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SYNTHESIS AND ANTITUBERCULAR ACTIVITY OF 4-OXO-THIAZOLIDINE DERIVATIVES OF 2-AMINO-5-NITROTHIAZOLE

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ABSTRACT. New series of *N*-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(substituted phenyl)-4-oxo-5-(substituted benzylidene)-1,3-thiazolidine-carboxamide, **5(a-j)** have been synthesized from 2-amino-5-nitrothiazole as a starting material. The structure of all the synthesized compounds were confirmed by chemical and spectral analyses such as IR, ^{1}H NMR, ^{13}C NMR and FAB-Mass. All the final synthesized compounds **5(a-j)** were screened for their antibacterial and antifungal activities against some selected bacteria and fungi with their MIC values and antitubercular activity screened against *M. tuberculosis.*

KEY WORDS: Synthesis, 2-Amino-5-nitrothiazole, Thiazolidinone, Antimicrobial, Antitubercular

INTRODUCTION

Molecules containing thiazole ring systems are widely studied because of its low toxicity. Thiazole moiety is the key pharmacophore for the synthesis of several biological important molecules. Thiazole containing derivatives plays an important role in biological activity of many compounds such as antimicrobial activity [1, 2], anti-inflammatory [3], antitumor activities [4], antiarrhythmic and anticoagulant activities [5]. We also knows that imine derivatives possess potent activities including antibacterial [6, 7], antifungal [8, 9] and antitubercular [10] activities. Thiazolidine-4-ones are an important subunit of heterocyclic compounds having valuable biological activities. The thiazolidinones and correlated motifs have high biological relevance since the discovery. They are present in both natural products and pharmaceutical compounds. Some synthesized thiazolidinone derivatives possess antimicrobial [11-14], antidiabetic agents [15], antiviral [16], anti-inflammatory [17] activities.

In the present study, we have synthesized new series of biologically active thiazolidine derivatives. We have described the synthesis of a new series of *N*-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(substituted phenyl)-4-oxo-5-(substituted benzylidene)-1,3-thiazolidine-carboxamide, compounds **5(a-j)** and other intermediate of the series compound **1**, **2**, **3(a-j)**, **4(a-j)** (Scheme 1). The structure of all the synthesized compounds were confirmed by chemical and spectral analyses such as IR, ^{1}H NMR, ^{13}C NMR and FAB-Mass. All the final synthesized compounds **5(a-j)** were screened for their antibacterial and antifungal activities against some selected bacteria and fungi with their MIC values and antitubercular activity screened against *M. tuberculosis.*

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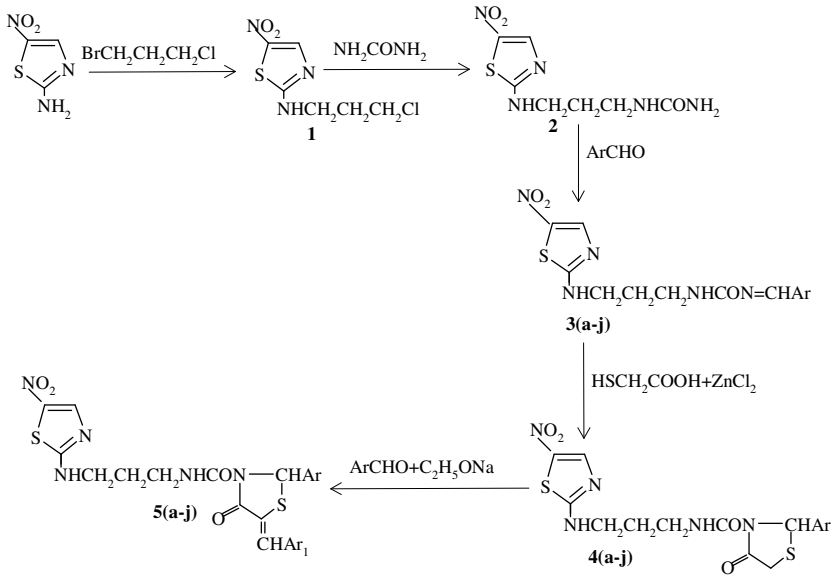
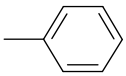
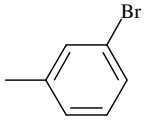
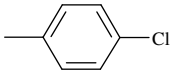
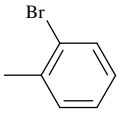
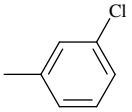
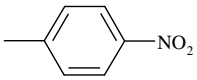
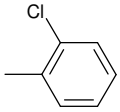
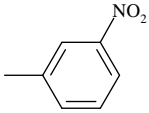
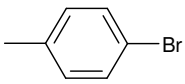
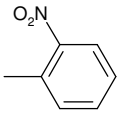


Scheme 1. Synthesis of compounds **1**, **2**, **3(a-j)**, **4(a-j)** and **5(a-j)**.

Compound	Ar = Ar_1	Compound	Ar = Ar_1
3a, **4a**, **5a**		**3f**, **4f**, **5f**	
3b, **4b**, **5b**		**3g**, **4g**, **5g**	
3c, **4c**, **5c**		**3h**, **4h**, **5h**	
3d, **4d**, **5d**		**3i**, **4i**, **5i**	
3e, **4e**, **5e**		**3j**, **4j**, **5j**	

RESULTS AND DISCUSSION

Synthesis

The reaction of 1-bromo-3-chloro-propane with 2-amino-5-nitrothiazole to afford a product compound **1** [18]. Spectroscopic analyses of compound **1** showed absorption peaks for N-CH and C-Cl at 1313 cm^{-1} and 727 cm^{-1} in the IR spectrum which confirms the formation of compound **1**. Compound **1** on the reaction with urea yielded compound **2** [19]. IR spectrum of compound **2** showed three absorption peaks for NH, NH_2 and CO at 3387, 3452 cm^{-1} and 1662 cm^{-1} respectively while absorption of C-Cl disappeared. This is clearly indicated that compound **1** gives the substitution reaction with urea. This fact was also supported by ^1H and ^{13}C NMR spectra because two signals appeared in the ^1H NMR spectrum for NH at δ 5.67 and 5.97 ppm, respectively. The formation of compound **2** was fully supported by a CO group which gives a signal at δ 163.3 ppm in the ^{13}C NMR spectrum. All the facts together are strong evidence for the synthesis of compound **2**. Compound **2** gives the condensation reaction with substituted benzaldehydes furnished compounds **3(a-j)** [20] which were confirmed by IR, ^1H NMR and ^{13}C NMR spectra. In the IR spectra an absorption found in the range of 1555-1573 cm^{-1} for N=C while a strong signal appeared in the range of δ 8.02-8.20 and δ 147.4-151.6 ppm in the ^1H NMR and ^{13}C NMR spectra respectively for N=CH of compounds **3(a-j)**. The facts also supported by the disappearance of the signal of NH_2 in the ^1H NMR spectrum of compound **2**. Compounds **3(a-j)** on reaction with thioglycolic acid in the presence of $ZnCl_2$ furnished compounds **4(a-j)**. Compounds **4(a-j)** showed a characteristic absorption of the cyclic carbonyl group (cyclic CO) in the range of 1739-1755 cm^{-1} in the IR spectra. The ^1H NMR spectra of compounds **4(a-j)** aroused our attention and clearly indicate the presence of the active methylene group ($-CH_2-$) in the thiazolidine ring in the range of δ 3.20-3.38 ppm. ^{13}C NMR spectra of compounds **4(a-j)** also supported the fact that cyclic carbonyl group (cyclic CO) present and a signal appeared in the range of δ 170.3-173.7 ppm. All these facts also supported by the two evidences that are (a) disappearance of N=CH proton and (b) appearance of N-CH proton in the range of δ 5.18-5.37 ppm in the ^1H NMR spectra of compounds **4(a-j)**. Compounds **4(a-j)** underwent the Knoevenagel condensation reaction with several selected series of substituted benzaldehydes in the presence of C_2H_5ONa to afford the compounds **5(a-j)**. In the ^1H NMR spectra of compounds **5(a-j)**, we found the disappearance of two methylene protons of compounds **4(a-j)** and an appearance of a new signal for C=<u>CH</u> in the range of δ 6.45-6.73 ppm in the ^1H NMR and two new signals for C=<u>CH</u> and <u>C</u>=CH appeared in the range of δ 135.9-141.7 and δ 140.2-143.8 ppm respectively in the ^{13}C NMR spectra of compounds **5(a-j)**. All these facts clearly confirmed the synthesis of all **1, 2, 3(a-j), 4(a-j)** and **5(a-j)** products.

Biological significance

The results of the all described activities (antibacterial, antifungal and antitubercular) are summarized in Tables 1. The results of the antimicrobial screening data revealed that all final compounds of the series compounds **5(a-j)** showed considerable and varied activity against the selected microorganism. A new series of *N*-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(substituted phenyl)-4-oxo-5-(substituted benzylidene)-1,3-thiazolidine-carboxamide, compounds **5(a-j)** were synthesized and screened for their antimicrobial and antitubercular activities data (as shown in Table 1) revealed that all the synthesized compounds **5(a-j)** have a structure activity relationship (SAR) because activities of compounds varies with substitution. Nitro group containing compounds **(5h**, **5i** and **5j)** showed higher activity than chloro **(5c**, **5d)** and bromo group containing compounds **(5e**, **5f)**. On the basis of SAR, we concluded that the sequence of the activity is following

$$NO_2 > Cl > Br > H$$

The investigation of antimicrobial (antibacterial, antifungal and antitubercular) data revealed that the compounds (**5c**), (**5d**), (**5e**), (**5f**), (**5h**), (**5i**) and (**5j**) displayed high activity in the series, the compounds (**5b**) and (**5g**) showed moderate activity and rest compounds showed less activity against all the strains compared with standard drugs.

Table 1. Antibacterial, antifungal and antitubercular activities of compounds **5(a-j)**.

Comp.	Antibacterial activity			Antifungal activity			Antitubercular activity
	B. subtilis	*E. coli*	*S. aureus*	*A. niger*	*A. flavus*	*C. albicans*	*M. tuberculosis*
5a	12.5	9.25	12.50	20.25	21.25	20.25	12.5
5b	3.75	6.25	3.25	15.75	13.25	15.25	2.50
5c	6.25	3.75	6.25	12.75	12.50	12.75	2.75
5d	3.75	6.25	3.25	12.50	12.25	13.50	2.50
5e	3.25	3.75	3.25	13.25	12.25	13.75	2.75
5f	6.25	3.25	3.25	12.75	13.25	12.75	2.75
5g	4.75	6.25	4.50	16.25	14.50	15.75	6.25
5h	3.25	3.75	3.25	12.50	13.50	12.75	2.50
5i	3.25	3.25	3.75	12.25	12.75	13.5	2.50
5j	3.25	3.75	3.25	12.75	12.50	13.50	2.75

The MIC values of standard streptomycin for all bacterial strain and griseofulvin for all fungal strain were in the range of 2.50-3.25 and 6.25-12.50 μg/mL, respectively. Isoniazid and rifampicin were used as standards, MIC values in the range of 1.25-2.50 μg/mL for *M. tuberculosis*.

CONCLUSION

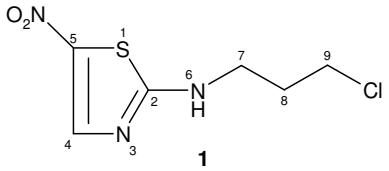
The present research study reports the successful synthesis of a new series of *N*-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(substituted phenyl)-4-oxo-5-(substituted benzylidene)-1,3-thiazolidine-carboxamide, compounds **5(a-j)**. Antimicrobial and antitubercular activities of newly synthesized compounds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

EXPERIMENTAL

Melting points were taken in open capillaries and are uncorrected. Progress of reaction was monitored by silica gel-G coated TLC plates in MeOH:$CHCl_3$ system (1:9). The spot was visualized by exposing dry plate in iodine vapours. IR spectra were recorded in KBr disc on a Schimadzu 8201 PC FTIR spectrophotometer (ν_{max} in cm^{-1}) and ^1H and ^{13}C NMR spectra were measured on a Brucker DRX-300 spectrometer in $CDCl_3$ 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 highly 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.

*Synthesis of 1-(3-chloropropyl)-2-amino-5-nitrothiazole, compound **1***

2-Amino-5-nitrothiazole (0.345 mol) and 1-bromo-3-chloropropane (0.345 mol) in methanol (100 mL) were stirred on a magnetic stirrer for about 6.5 h at room temperature. The completion of the reaction was monitored by silica gel-G coated TLC plates. After the completion of the reaction the product was filtered and purified over a silica gel packed column chromatography using $CHCl_3$:CH_3OH (8:2 v/v) system as eluant (120 mL). The purified product was dried under vacuo and recrystallized from ethanol at room temperature to yield compound **1** (Figure 1).



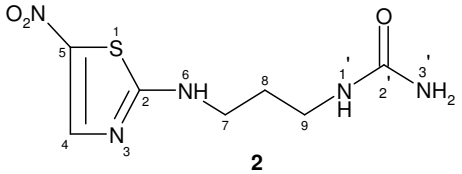
1

Figure 1. Structure of compound **1**.

*1-(3-Chloropropyl)-2-amino-5-nitrothiazole (**1**).* Yield: 62%; m.p. 173-175 ºC; IR (cm^{-1}): 727 (C-Cl), 881 (C-S), 968 (C-NO), 1313 (N-CH_2), 1362, 1532 (NO_2), 1559 (C=C), 1436, 2832, 2897 (CH_2), 3009 (CH-Ar), 3388 (NH); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ: 1.91-1.95 (m, 2H H-8), 3.27 (t, *J* 7.35 Hz, 2H, H-9), 3.85-3.89 (m, 2H, H-7), 7.71 (s, 1H, H-4), 7.83 (br, s, 1H, H-6); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ: 34.4 (C-8), 41.7 (C-9), 45.9 (C-7), 134.2 (C-4), 137.8 (C-5), 166.5 (C-2); FAB-Mass *(m/z)*: 221 [M^+]; anal. calc. for $C_6H_8N_3O_2SCl$: C 32.51, H 3.63, N 18.95; found: C 32.49, H 3.59, N 18.87%.

*Synthesis of N-[3-(2-amino-5-nitrothiazolyl)-propyl]-urea, compound **2***

Compound **1** (0.2256 mol) and urea (0.2256 mol) in methanol (100 mL) were stirred on a magnetic stirrer for about 6.5 h at room temperature. The completion of the reaction was monitored by silica gel-G coated TLC plates. After the completion of the reaction the product was filtered and purified over a silica gel packed column chromatography using $CHCl_3$:CH_3OH (8:2 v/v) system as eluent (120 mL). The purified product was dried under vacuo and recrystallized from ethanol at room temperature to yield compound **2** (Figure 2).



2

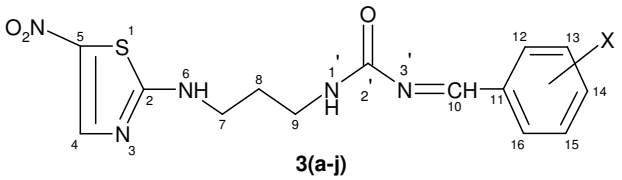
Figure 2. Structure of compound **2**.

*N-[3-(2-amino-5-nitrothiazolyl)-propyl]-urea (**2**).* Yield: 70%; m.p. 153-155 ºC; IR (cm^{-1}): 879 (C-S), 966 (C-NO), 1324 (N-CH_2), 1360, 1533 (NO_2), 1559 (C=C), 1662 (C=O), 1432, 2885, 2918 (CH_2), 3021 (CH-Ar), 3387 (NH), 3452 (NH_2); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ: 2.08-2.12 (m, 2H, H-8), 3.19-3.24 (m, 2H, H-9), 3.82-3.90 (m, 2H, H-7), 5.67 (s, 1H, H-1'), 5.97 (br s, 2H, H-3'), 7.65 (s, 1H, H-4), 7.80 (br, s, 1H, H-6); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ: 33.4 (C-8), 38.6 (C-9), 44.1 (C-7), 133.8 (C-4), 138.5 (C-5), 163.4 (C-2'), 165.3 (C-2); FAB-

Mass *(m/z)*: 245 [M^+]; anal. calc. for $C_7H_{11}N_5O_3S$: C 34.28, H 4.52, N 28.55; found: C 34.25, H 4.48, N 28.51%.

*Synthesis of N-[3-(1H-2-amino-5-nitrothiazolyl)-propyl]-N'-[(phenyl)-methyli dene]-urea, compound **3a***

Compound **2** (0.0330 mol) and benzaldehyde (0.0330 mol) in methanol (100 mL) in the presence of 2-4 drops of glacial acetic acid were first stirred on a magnetic stirrer for about 2 h followed by reflux on a steam bath for about 3.5 h. The completion of the reaction was monitored by silica gel-G coated TLC plates. The product was filtered and cooled at room temperature. The filtered product was purified over a silica gel packed column chromatography using CH_3OH:$CHCl_3$ (7:3 v/v) as eluent (75 mL). The purified product was dried under vacuo and recrystallized from ethanol at room temperature to furnish compound **3a** (Figure 3).



3(a-j)

Figure 3. Structure of compounds **3(a-j)**.

Compounds **3 (b-j)** have also been synthesized by using similar method as above.

*N-[3-(2-amino-5-nitrothiazolyl)-propyl]-N'-[(phenyl)-methyli dene]-urea (**3a**).* Yield: 62%; m.p. 148-149 ºC; IR (cm^{-1}): 856 (C-S), 961 (C-NO), 1329 (N-CH_2), 1356, 1531 (NO_2), 1547 (C=C), 1661 (C=O), 1427, 2878, 2912 (CH_2), 3016 (CH-Ar), 3382 (NH); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ: 2.02-2.07 (m, 2H, H-8), 3.20-3.25 (m, 2H, H-9), 3.80-3.85 (m, 2H, H-7), 5.60 (s, 1H, H-1'), 7.24 (s, 1H, H-4), 7.89 (s, 1H, H-6), 8.02 (s, 1H, H-10), 6.75-7.84 (m, 5H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ: 28.2 (C-8), 36.5 (C-9), 42.4 (C-7), 126.7 (C-12 and C-16), 128.4 (C-14), 129.3 (C-13 and C-15), 130.7 (C-4), 136.6 (C-5), 137.2 (C-11), 147.4 (C-10), 160.5 (C-2'), 168.8 (C-2); FAB-Mass *(m/z)*: 333 [M^+]; anal. calc. for $C_{14}H_{15}N_5O_3S$: C 50.44, H 4.53, N 21.00; found: C 50.35, H 4.55, N 20.95%.

*N-[3-(2-amino-5-nitrothiazolyl)-propyl]-N'-[(4-chlorophenyl)-methylidene]-urea (**3b**).* Yield: 62%; m.p. 178-179 ºC; IR (cm^{-1}): IR: 744 (C-Cl), 870 (C-S), 968 (C-NO), 1342 (N-CH_2), 1365, 1541 (NO_2), 1556 (C=C), 1670 (C=O), 1430, 2884, 2917 (CH_2), 3022 (CH-Ar), 3390 (NH); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ: 2.11-2.15 (m, 2H, H-8), 3.22-3.27 (m, 2H, H-9), 3.83-3.88 (m, 2H, H-7), 5.64 (s, 1H, H-1'), 7.89 (s, 1H, H-4), 7.98 (s, 1H, H-6), 8.13 (s, 1H, H-10), 6.94-7.65 (m, 4H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ: 28.6 (C-8), 40.1 (C-9), 43.2 (C-7), 126.6 (C-12 and C-16), 128.9 (C-14), 129.6 (C-13 and C-15), 130.9 (C-4), 135.2 (C-5), 141.4 (C-11), 147.7 (C-10), 160.2 (C-2'), 168.4 (C-2); FAB-Mass *(m/z)*: 367 [M^+]; anal. calc. for $C_{14}H_{14}N_5O_3SCl$: C 45.71, H 3.83, N 19.04; found: C 45.60, H 3.81, N 19.01%.

*N-[3-(2-amino-5-nitrothiazolyl)-propyl]-N'-[(3-chlorophenyl)-methylidene]-urea (**3c**).* Yield: 62%; m.p. 174-175 ºC; IR (cm^{-1}): 745 (C-Cl), 866 (C-S), 977 (C-NO), 1336 (N-CH_2), 1360, 1536 (NO_2), 1550 (C=C), 1667 (C=O),1434, 2892, 2930 (CH_2), 3026 (CH-Ar), 3386 (NH); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ: 2.11-2.15 (m, 2H, H-8), 3.28-3.32 (m, 2H, H-9), 3.84-3.89 (m, 2H, H-7), 5.72 (s, 1H, H-1'), 7.30 (s, 1H, H-4), 7.95 (s, 1H, H-6), 8.14 (s, 1H, H-

10), 6.82-7.93 (m, 4H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ: 30.3 (C-8), 39.6 (C-9), 43.5 (C-7), 127.7 (C-12), 128.4 (C-16), 129.4 (C-14), 130.3 (C-13), 131.7 (C-15), 133.4 (C-4), 137.1 (C-5), 141.9 (C-11), 151.2 (C-10), 161.3 (C-2'), 169.8 (C-2); FAB-Mass *(m/z)*: 367 [M^+]; anal. calc. for $C_{14}H_{14}N_5O_3SCl$: C 45.71, H 3.83, N 19.04; found: C 45.67, H 3.77, N 18.98%.

N-[3-(2-amino-5-nitrothiazolyl)-propyl]-N'-[(2-chlorophenyl)-methylidene]-urea ***(3d)***. Yield: 62%; m.p. 172-173 ºC; IR (cm^{-1}): 747 (C-Cl), 860 (C-S), 962 (C-NO), 1330 (N-CH_2), 1358, 1534 (NO_2), 1549 (C=C), 1663 (C=O), 1428, 2880, 2913 (CH_2), 3017 (CH-Ar), 3384 (NH); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ: 2.08-2.12 (m, 2H, H-8), 3.30-3.35 (m, 2H, H-9), 3.82-3.86 (m, 2H, H-7), 5.70 (s, 1H, H-1'), 7.31 (s, 1H, H-4), 7.91 (s, 1H, H-6), 8.18 (s, 1H, H-10), 6.86-7.84 (m, 4H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ: 31.2 (C-8), 38.8 (C-9), 44.7 (C-7), 127.3 (C-12), 128.6 (C-16), 129.7 (C-14), 130.4 (C-13), 132.5 (C-15), 134.5 (C-4), 138.2 (C-11), 138.9 (C-5), 151.6 (C-10), 162.4 (C-2'), 169.3 (C-2), (Ar); FAB-Mass *(m/z)*: 367 [M^+]; anal. calc. for $C_{14}H_{14}N_5O_3SCl$: C 45.71, H 3.83, N 19.04; found: C 45.65, H 3.75, N 19.02%.

N-[3-(2-amino-5-nitrothiazolyl)-propyl]-N'-[(4-bromophenyl)-methylidene]-urea ***(3e)***. Yield: 62%; m.p. 170-171 ºC; IR (cm^{-1}): 638 (C-Br), 858 (C-S), 970 (C-NO), 1335 (N-CH_2), 1370, 1537 (NO_2), 1551 (C=C), 1674 (C=O), 1440, 2886, 2921 (CH_2), 3019 (CH-Ar), 3387 (NH); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ: 2.07-2.12 (m, 2H, H-8), 3.29-3.34 (m, 2H, H-9), 3.81-3.85 (m, 2H, H-7), 5.73 (s, 1H, H-1'), 7.28 (s, 1H, H-4), 7.91 (s, 1H, H-6), 8.20 (s, 1H, H-10), 6.70-7.85 (m, 4H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ: 29.3 (C-8), 36.8 (C-9), 42.6 (C-7), 128.6 (C-12 and C-16), 130.5 (C-14), 131.2 (C-13 and C-15), 132.2 (C-4), 136.3 (C-5), 138.8 (C-11), 150.7 (C-10), 162.1 (C-2'), 170.4 (C-2); FAB-Mass *(m/z)*: 412 [M^+]; anal. calc. for $C_{14}H_{14}N_5O_3SBr$: C 40.78, H 3.42, N 16.98; found: C 45.75, H 3.39, N 6.92%.

N-[3-(2-amino-5-nitrothiazolyl)-propyl]-N'-[(3-bromophenyl)-methylidene]-urea ***(3f)***. Yield: 62%; m.p. 169-170 ºC; IR (cm^{-1}): 643 (C-Br), 860 (C-S), 963 (C-NO), 1337 (N-CH_2), 1374, 1540 (NO_2), 1554 (C=C), 1671 (C=O), 1432, 2888, 2922 (CH_2), 3025 (CH-Ar), 3388 (NH); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ: 2.10-2.17 (m, 2H, H-8), 3.30-3.36 (m, 2H, H-9), 3.87-3.92 (m, 2H, H-7), 5.67 (s, 1H, H-1'), 7.39 (s, 1H, H-4), 7.99 (s, 1H, H-6), 8.16 (s, 1H, H-10), 6.69-7.81 (m, 4H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ: 31.8 (C-8), 37.2 (C-9), 45.4 (C-7), 128.3 (C-12), 128.7 (C-16), 130.8 (C-14), 131.6 (C-13), 132.7 (C-4), 133.8 (C-15), 136.4 (C-5), 139.4 (C-11), 148.6 (C-10), 161.9 (C-2'), 170.7 (C-2); FAB-Mass *(m/z)*: 412 [M^+]; anal. calc. for $C_{14}H_{14}N_5O_3BrS$: C 40.78, H 3.42, N 16.98; found: C 40.73, H 3.37, N 16.94%.

N-[3-(2-amino-5-nitrothiazolyl)-propyl]-N'-[(2-bromophenyl)-methylidene]-urea ***(3g)***. Yield: 62%; m.p. 165-167 ºC; IR (cm^{-1}): 645 (C-Br), 871 (C-S), 965 (C-NO), 1332 (N-CH_2), 1359, 1533 (NO_2), 1552 (C=C), 1664 (C=O), 1437, 2883, 2914 (CH_2), 3024 (CH-Ar), 3385 (NH); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ: 2.11-2.16 (m, 2H, H-8), 3.25-3.29 (m, 2H, H-9), 3.88-3.93 (m, 2H, H-7), 5.71 (s, 1H, H-1'), 7.40 (s, 1H, H-4), 7.94 (s, 1H, H-6), 8.14 (s, 1H, H-10), 6.71-7.89 (m, 4H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ: 31.5 (C-8), 37.6 (C-9), 45.8 (C-7), 129.4 (C-12), 130.6 (C-16), 131.3 (C-14), 132.1 (C-13), 133.7 (C-15), 133.9 (C-4), 137.5 (C-5), 140.6 (C-11), 148.9 (C-10), 163.6 (C-2'), 171.4 (C-2); FAB-Mass *(m/z)*: 412 [M^+]; anal. calc. for $C_{14}H_{14}N_5O_3BrS$: C 40.78, H 3.42, N 16.98; found: C 40.70, H 3.36, N 16.93%.

N-[3-(2-amino-5-nitrothiazolyl)-propyl]-N'-[(4-nitrophenyl)-methylidene]-urea ***(3h)***. Yield: 62%; m.p. 167-168 ºC; IR (cm^{-1}): 865 (C-S), 974 (C-NO), 1340 (N-CH_2), 1367, 1532 (NO_2), 1560 (C=C), 1673 (C=O), 1435, 2891, 2925 (CH_2), 3021 (CH-Ar), 3393 (NH); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ: 2.12-2.15 (m, 2H, H-8), 3.24-3.30 (m, 2H, H-9), 3.91-3.96 (m, 2H, H-7), 5.65 (s, 1H, H-1'), 7.32 (s, 1H, H-4), 7.99 (s, 1H, H-6), 8.17 (s, 1H, H-10), 6.74-7.95 (m, 4H,

Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ: 29.8 (C-8), 40.4 (C-9), 44.5 (C-7), 129.8 (C-12 and C-16), 131.2 (C-14), 132.7 (C-13 and C-15), 134.8 (C-4), 138.6 (C-5), 140.3 (C-11), 150.7 (C-10), 160.4 (C-2'), 171.3 (C-2); FAB-Mass *(m/z)*: 378 [M^+]; anal. calc. for $C_{14}H_{14}N_6O_5S$: C 44.44, H 3.72, N 22.21; found: C 44.40, H 3.69, N 22.19%.

N-[3-(2-amino-5-nitrothiazolyl)-propyl]-N'-[(3-nitrophenyl)-methylidene]-urea ***(3i)***. Yield: 62%; m.p. 165-166 ºC; IR (cm^{-1}): 859 (C-S), 972 (C-NO), 1338 (N-CH_2), 1371, 1545 (NO_2), 1557 (C=C), 1665 (C=O), 1431, 2894, 2927 (CH_2), 3030 (CH-Ar), 3394 (NH); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ: 2.11-2.15 (m, 2H, H-8), 3.29-3.33 (m, 2H, H-9), 3.85-3.89 (m, 2H, H-7), 5.66 (s, 1H, H-1'), 7.33 (s, 1H, H-4), 7.92 (s, 1H, H-6), 8.15 (s, 1H, H-10), 6.78-7.86 (m, 4H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ: 30.7 (C-8), 38.3 (C-9), 45.8 (C-7), 131.4 (C-4), 130.1 (C-12), 130.9 (C-16), 132.6 (C-14), 133.4 (C-13), 134.1 (C-15), 136.9 (C-5), 137.5 (C-11), 149.2 (C-10), 163.6 (C-2'), 172.7 (C-2); FAB-Mass *(m/z)*: 378 [M^+]; anal. calc. for $C_{14}H_{14}N_6O_5S$: C 44.44, H 3.72, N 22.21; found: C 44.38, H 3.66, N 22.17%.

N-[3-(2-amino-5-nitrothiazolyl)-propyl]-N'-[(2-nitrophenyl)-methylidene]-urea ***(3j)***. Yield: 62%; m.p. 162-163 ºC; IR (cm^{-1}): 864 (C-S), 976 (C-NO), 1341 (N-CH_2), 1369, 1541 (NO_2), 1553 (C=C), 1669 (C=O), 1438, 2890, 2924 (CH_2), 3028 (CH-Ar), 3397 (NH); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ: 2.15-2.19 (m, 2H, H-8), 3.20-3.26 (m, 2H, H-9), 3.87-3.93 (m, 2H, H-7), 5.68 (s, 1H, H-1'), 7.36 (s, 1H, H-4), 7.96 (s, 1H, H-6), 8.10 (s, 1H, H-10), 6.80-7.90 (m, 4H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ: 30.7 (C-8), 39.7 (C-9), 44.5 (C-7), 131.8 (C-4), 130.5 (C-12), 131.6 (C-16), 132.4 (C-14), 133.6 (C-13), 134.5 (C-15), 137.3 (C-5), 139.7 (C-11), 149.9 (C-10), 163.2 (C-2'), 172.1 (C-2); FAB-Mass *(m/z)*: 378 [M^+]; anal. calc. for $C_{14}H_{14}N_6O_5S$: C 44.44, H 3.72, N 22.21; found: C 44.35, H 3.70, N 22.18%.

Synthesis of N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(phenyl)-4-oxo-1,3-thiazolidine-carboxamide, compound ***4a***

The compound **3a** (0.015 mol) and thioglycolic acid (0.015 mol) in methanol (50 mL) in the presence of $ZnCl_2$ (0.015 mol) were allowed to react at room temperature. The reaction mixture was first stirred on a magnetic stirrer for about 2 h followed by reflux on a steam bath for about 4 h. The product was filtered and cooled at room temperature. The completion of the reaction was monitored by silica gel-G coated TLC plates. The filtered product was purified over a silica gel packed column chromatography using CH_3OH:$CHCl_3$ (7:3 v/v) as eluent (80 mL). The purified product was dried under vacuo and recrystallized from ethanol at room temperature to furnish compound **4a** (Figure 4).

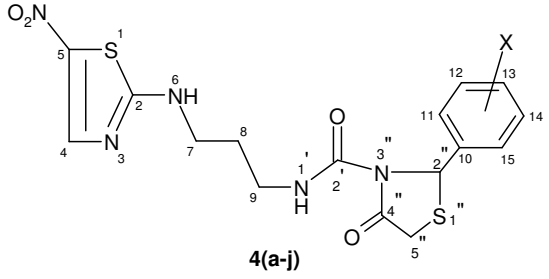


Figure 4. Structure of compounds **4(a-j)**.

Compounds **4 (b-j)** have also been synthesized by using similar method as above.

*N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(phenyl)-4-oxo-1,3-thiazolidine-carboxamide (**4a**)*. Yield: 64%; m.p. 159-160 ºC; IR (cm^{-1}): 698 (C-S-C), 1012 (C-NO), 1338 (N-CH_2), 1378, 1545 (NO_2), 1565 (C=C), 1657 (C=O), 1739 (CO cyclic), 1426, 2833, 2914 (CH_2), 2950 (S-CH_2), 3052 (CH-Ar), 3372 (NH); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ: 2.13-2.15 (m, 2H, H-8), 3.20 (s, 2H, H-5"), 3.34-3.37 (m, 2H, H-9), 3.95-3.99 (m, 2H, H-7), 5.18 (s, 1H, H-2"), 5.70 (s, 1H, H-1'), 7.85 (s, 1H, H-4), 7.97 (s, 1H, H-6), 6.66-7.72 (m, 5H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ: 30.2 (C-8), 34.3 (C-5"), 38.0 (C-9), 45.6 (C-7), 61.2 (C-2"), 128.4 (C-11 and C-16), 129.7 (C-15), 130.5 (C-12 and C-14), 133.5 (C-4), 137.3 (C-5), 139.2 (C-10), 162.4 (C-2'), 169.6 (C-2), 170.3 (C-4"); FAB-Mass *(m/z)*: 407 [M^+]; anal. calc. for $C_{16}H_{17}N_5O_4S_2$: C 47.16, H 4.20, N 17.18; found: C 47.12, H 4.18, N 17.16%.

*N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(4-chlorophenyl)-4-oxo-1,3-thiazolidine-carboxamide (**4b**)*. Yield: 61%; m.p. 185-187 ºC; IR (cm^{-1}): 682 (C-S-C), 734 (C-Cl), 867 (C-S), 972 (C-NO), 1339 (N-CH_2), 1369, 1540 (NO_2), 1556 (C=C), 1671 (C=O), 1755 (CO cyclic), 1440, 2894, 2924 (CH_2), 2963 (S-CH_2), 3025 (CH-Ar), 3393 (NH); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ: 2.13-2.18 (m, 2H, H-8), 3.26 (s, 2H, H-5"), 3.32-3.37 (m, 2H, H-9), 3.94-3.98 (m, 2H, H-7), 5.22 (s, 1H, H-2"), 5.73 (s, 1H, H-1'), 7.90 (s, 1H, H-4), 7.99 (s, 1H, H-6), 6.82-7.85 (m, 4H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ: 31.8 (C-8), 34.8 (C-5"), 40.5 (C-9), 45.9 (C-7), 61.5 (C-2"), 129.1 (C-11 and C-16), 130.5 (C-15), 130.9 (C-12 and C-14), 134.4 (C-4), 138.6 (C-10), 139.8 (C-5), 162.8 (C-2'), 170.5 (C-2), 170.7 (C-4"); FAB-Mass *(m/z)*: 442 [M^+]; anal. calc. for $C_{16}H_{16}N_5O_4S_2Cl$: C 43.48, H 3.64, N 15.84%; found: C 43.44, H 3.56, N 15.78%.

*N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(3-chlorophenyl)-4-oxo-1,3-thiazolidine-carboxamide (**4c**)*. Yield: 65; m.p. 180-181 ºC; IR (cm^{-1}): 679 (C-S-C), 745 (C-Cl), 868 (C-S), 975 (C-NO), 1339 (N-CH_2), 1373, 1543 (NO_2), 1557 (C=C), 1674 (C=O), 1752 (CO cyclic), 1442, 2892, 2925 (CH_2), 2966 (S-CH_2), 3030 (CH-Ar), 3394 (NH); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ: 2.13-2.19 (m, 2H, H-8), 3.26 (s, 2H, H-5"), 3.38-3.42 (m, 2H, H-9), 4.01-4.06 (m, 2H, H-7), 5.24 (s, 1H, H-2"), 5.76 (s, 1H, H-1'), 7.86 (s, 1H, H-4), 8.05 (s, 1H, H-6), 6.64-7.76 (m, 4H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ: 31.2 (C-8), 35.3 (C-5"), 39.2 (C-9), 46.3 (C-7), 65.6 (C-2"), 128.7 (C-11), 129.3 (C-16), 130.9 (C-15), 131.5 (C-12), 132.9 (C-14), 136.7 (C-4), 138.6 (C-5), 140.5 (C-10), 162.4 (C-2'), 172.1 (C-2), 171.3 (C-4"); FAB-Mass *(m/z)*: 442 [M^+]; anal. calc. for $C_{16}H_{16}N_5O_4S_2Cl$: C 43.48, H 3.64, N 15.84; found: C 43.45, H 3.58, N 15.77%.

*N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(2-chlorophenyl)-4-oxo-1,3-thiazolidine-carboxamide (**4d**)*. Yield: 64; m.p. 182-183 ºC; IR (cm^{-1}): 681 (C-S-C), 750 (C-Cl), 871 (C-S), 976 (C-NO), 1341 (N-CH_2), 1374, 1546 (NO_2), 1554 (C=C), 1677 (C=O), 1746 (CO cyclic), 1443, 2890, 2931 (CH_2), 2968 (S-CH_2), 3026 (CH-Ar), 3395 (NH); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ: 2.16-2.20 (m, 2H, H-8), 3.27 (s, 2H, H-5"), 3.37-3.43 (m, 2H, H-9), 4.03-4.08 (m, 2H, H-7), 5.32 (s, 1H, H-2"), 5.79 (s, 1H, H-1'), 7.91 (s, 1H, H-4), 8.07 (s, 1H, H-6), 6.66-7.72 (m, 4H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ: 30.5 (C-8), 37.2 (C-5"), 40.1 (C-9), 46.0 (C-7), 64.4 (C-2"), 137.2 (C-4), 130.3 (C-11), 130.8 (C-16), 131.5 (C-15), 131.7 (C-12), 132.6 (C-14), 140.2 (C-10), 141.1 (C-5), 164.6 (C-2'), 171.5 (C-2), 173.7 (C-4"); FAB-Mass *(m/z)*: 442 [M^+]; anal. calc. for $C_{16}H_{16}N_5O_4S_2Cl$: C 43.48, H 3.64, N 15.84; found: C 43.43, H 3.57, N 15.74%.

*N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(4-bromophenyl)-4-oxo-1,3-thiazolidine-carboxamide (**4e**)*. Yield: 67%; m.p. 176-177 ºC; IR (cm^{-1}): 652 (C-Br), 678 (C-S-C), 869 (C-S), 982 (C-NO), 1340 (N-CH_2), 1366, 1547 (NO_2), 1557 (C=C), 1680 (C=O), 1747 (CO cyclic), 1445, 2893, 2926 (CH_2), 2969 (S-CH_2), 3027 (CH-Ar), 3397 (NH) ^{1}H NMR (300 MHz, $CDCl_3$,

TMS) δ: 2.11-2.16 (m, 2H, H-8), 3.32 (s, 2H, H-5"), 3.42-3.48 (m, 2H, H-9), 4.05-4.09 (m, 2H, H-7), 5.35 (s, 1H, H-2"), 5.81 (s, 1H, H-1'), 7.97 (s, 1H, H-4), 8.13 (s, 1H, H-6), 6.72-7.84 (m, 4H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ: 32.7 (C-8), 37.6 (C-5"), 41.7 (C-9), 47.5 (C-7), 64.9 (C-2"), 130.7 (C-11 and C-16), 131.3 (C-15), 132.6 (C-12 and C-14), 137.5 (C-4), 141.4 (C-10), 141.6 (C-5), 165.4 (C-2'), 170.9 (C-2), 171.8 (C-4"); FAB-Mass *(m/z)*: 486 [M^+]; anal. calc. for $C_{16}H_{16}N_5O_4S_2Br$: C 39.51, H 3.31, N 14.39; found: C 39.47, H 3.29, N 14.36%.

*N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(3-bromophenyl)-4-oxo-1,3-thiazolidine-carboxamide (**4f**)*. Yield: 68%; m.p. 174-175 ºC; IR (cm^{-1}): 646 (C-Br), 678 (C-S-C), 870 (C-S), 977 (C-NO), 1342 (N-CH_2), 1367, 1542 (NO_2), 1555 (C=C), 1682 (C=O), 1750 (CO cyclic), 1443, 2897, 2927 (CH_2), 2964 (S-CH_2), 3028 (CH-Ar), 3392 (NH); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ: 2.15-2.20 (m, 2H, H-8), 3.38 (s, 2H, H-5"), 3.41-3.46 (m, 2H, H-9), 3.99-4.04 (m, 2H, H-7), 5.19 (s, 1H, H-2"), 5.83 (s, 1H, H-1'), 7.98 (s, 1H, H-4), 8.15 (s, 1H, H-6), 6.79-7.81 (m, 4H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ: 32.3 (C-8), 35.9 (C-5"), 38.4 (C-9), 47.4 (C-7), 62.9 (C-2"), 131.4 (C-11), 132.0 (C-16), 132.9 (C-15), 133.1 (C-12), 134.4 (C-14), 134.8 (C-4), 139.8 (C-10), 141.5 (C-5), 165.1 (C-2'), 172.6 (C-2), 171.5 (C-4"); FAB-Mass *(m/z)*: 486 [M^+]; anal. calc. for $C_{16}H_{16}N_5O_4S_2Br$: C 39.51, H 3.31, N 14.39; found: C 39.48, H 3.28, N 14.36%.

*N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(2-bromophenyl)-4-oxo-1,3-thiazolidine-carboxamide (**4g**)*. Yield: 62; m.p. 179-180 ºC IR (cm^{-1}): 645 (C-Br), 676 (C-S-C), 872 (C-S), 980 (C-NO), 1343 (N-CH_2), 1370, 1548 (NO_2), 1570 (C=C), 1672 (C=O), 1753 (CO cyclic), 1438, 2889, 2930 (CH_2), 2965 (S-CH_2), 3032 (CH-Ar), 3394 (NH); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ: 2.19-2.25 (m, 2H, H-8), 3.30 (s, 2H, H-5"), 3.44-3.49 (m, 2H, H-9), 4.10-4.16 (m, 2H, H-7), 5.20 (s, 1H, H-2"), 5.77 (s, 1H, H-1'), 7.87 (s, 1H, H-4), 8.00 (s, 1H, H-6), 6.70-7.62 (m, 4H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ: 33.9 (C-8), 36.8 (C-5"), 39.6 (C-9), 49.7 (C-7), 63.3 (C-2"), 131.4 (C-11), 131.9 (C-16), 132.5 (C-15), 133.2 (C-12), 133.6 (C-14), 136.1 (C-4), 137.4 (C-5), 163.6 (C-2'), 143.7 (C-10), 172.1 (C-2), 173.3 (C-4"); FAB-Mass *(m/z)*: 486 [M^+]; anal. calc. for $C_{16}H_{16}N_5O_4S_2Br$: C 39.51, H 3.31, N 14.39; found: C 39.45, H 3.27, N 14.36%.

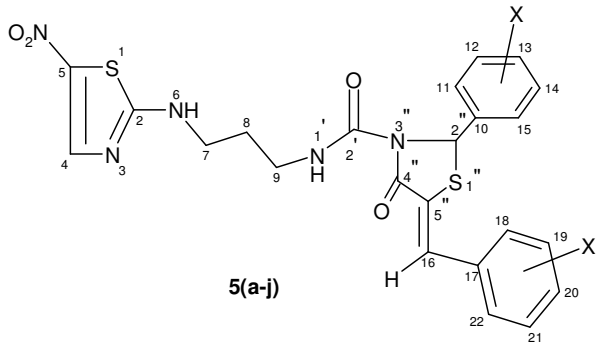
*N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(4-nitrophenyl)-4-oxo-1,3-thiazolidine-carboxamide (**4h**)*. Yield: 65%; m.p. 181-182 ºC; IR (cm^{-1}): 677 (C-S-C), 875 (C-S), 981 (C-NO), 1340 (N-CH_2), 1368, 1534 (NO_2), 1572 (C=C), 1675 (C=O), 1754 (CO cyclic), 1439, 2891, 2932 (CH_2), 2971 (S-CH_2), 3033 (CH-Ar), 3390 (NH); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ: 2.22-2.27 (m, 2H, H-8), 3.32 (s, 2H, H-5"), 3.44-3.48 (m, 2H, H-9), 3.97-4.03 (m, 2H, H-7), 5.24 (s, 1H, H-2"), 5.78 (s, 1H, H-1'), 7.93 (s, 1H, H-4), 8.03 (s, 1H, H-6), 6.65-7.70 (m, 4H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ: 33.4 (C-8), 36.2 (C-5"), 41.5 (C-9), 48.8 (C-7), 63.7 (C-2"), 132.1 (C-11 and C-16), 133.0 (C-15), 133.7 (C-12 and C-14), 135.7 (C-4), 139.2 (C-5), 141.7 (C-10), 164.1 (C-2'), 171.8 (C-2), 172.4 (C-4"); (Ar); FAB-Mass *(m/z)*: 452 [M^+]; anal. calc. for $C_{16}H_{16}N_6O_6S_2$: C 42.47, H 3.56, N 18.57; found: C 42.45, H 3.53, N 18.54%.

*N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(3-nitrophenyl)-4-oxo-1,3-thiazolidine-carboxamide (**4i**)*. Yield: 66%; m.p. 177-178 ºC; IR (cm^{-1}): 676 (C-S-C), 874 (C-S), 978 (C-NO), 1345 (N-CH_2), 1371, 1545 (NO_2), 1568 (C=C), 1676 (C=O), 1749 (CO cyclic), 1440, 2896, 2929 (CH_2), 2967 (S-CH_2), 3034 (CH-Ar), 3396 (NH); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ: 2.11-2.15 (m, 2H, H-8), 3.28 (s, 2H, H-5"), 3.32-3.39 (m, 2H, H-9), 4.09-4.13 (m, 2H, H-7), 5.31 (s, 1H, H-2"), 5.80 (s, 1H, H-1'), 7.95 (s, 1H, H-4), 8.06 (s, 1H, H-6), 6.80-7.86 (m, 4H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ: 34.6 (C-8), 38.1 (C-5"), 42.7 (C-9), 46.5 (C-7), 62.2 (C-2"), 132.8 (C-11), 133.5 (C-16), 134.2 (C-15), 134.8 (C-12), 135.2 (C-4), 135.7 (C-14), 140.7 (C-5), 142.2 (C-10), 165.7 (C-2'), 172.4 (C-2), 172.7 (C-4"); FAB-Mass *(m/z)*: 452 [M^+]; anal. calc. for $C_{16}H_{16}N_6O_6S_2$: C 42.47, H 3.56, N 18.57; found: C 42.41, H 3.52, N 18.54%.

*N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(2-nitrophenyl)-4-oxo-1,3-thiazolidine-carboxamide (**4j**).* Yield: 63%; m.p. 181-183 ºC; IR (cm^{-1}): 674 (C-S-C), 869 (C-S), 9784 (C-NO), 1344 (N-CH_2), 1372, 1541 (NO_2), 1569 (C=C), 1679 (C=O), 1750 (CO cyclic), 1441, 2899, 2932 (CH_2), 2970 (S-CH_2), 3035 (CH-Ar), 3398 (NH); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ: 2.13-2.19 (m, 2H, H-8), 3.35 (s, 2H, H-5"), 3.40-3.44 (m, 2H, H-9), 4.15-4.19 (m, 2H, H-7), 5.37 (s, 1H, H-2"), 5.84 (s, 1H, H-1'), 7.97 (s, 1H, H-4), 8.11 (s, 1H, H-6), 6.75-7.89 (m, 4H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ: 34.1 (C-8), 38.6 (C-5"), 42.2 (C-9), 47.6 (C-7), 65.1 (C-2"), 130.5 (C-11), 131.2 (C-16), 132.1 (C-15), 133.7 (C-4), 134.2 (C-12), 134.9 (C-14), 138.4 (C-5), 143.3 (C-10), 163.3 (C-2'), 173.6 (C-2), 172.9 (C-4"); FAB-Mass *(m/z)*: 452 [M^+]; anal. calc. for $C_{16}H_{16}N_6O_6S_2$: C 42.47, H 3.56, N 18.57; found: C 42.41, H 3.49, N 18.52%.

*Synthesis of N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(phenyl)-4-oxo-5-(benzylidene)-1,3-thiazolidine-carboxamide, compound **5a***

The compound **4a** (0.009 mol) and benzaldehyde (0.009 mol) in ethanol (50 mL) in the presence of CH_3CH_2ONa (0.009 mol) were allowed to react at room temperature. The reaction mixture was first stirred on a magnetic stirrer for about 2 h followed by reflux on a steam bath for about 5.5 h. The completion of the reaction was monitored by silica gel-G coated TLC plates. The product was filtered and cooled at room temperature. The filtered product was purified over a silica gel packed column chromatography using CH_3OH:$CHCl_3$ (7:3 v/v) as eluent (80 mL). The purified product was dried under vacuo and recrystallized from acetone at room temperature to furnish compound **5a** (Figure 5).



5(a-j)

Figure 5. Structure of compounds **5(a-j)**.

Compounds **5 (b-j)** have also been synthesized by using similar method as above.

*N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(substitutedphenyl)-4-oxo-5-(benzylidene)-1,3-thiazolidine-carboxamide (**5a**).* Yield: 60%; m.p. 155-156 ºC; IR (cm^{-1}): 872 (C-S), 977 (C-NO), 1345 (N-CH_2), 1371, 1542 (NO_2), 1567 (C=C), 1675 (C=O), 1750 (CO cyclic), 1441, 2840, 2926 (CH_2), 2966 (C=CH), 3027 (CH-Ar), 3393 (NH); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ: 2.06-2.09 (m, 2H, H-8), 3.35-3.39 (m, 2H, H-9), 3.97-4.02 (m, 2H, H-7), 5.22 (s, 1H, H-2"), 5.76 (s, 1H, H-1'), 6.45 (s, 1H, H-16), 7.80 (s, 1H, H-4), 8.05 (s, 1H, H-6), 6.65-7.78 (m, 10H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ: 31.2 (C-8), 39.5 (C-9), 46.2 (C-7), 62.4 (C-2"), 128.4 (C-18 and C-22), 129.1 (C-11 and C-15), 129.6 (C-13), 130.1 (C-20), 130.1 (C-19 and C-21), 132.7 (C-12 and C-14), 134.6 (C-4), 136.2 (C-16), 138.2 (C-17), 139.6 (C-5),140.6

(C-10), 141.5 (C-5"), 163.5 (C-2'), 169.7 (C-2), 172.7 (C-4"); FAB-Mass *(m/z)*: 495 [M^+]. anal. calc. for $C_{23}H_{21}N_5O_4S_2$: C 55.74, H 4.27, N 14.13; found: C 55.71, H 4.25, N 14.09%.

*N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(4-chlorophenyl)-4-oxo-5-(4-chlorobenzyl-idene)-1,3-thiazolidine-carboxamide (**5b**).* Yield: 64%; m.p. 180-181 ºC; IR (cm^{-1}): 752 (C-Cl), 876 (C-S), 979 (C-NO), 1350 (N-CH_2), 1375, 1543 (NO_2), 1570 (C=C), 1677 (C=O), 1752 (CO cyclic), 1443, 2854, 2930 (CH_2), 2969 (C=CH), 3028 (CH-Ar), 3397 (NH); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ: 2.11-2.14 (m, 2H, H-8), 3.41-3.47 (m, 2H, H-9), 3.98-4.03 (m, 2H, H-7), 5.25 (s, 1H, H-2"), 5.81 (s, 1H, H-1'), 6.51 (s, 1H, H-16), 7.83 (s, 1H, H-4), 8.06 (s, 1H, H-6), 6.67-7.80 (m, 8H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ: 31.8 (C-8), 40.2 (C-9), 49.5 (C-7), 62.9 (C-2"), 130.1 (C-18 and C-22), 131.3 (C-11 and C-15), 131.5 (C-19 and C-21), 132.1 (C-13), 133.9 (C-20), 134.1 (C-12 and C-14), 137.6 (C-4), 139.7 (C-16), 138.1 (C-5), 138.8 (C-17), 142.3 (C-10), 142.5 (C-5"), 167.4 (C-2'), 172.7 (C-2), 172.6 (C-4"); (Ar); FAB-Mass *(m/z)*: 564 [M^+]; anal. calc. for $C_{23}H_{19}N_5O_4S_2Cl_2$: C 48.94, H 3.39, N 12.40; found: C 48.91, H 3.32, N 12.38%.

*N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(3-chlorophenyl)-4-oxo-5-(3-chlorobenzyl-idene)-1,3-thiazolidine-carboxamide (**5c**).* Yield: 63%; m.p. 177-178 ºC; IR (cm^{-1}): 755 (C-Cl), 875 (C-S), 981 (C-NO), 1348 (N-CH_2), 1375, 1546 (NO_2), 1572 (C=C), 1678 (C=O), 1755 (CO cyclic), 1445, 2841, 2932 (CH_2), 2976 (C=CH), 3030 (CH-Ar), 3398 (NH); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ: 2.19-2.24 (m, 2H, H-8), 3.32-3.36 (m, 2H, H-9), 4.02-4.07 (m, 2H, H-7), 5.27 (s, 1H, H-2"), 5.87 (s, 1H, H-1'), 6.53 (s, 1H, H-16), 7.87 (s, 1H, H-4), 8.09 (s, 1H, H-6), 6.71-7.82 (m, 8H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ: 32.6 (C-8), 39.4 (C-9), 49.0 (C-7), 63.6 (C-2"), 135.7 (C-4), 139.6 (C-5), 167.5 (C-2'), 173.1 (C-2), 131.2 (C-11), 131.6 (C-15), 130.5 (C-18), 131.3 (C-22), 132.0 (C-19), 132.5 (C-21), 132.8 (C-13), 133.3 (C-20), 134.2 (C-12), 134.9 (C-14), 137.5 (C-16), 138.7 (C-17), 142.9 (C-10), 143.1 (C-5"), 173.8 (C-4"); FAB-Mass *(m/z)*: 564 [M^+]; anal. calc. for $C_{23}H_{19}N_5O_4S_2Cl_2$: C 48.94, H 3.39, N 12.40; found: C 48.89, H 3.32, N 12.35%.

*N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(2-chlorophenyl)-4-oxo-5-(2-chlorobenzyl-idene)-1,3-thiazolidine-carboxamide (**5d**).* Yield: 61%; m.p. 178-180 ºC; IR (cm^{-1}): 747 (C-Cl), 883 (C-S), 978 (C-NO), 1360 (N-CH_2), 1384, 1550 (NO_2), 1576 (C=C), 1681 (C=O), 1757 (CO cyclic), 1446, 2845, 2935 (CH_2), 2972 (C=CH), 3029 (CH-Ar), 3395 (NH); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ: 2.15-2.19 (m, 2H, H-8), 3.43-3.48 (m, 2H, H-9), 4.02-4.07 (m, 2H, H-7), 5.28 (s, 1H, H-2"), 5.96 (s, 1H, H-1'), 6.57 (s, 1H, H-16), 7.92 (s, 1H, H-4), 8.21 (s, 1H, H-6), 6.75-7.64 (m, 8H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ: 35.4 (C-8), 43.7 (C-9), 48.5 (C-7), 63.6 (C-2"), 128.5 (C-18), 128.9 (C-22), 129.8 (C-11), 130.3 (C-15), 130.9 (C-13), 131.1 (C-20), 132.7 (C-12), 132.2 (C-19 and C-21), 133.6 (C-14), 135.5 (C-4), 137.6 (C-16), 139.1 (C-5), 140.5 (C-17), 141.4 (C-10), 143.2 (C-5"), 166.7 (C-2'), 169.3 (C-2), 173.8 (C-4"); (Ar); FAB-Mass *(m/z)*: 564 [M^+]; anal. calc. for $C_{23}H_{19}N_5O_4S_2Cl_2$: C 48.94, H 3.39, N 12.40; found: C 48.88, H 3.36, N 12.36%.

*N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(4-bromophenyl)-4-oxo-5-(4-bromobenzyl-idene)-1,3-thiazolidine-carboxamide (**5e**).* Yield: 66%; m.p. 169-171 ºC; IR (cm^{-1}): 656 (C-Br), 877 (C-S), 983 (C-NO), 1346 (N-CH_2), 1373, 1557 (NO_2), 1581 (C=C), 1684 (C=O), 1761 (CO cyclic), 1455, 2837, 2937 (CH_2), 2973 (C=CH), 3040 (CH-Ar), 3399 (NH); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ: 2.12-2.17 (m, 2H, H-8), 3.48-3.54 (m, 2H, H-9), 4.02-4.09 (m, 2H, H-7), 5.40 (s, 1H, H-2"), 5.99 (s, 1H, H-1'), 6.60 (s, 1H, H-16), 7.85 (s, 1H, H-4), 8.12 (s, 1H, H-6), 6.77-7.75 (m, 8H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ: 35.3 (C-8), 43.3 (C-9), 47.4 (C-7), 64.2 (C-2"), 130.3 (C-18 and C-22), 131.1 (C-11 and C-15), 132.8 (C-13), 133.4 (C-20),

133.5 (C-12 and C-14), 134.8 (C-19 and C-21), 138.1 (C-4), 138.7 (C-16), 140.7 (C-5), 141.1 (C-10), 141.6 (C-17), 142.9 (C-5"), 163.6 (C-2'), 170.2 (C-2), 174.4 (C-4"); (Ar); FAB-Mass *(m/z)*: 653 [M^+]; anal. calc. for $C_{23}H_{19}N_5O_4S_2Br_2$: C 42.28, H 2.93, N 10.71; found: C 42.25, H 2.87, N 10.69%.

*N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(3-bromophenyl)-4-oxo-5-(3-bromobenzylidene)-1,3-thiazolidine-carboxamide (**5f**).* Yield: 60%; m.p. 166-167 ºC; IR (cm^{-1}): 649 (C-Br), 885 (C-S), 987 (C-NO), 1348 (N-CH_2), 1374, 1556 (NO_2), 1578 (C=C), 1685 (C=O), 1763 (CO cyclic), 1442, 2830, 2918 (CH_2), 2975 (C=CH), 3031 (CH-Ar), 3400 (NH); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ: 2.08-2.13 (m, 2H, H-8), 3.35-3.39 (m, 2H, H-9), 4.08-4.12 (m, 2H, H-7), 5.31 (s, 1H, H-2"), 5.85 (s, 1H, H-1'), 6.64 (s, 1H, H-16), 7.84 (s, 1H, H-4), 8.15 (s, 1H, H-6), 6.68-7.72 (m, 8H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ: 34.5 (C-8), 42.2 (C-9), 48.4 (C-7), 64.3 (C-2"), 128.8 (C-18), 129.1 (C-11), 129.8 (C-15), 130.4 (C-22), 130.7 (C-13), 131.1 (C-20), 132.5 (C-12), 132.9 (C-14), 134.1 (C-19), 134.9 (C-21), 135.2 (C-16), 138.3 (C-4), 140.1 (C-5), 138.6 (C-10), 140.8 (C-17), 143.3 (C-5"), 165.3 (C-2'), 173.2 (C-2), 174.7 (C-4"); (Ar); IR: FAB-Mass *(m/z)*: 653 [M^+]; anal. calc. for $C_{23}H_{19}N_5O_4S_2Br_2$: C 42.28, H 2.93, N 10.71; found: C 42.22, H 2.87, N 10.66%.

*N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(2-bromophenyl)-4-oxo-5-(2-bromobenzyl-idene)-1,3-thiazolidine-carboxamide (**5g**).* Yield: 62%; m.p. 165-167 ºC; IR (cm^{-1}): 652 (C-Br), 881 (C-S), 980 (C-NO), 1357 (N-CH_2), 1381, 1548 (NO_2), 1582 (C=C), 1680 (C=O), 1770 (CO cyclic), 1453, 2843, 2940 (CH_2), 2974 (C=CH), 3034 (CH-Ar), 3401 (NH); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ: 2.14-2.19 (m, 2H, H-8), 3.41-3.46 (m, 2H, H-9), 4.11-4.18 (m, 2H, H-7), 5.34 (s, 1H, H-2"), 5.80 (s, 1H, H-1'), 6.68 (s, 1H, H-16), 7.77 (s, 1H, H-4), 8.17 (s, 1H, H-6), 6.72-7.76 (m, 8H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ: 32.2 (C-8), 41.9 (C-9), 47.8 (C-7), 65.0 (C-2"), 128.7 (C-15), 129.7 (C-18), 130.5 (C-22), 130.6 (C-11), 131.4 (C-13), 132.5 (C-20), 132.7 (C-14), 133.9 (C-12), 134.0 (C-19), 134.5 (C-21), 135.0 (C-16), 136.9 (C-4), 138.2 (C-10), 140.0 (C-17), 140.2 (C-5"), 141.8 (C-5), 164.0 (C-2'), 170.7 (C-2), 175.8 (C-4"); (Ar); FAB-Mass *(m/z)*: 653 [M^+]; anal. calc. for $C_{23}H_{19}N_5O_4S_2Br_2$: C 42.28, H 2.93, N 10.71; found: C 42.21, H 2.87, N 10.65%.

*N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(4-nitrophenyl)-4-oxo-5-(4-nitrobenzylidene)-1,3-thiazolidine-carboxamide (**5h**).* Yield: 65%; m.p. 170-172 ºC; IR (cm^{-1}): 874 (C-S), 987 (C-NO), 1353 (N-CH_2), 1376, 1544 (NO_2), 1587 (C=C), 1679 (C=O), 1765 (CO cyclic), 1447, 2848, 2929 (CH_2), 2977 (C=CH), 3038 (CH-Ar), 3396 (NH); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ: 2.21-2.26 (m, 2H, H-8), 3.42-3.47 (m, 2H, H-9), 4.13-4.18 (m, 2H, H-7), 5.36 (s, 1H, H-2"), 5.79 (s, 1H, H-1'), 6.71 (s, 1H, H-16), 7.95 (s, 1H, H-4), 8.08 (s, 1H, H-6), 6.72-7.74 (m, 8H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ: 33.5 (C-8), 40.5 (C-9), 49.6 (C-7), 65.4 (C-2"), 128.1 (C-18 and C-22), 129.2 (C-11 and C-15), 130.3 (C-13), 131.0 (C-20), 132.6 (C-12 and C-14), 135.9 (C-19 and C-21), 136.1 (C-4), 138.2 (C-17), 140.1 (C-10), 141.7 (C-16), 141.9 (C-5), 143.8 (C-5"), 166.5 (C-2'), 172.4 (C-2), 175.6 (C-4"); FAB-Mass *(m/z)*: 586 [M^+]; anal. calc. for $C_{23}H_{19}N_7O_8S_2$: C 47.17, H 3.27, N 16.74; found: C 47.14, H 3.25, N 16.71%.

*N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(3-nitrophenyl)-4-oxo-5-(3-nitrobenzylidene)-1,3-thiazolidine-carboxamide (**5i**).* Yield: 64%; m.p 169-170 ºC; IR (cm^{-1}): 877 (C-S), 982 (C-NO), 1358 (N-CH_2), 1377, 1553 (NO_2), 1584 (C=C), 1682 (C=O), 1766 (CO cyclic), 1448, 2852, 2931 (CH_2), 2970 (C=CH), 3037 (CH-Ar), 3403 (NH); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ: 2.21-2.26 (m, 2H, H-8), 3.46-3.50 (m, 2H, H-9), 4.17-4.23 (m, 2H, H-7), 5.37 (s, 1H, H-2"), 5.97 (s, 1H, H-1'), 6.73 (s, 1H, H-16), 7.89 (s, 1H, H-4), 8.11 (s, 1H, H-6), 6.74-7.63 (m, 8H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ: 33.7 (C-8), 41.1 (C-9), 48.3 (C-7), 62.8 (C-2"),

128.3 (C-15), 129.2 (C-18), 130.4 (C-11), 130.9 (C-22), 131.3 (C-13), 131.7 (C-19), 132.2 (C-20), 132.6 (C-14), 133.5 (C-12), 133.8 (C-21), 137.3 (C-4), 138.6 (C-10), 139.3 (C-17), 139.7 (C-16), 140.2 (C-5), 142.6 (C-5"), 165.4 (C-2'), 171.7 (C-2), 176.8 (C-4"); FAB-Mass *(m/z)*: 586 [M^+]; anal. calc. for $C_{23}H_{19}N_7O_8S_2$: C 47.17, H 3.27, N 16.74; found: C 47.14, H 3.23, N 16.67%.

*N-[3-(2-amino-5-nitrothiazolyl)-propyl]-2-(2-nitrophenyl)-4-oxo-5-(2-nitrobenzylidene)-1,3-thiazolidine-carboxamide (**5j**)*. Yield: 63%; m.p. 166-168 ºC; IR (cm^{-1}): 880 (C-S), 996 (C-NO), 1356 (N-CH_2), 1380, 1552 (NO_2), 1585 (C=C), 1683 (C=O), 1769 (CO cyclic), 1449, 2853, 2934 (CH_2), 2967 (C=CH), 3036 (CH-Ar), 3394 (NH); ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ: 2.19-2.25 (m, 2H, H-8), 3.42-3.47 (m, 2H, H-9), 4.12-4.16 (m, 2H, H-7), 5.28 (s, 1H, H-2"), 5.80 (s, 1H, H-1'), 6.76 (s, 1H, H-16), 7.81 (s, 1H, H-4), 8.19 (s, 1H, H-6), 6.69-7.71 (m, 8H, Ar-H); ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ: 34.9 (C-8), 42.6 (C-9), 46.2 (C-7), 62.1 (C-2"), 127.5 (C-22), 128.7 (C-18), 129.9 (C-15), 130.8 (C-11), 131.1 (C-13), 132.7 (C-20), 133.0 (C-12), 133.8 (C-14), 134.8 (C-4), 135.1 (C-19), 135.6 (C-21), 137.9 (C-16), 138.7 (C-5), 139.1 (C-10), 139.6 (C-17), 143.1 (C-5"),164.3 (C-2'), 171.6 (C-2), 176.5 (C-4"); FAB-Mass *(m/z)*: 586 [M^+]; anal. calc. for $C_{23}H_{19}N_7O_8S_2$: C 47.17, H 3.27, N 16.74; found: C 47.16, H 3.23, N 16.71%.

Invitro study (antibacterial, antifungal and antitubrcular activities)

The antibacterial, antifungal and antitubercular activity of compound **5(a-j)** has been assayed in vitro against selected bacteria, *B. subtilis, E. coli, S. aureus* fungi *A. niger, A. flavus, C. albicans* and *M. tuberculosis* H37Rv strain, respectively. MIC values of compounds **5(a-j)** were determined using filter paper disc diffusion method (antibacterial and antifungal activities) and L. J. medium (conventional) method (antitubercular activity). Streptomycin and griseofulvin used as standard for antibacterial and antifungal activities respectively and for antitubercular activity, isoniazid and rifampicin were taken as standards. All standards were also screened under the similar condition for comparison. Results of given activities of above compounds are given in Table 1.

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