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A new approach for the N- and S-galactosylation of 5-arylidene-2-thioxo-4-thiazolidinones

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ABSTRACT

N- and S-galactosylation was carried out via the reaction of 5-((*Z*)-arylidene)-2-thioxo-4-thiazolidinones with 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide under alkaline conditions or under silylation conditions. Deacetylation of the N-galactosylation products was performed with concentrated hydrochloric acid in methanol (3.5%) or sodium methoxide in methanol without cleavage of the 2-thioxo-4-thiazolidinone ring by means of acid hydrolysis. The anomers were separated by flash column chromatography, and their configurations were assigned by NMR spectroscopy. The deprotected nucleosides were screened against leukemia L-1210 and were found inactive.

1. Introduction

The chemistry of 2-thioxo-4-thiazolidinone and its derivatives has been studied for over half a century because of its important chemical and biological applications. Derivatives of 2-thoxo-4-thiazolidinone have been demonstrated to possess antibacterial,[1–4] antifungal,[5,6] anticonvulsant,[7] anticancer,[8] antituberculosis,[9] anti-human immunodeficiency virus type 1 (HIV-1),[10–12] antimicrobial,[13] antidiabetic,[14] antitubercular,[15,16] antiparasitic,[17] hypnotic,[18] and anthelmintic activities.[19] 2-Thioxo-4-thiazolidinones also act as analogs of purine bases in nucleic acid synthesis.[20] During the last decade thiazole nucleoside analogs have been recognized as potent and increasingly important antimetabolite agents.[21,22] *N*-Galactosyl derivatives of 2-thioxo-4-thiazolidinones are not very well known, but *N*-(β-D-glucopyranosyl)-5-(4-nitrobenzylidene)-2-thioxo-4-thiazolidinone showed antiviral activity by inhibition of viral RNA synthesis.[23] Glycosyl derivatives of structurally similar heterocyclic systems have been reported before.[24–28] In continuation of our work on the synthesis of novel nucleosides as potential antiviral and antitumor agents, and keeping in mind the biological significance of 2-thioxo-4-thiazolidinones,[29–37] we hereby report the synthesis, antitumor screening, and spectroscopy of a series of N- and S-galactosylated analogs bearing 2-thioxo-4-thiazolidinone bases. This is the first time that *N*- and *S*-galactosyl derivatives of 2-thioxo-4-thiazolidinones have been prepared via new synthetic strategies. The previous work of Metwally et al.[13] was successful in preparing *N*-glycosyl derivatives of 2-thioxo-4-thiazolidinones without the S-glycosylation of 2-thioxo-4-thiazolidinone. At the same time, they did not succeed in the synthesis of the corresponding deprotected *N*-glycosyl derivatives of 2-thioxo-4-thiazolidinone.

2. Results and discussion

2-Thioxo-4-thiazolidinone (**1**) was condensed with the appropriate aromatic aldehydes (**2a**–**f**) in ethanol in the presence of piperidine as catalyst at room temperature to afford the corresponding 5-((*Z*)-arylidene)-2-thioxo-4-thiazolidinones (**3a**–**f**) (Scheme 1).

Treatment of **3a**–**f** with 1.1 equiv of NaH in anhyd acetonitrile furnished the sodium salts of 2-thioxo-4-thiazolidinones (**4a**–**f**), which in turn were treated with 2,3,4,6-tetra-*O*-acetyl-α-D-galactopyranosyl bromide (**6**) to afford nitrogen protected nucleosides **8a**–**f** and sulfur protected nucleosides **9a**–**f**, respectively. The N-isomers and S-isomers were isolated by silica gel column chromatography. The protected nucleosides **8a** and **9a** were independently synthesized through another pathway. The silylation of **3a** was accomplished with bis(trimethylsilyl)acetamide (BSA) in anhyd acetonitrile at 70–80 °C. Similar conditions furnished the trimethylsilylated derivative **5a**. This derivative **5a** was condensed with 1,2,3,4,6-penta-*O*-acetyl-α-D-galactopyaranose (**7**) in the presence

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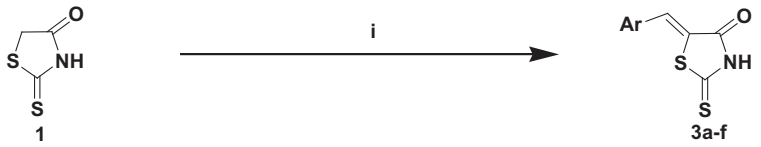


2,3	Ar	2,3	Ar
a	Phenyl	d	3,4-Ethylenedioxphenyl
b	2-Hydroxy-3-methoxyphenyl	e	2-Thienyl
c	3,4-Methylenedioxphenyl	f	5-Bromo-2-thienyl

Scheme 1. Reagents and condition: (i) Ar-CHO (**2a–f**), piperidine, EtOH, rt.

of trimethylsilyl trifluoromethanesulfonate (TMSOTf) as catalyst at 70–80 °C for 60 min. The protected nucleosides **8a** and **9a** were isolated by silica gel column chromatography in 32% and 26% yields, respectively.

The structures of **8a–f** and **9a–f** were established and confirmed by elemental analyses and spectral data (IR, ^{1}H NMR, ^{13}C NMR and MS). The absence of a signal for NH and the presence of signal for the thiocarbonyl group at ν_{max} 1210–1240 cm^{-1} were characteristic of the IR absorption spectra of **8a–f**, while the IR absorption spectra of **9a–f** were characterized by the absence of signals for the NH and CS groups. The ^{1}H NMR ($CDCl_3$) spectrum of compound **8d** showed a singlet at δ_H 7.62 assigned to the vinyl proton, indicating the presence of a *Z*-configuration for the exocyclic double bond and subsequent N-glycosylation. This is in agreement with the ^{1}H NMR ($CDCl_3$) spectrum of 5-((*Z*)-benzylidene)-3-methyl-2-thioxo-4-thiazolidinone whose vinyl proton appears at δ_H 7.75.[38] The anomeric proton appears as a doublet at δ_H 6.30 (J = 9.4 Hz), indicating the presence of the β-D-galactopyranose moiety and N-glycosylation. The ^{13}C NMR ($CDCl_3$) spectrum of **8d** showed a singlet at δ_C 166.36 and 194.4 assigned to the carbonyl carbon at C-4 and the thiocarbonyl group at C-2, respectively. These data are also in agreement with the ^{13}C NMR ($CDCl_3$) spectrum of 5-((*Z*)-hexylidene-4-oxo-2-thioxo-thiazolidinyl)acetic acid,[39] since the carbonyl at C-4 appears at δ_C 165.7 and the thiocarbonyl group at C-2 appears at δ_C 194.8, indicating the presence of N-glycosylation. The ^{1}H NMR ($CDCl_3$) spectrum of compound **9d** showed a singlet at δ_H 7.78 assigned to the vinyl proton, indicating the presence of a *Z*-configuration for the exocyclic double bond and S-glycosylation. This is in agreement with the ^{1}H NMR ($CDCl_3$) spectrum of 5-((*Z*)-benzylidene)-2-allylmercapto-4-thiazolidinone whose vinyl proton appears at δ_H 7.84.[40] The anomeric proton appears as a doublet at δ_H 5.98 (J = 10.4 Hz), indicating the presence of the β-D-galactopyranosyl moiety and S-glycosylation. The ^{13}C NMR ($CDCl_3$) spectrum of **9d** showed a singlet at δ_C 179.1 and 188.6 assigned to the carbonyl at C-4 and the thiocarbonyl group at C-2, respectively. These data are also in agreement with the ^{13}C NMR ($CDCl_3$) spectrum of 5-((*Z*)-benzylidene)-2-allylmercapto-4-thiazolidinone,[40] since the carbonyl at C-4 appears at δ_C 179.8 and the thiocarbonyl group at C-2 appears at δ_C 191.8, indicating the presence of S-glycosylation.

Removal of the acetyl groups from the glycon moiety of **8a–f** with a solution of concd HCl–MeOH (2%) at 50 °C for 2 h or NaOMe–MeOH at room temperature furnished 5-((*Z*)-arylidene)-3-(β-D-galactopyranosyl)-2-thioxo-4-thiazolidinones (**10a–f**), indicating the presence of N-glycosylation. Correspondingly, when the protected nucleoside **9c** was treated with concd HCl–MeOH (10%) at 50 °C or NaOMe–MeOH at room temperature. 5-((*Z*)-Methylenedioxy-benzylidene)-2,4-thazolidinedione (**11**) was obtained, indicating the presence of S-glycosylation. This type of cleavage explains why we were not successful in the preparation of the corresponding deprotected nucleosides of **9a–f** (Scheme 2). The nucleoside bases **1** and **3** can be utilized as starting materials for the synthesis of other carbohydrate derivatives such as deoxy, amino, and azido nucleosides.

In conclusion, we have carried out the successful synthesis of hitherto unreported 5-((*Z*)-arylidene)-3-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranosyl)-2-thioxo-4-thiazolidinones (**8a–f**), 5-((*Z*)-arylidene)-2-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranosyl)-2-thioxo-4-thiazolidinones (**9a–f**), and 5-((*Z*)-arylidene)-3-(β-D-galactopyranosyl)-2-thioxo-4-thiazolidinones (**10a–f**). The conformational analyses of their most stable configurations were established by NMR spectroscopy. Compounds **10a–f** were screened against leukemia-1210 and were found to be inactive.[41,42] The antiviral and further antitumor activities of the new prepared compounds are under investigation and will be reported in due time.

3. Experimental

3.1. General procedures

Melting points were determined on a Büchi apparatus and are uncorrected. TLC was carried out on aluminum backed Silica Gel 60 F_{254} (E. Merck) plates and detected by shortwave UV light. IR spectra were obtained as potassium bromide pellets using a Pye Unicam spectrometer 1000. ^{1}H NMR and ^{13}C NMR spectra were measured on a Bruker Avance DPX 300 MHz spectrometer in DMSO-d_6 or $CDCl_3$ using TMS as the internal standard. Chemical shifts are given in δ units (ppm) and J values in Hz. Analytical data were obtained using a Carlo Erba 1106 C,H,N elemental analyzer. Mass spectra were recorded by EI on a Varian MAT 112 spectrometer and FAB on a Kratos MS spectrometer.

3.2. 5-((*Z*)-Arylidene)-2-thioxo-4-thiazolidinones (3a–f). General procedure

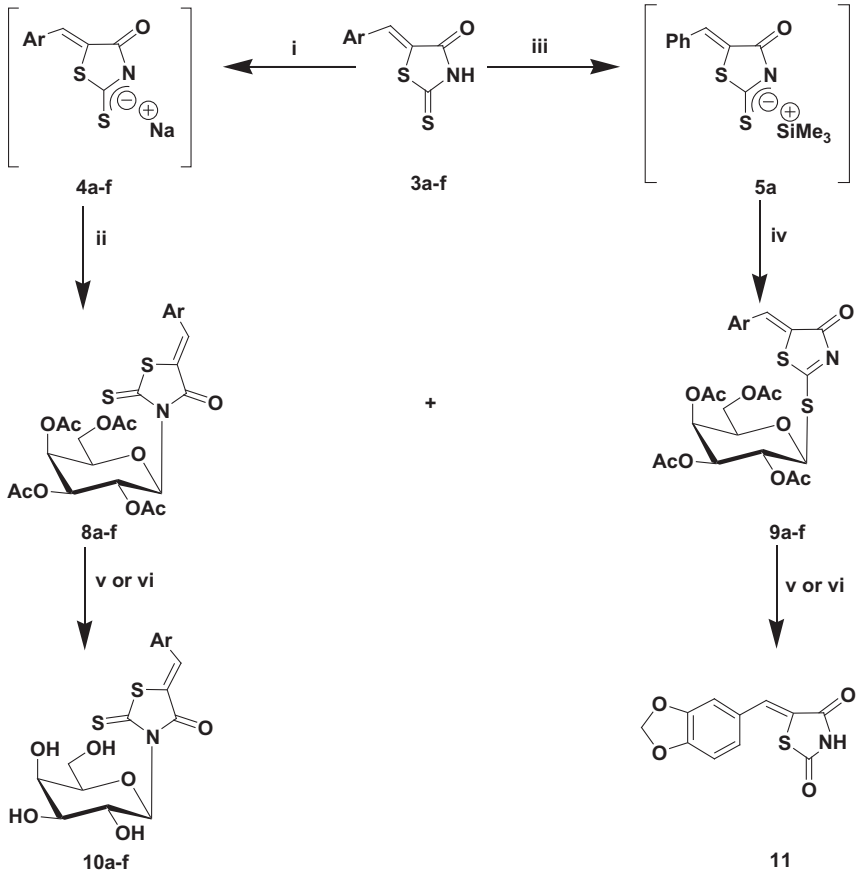
To a mixture of 2-thioxo-4-thiazolidinone (**1**) (1.33 g, 10 mmol), anhyd piperidine (0.9 g, 10 mmol) and anhyd EtOH (30 mL) were added the appropriate aromatic aldehydes (**2a–f**) (11 mmol). The mixture was stirred until the starting material was consumed (12 h; TLC). The reaction mixture was diluted with water and neutralized with dilute hydrochloric acid. The yellow solid that separated was collected by filtration and recrystallized from ethanol to give the products **3a–f** in quantitative yields.

3.2.1. Preparation of 5-((*Z*)-benzylidene)-2-thioxo-4-thiazolidinone (3a)

Yield 2.00 g (90%); mp 205–206 °C (lit.[40] yield 95%, mp 208–210 °C); IR: ν 3190 (NH), 1726 (C=O) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.49–7.59 (m, 5H, Ar-H), 7.62 (s, 1H, =CH), 13.85 (s, 1H, NH); ^{13}C NMR (300 MHz, DMSO-d_6): δ 125.90 (=CH), 129.84, 130.90, 131.14, 132.05, 133.36 (C-5, C-Ar), 169.76 (C-4), 196.07 (C-2).

3.2.2. Preparation of 5-((*Z*)-(2-hydroxy-3-methoxybenzylidene)-2-thioxo-4-thiazolidinone (3b)

Yield 2.25 g (84%); mp 197–198 °C (lit.[40] yield 86%, mp 194–196 °C); IR: ν 3190 (NH), 1728 (C=O) cm^{-1}; ^{1}H NMR (300 MHz,



3-10	Ar	3-10	Ar
a	Phenyl	**d**	3,4-Ethylenedioxphenyl
b	2-Hydroxy-3-methoxyphenyl	**e**	2-Thienyl
c	3,4-Methylenedioxphenyl	**f**	5-Bromo-2-thienyl

Scheme 2. Reagents and conditions: (i) CH_3CN, NaH; (ii) 1,2,3,4,6-penta-*O*-acetyl-α-D-galactopyranosyl bromide (**6**); (iii) CH_3CN, BSA, 70–80 °C, 30 min; (iv) 1,2,3,4,6-penta-*O*-acetyl-α-D-galactopyranose (**7**), TMSOTf, 70–80 °C, 60 min; (v), concd HCl–MeOH (3.5%), 0–50 °C, 2 h; (vi) NaOMe–MeOH, 0 °C, rt, 2 h.

DMSO-d_6): δ 3.86 (s, 3H, OMe), 6.86–7.15 (m, 3H, Ar-H), 7.94 (s, 1H, =CH), 9.89 (s, 1H, OH), 13.72 (s, 1H, NH); ^{13}C NMR (300 MHz, DMSO-d_6): δ 56.23 (OMe), 114.43, 119.99, 120.50, 124.70, 127.19, 147.19, 148.26 (=CH, C-5, C-Ar), 170.10 (C-4), 196.42 (C-2).

3.2.3. Preparation of 5-((*Z*)-3,4-methylenedioxybenzylidene)-2-thioxo-4-thiazolidinone (3c)

Yield 2.45 g (92%); mp 211–212 °C (lit.[43] yield 71%, mp 278–279 °C); IR (KBr) *v* 3194 (NH), 1732 (C=O) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ 6.13 (s, 2H, OCH_2O), 7.12 (m, 3H, Ar-H), 7.56 (s, 1H, =CH) 13.67 (s, 1H, NH).

3.2.4. 5-((*Z*)-3,4-Ethylenedioxybenzylidene)-2-thioxo-4-thiazolidinone (3d)

Yield 2.62 g (94%); mp 207–208 °C; IR (KBr) *v* 3196 (NH), 1736 (C=O) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ 4.26 (m, 4H, 2 × OCH_2), 6.94 (m, 3H, Ar-H), 7.38 (s, 1H, =CH) 13.65 (s, 1H, NH); ^{13}C NMR (300 MHz, DMSO-d_6) δ 64.14, 64.71 (2 × OCH_2), 118.19, 119.35, 122.99, 124.57, 125.69, 126.40, 131.79, 143.89, 146.15 (C-Ar, =CH, C-5), 169.52 (C-4), 195.46 (C-2); MS, *m*/*z* 279 (M^+); Anal. Calcd for $C_{12}H_9NO_3S_2$ (279.34): C, 51.60; H, 3.25; N, 5.01. Found: C, 51.86; H, 3.39; N, 4.76.

3.2.5. Preparation of 5-((*Z*)-2-thienylidene)-2-thioxo-4-thiazolidinone (3e)

Yield 2.15 g (95%); mp 220–221 °C; (lit.[40] yield 89% mp 218–220 °C); IR (KBr) *v* 3198 (NH), 1727 (C=O) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.27 (d, *J* = 3.83 Hz, 1H, 4′-H), 7.68 (t, *J* = 3.70 Hz, 1H, 3′-H), 7.90 (d, *J* = 3.78 Hz, 1H, 5′-H), 8.05 (s, 1H, =CH), 13.77 (s, 1H, NH); ^{13}C NMR (300 MHz, DMSO-d_6): δ 123.11, 124.86, 129.37, 134.37, 135.44, 137.56 (=CH, C-5, C-Ar), 169.11 (C-4), 194.68 (C-2).

3.2.6. 5-[(*Z*)-(5-Bromo-2-thienylidene)]-2-thioxo-4-thiazolidinone (3f)

Yield 2.72 g (89%); mp 220–221 °C; IR (KBr) *v* 3196 (NH), 1727 (C=O) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ 7.12–7.37 (m, 2H, Ar-H), 7.73 (s, 1H, =CH), 13.56 (s, 1H, NH); ^{13}C NMR (300 MHz, DMSO-d_6): δ 119.79 (=CH), 123.24 (C-5), 124.04, 132.14, 134.76, 139.25 (C-Ar), 168.91 (C-4), 193.77 (C-2); MS, *m*/*z* 306 (M^+); Anal. Calcd for $C_8H_4BrNOS_3$ (306.23): C, 31.38; H, 1.32; N, 4.57. Found: C, 31.46; H, 1.60; N, 4.28.

3.3. 5-((*Z*)-Benzylidene)-3-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranosyl)-2-thioxo-4-thiazolidinone (8a) and 5-((*Z*)-benzylidene)-2-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranosyl)-2-thioxo-4-thiazolidinone (9a). General procedures

3.3.1. Method A

5-((*Z*)-Benzylidene)-2-thioxo-4-thiazolidinone (**3a**) (1.10 g, 5.0 mmol) was suspended in anhyd MeCN (5 mL) at room temperature. To this suspension was added NaH (50%, 0.26 g, 5 mmol), and the mixture was stirred at room temperature for 30 min. The

mixture became clear after 15 min. 2,3,4,6-Tetra-*O*-acetyl-α-D-galactopyranosyl bromide (6, 2.26 g, 5.50 mmol) was added, and the mixture was stirred at room temperature for 12 h until the starting material was consumed (TLC). The reaction mixture was diluted with CH_2Cl_2 (200 mL), washed with cold satd aq $NaHCO_3$ (200 mL) and water (2 × 100 mL), and dried over anhyd Na_2SO_4. The mixture was concentrated in vacuo, and the residue was purified by flash chromatography (eluent 30–50% Et_2O–petroleum ether, bp 40–60 °C) to afford, respectively, 1.00 g (36%) of **8a** and 0.85 g (31%) of **9a** as yellow solids.

3.3.2. Method B

5-((*Z*)-Benzylidene)-2-thioxo-4-thiazolidinone (**3a**) (1.10 g, 5 mmol) was suspended in anhyd acetonitrile (25 mL) and BSA (1.25 mL, 5 mmol) was added, and the reaction mixture was heated at 70–80 °C for 30 min. The 1,2,3,4,6-penta-*O*-acetyl-α-D-galactopyranose (7,1.87 g, 5 mmol) dissolved in anhyd acetonitrile (25 mL) was added to the reaction mixture via a cannula. Finally TMSOTf (1.00 mL, 5 mmol) was added, and the reaction mixture was heated at 70–80 °C for 60 min. Then satd $NaHCO_3$ was added to quench the reaction, and the resulting mixture was extracted with CH_2Cl_2. The combined organic fractions were washed with satd NaCl solution, dried over $MgSO_4$, filtered, and evaporated to dryness. The solid obtained was purified by flash chromatography (eluent 10–50% Et_2O–petroleum ether, bp 40–60 °C) to give, respectively, 0.87 g (32%) of **8a** and 0.71 g (26%) of **9a** as yellow solids.

3.3.2.1. Data for 8a. Mp 103–105 °C; IR (KBr) *ν* 1749 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): *δ* 1.92 (s, 3H, Ac), 1.99 (s, 3H, Ac), 2.01 (s, 3H, Ac), 2.22 (s, 3H, Ac), 4.07–4.21 (m, 3H, 5′-H, 6′-H, 6″-H), 5.20 (dd, *J* = 3.26, 9.14 Hz, 1H, 4′-H), 5.48 (d, *J* = 3.17 Hz, 1H, 3′-H), 6.23 (t, *J* = 9.21 Hz, 1H, 2′-H), 6.30 (d, *J* = 9.15 Hz, 1H, 1′-H), 7.43 (m, 5H, Ar-H), 7.71 (s, 1H, =CH); ^{13}C NMR (300 MHz, $CDCl_3$): *δ* 20.33, 20.47, 20.58 (4Ac), 61.31 (C-6′), 65.54 (C-2′), 66.65 (C-3′), 71.42 (C-4′), 73.44 (C-5′), 82.06 (C-1′), 120.54 (=CH), 130.80 (C-5), 129.24, 130.58, 133.04, 133.73 (C-Ar), 165.90 (C-4), 169.80 169.87, 170.25, 170.29 (4Ac), 194.03 (C-2); MS: *m*/*z* 551 (M^+); Anal. Calcd for $C_{24}H_{25}NO_{10}S_2$ (551.59): C, 52.26; H, 4.57; N, 2.54. Found: C, 52.14; H, 4.80; N, 2.46.

3.3.2.2. Data for 9a. Mp 180–182 °C; IR (KBr) *ν* 1750 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): *δ* 2.01 (s, 3H, Ac), 2.03 (s, 3H, Ac), 2.08 (s, 3H, Ac), 2.18 (s, 3H, Ac), 4.10–4.23 (m, 3H, 5′-H, 6′-H, 6″-H), 5.20 (dd, *J* = 3.36, 9.92 Hz, 1H, 4′-H), 5.42 (t, *J* = 10.17 Hz, 2′-H), 5.50 (d, *J* = 3.32 Hz, 1H, 3′-H), 5.98 (d, *J* = 10.35 Hz, 1H, 1′-H), 7.42 (m, 5H, Ar-H), 7.70 (s, 1H, =CH); ^{13}C NMR (300 MHz, $CDCl_3$): *δ* 20.32, 20.45, 20.60 (4Ac), 61.11 (C-6′), 66.44 (C-2′), 66.94 (C-3′), 71.40 (C-4′), 75.12 (C-5′), 82.40 (C-1′), 120.50 (=CH), 130.82 (C-5), 129.26, 130.58, 133.05, 133.76 (C-Ar), 169.80 169.86, 170.27, 170.30 (4Ac), 179.30 (C-4), 188.40 (C-2); MS, *m*/*z* 551 (M^+); Anal. Calcd for $C_{24}H_{25}NO_{10}S_2$ (551.58): C, 52.26; H, 4.57; N, 2.54. Found: C, 52.07; H, 4.72; N, 2.50.

3.3.3. 5-((*Z*)-(2-Hydroxy-3-methoxybenzylidene)-3-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranosyl)-2-thioxo-4-thiazolidinone (8b) and 5-((*Z*)-(2-hydroxy-3-methoxybenzylidene)-2-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranosyl)-2-thioxo-4-thiazolidinone (9b)

Method A described for the synthesis of **8a** was utilized using 1.33 g (5 mmol) of **3b** instead of **3a** as the starting material. The product was purified by flash chromatography (eluent 30–50%, Et_2O–petroleum ether, 40–60 °C) to afford, respectively, 1.44 g (48%) of **8b** and 0.92 g (31%) of **9b** as yellow foams.

3.3.3.1. Data for 8b. IR (KBr) *ν* 1750 (C=O), 1744 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): *δ* 1.98 (s, 3H, Ac), 2.04 (s, 3H, Ac), 2.06 (s, 3H, Ac), 2.28 (s, 3H, Ac), 3.93 (s, 3H, OCH_3), 4.10–4.26 (m, 3H, 5′-H, 6′-H, 6″-H), 5.24 (dd, *J* = 3.36, 9.90 Hz, 1H, 4′-H), 5.52 (d, *J* = 3.26 Hz, 1H, 3′-H), 6.29 (t, *J* = 9.20 Hz, 1H, 2′-H), 6.33 (d, *J* = 9.60 Hz, 1H, 1′-H), 6.47 (s, 1H, OH), 6.92 (m, 3H, Ar-H), 8.18 (s, 1H, =CH); ^{13}C NMR (300 MHz, $CDCl_3$): *δ* 20.48, 20.61, 20.70, 20.73 (4Ac), 56.22 (OCH_3), 61.47 (C-6′), 65.68 (C-2′), 66.79 (C-3′), 71.63 (C-4′), 73.53 (C-5′), 81.16 (C-1′), 112.91, 119.79, 120.07, 120.12, 121.02, 125.90, 146.32, 146.91 (C-Ar, =CH, C-5), 166.01 (C-4), 169.88, 170.10, 170.45, 170.53 (4Ac), 194.85 (C-2); MS: *m*/*z* 597 (M^+); Anal. Calcd for $C_{25}H_{27}NO_{12}S_2$ (597.60): C, 50.24; H, 4.55; N, 2.34. Found: C, 50.16; H, 4.90; N, 2.08.

3.3.3.2. Data for 9b. IR (KBr) *ν* 1752 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): *δ* 2.01 (s, 3H, Ac), 2.04 (s, 3H, Ac), 2.07 (s, 3H, Ac), 2.18 (s, 3H, Ac), 3.94 (s, 3H, OCH_3), 4.09–4.21 (m, 3H, 5′-H, 6′-H, 6″-H), 5.16 (dd, *J* = 3.34, 9.91 Hz, 1H, 4′-H), 5.41 (t, *J* = 10.14 Hz, 1H, 2′-H), 5.50 (d, *J* = 3.16 Hz, 1H, 3′-H), 5.98 (d, *J* = 10.40 Hz, 1H, 1′-H), 6.32 (s, 1H, OH), 6.92–7.05 (m, 3H, Ar-H), 8.36 (s, 1H, =CH); MS: *m*/*z* 597 (M^+); Anal. Calcd for $C_{25}H_{27}NO_{12}S_2$ (597.60): C, 50.24; H, 4.55; N, 2.34. Found: C, 50.33; H, 4.78; N, 2.14.

3.3.4. 5-((*Z*)-3,4-Methylenedioxybenzylidene)-3-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranosyl)-2-thioxo-4-thiazolidinone (8c) and 5-((*Z*)-3,4-methylenedioxybenzylidene)-2-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranosyl)-2-thioxo-4-thiazolidinone (9c)

Method A described for the synthesis of **8a** was utilized using 1.32 g (5 mmol) of **3c** instead of **3a** as the starting material. The product was purified by flash chromatography (eluent 30–50%, Et_2O–petroleum ether, bp 40–60 °C) to afford, respectively 1.80 g (60%) of **8c** and 0.90 g (30%) of **9c** as yellow foams.

3.3.4.1. Data for 8c. IR (KBr) *ν* 1750 (C=O), 1746 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): *δ* 1.97 (s, 3H, Ac), 2.03 (s, 3H, Ac), 2.06 (s, 3H, Ac), 2.27 (s, 3H, Ac), 4.10–4.24 (m, 3H, 5′-H, 6′-H, 6″-H), 5.23 (dd, *J* = 3.36, 9.42 Hz, 1H, 4′-H), 5.51 (d, *J* = 3.24 Hz, 1H, 3′-H), 6.07 (s, 2H, OCH_2O), 6.26 (t, *J* = 9.36 Hz, 1H, 2′-H), 6.32 (d, *J* = 9.20 Hz, 1H, 1′-H), 6.89–7.04 (m, 3H, Ar-H), 7.64 (s, 1H, =CH); ^{13}C NMR (300 MHz, $CDCl_3$): *δ* 20.48, 20.61, 20.72 (4Ac), 61.43 (C-6′), 65.64 (C-2′), 66.76 (C-3′), 71.57 (C-4′), 73.54 (C-5′), 82.17 (C-1′), 102.09 (OCH_2O), 109.23, 109.36, 118.11, 127.51, 127.58, 133.93, 148.74, 150.21 (C-Ar, =CH, C-5), 166.15 (C-4), 170.04, 170.43 (4Ac), 193.88 (C-2); MS: *m*/*z* 595 (M^+); Anal. Calcd for $C_{25}H_{25}NO_{12}S_2$ (595.60): C, 50.41; H, 4.23; N, 2.35. Found: C, 50.27; H, 4.35; N, 2.30.

3.3.4.2. Data for 9c. IR (KBr) *ν* 1748 (C=O) cm^{-1}; MS: *m*/*z* 595 (M^+); Anal. Calcd for $C_{25}H_{25}NO_{12}S_2$ (595.60): C, 50.41; H, 4.23; N, 2.35. Found: C, 50.32; H, 4.44; N, 2.18.

3.3.5. 5-((*Z*)-3,4-Ethylenedioxybenzylidene)-3-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranosyl)-2-thioxo-4-thiazolidinone (8d) and 5-((*Z*)-3,4-ethylenedioxybenzylidene)-2-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranosyl)-2-thioxo-4-thiazolidinone (9d)

Method A described for the synthesis of **8a** was utilized using 1.40 g (5 mmol) of **3d** instead of **3a** as the starting material. The product was purified by flash chromatography (eluent 30–50% Et_2O–petroleum ether, bp 40–60 °C) to afford 1.80 g (58%) of **8d** and 0.80 g (26%) of **9d** as yellow foams.

3.3.5.1. Data for 8d. IR (KBr) *ν* 1750 (C=O), 1746 (C=O) cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): *δ* 1.95 (s, 3H, Ac), 2.02 (s, 3H, Ac), 2.05 (s, 3H, Ac), 2.26 (s, 3H, Ac), 4.10–4.33 (m, 7H, 5′-H, 6′-H, 6″-H, 2 × OCH_2), 5.22 (dd, *J* = 3.36, 8.67 Hz, 1H, 4′-H), 5.50 (d,

J = 3.24 Hz, 1H, 3′-H), 6.26 (t, J = 9.20 Hz, 1H, 2′-H), 6.30 (d, J = 9.40 Hz, 1H, 1′-H), 6.92–7.01 (m, 3H, Ar-H), 7.62 (s, 1H, =CH); ^{13}C NMR (300 MHz, $CDCl_3$): δ 20.67, 20.81, 20.92, 20.97 (4Ac), 61.65 (C-6′), 64.36, 64.92 (2 OCH_2), 65.85 (C-2′), 67.00 (C-3′), 71.82 (C-4′), 73.76 (C-5′), 82.39 (C-1′), 118.45, 118.50, 119.68, 125.39, 126.95, 134.06, 144.25, 146.65 (C-Ar, =CH, C-5), 166.36 (C-4), 170.07, 170.23, 170.60, 170.66 (4Ac), 194.40 (C-2); MS: m/z 609 (M^+); Anal. Calcd for $C_{26}H_{27}NO_{12}S_2$ (609.62): C, 51.22; H, 4.46; N, 2.30. Found: C, 51.12; H, 4.68; N, 2.37.

3.3.5.2. Data for 9d. IR (KBr) ν 1750 (C=O) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.02 (s, 3H, Ac), 2.05 (s, 3H, Ac), 2.08 (s, 3H, Ac), 2.20 (s, 3H, Ac), 4.10–4.34 (m, 7H, 5′-H, 6′-H, 6″-H, 2 × OCH_2), 5.28 (dd, J = 3.36, 9.92 Hz, 1H, 4′-H), 5.42 (t, J = 10.15 Hz, 1H, 2′-H), 5.50 (d, J = 3.26 Hz, 1H, 3′-H), 5.98 (d, J = 10.40 Hz, 1H, 1′-H), 6.90–7.10 (m, 3H, Ar-H), 7.78 (s, 1H, =CH); ^{13}C NMR (300 MHz, $CDCl_3$): δ 20.22, 20.33, 20.37 (4Ac), 60.99 (C-6′), 63.87 (OCH_2), 64.44 (OCH_2), 66.30 (C-2′), 66.88 (C-3′), 71.28 (C-4′), 75.03 (C-5′), 82.25 (C-1′), 117.96, 118.98, 122.90, 124.81, 126.44, 136.95, 143.75, 146.35 (C-Ar, =CH, C-5), 169.37, 169.41, 169.78, 170.06 (4Ac), 179.14 (C-4), 188.58 (C-2); MS: m/z 609 (M^+); Anal. Calcd for $C_{26}H_{27}NO_{12}S_2$ (609.62): C, 51.22; H, 4.46; N, 2.30. Found: C, 51.07; H, 4.72; N, 2.26.

3.3.6. 5-((*Z*)-2-Thienylidene)-3-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranosyl)-2-thioxo-4-thiazolidinone (8e) and 5-((*Z*)-2-thienylidene)-2-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranosyl)-2-thioxo-4-thiazolidinone (9e)

Method A described for the synthesis of **8a** was utilized using 1.13 g (5 mmol) of **3g** instead of **3a** as the starting material. The product was purified by flash chromatography (eluent 30–50%, Et_2O–petroleum ether, bp 40–60 °C) to afford, respectively, 1.17 g (42%) of **8e** and 0.89 g (32%) of **9e** as yellow foams.

3.3.6.1. Data for 8e. IR (KBr) ν 1752 (C=O), 1747 (C=O) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.96 (s, 3H, Ac), 2.03 (s, 3H, Ac), 2.04 (s, 3H, Ac), 2.26 (s, 3H, Ac), 4.14–4.24 (m, 3H, 5′-H, 6′-H, 6″-H), 5.22–5.52 (m, 2H, 4′-H, 3′-H), 6.26–6.30 (m, 2H, 2′-H, 1′-H), 7.18–7.90 (m, 4H, Ar-H, =CH); ^{13}C NMR (300 MHz, $CDCl_3$): δ 20.66, 20.79, 20.89 (4Ac), 61.66 (C-6′), 65.82 (C-2′), 67.01 (C-3′), 71.74 (C-4′), 73.74 (C-5′), 82.43 (C-1′), 118.79 (=CH), 126.30 (C-5), 129.19, 133.48, 134.55, 138.03 (C-Ar), 165.93 (C-4), 170.06, 170.15, 170.53 (4Ac), 193.54 (C-2); MS, m/z 557 (M^+); Anal. Calcd for $C_{22}H_{23}NO_{10}S_3$ (557.62): C, 47.39; H, 4.16; N, 2.51. Found: C, 47.25; H, 4.31; N, 2.39.

3.3.6.2. Data for 9e. IR (KBr) ν 1750 cm^{-1} (C=O); MS: m/z 557 (M^+); Anal. Calcd for $C_{22}H_{23}NO_{10}S_3$ (557.62): C, 47.39; H, 4.16; N, 2.51. Found: C, 47.30; H, 4.35; N, 2.46.

3.3.7. 5-[(*Z*)-(5-Bromo-2-thienylidene)]-3-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranosyl)-2-thioxo-4-thiazoli-dinone (8f) and 5-[(*Z*)-(5-bromo-2-thienylidene)]-2-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-galactopyranosyl)-2-thioxo-4-thiazolidinone (9f)

Method A described for the synthesis of **8a** was utilized using 1.53 g (5 mmol) of **3f** instead of **3a** as the starting material. The product was purified by flash chromatography (eluent 30–50%, Et_2O–petroleum ether, bp 40–60 °C) to afford, respectively, 1.87 g (60%) of **8f** and 0.62 g (20%) of **9f** as yellow foams.

3.3.7.1. Data for 8f. IR (KBr) ν 1750 (C=O), 1746 (C=O) cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.97 (s, 3H, Ac), 2.04 (s, 3H, Ac), 2.06 (s, 3H, Ac), 2.27 (s, 3H, Ac), 4.11–4.27 (m, 3H, 5′-H, 6′-H, 6″-H), 5.26 (dd, J = 3.31, 9.05, 1H, 4′-H), 5.53 (d, J = 3.23 Hz, 1H, 3′-H), 6.25–6.30 (m, 2H, 2′-H, 1′-H), 7.16 (m, 2H, Ar-H), 7.75 (s, 1H, =CH); ^{13}C NMR (300 MHz, $CDCl_3$): δ 20.65, 20.76, 20.87 (4Ac), 61.67 (C-6′), 65.80 (C-2′), 67.01 (C-3′), 71.68 (C-4′), 73.73 (C-5′), 82.42 (C-1′), 119.35 (=CH), 121.43 (C-5), 124.98, 132.18, 134.52, 139.57 (C-Ar), 165.74 (C-4), 170.09, 170.12, 170.51, 170.54 (4Ac), 192.77 (C-2); MS: m/z 636 (M^+); Anal. Calcd for $C_{22}H_{22}BrNO_{10}S_3$ (636.51): C, 41.51; H, 3.48; N, 2.20. Found: C, 41.42; H, 3.75; N, 2.08.

3.3.7.2. Data for 9f. IR (KBr) ν 1750 cm^{-1} (C=O); ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.01 (s, 3H, Ac), 2.04 (s, 3H, Ac), 2.05 (s, 3H, Ac), 2.08 (s, 3H, Ac), 4.08–4.22 (m, 3H, 5′-H, 6′-H, 6″-H), 5.20 (dd, J = 3.35, 9.90 Hz, 1H, 4′-H), 5.42 (t, J = 10.18 Hz, 1H, 2′-H), 5.50 (d, J = 3.24 Hz, 1H, 3′-H), 5.95 (d, J = 10.37 Hz, 1H, 1′-H), 7.16–7.31 (m, 2H, Ar-H), 7.93 (s, 1H, =CH); MS: m/z 636 (M^+); Anal. Calcd for $C_{22}H_{22}BrNO_{10}S_3$ (636.51): C, 41.51; H, 3.48; N, 2.20. Found: C, 41.36; H, 3.80; N, 2.27.

3.4. 5-((*Z*)-Benzylidene)-3-β-D-galactopyranosyl-2-thioxo-4-thiazolidinone (10a). General procedures

3.4.1. Method A

The protected nucleoside **8a** (551 mg, 1 mmol) was suspended in MeOH (15 mL), and concd HCl (0.5 mL) was added. The reaction mixture was stirred at 50 °C for 2 h, then cooled to room temperature. To the resulting solution was added an ion-exchange resin (Amberlite IR-120, HO^--form), previously washed with MeOH. After stirring for 5 min., the solution was filtered and evaporated in vacuo and the residue was purified by flash chromatography (eluent 0–5%, $CHCl_3$–MeOH) to afford 340 mg (89%) of **10a** as yellow solid: mp 203–205 °C; IR (KBr) ν 3400 (OH), 1719 (C=O) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.32–3.74 (m, 5H, 4′-H, 5′-H, 6′-H, 6″-H, 3′-H), 4.51 (m, 1H, 2′-H), 4.71 (t, J = 5.00 Hz, 1H, 6′-OH), 5.00 (d, J = 5.12 Hz, 1H, 4′-OH), 5.26 (d, J = 3.62 Hz, 1H, 3′-OH), 5.33 (d, J = 3.63 Hz, 1H, 2′-OH), 5.80 (d, J = 9.00 Hz, 1H, 1′-H), 7.52–7.80 (m, 5H, Ar-H); ^{13}C NMR (300 MHz, DMSO-d_6): δ 60.74 (C-6′), 65.29 (C-2′), 68.64 (C-3′), 74.56 (C-4′), 79.32 (C-5′), 85.79 (C-1′), 121.10 (=CH), 132.93 (C-5), 125.67, 129.80, 130.85, 133.18 (C-Ar), 166.01 (C-4), 195.82 (C-2); MS: m/z 383 (M^+); Anal. Calcd for $C_{16}H_{17}NO_6S_2$ (383.44): C, 50.12; H, 4.47; N, 3.65. Found: C, 49.94; H, 4.82; N, 3.57.

3.4.2. Method B

To a stirred suspension of the protected nucleoside **8a** (551 mg, 1 mmol) in anhyd MeOH (15 mL) was added portionwise NaOMe (0.06 g, 1.1 mmol) in anhyd MeOH (15 mL) at 0 °C. Then the reaction mixture was stirred for 2 h at room temperature. To the resulting solution was added an ion-exchange resin (Amberlite IR-120, H^+-form), previously washed with MeOH. After stirring for 5 min, the solution was filtered and evaporated in vacuo, and the residue was purified by flash chromatography (eluent 0–5%, $CHCl_3$–MeOH) to afford 330 mg (86%) of **10a** as yellow solid.

3.4.3. 5-((*Z*)-(2-Hydroxy-3-methoxybenzylidene)-3-β-D-galactopyranosyl-2-thioxo-4-thiazolidinone (10b)

Method A described for the synthesis of **10a** was utilized using 597 mg (1 mmol) of **8b** instead of **8a** as the starting material. The product was purified by flash chromatography (eluent 0–5%, $CHCl_3$–MeOH) to afford 334 mg (78%) of **10b** as yellow solid: mp 155–157 °C; IR (KBr) ν 3398 (OH), 1714 (C=O) cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6 + D_2O): δ 3.16–3.72 (m, 5H, 4′-H, 5′-H, 6′-H, 3′-H), 3.85 (s, 3H, OCH_3), 4.41 (t, J = 8.96 Hz, 1H, 2′-H), 5.86 (d, J = 9.33 Hz, 1H, 1′-H), 6.91–7.15 (m, 3H, Ar-H), 7.98 (s, 1H, =CH); ^{13}C NMR (300 MHz, DMSO-d_6): δ 55.96 (OCH_3), 60.88 (C-6′), 67.50 (C-2′), 69.72 (C-3′), 77.33 (C-4′), 80.64 (C-5′), 84.81 (C-1′), 114.40, 119.41, 119.80, 120.04, 120.54, 128.30, 146.84, 148.01 (=CH, C-5, C-Ar), 165.98 (C-4), 195.80 (C-2); MS: m/z 429 (M^+);

Anal. Calcd for $C_{17}H_{19}NO_8S_2$ (429.47): C, 47.54; H, 4.46; N, 3.26. Found: C, 47.33; H, 4.75; N, 3.13.

3.4.4. 5-((*Z*)-3,4-Methylenedioxybenzylidene)-3-β-D-galactopyranosyl-2-thioxo-4-thiazolidinone (10c)

Method A described for the synthesis of **8a** was utilized using 595 mg (1 mmol) of **8c** instead of **8a** as the starting material. The product was purified by flash chromatography (eluent 0–5%, $CHCl_3$–MeOH) to afford 350 mg (82%) of **10c** as yellow solid: mp 186–188 °C; IR (KBr) ν 3400 (OH), 1710 (C=O) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 3.14–3.82 (m, 5H, 4′-H, 5′-H, 6′-H, 6″H, 3′-H), 4.32 (m, 1H, 2′-H), 4.63 (m, 1H, 6′-OH), 4.77 (d, J = 4.23 Hz, 1H, 4′-OH), 4.86 (m, 1H, 3′-OH), 5.22 (d, J = 4.32 Hz, 1H, 2′-OH), 5.84 (d, J = 9.00 Hz, 1H, 1′-H), 6.13 (s, 2H, OCH_2O), 7.01–7.17 (m, 3H, Ar-H), 7.67 (s, 1H, =CH); ^{13}C NMR (300 MHz, DMSO-d_6): δ 60.56 (C-6′), 65.22 (C-2′), 68.50 (C-3′), 74.59 (C-4′), 78.94 (C-5′), 84.80 (C-1′), 102.07 (OCH_2O), 109.15, 109.30, 118.03, 126.88, 127.18, 132.44, 148.47, 149.84 (=CH, C-5, C-Ar), 165.99 (C-4), 194.640 (C-2); MS: m/z 427 (M^+); Anal. Calcd for $C_{17}H_{17}NO_8S_2$ (427.45): C, 47.77; H, 4.01; N, 3.28. Found: C, 47.61; H, 4.15; N, 3.22.

3.4.5. 5-((*Z*)-3,4-Ethylenedioxybenzylidene)-3-β-D-galactopyranosyl-2-thioxo-4-thiazolidinone (10d)

Method A described for the synthesis of **10a** was utilized using 609 mg (1 mmol) of **8d** instead of **8a** as the starting material. The product was purified by flash chromatography (eluent 0–5%, $CHCl_3$–MeOH) to afford 379 mg (86%) of **10d** as yellow solid: mp 194–196 °C; IR (KBr) ν 3398 (OH), 1709 (C=O) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 3.25–3.75 (m, 5H, 4′-H, 5′-H, 6′-H, 3′-H), 4.26–4.48 (m, 6H, 2 × OCH_2, 2′-H, 6′-OH), 4.60 (d, J = 5.38 Hz, 1H, 4′-OH), 5.00 (d, J = 4.50 Hz, 1H, 3′-OH), 5.20 (d, J = 4.83 Hz, 1H, 2′-OH), 5.78 (d, J = 9.30 Hz, 1H, 1′-H), 7.04–7.2 (m, 3H, Ar-H), 7.68 (s, 1H, =CH); ^{13}C NMR (300 MHz, DMSO-d_6): δ 60.68 (C-6′), 64.17 (2 OCH_2), 65.20 (C-2′), 68.50 (C-3′), 74.57 (C-4′), 79.24 (C-5′), 85.71 (C-1′), 118.46, 119.62, 124.67, 126.50, 132.86, 143.95, 146.47 (=CH, C-5, C-Ar), 166.00 (C-4), 195.54 (C-2); MS: m/z 441 (M^+); Anal. Calcd for $C_{18}H_{19}NO_8S_2$ (441.48): C, 48.97; H, 4.34; N, 3.17. Found: C, 48.83; H, 4.51; N, 3.12.

3.4.6. 5-((*Z*)-2-Thienylidene)-3-β-D-galactopyranosyl-2-thioxo-4-thiazolidinones (10e)

Method A described for the synthesis of **10a** was utilized using 557 mg (1 mmol) of **8e** instead of **8a** as the starting material. The product was purified by flash chromatography (eluent 0–5%, $CHCl_3$–MeOH) to afford 318 mg (82%) of **10e** as yellow solid: mp 180–182 °C; IR (KBr) ν 3400 (OH), 1710 (C=O) cm^{-1}; ^1H NMR (300 MHz, CD_3OD-d_4): δ 3.29–3.94 (m, 6H, 4′-H, 5′-H, 6′-H, 3′-H, 2′-H), 6.00 (d, J = 9.34 Hz, 1H, 1′-H), 7.24–7.94 (m, 4H, H-4″, H-3″, =CH, H-5″); ^{13}C NMR (300 MHz, CD_3OD): δ 62.40 (C-6′), 67.16 (C-2′), 70.63 (C-3′), 76.28 (C-4′), 80.22 (C-5′), 86.74 (C-1′), 120.36, 126.48, 130.15, 134.60, 135.80, 139.28 (=CH, C-5, C-Ar), 168.00 (C-4), 196.10 (C-2); MS: m/z 389 (M^+); Anal. Calcd for $C_{14}H_{15}NO_6S_3$ (389.47): C, 43.17; H, 3.88; N, 3.60. Found: C, 43.04; H, 4.11; N, 3.53.

3.4.7. 5-[(*Z*)-(5-Bromo-2-thienylidene)]-3-β-D-galactopyranosyl-2-thioxo-4-thiazolidinones (10f)

Method A described for the synthesis of **10a** was utilized using 636 mg (1 mmol) of **8f** instead of **8a** as the starting material. The product was purified by flash chromatography (eluent 0–5%, $CHCl_3$–MeOH) to afford 360 mg (77%) of **10f** as yellow solid: mp 178–180 °C; IR (KBr) ν 3398 (OH), 1702 (C=O) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 3.33–3.80 (m, 5H, 4′-H, 5′-H, 6′-H, 3′-H), 4.40 (m, 2H, 2′-H, 6′-OH), 4.71 (t, J = 9.06 Hz, 1H, 4′-OH), 4.94 (t, J = 9.20 Hz, 1H, 3′-OH), 5.21 (m, 1H, 2′-OH), 5.80 (d, J = 9.25 Hz, 1H, 1′-H), 7.33–7.55 (m, 2H, H-4″, H-3″), 7.89 (s, 1H, =CH); ^{13}C NMR (300 MHz, DMSO-d_6): δ 60.49 (C-6′), 65.11 (C-2′), 68.42 (C-3′), 74.49 (C-4′), 78.92 (C-5′), 85.58 (C-1′), 119.34, 120.20, 124.07, 132.43, 135.43, 139.11 (=CH, C-5, C-Ar), 165.51 (C-4), 193.72 (C-2); MS: m/z 468 (M^+); Anal. Calcd for $C_{14}H_{14}BrNO_6S_3$ (468.37): C, 35.90; H, 3.01; N, 2.99. Found: C, 35.76; H, 3.13; N, 2.78.

3.5. 5-((*Z*)-(3,4-Methylenedioxybenzylidene)-2,4-thiazolidindione (11)

The protected nucleoside **9c** (595 mg, 1 mmol) was suspended in MeOH (15 mL), and concd HCl (2 mL) was added. The reaction mixture was heated under reflux for 2 h until the starting material was consumed (TLC), then it was cooled to room temperature, and the separated yellow solid was collected by filtration and recrystallized from EtOH to give 212 mg (90%) of product **11**: mp 245–247 °C; IR (KBr) ν 3200 (NH), 1755 (CO), 1710 (CO) cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 6.15 (s, 2H, OCH_2O), 7.05–7.18 (m, 3H, Ar-H), 7.72 (s, 1H, =CH), 12.56 (s, 1H, NH); ^{13}C NMR (300 MHz, DMSO-d_6): δ 102.10, 109.12, 109.34, 118.06, 126.90, 127.26, 132.50, 148.60, 149.98 (C-Ar, C-5, =CH), 167.40 (C-4), 167.86 (C-2); MS: m/z 249 (M^+); Anal. Calcd for $C_{11}H_7NO_4S$ (249.24): C, 53.01; H, 2.83; N, 5.62. Found: C, 53.32; H, 3.04; N, 5.48.

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References

1. Kucukguzel, S. G.; Oruc, E. E.; Rollas, S.; Sahin, F.; Ozbek, A. *Eur. J. Med. Chem.* **2002**, *37*, 197–206.
2. Gualtieri, M.; Bastide, L.; Latouche, P. V.; Leonette, J. P. *J. Antimicrob. Chemother.* **2006**, *58*, 778–783.
3. Sim, M. M.; Ng, S. B.; Buss, A. D.; Crasta, S. C.; Goh, K. L.; Lee, S. K. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 697–699.
4. Petrikaite, V.; Tarasevicius, E.; Pavilonis, A. *Medicina* **2007**, *43*, 657–663.
5. Capan, G.; Ulusoy, N.; Ergenc, N.; Kiraz, M. *Monatsh. Chem.* **1999**, *130*, 1399–1407.
6. Sortino, M.; Delgado, P.; Juarez, S.; Quiroqa, J.; Abonia, R.; Insuasty, B.; Noqueras, M.; Rodero, L.; Garibatto, F. M.; Enriz, R. D.; Zacchino, S. A. *Bioorg. Med. Chem.* **2007**, *15*, 484–494.
7. Ergenc, N.; Capan, G. *Il Farmaco* **1994**, *49*, 133–135.
8. Bhatt, J. J.; Shah, B. R.; Shah, H. P.; Trivedi, P. B.; Undavia, N. K.; Desai, N. C. *Indian J. Chem., Sect. B* **1994**, *33*, 189–192.
9. Bukowski, L.; Janowiec, M.; Zwolska-Kwiek, Z.; Andrezejczyk, Z. *Pharmazie* **1998**, *53*, 373–376.
10. Barreca, M. L.; Chimirri, A.; Luca, L. D.; Monforte, A.; Monforte, P.; Rao, A.; Zappala, M.; Balzarini, J.; De Clercq, E.; Pannecouque, C.; Witvrouw, M. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 1793–1796.
11. Ozkirimli, S.; Kazan, F.; Tunali, Y. *J. Enzym. Inhib. Med. Chem.* **2009**, *24*, 447–452.
12. Chandrappa, S.; Benaka Prasad, S. B.; Vinaya, K.; Ananda Kumar, C. S.; Thimmegowda, N. R.; Rangappa, K. S. *Invest. New Drugs* **2008**, *26*, 437–444.
13. Metwally, N. H.; Abdalla, M. A.; Mosselhi, M. A. N.; El-Desoky, E. A. *Carbohydr. Res.* **2010**, *345*, 1135–1141.
14. Nurugan, R.; Anbazhagan, S.; Sriman Narayanan, S. *Eur. J. Med. Chem.* **2009**, *44*, 3272–3279.
15. Chandrappa, S.; Kavitha, C. V.; Shahabuddin, M. S.; Vinaya, K.; Ananda Kumar, C. S.; Ranganatha, S. R.; Raghavan, S. C.; Rangappa, K. S. *Bioorg. Med. Chem.* **2009**, *17*, 2576–2584.
16. Brooke, E. W.; Davies, S. G.; Mulvaney, A. W.; Okada, M.; Pompeo, F.; Sim, E.; Vickers, R. J.; Westwood, I. M. *Bioorg. Med. Chem.* **2003**, *13*, 2527–2530.
17. Rauter, A. P.; Padilha, M.; Figueiredo, J. A.; Ismael, M. I.; Justino, J.; Ferreira, H.; Ferreira, M. J.; Rajendran, C.; Wilkins, R.; Vaz, P. D.; Calhorda, M. J. *J. Carbohydr. Chem.* **2005**, *24*, 275–296.
18. Ergenc, N.; Capan, G.; Gunay, N. S.; Ozkirimli, S.; Gungor, M.; Ozbey, S.; Kendi, E. *Arch. Pharmacol.* **1999**, *332*, 343–347.
19. Verma, A.; Saraf, S. K. *Eur. J. Med. Chem.* **2008**, *43*, 897–905.
20. Hardy, R. W.; Marcotrigiano, J.; Blight, K. J.; Majors, J. K.; Rice, C. M. *J. Virol.* **2003**, *77*, 2029–2037.
21. Hallick, S. K.; Martin, A. R.; Lingard, R. G. *J. Med. Chem.* **1971**, *14*, 528–532.
22. Kumar, R.; Lown, J. W. *Eur. J. Org. Chem.* **2003**, *24*, 4842–4851.
23. Foye, W. O.; Tovivich, P. *J. Pharm. Sci.* **1977**, *66*, 1607–1611.

24. El-Barbary, A. A.; Khodair, A. I.; Pedersen, E. B.; Nielsen, C. *J. Med. Chem.* **1994**, *37*, 73–77.
25. Khodair, A. I.; EL-Subagh, H. I.; El-Emam, A. A. *Boll. Chim. Farm.* **1997**, *136*, 561–567.
26. Al-Obaid, A. M.; EL-Subagh, H. I.; Khodair, A. I.; Elmazar, M. M. A. *Anticancer Drugs* **1996**, *7*, 873–880.
27. Khodair, A. I. *Carbohydr. Res.* **2001**, *331*, 445–453.
28. Khodair, A. I. *Nucleos. Nucleot. Nucl.* **2001**, *20*, 1735–1750.
29. Zsolnai, T. *Arzneim.-Forsch.* **1969**, *19*, 558–560.
30. Taniyama, T.; Takemura, S.; Yasui, B.; Uchida, H. *J. Pharm. Soc. Jpn.* **1954**, *74*, 113–119.
31. Werbel, L. M.; Headen, N.; Elslager, E. F. *J. Med. Chem.* **1968**, *11*, 364–365.
32. Brown, F. C.; Bradsher, C. K.; Bond, S. M.; Granthan, R. J. *Ind. Eng. Chem.* **1954**, *46*, 1508–1512.
33. Takematsu, T.; Furushima, M.; Hasegawa, Y.; Morioka, M.; Tsuchiyama, T. Jpn. Pat. *7*,243,812, 1972.
34. Mackie, A.; Stewart, G. M. *Arch. Int. Pharmacodyn. Ther.* **1955**, *102*, 476–486.
35. Moers, F. G.; Goossens, J. W. M.; Langhout, J. P. M. *J. Inorg. Nucl. Chem.* **1973**, *35*, 855–859.
36. Brockman, R. W.; Sidwell, R. W.; Arnett, G.; Shaddix, S. *Proc. Soc. Exp. Biol. Med.* **1970**, *133*, 609–614.
37. Foye, W. O.; Lange, W. E.; Feldmann, E. G. *J. Am. Pharm. Assoc. Sci. Ed.* **1958**, *47*, 831–834.
38. Villemin, D.; Alloun, A. B. *Phosphorus, Sulfur Silicon Reat. Elem.* **1993**, *79*, 33–41.
39. Ishida, T.; In, Y.; Inoue, M.; Ueno, Y.; Tanaka, C. *Tetrahedron Lett.* **1989**, *30*, 959–962.
40. Khodair, A. I. *J. Heterocycl. Chem.* **2002**, *39*, 1153–1160.
41. Monks, A.; Scudiero, D.; Skehan, P.; Shoemaker, R.; Poull, K.; Vistica, D.; Hose, C.; Langly, J.; Cronise, P.; Viagro-Wolff, A.; Gray-Goodrish, M.; Compell, H.; Boyd, M. *J. Natl. Cancer Inst.* **1991**, *83*, 757–766.
42. Poull, K.; Boyd, M. *Drug Dev. Res.* **1995**, *34*, 91–109.
43. Zhou, J.-F.; Zhu, F.-X.; Song, Y.-Z.; Zhu, Y.-L. *ARKIVOC* **2006**, *xiv*, 175–180.