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# SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF 4-OXO-THIAZOLIDINES AND 5-ARYLIDENE DERIVATIVES OF 2-AMINO-5-ETHYL-1,3,4-THIADIAZOLE

SUNIL MAKWANE*, S.D. SRIVASTAVA[2], RAJIV DUA[3], AND S.K. SRIVASTAVA[4]

*Synthetic Organic Chemistry Laboratory, Department of Chemistry, School of Chemical sciences and Technology, Dr. Harisingh Gour University, Sagar (M.P) India*

ABSTRACT

A new series of 5-benzylidene-3-(5-ethyl-[1,3,4]thiadiazol-2-yl)-2-phenyl-thiazolidin-4-ones (**3a-3m**) were synthesized. The reaction of thioglycolic acid with benzylidene-(5-ethyl-[1,3,4] thiadiazol-2-yl)-amine **1a** in the presence of anhydrous $ZnCl_2$ afforded the new heterocyclic compounds 5-benzylidene-3-(5-ethyl-[1,3,4] thiadiazole-yl)-2-phenyl-thiazolidin-4-one, **2a.** The latter product on treatment with several selected substituted aromatic aldehydes in the presence of sodium ethoxide underwent the Knoevenagel reaction to yield 5-benzylidene-3-(5-ethyl-[1,3,4] thiadiazol-2-yl)-2-phenyl-thiazolidin-4-ones, **3a-3m.** The structures of the compounds were confirmed by IR, $^{1}$H-NMR, $^{13}$C-NMR and mass spectroscopy and by chemical analysis. All the above compounds were screened for their antimicrobial activity against some selected bacteria and fungi such as *E. coli, B. Subtilis, and S. Typhi bacteria and A.niger, A. Flavus* and *F. oxisporium Fungi.*

**Key words:** Thiadiazole, Benzylidene, Thiazolidinone and Antimicrobial activity

## INTRODUCTION

Heterocycles form by far the largest of classical divisions of organic chemistry and are of immense importance biologically and industrially. The majority of pharmaceuticals and biologically active agrochemicals as well as countless additives and modifiers used in industrial applications ranging from cosmetics, reprography, information storage and plastics are heterocyclic in nature (Dua *et al.* 2011). The 1,3,4 - thiadiazole nucleus is one of the most important and well - known heterocyclic nuclei, which is a common and integral feature of a variety of natural products and medicinal agents (Li Y. and Geng J. *et al.* 2013). Thiadiazole nucleus is present as a core structural component in an array of drug categories such as antimicrobial (Jain A. K. and Sharma S. *et al.* 2013) anti - inflammatory, analgesic (Shkair A. M. *et al.* 2016), antinociceptive (Mehlika D. A. *et al.* 2016), antidepressant, anxiolytic and anticonvulsant agents (Pattanayak P. *et al.* 2009; Rajak H. *et al.* 2009), antiviral (Zhuo C. e*t al.* 2010), antineoplastic (Eghbalian A. E. *et al.* 2013) and antitubercular agents ( Fu X. S. e*t al.* 2016). The broad and potent activity of thiadiazole and their derivatives has established them as pharmacologically significant scaffolds. Thiazolidinones scaffolds are reviewed extensively in literature for its vibrant activities such as antibacterial (Kandapalli V. G. *et al.* 2010), antifungal (Sharma R. *et al.* 2012), antioxidant (Parmeshwaran M. *et al.* 2009), cytotoxic (Jubie S. *et al.* 2009), anti-inflammatory (Goel B. *et al.* 1999), anticonvulsant (Chaudhary M. *et al.* 1976), anti-HIV (Rawal R. *et al.* 2005), anti-tubercular (Aamer S. *et al.* 2007), antiviral activities (Murugesan S. *et al.* 2012) and DNA Binding

* Corresponding author: <sanumkwn@gmail.com>.
[2,4] Synthetic Organic Chemistry Laboratory, Department of Chemistry, School of Chemical sciences and Technology, Dr. Harisingh Gour University, Sagar (M.P) India.
[3] Department of Chemistry, State Forensic Science Laboratory, Department of Home (Police), Goverment of Madhya Pradesh, Sagar (M.P) India.

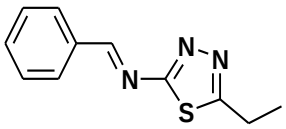
Agent (War J. *et al.* 2017). The incorporation of 4-oxothiazolidine and 5-arylidene moieties in 2-amino-5-ethyl-1,3,4-thiadiazole frame work has been found to enhance the activity. Keeping in view the biological importance of the above mentioned heterocyclic compounds and in continuation to our endeavour towards environmentally benign synthesis, we report herein the synthesis of several 3-(5-ethyl-[1,3,4]thiadiazole-2-yl)-2-phenyl-thiazolidin-4-one (**2a-2m**) and 3-(5-ethyl-[1,3,4] thiadiazole-2-yl)-2-phenyl-thiazolidin-4-one **(3a-3m)**. All the above synthesized compounds were characterized by using spectral techniques such as IR, $^{1}$H NMR, $^{13}$C-NMR and MS spectroscopy. Antibacterial and antifungal activities were performed on *E. coli, B. Subtilis,* and *S. Typhi bacteria and A.niger, A. Flavus* and *F. oxisporium Fungi.*

## MATERIALS AND METHODS

All the chemicals and reagents were of analytical grade of Sigma Aldrich, Merck, Chemi-loba and Himedia. The reagents and solvents were purified before using by standard methods. Melting points were taken in open capillaries and are uncorrected. Progress of reaction was monitored at various stages by silica gel-G coated TLC plates using MeOH: $CHCl_3$ system.The spot was visualized by exposing dry plate to iodine vapour and fluorescent indicator F 254 UV chamber. IR spectra are recorded in KBr disc on a Schimadzu 8201 PC, FTIR spectrophotometer (*v* max in $cm^{-1}$) and $^{1}$H NMR and $^{13}$C NMR spectra were measured on a Brucker DRX-300 spectrometer in $CDCl_3$ at 500 and 75 MHz respectively using TMS as an internal standard. All chemical shifts are reported on δ scale. The mass spectra were recorded on a Jeol SX–102 GC-MS mass spectrometer. Elemental analyses were performed on a Carlo Erba–1108 analyzer. All the synthesized compounds were purified by column chromatography using Merck silica Gel 60 (230-400 Mesh).

*Synthesis of Benzylidene- (5-ethyl- [1,3,4] thiadiazol-2-yl)-amine (**1a**)* **:** The compound **1a** was synthesized by standard method using equimolar mixture of 2-amino-5-ethyl-1,3,4-thiadiazole (0.008mole) and benzaldehyde (0.008 mole) in toluene (25mL) followed by continuous stirring on a magnetic stirrer for about 1 hr. Then the reaction mixture was refluxed on a heating mantle using dean stark apparatus for 2 hrs using glacial acetic acid as a catalyst. Molecular sieves were used to trap excess water molecule in the reaction mixture. After completion of the reaction, the flask was removed from dean stark apparatus and excess solvent was recovered by simple distillation method under reduced pressure at 115-120 $^{0}$C. A solid product was obtained which was purified over a silica gel column using chloroform: methanol (8:2 v/v) mixture as eluant. The elute was concentrated to give a product which was recrystallized from ethanol at room temperature to yield compound **1a**: white crystalline solid. m.p. 190-192$^{0}$C, yield 75%, IR: 1453($\nu_{C-C}$), 712 ($\nu_{C-S}$), 1670($\nu_{C=N}$), 1642($\nu_{N=C-}$), 1430($\nu_{C-N}$), 3118($\nu_{C-H}$),1310 ($\nu_{N-N}$). $^{1}$H NMR: δ (ppm) 1.20 (3H, $CH_3$ t, $J$ = 7.3 Hz), 3.06 (2H, $CH_2$, N=CH q, $J$ = 7.3 Hz), 7.40-8.06 (5H, Ar-H, m,), 9.39 (1H, s, CH acyclic; $^{13}$C NMR : δ (ppm) 12.35 ($CH_3$ acyclic), 28.93 ($CH_2$ acyclic), 127.7-134.61 (6C of aromatic ring), 158.91 (N=CH acyclic), 159.6 (CH acyclic), 156.7, 160.4,156.7 ($C_2$,$C_5$ of thiadiazole); Anal. Calcd for: $C_{11}H_{11}N_3S$ : C, 60.80, H, 5.10, N, 19.34 %;

found C, 60.76, H,5.77, N,19.14 %; Mass 217 ($M^+$).



**Compoud-1a**

The compounds **1b-1m** were synthesized by the similar method as reported for **1a.**

***2-Chloro-benzylidene-(5-ethyl-[1,3,4] thiadiazol-2-yl)-amine (1b)*:** m.p. 175-177 $^0$C, yield 66%, IR:1453 ($\nu_{C-C}$), 742 ($\nu_{C-S}$), 1647($\nu_{N=C}$), 1430($\nu_{C-N}$), 2989($\nu_{C-H}$),1310($\nu_{N-N}$). $^1$H NMR: δ (ppm)1.22 (3H, t, *J* = 7.3 Hz, $CH_3$), 3.03 (2H, q, *J* = 7.3 Hz $CH_2$), 7.35 - 8.05 (4H, m,) 9.41 (1H, s, N=CH); $^{13}$C NMR: δ (ppm) 13.05 ($CH_3$ acyclic), 27.93 ($CH_2$ acyclic), 128.8-136.7 (6C of aromatic ring), 159.50 (N=CH acyclic), 156.7, 160.4,156.7 ($C_2$,$C_5$ of thiadiazole); Anal. Calcd for : $C_{11}H_{10}N_3S$ : C, 52.48, H, 4.00, N, 16.69 %; found C, 52.28, H, 3.97, N, 16.54 %; Mass 251($M^+$).

***(3-Chloro-benzylidene)-(5-ethyl-[1,3,4] thiadiazol-2-yl)-amine (1c)*:** m.p.172-175 $^0$C, yield 62%, IR:1543($\nu_{C-C}$), 752 ($\nu_{C-S}$), 1655($\nu_{N=C}$), 1432($\nu_{C-N}$), 3018 ($\nu_{C-H}$), 1310 ($\nu_{N-N}$), 719 ($\nu_{C-Cl}$). $^1$H NMR: δ (ppm)1.20 (3H, t, *J* = 7.3 Hz $CH_3$), 3.04 (2H, q, *J* = 7.3 Hz $CH_2$), 7.46-7.99 (3H, m), 7.92 (1H, dt, J = 7.8 Hz), 9.43 (1H, s, N=CH acyclic). $^{13}$C NMR: δ (ppm) 12.55 ($CH_3$ acyclic), 26.93($CH_2$ acyclic), 127.8-130.7(C of aromatic ring), 158.91(N=CH acyclic),158.4,156.7 ($C_2$,$C_5$ of thiadiazole). Anal. Calcd for : $C_{11}H_{10}ClN_3S$: C, 52.48, H, 4.00, 14.08, N, 16.69; found C,52.18,H,3.92,N,16.50 %; Mass 251($M^+$).

***(4-Chloro-benzylidene)-(5-ethyl-[1,3,4] thiadiazol-2-yl)-amine (1d)*:** m.p.173-175 $^0$C, yield 67 %, IR: 1549($\nu_{C-C}$), 746 ($\nu_{C-S}$), 1661($\nu_{N=C}$), 1439($\nu_{C-N}$), 3108 ($\nu_{C-H}$),1316($\nu_{N-N}$), 717($\nu_{C-Cl}$). $^1$H NMR: δ(ppm) 1.26 (3H, t, *J* = 7.3 Hz $CH_3$), 3.03 (2H, q, *J* = 7.3 Hz $CH_2$), 7.66-8.00 (4H, m, Ar-H), 9.37 (1H, s, N=CH). $^{13}$C NMR:δ (ppm) 12.75 ($CH_3$ acyclic), 27.93 ($CH_2$ acyclic), 129.42-135.7(C of aromatic ring), 158.81 (N=CH acyclic), 158.4,156.7 ($C_2$,$C_5$ of thiadiazole), Anal. Calcd for : $C_{11}H_{10}ClN_3S$ : C, 52.48, H, 4.00, N, 16.69 %; found C, 52.24, H, 3.97, N, 16.51 %, Mass; 251($M^+$).

***(2-bromo-benzylidene)-(5-ethyl-[1,3,4] thiadiazol-2-yl)-amine (1e)*:** m.p. 180-181$^0$C, yield 71 %, IR:1546($\nu_{VC-C}$), 741 ($\nu_{C-S}$), 1669($\nu_{N=C}$), 1440($\nu_{C-N}$), 2950 ($\nu_{C-H}$),1320($\nu_{N-N}$), 549 ($\nu_{C-Br}$). $^1$H NMR: δ(ppm) 1.20 (3H, t, *J* = 6.6 Hz, $CH_3$), 3.04 (2H, q, *J* = 6.6 Hz, $CH_2$), 7.29-7.91 (4H, m,) Ar-H, 9.39 (1H, s, N=CH); $^{13}$C NMR: δ (ppm)12.65($CH_3$ acyclic), 28.83 ($CH_2$ acyclic), 158.51 (N=CH acyclic), 127.42-132.19(Cof aromatic ring),159.4,155.7($C_2$,$C_5$ of thiadiazole), Anal. Calcd for: $C_{11}H_{10}BrN_3S$ : C, 44.61, H, 3.40, N, 14.19 %; found C, 44.21, H, 3.27, N, 14.11 %; Mass 294 ($M^+$).

***(3-bromo-benzylidene)-(5-ethyl-[1,3,4] thiadiazol-2-yl)-amine (1f)*:** m.p.181-182$^0$C, yield 72 %, IR:1548($\nu_{C-C}$), 750 ($\nu_{C-S}$), 1645($\nu_{N=C}$), 1438($\nu_{C-N}$), 2952 ($\nu_{C-H}$),1320($\nu_{N-N}$), 551($\nu_{C-Br}$); $^1$H NMR: δ (ppm)1.21 (3H, t, *J* = 7.3 Hz, $CH_3$), 3.08 (2H, q, *J* = 7.3 Hz, $CH_2$), 7.45 -7.96 (4H, m, Ar-H), 9.42 (1H, s, N=CH); $^{13}$C NMRδ (ppm)12.75 ($CH_3$ acyclic), 27.93 ($CH_2$ acyclic), 128.41-133.19(C of aromatic ring), 159.41 N=CH acyclic, 156.4,158.7 ($C_2$,$C_5$ of thiadiazole), Anal. Calcd for: $C_{11}H_{10}BrN_3S$ : C, 44.61, H, 3.40, N, 14.19 %; found C, 44.21, H, 3.27, N, 14.15 %; Mass 294 ($M^+$).

***(4-bromo-benzylidene)-(5-ethyl-[1,3,4] thiadiazol-2-yl)-amine (1g)*:** m.p.182-183$^0$C, yield 68 %, IR : 1550($\nu_{C-C}$), 752 ($\nu_{C-S}$), 1667($\nu_{N=C}$), 1441($\nu_{C-N}$), 3072 ($\nu_{C-H}$),1316($\nu_{N-N}$), 549($\nu_{C-Br}$); $^1$H NMR: δ(ppm) 1.26 (3H, t, *J* = 7.3 Hz, $CH_3$), 3.06 (2H, q, *J* = 7.3 Hz $CH_2$), 7.67-

7.99 (4H, m, Ar-H), 9.42 (1H, s, N=CH). $^{13}$C NMR: δ (ppm) 13.76 ($CH_3$ acyclic), 29.73($CH_2$ acyclic), 124.09-134.59 (C of aromatic ring), 158.92(N=CH acyclic), 158.4, 159.9 ($C_2$,$C_5$ of thiadiazole), Anal. Calcd for: $C_{11}H_{10}BrN_3S$: C, 44.61, H, 3.40, N, 14.19 %; found C, 44.21, H, 3.19, N, 14.11 % ; Mass 294($M^+$).

***(2-nitro-benzylidene)-(5-ethyl-[1,3,4]thiadiazol-2-yl)-amine (1h)*:** m.p.176-179$^0$C, yield 80 %, IR:1552($\nu_{C-C}$), 753 ($\nu_{C-S}$), 1649($\nu_{N=C}$), 1436($\nu_{C-N}$), 3090 ($\nu_{C-H}$), 1321($\nu_{N-N}$), 1518 ($\nu$ C-$NO_2$) $^1$H NMR: δ 1.21 (3H, t, *J* = 7.1 Hz, $CH_3$), 3.06 (2H, q, *J* = 7.1 Hz, $CH_2$), 7.29-7.89 (4H, m, Ar-H,) 9.39 (1H, s, N=CH); $^{13}$C NMR: δ (ppm) 12.55($CH_3$ acyclic), 26.53($CH_2$ acyclic), 127.4.-148.40 (C of aromatic ring), 160.10(N=CH acyclic), 157.4,159.8 ($C_2$,$C_5$ of thiadiazole ring). Anal. Calcd for: $C_{11}H_{10}N_4O_2S$: C, 50.37, H, 3.84 N, 21.36 %; found C, 50.22, H, 3.59, N, 21.16 %; Mass 262 ($M^+$).

***(3-nitro-benzylidene)-(5-ethyl-[1,3,4]thiadiazol-2-yl)-amine (1i)* :**m.p.175-177$^0$C, yield 79 %, IR:1549($\nu_{C-C}$), 755 ($\nu_{C-S}$), 1647($\nu_{N=C}$), 1436($\nu_{C-N}$), 3110 ($\nu_{C-H}$), 1322 ($\nu_{N-N}$), 1521($\nu$C-$NO_2$), $^1$H NMR: δ (ppm) 1.25 (3H, t, *J* = 7.4 Hz, $CH_3$), 3.07 (2H, q, *J* = 7.4 Hz, $CH_2$), 7.33-7.83 (4H, m, Ar-H), 9.41 (1H, s, N=CH), $^{13}$C NMR δ (ppm) 14.75($CH_3$ acyclic), 29.93($CH_2$ acyclic), 158.71(N=CH acyclic), 117.1-140.50 (C of aromatic ring), 156.4,159.6 ($C_2$,$C_5$ of thiadiazole ring), Anal. Calcd for: $C_{11}H_{10}N_4O_2S$: C, 50.37, H, 3.84 N, 21.36 %; found C, 50.32, H, 3.49, N, 21.14, %; Mass 262 ($M^+$).

***(4-nitro-benzylidene)-(5-ethyl-[1,3,4] thiadiazol-2-yl)-amine (1j)* :**m.p.176-178 $^0$C, yield 81 %, IR:1550($\nu_{C-C}$), 754 ($\nu_{C-S}$), 1648($\nu_{N=C}$), 1433($\nu_{C-N}$), 3120 ($\nu_{C-H}$),1317($\nu_{N-N}$), 1526($\nu$C-$NO_2$); $^1$H NMR: δ(ppm) 1.27 (3H, t, *J* = 7.1 Hz, $CH_3$), 3.08 (2H, q, *J* = 7.1 Hz $CH_2$), 7.39-7.95 (4H, m, Ar-H), 9.46 (1H, s, N=CH); $^{13}$C NMR δ (ppm) 11.85($CH_3$ acyclic), 26.93 ($CH_2$ acyclic), 158.21(N=CH acyclic),117.1-140.20 (C of aromatic ring),157.7, 158.6 ($C_2$,$C_5$ of thiadiazole ring). Anal. Calcd for: $C_{11}H_{10}N_4O_2S$ : C, 50.37, H, 3.84 N, 21.36 %; found C, 50.22, H, 3.32, N, 21.21 %; Mass 262 ($M^+$).

***(2-methoxy-benzylidene)-(5-ethyl-[1,3,4] thiadiazol-2-yl)-amine(1k)*:** m.p.136-137$^0$C, yield 61%, IR: 1549($\nu_{C-C}$),752 ($\nu_{C-S}$), 1639($\nu_{N=C}$), 1439($\nu_{C-N}$), 3090 ($\nu_{C-H}$), 1314($\nu_{N-N}$), 2969($\nu OCH_3$); $^1$H NMR: δ (ppm)1.21 (3H, t, *J* = 7.1 Hz $CH_3$), 3.17 (2H, q, *J* = 7.1 Hz $CH_2$), 3.87 (3H, s, $OCH_3$), 7.03 -7.74 (4H, m,) Ar-H, 9.34(1H, s, N=CH); $^{13}$C NMR δ (ppm) 13.05 ($CH_3$ acyclic), 28.93($CH_2$ acyclic), 55.89($OCH_3$), 119.2-159.59(C of aromatic ring), 159.52 N=CH acyclic, 156.7, 158.9($C_2$, $C_5$ of thidiazole). Anal. Calcd for: $C_{12}H_{13}N_3OS$: C,58.28, H,5 .30 N,16.99 %; found C, 58.12, H, 5.18, N, 16.91 %; Mass 247 ($M^+$).

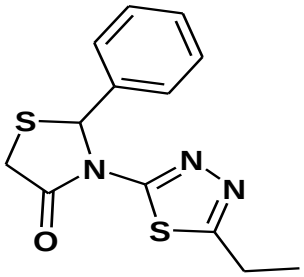
***(3-methoxy-benzylidene)-(5-ethyl-[1,3,4] thiadiazol-2-yl)-amine (1l)*:** m.p.134-136$^0$C, yield 59%, IR-1549 ($\nu_{C-C}$), 755 ($\nu_{C-S}$), 1651($\nu_{C=N}$), 1440($\nu_{C-N}$), 3085 ($\nu_{C-H}$), 1314($\nu_{N-N}$), 2973 ($\nu OCH_3$); $^1$H NMR: δ 1.19(ppm) (3H, t, *J* = 7.0 Hz $CH_3$), 2.97 (2H, q, *J* = 7.0 Hz $CH_2$), 3.77 (3H, s, $OCH_3$), 7.06-7.81 (4H, m,Ar-H) 9.41 (1H, s, N=CH), $^{13}$C NMR δ (ppm) 11.95 ($CH_3$ acyclic), 26.91($CH_2$ acyclic), 55.79 ($OCH_3$), 111.02-157.69 (C of aromatic ring), 158.71(N=CH acyclic), 156.5,159.4 ($C_2$,$C_5$ of thiadiazole). Anal. Calcd for:$C_{12}H_{13}N_3OS$ :C,58.28, H,5.30 N,16.99 %; found C, 58.12, H,16, N, 16.81 %; Mass 247 ($M^+$).

***(4-methoxy-benzylidene)-(5-ethyl-[1,3,4 ]thiadiazol-2-yl)-amine (1m)*:** m.p.136-138$^0$C, yield 57%, IR-1549($\nu_{C-C}$),755($\nu_{C-S}$), 1628($\nu_{C=N}$), 1441($\nu_{C-N}$), 3095 ($\nu_{C-H}$),1314($\nu_{N-N}$), 1109 ($\nu COCH_3$); $^1$H NMR: δ 1.26(ppm) (3H, t, *J* = 7.1 Hz ,$CH_3$), 3.17 (2H, q, *J* = 7.1 Hz $CH_2$), 3.84 (3H, s, $OCH_3$), 7.26-7.73 (4H, m, Ar-H), 9.35

(1H, s, N=CH); $^{13}$C NMR: δ (ppm) 11.95 ($CH_3$ acyclic), 26.98($CH_2$ acyclic), 55.51($OCH_3$), 114.5-160.40 (C of aromatic ring), 158.61(N=CH acyclic), 160.4, 156.7 ($C_2$,$C_5$ of thiadiazole). Anal. Calcd for: $C_{12}H_{13}N_3$ OS : C, 58.28, H, 5 .30 N, 16.99 %; found C, 58.12, H, 5.21, N, 16.11 % ; Mass 247 ($M^+$).

***Synthesis of 3-(5-ethyl-[1,3,4]thiadiazole-2-yl)-2-phenyl-thiazolidin-4-one (2a)*:**

Equimolar solution of the compound **1a** (0.004 mole) and mercaptoacetic acid (0.004 mole) in methanol (30 mL) and a pinch of anhydrous $ZnCl_2$ as a catalyst was first continuously stirred on a magnetic stirrer for about 02 hr followed by refluxing for about 11 hrs on a steam bath at 85-95$^0$C temperature. After the completion of the reaction the excess of methanol was removed and the product thus obtained was washed with water and purified over a silica gel column and the product recrystallized from ethanol to yield compound **2a**, yellow crystalline




**Compoun-2a**

compound. m.p.190-192$^0$C, yield 75 %, IR-1453($\nu_{C-C}$), 1590 ($\nu_{C=C}$), 1310($\nu_{N-N}$), 1670($\nu_{C=N}$), 712($\nu_{C-S}$), 1710 ($\nu_{C=O}$) 2949($\nu_{C-H}$); $^1$H NMR: δ(ppm)1.09 (3H, t, *J* = 7.3 Hz $CH_3$), 1.04 (2H, q, *J* = 7.3 Hz $CH_2$), 3.66 (2H, d, *J* = 15.8 Hz CH, thiazolidinone), 6.13 (1H, s) CH thiazolidinone, 7.32-7.48 (5H, m, Ar-H); $^{13}$C NMR: δ (ppm) 13.25($CH_3$ acyclic), 29.13($CH_2$ acyclic), 128.2-129.2(C of aromatic ring), 157.8,161.3 ($C_2$,$C_5$ of thiadiazole ring), 170.6(C=O cyclic thiazolidinone), 34.5($CH_2$ thiazolidinone), 69.7(CH cyclic thiazolidinone); Anal. Calcd for: $C_{13}H_{13}$ $N_3$ $OS_2$ : C, 53.58, H, 4.50, N, 14.42 %; found C, 53.41, H, 4.11, N, 14.21 %; Mass 291($M^+$).

The compounds **2b-2m** were synthesized by the similar method as described for **2a**.

***2-(2-chloro-phenyl)-3-(5-ethyl-[1,3,4] thiadiazole-2-yl)-thiazolidin-4-one (2b)*:**
m.p.175-177$^0$C, yield 65 %, IR:1451($\nu_{C-C}$), 1550 ($\nu_{C=C}$), 1308($\nu_{N-N}$), 1627 ($\nu_{C=N}$), 711($\nu_{C-S}$), 1712 ($\nu_{C=O}$) 720 ($\nu_{C-Cl}$); $^1$H NMR: δ(ppm) 1.09 (3H, t, *J* = 7.3 Hz, $CH_3$), 2.87 (2H, q, *J* = 7.3 Hz, $CH_2$), 3.67 (2H d, *J* = 15.8 Hz S-CH thiazolidinone), 6.12 (1H, s, CH thiazolidinone), 7.21-7.64 (4H, m, Ar-H); $^{13}$C NMR δ (ppm)12.15($CH_3$ acyclic), 29.98 ($CH_2$ acyclic), 127.6-133.2(C of aromatic ring), 161.3, 156.8($C_2$,$C_5$ of thiadiazole ring). 171.5(C=O cyclic thiazolidinone), 34.5($CH_2$ thiazolidinone), 69.0(CH cyclic thiazolidinone). Anal. Calcd for : $C_{13}H_{12}Cl$ $N_3$ $OS_2$: C, 47.92, H, 3.71, N, 12.90 %; found C, 46.91, H, 3.01, N, 11.71 %; Mass 325 ($M^+$).

***2-(3-chloro-phenyl)-3-(5-ethyl-[1,3,4] thiadiazole-2-yl)-thiazolidin-4-one (2c)*:**

m.p.172-175$^0$C, yield 55 %, IR:1450($\nu_{C-C}$), 1555 ($\nu_{C=C}$), 1316($\nu_{N-N}$), 1629 ($\nu_{C=N}$), 712($\nu_{C-S}$), 1714 ($\nu_{C=O}$), 730 ($\nu_{C-Cl}$); $^1$H NMR: δ (ppm)1.02 (3H, t, *J* = 7.3 Hz, $CH_3$), 2.88 (2H, q, *J* = 7.3 Hz, $CH_2$), 3.61 (2H, d, *J* = 15.9 Hz, S-CH thiazolidinone), 6.18 (1H, s, CH thiazolidinone), 7.22-7.40 (4H, m, Ar-H); $^{13}$C NMR :δ (ppm)13.39($CH_3$ acyclic), 28.23 ($CH_2$ acyclic), 127.6-137.0 (C of aromatic ring), 160.3, 157.2 ($C_2$,$C_5$ of thidiazole ring), 179.8 (C=O cyclic thiazolidinone), 34.8 ($CH_2$ thiazolidinone), 69.6 (CH cyclic thiazolidinone); Anal. Calcd. for: $C_{13}H_{12}$ Cl $N_3$ $OS_2$ C, 47.92, H, 3.71, N, 12.90 %; found C, 47.71, H, 3.43, N, 12.51 %; Mass 325 ($M^+$).

***2-(4-chloro-phenyl)-3-(5-ethyl-[1,3,4] thiadiazole-2-yl)-thiazolidin-4-one (2d)*:**
m.p.173-176$^0$C, yield 59 %, IR:1450 ($\nu_{C-C}$), 1542 ($\nu_{C=C}$), 1315($\nu_{N-N}$), 1630 ($\nu_{C=N}$), 711($\nu_{C-S}$), 1720 ($\nu_{C=O}$), 730 ($\nu_{C-Cl}$); $^1$H NMR: δ(ppm)1.07 (3H, t, *J* = 7.3 Hz $CH_3$), 2.88 (2H, q, *J* = 7.3 Hz $CH_2$), 3.70 (2H, d, *J* = 15.8 Hz, S-CH thiazolidinone,), 6.19 (1H, s, CH thiazolidinone), 7.54-7.56 (4H, m, Ar-H); $^{13}$C NMR: δ (ppm)129.5-139.3(C of aromatic ring),12.75($CH_3$ acyclic), 27.93 ($CH_2$ acyclic), 34.5($CH_2$ thiazolidinone), 67.9 (CH cyclic thiazolidinone) 159.4, 156.8 ($C_2$,$C_5$ of thiadiazole ring), 171.6 (C=O thiazolidinone); Anal. Calcd For: $C_{13}H_{12}$ Cl $N_3$ $OS_2$ : C, 47.92, H, 3.71, N, 12.90 %; found C, 47.51, H, 3.43, N, 12.81 % ; Mass 325($M^+$).

***2-(2-bromo-phenyl)-3-(5-ethyl-[1,3,4] thiadiazole-2-yl)-thiazolidin-4-one (2e)*:**

m.p.180-182$^0$C, yield 69 %, IR: 1446 ($\nu_{C-C}$), 1545 ($\nu_{C=C}$), 1318($\nu_{N-N}$), 1630 ($\nu_{C=N}$), 714($\nu_{C-S}$), 1719 ($\nu_{C=O}$), 545 ($\nu_{C-Br}$); $^1$H NMR: δ 1.06 (3H, t, *J* = 7.3 Hz, $CH_3$), 2.87 (2H, q, *J* = 7.3 Hz, $CH_2$) , 3.69 (2H, d, *J* = 15.9 Hz) S-CH thiazolidinone, 6.13 (1H, s, CH thiazolidinone), 7.03-7.48 (4H, m, Ar-H); $^{13}$C NMR δ (ppm)-120.7.2-132.7 (C of aromatic ring), 12.55 ($CH_3$ acyclic), 27.23 ($CH_2$ acyclic),160.3,155.3 ($C_2$,$C_5$ of thiadiazole ring), 170.2 (C=O cyclic thiazolidinone), 34.2 ($CH_2$ thiazolidinone), 68.5(CH cyclic thiazolidinone); Anal. Calcd for: $C_{13}H_{12}$ Br $N_3$ $OS_2$ : C, 42.17, H, 3.27, N, 11.35 %; found C, 42.01, H, 3.11, N, 11.01 %; Mass 370($M^+$).

***2-(3-bromo-phenyl)-3-(5-ethyl-[1,3,4] thiadiazole-2-yl)-thiazolidin-4-one (2f)*:**

m.p.181-184$^0$C, yield 65 %, IR:1448 ($\nu_{C-C}$), 1540 ($\nu_{C=C}$), 1313($\nu_{N-N}$), 1630 ($\nu_{C=N}$), 715($\nu_{C-S}$), 1712 ($\nu_{C=O}$), 525 ($\nu_{C-Br}$); $^1$H NMR: δ (ppm) 1.10(3H, t, *J* = 7.3 Hz, $CH_3$), 2.78 (2H, q, *J* = 7.3 Hz, $CH_2$), 3.70 (2H, d, *J* = 15.9 Hz, S-CH thiazolidinone), 6.15 (1H, s, CH thiazolidinone), 7.04-7.35 (4H, m, Ar-H); $^{13}$C NMR: δ (ppm) 118.2-137.0 (C of aromatic ring), 12.76 ($CH_3$ acyclic), 27.83 ($CH_2$ acyclic), 158.5, 157.4($C_2$,$C_5$ of thiadiazole ring), 168.9 (C=O cyclic thiazolidinone), 34.4 ($CH_2$ thiazolidinone), 69.1(cyclic CH thiazolidinone); Anal. Calcd for: $C_{13}H_{12}$ Br $N_3$ $OS_2$: C, 42.17, H,3. 27, N, 11.35 %; found C, 42.11, H, 3.21, N, 11.01 % ; Mass 370 ($M^+$).

***2-(4-bromo-phenyl)-3-(5-ethyl-[1,3,4] thiadiazole-2-yl)-thiazolidin-4-one (2g)*:**

m.p.182-183$^0$C, yield 67 %, IR:1441 ($\nu_{C-C}$), 1542 ($\nu_{C=C}$), 1314($\nu_{N-N}$), 1629 ($\nu_{C=N}$), 712 ($\nu_{C-S}$), 1713 ($\nu_{C=O}$), 542 ($\nu_{C-Br}$); $^1$H NMR: δ(ppm) 1.09 (3H, t, *J* = 7.3 Hz, $CH_3$), 2.78 (2H, q, *J* = 7.3 Hz, $CH_2$), 3.69 (2H, d, *J* = 15.9 Hz, S-CH thiazolidinone), 6.16 (1H, s, CH thiazolidinone), 7.30-7.63 (4H, m, Ar-H); $^{13}$C NMR: δ (ppm) 13.41 ($CH_3$ acyclic), 28.23 ($CH_2$ acyclic), 124.2-139.3 (C of aromatic ring), 169.2, 155.7 ($C_2$,$C_5$ of thiadiazole ring), 169.5 (C=O cyclic thiazolidinone), 33.5 ($CH_2$ thiazolidinone), 68.4 (cyclic CH thiazolidinone); Anal. Calcd for : $C_{13}H_{12}$ Br $N_3OS_2$: C, 42.17, H,3.27, N,11.35 %; found C, 42.01, H, 3.20, N, 11.01 %; Mass 370 ($M^+$).

***2-(2-nitro-phenyl)-3-(5-ethyl-[1,3,4] thiadiazole-2-yl)-thiazolidin-4-one(2h)*:**

m.p.176-179$^0$C, yield 65 %, IR:1446 ($\nu_{C-C}$), 1539 ($\nu_{C=C}$), 1316($\nu_{N-N}$), 1630 ($\nu_{C=N}$), 720 ($\nu_{C-S}$), 1716 ($\nu_{C=O}$), 1526(ν C-$NO_2$); $^1$H NMR: δ(ppm) 1.15 (3H, t, *J* = 7.3 Hz, $CH_3$), 2.81 (2H, q, *J* = 7.3 Hz, $CH_2$), 3.71 (2H, d, *J* = 15.9 Hz, CH thiazolidinone), 6.14 (1H, CH thiazolidinone, s), 7.50-8.08 (4H, m,) Ar-H; $^{13}$C NMR :δ (ppm) 13.05($CH_3$ acyclic), 28.83($CH_2$ acyclic), 127.6-148.4(C of aromatic ring),161.3, 156.8 ($C_2$,$C_5$ of thiadiazole ring), 170.9 (C=O cyclic thiazolidinone), 34.4($CH_2$ thiazolidinone),69.2 (CH cyclic thiazolidinone); Anal. Calcd for: $C_{13}H_{12}N_4O_3S_2$ : C, 46.42, H,3. 60, N, 16.66, O,

14.27, S, 19.06 %; found C, 45.21, H, 3.20, N, 15.80 %; Mass 336 ($M^+$).

***2-(3-nitro-phenyl)-3-(5-ethyl-[1,3,4] thiadiazole-2-yl)-thiazolidin-4-one (2i)*:**

m.p.175-177$^0$C, yield 85 %, IR:1441 ($\nu_{C-C}$), 1539 ($\nu_{C=C}$), 1311($\nu_{N-N}$), 1630 ($\nu_{C=N}$), 720 ($\nu_{C-S}$), 1715 ($\nu_{C=O}$), 1528 ($\nu$ C-$NO_2$); $^1$H NMR: δ(ppm) 1.08 (3H, t, *J* = 7.3 Hz, $CH_3$), 2.81 (2H, q, *J* = 7.3 Hz $CH_2$), 3.76 (2H, d, *J* = 15.9 Hz, CH thiazolidin-4-one), 6.31 (1H, s, CH thiazolidin-4-one,) 7.54-8.04 (4H, m, Ar-H); $^{13}$C NMR: δ (ppm) 13.35 ($CH_3$ acyclic), 28.97 ($CH_2$ acyclic), 117.3-140.5(C of aromatic ring), 159.4-158.2 ($C_2$, $C_5$ of thiadiazole), 171.6 (C=O Cyclic thiazolidinone), 34.4 ($CH_2$ thiazolidinone), 68.8 (CH cyclic thiazolidinone); Anal. Calcd for: $C_{13}H_{12}N_4O_3S_2$ : C, 46.42, H, 3. 60, N, 16.66 %; found C, 46.11, H, 3.18, N, 16.27 %; Mass 336. ($M^+$).

***2-(4-nitro-phenyl)-3-(5-ethyl-[1,3,4] thiadiazole-2-yl)-thiazolidin-4-one (2j)*:**

m.p. 176-179$^0$C, yield 83 %, IR:1442 ($\nu_{C-C}$), 1546 ($\nu_{C=C}$), 1319($\nu_{N-N}$), 1630 ($\nu_{C=N}$), 720 ($\nu_{C-S}$), 1717 ($\nu_{C=O}$), ,1539 ($\nu$ C-$NO_2$); $^1$H NMR: δ(ppm) 1.11 (3H, t, *J* = 7.3 Hz, $CH_3$), 2.84 (2H, q, *J* = 7.3 Hz, $CH_2$), 3.76 (2H, d, *J* = 15.8 Hz, CH thiazolidinone), 6.09 (1H, s, CH thiazolidinone), 7.42-8.08 (4H, m, Ar-H,); $^{13}$C NMR δ (ppm)12.76($CH_3$ acyclic), 27.93 ($CH_2$ acyclic), 117.3-140.5(C of aromatic ring), 160.4,157.8 ($C_2$,$C_5$ of thiadiazole ring), 171.5(C=O Cyclic thiazolidinone), 35.4($CH_2$ thiazolidinone), 67.9(CH cyclic thiazolidinone); Anal. Calcd for: $C_{13}H_{12}N_4O_3S_2$: C, 46.42, H,3. 60, N, 16.66 %; found C, 46.31, H, 3.24, N, 16.51 % ; Mass 336 ($M^+$).

***2-(2-methoxy-phenyl)-3-(5-ethyl-[1,3,4] thiadiazole-2-yl)-thiazolidin-4-one (2k)*:**

m.p.135-137$^0$C, yield 60 %, IR: 1449 ($\nu_{C-C}$), 1544 ($\nu_{C=C}$), 1317($\nu_{N-N}$), 1629 ($\nu_{C=N}$), 723 ($\nu_{C-S}$), 1711 ($\nu_{C=O}$) 2970 ($\nu$ $OCH_3$); $^1$H NMR: δ 1.08 (3H, t, J = 7.3 Hz, $CH_3$), 2.78 (2H, q, J = 7.3 Hz, $CH_2$ ), 3.71 (2H, d, J = 15.9 Hz, CH thiazolidinone), 3.79 (3H, s, $OCH_3$), 6.03 (1H, s, CH thiazolidinone), 6.89-7.37 (4H, m, Ar-H,); $^{13}$C NMR : δ (ppm) 12.25 ($CH_3$ acyclic), 27.93 ($CH_2$ acyclic), 55.4($OCH_3$), 113.7-155.8 (C of aromatic ring), 161.3,156.8 ($C_2$,$C_5$ of thiadiazole ring).172.5 (C=O cyclic thiazolidinone), 34.4 ($CH_2$ thiazolidinone), 69.7(CH cyclic thiazolidinone); Anal. Calcd for: $C_{14}H_{15}N_4O_2S_2$ C, 52.32, H,4. 70, N, 13.07 %; found C, 52.11, H, 4.24, N, 13.00 % ; Mass 321 ($M^+$).

***2-(3-methoxy-phenyl)-3-(5-ethyl-[1,3,4] thiadiazole-2-yl)-thiazolidin-4-one (2l):***

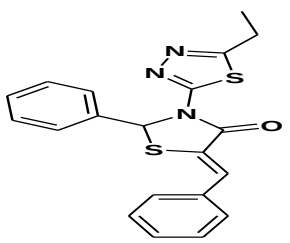
*m*.p.134-1136 $^0$C, yield 58 %, IR - 1441 ($\nu_{C-C}$), 1542 ($\nu_{C=C}$), 1313($\nu_{N-N}$), 1630 ($\nu_{C=N}$), 706 ($\nu_{C-S}$), 1712 ($\nu_{C=O}$) 2971 ($\nu$ $OCH_3$); $^1$H NMR: δ (ppm) 1.11 (3H, t, *J* = 7.3 Hz, $CH_3$), 2.79 (2H, q, *J* = 7.3 Hz, $CH_2$), 3.76 (2H, d, *J* = 15.8 Hz, CH thiazolidin-4-one), 3.73 (3H, s, $OCH_3$), 6.26 (1H, s CH thiazolidin-4-one), 6.88-7.24 (4H, m, Ar-H); $^{13}$C NMR :δ (ppm) 13.15($CH_3$ acyclic), 29.13($CH_2$ acyclic), 55.7($OCH_3$), 111.7-157.8 (C of aromatic ring), 169.3, 115.8 ($C_2$,$C_5$ of thiadiazole ring), 172.2 (C=O cyclic thiazolidinone), 34.4 ($CH_2$ thiazolidinone), 68.7(cyclic CH thiazolidinone); Anal. Calcd for: $C_{14}H_{15}N_4O_2S_2$:C, 52.32, H,4.70, N, 13.07 %; found C, 52.21, H, 4.14, N, 13.00 %; Mass 321($M^+$).

***2-(4-methoxy-phenyl)-3-(5-ethyl-[1,3,4] thiadiazole-2-yl)-thiazolidin-4-one (2m):***

m.p.136-137$^0$C, yield 55 %, IR: 1443 ($\nu_{C-C}$), 1565 ($\nu_{C=C}$), 1316($\nu_{N-N}$), 1632 ($\nu_{C=N}$), 707 ($\nu_{C-S}$), 1710 ($\nu_{C=O}$) 2968 ($\nu$ $OCH_3$); $^1$H NMR: δ (ppm)1.17 (3H, t, *J* = 7.3 Hz, $CH_3$), 2.83 (2H, q, *J* = 7.3 Hz, $CH_2$), 3.74 (2H, d, *J* = 15.8 Hz, CH thiazolidinone), 3.76 (3H, s $OCH_3$), 6.08 (1H, s CH thiazolidinone), 6.95-7.30 (4H, m, Ar-H); $^{13}$C NMR δ (ppm) 12.95 ($CH_3$ acyclic), 28.73 ($CH_2$ acyclic), 56.01($OCH_3$), 114.59-160.4 (C of

aromatic ring), 161.3, 156.8 ($C_2$,$C_5$ of thiadiazole ring), 170.9 (C=O Cyclic thiazolidinone), 34.3 ($CH_2$ thiazolidinone), 69.6 (CH cyclic thiazolidinone); Anal. Calcd. For: $C_{14}H_{15}N_4O_2S_2$: C, 52.32, H, 4.70, N, 13.07 %; found C, 52.21, H, 4.40, N, 13.02 %; Mass 321 ($M^+$).

***Synthesis of 5-benzylidene-3-(5-ethyl-[1,3,4] thiadiazol-2-yl)-2-phenyl-thiazolidin-4-ones (3a):*** The compound-**2** (0.002 mole,) and benzaldehyde (0.002 mole) in methanol (25 mL) in the presence of sodium ethoxide undergo Knovenagel condensation. The reaction mixture was first continuously stirred on magnetic stirrer for about 2-3 hrs, then it was kept on steam bath for reflux for about 10 hr. After the completion of the reaction the excess of methanol was removed and the product thus obtained was washed with water and purified over a silica gel column and recrystallized from ethanol to yield compound **3;** yellow crystals, m.p.-189-191$^0$C, Yield 71 % IR: 1453($\nu_{C-C}$), 1545 ($\nu_{C=C}$), 2949($\nu_{C-H}$), 1470($\nu_{C-N}$), 1310 ($\nu_{N-N}$), 1207($\nu_{C=N}$) 737 ($\nu_{C-S}$), 1710 ($\nu_{C=O}$); $^1$H NMR: δ (ppm)1.09 (3H, t, *J* = 7.3 Hz, $CH_3$), 2.79 (2H, q, *J* = 7.3 Hz, $CH_2$), 6.40 (1H, s, CH cyclic thiazolidinone), 7.21-7.65 (10H, m, Ar-H), 7.70 (1H, s, CH acyclic); $^{13}$C NMR: δ (ppm) 12.85 ($CH_3$ acyclic), 28.53($CH_2$ acyclic), 128.2-139.30 (C of aromatic ring), 161.3, 156.8 ($C_2$,$C_5$ of thiadiazole ring), 166.2 (C=O Cyclic thiazolidinone); 69.5(CH cyclic thiazolidinone), 126.5 (CH acyclic); Anal. Calcd. for : $C_{20}H_{17}N_3OS_2$: C, 63.30, H, 4. 52, N, 11.07, O, 4.22, S, 16.90 %; found C, 63.21, H, 4.34, N, 11.01 %; Mass 379 ($M^+$).



**Compound-3a**

The compounds **3b-3m** were synthesized by the similar method as reported for 3a.

***5-(2-chloro-benzylidene)-2-(2-chloro-phenyl)-3-(5-ethyl-[1,3,4]thiadiazole-2-yl)-thiazolidin-4-one (3b) :*** m.p.169-171$^0$C, yield 67 % IR : 1451($\nu_{C-C}$), 1555 ($\nu_{C=C}$), 2949($\nu_{C-H}$), 745($\nu_{C-Cl}$), 1310($\nu_{N-N}$), 1207($\nu_{C=N}$) 737($\nu_{C-S}$), 1714 ($\nu_{C=O}$); $^1$H NMR: δ (ppm) 1.18 (3H, t, *J* = 7.3 Hz, $CH_3$), 2.84 (2H, q, *J* = 7.3 Hz, $CH_2$), 6.39 (1H, s, CH thiazolidinone), 7.21-7.80 (8H,m, Ar-H), 7.75 (1H, s, CH acyclic); $^{13}$C NMR δ (ppm)13.65 ($CH_3$ acyclic), 28.83($CH_2$ acyclic), 127.1-134.3(C of aromatic ring), 160.4, 155.9 ($C_2$,$C_5$ of thiadiazole ring), 165.2(C=O cyclic thiazolidinone), 69.9 (CH cyclic thiazolidinone), 125.9 (CH acyclic); Anal. calcd. for: $C_{20}H_{15}Cl_2N_3OS_2$ : C, 53.57, H,3. 37, N, 9.37 %; found C, 53.31, H, 3.14, N, 9.22 %; Mass 447 ($M^+$).

***5-(3-chloro-benzylidene)-2-(3-chloro-phenyl)-3-(5-ethyl-[1,3,4]thiadiazole-2-yl)-thiazolidin-4-one (3c) :*** m.p.172-173 $^0$C, yield 65 %**,** IR :1451($\nu_{C-C}$), 1551 ($\nu_{C=C}$), 2959($\nu_{C-H}$), 735($\nu_{C-Cl}$), 1312($\nu_{N-N}$), 1209($\nu_{C=N}$) 736($\nu_{C-S}$), 1720 ($\nu_{C=O}$); $^1$H NMR: δ (ppm) 1.06 (3H, t, *J* = 7.3 Hz, $CH_3$), 2.88 (2H, q, *J* = 7.3 Hz, $CH_2$), 6.40 (1H, s, CH thiazolidin-4-one), 7.22-7.89 (8H, m Ar-H), 7.84 (1H, s, CH acyclic); $^{13}$C NMR: δ (ppm) 12.98($CH_3$ acyclic), 28.23($CH_2$ acyclic),127.8-132.2 (C of aromatic ring), 161.4, 156.9 ($C_2$,$C_5$ of thiadiazole) 167.2 C=O cyclic thiazolidinone, 68.5(CH cyclic thiazolidinone), 126.5 (CH acyclic); Anal. Calcd. For: $C_{20}H_{15}Cl_2N_3OS_2$: C, 53.57, H, 3. 37, N, 9.37 %; found C, 53.21, H, 3.21, N, 9.12 %, Mass 447($M^+$).

***5-(4-chloro-benzylidene)-2-(4-chloro-phenyl)-3-(5-ethyl-[1,3,4]thiadiazole-2-yl)-thiazolidin-4-one (3d):*** m.p.170-172 $^0$C, yield 66 % IR: 1453($\nu_{C-C}$), 1554 ($\nu_{C=C}$), 2979($\nu_{C-H}$), 741($\nu_{C-Cl}$), 1312 ($\nu_{N-N}$), 1209 ($\nu_{C=N}$), 734( $V_{C-S}$), 1713 ( $V_{C=O}$), $^1$H NMR: δ(ppm) 1.12 (3H, t, *J* = 7.3 Hz, $CH_3$), 2.82

(2H, q, *J* = 7.3 Hz, $CH_2$), 6.41 (1H, s, CH thiazolidinone ), 7.80 (1H, s, CH acyclic), 7.49-7.75 (8H, m, Ar-H); $^{13}$C NMR : δ (ppm) 13.25 ($CH_3$ acyclic), 28.03($CH_2$ acyclic), 129.5-139.3 (C of aromatic ring), 160.7, 156.2 ($C_2$,$C_5$ of thiadiazole ring), 166.5 (C=O cyclic thiazolidinone), 67.5(CH cyclic thiazolidinone),126.4 (CH acyclic); Anal. Calcd. for: $C_{20}H_{15}Cl_2N_3OS_2$ : C, 53.57, H, 3. 37, N, 09.37 %; found C, 53.31, H, 3.27, N, 9.20 % ;Mass 447 ($M^+$).

***5-(2-bromo-benzylidene)-2-(2-bromo-phenyl)-3-(5-ethyl-[1,3,4]thiadiazole-2-yl)-thiazolidin-4-one (3e) :*** m.p. 180-181 $^0$C, yield 70 % IR: 1448($\nu_{C-C}$), 1554 ($\nu_{C=C}$), 2952($\nu_{C-H}$), 535($\nu_{C-Br}$), 1316($\nu_{N-N}$), 1211($\nu_{C=N}$) 734($\nu_{C-S}$), 1711 ($\nu_{C=O}$); $^1$H NMR: δ (ppm) 1.16 (3H, t, *J* = 7.3 Hz, $CH_3$), 2.86 (2H, q, *J* = 7.3 Hz, $CH_2$), 6.41 (1H, s, CH thiazolidinone), 7.03-7.78 (8H, m, Ar-H) 7.78 (1H, s, CH acyclic); $^{13}$C NMR: δ (ppm) 13.75 ($CH_3$ acyclic), 29.33 ($CH_2$ acyclic), 120.6-132.5 (C of aromatic ring), 161.4, 158.1 ($C_2$,$C_5$ of thiadiazole ring), 165.2 (C=O cyclic thiazolidinone), 69.2 (CH cyclic thiazolidinone), 126.8 (CH acyclic); Anal. Calcd. for: $C_{20}H_{15}Br_2N_3OS_2$ : C, 44.71, H, 2.81, N,7.82 %; found C, 44.56, H, 2.57, N, 7.66 %, Mass 537 ($M^+$).

***5-(3-bromo-benzylidene)-2-(3-bromo-phenyl)-3-(5-ethyl-[1,3,4]thiadiazole-2-yl)-thiazolidin-4-one (3f):*** m.p.182-184 $^0$C, yield 72 %, IR:1445($\nu_{C-C}$), 1552 ($\nu_{C=C}$), 2962($\nu_{C-H}$), 540($\nu_{C-Br}$), 1313($\nu_{N-N}$), 1216($\nu_{C=N}$) 736 ($\nu_{C-S}$), 1715 ($\nu_{C=O}$); $^1$H NMR: δ(ppm) 1.08 (3H, t, *J* = 7.3 Hz, $CH_3$), 2.89 (2H, q, *J* = 7.3 Hz, $CH_2$), 6.41 (1H, s, CH thiazolidin-4-one), 7.03-7.82 (8H, m, Ar-H) 7.81 (1H, s, CH acyclic); $^{13}$C NMR δ (ppm) 11.95($CH_3$ acyclic), 26.83 ($CH_2$ acyclic), 118.2-137.5(C of aromatic ring),162.4, 158.6 ($C_2$,$C_5$ of thiadiazole),166.3 (C=O cyclic thiazolidinone), 68.5 (CH cyclic thiazolidinone),126.7 (CH acyclic); Anal. Calcd. for: $C_{20}H_{15}Br_2N_3OS_2$ : C, 44.71, H, 2.81, N, 7.82 %; found C, 44.56, H, 2.49, N, 7.50 %, Mass 537 ($M^+$).

***5-(4-bromo-benzylidene)-2-(4-bromo-phenyl)-3-(5-ethyl-[1,3,4]thiadiazole-2-yl)-thiazolidin-4-one (3g) :***m.p.181-183 $^0$C, yield 71 %, IR :1439($\nu_{C-C}$), 1548 ($\nu_{C=C}$), 2952($\nu_{C-H}$), 546($\nu_{C-Br}$), 1316($\nu_{N-N}$), 1226($\nu_{C=N}$) 733 ($\nu_{C-S}$), 1719 ($\nu_{C=O}$), $^1$H NMR: δ (ppm)1.07 (3H, t, *J* = 7.3 Hz, $CH_3$), 2.81 (2H, q, *J* = 7.3 Hz, $CH_2$), 6.40 (1H, s, CH thiazolidin-4-one), 7.30-7.74 (8H, m, Ar-H), 7.65 (1H, s, CH acyclic); $^{13}$C NMR δ (ppm) 11.91($CH_3$ acyclic), 26.89 ($CH_2$ acyclic), 127.8-139.3 (C of aromatic ring), 162.4, 158.6 ($C_2$,$C_5$ of thiadiazole ring), 166.2 (C=O cyclic thiazolidineone), 69.4 (CH cyclic thiazolidinone), 126.6(CH acyclic); Anal. Calcd. For: $C_{20}H_{15}Br_2N_3OS_2$: C, 44.71, H, 2.81, 74, N, 7.82 %; found C, 44.66, H, 2.59, N, 7.60 %; Mass 537 ($M^+$).

***5-(2-nitro-benzylidene)-2-(2-nitro-phenyl)-3-(5-ethyl-[1,3,4]thiadiazole-2-yl)-thiazolidin-4-one (3h) :*** m.p.185-187$^0$C, yield 60 %, IR:1448 ($\nu_{C-C}$), 1460 ($\nu_{C=C}$), 1314($\nu_{N-N}$), 1630 ($\nu_{C=N}$), 720 ($\nu_{C-S}$), 1716 ($\nu_{C=O}$) 1538 (ν C-$NO_2$), 735(ν $_{C-N}$), $^1$H NMR: δ (ppm)1.13 (3H, t, *J* = 7.3 Hz, $CH_3$), 2.84 (2H, q, *J* = 7.3 Hz, $CH_2$), 6.44 (1H, s, CH thiazolidinone), 7.53-8.20 (8H, m,) Ar-H, 8.50 (1H, s, CH acyclic); $^{13}$C NMR δ (ppm) 121.8-148.4(C of aromatic ring), 12.77 ($CH_3$ acyclic), 27.91($CH_2$ acyclic), 158.6,162.4 ($C_2$,$C_5$ of thiadiazole ring), 169.2 (C=O cyclic thiazolidinone), 69.5 (CH cyclic thiazolidinone), 127.1(CH acyclic); Anal. Calcd. for: $C_{20}H_{15}N_3O_5S_2$ C, 51.16, H, 3.22, N, 14.92, O,17.04, S, 13.66 %; found C, 51.06, H, 2.12, N, 13.32 %, Mass 469 ($M^+$).

***5-(3-nitro-benzylidene)-2-(3-nitro-phenyl)-3-(5-ethyl-[1,3,4]thiadiazole-2-yl)-thiazolidin-4-one (3i)*****:** m.p.183-185$^0$C, yield 64 %, IR-1443 ($\nu_{C-C}$), 1459 ($\nu_{C=C}$), 1311($\nu_{N-N}$), 1629 ($\nu_{C=N}$), 735 ($\nu_{C-S}$), 1715 ($\nu_{C=O}$) 1532 (ν C-$NO_2$),735($\nu_{C-N}$); $^1$H

NMR: δ (ppm)1.16 (3H, t, *J* = 7.3 Hz, $CH_3$), 2.86 (2H, q, *J* = 7.3 Hz $CH_2$), 6.46 (1H, s, CH thiazolidinone), 7.45-8.66 (8H, m, Ar-H), 7.96 (1H, s CH acyclic); $^{13}$C NMR: δ (ppm) 116.4-140.5 (C of aromatic ring), 12.72($CH_3$ acyclic), 27.83($CH_2$ acyclic),169.2, 159.5 ($C_2$,$C_5$ of thiadiazole ring), 167.2 (C=O cyclic thiazolidinone), 68.4(CH cyclic thiazolidinone), 126.8 (CH acyclic); Anal. Calcd. for : $C_{20}H_{15}N_3O_5S_2$ : C, 51.16, H, 3.22, N, 14.92 %; found C, 51.06, H, 3.11, N, 14.62 % ; Mass 469 ($M^+$).

***5-(4-nitro-benzylidene)-2-(4-nitro-phenyl)-3-(5-ethyl-[1,3,4]thiadiazole-2-yl)-thiazolidin-4-one(3j) :*** m.p.190-191$^0$C, yield 61 %, IR: 1439 ($\nu_{C-C}$), 1540 ($\nu_{C=C}$), 1321($\nu_{N-N}$), 1633 ($\nu_{C=N}$), 735 ($\nu_{C-S}$), 1717 ($\nu_{C=O}$),735($\nu_{C-N}$), 1529 (ν, C-$NO_2$); $^1$H NMR: δ(ppm) 1.17 (3H, t, *J* = 7.3 Hz, $CH_3$), 2.85 (2H, q, *J* = 7.3 Hz, $CH_2$), 6.45 (1H, s, CH thiazolidinone), 7.44-8020 (8H, m, Ar-H), 8.26 (1H, s, CH acyclic); $^{13}$C NMR : δ (ppm) 117.3-140.5 (C of aromatic ring), 12.70 ($CH_3$ acyclic), 27.73($CH_2$ acyclic), 169.2, 159.5 ($C_2$,$C_5$ of thiadiazole ring), 170.3 (C=O cyclic thiazolidinone), 67.8(CH cyclic thiazolidinone), 126.5 (CH acyclic); Anal. Calcd. For: $C_{20}H_{15}N_3O_5S_2$ : C, 51.16, H, 3.22, N, 14.92 %; found C, 51.06, H, 3.11, N, 14.52 %; Mass 469 ($M^+$).

***5-(2-methoxy-benzylidene)-2-(2-methoxy-phenyl)-3-(5-ethyl-[1,3,4]thiadiazole-2-yl)-thiazolidin-4-one (3k):*** m.p.133-135$^0$C, yield 76 %, IR:1439 ($\nu_{C-C}$), 1540 ($\nu_{C=C}$), 1319($\nu_{N-N}$), 1718 ($\nu_{C=O}$), 1633 ($\nu_{C=N}$), 734 ($\nu_{C-S}$), 2971, (ν, $OCH_3$); $^1$H NMR: δ (ppm) 1.13 (3H, t, *J* = 7.3 Hz, $CH_3$), 2.80 (2H, q, *J* = 7.3 Hz) $CH_2$, 3.71-3.86 (6H, s, $OCH_3$), 6.32 (1H, s, CH thiazolidinone ), 6.74-7.78 (8H, m, Ar-H). 7.59 (1H, s, CH acyclic); $^{13}$C NMR: δ (ppm) 12.71 ($CH_3$ acyclic), 26.83($CH_2$ acyclic), 55.4 ($OCH_3$), 111.4-156.4 (C of aromatic ring),168.3, 155.8 ($C_2$,$C_5$ of thiadiazole ring),170.2 (C=O cyclic thiazolidinone), 68.5 (CH cyclic thiazolidinone), 127.3 (CH acyclic); Anal. Calcd. for: $C_{22}H_{21}N_3O_3S_2$: C, 60.11, H, 4.28, N, 9.56 %; found C, 60.06, H, 4.19.01, N, 9.26.12 %; Mass 438 ($M^+$).

***5-(3-methoxy-benzylidene)-2-(3-methoxy-phenyl)-3-(5-ethyl-[1,3,4]thiadiazole-2-yl)-thiazolidin-4-one (3l)*** -m.p. 133-134 $^0$C, yield 75 %, IR: 1441 ($\nu_{C-C}$), 1542 ($\nu_{C=C}$), 1317($\nu_{N-N}$), 1712 ($\nu_{C=O}$), 1636 ($\nu_{C=N}$), 736 ($\nu_{C-S}$), 2970 (ν $OCH_3$); $^1$H NMR: δ(ppm) 1.14 (3H, t, *J* = 7.3 Hz, $CH_3$), 2.81 (2H, q, *J* = 7.3 Hz, $CH_2$), 3.73-3.75 (6H, s, $OCH_3$), 6.26 (1H, s, CH thiazolidin-4-one), 6.88-7.50 (8H,m, Ar-H), 7.81 (1H, s, CH acyclic); $^{13}$C NMR δ (ppm) 111.3-157.7(C of aromatic ring), 13.15 ($CH_3$ acyclic), 26.32 ($CH_2$ acyclic), 155.8, 168.3, ($C_2$,$C_5$ of thiadiazole ring), 167.6 (C=O cyclic thiazolidineone), 68.7(CH cyclic thiazolidinone),127.3(CH acyclic); Anal. Calcd. For: $C_{22}H_{21}N_3O_3S_2$ : C, 60.11, H,4.28, N, 9.56 %; found C, 60.06, H, 4.15, N, 9.36 %; Mass 439 ($M^+$).

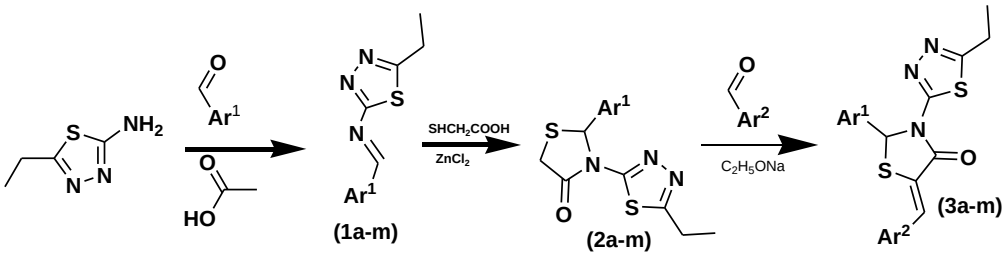
***5-(4-methoxy-benzylidene)-2-(4-methoxy-phenyl)-3-(5-ethyl-[1,3,4]thiadiazole-2-yl)-thiazolidin-4-one (3m) :***m.p.137-139 $^0$C, yield 75 %, IR: 1443 ($\nu_{C-C}$), 1540 ($\nu_{C=C}$), 1319($\nu_{N-N}$), 1715 ($\nu_{C=O}$),1638 ($\nu_{C=N}$), 734 ($\nu_{C-S}$), 2969 (ν $OCH_3$); $^1$H NMR: δ (ppm) 1.12 (3H, t, *J* = 7.3 Hz, $CH_3$), 2.78 (2H, q, *J* = 7.3 Hz, $CH_2$), 3.76-3.79 (6H, s, $OCH_3$), 6.38 (1H, s, CH thiazolidinone), 6.95-7.73 (8H, m, Ar-H). 7.65 (1H, s, CH cyclic); $^{13}$C NMR: δ (ppm) 114.3-160.3 (C of aromatic ring), 12.65($CH_3$ acyclic), 26.38 ($CH_2$ acyclic), 167.6, 156.9 ($C_2$, $C_5$ of thiadiazole ring), 169.4 (C=O cyclic thiazolidineone), 67.5(CHcyclic thiazolidinone), 126.3(CH acyclic); Anal. Calcd. For: $C_{22}H_{21}N_3O_3S_2$ : C, 60.11, H,4.28, N, 9.56 %; found C, 60.00, H, 4.15, N, 9.44%, Mass 439 ($M^+$).

## RESULTS AND DISCUSSION

The reaction of 2-amino-5-ethyl-1,3,4-thiadiazole and benzaldehyde afforded compound **1a.** The

spectroscopic analyses of compound **1a** showed absorption peaks for N–CH for Schiff bases N=CH are confirmed by IR, $^1$H NMR and $^{13}$C NMR spectra. ***1a–1m*** have been synthesized by taking various derivatives of benzaldehyde. In the IR spectra an absorption found in the range of 1665–1675 cm$^{-1}$, and a strong signal in the range of δ 9.34–9.46 and δ 158-161 ppm in the $^1$H NMR and $^{13}$C NMR spectra respectively supported the formation of compounds ***1a–1m***. The fact is also supported by the disappearance of the signal of $NH_2$ in the $^1$H NMR spectra.

The compounds ***1a–1m*** on reaction with equimolar amount of thioglycolic acid in the presence of $ZnCl_2$ in trace amount gives the cycloaddition reaction and produced a five membered thiazolidinone ring, ***2a–2m.*** The compound ***2a–2m*** showed a characteristic absorption of the cyclic carbonyl group in the range of 1710–1721 cm$^{-1}$ in the IR spectra. The $^1$H NMR spectra clearly indicate the presence of the active methylene group in the thiazolidine ring in the range of δ 3.61–3.96 ppm. The $^{13}$C NMR spectra of compounds ***2a–2m*** also supported the presence of cyclic carbonyl group where a $^{13}C$ signal appeared in the range of δ 165.4–175.2 ppm. These are supported by two evidences that are; (a) disappearance of N=CH proton and (b) appearance of N–CH proton in the range of δ 6.08-6.37 (acyclic CH) ppm. in the $^1$H NMR spectra of compounds ***2a–2m***. Compounds ***2a–2m*** underwent the Knoevenagel condensation reaction with substituted benzaldehydes in the presence of $C_2H_5ONa$ to afford compounds ***3a–3m***. In the $^1$H NMR spectra of the compounds disappearance of two methylene protons of ***2a–2m*** and appearance of a new signal for C=CH in the range of δ 7.39–8.50 ppm in the $^1$H NMR was observed. Two new signals for C=CH appeared in the range of δ 125– 130 ppm and C-H appeared in the range of δ 67-70 ppm in the $^{13}$C NMR spectra of ***3a–3m***. These facts clearly confirmed the formation of compounds ***2a–2m*** and ***3a–3m***.




**Ar$^1$,Ar$^2$=Various Substituted Aryl Groups**

*Antimicrobial activities*

The synthesized compounds ***2a–2m*** *and* ***3a–3m*** were evaluated *in vitro* for antibacterial activity by using filter paper disc diffusion method against different strains of bacteria viz. *B. substilis, E. Coli* and *S. tyhpi*. All the final products along with standard antibacterial streptomycin were used at 50 and 100 *ppm* concentrations. Antifungal activity against *A.niger, A. Flavus and F. oxisporium* at 50 and 100 mg/mL concentrations was also determined by filter paper disc technique. The minimum inhibitory concentration (MIC) values of the synthesized compounds were determined. Standard antibacterial Streptomycin and antifungal griseofulvin were also tested under the similar conditions for comparison **(Tables: 1, 2 and 3).**

Nitro group containing compounds showed higher activity in the order ***(3i> 3j > 3h)*** than chloro ***(3c>3b >3d),*** or bromo group containing compounds ***(3f> 3g > 3e).*** Similar order of activity for compounds ***2a–2m*** was observed. The chloro and bromo derivatives also have

higher activity than other compounds in the series. On the basis of Structural Activity Relationship (SAR),it can be concluded that the activity of compounds depends on electron withdrawing nature of the substituted groups, -$NO_2$ > -Cl >- Br > -$OCH_3$.

**Table 1. Antibacterial Activity (Inhibition zone diameter in mm) of Compounds 2a-2m and 3a-3m**

| Comp. | *E. coli* | | *B. subtilis* | | *S. Typhi* | |
|---|---|---|---|---|---|---|
| | 50 mg/mL | 100 mg/mL | 50 mg/mL | 100 mg/mL | 50 mg/mL | 100 mg/mL |
| 2a | 6 | 9 | 4 | 5.3 | 4 | 7 |
| 2b | 15.9 | 16 | 14.6 | 16.9 | 14 | 17 |
| 2c | 16.7 | 18.4 | 14 | 16.2 | 15.3 | 18 |
| 2d | 15.4 | 19 | 15 | 17.9 | 16 | 19.4 |
| 2e | 13 | 14.2 | 12.2 | 15.8 | 11.9 | 11.5 |
| 2f | 12.8 | 13.6 | 11.7 | 14.9 | 12 | 16 |
| 2g | 13.5 | 14.8 | 13 | 16.2 | 12.6 | 16.5 |
| 2h | 18 | 23.5 | 18.3 | 22.5 | 18.9 | 24.7 |
| 2i | 19 | 24.8 | 19 | 24 | 18.7 | 24.8 |
| 2j | 17.5 | 24.5 | 17.5 | 23.5 | 17.5 | 23.8 |
| 2k | 12.5 | 14 | 10 | 12.5 | 10.2 | 13.7 |
| 2l | 11.8 | 13.2 | 10.6 | 13.2 | 11 | 14.6 |
| 2m | 12.6 | 13.9 | 11.3 | 13.8 | 11.5 | 14.9 |
| 3a | 8.9 | 11.2 | 7 | 9.8 | 7.5 | 10.6 |
| 3b | 15.2 | 18.3 | 15.4 | 18.2 | 14.5 | 19.3 |
| 3c | 16.5 | 19.2 | 16 | 19.8 | 15 | 19 |
| 3d | 14.9 | 18 | 14.8 | 17.6 | 15.2 | 29.2 |
| 3e | 12.6 | 14.5 | 12.8 | 16.9 | 13 | 16 |
| 3f | 13 | 15.9 | 13 | 17 | 13.9 | 17 |
| 3g | 12.5 | 14.8 | 12.5 | 15.5 | 13.5 | 21.8 |
| 3h | 21.7 | 26.9 | 20.6 | 25.7 | 21.2 | 25 |
| 3i | 22.3 | 26 | 21.5 | 26.3 | 22.5 | 26 |
| 3j | 22 | 25.5 | 22.2 | 27 | 22 | 26.5 |
| 3k | 12 | 16 | 12.3 | 15 | 12 | 16 |
| 3l | 11 | 15 | 9.9 | 12.4 | 10.1 | 13.8 |
| 3m | 12.4 | 15.9 | 11.4 | 13.7 | 11.7 | 14.8 |
| SM[a] | 26.3 | 29.5 | 23 | 27 | 25 | 28 |

**Table 2. Antifungal Activity (Inhibition Zone diameter in mm) of the Compounds 2a-2m and 3a-3m**

| Comp. | *A. flavus* | | *A.niger* | | *F. oxisporium* | |
|---|---|---|---|---|---|---|
| | 50 mg/mL | 100 mg/mL | 50 mg/mL | 100 mg/mL | 50 mg/mL | 100 mg/mL |
| 2a | 6.0 | 9.0 | 6.5 | 8.7 | 8.6 | 10.2 |
| 2b | 14.7 | 17.0 | 14.5 | 17.5 | 15.5 | 18.4 |
| 2c | 14.9 | 17.5 | 15.9 | 18.6 | 14.6 | 17.7 |
| 2d | 14.2 | 20.5 | 16.0 | 18.6 | 16.2 | 19.5 |
| 2e | 12.5 | 16.8 | 10.0 | 13.3 | 11.0 | 13.9 |
| 2f | 11.6 | 14.5 | 10.5 | 14.5 | 12.8 | 16.6 |
| 2g | 13.0 | 17.9 | 11.9 | 14.5 | 13.0 | 16.2 |
| 2h | 17.4 | 24.0 | 18.5 | 23.5 | 18.5 | 24.0 |
| 2i | 17.5 | 24.5 | 19.0 | 25.0 | 19.5 | 24.5 |
| 2j | 17.2 | 23.0 | 18.0 | 24.0 | 18.0 | 23.5 |
| 2k | 10.9 | 14.1 | 10.0 | 13.5 | 12.0 | 15.2 |
| 2l | 8.8 | 11.5 | 7.0 | 10.0 | 10.3 | 13.4 |
| 2m | 11.2 | 13.6 | 8.6 | 11.5 | 10.4 | 13.9 |
| 3a | 9.0 | 11.5 | 7.0 | 9.5 | 8.0 | 11.0 |
| 3b | 16.0 | 20.0 | 14.8 | 19.5 | 17.0 | 21.5 |
| 3c | 18.0 | 23.4 | 16.4 | 22.0 | 16.5 | 23.2 |
| 3d | 17.5 | 22.5 | 15.2 | 21.4 | 17.5 | 21.8 |
| 3e | 12.8 | 18.9 | 13.5 | 16.8 | 11.5 | 14.6 |
| 3f | 13.0 | 16.8 | 12.6 | 15.0 | 13.8 | 16.7 |
| 3g | 14.9 | 18.2 | 11.4 | 13.6 | 12.0 | 15.0 |
| 3h | 21.7 | 27.0 | 21.0 | 26.5 | 21.0 | 27.0 |
| 3i | 22.5 | 26.8 | 21.5 | 26.0 | 20.5 | 26.0 |
| 3j | 20.0 | 26.0 | 20.5 | 26.8 | 22.0 | 26.5 |
| 3k | 11.0 | 14.0 | 10.0 | 13.3 | 10.3 | 14.5 |
| 3l | 10.5 | 14.4 | 11.4 | 14.6 | 11.0 | 15.5 |
| 3m | 11.5 | 15.4 | 11.4 | 14.4 | 10.5 | 15.4 |
| GF[b] | 27.0 | 30.0 | 25.0 | 28.0 | 28.0 | 32.0 |

## CONCLUSION

A new series of compounds **2a**–2**m** and **3a-3m** were synthesized and the synthesized compounds were screened for their biological study. The investigation of antimicrobial (antibacterial and antifungal) activities data revealed that the compounds follow the order **(2i > 2h > 2j >2c > 2b> 2d>2g) and (3i > 3j> 3h> 3c> 3d> 3b** and **3f) and** displayed excellent activity; the compounds follow the order (**2e >2f**

**Table 3. Minimal inhibitory concentrations (MIC) in mg/mL of synthesized compounds against bacterial and fungal strains**

| Compound | *E. coli* | *B. subtilis* | *S. typhi* | *A. flavus* | *A.niger* | *F. oxisporium* |
|---|---|---|---|---|---|---|
| 2a | 32 | 44 | 37 | 33 | 39 | 30 |
| 2b | 16 | 21 | 19 | 19 | 23 | 14 |
| 2c | 17 | 18 | 17 | 17 | 21 | 14 |
| 2d | 18 | 19 | 18 | 19 | 22 | 15 |
| 2e | 21 | 23 | 21 | 22 | 27 | 16 |
| 2f | 20 | 23 | 20 | 23 | 25 | 16 |
| 2g | 22 | 24 | 21 | 25 | 24 | 16 |
| 2h | 14 | 16 | 13 | 15 | 17 | 11 |
| 2i | 14 | 15 | 13 | 14 | 16 | 11 |
| 2j | 15 | 16 | 14 | 12 | 15 | 10 |
| 2k | 27 | 37 | 31 | 22 | 35 | 20 |
| 2l | 25 | 38 | 26 | 21 | 32 | 18 |
| 2m | 26 | 27 | 30 | 23 | 31 | 18 |
| 3a | 30 | 45 | 38 | 33 | 38 | 31 |
| 3b | 17 | 19 | 18 | 17 | 18 | 11 |
| 3c | 18 | 20 | 18 | 15 | 19 | 10 |
| 3d | 19 | 21 | 21 | 19 | 19 | 11 |
| 3e | 20 | 22 | 20 | 20 | 27 | 13 |
| 3f | 21 | 21 | 21 | 18 | 26 | 14 |
| 3g | 21 | 20 | 21 | 19 | 28 | 13 |
| 3h | 12 | 15 | 13 | 12 | 13 | 09 |
| 3i | 13 | 15 | 12 | 12 | 13 | 08 |
| 3j | 14 | 16 | 14 | 13 | 14 | 08 |
| 3k | 26 | 36 | 30 | 22 | 34 | 19 |
| 3l | 25 | 37 | 26 | 21 | 33 | 17 |
| 3m | 25 | 35 | 29 | 23 | 32 | 17 |
| Streptomycin | 9 | 13 | 11 | --- | --- | ---- |
| Griseofulvin | --- | --- | --- | 9 | 11 | 03 |

**> 2m > 2k)** and (**3e** > **3g> 3m >3k )** displayed moderate activity and the other compounds showed less activity compared with standard drugs.

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