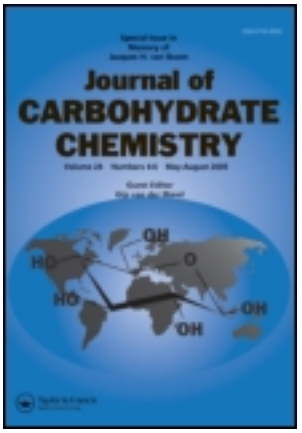

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Benzotriazole-Mediated Facile Synthesis of Novel Glycosyl Tetrazole

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A facile, simple, and high-yielding synthetic protocol for novel glycosyl tetrazoles has been devised from different carbohydrate-containing amides using benzotriazole methodology under mild reaction condition.

Keywords Carboxamide; Imidoylbenzotrizole; Tetrazole; Cyclization

INTRODUCTION

Carbohydrate-containing molecules are known for their great medicinal value.[1] Heterocycles coupled with the pendant sugar moiety through a C—C bond show a high chemotherapeutic potential,[2] represent a broad spectrum of biological activities such as antitumor and antiviral activities, and have been studied as building blocks in artificial DNA and RNA for various biochemical applications.[3] They have also been used as promising activating catalysts for phosphoramidites to facilitate the formation of *N*-acylphosphoramidate linkages through rapid condensation with carboxamides.[4] Carbohydrate coupled with tetrazole heterocycle may occupy a pivotal position in medicinal chemistry since several tetrazoles are known for their wide range of pharmacological activities (Fig. 1). The tetrazolyl group consists of nonclassical isosteres of carboxylic acid and thus has been a suitable substitution in drug design in recent years.[5] Tetrazole may serve as a substrate for N-glucuronidation of xenobiotics, which is an important pathway for the biological clearance of drugs.[6]

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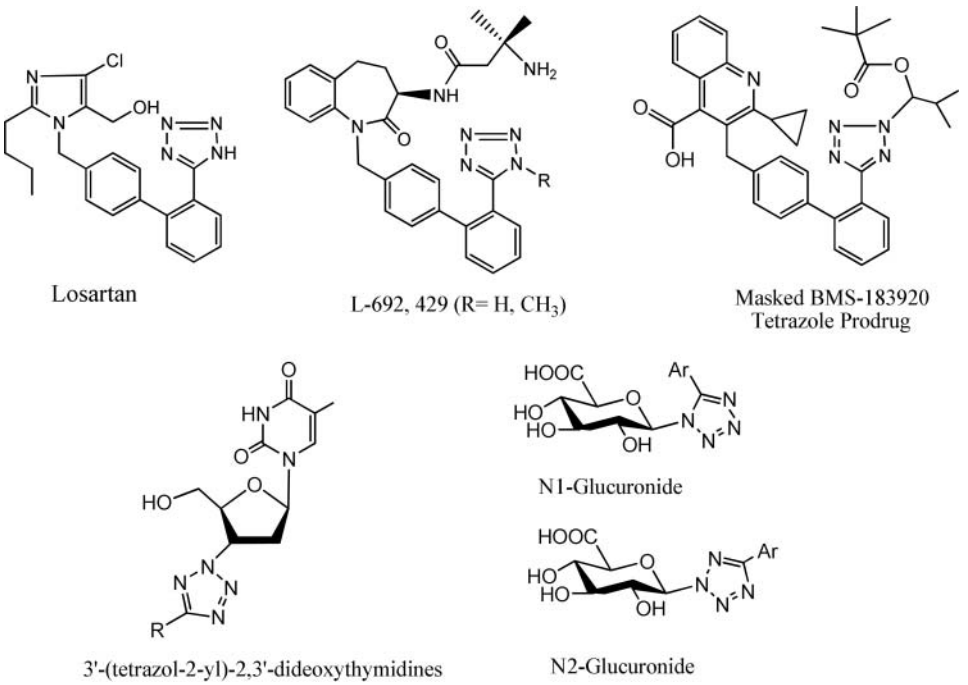


Figure 1: Tetrazole-containing biologically active molecules.

Nohara et al. identified tetrazole N1 β-glucuronide in the urine stream of several animals orally dosed with a chromone-derived tetrazole.[7] The majority of tetrazolic acid–based drugs are of the biphenyl tetrazole motif, which are basically analogs of DuPont's nonpeptidic selective angiotensin II receptor antagonist Losartan, a drug to treat hypertension.[8] A tetrazole-based nonpeptidyl growth hormone secretagogue L-692,429, developed by Merck & Company, provides an increased in vitro potency with an excellent oral absorption.[9] Physicochemical properties including the bioavailability of the angiotensin II receptor antagonist BMS-183920 may be improved even better than threefold (from 11% to 37%) by *N*-"bioreversible" protection of the tetrazole with a pivaloylisobutyl moiety.[10] Carbohydrate-containing tetrazole derivatives, for example, 3′-(5-substituted-tetrazol-2-yl)-2,3′-dideoxythymidines, have been used in drug development against viral infection.[11]

The common synthetic approaches for substituted triazole are based on Huisgen's 1,3-dipolar cycloaddition of azides with alkynes.[12a] These strategies were further extended to achieve the regioselective synthesis of various substituted triazoles under the catalysis of Cu(I) or Ru-complex.[12b,c] Although the synthesis of triazole skeleton has been well investigated in recent years, surprisingly less attention has been paid to the synthesis of the tetrazole ring. The synthesis of 5-substituted 1*H*-tetrazoles is known

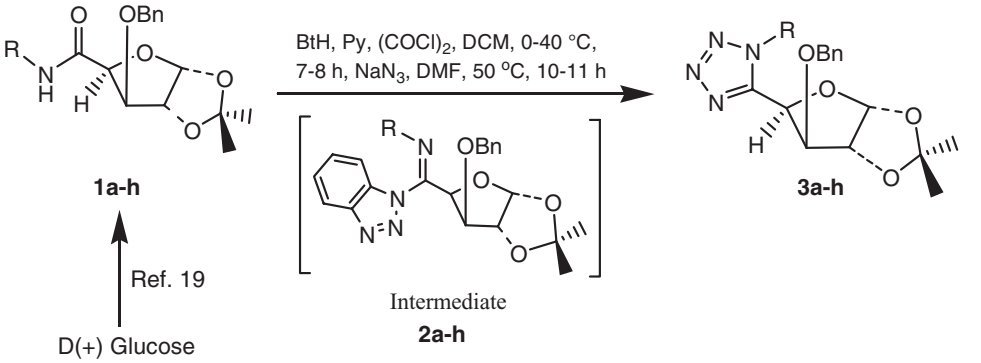
by I_2 or silica-supported $NaHSO_4$-catalyzed reaction of organic nitriles with azide[13a] or treatment of nitrile with triethylammonium chloride in nitrobenzene under microwave (MW) irradiation.[13b] $Yb(OTf)_3$-catalyzed multicomponent reaction of amines, NaN_3, and triethyl orthoformate gave good yields of 1-substituted 1*H*-tetrazole.[13c] Shie et al. successfully applied [2 + 3] cycloaddition reaction of nitriles, obtained in situ from primary alcohols or aldehydes, with dicyandiamide and NaN_3 to get a similar tetrazole skeleton.[14a] Katritzky et al. achieved 1,5-disubstituted tetrazoles on treatment of imidoylbenzotriazoles with NaN_3, where the protocol required 1 eq. TFA and 0.2 eq. TBAB in a (1:1) mixture of H_2O/CH_2Cl_2.[14b] Interestingly, imidoyl azides, obtained by the reaction of cyanogen azide with primary amines on intramolecular cyclization, also affords 1-substituted aminotetrazoles.[14c] Haira et al. reported $Zn(OTf)_2$-catalyzed one-pot reaction of nitriles, alkenes, NBS, and $TMSN_3$ to provide 1,5-disubstituted tetrazoles containing an additional α-bromo functionality of the *N*1-alkyl substituent.[15a] Treatment of isocyanide dibromides with NaN_3 followed by electrocyclization and a Suzuki coupling affords a good yield of tetrazoles.[15b] Synthesis of fused tetrazoles is also well documented in the literature. Representative examples include the synthesis of tetrazolo[1,5-α]pyridines starting from pyridine *N*-oxides on reaction with diphenyl phosphorazidate and pyridine (2 eq.) under solvent-free condition.[16] TBAF-catalyzed reaction of 2-halopyridines with $TMSN_3$ also gave similar fused heterocycles.[17]

Despite the huge potential of carbohydrate-containing tetrazole skeletons to offer promising chemotherapeutic potential, their syntheses through simple protocols is still challenging. The known methods have limitations, including requirement of an acidic catalyst that may cause removal of the isopropylidene protection of carbohydrate, involvement of two or more steps, average reaction yield, and, moreover, the limited availability of starting material. Based on a literature search, there is not a single report available to deal with the synthesis of carbohydrate-containing tetrazole using benzotriazole chemistry. Herein, we present a simple and facile protocol for the synthesis of a novel glycosyl tetrazole using benzotriazole methodology.

RESULTS AND DISCUSSION

Synthesis of glycosylated tetrazole surfaced due to our consistent interest in a long-standing research program on devising new synthetic strategies for pharmacologically important carbohydrate and heterocyclic scaffolds by employing benzotriazole methodology.[18] During the course of these studies we set out to explore the feasibility of utilizing recently developed glycosyl carboxamides[19] with sugar in furanose and pyranose form as precursors to access a broad range of diverse carbohydrate-containing tetrazoles. A close look at the structure of carboxamide inspired us to envisage two different strategies to furnish the

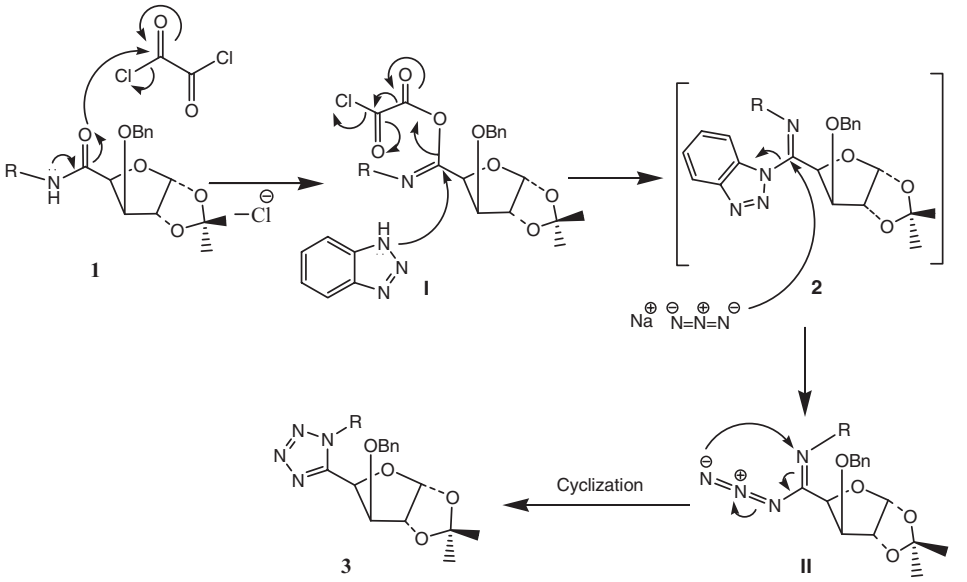
glycosylated tetrazole via an imidoylbenzotriazole intermediate. The strategy first encompasses the treatment of BtTMS complex with $SOCl_2$ at 0°C to afford the sulfenyl dibenzotriazole, which on further treatment with carboxamide yields imidoylbenzotriazole. This route was found to be very cumbersome and led to poor yield of the desired product. Then eventually we employed a second strategy to synthesize imidoylbenzotriazole, where carboxamide (**1**) was treated with oxalyl chloride, pyridine, and benzotriazole in anhydrous CH_2Cl_2 and the formed imidoylbenzotriazole (**2**) was directly used in next step as depicted in Scheme 1. In the above dried mass, anhydrous DMF and sodium azide were added and the reaction was continued for 10 to 11 h. The product was isolated by column chromatography (SiO_2) and characterized by ^1H and ^{13}C NMR, IR, and elemental analysis.



Scheme 1: Benzotriazole-mediated synthesis of glycosyl 1*H*-tetrazole *C*-nucleosides.

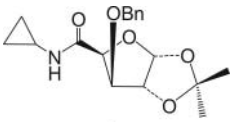
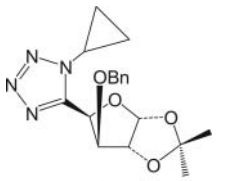
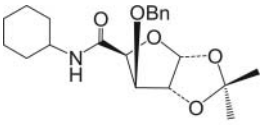
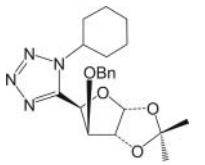
Next, we studied the individual effect of catalysts such as TFA (one to two drops) and TBAB, where no significant effect was noticed on the yield of the reaction. The 1,2-isopropylidene protection in the glycosyl imidoylbenzotrizole was found to be stable during the course of the reaction even in the presence of one to two drops of TFA. In order to find a suitable solvent, we investigated the effect of various solvents upon yield as well as reaction duration and observed that CH_2Cl_2, benzene, and $CHCl_3$ took more time to afford the desired glycosyl tetrazole, whereas DMF furnished the desired compound in good yield and proved to be the most suited solvent for this synthesis. Cyclization of imidoylbenzotrizole leading to the tetrazole ring is mechanistically driven by aromatization force. With optimum condition in hand, we treated cyclopropyl, cyclohexyl, *n*-hexadecyl, *n*-octyl, phenylethyl, 4-phenylthiazole, thiadiazole, and oxadiazole-containing glycosyl imidoylbenzotriazoles with NaN_3 in DMF to afford the desired glycosyl tetrazoles (**3a–h**) in good yields (Table 1).

The proposed reaction mechanism is presented in Scheme 2. At the outset of the reaction, the delocalization of a lone pair of electrons of nitrogen of carboxamide **1** initiates the attack on carbonyl carbon of oxalyl chloride to



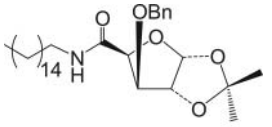
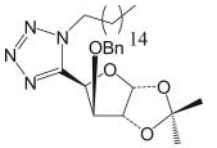
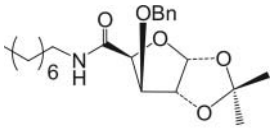
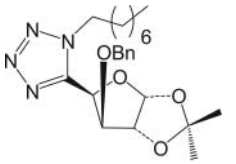
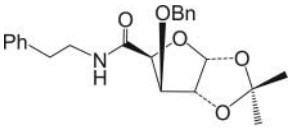
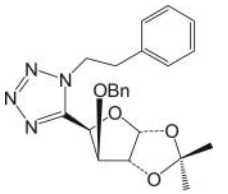
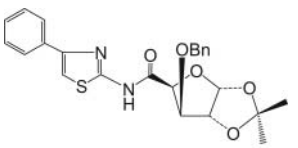
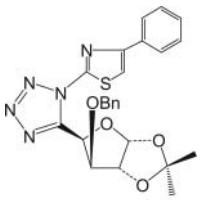
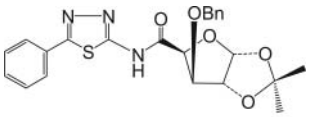
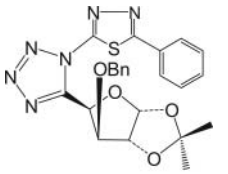
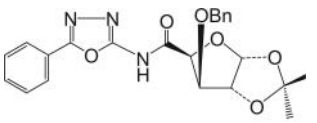
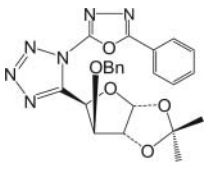
Scheme 2: Proposed reaction mechanism for the formation of glycosyl tetrazole **3.**

Table 1: Synthesis of glycosyl tetrazole **(3a–h)**

Entry	Glycosyl amide (**1a–h**)	Product (**3a–h**)	Reaction condition	Yield (%)[a]
1	 1a	 3a	Toluene, 15 h	55
2	**1a**	**3a**	C_6H_6, 15 h	40
3	**1a**	**3a**	CH_2Cl_2, 15 h	45
4	**1a**	**3a**	$CHCl_3$, 15 h	46
5	**1a**	**3a**	DMF, 11 h	80
6	**1a**	**3a**	DMF, TFA, 11 h	80
7	 1b	 3b	DMF, 11 h	78

(Continued on next page)

Table 1: Synthesis of glycosyl tetrazole **(3a–h)** *(Continued)*

Entry	Glycosyl amide (**1a–h**)	Product (**3a–h**)	Reaction condition	Yield (%)[a]
8	 **1c**	 **3c**	DMF, 10 h	73
9	 **1d**	 **3d**	DMF, 10 h	76
10	 **1e**	 **3e**	DMF, 10 h	77
11	 **1f**	 **3f**	DMF, 10 h	74
12	 **1g**	 **3g**	DMF,10 h	70
13	 **1h**	 **3h**	DMF, 10 h	71

[a]Yields refer to the isolated pure product.

give the ester intermediate I, which on substitution reaction by benzotriazole fetches the imidoylbenzotriazole intermediate **2**. Then benzotriazole is cleaved by addition of sodium azide to provide the intermediate II, which on subsequent cyclization leads to formation of desired glycosyl triazole **3**. The structures of the synthesized compounds were confirmed on the basis of IR and ^{1}H and ^{13}C NMR spectroscopic data. In the ^{13}C NMR spectra, quaternary carbon of tetrazole appeared in between δ 155 and 157 with other furanose peaks and thus clearly substantiated the formation of the desired glycosyl tetrazoles.

CONCLUSION

In conclusion, a facile protocol for diverse novel carbohydrate-containing tetrazole has been developed using benzotriazole methodology. The method is advantageous as it is one pot, involves mild reaction conditions, and affords the products in good to excellent yields. The developed glycosyl tetrazoles bearing different heterocyclic skeletons at 1-position may show promising bioactivities and can serve as a pharmacologically important carbohydrate-based scaffold.

EXPERIMENTAL SECTION

All the solvents and reagents were purchased from Sigma-Aldrich and purified by standard techniques. Thin layer chromatography (TLC) was performed using silica gel 60 F-254 plates with I_2 vapors as the detecting agent followed by H_2SO_4 spray. Crude products were purified by column chromatography on silica gel 230–400 mesh. Solvents were evaporated under reduced pressure at temperature $<55^{\circ}$C. *TMS* (0.0 ppm) was used as an internal standard in ^{1}H NMR and in ^{13}C NMR. Infrared spectra were recorded as KBr pellets by a Perkin Elmer RX-1 spectrometer. Elemental analyses were performed on a Perkin-Elmer 2400 C, H, N analyzer and values were found to be within $\pm 0.5\%$ of the calculated values.

Typical Experimental Procedure for Synthesis of Glycosyl Tetrazole (3a–h)

To a solution of *N*-cyclopropyl-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-xylofuranuron amide (**1a**, 0.5 g, 1.50 mmol) in dry CH_2Cl_2 (25 mL), pyridine (0.13 mL, 1.50 mmol) and oxalyl chloride (0.13 mL, 1.50 mmol) were added slowly at 0°C under constant stirring. After 15 min, benzotriazole (0.375 g, 3.153 mmol) was added and reaction was further stirred for 15 min and then allowed to be continued for 7 h at 40°C. Progress of reaction was monitored with TLC (20% EtOAc in *n*-hexane) and after completion, the reaction mixture was treated with 10% Na_2CO_3 aq. solution, extracted with CH_2Cl_2, and evaporated under

vacuum. Crude mass thus obtained was dissolved in dry DMF (20 mL) followed by the addition of NaN_3 (0.572 g, 8.94 mmol) at 50°C and kept under constant stirring. Progress of the reaction was monitored with TLC (40% EtOAc in *n*-hexane) and found to be completed after 10 h. Then the reaction mixture was concentrated under vacuum, extracted with CH_2Cl_2 (2 × 20 mL), and dried over anhydrous Na_2SO_4. The solvent was evaporated, and the crude product was subjected to flash column chromatography (SiO_2) to give desired glycosyl tetrazole (**3a**) in good yield.

N[1]-*Cyclopropyl-5-(3′*-O-*benzyl-1,2*-O-*isopropylidene-α-D-xylo-furano-4′-yl)-tetrazole (3a)*

Yield: 80%; IR (KBr): ν_{max} cm^{-1} 1673.6, 2921.1; ^1H NMR ($CDCl_3$, 300 MHz): $\delta = 0.53$ and 0.79 (each m, each 2 H, cyclopropyl-CH_2), 1.31 and 1.47 [each s, each 3 H, 2 × >C(CH_3)$_2$], 2.78 (m, 1 H, cyclopropyl-C*H*), 4.37 (d, $J = 3.0$ Hz, 1 H, H-3), 4.58 (m, two d merged, OCH_APh, 2 H, H-2 and OCH_BPh), 4.76 (d, $J = 3.3$ Hz, 1 H, H-4), 5.97 (d, $J = 3.3$ Hz, 1 H, H-1), 7.26–7.44 (m, 5 H, Ar-*H*); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 6.34$, 6.40, 22.11, 26.31, 26.91, 73.14, 81.04, 82.41, 82.45, 105.47, 112.77, 114.96, 127.67, 127.96, 128.27, 128.39, 137.04, 138.89, and 156.0 ppm. Anal. Calcd for $C_{18}H_{22}N_4O_4$: C 60.32, H 6.19, N 15.63; found C 60.61, H 6.05, N 15.84.

N[1]-*Cyclohexyl-5-(3′*-O-*benzyl-1,2*-O-*isopropylidene-α-D-xylofurano-4′-yl)-tetrazole (3b)*

Reaction of *N*-cyclohexyl-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-xylofuranu ronamide (**2b**) with oxalyl chloride, BtH followed by treatment with NaN_3, and workup as described above, and flash column chromatography gave glycosyl tetrazole **3b** as colorless foam. Yield: 78%; IR (KBr): ν_{max} cm^{-1} 1677.5, 2943.3; ^1H NMR ($CDCl_3$, 300 MHz): $\delta = 1.16$–1.87 [m, 16 H, cyclohexyl-CH_2 and 2 × >C(CH_3)$_2$ merged], 3.82 (m, 1 H, cyclohexyl-C*H*), 4.35 (d, $J = 3.0$ Hz, 1 H, H-3), 4.58 (d, $J = 8.1$ Hz, 1 H, OCH_APh), 4.59–4.65 (m, 2 H, OCH_BPh and H-2), 4.72 (d, $J = 2.7$ Hz, 1 H, H-4), 5.98 (d, $J = 3.3$ Hz, 1 H, H-1); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 24.63$, 24.66, 25.35, 26.30, 26.89, 32.68, 32.88, 47.98, 73.06, 80.97, 82.39, 82.45, 105.40, 112.68, 125.61, 127.66, 127.85, 128.27, 137.13, and 154.96 ppm. Anal. Calcd for $C_{21}H_{28}N_4O_4$: C 62.98, H 7.05, N 13.99; found C 63.17, H 7.11, N 14.06.

N[1]-n-*Hexadecyl-5-(3′*-O-*benzyl-1,2*-O-*isopropylidene-α-D-xylofurano-4′-yl)-tetrazole (3c)*

Reaction of *N*-hexadecyl-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-xylofuranu ronamide (**2c**) with oxalyl chloride, BtH followed by treatment with NaN_3 and workup as described above, and flash column chromatography gave glycosyl tetrazole **3c** as colorless foam. Yield 73%; IR (KBr): ν_{max} cm^{-1} 1671.3, 2918.4;

^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 0.88$ (t, $J = 6.6$ Hz, 3 H, CH_3), 1.25 (m, 28 H, CH_2), 1.31 and 1.48 (each s, each 3 H, 2 × >C(CH_3)$_2$), 3.29 (m, 2 H, CH_2), 4.35 (d, $J = 2.7$ Hz, 1 H, H-3), 4.59–4.61 (m, 3 H, H-2, OCH$_A$Ph and OCH$_B$Ph), 4.73 (d, $J = 2.7$ Hz, 1 H, H-4), 5.98 (d, $J = 3.3$ Hz, 1 H, H-1), 7.29 (m, 5 H, Ar-*H*); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 14.11$, 22.65, 26.34, 26.84, 26.92, 29.25, 29.33, 29.49, 29.57, 29.66, 31.89, 39.10, 73.17, 81.09, 82.38, 82.59, 105.40, 112.62, 127.68, 127.88, 128.36, 137.24, and 156.3 ppm. Anal. Calcd for $C_{31}H_{50}N_4O_4$: C 68.60, H 9.29, N 10.32; found C 68.73, H 9.36, N 10.42.

N^1-n-*Octyl-5-(3′*-O-*benzyl-1,2*-O-*isopropylidene-α-D-xylofurano-4′-yl)-tetrazole (3d)*

Reaction of *N*-octyl-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-xylo- furanuronamide (**2d**) with oxalyl chloride, BtH followed by treatment with NaN_3 and workup as described above, and flash column chromatography gave glycosyl tetrazole **3d** as colorless foam. Yield 76%; IR (KBr): ν_{max} cm^{-1} 1679.3, 2912.1; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 0.87$ (d, $J = 6.6$ Hz, 3 H, CH_3), 1.25 (m, 12 H, CH_2), 1.31 and 1.47 (each s, each 3 H, 2 × >C(CH_3)$_2$), 3.31 (t, $J = 6.6$ Hz, 2 H, NCH_2), 4.35 (d, $J = 3.0$ Hz, 1 H, H-3), 4.57 (d, $J = 3.6$ Hz, 1 H, H-2), 4.59 (d, $J = 11.7$ Hz, 1 H, OCH$_A$Ph), 4.65 (d, $J = 11.7$ Hz, 1 H, OCH$_B$Ph), 4.74 (d, $J = 3.0$ Hz, 1 H, H-4), 5.99 (d, $J = 3.6$ Hz, 1 H, H-1), 7.25–7.31 (m, 5 H, Ar-*H*); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 14.05$, 22.59, 26.35, 26.82, 26.93, 29.12, 29.19, 29.49, 31.76, 39.03, 73.18, 81.11, 82.41, 82.61, 105.44, 112.63, 127.69, 127.90, 128.37, 137.28, 138.0 and 155.89 ppm. Anal. Calcd for $C_{23}H_{34}N_4O_4$: C 64.16, H 7.96, N 13.01; found C 64.22, H 8.01, N 13.12.

N^1-*Phenylethyl-5-(3′*-O-*benzyl-1,2*-O-*isopropylidene-α-D-xylofurano-4′-yl)-tetrazole (3e)*

Reaction of *N*-phenylethyl-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-xylofura nuronamide (**2e**) with oxalyl chloride, BtH followed by treatment with NaN_3 and workup as described above, and flash column chromatography gave glycosyl tetrazole **3e** as colorless foam. Yield 77%; IR (KBr): ν_{max} cm^{-1} 1672.9, 2932.5; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 1.31$ and 1.47 [each s, each 3H, 2 × >C(CH_3)], 2.79 (t, $J = 6.6$, 2 H, CH_2), 3.58 (m, 2 H), 4.37 (d, $J = 3.3$ Hz, 1 H, H-3), 4.57 (d, $J = 10.8$ Hz, 1 H, OCH$_A$Ph), 4.58 (d, $J = 10.8$ Hz, 1 H, OCH$_B$Ph), 4.60 (d, $J = 3.6$ Hz, 1 H, H-2), 4.77 (d, $J = 3.0$ Hz, 1 H, H-4), 5.96 (d, $J = 3.6$ Hz, 1 H, H-1), 7.26–7.48 (m, 10 H, Ar-*H*); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 26.28$, 26.91, 35.66, 40.39, 73.08, 81.10, 82.32, 82.49, 105.50, 112.81, 125.98, 126.50, 127.71, 127.99, 128.39, 128.55, 128.63, 137.00, 138.77, 138.84, 138.90, and 156.23 ppm. Anal. Calcd for $C_{23}H_{26}N_4O_4$: C 65.39, H 6.20, N 13.26; found C 65.47, H 6.32, N 13.35.

N^{1}*-2-(4-Phenyl-thiazol-2-yl)-5-(3′-*O*-benzyl-1,2-*O*-isopropylidene-α-D-xylofurano-4′-yl)-tetrazole (3f)*

Reaction of *N*-2-(4-Phenyl-thiazol-2-yl)-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-xylofuranuronamide (**2f**) with oxalyl chloride, BtH followed by treatment with NaN_3 and workup as described above, and flash column chromatography gave glycosyl tetrazole **3f** as colorless foam. Yield: 74%; IR (KBr): ν_{max} cm^{-1} 1676.6, 2945.1; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 1.35$ and 1.60 [each s, each 3H, 2 × >C(CH_3)$_2$], 4.43 (d, $J = 3.0$ Hz, 1 H, H-3), 4.57–4.64 (m, 3 H, *O*CH_APh, *O*CH_BPh, H-4), 4.97 (d, $J = 3.3$ Hz, 1 H, H-2), 6.15 (d, $J = 3.0$ Hz, 1 H, H-1), 7.17–7.84 (m, 11 H, Ar-*H*); ^{13}C NMR ($CDCl_3$, 75 MHz): ^{1}H NMR ($CDCl_3$, 75 MHz): $\delta = 26.32$, 27.02, 73.01, 80.95, 82.34, 82.55, 105.96, 107.81, 113.04, 125.68, 126.03, 127.55, 127.92, 128.03, 128.32, 128.70, 134.23, 136.64, 150.07, and 156.56 ppm. Anal. Calcd for $C_{24}H_{23}N_5O_4S$: C 60.36, H 4.85, N 14.67; found C 60.45, H 4.80, N 14.74.

N^{1}*-(5-Phenyl-[1,3,4]thiadiazol-2-yl)-5-(3′-*O*-benz-yl-1,2-*O*-isopropylidene-α-D-xylofurano-4′-yl)-tetrazole (3g)*

Reaction of *N*-(5-Phenyl-[1,3,4] thiadiazol-2-yl)-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-xylofuranuronamide (**2g**) with oxalyl chloride, BtH followed by treatment with NaN_3 and workup as described above, and flash column chromatography gave glycosyl tetrazole **3g** as colorless foam. Yield 70%; IR (KBr): ν_{max} cm^{-1} 1673.9, 2934.2; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 1.31$ and 1.51 [each s, each 3 H, 2 × >C(CH_3)$_2$], 4.46 (d, $J = 3.3$ Hz, 1 H, H-3), 4.54 (d, $J = 11.7$ Hz, 1 H, *O*CH_APh), 4.58 (d, $J = 12.0$ Hz, 1 H, *O*CH_BPh), 4.64 (d, $J = 3.3$ Hz, 1 H, H-2), 5.02 (d, $J = 3.3$ Hz, 1 H, H-4), 6.18 (d, $J = 3.3$ Hz, 1 H, H-1), 7.16–7.96 (m, 10 H, Ar-*H*); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 26.28$, 26.99, 72.66, 80.97, 82.17, 82.49, 106.03, 112.90, 127.19, 127.48, 127.87, 128.25, 128.99, 130.26, 130.53, 136.48, and 156.62 ppm. Anal. Calcd for $C_{23}H_{22}N_6O_4S$: C 57.73, H 4.63, N 17.56; found C 57.86, H 4.69, N 17.64.

N^{1}*-(5-Phenyl-[1,3,4]thiadiazol-2-yl)-5-(3′-*O*-benzyl-1,2-*O*-isopropylidene-α-D-xylofurano-4′-yl)-tetrazole (3h)*

Reaction of *N*-(5-Phenyl-[1,3,4] thiadiazol-2-yl)-3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-xylofuranuronamide (**2h**) with oxalyl chloride, BtH followed by treatment with NaN_3 and workup as described above, and flash column chromatography gave glycosyl tetrazole **3h** as colorless foam. Yield 71%; IR (KBr): ν_{max} cm^{-1} 1671.7, 2929.1; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta = 1.33$ and 1.50 [each s, each 3 H, 2 × >C(CH_3)$_2$], 4.43 (d, $J = 3.3$ Hz, 1 H, H-3), 4.51–4.70 (m, 3 H, *OCH$_A$*Ph, H-2 and *OCH$_B$*Ph), 4.99 (d, $J = 3.3$ Hz, 1 H, H-4), 6.14 (d, $J = 3.3$ Hz, 1 H, H-1), 7.16–7.95 (m, 10 H, Ar-*H*); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 26.35$, 27.10, 73.16, 81.0, 82.32, 82.62, 106.09, 113.34, 127.12, 127.38, 127.59, 128.13, 128.40, 128.50,128.96, 129.17, 130.33, 130.75, 136.55,

and 155.26 ppm. Anal. Calcd for $C_{23}H_{22}N_6O_5$: C 59.73, H 4.79, N 18.17; found C 59.79, H 4.81, N 18.22.

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