Synthesis of 2-(3-methyl-2-oxoquinoxalin-1(2H)-yl)acetamide Based Thiazolidinone Derivatives as Potent Antibacterial and Antifungal Agents

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Abstract: Twelve compounds belonging to series 2-(3-methyl-2-oxoquinoxalin-1(2H)-yl)-N-[4-oxo-2-(substituted)phenyl]-1,3-thiazolidin-3-yl]acetamide (**5a-l**) were synthesized. These compounds were evaluated for their *in-vitro* antibacterial against *E. coli*, *S. aureus*, *K. pneumoniae*, *P. aeruginosa* & antifungal activity against *C. albicans*, *A. niger* & *A. flavus* by cup-plate method. Structures of all the newly synthesized compounds were confirmed by elemental analysis, ¹H-NMR & FT-IR spectral data interpretation. Compounds **5d** & **5h** having *p*-nitrophenyl & *p*-trifluoromethylphenyl group respectively on 2-position of thiazolidinone ring attached to N-atom of acetamido group on 1-position of 3-methyl-1H-quinoxaline-2-one, were found to be active against all the bacterial & fungal strains under investigation, while compound **5l** having *p*-chlorophenyl on 2-position of thiazolidinone nucleus was reported as least active compound against all bacterial & fungal strain under investigation.

Keywords: Quinoxaline, Thiazolidinone, Antibacterial, Antifungal.

Introduction

Nitrogen containing heterocyclic compounds are indispensable structural units for both the chemists & biochemists. Among the various classes of benzene fused six-membered

nitrogen containing heterocyclic compounds, quinoxaline derivatives form important classes of pharmacologically active compounds. Quinoxaline ring is a part of various antibiotics such as hinomycin, levomycin, and actinoleutin that are known to inhibit growth of gram positive bacteria and are active against various transplantable tumors.¹⁻⁷ Quinoxaline derivatives have also been found to be associated with a wide variety of biological activities including antifungal⁸⁻¹⁰, antibacterial¹⁰⁻¹⁴, antitubercular^{8,9,15-18}, anti-inflammatory agents¹⁹. Further hydrazinoquinoxalines & their cyclic analogues have been reported as antimicrobial agents²⁰. Five member nitrogen & sulphur containing thiazolidinone ring attached with other heterocyclic system have also been found to be associated with wide spectrum of pharmacological activities viz. antibacterial^{21,22,25,26}, antifungal²², anti-inflammatory²³, antitumor²⁴, anti-HIV²⁵, etc.

Keeping the above facts in view, it was thought worthwhile to design the synthesis of compound series viz. 2-(3-methyl-2-oxoquinoxalin-1(2*H*)-yl)-*N*-[4-oxo-2-(substituted)phenyl-1,3-thiazolidin-3-yl]acetamide (5a-l) wherein thiazolidinone rings have been attached to quinoxaline at 1 position with an acetamido amino linkage. All the synthesized have been screened for *in-vitro* antibacterial activity against gram positive bacteria *Staphylococcus aureus* (ATCC2913), gram negative bacteria *Klebsella pneumoniae* (ATCC700603), *Pseudomonas aeruginosa* (ATCC27853), *Escherichia coli* (ATCC25922) & antifungal activity against *Candida albicans* (MTCC3017), *Aspergillus niger* (MTCC281) and *Aspergillus flavus* (MTCC222) by using cup-plate method.

Experimental

General

Melting points were determined in open capillary tubes in a Hicon melting point apparatus and are uncorrected. All the Fourier Transform-Infra Red (FT-IR) spectra were recorded in KBr pellets on a Shimadzu-8400S spectrometer. The ¹H-NMR spectra were taken on a Bruker-Spectrospin DCX (300 MHz) NMR spectrometer. Chemical shifts (δ) are expressed in ppm relative to tetramethylsilane (TMS), used as an internal standard. The purity of the compounds was checked by thin layer chromatography (TLC) on Merck Silica Gel 60_{F254} precoated sheets. Iodine chamber and UV lamp were used for the visualization of TLC spots.

General procedure for the synthesis of titled compounds

3-Methyl-1*H*-quinoxaline-2-one (1): Pyruvic acid (0.1 mol) and *o*-phenylenediamine (0.1 mol), in 20% HCl (100 ml), were mixed properly and heated at 45°C with continuous stirring for about 5 hours. Product was filtered, dried and washed with water, dried and then purified by dissolving in 5% w/v NaOH (75 ml). Then, liquid was filtered and cooled to temperature below 5°C and acidified with glacial acetic acid to pH 6. Buff colored crystals appeared & then recrystallized with dimethylformamide (DMF). Pale yellow crystals, yield 60%, *R_f* (Ethylacetate : Hexane = 7 : 3) 0.73, m.p. 230°C, ¹H-NMR (DMSO-*d*₆, 300 MHz, δ ppm) : 7.624-7.651 (d, 1H, quinoxaline ring protons, *J* = 8.1 Hz), 7.391-7.441 (t, 1H, quinoxaline ring protons, *J* = 5.4-9.6 Hz), 7.188-7.250 (m, 2H, quinoxaline ring protons, *J* = 2.7-7.5 Hz), 2.364 (s, 3H, CH₃), 9.1 (s, 1H, NHCO); IR (KBr, cm⁻¹): 762 (*ortho*-disubstituted aromatic ring), 1390 (C-N), 1500 (aromatic C=C), 1544 (-NH), 1688 (>C=O), 3314 (-NH).

Ethyl-[3-methyl-2-oxo-quinoxaline-1-yl]acetate (2): Compound (1) (0.0642 mol), ethylchloroacetate (0.077 mol) and potassium carbonate (0.078 mol) were taken in round bottom flask and refluxed in acetone (100 ml) for 6 hours. After completion of reaction, acetone was removed by reduced pressure. The residue was added to ice cold water (300

ml), acidified with acetic acid, filtered, washed with cold water, dried and finally recrystallized with ethylacetate. Pale yellow crystals, yield 45%, R_f (Ethylacetate : Hexane = 7 : 3) 0.64, m.p. 112°C, $^1\text{H-NMR}$ (DMSO- d_6 , 300 MHz, δ ppm) : 7.739-7.766 (d, 1H, quinoxaline ring protons, J = 8.1 Hz), 7.532-7.559 (t, 1H, quinoxaline ring protons, J = 3.9-4.2 Hz), 7.436-7.46 (d, 1H, quinoxaline ring protons, J = 3 Hz), 7.314-7.364 (t, 1H, quinoxaline ring protons, J = 6.6-8.4 Hz), 4.118-4.189 (q, 2H, CH_2OCO), 3.386 (s, 2H, CH_2CO), 2.397 (s, 3H, CH_3), 1.149-1.196 (t, 3H, CH_3); IR (KBr, cm^{-1}): 763 (*ortho*-disubstituted aromatic ring), 962 (aromatic =C-H, bend), 1199 (=C-N), 1285 (C-O, coupled with H-C-H), 1380 (C-N), 1645 (CH=N), 1750 (>C=O), 2745 (C-C).

3-Methyl-2-oxo-quinoxaline-1(2H)-acetohydrazide (3): Compound 2 (0.02 mol) and hydrazine hydrate (0.03 mol) were dissolved in ethanol (50 ml) and refluxed for 6 hours. Reaction mixture was kept in deep freezer for overnight. Product was filtered, dried and finally recrystallized with DMF. Biege colored solid, yield 50%, R_f (TEF) 0.9, m.p. 200°C, $^1\text{H-NMR}$ (DMSO- d_6 , 300 MHz, δ ppm) : 7.729-7.755 (d, 1H, quinoxaline ring protons, J = 7.8 Hz), 7.494-7.545 (t, 1H, quinoxaline ring protons, J = 6.3-9 Hz), 7.262-7.354 (q, 2H, quinoxaline ring protons, J = 7.5-10.2 Hz), 4.843 (s, 2H, NHNH_2 , exchangeable protons), 4.284 (s, 2H, CH_2CO), 2.432 (s, 3H, CH_3); IR (KBr, cm^{-1}): 760 (*ortho*-disubstituted aromatic ring), 963 (aromatic =C-H, bend), 1198 (=C-N), 1385 (C-N), 1569 (-NH, bend), 1645 (CH=N), 1749 (>C=O), 2320 (N-N), 3245 (-NH. str.).

2-(3-Methyl-2-oxoquinoxalin-1(2H)-yl)-N'-[(substituted)phenylmethylidene]acetohydrazide (4a-l): Equimolar quantities of compound 3 (0.0044 mol) and aromatic aldehydes (0.0045 mol) were dissolved in methanol (25 ml) and refluxed for 6 hours. A solid appears with vigorous bumping in each case. Solid was filtered, washed with cold methanol, dried and recrystallized with DMF.

N'-benzylidene-2-(3-methyl-2-oxoquinoxalin-1(2H)-yl)acetohydrazide (4a): Light yellow solid, yield 54%, R_f (Benzene : Acetone = 8 : 2) 0.85, m.p. 234°C, $^1\text{H-NMR}$ (DMSO- d_6 , 300 MHz, δ ppm) : 8.061 (s, 1H, NHCO), 7.678-7.776 (m, 4H, quinoxaline ring protons, J = 3-7.5 Hz), 7.418-7.433 (m, 5H, Ar-H, J = 2.7 – 8.1 Hz), 5.425 (s, 2H, CH_2), 5.035 (s, 1H, CH=N), 2.545 (s, 3H, CH_3); IR (KBr, cm^{-1}): 723 (*mono*-substituted aromatic ring), 769 (*ortho*-disubstituted aromatic ring), 854 (aromatic C=C), 964 (aromatic =C-H, bend), 1199 (=C-N), 1388 (C-N), 1542 (-NH, bend), 1650 (CH=N), 1650 (CH=N), 1729 (>C=O), 2345 (N-N=), 3244 (-NH).

N'-(4-chlorobenzylidene)-2-(3-methyl-2-oxoquinoxalin-1(2H)-yl)acetohydrazide (4b): Light yellow solid, yield 48%, R_f (Benzene : Acetone = 8 : 2) 0.72, m.p. 230°C, $^1\text{H-NMR}$ (DMSO- d_6 , 300 MHz, δ ppm) : 8.032-8.067 (q, 4H, A_2B_2 pattern, Ar-H, J = 3.3-3.6 Hz), 8.188 (s, 1H, CONH), 7.578-7.768 (m, 4H, quinoxaline ring protons, J = 2.7-8.1 Hz), 5.425 (s, 2H, CH_2), 5.036 (s, 1H, CH=N), 2.354 (s, 3H, CH_3); IR (KBr, cm^{-1}): 765 (*ortho*-disubstituted aromatic ring), 823 (*para*-disubstituted aromatic ring), 865 (aromatic C=C), 965 (aromatic =C-H, bend), 1129 (Aryl C-Cl), 1203 (=C-N), 1385 (C-N), 1540 (-NH, bend), 1650 (CH=N), 1650 (CH=N), 1740 (>C=O), 2342 (N-N=), 3245 (-NH).

N'-(4-hydroxybenzylidene)-2-(3-methyl-2-oxoquinoxalin-1(2H)-yl)acetohydrazide (4c): Greenish yellow solid, yield 45%, R_f (Benzene : Acetone = 8 : 2) 0.76, m.p. 254°C, $^1\text{H-NMR}$ (DMSO- d_6 , 300 MHz, δ ppm) : 8.028-8.062 (q, 4H, A_2B_2 pattern, Ar-H, J = 3-3.6 Hz), 8.152 (s, 1H, CONH), 7.758-7.876 (m, 4H, quinoxaline ring protons, 2.1-8.4 Hz), 5.325 (s, 2H, CH_2), 5.135 (s, 1H, CH=N), 2.486 (s, 1H, OH), 2.354 (s, 3H, CH_3); IR (KBr, cm^{-1}): 764 (*ortho*-disubstituted aromatic ring), 825 (*para*-disubstituted aromatic ring), 863 (aromatic C=C), 960 (aromatic =C-H, bend), 1198 (=C-N), 1288 (C-O, coupled with H-C-H), 1382 (C-N), 1540 (-NH, bend), 1650 (CH=N), 1650 (CH=N), 1745 (>C=O), 2344 (N-N=), 3250 (-NH), 3675 (phenolic -OH).

2-(3-methyl-2-oxoquinoxalin-1(2H)-yl)-N'-(4-nitrobenzylidene)acetohydrazide

(4d): Grey solid, yield 52%, R_f (Benzene : Acetone = 8 : 2) 0.70, m.p. 220°C, $^1\text{H-NMR}$ (DMSO- d_6 , 300 MHz, δ ppm) : 8.033-0.64 (q, 4H, A_2B_2 pattern, Ar-H, J = 3-3.3 Hz), 8.154 (s, 1H, CONH), 7.778-7.876 (m, 4H, quinoxaline ring protons, J = 2.4-7.5 Hz), 5.525 (s, 2H, CH_2), 5.033 (s, 1H, $\text{CH}=\text{N}$), 2.543 (s, 3H, CH_3); IR (KBr, cm^{-1}): 723 (*ortho*-disubstituted aromatic ring), 829 (*para*-disubstituted aromatic ring), 864 (aromatic $\text{C}=\text{C}$), 969 (aromatic $=\text{C-H}$, bend), 1199 ($=\text{C-N}$), **1369** (aromatic $-\text{NO}_2$ *sym.* str.), 1385 (C-N), 1542 ($-\text{NH}$, bend), **1551** (aromatic $-\text{NO}_2$, *asym.* str.) 1648 ($\text{CH}=\text{N}$), 1748 ($>\text{C}=\text{O}$), 2341 (N-N=), 3247 ($-\text{NH}$).

N'-(4-methoxybenzylidene)-2-(3-methyl-2-oxoquinoxalin-1(2H)-yl)acetohydrazide

(4e): Light yellow solid, yield 43%, R_f (Benzene : Acetone = 8 : 2) 0.80, m.p. 218°C, $^1\text{H-NMR}$ (DMSO- d_6 , 300 MHz, δ ppm) : 8.020-8.052 (d, 4H, Ar-H, J = 9.6 Hz), 8.142 (s, 1H, CONH), 7.578-7.678 (m, 4H, quinoxaline ring protons, J = 2.4-7.5 Hz), 5.525 (s, 2H, CH_2), 5.024 (s, 1H, $\text{CH}=\text{N}$), 3.369 (s, 3H, OCH_3), 2.351 (s, 3H, CH_3); IR (KBr, cm^{-1}): 769 (*ortho*-disubstituted aromatic ring), 825 (*para*-disubstituted aromatic ring), 865 (aromatic $\text{C}=\text{C}$), 964 (aromatic $=\text{C-H}$, bend), **1040** (C-O-C, *sym.* str.), **1129** (aromatic C-O), 1198 ($=\text{C-N}$), **1240** (C-O-C, *asym.* str.), 1388 (C-N), 1540 ($-\text{NH}$, bend), 1648 ($\text{CH}=\text{N}$), 1745 ($>\text{C}=\text{O}$), 2344 (N-N=), 3250 ($-\text{NH}$).

N'-(3,4-dimethoxybenzylidene)-2-(3-methyl-2-oxoquinoxalin-1(2H)-yl)acetohydrazide (4f):

Light yellow solid, yield 40%, R_f (Benzene : Acetone = 8 : 2) 0.72, m.p. 208°C, $^1\text{H-NMR}$ (DMSO- d_6 , 300 MHz, δ ppm) : 8.112 (s, 1H, CONH), 7.812-7.998 (m, 4H, quinoxaline ring protons, J = 2.4-7.5 Hz), 7.775-7.796 (d, 1H, Ar-H, J = 6.3 Hz), 7.672-7.694 (d, 1H, Ar-H, J = 6.6 Hz), 7.625 (s, 1H, Ar-H), 5.335 (s, 2H, CH_2), 5.025 (s, 1H, $\text{CH}=\text{N}$), 3.624 (s, 6H, OCH_3), 2.454 (s, 3H, CH_3); IR (KBr, cm^{-1}): 768 (*ortho*-disubstituted aromatic ring), 830 (*para*-disubstituted aromatic ring), 863 (aromatic $\text{C}=\text{C}$), 965 (aromatic $=\text{C-H}$, bend), **1042** (C-O-C, *sym.* str.), **1132** (aromatic C-O), 1199 ($=\text{C-N}$), **1245** (C-O-C, *asym.* str.), 1385 (C-N), 1545 ($-\text{NH}$, bend), 1650 ($\text{CH}=\text{N}$), 1745 ($>\text{C}=\text{O}$), 2344 (N-N=), 3245 ($-\text{NH}$).

N'-(4-(dimethylamino)benzylidene)-2-(3-methyl-2-oxoquinoxalin-1(2H)-yl)acetohydrazide (4g):

Yellow solid, yield 54%, R_f (Benzene : Acetone = 8 : 2) 0.86, m.p. 228°C, $^1\text{H-NMR}$ (DMSO- d_6 , 300 MHz, δ ppm) : 7.033-7.080 (q, 4H, A_2B_2 pattern, Ar-H, J = 3 – 5.7 Hz), 7.812 (s, 1H, CONH), 7.558-7.678 (m, 4H, quinoxaline ring protons, J = 2.1-8.1 Hz), 5.225 (s, 2H, CH_2), 5.015 (s, 1H, $\text{CH}=\text{N}$), 2.353 (s, 3H, CH_3), 1.832 (s, 6H, N-CH_3); IR (KBr, cm^{-1}): 769 (*ortho*-disubstituted aromatic ring), 830 (*para*-disubstituted aromatic ring), 865 (aromatic $\text{C}=\text{C}$), 968 (aromatic $=\text{C-H}$, bend), 1199 ($=\text{C-N}$), 1384 (C-N), **1550** ($-\text{NH}$, bend), 1648 ($\text{CH}=\text{N}$), 1750 ($>\text{C}=\text{O}$), 2344 (N-N=), 3124 ($-\text{CH}_3$), **3245** ($-\text{NH}$).

2-(3-methyl-2-oxoquinoxalin-1(2H)-yl)-N'-(4-(trifluoromethyl)benzylidene)acetohydrazide (4h):

Light yellow solid, yield 46%, R_f (Benzene : Acetone = 8 : 2) 0.85, m.p. 238°C, $^1\text{H-NMR}$ (DMSO- d_6 , 300 MHz, δ ppm) : 8.184 (s, 1H, CONH), 7.868-8.072 (m, 4H, quinoxaline ring protons, J = 1.8-7.5 Hz), 8.133-8.177 (q, 4H, A_2B_2 pattern, Ar-H, J = 3-5.1 Hz), 5.325 (s, 2H, CH_2), 5.136 (s, 1H, $\text{CH}=\text{N}$), 2.645 (s, 3H, CH_3); IR (KBr, cm^{-1}): 768 (*ortho*-disubstituted aromatic ring), 845 (*para*-disubstituted aromatic ring), 869 (aromatic $\text{C}=\text{C}$), 968 (aromatic $=\text{C-H}$, bend), 1199 ($=\text{C-N}$), **1288** (aryl C-F), 1385 (C-N), 1548 ($-\text{NH}$, bend), 1650 ($\text{CH}=\text{N}$), 1745 ($>\text{C}=\text{O}$), 2344 (N-N=), 3245 ($-\text{NH}$).

N'-(2-hydroxybenzylidene)-2-(3-methyl-2-oxoquinoxalin-1(2H)-yl)acetohydrazide (4i):

Light yellow solid, yield 48%, R_f (Benzene : Acetone = 8 : 2) 0.80, m.p. 248°C, $^1\text{H-NMR}$ (DMSO- d_6 , 300 MHz, δ ppm) : 8.152 (s, 1H, CONH), 7.778-7.876 (m, 4H, quinoxaline ring protons, J = 1.8-6.9 Hz), 7.522-7.538 (d, 1H, Ar-H, J = 4.8 Hz), 7.333-7.359 (d, 1H, Ar-H, J = 7.8 Hz), 7.251-7.288 (t, 2H, Ar-H, J = 4.8 – 5.7 Hz), 5.525 (s, 2H, CH_2), 5.036 (s, 1H, $\text{CH}=\text{N}$), 2.486 (s, 1H, OH), 2.545 (s, 3H, CH_3); IR (KBr, cm^{-1}): 765 (*ortho*-disubstituted aromatic ring), 868 (aromatic $\text{C}=\text{C}$), 969 (aromatic $=\text{C-H}$, bend), 1198 ($=\text{C-N}$), **1258** (C-O,

str.) 1385 (C-N), 1545 (-NH, bend), 1649 (CH=N), 1748 (>C=O), 2340 (N-N=), 3250 (-NH), **3365** (phenolic -OH).

N'-(3-hydroxy-4-methoxybenzylidene)-2-(3-methyl-2-oxoquinoxalin-1(2H)-yl)acetohydrazide (4j): Yellow solid, yield 66%, R_f (Benzene : Acetone = 8 : 2) 0.87, m.p. 188°C, $^1\text{H-NMR}$ (DMSO- d_6 , 300 MHz, δ ppm) : 8.122 (s, 1H, CONH), 7.878-7.978 (m, 4H, quinoxaline ring protons, J = 2.1-8.4 Hz), 7.634 (s, 1H, Ar-H), 7.775-7.812 (t, 1H, Ar-H, J = 3-8.2 Hz), 7.824-7.846 (d, 1H, Ar-H, J = 6.6 Hz), 5.225 (s, 2H, CH₂), 5.125 (s, 1H, CH=N), 2.485 (s, 1H, OH), 2.545 (s, 3H, CH₃), 3.625 (s, 3H, OCH₃); IR (KBr, cm⁻¹): 769 (*ortho*-disubstituted aromatic ring), 849 (*para*-disubstituted aromatic ring), 869 (aromatic C=C), 968 (aromatic =C-H, bend), **1045** (C-O-C, *sym.* str.), **1132** (aromatic C-O), 1199 (=C-N), **1245** (C-O-C, *asym.* str.), 1252 (C-O, str.), 1384 (C-N), 1546 (-NH, bend), 1648 (CH=N), 1749 (>C=O), 2345 (N-N=), 3245 (-NH), **3352** (phenolic -OH).

N'-(2-fluorobenzylidene)-2-(3-methyl-2-oxoquinoxalin-1(2H)-yl)acetohydrazide (4k): Red solid, yield 53%, R_f (Benzene : Acetone = 8 : 2) 0.85, m.p. 248°C, $^1\text{H-NMR}$ (DMSO- d_6 , 300 MHz, δ ppm) : 8.148 (s, 1H, CONH), 7.881-7.986 (m, 4H, quinoxaline ring protons, J = 1.8-7.5 Hz), 7.623-7.651 (d, 1H, Ar-H, J = 8.4 Hz), 7.436-7.461 (d, 1H, Ar-H, J = 7.5 Hz), 7.551-7.592 (t, 2H, Ar-H, J = 2.4-5.1 Hz), 5.136 (s, 2H, CH₂), 5.235 (s, 1H, CH=N), 2.552 (s, 3H, CH₃); IR (KBr, cm⁻¹): 769 (*ortho*-disubstituted aromatic ring), 864 (aromatic C=C), 968 (aromatic =C-H, bend), 1199 (=C-N), **1285** (aryl C-F), 1387 (C-N), 1548 (-NH, bend), 1650 (CH=N), 1745 (>C=O), 2345 (N-N=), 3248 (-NH).

N'-(2-chlorobenzylidene)-2-(3-methyl-2-oxoquinoxalin-1(2H)-yl)acetohydrazide (4l): Light yellow solid, yield 43%, R_f (Benzene : Acetone = 8 : 2) 0.80, m.p. 218°C, $^1\text{H-NMR}$ (DMSO- d_6 , 300 MHz, δ ppm) : 8.136 (s, 1H, CONH), 7.782-7.880 (m, 4H, quinoxaline ring protons, J = 1.8-7.8 Hz), 7.523-7.556 (d, 1H, Ar-H, J = 9.9 Hz), 7.336-7.362 (d, 1H, Ar-H, J = 7.8 Hz), 7.452-7.496 (t, 2H, Ar-H, J = 6.6 Hz), 5.038 (s, 2H, CH₂), 5.136 (s, 1H, CH=N), 2.548 (s, 3H, CH₃); IR (KBr, cm⁻¹): 768 (*ortho*-disubstituted aromatic ring), 865 (aromatic C=C), 968 (aromatic =C-H, bend), **1106** (aryl C-Cl), 1198 (=C-N), 1385 (C-N), 1545 (-NH, bend), 1648 (CH=N), 1752 (>C=O), 2346 (N-N=), 3245 (-NH).

2-(3-methyl-2-oxoquinoxalin-1(2H)-yl)-N-[4-oxo-2-(substituted)phenyl-1,3-thiazolidin-3-yl]acetamide (5a-l): Compound (4a-l) (100 mg) and thioglycolic acid (10 ml) were refluxed on heavy petroleum ether bath at 200°C for 48 hours. Excess of thioglycolic acid was removed by vacuum distillation. Reaction mixture was neutralized with 10% sodium carbonate solution. Precipitate thus obtained was filtered, dried and recrystallized with DMF.

2-(3-methyl-2-oxoquinoxalin-1(2H)-yl)-N-(4-oxo-2-phenyl-1,3-thiazolidin-3-yl)acetamide (5a): Brown solid, yield 48%, R_f (TEF) 0.80, m.p. 200°C, $^1\text{H-NMR}$ (DMSO- d_6 , 300 MHz, δ ppm) : 8.124 (s, 1H, NHCO), 7.716-7.798 (m, 4H, quinoxaline ring protons, J = 1.8-7.2 Hz), 7.515-7.599 (m, 5H, Ar-H, J = 1.5-7.5 Hz), 5.406 (s, 2H, CH₂), 2.320 (s, 3H, CH₃), 3.745 (s, 1H, CH-Ar), 2.512 (s, 2H, CH₂-S); IR (KBr, cm⁻¹): 726 (*mono*-substituted aromatic ring), 762 (*ortho*-disubstituted aromatic ring), **799** (C-S, str.), 856 (aromatic C=C), 962 (aromatic =C-H, bend), 1199 (=C-N), 1385 (C-N), 1545 (-NH, bend), 1745 (>C=O), 3245 (-NH).

N-[2-(4-chlorophenyl)-4-oxo-1,3-thiazolidin-3-yl]-2-(3-methyl-2-oxoquinoxalin-1(2H)-yl)acetamide (5b): Brown solid, yield 51%, R_f (TEF) 0.81, m.p. 212°C, $^1\text{H-NMR}$ (DMSO- d_6 , 300 MHz, δ ppm) : 8.118 (s, 1H, NHCO), 7.712-7.794 (m, 4H, quinoxaline ring protons, J = 1.8-7.8 Hz), 7.527-7.581 (q, 4H, A₂B₂ pattern, Ar-H, J = 3-5.1 Hz), 5.410 (s, 2H, CH₂), 2.311 (s, 3H, CH₃), 3.788 (s, 1H, CH-Ar), 2.518 (s, 2H, CH₂-S); IR (KBr, cm⁻¹): 762 (*ortho*-disubstituted aromatic ring), **799** (C-S, str.), 837 (*para*-disubstituted aromatic ring), 852 (aromatic C=C), 966 (aromatic =C-H, bend), **1041** (aryl C-Cl, str.), 1198 (=C-N), 1388 (C-N), 1549 (-NH, bend), 1748 (>C=O), 3225 (-NH).

***N*-[2-(4-hydroxyphenyl)-4-oxo-1,3-thiazolidin-3-yl]-2-(3-methyl-2-oxoquinoxalin-1(2*H*)-yl)acetamide (5c):** Brown solid, yield 45%, $R_f(\text{TEF})$ 0.78, m.p. 215°C, $^1\text{H-NMR}$ (DMSO- d_6 , 300 MHz, δ ppm) : 8.128 (s, 1H, NHCO), 7.718-7.795 (m, 4H, quinoxaline ring protons, $J = 1.5$ -7.2 Hz), 7.427-7.494 (m, 4H, Ar-H, $J = 2.1$ -6.9 Hz), 5.418 (s, 2H, CH₂), 2.308 (s, 3H, CH₃), 3.772 (s, 1H, CH-Ar), 2.516 (s, 2H, CH₂-S), 3.261 (s, 1H, phenolic -OH); IR (KBr, cm⁻¹): 765 (*ortho*-disubstituted aromatic ring), 795 (C-S, str.), 838 (*para*-disubstituted aromatic ring), 851 (aromatic C=C), 969 (aromatic =C-H, bend), 1199 (=C-N), 1257 (C-O, str.), 1385 (C-N), 1555 (-NH, bend), 1732 (>C=O), 3240 (-NH), 3362 (phenolic -OH, str.).

2-(3-methyl-2-oxoquinoxalin-1(2*H*)-yl)-*N*-[2-(4-nitrophenyl)-4-oxo-1,3-thiazolidin-3-yl]acetamide (5d): Brown solid, yield 45%, $R_f(\text{TEF})$ 0.78, m.p. 215°C, $^1\text{H-NMR}$ (DMSO- d_6 , 300 MHz, δ ppm) : 8.132 (s, 1H, NHCO), 7.715-7.799 (m, 4H, quinoxaline ring protons, $J = 1.5$ -6.9 Hz), 7.456-7.489 (q, 4H, A₂B₂ pattern, Ar-H, $J = 3$ -3.9 Hz), 5.409 (s, 2H, CH₂), 2.308 (s, 3H, CH₃), 3.781 (s, 1H, CH-Ar), 2.532 (s, 2H, CH₂-S); IR (KBr, cm⁻¹): 769 (*ortho*-disubstituted aromatic ring), 798 (C-S, str.), 835 (*para*-disubstituted aromatic ring), 854 (aromatic C=C), 965 (aromatic =C-H, bend), 1197 (=C-N), 1342 (*sym.* aromatic -NO₂), 1388 (C-N), 1518 (*asym.* aromatic -NO₂, str.), 1542 (-NH, bend), 1749 (>C=O), 3245 (-NH).

***N*-[2-(4-methoxyphenyl)-4-oxo-1,3-thiazolidin-3-yl]-2-(3-methyl-2-oxoquinoxalin-1(2*H*)-yl)acetamide (5e):** Brown solid, yield 62%, $R_f(\text{TEF})$ 0.80, m.p. 223°C, $^1\text{H-NMR}$ (DMSO- d_6 , 300 MHz, δ ppm) : 8.124 (s, 1H, NHCO), 7.710-7.792 (m, 4H, quinoxaline ring protons, $J = 1.5$ -7.2 Hz), 7.426-7.488 (m, 4H, Ar-H, $J = 3$ -5.1 Hz), 5.411 (s, 2H, CH₂), 2.298 (s, 3H, CH₃), 3.755 (s, 1H, CH-Ar), 2.518 (s, 2H, CH₂-S), 2.380 (s, 3H, -OCH₃); IR (KBr, cm⁻¹): 764 (*ortho*-disubstituted aromatic ring), 792 (C-S, str.), 838 (*para*-disubstituted aromatic ring), 856 (aromatic C=C), 967 (aromatic =C-H, bend), 1092 (*sym.* C-O-C, str.), 1145 (aromatic C-O, str.), 1199 (=C-N), 1248 (*asym.* C-O-C, str.), 1381 (C-N), 1545 (-NH, bend), 1751 (>C=O), 3254 (-NH).

***N*-[2-(3,4-dimethoxyphenyl)-4-oxo-1,3-thiazolidin-3-yl]-2-(3-methyl-2-oxoquinoxalin-1(2*H*)-yl)acetamide (5f):** Brown solid, yield 65%, $R_f(\text{TEF})$ 0.72, m.p. 173°C, $^1\text{H-NMR}$ (DMSO- d_6 , 300 MHz, δ ppm) : 8.118 (s, 1H, NHCO), 7.718-7.788 (m, 4H, quinoxaline ring protons, $J = 1.8$ -7.5 Hz), 7.410-7.432 (d, 1H, Ar-H, $J = 6.6$ Hz), 7.465-7.487 (d, 1H, Ar-H, $J = 6.6$ Hz), 7.372-7.396 (d, 1H, Ar-H, $J = 7.2$ Hz), 5.413 (s, 2H, CH₂), 2.301 (s, 3H, CH₃), 3.749 (s, 1H, CH-Ar), 2.517 (s, 2H, CH₂-S), 2.384 (s, 6H, -OCH₃); IR (KBr, cm⁻¹): 762 (*ortho*-disubstituted aromatic ring), 790 (C-S, str.), 842 (*para*-disubstituted aromatic ring), 858 (aromatic C=C), 965 (aromatic =C-H, bend), 1088 (*sym.* C-O-C, str.), 1148 (aromatic C-O, str.), 1195 (=C-N), 1248 (*asym.* C-O-C, str.), 1380 (C-N), 1549 (-NH, bend), 1753 (>C=O), 3248 (-NH).

***N*-[2-(4-dimethylaminophenyl)-4-oxo-1,3-thiazolidin-3-yl]-2-(3-methyl-2-oxoquinoxalin-1(2*H*)-yl)acetamide (5g):** Brown solid, yield 64%, $R_f(\text{TEF})$ 0.82, m.p. 205°C, $^1\text{H-NMR}$ (DMSO- d_6 , 300 MHz, δ ppm) : 8.119 (s, 1H, NHCO), 7.719-7.801 (m, 4H, quinoxaline ring protons, $J = 1.8$ -7.5 Hz), 7.424-7.482 (q, 4H, A₂B₂ pattern, Ar-H, $J = 3$ -7.2 Hz), 5.408 (s, 2H, CH₂), 2.296 (s, 3H, CH₃), 3.745 (s, 1H, CH-Ar), 2.515 (s, 2H, CH₂-S), 2.374 (s, 6H, -N(CH₃)₂); IR (KBr, cm⁻¹): 766 (*ortho*-disubstituted aromatic ring), 791 (C-S, str.), 840 (*para*-disubstituted aromatic ring), 862 (aromatic C=C), 965 (aromatic =C-H, bend), 1198 (=C-N), 1385 (C-N), 1552 (-NH, bend), 1748 (>C=O), 3250 (-NH).

2-(3-methyl-2-oxoquinoxalin-1(2*H*)-yl)-*N*-[4-oxo-2-[4-(trifluoromethyl)phenyl]-1,3-thiazolidin-3-yl]acetamide (5h): Brown solid, yield 68%, $R_f(\text{TEF})$ 0.83, m.p. 235°C, $^1\text{H-NMR}$ (DMSO- d_6 , 300 MHz, δ ppm) : 8.121 (s, 1H, NHCO), 7.719-7.888 (m, 4H, quinoxaline ring protons, $J = 1.8$ -7.2 Hz), 7.512-7.466 (q, 4H, A₂B₂ pattern, Ar-H, $J = 3$ -6.6 Hz), 5.416 (s, 2H, CH₂), 2.302 (s, 3H, CH₃), 3.761 (s, 1H, CH-Ar), 2.518 (s, 2H, CH₂-S); IR

(KBr, cm^{-1}): 768 (*ortho*-disubstituted aromatic ring), 792 (C-S, str.), 845 (*para*-disubstituted aromatic ring), 861 (aromatic C=C), 962 (aromatic =C-H, bend), 1188 (=C-N), 1287 (aryl C-F, str.), 1392 (C-N), 1565 (-NH, bend), 1752 (>C=O), 3248 (-NH).

***N*-[2-(2-hydroxyphenyl)-4-oxo-1,3-thiazolidin-3-yl]-2-(3-methyl-2-oxoquinoxalin-1(2*H*)-yl)acetamide (5i):** Light brown solid, yield 58%, $R_f(\text{TEF})$ 0.74, m.p. 195°C, $^1\text{H-NMR}$ (DMSO- d_6 , 300 MHz, δ ppm) : 8.120 (s, 1H, NHCO), 7.715-7.792 (m, 4H, quinoxaline ring protons, $J = 1.5$ -7.8 Hz), 7.315-7.344 (dd, 2H, Ar-H), 7.409-7.445 (d, 1H, Ar-H, $J = 7.8$ Hz), 7.328-7.363 (t, 1H, Ar-H, $J = 3.3$ -7.2 Hz), 5.411 (s, 2H, CH_2), 2.291 (s, 3H, CH_3), 3.738 (s, 1H, CH-Ar), 2.518 (s, 2H, CH_2 -S), 2.824 (s, 1H, phenolic -OH); IR (KBr, cm^{-1}): 766 (*ortho*-disubstituted aromatic ring), 792 (C-S, str.), 864 (aromatic C=C), 963 (aromatic =C-H, bend), 1199 (=C-N), 1381 (C-N), 1550 (-NH, bend), 1752 (>C=O), 3255 (-NH), 3567 (phenolic -OH).

***N*-[2-(3-Hydroxy-4-methoxyphenyl)-4-oxo-1,3-thiazolidin-3-yl]-2-(3-methyl-2-oxoquinoxalin-1(2*H*)-yl)acetamide (5j):** Light brown solid, yield 70%, $R_f(\text{TEF})$ 0.78, m.p. 285°C, $^1\text{H-NMR}$ (DMSO- d_6 , 300 MHz, δ ppm) : 8.118 (s, 1H, NHCO), 7.715-7.798 (m, 4H, quinoxaline ring protons, $J = 1.8$ -8.1 Hz), 7.311-7.337 (t, 1H, Ar-H, $J = 1.8$ -6 Hz), 7.410 (s, 1H, Ar-H), 7.377-7.398 (d, 1H, Ar-H, $J = 6.3$ Hz), 5.418 (s, 2H, CH_2), 2.288 (s, 3H, CH_3), 3.741 (s, 1H, CH-Ar), 2.519 (s, 2H, CH_2 -S), 2.817 (s, 1H, phenolic -OH), 3.311 (s, 3H, -OCH₃); IR (KBr, cm^{-1}): 764 (*ortho*-disubstituted aromatic ring), 789 (C-S, str.), 865 (aromatic C=C), 964 (aromatic =C-H, bend), 1201 (=C-N), 1285 (C-O, str. coupled with H-C-H), 1385 (C-N), 1552 (-NH, bend), 1752 (>C=O), 3251 (-NH), 3542 (phenolic -OH).

***N*-[2-(2-fluorophenyl)-4-oxo-1,3-thiazolidin-3-yl]-2-(3-methyl-2-oxoquinoxalin-1(2*H*)-yl)acetamide (5k):** Dark brown solid, yield 50%, $R_f(\text{TEF})$ 0.76, m.p. 235°C, $^1\text{H-NMR}$ (DMSO- d_6 , 300 MHz, δ ppm) : 8.132 (s, 1H, NHCO), 7.715-7.812 (m, 4H, quinoxaline ring protons, $J = 1.2$ -8.1 Hz), 7.322-7.381 (dd, 2H, Ar-H), 7.411-7.446 (d, 1H, Ar-H, $J = 10.5$ Hz), 7.569-7.602 (t, 1H, Ar-H, $J = 3.3$ -6.6 Hz), 5.418 (s, 2H, CH_2), 2.288 (s, 3H, CH_3), 3.745 (s, 1H, CH-Ar), 2.522 (s, 2H, CH_2 -S); IR (KBr, cm^{-1}): 768 (*ortho*-disubstituted aromatic ring), 795 (C-S, str.), 868 (aromatic C=C), 962 (aromatic =C-H, bend), 1199 (=C-N), 1285 (aryl C-F, str.), 1385 (C-N), 1541 (-NH, bend), 1747 (>C=O), 3199 (-NH).

***N*-[2-(2-chlorophenyl)-4-oxo-1,3-thiazolidin-3-yl]-2-(3-methyl-2-oxoquinoxalin-1(2*H*)-yl)acetamide (5l):** Light brown solid, yield 52%, $R_f(\text{TEF})$ 0.78, m.p. 225°C, $^1\text{H-NMR}$ (DMSO- d_6 , 300 MHz, δ ppm) : 8.133 (s, 1H, NHCO), 7.710-7.798 (m, 4H, quinoxaline ring protons, $J = 1.2$ -8.1 Hz), 7.318-7.345 (dd, 2H, Ar-H), 7.408-7.435 (d, 1H, Ar-H, $J = 8.1$ Hz), 7.355-7.389 (t, 1H, Ar-H, $J = 3$ -7.2 Hz), 5.412 (s, 2H, CH_2), 2.287 (s, 3H, CH_3), 3.735 (s, 1H, CH-Ar), 2.525 (s, 2H, CH_2 -S); IR (KBr, cm^{-1}): 765 (*ortho*-disubstituted aromatic ring), 793 (C-S, str.), 872 (aromatic C=C), 965 (aromatic =C-H, bend), 1132 (aryl C-Cl, str.), 1201 (=C-N), 1286 (aryl C-F, str.), 1383 (C-N), 1541 (-NH, bend), 1747 (>C=O), 3199 (-NH).

Antibacterial & Antifungal Activity

All the synthesized have been screened for *in-vitro* antibacterial activity against gram positive bacteria *S. aureus* (ATCC2913), gram negative bacteria *K. pneumonia* (ATCC700603), *P. aeruginosa* (ATCC27853), *E. coli* (ATCC25922) and antifungal activity against *C. albicans* (MTCC3017), *A. niger* (MTCC281) and *A. flavus* (MTCC277) by using cup-plate method.

The growth media (Nutrient Agar media for bacterial growth & Sabouraud Dextrose Agar media for fungal growth) were prepared & sterilized in autoclave at 15 psig for 15 minutes. These media were poured into petri-plates under standard conditions & allowed to solidify. On the surface of media, test microorganisms were inoculated with sterilized nickel loop wire. Cups were made by boring on the surface of growth media with previously sterilized borer. Four cups were made on each petri-plate. These cups were filled with

different concentrations (50 µg/mL & 100 µg/mL in DMSO) of the test compounds, third with control (DMSO) & fourth one with standard drug. The plates were kept in cold for 1 hour to allow the diffusion of test compounds & then incubated at 35°C for 48 hours (for antifungal activity) & at 37°C for 24 hours (for antibacterial activity). The zones of inhibition formed around the cups after respective incubation were measured.

Results and Discussion

All the newly synthesized compounds have been evaluated for their antibacterial activity against *E. coli*, *S. aureus*, *K. pneumoniae*, *P. aeruginosa* and antifungal activity against *C. albicans*, *A. niger* and *A. flavus*. In the present communication, we have concentrated on “the effect of various substituents on phenyl ring attached to 2-position of thiazolidinone nucleus attached to N-atom of acetamido functionality on 1-position of 3-methyl-2-oxo-quinoxaline-1(2*H*)-acetamide”. Against *E. coli*, compounds with functionalities 4-Cl (**5b**), 4-OH (**5c**), 4-NO₂ (**5d**), 4-N(CH₃)₂ (**5g**), 4-CF₃ (**5h**), 2-F (**5k**) on phenyl ring attached to 2-position of thiazolidinone nucleus attached to above mentioned position in basic scaffold have exhibited maximal activity. Compound **5i** having -OH group at *ortho*-position on phenyl group at above mentioned position exhibited minimal activity. Thiazolidinone nucleus with electron withdrawing functional groups 4-Cl (**5b**), 4-OH (**5c**), 4-NO₂ (**5d**), 4-CF₃ (**5h**), 3-OH-4-OCH₃ (**5j**) and 2-F (**5k**) have shown good activity against *S. aureus*. However, -OH group at *ortho*-position of phenyl ring (**5i**) on 2-position of thiazolidinone ring exhibited minimal activity against *S. aureus*. Compounds with electron donating groups 4-OCH₃ (**5e**), 3,4-(OCH₃)₂ (**5f**) exhibited moderate activity against *S. aureus*. Against *K. pneumoniae*, compounds with functional groups 4-Cl (**5b**), 4-OH (**5c**), 4-NO₂ (**5d**), 4-N(CH₃)₂ (**5g**), 4-CF₃ (**5h**) on phenyl ring attached to 2-position of thiazolidinone ring exhibited fantastic activity. Additionally, among thiazolidinone derivatives, compounds with 4-OCH₃ (**5e**), 3-OH-4-OCH₃ (**5j**) on above mentioned position also exhibited better activity. Compounds **5f** and **5l** having 3,4-(OCH₃)₂-C₆H₃ and 2-Cl-C₆H₄ on 2-position of thiazolidinone ring respectively have shown minimal activity against *K. pneumoniae*. Most of newly synthesized compounds have shown good antibacterial activity against *P. aeruginosa*. Compounds having 4-Cl (**5b**), 4-OH (**5c**), 4-NO₂ (**5d**), 4-N(CH₃)₂ (**5g**), 4-CF₃ (**5h**), and 3-OH-4-OCH₃ (**5j**) on phenyl ring attached to above mentioned positions at thiazolidinone ring exhibited better activity. Thiazolidinone derivatives with 3,4-(OCH₃)₂-C₆H₃ (**5f**) and 2-Cl-C₆H₄ (**5l**) exhibited minimal activity.

Against fungal strains *C. albicans*, *A. niger*, *A. flavus*, most of the newly synthesized compound exhibited moderate activity. Against *C. albicans* compounds **5a**, **5b**, **5c**, **5d**, **5g** and **5h** having unsubstituted phenyl ring, 4-Cl-C₆H₄, 4-OH-C₆H₄, 4-NO₂-C₆H₄, 4-N(CH₃)₂-C₆H₄ and 4-CF₃-C₆H₄ groups in respective position exhibited fantastic activity. However, compound **5k** and **5l** having halogens F and Cl on *ortho*-positions on phenyl ring attached to 2-position of thiazolidinone ring exhibited minimal activity. Against *A. niger*, thiazolidinone derivatives, **5d**, **5h** and **5j** having 4-NO₂, 4-CF₃ and 3-OH-4-OCH₃ groups on phenyl ring were found to be more active. Thiazolidinone derivatives, **5i**, **5k** and **5l** having 2-OH, 2-F and 2-Cl on phenyl ring attached to 2-position of thiazolidinone ring exhibited minimal activity. Compounds with 4-Cl-C₆H₄ (**5b**), 4-OH-C₆H₄ (**5c**), 4-NO₂-C₆H₄ (**5d**) and 4-CF₃-C₆H₄ (**5h**), have shown better activity, while compounds with 3,4-(OCH₃)₂-C₆H₃ (**5f**), 2-OH-C₆H₄ (**5i**), 2-F-C₆H₄ (**5k**) and 2-Cl-C₆H₄ (**5l**) were reported as minimal active compounds. Against *A. flavus*, among thiazolidinone derivatives, **5b**, **5c**, **5d**, **5g** and **5h** with 4-Cl, 4-OH, 4-NO₂, 4-N(CH₃)₂ and 4-CF₃ substitutions on phenyl ring attached to N-atom of acetamido group on first position of 3-methyl-2-oxo-quinoxaline-1(2*H*)-acetamide exhibited fantastic activity against all bacterial strains under investigation.

Table 1. Zone of inhibition (mm) of different compounds.

Compound	<i>E. coli</i>		<i>S. aureus</i>		<i>K. pneumoniae</i>		<i>P. aeruginosa</i>		<i>C. albicans</i>		<i>A. niger</i>		<i>A. flavus</i>	
	50 µg/ml	100 µg/ml	50 µg/ml	100 µg/ml	50 µg/ml	100 µg/ml	50 µg/ml	100 µg/ml	50 µg/ml	100 µg/ml	50 µg/ml	100 µg/ml	50 µg/ml	100 µg/ml
5a	11	18	10	17	10	16	11	20	12	22	11	19	11	20
6b	13	22	13	21	14	24	14	25	12	21	11	19	13	23
6c	12	21	13	23	14	25	14	24	13	22	11	20	12	21
6d	13	23	13	23	13	22	13	23	12	21	13	23	13	20
6e	09	16	11	19	12	21	11	19	11	20	09	14	09	15
6f	10	17	09	16	08	14	09	14	10	18	10	17	08	13
6g	13	22	12	21	13	23	14	24	14	24	11	18	10	17
6h	14	25	14	24	14	24	14	25	14	24	13	22	14	24
6i	07	12	07	11	09	15	08	13	09	14	08	13	08	14
6j	11	18	13	22	12	21	12	22	11	20	12	21	10	18
6k	12	22	11	20	11	19	11	18	08	14	09	15	08	14
6l	09	16	09	15	07	12	08	14	07	12	07	11	08	14
Standard	27		28		27		27		26		26		25	
Control	02		02		02		02		02		03		02	

Standard Drugs:

For antibacterial activity: Ciprofloxacin, 30 µg/ml.

For antifungal activity: Voriconazole, 30 µg/ml.

Control: DMSO.

Compounds **5d** and **5h** were found to be more active against all fungal strains under investigation. Compounds **5d** and **5h** were also found to be more active against all bacterial and fungal strains under investigation. Compound **5l** having 2-Cl group on phenyl ring attached to 4-position of thiazolidinone ring showed minimal activity against all bacterial and fungal strains.

Conclusion

All the synthesized compounds were evaluated for their antibacterial activity against *E. coli*, *S. aureus*, *P. aeruginosa*, *K. pneumoniae* and antifungal activity against *C. albicans*, *A. niger* and *A. flavus* using cup-plate method. 2-(3-Methyl-2-oxoquinoxalin-1(2H)-yl)acetamide based thiazolidinone derivatives having aromatic phenyl ring substituted with 4-Cl, 4-OH, 4-NO₂, 4-N(CH₃)₂ and 4-CF₃ exhibited fantastic activity against all the bacterial strains under investigation. 2-(3-Methyl-2-oxoquinoxalin-1(2H)-yl)acetamide based thiazolidinone derivatives having aromatic phenyl ring substituted with 4-NO₂ and 4-CF₃ have exhibited better activity against all bacteria and fungi under investigation. These compounds may act as lead for future investigation.

Compound	4a, 5a	4b, 5b	4c, 5c	4d, 5d	4e, 5e	4f, 5f	4g, 5g	4h, 5h	4i, 5i	4j, 5j	4k, 5k	4l, 5l
R	H	4-Cl	4-OH	4-NO ₂	4-OMe	3,4-(OMe) ₂	4-NMe ₂	4-CF ₃	2-OH	3-OH-4-OMe	2-F	2-Cl

Reagents & Conditions: (i) 20%, HCl, 45-50°C, stirring (ii) ClCH₂COOEt, acetone, 40°C, reflux (iii) NH₂NH₂·H₂O, MeOH, reflux (iv) RCHO, EtOH, reflux (v) HSCH₂COOH, reflux in heavy petroleum ether bath

Figure 1. Reaction Scheme.

Graphical Representation

References

- Grande F, Aiello F, Grazia O D, Brizz,i A, Garofalo A, Neamati N, *Bioorg. Med. Chem.* 2007, **15**, 288.
- Amin K M, Ismail M M F, Noaman E, Soliman D H, Ammar Y A, *Bioorg. Med. Chem.* 2006, **14**, 6917.
- Zarranz B, Jaso A, Aldana I, Monge A, *Bioorg. Med. Chem.* 2004, **12**, 3711.
- Lee H, Cho S, Namgoong K, Jung J K, Yang S, *Bioorg. Med. Chem. Lett.* 2004, **14**, 1235.
- Diana P, Martorana A, Barraja P, Montalbaro A, *J. Med. Chem.* 2008, **51**, 2387.
- Chung H J, Jung O J, Chae M J, Hong S Y, Chung K H, Lee S K, *Bioorg. Med. Chem. Lett.* 2005, **15**, 3380.

7. Katsuyuki A, Obata T, Yamazaki Y, Mori Y, Hirokawa H, Koseki J, Hattori T, Niitsu K, Takeda S, Aburada M, Miyamoto K, *Chem. Pharm. Bulletin.* 2007, **55**, 255.
8. Carta A, Loriga M, Paglietti G, Mattana A, Fiori P L, Mollicotti P, Sechi L, Zanetti S, *Eur. J. Med. Chem.* 2004, **39**, 195.
9. Carta A, Paglietti G, Nikoogar M E R, Sanna P, Sechi L, Zanetti S, *Eur. J. Med. Chem.* 2002, **37**, 355.
10. Tandon V K, Yadav D B, Maurya H K, Chaturvedi A K, Shukla P K, *Bioorg. Med. Chem.* 2006, **14**, 6120.
11. Kotharkar S A, Shinde D B, *Bioorg. Med. Chem. Lett.* 2006, **16**, 6181.
12. Mashevskaya I V, Makhmudov R R, Aleksandrova G A, Golovnira O V, Duvalov A V, Maslivets A N, *Pharm. Chem. J.* 2001, **35**, 196.
13. Mashevskaya I V, Tolmacheva I A, Voronova E V, Odegova T F, Alkeksandrova G A, Goleneva A F, Kot'tsova S V, Maslivets A N, *Pharm. Chem. J.* 2002, **36**, 86.
14. Vyas D A, Chauhan N A, Parikh A R, *Indian J. Chem.* 2007, **46B**, 1699.
15. Jaso A, Zarranz B, Aldana I, Monge A, *Eur. J. Med. Chem.* 2003, **38**, 791.
16. Zarranz B, Jaso A, Aldana I, Monge A, *Bioorg. Med. Chem.* 2003, **11**, 2149.
17. Jaso A, Zarranz B, Aldana I, Monge A, *J. Med. Chem.* 2005, **48**, 2019.
18. Seitz L E, Suling W J, Reynolds R C, *J. Med. Chem.* 2002, **45**, 5604.
19. Burguete A, Pontiki E, Litina D H, Villar R, Vicente E, Solano B, Ancizu S, Aldana I, Monge A, *Bioorg. Med. Chem. Lett.* 2007, **17**, 6439.
20. El-Bendary E R, Goda F E, Maaronf A R, Badria F A, *Sci. Pharm.*, 2004, **72**, 175.
21. Palekar V S, Damle A J, Shukla S R, *Eur. J. Med. Chem.* 2009, **44**, 5112.
22. Omar K, Geronikaki A, Zoumpoulakis P, Camoutsis C, Soković M, Ćirić A J, Glamočlija J, *Bioorg. Med. Chem.* 2010, **18**, 426.
23. Kumar A, Rajput C S, Bhati S K, *Bioorg. Med. Chem.* 2007, **15**, 3089.
24. Hafez H N, El-Gazzar A R B A, *Bioorg. Med. Chem. Lett.* 2009, **19**, 4143.
25. Ravichandran V, Kumar B R P, Sankar S, Agrawal R K, *Eur. J. Med. Chem.* 2009, **44**, 1180.
26. El-Gaby M S A, El-Hag Ali G A M, El-Maghraby A A, El-Rahman M T A, Helal M H M, *Eur. J. Med. Chem.* 2009, **44**, 4148.