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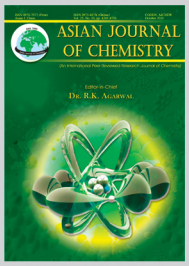

Synthesis of Some Novel Substituted (per-O-acetyl-β-D-Glucopyranosyl)thioureas from 2-Amino-4-(4-methoxyphenyl)-6-phenylpyrimidines

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Some tetra-O-acetyl-β-D-glucopyranosyl thioureas was synthesized from peracetylated β-D-glucopyranosyl isothiocyanate and corresponding 2-amino-4,6-diarylpyrimidines using conventional and microwave-assisted procedures. The second procedure afforded higher yields in much shorter reaction times.

Key Words: Isothiocyanate, Thioureas, Microwave-assisted method, D-Glucose.

INTRODUCTION

The preparations of compounds having pyrimidine ring are interested in organic synthesis due to remarkable biological activities of these substances[1]. Aminopyrimidine constitutes one of the important classes of pyrimidines and its various derivatives have displayed interesting antibacterial, antitumor and HIV-I inhibiting activity[2]. The pyrimidine and aminopyrimidine moieties are frequently occurring motifs in commercially available drugs such as antiatherosclerotic aronixil, antihistamine thonzylamine, antianxiolytic buspirone, antipsoriatic enazadrem and other medicinally relevant compounds[3]. Thiourea and its derivatives are biologically important compounds and are useful fungicides, herbicides and antibacterial agents[4]. They have also found use in organocatalysis[5].

One of the most popular and interesting approach in so called "green chemistry" field is employing the microwaves energy for conducting many chemical transformations[6]. The interaction of the matter with such kinds of electromagnetic waves results in higher speed of heating[7], much shorter reaction time or/and much smaller solvent volume, rather in solvent-free conditions and very often the higher selectivity of desired products.

Thiourea and its derivatives are biologically important compounds and are useful fungicides, herbicides[8] and antibacterial agents[9]. They have also found use in organocatalysis[10]. Thioureas have been synthesized by the reaction of primary and secondary amines with thiophosgene and isothiocyanates[11].

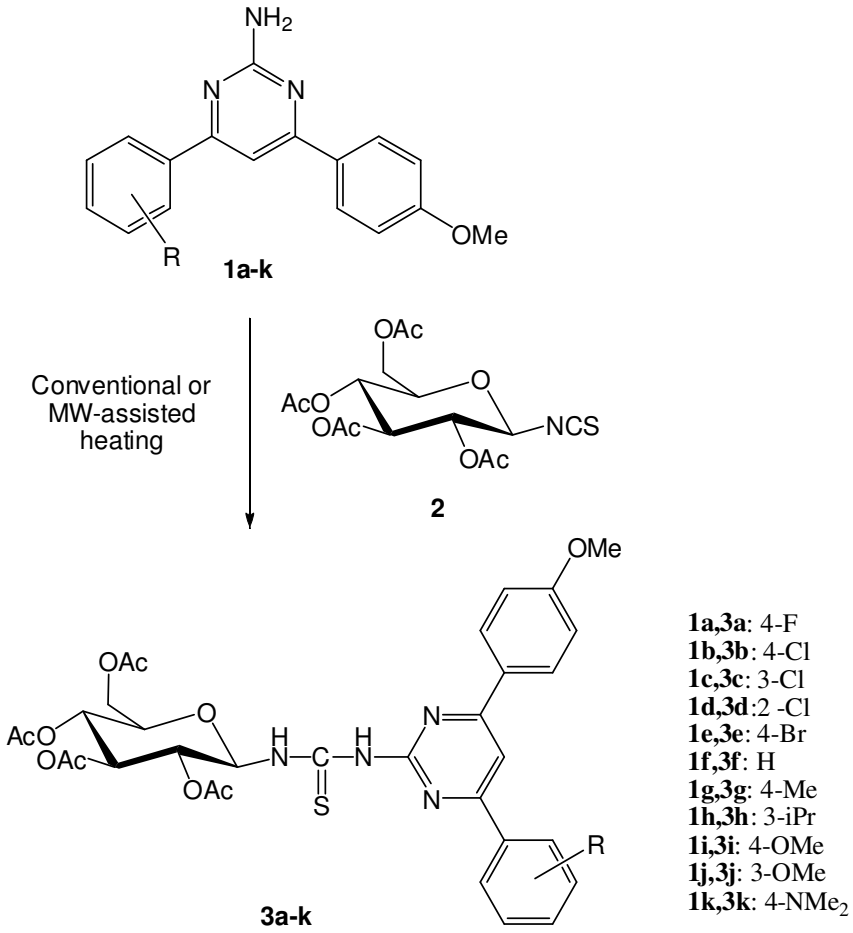
Glucopyranosyl thioureas containing heterocycles (such as thiazole, benzothiazole[12], thiadiazole[13]) were synthesized using conventional heating method. We report herein a facile synthetic method of some peracetylated glucopyranosyl thioureas containing pyrimidine nucleus (**Scheme-I**).

In continunation of our studied on the synthesis and the reactivity of peracetated glycopyranosyl isothiocyanate[14], we report here a systematic study for the synthesis and spectral characterization of a series of tetra-O-acetyl-β-D-glucopyranosyl)-thioureas using microwave-assisted method.

EXPERIMENTAL

Melting points were determined by open capillary method on STUART SMP3 instrument (BIBBY STERILIN-UK) and are uncorrected. IR spectra (KBr disc) were recorded on a Impact 410 FT-IR Spectrometer (Nicolet, USA). ^{1}H and ^{13}C NMR spectra were recorded on Bruker Avance Spectrometer AV500 (Bruker, Germany) at 500.13 and 125.77 MHz, respectively, using DMSO-d_6 as solvent and TMS as an internal standard. All the starting benzaldehydes for preparation of 2-amino-4,6-diarylpyrimidines (**1a-k**) were purchased from commercial suppliers (Merck-Germany) and used with no further purification. All other solvents and reagents were used as received or purified by standard protocols. Tetra-O-acetyl-β-glucopyranosyl isothiocyanate were prepared by the reaction of tetra-O-acetyl-β-glucopyranosyl bromide (prepared from D-glucose)[15] with lead thiocyanate in dried toluene[12]. Substituted 2-amino-4,6-diarylpyrimidines (**1a-k**)were prepared according to reference[14a].

General procedure for synthesis of *N*-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-*N'*-(4',6'-diarylpyrimidin-2'-yl)thioureas (3a-k)



Scheme-I: Preparation of per-O-acetyl-β-D-glucopyranosyl thioureas of 2-amino-4,6-diarylpyrimidines

Procedure A (under refluxing condition): A solution of 2-amino-4,6-diarylpyrimidine **1** (2 mmol) in anhydrous dioxane (10 mL) was added to a solution of 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl isothiocyanate **2** (2 mmol) in anhydrous dioxane (10 mL). The reaction mixture was heated at reflux for 8-10 h. Then the solvent was removed under reduced pressure and the residue was triturated with ethanol. The precipitate was filtered by suction and recrystallized with 1:1 EtOH-water to afford the title compounds **3** as ivory-white crystals.

Procedure B (under microwave-assisted and solvent-free conditions): A mixture of 2-amino-4,6-diarylpyrimidine **2** (2 mmol) **1** and 2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl isothiocyanate **2** (2 mmol) was grinded in a 5 mL porcelain beaker. Then the mixture was put into a domestic microwave oven (the power output is 750 W). The adjustor of the microwave oven was set to the proper temperature (about 50 ºC). The reactants were irradiated for a period of 5-7 min. The mixture became dark-yellow paste in reaction process. The reaction was traced with thin-layer chromatography. The reaction mixture was cooled to room temperature, triturated with ethanol, filtered by suction and recrystallized with ethanol/toluene (1:1) to afford the title compounds **3** as ivory-white or white crystals.

3a (R=4-F): IR (KBr, ν_{max}, cm^{-1}): 3414, 3170, 1755, 1601, 1590, 1524, 1511, 1496, 1365, 1223, 1243, 1038; ^{1}H NMR (DMSO-d_6) δ: 12.11 (d, 1H, J = 9.5 Hz, H_a), 11.03 (s, 1H, H_b), 6.18 (t, 1H, J = 9.5 Hz, H-1), 5.07 (t, 1H, J = 9.25 Hz, H-2), 5.51 (t, 1H, J = 9.5 Hz, H-3), 5.05 (t, 1H, J = 9.5 Hz, H-4), 4.23-4.20 (m, 2H, H-5, H-6a), 4.07-4.05 (m, 1H, H-6b), 8.22 (s, 1H, H-5'), 8.28-8.20 (m, 2H, H-2" and H-6"), 7.13 (d, 2H, J = 8.25 Hz, H-3" and H-5"), 8.36 (qd, 2H, J = 8.5, 1.75 Hz, H-2"' and H-6"'), 7.43 (t, 2H, J = 8.5 Hz, H-3"' and H-5"'), 1.95-2.03 (s, 12H, 4 × $COCH_3$), 3.88 (s, 3H, 4"-OCH_3); ^{13}C NMR (DMSO-d_6): δ 181.3 (C=S), 169.3-169.9 (4 × CH_3CO), 157.4 (C-2'), 165.2 (C-4'), 106.9 (C-5'), 164.5 (C-6'), 127.7 (C-1"), 129.3 (C-2" and C-6"), 162.3 (C-4"), 127.7 (C-3" and C-5"), 132.2 (C-1"'), 129.9 (J_{CF} = 8.68 Hz, C-2"' and C-6"'), 163.4 (J_{CF} = 34.96 Hz, C-4"'), 115.9 (J_{CF} = 9.18 Hz, C-3"' and C-5"'), 81.8 (C-1), 71.4 (C-2), 72.2 (C-3), 68.0 (C-4), 72.7 (C-5), 61.9 (C-6), 55.5 (4"-OCH_3), 20.2-20.4 (4 × CH_3CO).

3b (R=4-Cl): IR (KBr, ν_{max}, cm^{-1}): 3427, 3163, 1747, 1593, 1520, 1490, 1365, 1232, 1087; ^{1}H NMR (DMSO-d_6) δ: 12.06 (d, 1H, J = 9.0 Hz, H_a), 11.04 (s, 1H, H_b), 6.19 (t, 1H, J = 9.25 Hz, H-1), 5.08 (t, 1H, J = 10.0 Hz, H-2), 5.52 (t, 1H, J = 9.5 Hz, H-3), 5.06 (t, 1H, J = 9.5 Hz, H-4), 4.25-4.20 (m, 2H, H-5, H-6a), 4.07-4.00 (m, 1H, H-6b), 8.25 (s, 1H, H-5'), 8.30 (d, 2H, J = 8.75 Hz, H-2" and H-6"), 7.14 (d, 2H, J = 8.75 Hz, H-3" and H-5"), 8.32 (d, 2H, J = 8.5 Hz, H-2"' and H-6"'), 7.68 (t, 2H, J = 8.5 Hz, H-3"' and H-5"'), 1.96-2.04 (s, 12H, 4 × $COCH_3$), 3.89 (s, 3H, 4"-OCH_3); ^{13}C NMR (DMSO-d_6): δ 181.3 (C=S), 169.2-169.8 (4 × CH_3CO), 157.3 (C-2'), 164.7 (C-4'), 106.7 (C-5'), 163.2 (C-6'), 127.6 (C-1"), 129.1

(C-2" and C-6"), 162.3 (C-4"), 114.3 (C-3" and C-5"), 136.3 (C-1'"), 128.9 (C-2'" and C-6'"), 134.5 (C-4'"), 129.2 (C-3'" and C-5'"), 81.8 (C-1), 71.4 (C-2), 72.2 (C-3), 68.0 (C-4), 72.7 (C-5), 61.8 (C-6), 55.4 (4"-OCH_3), 20.1-20.3 (4 × CH_3CO).

3c (R=3-Cl): IR (KBr, ν_{max}, cm^{-1}): 3473, 3167, 1752, 1590, 1520, 1367, 1231, 1039; ^1H NMR (DMSO-d_6): δ 12.20 (d, 1H, *J* = 9.0 Hz, H_a), 11.09 (s, 1H, H_b), 6.19 (t, 1H, *J* = 9.25 Hz, H-1), 5.08 (t, 1H, *J* = 9.5 Hz, H-2), 5.55 (t, 1H, *J* = 9.75 Hz, H-3), 5.06 (t, 1H, *J* = 9.5 Hz, H-4), 4.24-4.19 (m, 2H, H-5, H-6a), 4.07-4.00 (m, 1H, H-6b), 8.37 (s, 1H, H-5'), 8.33 (d, 2H, *J* = 8.75 Hz, H-2" and H-6"), 7.15 (d, 2H, *J* = 8.75 Hz, H-3" and H-5"), 8.30 (d, 1H, *J* = 8.0 Hz, H-2'"), 7.64 (t, 1H, *J* = 7.75 Hz, H-4'"), 7,69 (dt, *J* = 8.0, 1.0 Hz, H-5'"), 8.3 (d, *J* = 8.0 Hz, H-6'"), 1.94-2.03 (s, 12H, 4 × $COCH_3$), 3.89 (s, 3H, 4"-OCH_3); ^{13}C NMR (DMSO-d_6): δ 181.3 (C=S), 169.2-169.8 (4 × CH_3CO), 157.3 (C-2'), 165.1 (C-4'), 106.8 (C-5'), 164.9 (C-6'), 126.9 (C-1"), 129.4 (C-2" and C-6"), 162.3 (C-4"), 114.3 (C-3" and C-5"), 134.0 (C-1'"), 130.7 (C-2'"), 131.1 (C-3'"), 127.6 (C-4'"), 131.1 (C-5'"), 126.0 (C-6'"), 81.7 (C-1), 71.5 (C-2), 71.9 (C-3), 68.0 (C-4), 72.6 (C-5), 61.7 (C-6), 55.4 (4"-OCH_3), 20.1-20.3 (4 × CH_3CO).

3d (R=2-Cl): IR (KBr, ν_{max}, cm^{-1}): 3437, 3166, 1748, 1599, 1515, 1367, 1230, 1039; ^1H NMR (DMSO-d_6) δ: 11.95 (d, 1H, *J* = 9.5 Hz, H_a), 11.08 (s, 1H, H_b), 6.16 (t, 1H, *J* = 9.0 Hz, H-1), 5.00 (t, 1H, *J* = 9.0 Hz, H-2), 5.49 (t, 1H, *J* = 9.5 Hz, H-3), 4.98 (t, 1H, *J* = 9.5 Hz, H-4), 4.18-4.15 (m, 2H, H-5, H-6a), 4.05-4.00 (m, 1H, H-6b), 7.95 (s, 1H, H-5'), 8.32 (d, 2H, *J* = 9.0 Hz, H-2" and H-6"), 7.13 (d, 2H, *J* = 9.0 Hz, H-3" and H-5"), 7.69 (dd, 1H, *J* = 8.5, 0.5 Hz, H-3'"), 7.55 (tt, 1H, *J* = 9.0, 0.5 Hz, H-4'"), 7,59 (td, *J* = 7.5, 2.0 Hz, H-5'"), 7.79 (dd, *J* = 7.5, 1.5 Hz, H-6'"), 1.93-2.03 (s, 12H, 4 × $COCH_3$), 3.88 (s, 3H, 4"-OCH_3); ^{13}C NMR (DMSO-d_6): δ 181.4 (C=S), 169.2-169.7 (4 × CH_3CO), 156.9 (C-2'), 164.4 (C-4'), 111.0 (C-5'), 164.4 (C-6'), 127.5 (C-1"), 129.2 (C-2" and C-6"), 162.3 (C-4"), 114.4 (C-3" and C-5"), 131.1 (C-1'"), 135.7 (C-2'"), 131.4 (C-3'"), 127.4 (C-4'"), 127.4 (C-5'"), 130.3 (C-6'"), 81.7 (C-1), 71.0 (C-2), 72.2 (C-3), 67.9 (C-4), 72.5 (C-5), 61.5 (C-6), 55.4 (4"-OCH_3), 20.1-20.3 (4 × CH_3CO).

3e (R=4-Br): IR (KBr, ν_{max}, cm^{-1}): 3414, 3170, 1755, 1590, 1524, 1511, 1496, 1365, 1223, 1243, 1038; ^1H NMR (DMSO-d_6) δ: 12.06 (d, 1H, *J* = 9.5 Hz, H_a), 11.04 (s, 1H, H_b), 6.19 (t, 1H, *J* = 9.25 Hz, H-1), 5.08 (t, 1H, *J* = 9.75 Hz, H-2), 5.51 (t, 1H, *J* = 9.75 Hz, H-3), 5.06 (t, 1H, *J* = 9.5 Hz, H-4), 4.25-4.20 (m, 2H, H-5, H-6a), 4.06-4.00 (m, 1H, H-6b), 8.26 (s, 1H, H-5'), 8.25 (d, 2H, *J*= 9.0 Hz, H-2" and H-6"), 7.14 (d, 2H, *J* = 9.0 Hz, H-3" and H-5"), 8.30 (d, 2H, *J* = 8.25 Hz, H-2'" and H-6'"), 7.82 (d, 2H, *J* = 8.25 Hz, H-3'" and H-5'"), 1.96-2.04 (s, 12H, 4 × $COCH_3$), 3.89 (s, 3H, 4"-OCH_3); ^{13}C NMR (DMSO-d_6): δ 181.2 (C=S), 169.2-169.7 (4 × CH_3CO), 157.3 (C-2'), 164.7 (C-4'), 106.6 (C-5'), 163.3 (C-6'), 127.6 (C-1"), 129.3 (C-2" and C-6"), 162.3 (C-4"), 114.3 (C-3" and C-5"), 134.8 (C-1'"), 129.2 (C-2'" and C-6'"), 125.2 (C-4'"), 131.8 (C-3'" and C-5'"), 81.8 (C-1), 71.3 (C-2), 72.2 (C-3), 68.0 (C-4), 72.7 (C-5), 61.8 (C-6), 55.4 (4"-OCH_3), 20.1-20.3 (4 × CH_3CO).

3f (R=H): IR (KBr, ν_{max}, cm^{-1}): 3435, 3170, 1750, 1595, 1515, 1493, 1364, 1243, 1223, 1059, 1041; ^1H NMR (DMSO-d_6) δ: 12.22 (d, 1H, *J* = 9.0 Hz, H_a), 11.06 (s,1H, H_b), 6.19 (t, 1H, *J* = 9.25 Hz, H-1), 5.04 (t, 1H, *J* = 9.5 Hz, H-2), 5.52 (t, 1H, *J* = 9.5 Hz, H-3), 5.02 (t, 1H, *J* = 9.5 Hz, H-4), 4.21-4.20 (m, 2H, H-5, H-6a), 4.05-4.00 (m, 1H, H-6b), 8.25 (s, 1H, H-5'), 8.30 (td, 2H, *J*= 8.0, 2.0 Hz, H-2" and H-6"), 7.64-7.60 (m, 3H, H-3", H-4" and H-5"), 8.32 (d, 2H, *J* = 9.5 Hz, H-2'" and H-6'"), 7.15 (d, 2H, *J* = 9.0 Hz, H-3'" and H-5'"), 1.95-2.03 (s, 12H, 4 × $COCH_3$), 3.89 (s, 3H, 4"-OCH_3); ^{13}C NMR (DMSO-d_6): δ 181.3 (C=S), 169.2-169.8 (4 × CH_3CO), 162.3 (C-2'), 164.7 (C-4'), 106.7 (C-5'), 164.4 (C-6'), 127.8 (C-1"), 127.4 (C-2" and C-6"), 157.5 (C-4"), 114.3 (C-3" and C-5"), 135.7 (C-1'"), 127.4 (C-2'" and C-6'"), 131.6 (C-4'"), 129.3 (C-3'" and C-5'"), 81.7 (C-1), 71.5 (C-2), 72.1 (C-3), 68.0 (C-4), 72.6 (C-5), 61.8 (C-6), 55.3 (4"-OCH_3), 20.1-20.3 (4 × CH_3CO).

3g (R=4-Me): IR (KBr, ν_{max}, cm^{-1}): 3433, 1749, 1595, 1524, 1501, 1363, 1249, 1225, 1043; ^1H NMR (DMSO-d_6) δ: 12.24 (d, 1H, *J* = 9.5 Hz, H_a), 11.94 (s, 1H, H_b), 6.24 (t, 1H, *J* = 9.0 Hz, H-1), 5.09 (t, 1H, *J* = 9.75 Hz, H-2), 5.56 (t, 1H, *J* = 9.25 Hz, H-3), 5.07 (t, 1H, *J* = 9.0 Hz, H-4), 4.26-4.23 (m, 2H, H-5, H-6a), 4.09-4.00 (m, 1H, H-6b), 8.16 (s, 1H, H-5'), 8.29 (d, 2H, *J* = 8.75 Hz, H-2" and H-6"), 7.13 (d, 2H, *J* = 8.75 Hz, H-3" and H-5"), 8.17 (d, 2H, *J* = 8.0 Hz, H-2'" and H-6'"), 7.41 (d, 2H, *J* = 8.0 Hz, H-3'" and H-5'"), 1.97-2.06 (s, 12H, 4 × $COCH_3$), 3.88 (s, 3H, 4"-OCH_3), 2.42 (s, 3H, 4'"-CH_3); ^{13}C NMR (DMSO-d_6): δ 181.9 (C=S), 169.2-169.8 (4 × CH_3CO), 157.9 (C-2'), 165.1 (C-4'), 106.8 (C-5'), 164.8 (C-6'), 128.4 (C-1"), 130.0 (C-2" and C-6"), 162.7 (C-4"), 114.8 (C-3" and C-5"), 133.4 (C-1'"), 127.8 (C-2'" and C-6'"), 142.2 (C-4'"), 129.7 (C-3'" and C-5'"), 82.4 (C-1), 72.0 (C-2), 72.8 (C-3), 68.6 (C-4), 73.3 (C-5), 62.3 (C-6), 55.9 (4"-OCH_3), 21.5 (s, 3H, 4'"-Me), 20.1-20.3 (4 × CH_3CO).

3h (R=4-iPr): IR (KBr, ν_{max}, cm^{-1}): 3328, 3170, 1755, 1592, 1524, 1509, 1366, 1233, 1037; ^1H NMR (DMSO-d_6) δ: 12.23 (d, 1H, *J* = 9.0 Hz, H_a), 10.98 (s, 1H, H_b), 6.20 (t, 1H, *J* = 9.0 Hz, H-1), 5.06 (t, 1H, *J* = 9.5 Hz, H-2), 5.52 (t, 1H, *J* = 9.5 Hz, H-3), 5.04 (t, 1H, *J* = 9.5 Hz, H-4), 4.24-4.20 (m, 2H, H-5, H-6a), 4.07-4.00 (m, 1H, H-6b), 8.20 (s, 1H, H-5'), 8.23 (d, 2H, *J* = 8.25 Hz, H-2" and H-6"), 7.14 (d, 2H, *J* = 9.0 Hz, H-3" and H-5"), 8.30 (d, 2H, *J* = 9.0 Hz, H-2'" and H-6'"), 7.48 (d, 2H, *J* = 8.25 Hz, H-3'" and H-5'"), 1.96-2.04 (s, 12H, 4 × $COCH_3$), 3.88 (s, 3H, 4"-OCH_3), 3.02 [d, 1H, *J* = 7.0 Hz, $CH(CH_3)_2$], 2.42 (s, 3H, 4'"-CH_3), 1.27 [d, 6H, *J* = 7.0 Hz, $CH(CH_3)_2$]; ^{13}C NMR (DMSO-d_6): δ 181.3 (C=S), 169.2-169.8 (4 × CH_3CO), 157.9 (C-2'), 164.4 (C-4'), 106.4 (C-5'), 162.2 (C-6'), 127.8 (C-1"), 129.2 (C-2" and C-6"), 162.2 (C-4"), 114.3 (C-3" and C-5"), 133.2 (C-1'"), 126.8 (C-2'" and C-6'"), 127.4 (C-3'" and C-5'"), 81.8 (C-1), 71.5 (C-2), 72.1 (C-3), 68.0 (C-4), 72.6 (C-5), 61.7 (C-6), 55.4 (4"-OCH_3), 33.3[4'"-$CH(CH_3)_2$], 23.5 [4'"-$CH(CH_3)_2$], 20.1-20.3 (4 × CH_3CO).

3i (R=4-OMe): IR (KBr, ν_{max}, cm^{-1}): 3338, 3146, 1750, 1591, 1510, 1363, 1226, 1243, 1031; ^1H NMR (DMSO-d_6) δ: 12.25 (d, 1H, *J* = 9.0 Hz, H_a), 10.93 (s, 1H, H_b), 6.19 (t, 1H, *J* = 9.0 Hz, H-1), 5.06 (t, 1H, *J* = 9.5 Hz, H-2), 5.52 (t, 1H, *J* = 9.5 Hz, H-3), 5.04 (t, 1H, *J*= 9.5 Hz, H-4), 4.23-4.21 (m, 2H, H-5, H-6a), 4.07-4.00 (m, 1H, H-6b), 8.16 (s, 1H, H-5'), 8.28 (dd, 4H, *J* = 7.0, 1.5 Hz, H-2" and H-6"), 7.14 (dd, 4H, *J* = 7.0, 1.5 Hz, H-3" and H-5"), 1.95-2.04 (s, 12H, 4 × $COCH_3$), 3.89 (s, 6H, 4"-OCH_3 and 4'"-OCH_3); ^{13}C NMR (DMSO-d_6): δ 181.3 (C=S), 169.2-169.8 (4 × CH_3CO), 157.3 (C-2'), 164.1 (C-4'), 105.8 (C-5'), 164.1 (C-6'), 127.6 (C-1"), 129.1 (C-2"

and C-6", C-2'" and C-6'"), 162.2 (C-4" and C-4'"), 114.4 (C-3" and C-5", C-3'" and C-5'"), 81.8 (C-1), 71.5 (C-2), 71.2 (C-3), 68.0 (C-4), 72.6 (C-5), 61.8 (C-6), 55.4 (4"-OCH_3 and 4'"-OCH_3), 20.1-20.3 (4 × CH_3CO).

3j (R=3-OMe): IR (KBr, ν_{max}, cm^{-1}): 3414, 3165, 1753, 1590, 1521, 1365, 1222, 1039; 1H-NMR (DMSO-d_6) δ: 12.29 (d, 1H, *J* = 9.0 Hz, H_a), 10.98 (s, 1H, H_b), 6.20 (t, 1H, *J* = 9.0 Hz, H-1), 5.05 (t, 1H, *J* = 9.5 Hz, H-2), 5.54 (t, 1H, *J* = 9.5 Hz, H-3), 5.04 (t, 1H, *J* = 9.5 Hz, H-4), 4.24 (dq, 1H, *J* = 9.5, 2.0 Hz, H-5), 4.20 (dd, 1H, *J* = 12.5, 4.5 Hz, H-6a), 4.08 (dd, 1H, *J* = 12.5, 2.0 Hz, H-6b), 8.22 (s, 1H, H-5'), 8.32 (d, 2H, *J* = 9.0 Hz, H-2" and H-6"), 7.14 (d, 2H, *J* = 9.0 Hz, H-3" and H-5"), 7.84 (d, 1H, *J* = 2.0 Hz, H-2'"), 7.20 (dd,1H, *J* = 8.0, 2.0 Hz, H-4'"), 7.89 (d, *J* = 7.5 Hz, H-5'"), 7.52 (t, *J* = 8.0 Hz, H-6'"), 1.95-2.04 (s, 12H, 4 × $COCH_3$), 3.92 (s, 3H, 3'"-OCH_3), 3.89 (s, 3H, 4"-OCH_3); ^{13}C NMR (DMSO-d_6): δ 181.2 (C=S), 169.2-169.9 (4 × CH_3CO), 157.3 (C-2'), 164.8 (C-4'), 106.7 (C-5'), 164.0 (C-6'), 127.8 (C-1"), 129.3 (C-2" and C-6"), 162.2 (C-4"), 114.4 (C-3" and C-5"), 137.0 (C-1'"), 112.8 (C-2'"), 159.8 (C-3'"), 117.0 (C-4'"), 129.9 (C-5'"), 119.7 (C-6'"), 81.7 (C-1), 71.6 (C-2), 72.0 (C-3), 68.0 (C-4), 72.6 (C-5), 61.7 (C-6), 55.4 (4"-OCH_3), 55.3 (3'"-OCH_3), 20.1-20.3 (4 × CH_3CO).

3k (R=4-NMe_2): IR (KBr, ν_{max}, cm^{-1}): 3414, 3170, 1755, 1601, 1585, 1504, 1496, 1372, 1223, 1243, 1037; ^1H NMR (DMSO-d_6) δ: 12.43 (d, 1H, *J* = 9.5 Hz, H_a), 10.77 (s, 1H, H_b), 6.18 (t, 1H, *J* = 9.0 Hz, H-1), 5.07 (t, 1H, *J* = 9.25 Hz, H-2), 5.52 (t, 1H, *J* = 9.5 Hz, H-3), 5.03 (t, 1H, *J* = 9.25 Hz, H-4), 4.24-4.20 (m, 2H, H-5 and H-6a), 4.07-4.00 (m, 1H, H-6b), 8.04 (s, 1H, H-5'), 8.17 (d, 2H, *J*= 9.25 Hz, H-2" and H-6"), 6.88 (d, 2H, *J* = 9.0 Hz, H-3" and H-5"), 8.25 (d, 2H, *J* = 8.75 Hz, H-2'" and H-6'"), 7.12 (d, 2H, *J* = 8.75 Hz, H-3'" and H-5'"), 2.51-2.48 (s, 12H, 4 × $COCH_3$), 3.88 (s, 3H, 4'"-OCH_3), 3.05 [s, 3H, 4"-$N(CH_3)_2$]; ^{13}C NMR (DMSO-d_6): δ 181.3 (C=S), 169.3-169.8 (4 × CH_3CO), 157.9 (C-2'), 164.5 (C-4'), 104.6 (C-5'), 157.9 (C-6'), 128.8 (C-1"), 128.9 (C-2" and C-6"), 161.9 (C-4"), 114.2 (C-3" and C-5"), 128.1 (C-1'"), 111.4 (C-2'" and C-6'"), 128.7 (C-3'" and C-5'"), 81.8 (C-1), 71.6 (C-2), 72.1 (C-3), 68.0 (C-4), 72.5 (C-5), 61.8 (C-6), 55.4 (4"-OCH_3), 40.0 [4'"-$N(Me)_2$], 20.1-20.3 (4 × CH_3CO).

RESULTS AND DISCUSSION

Some 2-amino-4,6-diarylpyrimidines were prepared according to previous procedure by reaction of substituted chalcones and guanidine. These chalcones were synthesized from 4-methoxyacetophenone and substituted benzaldehydes. We prepared required 2-amino-4,6-diarylpyrimidines **1a-k** by ring-closure condensation of substituted chalcones and guanidine hydrochloride in the presence of sodium hydroxide in ethanol under microwave-assisted method[14a].

N-(2,3,4,6-Tetra-O-acetyl-β-D-glucopyranosyl)-*N*'-(4',6'-diarylpyrimidine-2'-yl)thioureas **3a-k** were synthesized by the condensation of tetra-O-acetyl-β-D-glucopyranosyl isothiocyanate (**2**) and corresponding 2-amino-4,6-diarylpyrimidines (**1a-k**). We performed this reaction by using two methods, by refluxing in anhydrous dioxane or by executing in microwave oven (**Scheme-I**).

The reaction results with or without microwave irradiation are shown in Table-1. It can be seen that the presence of microwave irradiation both accelerated the reactions and gave higher yields, in 55-77 and 68-82 %, respectively. The reaction time for synthesis of compounds **3a-k** was shortened from 14 h to only 3 min with the solvent-free procedure (Table-1).

In the refluxing cases, 2-aminopyrimidines and peracetylated glucopyranosyl isothiocyanate were dissolved in anhydrous dioxane for first several minutes of microwave irradiation and then the reaction mixture became pasty. The solvent was distilled off and resultant sticky residue was triturated with ethanol to afford title compound **3a-k** that were recrystallized with ethanol:toluene (1:1). In microwave irradiation cases, a mixture of 2-aminopyrimidine and peracetylated glucopyranosyl isothiocyanate was grinded together and irradiated in microwave oven. Reaction yields were high in both the methods (refluxing and using microwave oven), in 60-68 and 72-77 %, respectively. All these obtained thioureas are soluble in common organic solvents (such as ethanol, methanol, toluene, benzene, DMF, *etc.*). Their structures have been confirmed by spectral data (such as IR, NMR spectra).

IR spectra show characteristic bands in ranges of 3437-3414 and 3170-3163 (νNH), 1755-1747 (νC=O), 1594, 1578, 1526, 1495 (νC=C), 1367-1363 (νC=S), 1243-1223 and 1087-1038 cm^{-1} (νCOC). ^1H NMR spectra show resonance signals which are specified for protons in thiourea-NH groups at δ = 12.43-11.95 ppm in doublet with coupling constants *J* = 9.5-9.0 Hz which belongs to proton NH_a and δ = 1.08-10.77 ppm in singlet which belongs to proton NH_b. Some resonance signals are in region δ = 8.37-6.88 ppm which belong to some

TABLE 1
N-(2,3,4,6-TETRA-O-ACETYL-β-D-GLUCOPYRANOSYL)-*N*'-4',6'- DIARYLPYRIMIDIN -2'-YL)THIOUREAS (**3a-k**)

Entry	R	m.p. (ºC)	Yield (%)		Reaction time	
			Proc-1	Proc-2	Proc-1 (h)	Proc-1 (min)
3a	4-F	187-190	70	80	14	2
3b	4-Cl	182-185	66	72	14	3
3c	3-Cl	174-175	70	77	14	3
3d	2-Cl	203-204	55	68	14	3
3e	4-Br	193-194	70	77	14	3
3f	H	213-214	68	77	14	2
3g	4-Me	188-190	66	78	14	5
3h	4-iPr	178-180	77	82	14	3
3i	4-OMe	170-171	69	70	14	7
3j	3-OMe	152-154	65	72	14	7
3k	4-$N(Me)_2$	197-198	65	80	14	3

Note: Proc-1: Conventional heating; Proc-2: solvent-free MW-assisted heating.

aromatic protons in amino component. Protons C-H in pyranose ring of monosaccharide have some resonance peaks with chemical shifts from 6.24-4.20 ppm as observed in ^{1}H NMR spectra of monosaccharide compounds[4]. Proton H-1 has chemical shift in region δ = 6.24-6.16 ppm (in triplet) with couple constant J_{12} = 9.0-9.5 Hz. Resonance signal of proton H-2 appears in triplet in region δ = 5.08-5.00 ppm with $J_{2,1}$ = 9.0-9.5 Hz. The values of coupling constant are appropriate to *trans*-H-H couple interaction and indicate β-anomer configuration of NH-thiourea group[13,14]. Another protons such as H-3, H-4 have triplet resonance signals in regions δ = 5.52-5.53 ppm (with coupling constants $J_{3,4}$ = 9.5 Hz) and δ = 5.02-5.04 ppm (with coupling constants $J_{4,3}$ = $J_{4,5}$ = 9.5 Hz), respectively.

^{13}C NMR spectra show four-parted regions at δ 181.3-169.2, 165.1-104.6, 82.4-61.7 and 20.4-20.1 ppm. The magnetic resonance signals of the carbonyl bonds C=O in acetyl groups have appeared in the low-field regions at δ = 169.9-169.2 ppm. In addition, there were some resonance peaks in high-field region at δ = 20.4-20.1 ppm that's indicated the present of methyl groups on acetyl functions. The aromatic and hetero-aromatic carbon atoms had chemical shifts in region at δ = 165.1-104.6 ppm. Six carbon atoms in pyranose ring had clearly resonance signals in region at δ = 82.4-61.7 ppm.

Conclusion

In summary, we developed the new method for preparation of *N*-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-*N*'-(4,6-diarylpyrimidine-2-yl)thioureas (**3a-k**) using microwave irradiation. This heating method offers several advantages: faster reaction rates (only in 2-7 min) and high yields (68-82 % *versus* 55-77 %), while the classical method of formation of these thioureas involves long reaction times (until 14 h). All compounds **3a-k** were characterized by spectroscopic methods.

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REFERENCES

1. K.L. Sayle, J. Bentley, F.T. Boyle, A.H. Calvert, Y. Cheng, N.J. Curtin, J.A. Endicott, B.T. Golding, I.R. Hardcastle and P. Jewbury, *Bioorg. Med. Chem. Lett*., **13**, 3079 (2003).
2. (a) S. Chandrasekaran and S. Nagarajan, *IL Farmaco*, **60**, 279 (2005); (b) M.T. Cocco, C. Congiu, V. Liliu and V. Onnis, *Bioorg. Med. Chem*., **14**, 366 (2006); (c) V.R. Gadhachanda, B. Wu, Z. Wang, K.L. Kuhen, J. Caldwell, H. Zondler, H. Walter, M. Havenhand and Y. He, *Bioorg. Med. Chem. Lett*., **17**, 260 (2007).
3. G.S. Rashinkar, S.B. Pore, K.B. Mote and R.S. Salunkhe, *Indian J. Chem*., **48B**, 606 (2009).
4. (a) C. Walpole, S.Y. Ko, M. Brown, D. Beattie, E. Campbell, F. Dickenson, S. Ewan, G.A. Hughes, M. Lemaira, J. Lerpiniere, S. Patel and L. Urban, *J. Med. Chem*., **41**, 3159 (1998); (b) E.G. Chalina and L. Chakarova, *Eur. J. Med. Chem*., **33**, 975 (1998).
5. J. Wang, H. Li, X. Yu, L. Zu and W. Wang, *Org. Lett*., **7**, 4293 (2005).
6. R.A. Abramovitch, *Org. Prep. Proc. Int*., **23**, 683 (1991); (b) A. Loupy, Microwaves in Organic Synthesis, Wiley-VCH, Weinheim, edn. 2, 306 (2006).
7. (a) C. Gabriel, S. Gabriel, E. Grant, B.S.J. Halstead and D. Mingos, *Chem. Soc. Rev*., **27**, 213 (1997); (b) P. Lidstorm, J. Tierney, B. Wathey and J. Westman, *Tetrahedron*, **57**, 9225 (2001).
8. C. Walpole, S.Y. Ko, M. Brown, D. Beattie, E. Campbell, F. Dickenson, S. Ewan, G.A. Hughes, M. Lemaira, J. Lerpiniere, S. Patel and L. Urban, *J. Med. Chem*., **41**, 3159 (1998).
9. (a) E.G. Chalina and L. Chakarova, *Eur. J. Med. Chem*., **33**, 975 (1998); (b) H. Stark, K. Purand, X. Ligneau, A. Rouleau, J.-M. Arrang, M. Garbarg, J.-C. Schwartz and W. Schunack, *J. Med. Chem*., **39**, 1157 (1996).
10. (a) J. Wang, H. Li, X. Yu, L. Zu and W. Wang, *Org. Lett*., **7**, 4293 (2005); (b) J. Seayad and B. List, *Org. Biomol. Chem*., **3**, 719 (2005); (c) P.M. Pihko, *Angew. Chem. Int. Ed*., **43**, 2062 (2004); (d) T.P. Yoon and E.N. Jacobsen, *Angew. Chem. Int. Ed*., **44**, 466 (2005).
11. (a) P.K. Mohanta, S. Dhar, S.K. Samal, H. Ila and H. Junjappa, *Tetrahedron*, **56**, 629 (2000); (b) T. Aoyama, S. Murata, Y. Nagata, T. Takido and M. Kodamari, *Tetrahedron Lett*., **46**, 4875 (2005); (c) M. Kodomari, M. Suzuki, K. Tanigawa and T. Aoyama, *Tetrahedron Lett*., **46**, 5841 (2005); (d) K. Bhandari, S. Srivatsava and G. Shankar, *Bioorg. Med. Chem*., **12**, 4189 (2004).
12. K.G. Bama and K.B. Rajani, *Indian J. Chem*., **27B**, 1157 (1988).
13. Yong-Hua Liu and Ling-Hua Cao, *Carbohydr. Res*., **343**, 615 (2008).
14. (a) N.D. Thanh and N.T.T. Mai, *Carbohydr. Res*., **344**, 2399 (2009); (b) N.D. Thanh, N.T.K. Giang and L.T. Hoai, *E-J. Chem*., **7**, 899 (2010).
15. R.L. Lemieux, In eds. R.L. Whistler and M.L. Wolfrom, Methods in Carbohydrate Chemistry, Academic Press, New York, Vol. 2, p. 221 (1963).