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Synthesis of Glycoconjugate Benzothiazoles via Cleavage of Benzotriazole Ring

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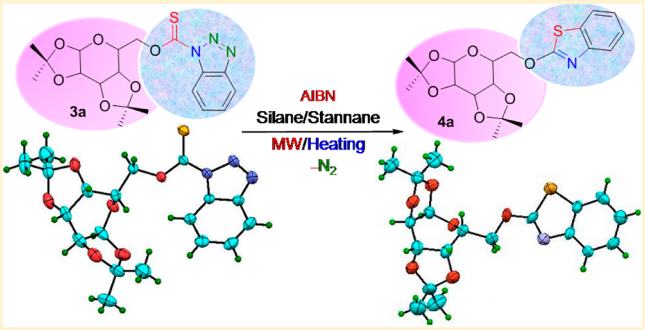
Supporting Information

ABSTRACT: A concise and efficacious benzotriazole-mediated novel two-step protocol has been developed for easy access to glycoconjugate benzothiazoles from protected carbohydrates. The benzotriazolemethanethione **3**, prepared by the reaction of free alcohol with bis(1*H*-benzo[1,2,3]triazol-1-yl)methanethione, on treatment with silanes or stannane under heating or microwave irradiation undergoes free radical *β*-scission of *N*−*N* bond and affords diverse range of 2-*O*-substituted benzothiazoles **4** via cyclative elimination of molecular nitrogen. The structures of all of the compounds have been elucidated using IR, NMR, MS, and elemental analysis, and five of them have been characterized by single-crystal X-ray analysis.



INTRODUCTION

Benzotriazole methodology, a versatile, useful, and one of the most successful synthetic protocol investigated so far, has grown from an obscure level to very high popularity.[1,2] Despite the high stability of benzotriazole in synthetic transformations,[3] there are few reactions reported to involve the disruption of the benzotriazole ring, i.e., in the synthesis of indoles, benzoazines, quinazolines, 3,4-dihydroquinazolines, and quinazoline-4-thiones.[4] Such ring-opening of benzotriazole derivatives provide an attractive way to generate a wide variety of benzoheterocycles.[1f,2] Thus, we envisioned exploring the feasibility of utilizing benzotriazole methodology for construction of benzothiazole ring on protected sugars to afford glycoconjugate benzothiazoles in an elegant and efficient way.

Benzothiazole is a privileged bicyclic ring system in myriad compounds of value to medicine and agriculture.[5−7] The benzothiazole conjugation would be effectively utilized for improving the inhibition of carbohydrate-based glycosidase inhibitors and enhance the interaction of carbohydrate-based ligands to carbohydrate-binding proteins. However, reports on 2-*O*-substitued benzothiazoles are highly scarce and pose significant challenges for their sustainable development. The customary methods to access benzothiazoles involve the condensation of *o*-aminothiophenols with substituted nitriles, aldehydes, acyl chlorides, carboxylic acids, or esters,[8] but difficulty in the synthesis of readily oxidizable *o*-aminothiophenols restricts their pervasive applications. Oxidative cyclization of thiobenzanilides using various oxidants, including Jacobson's and Hugershoff's methods, are other routes to access benzothiazoles.[9] However, low functional group tolerance limits the utility of these approaches. Other methods include the reaction of *o*-aminothiophenol with dibenzyl disulfides and *β*-chlorocinnamaldehydes, reaction of *S*-aryl thiobenzoate with arylhaloamines, from 1,2,3-benzodithiazole-2-oxides, radical cyclization of benzyne intermediates, reduction of *o*,*o*′-dinitrodiphenyl disulfide, and Grignard reactions of arylisothiocyanates.[10−13] Intramolecular cyclization of thioformanilides using hypervalent iodine reagents and Pd/Cu-catalyzed cyclization of 2-halophenylthiobenzamides also provides an easy access to benzothiazoles.[14] However, the prefunctionalization of starting material and poor performance in gram scale synthesis are among the major drawbacks of these approaches.

Over recent years, there is an increasing demand for new carbohydrate scaffolds for the numerous biological, medicinal, and pharmacological investigations.[15] As part of our ongoing work on development of new benzotriazole methodologies for the synthesis of heterocyclic and carbohydrate-based scaffolds of multifaceted biological profiles,[16] we herein describe a novel two-step protocol for an easy access to diverse 2-*O*-substituted glycoconjugate benzothiazoles **4** from carbohydrate based benzotriazolemethanethiones **3**, readily prepared from protected sugars **1** using benzotriazole as a synthetic auxiliary (Scheme 1).

RESULTS AND DISCUSSION

We began our study by examining a model reaction of 1,2:3,4-di-*O*-isopropylidene-*α*-D-galactopyranose **1a** with bis-benzotriazole methanethione **2** in presence of Et_3N (0.2 equiv) and pyridine (0.3 equiv) in dichloromethane at room temperature to afford 6-*O*-(1,2:3,4-di-*O*-isopropylidine-*α*-D-galactopyranose)-1*H*-benzo[d][1,2,3]triazole-1-carbothioate (**3a**) in sig-

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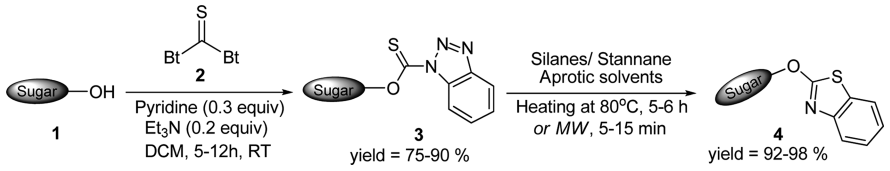
Scheme 1. Reaction of Protected Sugars 1 with Bis(1*H*-benzo[1,2,3]triazol-1-yl)methanethione 2



nificant yield. The high stability of resulting adduct **3a** prevented it to be further attacked by another sugar molecule, and indeed, no bisubstituted products were observed during synthesis of carbohydrate based benzotriazolemethanethiones **3a–k** (Table 1) via reaction of protected sugars **1a–k** and compound **2**. Using extensive spectral studies (IR, ^{1}H, and ^{13}C NMR), the structures of compounds **3a–k** were elucidated. A single-crystal X-ray analysis[17] evidenced the unambiguous structure of compound **3a** (see the Supporting Information, Figure S1).

However, reaction of 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranos-5-ulose (**5**) with compound **2** to access the corresponding carbohydrate-based benzotriazolemethanethione **3** under our standardized reaction condition was not successful, rather a mixture of two regioisomers, 5-(1′*H*-benzo[1,2,3]-triazol-1′-yl)-3-*O*-benzyl-1,2-di-*O*-isopropylidene-5,6-*O*-thiocarbonate-α-D-glucofuranose (**6**) and 5-(2*H*-benzo[1,2,3]triazol-2-yl)-3-*O*-benzyl-1,2-di-*O*-isopropylidene-5,6-*O*-thiocarbonate-α-D-glucofuranose (**7**) were obtained in a ratio of 73:27%, respectively (Scheme 2).

A plausible mechanism involves the initial nucleophilic attack by hydroxyl group of hydroxy ketone **5** on thiocarbonyl carbon of compound **3** to afford a carbohydrate based benzotriazolemethanethione intermediate **I** that readily passes to a transition state (TS) via nucleophilic attack of benzotriazole moiety through *N*1 or *N*2 and subsequent nucleophilic addition of carbonyl oxygen on thiocarbonyl carbon as outlined in Scheme 3. The benzotriazole moiety by virtue of π–π interaction with phenyl ring facilitates a preferred *Si*-face attack and results in an observed stereochemistry of products, also confirmed by single crystal X-ray analysis (Figure 1). The structures of compounds **6** and **7** were elucidated using extensive spectral studies (IR, ^{1}H, and ^{13}C NMR) and single-crystal X-ray analysis (see Figure 2).

Treatment of compound **3a** with reagents capable of inducing a free-radical mechanism furnished 6-*O*-(benzothiazol-2′-yl)-1,2:3,4-di-*O*-isopropylidine-α-D-galactopyranose **4a** in good to excellent yield. We briefly studied the effect of various reagents (e.g., silanes and stannane) in terms of yield and reaction time. The cyclization of **3a** using Bu_3SnH at 80 °C in toluene furnished **4a** quantitatively in 5 h. Encouraged by this result, we further examined this reaction in the presence of AIBN (5 mol %) as radical initiator and obtained high yield of product **4a** in significantly reduced reaction time (entry 11, Table 2). Although simple, low molecular weight silanes would be very acceptable alternatives, despite the greater strength of the Si–H (377 kJ mol^{-1}) in Et_3SiH compared with Sn–H bond (310 kJ mol^{-1}) in *n*-Bu_3SnH, such cyclizations are observed to be comparatively slow and require considerably high temperature or added initiators.[18a] In our investigation, the cyclizations with Et_3SiH and Pr^i_3SiH resulted in poor yields of products, unless 5 mol % of AIBN was used as initiator. However, the reactions carried out in the presence of silanes having radical stabilizing groups, i.e., phenyl substituent in $MePh_2SiH$, Bu^tPh_2SiH, and Ph_3SiH, afforded a moderate yield of products in 5–6 h, even without using radical initiator, which suggested that the bond-weakening effects operative on phenyl substitution.[18b] The uniformity of Si–H bond strengths between Et_3SiH and Pr^i_3SiH gives almost the similar results. However, results obtained with phenyl-substituted silanes are quite noticeable, particularly due to the radical stabilization by π-conjugation of phenyl group(s) that weakens the Si–H bond. Further, using AIBN as initiator for cyclization dramatically accelerated the reaction and furnished product in a quantitative yield with significant reduction of reaction time (Table 2). Bu_3SnH proved to be best among an array of reagent tested and addition of AIBN was crucial for aforementioned conversion (entry 11, Table 2). In the reaction optimization study executed by varying the ratio of Bu_3SnH under refluxing condition, an increase in total yield of **4a** was observed while increasing the reagent quantitatively. The yield of compound **4a** was optimum using 2 equiv of Bu_3SnH at 80 °C. In addition, we investigated the reaction under microwave (MW) condition, where significant reduction in reaction time ranging from 5 to 15 min was observed (Table 2).

The solvent effect was briefly investigated using various solvents in the presence of AIBN (5 mol %) and Bu_3SnH (2 molar equiv) at 80 °C (Table 3). The results illustrated the poor performance of cyclohexane, *n*-hexane, benzene, 1,4-dioxane, dichloromethane and chloroform in terms of yield and reaction time. Using toluene as a solvent, the reaction accomplished in significantly less time with much higher yield of product, which suggested the toluene as solvent of choice for cyclization to product **4a**.

The extensive spectral studies (IR, ^{1}H and ^{13}C NMR, and MS) evidenced the unambiguous structure of compound **4a**. Like ^{1}H NMR spectra of compound **3a** having four separate resonances (one proton each) for the characteristic benzotriazolyl C–H protons, the compound **4a** also exhibited four proton resonances in aromatic region with a different splitting pattern, thus ruled out the formation of possible deoxy product[19] under our standardized conditions. In addition, the mass spectrum of **4a** exhibited an $[M + H]^+$ peak at *m*/*z* 394, which was 28 units less than the molecular ion peak $[M + H]^+$ of **3a** observed at *m*/*z* 422. Therefore, the compound **4a** might have been formed by the loss of molecular nitrogen (N_2) from **3a**, also evidenced by their respective single-crystal X-ray analysis (see Figure 3).

Thus, under optimized reaction conditions, all the developed carbohydrate based benzotriazolemethanethione **3a–k** were cyclized to their respective glycoconjugate benzothiazoles **4a–k** in excellent yields ranging from 92 to 98% (Table 4). The structure of compounds **4a–k** were deduced from their extensive spectral studies (IR, NMR, and MS), and single-crystal X-ray analysis.

Apart from highly functionalized carbohydrates, we next synthesized *O*-cholesteryl methanethione **9** by the reaction of cholesterol **8** with bis(1*H*-benzo[1,2,3]triazol-1-yl)-methanethione (**2**) and successfully executed the synthesis of

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Table 1. Synthesis of Carbohydrate-Based Benzotriazolemethanethiones 3a–k

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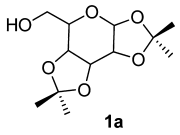
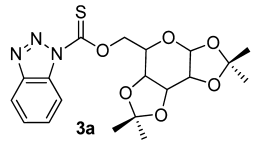
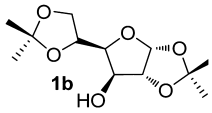
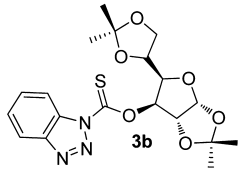
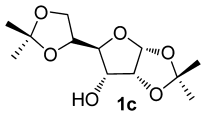
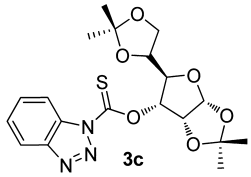
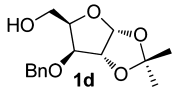
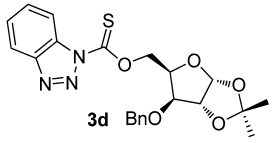
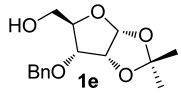
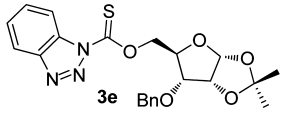
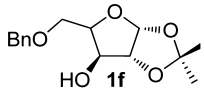
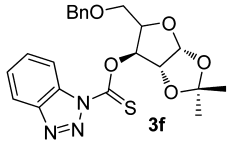
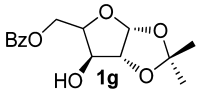
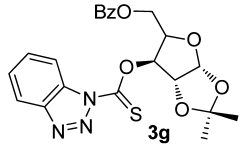
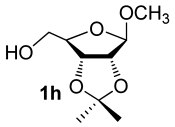
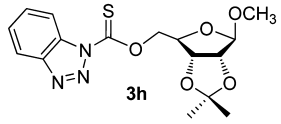
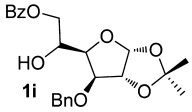
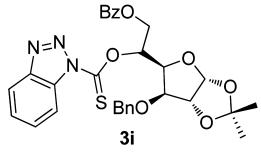
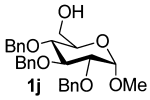
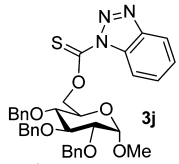
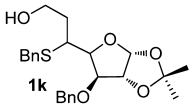
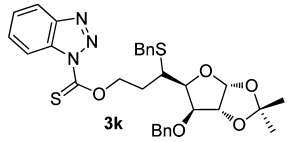
1	 1a	 3a	5	90
2	 1b	 3b	6	89
3	 1c	 3c	6	87
4	 1d	 3d	5	86
5	 1e	 3e	5	87
6	 1f	 3f	12	78
7	 1g	 3g	10	82
8	 1h	 3h	5	87
9	 1i	 3i	24	75
10	 1j	 3j	6	82
11	 1k	 3k	6	81

[a]Molar ratios: protected sugar, Et_3N, *bis*-benzotriazole methanethiones. [b]Carbohydrate based benzotriazolemethanethiones. [c]Reaction time. [d]Yield reported after purification by column chromatography.

O-cholesteryl benzothiazole **10** in quantitative yield via radical cyclization under our standardized conditions (Scheme 4). Thus, the developed methodology is well tolerated to a number of functional groups such ethers, acetals, thioethers, esters, and

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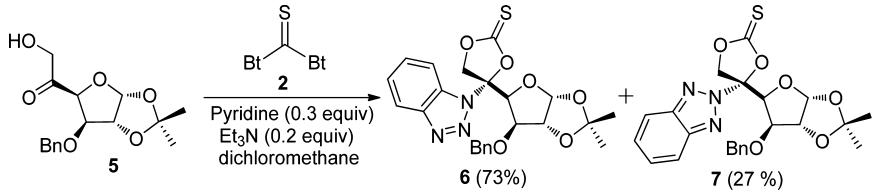
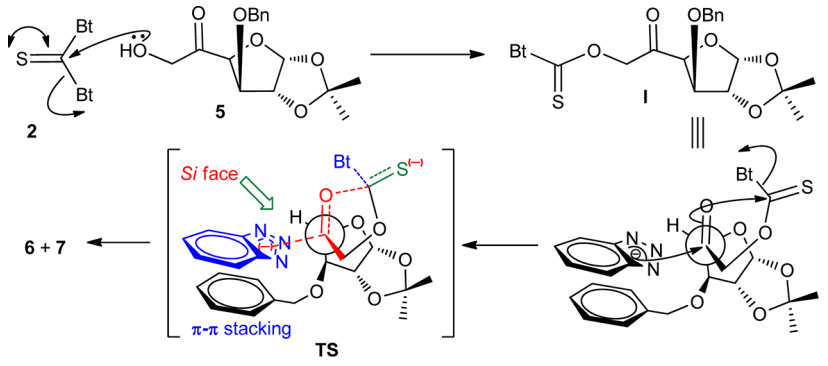
Scheme 2. Reaction of 3-*O*-Benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranos-5-ulose 5 with Compound 2



Scheme 3. Plausible Mechanism for the Formation of Regioisomers 6 and 7



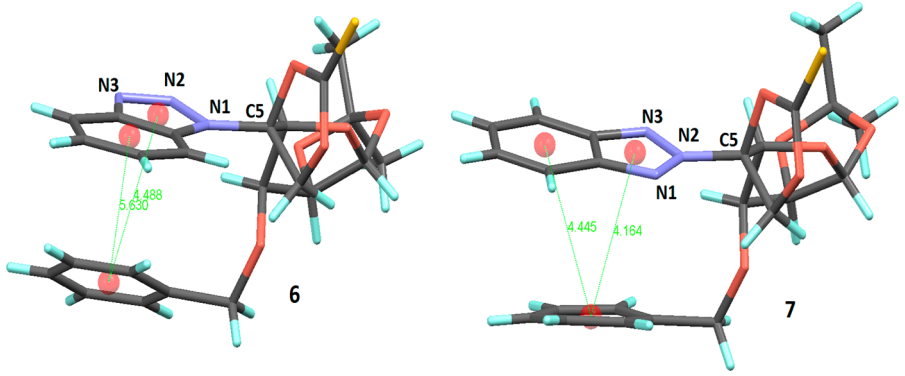


Figure 1. Offset π−π stacking interactions in regioisomers **6** and 7.

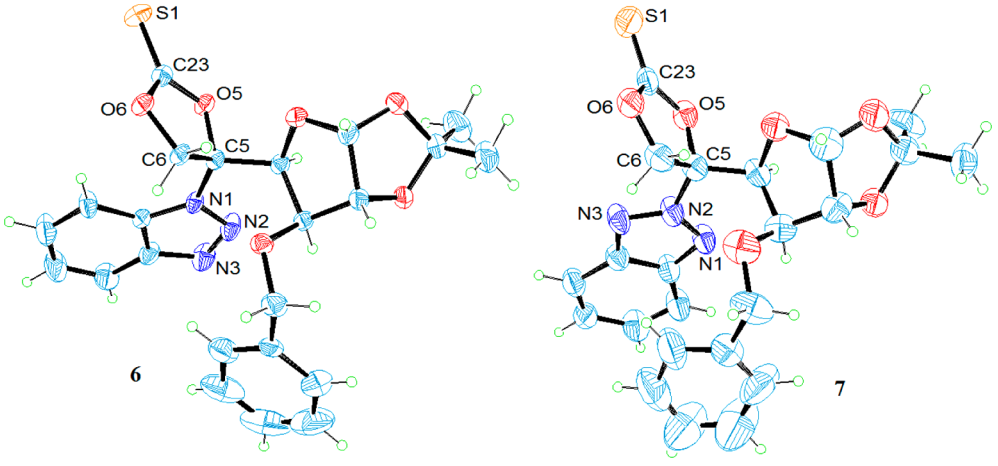


Figure 2. Molecular structure of **6** and 7. Thermal ellipsoids of C, N, S, and O are set at 40 % probability.

alkenes. Extensive spectral studies (IR, ^{1}H, and ^{13}C NMR) and single-crystal X-ray analysis evidenced the formation of benzothiazole ring in the compound **10** (see Figure 4).

Although a detailed understanding of the mechanism will require additional studies, we assume that the transformation of carbohydrate based benzotriazolemethanethione **3** to glycoconjugate benzothiazole **4** proceeds via free radical cyclization as outlined in Scheme 5. The homolytic cleavage of tributylstannane initiates a radical reaction, which is propagated by subsequent addition of stannanyl radical to sulfur of

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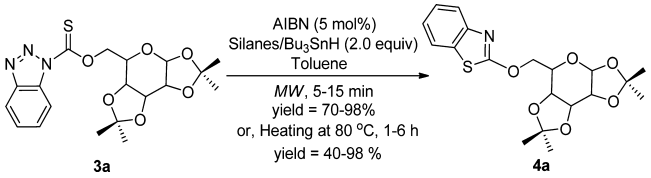
Table 2. Optimization of Radical Conversion to 4a Using 2 molar equiv of Reagents



entry	reagent	initiator[a] (mol %)	temp[b] (°C)	yield (%) (time)[c]	yield % (time)[d]
1	Et_3SiH	5	80	40 (4)	70 (15)
2	Et_3SiH	0	150	0 (6)	0 (15)
3	Pr^i_3SiH	5	80	45 (4)	75 (15)
4	Pr^i_3SiH	0	150	5 (6)	18 (15)
5	$MePh_2SiH$	5	80	60 (4)	89 (15)
6	$MePh_2SiH$	0	150	49 (6)	63 (15)
7	Bu^tPh_2SiH	5	80	89 (4)	96 (15)
8	Bu^tPh_2SiH	0	150	50 (5)	65 (15)
9	Ph_3SiH	5	80	90 (3)	98 (10)
10	Ph_3SiH	0	150	60 (5)	74 (10)
11	Bu_3SnH	5	80	98 (1)	98 (5)
12	Bu_3SnH	0	80	92 (5)	97 (10)

[a]AIBN (azobisisobutyronitrile) was used as radical initiator. [b]Reaction temperature 80−150 °C. [c]Reaction time in hours under heating conditions. [d]Reaction time in minutes under microwave conditions.

Table 3. Solvent Optimization for Conversion from 3a to 4a using Bu_3SnH (2 molar equiv) in the Presence of AIBN (5 mol %)

entry	solvent[a]	time[b] (h)	yield[c] (%)
1	cyclohexane	6	75
2	*n*-hexane	5	75[d]
3	benzene	5	85
4	toluene	1	98
5	1,4-dioxane	8	80
6	dichloromethane	12	60[d]
7	chloroform	12	62[d]

[a]2.0 mL of solvent was used for 1 mmol of **3a**. [b]Reaction time 1−12 h. [c]Isolated yield 60−98%. [d]Reaction in sealed tube.

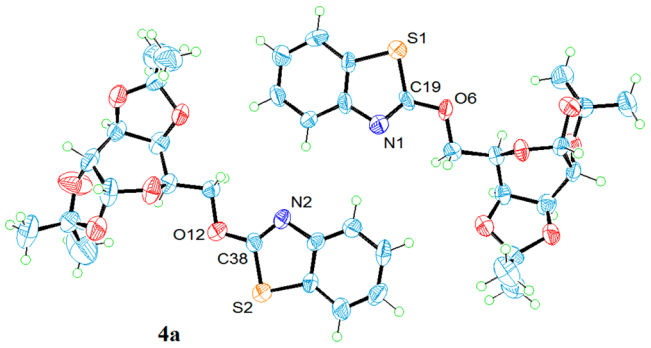


Figure 3. Molecular structure of **4a**. Thermal ellipsoids of C, N, S, and O are set at 50% probability.

thiocarbonyl[20] forming an intermediate **A** that rapidly adds a hydrogen radical to furnish an intermediate **B**. The β-scission by the radical cleavage of benzotriazole ring results in the formation of an intermediate **C**. Elimination of a nitrogen molecule (N_2) from biradical intermediate **C** affords a resonance stabilized aryl radical intermediate **D** that cyclizes to furnish benzothiazole **4** via a thermodynamically favorable and thermally induced oxidation process leading to aromatization at the cost of 2σ-bond to a resulted π-bond in final product. The trialkylsilyl radicals also add rapidly to sulfur in thiocarbonyl compounds, and possibly follow the same mechanistic pathway. However, addition of $R_3Si^\bullet$ is likely to be much less readily reversible than the corresponding addition of $Bu_3Sn^\bullet$, because the Si−S bond is appreciably stronger than the Sn−S bond.[21] Therefore, this may reduce the rate of decay for biradical intermediate **C** to furnish **D** that cyclizes to glycoconjugate benzothiazole **4**.

CONCLUSION

In conclusion, a concise and efficacious benzotriazole-mediated novel two-step protocol for an easy access to diverse glycoconjugate benzothiazoles from protected carbohydrates has been developed. The short reaction period, simple workup, good yield, and mild conditions of this methodology demonstrate significant compatibility toward acid and base sensitive functionalities. Unlike carbohydrate derivatives, e.g., *O*-(*S*-methyldithiocarbonate)-, *O*-phenoxythiocarbonyl, phenyl-1-thio, *O*-pentafluorophenylthionocarbonate, *O*-thiocarbonyl imidazolide, etc., utilized previously for deoxygenation,[19] the developed methodology described herein does not give deoxy products even in trace amounts. In addition to the generality with respect to the substrate scope, facile accessibility to the starting materials is also highly appealing. The synthesis of benzothiazoles via benzotriazole ring cleavage has not been realized so far, thus, this approach should be of further interest to synthetic and medicinal chemists. The developed methodology performs well in small as well as gram scale synthesis of benzothiazoles, thus may have industrial significance. The biological screening of all the developed glycoconjugate benzothiazoles is under way.

EXPERIMENTAL SECTION

General Remarks. All of the reactions were executed in anhydrous solvents under an argon atmosphere in one hour oven-dried glassware at 100 °C. All reagents and solvents were of pure analytical grade. Thin-layer chromatography (TLC) was performed on 60 F_{254} silica gel, precoated on aluminum plates and revealed with either a UV lamp (λ_{max} = 254 nm) or a specific color reagent (Draggendorff reagent or iodine vapors) or by spraying with methanolic H_2SO_4 solution and subsequent charring by heating at 100 °C. ^1H and ^{13}C NMR were recorded at 300 and 75 MHz, respectively. Chemical shifts given in ppm downfield from internal TMS; *J* values in Hz. Mass spectra recorded using electrospray ionization mass spectrometry (ESI-MS). Infrared spectra recorded as Nujol mulls in KBr plates. Elemental analysis was performed using a C, H, N analyzer, and results were found to be within ±0.4% of the calculated values. Reactions under microwave were carried out in a single-mode microwave reactor from CEM Discover LabMate, Wattage: 300 W, *T* 300 °C. Single-crystal X-ray data collected on Xcalibur Eos (Oxford) CCD-diffractometer.

Procedure for the Synthesis of Protected Sugars (1a−k and 5). Compounds **1a−j** and **5** were prepared from readily available carbohydrates (D-glucose, D-galactose, D-ribose, and D-xylose) using standard protection methodologies.[22]

3-*O*-Benzyl-5-benzylthio-5,6-dideoxy-1,2-*O*-isoproyledene-α-D-*xylo*-heptofuranuronose (1k). Ethyl 3-*O*-benzyl-5-benzylthio-5,6-dideoxy-1,2-*O*-isoproyledene-α-D-*xylo*-heptofuranuronoate[23a] (1.56 g, 3.30 mmol), prepared by the 1,4-conjugate addition of benzylmercaptan to ethyl (3-*O*-benzyl-1,2-*O*-isopropylidene-1,4-pentofuranose-4-yl)-hept-5-enoate,[23b] was taken in anhydrous THF and added dropwise to the stirring slurry of $LiAlH_4$ (250 mg, 6.60 mmol) in anhydrous THF at 0 °C under a nitrogen atmosphere. The reaction mixture was stirred for 30 min at 0 °C followed by further stirring at

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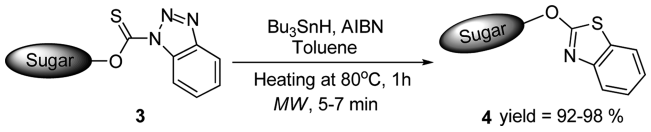
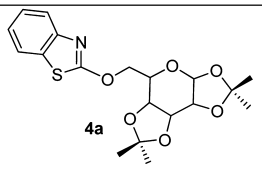
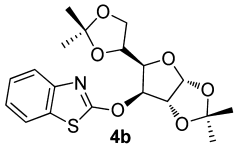
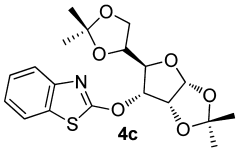
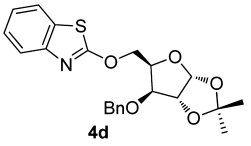
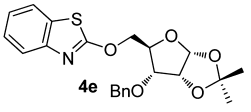
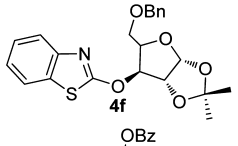
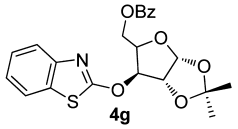
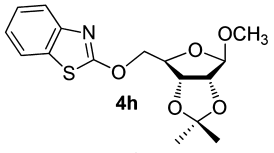
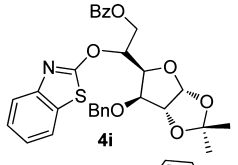
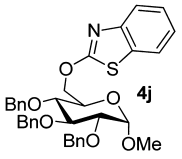
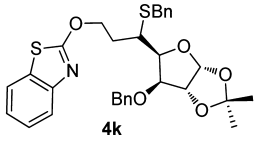
Table 4. Synthesis of Glycoconjugate Benzothiazoles 4a–k



3 4 yield = 92-98 %

entry	substrate[a]	product	yield % (time)[b]	yield % (time)[c]
1	**3a**	 **4a**	98(1)	98(5)
2	**3b**	 **4b**	95(1)	97(5)
3	**3c**	 **4c**	96(1)	98(5)
4	**3d**	 **4d**	94(1)	97(6)
5	**3e**	 **4e**	95(1)	97(5)
6	**3f**	 **4f**	97(1)	98(6)
7	**3g**	 **4g**	95(1)	97(5)
8	**3h**	 **4h**	96(1)	98(5)
9	**3i**	 **4i**	96(1)	98(7)
10	**3j**	 **4j**	92(1)	95(5)
11	**3k**	 **4k**	94(1)	96(6)

[a]Molar ratios: carbohydrate-based benzotriazolemethanethiones **3a–k**, Bu_3SnH (1:2 equivalent), and AIBN (5 mol %). [b]Reaction time in hours under heating conditions. [c]Reaction time in minutes under microwave conditions.

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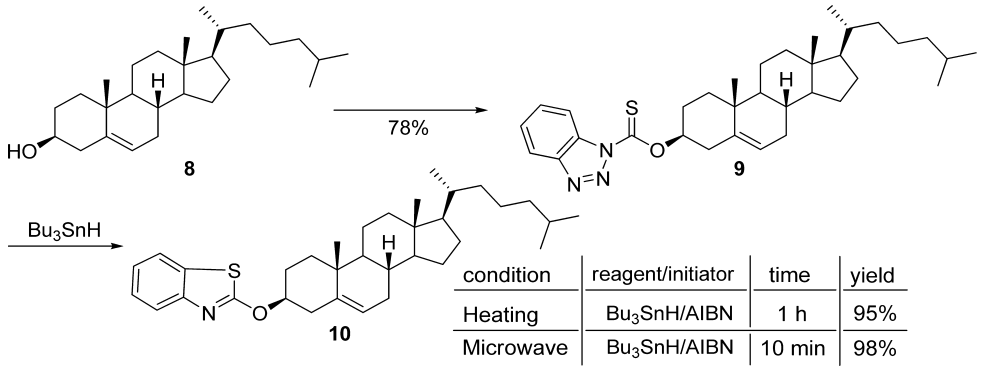
Scheme 4. Synthesis of *O*-Cholesteryl Benzothiazole 10



condition	reagent/initiator	time	yield
Heating	Bu_3SnH/AIBN	1 h	95%
Microwave	Bu_3SnH/AIBN	10 min	98%

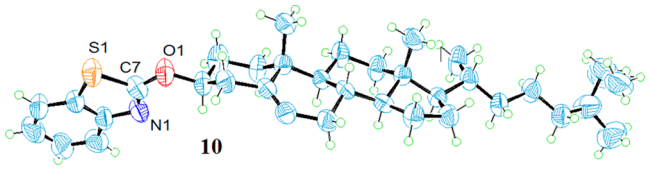
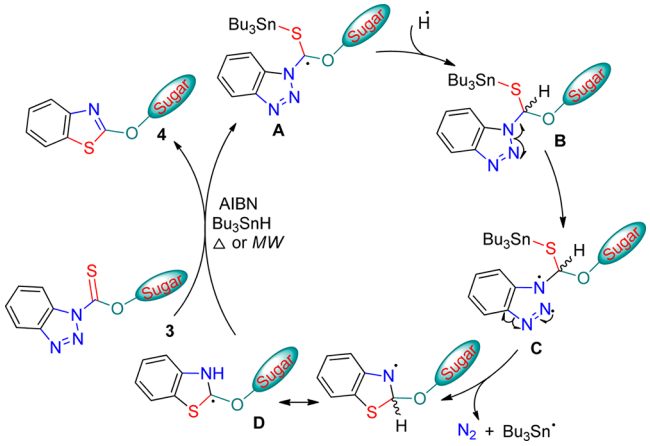


Figure 4. Molecular structure of **10**. Thermal ellipsoids of C, N, S, and O are set at 50% probability.

Scheme 5. Postulated Mechanism for the Formation of Benzothiazoles



ambient temperature for 3 h. On completion (monitored by TLC), the reaction was quenched by adding saturated aqueous Na_2SO_4 solution and filtered. The solid cake was washed with THF, and the filtrate was concentrated under reduced pressure followed by extraction with chloroform (2 × 100 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Further purification using flash column chromatography using gradient mixtures of ethylacetate and *n*-hexane afforded pure compound **1k** (1.35 g, yield 95%) as viscous liquid: R_f = 0.5 (40% ethyl acetate/*n*-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33−7.21 (m, 10H), 5.89 (d, J = 3.6 Hz, 1H), 4.67 (d, J = 11.0 Hz, 1H), 4.56 (d, J = 4.2 Hz, 1H), 4.55 (d, J = 11.0 Hz, 1H), 4.10 (d, J = 12.6 Hz, 2H), 3.73−3.68 (m, 4H), 3.17−3.12 (m, 1H), 3.17−3.12 (m, 1H), 2.16−2.09 (m, 1H), 1.89−1.84 (m, 2H), 1.45, 1.29 (each s, each 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 138.5, 137.3, 128.8, 128.5 (2C), 128.4 (2C), 127.9 (2C), 127.7 (2C), 127.1 (2C), 111.6, 105.0, 82.6, 82.2, 81.3, 72.1, 60.6, 40.4, 34.6, 26.7, 26.1. Anal. Calcd for $C_{24}H_{30}O_5S$: C, 66.95; H, 7.02. Found: C, 67.26; H, 7.31.

Procedure for the Synthesis of Carbohydrate-Based Benzotriazolemethanethione (3a−k) and Compounds 6, 7, and 9. A stirring solution of free alcohol (**1a−k** and **8**) in dry CH_2Cl_2 was treated with bis-benzotriazole methanethiones **2** in the presence of pyridine and Et_3N under inert atmosphere. After completion of reaction (monitored by TLC), the reaction mixture was concentrated in vacuo. After extraction with CH_2Cl_2, washing with 10% Na_2CO_3, water, and brine solution followed by drying over anhydrous Na_2SO_4, the organic layer was concentrated under reduced pressure. Further purification using flash column chromatography using gradient mixtures of ethyl acetate and *n*-hexane afforded pure benzotriazole methanethiones.

6-*O*-(1,2:3,4-Di-*O*-isopropylidine-α-D-galactopyranose)-1*H*-benzo[*d*][1,2,3]triazole-1-carbothioate (3a). A stirring solution of compound **1a** (1.93 g, 7.43 mmol) in dry CH_2Cl_2 (10 mL) was added with **2** (2.50 g, 8.92 mmol), pyridine (179 μL, 2.23 mmol), and triethylamine (206 μL, 1.49 mmol) under inert atmosphere:hite crystals, 2.8 g, yield 90%; mp 110−112 °C; R_f = 0.6 (30% ethyl acetate/*n*-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.41 (d, J = 8.4 Hz, 1H), 8.11 (d, J = 8.4 Hz, 1H), 7.64 (dd, J = 7.8, 7.5 Hz, 1H), 7.48 (dd, J = 7.8, 7.5 Hz, 1H), 5.64 (d, J = 5.1 Hz, 1H), 5.03−4.98 (m, 1H), 4.92−4.85 (m, 1H), 4.71 (dd, J = 2.4, 7.2 Hz, 1H), 4.42−4.37 (m, 3H), 1.56, 1.54, 1.50, 1.38 (each s, each 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 183.0, 146.3, 130.7, 130.5, 125.9, 120.4, 115.4, 110.0, 109.0, 96.3, 72.2, 70.9, 70.7, 70.8, 65.7, 26.0, 25.9, 24.9, 24.4; IR (KBr) ν_{max} 1595, 1068, 1002, 989, 962, 888, 777, 744 cm^{-1}; MS m/z 422 [M + H]$^+$. Anal. Calcd for $C_{19}H_{23}N_3O_6S$: C, 54.14; H, 5.50; N, 9.98. Found: C, 53.75; H, 5.76; N, 9.61.

3-*O*-(1,2:5,6-Di-*O*-isopropylidine-α-D-glucofuranose)-1*H*-benzo[*d*][1,2,3]triazole-1-carbothioate (3b). A stirring solution of compound **1b** (20.0 g, 76.84 mmol) in dry CH_2Cl_2 (160 mL) was added with **2** (23.7 g, 84.52 mmol), pyridine (1.66 mL, 15.37 mmol), and Et_3N (2.14 mL, 15.37 mmol) under inert atmosphere: liquid, 28.8 g, yield 89%; R_f = 0.6 (30% ethyl acetate/*n*-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.47 (d, J = 8.4 Hz, 1H), 8.15 (d, J = 8.4 Hz, 1H), 7.69 (t, J = 7.5 Hz, 1H), 7.52 (t, J = 7.5 Hz, 1H), 6.03 (d, J = 3.0 Hz, 2H), 4.84 (d, J = 3.6 Hz, 1H), 4.50−4.57 (m, 1H), 4.40−4.23 (m, 1H), 4.11−4.22 (m, 2H), 1.60, 1.42, 1.36, 1.25 (each s, each 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 181.1, 146.4, 131.5, 130.6, 126.1, 120.7, 114.6, 112.6, 109.4, 105.1, 84.1, 82.7, 79.8, 72.1, 67.2, 26.9, 26.5, 26.1, 25.0; IR (Nujol) ν_{max} 1610, 1590,1066, 984, 986, 973, 954, 732 cm^{-1}; MS m/z 422 [M + H]$^+$. Anal. Calcd for $C_{19}H_{23}N_3O_6S$: C, 54.14; H, 5.50; N, 9.98. Found: C, 54.51; H, 5.87; N, 9.66.

3-*O*-(1,2:5,6-Di-*O*-isopropylidine-α-D-allofuranose)-1*H*-benzo[*d*][1,2,3]triazole-1-carbothioate (3c). A stirring solution of compound **1c** (1.0 g, 3.84 mmol) in dry CH_2Cl_2 (10 mL) was added with **2** (1.29 g, 4.61 mmol), pyridine (92 μL, 1.15 mmol), and Et_3N (107 μL, 0.77 mmol) under inert atmosphere: white solid, 1.41 g, yield 87%; mp 82−84 °C; R_f = 0.6 (30% ethyl acetate/*n*-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.46 (d, J = 8.1 Hz, 1H), 8.13 (d, J = 8.4 Hz, 1H), 7.66 (two d's merged, J = 7.8, 7.5 Hz, 1H), 7.51 (two d's merged,

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J = 7.8, 7.2 Hz, 1H), 5.96 (d, J = 3.6 Hz, 1H), 5.72 (dd, J = 5.1, 8.1 Hz, 1H), 5.18 (dd, J = 3.9, 8.7 Hz, 1H), 4.56 (dd, J = 4.5, 8.4 Hz, 1H), 4.44 (d, J = 4.8 Hz, 1H), 4.14−4.09 (m, 2H), 1.57, 1.39, 1.34, 1.32 (each s, each 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 181.5, 146.4, 131.4, 130.4, 126.1, 120.6, 114.9, 113.6, 110.1, 104.2, 79.1, 77.6, 76.5, 74.5, 65.7, 26.7, 26.5, 26.2, 24.6; IR (KBr) ν_{max} 1614, 1593,1103, 1121, 996, 962, 741 cm^{-1}; MS m/z 422 $[M + H]^+$. Anal. Calcd for $C_{19}H_{23}N_3O_6S$: C, 54.14; H, 5.50; N, 9.98. Found: C, 54.34; H, 5.28; N, 9.63.

6-*O*-(3-*O*-Benzyl-1,2-*O*-isopropylidine-α-D-xylofuranose)-1*H*-benzo[*d*][1,2,3]triazole-1-carbothioate (3d). A stirring solution of compound **1d** (730 mg, 2.60 mmol) in dry CH_2Cl_2 (10 mL) was added with **2** (875 mg, 3.13 mmol), pyridine (63 μL, 0.78 mmol), and Et_3N (71 μL, 0.53 mmol) under inert atmosphere: white solid, 991 mg, yield 86%; mp 90−92 °C; R_f = 0.6 (20% ethyl acetate/*n*-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.34 (d, J = 8.4 Hz, 1H), 8.12 (d, J = 8.1 Hz, 1H), 7.64 (two d's merged, J = 7.5, 7.8 Hz, 1H), 7.48 (two d's merged, J = 8.1 Hz, 1H), 7.29−7.13 (m, 5H), 6.04 (d, J = 3.3 Hz, 1H), 5.07−4.94 (m, 2H), 4.74 (d, J = 12.0 Hz, 2H), 4.70 (d, J = 3.6 Hz, 1H), 4.51 (d, J = 12.0 Hz, 1H), 4.16 (d, J = 2.7 Hz, 1H), 1.52, 1.36 (each s, each 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 182.6, 146.3, 136.8, 131.2, 130.5, 128.4 (2C), 128.0, 127.8 (2C), 125.9, 120.5, 114.9, 112.1, 105.4, 82.2, 81.3, 77.1, 72.0, 70.3, 26.9, 26.2; IR (KBr) ν_{max} 1618, 1595,1072, 1060, 992, 983, 974, 756 cm^{-1}; MS m/z 442 $[M + H]^+$. Anal. Calcd for $C_{22}H_{23}N_3O_5S$: C, 59.85; H, 5.25; N, 9.52. Found: C, 60.32; H, 4.81; N, 9.17.

5-*O*-(3-*O*-Benzyl-1,2-*O*-isopropylidine-α-D-ribofuranose)-1*H*-benzo[*d*][1,2,3]triazole-1-carbothioate (3e). A stirring solution of compound **1e** (925 mg, 3.30 mmol) in dry CH_2Cl_2 (10 mL) was added with **2** (1.11 g, 3.96 mmol), pyridine (80 μL, 0.99 mmol), and Et_3N (67 μL, 0.66 mmol) under inert atmosphere: liquid, 1.27 g, yield 87%; R_f = 0.6 (20% ethyl acetate/*n*-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.36 (d, J = 7.8 Hz, 1H), 8.12 (d, J = 8.1 Hz, 1H), 7.63 (two d's merged, J = 7.8, 7.5 Hz, 1H), 7.49 (two d's merged, J = 7.8 Hz, 1H), 7.29 (d, J = 7.2 Hz, 2H), 7.13 (t, J = 7.5 Hz, 2H), 7.00 (t, J = 7.5 Hz, 1H), 5.85 (d, J = 3.3 Hz, 1H), 4.98 (d, J = 11.7 Hz, 1H), 4.82 (d, J = 12.0 Hz, 1H), 4.77 (d, J = 3.3, 12.0 Hz, 1H), 4.70 (m, 1H), 4.52 (d, J = 12.0 Hz, 1H), 4.47 (m, 1H), 3.99 (dd, J = 3.9, 9.0 Hz, 1H), 1.64, 1.40 (each s, each 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 182.4, 146.3, 136.9, 130.4, 128.3 (2C), 128.0 (3C), 127.9, 125.9, 120.5, 114.8, 113.3, 104.1, 77.0 (2C), 75.8, 72.4, 70.4, 26.8, 26.4; IR (Nujol) ν_{max} 1625, 1590, 1162, 1140, 997, 981, 962, 754 cm^{-1}; MS m/z 442 $[M + H]^+$. Anal. Calcd for $C_{22}H_{23}N_3O_5S$: C, 59.85; H, 5.25; N, 9.52. Found: C, 59.59; H, 4.80; N, 9.91.

3-*O*-(5-*O*-Benzyl-1,2-*O*-isopropylidine-α-D-xylofuranose)-1*H*-benzo[*d*][1,2,3]triazole-1-carbothioate (3f). A stirring solution of compound **1f** (947 mg, 3.38 mmol) in dry CH_2Cl_2 (10 mL) was added with **2** (1.14 g, 4.05 mmol), pyridine (81 μL, 1.01 mmol), and Et_3N (91 μL, 0.68 mmol) under inert atmosphere: liquid, 1.16 g, yield 78%; R_f = 0.7 (30% ethyl acetate/*n*-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.22 (d, J = 8.4 Hz, 1H), 8.11 (d, J = 8.1 Hz, 1H), 7.62 (two d's merged, J = 7.8, 7.5 Hz, 1H), 7.49 (two d's merged, J = 7.8, 7.2 Hz, 1H), 7.14 (d, J = 6.9 Hz, 2H), 7.04 (dd, J = 7.2, 7.5 Hz, 2H), 6.96 (d, J = 7.2 Hz, 1H), 6.11 (d, J = 2.4 Hz, 1H), 6.06 (d, J = 3.6 Hz, 1H), 4.81 (d, J = 3.6 Hz, 1H), 4.71 (m, 1H), 4.57−4.51 (m, 1H), 4.36 (d, J = 11.7 Hz, 1H), 3.87−3.85 (m, 2H), 1.58, 1.35 (each s, each 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 181.2, 146.2, 137.1, 130.6, 128.3, 127.9 (2C), 127.7 (2C), 127.4, 126.0, 120.6, 114.5, 112.5, 104.7, 83.9, 82.6, 77.5, 73.3, 65.9, 26.4, 26.1; IR (Nujol) ν_{max} 1627, 1591,1098, 1078, 1063, 1012, 996, 964, 736 cm^{-1}; MS m/z 442 $[M + H]^+$. Anal. Calcd for $C_{22}H_{23}N_3O_5S$: C, 59.85; H, 5.25; N, 9.52. Found: C, 60.21; H, 5.67; N, 9.11.

3-*O*-(5-*O*-Benzoyl-1,2-*O*-isopropylidine-α-D-xylofuranose)-1*H*-benzo[*d*][1,2,3]triazole-1-carbothioate (3g). A stirring solution of compound **1g** (1.04 g, 3.54 mmol) in dry CH_2Cl_2 (10 mL) was added with **2** (1.19 g, 4.25 mmol), pyridine (85 μL, 1.06 mmol), and Et_3N (98 μL, 0.71 mmol) under inert atmosphere: white solid, 1.3 g, yield 82%; mp 94−96 °C; R_f = 0.7 (30% ethyl acetate/*n*-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.34 (d, J = 8.1 Hz, 1H), 8.12 (d, J = 8.1 Hz, 1H), 7.95 (d, J = 7.5 Hz, 2H), 7.66 (two d's merged, J = 7.5, 7.8 Hz, 1H), 7.49 (t, J = 7.5 Hz, 2H), 7.35 (t, J = 7.5 Hz, 2H), 6.21 (s, 1H), 6.14 (d, J = 3.3 Hz, 1H), 4.88−4.84 (m, 2H), 4.72 (m, 2H), 1.36, 1.23 (each s, each 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 181.1, 165.9, 146.4, 133.1, 131.3, 130.8 (2C), 129.6 (2C), 129.2, 128.2, 126.2, 120.8, 114.5, 112.7, 104.9, 83.8, 82.8, 76.9, 61.3, 26.5, 26.1; IR (KBr) ν_{max} 1744, 1616, 1579, 1088, 1067, 1054, 986, 974, 734 cm^{-1}; MS m/z 456 $[M + H]^+$. Anal. Calcd for $C_{22}H_{21}N_3O_6S$: C, 58.01; H, 4.65; N, 9.23. Found: C, 57.61; H, 5.02; N, 9.54.

5-*O*-(Methyl-2,3-isopropylidine-β-D-ribofuranoside)-1*H*-benzo[*d*][1,2,3]triazole-1-carbothioate (3h). A stirring solution of compound **1h** (1.01 g, 4.94 mmol) in dry CH_2Cl_2 (10 mL) was added with **2**, pyridine (119 μL, 1.48 mmol), and Et_3N (137 μL, 0.99 mmol) under inert atmosphere: white solid, 1.5 g, yield 87%; mp 88−90 °C; R_f = 0.6 (30% ethyl acetate/*n*-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.43 (d, J = 8.4 Hz, 1H), 8.14 (d, J = 7.8 Hz, 1H), 7.68 (t, J = 7.5 Hz, 1H), 7.51 (t, J = 7.5 Hz, 1H), 5.08 (s, 1H), 4.70−4.91 (m, 3H), 4.43−4.50 (m, 2H), 3.35 (s, 3H), 1.53, 1.35 (each s, each 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.7, 182.5, 146.4, 130.6, 126.0, 120.6, 114.8, 112.6, 109.3, 85.0, 83.3, 81.6, 72.7, 55.0, 26.3, 24.8; IR (KBr) ν_{max} 1615, 1587, 1132, 1113, 976, 961, 954, 727 cm^{-1}; MS m/z 366 $[M + H]^+$. Anal. Calcd for $C_{16}H_{19}N_3O_5S$: C, 52.59; H, 5.24; N, 11.50. Found: C, 53.02; H, 5.62; N, 11.94.

5-*O*-(6-*O*-Benzoyl-3-*O*-benzyl-1,2-*O*-isopropylidine-α-D-glucofuranose)-1*H*-benzo[*d*][1,2,3]triazole-1-carbothioate (3i). A stirring solution of compound **1i** (910 mg, 2.20 mmol) in dry CH_2Cl_2 (10 mL) was added with **2** (738 mg, 2.63 mmol), pyridine (53 μL, 0.66 mmol), and Et_3N (61 μL, 0.44 mmol) under inert atmosphere: liquid, 947 mg, yield 75%; R_f = 0.7 (30% ethyl acetate/*n*-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.20 (d, J = 8.4 Hz, 1H), 8.01 (d, J = 8.1 Hz, 1H), 7.88 (d, J = 7.2 Hz, 2H), 7.51−7.25 (m, 5H), 7.10−7.01 (m, 3H), 6.87 (t, J = 7.2 Hz, 2H), 6.17 (s, 1H), 5.93 (s, 1H), 5.18−5.11 (m, 1H), 4.82 (m, 1H), 4.61 (m, 2H), 4.53 (d, J = 11.4 Hz, 1H), 4.27 (d, J = 11.4 Hz, 1H), 4.14 (s, 1H), 1.43, 1.26 (each s, each 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 181.2, 165.9, 146.3, 136.0, 133.0, 131.4, 130.3, 129.7, 129.5, 128.3, 128.2, 128.0, 127.7, 125.9, 120.4, 114.8, 112.2, 105.4, 81.7, 80.1, 77.4, 77.2, 71.8, 68.6, 62.6, 26.8, 26.2; IR (Nujol) ν_{max} 1739, 1631, 1588, 1121, 1103, 993, 972, 960, 853, 731 cm^{-1}; MS m/z 576 $[M + H]^+$. Anal. Calcd for $C_{30}H_{29}N_3O_7S$: C, 62.60; H, 5.08; N, 7.30. Found: C, 62.91; H, 5.47; N, 7.64.

6-*O*-(Methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside)-1*H*-benzo[*d*][1,2,3]triazole-1-carbothioate (3j). A stirring solution of compound **1j** (1.21 g, 2.60 mmol) in dry CH_2Cl_2 (10 mL) was added with **2** (874 mg, 3.12 mmol), pyridine (60 μL, 0.75 mmol). and Et_3N (72 μL, 0.52 mmol) under inert atmosphere: white solid, 1.3 g, yield 82%; mp 108−110 °C; R_f = 0.7 (30% ethyl acetate/*n*-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.33 (d, J = 8.1 Hz, 1H), 8.12 (d, J = 8.1 Hz, 1H), 7.55 (two d's merged, J = 7.8, 7.4 Hz, 1H), 7.48 (two d's merged, J = 7.8, 7.4 Hz, 1H), 7.37−7.04 (m, 15 H), 5.03 (d, J = 10.8 Hz, 1H), 4.87−4.71 (m, 5H), 4.71−4.61 (m, 3H), 4.06 (d, J = 8.7 Hz, 2H), 3.66 (d, J = 9.1 Hz, 1H), 3.61 (dd, J = 10.2, 9.3 Hz, 1H), 3.42 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 182.4, 146.3, 138.4, 137.9, 137.4, 131.2, 130.2, 128.4 (4C), 128.3 (4C), 128.1 (2C), 127.9 (2C), 127.7 (2C), 127.6, 125.8, 120.5, 114.7, 98.2, 82.1, 79.8, 76.4, 75.8, 74.8, 73.4, 71.5, 68.1, 55.5; IR (KBr) ν_{max} 1739, 1631, 1588, 1121, 1103, 993, 972, 960, 853, 731 cm^{-1}; MS m/z 626 $[M + H]^+$. Anal. Calcd for $C_{35}H_{35}N_3O_6S$: C, 67.18; H, 5.64; N, 6.72. Found: C, 67.64; H, 5.27; N, 7.03.

7-*O*-(3-*O*-Benzyl-5-benzylthio-5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-heptofuranuronose)-1*H*-benzo[*d*][1,2,3]triazole-1-carbothioate (3k). A stirring solution of compound **1k** (802 mg, 1.86 mmol) in dry CH_2Cl_2 (10 mL) was added with **2** (874 mg, 2.24 mmol), pyridine (60 μL, 0.56 mmol), and Et_3N (51 μL, 0.37 mmol) under inert atmosphere: white solid, 892 mg, yield 81%; mp 94−96 °C; R_f = 0.6 (30% ethyl acetate/*n*-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.24 (d, J = 8.1 Hz, 1H), 8.12 (d, J = 7.8 Hz, 1H), 7.57 (two d's merged, J = 7.2, 7.8 Hz, 1H), 7.46 (two d's merged, J = 7.5, 6.9 Hz, 1H), 7.27 (m, 5H), 7.09−7.02 (m, 5H), 5.94 (s, 1H), 4.91 (m, 1H), 4.71 (d, J = 11.7 Hz, 2H), 4.61−4.55 (m, 2H), 4.19−4.15 (m, 2H), 3.70 (s, 2H), 3.24 (m, 1H), 2.64 (m, 1H), 2.0 (m, 1H), 1.47, 1.31 (each s, each 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 182.9, 146.3, 138.2, 137.2, 130.3, 128.7 (2C), 128.4 (4C), 127.9 (2C), 127.6, 127.1 (2C),

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125.7, 120.4, 115.0, 111.6, 105.1, 83.0, 82.1, 81.3, 71.9, 71.4, 39.3, 34.9, 30.6, 26.7, 26.1; IR (KBr) ν_{max} 1734, 1640, 1580, 1127, 1110, 990, 970, 846, 737 cm^{-1}; MS m/z 592 $[M + H]^+$. Anal. Calcd for $C_{31}H_{33}N_3O_5S_2$: C, 62.92; H, 5.62; N, 7.10. Found: C, 63.35; H, 5.5.28; N, 7.57.

5-(1′*H*-Benzo[1′,2′,3′]triazol-1′-yl)-3-*O*-benzyl-5-deoxy-1,2-*O*-isopropylidene-α-D-glucofuranose (6) and 5-(2′*H*-Benzo-[1′,2′,3′]triazol-2′-yl)-3-*O*-benzyl-5-deoxy-1,2-*O*-*iso*propylidene-α-D-glucofuranose (7). A stirring solution of compound **5** (1.15 g, 3.73 mmol) in dry CH_2Cl_2 (12 mL) was added with **2** (1.25 g, 4.48 mmol), pyridine (90 μL, 1.12 mmol), and Et_3N (103 μL, 0.75 mmol) under inert atmosphere.

5-(1′*H*-Benzo[1′,2′,3′]triazol-1′-yl)-3-*O*-benzyl-5-deoxy-1,2-*O*-isopropylidene-α-D-glucofuranose (6): colorless crystals, mp 158−160 °C; R_f = 0.6 (30% ethyl acetate/*n*-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.15 (d, J = 8.4 Hz, 1H), 7.69 (d, J = 8.1 Hz, 1H), 7.61 (two d's merged, J = 6.9, 8.7 Hz, 1H), 7.50 (two d's merged, J = 7.8, 6.9 Hz, 1H), 7.19−7.09 (m, 3H), 6.91 (d, J = 7.2 Hz, 2H), 6.12 (d, J = 3.3 Hz, 1H), 5.56 (d, J = 3.3 Hz, 1H), 5.37 (d, J = 11.1 Hz, 1H), 5.28 (d, J = 11.1 Hz, 1H), 4.62 (d, J = 3.0 Hz, 1H), 4.40 (d, J = 10.8 Hz, 1H), 4.15 (d, J = 10.8 Hz, 1H), 4.14 (d, J = 2.7 Hz, 1H), 1.55, 1.35 (each s, each 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 187.9, 148.5, 135.7, 129.6, 128.4, 128.1, 125.3, 120.9, 113.2, 110.3, 105.9, 82.2, 81.8, 80.1, 73.0, 72.7, 27.1, 26.4; IR (KBr) ν_{max} 1610, 1589, 1108, 1075, 1025, 975, 926, 741, 696 cm^{-1}; MS m/z 470 $[M + H]^+$. Anal. Calcd for $C_{23}H_{23}N_3O_6S$: C, 58.84; H, 4.94; N, 8.95. Found: C, 58.55; H, 5.25; N, 9.31.

5-(2′*H*-Benzo[1′,2′,3′]triazol-2′-yl)-3-*O*-benzyl-5-deoxy-1,2-*O*-isopropylidene-α-D-glucofuranose (7): colorless crystals, mp 162−164 °C; R_f = 0.6 (30% ethyl acetate/*n*-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.81 (d, J = 6.6 Hz, 1H), 7.80 (d, J = 6.3 Hz, 1H), 7.45 (d, J = 6.6 Hz, 1H), 7.44 (d, J = 6.6 Hz, 1H), 76.95−6.84 (m, 3H), 6.62 (d, 2H), 6.13 (d, J = 2.7 Hz, 1H), 5.79 (d, J = 3.0 Hz, 1H), 5.69 (d, J = 10.5 Hz, 1H), 5.23 (d, J = 10.5 Hz, 1H), 4.67 (s, 1H), 4.34 (d, J = 11.7 Hz, 1H), 4.33 (s, 1H), 3.87 (d, J = 11.7 Hz, 1H), 1.62, 1.39 (each s, each 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.3, 144.5, 134.9, 128.27, 128.21, 128.1, 128.0, 118.8, 113.2, 106.0, 100.7, 81.6, 81.0, 80.0, 73.8, 72.0, 27.1, 26.4; IR (KBr) ν_{max} 1562, 1455, 1071, 1036, 994, 967, 876, 847, 753, 696, 641 cm^{-1}; MS m/z 470 $[M + H]^+$. Anal. Calcd for $C_{23}H_{23}N_3O_6S$: C, 58.84; H, 4.94; N, 8.95. Found: C, 58.47; H, 4.69; N, 8.62.

***O*-Cholesteryl-(1*H*-benzo[1′,2′,3′]triazol-1′-yl)-methanethione (9).** A stirring solution of compound **8** (1.50 g, 3.88 mmol) in dry CH_2Cl_2 (10 mL) was added with **2** (1.30 g, 4.66 mmol), pyridine (93 μL, 1.17 mmol), and Et_3N (108 μL, 0.78 mmol) under inert atmosphere: white crystals, 1.66 g, yield 78%; mp 170−172 °C; R_f = 0.7 (30% ethyl acetate/*n*-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.38 (d, J = 8.4 Hz, 1H), 8.13 (d, J = 8.1 Hz, 1H), 7.65 (two d's merged, J = 7.2, 7.8 Hz, 1H), 7.49 (t, J = 7.0 Hz, 1H), 5.50 (m, 2H), 2.72 (d, J = 7.5 Hz, 2H), 2.26 (m, 1H), 2.02−1.83 (m, 5H), 1.56−1.52 (m, 9H), 1.33−1.01 (m, 14H), 0.93 (d, J = 9.3 Hz, 3H), 0.87 (s, 3H), 0.85 (s, 3H), 0.73 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 182.2, 146.4, 138.6, 131.3, 130.2, 125.8, 123.8, 120.5, 114.9, 83.8, 56.6, 56.1, 49.9, 42.2, 39.6, 39.4, 37.3, 36.8, 36.6, 36.1, 35.7, 31.9, 31.8, 28.1, 27.9, 27.1, 24.2, 23.8, 22.7, 22.5, 21.0, 19.3, 18.7, 11.8; IR (KBr) ν_{max} 1611, 1070, 1021, 974, 723, 685 cm^{-1}; MS m/z 548 $[M + H]^+$. Anal. Calcd for $C_{34}H_{49}N_3OS$: C, 74.54; H, 9.02; N, 7.67. Found: C, 74.87; H, 9.41; N, 8.07.

Procedure for the Synthesis of Glycoconjugate Benzothiazoles (4a−k) and Compound 10. A stirring solution of benzotriazolemethanethione (**3a−k** and **9**) in toluene was added with stannanyl/silyl hydride (2.0 equiv) and AIBN (5 mol %) under inert atmosphere. The reaction was stirred under heating at 80 °C as well as exposure to microwave CEM Discover LabMate at 100 °C. After completion of the reaction (monitored by TLC), the reaction mixture was concentrated in vacuo, extracted with CH_2Cl_2, and washed with 10% LiOH, water, and brine solutions. After drying over anhydrous Na_2SO_4, the organic layer was concentrated in vacuo. Purification using flash column chromatography afforded glycoconjugate benzothiazoles.

6-*O*-(Benzothiazol-2′-yl)-1,2:3,4-di-*O*-isopropylidine-α-D-galactopyranose (4a). A stirring solution of **3a** (400 mg, 0.95 mmol) in toluene was added with tributyltin hydride (0.55 mL, 1.90 mmol) and AIBN (5 mol %) under inert atmosphere: white crystals, 365 mg, yield 98%; mp 100−102 °C; R_f = 0.8 (20% ethyl acetate/*n*-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (t, J = 8.7 Hz, 2H), 7.34 (dd, J = 7.2, 7.5 Hz, 1H), 7.22 (two d's merged, J = 7.5, 7.2 Hz, 1H), 5.57 (d, J = 4.8 Hz, 1H), 4.79−4.73 (m, 3H), 4.69−4.64 (m, 3H), 1.48, 1.48, 1.35, 1.32 (each s, each 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.5, 149.1, 132.0, 125.8, 123.4, 121.2, 120.8, 109.6, 108.8, 96.3, 70.9, 70.6, 70.4, 70.2, 65.5, 25.9, 25.9, 24.9, 24.4; IR (KBr) ν_{max} 1597, 1536, 1067, 1007, 959, 891, 728, 692, 650 cm^{-1}; MS m/z 394 $[M + H]^+$. Anal. Calcd for $C_{19}H_{23}NO_6S$: C, 58.00; H, 5.89; N, 3.56. Found: C, 58.29; H, 5.51; N, 3.33.

3-*O*-(Benzothiazol-2′-yl)-1,2;5,6-di-*O*-isopropylidine-α-D-glucofuranose (4b). A stirring solution of **3b** (10.0 g, 23.72 mmol) in toluene was added with tributyltin hydride (12.76 mL, 47.45 mmol) and AIBN (5 mol %) under inert atmosphere: liquid, 8.86 g, yield 95%; R_f = 0.7 (20% ethyl acetate/*n*-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 (d, J = 9.1 Hz, 1H), 7.64 (d, J = 9.1 Hz, 1H), 7.37 (t, J = 7.5 Hz, 1H), 7.24 (t, J = 7.5 Hz, 1H), 5.95 (d, J = 3.6 Hz, 1H), 5.63 (d, J = 2.4 Hz, 1H), 4.83 (d, J = 3.6 Hz, 1H), 4.32−4.45 (m, 2H), 4.05−4.15 (m, 2H), 1.56, 1.42, 1.33, 1.30 (each s, each 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.1, 149.0, 132.0, 126.0, 123.8, 121.0, 112.3, 109.3, 105.0, 82.9, 82.6, 79.8, 72.2, 67.0, 26.8, 26.7, 26.2, 25.2; IR (Nujol) ν_{max} 1598, 1535, 1075, 1021, 845, 756, 644 cm^{-1}; MS m/z 394 $[M + H]^+$. Anal. Calcd for $C_{19}H_{23}NO_6S$: C, 58.00; H, 5.89; N, 3.56. Found: C, 58.35; H, 6.22; N, 3.91.

3-*O*-(Benzothiazol-2′-yl)-1,2:5,6-di-*O*-isopropylidine-α-D-allofuranose (4c). A stirring solution of **3c** (300 mg, 0.71 mmol) in toluene was added with tributyltin hydride (0.38 mL, 1.42 mmol) and AIBN (5 mol %) under inert atmosphere: white solid, 268 mg, yield 96%; mp 78−80 °C; R_f = 0.6 (20% ethyl acetate/*n*-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 (t, J = 8.7 Hz, 2H), 7.35 (d, J = 7.5 Hz, 1H), 7.25 (d, J = 7.2, 1H), 5.90 (d, J = 3.3, 1H), 5.38 (dd, J = 5.1, 8.4 Hz, 1H), 5.13 (t, J = 4.2, 1H), 4.40−4.32 (m, 2H), 4.09 (d, J = 6.6 Hz, 1H), 4.00 (d, J = 5.7 Hz, 1H), 1.59, 1.39, 1.33, 1.33 (each s, each 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.2, 148.9, 132.3, 125.9, 123.7, 121.3, 121.0, 113.3, 109.9, 104.0, 78.3, 77.5, 77.4, 74.9, 65.4, 26.6, 26.1, 25.0; IR (KBr) ν_{max} 1596, 1536, 1073, 1023, 851, 755, 639 cm^{-1}; MS m/z 394 $[M + H]^+$. Anal. Calcd for $C_{19}H_{23}NO_6S$: C, 58.00; H, 5.89; N, 3.56. Found: C, 57.73; H, 6.23; N, 3.17.

5-*O*-(Benzothiazol-2′-yl)-3-*O*-benzyl-1,2-*O*-isopropylidine-α-D-xylofuranose (4d). A stirring solution of **3d** (400 mg, 0.91 mmol) in toluene was added with tributyltin hydride (0.49 mL, 1.81 mmol) and AIBN (5 mol %) under inert atmosphere: liquid, 352 mg, yield 94%; R_f = 0.7 (20% ethyl acetate/*n*-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (d, J = 8.1 Hz, 1H), 7.62 (d, J = 7.8 Hz, 1H), 7.37−7.19 (m, 7H), 6.00 (d, J = 3.6 Hz, 1H), 4.88 (dd, 1H), 4.79 (d, J = 6.6 Hz, 1H), 4.74 (d, J = 12.9 Hz, 1H), 4.68−4.64 (m, 2H), 4.54 (d, J = 12.0 Hz, 1H), 4.08 (d, J = 3.0 Hz, 1H), 1.50, 1.33 (each s, each 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.3, 149.1, 137.0, 132.0, 128.4, 127.9, 127.7, 125.9, 123.5, 121.2, 120.8, 111.9, 105.2, 82.1, 81.5, 77.9, 71.9, 68.9, 26.8, 26.2; IR (Nujol) ν_{max} 1598, 1537, 1113, 1067, 968, 912, 784, 737, 649 cm^{-1}; MS m/z 414 $[M + H]^+$. Anal. Calcd for $C_{22}H_{23}NO_5S$: C, 63.91; H, 5.61; N, 3.39. Found: C, 64.27; H, 5.29; N, 3.62.

5-*O*-(Benzothiazol-2′-yl)-3-*O*-benzyl-1,2-*O*-isopropylidine-α-D-ribofuranose (4e). A stirring solution of **3e** (400 mg, 0.91 mmol) in toluene was added with tributyltin hydride (0.49 mL, 1.81 mmol) and AIBN (5 mol %) under inert atmosphere: liquid, 355 mg, yield 95%; R_f = 0.7 (20% ethyl acetate/*n*-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.67 (d, J = 8.1 Hz, 1H), 7.63 (d, J = 7.8 Hz, 1H), 7.39−7.20 (m, 7H), 5.79 (d, J = 3.3 Hz, 1H), 4.83−4.75 (m, 2H), 4.66 (dd, J = 4.2, 11.7 Hz, 1H), 4.61 (dd, J = 3.6, 7.5 Hz, 1H), 4.56 (d, J = 11.7 Hz, 1H), 4.39 (d, J = 6.6 Hz, 1H), 3.85 (dd, J = 4.2, 9.0 Hz, 1H), 1.63, 1.38 (each s, each 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.5, 149.0, 137.1, 132.0, 128.4, 127.9, 125.9, 123.5, 121.2, 120.8, 113.2, 104.2, 72.3, 69.4, 26.8, 26.5; IR (Nujol) ν_{max} 1596, 1531, 1107, 1055, 914, 774, 736, 650

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cm^{-1}; MS m/z 414 [M + H]$^+$. Anal. Calcd for $C_{22}H_{23}NO_5S$: C, 63.91; H, 5.61; N, 3.39. Found: C, 63.46; H, 5.98; N, 3.83.

5-*O*-Benzyl-3-*O*-(benzothiazol-2′-yl)-1,2-*O*-isopropylidine-α-D-xylofuranose (4f). A stirring solution of **3f** (364 mg, 0.82 mmol) in toluene was added with tributyltin hydride (0.48 mL, 1.65 mmol) under inert atmosphere: liquid, 330 mg, yield 97%; R_f = 0.7 (20% ethyl acetate/hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63 (d, J = 7.8 Hz, 1H), 7.54 (d, J = 7.8 Hz, 1H), 7.28 (two d's merged, J = 7.8, 7.5 Hz, 1H), 7.14 (m, 6H), 5.91 (s, 1H), 5.60 (s, 1H), 4.72 (s, 1H), 4.51−4.70 (m, 2H), 4.36 (d, J = 12.0 Hz, 1H), 3.71 (two d's merged, J = 2.4, 2.7 Hz, 2H), 1.47, 1.24 (each s, each 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.1, 148.9, 137.6, 132.0, 128.2 (2C), 127.6 (2C), 127.6, 126.0, 123.8, 121.3, 121.2, 112.2, 104.8, 83.0, 82.7, 78.2, 73.5, 66.9, 26.6, 26.2; IR (Nujol) ν_{max} 1598, 1530, 1097, 1046, 923, 761, 732, 644 cm^{-1}; MS m/z 414 [M + H]$^+$. Anal. Calcd for $C_{22}H_{23}NO_5S$: C, 63.91; H, 5.61; N, 3.39. Found: C, 64.25; H, 5.95; N, 3.66.

5-*O*-Benzoyl-3-*O*-(benzothiazol-2′-yl)-1,2-*O*-isopropylidine-α-D-xylofuranose (4g). A stirring solution of **3g** (352 mg, 1.20 mmol) in toluene was added with tributyltin hydride (0.70 mL, 2.40 mmol) and AIBN (5 mol %) under inert atmosphere: white solid, 313 mg, yield 95%; mp 78−80 °C; R_f = 0.7 (20% ethyl acetate/n-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.92 (d, J = 8.1 Hz, 2H),7.61−7.42 (m, 3H), 7.36−7.29 (m, 3H), 7.18−7.14 (m, 1H), 5.99 (d, J = 2.7 Hz, 1H), 5.72 (s, 1H), 4.80 (d, J = 2.7 Hz, 1H), 4.69 (m, 1H), 4.57 (d, J = 5.7 Hz, 2H), 1.50, 1.33 (each s, each 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.1, 166.0, 148.7, 133.0, 132.0, 129.7, 129.5, 128.5, 128.2, 126.1, 123.9, 121.3, 112.4, 105.0, 83.0, 82.8, 77.1, 61.3, 26.5, 26.1; IR (KBr) ν_{max} 1733, 1595, 1531, 1102, 987, 911, 749, 756, 645 cm^{-1}; MS m/z 428 [M + H]$^+$. Anal. Calcd for $C_{22}H_{21}NO_6S$: C, 61.82; H, 4.95; N, 3.28. Found: C, 61.40; H, 5.34; N, 3.73.

Methyl 5-*O*-(Benzothiazol-2′-yl)-2,3-*O*-isopropylidine-β-D-ribofuranoside (4h). A stirring solution of **3h** (408 mg, 1.12 mmol) in toluene was added with tributyltin hydride (0.60 mL, 2.23 mmol) and AIBN (5 mol %) under inert atmosphere: liquid, 361 mg, yield 96%; R_f = 0.7 (20% ethyl acetate/n-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (two d's merged, J = 8.1, 8.2 Hz, 2H), 7.36 (t, J = 7.4 Hz, 1H), 7.22 (t, J = 7.8 Hz, 1H), 5.03 (s, 1H), 4.79 (d, 1H), 4.59−4.67 (m, 4H), 3.34 (s, 3H), 1.34, 1.50 (each s, each 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.3, 149.0, 132.0, 125.9, 123.6, 121.2, 120.9, 112.6, 109.4, 85.1, 83.9, 81.7, 71.4, 55.0, 26.4, 24.9; IR (Nujol) ν_{max} 1733, 1595, 1531, 1102, 987, 911, 749, 756, 645 cm^{-1}; MS m/z 338 [M + H]$^+$. Anal. Calcd for $C_{16}H_{19}NO_5S$: C, 56.96; H, 5.68; N, 4.15. Found: C, 57.42; H, 5.36; N, 3.72.

6-*O*-Benzoyl-5-*O*-(benzothiazol-2′-yl)-3-*O*-benzyl-1,2-*O*-isopropylidine-α-D-glucofuranose (4i). A stirring solution of **3i** (381 mg, 0.66 mmol) in toluene was added with tributyltin hydride (0.36 mL, 1.32 mmol) and AIBN (5 mol %) under inert atmosphere: liquid, 347 mg, yield 96%; R_f = 0.8, 20% ethyl acetate/n-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 (d, J = 7.2 Hz, 2H), 7.60−7.59 (m, 2H), 7.47 (m, 1H), 7.35−7.19 (m, 5H), 7.11−7.01 (m, 4H), 5.97 (s, 2H), 5.13 (d, J = 12.6 Hz, 1H), 4.66−4.56 (m, 4H), 4.38 (d, J = 11.1 Hz, 1H), 4.14 (s, 1H), 1.51, 1.34 (each s, each 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.4, 166.0, 149.0, 136.6, 132.8, 132.0, 129.9, 129.7, 129.6, 128.3, 128.2, 128.1, 127.9, 127.8, 125.9, 123.5, 121.1 (2C), 112.1, 105.4, 81.8, 81.0, 77.8, 75.8, 72.3, 63.6, 26.8, 26.3; IR (Nujol) ν_{max} 1742, 1596, 1530, 1114, 1075, 970, 911, 755, 736, 688, 642 cm^{-1}; MS m/z 548 [M + H]$^+$. Anal. Calcd for $C_{30}H_{29}NO_7S$: C, 65.80; H, 5.34; N, 2.56. Found: C, 65.47; H, 4.97; N, 2.15.

Methyl 6-*O*-(Benzothiazol-2′-yl)-2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (4j). A stirring solution of **3j** (402 mg, 0.64 mmol) in toluene was added with tributyltin hydride (0.35 mL, 1.28 mmol) and AIBN (5 mol %) under inert atmosphere: white crystals, 357 mg, yield 92%; mp 88−90 °C; R_f = 0.8 (20% ethyl acetate/n-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (two d's merged, J = 8.7 Hz, 2H), 7.35−7.23 (m, 17H), 5.01 (d, J = 10.8 Hz, 1H), 4.89−4.66 (m, 4H), 4.69−4.55 (m, 4H), 4.04 (t, J = 9.3 Hz, 1H), 3.95 (d, J = 9.9 Hz, 1H), 3.67- 3.57 (m, 2H), 3.39 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.5, 149.0, 138.5, 137.7, 131.9, 128.4 (4C), 128.3 (2C), 128.1 (2C), 128.0 (2C), 127.9 (2C), 127.8 (4C), 127.6, 125.9, 123.5, 121.2, 120.8, 98.1, 82.0, 79.8, 75.7, 75.1, 73.4, 70.0, 68.8, 55.3; IR (KBr) ν_{max} 1596, 1564, 1534, 1115, 1065, 1013, 751, 738, 696, 653 cm^{-1}; MS m/z 598 [M + H]$^+$; Anal. Calcd for $C_{35}H_{35}NO_6S$: C, 70.33; H, 5.90; N, 2.34; Found: C, 70.68; H, 6.27; N, 1.95.

7-*O*-(Benzothiazol-2′-yl)-3-*O*-benzyl-5-benzylthio-5,6-dideoxy-1,2-*O*-isoproyledene-α-D-*xylo*-heptofuranuronose (4k). A stirring solution of **3k** (400 mg, 0.68 mmol) in toluene was added with tributyltin hydride (0.36 mL, 1.35 mmol) and AIBN (5 mol %) under inert atmosphere. Liquid, 358 mg, yield 94%; R_f = 0.8 (20% ethyl acetate/n-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 (d, J = 8.1 Hz, 1H), 7.62 (d, J = 8.4 Hz, 1H), 7.24−7.08 (m, 12H), 5.89 (s, 1H), 4.68−4.54 (m, 5H), 4.12−4.08 (m, 2H), 3.73 (s, 2H), 3.23 (m, 1H), 2.47 (m, 1H), 2.07 (m, 1H), 1.45, 1.29 (each s, each 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.6, 149.3, 138.3, 137.3, 131.8, 128.7 (2C), 128.4 (4C), 127.8, 127.7 (2C), 126.9, 125.7, 123.2, 121.1, 120.6, 111.4, 105.0, 82.7, 82.2, 81.3, 72.1, 69.5, 39.7, 34.5, 30.7, 26.7, 26.1; IR (Nujol) ν_{max} 1597, 1529, 1118, 1095, 978, 932, 784, 764, 736, 654 cm^{-1}; MS m/z 564 [M + H]$^+$. Anal. Calcd for $C_{31}H_{33}NO_5S_2$: C, 66.05; H, 5.90; N, 2.48. Found: C, 65.72; H, 6.27; N, 2.07.

***O*-Cholesteryl Benzothiazole (10).** A stirring solution of **9** (407 mg, 0.74 mmol) in toluene was added with tributyltin hydride (0.40 mL, 1.49 mmol) and AIBN (5 mol %) under inert atmosphere: white crystals, 370 mg, yield 95%; mp 106−108 °C; R_f = 0.7 (20% ethyl acetate/n-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.63 (two d's merged, J = 8.7, 9.0 Hz, 2H), 7.33 (t, J = 7.5 Hz, 1H), 7.18 (two d's merged, J = 7.8, 7.2 Hz, 1H), 5.45 (m, 1H), 5.01 (m, 1H), 2.68−2.64 (m, 1H), 2.53−2.45 (m, 1H), 2.16 (m, 1H), 2.04−1.69 (m, 5H), 1.57−0.85 (m, 32H), 0.68 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.2, 149.6, 139.3, 131.7, 125.8, 123.1, 123.1, 121.1, 120.6, 81.7, 56.6, 56.1, 50.0, 42.3, 39.7, 39.5, 38.1, 37.9, 36.6, 36.1, 35.7, 31.9, 31.8, 28.2, 28.0, 27.8, 24.2, 23.8, 22.8, 22.5, 22.0, 19.3, 18.7, 11.8; IR (KBr) ν_{max} 1597, 1529, 1112, 1070, 731, 651 cm^{-1}; MS m/z 520 [M + H]$^+$. Anal. Calcd for $C_{34}H_{49}NOS$: C, 78.56; H, 9.51; N, 2.70. Found: C, 78.32; H, 9.19; N, 2.32.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra for all the new compounds and X-ray crystallographic data for **3a**, **4a**, **6**, **7**, and **10** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ DEDICATION

Dedicated to Prof. Alan R. Katritzky, Director, Centre for Heterocyclic Compounds, University of Florida, Gainesville, FL

■ REFERENCES

(1) (a) Katritzky, A. R.; Rachwal, S.; Rachwal, B. *J. Chem. Soc., Perkin Trans. 1* **1987**, 805. (b) Katritzky, A. R.; Kuzmierkiewicz, W. *J. Chem. Soc., Perkin Trans. 1* **1987**, 819. (c) Katritzky, A. R.; Drewniak, M. *J. Chem. Soc., Perkin Trans. 1* **1988**, 2339. (d) Katritzky, A. R.; Lan, X. F.; Yang, J. Z.; Denisko, O. V. *Chem. Rev.* **1998**, *98*, 409. (e) Katritzky, A. R.; Rachwal, S. *Chem. Rev.* **2010**, *110*, 1564. (f) Katritzky, A. R.; Rachwal, S. *Chem. Rev.* **2011**, *111*, 7063.

(2) Kale, R. R.; Prasad, V.; Mohapatra, P. P.; Tiwari, V. K. *Monatsh. Chem.* **2010**, *141*, 1159.
(3) (a) Katritzky, A. R.; Kim, M. S.; Widyana, K. *ARKIVOC* **2008**, *iii*, 91. (b) Verma, A. K.; Singh, J.; Sankar, V. K.; Chaudhary, R.; Chandra, R. *Tetrahedron Lett.* **2007**, *48*, 4207. (c) Verma, A. K.; Singh, J.; Chaudhary, R. *Tetrahedron Lett.* **2007**, *48*, 7199. (d) Verma, A. K.; Kesharwani, T.; Singh, J.; Tandon, V.; Larock, R. C. *Angew. Chem., Int. Ed.* **2009**, *48*, 1138.
(4) (a) Katritzky, A. R.; Yang, B.; Jiang, J.; Steel, P. J. *J. Org. Chem.* **1995**, *60*, 246. (b) Katritzky, A. R.; Zhang, G.; Jiang, J.; Steel, P. J. *J. Org. Chem.* **1995**, *60*, 7625. (c) Nakamura, I.; Nemoto, T.; Shiraiwa, N.; Terada, M. *Org. Lett.* **2009**, *11*, 1055. (d) Katritzky, A. R.; Huang, T. B.; Denisko, O. V.; Steel, P. J. *J. Org. Chem.* **2002**, *67*, 3118. (e) Al-Awadi, N. A.; George, B. J.; Dib, H. H.; Ibrahim, M. R.; Ibrahim, Y. A.; El-Dusouqui, O. M. E. *Tetrahedron* **2005**, *61*, 8257. (f) Katritzky, A. R.; Witek, R. M.; Rodriguez-Garcia, V.; Mohapatra, P. P.; Rogers, J. W.; Cusido, J.; Abdel-Fattah, A. A. A.; Steel, P. J. *J. Org. Chem.* **2005**, *70*, 7866.
(5) (a) Yogeeswari, P.; Sriram, D.; Ramamoorthy, L.; Sunil, J. J.; Satish, K. S.; Stables, J. P. *Eur. J. Med. Chem.* **2002**, *37*, 231. (b) Mishra, B. B.; Tiwari, V. K. *Eur. J. Med. Chem.* **2011**, *46*, 4769.
(6) (a) Tanaka, K.; Kumagai, T.; Aoki, H.; Deguchi, M.; Iwata, S. *J. Org. Chem.* **2001**, *66*, 7328. (b) Yu, G.; Yin, S.; Liu, Y.; Shuai, Z.; Zhu, D. *J. Am. Chem. Soc.* **2003**, *125*, 14816. (c) Reddy, P. V. G.; Lin, Y.-W.; Chang, H.-T. *ARKIVOC* **2007**, *xvi*, 113. (d) Lu, Y.-J.; Yan, S.-C.; Chan, F.-Y.; Zou, L.; Chung, W.-H.; Wong, W.-L.; Qiu, B.; Sun, N.; Chan, P.-H.; Huang, Z.-S.; Gu, L.-Q.; Wong, K.-Y. *Chem. Commun.* **2011**, *47*, 4971.
(7) (a) Satish, G.; Reddy, K. H. V.; Ramesh, K.; Karnakar, K.; Nageswar, Y. V. D. *Tetrahedron Lett.* **2012**, *53*, 2518. (b) Massari, S.; Daelemans, D.; Barreca, M. L.; Knezevich, A.; Sabatini, S.; Cecchetti, V.; Marcello, A.; Pannecouque, C.; Tabarrini, O. *J. Med. Chem.* **2010**, *53*, 641. (c) Stewart, G. W.; Baxter, C. A.; Cleator, E.; Sheen, F. J. *J. Org. Chem.* **2009**, *74*, 3229. (d) Caleta, I.; Kralj, M.; Marjanovic, M.; Bertosa, B.; Tomic, S.; Pavlovic, G.; Zamola, G. K. *J. Med. Chem.* **2009**, *52*, 1744.
(8) Ben-Alloum, A.; Bakkas, S.; Soufiaoui, M. *Tetrahedron Lett.* **1997**, *38*, 6395.
(9) (a) Thiel, O. R.; Bernard, C.; King, T.; Dilmeghani-Seran, M.; Bostick, T.; Larsen, R. D.; Faul, M. M. *J. Org. Chem.* **2008**, *73*, 3508. (b) Bose, D. S.; Idrees, M.; Srikanth, B. *Synthesis* **2007**, 819. (c) Wang, M.; Gao, M.; Mock, B. H.; Miller, K. D.; Sledge, G. W.; Hutchins, G. D.; Zheng, Q.-H. *Bioorg. Med. Chem.* **2006**, *14*, 8599.
(10) (a) Bose, D. S.; Idrees, M. *J. Org. Chem.* **2006**, *71*, 8261. (b) Paul, S.; Gupta, M.; Gupta, R. *Synth. Commun.* **2002**, *32*, 3541.
(11) Roe, A.; Tucker, W. P. *J. Heterocycl. Chem.* **1965**, *2*, 148.
(12) Stanetty, P.; Krumpark, B. *J. Org. Chem.* **1996**, *61*, 5130.
(13) Majo, V. J.; Prabhakaran, J.; Mann, J. J.; Kumar, J. S. D. *Tetrahedron Lett.* **2003**, *44*, 8535.
(14) (a) Vera, M. D.; Pelletier, J. C. *J. Comb. Chem.* **2007**, *9*, 569. (b) Evindar, G.; Batey, R. A. *J. Org. Chem.* **2006**, *71*, 1802. (c) Joyce, L. L.; Evindar, G.; Batey, R. A. *Chem. Commun.* **2004**, 446. (d) Inamoto, K.; Hasegawa, C.; Hiroya, K.; Doi, T. *Org. Lett.* **2008**, *10*, 5147.
(15) (a) Tiwari, V. K.; Mishra, R. C.; Sharma, A.; Tripathi, R. P. *Mini-Rev. Med. Chem.* **2012**, *12*, 1497. (b) Varki, A. *Glycobiology* **1993**, *3*, 97. (c) Yu, H.; Cheng, J.; Ding, L.; Khedri, Z.; Chen, Y.; Lau, K.; Tiwari, V. K.; Chen, X. *J. Am. Chem. Soc.* **2009**, *131*, 18467. (d) Tiwari, V. K.; Kumar, A.; Schmidt, R. R. *Eur. J. Org. Chem.* **2012**, 2945.
(16) (a) Tiwari, V. K.; Singh, A.; Hussain, H. A.; Mishra, B. B.; Tripathi, V. *Monatsh. Chem.* **2007**, *138*, 653. (b) Tiwari, V. K.; Singh, D. D.; Hussain, H. A.; Mishra, B. B.; Singh, A. *Monatsh. Chem.* **2008**, *139*, 43. (c) Tiwari, V. K.; Kale, R. R.; Mishra, B. B.; Singh, A. *Arkivoc* **2008**, *xiv*, 27. (d) Kale, R. R.; Hussain, H. A.; Prasad, V.; Tiwari, V. K. *Tetrahedron Lett.* **2010**, *51*, 5740. (e) Kale, R. R.; Prasad, V.; Tiwari, V. K. *Lett. Org. Chem.* **2010**, *7*, 136. (f) Kale, R. R.; Prasad, V.; Tiwari, V. K. *Synlett* **2011**, 195. (g) Kale, R. R.; Prasad, V.; Kushwaha, D.; Tiwari, V. K. *J. Carbohydr. Chem.* **2012**, *31*, 130.
(17) Sheldrick, G. M. *Acta Crystallogr.* **2008**, *A64*, 112.
(18) (a) Cole, S. J.; Kirwan, J. N.; Roberts, B. P.; Willis, C. R. *J. Chem. Soc., Perkin Trans. 1* **1991**, 103. (b) Chatgilialoglu, C. *Chem. Rev.* **1995**, *95*, 1229.
(19) (a) Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc., Perkin Trans. 1* **1976**, 1574. (b) Haskell, T. H.; Woo, P. W. K.; Watson, D. R. *J. Org. Chem.* **1977**, *42*, 1302. (c) Yu, H.; Cao, H.; Tiwari, V. K.; Li, Y.; Chen, X. *Bio-Org. Med. Chem. Lett.* **2011**, *21*, 5037. (d) Postigo, A.; Kopsov, S.; Ferreri, C.; Chatgilialoglu, C. *Org. Lett.* **2007**, *9*, 5159. (e) Muramatsu, W.; Tanigawa, S.; Takemoto, Y.; Yoshimatsu, H.; Onomura, O. *Chem.—Eur. J.* **2012**, *18*, 4850.
(20) (a) Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1574. (b) Barton, D. H. R.; Motherwell, W. B.; Stange, A. S. *Synthesis* **1981**, 743.
(21) (a) Scaiano, J. C.; Ingold, K. U. *J. Am. Chem. Soc.* **1976**, *98*, 4727. (b) Forrest, D.; Ingold, K. U. *J. Am. Chem. Soc.* **1978**, *100*, 3868.
(22) (a) Bajza, I.; Borbas, A.; Liptak, A. In *Comprehensive Glycoscience*; Kamerling, J. P., Ed.; Elsevier Science: New York, 2007; Vol. *1*, pp 203−259. (b) Mancuso, A. J.; Huang, S.-L.; Swern, D. *J. Org. Chem.* **1978**, *43*, 2480. (c) Gregorio, S. C.; Hernandez, L.; Vargas, M.; Quintero, L.; Piscil, F. S. *J. Mex. Chem. Soc.* **2005**, *49*, 20. (d) Schworer, C. J.; Oberthur, M. *Eur. J. Org. Chem.* **2009**, *35*, 6129. (e) Enholm, E. J.; Gallagher, M. E.; Jiang, S.; Batson, W. A. *Org. Lett.* **2000**, *21*, 3355. (f) Alper, P. B.; Hendrix, M.; Sears, P.; Wong, C.-H. *J. Am. Chem. Soc.* **1998**, *9*, 1965. (g) Follmann, H.; Hogenkamp, H. P. C. *J. Am. Chem. Soc.* **1970**, *3*, 671. (h) Schmidt, R. R.; Gohl, A.; Karg, J. *Eur. J. Org. Chem.* **1979**, *5*, 1705. (i) Goda, S. K.; Al-Feel, W.; Akhtar, M. *J. Chem. Soc., Perkin Trans. 1* **1986**, 1383.
(23) (a) Tiwari, V. K.; Singh, B. K.; Chaturvedi, V.; Manju, Y. K.; Srivatava, A. K.; Sinha, S.; Gaikwad, A.; Tripathi, R. P. *Org. Chem. Ind. J.* **2007**, *3*, 84. (b) Singh, A.; Mishra, B. B.; Kale, R. R.; Kushwaha, D.; Tiwari, V. K. *Synth. Commun.* **2012**, *42*, 3598.