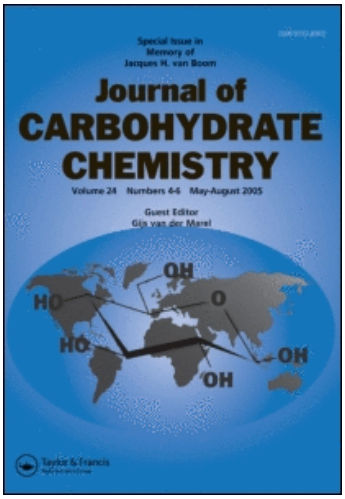

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Efficient Synthesis of Some Unsaturated (1,2,3)-Triazole-Linked Glycoconjugates

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Thermal 1,3-dipolar cycloaddition of ethyl 4-azido-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranosides with diethyl acetylenedicarboxylate or copper-catalyzed reaction with various functionalized alkynes gave the corresponding 1-(ethyl 2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranosid-4-yl)-1*H*-1,2,3-triazole derivatives in quite good yields. These unsaturated compounds could be transformed into 1-(ethyl 2,3-di-*O*-acetyl-4-deoxy-α-D-mannopyranosid-4-yl)-1*H*-1,2,3-triazoles by a simple dihydroxylation reaction. Copper-catalyzed condensation of ethyl 6-*O*-acetyl-4-azido-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranoside with 1,3,5-triethynylbenzene or 1,3,5-tris(prop-2-ynyloxy)benzene afforded the corresponding trivalent glycoconjugate clusters.

Keywords Cu-catalyst, [3+2] Cycloaddition, Hexenopyranoside, 1,2,3-Triazole based-carbohydrate

INTRODUCTION

Glycoconjugates exert important roles in many biological processes,[1–3] including particularly cellular recognition in the case of inflammation,[4–6] tumor metastasis,[7] immune response,[8,9] and bacterial and viral infections.[1] In the course of a project involving the synthesis and biological evaluation of a series of new aminosugars,[10–13] we were attracted by *N*-triazole derivatives of unsaturated carbohydrates where the azole nucleus is located at C-4 of the pyranosyl

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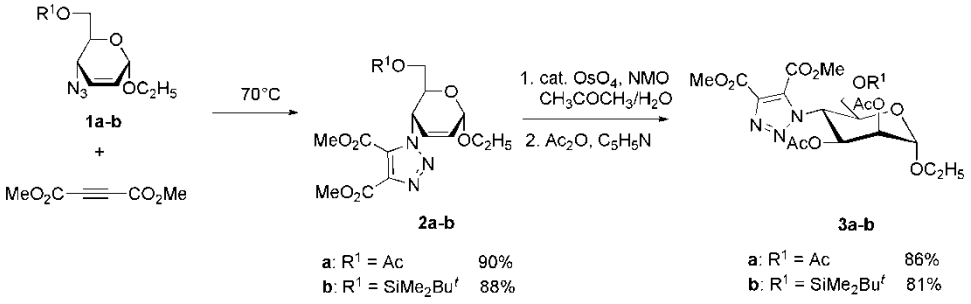
structure. Recently, we have published a very convenient access to 4-amino and 2-aminocarbohydrates via a palladium-catalyzed substitution of allylic acetates or carbonates using NaN_3 or Me_3SiN_3 as the azide source.[14] We perceived that these azido unsaturated carbohydrates could be valuable precursors to 1-(2,3-unsaturated pyranosid-4-yl)triazoles. Substituted triazoles have been shown to display diversified biological activities against different targets.[15–18] Surprisingly, in view of the easy availability of these glycomimetics, examples of triazole-substituted carbohydrates are scarce. Triazolylglycosides have been prepared from the corresponding azidoglycosides via a thermal[16,19–21] or a copper(I)-catalyzed cycloaddition[22,23] with acetylenic derivatives. The opposite approach (i.e. the cycloaddition of an acetylenic glycoside with azide derivatives leading to the *C*-glycosyl triazoles) is well documented.[22,24] Carbohydrates bearing the *N*-triazole substituent at position 3 or 4 have also been prepared.[20,25] Various multivalent neoglycoconjugates have been obtained by the regiospecific 1,3-dipolar cycloaddition of carbohydrates bearing an alkyne function to substituted azides, or vice versa.[26–29] Recently various pseudo-oligosaccharides and amino acid glycoconjugates were synthesized via an intermolecular 1,3-dipolar cycloaddition reaction using easily accessible carbohydrate and amino acid-derived azides and alkynes as building blocks.[30]

We recently disclosed some preliminary results concerning the synthesis of 1-(ethyl 6-*O*-acetyl-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranosid-4-yl)-1*H*-1,2,3-triazole derivatives[31]; we describe therein a full account concerning this approach and some applications.

RESULTS AND DISCUSSION

The starting materials, namely ethyl 4-azido-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranosides **1a** and **1b**, were prepared according to the method described previously.[14] The thermal 1,3-dipolar cycloaddition of azidosugars **1a–b** with diethyl acetylenedicarboxylate was first studied; effectively the corresponding 1-(glycosid-4-yl)-1*H*-1,2,3-triazoles **2a** and **2b** were obtained at 70°C in quite good chemical yields: 90% and 88%, respectively (Sch. 1). 1-(Glycosid-4-yl)-1,2,3-triazole **2b** was also obtained in a one-pot procedure starting from ethyl 6-*O*-(*tert*-butyldimethylsilyl)-4-*O*-methoxycarbonyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside, without isolation of the intermediate azide derivative. Reaction of this unsaturated carbonate with $TMSN_3$ in THF at rt in the presence of a catalytic amount of $Pd_2(dba)_3$ and PPh_3 afforded the crude unsaturated azidocarbohydrate **1b**. Reaction of this crude compound **1b** with dimethyl acetylenedicarboxylate under the above mentioned conditions gave compound **2b** in 64% overall yield.

These 1-(glycosid-4-yl)-1,2,3-triazoles **2a–b** were subjected to the dihydroxylation reaction in the presence of a catalytic amount of OsO_4 and *N*-methyl morpholine oxide followed by acetylation of the crude mixture



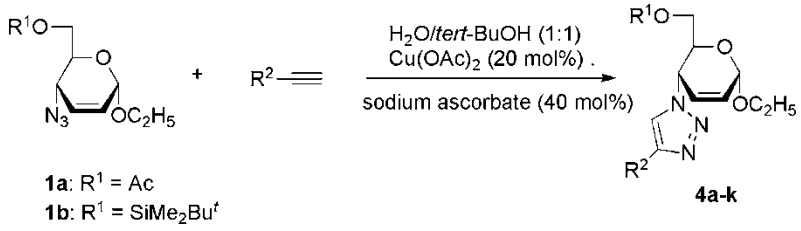
Scheme 1: Thermal synthesis of 1-(glycopyranosid-4-yl)-1*H*-1,2,3-triazole derivatives **2** and **3**.

(Sch. 1). As expected, the corresponding (ethyl 2,3-di-*O*-acetyl-4-deoxy-α-D-mannopyranosid-4-yl)-1*H*-1,2,3-triazoles derivatives **3a**–**b** were obtained as the sole products in 86% and 81% yield, respectively. Compounds **3a**–**b** resulted from the dihydroxylation of the double bond on the less hindered side, in agreement with the previous findings in this field.[32,33] The assigned configurations for compounds **3a**–**b** are mainly based on the coupling constant ($J_{4,5} = 10.5$ and 10.9 Hz, and $J_{3,4} = 10.9$ Hz, respectively), characteristic of an axial-axial disposition for H-3, H-4, and H-5.

However, in order to extend this methodology to the preparation of a large range of 1-(glycosid-4-yl)-1*H*-1,2,3-triazoles, we have to use the copper(I)-catalyzed condensation of 4-azidocarbohydrates **1** with various acetylenic compounds. This methodology, described as "click" chemistry,[34–37] generally afforded the corresponding triazole derivatives quantitatively under very mild conditions with a very high regioselectivity and a high tolerance of other functionalities. The condensation of ethyl 6-*O*-*tert*-butyldimethylsilyl-4-azido-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranoside (**1b**)[14] with ethynylbenzene in the presence of $Cu(OAc)_2$ and sodium ascorbate in a 1:1 mixture of *tert*-butanol and water at rt under nitrogen overnight afforded 1*H*-1,2,3-triazole derivative **4b** as the exclusive product in 75% yield after column chromatography (Sch. 2), quite close to the value obtained starting from unsaturated azido carbohydrate **1a** (80%).[31] The regioselectivity of the 1,3-dipolar cycloaddition reaction was assigned according to the previous results using this methodology and to the mechanism proposed by Rostovtsev et al.[35]

p-Bromoethynylbenzene reacted with 4-azidocarbohydrate **1b** under the same conditions to afford 1-(glycosid-4-yl)-1*H*-1,2,3-triazole **4c** in 85% yield, when **4b** was obtained in 67% chemical yield starting from **1a**.[31]

Functionalization of unsaturated glycosidyltriazole **4b** with arylboronic acid such as phenylboronic acid could be performed very easily at 70°C in the presence of a catalytic amount of palladium(0)-catalyst to afford the coupling product **5** in 64% yield after purification (Sch. 3); this methodology leads to



1a: R^1 = Ac
1b: R^1 = $SiMe_2Bu^t$

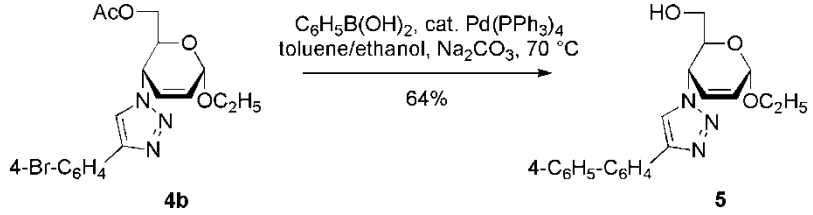
4a-k

4a:	$R^1 = SiMe_2Bu^t$; $R^2 = C_6H_5$	75%
4b:	R^1 = Ac; R^2 = 4-BrC_6H_4	67%[31]
4c:	$R^1 = SiMe_2Bu^t$; R^2 = 4-BrC_6H_4	85%
4d:	$R^1 = SiMe_2Bu^t$; $R^2 = CH_2OH$	70%
4e:	$R^1 = SiMe_2Bu^t$; $R^2 = CH_2OCO_2Me$	79%
4f:	$R^1 = SiMe_2Bu^t$; R^2 = (*R,S*)-$CHOHCH_3$	75%
4g:	$R^1 = SiMe_2Bu^t$; $R^2 = CO_2Me$	78%
4h:	R^1 = H; $R^2 = CO_2H$	35%
4i:	R^1 = Ac; R^2 = Pht-OCH_2	80%
4j:	R^1 = Ac; $R^2 = SiMe_3$	30%
4k:	R^1 = Ac; R^2 = H	53%

Scheme 2: Copper-catalyzed synthesis of 1-(glycopyranosid-4-yl)-1*H*-1,2,3-triazole derivatives **4**.

an easy entry to a large variety of 4-aryl-1-(ethyl 2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranosid-4-yl)-1*H*-1,2,3-triazoles.

Propargylic alcohol and its methyl carbonate also reacted with 4-azidocarbohydrate **1b** under the above described conditions to give the corresponding 1-(glycosid-4-yl)-1*H*-1,2,3-triazoles **4d** and **4e** in 70% and 79% yield, respectively. Unfortunatly, all attempts to functionalize carbonate **4e** failed. When racemic but-3-yn-2-ol was used as the acetylenic compound, triazole **4f** was obtained as a 1 : 1 mixture of the two epimers, in 75% yield. When copper-catalyzed condensation of methyl propiolate with 4-azidocarbohydrate **1b** gave the corresponding triazole derivative **4g** in 78% yield, the condensation of propiolic acid with unsaturated 4-azidocarbohydrate **1a** afforded triazole **4h** in moderate yield only (35%); it is to be noted that the cleavage of the acetoxy group, in this case, is probably due to the final treatment of the mixture at the end of the reaction.



4b **5**

Scheme 3: Synthesis of 1-(glycopyranosid-4-yl)-1*H*-1,2,3-triazole derivative **5**.

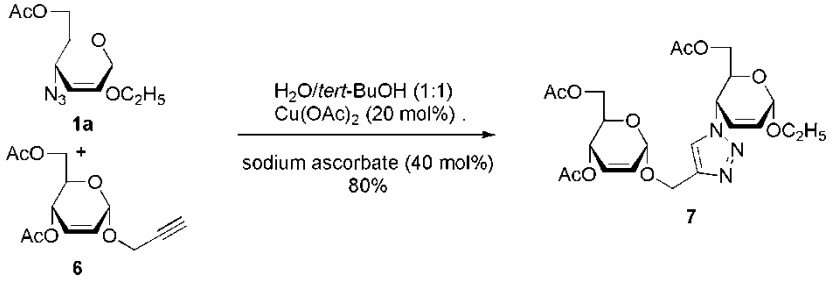
Copper-catalyzed condensation of 2-(ethynyloxy)isoindoline-1,3-dione with 4-azidocarbohydrate **1a** afforded compound **4i** in 80% yield. Under the same conditions, ethynyltrimethylsilane gave a mixture of silylated triazole **4j** and desilylated triazole **4k** in 30% and 53% yield, respectively. The formation of compound **4k** could be explained by the reaction of a copper-acetylide intermediate formed from the alkyne and CuCl with extrusion of TMSCl at the initial stage of the catalytic cycle, and not the formation of the expected copper-TMS acetylide intermediate leading to the formation of **4j**.[38]

We extended this reaction to more complex propargylic substrates. Unsaturated 4-azidocarbohydrate **1a** reacted smoothly with other carbohydrate moiety such as propargyl 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (**6**)[39] to afford the corresponding disaccharide **7** in 80% yield (Sch. 4).

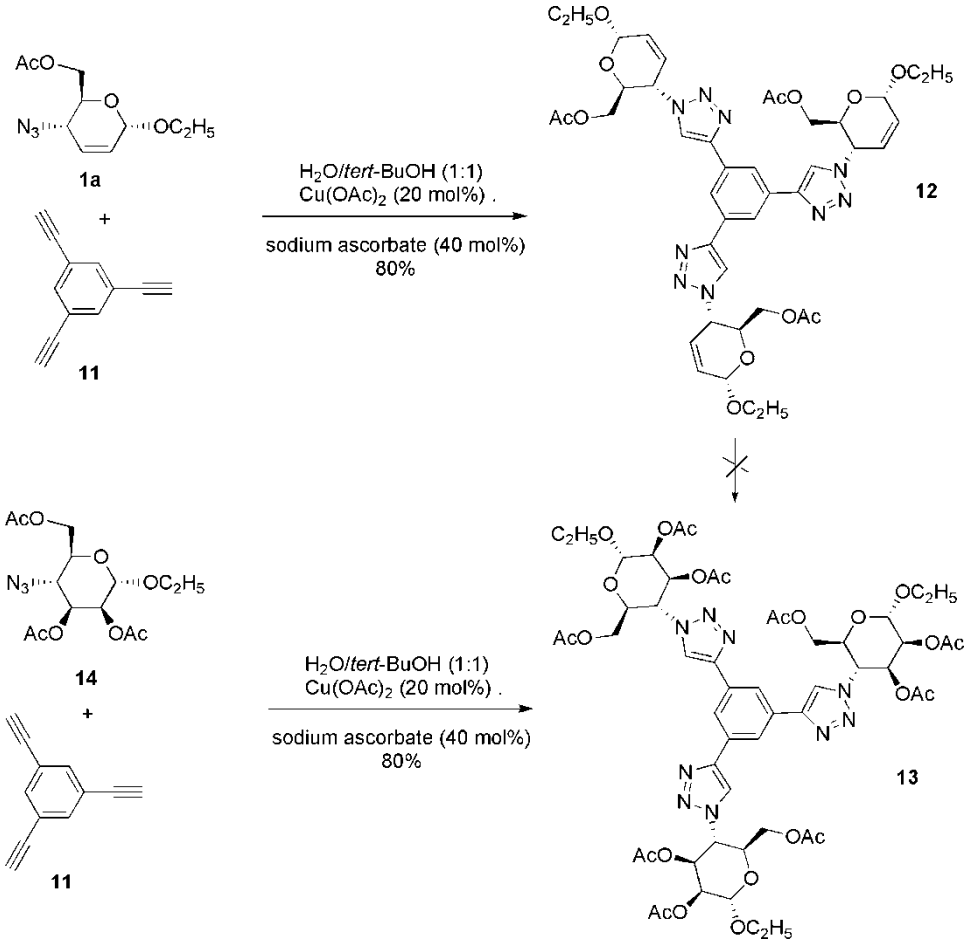
This cycloaddition reaction was also extended to multivalent alkynes, to investigate the potentiality of this methodology for the preparation of polyvalent glycoconjugate clusters. It is well known that interactions between glycoconjugates and receptors play an important role in biological systems.[40] The copper-catalyzed condensation of unsaturated 4-azidocarbohydrate **1a**, used in excess, occurred readily with 1,3,5-triethynylbenzene (**11**) or with 1,3,5-tris(prop-2-ynyloxy)benzene (**16**) to afford a single product **12** or **17** in 80% and 61% yields, respectively, after column chromatography (Sch. 5 and 6). However, all attempts to dihydroxylate compounds **12** and **17** under the above mentioned conditions were unsuccessful. Fortunately, the copper-catalyzed condensation of ethyl 4-azidomannopyranoside **14**, obtained by bishydroxylation of unsaturated azidopyranoside **1a**,[14] with unsaturated benzene derivatives **11** or **16** afforded conveniently the corresponding tris[4-(ethyl—2,3,6-tri-*O*-acetyl-4-deoxy-α-D-mannopyranosid-4-yl)-1*H*-1,2,3-triazol-1-yl] derivatives **13** or **18** in 80% chemical yield after column chromatography (Sch. 5 and 6).

CONCLUSION

In conclusion, thermal 1,3-dipolar cycloaddition of ethyl 4-azido-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranosides with diethyl acetylenedicarboxylate followed

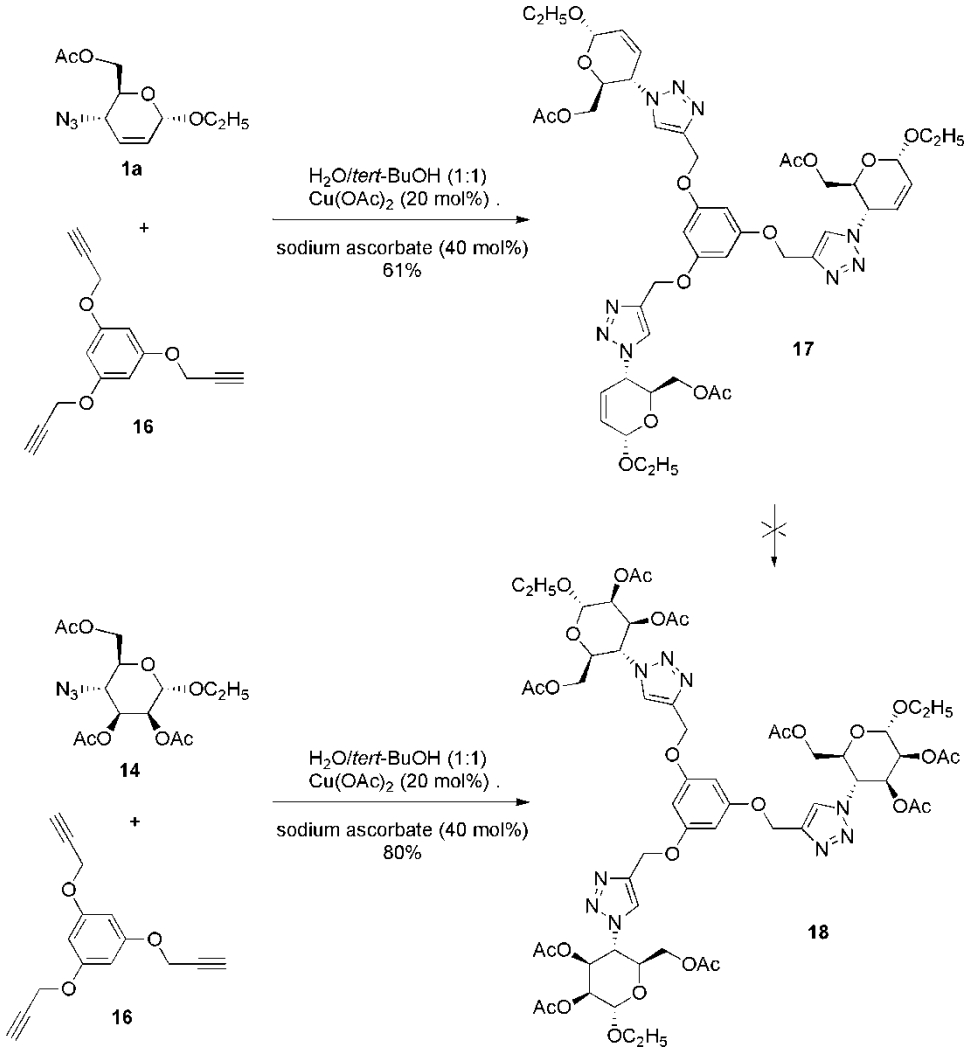


Scheme 4: Copper-catalyzed synthesis of 1,2,3-triazole derivative **7**.



Scheme 5: Copper-catalyzed synthesis of tris(1,2,3-triazole) derivatives **12** and **13**.

by dihydroxylation of the obtained 1-(ethyl 2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranosid-4-yl)-1*H*-1,2,3-triazoles afforded 1-(ethyl 2,3-di-*O*-acetyl-4-deoxy-α-D-mannopyranosid-4-yl)-1*H*-1,2,3-triazoles in quite good yields. Copper-catalyzed reaction of ethyl 6-*O*-acetyl-4-azido-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranoside with various functionalized alkynes gave the corresponding 1-(ethyl 2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranosid-4-yl)-1*H*-1,2,3-triazole derivatives bearing different functionnalities. These unsaturated compounds could also be transformed into 1-(ethyl 2,3-di-*O*-acetyl-4-deoxy-α-D-mannopyranosid-4-yl)-1*H*-1,2,3-triazoles by usual dihydroxylation. Copper-catalyzed condensation of ethyl 6-*O*-acetyl-4-azido-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranoside with 1,3,5-triethynylbenzene or 1,3,5-tris(prop-2-ynyloxy)benzene afforded the corresponding trivalent unsaturated glycoconjugate clusters, when the same reaction performed with ethyl 2,3,6-tri-*O*-acetyl-4-azido-4-deoxy-α-D-mannopyranoside



Scheme 6: Copper-catalyzed synthesis of tris(1,2,3-triazole) derivatives **17** and **18**.

allowed the preparation of the corresponding tris[4-(ethyl 2,3,6-tri-*O*-acetyl-4-deoxy-α-D-mannopyranosid-4-yl)-1*H*-1,2,3-triazol-1-yl] derivatives.

EXPERIMENTAL

General Procedure

All commercially available reagents were used as received. All reactions were monitored by TLC analysis (TLC plates GF_{254} Merck). Air- and

moisture-sensitive reactions were performed under inert atmosphere. Melting points were determined on a Büchi apparatus and are uncorrected. Column chromatography was performed on silica gel 60 (230-240 mesh, Merck). Optical rotations were recorded using a Perkin-Elmer 241 polarimeter. NMR spectra were recorded with a Bruker AMX 300 spectrometer and referenced as following: ^{1}H (300 MHz), internal $SiMe_4$ at $\delta = 0.00$ ppm, ^{13}C (75 MHz), internal standard at $\delta = 77.23$ ppm. Exact mass measurements of the molecular ions were obtained on a Finnigan Mat 95 XL spectrometer. 1,3,5-Triethynylbenzene (**11**) was commercially available. Ethyl 4-azido-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranosides **1a** and **1b**,[14] ethyl 2,3,6-tri-*O*-acetyl-4-azido-4-deoxy-α-D-mannopyranoside (**14**),[14] 3-butynyl 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside,[41] methyl prop-2-ynyl carbonate,[42] methyl propiolate,[43] and 1,3,5-tris(pro-2-ynyloxy)benzene (**16**)[44] were prepared according to the literature. The preparation and characterization of triazole derivative **4b** has already been described.[31]

General procedure for the preparation of (ethyl α-D-*erythro*-hex-2-enopyranosid-4-yl)-triazoles 2. A mixture of azido carbohydrate **1** (0.16 mmol) and dimethyl acetylenedicarboxylate (34 mg, 0.24 mmol) was heated at 70°C for 5 h. The crude product was directly purified by column chromatography on silica to afford the corresponding triazole derivatives **2**.

4,5-Di(methoxycarbonyl)-1-(ethyl 6-*O*-acetyl-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranosid-4-yl)-1*H*-1,2,3-triazole (2a). Yield 90%; colorless solid; mp 66–68°C; R_f 0.3 (petroleum ether/EtOAc 6 : 4); $[\alpha]_D^{20} + 68$ ($c = 1$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): 1.27 (t, $J = 7.1$ Hz, 3 H, CH_2CH_3), 2.01 (s, 3 H, CH_3CO), 3.60 (dq, $J = 9.6$, 7.1 Hz, 1 H, OCH_2CH_3), 3.86 (dq, $J = 9.6$, 7.1 Hz, 1 H, OCH_2CH_3), 3.96 (s, 3 H, CH_3O), 3.99 (s, 3 H, CH_3O), 4.04 (dd, $J = 12.2$, 3.8 Hz, 1 H, H-6), 4.08 (dd, $J = 12.2$, 3.8 Hz, 1 H, H-6), 4.74 (ddd, $J = 9.9$, 3.8, 3.8 Hz, 1 H, H-5), 5.15 (br s, 1 H, H-1), 5.67 (ddd, $J = 9.9$, 3.8, 1.5 Hz, 1 H, H-4), 5.92 (br d, $J = 10.2$ Hz, 1 H, H-3), 6.02 (ddd, $J = 10.2$, 2.5, 2.5 Hz, 1 H, H-2); ^{13}C NMR (75.5 MHz, $CDCl_3$): 15.6, 20.9, 53.1, 54.1, 56.0, 63.0, 65.0, 67.7, 94.6, 127.5, 129.0, 131.6, 139.9, 159.3, 160.6, 170.7.

Anal. Calcd for $C_{16}H_{21}O_8N_3$ (383.353): C, 50.13; H, 5.52. Found: C, 50.34; H, 5.53.

4,5-Di(methoxycarbonyl)-1-(ethyl 6-*O*-*tert*-butyldimethylsilyl-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranosid-4-yl)-1*H*-1,2,3-triazole (2b). Yield 88%; colorless oil; R_f 0.5 (petroleum ether/EtOAc 7 : 3); $[\alpha]_D^{20} + 58$ ($c = 2.4$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): $_\delta$-0.03 (s, 6 H, $SiMe_2$), 0.80 (s, 9 H, CMe_3), 1.26 (t, $J = 7.1$ Hz, 3 H, CH_2CH_3), 3.52 (dd, $J = 11.7$, 3.8 Hz, 1 H, H-6), 3.60 (dq, $J = 9.6$, 7.1 Hz, 1 H, OCH_2CH_3), 3.69 (dd, $J = 11.7$, 2.8 Hz, 1 H, H-6), 3.87 (dq, $J = 9.6$, 7.1 Hz, 1 H, OCH_2CH_3), 3.96 (s, 3 H,

CH_3O), 3.98 (s, 3 H, CH_3O), 4.55 (ddd, $J = 9.7, 3.8, 2.8$ Hz, 1 H, H-5), 5.11 (br s, 1 H, H-1), 5.7 (br dd, $J = 9.7, 1.1$ Hz, 1 H, H-4), 5.93 (br d, $J = 10.2$ Hz, 1 H, H-3), 5.98 (ddd, $J = 10.2, 2.2, 2.2$ Hz, 1 H, H-2); ^{13}C NMR (75.5 MHz, $CDCl_3$): $_{\delta}$-5.1, 15.6, 18.7, 26.2, 53.0, 54.0, 55.7, 62.8, 64.6, 69.9, 94.5, 128.0, 128.9, 132.0, 139.6, 159.4, 160.7.

Anal. Calcd for $C_{20}H_{33}O_7N_3Si$ (455.577): C, 52.73; H, 7.30. Found: C, 52.61; H, 7.14.

Procedure for the one-pot synthesis of compound 2b. To a mixture of $Pd_2(dba)_3$ (13 mg, 14 μmol) and PPh_3 (30 mg, 112 μmol) in THF (2 mL) was added a solution of ethyl 6-*O*-(*tert*-butyldimethylsilyl)-4-*O*-methoxycarbonyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (98 mg, 0.28 mmol) in THF (1 mL), followed by $TMSN_3$ (102 mg, 0.84 mmol). The solution was stirred at 50°C for 2 h. Elimination of the solvent under reduced pressure afforded the crude azido compound **1b**. Dimethyl acetylenedicarboxylate (120 mg, 0.84 mmol) was added to this residue, and the mixture was heated at 70°C for 2 h. The crude product was purified by column chromatography on silica using petroleum ether/EtOAc (7 : 3) as the eluent to give compound **2b** (82 mg, 64%).

General procedure for the dihydroxylation of (ethyl α-D-*erythro*-hex-2-enopyranosid-4-yl)-triazoles 2. To a solution of unsaturated 4-triazolyl carbohydrate derivative **2** (1 mmol) in a 4 : 1 mixture of acetone/water (2 mL) were added OsO_4 (0.25 mg, 1 mmol, 2 mol%) and *N*-methylmorpholine-*N*-oxide (465 mg, 4 mmol) at 0°C. The reaction mixture was stirred overnight at rt, $NaHSO_3$ (500 mg) was added, and the contents were stirred for 30 min at rt. The reaction mixture was diluted with water (5 mL), and extracted with EtOAc (2 × 10 mL). The organic phase was separated and dried over Na_2SO_4, and the solvent was evaporated to give the corresponding diol. The crude residue was directly acetylated using Ac_2O (306 mg, 3 mmol) in pyridine (4 mL) for 1 day. After removing the solvent under reduced pressure, the residue was purified by column chromatography on silica using the corresponding eluent to afford the 4-triazolyl carbohydrate **3**.

4,5-Di(methoxycarbonyl)-1-(ethyl 2,3,6-tri-*O*-acetyl-4-deoxy-α-D-mannopyranosid-4-yl)-1*H*-1,2,3-triazole (3a). Yield 86%; colorless solid; mp 124–127°C; R_f 0.3 (petroleum ether/EtOAc 1 : 1); $[\alpha]_D^{20} + 80$ ($c = 0.5$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): 1.31 (t, $J = 7.0$ Hz, 3 H, CH_2CH_3), 1.82 (s, 3 H, CH_3CO), 2.04 (s, 3 H, CH_3CO), 2.19 (s, 3 H, CH_3CO), 3.61 (dq, $J = 9.8$, 7.0 Hz, 1 H, OCH_2CH_3), 3.85 (dq, $J = 9.8$, 7.0 Hz, 1 H, OCH_2CH_3), 3.98 (s, 3 H, CH_3O), 4.02 (s, 3 H, CH_3O), 4.07 (dd, $J = 12.4$, 3.5 Hz, 1 H, H-6), 4.12 (dd, $J = 12.4$, 3.3 Hz, 1 H, H-6), 4.93 (ddd, $J = 10.5$, 3.5, 3.3 Hz, 1 H, H-5), 4.95 (d, $J = 1.7$ Hz, 1 H, H-1), 5.36 (dd, $J = 3.2$, 1.7 Hz, 1 H, H-2), 5.38 (dd,

$J = 10.9$, 10.5 Hz, 1 H, H-4), 5.72 (dd, $J = 10.9$, 3.2 Hz, 1 H, H-3); ^{13}C NMR (75.5 MHz, $CDCl_3$): $_{\delta}$ 14.7, 19.6, 19.8, 20.0, 52.1, 52.8, 61.6, 63.7, 67.3, 68.0, 96.9, 158.1, 159.4, 167.9, 169.0, 169.5.

Anal. Calcd for $C_{20}H_{27}O_{12}N_3$ (501.441): C, 47.90; H, 5.43. Found: C, 47.71; H, 5.61.

4,5-Di(methoxycarbonyl)-1-(ethyl 2,3-di-*O*-acetyl-6-*O*-*tert*-butyldimethylsilyl-α-D-mannopyranosid-4-yl)-1*H*-1,2,3-triazole (3b). Yield 81%; colorles solid; mp 101–103°C; R_f 0.4 (petroleum ether/EtOAc 7 : 3); $[\alpha]_D^{20} + 99$ ($c = 1.2$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): 0.02 (s, 6 H, $SiMe_2$), 0.87 (s, 9 H, CMe_3), 1.30 (t, $J = 7.0$ Hz, 3 H, CH_2CH_3), 1.84 (s, 3 H, CH_3CO), 2.17 (s, 3 H, CH_3CO), 3.46 (dd, $J = 11.9$, 3.2 Hz, 1 H, H-6), 3.58 (dq, $J = 9.7$, 7.0 Hz, 1 H, OCH_2CH_3), 3.70 (dd, $J = 11.9$, 2.1 Hz, 1 H, H-6), 3.82 (dq, $J = 9.7$, 7.0 Hz, 1 H, OCH_2CH_3), 3.98 (s, 3 H, CH_3O), 4.00 (s, 3 H, CH_3O), 4.69 (br d, $J = 10.9$ Hz, 1 H, H-5), 4.91 (d, $J = 1.6$ Hz, 1 H, H-1), 5.35 (dd, $J = 3.1$, 1.6 Hz, 1 H, H-2), 5.49 (dd, J =10.9, 10.9 Hz, 1 H, H-4), 5.73 (dd, $J = 10.9$, 3.1 Hz, 1 H, H-3); ^{13}C NMR (75.5 MHz, $CDCl_3$): -5.1, 15.3, 18.7, 20.8, 21.1, 26.1, 53.1, 53.7, 62.2, 64.3, 69.4, 71.0, 97.8, 137.1, 139.6, 160.7, 169.3, 170.2, 170.8.

Anal. Calcd for $C_{24}H_{39}O_{11}N_3Si$ (573.665): C, 50.25; H, 6.85. Found: C, 50.68; H, 7.05.

General procedure for the preparation of (ethyl α-D-*erythro*-hex-2-enopyranosid-4-yl)-triazoles 4. The 4-azido sugar **1** (1 mmol) and the alcyne derivative (3 mmol) were suspended in a 1 : 1 mixture of *tert*-butanol and water (4 mL), and THF (2 mL). To this solution was added a mixture of $Cu(OAc)_2$ (36 mg, 0.2 mmol) and sodium ascorbate (79 mg, 0.4 mmol) in *tert*-$BuOH/H_2O$ (1 mL). The reaction was stirred under nitrogen at rt until TLC analysis indicated complete consumption of the product; water (3 mL) was added, and the product was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were dried over Na_2SO_4. Evaporation of the solvent under reduced pressure gave a residue that was purified by column chromatography on silica using the indicated eluent to give the corresponding compounds **4**.

1-(Ethyl 6-*O*-*tert*-butyldimethylsilyl-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranosid-4-yl)-4-phenyl-1*H*-1,2,3-triazole (4a). Yield 75%; yellow oil; R_f 0.4 (petroleum ether/EtOAc 9 : 1); $[\alpha]_D^{20} + 119$ ($c = 1.2$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): −0.02 (s, 3 H, $SiMe_2$), 0.00 (s, 3 H, $SiMe_2$), 0.84 (s, 9 H, CMe_3), 1.24 (t, $J = 7.1$ Hz, 3 H, CH_2CH_3), 3.53–3.63 (m, 2 H, H-6, OCH_2CH_3), 3.68 (dd, $J = 11.7$, 2.2 Hz, 1 H, H-6), 3.88 (dq, $J = 9.6$, 7.1 Hz, 1 H, OCH_2CH_3), 4.11 (ddd, $J = 9.8$, 5.0, 2.2 Hz, 1 H, H-5), 5.13 (br s, 1 H, H-1), 5.38 (br dd, $J = 9.8$, 1.7 Hz, 1 H, H-4), 5.98 (br d, $J = 10.0$ Hz, 1 H, H-3), 6.05 (ddd, $J = 10.0$, 2.5, 2.5 Hz, 1 H, H-2), 7.30–7.42 (m, 3 H, H_{arom}), 7.78–7.81

(m, 3 H, H_{arom}, =CH-N); ^{13}C NMR (75.5 MHz, $CDCl_3$): −5.0, 15.6, 18.7, 26.3, 55.3, 62.8, 64.7, 71.6, 94.2, 118.7, 126.1, 129.3, 128.3, 128.7, 129.8, 130.8, 148.5.

Anal. Calcd for $C_{22}H_{33}O_3N_3Si$ (415.601): C, 63.58; H, 8.00. Found: C, 64.17; H, 8.32.

1-(Ethyl 6-*O*-*tert*-butyldimethylsilyl-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranosid-4-yl)-4-(4-bromophenyl)-1*H*-1,2,3-triazole (4c). Yield 85%; colorless oil; R_f 0.4 (petroleum ether/EtOAc 9 : 1); $[\alpha]_D^{20} + 133$ ($c = 2.8$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): $_\delta$ 0.02 (s, 6 H, $SiMe_2$), 0.86 (s, 9 H, CMe_3), 1.29 (t, $J = 7.2$ Hz, 3 H, CH_2CH_3), 3.55–3.66 (m, 2 H, OCH_2CH_3, H-6), 3.70 (dd, $J = 11.7$, 2.3 Hz, 1 H, H-6), 3.90 (dq, $J = 9.6$, 7.1 Hz, 1 H, OCH_2CH_3), 4.12 (ddd, $J = 9.8$, 4.7, 2.3 Hz, 1 H, H-5), 5.14 (br s, 1 H, H-1), 5.40 (ddd, $J = 9.8$, 3.4, 1.7 Hz, 1 H, H-4), 5.99 (br d, $J = 10.2$ Hz, 1 H, H-3), 6.07 (ddd, $J = 10.2$, 2.5, 2.5 Hz, 1 H, H-2), 7.53 (dd, $J = 6.6$, 1.9 Hz, 2 H, H_{arom}), 7.69 (dd, $J = 6.6$, 1.9 Hz, 2 H, H_{arom}), 7.82 (s, 1 H, =CH-N); ^{13}C NMR (75.5 MHz $CDCl_3$): −5.0, 15.6, 18.7, 26.2, 55.4, 62.8, 64.7, 71.6, 94.2, 118.8, 122.7, 127.6, 128.1, 129.8, 129.9, 132.4, 147.5.

Anal. Calcd for $C_{22}H_{32}O_3BrN_3Si$ (494.497): C, 53.44; H, 6.52. Found: C, 53.44; H, 6.84.

1-(Ethyl 6-*O*-*tert*-butyldimethylsilyl-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranosid-4-yl)-4-(hydroxymethyl)-1*H*-1,2,3-triazole (4d). Yield 70%; colorless oil; R_f 0.3 (petroleum ether/EtOAc 4 : 6); $[\alpha]_D^{20} + 80$ ($c = 0.5$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): −0.01 (s, 6 H, $SiMe_2$), 0.85 (s, 9 H, CMe_3), 1.23 (t, $J = 7.1$ Hz, 3 H, CH_2CH_3), 2.49 (t, $J = 5.8$ Hz, 1 H, OH), 3.53–3.60 (m, 2 H, H-6, OCH_2CH_3), 3.65 (dd, $J = 11.7$, 2.3 Hz, 1 H, H-6), 3.85 (dq, $J = 9.4$, 7.0 Hz, 1 H, OCH_2CH_3), 4.07 (ddd, $J = 9.8$, 4.9, 2.3 Hz, 1 H, H-5), 4.77 (d, $J = 5.8$ Hz, 2 H, CH_2OH), 5.11 (br s, 1 H, H-1), 5.34 (dd, $J = 9.8$, 1.7 Hz, 1 H, H-4), 5.92 (br d, $J = 10.4$ Hz, 1 H, H-3), 6.02 (ddd, $J = 10.4$, 2.6, 2.6 Hz, 1 H, H-2), 7.59 (s, 1 H, =CH-N); ^{13}C NMR (75.5 MHz, $CDCl_3$): −5.0, 15.6, 18.7, 26.3, 55.2, 57.0, 62.8, 64.6, 71.5, 94.2, 121.0, 128.1, 129.7, 148.3.

Anal. Calcd for $C_{17}H_{31}O_4N_3Si$ (369.531): C, 55.25; H, 8.46. Found: C, 55.77; H, 8.29.

1-(Ethyl 6-*O*-*tert*-butyldimethylsilyl-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranosid-4-yl)-4-(methoxymethylcarbonyl)-1*H*-1,2,3-triazole (4e). Yield 79%; colorless oil; R_f 0.6 (petroleum ether/EtOAc 6 : 4); $[\alpha]_D^{20} + 65$ ($c = 2.0$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): 0.04 (s, 3 H, $SiMe_2$), 0.05 (s, 3 H, $SiMe_2$), 0.85 (s, 9 H, CMe_3), 1.24 (t, $J = 7.2$ Hz, 3H, CH_3CH_2), 3.52–3.60 (m, 2H, H-6, OCH_2CH_3), 3.65 (dd, $J = 11.7$, 2.1 Hz, 1H, H-6), 3.78 (s, 3 H, OCH_3), 3.87 (dq, $J = 7.3$, 9.6 Hz, 1 H, OCH_2CH_3), 4.07 (ddd, $J = 9.9$, 4.9, 2.1 Hz, 1 H, H-5), 5.11 (br s, 1 H, H-1), 5.26 (br s, 2 H, CH_2OCO_2Me), 5.34

(br dd, $J = 9.9$, 1.5 Hz, 1 H, H-4), 5.92 (br d, $J = 10.0$ Hz, 1 H, H-3), 6.01 (ddd, $J = 10.0$, 2.8, 2.8 Hz, 1 H, H-2), 7.69 (s, 1 H, =CH-N); ^{13}C NMR (75.5 MHz, $CDCl_3$): −5.1, −5.0, 15.6, 18.7, 26.2, 55.3, 55.4, 61.3, 62.8, 64.6, 71.4, 94.2, 123.0, 127.9, 129.8, 143.0, 156.0.

Anal. Calcd for $C_{19}H_{33}O_6N_3Si$ (427.567): C, 53.37; H, 7.78. Found: C, 53.91; H, 8.16.

1-(Ethyl 6-*O*-*tert*-butyldimethylsilyl-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranosid-4-yl)-4-[(*R*,*S*)-1-hydroxyethyl]-1*H*-1,2,3-triazole (4f). Yield 75%; colorless oil; R_f 0.4 (petroleum ether/EtOAc 4 : 6); ^{1}H NMR (300 MHz, $CDCl_3$): − 0.01 (s, 6 H, $SiMe_2$), 0.84 (s, 9 H, CMe_3), 1.21 (t, $J = 7.1$ Hz, 3 H, CH_2CH_3,), 1.55 (d, $J = 6.4$ Hz, 3 H, CH_3CHOH), 2.58 (d, $J = 4.5$ Hz, 0.5 H, OH), 2.61 (d, $J = 4.5$ Hz, 0.5 H, OH), 3.53–3.60 (m, 2 H, H-6, OCH_2CH_3), 3.64 (dd, $J = 11.7$, 2.5 Hz, 1 H, H-6), 3.86 (dq, $J = 9.6$, 7.1 Hz, 1 H, OCH_2CH_3), 4.06 (ddd, $J = 9.8$, 5.1, 2.5 Hz, 1 H, H-5), 5.06 (dq, $J = 6.4$, 4.5 Hz, 1 H, CHOH), 5.11 (br s, 1 H, H-1), 5.31 (br d, $J = 9.8$ Hz, 1 H, H-4), 5.92 (br d, $J = 10.2$ Hz, 1 H, H-3), 6.02 (ddd, J =10.2, 2.5, 2.5 Hz, 1 H, H-2), 7.53 (s, 1 H, =CH-N); ^{13}C NMR (75.5 MHz, $CDCl_3$): −5.0, 15.6, 18.7, 23.4 (0.5 CHOH), 23.5 (0.5 CHOH), 26.3, 55.2 (0.5 C-4), 55.3 (0.5 C-4), 62.8, 64.5, 71.5 (0.5 C-5), 71.4 (0.5 C-5), 94.1, 119.2, 119.3, 128.1, 129.6.

Anal; Calcd for $C_{18}H_{33}O_4N_3Si$ (383.558): C, 56.37; H, 8.67. Found: C, 56.64; H, 8.66.

1-(Ethyl 6-*O*-*tert*-butyldimethylsilyl-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranosid-4-yl)-4-(methoxycarbonyl)-1*H*-1,2,3-triazole (4g). Yield 78%; colorless oil; R_f 0.6 (petroleum ether/EtOAc 6 : 4); $[\alpha]_D^{20} + 81$ ($c = 1.1$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): −0.01 (s, 6 H, $SiMe_2$), 0.85 (s, 9 H, CMe_3), 1.24 (t, $J = 7.1$ Hz, 3 H, CH_2CH_3), 3.55 (dd, $J = 11.7$, 4.7 Hz, 1 H, H-6), 3.60 (dq, $J = 9.8$, 7.1 Hz, 1 H, OCH_2CH_3), 3.68 (dd, $J = 11.7$, 2.4 Hz, 1 H, H-6), 3.88 (dq, $J = 9.8$, 7.1 Hz, 1 H, OCH_2CH_3), 3.94 (s, 3 H, OCH_3), 4.08 (ddd, $J = 9.7$, 4.7, 2.4 Hz, 1 H, H-5), 5.12 (br s, 1 H, H-1), 5.43 (dd, $J = 9.7$, 1.7 Hz, 1 H, H-4), 5.93 (br d, $J = 10.1$ Hz, 1 H, H-3), 6.07 (ddd, $J = 10.1$, 2.6, 2.6 Hz, 1 H, H-2), 8.15 (s, 1 H, =CH-N); ^{13}C NMR (75.5 MHz, $CDCl_3$): −5.1, 15.6, 18.7, 26.2, 52.6, 55.5, 62.6, 64.7, 71.4, 94.2, 127.0, 127.3, 130.3, 140.6, 161.4.

HRMS-FAB Calcd for $C_{28}H_{31}O_5N_3Si$: 398.2111. Found: 398.2107.

4-(Carboxylic acid)-1-(ethyl 2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranosid-4-yl)-1*H*-1,2,3-triazole (4h). Yield 35%; colorless solid; mp 155°C (decomposition); R_f 0.3 (methanol/EtOAc 1 : 1); $[\alpha]_D^{20} + 104$ ($c = 0.5$, CH_3OH); ^{1}H NMR (300 MHz, CD_3OD): 1.26 (t, $J = 7.1$ Hz, 3 H, CH_2CH_3,), 3.45 (dd, $J = 12.4$, 4.6 Hz, 1 H, H-6), 3.41 (dd, $J = 12.4$, 2.1 Hz, 1 H, H-6), 3.64 (dq, $J = 9.6$, 7.1 Hz, 1 H, OCH_2CH_3), 3.91 (dq, $J = 9.6$, 7.1 Hz, 1 H, OCH_2CH_3),

4.18 (ddd, $J = 9.9$, 4.6, 2.1 Hz, 1 H, H-5), 5.19 (br s, 1 H, H-1), 5.42 (br d, $J = 9.9$ Hz, 1 H, H-4), 6.03 (br d, $J = 10.2$ Hz, 1 H, H-3), 6.08 (br dd, $J = 10.2$, 2.1 Hz, 1 H, H-2), 8.15 (s, 1 H, =CH-N); ^{13}C NMR (75.5 MHz, CD_3OD): 16.0, 56.5, 62.1, 65.7, 72.5, 95.8, 127.0, 129.2, 130.5, 148.0, 168.3.

HRMS-FAB Calcd for $C_{11}H_{16}O_5N_3$: 270.1090. Found: 270.1091.

4-{[(1,3-Dioxo-1,3-dihydro-2*H*-isoindol-2-yl)oxy]methyl}-1-(ethyl 6-*O*-acetyl-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranosid-4-yl)-1*H*-1,2,3-triazole (4i). Yield 80%; colorless solid; mp 86–88°C; R_f 0.6 (petroleum ether/EtOAc 1 : 1); $[\alpha]_D^{20} + 52$ ($c = 1.2$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): $_\delta$ 1.28 (t, $J = 7.1$ Hz, 3 H, CH_2CH_3), 2.09 (s, 3 H, CH_3CO), 3.63 (dq, $J = 9.6$, 7.1 Hz, 1 H, OCH_2CH_3,), 3.87 (dq, $J = 9.6$, 7.1 Hz, 1 H, OCH_2CH_3), 3.99 (dd, $J = 12.4$, 4.8 Hz, 1 H, H-6), 4.19 (dd, $J = 12.4$, 2.5 Hz, 1 H, H-6), 4.34 (ddd, $J = 10.0$, 4.8, 2.5 Hz, 1 H, H-5), 5.17 (br s, 1 H, H-1), 5.34 (s, 2 H, CH_2OPhth), 5.43 (dd, $J = 10.0$, 1.5 Hz, 1 H, H-4), 5.98 (br d, $J = 10.2$ Hz, 1 H, H-3), 6.10 (ddd, $J = 10.2$, 2.6, 2.6 Hz, 1 H, H-2), 7.71–7.76 (m, 2 H, H_{arom}), 7.77–7.81 (m, 2 H, H_{arom}), 7.95 (s, 1 H, =CH-N); ^{13}C NMR (75.5 MHz $CDCl_3$): 15.7, 21.2, 55.6, 63.0, 65.0, 70.5, 68.8, 94.5, 124.0, 129.1, 127.5, 130.1, 134.9, 142.7, 140.90, 163.8, 170.9.

Anal. Calcd for $C_{14}H_{19}O_6N_3$ (325.317): C, 57.01; H, 5.01. Found C, 56.31; H, 5.02.

1-(Ethyl 6-*O*-acetyl-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranosid-4-yl)-4-trimethylsilyl-1*H*-1,2,3-triazole (4j). Yield 30%; colorless oil; R_f 0.8 (petroleum ether/EtOAc 1 : 1); $[\alpha]_D^{20} + 99$ ($c = 1.8$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): 0.34 (s, 9 H, $SiMe_3$), 1.30 (t, $J = 7.1$ Hz, 3 H, CH_2CH_3), 2.07 (s, 3 H, CH_3CO), 3.65 (dq, $J = 9.7$, 7.1 Hz, 1 H, OCH_2CH_3), 3.88 (dq, $J = 7.1$, 9.7 Hz, 1 H, OCH_2CH_3), 4.07 (dd, $J = 12.2$, 5.3 Hz, 1 H, H-6), 4.17 (dd, $J = 12.2$, 2.9 Hz, 1 H, H-6), 4.29 (ddd, $J = 10.0$, 5.3, 3.0 Hz, 1 H, H-5), 5.18 (br s, 1 H, H-1), 5.48 (dd, $J = 10.0$, 1.9 Hz, 1 H, H-4), 5.98 (br d, $J = 10.0$ Hz, 1 H, H-3), 6.09 (ddd, $J = 10.0$, 2.6 Hz, 1 H, H-2), 7.58 (s, 1 H, =CH-N); ^{13}C NMR (75.5 MHz, $CDCl_3$): 0.0, 16.4, 21.8, 55.9, 64.1, 65.8, 69.5, 95.2, 128.2, 128.9, 130.3, 148.6, 171.6.

Anal. Calcd for $C_{15}H_{25}O_4N_3Si$ (339.462): C, 53.07; H, 7.42. Found: C, 53.11; H, 7.50.

1-(Ethyl 6-*O*-acetyl-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranosid-4-yl)-1*H*-1,2,3-triazole (4k). Yield 53%; colorless oil; R_f 0.4 (petroleum ether/EtOAc 1 : 1); $[\alpha]_D^{20} + 43$ ($c = 1.2$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): 1.27 (t, $J = 7.1$ Hz, 3 H, CH_2CH_3), 2.06 (s, 3 H, CH_3CO), 3.63 (dq, $J = 9.8$, 7.1 Hz, 1 H, OCH_2CH_3), 3.86 (dq, $J = 7.1$, 9.8 Hz, 1 H, OCH_2CH_3), 4.02 (dd, $J = 12.1$, 5.1 Hz, 1 H, H-6), 4.17 (dd, $J = 12.1$, 2.7 Hz, 1 H, H-6), 4.29 (ddd, $J = 10.0$, 5.1, 2.7 Hz, 1 H, H-5), 5.16 (br s, 1 H, H-1), 5.45 (dd, $J = 10.0$,

1.5 Hz, 1 H, H-4), 5.97 (br d, $J = 10.2$ Hz, 1 H, H-3), 6.09 (ddd, $J = 10.2$, 2.6, 2.6 Hz, 1 H, H-2), 7.63 (s, 1 H, =CH-N=), 7.76 (s, 1 H, =CH-N); ^{13}C NMR (75.5 MHz, $CDCl_3$): 15.6, 21.1, 55.5, 63.2, 65.0, 68.7, 94.4, 122.7, 127.7, 129.9, 134.8, 170.8.

Anal. Calcd for $C_{16}H_{21}O_8N_3$ (353.383): C, 53.92; H, 6.41. Found: C, 54.35; H, 6.56.

4-Biphenyl-1-(ethyl 2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranosid-4-yl)-1*H*-1,2,3-triazole (5). To a solution of carbohydrate **4b** (80 mg, 0.19 mmol), phenyl boronic acid (35 mg, 0.286 mmol), and Pd $(PPh_3)_4$ (14 mg, 12 μmol), in a mixture of toluene (2 mL) and ethanol (1 mL) in a Schlenk tube under argon, was added a solution of Na_2CO_3 (76 mg, 0.714 mmol) in water (0.5 mL). The mixture was stirred at 70°C for 4 h. After cooling the contents to rt, a 1:1 solution of ethanol/water (4 mL) was added, the solution was extracted with toluene (3 × 10 mL), and the organic phase was dried over Na_2SO_4. Solvent evaporation under reduced pressure gave a residue that was purified by column chromatography on silica using petroleum ether/EtOAc 6:4) as the eluent to provide compound **5**. Yield: 46 mg (64%, colorless solid); mp 143–145°C; R_f 0.3 (petroleum ether/EtOAc 6:4); $[\alpha]_D^{20} + 145$ ($c = 1.2$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): $_\delta$ 1.28 (t, $J = 7.1$ Hz, 3 H, CH_2CH_3), 3.59–3.69 (m, 2 H, H-6, OCH_2CH_3), 3.76 (br d, $J = 12.5$ Hz, 1 H, H-6), 3.89 (dq, $J = 9.6$, 7.1 Hz, 1 H, OCH_2CH_3), 4.15 (ddd, $J = 9.9$, 4.0, 2.4 Hz, 1 H, H-5), 5.20 (br s, 1 H, H-1), 5.55 (dd, $J = 9.9$, 1.1 Hz, 1 H, H-4), 6.08 (br d, $J = 10.5$ Hz, 1 H, H-3), 6.13 (ddd, $J = 10.5$, 2.1, 2.1 Hz, 1 H, H-2), 7.26 (m, 1 H, H_{arom}), 7.46 (m, 2 H, H_{arom}), 7.65 (m, 4 H, H_{arom}), 7.88–7.92 (m, 3 H, H_{arom}, =CH-N); ^{13}C NMR (75.5 MHz, $CDCl_3$): 15.7, 54.9, 61.9, 65.0, 71.0, 94.4, 118.7, 126.5, 127.4, 127.9, 128.0, 129.2, 129.6, 129.9, 140.9, 141.5, 148.4.

Anal. Calcd for $C_{22}H_{23}O_3N_3$ (377.436): C, 70.01; H, 6.14. Found: C, 70.31; H, 6.40.

Ethyl 6-*O*-acetyl-2,3,4-trideoxy-4-(4-{[(4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosyl)oxy]methyl}-1*H*-1,2,3-triazol-1-yl)-α-D-*erythro*-hex-2-enopyranoside (7). Yield 80%; colorless solid; mp 99–101°C; R_f 0.3 (petroleum ether/EtOAc 4:6); $[\alpha]_D^{20} + 99$ ($c = 2.8$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): 1.28 (t, $J = 7.1$ Hz, 3 H, CH_2CH_3), 2.07 (s, 3 H, CH_3CO), 2.09 (s, 3 H, CH_3CO), 2.12 (s, 3 H, CH_3CO), 3.63 (dq, $J = 9.7$, 7.1 Hz, 1 H, OCH_2CH_3), 3.86 (dq, $J = 9.7$, 7.1 Hz, 1 H, OCH_2CH_3), 4.05 (dd, $J = 12.2$, 5.3 Hz, 1 H, H-6), 4.10–4.31 (m, 5 H, 2 X H-5, 3 X H-6), 4.71 (d, $J = 12.2$ Hz, 1 H, CH_2), 4.94 (d, $J = 12.2$ Hz, 1 H, CH_2), 5.16 (s, 1 H, H-1), 5.19 (br s, 1 H, H-1), 5.35 (dd, $J = 9.6$, 1.3 Hz, 1 H, CH-N), 5.40 (dd, $J = 9.9$, 1.5 Hz, 1 H, OCHOCH=), 5.85 (ddd, $J = 10.3$, 2.3, 2.3 Hz, 1 H, H-2), 5.92 (br d, $J = 10.3$ Hz, 1 H, H-3), 5.96 (br d, $J = 10.3$ Hz, 1 H, H-3), 6.09 (ddd, $J = 10.0$,

2.6, 2.6 Hz, 1 H, H-2), 7.63 (s, 1 H, =CH-N); ^{13}C NMR (75.5 MHz, $CDCl_3$): 15.6, 21.1, 21.2, 21.3, 55.6, 62.0, 63.1, 63.2, 65.0, 65.6, 67.4, 68.6, 94.3, 94.4, 121.5, 127.6, 127.7, 130.0, 145.6, 170.6, 170.8, 171.2.

Anal. Calcd for $C_{23}H_{31}O_{10}N_3$ (509.506): C, 54.22; H, 6.13. Found: C, 54.17; H, 6.14.

General procedure for the synthesis of compounds 12, 13, 17, and 18. 4-Azido sugar **1a** (386 mg, 1.6 mmol) or **14** (574.4 mg, 1.6 mmol) and the alkyne derivative (0.4 mmol) were suspended in 1 : 1 mixture of *tert*-butanol and water (4 mL). To this solution was added a mixture of $Cu(OAc)_2$ (43 mg, 0.24 mmol) and sodium ascorbate (95 mg, 0.48 mmol) in *tert*-BuOH/H_2O (1 mL). The reaction was stirred under nitrogen at rt until TLC analysis indicated complete consumption of the product; water (3 mL) was added, and the product was extracted with CH_2Cl_2 (3 × 5 mL). The combined organic layers were dried over Na_2SO_4. Evaporation of the solvent under reduced pressure gave a residue that was purified by column chromatography on silica using the indicated eluent to give the corresponding triazole derivatives.

1,3,5-Tris[4-(ethyl 6-*O*-acetyl-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranosid-4-yl)-1*H*-1,2,3-triazol-1-yl]benzene (12). Yield 80%; colorles solid; mp 98–100°C; R_f 0.6 (EtOAc); $[\alpha]_D^{20} + 280$ ($c = 0.5$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.32 (t, $J = 7.2$ Hz, 9 H, CH_2CH_3), 2.09 (s, 9 H, CH_3CO), 3.67 (dq, $J = 9.6$, 7.2 Hz, 9 H, OCH_2CH_3), 3.90 (dq, $J = 9.6$, 7.2 Hz, 3 H, OCH_2CH_3), 4.12 (dd, $J = 12.2$, 5.0 Hz, 3 H, H-6), 4.23 (dd, $J = 12.2$, 2.6 Hz, 3 H, H-6), 4.38 (ddd, $J = 10.0$, 5.0, 2.6 Hz, 3 H, H-5), 5.20 (br s, 3 H, H-1), 5.49 (br d, $J = 10.0$ Hz, 3 H, H-4), 6.04 (br d, $J = 10.1$ Hz, 1 H, H-3), 6.17 (ddd, $J = 10.1$, 2.5, 2.5 Hz, 1 H, H-2), 8.06 (s, 3 H, =CH-N), 8.32 (s, 3 H, H_{arom}); ^{13}C NMR (75.5 MHz, $CDCl_3$): 15.6, 21.1, 55.8, 63.2, 65.0, 68.7, 94.4, 119.2, 122.8, 131.9, 127.4, 130.2, 147.9, 170.8.

HRMS Calcd for $C_{42}H_{52}O_{12}N_9$: 874.3735. Found: 874.3730.

1,3,5-Tris{methylenoxy[4-(ethyl 6-*O*-acetyl-2,3,4-trideoxy-α-D-*erythro*-hex-2-enopyranosid-4-yl)-1*H*-1,2,3-triazol-1-yl]}benzene (17). Yield 61%; colorless oil; R_f 0.5 (EtOAc); $[\alpha]_D^{20} + 123$ ($c = 1.5$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.27 (t, $J = 7.1$ Hz, 9 H, CH_2CH_3), 2.07 (s, 6 H, CH_3CO), 3.62 (dq, $J = 9.6$, 7.1 Hz, 3 H, OCH_2CH_3), 3.86 (dq, $J = 9.6$, 7.1 Hz, 3 H, OCH_2CH_3), 4.05 (dd, $J = 12.2$, 5.0 Hz, 3 H, H-6), 4.19 (dd, $J = 12.2$, 2.6 Hz, 3 H, H-6), 4.31 (ddd, $J = 9.9$, 5.0, 2.6 Hz, 3 H, H-5), 5.15 (br s, 9 H, H-1, CH_2OAr), 5.42 (dd, $J = 9.9$, 1.7 Hz, 3 H, H-4), 5.98 (br d, $J = 10.2$ Hz, 3 H, H-3), 6.09 (ddd, $J = 10.2$, 2.6, 2.6 Hz, 3 H, H-2), 6.29 (s, 3H, H_{arom}), 7.73 (s, 3 H, =CH-N); ^{13}C NMR (75.5 MHz, $CDCl_3$): 15.7, 21.1, 55.8, 62.5, 63.2, 65.0, 68.6, 94.4, 95.4, 121.8, 127.6, 130.0, 144.9, 160.5, 170.8.

Anal. Calcd for $C_{45}H_{57}O_{15}N_9$ (963.985): C, 56.07; H, 5.96. Found: C, 55.77; H, 6.17.

HRMS Calcd for $C_{45}H_{58}O_{15}N_9$: 964.4052. Found: 964.4059.

1,3,5-Tris[4-(ethyl 2,3,6-tri-*O*-acetyl-4-deoxy-α-D-mannopyranosid-4-yl)-1*H*-1,2,3-triazol-1-yl]benzene (13). Yield 80%; colorles solid; mp $> 250^{\circ}$C; R_f 0.4 (petroleum ether/EtOAc 1:4); $[\alpha]_D^{20} + 51$ ($c = 2.0$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): $_\delta$ 1.29 (t, $J = 7.0$ Hz, 9 H, CH_2CH_3), 1.98 (s, 9 H, CH_3CO), 2.27 (s, 18 H, CH_3CO), 3.70 (dq, $J = 10.1$, 7.1 Hz, 3 H, OCH_2CH_3), 3.82 (dq, $J = 10.1$, 7.1 Hz, 3 H, OCH_2CH_3), 3.91 (br s, 6 H, H-6), 4.50 (br d, $J = 10.5$ Hz, 3 H, H-5), 5.00 (br s, 3 H, H-1), 5.27 (dd, $J = 10.7$, 10.5 Hz, 3 H, H-4), 5.40 (br s, 3 H, H-2), 6.31 (br d, $J = 10.7$ Hz, 3 H, H-3), 7.62 (br s, 3 H, H_{arom}), 8.74 (br s, 3 H, =CH-N); ^{13}C NMR (75.5 MHz, $CDCl_3$): 15.1, 21.0, 21.4, 21.5, 58, 63.1, 64.3, 68.0, 69.2, 69.7, 97.9, 119.3, 131.5, 147.8, 170.4, 170.7.

Anal. Calcd for $C_{54}H_{69}O_{24}N_9$ (1228.172): C, 52.81; H, 5.66. Found: C, 51.91; H, 5.71.

HRMS-FAB Calcd for $C_{54}H_{70}O_{24}N_9$: 1228.4534. Found: 1228.4539.

1,3,5-Tris{methylenoxy[4-(ethyl 2,3,6-tri-*O*-acetyl-4-deoxy-α-D-manno-pyranosid-4-yl)-1*H*-1,2,3-triazol-1-yl]}benzene (18). Yield 80%; colorles solid; mp 93-95°C; R_f 0.3 (petroleum ether/EtOAc 2:8); $[\alpha]_D^{20} + 48$ ($c = 1.8$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): $_\delta$ 1.29 (t, $J = 7.1$ Hz, 9 H, CH_2CH_3), 1.77 (s, 9 H, CH_3CO), 2.04 (s, 9 H, CH_3CO), 2.18 (s, 9 H, CH_3CO), 3.60 (dq, $J = 9.6$, 7.1 Hz, 3 H, OCH_2CH_3), 3.80 (dq, $J = 9.6$, 7.1 Hz, 3 H, OCH_2CH_3), 3.92 (dd, $J = 12.3$, 4.2 Hz, 3 H, H-6), 4.15 (dd, $J = 12.3$, 2.6 Hz, 3 H, H-6), 4.35 (ddd, $J = 10.4$, 4.2, 3.0 Hz, 3 H, H-5), 4.93 (br s, 3 H, H-1), 4.90 (dd, $J = 11.0$, 10.2 Hz, 3 H, H-4), 5.13 (br s, 6 H, CH_2OAr), 5.32 (dd, $J = 3.2$, 1.7 Hz, 3 H, H-2), 5.81 (br d, $J = 11.0$, 3.2 Hz, 3 H, H-3), 6.20 (s, 3 H, H_{arom}), 7.70 (s, 3 H, =CH-N); ^{13}C NMR (75.5 MHz, $CDCl_3$): 15.3, 20.6, 21.0, 21.2, 57.7, 62.4, 62.9, 64.7, 68.8, 68.9, 69.2, 95.4, 97.9, 123.3, 144.5, 160.4, 169.4, 170.2, 170.7.

HRMS-FAB Calcd for $C_{57}H_{76}O_{27}N_9$: 1318.4851. Found: 1318.4846.

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