A Short Synthetic Route to β-*C*-Glycosides of *N*-Acetylglucosamine

Stéphanie Rat, Stéphanie Norsikian*

Laboratoire de Chimie Organique Multifonctionnelle, UMR CNRS-UPS 8614 'Glycochimie Moléculaire', Bât. 420, Université Paris Sud, 91405 Orsay Cedex, France
Fax +33(1)69154715; E-mail: stephnorsikian@icmo.u-psud.fr
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Abstract: A short and efficient process is described for the synthesis of protected and unprotected 1-formyl-*C*-glycosides of *N*-acetylglucosamine.

Key words: carbohydrates, glycosides, aldehydes, oxidations, enols

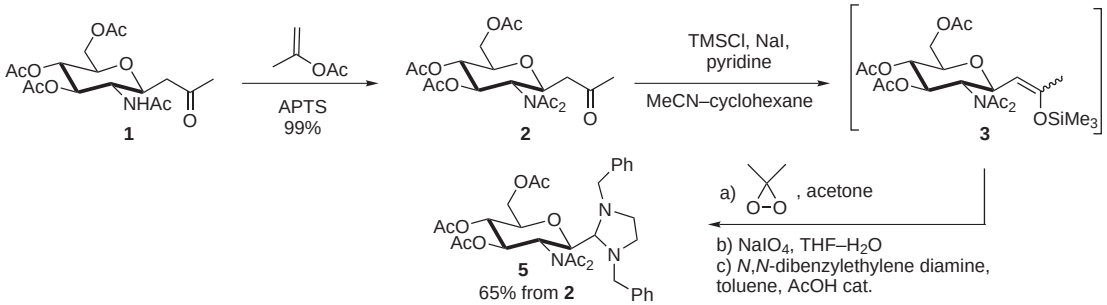
C-Glycosides, in which the *exo*-anomeric oxygen atom is replaced by a methylene group, have been the subject of considerable interest in carbohydrate chemistry and biochemistry.[1] Since they are stable to acid-, base-, and enzymatic-catalyzed hydrolysis, they can serve as analogues for biological recognition studies or as biologically active agents. Despite structural investigations that revealed notable conformational differences between the natural and unnatural glycosides,[2] a number of studies have shown that the biological properties of *C*-glycoside are retained and sometimes are even superior.[1e,3] Of particular interest is the synthesis of *C*-glycoside compounds of GlcNAc. Indeed, amino sugars are widely distributed in biological systems and are fundamental constituents of glycoproteins, a class of natural products with crucial roles in biological recognition phenomena.[4] Efficient methods for the construction of *C*-glycoside compounds of GlcNAc are therefore necessary. One way for achieving the formation of C–C bonds at the anomeric position, is the coupling between 1-formyl-*C*-glycosides and another sugar moiety or an aglycone residue.[5] Thus, an efficient protocol for incorporating a formyl group at the anomeric position of GlcNAc derivatives may serve as a tool toward the synthesis of more complex 2-amino-*C*-glycosides or *C*-disaccharides of biological relevance.

The preparation of 1-formyl-*C*-glycosides of 2-amino sugars has proven to be difficult and consequently, relatively few methods have been reported.[6] Recently, we have described a convenient route to 1-formyl-β-D-glucopyranosides based on the utilisation of 1-*C*-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyl)-propane-2-one.[7] Indeed, after enolization of the ketone and oxidation of the double bond, we could access various protected and unprotected 1-formyl-*C*-glucopyranosides.

In this letter, we wish to report the extension of this methodology to the preparation of highly-coveted GlcNAc derivatives from 1-*C*-(2-*N*-acetamido-2-deoxy-3,4,6-tri-*O*-acetyl-β-D-glucopyranosyl)-propane-2-one (**1**), which can be easily synthesized in only two steps from *N*-acetyl-D-glucosamine and in large scale.[8]

In the first instance, the enolization of the ketone **1** was studied. However, under various conditions, no reaction was observed. A second acetate group was then introduced onto the nitrogen center by treating the compound **1** with isopropenyl acetate in the presence of APTS to afford the *N*,*N*-diacetate derivative **2** in 99% yield (Scheme 1).[9]

We first carried out the enolization reaction of the ketone **2** using the conditions that we described for the D-glucose series. With Me_3SiCl–NaI–pyridine reagent, the reaction was performed at 52 °C in a mixture of MeCN–pentane. Since the reaction was not complete, we replaced pentane by cyclohexane and the reaction was carried out at 70 °C overnight. In this case, conversion was observed (according to ^1H NMR spectra) and the reaction led only to the thermodynamic compound **3** as a mixture of *E*/*Z* stereoisomers.



Scheme 1

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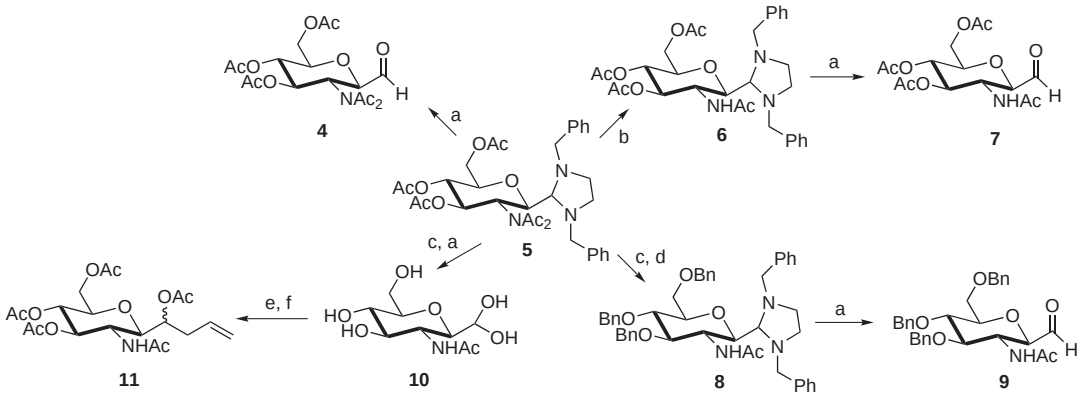

Scheme 2 *Reagents and conditions*: (a) Dowex H^+ resin, H_2O–THF; (b) $NH_2NH_2{\cdot}H_2O$, CH_2Cl_2 (**6**, 88%); (c) MeONa, MeOH (d) NaH, BnBr, DMF (**8**, 75%); (e) allylbromide, In, H_2O–THF; (f) Ac_2O, pyridine (**11**, 87% from **5**).

The resulting enoxysilane **3** was then directly engaged (without purification) in the oxidation reaction using a freshly prepared solution of dimethyldioxirane.[10] Further treatment with sodium metaperiodate in THF–water provided the aldehyde **4**, which was converted for storage into the aminal **5** in 65% overall yield from **2**.[11] Indeed, the aldehyde **4** can be regenerated by simple treatment with Dowex-H^+ resin and can be used directly without further purification (Scheme 2).[12] In order to achieve the synthesis of the aldehyde **7**, the aminal **5** was treated with hydrazine monohydrate in a mixture of MeOH–THF as described by Burk et al.[13] However, using theses conditions, some decomposition occurred and the aminal **6** was obtained in a modest 54% yield. In contrast, performing the reaction in pure CH_2Cl_2 allowed us to obtain the aminal **6** in 88% yield.[14] The deprotection of the aminal function with Dowex H^+ resin led quantitatively to **7**, which can be used without purification.[15]

The aminal **5** can also serve as a precursor of other aldehydes such as the benzylated aldehyde **9** and the free aldehyde **10**. Indeed, after deacetylation of **5** (MeONa in MeOH), a benzylation step carried out with NaH in DMF produced **8** in 75% yield over two steps.[16] Further treatment of **8** with Dowex H^+ resin gave the desired aldehyde **9** quantitatively.[17] Finally, the synthesis of free **10** was achieved after deprotection of the alcohols followed directly by removal of the aminal function. Compound **10** was found to be rather unstable and was not isolated but for proof of efficiency it was allowed to react with allylbromide in the presence of indium in a mixture of THF–water (1:1). After acetylation of the reaction mixture, the allylated compound **11**[18] was obtained as a mixture of diastereoisomers (75:25) in 87% yield over four steps.

In summary, we have reported an efficient protocol for the installation of a formyl group at the anomeric position of *N*-acetylglucosamine. From 1-*C*-[2′-(*N*-acetamido)-2′-deoxy-3′,4′,6′-tri-*O*-acetyl-β-D-glucopyranosyl]-propane-2-one, only a few steps are required to access synthetically useful protected or unprotected 2-(*N*-acetamido)-2-deoxy-1-formyl-β-D-glucopyranosides in 48–64% yields. Further applications of the above method for the synthesis of more complex 2-amino-*C*-glycosides or *C*-disaccharides of biological relevance will be presented in due course.

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References and Notes

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(9) **Preparation of 1-(2′-*N*-Acetylacetamido)-2′-deoxy-3′,4′,6′-tri-*O*-acetyl-β-D-glucopyranosyl)propane-2-one (2).**

To a solution of **1** (1.16 g, 3 mmol) in isopropenyl acetate (35 mL) was added *p*-TSA (0.27 g, 1.4 mmol, 0.47 equiv). After stirring for 5 h at 65 °C, the reaction mixture was cooled to r.t. before addition of Et_3N (8 mL). After evaporation of the solvents under reduced pressure, the crude residue was purified by flash chromatography (SiO_2, PE–EtOAc, = 6:4 + 0.1% Et_3N) to afford **2** (1.26 g, 99%) as a white solid. Mp 127 °C; $[\alpha]_D^{20}$ +12.4 (*c* 1, $CHCl_3$). IR (KBr): 2937, 2890, 1743, 1716, 1697, 1365, 1241, 1065 cm^{-1}. ^1H NMR (360 MHz, $CDCl_3$): δ = 5.78 (dd, 1 H, *J* = 9, 10 Hz, H-3′), 5.03 (dd, 1 H, *J* = 9, 10 Hz, H-4′), 4.91 (ddd, 1 H, *J* = 4, 7, 11 Hz, H-1′), 4.23 (dd, 1 H, *J* = 5, 12 Hz, H-6′a), 4.06 (dd, 1 H, *J* = 2, 12 Hz, H-6′b), 3.89 (t, 1 H, *J* = 10 Hz, H-2′), 3.77 (ddd, 1 H, *J* = 2, 5, 10 Hz, H-5′), 2.62 (dd, 1 H, *J* = 4, 15 Hz, H-1a), 2.47 (dd, 1 H, *J* = 7, 15 Hz, H-1b), 2.42 (s, 3 H, COCH_3), 2.32 (s, 3 H, COCH_3), 2.17 (s, 3 H, COCH_3), 2.07 (s, 3 H, COCH_3), 2.02 (s, 3 H, COCH_3), 1.99 (s, 3 H, COCH_3). ^{13}C NMR (90 MHz, $CDCl_3$): δ = 205.2 (C-3), 174.2 (*C*OCH$_3$), 174.1 (*C*OCH$_3$), 170.5 (*C*OCH$_3$), 169.6 (*C*OCH$_3$), 169.5 (*C*OCH$_3$), 75.9 (C-5′), 73.2 (C-1′), 71.2 (C-3′), 69.6 (C-4′), 62.1 (C-6′), 60.9 (C-2′), 44.1 (C-1), 31.1 (C-3), 27.5 (CO*C*H$_3$), 25.1 (CO*C*H$_3$), 20.6 (CO*C*H$_3$), 20.5 (CO*C*H$_3$), 20.4 (CO*C*H$_3$). MS (ES): *m/z* (%) = 452 (100) $[M + Na]^+$. Anal. Calcd for $C_{19}H_{27}O_{10}N$: C, 53.14; H, 6.34; O, 37.26; N, 3.26. Found: C, 52.97; H, 6.27; O, 37.34; N, 3.12.

(10) Prepared according to: Adam, W.; Bialas, J.; Hadjiarapoglou, L. *Chem. Ber.* **1991**, *124*, 2377.

(11) **Preparation of 2-(2′-*N*-Acetylacetamido)-2′-deoxy-3′,4′,6′-tri-*O*-acetyl-β-D-glucopyranosyl)-1,3-bis(phenylmethyl)imidazolidine (4).**

To a solution of **2** (0.429 g, 1 mmol) in a mixture of MeCN (1.9 mL) and cyclohexane (1.6 mL) was added successively pyridine (0.4 mL, 5 mmol, 5 equiv), TMSCl (0.64 mL, 5 mmol, 5 equiv) and NaI (0.74 g, 5 mmol, 5 equiv). After stirring overnight at 70 °C, the reaction mixture was cooled to r.t. and was poured into sat. aq $NaHCO_3$ (20 mL). The aqueous phase was extracted with EtOAc (3 × 20 mL) and the combined organic layers were washed with brine (2 × 20 mL). The organic phase was then dried (Na_2SO_4), filtered and concentrated to afford crude enoxysilane, which was used without further purification. To this crude residue was added a solution of dimethyldioxirane (30 mL, 0.1 M in acetone, 3 equiv). The solution was stirred for 2 h at r.t. and concentrated. The residue was then diluted in a mixture of THF (3 mL) and H_2O (1.5 mL) and sodium metaperiodate (0.64 g, 3 mmol, 3 equiv) was added. After stirring for 3 h at r.t., a sat. aq $NaHCO_3$ was added until pH = 7. After addition of brine (10 mL), the aqueous phase was extracted with EtOAc (3 × 10 mL). The combined organic phases were washed with brine (2 × 10 mL), dried (Na_2SO_4), filtered and concentrated. Toluene (10 mL), *N,N*-dibenzylethylenediamine (0.25 mL, 1.05 mmol, 1.05 equiv) and glacial AcOH (2 drops) were then added to the crude aldehyde. The solution was immediately concentrated under reduced pressure and toluene was added and evaporated twice (2 × 10 mL). The pure aminal **5** (0.405 g, 65% from **2**) was obtained after flash chromatography on silica gel (PE–EtOAc = 8:2 + 0.5% Et_3N). $[\alpha]_D^{20}$ +19.8 (*c* 1, $CHCl_3$). IR (NaCl): 2940, 2883, 2807, 1749, 1700, 1367, 1227, 1060, 704 cm^{-1}. ^1H NMR (360 MHz, $CDCl_3$): δ = 7.35–7.20 (m, 5 H, Ph), 6.01 (dd, 1 H, *J* = 9, 10 Hz, H-3′), 5.13 (dd, 1 H, *J* = 9, 10 Hz, H-4′), 4.91 (d, 1 H, *J* = 9 Hz, H-1′), 4.41 (dd, 1 H, *J* = 9, 10 Hz, H-2′), 4.25–4.15 (m, 3 H, H-6′a, H-6′b, CH_2Ph), 3.92 (d, 1 H, *J* = 13 Hz, CH_2Ph), 3.80 (td, 1 H, *J* = 4, 10 Hz, H-5′), 3.54 (s, 1 H, H-1), 3.52 (d, 1 H, *J* = 13 Hz, CH_2Ph), 3.29 (d, 1 H, *J* = 13 Hz, CH_2Ph), 2.75–2.65 (m, 2 H, CH_2N), 2.63–2.55 (m, 2 H, CH_2N), 2.30 (s, 3 H, CH_3), 2.20 (s, 3 H, CH_3), 2.04 (s, 3 H, CH_3), 2.00 (s, 6 H, 2 × CH_3). ^{13}C NMR (90 MHz, $CDCl_3$): δ = 174.9 (*C*OCH$_3$), 174.7 (*C*OCH$_3$), 170.6 (*C*OCH$_3$), 169.9 (*C*OCH$_3$), 169.6 (*C*OCH$_3$), 138.6 (Cq Ph), 137.8 (Cq Ph), 129.3 (*C*H Ph), 129.2 (*C*H Ph), 128.3 (*C*H Ph), 128.0 (*C*H Ph), 127.2 (*C*H Ph), 127.2 (*C*H Ph), 127.1 (*C*H Ph), 86.7 (C-1), 75.9 (C-5′), 75.7 (C-1′), 72.3 (C-3′), 69.8 (C-4′), 62.1 (C-6′), 60.0 (CH_2Ph), 59.2 (CH_2Ph), 57.9 (C-2′), 50.4 (CH_2N), 50.0 (CH_2N), 28.2 (CO*C*H$_3$), 24.6, 28.2 (CO*C*H$_3$), 20.7, 28.2 (CO*C*H$_3$), 20.6 (CO*C*H$_3$), 20.4 (CO*C*H$_3$). MS (ES): *m/z* (%) = 646 (100) $[M + Na]^+$. Anal. Calcd for $C_{33}H_{41}O_9N_3$: C, 63.55; H, 6.63; O, 37.26; N, 6.74. Found: C, 63.93; H, 6.81; N, 6.53.

(12) **Preparation of 2-(*N*-Acetylacetamido)-2-deoxy-1-formyl-3,4,6-tri-*O*-acetyl-β-D-glucopyranoside (5).**

To a solution of the aminal **5** (75 mg, 0.12 mmol) in a mixture of THF (2 mL) and H_2O (2 mL) was added Dowex-50 (H^+) resin (150 mg). After stirring for 1 h at r.t., the reaction mixture was filtered, concentrated and coevaporated with toluene (3 × 10 mL). The aldehyde **4** (48 mg) was obtained quantitatively. ^1H NMR (360 MHz, $CDCl_3$): δ = 9.67 (s, 1 H, C*H*O), 5.88 (t, 1 H, *J* = 10 Hz, H-3), 5.08 (t, 1 H, *J* = 10 Hz, H-4), 5.03 (d, 1 H, *J* = 10 Hz, H-1), 4.33 (dd, 1 H, *J* = 5, 12 Hz, H-6a), 4.18 (dd, 1 H, *J* = 2, 12 Hz, H-6b), 4.04 (t, 1 H, *J* = 10 Hz, H-2), 3.90 (ddd, 1 H, *J* = 2, 5, 10 Hz, H-5), 2.41 (s, 6 H, COCH_3), 2.11 (s, 3 H, COCH_3), 2.04 (s, 3 H, COCH_3), 2.00 (s, 3 H, COCH_3). ^{13}C NMR (90 MHz, $CDCl_3$): δ = 197.8 (C-7), 170.6 (*C*OCH$_3$), 169.8 (*C*OCH$_3$), 169.7 (*C*OCH$_3$), 77.0 (C-1), 76.1 (C-5), 71.1 (C-3), 68.9 (C-4), 62.0 (C-6), 57.3 (C-2), 20.7 (CO*C*H$_3$), 20.6 (CO*C*H$_3$), 20.4 (CO*C*H$_3$).

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(14) **Preparation of 2-(2′-*N*-Acetyl)-2′-deoxy-3′,4′,6′-tri-*O*-acetyl-β-D-glucopyranosyl)-1,3-bis(phenylmethyl)imidazolidine (6).**

To a solution of the aminal **5** (0.156 g, 0.25 mmol) in CH_2Cl_2 (3.1 mL) was added hydrazine monohydrate (85 μL, 1.75 mmol, 7 equiv). After stirring for 24 h at r.t., brine (10 mL) was added and the aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL). The combined organic phases were dried (Na_2SO_4), filtered and concentrated. The pure aminal **6** (0.128 g, 88%) was obtained after flash chromatography on silica gel (PE–EtOAc = 4:6 to 3:7 + 0.1% Et_3N). $[\alpha]_D^{20}$ +0.6 (*c* 1, $CHCl_3$). IR (NaCl): 3329, 2935, 1745, 1653, 1531, 1371, 1240, 1056, 1034, 739, 701 cm^{-1}. ^1H NMR (360 MHz, $CDCl_3$): δ = 7.35–7.10 (m, 10 H, Ph), 5.79 (d, 1 H, *J* = 7 Hz, N*H*), 5.22 (t, 1 H, *J* = 10 Hz, H-3), 5.07 (t, 1 H, *J* = 10 Hz,

H-4), 4.30–4.05 (m, 4 H, H-2, H-6, H-6′ and CH_2Ph), 3.96 (d, 1 H, *J* = 13 Hz, CH_2Ph), 3.65–3.50 (m, 4 H, H-5, H-7 and 2 × CH_2Ph), 2.95–2.85 (m, 2 H, CH_2N), 2.60–2.50 (m, 2 H, CH_2N), 2.03 (s, 3 H, COCH_3), 2.01 (s, 3 H, COCH_3), 1.99 (s, 3 H, COCH_3), 1.75 (s, 3 H, COCH_3). ^{13}C NMR (90 MHz, $CDCl_3$): δ = 170.9 (*C*OCH$_3$), 170.5 (*C*OCH$_3$), 169.9 (*C*OCH$_3$), 169.3 (*C*OCH$_3$), 139.0 (Cq Ph), 138.8 (Cq Ph), 128.7 (*C*H Ph), 128.4 (*C*H Ph), 128.2 (*C*H Ph), 127.2 (*C*H Ph), 126.8 (*C*H Ph), 84.9 (C-7), 78.0 (C-1), 75.9 (C-5), 75.0 (C-3), 68.6 (C-4), 62.2 (C-6), 60.1 (*C*H$_2$Ph), 58.5 (*C*H$_2$Ph), 51.7 (C-2), 51.0 (*C*H$_2$N), 50.6 (*C*H$_2$N), 23.3 (CO*C*H$_3$), 20.7 (CO*C*H$_3$), 20.5 (CO*C*H$_3$). MS (ES): *m/z* (%) = 582 (100) [M + H]$^+$, 604 (50) [M + Na]$^+$. Anal. Calcd for $C_{31}H_{39}O_8N_3$: C, 64.01; H, 6.76; O, 22.01; N, 7.22. Found: C, 63.84; H, 7.06; O, 22.09; N, 6.88.

(15) **Preparation of 2-(*N*-Acetyl)-2-deoxy-1-formyl-3′,4′,6′-tri-*O*-acetyl-β-D-glucopyranoside (7).**
To a solution of the aminal **6** (75 mg, 0.13 mmol) in a mixture of THF (2 mL) and H_2O (2 mL) is added Dowex-50 (H^+) resin (150 mg). After stirring for 1 h at r.t., the reaction mixture was filtered, concentrated and coevaporated with toluene (3 × 10 mL). The aldehyde **7** (46 mg) was obtained quantitatively. ^{1}H NMR (360 MHz, $CDCl_3$): δ = 9.52 (d, 1 H, *J* = 3 Hz, H-7), 5.79 (d, 1 H, *J* = 9 Hz, N*H*), 5.20–5.10 (m, 2 H, H-4 and H-3), 4.35–4.20 (m, 2 H, H-6 and H-2), 4.17 (dd, 1 H, *J* = 2, 12 Hz, H-6′), 3.75–3.65 (m, 1 H, H-5), 3.67 (dd, 1 H, *J* = 3, 10 Hz, H-1), 2.14 (s, 3 H, COCH_3), 2.06 (s, 3 H, COCH_3), 2.04 (s, 3 H, COCH_3), 1.93 (s, 3 H, COCH_3). ^{13}C NMR (90 MHz, $CDCl_3$): δ = 195.8 (C-7), 171.6 (*C*OCH$_3$), 170.7 (*C*OCH$_3$), 170.6 (*C*OCH$_3$), 169.2 (*C*OCH$_3$), 82.0 (C-1), 75.9 (C-5), 73.1 (C-3 or C-4), 67.8 (C-3 or C-4), 61.8 (C-6), 50.3 (C-2), 23.0 (CO*C*H$_3$), 20.8 (CO*C*H$_3$), 20.7 (CO*C*H$_3$), 20.6 (CO*C*H$_3$).

(16) **Preparation of 2-(2′-*N*-Acetyl)-2′-deoxy-3′,4′,6′-tri-*O*-benzyl-β-D-glucopyranosyl)-1,3-bis(phenylmethyl)imidazolidine (8).**
To a solution of the aminal **5** (0.137 g, 0.22 mmol) in MeOH (2.2 mL) was added MeONa (2 mg). After stirring for 2 h at r.t., the solvents were coevaporated under reduced pressure with toluene (2 × 5 mL). DMF (4.4 mL), NaH (60% dispersion in mineral oil, 34 mg, 0.86 mmol) and benzyl bromide (82 μL, 0.68 mmol) were then added. After stirring for 2 h at r.t., MeOH (1 mL) and H_2O (10 mL) were added and the aqueous phase was extracted with EtOAc (4 × 10 mL). The combined organic phases were then dried (Na_2SO_4), filtered and concentrated. Flash chromatography (SiO_2, PE–EtOAc +1% Et_3N = 7:3 to 5:5) of the crude residue afforded the pure aminal **8** (0.120 mg, 75% from **4**) as a white solid. Mp 116 °C. $[\alpha]_D^{20}$ +16.7 (*c* 0.6, $CHCl_3$). IR (ATR-FTIR, diamond prism): 3278, 3028, 2909, 2854, 1643, 1598, 1552, 1102, 1088, 1070, 745, 694 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45–7.15 (m, 25 H, Ph), 5.36 (d, 1 H, *J* = 5 Hz, N*H*), 4.83 (d, 2 H, *J* = 12 Hz, 2 × CH_2Ph), 4.70 (d, 1 H, *J* = 11 Hz, CH_2Ph), 4.59 (d, 2 H, *J* = 11 Hz, 2 × CH_2Ph), 4.54 (d, 1 H, *J* = 12 Hz, CH_2Ph), 4.22 (d, 1 H, *J* = 14 Hz, CH_2Ph), 4.08 (t, 1 H, *J* = 9 Hz, H-3′), 3.95 (d, 2 H, *J* = 13 Hz, 2 × CH_2Ph), 3.89–3.82 (m, 2 H, H-1′, H-2′), 3.74 (dd, 1 H, *J* = 2, 11 Hz, H-6′a), 3.69 (dd, 1 H, *J* = 4, 11 Hz, H-6′b), 3.62–3.51 (m, 5 H, H-4′, H-5′, H-1, 2 × CH_2Ph), 3.10–3.02 (m, 1 H, CH_2N), 3.00–2.90 (m, 1 H, CH_2N), 2.65–2.55 (m, 2 H, 2 × CH_2N), 1.68 (s, 3 H, COCH_3). ^{13}C NMR (90 MHz, $CDCl_3$): δ = 170.3 (*C*OCH$_3$), 139.7 (Cq Ph), 139.3 (Cq Ph), 138.9 (Cq Ph), 138.5 (Cq Ph), 129.1 (*C*H Ph), 128.7 (*C*H Ph), 128.3 (*C*H Ph), 128.0 (*C*H Ph), 127.8 (*C*H Ph), 127.5 (*C*H Ph), 127.4 (*C*H Ph), 127.1 (*C*H Ph), 126.8 (*C*H Ph), 85.1 (C-1), 83. 5 (C-3′), 79.5 (C-5′), 79.0 (C-4′), 77.2 (C-1′), 75.0 (*C*H$_2$Ph), 74.6 (*C*H$_2$Ph), 73.3 (*C*H$_2$Ph), 69.7 (C-6′), 60.4 (*C*H$_2$Ph), 58.6 (*C*H$_2$Ph), 54.2 (C-2′), 51.7 (*C*H$_2$N), 50.8 (*C*H$_2$N), 23.8 (CO*C*H$_3$). MS (ESI): m/z (%) = 726.2 (100) [M + H]$^+$, 748.2 (35) [M + Na]$^+$. HRMS (ESI high resolution): *m/z* calcd for $C_{46}H_{52}O_5N_3$: 726.3901; found: 726.3914. Anal. Calcd for $C_{46}H_{51}O_5N_3$: C, 76.11; H, 7.08; O, 11.02; N, 5.79. Found: C, 76.02; H, 6.83; N, 5.76.

(17) **Preparation of 2-(*N*-Acetyl)-2-deoxy-1-formyl-3,4,6-tri-*O*-benzyl-β-D-glucopyranoside (9).**
To a solution of the aminal **8** (30 mg, 0.04 mmol) in a mixture of THF (1 mL) and H_2O (1 mL) was added Dowex-50 (H^+) resin (100 mg). After stirring for 1 h at r.t., the suspension was filtered, concentrated and coevaporated with toluene (3 × 10 mL). The aldehyde **9** (20 mg) was obtained quantitatively. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.53 (d, 1 H, *J* = 2 Hz, H-7), 7.45–7.15 (m, 15 H, Ph), 5.24 (d, 1 H, *J* = 8 Hz, N*H*), 4.86 (d, 1 H, *J* = 12 Hz, CH_2Ph), 4.82 (d, 1 H, *J* = 11 Hz, CH_2Ph), 4.65 (d, 1 H, *J* = 12 Hz, CH_2Ph), 4.63 (d, 1 H, *J* = 12 Hz, CH_2Ph), 4.60 (d, 1 H, *J* = 11 Hz, CH_2Ph), 4.57 (d, 1 H, *J* = 12 Hz, CH_2Ph), 3.96 (q, 1 H, *J* = 8 Hz, H-2), 3.75 (d, 2 H, *J* = 3 Hz, 2 × H-6), 3.73–3.69 (m, 2 H, H-3 and H-4), 3.65 (dd, 1 H, *J* = 2, 10 Hz, H-1), 3.55 (dt, 1 H, *J* = 3, 9 Hz, H-5), 1.75 (s, 3 H, COCH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.4 (C-7), 170.5 (*C*OCH$_3$), 138.0 (Cq Ph), 137.8 (Cq Ph), 137.7 (Cq Ph), 128.7 (*C*H Ph), 128.5 (*C*H Ph), 128.4 (*C*H Ph), 128.2 (*C*H Ph), 128.0 (*C*H Ph), 127.8 (*C*H Ph), 127.7 (*C*H Ph), 81.9 (C-1), 81.5 (C-3 or C-4), 78.9 (C-5), 78.2 (C-3 or C-4), 75.0 (*C*H$_2$Ph), 74.6 (*C*H$_2$Ph), 73.5 (*C*H$_2$Ph), 68.6 (C-6), 51.0 (C-2), 23.1 (CO*C*H$_3$).

(18) **Preparation of (1*R*)- and (1*S*)-1-(2′-*N*-Acetyl)-2′-deoxy-3′,4′,6′-tri-*O*-acetyl-β-D-glucopyranosyl)-1-acetoxy-1-but-3-ene (11).**
To a solution of the aminal **5** (0.32 mmol, 200 mg) in MeOH (3 mL) was added sodium methoxide (2 mg). After stirring for 1 h at r.t. MeOH was evaporated. THF (1.6 mL), H_2O (1.6 mL) and Dowex-50 (H^+) resin (400 mg) were added. After stirring for 1 h at r.t., the suspension was filtered, concentrated and coevaporated with toluene (3 × 10 mL). The residue was dissolved in a 1:1 mixture of THF–H_2O (3.2 mL) and allyl bromide (0.64 mmol, 55 mL) and In (0.96 mmol, 110 mg) were added. After stirring for 12 h at r.t., the suspension was filtered over Celite®. After washing with EtOH and evaporation of the solvents under reduced pressure, the residue was dissolved in a 2:1 mixture of pyridine and Ac_2O (1.5 mL). After stirring for 12 h at r.t., the reaction mixture was concentrated and coevaporated with toluene. Then, EtOAc (15 mL) was added and the mixture was washed with aq HCl (0.1 N, 5 mL) then with brine (10 mL). The organic phase was dried (Na_2SO_4) and concentrated. The crude residue was purified by flash chromatography (PE–EtOAc = 3:7 to 2:8) to afford **11** as a mixture of two diastereomers (87% from **5**).
Diastereomer 1 (32 mg, white solid): mp 124 °C; $[\alpha]_D^{20}$ –44.3 (*c* 0.3, $CHCl_3$). IR (ATR-FTIR, diamond prism): 3258, 3075, 2863, 1752, 1734, 1635, 1560, 1453, 1358, 1314, 1101, 1054, 735, 695 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.85–5.60 (m, 2 H, H-3 and N*H*), 5.11 (dd, 1 H, *J* = 1, 17 Hz, H-4a), 5.09–5.05 (m, 2 H, H-4′, H-4b), 5.01 (t, 1 H, *J* = 10 Hz, H-3′), 4.88 (ddd, 1 H, *J* = 1, 4, 9 Hz, H-1), 4.23 (dd, 1 H, *J* = 4, 12 Hz, H-6′a), 4.19–4.09 (m, 2 H, H-2 and H-6′b), 3.57 (ddd, 1 H, *J* = 2, 4, 10 Hz, H-5′), 3.51 (dd, 1 H, *J* = 2, 11 Hz, H-1′), 2.60–2.45 (m, 2 H, 2 × H-2), 2.08 (s, 3 H, COCH_3), 2.05 (s, 3 H, COCH_3), 2.02 (s, 3 H, COCH_3), 2.01 (s, 3 H, COCH_3), 1.96 (s, 3 H, COCH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.3 (*C*OCH$_3$), 171.0 (*C*OCH$_3$), 170.6 (*C*OCH$_3$), 170.2 (*C*OCH$_3$), 169.2 (*C*OCH$_3$),

133.9 (C-3), 117.8 (C-4), 79.8 (C-1′), 75.7 (C-5′), 74.4 (C-3′), 72.6 (C-1), 68.3 (C-4′), 62.2 (C-6′), 50.9 (C-2′), 31.9 (C-2), 23.1 (CO*C*H$_3$), 21.0 (CO*C*H$_3$), 20.7 (CO*C*H$_3$), 20.6 (CO*C*H$_3$), 20.5 (CO*C*H$_3$). MS (ESI): *m/z* (%) = 466.2 (100) [M + Na]$^+$. HRMS (ESI high resolution): *m/z* calcd for $C_{20}H_{29}O_{10}NNa$: 466.1684; found: 466.1695.

Diastereomer 2 (91 mg, white solid): mp 165 °C; $[\alpha]_D^{20}$ +16.2 (*c* 0.6, $CHCl_3$). IR (ATR-FTIR, diamond prism): 3273, 3087, 2858, 1778, 1743, 1645, 1563, 1453, 1358, 1314, 1101, 1065, 745, 690 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.76–5.64 (m, 1 H, H-3), 5.49 (d, 1 H, *J* = 10 Hz, N*H*), 5.18–5.01 (m, 4 H, H-3′, H-4′, 2 × H-4), 4.96 (td, 1 H, *J* = 2, 7 Hz, H-1), 4.23 (dd, 1 H, *J* = 6, 12 Hz, H-6′a), 4.19 (q, 1 H, *J* = 10 Hz, H-2′), 4.14 (dd, 1 H, *J* = 2, 12 Hz, H-6′), 3.59 (ddd, 1 H, *J* = 2, 6, 10 Hz, H-5′), 3.52 (dd, 1 H, *J* = 2, 10 Hz, H-1′), 2.46 (t, 2 H, *J* = 7 Hz, 2 × H-2), 2.09 (s, 3 H, COC*H*$_3$), 2.07 (s, 3 H, COC*H*$_3$), 2.01 (s, 3 H, COC*H*$_3$), 2.00 (s, 3 H, COC*H*$_3$), 1.88 (s, 3 H, COC*H*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.2 (*C*OCH$_3$), 170.8 (*C*OCH$_3$), 170.6 (*C*OCH$_3$), 169.9 (*C*OCH$_3$), 169.3 (*C*OCH$_3$), 132.9 (C-3), 118.6 (C-4), 77.4 (C-1′), 76.3 (C-5′), 74.4 (C-3′), 69.2 (C-1), 68.9 (C-4′), 62.7 (C-6′), 49.9 (C-2′), 34.6 (C-2), 23.1 (CO*C*H$_3$), 21.0 (CO*C*H$_3$), 20.7 (CO*C*H$_3$), 20.6 (CO*C*H$_3$), 20.5 (CO*C*H$_3$). MS (ESI): *m/z* = 466.2 (100) [M + Na]$^+$. HRMS (ESI high resolution): *m/z* calcd for $C_{20}H_{29}O_{10}NNa$: 466.1684; found: 466.1695. Anal. Calcd for $C_{20}H_{28}O_{10}N$: C, 54.17; H, 6.59; O, 36.08; N, 3.16. Found: C, 53.72; H, 6.64; N, 3.06.