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Synthesis of Differentially Protected Glucosamine Building Blocks and Their Evaluation as Glycosylating Agents

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The modular assembly of heparin oligosaccharides requires glucosamine building blocks with amine protecting groups for α-selective glycosylations that can be readily removed. The synthesis of *N*-4-nitrobenzensulphonamide (nosyl)- and *N*-2,4-dinitrophenyl (DNP)-protected glucosamine building blocks and their evaluation as glycosylating agents is described. The *N*-nosyl-protected glucosamine building blocks were challenging to prepare and their glycosylations resulted in inseparable mixtures of products. The *N*-DNP-protected glucosamines, however, were readily synthesized and resulted in α-selective couplings to protected L-iduronic acid derivatives.

Keywords Heparin; Oligosaccharides; Carbohydrates; Glycosylation; 4-Nitrobenzenesulphonamide protecting group; 2,4-Dinitrophenyl protecting group

INTRODUCTION

Glycosaminoglycans (GAGs) are a large class of polysaccharides that are found on the cell surface and in the extracellular matrix. GAGs are attached to proteins to form proteoglycans. Heparin and heparan sulfate are the most complex GAGs, a family of molecules that also includes chondroitin sulfate,

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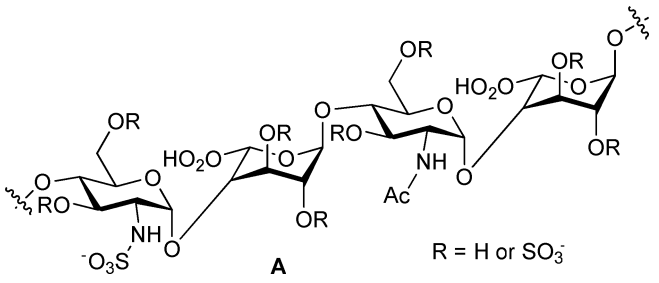


Figure 1: General heparin target structure **A** with differently functionalized amine groups.

keratin sulfate, and dermatan sulfate. The various biological roles of GAGs are dependent on their ability to bind selectively to different growth factors, enzymes, morphogens, cell adhesion molecules, and cytokines.[1] Many aspects of GAG chemistry,[2] biology[1,3] and structure-activity relationships (SARs)[4] have been reviewed.

The unbranched, highly sulfated polysaccharide heparin is composed of disaccharide units consisting of a uronic acid (UA) 1,4-linked to a D-glucosamine (GlcN) unit. L-Iduronic acid (IdoA, 90%) predominates over its C-5-epimer D-glucuronic acid (GlcA, 10%). Typically, a heparin disaccharide contains several sulfate groups: *O*-sulfation occurs at the C-2 hydroxyl and/or C-3 hydroxyl of the uronic acids, as well as at the C-3 hydroxyl and/or C-6 hydroxyl of the amino sugar. Additionally, the glucosamine unit can be *N*-sulfated or *N*-acetylated or, in rare cases, remains unmodified.

The azido group is usually the only group used for masking the amine for the modular assembly of heparin oligosaccharides by chemical means.[2,4a,5] Therefore, the amines generally cannot be differentiated in the final deprotection and functionalization steps,[6] resulting in either an all *N*-acetylated or an all *N*-sulfated oligosaccharide.[7] In order to differentiate the amines and to introduce both *N*-acetate and *N*-sulfate groups in the same oligosaccharide, leading to a structural motive such as **A** (Fig. 1), a second protecting group for the amine is required. This protecting group has to fulfill several requirements:

1. It has to be nonparticipating, in order to yield preferentially the desired α-linked product when coupled to an L-iduronic acid acceptor.
2. It has to be orthogonal to the azido group.
3. It has to be electron withdrawing to lower the basicity of the amine group for compatibility with TMSOTf-catalyzed couplings, and to avoid the formation of an aziridinium intermediate that would lead to 1,2-*trans* glycosylation.

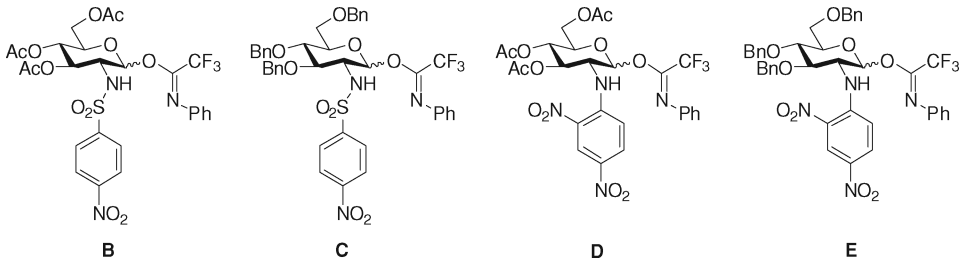


Figure 2: *N*-nosyl-protected (**B**, **C**) and *N*-DNP-protected (**D**, **E**), tri-*O*-acetylated and tri-*O*-benzylated glucosamine *N*-phenyltrifluoroacetimidate glycosylating agents.

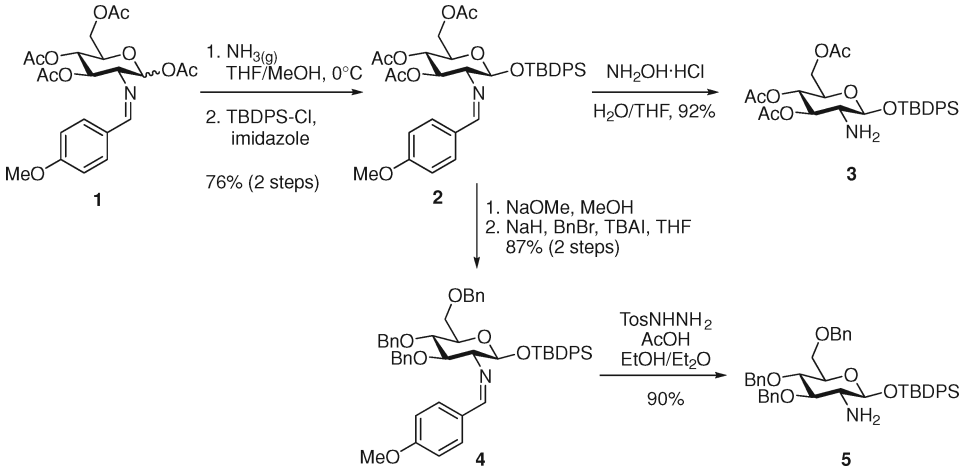
Two possible protecting groups that may meet these criteria were evaluated: *N*-4-nitrobenzensulphonamide (nosyl, Nos)[8] and *N*-2,4-dinitrophenyl (DNP)[9] (Fig. 2).

Both protecting groups have already been applied to the synthesis of oligosaccharides: The *N*-DNP group was used for the protection of glucosamines and was shown to be stable to Königs-Knorr coupling conditions.[9] The *N*-DNP group resists treatment with numerous amines[10] and is compatible with the conditions used for Fmoc- and Lev-cleavage used for the assembly of oligosaccharides.[11] Cleavage of *N*-DNP by basic resin[9d,9f,9g] fits well into the standard deprotection scheme for heparin oligosaccharides.[4a,5c] The *N*-nosyl group was used by Fügedi et al. for the protection of an aza-glycoside and was shown to be stable to TMSOTf-catalyzed couplings.[12] Deprotection of the *N*-nosyl group using PhSH and K_2CO_3 or Cs_2CO_3[8b,8c,8e] renders this group orthogonal to the azido group.[13]

The aim of this study was to evaluate whether *N*-nosyl and *N*-DNP are suitable protecting groups for the amine of glucosamine. Four glycosylating agents **B**-**E** (Fig. 2) were to be synthesized from D-glucosamine to examine their influence on the α/β-selectivity of glycosylation reactions. It is of particular interest to determine whether these protected glucosamine glycosylating agents yield preferentially the desired α-coupling product when glycosylating L-iduronic acid, as observed for C-2 azide glucosamines.[2,5c] Glycosyl *N*-phenyltrifluoroacetimidates were chosen as glycosylating agents, an attractive alternative[14] to the commonly used glycosyl trichloroacetimidates.[15] Tri-*O*-acetylated (**B**, **D**) or tri-*O*-benzylated (**C**, **E**) glucosamines represent disarmed and armed glycosides, respectively.[16]

RESULTS AND DISCUSSION

The synthesis of the glucosamine building blocks started from crystalline, glucosamine acetate **1**[17] that is readily available on a 100-g scale from D-glucosamine hydrochloride (Sch. 1). Selective cleavage of the anomeric acetyl

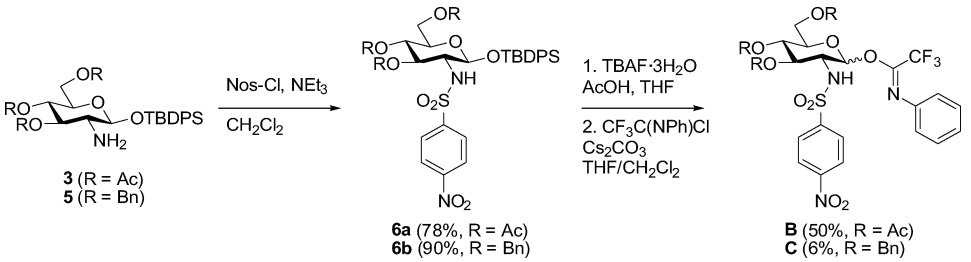


Scheme 1: Synthesis of glucosamines **3** and **5**.

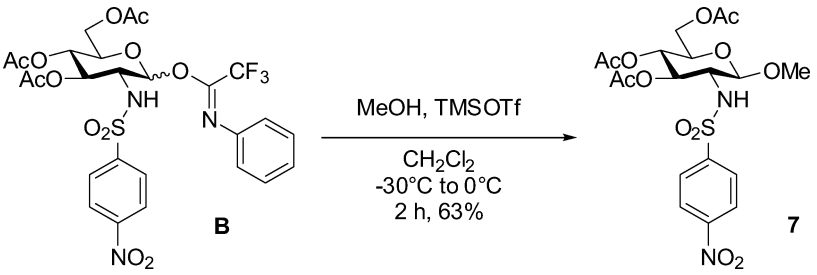
group, using gaseous ammonia,[18] was followed by TBDPS protection of the resulting hemiacetal to afford imine **2**. Hydrolysis of **2** was achieved by treatment with hydroxylamine hydrochloride in THF and water to afford amine **3** in 92% yield. Alternatively, imine **2** was subjected to Zemplén conditions[19] and tri-*O*-benzylated to obtain imine **4** in 87% yield over two steps (Sch. 1). Hydrolysis of the imino group of **4** using *p*-toluenesulfonyl hydrazine and acetic acid in a mixture of diethyl ether and ethanol[20] furnished amine **5** in 90% yield.

The *N*-nosyl-protecting group was installed by reacting amine **3** with 4-nitrobenzenesulfonyl chloride and triethylamine[8c] to afford *N*-nosyl-protected amine **6a** in 78% yield (Sch. 2). Cleavage of the anomeric silyl group using TBAF/acetic acid in THF followed by reaction of the resulting hemiacetal with trifluoro-*N*-phenylacetimidoyl chloride and Cs_2CO_3 in a mixture of CH_2Cl_2 and THF furnished glycosylating agent **B** in 50% yield over two steps.

Following the same reaction path, tri-*O*-benzylated amine **5** was converted into glycosylating agent **C** (Sch. 2). However, the two-step manipulation of the



Scheme 2: Synthesis of *N*-nosyl-protected glycosylating agents **B** and **C**.



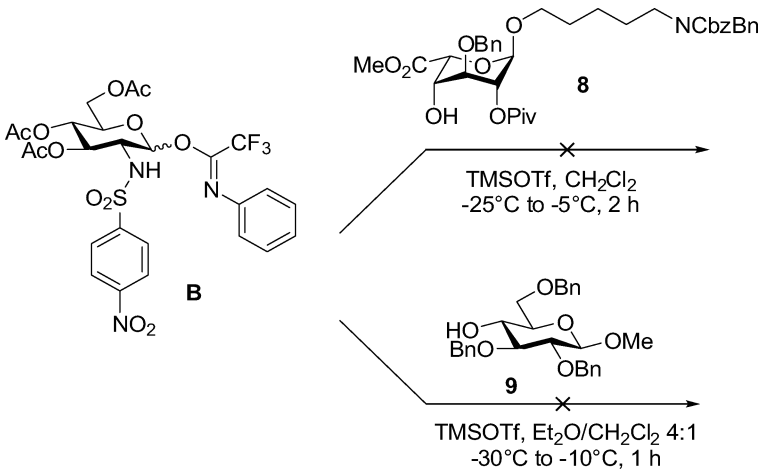
Scheme 3: β-Selective glycosylation of *N*-nosyl-protected glycosylating agent **B**.

anomeric hydroxyl group was found to proceed in only 6% yield due to multiple side reactions. Therefore, it was decided to evaluate solely tri-*O*-acetylated derivative **B** in glycosylation reactions.

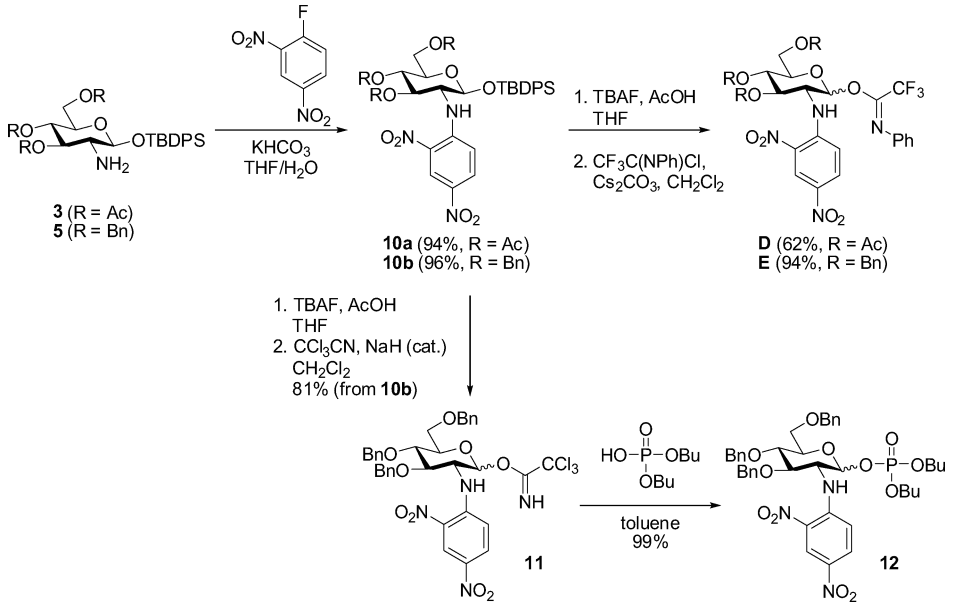
In a first reaction, glycosylating agent **B** was coupled with methanol in CH_2Cl_2 using TMSOTf as activator to yield methyl glycoside **7** exclusively as β-anomer in 63% yield (Sch. 3).

Coupling of glycosylating agent **B** with either linker-equipped[5c,21] L-iduronic acid acceptor **8**[5c] or methyl glycoside **9**[22] resulted in an inseparable mixture of products (Sch. 4). This result was attributed to side reactions involving the *N*-nosyl-protecting group.

The problems observed during the preparation of *N*-nosyl-protected glycosylating agents **B** and **C**, as well as the unselective coupling behavior of tri-*O*-acetyl derivative **B**, may be attributed to the acidic nature of the sulfonamide proton.



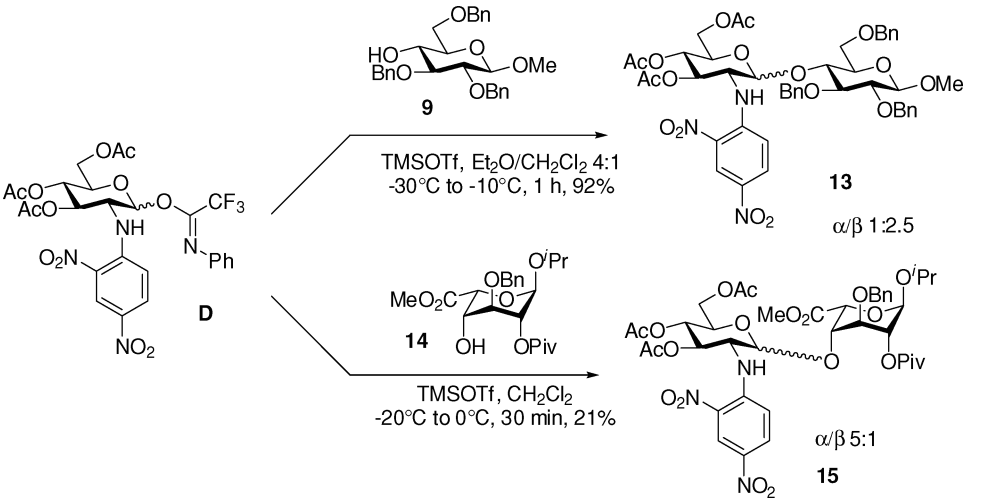
Scheme 4: Glycosylation attempts with *N*-nosyl-protected glycosylating agent **B**.



Scheme 5: Synthesis of *N*-DNP-protected glycosylating agents **D**, **E**, **11,** and **12**.

The *N*-2,4-dinitrophenyl (DNP)-protecting group was investigated next. Amine **3** was protected by nucleophilic aromatic substitution using 1-fluoro-2,4-dinitrobenzene (Sanger's reagent)[23] and $KHCO_3$ as base in THF and H_2O[9] to obtain masked amine **10a** in 94% yield (Sch. 5). *N*-DNP-protected glucosamine **10a** was then converted into glycosylating agent **D** by cleavage of the anomeric silyl group using TBAF/acetic acid in THF followed by reaction of the resulting hemiacetal with trifluoro-*N*-phenylacetimidoyl chloride and Cs_2CO_3 in CH_2Cl_2 (62% yield, two steps). Similarly, tri-*O*-benzylated amine **5** reacted with Sanger's reagent to furnish *N*-DNP-protected **10b** in 96% yield (Sch. 5). Intermediate **10b** was converted to three different glycosylating agents: Cleavage of the anomeric silyl group using TBAF/acetic acid in THF was followed by reaction of the resulting hemiacetal either with trifluoro-*N*-phenylacetimidoyl chloride and Cs_2CO_3 in CH_2Cl_2 to afford *N*-phenyltrifluoroacetimidate **E** (94% yield, two steps) or with trichloroacetonitrile and substoichiometric amounts of sodium hydride to obtain trichloroacetimidate **11** (81% yield, two steps). Glycosylating agent **11** was subsequently converted in 99% yield into dibutyl phosphate **12** by reacting **11** with dibutyl phosphate in toluene.[24]

In comparison with the synthesis of *N*-nosyl-protected derivatives **B** and **C**, the protection of the primary amine as *N*-DNP group and conversion to the corresponding glycosylating agents proceeded well, both for tri-*O*-acetylated derivative **D** and tri-*O*-benzylated glycosylating agents **E**, **11,** and **12**. In

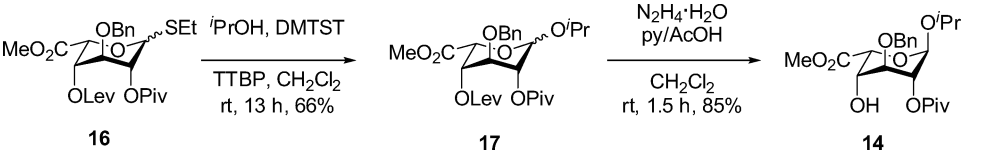


Scheme 6: Glycosylations of *N*-DNP-protected glycosylating agent **D**.

addition, all *N*-DNP-protected compounds displayed a bright yellow color permitting easy detection after column chromatography.

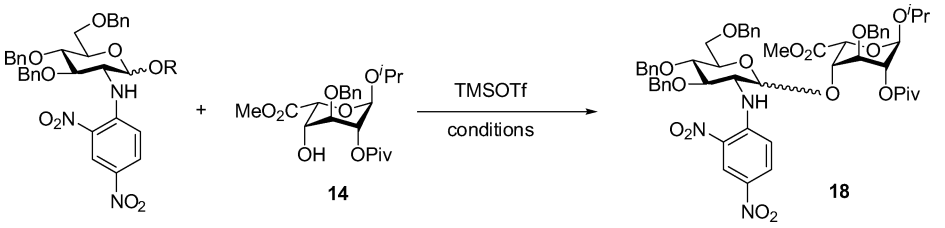
First, tri-*O*-acetylated glucosamine building block **D** was evaluated. Coupling with methylglycoside **9**[22] using TMSOTf as activator afforded disaccharide **13** as a mixture of α/β-anomers (α/β 1:2.5) in excellent yield (92%, Sch. 6). Attempts to enhance the α-selectivity using diethyl ether as cosolvent[25] did not meet with success, as mainly the β-product was obtained. This coupling prompted extended investigations to couplings involving L-iduronic acid **14** as acceptor.

Preparation of iduronic acid **14** commenced with the glycosylation of thioglycoside **16**[26] with ^{i}PrOH using dimethylsulfonium triflate (DMTST)[27] as activator and tri-*tert*-butylpyrimidine (TTBP) as base to yield **17** in 66% yield (Sch. 7). Despite the participating pivaloyl ester at the C2 hydroxyl, **17** was obtained as an inseparable mixture of anomers (α/β 8:1).[26] Cleavage of the levulinoyl ester was achieved by treatment of **17** with hydrazine monohydrate and a mixture of pyridine and acetic acid as buffer in CH_2Cl_2 to afford acceptor **14** in 85% yield. Glycosylating agent **D** was then coupled with **14** in CH_2Cl_2 using TMSOTf as activator. At this stage, no diethyl ether was



Scheme 7: Synthesis of L-iduronic acid acceptor **14**.

Table 1: TMSOTf-catalyzed couplings of glycosylating agents **E**, **11**, and **12** to L-iduronic acid **14**.



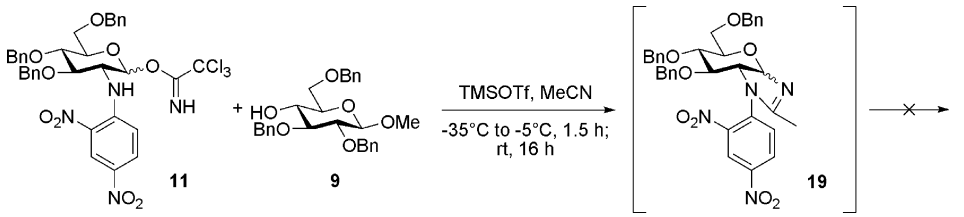
Entry	Glycosylating Agent	Conditions	Yield (%)	α/β-ratio
1	**E** (R = C(NPh)CF_3)	−30°C to −5°C, 45 min, CH_2Cl_2	58	5:1
2	**E** (R = C(NPh)CF_3)	−30°C to −10°C, 45 min, Et_2O/CH_2Cl_2	87	2.5:1
3	**11** (R = C(NH)CCl_3)	−35°C to −10°C, 45 min, CH_2Cl_2	41	3.5:1
4	**11** (R = C(NH)CCl_3)	−30°C to −10°C, 45 min, Et_2O/CH_2Cl_2	57	3.5:1
5	**12** (R = P(O)$(OBu)_2$)	−78°C to −50°C, 30 min, CH_2Cl_2	89	1.5:1

employed, in the hope that L-iduronic acid acceptor **14** would induce complete α-selectivity.[5b,5c,18b,28] As expected, preferably α-linked disaccharide **15** was obtained (ratio of α/β-anomers: 5:1) in 21% yield (Sch. 6).

Moreover, the couplings of tri-*O*-benzylated *N*-DNP-protected glucosamine building blocks **E**, **11,** and **12** with L-iduronic acid **14** were investigated and optimized (Table 1). When *N*-phenyltrifluoroacetimidate **E** was used in CH_2Cl_2 alone, disaccharide **18** was obtained in moderate yield (58%), but with good α-selectivity (α/β 5:1, entry 1). Using diethyl ether as cosolvent distinctively increased the yield to 87%. However, the α-selectivity dropped to α/β = 2.5:1 (entry 2). In the case of couplings with trichloroacetimidate **11,** no significant difference in α/β ratios was obtained by varying the solvent (α/β 3.5:1). Again, the use of diethyl ether as cosolvent to CH_2Cl_2 significantly raised the yield from 41% to 57% (entries 3 and 4). Couplings involving glycosyl phosphate **12** could be performed at very low temperature (−78°C to −50°C), resulting in 89% yield. However, the α-selectivity dropped (α/β 1.5:1, entry 5).

L-Iduronic acid acceptors are known to induce α-selectivity upon reaction with C-2- azide glycosylating agents.[5b,5c,18b,28] Likewise, the coupling of disarmed tri-*O*-acetylated glycosylating agent **D** with acceptor **14** preferentially yielded α-linked disaccharide **15**. When armed glycosylating agents **E**, **11,** and **12** were coupled with **14,** corresponding disaccharide **18** was furnished with good to very good α-selectivity.

In nature, β-linked glucosamines are prominently found in many carbohydrate structures. Although synthetically less challenging than α-linkages to glucosamine, additional orthogonal amine-protecting groups that selectively yield β-linked glucosamines would be useful.[29] Reaction of trichloroacetimidate **11** with methyl glycoside **9**[22] using TMSOTf as activator and



Scheme 8: Glycosylation attempt of *N*-DNP-protected glycosylating agent **11** in acetonitrile.

acetonitrile as solvent was investigated (Sch. 8). Acetonitrile is well known to increase β-selectivity in coupling reactions.[30] In the course of the reaction, glycosylating agent **11** was consumed; however, even after prolonged reaction time at room temperature, no disaccharide was formed. ESI-mass analysis of the reaction mixture hinted at the formation of acetonitrile-adduct **19** (Sch. 8).[31,32]

CONCLUSION

Reported is the synthesis of *N*-nosyl- and *N*-DNP-protected glucosamine building blocks and their evaluation in glycosylation reactions. Readily accessible glucosamines **3** and **5** may serve as intermediates for the synthesis and subsequent evaluation of multiple other amine-protecting groups.

During the first investigations on *N*-nosyl as protecting group for a glucosamine glycosylating agent reported here, several challenges were encountered: The synthesis of glycosylating agents **B** and **C** turned out to be challenging. Glycosylations involving tri-*O*-acetyl derivative **B** either yielded undesired β-linked product **7** exclusively or resulted in inseparable mixtures of products. On the other hand, *N*-DNP-protected *N*-phenyltrifloroacetimidates **D** and **E**, as well as trichloroacetimidate **11** and phosphate **12**, were prepared in high yield. The glycosylations of disarmed tri-*O*-acetyl derivative **D**, as well as armed tri-*O*-benzyl derivatives **E**, **11,** and **12**, showed the expected preference for α-selective couplings to L-iduronic acid derivative **14**.

Future investigations will reveal whether incorporating *N*-DNP-protected glucosamine building blocks into the modular assembly of heparin oligosaccharides is feasible to increase the diversity of synthetic heparin oligosaccharides.

EXPERIMENTAL

General

All chemicals used were reagent grade and used as supplied except where noted. Dichloromethane (CH_2Cl_2), diethyleter (Et_2O), toluene, and

tetrahydrofuran (THF) were purified by a J.C. Meyer Cycle-Tainer Solvent Delivery System. Pyridine, acetonitrile, and triethylamine were distilled over CaH_2 prior to use. Trichloroacetonitrile (CCl_3CN) was distilled over P_2O_5 under Ar and stored at 0°C. Reactions were performed under an Ar-atmosphere except where noted. Analytical thin layer chromatography (TLC) was performed on Merck silica gel 60 F_{254} plates (0.25 mm). Compounds were visualized by UV irradiation or dipping the plate in a cerium (IV) sulfate/ammonium molybdate/H_2O/H_2SO_4 solution followed by heating. Flash column chromatography was carried out using forced flow of the indicated solvent on Fluka Kieselgel 60 (230–400 mesh). Recycling preparative HPLC (LC-9101, Japan Analytical Industry Co., Ltd.); flow rate: 3.5 mL/min; solvent: $CHCl_3$. ^{1}H NMR spectra were recorded on a Varian VXR-300 (300 MHz) or Bruker DRX400 (400 MHz) spectrometer and are reported in ppm (δ) relative to $CHCl_3$ (7.25 ppm) as internal reference. Coupling constants (J) are reported in Hz. ^{13}C NMR spectra were obtained using a Varian VXR-300 (75 MHz) or Bruker DRX400 (100 MHz) and are reported in ppm (δ) relative to $CDCl_3$ (77 ppm). MALDI and ESI high-resolution mass spectra were performed by the MS-service at the Laboratory for Organic Chemistry (ETH Zürich). IR spectra were recorded on a Perkin-Elmer 1600 FTIR spectrometer (neat) or on a Perkin-Elmer Spectrum 100 Series spectrometer ($CHCl_3$). Optical rotations were measured using a Perkin-Elmer 241 polarimeter (10 cm, 1-mL cell); solvents and concentrations (in g/100 mL) are indicated.

General Procedures

tert-*Butyldiphenylsilyl 3,4,6-Tri*-O-*acetyl-2-deoxy-2-(4-methoxy-benzylideneamino)-β*-D-*glucopyranose (2)*

Through a solution of **1**[17b] (30.4 g, 65.3 mmol) in THF (180 mL) and MeOH (78 mL) at 0°C was bubbled anhydrous ammonia at a modest rate. After 1.5 h, nitrogen was bubbled through the solution to remove excess ammonia and the solvent was removed in vacuo to afford a dark orange oil. The residue was co-evaporated three times with toluene and once with CH_2Cl_2 and dried in vacuo for 12 h to get a yellow solid that was dissolved in CH_2Cl_2 (130 mL). At rt, imidazole (8.89 g, 131 mmol) and TBDPS-Cl (18.7 mL, 72 mmol) were added. The mixture was stirred for 2 h at rt, diluted with EtOAc (500 mL), washed with saturated aqueous NH_4Cl solution (2 × 200 mL) and brine (200 mL), dried over $MgSO_4$, and concentrated. Flash column chromatography on silica gel (3:1 → 2:1 cyclohexane/EtOAc) afforded **2** (32.8 g, 76%) as a yellow foam. R_f 0.49 (cyclohexane/EtOAc 3:2). $[\alpha]_D^{r.t.}$: +49.4 (c = 1.0, $CHCl_3$). IR ($CHCl_3$): 3008, 2960, 2860, 1749, 1649, 1606, 1579, 1513, 1464, 1428, 1366, 1308, 1113, 1035, 909 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.98 (s, 9H, ^{t}Bu), 1.87 (s, 3H, Ac), 1.99 (s, 3H, Ac), 2.02 (s, 3H, Ac), 3.43 (dd, J = 9.7, 7.5 Hz, 1H, H-2), 3.54 (ddd, J =

10.0, 5.6, 2.5 Hz, 1H, H-5), 3.86 (s, 3H, OMe), 4.00 (dd, J = 12.1, 2.5 Hz, 1H, H-6), 4.17 (dd, J = 12.1, 5.6 Hz, 1H, H-6′), 4.93 (d, J = 7.5 Hz, 1H, H-1), 5.08 (t, J = 9.8 Hz, 1H, H-4), 5.32 (t, J = 9.6 Hz, 1H, H-3), 6.91–6.95 (m, 2H, H_{Ar}), 7.17–7.43 (m, 6H, H_{Ar}), 7.58–7.61 (m, 2H, H_{Ar}), 7.65–7.71 (m, 4H, H_{Ar}), 8.24 (s, 1H, N = C-H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 19.3, 20.7, 20.8, 26.8, 55.4, 62.6, 69.0, 71.6, 73.6, 76.5, 96.7, 113.9, 127.3, 127.4, 128.7, 129.6, 130.1, 132.5, 132.9, 135.7, 135.9, 161.8, 163.7, 169.6, 169.8, 170.5. MALDI-HRMS: m/z calcd for $C_{36}H_{44}NO_9Si$ $[M+H]^+$ 662.2780, obsd 662.2775.

tert-*Butyldiphenylsilyl 3,4,6-Tri*-O-*acetyl-2-amino-2-deoxy-β*-D-*glucopyranose (3)*

To a solution of **2** (250 mg, 0.378 mmol) in THF (1.8 mL) was added $NH_2OH{\cdot}HCl$ (79 mg, 1.3 mmol) in H_2O (2.2 mL). The mixture was stirred for 45 min at rt, diluted with EtOAc, and washed with saturated aqueous $NaHCO_3$ solution. The aqueous phase was re-extracted twice with EtOAc. The combined organic phases were dried over $MgSO_4$ and concentrated. The residue was purified by flash column chromatography on silica gel (7:3 → 2:3 cyclohexane/EtOAc) to afford **3** (189 mg, 92%) as a yellow, viscous oil. R_f 0.42 (cyclohexane/EtOAc 3:7). $[\alpha]_D^{r.t.}$: +3.0 (c = 1.0, $CHCl_3$). IR ($CHCl_3$): 3008, 2962, 2860, 1748, 1428, 1367, 1113, 1042, 909 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.10 (s, 9H), 1.25 (br. s, 2H), 1.95 (s, 3H), 1.96 (s, 3H), 2.04 (s, 3H), 2.98 (dd, J = 10.3, 7.8 Hz, 1H), 3.37 (ddd, J = 9.8, 5.8, 2.3 Hz, 1H), 3.90 (dd, J = 12.0, 2.3 Hz, 1H), 4.06 (dd, J = 12.1, 5.6 Hz, 1H), 4.37 (d, J = 7.8 Hz, 1H), 4.82 (t, J = 9.7 Hz, 1H), 4.96 (t, J = 9.7 Hz, 1H), 7.32–7.46 (m, 6H), 7.66–7.70 (m, 4H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 19.3, 20.7, 20.8, 20.9, 27.0, 58.0, 62.5, 69.1, 71.6, 75.1, 98.9, 127.3, 127.6, 129.8, 129.9, 132.7, 132.8, 135.6, 135.8, 169.6, 170.4, 170.5. MALDI-HRMS: m/z calcd for $C_{28}H_{38}NO_8Si$ $[M+H]^+$ 544.2361, obsd 544.2356.

tert-*Butyldiphenylsilyl 3,4,6-Tri*-O-*benzyl-2-deoxy-2-(4-methoxy-benzylideneamino)-β*-D-*glucopyranose (4)*

At rt, a solution of **2** (5.0 g, 7.56 mmol) in MeOH (75 mL) and CH_2Cl_2 (38 mL) was treated with a solution of sodium (73 mg, 3.17 mmol) in MeOH (10 mL). After 2.5 h, more sodium (36 mg, 1.59 mmol) in MeOH (5 mL) was added. After 30 min stirring at rt, the mixture was neutralized with IR-120-H^+ Amberlite resin to pH 6, filtered, and concentrated. The residue was co-evaporated three times with toluene and dissolved in THF (75 mL). At 0°C, NaH (2.12 g, 52.9 mmol, 60% dispersion in mineral oil) and benzyl bromide (7.2 mL, 60.5 mmol, filtered over alumina) were added. After warming to rt, TBAI (28 mg, 76 μmol) was added and the mixture was heated at reflux. After 2 h, the reaction was allowed to cool to rt, quenched with MeOH (50 mL), diluted with CH_2Cl_2, and washed with saturated aqueous $NaHCO_3$ solution.

The aqueous phase was re-extracted once with CH_2Cl_2. The combined organic phases were dried over $MgSO_4$ and concentrated. Flash column chromatography on silica gel (1:1 → 0:1 cyclohexane/CH_2Cl_2 and then 12:1 to 9:1 cyclohexane/EtOAc) afforded **4** (5.31 g, 87%) as a colorless oil. R_f 0.18 (cyclohexane/EtOAc 9:1). $[\alpha]_D^{r.t.}$: +80.7 (c = 1.0, $CHCl_3$). IR ($CHCl_3$): 3067, 3008, 2933, 2860, 1648, 1606, 1579, 1513, 1454, 1428, 1390, 1361, 1307, 1113, 1061 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 0.99 (s, 9H, ^{t}Bu), 3.25–3.29 (m, 1H, H-5), 3.40 (t, J = 8.1 Hz, 1H, H-2), 3.52 (dd, J = 10.9, 1.9 Hz, 1H, H-6), 3.67 (dd, J = 11.1, 4.2 Hz, 1H, H-6′), 3.74 (t, J = 8.9 Hz, 1H, H-4), 3.80 (t, J = 9.0 Hz, 1H, H-3), 3.89 (s, 3H, OMe), 4.45 (d, J = 12.1 Hz, 1H,C*H*Ph), 4.54 (d, J = 10.9 Hz, 1H, C*H*Ph), 4.56 (d, J = 12.1 Hz, 1H, C*H*Ph), 4.62 (d, J = 10.9 Hz, 1H, C*H*Ph), 4.63 (d, J = 10.6 Hz, 1H, C*H*Ph), 4.85 (d, J = 11.2 Hz, 1H, C*H*Ph), 4.85 (d, J = 7.5 Hz, 1H, H-1), 6.94–6.98 (m, 2H, H_{Ar}), 7.08–7.38 (m, 21H, H_{Ar}), 7.62–7.66 (m, 2H, H_{Ar}), 7.69–7.74 (m, 4H, H_{Ar}), 8.33 (s, 1H, N = C-H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 19.4, 27.0, 55.5, 68.9, 73.6, 74.9, 75.1, 75.2, 77.8, 79.3, 83.9, 96.9, 113.9, 127.2, 127.3, 127.4, 127.5, 127.6, 127.8, 128.2, 128.2, 128.2, 128.3, 129.3, 129.5, 130.0, 133.0, 133.5, 136.0, 136.0, 138.2, 138.4, 138.5, 161.6, 163.1. MALDI-HRMS: m/z calcd for $C_{51}H_{56}NO_6Si$ $[M+H]^+$ 806.3871, obsd 806.3888.

tert-*Butyldiphenylsilyl 2-Amino-3,4,6-tri*-O-*benzyl-2-deoxy-β*-D-*glucopyranose (5)*

A solution of **4** (3.99 g, 4.95 mmol) in Et_2O (15 mL) and EtOH (22 mL) was cooled to 0°C. AcOH (2.6 mL) and $TosNHNH_2$ (1.88 g, 9.89 mmol) were added. The mixture was stirred for 3.5 h at rt, diluted with EtOAc, and washed with saturated aqueous $NaHCO_3$ solution. The aqueous phase was re-extracted with EtOAc. The combined organic phases were dried over $MgSO_4$ and concentrated. Flash column chromatography on silica gel (4:1 → 7:3 cyclohexane/EtOAc) afforded **5** (3.07 g, 90%) as a yellow, viscous oil. R_f 0.42 (cyclohexane/EtOAc 3:1). $[\alpha]_D^{r.t.}$: −6.3 (c = 1.0, $CHCl_3$). IR ($CHCl_3$): 3385, 3067, 3008, 2933, 2860, 1589, 1496, 1454, 1428, 1362, 1110, 1062, 1028 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 1.15 (s, 9H), 1.60 (br. s, 2H), 3.04 (dd, J = 9.8, 7.6 Hz, 1H), 3.13 (ddd, J = 9.8, 3.7, 1.7 Hz, 1H), 3.37 (t, J = 9.3 Hz, 1H), 3.45 (dd, J = 11.1, 1.7 Hz, 1H), 3.65 (dd, J = 11.2, 4.0 Hz, 1H), 3.75 (t, J = 9.3 Hz, 1H), 4.37 (d, J = 12.1 Hz, 1H), 4.41 (d, J = 7.5 Hz, 1H), 4.51 (d, J = 12.1 Hz, 1H), 4.65 (d, J = 10.9 Hz, 1H), 4.73 (d, J = 11.2 Hz, 1H), 4.81 (d, J = 10.9 Hz, 1H), 4.96 (d, J = 11.5 Hz, 1H), 7.22–7.45 (m, 21H), 7.72–7.79 (m, 4H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 19.4, 27.2, 59.1, 68.6, 73.6, 74.7, 75.3, 78.5, 85.2, 98.9, 127.3, 127.4, 127.5, 127.5, 127.6, 127.7, 127.8, 128.2, 128.4, 128.4, 129.5, 129.7, 132.9, 133.6, 135.8, 135.9, 138.1, 138.4, 138.5. MALDI-HRMS: m/z calcd for $C_{43}H_{49}NO_5SiNa$ $[M+Na]^+$ 710.3272, obsd 710.3254.

tert-*Butyldiphenylsilyl 3,4,6-Tri*-O-*acetyl-2-deoxy-2-(4-nitrobenzenesulfonylamino)-β*-D-*glucopyranose (6a)*

A solution of **3** (2.02 g, 3.71 mmol) in CH_2Cl_2 (35 mL) was cooled to 0°C and treated with NEt_3 (2.1 mL, 14.8 mmol) and 4-nitrobenzenesulphonyl chloride (2.88 g, 13.0 mmol). The reaction was stirred for 3 h at rt. Then, more NEt_3 (0.5 mL, 3.7 mmol) and 4-nitrobenzenesulphonyl chloride (0.82 g, 3.7 mmol) were added and the mixture was stirred for additional 2 h at rt, diluted with CH_2Cl_2, and washed with saturated aqueous NH_4Cl solution. The aqueous phase was re-extracted once with CH_2Cl_2 and the combined organic phases were dried over $MgSO_4$ and concentrated. Flash column chromatography on silica gel (4:1 → 3:2 cyclohexane/EtOAc) afforded **6a** (2.12 g, 78%) as a pale yellow foam. R_f 0.37 (cyclohexane/EtOAc 3:2). $[\alpha]_D^{r.t.}$: +2.0 (c = 1.0, $CHCl_3$). IR ($CHCl_3$): 3364, 3032, 2934, 2861, 1750, 1533, 1428, 1350, 1312, 1114, 1091, 1046, 909 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 1.02 (s, 9H, ^{t}Bu), 1.83 (s, 3H, Ac), 1.96 (s, 3H, Ac), 2.01 (s, 3H, Ac), 3.40 (ddd, J = 9.6, 5.3, 2.5 Hz, 1H, H-5), 3.76–3.85 (m, 1H, H-2), 3.95 (dd, J = 12.1, 2.5 Hz, 1H, H-6), 4.05 (dd, J = 12.1, 5.3 Hz, 1H, H-6′), 4.61 (d, J = 7.8 Hz, 1H, H-1), 4.90 (d, J = 9.3 Hz, 1H, NH), 4.96 (t, J = 9.8 Hz, 1H, H-3), 5.07 (t, J = 9.5 Hz, 1H, H-4), 7.29–7.55 (m, 10H, H_{Ar}), 7.86–7.95 (m, 4H, H_{Ar}). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 19.3, 20.7, 20.8, 20.8, 26.7, 60.6, 62.1, 68.7, 71.5, 73.3, 95.9, 124.0, 127.5, 127.6, 127.9, 129.9, 130.0, 132.6, 132.8, 135.3, 135.5, 146.6, 149.4, 169.1, 170.4, 170.6. MALDI-HRMS: m/z calcd for $C_{34}H_{40}N_2O_{12}SSiNa$ $[M+Na]^+$ 751.1963, obsd 751.1978.

3,4,6-Tri-O-*acetyl-2-deoxy-2-(4-nitrobenzenesulfonylamino)-β*-D-*glucopyranosyl* N-*Phenyl trifluoroacetimidate (B)*

A solution of **6a** (166 mg, 0.228 mmol) in THF (4.6 mL) was treated with AcOH (0.13 mL, 2.28 mmol) and a 1M solution of TBAF in THF (0.91 mL, 0.91 mmol). The mixture was stirred for 2 h at rt, diluted with EtOAc, washed with saturated aqueous $NaHCO_3$ solution and brine, dried over $MgSO_4$, and concentrated. The residue was purified by flash column chromatography on silica gel (3:2 → 1:1 toluene/EtOAc) to yield the hemiacetal (92 mg, 82%) as a pale yellow foam. An aliquot of the resulting hemiacetal (75 mg, 0.153 mmol) was dissolved in THF (1 mL) and CH_2Cl_2 (1 mL). At 0°C, the solution was treated with $CF_3C(NPh)Cl$[33] (0.10 mL, 0.63 mmol) and Cs_2CO_3 (0.10 g, 0.31 mmol) and stirred for 15 min at 0°C. After stirring for 45 min at rt, the mixture was filtered through Celite (CH_2Cl_2) and concentrated. The residue was purified by column chromatography (7:3 → 3:2 cyclohexane/EtOAc) to afford **B** (62 mg, 61% [50% over two steps]) as a mixture of α/β-anomers (α/β = 1:>20). Colorless, viscous oil. R_f 0.18 (cyclohexane/EtOAc 7:3). IR (neat): 3257, 2959, 1730, 1597, 1533, 1489, 1452, 1351, 1311, 1165, 1044 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz, only signals of β-anomer) δ 1.85 (s, 3H), 1.97 (s, 3H), 2.07 (s, 3H), 3.85 (br, 1H), 4.02–4.09 (m, 2H), 4.26 (dd, J = 12.7 Hz, 4.4 Hz, 1H), 5.15 (t, J =

9.9 Hz, 1H), 5.34 (t, J = 10.1 Hz, 1H), 6.25 (br. s, 1H), 6.55 (d, J = 9.1 Hz, 1H), 6.69–6.71 (m, 2H), 7.09–7.14 (m, 1H), 7.25–7.30 (m, 2H), 8.02–8.05 (m, 2H), 8.25–8.29 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz, only signals of β-anomer) δ 20.4, 20.5, 20.7, 55.6, 61.3, 67.2, 69.8, 70.0, 93.9, 119.0, 120.3, 124.4, 124.9, 126.2, 128.0, 128.8, 129.2, 142.2, 146.3, 149.9, 169.0, 170.3, 171.3. ESI-HRMS: m/z calcd for $C_{26}H_{26}F_3N_3O_{12}SNa$ $[M+Na]^+$ 684.1082, obsd 684.1077.

tert-*Butyldiphenylsilyl 3,4,6-Tri*-O-*benzyl-2-deoxy-2-(4-nitrobenzenesulfonylamino)-β*-D-*glucopyranose (6b)*

At 0°C, a solution of **5** (3.07 g, 4.46 mmol) in CH_2Cl_2 (60 mL) was portionwise treated with NEt_3 (2.5 mL, 17.8 mmol) and 4-nitrobenzenesulphonyl chloride (3.46 g, 15.6 mmol). The reaction was stirred for 4 h at rt, diluted with CH_2Cl_2, and washed with saturated aqueous NH_4Cl solution. The aqueous phase was re-extracted once with CH_2Cl_2 and the combined organic phases were dried over $MgSO_4$ and concentrated. Flash column chromatography on silica gel (9:1 → 7:3 cyclohexane/EtOAc) afforded **6b** (3.49 g, 90%) as a pale yellow foam. R_f 0.44 (cyclohexane/EtOAc 7:3). $[\alpha]_D^{r.t.}$: −33.1 (c = 1.0, $CHCl_3$). IR (neat): 3330, 3031, 2932, 2859, 1607, 1530, 1454, 1348, 1162, 1092 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.02 (s, 9H, ^{t}Bu), 3.02–3.05 (m, 1H, H-5), 3.19 (t, J = 8.8 Hz, 1H, H-3), 3.37 (dd, J = 10.9, 2.6 Hz, 1H, H-6), 3.49 (dd, J = 10.9, 3.8 Hz, 1H, H-6′), 3.57–3.64 (m, 1H, H-2), 3.68 (t, J = 8.5 Hz, 1H, H-4), 4.22 (d, J = 11.6 Hz, 1H, C*H*Ph), 4.28 (d, J = 12.1 Hz, 1H, C*H*Ph), 4.35 (d, J = 7.3 Hz, 1H, H-1), 4.38 (d, J = 12.8 Hz, 1H, C*H*Ph), 4.46 (d, J = 10.8 Hz, 1H, C*H*Ph), 4.52 (d, J = 10.8 Hz, 1H, C*H*Ph), 4.56 (d, J = 7.7 Hz, 1H, NH), 4.58 (d, J = 11.4 Hz, 1H, C*H*Ph), 6.90–6.96 (m, 4H, H_{Ar}), 7.10–7.36 (m, 17H, H_{Ar}), 7.59–7.63 (m, 4H, H_{Ar}), 7.71–7.76 (m, 4H, H_{Ar}). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 19.2, 26.8, 60.5, 68.5, 73.6, 74.1, 74.5, 74.8, 78.0, 81.9, 96.4, 123.8, 125.0, 126.5, 127.4, 127.6, 127.6, 127.7, 127.8, 128.2, 128.4, 128.4, 129.8, 130.0, 132.8, 133.2, 136.0, 137.5, 137.6, 138.2, 147.1, 149.3. MALDI-HRMS: m/z calcd for $C_{49}H_{52}N_2O_9SSiNa$ $[M+Na]^+$ 895.3055, obsd 895.3040.

3,4,6-Tri-O-*benzyl-2-deoxy-2-(4-nitrobenzenesulfonylamino)*-D-*glucopyranosyl* N-*Phenyl trifluoroacetimidate (C)*

At rt, a solution of **6b** (200 mg, 0.229 mmol) in THF (5 mL) was treated with AcOH (131 μL, 2.29 mmol) and TBAF·$3H_2O$ (0.29 g, 0.92 mmol). The mixture was stirred at rt for 4 h. Then, TBAF·H_2O (0.39 g, 1.37 mmol) and H_2O (0.05 mL) were added, and the mixture was stirred for additional 15 h at rt, diluted with EtOAc, and washed with saturated aqueous NH_4Cl solution. The aqueous phase was re-extracted once with EtOAc. The combined organic phases were dried over $MgSO_4$ and concentrated. The residue was purified by flash column chromatography on silica gel (7:3 → 3:2 cyclohexane/EtOAc) to afford the hemiacetal (94 mg, 65%) that was dissolved in THF (1 mL) and CH_2Cl_2 (2 mL). At 0°C, the solution was treated with $CF_3C(NPh)Cl$[33] (47 μL,

0.30 mmol) and Cs_2CO_3 (145 mg, 0.44 mmol) and stirred for 1.5 h at 0°C and for 4 h at rt. Then, the mixture was filtered through Celite (CH_2Cl_2) and concentrated. The residue was purified by flash column chromatography on silica gel (1:0 → 4:1 cyclohexane/EtOAc) to afford **C** (11 mg, 9% [6% over two steps.) as a mixture of α/β-anomers. Yellow solid. R_f 0.51 (cyclohexane/EtOAc 7:3). IR (neat): 3317, 3034, 2870, 1718, 1607, 1530, 1498, 1453, 1349, 1312, 1208, 1071 cm^{-1}. ^1H NMR ($CDCl_3$, 300 MHz) δ 3.28–3.97 (m, 6H), 3.97–4.96 (m, 7H), 6.36–8.36 (m, 25H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 56.7, 67.7, 72.1, 73.2, 74.8, 75.3, 78.7, 94.4, 95.1, 113.7, 117.5, 119.1, 120.4, 122.8, 123.4, 123.8, 123.9, 124.4, 124.6, 126.2, 126.9, 127.6, 127.9, 129.1, 130.2, 134.9, 137.0, 137.3, 142.7, 145.4, 148.9, 149.4. MALDI-HRMS: m/z calcd for $C_{41}H_{38}F_3N_3O_9SNa$ $[M+Na]^+$ 828.2173, obsd 828.2175.

*Methyl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-(4-nitrobenzenesulfonylamino)-β-*D*-glucopyranoside (7)*

N-Phenyl trifluoroacetimidate **B** (58 mg, 0.088 mmol) was coevaporated three times with toluene, dried in vacuo for 1 h, and dissolved in CH_2Cl_2 (2 mL). At −30°C, MeOH (5.4 μL, 0.132 mmol) and TMSOTf (2.4 μL, 13 μmol) were added. The reaction was warmed to 0°C over 2 h, quenched with NEt_3 (0.1 mL), and concentrated. The residue was coevaporated twice with toluene and purified by flash column chromatography on silica gel (9:1 → 7:3 cyclohexane/EtOAc) to afford **7** (28 mg, 63%) as pure β-anomer (colorless oil). R_f 0.53 (cyclohexane/EtOAc 7:3). $[\alpha]_D^{r.t.}$: −36.4 (c = 1.0, $CHCl_3$). IR (neat): 3275, 3108, 2926, 1748, 1531, 1451, 1350, 1312, 1229, 1166, 1090 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ 1.97 (s, 3H, Ac), 2.01 (s, 3H, Ac), 2.04 (s, 3H, Ac), 3.00 (s, 3H, OMe), 3.38–3.50 (m, 1H, H-2), 3.57–3.62 (m, 1H, H-5), 4.03 (dd, J = 12.4, 2.4 Hz, 1H, H-6), 4.11 (d, J = 8.3 Hz, 1H, H-1), 4.19 (dd, J = 12.4, 4.7 Hz, 1H, H-6′), 4.99–5.03 (m, 2H, H-3/H-4), 5.42 (d, J = 8.9 Hz, 1H, NH), 7.96–8.00 (m, 2H, H_{Ar}), 8.24–8.27 (m, 2H, H_{Ar}). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 20.6, 20.7, 20.8, 56.8, 58.5, 61.8, 68.2, 71.8, 72.6, 102.3, 123.8, 128.6, 147.0, 149.9, 169.2, 170.7, 171.7. MALDI-HRMS: m/z calcd for $C_{19}H_{24}N_2O_{12}SNa$ $[M+Na]^+$ 527.0942, obsd 527.0936.

tert-*Butyldiphenylsilyl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-(2,4-dinitrophenylamino)-β-*D*-glucopyranose (10a)*

A solution of **3** (2.20 g, 4.04 mmol) in THF (21 mL) and H_2O (5.3 mL) was treated with $KHCO_3$ (405 mg, 4.04 mmol) and 1-fluoro-2,4-dinitrobenzene (1.53 mL, 12.1 mmol) and stirred for 2 h at rt. Then, more 1-fluoro-2,4-dinitrobenzene (0.51 mL, 4.04 mmol) was added. The mixture was stirred for an additional 4 h at rt, diluted with EtOAc, and washed with saturated aqueous NH_4Cl solution. The aqueous phase was re-extracted once with EtOAc, and the combined organic phases were dried over $MgSO_4$ and concentrated. Flash column chromatography on silica gel (9:1 → 3:1 cyclohexane/EtOAc)

afforded **10a** (2.69 g, 94%) as a yellow foam. R_f 0.66 (cyclohexane/EtOAc 1:1). $[\alpha]_D^{r.t.}$: −7.3 (c = 1.0, $CHCl_3$). IR (neat): 3318, 3075, 2934, 1747, 1618, 1593, 1524, 1428, 1334, 1112, 1042 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ 0.98 (s, 9H, ^{t}Bu), 1.90 (s, 3H, Ac), 2.01 (s, 3H, Ac), 2.06 (s, 3H, Ac), 3.52–3.56 (m, 1H, H-5), 4.02–4.08 (m, 2H, H-2, H-6), 4.22 (dd, J = 12.2, 5.6 Hz, 1H, H-6′), 4.75 (d, J = 7.7 Hz, 1H, H-1), 5.15 (t, J = 9.3 Hz, 1H, H-4), 5.19 (t, J = 9.5 Hz, 1H, H-3), 7.20–7.42 (m, 8H, H_{Ar}), 7.56–7.58 (m, 2H, H_{Ar}), 8.15 (dd, J = 9.5, 2.5 Hz, 1H, DNP), 8.44 (d, J = 9.3 Hz, 1H, DNP), 9.01 (d, J = 2.7 Hz, 1H, DNP). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 18.9, 20.4, 20.5, 20.6, 26.6, 59.2, 62.1, 68.5, 71.9, 97.5, 115.5, 123.8, 127.6, 127.6, 129.7, 130.3, 130.3, 131.8, 135.3, 135.8, 136.8, 148.3, 169.4, 170.2, 170.4. MALDI-HRMS: m/z calcd for $C_{34}H_{39}N_3O_{12}SiNa$ $[M+Na]^+$ 732.2195, obsd 732.2209.

*3,4,6-Tri-*O*-acetyl-2-deoxy-2-(2,4-dinitrophenylamino)-*D*-glucopyranosyl* N*-Phenyl trifluoroacetimidate (D)*

A solution of **10a** (200 mg, 0.282 mmol) in THF (5 mL) was treated with AcOH (0.16 mL, 2.82 mmol) and TBAF·$3H_2O$ (360 mg, 1.13 mmol). The mixture was stirred for 1.5 h at rt, diluted with EtOAc, and washed with saturated aqueous $NaHCO_3$ solution. The aqueous layer was re-extracted once with EtOAc, and the combined organic phases were dried over $MgSO_4$ and concentrated. The residue was purified by flash column chromatography on silica gel (7:3 → 1:1 cyclohexane/EtOAc) to yield the hemiacetal (94 mg, 71%) as a yellow foam. Combined samples of the resulting hemiacetal (654 mg, 1.39 mmol) were dissolved in CH_2Cl_2 (26 mL). At 0°C, the solution was treated with $CF_3C(NPh)Cl$[33] (0.86 mL, 5.4 mmol) and Cs_2CO_3 (904 mg, 2.77 mmol) and stirred for 15 min at 0°C and for 75 min at rt. Then, the mixture was filtered through Celite (CH_2Cl_2) and concentrated. The residue was purified by flash column chromatography on silica gel (9:1 → 3:2 cyclohexane/EtOAc) to yield **D** (783 mg, 88% [62% over two steps]) as a mixture of α/β-anomers. Yellow foam. R_f 0.50 (cyclohexane/EtOAc 1:1). IR (neat): 3333, 2964, 1748, 1617, 1594, 1524, 1337, 1153, 1114, 1043 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ 1.89 (s, 3H), 2.09 (s, 3H), 2.13 (s, 3H), 4.11–4.19 (m, 2H), 4.35–4.43 (m, 2H), 5.31 (t, J = 9.8 Hz, 1H), 5.55 (t, J = 9.9 Hz, 1H), 6.52 (br. s, 1H), 6.72–6.74 (m, 2H), 7.09–7.14 (m, 1H), 7.17 (d, J = 9.6, 1H), 7.25–7.30 (m, 2H), 8.30 (dd, J = 9.5, 2.7 Hz, 1H), 8.74 (d, J = 9.6 Hz, 1H), 9.14 (d, J = 2.7 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 20.7, 20.9, 54.7, 61.4, 67.3, 70.3, 72.0, 92.8, 114.0, 118.8, 124.0, 124.8, 128.7, 130.0, 131.4, 137.0, 142.1, 147.0, 169.2, 169.4, 170.0. MALDI-HRMS: m/z calcd for $C_{26}H_{25}F_3N_4O_{12}Na$ $[M+Na]^+$ 665.1313, obsd 665.1318.

tert-*Butyldiphenylsilyl 3,4,6-Tri-*O*-benzyl-2-deoxy-2-(2,4-dinitrophenylamino)-*β*-*D*-glucopyranose (10b)*

A solution of **5** (3.77 g, 5.48 mmol) in THF (16 mL) and H_2O (4 mL) was treated with $KHCO_3$ (549 mg, 5.48 mmol) and 1-fluoro-2,4-dinitrobenzene

(2.11 mL, 16.5 mmol) and stirred for 2 h at rt. Then, the reaction was diluted with EtOAc and washed with saturated aqueous NH_4Cl solution. The aqueous phase was re-extracted once with EtOAc, and the combined organic phases were dried over $MgSO_4$ and concentrated. Flash column chromatography on silica gel (1:1 → 1:9 cyclohexane/CH_2Cl_2 and then 17:3 → 4:1 cyclohexane/EtOAc) afforded **10b** (4.49 g, 96%) as a yellow foam. R_f 0.39 (cyclohexane/EtOAc 4:1). $[\alpha]_D^{r.t.}$: +21.8 (c = 1.0, $CHCl_3$). IR (neat): 3327, 3031, 2859, 1618, 1592, 1522, 1428, 1332, 1279, 1113, 1065 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ 0.98 (s, 9H, ^{t}Bu), 3.25–3.27 (m, 1H, H-5), 3.52–3.59 (m, 2H, H-3, H-6), 3.71 (dd, J = 10.9, 3.9 Hz, 1H, H-6′), 3.83–3.93 (m, 2H, H-2, H-4), 4.52 (d, J = 11.4 Hz, 1H, C*H*Ph), 4.52 (d, J = 13.3 Hz, 1H, C*H*Ph), 4.59 (d, J = 11.5 Hz, 1H, C*H*Ph), 4.60 (d, J = 7.85 Hz, 1H, H-1), 4.68 (d, J = 11.0 Hz, 1H, C*H*Ph), 4.81 (d, J = 12.8, 1H, C*H*Ph), 4.84 (d, J = 11.2, 1H, C*H*Ph), 6.97–6.99 (m, 2H, H_{Ar}), 7.09–7.45 (m, 21H, H_{Ar}), 7.62–7.64 (m, 22H, H_{Ar}), 8.11 (dd, J = 9.6, 2.6 Hz, 1H, DNP), 8.34 (d, J = 9.4 Hz, 1H, DNP), 8.99 (d, J = 2.7 Hz, 1H, DNP). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 18.9, 26.6, 60.8, 68.2, 73.6, 74.9, 75.0, 75.7, 83.8, 97.4, 116.0, 123.8, 127.5, 127.5, 127.7, 127.8, 127.9, 128.6, 129.4, 130.0, 130.1, 130.2, 132.3, 132.3, 135.5, 136.0, 136.3, 137.3, 137.9, 138.1, 149.0. MALDI-HRMS: m/z calcd for $C_{49}H_{51}N_3O_9SiNa$ $[M+Na]^+$ 876.3287, obsd 876.3287.

*3,4,6-Tri-*O*-benzyl-2-deoxy-2-(2,4-dinitrophenylamino)-*D*-glucopyranosyl* N*-Phenyl trifluoroacetimidate (E)*

At rt, a solution of **10b** (4.32 g, 5.06 mmol) in THF (140 mL) was treated with AcOH (2.9 mL, 50.6 mmol) and TBAF·$3H_2O$ (6.45 g, 20.2 mmol). The mixture was stirred for 1 h at rt, diluted with EtOAc, and washed with saturated aqueous $NaHCO_3$ solution. The aqueous layer was re-extracted once with EtOAc, and the combined organic phases were dried over $MgSO_4$ and concentrated. The residue was purified by flash column chromatography on silica gel (4:1 → 2:1 cyclohexane/EtOAc) to yield hemiacetal 20 (3.01 g, 96%) as a yellow foam. An aliquot of hemiacetal 20 (616 mg, 1.0 mmol) was dissolved in CH_2Cl_2 (20 mL), treated at 0°C with $CF_3C(NPh)Cl$[33] (0.62 mL, 3.9 mmol) and Cs_2CO_3 (655 mg, 2.0 mmol), and stirred for 15 min at 0°C. After stirring for 12 h at rt, the mixture was filtered through Celite (CH_2Cl_2) and concentrated. The residue was purified by flash column chromatography on silica gel (9:1 → 4:1 cyclohexane/EtOAc) to yield **E** (766 mg, 97% [94% over two steps]) as a mixture of α/β-anomers (α/β = 1:2.5). Yellow foam. R_f 0.55 (cyclohexane/EtOAc 7:3). IR (neat): 3332, 3062, 2871, 1718, 1617, 1591, 1522, 1332, 1207, 1115 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz, only signals of β-anomer) δ 3.77–4.12 (m, 6H), 4.55 (d, J = 11.4 Hz, 1H), 4.60 (d, J = 11.1 Hz, 1H), 4.66–4.71 (m, 2H), 4.83–4.93 (m, 2H), 6.41 (br. s, 1H), 6.76–6.77 (m, 2H), 6.94–7.41 (m, 19H), 8.14 (dd, J = 9.4, 2.5 Hz, 1H), 8.61 (d, J = 9.3 Hz, 1H), 9.06 (d, J = 2.7 Hz, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz, only signals of β-anomer) δ 55.7, 57.5, 67.8, 68.0, 73.6, 73.7, 74.8, 75.4, 75.6, 75.9, 76.2, 81.8, 82.8, 94.2, 115.5, 115.6, 119.1, 123.8, 123.9,

124.7, 124.7, 127.8, 128.0, 128.1, 128.3, 128.5, 129.7, 130.9, 131.0, 136.7, 136.9, 137.0, 137.4, 137.5, 137.6, 137.7, 142.8, 148.1, 148.3. MALDI-HRMS: m/z calcd for $C_{41}H_{37}F_3N_4O_9Na$ $[M+Na]^+$ 809.2405, obsd 809.2420.

*3,4,6-Tri-*O*-benzyl-2-deoxy-2-(2,4-dinitrophenylamino)-*D*-glucopyranosyl trichloroacetimidate (11)*

An aliquot of hemiacetal 20 (616 mg, 1.0 mmol) was dissolved in CH_2Cl_2 (10 mL), treated at 0°C with Cl_3CCN (1.44 mL, 10 mmol) and NaH (spatula tip), and stirred for 1.5 h at 0°C. After stirring for 12 h at rt, the mixture was cooled again to 0°C and more NaH (spatula tip) was added. After stirring at rt for an additional 4 h, the reaction was filtered through Celite (CH_2Cl_2) and concentrated. The residue was purified by flash column chromatography on silica gel (9:1 → 7:3 cyclohexane/EtOAc) to afford **11** (642 mg, 84% [81% over two steps]) as a mixture of α/β-anomers ($\alpha/\beta = 4{:}1$). Yellow foam. R_f 0.39 (cyclohexane/EtOAc 7:3). IR (neat): 3330, 3031, 2872, 1676, 1591, 1522, 1333, 1285, 1135, 1059, 1026 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ 3.73–4.20 (m, 6H), 4.53–4.92 (m, 6H), 5.90 (d, $J = 7.5$ Hz, 0.2H), 6.43 (d, $J = 3.4$ Hz, 0.8H), 6.90–7.38 (m, 16H), 8.16 (dd, $J = 9.4$, 2.5 Hz, 0.8H), 8.20 (dd, $J = 9.8$, 2.9 Hz, 0.2H), 8.52 (d, $J = 9.5$ Hz, 0.8H), 8.61 (d, $J = 9.3$ Hz, 0.2H), 8.69 (s, 0.2 H), 8.80 (s, 0.8H), 9.03–9.04 (m, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 55.8, 57.3, 67.7, 68.2, 73.6, 73.7, 73.7, 74.7, 75.5, 76.0, 76.1, 81.5, 82.4, 90.7, 95.0, 97.1, 115.6, 115.8, 123.7, 123.9, 127.8, 128.0, 128.1, 128.1, 128.5, 129.7, 130.8, 136.7, 136.8, 136.9, 137.0, 137.5, 137.6, 137.6, 137.8, 148.2, 148.4, 160.5, 161.0. MALDI-HRMS: m/z calcd for $C_{35}H_{33}Cl_3N_4O_9Na$ $[M+Na]^+$ 781.1205, obsd 781.1217.

*3,4,6-Tri-*O*-benzyl-2-deoxy-2-(2,4-dinitrophenylamino)-*D*-glucopyranosyl dibutylphosphate (12)*

Trichloroacetimidate **11** (110 mg, 145 μmol) was coevaporated three times with toluene and taken up in toluene (7 mL). Dibutyl phosphate (38 μL, 188 μmmol) was added dropwise at rt. The reaction mixture was stirred for 3 h at rt and concentrated. The crude product was purified by flash column chromatography on silica gel (9:1 → 3:1 cyclohexane/EtOAc) to yield **12** (116 mg, 99%) as a mixture of anomers ($\alpha/\beta = 0.45/0.55$). Yellow solid. R_f 0.24 (cyclohexane/EtOAc 7:3). IR (neat): 3340, 2963, 1729, 1618, 1592, 1523, 1454, 1275, 1135, 1028, 941 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ 0.72–1.81 (m, 14H), 3.68–4.02 (m, 10H), 4.47–4.67 (m, 4H), 4.80–4.89 (m, 2H), 5.30 (t, $J = 7.8$ Hz, 0.55H), 5.78 (dd, $J = 5.4$, 3.1 Hz, 0.45H), 6.43 (br. s, 0.45H), 6.64 (br. s, 0.55H), 6.88–7.34 (m, 15H), 8.12 (dd, $J = 9.6$, 2.7 Hz, 0.45H), 8.17 (dd, $J = 9.6$, 2.7 Hz, 0.55H), 8.51 (d, $J = 9.3$ Hz, 0.55H), 8.58 (d, $J = 9.2$ Hz, 0.45H), 9.02 (d, $J = 2.6$ Hz, 0.45H), 9.03 (d, $J = 2.6$ Hz, 0.55H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 13.4, 13.5, 18.4, 18.6, 31.9, 32.2, 56.2, 59.0, 68.1, 68.4, 72.9, 73.7, 75.0, 75.7, 75.9, 81.5, 83.2, 96.0, 97.7, 115.7, 123.7, 123.9, 127.9, 128.0, 128.2, 128.5, 129.7,

130.8, 136.6, 136.9, 137.6. ^{31}P NMR ($CDCl_3$, 162 MHz) δ −2.51, −1.85. MALDI-HRMS: m/z calcd for $C_{41}H_{50}N_3O_{12}PNa$ $[M+Na]^+$ 830.3024, obsd 830.3008.

*Methyl 3,4,6-Tri-*O*-acetyl-2-deoxy-2-(2,4-dinitrophenylamino)-*D*-glucopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-β-*D*-glucosaminopyranoside (13)*

Methyl glycoside **9**[22] (50 mg, 0.108 mmol) and *N*-phenyl trifluoroacetimidate **D** (90 mg, 0.140 mmol) were coevaporated three times with toluene, dried in vacuo for 1 h, and dissolved in CH_2Cl_2 (0.8 mL) and Et_2O (3.2 mL). Freshly activated acid-washed 4 molecular sieves (140 mg) were added. At −30°C, the mixture was treated with TMSOTf (3.9 μL, 22 μmol). The reaction was warmed to −10°C over 1 h, quenched with pyridine (0.1 mL), filtered through Celite (CH_2Cl_2), and concentrated. The residue was coevaporated twice with toluene and purified by flash column chromatography on silica (4:1 → 1:1 cyclohexane/EtOAc) and recycling preparative HPLC ($CHCl_3$) to afford **13** (96 mg, 92%) as a pale yellow solid (α/β-ratio: 1:2.5). R_f 0.04 (cyclohexane/EtOAc 4:1). IR (neat): 3332, 3022, 2878, 1748, 1617, 1593, 1523, 1337, 1215, 1039 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.65 (s, 0.9H), 1.71 (s, 0.9H), 1.90 (s, 2.1H), 2.00 (s, 0.9H), 2.03 (s, 2.1H), 2.06 (s, 2.1H), 2.87 (d, J = 9.7 Hz, 0.7H), 3.24–5.13 (m, 21.7H), 5.29 (t, J = 9.9 Hz, 0.3H), 5.88 (d, J = 4.0 Hz, 0.3H), 6.76–6.98 (m, 2.7H), 7.26–7.51 (m, 13.3H), 8.05 (dd, J = 9.6, 2.7 Hz, 1H), 8.26 (d, J = 8.9 Hz, 0.7H), 8.78 (d, J = 9.6 Hz, 0.3H), 9.01 (d, J = 2.7 Hz, 0.3H), 9.05 (d, J = 0.7H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 20.5, 20.5, 20.6, 20.7, 20.7, 53.4, 54.7, 57.1, 57.8, 61.3, 61.6, 67.6, 67.7, 67.9, 68.4, 68.9, 71.5, 72.5, 73.6, 74.1, 74.6, 81.5, 81.9, 82.5, 84.6, 96.4, 100.9, 104.7, 114.3, 115.8, 123.8, 124.2, 126.1, 127.1, 127.8, 128.1, 128.3, 128.5, 129.0, 130.8, 130.9, 136.5, 137.0, 137.6, 137.9, 138.1, 138.2, 138.4, 139.0, 147.3, 148.2, 169.4, 169.5, 169.6, 170.1, 170.4, 170.5. MALDI-HRMS: m/z calcd for $C_{46}H_{51}N_3O_{17}Na$ $[M+Na]^+$ 940.3111, obsd 940.3102.

Iso-*propyl (Methyl* 3-O-*Benzyl-4-*O*-levulinoyl-2-*O*-pivaloyl-*L*-idopyranosyluronate) (17)*

Thioglycoside **16**[26] (500 mg, 0.95 mmol) and tri-*tert*-butylpyrimidine (TTBP, 1.18 g, 4.8 mmol) were coevaporated twice with toluene and dissolved in CH_2Cl_2 (19 mL), freshly activated 4 molecular sieves and ^{i}PrOH (365 μL, 4.8 mmol) were added, and the mixture was stirred at rt for 15 min. At 0°C, MeSSMe (0.42 mL, 4.8 mmol) and MeOTf (0.6 mL, 4.8 mmol) were added dropwise and the reaction was stirred at rt for 10 h. Then, more ^{i}PrOH (0.72 mL, 48 mmol) was added and the reaction was stirred for an additional 3 h at rt, filtered through Celite (CH_2Cl_2), and washed with a 1:1 mixture of saturated aqueous $NaHCO_3$ and saturated aqueous $Na_2S_2O_3$ solutions. The aqueous layer was re-extracted once with CH_2Cl_2, and the combined organic phases were dried over $MgSO_4$, filtered, and concentrated. Flash column chromatography on silica gel (9:1 → 4:1, cyclohexane/EtOAc) afforded **17** (330 mg, 66%)

as a colorless oil (ratio of α/β-anomers: 8:1). R_f 0.54 (cyclohexane/EtOAc 1:1). ^{1}H NMR ($CDCl_3$, 300 MHz, only signals of α-anomer) δ 1.18–1.23 (m, 15H), 2.50–2.82 (m, 4H), 3.71 (t, J = 2.6 Hz, 1H), 3.78 (s, 3H), 3.93–4.01 (m, 1H), 4.67 (d, J = 11.7 Hz, 1H), 4.80 (d, J = 11.7 Hz, 1H), 4.87 (br., 1H), 4.93 (d, J = 2.4 Hz, 1H), 5.08 (br. s, 1H), 5.22 (t, J = 2.6 Hz, 1H), 7.26–7.38 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 14.9, 21.4, 23.2, 26.5, 27.1, 27.1, 27.9, 29.7, 29.7, 37.7, 38.7, 38.8, 52.3, 52.4, 66.4, 66.6, 67.4, 68.2, 68.5, 70.5, 72.0, 72.6, 73.5, 77.2, 82.8, 96.7, 127.4, 127.5, 127.6, 127.7, 127.8, 128.2, 128.4, 128.5, 137.2, 137.8, 168.9, 169.2, 171.6, 171.6, 177.3, 177.3, 205.8, 205.9. MALDI-HRMS: m/z calcd for $C_{27}H_{38}O_{10}Na$ $[M+Na]^+$ 545.2357, obsd 545.2358.

Iso-*propyl (Methyl* 3-O-*Benzyl-2*-O-*pivaloyl-α*-L-*idopyranosyluronate) (14)*

To a solution of **17** (255 mg, 488 μmol) in CH_2Cl_2 (4.9 mL) at rt was added pyridine (1.18 mL), AcOH (0.78 mL), and hydrazine monohydrate (47.4 μL, 976 μmol). The solution was stirred for 1.5 h at rt, quenched with acetone (1 mL), and concentrated. The residue was coevaporated twice with toluene and purified by flash column chromatography on silica gel (6:1 $\rightarrow$ 3:1, cyclohexane/EtOAc) to afford **14** (176 mg, 85%) as a colorless oil. R_f 0.63 (cyclohexane/EtOAc 1:1). $[\alpha]_D^{r.t.}$: -46.9 (c = 1.0, $CHCl_3$). IR (neat): 3505, 2973, 2934, 1739, 1456, 1370, 1279, 1210, 1104, 1049, 942 cm^{-1}. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.18–1.24 (m, 15H), 2.69 (d, J = 11.9 Hz, 1H), 3.68 (br. s, 1H), 3.79 (s, 3H), 3.96–4.06 (m, 2H), 4.58 (d, J = 11.5 Hz, 1H), 4.80 (d, J = 11.5 Hz, 1H), 4.90 (br. s, 1H), 4.94 (br. s, 1H), 5.04 (br. s, 1H), 7.27–7.35 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.4, 23.1, 23.3, 27.1, 38.8, 52.3, 53.4, 67.2, 67.8, 68.3, 68.4, 70.6, 71.6, 74.5, 97.0, 127.5, 127.7, 128.3, 137.8, 170.1, 176.7. MALDI-HRMS: m/z calcd for $C_{22}H_{32}O_8Na$ $[M+Na]^+$ 447.1989, obsd 447.1992.

Iso-*propyl 3,4,6-Tri*-O-*acetyl-2-deoxy-2-(2,4-dinitrophenylamino)*-D-*glucopyranosyl-(1→4)-(Methyl 3*-O-*Benzyl-2*-O-*pivaloyl-α*-L-*idopyranosyluronate) (15)*

L-Iduronic acid acceptor **14** (37 mg, 87 μmol) and *N*-phenyl trifluoroacetimidate **D** (114 mg, 177 μmol) were coevaporated three times with toluene and dried in vacuo for 1 h. Freshly activated acid-washed 4 molecular sieves (150 mg) were added and the mixture was dissolved in CH_2Cl_2 (5 mL). At -20°C, TMSOTf (5 μL, 27 μmol) was added. The reaction was warmed to $+5^\circ$C over 1 h, quenched with pyridine (0.1 mL), filtered through Celite (CH_2Cl_2), and concentrated. The residue was coevaporated once with toluene and purified by flash column chromatography on silica (9:1 $\rightarrow$ 3:2 cyclohexane/EtOAc) and recycling preparative HPLC ($CHCl_3$) to afford **15** (16 mg, 21%) as a pale yellow oil (ratio of α/β-anomers: 5:1). R_f 0.23 (cyclohexane/EtOAc 13:7). IR (neat): 3333, 2972, 2931, 1740, 1616, 1592, 1523, 1335, 1218, 1106, 1029 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz, only signals of α-anomer) δ 1.07–1.16 (m, 6H, $(CH_3)_2CH$),

1.14 (s, 9H, Piv), 1.67 (s, 3H, Ac), 1.96, (s, 3H, Ac), 2.05 (s, 3H, Ac), 3.82 (s, 3H, OMe), 3.86–3.91 (m, 1H, $(CH_3)_2CH$), 3.95 (td, $J = 9.9, 3.7$, H-2^2), 4.07–4.11 (m, 2H, H-3^1, H-6^2), 4.18–4.21 (m, 1H, H-5^2), 4.25 (dd, $J = 7.0, 5.3$, 1H, H-4^1), 4.31 (dd, $J = 12.4, 4.1$, 1H, H-$6'^2$), 4.32 (d, $J = 11.8$, 1H, C*H*HPh), 4.69 (d, $J = 13.3$, 1H, C*H*HPh), 4.71 (d, $J = 5.3$, 1H, H-5^1), 4.92 (dd, $J = 6.2, 4.5$, 1H, H-2^1), 5.07 (t, $J = 9.9$, 1H, H-4^2), 5.16 (d, $J = 4.5$, 1H, H-1^1), 5.26 (t, $J = 9.9$, 1H, H-3^2), 5.27 (d, $J = 4.1$, 1H, H-1^2), 6.89–7.02 (m, 5H, H_{Ar}), 8.08 (dd, $J = 9.5, 2.6$, 1H, DNP), 8.66 (d, $J = 9.7$, 1H, DNP), 8.93, (d, $J = 2.7$, 1H, DNP). ^{13}C NMR ($CDCl_3$, 100 MHz, only signals of α-anomer) δ 20.4, 20.5, 20.7, 21.8, 27.1, 38.8, 52.5, 54.9, 61.5, 67.7, 68.9, 70.5, 71.6, 71.8, 72.5, 72.9, 73.8, 77.8, 97.7, 97.8, 114.0, 124.2, 126.3, 127.3, 128.0, 129.8, 130.9, 136.7, 137.5, 147.3, 169.5, 169.6, 169.9, 170.5, 177.2. MALDI-HRMS: m/z calcd for $C_{40}H_{51}N_3O_{19}Na$ $[M+Na]^+$ 900.3009, obsd 900.3004.

Iso-*propyl 3,4,6-Tri*-O-*benzyl-2-deoxy-2-(2,4-dinitrophenylamino)*-D-*glucopyranosyl-(1→4)-(Methyl* 3-O-*Benzyl-2*-O-*pivaloyl-α*-L-*idopyranosyluronate) (18)*

L-Iduronic acid acceptor **14** (33 mg, 78 μmol) and *N*-phenyl trifluoroacetimidate **E** (122 mg, 155 μmol) were coevaporated three times with toluene and dried in vacuo for 1 h. Freshly activated acid-washed 4 molecular sieves (155 mg) were added and the mixture was dissolved in CH_2Cl_2 (4.6 mL). At -30°C, TMSOTf (4 μL, 22 μmol) was added. The reaction was warmed to -5°C over 45 min, quenched with pyridine (0.1 mL), filtered through Celite (CH_2Cl_2), and concentrated. The residue was coevaporated twice with toluene and purified by flash column chromatography on silica gel (1:0 → 4:1 cyclohexane/EtOAc) and recycling preparative HPLC ($CHCl_3$) to afford **18** (46 mg, 58%) as a yellow solid (ratio of α/β-anomers: 5:1). R_f 0.32 (cyclohexane/EtOAc 4:1). IR (neat): 3332, 2931, 1738, 1618, 1590, 1523, 1454, 1334, 1131, 1029 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.15–1.30 (m, 15H), 3.49 (s, 0.51H), 3.52–4.04 (m, 7H), 3.83 (s, 2.49H), 4.16–4.20 (m, 0.17H), 4.18 (t, $J = 7.0$ Hz, 0.83H), 4.33 (dd, $J = 7.3, 5.6$ Hz, 0.83H), 4.36–4.88 (m, 9.34H), 4.90 (br. s, 0.17H), 4.94 (br. s, 0.17H, H-1-IdoA), 5.01 (dd, $J = 6.6, 5.2$ Hz, 0.83H), 5.21 (d, $J = 5.1$ Hz, 0.83H), 5.29 (d, $J = 3.7$ Hz, 0.83H), 6.80–6.82 (m, 2H), 6.94–7.38 (m, 19H), 8.00 (dd, $J = 9.6, 2.6$ Hz, 0.83H), 8.13 (dd, $J = 9.6, 2.7$ Hz, 0.17H), 8.43 (d, $J = 8.1$ Hz, 0.17H), 8.74 (d, $J = 9.5$ Hz, 0.83H), 8.92 (d, $J = 2.7$ Hz, 0.17H), 9.06 (d, $J = 2.7$ Hz, 0.83H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.5, 21.8, 23.3, 23.3, 27.2, 27.3, 38.7, 38.8, 51.8, 52.2, 56.0, 59.3, 66.9, 67.1, 67.8, 68.5, 70.3, 71.2, 71.8, 73.0, 73.4, 74.7, 76.0, 76.2, 78.0, 78.3, 82.3, 84.0, 96.8, 97.5, 98.2, 104.4, 115.5, 116.2, 123.7, 123.9, 126.3, 126.4, 127.2, 128.1, 129.4, 129.7, 130.1, 130.6, 136.1, 136.7, 136.9, 137.0, 137.6, 137.7, 137.9, 138.0, 138.3, 148.1, 148.9, 169.5, 169.6, 177.0, 177.3. MALDI-HRMS: m/z calcd for $C_{55}H_{63}N_3O_{16}Na$ $[M+Na]^+$ 1044.4101, obsd 1044.4124.

Entry 2: Acceptor **14** (31 mg, 73 μmol) and *N*-phenyl trifluoroacetimidate **E** (115 mg, 146 μmol) were coevaporated three times with toluene and dried in vacuo for 1 h. Freshly activated acid-washed 4 molecular sieves (145 mg) were added and the mixture was dissolved in Et_2O (3.5 mL) and CH_2Cl_2 (0.9 mL). At -30°C, TMSOTf (4 μL, 22 μmol) was added. The reaction was warmed to -10°C over 45 min, quenched with pyridine (0.1 mL), filtered through Celite (CH_2Cl_2), and concentrated. The residue was coevaporated twice with toluene and purified by flash column chromatography on silica gel (1:0 $\rightarrow$ 4:1 cyclohexane/EtOAc) and recycling preparative HPLC ($CHCl_3$) to afford **18** (65 mg, 87%) as a yellow solid (ratio of α/β-anomers: 2.5:1).

Entry 3: Acceptor **14** (32 mg, 75 μmol) and trichloroacetimidate **11** (115 mg, 151 μmol) were coevaporated three times with toluene and dried in vacuo for 1 h. Freshly activated acid-washed 4 molecular sieves (150 mg) were added and the mixture was dissolved in Et_2O (3.7 mL) and CH_2Cl_2 (0.9 mL). At -29°C, TMSOTf (4 μL, 23 μmol) was added. The reaction was warmed to -10°C over 45 min, quenched with pyridine (0.1 mL), filtered through Celite (CH_2Cl_2), and concentrated. The residue was coevaporated twice with toluene and purified by flash column chromatography on silica gel (1:0 $\rightarrow$ 4:1 cyclohexane/EtOAc) and recycling preparative HPLC ($CHCl_3$) to afford **18** (44 mg, 57%) as a yellow solid (ratio of α/β-anomers: 3.5:1).

Entry 4: Acceptor **14** (39 mg, 92 μmol) and trichloroacetimidate **11** (91 mg, 119 μmol) were coevaporated three times with toluene and dried in vacuo for 1 h. Freshly activated acid-washed 4 molecular sieves (150 mg) were added and the mixture was dissolved in CH_2Cl_2 (4.2 mL). At -35°C, TMSOTf (3.3 μL, 18 μmol) was added. The reaction was warmed to -10°C over 45 min, quenched with pyridine (0.1 mL), filtered through Celite (CH_2Cl_2), and concentrated. The residue was coevaporated twice with toluene and purified by flash column chromatography on silica gel (1:0 $\rightarrow$ 4:1 cyclohexane/EtOAc) and recycling preparative HPLC ($CHCl_3$) to afford **18** (39 mg, 41%) as a yellow solid (ratio of α/β-anomers: 3.5:1).

Entry 5: Acceptor **14** (29 mg, 68 μmol) and phosphate **12** (100 mg, 124 μmol) were coevaporated three times with toluene and dried in vacuo for 1 h. Freshly activated acid-washed 4 molecular sieves (130 mg) were added and the mixture was dissolved in CH_2Cl_2 (3.9 mL). At -78°C, TMSOTf (4 μL, 22 μmol) was added. The reaction was warmed to -50°C over 30 min, quenched with pyridine (0.1 mL), filtered through Celite (CH_2Cl_2), and concentrated. The residue was coevaporated twice with toluene and purified by flash column chromatography on silica gel (1:0 $\rightarrow$ 4:1 cyclohexane/EtOAc) and recycling preparative HPLC ($CHCl_3$) to afford **18** (62 mg, 89%) as a yellow solid (ratio of α/β-anomers: 1.5:1).

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