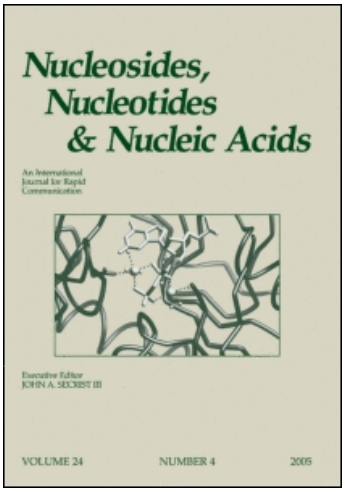

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SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF SOME *S*-β-D-GLUCOSIDES OF 4-MERCAPTOPYRIMIDINE

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□ *5-Acetyl-2-aryl-6-methyl-4-(2,3,4,6-tetra-*O*-acetyl-β-**D**-glucopyranosylmercapto)pyramidines* ***3a–c*** *were obtained by the reaction of 5-acetyl-2-aryl-6-methyl-pyrimidine thiol* ***1a–c*** *with 2,3,4,6-tetra-*O*-acetyl-α-**D**-glucopyranosyl bromide (****2****) in aq. KOH/acetone. The reaction of* ***1a–c*** *with peracetylated galactose* ***5*** *and peracetylated ribose* ***8*** *under MW irradiation gave 5-acetyl-2-aryl-6-methyl-4-(2,3,4,6-tetra-*O*-acetyl-β-**D**-galactopyranosylmercapto)pyrimidine* ***6a–c*** *and 5-acetyl-2-aryl-6-methyl-4-(2,3,5-tri-*O*-acetyl-β-**D**-ribofuranosylmercapto)pyrimidines* ***9a–c****. The deprotection of* ***3a–c****,* ***6a–c****, and* ***9a–c*** *in the presence of methanol and TEA/H_2O yielded the deprotected products* ***4a–c****,* ***7a–c****, and* ***10a–c****. The structures of the compounds were confirmed by using IR, ^1H, ^{13}C spectra and microanalysis. Selected members of these compounds were screened for antimicrobial activity.*

Keywords Glycosides; microwave; antimicrobial activity

INTRODUCTION

The pyrimidines and their nucleosides are interesting classes in medicinal and agricultural chemistry. Some pyrimidine nucleosides are known as antiviral,[1–3] antibacterials,[4,5] antitumor,[6] antipyretic,[7] antiinflammatory drugs,[8] pesticides,[9] and plant growth regulators.[10]

Glycosylthio-heterocycles have attracted much attention because of their abilities to function as biological inhibitors, inducers, and ligands for affinity of chromatography of carbohydrate-process enzymes and proteins.[11] The utility of microwave (MW) as a nonconventional energy source has advantages such as significant rate enhancements of reactions, higher product yields, and greater selectivity of organic reactions.[12–14] The combination of solvent-free reaction conditions and microwave irradiation has also been investigated.[15–17]

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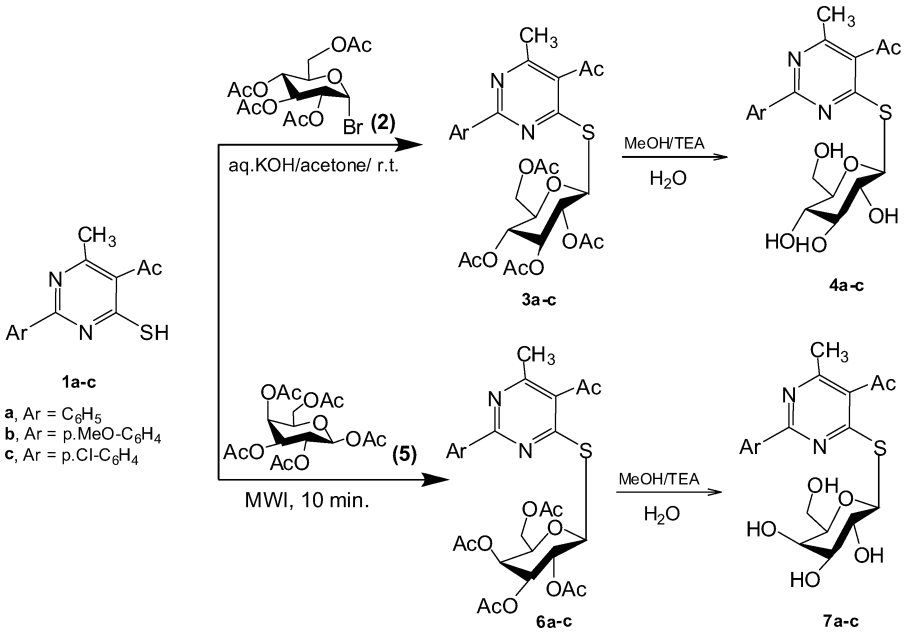


SCHEME 1

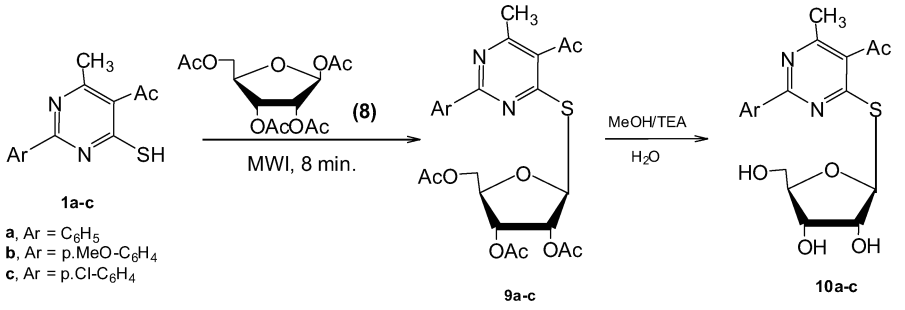
RESULTS AND DISCUSSION

The syntheses of 5–acetyl-6-methyl-2-arylpyrimidine-4-thiols **1a–c** have been achieved as reported in literature.[18] Reaction of **1a–c** with glycosyl bromide **2** in the presence of aqueous potassium hydroxide/acetone[4,5] gave 5-acetyl-6-methyl-2-aryl-4-(2,3,4,6 -tetra-***O***-acetyl-β-**D**-glycopyranosylthio)pyrimidines **(3a–c)** (Scheme 1). Irradiation of **1a–c** with **5** in the presence of silica gel as a solid support in MW oven[4,19] for 10 minutes gave the corresponding thiogalactosides **6a–c** in 40–45% yield (Scheme 1).

The structure of compounds **3a–c** was confirmed on the basis of their elemental analysis and spectral data. Their IR spectra showed a band at 1765–1745 cm^{-1} for the acetoxy carbonyl groups in addition to a band at 1695cm^{-1} due to the carbonyl of 5-aceylpyrimidine.

The ^{1}H NMR spectrum of **3a** showed the presence of signals at δ 1.53, 1.96, 2.00, and 2.02 ppm characteristic for 4 CH_3 of OAc groups, in addition to 2 CH_3 at δ 2.36, 2.58 ppm and a doublet at δ 6.23 ppm for anomeric proton with $J_{1',2'} = 8.97$ Hz, which confirmed the presence of the β-configuration. The ^{13}C NMR spectrum of **3a** showed peak at δ 80.1 ppm, characteristic for anomeric carbon, and absence of C=S group, which indicates the formation of S-glycoside not N-glycoside.

The ^{1}H NMR spectrum of **3b** and **3c** showed similar results. Also the glycosides **6a–c** showed spectral characteristic conforming their



SCHEME 2

β-configuration. On the other hand, reaction of **1a–c** with **8** under MW irradiation in the presence of silica gel as a solid support[4,20] for 8 minutes gave the corresponding ribosides **9a–c** in 40–45% yield (Scheme 2).

The ^{1}H NMR spectrum of **9a** showed signals at δ 2.06, 2.07, and 2.15 ppm for 3 CH_3 of OAc groups, and doublet at δ 6.46 ppm for anomeric proton with coupling constant $J_{1',2'} = 2.80$ Hz indicating the presence of β-configuration. Similarly **9b** and **9c** gave similar results. Deprotection of the previous prepared S-glucosides **3a–c**, **6a–c**, and **9a–c** using triethylamine in presence of methanol and few drops of water[4,5,20] gave the deprotected glycosides **4a–c**, **7a–c**, and **10a–c** (Schemes 1and 2).

The ^{1}H, ^{13}C NMR spectra for **4a–c** showed the absence of the four signals of the 4 OAc groups and presence of signals at δ 4.53, 5.11, 5.24, and 5.51 ppm for 4 OH groups of sugar moieties, in addition of doublet at δ 5.61, 5.68, and 6.26 ppm for the anomeric protons of **4a–c**. The IR spectra of **4a–c** showed the appearance of the broad band at 3417 cm^{-1} for 4 OH groups. Similar results were obtained for **7a–c** and **10a–c**.

Antimicrobial Activity

Compound **3c** showed higher activity against *B. subtitlis* as gram positive and *E. coli* as gram negative bacteria, while **3a**,**b** and **6b** showed only moderate activity. Compounds **3** and **9a** showed activity towards fungi (e.g., *Penicillium sp.* and *aspergillus sp.*). Compounds **6a**,**c** and **9b**,**c** did not show any activity against the tested microorganisms (Table 1).

EXPERIMENTAL

All melting points are uncorrected and were measured using an Electrothermal IA 9100 apparatus. Thin layer chromatography (TLC) was performed on Merck Silica Gel 60F_{254} with detection by UV light and charring with H_2SO_4/EtOH (5:95); The IR spectra (KBr disc) were recorded on a Pye Unicam Sp-3-300 and Shimadzu FTIR 8101 PC infrared

TABLE 1 Antimicrobial activity of tested compounds (inhibition zones [mm], minimum inhibitory concentration [μg/mL])

Compound no.	*E. Coli*	*B. Subtilis*	*Penicillium Sp.*	*Aspergillus Sp.*
3a	—	15	15	10
3b	—	10	—	—
3c	10	25	—	—
6a	—	—	—	—
6b	—	5	—	—
6c	—	—	—	—
9a	—	10	10	8
9b	—	—	—	—
9c	—	—	—	—

spectrophotometer. The ultraviolet (UV) spectra were recorded by UV-160A, UV-visible recording spectrometer Shimadzu using EtOH 95% as a solvent. The ^{1}H and ^{13}C NMR spectra were recorded on a Varian Mercury VX-NMR 300 & 100 MHz spectrometer. Chemical shifts are expressed on the δ(ppm) scale using TMS as the standard and coupling-constant values are given in Hz. Elemental analyses were determined on a Perkin Elmer 240.

General Methods for Preparation of Glucosides

Method A

To a solution of pyrimidinethiol **1a–c** (0.01 mol) in aq. KOH [0.01 mol in distilled water (6 mL)] was added a solution of 2,3,4,6-tetra-***O***-acetyl-α-**D**-glucopyranosyl bromide (**2**) (0.011 mol) in acetone (30 mL). The reaction mixture was stirred at room temperature and followed by *tlc* until the reaction was finished (4.5–5 hours), the reaction mixture was evaporated under reduced pressure and the residue was washed with distilled water to remove potassium bromide. The product was dried and crystallized from the appropriate solvent.

Method B

A mixture of pyrimidinethiol **1a–c** (0.001 mol) and (0.001 mol) of per acetylated galactose (**5**) or ribose (**8**) was dissolved in methylene chloride, then 1 gm of silica gel (200–400 mesh) was added, the solvent was removed by evaporation, and then the dried residue was transferred into a glass beaker and irradiated for (8–10 minutes) in a domestic microwave oven. The product was extracted with methylene chloride, evaporated to dryness, and crystallized from appropriate solvent.

5-Acetyl-6-methyl-2-phenyl-4-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl-thio)pyrimidine (3a). *Method A:* yield 26%. As colorless crystals from ethanol; m.p. 105–107°C; λ_{max} = 300 nm. ^{1}H NMR (DMSO-d_6, 300 MHz):

δ 1.53, 1.96, 2.00, 2.02 (4s, 12 H, 4 CH_3CO), 2.36 (s, 3 H, CH_3 pyrimidine), 2.58 (s, 3 H, CH_3CO pyrimidine), 4.00 (m, 1 H, H-5′), 4.13(dd, 1 H, $J_{6'',5'}$ = 2.10, $J_{6'',6'}$ = 12.32 Hz, H-6″), 4.26 (dd, 1 H, $J_{6',5'}$ = 5.96, $J_{6',6''}$ = 12.3 Hz, H-6′), 5.12 (t, 1 H, $J_{4',3'}$ = 8.78, $J_{4',5'}$ = 9.13 Hz, H-4′), 5.31 (t, 1 H, $J_{2',1'}$ = 7.70, $J_{2',3'}$ = 9.20 Hz, H-2′), 5.63 (t, 1 H, $J_{3',2'}$ = 9.20, $J_{3',4'}$ = 8.78 Hz, H-3′), 6.23 (d, 1 H, $J_{1',2'}$ = 8.97 Hz, H-1′), 7.56 (m, 3 H, Ar−H), 8.58 (m, 2 H, Ar−H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 20.8, 21.1, 21.2, 21.4, 23.8, 32.2 (6 CH_3), 62.8 (C-6′), 69.2 (C-2′), 69.8 (C-4′), 73.8 (C-3′), 75.9 (C-5′), 80.1 (C-1′), 129.4, 129.6, 130.9, 132.4, 136.7, 162.54, 163.1, 163.6, 170.1, 170.4, 170.6 and 202.8 (Ar−C, 2 C=N and 5 C=O). Anal. Calcd for $C_{27}H_{30}N_2O_{10}S$ (574.6): C, 56.44; H, 5.26; N, 4.88. Found: C, 56.68; H, 5.31; N, 5.03.

5-Acetyl-6-methyl-2-(4-methoxyphenyl)-4-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylthio)pyrimidine (3b). *Method A:* yield 24%. As colorless crystals from ethanol; m.p. 100–103°C; λ_{max} = 301.4 nm. ^{1}H NMR (DMSO-d_6, 300 MHz): δ 1.54, 1.95, 2.00, 2.02 (4s, 12 H, 4 CH_3CO), 2.34 (s, 3 H, CH_3 pyrimidine), 2.59 (s, 3 H, CH_3CO pyrimidine), 3.89 (s, 3 H, OCH_3), 3.98 (m, 1 H, H-5′), 4.12 (dd, 1 H, $J_{6'',5'}$ = 2.10, $J_{6'',6'}$ = 12.3 Hz, H-6″), 4.26 (dd, 1 H, $J_{6',5'}$ = 5.96, $J_{6',6''}$ = 12.3 Hz, H-6′), 5.12 (t, 1 H, $J_{4',3'}$ = 8.97, $J_{4',5'}$ = 9.13 Hz, H-4′), 5.31 (t, 1 H, $J_{2',1'}$ = 7.90, $J_{2',3'}$ = 9.22 Hz, H-2′), 5.62 (t, 1 H, $J_{3',2'}$ = 9.22, $J_{3',4'}$ = 8.78 Hz, H-3′), 6.24 (d, 1 H, $J_{1',2'}$ = 8.87 Hz, H-1′), 7.10 (d, 2 H, J = 9.0 Ar−H), 8.40 (d, 2 H, J = 9.0 Hz, Ar−H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 20.8, 21.1, 21.2, 21.4, 23.9, 32.3 (6 CH_3), 56.2 (OCH_3), 62.8 (C-6′), 69.2 (C-2′), 69.8 (C-4′), 73.8 (C-3′), 75.9 (C-5′), 80.0 (C-1′), 129.2, 130.0, 131.3, 131.7, 162.3, 163.0, 163.1, 163.6, 170.1, 170.2, 170.4, 170.6 and 202.7 (Ar−C, 2 C=N and 5 C=O). Anal. Calcd for $C_{28}H_{32}N_2O_{11}S$ (604.63): C, 55.62; H, 5.33; N, 4.63. Found: C, 55.50; H, 5.68; N, 4.60.

5-Acetyl-2-(4-chlorophenyl)-6-methyl-4-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosylthio)pyrimidine (3c). *Method A:* yield 34%. As colorless crystals from ethanol; m.p. 104–106°C; λ_{max} = 300 nm. IR (KBr): 1749 (C=O, esters) cm^{-1}, 1697(C=O, acetyl) cm^{-1}. ^{1}H NMR (DMSO-d_6, 300 MHz): δ 1.53, 1.95, 2.00, 2.02 (4s, 12 H, 4 CH_3CO), 2.45 (s, 3 H, CH_3 pyrimidine), 2.55 (s, 3 H, CH_3CO pyrimidine), 3.98 (m, 1 H, H-5′), 4.12 (dd, 1 H, $J_{6'',5'}$ = 2.10, $J_{6'',6'}$ = 12.3 Hz, H-6″), 4.27 (dd, 1 H, $J_{6',5'}$ = 5.96, $J_{6',6''}$ = 12.3 Hz, H-6′), 4.92 (t, 1 H, $J_{4',3'}$ = 8.97, $J_{4',5'}$ = 9.13 Hz, H-4′), 5.08 (t, 1 H, $J_{2',1'}$ = 7.90, $J_{2',3'}$ = 9.22 Hz, H-2′), 5.67 (t, 1 H, $J_{3',2'}$ = 9.22, $J_{3',4'}$ = 8.78 Hz, H-3′), 6.21(d, 1 H, $J_{1',2'}$ = 7.89 Hz, H-1′), 7.59 (d, 2 H, J = 8.90 Ar−H), 8.49 (d, 2 H, J = 8.90 Ar−H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 20.2, 20.3, 20.4, 22.8, 22.9, 31.3 (6 CH_3), 61.9 (C-6′), 68.2 (C-2′), 68.9 (C-4′), 72.9 (C-3′), 74.9 (C-5′), 79.2 (C-1′), 128.8, 128.9, 130.3, 130.4, 134.7, 136.5, 160.6, 162.7, 162.9, 169.4, 169.5, 169.6 and 201.9 (Ar−C, 2 C=N and 5 C=O). Anal. Calcd for $C_{27}H_{29}ClN_2O_{10}S$ (609.04): C, 53.25; H, 4.80; N, 6.40. Found: C, 53.12; H, 4.57; N, 6.21.

5-Acetyl-6-methyl-2-phenyl-4-(β-D-glucopyranosylthio)pyrimidine (4a). *General method for deprotection of acetyl groups*: Triethylamine (1ml) was added to 10 ml a solution of glucosides or ribosides (0.001mol) in ($MeOH/H_2O$). The mixture was stirred overnight at room temperature; it was evaporated under reduced pressure and co-evaporated with MeOH until the excess of Et_3N was removed. The residue was then crystallized from the proper solvent to give the desired product with yield >85%. Colourless crystals from ethanol; m.p. 115–117°C; IR (KBr): 3417 (br. 4 OH) cm^{-1} and 1689 (C=O) cm^{-1}. ^1H NMR (DMSO-d_6/D_2O, 300 MHz): δ 2.46 (s, 3 H, CH_3 pyrimidine), 2.60 (s, 3 H, CH_3CO pyrimidine), 3.24–3.85 (m, 6 H, H-6′, H-6″, H-5′, H-4′, H-3′ and H-2′), 5.69 (d, 1 H, $J_{1',2'} = 8.97$ Hz, H-1′),7.45 (m, 3 H, Ar−H), 8.42 (m, 2 H, Ar−H). ^{13}C NMR (DMSO-d_6,300 MHz): δ 22.5, 31.4 (2 CH_3), 61.6 (C-6′), 69.6 (C-2′), 71.7 (C-4′), 78.5 (C-3′), 81.8 (C-5′), 83.0 (C-1′), 128.2, 128.8, 128.9, 130.3, 131.4, 136.3, 161.6, 163.7 and 202.6 (Ar−C, 2 C=N and C=O). Anal. Calcd for $C_{19}H_{22}N_2O_6S$ (406.45): C, 56.15; H, 5.46; N, 6.89. Found: C, 55.91; H, 5.55; N, 6.93.

5-Acetyl-6-methyl-2-(4-methoxyphenyl)-4-(β-D-glucopyranosylthio) pyrimidine (4b). As for **4a**, colorless crystals from ethanol; m.p. 110–111°C; IR (KBr): 3415 (br. 4 OH) cm^{-1} and 1690 (C=O) cm^{-1}. ^1H NMR (DMSO-d_6/D_2O, 300 MHz): δ 2.45 (s, 3 H, CH_3 pyrimidine), 2.62 (s, 3 H, CH_3CO pyrimidine), 3.23–3.85 (m, 6 H, H-6′, H-6″, H-5′, H-4′, H-3′ and H-2′), 3.89 (s, 3 H, OCH_3), 6.21 (d, 1 H, $J_{1',2'} = 8.90$ Hz, H-1′), 7.10 (d, 2 H, J = 8.62 Hz, Ar−H), 8.40 (d, 2 H, J = 8.62 Hz, Ar−H). Anal. Calcd for $C_{20}H_{24}N_2O_7S$ (436.48): C, 55.03; H, 5.54; N, 6.42. Found: C, 55.23; H, 5.44; N, 6.50.

5-Acetyl-2-(4-chlorophenyl)-6-methyl-4-(β-D-glucopyranosylthio)pyrimidine (4c). As for **4a**, colorless crystals from ethanol; m.p. 114–116°C; IR (KBr): 3417 (br. 4 OH) cm^{-1} and 1700 (C=O) cm^{-1}. ^1H NMR (DMSO-d_6, 300 MHz): δ 2.46 (s, 3 H, CH_3 pyrimidine), 2.59 (s, 3 H, CH_3CO pyrimidine), 3.13–3.46 (m, 6 H, H-6′, H-6″, H-5′, H-4′, H-3′ and H-2′), 4.53 (t, 1 H, J = 3.56 Hz, OH-6′), 5.11 (d, J = 4.34 Hz, 1 H, OH-4′), 5.24 (d, 1 H, J = 5.24 Hz, OH-3′), 5.51 (d, 1 H, J = 4.96 Hz, OH-2′), 6.24 (d, 1 H, $J_{1',2'} = 8.89$ Hz, H-1′), 7.60 (d, 2 H, J = 8.91 Hz, Ar−H), 8.39 (d, 2 H, J = 8.91 Hz, Ar−H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 22.4, 31.3 (2 CH_3), 60.7 (C-6′), 69.6 (C-2′), 71.6 (C-4′), 78.4 (C-3′), 81.9 (C-5′), 83.1 (C-1′), 128.9, 130.0, 130.4, 135.2, 136.3, 160.6, 161.7, 163.9 and 202.5 (Ar−C, 2 C=N and C=O). Anal. Calcd for $C_{19}H_{21}ClN_2O_6S$ (440.90): C, 51.76; H, 4.80; N, 6.35. Found: C, 51.42; H, 4.36; N, 6.17.

5-Acetyl-6-methyl-2-phenyl-4-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosylthio)pyrimidine (6a). *Method B:* yield 40%. As colorless crystals from ethanol; m.p. 102–103°C; $\lambda_{max} = 303.2$ nm. ^1H NMR (DMSO-d_6, 300 MHz): δ 1.50, 1.95, 2.03, 2.13 (4s, 12 H, 4 CH_3CO), 2.46 (s, 3 H, CH_3 pyrimidine), 2.59 (s, 3 H, CH_3CO pyrimidine), 3.95 (m, 1 H, H-5′), 4.12 (dd, 1 H, $J_{6'',5'} = 6.50$, $J_{6',6''} = 12.0$ Hz, H-6″), 4.25 (dd, 1 H, $J_{6',5'} = 5.60$, $J_{6',6''} = 12.0$ Hz, H-6′),

5.21 (t, 1 H, $J_{3',2'} = 10.0$, $J_{3',4'} = 3.50$ Hz, H-3′), 5.41 (t, 1 H, $J_{2',1'} = 8.20$, $J_{2',3'} = 10.0$ Hz, H-2′), 5.62 (t, 1 H, $J_{4',3'} = 3.50$, $J_{4',5'} = 1.00$ Hz, H-4′), 6.26 (d, 1 H, $J_{1',2'} = 8.20$ Hz, H-1′), 7.57 (m, 3 H, Ar−H), 8.56 (d, 2 H, Ar−H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 20.1, 20.3, 20.4, 22.7, 22.9, 31.3 (6 $\underline{C}H_3$), 62.0 (C-6′), 69.1 (C-2′), 68.9 (C-4′), 73.8 (C-3′), 75.9 (C-5′), 80.1 (C-1′), 129.3, 129.6, 130.8, 132.3, 136.7, 162.5, 163.1, 163.5, 170.2, 170.3, 170.4, 170.6 and 202.6 (Ar−C, 2 C=N and 5 C=O). Anal. Calcd for $C_{27}H_{30}N_2O_{10}S$ (574.6): C, 56.44; H, 5.26; N, 4.88. Found: C, 56.53; H, 5.33; N, 5.23.

5-Acetyl-6-methyl-2-(4-methoxyphenyl)-4-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosylthio)pyrimidine (6b). *Method B:* yield 41%. As colorless crystals from ethanol; m.p. 98–99°C; $\lambda_{max} = 302.8$ nm. ^{1}H NMR (DMSO-d_6, 300 MHz): δ 1.51, 1.59, 2.03, 2.13 (4s, 12 H, 4 $C\underline{H}_3CO$), 2.49 (s, 3 H, CH_3 pyrimidine), 2.57 (s, 3 H, $C\underline{H}_3CO$ pyrimidine), 3.85 (s, 3 H, OCH_3), 3.95 (m, 1H, H-5′), 4.13 (dd, 1 H, $J_{6'',5'} = 6.50$, $J_{6',6''} = 12.0$ Hz, H-6″), 4.26 (dd, 1 H, $J_{6',5'} = 5.60$, $J_{6',6''} = 12.0$ Hz, H-6′), 5.22 (t, 1 H, $J_{3',2'} = 10.0$, $J_{3',4'} = 3.50$ Hz, H-3′), 5.41 (t, 1 H, $J_{2',1'} = 8.20$, $J_{2',3'} = 10.0$ Hz, H-2′), 5.62 (t, 1 H, $J_{4',3'} = 3.50$, $J_{4',5'} = 1.00$ Hz, H-4′), 6.26 (d, 1 H, $J_{1',2'} = 8.22$ Hz, H-1′), 7.08 (d, 2 H, J = 8.63 Hz, Ar−H), 8.48 (d, 2 H, J = 8.63 Hz, Ar−H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 20.1, 20.2, 20.4, 22.6, 22.8, 31.2 (6 $\underline{C}H_3$), 56.2 ($O\underline{C}H_3$), 61.8 (C-6′), 66.4 (C-2′), 70.9 (C-4′), 72.4 (C-3′), 74.4 (C-5′), 79.6 (C-1′), 128.3, 129.2, 130.4, 131.7, 161.4, 162.1, 162.7, 169.4, 169.5, 169.7, 169.8, 170.0 and 201.8 (Ar−C, 2 C=N and 5 C=O). Anal. Calcd for $C_{28}H_{32}N_2O_{11}S$ (604.63): C, 55.62; H, 5.33; N, 4.63. Found: C, 55.51; H, 5.48; N, 4.60.

5-Acetyl-2-(4-chlorophenyl)-6-methyl-4-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosylthio)pyrimidine (6c). *Method B:* yield 45%. As colorless crystals from ethanol; m.p. 106–109°C; $\lambda_{max} = 301.4$ nm. ^{1}H NMR (DMSO-d_6, 300 MHz): δ 1.49, 1.58, 2.03, 2.14 (4s, 12 H, 4 $C\underline{H}_3CO$), 2.48 (s, 3 H, $C\underline{H}_3$ pyrimidine), 2.59 (s, 3 H, $C\underline{H}_3CO$ pyrimidine), 3.98 (m, 1 H, H-5′), 4.14 (dd, 1 H, $J_{6'',5'} = 6.50$, $J_{6',6''} = 12.0$ Hz, H-6″), 4.27 (dd, 1 H, $J_{6',5'} = 5.60$, $J_{6',6''} = 12.0$ Hz, H-6′), 5.23 (t, 1 H, $J_{3',2'} = 10.0$, $J_{3',4'} = 3.50$ Hz, H-3′), 5.42 (t, 1 H, $J_{2',1'} = 8.20$, $J_{2',3'} = 10.0$ Hz, H-2′), 5.65 (t, 1 H, $J_{4',3'} = 3.50$, $J_{4',5'} = 1.00$ Hz, H-4′), 6.36 (d, 1 H, $J_{1',2'} = 8.22$ Hz, H-1′), 7.53 (d, 2 H, J = 8.90 Hz, Ar−H), 8.49 (d, 2 H, J = 8.90 Hz, Ar−H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 20.1, 20.2, 20.4, 22.6, 22.8, 31.1 (6 $\underline{C}H_3$), 61.6 (C-6′), 66.8 (C-2′), 69.6 (C-4′), 70.5 (C-3′), 70.6 (C-5′), 79.3 (C-1′), 128.5, 130.1, 134.4, 134.5, 160.3, 162.1, 162.6, 168.5, 168.9, 169.2, 169.3, 169.5 and 201.6 (Ar−C, 2 C=N and 5 C=O). Anal. Calcd for $C_{27}H_{29}ClN_2O_{10}S$ (609.04): C, 53.25; H, 4.80; N, 6.40. Found: C, 53.52; H, 4.78; N, 6.33.

5-Acetyl-6-methyl-2-phenyl-4-(β-D-galactopyranosylthio) pyrimidine (7a). As for **4a**, colorless crystals from ethanol; m.p. 118–119°C; IR (KBr): 3417 (br 4 OH) cm^{-1} and 1690 (C=O) cm^{-1}. ^{1}H NMR (DMSO-d_6/D_2O, 300 MHz): δ 2.45 (s, 3 H, $C\underline{H}_3$ pyrimidine), 2.59 (s, 3 H, $C\underline{H}_3CO$ pyrimidine), 3.23–3.84 (m, 6 H, H-6′, H-6″, H-5′, H-4′, H-3′ and H-2′), 6.21 (d, 1 H, $J_{1',2'} =$

8.40 Hz, H-1′), 7.57 (m, 3 H, Ar−H), 8.53 (m, 2 H, Ar−H). Anal. Calcd for $C_{19}H_{22}N_2O_6S$ (406.45): C, 56.15; H, 5.46; N, 6.89. Found: C, 55.90; H, 5.45; N, 6.93.

5-Acetyl-6-methyl-2-(4-methoxyphenyl)-4-(β-D-galactopyranosylthio)pyrimidine (7b). As for **4a**, colorless crystals from ethanol; m.p. 112–114°C; IR (KBr): 3415 (br 4 OH) cm^{-1} and 1695 (C=O) cm^{-1}. ^1H NMR (DMSO-d_6/D_2O, 300 MHz): δ 2.45 (s, 3 H, CH_3 pyrimidine), 2.59 (s, 3 H, CH_3CO pyrimidine), 3.24–3.75 (m, 6 H, H-6′, H-6″, H-5′, H-4′, H-3′ and H-2′), 3.85 (s, 3 H, OCH_3), 6.23 (d, 1H, $J_{1',2'} = 8.51$ Hz, H-1′), 7.52 (d, 2 H, J = 8.90 Hz, Ar−H), 8.48 (d, 2 H, J = 8.90 Hz, Ar−H). Anal. Calcd for $C_{20}H_{24}N_2O_7S$ (436.48): C, 55.03; H, 5.54; N, 6.42. Found: C, 55.43; H, 5.44; N, 6.52.

5-Acetyl-2-(4-chlorophenyl)-6-methyl-4-(β-D-galactopyranosylthio) pyrimidine (7c). As for **4a**, colorless crystals from ethanol; m.p. 119–120°C; IR (KBr): 3418 (br. 4 OH) cm^{-1} and 1692 (C=O) cm^{-1}. ^1H NMR (DMSO-d_6/D_2O, 300 MHz): δ 2.45 (s, 3 H, CH_3 pyrimidine), 2.58 (s, 3 H, CH_3CO pyrimidine), 3.35–3.85 (m, 6 H, H-6′, H-6″, H-5′, H-4′, H-3′ and H-2′), 6.22 (d, 1 H, $J_{1',2'} = 8.45$ Hz, H-1′), 7.53 (d, 2 H, J = 8.90 Hz, Ar−H), 8.48 (d, 2 H, J = 8.90 Hz, Ar−H). Anal. Calcd for $C_{19}H_{21}ClN_2O_6S$ (440.90): C, 51.76; H, 4.80; N, 6.35. Found: C, 51.44; H, 4.32; N, 6.27.

5-Acetyl-6-methyl-2-phenyl-4-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosylthio)pyrimidine (9a). *Method B:* yield 41%; as colorless crystals from methanol; m.p. 111–113°C; $\lambda_{max} = 300$ nm. ^1H NMR (DMSO-d_6, 300 MHz): δ 2.06, 2.07, 2.15 (3s, 9 H, 3 CH_3CO), 2.43 (s, 3 H, CH_3 pyrimidine), 2.59 (s, 3 H, CH_3CO pyrimidine), 4.10 (dd, 1 H, $J_{5',4'} = 3.40$, $J_{5',5''} = 11.6$ Hz, H-5′), 4.16 (dd, 2 H, $J_{5'',4'} = 3.60$, $J_{5'',5'} = 11.6$ Hz, H-5″), 4.41 (m, 1 H, H-4′), 5.54 (t, 1 H, $J_{3',2'} = 2.71$, $J_{3',4'} = 6.62$ Hz, H-3′), 5.63 (dd, 1 H, $J_{2',1'} = 2.60$, $J_{2',3'} = 2.80$ Hz, H-2′), 6.46 (d, 1 H, $J_{1',2'} = 2.80$ Hz, H-1′), 7.45–8.40 (m, 5 H, Ar−H). Anal. Calcd for $C_{24}H_{26}N_2O_8S$ (502.54): C, 57.36; H, 5.52; N, 5.57. Found: C, 57.14; H, 5.11; N, 5.75.

5-Acetyl-6-methyl-2-(4-methoxyphenyl)-4-(2,3,5-tri-*O*-acetyl-β-*D*-ribofuranosylthio)pyrimidine (9b). *Method B:* yield 36%, as colorless crystals from methanol ; m.p. 107–109°C; UV; $\lambda_{max} = 299$ nm. ^1H NMR (DMSO-d_6, 300 MHz): δ 2.05, 2.07, 2.16 (3s, 9 H, 3 CH_3CO), 2.51 (s, 3 H, CH_3CO pyrimidine), 2.62 (s, 3 H, CH_3 pyrimidine), 3.34 (s, 3 H, OCH_3), 4.10 (dd, 1 H, $J_{5',4'} = 3.40$, $J_{5',5''} = 11.6$ Hz, H-5′), 4.14 (dd, 1 H, $J_{5'',4'} = 3.60$, $J_{5',5''} = 11.6$ Hz, H-5″), 4.41 (m, 1 H, H-4′), 5.43 (t, 1 H, $J_{3',2'} = 2.71$, $J_{3',4'} = 6.62$ Hz, H-3′), 5.56 (dd, 1 H, $J_{2',1'} = 2.60$, $J_{2',3'} = 2.80$ Hz, H-2′), 6.43 (d, 1 H, $J_{1',2'} = 2.75$ Hz, H-1′) 7.61 (d, 2 H, J = 8.90 Hz, Ar−H), 8.31 (d, 2 H, J = 8.90 Hz, Ar−H). Anal. Calcd for $C_{25}H_{28}N_2O_9S$ (532.56): C, 56.38; H, 5.30; N, 5.26. Found: C, 56.10; H, 5.32; N, 5.19.

5-Acetyl-2-(4-chlorophenyl)-6-methyl-4-(2′,3′,5′-tri-*O*-acetyl-β-D-ribofuranosylthio)pyrimidine (9c). *Method B:* yield 40%, as colorless crystals from methanol ; m.p. 105–107°C; UV; λ_{max} 299 nm. ^1H NMR

(DMSO-d_6, 300 MHz): δ 2.05, 2.07, 2.16 (3s, 9 H, 3 CH_3CO), 2.62 (s, 3 H, CH_3CO pyrimidine), 2.51 (s, 3 H, CH_3 pyrimidine), 4.06 (dd, 1 H, $J_{5',4'}$ = 3.40, $J_{5',5''}$ = 11.6 Hz, H-5′), 4.12 (dd, 1 H, $J_{5'',4'}$ = 3.60, $J_{5'',5'}$ = 11.6 Hz, H-5″), 4.45 (m, 1 H, H-4′), 5.42 (t, 1 H, $J_{3',2'}$ = 2.71, $J_{3',4'}$ = 6.62 Hz, H-3′), 5.55 (dd, 1 H, $J_{2',1'}$ = 2.60, $J_{2',3'}$ = 2.80 Hz, H-2′), 6.42 (d, 1 H, $J_{1',2'}$ = 2.60 Hz, H-1′), 7.60 (d, 2 H, J = 8.80 Hz, Ar−H), 8.34 (d, 2 H, J = 8.80 Hz, Ar−H). ^{13}C NMR (DMSO-d_6, 100 MHz); δ 20.7, 20.8, 21.0, 23.4, 31.8 (5 CH_3), 62.7 (C-5′), 70.5 (C-3′), 75.6 (C-2′), 79.6 (C-4′), 85.4 (C-1′), 129.3, 130.2, 135.2, 137.0, 160.9, 163.3, 164.1, 166.5, 169.7, 169.8, 170.3 and 202.1 (Ar−C, 2 C=N and 4 C=O). Anal. Calcd for $C_{24}H_{25}ClN_2O_8S$ (536.98): C, 53.68; H, 4.69; N, 5.22. Found: C, 53.61; H, 4.81; N, 4.93.

5-Acetyl-6-methyl-2-phenyl-4-(β-D-ribofuranosylthio)pyrimidine (10a). As for **4a**, colorless crystals from ethanol; m.p. 124–126°C. IR (KBr): 3419 (3 OH) cm^{-1}, 1692 (C=O) cm^{-1}. ^{1}H NMR (DMSO-d_6/D_2O, 300 MHz): δ 2.41 (s, 3 H, CH_3 pyrimidine), 2.54 (s, 3 H, CH_3CO pyrimidine), 3.46 -3.73 (m, 2 H, H-5′ 5 Prime;), 3.97 (m, 1 H, H-4′), 4.12 (dd, 1 H, $J_{3',4'}$ = 6.60, $J_{3',2'}$ = 2.70 Hz, H-3′), 4.23 (dd, 1 H, $J_{2',1'}$ = 2.60, $J_{2',3'}$ = 2.70 Hz, H-2′), 6.21 (d, 1 H, $J_{1',2'}$ = 2.80 Hz, H-1′), 7.53–8.37 (m, 5 H, Ar−H). Anal. Calcd for $C_{189}H_{20}N_2O_5S$ (376.43): C, 57.43; H, 5.36; N, 7.44. Found: C, 57.40; H, 4.98; N, 7.47.

5-Acetyl-6-methyl-2-(4-methoxyphenyl)-4-(β-D-ribofuranosylthio) pyrimidine (10b). As for **4a**, colorless crystals from ethanol; m.p. 117–119°C; IR (KBr): 3420 (3 OH) cm^{-1}, 1695 (C=O) cm^{-1}. ^{1}H NMR (DMSO-d_6/D_2O, 300 MHz): δ 2.45 (s, 3 H, CH_3 pyrimidine), 2.54 (s, 3 H, CH_3CO pyrimidine), 3.41–3.83 (m, 2 H, H-5′ H-5 Prime;), 3.89 (s, 3 H, OCH_3), 3.96 (m, 1 H, H-4′), 4.10 (dd, 1 H, $J_{3',4'}$ = 6.59, $J_{3',2'}$ = 2.70 Hz, H-3′), 4.20 (t, 1 H, $J_{2',1'}$ = 2.60, $J_{2',3'}$ = 2.70 Hz, H-2′), 6.22 (d, 1 H, $J_{1',2'}$ = 2.8 Hz, H-1′), 7.54 (d, 2 H, J = 8.90 Hz, Ar−H), 8.36 (d, 2 H, J = 8.90 Hz, Ar−H). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 20.0, 31.0 (2 CH_3), 56.3 (OCH_3), 61.5 (C-5′), 70.4 (C-3′), 75.3 (C-2′), 75.8 (C-4′), 74.0 (C-1′), 120.9, 121.3, 128.7, 129.8, 136.5, 136.9, 161.9, 169.9, and 201.8 (Ar−C, 2 C=N and C=O). Anal. Calcd for $C_{19}H_{22}N_2O_6S$ (406.45): C, 56.15; H, 5.46; N, 6.89. Found: C, 56.43; H, 5.32; N, 6.70.

5-Acetyl-2-(4-chlorophenyl)-6-methyl-4-(β-D-ribofuranosylthio)pyrimidine (10c). As for **4a**, colourless crystals from ethanol; m.p. 123–125°C; IR (KBr): 3422 (OH) cm^{-1}, 1690 (C=O) cm^{-1}. ^{1}H NMR (DMSO-d_6/D_2O, 300 MHz): δ 2.43 (s, 3 H, CH_3 pyrimidine), 2.57 (s, 3 H, CH_3CO pyrimidine), 3.42–3.83 (m, 2 H, H-5′ 5Prime;), 3.95 (m, 1 H, H-4′), 4.12 (dd, 1 H, $J_{3',4'}$ = 6.58, $J_{3',2'}$ = 2.75 Hz, H-3′), 4.20 (t, 1 H, $J_{2',1'}$ = 2.60, $J_{2',3'}$ = 2.70 Hz, H-2′), 6.23 (d, 1 H, $J_{1',2'}$ = 2.80 Hz, H-1′),7.25 (d, 2 H, J = 8.98 Hz, Ar−H), 8.05 (d, 2 H, J = 8.98 Hz, Ar−H). Anal. Calcd for $C_{18}H_{19}ClN_2O_5S$ (410.87): C, 52.62; H, 4.66; N, 6.82. Found: C, 52.34; H, 4.54; N, 6.76.

Antibacterial Screening

The antimicrobial activities of some newly synthesized compounds were screened for their antibacterial activity against three species of bacteria, namely *(E. coli*) as Gram positive, (*B. Subtilis*) as Gram negativeve and *(Penicillium Sp.)* and *(Asperagillus Sp.)* as fungi, using saturated disks according to the a dapted method.[21] The tested compounds were dissolved in chloroform to get a solution of 1 mg/mL concentration. The inhibition zones were measured in (mm) at the end of an incubation period of 48 hours at 37°C. Chloroform showed no inhibition zones. The fungi cultures were maintained on dextrose agar medium.

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