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Synthesis of Glycoconjugate Benzothiazoles *via* Cleavage of Benzotriazole Ring

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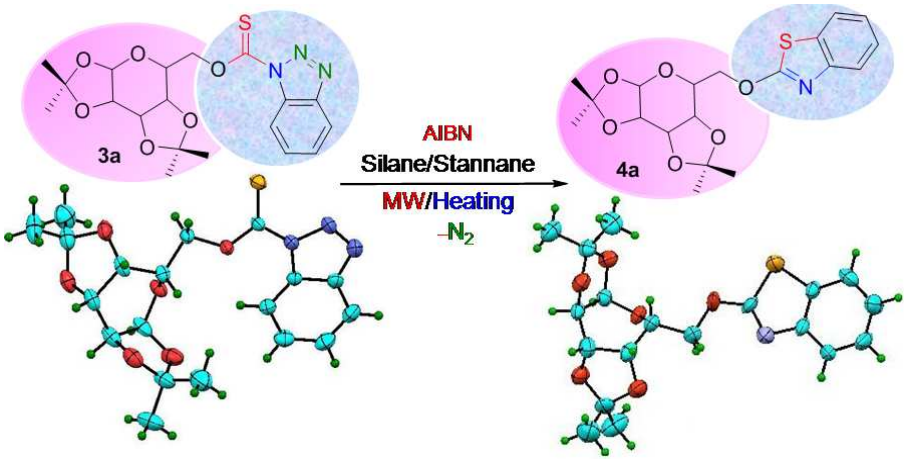


Abstract: A concise and efficacious benzotriazole mediated novel two-step protocol has been developed for an easy access to glycoconjugate benzothiazoles from protected carbohydrates. The benzotriazolemethanethione **3**, prepared by the reaction of free alcohol with *bis*(1*H*-benzo[1,2,3]triazol-1-yl)methanethione, 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. Structure of all the compounds has been elucidated using IR, NMR, MS and elemental analysis, where five of them have been characterized by single crystal X-ray analysis.

Keywords: benzotriazole, cyclization, elimination, glycoconjugate, benzothiazoles, heterocycle

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

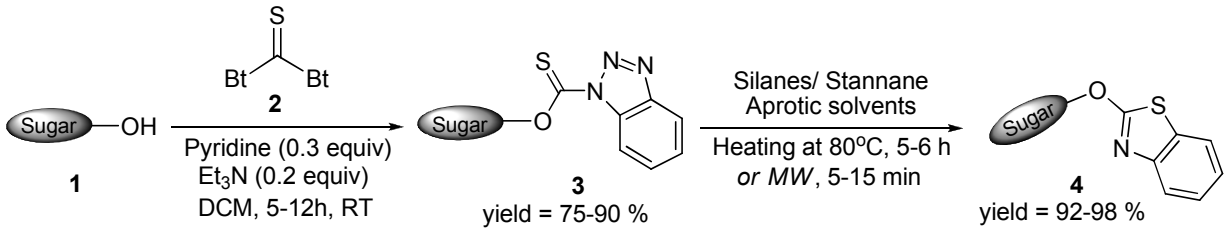
INTRODUCTION

Benzotriazole methodology, a versatile, useful, and one of the most successful synthetic protocol investigated so far, has now 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 provide an easy access to benzothiazoles.[14] However, the pre-functionalization 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*-substitued glycoconjugate benzothiazoles **4** from carbohydrate based benzotriazolemethanethiones **3**, readily prepared from protected sugars **1** using benzotriazole as a synthetic auxiliary (Scheme 1).



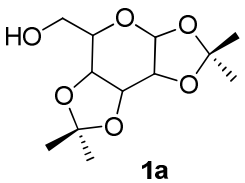
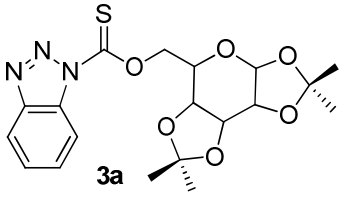
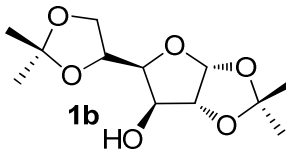
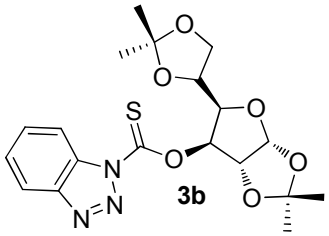
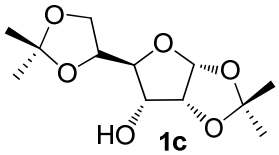
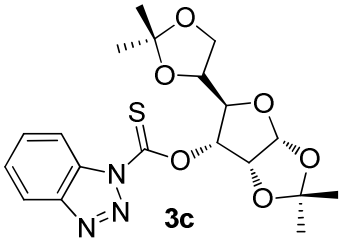
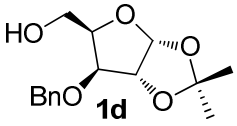
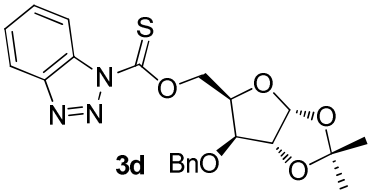
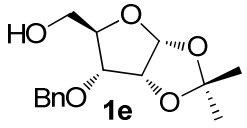
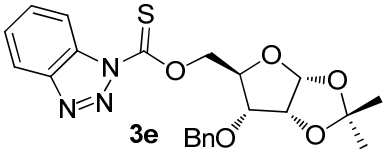
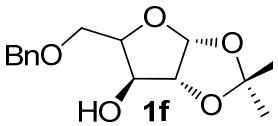
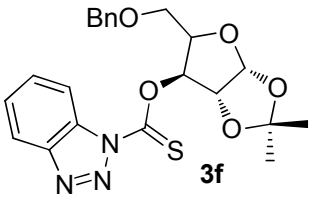
Scheme 1. The reaction of protected sugars **1** with *bis*(1*H*-benzo[1,2,3]triazol-1-yl)methanethione **2**

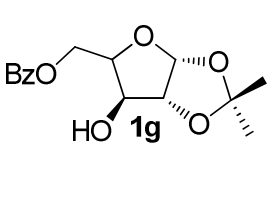
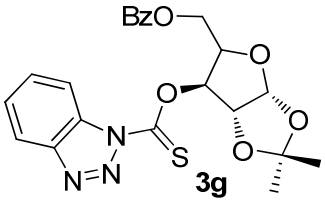
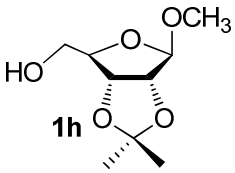
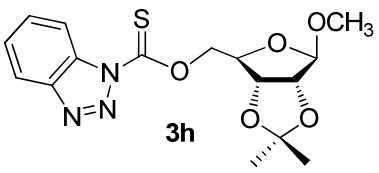
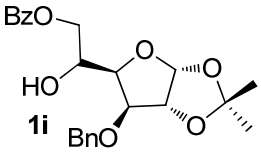
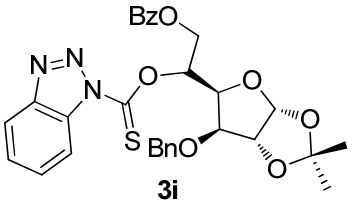
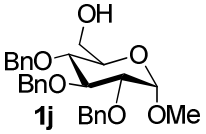
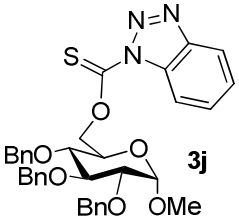
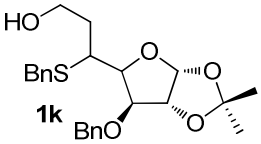
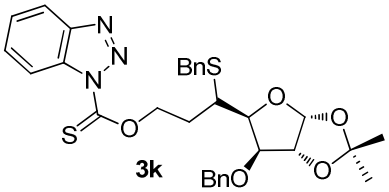
RESULTS AND DISCUSSION

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 significant 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).

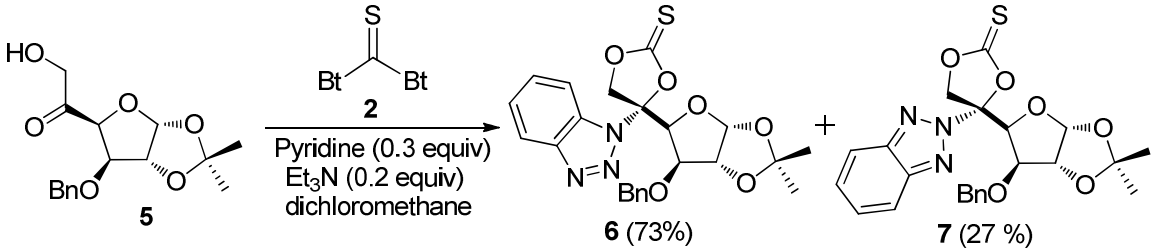
Table 1. Synthesis of carbohydrate based benzotriazolemethanethiones **3a-k**

entry[a]	substrate	product[b]	time (h)[c]	yield (%)[d]
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			10	82
8			5	87
9			24	75
10			6	82
11			6	81

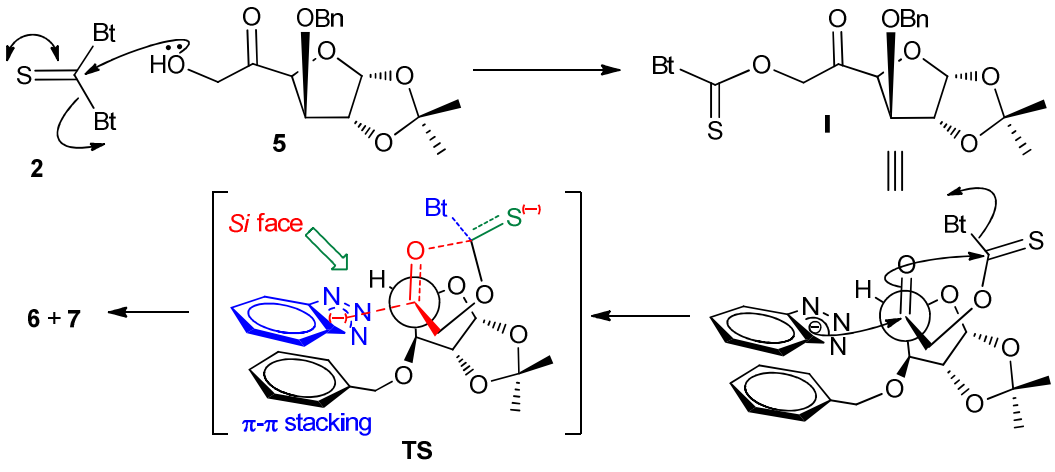
[a]Molar ratios: protected sugar, Et_3N, *bis*-benzotriazole methanethiones. [b]Carbohydrate based benzotriazolemethanethiones. [c]Reaction time. [d]Yield reported after purification by column chromatography.

However, reaction of 3-*O*-benzyl-1,2-*O*-isopropylidene-*α*-D-*xylo*-hexofuranos-5-ulose **5** with compound **2** to access 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).



Scheme 2. Reaction of 3-*O*-benzyl-1,2-*O*-isopropylidene-*α*-D-*xylo*-hexofuranos-5-ulose **5** with compound **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** & **7** were elucidated using extensive spectral studies (IR, ^{1}H, and ^{13}C NMR) and single crystal X-ray analysis (see the Supporting Information, Figure S2 and S3).



Scheme 3. The plausible mechanism for the formation of regioisomers **6** & **7**

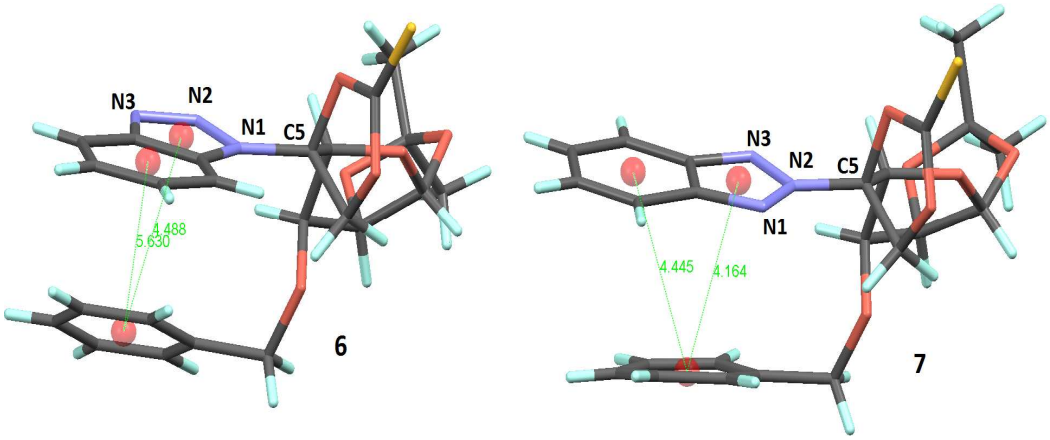
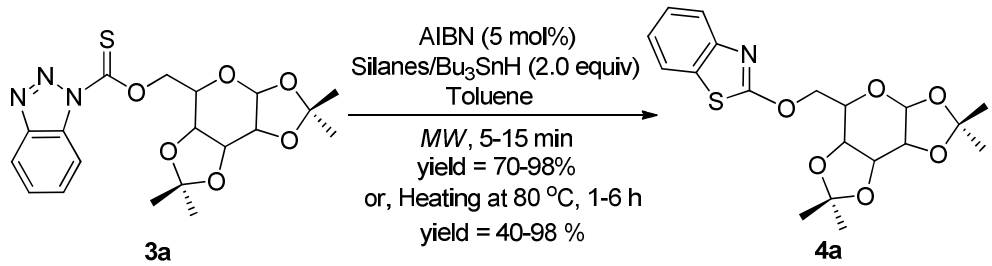


Figure 1. Offset π-π stacking interactions in regioisomers **6** & **7**

Treatment of compound **3a** with reagents capable of inducing 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, however 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 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 presence of silanes having radical stabilizing groups i.e. phenyl-substituent in $MePh_2SiH$, Bu^tPh_2SiH and Ph_3SiH afforded 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 two equivalents of Bu_3SnH at 80 °C. In addition, we investigated the reaction under microwave (MW) condition, where significant reduction in reaction time ranging from 5-15 min was observed (Table 2).

Table 2. Optimization of radical conversion to **4a** using 2 molar equivalents of reagents



3a **4a**

entry	reagent	initiator[a] (Mol%)	temp (°C)[b]	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 condition, [d]Reaction time in minutes under microwave condition.

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**.

Table 3. Solvent optimization for conversion from **3a** to **4a** using Bu_3SnH (2 molar equiv) in presence of AIBN (5 mol %)

entry	**solvent**[a]	**time (h)**[b]	**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]

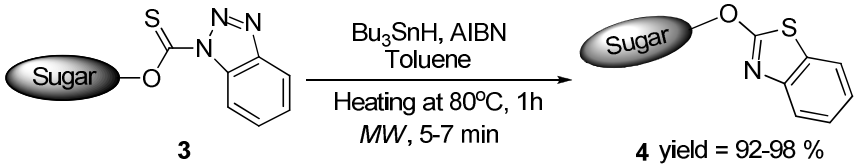
[a]2.0 mL of solvent was used for 1 mmol of **3a**. [b]Reaction time 1-12 h. [c]Isolated yield 60-98%. [d]Reaction in sealed tube.

The extensive spectral studies (IR, ^1H, ^{13}C NMR and MS) evidenced the unambiguous structure of compound **4a**. Like ^1H NMR spectra of compound **3a** having four separate resonances (one

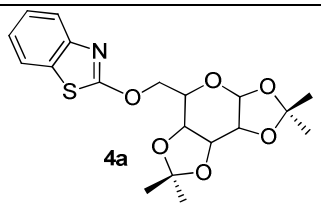
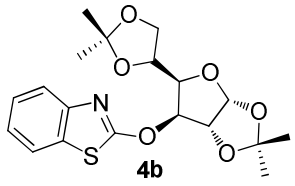
proton each) for the characteristic benzotriazolyl C-H protons, the compound **4a** also exhibited four proton resonances in aromatic region with a different splitting pattern, thus ruled out the formation of possible deoxy product[19] under our standardized conditions. Also, the mass spectrum of **4a** exhibited $[M+H]^+$ 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 the Supporting Information, Figure S1 and S4).

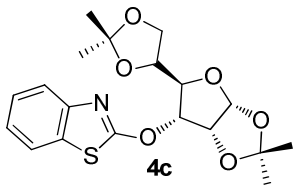
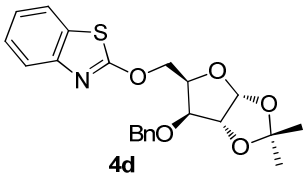
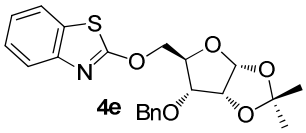
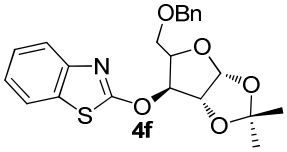
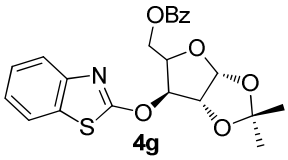
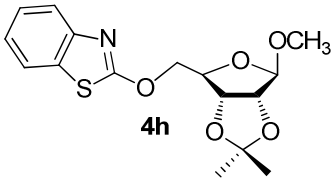
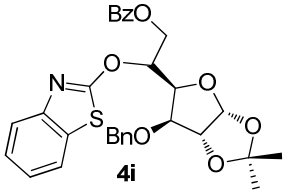
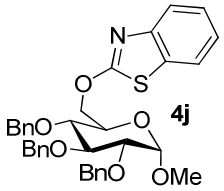
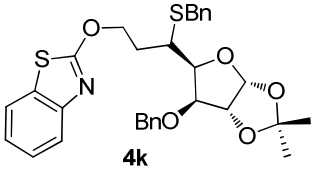
Thus, under optimized reaction conditions, all the developed carbohydrate based benzotriazolemethanethione **3a-k** were cyclized to their respective glycoconjugate benzothiazoles **4a-k** in excellent yields ranging from 92-98% (Table 4). The structure of compounds **4a-k** were deduced from their extensive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

Table 4. Synthesis of glycoconjugate benzothiazoles **4a-k**



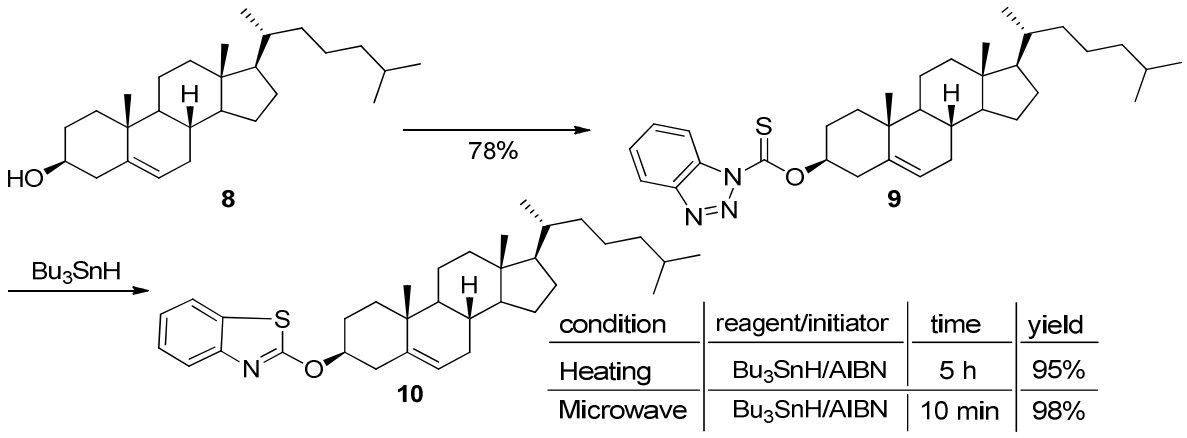
3 **4** yield = 92-98 %

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 condition. [c]Reaction time in minutes under microwave condition.

A part 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 *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 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 the Supporting Information, Figure S5).

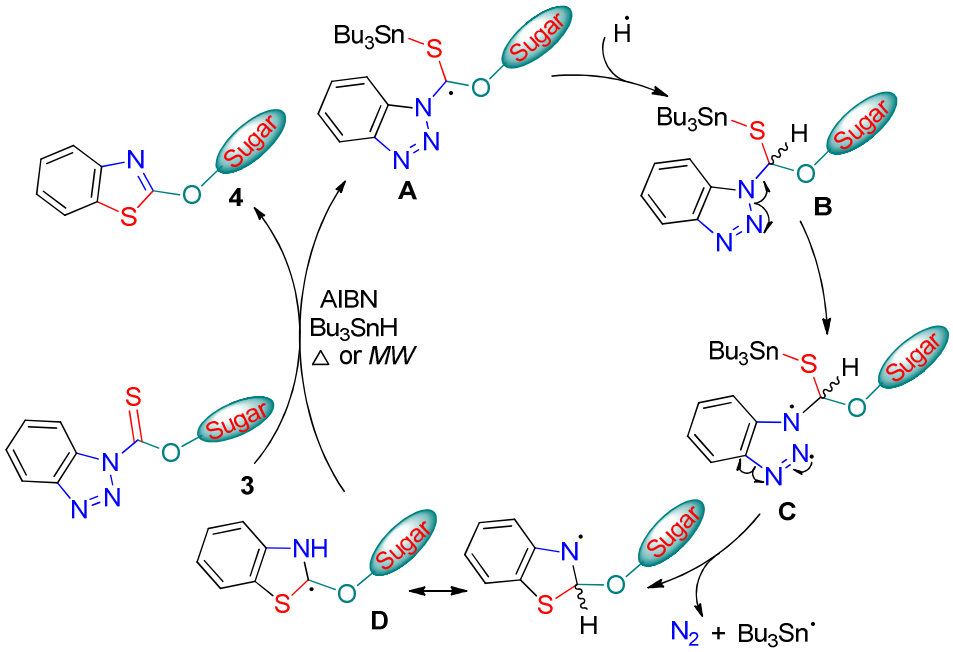


condition	reagent/initiator	time	yield
Heating	Bu_3SnH/AIBN	5 h	95%
Microwave	Bu_3SnH/AIBN	10 min	98%

Scheme 4. Synthesis of *O*-cholesteryl benzothiazole **10**

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 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**.



Scheme 5. The postulated mechanism for the formation of benzothiazoles

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 towards acid and base sensitive

functionalities. Unlike carbohydrate derivatives e.g. *O*-(*S*-methyldithiocarbonate)-, *O*-phenoxythiocarbonyl, pheny-1-thio, *O*-pentafluorophenylthionocarbonate, *O*-thiocarbonyl imidazolide etc. utilized earlier 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 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, pre-coated on aluminum plates and revealed with either a UV lamp (λ_{max} = 254 nm) or a specific colour reagent (*Draggendorff* reagent or iodine vapours) or by spraying with methanolic-H_2SO_4 solution and subsequent charring by heating at 100 °C. ^{1}H 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 & 5). The compounds **1a-j** & **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 benzyl mercapton 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 drop-wise 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 ambient temperature for 3h. 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 x100mL). 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 & 9. A stirring solution of free alcohol (**1a-k** and **8**) in dry CH_2Cl_2 was treated with *bis*-benzotriazole methanethiones **2** in presence of pyridine and Et_3N under inert atmosphere. After completion of reaction (monitored by TLC), the reaction mixture was *in vacuo* concentrated. 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 triethyl amine (206 μL, 1.49 mmol) under inert atmosphere. White 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) v_{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, 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) v_{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*-isoproyledene-*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), 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*-*iso*propylidene-*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) v_{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) v_{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 & 9)** in toluene was added with stannanyl/silyl hydride (2.0 equiv) and AIBN (5 mol %) under inert atmosphere. The reaction stirred under heating at 80 °C as well as exposure to microwave CEM Discover® LabMate at 100°C. After completion of reaction (monitored by TLC), the reaction mixture was *in vacuo*

concentrated, 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 *in vacuo* concentrated. 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) v_{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) v_{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) v_{max} 1596, 1531, 1107, 1055, 914, 774, 736, 650 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) v_{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.

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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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