

SYNTHESIS OF SOME NOVEL *N*-RIBOSYL-1,2,4-TRIAZIN-6(1*H*)-/ONES OR THIONES AS POTENTIAL ANTIBACTERIAL AND ANTIFUNGAL CHEMOTHERAPEUTICS

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□ Ribosylation of 3-aryl-5-benzyl(or substituted benzyl)-1,2,4-triazin-6(1H)-/ones or thiones with 1-O-acetyl-2,3,5-tri-O-benzoyl-β-D-ribofuranose gave the corresponding 3-aryl-5-benzyl(or substituted benzyl)-1.(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-1,2,4-triazin-6(1H)-/ones or thiones. The structure of the new ribosides was confirmed chemically and spectroscopically.

Keywords Synthesis, β -D-Ribosyls, 1,2,4-Triazines, Antibacterial, Antifungal

INTRODUCTION

N-Glycosides of 1,2,4-triazines are considered to be one of the most biologically active classes of compounds, possessing a wide spectrum of activities such as cytotoxics, antivirals, enzyme inhibitors, immunosuppressives, antipsoriatics, bacteriostatics, antitumors, as well as floor and wall disinfectants.^[1-10] Therefore, it would be of interest to synthesize some novel *N*-ribosides of 3-aryl-5-benzyl(or substituted benzyl)-1,2,4-triazin-6(1*H*)-/ones or thiones of expected interesting biological activities and report the antimicrobial screening of three selected compounds. The glucosyl and galactosyl analogues are reported.^[11,12]

RESULTS AND DISCUSSION

In the present investigation, the starting 3-aryl-5-benzyl(or substituted benzyl)-1,2,4-triazin-6(1*H*)-/ones **1a-d** or thiones **5a-d** were allowed to react with 1-Oacetyl-2,3,5-tri-O-benzoyl- β -D-ribofuranose **2** to give the corresponding 3-aryl-5-benzyl (or substituted benzyl)-1-(2,3,5-tri-O-benzoyl- β -D-ribofuranosyl)-1,2,4-triazin-6(1*H*)-/ ones **3a-d** or thiones **6a-d** following a simplified one-step/one-pot nucleoside

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SCHEME 1 Synthesis of N-ribosyl-1,2,4-triazin-6(1H)/ones or thiones.

synthesis as shown in Scheme 1. The structures of compounds **3a-d**, **6a-d** were assigned based on the following evidences:

- 1. The β -configuration of compounds **3a–d**, **6a–d** is confirmed from their ¹H NMR spectral data, which revealed the anomeric proton at δ 6.82–6.62 with a coupling constant consistent with similar reported data.^[13–16]
- 2. The IR spectra of compounds 3a-d showed the amide carbonyl function at 1674-1666 cm⁻¹.
- 3. Thiation of compounds $3\mathbf{a}-\mathbf{d}$ gave the corresponding thiones $6\mathbf{a}-\mathbf{d}$, which their IR spectra showed the absence of the amide carbonyl function at 1674–1666 cm⁻¹.

Debenzoylation of compounds **3a–d**, **6a–d** was achieved via their treatment with methanolic ammonia to give the free ribosides **4a–d**, **7a–d**, respectively. The structure of compounds **4a–d**, **7a–d** was confirmed based on their analytical and spectral data. Thus, the IR spectra of these compounds not only showed the absence of the ester carbonyl function at 1728 cm⁻¹, but also showed the appearance of the hydroxyl function at 3669–3400 cm⁻¹. Moreover, the ¹H NMR data of these compounds revealed the absence of the aromatic protons of the benzoate groups at δ 8.30–7.02 (via calculation of proton integration ratios) and the appearance of the exchangeable OH protons' signals at δ 5.18–4.59.

Biological Evaluation

As a part of our program directed toward the synthesis of new 1,2,4-triazine nucleosides with possible potential biological activity, $^{[9,10,12,17,18]}$ compounds **7b d** were tested for antimicrobial activity (in vitro) against against Aspergillus fumigatus, Penicillium italicum, Syncephalastrum racemosum, Candida albicans, Staphylococcus aureus, Pseudomonas aeruginosa, Bacillus subtilis, Escherichia coli. Table 1 shows the inhibitory effects of compounds **7bd** against these organisms. The screening results of these compounds showed that compound **7d** having a Cl atom has the greatest inhibitory effect against one or more types of microorganisms followed by compound **7c** having a methoxy group then compound **7b** having a methyl group. Thus, compound **7b** showed moderate activity against Aspergillus fumigatus (at all tested concentrations; 5, 2.5, 1 mg/mL), Penicillium italicum (at concentration 5 mg/mL), Syncephalastrum racemosum (at concentration 5 mg/mL), and *Escherichia coli* (at concentration 5 mg/mL). Compound **7c** showed activity against Aspergillus fumigatus (promising activity at concentration 5 mg/mL; moderate activity at concentration 2.5 mg/mL), Penicillium italicum (moderate activity at concentration 5 mg/mL), Candida albicans (moderate activity at all tested concentrations; 5, 2.5, 1 mg/mL), and Escherichia coli (promising activity at concentration 5 mg/mL; moderate activity at concentration 2.5 mg/mL). Compound 7d showed activity against Aspergillus fumigatus (promising activity at concentrations 5, 2.5 mg/mL; moderate activity at concentration 1 mg/mL), Penicillium italicum

Test organisms	Compounds											
	7b ^{<i>a</i>}			$\mathbf{7c}^{a}$			$\mathbf{7d}^{a}$			St. ^b		
	5	2.5	1	5	2.5	1	5	2.5	1	5	2.5	1
Aspergillus fumigatus	+	+	+	++	+	0	++	++	+	+++	+++	++
Penicillium italicum	+	0	0	+	0	0	++	++	+	+++	+++	++
Syncephalastrum racemosum	+	0	0	0	0	0	0	0	0	+++	+++	+++
Candida albicans	0	0	0	+	+	+	+	+	+	++	++	++
Staphylococcus aureus	0	0	0	0	0	0	0	0	0	++	++	++
Pseudomonas aeruginosa	0	0	0	+	+	+	0	0	0	+++	++	++
Bacillus subtilis	0	0	0	+	0	0	0	0	0	++	++	++
Escherichia coli	+	0	0	++	+	0	+++	++	++	+++	++	++

TABLE 1 Antimicrobial Activity of Compounds 7b = d Compared to Standard Antimicrobial Agents

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 = 1.1-1.5 cm beyond control = +++; 0 = not detected.

^a100 µl of each conc. (5, 2.5, 1 mg/mL) was tested.

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

(promising activity at concentrations 5, 2.5 mg/mL; moderate activity at concentration 1 mg/mL), *Candida albicans* (moderate activity at all tested concentrations; 5, 2.5, 1 mg/mL), and *Escherichia coli* (as potent as standard chloramphenicol at all tested concentrations).

EXPERIMENTAL

All melting points are uncorrected. IR spectra were recorded on a Perkin-Elmer 1430 spectrometer. ¹H NMR spectra were recorded at 200 MHz with a Varian GEMINI 200 spectrometer. The abbreviations pt and pq denote pseudotriplet and pseudoquartet signals, respectively. The starting compounds 1a-d,^[19,20] 5a-d^[11] were prepared as reported. TLC was performed on Fluka silica gel 60 F₂₅₄ aluminum sheets, and products were detected using 254 nm light. Fluka silica gel 60 (70–230 mesh) was used for column chromatography. Elemental analyses were carried out at the Micro Analytical Center, Cairo University, Giza, Egypt. Antimicrobial screening of compounds **7b d** was carried out at the Medical Mycology Lab, the Regional Center for Mycology and Biotechnology, Al Azhar University, Cairo, Egypt.

5-Benzyl (or substituted benzyl)-3-phenyl-1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-1,2,4-triazin-6(1*H*)-ones (3a-d).

General Procedure. To a mixture of each of compounds **1a–d** (2 mmol) and 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (**2**) (2 mmol) in acetonitrile (20 mL) were added consecutively hexamethyldisilazane (2.2 mmol), trimethylchlorosilane (2.2 mmol), and trifluoromethanesulfonic acid (2.4 mmol). The reaction mixture was heated at reflux temperature with exclusion of humidity (using CaCl₂ guard tube fitted over the refluxing condenser) until the reaction was judged complete by TLC (18–24 h), using petroleum ether (bp 40–60°C)/EtOAc (60:40, v/v) as a developing system. The excess acetonitrile was evaporated on a rotavap and the formed residue was dissolved in dichloromethane (30 mL), washed (NaHCO₃, brine), dried (Na₂SO₄), evaporated, column chromatographed (petroleum ether [bp 40–60°C] \rightarrow 60% EtOAc/petroleum ether [bp 40–60°C]), and recrystallized from dichloromethane/petroleum ether (bp 40–60°C) to give pale yellow crystals of compounds **3a–d**.

5-Benzyl-3-phenyl-1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-**1,2,4-triazin-6(1***H***)-one (3a).** Using the general procedure, **1a** gave **3a** (75%); $R_f = 0.87$; mp 114°C; IR (KBr) 1728 (C = O benzoate), 1674 (C = O amide) cm⁻¹; ¹H NMR (DMSO-d₆) δ 8.14–7.17 (m, 25H, ArH), 6.74 (d, 1H, J = 4.8 Hz, H-1'), 6.32 (pt, 1H, J = 5.5 Hz, H-2'), 6.24 (pt, 1H, J = 5.3 Hz, H-3'), 4.76 (m, 1H, H-4'), 4.68 (dd, 1H, J = 4.0 Hz, 11.5 Hz, H-5'), 4.48 (dd, 1H, J = 4.5 Hz, 11.7 Hz, H-5"), 4.23 (s, 2H, C₆H₅CH₂). Anal. Calcd. for C₄₂H₃₃N₃O₈: C, 71.28; H, 4.70; N, 5.94. Found: C, 71.44; H, 4.63; N, 5.68.

5-(4-Methylbenzyl)-3-phenyl-1-(2,3,5-tri-*O***-benzoyl-β-D-ribofuranosyl)-1,2,4-triazin-6(1***H***)-one (3b).** Using the general procedure, **1b** gave **3b** (72%); $R_f = 0.85$; mp 130°C; IR (KBr) 1728 (C = O benzoate), 1666 (C = O amide) cm⁻¹; ¹H NMR (DMSO-d₆) δ 8.3–7.02 (m, 24H, ArH), 6.62 (d, 1H, J = 5.0 Hz, H-1'), 6.29 (pt, 1H, J = 5.2 Hz, H-2'), 6.16 (pt, 1H, J = 5.3 Hz, H-3'), 4.82 (m, 1H, H-4'), 4.66 (dd, 1H, J = 4.1 Hz, 11.3 Hz, H-5'), 4.44 (dd, 1H, J = 4.3 Hz, 11.5 Hz, H-5"), 4.12 (s, 2H, 4-CH₃C₆H₄CH₂), 2.28 (s, 3H, 4-CH₃C₆H₄CH₂). Anal. Calcd. for C₄₃H₃₅N₃O₈: C, 71.56; H, 4.89; N, 5.82. Found: C, 71.71; H, 4.83; N, 5.77.

5-(4-Methoxybenzyl)-3-phenyl-1-(2,3,5-tri-*O***-benzoyl-β-D-ribo-furanosyl)-1,2,4-triazin-6(1***H***)-one (3c).** Using the general procedure, **1c** gave **3c** (83%); $R_f = 0.84$; mp 116°C; IR (KBr) 1728 (C = O benzoate), 1674 (C = O amide) cm⁻¹; ¹H NMR (DMSO-d₆) δ 8.11–7.36 (m, 24H, ArH), 6.75 (d, 1H, *J* = 4.9 Hz, H-1'), 6.35 (pt, 1H, *J* = 5.6 Hz, H-2'), 6.19 (pt, 1H, *J* = 5.4 Hz, H-3'), 4.89 (m, 1H, H-4'), 4.61 (dd, 1H, *J* = 4.2 Hz, 11.4 Hz, H-5'), 4.52 (dd, 1H, *J* = 4.4 Hz, 11.9 Hz, H-5''), 3.90 (s, 2H, 4-CH₃OC₆H₄CH₂), 3.76 (s, 3H, 4-CH₃OC₆H₄CH₂). Anal. Calcd. for C₄₃H₃₅N₃O₉: C, 70.01; H, 4.78; N, 5.70. Found: C, 70.20; H, 4.69; N, 5.74.

5-(4-Chlorobenzyl)-3-phenyl-1-(2,3,5-tri-*O***-benzoyl-β-D-ribofuranosyl)-1,2,4-triazin-6(1***H***)-one (3d).** Using the general procedure, **1d** gave **3d** (85%); $R_f = 0.79$; mp 117°C; IR (KBr) 1728 (C = O benzoate), 1674 (C = O amide) cm⁻¹; ¹H NMR (DMSO-d₆) δ 8.14–7.14 (m, 24H, ArH), 6.74 (d, 1H, J = 4.8 Hz, H-1'), 6.34 (pt, 1H, J = 5.3 Hz, H-2'), 6.16 (pt, 1H, J = 5.5 Hz, H-3'), 4.85 (m, 1H, H-4'), 4.64 (dd, 1H, J = 4.2 Hz, 11.4 Hz, H-5'), 4.56 (dd, 1H, J = 4.4 Hz, 11.7 Hz, H-5"), 4.23 (s, 2H, 4-ClC₆H₄CH₂). Anal. Calcd. for C₄₂H₃₂ClN₃O₈: C, 67.97; H, 4.35; N, 5.66. Found: C, 68.02; H, 4.44; N, 5.75.

5-Benzyl (or substituted benzyl)-3-phenyl-1-(2,3,5-tri-O-benzoyl- β -D-ribofuranosyl)1,2,4-triazin-6(1H)-thiones (6a-d).

General Procedure (A). To a mixture of each of compounds $5\mathbf{a}-\mathbf{d}$ (2 mmol) and 1-O-acetyl-2,3,5-tri-O-benzoyl- β -D-ribofuranose (2) (2 mmol) in acetonitrile (20 mL) were added consecutively hexamethyldisilazane (2.2 mmol), trimethylchlorosilane (2.4 mmol), and trifluoromethanesulfonic acid (2.4 mmol). The reaction mixture was heated at reflux temperature with exclusion of humidity (using CaCl₂ guard tube fitted over the refluxing condenser) until the reaction was judged complete by TLC (18–24 h), using petroleum ether (bp 40–60°C)/EtOAc (60:40, v/v) as a developing system. The excess acetonitrile was evaporated on a rotavap and the formed residue was dissolved in dichloromethane (30 mL), washed (NaHCO₃, brine), dried (Na₂SO₄), evaporated, column chromatographed (petroleum ether [bp 40–60°C] \rightarrow 60% EtOAc/petroleum ether [bp 40–60°C]) and recrystallized from dichloromethane/petroleum ether (bp 40–60°C) to give yellow crystals of compounds **6a–d**.

General Procedure (B). To a solution of each of compounds 3a-d (1 mmol) in dry pyridine (5 mL) was added phosphorous pentasulfide (2 mmol). The reaction mixture was heated at reflux temperature for 6 h. After cooling, the products were extracted from the oily materials with ethanol (10 mL). The supernatant solutions were decanted, acidified with acetic acid (0.5 mL), concentrated, and diluted with water. The precipitates were collected by filtration, dried at room temperature, dissolved in diethyl ether, and treated with charcoal (0.5 g), filtered, and the filtrates evaporated at room temperature. The resulting solids were recrystallized from diethyl ether/petroleum ether (bp $40-60^{\circ}$ C) to give yellow crystals of compounds 6a-d.

5-Benzyl-3-phenyl-1-(2,3,5-tri-*O*-**benzoyl-β-D**-**ribofuranosyl)-1,2,4-triazin-6(1***H***)-thione (6a).** Using the general procedure (A) or (B) with **5a** or **3a**, respectively, gave **6a** (77% or 55%); $R_f = 0.89$; mp 122°C; IR (KBr) 1728 (C = O benzoate) cm⁻¹; ¹H NMR (DMSO-d₆) δ 8.12–7.13 (m, 25H, ArH), 6.77 (d, 1H, J = 4.9 Hz, H-1'), 6.37 (pt, 1H, J = 5.1 Hz, H-2'), 6.19 (pt, 1H, J = 5.4 Hz, H-3'), 4.82 (m, 1H, H-4'), 4.69 (dd, 1H, J = 4.2 Hz, 11.4 Hz, H-5'), 4.48 (dd, 1H, J = 4.4 Hz, 11.5 Hz, H-5″), 4.22 (s, 2H, C₆H₅CH₂). Anal. Calcd. for C₄₂H₃₃N₃O₇S: C, 69.70; H, 4.60; N, 5.81; S, 4.43. Found: C, 69.84; H, 4.72; N, 5.92; S; 4.52. **5-(4-Methylbenzyl)-3-phenyl-1-(2,3,5-tri-***O***-benzoyl-β-D-ribofuranosyl)-1,2,4-triazin-6(1***H***)-thione (6b).** Using the general procedure (A) or (B) with **5b** or **3b**, respectively, gave **6b** (75% or 54%); $R_f = 0.83$; mp 146°C; IR (KBr) 1728 (C = O benzoate) cm⁻¹; ¹H NMR (DMSO-d₆) δ 8.29–7.13 (m, 24H, ArH), 6.74 (d, 1H, J = 5.3 Hz, H-1'), 6.25 (pt, 1H, J = 5.2 Hz, H-2'), 6.19 (pt, 1H, J = 5.4 Hz, H-3'), 4.88 (m, 1H, H-4'), 4.66 (dd, 1H, J = 4.1 Hz, 11.0 Hz, H-5'), 4.44 (dd, 1H, J = 4.3 Hz, 11.2 Hz, H-5"), 4.19 (s, 2H, 4-CH₃C₆H₄CH₂), 2.25 (s, 3H, 4-CH₃C₆H₄CH₂). Anal. Calcd. for C₄₃H₃₅N₃O₇S: C, 70.00; H, 4.78; N, 5.70; S, 4.35. Found: C, 69.92; H, 4.89; N, 5.61; S, 4.44.

5-(4-Methoxybenzyl)-3-phenyl-1-(2,3,5-tri-*O***-benzoyl-β-D-ribo-furanosyl)-1,2,4-triazin-6(1***H***)-thione (6c).** Using the general procedure (A) or (B) with **5c** or **3c**, respectively, gave **6c** (85% or 57%); $R_f = 0.79$; mp 122°C; IR (KBr) 1728 (C = O benzoate) cm⁻¹; ¹H NMR (DMSO-d₆) δ 8.14–7.30 (m, 24H, ArH), 6.82 (d, 1H, J = 5.0 Hz, H-1'), 6.32 (pt, 1H, J = 5.1 Hz, H-2'), 6.22 (pt, 1H, J = 5.5 Hz, H-3'), 4.84 (m, 1H, H-4'), 4.63 (dd, 1H, J = 4.1 Hz, 11.2 Hz, H-5'), 4.55 (dd, 1H, J = 4.3 Hz, 11.6 Hz, H-5"), 3.96 (s, 2H, 4-CH₃OC₆H₄CH₂), 3.78 (s, 3H, 4-CH₃OC₆H₄CH₂). Anal. Calcd. for C₄₃H₃₅N₃O₈S: C, 68.51; H, 4.68; N, 5.57; S, 4.25. Found: C, 68.54; H, 4.79; N, 5.48; S, 4.18.

5-(4-Chlorobenzyl)-3-phenyl-1-(2,3,5-tri-*O***-benzoyl-β-D-ribofuranosyl)-1,2,4-triazin-6(1***H***)-thione (6d).** Using the general procedure (A) or (B) with **5d** or **3d**, respectively, gave **6d** (86% or 60%); $R_f = 0.79$; mp 128–130°C; IR (KBr) 1728 (C = O benzoate) cm⁻¹; ¹H NMR (DMSO-d₆) δ 8.12–7.15 (m, 24H, ArH), 6.72 (d, 1H, J = 4.9 HzH-1'), 6.31 (pt, 1H J = 5.6 Hz, H-2'), 6.14 (pt, 1H, J = 5.7 Hz, H-3'), 4.80 (m, 1H, H-4'), 4.62 (dd, 1H, J = 4.2 Hz, 11.1 Hz, H-5'), 4.56 (dd, 1H, J = 4.3 Hz, 11.6 Hz, H-5"), 4.25 (s, 2H, 4-ClC₆H₄CH₂). Anal. Calcd. for C₄₂H₃₂ClN₃O₇S: C, 66.53; H, 4.25; N, 5.54; S, 4.23. Found: C, 66.48; H, 4.39; N, 5.66; S, 4.34.

5-Benzyl-3-phenyl-1- β -D-ribofuranosyl-1,2,4-triazin-6(1*H*)-ones (4a-d)/or thiones (7a-d).

General Procedure. Dry gaseous ammonia was passed through a solution of each of compounds 3a-d or 6a-d (1 mmol) in dry methanol (10 mL) for about 1 h while cooling and stirring. The reaction mixture was kept stirring at room temperature until complete as shown by TLC (10 to 24 h), using chloroform/methanol (80:20, v/v) as a developing system. The resulting mixture was then concentrated at reduced pressure to afford a semisolid residue, which was boiled in chloroform (100 mL), collected by discarding chloroform via decantation, washed several times with boiled chloroform, collected again by discarding chloroform via decantation, dried at room temperature, column chromatographed

(chloroform $\rightarrow 20\%$ methanol/chloroform), and recrystallized from methanol to give pale crystals of compounds **4a**–**d** and pale yellow crystals of compounds **7a**–**d**.

5-Benzyl-3-phenyl-1-β-D-ribofuranosyl-1,2,4-triazin-6(1*H***)-one (4a). Using the general procedure, 3a** gave **4a** (80%); $R_f = 0.92$; mp 175°C; IR (KBr) 3663–3429 (OH), 1673 (C = O amide) cm⁻¹; ¹H NMR (DMSO-d₆) δ 8.09–7.11 (m, 10H, ArH), 6.56 (d, 1H, J = 4.0 Hz, H-1'), 5.11 (d, 1H, J = 5.6 Hz, 2'-OH-exchangeable), 4.92 (d, 1H, J = 6.5 Hz, 3'-OH-exchangeable), 4.62 (t, 1H, J = 5.3 Hz, 5'-OH-exchangeable), 4.56 (pt, 1H, J = 5.2 Hz, H-2'), 4.19 (pq, 1H, H-3'), 3.78 (m, 1H, H-4'), 3.66 (dd, 1H, J = 4.5 Hz, 11.6 Hz, H-5'), 3.53 (dd, 1H, J = 4.7 Hz, 11.6 Hz, H-5''), 4.21 (s, 2H, C₆H₅CH₂). Anal. Calcd. for C₂₁H₂₁N₃O₅: C, 63.79; H, 5.35; N, 10.63. Found: C, 63.66; H, 5.24; N, 10.74.

5-(4-Methylbenzyl)-3-phenyl-1-β-D-ribofuranosyl-1,2,4-triazin-6(1*H***)-one (4b). Using the general procedure, 3b** gave **4b** (78%); $R_f = 0.88$; mp 197°C; IR (KBr) 3661–3422 (OH), 1673 (C = O amide) cm⁻¹; ¹H NMR (DMSO-d₆) δ 8.12–7.14 (m, 9H, ArH), 6.59 (d, 1H, J = 4.1 Hz, H-1'), 5.14 (d, 1H, J = 5.2 Hz, 2'-OH-exchangeable), 4.99 (d, 1H, J = 6.2 Hz, 3'-OH-exchangeable), 4.61 (t, 1H, J = 5.2 Hz, 5'-OH-exchangeable), 4.55 (pt, 1H, J = 5.4 Hz, H-2'), 4.29 (pq, 1H, H-3'), 3.79 (m, 1H, H-4'), 4.18 (s, 2H, 4-CH₃C₆H₄CH₂), 3.61 (dd, 1H, J = 4.4 Hz, 11.4 Hz, H-5'), 3.52 (dd, 1H, J = 4.4 Hz, 11.7 Hz, H-5"), 2.25 (s, 3H, 4-CH₃C₆H₄CH₂). Anal. Calcd. for C₂₂H₂₃N₃O₅: C, 64.54; H, 5.66; N, 10.26. Found: C, 64.44; H, 5.49; N, 10.37.

5-(4-Methoxybenzyl)-3-phenyl-1-β-D-ribofuranosyl-1,2,4-triazin-6(1*H***)-one (4c). Using the general procedure, 3c** gave **4c** (78%); $R_f = 0.87$; mp. 201–202°C; IR (KBr) 3661–3400 (OH), 1673 (C = O amide) cm⁻¹; 1H NMR (DMSO-d₆) δ 8.07–7.16 (m, 9H, ArH), 6.61 (d, 1H, J = 4.7 Hz, H-1'), 5.17 (d, 1H, J = 5.5 Hz, 2'-OH-exchangeable), 4.91 (d, 1H, J = 6.7 Hz, 3'-OH-exchangeable), 4.59 (t,1H, J = 5.0 Hz, 5'-OH-exchangeable), 4.62 (pt, 1H, J = 5.4 Hz, H-2'), 4.26 (pq, 1H, H-3'), 3.92 (s, 3H, 4-CH₃OC₆H₄CH₂), 3.78 (s, 2H, 4-CH₃OC₆H₄CH₂), 3.71 (m, 1H, H-4'), 3.66 (dd, 1H, J = 4.4 Hz, 11.3 Hz, H-5'), 3.53 (dd, 1H, J = 4.2 Hz, 11.3 Hz, H-5''). Anal. Calcd. for C₂₂H₂₃N₃O₆: C, 62.11; H, 5.45; N, 9.88. Found: C, 62.01; H, 5.64; N, 10.02.

5-(4-Chlorobenzyl)-3-phenyl-1-β-D-ribofuranosyl-1,2,4-triazin-6(1*H***)-thione (4d). Using the general procedure, 3d** gave **4d** (78%); $R_f = 0.90$; mp 194–196°C; 3670–3421 (OH), 1673 (C = O amide) cm⁻¹; 1H NMR (DMSO-d₆) δ 8.11–7.06 (m, 9H, ArH), 6.57 (d, 1H, J = 4.5 Hz, H-1'), 5.18 (d, 1H, J = 5.6 Hz, 2'-OH-exchangeable), 4.97 (d, 1H, J = 6.4 Hz, 3'-OHexchangeable), 4.62 (t, 1H, J = 5.1 Hz, 5'-OH-exchangeable), 4.55 (pt, 1H, J = 5.2Hz, H-2'), 4.24 (pq, 1H, H-3'), 3.76 (m, 1H, H-4'), 3.62 (dd, 1H, J = 4.6 Hz, 11.3 Hz, H-5'), 3.53 (dd, 1H, J = 4.7 Hz, 11.4 Hz, H-5"), 4.17 (s, 2H, 4-ClC₆H₄CH₂). Anal. Calcd. for C₂₁H₂₀ClN₃O₅: C, 58.68; H, 4.69; N, 9.78. Found: C, 58.84; H, 4.51; N, 9.66.

5-Benzyl-3-phenyl-1-β-D-ribofuranosyl-1,2,4-triazin-6(1H)-thione (7a). Using the general procedure, **6a** gave **7a** (79%); $R_f = 0.96$; mp 152–154°C; IR (KBr) 3660–3425 (OH) cm⁻¹; ¹H NMR (DMSO-d₆) δ 8.14–7.17 (m, 10H, ArH), 6.54 (d, 1H, J = 4.3 Hz, H-1′), 5.14 (d, 1H, J = 5.9 Hz, 2′-OH-exchangeable), 4.96 (d, 1H, J = 6.7 Hz, 3′-OH-exchangeable), 4.66 (t, 1H, J = 5.0 Hz, 5′-OH-exchangeable), 4.58 (pt, 1H, J = 5.5 Hz, H-2′), 4.25 (pq, 1H, H-3′), 3.76 (m, 1H, H-4′), 3.68 (dd, 1H, J = 4.7 Hz, 11.7 Hz, H-5′), 3.51 (dd, 1H, J = 4.8 Hz, 11.9 Hz, H-5″), 4.23 (s, 2H, C₆H₅CH₂). Anal. Calcd. for C₂₁H₂₁N₃O₄S: C, 61.30; H, 5.14; N, 10.21; S, 7.79. Found: C, 61.24; H, 5.02; N, 10.34; S, 7.95.

5-(4-Methylbenzyl)-3-phenyl-1-β-D-ribofuranosyl-1,2,4-triazin-6(1H)-thione (7b). Using the general procedure, **6b** gave **7b** (75%); $R_f = 0.95$; mp 169°C IR (KBr) 3667–3425 (OH) cm⁻¹; 1H NMR (DMSO-d₆) δ 8.19–7.11 (m, 9H, ArH), 6.64 (d, 1H, J = 4.5 Hz, H-1′), 5.16 (d, 1H, J = 5.7 Hz, 2′-OH-exchangeable), 4.98 (d, 1H, J = 6.5 Hz, 3′-OH-exchangeable), 4.63 (t, 1H, J = 5.7 Hz, 5′-OH-exchangeable), 4.58 (pt, 1H, J = 5.3 Hz, H-2′), 4.27 (pq, 1H, H-3′), 3.78 (m, 1H, H-4′), 4.23 (s, 2H, 4-CH₃C₆H₄CH₂), 3.67 (dd, 1H, J = 4.5 Hz, 11.6 Hz, H-5′), 3.52 (dd, 1H, J = 4.7 Hz, 11.8 Hz, H-5″), 2.27 (s, 3H, 4-CH₃C₆H₄CH₂). Anal. Calcd. for C₂₂H₂₃N₃O₄S: C, 62.10; H, 5.45; N, 9.88; S, 7.54. Found: C, 62.23; H, 5.56; N, 9.62; S, 7.68.

5-(4-Methoxybenzyl)-3-phenyl-1-β-D-ribofuranosyl-1,2,4-triazin-6(1*H***)-thione (7c). Using the general procedure, 6c** gave **7c** (87%); $R_f = 0.89$; mp 201–203°C; IR (KBr) 3669–3438 cm⁻¹; ¹H NMR (DMSO-d₆) δ 8.11–7.23 (m, 9H, ArH), 6.54 (d, 1H, J = 4.5 Hz, H-1'), 5.12 (d, 1H, J = 5.6 Hz, 2'-OH-exchangeable), 4.94 (d, 1H, J = 6.6 Hz, 3'-OH-exchangeable), 4.62 (t, 1H, J = 5.3 Hz, 5'-OH-exchangeable), 4.60 (pt, 1H, J = 5.4 Hz, H-2'), 4.26 (pq, 1H, H-3'), 3.97 (s, 2H, 4-CH₃OC₆H₄CH₂), 3.77 (s, 3H, 4-CH₃OC₆H₄CH₂), 3.74 (m, 1H, H-4'), 3.65 (dd, 1H, J = 4.5 Hz, 11.7 Hz, H-5'), 3.51 (dd, 1H, J = 4.8 Hz, 11.6 Hz, H-5"). Anal. Calcd. for C₂₂H₂₃N₃O₅S: C, 59.85; H, 5.25; N, 9.52; S, 7.26. Found: C, 60.03; H, 5.22; N, 9.74; S, 7.19.

5-(4-Chlorobenzyl)-3-phenyl-1-β-D-ribofuranosyl-1,2,4-triazin-6(1*H*)-thione (7d). Using the general procedure, 6d gave 7d (81%); $R_f = 0.93$; mp 222°C; 3660-3425 (OH) cm⁻¹; ¹H NMR (DMSO-d₆) δ 8.17-7.12 (m, 9H, ArH), 6.62 (d, 1H, J = 4.3 Hz, H-1'), 5.16 (d, 1H, J = 5.8 Hz, 2'-OHexchangeable), 4.96 (d, 1H, J = 6.8 Hz, 3'-OH-exchangeable), 4.67 (t, 1H, J = 5.0Hz, 5'-OH-exchangeable), 4.58 (pt, 1H, J = 5.3 Hz, H-2'), 4.24 (pq, 1H, H- 3'), 3.76 (m, 1H, H-4'), 3.67 (dd, 1H, J = 4.7 Hz, 11.6 Hz, H-5'), 3.53 (dd, 1H, J = 4.7 Hz, 11.9 Hz, H-5"), 4.21 (s, 2H, 4-ClC₆H₄CH₂). Anal. Calcd. for C₂₁H₂₀ClN₃O₄S: C, 56.56; H, 4.52; N, 9.42; S, 7.19. Found: C, 56.61; H, 4.42; N, 9.63, S, 7.34.

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