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A Simple Procedure for Connecting Two Carbohydrate Moieties by Click Chemistry Techniques

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We describe a procedure to link two saccharides by click chemistry techniques. This methodology allows the generation of new molecules in which two carbohydrates are connected through a triazole ring.

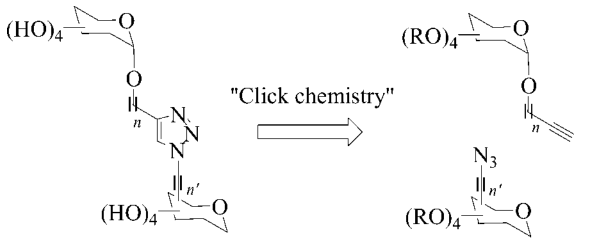
Introduction

Carbohydrate–protein interactions have been extensively investigated. Oligosaccharides serve to mediate a host of biological events, including cell–cell recognition, adhesion, and modulation of signal transduction pathways.[1] Many proteins and lipids are glycosylated and this affects the functions of the proteins to which they are attached.

In the area of multivalency, the development of multivalent carbohydrates of varying size as effectors of biological processes through clustering of receptors has been a topic of interest. Generally, carbohydrates involved in the binding are connected together through linkers.[2]

The Huisgen 1,3-dipolar cycloaddition between azides and alkynes to afford triazoles is probably the most powerful "click" reaction for such linkages.[3] Interest in this reaction became clear after the recent discovery of the advantages of Cu^{I} as catalyst, reported independently by Sharpless's[4] and Meldal's[5] groups. This reaction in part owes its usefulness to its high compatibility with functional groups (alcohols, carboxylic acids, amines) in different solvent systems, including water. In the field of carbohydrate chemistry, click chemistry has been used for the synthesis of glycoconjugates[6,7] and carbohydrate macrocycles[8] in which a sugar possessing an azido function is grafted onto a saccharide,[9] a peptide,[10] or a polymeric chain.[11] This methodology has also been employed for the synthesis of glycosidase inhibitors.[12]

We are currently involved in a research program dealing with the construction of new probes for studying multivalency in carbohydrate–protein interactions. In this context, it was necessary to develop a general method to connect carbohydrates bearing a variety of protecting groups. Recent success in the synthesis of glycoconjugates[10,13] by "click chemistry" inspired us to envisage this approach to constructing our molecules, and here we describe a fast procedure to connect saccharides through triazole rings (Scheme 1).



Scheme 1.

Results and Discussion

To demonstrate the broad compatibility of our technique, we have synthesized four azidoalkyl-saccharides (Scheme 2). Azides have been introduced at different positions (C-2, C-5, C-6) in carbohydrate derivatives in their pyranose or furanose forms, in the presence of a range of protecting groups commonly used in oligosaccharide synthesis.

Compounds **1** and **2** were obtained as described previously,[14,15] while the azido derivative **3** was prepared by standard acetylation (pyridine/acetic anhydride, 96% yield) of the 3-OH precursor, easily obtained in five steps from glucosamine, as previously reported.[16]

Azide **4** was synthesized as shown in Scheme 3. Regioselective reductive opening of the 4,6-benzylidene acetal **5**[17,18] with TFA/TES gave the known alcohol **6**,[19] which was converted into **7** by treatment with an excess of levulinic anhydride.[20] First attempts to remove the benzyl group were conducted with Pd–C in methanol under positive hydrogen pressure. Unfortunately, though, compound **8** was

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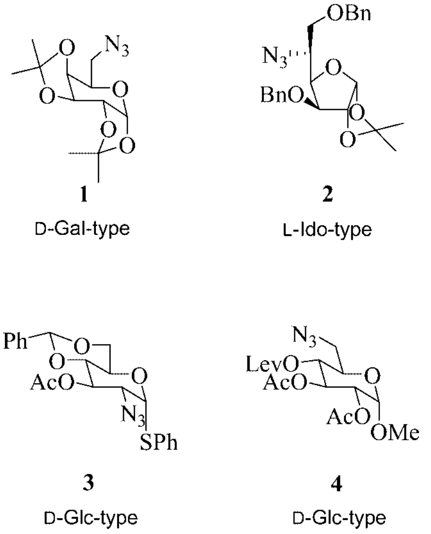
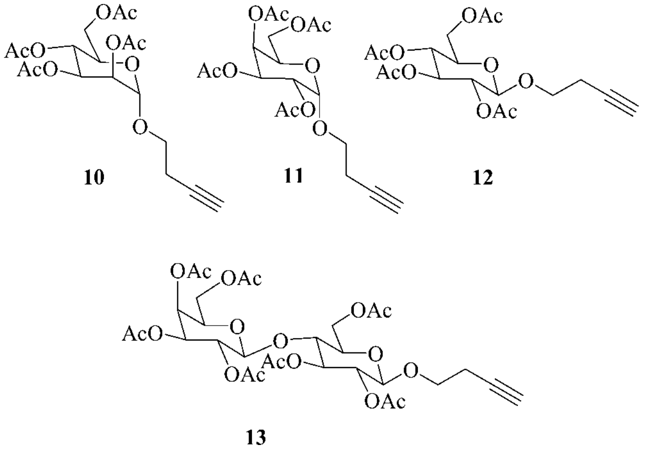


Scheme 2.



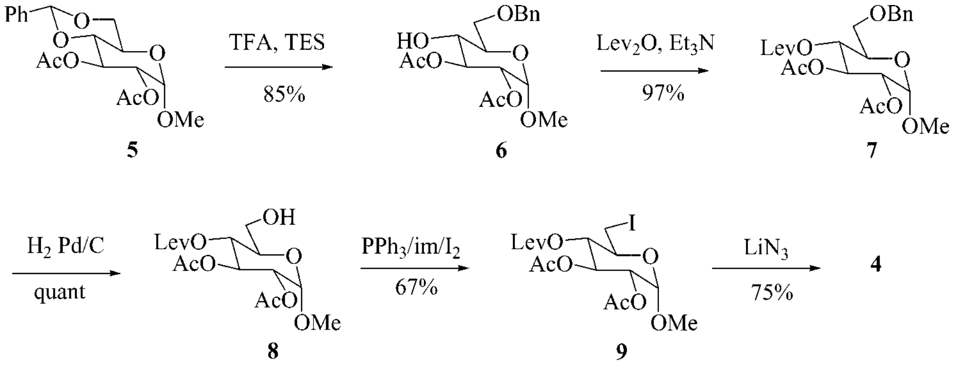
Scheme 4.

unstable under these conditions and migration of the Lev group from *O*-5 to *O*-6 occurred. The same approach in THF, however, allowed us to isolate **8** in quantitative yield. After conversion of the hydroxy group into the iodide **9** by treatment with $PPh_3/I_2/Im$,[21] the synthesis of **4** was achieved by addition of LiN_3 in DMF.

Conversely, four different alkynyl saccharides were selected: the mannoside **10**,[22] the galactoside **11**, the glucoside **12**,[23] and the lactoside **13** (Scheme 4), all easily obtained from the corresponding peracetylated sugars by treatment with but-3-yn-1-ol in the presence of boron trifluoride etherate.[23]

The first attempted cycloadditions between saccharides **4** and **10** are summarized in Table 1 and Scheme 5. Nitrogen donors including bases such as DIPEA and some solvents such as acetonitrile have been reported to improve results in Cu^I-catalyzed alkyne–azide coupling by helping to prevent degradation of Cu^I by disproportionation or oxidation.[24] In our hands, these experimental conditions were inappropriate, no reaction having occurred after 2 h in THF with a catalytic amount of Cu^I (Entry 1). In the presence of an excess of CuI (Entry 3), however, the expected compound **14** was obtained in moderate yield after 4 h in THF (Entry 2) or 1 h in acetonitrile, although the reactions did not go to completion. To overcome the instability of Cu^I, it was generated by in situ reduction of Cu^{II} salts (copper sulfate) with the aid of sodium ascorbate,[25] but no reaction had been observed in *sec*-butanol or in anhydrous DMF after 3 and 2 h, respectively (Entries 4 and 6). Fortunately, though, we observed dramatic increases in the reaction rates when water was added to the *sec*-butanol or DMF (Entries 5 and 7), and only the expected triazole **14** was formed (71 % and 88 % yields, respectively, after flash chromatography). These results demonstrate the high sensitivity of the reaction to the experimental conditions and corroborate precedent reports on the positive effect of water.[26]

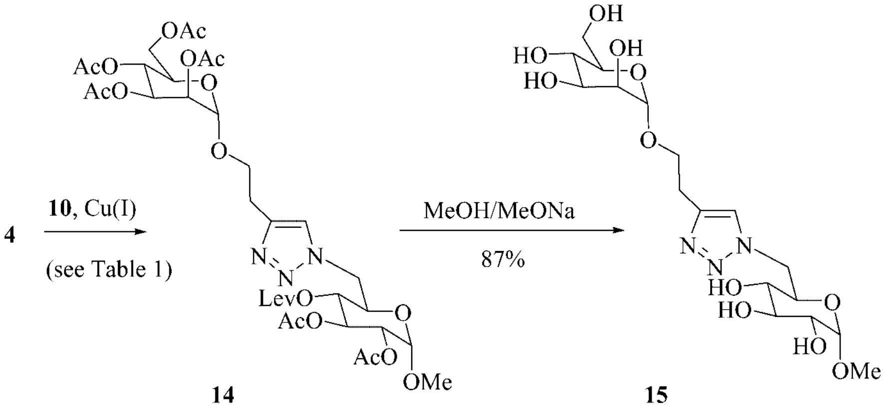
As previously observed, the catalyzed Huisgen reaction was found to be highly regioselective, yielding 1,4-disubstituted 1,2,3-triazole-containing carbohydrates.[5] In each cycloadduct, the olefinic proton associated with the 1,2,3-triazole moiety was identified as a singlet between δ = 7.25 and 7.65 ppm, while allylic methylene resonances were observed around δ = 3 ppm. ^{13}C NMR analysis of the compounds were also carried out: the large Δ (δ_{C4}–δ_{C5}) values for the different triazoles, ranging from 20.4 to 22.5 ppm, corroborated the 1,4-disubstituted structure, since much smaller values would be expected for 1,5-disubstituted regioisomers.[27]



Scheme 3.

Table 1. Evaluation of different conditions for the cycloaddition.

Entry	Equiv. of alkyne	Equiv. of DIPEA	Na ascorbate	Catalyst	Solvent	Time / h	% Yield
1	1	3	–	0.2 equiv. CuI	THF	2	no reaction
2	1.2	4	–	0.2 equiv. CuI	THF	4	55
3	1	3	–	2.0 equiv. CuI	CH_3CN	1	49
4	1	–	0.4 equiv.	0.2 equiv. $CuSO_4$	*s*Bu	3	no reaction
5	1	–	0.4 equiv.	0.2 equiv. $CuSO_4$	*s*Bu/H_2O	1.1	71
6	1	–	0.4 equiv.	0.2 equiv. $CuSO_4$	DMF	2	no reaction
7	1	–	0.4 equiv.	0.2 equiv. $CuSO_4$	DMF/H_2O	1.5	88



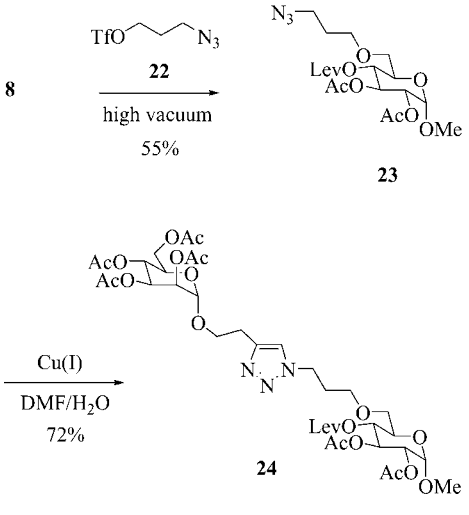
Scheme 5.

Removal of the protecting groups from **14** with a catalytic quantity of sodium methoxide in methanol gave the compound **15** in 87% yield. The triazole ring was not affected by the basic conditions and no degradation occurred.

The best experimental conditions (Table 1, Entry 7) found were applied to couplings of azido sugars **1**–**4** with alkynyl derivatives **10**–**13**, and the results are summarized in Table 2.

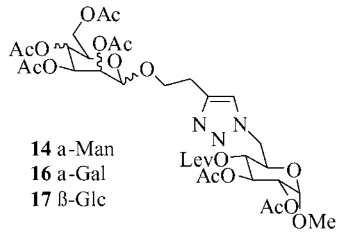
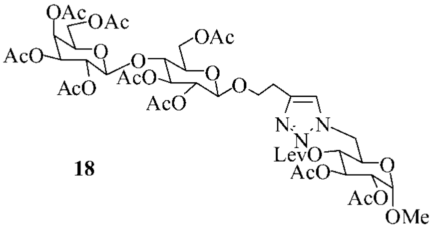
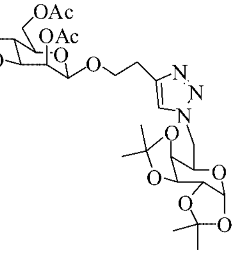
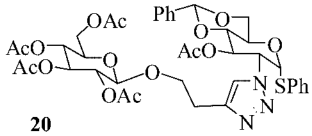
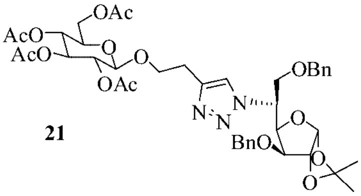
All the reactions had gone to completion within 5 h at room temperature, with use of equimolar ratios of azide and alkyne and catalytic quantities of copper sulfate. Yields ranged from 70 to 100% after flash chromatography (Table 2). Different cycloaddition trials on compound **4** showed similar yields independently of the α,β stereochemistry of the alkynyl saccharide employed (Entries 1, 2, 3). The reaction time with alkynyl lactoside **13** was slightly higher because of its lower solubility in the DMF/water mixture (Entry 4). Notably, compound **4** (Entry 6) contains a thiophenyl group, which can be activated for further glycosylation. Under our conditions, the intermolecular 1,3-dipolar cycloadditions tolerated the presence of a variety of protecting groups (i.e., acetate or levulinate esters, benzyl ethers, benzylidene or isopropylidene acetals). Azide groups linked to secondary carbons atoms, on the other hand, provided the corresponding oligosaccharide analogues in very good to excellent yields (Entries 6 and 7).

In order to modulate the distance between the monosaccharides, we connected the azido group through a spacer (Scheme 6). Alkylation of **8** with the azide derivative **22,** freshly prepared as described previously,[28] was problematic in the presence of base, probably due to the sensitivity of acetates to the alkaline medium. The reaction was therefore conducted in the absence of base and under vacuum, by a method previously described.[29,30] Compound **23** was isolated in 55% yield. In spite of the moderate yield obtained, this reaction is particularly interesting as the starting material can be recycled. The general procedure for the click reaction was employed and product **24** was isolated in 72% yield.



Scheme 6.

Table 2. Structures of the cycloadducts obtained and experimental conditions.

Entry	Product	CuSO$_4$	Na asc.	Time	Yield
1	 **14** a-Man **16** a-Gal **17** ß-Glc	0.2 equiv.	0.4 equiv.	1.5 h	**14** a-Man 88%
2		0.4 equiv.	0.8 equiv.	3 h	**16** a-Gal 76%
3		0.2 equiv.	0.4 equiv.	1.6 h	**17** ß-Glc 75%
4	 **18**	0.4 equiv.	0.8 equiv.	5 h	70%
5	 **19**	0.2 equiv.	0.4 equiv.	2.5 h	100%
6	 **20**	0.2 equiv.	0.4 equiv.	3 h	100%
7	 **21**	0.4 equiv.	0.8 equiv.	1.1 h	75%

Conclusion

In summary, we have developed a procedure for the connection of saccharides by click chemistry techniques. This approach shows that different sugars bearing azide substituents on C-2, C-5, or C-6 can be used as building blocks. The reactions tolerate the presence of a range of protecting groups commonly used in carbohydrate chemistry. Moreover, they can be conducted at room temperature, with equimolar ratios of reagents, and products are obtained in high yields. The high solubilities of the protected sugars in DMF allowed us to add 30% water to the mixtures, which greatly accelerated the cycloaddition reactions. Furthermore, we have also demonstrated the possibility of varying the distances between triazole-linked saccharides units, through the use of spacers to attach the azido group.

Experimental Section

General: All purchased materials were used without further purification. Dichloromethane was distilled from calcium hydride, tetrahydrofuran over sodium and benzophenone. Analytical thin-layer chromatography (TLC) was carried out on Merck D.C.-Alufolien (Kieselgel 60 F$_{254}$). Flash chromatography was performed on Geduran Si 60 (0.040–0.060 mm pore size) with distilled solvents. ^{1}H, ^{13}C nuclear magnetic resonance (NMR) spectra were recorded on a Bruker AC 300 spectrometer, and chemical shifts are reported in parts per million relative to tetramethylsilane or a residual solvent (CHCl$_3$) peak (^{1}H: δ = 7.26 ppm, ^{13}C: δ = 77.2 ppm). Assignments of ^{1}H and ^{13}C were assisted by 2D ^{1}H COSY and 2D ^{1}H–^{13}C CORR experiments. High resolution mass spectra HRMS were obtained by Electrospray Ionization (ESI) with a Micromass–Waters Q-TOF Ultima Global instrument. Optical rotations were measured on a Perkin–Elmer 343 machine at 20 °C in a 1-cm cell in the stated solvent. $[\alpha]_{\mathrm{D}}$ values are given in $10^{-1}\ \mathrm{deg\,cm^2\,g^{-1}}$ (concentration *c* given as g/100 mL).

Phenyl 3-Acetyl-2-azido-2-deoxy-4,6-*O*-benzylidene-1-thio-α-D-glucopyranoside (3): The known phenyl 2-azido-4,6-*O*-benzylidene-2-deoxy-1-thio-α-D-glucopyranoside[16] (1.49 g, 3.9 mmol) was dissolved in a mixture of acetic anhydride (20 mL) and pyridine (25 mL) and the mixture was stirred at room temp. for 18 h. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (cyclohexane/EtOAc, 9:1) to afford **3** as a white solid (1.6 g, 96%). $[\alpha]_{\mathrm{D}}^{20} = +145$ ($c = 1$, $\mathrm{CH_2Cl_2}$). ^{1}H NMR (300 MHz, $\mathrm{CDCl_3}$): $\delta = 7.44$ (m, 10 H, arom. H), 5.65 (d, $J_{1,2} = 6.0$ Hz, 1 H, 1-H), 5.54 (s, 1 H, $\mathrm{PhC}\mathit{H}$), 5.53 (dd, $J_{2,3} = J_{3,4} = 10.0$ Hz, 1 H, 3-H), 4.51 (ddd, $J_{4,5} = 10.0$, $J_{5,6a} = 5.0$, $J_{5,6b} = 10.0$ Hz, 1 H, 5-H), 4.26 (dd, $J_{6a,6b} = 10.0$ Hz, 1 H, 6a-H), 4.07 (dd, 1 H, 2-H), 3.80 (dd, 1 H, 6b-H), 3.70 (dd, 1 H, 4-H), 2.18 (s, 3 H, $\mathrm{C}\mathit{H}_3$) ppm. ^{13}C NMR (75 MHz, $\mathrm{CDCl_3}$): $\delta = 169.9$ (CO), 137.2, 134.2, 133.1, 128.6, 126.6 (arom. C), 102.1 ($\mathrm{Ph}\mathit{C}\mathrm{H}$), 88.2 (C-1), 80.0 (C-4), 70.9 (C-3), 68.8 (C-6), 64.3 (C-5), 62.7 (C-2), 21.3 ($\mathit{C}\mathrm{H_3}$) ppm. HRMS: *m*/*z*: found 450.1114; $\mathrm{C_{21}H_{21}O_5N_3NaS}$ requires 450.1100 $[\mathrm{M + Na}]^+$.

Methyl 2,3-Di-*O*-acetyl-6-*O*-benzyl-4-*O*-levulinyl-α-D-glucopyranoside (7): Levulinic anhydride (1.8 g, 8.41 mmol) in dichloromethane (5 mL), $\mathrm{Et_3N}$ (2.36 mL, 16.8 mmol), and DMAP (25 mg, 0.20 mmol) were added under argon to a solution of compound **6** (1.55 g, 4.21 mmol) in dry dichloromethane (20 mL), and the mixture was stirred for 16 h at room temp. The solvent was removed under reduced pressure and the residue was purified by flash chromatography (cyclohexane/EtOAc, 7:3 to 13:7) to afford **7** as a colorless oil (1.91 g, 97%). $[\alpha]_{\mathrm{D}}^{20} = +118$ ($c = 0.2$, $\mathrm{CH_2Cl_2}$). ^{1}H NMR (300 MHz, $\mathrm{CDCl_3}$): $\delta = 7.30$ (m, 5 H, arom. H), 5.49 (dd, $J_{2,3} = 10.0$, $J_{3,4} = 9.5$ Hz, 1 H, 3-H), 5.15 (dd, $J_{4,5} = 10.0$ Hz, 1 H, 4-H), 4.93 (d, $J_{1,2} = 3.6$ Hz, 1 H, 1-H), 4.91 (dd, 1 H, 2-H), 4.54 (s, 2 H, $\mathrm{C}\mathit{H}_2\mathrm{Ph}$), 3.94 (m, 1 H, 5-H), 3.56 (m, 2 H, 6-a, 6b-H), 3.42 (s, 3 H, $\mathrm{C}\mathit{H}_3\mathrm{O}$), 2.67 (t, $J = 6.3$ Hz, 2 H, $\mathrm{CH_3COC}\mathit{H}_2\mathrm{CH_2}$), 2.40 (t, $J = 6.3$ Hz, 2 H, $\mathrm{CH_3COCH_2C}\mathit{H}_2$), 2.15 (s, 3 H, $\mathrm{C}\mathit{H}_3\mathrm{Lev}$), 2.07, 2.04 (2 × s, 3 H each, 2 × $\mathrm{C}\mathit{H}_3\mathrm{CO}$) ppm. ^{13}C NMR (75 MHz, $\mathrm{CDCl_3}$): $\delta = 206.1$ ($\mathrm{CH_3}\mathit{C}\mathrm{OCH_2}$), 171.8, 170.7 ($\mathrm{CH_3}\mathit{C}\mathrm{O}$), 170.6 ($\mathit{C}\mathrm{OCH_2CH_2}$), 138.2, 128.7, 128.3, 128.1 (arom. C), 97.1 (C-1), 74.0 ($\mathrm{Ph}\mathit{C}\mathrm{H_2}$), 71.4 (C-2), 70.4 (C-3), 69.6 (C-4), 68.8 (C-5, -6), 55.8 ($\mathit{C}\mathrm{H_3O}$), 38.1 ($\mathrm{CH_3CO}\mathit{C}\mathrm{H_2CH_2}$), 29.1 ($\mathrm{C}\mathit{H}_3\mathrm{Lev}$), 28.2 ($\mathrm{CH_3COCH_2}\mathit{C}\mathrm{H_2}$), 21.1 ($\mathit{C}\mathrm{H_3CO}$) ppm. HRMS: *m*/*z*: found 489.1715; $\mathrm{C_{23}H_{30}NaO_{10}}$ requires 489.1737 $[\mathrm{M + Na}]^+$.

Methyl 2,3-Di-*O*-acetyl-4-*O*-levulinyl-α-D-glucopyranoside (8): A mixture of compound **7** (200 mg, 0.429 mmol) and Pd/C (10%, 20 mg) in THF (6 mL) was stirred for 40 min at room temp. under a positive pressure of hydrogen. The mixture was filtered through celite, and the solvent was removed under reduced pressure to give **7** as a colorless oil (161 mg, quant). $[\alpha]_{\mathrm{D}}^{20} = +94$ ($c = 0.2$, $\mathrm{CH_2Cl_2}$). ^{1}H NMR (300 MHz, $\mathrm{CDCl_3}$): $\delta = 5.55$ (dd, $J_{2,3} = J_{3,4} = 9.8$ Hz, 1 H, 3-H), 5.03 (dd, $J_{4,5}$ 9.8 Hz, 1 H, 4-H), 4.96 (d, $J_{1,2} = 3.6$ Hz, 1 H, 1-H), 4.86 (dd, 1 H, 2-H), 3.78–3.62 (m, 3 H, 5-, 6a-, 6b-H), 3.40 (s, 3 H, $\mathrm{C}\mathit{H}_3\mathrm{O}$), 2.74 (m, 2 H, $\mathrm{CH_3COC}\mathit{H}_2\mathrm{CH_2}$), 2.50 (m, 2 H, $\mathrm{CH_3COCH_2C}\mathit{H}_2$), 2.17 (s, 3 H, $\mathrm{C}\mathit{H}_3\mathrm{Lev}$), 2.07, 2.04 (2 × s, 3 H each, $\mathrm{C}\mathit{H}_3\mathrm{CO}$) ppm. ^{13}C NMR (75 MHz, $\mathrm{CDCl_3}$): $\delta = 172.9$, 170.6 ($\mathit{C}\mathrm{O}$), 97.2 (C-1), 71.5 (C-2), 70.1, 69.9, 69.8 (C-3, -4, -5), 61.3 (C-6), 55.8 ($\mathit{C}\mathrm{H_3O}$), 38.1 ($\mathrm{CH_3CO}\mathit{C}\mathrm{H_2CH_2}$), 30.0 ($\mathrm{C}\mathit{H}_3\mathrm{Lev}$), 28.2 ($\mathrm{CH_3COCH_2}\mathit{C}\mathrm{H_2}$), 21.1 ($\mathit{C}\mathrm{H_3CO}$) ppm. HRMS: *m*/*z*: found 399.1256; $\mathrm{C_{16}H_{24}NaO_{10}}$ requires 399.1267 $[\mathrm{M + Na}]^+$.

Methyl 2,3-Di-*O*-acetyl-6-*O*-iodo-4-*O*-levulinyl-α-D-glucopyranoside (9): A solution of compound **8** (3.3 g, 8.8 mmol), $\mathrm{PPh_3}$ (6.9 g, 26 mmol), imidazole (2.38 g, 35 mmol), and $\mathrm{I_2}$ (5.57 g, 21.9 mmol) in anhydrous toluene (160 mL) was stirred at room temp. for 6 h. The reaction mixture was cooled and satd. $\mathrm{NaHCO_3}$ (160 mL) was added. After the mixture had been stirred for 5 min, $\mathrm{I_2}$ (16.5 g, 65 mmol) was added and after an additional 10 min excess iodine was removed by addition of a sodium thiosulfate solution (100 mL). The organic layer was diluted with toluene, separated, washed with water, dried with $\mathrm{Na_2SO_4}$, and filtered, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography (cyclohexane/EtOAc, 3:1) to afford **9** as a colorless oil (2.89 g, 67%). $[\alpha]_{\mathrm{D}}^{20} = +73$ ($c = 0.3$, $\mathrm{CH_2Cl_2}$). ^{1}H NMR (300 MHz, $\mathrm{CDCl_3}$): $\delta = 5.47$ (dd, $J_{2,3} = J_{3,4} = 9.5$ Hz, 1 H, 3-H), 4.94 (d, $J_{1,2} = 3.6$ Hz, 1 H, 1-H), 4.88 (dd, $J_{4,5} = 9.5$ Hz, 1 H, 4-H), 4.82 (dd, 1 H, 2-H), 3.77 (m, 1 H, 5-H), 3.46 (s, 3 H, $\mathrm{C}\mathit{H}_3\mathrm{O}$), 3.60 (dd, $J_{5,6a} = 2.4$, $J_{6a,6b} = 10.9$ Hz, 1 H, 6a-H), 3.60 (dd, $J_{5,6b} = 8.4$ Hz, 1 H, 6b-H), 2.72 (m, 2 H, $\mathrm{CH_3COC}\mathit{H}_2\mathrm{CH_2}$), 2.49 (m, 2 H, $\mathrm{CH_3COCH_2C}\mathit{H}_2$), 2.17 (s, 3 H, $\mathrm{C}\mathit{H}_3\mathrm{Lev}$), 2.06, 2.02 (2 × s, 3 H each, 2 × $\mathrm{CH_3CO}$) ppm. ^{13}C NMR (75 MHz $\mathrm{CDCl_3}$): $\delta = 206.2$ ($\mathrm{CH_3}\mathit{C}\mathrm{O}$), 171.6, 170.1 ($\mathit{C}\mathrm{O}$), 96.8(C-1), 72.5, 71.1 (C-2, C-4), 69.4 (C-3), 68.9 (C-5), 55.8 ($\mathit{C}\mathrm{H_3O}$), 38.9 ($\mathrm{CH_3CO}\mathit{C}\mathrm{H_2CH_2}$), 30.8 ($\mathrm{C}\mathit{H}_3\mathrm{Lev}$), 27.1 ($\mathrm{CH_3COCH_2}\mathit{C}\mathrm{H_2}$), 20.8 ($\mathit{C}\mathrm{H_3CO}$), 3.9 (C-6) ppm. HRMS: *m*/*z*: found 509.0294; $\mathrm{C_{16}H_{23}INaO_9}$ requires 509.0285 $[\mathrm{M + Na}]^+$.

Methyl 2,3-Di-*O*-acetyl-6-azido-6-deoxy-4-*O*-levulinyl-α-D-glucopyranoside (4): A mixture of compound **9** (150 mg, 0.3 mmol) and $\mathrm{LiN_3}$ (20% in water, 377 μL, 1.5 mmol) in dry DMF (5 mL) was stirred under argon at 50 °C until total consumption of starting material. EtOAc (20 mL) was added and the organic layer was washed with water (20 mL). The aqueous layer was extracted three times with EtOAc (3 × 10 mL). The organic layers were combined, dried with $\mathrm{Na_2SO_4}$, and filtered, and the solvent was removed under reduced pressure to afford **4** (90 mg, 75%). $[\alpha]_{\mathrm{D}}^{20} = +107$ ($c = 0.2$, $\mathrm{CH_2Cl_2}$). ^{1}H NMR (300 MHz, $\mathrm{CDCl_3}$): $\delta = 5.56$ (dd, $J_{2,3} = 10$, $J_{3,4} = 9.6$ Hz, 1 H, 3-H), 5.09 (dd, $J_{4,5} = 9.5$ Hz, 1 H, 4-H), 5.04 (d, $J_{1,2} = 3.7$ Hz, 1 H, 1-H), 4.94 (dd, 1 H, 2-H), 4.02 (dt, $J_{5,6a} = J_{5,6b} = 5.0$ Hz, 1 H, 5-H), 3.52 (s, 3 H, $\mathrm{C}\mathit{H}_3\mathrm{O}$), 3.44 (d, 2 H, 6a-, 6b-H), 2.80 (m, 2 H, $\mathrm{CH_3COC}\mathit{H}_2\mathrm{CH_2}$), 2.54 (m, 2 H, $\mathrm{CH_3COCH_2C}\mathit{H}_2$), 2.24 (s, 3 H, $\mathrm{C}\mathit{H}_3\mathrm{Lev}$), 2.15, 2.12 (2 × s, 3 H each, 2 × $\mathrm{CH_3CO}$) ppm. ^{13}C NMR (75 MHz, $\mathrm{CDCl_3}$): $\delta = 206.4$ ($\mathrm{CH_3}\mathit{C}\mathrm{O}$), 171.7, 170.3, 170.2, ($\mathit{C}\mathrm{O}$), 96.7(C-1), 70.9 (C-2), 69.7, 69.5 (C-3, -4), 68.7 (C-5), 55.6 ($\mathit{C}\mathrm{H_3O}$), 50.9 (C-6), 38.9 ($\mathrm{CH_3CO}\mathit{C}\mathrm{H_2CH_2}$), 30.8 ($\mathrm{C}\mathit{H}_3\mathrm{Lev}$), 27.8 ($\mathrm{CH_3COCH_2}\mathit{C}\mathrm{H_2}$), 20.8 ($\mathit{C}\mathrm{H_3CO}$) ppm. HRMS: *m*/*z*: found 424.1346; $\mathrm{C_{16}H_{23}N_3NaO_9}$ requires 424.1332 $[\mathrm{M + Na}]^+$.

But-3-ynyl 2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranoside (11): This compound was obtained by the procedure described in ref.[22]. The pure α anomer was separated from the α/β mixture by flash chromatography (dichloromethane/EtOAc, 98:2, 20% yield). $[\alpha]_{\mathrm{D}}^{20} = +130$ ($c = 0.1$, $\mathrm{CH_2Cl_2}$). ^{1}H NMR (300 MHz, $\mathrm{CDCl_3}$): $\delta = 5.43$ (br d, $J_{3,4} = 3.0$ Hz, $J_{4,5} < 1$ Hz, 1 H, 4-H), 5.33 (dd, $J_{2,3} = 11.0$ Hz, 1 H, 3-H), 5.15 (d, $J_{1,2} = 4.0$ Hz, 1 H, 1-H), 5.09 (dd, 1 H, 2-H), 4.28 (t, $J_{5,6a} = J_{5,6b} = 7.0$ Hz, 1 H, 5-H), 4.09–4.04 (m, 2 H, 6a-, 6b-H), 3.75 (dt, $J = 7$, $J = 10$ Hz, 1 H, $\mathrm{OC}\mathit{H}\mathrm{HCH_2}$), 3.60 (dt, $J = 7$, $J = 10$ Hz, 1 H, $\mathrm{OCH}\mathit{H}\mathrm{CH_2}$), 2.47 (dt, $J = 3$, $J = 7$ Hz, 2 H, $\mathrm{OCH_2C}\mathit{H}_2$), 2.11, 2.05, 2.02, 1.97 (4 × s, 3 H each, 4 × $\mathrm{C}\mathit{H}_3\mathrm{CO}$), 1.95 (m, 1 H, $\mathrm{CC}\mathit{H}$) ppm. ^{13}C NMR (75 MHz, $\mathrm{CDCl_3}$): $\delta = 170.5$, 170.3, 170.0 ($\mathit{C}\mathrm{O}$), 96.3 (C-1), 80.8 ($\mathrm{CH_2}\mathit{C}\mathrm{CH}$), 69.8 ($\mathrm{CH_2C}\mathit{C}\mathrm{H}$), 68.2 (C-2, -4), 67.6 (C-3), 66.7 ($\mathrm{O}\mathit{C}\mathrm{H_2CH_2CCH}$), 66.6 (C-5), 61.8 (C-6), 20.9, 20.7 ($\mathit{C}\mathrm{H_3CO}$), 19.8 ($\mathrm{OCH_2}\mathit{C}\mathrm{H_2}$) ppm. HRMS: *m*/*z*: found 423.1282; $\mathrm{C_{18}H_{24}NaO_{10}}$ requires 423.1267 $[\mathrm{M + Na}]^+$.

But-3-ynyl 2,3,4,6,2′,3′,6′-Hepta-*O*-acetyl-β-D-lactopyranoside (13): This compound was obtained by the procedure described in ref.[22] The pure β product was isolated by flash chromatography (cyclohexane/EtOAc, 2:3 to 1:1, 43% yield). $[\alpha]_{\mathrm{D}}^{20} = -9$ ($c = 0.4$, $\mathrm{CH_2Cl_2}$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.31 (br d, $J_{3',4'}$ = 3 Hz, $J_{4',5'}$ < 1 Hz, 1 H, 4′-H), 5.13 (dd, $J_{2,3}$ = $J_{3,4}$ = 9.0 Hz, 1 H, 3-H), 5.06 (dd, $J_{1',2'}$ = $J_{2',3'}$ = 8.0 Hz, 1 H, 2′-H), 4.90 (dd, 1 H, 3′-H), 4.85 (dd, $J_{1,2}$ = 8 Hz, 1 H, 2-H), 4.50 (d, 1 H, 1-H), 4.50 (m, 2 H, 1′-, 6a-H), 4.09–4.03 (m, 4 H, 6b-, 5′-, 6′a- 6′b-H), 3.88–3.75 (m, 2 H, 5′-H, OC*H*HCH$_2$), 3.74 (dd, 1 H, $J_{4,5}$ = 9 Hz, 4-H), 3.63–3.59 (m, 2 H, 5-H, OCH*H*CH$_2$), 2.42 (dt, 2 H, *J* = 3.0, *J* = 7.0 Hz, OCH$_2$C*H*$_2$), 2.11, 2.08 (×2), 2.02, 2.01(×2), 1.92 (7×s, 3 H each, 7×C*H*$_3$CO), 1.92 (m, 1 H, CC*H*) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.7, 170.5, 170.4, 170.1, 170.0, 169.4 (*C*O), 101.4 (C-1′), 101.0 (C-1), 80.9 (*C*CH), 76.6 (C-4), 73.0 (C-3), 71.9 (C-2), 71.4 (C-3′), 71.0 (C-5′), 69.9 (CH$_2$C*C*H), 69.5 (C-2′), 68.3 (O*C*H$_2$CH$_2$CCH), 67.0 (C-4′), 62.3, 61.2 (C-6, -6′), 21.1, 21.1, 21.0, 20.9 (*C*H$_3$CO), 20.2 (OCH$_2$*C*H$_2$) ppm. HRMS: *m*/*z*: found 711.2089; $C_{30}H_{40}NaO_{18}$ requires 711.2112 [M + Na]$^+$.

General Procedure for the Huisgen Cycloadditions: Compounds **14**–**21** and **24** were synthesized by this procedure. Alkynyl-saccharide (0.13 mmol) and azido-saccharide (0.13 mmol) were dissolved in a DMF/H_2O mixture (4+1.3 mL). Copper sulfate (0.2 or 0.4 equiv.) and sodium ascorbate (0.4 or 0.8 equiv.) were added and the mixture was stirred at room temp. until TLC indicated the disappearance of the starting materials. The mixture was poured into H_2O/satd. NH_4Cl solution (1:1, 20 mL) and the product was extracted four times with EtOAc. The organic layer was dried with Na_2SO_4 and filtered, and the solvent was removed under reduced pressure. The residue was purified by flash chromatography.

1-(2′,3′,4′,6′-Tetra-*O*-acetyl-α-D-mannopyranosyloxyethyl)-4-(methyl 2′′,3′′-di-*O*-acetyl-6′′-deoxy-4′′-*O*-levulinyl-α-D-glucopyranosid-6-yl)-1*H*-1,2,3-triazole (14): Flash chromatography (EtOAc/cyclohexane, 4:1 to EtOAc). $[\alpha]_D^{20}$ = +80 (*c* = 0.4, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.55 (s, 1 H, C*H*N), 5.46 (dd, $J_{2,3}$ = $J_{3,4}$ = 10.0 Hz, 1 H, 3-H), 5.27–5.15 (m, 5 H, 2′-, 3′-, 4′-H), 4.89 (d, $J_{1',2'}$ = 3.0 Hz, 1 H, 1′-H), 4.86–4.79 (m, 3 H, 1-, 2-, 4-H), 4.59 (br d, $J_{5,6a}$ < 1, $J_{6a,6b}$ = 13.9 Hz, 1 H, 6a-H), 4.50–3.90 (m, 5 H, 5-, 6b-, 6′a-, 6′b-H, OC*H*HCH$_2$), 3.80–3.73 (m, 2 H, 5′-H, OCH*H*CH$_2$), 3.09 (s, 3 H, C*H*$_3$O), 3.05–3.01 (m, 2 H, OCH$_2$CH$_2$), 2.75 (m, 2 H, CH$_3$COC*H*$_2$CH$_2$), 2.52 (m, 2 H, CH$_3$COCH$_2$C*H*$_2$), 2.15 (s, 3 H, C*H*$_3$Lev), 2.14, 2.12, 2.06, 2.02, 2.01, 1.97 (6×s, 3 H each, 6×C*H*$_3$CO) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 206.7 (CH$_3$*C*O), 171.9, 170.8, 170.2, 169.7 (*C*O), 144.2 (N*C*=CH), 123.8 (NC=*C*H), 97.5 (C-1′), 96.6 (C-1), 70.8 (C-2), 70.2 (C-4), 69.6, 69.5, 66.1 (C-2′, -3′, -4′), 69.1 (C-5′), 68.8 (C-5), 68.1 (C-3′), 67.0 (O*C*H$_2$CH$_2$), 62.4 (C-6′), 55.3 (*C*H$_3$O), 50.6 (C-6), 37.9 (CH$_3$CO*C*H$_2$CH$_2$), 29.7 (*C*H$_3$Lev), 28.0 (CH$_3$COCH$_2$*C*H$_2$), 26.2 (OCH$_2$*C*H$_2$), 20.9 (*C*H$_3$CO) ppm. HRMS: *m*/*z*: found 824.2686; $C_{34}H_{47}N_3NaO_{19}$ requires 824.2701 [M + Na]$^+$.

1-(α-D-Mannopyranosyloxyethyl)-4-(methyl 6′′-deoxy-α-D-glucopyranosid-6-yl)-1*H*-1,2,3-triazole (15): Flash chromatography (EtOAc/cyclohexane, 4:1 to EtOAc). $[\alpha]_D^{20}$ = +59 (*c* = 0.1, D_2O). ^{1}H NMR (300 MHz, CD_3OD): δ = 7.26 (s, 1 H, C*H*N), 4.28 (dd, $J_{5,6a}$ = 7.7, $J_{6a,6b}$ = 14.2 Hz, 1 H, 6a-H), 4.19 (d, $J_{1',2'}$ = 2.0 Hz, 1 H, 1′-H), 4.10 (d, $J_{1,2}$ = 4.0 Hz, 1 H, 1-H), 3.98 (dd, 1 H, $J_{5,6b}$ = 8.0 Hz, 6b-H), 3.42–3.36 (m, 1 H, OCH*H*CH$_2$), 3.30–2.50 (m, 11 H, 2-, 3-, 4-, 5-, 2′-, 3′-, 4′-, 5′-, 6′a-, 6′b-H, OCH*H*CH$_2$), 2.60 (s, 3 H, C*H*$_3$O), 2.43 (m, 2 H, OCH$_2$C*H*$_2$) ppm. ^{13}C NMR (75 MHz, CD_3OD): δ = 146.0 (N*C*=CH), 125.5 (NC=*C*H), 101.6 (C-1′), 101.2 (C-1), 74.9, 74.8, 73.3, 72.8, 72.5, 72.0, 71.6, 68.5 (C-2, -3, -4, -5, -2′, -3′, -4′, -5′), 67.4 (O*C*H$_2$CH$_2$), 62.9 (C-6′), 55.3 (*C*H$_3$O), 52.3 (C-6), 27.0 (OCH$_2$*C*H$_2$) ppm. HRMS: *m*/*z*: found 474.1704; $C_{17}H_{29}N_3NaO_{11}$ requires 474.1700 [M + Na]$^+$.

1-(2′,3′,4′,6′-Tetra-*O*-acetyl-α-D-galactopyranosyloxyethyl)-4-(methyl 2′′,3′′-di-*O*-acetyl-6′′-deoxy-4′′-*O*-levulinyl-α-D-glucopyranosid-6-yl)-1*H*-1,2,3-triazole (16): Flash chromatography (EtOAc/cyclohexane, 4:1 to EtOAc). $[\alpha]_D^{20}$ = +110 (*c* = 0.2, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.50 (s, 1 H, C*H*N), 5.44 (dd, $J_{2,3}$ = $J_{3,4}$ = 10.0 Hz, 1 H, 3-H), 5.43 (br d, $J_{3',4'}$ = 3.0, $J_{4,5}$ < 1 Hz, 1 H, 4′-H), 5.26 (dd, $J_{2',3'}$ = 11, $J_{3',4'}$ = 3.0 Hz, 1 H, 3′-H), 5.09 (d, $J_{1',2'}$ = 4.0 Hz, 1 H, 1′-H), 5.08 (dd, $J_{1',2'}$ = 4.0 Hz, 1 H, 2′-H), 4.79 (m, 3 H, 1-, 2-, 4-H), 4.59 (dd, $J_{5,6a}$ = 2.2, $J_{6a,6b}$ = 14.3 Hz, 1 H, 6a-H), 4.25 (dd, $J_{5,6b}$ = 8.3 Hz, 1 H, 6b-H), 4.20–3.90 (m, 5 H, 5-, 5′-, 6′a-, 6′b-, OC*H*HCH$_2$), 3.75 (dt, *J* = 7.0, *J* = 10.0 Hz, 1 H, OC*H*HCH$_2$), 3.08 (s, 3 H, C*H*$_3$O), 3.02 (t, *J* = 7.0 Hz, 2 H, OCH$_2$C*H*$_2$), 2.73 (m, 2 H, CH$_3$COC*H*$_2$CH$_2$), 2.50 (m, 2 H, CH$_3$COCH$_2$C*H*$_2$), 2.14 (s, 3 H, C*H*$_3$Lev), 2.09 (×2), 1.99, 1.95 (×2), 1.93 (6×s, 3 H each, 6×C*H*$_3$CO) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 206.7 (CH$_3$*C*O), 171.8, 170.5, 170.3, 170.1 (*C*O), 144.3 (N*C*=CH), 123.3 (NC=*C*H), 97.5 (C-1′), 96.6 (C-1), 96.2 (C-1′), 70.8 (C-2), 70.0 (C-4), 69.4 (C-3), 68.1 (C-2′, -4′), 66.4 (C-5′), 67.5 (C-3′), 67.4 (O*C*H$_2$CH$_2$), 66.4 (C-5), 62.1 (C-6′), 55.7 (*C*H$_3$O), 50.8 (C-6), 38.2 (CH$_3$CO*C*H$_2$CH$_2$), 29.9 (*C*H$_3$Lev), 28.3 (CH$_3$COCH$_2$*C*H$_2$), 26.5 (OCH$_2$*C*H$_2$), 21.0 (*C*H$_3$CO) ppm. HRMS: *m*/*z*: found 824.2682; $C_{34}H_{47}N_3NaO_{19}$ requires 824.2701 [M + Na]$^+$.

1-(2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-glucopyranosyloxyethyl)-4-(methyl 2′′,3′′-di-*O*-acetyl-6′′-deoxy-4′′-*O*-levulinyl-α-D-glucopyranosid-6-yl)-1*H*-1,2,3-triazole (17): Flash chromatography (EtOAc/cyclohexane, 4:1 to EtOAc). $[\alpha]_D^{20}$ = +32 (*c* = 0.3, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.49 (s, 1 H, C*H*N), 5.45 (dd, $J_{2,3}$ = $J_{3,4}$ = 9.0 Hz, 1 H, 3-H), 5.13 (dd, $J_{2',3'}$ = $J_{3',4'}$ = 10.0 Hz, 1 H, 3′-H), 5.13 (dd, $J_{3',4'}$ = $J_{4',5'}$ = 10.0 Hz, 1 H, 4′-H), 5.12–4.79 (m, 4 H, 1-, 2-, 2′-, 4-H), 4.59 (dd, $J_{5,6a}$ = 2.2, $J_{6a,6b}$ = 14.2 Hz, 1 H, 6a-H), 4.50 (d, $J_{1',2'}$ = 8.0 Hz, 1 H, 1′-H), 4.35–4.00 (m, 5 H, 5-, 6b-, 6′a-, 6′b-H, OC*H*HCH$_2$), 3.75 (m, 2 H, 5′-H, OC*H*HCH$_2$), 3.10 (s, 3 H, C*H*$_3$O), 2.93 (t, 2 H, *J* = 7.0 Hz, OCH$_2$C*H*$_2$), 2.75 (m, 2 H, CH$_3$COC*H*$_2$CH$_2$), 2.50 (m, 2 H, CH$_3$COCH$_2$C*H*$_2$), 2.15 (s, 3 H, C*H*$_3$Lev), 2.09, 2.05, 2.03, 1.98, 1.96, 1.95 (6×s, 3 H each, 6×C*H*$_3$CO) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 206.7 (CH$_3$*C*O), 171.9, 170.7, 170.2, 169.5, 169.4 (*C*O), 144.4 (N*C*=CH), 123.8 (NC=*C*H), 100.9 (C-1′), 96.6 (C-1), 72.8 (C-3′), 71.9 (C-5′), 71.3 (C-2′), 70.8 (C-2), 70.0 (C-4), 69.5 (C-3), 69.0 (O*C*H$_2$CH$_2$), 68.5 (C-4′), 68.0 (C-5), 61.2 (C-6′), 55.5 (*C*H$_3$O), 50.5 (C-6), 37.9 (CH$_3$CO*C*H$_2$CH$_2$), 29.7 (*C*H$_3$Lev), 28.0 (CH$_3$COCH$_2$*C*H$_2$), 26.5 (OCH$_2$*C*H$_2$), 20.8 (*C*H$_3$CO) ppm. HRMS: *m*/*z*: found 824.2695; $C_{34}H_{47}N_3NaO_{19}$ requires 824.2701 [M + Na]$^+$.

1-(2′,3′,4′,6′,2′′,3′′,6′′-Hepta-*O*-acetyl-β-D-lactopyranosyloxyethyl)-4-(methyl 2′′′,3′′′-di-*O*-acetyl-6′′-deoxy-4′′-*O*-levulinyl-α-D-glucopyranosid-6-yl)-1*H*-1,2,3-triazole (18): Flash chromatography (EtOAc/cyclohexane, 4:1 to EtOAc). $[\alpha]_D^{20}$ = +13 (*c* = 0.3, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.49 (s, 1 H, C*H*N), 5.43 (dd, $J_{2,3}$ = $J_{3,4}$ = 9.0 Hz, 1 H, 3-H), 5.30 (br d, 1 H, $J_{3'',4''}$ = 3.0, $J_{4'',5''}$ < 1 Hz, 4′′-H), 5.13 (dd, $J_{2',3'}$ = $J_{3',4'}$ = 9.0 Hz, 1 H, 3′-H), 5.06 (dd, $J_{1'',2''}$ = $J_{2'',3''}$ = 8.0 Hz, 1 H, 2′′-H), 4.90–4.78 (m, 5 H, 1-, 2-, 2′-, 3′′-, 4-H), 4.59 (dd, $J_{5,6a}$ = 2.3, $J_{6a,6b}$ = 14.3 Hz, 1 H, 6a-H), 4.44 (m, 3 H, 1′-, 1′′-, 6′a-H), 4.25 (dd, $J_{5,6b}$ = 8.4 Hz, 1 H, 6b-H), 4.20–4.00 (m, 5 H, 5-, 6′b-, 6′′a-, 6′′b-H, OC*H*HCH$_2$), 3.80 (m, 1 H, 5′′-H), 3.74 (m, 2 H, 4′-H, OC*H*HCH$_2$), 3.52 (m, 1 H, 5′-H), 3.07 (s, 3 H, C*H*$_3$O), 2.91 (t, *J* = 7.0 Hz, 2 H, OCH$_2$C*H*$_2$), 2.72 (m, 2 H, CH$_3$COC*H*$_2$CH$_2$), 2.50 (m, 2 H, CH$_3$COCH$_2$C*H*$_2$), 2.14 (s, 3 H, C*H*$_3$Lev), 2.10, 2.08, 2.01 (×2), 1.98, 1.97 (×2), 1.93, 1.91 (9×s, 3 H each, 9×C*H*$_3$CO) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 206.7 (CH$_3$*C*O), 172, 170.7, 170.5, 170.4, 170.0, 169.5 (*C*O), 144.8 (N*C*=CH), 124.0 (NC=*C*H), 101.4 (C-1′′), 101.0 (C-1′), 96.9 (C-1), 76.7 (C-4′), 72.7 (C-3′, -5′), 71.6 (C-2′), 71.0, 70.8, 70.7, 70.0 (C-2, -4, -3′′, -5′′), 69.5 (C-3), 69.2 (C-2′′), 69.1 (O*C*H$_2$CH$_2$), 68.9 (C-5), 67.0 (C-4′′), 62.3, 61.2 (C-6′, -6′′), 55.7

(CH_3O), 50.8 (C-6), 38.1 ($CH_3COCH_2CH_2$), 29.7 (CH_3Lev), 28.3 ($CH_3COCH_2CH_2$), 26.7 (OCH_2CH_2), 21.0 (CH_3CO) ppm. HRMS: *m*/*z*: found 1112.3516; $C_{46}H_{63}N_3NaO_{27}$ requires 1112.3547 [M + Na]$^+$.

1-(2′,3′,4′,6′-Tetra-*O*-acetyl-α-D-mannopyranosyloxyethyl)-4-(6-azido-1′′,2′′:3′′,4′′-di-*O*-isopropylidene-6-deoxy-α-D-galactopyranosid-6-yl)-1*H*-1,2,3-triazole (19): Flash chromatography (EtOAc/cyclohexane, 4:1 to EtOAc). $[\alpha]_D^{20}$ = –3 (*c* = 0.3, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.63 (s, 1 H, C*H*N), 5.46 (d, $J_{1,2}$ = 5.0 Hz, 1 H, 1-H), 5.25–5.16 (m, 3 H, 2′-, 3′-, 4′-H), 4.79 (s, 1 H, 1′-H), 4.59 (dd, $J_{2,3}$ = 3.0, $J_{3,4}$ = 8.0 Hz, 1 H, 3-H), 4.54 (dd, $J_{5,6a}$ = 4.0, $J_{6a,6b}$ = 14.0 Hz, 1 H, 6a-H), 4.27 (dd, $J_{5,6b}$ = 8.0 Hz, 1 H, 6b-H), 4.27 (dd, 1 H, 2-H), 4.23–4.04 (m, 5 H, 4-, 5-, 6′a-, 6′b-H, OC*H*HCH$_2$), 4.00 (dt, *J* = 6.0, *J* = 10.0 Hz, 1 H, OC*H*HCH$_2$), 3.80 (m, 1 H, 5′-H), 3.67 (dt, *J* = 6.0, *J* = 10.0 Hz, 1 H, OCH*H*CH$_2$), 3.01 (t, *J* = 7.0 Hz, 2 H, OCH_2CH_2), 2.12, 2.05, 1.99, 1.94 (4 × s, 3 H each, 4 × CH_3CO), 1.45, 1.33, 1.31, 1.23 (4 × s, 3 H each, 4 × CH_3C) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.7, 170.0, 169.9, 169.7 (*C*O), 143.9 (N*C*=CH), 123.2 (NC=*C*H), 97.5 (C-1′), 96.6 (C-1), 71.3 (C-5′), 70.8 (C-3), 70.4 (C-2), 69.6, 69.1, 66.1 (C-4, -2′, -3′, -4′), 68.6 (C-5′), 67.3 (C-5), 67.2 (OCH_2CH_2), 62.4 (C-6′), 50.5 (C-6), 28.0 ($CH_3COCH_2CH_2$), 26.2 (OCH_2CH_2), 26.0, 25.9, 24.9, 24.5 (*C*H$_3$C), 20.9, 20.7 (*C*H$_3$CO) ppm. HRMS: *m*/*z*: found 708.2618; $C_{30}H_{43}N_3NaO_{15}$ requires 708.2592 [M + Na]$^+$.

2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-glucopyranosyloxyethyl)-4-(phenyl 2′′-deoxy-4,6-*O*-benzylidene-1-thio-α-D-glucopyranosid-2-yl)-1*H*-1,2,3-triazole (20): Flash chromatography (dichloromethane, then EtOAc). $[\alpha]_D^{20}$ = +48 (*c* = 0.4, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.49 (s, 1 H, C*H*N), 7.44–7.22 (m, 10 H, arom. H), 5.95 (dd, $J_{2,3}$ = $J_{3,4}$ = 10.0 Hz, 1 H, 3-H), 5.77 (d, $J_{1,2}$ = 5.0 Hz, 1 H, 1-H), 5.55 (s, 1 H, PhC*H*), 5.34 (dd, 1 H, 2-H), 5.17 (dd, $J_{2',3'}$ = $J_{3',4'}$ = 10.0 Hz, 1 H, 3′-H), 5.08 (dd, $J_{4',5'}$ = 10.0 Hz, 1 H, 4′-H), 4.97 (dd, $J_{1',2'}$ = 10.0 Hz, 1 H, 2′-H), 4.54–4.49 (m, 2 H, 1′-, 5-H), 4.30–4.27 (m, 2 H, 6a-, 6′a-H), 4.02–3.98 (m, 2 H, 6′-H, OC*H*HCH$_2$), 3.88–3.85 (m, 3 H, 4-, 6-H, OC*H*HCH$_2$), 3.72–3.69 (m, 1 H, 5′-H), 3.02 (t, *J* = 7 Hz, 2 H, OCH_2CH_2), 2.07, 2.05, 2.04 (× 2), 1.99, 1.97 (6 × s, 3 H each, 6 × CH_3CO) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.5, 170.1, 169.7, 169.2, 169.1 (*C*O), 144.0 (N*C*=CH), 137.5, 134.0, 133.3, 128.9, 128.2, 126.0 (arom. C), 121.5 (NC=*C*H), 101.6 (Ph*C*H), 100.5 (C-1′), 88.2 (C-1), 79.8 (C-4), 72.7 (C-3′), 71.7 (C-5′), 71.3 (C-2′), 70.9 (C-3), 69.0 (OCH_2CH_2), 68.6 (C-6), 68.2 (C-4′), 64.3 (C-5), 62.9 (C-2), 61.8 (C-6′), 26.3 (OCH_2CH_2), 20.4 (*C*H$_3$CO) ppm. HRMS: *m*/*z*: found 850.2477; $C_{39}H_{45}N_3NaO_{15}S$ requires 850.2469 [M + Na]$^+$.

2′,3′,4′,6′-Tetra-*O*-acetyl-β-D-glucopyranosyloxyethyl)-4-(5-azido-5-deoxy-1,2-*O*-isopropylidene-3,6-di-*O*-benzyl-β-L-idofuranosid-5-yl)-1*H*-1,2,3-triazole (21): Flash chromatography (EtOAc). $[\alpha]_D^{20}$ = –24 (*c* = 0.2, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.52 (s, 1 H, C*H*N), 7.34–7.19 (m, 10 H, arom. H), 5.88 (d, $J_{1,2}$ = 4.0 Hz, 1 H, 1-H), 5.18 (dd, $J_{2',3'}$ = $J_{3',4'}$ = 9.0 Hz, 1 H, 3′-H), 5.02 (dd, $J_{4',5'}$ = 9.0 Hz, 1 H, 4′-H), 4.99 (m, 2 H, 2′-, 5-H), 4.62 (dd, $J_{3,4}$ = 4.0, $J_{4,5}$ = 13.0 Hz, 1 H, 4-H), 4.59 (dd, $J_{2,3}$ = 3.0 Hz, 1 H, 2-H), 4.56 (m, 2 H, 1′-H, PhC*H*), 4.39 (d, *J* = 12.1 Hz, 1 H, PhC*H*), 4.30–4.22 (m, 3 H, 6′-H, 2 PhC*H*), 4.13–3.94 (m, 2 H, 6′-H, OC*H*CH$_2$), 3.94 (d, 1 H, 3-H), 3.90–3.60 (m, 4 H, OC*H*CH$_2$, 5′-, 6a-, 6b-H), 3.01 (t, *J* = 7.0 Hz, 2 H, OCH_2CH_2), 2.06, 2.02, 1.99, 1.97 (4 × s, 3 H each, 4 × CH_3CO) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.8, 170.3, 169.5 (*C*O), 143.5 (N*C*=CH), 137.3, 136.7, 128.7, 128.5, 128.3 (arom. C), 122.7 (NC=*C*H), 112.0 (CH_3CCH_3), 104.8 (C-1), 100.9 (C-1′), 81.8 (C-2), 81.3 (C-3), 78.7 (C-4), 73.4 (Ph*C*H$_2$), 72.9 (C-3′), 71.8 (C-5′), 71.7 (Ph*C*H$_2$), 71.3 (C-2′), 69.1 (OCH_2CH_2), 68.7 (C-6), 68.5 (C-4′), 62.0 (C-6′), 60.5 (C-5), 26.8 (*C*H$_3$C), 26.5 (OCH_2CH_2), 26.3 (*C*H$_3$C), 20.8 (*C*H$_3$CO) ppm. HRMS: *m*/*z*: found 848.3218; $C_{41}H_{51}N_3NaO_{15}$ requires 848.3218 [M + Na]$^+$.

Methyl 2,3-Di-*O*-acetyl-6-*O*-azidopropyl-4-*O*-levulinyl-α-D-glucopyranoside (23): 3-Azidopropan-1-ol (691 mg, 6.84 mmol, prepared from 3-chloropropan-1-ol as in ref.[29]) and 2,6-di-*tert*-butyl-4-methylpyridine (1.4 g, 6.84 mmol) were dissolved in dry dichloromethane (37 mL). Tf_2O (1.135 mL, 6.84 mmol) was added at 0 °C and the mixture was stirred at room temp. for 15 min. Water (100 mL) was added and the product **22** was extracted with CH_2Cl_2 (2 × 150 mL). The organic layer was dried with $MgSO_4$ and concentrated to 310 mL (*c* = 22.5 mM). Compound **8** (507 mg, 1.35 mmol), was added to the solution (60 mL) and the solvent was removed on a rotavapor and under high vacuum. The procedure was repeated three times. The residue was purified by flash chromatography (cyclohexane/EtOAc, 3:1 to 1:1) to afford **23** as a colorless oil (340 mg, 55%). $[\alpha]_D^{20}$ = +121 (*c* = 0.2, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 5.46 (dd, $J_{2,3}$ = $J_{3,4}$ = 10.0 Hz, 1 H, 3-H), 5.11 (dd, $J_{4,5}$ = 9.6 Hz, 1 H, 4-H), 4.94 (d, $J_{1,2}$ = 3.7 Hz, 1 H, 1-H), 4.86 (dd, 1 H, 2-H), 3.86 (m, 1 H, 5-H), 3.54–3.36 (m, 6 H, 6a-, 6b-H, CH_2CH_2O, $CH_2CH_2N_3$), 3.40 (s, 3 H, C*H*$_3$O), 2.69 (m, 2 H, $CH_3COCH_2CH_2$), 2.48 (m, 2 H, $CH_3COCH_2CH_2$), 2.15 (s, 3 H, C*H*$_3$Lev), 2.04, 2.02 (2 × s, 3 H each, C*H*$_3$CO), 1.83 (m, 2 H, $OCH_2CH_2CH_2N_3$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.4, 170.4, 170.2 (*C*O), 96.9 (C-1), 71.0 (C-2), 70.1 (C-3), 69.0 (*C*H$_2$), 68.9, 68.5, 68.4 (*C*-4, -5, *C*H$_2$), 55.5 (*C*H$_3$O), 48.4 (*C*H$_2$N$_3$), 37.8 ($CH_3COCH_2CH_2$), 29.8 (*C*H$_3$Lev), 29.2 ($OCH_2CH_2CH_2N_3$), 27.9 ($CH_3COCH_2CH_2$), 20.8 (*C*H$_3$CO) ppm. HRMS: *m*/*z*: found 482.1765; $C_{19}H_{29}N_3NaO_{10}$ requires 482.1751 [M + Na]$^+$.

1-(2′,3′,4′,6′-Tetra-*O*-acetyl-α-D-mannopyranosyloxyethyl)-4-{3-(methyl 2′′,3′′-di-*O*-acetyl-6′′-*O*-levulinyl-α-D-glucopyranoside)-propyl}-1*H*-1,2,3-triazole (24): Flash chromatography (EtOAc). $[\alpha]_D^{20}$ = +56 (*c* = 0.3, CH_2Cl_2). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.4 (br s, 1 H, C*H*N), 5.48 (dd, $J_{2,3}$ = $J_{3,4}$ = 10.0 Hz, 1 H, 3-H), 5.27–5.14 (m, 5 H, 4-, 2′-, 3′-, 4′-H), 4.95 (d, $J_{1,2}$ = 3.6 Hz, 1 H, *H*-1), 4.88 (dd, 1 H, 2-H), 4.82 (br s, $J_{1',2'}$ < 1 Hz, 1 H, *H*-1′), 4.47 (m, 2 H, CH$_2$), 4.24 (m, 1 H, 6a′-H), 4.09 (m, 2 H, 5′-, 6′b-H), 3.90–3.40 (m, 9 H, 5-, 6a-, 6b-H, $NCH_2CH_2CH_2O$, $NCH_2CH_2CH_2O$, OCH_2CH_2), 3.36 (s, 3 H, C*H*$_3$O), 3.02 (m, 2 H, OCH_2CH_2), 2.70 (m, 2 H, $CH_3COCH_2CH_2$), 2.49 (m, 2 H, $CH_3COCH_2CH_2$), 2.15 (s, 3 H, C*H*$_3$Lev), 2.14, 2.12, 2.09, 2.06, 2.03, 1.98 (6 × s, 3H each, 6 × C*H*$_3$CO), 1.91 (m, 2 H, $OCH_2CH_2CH_2N$) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.6, 170.8, 170.2, 169.8 (*C*O), 144.0 (N*C*=CH), 122.6 (NC=*C*H), 97.6 (C-1′), 96.9 (C-1), 71.0 (C-2), 70.2 (C-3), 69.6, 69.2, 68.8, 68.5, 66.1 (C-4, -5, -2′, -3′, -4′, -5′, *C*H$_2$), 67.9, 67.0 (2*C*H$_2$), 62.5 (*C*-6′), 55.5 (*C*H$_3$O), 37.8 ($CH_3COCH_2CH_2$), 30.4 (NCH_2CH_2), 29.8 (*C*H$_3$Lev), 28.0 ($CH_3COCH_2CH_2$), 26.1 ($NCCH_2$), 21.0 (*C*H$_3$CO) ppm. HRMS: *m*/*z*: found 882.3087, $C_{37}H_{53}N_3NaO_{20}$ requires 882.3120 [M + Na]$^+$.

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