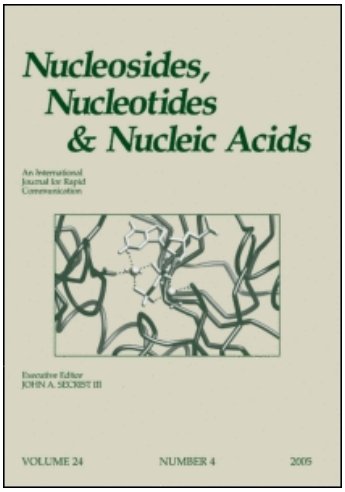

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First Synthesis And Antimicrobial Activity Of *N*- and *S*-α-L-Arabinopyranosyl-1,2,4-Triazoles

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FIRST SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF *N*- AND *S*-α-L-ARABINOPYRANOSYL-1,2,4-TRIAZOLES

Nasser S. A. M. Khalil □ *Regional Center for Food and Feed, Agricultural Research Center, Giza, Egypt*

□ *Arabinosylation of some 4-amino- and 4-arylideneamino-5-(pyridin-3-yl)-2,4-dihydro-[1,2,4]-triazole-3-thiones with 2,3,4-tri-O-acetyl-β-L-arabinopyranosyl bromide led to an efficient synthetic approach to the corresponding N- and S-α-L-arabinopyranosides. Structure assignment of these two regiosiomers was based on chemical and spectroscopic evidences. Antimicrobial activities of two selected regioisomeric N- and S-α-L-arabinopyranosides were compared. The N-α-L-arabinopyranoside showed higher inhibitory effect than its regioisomeric S-α-L-arabinopyranoside against Aspergillus fumigatus, Penicillium italicum, Staphylococcus aureus, and Pseudomonas aeruginosa.*

Keywords Synthesis; arabinosylation; 1,2,4-triazoles; deamination; deacetylation; antibacterial activity; antifungal activity

INTRODUCTION

The discovery of novel nucleosides for use as antimicrobial and anticancer agents has been the ambition of nucleoside chemists for decades. Extensive efforts have been concentrated on various modifications of the sugar moiety of nucleosides, which have resulted in FDA approved anti-HIV (such as AZT,[1] ddC,[2] ddI,[3] d4T,[4] 3TC,[5] Abacavir,[6] Bis(POC) PMPA[7]), and anti-HBV (including L-F-ddC[8] and L-FMAU[9]) agents.

Several β-L-nucleosides[10–13] have been synthesized and found to be more active and less toxic than their D-isomers[13,14] against HIV-1 and HBV[15,16] viruses. Biochemically some L-nucleosides are substrates for cellular kinases[17,18] and have greater stability for catabolizing enzymes such as cytidine and adenosine deaminase.[19]

While many routes exist for synthesis of *N*-ß-nucleosides, there are few methods available for the α-anomers. Mukaiyama et al.[20] showed that the reaction of 1-hydroxy sugars such as 2,3-*O*-(1-methylethylidene-5-*O*-(triphenylmethyl)-α/β-D-ribofuranose[21] or 5-*O*-benzoyl-2,3-*O*-(1-methyl-

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ethylidene)-D-ribofuranose[22] with trimethylsilylated benzimidazole and other nitrogenous bases including nucleoside bases and azides, using 2-fluoro-1-methylpyridinium tosylate as condensing reagent, gives predominantly α-ribonucleosides. However, as much as 47% of the β- anomer is obtained, requiring difficult separations of these isomeric mixtures by column chromatography. So far, no full characterization and isolation of these compounds have been reported. There are reports[22,23] of the use of ribofuranosyl chlorides for α-glycosylation, but these also produce mixtures of α- and ß-*N*-glycosides. Recently, we reported a simple base induced regeoselective method for the α-arabinopyranosylation of different ß-lactams[24] and 1,2,4-triazines[25] that resulted in the synthesis of many antimicrobial[24] and antitumor[25] α-nucleosides.

Various 1,2,4-triazoles,[26–45] their ribosides,[46–49] and glucosides[50,51] have been reported to possess antibacterial, antifungal, antiviral, antiinflammatory, anticonvulsant, antidepressant, antitubercular, antihypertensive, analgesic, hypoglycemic, herbicidal, and sedative properties.

To date there has not been a single report of reactions that produce the α-nucleosides of 1,2,4-triazole. Thus, in this article, and in continuation of our ongoing program[24,25,50–57] of research on the synthesis of some biologically active compounds, we report here the first synthesis, antifungal and antibacterial activities of some novel unusual *N*- and *S*-α-L-arabinopyranosyl-1,2,4-triazoles.

RESULTS AND DISCUSSION

Arabinosidation of 4-amino- and/or 4-arylideneamino-5-(pyridin-3-yl)-2,4-dihydro-[1,2,4]-triazole-3-thiones (**1** and/or **2a–d**) with 1.2 molar equivalent of 2,3,4-tri-*O*-acetyl-β-L-arabinopyranosyl bromide (**3**) gave a chromatographically separable mixture (53–77% overall yield) of two products namely, 2-(2,3,4,-tri-*O*-acetyl-α-L-arabinopyranosyl)-4-amino- and/or 4-arylideneamino-5-(pyridin-3-yl)-2,4-dihydro-[1,2,4]-triazole-3-thiones (**4** and/or **6a–d**) and 3-(2,3,4-tri-*O*-acetyl-α-L-arabinopyranosyl-1-thio)-4-amino- and/or 4-arylideneamino-5-(pyridin-3-yl)-4*H*-[1,2,4]-triazoles (**5** and/or **7a–d**).

The structures of compounds **4–7** were established based on spectroscopic and chemical evidences. Thus, the position of the anomeric proton of compounds **4** and **6a–d** at δ 6.02–6.20 with a coupling constant value of 9.0–9.3 Hz consistent with similar reported data[24,25,50–55,57,58] proves that the anomeric proton is of *N*-type in a trans position with respect to the proton on position 2 of the L-arabinopyranosyl ring, a fact that assigns its *N*-α-configuration. The *S*-α-configuration of compounds **5** and **7a–d** is similarly assigned from their ^{1}H NMR data. Thus, the ^{1}H NMR data of compounds **5** and **7a–d** showed the anomeric proton at δ 5.09–5.60

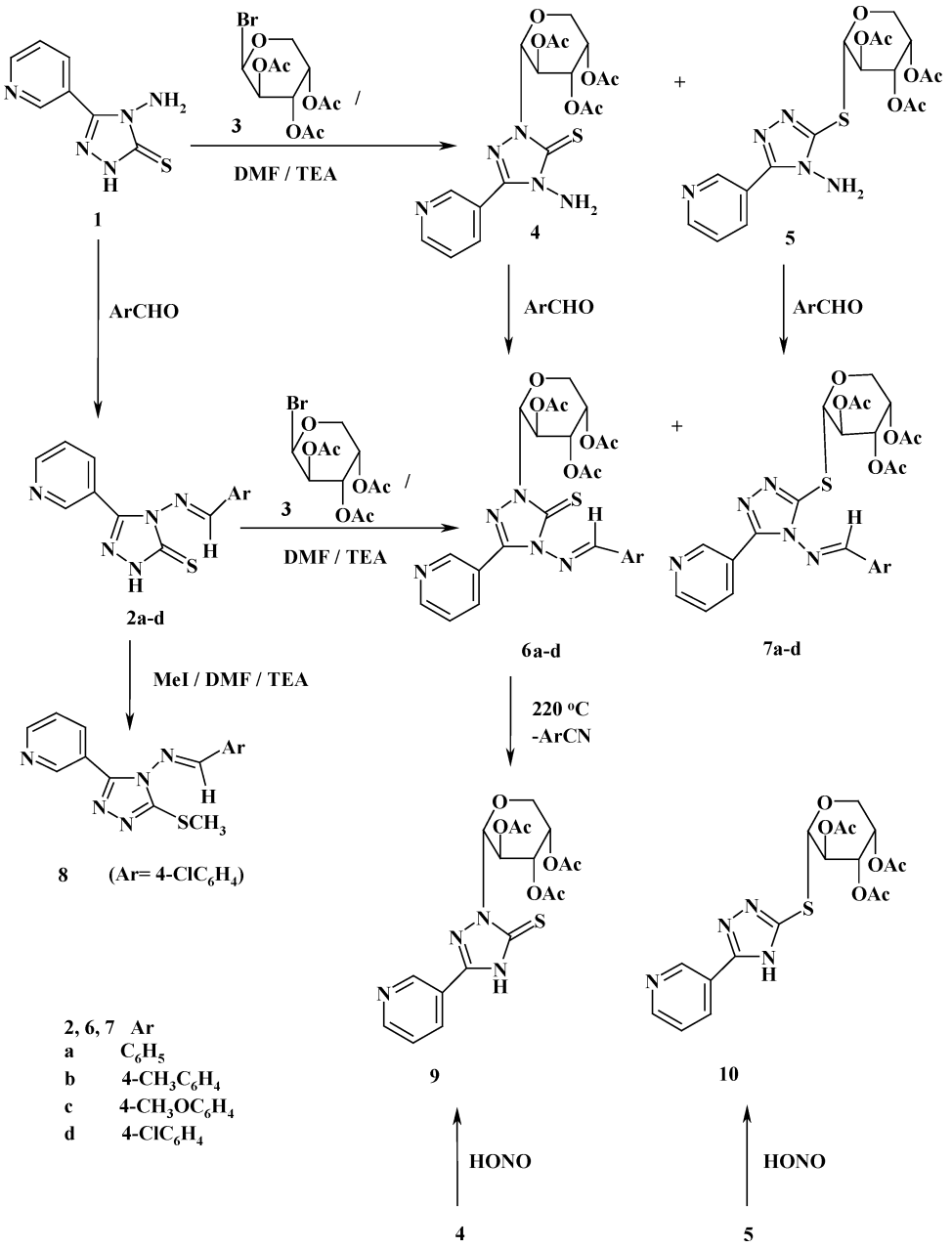
with a coupling constant value 7.2–8.7 Hz consistent with reported data for *S*-glucosides having their anomeric proton in a trans position with respect to the proton on position 2 of the pyranosyl ring.[50,51] For all the *N*-arabinosides **6a–d**, the CH = N and the anomeric protons appear at δ 9.89–10.28 and 6.19–6.20 more downfield than those for the *S*-arabinosides **7a–d** which appear at δ 8.47–8.65 and 5.51–5.60, respectively. Such downfield shifts in *N*-arabinosyl derivatives is 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 was reported for pyrimidine[59–61] and 1,2,4-triazole nucleosides[50,51]). Further evidence comes from studying the ^{1}HNMR spectra of the *N*- glucosides **6a–d** and *S*- glucosides **7a–d** in comparison with the previously reported ^{1}HNMR spectrum of the 4-(4-chlorobenzyideneamino)-3-methylthio-5-(pyridin-3-yl)-4 *H*-[1,2,4]-triazole (**8**).[50] Thus, the appearance of CH = N proton signal of compound **8** at δ 8.58[50] confirms the assigned structure of compounds **7a–d.**

Compounds **6a–d** and **7a–d** were alternatively synthesized in excellent yields via condensation of compounds **4** and **5** with the appropriate aryl aldehydes.

Deamination of compounds **4** and **5** into compounds **9** and **10** was carried out in excellent yields by the action of nitrous acid in acetic acid (Scheme 1). Thermolysis of compounds **6a–d** showed also an efficient alternative pathway to the deaminated product **9.** The structure of compounds **9** and **10** was assigned from their correct analytical and spectral data. Thus, the ^{1}HNMR data of these compounds showed the absence of the NH_2 protons at δ 4.98–5.46 and revealed the presence of the D_2O exchangeable NH proton signal at δ 8.33–8.37. Moreover, the IR data of compounds **9** and **10** showed the disappearance of NH_2 bands at 3336–3328, 3250–3205 cm^{-1} and revealed the appearance of the characteristic NH band at 3474–3337 cm^{-1}.

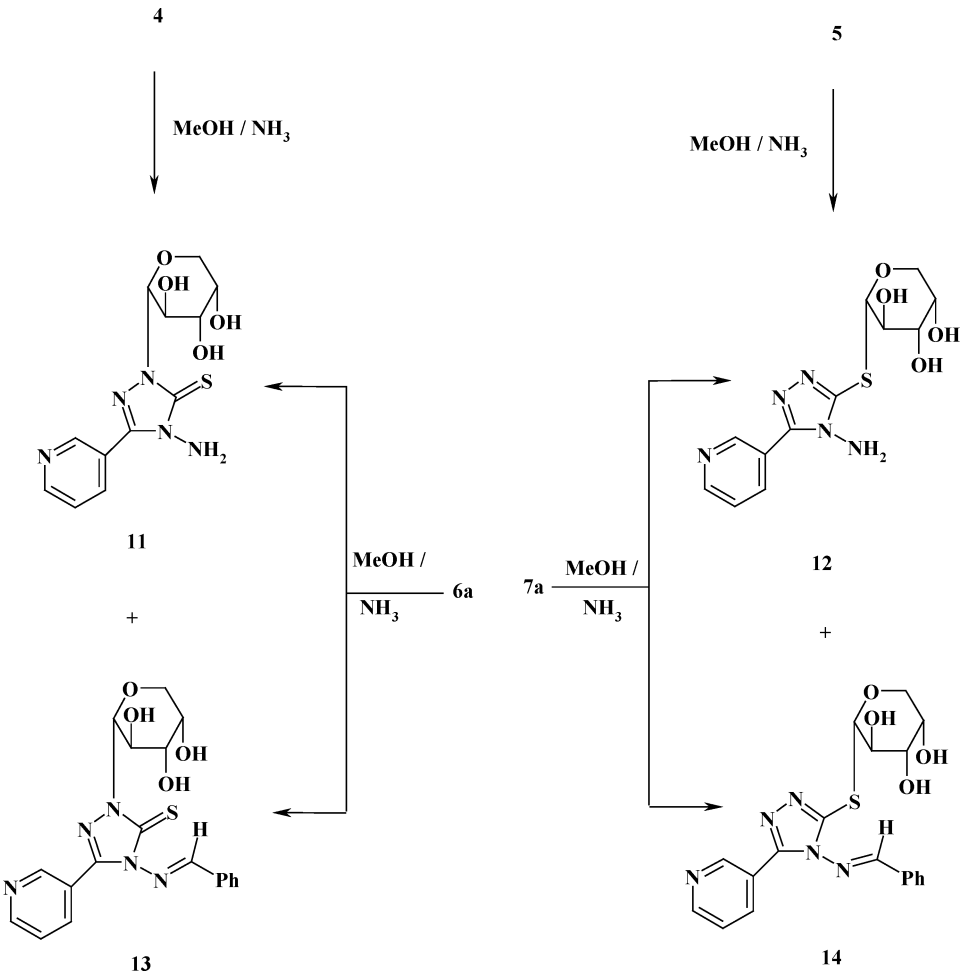
Deacetylation of compounds **4** and **5** (Scheme 2) via methanolic ammonia treatment led to the formation of the expected free nucleosides **11** and **12**, respectively. On the other hand, deacetylation of compounds **6a** and **7a** gave a mixture of the expected deacetylated products **13** and **14** along with the 4-amino free nucleosides **11** and **12**, respectively. The ^{1}HNMR data of the compounds **11–14** revealed the absence of the acetyl protons at δ 1.89–2.18 and the appearance of the D_2O exchangeable OH protons at δ 4.22–5.14. The IR data of compound **11** as a typical example showed also the absence of the acetyl carbonyl function at 1743 cm^{-1} and the appearance of the characteristic OH band at 3424 (br) cm^{-1}.

Compounds **6d** and **7d** were 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.



SCHEME 1 Synthesis of *N*- and *S*-α-L-arabinopyranosyl-1,2,4-triazoles.

The inhibitory effect of *N*-α-L-arabinoside **6d** was studied in comparison with similar effect due to *S*-α-L-arabinoide **7d**. Thus, compound **6d** showed higher inhibitory effect against *Aspergillus fumigatus*, *Penicillium italicum*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*. Compound **7d** showed



SCHEME 2 Deacetylation of compounds **4**, **5**, **6a**, and **7a**.

only a moderate activity against *Penicillium italicum* at concentrations 2.5 and 5.0 mg/mL.

CONCLUSIONS

The present article describes first synthesis and efficient routes for different novel and unusual functionalized *N*- and *S*-α-L-arabinosyl-1,2,4-triazoles with potential antimicrobial activities. These compounds could serve 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 infection.

TABLE 1 Antimicrobial activity of compounds **6d** and **7d** compared to standard antimicrobial agents

	Compound								
	6d[a]			**7d**[a]			**St.**[b]		
	Concentration (mg/mL)								
Test organisms	1	2.5	5	1	2.5	5	1	2.5	5
Aspergillus fumigatus	0	+	++	0	0	0	++	+++	+++
Penicillium italicum	0	+	++	0	+	+	++	+++	+++
Syncephalastrum racemosum	0	0	0	0	0	0	+++	+++	+++
Candida albicans	0	0	0	0	0	0	++	++	++
Staphylococcus aureus	0	+	+	0	0	0	++	++	++
Pseudomonas aeruginosa	0	+	+	0	0	0	++	+++	+++
Bacillus subtilis	0	0	0	0	0	0	++	+++	+++
Escherichia coli	0	0	0	0	0	0	++	++	++

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 conc. 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.

EXPERIMENTAL

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. Elemental analyses were carried out at the Micro Analytical Center, Cairo University, Giza, Egypt. Antimicrobial screening of compounds **6d** and **7d** was carried out at the Medical Mycology Laboratory, Regional Center for Mycology and Biotechnology, Al Azhar University, Cairo, Egypt. The starting 4-amino- and/or 4-arylideneamino-5-(pyridin-3-yl)-2,4-dihydro-[1,2,4]-triazole-3-thiones (**1** and/or **2a–d**)[50] and 2,3,4-tri-*O*-acetyl-β-L-arabinopyranosyl bromide **(3)**[62]were prepared as reported. TLC was performed on Fluka silica gel 60 F_{254} aluminum sheets, and products were detected using 254 nm light. Fluka silica gel 60 (70–230 mesh) was used for column chromatography.

General Procedure for the Synthesis of Compounds 4 and 5

To a solution of compound **1** (1.93 g, 10 mmol) in *N*,*N*-dimethylformamide (10 mL) and triethylamine (1.7 mL, 12 mmol) was added 2,3,4-tri-*O*-acetyl-β-L-arabinopyranosyl bromide **(3)** (4.07 g, 12 mmol)

and the reaction mixture was stirred overnight. The next day, the reaction mixture was dried under reduced pressure, diluted with dichloromethane (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 **4** was eluted first with 80% ethyl acetate/petroleum ether (b.p. 40–60°C) → 90% ethyl acetate/petroleum ether (b.p. 40–60°C), followed by compound **5** with ethyl acetate → 20% methanol/ethyl acetate. The chromatographically separated crude products were recrystallized from dichloromethane/petroleum ether (b.p. 40–60°C) and their R_f values were determined on TLC aluminum sheets using ethyl acetate/petroleum ether (b.p. 40–60°C) [60:40, v/v] as a developing system.

2-(2,3,4-Tri-*O*-acetyl-α-L-arabinopyranosyl)-4-amino-5-(pyridin-3-yl)-2,4-dihydro-[1,2,4]-triazole-3-thione (4): Yield 1.08 g (24%); colorless crystals, m.p. 190–192°C ($R_f = 0.63$). IR: 3328, 3250, 3093, 3053, 2970, 2941, 2858, 2739, 2500, 2380, 1948, 1743, 1431, 1369, 1223, 1057, 1026, 937, 879, 852, 814, 760, 702, 663, 606, 521, 486; ^{1}H NMR ($CDCl_3$) δ 1.89, 2.00, 2.17 (3s, 9H, CH_3CO), 3.95 (dd, 1H, $J_{H\text{-}5'\text{-}H\text{-}4'} = 0.9$ Hz, $J_{H\text{-}5'\text{-}H\text{-}5''} = 13.5$ Hz, H-5′), 4.14 (dd, 1H, $J_{H\text{-}5''\text{-}H\text{-}4'} = 1.8$ Hz, $J_{H\text{-}5''\text{-}H\text{-}5'} = 13.5$ Hz, H-5″), 4.98 (s, 2H, D_2O exchangeable NH_2), 5.25 (dd, 1H, $J_{H\text{-}3'\text{-}H\text{-}4'} = 3.6$ Hz, $J_{H\text{-}3'\text{-}H\text{-}2'} = 9.6$ Hz, H-3′), 5.38 (dd, 1H, $J_{H\text{-}4'\text{-}H\text{-}3'} = 3.6$ Hz, $J_{H\text{-}4'\text{-}H\text{-}5''} = 1.8$ Hz, H-4′), 5.94 (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′), 6.02 (d, 1H, $J_{H\text{-}1'\text{-}H\text{-}2'} = 9.3$ Hz, H-1′), 7.39 (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.), 8.40 (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.), 8.70 (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.), 9.34 (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 $C_{18}H_{21}N_5O_7S$ (451.5): C, 47.89; H, 4.69; N, 15.51; S, 7.10. Found: C, 47.79; H, 4.63; N, 15.47; S, 6.94.

3-(2,3,4-Tri-*O*-acetyl-α-L-arabinopyranosylthio)-4-amino-5-(pyridin-3-yl)-4*H*-[1,2,4]-triazole (5): Yield 1.85 g (41%); pale crystals, m.p. 130–132°C ($R_f = 0.04$). IR: 3336, 3205, 3032, 2983, 2935, 1747, 1632, 1578, 1431, 1373, 1223, 1061, 1022, 937, 814, 756, 706, 602, 494, 417; ^{1}H NMR ($CDCl_3$) δ 1.96, 2.02, 2.04 (3s, 9H, CH_3CO), 3.68 (d, 1H, $J_{H\text{-}5'\text{-}H\text{-}5''} = 12.9$ Hz, H-5′), 3.98 (dd, 1H, $J_{H\text{-}5''\text{-}H\text{-}4'} = 3.3$ Hz, $J_{H\text{-}5''\text{-}H\text{-}5'} = 12.9$ Hz, H-5″), 5.05 (dd, 1H, $J_{H\text{-}3'\text{-}H\text{-}4'} = 3.3$ Hz, $J_{H\text{-}3'\text{-}H\text{-}2'} = 8.4$ Hz, H-3′), 5.09 (d, 1H, $J_{H\text{-}1'\text{-}H\text{-}2'} = 8.7$ Hz, H-1′), 5.19 (m, 1H, H-4′), 5.20 (t, 1H, $J_{H\text{-}2'\text{-}H\text{-}3'} = 8.4$ Hz, $J_{H\text{-}2'\text{-}H\text{-}1'} = 8.7$ Hz, H-2′), 5.46 (s, 2H, D_2O exchangeable NH_2), 7.32 1H, (dd, $J_{H\text{-}5\text{ pyrid.}\text{-}H\text{-}6\text{ pyrid.}} = 4.8$ Hz, $J_{H\text{-}5\text{ pyrid.}\text{-}H\text{-}4\text{ pyrid.}} = 8.1$ Hz, H-5 pyrid.), 8.35 (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.), 8.55 (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.), 9.24 (dd, 1H, $J_{H\text{-}2\text{ pyrid.}\text{-}H\text{-}4\text{ pyrid.}} = 2.1$ Hz, H-2 pyrid.). Anal. Calcd for $C_{18}H_{21}N_5O_7S$ (451.5): C, 47.89; H, 4.69; N, 15.51; S, 7.10. Found: C, 47.67; H, 4.54; N, 15.54; S, 6.99.

General Procedures for the Synthesis of Compounds 6a–d and 7a–d

A) To a solution of each of compounds **2a–d** (3.6 mmol) in *N*,*N*-dimethylformamide (4 mL) and triethylamine (0.6 mL, 4.3 mmol) was added 2,3,4-tri-*O*-acetyl-β-L-arabinopyranosyl bromide (**3**) (1.46 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 several times with water and dried at room temperature. The product was extracted from dichloromethane and subjected to silica gel (70–230 mesh) column chromatography. Compounds **6a–d** were eluted first with 50% ethyl acetate/petroleum ether (b.p. 40–60°C) → 100% ethyl acetate followed by compounds **7a–d** with ethyl acetate → 20% methanol/ethyl acetate. The chromatographically separated crude products were recrystallized from dichloromethane/petroleum ether (b.p. 40–60°C) and their R_f values were determined on TLC aluminum sheets using ethyl acetate/petroleum ether (b.p. 40–60°C) [60:40, v/v] as a developing system.

B) An equimolecular mixture of each of compounds **4**, **5** (100 mg, 0.2 mmol) and the appropriate aldehyde (0.2 mmol) was heated at 160°C for 5–10 minutes. After cooling the products were recrystallized from dichloromethane/petroleum ether (b.p. 40–60°C) to give the corresponding arylideneamino derivatives 6a–d and 7a–d, respectively.

2-(2,3,4-Tri-*O*-acetyl-α-L-arabinopyranosyl)-4-benzylideneamino-5-(pyridin-3-yl)-2,4-dihydro-[1,2,4]-triazole-3-thione (6a). Yield 485 mg (25%, A); 102 mg (86%, B); colorless crystals, m.p. 174–176°C ($R_f = 0.53$). IR: 3086, 3054, 3012, 2932, 2870, 2750, 1747, 1601, 1578, 1547, 1423, 1369, 1323, 1246, 1223, 1119, 1092, 1061, 1022, 960, 937, 876, 845, 818, 756, 733, 698, 613, 525, 490, 428; ^{1}H NMR ($CDCl_3$) δ 1.93, 2.01, 2.18 (3s, 9H, CH_3CO), 3.98 (d, 1H, $J_{H\text{-}5'\text{-}H\text{-}5''} = 13.5$ Hz, H-5′), 4.17 (d, 1H, $J_{H\text{-}5''\text{-}H\text{-}5'} = 13.5$ Hz, H-5″), 5.29 (dd, 1H, $J_{H\text{-}3'\text{-}H\text{-}4'} = 3.3$ Hz, $J_{H\text{-}3'\text{-}H\text{-}2'} = 9.6$ Hz, H-3′), 5.41 (d, 1H, $J_{H\text{-}4'\text{-}H\text{-}3'} = 3.3$ Hz, H-4′), 6.01 (t, 1H, $J_{H\text{-}2'\text{-}H\text{-}1'} = 9.0$ Hz, $J_{H\text{-}2'\text{-}H\text{-}3'} = 9.6$ Hz, H-2′), 6.20 (d, 1H, $J_{H\text{-}1'\text{-}H\text{-}2'} = 9.0$ Hz, H-1′), 7.46 (m, 4 H, ArH, H-5 pyrid.), 7.81 (d, 2H, $J = 7.2$ Hz, ArH), 8.28 (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.), 8.71 (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.), 9.22 (d, 1H, $J_{H\text{-}2\ pyrid.\text{-}H\text{-}4\ pyrid.} = 2.1$ Hz, H-2 pyrid.), 10.17 (s, 1H, CH = N). Anal. Calcd for $C_{25}H_{25}N_5O_7S$ (539.6): C, 55.65; H, 4.67; N, 12.98; S, 5.94. Found: C, 55.74; H, 4.54; N, 13.05; S, 5.83.

2-(2,3,4-Tri-*O*-acetyl-α-L-arabinopyranosyl)-4-(4-methylbenzylideneamino)-5-(pyridin-3-yl)-2,4-dihydro-[1,2,4]-triazole-3-thione (6b). Yield 657 mg (33%, A); 108 mg (88%, B); colorless crystals, m.p. 180–182°C ($R_f = 0.54$). IR: 3074, 3049, 3005, 2924, 2858, 1747, 1616, 1570, 1423, 1373, 1327, 1246, 1223, 1119, 1092, 1061, 1018, 918, 879, 849, 814, 756, 702, 617, 486; ^{1}H

NMR ($CDCl_3$) δ 1.93, 2.01, 2.19 (3s, 9H, CH_3CO), 2.39 (s, 3H, CH_3), 3.97 (d, 1H, $J_{H\text{-}5'\text{-}H\text{-}5''} = 13.5$ Hz, H-5′), 4.17 (dd, 1H, $J_{H\text{-}5''\text{-}H\text{-}4'} = 1.8$ Hz, $J_{H\text{-}5''\text{-}H\text{-}5'} = 13.5$ Hz, H-5″), 5.29 (dd, 1H, $J_{H\text{-}3'\text{-}H\text{-}4'} = 3.3$ Hz, $J_{H\text{-}3'\text{-}H\text{-}2'} = 9.9$ Hz, H-3′), 5.41 (d, 1H, $J_{H\text{-}4'\text{-}H\text{-}3'} = 3.3$ Hz, H-4′), 6.01 (t, 1H, $J_{H\text{-}2'\text{-}H\text{-}1'} = 9.0$ Hz, $J_{H\text{-}2'\text{-}H\text{-}3'} = 9.9$ Hz, H-2′), 6.20 (d, 1H, $J_{H\text{-}1'\text{-}H\text{-}2'} = 9.0$ Hz, H-1′), 7.25 (d, 2H, $J = 8.1$ Hz, ArH), 7.39 (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.), 7.71 (d, 2H, $J = 8.1$ Hz, ArH), 8.28 (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.), 8.69 (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.), 9.21 (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.), 10.04 (s, 1H, CH = N). Anal. Calcd for $C_{26}H_{27}N_5O_7S$ (553.6): C, 56.41; H, 4.92; N, 12.65; S, 5.79. Found: C, 56.53; H, 4.88; N, 12.69; S, 5.64.

2-(2,3,4-Tri-*O*-acetyl-α-L-arabinopyranosyl)-4-(4-methoxybenzylideneamino)-5-(pyridin-3-yl)-2,4-dihydro-[1,2,4]-triazole-3-thione (6c). Yield 553 mg (27% A); 105 mg (83%, B); colorless crystals, m.p. 158–160°C ($R_f = 0.56$). IR: 3088, 3029, 2932, 2839, 1747, 1612, 1570, 1512, 1423, 1369, 1323, 1254, 1219, 1169, 1061, 1022, 933, 879, 829, 752, 702, 606, 525, 482; ^{1}H NMR ($CDCl_3$) δ 1.92, 2.01, 2.18 (3s, 9H, CH_3CO), 3.83 (s, 3H, OCH_3), 3.97 (d, 1H, $J_{H\text{-}5'\text{-}H\text{-}5''} = 13.5$ Hz, H-5′), 4.17 (d, 1H, $J_{H\text{-}5''\text{-}H\text{-}5'} = 13.5$ Hz, H-5″), 5.28 (dd, 1H, $J_{H\text{-}3'\text{-}H\text{-}4'} = 3.3$ Hz, $J_{H\text{-}3'\text{-}H\text{-}2'} = 9.6$ Hz, H-3′), 5.40 (d, 1H, $J_{H\text{-}4'\text{-}H\text{-}3'} = 3.3$ Hz, H-4′), 6.01 (t, 1H, $J_{H\text{-}2'\text{-}H\text{-}1'} = 9.0$ Hz, $J_{H\text{-}2'\text{-}H\text{-}3'} = 9.6$ Hz, H-2′), 6.19 (d, 1H, $J_{H\text{-}1'\text{-}H\text{-}2'} = 9.0$ Hz, H-1′), 6.94 (d, 2H, $J = 8.4$ Hz, ArH), 7.38 (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.), 7.77 (d, 2H, $J = 8.4$ Hz, ArH), 8.27 (d, 1H, $J_{H\text{-}4\text{ pyrid.}\text{-}H\text{-}5\text{ pyrid.}} = 7.8$ Hz, H-4 pyrid.), 8.69 (d, 1H, $J_{H\text{-}6\text{ pyrid.}\text{-}H\text{-}5\text{ pyrid.}} = 4.8$ Hz, H-6 pyrid.), 9.21 (s, 1H, H-2 pyrid.), 9.89 (s, 1H, CH = N). Anal. Calcd for $C_{26}H_{27}N_5O_8$ S (569.6): C, 54.83; H, 4.78; N, 12.30; S, 5.63. Found: C, 54.77; H, 4.77; N, 12.24; S, 5.74.

2-(2,3,4-Tri-*O*-acetyl-α-L-arabinopyranosyl)-4-(4-chlorobenzylideneamino)-5-(pyridin-3-yl)-2,4-dihydro-[1,2,4]-triazole-3-thione (6d). Yield 827 mg (40% A); 110 mg (87%, B); colorless crystals, m.p. 94–96°C ($R_f = 0.54$). IR: 3067, 3025, 2928, 2858, 1751, 1597, 1489, 1419, 1369, 1342, 1323, 1246, 1219, 1119, 1092, 1061, 1018, 960, 933, 895, 876, 845, 825, 741, 706, 667, 598, 563, 517, 420; ^{1}H NMR ($CDCl_3$) δ 1.94, 2.03, 2.20 (3s, 9H, CH_3CO), 3.98 (d, 1H, $J_{H\text{-}5'\text{-}H\text{-}5''} = 13.5$ Hz, H-5′), 4.19 (d, 1H, $J_{H\text{-}5''\text{-}H\text{-}5'} = 13.5$ Hz, H-5″), 5.29 (dd, 1H, $J_{H\text{-}3'\text{-}H\text{-}4'} = 3.3$ Hz, $J_{H\text{-}3'\text{-}H\text{-}2'} = 9.6$ Hz, H-3′), 5.42 (d, 1H, $J_{H\text{-}4'\text{-}H\text{-}3'} = 3.3$ Hz, H-4′), 6.01 (t, 1H, $J_{H\text{-}2'\text{-}H\text{-}1'} = 9.0$ Hz, $J_{H\text{-}2'\text{-}H\text{-}3'} = 9.6$ Hz, H-2′), 6.19 (d, 1H, $J_{H\text{-}1'\text{-}H\text{-}2'} = 9.0$ Hz, H-1′), 7.42 (dd, 1H, $J_{H\text{-}5\text{ pyrid.}\text{-}H\text{-}6\text{ pyrid.}} = 4.8$ Hz, $J_{H\text{-}5\text{ pyrid.}\text{-}H\text{-}4\text{ pyrid.}} = 8.1$ Hz, H-5 pyrid.), 7.44 (d, 2H, $J = 8.4$ Hz, ArH), 7.77 (d, 2H, $J = 8.4$ Hz, ArH), 8.28 (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.), 8.73 (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.), 9.20 (d, 1H, $J_{H\text{-}2\text{ pyrid.}\text{-}H\text{-}4\text{ pyrid.}} = 2.1$ Hz, H-2 pyrid.), 10.28 (s, 1H, CH = N). Anal.

Calcd for $C_{25}H_{24}ClN_5O_7S$ (574): C, 52.31; H, 4.21; N, 12.20; S, 5.59. Found: C, 52.23; H, 4.17; N, 12.18; S, 5.44.

3-(2,3,4-Tri-*O*-acetyl-α-L-arabinopyranosyl-1-thio)-4-benzylideneamino-5-(pyridin-3-yl)-4*H*-[1,2,4]-triazole (7a). Yield 543 mg (28% A); 98 mg (82%, B); pale crystals, m.p. 84–86°C ($R_f = 0.06$). IR: 3074, 3022, 2935, 2743, 1747, 1612, 1574, 1435, 1373, 1219, 1057, 968, 922, 876, 814, 756, 698, 609, 478; ^{1}H NMR ($CDCl_3$) δ 1.98, 2.00, 2.02 (3s, 9H, CH_3CO), 3.70 (dd, 1H, $J_{H\text{-}5'\text{-}H\text{-}4'} = 1.8$ Hz, $J_{H\text{-}5'\text{-}H\text{-}5''} = 12.6$ Hz, H-5′), 4.02 (dd, 1H, $J_{H\text{-}5''\text{-}H\text{-}4'} = 4.6$ Hz, $J_{H\text{-}5''\text{-}H\text{-}5'} = 12.6$ Hz, H-5″), 5.12 (dd, 1H, $J_{H\text{-}3'\text{-}H\text{-}4'} = 3.3$ Hz, $J_{H\text{-}3'\text{-}H\text{-}2'} = 7.8$ Hz, H-3′), 5.23 (dd, 1H, $J_{H\text{-}4'\text{-}H\text{-}3'} = 3.3$ Hz, $J_{H\text{-}4'\text{-}H\text{-}5''} = 4.6$ Hz, H-4′), 5.25 (t, 1H, $J_{H\text{-}2'\text{-}H\text{-}1'} = 7.2$ Hz, $J_{H\text{-}2'\text{-}H\text{-}3'} = 7.8$ Hz, H-2′), 5.55 (d, 1H, $J_{H\text{-}1'\text{-}H\text{-}2'} = 7.2$ Hz, H-1′), 7.34 (dd, 1H, $J_{H\text{-}5\text{ pyrid.}\text{-}H\text{-}6\text{ pyrid.}} = 4.8$ Hz, $J_{H\text{-}5\text{ pyrid.}\text{-}H\text{-}4\text{ pyrid.}} = 8.1$ Hz, H-5 pyrid.), 7.47 (dt, 2H, $J = 1.0$, 7.7 Hz, ArH), 7.56 (dt, 1H, $J = 1.0$, 7.7 Hz, ArH), 7.82 (d, 2H, $J = 7.7$ Hz, ArH), 8.25 (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.), 8.60 (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.), 8.64 (s, 1H, CH = N), 9.14 (d, 1H, $J_{H\text{-}2\text{ pyrid.}\text{-}H\text{-}4\text{ pyrid.}} = 2.1$ Hz, H-2 pyrid.). Anal. Calcd for $C_{25}H_{25}N_5O_7S$ (539.6): C, 55.65; H, 4.67; N, 12.98; S, 5.94. Found: C, 55.52; H, 4.63; N, 13.15; S, 5.77.

3-(2,3,4-Tri-*O*-acetyl-α-L-arabinopyranosyl-1-thio)-4-(4-methylbenzylideneamino)-5-(pyridin-3-yl)-4*H*-[1,2,4]-triazole (7b). Yield 876 mg (44%, A); 98 mg (80%, B); pale crystals, m.p. 154–156°C ($R_f = 0.05$). IR: 3030, 2943, 2870, 2716, 1747, 1601, 1566, 1508, 1427, 1369, 1246, 1223, 1057, 1014, 960, 933, 906, 879, 814, 752, 702, 663, 621, 594, 513, 474, 447; ^{1}H NMR ($CDCl_3$) δ 1.97, 1.98, 2.01 (3s, 9H, CH_3CO), 2.37 (s, 3H, CH_3), 3.68 (dd, 1H, $J_{H\text{-}5'\text{-}H\text{-}4'} = 2.4$ Hz, $J_{H\text{-}5'\text{-}H\text{-}5''} = 12.6$ Hz, H-5′), 4.00 (dd, 1H, $J_{H\text{-}5''\text{-}H\text{-}4'} = 4.8$ Hz, $J_{H\text{-}5''\text{-}H\text{-}5'} = 12.6$ Hz, H-5″), 5.10 (dd, 1H, $J_{H\text{-}3'\text{-}H\text{-}4'} = 3.3$ Hz, $J_{H\text{-}3'\text{-}H\text{-}2'} = 7.8$ Hz, H-3′), 5.21 (dd, 1H, $J_{H\text{-}4'\text{-}H\text{-}3'} = 3.3$ Hz, $J_{H\text{-}4'\text{-}H\text{-}5''} = 4.8$ Hz, H-4′), 5.22 (t, 1H, $J_{H\text{-}2'\text{-}H\text{-}1'} = 7.2$ Hz, $J_{H\text{-}2'\text{-}H\text{-}3'} = 7.8$ Hz, H-2′), 5.52 (d, 1H, $J_{H\text{-}1'\text{-}H\text{-}2'} = 7.2$ Hz, H-1′), 7.25 (d, 2H, $J = 8.1$ Hz, ArH), 7.31 (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.), 7.70 (d, 2H, $J = 8.1$ 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.), 8.56 (s, 1H, CH = N), 8.57 (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.), 9.12 (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 $C_{26}H_{27}N_5O_7S$ (553.6): C, 56.41; H, 4.92; N, 12.65; S, 5.79. Found: C, 56.37; H, 5.02; N, 12.62; S, 5.69.

3-(2,3,4-Tri-*O*-acetyl-α-L-arabinopyranosyl-1-thio)-4-(4-methoxybenzylideneamino)-5-(pyridin-3-yl)-4*H*-[1,2,4]-triazole (7c). Yield 737 mg (36%, A); 99 mg (79%, B); pale crystals, m.p. 86–88°C ($R_f = 0.08$). IR: 3092, 3035, 2935, 2843, 2770, 1747, 1601, 1566, 1516, 1431, 1373, 1311, 1254, 1219, 1169, 1057, 1022, 968, 914, 879, 837, 814, 752, 706, 598, 528, 494, 424; ^{1}H NMR ($CDCl_3$) δ 1.95, 1.96, 1.99 (3s, 9H, CH_3CO), 3.67 (dd, 1H,

$J_{H\text{-}5'\text{-}H\text{-}4'} = 2.4$ Hz, $J_{H\text{-}5'\text{-}H\text{-}5''} = 12.6$ Hz, H-5′), 3.81 (s, 3 H, OCH_3), 4.00 (dd, 1H, $J_{H\text{-}5''\text{-}H\text{-}4'} = 4.8$ Hz, $J_{H\text{-}5''\text{-}H\text{-}5'} = 12.6$ Hz, H-5″), 5.09 (dd, 1H, $J_{H\text{-}3'\text{-}H\text{-}4'} = 3.3$ Hz, $J_{H\text{-}3'\text{-}H\text{-}2'} = 8.1$ Hz, H-3′), 5.20 (dd, 1H, $J_{H\text{-}4'\text{-}H\text{-}3'} = 3.3$ Hz, $J_{H\text{-}4'\text{-}H\text{-}5''} = 4.8$ Hz, H-4′), 5.21 (t, 1H, $J_{H\text{-}2'\text{-}H\text{-}1'} = 7.2$ Hz, $J_{H\text{-}2'\text{-}H\text{-}3'} = 8.1$ Hz, H-2′), 5.51 (d, 1H, $J_{H\text{-}1'\text{-}H\text{-}2'} = 7.2$ Hz, H-1′), 6.93 (d, 2H, $J = 8.7$ Hz, ArH), 7.29 (dd, 1H, $J_{H\text{-}5\text{ pyrid.}\text{-}H\text{-}6\text{ pyrid.}} = 4.8$ Hz, $J_{H\text{-}5\text{ pyrid.}\text{-}H\text{-}4\text{ pyrid.}} = 8.1$ Hz, H-5 pyrid.), 7.75 (d, 2H, $J = 8.7$ Hz, ArH), 8.21 (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.), 8.47 (s, 1H, CH = N), 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.), 9.11 (d, 1H, $J_{H\text{-}2\text{ pyrid.}\text{-}H\text{-}4\text{ pyrid.}} = 2.1$ Hz, H-2 pyrid.). Anal. Calcd for $C_{26}H_{27}N_5O_8S$ (569.6): C, 54.83; H, 4.78; N, 12.30; S, 5.63. Found: C, 54.92; H, 4.68; N, 12.44; S, 5.55.

3-(2,3,4-Tri-*O*-acetyl-α-L-arabinopyranosyl-1-thio)-4-(4-chlorobenzyidene-amino)-5-(pyridin-3-yl)-4*H*-[1,2,4]-triazole (7d). Yield 372 mg (18% A); 112 mg (88%, B); yellow crystals, m.p. 230–232°C ($R_f = 0.06$). IR: 3075, 2936, 2873, 1743, 1593, 1554, 1516, 1481, 1423, 1362, 1223, 1090, 1007, 964, 937, 876, 818, 775, 733, 694, 633, 517, 471; ^{1}H NMR ($CDCl_3$) δ 2.04, 2.08, 2.09 (3s, 9H, CH_3CO), 3.74 (dd, 1H, $J_{H\text{-}5'\text{-}H\text{-}4'} = 2.4$ Hz, $J_{H\text{-}5'\text{-}H\text{-}5''} = 12.6$ Hz, H-5′), 4.08 (dd, 1H, $J_{H\text{-}5''\text{-}H\text{-}4'} = 4.8$ Hz, $J_{H\text{-}5''\text{-}H\text{-}5'} = 12.6$ Hz, H-5″), 5.17 (dd, 1H, $J_{H\text{-}3'\text{-}H\text{-}4'} = 3.3$ Hz, $J_{H\text{-}3'\text{-}H\text{-}2'} = 7.8$ Hz, H-3′), 5.29 (dd, 1H, $J_{H\text{-}4'\text{-}H\text{-}3'} = 3.3$ Hz, $J_{H\text{-}4'\text{-}H\text{-}5''} = 4.8$ Hz, H-4′), 5.30 (t, 1H, $J_{H\text{-}2'\text{-}H\text{-}1'} = 7.2$ Hz, $J_{H\text{-}2'\text{-}H\text{-}3'} = 7.8$ Hz, H-2′), 5.60 (d, 1H, $J_{H\text{-}1'\text{-}H\text{-}2'} = 7.2$ Hz, H-1′), 7.41 (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.), 7.50 (td, 2H, $J = 1.9$, 8.7Hz, ArH), 7.81 (td, 2H, $J = 1.9$, 8.7 Hz, ArH), 8.30 (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.), 8.65 (s, 1H, CH = N), 8.67 (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.), 9.18 (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 $C_{25}H_{24}ClN_5O_7S$ (574): C, 52.31; H, 4.21; N, 12.20; S, 5.59. Found: C, 52.12; H, 4.24; N, 12.29; S, 5.65.

Synthesis of Compounds 9 and 10

General Procedures

A) To a cold stirred solution (at 0°C) of each of compounds **4** and **5** (2.37 g, 5.25 mmol) in acetic acid (30 mL) was added dropwise, while stirring, a solution of sodium nitrite (3 g in 5 mL water) over a period of 1 hour. The reaction mixture was kept in the refrigerator overnight, dried under reduced pressure, diluted with dichloromethane (150 mL) and washed with water (3 × 150 mL). The organic layer was dried (Na_2SO_4), filtered, evaporated under reduced pressure, and the formed residue was recrystallized from dichloromethane/petroleum ether (b.p. 40–60°C). R_f values of compounds **9** and **10** were determined on TLC aluminum sheets

using ethyl acetate/petroleum ether (b.p. 40–60°C) [60:40, v/v] as a developing system.

B) Each of compounds **6a–d** (1 mmol) was heated at 220°C in an oil bath under vacuum in a micro distillation system for 15 minutes. After cooling, the remaining solid was recrystallized from dichloromethane/petroleum ether (b.p. 40–60°C). The expected nitriles were collected in the distillates and identified by ^{1}H NMR.

2-(2,3,4-Tri-*O*-acetyl-α-L-arabinopyranosyl)-5-(pyridin-3-yl)-2,4-dihydro-[1,2,4]-triazole-3-thione (9). Yield 1.92 g (84%, A); 401 mg (92%, B using Compound **7a**); 380 mg (87%, B using Compound **7b**); 406 mg (93%, B using Compound **7c**); 393 mg (90%, B using Compound **7d**); Orange yellow crystals, m.p. 62–64°C ($R_f = 0.33$). IR: 3474, 3124, 2988, 2937, 1751, 1638, 1603, 1578, 1519, 1486, 1447, 1412, 1373, 1340, 1224, 1161, 1116, 1092, 1063, 962, 936, 918, 873, 821, 749, 709, 656, 622, 600, 558, 495; ^{1}H NMR ($CDCl_3$) δ 1.94, 1.99, 2.12 (3s, 9H, CH_3CO), 3.90 (dd, 1H, $J_{H\text{-}5'\text{-}H\text{-}4'} = 0.9$ Hz, $J_{H\text{-}5'\text{-}H\text{-}5''} = 13.5$ Hz, H-5′), 4.12 (dd, 1H, $J_{H\text{-}5''\text{-}H\text{-}4'} = 1.8$ Hz, $J_{H\text{-}5''\text{-}H\text{-}5'} = 13.5$ Hz, H-5″), 5.19 (dd, 1H, $J_{H\text{-}3'\text{-}H\text{-}4'} = 3.6$ Hz, $J_{H\text{-}3'\text{-}H\text{-}2'} = 10.0$ Hz, H-3′), 5.34 (dd, 1H, $J_{H\text{-}4'\text{-}H\text{-}3'} = 3.6$ Hz, $J_{H\text{-}4'\text{-}H\text{-}5''} = 1.8$ Hz, H-4′), 5.50 (d, 1H, $J_{H\text{-}1'\text{-}H\text{-}2'} = 9.0$ Hz, H-1′), 5.73 (t, 1H, $J_{H\text{-}2'\text{-}H\text{-}1'} = 9.0$ Hz, $J_{H\text{-}2'\text{-}H\text{-}3'} = 10.0$ Hz, H-2′), 7.31 (dd, 1H, $J_{H\text{-}5\text{ pyrid.}\text{-}H\text{-}6\text{ pyrid.}} = 4.8$ Hz, $J_{H\text{-}5\text{ pyrid.}\text{-}H\text{-}4\text{ pyrid.}} = 8.1$ Hz, H-5 pyrid.), 8.30 (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.), 8.37 (s, 1H, D_2O exchangeable NH), 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.), 9.24 (d, 1H, $J_{H\text{-}2\text{ pyrid.}\text{-}H\text{-}4\text{ pyrid.}} = 2.1$ Hz, H-2 pyrid.). Anal. Calcd for $C_{18}H_{20}N_4O_7S$ (436.4): C, 49.54; H, 4.62; N, 12.84; S, 7.35. Found: C, 49.41; H, 4.58; N, 13.00; S, 7.24.

3-(2,3,4-Tri-*O*-acetyl-α-L-arabinopyranosyl-1-thio)-5-(pyridin-3-yl)-4*H*-[1,2,4]-triazole (10). Yield 1.65 g (72%, A); brownish yellow crystals, m.p. 118–120°C ($R_f = 0.06$). IR: 3337, 2928, 1747, 1631, 1577, 1436, 1372, 1221, 1158, 1060, 935, 817, 747, 708, 654, 623, 602, 493; ^{1}H NMR ($CDCl_3$) δ 2.07, 2.11, 2.14 (3s, 9H, CH_3CO), 3.70 (dd, 1H, $J_{H\text{-}5'\text{-}H\text{-}4'} = 1.8$ Hz, $J_{H\text{-}5'\text{-}H\text{-}5''} = 12.9$ Hz, H-5′), 4.05 (dd, 1H, $J_{H\text{-}5''\text{-}H\text{-}4'} = 3.3$ Hz, $J_{H\text{-}5''\text{-}H\text{-}5'} = 12.9$ Hz, H-5″), 5.09 (dd, 1H, $J_{H\text{-}3'\text{-}H\text{-}4'} = 3.3$ Hz, $J_{H\text{-}3'\text{-}H\text{-}2'} = 8.7$ Hz, H-3′), 5.27 (dd, 1H, $J_{H\text{-}4'\text{-}H\text{-}3'} = 3.3$ Hz, $J_{H\text{-}4'\text{-}H\text{-}5''} = 4.8$ Hz, H-4′), 5.29 (t, 1H, $J_{H\text{-}2'\text{-}H\text{-}3'} = 8.4$ Hz, $J_{H\text{-}2'\text{-}H\text{-}1'} = 8.7$ Hz, H-2′), 5.33 (d, 1H, $J_{H\text{-}1'\text{-}H\text{-}2'} = 8.7$ Hz, H-1′), 7.40 (dd, 1H, $J_{H\text{-}5\text{ pyrid.}\text{-}H\text{-}6\text{ pyrid.}} = 4.8$ Hz, $J_{H\text{-}5\text{ pyrid.}\text{-}H\text{-}4\text{ pyrid.}} = 8.1$ Hz, H-5 pyrid.), 8.33 (s, 1H, D_2O exchangeable NH), 8.43 (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.), 8.63 (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.), 9.30 (d, 1H, $J_{H\text{-}2\text{ pyrid.}\text{-}H\text{-}4\text{ pyrid.}} = 2.1$ Hz, H-2 pyrid.). Anal. Calcd for $C_{18}H_{20}N_4O_7S$ (436.4): C, 49.54; H, 4.62; N, 12.84; S, 7.35. Found: C, 49.61; H, 4.66; N, 12.74; S, 7.48.

Deacetylation of Compounds 4, 5, 6a, and 7a

General Procedures

A) Deacetylation of compounds **4** and **5**: Dry gaseous ammonia was passed through a solution of each of compounds **4** and **5** (1 mmol) in dry methanol (10 mL) for about 1 hour with cooling and stirring then the reaction mixture was stirred at room temperature over night. 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 and column chromatographed. Compound **11** was eluted using 25% methanol/chloroform →35% methanol/chloroform), and recrystallized from methanol. Compound **12** was eluted using 40% methanol/chloroform →60% methanol/chloroform and recrystallized from methanol. R_f values of compounds **11** and **12** were determined on TLC aluminum sheets using chloroform/methanol (80:20, v/v) as a developing system.

B) Deacetylation of compounds **6a** and **7a**: using the same general procedure A, deacetylation of compounds **6a** and **7a** (1 mmol) gave a mixture of compounds **11**, **13**, and **12**, **14**, respectively. Compounds **11** and **13** were eluted first with 25% methanol/chloroform →35% methanol/chloroform followed by compounds **12** and **14** with 40% methanol/chloroform →60% methanol/chloroform. Compounds **11–14** were recrystallized from methanol and their R_f values were determined on TLC aluminum sheets using chloroform/methanol (80:20, v/v) as a developing system.

2-α-L-Arabinopyranosyl-4-amino-5-(pyridin-3-yl)-2,4-dihydro-[1,2,4]-triazole-3-thione (11). Yield 299 mg (92% A); 169 mg (52%, B); colorless crystals, m.p. 140–142°C (R_f = 0.47). IR: 3424 (br), 2922, 2848, 1638, 1543, 1428, 1366, 1078, 887, 847, 703, 562, 412; ^{1}H NMR (DMSO-d_6) δ 3.42–4.26 (m, 3H, H-2′, H-3′, H-4′), 3.66 (d, 1H, $J_{\text{H-5′-H-5″}}$ = 12.9 Hz, H-5′), 3.81 (dd, 1H, $J_{\text{H-5″-H-4′}}$ = 1.2 Hz, $J_{\text{H-5″-H-5′}}$ = 12.9 Hz, H-5″), 4.76 (br s, 1H, D_2O exchangeable OH), 4.91 (br s, 1H, D_2O exchangeable OH), 5.14 (br s, 1H, D_2O exchangeable OH), 5.53 (d, 1H, $J_{\text{H-1′-H-2′}}$ = 9.0 Hz, H-1′), 5.91 (s, 2H, D_2O exchangeable NH_2), 7.60 (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.), 8.39 (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.), 8.74 (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.), 9.16 (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 $C_{12}H_{15}N_5O_4S$ (325.3): C, 44.30; H, 4.65; N, 21.53; S, 9.86. Found: C, 44.38; H, 4.72; N, 21.74; S, 9.79.

3-(α-L-Arabinopyranosyl-1-thio)-4-amino-5-(pyridin-3-yl)-4*H*-[1,2,4]-triazole (12). Yield 244 mg (75%, A); 146 mg (45%, B); pale crystals, m.p. 136–138°C (R_f = 0.08). ^{1}H NMR (DMSO-d_6) δ 3.40–4.22 (m, 5H, H-2′, H-3′, H-4′, H-5′, H-5″), 4.75 (br s, 1H, D_2O exchangeable OH), 4.90 (br

s, 1H, D_2O exchangeable OH), 5.13 (br s, 1H, D_2O exchangeable OH), 5.19 (d, 1H, $J_{H\text{-}1'\text{-}H\text{-}2'} = 9.0$ Hz, H-1′), 5.77 (s, 2H, D_2O exchangeable NH_2), 7.59 (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.), 8.37 (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.), 8.72 (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.). Anal. Calcd for $C_{12}H_{15}N_5O_4S$ (325.3): C, 44.30; H, 4.65; N, 21.53; S, 9.86. Found: C, 44.29; H, 4.54; N, 21.66; S, 9.74.

2-α-L-Arabinopyranosyl-4-benzylideneamino-5-(pyridin-3-yl)-2,4-dihydro-[1,2,4]-triazole-3-thione (13). Yield 157 mg (38%, B); colorless crystals, m.p. 148–150°C ($R_f = 0.46$). ^{1}H NMR (DMSO-d_6) δ 4.0–3.0 (m, 5H, H-2′, H-3′, H-4′, H-5′, H-5″), 4.22 (d, 1H, $J = 6.0$ Hz, D_2O exchangeable OH), 4.56 (d, 1H, $J = 6.0$ Hz, D_2O exchangeable OH), 5.07 (d, 1H, $J = 6.3$ Hz, D_2O exchangeable OH), 5.42 (d, 1H, $J_{H\text{-}1'\text{-}H\text{-}2'} = 7.5$ Hz, H-1′), 7.60 (m, 4H, ArH, H-5 pyrid.), 8.05 (t, 2H, $J = 8.1$ Hz, ArH), 8.46 (s, 1H, CH = N), 8.39 (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.), 8.73 (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.), 9.21 (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.). Anal. Calcd for $C_{19}H_{19}N_5O_4S$ (413.5): C, 55.20; H, 4.63; N, 16.94; S, 7.76. Found: C, 55.18; H, 4.64; N, 16.82; S, 7.81.

3-α-L-Arabinopyranosylthio-4-benzylideneamino-5-(pyridin-3-yl)-4*H*-[1,2,4]-triazole (14). Yield 124 mg (30%, B); pale crystals, m.p. 141–143°C ($R_f = 0.06$). ^{1}H NMR (DMSO-d_6) δ 4.0–3.0 (m, 5H, H-2′, H-3′, H-4′, H-5′, H-5″), 4.22 (d, 1H, $J = 6.0$ Hz, D_2O exchangeable OH), 4.56 (d, 1H, $J = 6.0$ Hz, D_2O exchangeable OH), 5.07 (d, 1H, $J = 6.3$ Hz, D_2O exchangeable OH), 5.37 (d, 1H, $J_{H\text{-}1'\text{-}H\text{-}2'} = 7.8$ Hz, H-1′), 7.55 (m, 4 H, ArH, H-5 pyrid.), 8.05 (t, 2H, $J = 8.1$ Hz, ArH), 8.36 (s, 1H, CH = N), 8.37 (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.), 8.71 (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 (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.). Anal. Calcd for $C_{19}H_{19}N_5O_4S$ (413.5): C, 55.20; H, 4.63; N, 16.94; S, 7.76. Found: C, 55.24; H, 4.61; N, 16.99; S, 7.69.

REFERENCES

1. Furman, P.A.; Fyfe, J.A.; St. Clair, M.H.; Weinhold, K.; Rideout, J.L.; Freeman, G.A.; Lehrman, S. N.; Bolognesi, D.P.; Broder, S.; Mitsuya, H.; Barry, D.W. Phosphorylation of 3′-azido-3′-deoxythymidine and selective interaction of the 5′-triphosphate with human immunodeficiency virus reverse transciptase. *Proc. Natl. Acad. Sci. USA* **1986**, 83, 8333–8337.
2. Yarchoan, R.; Perno, C.F.; Thomas, R.V.; Klecker, R.W.; Allain, J.P.; Wills, R.J.; McAtee, N.; Leuther, M.; Collins, J.M.; Broder, S.; Fischl, M.A.; Dubinsky, R.; McNeeLy, M.C.; Mitsuya, H.; Lawley, T.J.; Safai, B.; Myers, C.E. Phase 1 studies of 2′,3′-dideoxycytidine in severe human immunodeficiency virus infection as a single agent and alternating with zidovudine (AZT). *Lancet* **1988**, 1, 76–81.

3. Yarchoan, R.; Mitsuya, H.; Thomas, R.V.; Pluda, J.M.; Hartman, N.R.; Perno, C.F.; Marczyk, K.S.; Allain, J.P.; Johns, D.G.; Broder, S. In vivo activity against HIV and favorable toxicity profile of 2′,3′-dideoxyinosine. *Science* **1989**, 245, 412–415.
4. Lin, T.S.; Schinazi, R.F.; Prusoff, W.H. Potent and selective in vitro activity of 3′-deoxythymidin-2′-ene (3′-deoxy-2′,3′-didehydrothymidine) against human immunodeficiency virus. *Biochem. Pharmacol.* **1987**, 36, 2713–2718.
5. Schinazi, R.F.; Chu, C.K.; Peck, A.; McMillan, A.; Mathis, R.; Cannon, D.; Jeong, L.S.; Beach, J.W.; Choi, W.B.; Yeola, S.; Liotta, D.C. Activities of the four optical isomers of 2′,3′-dideoxy-3′-thiacytidine (BCH-189) against human immunodeficiency virus type 1 in human lymphocytes. *Antimicrob. Agents Chemother.* **1992**, 36, 672–676.
6. Daluge, S.M.; Good, S.S.; Faletto, M.B.; Miller, W.H.; StClair, M.H.; Boone, L.R.; Tisdale, M.; Parry, N.R.; Reardon, J.E.; Dornsife, R.E.; Averett, D.R.; Krenitsky, T.A. 1592U89, a novel carbocyclic nucleoside analog with potent, selective anti-human immunodeficiency virus activity. *Antimicrob. Agents Chemother.* **1997**, 41, 1082–1093.
7. Arimilli, M.N.; Kim, C.U.; Dougherty, J.; Mulato, A.; Oliyai, R.; Shaw, J.P.; Cundy, K.C.; Bischofberger, N. Synthesis, in vitro biological evaluation, and oral bioavailability of 9-[2-(phosphonomethoxy)propyl]adenine (PMPA) prodrugs. *Antiviral. Chem. Chemother.* **1997**, 8, 557–564.
8. Lin, T.S.; Luo, M.Z.; Liu, M.C.; Pai, S.B.; Dutschman, G.E.; Cheng, Y.C. Synthesis and biological evaluation of 2′,3′-dideoxy-L-pyrimidine nucleosides as potential antiviral agents against human immunodeficiency virus (HIV) and hepatitis B virus (HBV). *J. Med. Chem.* **1994**, 37, 798–803.
9. Chu, C,K.; Ma, T.W.; Shanmuganthan, K.; Wang, C.G.; Xiang, Y.J.; Pai, S.B.; Yao, G.Q.; Sommadossi, J.P.; Cheng, Y.C. Use of 2′-fluoro-5-methyl-β-L-araninofuranosyl uracil as a novel antiviral agent for hepatitis B virus and Epstein-Barr virus. *Antimicrob. Agents Chemother.* **1995**, 39, 979–981.
10. Chang, C.N.; Doong, S.L.; Zhou, J.H.; Beach, J.W.; Jeong, L.S.; Chu, C.K.; Tsai, C.H.; Cheng, Y.C. Deoxycytidine deaminase–resistant stereoisomer is the active form of (±)-2′,3′-dideoxy-3′-thiacytidine in the inhibitation of hepatitis B virus replication. *J. Biol. Chem.* **1992**, 267, 13938–13942.
11. Belleau, B.; Dixit, D.; Ngueyn-Ba, N.; Karus, J.L. Purinyl- and pyrimidinyl-1,3-dioxolanes as anti-retrovirals. *Eur. Pat.* 337, 713, Oct 18, 1989; *Chem. Abstr.* **1990**, 112, 198359 w.
12. Furman, P.A.; Davis, M.; Liotta, D.C.; Paff, M.; Frick, L.W.; Nelson, D.J.; Dornsife, R.E.; Wurster, J.A.; Wilson, L.J.; Fyfe, J.A.; Tuttle, J.V.; Miller, W.H.; Condreay, L.; Avereet, D.R.; Schinazi R.F.; Painter, G.R. The antihepatitis B virus activities, cytotoxicities, and anabolic profiles of the (−) and (+) enantiomers of cis-5-fluoro-1-[2-(hydroxymethyl)-1,3-oxothiolan-5-yl]-cytosine. *Antimicrob. Agents Chemother.* **1992**, 36, 2686–2692.
13. Schinazi, R.F.; Gosselin, G.; Faraj. A.; Korba, B.E.; Liotta, D.C.; Chu, C.K.; Mathe, C.; Imbach, J.; Sommadossi, J. Pure nucleoside enantiomers of β-2′,3′-dideoxycytidine analogs are selective inhibitors of hepatitis B virus in vitro. *Antimicrob. Agents Chemother.* **1994**, 38, 2172–2174.
14. Coates, J.A.V.; Cammack, N.; Jenkinson, H.J.; Jowett, A.J.; Jowett, M.I.; Pearson, B.A.; Penn, C.R.; Rouse, P. L.; Viner, K.C.; Cameron, J.M. (−)-2′-Deoxy-3′-thiacytidine is a potent, highly selective inhibitor of human immunodeficiency virus type 1 and type 2 replication in vitro. *Antimicrob. Agents Chemother.* **1992**, 36, 733–739.
15. Doong, S.L.; Tsai, C.H.; Schinazi R.F.; Liotta, D.C.; Cheng, Y.C. Inhibition of the replication of hepatitis B virus in vitro by 2′,3′-dideoxy-3′-thiacytidine and related analog. *Proc. Natl. Acad. Sci. USA* **1991**, 88, 8495–8499.
16. Chang, C.N.; Skalski, V.; Zhou, J.H.; Cheng, Y.C. Biochemical pharmacology of the (+) and (−)-2′,3′-dideoxy-3′-thiacytidine as antihepatitis B virus agents. *J. Biol. Chem.* **1992**, 267, 22414–22420.
17. Grove, K.L.; Guo, X.; Liu, S.H.; Gao, Z.; Chu, C.K.; Cheng, Y.C. Anticancer activity of β-L-dioxolanecytidine, a novel nucleoside analog with the unnatural L configuration. *Cancer Res.* **1995**, 55, 3008–3011.
18. Pai, S.B.; Liu, S. H.; Zhu, Y. L.; Chu, C. K.; Cheng, Y. C. Inhibition of hepatitis B virus by a novel L-nucleoside, 2′-fluoro-5-methyl-β-L-arabinofuranosyluracil. *Antimicrob. Agents Chemother.* **1996**, 40, 380–386.
19. Pelicano, H.; Pierra, C.; Eriksson, S.; Gosselin, G.; Imbach, J. L.; Maury, G. Enzymatic properties of the unnatural β-L-enantiomers of 2′,3′-dideoxyadenosine and 2′,3′-didehydro-2′,3′-dideoxyadenosine. *J. Med. Chem*, **1997**, 40, 3969–3973.
20. Mukaiyama, T.; Hashimoto, Y.; Hayashi, Y.; Shoda, S. Stereoselective synthesis of α-ribonucleosides from 1-hydroxy sugars by using 2-fluoropyridinium tosylate. *Chem. Lett.* **1984**, 4, 557–560.

21. Klein, R.S.; Ohrui, H.; Fox, J.J. Synthesis of 2,3-*O*-isopropylidene-5-*O*-trityl-β-D-ribofuranosyl chloride. *J.Carbohydr. Nucleosides Nucleotides* **1974**, 1, 265–269.
22. Haga, M.; Ness, R.K.; Fletcher, H.G. Syntheses with partially benzylated sugars. XII. 3,5-Di-*O*-benzyl-beta-D-ribofuranose and its use as an intermediate in the synthesis of partially substituted ribonucleosides. *J. Org. Chem.* **1968**, 33, 1810–1815.
23. Stevens, J.D.; Ness, R.K.; Fletcher, H.G. Syntheses with partially benzylated sugars. XI. Studies on the synthesis of anomeric 5,6-dimethyl-1-D-ribofuranosylbenzimidazoles (ribazoles). Comparison of the condensation of 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl bromide and 2,3,5-tri-*O*-benzoyl-D-ribofuranosyl chloride with 5,6-dimethylbenzimidazole. *J. Org. Chem.* **1968**, 33, 1806–1810.
24. Khalil, N.S.A.M. Synthesis of novel α-L-arabinopyranosides of β-lactams with potential antimicrobial activity. *Nucleosides Nucleotides Nucleic Acids* **2005**, 24, 1277–1287.
25. Mansour, A.K.; Eid, M.M.; Khalil, N.S.A.M. Synthesis of some new 2-α-L-arabinopyranosyl-1,2,4-triazines as potential antitumor chemotherapeutics. *Nucleosides Nucleotides Nucleic Acids* **2003**, 22, 1805–1823.
26. Jones, D.H.; Slack, R.; Squires, S.; Wooldridge, K.R.H. Antiviral chemotherapy. I. The activity of pyridine and quinoline derivatives against neurovaccina in mice. *J. Med. Chem.* **1965**, 8, 676–680.
27. Goswami, B.N.; Kataky, J.C.S.; Baruah, J.N. Synthesis and antibacterial activity of 1-(2,4-dichlorobenzoyl)-4-substituted thiosemicarbazides, 1,2,4-triazoles and their methyl derivatives. *J. Heterocycl. Chem.* **1984**, 21, 1225–1229.
28. Holla, B.S.; Kalluraya, B.; Sridhar, K.R. Synthesis of 4-(5-nitro-2-furfurylidene)amino-3-mercapto-5-(substituted)-1,2,4-triazoles as possible antibacterial agents. *Curr. Sci.* **1987**, 56, 236–238.
29. Holla, B.S.; Poojary, K.N.; Kalluraya, B.; Gowda, P.V. Synthesis, characterisation and antifungal activity of some *N*-bridged heterocycles derived from 3-(3-bromo-4-methoxyphenyl)-4-amino-5-mercapto-1,2,4-triazole. *Farmaco* **1996**, 51, 793–799.
30. Abdou, N.A.; Amin, F.M. Synthesis and biological activity of certain 5-mercapto-3-(3-pyridyl)-4*H*-1,2,4-triazole derivatives. *Mansoura J. Pharm. Sci.* **1990**, 6, 25–29.
31. Mishra, R.K.; Tewari, R.K.; Srivastava, S.K.; Bahel, S.C. Synthesis and antifungal activity of some 1,4-disubstitued-thiosemicarbazides, 2,5-disubstituted-1,3,4-thiadiazoles and 3,4-disubstituted-5-mercapto-1,2,4-triazoles. *J. Indian Chem. Soc.* **1991**, 68, 110–112.
32. Unangst, P.C.; Shurum, G.P.; Connor, D.T.; Dyer, R.D.; Schrier, D.J. Novel 1,2,4-oxadiazoles and 1,2,4-thiadiazoles as dual 5-lipoxygenase and cyclooxygenase inhibitors. *J. Med. Chem.* **1992**, 35, 3691–3698.
33. Mullican, M.D.; Wilson, M.W.; Connor, D.T.; Kostlan, C.R.; Schrier, D.J.; Dyer, R.D. Design of 5-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1,3,4-thiadiazoles, -1,3,4-oxadiazoles, and -1,2,4-triazoles as orally active, nonulcerogenic antiinflammatory agents. *J. Med. Chem.* **1993**, 36, 1090–1099.
34. Sugden, J.K.; Yoloye, T.O. Medicinal applications of indole derivatives. *Pharm. Acta Helv.* **1978**, 53, 65–92.
35. Shams El-Dine, Sh. A.; Hazzaa, A.A.B. Synthesis of compounds with potential fungicidal activity. *Pharmazie* **1974**, 29, 761–763.
36. Misato, T.; Ko, K.; Honma, Y.; Konno, K.; Taniyama, E. 1,3,4-thiadiazole derivatives as fungicides. Jpn. Kokai Tokkyo Koho 77 25,028, 1977. *Chem. Abstr.* **1977**, 87, 147054 a.
37. Cansiz, A.; Servi, S.; Koparir, M.; Altintas, M.; Digrak, M. Synthesis and biological activities of some Mannich bases of 5-(2-furyl)-1,2,4-triazole-3-thiones. *J. Chem. Soc. Pak.* **2001**, 23, 237–240.
38. Stillings, M.R.; Welbourn, A.P.; Walter, D.S. Substituted 1,3,4-thiadiazoles with anticonvulsant activity. 2. Aminoalkyl derivatives. *J. Med. Chem.* **1986**, 29, 2280–2284.
39. Kane, J.M.; Dudley, M.W.; Sorensen, S.M.; Miller, F.P. 2,4-Dihydro-3*H*-1,2,4-triazole-3-thiones as potential antidepressant agents. *J. Med. Chem.* **1988**, 31, 1253–1258.
40. George, T.; Mehta, D.V.; Tahilramani R.; David, J.; Talwalker, P.K. Synthesis of some s-triazoles with potential analgesic and antiinflammatory activities. *J. Med. Chem.* **1971**, 14, 335–338.
41. Srivastava, U.; Khan, R.H.; Bahel, S.C. Synthesis of fungicidal 1,2,4-triazoles and related compounds. *Bokin Bobai.* **1979**, 7, T414-T417.
42. Rudnicka, W.; Osmailowska, Z. Cyanoalkylation of 4-amino-1,2,4-triazol-3-thione. *Acta Pol. Pharm.* **1979**, 36, 411–419.
43. Shu-Qing, K.; Sun-Yung, T.; Hung-Shan, T.; Ki, C. *Wei Sheng Wu Hsueh Pao* **1980**, 20, 208–212.
44. Singh, H.; Yadav, L.D.S.; Bhattacharya, B.K. Synthesis of some new bis(1,2,4-triazol-3-yl) disulfides, sulfides and sulfones as potential pestcides. *J. Indian Chem. Soc.* **1979**, 56, 1013–1016.
45. Gall, M.; Lahti, R.A.; Rudzik, A.D.; Duchamp, D.J.; Chidester, C.; Scahill, T. Novel anxiolytic agents derived from alpha.-amino-.alpha.-phenyl-o-tolyl-4*H*-triazoles and –imidazoles. *J. Med. Chem.* **1978**, 21, 542–548.

46. Witkowski, J.T.; Robins, R.K.; Sidwell, R.W.; Simon, L.N. Design, synthesis, and broad spectrum antiviral activity of 1-β-D-ribofuranosyl-1,2,4-triazole-3-carboxamide and related nucleosides. *J. Med. Chem.* **1972**, 15, 1150–1154.
47. Smith, R.A.; Kirkpatrick, W., eds. *The pharmacology of ribavirin*, Academic Press, London, 1980, pp. 133–156,
48. Sidwell, R.W., ed. *In vitro and in vivo Inhibition of DNA Viruses by Ribavirin*, Academic Press, Orlando, FL, 1984, pp. 19–32.
49. Smith, R.A.; Knight, V.; Smith, J.A.D., eds. *Clinical Applications of Ribavirin,* Academic Press, Orlando, FL, 1984, pp. 222.
50. Khalil, N.S.A.M. Efficient synthesis, structure, and antimicrobial activity of some novel *N*- and *S*-β-D-glucosides of 5-pyridin-3-yl-1,2,4-triazoles. *Carbohydr. Res.* **2006**, 341, 2187–2199.
51. Abbas, A.A.; Khalil, N.S.A.M. Synthesis of some new 1,3/ or 1,4-bis(glucopyranosyl-1,2,4-triazol-5-ylthio)propanes/or butanes as potential antimicrobial agents. *Nucleosides Nucleotides Nucleic Acids* **2005**, 24, 1353–1372.
52. Khalil, N.S.A.M.; Mansour, A.K.; Eid, M.M. Synthesis of some novel 6-benzyl(or substituted benzyl)-2-β-D-glucopyranosyl-1,2,4-triazolo[4,3-*b*][1,2,4]triazines as potential antimicrobial chemotherapeutics. *Nucleosides Nucleotides Nucleic Acids* **2004**, 23, 1889–1910.
53. Khalil, N.S.A.M. Synthesis of some novel *N*-ribosyl-1,2,4-triazin-6(1*H*)-/ones or thiones as potential antibacterial and antifungal chemotherapeutics. *Nucleosides Nucleotides Nucleic Acids* **2005**, 24, 111–120.
54. Mansour, A.K.; Eid, M.M.; Khalil, N.S.A.M. Selective synthesis and reactions of 6-substituted-2-β-galactosyl-1,2,4-triazines of potential anticancer activity. *Nucleosides Nucleotides Nucleic Acids* **2003**, 22, 21–44.
55. Mansour, A.K.; Eid, M.M.; Khalil, N.S.A.M. Synthesis of some *N*-galactosides of 3-aryl-5-benzyl (or substituted benzyl)-1,2,4-triazin-6(1*H*)-/ones or thiones of expected biological activity. *Nucleosides Nucleotides Nucleic Acids* **2003**, 22, 1825–1833.
56. Mansour, A.K.; Eid, M.M.; Khalil, N.S.A.M. Synthesis and reactions of some new heterocyclic carbohydrazides and related compounds as potential anticancer agents. *Molecules* **2003**, 8, 744–755.
57. Mansour, A.K.; Ibrahim, Y.A.; Khalil, N.S.A.M. Selective synthesis and structure of 6-arylvinyl-2- and 4- glucosyl-1,2,4-triazines of expected interesting biological activity. *Nucleosides Nucleotides* **1999**, 18, 2265–2283.
58. Niedballa, U.; Vorbrüggen. H. A general synthesis of *N*-glycosides. I. Synthesis of pyrimidine nucleosides. *J. Org. Chem.* **1974**, *39*, 3654–3660; and references cited therein.
59. Cleve, G.; Hoyer, G.A.; Schulz, G.; Vorbrüggen, H. Synthesis of nucleosides. VIII. NMR and CD spectra of pyrimidine nucleosides and their 2-thio analogs. *Chem. Ber.* **1973**, 106, 3062–3072.
60. Vorbrüggen. H.; Strehlke, P.; Schulz, G. A simple new synthesis of 2-thiopyrimidine nucleosides. *Angew. Chem. Internat. Edit.* **1969**, 8, 976–977.
61. Walter, W.; Maerten, G. Structure of thioamides and their derivatives. I. Configuration studies of substituted thioformamides and formamides by N.M.R. spectroscopy. *Justus Liebigs Ann. Chem.* **1968**, 712, 58–66.
62. Furniss, B.S.; Hannaford, A.J.; Smith, P.W.G.; Tatchell, A.R.; eds. *Vogel's Textbook of Practical Organic Chemistry*, Longman Group UK, Ltd., England, 1989, 5th ed., pp. 648.