Regioselective Acylation of 3,4-OH Free D-Glucosamines: A Rapid Access to Orthogonally Functionalized Building Blocks

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Abstract: A method for the regioselective O-acylation of 3,4-OH free D-glucosamines via stannylene acetal methodology was developed. From fully acetylated 2-*N*-trichloroacetyl-D-glucosamine, 4-OH free D-glucosamine derivatives bearing orthogonal protecting group patterns were prepared.

Key words: carbohydrates, protecting groups, regioselectivity, stannylene acetals, glycosylaminoglycans

Carbohydrate-based structures, glycans, have been recognized as key elements in a plethora of recognition events at the cellular level[1] and in numerous interactions of pathogens with an infected host.[2] While the relevance of these interactions is indisputable, their study still is severely hampered by the lack of sufficient material for in-depth studies of the underlying mechanisms at the molecular level. The rapid synthesis of complex carbohydrate structures requires not only high-yielding and stereoselective glycosylation reactions, but also an efficient and inexpensive access to the required monosaccharidic building blocks. The work presented here is focused on an efficient preparation of building blocks for the →4)-2-acetamido-2-deoxy-β-D-glucopyranosyl-(1→ motif [abbreviated as →4)-GlcNAcβ(1→; structure **1** in Figure 1]. Such 1,4-linked D-glucosamines appear as structural motifs in a variety of biologically relevant glycan structures. For example, 1,4-linked *N*-acyl-D-glucosamine derivatives appear as the carbohydrate repeating unit in bacterial peptidoglycan[3] or within the neutral core region of glycosphingolipids (e.g., in the *neolacto*-series).[4] In eukaryotic organisms the core region of N-glycosylated glycoproteins contains an *N*-acetyl-D-glucosamine dimer linked to asparagine,[5] and the glycosaminoglycan keratan sulfate is composed of repetitive →4)-GlcNAcβ(1→3)Galβ(→ dimers.[6]

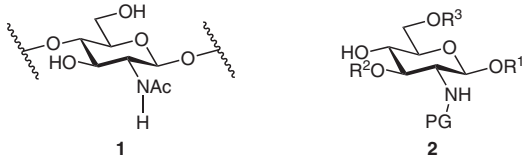

Figure 1 Structures of the 1,4-linked *N*-acetylglucosamine motif **1** and the desired building blocks of type **2**

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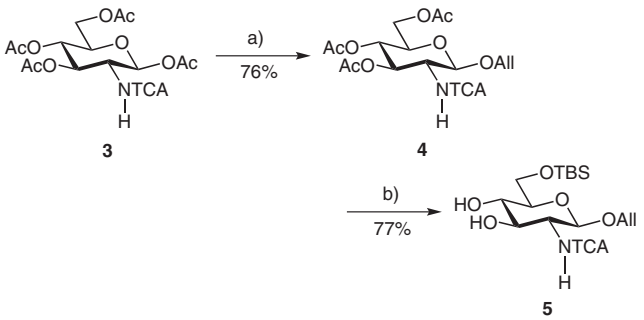
Within our current research, we required an easy access to D-glucosamine building blocks for such motifs. At first these units should function as glycosyl acceptors, while allowing rapid conversion into glycosyl donors at a later stage to access 1,2-*trans*-configured linkages. Ideally the installed protecting group pattern should also allow for the selective liberation of the hydroxy groups at C3 and C6 later on. These requirements can be consolidated into a general structure **2** (Figure 1) with the following features: (i) an N-protecting group at C2 that can participate as a neighboring group during subsequent glycosylations, (ii) the free 4-OH group functions as glycosyl acceptor, and (iii) a set of orthogonal protecting groups on the hydroxy groups at C1, C3, and C6 has been installed.

In our case the trichloroacetyl (TCA) group was used as an N-protecting group; this electron-withdrawing group is able to participate in glycosylation reactions at later stages (→1,2-*trans*-linked glycosides).[7] While the 4-OH group stayed unprotected, an orthogonal set of O-protecting groups for the remaining hydroxy groups was chosen. This consisted of the *O*-allyl group at the reducing end, an *O*-silyl ether at C6, and an *O*-acyl based group at C3 (**2** in Figure 1 with PG = TCA, R^1 = All, R^2 = acyl, R^3 = TBS).

To obtain the desired 4-OH free substitution pattern, we decided to follow an approach based on the stannylene acetal methodology.[8] The differentiation between the 3- and 4-OH groups results from the regioselective opening of a *trans*-fused stannylene acetal spanning the 3- and 4-positions of the carbohydrate ring with an electrophile (EX). This approach markedly differs from the sequence usually employed to access 4-OH free building blocks



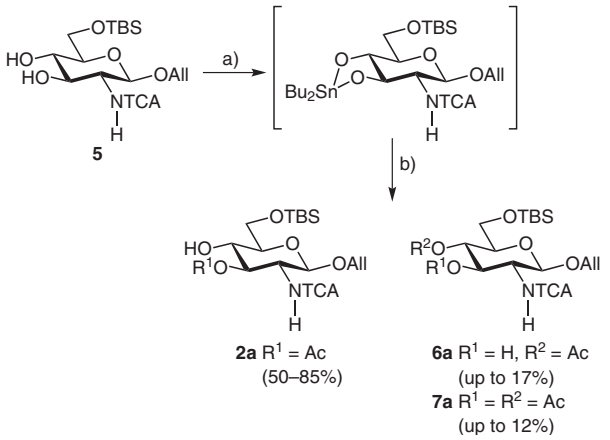
Scheme 1 Synthesis of the partially protected diol **5** from the fully acylated precursor **3**. *Reaction conditions:* (a) $FeCl_3$, drierite, allyl alcohol, MeCN, r.t., overnight, 76%; (b) 1. NaOMe (~0.02 M), MeOH, r.t., 2 h; 2. TBSCl, imidazole, DMF, 0 °C to r.t., overnight, 77% over two steps.

from 3,4,6-OH free triols[9] and, to our knowledge, this use of the stannylene acetal method on D-glucosamine derivatives has no literature precedent.

Our synthesis of the 4-OH free glucosamine derivatives **2** started from known, fully protected *N*-trichloroacetyl derivative **3** (Scheme 1).[7a,c,10] Compound **3** was transformed into the known *O*-allyl glycoside **4**[7d] by the action of iron(III) chloride in the presence of allyl alcohol.[11]

Afterwards fully protected **4** was partially deprotected under Zemplén conditions[12] and the primary alcohol (6-OH group) in the resultant triol was immediately O-silylated to afford the diol **5** in 58% overall yield from **3** (Scheme 1).

With diol **5** available in sufficient amounts, we explored the formation and the regioselective opening of the 3,4-stannylene acetal with electrophiles (Scheme 2). In a first series of experiments, different conditions for forming the stannylene acetal and different acetylating agents were investigated.



Scheme 2 Regioselective acylation of diol **5** using the stannylene acetal method. *Reaction conditions:* (a) Bu_2SnO, benzene, reflux, 1 h; (b) EX, benzene, r.t., 1 h.

The direct treatment of **5** with acetyl chloride without addition of the tin reagent afforded the monoacetylated product in 54% yield (Table 1, entry 1). When the stannylene acetal was formed, the monoacetylation, leading to **2a** and **6a**, proceeded in good to excellent yields under all conditions studied (Table 1, entries 2–5). The formation of the acetal proceeded rapidly and usually was finished after one hour. The best yield (94%) was obtained using stoichiometric amounts of acetic anhydride as the acetylating agent. In all experiments high regioselectivity (>9:1) was observed. The regioselective acetylation of the diol **5** in the tin-free experiment can perhaps be explained by the differing nucleophilicity of the 3- and 4-OH groups of D-glucosamine.[9c,13] Other regioselective preparations of 4-OH free D-glucosamine derivatives by selective protection of the 3-OH group have been previously reported.[14]

Table 1 Regioselective O-Acetylation of Diol **5**[a]

Entry	EX (equiv)	Yield (%)		Regioselectivity[d]
		2a + **6a**[b,c]	**7a**[b]	**2a**/**6a**
1[e,f]	AcCl (1.0), Et_3N (1.0), overnight	54	6	
2[g]	AcCl (1.0), 1 h	72	10	
3	AcCl (1.0), 1 h	71	12	>9:1
4	AcCl (1.5), 1 h	80	–	
5	Ac_2O (1.0), 1 h	94	–	

[a] Stannylene acetal formation: Bu_2SnO (1.02 equiv), reflux, overnight (entry 2) or 1.5 h (entries 3–5).
[b] Yield after chromatography.
[c] Yield for both diastereoisomers.
[d] Determined by ^1H NMR.
[e] Acetylation performed without addition of Bu_2SnO.
[f] Starting material (29%) recovered.
[g] Starting material (8%) recovered.

Based on these promising results, the scope of the reaction with regard to the electrophile employed in the stannylene acetal opening was investigated in a second series of experiments (Table 2).

Table 2 Regioselective O-Acylation of Diol **5**[a]

Entry	EX (equiv)	Yield (%)		Regioselectivity[d]
		2 + **6**[b,c]	**7**[b]	**2**/**6**
1[e]	CA_2O[f] (1.0), 1 h	68 **2b** R^1 = CA	–	~9:1
2	Lev_2O[f] (2.5), 1.5 h	74 **2c** R^1 = Lev	–	>9:1
3	PivCl[f] (1.0), 1 h	58 **2d** R^1 = Piv	–	~9:1
4	BzCl[f] (1.0), 1 h	68 **2e** R^1 = Bz	–	~3:1[g]

[a] Stannylene acetal formation: Bu_2SnO (1.02 equiv), reflux, 1 h.
[b] Yield after chromatography.
[c] Yield for both diastereoisomers.
[d] Determined by ^1H NMR.
[e] Starting material (31%) recovered.
[f] CA = chloroacetyl; Lev = levulinoyl (4-oxopentanoyl); Piv = pivaloyl; Bz = benzoyl.
[g] Regioisomers not separated.

To our delight, all electrophiles investigated were readily incorporated and afforded the acylated compounds in synthetically useful yields (Table 2, entries 1–4). However, the high 3-OH/4-OH regioselectivity already observed for the formation of **2a** was not retained in all cases. Although the formation of the bulky monopivaloyl derivatives afforded essentially the 4-OH free compound **2d**, albeit obtained with the lowest yield (entry 3), the sterically less encumbered benzoyl derivative **2e** was only formed as a 3:1 mixture of the regioisomers (entry 4). Especially note-

worthy is the introduction of the 3-*O*-chloroacetyl[15] and the 3-*O*-levulinoyl[16] residues (entries 1 and 2), as they are susceptible to cleavage reactions distinctive from the usual nucleophilic cleavage of *O*-acyl protecting groups. Thus an additional orthogonal dimension could be installed in the protecting group schemes of **2b** and **2c**.

In conclusion, we have developed an efficient access to highly functionalized D-glucosamine derivatives of the general structure **2** in five steps, with three purifications required, from known starting material **3**. The key step in this sequence, electrophilic opening of the *trans*-fused 3,4-*O*-stannylene acetal, proceeds with high regioselectivity to afford the 4-OH free compounds. The versatile incorporation of different 3-*O*-acyl groups permits the installation of fully orthogonal sets of protecting groups.

All moisture-sensitive reactions were carried out under O_2-free argon or N_2 using oven-dried glassware and a vacuum line. Flash column chromatography used Merck silica gel 60 (230–400 mesh) and TLC used commercially available Merck F_{254} pre-coated sheets. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker Cryospek WM-250 or an AM 400 with reported relative residual solvent protons or TMS as internal standard. Assignments of proton and carbon chemical shifts were carried out with the aid of 2D NMR experiments: COSY or HMQC. Multiplicities are reported as they appear in the spectra. FAB and HRMS (FAB from 3-NBA) were recorded with a Finnigan MAT-90 machine. Optical rotations were recorded with a Perkin-Elmer 241 polarimeter (Na_D line at 589 nm), and specific optical rotations $[\alpha]_D^{20}$ are given in units of 10^{-1} deg cm^2 g^{-1}.

Regioselective Protection of 3,4-OH Free Glucosamine Derivatives; General Procedure

Diol **5** (800 mg, 1.67 mmol, 1.0 equiv) was dissolved in benzene (20 mL) and Bu_2SnO (426 mg, 1.71 mmol, 1.02 equiv) was added. The mixture was heated to reflux for 1.5 h using a Dean–Stark apparatus, solvent (3 × 3 mL) was removed from the Dean–Stark trap. After cooling to r.t., the obtained suspension was transferred into a graduated cylinder, diluted with benzene to 16 mL and divided into four aliquots. The appropriate acylating agent was added to each flask and the mixture was stirred at r.t. The reaction was monitored by TLC (silica gel; hexanes–EtOAc, 1:1) and upon complete conversion the solvent was removed under reduced pressure. The residue was purified by flash chromatography (silica gel; hexanes–EtOAc, 3:1 to 1:1) to afford mixtures of the diastereoisomers containing primarily the 3-O-monoacylated compound.

Allyl 3-*O*-Acetyl-6-*O*-*tert*-butyldimethylsilyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (2a)

Compound **2a** was prepared according to the general procedure from diol **5** and Ac_2O (39 μL, 43 mg, 0.42 mmol); stirring was continued for 1 h. The product was obtained as a white solid (205 mg, 0.39 mmol, 94%; **2a**/**6a** >9:1).

R_f = 0.30 (silica gel; hexanes–EtOAc, 2:1).

$[\alpha]_D^{20}$ –42.5 (*c* 1.1, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.07 (s, 3 H, OTBS), 0.08 (s, 3 H, OTBS), 0.87 (s, 9 H, OTBS), 2.07 (s, 3 H, OAc), 3.43 (bs, 1 H, 4-OH), 3.45 (ddd, ^3J = 9.4, 5.9, 5.0 Hz, 1 H, 5-H), 3.75 (t, ^3J = 9.4 Hz, 1 H, 4-H), 3.83 (dd, ^2J = 10.5 Hz, ^3J = 5.9 Hz, 1 H, 6-H$_a$), 3.93 (dd, ^2J = 10.5 Hz, ^3J = 5.0 Hz, 1 H, 6-H$_b$), 3.96 (ddd, ^3J = 10.5, 9.1, 8.3 Hz, 1 H, 2-H), 4.02 (ddt, ^2J = 13.1 Hz, ^3J = 6.2 Hz, ^4J = 1.4 Hz, 1 H, OAll), 4.29 (ddt, ^2J = 13.1 Hz, ^3J = 4.9 Hz, ^4J = 1.5 Hz, 1 H, OAll), 4.56 (d, ^3J = 8.3 Hz, 1 H, 1-H), 5.14 (dq, $^2J \approx {}^4J$ = 1.4 Hz, ^3J = 10.5 Hz, ^4J = 1.3 Hz, 1 H, OAll), 5.22 (dd, ^3J = 10.5, 9.4 Hz, 1 H, 3-H), 5.23 (dq, $^2J \approx {}^4J$ = 1.6 Hz, ^3J = 17.2 Hz, 1 H, OAll), 5.79 (dddd, ^3J = 17.2, 10.5, 6.2, 4.9 Hz, 1 H, OAll), 7.02 (d, ^3J = 9.1 Hz, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –5.3 (2 C, OTBS), 18.4 (OTBS), 21.1 (OAc), 26.0 (OTBS), 55.7 (C2), 64.8 (C6), 70.1 (OAll), 71.7 (C4), 74.4 (C5), 74.7 (C3), 92.7 (*C*Cl_3), 99.8 (C1), 118.0 (OAll), 133.6 (OAll), 162.3, 172.1.

MS (FAB): *m*/*z* (%) = 546 (22) [$^{35}Cl^{37}Cl_2M$ + Na]$^+$, 544 (61) [$^{35}Cl_2{}^{37}ClM$ + Na]$^+$, 542 (57) [$^{35}Cl_3M$ + Na]$^+$, 466 (15) [$^{35}Cl^{37}Cl_2M$ – OAll]$^+$, 464 (43) [$^{35}Cl_2{}^{37}ClM$ – OAll]$^+$, 462 (41) [$^{35}Cl_3M$ – OAll]$^+$, 406 (12) [$^{35}Cl^{37}Cl_2M$ – OAll – AcOH]$^+$, 404 (28) [$^{35}Cl_2{}^{37}ClM$ – OAll – AcOH]$^+$, 402 (19) [$^{35}Cl_3M$ – OAll – AcOH]$^+$, 117 (100); $C_{19}H_{32}Cl_3NO_7Si$ (520.9).

HRMS (FAB): *m*/*z* [$^{35}Cl_3M$ + Na]$^+$ calcd for $C_{19}H_{32}{}^{35}Cl_3NNaO_7Si$: 542.0911; found: 542.0913.

Allyl 6-*O*-*tert*-Butyldimethylsilyl-3-*O*-chloroacetyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (2b)

Compound **2b** was prepared according to the general procedure from diol **5** and chloroacetic anhydride (71 mg, 0.42 mmol); stirring was continued for 1 h. The product was obtained as a colorless oil (158 mg, 0.28 mmol, 68%; **2b**/**6b** ~9:1); some starting material (62 mg, 0.13 mmol, 31%) was recovered.

R_f = 0.51 (silica gel; hexanes–EtOAc, 2:1).

$[\alpha]_D^{20}$ –42.2 (*c* 1.0, $CHCl_3$).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.06 (s, 3 H, OTBS), 0.07 (s, 3 H, OTBS), 0.86 (s, 9 H, OTBS), 3.45 (dt, ^3J = 9.9, 5.0 Hz, 1 H, 5-H), 3.71–4.13 (m, 7 H, 2 OCA, 4-OH, 6-H$_{a/b}$, 2-H, OAll), 3.76 (dd, ^3J = 9.2, 9.9 Hz, 1 H, 4-H), 4.28 (ddt, ^2J = 13.1 Hz, ^3J = 5.0 Hz, ^4J = 1.5 Hz, 1 H, OAll), 4.64 (d, ^3J = 8.3 Hz, 1 H, 1-H), 5.13 (dq, $^2J \approx {}^4J$ = 1.4 Hz, ^3J = 10.5 Hz, 1 H, OAll), 5.22 (dq, $^2J \approx {}^4J$ = 1.6 Hz, ^3J = 17.2 Hz, 1 H, OAll), 5.44 (dd, ^3J = 10.7, 9.2 Hz, 1 H, 3-H), 5.82 (dddd, ^3J = 17.2, 10.5, 6.0, 5.0 Hz, 1 H, OAll), 7.23 (d, ^3J = 9.3 Hz, 1 H, NH).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = –5.3 (2 C, OTBS), 18.4 (OTBS), 26.0 (OTBS), 41.0 (OCA), 55.8 (C2), 64.2 (C6), 70.3 (OAll), 71.1 (C4), 74.5 (C5), 76.9 (C3), 92.5 (*C*Cl_3), 99.4 (C1), 118.0 (OAll), 133.5 (OAll), 162.7, 168.7.

MS (FAB): *m*/*z* (%) = 578 (2) [$^{35}Cl_3{}^{37}ClM$ + Na]$^+$, 576 (1) [$^{35}Cl_4M$ + Na]$^+$, 500 (16) [$^{35}Cl_2{}^{37}Cl_2M$ – OAll]$^+$, 498 (26) [$^{35}Cl_3{}^{37}ClM$ – OAll]$^+$, 496 (18) [$^{35}Cl_4M$ – OAll]$^+$, 442 (12) [$^{35}Cl_2{}^{37}Cl_2M$ – TBS]$^+$, 440 (21) [$^{35}Cl_3{}^{37}ClM$ – TBS]$^+$, 438 (14) [$^{35}Cl_4M$ – TBS]$^+$, 406 (8) [$^{35}Cl^{37}Cl_2M$ – OAll – CAOH]$^+$, 404 (26) [$^{35}Cl_2{}^{37}ClM$ – OAll – CAOH]$^+$, 402 (24) [$^{35}Cl_3M$ – OAll – CAOH]$^+$, 117 (100); $C_{19}H_{31}Cl_4NO_7Si$ (555.4).

HRMS (FAB): *m*/*z* [$^{35}Cl_4M$ + Na]$^+$ calcd for $C_{19}H_{31}{}^{35}Cl_4NNaO_7Si$: 576.0522; found: 576.0524.

Allyl 6-*O*-*tert*-Butyldimethylsilyl-2-deoxy-3-*O*-levulinoyl-2-trichloroacetamido-β-D-glucopyranoside (2c)

Compound **2c** was prepared according to the general procedure from diol **5** and levulinic anhydride[16a] (134 mg, 0.63 mmol); stirring was continued for 1 h. Additional anhydride (89 mg, 0.42 mmol) was added and stirring was continued for 30 min. The product was obtained as a colorless oil (179 mg, 0.31 mmol, 74%; **2c**/**6c** >9:1).

R_f = 0.23 (silica gel; hexanes–EtOAc, 2:1).

$[\alpha]_D^{20}$ –32.4 (*c* 1.1, $CHCl_3$).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.06 (s, 3 H, OTBS), 0.06 (s, 3 H, OTBS), 0.87 (s, 9 H, OTBS), 2.13 (s, 3 H, OAc), 2.40–2.62 (m, 2 H, 2 OLev), 2.67–2.80 (m, 2 H, OLev), 3.45 (dt, ^3J = 9.2, 4.5 Hz, 1 H, 5-H), 3.54 (d, ^3J = 3.6 Hz, 1 H, 4-OH), 3.69 (td, ^3J = 9.2, 3.6 Hz, 1 H, 4-H), 3.85–3.88 (m, 2 H, 6-H$_{a/b}$), 3.93 (m, 1 H, 2-H), 4.02 (ddt, ^2J = 13.2 Hz, ^3J = 6.0 Hz, ^4J = 1.4 Hz, 1 H, OAll), 4.28 (ddt, ^2J = 13.1 Hz, ^3J = 4.9 Hz, ^4J = 1.5 Hz, 1 H, OAll), 4.59 (d, ^3J = 8.3

Hz, 1 H, 1-H), 5.11 (dq, $^2J \approx {}^4J$ = 1.3 Hz, ^3J = 10.5 Hz, 1 H, OAll), 5.22 (dq, $^2J \approx {}^4J$ = 1.7 Hz, ^3J = 17.3 Hz, ^4J = 1.7 Hz, 1 H, OAll), 5.27 (dd, ^3J = 10.7, 8.9 Hz, 1 H, 3-H), 5.80 (dddd, ^3J = 17.3, 10.5, 5.9, 5.0 Hz, 1 H, OAll), 7.23 (d, ^3J = 9.2 Hz, 1 H, NH).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = –5.3 (OTBS), –5.2 (OTBS), 18.4 (OTBS), 26.0 (OTBS), 28.4 (OLev), 29.9 (OLev), 38.3 (OLev), 55.6 (C2), 63.7 (C6), 69.9 (OAll), 70.5 (C4), 75.1 (C5), 75.5 (C3), 92.7 (*C*Cl_3), 99.5 (C1), 117.6 (OAll), 133.7 (OAll), 162.3, 173.6, 207.6.

MS (FAB): *m/z* (%) = 600 (2) [$^{35}Cl_2{}^{37}ClM$ + Na]$^+$, 598 (1) [$^{35}Cl_3M$ + Na]$^+$, 522 (8) [$^{35}Cl^{37}Cl_2M$ – OAll]$^+$, 520 (21) [$^{35}Cl_2{}^{37}ClM$ – OAll]$^+$, 518 (22) [$^{35}Cl_3M$ – OAll]$^+$, 406 (6) [$^{35}Cl^{37}Cl_2M$ – OAll – LevOH]$^+$, 404 (24) [$^{35}Cl_2{}^{37}ClM$ – OAll – LevOH]$^+$, 402 (24) [$^{35}Cl_3M$ – OAll – LevOH]$^+$, 117 (43), 99 (100); $C_{22}H_{36}Cl_3NO_8Si$ (577.0).

HRMS (FAB): *m/z* [$^{35}Cl_3M$ + Na]$^+$ calcd for $C_{22}H_{36}{}^{35}Cl_3NNaO_8Si$: 598.1173; found: 598.1178.

Allyl 6-*O*-*tert*-Butyldimethylsilyl-2-deoxy-3-*O*-pivaloyl-2-trichloroacetamido-β-D-glucopyranoside (2d)

Compound **2d** was prepared according to the general procedure from diol **5** and pivaloyl chloride (51 μL, 50 mg, 0.42 mmol); stirring was continued for 2 h. As the reaction had not run to completion, stirring was continued overnight. The product was obtained as clear syrup (137 mg, 0.24 mmol, 58%; **2d/6d** ~9:1).

R_f = 0.51 (silica gel; hexanes–EtOAc, 2:1).

$[\alpha]_D{}^{20}$ –35.3 (*c* 1.2, $CHCl_3$).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.08 (s, 3 H, OTBS), 0.09 (s, 3 H, OTBS), 0.89 (s, 9 H, OTBS), 1.19 (s, 9 H, OPiv), 3.27 (bs, 1 H, 4-OH), 3.45 (dt, ^3J = 9.6, 5.1 Hz, 1 H, 5-H), 3.72 (dd, ^3J = 9.2, 9.6 Hz, 1 H, 4-H), 3.87–3.90 (m, 2 H, 6-$H_{a/b}$), 3.97–4.10 (m, 2 H, 2-H, OAll), 4.31 (ddt, ^2J = 13.2 Hz, ^3J = 4.9 Hz, ^4J = 1.5 Hz, 1 H, OAll), 4.59 (d, ^3J = 8.3 Hz, 1 H, 1-H), 5.14 (dq, $^2J \approx {}^4J$ = 1.5 Hz, ^3J = 10.4 Hz, 1 H, OAll), 5.22 (dq, $^2J \approx {}^4J$ = 1.7 Hz, ^3J = 17.3 Hz, 1 H, OAll), 5.37 (dd, ^3J = 10.7, 9.2 Hz, 1 H, 3-H), 5.82 (dddd, ^3J = 17.3, 10.4, 6.1, 5.0 Hz, 1 H, OAll), 7.18 (d, ^3J = 9.6 Hz, 1 H, NH).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = –5.3 (2 C, OTBS), 18.4 (OTBS), 26.0 (OTBS), 27.2 (OPiv), 39.1 (OPiv), 55.7 (C2), 64.5 (C6), 70.1 (OAll), 71.7 (C4), 74.4 (C3), 74.8 (C5), 92.6 (*C*Cl_3), 99.8 (C1), 117.8 (OAll), 133.6 (OAll), 162.2, 179.7.

MS (FAB): *m/z* (%) = 588 (1) [$^{35}Cl^{37}Cl_2M$ + Na]$^+$, 586 (3) [$^{35}Cl_2{}^{37}ClM$ + Na]$^+$, 584 (3) [$^{35}Cl_3M$ + Na]$^+$, 508 (22) [$^{35}Cl^{37}Cl_2M$ – OAll]$^+$, 506 (51) [$^{35}Cl_2{}^{37}ClM$ – OAll]$^+$, 504 (50) [$^{35}Cl_3M$ – OAll]$^+$, 406 (18) [$^{35}Cl^{37}Cl_2M$ – OAll – PivOH]$^+$, 404 (49) [$^{35}Cl_2{}^{37}ClM$ – OAll – PivOH]$^+$, 402 (50) [$^{35}Cl_3M$ – OAll – PivOH]$^+$, 117 (100); $C_{22}H_{38}Cl_3NO_7Si$ (563.0).

HRMS (FAB): *m/z* [$^{35}Cl_3M$]$^+$ calcd for $C_{22}H_{38}{}^{35}Cl_3NO_7Si$: 562.1561; found: 562.1564.

Allyl 3-*O*-Benzoyl-6-*O*-*tert*-butyldimethylsilyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (2e)

Compound **2e** was prepared according to the general procedure from diol **5** and BzCl (48 μL, 59 mg, 0.42 mmol); stirring was continued for 1 h. After chromatography the product was obtained as a mixture of the regioisomers (163 mg, 0.28 mmol, 68%; **2e/6e** ~3:1), that was not further purified.

R_f = 0.49 (silica gel; hexanes–EtOAc, 2:1).

^{1}H NMR (250 MHz, $CDCl_3$): δ = 4.71 (d, ^3J = 8.3 Hz, 1 H, 1-H **2e**), 4.92 (d, ^3J = 8.3 Hz, 1 H, 1-H **6e**).

MS (FAB): *m/z* (%) = 608 (1) [$^{35}Cl^{37}Cl_2M$ + Na]$^+$, 606 (3) [$^{35}Cl_2{}^{37}ClM$ + Na]$^+$, 604 (3) [$^{35}Cl_3M$ + Na]$^+$, 528 (6) [$^{35}Cl^{37}Cl_2M$ – OAll]$^+$, 526 (13) [$^{35}Cl_2{}^{37}ClM$ – OAll]$^+$, 524 (12) [$^{35}Cl_3M$ – OAll]$^+$, 406 (5) [$^{35}Cl^{37}Cl_2M$ – OAll – BzOH]$^+$, 404 (16) [$^{35}Cl_2{}^{37}ClM$ – OAll – BzOH]$^+$, 402 (16) [$^{35}Cl_3M$ – OAll – BzOH]$^+$, 117 (27), 105 (100); $C_{24}H_{34}Cl_3NO_7Si$ (583.0).

HRMS (FAB): *m/z* [$^{35}Cl_3M$ + Na]$^+$ calcd for $C_{24}H_{34}{}^{35}Cl_3NNaO_7Si$: 604.1068; found: 604.1063.

Allyl 6-*O*-*tert*-Butyldimethylsilyl-2-deoxy-2-trichloroacetamido-β-D-glucopyranoside (5)

Fully protected glucosamine **4** (610 mg, 1.24 mmol) was dissolved in MeOH (5 mL) and Na (3 mg, 0.12 mmol) was added. The soln was stirred at r.t. for 2 h. The mixture was neutralized with Lewatite ion exchange resin (H^+ form), the mixture was filtered through Celite and the volatiles were removed. The resulting residue was dissolved under an argon atmosphere in anhyd DMF (3 mL) and cooled in an ice bath. Imidazole (169 mg, 2.49 mmol) and TBSCl (206 mg, 1.37 mmol) were added, the mixture slowly came to r.t. and was stirred overnight. The mixture was diluted with H_2O (40 mL) and extracted with EtOAc (3 × 30 mL). The combined organic layers were successively washed with brine, sat. aq NH_4Cl, sat. aq $NaHCO_3$, and brine (40 mL each), dried (Na_2SO_4) and the solvent was removed under reduced pressure. The residue was purified by flash column chromatography (silica gel; hexanes–EtOAc, 1:1) to afford the product as an off-white solid (464 mg, 0.97 mmol, 77%).

R_f = 0.35 (silica gel; hexanes–EtOAc, 1:1).

$[\alpha]_D{}^{20}$ –37.4 (*c* 1.1, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.07 (s, 3 H, OTBS), 0.08 (s, 3 H, OTBS), 0.88 (s, 9 H, OTBS), 3.37 (dt, ^3J = 9.8, 5.2 Hz, 1 H, 5-H), 3.47 (ddd, ^3J = 10.5, 8.3, 7.0 Hz, 1 H, 2-H), 3.52 (dd, ^3J = 9.8, 8.6 Hz, 1 H, 4-H), 3.78–3.91 (bs, 2 H, 2 OH), 3.87–3.89 (m, 2 H, 6-$H_{a/b}$), 3.98 (dd, ^3J = 10.5, 8.6 Hz, 1 H, 3-H), 4.04 (ddt, ^2J = 12.8 Hz, ^3J = 6.4 Hz, ^4J = 1.4 Hz, 1 H, OAll), 4.29 (ddt, ^2J = 12.8 Hz, ^3J = 5.2 Hz, ^4J = 1.4 Hz, 1 H, OAll), 4.72 (d, ^3J = 8.3 Hz, 1 H, 1-H), 5.16 (dq, $^2J \approx {}^4J$ = 1.3 Hz, ^3J = 10.4 Hz, 1 H, OAll), 5.24 (dq, $^2J \approx {}^4J$ = 1.6 Hz, ^3J = 17.2 Hz, ^4J = 1.5 Hz, 1 H, OAll), 5.82 (dddd, ^3J = 17.2, 10.4, 6.4, 5.2 Hz, 1 H, OAll), 7.16 (d, ^3J = 7.0 Hz, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = –5.2 (2 C, OTBS), 18.5 (OTBS), 26.1 (OTBS), 58.8 (C2), 64.5 (C6), 70.3 (OAll), 73.1 (C3), 73.8 (C4), 74.7 (C5), 92.7 (*C*Cl_3), 98.8 (C1), 118.4 (OAll), 133.6 (OAll), 162.8.

MS (FAB): m/z (%) = 504 (3) [$^{35}Cl^{37}Cl_2M$ + Na]$^+$, 502 (13) [$^{35}Cl_2{}^{37}ClM$ + Na]$^+$, 500 (11) [$^{35}Cl_3M$ + Na]$^+$, 424 (22) [$^{35}Cl^{37}Cl_2M$ – OAll]$^+$, 422 (86) [$^{35}Cl_2{}^{37}ClM$ – OAll]$^+$, 420 (82) [$^{35}Cl_3M$ – OAll]$^+$, 406 (17) [$^{35}Cl^{37}Cl_2M$ – OAll – H_2O]$^+$, 404 (40) [$^{35}Cl_2{}^{37}ClM$ – OAll – H_2O]$^+$, 402 (35) [$^{35}Cl_3M$ – OAll – H_2O]$^+$, 366 (9) [$^{35}Cl^{37}Cl_2M$ – TBS]$^+$, 364 (34) [$^{35}Cl_2{}^{37}ClM$ – TBS]$^+$, 362 (36) [$^{35}Cl_3M$ – TBS]$^+$, 117 (100); $C_{17}H_{30}Cl_3NO_6Si$ (478.9).

HRMS (FAB): *m/z* [$^{35}Cl_3M$]$^+$ calcd for $C_{17}H_{30}{}^{35}Cl_3NO_6Si$: 478.0986; found: 478.0983.

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