

Synthesis of new series of N-3-[-{2-(substituted phenyl-4-oxo-5-(substituted benzylidene)-1,3-thiazolidine)-carbamyl]-propyl-2-aminothiazole and their biological importance

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Abstract. Synthesis of new series of N-3-[-{2-(substituted phenyl-4-oxo-5-(substituted benzylidene)-1,3-thiazolidine)-carbamyl]-propyl-2-aminothiazole, **5(a-s)** have been developed. The cycloaddition reaction of thioglycolic acid with N-{3-(substituted benzylidene-carbamyl)-propyl}-2-aminothiazole, **3(a-s)** in the presence of anhydrous ZnCl_2 afforded new heterocyclic compounds N¹-3-[-{2-(substituted phenyl-4-oxo-1,3-thiazolidine)-carbamyl]-propyl-2-aminothiazole **4(a-s)**. The latter product on treatment with several selected substituted aromatic aldehydes in the presence of $\text{C}_2\text{H}_5\text{ONa}$ undergoes Knoevenagel reaction to yield **5(a-s)**. The structure of compounds **1**, **2**, **3(a-s)**, **4(a-s)** and **5(a-s)** were confirmed by IR, ^1H NMR, ^{13}C NMR, FAB mass and chemical analysis. All final compounds were screened for their antimicrobial activity against some selected bacteria and fungi and antituberculosis study against *M. tuberculosis*, gave acceptable activity.

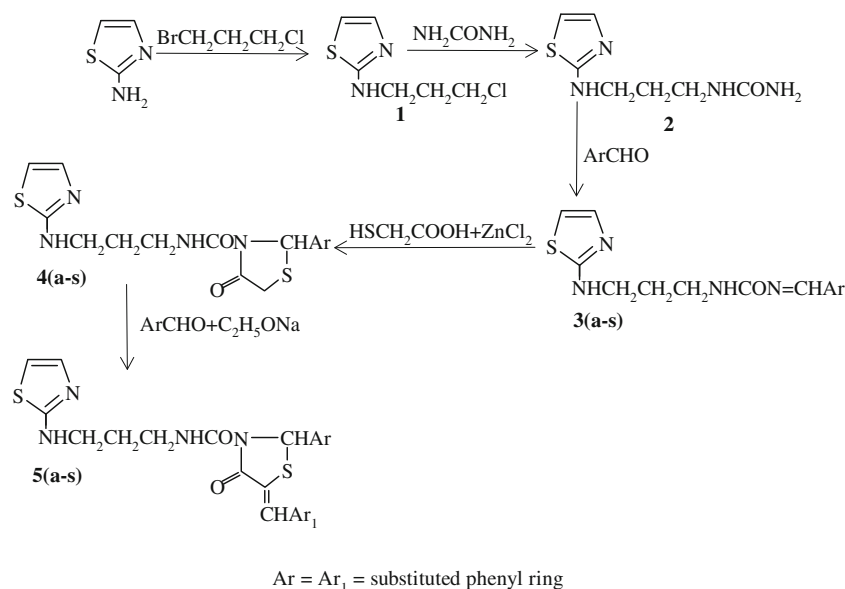
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1. Introduction

Thiazolidinone has an important role as a widely exploited pharmacophore in medicinal chemistry having varied biological activity such as antifungal,¹ antibacterial,^{2,3} antimycobacterial,⁴ antipsychotic,⁵ anti-inflammatory⁶ have been found to be associated with thiazolidinone derivatives. Substituted thiazolidine derivatives represent important key intermediates for the synthesis of pharmacologically active drug. Thiazoles are amongst the most frequently encountered heterocycles in compounds of biological interest along with many other applications. They have been shown to possess a broad spectrum of biological activity depending on their particular structure. Anticonvulsants⁷, anti-inflammatory⁸ activities are observed in thiazole derivatives. Some synthetic thiazoles have exhibited a range of biological activities such as antimicrobial,⁹ biological activities,¹⁰ antibacterial, antifungal.^{11–13} Some recent studies have shown the synthesis of some new thiazoles candidates used as antimicrobial and anticancer agent. We have decided to synthesize a new series of N-3-[-{2-(substituted phenyl-4-oxo-

5-substituted benzylidene-1,3-thiazolidine)-carbamyl]-propyl-2-aminothiazole as shown in scheme 1. The starting material, 2-aminothiazole with 1-bromo-3-chloropropane undergoes electrophilic substitution reaction yielded N-(3-chloropropyl)-2-aminothiazole, compound **1**. The compound **1** on the reaction with urea afforded N¹-{3-(aminocarbamyl)-propyl}-2-aminothiazole, compound **2**. The compound **2** on reaction with several selected substituted benzaldehydes undergoes condensation reaction to afford N-{3-(substituted benzylidene-carbamyl)-propyl}-2-aminothiazole, compound **3(a-s)**. The cycloaddition reaction of thioglycolic acid with compound **3(a-s)** in the presence of anhydrous ZnCl_2 gave new heterocyclic compounds N-3-[-{2-(substituted phenyl-4-oxo-1,3-thiazolidine)-carbamyl]-propyl-2-aminothiazole, compound **4(a-s)**. The compound **4(a-s)** on treatment with various selected substituted benzaldehydes in the presence of $\text{C}_2\text{H}_5\text{ONa}$ undergo Knoevenagel condensation reaction yielded compound **5(a-s)**. The structure of compounds **1**, **2**, **3(a-s)**, **4(a-s)** and **5(a-s)** were confirmed by IR, ^1H NMR, ^{13}C NMR, FAB mass and chemical analysis. All the above compounds were screened for their

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Scheme 1. Synthesis of compounds **1**, **2**, **3(a-s)**, **4(a-s)** and **5(a-s)**.

antimicrobial activity against some selected bacteria and fungi and antituberculosis study against *M. tuberculosis*.

2. Materials and methods

Melting points were taken in open capillaries and are uncorrected. Progress of reaction was monitored by silica gel-G coated TLC plates in MeOH: CHCl₃ system (1:9). The spot was visualized by exposing dry plate in iodine vapours. IR spectra were recorded in KBr disc on a Shimadzu 8201 PC, FTIR spectrophotometer (ν_{\max} in cm⁻¹) and ¹H and ¹³C NMR spectra were measured on a Bruker DRX-300 spectrometer in CDCl₃ at 300 and 75 MHz respectively using TMS as an internal standard. All chemical shifts were reported on δ scales. The FAB mass spectra were recorded on a Jeol SX-102 mass spectrometer. Elemental analyses were performed on a Carlo Erba-1108 analyzer. The analytical data of all the compounds were satisfactory. For column chromatographic purification of the products, Merck silica Gel 60 (230–400 Mesh) was used. The reagent grade chemicals were purchased from the commercial sources and further purified before use.

2.1 Method for synthesis of the compound **1**

A mixture of 2-aminothiazole and 1-bromo-3-chloropropane (1:1 mole) was dissolved in methanol at

room temperature. The reaction mixture was continuously stirred on a magnetic stirrer for about 8 h. The product was filtered and purified over a column chromatography. The purified product was recrystallized from ethanol at room temperature to yield compound **1**.

2.2 Method for synthesis of compound **2**

A mixture of compound **1** and urea (1:1 mole) was dissolved in methanol at room temperature. The reaction mixture was continuously stirred on a magnetic stirrer for about 8 h. The product was filtered and purified over a column chromatography. The purified product was recrystallized from ethanol at room temperature to yield compound **2**.

2.3 General method for the synthesis of compound **3(a-s)**

A mixture of compound **2** and substituted benzaldehydes (1:1 mole) was dissolved in methanol at room temperature and allowed to react. The reaction mixture was first continuously stirred on a magnetic stirrer for about 2 to 3 h then kept on a steam bath for about 1.30–4.15 h. The products were cooled and filtered. The products were purified over a column chromatography and recrystallized from ethanol at room temperature to yield compound **3(a-s)**.

2.4 General method for the synthesis of compounds 4(a–s)

A mixture of compound 3(a–s) and thioglycolic acid (1:1 mole) dissolved in methanol was allowed to react in the presence of catalytic amount of ZnCl_2 . The reaction mixture was first continuously stirred on a magnetic stirrer for about 2 to 3.5 h then kept on steam bath for about 1.45–4.15 h at 80–90°C. The products were cooled and filtered at room temperature. The filtered products were purified over column chromatography and recrystallized from ethanol at room temperature to yield compound 4(a–s).

2.5 General method for the synthesis of compound 5(a–s)

A mixture of compound 4(a–s) and substituted benzaldehydes (1:1 mole) was dissolved in methanol in the presence of alkali metal alkoxide ($\text{C}_2\text{H}_5\text{ONa}$) and allow to react. The reaction mixture was first continuously stirred on a magnetic stirrer for about 2 to 3.5 h then kept on steam bath for about 1.45–4.15 h at 80–90°C. The products were cooled and filtered at room temperature. The filtered products were purified over column chromatography and recrystallized from ethanol at room temperature to yield final products compound 5(a–s).

3. Biological study

Series of newly synthesized compounds were active against selected microorganisms. The minimal inhibition diameters were determined using the filter paper disc diffusion method and the concentrations have been

used in ppm. All the final synthesized compounds 5(a–s) have been screened *in vitro* for their antibacterial activity against *B. subtilis*, *E. coli* and *S. aureus* and antifungal activity against *A. niger*, *A. flavus* and *C. albicans*. Standards for antibacterial and antifungal activity streptomycin and griseofulvin were used respectively. Standards also screened under the similar conditions for comparison. The antitubercular activity was screened against the *M. tuberculosis*. For the antitubercular activity isoniazid and rifampicin were used as standard and also screened under the similar conditions.

3.1 Antibacterial activity

The above synthesized compound 5(a–s) were screened against some selected bacteria and examined for the inhibition of growth of the organism. The concentrations of the compounds were given in ppm. The diameter of the inhibition zones in (mm) are given in table 1.

3.2 Antifungal activity

The above synthesized compound 5(a–s) were screened against selected fungi and determined their minimal inhibition zones in (mm) were presented in table 2 and concentrations of the compounds were given in ppm.

3.3 Antitubercular activity

The above synthesized compound 5(a–s) were screened against *M. tuberculosis* using L. J. medium (Conventional) method at 50 µg/mL and lower concentrations

Table 1. Antibacterial activity of compounds 5(a–s).

Compound	<i>B. subtilis</i>		<i>E. coli</i>		<i>S. aureus</i>		Compound	<i>B. subtilis</i>		<i>E. coli</i>		<i>S. aureus</i>	
	50 ppm	100 ppm	50 ppm	100 ppm	50 ppm	100 ppm		50 ppm	100 ppm	50 ppm	100 ppm	50 ppm	100 ppm
5a	10	25	07	22	10	23	5k	08	25	09	18	08	20
5b	15	32	10	30	15	32	5l	11	24	12	19	12	28
5c	13	34	12	30	14	30	5m	13	25	15	19	14	26
5d	15	33	10	31	13	27	5n	14	18	14	13	16	27
5e	12	30	12	28	15	31	5o	12	19	14	12	15	20
5f	11	30	11	27	14	28	5p	14	20	15	11	14	19
5g	20	28	10	26	10	27	5q	12	25	13	15	12	18
5h	22	29	09	25	12	29	5r	13	23	14	17	13	21
5i	20	27	10	25	12	26	5s	11	22	12	15	11	20
5j	24	27	11	24	10	25	-	-	-	-	-	-	-
Streptomycin	28	37	26	34	27	35	Streptomycin	28	37	26	34	27	35

Table 2. Antifungal activity of compounds **5(a–s)**.

Compound	<i>A. niger</i>		<i>A. flavus</i>		<i>C. albicans</i>		Compound	<i>A. niger</i>		<i>A. flavus</i>		<i>C. albicans</i>	
	50 ppm	100 ppm	50 ppm	100 ppm	50 ppm	100 ppm		50 ppm	100 ppm	50 ppm	100 ppm	50 ppm	100 ppm
5a	07	15	07	12	10	14	5k	11	15	10	18	11	20
5b	12	22	10	20	14	24	5l	10	14	12	19	12	18
5c	10	24	12	20	14	22	5m	13	15	13	19	12	16
5d	11	23	10	21	13	21	5n	10	15	10	13	10	17
5e	10	22	12	18	15	21	5o	09	14	09	12	11	15
5f	11	20	11	17	14	20	5p	08	12	10	11	09	13
5g	10	18	10	16	10	22	5q	14	15	13	15	12	12
5h	08	19	09	15	12	20	5r	13	18	13	17	13	14
5i	12	17	10	15	12	21	5s	12	22	10	15	11	16
5j	13	17	11	14	10	20		-	-	-	-	-	-
Griseofulvin	22	32	20	35	24	36	Griseofulvin	22	32	20	35	24	36

using *M. tuberculosis* H37Rv strain. The results are shown in table 3. The standard antitubercular drugs isoniazid and rifampicin were taken as standards.

3.3a *N*-(3-chloropropyl)-2-aminothiazole (**1**): Yield: 63%; m.p. 77–79°C; Anal. Calcd for C₆H₉N₂SCl: C, 40.79, H, 5.13, N, 15.85%; found C, 40.74, H, 5.09, N, 15.80%; IR (cm⁻¹): 748 (C–Cl), 886 (C–S), 1339 (N–CH₂), 1568 (C=C), 2888, 3046 (CH), 3482 (NH); ¹H NMR (δ): 2.30 (m, 2H, CH₂CH₂CH₂), 3.46(t, 2H, J = 7.41 Hz, CH₂CH₂CH₂–Cl), 4.23 (m, 2H, N–CH₂CH₂CH₂), 6.90 (t, J = 5.10 Hz, 1H, NH), 6.76 (d, 1H, J = 4.36 Hz, C₅H of thiazole), 7.18 (d, 1H, J = 4.36 Hz, C₄H of thiazole), ¹³C NMR (δ): 32.6 (CH₂CH₂CH₂), 41.8 (CH₂CH₂CH₂–Cl), 46.6 (N–CH₂CH₂CH₂), 109.5 (C₅ of thiazole), 139.5 (C₄ of thiazole), 169.6 (C₂ of thiazole), Mass (FAB): 176M⁺.

3.3b *N*-(3-(aminocarbamyl)-propyl)-2-aminothiazole (**2**): Yield: 72%; m.p. 58–60°C; Anal. Calcd for C₇H₁₂N₄OS: C, 41.98, H, 6.03, N, 27.97%; found C, 41.89, H, 5.97, N, 27.88%; IR: 872 (C–S), 1232 (C–N), 1642 (C=O), 3378 (NH), 3424 (NH₂); ¹H

NMR (δ): 2.24 (m, 2H, CH₂CH₂CH₂), 3.46 (m, 2H, CH₂CH₂CH₂–NH), 4.25 (m, 2H, N–CH₂CH₂CH₂), 5.63 (t, J = 4.60 Hz, 1H, NHCO), 5.96 (s, 2H, NH₂), 7.76 (t, J = 5.10 Hz, 1H, NH), 6.76 (d, 1H, J = 4.82 Hz, C₅H of thiazole), 7.18 (d, 1H, J = 4.82 Hz, C₄H of thiazole), ¹³C NMR (δ): 32.9 (CH₂CH₂CH₂), 39.6 (CH₂CH₂CH₂–NH), 44.8 (N–CH₂CH₂CH₂), 109.5 (C₅ of thiazole), 138.6 (C₄ of thiazole), 163.8 (CO), 168.2 (C₂ of thiazole); Mass(FAB): 200M⁺.

3.3c *N*-(3-(benzylidencarbamyl)-propyl)-2-aminothiazole (**3a**): Yield: 61%; m.p. 67–68°C; Anal. Calcd for C₁₄H₁₆N₄OS: C, 58.31, H, 5.59, N, 19.42%; found C, 58.27, H, 5.52, N, 19.37%; IR: 3369 (NH), 1664 (C=O), 1558 (N=CH); ¹H NMR (δ): 2.26 (m, 2H, CH₂CH₂CH₂), 3.42 (t, 2H, J = 7.40 Hz, CH₂CH₂CH₂–N), 4.22 (t, 2H, J = 7.40 Hz, N–CH₂CH₂CH₂), 5.58 (t, J = 4.60 Hz, 1H, NHCO), 7.24 (d, 1H, J = 4.84 Hz, C₄H of thiazole), 6.62 (d, 1H, J = 4.84 Hz, C₅H of thiazole), 7.78 (t, J = 5.10 Hz, 1H, NH), 7.86 (s, 1H, N=CH), 6.30–7.21 (m, 5H, Ar–H); ¹³C NMR (δ): 32.8 (CH₂CH₂CH₂), 39.7 (CH₂CH₂CH₂–N), 45.6 (N–CH₂CH₂CH₂), 113.6 (C₅ of thiazole), 140.5 (C₄ of

Table 3. Antitubercular activity of compounds **5(a–s)**.

Compound	% Activity		Compound	% Activity		Compound	% Activity		Compound	% Activity	
	25 ppm	50 ppm		25 ppm	50 ppm		25 ppm	50 ppm		25 ppm	50 ppm
5a	22	45	5f	30	79	5k	28	60	5p	20	47
5b	32	82	5g	29	76	5l	30	63	5q	24	56
5c	33	80	5h	32	82	5m	31	65	5r	27	60
5d	32	80	5i	27	83	5n	22	45	5s	25	55
5e	30	78	5j	28	81	5o	18	49	-	-	-
Standard	100	100	Standard	100	100	Standard	100	100	Standard	100	100

thiazole), 144.5 (N=CH), 162.7 (CO), 169.7 (C2 of thiazole), 124.5, 125.8, 127.6, 129.7, 131.5, 137.6 (6C, Ar); Mass (FAB): 288M⁺.

3.3d *N*-{3-(4-chlorobenzylidencarbamyl)-propyl}-2-aminothiazole (**3b**): Yield: 63%; m.p. 80–82°C; Anal. Calcd for C₁₄H₁₅N₄OSCl: C, 52.08, H, 4.68, N, 17.35%; found C, 52.05, H, 4.65, N, 17.30%; IR: 3375 (NH), 1675 (C=O), 1565 (N=CH), 742 (C–Cl); ¹H NMR (δ): 2.35 (m, 2H, J = 7.43 Hz, CH₂CH₂CH₂), 3.52 (m, 2H, CH₂CH₂CH₂-N), 4.33 (m, 2H, N-CH₂CH₂CH₂), 5.57 (t, J = 4.60 Hz, 1H, NHCO), 7.40 (d, 1H, J = 4.86 Hz, C₄H of thiazole), 7.20 (d, 1H, J = 4.86 Hz, C₅H of thiazole), 7.05 (t, J = 5.10 Hz, 1H, NH), 7.95 (s, 1H, N=CH), 6.70–7.80 (m, 4H, Ar-H); ¹³C NMR (δ): 34.7 (CH₂CH₂CH₂), 41.5 (CH₂CH₂CH₂-NH), 47.5 (N-CH₂CH₂CH₂), 115.5 (C₅ of thiazole), 143.9 (C₄ of thiazole), 151 (N=CH), 166.5 (CO), 172.5 (C₂ of thiazole), 125.5, 128.5, 129.5, 130.4, 134.3, 140.5 (6C, Ar); Mass (FAB): 322M⁺.

3.3e *N*-{3-(3-chlorobenzylidencarbamyl)-propyl}-2-aminothiazole (**3c**): Yield: 65%; m.p. 84–87°C; Anal. Calcd for C₁₄H₁₅N₄OSCl: C, 52.08, H, 4.68, N, 17.35%; found C, 52.04, H, 4.64, N, 1.25%; IR: 745 (C–Cl), 1560 (N=CH), 1674 (C=O), 3375 (NH); ¹H NMR (δ): 2.44 (m, 2H, J = 7.42 Hz, CH₂CH₂CH₂), 3.50 (m, 2H, CH₂CH₂CH₂-N), 3.85 (m, 2H, N-CH₂CH₂CH₂), 5.62 (t, J = 4.60 Hz, 1H, NHCO), 7.15 (d, 1H, J = 4.84 Hz, C₅H of thiazole), 7.30 (d, 1H, J = 4.84 Hz, C₄H of thiazole), 7.74 (t, J = 5.10 Hz, 1H, NH), 7.95 (s, 1H, N=CH), 7.3–7.5 (m, 4H, Ar-H); ¹³C NMR (δ): 33.5 (CH₂CH₂CH₂), 43.5 (CH₂CH₂CH₂-N), 47.1 (N-CH₂CH₂CH₂), 113 (C₅ of thiazole), 141.8 (C₄ of thiazole), 147.5 (N=CH), 164 (CO), 170 (C₂ of thiazole), 126.5, 128.5, 130.5, 132.5, 136.3, 137.5 (6C, Ar); Mass (FAB): 322M⁺.

3.3f *N*-{3-(2-chlorobenzylidencarbamyl)-propyl}-2-aminothiazole (**3d**): Yield: 66%; m.p. 81–82°C; Anal. Calcd for C₁₄H₁₅N₄OSCl: C, 52.08, H, 4.68, N, 17.35%; found C, 52.1, H, 4.60, N, 17.36%; IR: 742 (C–Cl), 1565 (N=CH), 1675 (C=O), 3380 (NH); ¹H NMR (δ): 2.45 (m, 2H, CH₂CH₂CH₂), 3.45 (m, 2H, CH₂CH₂CH₂-NH), 3.78 (m, 2H, N-CH₂CH₂CH₂), 5.85 (t, J = 4.60 Hz, 1H, NHCO), 7.12 (d, 1H, J = 4.81 Hz, C₅H of thiazole), 7.35 (d, 1H, J = 4.81 Hz, C₄H of thiazole), 7.77 (t, J = 5.10 Hz, 1H, NH), 7.85 (s, 1H, N=CH), 7.5–7.8 (m, 4H, Ar-H); ¹³C NMR (δ): 33.5 (CH₂CH₂CH₂), 44.5 (CH₂CH₂CH₂-N), 47.8 (N-CH₂CH₂CH₂), 111.5 (C₅ of thiazole), 141.5 (C₄ of thiazole), 150.5 (N=CH), 164.3 (CO), 170.3 (C₂ of

thiazole), 126.5, 128.7, 128.5, 129.5, 132.4, 139.5 (6C, Ar); Mass (FAB): 322M⁺.

3.3g *N*-{3-(4-bromobenzylidencarbamyl)-propyl}-2-aminothiazole (**3e**): Yield: 68%; m.p. 75–77°C; Anal. Calcd for C₁₄H₁₅N₄OSBr: C, 45.78, H, 4.11, N, 15.25%; found C, 45.74, H, 4.06, N, 15.19%; IR: 639 (C–Br), 1555 (N=CH), 1678 (C=O), 3388 (NH); ¹H NMR (δ): 2.35 (m, 2H, J = 7.39 Hz, CH₂CH₂CH₂), 3.52 (m, 2H, CH₂CH₂CH₂-NH), 4.26 (m, 2H, N-CH₂CH₂CH₂), 5.69 (t, J = 4.60 Hz, 1H, NHCO), 7.04 (d, 1H, J = 4.78 Hz, C₅H of thiazole), 7.27 (d, 1H, J = 4.78 Hz, C₄H of thiazole), 7.78 (t, J = 5.10 Hz, 1H, NH), 7.94 (s, 1H, N=CH) 7.19–7.69 (m, 4H, Ar-H); ¹³C NMR (δ): 33.4 (CH₂CH₂CH₂), 43.7 (CH₂CH₂CH₂-NH), 46.8 (N-CH₂CH₂CH₂), 112.7 (C₅ of thiazole), 140.9 (C₄ of thiazole), 150.6 (N=CH), 164.1 (CO), 169.5 (C₂ of thiazole), 123.5, 126.5, 129.2, 132.8, 133.6, 137.6 (6C, Ar); Mass (FAB): 367M⁺.

3.3h *N*-{3-(3-bromobenzylidencarbamyl)-propyl}-2-aminothiazole (**3f**): Yield: 64%; m.p. 72–73°C; Anal. Calcd for C₁₄H₁₅N₄OSBr: C, 45.78, H, 4.11, N, 15.25%; found C, 45.72, H, 4.04, N, 15.22%; IR: 642 (C–Br), 1563 (N=CH), 1679 (C=O), 3366 (NH); ¹H NMR (δ): 2.39 (m, 2H, CH₂CH₂CH₂), 3.50 (m, 2H, CH₂CH₂CH₂-NH), 4.28 (m, 2H, N-CH₂CH₂CH₂), 5.55 (t, J = 4.60 Hz, 1H, NHCO), 7.07 (d, 1H, J = 4.82 Hz, C₅H of thiazole), 7.29 (d, 1H, J = 4.82 Hz, C₄H of thiazole), 7.75 (t, J = 5.10 Hz, 1H, NH), 7.88 (s, 1H, N=CH), 7.23–7.90 (m, 4H, Ar-H); ¹³C NMR (δ): 41.3 (CH₂CH₂CH₂), 49.4 (CH₂CH₂CH₂-N), 47.1 (N-CH₂CH₂CH₂), 112.6 (C₅ of thiazole), 141.5 (C₄ of thiazole), 151.6 (N=CH), 163.9 (CO), 172.4 (C₂ of thiazole), 124.1, 126.7, 129.2, 131.5, 137.7, 141.2 (6C, Ar); Mass (FAB): 367M⁺.

3.3i *N*-{3-(2-bromobenzylidencarbamyl)-propyl}-2-aminothiazole (**3h**): Yield: 62%; m.p. 70–71°C; Anal. Calcd for C₁₄H₁₅N₄OSBr: C, 45.78, H, 4.11, N, 15.25%; found C, 45.74, H, 4.05, N, 15.18%; IR: 632 (C–Br), 1554 (N=CH), 1672 (C=O), 3378 (NH); ¹H NMR (δ): 2.30 (m, 2H, CH₂CH₂CH₂), 3.41 (m, 2H, CH₂CH₂CH₂-NH), 4.27 (m, 2H, N-CH₂CH₂CH₂), 5.69 (t, J = 4.60 Hz, 1H, NHCO), 7.06 (d, 1H, J = 4.83 Hz, C₅H of thiazole), 7.28 (d, 1H, J = 4.83 Hz, C₄H of thiazole), 7.70 (t, J = 5.10 Hz, 1H, NH), 8.02 (s, 1H, N=CH), 7.21–7.73 (m, 4H, Ar-H); ¹³C NMR (δ): 35.9 (CH₂CH₂CH₂), 42.1 (CH₂CH₂CH₂-NH), 51.4 (N-CH₂CH₂CH₂), 109.7 (C₅ of thiazole), 139.9 (C₄ of thiazole), 152 (N=CH), 164.1 (CO), 171.6 (C₂ of

thiazole), 126.8, 128.5, 129.5, 131.7, 133.9, 145.4 (6C, Ar); Mass (FAB): 367M⁺.

3.3j *N*-{3-(4-nitrobenzylidencarbamyl)-propyl}-2-aminothiazole (**3i**): Yield: 65%; m.p. 80–81°C; Anal. Calcd for C₁₄H₁₅N₅O₃S: C, 50.44, H, 4.53, N, 21.00%; found C, 50.35, H, 4.48, N, 20.90%; IR: 849 (C-N), 1532 (N=O), 1578 (N=CH), 1677 (C=O), 3378 (NH); ¹H NMR (δ): 2.37 (m, 2H, J = 7.45 Hz, CH₂CH₂CH₂), 3.57 (m, 2H, CH₂CH₂CH₂-N), 4.24 (m, 2H, N-CH₂CH₂CH₂), 5.81 (t, J = 4.60 Hz, 1H, NHCO), 7.20 (d, 1H, J = 4.83 Hz, C₅H of thiazole), 7.45 (d, 1H, J = 4.83 Hz, C₄H of thiazole), 7.80 (t, J = 5.10 Hz, 1H, NH), 8.10 (s, 1H, N=CH), 7.22–7.91 (m, 4H, Ar-H); ¹³C NMR (δ): 38.9 (CH₂CH₂CH₂), 44.3 (CH₂CH₂CH₂-N), 48.3 (N-CH₂CH₂CH₂), 114.7 (C₅ of thiazole), 141.6 (C₄ of thiazole), 155.4 (N=CH), 165.4 (CO), 171.9 (C₂ of thiazole), 122.4, 124.9, 128.7, 129.5, 138.8, 147.9 (6C, Ar); Mass (FAB): 333M⁺.

3.3k *N*-{3-(3-nitrobenzylidencarbamyl)-propyl}-2-aminothiazole (**3j**): Yield: 61%; m.p. 77–79°C; Anal. Calcd for C₁₄H₁₅N₅O₃S: C, 50.44, H, 4.53, N, 21.00%; found C, 50.37, H, 4.45, N, 20.92%; IR: 3371 (NH), 1668 (C=O), 1528 (N=O), 1574 (N=CH), 844 (C-N); ¹H NMR (δ): 2.35 (m, CH₂CH₂CH₂), 3.56 (m, 2H, CH₂CH₂CH₂-NH), 4.32 (m, 2H, N-CH₂CH₂CH₂), 5.78 (t, J = 4.60 Hz, 1H, NHCO), 7.40 (d, 1H, J = 4.87 Hz, C₄H of thiazole), 7.18 (d, 1H, J = 4.87 Hz, C₅H of thiazole), 7.87 (t, J = 5.10 Hz, 1H, NH), 8.07 (s, 1H, N=CH), 7.21–7.86 (m, 4H, Ar-H); ¹³C NMR (δ): 39.7 (CH₂CH₂CH₂), 45.2 (CH₂CH₂CH₂-NH), 51.1 (N-CH₂CH₂CH₂), 112.6 (C₅ of thiazole), 140 (C₄ of thiazole), 154.7 (N=CH), 165.2 (CO), 171.3 (C₂ of thiazole), 122.3, 125.2, 128.4, 133.4, 137.5, 150.5 (6C, Ar); Mass (FAB): 333M⁺.

3.3l *N*-{3-(2-nitrobenzylidencarbamyl)-propyl}-2-aminothiazole (**3k**): Yield: 60%; m.p. 72–74°C; Anal. Calcd for C₁₄H₁₅N₅O₃S: C, 50.44, H, 4.53, N, 21%; found C, 50.40, H, 4.47, N, 20.95%; IR: 847 (C-N), 1538 (N=O), 1572 (N=CH), 1664 (C=O), 3358 (NH); ¹H NMR (δ): 2.34 (m, 2H, J = 7.51 Hz, CH₂CH₂CH₂), 3.45 (m, 2H, CH₂CH₂CH₂-N), 4.29 (m, 2H, N-CH₂CH₂CH₂), 5.73 (t, J = 4.60 Hz, 1H, NHCO), 7.16 (d, 1H, J = 4.88 Hz, C₅H of thiazole), 7.31 (d, 1H, J = 4.88 Hz, C₄H of thiazole), 7.82 (t, J = 5.10 Hz, 1H, NH), 8.11 (s, 1H, N=CH), 7.26–7.99 (m, 4H, Ar-H); ¹³C NMR (δ): 40.2 (CH₂CH₂CH₂), 47.1 (CH₂CH₂CH₂-N), 52.3 (N-CH₂CH₂CH₂), 111.7 (C₅ of thiazole), 139.8 (C₄ of thiazole), 155.7 (N=CH),

165 (CO), 171.5 (C₂ of thiazole), 122.8, 125.6, 127.8, 133.7, 137.9, 149.6 (6C, Ar); Mass (FAB): 333M⁺.

3.3m *N*-{3-(4-methoxybenzylidencarbamyl)-propyl}-2-aminothiazole (**3l**): Yield: 61%; m.p. 75–77°C; Anal. Calcd for C₁₅H₁₈N₄O₂S: C, 56.58, H, 5.69, N, 17.59%; found C, 56.50, H, 5.61, N, 17.56%; IR: 1564 (N=CH), 2949 (OCH₃), 3359 (NH); ¹H NMR (δ): 2.16 (m, 2H, CH₂CH₂CH₂), 3.38 (m, 2H, CH₂CH₂CH₂-NH), 3.59 (s, 3H, OCH₃), 4.23 (t, 2H, m, 2H, N-CH₂CH₂CH₂), 5.68 (t, J = 4.60 Hz, 1H, NHCO), 7.10 (d, 1H, J = 4.82 Hz, C₅H of thiazole), 7.39 (d, 1H, J = 4.82 Hz, C₄H of thiazole), 7.84 (t, J = 5.10 Hz, 1H, NH), 7.95 (s, 1H, N=CH), 7.24–7.88 (m, 4H, Ar-H); ¹³C NMR (δ): 35.2 (CH₂CH₂CH₂), 44.6 (CH₂CH₂CH₂-NH), 47.6 (N-CH₂CH₂CH₂), 51.7 (OCH₃), 109.8 (C₅ of thiazole), 139.5 (C₄ of thiazole), 154.8 (N=CH), 162.5 (CO), 169.6 (C₂ of thiazole), 114.7, 117.6, 126.8, 128.7, 130.6, 159.9 (6C, Ar); Mass (FAB): 318M⁺.

3.3n *N*-{3-(2-methoxybenzylidencarbamyl)-propyl}-2-aminothiazole (**3m**): Yield: 63%; m.p. 68–69°C; Anal. Calcd for C₁₅H₁₈N₄O₂S: C, 56.58, H, 5.69, N, 17.59%; found C, 56.54, H, 5.62, N, 17.53%; IR: 3366 (NH), 2940 (OCH₃), 1558 (N=CH); ¹H NMR (δ): 2.14 (m, 2H, CH₂CH₂CH₂), 3.42 (m, 2H, CH₂CH₂CH₂-NH), 3.64 (s, 3H, OCH₃), 4.14 (m, 2H, N-CH₂CH₂CH₂), 5.64 (t, J = 4.60 Hz, 1H, NHCO), 7.28 (d, 1H, J = 4.80 Hz, C₄H of thiazole), 6.82 (d, 1H, J = 4.80 Hz, C₅H of thiazole), 7.68 (t, J = 5.10 Hz, 1H, NH), 7.79 (s, 1H, N=CH), 7.22–7.92 (m, 4H, Ar-H); ¹³C NMR (δ): 38.1 (N-CH₂CH₂CH₂), 42.8 (CH₂CH₂CH₂), 49.7 (CH₂CH₂CH₂-NH), 54.7 (OCH₃), 161.1 (CO), 153.5 (N=CH), 170.2 (C₂ of thiazole), 109.4 (C₅ of thiazole), 138.3 (C₄ of thiazole), 112.3, 116.8, 122.7, 128.5, 137.7, 159.9 (6C, Ar); Mass (FAB): 318M⁺.

3.3o *N*-{3-(3-methoxybenzylidencarbamyl)-propyl}-2-aminothiazole (**3n**): Yield: 64%; m.p. 70–72°C; Anal. Calcd for C₁₅H₁₈N₄O₂S: C, 56.58, H, 5.69, N, 17.59%; found C, 56.52, H, 5.64, N, 17.50%; IR: 1554 (N=CH), 2947 (OCH₃), 3368 (NH); ¹H NMR (δ): 2.11 (m, 2H, CH₂CH₂CH₂), 3.42 (m, 2H, CH₂CH₂CH₂-NH), 3.68 (s, 3H, OCH₃), 4.18 (m, 2H, N-CH₂CH₂CH₂), 5.69 (t, J = 4.60 Hz, 1H, NHCO), 7.11 (d, 1H, J = 4.82 Hz, C₅H of thiazole), 7.29 (d, 1H, J = 4.82 Hz, C₄H of thiazole), 7.72 (t, J = 5.10 Hz, 1H, NH), 7.96 (s, 1H, N=CH), 7.41–7.82 (m, 4H, Ar-H); ¹³C NMR (δ): 36.2 (CH₂CH₂CH₂), 44.6 (CH₂CH₂CH₂-NH), 48.7 (N-CH₂CH₂CH₂), 54.5 (OCH₃), 109.8 (C₅ of thiazole), 137.8 (C₄ of thiazole), 153.9 (N=CH),

161.9 (CO), 168.2 (C₂ of thiazole), 112.8, 117.9, 123.6, 129.7, 138.9, 160.5 (6C, Ar); Mass (FAB): 318M⁺.

3.3p *N*-{3-(4-methylbenzylidencarbamyl)-propyl}-2-aminothiazole (**3n**): Yield: 62%; m.p. 64–65°C; Anal. Calcd for C₁₅H₁₈N₄OS: C, 59.58, H, 5.99, N, 18.52%; found C, 59.50, H, 5.92, N, 18.48%; IR: 1552 (N=CH), 2927 (CH₃), 3352 (NH); ¹H NMR (δ): 2.09 (m, 2H, CH₂CH₂CH₂), 3.34 (m, 2H, CH₂CH₂CH₂-NH), 2.60 (s, 3H, CH₃), 4.02 (m, 2H, N-CH₂CH₂CH₂), 5.68 (t, J = 4.60 Hz, 1H, NHCO), 6.81 (d, 1H, J = 4.88 Hz, C₅H of thiazole), 7.14 (d, 1H, J = 4.88 Hz, C₄H of thiazole), 7.69 (t, J = 5.10 Hz, 1H, NH), 7.84 (s, 1H, N=CH), 7.29–7.79 (m, 4H, Ar-H); ¹³C NMR (δ): 24.9 (CH₃), 34.4 (CH₂CH₂CH₂), 43.3 (CH₂CH₂CH₂-NH), 46.7 (N-CH₂CH₂CH₂), 151.7 (N=CH), 160.8 (CO), 171.2 (C₂ of thiazole), 109.5 (C₅ of thiazole), 139.8 (C₄ of thiazole), 125.8, 127.4, 129.8, 130.7, 134.9, 139.6 (6C, Ar); Mass (FAB): 302M⁺.

3.3q *N*-{3-(3-methylbenzylidencarbamyl)-propyl}-2-aminothiazole (**3o**): Yield: 61%; m.p. 61–62°C; Anal. Calcd for C₁₅H₁₈N₄OS: C, 59.58, H, 5.99, N, 18.52%; found C, 59.52, H, 5.90, N, 18.45%; IR: 1545 (N=CH), 2920 (CH₃), 3347 (NH); ¹H NMR (δ): 2.60 (s, 3H, CH₃), 2.05 (m, 2H, CH₂CH₂CH₂), 3.45 (m, 2H, CH₂CH₂CH₂-NH), 3.78 (m, 2H, N-CH₂CH₂CH₂), 5.40 (t, J = 4.60 Hz, 1H, NHCO), 6.88 (d, 1H, J = 4.86 Hz, C₅H of thiazole), 7.25 (d, 1H, J = 4.86 Hz, C₄H of thiazole), 7.65 (t, J = 5.10 Hz, 1H, NH), 7.80 (s, 1H, N=CH), 7.32–7.85 (m, 4H, Ar-H); ¹³C NMR (δ): 21.9 (CH₃), 39.1 (CH₂CH₂CH₂), 52.1 (CH₂CH₂CH₂-NH), 45.7 (N-CH₂CH₂CH₂), 109.8 (C₅ of thiazole), 140.1 (C₄ of thiazole), 151 (N=CH), 159.5 (CO), 171 (C₂ of thiazole), 125.2, 129.6, 128.5, 129.8, 134.3, 137.4 (6C, Ar); Mass (FAB): 302M⁺.

3.3r *N*-{3-(2-methylbenzylidencarbamyl)-propyl}-2-aminothiazole (**3p**): Yield: 64%; m.p. 57–58°C; Anal. Calcd for C₁₅H₁₈N₄OS: C, 59.58, H, 5.99, N, 18.52%; found C, 59.55, H, 5.93, N, 18.46%; IR: 1555 (N=CH), 2910 (CH₃), 3345 (NH); ¹H NMR (δ): 2.63 (s, 3H, CH₃), 2.05 (m, 2H, CH₂CH₂CH₂), 3.40 (m, 2H, CH₂CH₂CH₂-NH), 3.70 (m, 2H, N-CH₂CH₂CH₂), 5.55 (t, J = 4.60 Hz, 1H, NHCO), 6.85 (d, 1H, J = 4.82 Hz, C₅H of thiazole), 7.22 (d, 1H, J = 4.82 Hz, C₄H of thiazole), 7.67 (t, J = 5.10 Hz, 1H, NH), 7.75 (s, 1H, N=CH), 7.24–7.75 (m, 10H, Ar-H); ¹³C NMR (δ): 22.9 (CH₃), 35.2 (CH₂CH₂CH₂), 42.3 (CH₂CH₂CH₂-NH), 46.5 (N-CH₂CH₂CH₂), 105.2 (C₅ of thiazole), 139.4 (C₄ of thiazole), 155.5 (N=CH), 160.2 (CO), 169.5 (C₂

of thiazole), 124.3, 126.4, 128.7, 130.8, 134.7, 137.8 (6C, Ar); Mass (FAB): 302M⁺.

3.3s *N*-{3-(4-hydroxybenzylidencarbamyl)-propyl}-2-aminothiazole (**3q**): Yield: 61%; m.p. 72–74°C; Anal. Calcd for C₁₄H₁₅N₄O₂S: C, 55.24, H, 4.96, N, 18.40%; found C, 55.19, H, 4.90, N, 18.30%; IR: 1559 (N=CH), 3382 (NH), 3470 (OH); ¹H NMR (δ): 2.29 (m, 2H, CH₂CH₂CH₂), 3.47 (m, 2H, CH₂CH₂CH₂-NH), 4.29 (m, 2H, N-CH₂CH₂CH₂), 4.17 (s, 1H, OH), 5.82 (t, J = 4.60 Hz, 1H, NHCO), 7.15 (d, 1H, J = 4.81 Hz, C₅H of thiazole), 7.36 (d, 1H, J = 4.81 Hz, C₄H of thiazole), 7.84 (t, J = 5.10 Hz, 1H, NH), 8.07 (s, 1H, N=CH), 7.22–7.99 (m, 4H, Ar-H); ¹³C NMR (δ): 39.9 (CH₂CH₂CH₂), 45.1 (CH₂CH₂CH₂-NH), 51.1 (N-CH₂CH₂CH₂), 110.7 (C₅ of thiazole), 138.6 (C₄ of thiazole), 156.3 (N=CH), 164.7 (CO), 169.1 (C₂ of thiazole), 116.7, 118.9, 126.9, 129.8, 130.7, 154.8 (6C, Ar); Mass (FAB): 304M⁺.

3.3t *N*-{3-(3-hydroxybenzylidencarbamyl)-propyl}-2-aminothiazole (**3r**): Yield: 66%; m.p. 70–71°C; Anal. Calcd for C₁₄H₁₅N₄O₂S: C, 55.24, H, 4.96, N, 18.40%; found C, 55.20, H, 4.88, N, 18.36%; IR: 1564 (N=CH), 3379 (NH), 3462 (OH); ¹H NMR (δ): 2.28 (m, 2H, CH₂CH₂CH₂), 3.48 (m, 2H, CH₂CH₂CH₂-N), 4.28 (m, 2H, N-CH₂CH₂CH₂), 4.26 (s, 1H, OH), 5.96 (t, J = 4.60 Hz, 1H, NHCO), 7.05 (d, 1H, J = 4.90 Hz, C₅H of thiazole), 7.34 (d, 1H, J = 4.90 Hz, C₄H of thiazole), 7.87 (t, J = 5.10 Hz, 1H, NH), 8.01 (s, 1H, N=CH), 7.26–8.14 (m, 4H, Ar-H); ¹³C NMR (δ): 38.4 (CH₂CH₂CH₂), 46.7 (CH₂CH₂CH₂-N), 53.4 (N-CH₂CH₂CH₂), 111.2 (C₅ of thiazole), 139.6 (C₄ of thiazole), 154.2 (N=CH), 163.7 (CO), 168.1 (C₂ of thiazole), 113.4, 115.8, 119.9, 129.4, 138.8, 155.7 (6C, Ar); Mass (FAB): 304M⁺.

3.3u *N*-{3-(2-hydroxybenzylidencarbamyl)-propyl}-2-aminothiazole (**3s**): Yield: 65%; m.p. 78–80°C; Anal. Calcd for C₁₄H₁₅N₄O₂S: C, 55.24, H, 4.96, N, 18.40%; found C, 55.20, H, 4.92, N, 18.32%; IR: 1565 (N=CH), 3381 (NH), 3468 (OH); ¹H NMR (δ): 2.21 (m, 2H, CH₂CH₂CH₂), 3.44 (m, 2H, CH₂CH₂CH₂-NH), 4.26 (m, 2H, N-CH₂CH₂CH₂), 4.28 (s, 1H, OH), 5.83 (t, J = 4.60 Hz, 1H, NHCO), 7.12 (d, 1H, J = 4.89 Hz, C₅H of thiazole), 7.39 (d, 1H, J = 4.89 Hz, C₄H of thiazole), 7.79 (t, J = 5.10 Hz, 1H, NH), 7.97 (s, 1H, N=CH), 7.25–8.06 (m, 4H, Ar-H); ¹³C NMR (δ): 38.4 (CH₂CH₂CH₂), 47.3 (CH₂CH₂CH₂-NH), 52.1 (N-CH₂CH₂CH₂), 109.6 (C₅ of thiazole), 140.2 (C₄ of thiazole), 151.3 (N=CH), 164.1 (CO), 168.3 (C₂ of

thiazole), 112.7, 123.4, 124.3, 127.7, 131.5, 154.9 (6C, Ar); Mass (FAB): 304M⁺.

3.4 Compounds 4(a–s)

3.4a *N*-3-[*-(2-phenyl-4-oxo-1,3-thiazolidine)-carbamyl*]-propyl-2-aminothiazole (**4a**): Yield: 62%; m.p. 75–77°C; Anal. Calcd for C₁₆H₁₈N₄O₂S₂: C, 53.01, H, 5.00, N, 15.45%; found C, 52.97, H, 4.95, N, 15.41%; IR: 674 (C-S-C), 1329 (C-N), 1735 (CO cyclic), 2930 (S-CH₂); ¹H NMR: 3.49 (s, 2H, S-CH₂), 5.32 (d, 1H, N-CH), 6.96 (d, 1H, J = 4.90 Hz, C₅H of thiazole), 7.35 (d, 1H, J = 4.90 Hz, C₄H of thiazole), 6.74–7.69 (m, 4H, Ar-H); ¹³C NMR (δ): 52.6 (CH₂-S), 63.5 (N-CH), 109.5 (C₅ of thiazole), 140.1 (C₄ of thiazole), 171.6 (CO, cyclic), 172 (C₂ of thiazole), 125.4, 126.4, 127, 128.2, 130, 137.2 (6C, Ar); Mass (FAB): 362M⁺.

3.4b *N*-3-[*-(2-(4-chlorophenyl)-4-oxo-1,3-thiazolidine)-carbamyl*]-propyl-2-aminothiazole (**4b**): Yield: 63%; m.p. 92–93°C; Anal. Calcd for C₁₆H₁₇N₄O₂S₂Cl: C, 48.41, H, 4.31, N, 14.11% found C, 48.39, H, 4.27, N, 14.08%; IR: 671 (C-S-C), 743 (C-Cl), 1325 (C-N), 1736 (CO cyclic), 2933 (S-CH₂); ¹H NMR: 3.52 (s, 2H, S-CH₂), 5.46 (d, 1H, N-CH), 6.96 (d, 1H, J = 4.91 Hz, C₅H of thiazole), 7.41 (d, 1H, J = 4.91 Hz, C₄H of thiazole), 6.71–7.84 (m, 4H, Ar-H); ¹³C NMR (δ): 53.5 (CH₂-S), 64.3 (N-CH), 112.6 (C₅ of thiazole), 138.1 (C₄ of thiazole), 174 (CO, cyclic), 170.5 (C₂ of thiazole), 126.7, 127.5, 128.3, 129.4, 130.1, 138.6 (6C, Ar); Mass (FAB): 397M⁺.

3.4c *N*-3-[*-(2-(3-chlorophenyl)-4-oxo-1,3-thiazolidine)-carbamyl*]-propyl-2-aminothiazole (**4c**): Yield: 62%; m.p. 88–89°C; Anal. Calcd for C₁₆H₁₇N₄O₂S₂Cl: C, 48.41, H, 4.31, N, 14.11%; found C, 48.36, H, 4.25, N, 14.10%; IR: 675 (C-S-C), 746 (C-Cl), 1329 (C-N), 1738 (CO cyclic), 2932 (S-CH₂); ¹H NMR: 3.51 (s, 2H, S-CH₂), 5.42 (d, 1H, N-CH), 6.89 (d, 1H, J = 4.95 Hz, C₅H of thiazole), 7.38 (d, 1H, J = 4.95 Hz, C₄H of thiazole), 6.81–7.82 (m, 4H, Ar-H); ¹³C NMR (δ): 55.6 (CH₂-S), 63.2 (N-CH), 113.4 (C₅ of thiazole), 139.4 (C₄ of thiazole), 173.5 (CO, cyclic), 171 (C₂ of thiazole), 125.4, 126, 127.7, 128.6, 129.4, 137 (6C, Ar); Mass (FAB): 397M⁺.

3.4d *N*-3-[*-(2-(2-chlorophenyl)-4-oxo-1,3-thiazolidine)-carbamyl*]-propyl-2-aminothiazole (**4d**): Yield: 68%; m.p. 85–86°C; Anal. Calcd for C₁₆H₁₇N₄O₂S₂Cl: C, 48.41, H, 4.31, N, 14.11%; found C, 48.38, H, 4.28, N, 14.05%; IR: 676 (C-S-C), 748 (C-Cl), 1325 (C-N), 1735 (CO cyclic), 2936 (S-CH₂); ¹H NMR: 3.55 (s,

2H, S-CH₂), 5.49 (d, 1H, N-CH), 6.98 (d, 1H, J = 4.98 Hz, C₅H of thiazole), 7.38 (d, 1H, J = 4.98 Hz, C₄H of thiazole), 6.72–7.86 (m, 4H, Ar-H); ¹³C NMR (δ): 54 (CH₂-S), 63.2 (N-CH), 113.5 (C₅ of thiazole), 139.4 (C₄ of thiazole), 173.6 (CO, cyclic), 171.3 (C₂ of thiazole), 126.4, 127.8, 128.5, 129.2, 130.5, 139 (6C, Ar); Mass (FAB): 397M⁺.

3.4e *N*-3-[*-(2-(4-bromophenyl)-4-oxo-1,3-thiazolidine)-carbamyl*]-propyl-2-aminothiazole (**4e**): Yield: 62%; m.p. 80–82°C; Anal. Calcd for C₁₆H₁₇N₄O₂S₂Br: C, 43.54, H, 3.88, N, 12.69%; found C, 43.51, H, 3.82, N, 12.66%; IR: 670 (C-S-C), 741 (C-Br), 1324 (C-N), 1732 (CO cyclic), 2931 (S-CH₂); ¹H NMR: 3.59 (s, 2H, S-CH₂), 5.41 (d, 1H, N-CH), 6.86 (d, 1H, J = 4.89 Hz, C₅H of thiazole), 7.41 (d, 1H, J = 4.89 Hz, C₄H of thiazole), 6.81–7.79 (m, 4H, Ar-H); ¹³C NMR (δ): 52.4 (CH₂-S), 65.1 (N-CH), 113.3 (C₅ of thiazole), 138.2 (C₄ of thiazole), 172.6 (CO, cyclic), 170.6 (C₂ of thiazole), 126.5, 127.9, 128.5, 129.4, 130.9, 139.2 (6C, Ar); Mass (FAB): 441M⁺.

3.4f *N*-3-[*-(2-(3-bromophenyl)-4-oxo-1,3-thiazolidine)-carbamyl*]-propyl-2-aminothiazole (**4f**): Yield: 65%; m.p. 87–88°C; Anal. Calcd for C₁₆H₁₇N₄O₂S₂Br: C, 43.54, H, 3.88, N, 12.69%; found C, 43.49, H, 3.81, N, 12.67%; IR: 672 (C-S-C), 742 (C-Br), 1327 (C-N), 1738 (CO cyclic), 2981 (S-CH₂); ¹H NMR: 3.51 (s, 2H, S-CH₂), 5.45 (d, 1H, N-CH), 6.87 (d, 1H, J = 4.91 Hz, C₅H of thiazole), 7.37 (d, 1H, J = 4.91 Hz, C₄H of thiazole), 6.65–7.79 (m, 4H, Ar-H); ¹³C NMR (δ): 55.7 (CH₂-S), 65.6 (N-CH), 113.4 (C₅ of thiazole), 140.3 (C₄ of thiazole), 172.4 (CO, cyclic), 169.5 (C₂ of thiazole), 126.7, 127.5, 128, 128.7, 129.3, 138.5 (6C, Ar); Mass (FAB): 441M⁺.

3.4g *N*-3-[*-(2-(2-bromophenyl)-4-oxo-1,3-thiazolidine)-carbamyl*]-propyl-2-aminothiazole (**4g**): Yield: 67%; m.p. 89–91°C, Anal. Calcd for C₁₆H₁₇N₄O₂S₂Br: C, 43.54, H, 3.88, N, 12.69%; found C, 43.48, H, 3.84, N, 12.66%; IR: 677 (C-S-C), 748 (C-Br), 1322 (C-N), 1740 (CO cyclic), 2937 (S-CH₂); ¹H NMR: 3.46 (s, 2H, S-CH₂), 5.41 (d, 1H, N-CH), 6.87 (d, 1H, J = 4.88 Hz, C₅H of thiazole), 7.35 (d, 1H, J = 4.88 Hz, C₄H of thiazole), 6.77–7.91 (m, 4H, Ar-H); ¹³C NMR (δ): 54.5 (CH₂-S), 63.3 (N-CH), 109.6 (C₅ of thiazole), 138.3 (C₄ of thiazole), 170.2 (CO, cyclic), 169.6 (C₂ of thiazole), 126.4, 127.2, 128.7, 129.1, 129.9, 137.6 (6C, Ar); Mass (FAB): 441M⁺.

3.4h *N*-3-[*-(2-(4-nitrophenyl)-4-oxo-1,3-thiazolidine)-carbamyl*]-propyl-2-aminothiazole (**4h**): Yield: 66%;

m.p. 83–85°C; Anal. Calcd for $C_{16}H_{17}N_5O_4S_2$: C, 47.16, H, 4.20, N, 17.18%; found C, 47.14, H, 4.12, N, 17.15%; IR: 669 (C-S-C), 841 (C-NO), 1324 (C-N), 1516 (NO₂), 1736 (CO cyclic), 2928 (S-CH₂); ¹H NMR: 3.44 (s, 2H, S-CH₂), 5.38 (d, 1H, N-CH), 6.87 (d, 1H, J = 4.94 Hz, C₅H of thiazole), 7.36 (d, 1H, J = 4.94 Hz, C₄H of thiazole), 6.78–7.84 (m, 4H, Ar-H); ¹³C NMR (δ): 51.7 (CH₂-S), 623.5 (N-CH), 113.3 (C₅ of thiazole), 138.1 (C₄ of thiazole), 170.7 (CO, cyclic), 169.2 (C₂ of thiazole), 125.1, 126.4, 127.1, 128.7, 129.9, 137.4 (6C, Ar); Mass (FAB): 407M⁺.

3.4i *N*-3-[-{2-(3-nitrophenyl-4-oxo-1,3-thiazolidine)-carbamyl]-propyl-2-aminothiazole (**4i**): Yield: 62%; m.p. 87–89°C; Anal. Calcd for $C_{16}H_{17}N_5O_4S_2$: C, 47.16, H, 4.20, N, 17.18%; found C, 47.14, H, 4.11, N, 17.16%; IR: 679 (C-S-C), 866 (C-NO), 1325 (C-N), 1529 (NO₂), 1732 (CO cyclic), 2927 (S-CH₂); ¹H NMR: 3.41 (s, 2H, S-CH₂), 5.36 (d, 1H, N-CH), 6.85 (d, 1H, J = 4.92 Hz, C₅H of thiazole), 7.39 (d, 1H, J = 4.92 Hz, C₄H of thiazole), 6.68–7.77 (m, 4H, Ar-H); ¹³C NMR (δ): 55.7 (CH₂-S), 62 (N-CH), 110.7 (C₅ of thiazole), 139.8 (C₄ of thiazole), 169.8 (CO, cyclic), 168.5 (C₂ of thiazole), 126.5, 127.8, 128.6, 129.6, 130.5, 139.5 (6C, Ar); Mass (FAB): 407 M⁺.

3.4j *N*-3-[-{2-(2-nitrophenyl-4-oxo-1,3-thiazolidine)-carbamyl]-propyl-2-aminothiazole (**4j**): Yield: 63%; m.p. 80–81°C; Anal. Calcd for $C_{16}H_{17}N_5O_4S_2$: C, 47.16, H, 4.20, N, 17.18%; found C, 47.12, H, 4.14, N, 17.13%; IR: 677 (C-S-C), 842 (C-NO), 1325 (C-N), 1532 (NO₂), 1735 (CO cyclic), 2927 (S-CH₂); ¹H NMR: 3.38 (s, 2H, S-CH₂), 5.31 (d, 1H, N-CH), 6.86 (d, 1H, J = 4.98 Hz, C₅H of thiazole), 7.34 (d, 1H, J = 4.98 Hz, C₄H of thiazole), 6.82–7.68 (m, 4H, Ar-H); ¹³C NMR (δ): 53.4 (CH₂-S), 62.6 (N-CH), 110.7 (C₅ of thiazole), 138.5 (C₄ of thiazole), 169.7 (CO, cyclic), 170.2 (C₂ of thiazole), 126.1, 127.2, 128.2, 128.6, 129, 138.2 (6C, Ar); Mass (FAB): 407M⁺.

3.4k *N*-3-[-{2-(4-methoxyphenyl-4-oxo-1,3-thiazolidine)-carbamyl]-propyl-2-aminothiazole (**4k**): Yield: 65%; m.p. 78–79°C; Anal. Calcd for $C_{17}H_{18}N_4O_3S_2$: C, 52.04, H, 4.51, N, 14.28%; found C, 52.01, H, 4.48, N, 14.25%; IR: 670 (C-S-C), 1324 (C-N), 1736 (CO cyclic), 2928 (S-CH₂), 2968 (OCH₃); ¹H NMR: 3.38 (s, 2H, S-CH₂), 3.67 (s, 3H, OCH₃), 5.38 (d, 1H, N-CH), 6.85 (d, 1H, J = 4.82 Hz, C₅H of thiazole), 7.35 (d, 1H, J = 4.82 Hz, C₄H of thiazole), 6.89–7.87 (m, 4H, Ar-H); ¹³C NMR (δ): 54 (CH₂-S), 62 (N-CH), 110.7 (C₅ of thiazole), 138.4 (C₄ of thiazole), 168.7

(CO, cyclic), 171.2 (C₂ of thiazole), 126, 127.5, 128, 128.8, 129.6, 138 (6C, Ar); Mass (FAB): 392M⁺.

3.4l *N*-3-[-{2-(3-methoxyphenyl-4-oxo-1,3-thiazolidine)-carbamyl]-propyl-2-aminothiazole (**4l**): Yield: 61%; m.p. 80–81°C; Anal. Calcd for $C_{17}H_{18}N_4O_3S_2$: C, 52.04, H, 4.51, N, 14.28%; found C, 51.99, H, 4.46, N, 14.23%; IR: 669 (C-S-C), 1331 (C-N), 1734 (CO cyclic), 2981 (S-CH₂), 2961 (OCH₃); ¹H NMR: 3.32 (s, 2H, S-CH₂), 3.58 (s, 2H, OCH₃), 5.38 (d, 1H, N-CH), 6.87 (d, 1H, J = 4.86 Hz, C₅H of thiazole), 7.37 (d, 1H, J = 4.86 Hz, C₄H of thiazole), 6.87–7.81 (m, 4H, Ar-H); ¹³C NMR (δ): 53 (CH₂-S), 64.6 (N-CH), 112.5 (C₅ of thiazole), 140.4 (C₄ of thiazole), 169.7 (CO, cyclic), 170.1 (C₂ of thiazole), 125.1, 127.2, 128.7, 129.2, 130.6, 137.2 (6C, Ar); Mass (FAB): 392M⁺.

3.4m *N*-3-[-{2-(2-methoxyphenyl-4-oxo-1,3-thiazolidine)-carbamyl]-propyl-2-aminothiazole (**4m**): Yield: 62%; m.p. 77–78°C; Anal. Calcd for $C_{17}H_{18}N_4O_3S_2$: C, 52.04, H, 4.51, N, 14.28%; found C, 52.02, H, 4.44, N, 14.21%; IR: 676 (C-S-C), 1328 (C-N), 1736 (CO cyclic), 2939 (S-CH₂), 2959 (OCH₃); ¹H NMR: 3.38 (s, 2H, S-CH₂), 3.54 (s, 2H, OCH₃), 5.38 (d, 1H, N-CH), 6.85 (d, 1H, J = 4.89 Hz, C₅H of thiazole), 7.39 (d, 1H, J = 4.89 Hz, C₄H of thiazole), 6.78–7.84 (m, 4H, Ar-H); ¹³C NMR (δ): 53.4 (CH₂-S), 62.7 (N-CH), 110.6 (C₅ of thiazole), 139 (C₄ of thiazole), 169.2 (CO, cyclic), 171.2 (C₂ of thiazole), 126, 127, 128.5, 129.6, 130, 131.5, 139.4 (6C, Ar); Mass (FAB): 392M⁺.

3.4n *N*-3-[-{2-(4-methylphenyl-4-oxo-1,3-thiazolidine)-carbamyl]-propyl-2-aminothiazole (**4n**): Yield: 64%; m.p. 174–175°C; Anal. Calcd for $C_{17}H_{20}N_4O_2S_2$: C, 54.25, H, 5.31, N, 14.89%; found C, 54.21, H, 5.29, N, 14.86%; IR: 672 (C-S-C), 1327 (C-N), 1738 (CO cyclic), 2981 (S-CH₂), 2976 (CH₃); ¹H NMR: 2.85 (s, 3H, CH₃), 3.34 (s, 2H, S-CH₂), 5.28 (d, 1H, N-CH), 6.89 (d, 1H, J = 4.83 Hz, C₅H of thiazole), 7.35 (d, 1H, J = 4.83 Hz, C₄H of thiazole), 6.79–7.81 (m, 4H, Ar-H); ¹³C NMR (δ): 25.6 (CH₃), 53.2 (CH₂-S), 63.6 (N-CH), 111.7 (C₅ of thiazole), 138.1 (C₄ of thiazole), 169.2 (CO, cyclic), 167.4 (C₂ of thiazole), 124, 125.2, 127.4, 129.4, 130.4, 131.2, 137.4 (6C, Ar); Mass (FAB): 376M⁺.

3.4o *N*-3-[-{2-(3-methylphenyl-4-oxo-1,3-thiazolidine)-carbamyl]-propyl-2-aminothiazole (**4o**): Yield: 63%; m.p. 67–68°C; Anal. Calcd for $C_{17}H_{20}N_4O_2S_2$: C, 54.25, H, 5.31, N, 14.89%; found C, 54.19, H, 5.26,

N, 14.85%; IR: 667 (C-S-C), 1324 (C-N), 1739 (CO cyclic), 2924 (S-CH₂), 2968 (CH₃); ¹H NMR: 2.78 (CH₃), 3.32 (s, 2H, S-CH₂), 5.25 (d, 1H, N-CH), 6.82 (d, 1H, J = 4.84 Hz, C₅H of thiazole), 7.38 (d, 1H, J = 4.84 Hz, C₄H of thiazole), 6.75–7.69 (m, 4H, Ar-H); ¹³C NMR (δ): 25.3 (CH₃), 52.2 (CH₂-S), 60.4 (N-CH), 108.2 (C₅ of thiazole), 136.4 (C₄ of thiazole), 168.7 (CO, cyclic), 169.1 (C₂ of thiazole), 124.6, 126.8, 127.9, 129.4, 130.8, 132.5, 140.2 (6C, Ar); Mass (FAB): 376M⁺.

3.4p *N*-3-[-{2-(2-methylphenyl-4-oxo-1,3-thiazolidine)-carbamyl]-propyl-2-aminothiazole (**4p**): Yield: 62%; m.p. 70–72°C; Anal. Calcd for C₁₇H₂₀N₄O₂S₂: C, 54.25, H, 5.31, N, 14.89%; found C, 54.18, H, 5.22, N, 14.81%; IR: 669 (C-S-C), 1324 (C-N), 1733 (CO cyclic), 2922 (S-CH₂), 2956 (CH₃); ¹H NMR: 2.68 (CH₃), 3.21 (s, 2H, S-CH₂), 5.18 (d, 1H, N-CH), 6.89 (d, 1H, J = 4.87 Hz, C₅H of thiazole), 7.31 (d, 1H, J = 4.87 Hz, C₄H of thiazole), 6.76–7.68 (m, 4H, Ar-H); ¹³C NMR (δ): 25.8 (CH₃), 52.7 (CH₂-S), 63.4 (N-CH), 112.7 (C₅ of thiazole), 140.1 (C₄ of thiazole), 168.2 (CO, cyclic), 171 (C₂ of thiazole), 124.5, 125.8, 127.9, 128.6, 129, 137.8 (6C, Ar); Mass (FAB): 376M⁺.

3.4q *N*-3-[-{2-(4-hydroxyphenyl-4-oxo-1,3-thiazolidine)-carbamyl]-propyl-2-aminothiazole (**4q**): Yield: 66%; m.p. 79–81°C; Anal. Calcd for C₁₆H₁₈N₄O₃S₂: C, 50.79, H, 4.76, N, 14.81%; found C, 50.77, H, 4.74, N, 14.79%; IR: 668 (C-S-C), 1324 (C-N), 1732 (CO cyclic), 2925 (S-CH₂), 3482 (OH); ¹H NMR: 3.35 (s, 2H, S-CH₂), 4.92 (s, 1H, OH), 5.27 (d, 1H, N-CH), 6.82 (d, 1H, J = 4.91 Hz, C₅H of thiazole), 7.35 (d, 1H, J = 4.91 Hz, C₄H of thiazole), 6.77–7.71 (m, 4H, Ar-H); ¹³C NMR (δ): 53.2 (CH₂-S), 63.4 (N-CH), 110.5 (C₅ of thiazole), 138.4 (C₄ of thiazole), 169.7 (CO, cyclic), 168 (C₂ of thiazole), 124.4, 125.2, 127.2, 128.6, 129.6, 137.8 (6C, Ar); Mass (FAB) : 378M⁺.

3.4r *N*-3-[-{2-(3-hydroxyphenyl-4-oxo-1,3-thiazolidine)-carbamyl]-propyl-2-aminothiazole (**4r**): Yield: 63%; m.p. 85–87°C; Anal. Calcd for C₁₆H₁₈N₄O₃S₂: C, 50.79, H, 4.76, N, 14.81%; found C, 50.75, H, 4.72, N, 14.73%; IR: 668 (C-S-C), 1325 (C-N), 1733 (CO cyclic), 2988 (S-CH₂), 3477 (OH); ¹H NMR: 3.31 (s, 2H, S-CH₂), 4.94 (s, 1H, OH), 5.18 (d, 1H, N-CH), 6.85 (d, 1H, J = 4.94 Hz, C₅H of thiazole), 7.22 (d, 1H, J = 4.94 Hz, C₄H of thiazole), 6.75–7.68 (m, 4H, Ar-H); ¹³C NMR (δ): 51.4 (CH₂-S), 60.2 (N-CH), 108.2 (C₅ of thiazole), 137.4 (C₄ of thiazole), 168.1 (CO, cyclic),

167 (C₂ of thiazole), 124, 125.4, 126.2, 128.6, 130, 139 (6C, Ar); Mass (FAB): 378M⁺.

3.4s *N*-3-[-{2-(2-hydroxyphenyl-4-oxo-1,3-thiazolidine)-carbamyl]-propyl-2-aminothiazole (**4s**): Yield: 61%; m.p. 80–81°C; Anal. Calcd for C₁₆H₁₈N₄O₃S₂: C, 50.79, H, 4.76, N, 14.81%; found C, 50.72, H, 4.71, N, 14.75%; IR: 667 (C-S-C), 1322 (C-N), 1733 (CO cyclic), 2928 (S-CH₂), 3456 (OH); ¹H NMR: 3.29 (s, 2H, S-CH₂), 4.78 (s, 1H, OH), 5.15 (d, 1H, N-CH), 6.83 (d, 1H, J = 4.90 Hz, C₅H of thiazole), 7.27 (d, 1H, J = 4.90 Hz, C₄H of thiazole), 6.71–7.64 (m, 4H, Ar-H); ¹³C NMR (δ): 50.5 (CH₂-S), 59.2 (N-CH), 107.4 (C₅ of thiazole), 136.1 (C₄ of thiazole), 168.1 (CO, cyclic), 166 (C₂ of thiazole), 124.6, 126.7, 128.5, 129.3, 131.2, 137 (6C, Ar); Mass (FAB): 378M⁺.

3.5 Compounds 5(a–s)

3.5a *N*-3-[-{2-phenyl-4-oxo-5-benzylidene-1,3-thiazolidine)-carbamyl]-propyl-2-aminothiazole (**5a**): Yield: 64%; m.p. 71–73°C; Anal. Calcd for C₂₃H₂₂N₄O₂S₂: C, 61.30, H, 4.92, N, 12.43%; found C, 61.27, H, 4.85, N, 12.39%; IR: 1608 (C=CH), 2968 (C=CH); ¹H NMR: 6.40 (s, 1H, C=CH), 6.91 (d, 1H, J = 4.88 Hz, C₅H of thiazole), 7.27 (d, 1H, J = 4.88 Hz, C₄H of thiazole), 6.71–7.92 (m, 10H, Ar-H); ¹³C NMR (δ): 110.4 (C₅ of thiazole), 138.4 (C₄ of thiazole), 143.2 (C=CH), 146.2 (C=CH), 169.2 (C₂ of thiazole), 124.8, 125.3, 126.1, 126.8, 127.2, 127.6, 128.2, 128.6, 129, 130.4, 137.6, 138.2 (12C, Ar); Mass (FAB): 490M⁺.

3.5b *N*-3-[-{2-(4-chlorophenyl)-4-oxo-5-(4-chlorobenzylidene)-1,3-thiazolidine)-carbamyl]-propyl-2-aminothiazole (**5b**): Yield: 62%; m.p. 89–91°C; Anal. Calcd for C₂₃H₂₀N₄O₂S₂Cl₂: C, 53.17, H, 3.88, N, 10.78%; found C, 53.12, H, 3.81, N, 10.74%; IR: 769 (C–Cl), 1615 (C=CH), 2981 (C=CH); ¹H NMR: 6.45 (s, 1H, C=CH), 6.92 (d, 1H, J = 4.81 Hz, C₅H of thiazole), 7.32 (d, 1H, J = 4.81 Hz, C₄H of thiazole), 6.85–7.72 (m, 8H, Ar-H); ¹³C NMR (δ): 110.2 (C₅ of thiazole), 139.4 (C₄ of thiazole), 143.1 (C=CH), 146.5 (C=CH), 170 (C₂ of thiazole), 125.1, 126.3, 126.7, 127, 127.8, 128, 128.9, 129, 130.5, 131.2, 138.4, 139.2 (12C, Ar); Mass (FAB): 519M⁺.

3.5c *N*-3-[-{5-(3-chlorobenzylidene)-2-(3-chlorophenyl)-4-oxo-1,3-thiazolidine)-carbamyl]-propyl-2-aminothiazole (**5c**): Yield: 61%; m.p. 84–85°C; Anal. Calcd for C₂₃H₂₀N₄O₂S₂Cl₂: C, 53.17, H, 3.88, N,

10.78%; found C, 53.14, H, 3.78, N, 10.73%; IR: 775 (C–Cl), 1625 (C=CH), 2983 (C=CH); ^1H NMR: 6.49 (s, 1H, C=CH), 7.02 (d, 1H, $J = 4.85$ Hz, C_5H of thiazole), 7.36 (d, 1H, $J = 4.85$ Hz, C_4H of thiazole), 6.71–7.63 (m, 8H, Ar-H); ^{13}C NMR (δ): 51.7 ($\text{CH}_2\text{-S}$), 63.6 (N-CH), 109.7 (C_5 of thiazole), 140.1 (C_4 of thiazole), 144.6 (C=CH), 148.3 (C=CH), 172 (C_2 of thiazole), 123.2, 124.5, 125.4, 125.8, 126, 126.7, 127.3, 128.5, 129, 129.8, 138.2, 139.7 (12C, Ar); Mass (FAB) 519M^+ .

3.5d *N*-3-[-{2-(2-chlorophenyl-4-oxo-5-(2-chlorobenzylidene)-1,3-thiazolidine)-carbamyl]-propyl-2-aminothiazole (**5d**): Yield: 63%; m.p. 81–82°C; Anal. Calcd for $\text{C}_{23}\text{H}_{20}\text{N}_4\text{O}_2\text{S}_2\text{Cl}_2$: C, 53.17, H, 3.88, N, 10.78%; found C, 53.11, H, 3.82, N, 10.76%; IR: 762 (C–Cl), 1618 (C=CH), 2983 (C=CH); ^1H NMR: 6.47 (s, 1H, C=CH), 6.97 (d, 1H, $J = 4.80$ Hz, C_5H of thiazole), 7.36 (d, 1H, $J = 4.80$ Hz, C_4H of thiazole), 6.71–7.63 (m, 8H, Ar-H); ^{13}C NMR (δ): 107.9 (C_5 of thiazole), 136.2 (C_4 of thiazole), 144.6 (C=CH), 143.2 (C=CH), 172 (C_2 of thiazole), 124.2, 125.6, 126.3, 127, 127.8, 128.4, 128.6, 130, 130.8, 131.2, 138.6, 140.1 (12C, Ar); Mass (FAB): 519M^+ .

3.5e *N*-3-[-{2-(4-bromophenyl-4-oxo-5-(4-bromobenzylidene)-1,3-thiazolidine)-carbamyl]-propyl-2-aminothiazole (**5e**): Yield: 62%; m.p. 78–79°C; Anal. Calcd for $\text{C}_{23}\text{H}_{20}\text{N}_4\text{O}_2\text{S}_2\text{Br}_2$: C, 45.40, H, 3.31, N, 9.20%; found C, 45.33, H, 3.25, N, 9.18%; IR: 635 (C–Br), 1627 (C=CH), 2986 (C=CH); ^1H NMR: 6.43 (s, 1H, C=CH), 6.90 (d, 1H, $J = 4.89$ Hz, C_5H of thiazole), 7.31 (d, 1H, $J = 4.89$ Hz, C_4H of thiazole), 6.80–7.77 (m, 8H, Ar-H); ^{13}C NMR (δ): 110.9 (C_5 of thiazole), 138.1 (C_4 of thiazole), 144.3 (C=CH), 146.8 (C=CH), 170 (C_2 of thiazole), 120.4, 121.3, 124.7, 125.3, 126.8, 127.2, 127.7, 128.3, 130.2, 131, 137.4, 139.1 (12C, Ar); Mass (FAB) 608M^+ .

3.5f *N*-3-[-{2-(3-bromophenyl-4-oxo-5-(3-bromobenzylidene)-1,3-thiazolidine)-carbamyl]-propyl-2-aminothiazole (**5f**): Yield: 66%; m.p. 79–81°C; Anal. Calcd for $\text{C}_{23}\text{H}_{20}\text{N}_4\text{O}_2\text{S}_2\text{Br}_2$: C, 45.40, H, 3.31, N, 9.20%; found C, 45.34, H, 3.24, N, 9.15%; IR: 641 (C–Br), 1624 (C=CH), 2987 (C=CH); ^1H NMR: 6.49 (s, 1H, C=CH), 6.98 (d, 1H, $J = 4.87$ Hz, C_5H of thiazole), 7.37 (d, 1H, $J = 4.87$ Hz, C_4H of thiazole), 6.78–7.79 (m, 8H, Ar-H); ^{13}C NMR (δ): 113.1 (C_5 of thiazole), 140.4 (C_4 of thiazole), 142.1 (C=CH), 147 (C=CH), 173 (C_2 of thiazole), 121.7, 123.4, 125.4, 126.3, 127.1,

127.5, 128.2, 128.7, 131, 132.5, 138.4, 140.2 (12C, Ar); Mass (FAB): 608M^+ .

3.5g *N*-3-[-{2-(2-bromophenyl-4-oxo-5-(2-bromobenzylidene)-1,3-thiazolidine)-carbamyl]-propyl-2-aminothiazole (**5g**): Yield: 65%; m.p. 80–81°C; Anal. Calcd for $\text{C}_{23}\text{H}_{20}\text{N}_4\text{O}_2\text{S}_2\text{Br}_2$: C, 45.40, H, 3.31, N, 9.20%; found C, 45.31, H, 3.26, N, 9.16%; IR: 639 (C–Br), 1620 (C=CH), 2989 (C=CH); ^1H NMR: 6.50 (s, 1H, C=CH), 6.98 (d, 1H, $J = 4.85$ Hz, C_5H of thiazole), 7.37 (d, 1H, $J = 4.85$ Hz, C_4H of thiazole), 6.79–7.75 (m, 8H, Ar-H); ^{13}C NMR (δ): 113.5 (C_5 of thiazole), 142.3 (C_4 of thiazole), 144.1 (C=CH), 147.3 (C=CH), 173 (C_2 of thiazole), 122.3, 124.3, 125.3, 126.6, 127.4, 128.6, 129.3, 130.4, 131.7, 132.2, 137.5, 138 (12C, Ar); Mass (FAB): 608M^+ .

3.5h *N*-3-[-{2-(4-nitrophenyl-4-oxo-5-(4-nitrobenzylidene)-1,3-thiazolidine)-carbamyl]-propyl-2-aminothiazole (**5h**): Yield: 61%; m.p. 77–79°C; Anal. Calcd for $\text{C}_{23}\text{H}_{20}\text{N}_6\text{O}_6\text{S}_2$: C, 51.10, H, 3.72, N, 15.54%; found C, 51.07, H, 3.69, N, 15.51%; IR: 852 (C–NO), 1522 (NO_2), 1622 (C=CH), 2990 (C=CH); ^1H NMR: 6.52 (s, 1H, C=CH), 7.06 (d, 1H, $J = 4.92$ Hz, C_5H of thiazole), 7.42 (d, 1H, $J = 4.92$ Hz, C_4H of thiazole), 6.89–7.81 (m, 8H, Ar-H); ^{13}C NMR (δ): 57.4 ($\text{CH}_2\text{-S}$), 64 (N-CH), 111.6 (C_5 of thiazole), 141.2 (C_4 of thiazole), 145.3 (C=CH), 147.3 (C=CH), 172 (C_2 of thiazole), 122.7, 123.5, 125.3, 126, 126.8, 127.2, 127.9, 128.7, 129.3, 130.6, 137.4, 138.4 (12C, Ar); Mass (FAB): 540M^+ .

3.5i *N*-3-[-{2-(3-nitrophenyl-4-oxo-5-(3-nitrobenzylidene)-1,3-thiazolidine)-carbamyl]-propyl-2-aminothiazole (**5i**): Yield: 65%; m.p. 75–76°C; Anal. Calcd for $\text{C}_{23}\text{H}_{20}\text{N}_6\text{O}_6\text{S}_2$: C, 51.10, H, 3.72, N, 15.54%; found C, 51.08, H, 3.66, N, 15.49%; IR: 859 (C–NO), 1518 (NO_2), 1628 (C=CH), 2985 (C=CH); ^1H NMR: 6.51 (s, 1H, C=CH), 7.03 (d, 1H, $J = 4.94$ Hz, C_5H of thiazole), 7.41 (d, 1H, $J = 4.94$ Hz, C_4H of thiazole), 6.87–7.86 (m, 8H, Ar-H); ^{13}C NMR (δ): 56 ($\text{CH}_2\text{-S}$), 63.2 (N-CH), 112 (C_5 of thiazole), 140.2 (C_4 of thiazole), 144.3 (C=CH), 147.2 (C=CH), 173 (C_2 of thiazole), 120.7, 122.4, 123.3, 125.1, 125.9, 127.8, 128.9, 129.4, 131.3, 132.2, 135.4, 136.2 (12C, Ar); Mass (FAB) 540M^+ .

3.5j *N*-3-[-{2-(2-nitrophenyl-4-oxo-5-(2-nitrobenzylidene)-1,3-thiazolidine)-carbamyl]-propyl-2-aminothiazole (**5j**): Yield: 62%; m.p. 81–82°C; Anal. Calcd for $\text{C}_{23}\text{H}_{20}\text{N}_6\text{O}_6\text{S}_2$: C, 51.10, H, 3.72, N, 15.54%;

found C, 51.04, H, 3.64, N, 15.46%; IR: 863 (C-NO), 1526 (NO₂), 1625 (C=CH), 2988 (C=CH); ¹H NMR: 6.49 (s, 1H, C=CH), 6.98 (d, 1H, J = 4.93 Hz, C₅H of thiazole), 7.37 (d, 1H, J = 4.93 Hz, C₄H of thiazole), 6.88–7.81 (m, 8H, Ar-H); ¹³C NMR (δ): 56.1 (CH₂-S), 63.2 (N-CH), 112.6 (C₅ of thiazole), 141.2 (C₄ of thiazole), 145 (C=CH), 147.3 (C=CH), 172 (C₂ of thiazole), 123.3, 124.6, 125.6, 126, 126.8, 127.2, 128.4, 128.7, 129.4, 132.5, 137, 139.7 (12C, Ar); Mass (FAB): 540M⁺.

3.5k *N*-3-[-{2-(4-methoxyphenyl-4-oxo-5-(4-methoxybenzylidene)-1,3-thiazolidine)-carbonyl]-propyl-2-aminothiazole (**5k**): Yield: 65%; m.p. 74–76°C; Anal. Calcd for C₂₅H₂₆N₄O₄S₂: C, 58.82, H, 5.09, N, 10.98%; found C, 58.77, H, 5.06, N, 10.95%; IR: 1596 (C=CH), 2985 (C=CH), 2970 (OCH₃); ¹H NMR: 3.63 (s, 3H, OCH₃), 6.47 (s, 1H, C=CH), 6.98 (d, 1H, J = 4.88 Hz, C₅H of thiazole), 7.38 (d, 1H, J = 4.88 Hz, C₄H of thiazole), 6.82–7.78 (m, 8H, Ar-H); ¹³C NMR (δ): 51.6 (CH₂-S), 63.2 (N-CH), 109.6 (C₅ of thiazole), 138.1 (C₄ of thiazole), 142.1 (C=CH), 146.5 (C=CH), 170 (C₂ of thiazole), 110.7, 112.4, 113.2, 114.5, 124.5, 125.9, 127, 128.6, 129, 138.1, 154.8, 157.3 (12C, Ar); Mass (FAB) 511M⁺.

3.5l *N*-3-[-{2-(3-methoxyphenyl-4-oxo-5-(3-methoxybenzylidene)-1,3-thiazolidine)-carbonyl]-propyl-2-aminothiazole (**5l**): Yield: 60%; m.p. 75–76°C; Anal. Calcd for C₂₅H₂₆N₄O₄S₂: C, 58.82, H, 5.09, N, 10.98%; found C, 58.76, H, 5.04, N, 10.93%; IR: 1592 (C=CH), 2982 (C=CH), 2977 (OCH₃); ¹H NMR: 3.67 (s, 3H, OCH₃), 6.40 (s, 1H, C=CH), 6.96 (d, 1H, J = 4.91 Hz, C₅H of thiazole), 7.38 (d, 1H, J = 4.91 Hz, C₄H of thiazole), 6.87–7.79 (m, 8H, Ar-H); ¹³C NMR (δ): 110.7 (C₅ of thiazole), 138.1 (C₄ of thiazole), 142.5 (C=CH), 144.7 (C=CH), 168.6 (C₂ of thiazole), 114.2, 116.3, 118.4, 120.3, 122.5, 123.6, 125.4, 127.4, 128, 136.6, 158.1, 160.2 (12C, Ar); Mass (FAB) 511M⁺.

3.5m *N*-3-[-{2-(2-methoxyphenyl-4-oxo-5-(2-methoxybenzylidene)-1,3-thiazolidine)-carbonyl]-propyl-2-aminothiazole (**5m**): Yield: 61%; m.p. 72–73°C; Anal. Calcd for C₂₅H₂₆N₄O₄S₂: C, 58.82, H, 5.09, N, 10.98%; found C, 58.71, H, 5.01, N, 10.94%; IR: 1597 (C=CH), 2983 (C=CH) 2969 (OCH₃); ¹H NMR: 3.61 (s, 3H, OCH₃), 6.47 (s, 1H, C=CH), 6.93 (d, 1H, J = 4.96 Hz, C₅H of thiazole), 7.33 (d, 1H, J = 4.96 Hz, C₄H of thiazole), 6.82–7.77 (m, 8H, Ar-H); ¹³C NMR (δ): 109.4 (C₅ of thiazole), 139 (C₄ of thiazole), 142.6 (C=CH), 147.4 (C=CH), 171 (C₂ of thiazole), 115.3,

118.6, 120.5, 121.3, 124.1, 126.3, 127, 128.4, 129.3, 136, 155.3, 157.2 (12C, Ar); Mass (FAB) 511M⁺.

3.5n *N*-3-[-{2-(4-methylphenyl-4-oxo-5-(4-methylbenzylidene)-1,3-thiazolidine)-carbonyl]-propyl-2-aminothiazole (**5n**): Yield: 62%; m.p. 69–71°C; Anal. Calcd for C₂₅H₂₆N₄O₂S₂: C, 62.76, H, 5.43, N, 11.71%; found C, 62.72, H, 5.41, N, 11.68 IR: 1588 (C=CH), 2979 (C=CH) 1341 (CH₃); ¹H NMR: 2.81 (s, 3H, CH₃) 6.42 (s, 1H, C=CH), 6.93 (d, 1H, J = 4.87 Hz, C₅H of thiazole), 7.36 (d, 1H, J = 4.87 Hz, C₄H of thiazole), 6.79–7.67 (m, 8H, Ar-H); ¹³C NMR (δ): 107.5 (C₅ of thiazole), 137.1 (C₄ of thiazole), 140.5 (C=CH), 144.2 (C=CH), 171 (C₂ of thiazole), 122.9, 124.3, 125.2, 126.2, 127.4, 128.6, 129.6, 130, 133.8, 134.6, 135.2, 137.6 (12C, Ar); Mass (FAB) 479M⁺.

3.5o *N*-3-[-{2-(3-methylphenyl-4-oxo-5-(3-methylbenzylidene)-1,3-thiazolidine)-carbonyl]-propyl-2-aminothiazole (**5o**): Yield: 65%; m.p. 61–63°C; Anal. Calcd for C₂₅H₂₆N₄O₂S₂: C, 62.76, H, 5.43, N, 11.71%; found C, 62.73, H, 5.39, N, 11.65%; IR: 1592 (C=CH), 2977 (C=CH), 1325 (CH₃); ¹H NMR: 2.86 (s, 3H, CH₃), 6.38 (s, 1H, C=CH), 6.91 (d, 1H, J = 4.86 Hz, C₅H of thiazole), 7.30 (d, 1H, J = 4.86 Hz, C₄H of thiazole), 6.80–7.71 (m, 8H, Ar-H); ¹³C NMR (δ): 52.5 (CH₂-S), 62 (N-CH), 110.7 (C₅ of thiazole), 138.1 (C₄ of thiazole), 142.4 (C=CH), 144.3 (C=CH), 168 (C₂ of thiazole), 122.4, 124.5, 125.6, 126.5, 127.6, 128.2, 128.7, 130.4, 131, 132.8, 135.9, 137.2 (12C, Ar); Mass (FAB) 479M⁺.

3.5p *N*-3-[-{2-(2-methylphenyl-4-oxo-5-(2-methylbenzylidene)-1,3-thiazolidine)-carbonyl]-propyl-2-aminothiazole (**5p**): Yield: 63%; m.p. 65–66°C; Anal. Calcd for C₂₅H₂₆N₄O₂S₂: C, 62.76, H, 5.43, N, 11.71%; found C, 62.69, H, 5.38, N, 11.66%; IR: 1590 (C=CH), 2980 (C=CH), 1338 (CH₃); ¹H NMR: 2.79 (s, 3H, CH₃) 6.41 (s, 1H, C=CH), 6.88 (d, 1H, J = 4.90 Hz, C₅H of thiazole), 7.35 (d, 1H, J = 4.90 Hz, C₄H of thiazole), 6.81–7.75 (m, 8H, Ar-H); ¹³C NMR (δ): 109.2 (C₅ of thiazole), 135.4 (C₄ of thiazole), 140.5 (C=CH), 145.4 (C=CH), 170 (C₂ of thiazole), 123.5, 124.6, 125.3, 126.4, 127.6, 128, 128.7, 129.6, 132.5, 135.8, 136, 139.1 (12C, Ar); Mass (FAB) 479M⁺.

3.5q *N*-3-[-{2-(4-hydroxyphenyl-4-oxo-5-(4-hydroxybenzylidene)-1,3-thiazolidine)-carbonyl]-propyl-2-aminothiazole (**5q**): Yield: 65%; m.p. 79–81°C; Anal. Calcd for C₂₃H₂₂N₄O₄S₂: C, 57.26, H, 4.56, N, 11.61%; found C, 57.22, H, 4.54, N, 11.57%; IR: 1625 (C=CH),

2978 (C=CH), 3612 (OH); ^1H NMR: 4.82 (s, 1H, OH), 6.34 (s, 1H, C=CH), 6.89 (d, 1H, $J = 4.92$ Hz, C_5H of thiazole), 7.36 (d, 1H, $J = 4.92$ Hz, C_4H of thiazole), 6.71–7.62 (m, 8H, Ar-H); ^{13}C NMR (δ): 108.6 (C_5 of thiazole), 136.2 (C_4 of thiazole), 139.3 (C=CH), 143.4 (C=CH), 169 (C_2 of thiazole), 116.5, 120.3, 122.8, 123.2, 124.2, 126.8, 127.6, 128.7, 130.5, 137, 155.6, 157.4 (12C, Ar); Mass (FAB) 581M^+ .

3.5r *N*-3-[-{2-(3-hydroxyphenyl-4-oxo-5-(3-hydroxybenzylidene)-1,3-thiazolidine)-carbonyl]-propyl-2-aminothiazole (**5r**): Yield: 61%; m.p. 73–74°C; Anal. Calcd for $\text{C}_{23}\text{H}_{22}\text{N}_4\text{O}_4\text{S}_2$: C, 57.26, H, 4.56, N, 11.61%; found C, 57.22, H, 4.51, N, 11.54%; IR: 1624 (C=CH), 2979 (C=CH), 3626 (OH); ^1H NMR: 4.91 (s, 1H, OH), 6.38 (s, 1H, C=CH), 6.86 (d, 1H, $J = 4.85$ Hz, C_5H of thiazole), 7.37 (d, 1H, $J = 4.85$ Hz, C_4H of thiazole), 6.76–7.69 (m, 8H, Ar-H); ^{13}C NMR (δ): 108.4 (C_5 of thiazole), 137.1 (C_4 of thiazole), 141.3 (C=CH), 143.3 (C=CH), 168.5 (C_2 of thiazole), 117.2, 118.5, 122, 123.7, 124.2, 125, 12.6, 127.1, 130, 136.5, 154.6, 156.9 (12C, Ar); Mass (FAB) 581M^+ .

3.5s *N*-3-[-{2-(2-hydroxyphenyl-4-oxo-5-(2-hydroxybenzylidene)-1,3-thiazolidine)-carbonyl]-propyl-2-aminothiazole (**5s**): Yield: 62%; m.p. 75–76°C; Anal. Calcd for $\text{C}_{23}\text{H}_{22}\text{N}_4\text{O}_4\text{S}_2$: C, 57.26, H, 4.56, N, 11.61%; found C, 57.20, H, 4.51, N, 11.52%; IR: 1632 (C=CH), 2977 (C=CH), 3618 (OH); ^1H NMR: 4.87 (s, 1H, OH), 6.35 (s, 1H, C=CH), 6.86 (d, 1H, $J = 4.80$ Hz, C_5H of thiazole), 7.25 (d, 1H, $J = 4.80$ Hz, C_4H of thiazole), 6.69–7.65 (m, 8H, Ar-H); ^{13}C NMR (δ): 107.6 (C_5 of thiazole), 132.1 (C_4 of thiazole), 139.3 (C=CH), 140.2 (C=CH), 165 (C_2 of thiazole), 120.4, 122.7, 123.4, 124.1, 125.7, 126.6, 127.6, 128.4, 129.2, 137.7, 153.9, 155.2 (12C, Ar); Mass (FAB) 581M^+ .

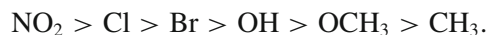
4. Results and discussion

The reaction of 1-bromo-3-chloro-propane with 2-aminothiazole afforded a product compound **1**. The spectroscopic analyses of compound **1** showed absorption peaks for N–CH and C–Cl at 1339 and 748 cm^{-1} respectively in the IR spectrum and confirms the formation of compound **1**. The compound **1** on the reaction with urea with continuous stirring at room temperature yielded compound **2**. In the spectroscopic analyses of compound **2** we found three absorption peaks in IR spectrum for NH, NH_2 and CO at 3378 , 3424 cm^{-1} and 1642 cm^{-1} respectively while absorption of C–Cl has

been disappeared. This is clearly indicated that compound **1** gives the substitution reaction with urea. This was also supported by ^1H and ^{13}C NMR spectra because two signals appeared in the ^1H NMR spectrum for NH and NH_2 at δ 5.63 and 5.96 ppm respectively. The formation of the compound **2** was fully supported by a CO group gives a signal at δ 163.8 ppm in the ^{13}C NMR spectrum. All these are strong evidences for the synthesis of compound **2**. Substituted benzaldehydes give the condensation reaction with compound **2** resultant the production of Schiff bases $\text{N}=\text{CH}$ took place which was confirmed by IR, ^1H NMR and ^{13}C NMR spectra of compound **3(a–s)**. In the IR spectra an absorption found in the range of 1552 – 1589 cm^{-1} while a strong signal appeared in the range of δ 7.78–8.24 and δ 145–155.4 ppm in the ^1H NMR and ^{13}C NMR spectra of compound **3(a–s)** respectively. The facts also supported by the disappearance of the signal of NH_2 in the ^1H NMR spectra. The compound **3(a–s)** on reaction with equimolar amount of thioglycolic acid in the presence of ZnCl_2 (act as a catalyst) in the trace amount gives the cycloaddition reaction and produced a five-membered thiazolidinone ring, **4(a–s)**. The compound **4(a–s)** showed a characteristic absorption of the cyclic carbonyl group in the range of 1736 – 1758 cm^{-1} in the IR spectra. The ^1H NMR spectra drawn attention and clearly indicate the presence of the active methylene group in the thiazolidine ring in the range of δ 3.26–3.49 ppm. The ^{13}C NMR spectra of compound **4(a–s)** also supported the fact that cyclic carbonyl group present and a signal appeared in the range of δ 165.4–175.2 ppm. These were supported by two evidences that are; (i) disappearance of $\text{N}=\text{CH}$ proton and (ii) appearance of N–CH proton in the range of δ 5.23–5.47 ppm in the ^1H NMR spectra of compound **4(a–s)**. Compound **4(a–s)** underwent the Knoevenagel condensation reaction with substituted benzaldehydes in the presence of alkali metal alkoxide ($\text{C}_2\text{H}_5\text{ONa}$) to afford compound **5(a–s)**. In the ^1H NMR spectra of the compound **5(a–s)**, we found the disappearance of two methylene protons of compounds **4(a–s)** and an appearance of a new signal for C=CH in the range of δ 6.44–6.77 ppm in the ^1H NMR and two new signals for C=CH and C=CH appeared in the range of δ 135.7–143.2 and δ 141.1–149.2 ppm in the ^{13}C NMR spectra of the compounds **5(a–s)**. These facts clearly confirmed the synthesis of all final products. Compounds **5(a–s)** were synthesized and screened for their antibacterial and antifungal activity against some selected bacteria and fungi respectively and antitubercular activity against *M. tuberculosis* (H37Rv strain). The investigation of antimicrobial and antitubercular data revealed

that the compounds (**5c**), (**5d**), (**5e**), (**5f**), (**5h**), (**5i**) and (**5j**) have shown more activity in the series, the compounds (**5b**), (**5g**) and (**5s**) showed moderate activity and rest of the compounds showed less activity against all the strains compared with standard drugs.

Our investigations have shown that the compounds have a structure–activity relationship because activity of compounds varied with substitution. Nitro group containing compounds (**5h**, **5i** and **5j**) showed higher activity than chloro (**5c**, **5d**), or bromo group containing compounds (**5e**, **5f**). Chloro and bromo derivatives also have higher activity than other compounds. On the basis of Structural Activity Relationship (SAR), concluded that the activity of compounds depends on electron withdrawing nature of the substituted groups. The sequence of the activity is given below.



5. Conclusions

The present study reports the synthesis of a new series of N-3-[-{2-(substituted phenyl-4-oxo-5-(substituted benzylidene)-1,3-thiazolidine)-carbonyl]-propyl-2-aminothiazole, **5(a–s)**. Antimicrobial and antitubercular activity of the new synthesized compounds bearing thiazolidine moiety, revealed that all tested compounds showed moderate to good antibacterial, antifungal and antitubercular activities against selected microbial strains.

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