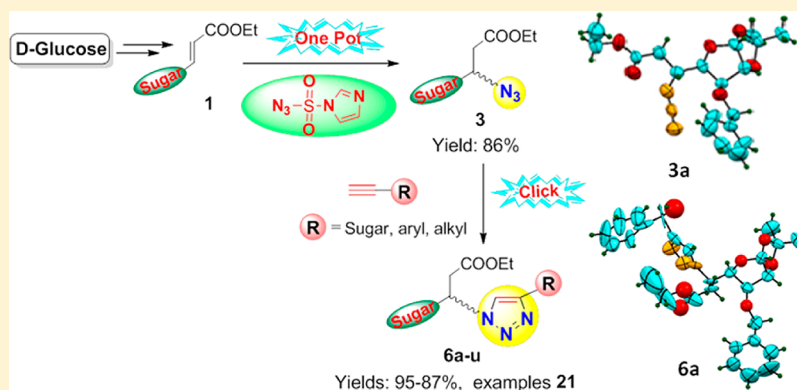


One-Pot Synthesis of Glycosyl- β -azido Ester via Diazotransfer Reaction Toward Access of Glycosyl- β -triazolyl Ester

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S Supporting Information



ABSTRACT: A concise and efficacious one-pot protocol for the synthesis of novel glycosyl- β -azido ester **3** from glycosyl olefinic ester **1** under mild conditions has been devised. The β -aminoester, formed by the conjugate addition of ammonia on olefinic ester, undergoes a metal-catalyzed diazotransfer reaction to furnish glycosyl- β -azido ester. The optimized conditions for diazotransfer reaction indicate that imidazole-1-sulphonyl azide and K_2CO_3 give the best results in the presence of $ZnCl_2$. A diverse range of novel regioselective triazolyl glycoconjugates **6a–u** have been achieved in high yields via 1,3-dipolar cycloaddition of compound **3** with various alkynes in the presence of $CuI/DIPEA$. Structures of all the compounds have been elucidated using IR, NMR, MS, and elemental analysis, and four of them (**3a**, **3b**, **4b**, and **6a**) have also been characterized by single crystal X-ray diffraction analysis.

INTRODUCTION

1,2,3-Triazoles are one of the most important classes of heterocycles that have been studied over the past decade because of their wide applicability in material science, biological research, and medicinal chemistry.¹ They possess antitumor,² anti-HIV,³ cytostatic,⁴ and antibactericidal properties⁵ and can also act as glycosidase⁶ and GABA inhibitors.⁷ The triazole moiety, because of its close electronic and chemical resemblance to an amide bond, serves as a bioisostere of peptide functionality and hence plays a major role in the elaboration and composition of biological systems.⁸

Carbohydrates and their conjugates play a fundamental role in normal cell functions, including energy storage, modulation of protein function, transport, adhesion, signal transduction, as well as viral and bacterial cell surface recognition. Their role in biodynamic applications has led to increased demand of carbohydrate-based molecules for complete chemical, medicinal, biological, and pharmacological investigations.⁹ In this context, sugar derivatives with substituted C-5 amide functionality possess significant bioactivity, such as antitubercular, antifilarial, and α -glucosidase inhibition.^{9d,10,11} Thus, the pursuit of introducing a triazole ring at the C-5 position of sugar derivatives is quite relevant and demanding. In this perspective, the Huisgen 1,3-dipolar cycloaddition of terminal alkynes and organic azides

(click chemistry) has been extensively used in joining two distinct building blocks, enabling easy access to regioselective novel 1,4-disubstituted-1,2,3-triazolyl conjugates of simple to complex molecular-level architectures.^{12–14} Although this chemistry has exponentially expanding applications in various disciplines of science, ranging from organic synthesis, material science, and catalysis to chemical biology; however, special attention has been received in the field of glycoscience because it leads to an easy route for triazolyl glycoconjugation in diverse applications.^{13e}

The role of azides in the click reaction is well established.¹⁵ For the introduction of a triazole skeleton at the β -position (C-5) of glycosyl olefinic ester, the presence of an azide group is necessary. However, the introduction of azide functionality at the β -position of olefinic esters is still a challenging task. Several established strategies for the β -azidation of α,β -unsaturated carbonyl compounds include conjugate addition of the azide via HN_3 in $HOAc$, HN_3 with Lewis bases, and $TMSN_3$ with $HOAc$. These methods suffer from some limitations, including poor reaction yields, requiring elevated temperature (353 K) and long reaction times.^{16–18} A search of the available literature revealed that there

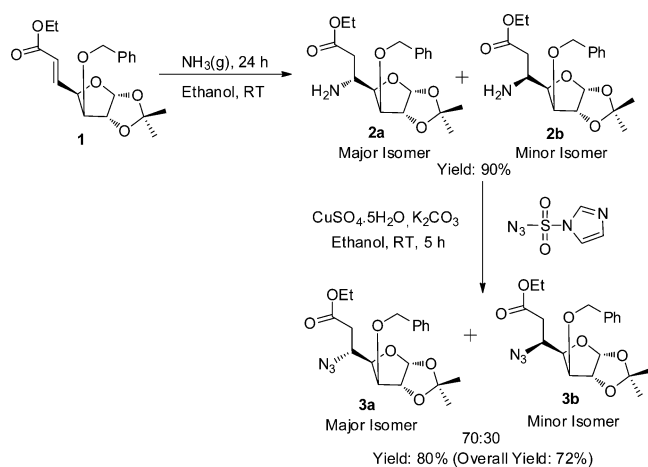
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is no report on the β -azidation of glycosyl olefinic esters. Our current interest in azide chemistry, and the need for new and specific flexible strategies that would provide potentially useful routes for triazole synthesis, prompted us to determine a new methodology for this purpose. In this article, we report a new and remarkably mild synthesis of novel glycosyl- β -azido ester and its application for the development of glycosyl- β -triazolyl esters in good to excellent yields.

RESULTS AND DISCUSSION

We first investigated the conjugate addition of azide to glycosyl olefinic ester **1** using previously reported reagents and reaction conditions for β -azidation of α,β -unsaturated carbonyl compounds.^{16–18} To our surprise, the reaction of compound **1** with hydrogen azide in acidic media (HOAc)¹⁶ using a Lewis base catalyst (Et₃N) at two different temperatures (30 and 80 °C),¹⁷ TMSN₃, HOAc with tertiary amine (Et₃N) as catalyst,^{18a} and NaN₃ in dry DMF at 80 °C, indicated the absence of product. These results indicate that synthesis of glycosyl- β -azido ester was indeed challenging using these earlier methods. Therefore, a different route was developed for the synthesis of glycosyl- β -azido ester.

Scheme 1. Synthesis of Novel Glycosyl- β -azido Ester **3**



It is known that azides can formally be considered diazoamines¹⁵ and can be prepared by a diazotransfer reaction of amines. In light of this fact, we attempted a 1,4-conjugate

addition of amine on glycosyl olefinic ester followed by a metal-catalyzed diazotransfer reaction of amine. Expectedly, the reaction led to the formation of glycosyl- β -azido ester with significant ease. Our synthetic protocol started from a cheap and readily available compound, D-glucose, which undergoes a number of high-yielding steps, such as isopropylidene protection, 3-O-benzyl protection, selective 5,6-isopropylidene deprotection followed by NaIO₄ oxidation, and finally Horner–Emmons–Wadsworth Wittig olefination affording the glycosyl olefinic ester (1*R*,2*R*,3*S*,4*R*)-ethyl-[3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene- α -D-glucO]-heptofuran-5-en-uronate **1**.¹⁹ Further, 1,4-conjugate addition of olefinic ester **1** with ammonia in dry ethanol yielded (1*R*,2*R*,3*S*,4*R*)-ethyl-[5-amino-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene]- α -D-glucO- and - β -L-ido-heptofuranuronate **2a** and **2b** as a diastereomeric mixture (70:30) in good yield (Scheme 1).^{19,20} The diastereoselectivity ratio was determined by literature precedent.^{19,20} The major and minor isomers were successfully isolated in pure form by flash column chromatography. The observed diastereoselectivity can be rationalized by Felkin–Anh-like transition states based on an alkene–arene π stacking interaction as described by earlier studies.^{20,21} The synthesized glycosyl- β -amino ester can undergo a diazotransfer reaction to form glycosyl- β -azido ester. To achieve an efficient, practical, and easy synthesis of novel glycosyl- β -azido esters, we focused on the diazotransfer reaction and related chemistry. The major isomer **2a** was further used for the optimization studies. The intermolecular diazotransfer reaction of compound **2** with imidazole-1-sulfonyl azide²² as the donor of a diazo group in the presence of CuSO₄·5H₂O and K₂CO₃ in dry ethanol afforded ethyl-[5-azido-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene]- α -D-glucO- and - β -L-ido-heptofuranuronate **3** in 80% yield (Scheme 1). Separation of major and minor isomers was achieved by flash column chromatography, and the structure was confirmed by NMR (¹H and ¹³C). Lastly, single crystal X-ray analysis confirmed the unambiguous structure and stereochemistry at the C-5 center in compounds **3a** and **3b** (Figure 1).

The success of this reaction prompted us toward the synthesis of a new diazotransfer reagent. Hence, the reaction of indole-3-carboxaldehyde (2.0 equiv) with chlorosulfonyl azide, prepared in situ by the reaction of equimolar quantities of sodium azide and sulfur chloride in MeCN, gave indole-3-carboxaldehyde-1-sulfonyl azide **I** (40%, obtained after aqueous workup and purification by flash column chromatography) as a yellow solid (mp 174–176 °C) (Scheme 2).

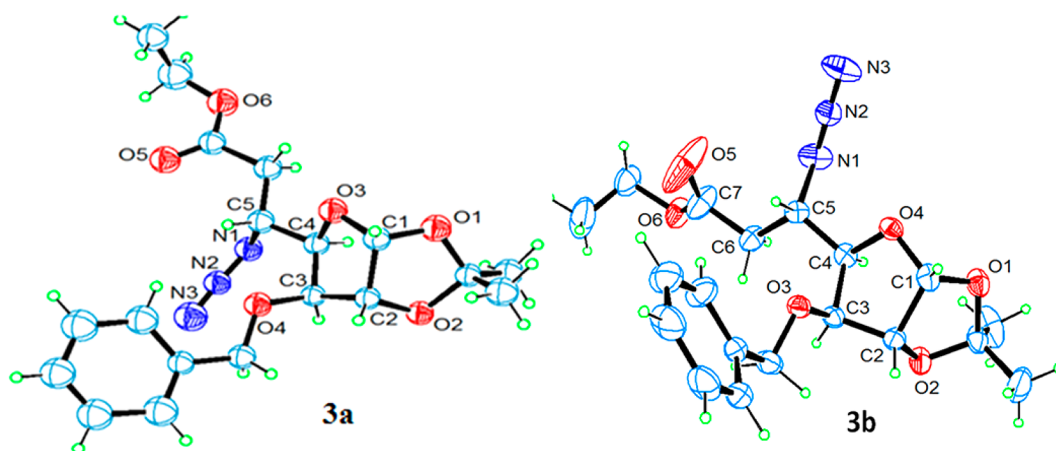
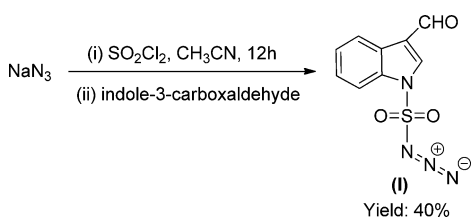


Figure 1. Molecular structure of **3a** and **3b**. Thermal ellipsoids of C, N, and O are set at 40% probability.

Scheme 2. Synthesis of Indole-3-carboxaldehyde-1-sulphonyl Azide I



Then, the diazotransfer reaction of primary amines (1.0 equiv) with indole-3-carboxaldehyde-1-sulphonyl azide I (1.2 equiv) in the presence of $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ catalyst (5 mol %) and K_2CO_3 (2.0 equiv) in dry methanol at room temperature was investigated, which gave the corresponding azides (Table 1). Consequently,

Table 1. Synthesis of Azides from Primary Amines Utilizing Indole-3-carboxaldehyde-1-sulphonyl Azide I (1.2 equiv), K_2CO_3 (2.0 equiv), and $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ Catalyst (5 mol %)

S.N.	Substrate	Product	Time ^a	Yield (%) ^b
1.			6	30
2.			7	40
3.			6	25

^aReaction time in hours. ^bIsolated yield of product obtained after purification by column chromatography.

the diazotransfer reagent I was tested on glycosyl-β-amino ester 2a under same reaction conditions to give glycosyl-β-azido ester 3a in 25% yield (entry 3, Table 1). The NMR data of compound 3a matched with that of the major isomer obtained in Scheme 1.

We then compared the efficiency of conversion of glycosyl-β-amino ester to glycosyl-β-azido ester in the presence of various diazotransfer reagents, such as imidazole-1-sulphonyl azide,²² indole-3-carboxaldehyde-1-sulphonyl azide, or benzotriazole-1-sulphonyl azide²³ with $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ and K_2CO_3 for all reagents except for benzotriazole-1-sulphonyl azide with which no base was used. The observed results indicated that the best reaction yields and efficiency were achieved when imidazole-1-sulphonyl azide was used as the diazotransfer reagent (entry 1, Table 2).

Then, with imidazole-1-sulphonyl azide as the well suited diazotransfer reagent, we performed the next experiment intended to determine the feasibility of screening metal catalysts for this reaction. In one set of experiments, zinc chloride and zinc nitrate were tested under homogeneous reaction conditions. It was observed that the products were obtained in the same yields with both metal salts having zinc in the +2 oxidation state but different counterions. Thus, it can be concluded that the counterion of zinc does not significantly affect the reaction because it exhibits a similar effect.

In the other set of experiments, out of the several metal ions tested under homogeneous reaction conditions given in Scheme 3, zinc chloride (5 mol %) gave the best result as the product was

Table 2. Diazotransfer Reaction of Glycosyl-β-amino Ester 2a in the Presence of Various Diazotransfer Reagents

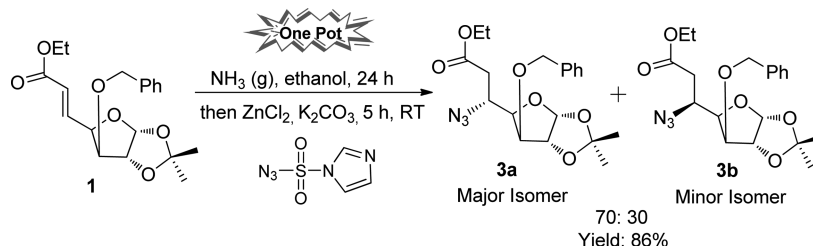
S.N.	Diazotransfer reagents ^a	Time ^b	Yield (%) ^c
1.		5	80
2.		6	25
3.		8	70

^aReaction conditions: Glycosyl-β-amino ester 2a (1.0 equiv), diazotransfer reagent (1.2 equiv), K_2CO_3 (2.0 equiv) [for all reagents except benzotriazole-1-sulphonyl azide] and $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ catalyst (5 mol %). ^bReaction time in hours. ^cIsolated yield of product obtained after purification by column chromatography.

obtained in excellent yield (86%). This was followed by copper (80%), and decent results were also observed using nickel over a 5 h duration (Table 3). In a control experiment in which the metal catalyst was omitted completely, the product was obtained in low yields, indicating a decrease in the efficiency of the reaction. The other metals, Mg^{II} , Co^{II} , Pd^{II} , and Ca^{II} , had a negligible effect with nearly the same reaction yield as that in the absence of metal catalyst (entries 4–8, Table 3). Os(III) and Ru(III) also have no effect on the reaction (Cu as sulfate, Zn, Mg, Co, Ni, Ca, Pd, Os, and Ru as chlorides). These observations suggest that the metal catalyst might increase the rate of the reaction by lowering the activation energy barrier for the reaction. It might also act as a Lewis acid catalyst to activate the imidazole-1-sulphonyl azide toward the probable reaction via the nucleophilic mechanism.²⁴

Next, the effect of different bases was investigated. Upon scanning the reaction for various inorganic/organic bases, it was revealed that 2.0 equiv of either bicarbonate or carbonate bases resulted in comparable product formation as was evident from the results obtained in Table 4 (entries 1–3). Amine bases do not affect the reaction to a great extent, and thus, low product yield was obtained.

Finally, the reaction was screened for a variety of organic solvents; the results are summarized in Table 5. It was observed that the reaction performed well in terms of efficiency and had good yields using ethanol and methanol solvents (entries 1 and 3, Table 5). However, ethanol proved to be the solvent of choice for the prescribed diazotransfer reaction because ethyl functionality of the ester group in glycosyl-β-amino ester is preserved in the product. Using methanol as the solvent, hydrolysis of the ester functional group occurred by a B_{AC}^2 (bimolecular base-catalyzed hydrolysis via acyl oxygen cleavage) mechanism. As a result, the ethyl group present on the ester functionality was replaced by a methyl group to afford methyl-[5-azido-3-O-benzyl-5,6-dideoxy-1,2-O-isopropylidene]-α-D-glucopyranoside and β-L-idopyranoside (4a,b). The ¹H NMR data of compound 4b corresponding to 23 proton resonances and a sharp singlet integrated to 3 proton resonances appearing at δ 3.63 evidenced the presence of the methyl group. The molecular ion peak $[\text{M} + \text{H}]^+$ observed at m/z 378 and single crystal X-ray analysis confirmed the unambiguous

Scheme 3. One-Pot Synthesis for Novel Glycosyl- β -azido Ester 3Table 3. Diazotransfer Reaction of Glycosyl- β -amino Ester in the Presence of Various Metal Catalysts

entry	metal (M ²⁺)	time ^a	yield (%) ^b
1	Cu	5	80
2	Ni	5	60
3	Zn	5	86
4	Ca	5	45
5	Mg	5	45
6	Co	5	45
7	Pd	5	40
8		5	45

^aReaction time in hours. ^bIsolated yield of product 3a.Table 4. Diazotransfer Reaction of Glycosyl- β -amino Ester in the Presence of Various Bases

entry	solvent	time ^a	yield (%) ^b
1	Na ₂ CO ₃	5	>80
2	K ₂ CO ₃	5	>85
3	NaHCO ₃	5	>80
4	DMAP	5	40
5	DIPEA	5	40
6	DBU	5	40
7	DABCO	5	40
8	Et ₃ N	5	<30
9	pyridine	5	<30

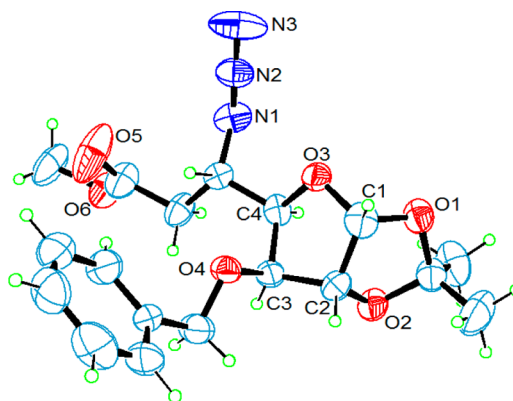
^aReaction time in hours. ^bIsolated yield of product 3a.

structure of compound **4b** and the presence of the methyl group at the ester functionality (Figure 2).

Therefore, efficient synthesis of glycosyl- β -azido ester from glycosyl- β -amino ester (1.0 equiv) was achieved in ethanol with imidazole-1-sulfonyl azide (1.2 equiv), K₂CO₃ (2.0 equiv), and ZnCl₂ (5 mol %). Upon observing the formation of glycosyl- β -azido ester from olefinic ester **1**, we found that both steps involved in the reaction sequence proceeded in the same solvent. Thus, after the conjugate addition of ammonia (24 h) in ethanol, the reagents for the second step (diazotransfer reaction) were added, and the reaction was stirred for the appropriate amount of

Table 5. Diazotransfer Reaction of Glycosyl- β -amino Ester (1.0 equiv) with Imidazole-1-sulfonyl Azide (1.2 equiv), K₂CO₃ (2.0 equiv), and ZnCl₂ (5 mol %)

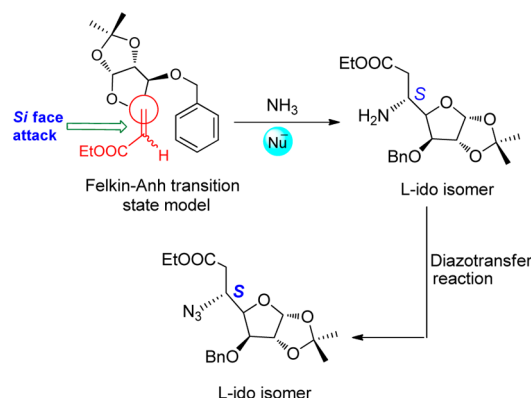
entry	solvent	time ^a	yield (%) ^b
1	ethanol	5	>85
2	DCM	5	50
3	methanol	5	>85
4	THF	5	>40
5	acetone	5	30
6	DMF	5	20
7	Et ₂ O	5	30
8	acetonitrile	5	35

^aReaction time in hours. ^bIsolated yield of product 3a.Figure 2. Molecular structure of **4b**. Thermal ellipsoids of C, N, and O are set at 40% probability.

time. The process gave compound **3** in good yields at room temperature. Thus, a facile and efficacious one-pot methodology for the synthesis of novel glycosyl- β -azido ester **3** from glycosyl olefinic ester **1** has been developed (Scheme 3).

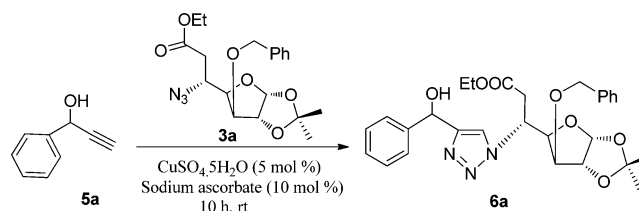
The stereochemistry at the C-5 stereogenic center has been tentatively predicted on the basis of a precedent set in the literature and mechanistic grounds.^{20,21} On the basis of Felkin–Anh and Cram’s transition states, it can be predicted that the major attack of nucleophilic ammonia at C-5 in olefinic ester would take place from the side of the least bulky group (hydrogen attached to C-4 of the furanose ring, the *Si* diastereoface). Thus, the major reaction product has an *S* configuration at C-5, whereas that of the minor one is *R* (Scheme 4). The diazotransfer reaction does not involve a change in stereochemistry²⁵ at the carbon (C-5) center, so the configuration at this stereocenter should be the same as that in the glycosyl- β -amino ester previously established. The ¹H NMR spectra of azide **3a** (major isomer) showed *J*_{4,5} = 9.9 Hz, evidenced a *threo* relationship between protons at C-4 and C-5, and *S* configuration at new stereogenic center C-5 has been

Scheme 4. Formation of L-Ido Isomer from Si Face Attack



assigned to this isomer. Consequently, for the second isomer (erythro) isolated as a minor ratio, the *R* stereochemistry could easily be established at C-5. Therefore, the diazotransfer reaction on glycosyl-β-amino ester **2a** affords the corresponding glycosyl-β-azido ester (1*R*,2*R*,3*S*,4*R*,5*S*)-ethyl-[5-azido-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene]-β-*L*-ido-heptofuranurinate **3a**. The ¹H NMR spectrum of compound **3a** corresponds to 25 protons, and a multiplet at δ 7.35 was observed for five Ar-*H* protons. A doublet at δ 5.87 (*J* = 3.0 Hz) was identified for the anomeric proton. The remaining 14 protons of glycosyl-β-azido ester appeared in the range of δ 2.26–4.69 along with the six protons of isopropylidene moiety, which appeared as singlets at δ 1.41 and 1.31. A triplet integrated to 3 proton resonances was observed at δ 1.27 (*J* = 6.9 Hz) for the –CH₂CH₃ group. The IR spectra showed a sharp absorption band at 2134 cm^{−1}, indicating the presence of an azide (–N₃) group, and 19 carbon resonances appeared in ¹³C NMR in addition to the molecular ion peak [*M* + *H*]⁺ observed at *m/z* 392. Further, single crystal X-ray analysis confirmed the unambiguous structure of compounds **3a** and **3b** (Figure 1).

Once the synthesis of glycosyl-β-azido ester **3** was achieved in excellent yields, we next turned our focus toward the application of this compound for CuAAC click reactions. Such reactions, in general, require a Cu(I) source directly introduced in the reaction medium from CuI or by the reduction of Cu(II) salts in form of CuSO₄·5H₂O or copper acetate in the presence of sodium ascorbate, which is the most frequently used reducing agent utilized in 3–4 fold excess to give commendable results in aqueous medium. The latter reagents are more effective because they maintain a high Cu(I) concentration during the reaction course, and they are not affected by oxidizing atmosphere. Thus, we primarily investigated the click reaction between the developed compound **3a** and 1-phenyl-2-propyn-1-ol **5a** using MeOH/H₂O, *t*-BuOH/H₂O, CH₂Cl₂/H₂O, Et₂O/H₂O, THF/H₂O, and acetone/H₂O as solvent mixtures. It is easy to verify that most of the reactions afforded the corresponding glycoconjugated triazole **6a** using a variety of organic solvents in combination with H₂O (Table 6). However, the optimal yield of **6a** was achieved using a mixture of acetone/H₂O (1:1) as the solvent. A remarkable feature of this reaction is the H₂O dependence of the triazolyl glycoconjugate synthesis (tolerant to pH range 6–9). Reactions using a mixture of acetone/H₂O (1:0.5) or acetone alone resulted in poor yield of desired product **6a** (entries 7 and 8, Table 6). The probable reason is the dependency toward aqueous media of the in situ generation of Cu(I) species from the combination of CuSO₄·5H₂O and sodium ascorbate. However, when the reaction was performed

Table 6. Study of the Solvent Effect on CuAAC of Glycosyl-β-azido Ester **3a** with **5a**

entry	reaction conditions	yield (%) ^a
1	MeOH/H ₂ O (1:1)	<20
2	<i>t</i> -BuOH/H ₂ O (1:1)	30
3	CH ₂ Cl ₂ /H ₂ O (1:1)	>70
4	Et ₂ O/H ₂ O (1:1)	>70
5	THF/H ₂ O (1:1)	60
6	acetone/H ₂ O (1:1)	>80
7	acetone/H ₂ O (1:0.5)	40
8	acetone	nd ^b
9	H ₂ O	ta ^b
10	acetone/H ₂ O (1:1) ^b	>70

^aIsolated yields in 10 h. ^bReaction under an argon atmosphere; ta = trace amount, nd = not detected.

only in H₂O, the formation of product **6a** was not observed (entry 9, Table 6) because of the decreased solubility of compound **3a** in aqueous media compared to that in the organic phase. These observations suggest that in the solvent mixture of acetone and H₂O, the Cu(I) species is generated in situ in aqueous medium from CuSO₄·5H₂O and sodium ascorbate and then catalyzes the click reaction between compounds **3a** and **6a**, which are soluble in the organic phase. It is important to note that the reactions are not very air sensitive, allowing for preparation of the respective triazole **6a** in an open atmosphere (entry 10, Table 6).

For the yield to be improved further, the reaction of **3a** (400 mg, 1.02 mmol) with **5a** (0.149 mL, 1.22 mmol) under catalysis by CuI (5 mol %) and DIPEA (10 mol %) at room temperature under inert reaction conditions was screened for a variety of organic solvents to afford **6a** in good to significant yields. The results illustrated poor performance of *t*-BuOH, toluene, benzene, DMF, and methanol in terms of yield and reaction time (Table 7). Maximum yields of triazolyl glycoconjugate were obtained using acetone and DCM (entries 1 and 3, Table 7).

Thus, under optimized conditions, alkyne **5a** reacted with **3a** in the presence of CuI (5 mol %) and DIPEA (10 mol %) as click

Table 7. Optimization of Solvent for 1,3-Dipolar Cycloaddition of Glycosyl-β-azido Ester **3a** with **5a** in the presence of CuI and DIPEA

entry	solvent	time ^a	yield (%) ^b
1	acetone	8	>80
2	<i>t</i> -BuOH	18	30
3	CH ₂ Cl ₂	8	>85
4	MeCN	8	>75
5	THF	9	70
6	toluene	12	25
7	benzene	15	20
8	MeOH	12	35
9	DMF	12	10

^aReaction time in hours. ^bIsolated yield of product **6a**.

catalysts in anhydrous CH_2Cl_2 under an argon atmosphere at ambient temperature afforded corresponding 1-[ethyl-(3'-O-benzyl-5',6'-dideoxy-1',2'-O-isopropylidene)- β -L-ido-heptofuranurate-5-yl]-4-(1''-phenylmethan-1''-ol-1''-yl)-1H-[1,2,3]-triazole **6a** regioselectively in 94% yield. The regioisomeric nature of compound **6a** was established based on its spectroscopic data. In mass spectrum, compound **6a** displayed a molecular ion peak $[\text{M} + \text{H}]^+$ at m/z 524, which corresponded to the molecular formula $\text{C}_{28}\text{H}_{33}\text{N}_3\text{O}_7$. In the ^1H NMR spectrum, the signal for the triazolyl proton and 8 phenyl protons were observed as a multiplet in the range δ 7.17–7.38 and the remaining two Ar-H protons appeared as multiplets at δ 7.08. The anomeric proton (H-1) along with the proton at the hydroxyl group bearing the carbon atom of alkyne appeared as a multiplet in the range δ 5.91–5.98. The remaining 11 protons of the cycloadduct resonated between δ 3.35–5.17 along with the six protons of isopropylidene moiety, which appeared as singlets at δ 1.49 and 1.29. A triplet of 3 protons appearing at δ 1.11 ($J = 6.9$ Hz) was identified for $-\text{CH}_2\text{CH}_x$. The ^{13}C NMR spectrum showed a signal at δ 170.3 for carbonyl carbon, whereas the anomeric carbon (C-1) of the furanose sugar resonated at δ 105.2. Single-crystal X-ray analysis further confirmed the unambiguous structure of compound **6a** (Figure 3).

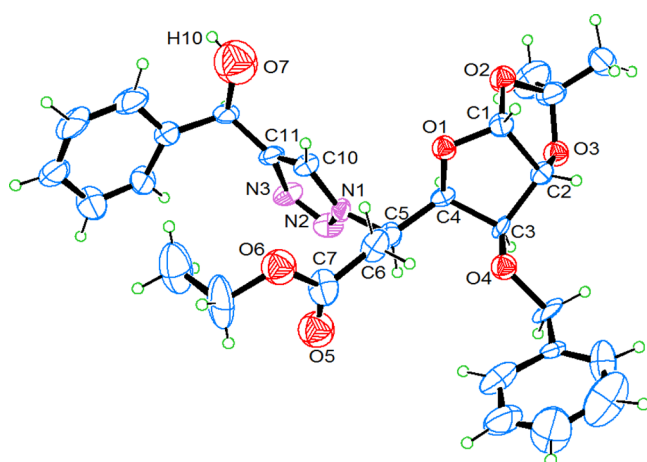


Figure 3. Molecular structure of **6a**. Thermal ellipsoids of C, N, and O are set at 40% probability.

Utilizing the reaction conditions established above for the regioselective cycloaddition of alkyne **5a** and glycosyl- β -azido ester **3a**, we further explored the scope and possibility of using various alkyl, aryl, and sugar-substituted terminal alkynes²⁶ in such a cycloaddition and prepared a library of glycoconjugated triazoles **6a–u** in efficient yields (Table 8). The structures of compounds **6a–u** were deduced using extensive spectral studies (IR, ^1H and ^{13}C NMR, and MS) and single crystal X-ray analysis for compound **6a**.

After successfully isolating the triazole made from the highly functionalized carbohydrates as well as aromatic and aliphatic side chains in excellent yields, we next synthesized 1'-1''-[ethyl-(3''-O-benzyl-5'',6''-dideoxy-1'',2''-O-isopropylidene)- α -D-glucoheptofuranurate-5-yl]-ethisterone-1,2,3-triazole **6u** by the reaction of ethisterone **5u** with glycosyl- β -azido ester **3a** and successfully executed the synthesis of ethisterone triazolyl glycoconjugate in excellent yield under our standardized conditions for click reactions (Scheme 5). Thus, the methodology is equally applicable to complex steroidal moieties. Analysis

of extensive spectral studies (IR, ^1H , and ^{13}C NMR) evidenced the formation of the triazole ring in compound **6u**.

Mechanistic Consideration. Ammonia adds to olefinic ester via 1,4 conjugate additions, and its formation can be rationalized by Felkin–Anh-like transition states based on alkene-arene π stacking interactions as described in the literature.^{19–21} The next step includes the diazotransfer reaction with imidazole-1-sulphonyl azide. Imidazole-1-sulphonyl azide is an efficient diazotransfer reagent that has the ability to transfer the diazo group directly to the primary amine function to form the corresponding azide.²² The exact mechanism of the diazotransfer reaction is to date still controversial; however, close examination of previous reports for these reactions suggests that a dianionic tetrazene intermediate is formed during this reaction and is stabilized by two monovalent metal ions (e.g., sodium).²⁷ This proposed mechanism has been further extended by Nyffeler et al. to incorporate a divalent metal ion in place of the two monovalent ions.²⁸ On the basis of these reports, we propose a plausible mechanism for the transition metal-catalyzed diazotransfer reaction of glycosyl- β -azido ester formation. The mechanism proceeds via the initial complexation of the amine substrate with the metal catalyst under basic conditions to give **7**. The amine of complex **7** undergoes nucleophilic attack on the highly electrophilic imidazole-1-sulphonyl azide that, upon further deprotonation, may possibly form zinc-stabilized mixed tetrazene **8**.^{29b} This zinc-stabilized tetrazene undergoes breakdown possibly by a reverse [3 + 2] dipolar cycloaddition, which leads to the formation of product glycosyl- β -azido ester and zinc–imidazole sulphonyl imido complex **9**. The computational work on such similar structures by Brandt et al. suggests that complex **9** would be in equilibrium with complex **11**.²⁹ From here, two possible pathways could be operating: one leads to amine complexation followed by consequent proton transfer to give **9** and the other forms zinc–imido complex **11** via the transamination of **10**. Further, this zinc–imido complex is employed in a [3 + 2] dipolar cycloaddition with imidazole-1-sulphonyl azide to alternatively give **8** (Figure 4).

CONCLUSION

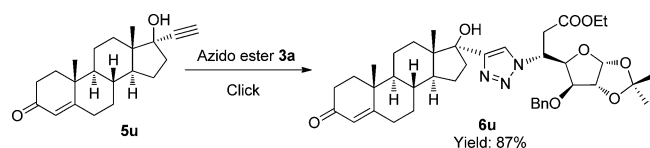
In conclusion, we have developed a concise and readily adaptable novel one-pot protocol for easy access to glycosyl- β -azido ester from glycosyl olefinic ester under mild reaction conditions. This method demonstrates high efficiency in terms of product yields. The developed glycosyl- β -azido ester has been utilized for the development of a diverse range of novel triazolyl glycoconjugates. On the basis of the presence of a substituted triazole moiety incorporating various sugar, aryl, and alkyl side chains in the glycoconjugates, they might prove to be potent scaffolds for biological and pharmaceutical investigations. The short reaction period, simple workup, high yield, and mild conditions of this methodology underscore its significance. In addition, the generality with respect to substrate scope and facile accessibility to the starting materials is also highly appealing. Synthesis of a novel glycosyl- β -azido ester from glycosyl olefinic ester has not yet been realized for one-pot conditions; thus, this approach should also be of interest to synthetic chemists. The developed methodology also performs well in small as well as gram scale synthesis of glycosyl- β -azido ester, suggesting that it may have industrial significance. Biological screening of the developed glycosyl- β -triazolyl esters is currently under way.

Table 8. Synthesis of Glycoconjugate Triazoles 6a–t via CuAAC Reaction

entry	alkyne ^a	cycloadduct ^b	time ^c	yield (%) ^d	entry	alkyne ^a	cycloadduct ^b	time ^c	yield (%) ^d
1			9	94	11			9	92
2			10	90	12			9	93
3			10	93	13			9	94
4			14	88	14			10	92
5			12	90	15			12	93
6			10	91	16			10	94
7			10	95	17			12	93
8			16	87	18			12	92
9			12	92	19			10	94
10			9	93	20			12	90

^aMolar ratios: alkynes, glycosyl-β-azido ester (1.2:1.0 equiv), CuI (5 mol %), and DIPEA (10 mol %). ^bTriazolyl glycoconjugates. ^cReaction time: in hours. ^dIsolated yield of triazolyl glycoconjugates after purification by column chromatography.

Scheme 5. Synthesis of Glycosyl-β-triazolyl Ester with Steroidal Functionality



EXPERIMENTAL SECTION

General Remarks. All of the reactions were executed in anhydrous solvents under an argon atmosphere in glassware that was oven-dried for 1 h at 100 °C. All reagents and solvents were of pure analytical grade. Thin layer chromatography (TLC) was performed on 60 F₂₅₄ silica gel precoated on aluminum plates and revealed with either a UV lamp ($\lambda_{\text{max}} = 254 \text{ nm}$), a specific color reagent (Dragendorff reagent or iodine vapors), or by spraying with a methanolic-H₂SO₄ solution and subsequent charring by heating at 100 °C. ¹H and ¹³C NMR were recorded at 300 and 75 MHz, respectively. Chemical shifts are given in ppm downfield from internal TMS, and *J* values are in Hz. Mass spectra were recorded using electrospray ionization mass spectrometry (ESI-

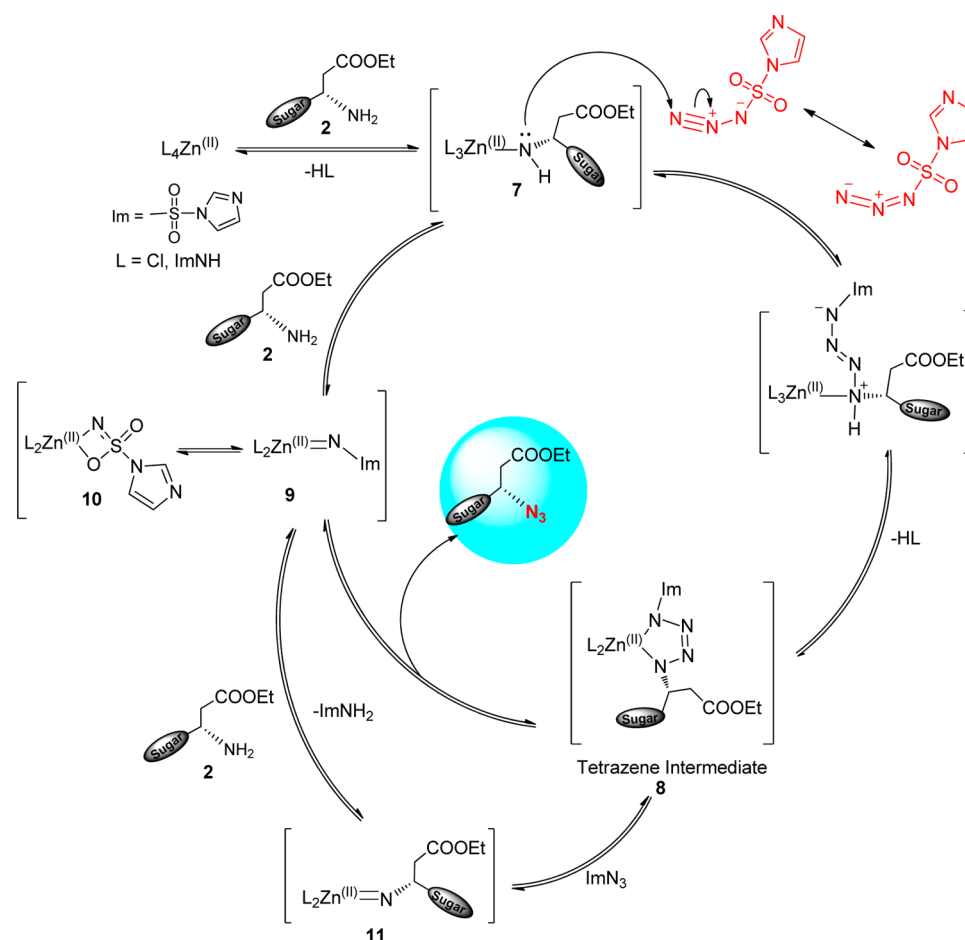


Figure 4. Proposed mechanism of the diazotransfer reaction of glycosyl- β -amino ester with imidazole-1-sulphonyl azide and zinc chloride as the catalyst.

MS). Infrared spectra were recorded as Nujol mulls in KBr plates. Elemental analysis was performed using a C, H, N analyzer, and the results were found to be within $\pm 0.4\%$ of the calculated values. Single-crystal X-ray data was collected on a CCD diffractometer.

Procedure for the Synthesis of Indole-3-carboxaldehyde-1-sulphonyl Azide (I). Sulfuryl chloride (1.10 mL, 13.6 mmol) was added dropwise to an ice-cooled suspension of NaN_3 (0.89 g, 13.6 mmol) in CH_3CN (5.0 mL), and the mixture was stirred for 12 h at room temperature. Indole-3-carboxaldehyde (3.97 g, 27.3 mmol) was added to the ice-cooled reaction mixture, and the resulting slurry was stirred at room temperature for 5 h. The mixture was diluted with EtOAc (40 mL) and H_2O (40 mL) and separated. The organic layer was washed with H_2O (40 mL) followed by saturated aqueous NaHCO_3 (2×30 mL), dried over anhydrous Na_2SO_4 , and concentrated under reduced pressure. The crude mass obtained was subjected to flash chromatography using gradient mixtures of ethyl acetate and *n*-hexane to afford pure compound I as a yellow solid; mp 174–176 °C; 1.36 g, 40% yield; $R_f = 0.48$ (30% ethyl acetate/*n*-hexane); ^1H NMR (300 MHz, CDCl_3) δ 8.86 (s, 1H), 7.78 (d, $J = 6.6$ Hz, 1H), 7.74–7.31 (m, 1H), 7.47 (d, $J = 7.2$ Hz, 1H), 7.36–7.25 (m, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 180.1, 134.8, 131.8, 126.9, 124.3, 122.3, 119.6, 115.8, 112.0; IR (KBr) ν_{max} 3257, 2924, 2223 (azide- N_3), 1709 (C=O), 1621, 1583, 1522, 1433, 1239, 1110, 745, 737 cm^{-1} ; MS (m/z) 251 [$\text{M} + \text{H}$] $^+$; Anal. Calcd for $\text{C}_9\text{H}_6\text{N}_4\text{O}_3\text{S}$ C 43.20, H 2.42, N 22.39; found C 43.30, H 2.48, N 22.41.

General Procedure for the Synthesis of Azides. To a stirred solution of amine or ammonium salt substrate (1.0 equiv) in dry MeOH were added indole-3-carboxaldehyde-1-sulphonyl azide I (1.2 equiv), K_2CO_3 (2.0 equiv), and $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ (5 mol %), and the resulting reaction mixture was stirred at room temperature for 6–7 h. The mixture was concentrated in vacuo, diluted with H_2O , acidified with concentrated HCl and extracted with EtOAc 3 times. The combined organic layers were dried on anhydrous Na_2SO_4 , filtered, and concentrated. Flash

chromatography using gradient mixtures of ethyl acetate and *n*-hexane afforded pure azides.

1,2-Diazo-4,5-dimethyl-benzene (II). To a stirred solution of 1,2-diamino-4,5-dimethyl-benzene (150 mg, 1.10 mmol) in dry MeOH (5.0 mL) were added indole-3-carboxaldehyde-1-sulphonyl azide I (330 mg, 1.32 mmol), K_2CO_3 (304 mg, 2.20 mmol), and $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ (5 mol %), and the resulting reaction mixture was stirred at room temperature for 6 h. Aqueous workup and purification by flash chromatography as described above afforded pure azide as a liquid; 62 mg, 30% yield; $R_f = 0.55$ (30% ethyl acetate/*n*-hexane); ^1H NMR (300 MHz, CDCl_3) δ 7.91 (s, 2H), 2.53 (s, 6H); ^{13}C NMR (75 MHz, CDCl_3) δ 142.4, 140.8, 127.8 (2C), 127.7 (2C), 20.6 (2C); IR (KBr) ν_{max} 2923, 2824, 2107 (azide- N_3), 1491, 1453, 1359, 1027, 998, 859 cm^{-1} ; Anal. Calcd for $\text{C}_8\text{H}_8\text{N}_6$ C 51.06, H 4.28, N 44.66; found C 51.03, H 4.32, N 44.65.

Methyl-2-azido-propan-1-oate (III). To a stirred solution of amine substrate (150 mg, 1.45 mmol) in dry MeOH (5 mL) was added indole-3-carboxaldehyde-1-sulphonyl azide I (436 mg, 1.74 mmol), K_2CO_3 (402 mg, 2.91 mmol), and $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ (5 mol %), and the resulting reaction mixture was stirred at room temperature for 7 h. Aqueous workup and purification by flash chromatography as described above afforded pure azide as a colorless liquid; 75 mg, 40% yield; $R_f = 0.49$ (25% ethyl acetate/*n*-hexane); ^1H and ^{13}C NMR spectroscopic data were in agreement with published results;³⁰ IR (KBr) ν_{max} 2852, 2118 (azide- N_3), 1463, 1257, 1054, 631 cm^{-1} ; Anal. Calcd for $\text{C}_4\text{H}_7\text{N}_3\text{O}_2$ C 37.21, H 5.46, N 32.54; found C 37.26, H 5.50, N 32.58.

Procedure for the Synthesis of Orthogonally Protected Sugars. The protected sugars were prepared from readily available carbohydrates (D-glucose, D-galactose, D-mannose, D-fructose, and D-xylose) using standard protection methodologies.^{31,32}

General Procedure for the Synthesis of O-Propargyl Ethers of Orthogonally Protected Sugars (5j–n). To a stirred solution of orthogonally protected sugars (1.0 mmol) in dry DMF (10 mL) was

added NaH (2.1 mmol) fractionwise at 0 °C, and the reaction was allowed to stir for 10–15 min. Then, propargyl bromide (1.3 mmol) and TBAB (50 mg, catalytic amount) were added to the reaction mixture and stirring continued at room temperature for 10–12 h. Completion of the reaction was confirmed by TLC (*n*-hexane/ethyl acetate 9:1); the reaction mixture was extracted with ethyl acetate and dried over anhydrous Na₂SO₄. Solvent evaporated under reduced pressure below 55 °C. Column chromatography (SiO₂) of crude product was performed using gradient mixtures of *n*-hexane/ethyl acetate (9:1) as eluant, which afforded the desired sugar alkynes **5j–n**.²⁶

General Procedure for the Synthesis of Glycosyl- β -azido Ester (3a**, **b**).** To a stirred solution of ethyl-[3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene- α -D-glucopyranosyl]-heptofuran-5-en-uronate **1**¹⁹ dissolved in dry ethanol was passed NH₃ gas for 3 h, and the reaction was allowed to stir at room temperature for 24 h to afford ethyl-[5-amino-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene]- α -D-glucopyranosyl- and - β -L-ido-heptofuranuronate^{19,20} (**2a**, **2b**) as diastereomeric mixture. Then, in the same reaction pot having glycosyl- β -aminoester **2** (1.0 equiv), imidazole-1-sulphonyl azide²² (1.2 equiv), K₂CO₃ (2.0 equiv), and ZnCl₂ in a catalytic amount (5 mol %) were added and stirring continued for additional 5 h to afford glycosyl- β -azido ester **3a** and **3b** with a major to minor ratio of 70:30. After completion of the reaction (monitored by TLC), the reaction mixture was concentrated in vacuo, diluted with H₂O, extracted with EtOAc, washed with brine solution, and dried over anhydrous Na₂SO₄. The organic layer was concentrated under reduced pressure. Further purification and separation using flash column chromatography using gradient mixtures of ethyl acetate and *n*-hexane afforded pure compound **3** with 86% yield.

Ethyl-[5-(S)-azido-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene]- β -L-ido-heptofuranuronate (3a**, major isomer).** To a stirred solution of glycosyl- β -olefinic ester **1** (5.0 g, 0.014 mol) dissolved in dry ethanol (50.0 mL) was passed NH₃ gas for 3 h, and the reaction was allowed to stir at room temperature for 24 h to afford ethyl-[5-amino-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene]- α -D-glucopyranosyl- and - β -L-ido-heptofuranuronate (**2a**, **2b**) as a diastereomeric mixture. Then, in the same reaction pot, glycosyl- β -aminoester **2**, imidazole-1-sulphonyl azide (2.67g, 0.015 mol), K₂CO₃ (3.56g, 0.025 mol), and ZnCl₂ in a catalytic amount (5 mol %) were added and stirring continued for an additional 5 h to afford glycosyl- β -azido ester **3** (86% yield) with a major to minor ratio of 70:30, which was separated by purification as described earlier to afford **3a** as white crystals; mp 82–84 °C; *R*_f = 0.52 (10% ethyl acetate/*n*-hexane); ¹H NMR (300 MHz, CDCl₃) δ 7.35 (m, 5H), 5.87 (d, *J* = 3.0 Hz, 1H), 4.69–4.62 (m, 3H), 4.28 (dd, *J* = 9.9, 19.2 Hz, 1H), 4.18 (q, *J* = 6.9 Hz, 2H), 4.06 (m, 1H), 3.99 (d, *J* = 9.6 Hz, 1H), 2.90 (d, *J* = 16.5 Hz, 1H), 2.46 (dd, *J* = 10.2, 16.8 Hz, 1H), 1.48 (s, 3H), 1.31 (s, 3H), 1.27 (t, *J* = 6.9 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 170.8, 136.9, 128.4 (2C), 128.0, 127.9 (2C), 111.9, 105.1, 81.8, 81.4, 80.8, 71.9, 60.7, 56.5, 37.4, 26.8, 26.1, 14.0; IR (KBr) ν_{max} 2980, 2933, 2134 (azide- N₃), 2096, 1742 (C=O), 1465, 1399, 1081, 1037, 731 cm⁻¹; MS (*m/z*) 392 [*M* + *H*]⁺; Anal. Calcd for C₁₉H₂₅N₃O₆ C 58.30, H 6.44, N 10.74; found C 58.45, H 6.48, N 10.78.

Ethyl-[5-(R)-azido-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene]- α -D-glucopyranuronate (3b**, minor isomer).** White crystalline solid; mp 78 °C, *R*_f = 0.56 (10% ethyl acetate/*n*-hexane); ¹H NMR (300 MHz, CDCl₃) δ 7.32–7.25 (m, 5H), 5.98 (d, *J* = 3.3 Hz, 1H), 4.72 (d, *J* = 11.7 Hz, 1H), 4.66 (d, *J* = 3.6 Hz, 1H), 4.41 (d, *J* = 11.7 Hz, 1H), 4.20–4.18 (m, 2H), 4.15–4.10 (m, 2H), 3.85 (m, 1H), 2.26–2.12 (m, 2H), 1.49 (s, 3H), 1.33 (s, 3H), 1.27 (t, *J* = 6.9 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 169.9, 136.5, 128.5 (2C), 128.3, 128.0 (2C), 112.0, 105.0, 81.9, 81.7, 81.0, 71.5, 60.9, 58.2, 35.8, 26.7, 26.2, 14.1; IR (KBr) ν_{max} 2990, 2912, 2129 (azide- N₃), 2091, 1736 (C=O), 1455, 1381, 1081, 742, 698 cm⁻¹; MS (*m/z*) 392 [*M* + *H*]⁺; Anal. Calcd for C₁₉H₂₅N₃O₆ C 58.30, H 6.44, N 10.74; found C 58.40, H 6.50, N 10.76.

Methyl-[5-(R)-azido-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene]- α -D-glucopyranuronate (4b**, minor).** To a stirred solution of glycosyl- β -olefinic ester **1** (0.8 g, 1.43 mmol) dissolved in dry methanol (8.0 mL) was passed NH₃ gas for 3 h, and the reaction was allowed to stir at room temperature for 24 h. Then, in the same reaction pot, glycosyl- β -aminoester, imidazole-1-sulphonyl azide (0.42 g, 0.46 mmol), K₂CO₃ (0.56, 4.10 mmol), and ZnCl₂ in a catalytic amount (5

mol %) were added to the reaction mixture and stirring continued for additional 5 h to afford **4b** as thin white crystals after purification as described above; *R*_f = 0.57 (10% ethyl acetate/*n*-hexane); ¹H NMR (300 MHz, CDCl₃) δ 7.25–7.24 (m, 5H), 5.91 (d, *J* = 3.6 Hz, 1H), 4.65 (d, *J* = 12 Hz, 1H), 4.59 (d, *J* = 3.6 Hz, 1H), 4.34 (d, *J* = 12 Hz, 1H), 4.16–4.09 (m, 1H), 4.06–4.02 (m, 1H), 3.77 (d, *J* = 3.0 Hz, 1H), 3.63 (s, 3H), 2.20–2.04 (m, 2H), 1.42 (s, 3H), 1.26 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 168.9, 136.5, 128.9 (2C), 128.6, 128.1 (2C), 111.3, 104.9, 81.9, 81.5, 80.9, 73.3, 65.5, 58.1, 35.5, 26.8, 26.3; IR (KBr) ν_{max} 2992, 2915, 2125 (azide- N₃), 2092, 1732 (C=O), 1453, 1386, 1084, 745, 696 cm⁻¹; MS (*m/z*) 378 [*M* + *H*]⁺; Anal. Calcd for C₁₈H₂₃N₃O₆ C 57.29, H 6.14, N 11.13; found C 57.35, H 6.20, N 11.15.

General Procedure for the Synthesis of Glycosyl- β -triazolyl Esters (6a–u**).** To a stirred solution of glycosyl- β -azido ester **3** (1.0 equiv) in dry CH₂Cl₂ (10 mL) was added alkynes **5a–u** (1.2 equiv) in the presence of DIPEA (10 mol %) and CuI (5 mol %), and the reaction mixture was allowed to stir at room temperature for 9–14 h under an argon atmosphere. After completion of the reaction (monitored by TLC), the reaction mixture was concentrated to obtain a crude residue that was further purified by flash column chromatography using gradient mixtures of ethyl acetate and *n*-hexane to afford pure compounds **6a–u** in good to excellent yields.

1-[Ethyl-(3'-*O*-benzyl-5',6'-dideoxy-1',2'-*O*-isopropylidene)- β -L-ido-heptofuranuronate-5-yl]-4-(1''-phenylmethan-1''-ol-1''-yl)-1H-[1,2,3]-triazole (6a**).** To a stirred solution of ethyl-[5-(S)-azido-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene]- β -L-ido-heptofuranuronate **3a** (400 mg, 1.021 mmol) in dry dichloromethane (10 mL) was added 1-phenyl-2-propyn-1-ol **5a** (0.149 mL, 1.226 mmol) in the presence of DIPEA (0.017 mL, 0.102 mmol) and CuI (5 mol %), and the reaction was allowed to stir at room temperature under an argon atmosphere for 9 h followed by purification described above to afford compound **6a** as a white crystalline solid; mp 128–130 °C; 502 mg, 94% yield; *R*_f = 0.45 (45% ethyl acetate/*n*-hexane); ¹H NMR (300 MHz, CDCl₃) δ 7.38–7.17 (m, 9H), 7.08 (m, 2H), 5.98–5.91 (m, 2H), 5.17–5.08 (m, 1H), 4.71 (d, *J* = 9.9 Hz, 1H), 4.54–4.51 (m, 1H), 4.40–4.31 (m, 1H), 4.02–3.84 (m, 3H), 3.46 (d, *J* = 9.9 Hz, 1H), 3.35 (s, 1H), 3.22–3.16 (m, 2H), 1.49 (s, 3H), 1.29 (s, 3H), 1.11 (t, *J* = 6.9 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 170.3, 150.1, 141.9, 136.5, 128.5 (4C), 128.0 127.9, 127.8, 127.6, 126.3, 126.1, 123.1, 112.2, 105.2, 81.7, 81.1, 80.5, 72.0, 68.9, 60.8, 55.6, 37.2, 26.8, 26.1, 13.9; IR (KBr) ν_{max} 3412, 2990, 3065, 1690 (C=O), 1610, 1563, 1478, 1420, 1282, 1108, 1072, 845, 786, 562; MS (*m/z*) 524 [*M* + *H*]⁺; Anal. Calcd for C₂₈H₃₃N₃O₇ C 64.23, H 6.35, N 8.03; found C 64.35, H 6.38, N 8.05.

A click reaction between glycosyl- β -azido ester **3a** and alkyne **5a** using CuSO₄·5H₂O/sodium ascorbate in aqueous medium at room temperature affords glycosyl- β -triazolyl ester **6a** in good yields. The physical data closely matched that of developed molecule **6a**, where the reaction was carried out in dry CH₂Cl₂ solvent under an inert atmosphere at room temperature.

1-[Ethyl-(3'-*O*-benzyl-5',6'-dideoxy-1',2'-*O*-isopropylidene)- α -D-glucopyranuronate-5-yl]-4-(phenyl-1''-yl)-1H-[1,2,3]-triazole (6b**).** To a stirred solution of ethyl-[5-(R)-azido-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene]- α -D-glucopyranuronate **3b** (400 mg, 1.021 mmol) in dry dichloromethane (10 mL) was added phenylacetylene **5b** (0.134 mL, 1.226 mmol) in the presence of DIPEA (0.017 mL, 0.102 mmol) and CuI (5 mol %), and the reaction was allowed to stir at room temperature under an argon atmosphere for 10 h followed by purification as described above to afford compound **6b** as a yellow solid; mp 124–126 °C; 454 mg, 90% yield; *R*_f = 0.41 (50% ethyl acetate/*n*-hexane); ¹H NMR (300 MHz, CDCl₃) δ 7.88 (s, 1H), 7.82–7.79 (m, 2H), 7.40–7.28 (m, 8H), 5.91 (d, *J* = 3.6 Hz, 1H), 5.20–5.13 (m, 1H), 4.76 (d, *J* = 12 Hz, 1H), 4.68 (d, *J* = 3.3 Hz, 1H), 4.63 (dd, *J* = 3, 9.3 Hz, 1H), 4.47 (d, *J* = 11.4 Hz, 1H), 4.02–4.01 (m, 2H), 3.57 (m, 1H), 3.29–3.20 (m, 1H), 2.45 (dd, *J* = 2.4, 16.5 Hz, 1H), 1.43 (s, 3H), 1.29 (s, 3H), 1.14 (t, *J* = 6.9 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 169.4, 146.6, 136.3, 130.8, 128.68 (2C), 128.61 (2C), 128.4 (2C), 128.2 (2C), 127.8, 125.6, 121.9, 112.2, 105.0, 81.6, 81.5, 80.6, 71.6, 60.9, 57.3, 34.8, 26.7, 26.2, 13.9; IR (KBr) ν_{max} 3414, 3077, 1695 (C=O), 1607, 1565, 1484, 1449, 1424, 1279, 1101, 1075, 850, 784, 574; MS (*m/*

z) 494 [M + H]⁺; Anal. Calcd for C₂₇H₃₁N₃O₆ C 65.71, H 6.33, N 8.51; found C 65.56, H 6.45, N 8.63.

1-[Ethyl-(3'-O-benzyl-5',6'-dideoxy-1',2'-O-isopropylidene)- α -D-glucopyranuronate-5'-yl]-4-(toluene-4"-yl)-1H-[1,2,3]-triazole (6c). To a stirred solution of ethyl-[5-(R)-azido-3-O-benzyl-5,6-dideoxy-1,2-O-isopropylidene]- α -D-glucopyranuronate **3b** (500 mg, 1.277 mmol) in dry dichloromethane (10 mL) was added 4-ethynyl toluene **5c** (0.194 mL, 1.532 mmol) in the presence of DIPEA (0.022 mL, 0.127 mmol) and CuI (5 mol %), and the reaction was allowed to stir at room temperature under an argon atmosphere for 10 h followed by purification as described above to afford title compound **6c** as a yellow liquid; 602 mg, 93% yield; *R*_f = 0.41 (50% ethyl acetate/*n*-hexane); ¹H NMR (300 MHz, CDCl₃) δ 7.83 (s, 1H), 7.70–7.68 (m, 2H), 7.34 (m, 5H), 7.20–7.17 (m, 2H), 5.91 (d, *J* = 3.6 Hz, 1H), 5.18–5.12 (m, 1H), 4.76 (d, *J* = 11.7 Hz, 1H), 4.68 (d, *J* = 3.6 Hz, 1H), 4.63 (dd, *J* = 3, 9.3 Hz, 1H), 4.47 (d, *J* = 11.7 Hz, 1H), 4.01 (d, *J* = 2.7 Hz, 2H), 3.56 (m, 1H), 3.24 (dd, *J* = 10.8, 16.8 Hz, 1H), 2.47 (d, *J* = 13.8 Hz, 1H), 2.35 (s, 3H), 1.43 (s, 3H), 1.29 (s, 3H), 1.14 (t, *J* = 6.9 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 169.4, 146.7, 137.5, 136.3, 129.3 (2C), 128.6 (2C), 128.4, 128.2 (2C), 127.9, 125.5 (2C), 121.5, 112.2, 104.8, 81.5, 80.7, 80.6, 71.6, 60.9, 57.2, 34.9, 26.7, 26.2, 21.2, 13.9; IR (KBr) ν_{max} 3409, 3065, 1706 (C=O), 1603, 1567, 1489, 1453, 1419, 1225, 1105, 855, 570; MS (*m/z*) 508 [M + H]⁺; Anal. Calcd for C₂₈H₃₃N₃O₆ C 66.26, H 6.55, N 8.28; found C 66.37, H 6.71, N 8.41.

1-[Ethyl-(3'-O-benzyl-5',6'-dideoxy-1',2'-O-isopropylidene)- β -L-ido-heptofuranuronate-5-yl]-4-(fluorobenzene-4"-yl)-1H-[1,2,3]-triazole (6d). To a stirred solution of ethyl-[5-(S)-azido-3-O-benzyl-5,6-dideoxy-1,2-O-isopropylidene]- β -L-ido-heptofuranuronate **3a** (500 mg, 1.277 mmol) in dry dichloromethane (10 mL) was added 1-ethynyl-4-fluorobenzene **5d** (0.175 mL, 1.532 mmol) in the presence of DIPEA (0.022 mL, 0.127 mmol) and CuI (5 mol %), and the reaction was allowed to stir at room temperature under an argon atmosphere for 14 h followed by purification as described above to afford desired compound **6d** as a yellow liquid; 575 mg, 88% yield; *R*_f = 0.43 (55% ethyl acetate/*n*-hexane); ¹H NMR (300 MHz, CDCl₃) δ 7.68–7.57 (m, 2H), 7.40–6.99 (m, 8H), 5.98 (d, *J* = 3 Hz, 1H), 5.23 (dd, *J* = 8.4, 14.1 Hz, 1H), 4.82 (d, *J* = 9.9 Hz, 1H), 4.62 (d, *J* = 3 Hz, 1H), 4.56 (d, *J* = 11.7 Hz, 1H), 4.06 (d, *J* = 11.1 Hz, 1H), 4.01 (d, *J* = 7.5 Hz, 2H), 3.64 (d, *J* = 2.7 Hz, 1H), 3.25 (d, *J* = 6 Hz, 2H), 1.52 (s, 3H), 1.32 (s, 3H), 1.14 (t, *J* = 6.9 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 170.5, 162.5 (d, *J* = 246 Hz), 145.5, 136.6, 134.1, 128.5 (2C), 128.1, 127.7 (2C), 127.3 (d, *J* = 8.9 Hz), 126.65, 126.61, 121.4, 115.5 (d, *J* = 21.6 Hz), 112.2, 105.3, 81.6, 81.2, 80.2, 72.1, 60.8, 55.7, 37.4, 26.8, 26.2, 13.9; IR (KBr) ν_{max} 3412, 3079, 1701 (C=O), 1604, 1562, 1479, 1452, 1276, 1085, 1106, 1079, 858, 786, 576; MS (*m/z*) 512 [M + H]⁺; Anal. Calcd for C₂₇H₃₀FN₃O₆ C 63.39, H 5.91, N 8.21; found C 63.55, H 5.99, N 8.17.

1-[Ethyl-(3'-O-benzyl-5',6'-dideoxy-1',2'-O-isopropylidene)- β -L-ido-heptofuranuronate-5-yl]-4-(pyridine-3"-yl)-1H-[1,2,3]-triazole (6e). To a stirred solution of ethyl-[5-(S)-azido-3-O-benzyl-5,6-dideoxy-1,2-O-isopropylidene]- β -L-ido-heptofuranuronate **3a** (500 mg, 1.277 mmol) in dry dichloromethane (10 mL) was added 3-ethynylpyridine **5e** (158 mg, 1.532 mmol) in the presence of DIPEA (0.022 mL, 0.127 mmol) and CuI (5 mol %), and the reaction was allowed to stir at room temperature under an argon atmosphere for 12 h followed by purification as described above to afford compound **6e** as a yellow solid; mp 120–124 °C; 568 mg, 90% yield; *R*_f = 0.45 (65% ethyl acetate/*n*-hexane); ¹H NMR (300 MHz, CDCl₃) δ 8.84 (m, 1H), 8.56 (d, *J* = 4.5 Hz, 1H), 8.08 (d, *J* = 7.8 Hz, 1H), 7.65 (m, 1H), 7.37–7.26 (m, 5H), 7.18 (d, *J* = 6.3 Hz, 1H), 5.99 (d, *J* = 3.3 Hz, 1H), 5.25 (dd, *J* = 9.6, 14.7 Hz, 1H), 4.82 (d, *J* = 9.9 Hz, 1H), 4.64 (d, *J* = 3 Hz, 1H), 4.59 (d, *J* = 11.4, 1H), 4.08–4.00 (m, 3H), 3.64 (m, 1H), 3.27 (d, *J* = 5.1 Hz, 2H), 1.52 (s, 3H), 1.32 (s, 3H), 1.14 (t, *J* = 6.9 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 170.4, 149.0, 146.9, 143.3, 136.4, 132.8, 128.6 (2C), 128.3, 127.7 (2C), 126.5, 123.6, 122.1, 112.3, 105.3, 81.7, 81.5, 80.2, 72.1, 60.9, 55.7, 37.3, 26.8, 26.2, 13.9; IR (KBr) ν_{max} 3440, 3064, 2926, 1736 (C=O), 1605, 1574, 1455, 1409, 1376, 1220, 1164, 803, 707; MS (*m/z*) 495 [M + H]⁺; Anal. Calcd for C₂₆H₃₀N₄O₆ C 63.15, H 6.11, N 11.33; found C 63.44, H 6.01, N 11.22.

1-[Ethyl-(3'-O-benzyl-5',6'-dideoxy-1',2'-O-isopropylidene)- α -D-glucopyranuronate-5'-yl]-4-(1"-phenyl-methan-1"-yl)-1H-[1,2,3]-triazole (6f). To a stirred solution of ethyl-[5-(R)-azido-3-O-

benzyl-5,6-dideoxy-1,2-O-isopropylidene]- α -D-glucopyranuronate **3b** (400 mg, 1.021 mmol) in dry dichloromethane (10 mL) was added 3-phenyl-1-propyne **5f** (0.152 mL, 1.226 mmol) in the presence of DIPEA (0.017 mL, 0.102 mmol) and CuI (5 mol %), and the reaction was allowed to stir at room temperature under an argon atmosphere for 10 h followed by purification as described above to afford compound **6f** as a white solid; mp 138–140 °C, 471 mg, 91% yield; *R*_f = 0.46 (45% ethyl acetate/*n*-hexane); ¹H NMR (300 MHz, CDCl₃) δ 7.33–7.22 (m, 11H), 5.87 (d, *J* = 3 Hz, 1H), 5.07–5.00 (m, 1H), 4.72 (d, *J* = 11.7 Hz, 1H), 4.65 (d, *J* = 3 Hz, 1H), 4.57 (d, *J* = 9.3 Hz, 1H), 4.43 (d, *J* = 11.7 Hz, 1H), 4.05–3.97 (m, 5H), 3.17 (dd, *J* = 10.8, 16.5 Hz, 1H), 2.41 (d, *J* = 15.9 Hz, 1H), 1.43 (s, 3H), 1.29 (s, 3H), 1.14 (t, *J* = 6.9 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 169.4, 146.3, 139.0, 136.3, 128.7 (2C), 128.6, 128.44 (2C), 128.40 (2C), 128.1 (2C), 126.2, 123.6, 112.1, 104.9, 81.6, 81.4, 80.6, 71.6, 60.8, 57.1, 35.0, 32.1, 26.6, 26.2, 13.8; IR (KBr) ν_{max} 3412, 3076, 1698 (C=O), 1603, 1561, 1482, 1451, 1423, 1276, 1105, 1075, 856, 784; MS (*m/z*) 508 [M + H]⁺; Anal. Calcd for C₂₈H₃₃N₃O₆ C 66.26, H 6.55, N 8.28; found C 66.53, H 6.49, N 8.23.

1-[Ethyl-(3'-O-benzyl-5',6'-dideoxy-1',2'-O-isopropylidene)- β -L-ido-heptofuranuronate-5-yl]-4-(cyclohexan-1"-ol-1"-yl)-1H-[1,2,3]-triazole (6g). To a stirred solution of ethyl-[5-(S)-azido-3-O-benzyl-5,6-dideoxy-1,2-O-isopropylidene]- β -L-ido-heptofuranuronate **3a** (300 mg, 0.766 mmol) in dry dichloromethane (10 mL) was added 1-ethynylcyclohexanol **5g** (114 mg, 0.919 mmol) in the presence of DIPEA (0.013 mL, 0.076 mmol) and CuI (5 mol %), and the reaction was allowed to stir at room temperature under an argon atmosphere for 10 h followed by purification as described above to afford compound **6g** as a yellow liquid; 375 mg, 95% yield; *R*_f = 0.52 (75% ethyl acetate/*n*-hexane); ¹H NMR (300 MHz, CDCl₃) δ 7.37–7.26 (m, 6H), 5.94 (m, 1H), 5.29–5.17 (m, 2H), 4.76 (d, *J* = 9.3 Hz, 1H), 4.57 (d, *J* = 3 Hz, 1H), 4.51 (d, *J* = 11.1 Hz, 1H), 4.09 (d, *J* = 11.7 Hz, 2H), 4.02 (dd, *J* = 6.9, 13.2 Hz, 1H), 3.56 (s, 1H), 3.22 (d, *J* = 6.9 Hz, 2H), 2.33 (m, 1H), 1.81 (m, 5H), 1.50 (m, 5H), 1.30 (s, 5H), 1.14 (t, *J* = 6.9 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 170.4, 154.2, 136.7, 128.6 (2C), 128.0, 127.4 (2C), 121.4, 112.2, 105.1, 81.8, 81.3, 80.5, 72.1, 60.8, 55.5, 38.1 (3C), 37.4, 26.7, 26.2, 25.3, 21.9 (2C), 13.9; IR (KBr) ν_{max} 3443, 2929, 2855, 1737 (C=O), 1607, 1498, 1454, 1376, 1221, 1164, 1075, 1026, 738; MS (*m/z*) 516 [M + H]⁺; Anal. Calcd for C₂₇H₃₇N₃O₇ C 62.90, H 7.23, N 8.15; found C 63.21, H 7.28, N 8.27.

1-[Ethyl-(3'-O-benzyl-5',6'-dideoxy-1',2'-O-isopropylidene)- α -D-glucopyranuronate-5'-yl]-4-(1"-4-methylpiperazin)-methan-1"-yl)-1H-[1,2,3]-triazole (6h). To a stirred solution of ethyl-[5-(R)-azido-3-O-benzyl-5,6-dideoxy-1,2-O-isopropylidene]- α -D-glucopyranuronate **3b** (500 mg, 1.277 mmol) in dry dichloromethane (9.0 mL) was added *N*-methyl,*N*-propargyl piperazine **5h** (0.194 mL, 1.532 mmol) in the presence of DIPEA (0.022 mL, 0.127 mmol) and CuI (5 mol %), and the reaction was allowed to stir at room temperature under an argon atmosphere for 16 h followed by purification as described above to afford compound **6h** as a yellow liquid; 588 mg, 87% yield; *R*_f = 0.41 (50% ethyl acetate/*n*-hexane); ¹H NMR (300 MHz, CDCl₃) δ 7.63 (s, 1H), 7.35 (m, 5H), 5.89 (s, 1H), 5.12–5.09 (m, 1H), 4.76 (d, *J* = 15 Hz, 1H), 4.69 (m, 1H), 4.56 (m, 1H), 4.45 (d, *J* = 11.7 Hz, 1H), 4.04 (d, *J* = 8.1 Hz, 2H), 4.00 (d, *J* = 6.6 Hz, 1H), 3.76–3.69 (m, 2H), 3.05–2.91 (m, 8H), 2.65 (s, 3H), 2.44–2.32 (m, 1H), 2.03 (d, *J* = 6.9 Hz, 1H), 1.41 (s, 3H), 1.25–1.14 (m, 6H); ¹³C NMR (75 MHz, CDCl₃) δ 169.3, 141.5, 136.3, 128.7 (2C), 128.5, 128.2 (2C), 125.4, 112.1, 104.9, 81.6, 81.5, 80.6, 71.6, 60.9, 57.1, 53.5 (2C), 52.2, 49.8 (2C), 43.8, 34.8, 26.7, 26.2, 14.0; MS (*m/z*) 530 [M + H]⁺; Anal. Calcd for C₂₇H₃₉N₅O₆ C 61.23, H 7.42, N 13.22; found C 61.30, H 7.38, N 13.21.

1-[Ethyl-(3'-O-benzyl-5',6'-dideoxy-1',2'-O-isopropylidene)- β -L-ido-heptofuranuronate-5-yl]-4-(cyclohexene-1"-yl)-1H-[1,2,3]-triazole (6i). To a stirred solution of ethyl-[5-(S)-azido-3-O-benzyl-5,6-dideoxy-1,2-O-isopropylidene]- β -L-ido-heptofuranuronate **3a** (300 mg, 0.766 mmol) in dry dichloromethane (10 mL) was added 1-ethynylcyclohexene **5i** (0.108 mL, 0.919 mmol) in the presence of DIPEA (0.013 mL, 0.076 mmol) and CuI (5 mol %), and the reaction was allowed to stir at room temperature under an argon atmosphere for 12 h followed by purification as described above to afford compound **6i** as a yellow liquid; 350 mg, 92% yield; *R*_f = 0.32 (45% ethyl acetate/*n*-

hexane); ^1H NMR (300 MHz, CDCl_3) δ 7.32–7.30 (m, 4H), 7.23–7.21 (m, 2H), 6.43 (s, 1H), 5.94 (s, 1H), 5.18 (dd, J = 8.4, 15.6 Hz, 1H), 4.77 (d, J = 6.9 Hz, 1H), 4.58 (m, 1H), 4.52 (d, J = 11.1 Hz, 1H), 4.11 (m, 1H), 4.06 (d, J = 9 Hz, 1H), 4.01 (d, J = 6 Hz, 1H), 3.59 (m, 1H), 3.21 (d, J = 6 Hz, 2H), 2.25–2.09 (m, 4H), 1.73 (m, 2H), 1.66 (d, J = 5.7 Hz, 2H), 1.50 (s, 3H), 1.30 (s, 3H), 1.15 (t, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 170.5, 148.1, 136.7, 128.5 (2C), 128.0, 127.6 (2C), 127.0, 124.8, 120.3, 112.2, 105.1, 81.7, 81.2, 80.3, 72.1, 60.7, 55.2, 37.4, 29.6, 26.7, 26.2, 25.2, 22.4, 22.1, 13.9; IR (KBr) ν_{max} 3449, 2926, 2855, 1736 (C=O), 1655, 1497, 1455, 1376, 1220, 1164, 1074, 1024, 854, 740; MS (m/z) 498 [$\text{M} + \text{H}$] $^+$; Anal. Calcd for $\text{C}_{27}\text{H}_{35}\text{N}_3\text{O}_6$ C 65.17, H 7.09, N 8.44; found C 64.99, H 7.23, N 8.57.

1-[Ethyl-(3'-O-benzyl-5',6'-dideoxy-1',2'-O-isopropylidene)- α -D-glucopyranurinate-5'-yl]-4-(1'',2'':3'',4''-di-O-isopropylidene-6''-O-methyl- α -D-galacto-pyranose-6''-yl)-1H-[1,2,3]-triazole (**6j**). To a stirred solution of ethyl-[5-(R)-azido-3-O-benzyl-5,6-dideoxy-1,2-O-isopropylidene]- α -D-glucopyranurinate **3b** (500 mg, 1.277 mmol) in dry dichloromethane (10 mL) was added 1,2:3,4-di-O-isopropylidene-6-O-propargyl- α -D-galacto-pyranose **5j** (456 mg, 1.532 mmol) in the presence of DIPEA (0.022 mL, 0.127 mmol) and CuI (5 mol %), and the reaction was allowed to stir at room temperature under an argon atmosphere for 9 h followed by purification described earlier to afford title compound **6j** as a yellow liquid; 819 mg, 93% yield; R_f = 0.50 (60% ethyl acetate/*n*-hexane); ^1H NMR (300 MHz, CDCl_3) δ 7.65 (s, 1H), 7.33 (m, 5H), 5.88 (s, 1H), 5.52 (s, 1H), 5.13–5.07 (m, 1H), 4.75 (d, J = 12.6 Hz, 2H), 4.67 (d, J = 7.5 Hz, 2H), 4.58 (d, J = 7.8 Hz, 2H), 4.45 (d, J = 12 Hz, 1H), 4.29–4.23 (m, 2H), 3.99 (m, 4H), 3.71–3.65 (m, 2H), 3.18 (dd, J = 10.8, 16.5 Hz, 1H), 2.43 (d, J = 16.8 Hz, 1H), 1.53 (s, 6H), 1.42 (s, 6H), 1.30 (s, 6H), 1.14 (t, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 169.2, 143.9, 136.3, 128.5 (2C), 128.3, 128.1 (2C), 124.5, 112.0, 109.0, 108.4, 104.9, 96.3, 81.5, 81.3, 80.6, 80.5, 71.5, 70.9, 70.5, 69.0, 66.5, 64.7, 60.8, 57.1, 34.9, 26.5, 26.1, 25.9, 25.8, 24.7, 24.3, 13.8; IR (KBr) ν_{max} 3450, 2930, 1732 (C=O), 1635, 1452, 1376, 1222, 1112, 1082, 856; MS (m/z) 690 [$\text{M} + \text{H}$] $^+$; Anal. Calcd for $\text{C}_{34}\text{H}_{47}\text{N}_3\text{O}_{12}$ C 59.20, H 6.87, N 6.09; found C 58.92, H 6.83, N 6.06.

1-[Ethyl-(3'-O-benzyl-5',6'-dideoxy-1',2'-O-isopropylidene)- α -D-glucopyranurinate-5'-yl]-4-(1'',2'':5'',6''-di-O-isopropylidene-3''-O-methyl- α -D-glucopyranose-3''-yl)-1H-[1,2,3]-triazole (**6k**). To a stirred solution of ethyl-[5-(R)-azido-3-O-benzyl-5,6-dideoxy-1,2-O-isopropylidene]- α -D-glucopyranurinate **3b** (500 mg, 1.277 mmol) in dry dichloromethane (10 mL) was added 1,2:5,6-di-O-isopropylidene-3-O-propargyl- α -D-glucopyranose **5k** (456 mg, 1.532 mmol) in the presence of DIPEA (0.022 mL, 0.127 mmol) and CuI (5 mol %), and the reaction was allowed to stir at room temperature under an argon atmosphere for 9 h followed by purification as described above to afford compound **6k** as a yellow liquid; 810 mg, 92% yield; R_f = 0.46 (60% ethyl acetate/*n*-hexane); ^1H NMR (300 MHz, CDCl_3) δ 7.71 (s, 1H), 7.34–7.27 (m, 5H), 5.89–5.86 (m, 2H), 5.08 (d, J = 9.6 Hz, 1H), 4.76–4.68 (m, 4H), 4.57–4.35 (m, 2H), 4.32 (dd, J = 6, 13.2 Hz, 1H), 4.13–3.99 (m, 7H), 3.57 (m, 1H), 3.21 (dd, J = 10.8, 16.5 Hz, 1H), 2.44 (d, J = 16.5 Hz, 1H), 1.48 (s, 3H), 1.42 (s, 6H), 1.36 (s, 3H), 1.29 (s, 6H), 1.15 (t, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 169.2, 143.7, 136.3, 128.6 (2C), 128.4, 128.1 (2C), 124.7, 112.1, 111.7, 108.9, 105.2, 104.8, 82.4, 81.9, 81.7, 81.4, 81.1, 80.6, 72.3, 71.6, 67.2, 64.2, 60.8, 57.1, 34.7, 26.6 (2C), 26.1 (2C), 25.3 (2C), 13.9; IR (KBr) ν_{max} 3453, 2926, 1739 (C=O), 1640, 1457, 1380, 1220, 1117, 1080, 853; MS (m/z) 690 [$\text{M} + \text{H}$] $^+$; Anal. Calcd for $\text{C}_{34}\text{H}_{47}\text{N}_3\text{O}_{12}$ C 59.20, H 6.87, N 6.09; found C 58.88, H 6.81, N 6.15.

1-[Ethyl-(3'-O-benzyl-5',6'-dideoxy-1',2'-O-isopropylidene)- α -D-glucopyranurinate-5'-yl]-4-(1'',2'':4'',5''-di-O-isopropylidene-3''-O-methyl- α -D-fructo-pyranose-1''-yl)-1H-[1,2,3]-triazole (**6l**). To a stirred solution of ethyl-[5-(R)-azido-3-O-benzyl-5,6-dideoxy-1,2-O-isopropylidene]- α -D-glucopyranurinate **3b** (500 mg, 1.277 mmol) in dry dichloromethane (10 mL) was added 1,2:4,5-di-O-isopropylidene-3-O-propargyl- α -D-fructo-pyranose **5l** (456 mg, 1.532 mmol) in the presence of DIPEA (0.022 mL, 0.127 mmol) and CuI (5 mol %), and the reaction was allowed to stir at room temperature under an argon atmosphere for 9 h followed by purification as described above to afford compound **6l** as a yellow liquid; 819 mg, 93% yield; R_f = 0.45 (65% ethyl acetate/*n*-hexane); ^1H NMR (300 MHz, CDCl_3) δ 7.63

(s, 1H), 7.34 (m, 5H), 5.87 (d, J = 3 Hz, 1H), 5.12–5.06 (m, 1H), 5.02 (d, J = 12.9 Hz, 1H), 4.81 (d, J = 12.9 Hz, 1H), 4.78 (d, J = 11.7 Hz, 1H), 4.66 (d, J = 3 Hz, 1H), 4.54 (d, J = 9.3 Hz, 1H), 4.45 (d, J = 12 Hz, 1H), 4.35 (dd, J = 6.3, 12.9 Hz, 1H), 4.20–4.02 (m, 4H), 3.98 (d, J = 6.3 Hz, 2H), 3.81 (d, J = 8.7 Hz, 1H), 3.56 (m, 2H), 3.19 (dd, J = 11.4, 16.8 Hz, 1H), 2.41 (d, J = 16.8 Hz, 1H), 1.57 (s, 3H), 1.47 (s, 3H), 1.42 (s, 3H), 1.37 (s, 3H), 1.29 (s, 6H), 1.15 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 169.2, 144.0, 136.2, 128.6 (2C), 128.4, 128.2 (2C), 124.5, 112.1, 111.9, 109.0, 104.7, 104.1, 81.6, 81.5, 80.5, 75.7, 73.7, 71.6, 71.5, 64.8, 60.8, 60.0, 57.0, 51.8, 34.7, 28.0, 26.8, 26.6, 26.1 (2C), 25.8, 13.9; IR (KBr) ν_{max} 3453, 2926, 1739 (C=O), 1640, 1457, 1380, 1220, 1117, 1080, 853; MS (m/z) 690 [$\text{M} + \text{H}$] $^+$; Anal. Calcd for $\text{C}_{34}\text{H}_{47}\text{N}_3\text{O}_{12}$ C 59.20, H 6.87, N 6.09; found C 59.36, H 6.89, N 6.11.

1-[Ethyl-(3'-O-benzyl-5',6'-dideoxy-1',2'-O-isopropylidene)- α -D-glucopyranurinate-5'-yl]-4-(5''-O-benzyl-1'',2''-O-isopropylidene-3''-O-methyl- α -D-xylo-furanose-3''-yl)-1H-[1,2,3]-triazole (**6m**). To a stirred solution of ethyl-[5-(R)-azido-3-O-benzyl-5,6-dideoxy-1,2-O-isopropylidene]- α -D-glucopyranurinate **3b** (500 mg, 1.277 mmol) in dry dichloromethane (10 mL) was added 5-O-benzyl-1,2-O-isopropylidene-3-O-propargyl- α -D-xylo-furanose **5m** (456 mg, 1.532 mmol) in the presence of DIPEA (0.022 mL, 0.127 mmol) and CuI (5 mol %), and the reaction was allowed to stir at room temperature under an argon atmosphere for 9 h followed by purification described earlier to afford compound **6m** as a yellow liquid; 853 mg, 94% yield; R_f = 0.50 (60% ethyl acetate/*n*-hexane); ^1H NMR (300 MHz, CDCl_3) δ 7.59 (s, 1H), 7.33–7.26 (m, 10H), 5.89 (s, 2H), 5.11–5.05 (m, 1H), 4.75 (d, J = 11.7 Hz, 1H), 4.69–4.54 (m, 8H), 4.49 (d, J = 10.2 Hz, 2H), 4.41 (d, J = 14.4 Hz, 1H), 4.00 (d, J = 7.5 Hz, 3H), 3.70 (d, J = 4.8 Hz, 2H), 3.18 (dd, J = 10.8, 16.8 Hz, 1H), 2.41 (d, J = 15.9 Hz, 1H), 1.47 (s, 3H), 1.41 (s, 3H), 1.29 (s, 6H), 1.13 (t, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 169.2, 143.5, 138.0, 136.2, 128.6 (2C), 128.4 (2C), 128.2 (2C), 128.1 (2C), 127.7, 127.5, 124.5, 112.1, 111.5, 105.0, 104.9, 82.3, 82.1, 81.5, 80.7, 80.6, 79.0, 73.3, 71.6, 67.5, 63.9, 60.8, 57.1, 34.7, 26.67, 26.62, 26.2, 26.1, 13.9; IR (KBr) ν_{max} 3451, 2927, 1740 (C=O), 1625, 1456, 1379, 1260, 1165, 1077, 1023, 851; MS (m/z) 711 [$\text{M} + \text{H}$] $^+$; Anal. Calcd for $\text{C}_{37}\text{H}_{48}\text{N}_3\text{O}_{11}$ C 62.52, H 6.81, N 5.91; found C 62.57, H 6.76, N 5.90.

1-[Ethyl-(3'-O-benzyl-5',6'-dideoxy-1',2'-O-isopropylidene)- α -D-glucopyranurinate-5'-yl]-4-(2'',3'':5'',6''-di-O-isopropylidene-1''-O-methyl- α -manno-furanose-1''-yl)-1H-[1,2,3]-triazole (**6n**). To a stirred solution of ethyl-[5-(R)-azido-3-O-benzyl-5,6-dideoxy-1,2-O-isopropylidene]- α -D-glucopyranurinate **3b** (500 mg, 1.277 mmol) in dry dichloromethane (9.0 mL) was added 2,3:5,6-di-O-isopropylidene-1-O-propargyl- α -manno-furanose **5n** (456 mg, 1.532 mmol) in the presence of DIPEA (0.022 mL, 0.127 mmol) and CuI (5 mol %), and the reaction was allowed to stir at room temperature under an argon atmosphere for 10 h followed by purification as described above to afford compound **6n** as a white solid; mp 142–144 °C; 810 mg, 92% yield; R_f = 0.48 (60% ethyl acetate/*n*-hexane); ^1H NMR (300 MHz, CDCl_3) δ 7.63 (s, 1H), 7.34–7.33 (m, 5H), 5.89 (d, J = 3.3 Hz, 1H), 5.09 (m, 2H), 4.76–4.53 (m, 7H), 4.46 (d, J = 15.3 Hz, 1H), 4.40 (d, J = 6 Hz, 1H), 4.14–3.99 (m, 6H), 3.19 (dd, J = 10.5 Hz, 16.5 Hz, 1H), 2.44 (d, J = 16.5 Hz, 1H), 1.45 (s, 6H), 1.43 (s, 3H), 1.38 (s, 3H), 1.38 (s, 3H), 1.30 (s, 3H), 1.15 (t, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 169.3, 142.9, 136.3, 128.6 (2C), 128.4, 128.1 (2C), 124.9, 112.5, 112.1, 109.1, 105.8, 105.0, 85.0, 81.6, 81.4, 80.7, 80.6, 79.5, 73.0, 71.6, 66.9, 60.9, 60.4, 57.1, 34.9, 26.7, 26.6, 26.2, 25.8, 25.1, 24.4, 13.9; IR (KBr) ν_{max} 3459, 2925, 1735 (C=O), 1622, 1459, 1365, 1259, 1163, 1068, 1025, 858; MS (m/z) 690 [$\text{M} + \text{H}$] $^+$; Anal. Calcd for $\text{C}_{34}\text{H}_{47}\text{N}_3\text{O}_{12}$ C 59.20, H 6.87, N 6.09; found C 59.15, H 6.80, N 6.07.

1-[Ethyl-(3'-O-benzyl-5',6'-dideoxy-1',2'-O-isopropylidene)- α -D-glucopyranurinate-5'-yl]-4-(octan-1''-ol-8''-yl)-1H-[1,2,3]-triazole (**6o**). To a stirred solution of ethyl-[5-(R)-azido-3-O-benzyl-5,6-dideoxy-1,2-O-isopropylidene]- α -D-glucopyranurinate **3b** (500 mg, 1.277 mmol) in dry dichloromethane (9.0 mL) was added dec-9-yn-1-ol **5o** (0.271 mL, 1.532 mmol) in the presence of DIPEA (0.022 mL, 0.127 mmol) and CuI (5 mol %), and the reaction was allowed to stir at room temperature under an argon atmosphere for 12 h followed by purification as described above to afford compound **6o** as a yellow liquid; 648 mg, 93% yield; R_f = 0.48 (45% ethyl acetate/*n*-hexane); ^1H NMR (300 MHz, CDCl_3) δ 7.36–7.33 (m, 5H), 5.90–5.87 (m, 1H),

5.07–5.04 (m, 1H), 4.80 (d, $J = 12$ Hz, 1H), 4.77 (dd, $J = 12, 26.7$ Hz, 1H), 4.66 (d, $J = 3.9$ Hz, 1H), 4.58 (dd, $J = 3, 9.3$ Hz, 1H), 4.51–4.42 (m, 1H), 4.05–3.96 (m, 3H), 3.65–3.54 (m, 3H), 3.29–3.15 (m, 1H), 2.69–2.60 (m, 2H), 2.42 (dd, $J = 2.4, 16.5$ Hz, 1H), 1.57–1.55 (m, 6H), 1.42 (d, $J = 5.4$ Hz, 2H), 1.32–1.10 (m, 13H); ^{13}C NMR (75 MHz, CDCl_3) δ 169.5, 147.1, 136.3, 128.6 (2C), 128.4, 128.1 (2C), 122.7, 112.1, 104.9, 81.6, 81.4, 80.7, 71.6, 71.5, 62.8, 60.8, 56.8, 34.9, 32.6, 29.6, 29.1 (2C), 26.6, 26.1, 26.0, 25.7, 13.8; IR (KBr) ν_{max} 3310, 2928, 2856, 1738 (C=O), 1457, 1378, 1223, 1164, 1075, 1028, 888, 856; MS (m/z) 546 [$\text{M} + \text{H}$] $^+$; Anal. Calcd for $\text{C}_{29}\text{H}_{43}\text{N}_3\text{O}_7$ C 63.83, H 7.94, N 7.70; found C 63.90, H 7.82, N 7.65.

1-[Ethyl-(3'-O-benzyl-5',6'-dideoxy-1',2'-O-isopropylidene)- α -D-glucio-heptofuranurnate-5'-yl]-4-(hexan-1"-yl)-1H-[1,2,3]-triazole (6p). To a stirred solution of ethyl-[5-(R)-azido-3-O-benzyl-5,6-dideoxy-1,2-O-isopropylidene]- α -D-glucio-heptofuranurnate **3b** (400 mg, 1.021 mmol) in dry dichloromethane (10 mL) was added 1-octyne **5p** (0.180 mL, 1.226 mmol) in the presence of DIPEA (0.017 mL, 0.102 mmol) and CuI (5 mol %), and the reaction was allowed to stir at room temperature under an argon atmosphere for 10 h followed by purification as described above to afford compound **6p** as a yellow semisolid; 481 mg, 94% yield; $R_f = 0.48$ (50% ethyl acetate/*n*-hexane); ^1H NMR (300 MHz, CDCl_3) δ 7.26–7.19 (m, 6H), 5.82 (d, $J = 3.3$ Hz, 1H), 4.98 (d, $J = 9.3$ Hz, 1H), 4.67 (d, $J = 11.7$ Hz, 1H), 4.59 (d, $J = 3.3$ Hz, 1H), 4.51 (d, $J = 6.3$ Hz, 1H), 4.38 (d, $J = 11.7$ Hz, 1H), 3.93 (d, $J = 10.5$ Hz, 2H), 3.48 (m, 1H), 3.11 (dd, $J = 10.5, 16.5$ Hz, 1H), 2.61–2.56 (m, 2H), 2.36 (d, $J = 14.7$ Hz, 1H), 1.57 (m, 2H), 1.35 (m, 2H), 1.22–1.85 (m, 10H), 1.06 (t, $J = 6.9$ Hz, 3H), 0.80 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 169.5, 136.3, 128.6 (2C), 128.3, 128.1 (2C), 122.7, 112.1, 104.9, 81.6, 81.4, 80.6, 71.6, 60.8, 56.9, 34.9, 31.4, 29.0, 28.8, 26.6, 26.2, 25.6 (2C), 22.4, 13.9 (2C); IR (KBr) ν_{max} 3426, 2925, 2856, 1732 (C=O), 1451, 1372, 1225, 1161, 1074, 1031, 879, 852, 702; MS (m/z) 502 [$\text{M} + \text{H}$] $^+$; Anal. Calcd for $\text{C}_{27}\text{H}_{39}\text{N}_3\text{O}_6$ C 64.65, H 7.84, N 8.38; found C 64.70, H 7.80, N 8.39.

1-[Ethyl-(3'-O-benzyl-5',6'-dideoxy-1',2'-O-isopropylidene)- α -D-glucio-heptofuranurnate-5'-yl]-4-(3"-cyanopropan-1"-yl)-1H-[1,2,3]-triazole (6q). To a stirred solution of ethyl-[5-(R)-azido-3-O-benzyl-5,6-dideoxy-1,2-O-isopropylidene]- α -D-glucio-heptofuranurnate **3b** (500 mg, 1.277 mmol) in dry dichloromethane (10 mL) was added 5-cyanopentyn-1-ol **5q** (0.160 mL, 1.532 mmol) in the presence of DIPEA (0.022 mL, 0.127 mmol) and CuI (5 mol %), and the reaction was allowed to stir at room temperature under an argon atmosphere for 12 h followed by purification as described above to afford compound **6q** as a yellow liquid; 575 mg, 93% yield; $R_f = 0.51$ (55% ethyl acetate/*n*-hexane); ^1H NMR (300 MHz, CDCl_3) δ 7.44 (s, 1H), 7.34–7.33 (m, 5H), 5.89 (d, $J = 3.9$ Hz, 1H), 5.06 (d, $J = 9.6$ Hz, 1H), 4.75 (d, $J = 11.7$ Hz, 1H), 4.67 (d, $J = 3.6$ Hz, 1H), 4.56 (dd, $J = 3.0, 9.6$ Hz, 1H), 4.47–4.43 (m, 1H), 4.03–3.99 (m, 3H), 3.21–3.12 (m, 1H), 2.85–2.80 (m, 2H), 2.45–2.40 (m, 2H), 2.37 (d, $J = 6.9$ Hz, 1H), 2.05 (t, $J = 6.9$ Hz, 2H), 1.43 (s, 3H), 1.30 (s, 3H), 1.15 (t, $J = 6.9$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 169.4, 144.3, 136.3, 128.6 (2C), 128.4, 128.2 (2C), 123.4, 119.3, 112.1, 104.9, 81.6, 81.4, 80.6, 71.6, 60.8, 57.1, 34.8, 29.6, 26.6, 26.1, 24.1, 16.4, 13.9; IR (KBr) ν_{max} 3429, 2927, 2855, 2246 (C \equiv N), 1737 (C=O), 1455, 1379, 1217, 1165, 1075, 1028, 856, 701; MS (m/z) 485 [$\text{M} + \text{H}$] $^+$; Anal. Calcd for $\text{C}_{25}\text{H}_{32}\text{N}_4\text{O}_6$ C 61.97, H 6.66, N 11.56; found C 62.05, H 6.65, N 11.60.

1-[Ethyl-(3'-O-benzyl-5',6'-dideoxy-1',2'-O-isopropylidene)- α -D-glucio-heptofuranurnate-5'-yl]-4-(propan-1"-yl)-1H-[1,2,3]-triazole (6r). To a stirred solution of ethyl-[5-(R)-azido-3-O-benzyl-5,6-dideoxy-1,2-O-isopropylidene]- α -D-glucio-heptofuranurnate **3b** (700 mg, 1.788 mmol) in dry dichloromethane (10.0 mL) was added 1-pentyn-1-ol **5r** (0.228 mL, 2.146 mmol) in the presence of DIPEA (0.031 mL, 0.178 mmol) and CuI (5 mol %), and the reaction was allowed to stir at room temperature under an argon atmosphere for 12 h followed by purification as described above to afford compound **6r** as a white solid; mp 158–160 $^{\circ}\text{C}$; 755 mg, 92% yield; $R_f = 0.48$ (60% ethyl acetate/*n*-hexane); ^1H NMR (300 MHz, CDCl_3) δ 7.55 (s, 1H), 7.34–7.33 (m, 5H), 5.88 (m, 1H), 5.13–5.06 (m, 1H), 4.75 (d, $J = 11.4$ Hz, 2H), 4.67 (d, $J = 3.3$ Hz, 1H), 4.57 (d, $J = 9.3$ Hz, 1H), 4.45 (d, $J = 12$ Hz, 1H), 4.01 (d, $J = 11.1$ Hz, 3H), 3.17 (dd, $J = 10.8, 16.5$ Hz, 1H), 2.44 (d, $J = 16.2$ Hz, 2H), 1.87–1.81 (m, 2H), 1.43 (s, 3H), 1.29 (s, 3H), 1.14 (t, $J = 6.9$

Hz, 3H), 0.096 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 169.3, 149.9, 136.3, 128.6 (2C), 128.4, 128.2 (2C), 122.5, 112.1, 105.0, 81.6, 80.7, 80.6, 71.6, 68.3, 60.9, 57.1, 35.0, 30.1, 26.6, 26.2, 13.9, 9.7; IR (KBr) ν_{max} 3426, 2925, 2853, 1733 (C=O), 1453, 1377, 1216, 1162, 1071, 1025, 851, 702; MS (m/z) 460 [$\text{M} + \text{H}$] $^+$; Anal. Calcd for $\text{C}_{24}\text{H}_{33}\text{N}_3\text{O}_6$ C 62.73, H 7.24, N 9.14; found C 62.79, H 7.21, N 9.10.

1-[Ethyl-(3'-O-benzyl-5',6'-dideoxy-1',2'-O-isopropylidene)- α -D-glucio-heptofuranurnate-5'-yl]-4-(meth-1"-ol-1"-yl)-1H-[1,2,3]-triazole (6s). To a stirred solution of ethyl-[5-(R)-azido-3-O-benzyl-5,6-dideoxy-1,2-O-isopropylidene]- α -D-glucio-heptofuranurnate **3b** (300 mg, 0.766 mmol) in dry dichloromethane (10 mL) was added propargyl alcohol **5s** (0.057 mL, 0.996 mmol) in the presence of DIPEA (0.013 mL, 0.076 mmol) and CuI (5 mol %), and the reaction was allowed to stir at room temperature under an argon atmosphere for 10 h followed by purification as described above to afford compound **6s** as a white solid; mp 150–152 $^{\circ}\text{C}$; 322 mg, 94% yield; $R_f = 0.51$ (80% ethyl acetate/*n*-hexane); ^1H NMR (300 MHz, CDCl_3) δ 7.59 (s, 1H), 7.35–7.26 (m, 5H), 5.88 (d, $J = 3.6$ Hz, 1H), 5.14–5.02 (m, 1H), 4.77–4.67 (m, 4H), 4.56 (dd, $J = 3, 9.6$ Hz, 1H), 4.45 (d, $J = 11.7$ Hz, 1H), 4.03–3.98 (m, 3H), 3.18 (dd, $J = 10.8, 16.5$ Hz, 1H), 2.56 (s, 1H), 2.42 (d, $J = 16.8$ Hz, 1H), 1.42 (s, 3H), 1.29 (s, 3H), 1.15 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 169.3, 146.5, 136.3, 128.6 (2C), 128.4, 128.2 (2C), 123.7, 112.2, 104.8, 81.6, 81.4, 80.6, 71.6, 60.9, 57.2, 56.6, 34.8, 26.7, 26.2, 13.9; IR (KBr) ν_{max} 3312, 2926, 2859, 1737 (C=O), 1455, 1376, 1225, 1162, 1074, 1025, 883, 854; MS (m/z) 448 [$\text{M} + \text{H}$] $^+$; Anal. Calcd for $\text{C}_{22}\text{H}_{29}\text{N}_3\text{O}_7$ C 59.05, H 6.53, N 9.39; found C 59.10, H 6.56, N 9.43.

1-[Ethyl-(3'-O-benzyl-5',6'-dideoxy-1',2'-O-isopropylidene)- α -D-glucio-heptofuranurnate-5'-yl]-4-(butan-1"-yl)-1H-[1,2,3]-triazole (6t). To a stirred solution of ethyl-[5-(R)-azido-3-O-benzyl-5,6-dideoxy-1,2-O-isopropylidene]- α -D-glucio-heptofuranurnate **3b** (500 mg, 1.277 mmol) in dry dichloromethane (9.0 mL) was added 1-hexyne **5t** (0.174 mL, 1.532 mmol) in the presence of DIPEA (0.022 mL, 0.127 mmol) and CuI (5 mol %), and the reaction was allowed to stir at room temperature under an argon atmosphere for 12 h followed by purification as described above to afford compound **6t** as a yellow liquid; 544 mg, 90% yield; $R_f = 0.43$ (55% ethyl acetate/*n*-hexane); ^1H NMR (300 MHz, CDCl_3) δ 8.14 (s, 1H), 7.35–7.33 (m, 5H), 5.88 (d, $J = 3.6$ Hz, 1H), 5.16–5.10 (m, 1H), 4.76 (d, $J = 12$ Hz, 1H), 4.68 (d, $J = 3.3$ Hz, 1H), 4.57–4.54 (m, 1H), 4.44 (d, $J = 11.7$ Hz, 1H), 4.04–3.99 (m, 3H), 3.17 (dd, $J = 11.1, 16.5$ Hz, 1H), 3.08–3.03 (m, 1H), 2.66 (d, $J = 7.2$ Hz, 1H), 2.41 (d, $J = 16.8$ Hz, 1H), 1.79–1.72 (m, 2H), 1.42 (s, 3H), 1.25 (s, 6H), 1.15 (t, $J = 6.9$ Hz, 3H), 1.01–0.96 (m, 2H); ^{13}C NMR (75 MHz, CDCl_3) δ 169.0, 147.0, 136.2, 128.7 (2C), 128.5, 128.3 (2C), 127.6, 112.2, 105.0, 81.5, 80.4, 80.2, 71.6, 61.0, 57.7, 41.3, 34.6, 29.6, 26.6, 26.2, 25.3, 17.2, 13.9; IR (KBr) ν_{max} 3424, 2921, 2857, 1737 (C=O), 1454, 1376, 1215, 1161, 1072, 1023, 886, 856, 701; MS (m/z) 474 [$\text{M} + \text{H}$] $^+$; Anal. Calcd for $\text{C}_{25}\text{H}_{35}\text{N}_3\text{O}_6$ C 63.41, H 7.45, N 8.87; found C 63.52, H 7.48, N 8.89.

1-[Ethyl-(3'-O-benzyl-5',6'-dideoxy-1',2'-O-isopropylidene)- β -L-ido-heptofuranurnate-5'-yl]-4-(ethisterone-1"-yl)-1H-[1,2,3]-triazole (6u). To a stirred solution of ethyl-[5-(S)-azido-3-O-benzyl-5,6-dideoxy-1,2-O-isopropylidene]- β -L-ido-heptofuranurnate **3a** (500 mg, 1.277 mmol) in dry dichloromethane (10 mL) was added ethisterone **5u** (478 mg, 1.532 mmol) in the presence of DIPEA (0.022 mL, 0.127 mmol) and CuI (5 mol %), and the reaction was allowed to stir at room temperature under an argon atmosphere for 12 h followed by purification as described above to afford compound **6u** as a yellow liquid; 782 mg, 87% yield; $R_f = 0.45$ (50% ethyl acetate/*n*-hexane); ^1H NMR (300 MHz, CDCl_3) δ 7.45 (s, 1H), 7.34–7.33 (m, 5H), 5.87 (d, $J = 3.3$ Hz, 1H), 5.69 (m, 1H), 5.11–5.05 (m, 1H), 4.74 (d, $J = 11.5$ Hz, 1H), 4.66 (d, $J = 3.6$ Hz, 1H), 4.55 (d, $J = 9.3$ Hz, 1H), 4.44 (d, $J = 11.7$ Hz, 1H), 4.01–3.94 (m, 3H), 3.13 (dd, $J = 10.5, 16.5$ Hz, 1H), 3.05 (m, 1H), 2.45–1.77 (m, 11H), 1.62–1.47 (m, 7H), 1.41 (s, 3H), 1.27 (s, 3H), 1.12 (s, 3H), 1.07 (m, 3H), 1.03 (s, 3H), 0.68 (m, 1H), 0.37 (m, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 199.5, 171.4, 169.2, 152.0, 136.3, 128.6 (2C), 128.4, 128.2 (2C), 123.7, 123.1, 112.2, 104.7, 81.7, 81.5, 80.6, 80.5, 71.7, 60.8, 57.2, 53.3, 48.9, 46.8, 38.5, 37.3, 36.1, 35.5, 35.0, 33.8, 32.8, 32.4, 31.6, 26.7, 26.2, 23.4, 20.6, 17.3, 14.17, 14.10; MS (m/z) 704 [$\text{M} + \text{H}$] $^+$; Anal. Calcd for $\text{C}_{40}\text{H}_{53}\text{N}_3\text{O}_8$ C 68.26, H 7.59, N 5.97; found C 68.20, H 7.55, N 5.95.

■ ASSOCIATED CONTENT

■ Supporting Information

Copies of ^1H and ^{13}C NMR spectra for all the new compounds and X-ray crystallographic data for **3a**, **3b**, **4b**, and **6a** (CIF) are given. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00179.

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Notes

The authors declare no competing financial interest.

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