13rd International Electronic Conference on Synthetic Organic Chemistry (ECSOC-13), 1-30 November 2009.
http://www.mdpi.org/ecsoc-13/ & http://www.usc.es/congresos/ecsoc/13/

[e005]

Microwave-Assisted Synthesis of *N*-Tetra-*O*-Acetyl-β-D-Glucopyranosyl-*N*'-(4',6'-Diarylpyrimidine-2'-yl)thioureas

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Abstract. Some 2-amino-4,6-diarylpyrimidines **2** have been prepared from substituted benzylideneacetophenones and guanidine hydrochloride in presence of alkali by conventional heating in alcoholic medium and microwave heating in solvent-free conditions. *N*-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-*N'*-(4',6'-diarylpyrimidine-2'-yl)thioureas **4** have been synthesized by reaction of per-*O*-acetylated glucopyranosyl isothiocyanate **1** and substituted 2-amino-4,6-diarylpyrimidines **2**. Two different methods have been used, namely refluxing in anhydrous dioxane and solvent-free microwave-assisted coupling. The second procedure afforded higher yields in much shorter reaction times. The compounds **2** and **4** were tested for their antibacterial and antifungal activities *in vitro* against *Staphylococcus epidermidis*, *Enterobacter aerogenes* and *Candida albicans* by disc diffusion method.

Keywords: pyrimidine; glucopyranosyl thiourea; glucopyranosyl isothiocyanate; microwave-assisted method

The pyrimidine structural motif is a fundamental part of nucleic acids and has been associated with a number of biological activities.[1,2] Aminopyrimidine derivatives have displayed interesting antibacterial, antitumor and HIV-I inhibiting activity.[2] Both pyrimidine and aminopyrimidine moieties occur in commercially available drugs such as anti-atherosclerotic Aronixil®, anti-histamine Thonzylamine®, anti-anxiolytic Buspirone® and other medicinally relevant compounds.[3]

In other hand, sugar isothiocyanates are among the most versatile synthetic intermediates in carbohydrate chemistry.[4] They play a pivotal role in the preparation of a broad series of functional groups such as amide, isonitrile, carbodiimide, and *N*-thiocarbonyl derivatives allowing, simultaneously, the covalent coupling of a quite unrestricted variety of structures to the saccharide part.[5] Moreover, isothiocyanates are important reagents in heterocyclic chemistry, which may be exploited in the synthesis of nucleosides and other *N*-glycosyl structures.[6,7]

One of the most popular and interesting approach in the context "green chemistry" is employing microwave energy for conducting chemical transformations, which allows a higher speed of heating, shorter reaction times, is compatible with solvent-free conditions and very often lead to higher selectivities.[8-11]

Thioureas and its derivatives are biologically important compounds and are useful fungicides, herbicides,[12] and antibacterial agents.[13] They have also found use in organocatalysis.[14,15] Thioureas have been synthesized by the reaction of primary and secondary amines with thiophosgene and isothiocyanates.[4,5,16-19]

Glucopyranosyl thioureas containing heterocycles (such as thiazole, benzothiazole,[20]

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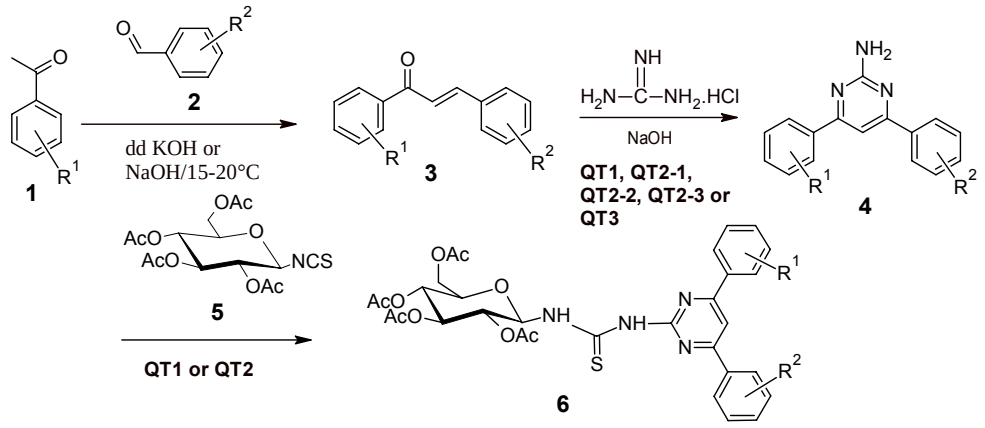
thiadiazole[21]) were synthesized using conventional heating method. We report herein the preparation of some peracetylated glucopyranosyl thioureas containing pyrimidine nucleus both under classical heating and solvent-free microwave irradiation conditions.



where 3, **4**, **5** and **6**:
+ with R^1=H, R^2=H (**a1**), 4-F (**b1**), 4-Cl (**c1**), 3-Cl (**d1**), 2-Cl (**e1**), 4-Br (**f1**), 4-Me (**g1**), 4-iPr (**h1**), 4-OMe (**i1**), 3-OMe (**j1**), 2-OMe (**k1**), 3,4-O_2CH_2 (**l1**), 4-OH (**m1**), 3-OH (**n1**), 2-OH (**o1**), 4-N(Me)$_2$ (**p1**);
+ with R^1=4-OMe, R^2=H (**a2=i1**), 4-F (**b2**), 4-Cl (**c2**), 3-Cl (**d2**), 2-Cl (**e2**), 4-Br (**f2**), 4-Me (**g2**), 4-iPr (**h2**), 4-OMe (**i2**), 3-OMe (**j2**), 2-OMe (**k2**), 3,4-O_2CH_2 (**l2**), 4-OH (**m2**), 3-OH (**n2**), 2-OH (**o2**), 4-N(Me)$_2$ (**p2**);
+ with R^1=4-Br, R^2=H (**a3=f1**), 4-F (**b3**), 4-Cl (**c3**), 3-Cl (**d3**), 2-Cl (**e3**), 4-Br (**f3**), 4-Me (**g3**), 4-iPr (**h3**), 4-OMe (**i3**), 3-OMe (**j3**), 2-OMe (**k3**), 3,4-O_2CH_2 (**l3**), 4-OH (**m3**), 3-OH (**n3**), 2-OH (**o3**), 4-N(Me)$_2$ (**p3**).

QT1: Convernient heating with refluxing method in 96% ethanol; **QT2-1**: Heating with refluxing in MW oven; **QT2-2**: Microwave-assisted with solvent method; QT2-3: Microwave-assisted solventless method; QT3: Microwave-assisted 'one-pot' method.

Scheme 1

2-Aminopyrimidines were prepared previously by reaction of substituted benzylideneacetophenones **3**[22] with guanidine under reflux in ethanol.[3,23] For the purpose of this work we have prepared new 2-amino-4,6-diarylpyrimidines **4a-p** by ring-closure condensation of substituted benzylideneacetophenones and guanidine hydrochloride in the presence of sodium hydroxide under microwave-assisted conditions and compare the results with the classical procedures (Scheme 1 and Table 1,2). *N*-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-*N'*-(4',6'-diarylpyrimidine-2'-yl)thioureas **6a-p** were subsequently synthesized by the condensation of tetra-*O*-acetyl-*β*-D-glucopyranosyl isothiocyanate and corresponding 2-aminopyrimidines **4a-p**. We performed this reaction by using two methods: by refluxing in anhydrous dioxane for 8-10 h or by irradiation in a domestic microwave oven for a few minutes in solvent-free condition (Scheme 1 and Table 3-5). The last method accelerates the reactions and gave higher yields. We realized that 2-amino-4,6-diphenylpyrimidines with electron-withdrawing group (such NO_2, except halogens) cannot be formed; we tried to perform the reaction of benzylidenacetophenones having nitro-group with guanidine, but the reactions were unsuccessful.

Table 1. Synthetic results of 2-amino-4,6-diarylpyrimidines 4a-q

Entry	mp, ºC	Yield (%)				Reaction time				IR Spectra (cm^{-1})
		QT1	QT2-1	QT2-2	QT2-3	QT1 (h)	QT2-1 (min)	QT2-2 (min)	QT2-3 (min)	ν_{N-H}
4a1	118-119	67	77	81	62	14	5-7	1	9-10	3469;3320
4b1	132-133	67	76	80	65	14	5-7	2	9-10	3501;3338
4c1	160-161	75	75	79	67	14	5-7	3	9-10	3493;3314
4d1	118-119	67	78	88	70	14	5-7	3	9-10	3491;3315
4f1	171-172	70	74	86	69	14	5-7	2	9-10	3493;3293
4g1	127-128	75	75	80	65	14	5-7	1	8-10	3316-3210
4h1	142-143	-	-	-	-	-	-	-	-	3512;3314
4i1	151-152	67	70	88	70	14	5-7	1	5-7	3369;3326
4j1	138-140	68	77	83	66	14	5-7	1	5-7	3429;3301
4l1	190-192	77	78	80	69	14	5-7	4	8-10	3493;3306
4m1	239-240	54	77	82	65	14	5-7	4	8-10	3505;3397
4n1	231-232	55	74	80	66	14	5-7	4	8-10	3325;3194
4o1	181-182	45	82	88	67	14	5-7	4	8-10	3401;3570
4p1	140-142	69	76	79	56	14	5-7	3	8-10	3480;3281
4b2	189-190	65	80	78	-	10	7-10	10-15	-	3319;3480
4c2	156-157	75	78	76	-	10	7-10	10-15	-	3329;3208
4d2	130-131	74	80	82	-	10	7-10	10-15	-	3327;3199
4e2	161-162	55	67	65	-	10	7-10	10-15	-	3326;3194
4f2	167-168	76	82	76	-	10	7-10	10-15	-	3330;3209
4g2	125-126	68	68	65	-	10	7-10	10-15	-	3508;3303
4h2	126-127	71	79	80	-	10	7-10	10-15	-	3380;3309
4i2	179-180	80	84	88	-	10	7-10	10-15	-	3487;3387
4j2	140-141	79	82	78	-	10	7-10	10-15	-	3430;3190
4p2	175-176	78	80	82	-	10	7-10	10-15	-	3482;3297
4b4	198-199	76	79	76	--	10	7-10	10-15	-	3492;3329
4c4	219-220	82	82	76	-	10	7-10	10-15	-	3467;3306
4d4	184-185	79	81	78	-	10	7-10	10-15	-	3464;3316
4e4	170-171	61	77	56	-	10	7-10	10-15	-	3486;3322
4f4	225-226	78	78	68	-	10	7-10	10-15	-	3495;3316
4g4	152-153	75	78	77	-	10	7-10	10-15	-	3498;3302
4h4	155-156	80	81	76	-	10	7-10	10-15	-	3494;3316
4i4	171-172	80	80	77	-	10	7-10	10-15	-	3484;3314
4j4	182-183	77	80	80	-	10	7-10	10-15	-	3328;3305
4k4	150-151	76	77	80	-	10	7-10	10-15	-	3484;3314
4p4	185-186	80	80	82	-	10	7-10	10-15	-	3493;3316
4q	160-161	77	79	76	-	10	7-10	10-15	-	3479;3390

In the refluxing cases, 2-aminopyrimidines **4** and peracetylated glucopyranosyl isothiocyanate **5** were dissolved in anhydrous dioxane. After reaction, the solvent was distilled off, and resultant sticky residue was triturated with ethanol to afford thioureas **6a-p** that were recrystallized with ethanol:toluene (1:1). In MW irradiation cases, a mixture of 2-aminopyrimidine and peracetylated glucopyranosyl isothiocyanate was grinded together and

irradiated in domestic MW oven (750 W). For first several minutes of microwave irradiation (MWI), and then the reaction mixture became pasty. Reaction yields increased using MW oven from 60-68% to 68-80%. All the obtained thioureas were soluble in common organic solvents (such as ethanol, methanol, toluene, benzene, DMF,…). Their structures have been confirmed by spectral (IR, NMR and MS) data.

Table 2. Selected ^{1}H-NMR of 2-amino-4,6-diarylpyrimidin 4 a1-p1

Entry	^{1}H-NMR spectra, δ (ppm)
4a1	8,22-8,20 (m, 4H, *J* 3,5 Hz, H-3' & H5' and H-3"& H-5"); 7,70 (s, 1H, H-5); 7,53-7,52 (m, 6H, *J* 3,0 Hz, H-2', H 4' & H-6' and H-2", H 4" & H-6")
4d1	8,30 (s, 1H, H-2'); 8,25-8,23 (m, 2H, *J* 2,75 Hz, H-3" & H-5"); 8,20 (d, 1H, *J* 7,5 Hz, H-4'); 7,78 (s, 1H, H-5); 7,591-7,75 (m, 2H, *J* 7,5 Hz & 3,0 Hz, H-5' & H6'); 7,53-7,52 (t, 3H, *J* 3,0 Hz, H-2", H 4" & H-6"); 6,80 (s, 2H, NH_2)
4f1	8,22-8,21 (m, 2H, *J* 3,0 Hz, H-3" & H-5"); 8,18 (d, 2H, *J* 8,5 Hz, H-3' & H5'); 7,72 (s, 1H, H-5); 7,72 (d, 2H, *J* 8,5 Hz, H-2' & H6'); 7,53-7,51 (m, 3H, *J* 3,5 Hz, H-2", H 4" & H-6"); 6,76 (s, 2H, NH_2)
4i1	8,20-8,18 (m, 2H, *J* 2,5 Hz, H-3" & H-5"); 8,19 (d, 2H, *J* 9,0 Hz, H-3' & H5'); 7,64 (s, 1H, H-5); 7,52-7,50 (m, 3H, *J* 3,0 Hz, H-2", H 4" & H-6"); 7,06 (d, 2H, *J* 9,0 Hz, H-2' & H6'); 6,61 (s, 2H, NH_2); 3,84 (s, 3H, OMe)
4l1	8,22-8,20 (m, 2H, *J* 4,0 Hz & 1,5 Hz, H-3" & H-5"); 7,84 (dd, 1H, *J* 8,5 Hz & 1,25 Hz, H-6'); 7,80 (d, 1H, *J* 1,5, H-2'); 7,65 (s, 1H, H-5); 7,52-7,50 (m, 3H, *J* 3,25 Hz, H-2", H 4" & H-6"); 7,05 (d, 1H, *J* 8,0 Hz, H-5'); 6,64 (s, 2H, NH_2); 6,11 (s, 2H, OCH_2O)
4m1	9,90 (s, 1H, OH); 8,19-8,17 (m, 2H, *J* 2,25 Hz, H-3" & H-5"); 8,08 (d, 2H, *J* 9,0 Hz, H-3' & H5'); 7,59 (s, 1H, H-5); 7,51-7,50 (m, 3H, *J* 2,5 Hz, H-2", H 4" & H-6"); 6,87 (d, 2H, *J* 8,5 Hz, H-2' & H6'); 6,60 (s, 2H, NH_2)
4n1	9,59 (s, 1H, OH); 8,20-8,18 (m, 2H, *J* 2,75 Hz, H-3" & H-5"); 7,61 (s, 1H, *J* 1,0 Hz, H-2'); 7,60 (m, 1H, *J* 7,5 Hz & 4,5 Hz, H-4'); 7,59 (s, 1H, H-5); 7,52-7,51 (t, 3H, *J* 3,25 Hz, H-2", H 4" & H-6"); 7,30 (t, 1H, *J* 2,75 Hz, H-6'); 6,91 (ddd, 1H, *J* 8,0 Hz, 2,5 Hz & 1,0 Hz, H-5'); 6,68 (s, 2H, NH_2)
4o1	8,25-8,21 (m, 3H, *J* 2,5 Hz, 2,0 Hz & 1,5 Hz, H-3", H-5" & H-3'); 7,86 (s, 1H, H-5); 7,54-7,53 (m, 3H, *J* 2,5 Hz & 1,0 Hz, H-2", H 4" & H-6"); 7,37-7,34 (td, 1H, *J* 8,5 Hz & 1,5 Hz, H-6'); 7,18 (br,, OH & NH_2); 6,90 (t, 1H, *J* 7,0 Hz, H-5'); 6,90 (dd, 1H, *J* 8,5 Hz & 1,25 Hz, H-4')
4p1	8,19-8,17 (m, 2H, *J* 4,0 Hz & 1,5 Hz, H-3" & H-5"); 8,10 (d, 2H, *J* 9,0 Hz, H-3' & H5'); 7,60 (s, 1H, H-5); 7,50-7,49 (m, 3H, *J* 3,5 Hz & 1,5 Hz, H-2", H 4" & H-6"); 6,79 (d, 2H, *J* 8,5 Hz, H-2' & H6'); 6,50 (s, 2H, NH_2); 3,00 (s, 6H, $N(Me)_2$)

The IR spectra showed characteristic bands at 3522-3410 (ν_{NH}), 1754-1748 ($\nu_{C=O}$), 1594, 1578, 1526, 1495 ($\nu_{C=C}$), 1364-1362 ($\nu_{C=S}$), 1232-1222 and 1070-1041 cm^{-1} (ν_{COC}). The ^{1}H NMR spectra show resonance signals which are specified for protons in thiourea-NH groups at δ=11.16-12.04 ppm. Proton H-1 has chemical shift at δ=6.19-6.21 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=5.02-5.06 ppm with J_{21}=9.0-9.5 Hz. The coupling constant values about the pyranose ring agreed with *trans*-H–H disposition and the β-anomeric configuration. The ^{13}C NMR spectra

showed signal of thiocarbonyl group at δ=181.3-181.4 ppm.[24] The mass spectra showed M^+ peak at respective molecular weights of the compounds. Some of them were subjected to HREIMS to obtain respective molecular weights.

Table 3. Synthetic results of *N*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-*N'*-4',6'-diarylpyrimidin-2'-yl)thioureas

Entry	mp, °C		Yield (%)		Reaction time	
	QT1	QT2	QT1	QT2	QT1 (h)	QT2 (min)
6a1	229-230	229-203	60	75	14	2
6b1	223-224	223-224	68	87	14	3
6c1	218-219	218-219	68	76	14	3
6d1	190-191	190-191	67	72	14	2
6f1	223-224	223-224	66	76	14	3
6g1	209-210	209-210	69	80	14	3
6h1	151-152	151-152	66	79	14	5
6i1	213-214	213-214	68	77	14	2
6j1	165-166	165-166	72	83	14	2
6o1	293-294	293-294	56	80	18	5
6b2	221-222	221-222	70	80	14	2
6c2	182-185	182-185	66	72	14	3
6d2	174-175	174-175	70	77	14	3
6e2	203-204	203-204	55	68	14	3
6f2	193-194	193-194	70	77	14	3
6g2	188-190	188-190	66	78	14	5
6h2	178-180	178-180	77	82	14	3
6i2	170-171	170-171	69	70	14	7
6j2	152-154	152-154	65	72	14	7
6p2	197-198	197-198	65	80	14	3
6b3	201-202	201-202	76	79	14	5
6c3	-	221-222	-	67	-	10
6d3	132-133	132-133	76	76	14	5
6e3	220-221	220-221	59	67	14	8
6f3	232-233	232-233	76	79	14	3
6g3	225-226	225-226	67	80	14	5
6h3	218-219	218-219	71	82	14	3
6i3	195-196	195-196	72	72	14	3
6j3	226-227	226-227	69	75	14	3
6k3	253-254	253-254	54	73	14	3
6p3	199-200	199-200	69	80	14	9
6q	220-221	220-221	70	71	14	3

Table 4. Selected ^{1}H-NMR spectral data of some *N*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-*N'*-(4,6-diarylpyrimidine-2-yl)thioureas

Entry	δ_H (ppm)
6a1	12.181(d, 1H, $J_{a,1}$=9.5 Hz, H_a), 11.107 (s, 1H, H_b), 8.317-8.298 (m, 4H, H-2", H-6" & H-2'", H-6'"), 8.291 (s, 1H, H-5'), 7.651-7.597 (m, 6H, H-3", H-4", H-5" & H-3'", H-4'", H-5'"), 6.212 (t, 1H, $J_{1,Ha}$=9.5 Hz, $J_{1,2}$ =9.5 Hz, H-1), 5.531 (t, 1H, $J_{4,3}$ =9.5 Hz, $J_{3,2}$ =9.5 Hz, H-3), 5.036 (t, 1H, $J_{2,3}$ =9.5 Hz, $J_{2,1}$ =9.0 Hz, H-2), 5.034 (t, 1H, $J_{3,4}$ =9.5 Hz, $J_{4,5}$ =9.5 Hz, H-4), 4.233 (m, 1H, $J_{5,4}$ 9.5 Hz, H-5), 4.065 (d, 1H, $J_{6a,\ 6b}$ 10.0 Hz, H_a-6), 4.233 (d, 1H, $J_{6b,6a}$ 10.0 Hz, H_b-6), 2.030, 1.989, 1.955, 1,950 (s, 4xCH_3CO)
6c1	12.036 (d, 1H, $J_{a,1}$ 9.0 Hz, H_a), 11.157 (s, 1H, H_b), 8.348 (d, 2H, $J_{2",3"}$=$J_{6",5"}$=9.0 Hz, H-2" & H-6"), 8.334 (s, 1H, H-5'), 8.309 (dd, 2H, $J_{2'",3'"}$=$J_{6'",5'"}$=8.0 Hz, $J_{2'",4'"}$=$J_{6'",\ 4'"}$=2.0 Hz, H-2'" & H-6'"), 7.691 (d, 2H $J_{3",2"}$=$J_{5",6"}$=9.0 Hz, H-3" & H-5"), 7.625 (ddd, 3H, $J_{3'",2'"}$=$J_{5'",6'"}$=8.0 Hz, $J_{3',4'}$=7.5 Hz, H-3'", H-4'" & H-5'"), 6.197 (t, 1H, $J_{1,Ha}$ 9.0 Hz, $J_{1,\ 2}$ 9.0 Hz, H-1), 5.522 (t, 1H, $J_{4,3}$ 9.5 Hz, $J_{4,}$ =9.5 Hz, H-3), 5.064 (t, 1H, $J_{2,3}$ 9.5 Hz, $J_{2,1}$=9.0 Hz, H-2), 5.044 (t, 1H, $J_{3,4}$=$J_{4,5}$=9.5 Hz, H-4), 4.217 (t, 1H, $J_{5,4}$=9.5 Hz, $J_{2,1}$ =9.0 Hz, H-5), 4.054 (dd, 1H, $J_{6a,6b}$=10.0 Hz, H_a-6), 4.207 (dd, 1H, $J_{6b,6a}$=10.0 Hz, H_b-6), 2.030, 1.991, 1.962, 1.952 (s, 4xCH_3CO)
6d1	12.163 (d, 1H, $J_{a,1}$=9.5 Hz, H_a), 11.224 (s, 1H, H_b), 8.395 (m, 2H, H-2" & H-5'), 8.347-8.319 (m, 3H, H-2'", H-4'" & H-6'"), 7.704 (m, 1H, H-6"), 7.664-7.601 (m, 4H, H-4", H-5" & H-3'", H-5'"), 6.198 (t, 1H, $J_{1,Ha}$=9.5 Hz, $J_{1,2}$=9.5 Hz, H-1), 5.556 (t, 1H, $J_{4,3}$=9.5 Hz, $J_{4,5}$=9.5 Hz, H-3), 5.062 (t, 1H, $J_{3,4}$=9.5 Hz, $J_{3,2}$=9.5 Hz, H-4), 5.046 (t, 1H, $J_{2,\ 3}$ =9,5; $J_{2,\ 1}$=9,5 Hz, H-2), 4.21 (octet, 1H, $J_{5,4}$=9.5 Hz, $J_{5,6b}$=5.0 Hz, $J_{5,6a}$=2.0 Hz, , H-5), 4.219 (dd, 1H, $J_{6b,6a}$=12.5 Hz, $J_{6b,5}$=4.75 Hz, H_b-6), 4.054 (dd, 1H, $J_{6a,6b}$=12.5 Hz, $J_{6b,5}$=1.75 Hz, H_a-6), 2.030, 1.991, 1.962, 1.952 (s, 4xCH_3CO)
6f1	12.031 (d, 1H, $J_{Ha,1}$=9.5 Hz, H_a), 11.180 (s, 1H, H_b), 8.350 (s, 1H, H-5'), 8.314 (dd, 2H, $J_{2'",3'"}$=$J_{6'",5'"}$=8.5 Hz, $J_{2',4'}$=$J_{6',4'}$=2.0 Hz, H-2'" & H-6'"), 8.282 (d, 2H, $J_{2,3}$=$J_{6,5}$=9.0 Hz, H-2" & H-6"), 7.831(d, 2H, $J_{3,2}$=$J_{5,6}$=9.0 Hz, H-3" & H-5"), 7.627 (m, 3H, H-3'", H-4'" & H-5'"), 6.188 (t, 1H, $J_{1,Ha}$=9.5 Hz, $J_{1,2}$=9.5 Hz, H-1), 5.516 (t, 1H, $J_{3,4}$=9.5 Hz, $J_{3,4}$=9.5 Hz, H-3), 5.053 (t, 1H, $J_{2,1}$ =9.5 Hz, $J_{2,3}$=9.5 Hz, H-2), 5.039 (t, 1H, $J_{4,3}$ =9.5 Hz, $J_{4,5}$ =9.5 Hz, H-4), 4.217 (dd, 1H, $J_{6b,6a}$ =14.5 Hz, H_b-6), 4.214 (t, 1H $J_{5,4}$ =9.5 Hz, $J_{5,6}$ =9.5 Hz, H-5), 4.046 (dd, 1H $J_{6a,6b}$ =14.5 Hz, H_a-6), 2.027, 1.988, 1.963, 1.947 (s, 4xCH_3CO)
6o1	12.115 (d, 1H, $J_{Ha,1}$ 9.5 Hz, H_a), 11.850 (s, 1H, H_b), 11.832 (s, 1H, OH), 8.335 (s, 1H, H-5'), 8.307 (dd, 1H, $J_{3",4"}$=8.5 Hz, $J_{3,5}$=1.5 Hz, H-3"), 8.244-8.228 (m, 2H, H-3'" & H-5'"), 7.676-7.624 (m, 3H, H-2'", H-4'" & H-6'"), 7.549 (td, 1H, $J_{6",5"}$=8.0 Hz, $J_{6",4"}$=1.5 Hz, H-6"), 7.015 (d, 1H, J=7.5 Hz, H-4"), 7.003 (d, 1H, J=8.0 Hz, H-5"), 6.198 (t, 1H, $J_{1,Ha}$=9.0 Hz, $J_{1,2}$=9.5 Hz, H-1), 5.521 (t, 1H $J_{3,2}$=9.5 Hz, $J_{3,4}$ =9.5 Hz, H-3), 5.021 (m, 2H, H-2 & H-4), 4.234-4.175 (m, 2H, H-5 & H_b-6), 4.062-4.041 (m, 1H, H_a-6), 2.027, 1.984, 1.953 (s, 4xCH_3CO)
6i1	12.218 (d, 1H, $J_{Ha,1}$ 9.0 Hz, H_a), 11.063 (s, 1H, H_b), 8.316 (d, 2H, $J_{2",3"}$=$J_{6",5"}$=9.5 Hz, H-2" & H-6"), 8.298 (td, 2H, $J_{2'",3'"}$=$J_{6'",5'"}$=8.0 Hz, $J_{2'",4'"}$=$J_{6'",4'"}$=2.0 Hz, H-2'" & H6'"), 8.251 (s, 1H, H-5'), 7.639-7.600 (m, 3H, H-3'", H-4'" & H-5'"), 7.147 (d, 2H, $J_{3",2"}$=$J_{5",6"}$=9.0 Hz, H-3" & H-5"), 6.192 (t, 1H, $J_{1,Ha}$=9.0 Hz, $J_{1,2}$=9.5 Hz, H-1), 5.522 (t, 1H $J_{3,2}$=9.5 Hz, $J_{3,4}$=9.5 Hz, H-3), 5.035 (t, 1H, $J_{2,3}$=9.5 Hz, $J_{2,1}$=9.5 Hz, H-2), 5.020 (t, 1H, $J_{4,3}$=9.5 Hz, $J_{4,5}$=9.5 Hz, H-4), 4.208 (m, 1H, H_b-6), 4.204 (m, 1H, H-5), 4.052 (m, 1H, H_a-6), 3.888 (s, 3H, OCH_3 Ar), 2.028, 1.984, 1.956, 1.949 (s, 4xCH_3CO)
6g1	12.185 (d, 1H, $J_{Ha,1}$=9.0 Hz, H_a), 11.047 (s, 1H, H_b), 8.296 (dd, 2H, $J_{2",3"}$=$J_{6",5"}$=8.0 Hz, $J_{2",4"}$=$J_{6",4"}$=1.75 Hz, H-2" & H-6"), 8.242 (s, 1H, H-5'), 8.207 (d, 2H, $J_{2",3"}$=$J_{6",5"}$=8.0 Hz, H-2" & H6"), 7.598 (m, 3H, H-3'", H-4'" & H-5'"), 7.405 (d, 2H, $J_{3",2"}$=$J_{5",6"}$=8.0 Hz, H-3" & H-5"), 6.218 (t, 1H, $J_{1,Ha}$=9.0 Hz, $J_{1,2}$ 9.5 Hz, H-1), 5.535 (t, 1H $J_{3,2}$=9.5 Hz, $J_{3,4}$=9.5 Hz, H-3), 5.041 (t, 1H, $J_{2,3}$=9.5 Hz, $J_{2,1}$=9.5 Hz, H-2), 5.034 (t, 1H, $J_{4,3}$=9.5 Hz, $J_{4,5}$=9.0 Hz, H-4), 4.246-4.197 (m, 2H, H_b-6 & H-5), 4.070 (dd, 1H, $J_{6b,6a}$ =10.5 Hz, $J_{6a,5}$=3.5 Hz, H_a-6), 2.414 (s, 3H, CH_3), 2.033, 1.993, 1.956, 1.956 (s, 4xCH_3CO)

Entry	δ_H (ppm)
6h1	12.185 (d, 1H, $J_{Ha,1}$=9.5 Hz, H_a), 11.051 (s, 1H, H_b), 8.307 (dd, 2H, $J_{2",3"}$=$J_{6",5"}$=8.5 Hz, $J_{2",4"}$=$J_{6",4"}$=1.75 Hz, H-2" & H-6"), 8.269 (s, 1H, H-5'), 8.255 (d, 2H, $J_{2",3"}$=$J_{6",5"}$=8.5 Hz, H-2'" & H6'"), 7.621 (m, 3H, H-3'", H-4'" & H-5'"), 7.485 (d, 2H, $J_{3",2"}$=$J_{5",6"}$=8.5 Hz, H-3" & H-5"), 6.213 (t, 1H, $J_{1,Ha}$=9.0 Hz, $J_{1,2}$ 9.0 Hz, H-1), 5.530 (t, 1H $J_{3,2}$=9.5 Hz, $J_{3,4}$=9.5 Hz, H-3), 5.052 (t, 1H, $J_{2,3}$=9.5 Hz, $J_{2,1}$=9.5 Hz, H-2), 5.045 (t, 1H, $J_{4,3}$=9.5 Hz, $J_{4,5}$=9.0 Hz, H-4), 4.229-4.194 (m, 2H, H_b-6 & H-5), 4.081 (m, 1H, H_a-6), 3.019 (quintet, 1H, *J*=7.0 Hz, C*H*$(CH_3)_2$), 2.037, 1.994, 1.960, 1.953 (s, 4xCH_3CO), 1.275 (s, 6H, *J*=7.0 Hz, CH(CH_3)$_2$).

Table 5. Selected ^{13}C-NMR spectral data of some *N*-(2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl)-*N'*-(4,6-diarylpyrimidine-2-yl)thioureas

Carbon	Thioureas							
	6a1	**6c1**	**6d1**	**6f1**	**6g1**	**6h1**	**6i1**	**6o1**
C=S	181.39	181.32	181.30	181.31	181.28	181.29	181.33	181.37
C-1	81.72	81.17	81.63	81.73	81.72	81.75	81.71	81.63
C-2	71.48	71.38	71.88	71.34	71.41	71.47	71.48	71.42
C-3	72.14	72.20	71.53	72.17	72.11	72.28	72.11	72.15
C-4	67.98	67.99	67.98	67.97	67.97	67.96	67.97	67.96
C-5	72.61	72.67	72.57	72.66	72.61	72.59	72.59	72.61
C-6	61.75	61.79	61.72	61.79	61.75	61.69	61.77	61.73
C-2'	157.55	157.46	157.46	157.48	157.43	157.45	162.26	159.22
C-4'	164.97	163.82	163.14	163.93	164.82	164.71	164.38	163.55
C-5'	107.66	107.62	107.81	107.60	107.16	107.27	106.74	107.15
C-6'	164.97	165.02	165.45	165.06	164.82	164.94	164.68	166.13
C-1"	135.53	134.34	134.05	131.80	132.67	133.10	131.58	118.36
C-2"	128.96	128.97	131.86	129.46	129.48	127.53	127.39	155.91
C-3"	127.49	129.25	137.53	131.94	131.55	128.85	114.32	117.93
C-4"	131.73	136.56	126.16	136.41	141.80	152.47	157.49	131.77
C-5"	127.49	129.25	131.38	131.94	131.55	128.85	114.32	119.22
C-6"	128.96	128.97	127.08	129.46	129.48	127.53	127.39	133.68
C-1'"	135.53	135.40	135.39	134.72	135.52	135.53	135.66	135.48
C-2'"	128.96	127.46	127.57	127.49	127.36	126.82	128.93	127.37
C-3'"	127.49	128.93	128.95	128.95	128.83	127.36	129.32	129.07
C-4'"	131.73	131.76	130.83	125.53	131.46	131.55	127.78	129.14
C-5'"	127.49	128.93	128.95	128.95	128.83	127.36	129.32	129.07
C-6'"	128.96	127.46	127.57	127.49	127.36	126.82	128.93	127.37
CH_3CO	20.43, 20.40, 20.32,	20.39, 20.36,	20.39, 20.39,	20.42, 20.38,	20.990, 20.386,	20.29, 20,29	20.42, 20.39,	20.40, 20.36,

Carbon	Thioureas							
	6a1	**6c1**	**6d1**	**6f1**	**6g1**	**6h1**	**6i1**	**6o1**
	20.229	20.29, 20.21	20.28, 20.17	20.30, 20.21	20.293, 20.203	20.20, 20.12	20.31, 20.21	20.28, 20.20
CH_3CO	169.93, 169.57, 169.50, 169.35	169.883, 169.566, 169.470, 169.303	169.90, 169.57, 169.45, 169.30	169.90, 169.58, 169.48, 169.31	169.78, 169.41, 169.35, 169.21	196.77, 169.43, 169.36, 169.22	169.91, 169.53, 169.48, 169.34	169.90, 169.51, 169.46, 169.31
C others					20.29 (CH_3 Ar)	33.29 [CH(CH_3)$_2$ Ar], 23.45 [CH(CH_3)$_2$ Ar]	55.48 (OCH_3 Ar)	

Compounds **4** and **6** were screened for their antibacterial and antifungal activities *in vitro* against *Staphyloccus epidermidis*, *Enterobacter aerogenes* and *Candida albicans* by disc diffusion method. All amines **4** have significant biological activities against *E. aerogenes*, *S. epidermidis* and *C. albicans*. Compounds **4a-p** showed highest antibacterial activity against *S. Epidermidis* (Table 6). Almost all compounds **6** have remarkable biological activity, except compound **6b** which exhibited no antifungal activity against *E. aerogenes* and compound **6g** against *C. albicans*. Especially, the antibacterial activity against *S. epidermidis* proved significantly in these compounds (Table 7).

Table 6. Response of various micro-organisms to some new selected substituted amino-4,6-diarylpyrimidine

Entry	R	Diameter of zone inhibition (mm)[a)]		
		E. aerogenes	*S. epidermidis*	*C. albicans*
4a	H	15	30	20
4b	*p*-F	26	30	25
4c	*p*-Cl	20	29	17
4d	*m*-Cl	18	30	20
4e	*p*-Br	15	28	15
4f	*p*-Me	23	27	26
4g	*p*-iPr	22	26	25
4h	*o*-OH	18	23	24
4i	*p*-OMe	18	29	18
4j	*m*-OMe	19	25	22
ref.	-	25[b)]	25[c)]	35[d)]

[a)] DMF used as control; Concentration used=100 μg/mL of DMF.
ref= [b)] ampicillin; [c)] methicillin; [d)] clotrimazole.

Table 7. Response of various micro-organisms to some new selected substituted *N*-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)-*N'*-(4',6'-diarylpyrimidine-2'-yl)thioureas

Entry	R	Diameter of zone inhibition (mm)[a)]		
		E. aerogenes	*S. epidermidis*	*C. albicans*
6a	H	15	27	15
6b	*p*-F	17	28	16
6c	*p*-Cl	0	30	14
6d	*m*-Cl	13	28	19
6e	*p*-Br	18	30	21
6f	*p*-Me	20	28	20
6g	*p*-iPr	22	29	22
6h	*o*-OH	20	27	21
6i	*p*-OMe	23	29	0
6j	*m*-OMe	22	24	22
ref.	-	35[b)]	35[c)]	45[d)]

[a)] DMF used as control; Concentration used=100μg/mL of DMF.
ref= [b)] ampicillin; [c)] methicillin; [d)] clotrimazole.

In summary, the present new method of the formation of 2-amino-4,6-diarylpyrimidines **4** and *N*-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)-*N'*-(4',6'-diarylpyrimidine-2'-yl)thioureas **6** under microwave irradiation offers several advantages: faster reaction rates (1-2 min for **4** and 5-7 min for **6**) and high yields (80-89% for **4** and 72-83% for **6**), while the conventional method of formation of these thioureas involves long reaction times (8-10 h and 60-68% for **6**).

1. Experimental

1.1. General methods

Melting points were determined on a STUART SMP3 apparatus (BIBBY STERILIN-UK). The FTIR-spectra were recorded on a Magna 760 FT-IR Spectrometer (NICOLET, USA) in KBr pellets. The ^{1}H NMR (500.13 MHz) and ^{13}C NMR (125.77 MHz) spectra were recorded on an AVANCE500 Spectrometer (BRUKER, Germany) in DMSO-d_6 solution in ppm compared to TMS as internal reference at 300K. The assignments of ^{1}H and ^{13}C were confirmed using HMBC and HSQC methods. The high-resolution mass spectra were recorded on AutoSpec Premier instrument (WATERS, USA) using EI. Optical rotation were measured on a POLAX-2L polarimeter (ATAGO-Japan) in DMSO solution. Analytical thin-layer chromatography (TLC) was performed on silica gel $60F_{254}$ No. 5715 (Merck, Germany) with EtOAc and light petroleum (bp 60–90 °C). The spots were visualized by exposure to UV light or by spraying the plats with 10% (v/v) H_2SO_4 in EtOH, followed by heating. 2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl isothiocyanate **3** was prepared by the reaction of per-*O*-acetylated-β-D-glucopyranosyl bromide (prepared from D-glucose)[25] with lead thiocyanate in dried toluene.[20] Other reagents were supplied by Merck and used as is.

1.2. General procedure for synthesis of 2-amino-4,6-diarylpyrimidines (2a-p)

Procedure A (under refluxing condition)

A solution of substituted benzylideneacetophenone **3** (10 mmol) in ethanol (5 mL) was added to a solution of guanidine hydrochloride (15 mmol) and sodium hydroxide (45 mmol) in water (2 mL). The reaction mixture was refluxed for 10 min in domestic microwave oven. Solvent was removed under reduced pressure and the residue was triturated with water, the precipitate was filtered by suction and washed with water until neutral to afford the title compounds **4**, which were recrystallized from ethanol: toluene (1:1) to give ivory-white crystals.

Procedure B (under microwave-assisted and solvent-free conditions)

Substituted benzylideneacetophenone **3** (10 mmol), guanidine hydrochloride (15 mmol) and sodium hydroxide (45 mmol) were mixed carefully with a little water. Obtained mixture was irradiated under domestic microwave oven. After some minutes (1-2 min) the reaction mixture had become dark-yellow, and then the irradiation was continued in given time. Upon completion, monitored by TLC, the reaction mixture was cooled to room temperature and then triturated with water; formed precipitate was filtered by suction and washed with water until neutral to afford the title compounds **4**, which were recrystallized from ethanol: toluene (1:1) to give ivory-white crystals.

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

Procedure A (under refluxing condition)

A solution of 2-amino-4,6-diarylpyrimidine **4** (2 mmol) in anhydrous dioxane (10 mL) was added to a solution of 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl isothiocyanate **5** (2 mmol) in anhydrous dioxane (10 mL). The reaction mixture was heated in refluxing for 8-10 h. Then solvent was removed under reduced pressure, and the residue was triturated with ethanol. The precipitate was filtered by suction and recrystallized with ethanol: toluene (1:1) to afford the title compounds **6** as ivory-white crystals.

Procedure B (under microwave-assisted and solvent-free conditions)

A mixture of 2-amino-4,6-diarylpyrimidine **4** (2 mmol) and 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl isothiocyanate **5** (2 mmol) was grinded in 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 °C). The reactants were irradiated for a period of 5-7 min. The mixture became dark-yellow pasty 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 **6** as ivory-white crystals.

Acknowledgements

Financial support for this work was provided by Scientific Research Fund-Hanoi National University (Grant QGTD.08.03).

References

1. Sayle, K. L.; Bentley, J.; Boyle, F. T.; Calvert, A. H.; Cheng, Y.; Curtin, N. J.; Endicott, J. A.; Golding, B. T.; Hardcastle I. R.; Jewbury, P.; Mesguiche, V.; Newell, D. R.; Noble, M. E. M.; Parsons, R. J.; Pratt, D. J.; Wang, L. Z.; Griffin R. J. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 3079–3082; (c) Balasankar, T.; Nagarajan, S. *Heterocycl. Commun.* **2004**, *10*, 465–468.

2. (a) Chandrasekaran S. & Nagarajan, S. *Il Farmaco* **2005**, *60*, 279–282; (b) Cocco, M. T., Congiu, C.; Liliu V. & Onnis, V. *Bioorg. Med. Chem.* **2006**, *14*, 366–372; (c) Gadhachanda, V. R.; Wu, B.; Wang, Z.; Kuhen, K. L.; Caldwell, J.; Zondler, H.; Walter, Havenhand, H. M. & He, Y. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 260–265.

3. (a) El-Hashash, M. A.; Mahhmoud M. R.; Madboli, S. A. *Indian J. Chem.* **1993**, *32B*, 449–453; (b) Wustrow, D.; Akunne, H.; Belliotti, T.; Davis, M. D.; Heffner, T.; Kesten, S.; Meltzer, L.; Pugsley, T.; Wise, L. *Eur. Neuropsychopharm.* **1996**, *6*, S4; (c) Rashinkar, G. S.; Pore, S. B.; Mote K. B. & Salunkhe, R. S. *Indian J. Chem.* **2009**, *48B*, 606–610.

4. (a) Witczak, Z. J. In *Adv. Carbohydr. Chem. Biochem.*, Tipson, S., Ed.; Academic Press: New York, 1986; Vol. 44, pp. 91–145; (b) Lindhorst, T. K.; Kieburg, C. *Synthesis* **1995**, 1228–1230; (c) Jiménez Blanco, J. L.; Balla Sylla; Ortiz-Mellet, C. and García Fernández, J. M. *J. Org. Chem.* **2007**, *72*, 4547–4550; (d) Kühne, M.; Györgydeák, Z.; Lindhorst, T. K. *Synthesis* **2006**, 949–951.

5. (a) García-Fernández, J. M.; Ortiz-Mellet, C. *Sulfur Rep.* **1996**, *19*, 61–159; (b) García-Fernández, J. M.; Ortiz-Mellet, C. In *Adv. Carbohydr. Chem. Biochem.*, Horton, D., Ed.; Academic Press: New York, 2000; Vol. 55, pp. 36–135.

6 . (a) Naito, T.; Sano, M. *Chem. Pharm. Bull.* **1961**, *9*, 709–714; (b) Ukita, T.; Hamada, A.; Yoshida, M. *Chem. Pharm. Bull.* **1964**, *12*, 454–459; (c) Ogura, H.; Takahashi, H. *Heterocycles* **1977**, *8*, 125–146.

7. (a) Camarasa, M. J.; Fernandez-Resa, P.; Garcia-Lopez, M. T.; de las Heras, F. G.; Mendez-Castrillon, P. P.; San Felix, A. *Synthesis* **1984**, 509–510; (b) Prata, C.; Mora, N.;Lacombe,J. -M.; Maurizis, J. -C.; Pucci, B. *Carbohydr. Res.* **1999**, *321*, 4–14.

8. (a) Abramovitch, R. A. *Org. Prep. Proc. Int.* **1991**, *23*, 683–712; (b) Larhed, M.; Moberg, C.; Hallberg, A. *Acc. Chem. Res.,* **2002**, *35*, 717; (c) Lidström, P.; Tierney, J.; Wathey, B.; Westman, J. *Tetrahedron,* **2001**, *57*, 9225–9283.

9. Loupy, A. *Microwaves in Organic Synthesis*, 2nd ed., Wiley and Sons Ltd-VCH: Weinheim, 2006; pp 306–307; b) Kingston, H. M.; Haswell, S. J. (Eds), *Microwave-Enhanced Chemistry: Fundamental, Sample Preparation, and Applications*, American Chemical Society: New York, 1997.

10. a) Gedye, R.; Smith, F.; Westaway, K.; Ali, H.; Baldisera, L.; Laberge, L.; Roussel, J. *Tetrahedron Lett*., **1986**, *27*, 279–279; b) Caddick, S. *Tetrahedron,* **1995**, *51*, 10403–10432; (c) Gabriel, C.; Gabriel, S.; Grant, E.; Halstead, B. S. J.; Mingos, D. *Chem. Soc. Rev.* **1997**, *27*, 213–224.

11. (a) Chen, S.-T.; Sookkheo, B.; Phutrahul, S.; Wang, K.-T. *Methods in Biotechnology* **2001**, *15*, 373; (b) Soderberg, E.; Westman, J.; Oscarson, S. *J. Carbohydr. Chem.* **2001**, *20*, 397; (c) Lidstorm, P.; Tierney, J.; Wathey, B.; Westman, J. *Tetrahedron* **2001**, *57*, 9225–9283.

12. Walpole, C.; Ko, S. Y.; Brown, M.; Beattie, D.; Campbell, E.; Dickenson, F.; Ewan, S.; Hughes, G. A.; Lemaira, M.; Lerpiniere, J.; Patel, S.; Urban, L. *J. Med. Chem.* **1998**, *41*, 3159–3173.
13. (a) Chalina, E. G.; Chakarova, L. *Eur. J. Med. Chem.* **1998**, *33*, 975–983; (b) Stark, H.; Purand, K.; Ligneau, X.; Rouleau, A.; Arrang, J. -M.; Garbarg, M.; Schwartz, J. -C.; Schunack, W. *J. Med. Chem.* **1996**, *39*, 1157–1163.
14. (a) Wang, J.; Li, H.; Yu, X.; Zu, L.; Wang, W. *Org. Lett.* **2005**, *7*, 4293–4296; (b) Seayad, J.; List, B. *Org. Biomol. Chem.* **2005**, *3*, 719–724; (c) Pihko, P. M. *Angew. Chem., Int. Ed.* **2004**, *43*, 2062–2064.
15. (a) Staab, H. A. *Angew. Chem., Int. Ed. Engl.* **1962**, *1*, 351–367; (b) Staab, H. A.; Walther, G. *Leibigs Ann. Chem.* **1962**, *657*, 98–103; (c) Yoon, T. P.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2005**, *44*, 466–468.
16. (a) Mohanta, P. K.; Dhar, S.; Samal, S. K.; Ila, H.; Junjappa, H. *Tetrahedron* **2000**, *56*, 629–637; (b) Aoyama, T.; Murata, S.; Nagata, Y.; Takido, T.; Kodamari, M. *Tetrahedron Lett.* **2005**, *46*, 4875–4878.
17. (a) Rodríguez-Lucena, D.; Benito, J. M.; Ortiz-Mellet C. and García Fernández, J. M. *Chem. Commun.* **2007**, 831–833; (c) Jiménez Blanco, J. L.; Bootello, P.; Gutiérrez Gallego, R.; Ortiz-Mellet, C.; García Fernández, J. M. *Synthesis* **2007**, 2545–2558.
18. (a) Sharma, S. *Synthesis* **1978**, 803; (b) Bhandari, K.; Srivatsava, S.; Shankar, G. *Bioorg. Med. Chem.* **2004**, *12*, 4189–4196; (c) Kodomari, M.; Suzuki, M.; Tanigawa, K.; Aoyama, T. *Tetrahedron Lett.* **2005**, *46*, 5841–5843.
20. Bama K. G. & Rajani, K. B. *Indian J. Chem.* **1988**, *27B*, 1157–1158.
21. Yong-Hua Liu, Ling-Hua Cao *Carbohydr. Res.* **2008**, *343*, 615–625.
22. (a) Furniss, B. A.; Hannaford, A. J.; Smith, P. W.; Tatchell, A. R. *Vogel's Text-Book of Practical Organic Chemistry*, 5th ed., Longmann Scietific & Technical: Harlow, 1989; p 1034; (b) Oyedapo, A. O.; Makanju, V. O.; Adewunmi, C. O.; Iwalewa, E. O.; Adenowo, T. K. *Afr. J. Trad. CAM* **2004**, *1*, 55; (c) Adewunmi, C. O.; Ogungbamila, F. O.; Oluwadiya, J. O. *Planta. Med.* **1987**, *53*, 110.
23. El-Hashash, M. A.; Mahhmoud M. R. and Madboli, S. A. *Indian J. Chem.* **1993**, *32B*, 449–452.
24. Pretsch, E.; Buhlmann, P.; Affolter, C. *Structure Determination of Organic Compounds*, 2nd ed., Springer-Verlag: Berlin, 2000; pp 152, 236.
25. Lemieux, R. L. *Methods in Carbohydrate Chemistry*, Whistler, R. L.; Wolfrom, M. L., Eds.; Academic Press: New York, 1963; Vol. 2, pp 221–222.