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Synthesis of New Gluco-, Galacto-, and Mannopyranosylthiazoles, Thiazolidinones, and Pyranosylthiazlidin-4-ones from Sugar Thiosemicarbazone Derivatives

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ABSTRACT: *A new series of potentially biological active derivatives, namely alkyl-2-((4-oxo-2-(phenylimino)-3-(β-D-pyranosyl-2-ylamino)thiazolidine-5-ylidene)acetate (**5a–f**), 4-(4-bromophenyl) thiazol-2(3H)-ylidene)hydrazinyl)-β-D-pyranosyl (**4a–c**), and 5-(4-bromophenyl)-2-(phenylimino)-3-(β-D-pyranosyl-2-ylamino)thiazolidine-4-one (**6**) were synthesized via a reaction of the sugar thiosemicarbazone derivatives with 2,4′-dibromoacetophenone, dialkylacetylenedicarboxylate, and ethylbromoacetate, respectively. The structures of the synthesized compounds were established by spectroscopic methods (FT-IR, ^{1}H NMR, ^{13}C NMR, and 2D NMR) and elemental analyses. Furthermore, the effect of various solvents at reflux and also ambient temperature on the reactions of the sugar thiosemicarbazone with 2,4′dibromoacetophenone, diethyl acetylenedicarboxylate, and dimethyl acetylenedicarboxylate was investigated.* © 2013 Wiley Periodicals, Inc. Heteroatom Chem. 00:1–8, 2013; View this article online at wileyonlinelibrary.com. DOI 10.1002/hc.21083

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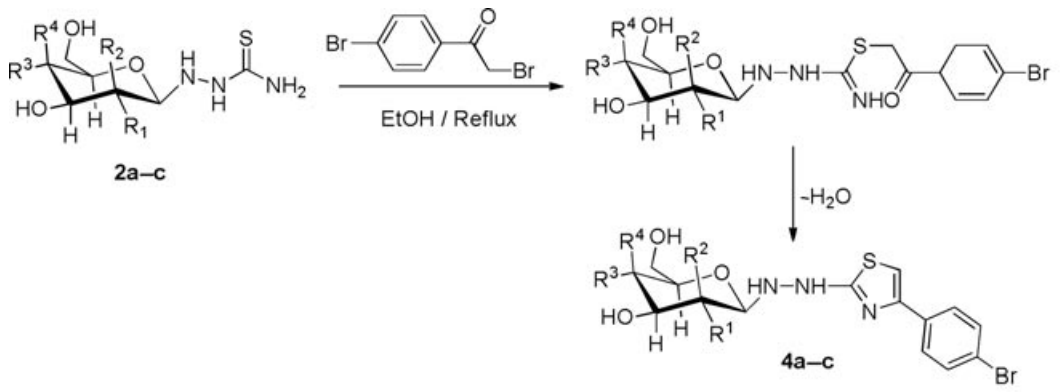
INTRODUCTION

Thiazoles are general heterocyclic compounds that are found in various biologically active and natural products like vitamin B_1 (thiamine) [1]. The thiazole ring in the presence of its coenzyme also plays an important role as an electron sink in the decarboxylation of α-keto acid [2]. Thiazole derivatives, thiazolidine-4-one, and organic compounds containing the thiazole and thiazolidinone ring system are used as antiviral agents, and some are used as pesticides [3], antitumor, cytotoxic [4], antifungal [5], antibacterial [6], antiparasitic [7], antitubercular [8], analgesic, and anticancer [9] agents. Therefore, studies of the synthesis and pharmacology of thiazol-2-imine derivatives and thiazolidine-4-one have attracted increasing interest in recent years.

In the past few decades, the literature has been enriched with increasing amounts of information about the anticonvulsive activities of various substituted thiazole derivatives [10], the synthesis of thiazole derivatives by various methods, and their biological evaluation [11]. In 2003, a series of arylaminothiazoles were synthesized by Holla et al. and found to be effective antibacterial and antiinflammatory agents [12]. Recently, the quantitative structural–activity relationship analyses for fungicidal activities of 2-phenylimino-1 and 3-thiazolines derivatives were carried out by Hahn and coworkers [13]. The glycoconjugates also exerted important effects on many complex biological events [14] including cellular recognition in the processes of immune



Entry	R^1	R^2	R^3	R^4	Product	Yields (%)
2a	OH	H	OH	H	**4a**	61
2b	H	OH	OH	H	**4b**	62
c	OH	H	H	OH	**4c**	72

SCHEME 1 Synthesis of 4-bromothiazol-2-ylidene derivative.

response [15], inflammation, tumor metastasis, and viral infections [16].

In addition, glycosylation of proteins and lipids is a key factor in modulating their structures and functions [17]. However, there are a few reports on the synthesis and pharmacology of the thiazol-2-imines containing sugar moieties. Since thiazole and thiazolidinone ring systems are known to be biologically active, we turned our attention to the synthesis of such thiazol-2-imine derivatives for investigating their biological activities and developing structure–activity relationships. Our research group is hopeful that this synthesis will provide new and fascinating sulfur-containing drug candidates.

RESULTS AND DISCUSSION

β-D-Pyranosylhydrazinecarbothioamide **2a–2c** and *N*-phenyl-β-D-pyranosyl hydrazine carbothioamide **3a–3c** were used as starting materials. These compounds (**2a–c** and **3a–c)** were obtained from the reaction of D-glycopyranos derivatives and thiosemicarbazide or phenylthiosemicarbazide, respectively, according to the known procedure in the literature [18–20].

The reaction of **2a–c** with 2,4′-dibromoacetophenone was investigated (Scheme 1). First, different solvents such as chloroform and dichloromethane were used as the reaction medium. In these reactions, cyclization products were not obtained; however, the use of absolute ethanol as a solvent gave the desired products. The structures of compounds **4a–c** were deduced from their elemental analysis and their IR and ^{1}H and ^{13}C NMR spectral data. In the ^{1}H NMR spectra of compounds **4a–c**, the expected two doublets around 7 and 8 ppm corresponding to the NH groups and one singlet at 7 ppm corresponding to the H—C=C thiazole ring were observed whereas their ^{13}C NMR showed signals of thiazole ring imino groups around 170 ppm.

The formation of the 4-bromothiazol-2-ylidene derivatives was verified by C—H correlations experiments. Figure 1 shows the C—H correlations spectra of **4a**. Based on the C—H correlations in Fig. 1, we can unambiguously assign all chemical shift values of carbon and proton atoms in the sugar ring.

To obtain thiazolidine derivatives, a series of 4-oxothiazolidine-5-ylidene derivatives **5a–f** were synthesized (Scheme 2). Compounds **5a–f** were obtained by the reaction of dialkylacetylenedicarboxylate with a series of *N*-phenyl-β-D-pyranosidehydrazinecarbothioamides. Several reports regarding the condensation of thiosemicarbazones with alkyl halides have pointed out that the main products are of type **5a–f** [21], resulting

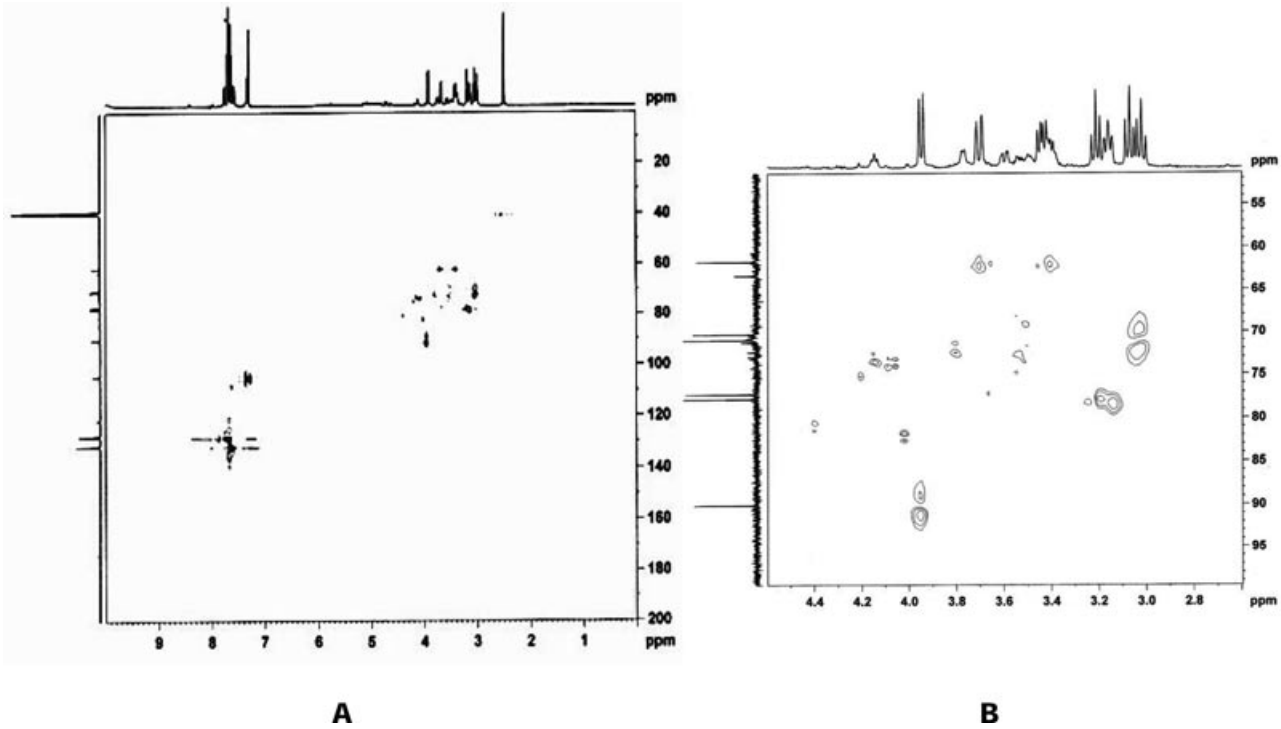


FIGURE 1 (A) ^{1}H-^{13}C correlations spectra of 2-[*N*-(4-(4-bromo-phenyl)-3*H*-thiazol-2-ylidene]-D-glucopyranosyl, (B) sugar part (expanded)

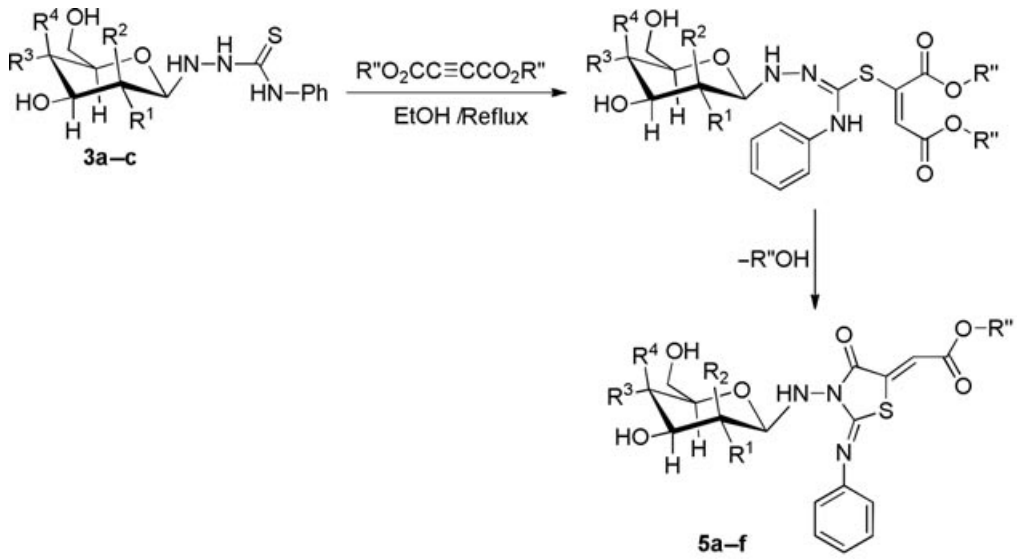
from cyclization at *N*-4. 2-(Dimethylhydrazono)-3-phenylthiazol-4-one was obtained by refluxing thiosemicarbazide with ethyl bromoacetate for 7 days in dichloromethane [22]. Saleh et al. reported that substituted thioureas reacted with chloroacetic acid in the presence of a weak base to produce thiazolidine-4-one compounds with substitution at *N*-4 [23].

Conversely, the cyclization at *N*-2 has been scarcely reported. Moghaddam and Hojabri [24] have reported cyclization at the *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 [25]. In conclusion, the reaction is mainly condensation followed by cyclization. Initially, the sulfur atom from β-D-pyranosylhydrazinecarbothioamide **2a–2c** or *N*-phenyl-β-D-pyranosyl hydrazine carbothioamide **3a–3** attacks on the carbon triplet bond of acetylenic ester dimethylacetylenedicarboxylate, and diethylacetylenedicarboxylate, or methyl bromide of 2,4′-dibromoacetophenone, which are prone to nucleophilic attack. Then cyclization proceeds on to the esteric (CO_2R) or carbonyl (CO) functional groups to give products **4a–c** and **5a–f** in good yield (Schemes 1 and 2).

The ^{1}H NMR spectrum of **5a** in DMSO showed two multiplets for the sugar ring CH and CH_2 protons at $\delta = 3.38$–3.65 and 3.00–3.25 ppm, a methoxy at $\delta = 3.72$ ppm, hydroxyl groups at $\delta = 4.21$–5.02 ppm, one doublet for NH at $\delta = 6.66$ ppm, and olefinic protons at $\delta = 6.82$ ppm, along with one doublet at $\delta = 7.00$ ppm and two triplets at $\delta = 7.22$ and 7.41 ppm for the aromatic protons. The ^{13}C NMR spectrum of **5a** showed 12 signals, which are in agreement with the proposed structure. Partial assignments of these resonances are given in the Experimental section. The ^{1}H and ^{13}C NMR spectra **5b–f** are similar to those for **5a**, except for the ester moiety, which exhibits characteristic signals at appropriate chemical shifts.

On the basis of well-established chemistry of electrophilic acetylenes, it is reasonable to assume that compound **5** results from the initial conjugate addition of the sulfur atom of **3** to the acetylenic ester. Subsequently, the ester group of this intermediate is attacked by the amino moiety to yield **5** with the elimination of ROH.

To extend the study to other thiazole derivatives, 3-phenyl-2-(β-D-galactopyranosyl) hydrazonothiazolidine-4-one was synthesized according to the synthetic pathway shown in Scheme 3. The



Entry	R^1	R^2	R^3	R^4	R"	Product	Yields (%)
3a	OH	H	OH	H	CH_3	**5a**	43
3a	OH	H	OH	H	CH_2CH_3	**5b**	48
3b	H	OH	OH	H	CH_3	**5c**	57
3b	H	OH	OH	H	CH_2CH_3	**5d**	58
3c	OH	H	H	OH	CH_3	**5e**	60
3c	OH	H	H	OH	CH_2CH_3	**5f**	46

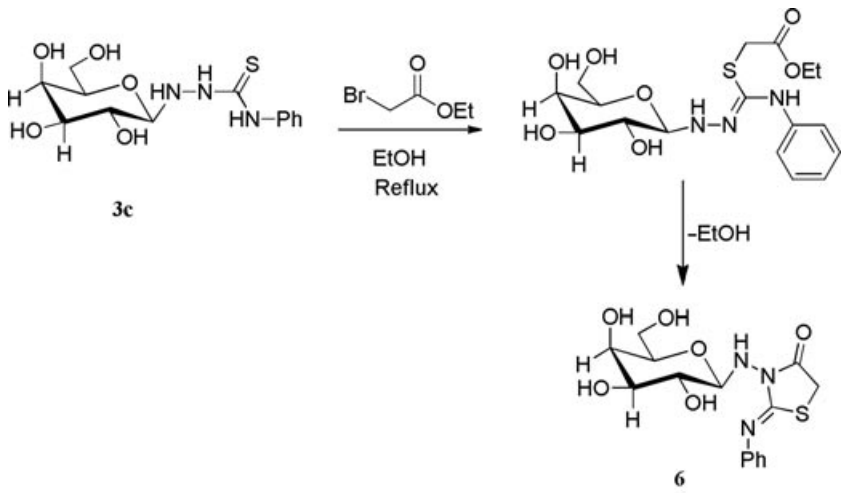
SCHEME 2 Synthesis of 4-oxothiazolidin-5-ylidene derivatives.

reaction of compound **3c** with ethylbromoacetate led to the intermediate **3c′** (Scheme 3), which, by a further intermolecular cyclization, gave the corresponding 3-phenyl-2-(β-D-galactopyranosyl)hydrazonothiazolidine-4-one **6** in quantitative yield. The IR and ^{1}H and ^{13}C NMR spectra are in agreement with the proposed structure.

IR spectra of **6** showed bands at ν_{max} = 1569 cm^{-1} (C=N), 1640, 1718 cm^{-1} (C=O), and 3300–3510 cm^{-1} (NH, OH). In the ^{1}H NMR spectra of **6**, one singlet and a doublet signal observed at $\delta = 4.19$ ppm (methylene protons, CH_2 thiazolidine ring) and 7.57 ppm (NH proton) are in good agreement with the values expected for these protons upon comparison with similar compounds [26]. In the ^{13}C NMR spectra of compound **6**, the signals were observed at $\delta = 32.69$ ppm (CH_2 thiazolidine ring), $\delta = 165.03$ ppm (imino group), and $\delta = 172.45$ (carbonyl group), confirming that the intermolecular cyclization had occurred.

CONCLUSIONS

In summary, we described here a straightforward synthesis of β-D-gluco-, galacto-, and mannopyranosylthiazoles, thiazolidinones, and pyranosylthiazlidin-4-ones derivatives based on the condensation of α-halocarbonyl compounds or dialkylacetylenedicarboxylate with unprotected β-D-pyranosylhydrazinecarbothioamide and *N*-phenyl-β-D-pyranosyl hydrazine carbothioamide. This method allowed us to prepare glucose, galactose,



Entry	Product	Yields (%)
3c	**6**	44

SCHEME 3 Synthesis of 3-phenyl-2-(β-D-galactopyranosyl)hydrazonothiazolidin-4-one.

and maltose derivatives bearing C-linked to thiazoles, thiazolidinones, and pyranosylthiazlidin-4-ones rings. These compounds can be potentially biological active.

EXPERIMENTAL

Chemicals and solvents such as EtOAC, EtOH, DMF, and MeOH were obtained from Merck Chemical Co (Merck Chemical Co. representative in Tehran (kimiaexir), Iran) and used without further purification. Sugar thiosemicarbazone derivatives were prepared according to a known procedure [18, 19]. Melting points were determined on a Melt-Temp II melting point apparatus and are uncorrected. IR spectra were obtained on a Matson-1000 FT-IR spectrometer. Peaks are reported in wavenumbers (cm^{-1}). All of the NMR spectra were recorded on a Bruker model DRX-500 AVANCE (^1H: 500 MHz) (^{13}C: 125 MHz) (Trabiatmodares University, Tehran, Iran) and a Bruker model DRX-400 AVANCE (^1H: 400 MHz) (^{13}C: 100 MHz) (Kashan University, Kashan, Iran) NMR spectrometer. Chemical shifts are reported in parts per million (ppm) from tetramethylsilane as an internal standard in DMSO-d_6 as a solvent. Assignments were confirmed with the aid of two-dimensional techniques NMR (C—H correlation). Element analyses (C, H, and N) were performed with a Heracus CHN-O-Rapid analyzer (Trabiatmoalem University, Tehran, Iran). The purity of the compounds was checked by thin layer chromatography (TLC) on Merck silica gel 60 F_{254} precoated sheets in *n*-hexane/ethyl acetate mixture, and spots were developed using iodine vapors and ultraviolet light as visualizing agents.

*General Procedure for Synthesis of 4-Bromothiazol-2-ylidene Derivatives (**4a–c**)*

A solution of β-D-pyranosylhydrazinecarbothioamide (0.25 g, 1 mmol) in 8 mL of absolute ethanol was stirred at ambient temperature for 20 min. Then 2,4′-dibromoacetophenone (0.27 g, 1 mmol) was added to this mixture and was refluxed for 12–18 h (the reaction was monitored by TLC 4:8 *n*-hexane/ethyl acetate). The mixture was cooled, and the precipitate was filtered off and recrystallized from EtOH, affording 4-bromothiazol-2-ylidene derivatives (**4a–c**).

*2-[N-(4-(4-Bromophenyl)-3H-thiazol-2-ylidene]β-D-glucopyranoside (**4a**).* mp = 148°C, yield = 61%. Anal. Calcd. for $C_{15}H_{18}BrN_3O_5S$: C, 41.68; H, 4.20; N, 9.72; found: C, 41.57; H, 4.24; N, 9.80. FT-IR (KBr) ν_{max} (cm^{-1}) 1629 (C=N), 3250–3500 (NH, OH). ^1H NMR (DMSO-d_6, 500 MHz); δ (ppm): 2.96–2.98 (m, 1H, H-4′), 3.04 (t, J = 8.8, 1H, H-5′), 3.11 (t, J = 8.8, 1H, H-2′), 3.17–3.19 (m, 1H, H-3′), 3.52 (d, J = 11.35, 2H, H-6′), 3.91 (d, J = 8.8, 1H, H-1′), 3.34–4.11 (m, 4H, OH), 7.29 (s, 1H, C=CH), 7.56 (d, J = 8.3, 1H, NH), 7.62 (d, J = 8.5, 2H arom), 7.67–7.69 (d, J = 8.5, 2H arom), 7.75 (d, J = 8.5, 1H, NH). ^{13}C NMR (DMSO-d_6, 125.77 MHz); δ (ppm): 61.7 (1C, C-6′), 70.3(1C, C-4′), 71.0 (1C, C-5′), 77.3 (1C, C-2′), 77.8 (1C, C-3′), 90.1 (1C,

C-1′), 104.2 (CH thiazole), 121.5 (C thiazole), 127.5, 127.8 (2CH arom), 131.4, 131.7 (2CH arom), 173.9 (C=N).

*2-[N-(4-(4-Bromophenyl)-3H-thiazol-2-ylidene] β-D-mannopyranoside (***4b***).* Pale brown solid, mp = 185–188°C, yield = 62%. Anal. Calcd. for $C_{15}H_{18}BrN_3O_5S$: C, 41.68; H, 4.20; N, 9.72. Found: C, 41.73; H, 4.18; N, 9.69. FT-IR (KBr); ν_{max} (cm^{-1}): 1614 (C=N), 3250–3500 (NH, OH). ^{1}H NMR (DMSO-d_6, 400 MHz); δ (ppm): 2.72–3.30 (m, 4H, OH), 3.65–3.69 (m, 2H, H-6′, OH), 4.08–4.11 (m, 1H, H-5′), 4.57–4.89 (m, 4H, H-2′, H-3′, H-4′, H-1′), 7.21 (s, 1H=CH), 7.32 (d, J = 8.3, 1H, NH), 7.58–7.87 (m, 4H, arom), 7.92 (d, J = 8.3, 1H, NH). ^{13}C NMR (DMSO-d_6, 100 MHz); δ (ppm) 62.5 (1C, C-6′), 63.7 (1C, C-4′), 67.7 (1C, C-5′), 70.0 (1C, C-2′), 74.0 (1C, C-3′), 78.2 (1C, C-1′), 103.3 (=CH), 120.0 (C=C), 127.4, 127.4, 131.3, 131.4, 134.2 (arom), 174.1 (C=N).

*2-[N-(4-(4-Bromophenyl)-3H-thiazol-2-ylidene] β-D-galactopyranoside (***4c***).* Light brown solid, mp = 148–156°C, yield = 72%, Anal. Calcd. for $C_{15}H_{18}BrN_3O_5S$: C, 41.68; H, 4.20; N, 9.72; Found: C, 41.87; H, 4.30; N, 9.67. FT-IR (KBr); ν_{max} (cm^{-1}): 1645 (C=N), 3250–3400 (NH, OH). ^{1}H NMR (DMSO-d_6, 400 MHz); δ (ppm): 3.37–4.31 (m, 11H, 7H, 4OH), 7.32 (s, 1H,=CH), 7.43 (d, J = 6.4, 1H, NH), 7.56–7.77 (m, 4H, arom), 7.65 (d, J = 8.8, 1H, NH). ^{13}C NMR (DMSO-d_6, 100 MHz); δ (ppm): 61.0 (1C, C-6′), 63.4 (1C, C-2′), 68.6 (1C, C-4′), 74.4 (1C, C-5′), 77.9 (1C, C-3′), 91.0 (1C, C-1′), 104.8 (=CH), 121.3 (C=C), 128.2, 128.6, 128.8, 132.0, 132.3, 133.4 (6C, arom), 169.1(C=N).

*General Procedure for Synthesis of 4-Oxothiazolidine-5-ylidene Derivatives (***5a–f***)*

A solution of *N*-phenyl-β-D-pyranosylhydrazinecarbothioamide (0.32 g, 1 mmol) in 8 mL of absolute ethanol was well stirred at ambient temperature for 20 min. Then dimethyl acetylenedicarboxylate (0.12 mL, 1 mmol) or diethyl acetylenedicarboxylate (0.16 mL, 1 mmol) was added to this mixture and was refluxed for 8–12 h (the reaction was monitored by TLC 4:8 *n*-hexane/ethyl acetate). The mixture was cooled, and the precipitate was filtered off and recrystallized from methanol, affording the 4-oxothiazolidine-5-ylidene derivatives (**5a–c**) as yellow light or white crystals.

*Methyl 2-((4-Oxo-2-(phenylimino)-3-(β-D-glucopyranosyl-2-ylamino) thiazolidine-5-ylidene) acetate (***5a***).* mp = 136–137°C, Yield = 43%, Anal. Calcd. for $C_{18}H_{21}N_3O_8S$: C, 49.20; H, 4.82; N, 9.56; Found: C, 49.43; H, 5.02; N, 9.52. FT-IR (KBr); ν_{max} (cm^{-1}): 1642 (C=N), 1692, 1731 (C=O), 3260–3500 (NH, OH). ^{1}H NMR (DMSO-d_6, 400 MHz); δ (ppm): 3.38–3.65(m, 2H), 3.00–3.25 (m, 3H), 3.72(s, 3H, CH_3), 4.21–5.02 (m, 5H, H, OH), 6.66(d, J = 4, 1H, NH), 6.82(s, 1H,=CH), 7.00 (d, J = 7.6, 2H, arom), 7.22 (t, J = 8, 2H arom), 7.41(t, J = 8, 2H arom). ^{13}C NMR (DMSO-d_6, 100 MHz); δ (ppm); 53.0(CH_2), 61.8(1C, C-6′), 70.6 (1C, C-4′), 72.5 (1C, C-5′), 77.3 (1C, C-2′), 78.7 (1C, C-3′), 79.6(1C, C-1′), 115.0(=CH), 121.3 (C=C), 128.4, 129.4, 129.9(arom).

*Ethyl 2-((4-Oxo-2-(phenylimino)-3-(β-D-glucopyranosyl-2-ylamino) thiazolidine-5-ylidene) acetate (***5b***).* Yellow light solid, mp = 131–135°C, yield = 48%. Anal. Calcd. for $C_{19}H_{23}N_3O_8S$: C, 50.32; H, 5.11; N, 9.27; Found: C, 50.57; H, 5.17; N, 9.38. FT-IR (KBr); ν_{max} (cm^{-1}): 1647 (C=N), 1691, 1728 (C=O), 3260–3500 (NH, OH). ^{1}H NMR (DMSO-d_6, 400 MHz); δ (pp): 1.18–1.22 (t, J = 6.8, 3H, CH_3), 2.96–3.15 (m, 4H, H-4′, H-5′, H-2′, H-3′), 3.16–3.25 (m, 1H, H-1′), 3.50–3.68 (m, 2H, H-6′), 4.18 (q, J = 6.8, 2H, CH_2), 4.21–5.02 (m, 7H, OH), 6.67 (NH), 6.79 (s, 1H, C=CH), 7.00 (t, J = 8.0, 2H arom), 7.21 (t, J = 8.0, 1H arom), 7.40–7.50 (m, 3H, 2H arom, NH) ppm. ^{13}C NMR (DMSO-d_6, 100 MHz); δ (ppm): 14.4 (CH_3), 61.8 (CH_2), 62.0 (1C, C-6′), 70.7 (1C, C-4′), 72.5 (1C, C-5′), 77.3(1C, C-2′), 78.7 (1C, C-3′), 89.1 (1C, C-1′), 116.5 (=CH), 121.3 (C thiazole), 129.6, 129.9, 139.6, 147.6 (arom), 150.3 (C=O ester), 162.4 (C=O amide), 165.7 (C=N).

*Methyl 2-((4-Oxo-2-(phenylimino)-3-(β-D-mannopyranosyl-2-ylamino) thiazolidine-5-ylidene) acetate (***5c***).* White solid, mp = 207–208°C, Yield = 57%, Anal. Calcd. for $C_{18}H_{21}N_3O_8S$ C, 49.20; H, 4.82; N, 9.56 Found: C, 49.63; H, 4.75; N, 9.62. FT-IR (KBr); ν_{max} (cm^{-1}): 1594 (C=N), 1647, 1711, 3300–3509 (NH, OH), ^{1}H NMR (DMSO-d_6, 400 MHz); δ (ppm): 3.40–3.70 (m, 4H), 3.80 (s, 3H, CH_3), 4.08–5.43 (m, 2H, H, OH), 4.28–4.43 (m, 4H), 6.78 (s, 1H,=CH), 7.47–7.53 (m, 5H, arom), 7.62 (m, 1H, NH). ^{13}C NMR (DMSO-d_6 100 MHz); δ (ppm): 53.1 (CH_3), 64.3 (1C, C-6′), 69.8 (1C, C-4′), 70.5 (1C, C-5′), 71.1 (1C, C-2′), 71.5 (1C, C-3′), 115.3 (=CH), 128.6, 129.6, 134.7, 142.3(4C, arom), 160.4 (C=C), 164.7 (C=O ester), 166.4(C=O amide), 166.7 (C=N).

*Ethyl 2-((4-Oxo-2-(phenylimino)-3-(β-D-mannopyranosyl-2-ylamino) thiazolidine-5-ylidene) acetate (***5d***).* White solid, mp = 214–216°C, Yield = 58%, Anal. Calcd. for $C_{19}H_{23}N_3O_8S$ C, 50.32; H, 5.11; N, 9.27; Found: C, 50.65; H, 5.24; N, 9.41.FT-IR

(KBr); ν_{max} (cm^{-1}): 1537 (C=N), 1645, 1717 (C=O), 3337–3500 (NH, OH), ^1H NMR (DMSO-d_6, 500 MHz); δ (ppm): 1.27 (t, J = 6.8, 3H, CH_3), 3.4–3.52 (m, 3H), 4.10–4.20 (q, J = 6.8, 2H, CH_2), 4.27–5.32 (m, 7H, H, OH), 6.75 (s, 1H, C=CH), 7.47–7.52 (m, 5H, arom), 7.60 (d, J = 4.0, 1H, NH). ^{13}C NMR (DMSO-d_6, 125.77 MHz); δ (ppm): 14.5 (CH_3), 61.9 (CH_2), 64.7 (1C, C-6′), 69.8 (1C, C-4′), 70.5 (1C, C-5′), 71.1 (1C, C-2′), 71.5 (1C, C-3′), 115.6 (=CH), 128.6, 129.6, 134.7, 142.1 (arom), 160.5 (C=C), 164.7 (C=O ester), 165.9 (C=O amide), 166.6 (C=N).

*Methyl 2-((4-Oxo-2-(phenylimino)-3-(β-D-galactopyranosyl-2-ylamino)thiazolidine-5-ylidene) acetate (**5e**).* White solid, mp = 220–225°C, yield = 60%. Anal. Calcd. for $C_{18}H_{21}N_3O_8S$ C, 49.20; H, 4.82; N, 9.56; Found: C, 4941; H, 4.72; N, 9.68. FT-IR (KBr); ν_{max} (cm^{-1}): 1645 (C=N), 1645, 1704 (C=O), 3330–3496 (NH, OH). ^1H NMR (DMSO-d_6 400 MHz); δ (ppm): 3.37, 3.39 (m, 2H, H-4′, H-5′), 3.51, 3.52 (m, 2H), 3.65–4.63 (m, 2H, H, OH), 3.81 (s, 3H, CH_3), 4.15–4.17 (d, J = 6.8, 1H, H-2′), 4.41–4.43 (m, 2H), 4.97–4.99 (m, 1H), 6.79 (s, 1H,=CH), 7.45–7.53 (m, 5H arom), 7.70 (d, J = 5.6, 1H, NH). ^{13}C NMR (DMSO-d_6, 100 MHz); δ (ppm): 53.0 (CH_3), 63.5 (1C, C-6′), 69.4 (1C, C-2′), 70.1 (1C, C-4′), 70.7 (1C, C-5′), 72.8 (C-3′), 115.3 (=CH), 128.6, 129.6, 134.7, 142.2, 145.2 (5C, arom), 168.3 (C=N).

*Ethyl 2-((4-Oxo-2-(phenylimino)-3-(β-D-galactopyranosyl-2-ylamino)thiazolidine-5-ylidene) acetate (**5f**).* White solid, mp = 157–159°C, yield = 46%. Anal. Calcd. for $C_{19}H_{23}N_3O_8S$ C, 50.32; H, 5.11; N, 9.27; Found: C, 50.47; H, 5.08; N, 9.59. FT-IR (KBr) ν_{max} = 1582 (C=N), 1694, 1723 (C=O), 3300–3500 (NH, OH). ^1H NMR (DMSO-d_6, 400 MHz); δ (ppm): 1.24–1.29 (t, J = 6.8, 3H, CH_3), 3.31–3.69 (m, 6H, H, OH), 4.27 (q, J = 6.8, 2H, CH_2), 4.58–4.98 (m, 2H, H, OH), 6.75 (s, 1H,=CH), 7.45–7.55 (arom), 7.69 (d, J = 6.0, 1H, NH) ppm. ^{13}C NMR (DMSO-d_6, 100 MHz); δ (ppm): 14.5 (CH_3), 61.9 (CH_2), 63.5 (1C, C-6′), 69.4 (1C, C-2′), 70.1 (1C, C-4′), 70.7 (1C, C-5′), 72.9 (1C, C-3′), 115.6 (=CH), 128.6, 129.6, 134.6, 142.1 (5C, arom), 160.5(C=C), 164.6 (C=O ester), 165.9 (C=O amide), 167.6 (C=N).

*Synthesis of 3-Phenyl-2-(β-D-galactopyranosyl) hydrazono thiazolidine-4-one (**6**)*

A solution of *N*-phenyl-β-D-galactopyranosyl hydrazine carbothioamide (0.16 g, 0.5 mmol) in 8 mL of absolute ethanol and calcium carbonate (0.69 g, 0.5 mmol) was stirred at ambient temperature for 20 min. Then ethyl bromoacetate (0.05 mL, 0.5 mmol) was added to this mixture and was refluxed for 24 h (the reaction was monitored by TLC 4:8 *n*-hexane/ethyl acetate). The mixture was cooled, and the precipitate was filtered off and purified from water affording 3-phenyl-2-D-galactopyranosylthiazolidine-4-one **6.**

White solid, mp = 229–230°C, yield = 44%. Anal. Calcd. for $C_{15}H_{19}N_3O_6S$: C, 48.77; H, 5.18; N, 11.38. Found: C, 48.39; H, 5.14; N, 11.55. FT-IR (KBr); ν_{max} (cm^{-1}): 1569 (C=N), 1640, 1718 (C=O), 3300–3510 (NH, OH) cm^{-1}. ^1H NMR (DMSO-d_6, 400 MHz); δ (ppm): 3.44–3.48 (m, 2H, CH_2), 3.67–4.05 (3H, 2H, 1OH), 3.67(d, J = 5.6, 1H), 4.05–4.86 (3H, OH), 4.14(d, J = 5.6, 1H), 4.22 (d, J = 0.6, 1H), 4.36 (d, J = 0.6, 1H), 4.55 (d, J = 5.6, 1H), 7.33 (d, J = 7.2, 2H arom), 7.44 (d, 1H arom), 7.48–7.49 (m, 2H arom), 7.57 (d, J = 6.0, 1H, NH). ^{13}C NMR (DMSO-d_6, 100 MHz); δ (ppm): 32.7(1C, CH_2), 63.5 (1C, C-6′), 69.3 (1C, C-4′), 70.1 (1C, C-5′), 70.5 (1C, C-2′), 72.8 (1C, C-3′), 79.6 (1C, C-1′), 128.7, 129.1, 129.3, 129.5, 135.5 (5C, arom), 165.0 (C=N), 172.4 (C=O).

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