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Regioselectivity in the glycosylation of 5-(3-chlorobenzo[*b*]thien-2-yl)-4*H*-1,2,4-triazole-3-thiol

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ABSTRACT

The glycosylation of 5-(3-chlorobenzo[*b*]thien-2-yl)-4*H*-1,2,4-triazole-3-thiol (**1**) and its 3-benzylsulfanyl and 3-methylsulfanyl derivatives with different glycosyl halides **2–4** has been studied in presence of base. The S-glycosides **5–7** were obtained in the presence of triethylamine, whereas the respective *S*,N^4-bis(glycosyl) derivatives **8–10** were synthesized in the presence of potassium carbonate; the *S*,N^2-bis(glycosyl) isomer **11** could also be isolated in the case of the galactosyl analog. Similarly, after protecting **1** as 3-benzyl(methyl)sulfanyl derivatives **12** or **13**, the N^4-glycosyl analogs **14–19** as well as minor amounts of *S*,N^2-bis(galactosyl) isomers **20** and **21** were formed. The theoretical calculations using AM1 semiempirical methods agreed with the experimental results. Microwave irradiation (MWI) led to higher yields in much less time than the conventional methods, and no change in regioselectivity has been noticed.

1. Introduction

Glycosylsulfanyl heterocycles have attracted much attention because of their biological activity and in particular because of their inhibition of the activity of enzymes.[1–6] They have excellent chemoselectivity in glycosylation processes as both donors and acceptors,[7] particularly via reaction processes that involve active and latent glycosylation[8] protocols. Thus, these compounds serve as useful intermediates for the synthesis of oligosaccharides.[6–14]

On the other hand, the 1,2,4-triazole nucleus is found in many drug structures such as anastrozole, estazolam, ribavirin, and triazolam. In addition, these compounds show antiseptic, analgesic, and anticonvulsant properties.[15] Considerable attention has been devoted to the synthesis of benzothiophene derivatives that possess diverse pharmacological properties, such as antibiotic, analgesic, antiallergic, anti-inflammatory, diuretic and enzyme inhibition activities.[16,17]

On the basis of these findings, it is interesting to report the synthesis and spectroscopic analysis of a new series of compounds in which the glycosyl moieties have been used as carriers for the heterocycle, having the triazole ring linked to the benzothiophene ring, as in 5-(3-chlorobenzo[*b*]thien-2-yl)-4*H*-1,2,4-triazole. The effects of base and microwave irradiation (MWI) on the glycosylation with various glycosyl halides have been investigated as a continuation of our previous work using microwave technology.[18–27] Microwave-assisted organic reactions constitute an emerging technology that makes experimentally and industrially important organic syntheses more effective and more ecofriendly than conventional reactions.[28–32]

2. Results and discussion

The optimum conditions have been determined for the selective glycosylation of 5-(3-chlorobenzo[*b*]thien-2-yl)-4*H*-1,2,4-triazole-3-thiol (**1**),[33] which is readily available[34] from MWI-assisted synthesis, as well as of its 3-benzylsulfanyl- and methylsulfanyl derivatives **12**[34] and **13**,[33] which are prepared by both conventional and MWI methods. Coupling of **1** with one or two equivalents of glycosyl halides **2–4** takes place in the presence of triethylamine with acetone as solvent to give the *S*-glycosyl compounds **5–7** in 77–80% yield (Scheme 1). More efficiently, MWI of a mixture of the reactants provided **5–7** in higher yields (90–93%) within 3–4 min with no change in regioselectivity.

The ^{1}H NMR spectra of **5–7** confirmed that a monoglycosylation of **1** had taken place by showing one exchangeable proton in the

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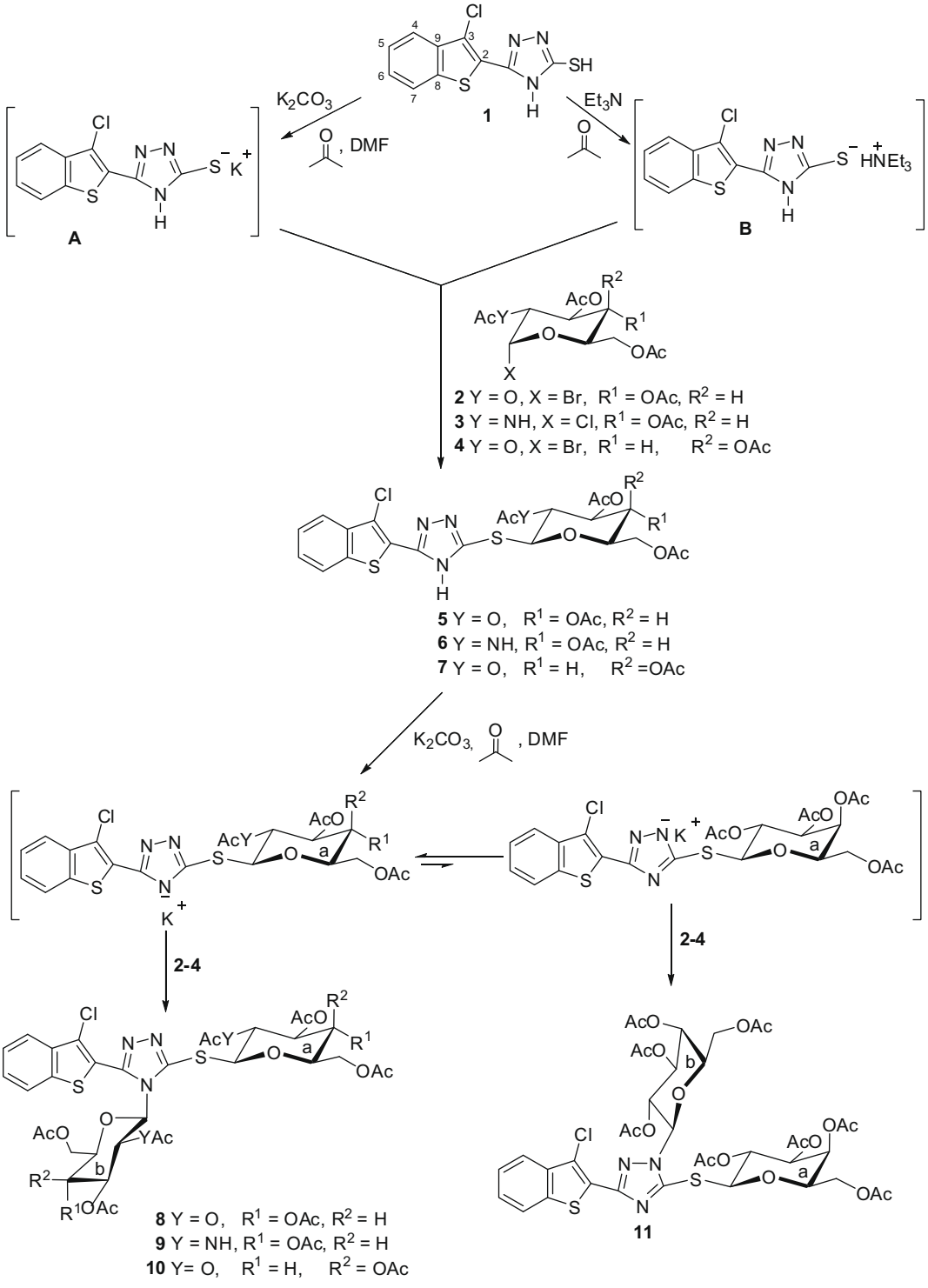


Scheme 1.

downfield region at 12.08–14.62 ppm due to the NH-proton of the triazole ring. The anomeric protons of **5–7** were assigned to the doublet at 5.27–5.46 ppm with $J_{1',2'}$ 9.9–10.7 Hz, confirming the β-configuration. The heteromultiple bond correlation $^{1}H–^{1}H$ DQF-COSY and $^{1}H–^{13}C$ HMQC experiments facilitated the spectral assignment of **5–7** (Section 4).

Reaction of **1** with 1.1 equiv of glycosyl halides **2–4** in the presence of K_2CO_3 did not afford the expected *S*-glycopyranosyl products only, but they were accompanied by the *S*,*N*^{4}-bis(glycopyranosyl) analogs, along with the recovery of some starting material **1**. Under the same reaction conditions, but using 2.2 equiv of glycosyl halides **2** or **3,** the *S*,*N*^{4}-bis(glycopyranosyl) derivatives **8** and **9**, respectively, were obtained. On the other hand, reaction of **1** with tetra-*O*-acetyl-α-D-galactopyranosyl bromide (**4**) afforded a mixture of *S*,*N*^{4}- **10** and *S*,*N*^{2}-bis(galactopyranosyl) **11** derivatives as major and minor products, respectively, in 75% overall yield, which were separated by column chromatography ($R_f^{N-4} > R_f^{N-2}$). Improvement of the yields of the bis(glycosides) to 89–92% and

significant reduction in reaction times to 4–5 min were achieved under microwave irradiation (MWI), but with no recognized change in the ratio of isomers.

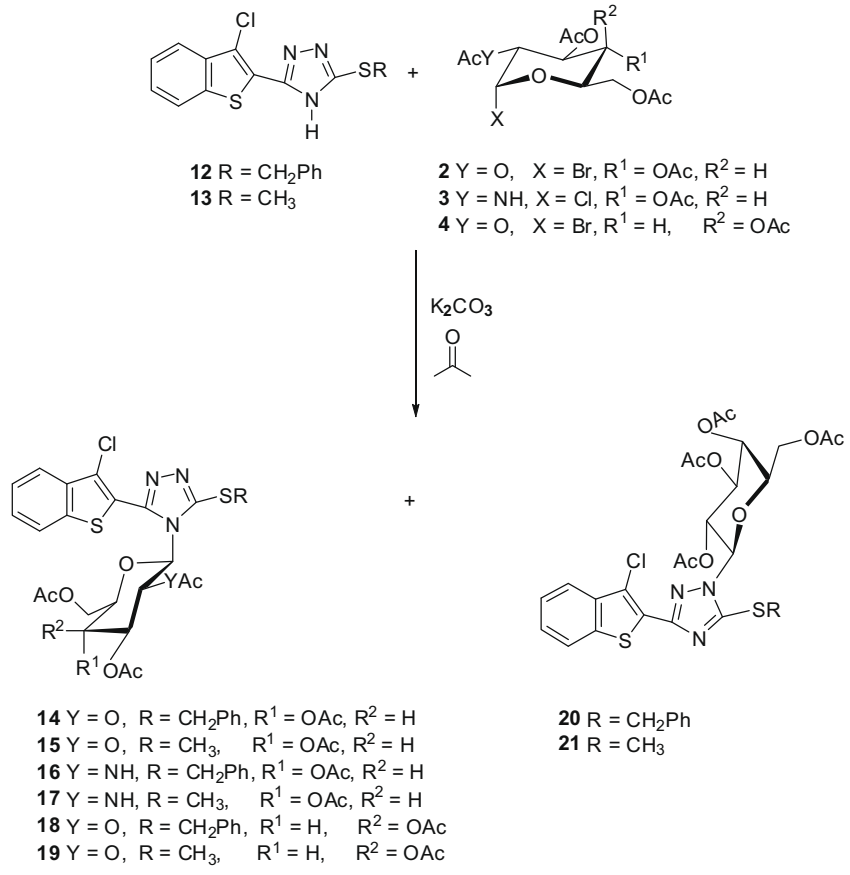
The structures of compounds **8–11** were established on the basis of their elemental analyses and spectral data, which indicated the presence of two glycosyl residues and the absence of the signal of an NH-triazole. The ^{1}H NMR spectra of **8–11** showed the presence of two doublets in the region 5.51–5.70 and 5.48–6.03 ppm with $J_{1',2'}$ 9.2–10.7 Hz for H-1′a and H-1′b, confirming that the glycosyl residues were in the β-configuration. The heteromutiple bond correlation facilitated the spectral assignment. In the ^{1}H NMR spectrum of compound **9**, there are eight signals in the upper-field region corresponding to the methyl groups of the two acetamido and six acetoxy groups. The two anomeric protons correlated with 83.3 and 84.5 ppm for C-1′a and C-1′b, respectively. Resonances for the other proton and carbon atom were in their appropriate positions (Section 4).

In order to help in assigning the H-1′ in the ^{1}H NMR of *S*,*N*^{4}- and *S*,*N*^{2}-bis(glycosides), latent glycosylations of the S-protected **12** and **13** with glycosyl halides **2–4** were carried out in presence of K_2CO_3 under MWI for 4–6 min to give the respective glycosides **14–19** in 86–90% yield (Scheme 2); conventional methods required longer times (18–21 h) to give 71–76% yields of the same products. It has also been found that the galactosyl derivatives gave in addition, the minor galactosyl derivatives at N^2 **20** and **21**.

Attempted use of the chemical shifts of H-1′ of both the S- and N-glycosides for differentiation was not reliable because of their close values. Thus, the spectra showed the anomeric protons as doublets at 5.50–5.51 ppm for **18** and **19**, and 5.46–5.45 ppm for **20** and **21**; the thioglycoside showed them at 5.51–5.70 ppm.

In order to assign the site of glycosylation, we have initiated a study of the tautomerism in 5-(3-chlorobenzo[*b*]thien-2-yl)-4*H*-1,2,4-triazole-3-thiol (**1**),[34] which indicated the preference of the thiol tautomer. In the present work, the theoretical approach has been considered for the tautomers **5–7** and the transition state by means of the semiempirical AM1 method. The computations were carried out with the MOPAC7 package.[35] Thus, the heat of formation, dipole moment, the highest occupied molecular orbital energies (E_{HOMO}), the lowest unoccupied molecular orbital energies (E_{LUMO}), and the charge density on triazole heteroatoms, as well as the relative stabilities, have been calculated (Tables 1 and 2).

On the basis of the regioselective alkylation of **1**,[34] we could assume that the glycosylation of **1** would give, due to the higher nucleophilic properties and the lower electronegativity of the sulfur atom,[36] the S-glycosylated products **5–7**, which could be the precursors for the bis(glycosylated) products **8–11**. Further, reaction of **5–7** in presence of potassium carbonate could generate one or more of the equilibrated anionic transition states, which upon reaction with glycosyl halides **2–4** gave the corresponding bis(glycosylated) derivatives **8–11** (Scheme 3). Since this glycosylation occurred from a nucleophilic substitution, we have analyzed the charge density distribution in the tautomers, their anionic forms and the calculated relative stabilities (Scheme 3). The transition states and tautomers of **5–7** have the negative charge more localized at the N^4 atom, followed by N^2 and then N^1 (Tables 1 and 2), thus explaining the favored regioselective glycosylation at N^4, and to minor extent at N^2 such as *S*,*N*^{2}-bis(galactopyranosyl) **11**. Moreover, the calculated relative stability (Tables 1 and 2) based on the energy difference for possible alkylation on N^4, N^2 and N^1 also coincides with the experimental results.



Scheme 2.

Table 1
Calculated (AM1) heat of formation (kcal), relative stability (kcal), dipole moments, (μ, Debye), HOMO orbital energies (E_{HOMO}, eV) and charge density on triazole heteroatoms for the tautomers **5**–**7**

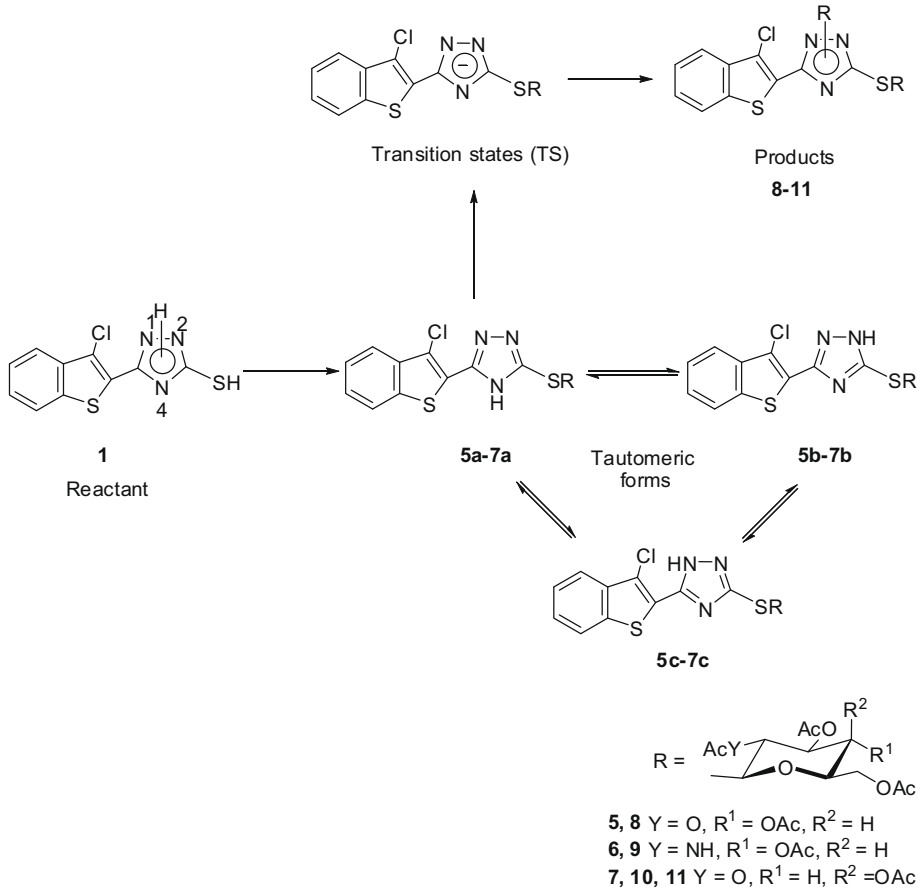
Tautomer No.	Heat of formation (ΔH_f, kcal)	μ (Debye)	E_{HOMO} (eV)	E_{LUMO} (eV)	Charge density on triazole heteroatoms	Relative stability[a] (RS, kcal)
5a	−254.133	2.887	−8.509	−0.933	−0.181 (N-4) −0.091 (N-2) −0.039 (N-1)	−1.841 (**5a**–**5b**) −3.618 (**5a**–**5c**)
5b	−252.292	5.977	−8.441	−0.777	−0.168 (N-4) −0.167 (N-2) −0.047 (N-1)	−1.777 (**5b**–**5c**)
5c	−250.515	5.277	−8.545	−1.114	−0.130 (N-4) −0.104 (N-2) −0.153 (N-1)	
6a	−214.017	4.777	−8.583	−1.090	−0.178 (N-4) −0.097 (N-2) −0.048 (N-1)	−2.194 (**6a**–**6b**) −5.077 (**6a**–6b)
6b	−211.823	5.398	−8.211	−0.518	−0.099 (N-4) −0.134 (N-2) −0.028 (N-1)	−2.883 (**6b**–**6c**)
6c	−208.940	8.576	−8.492	−1.211	−0.121 (N-4) −0.116 (N-2) −0.155 (N-1)	
7a	−258.733	4.829	−8.575	−1.082	−0.180 (N-4) −0.087 (N-2) −0.038 (N-1)	−4.547 (**7a**–**7b**) −6.158 (**7a**–**7c**)
7b	−254.186	7.767	−8.217	−0.524	−0.097 (N-4) −0.132 (N-2) −0.028 (N-1)	−1.611 (**7b**–**7c**)
7c	−252.575	2.634	−8.635	−1.083	−0.112 (N-4) −0.072 (N-2) −0.152 (N-1)	

[a] RS = The difference in the heat of formation between each of two possible tautomers.

Table 2
Calculated (AM1) heat of formation (kcal), relative stability (kcal), dipole moments, (μ, Debye), HOMO orbital energies (E_{HOMO}, eV) and charge density on triazole heteroatoms for the transition states (TS) TS **5**–**7**

TS of tautomer No.	Heat of formation (ΔH_f, kcal)	μ (Debye)	E_{HOMO} (eV)	E_{LUMO} (eV)	Charge density on triazole heteroatoms	Relative stability[a] (RS, kcal)
TS **5a**	−305.670	14.026	−4.619	2.351	−0.118 (N-4) −0.116 (N-2) −0.093 (N-1)	−0.234 (**5a**–**5b**) −0.842 (**5b**–**5c**)
TS **5b**	−305.436	14.378	−4.701	2.321	−0.115 (N-4) −0.105 (N-2) −0.095 (N-1)	−0.608 (**5a**–**5c**)
TS **5c**	−304.828	14.794	−4.729	2.296	−0.129 (N-4) −0.096 (N-2) −0.097 (N-1)	
TS **6a**	−267.928	9.255	−4.836	2.202	−0.111 (N-4) −0.096 (N-2) −0.090 (N-1)	−0.375 (**6a**–**6b**) −1.943 (**6a**–**6b**)
TS **6b**	−267.553	9.601	−4.952	2.165	−0.116 (N-4) −0.137 (N-2) −0.095 (N-1)	−1.568 (**6b**–**6c**)
TS **6c**	−265.985	9.731	−4.733	2.143	−0.141 (N-4) −0.122 (N-2) −0.091 (N-1)	
TS **7a**	−311.560	13.847	−4.667	2.325	−0.116 (N-4) −0.111 (N-2) −0.093 (N-1)	−3.175 (**7a**–**7b**) −4.345 (**7b**–**7c**)
TS **7b**	−308.385	14.947	−4.626	2.367	−0.112 (N-4) −0.113 (N-2) −0.094 (N-1)	−1.170 (**7b**–**7c**)
TS **7c**	−307.215	9.387	−4.780	2.226	−0.139 (N-4) −0.098 (N-2) −0.095 (N-1)	

[a] RS = The difference in the heat of formation between each of two possible TS.



Scheme 3.

On the other hand, AM1 optimization of the structure of tautomers **5**–**7** could justify the possibility of intramolecular hydrogen bonding between the mobile hydrogen atom of the triazole ring and the chlorine atom. Since the benzothiophene and triazole rings are not planar, the N–H···Cl distance was found to be smaller in case of tautomer **5c** (2.00 Å) when compared to tautomers **5a** (4.99 Å) and **5b** (4.87 Å) (Table 3). Accordingly, the tendency of intramolecular H-bonding seems to be higher in case of **5c**, and hence its proton-donating power is weakened (i.e., becoming less acidic), thus diminishing the possibility of its alkylation (Fig. 1).

The preferential formation of *S*,N^4-bis(glycopyranosyl) more than *S*,N^2-bis(glycopyranosyl) is presumably due to the higher acidity of N^4–H. After the introduction of the glycosyl residue on the sulfur atom, the second glycosyl residue will be directed to N^4. In case of the galactosyl derivative, the higher reactivity of the donor could be a reason for further galactosylation at N^2. Such isomers from other sugars were undetectable. The difference in the effect of the triethylamine and potassium carbonate in the glycosylation steps can be due to the extent of abstraction of a proton from N^4–H or N^2–H.

3. Conclusions

In conclusion, regioselective glycosylation of 5-(3-chlorobenzo[*b*]thien-2-yl)-4*H*-1,2,4-triazole-3-thiol (**1**) with glycosyl halides **2–4** to give the corresponding S-glycosides **5–7** took place in presence of triethylamine. In the presence of potassium carbonate, the respective *S*,N^4-bis(glycosyl) derivatives **8–10** were obtained; the galactopyranosyl analogue gave, in addition, minor products of *S*,N^2-bis(glycosyl) isomer **11**. MWI led to higher yields in much less time than the conventional methods, and no change in regioselectivity has been noticed.

Table 3
Selected bond length (Å) and angles (°)

Tautomer No.	Bond length NH···Cl	Bond angle		Tetrahedral angle	
		Cl(16)–C(15)–C(14)	C(15)–C(14)–C(1)–N(5)	C(1)–C(14)–C(15)–Cl(16)	C(15)–Cl(16)–H(6)–N(5)
5a	4.987	125.7	41.2	1.6	–
5b	4.872	126.2	−0.4	0.0	–
5c	2.000	126.4	1.5	0.0	3.8
6a	5.092	125.8	34.6	1.3	–
6b	4.861	126.3	4.3	0.0	–
6c	2.000	126.3	−3.9	0.0	−7.8
7a	4.951	125.6	43.7	1.7	–
7b	4.861	126.3	7.2	0.0	–
7c	2.000	126.3	−3.2	0.0	−6.4

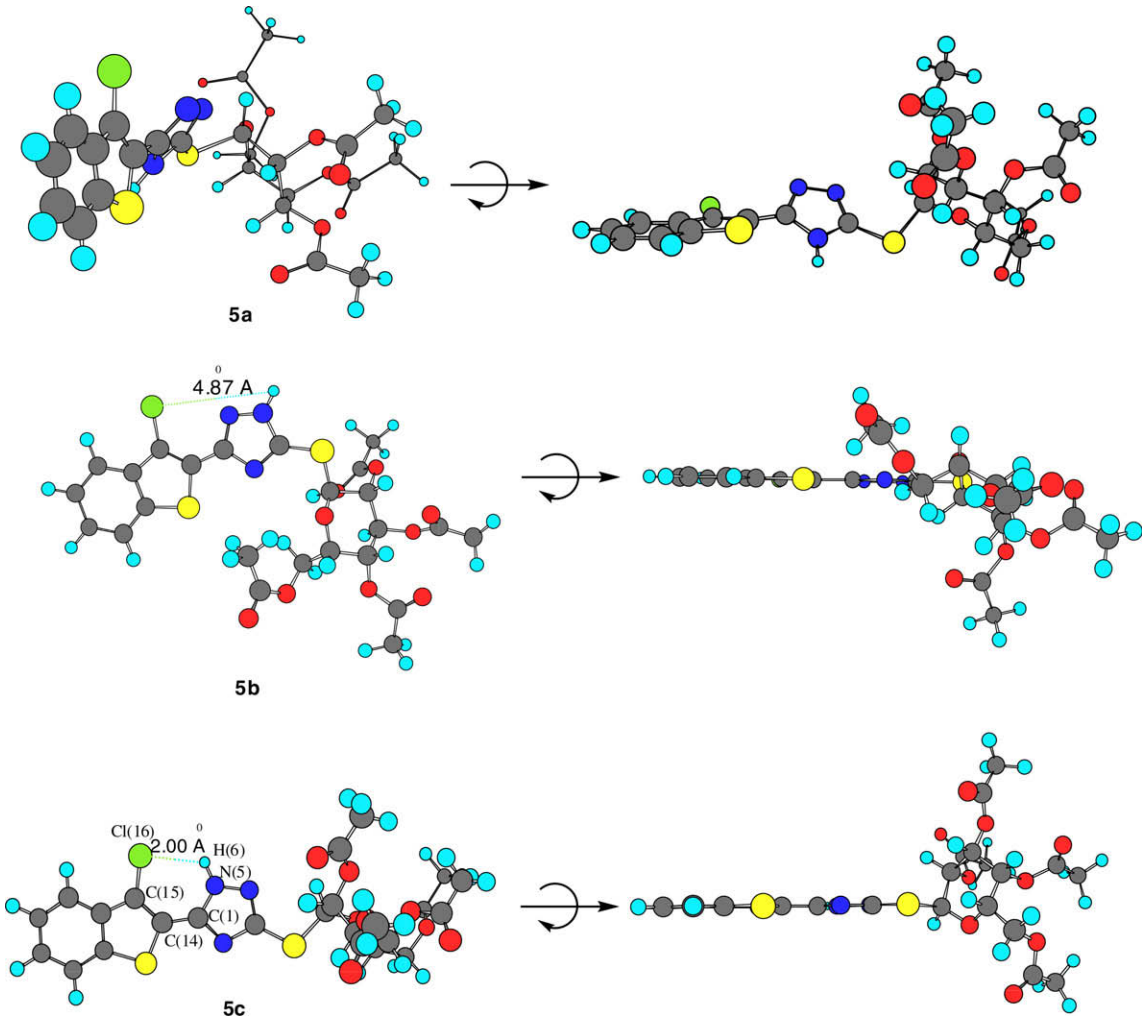


Figure 1.

The AM1 computational data are in agreement with the resulting isomeric ratio distribution observed in the experimental data, where the glycosylation occurred predominantly at the N^4 and to lesser extent at the N^2 atom, which was noticed in the case of galactopyranosyl derivatives.

4. Experimental

4.1. General methods and materials

Melting points were determined with a Melt-Temp apparatus, and are uncorrected. TLC was performed on Baker-Flex silica gel 1B-F plates using EtOAc–hexane as the developing solvent, and the spots were detected by UV light absorption. Irradiation was done in a domestic microwave oven EM-230M (1200 W output power under 'defrost' setting). The irradiation was done, unless otherwise stated, in a closed Teflon cylindrical vessel that was placed at the center of a rotating plate inside the oven. The vessel was supported by a frame for safety. The vessel had an outside diameter of 6.5 cm and a length of 6.0 cm, whereas the space inside the vessel was 3.0 cm in width and 2.0 cm in length. An additional 2.0 cm in length inside the vessel was used for the screw cap that was tightened. The oven was set in the defrost mode with fixed output power. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Jeol spectrometer (500 MHz). The assignment of ^{1}H NMR spectra was based on chemical shift correlation DQFCOSY spectra, while the assignment of ^{13}C NMR spectra was based on HMQC experiments. Chemical shifts (δ) are given in ppm relative to the signal for TMS as internal standard. Elemental analyses were performed in the Microanalyses unit at the Faculty of Science, Cairo University. Numbering of the ring systems in derivatives follows that of the starting material **1** regardless of IUPAC rules.

4.2. General procedure: reaction of 5-(3-chlorobenzo[*b*]thien-2-yl)-4*H*-1,2,4-triazole-3-thiol (1) with glycosyl halides 2–4 in the presence of Et_3N

4.2.1. Conventional method (CM)

A mixture of compound **1** (1 mmol) and Et_3N (1 mmol, 0.14 mL) in dry acetone (25 mL) was stirred for 1 h, then glycosyl halides **2–4** (1.1 mmol) were added. Stirring was continued overnight with **2**, whereas with **3** and **4**, the reaction mixture was heated under reflux for 2 and 3 h, respectively. The mixture was filtered, the solids were washed with acetone, the filtrate was evaporated under reduced pressure, and the crude product was recrystallized from EtOH to give the S-glycosides **5–7**.

4.2.2. Microwave irradiation (MWI) method

A mixture of compound **1** (0.5 mmol), Et_3N (0.5 mmol, 0.07 mL), and glycosyl halides **2–4** (0.55 mmol) in dry acetone (5 mL) in a closed Teflon vessel was irradiated for 3–4 min. The reaction mixture was cooled and processed as described above to give **5–7**.

4.2.3. 5-(3-Chlorobenzo[*b*]thien-2-yl)-3-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylsulfanyl)-4*H*-1,2,4-triazole (5)

Colorless plates; yield: CM (80%), MW (93%); mp 214–215 °C; TLC, R_f 0.18 (1:1 hexane–EtOAc). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.01, 2.03, 2.07, 2.09 (4 × s, 12H, 4 × CH_3CO), 3.86 (ddd, 1H, $J_{5',6'}$ 4.6, $J_{5',6''}$ 2.3, $J_{5',4'}$ 9.9 Hz, H-5′), 4.22 (dd, 1H, $J_{6',5'}$ 4.6, $J_{6',6''}$ 12.2 Hz, H-6′), 4.28 (dd, 1H, $J_{6'',5'}$ 2.3, $J_{6'',6'}$ 12.2 Hz, H-6″), 5.14 (dd, 1H, $J_{4',3'}$ 9.2, $J_{4',5'}$ 9.9 Hz, H-4′), 5.17 (dd, 1H, $J_{2',3'}$ 9.2 Hz, $J_{2',1'}$ 9.9 Hz, H-2′), 5.27 (d, 1H, $J_{1',2'}$ 9.9 Hz, H-1′), 5.31 (t, 1H, $J_{3',4'}$ 9.2 Hz, H-3′), 7.43–7.48 (m, 2H, H-5, H-6 benzothiophene), 7.82 (dd, 1H, *J* 2.3, *J* 6.1 Hz, H-4 benzothiophene), 7.87 (dd, 1H, *J* 2.3, *J* 6.1 Hz, H-7 benzothiophene), 12.08 (s, 1H, D_2O exchangeable, NH). ^{13}C NMR ($CDCl_3$, 125.7 MHz): δ 20.7, 20.8 (4 × *CH*$_3$CO), 61.9 (C-6′), 68.1 (C-4′), 69.9 (C-2″), 73.6 (C-3′), 76.3 (C-5′), 83.3 (C-1′), 120.0 (C-9), 122.6 (C-4), 122.7 (C-7), 125.5 (C-5), 126.1 (C-8), 126.9 (C-6), 137.0 (C-3), 137.6 (C-2), 169.5, 169.6, 170.2, 171.1 (4 × CH_3*CO*). Anal. Calcd for $C_{24}H_{24}ClN_3O_9S_2$: C, 48.20; H, 4.04; N, 7.03. Found: C, 48.12; H, 4.10; N, 6.81.

4.2.4. 3-(2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosylsulfanyl)-5-(3-chlorobenzo[*b*]thien-2-yl)-4*H*-1,2,4-triazole (6)

Colorless plates; yield: CM (78%), MW (92%); mp 222–223 °C, R_f 0.68 (1:5 hexane–EtOAc). ^{1}H NMR (DMSO-d_6, 500 MHz): δ 1.79, 1.88, 1.92, 1.95 (4 × s, 12H, NCH_3CO, 3 × CH_3CO), 3.90–3.93 (m, 1H, H-5′), 3.98 (dd, 1H, $J_{6',5'}$ 1.5, $J_{6',6''}$ 12.2 Hz, H-6′), 4.09 (ddd, 1H, $J_{2',3'}$ 9.9, $J_{2',1'}$ 10.7, $J_{2',NH}$ 9.2 Hz, H-2′), 4.18 (dd, 1H, $J_{6'',5'}$ 5.3, $J_{6'',6'}$ 12.2 Hz, H-6″), 4.92 (t, 1H, $J_{4',3'}$ $J_{4',5'}$ 9.9 Hz, H-4′), 5.19 (dd, 1H, $J_{3',2'}$ 9.9 Hz, H-3′), 5.46 (d, 1H, $J_{1',2'}$ 10.7 Hz, H-1′), 7.49–7.54 (m, 2H, H-5, H-6 benzothiophene), 7.84 (dd, 1H, *J* 1.5, *J* 6.9 Hz, H-4 benzothiophene), 8.06 (dd, 1H, *J* 1.5, *J* 7.6 Hz, H-7 benzothiophene), 8.24 (d, 1H, $J_{NH,2'}$ 9.2 Hz, D_2O exchangeable, NHAc), 14.62 (s, 1H, D_2O exchangeable, NH). ^{13}C NMR (DMSO-d_6, 125.7 MHz): δ 20.8, 20.9, 23.1 (4 × *CH*$_3$CO), 52.5 (C-2′), 62.3 (C-6′), 68.8 (C-4′), 73.6 (C-3′), 75.6 (C-5′), 84.1 (C-1′), 119.9 (C-9), 122.5 (C-4), 123.7 (C-7), 126.3 (C-5), 126.8 (C-8), 127.3 (C-6), 136.9 (C-3), 137.2 (C-2), 169.8, 170.1, 170.4 (4 × CH_3*CO*). Anal. Calcd for $C_{24}H_{25}ClN_4O_8S_2$: C, 48.28; H, 4.22; N, 9.38. Found: C, 48.05; H, 4.44; N, 9.25.

4.2.5. 5-(3-Chlorobenzo[*b*]thien-2-yl)-3-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosylsulfanyl)- 4*H*-1,2,4-triazole (7)

Colorless crystals; yield: CM (77%), MW (90%); mp 200–201 °C, R_f 0.50 (1:2.5 hexane–EtOAc). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.98, 2.04, 2.08, 2.15 (4 × s, 12H, 4 × CH_3CO), 4.06–4.09 (m, 1H, H-5′), 4.13–4.20 (m, 2H, H-6′, H-6″), 5.16 (dd, 1H, $J_{3',2'}$ 9.9, $J_{3',4'}$ 3.1 Hz, H-3′), 5.29 (d, 1H, $J_{1',2'}$ 9.9 Hz, H-1′), 5.36 (t, 1H, $J_{2',3'}$ 9.9 Hz, H-2′), 5.48 (d, 1H, $J_{4',3'}$ 3.1 Hz, H-4′), 7.42–7.47 (m, 2H, H-5, H-6 benzothiophene), 7.81 (dd, 1 H, *J* 2.3, *J* 6.9 Hz, H-4 benzothiophene), 7.86 (dd, 1H, *J* 2.3, *J* 6.9 Hz, H-7 benzothiophene), 12.18 (s, 1H, D_2O exchangeable, NH). ^{13}C NMR ($CDCl_3$, 125.7 MHz): δ 20.6, 20.7, 20.8 (4 × *CH*$_3$CO), 61.7 (C-6′), 67.3 (C-4′, C-2′), 71.7 (C-3′), 75.2 (C-5′), 83.8 (C-1′), 120.0 (C-9), 122.6 (C-4), 122.7 (C-7), 125.5 (C-5), 125.9 (C-8), 126.9 (C-6), 137.1 (C-3), 137.5 (C-2), 169.8, 170.1, 170.3, 170.7 (4 × *CO*CH_3). Anal. Calcd for $C_{24}H_{24}ClN_3O_9S_2$: C, 48.20; H, 4.04; N, 7.03. Found: C, 48.34; H, 4.29; N, 6.88.

4.3. General procedure: reaction of 5-(3-chlorobenzo[*b*]thien-2-yl)-4*H*-1,2,4-triazole-3-thiol (1) with glycosyl halides 2–4 in presence of K_2CO_3

4.3.1. Conventional method (CM)

A mixture of compound **1** (1 mmol) and potassium carbonate (2 mmol, 0.276 g) in dry acetone (25 mL) and 5 drops of DMF were stirred for 1 h, then glycosyl halides **2–4** (2.2 mmol) were added. Stirring was continued overnight, and then the reaction mixture was heated under reflux for 2–4 h. The mixture was filtered, the solids were washed with acetone, the filtrate was evaporated under reduced pressure, and the crude product was recrystallized from EtOH to afford **8** and **9** from **2** and **3**, respectively, whereas **10** and **11** from **4** were separated by column chromatography using 30:70 hexane–EtOAc as eluant, and the products were recrystallized from EtOH.

4.3.2. Microwave irradiation (MWI) method

A mixture of compound **1** (0.5 mmol), potassium carbonate (1 mmol, 0.138 g), and glycosyl halides **2–4** (1.1 mmol) in dry acetone (5 mL) and a few drops of DMF in a closed Teflon vessel were irradiated for 4–5 min. The reaction mixture was cooled and processed as described above to give **8–11**.

4.3.3. 5-(3-Chlorobenzo[*b*]thien-2-yl)-4-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-3-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylsulfanyl)-4*H*-1,2,4-triazole (8)

Colorless crystals; yield: CM (77%), MW (92%); mp 172–173 °C, R_f 0.10 (1:1 hexane–EtOAc). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.87, 1.97, 1.99, 2.01, 2.02, 2.04, 2.07, 2.08 (8 × s, 24H, 8 × CH_3CO), 3.87 (ddd, 1H, $J_{5'a,6'a}$ 2.3, $J_{5'a,6''a}$ 4.6, $J_{5'a,4'a}$ 9.9 Hz, H-5′a), 3.98 (ddd, 1H, $J_{5'b,6'b}$ 2.3, $J_{5'b,6''b}$ 4.6, $J_{5'b,4'b}$ 9.9 Hz, H-5′b), 4.10 (dd, 1H, $J_{6'a,5'a}$ 2.3, $J_{6'a,6''a}$ 12.2 Hz, H-6′a), 4.17 (dd, 1H, $J_{6'b,5'b}$ 2.3, $J_{6'b,6''b}$ 12.2 Hz, H-6′b), 4.28 (dd, 1H, $J_{6''a,5'a}$ 4.6, $J_{6''a,6'a}$ 12.2 Hz, H-6″a), 4.32 (dd, 1H, $J_{6''b,5'b}$ 4.6, $J_{6''b,6'b}$ 12.2 Hz, H-6″b), 5.14 (dd, 1H, $J_{4'a,3'a}$ 9.2, $J_{4'a,5'a}$ 9.9 Hz, H-4′a), 5.20 (dd, 1H, $J_{2'a,1'a}$ 10.7, $J_{2'a,3'a}$ 9.9 Hz, H-2′a), 5.29 (dd, 1H, $J_{4'b,3'b}$ 9.2, $J_{4'b,5'b}$ 9.9 Hz, H-4′b), 5.32 (dd, 1H, $J_{3'a,2'a}$ 9.9, $J_{3'a,4'a}$ 9.2 Hz, H-3′a), 5.37 (t, 1H, $J_{3'b,2'b} = J_{3'b,4'b}$ 9.2 Hz, H-3′b), 5.58 (d, 1H, $J_{1'a,2'a}$ 10.7 Hz, H-1′a), 5.65 (d, 1H, $J_{1'b,2'b}$ 9.2 Hz, H-1′b), 5.82 (t, 1H, $J_{2'b,1'b} = J_{2'b,3'b}$ 9.2 Hz, H-2′b), 7.41–7.46 (m, 2H, H-5, H-6 benzothiophene), 7.79 (dd, 1H, *J* 1.5, *J* 6.9 Hz, H-4 benzothiophene), 7.89 (dd, 1H, *J* 1.5, *J* 6.9 Hz, H-7 benzothiophene). ^{13}C NMR ($CDCl_3$, 125.7 MHz): δ 20.4, 20.6, 20.7 (8×*CH*$_3$CO), 61.4 (C-6′b), 61.7 (C-6′a), 67.4 (C-4′b), 68.0 (C-4′a), 69.6 (C-2′a), 69.8 (C-2′b), 73.1 (C-3′b), 73.8 (C-3′b), 74.9 (C-5′b), 76.7 (C-5′a), 84.1 (C-1′a), 84.3 (C-1′b), 120.8 (C-9), 122.6 (C-4), 122.8 (C-7), 125.2 (C-5), 125.8 (C-8), 126.6 (C-6), 137.4 (C-3), 137.6 (C-2), 168.4, 169.3, 169.4, 169.6, 170.1, 170.3, 170.7 (8 × CH_3*CO*). Anal. Calcd for $C_{38}H_{42}ClN_3O_{18}S_2$: C, 49.16; H, 4.56; N, 4.53. Found: C, 48.97; H, 4.65; N, 4.54.

4.3.4. 4-(2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-3-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosylsulfanyl)-5-(3-chlorobenzo[*b*]thien-2-yl)-4*H*-1,2,4-triazole (9)

Colorless crystals; yield: CM (76%), MW (90%); mp 116–118 °C; R_f 0.16 (1:5 hexane–EtOAc); ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.80, 1.94, 2.01, 2.03, 2.04, 2.06, 2.07, 2.08 (8 × s, 24H, 2 × NCH_3CO, 6 × CH_3CO), 3.84 (ddd, 1H, $J_{5'a,6'a}$ 2.3, $J_{5'a,6''a}$ 5.3, $J_{5'a,4'a}$ 9.2 Hz, H-5′a), 4.01 (ddd, 1H, $J_{5'b,6'b}$ 2.3, $J_{5'b,6''b}$ 4.6, $J_{5'b,4'b}$ 9.9 Hz, H-5′b), 4.12 (dd, 1H, $J_{6'a,5'a}$ 2.3, $J_{6'a,6''a}$ 12.2 Hz, H-6′a), 4.18 (dd, 1H, $J_{6'b,5'b}$ 2.3, $J_{6'b,6''b}$ 12.2 Hz, H-6′b), 4.22 (dd, 1H, $J_{6''a,5'a}$ 5.3, $J_{6''a,6'a}$ 12.2 Hz, H-6″a), 4.26 (dd, 1H, $J_{6''b,5'b}$ 4.6, $J_{6''b,6'b}$ 12.2 Hz, H-6″b), 4.40 (ddd, 1H, $J_{2'a,1'a}$ 9.9, $J_{2'a,3'a}$ 9.9, $J_{2'a,NHa}$ 7.7 Hz, H-2′a), 4.56 (ddd, 1H, $J_{2'b,1'b}$ 9.9, $J_{2'b,3'b}$ 9.9, $J_{2'b,NHb}$ 7.7 Hz, H-2′b), 5.16 (dd, 1H, $J_{4'a,3'a}$ 9.9, $J_{4'a,5'a}$ 9.2 Hz, H-4′a), 5.22 (t, 1H, $J_{3'a,2'a} = J_{3'a,4'a}$ 9.9 Hz, H-3′a), 5.41 (t, 1H, $J_{3'b,2'b} = J_{3'b,4'b}$ 9.9 Hz, H-3′b), 5.53 (d, 1H, $J_{1'a,2'a}$ 9.9 Hz, H-1′a), 5.64 (t, 1H, $J_{4'b,3'b} = J_{4'b,5'b}$ 9.9 Hz, H-4′b), 6.03 (d, 1H, $J_{1'b,2'b}$ 9.9 Hz, H-1′b), 6.49 (d, 1H, $J_{NHb,2'b}$ 7.7 Hz, D_2O exchangeable, NHAc), 7.42–7.53 (m, 2H, H-5, H-6 benzothiophene), 7.69 (dd, 1H, *J* 3.1, *J* 8.4 Hz, H-4 benzothiophene), 7.80 (d, 1H, $J_{NHa,2'a}$ 7.7 Hz, D_2O exchangeable, NHAc), 7.89 (dd, 1H, *J* 1.5, *J* 6.9 Hz, H-7 benzothiophene). ^{13}C NMR ($CDCl_3$, 125.7 MHz): δ 20.7, 20.8 (8×*CH*$_3$CO), 53.6 (C-2′a), 54.5 (C-2′b), 62.0 (C-6′a), 62.1 (C-6′b), 68.2 (C-4′b),

68.4 (C-4′a), 71.4 (C-3′b), 73.4 (C-3′a), 74.5 (C-5′b), 76.3 (C-5′a), 83.3 (C-1′a), 84.5 (C-1′b), 120.4 (C-9), 122.6 (C-4), 122.7 (C-7), 125.4 (C-5), 125.9 (C-8), 126.10 (C-6), 136.0 (C-3), 137.5 (C-2), 170.5, 170.7, 170.8, 171.0, 171.1 ($8 \times CH_3CO$). Anal. Calcd for $C_{38}H_{44}ClN_5O_{16}S_2$: C, 49.27; H, 4.79; N, 7.56. Found: C, 48.85; H, 5.02; N, 7.45.

4.3.5. 5-(3-Chlorobenzo[*b*]thien-2-yl)-4-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-3-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosylsulfanyl)-4*H*-1,2,4-triazole (10) and 5-(chlorobenzo[*b*]thien-2-yl)-2-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-3-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosylsulfanyl)-4*H*-1,2,4-triazole (11)

Yield of the crude: CM (75%), MW (89%); eluant: 30:70 hexane–EtOAc; the first fraction gave colorless crystals of **10** in 68% yield; mp 118–119 °C; R_f 0.43 (1:2.5 hexane–EtOAc). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.88, 1.90, 1.99, 2.00, 2.05, 2.08, 2.14, 2.27 (8s, 24H, $8 \times CH_3CO$), 4.11–4.18 (m, 6H, H-5′a, H-5′b, H-6′a, H-6′b, H-6″a, H-6″b), 5.20 (dd, 1H, $J_{3'b,2'b}$ 9.9, $J_{3'b,4'b}$ 3.1 Hz, H-3′b), 5.21 (dd, 1H, $J_{3'a,2'a}$ 9.9, $J_{3'a,4'a}$ 3.1 Hz, H-3′a), 5.43 (dd, 1H, $J_{2'a,1'a}$ 10.7, $J_{2'a,3'a}$ 9.9 Hz, H-2′a), 5.49 (d, 1H, $J_{4'a,3'a}$ 3.1 Hz, H-4′a), 5.51 (d, 1H, $J_{4'b,3'b}$ 3.1 Hz, H-4′b), 5.59 (d, 1H, $J_{1'b,2'b}$ 9.2 Hz, H-1′b), 5.70 (d, 1H, $J_{1'a,2'a}$ 10.7 Hz, H-1′a), 5.95 (dd, 1H, $J_{2'b,1'b}$ 9.2, $J_{2'b,3'b}$ 9.9 Hz, H-2′b), 7.42–7.47 (m, 2H, H-5, H-6 benzothiophene), 7.81 (dd, 1H, *J* 1.5, *J* 6.9 Hz, H-4 benzothiophene), 7.90 (dd, 1H, *J* 1.5, *J* 6.9 Hz, H-7 benzothiophene). ^{13}C NMR ($CDCl_3$, 125.7 MHz): δ 20.4, 20.6, 20.7, 20.8 ($8 \times CH_3CO$), 61.1 (C-6′a), 61.3 (C-6′b), 66.8 (C-2′a), 67.1 (C-2′b), 67.3 (C-4′a, C-4′b), 71.1 (C-3′a), 71.7 (C-3′b), 73.8 (C-5′a), 75.3 (C-5′b), 84.8 (C-1′a), 85.6 (C-1′b), 120.5 (C-9), 122.6 (C-4), 122.7 (C-7), 125.2 (C-5), 126.0 (C-8), 126.6 (C-6), 137.4 (C-3), 137.6 (C-2), 168.4, 169.9, 170.0, 170.1, 170.2, 170.4 ($8 \times CH_3CO$). Anal. Calcd for $C_{38}H_{42}ClN_3O_{18}S_2$: C, 49.16; H, 4.56; N, 4.53. Found: C, 49.08; H, 4.69; N, 4.48.

The second fraction gave **11**; colorless crystals (3% yield); mp 112–114 °C; R_f 0.37 (1:2.5 hexane–EtOAc). ^{1}H NM ($CDCl_3$, 500 MHz): δ 1.88, 1.97, 1.98, 2.00, 2.01, 2.04, 2.16 ($7 \times$ s, 24 H, $8 \times CH_3CO$), 4.19 (m, 6H, H-5′a, H-5′b, H-6′a, H-6′b, H-6″a, H-6″b), 5.08 (dd, 1H, $J_{3'b,2'b}$ 9.9, $J_{3'b,4'b}$ 3.1 Hz, H-3′b), 5.18 (dd, 1H, $J_{3'a,2'a}$ 9.9, $J_{3'a,4'a}$ 3.1 Hz, H-3′a), 5.43 (dd, 1H, $J_{2'a,1'a}$ 10.7, $J_{2'a,3'a}$ 9.2 Hz, H-2′a), 5.45 (d, 1H, $J_{4'b,3'b}$ 3.1 Hz, H-4′b), 5.48 (2d, 2H, $J_{4'a,3'a}$ 3.1, $J_{1'b,2'b}$ 9.2 Hz, H-4′a, H-1′b), 5.51 (d, 1H, $J_{1'a,2'a}$ 10.7 Hz, H-1′a), 6.00 (dd, 1H, $J_{2'b,1'b}$ 9.2, $J_{2'b,3'b}$ 9.9 Hz, H-2′b), 7.55–7.59 (m, 2H, H-5, H-6 benzothiophene), 7.87–7.90 (m, 1H, H-4 benzothiophene), 7.96–7.98 (m, 1H, H-7 benzothiophene). ^{13}C NMR ($CDCl_3$, 125.7 MHz): δ 20.5, 20.6, 20.7, 20.8 ($8 \times CH_3CO$), 61.1 (C-6′a), 61.4 (C-6′b), 66.9 (C-2′a), 67.3 (C-4′a, C-4′b), 67.6 (C-2′b), 71.4 (C-3′a), 72.0 (C-3′b), 73.9 (C-5′a), 74.7 (C-5′b), 84.3 (C-1′a), 84.5 (C-1′b), 120.0 (C-9), 122.7 (C-4), 123.3 (C-7), 124.2 (C-8), 126.1 (C-5), 127.6 (C-6), 136.1 (C-3), 138.6 (C-2), 168.3, 169.6, 170.0, 170.3, 170.4 ($8 \times CO$). Anal. Calcd for $C_{38}H_{42}ClN_3O_{18}S_2$: C, 49.16; H, 4.56; N, 4.53. Found: C, 49.10; H, 4.33; N, 4.28.

4.4. General procedure: reaction of 5-(3-chlorobenzo[*b*]thien-2-yl)-3-benzylsulfanyl-4*H*-1,2,4-triazole (12) and 5-(3-chlorobenzo[*b*]thien-2-yl)-3-methylsulfanyl-4*H*-1,2,4-triazole (13) with glycosyl halides 2–4

4.4.1. Conventional method (CM)

A mixture of compound **12** or **13** (1 mmol) and potassium carbonate (1 mmol, 0.138 g) in dry acetone (25 mL) was stirred for 1 h, then glycosyl halides **2–4** (1.1 mmol) were added. Stirring was continued overnight, then the mixture was heated under reflux for 2–5 h. The mixture was filtered, and the solids were washed with acetone. The acetone was evaporated under reduced pressure, and the crude product was recrystallized from EtOH or subjected to column chromatography to afford the respective derivatives, which were recrystallized from EtOH.

4.4.2. Microwave irradiation (MWI) method

A mixture of compound **12** or **13** (0.5 mmol), potassium carbonate (0.5 mmol, 0.069 g), and glycosyl halides **2–4** (0.55 mmol) in dry acetone (5 mL) in a closed Teflon vessel was irradiated by MW for 4–6 min. The reaction mixture was cooled and processed as described above to give **14–21**.

4.4.3. 3-Benzylsulfanyl-5-(3-chlorobenzo[*b*]thien-2-yl)-4-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-4*H*-1,2,4-triazole (14)

Colorless crystals; yield: CM (76%), MW (90%); mp 198–200 °C; R_f 0.33 (1:1 hexane–EtOAc). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.82, 2.01, 2.03, 2.05 (4s, 12H, $4 \times CH_3CO$), 3.92 (ddd, 1H, $J_{5',6'}$ 2.3, $J_{5',6''}$ 5.3, $J_{5',4'}$ 9.9 Hz, H-5′), 4.16 (dd, 1H, $J_{6',5'}$ 2.3, $J_{6',6''}$ 12.2 Hz, H-6′), 4.25 (dd, 1H, $J_{6'',5'}$ 5.3, $J_{6'',6'}$ 12.2 Hz, H-6″), 4.55, 4.62 (2d, 2H, *J* 13.0 Hz, CH_2Ph), 5.26 (dd, 1H, $J_{4',3'} = J_{4',5'}$ 9.9 Hz, H-4′), 5.36 (dd, 1H, $J_{3',2'}$ 9.2, $J_{3',4'}$ 9.9 Hz, H-3′), 5.51 (d, 1H, $J_{1',2'}$ 9.9 Hz, H-1′), 5.90 (dd, 1H, $J_{2',1'}$ 9.9, $J_{2',3'}$ 9.2 Hz, H-2′), 7.27–7.34 (m, 3H, 3 Ph-H), 7.42–7.48 (m, 4H, 2 Ph-H, H-5, H-6 benzothiophene), 7.82 (dd, 1H, *J* 1.5, *J* 6.9 Hz, H-4 benzothiophene), 7.91 (dd, 1H, *J* 1.5, *J* 6.9 Hz, H-7 benzothiophene). Anal. Calcd for $C_{31}H_{30}ClN_3O_9S_2$: C, 54.10; H, 4.39; N, 6.11. Found: C, 54.06; H, 4.65; N, 5.72.

4.4.4. 5-(3-Chlorobenzo[*b*]thien-2-yl)-3-methylsulfanyl-4-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-4*H*-1,2,4-triazole (15)

Colorless crystals; yield: CM (74%), MW (88%); mp 186–188 °C; R_f 0.27 (1:1 hexane–EtOAc). ^{1}H NM ($CDCl_3$, 500 MHz): δ 1.89, 2.04, 2.06, 2.08 ($4 \times$ s, 12H, $4 \times CH_3CO$), 2.80 (s, 3H, SCH_3), 3.97 (ddd, 1H, $J_{5',6'}$ 2.3, $J_{5',6''}$ 4.6, $J_{5',4'}$ 9.9 Hz, H-5′), 4.21 (dd, 1H, $J_{6',5'}$ 2.3, $J_{6',6''}$ 12.2 Hz, H-6′), 4.29 (dd, 1H, $J_{6'',5'}$ 4.6, $J_{6'',6'}$ 12.2 Hz, H-6″), 5.28 (t, 1H, $J_{4',3'} = J_{4',5'}$ 9.9 Hz, H-4′), 5.41 (dd, 1H, $J_{3',2'}$ 9.2, $J_{3',4'}$ 9.9 Hz, H-3′), 5.57 (d, 1H, $J_{1',2'}$ 9.2 Hz, H-1′), 5.92 (dd, 1H, $J_{2',1'} = J_{2',3'}$ 9.2 Hz, H-2′), 7.40–7.47 (m, 2H, H-5, H-6 benzothiophene), 7.80 (dd, 1H, *J* 1.5, *J* 6.9 Hz, H-4 benzothiophene), 7.90 (dd, 1H, *J* 1.5, *J* 6.9 Hz, H-7 benzothiophene). Anal. Calcd for $C_{25}H_{26}ClN_3O_9S_2$: C, 49.06; H, 4.28; N, 6.87. Found: C, 49.04; H, 4.35; N, 6.80.

4.4.5. 4-(2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-3-benzylsulfanyl-5-(3-chlorobenzo[*b*]thien-2-yl)-4*H*-1,2,4-triazole (16)

Colorless plates; yield: CM (74%), MW (89%); mp: 248–250 °C, TLC R_f 0.57 (1:1 hexane–EtOAc). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.74, 2.00, 2.04, 2.06 (4s, 12H, NCH_3CO, $3 \times CH_3CO$), 4.00 (ddd, 1H, $J_{5',6'}$ 2.3, $J_{5',6''}$ 4.6, $J_{5',4'}$ 10.7 Hz, H-5′), 4.15 (dd, 1H, $J_{6',5'}$ 2.3, $J_{6',6''}$ 12.2 Hz, H-6′), 4.26 (dd, 1H, $J_{6'',5'}$ 4.6, $J_{6'',6'}$ 12.2 Hz, H-6″), 4.43 (ddd, 1H, $J_{2',1'}$ 9.9, $J_{2',3'}$ 9.9, $J_{2',NH}$ 7.7 Hz, H-2′), 4.54, 4.57 (2d, 2H, *J* 13.0 Hz, CH_2Ph), 5.19 (t, 1H, $J_{3',2'} = J_{3',4'}$ 9.9 Hz, H-3′), 5.59 (d, 1H, $J_{NH,2'}$ 7.7 Hz, D_2O exchangeable, $NHCH_3CO$), 5.83 (dd, 1H, $J_{4',3'}$ 9.9, $J_{4',5'}$ 10.7 Hz, H-4′), 6.14 (d, 1H, $J_{1',2'}$ 9.9 Hz, H-1′), 7.26–7.33 (m, 3H, 3 Ph-H), 7.43–7.49 (m, 4H, 2 Ph-H, H-5, H-6 benzothiophene), 7.83 (dd, 1 H, *J* 1.5, *J* 8.4 Hz, H-4 benzothiophene), 7.91 (dd, 1H, *J* 1.5, *J* 6.9 Hz, H-7 benzothiophene). Anal. Calcd for $C_{31}H_{31}ClN_4O_8S_2$: C, 54.18; H, 4.55; N, 8.15. Found: C, 54.52; H, 4.77; N, 8.02.

4.4.6. 4-(2-Acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-5-(3-chlorobenzo[*b*]thien-2-yl)-3-methylsulfanyl-4*H*-1,2,4-triazole (17)

Colorless crystals; yield: CM (72%), MW (87%); mp 178–180 °C; R_f 0.52 (1:2 hexane–EtOAc). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.80, 2.06, 2.07, 2.08 ($4 \times$ s, 12H, NCH_3CO, $3 \times CH_3CO$), 2.77 (s,

3H, SCH_3), 4.04 (ddd, 1H, $J_{5',6'}$ 2.3, $J_{5',6''}$ 4.6, $J_{5',4'}$ 10.7 Hz, H-5′), 4.23 (dd, 1H, $J_{6',5'}$ 2.3, $J_{6',6''}$ 12.2 Hz, H-6′), 4.30 (dd, 1H, $J_{6'',5'}$ 4.6, $J_{6'',6'}$ 12.2 Hz, H-6″), 4.50 (ddd, 1H, $J_{2',1'} = J_{2',3'}$ 9.9, $J_{2',NH}$ 7.7 Hz, H-2′), 5.22 (t, 1H, $J_{3',2'} = J_{3',4'}$ 9.9 Hz, H-3′), 5.75 (d, 1H, $J_{NH,2'}$ 7.7 Hz, D_2O exchangeable, NHAc), 5.84 (dd, 1H, $J_{4',3'}$ 9.9, $J_{4',5'}$ 10.7 Hz, H-4′), 6.17 (d, 1H, $J_{1',2'}$ 9.9 Hz, H-1′), 7.41–7.48 (m, 2H, H-5, H-6 benzothiophene), 7.81 (dd, 1H, *J* 1.5, *J* 6.9 Hz, H-4 benzothiophene), 7.90 (dd, 1H, *J* 1.5, *J* 6.9 Hz, H-7 benzothiophene). Anal. Calcd for $C_{25}H_{27}ClN_4O_8S_2$: C, 49.14; H, 4.45; N, 9.17. Found: C, 49.52; H, 4.77; N, 8.98.

4.4.7. 3-Benzylsulfanyl-5-(3-chlorobenzo[*b*]thien-2-yl)-4-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-4*H*-1,2,4-triazole (18) and 3-benzylsulfanyl-5-(3-chlorobenzo[*b*]thien-2-yl)-2-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)- 4*H*-1,2,4-triazole (20)

Yield of the crude product: CM (73%), MW (87%); eluant: 85:15 hexane–EtOAc, the first fraction gives **18**, colorless crystals in 62% yield; mp 80–81 °C; TLC R_f 0.310 (2:1 hexane–EtOAc). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.85, 2.00, 2.01, 2.14 (4 × s, 12H, 4 × CH_3CO), 4.11–4.19 (m, 3H, H-5′, H-6′, H-6″), 4.55, 4.64 (2d, 2H, *J* 13.0 Hz, CH_2Ph), 5.19 (dd, 1H, $J_{3',2'}$ 9.9, $J_{3',4'}$ 3.1 Hz, H-3′), 5.49 (d, 1H, $J_{4',3'}$ 3.1 Hz, H-4′), 5.50 (d, 1H, $J_{1',2'}$ 9.9 Hz, H-1′), 6.05 (t, 1H, $J_{2',1'} = J_{2',3'}$ 9.9 Hz, H-2′), 7.26–7.34 (m, 3H, 3Ph-H), 7.42–7.49 (m, 4H, 2Ph-H, H-5, H-6 benzothiophene), 7.81 (d, 1H, *J* 7.7 Hz, H-4 benzothiophene), 7.91 (dd, 1H, *J* 3.1, *J* 6.9 Hz, H-7 benzothiophene). Anal. Calcd For $C_{31}H_{30}ClN_3O_9S_2$: C, 54.10; H, 4.39; N, 6.11. Found: C, 54.29; H, 4.59; N, 5.97.

The second fraction gave **20**; white crystals in 6% yield; mp 72–74 °C; TLC R_f 0.243 (2:1 hexane–EtOAc). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.83, 1.97, 2.04, 2.17 (4 × s, 12H, 4 × CH_3CO), 4.06–4.18 (m, 3H, H-5′, H-6′, H-6″), 4.39, 4.50 (2d, 2H, *J* 13.0 Hz, CH_2Ph), 5.09 (dd, 1H, $J_{3',2'}$ 9.9, $J_{3',4'}$ 3.1 Hz, H-3′), 5.45 (d, 1H, $J_{4',3'}$ 3.1 Hz, H-4′), 5.46 (d, 1H, $J_{1',2'}$ 9.9 Hz, H-1′), 5.98 (t, 1H, $J_{2',1'} = J_{2',3'}$ 9.9 Hz, H-2′), 7.24–7.33 (m, 3H, 3 Ph-H), 7.45–7.57 (m, 4H, 2 Ph-H, H-5, H-6 benzothiophene), 7.89 (dd, 1H, *J* 3.1, *J* 6.9 Hz, H-4 benzothiophene), 7.97 (dd, 1H, *J* 3.1, *J* 6.9 Hz, H-7 benzothiophene). Anal. Calcd for $C_{31}H_{30}ClN_3O_9S_2$: C, 54.10; H, 4.39; N, 6.11. Found: C, 54.27; H, 4.40; N, 6.00.

4.4.8. 5-(3-Chlorobenzo[*b*]thien-2-yl)-3-methylsulfanyl-4-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-4*H*-1,2,4-triazole (19) and 5-(3-chlorobenzo[*b*]thien-2-yl)-3-methylsulfanyl-2-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-4*H*-1,2,4-triazole (21)

Yield of the crude: CM (71%), MW (86%); eluant: 85:15 hexane–EtOAc; the first fraction gives **19**; colorless crystals in 60% yield; mp 60–61 °C; R_f 0.30 (2:1 hexane–EtOAc). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.90, 2.01, 2.05, 2.22 (4 × s, 12H, 4 × CH_3CO), 2.80 (s, 3H, SCH_3), 4.16–4.21 (m, 3H, H-5′, H-6′, H-6″), 5.23 (dd, 1H, $J_{3',2'}$ 9.9, $J_{3',4'}$ 3.1 Hz, H-3′), 5.52 (d, 1H, $J_{4',3'}$ 3.1 Hz, H-4′), 5.55 (d, 1H, $J_{1',2'}$ 9.2 Hz, H-1′), 6.07 (dd, 1H, $J_{2',1'}$ 9.2, $J_{2',3'}$ 9.9 Hz, H-2′), 7.40–7.46 (m, 2H, H-5, H-6 benzothiophene), 7.80 (dd, 1H, *J* 1.5, *J* 7.7 Hz, H-4 benzothiophene), 7.89 (dd, 1H, *J* 1.5, *J* 7.7 Hz, H-7 benzothiophene). Anal. Calcd for $C_{25}H_{26}ClN_3O_9S_2$: C, 49.06; H, 4.28; N, 6.87. Found: C, 49.28; H, 4.25; N, 6.76.

The second fraction gave **21**; white crystals in 5% yield; mp 53–54 °C; R_f 0.18 (2:1 hexane–EtOAc). ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.87, 1.96, 2.03, 2.18 (4 × s, 12H, 4 × CH_3CO), 2.64 (s, 3H, SCH_3), 4.05–4.08 (m, 3H, H-5′, H-6′, H-6″), 5.08 (dd, 1H, $J_{3',2'}$ 9.9, $J_{3',4'}$ 3.1 Hz, H-3′), 5.45, 5.47 (2d, 2H, $J_{1',2'}$ 9.9, $J_{4',3'}$ 3.1 Hz, H-1′, H-4′), 6.01 (dd, 1H, $J_{2',1'}$ 9.9, $J_{2',3'}$ 9.9 Hz, H-2′), 7.55–7.57 (m, 2H, H-5, H-6 benzothiophene), 7.88 (dd, 1H, *J* 3.1, *J* 6.9 Hz, H-4 benzothiophene), 7.96 (dd, 1H, *J* 3.1, *J* 6.9 Hz, H-7 benzothiophene). Anal. Calcd for $C_{25}H_{26}ClN_3O_9S_2$: C, 49.06; H, 4.28; N, 6.87. Found: C, 48.98; H, 4.20; N, 6.79.

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