



## Reaction of *N*-(Per-*O*-acetyl- $\beta$ -*D*-glucopyranosyl)-*N'*-(4',6'-diarylpyrimidine-2'-yl)thioureas with Ethyl Bromoacetate

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**Abstract:** Some new 2-iminothiazolidin-4-ones having pyrimidine ring have been synthesized by reaction of substituted *N*-(per-*O*-acetyl- $\beta$ -*D*-glucopyranosyl)-*N'*-(4',6'-diarylpyrimidine-2'-yl)thioureas with ethyl bromoacetate. The structure of isomeric products has been confirmed by spectroscopic methods, such as IR, <sup>1</sup>H and <sup>13</sup>C NMR.

**Keywords:** Glucopyranosyl thiourea, Thiazolidin-4-one, Ethyl bromoacetate, 2-Iminothiazolidin-4-one

### Introduction

Thiazolidin-4-one represents a prevalent scaffold in drug discovery. A survey of the most recent literature indicate that chemicals containing this moiety are potential antibacterial, antimycobacterial, anticonvulsant, antiparasitic, anti-inflammatory, analgesic and herbicidal agents. Moreover, it has been reported that thioureas can serve as the precursor of thiazolidin-4-one derivatives<sup>1</sup>. Interestingly, Garnaik *et al.*<sup>2</sup> reported that several 2-(arylimino)-4-tetra-*O*-acetyl- $\beta$ -*D*-glucopyranosyl-4-thiazolidinones showed promising antimicrobial and antifungal activities. Thiazolidin-4-one could be obtained from cyclization of substituted thiourea with chloroacetic acid (in the presence of weak base). Several reports regarding the condensation of thiosemicarbazides with alkyl halides have pointed that main products are of compound types<sup>3</sup> resulting from cyclization at *N*-4. In the presence of a weak base, Saleh *et al.*<sup>4</sup> cyclized substituted thioureas with chloroacetic acid, giving thiazolidin-4-one compounds substituted at *N*-4. Conversely, the cyclization at *N*-2 has been more scarcely reported. Moghaddam and Hojabri<sup>5</sup> and Rajanarendar *et al.*<sup>6</sup> have reported cyclizations at *N*-2 position. A detailed study of the condensation of thiosemicarbazides with ethyl bromoacetate to give *N*-2 isomers as major products has been reported<sup>7</sup>. Yu Xin Li *et al.*<sup>8</sup> have reported cyclizations at *N*-2 position in 1-alkoxy(phenyl) thiophosphoryl-4-(per-*O*-acetylglycosyl)thiosemicarbazides to give 3-alkoxy(phenyl)-thiophosphorylamido-2-(per-*O*-acetylglycosyl-1'-imino)thiazolidin-4-one and at *N*-4 position

in 1-arylsulfonyl-4-(*N*-per-*O*-acetyl- $\beta$ -*D*-glucopyranosyl) thiosemicarbazides to afford 2-phenylsulfonylhydrazono-3-(per-*O*-acetyl- $\beta$ -*D*-glucopyranosyl) thiazolidin-4-ones.

Continuing our studies<sup>9</sup> on the synthesis of peracetylated glucopyranosyl isothiocyanate and conversion into corresponding thioureas containing pyrimidine ring, we report here the synthesis and spectral characterization of some iminothiazolidin-4-one compounds from *N*-(2,3,4,6-tetra-*O*-acetyl- $\beta$ -*D*-glucopyranosyl)-*N'*-(4',6'-diarylpyrimidine-2'-yl)thioureas.

## Experimental

All the starting materials and reagents were purchased from commercial suppliers and used after further purification. 2,3,4,6-Tetra-*O*-acetyl- $\beta$ -*D*-glucopyranosyl isothiocyanate was prepared by the reaction of per-*O*-acetylated- $\beta$ -*D*-glucopyranosyl bromide (prepared from *D*-glucose)<sup>10</sup> with lead thiocyanate in dried toluene<sup>2</sup> and *N*-(2,3,4,6-tetra-*O*-acetyl- $\beta$ -*D*-glucopyranosyl)-*N'*-(4',6'-diarylpyrimidine-2'-yl)thioureas by our method<sup>9</sup>.

### Physical measurements

Melting points were measured on STUART SMP3 (BIBBY STERILIN-UK). The FTIS-spectra was recorded on Impact 410 FT-IR Spectrometer (Nicolet, USA) in form of KBr and using reflex-measure method. The <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were recorded on an Avance spectrometer AV500 (Bruker, Germany) at 500.13 MHz and 125.77 MHz, respectively, using DMSO-*d*<sub>6</sub> as solvent and TMS as an internal reference. MS spectra were recorded on mass spectrometer LC-MS 1100 LC-MSD Trap-SL (Agilent technologies, USA) in metanol. Analytical thin-layer chromatography (TLC) was performed on silica gel 60F<sub>254</sub> 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<sub>2</sub>SO<sub>4</sub> in EtOH, followed by heating.

*General synthetic method of (Z)-3-(2',3',4',6'-tetra-*O*-acetyl- $\beta$ -*D*-glucopyranosyl)-2-(4'',6''-diphenylpyrimidin-2''-ylimino)-thiazolidin-4-ones (2a-g) and (Z)-2-(2',3',4',6'-tetra-*O*-acetyl- $\beta$ -*D*-glucopyranosyl)-1'-imino)-3-(4'',6''-diphenylpyrimidin-2''-yl)-thiazolidin-4-ones (2'a-g)*

To a solution of thioureas **1** (5 mmol) in CHCl<sub>3</sub> (20 mL), ethyl bromoacetate (1.0 g, 0.2 mL, 6 mmol) was added drop wise with stirring. The mixture was heated at reflux for 8-10 h and the solvent was removed under diminished pressure until the volume was 10 mL and ethanol (20 mL) was added and left overnight. A white separated crude product was filtered and purified by recrystallization from toluene: ethanol (1:1) to afford the title isomeric compounds **2** and **2'**.

Compounds **2a/2'a**: Yield 59%; mp. 180–185 °C, ratio of **2a/2'a** isomers 7.7/2.3; IR (KBr, cm<sup>-1</sup>):  $\nu$  1752, 1740, 1591, 1577, 1567, 1513, 1237, 1032; (**2a**): <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>):  $\delta$  8.50–8.41 (m, 4H, H-2''', H-6''', H-2''', H-6'''), 8.40 (s, 1H, H-5''), 7.46–7.42 (m, 3H, H-3''', H-4''', H-5'''), 7.27–7.13 (m, 2H, H-3''', H-5'''), 6.38 (d, 1H, *J* 9.5 Hz, H-1'), 5.92 (t, 1H, *J* 9.5 Hz, H-2'), 5.64 (t, 1H, 9.5 Hz, H-3'), 5.01 (t, 1H, *J* 10.0 Hz, H-4'), 4.40–4.36 (m, 1H, H-5'), 4.18–4.12 (m, 2H, H-6'a, H-6'b), 4.16 (d, 1H, *J* 17.75 Hz, H-5a), 3.95 (d, 1H, *J* 17.75 Hz, H-5b), 2.04–1.91 (4×CH<sub>3</sub>CO); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>):  $\delta$  171.7 (C=O lactam), 170.0–169.4 (4×COCH<sub>3</sub>), 165.5 (C-6''), 164.4 (C-1''), 163.3 (C-2''), 163.1 (C-2, C=N), 163.0 (C-4'''), 136.1 (C-1'''), 131.3 (C-1'''), 130.1 (d, *J* 8.80 Hz, C-2''', C-6'''), 128.9 (C-4'''), 128.8 (C-3''', C-5'''), 128.2 (C-2''', C-6'''), 115.9 (d, *JCF* 21.63 Hz, C-3''',

C-5'''), 110.4 (C-5''), 80.3 (C-1'), 72.9 (C-5'), 72.2 (C-3'), 67.6 (C-2'), 67.5 (C-4'), 61.6 (C-6'), 32.7 (C-5), 21.0–20.1 (4×COCH<sub>3</sub>). (**2'a**): <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): δ 8.50–8.41 (m, 4H, H-2'''' & H-6''', H-2'''' & H-6'''), 8.40 (s, 1H, H-5''), 7.46–7.42 (m, 3H, H-3'''' & H-4'''' & H-5'''), 7.27–7.13 (m, 2H, H-3''', H-5'''), 6.47 (t, 1H, *J* 9.25 Hz, H-2'), 5.92 (t, 1H, *J* 9.5 Hz, H-1'), 5.54 (t, 1H, 9.5 Hz, H-3'), 5.19 (t, 1H, *J* 9.75 Hz, H-4'), 4.35–4.30 (m, 1H, H-5'), 4.18–4.12 (m, 2H, H-6'a, H-6'b), 4.16 (d, 1H, *J* 17.75 Hz, H-5a), 3.95 (d, 1H, *J* 17.75 Hz, H-5b), 2.04–1.91 (4×CH<sub>3</sub>CO); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): δ 171.7 (C=O lactam), 169.9–169.4 (4×COCH<sub>3</sub>), 165.5 (C-6''), 164.4 (C-1''), 163.3 (C-2''), 163.1 (C-2, C=N), 163.0 (C-4'''), 136.1 (C-1'''), 131.3 (C-1'''), 130.1 (d, *J* 8.80 Hz, C-2''', C-6'''), 128.9 (C-4'''), 128.8 (C-3'''' & C-5'''), 128.2 (C-2'''' & C-6'''), 115.9 (d, *J*<sub>CF</sub> 21.63 Hz, C-3''', C-5'''), 110.4 (C-5''), 80.0 (C-1'), 73.0 (C-5'), 72.2 (C-3'), 67.6 (C-2'), 67.4 (C-4'), 61.6 (C-6'), 32.7 (C-5), 21.0–20.1 (4×COCH<sub>3</sub>).

Compounds **2b/2'b**: Yield 68%; mp. 190–193 °C, ratio of **2b/2'b** isomers 7.5/2.5; IR (KBr, cm<sup>-1</sup>): ν 1752, 1740, 1591, 1577, 1567, 1513, 1237, 1032; (**2b**): <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): δ 8.44 (s, 1H, H-5''), 8.40 (d, 2H, *J* 8.5 Hz, H-2''', H-6'''), 8.44–8.39 (m, 2H, H-2'''' & H-6'''), 7.84 (d, 2H, *J* 8.5 Hz, H-3''', H-5'''), 7.65–7.64 (m, 3H, H-3'''' & H-4'''' & H-5'''), 6.42 (d, 1H, *J* 9.0 Hz, H-1'), 5.97 (t, 1H, *J* 9.25 Hz, H-2'), 5.68 (t, 1H, 9.25 Hz, H-3'), 5.06 (t, 1H, *J* 10.0 Hz, H-4'), 4.43–4.41 (m, 1H, H-5), 4.22–4.15 (m, 2H, H-6'a, H-6'b), 4.19 (d, 1H, *J* 17.75 Hz, H-5a), 4.01 (d, 1H, *J* 17.75 Hz, H-5b), 2.08–1.95 (4×CH<sub>3</sub>CO); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): δ 171.7 (C=O lactam), 169.9–169.4 (4×COCH<sub>3</sub>), 165.7 (C-6''), 164.4 (C-1''), 163.2 (C-2''), 163.1 (C-2, C=N), 136.0 (C-1'''), 135.4 (C-1'''), 131.9 (C-3''', C-5'''), 131.4 (C-4'''), 129.5 (C-2'''' & C-6'''), 128.9 (C-3'''' & C-5'''), 127.6 (C-2'''' & C-6'''), 125.1 (C-4'''), 108.4 (C-5''), 80.3 (C-1'), 72.9 (C-5'), 72.2 (C-3'), 67.6 (C-2'), 67.5 (C-4'), 61.6 (C-6'), 32.7 (C-5), 20.5–20.1 (4×COCH<sub>3</sub>). (**2'b**): <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): δ 8.44 (s, 1H, H-5''), 8.40 (d, 2H, *J* 8.5 Hz, H-2''', H-6'''), 8.44–8.39 (m, 2H, H-2'''' & H-6'''), 7.84 (d, 2H, *J* 8.5 Hz, H-3''', H-5'''), 7.65–7.64 (m, 3H, H-3'''' & H-4'''' & H-5'''), 6.51 (d, 1H, *J* 9.25 Hz, H-2'), 5.97 (t, 1H, *J* 9.25 Hz, H-1'), 5.59 (t, 1H, 9.5 Hz, H-3'), 5.25 (t, 1H, *J* 9.75 Hz, H-4'), 4.37–4.36 (m, 1H, H-5'), 4.22–4.15 (m, 2H, H-6'a, H-6'b), 4.19 (d, 1H, *J* 17.75 Hz, H-5a), 4.01 (d, 1H, *J* 17.75 Hz, H-5b), 2.01–1.97 (4×CH<sub>3</sub>CO); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): δ 171.7 (C=O lactam), 169.9–169.4 (4×COCH<sub>3</sub>), 165.7 (C-6''), 164.4 (C-1''), 163.2 (C-2''), 163.1 (C-2, C=N), 136.0 (C-1'''), 135.4 (C-1'''), 131.9 (C-3''', C-5'''), 131.4 (C-4'''), 129.5 (C-2'''' & C-6'''), 128.9 (C-3'''' & C-5'''), 127.6 (C-2'''' & C-6'''), 125.1 (C-4'''), 108.4 (C-5''), 79.5 (C-1'), 73.0 (C-5'), 72.5 (C-3'), 67.3 (C-2'), 67.0 (C-4'), 61.6 (C-6'), 32.7 (C-5), 20.5–20.1 (4×COCH<sub>3</sub>).

Compounds **2c/2'c**: Yield 66%; mp. 175–180 °C, ratio of **2c/2'c** isomers 7.5/2.5; IR (KBr, cm<sup>-1</sup>): ν 1751, 1610, 1574, 1508, 1227, 1035; (**2c**): <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): δ 8.40–8.33 (m, 2H, *J* 7.75 Hz, H-2'''' & H-6'''), 8.35 (s, 1H, H-5''), 8.34 (d, 2H, *J* 7.75 Hz, H-2'''' & H-6'''), 7.62–7.60 (m, 3H, H-3'''' & H-4'''' & H-5'''), 7.47 (d, 2H, *J* 7.75 Hz, H-3''', H-5'''), 6.38 (d, 1H, *J* 9.0 Hz, H-1'), 5.94 (t, 1H, *J* 9.25 Hz, H-2'), 5.65 (t, 1H, 9.5 Hz, H-3'), 5.02 (t, 1H, *J* 9.75 Hz, H-4'), 4.39–4.38 (m, 1H, H-5'), 4.18–4.11 (m, 2H, H-6'a, H-6'b), 4.15 (d, 1H, *J* 18.0 Hz, H-5a), 3.96 (d, 1H, *J* 18.0 Hz, H-5b), 3.01 [septet, 1H, *J* 7.0 Hz, 4''-CH(CH<sub>3</sub>)<sub>2</sub>], 2.05–1.92 (4×CH<sub>3</sub>CO), 1.28 [d, 6H, *J* 7.0 Hz, 4''-CH(CH<sub>3</sub>)<sub>2</sub>]; <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): δ 171.7 (C=O lactam), 170.0–169.4 (4×COCH<sub>3</sub>), 165.7 (C-2''), 165.3 (C-6''), 163.3 (C-1''), 162.8 (C-2, C=N), 152.1 (C-4'''), 136.2 (C-1'''), 133.8 (C-1'''), 131.2 (C-4'''), 128.9 (C-3'''' & C-5'''), 127.7 (C-3'''' & C-5'''), 127.5 (C-2'''' & C-6'''), 126.9 (C-2'''' & C-6'''), 108.2 (C-5''), 80.3 (C-1'), 72.9 (C-5'), 72.2 (C-3'), 67.6 (C-2'), 67.5 (C-4'), 61.6 (C-6'), 33.4 [4''-CH(CH<sub>3</sub>)<sub>2</sub>], 32.7 (C-5), 23.6 [4''-CH(CH<sub>3</sub>)<sub>2</sub>], 20.5–20.1 (4×COCH<sub>3</sub>). (**2'c**): <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): δ 8.40–8.33 (m, 2H, *J* 7.75 Hz, H-2'''' & H-6'''), 8.35 (s, 1H, H-5''), 8.34 (d, 2H, *J* 7.75 Hz, H-2'''' & H-6'''),

H-6'''), 7.62–7.60 (m, 3H, H-3''', H-4'''' & H-5''''), 7.47 (d, 2H, *J* 7.75 Hz, H-3''', H-5'''), 6.50 (t, 1H, *J* 9.25 Hz, H-2'), 5.94 (t, 1H, *J* 9.25 Hz, H-1'), 5.55 (t, 1H, 9.5 Hz, H-3'), 5.21 (t, 1H, *J* 9.75 Hz, H-4'), 4.33–4.32 (m, 1H, H-5'), 4.18–4.11 (m, 2H, H-6'a, H-6'b), 4.15 (d, 1H, *J* 18.0 Hz, H-5a), 3.96 (d, 1H, *J* 18.0 Hz, H-5b), 3.01 [septet, 1H, *J* 7.0 Hz, 4''-CH(CH<sub>3</sub>)<sub>2</sub>], 2.00–1.96 (4×CH<sub>3</sub>CO), 1.28 [d, 6H, *J* 7.0 Hz, 4''-CH(CH<sub>3</sub>)<sub>2</sub>]; <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): δ 171.7 (C=O lactam), 170.0–169.4 (4×COCH<sub>3</sub>), 165.7 (C-2''), 165.3 (C-6''), 163.3 (C-1''), 162.8 (C-2, C=N), 152.1 (C-4'''), 136.2 (C-1''''), 133.8 (C-1'''), 131.2 (C-4''''), 128.9 (C-3''''), C-5''''), 127.7 (C-3''', C-5'''), 127.5 (C-2''''), C-6''''), 126.9 (C-2''''), C-6''''), 108.2 (C-5''), 79.8 (C-1'), 73.0 (C-5'), 72.2 (C-3'), 67.6 (C-2'), 67.5 (C-4'), 61.6 (C-6'), 33.4 [4''-CH(CH<sub>3</sub>)<sub>2</sub>], 32.7 (C-5), 23.6 [4''-CH(CH<sub>3</sub>)<sub>2</sub>], 20.5–20.1 (4×COCH<sub>3</sub>).

Compounds **2d/2'd**: Yield 59%; mp. 226–230 °C, ratio of **2d/2'd** isomers 7.5/2.5; IR (KBr, cm<sup>-1</sup>): ν 1751, 1736, 1610, 1579, 1519, 1497, 1226, 1037; (**2d**): <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): δ 8.52 (s, 1H, H-5''), 7.61 (s, 2'''-OH), 7.46–7.41 (m, 2H, H-2''''), H-6''''), 7.04–6.96 (m, 3H, H-3''', H-4'''' & H-5''''), 8.36–8.26 (d, 4H, H-4''', H-6''', H-2''''), H-6''''), 6.35 (d, 1H, *J* 9.0 Hz, H-1'), 5.93 (t, 1H, *J* 9.25 Hz, H-2'), 5.63 (t, 1H, 9.5 Hz, H-3'), 5.02 (t, 1H, *J* 10.0 Hz, H-4'), 4.40–4.38 (m, 1H, H-5'), 4.23–4.11 (m, 2H, H-6'a, H-6'b), 4.16 (d, 1H, *J* 18.0 Hz, H-5a), 4.00 (d, 1H, *J* 18.0 Hz, H-5b), 2.05–1.92 (4×CH<sub>3</sub>CO); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): δ 171.6 (C=O lactam), 170.0–169.4 (4×COCH<sub>3</sub>), 164.7 (C-2''), 164.6 (C-6''), 164.0 (C-1''), 159.8 (C-2, C=N), 156.1 (C-2'''), 135.9 (C-1''''), 131.5 (C-6'''), 129.0 (C-4''', C-3''''), C-5''''), 128.7 (C-4''''), 127.7 (C-2''''), C-6''''), 119.2 (C-5'''), 118.4 (C-1'''), 117.6 (C-3'''), 108.2 (C-5''), 80.3 (C-1'), 72.9 (C-5'), 72.2 (C-3'), 67.6 (C-2'), 67.5 (C-4'), 61.6 (C-6'), 32.7 (C-5), 20.5–20.1 (4×COCH<sub>3</sub>). (**2'd**): <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): δ 8.52 (s, 1H, H-5''), 7.61 (s, 2'''-OH), 7.46–7.41 (m, 2H, H-2''''), H-6''''), 7.04–6.96 (m, 3H, H-3''', H-4'''' & H-5''''), 8.36–8.26 (d, 4H, H-4''', H-6''', H-2''''), H-6''''), 6.44 (d, 1H, *J* 9.5 Hz, H-2'), 5.92 (t, 1H, *J* 9.0 Hz, H-1'), 5.56 (t, 1H, 9.25 Hz, H-3'), 5.10 (t, 1H, *J* 9.75 Hz, H-4'), 4.34–4.32 (m, 1H, H-5'), 4.23–4.11 (m, 2H, H-6'a, H-6'b), 4.16 (d, 1H, *J* 18.0 Hz, H-5a), 4.00 (d, 1H, *J* 18.0 Hz, H-5b), 2.05–1.92 (4×CH<sub>3</sub>CO); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): δ 172.0 (C=O lactam), 170.0–169.4 (4×COCH<sub>3</sub>), 164.7 (C-2''), 164.6 (C-6''), 164.0 (C-1''), 159.8 (C-2, C=N), 156.1 (C-2'''), 135.9 (C-1''''), 131.5 (C-6'''), 129.0 (C-4''', C-3''''), C-5''''), 128.7 (C-4''''), 127.7 (C-2''''), C-6''''), 119.2 (C-5'''), 118.4 (C-1'''), 117.6 (C-3'''), 108.2 (C-5''), 80.3 (C-1'), 72.9 (C-5'), 72.2 (C-3'), 67.6 (C-2'), 67.5 (C-4'), 61.6 (C-6'), 32.7 (C-5), 20.5–20.1 (4×COCH<sub>3</sub>).

Compounds **2e/2'e**: Yield 54%; mp. 183–183 °C, ratio of **2e/2'e** isomers 7.5/2.5; IR (KBr, cm<sup>-1</sup>): ν 1749, 1742, 1694, 1607, 1580, 1568, 1518, 1508, 1237, 1033; (**2e**): <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): 8.46–8.37 (m, 2H, H-2''''), H-6''''), 8.42 (d, 2H, *J* 8.25 Hz, H-2''''), H-6''''), 8.37 (s, 1H, H-5''), 8.44–8.39 (m, 2H, H-2''', H-6'''), 7.66–7.61 (m, 2H, H-4''''), H-5''''), 7.15 (d, 2H, *J* 8.25 Hz, H-3''''), H-5''''), 6.42 (d, 1H, *J* 9.0 Hz, H-1'), 5.97 (t, 1H, *J* 9.25 Hz, H-2'), 5.68 (t, 1H, 9.25 Hz, H-3'), 5.02 (t, 1H, *J* 9.75 Hz, H-4'), 4.40–4.38 (m, 1H, H-5'), 4.17–4.11 (m, 2H, H-6'a, H-6'b), 4.19 (d, 1H, *J* 17.75 Hz, H-5a), 4.01 (d, 1H, *J* 17.75 Hz, H-5b), 3.88 (4''''-OCH<sub>3</sub>), 2.05–1.92 (4×CH<sub>3</sub>CO); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): δ 171.7 (C=O lactam), 169.9–169.4 (4×COCH<sub>3</sub>), 165.3 (C-2''), 163.7 (C-6''), 163.2 (C-1''), 162.8 (C-2, C=N), 162.0 (C-4''''), 134.5 (C-1'''), 133.9 (C-3''''), 130.8 (C-2'''), 130.7 (C-5''''), 129.4 (C-2''''), C-6''''), 128.3 (C-4''''), 127.9 (C-1''''), 126.0 (C-6'''), 114.3 (C-3''''), C-5''''), 107.8 (C-5''), 80.3 (C-1'), 72.9 (C-5'), 72.3 (C-3'), 67.6 (C-2'), 67.5 (C-4'), 61.6 (C-6'), 55.4 (4''''-OCH<sub>3</sub>), 32.7 (C-5), 20.5–20.1 (4×COCH<sub>3</sub>). (**2'e**): <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): 8.46–8.37 (m, 2H, H-2''''), H-6''''), 8.42 (d, 2H, *J* 8.25 Hz, H-2''''), H-6''''), 8.37 (s, 1H, H-5''), 8.44–8.39 (m, 2H, H-2''', H-6'''), 7.66–7.61 (m, 2H, H-4''''), H-5''''), 7.15 (d, 2H, *J* 8.25 Hz, H-3''''), H-5''''), 6.49 (d, 1H, *J* 9.0

Hz, H-2'), 5.97 (t, 1H, *J* 9.25 Hz, H-1'), 5.56 (t, 1H, 9.25 Hz, H-3'), 5.22 (t, 1H, *J* 9.75 Hz, H-4'), 4.34–4.32 (m, 1H, H-5'), 4.17–4.11 (m, 2H, H-6'a, H-6'b), 4.19 (d, 1H, *J* 17.75 Hz, H-5a), 4.01 (d, 1H, *J* 17.75 Hz, H-5b), 3.88 (4''''-OCH<sub>3</sub>), 1.98–1.95 (4×CH<sub>3</sub>CO); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): δ 171.7 (C=O lactam), 169.9–169.4 (4×COCH<sub>3</sub>), 165.3 (C-2''), 163.7 (C-6''), 163.2 (C-1'''), 162.8 (C-2, C=N), 162.0 (C-4'''), 134.5 (C-1'''), 133.9 (C-3'''), 130.8 (C-2'''), 130.7 (C-5'''), 129.4 (C-2''', C-6'''), 128.3 (C-4'''), 127.9 (C-1'''), 126.0 (C-6'''), 114.3 (C-3''', C-5'''), 107.8 (C-5''), 79.9 (C-1'), 73.0 (C-5'), 72.3 (C-3'), 67.6 (C-2'), 67.5 (C-4'), 61.2 (C-6'), 55.4 (4''''-OCH<sub>3</sub>), 32.7 (C-5), 20.5–20.1 (4×COCH<sub>3</sub>).

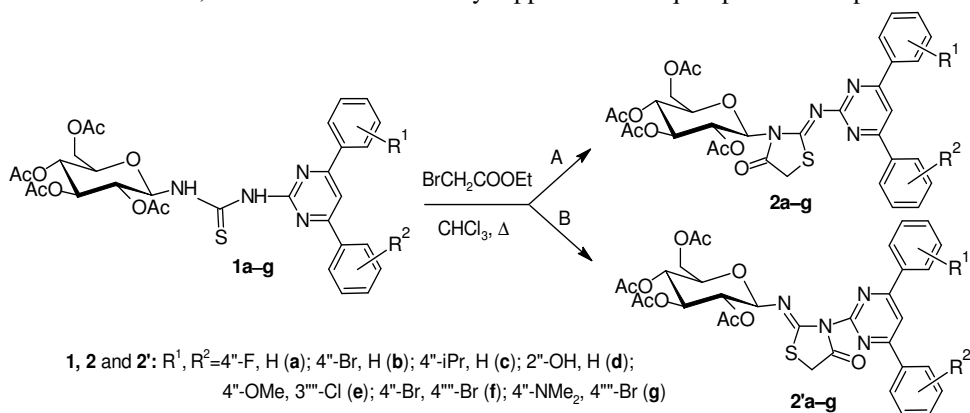
Compounds **2f/2'f**: Yield 66%; mp. 219–221 °C, ratio of **2f/2'f** isomers 7.6/2.4; IR (KBr, cm<sup>-1</sup>): ν 1752, 1740, 1591, 1577, 1567, 1513, 1237, 1223, 1032; (**2f**): <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): δ 8.41 (s, 1H, H-5''), 8.35 (d, 4H, *J* 8.25 Hz, H-2''', H-6''', H-2''', H-6'''), 7.80 (d, 4H, *J* 8.25 Hz, H-3''', H-5''', H-3''', H-5'''), 6.38 (d, 1H, *J* 9.0 Hz, H-1'), 5.93 (t, 1H, *J* 9.25 Hz, H-2'), 5.65 (t, 1H, 9.5 Hz, H-3'), 5.02 (t, 1H, *J* 9.75 Hz, H-4'), 4.39–4.37 (m, 1H, H-5'), 4.18–4.11 (m, 2H, H-6'a, H-6'b), 4.16 (d, 1H, *J* 18.0 Hz, H-5a), 3.97 (d, 1H, *J* 18.0 Hz, H-5b), 2.05–1.92 (4×CH<sub>3</sub>CO); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): δ 171.7 (C=O lactam), 169.9–169.4 (4×COCH<sub>3</sub>), 164.6 (C-4'', C-6''), 163.3 (C-2''), 163.1 (C-2, C=N), 135.3 (C-1''', C-1'''), 131.9 (C-3''', C-5''', C-3''', C-5'''), 129.6 (C-2''', C-6''', C-2''', C-6'''), 125.2 (C-4''', C-4'''), 108.4 (C-5''), 80.3 (C-1'), 72.9 (C-5'), 72.2 (C-3'), 67.6 (C-2'), 67.5 (C-4'), 61.6 (C-6'), 32.7 (C-5), 20.5–20.1 (4×COCH<sub>3</sub>). (**2'f**): <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): δ 8.41 (s, 1H, H-5''), 8.35 (d, 4H, *J* 8.25 Hz, H-2''', H-6''', H-2''', H-6'''), 7.80 (d, 4H, *J* 8.25 Hz, H-3''', H-5''', H-3''', H-5'''), 6.47 (t, 1H, *J* 9.25 Hz, H-2'), 5.93 (t, 1H, *J* 9.25 Hz, H-1'), 5.55 (t, 1H, 9.25 Hz, H-3'), 5.21 (t, 1H, *J* 9.75 Hz, H-4'), 4.34–4.32 (m, 1H, H-5'), 4.18–4.11 (m, 2H, H-6'a, H-6'b), 4.16 (d, 1H, *J* 18.0 Hz, H-5a), 3.97 (d, 1H, *J* 18.0 Hz, H-5b), 2.05–1.92 (4×CH<sub>3</sub>CO); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): δ 171.7 (C=O lactam), 169.9–169.4 (4×COCH<sub>3</sub>), 164.6 (C-1'', C-6''), 163.3 (C-2''), 163.1 (C-2, C=N), 135.3 (C-1''', C-1'''), 131.9 (C-3''', C-5''', C-3''', C-5'''), 129.6 (C-2''', C-6''', C-2''', C-6'''), 125.2 (C-4''', C-4'''), 108.4 (C-5''), 79.8 (C-1'), 72.9 (C-5'), 72.2 (C-3'), 67.6 (C-2'), 67.5 (C-4'), 61.6 (C-6'), 32.7 (C-5), 20.5–20.1 (4×COCH<sub>3</sub>).

Compounds **2g/2'g**: Yield 68%; mp. 229–231 °C, ratio of **2g/2'g** isomers 7.5/2.5; IR (KBr, cm<sup>-1</sup>): ν 1747, 1739, 1694, 1610, 1591, 1571, 1530, 1500, 1239, 1068; (**2g**): <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): δ 8.32 (d, 2H, *J* 8.5 Hz, H-2''', H-6'''), 8.28 (d, 2H, *J* 8.5 Hz, H-2''', H-6'''), 8.12 (s, 1H, H-5''), 7.78 (d, 2H, *J* 8.5 Hz, H-3''', H-5'''), 6.84 (d, 2H, *J* 8.5 Hz, H-3''', H-5'''), 6.36 (d, 1H, *J* 9.0 Hz, H-1'), 5.93 (t, 1H, *J* 9.5 Hz, H-2'), 5.64 (t, 1H, 9.75 Hz, H-3'), 5.00 (t, 1H, *J* 10.0 Hz, H-4'), 4.38–4.37 (m, 1H, H-5'), 4.17–4.10 (m, 2H, H-6'a, H-6'b), 4.13 (d, 1H, *J* 17.75 Hz, H-5a), 3.95 (d, 1H, *J* 17.75 Hz, H-5b), 3.04 (s, 6H, 4'''-NMe<sub>2</sub>), 2.06–1.92 (4×CH<sub>3</sub>CO); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): δ 171.7 (C=O lactam), 169.9–169.4 (4×COCH<sub>3</sub>), 165.7 (C-6''), 163.4 (C-4''), 163.2 (C-2''), 162.3 (C-2, C=N), 152.4 (C-4'''), 135.8 (C-1'''), 131.8 (C-3''', C-5'''), 129.5 (C-2''', C-6'''), 128.9 (C-2''', C-6'''), 124.6 (C-1'''), 122.6 (C-4'''), 108.4 (C-5''), 80.3 (C-1'), 72.9 (C-5'), 72.3 (C-3'), 67.6 (C-2'), 67.5 (C-4'), 61.7 (C-6'), 40.0 (4'''-NMe<sub>2</sub>), 32.6 (C-5), 20.5–20.1 (4×COCH<sub>3</sub>). (**2'g**): <sup>1</sup>H NMR (DMSO-*d*<sub>6</sub>): δ 8.32 (d, 2H, *J* 8.5 Hz, H-2''', H-6'''), 8.28 (d, 2H, *J* 8.5 Hz, H-2''', H-6'''), 8.12 (s, 1H, H-5''), 7.78 (d, 2H, *J* 8.5 Hz, H-3''', H-5'''), 6.84 (d, 2H, *J* 8.5 Hz, H-3''', H-5'''), 6.48 (d, 1H, *J* 9.25 Hz, H-2'), 5.93 (t, 1H, *J* 9.5 Hz, H-1'), 5.54 (t, 1H, 9.75 Hz, H-3'), 5.20 (t, 1H, *J* 10.0 Hz, H-4'), 4.35–4.30 (m, 1H, H-5'), 4.17–4.10 (m, 2H, H-6'a, H-6'b), 4.13 (d, 1H, *J* 17.75 Hz, H-5a), 3.95 (d, 1H, *J* 17.75 Hz, H-5b), 3.04 (s, 6H, 4'''-NMe<sub>2</sub>), 1.98–1.93 (4×CH<sub>3</sub>CO); <sup>13</sup>C NMR (DMSO-*d*<sub>6</sub>): δ 171.7 (C=O lactam), 169.9–169.4

( $4 \times \text{COCH}_3$ ), 165.7 (C-6''), 163.4 (C-1''), 163.2 (C-2''), 162.3 (C-2, C=N), 152.4 (C-4'''), 135.8 (C-1'''), 131.8 (C-3''', C-5'''), 129.5 (C-2''', C-6'''), 128.9 (C-2''', C-6'''), 124.6 (C-1'''), 122.6 (C-4'''), 108.4 (C-5'''), 80.3 (C-1'), 72.9 (C-5'), 72.3 (C-3'), 67.6 (C-2'), 67.5 (C-4'), 61.7 (C-6'), 40.0 (4''''-NMe<sub>2</sub>), 32.6 (C-5), 20.5–20.1 ( $4 \times \text{COCH}_3$ ).

## Results and Discussion

Required *N*-(per-*O*-acetyl- $\beta$ -*D*-glucopyranosyl)-*N'*-(4',6'-diarylpyrimidine-2'-yl)thioureas (**1a-g**) were prepared as already described in 7 steps<sup>9</sup> by the nucleophilic addition of corresponding 2-amino-4',6'-diarylpyrimidines on 2,3,4,6-tetra-*O*-acetyl- $\beta$ -*D*-glucopyranosyl isothiocyanate using microwave assisted method for several minutes in dried dioxane. The reaction of ethyl bromoacetate with corresponding thioureas (**1a-g**) lead to new 3-(2',3',4',6'-tetra-*O*-acetyl- $\beta$ -*D*-glucopyranosyl)-2-(4'',6''-diphenylpyrimidin-2''-ylimino)thiazolidin-4-ones (**2a-g**) and 2-(2',3',4',6'-tetra-*O*-acetyl- $\beta$ -*D*-glucopyranosyl-1'-imino)-3-(4'',6''-diphenylpyrimidin-2''-yl)thiazolidin-4-ones (**2'a-g**) (Scheme 1). We used chloroform as the reaction medium and molar ratios of ethyl bromoacetate and thioureas **1a-g** in 3:1 ratio in order to obtain the higher transformation yields. Reaction mixtures were stirred in room temperature for one hour, after that, heated with reflux for 8-10 h. A reaction time of over 10 h at reflux in chloroform was kept since a longer time did not improve the yield. The appearance of white precipitate in the reaction beginning was the evidence indicating the reaction was taken place. The isomeric products **2a-g** and **2'a-g** were insoluble in ethanol, methanol, it facilitated for purification. Reaction yields are 50-68%. These isomers have some similar features in structure which made the separation of these isomers to become difficult. When solvent systems were changed from *n*-hexane-acetone to toluene-ethyl acetate-formic acid, these isomers were always appeared in unique spot on TLC plate.



Scheme 1

IR spectra show the characteristic absorption bands at  $\nu=1752\text{--}1739\text{ cm}^{-1}$  ( $\nu_{\text{C=O}}$  ester),  $1694\text{--}1690\text{ cm}^{-1}$  ( $\nu_{\text{C=O}}$  lactam),  $1610\text{--}1607\text{ cm}^{-1}$  ( $\nu_{\text{C=N}}$ ),  $1575\text{--}1508\text{ cm}^{-1}$  ( $\nu_{\text{C=C}}$ ),  $1239\text{--}1227$  and  $1033\text{--}1035\text{ cm}^{-1}$  ( $\nu_{\text{COC}}$  ester). The evidences that confirm the success of reactions are the absence of NH bands in IR spectra at  $\nu=3340\text{--}3320\text{ cm}^{-1}$  and chemical shifts of NH (thiourea) at  $\delta=9\text{--}10\text{ ppm}$  (in <sup>1</sup>H NMR spectra). Other evidence is the disappearance of C=S signals at  $\delta=206\text{--}208\text{ ppm}$  and the appearance of C=N signals at  $\delta=163.9\text{--}160.0\text{ ppm}$  (in <sup>13</sup>C NMR spectra). The <sup>1</sup>H and <sup>13</sup>C NMR spectral elucidations of these products indicated the presence of two isomers in each obtained product. The isomers **2a-g** and **2'a-g** were distinguished

one isomer from another by chemical shifts of protons *H*-1' and *H*-2' on pyranose ring. In isomer **2a-g** resonance signals of proton *H*-1' show at  $\delta=6.42-6.35$  ppm and the one of proton *H*-2' show at  $\delta=5.97-5.92$  ppm, while protons *H*-1' and *H*-2' in isomer **2'a-g** had chemical shifts at  $\delta=5.97-5.92$  ppm and  $6.51-6.44$  ppm, respectively. Proton *H*-1' in isomers **2'a-g** were shielded more strongly by diamagnetic anisotropy of imino group and its resonance signal was upfield, while this effect was absent in isomer **2a-g**, so the resonance signals of proton *H*-1' was downfield.

## Conclusion

We have performed an efficient method for the reaction of (2,3,4,6-tetra-*O*-acetyl- $\beta$ -*D*-glucopyranosyl)thioureas containing pyrimidine ring with ethyl bromoacetate under refluxing conditions. It shows that the obtained 2-minothiazolidin-4-ones were two isomers and their ratio could be found using <sup>1</sup>H NMR spectra.

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