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Efficient synthesis, structure, and antimicrobial activity of some novel N- and S-β-D-glucosides of 5-pyridin-3-yl-1,2,4-triazoles

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Abstract—Glucosidation of some 4-amino- and 4-arylideneamino-5-(pyridin-3-yl)-2,4-dihydro-[1,2,4]-triazole-3-thiones with 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide followed by chromatographic separation gave the corresponding N- and S-β-D-glucosides. The structure of these two regiosiomers was established chemically and spectroscopically. Deamination as well as deacetylation of some selected nucleosides have been achieved. Antimicrobial screening of 14 selected compounds resulted in their activity against *Aspergillus fumigatus*, *Penicillium italicum*, *Syncephalastrum racemosum*, *Candida albicans*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Bacillus subtilis*, and *Escherichia coli*.

Keywords: Synthesis; Glucosidation; 1,2,4-Triazoles; Deamination; Deacetylation; Antibacterial activity; Antifungal activity

1. Introduction

Several base-modified nucleosides have been reported to act as antiviral and anticancer agents most likely due to their capability to mimic natural counterparts and function.[1] The synthesis and biological activities of sugar-modified nucleoside analogs have been active research areas for many years, since many of these compounds have found useful application in the chemotherapy of cancer and viral infections. A variety of nucleoside derivatives have been prepared through the deletion or change in nature of the functional group present on the heterocyclic base or their sugar moieties. Such analogs permit the synthesis of oligonucleotides in which a single functional group at a preselected position has been deleted or otherwise altered.

It has been found that many 1,2,4-triazoles possess a wide spectrum of activities including antibacterial, antifungal, antiviral, antiinflammatory, anticonvulsant, antidepressant, antihypertensive, analgesic, and hypoglycemic properties.[2–14] The synthesis and investigation of biological activity of 1,2,4-triazole glycosides[15–18] have been stimulated by the finding that Ribavirin (β-D-ribofuranosyl-1,2,4-triazole-3-carboxamide)[15] is remarkable in its broad spectral activity against DNA and RNA viruses.[16,17] Ribavirin has been developed clinically[18] and approved for human use in many pharmaceutical preparations.

Encouraged by these interesting structures and biological activities and as a part of our ongoing program[19–27] addressed to prepare some new biologically active compounds, we found that it would be of great interest to synthesize some novel 1,2,4-triazole glucosides to investigate their antibacterial and antifungal activities.

2. Results and discussion

In the present work, the reaction of some 4-substituted-2,4-dihydro-1,2,4-triazol-3-thiones with 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**4**) as well as the biological activity of the resulting glucosides was studied. Scheme 1 illustrates our attempt to design suitable starting 4-amino- and/or 4-arylideneamino-5-(pyridin-3-yl)-2,4-dihydro-[1,2,4]-triazole-3-thiones (**2** and/ or **3a–d**)

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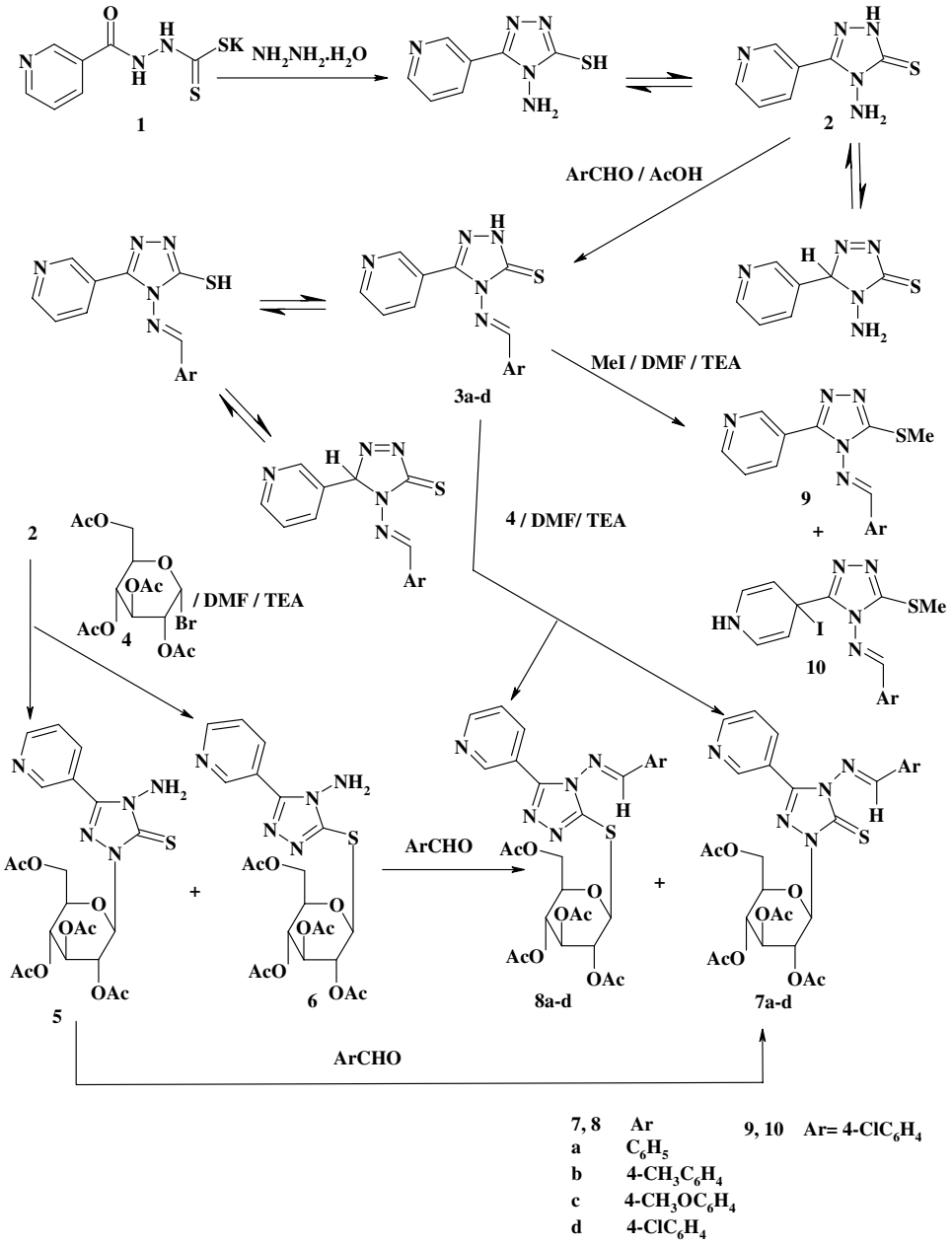


Scheme 1.

for use in the present objectives. Thus, consecutive hydrazinolysis and acidification of potassium 3-nicotinoyldithiocarbazate (**1**) gave the corresponding 4-amino-5-(pyridin-3-yl)-2,4-dihydro-[1,2,4]-triazole-3-thione (**2**).

While 1,2,4-triazole-3-thiones may exist in thione-thiol tautomeric structures, our investigations showed that compound **2** has three possible tautomeric structures, two of them are thione forms (2,4-dihydrothione and 4,5-dihydrothione) and the third is the thiol form as indicated by IR and NMR data of compound **2**. Thus, in its solid state, the IR spectrum of compound **2** showed absorption bands at 2924 (CH aliphatic of the 4,5-dihydrothione tautomeric structure), 2493 (SH of the thiol tautomeric structure consistent with similar reported data[28]), 1338 (C=S of both thione tautomeric structures consistent with similar reported data[29–31]), and 3232 cm^{-1} (NH of 2,4-dihydrothione tautomeric structure consistent with similar reported data[28]). The ^1H NMR spectrum of compound **2** showed the predominant 2,4-dihydrothione form in DMSO-d_6 as indicated by the appearance of NH proton signal at δ 5.27 (s, 1H, D_2O exchangeable).

Condensation of compound **2** with the appropriate aryl aldehydes gave the corresponding 4-arylidene-

amino-5-(pyridin-3-yl)-2,4-dihydro-[1,2,4]-triazole-3-thiones (**3a–d**). The latter compounds exist similarly in the three tautomeric forms in the solid state as indicated by their IR spectra. On the other hand, the ^{1}H NMR spectra of these compounds (measured in DMSO-d_6) support the predominant 2,4-dihydrothione structure (NH signals of these compounds appeared as a singlet at δ 14.30–14.38, consistent with similar reported thione structures[31–33]). Furthermore, the appearance of the CH=N proton signal of compounds **3a–d** in DMSO-d_6 at δ 9.61–9.90 confirms their presence in the 2,4-dihydrothione form as will be seen later compared to the CH=N proton signal of compound **9** at δ 8.58.

Compounds **2** and **3a–d** were used as starting materials to prepare new functionalized 1,2,4-triazole N- and S-β-D-glucosides. Thus, glucosidation of compounds **2** and/or **3a–d** with 1.1 M equiv of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**4**) afforded a chromatographically separable mixture (94–99% over-all yield) of two products, namely, 2-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-4-amino- and/or 4-arylideneamino-5-(pyridin-3-yl)-2,4-dihydro-[1,2,4]-triazole-3-thiones (**5** and/or **7a–d**) and 3-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl-1-thio)-4-amino- and/or 4-arylideneamino-5-(pyridin-3-yl)-4*H*-[1,2,4]-triazoles (**6** and/or **8a–d**).

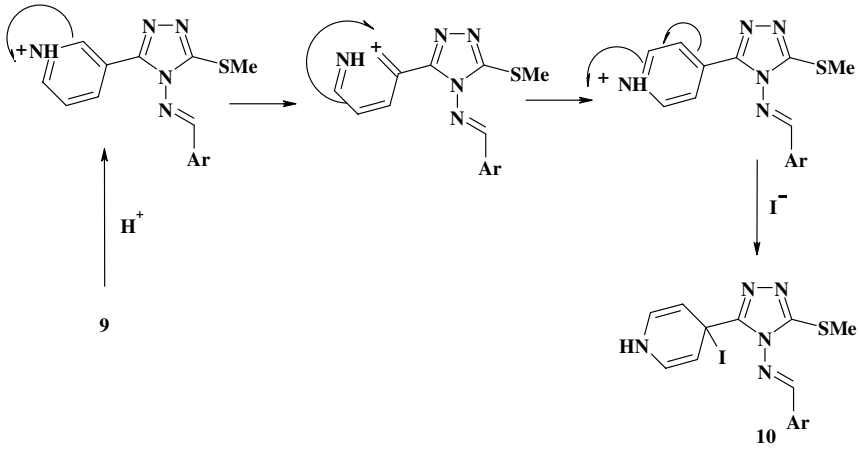
The structures assigned for compounds **5–8** were based on spectroscopic and chemical evidences. Thus, the N-β-D-configuration of compounds **5** and **7a–d** is supported by their ^{1}H NMR data, which revealed the anomeric proton signal around δ 6.4 with a coupling constant value of 6.6–9.3 Hz consistent with the reported data for N-β-D-glycosides.[20–23,25–27,34] The S-β-D-configuration of compounds **6** and **8a–d** is similarly assigned from their ^{1}H NMR data. The ^{1}H NMR data of compounds **8a–d** showed a signal of the anomeric proton around δ 5.4 with a coupling constant value of 9.9–10.5 consistent with the reported data for S-β-D-glycosides.[22]

For all the N-glucosides **7a–d**, the CH=N and the anomeric protons appear around δ 9.8 and 6.4 more downfield than those for the S-glucosides **8a–d**, which appear around δ 8.6 and 5.4, respectively. Such downfield shifts in *N*-glucosyl derivatives are readily explained by the anisotropic deshielding by the C=S (similar downfield shifts of the anomeric proton and the CH=N proton by an adjacent C=S were reported for pyrimidine[35] and 1,2,4-triazole nucleosides).[22]

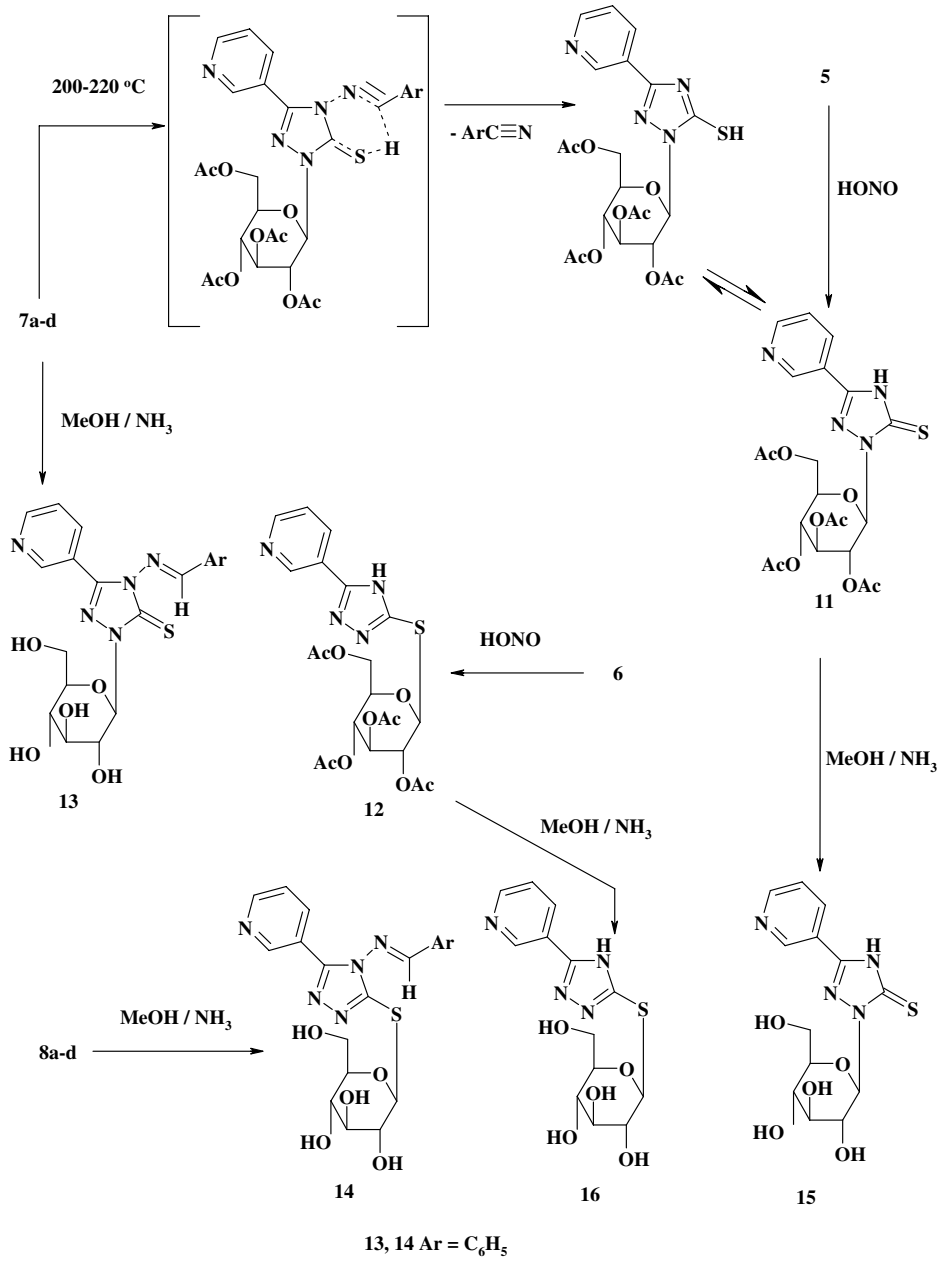
In order to support the latter evidence, methylation of compound **3d** with methyl iodide in *N*,*N*-dimethylformamide containing triethylamine was conducted to give the chromatographically separable 3-methylthio derivatives **9** and **10**. A careful study of the ^{1}H NMR spectra of the N-glucosides **7a–d** and S-glucosides **8a–d** in comparison with 4-(4-chlorobenzylideneamino)-3-methylthio-5-(pyridin-3-yl)-4*H*-[1,2,4]-triazole (**9**) establishes their structures. Thus, the appearance of CH=N proton signal of compound **9** at δ 8.58 confirms the assigned structure of compounds **8a–d** and adds another evidence to the existence of compounds **3a–d** in their thione tautomeric form in DMSO-d_6 as previously mentioned. Compounds **7a–d** and **8a–d** were alternatively synthesized in excellent yields via condensation of compounds **5** and **6** with the appropriate aryl aldehydes.

The proposed mechanism for the formation of compound **10** during methylation of compound **3d** is illustrated in Scheme 2. Thus, the reaction presumably proceeds to give first the 3-methylthio derivative **9**, which is then protonated (by the resulting hydroiodic acid) followed by ring opening and sigmatropic rearrangement to give an intermediate pyridinium cation. The latter is attacked by the iodide anion to afford compound **10**.

Deamination of compounds **5** and **6** into compounds **11** and **12**, respectively (Scheme 3), was achieved almost quantitatively by the action of nitrous acid in acetic acid. Compound **11** was alternatively prepared, also in an excellent yield, via thermolysis of compounds **7a–d**.



Scheme 2.



Scheme 3.

The structure of compounds **11** and **12** was inferred from their correct analytical and spectral data. Thus, the ^{1}H NMR data of these compounds not only showed the absence of the NH_2 protons at δ 5.91–5.45, but also revealed the presence of the D_2O exchangeable NH proton signal at δ 8.3. Further evidence comes from the disappearance of NH_2 bands at 3325–3313, 3229–3202 cm^{-1} and the appearance of the characteristic NH band at 3418–3259 cm^{-1} in the IR spectra of compounds **11** and **12**.

Deacetylation of compounds **7a**, **8a**, **11** and **12** (Scheme 3) via methanolic ammonia treatment led to the formation of the free nucleosides **13**–**16**. The ^{1}H NMR data of the latter compounds revealed the absence of the acetyl protons at δ 1.87–2.04 and the appearance of the D_2O exchangeable OH protons at δ 4.43–5.52. The IR data of these compounds also showed the absence of the acetyl carbonyl function at 1755–1747 cm^{-1} and the appearance of the characteristic OH band at 3600–3200 cm^{-1}.

Compounds **5**, **6**, **7a**–**d**, **8a**–**d**, **9**, **11**, **13**, and **15** have been evaluated for their antifungal and antibacterial activities against *Aspergillus fumigatus*, *Penicillium italicum*, *Syncephalastrum racemosum*, *Candida albicans*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Bacillus subtilis*, and *Escherichia coli*. The inhibitory effects of the tested compounds against the mentioned organisms are given in Table 1. The screening results indicate that

all compounds exhibited antifungal and antibacterial activities. The inhibitory effects of N-glucosides **5** and **7a–c** were studied in comparison with similar effects due to S-glucosides **6** and **8a–d**. Thus, compound **6** showed higher inhibitory effect against *Aspergillus fumigatus*, *Syncephalastrum racemosum*, and *Staphylococcus aureus* as well as lower inhibitory effect against *Penicillium italicum* and *Bacillus subtilis*, compared to compound **5**.

Compound **8a** revealed higher inhibitory effect against *Candida albicans*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Bacillus subtilis* as well as lower inhibitory effect against *Penicillium italicum*, compared to compound **7a**. Compared to compound **7b**, compound

Table 1. Antimicrobial activity of compounds **5**, **6**, **7a–d**, **8a–d**, **9**, **11**, **13**, and **15** (at a concentration of 1, 2.5, 5 mg/mL) compared to standard antimicrobial agents

Test organisms	Compd **5**[a]			Compd **6**[a]			Compd **7a**[a]		
	1	2.5	5	1	2.5	5	1	2.5	5
Aspergillus fumigatus	0	+	+	+	+	+	+	+	++
Penicillium italicum	0	+	+	0	0	+	+	+	+
Syncephalastrum racemosum	0	0	+	+	+	+	+	+	+
Candida albicans	+	+	+	+	+	+	0	0	+
Staphylococcus aureus	+	+	+	+	+	++	+	+	++
Pseudomonas aeruginosa	0	0	+	0	0	+	0	0	0
Bacillus subtilis	0	+	+	0	0	+	0	0	+
Escherichia coli	++	++	++	++	++	++	+	++	++
	Compd **7b**[a]			Compd **7c**[a]			Compd **7d**[a]		
Aspergillus fumigatus	+	+	+	0	+	++	+	+	++
Penicillium italicum	+	+	+	0	0	+	+	+	+
Syncephalastrum racemosum	+	+	+	+	+	+	+	+	+
Candida albicans	0	0	+	+	+	+	0	0	+
Staphylococcus aureus	+	+	++	+	+	++	+	+	++
Pseudomonas aeruginosa	0	0	0	0	0	0	0	0	+
Bacillus subtilis	0	0	+	+	+	+	0	0	+
Escherichia coli	+	+	++	++	++	++	+	++	++
	Compd **8a**[a]			Compd **8b**[a]			Compd **8c**[a]		
Aspergillus fumigatus	+	+	++	+	+	+	+	+	+
Penicillium italicum	0	+	+	+	+	+	0	0	+
Syncephalastrum racemosum	+	+	+	+	+	+	+	+	+
Candida albicans	+	+	+	0	0	+	0	0	+
Staphylococcus aureus	+	++	++	+	+	++	+	+	+
Pseudomonas aeruginosa	0	0	+	0	0	0	0	0	0
Bacillus subtilis	0	+	++	0	0	+	0	0	+
Escherichia coli	+	++	++	+	+	++	+	++	++
	Compd **8d**[a]			Compd **9**[a]			Compd **11**[a]		
Aspergillus fumigatus	+	+	+	0	+	+	+	+	+
Penicillium italicum	+	+	+	0	0	+	+	+	+
Syncephalastrum racemosum	+	+	+	+	++	++	+	+	++
Candida albicans	0	0	0	0	0	0	+	+	+
Staphylococcus aureus	+	+	++	+	+	++	+	+	++
Pseudomonas aeruginosa	0	0	0	0	0	0	0	+	+
Bacillus subtilis	0	0	+	0	0	0	+	+	++
Escherichia coli	+	+	++	+	+	+	+	++	++
	Compd **13**[a]			Compd **15**[a]			St.[b]		
Aspergillus fumigatus	+	+	+	0	0	+	++	+++	+++
Penicillium italicum	+	+	+	0	0	+	++	+++	+++
Syncephalastrum racemosum	++	++	++	++	++	++	+++	+++	+++
Candida albicans	0	0	0	+	+	+	++	++	++
Staphylococcus aureus	+	++	++	+	+	++	++	++	++
Pseudomonas aeruginosa	0	0	0	0	0	0	++	+++	+++
Bacillus subtilis	+	+	+	0	0	+	++	+++	+++
Escherichia coli	+	++	++	+	++	++	++	++	++

Note: The test was done using the diffusion agar technique. Inhibition values = 0.1–0.5 cm beyond control = +; inhibition values = 0.6–1.0 cm beyond control = ++; inhibition values = 1.0–1.5 cm beyond control = +++; 0 = not detected.

[a] 100 μL of each concn was tested (5, 2.5, 1.0 mg/mL); well diameter = 0.6 cm.

[b] St. = Reference standard; Chloramphenicol was used as a standard antibacterial agent and Terbinafin was used as a standard antifungal agent.

8b exhibited the same inhibitory effect against all the test organisms. Compound **7c** showed higher inhibitory effect against *Aspergillus fumigatus*, *Candida albicans*, *Staphylococcus aureus*, *Bacillus subtilis*, and *Escherichia coli*, compared to compound **8c**.

Compound **7d** showed higher inhibitory effect against *Aspergillus fumigatus*, *Candida albicans*, *Pseudomonas aeruginosa*, and *Escherichia coli*, compared to compound **8d**.

From the previous biological results, we can conclude that the inhibitory effects of N-glucosides **7a–d** and those of S-glucosides **8a–d** depend on the substituents on the aromatic ring.

To see the role of the sugar moiety on the antimicrobial activity, we compared the inhibitory effect of compound **8d** with that of compound **9**. Thus, compound **8d** showed higher inhibitory effect against *Aspergillus fumigatus*, *Penicillium italicum*, *Bacillus subtilis*, and *Escherichia coli* as well as lower inhibitory effect against *Syncephalastrum racemosum*, compared to compound **9**.

We can also compare the inhibitory effect of compound **5** with the similar effect of its deaminated product **11**. Thus, compound **11** revealed higher inhibitory effect against *Aspergillus fumigatus*, *Penicillium italicum*, *Syncephalastrum racemosum*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, and *Bacillus subtilis* as well as lower inhibitory effect against *Escherichia coli*, compared to compound **5**.

The inhibitory effects of the acylated nucleosides **7a** and **11** can further be compared with their deacylated analogs **13** and **15**, respectively. Thus, compound **13** showed higher inhibitory effect against *Syncephalastrum racemosum*, *Staphylococcus aureus*, and *Bacillus subtilis* as well as lower inhibitory effect against *Aspergillus fumigatus* and *Candida albicans*, compared to compound **7a**. Compared to compound **15**, compound **11** exhibited higher inhibitory effect against *Aspergillus fumigatus*, *Penicillium italicum*, *Pseudomonas aeruginosa*, and *Bacillus subtilis* as well as lower inhibitory effect against *Syncephalastrum racemosum*.

The present work describes an efficient synthetic access to N- and S-β-D-glucosides of various functionalized 1,2,4-triazoles with potential antimicrobial activities and as starting materials for further synthetic transformations. It also expands the synthesis as well as the utility of both base-modified and sugar-modified nucleosides of possible application in the chemotherapy of cancer and viral infections.

3. Experimental

3.1. General

All melting points are uncorrected. IR spectra were recorded on a Perkin–Elmer 1430 spectrometer. ^{1}H NMR spectra were recorded at 300 MHz with a Varian Mercury 300 spectrometer. Mass spectrum of compound **10** was recorded on a GCMS-QP 1000 EX (70EV) spectrometer. Elemental analyses were carried out at the Micro Analytical Center, Cairo University, Giza, Egypt. Antimicrobial screening of compounds **5**, **6**, **7a–d**, **8a–d**, **9**, **11**, **13**, and **15** was carried out at the Medical Mycology Lab., The Regional Center for Mycology and Biotechnology, Al Azhar University, Cairo, Egypt. The starting 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**4**) was prepared as reported.[36] TLC was performed on Fluka silica gel 60 F_{254} aluminum sheets, and the products were detected using 254 nm light. Fluka silica gel 60 (70–230 mesh) was used for column chromatography.

3.1.1. Potassium 3-nicotinoyldithiocarbazate (1). To a cold solution (0–5 °C) of potassium hydroxide (19.6 g, 349.3 mmol) and nicotinic acid hydrazide (30 g, 219 mmol) in absolute ethanol (470 mL) was added dropwise while stirring carbon disulfide (15.8 g, 207.8 mmol). The mixture was diluted with 350 mL of absolute ethanol and stirred overnight. The reaction mixture was then diluted with 470 mL of ether and the precipitated solids were collected by filtration, washed with ether (2 × 120 mL), and dried in an air oven at 105 °C for 1 h. The obtained yellow salt (55.0 g, 100%) was used in the next step without any further purification; mp 258 °C. Anal. Calcd for $C_7H_6KN_3OS_2$ (251.4): C, 33.45; H, 2.41; N, 16.72; S, 25.51. Found: C, 33.38; H, 2.44; N, 16.57; S, 25.66.

3.1.2. 4-Amino-5-(pyridin-3-yl)-2,4-dihydro-[1,2,4]-triazole-3-thione (2). A suspension of compound **1** (55.1 g, 219.2 mmol) and 99.8% hydrazine hydrate (102.7 g, 2.05 mol) was heated at reflux temperature with stirring for 12 h. The color of the reaction mixture changed to green, hydrogen sulfide was evolved (lead acetate paper and color), and a homogeneous solution resulted. The reaction mixture was diluted with 100 mL cold water and acidified with concentrated hydrochloric acid, and the formed product was collected by filtration, washed several times with cold water, dried at room temperature, and recrystallized from *N*,*N*-dimethylformamide to give 22.1 g (52%) of compound **2**, colorless crystals, mp 208 °C (dec). IR: 3414, 3232, 3148, 3078, 2924, 2493, 1836, 1647, 1597, 1566, 1508, 1439, 1416, 1338, 1234, 1192, 1161, 1126, 1084, 1045, 999, 980, 930, 806, 741, 698, 633, 602, 509, 474; ^{1}H NMR (DMSO-d_6) δ 5.27 (s, 1H, D_2O exchangeable NH), 5.79 (s, 2H, D_2O exchangeable NH_2), 7.56 (dd, 1H, $J_{\text{H-5 pyrid.–H-6 pyrid.}} = 4.8$ Hz, $J_{\text{H-5 pyrid.–H-4 pyrid.}} = 8.1$ Hz, H-5 pyrid.), 8.37 (td, 1H, $J_{\text{H-4 pyrid.–H-6 pyrid.}} = 1.8$ Hz, $J_{\text{H-4 pyrid.–H-2 pyrid.}} = 2.1$ Hz, $J_{\text{H-4 pyrid.–H-5 pyrid.}} = 8.1$ Hz, H-4 pyrid.), 8.70 (dd, 1H, $J_{\text{H-6 pyrid.–H-4 pyrid.}} = 1.8$ Hz, $J_{\text{H-6 pyrid.–H-5 pyrid.}} = 4.8$ Hz, H-6 pyrid.),

9.15 (dd, 1H, $J_{\text{H-2 pyrid.–H-5 pyrid.}} = 0.9$ Hz, $J_{\text{H-2 pyrid.–H-4 pyrid.}} = 2.1$ Hz, H-2 pyrid.). Anal. Calcd for $C_7H_7N_5S$ (193.2): C, 43.51; H, 3.65; N, 36.24; S, 16.59. Found: C, 43.55; H, 3.71; N, 36.44; S, 16.39.

3.1.3. 4-Arylideneamino-5-(pyridin-3-yl)-2,4-dihydro-[1,2,4]-triazole-3-thiones (3a–d). General procedure. To a solution of compound **2** (1 g, 5.2 mmol) in acetic acid (10 mL) was added the appropriate aldehyde (5.2 mmol), and the reaction mixture was heated at reflux temperature for 2 h. After cooling, the formed product was collected by filtration and recrystallized from acetic acid.

3.1.3.1. 4-Benzylideneamino-5-(pyridin-3-yl)-2,4-dihydro-[1,2,4]-triazole-3-thione (3a). Yield 0.95 g (65%); pale yellow crystals, mp 272–274 °C. IR: 3414, 3279, 3032, 2874, 2708, 2584, 2365, 1601, 1551, 1504, 1416, 1277, 1223, 1184, 1122, 1080, 1030, 964, 906, 876, 810, 756, 690, 625, 582, 505; ^{1}H NMR (DMSO-d_6) δ 7.56 (dd, 1H, $J_{\text{H-5 pyrid.–H-6 pyrid.}} = 4.8$ Hz, $J_{\text{H-5 pyrid.–H-4 pyrid.}} = 8.1$ Hz, H-5 pyrid.), 7.52–7.65 (m, 3H, ArH), 7.88 (m, 2H, ArH), 8.26 (td, 1H, $J_{\text{H-4 pyrid.–H-6 pyrid.}} = 1.8$ Hz, $J_{\text{H-4 pyrid.–H-2 pyrid.}} = 2.1$ Hz, $J_{\text{H-4 pyrid.–H-5 pyrid.}} = 8.1$ Hz, H-4 pyrid.), 8.71 (dd, 1H, $J_{\text{H-6 pyrid.–H-4 pyrid.}} = 1.8$ Hz, $J_{\text{H-6 pyrid.–H-5 pyrid.}} = 4.8$ Hz, H-6 pyrid.), 9.05 (d, 1H, $J_{\text{H-2 pyrid.–H-4 pyrid.}} = 2.1$ Hz, H-2 pyrid.), 9.85 (s, 1H, CH=N), 14.36 (s, 1H, D_2O exchangeable NH). Anal. Calcd for $C_{14}H_{11}N_5S$ (281.3): C, 59.77; H, 3.94; N, 24.89; S, 11.40. Found: C, 59.61; H, 3.86; N, 24.97; S, 11.39.

3.1.3.2. 4-(4-Methylbenzylideneamino)-5-(pyridin-3-yl)-2,4-dihydro-[1,2,4]-triazole-3-thione (3b). Yield 1.34 g (87%); pale yellow crystals, mp >300 °C. IR: 3445, 3201, 3013, 2870, 2831, 2716, 2592, 2365, 1600, 1599, 1489, 1419, 1381, 1362, 1335, 1300, 1277, 1223, 1173, 1122, 1092, 1041, 968, 906, 879, 810, 694, 636, 513, 444, 420; ^{1}H NMR (DMSO-d_6) δ 2.40 (s, 3H, CH_3), 7.38 (d, 2H, $J = 7.9$ Hz, ArH), 7.57 (ddd, 1H, $J_{\text{H-5 pyrid.–H-2 pyrid.}} = 0.9$ Hz, $J_{\text{H-5 pyrid.–H-6 pyrid.}} = 4.8$ Hz, $J_{\text{H-5 pyrid.–H-4 pyrid.}} = 8.1$ Hz, H-5 pyrid.), 7.78 (d, 2H, $J = 7.9$ Hz, ArH), 8.25 (td, 1H, $J_{\text{H-4 pyrid.–H-6 pyrid.}} = 1.8$ Hz, $J_{\text{H-4 pyrid.–H-2 pyrid.}} = 2.1$ Hz, $J_{\text{H-4 pyrid.–H-5 pyrid.}} = 8.1$ Hz, H-4 pyrid.), 8.71 (dd, 1H, $J_{\text{H-6 pyrid.–H-4 pyrid.}} = 1.8$ Hz, $J_{\text{H-6 pyrid.–H-5 pyrid.}} = 4.8$ Hz, H-6 pyrid.), 9.03 (dd, 1H, $J_{\text{H-2 pyrid.–H-5 pyrid.}} = 0.9$ Hz, $J_{\text{H-2 pyrid.–H-4 pyrid.}} = 2.1$ Hz, H-2 pyrid.), 9.73 (s, 1H, CH=N), 14.35 (s, 1H, D_2O exchangeable NH). Anal. Calcd for $C_{15}H_{13}N_5S$ (295.4): C, 61.00; H, 4.44; N, 23.71; S, 10.86. Found: C, 61.14; H, 4.51; N, 23.64; S, 10.75.

3.1.3.3. 4-(4-Methoxybenzylideneamino)-5-(pyridin-3-yl)-2,4-dihydro-[1,2,4]-triazole-3-thione (3c). Yield 1.31 g (81%); pale yellow crystals, mp 256 °C. IR: 3445, 3067, 2901, 2835, 2716, 2667, 2617, 2588, 2365, 1635, 1601, 1566, 1508, 1423, 1365, 1304, 1254, 1169, 1095, 1030, 964, 937, 879, 829, 744, 694, 636, 559, 528, 424; ^{1}H NMR (DMSO-d_6) δ 3.86 (s, 3H, OCH_3), 7.11 (d, 2H, $J = 8.8$ Hz, ArH), 7.57 (ddd, 1H, $J_{\text{H-5 pyrid.–H-2 pyrid.}} = 0.9$ Hz, $J_{\text{H-5 pyrid.–H-6 pyrid}} = 4.8$ Hz, $J_{\text{H-5 pyrid.–H-4 pyrid.}} = 8.1$ Hz, H-5 pyrid.), 7.85 (d, 2H, $J = 8.8$ Hz, ArH), 8.27 (td, 1H, $J_{\text{H-4 pyrid.–H-6 pyrid·}} = 1.8$ Hz, $J_{\text{H-4 pyrid.–H-2 pyrid.}} = 2.1$, $J_{\text{H-4 pyrid.–H-5 pyrid.}} = 8.1$ Hz, H-4 pyrid.), 8.71 (dd, 1H, $J_{\text{H-6 pyrid.–H-4 pyrid.}} = 1.8$ Hz, $J_{\text{H-6 pyrid.–H-5 pyrid.}} = 4.8$ Hz, H-6 pyrid.), 9.03 (dd, 1H, $J_{\text{H-2 pyrid.–H-5 pyrid}} = 0.9$ Hz, $J_{\text{H-2 pyrid.–H-4 pyrid.}} = 2.1$ Hz, H-2 pyrid.), 9.61 (s, 1H, CH=N), 14.30 (s, 1H, D_2O exchangeable NH). Anal. Calcd for $C_{15}H_{13}N_5OS$ (311.4): C, 57.86; H, 4.21; N, 22.49; S, 10.30. Found: C, 57.92; H, 4.42; N, 22.32; S, 10.24.

3.1.3.4. 4-(4-Chlorobenzylideneamino)-5-(pyridin-3-yl)-2,4-dihydro-[1,2,4]-triazole-3-thione (3d). Yield 1.44 g (88%); yellow crystals, mp 248–250 °C. IR: 3469, 3074, 2874, 2827, 2584, 2511, 1589, 1558, 1516, 1481, 1423, 1354, 1304, 1281, 1219, 1169, 1126, 1084, 1034, 1007, 964, 941, 876, 810, 783, 733, 694, 636, 517, 471, 424; ^{1}H NMR (DMSO-d_6) δ 7.57 (dd, 1H, $J_{\text{H-5 pyrid.–H-6 pyrid.}} = 4.8$ Hz, $J_{\text{H-5 pyrid.–H-4 pyrid.}} = 8.1$ Hz, H-5 pyrid.), 7.62 (d, 2H, $J = 8.5$ Hz, ArH), 7.90 (d, 2H, $J = 8.5$ Hz, ArH), 8.25 (td, 1H, $J_{\text{H-4 pyrid.–H-6 pyrid.}} = 1.8$ Hz, $J_{\text{H-4 pyrid.–H-2 pyrid.}} = 2.1$ Hz, $J_{\text{H-4 pyrid.–H-5 pyrid.}} = 8.1$ Hz, H-4 pyrid.), 8.72 (dd, 1H, $J_{\text{H-6 pyrid.–H-4 pyrid.}} = 1.8$ Hz, $J_{\text{H-6 pyrid.–H-5 pyrid.}} = 4.8$ Hz, H-6 pyrid.), 9.03 (d, 1H, $J_{\text{H-2 pyrid.–H-4 pyrid.}} = 2.1$ Hz, H-2 pyrid.), 9.90 (s, 1H, CH=N), 14.38 (s, 1H, D_2O exchangeable NH). Anal. Calcd for $C_{14}H_{10}ClN_5S$ (315.8): C, 53.25; H, 3.19; N, 22.18; S, 10.15. Found: C, 53.17; H, 3.02; N, 21.97; S, 10.31.

3.1.4. General procedure for the synthesis of compounds 5 and 6. To a solution of compound **2** (1.93 g, 10 mmol) in *N*,*N*-dimethylformamide (10 mL) and Et_3N (1.7 mL, 12 mmol) was added 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**4**) (4.93 g, 12 mmol), and the reaction mixture was stirred overnight. The next day, the reaction mixture was concentrated under reduced pressure, diluted with CH_2Cl_2 (100 mL), and washed with water (3 × 100 mL). The organic layer was dried (Na_2SO_4), filtered, evaporated under reduced pressure, and subjected to silica gel (70–230 mesh) column chromatography. Compound **5** was eluted first with petroleum ether (bp 40–60 °C)→70% ethyl acetate/petroleum ether (bp 40–60 °C), followed by compound **6** with 80% ethyl acetate/petroleum ether (bp 40–60 °C)→20% methanol/ethyl acetate. The chromatographically separated crude products were recrystallized from CH_2Cl_2/petroleum ether (bp 40–60 °C). R_f values of the latter compounds were determined on TLC aluminum sheets using ethyl acetate/petroleum ether (bp 40–60 °C) [60:40, v/v] as a developing system.

3.1.4.1. 2-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-4-amino-5-(pyridin-3-yl)-2,4-dihydro-[1,2,4]-triazole-3-thione (5). Yield 2.10 g (40%); colorless crystals, mp 214 °C ($R_f = 0.61$). IR: 3313, 3229, 3078, 2988, 2920, 2854, 1747, 1651, 1601, 1516, 1435, 1373, 1254, 1227, 1041, 987, 922, 856, 814, 698, 663, 617, 544, 467, 413; ^{1}H NMR (DMSO-d_6) δ 1.86, 1.96, 1.99, 2.03 (4s, 12H, CH_3CO), 4.03 (dd, 1H, $J_{H\text{-}6'\text{–}H\text{-}5'} = 2.1$ Hz, $J_{H\text{-}6'\text{–}H\text{-}6''} = 12.6$ Hz, H-6′), 4.20 (dd, 1H, $J_{H\text{-}6''\text{–}H\text{-}5'} = 4.8$ Hz, $J_{H\text{-}6''\text{–}H\text{-}6'} = 12.6$ Hz, H-6″), 4.40 (ddd, 1H, $J_{H\text{-}5'\text{–}H\text{-}6'} = 2.1$ Hz, $J_{H\text{-}5'\text{–}H\text{-}6''} = 4.8$ Hz, $J_{H\text{-}5'\text{–}H\text{-}4'} = 9.9$ Hz, H-5′), 5.05 (dt, 1H, $J_{H\text{-}4'\text{–}H\text{-}2'} = 2.7$ Hz, $J_{H\text{-}4'\text{–}H\text{-}3'} = 6.6$ Hz, $J_{H\text{-}4'\text{–}H\text{-}5'} = 9.9$ Hz, H-4′), 5.65 (dd, 2H, $J_{H\text{-}2'\text{–}H\text{-}4'} = J_{H\text{-}3'\text{–}H\text{-}1'} = 2.7$ Hz, $J_{H\text{-}2'\text{–}H\text{-}1'} = J_{H\text{-}2'\text{–}H\text{-}3'} = 6.6$ Hz, H-2′, H-3′), 5.91 (br s, 2H, D_2O exchangeable NH_2), 6.39 (dd, 1H, $J_{H\text{-}1'\text{–}H\text{-}3'} = 2.7$ Hz, $J_{H\text{-}1'\text{–}H\text{-}2'} = 6.6$ Hz, H-1′), 7.62 (ddd, 1H, $J_{H\text{-}5\ \text{pyrid.}\text{–}H\text{-}2\ \text{pyrid.}} = 0.9$ Hz, $J_{H\text{-}5\ \text{pyrid.}\text{–}H\text{-}6\ \text{pyrid.}} = 4.8$ Hz, $J_{H\text{-}5\ \text{pyrid.}\text{–}H\text{-}4\ \text{pyrid.}} = 8.1$ Hz, H-5 pyrid.), 8.34 (td, 1H, $J_{H\text{-}4\ \text{pyrid.}\text{–}H\text{-}6\ \text{pyrid.}} = 1.8$ Hz, $J_{H\text{-}4\ \text{pyrid.}\text{–}H\text{-}2\ \text{pyrid.}} = 2.1$ Hz, $J_{H\text{-}4\ \text{pyrid.}\text{–}H\text{-}5\ \text{pyrid.}} = 8.1$ Hz, H-4 pyrid.), 8.76 (dd, 1H, $J_{H\text{-}6\ \text{pyrid.}\text{–}H\text{-}4\ \text{pyrid.}} = 1.8$ Hz, $J_{H\text{-}6\ \text{pyrid.}\text{–}H\text{-}5\ \text{pyrid.}} = 4.8$ Hz, H-6 pyrid.), 9.10 (dd, 1H, $J_{H\text{-}2\ \text{pyrid.}\text{–}H\text{-}5\ \text{pyrid.}} = 0.9$ Hz, $J_{H\text{-}2\ \text{pyrid.}\text{–}H\text{-}4\ \text{pyrid.}} = 2.1$ Hz, H-2 pyrid.). Anal. Calcd for $C_{21}H_{25}N_5O_9S$ (523.5): C, 48.18; H, 4.81; N, 13.38; S, 6.12. Found: C, 48.02; H, 4.92; N, 13.47; S, 5.99.

3.1.4.2. 3-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl-1-thio)-4-amino-5-(pyridin-3-yl)-4*H*-[1,2,4]-triazole (6). Yield 3.0 g (57%); colorless crystals, mp 78–80 °C ($R_f = 0.10$). IR; 3325, 3202, 3037, 2947, 1751, 1632, 1601, 1574, 1439, 1373, 1230, 1038, 984, 914, 818, 706, 602, 548, 486, 420; ^{1}H NMR ($CDCl_3$) δ 1.78, 1.90, 1.93, 2.02 (4s, 12H, CH_3CO), 3.69 (ddd, 1H, $J_{H\text{-}5'\text{–}H\text{-}6''} = 2.4$ Hz, $J_{H\text{-}5'\text{–}H\text{-}6'} = 5.1$ Hz, $J_{H\text{-}5'\text{–}H\text{-}4'} = 10.0$ Hz, H-5′), 4.01 (dd, 1H, $J_{H\text{-}6'\text{–}H\text{-}5'} = 5.1$ Hz, $J_{H\text{-}6'\text{–}H\text{-}6''} = 12.6$ Hz, H-6′), 4.11 (dd, 1H, $J_{H\text{-}6''\text{–}H\text{-}5'} = 2.4$ Hz, $J_{H\text{-}6''\text{–}H\text{-}6'} = 12.6$ Hz, H-6″), 4.89-5.00 (m, 3H, H-4′, H-3′, H-1′), 5.14 (dt, 1H, $J_{H\text{-}2'\text{–}H\text{-}4'} = 1.0$ Hz, $J_{H\text{-}2'\text{–}H\text{-}1'} = 9.0$ Hz, H-2′), 5.45 (s, 2H, D_2O exchangeable NH_2), 7.31 (dd, 1H, $J_{H\text{-}5\ \text{pyrid.}\text{–}H\text{-}6\ \text{pyrid.}} = 4.8$ Hz, $J_{H\text{-}5\ \text{pyrid.}\text{–}H\text{-}4\ \text{pyrid.}} = 7.8$ Hz, H-5 pyrid.), 8.39 (td, 1H, $J_{H\text{-}4\ \text{pyrid.}\text{–}H\text{-}6\ \text{pyrid.}} = 1.8$ Hz, $J_{H\text{-}4\ \text{pyrid.}\text{–}H\text{-}5\ \text{pyrid.}} = 7.8$ Hz, H-4 pyrid.), 8.55 (dd, 1H, $J_{H\text{-}6\ \text{pyrid.}\text{–}H\text{-}4\ \text{pyrid.}} = 1.8$ Hz, $J_{H\text{-}6\ \text{pyrid.}\text{–}H\text{-}5\ \text{pyrid.}} = 4.8$ Hz, H-6 pyrid.), 9.28 (s, 1H, H-2 pyrid.). Anal. Calcd for $C_{21}H_{25}N_5O_9S$ (523.5): C, 48.18; H, 4.81; N, 13.38; S, 6.12. Found: C, 47.99; H, 4.77; N, 13.21; S, 6.28.

3.1.5. General procedures for the synthesis of compounds 7a–d and 8a–d. A) To a solution of each of compounds **3a–d** (3.6 mmol) in *N*,*N*-dimethylformamide (4 mL) and Et_3N (0.6 mL, 4.3 mmol) was added 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide (**4**) (1.77 g, 4.3 mmol), and the reaction mixture was stirred overnight. The next day, the reaction mixture was diluted with water and the formed precipitate was collected by filtration, washed with water several times and dried at room temperature. The precipitate was extracted with CH_2Cl_2, the solution was concentrated and the residue subjected to silica gel (70–230 mesh) column chromatography. Compounds **7a–d** were eluted first with petroleum ether (bp 40–60 °C)→70% ethyl acetate/petroleum ether (bp 40–60 °C), followed by compounds **8a–d** with 80% ethyl acetate/petroleum ether (bp 40–60 °C)→20% methanol/ethyl acetate. The chromatographically separated crude products were recrystallized from CH_2Cl_2/petroleum ether (bp 40–60 °C). R_f values of the latter compounds were determined on TLC aluminum sheets using ethyl acetate/petroleum ether (bp 40–60 °C) [60:40, v/v] as a developing system.

B) An intimate mixture of equimolecular amounts of each of compounds **5**, **6** (104.7 mg, 0.2 mmol) and the appropriate aryl aldehyde (0.2 mmol) was heated at 160 °C in an oil bath for 5 min. After cooling the product was recrystallized from CH_2Cl_2/petroleum ether (bp 40–60 °C) to give the corresponding arylideneamino derivatives **7a–d** and **8a–d**, respectively.

3.1.5.1. 2-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-4-benzylideneamino-5-(pyridin-3-yl)-2,4-dihydro-[1,2,4]-triazole-3-thione (7a). Yield 1.12 g (51%, A); 100 mg (82%, B); colorless crystals, mp 181–182 °C ($R_f = 0.5$). IR: 3062, 3012, 2970, 2947, 2854, 1747, 1646, 1605, 1578, 1423, 1369, 1319, 1230, 1099, 1065, 1038, 922, 899, 849, 814, 756, 694 644, 617, 544, 498, 451; ^{1}H NMR (DMSO-d_6) δ 1.91, 1.98, 2.00, 2.04 (4s, 12H, CH_3CO), 4.06 (dd, 1H, $J_{H\text{-}6'\text{–}H\text{-}5'} = 2.1$ Hz, $J_{H\text{-}6'\text{–}H\text{-}6''} = 12.6$ Hz, H-6′), 4.23 (dd, 1H, $J_{H\text{-}6''\text{–}H\text{-}5'} = 4.8$ Hz, $J_{H\text{-}6''\text{–}H\text{-}6'} = 12.6$ Hz, H-6″), 4.44 (ddd, 1H, $J_{H\text{-}5'\text{–}H\text{-}6'} = 2.1$ Hz, $J_{H\text{-}5'\text{–}H\text{-}6''} = 4.8$ Hz, $J_{H\text{-}5'\text{–}H\text{-}4'} = 9.6$ Hz, H-5′), 5.09 (t, 1H, $J_{H\text{-}4'\text{–}H\text{-}5'} = J_{H\text{-}4'\text{–}H\text{-}3'} = 9.6$ Hz, H-4′), 5.68 (t, 1H, $J_{H\text{-}3'\text{–}H\text{-}4'} = J_{H\text{-}3'\text{–}H\text{-}2'} = 9.6$ Hz, H-3′), 5.70 (t, 1H, $J_{H\text{-}2'\text{–}H\text{-}1'} = 9.3$ Hz, $J_{H\text{-}2'\text{–}H\text{-}3'} = 9.6$ Hz, H-2′), 6.52 (d, 1H, $J_{H\text{-}1'\text{–}H\text{-}2'} = 9.3$ Hz, H-1′), 7.55–7.69 (m, 4H, ArH, H-5 pyrid.), 7.91 (dd, 2H, $J = 1.5$, 8.4 Hz, ArH), 8.22 (td, 1H, $J_{H\text{-}4\ \text{pyrid.}\text{–}H\text{-}6\ \text{pyrid.}} = 1.8$ Hz, $J_{H\text{-}4\ \text{pyrid.}\text{–}H\text{-}2\ \text{pyrid.}} = 2.1$ Hz, $J_{H\text{-}4\ \text{pyrid.}\text{–}H\text{-}5\ \text{pyrid.}} = 8.1$ Hz, H-4 pyrid.), 8.76 (dd, 1H, $J_{H\text{-}6\ \text{pyrid.}\text{–}H\text{-}4\ \text{pyrid.}} = 1.8$ Hz, $J_{H\text{-}6\ \text{pyrid.}\text{–}H\text{-}5\ \text{pyrid.}} = 4.8$ Hz, H-6 pyrid.), 8.99 (dd, 1H, $J_{H\text{-}2\ \text{pyrid.}\text{–}H\text{-}5\ \text{pyrid}} = 0.9$ Hz, $J_{H\text{-}2\ \text{pyrid.}\text{–}H\text{-}4\ \text{pyrid.}} = 2.1$ Hz, H-2 pyrid.), 9.75 (s, 1H, CH=N). Anal. Calcd for $C_{28}H_{29}N_5O_9S$ (611.6): C, 54.99; H, 4.78; N, 11.45; S, 5.24. Found: C, 55.07; H, 4.68; N, 11.24; S, 5.19.

3.1.5.2. 2-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-4-(4-methylbenzylideneamino)-5-(pyridin-3-yl)-2,4-dihydro-[1,2,4]-triazole-3-thione (7b). Yield 1.28 g (57%, A); 110 mg (88%, B); colorless crystals, mp 180–182 °C ($R_f = 0.74$). IR: 3061, 3036, 3012, 2970, 2924, 2854, 1747, 1646, 1605, 1512, 1423, 1369, 1319, 1230, 1099,

1067, 1038, 922, 885, 852, 814, 702, 602, 459, 498; ^{1}H NMR (DMSO-d_6) δ 1.91, 1.98, 2.00, 2.04 (4s, 12H, CH_3CO), 2.40 (s, 3H, CH_3), 4.05 (dd, 1H, $J_{H\text{-}6'\text{–}H\text{-}5'} = 2.1$ Hz, $J_{H\text{-}6'\text{–}H\text{-}6''} = 12.6$ Hz, H-6′), 4.23 (dd, 1H, $J_{H\text{-}6''\text{–}H\text{-}5'} = 4.8$ Hz, $J_{H\text{-}6''\text{–}H\text{-}6'} = 12.6$ Hz, H-6″), 4.42 (ddd, 1H, $J_{H\text{-}5'\text{–}H\text{-}6'} = 2.1$ Hz, $J_{H\text{-}5'\text{–}H\text{-}6''} = 4.8$ Hz, $J_{H\text{-}5'\text{–}H\text{-}4'} = 9.3$ Hz, H-5′), 5.08 (t, 1H, $J_{H\text{-}4'\text{–}H\text{-}5'} = 9.3$ Hz, $J_{H\text{-}4'\text{–}H\text{-}3'} = 9.0$ Hz, H-4′), 5.67 (t, 1H, $J_{H\text{-}3'\text{–}H\text{-}4'} = 9.0$ Hz, $J_{H\text{-}3'\text{–}H\text{-}2'} = 9.1$ Hz, H-3′), 5.70 (t, 1H, $J_{H\text{-}2'\text{–}H\text{-}1'} = 8.1$ Hz, $J_{H\text{-}2'\text{–}H\text{-}3'} = 9.1$ Hz, H-2′), 6.51 (d, 1H, $J_{H\text{-}1'\text{–}H\text{-}2'} = 8.1$ Hz, H-1′), 7.39 (d, 2H, $J =$ 8.1 Hz, ArH), 7.61 (ddd, 1H, $J_{H\text{-}5\ pyrid.\text{–}H\text{-}2\ pyrid.} =$ 0.9 Hz, $J_{H\text{-}5\ pyrid.\text{–}H\text{-}6\ pyrid.} = 5.1$ Hz, $J_{H\text{-}5\ pyrid.\text{–}H\text{-}4\ pyrid.} =$ 7.8 Hz, H-5 pyrid.), 7.80 (d, 2H, $J = 8.1$ Hz, ArH), 8.21 (td, 1H, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}6\ pyrid.} = 1.5$ Hz, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}2\ pyrid.} =$ 1.8 Hz, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}5\ pyrid.} = 7.8$ Hz, H-4 pyrid.), 8.76 (dd, 1H, $J_{H\text{-}6\ pyrid.\text{–}H\text{-}4\ pyrid.} = 1.5$ Hz, $J_{H\text{-}6\ pyrid.\text{–}H\text{-}5\ pyrid.} =$ 5.1 Hz, H-6 pyrid.), 8.98 (dd, 1H, $J_{H\text{-}2\ pyrid.\text{–}H\text{-}5\ pyrid.} =$ 0.9 Hz, $J_{H\text{-}2\ pyrid.\text{–}H\text{-}4\ pyrid.} = 1.8$ Hz, H-2 pyrid.), 9.64 (s, 1H, CH=N). Anal. Calcd for $C_{29}H_{31}N_5O_9S$ (625.7): C, 55.67; H, 4.99; N, 11.19; S, 5.12. Found: C, 55.54; H, 4.84; N, 11.17; S, 5.00.

3.1.5.3. 2-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-4-(4-methoxybenzylideneamino)-5-(pyridin-3-yl)-2,4-dihydro-[1,2,4]-triazole-3-thione (7c). Yield 1.04 g (45%, A); 109 mg (85%, B); yellow crystals, mp 176 °C ($R_f = 0.78$). IR: 3073, 3017 2976, 2939, 2843, 1751, 1601, 1570, 1516, 1423, 1369, 1315, 1259, 1223, 1173, 1099, 1034, 922, 833, 702, 675, 606 532, 499; ^{1}H NMR ($CDCl_3$) δ 1.88, 1.95, 1.98, 2.01 (4s, 12H, CH_3CO), 3.81 (s, 3H, CH_3O), 3.99 (ddd, 1H, $J_{H\text{-}5'\text{–}H\text{-}6'} = 2.1$ Hz, $J_{H\text{-}5'\text{–}H\text{-}6''} = 4.8$ Hz, $J_{H\text{-}5'\text{–}H\text{-}4'} = 9.9$ Hz, H-5′), 4.13 (dd, 1H, $J_{H\text{-}6'\text{–}H\text{-}5'} = 2.1$ Hz, $J_{H\text{-}6'\text{–}H\text{-}6''} = 12.6$ Hz, H-6′), 4.27 (dd, 1H, $J_{H\text{-}6''\text{–}H\text{-}5'} = 4.8$ Hz, $J_{H\text{-}6''\text{–}H\text{-}6'} = 12.6$ Hz, H-6″), 5.23 (t, 1H, $J_{H\text{-}4'\text{–}H\text{-}3'} = 9.6$ Hz, $J_{H\text{-}4'\text{–}H\text{-}5'} = 9.9$ Hz, H-4′), 5.41 (t, 1H, $J_{H\text{-}3'\text{–}H\text{-}2'} = 9.3$ Hz, $J_{H\text{-}3'\text{–}H\text{-}4'} = 9.6$ Hz, H-3′), 5.86 (t, 1H, $J_{H\text{-}2'\text{–}H\text{-}1'} = J_{H\text{-}2'\text{–}H\text{-}3'} = 9.3$ Hz, H-2′), 6.26 (d, 1H, $J_{H\text{-}1'\text{–}H\text{-}2'} = 9.3$ Hz, H-1′), 6.92 (d, 2H, $J =$ 8.7 Hz, ArH), 7.35 (dd, 1H, $J_{H\text{-}5\ pyrid.\text{–}H\text{-}4\ pyrid.} = 8.1$ Hz, $J_{H\text{-}5\ pyrid.\text{–}H\text{-}6\ pyrid.} = 4.8$ Hz, H-5 pyrid.), 7.74 (d, 2H, $J = 8.7$ Hz, ArH), 8.21 (td, 1H, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}6\ pyrid.} =$ 1.8 Hz, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}2\ pyrid.} = 2.1$ Hz, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}5\ pyrid.} =$ 8.1 Hz, H-4 pyrid.), 8.66 (dd, 1H, $J_{H\text{-}6\ pyrid.\text{–}H\text{-}4\ pyrid.} =$ 1.8 Hz, $J_{H\text{-}6\ pyrid.\text{–}H\text{-}5\ pyrid.} = 4.8$ Hz, H-6 pyrid.), 9.16 (d, 1H, $J_{H\text{-}2\ pyrid.\text{–}H\text{-}4\ pyrid.} = 2.1$ Hz, H-2 pyrid.), 9.87 (s, 1H, CH=N). Anal. Calcd for $C_{29}H_{31}N_5O_{10}S$ (641.7): C, 54.28; H, 4.87; N, 10.91; S, 5.00. Found: C, 54.17; H, 4.74; N, 11.00; S, 4.93.

3.1.5.4. 2-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-4-(4-chlorobenzylideneamino)-5-(pyridin-3-yl)-2,4-dihydro-[1,2,4]-triazole-3-thione (7d). Yield 1.30 g (56%, A); 116 mg (90%, B); yellow crystals, mp 178–180 °C ($R_f = 0.75$). IR: 3073, 3012, 2975, 2947, 2858, 1751, 1597, 1489, 1423, 1369, 1315, 1227, 1095, 1074, 1038, 922, 849, 822, 771, 706, 602, 552, 513, 486 459; ^{1}H NMR (DMSO-d_6) δ 1.91, 1.98, 1.99, 2.04 (4s, 12H, CH_3CO), 4.05 (dd, 1H, $J_{H\text{-}6'\text{–}H\text{-}5'} = 1.8$ Hz, $J_{H\text{-}6'\text{–}H\text{-}6''} =$ 12.6 Hz, H-6′), 4.23 (dd, 1H, $J_{H\text{-}6''\text{–}H\text{-}5'} = 4.8$ Hz, $J_{H\text{-}6''\text{–}H\text{-}6'} = 12.6$ Hz, H-6″), 4.44 (ddd, 1H, $J_{H\text{-}5'\text{–}H\text{-}6'} =$ 1.8 Hz, $J_{H\text{-}5'\text{–}H\text{-}6''} = 4.8$ Hz, $J_{H\text{-}5'\text{–}H\text{-}4'} = 9.9$ Hz, H-5′), 5.08 (t, 1H, $J_{H\text{-}4'\text{–}H\text{-}3'} = 9.6$ Hz, $J_{H\text{-}4'\text{–}H\text{-}5'} = 9.9$ Hz, H-4′), 5.68 (t, 1H, $J_{H\text{-}3'\text{–}H\text{-}2'} = 9.0$ Hz, $J_{H\text{-}3'\text{–}H\text{-}4'} = 9.6$ Hz, H-3′), 5.71 (t, 1H, $J_{H\text{-}2'\text{–}H\text{-}1'} = 8.7$ Hz, $J_{H\text{-}2'\text{–}H\text{-}3'} =$ 9.0 Hz, H-2′), 6.52 (d, 1H, $J_{H\text{-}1'\text{–}H\text{-}2'} = 8.7$ Hz, H-1′), 7.61 (dd, 1H, $J_{H\text{-}5\ pyrid.\text{–}H\text{-}4\ pyrid.} = 8.1$ Hz, $J_{H\text{-}5\ pyrid.\text{–}H\text{-}6\ pyrid.} = 4.8$ Hz, H-5 pyrid.), 7.65 (d, 2H, $J = 8.4$ Hz, ArH), 7.93 (d, 2H, $J = 8.4$ Hz, ArH), 8.21 (td, 1H, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}6\ pyrid.} = 1.8$ Hz, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}2\ pyrid.} =$ 2.4 Hz, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}5\ pyrid.} = 8.1$ Hz, H-4 pyrid.), 8.77 (dd, 1H, $J_{H\text{-}6\ pyrid.\text{–}H\text{-}4\ pyrid.} = 1.8$ Hz, $J_{H\text{-}6\ pyrid.\text{–}H\text{-}5\ pyrid.} =$ 4.8 Hz, H-6 pyrid.), 8.97 (d, 1H, $J_{H\text{-}2\ pyrid.\text{–}H\text{-}4\ pyrid.} =$ 2.4 Hz, H-2 pyrid.), 9.80 (s, 1H, CH=N). Anal. Calcd for $C_{28}H_{28}ClN_5O_9S$ (646.1): C, 52.05; H, 4.37; N, 10.84; S, 4.96. Found: C, 51.98; H, 4.31; N, 10.97; S, 4.88.

3.1.5.5. 3-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl-1-thio)-4-benzylideneamino-5-(pyridin-3-yl)-4*H*-[1,2,4]-triazole (8a). Yield 0.94 g (43%, A); 106 mg (87%, B); pale crystals, mp 92 °C ($R_f = 0.10$). IR: 3090, 3020, 2951, 2908, 1755, 1651, 1605, 1574, 1431, 1373, 1322, 1219, 1122, 1057, 976, 910, 845, 814, 756, 687, 636, 602, 575, 528, 509, 490, 440; ^{1}H NMR ($CDCl_3$) δ 1.87, 1.92, 1.94, 1.97 (4s, 12H, CH_3CO), 3.74 (ddd, 1H, $J_{H\text{-}5'\text{–}H\text{-}6'} = 1.8$ Hz, $J_{H\text{-}5'\text{–}H\text{-}6''} = 4.8$ Hz, $J_{H\text{-}5'\text{–}H\text{-}4'} =$ 9.9 Hz, H-5′), 3.96 (dd, 1H, $J_{H\text{-}6'\text{–}H\text{-}5'} = 1.8$ Hz, $J_{H\text{-}6'\text{–}H\text{-}6''} = 12.6$ Hz, H-6′), 4.18 (dd, 1H, $J_{H\text{-}6''\text{–}H\text{-}5'} =$ 4.8 Hz, $J_{H\text{-}6''\text{–}H\text{-}6'} = 12.6$ Hz, H-6″), 5.03 (t, 1H, $J_{H\text{-}4'\text{–}H\text{-}3'} = 9.6$ Hz, $J_{H\text{-}4'\text{–}H\text{-}5'} = 9.9$ Hz, H-4′), 5.06 (t, 1H, $J_{H\text{-}3'\text{–}H\text{-}2'} = 9.3$ Hz, $J_{H\text{-}3'\text{–}H\text{-}4'} = 9.6$ Hz, H-3′), 5.21 (t, 1H, $J_{H\text{-}2'\text{–}H\text{-}1'} = 10.5$ Hz, $J_{H\text{-}2'\text{–}H\text{-}3'} = 9.3$ Hz, H-2′), 5.36 (d, 1H, $J_{H\text{-}1'\text{–}H\text{-}2'} = 10.5$ Hz, H-1′), 7.34 (dd, 1H, $J_{H\text{-}5\ pyrid.\text{–}H\text{-}6\ pyrid.} = 4.8$ Hz, $J_{H\text{-}5\ pyrid.\text{–}H\text{-}4\ pyrid.} =$ 8.1 Hz, H-5 pyrid.), 7.45 (t, 2H, $J = 8.0$ Hz, ArH), 7.54 (dt, 1H, $J = 2.1$, 8.0 Hz, ArH), 7.80 (dd, 2H, $J = 1.2$, 8.0 Hz, ArH), 8.25 (td, 1H, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}6\ pyrid.} =$ 1.8 Hz, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}2\ pyrid.} = 2.1$ Hz, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}5\ pyrid.} =$ 8.1 Hz, H-4 pyrid.), 8.60 (dd, 1H, $J_{H\text{-}6\ pyrid.\text{–}H\text{-}4\ pyrid.} =$ 1.8 Hz, $J_{H\text{-}6\ pyrid.\text{–}H\text{-}5\ pyrid.} = 4.8$ Hz, H-6 pyrid.), 8.71 (s, 1H, CH=N), 9.14 (d, 1H, $J_{H\text{-}2\ pyrid.\text{–}H\text{-}4\ pyrid.} =$ 2.1 Hz, H-2 pyrid.). Anal. Calcd for $C_{28}H_{29}N_5O_9S$ (611.6): C, 54.99; H, 4.78; N, 11.45; S, 5.24. Found: C, 54.84; H, 4.84; N, 11.57; S, 5.34.

3.1.5.6. 3-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl-1-thio)-4-(4-methylbenzylideneamino)-5-(pyridin-3-yl)-4*H*-[1,2,4]-triazole (8b). Yield 0.91 g (40%, A); 111 mg (89%, B); pale crystals, mp 118–120 °C ($R_f = 0.11$). IR: 3098, 3061, 2947, 2888, 2743, 1751, 1642, 1605, 1566, 1435, 1373, 1227, 1086, 1041, 968, 910, 818, 706, 679,

644, 602, 563, 513, 482, 455; ^{1}H NMR ($CDCl_3$) δ 1.89, 1.94, 1.96, 1.99 (4s, 12H, CH_3CO), 2.39 (s, 3H, CH_3), 3.74 (ddd, 1H, $J_{H\text{-}5'\text{–}H\text{-}6'} = 1.8$ Hz, $J_{H\text{-}5'\text{–}H\text{-}6''} = 4.8$ Hz, $J_{H\text{-}5'\text{–}H\text{-}4'} = 9.9$ Hz, H-5′), 3.97 (dd, 1H, $J_{H\text{-}6'\text{–}H\text{-}5'} = 1.8$ Hz, $J_{H\text{-}6'\text{–}H\text{-}6''} = 12.6$ Hz, H-6′), 4.19 (dd, 1H, $J_{H\text{-}6''\text{–}H\text{-}5'} = 4.8$ Hz, $J_{H\text{-}6''\text{–}H\text{-}6'} = 12.6$ Hz, H-6″), 5.04 (t, 1H, $J_{H\text{-}4'\text{–}H\text{-}3'} = 9.6$ Hz, $J_{H\text{-}4'\text{–}H\text{-}5'} = 9.9$ Hz, H-4′), 5.08 (t, 1H, $J_{H\text{-}3'\text{–}H\text{-}2'} = 9.3$ Hz, $J_{H\text{-}3'\text{–}H\text{-}4'} = 9.6$ Hz, H-3′), 5.22 (t, 1H, $J_{H\text{-}2'\text{–}H\text{-}1'} = 10.2$ Hz, $J_{H\text{-}2'\text{–}H\text{-}3'} = 9.3$ Hz, H-2′), 5.38 (d, 1H, $J_{H\text{-}1'\text{–}H\text{-}2'} = 10.2$ Hz, H-1′), 7.26 (d, 2H, $J = 7.8$ Hz, ArH), 7.34 (dd, 1H, $J_{H\text{-}5\ pyrid.\text{–}H\text{-}4\ pyrid.} = 8.1$ Hz, $J_{H\text{-}5\ pyrid.\text{–}H\text{-}6\ pyrid.} = 4.8$ Hz, H-5 pyrid.), 7.70 (d, 2H, $J = 7.8$ Hz, ArH), 8.25 (td, 1H, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}6\ pyrid.} = 1.8$ Hz, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}2\ pyrid.} = 2.1$ Hz, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}5\ pyrid.} = 8.1$ Hz, H-4 pyrid.), 8.60 (dd, 1H, $J_{H\text{-}6\ pyrid.\text{–}H\text{-}4\ pyrid.} = 1.8$ Hz, $J_{H\text{-}6\ pyrid.\text{–}H\text{-}5\ pyrid.} = 4.8$ Hz, H-6 pyrid.), 8.65 (s, 1H, CH=N), 9.16 (d, 1H, $J_{H\text{-}2\ pyrid.\text{–}H\text{-}4\ pyrid.} = 2.1$ Hz, H-2 pyrid.). Anal. Calcd for $C_{29}H_{31}N_5O_9S$ (625.7): C, 55.67; H, 4.99; N, 11.19; S, 5.12. Found: C, 55.71; H, 5.02; N, 11.09; S, 5.17.

3.1.5.7. 3-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl-1-thio)-4-(4-methoxybenzylideneamino)-5-(pyridin-3-yl)-4*H*-[1,2,4]-triazole (8c). Yield 1.24 g (54%, A); 110 mg (86%, B); pale crystals, mp 98–100 °C ($R_f = 0.10$). IR: 3067, 3008, 2943, 2843, 1751, 1601, 1566, 1516, 1431, 1373, 1311, 1223, 1169, 1034, 968, 910, 837, 814, 752, 706, 675, 602, 555, 528, 482; ^{1}H NMR ($CDCl_3$) δ 1.85, 1.90, 1.91, 1.94 (4s, 12H, CH_3CO), 3.73 (ddd, 1H, $J_{H\text{-}5'\text{–}H\text{-}6'} = 1.8$ Hz, $J_{H\text{-}5'\text{–}H\text{-}6''} = 4.8$ Hz, $J_{H\text{-}5'\text{–}H\text{-}4'} = 10.2$ Hz, H-5′), 3.79 (s, 3H, OCH_3), 3.94 (dd, 1H, $J_{H\text{-}6'\text{–}H\text{-}5'} = 1.8$ Hz, $J_{H\text{-}6'\text{–}H\text{-}6''} = 12.6$ Hz, H-6′), 4.15 (dd, 1H, $J_{H\text{-}6''\text{–}H\text{-}5'} = 4.8$ Hz, $J_{H\text{-}6''\text{–}H\text{-}6'} = 12.6$ Hz, H-6″), 5.00 (t, 1H, $J_{H\text{-}4'\text{–}H\text{-}3'} = 9.9$ Hz, $J_{H\text{-}4'\text{–}H\text{-}5'} = 10.2$ Hz, H-4′), 5.03 (t, 1H, $J_{H\text{-}3'\text{–}H\text{-}2'} = 9.3$ Hz, $J_{H\text{-}3'\text{–}H\text{-}4'} = 9.9$ Hz, H-3′), 5.18 (t, 1H, $J_{H\text{-}2'\text{–}H\text{-}1'} = 9.9$ Hz, $J_{H\text{-}2'\text{–}H\text{-}3'} = 9.3$ Hz, H-2′), 5.33 (d, 1H, $J_{H\text{-}1'\text{–}H\text{-}2'} = 9.9$ Hz, H-1′), 6.91 (d, 2H, $J = 8.7$ Hz, ArH), 7.29 (dd, 1H, $J_{H\text{-}5\ pyrid.\text{–}H\text{-}4\ pyrid.} = 8.1$ Hz, $J_{H\text{-}5\ pyrid.\text{–}H\text{-}6\ pyrid.} = 4.8$ Hz, H-5 pyrid.), 7.72 (d, 2H, $J = 8.7$ Hz, ArH), 8.20 (td, 1H, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}2\ pyrid.} = 1.5$ Hz, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}6\ pyrid.} = 1.8$ Hz, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}5\ pyrid.} = 8.1$ Hz, H-4 pyrid.), 8.54 (s, 1H, CH=N), 8.55 (dd, 1H, $J_{H\text{-}6\ pyrid.\text{–}H\text{-}4\ pyrid.} = 1.8$ Hz, $J_{H\text{-}6\ pyrid.\text{–}H\text{-}5\ pyrid.} = 4.8$ Hz, H-6 pyrid.), 9.11 (d, 1H, $J_{H\text{-}2\ pyrid.\text{–}H\text{-}4\ pyrid.} = 1.5$ Hz, H-2 pyrid.). Anal. Calcd for $C_{29}H_{31}N_5O_{10}S$ (641.7): C, 54.28; H, 4.87; N, 10.91; S, 5.00. Found: C, 54.31; H, 4.97; N, 10.84; S, 5.03.

3.1.5.8. 3-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl-1-thio)-4-(4-chlorobenzylideneamino)-5-(pyridin-3-yl)-4*H*-[1,2,4]-triazole (8d). Yield 0.94 g (40%, A); 105 mg (81%, B); pale crystals, mp 110 °C ($R_f = 0.13$). IR: 3113, 3025, 2943, 2844, 2750, 1751, 1616, 1570, 1488, 1435, 1373, 1227, 1088, 1041, 972, 910, 822, 775, 706, 606, 517, 409, 471; ^{1}H NMR ($CDCl_3$) δ 1.90, 1.96, 1.98, 2.03 (4s, 12H, CH_3CO), 3.74 (ddd, 1H, $J_{H\text{-}5'\text{–}H\text{-}6'} = 1.8$ Hz, $J_{H\text{-}5'\text{–}H\text{-}6''} = 4.8$ Hz, $J_{H\text{-}5'\text{–}H\text{-}4'} = 9.9$ Hz, H-5′), 3.99 (dd, 1H, $J_{H\text{-}6'\text{–}H\text{-}5'} = 1.8$ Hz, $J_{H\text{-}6'\text{–}H\text{-}6''} = 12.6$ Hz, H-6′), 4.21 (dd, 1H, $J_{H\text{-}6''\text{–}H\text{-}5'} = 4.8$ Hz, $J_{H\text{-}6''\text{–}H\text{-}6'} = 12.6$ Hz, H-6″), 5.05 (t, 1H, $J_{H\text{-}4'\text{–}H\text{-}3'} = 9.6$ Hz, $J_{H\text{-}4'\text{–}H\text{-}5'} = 9.9$ Hz, H-4′), 5.10 (t, 1H, $J_{H\text{-}3'\text{–}H\text{-}2'} = 9.3$ Hz, $J_{H\text{-}3'\text{–}H\text{-}4'} = 9.6$ Hz, H-3′), 5.24 (t, 1H, $J_{H\text{-}2'\text{–}H\text{-}1'} = 10.2$ Hz, $J_{H\text{-}2'\text{–}H\text{-}3'} = 9.3$ Hz, H-2′), 5.40 (d, 1H, $J_{H\text{-}1'\text{–}H\text{-}2'} = 10.2$ Hz, H-1′), 7.38 (dd, 1H, $J_{H\text{-}5\ pyrid.\text{–}H\text{-}6\ pyrid.} = 4.8$ Hz, $J_{H\text{-}5\ pyrid.\text{–}H\text{-}4\ pyrid.} = 8.1$ Hz, H-5 pyrid.), 7.47 (d, 2H, $J = 8.4$ Hz, ArH), 7.78 (d, 2H, $J = 8.4$ Hz, ArH), 8.27 (td, 1H, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}6\ pyrid.} = 1.8$ Hz, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}2\ pyrid.} = 2.1$ Hz, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}5\ pyrid.} = 8.1$ Hz, H-4 pyrid.), 8.65 (dd, 1H, $J_{H\text{-}6\ pyrid.\text{–}H\text{-}4\ pyrid.} = 1.8$ Hz, $J_{H\text{-}6\ pyrid.\text{–}H\text{-}5\ pyrid.} = 4.8$ Hz, H-6 pyrid.), 8.72 (s, 1H, CH=N), 9.15 (d, 1H, $J_{H\text{-}2\ pyrid.\text{–}H\text{-}4\ pyrid.} = 2.1$ Hz, H-2 pyrid.). Anal. Calcd for $C_{28}H_{28}ClN_5O_9S$ (646.1): C, 52.05; H, 4.37; N, 10.84; S, 4.96. Found: C, 52.12; H, 4.42; N, 10.81; S, 5.02.

3.1.6. General procedure for the synthesis of compounds 9 and 10. To a solution of compound **3d** (505 mg, 1.6 mmol) in *N*,*N*-dimethylformamide (8 mL) and Et_3N (0.3 mL, 2.1 mmol) was added methyl iodide (0.12 mL, 1.9 mmol), and the reaction mixture was stirred overnight. The next day, the reaction mixture was dried under reduced pressure, diluted with CH_2Cl_2 (100 mL) and washed with water (3 × 100 mL). The organic layer was dried (Na_2SO_4), filtered, evaporated under reduced pressure, and subjected to silica gel (70–230 mesh) column chromatography. Compound **10** eluted first with petroleum ether (bp 40–60 °C)→30% ethyl acetate/petroleum ether (bp 40–60 °C), followed by compound **9** with ethyl acetate→20% methanol/ethyl acetate. The chromatographically separated crude products were recrystallized from CH_2Cl_2/petroleum ether (bp 40–60 °C). R_f values of compounds **9** and **10** were determined on TLC aluminum sheets using ethyl acetate/petroleum ether (bp 40–60 °C) [60:40, v/v] as a developing system.

3.1.6.1. 4-(4-Chlorobenzylideneamino)-3-methylthio-5-(pyridin-3-yl)-4*H*-[1,2,4]-triazole (9). Yield 245 mg (46%); pale crystals, mp 150–152 °C ($R_f = 0.10$). IR: 3059, 3022, 2977, 2924, 2854, 1574, 1493, 1450, 1412, 1350, 1315, 1284, 1242, 1180, 1084, 1014, 960, 933, 879, 829, 810, 771, 702, 667, 633, 606, 517, 467; ^{1}H NMR ($CDCl_3$) δ 2.73 (s, 3H, SCH_3), 7.34 (ddd, 1H, $J_{H\text{-}5\ pyrid.\text{–}H\text{-}4\ pyrid.} = 8.1$ Hz, $J_{H\text{-}5\ pyrid.\text{–}H\text{-}6\ pyrid.} = 4.8$ Hz, $J_{H\text{-}5\ pyrid.\text{–}H\text{-}2\ pyrid.} = 0.6$ Hz, H-5 pyrid.), 7.41 (td, 2H, $J_{H\text{-}2\ ArH\text{–}H\text{-}3\ ArH} = 8.4$ Hz, $J_{H\text{-}2\ ArH\text{–}H\text{-}6\ ArH} = 2.1$ Hz, $J_{H\text{-}2\ ArH\text{–}H\text{-}5\ ArH} = 1.8$ Hz, ArH), 7.76 (td, 2H, $J_{H\text{-}5\ ArH\text{–}H\text{-}2\ ArH} = 1.8$ Hz, $J_{H\text{-}6\ ArH\text{–}H\text{-}2\ ArH} = 2.1$ Hz, $J_{H\text{-}3\ ArH\text{–}H\text{-}2\ ArH} = 8.4$ Hz, ArH), 8.21 (td, 1H, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}6\ pyrid.} = 1.8$ Hz, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}2\ pyrid.} = 2.1$ Hz, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}5\ pyrid.} = 8.1$ Hz, H-4 pyrid.), 8.58

(s, 1H, CH=N), 8.61 (dd, 1H, $J_{\text{H-6 pyrid.–H-4 pyrid.}} = 1.8$ Hz, $J_{\text{H-6 pyrid.–H-5 pyrid.}} = 4.8$ Hz, H-6 pyrid.), 9.12 (dd, 1H, $J_{\text{H-2 pyrid.–H-4 pyrid.}} = 2.1$ Hz, $J_{\text{H-2 pyrid.–H-5 pyrid.}} = 0.6$ Hz, H-2 pyrid.). Anal. Calcd for $C_{15}H_{12}ClN_5S$ (329.8): C, 54.63; H, 3.67; N, 21.23; S, 9.72. Found: C, 54.48; H, 3.61; N, 21.36; S, 9.84.

3.1.6.2. 4-(4-Chlorobenzylideneamino)-5-(4-iodo-1, 4-dihydropyridin-4-yl)-3-methylthio-4*H*-[1,2,4]-triazole (10). Yield 239 mg (33%); yellow crystals, mp 180–182 °C ($R_f = 0.94$). IR: 3391, 3061, 3016, 2924, 2851, 1628, 1581, 1539, 1489, 1416, 1342, 1219, 1180, 1084, 1053, 1011, 895, 868, 822, 756, 706, 671, 644, 505, 459, 413; ^{1}H NMR ($CDCl_3$) δ 2.58 (s, 3H, SCH_3), 7.33, 7.41, 7.61, 7.73 (4d, 2H each, $J = 8.4$ Hz, ArH, Pyrid. H), 8.32 (s, 1H, CH=N), 9.85 (s, 1H, D_2O exchangeable NH); Ms; 408 [M−(CH_3SH, H), 5%]. Anal. Calcd for $C_{15}H_{13}ClIN_5S$ (457.7): C, 39.36; H, 2.86; N, 15.30; S, 7.01. Found: C, 39.16; H, 3.01; N, 15.47; S, 6.94.

3.1.7. Synthesis of compounds 11 and 12. General procedures

(A) To a cold stirred solution (at 0 °C) of each of compounds **5** and **6** (523 mg, 1 mmol) in acetic acid (10 mL) was added dropwise, while stirring, a solution of sodium nitrite (0.6 g in 1 mL water) over a period of 1 h. The reaction mixture was kept in the refrigerator overnight, dried under reduced pressure, diluted with CH_2Cl_2 (100 mL), and washed with water (3 × 100 mL). The organic layer was dried (Na_2SO_4), filtered, evaporated under reduced pressure, and the formed residue was recrystallized from CH_2Cl_2/petroleum ether (bp 40–60 °C) to give colorless crystals of compounds **11** and **12**. R_f values of compounds **11** and **12** were determined on TLC aluminum sheets using ethyl acetate/petroleum ether (bp 40–60 °C) [60:40, v/v] as a developing system.

(B) Each of compounds **7a**–**d** (1 mmol) was heated at 210–220 °C in an oil bath under vacuum in a micro-distillation system for 15 min. After cooling, the remaining solid was recrystallized from CH_2Cl_2/petroleum ether (bp 40–60 °C) to give colorless crystals of compound **11**. The expected nitriles were collected in the distillates and identified by ^{1}H NMR.

3.1.7.1. 2-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-5-(pyridin-3-yl)-2,4-dihydro-[1,2,4]-triazole-3-thione (11). Yield 431 mg (85%, A); 482 mg (95%, B using **7a**); 467 mg (92%, B using **7b**); 480 mg (94%, B using **7c**); 477 mg (94%, B using **7d**); colorless crystals, mp 96-98 °C ($R_f = 0.51$). IR: 3259, 3082, 2947, 2885, 2739, 1751, 1647, 1605, 1578, 1489, 1439, 1416, 1373, 1223, 1095, 1038, 984, 914, 818, 748, 706, 606, 525, 463, 494; ^{1}H NMR ($CDCl_3$) δ 1.87, 1.88, 1.89, 1.93 (4s, 12H, CH_3CO), 3.96 (ddd, 1H, $J_{\text{H-5′–H-6′}} = 2.1$ Hz, $J_{\text{H-5′–H-6″}} = 4.8$ Hz, $J_{\text{H-5′–H-4′}} = 9.9$ Hz, H-5′), 4.05 (dd, 1H, $J_{\text{H-6′–H-5′}} = 2.1$ Hz, $J_{\text{H-6′–H-6″}} = 12.6$ Hz, H-6′), 4.19 (dd, 1H, $J_{\text{H-6″–H-5′}} = 4.8$ Hz, $J_{\text{H-6″–H-6′}} = 12.6$ Hz, H-6″), 5.20 (t, 1H, $J_{\text{H-4′–H-3′}} = 9.6$ Hz, $J_{\text{H-4′–H-5′}} = 9.9$ Hz, H-4′), 5.31 (t, 1H, $J_{\text{H-3′–H-2′}} = 8.7$ Hz, $J_{\text{H-3′–H-4′}} = 9.6$ Hz, H-3′), 5.58 (t, 1H, $J_{\text{H-2′–H-1′}} = 9.3$ Hz, $J_{\text{H-2′–H-3′}} = 8.7$ Hz, H-2′), 5.64 (d, 1H, $J_{\text{H-1′–H-2′}} = 9.3$ Hz, H-1′), 7.29 (dd, 1H, $J_{\text{H-5 pyrid.–H-4 pyrid.}} = 8.1$ Hz, $J_{\text{H-5 pyrid.–H-6 pyrid.}} = 4.8$ Hz, H-5 pyrid.), 8.30 (td, 1H, $J_{\text{H-4 pyrid.–H-6 pyrid.}} = 1.8$ Hz, $J_{\text{H-4 pyrid.–H-2 pyrid.}} = 2.1$ Hz, $J_{\text{H-4 pyrid.–H-5 pyrid.}} = 8.1$ Hz, H-4 pyrid.), 8.34 (s, 1H, D_2O-exchangeable NH), 8.52 (d, 1H, $J_{\text{H-6 pyrid.–H-5 pyrid.}} = 4.8$ Hz, H-6 pyrid.), 9.21 (d, 1H, $J_{\text{H-2 pyrid.–H-4 pyrid.}} = 2.1$ Hz, H-2 pyrid.). Anal. Calcd for $C_{21}H_{24}N_4O_9S$ (508.5): C, 49.60; H, 4.76; N, 11.02; S, 6.31. Found: C, 49.58; H, 4.70; N, 10.97; S, 6.29.

3.1.7.2. 3-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl-1-thio)-5-(pyridin-3-yl)-4*H*-[1,2,4]-triazole (12). Yield 381 mg (75%, A); colorless crystals, mp 232 °C ($R_f = 0.1$). IR: 3418, 3082, 2935, 2854, 2750, 1751, 1616, 1416, 1381, 1234, 1038, 918, 606, 474; ^{1}H NMR ($CDCl_3$) δ 1.99, 2.00, 2.01, 2.04 (4s, 12H, CH_3CO), 3.75 (ddd, 1H, $J_{\text{H-5′–H-6′}} = 2.1$ Hz, $J_{\text{H-5′–H-6″}} = 4.8$ Hz, $J_{\text{H-5′–H-4′}} = 9.6$ Hz, H-5′), 3.98 (dd, 1H, $J_{\text{H-6′–H-5′}} = 2.1$ Hz, $J_{\text{H-6′–H-6″}} = 12.6$ Hz, H-6′), 4.12 (dd, 1H, $J_{\text{H-6″–H-5′}} = 4.8$ Hz, $J_{\text{H-6″–H-6′}} = 12.6$ Hz, H-6″), 5.00 (t, 1H, $J_{\text{H-4′–H-3′}} = 9.6$ Hz, H-4′), 5.02 (t, 1H, $J_{\text{H-3′–H-2′}} = 9.3$ Hz, $J_{\text{H-3′–H-4′}} = 9.6$ Hz, H-3′), 5.19 (t, 1H, $J_{\text{H-2′–H-1′}} = 10.2$ Hz, $J_{\text{H-2′–H-3′}} = 9.3$ Hz, H-2′), 5.22 (d, 1H, $J_{\text{H-1′–H-2′}} = 10.2$ Hz, H-1′), 7.29 (dd, 1H, $J_{\text{H-5 pyrid.–H-4 pyrid.}} = 8.1$ Hz, $J_{\text{H-5 pyrid.–H-6 pyrid.}} = 4.8$ Hz, H-5 pyrid.), 8.25 (td, 1H, $J_{\text{H-4 pyrid.–H-6 pyrid.}} = 2.1$ Hz, $J_{\text{H-4 pyrid.–H-5 pyrid.}} = 8.1$ Hz, H-4 pyrid.), 8.33 (s, 1H, D_2O-exchangeable NH), 8.50 (d, 1H, $J_{\text{H-6 pyrid.–H-5 pyrid.}} = 4.8$ Hz, H-6 pyrid.), 9.20 (d, 1H, $J_{\text{H-2 pyrid.–H-4 pyrid.}} = 2.1$ Hz, H-2 pyrid.). Anal. Calcd for $C_{21}H_{24}N_4O_9S$ (508.5): C, 49.60; H, 4.76; N, 11.02; S, 6.31. Found: C, 49.74; H, 4.65; N, 10.91; S, 6.45.

3.1.8. Deacetylation of compounds 7a, 8a, 11, and 12. General procedure. Dry gaseous ammonia was passed through a solution of each of compounds **7a**, **8a**, **11**, and **12** (1 mmol) in dry methanol (10 mL) for about 1 h with cooling and stirring, then the reaction mixture was stirred at room temperature overnight. The resulting mixture was then concentrated at reduced pressure to afford a solid residue, which was washed several times via boiling in chloroform (100 mL) and decantation. The residue was dried at room temperature, column chromatographed (chloroform→20% methanol/chloroform), and recrystallized from methanol to give colorless crystals of compounds **13** and **15** as well as pale crystals of compounds **14** and **16**. R_f values of the latter

compounds were determined using TLC aluminum sheets and chloroform/methanol (60:40, v/v) as a developing system.

3.1.8.1. 2-β-D-Glucopyranosyl-4-benzylideneamino-5-(pyridin-3-yl)-2,4-dihydro-[1,2,4]-triazole-3-thione (13). Yield 381 mg (86%); pale colorless crystals, mp 172 °C ($R_f = 0.58$). IR: 3500–3200, 3256, 3082, 2874, 2519, 2206, 1655, 1601, 1508, 1419, 1350, 1308, 1257, 1215, 1080, 1026, 906, 845, 756, 694, 667, 621, 517, 474, 428; ^{1}H NMR (DMSO-d_6) δ 3.22–3.52 (m, 4H, H-2′, H-3′, H-4′, H-5′), 3.73 (dd, 1H, $J_{H\text{-}6'\text{–}H\text{-}5'} =$ 4.8 Hz, $J_{H\text{-}6'\text{–}H\text{-}6''} = 12.6$ Hz, H-6′), 3.97 (ddd, 1H, $J_{H\text{-}6''\text{–}H\text{-}5'} =$ 4.8 Hz, $J_{H\text{-}6''\text{–}OH} = 5.7$ Hz, $J_{H\text{-}6''\text{–}H\text{-}6'} = 12.6$ Hz, 6″), 4.60 (t, 1H, $J_{OH\text{–}H\text{-}6''} = 5.7$ Hz, D_2O-exchangeable 6′-OH), 5.08 (d, 1H, $J = 5.4$ Hz, D_2O-exchangeable OH), 5.19 (d, 1H, $J = 5.1$ Hz, D_2O-exchangeable OH), 5.32 (d, 1H, $J = 5.4$ Hz, D_2O-exchangeable OH), 5.79 (d, 1H, $J_{H\text{-}1'\text{–}H\text{-}2'} = 9.3$ Hz, H-1′), 7.55-7.68 (m, 4H, ArH, H-5 pyrid.), 7.91 (d, 2H, $J = 7.2$ Hz, ArH), 8.29 (td, 1H, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}6\ pyrid.} = 1.8$ Hz, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}2\ pyrid.} =$ 2.1 Hz, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}5\ pyrid.} = 8.1$ Hz, H-4 pyrid.), 8.76 (dd, 1H, $J_{H\text{-}6\ pyrid.\text{–}H\text{-}4\ pyrid.} = 1.8$ Hz, $J_{H\text{-}6\ pyrid.\text{–}H\text{-}5\ pyrid.} =$ 4.8 Hz, H-6 pyrid.), 9.06 (d, 1H, $J_{H\text{-}2\ pyrid.\text{–}H\text{-}4\ pyrid.} =$ 2.1 Hz, H-2 pyrid.), 9.79 (s, 1H, CH=N). Anal. Calcd for $C_{20}H_{21}N_5O_5S$ (443.5): C, 54.17; H, 4.77; N, 15.79; S, 7.23. Found: C, 53.95; H, 4.71; N, 15.77; S, 7.18.

3.1.8.2. 3-β-D-Glucopyranosyl-1-thio-4-benzylideneamino-5-(pyridin-3-yl)-4*H*-[1,2,4]-triazole (14). Yield 288 mg (65%); pale crystals, mp 102–104 °C ($R_f = 0.10$). IR: 3500–3200, 3549, 3414, 3240, 2928, 2361, 2338, 1640, 1616, 1543, 1419, 1381, 1250, 1034, 814, 760, 617, 474, 444; ^{1}H NMR (DMSO-d_6) δ 4.00-3.00 (m, 6H, H-2′, H-3′, H-4′, H-5′, H-6′, H-6″), 4.65 (t, 1H, $J_{OH\text{–}H\text{-}6'} = 5.7$ Hz, D_2O-exchangeable 6′-OH), 4.80 (d, 1H, $J_{H\text{-}1'\text{–}H\text{-}2'} = 9.9$ Hz, H-1′), 5.05 (d, 1H, $J = 5.4$ Hz, D_2O-exchangeable OH), 5.13 (d, 1H, $J = 5.1$ Hz, D_2O-exchangeable OH), 5.26 (d, 1H, $J = 5.4$ Hz, D_2O-exchangeable OH), 7.38 (dd, 1H, $J_{H\text{-}5\ pyrid.\text{–}H\text{-}4\ pyrid.} = 8.1$ Hz, $J_{H\text{-}5\ pyrid.\text{–}H\text{-}6\ pyrid.} =$ 4.8 Hz, H-5 pyrid.), 7.58 (m, 3H, ArH), 7.89 (dd, 2H, J=1.2, 8.1 Hz, ArH), 8.31 (s, 1H, CH=N), 8.38 (td, 1H, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}6\ pyrid.} = 1.8$ Hz, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}2\ pyrid.} =$ 2.1 Hz, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}5\ pyrid.} = 8.1$ Hz, H-4 pyrid.), 8.68 (dd, 1H, $J_{H\text{-}6\ pyrid.\text{–}H\text{-}4\ pyrid.} = 1.8$ Hz, $J_{H\text{-}6\ pyrid.\text{–}H\text{-}5\ pyrid.} =$ 4.8 Hz, H-6 pyrid.), 9.15 (d, 1H, $J_{H\text{-}2\ pyrid.\text{–}H\text{-}4\ pyrid.} =$ 2.1 Hz, H-2 pyrid.). Anal. Calcd for $C_{20}H_{21}N_5O_5S$ (443.5): C, 54.17; H, 4.77; N, 15.79; S, 7.23. Found: C, 54.41; H, 4.82; N, 15.66; S, 7.17.

3.1.8.3. 2-β-D-Glucopyranosyl-5-(pyridin-3-yl)-2,4-dihydro-[1,2,4]-triazole-3-thione (15). Yield 299 mg (88%); colorless crystals, mp 206–208 °C ($R_f = 0.5$). IR: 3500–3200, 3364, 3132, 2870, 2704, 1601, 1477, 1439, 1342, 1308, 1242, 1084, 1041, 995, 895, 833, 702, 629, 555, 525, 478; ^{1}H NMR (DMSO-d_6) δ 3.13–3.38 (m, 4H, H-2′, H-3′, H-4′, H-5′), 3.45 (dd, 1H, $J_{H\text{-}6'\text{–}OH} = 5.7$ Hz, $J_{H\text{-}6'\text{–}H\text{-}6''} = 11.7$ Hz), 3.64 (dd, 1H, $J_{H\text{-}6''\text{–}H\text{-}5'} = 2.3$ Hz, $J_{H\text{-}6''\text{–}H\text{-}6'} = 11.7$ Hz, H-6″), 4.55 (br, 1H, D_2O-exchangeable OH), 5.00 (d, 1H, $J = 5.4$ Hz, D_2O-exchangeable OH), 5.08 (d, 1H, $J_{H\text{-}1'\text{–}H\text{-}2'} =$ 9.3 Hz, H-1′), 5.14 (d, 1H, $J = 4.8$ Hz, D_2O-exchangeable OH), 5.52 (br, 1H, D_2O-exchangeable OH), 7.52 (ddd 1H, $J_{H\text{-}5\ pyrid.\text{–}H\text{-}2\ pyrid.} = 0.9$ Hz, $J_{H\text{-}5\ pyrid.\text{–}H\text{-}6\ pyrid.} =$ 4.8 Hz, $J_{H\text{-}5\ pyrid.\text{–}H\text{-}4\ pyrid.} = 8.1$ Hz, H-5 pyrid.), 8.29 (td, 1H, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}6\ pyrid.} = 1.8$ Hz, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}2\ pyrid.} =$ 2.1 Hz, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}5\ pyrid.} = 8.1$ Hz, H-4 pyrid.), 8.64 (dd, 1H, $J_{H\text{-}6\ pyrid.\text{–}H\text{-}4\ pyrid.} = 1.8$ Hz, $J_{H\text{-}6\ pyrid.\text{–}H\text{-}5\ pyrid.} =$ 4.8 Hz, H-6 pyrid.), 9.14 (dd, 1H, $J_{H\text{-}2\ pyrid.\text{–}H\text{-}5\ pyrid.} =$ 0.9 Hz, $J_{H\text{-}2\ pyrid.\text{–}H\text{-}4\ pyrid.} = 2.1$ Hz, H-2 pyrid.), 14.24 (br, 1H, D_2O-exchangeable NH). Anal. Calcd for $C_{13}H_{16}N_4O_5S$ (340.4): C, 45.88; H, 4.74; N, 16.46; S, 9.42. Found: C, 45.77; H, 4.81; N, 16.48; S, 9.49.

3.1.8.4. 3-β-D-Glucopyranosyl-1-thio-5-(pyridin-3-yl)-4*H*-[1,2,4]-triazole (16). Yield 238 mg (70%); pale brown crystals, mp 107 °C ($R_f = 0.10$). IR: 3600–3200, 3414, 2932, 2858, 2361, 1620, 1520, 1419, 1084, 1045, 613, 474; ^{1}H NMR (DMSO-d_6) δ 4.00–3.00 (m, 6H, H-2′, H-3′, H-4′, H-5′, H-6′, H-6″), 4.43 (br, 1H, D_2O-exchangeable OH), 4.65 (br, 1H, D_2O-exchangeable OH), 4.79 (d, 1H, $J_{H\text{-}1'\text{–}H\text{-}2'} = 9.3$ Hz, H-1′), 4.93 (br, 1H, D_2O-exchangeable OH), 5.45 (dd, 1H, $J = 5.1$, 7.8 Hz, D_2O-exchangeable OH), 7.50 (dd, 1H, $J_{H\text{-}5\ pyrid.\text{–}H\text{-}4\ pyrid.} = 8.1$ Hz, $J_{H\text{-}5\ pyrid.\text{–}H\text{-}6\ pyrid.} =$ 4.8 Hz, H-5 pyrid.), 8.27 (td, 1H, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}6\ pyrid.} =$ 1.8 Hz, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}2\ pyrid.} = 2.1$ Hz, $J_{H\text{-}4\ pyrid.\text{–}H\text{-}5\ pyrid.} =$ 8.1 Hz, H-4 pyrid.), 8.32 (s, 1H, D_2O-exchangeable NH), 8.62 (dd, 1H, $J_{H\text{-}6\ pyrid.\text{–}H\text{-}4\ pyrid.} = 1.8$ Hz, $J_{H\text{-}6\ pyrid.\text{–}H\text{-}5\ pyrid.} = 4.8$ Hz, H-6 pyrid.), 9.11 (d, 1H, $J_{H\text{-}2\ pyrid.\text{–}H\text{-}4\ pyrid.} = 2.1$ Hz, H-2 pyrid.). Anal. Calcd for $C_{13}H_{16}N_4O_5S$ (340.4): C, 45.88; H, 4.74; N, 16.46; S, 9.42. Found: C, 45.99; H, 4.77; N, 16.39; S, 9.34.

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