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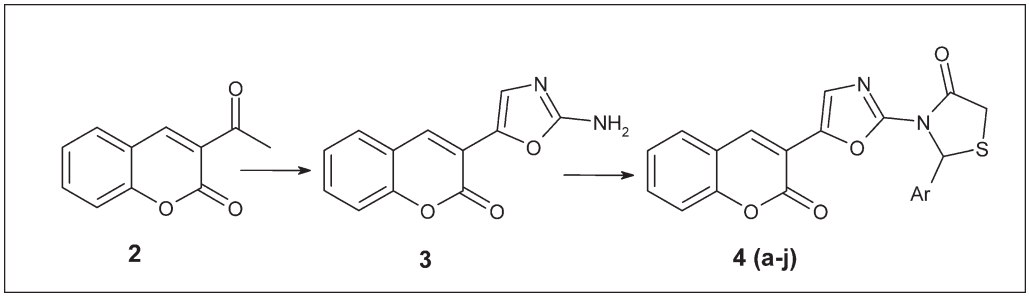

A series of novel 2-(aryl)-3-[5-(2-oxo-2*H*-3-chromenyl)-1,3-oxazol-2-yl]-1,3-thiazolan-4-ones **4a–j** have been synthesized and assayed for their antibacterial activity against Gram-positive bacteria *viz*. *Bacillus subtilis* (ATCC 6633), *Staphylococcus aureus* (ATCC 6538p), *Micrococcus luteus* (IFC 12708), and Gram-negative bacteria *viz*. *Proteus vulgaris* (ATCC 3851), *Salmonella typhimurium* (ATCC 14028), *Escherichia coli* (ATCC 25922), and also antifungal activity against *Candida albicans* (ATCC 10231), *Aspergillus fumigatus* (HIC 6094), *Trichophyton rubrum* (IFO 9185), and *Trichophyton mentagrophytes* (IFO 40996). Among the screened compounds, **4d**, **4e**, **4f**, **4g**, and **4j** exhibited potent inhibitory activity compared with the standard drug at the tested concentrations. The results reveal that, the presence of difluorophenyl in **4f** and pipernyl ring in **4j** at 2-position of thiazolidine-4-one ring show significant inhibitory activity. The other compounds also showed appreciable activity against the test bacteria and fungi and emerged as potential molecules for further development.

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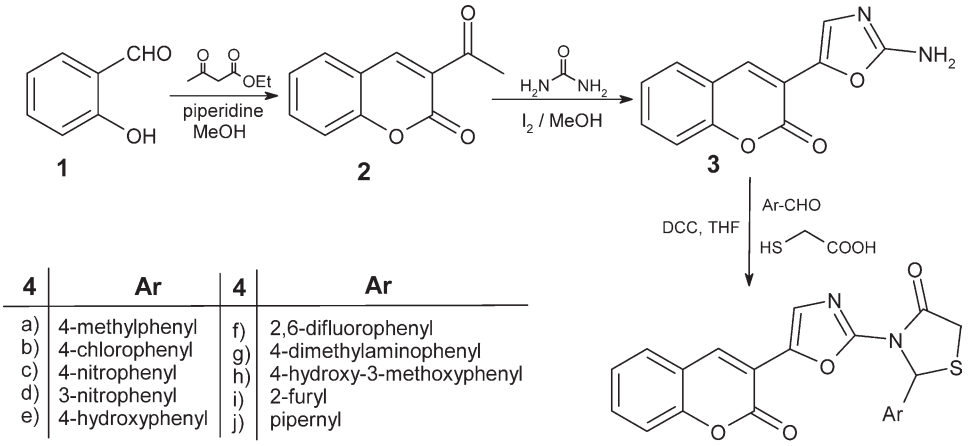
INTRODUCTION

The structural and therapeutic diversity coupled with commercial viability of small molecules have fascinated the organic and medicinal chemists. Coumarins are a class of compounds with biological activity, such as analgesics [1,2], anticoagulant [3], specific inhibitors of α-chymotripsin [4], human leukocyte elastase [5], diuretics [6], platelet aggregation [7], anticancer [8], inhibitor of HIV-1 protease [9], and antibacterial [10,11]. Further, there is a considerable interest in the chemistry of thiazolidine-4-one ring system, which is a core structure in various synthetic pharmaceuticals displaying a broad spectrum of biological activities [12–14], such as anticonvulsant [15], antidiarrheal [16], antiplatelet activating factor [17–19], antihistaminic [20,21], antimicrobial [22,23], antidiabetic, [24] cyclooxygenase (COX) inhibitory [25], Ca^{2+}-channel blocker [26], platelet activating factor (PAF) antagonist [27], cardioprotective [28], antiischemic [29], anticancer [30], tumor necrosis factor-α antagonist [31], and nematicidal [32]. Therefore, the simple and efficient method for rapid synthesis of thiazolidine-4-ones would be greatly advantageous and warrants for further investigation in drug discovery. In view of the biological significance of thiazolidine-4-one, pyrazole and in continuation of our work on the synthesis of biologically active heterocyclics [33–35], we herein, report the synthesis of a series of thiazolidine-4-one **4a–j**, with different pharmacologically active groups, in one-pot three-component system using 3-(2-amino-1,3-oxazol-5-yl)-2*H*-2-chromenone **3**, different aromatic aldehydes and thioglycolic acid in the presence of dicyclohexylcarbodiimide as the cyclizing agent. Furthur, all the newly synthesized compounds were evaluated for their *in vitro* antimicrobial activity by the disk diffusion and micro dilution methods against pathogenic strains.

RESULTS AND DISCUSSION

The compound **2** required for the synthesis of the title compounds was prepared by cyclocondensation of salicylaldehyde **1** with ethylacetoacetate in the presence of piperidine in methanol [36]. The compound **2** on cyclocondensation with urea in the presence of iodine in methanol at reflux for 8 h, results 3-(2-amino-1,3-

Scheme 1



4	Ar	4	Ar
a)	4-methylphenyl	f)	2,6-difluorophenyl
b)	4-chlorophenyl	g)	4-dimethylaminophenyl
c)	4-nitrophenyl	h)	4-hydroxy-3-methoxyphenyl
d)	3-nitrophenyl	i)	2-furyl
e)	4-hydroxyphenyl	j)	pipernyl

oxazol-5-yl)-2*H*-2-chromenone **3**. The one-pot, three-component condensation of **3** with different aromatic aldehydes and thioglycolic acid in the presence of dicyclohexylcarbodiimide as cyclizing agent in tetrahydrofuran solvent at room temperature, resulted the new series of 2-(aryl)-3-[5-(2-oxo-2*H*-3-chromenyl)-1,3-oxazol-2-yl]-1,3-thiazolan-4-ones **4a–j** in high-yields. The heterocyclic aldehyde, such as 2-furfuraldehyde, was also used to construct the new thiazolidine-4-one (Scheme 1). However, the two step reaction as reported [35], involving condensation of amino compounds with aromatic aldehydes in acetic acid resulted the Schiff's base, which on cyclocondensation with thioglycolic acid in presence of $ZnCl_2$ in toluene, at high-temperature, resulted thiazolidine-4-one derivatives in lower yields.

The structures of the compounds **4a–j** were deduced from their IR, NMR, and MS spectra. In the IR spectra of compounds **4a–j**, the disappearance of the absorption band at 3420 cm^{-1} corresponding to —NH_2 group, which was present in compound **3**, indicates the cyclization has occurred involving the —NH_2 group. The presence of vibrational frequency of C=O in the range of 1690 – 1700 cm^{-1} clearly demonstrate the formation of thiazolidine-4-one ring. In the ^1H NMR spectra, the CH_2—CO protons, N—CH—S proton of thiazolidine-4-one ring, appeared as singlet at 3.66 and 5.82–6.00 ppm, respectively. These signals clearly demonstrate the formation of thiazolidine-4-one ring. The proton of N—CH—S moiety appeared at a higher field owing to the shielding effect of the nearly coplanar sulfur orbital. Further support was obtained from ^{13}C NMR spectra. For all the compounds the signals corresponding to the carbons of thiazolidine-4-one appeared at ~172.4, ~72.0, 33.7 ppm. The other signals were observed at the expected chemical shifts and integral values. In addition, elemental analyses are consistent with the structures proposed for the compounds **4a–j**.

Antibacterial assay. All the compounds **4a–j** were assayed for their antibacterial activity against Gram-positive bacteria *viz*. *Bacillus Subtilis* (MTCC 441), *Bacillus Sphaericus* (MTCC 11), *Staphylococcus Aureus* (MTCC 96), and Gram-negative bacteria *viz*. *Pseudomonas Aeruginosa* (MTCC 741), *Klobsinella Aerogenes* (MTCC 39), *Chromobacterium Violaceum* (MTCC 2656) by disc diffusion, microdilution/ turbidometric methods [37]. For the antibacterial assay standard inoculums (1–2 × 10^7 c.f.u/mL 0.5 Mc Farland standards) were introduced on to the surface of sterile agar plates, and a sterile glass spreader was used for even distribution of the inoculums. The discs measuring 6.26 mm in diameter were prepared from Whatman no.1 filter paper and sterilized by dry heat at 140°C for 1 h. The sterile discs previously soaked in a known concentration of the test compounds were placed in nutrient agar medium. The plates were inverted and incubated for 24 h at 37°C. The inhibition zones were measured and compared with the standard. For the determination of MIC, bacteria were grown over night in Luria Bertani (LB) broth at 37°C harvested by centrifugation, and then washed twice with sterile distilled water. Stock solutions of the series of compounds were prepared in DMSO. Each stock solution was diluted with standard method broth (Difco) to prepare serial two-fold dilutions in the range of 50–0.8 μg/mL. 10 mL of the broth containing about 10^5 c.f.u/mL of test bacteria was added to each well of 96-well microtiter plate. Culture plates were incubated for 24 h at 37°C, and the growth was monitored visually and spectrometrically. The lowest concentration required to arrest the growth of bacteria was regarded as minimum inhibitory concentration (MIC,

Table 1

Antibacterial activity of compounds **4a–j**.

Compound	Minimal inhibitory concentration (MIC) (μg/mL)[a]					
	B. subtilis	*B. sphaericus*	*S. aureus*	*P. aeruginosa*	*K. aerogenes*	*C. violaceum*
4a	25 ± 1.1	23 ± 0.8	22 ± 0.8	14 ± 0.5	22 ± 1.1	20 ± 1.0
4b	32 ± 1.2	30 ± 1.0	26 ± 1.1	20 ± 0.7	26 ± 1.2	12 ± 0.4
4c	28 ± 1.1	25 ± 1.1	25 ± 1.0	17 ± 0.4	25 ± 0.5	10 ± 0.8
4d	13 ± 0.5	15 ± 0.6	12 ± 0.5	12 ± 0.5	13 ± 0.8	18 ± 0.7
4e	18 ± 0.8	20 ± 1.0	18 ± 0.8	15 ± 0.5	16 ± 1.0	22 ± 0.4
4f	8 ± 0.3	10 ± 0.4	10 ± 0.4	10 ± 0.4	10 ± 0.5	15 ± 0.34
4g	10 ± 0.4	13 ± 0.5	10 ± 0.5	10 ± 0.3	10 ± 1.0	30 ± 1.1
4h	28 ± 1.0	25 ± 1.0	25 ± 0.8	22 ± 0.8	26 ± 1.1	10 ± 1.2
4i	30 ± 0.9	26 ± 1.1	25 ± 1.0	25 ± 1.0	24 ± 0.6	17 ± 1.0
4j	10 ± 0.4	10 ± 0.4	10 ± 0.4	10 ± 0.4	10 ± 0.8	22 ± 0.9
Streptomycin	15 ± 0.5	19 ± 0.8	18 ± 0.8	20 ± 0.5	20 ± 1.0	18 ± 0.5

[a] Values are means of three determinations, the ranges of which are less than 5% of the mean in all cases.

μg/mL), and mean inhibition zone were also determined and compared with the standard drug streptomycin. The MIC and MZI data are presented in Table 1 and Table 2.

The investigation of antibacterial screening data reveal that, almost all the compounds **4a-j** are active and showing moderate to good antibacterial activity. Compounds **4d**, **4e**, **4f**, **4g**, and **4j** exhibited potent inhibitory activity compared to the standard drug at the tested concentrations. The obtained results reveal that the presence of difluorophenyl in **4f** and pipernyl ring in **4j** at 2-position of thiazolidine-4-one ring, might be the reason for the significant inhibitory activity. Also, the presence of hydroxyphenyl in the molecules would enhance the inhibitory activity stoichiometrically as shown by **4e**. Presence of chlophenyl in **4b** and nitrophenyl in **4c** did not show significant inhibition. But in **4a**, presence of the methylphenyl group and in **4g** presence of dimethylaminophenyl group showed considerable inhibitory activity.

Antifungal assay. The compounds **4a–j** were also screened for their antifungal activity against *Candida Albicans* (ATCC 10231), *Aspergillus Fumigatus* (HIC 6094), *Trichophyton rubrum* (IFO 9185), and *Trichophyton Mentagrophytes* (IFO 40996) in DMSO by agar diffusion and broth dilution methods [37]. For the antifungal assay, Sabourands agar media was prepared by dissolving peptone (1 g), D-glucose (4 g), and agar (2 g) in distilled water (100 mL) and adjusting the pH to 5.7. Normal saline was used to make a suspension of spore of fungal strain for lawning. A loopful of particular fungal strain was transferred to 3 mL saline to get a suspension of corresponding species. 20 mL of agar media was poured into each petri-dish, excess of suspension was decanted, and the plates were dried by placing in an incubator at 37°C for 1 h. Using an agar punch wells

Table 2

Antibacterial activity of compounds **4a–j**.

Compound	Mean zone inhibition (MZI) (mm)[a]					
	B. subtilis	*B. sphaericus*	*S. aureus*	*P. aeruginosa*	*K. aerogenes*	*C. violaceum*
4a	13 ± 0.4	12 ± 0.5	14 ± 0.5	10 ± 0.5	12 ± 0.4	14 ± 0.2
4b	8 ± 0.2	8 ± 0.3	9 ± 1.1	8 ± 0.4	5 ± 0.2	23 ± 1.0
4c	10 ± 0.3	8 ± 0.3	10 ± 0.7	5 ± 0.5	6 ± 0.3	5 ± 1.2
4d	22 ± 0.8	20 ± 1.0	21 ± 1.1	19 ± 0.8	22 ± 1.1	18 ± 0.6
4e	18 ± 0.5	16 ± 0.7	20 ± 1.0	18 ± 0.5	20 ± 0.8	14 ± 1.0
4f	25 ± 1.0	22 ± 1.1	26 ± 0.4	20 ± 1.2	26 ± 1.0	25 ± 0.3
4g	21 ± 1.0	23 ± 1.1	24 ± 0.5	22 ± 1.0	20 ± 0.3	10 ± 0.4
4h	10 ± 0.4	8 ± 0.3	10 ± 1.2	8 ± 0.3	7 ± 1.2	12 ± 1.2
4i	4 ± 0.2	10 ± 0.2	8 ± 0.3	6 ± 0.4	10 ± 0.3	24 ± 0.7
4j	20 ± 1.0	20 ± 1.0	23 ± 1.0	22 ± 1.1	20 ± 1.2	18 ± 0.2
Streptomycin	15 ± 0.5	17 ± 0.5	20 ± 1.0	18 ± 0.6	16 ± 0.8	20 ± 0.5

Streptomycin (25 μg/disc) and compounds **4a-j** (50 μg/disc) were used for the assay.
[a] Values are means of three determinations, the ranges of which are less than 5% of the mean in all cases.

Table 3

Antifungal activity of compounds **4a–j**.

Compound	Minimal inhibitory concentration (MIC) (μg/mL)[a]			
	C. albicans	*A. fumigatus*	*T. rubrum*	*T. mentagrophytes*
4a	25 ± 1.2	30 ± 1.4	35 ± 1.6	28 ± 1.2
4b	36 ± 1.1	36 ± 1.2	45 ± 1.4	52 ± 2.0
4c	16 ± 0.6	18 ± 0.6	18 ± 0.6	14 ± 0.6
4d	20 ± 1.0	20 ± 0.7	26 ± 1.0	26 ± 0.9
4e	21 ± 0.8	20 ± 1.0	36 ± 1.2	24 ± 0.7
4f	30 ± 1.2	32 ± 1.2	21 ± 1.6	30 ± 1.2
4g	20 ± 0.8	20 ± 0.6	32 ± 1.0	16 ± 0.8
4h	28 ± 1.0	30 ± 1.2	50 ± 1.4	30 ± 1.6
4i	32 ± 1.6	25 ± 1.6	20 ± 1.5	42 ± 0.8
4j	18 ± 0.8	20 ± 0.8	36 ± 0.9	18 ± 1.0
Amphotericin B	15 ± 1.1	20 ± 1.0	22 ± 1.3	18 ± 0.8

[a] Values are means of three determinations, the ranges of which are less than 5% of the mean in all cases.

were made and each well was labeled. A control was also prepared in triplicate and maintained at 37°C for 3–4 days. The *C. albicans* was grown for 48 h at 28°C in YPD broth (1% yeast extract, 2% peptone, and 2% dextrose), harvested by centrifugation and then washed twice with sterile distilled water. *A. fumigatus*, *T. rubrum*, and *T. mentagrophytes* were plated in potato dextrose agar (PDA) (Difco) and incubated at 28°C for 2 weeks. Spores were washed three times with sterile distilled water and resuspended in distilled water to obtain an initial inoculums size of 10^5 spores/mL. Each test compound was dissolved in DMSO and diluted with potato dextrose broth (Difco) to prepare serial two-fold dilutions in the range 100–0.8 μg/mL. 10 mL of the broth containing about 10^3 (for yeast) and 10^4 (for filamentous fungi) cells/mL of test fungi was added to each well of a 96-well microtiter plate. Culture plates were incubated for about 48–72 h at 28°C. The lowest concentration required to arrest the growth of fungi was regarded as minimum inhibitory concentration (MIC, μg/mL), and mean inhibition zone were also determined and compared with the standards drug Amphotericin B. The MIC and MZI data are presented in Table 3 and Table 4.

The antifungal screening data reveal that, most of the new compounds are active and show moderate to good antifungal activity. Among the screened compounds, the compounds **4c** and **4d** with nitrophenyl group at 2-position of thiazolidine-4-one ring showed highest activity against all the microorganisms employed. The activity of these compounds is almost equal to the standard. Compounds **4g** and **4j** also showed good inhibition toward *A. fumigatus* and *T. mentagrophytes*.

In conclusion, a series of novel 2-(aryl)-3-[5-(2-oxo-2*H*-3-chromenyl)-1,3-oxazol-2-yl]-1,3-thiazolan-4-ones **4a–j** have been synthesized and evaluated for their antibacterial

Table 4

Antifungal activity of compounds **4a–j**.

Compound	Mean zone inhibition (MZI) (mm)[a]			
	C. albicans	*A. fumigatus*	*T. rubrum*	*T. mentagrophytes*
4a	10 ± 0.6	14 ± 1.4	17 ± 1.0	16 ± 0.8
4b	6 ± 0.4	8 ± 1.2	6 ± 1.1	8 ± 1.2
4c	18 ± 1.0	20 ± 0.6	25 ± 0.5	26 ± 0.4
4d	20 ± 0.6	16 ± 0.7	20 ± 1.1	18 ± 0.7
4e	14 ± 0.7	18 ± 1.0	14 ± 1.0	18 ± 0.5
4f	10 ± 0.6	12 ± 1.2	14 ± 0.6	12 ± 1.0
4g	16 ± 0.8	18 ± 0.6	12 ± 1.0	26 ± 0.7
4h	14 ± 0.5	10 ± 1.2	6 ± 1.2	19 ± 0.5
4i	8 ± 0.3	8 ± 1.6	14 ± 0.9	10 ± 0.6
4j	16 ± 0.9	18 ± 0.8	8 ± 0.7	20 ± 1.0
Amphotericin B	20 ± 1.0	19 ± 1.0	18 ± 1.1	22 ± 0.6

Amphotericin B (50 μg/disc) and compounds **4a–j** (100 μg/disc) were used for assay.
[a] Values are means of three determinations, the ranges of which are less than 5% of the mean in all cases.

(MIC/MZI) activity and antifungal (MIC/ MZI) activity against various bacteria and fungi. Many of the synthesized compounds showed good activity against the test bacteria and fungi

EXPERIMENTAL

Reagents were commercial grade and were used as supplied. Reactions were monitored by thin-layer chromatography (TLC) on precoated silica gel F_{254} plates from Merck and compounds visualized either by exposure to UV light or dipping in 1% aqueous potassium permanganate solution. Chromatographic columns 70–230 mesh silica gel for separations were used. Melting points were determined through a Fisher–Johns apparatus and are uncorrected. IR spectra were recorded using KBr disk on a Perkin–Elmer FTIR spectrometer. The ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded on a Varian Gemini spectrometer. Chemical shifts are reported in δ ppm units with respect to TMS as internal standard and coupling constants (*J*) are reported in Hz units. Mass spectra were recorded on a VG micro mass 7070H spectrometer. Elemental analyses (C, H, N) determined by means of a Perkin–Elmer 240 CHN elemental analyzer, were within ± 0.4% of theory.

3-(2-amino-1,3-oxazol-5-yl)-2*H*-2-chromenone (3). A mixture of urea (0.02 mol) and Iodine (0.01 mol) were triturated and mixed with a solution of 3-acetyl-2*H*-2-chromenone **2** (0.01 mol) in methanol (20 mL). The mixture was heated on a water bath with occasional stirring for 8 h. The obtained solid was triturated with diethyl ether to remove unreacted compound **2**, washed the residue with aqueous sodium thiosulfate and then water to remove excess iodine. The crude product was dissolved in hot water, filtered to remove the sulphone, and the product was precipitated by addition of NH_3. The crude solid obtained on evaporation of the solvent under reduced pressure was recrystallized from methanol to furnish the pure compound **3** as yellow crystals; Yield 65%, mp 144–46°C; IR (KBr): ν 3420, 3240, 3072, 1698, 1560, 1070, 770 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 7.67 (s, 1H, ArH), 7.50–7.45 (m, 2H, ArH), 7.30–7.20 (m, 3H, ArH), 4.24 (bs, 2H, NH_2); ^{13}C NMR (DMSO-d_6): δ 163.2, 158.6, 155.2, 143.1, 128.6, 127.6, 125.7, 123.4, 120.8, 114.8, 111.8; MS: *m*/*z* 228 (M^+). Anal. Calcd for $C_{12}H_8N_2O_3$: C, 63.16; H, 3.53; N, 12.28. Found: C, 63.11; H, 3.60; N, 12.23.

2-(aryl)-3-[5-(2-oxo-2*H*-3-chromenyl)-1,3-oxazol-2-yl]-1,3-thiazolan-4-one (4a–j). A mixture of 3-(2-amino-1,3-oxazol-5-yl)-2*H*-2-chromenone **3** (0.01 mol) and corresponding arylde-hyde (0.012 mol) in dry tetrahydrofuran was stirred with ice cooling for 10 min, followed by the addition of thioglycolic acid (0.015 mol). After 10 min, dicyclohexylcarbodiimide (0.015 mol) was added to the reaction mixture at 0°C and the reaction mixture was stirred for about 5–6 h at room temperature to complete the reaction. The precipitated dicyclohexylurea was filtered off; the filtrate was concentrated to dryness under reduced pressure. Deionized water was added to the residue and extracted with dichloromethane. The organic layer was washed with 5% $NaHCO_3$ solution/citric acid solution and dried over anhydrous Na_2SO_4. The crude solid obtained on evaporation of the solvent under reduced pressure was recrystallized from methanol to furnish the pure compound.

2-(4-methylphenyl)-3-[5-(2-oxo-2*H*-3-chromenyl)-1,3-oxazol-2-yl]-1,3-thiazolan-4-one (4a). This was obtained as yellow solid; Yield 71%; mp 130–32°C; IR (KBr): ν 3065, 1705, 1695, 1560, 1180, 718 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 7.50–7.40 (m, 2H, ArH), 7.30–7.15 (m, 7H, ArH), 6.84 (s, 1H, ArH), 5.82 (s, 1H, N—CH—S), 3.66 (s, 2H, CH_2CO), 2.30 (s, 3H, CH_3); ^{13}C NMR (DMSO-d_6): δ 171.5, 158.6, 155.4, 153.5, 136.9, 134.6, 129.6, 128.0, 127.9, 127.5, 127.0, 125.4, 123.1, 114.5, 113.2, 112.2, 105.4, 70.6, 33.7, 22.0; MS: *m*/*z* 404 (M^+). Anal. Calcd for $C_{22}H_{16}N_2O_4S$: C, 65.34; H, 3.99; N, 6.93. Found: C, 65.39; H, 3.93; N, 6.85.

2-(4-chlorophenyl)-3-[5-(2-oxo-2*H*-3-chromenyl)-1,3-oxazol-2-yl]-1,3-thiazolan-4-one (4b). This was obtained as yellow solid; Yield 66%; mp 138–40°C; IR (KBr): ν 3065, 1700, 1695, 1560, 1180, 718, 685 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 7.50–7.40 (m, 2H, ArH), 7.30–7.20 (m, 7H, ArH), 6.86 (s, 1H, ArH), 5.82 (s, 1H, N—CH—S), 3.66 (s, 2H, CH_2CO); ^{13}C NMR (DMSO-d_6): δ 171.5, 158.6, 155.3, 153.7, 137.6, 134.1, 129.6, 129.0, 128.5, 128.0, 127.8, 127.0, 123.1, 114.5, 113.2, 112.2, 105.4, 70.6, 33.7; MS: *m*/*z* 424 (M^+). Anal. Calcd for $C_{22}H_{13}ClN_2O_4S$: C, 59.37; H, 3.08; N, 6.59. Found: C, 59.31; H, 3.00; N, 6.55.

2-(4-nitrophenyl)-3-[5-(2-oxo-2*H*-3-chromenyl)-1,3-oxazol-2-yl]-1,3-thiazolan-4-one (4c). This was obtained as brown solid; Yield 72%; mp 124–26°C; IR (KBr): ν 3066, 1702, 1695, 1560, 1370, 1180, 712 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 7.62 (d, J = 8.2 Hz, 2H, ArH), 7.50–7.40 (m, 4H, ArH), 7.30–7.20 (m, 3H, ArH), 6.82 (s, 1H, ArH), 5.82 (s, 1H, N—CH—S), 3.66 (s, 2H, CH_2CO); ^{13}C NMR (DMSO-d_6): δ 171.4, 158.5, 155.4, 153.5, 148.7, 144.8, 129.6, 128.0, 127.8, 127.0, 126.8, 124.1, 123.2, 114.5, 113.2, 112.2, 105.4, 70.5, 33.6; MS: *m*/*z* 435 (M^+). Anal. Calcd for $C_{21}H_{13}N_3O_6S$: C, 57.93; H, 3.01; N, 9.65. Found: C, 57.90; H, 3.10; N, 9.60.

2-(3-nitrophenyl)-3-[5-(2-oxo-2*H*-3-chromenyl)-1,3-oxazol-2-yl]-1,3-thiazolan-4-one (4d). This was obtained as pink solid; Yield 66%; mp 130–32°C; IR (KBr): ν 3062, 1700, 1697, 1565, 1370, 1180, 715 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 8.20 (s, 1H, ArH), 8.05 (s, 1H, ArH), 7.60–7.50 (m, 4H, ArH), 7.37 (s, 1H, CH=C), 7.20–7.15 (m, 2H, ArH), 6.84 (s, 1H, ArH), 5.99 (s, 1H, N—CH—S), 3.66 (s, 2H, CH_2CO); ^{13}C NMR (DMSO-d_6): δ 171.5, 158.4, 155.3, 153.6, 148.4, 140.4, 131.4, 133.4, 129.6, 128.0, 127.0, 126.7, 123.9, 123.1, 121.0, 114.5, 113.1, 112.2, 105.5, 71.1, 33.6; MS: *m*/*z* 435 (M^+). Anal. Calcd for $C_{21}H_{13}N_3O_6S$: C, 57.93; H, 3.01; N, 9.65. Found: C, 57.95; H, 3.00; N, 9.62.

2-(4-hydroxyphenyl)-3-[5-(2-oxo-2*H*-3-chromenyl)-1,3-oxazol-2-yl]-1,3-thiazolan-4-one (4e). This was obtained as pale yellow solid; Yield 67%; mp 122–24°C; IR (KBr): ν 3339, 3060, 1704, 1696, 1565, 1180, 715 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 7.50–7.40 (m, 3H, ArH), 7.20–7.15 (m, 4H, ArH), 6.91 (d, J = 8.1 Hz, 2H, ArH), 6.84 (s, 1H, ArH), 5.82 (s, 1H, N—CH—S), 5.05 (s, 1H, OH), 3.66 (s, 2H, CH_2CO); ^{13}C NMR (DMSO-d_6): δ 171.9, 160.1, 158.3, 155.4, 153.7, 134.0, 129.6, 128.1, 127.6, 127.0, 126.7, 123.2, 115.9, 114.5, 113.7, 112.2, 105.4, 70.6, 33.5; MS: *m*/*z* 406 (M^+). Anal. Calcd for $C_{21}H_{14}N_2O_5S$: C, 62.06; H, 3.47; N, 6.89. Found: C, 62.00; H, 3.50; N, 6.83.

2-(2,6-difluorophenyl)-3-[5-(2-oxo-2*H*-3-chromenyl)-1,3-oxzol-2-yl]-1,3-thiazolan-4-one (4f). This was obtained as yellow solid; Yield 69%; mp 167–69°C; IR (KBr): ν 3065, 1705, 1692, 1562, 1180, 811, 715 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 7.50–7.40 (m, 3H, ArH), 7.30–7.25 (m, 3H, ArH), 6.86 (s, 1H, ArH), 6.67 (d, J = 7.9 Hz, 2H, ArH), 6.41 (s, 1H, N—CH—S),

3.66 (s, 2H, CH_2CO); ^{13}C NMR (DMSO-d_6): δ 171.0, 158.4, 155.4, 154.7, 153.6, 129.8, 129.0, 128.0, 127.0, 126.7, 123.1, 116.5, 114.5, 113.9, 113.7, 112.2, 105.9, 71.0, 33.4; MS: *m*/*z* 426 (M^+). Anal. Calcd for $C_{21}H_{12}F_2N_2O_4S$: C, 59.15; H, 2.84; N, 6.57. Found: C, 59.19; H, 2.80; N, 6.60.

2-[4-(dimethylamino)phenyl]-3-[5-(2-oxo-2*H*-3-chromenyl)-1,3-oxazol-2-yl]-1,3-thiazolan-4-one (4g). This was obtained as red solid; Yield 70%; mp 144–46°C; IR (KBr): ν 3062, 1705, 1695, 1561, 1407, 1185, 715 cm^{-1}; ^1H NMR (DMSO-d_6): δ 7.50–7.45 (m, 2H, ArH), 7.32 (s, 1H, CH═C), 7.20–7.15 (m, 4H, ArH), 6.84 (s, 1H, ArH), 6.40 (d, J = 8.1 Hz, 2H, ArH), 5.82 (s, 1H, N─CH─S), 3.66 (s, 2H, CH_2CO), 2.89 (s, 6H, CH_3); ^{13}C NMR (DMSO-d_6): δ 171.2, 158.4, 155.4, 153.5, 144.0, 135.6, 129.6, 128.9, 128.0, 127.0, 126.7, 123.1, 114.5, 113.9, 113.2, 112.2, 105.9, 70.6, 46.1, 33.4; MS: *m*/*z* 433 (M^+). Anal. Calcd for $C_{23}H_{19}N_3O_4S$: C, 63.73; H, 4.42; N, 9.69. Found: C, 63.75; H, 4.36; N, 9.62.

2-(4-hydroxy-3-methoxyphenyl)-3-[5-(2-oxo-2*H*-3-chromen-yl)-1,3-oxazol-2-yl]-1,3-thiazolan-4-one (4h). This was obtained as orange solid; Yield 67%; mp 163–65°C; IR (KBr): ν 3334, 3066, 1700, 1695, 1561, 1185, 1070, 711 cm^{-1}; ^1H NMR (DMSO-d_6): δ 7.50–7.40 (m, 2H, ArH), 7.30–7.20 (m, 3H, ArH), 7.10–7.05 (m, 2H, ArH), 6.91 (s, 1H, ArH), 6.86 (s, 1H, ArH), 5.82 (s, 1H, N─CH─S), 4.85 (s, 1H, OH), 3.81 (s, 3H, OCH_3), 3.66 (s, 2H, CH_2CO); ^{13}C NMR (DMSO-d_6): δ 171.4, 158.5, 155.4, 153.7, 151.7, 149.6, 135.4, 129.6, 128.0, 127.0, 126.6, 123.1, 120.4, 119.1, 114.4, 113.2, 112.2, 108.4, 105.6, 73.1, 57.1, 33.5; MS: *m*/*z* 436 (M^+). Anal. Calcd for $C_{22}H_{16}N_2O_6S$: C, 60.55; H, 3.70; N, 6.42. Found: C, 60.51; H, 3.76; N, 6.40.

2-(2-furyl)-3-[5-(2-oxo-2*H*-3-chromenyl)-1,3-oxazol-2-yl]-1, 3-thiazolan-4-one (4i). This was obtained as black solid; Yield 69%; mp 142–44°C; IR (KBr): ν 3064, 1700, 1696, 1560, 1410, 1182, 1070, 715 cm^{-1}; ^1H NMR (DMSO-d_6): δ 7.55–7.45 (m, 3H, ArH), 7.30–7.20 (m, 3H, ArH), 6.88 (s, 1H, ArH), 6.42 (d, J = 7.7 Hz, 1H, ArH), 6.11 (d, J = 7.7 Hz, 1H, ArH), 6.07 (s, 1H, N─CH─S), 3.66 (s, 2H, CH_2CO); ^{13}C NMR (DMSO-d_6): δ 171.2, 158.4, 155.4, 153.6, 149.3, 146.4, 129.6, 128.0, 127.0, 126.5, 123.8, 123.1, 114.4, 113.1, 112.2, 109.2, 105.4, 57.9, 33.6; MS: *m*/*z* 380 (M^+). Anal. Calcd for $C_{19}H_{12}N_2O_5S$: C, 60.00; H, 3.18; N, 7.36. Found: C, 59.95; H, 3.20; N, 7.40.

2-(1,3-benzodioxol-5-yl)-3-[5-(2-oxo-2*H*-3-chromenyl)-1,3-oxazol-2-yl]-1,3-thiazolan-4-one (4j). This was obtained as black solid; Yield 71%; mp 133–35°C; IR (KBr): ν 3064, 1700, 1694, 1560, 1182, 715 cm^{-1}; ^1H NMR (DMSO-d_6): δ 7.50–7.40 (m, 3H, ArH), 7.30–7.20 (m, 3H, ArH), 7.10 (d, J = 8.2 Hz, 1H, ArH), 6.90–6.85 (m, 2H, ArH), 6.81 (s, 1H, ArH), 5.80 (s, 1H, N─CH─S), 5.49 (s, 2H, O─CH_2─O), 3.66 (s, 2H, CH_2CO); ^{13}C NMR (DMSO-d_6): δ 171.4, 158.3, 155.4, 153.7, 149.1, 148.5, 136.0, 129.6, 128.0, 127.0, 126.9, 123.1, 120.6, 114.6, 113.2, 112.2, 111.2, 107.1, 105.5, 101.2, 74.1, 33.4; MS: *m*/*z* 434 (M^+). Anal. Calcd for $C_{22}H_{14}N_2O_6S$: C, 60.83; H, 3.25; N, 6.45. Found: C, 60.86; H, 3.29; N, 6.50.

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