Lett.* **2000**, *41*, 169–173.

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