Copper(II)-Mediated Activation of Sugar Oxazolines: Mild and Efficient Synthesis of β-Glycosides of *N*-Acetylglucosamine

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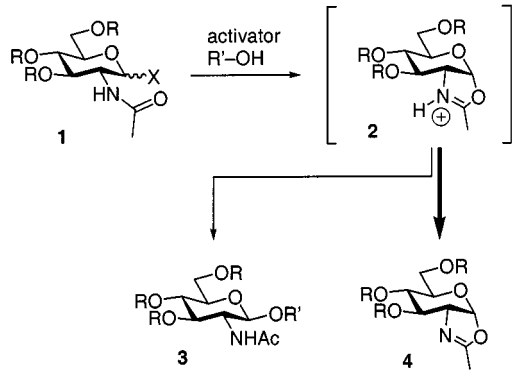
2-Methyl-(3,4,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucopyrano)-[2,1-*d*]-2-oxazoline (**5**) was reacted with glycosyl acceptors bearing primary (**6**, **8**, **10**, **20**) or secondary hydroxy groups (**12**, **14**, **16**, **18**) in the presence of anhydrous cupric bromide or cupric chloride at elevated temperature to provide 2-acetamido-2-deoxy-β-D-glucopyranosides in 36–92% yield. The reaction conditions are milder than those previously described for oxazoline activation employing *p*-toluenesulfonic acid or ferric chloride. Treatment of the oxazoline with trimethylsilyl azide (**22**) and $CuCl_2$ leads to 2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl azide (**23**) in 69% yield.

Introduction

2-Acetamido-2-deoxy-D-glucose (*N*-acetylglucosamine, GlcNAc) is a ubiquitous constituent of biologically important oligosaccharides and glycoconjugates, including glycoproteins and -lipids, glycosaminoglycans, and peptidoglycan.[1,2] Accordingly, the preparation of 2-acetamido-2-deoxyglycosides has been a major task in carbohydrate chemistry.[3] Glycosylation reactions with GlcNAc-derived donors such as **1** proceed with neighboring-group participation to give the oxazolinium intermediate **2** (Scheme 1), which is a poor glycosyl donor; this reaction is accompanied by the formation of oxazoline **4**, which in many cases is the main reaction product (Scheme 1). To circumvent the problem of oxazoline formation, a variety of different N^2-protecting groups[4] have been investigated, such as phthaloyl,[5] tetrachlorophthaloyl,[6] 4,5-dichlorophthaloyl,[7] dithiasuccinoyl,[8] trichloro-[9] and trifluoroacetyl,[9a,10] trichloroethoxycarbonyl,[11] diacetyl,[12] dimethylmaleoyl[13] or thiodiglycoloyl[14] groups, although additional synthetic steps are required for their introduction and subsequent replacement by an acetyl group. The 2-azido group has also been extensively used in this regard.[2,15,16]

The conversion of **4**, which is accessible in high yields by Jeanloz' procedure,[17] into glycosides **3** is known as the oxazoline method.[18] It has the conceptual advantage that the natural 2-acetamido group is obtained directly in the glycosylation step. However, due to the low reactivity of **4**, harsh reaction conditions are required, for example *p*-toluenesulfonic acid in refluxing nitromethane or toluene,[3,18] leading to decomposition of **3** and **4** and, therefore, moderate yields. Some improvement has been achieved by the use of 1,2-dichloroethane as solvent[19] or ferric chloride[20] or trimethylsilyl triflate[21] as the promoter. We now report on the use of anhydrous $CuBr_2$ and $CuCl_2$ as a means of mild activation of oxazoline **4** (R = Ac). Under these conditions, even reaction times of several days do not lead to decomposition of **4**, and the glycosides **3** are normally obtained in high yield and purity.



Scheme 1

Results and Discussion

During the synthesis of neoglycopeptide-based lectin ligands[22] we became interested in the synthesis of hydroxybutenyl glycoside (**7**). Using established methods for oxazoline activation,[3] **7** was obtained from **5** in a maximum yield of 39% (Scheme 2, condition a). Since oxazolines are known to be good complex ligands of copper(II),[23] we reasoned copper(II) salts to be potential candidates for oxazo-

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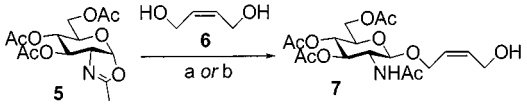
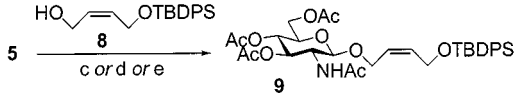
line activation by means of coordination to the nitrogen. Indeed, when **5** was treated for 45 min with one equivalent of $CuBr_2$ and five equivalents of diol **6** in THF at 50 °C, the singly glycosylated product **7** was obtained in 87% yield after chromatographic purification (condition b). The reaction conditions were further optimized by employing the mono TBDPS-protected butene diol **8** as the glycosyl acceptor. The prolonged reaction times that are needed if a smaller excess of acceptor (or donor) is used lead to significantly decreased yields of **9** (e.g. 32%, condition c), probably due to bromination of the olefin. This effect could be completely abolished by replacement of $CuBr_2$ with $CuCl_2$. Other copper(II) salts such as $Cu(OTf)_2$, $CuSO_4$, or $Cu(OAc)_2$ were essentially ineffective. Of the several solvents compared, chloroform gave slightly higher coupling rates than THF, acetonitrile or 1,2-dichloroethane. Thus, **9** is accessible in 88−92% yield using $CuCl_2$ in refluxing chloroform (conditions d and e).

The excellent yields of **7** and **9** and the high purity of the crude products prompted us to evaluate the scope of this novel procedure for oxazoline activation. Oxazoline **5** was reacted with a series of glycosyl acceptors bearing primary or secondary hydroxy groups (Table 1). Glycosylation of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**10**) nicely



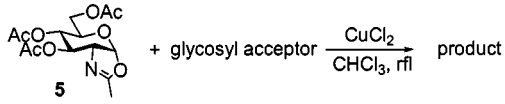
(a) 1 equiv. **5**, 20 equiv. **6**, 0.1 equiv. *p*-TsOH, THF, 50 °C, 14 h (39 %)
(b) 1 equiv. **5**, 5 equiv. **6**, 1 equiv. $CuBr_2$, THF, 50 °C, 45 min (87 %)

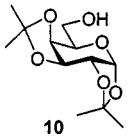
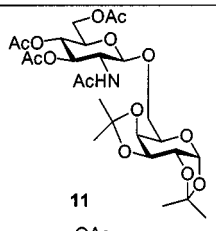
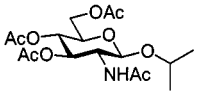
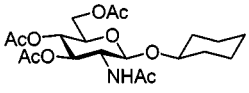
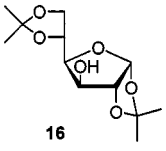
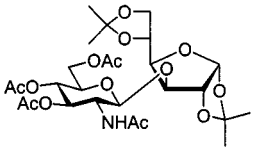
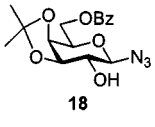
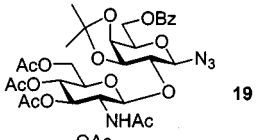
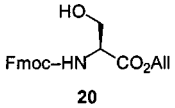
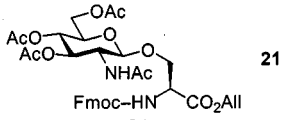
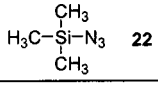
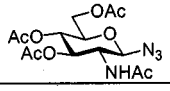


(c) 1 equiv. **5**, 1.5 equiv. **8**, 1 equiv. $CuBr_2$, THF, 50 °C, 17 h (32 %)
(d) 1.5 equiv. **5**, 1 equiv. **8**, 1.5 equiv. $CuCl_2$, $CHCl_3$, rfl, 16 h (88 %)
(e) 4 equiv. **5**, 1 equiv. **8**, 4 equiv. $CuCl_2$, $CHCl_3$, rfl, 2 h (92 %)

Scheme 2

Table 1. Reaction of oxazoline **5** with various glycosyl acceptors



Entry	Glycosyl acceptor	Product	Oxazoline/ acceptor ratio	Reaction time [h]	Yield (%)
1	 **10**	 **11**	1.5:1	43	92
2	 **12**	 **13**	1:4	2	80
3	 **14**	 **15**	1:4	2	86
4	 **16**	 **17**	1:4	18	36
5	 **18**	 **19**	2.5:1	19	61
6	 **20**	 **21**	4:1	74	77
7	 **22**	 **23**	1:12	3.5	69

demonstrates the advantage of cupric chloride activation (92% yield, entry 1) over the use of ferric chloride (67% yield[20b]). Acetonide cleavage was not observed, although catalytic amounts of $CuCl_2 \cdot 2H_2O$ in acetonitrile have been demonstrated to cleave acetals efficiently.[24] Isopropanol (**12**) and cyclohexanol (**14**) reacted smoothly with **5** to give the glycosides **13** and **15**, respectively (entries 2 and 3). Glycosylation of the sterically hindered 3-OH group of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**16**), however, proceeded sluggishly and was accompanied by partial cleavage of the sensitive 5,6-*O*-isopropylidene group, lowering the yield of **17** to 36% (entry 4). The galactosyl azide **18**, on the other hand, was converted into disaccharide **19** in 61% yield (entry 5).

When Fmoc-Ser-OAll (**20**) was reacted with **5**, the glycosyl amino acid **21** was formed in a slow but clean reaction (77% yield, entry 6). Glycosylation of serine derivatives with (intermediately formed) oxazolines has been carried out before in yields of up to 55%.[25] Finally, **5** was treated with $CuCl_2$ and an excess of trimethylsilyl azide (**22**) to give the glycosyl azide **23** in 69% yield (entry 7); no reaction was observed in the absence of $CuCl_2$.

In the case of water-insoluble compounds (such as **9**, **11**, **15**, **17**, **19**, **21**), workup of the glycosylation reaction is easily achieved by washing with dilute HCl in order to remove cupric compounds and excess of **5**. For water-soluble products (such as **7**, **13**, and **23**) an alternative workup procedure was developed based on the precipitation of copper(II) as basic carbonates ($CuCO_3 \cdot x CuO \cdot y H_2O$) upon addition of a sodium bicarbonate solution.

Conclusion

In summary, we have discovered a new procedure for the activation of glucosamine-derived oxazoline **5** to provide β-glycosides with the natural 2-acetamido functionality. Compared with known procedures, the reactivity of **5** is not enhanced, but the reaction conditions are milder, allowing prolonged reaction times without formation of decomposition products, leading to higher yields. Thus, our copper(II)-mediated glycosylation with oxazoline **5** is a useful alternative to known syntheses of 2-acetamido-2-deoxy-β-D-glucopyranosides.

Experimental Section

General Methods: 1,2:3,4-Di-*O*-isopropylidene-α-D-galactopyranose (**10**) and 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**16**) were purchased from Fluka (Buchs, Switzerland). Flash chromatography (FC): Merck silica gel 60 (40−63 μm); TLC: Merck silica gel 60 F_{254} pre-coated glass plates; NMR: Bruker AM-250 or AMX-400. ^1H chemical shifts are referenced to residual protic solvent ($CDCl_3$: $\delta_H = 7.26$) or internal standard TMS ($\delta_H = 0.00$). ^{13}C chemical shifts are referenced to the solvent signal ($CDCl_3$: $\delta_C = 77.0$). ESI-MS: Fisons (now Micromass) VG Platform II. MALDI-MS: Fisons (now Micromass) VG Tofspec. Elemental analyses (carried out at the Institut für Organische Chemie, Universität Frankfurt): Foss-Heraeus CHN-O-Rapid.

2-Methyl-(3,4,6-tri-*O*-acetyl-1,2-dideoxy-α-D-glucopyrano)-[2,1-*d*]-2-oxazoline (5): Oxazoline **5** was obtained in two steps from glucosamine hydrochloride according to published procedures: (1) Ac_2O, pyr, 3 days (86%);[26] (2) TMS-OTf, $ClCH_2CH_2Cl$, 50 °C, 20 h (90%).[17]

4-Hydroxy-(*Z*)-but-2-enyl 2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranoside (7): Oxazoline **5** (50 mg, 0.152 mmol) and *cis*-but-2-en-1,4-diol **6** (62 μL, 0.754 mmol) were dissolved in dry THF (1.5 mL). Anhydrous $CuBr_2$ (35 mg, 0.157 mmol) was then added and the resulting deep greenish-blue colored solution was heated for 45 min at 50 °C. After cooling to room temp., the solvent was removed and the residue purified by FC (CH_2Cl_2/MeOH, 9:1) to give **7** (55 mg, 87%) as a white solid. For gram-scale reactions, a workup procedure as described for the preparation of **13** is recommended due to the water solubility of **7**. M.p. 114−115 °C (ethyl acetate/hexane); $R_f = 0.16$ (CH_2Cl_2/MeOH, 95:5). ^1H NMR (400 MHz, $CDCl_3$): δ = 6.33 (d, $J = 8.7$ Hz, 1 H, NH), 5.89−5.83 (m, 1 H, vinyl-H), 5.66−5.60 (m, 1 H, vinyl-H), 5.31 (dd, $J = 9.3$, 10.5 Hz, 1 H), 5.07 ('t', $J \approx 9.6$ Hz, 1 H), 4.78 (d, $J = 8.4$ Hz, 1 H, 1-H), 4.38−4.24 (m, 3 H), 4.20−4.15 (m, 3 H), 3.89 (ddd, J = 8.4, 8.7, 10.6 Hz, 1 H, 2-H), 3.77 (ddd, $J = 2.5$, 4.9, 10.0 Hz, 1 H, 5-H), 3.01 (br. s, 1 H, OH), 2.10 [s, 3 H, $C(O)CH_3$], 2.04 [s, 3 H, $C(O)CH_3$], 2.03 [s, 3 H, $C(O)CH_3$], 1.97 [s, 3 H, $C(O)CH_3$]. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 171.0, 170.8, 170.7, 169.4, 133.6, 126.5, 99.2, 72.4, 71.8, 68.8, 64.0, 62.2, 58.2, 54.6, 23.1, 20.7, 20.6, 20.6. ESI-MS ($C_{18}H_{26}NO_{10}$ $[M - H]^-$): calcd. 416.2; found 416.2. $C_{18}H_{27}NO_{10}$ (417.4): C 51.79, H 6.52, N 3.36; found C 51.75, H 6.57, N 3.54.

(*Z*)-4-(*tert*-Butyldiphenylsilyloxy)but-2-en-1-yl 2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranoside (9): Oxazoline **5** (454 mg, 1.38 mmol) and (*Z*)-4-(*tert*-butyldiphenylsilyloxy)but-2-en-1-ol[27] (**8**) (300 mg, 0.919 mmol) were coevaporated with toluene. Anhydrous $CuCl_2$ (204 mg, 1.52 mmol) and anhydrous $CHCl_3$ (2.5 mL) were then added and the resulting greenish-blue colored solution was refluxed for 16 h. After cooling to room temperature, the solvent was removed, ethyl acetate was added, and the mixture was washed twice with 1 N HCl, once with sat. aq. $NaHCO_3$, and once with brine. The organic layer was dried (Na_2SO_4), evaporated, and purified by FC (hexane/ethyl acetate, 1:2 → 1:6) to give **9** (528 mg, 88%) as a white amorphous solid after co-evaporation with Et_2O. M.p. 88−95 °C; $R_f = 0.24$ (hexane/ethyl acetate 1:2). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.68−7.65 (m, 4 H, arenes), 7.46−7.37 (m, 6 H, arenes), 5.78 (dtt, $J = 1.4$, 5.9, 11.3 Hz, 1 H, vinyl-H), 5.53−5.46 (m, 1 H, vinyl-H), 5.43 (d, $J = 8.7$ Hz, 1 H, NH), 5.23 (dd, $J = 9.3$, 10.5 Hz, 1 H), 5.02 ('t', $J \approx 9.6$ Hz, 1 H), 4.55 (d, $J = 8.3$ Hz, 1 H, 1-H), 4.25−4.16 (m, 5 H), 4.10−4.05 (m, 1 H), 3.99 (dd, $J = 2.4$, 12.3 Hz, 1 H), 3.76 (ddd, $J = 8.3$, 8.7, 10.6 Hz, 1 H, 2-H), 3.52 (ddd, $J = 2.4$, 4.5, 10.0 Hz, 1 H, 5-H), 2.013 [s, 3 H, $C(O)CH_3$], 2.008 [s, 3 H, $C(O)CH_3$], 2.004 [s, 3 H, $C(O)CH_3$], 1.86 [s, 3 H, $C(O)CH_3$], 1.03 [s, 9 H, $C(CH_3)_3$]. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 170.8, 170.6, 170.1, 169.3, 135.5, 135.5, 133.5, 133.4, 133.2, 129.8, 127.7, 125.7, 99.3, 72.3, 71.7, 68.5, 64.7, 61.9, 60.4, 54.7, 26.7, 23.2, 20.6, 20.6, 19.1. ESI-MS ($C_{34}H_{44}NO_{10}Si$ $[M - H]^-$): calcd. 654.3; found 654.4. $C_{34}H_{45}NO_{10}Si$ (655.8): C 62.27, H 6.92, N 2.14; found C 62.40, H 6.95, N 2.02.

6-*O*-(2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (11): Oxazoline **5** (379 mg, 1.15 mmol), 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose (**10**) (200 mg, 0.768 mmol), anhydrous $CuCl_2$ (155 mg,

1.15 mmol), and anhydrous $CHCl_3$ (2.5 mL) were subjected to the reaction and workup conditions described for **9** (reaction time: 43 h). FC (hexane/ethyl acetate 1:3 then ethyl acetate/$CHCl_3$ 9:1) gave **11** (416 mg, 92%). R_f = 0.54 (ethyl acetate/MeOH, 95:5), 0.20 (hexane/ethyl acetate, 1:3). The ^1H and ^{13}C NMR spectroscopic data were in agreement with those published.[28]

Isopropyl 2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranoside (13): Oxazoline **5** (523 mg, 1.59 mmol) and anhydrous $CuCl_2$ (222 mg, 1.59 mmol) were coevaporated with toluene. Anhydrous $CHCl_3$ (3 mL) and anhydrous 2-propanol **12** (496 μL, 6.5 mmol) were then added and the resulting mixture was refluxed for 2 h. After cooling to room temp., the mixture was diluted with acetone (ca. 50 mL) and sat. aq. $NaHCO_3$ (25 mL) was added. Precipitated $CuCO_3 \cdot x CuO \cdot y H_2O$ was removed by filtration through Celite® and washed with acetone. The filtrate was evaporated and residual water was removed by co-evaporation with toluene. The remainder was shaken with $CHCl_3$ and weakly acidic ion-exchange resin (Amberlite IRC-86, ca. 5 g) in order to remove remaining **5** and $NaHCO_3$. Evaporation and purification by FC (hexane/ethyl acetate, 1:3) gave **13** (493 mg, 80%) as a white solid. R_f = 0.24 (hexane/ethyl acetate, 1:3). ^1H NMR (250 MHz, $CDCl_3$): δ = 5.80 (d, *J* = 8.4 Hz, 1 H, NH), 5.38 (dd, *J* = 9.3, 10.6 Hz, 1 H, 3-H), 5.01 ('t', *J* ≈ 9.6 Hz, 1 H, 4-H), 4.82 (d, *J* = 8.3 Hz, 1 H, 1-H), 4.22 (dd, *J* = 5.1, 12.2 Hz, 1 H, 6^a-H), 4.09 (dd, *J* = 2.6, 12.1 Hz, 1 H, 6^b-H), 3.91 [sept, *J* = 6.2 Hz, 1 H, C*H*$(CH_3)_2$], 3.71 (ddd, *J* = 2.6, 5.1, 10.0 Hz, 1 H, 5-H), 3.65 (ddd, *J* = 8.3, 8.4, 10.6 Hz, 1 H, 2-H), 2.05 [s, 3 H, C(O)CH_3], 2.005 [s, 3 H, C(O)CH_3], 1.996 [s, 3 H, C(O)CH_3], 1.92 [s, 3 H, C(O)CH_3], 1.20 and 1.11 [each d, *J* = 6.2 Hz, each 3 H, CH(C*H*$_3)_2$]. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 170.6, 170.5, 170.2, 169.3, 99.0, 72.4, 72.1, 71.4, 68.9, 62.2, 55.3, 23.1, 21.8, 20.6, 20.5, 20.5. ESI-MS ($C_{17}H_{28}NO_9$ $[M + H]^+$): calcd. 390.2; found 390.3. $C_{17}H_{27}NO_9$ (389.4): C 52.44, H 6.99, N 3.60; found C 52.48, H 6.83, N 3.43.

Cyclohexyl 2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranoside (15): Oxazoline **5** (231 mg, 0.666 mmol) and anhydrous $CuCl_2$ (90 mg, 0.666 mmol) were coevaporated with toluene. Anhydrous $CHCl_3$ (1.5 mL) and anhydrous cyclohexanol **14** (267 mg, 2.67 mmol) were then added and the resulting mixture was refluxed for 2 h. Workup was carried out as described for **9**. Purification by FC (hexane/ethyl acetate, 1:3) gave **15** (246 mg, 86%) as a white solid. R_f = 0.35 (hexane/ethyl acetate, 1:3). The ^1H and ^{13}C NMR spectroscopic data were in agreement with those reported previously.[29]

3-*O*-(2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (17): Oxazoline **5** (330 mg, 1.00 mmol), 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose (**16**) (1.054 g, 4.05 mmol), anhydrous $CuCl_2$ (141 mg, 1.02 mmol), and anhydrous $CHCl_3$ (2 mL) were subjected to the reaction and workup conditions described for **9** (reaction temperature: 55 °C, reaction time: 18 h). FC (hexane/ethyl acetate, 1:3), followed by a second FC (CH_2Cl_2/MeOH, 95:5) gave **17** (218 mg, 36%). R_f = 0.22 (CH_2Cl_2/MeOH, 95:5). ^1H NMR (400 MHz, $CDCl_3$, 300 K): δ = 5.93 (d, *J* = 3.7 Hz, 1 H, Glc 1-H), 5.83 (d, *J* = 7.2 Hz, 1 H, NH), 5.21 (dd, *J* = 9.4, 10.4 Hz, 1 H, GlcN 3-H), 5.03 (dd, *J* = 9.4, 9.7 Hz, 1 H, GlcN 4-H), 4.67 (d, *J* = 8.3 Hz, 1 H, GlcN 1-H), 4.52 (d, *J* = 3.7 Hz, 1 H, Glc 2-H), 4.22−4.18 (m, 2 H, GlcN 6^a-H, Glc 4-H), 4.15 (d, *J* = 3.8 Hz, 1 H, Glc 3-H), 4.09 (m, 1 H, GlcN 6^b-H), 3.92−3.85 (m, 2 H, GlcN 2-H, Glc 6^a-H), 3.76−3.65 (m, 3 H, GlcN 5-H, Glc 5-H and 6^b-H), 2.03 [s, 3 H, C(O)CH_3], 1.97 [s, 3 H, C(O)CH_3], 1.96 [s, 3 H, C(O)CH_3], 1.89 [s, 3 H, C(O)CH_3], 1.41 [s, 3 H, $C(CH_3)_2$], 1.30 [s, 3 H, $C(CH_3)_2$], 1.28 [s, 3 H, $C(CH_3)_2$], 1.26 [s, 3 H, $C(CH_3)_2$]. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 170.7, 170.6, 170.2, 169.3, 112.0, 106.2, 100.7, 100.5, 83.7, 79.6, 74.8, 72.6, 71.7, 70.7, 69.4, 68.6, 62.1, 54.3, 27.0, 26.3, 23.9, 23.9, 23.2, 20.6, 20.6, 20.5. $C_{26}H_{39}NO_{14}$ (589.6): C 52.97, H 6.67, N 2.38; found C 52.81, H 6.75, N 2.42.

6-*O*-Benzoyl-3,4-*O*-isopropylidene-β-D-galactopyranosyl Azide (18): 3,4-*O*-Isopropylidene-β-D-galactopyranosyl azide[30] (400 mg, 1.63 mmol) was dissolved in dry pyridine (6 mL) and cooled to −20 °C. Benzoyl chloride (210 μL, 1.79 mmol) was then added dropwise in the course of 1 h. The mixture was stirred for 4 h at −20 °C → 0 °C and 2 h at 0 °C → room temp. A small amount of water was added and the solvents were evaporated. Ethyl acetate was added to the remainder and the mixture was washed once with 1 N HCl, twice with sat. aq. $NaHCO_3$, and once with brine. The organic layer was dried (Na_2SO_4), evaporated, and purified by FC (hexane/ethyl acetate, 2.5:1 → 1:2) to give 2,6-di-*O*-benzoyl-3,4-*O*-isopropylidene-β-D-galactopyranosyl azide (135 mg, 18%), followed by **18** (370 mg, 65%) and its regio isomer 2-*O*-benzoyl-3,4-*O*-isopropylidene-β-D-galactopyranosyl azide (20 mg, 3.5%).

18: White needles (ethyl acetate/hexane); m.p. 139 °C; R_f = 0.55 (hexane/ethyl acetate, 1:2). ^1H NMR (250 MHz, $CDCl_3$): δ = 8.08−8.01 (m, 2 H, Bz), 7.61−7.54 (m, 1 H, Bz), 7.48−7.41 (m, 2 H, Bz), 4.67 (dd, *J* = 4.5, 11.8 Hz, 1 H, 6-H), 4.61−4.56 (m, 1 H), 4.51 (d, *J* = 8.8 Hz, 1 H, 1-H), 4.29−4.20 (m, 2 H), 4.13 (dd, *J* = 5.5, 7.0 Hz, 1 H), 3.53 (ddd, *J* = 3.4, 7.1, 8.8 Hz, 1 H, 2-H), 2.93 (d, *J* = 3.4 Hz, 1 H, OH), 1.53 (s, 3 H, CH_3), 1.37 (s, 3 H, CH_3). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 166.4, 133.2, 129.7, 128.4, 110.7, 89.5, 78.4, 73.3, 72.9, 63.6, 27.9, 26.1. MALDI-MS ($C_{16}H_{19}N_3O_6Na$ $[M + Na]^+$): calcd. 372.1; found 371.9. $C_{16}H_{19}N_3O_6$ (349.3): C 55.01, H 5.48, N 12.03; found C 55.18, H 5.48, N 12.08.

2-*O*-(2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-6-*O*-benzoyl-3,4-*O*-isopropylidene-β-D-galactopyranosyl Azide (19): Oxazoline **5** (353 mg, 1.07 mmol), azide **18** (150 mg, 0.429 mmol), anhydrous $CuCl_2$ (144 mg, 1.07 mmol), and anhydrous $CHCl_3$ (2 mL) were subjected to the reaction and workup conditions described for **9** (reaction time: 19 h). FC (hexane/ethyl acetate, 1:10 → 5:95) gave **19** (178 mg, 61%) as a white amorphous solid (from ethyl acetate/hexane); m.p. 174.5−175.5 °C; R_f = 0.33 (hexane/ethyl acetate, 1:10). ^1H NMR (250 MHz, $CDCl_3$): δ = 8.05−8.02 (m, 2 H, Bz), 7.60−7.54 (m, 1 H, Bz), 7.47−7.41 (m, 2 H, Bz), 5.71 (d, *J* = 9.0 Hz, 1 H), 5.19 ('t', *J* ≈ 9.8 Hz, 1 H), 5.07 ('t', *J* ≈ 9.5 Hz, 1 H), 4.87 (d, *J* = 8.4 Hz, 1 H), 4.61 (dd, *J* = 4.6, 11.8 Hz, 1 H), 4.55−4.46 (m, 2 H), 4.27−4.09 (m, 5 H), 4.06−3.94 (m, 1 H), 3.74−3.64 (m, 2 H), 2.05 [s, 3 H, C(O)CH_3], 2.02 [s, 3 H, C(O)CH_3], 2.01 [s, 3 H, C(O)CH_3], 1.95 [s, 3 H, C(O)CH_3], 1.53 and 1.35 [each s, each 3 H, $C(CH_3)_2$]. ^{13}C NMR (62.9 MHz, $CDCl_3$): δ = 171.0, 170.7, 170.1, 169.3, 166.3, 133.2, 129.7, 129.6, 128.4, 110.6, 101.4, 87.5, 79.4, 78.2, 73.3, 72.6, 72.5, 72.1, 68.4, 63.5, 62.2, 54.5, 27.8, 26.1, 23.2, 20.6, 20.5. ESI-MS ($C_{30}H_{39}N_4O_{14}$ $[M + H]^+$): calcd. 679.2; found 679.6. $C_{30}H_{38}N_4O_{14}$ (678.6): C 53.10, H 5.64, N 8.26; found C 53.02, H 5.65, N 8.03.

***O*-(2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-*N*-(9-fluorenylmethyloxycarbonyl)-L-serine Allyl Ester (21):** Oxazoline **5** (505 mg, 1.533 mmol), Fmoc-Ser-OAll **20** (140 mg, 0.383 mmol), anhydrous $CuCl_2$ (197 mg, 1.465 mmol), and anhydrous $CHCl_3$ (2.8 mL) were subjected to the reaction and workup conditions described for **9** (reaction time: 74 h). FC (hexane/ethyl acetate, 1:3) gave **21** (206 mg, 77%). R_f = 0.19 (hexane/ethyl acetate, 1:3). The ^1H and ^{13}C NMR spectroscopic data were in agreement with those published.[31]

2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl Azide (23): Oxazoline **5** (577 mg, 1.75 mmol) and anhydrous $CuCl_2$ (236 mg, 1.75 mmol) were coevaporated with toluene. Anhydrous $CHCl_3$ (3.5 mL) and TMS-N_3 **22** (3 mL, 22.1 mmol) were added and the resulting mixture was refluxed for 3.5 h. After cooling to room temp., the mixture was diluted with acetone (ca. 50 mL) and sat. aq. $NaHCO_3$ (25 mL) was added. Precipitated $CuCO_3 \cdot x CuO \cdot y H_2O$ was removed by filtration through Celite® and washed with acetone. The filtrate was evaporated and residual water was removed by co-evaporation with toluene. Purification by FC (hexane/ethyl acetate, 1:3) gave **23** (448 mg, 69%) as a white solid. $R_f = 0.22$ (hexane/ethyl acetate, 1:3). The ^1H and ^{13}C NMR spectroscopic data were in agreement with those published.[32]

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