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# SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF NOVEL 5-((1*H*-INDOL-3-YL) METHYLENE)-2-((4-(3A, 4, 5, 6, 7, 7A-HEXAHYDRO-4, 7-METHANEBENZO[D] ISOOXAZOL-3-YL) PHENYL) IMINO)-3-METHYLTHIAZOLIDIN-4-ONE DERIVATIVES

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**Abstract**- A series of novel 5-((1*H*-indol-3-yl) methylene)-2-((4-(3a, 4, 5, 6, 7, 7a-hexahydro-4, 7-methanebenzo[d] isooxazol-3-yl) phenyl) imino)-3-methylthiazolidin-4-one derivatives were synthesized and evaluated for their antibacterial and antifungal activity. The structures of the synthesised compounds were determined by IR, NMR, mass spectroscopy and elemental analysis. They were screened for activities against bacterial and fungal strains. Amongst the synthesised compounds **9b**, **9e**, **9i**, **10g**, **10h** & **10i** were found to be active.

**Keywords:** Thiazolidin-4-one, Indole, Isoxazolines, Antimicrobial, Antifungal

## Introduction

Thiazolidinones are a class of important heterocyclics containing sulphur and nitrogen in a five member ring, and has been considered as a magic moiety (wonder nucleus) which posses almost all types of biological activities.

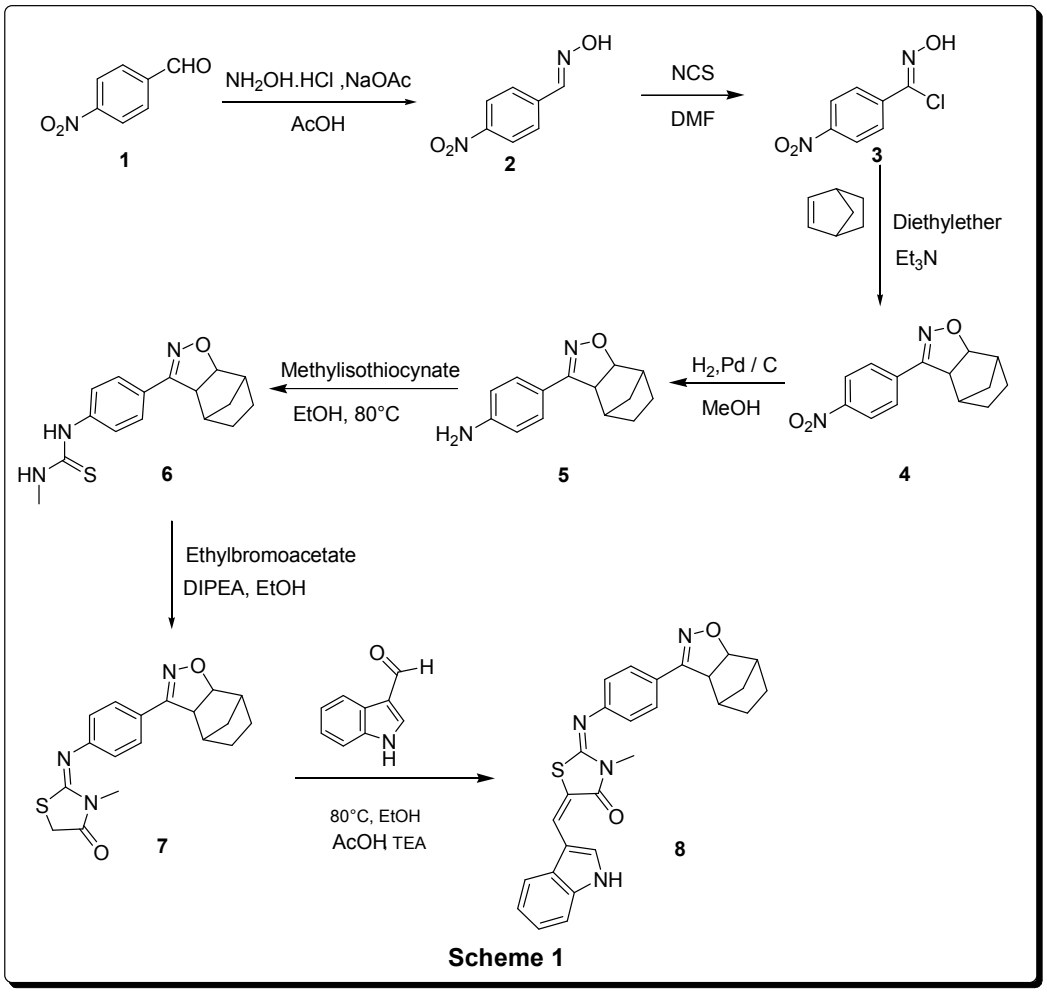
Among five-membered heterocycles, isoxazolines represent a class of compounds of great biological importance. For instance, isoxazolines possess a broad spectrum of biological activity[1,2]. Isoxazoline also serves as an important building block for the synthesis of biologically active molecules[2] and serves as a prodrug for an antiarthritic agent[3]. In fact, "Valdecoxib" is an isoxazoline derivative, now widely used in the market as an anti-inflammatory drug[4]. Isoxazoline derivatives have been reported to possess antifungal[5], antibacterial[6], anticonvulsant[7], anti-inflammatory[8], antiviral[9], analgesic[10], antitumor[11], chemotherapy [12] activity. Isoxazoline derivatives also show a good potency in animal models of thrombosis[13]. In addition, isoxazoline derivatives have played a crucial role in the theoretical development of heterocyclic chemistry and are also used extensively in organic synthesis[14,15]. 1, 3-Dipolar cycloaddition reactions are useful tools for the construction of biologically potent five-member heterocycles[2], and nitrile oxides serve as excellent 1,3-dipoles. Cycloaddition of nitrile oxides to olefinic compounds are of synthetic interest, since the resulting isoxazolines are versatile intermediates for the synthesis of bifunctional compounds[16]. Nitrile oxides can be generated by dehydrogenation of aryl

aldoximes with mercuric acetate[17], manganese dioxide[18], *tert*-butyl hypochlorite[19], chloramine-T[20], NCS, and TEA[21].

The wide applications of thiazolidin-4-one and Indole have prompted us to work in the area of thiazolidinone chemistry. In continuation of our work[22], we have prepared Indole-thiazolidin-4-ones having isoxazoline as a side chain and their various sulfonyl, acyl and benzoyl derivatives. All the synthesized compounds were screened for their biological evaluation.

**5.1.2: Result and Discussion**

The synthesis starts with reaction of 4-nitrobenzaldehyde **1** with hydroxyl amine hydrochloride and sodium acetate in AcOH to afford 4-nitrobenzaldehyde oxime **2**. The product was confirms by mass spectroscopy, which shows *m/z* at 167.2 for [M+1]. The 4-nitrobenzaldehyde oxime **2** was treated with NCS in DMF at rt to get N-hydroxy-4-nitrobenzimidoyl chloride **3**. The product was confirms by mass spectroscopy, it shows *m/z* at 201.5 for [M+1]. The N-hydroxy-4-nitrobenzimidoyl chloride **3** was further treated with TEA and bicyclo [2.2.1] hept-2-ene in diethylether at 0 $^{o}$C to get nitrophenyl-4-(3a, 4, 5, 6, 7, 7a-hexahydro-4,7-methanobenzo[d]isooxazol-3-yl) **4**. The formation of product was confirms by the mass spectroscopy, it shows *m/z* at 259.2 for [M+1]. The nitrophenyl-4-(3a, 4, 5, 6, 7, 7a-hexahydro-4, 7-methanobenzo[d] isooxazol-3-yl) **4** on catalytic reduction by using $H_2$, Pd/C in MeOH afforded 4-(3a, 4, 5, 6, 7, 7a-hexahydro-4,7-methanobenzo[d] isooxazol-3-yl)-benzamine **5**. The product shows *m/z* at 229.3 for [M+1]. The 4-(3a,4,5,6,7,7a-hexahydro-4,7-methanobenzo[d]isooxazol-3-yl)-benzamine **5** was further treated with methyl-isothiocynate in EtOH at 80$^{o}$C to afford the 4-(3a,4,5,6,7,7a-hexahydro-4,7-methanobenzo[d]isooxazol-3-yl) phenyl)-3-methylthiourea **6**. The formation of product was confirms by the mass spectroscopy, it shows *m/z* at 301.90 for [M+1]. The (4-(3a,4,5,6,7,7a-hexahydro-4,7-methano- benzo [d] isooxazol-3-yl)-phenyl)-3-methylthiourea **6** was treated with ethyl bromoacetate in presence of DIPEA in refluxing EtOH afforded the key intermediate 2-((4-(3a,4,5,6,7,7a-hexahydro-4,7-methanobenzo [d]isooxazol-3-yl)phenyl) imino)-3-methylthiazolidin-4-one **7** with 69% yield.

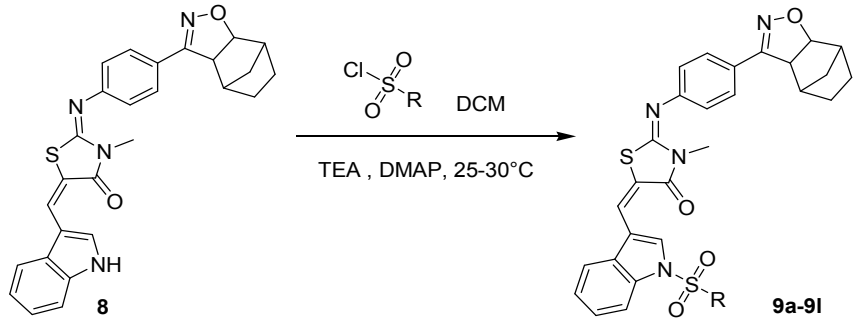



**Scheme 1**

In the IR spectrum of the compound **7** the strong absorption bands at 1726 $cm^{-1}$ (C=O), 1631 $cm^{-1}$ (C=C), 1612 $cm^{-1}$ (C=N) and 617 $cm^{-1}$ (C-S-C) confirmed the presence of C=O, C=C, C=N and C-S-C functional groups respectively. The $^1$HNMR spectrum of compound **7** shows three multiplets between 1.11-1.15, 1.26-1.43 and 1.45-1.50 ppm each integrating for two protons each respectively was due to the protons of three methylene groups of bicyclic ring. Two singlets each integrating for one proton resonated at 2.41 and 2.46 ppm were due to methine protons of bicyclic ring. A singlet at 3.16 ppm was due to methyl group attached to nitrogen for three protons. Two doublets each integrating for one proton at 3.65-3.67 (=C-C**H**) and 4.57-4.59 (O-C**H**) ppm were assigned to the methine protons at bicyclic and isooxazoline ring fusion. Another singlet at 4.03 ppm integrating for two protons was due to the protons of methylene group attached to S-atom of iminothiazolidin-4-one ring. Aromatic protons shows two doublets between 7.00- 7.02 and 7.68-7.70 ppm each integrating for two protons with coupling constant of 8Hz. The mass spectrum shows a peak at *m/z*= 342.0 [M+1] was in tune with the molecular formula $C_{18}H_{19}N_3O_2S$. All these spectral values and analysis data confirmed the gross structure of the key intermediate 2-((4-(3a, 4, 5, 6, 7, 7a-hexahydro-4,7-methanobenzo[d] isooxazol-3-yl) phenyl) imino)-3-methylthiazolidin-4-one **7**.

The key intermediate 2-((4-(3a, 4, 5, 6, 7, 7a-hexahydro-4,7-methanobenzo[d] isooxazol-3-yl) phenyl) imino)-3-methylthiazolidin-4-one **7** was then subjected to Knoevengel

condensation with Indole-3-carboxyladehyde with piperidine, AcOH and absolute EtOH at 80°C to give 5-((1H-indol-3-yl) methylene)-2-((4-(3a, 4, 5, 6, 7, 7a-hexahydro-4, 7-methanebenzo [d] isooxazol-3-yl) phenyl) imino)-3-methylthiazolidin-4-one 15[23]. In the IR spectrum of the compound **8** the strong absorption bands at 3309 $cm^{-1}$ (N-H), 1689 $cm^{-1}$ (C=O), 1641 $cm^{-1}$ (C=C), 1593 $cm^{-1}$ (C=N) and 609 $cm^{-1}$ (C-S-C) confirms the presence of N-H, C=O, C=C, C=N and C-S-C functional groups respectively. In $^{13}$CNMR spectra, methyl group attached to nitrogen observed at 29.92 ppm. Imino carbon of thiazolidin-4-one observed at 156.74 ppm. The olefinic carbon observed at 151.47 ppm. The carbonyl carbon of thiazolidin-4-one ring observed at 166.41 ppm. The $^{1}$HNMR spectrum of compound **8** shows two multiplets between 1.12-1.17, 1.30-1.51 ppm integrating for two and four protons respectively was due to the three methylene groups of bicyclic ring. Two singlets each integrating for one proton resonated at 2.41 and 2.46 ppm was due to methine protons of bicyclic ring. Singlet at 3.16 ppm was due to methyl group attached to nitrogen for three protons. Two doublets each integrating for one proton at 3.67-3.69 (=C-C**H**) and 4.58-4.60 (O-C**H**) ppm was assigned to the methine protons at bicyclic and isooxazoline ring fusion. Aromatic protons shows two doublets between 7.08- 7.10 and 7.73-7.75 ppm each integrating for two protons with J=8Hz. Two aromatic protons shows a multiplet at 7.12-7.24 ppm intregating for two protons. Two doblet observed at 7.47-7.49 and 7.85-7.87 ppm intregating for one proton each respectively with J=8 Hz. A sharp singlet at 7.64 ppm was due to olefinic proton. Another sharp singlet at 8.02 ppm was due to aromatic proton near to Indole nitrogen. A broad singlet at 11.95 ppm exchangeable with $D_2O$ was due to Indole NH. The mass spectrum shows a peak at *m/z*= 469.3 [M+1] in positive polarity and a peak at *m/z*= 467.3 [M-1] in negative polarity was in tune with the molecular formula $C_{27}H_{24}N_4O_2S$. All the spectral values and analysis data confirmed the gross structure of the key intermediate 2-((4-(3a, 4, 5, 6, 7, 7a-hexahydro-4,7-methanobenzo[d] isooxazol-3-yl) phenyl) imino)-3-methylthiazolidin-4-one **8**.




R= Ph-Me, Ph-$NO_2$, Me, Ph-OEt, Ph-F, Ph-Cl, Ph-Br, Ph-I, Ph-OMe, Ph, Ph-Et, $CH_2$-Ph

**Scheme 2**

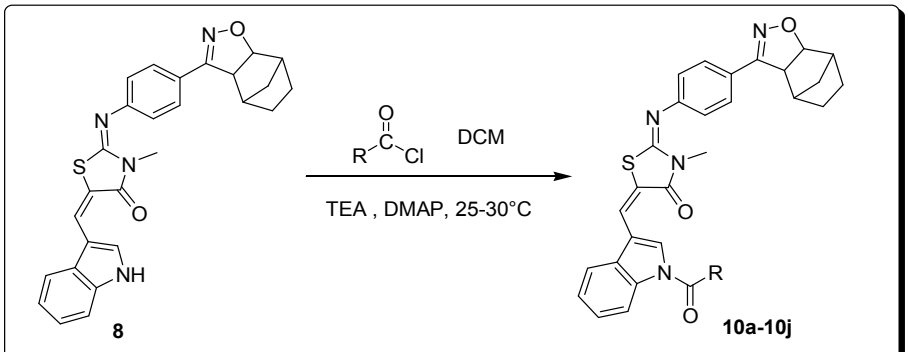
To complete the synthesis of various derivatives, the title compound **8** reacted with sulfonyl chlorides in presence of TEA and DMAP in a catalytic amount at rt to afford the sulfonyl derivatives **9a-9l** as shown in **Scheme 2.** Interestingly, all N-sulphonylated products formed in excellent yields (**Table 1**). Furthermore all the reaction has been done at rt in shortest period of time (**Table 1**). All these derivatives were prepared by reaction of **8** with various sulfonyl chlorides in DCM as a solvent in presence of TEA (2.0 mol.) and DMAP (0.10 mol.) as a catalyst at rt to afford the compounds **9a-9l** with excellent yields. (**Table 1**). The crude product obtained was recrystallised in EtOH. The yields obtained and the time required to complete the

conversion is presented in the **Table 1**. All compounds obtained are solid and having colour in the range of pale yellow to dark yellow. The yields and melting points are summerised in the **Table 1.**

**Table 1: Physical characterization data of compound 9a-9l**

| Compound | Physical State | Mp (°C) | Yield (%) | Molecular Formula | CHN Analysis (%) Calculated Found | | |
|---|---|---|---|---|---|---|---|
| | | | | | C | H | N |
| **9a** | Yellow Solid | 195-197 | 72 | $C_{30}H_{30}N_4O_4S_2$ | 65.57 | 4.86 | 9.00 |
| | | | | | 65.60 | 4.96 | 8.91 |
| **9b** | Yellow Solid | 213-215 | 64 | $C_{33}H_{27}N_5O_6S_2$ | 60.63 | 4.16 | 10.71 |
| | | | | | 60.60 | 4.11 | 10.68 |
| **9c** | Yellow Solid | 177-178 | 72 | $C_{28}H_{26}N_4O_4S_2$ | 61.52 | 4.79 | 10.25 |
| | | | | | 61.70 | 4.85 | 10.23 |
| **9d** | Yellow Solid | 176-178 | 68 | $C_{35}H_{32}N_4O_5S_2$ | 64.40 | 4.94 | 8.58 |
| | | | | | 64.33 | 4.88 | 8.60 |
| **9e** | Yellow Solid | 185-187 | 66 | $C_{33}H_{27}FN_4O_4S_2$ | 63.24 | 4.34 | 8.94 |
| | | | | | 63.32 | 4.24 | 8.99 |
| **9f** | Yellow Solid | 194-196 | 60 | $C_{33}H_{27}ClN_4O_4S_2$ | 61.62 | 4.23 | 8.71 |
| | | | | | 61.59 | 4.33 | 8.70 |
| **9g** | Yellow Solid | 189-192 | 68 | $C_{33}H_{27}BrN_4O_4S_2$ | 57.64 | 3.96 | 8.15 |
| | | | | | 57.71 | 4.01 | 8.19 |
| **9h** | Yellow Solid | 198-200 | 59 | $C_{33}H_{27}IN_4O_4S_2$ | 53.95 | 3.70 | 7.63 |
| | | | | | 53.86 | 3.85 | 7.70 |
| **9i** | Yellow Solid | 173-175 | 67 | $C_{34}H_{30}N_4O_5S_2$ | 63.93 | 4.73 | 8.77 |
| | | | | | 63.99 | 4.79 | 8.88 |
| **9j** | Yellow Solid | 180-182 | 78 | $C_{33}H_{28}N_4O_4S_2$ | 65.11 | 4.64 | 9.20 |
| | | | | | 65.23 | 4.73 | 9.23 |
| **9k** | Yellow Solid | 190-192 | 72 | $C_{35}H_{32}N_4O_4S_2$ | 66.02 | 5.07 | 8.80 |
| | | | | | 66.00 | 5.09 | 8.77 |
| **9l** | Yellow Solid | 188-190 | 73 | $C_{34}H_{30}N_4O_4S_2$ | 65.67 | 5.86 | 9.00 |
| | | | | | 65.65 | 5.90 | 9.05 |

In IR spectrum of the compound **9c,** the strong absorption bands at 1709 $cm^{-1}$ (C=O), 1639 $cm^{-1}$ (C=C), 1597 $cm^{-1}$ (C=N), 1369 & 1172 $cm^{-1}$ ($SO_2$), and 609 $cm^{-1}$ (C-S-C) confirmed the presence of C=O, C=C, C=N, $SO_2$ and C-S-C functional groups respectively. The $^1$HNMR spectrum of compound **9c** shows two multiplets between 1.03-1.17, 1.30-1.50 ppm integrating for three and four protons respectively was due to the three methylene protons and a methine proton of bicyclic ring. A singlet observed at 2.44 ppm was due to another methine proton of bicyclic ring. A sharp singlet at 3.31 ppm was due to methyl group attached to nitrogen for three protons. Another sharp singlet for three protons at 3.59 ppm was due to methyl group attached to sulfonyl group. Two doublets integrating for one proton each at 3.69-3.71 (=C-C**H**) and 4.59-4.61 (O-C**H**) ppm was assigned to the methine protons at bicyclic and isooxazoline ring fusion. Aromatic protons of phenyl ring attached to isooxazoline shows two doublets between 7.12-7.14 and 7.75-7.77 ppm each integrating for two protons with J=8Hz. Two aromatic protons show a multiplet at 7.12-7.24 ppm intregating for two protons. Two doublet observed at 7.47-7.49 and 7.85-7.87 ppm intregating for one proton each respectively with J=8 Hz. A multiplet at 7.40-7.51 ppm was due to two aromatic protons. A sharp singlet at 7.58 ppm was due to olefinic proton. Two doublets each integrating for one proton at 7.86-7.88 and 8.03-8.05 ppm was due to aromatic protons. Another sharp singlet at 7.97 ppm was due to aromatic proton next to Indole nitrogen. The mass spectrum shows a peaks at *m/z*= 547.3 [M+1], 548.2 [M+2], 549.2 [M+3] in positive polarity. All the spectral values and analysis data confirmed the gross structure of the key intermediate 2-((4-(3a, 4, 5, 6, 7, 7a-hexahydro-4,7-methanobenzo[d] isooxazol-3-yl) phenyl) imino)-3-methylthiazolidin-4-one **9c**.




**Scheme 3**

The title compound **8** reacted with different acyl and substituted benzoyl chlorides in DCM with TEA and DMAP in a catalytic amount at rt to afford the **10a-10j** in excellent yields **(Scheme 3, Table 2)**. In IR spectrum of the compound **10c,** the strong absorption bands at 1678 $cm^{-1}$ (C=O), 1639 $cm^{-1}$ (C=C) and 1597 $cm^{-1}$ (C=N) confirmed the presence of C=O, C=C and C=N functional groups respectively. The $^1$HNMR spectrum of compound **10c** shows two multiplets between 1.23-1.27, 1.55-1.62 ppm integrating for two and five protons respectively was due to the three methylene protons and a methine proton of bicyclic ring. Two singlets observed at 2.60 and 2.68 ppm was due to another two methine protons of bicyclic ring. A sharp singlet at 3.46 ppm was due to methyl group attached to nitrogen for three protons. Two doublets integrating for one proton each at 3.52-3.54 (=C-C**H**) and 4.69-4.71 (O-C**H**) ppm was assigned to the methine protons at bicyclic and isooxazoline ring fusion. Aromatic protons of phenyl ring

attached to isooxazoline shows a doublet between 7.01-7.03 integrating for two protons with J=8Hz. Three aromatic protons show a multiplet at 7.26-7.45 ppm intregating for three protons. A sharp singlet at 7.50 ppm was due to aromatic proton. A multiplet at 7.59-7.61 integrating for one proton was also due to the aromatic proton. Another multiplet integrating for five aromatic protons of phenyl ring attached to carbonyl carbon at 7.69-7.80 ppm. A sharp singlet at 7.95 ppm was due to olefinic proton. One doublets integrating for one proton at 8.29-8.31 ppm was due to aromatic protons. The mass spectrum shows a peaks at *m/z*= 573.3 [M+1], 574.4 [M+2] in positive polarity. All the spectral values and analysis data confirms the gross structure of the key intermediate 2-((4-(3a, 4, 5, 6, 7, 7a-hexahydro-4,7-methanobenzo[d] isooxazol-3-yl) phenyl) imino)-3-methylthiazolidin-4-one **10c**.

**Table 2: Physical characterization data of compound 10a-10j**

| Compound | Physical State | Mp (°C) | Yield (%) | Molecular Formula | CHN Analysis (%) Calculated Found | | |
|---|---|---|---|---|---|---|---|
| | | | | | C | H | N |
| **10a** | Yellow Solid | 183-184 | 73 | $C_{29}H_{26}N_4O_3S$ | 68.21 | 5.13 | 10.97 |
| | | | | | 68.28 | 5.23 | 10.90 |
| **10b** | Yellow Solid | 195-197 | 76 | $C_{30}H_{28}N_4O_3S$ | 68.68 | 5.38 | 10.68 |
| | | | | | 68.80 | 5.32 | 10.72 |
| **10c** | Yellow Solid | 172-173 | 75 | $C_{34}H_{28}N_4O_3S$ | 71.31 | 4.93 | 9.78 |
| | | | | | 71.23 | 5.00 | 9.80 |
| **10d** | Yellow Solid | 181-183 | 64 | $C_{34}H_{27}ClN_4O_3S$ | 67.26 | 4.48 | 9.23 |
| | | | | | 67.20 | 4.51 | 9.14 |
| **10e** | Yellow Solid | 196-198 | 62 | $C_{34}H_{27}BrN_4O_3S$ | 62.67 | 4.18 | 8.60 |
| | | | | | 62.70 | 4.24 | 8.71 |
| **10f** | Yellow Solid | 204-206 | 60 | $C_{34}H_{27}IN_4O_3S$ | 58.46 | 3.90 | 8.02 |
| | | | | | 58.58 | 3.88 | 8.10 |
| **10g** | Yellow Solid | 197-199 | 62 | $C_{34}H_{27}FN_4O_3S$ | 69.14 | 4.61 | 9.49 |
| | | | | | 69.23 | 4.59 | 9.55 |
| **10h** | Yellow Solid | 228-230 | 62 | $C_{34}H_{27}N_5O_5S$ | 66.11 | 4.41 | 11.34 |
| | | | | | 66.23 | 4.51 | 11.23 |
| **10i** | Yellow Solid | 215-217 | 64 | $C_{35}H_{30}N_4O_4S$ | 69.75 | 5.02 | 9.30 |
| | | | | | 69.66 | 5.07 | 9.42 |
| **10j** | Yellow Solid | 226-228 | 75 | $C_{36}H_{32}N_4O_4S$ | 70.11 | 5.23 | 9.08 |
| | | | | | 70.23 | 5.21 | 9.16 |

**Experimental Section**

The newly synthesized compounds were characterized on the basis of IR, $^1$HNMR and mass spectroscopy method. IR spectrums were recorded on Schimadzu 8201 PC, FTIR spectrophotometer in KBr phase. Proton NMR spectrum were recorded on Bruker Advance II 400 & 200 MHz NMR Ultra Shield Spectrometer using DMSO-$d_6$/$CDCl_3$ as a solvent and tetramethyl silane (TMS) as internal standard. Chemical shift values are expressed in parts per million (ppm). Melting points were determined with Buchi B-545 melting point apparatus in degree celsius and are uncorrected. Mass spectra were recorded on either Buker daltanoics Micro TOFQ or Quattro Primer XE. Elemental analyses were performed on a Heraeus CHN-O rapid analyzer. All the reactions were monitored by using precoated silica gel plates, followed by UV detection at 254nm, exposure to iodine vapours.

**Synthesis of 4-nitrobezaldoxime (2)**

A mixture of 4-nitrobenzaldehyde **1** (10 gm, 0.066 mol.), hydroxylamine hydro chloride (6.85 gm, 0.099 mol.) and Sodium acetate (11.9 gm, 0.145 mol.) in AcOH was stirred at rt for 2.5 hours. After completion of reaction (TLC check; 50% EtOAc: hexane), reaction mixture was poured in water and the solid precipitated was separated by filtration and dried under vacuum to get 10.2 gm 4-nitrobezaldoxime **2**.

Yellow powder, (90% Yield), EI-MS (m/z): 167.1 [M+1]

**Synthesis of N-hydroxy-4-nitrobenzimidoyl chloride (3)**

A mixture of 4-nitrobezaldoxime **2** (10 gm, 0.06 mol.) and NCS (9.31 gm, 0.07 mol.) in DMF was stirred at rt for 2.5 hours, after completion of reaction (TLC check; 50% EtOAc: hexane), reaction mixture was poured in water and aqueous layer was extracted with EtOAc (3 × 25ml). Organic layer was washed with 25% brine solution and evaporated to get 10.2 gm N-hydroxy-4-nitrobenzimidoyl chloride **3** with 85% yield.

Yellow powder, (85% Yield), EI-MS (m/z): 201.5 [M+1]

**Synthesis of (nitrophenyl)-((4-(3a, 4, 5, 6, 7, 7a-hexahydro-4,7-methano- benzo[d] isooxazol-3-yl) (4)**

To a solution of N-hydroxy-4-nitrobenzimidoyl chloride **3** (10 gm, 0.05 mol.) in diethylether was added bicyclo [2,2,1] hept-2-ene (5.17 gm, 0.055 mol.) and reaction mixture was cooled to 0$^o$C for 10 min. TEA (15.34 ml, 0.11 mol.) was added to it and reaction mixture was allowed to come at rt. After completion of reaction (TLC check; 1:1 Hexane:EtOAc) reaction mixture was partitioned between diethylether and water, organic layer seperated, washed with 25% brine solution and evaporated to get yellow solid. Crude yellow solid was stirred in 250 ml hexane for 15 min, filtered and dried under vacuum to get 10.6 gm of (nitrophenyl)- ((4-(3a,4,5,6,7,7a-hexahydro-4,7-methanobenzo [d] isooxazol-3-yl) **4**.

Pale Yellow powder, (73% Yield), EI-MS (m/z): 259.1 [M+1]

**Synthesis of (4-(3a,4,5,6,7,7a-hexahydro-4,7-methanobenzo[d] isooxa- zol-3-yl) benzamine (5)**

To a solution of (nitrophenyl)-((4-(3a,4,5,6,7,7a-hexahydro-4,7-methanobenzo[d] isooxazol-3-yl) **4** (10 gm, 0.039 mol.) in MeOH (50ml) Pd/C (1 gm, 10% w/w) was added and reaction mixture was stirred under $H_2$ atmosphere at rt for 12 hours. After completion of reaction

(TLC check; 1:1 Hexane:EtOAc), reaction mixture was cooled, filtered through a pad of celite and washed with MeOH. Filtrate was evaporated to get reddish residue. The residue was diluted with water and extracted with EtOAc (3 × 50 ml). The organic layer was evaporated to get sticky red solid. Crude solid was stirred in 250 ml hexane for 15 min, filtered and dried under vacuum to get 7.1 gm of (4-(3a,4,5,6,7, 7a-hexahydro-4,7-methanobenzo[d]isooxazol-3-yl) benzamine **5.**
Light pale yellow powder, (80% Yield), EI-MS (m/z): 229.1 [M+1]

**Synthesis of (4-(3a,4,5,6,7,7a-hexahydro-4,7-methanobenzo[d]isooxa- zol-3-yl) phenyl)-3-methylthiourea (6)**

To a solution of (4-(3a,4,5,6,7,7a-hexahydro-4,7-methanobenzo[d]isooxazol-3-yl) benzamine **5** (5 gm, 0.021 mol.) in EtOH (30 ml) methylisothiocynate (1.6 gm, 0.027 mol.) was added and reaction mixture was heated at 80-85$^{o}$C for 6 hour. After completion of reaction (TLC check; 1:1 Hexane:EtOAc), reaction mixture was cooled to rt and EtOH was removed under vacuum. Water (30 ml) was added to the residue and stirred for 15 min. The solid separated was filtered and trituted with 50% EtOH in water (20 ml). The solid was filtered and dried under vacuum to give 5.7 gm of 4-(3a, 4, 5, 6, 7, 7a-hexahydro-4, 7-methanobenzo [d] isooxazol-3-yl) phenyl) -3-methylthiourea **6**.
Off-white powder, (86% Yield), EI-MS (m/z): 301.90 [M+1]

**Synthesis of 2-((4-(3a,4,5,6,7,7a-hexahydro-4,7-methanobenzo[d]iso- oxazol-3-yl) phenyl) imino)-3-methylthiazolidin-4-one (7)**

To a solution of (4-(3a,4,5,6,7,7a-hexahydro-4,7-methanobenzo[d]isooxazol-3-yl) phenyl)-3-methylthiourea **6** (5 gm, 0.016 mol.) in EtOH ( 30 ml) was added ethylbromoacetate (3.2 gm, 0.019 mol.) and DIPEA (3.3 gm, 0.024 mol.), reaction mixture was heated at 80-85 $^{o}$C for 6 hour. After completion of reaction (TLC check; 1:1 Hexane:EtOAc), reaction mixture cooled to rt and EtOH was removed under vacuum. Water (30 ml) was added to the residue and stirred for 15 min and extracted with EtOAc (3 × 20ml). The organic layer was evaporated to get sticky reddish solid. It was then recrystalised using EtOH to give 3.95 gm pure product 2-((4-(3a, 4, 5, 6, 7, 7a-hexahydro-4, 7-methanobenzo[d]isooxazol-3-yl) phenyl) imino)-3-methylthiazolidin-4-one **7**.
Yellow solid, (69% yield), Mp: 112-114$^{o}$C; EI-MS (m/z) : 342.05 [M +1], IR (cm$^{-1}$, KBr) : 1726 (C=O), 1631 (C=C), 1612 (C=N) and 617 (C-S-C) cm$^{-1}$, $^{1}$HNMR (DMSO-$d_{6,}$ 400MHz) :1.11-1.15 (m,2H), 1.26-1.43 (m, 2H), 1.45- 1.50 (m, 2H), 2.41 (s,1H), 2.46 (s,1H), 3.16 (s,3H), 3.65-3.67 (d, 1H) , 4.03 (s,2H), 4.57-4.59 (d, 1H), 7.00- 7.02 (d, J=8Hz,2H), 7.68- 7.70 (d, J=8Hz,2H)

**5-((1H-indol-3-yl) methylene)-2-((4-(3a, 4, 5, 6, 7, 7a-hexahydro-4, 7-methanebenzo[d] isooxazol-3-yl) phenyl) imino)-3-methylthiazolidin-4-one (8)**

A well stirred solution of 2-((4-(3a, 4, 5, 6, 7, 7a-hexahydro-4, 7-methanobenzo[d]isooxazol-3-yl) phenyl) imino)-3-methylthiazolidin-4-one **7** (8.5 gm, 0.026 mol.) in 136 ml of EtOH , piperidine (0.64 gm 0.0075 mol.), AcOH (0.47 gm, 0.008mol.) and Indole-3-carboxaldehyde (3.77 gm, 0.026 mol.) was refluxed till (5-7 hrs) the completion of the reaction, monitored by TLC. The reaction mixture was then cooled to rt and solid collected by filtration to give 9.3 gm **8**.
Yellow solid, (78.7% yield), Mp: 180-182$^{o}$C; EI-MS (m/z) : 469.3 [M+1], IR (cm$^{-1}$, KBr) : 3309 (N-H), 1689 (C=O), 1641 (C=C), 1593 (C=N) and 609 (C-S-C) cm$^{-1}$, $^{1}$HNMR (DMSO-$d_{6,}$ 400 MHz) : 1.12-1.17 (m, 2H), 1.30-1.51 (m,4H), 2.41 (s,1H), 2.46 (s,1H), 3.16 (s, 3H), 3.67-3.69

(d,1H), 4.58-4.60 (d, 1H), 7.08-7.10 (d, *J* = 8Hz, 2H), 7.12-7.24 (m, 2H), 7.47-7.49 (d,1H), 7.64 (s,1H), 7.73-7.75 (d, *J* = 8Hz, 2H), 7.85-7.87 (d, 1H), 8.02 (s,1H), 11.95 (bs,1H,exchangeable with $D_2O$), $^{13}$CNMR (DMSO-d6; $Cl_3$,, 100 MHz): 22.60, 27.19, 29.92, 32.38, 43.17, 56.57, 87.50, 110.81, 112.84, 114.34, 118.71, 121.35, 122.22, 123.34, 123.40, 125.68, 127.20, 128.40, 128.78, 136.58, 149.81, 151.47, 156.74, 166.41

**General procedure for synthesis of 9a-9l**

A solution of 2-((4-(3a,4,5,6,7,7a-hexahydro-4,7-methanobenzo[d]isooxazol-3-yl) phenyl) imino)-3-methylthiazolidin-4-one **8** (0.15 gm, 0.00032 mol.) in DCM (1.5 ml), TEA (0.065 gm, 0.00064 mol.), DMAP (0.004 gm, 0.000032 mol.) and appropriate sulfonyl chloride (0.00034 mol.) was stirred over different periods till the completion of the reaction (monitored by TLC). The reaction mixture was then distilled out to get oil/solid, which then recrystallized using EtOH to get **9a-9l**.

**2-(4-(3a, 4, 5, 6, 7, 7a-hexahydro-4, 7-methanebenzo[d] isooxazol-3-yl) phenylimino)-3-methyl-5-((1-tosyl-1H-indol-3-yl) methylene) thiazolidin-4-one (9a)**

Yellow solid, (72% yield), Mp: 195-197$^o$C; EI-MS (m/z) : 623.6 [M+1], IR ($cm^{-1}$, KBr) : 1707 (C=O), 1639 (C=C), 1612 (C=N), 1373 & 1172 ($SO_2$) $cm^{-1}$

**2-(4-(3a, 4, 5, 6, 7, 7a-hexahydro-4, 7-methanebenzo[d] isooxazol-3-yl) phenylimino)-3-methyl-5-((1-(4-nitrophenylsulfonyl)-1H-indol-3-yl) methylene) thiazolidin-4-one (9b)**

Yellow solid, (64% yield), Mp: 213-215$^o$C; EI-MS (m/z) : 654.5 [M+1], IR ($cm^{-1}$, KBr) : 1720 (C=O), 1639 (C=C), 1607 (C=N), 1375 & 1174 ($SO_2$) $cm^{-1}$

**2-(4-(3a, 4, 5, 6, 7, 7a-hexahydro-4, 7-methanebenzo[d] isooxazol-3-yl) phenylimino)-3-methyl-5-((1-(methylsulfonyl)-1H-indol-3-yl) methylene) thiazolidin-4-one (9c)**

Yellow solid, (72% yield), Mp: 177-178$^o$C; EI-MS (m/z) : 547.3 [M+1], 548.2 [M+2], 549.2 [M+3], IR ($cm^{-1}$, KBr) : 1709 (C=O), 1639 (C=C), 1597 (C=N), 1369, 1172 ($SO_2$), 609 (C-S-C) $cm^{-1}$, $^1$HNMR (DMSO-d6, 400 MHz): 1.03-1.17 (m, 3H), 1.30-1.50 (m, 4H), 2.44(s, 1H) 3.31 (s,3H), 3.59 (s,3H), 3.69-3.71 (d,1H), 4.59-4.61 (d,1H), 7.12-7.14 (d, J=8Hz,2H), 7.40-7.51 (m,2H), 7.58 (s,1H), 7.75-7.77 (d, J=8Hz,2H), 7.86-7.88 (d,1H), 7.97 (s,1H), 8.03-8.05 (d,1H)

**2-(4-(3a, 4, 5, 6, 7, 7a-hexahydro-4, 7-methanebenzo[d] isooxazol-3-yl) phenylimino)-5-((1-(4-ethoxyphenylsulfonyl)-1H-indol-3-yl) methylene)-3-methylthiazolidin-4-one (9d)**

Yellow solid, (68% yield), Mp: 176-178$^o$C; EI-MS (m/z) : 653.6 [M+1], IR ($cm^{-1}$, KBr) : 1708 (C=O), 1631 (C=C), 1610 (C=N).1365 & 1167 ($SO_2$) $cm^{-1}$

**2-(4-(3a, 4, 5, 6, 7, 7a-hexahydro-4, 7-methanebenzo[d] isooxazol-3-yl) phenylimino)-5-((1-(4-fluorophenylsulfonyl)-1H-indol-3-yl) methylene)-3-methylthiazolidin-4-one (9e)**

Yellow solid, (66% yield), Mp: 185-187$^o$C; EI-MS (m/z) : 627.35 [M+1], 628.40 [M+2], IR ($cm^{-1}$, KBr) : 1713 (C=O), 1639(C=C), 1597 (C=N), 1369, 1180 ($SO_2$), 671 (C-S-C) $cm^{-1}$, $^1$HNMR (DMSO-d6, 400 MHz): 1.12-1.15 (d,3H), 1.27-1.29 (d,1H), 1.37-1.48 (m, 3H), 2.42 (d,1H) 3.34 (s,3H), 3.68-3.70 (d,1H), 4.57-4.59 (d,1H), 7.13-7.15 (d, J=8Hz, 2H), 7.35-7.46 (m,4H), 7.76-7.78 (s,3H), 7.87-7.93 (m,3H), 8.13-8.16 (m,2H)

**2-(4-(3a, 4, 5, 6, 7, 7a-hexahydro-4, 7-methanebenzo[d] isooxazol-3-yl) phenylimino)-5-((1-(4-chlorophenylsulfonyl)-1H-indol-3-yl) methylene)-3-methylthiazolidin-4-one (9f)**

Yellow solid, (60% yield), Mp: 194-196$^o$C; EI-MS (m/z) : 644.0 [M+1], IR ($cm^{-1}$, KBr) : 1693 (C=O), 1629 (C=C), 1612 (C=N), 1373 & 1166 ($SO_2$) $cm^{-1}$

**2-(4-(3a, 4, 5, 6, 7, 7a-hexahydro-4, 7-methanebenzo[d] isooxazol-3-yl) phenylimino)-5-((1-(4-bromophenylsulfonyl)-1H-indol-3-yl) methylene)-3-methylthiazolidin-4-one (9g)**

Yellow solid, (68% yield), Mp: 189-192$^o$C; EI-MS (m/z) : 688.5 [M+1], IR ($cm^{-1}$, KBr) : 1716 (C=O), 1637(C=C), 1608 (C=N), 1367 & 1176 ($SO_2$) $cm^{-1}$

**2-(4-(3a, 4, 5, 6, 7, 7a-hexahydro-4, 7-methanebenzo[d] isooxazol-3-yl) phenylimino)-5-((1-(4-iodophenylsulfonyl)-1H-indol-3-yl) methylene)-3-methylthiazolidin-4-one (9h)**
Yellow solid, (59% yield), Mp: 198-200$^{o}$C; EI-MS (m/z) : 735.5 [M+1], IR (cm$^{-1}$, KBr) : 1688(C=O), 1633 (C=C), 1600 (C=N), 1368 & 1178 ($SO_2$) cm$^{-1}$
**2-(4-(3a, 4, 5, 6, 7, 7a-hexahydro-4, 7-methanebenzo[d] isooxazol-3-yl) phenylimino)-5-((1-(4-methoxyphenylsulfonyl)-1H-indol-3-yl) methylene)-3-methylthiazolidin-4-one (9i)**
Yellow solid, (67% yield), Mp: 173-175$^{o}$C; EI-MS (m/z) : 639.30 [M+1], 640.40 [M+2], 641.40 [M+3], IR (cm$^{-1}$, KBr) : 1709 (C=O), 1639 (C=C), 1597 (C=N), 1369 & 1168 ($SO_2$), 671 (C-S-C) cm$^{-1}$, $^{1}$HNMR (DMSO-d6, 400 MHz): 1.12-1.14 (d,2H), 1.27-1.30 (d,1H), 1.37-1.47 (m, 3H), 2.43 (S,2H), 3.34 (s,3H), 3.68-3.70 (d,1H), 3.74 (s,3H), 4.50-4.59 (d,1H), 7.00-7.02 (d, J=8Hz,2H), 7.14-7.16 (d, J=8Hz,2H), 7.33-7.37 (m, 1H), 7.41-7.43 (m, 1H), 7.74-7.78 (m, 3H), 7.88-7.97 (m,5H)
**2-(4-(3a, 4, 5, 6, 7, 7a-hexahydro-4, 7-methanebenzo[d] isooxazol-3-yl) phenylimino)-3-methyl-5-((1-(phenylsulfonyl)-1H-indol-3-yl) methylene) thiazolidin-4-one (9j)**
Yellow solid, (78% yield), Mp: 180-182$^{o}$C; EI-MS (m/z) : 623.5 [M+1], IR (cm$^{-1}$, KBr) : 1708 (C=O), 1639 (C=C), 1608 (C=N), 1369 & 1172 ($SO_2$) cm$^{-1}$
**2-(4-(3a, 4, 5, 6, 7, 7a-hexahydro-4, 7-methanebenzo[d] isooxazol-3-yl) phenylimino)-5-((1-(4-ethylphenylsulfonyl)-1H-indol-3-yl) methylene)-3-methylthiazolidin-4-one (9k)**
Yellow solid, (72% yield), Mp: 190-192$^{o}$C; EI-MS (m/z) : 637.5 [M+1], IR (cm$^{-1}$, KBr) : 1697 (C=O), 1639 (C=C), 1609 (C=N), 1377 & 1169 ($SO_2$) cm$^{-1}$
**2-(4-(3a, 4, 5, 6, 7, 7a-hexahydro-4, 7-methanebenzo[d] isooxazol-3-yl) phenylimino)-5-((1-(benzylsulfonyl)-1H-indol-3-yl) methylene)-3-methylthiazolidin-4-one (9l)**
Yellow solid, (73% yield), Mp: 188-190$^{o}$C; EI-MS (m/z) : 623.5 [M+1], IR (cm$^{-1}$, KBr) : 1700 (C=O), 1645 (C=C), 1616 (C=N), 1388 & 1170 ($SO_2$) cm$^{-1}$

**General procedure for synthesis of 10a-10j**

A solution of 2-((4-(3a,4,5,6,7,7a-hexahydro-4,7-methanobenzo[d]isooxazol-3-yl) phenyl) imino)-3-methylthiazolidin-4-one **8** (0.15 gm, 0.00032 mol.) in DCM (1.5 ml), TEA (0.065 gm, 0.00064 mol.), DMAP (0.004 gm, 0.000032 mol.) and appropriate acyl/benzoyl chloride (0.00034 mol.) was stirred over different periods till the completion of the reaction (monitored by TLC). The reaction mixture was then distilled out to get oil/solid, which then recrystallized using EtOH to get **10a-10j**.

**2-(4-(3a, 4, 5, 6, 7, 7a-hexahydro-4, 7-methanebenzo[d] isooxazol-3-yl) phenylimino)-5-((1-acetyl-1H-indol-3-yl) methylene)-3-methylthiazolidin-4-one (10a)**
Yellow solid, (73% yield), Mp: 183-184$^{o}$C; EI-MS (m/z) : 511.3 [M+1], 512.1 [M+2], IR (cm$^{-1}$, KBr) : 1708 (C=O), 1639 (C=C), 1597 (C=N), 655 (C-S-C) cm$^{-1}$, $^{1}$HNMR ($CDCl_3$, 400 MHz): 1.21-1.24 (m,2H), 1.55-1.58 (m,1H), 1.59-1.60 (m,3H), 2.57 (s,2H), 2.65 (s,3H) 3.49 (s,3H), 3.68-3.70 (d,1H), 4.65-4.67 (d,1H), 7.06-7.08 (d, J=8Hz,2H), 7.39-7.44 (m,2H), 7.51 (s,1H), 7.74-7.79 (m,3H), 7.99 (s,1H), 8.39-8.41 (d,1H)
**2-(4-(3a, 4, 5, 6, 7, 7a-hexahydro-4, 7-methanebenzo[d] isooxazol-3-yl) phenylimino)-3-methyl-5-((1-propionyl-1H-indol-3-yl) methylene) thiazolidin-4-one (10b)**
Yellow solid, (76% yield), Mp: 195-197$^{o}$C; EI-MS (m/z) : 525.5 [M+23], IR (cm$^{-1}$, KBr) : 1685 (C=O), 1630 (C=C), 1606 (C=N) cm$^{-1}$
**2-(4-(3a, 4, 5, 6, 7, 7a-hexahydro-4, 7-methanebenzo[d] isooxazol-3-yl) phenylimino)-5-((1-benzoyl-1H-indol-3-yl) methylene)-3-methylthiazolidin-4-one (10c)**

Yellow solid, (75% yield), Mp: 172-173$^{o}$C; EI-MS (m/z) : 573.3 [M+1], 574.4 [M+2], IR (cm$^{-1}$, KBr) : 1678 (C=O), 1639 (C=C), 1597 (C=N) cm$^{-1}$, $^{1}$HNMR ($CDCl_3$, 400 MHz): 1.23-1.27 (m, 2H), 1.55-1.62 (m, 5H), 2.60 (s,1H), 2.68 (s,1H) 3.46 (s,3H), 3.52-3.54 (d,1H), 4.69-4.71 (d,1H), 7.01-7.03 (d, J=8Hz,2H), 7.26-7.45 (m,3H), 7.50 (s,1H), 7.59-7.61 (m,1H), 7.69-7.80 (m,5H), 7.95 (s,1H), 8.29-8.31 (d,1H)

**2-(4-(3a, 4, 5, 6, 7, 7a-hexahydro-4, 7-methanebenzo[d] isooxazol-3-yl) phenylimino)-5-((1-(4-chlorobenzoyl)-1H-indol-3-yl) methylene)-3-methylthiazolidin-4-one (10d)**

Yellow solid, (64% yield), Mp: 181-183$^{o}$C; EI-MS (m/z) : 608.0 [M+1], IR (cm$^{-1}$, KBr) : 1712 (C=O), 1639 (C=C), 1605 (C=C) cm$^{-1}$

**2-(4-(3a, 4, 5, 6, 7, 7a-hexahydro-4, 7-methanebenzo[d] isooxazol-3-yl) phenylimino)-5-((1-(4-bromobenzoyl)-1H-indol-3-yl) methylene)-3-methylthiazolidin-4-one (10e)**

Yellow solid, (62% yield), Mp: 196-198$^{o}$C; EI-MS (m/z) : 652.4 [M+1], IR (cm$^{-1}$, KBr) : 1709 (C=O), 1658 (C=C), 1606 (C=N) cm$^{-1}$

**2-(4-(3a, 4, 5, 6, 7, 7a-hexahydro-4, 7-methanebenzo[d] isooxazol-3-yl) phenylimino)-5-((1-(4-iodobenzoyl)-1H-indol-3-yl) methylene)-3-methylthiazolidin-4-one (10f)**

Yellow solid, (60% yield), Mp: 204-206$^{o}$C; EI-MS (m/z) : 699.1 [M+1], IR (cm$^{-1}$, KBr) : 1710 (C=O), 1632 (C=C), 1601 (C=N) cm$^{-1}$

**2-(4-(3a, 4, 5, 6, 7, 7a-hexahydro-4, 7-methanebenzo[d] isooxazol-3-yl) phenylimino)-5-((1-(4-fluorobenzoyl)-1H-indol-3-yl) methylene)-3-methylthiazolidin-4-one (10g)**

Yellow solid, (62% yield), Mp: 197-199$^{o}$C; EI-MS (m/z) : 591.6 [M+1], IR (cm$^{-1}$, KBr) : 1701 (C=O), 1654 (C=C), 1612 (C=N) cm$^{-1}$

**2-(4-(3a, 4, 5, 6, 7, 7a-hexahydro-4, 7-methanebenzo[d] isooxazol-3-yl) phenylimino)-3-methyl-5-((1-(4-nitrobenzoyl)-1H-indol-3-yl) methylene) thiazolidin-4-one (10h)**

Yellow solid, (62% yield), Mp: 228-230$^{o}$C; EI-MS (m/z) : 618.5 [M+1], IR (cm$^{-1}$, KBr) : 1725(C=O), 1646 (C=C), 1616 (C=N) cm$^{-1}$

**2-(4-(3a, 4, 5, 6, 7, 7a-hexahydro-4, 7-methanebenzo[d] isooxazol-3-yl) phenylimino)-5-((1-(4-methoxybenzoyl)-1H-indol-3-yl) methylene)-3-methylthiazolidin-4-one (10i)**

Yellow solid, (64% yield), Mp: 215-217$^{o}$C; EI-MS (m/z) : 603.5 [M+1], IR (cm$^{-1}$, KBr) : 1701 (C=O), 1631 (C=C), 1597 (C=N) cm$^{-1}$

**2-(4-(3a, 4, 5, 6, 7, 7a-hexahydro-4, 7-methanebenzo[d] isooxazol-3-yl) phenylimino)-5-((1-(4-ethoxybenzoyl)-1H-indol-3-yl) methylene)-3-methylthiazolidin-4-one (10j)**

Yellow solid, (75% yield), Mp: 226-228$^{o}$C; EI-MS (m/z) : 617.3 [M+1], IR (cm$^{-1}$, KBr) : 1712(C=O), 1634 (C=C), 1605(C=N) cm$^{-1}$

**Antimicrobial activity**

The various sulfonyl, acyl and benzoyl derivatives of Indole-thiazolidin-4-one were tested for their potential to inhibit growth of different bacterial and fungal species at doses of 100 µg/ml in DMSO as a solvent, against bacterial and fungal cultures. All the compounds were found to have antimicrobial activities against different species of bacteria and fungi in our studies.

**Antimicrobial activity of sulfonyl derivatives (9a-9l)**

Synthesized compounds **9a-9l** were tested to evaluate their antibacterial and antifungal activity. The newly synthesized compounds were found to exhibit very good antibacterial and antifungal activity against different species of bacteria and fungi. From the activity data **(Table 3)** it was observed that compound **9b, 9e & 9i** shows good activity against all the tested bacteria and fungi. Among all tested bacteria and fungi, compound **9b** shows very good activity against

*Staphylococcus aureus*, (inhibition 12 mm, standard shows 12 mm), *Bacillus subtillis* (inhibition 12 mm, standard shows 12 mm) and against *Escherichia coli* bacteria (inhibition 11 mm, standard shows 12 mm). Also against *Aspergillius Niger* fungi (inhibition 9 mm, standard shows 10 mm), against *Rhizopus Ostoyae* fungi (inhibition 8 mm, standard shows 10 mm). Compound **9e** shows very good activity against *Staphylococcus aureus*, (inhibition 10 mm, standard shows 12 mm), *Bacillus subtillis* (inhibition 11 mm, standard shows 12 mm) and against *Escherichia coli* bacteria (inhibition 11 mm, standard shows 12 mm). Also against *Aspergillius Niger* fungi (inhibition 8 mm, standard shows 10 mm), against *Rhizopus Ostoyae* fungi (inhibition 7 mm, standard shows 10 mm). Whereas compound **9i** shows good activity against *Staphylococcus aureus*, (inhibition 9 mm, standard shows 12 mm), *Bacillus subtillis* (inhibition 10 mm, standard shows 10 mm) and against *Escherichia coli* bacteria (inhibition 8 mm, standard shows 12 mm). Also against *Aspergillius Niger* fungi (inhibition 9 mm, standard shows 10 mm), against *Rhizopus Ostoyae* fungi (inhibition 8 mm, standard shows 10 mm).

Compounds **9a, 9c, 9d, 9f, 9g, 9h, 9j, 9k & 9l** shows moderate activity against *Staphylococcus aureus* bacteria, *Bacillus subtillis* bacteria and *Escherichia coli* bacteria as well as against *Aspergillius Niger* and *Rhizopus Ostoyae* fungi.

**Table 3: Antimicrobial activity of sulfonyl derivatives (9a-9l) of 5-((1H-indol-3-yl) methylene)-2-((4-(3a, 4, 5, 6, 7, 7a-hexahydro-4,7-methanebenzo[d]isooxazol-3-yl) phenyl) imino)-3-methylthiazolidin-4-one.**

| Compound Code | Zone of Inhibition (mm) | | | | |
|---|---|---|---|---|---|
| | Bacteria | | | Fungi | |
| | ***S. A.*** *NCLM No.2602* | ***B. S.*** *NCLM No.2458* | ***E. C.*** *NCLM No.2809* | ***A. N.*** *NCLM No.617* | ***R.O.*** *NCLM No.1299* |
| **9a** | 7 | 8 | 7 | 8 | 6 |
| **9b** | 12 | 12 | 11 | 9 | 8 |
| **9c** | 6 | 6 | 5 | 6 | 5 |
| **9d** | 8 | 8 | 9 | 8 | 6 |
| **9e** | 10 | 11 | 11 | 8 | 7 |
| **9f** | 8 | 7 | 5 | 5 | 4 |
| **9g** | 7 | 6 | 5 | 5 | 5 |
| **9h** | 6 | 5 | 5 | 5 | 5 |
| **9i** | 9 | 10 | 8 | 9 | 8 |
| **9j** | 7 | 7 | 7 | 7 | 6 |
| **9k** | 7 | 6 | 7 | 4 | 4 |
| **9l** | 6 | 6 | 5 | 6 | 5 |
| **Standard** | **12** | **12** | **12** | **10** | **10** |

**Antimicrobial activity of acyl & benzoyl derivatives (10a-10j):**

Synthesized compounds **10a-10j** were tested to evaluate their antibacterial and antifungal activity. The newly synthesized compounds were found to exhibit very good antibacterial and antifungal activity against different species of bacteria and fungi. From the activity data **(Table 4),** it was observed that compound **10h & 10i** shows good activity against all the tested bacteria

and fungi. Among all tested bacteria and fungi, compound **10h** shows very good activity against *Staphylococcus aureus*, (inhibition 10 mm, standard shows 12 mm), *Bacillus subtillis* (inhibition 10 mm, standard shows 12 mm) and against *Escherichia coli* bacteria (inhibition 9 mm, standard shows 12 mm). Also against *Aspergillius Niger* fungi (inhibition 8 mm, standard shows 10 mm), against *Rhizopus Ostoyae* fungi (inhibition 8 mm, standard shows 10 mm). Whereas compound **10i** shows very good activity against *Staphylococcus aureus*, (inhibition 9 mm, standard shows 12 mm), *Bacillus subtillis* (inhibition 9 mm, standard shows 12 mm) and against *Escherichia coli* bacteria (inhibition 8 mm, standard shows 12 mm). Also against *Aspergillius Niger* fungi (inhibition 8 mm, standard shows 10 mm), against *Rhizopus Ostoyae* fungi (inhibition 7 mm, standard shows 10 mm).

Compounds **10a, 10b, 10c, 10d, 10e, 10f, 10g & 10j** shows moderate activity against *Staphylococcus aureus* bacteria, *Bacillus subtillis* bacteria and *Escherichia coli* bacteria as well as against *Aspergillius Niger* and *Rhizopus Ostoyae* fungi.

**Table 4: Antimicrobial activity of acyl and benzoyl derivatives (10a-10j) of 5-((1H-indol-3-yl) methylene)-2-((4-(3a,4,5,6, 7, 7a-hexahydro-4,7-methanebenzo[d]isooxazol-3-yl) phenyl) imino)-3-methylthiazolidin-4-one.**

| Compound Code | Zone of Inhibition (mm) | | | | |
|---|---|---|---|---|---|
| | Bacteria | | | Fungi | |
| | ***S. A.*** *NCLM No.2602* | ***B. S.*** *NCLM No.2458* | ***E. C.*** *NCLM No.2809* | ***A. N.*** *NCLM No.617* | ***R.O.*** *NCLM No.1299* |
| **10a** | 6 | 6 | 5 | 6 | 5 |
| **10b** | 5 | 5 | 5 | 5 | 5 |
| **10c** | 7 | 7 | 8 | 7 | 6 |
| **10d** | 6 | 6 | 6 | 5 | 5 |
| **10e** | 5 | 6 | 4 | 4 | 4 |
| **10f** | 6 | 5 | 3 | 5 | 5 |
| **10g** | 8 | 9 | 8 | 8 | 7 |
| **10h** | 10 | 10 | 9 | 8 | 8 |
| **10i** | 9 | 9 | 8 | 8 | 7 |
| **10j** | 7 | 8 | 7 | 6 | 6 |
| **Standard** | **12** | **12** | **12** | **10** | **10** |

## Conclusion

In this communication all synthesized compounds reported first time and describe the simple route of their synthesis in mild condition with good yield .The present study showed that all the title compounds were exhibiting significant antibacterial and antifungal activities. However, further studies are required to establish the mechanism of action of the title compounds. From the screening data it was found that **9b**, **9e**, **9i**, **10g**, **10h** & **10i** derivative have encouraging antibacterial and antifungal activity, which need to be further investigation to get better antibacterial and antifungal agents. We herein also reported the synthesis of series of novel sulfonyl, acyl and benzoyl derivatives of 5-((1*H*-indol-3-yl) methylene)-2-((4-(3a, 4, 5, 6, 7, 7a-hexahydro-4, 7-methanebenzo[d] isooxazol-3-yl) phenyl) imino)-3-methylthiazolidin-4-one

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