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Synthesis and characterization of coumarin-4-thiazolidinone scaffolds as new class of anti-tuberculosis and antibacterial agents

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Abstract: *Our recent research target was to design biological active coumarin-4-thiazolidinone derivatives by using coumarin Schiff base which is pharmacologically and medicinally important scaffold. Synthesized novel coumarin-4-thiazolidinone derivatives were evaluated for their in vitro anti-tuberculosis activity against Mycobacterium tuberculosis strain $H_{37}Rv$ and showed moderate activity with MIC 25-100μg/mL. The antibacterial activity were also evaluated for synthesized compounds, among them compounds **5a** and **5o** showed the highest activity with MIC 1.6μg/mL and 0.8μg/mL respectively and these two are found to be more sensitive compounds against Gram positive bacterial strains S.aureus and B.subtilis.*

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I. Introduction

Now a day's science and technology has made implausible improvement in the field of medicine and developed various drugs against several diseases. Antibiotics are playing important role against infectious diseases and life threatening multi-drug resistant microorganisms[1], Moreover, the continuous increase in antibiotic resistant strain has provoked the advance development of alternative bacterial infection therapies to keep control over microorganism resistance. Therefore, there is a requirement to design novel drug molecules with different mode of action[2,3] and most of the essential steps in research program are directed towards the development of new drugs[4].

Tuberculosis (TB) is one of the serious infectious diseases caused by microorganism bacillus *mycobacterium tuberculosis*[5] whereas; *staphylococcus aureus* is one more Gram positive bacteria, which is responsible for variety of infections[6]. *Mycobacterium tuberculosis* and *S.aureus* annoyed the species wall to infect the humans, thus these bacterial pathogens highlights the requirement for innovative class of drugs[7,8].

Heterocyclic compounds, especially nitrogen and sulfur containing small ring heterocycles have been under exploration for a long time due to their importance in medicinal chemistry[9]. Among all bioactive heterocyclic moieties, thiazolidinone analogs are taken unique place in drug design and discovery. 4-Thiazolidinone has been subjected to extensive study in the recent year, because it is core structure present in several biosynthetic and semi-synthetic products, for examples benzylpencillin, dicloxacillin and cloxacilin. Besides, 4-thiazolidinone having N-C-S linkage[10,11] showed antibacterial, antifungal[12], anticancer[13], anti-inflammatory, antiulcer, analgesic[14] antioxidant[15], anti-tuberculosis, antiviral[16] and antileukaemic[17] activity so it is called as magic moiety due to its versatile biological activities[18]. Recent literature reported, 4-thiazolidinone is considered as good inhibitors of bacterial enzyme Mur B at micromolar level[19]. Natural penicillin and its related derivatives like sulbactam and tazobactam containing thiazolidine ring shows enormous biological activity[20].

On other hand oxygen containing coumarin heterocycles exhibited as interesting pharmacological properties[21] such as, antibacteria, antifungal[22] anti-inflammatory, antioxidant[23], antiviral[24], anticancer, anti-HIV[25], antidiabetics[26], and anti-tuberculosis[27] activity. It is also recognized that naturally occurring coumarin derivatives such as warfarin, mercumatilin, 677cumate, psoralen and calanolides are found to be pharmacologically and biologically active. While, novobiocin1 containing coumarin nucleus is strong DNA-gyrase inhibitors show terrific activity against Gram positive bacteria mainly *S.aureus*[28]. Whereas, (+)-calanolide A showed good anti-tubercular activity against all Mycobacterium tuberculosis strains and is the first compound to show anti-tuberculosis activity[29]. Thus, inspiring by anti-tubercular activity of calanolide, we were encouraged to design coumarin framework as anti-tubercular agents.

Our ongoing research on bioactive molecules[30,31] and to control bacterial resistance there is a need to associate antibiotics with modulators of drug resistance. Moreover, it is well recognized that slight alteration in the parent compounds enhances the activity and eliminates the toxicity of parent compounds[32]. Based upon review our goal has to combine above mentioned biolabile coumarin and thiazolidine-4-one heterocyclic ring together in one molecular framework, to enhance the bio-activity of fused heterocycles. Wherein, thiazolidinone 2-position fused with coumarin nucleus (**5**), exhibited as antibacterial and anti-tuberculosis activity, some of the structurally similar biological active 4-thiazolidinone and coumarin containing 4-thiazolidinone moiety are represented in **Figure 1**.

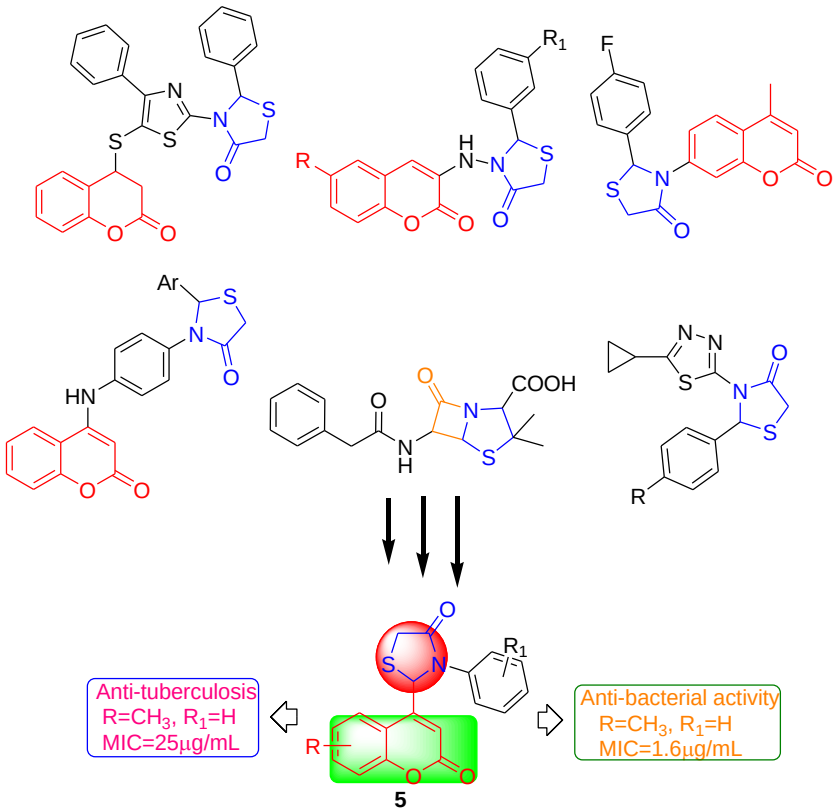


Figure 1. Targate compound (**5**) and structurally related bioactive coumarin containing thiazolidinone scaffolds.

II. Material and Methods

All the chemicals and solvent used for the research work were purchased from available commercial sources, and used without purification unless otherwise stated. Purity of the developed novel compounds were checked by thin layer chromatography (TLC) using Merck Silica Gel 60 F254 and visualized under UV light chamber. Melting point was recorded for all synthesized compounds by open capillary method and is uncorrected. The IR spectra (KBr disc) were recorded on a Nicolet 5700 FT-IR spectrophotometer and mass spectra were recorded using Agilent-singal Quartz GC-MS. Spectral analysis like ^{1}H-NMR and ^{13}C-NMR spectrum were recorded on Jeol and Bruker (400MHz) spectrometer using solvent DMSO-d_6 and internal standard TMS.

Synthesis

General experimental procedure for the synthesis of coumarin Schiff base (3a-o).

A mixture of 4-formylcoumarin (**1**) (1mmol) and aromatic aniline (**2**) (1 mmol) in ethanol were taken in 50ml round bottom flask and stirred for 15 to 20min at room temperature. The progress of the reaction was checked by TLC and after completion of the reaction, the solid obtained in the round bottom flask. Obtained solid was filtered and washed with cold ethanol to obtained pure Schiff base which was further used to synthesize coumarin thiazolidinone.

General experimental procedure for the synthesis of coumarin thiazolidine-4-one (5a-o).

A mixture of coumarin Schiff base (**3**) (1 mmol) and thioglycolic acid (**4**) (1.2 mmol) in dry toluene were taken in round bottom flask and refluxed for 8 to 10h at 110°C. The progress of the reaction was monitored by TLC and after completion of the reaction; excess toluene was removed by using rota evaporator. After removing solvent completely the solid obtained in the round bottom flask was washed with ethanol. The obtained coumarin-4-thiazolidinone is pure enough for all further characterization.

2-(6-methyl-2-oxo-2H-chromen-4-yl)-3-phenylthiazolidin-4-one (5a)

Cream solid: Yield-88%; mp-262-264; IR (KBr): 1724cm^{-1} and 1693cm^{-1}; ^{1}H-NMR (400 MHz, DMSO-d_6) δ ppm: 2.37(s, 3H, C_6-CH of coumarin), 3.82(d, 1H, *J*=13.2Hz, CH_2 of thiazolidinone), 4.02(d, 1H, *J*=16Hz, CH_2 of thiazolidinone), 6.18(s, 1H, CH of thiazolidinone), 7.03 (s, 1H, C_3-H of coumarin), 7.21 (dd, 1H, *J*=7.6Hz & *J*=1.2Hz, C_7-H of coumarin), 7.30 (d, 1H, *J*=8.8Hz, C_8-H of coumarin), 7.61(s, 1H, C_5-H of coumarin), 7.35(d, 2H, *J*=7.6Hz, CH of Phenyl ring), 7.52(d, 2H, *J*=7.6Hz, CH of Phenyl ring), 7.45(dd, 1H, *J*=8.4Hz & *J*=1.6Hz, CH of Phenyl ring); ^{13}C-NMR (400 MHz, DMSO-d_6) δ: 21.07, 32.63, 56.54, 116.59, 117.34, 124.08, 124.77, 126.90, 129.69, 133.96, 134.54, 137.92, 145.63, 152.18, 155.69, 160.11, 165.50, 171.44, 187.91; M/Z=337.

3-(3,4-dimethylphenyl)-2-(6-methyl-2-oxo-2H-chromen-4-yl)thiazolidin-4-one (5b)

Cream solid: Yield-87%; mp-257-259; IR (KBr): 1713cm^{-1} and 1692cm^{-1}; 1H-NMR (400 MHz, DMSO-d_6) δ ppm: 2.12 (s, 3H, C_3-CH_3 of phenyl ring), 2.14 (s, 3H, C_4-CH_3 of phenyl ring), 2.37 (s, 3H, C_6-CH_3 of coumarin), 3.78 (d, 1H, *J*=16Hz, CH of thiazolidinone), 4.03 (d, 1H, *J*=15.6Hz, CH of thiazolidinone), 6.18 (s, 1H, CH of thiazolidinone), 6.97 (s, 1H, C_3-H of coumarin), 7.11 (d, 1H, *J*=8.4Hz, CH of phenyl ring), 7.20 (d, 1H, *J*=7.6Hz, CH of phenyl ring), 7.35 (s, 1H, CH of phenyl ring), 7.30 (d, 1H, *J*=8.4Hz, C_8-H of coumarin), 7.45 (dd, 1H, *J*=8.4Hz, *J*=1.6Hz, C_7-H of coumarin), 7.64 (s, 1H, C_5-H of coumarin); ^{13}C-NMR (400 MHz, DMSO-d_6) δ: 19.37, 20.09, 21.08, 32.58, 116.65, 117.32, 121.74, 124.75, 125.28, 128.74, 129.43, 130.45, 133.93, 134.51, 135.55, 137.63, 152.59, 153.06, 160.15, 171.25; M/Z=365.

3-(4-methoxyphenyl)-2-(6-methyl-2-oxo-2H-chromen-4-yl)thiazolidin-4-one (5c)

Cream solid: Yield-85%; mp-238-240; IR (KBr): 1709cm^{-1} and 1689cm^{-1}; 1H-NMR (400 MHz, DMSO-d_6) δ ppm: 2.37 (s, 3H, C_6-CH_3 of coumarin), 3.71 (s, 3H, C_4-OCH_3 of phenyl ring), 3.76 (d, 1H, *J*=16Hz, CH of thiazolidinone), 4.01 (d, 1H, *J*=16Hz, CH of thiazolidinone), 6.17 (s, 1H, CH of thiazolidinone), 7.03 (s, 1H, C_3-H of coumarin), 7.12 (d, 1H, *J*=8Hz, C_8-H of coumarin), 7.20 (dd, 2H, *J*=9.6Hz, J=2.8Hz, CH of phenyl ring), 7.28 (dd, 2H, *J*=8.8Hz, *J*=2.8Hz, CH of phenyl ring), 7.36 (d, 1H, *J*=8.8Hz, C_7-H of coumarin), 7.30 (s, 1H, C_5-H of coumarin), ^{13}C-NMR (400 MHz, DMSO-d_6) δ: 21.08, 33.98, 55.78, 116.48, 118.07, 122.13, 124.45, 124.76, 128.34, 128.83, 131.14, 133.57, 134.21, 135.09, 135.49, 138.17, 152.79, 153.32, 159.67, 170.85; M/Z=367.

3-(4-methoxy-2-nitrophenyl)-2-(6-methyl-2-oxo-2H-chromen-4-yl)thiazolidin-4-one (5d)

Gray solid: Yield-86%; mp-244-246; IR (KBr): 1701cm^{-1} and 1692cm^{-1}; 1H-NMR (400 MHz, DMSO-d_6) δ ppm: 2.39 (s, 3H, C_6-CH_3 of coumarin), 3.52 (d, 1H, *J*=14.4Hz, CH of thiazolidinone), 3.70 (d. 1H, *J*=14.4Hz, CH of thiazolidinone), 3.76 (s, 3H, C_4-OCH_3 of phenyl ring), 5.72 (s, 1H, CH of thiazolidinone), 6.45 (s, 1H, C_3-H of coumarin), 7.26 (d, 1H, *J*=7.2Hz, CH of phenyl ring), 7.32 (dd, 2H, *J*=8.4Hz, CH of phenyl ring), 7.45 (d, 1H, *J*=8Hz, C_7-H of coumarin), 7.56 (s, 1H, C_5-H of coumarin), 8.04 (s, 1H, CH of phenyl ring), 8.32 (d, 1H, *J*=6.8Hz, C_8-H of coumarin); ^{13}C-NMR (400 MHz, DMSO-d_6) δ: 21.08, 33.98, 55.78, 55.77, 118.80, 121.32, 123.15, 124.43, 127.57 128.76, 131.22, 133.27, 134.87, 135.31, 137.67, 152.75, 153.23, 160.71, 169.37; M/Z=412.

3-(4-chlorophenyl)-2-(6-methyl-2-oxo-2H-chromen-4-yl)thiazolidin-4-one (5e)

Gray solid: Yield-88%; mp-244-246; IR (KBr): 1701cm^{-1} and 1698cm^{-1}; 1H-NMR (400 MHz, DMSO-d_6) δ ppm: 2.37 (s, 3H, C_6- CH_3 of coumarin), 3.82 (d, 1H, *J*=15.2Hz, CH of thiazolidinone), 4.04 (d. 1H, *J*=16Hz, CH of thiazolidinone), 6.16 (s, 1H, CH of thiazolidinone), 7.04 (s, 1H, C_3-H of coumarin), 7.32 (d, 1H, *J*=8.4Hz, C_7-H of coumarin), 7.43 (d, 2H, *J*=8.8Hz, CH of phenyl ring), 7.47 (d, 1H, *J*=7.6Hz, C_8-H of coumarin), 7.56 (d, 2H, *J*=8.8Hz, CH of phenyl ring), 7.64 (s, 1H, C_5-H of coumarin); ^{13}C-NMR (400 MHz, DMSO-d_6) δ: 21.09, 32.56, 57.21, 101.81, 117.37, 124.74, 125.65, 127.57 129.65, 131.22, 133.27, 134.87, 135.31, 136.78, 152.69, 152.20, 153.23, 160.07, 169.37; M/Z=372.

2-(2-oxo-2H-benzo[h]chromen-4-yl)-3-phenylthiazolidin-4-one (5f)

Cream solid: Yield-89%; mp-258-260; IR (KBr): 1724cm^{-1} and 1671cm^{-1}; 1H-NMR (400 MHz, DMSO-d_6) δ ppm: 3.87 (d, 1H, *J*=16Hz, CH of thiazolidinone), 4.10 (d. 1H, *J*=16Hz, CH of thiazolidinone), 6.31(s, 1H, CH of thiazolidinone), 7.14 (s, 1H, C_3-H of coumarin), 7.17-7.39 (3, 3H, of coumarin), 7.55 (d, 2H, *J*=8.4Hz, C_5 & C_6-H of coumarin), 7.68-8.03 (m, 5H, of phenyl ring), 8.30(d, 1H, *J*=8.4Hz, C_{10}-H of coumarin); ^{13}C-NMR (400 MHz, DMSO-d_6) δ: 32.65,112.59, 120.72, 122.20, 122.83, 123.57, 124.17, 124.19, 124.85, 126.92, 128.26, 128.54, 128.74, 129.43, 129.68, 129.72, 124.86, 133.46, 137.94, 151.19, 159.88, 171.48.; M/Z=373.

3-(3,4-dimethylphenyl)-2-(2-oxo-2H-benzo[h]chromen-4-yl)thiazolidin-4-one (5g)

Cream solid: Yield-87%; mp-258-260; IR (KBr): 1716cm^{-1} and 1695cm^{-1}; 1H-NMR (400 MHz, DMSO-d_6) δ ppm: 2.11 (s, 3H, C_3-CH_3 of phenyl ring), 2.14 (s, 3H, C_4-CH_3 of phenyl ring), 3.80 (d, 1H, *J*=16Hz, CH of thiazolidinone), 4.04 (d. 1H, *J*=16Hz, CH of thiazolidinone), 6.31(s, 1H, CH of thiazolidinone), 7.09 (s, 1H, C_3-H of coumarin), 7.11 (s, 1H, *J*=8.4Hz, C_5-H, of coumarin), 7.38 (s, 1H, CH phenyl ring), 7.66-7.73 (m, 2H, of coumarin), 7.83(d, 1H, *J*=8.8Hz, CH of phenyl ring), 7.89 (d, 1H, *J*=8.8Hz, CH of phenyl ring), 8.03 (dd, 2H, *J*=6.8Hz, *J*=1.6Hz, CH of coumarin), 8.30 (d, 1H, *J*=7.6Hz, CH of coumarin); ^{13}C-NMR (400 MHz, DMSO-d_6) δ:19.37, 20.07, 32.60, 55.45, 59.32, 106.29, 112.64, 114.81, 116.00, 120.73, 122.22, 122.83, 124.84, 128.25, 128.54, 129.43, 129.71, 130.45, 134.85, 135.28, 137.63, 151.16, 159.92, 188.21; M/Z=401.

3-(4-methoxyphenyl)-2-(2-oxo-2H-benzo[h]chromen-4-yl)thiazolidin-4-one (5h)

Cream solid: Yield-85%; mp-258-260; IR (KBr): 1727cm^{-1} and 1667cm^{-1}; 1H-NMR (400 MHz, DMSO-d_6) δ ppm: 3.67 (s, 3H, C_4-OCH_3 of phenyl ring), 3.80 (d, 1H, *J*=16.4Hz, CH of thiazolidinone), 4.03 (d. 1H, *J*=16.4Hz, CH of thiazolidinone), 6.36 (s, 1H, CH of thiazolidinone), 6.90 (s, 1H, C_3-H of coumarin), 6.92 (d, 1H, *J*=8.8Hz, CH of phenyl ring), 7.08(d, 1H, *J*=8.8Hz, CH phenyl ring), 7.46-7.47 (m, 2H, of coumarin), 7.68-7.73(m, 2H, CH of coumarin), 7.89 (d, 2H, *J*=8.8Hz, CH of coumarin), 8.03 (dd, 1H, *J*=6.8Hz, *J*=2Hz, CH of coumarin), 8.32 (d, 1H, *J*=7.6Hz, CH of coumarin); ^{13}C-NMR (400 MHz, DMSO-d_6) δ:19.36, 20.14, 31.60, 55.65, 111.78, 115.21, 116.42, 121.04, 122.32, 122.37, 124.54, 127.88, 128.73, 130.03, 130.71, 131.45, 135.22, 135.38, 136.77, 152.89, 160.02, 186.46, 188.73; M/Z=403.

3-(4-methoxy-2-nitrophenyl)-2-(2-oxo-2H-benzo[h]chromen-4-yl)thiazolidin-4-one(5i)

Gray solid: Yield-83%; mp-263-265; IR (KBr): 1716cm^{-1} and 1695cm^{-1}; 1H-NMR (400 MHz, DMSO-d_6) δ ppm: 3.65 (s, 3H, C_4-OCH_3 of phenyl ring), 3.87 (d, 1H, *J*=16.4Hz, CH of thiazolidinone), 4.02 (d. 1H, *J*=16.4Hz, CH of thiazolidinone), 6.38 (s, 1H, CH of thiazolidinone), 7.02 (s, 1H, C_3-H of coumarin), 7.09 (d, 2H, *J*=8Hz, CH of phenyl ring), 7.21(s, 1H, CH phenyl ring), 7.32-7.45 (m, 4H, of coumarin), 7.52-7.62(m, 2H, CH of coumarin), ^{13}C-NMR (400 MHz, DMSO-d_6) δ:20.08, 21.24, 31.54, 55.46, 59.37, 115.23, 116.22, 122.14, 122.78, 123.64, 125.37, 127.84, 128.56, 130.34, 130.96, 131.76, 135.47, 135.63, 136.68, 155.31, 160.23, 187.57, 188.16; M/Z=418.

3-(4-chlorophenyl)-2-(2-oxo-2H-benzo[h]chromen-4-yl)thiazolidin-4-one(5j)

Cream solid: Yield-85%; mp-236-238; IR (KBr): 1724cm^{-1} and 1672cm^{-1}; 1H-NMR (400 MHz, DMSO-d_6) δ ppm: 3.78 (d, 1H, *J*=16.4Hz, CH of thiazolidinone), 4.01 (d. 1H, *J*=16.4Hz, CH of thiazolidinone), 6.38 (s, 1H, CH of thiazolidinone), 7.06 (s, 1H, C_3-H of coumarin), 7.18 (d, 2H, *J*=8Hz, CH of phenyl ring), 7.32 (d, 2H, *J*=8Hz, CH phenyl ring), 7.37-7.49 (m, 2H, of coumarin), 7.52-7.88 (m, 2H, CH of coumarin), 8.09 (d, 2H, *J*=8Hz, CH of coumarin ^{13}C-NMR (400 MHz, DMSO-d_6) δ: 55.52, 60.59, 106.47, 110.58, 115.18, 116.37, 122.42, 122.21, 122.73, 124.64, 125.68, 128.97, 130.18, 130.86, 132.62, 135.32, 135.78, 136.41, 153.19, 160.21, 185.08, 187.23; M/Z=408.

2-(6-methoxy-2-oxo-2H-chromen-4-yl)-3-phenylthiazolidin-4-one (5k)

Gray solid: Yield-87%; mp-236-238; IR (KBr): 1709cm^{-1} and 1698cm^{-1}; 1H-NMR (400 MHz, DMSO-d_6) δ ppm: 3.84 (d, 1H, *J*=15.6Hz, CH of thiazolidinone), 3.82 (s, 3H, C_6-OCH_3 of coumarin), 4.06 (d. 1H, *J*=16Hz, CH of thiazolidinone), 6.20 (s, 1H, CH of thiazolidinone), 7.09 (s, 1H, C_3-H of coumarin), 7.18-7.26 (m, 2H, CH of phenyl ring), 7.30-7.37 (m, 3H, CH phenyl ring), 7.39 (s, 1H, C_5-H of coumarin), 7.54 (d, 2H, *J*=8Hz, C_7 & C_8-H of coumarin); ^{13}C-NMR (400 MHz, DMSO-d_6) δ: 32.61, 56.50, 99.99, 108.16, 117.33, 118.67, 120.12, 124.00, 125.32, 126.88, 129.70, 135.46, 137.92, 148.33, 156.22, 160.10, 171.44, 187.81, 189.07; M/Z=353.

3-(3,4-dimethylphenyl)-2-(6-methoxy-2-oxo-2H-chromen-4-yl)thiazolidin-4-one (5l)

Gray solid: Yield-89%; mp-232-234; IR (KBr): 1702cm^{-1} and 1697cm^{-1}; 1H-NMR (400 MHz, DMSO-d_6) δ ppm: 2.12 (s, 3H, C_3-CH_3 of phenyl ring), 2.15 (s, 3H, C_4-CH_3 of coumarin), 3.80 (d, 1H, *J*=16Hz, CH of thiazolidinone), 3.82 (s, 3H, C_6-OCH_3 of coumarin), 4.03 (d. 1H, *J*=15.6Hz, CH of thiazolidinone), 6.20 (s, 1H,

CH of thiazolidinone), 7.03 (s, 1H, C_3-H of coumarin), 7.12 (d, 1H, *J*=8Hz, CH of phenyl ring), 7.20 (s, 1H, CH phenyl ring), 7.25 (dd, 1H, *J*=8.8Hz, J=2.8Hz, C_7-H of coumarin), 7.28 (d, 1H, *J*=8Hz, CH of phenyl ring), 7.34 (s, 1H, C_5-H of coumarin), 7.36 (d, 1H, *J*=8Hz, C_8-H of coumarin); ^{13}C-NMR (400 MHz, DMSO-d_6) δ: 19.37, 20.10, 32.57, 56.50, 118.65, 120.00, 121.64, 125.17, 130.46, 135.26, 135.56, 137.63, 148.30, 154.52, 155.13, 155.83, 156.20, 160.01, 160.13, 170.92, 171.26; M/Z=381.44.

2-(6-methoxy-2-oxo-2H-chromen-4-yl)-3-(4-methoxyphenyl)thiazolidin-4-one (5m)

Gray solid: Yield-89%; mp-232-234; IR (KBr): 1712cm^{-1} and 1686cm^{-1}; 1H-NMR (400 MHz, DMSO-d_6) δ ppm: 3.68 (s, 3H, C_4-OCH_3 of phenyl ring), 3.80 (s, 3H, C_6-OCH_3 of coumarin), 3.8 (d, 1H, *J*=14Hz, CH of thiazolidinone), 4.03 (d. 1H, *J*=16Hz, CH of thiazolidinone), 6.24 (s, 1H, CH of thiazolidinone), 6.92 (d, 2H, *J*=7.2Hz, CH of phenyl ring), 7.01 (s, 1H, C_3-H of coumarin), 7.28 (d, 1H, *J*=8Hz, CH of phenyl ring), 7.25 (dd, 1H, *J*=8Hz, *J*=2.8Hz, C_7-H of coumarin), 7.36 (d, 1H, *J*=8.8Hz, CH of phenyl ring), 7.45 (d, 1H, *J*=8Hz, C_8-H of coumarin), 7.43 (s, 1H, C_5-H of coumarin); ^{13}C-NMR (400 MHz, DMSO-d_6) δ: 32.47, 55.79, 56.49, 100.00, 108.09, 114.83, 118.68, 120.09, 121.64, 125.17, 126.02, 130.46, 135.26, 135.56, 137.63, 148.31, 156.25, 157.94, 160.13, 171.20; M/Z=383.

2-(6-methoxy-2-oxo-2H-chromen-4-yl)-3-(4-nitrophenyl)thiazolidin-4-one (5n)

Gray solid: Yield-83%; mp-252-254; IR (KBr): 1716cm^{-1} and 1696cm^{-1}; 1H-NMR (400 MHz, DMSO-d_6) δ ppm: 3.79 (s, 6H, C_4 & C_6-OCH_3 of phenyl ring and coumarin), 3.38 (d, 1H, *J*=16Hz, CH of thiazolidinone), 3.61 (d. 1H, *J*=16Hz, CH of thiazolidinone), 6.35 (s, 1H, CH of thiazolidinone), 6.52 (s, 1H, C_3-H of coumarin), 7.16 (s, 1H, CH of phenyl ring), 7.17 (d, 1H, *J*=8Hz, CH of phenyl ring), 7.19 (d, 1H, *J*=8Hz, CH of phenyl ring), 7.33 (d, 2H, *J*=9.2Hz, C_7 & C_8-H of coumarin), 7.50 (d, 1H, *J*=8.8Hz, C_5-H of coumarin); ^{13}C-NMR (400 MHz, DMSO-d_6) δ: 32.10, 56.50, 108.23, 118.64, 120.00, 121.63, 125.17, 127.62, 130.46, 135.25, 135.56, 137.63, 148.30, 152.67, 153.16, 156.20, 160.13, 170.92, 171.25; M/Z=398.

3-(4-chlorophenyl)-2-(6-methoxy-2-oxo-2H-chromen-4-yl)thiazolidin-4-one (5o)

Gray solid: Yield-82%; mp-236-238; IR (KBr): 1706cm^{-1} and 1698cm^{-1}; 1H-NMR (400 MHz, DMSO-d_6) δ ppm: 3.82 (s, 3H, C_6-OCH_3 of coumarin), 3.85 (d, 1H, *J*=14Hz, CH of thiazolidinone), 3.06 (d. 1H, *J*=16Hz, CH of thiazolidinone), 6.18 (s, 1H, CH of thiazolidinone), 7.09 (s, 1H, C_3-H of coumarin), 7.24 (d, 1H, *J*=8.8Hz, CH of phenyl ring), 7.28 (d, 1H, *J*=6.8Hz, CH of phenyl ring), 7.37 (d, 1H, *J*=8.8Hz, C_6-H of coumarin), 7.46 (d, 2H, *J*=9.2Hz, CH of phenyl ring), 7.56 (d, 1H, *J*=8.8Hz, C_5-H of coumarin), 7.59 (d, 1H, *J*=8.8Hz, C_8-H of coumarin); ^{13}C-NMR (400 MHz, DMSO-d_6) δ: 32.55, 56.49, 108.17, 117.29, 118.69, 120.10, 122.12, 125.57, 127.53, 129.66, 130.90, 135.23, 136.78, 148.35, 152.43, 153.67, 156.21, 160.06, 171.51; M/Z=387.

Biological protocoal

Anti-tuberculosis activity

Anti-tuberculosis activity was assessed against M. tuberculosis for all the newly synthesized compounds using standard drugs Pyrazinamide, Ciprofloxicin and Streptomycin.

The anti-mycobacterial activity of all the synthesized compounds was evaluated against M. tuberculosis using Microplate Almar Blue Assay (MABA). In this methodology uses thermally stable reagent and this is non toxic, shows good correlation with propotional and BACTEC radiometric method. Firstly, 200µl of sterile deionzed water was added to all outer perimeter wells of sterile 96 wells plate to minimized evaporation of medium in the test wells during incubation. The 96 wells plate received 100µl of the Middlebrok 7H9 broth and serial dilution of compounds were made directly on plate. The final drug concentrations tested were 100 to 0.2µg/mL. Plates were covered and sealed with parafilm and incubated at 37°C for five days. After this, 25µl of freshly prepared 1:1 mixture of Almar Blue reagent and 10% tween 80 was added to the plate and incubated for 24h. A blue color in the well was interpreted as no bacterial growth and pink color was scored as growth. The MIC was defined as lowest drug concentration which prevented the color changes from blue to pink.

Antibacterial activity

The synthesized compounds are evaluated for their *in vitro* antibacterial activity against standard Ciprofloxacin drug using minimum inhibition method (MIC) method.

Nine dilutions for each drug have to be done with BHI for MIC. In the initial tube 20µl of drug was added into the 380µl of Brain Heart infusion (BHI) broth. For dilutions 200µl of BHI broth was added into the next nine tubes separately. Then from the initial tube 200µl was transferred to the first tube containing 200µl of

BHI broth. This was considered as 10^{-1} dilution. From 10^{-1} diluted tube containing 200µl was transferred to second tube to make it 10^{-2} dilution. The serial dilution was repeated up to 10^{-9} dilution for each drug. From the remaining stock cultures of required organisms, 5µl was taken and added into 2ml of BHI broth. In each serially diluted tube 200µl of above culture suspension was added. The tubes were incubated for 24h and observed for turbidity.

III. Results

The coumarin Schiff base (**3b**) was confirmed by its spectral characterization, IR stretching frequency of lactone carbonyl group of coumarin is observed at 1721cm^{-1} and GC-mass spectrum of compound **3b** is observed as m/z 291. Further title compound was also confirmed by ^{1}H NMR spectroscopy wherein, two methyl group of phenyl ring are resonated as singlet at δ 2.21ppm and δ 2.24ppm and C_6-CH_3 of coumarin resonated as a singlet at δ 2.36ppm respectively. C_3-H of coumarin resonated as a singlet at δ 6.90ppm and C_7-H of coumarin resonated as a doublet of doublet at δ 7.45ppm (*J*=8.4Hz & *J*=1.6Hz). The C_8-H of coumarin resonated as doublet at δ 7.32ppm (*J*=8.4Hz) and singlet at δ 8.59ppm due to C_5-H of coumarin. Whereas, two a doublets at δ 7.20ppm (*J*=8Hz) and δ 7.17ppm (*J*=8Hz) due to pheyl ring protons and one proton of phenyl ring resonated as a singlet at δ 7.24ppm.

The compound **5a** was confirmed by its spectral analysis, IR stretching frequency of lactone carbonyl and amide carbonyl group observed at 1724cm^{-1} and 1693cm^{-1} respectively. GC-MS of compound **5a** molecular weight is observed at m/z 337. Further, the compound is confirmed by ^{1}H NMR spectroscopy wherein, C_6-CH_3 of coumarin resonated as a singlet at around δ 2.37ppm and C_5-CH_2 proton of thiazolidinone resonated as doublet due to geminal coupling at δ 3.82ppm (*J*=16Hz) and δ 4.02ppm (*J*=16Hz) respectively. The C_2-H of thiazolidinone resonated as a singlet at δ 6.18ppm and C_3-H of coumarin resonated as a singlet at δ 7.03ppm. The C_7-H of coumarin resonated as doublet of doublet at δ 7.21ppm (*J*=7.6Hz and *J*=1.2Hz) and C_8-H of coumarin resonated as doublet at δ 7.30ppm (*J*=8.8Hz) whereas, C_5-H coumarin resonated as a singlet at δ 7.61ppm. The phenyl ring protons resonated as doublet at δ 7.35ppm (*J*=7.6Hz) and two proton resonated as doublet at δ 7.52ppm (*J*=7.6Hz) due to phenyl ring proton. Whereas, C_4-H of phenyl ring resonated as doublet of doublet at δ 7.45ppm (*J*=8.4Hz and *J*=1.6Hz). The chemical shift and possible coupling constant values are assigned for compounds **3b** and **5a** in Figure **2** and **3**.

Chemical shift in δ ppm	**Structural information**
2.21 (s, 3H)	:-CH_3 of Phenyl ring
2.24 (s, 3H)	:-CH_3 of Phenyl ring
2.36 (s, 3H)	:C_6-CH_3 of coumarin
6.90 (s, 1H)	:C_3-H of coumarin
7.17 (d, 1H, *J*=8Hz)	: Phenyl ring
7.20 (d, 1H, *J*=8Hz)	: Phenyl ring
7.24 (s, 1H)	: Phenyl ring
7.32 (d, 1H, *J*=8.4Hz)	:C_8-H of coumarin
7.45 (dd, 1H, *J*=8.4Hz, *J*=1.6Hz)	:C_7-H of coumarin
8.59 (s, 1H)	:C_5-H of coumarin
8.90 (s, 1H)	: CH of imine

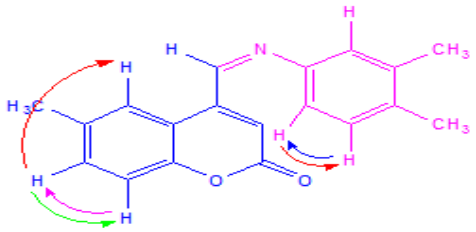


Figure 2 Chemical shift and coupling constant values of compound **3b**

Chemical shift in δ ppm	**Structural information**
2.37 (s, 3H)	: -CH_3 of coumarin
3.82 (d, 1H, *J*=16Hz)	: -CH_2 of thiazolidinone
4.02 (d, 1H, *J*=16Hz)	: -CH_2 of thiazolidinone
6.18 (s, 1H)	: -CH of thiazolidinone
7.03 (s, 1H)	: C_3-H of coumarin
7.21 (dd, 1H, *J*=7.6Hz & *J*=1.2Hz)	:C_7-H of coumarin
7.30 (d, 1H, *J*=8.8Hz)	: C_8-H of coumarin

7.61 (s, 1H) : C_5-H of coumarin
7.35 (d, 2H, *J*=7.6Hz) : Phenyl ring
7.52 (d, 2H, *J*=7.6Hz) : Phenyl ring
7.45 (d, 1H, *J*=8.4Hz & *J*=1.6Hz) : Phenyl ring

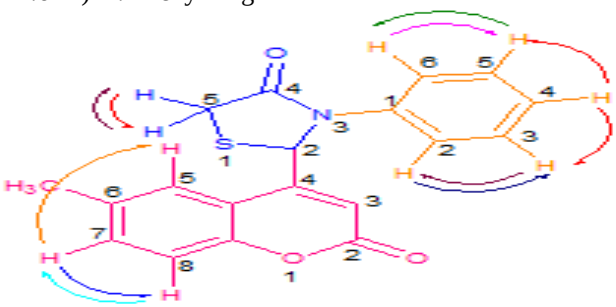
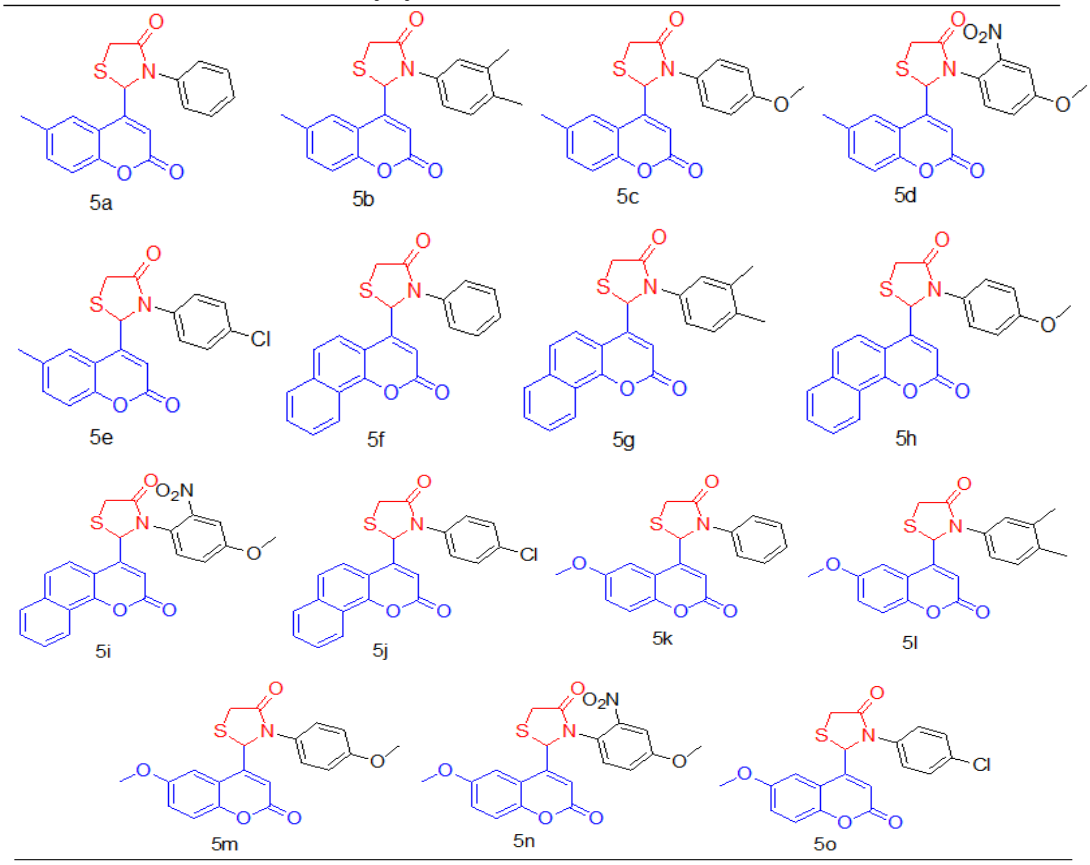


Figure 3 Chemical shift and coupling constant values of compound **5a**

Table 1 List of newly synthesized coumarin-4-thiazolidinone derivatives.



Biological screening

Anti-tubercular activity

Coumarin-4-thiazolidinone derivatives (**5a-o**) were assessed for their *in vitro* anti-tuberculosis activity against Mycobacterium tuberculosis strain $H_{37}Rv$ by MABA (Microplate Alamar Blue Assay) whereas; Pyrazinamide, Ciprofloxacine and Streptomycin are used as standard drugs. This methodology is non toxic, thermally stable and activity results are expressed in minimum inhibitory concentration (MIC) in µg/mL.

Table 2 reveals all the newly synthesized target compounds (**5a-o**) showed moderate activity against anti-tubercular strains with MIC 25 to 100µg/mL. Compound **5a** (6-CH_3 substitution on coumarin and aniline), **5c** (6-CH_3 substitution on coumarin and 3,4-di-CH_3 substitution on aniline) and **5o** (C_6-OCH_3 substitution on coumarin and C_4-Cl substitution on aniline) are showed good anti-tubercular activity with MIC 25µg/mL whereas compound **5b** (C_6-CH_3 substitution on coumarin and C_3,C_4-di-CH_3 substitution on aniline) and **5i** (7,8 benzo- substitution on coumarin and C_2-NO_2 & C_4-OCH_3 substitution on aniline) showed ten to twenty fold less activity then standard drugs. And all other compounds are moderately active with MIC 50µg/mL. **Figure 4**

indicates graphical presentation of the anti-tubercular activity results of all the compounds in comparison with the standard.

Table 2 Anti-tubercular activity of newly synthesized coumarin-4-thiazolidinone derivatives (**5a-o**).

Entry	Product Code	R	R_1	MIC (µg/mL)
1	5a	6-CH_3	H	25
2	5b	6-CH_3	3,4-di-CH_3	100
3	5c	6-CH_3	4-OCH_3	25
4	5d	6-CH_3	2-NO_2, 4-OCH_3	50
5	5e	6-CH_3	4-Cl	50
6	5f	7,8-Benzo	H	50
7	5g	7,8-Benzo	3,4- di-CH_3	50
8	5h	7,8-Benzo	4-OCH_3	50
9	5i	7,8-Benzo	2-NO_2, 4-OCH_3	100
10	5j	7,8-Benzo	4-Cl	50
11	5k	6-OCH_3	H	50
12	5l	6-OCH_3	3,4- di-CH_3	50
13	5m	6-OCH_3	4-OCH_3	50
14	5n	6-OCH_3	2-NO_2, 4-OCH_3	50
15	5o	6-OCH_3	4-Cl	25
Pyrazinamide				**3.125**
Ciprofloxacine				**3.125**
Streptomycin				**6.25**

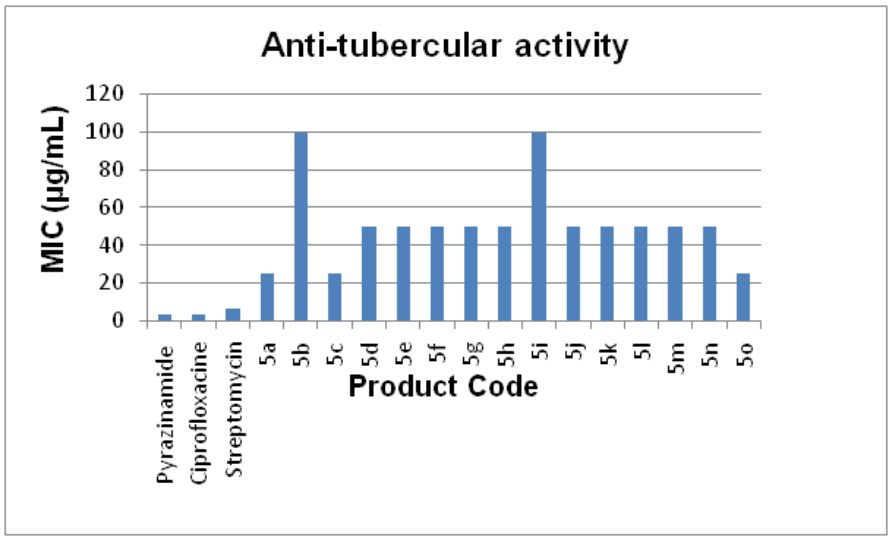


Figure 4 Graphical presentation of minimum inhibitory concentration (MIC) of all the compounds against Mycobacterium tuberculosis strain $H_{37}Rv$

***In vitro* antibacterial activity**

All the synthesized coumarin-4-thiazolidinone derivatives (**5a-o**) were examined for *in vitro* antibacterial activity by broth dilution method against Gram positive (*S.aureus and B.subtilis*) and Gram negative (*E.coli and P.aeruginosa*) bacterial strains. The Minimum inhibitory concentration (MIC) was determined and results of all synthesized compounds are summarized in **table 3**. All coumarin thiazolidinone compounds (**5a-o**) showed excellent activity against Gram positive bacterial strains with MIC **1.6** to **6.25**µg/mL whereas moderate activity against Gram negative bacterial strains with MIC **25** to **100**µg/mL, while Ciprofloxicine standard drug with MIC **2**µg/mL and **4**µg/mL respectively.

Table 3 reveals that the all compounds found to be significant effect on bacterial strains. Compound **5a** having methyl substitution on coumarin found to be more active with MIC **1.6**µg/mL compare to standard drug with MIC **2**µg/mL. Further, the methoxy substitution on coumarin and chloro substitution on aniline (**5o**) showed promising activity with MIC **0.8**µg/mL which was found to be highly active compound against *S.aureus* compare to all THE synthesized compound and **5o** showed moderate activity against *B.subtilis* with MIC 25µg/mL. Similarly, the compounds **5c** and **5m** having methyl and methoxy substitution on coumarin and methoxy substitution on aniline respectively are found to be active against both Gram positive bacterial strains with MIC 3.25µg/Ml. Whereas, the compounds **5b, 5d, 5k** and **5n** having methyl and methoxy substitution on coumarin and aniline with nitro and 3,4-di-CH_3 substitution are showed good activity against *S.aureus* with MIC

3.25Mg/mL and MIC 6.25-12.5µg/mL against *B.subtilis*. While, **5g, 5i** and **5l** having 7,8 benzo and methoxy substitution on coumarin and aniline with nitro, methoxy and 3,4-di-CH_3 substitution showed good activity against both tested Gram positive bacterial strains (*B.subtilis and S.aureus*) with MIC 3.25µg/mL and 6.25µg/mL respectively. The compounds **5e, 5f, 5h** and **5j** are showed least activity against both Gram positive bacterial strains and considered to be inactive compounds.

Antibacterial activity results reveal that, all the synthesized compounds are not active against both the Gram negative bacterial strains. From above observation we conclude that, electron donating groups like methyl and methoxy substitution on coumarin enhances the antibacterial activity whereas electron withdrawing group like nitro and chloro substitution on phenyl ring affect the antibacterial activity. The most sensitive bacterial species to our synthesized compounds were *S.aureus* and *B.subtilis* while, both Gram negative bacterial strains are most resistant to our compounds. The epigrammatic structure activity relationship (SAR) of all the compounds is drawn in **Figure 6** and antibacterial activity results with standard drug are presented in **Figure 5.**

Table 3 Antibacterial activity of newly synthesized coumarin-4-thiazolidinone derivatives (**5a-o**).

Entry	**Product Code**	**R**	**R_1**	**Minimum inhibitory concentration(MIC) µg/mL**			
				Gram (+)		**Gram (-)**	
				S.aureus	***B.subtilis***	***E.coli***	***P.aeruginosa***
1	5a	6-CH_3	H	**1.6**	**1.6**	50	50
2	5b	6-CH_3	3,4- di-CH_3	3.25	12.5	100	100
3	5c	6-CH_3	4-OCH_3	3.25	3.25	100	100
4	5d	6-CH_3	2-NO_2, 4-OCH_3	6.25	12.5	100	100
5	5e	6-CH_3	4-Cl	50	50	100	100
6	5f	7,8-Benzo	H	25	50	50	50
7	5g	7,8-Benzo	3,4- di-CH_3	25	6.25	100	100
8	5h	7,8-Benzo	4-OCH_3	50	100	100	100
9	5i	7,8-Benzo	2-NO_2, 4-OCH_3	12.5	6.25	100	100
10	5j	7,8-Benzo	4-Cl	50	25	100	100
11	5k	6-OCH_3	H	3.25	12.5	50	50
12	5l	6-OCH_3	3,4- di-CH_3	25	3.25	100	100
13	5m	6-OCH_3	4-OCH_3	3.25	3.25	50	100
14	5n	6-OCH_3	2-NO_2, 4-OCH_3	3.25	6.25	100	100
15	5o	6-OCH_3	4-Cl	**0.8**	25	100	100
Ciprofloxacin				**2**	**2**	**2**	**>4**

*Bold value represents the significant activity result for each bacterial strain.

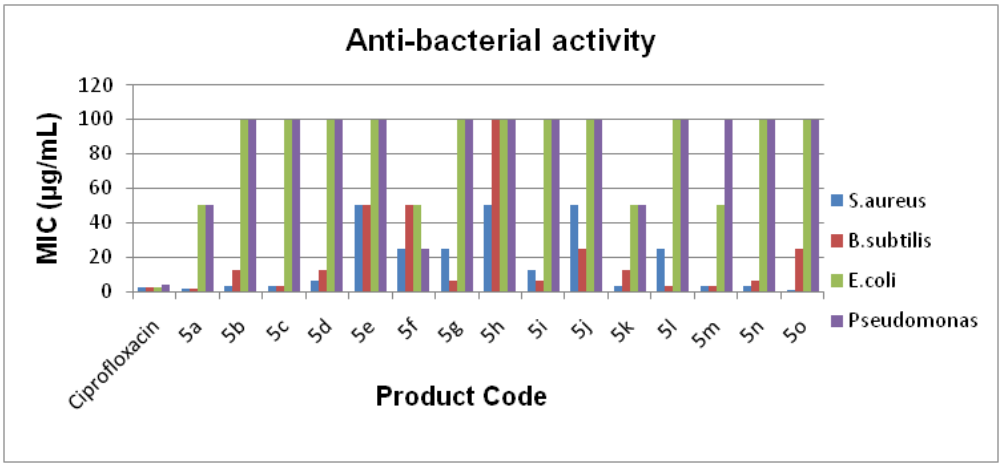


Figure 5 Graphical presentation of minimum inhibitory concentration (MIC) of all the compounds against *S.aureus, B.subtiles, E.coli* and *P.aeruginosa*.

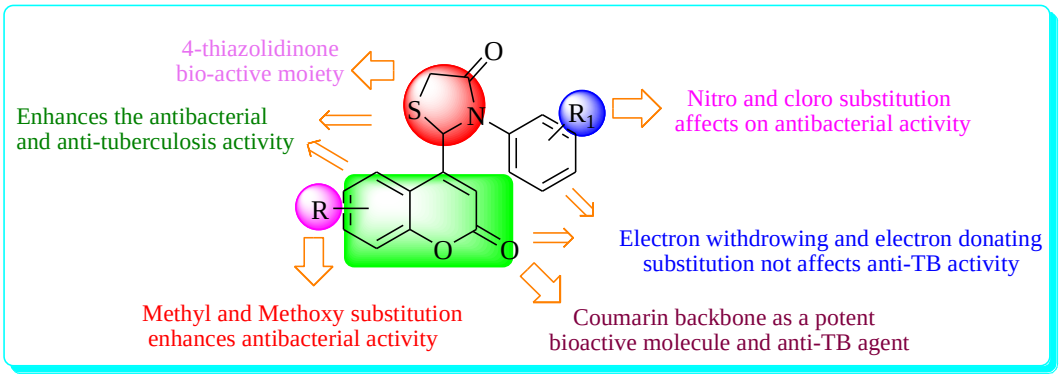


Figure 6 SAR study of coumarin-4-thiazolidinone derivatives

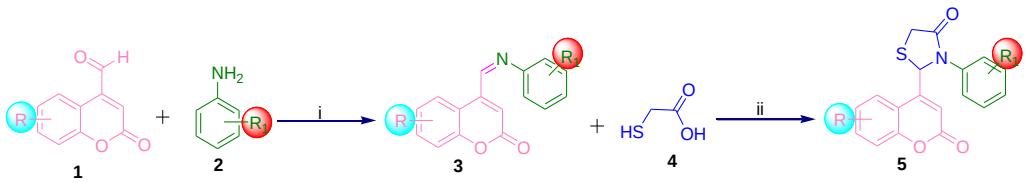
IV. Discussion

Chemistry

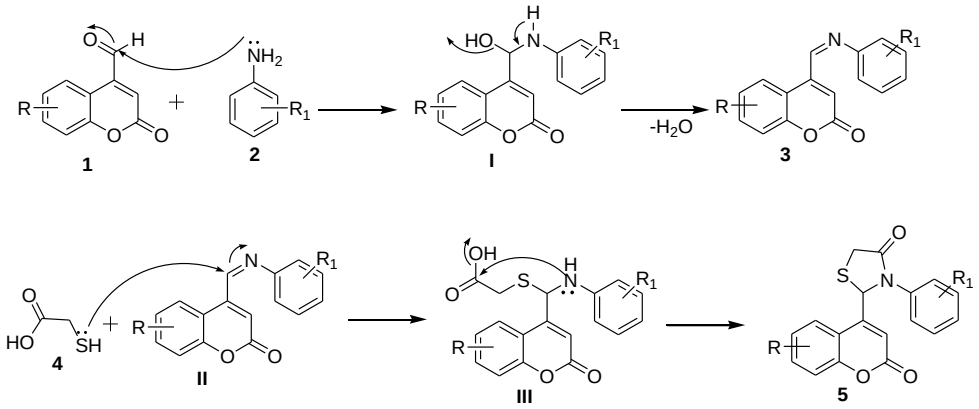
The targeted coumarin-4-thiazolidinones (**5**) are synthesized sequentially and synthetic route is outlined in **Scheme 1**. Coumarin-4-thiazolidinone derivatives (**5**) have been synthesized from Schiff bases which were prepared using different substituted aromatic anilines (**2**) and 4-formylcoumarin (**1**) in ethanol at room temperature without using any catalyst in 80% yield. Further, Schiff base (**3**) and thioglycolic acid (**4**) was refluxed on oil bath for 8h at 110°C, in the presence of dry toluene afforded desired coumarin thiazolidin-4-one (**5**) with excellent yield (**Table 1**). Synthesized coumarin Schiff bases (**3**) and final targeted coumarin-4-thiazolidinone compounds (**5**) are characterized by IR, Mass, ^{1}H-NMR and ^{13}C-NMR spectral analysis.

The plausible reaction mechanism for the synthesis of coumarin thiazolidine-4-one derivatives (**5**) from Schiff base is illustrated in **Scheme 2**. Mechanically, in first step of reaction, there is a condensation reaction takes place between 4-formylcoumarin (**1**) and aromatic aniline (**2**) to form imine (**3**) by eliminating water molecules. In second step of reaction, the formed imine (**3**) undergoes cyclocondensation reaction with thioglycolic acid, followed dehydration at higher temperature led to stable coumarin thiazolidinone (**5**).

Scheme 1. Synthesis of compounds **3a-o**, **5a-o**, (i) 15-20min at RT, ethanol. (ii) Thioglycolic acid, 8h, toluene, reflux.



Scheme 2. Plausible mechanism for the formation of coumarin-4-thiazolidinone.



V. Conclusion

Present research work is based on the discovery of novel antibacterial and anti-tuberculosis agent coumarin thiazolidin-4-one using thioglycolic acid by sequential method. The anti-tuberculosis evaluation was performed against all fifteen synthesized derivatives against Mycobacterium tuberculosis strain $H_{37}Rv$, among all compounds (**5a-o**) **5a, 5c** and **5o** are found to be moderately active with MIC 25µg/mL. Compounds **5a-o** exhibited a significant growth of inhibition against a wide spectrum of Gram positive bacterial strains. Compounds **5a** and **5o** are found to be as more active and promising antibacterial agents against both Gram positive bacterial strains *S.aureus and B.subtilis* with MIC 0.8-1.6µg/mL, whereas all other compounds showed good activity with MIC ranging from 3.25 to 12.5µg/mL. It is interesting to note that, *E.coli* and *P.aeruginosa* are most resistant towards our synthesized compounds and it is observed that, antibacterial activity result against Gram positive bacterial strain shows a discrepancy to every compound based on different substitution group present on both coumarin and aniline ring. Most of the compounds with methoxy and methyl group substitution on coumarin and aniline ring showed good activity and more sensitive towards Gram positive bacterial strain.

Acknowledgment

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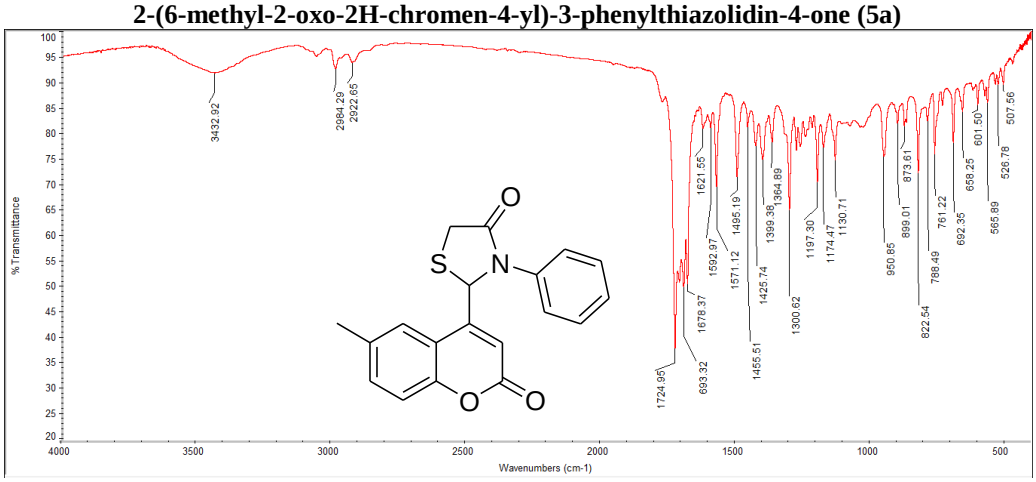
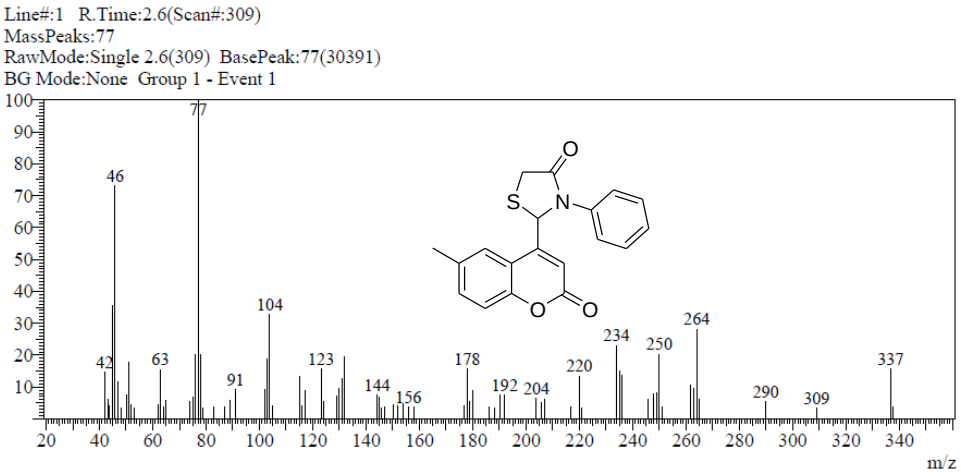
Supplimentary Information

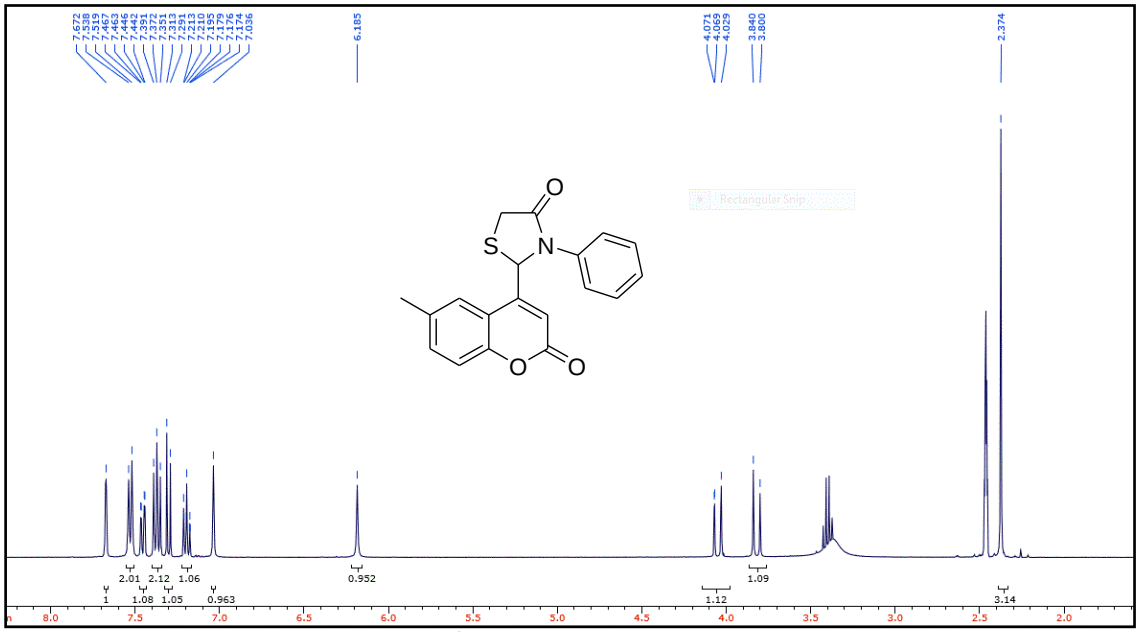
2-(6-methyl-2-oxo-2H-chromen-4-yl)-3-phenylthiazolidin-4-one (5a)



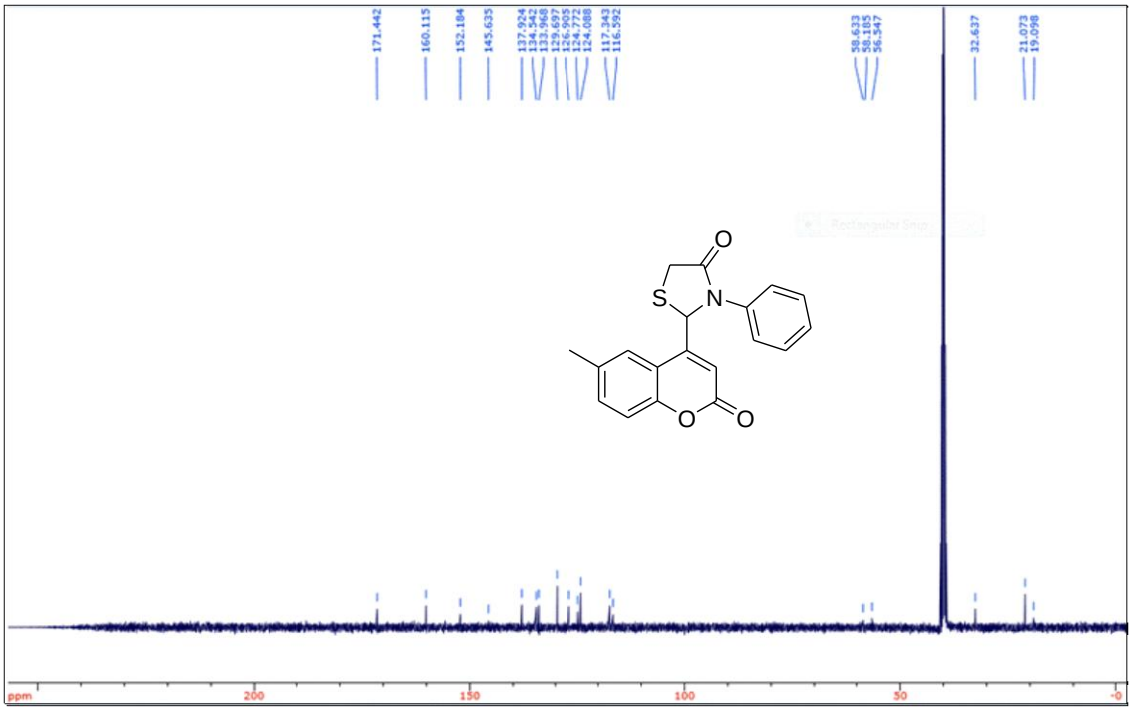
Spectrum-1: IR spectrum of compound **5a**



Spectrum-2: GC-MS spectrum of compound **5a**

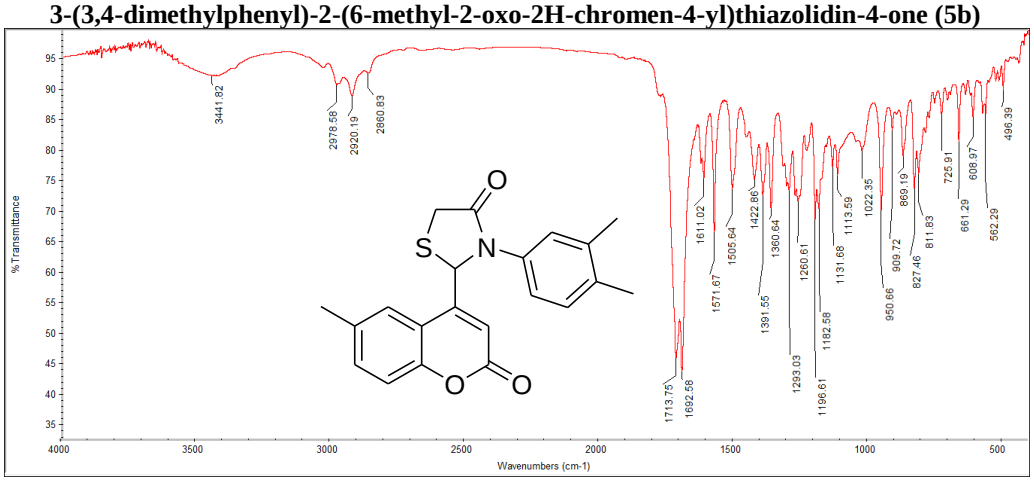


Spectrum-3: ^{1}H NMR spectrum of compound **5a**

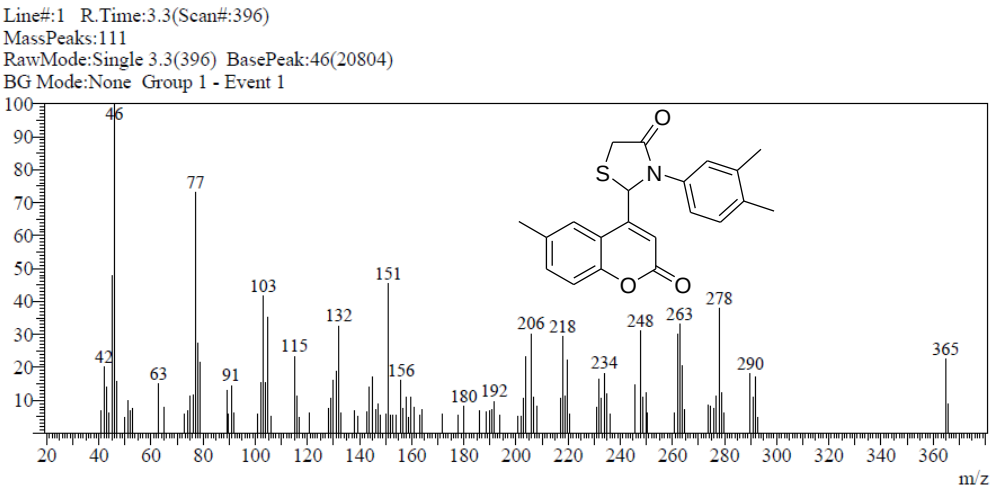


Spectrum-4: ^{13}C NMR spectrum of compound **5a**

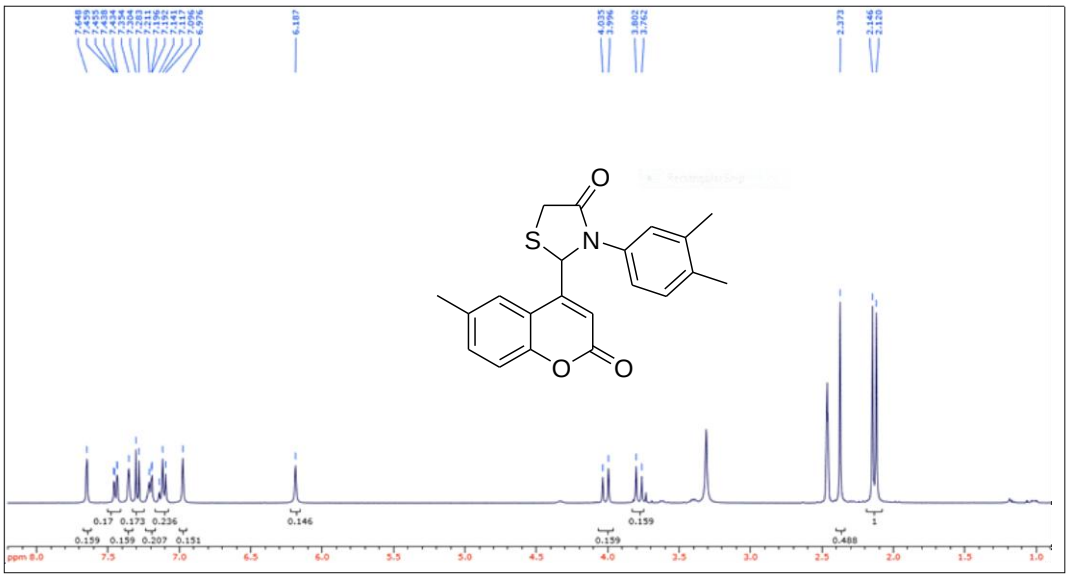
3-(3,4-dimethylphenyl)-2-(6-methyl-2-oxo-2H-chromen-4-yl)thiazolidin-4-one (5b)



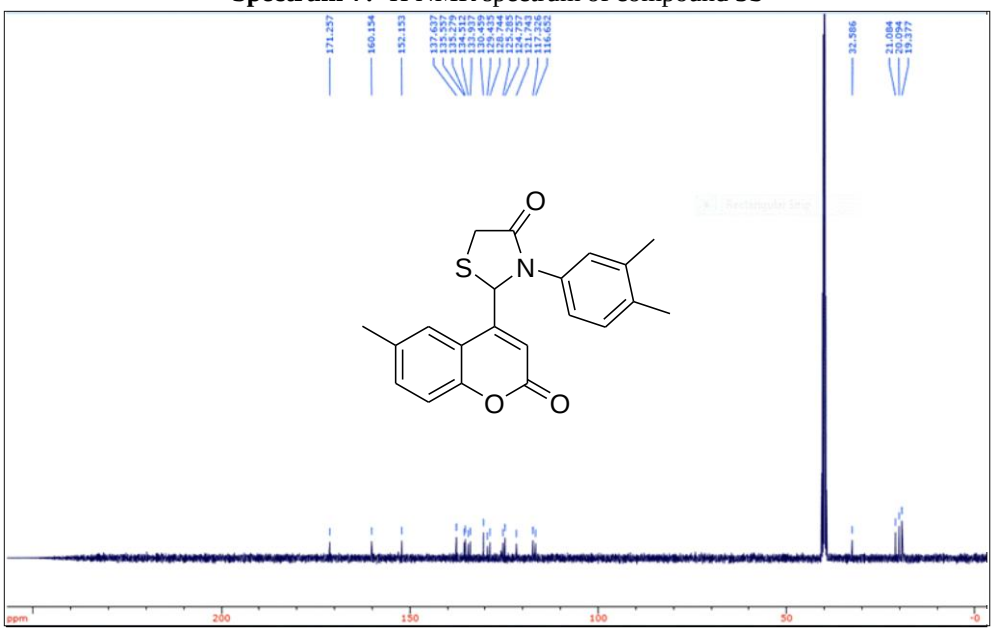
Spectrum-5: IR spectrum of compound **5b**



Spectrum-6: GC-MS spectrum of compound **5b**

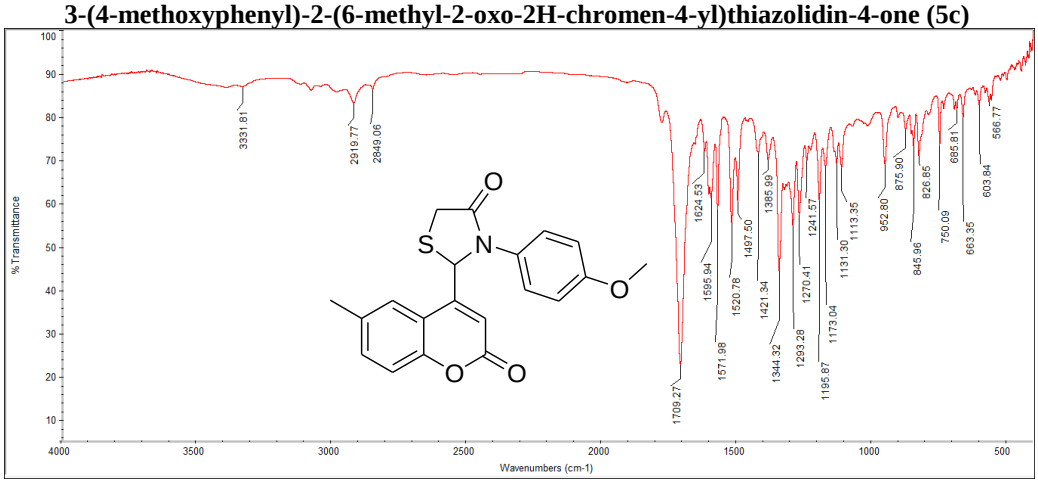


Spectrum-7: ^{1}H NMR spectrum of compound **5b**



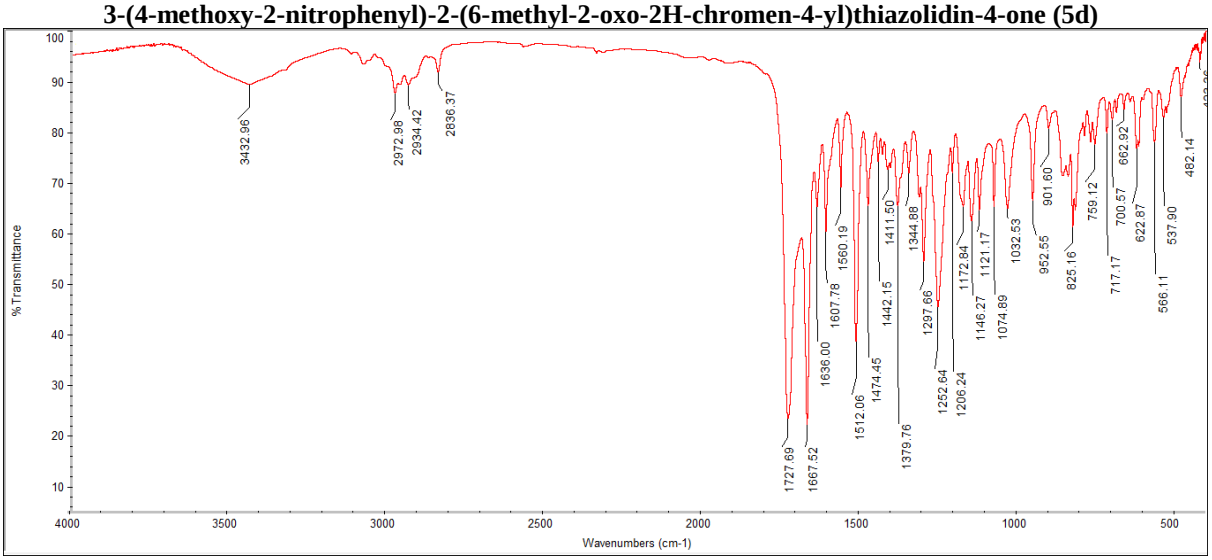
Spectrum-8: ^{13}C NMR spectrum of compound **5b**

3-(4-methoxyphenyl)-2-(6-methyl-2-oxo-2H-chromen-4-yl)thiazolidin-4-one (5c)

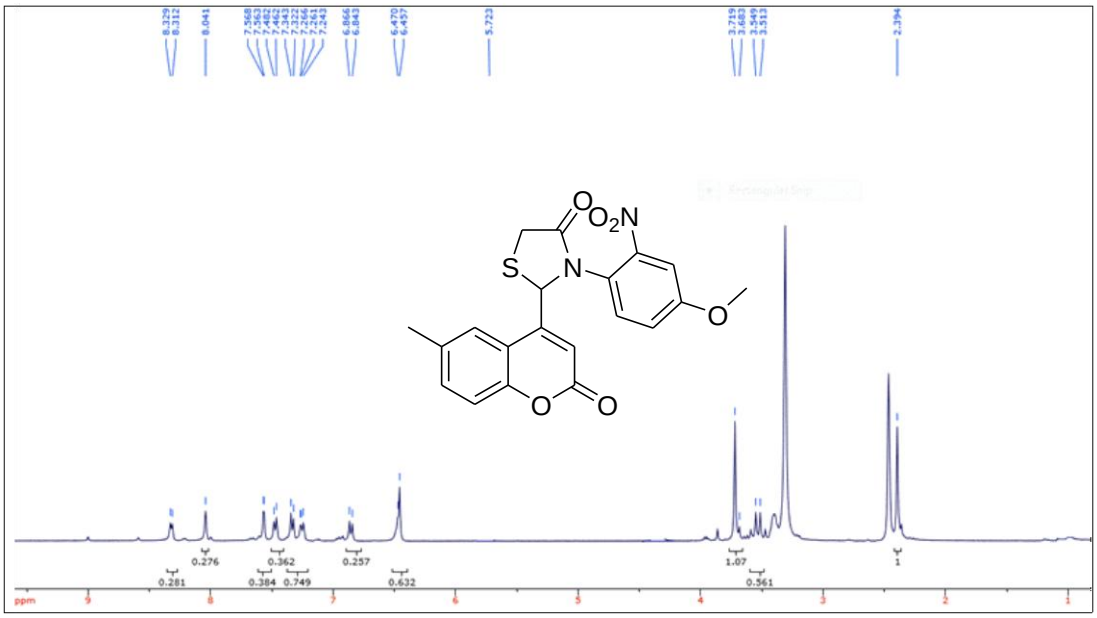


Spectrum-9: IR spectrum of compound **5c**

3-(4-methoxy-2-nitrophenyl)-2-(6-methyl-2-oxo-2H-chromen-4-yl)thiazolidin-4-one (5d)

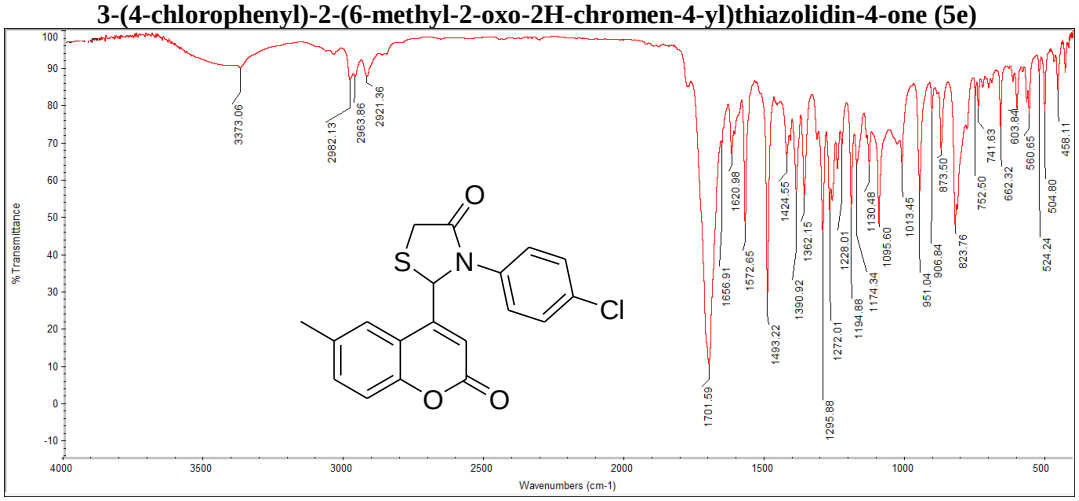


Spectrum-10: IR spectrum of compound **5d**

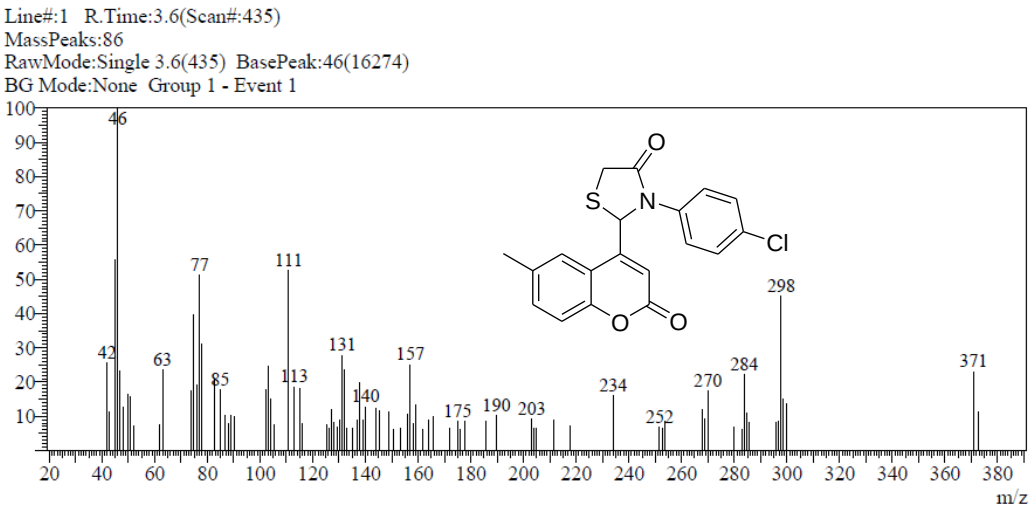


Spectrum-11: ^{1}H NMR spectrum of compound **5d**

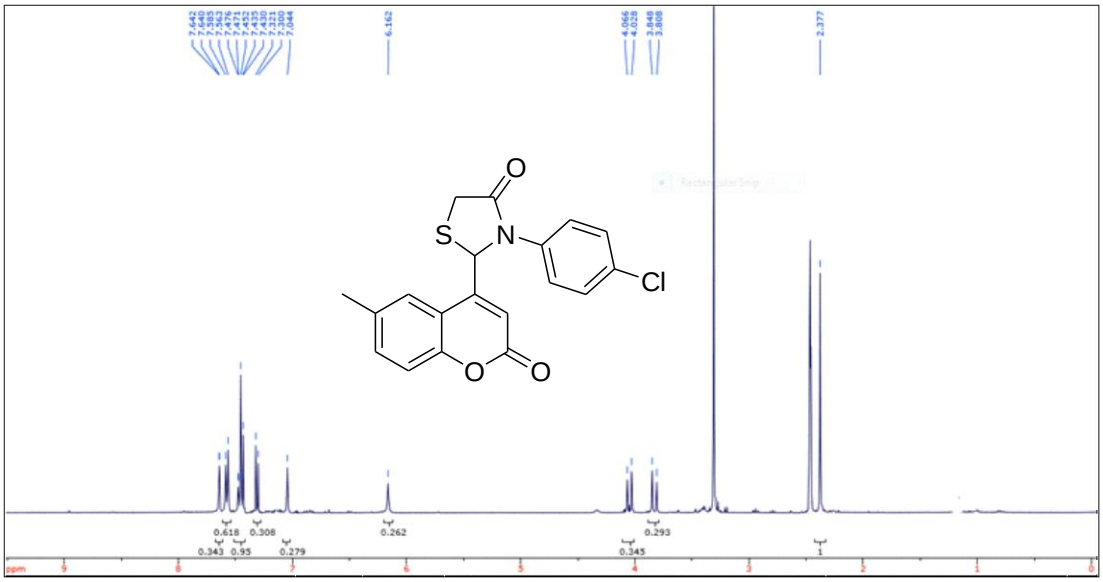
3-(4-chlorophenyl)-2-(6-methyl-2-oxo-2H-chromen-4-yl)thiazolidin-4-one (5e)



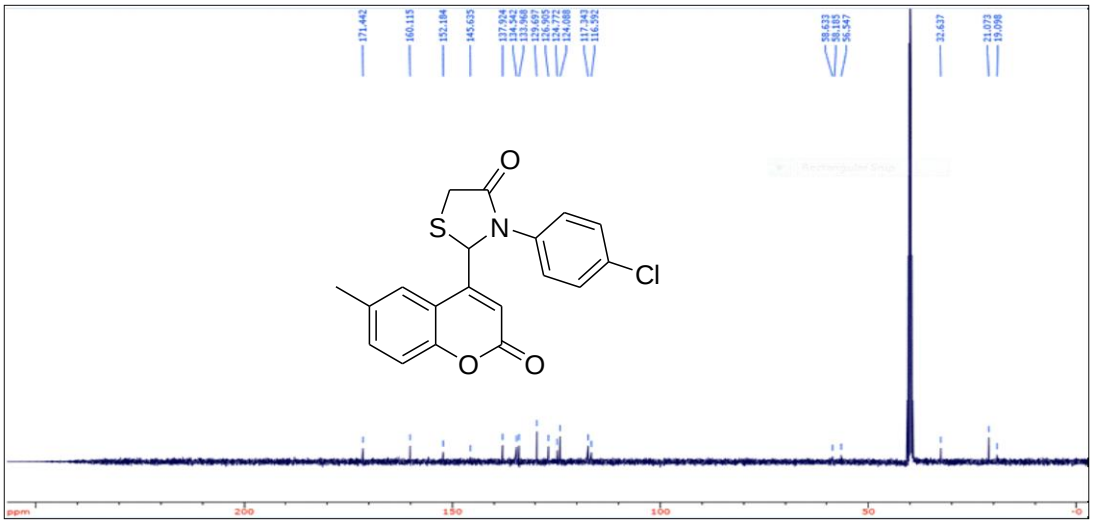
Spectrum-12: IR spectrum of compound **5e**



Spectrum-13: GC-MS spectrum of compound **5e**

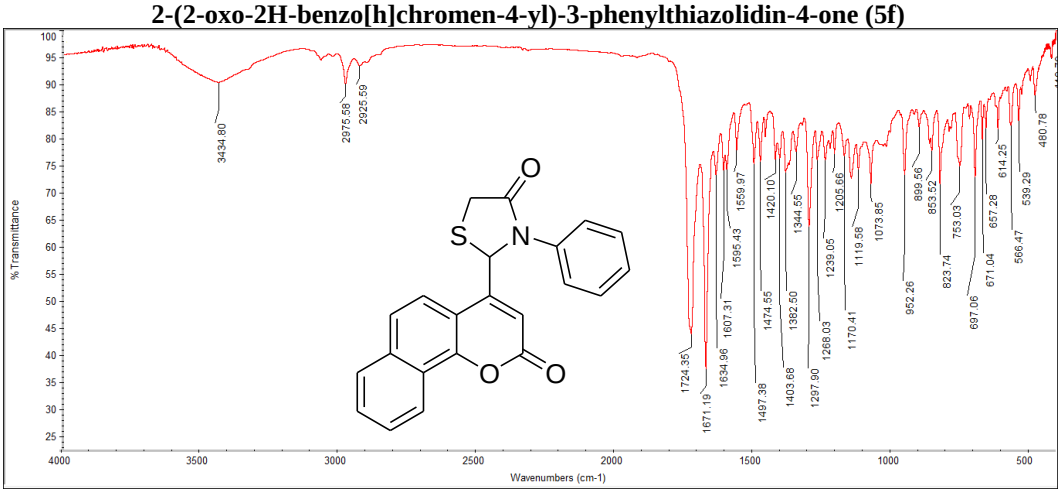


Spectrum-14: ^{1}H NMR spectrum of compound **5e**

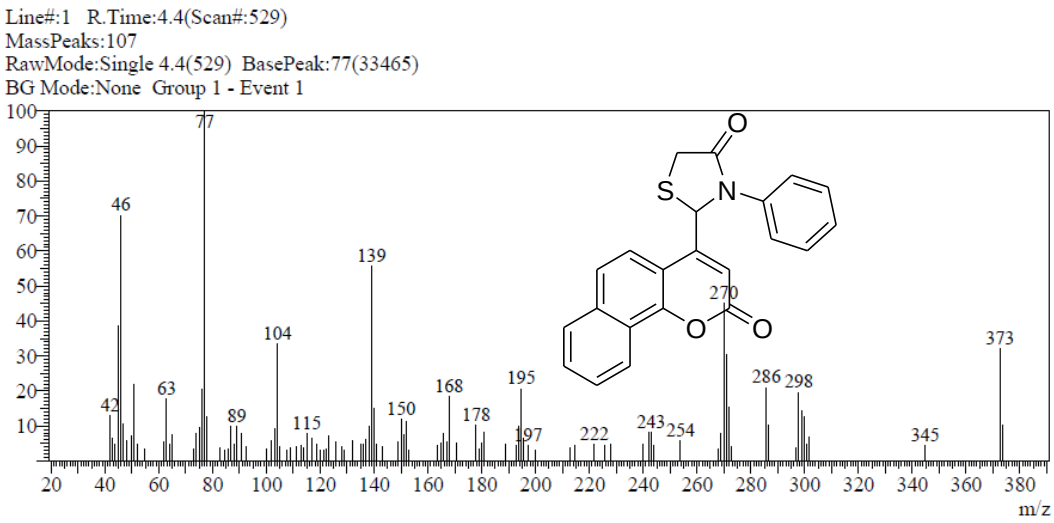


Spectrum-15: ^{13}C NMR spectrum of compound **5e**

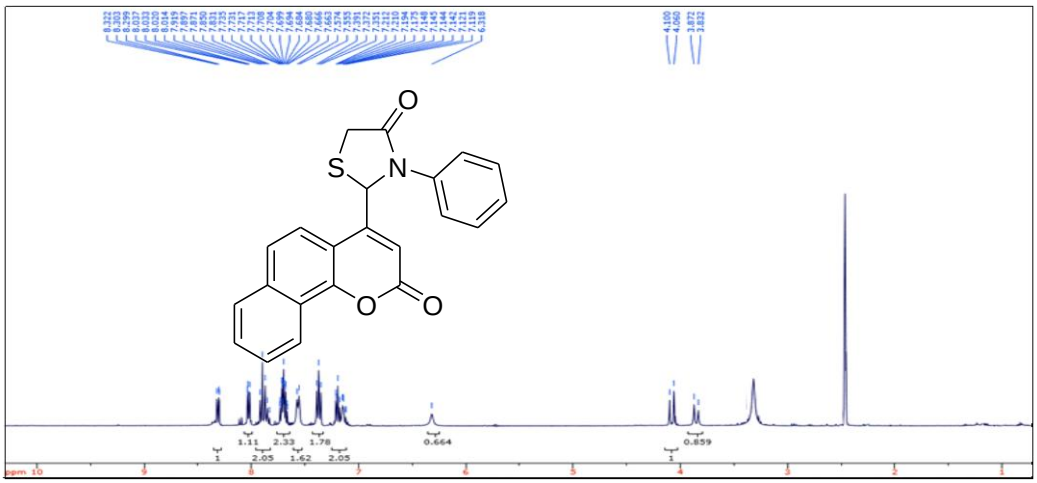
2-(2-oxo-2H-benzo[h]chromen-4-yl)-3-phenylthiazolidin-4-one (5f)



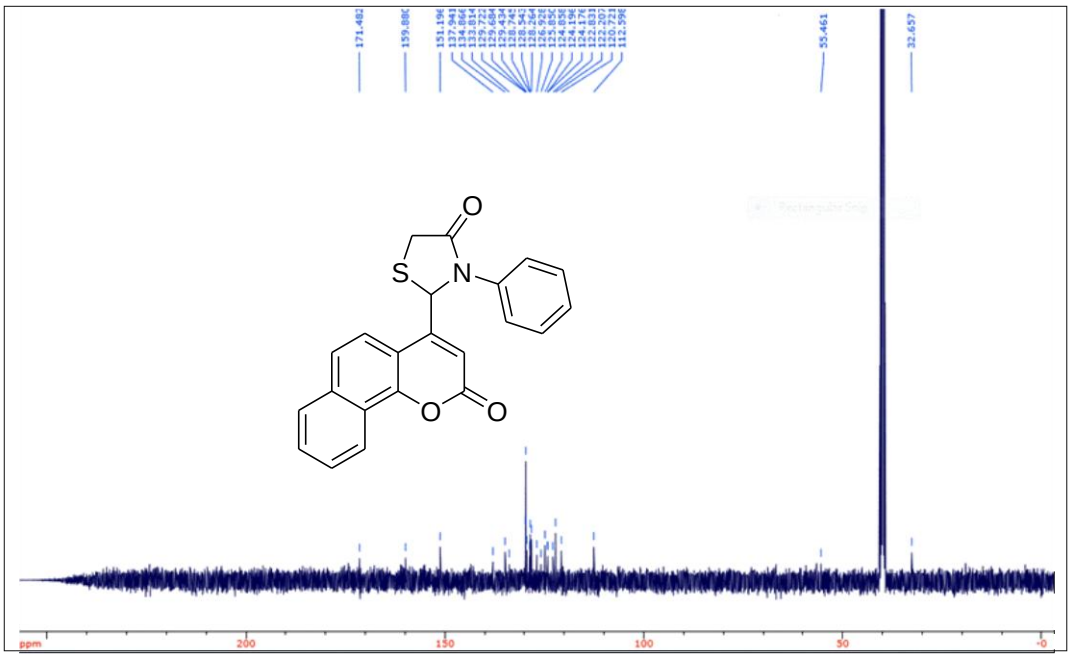
Spectrum-16: IR spectrum of compound **5f**



Spectrum-17: GC-MS spectrum of compound **5f**

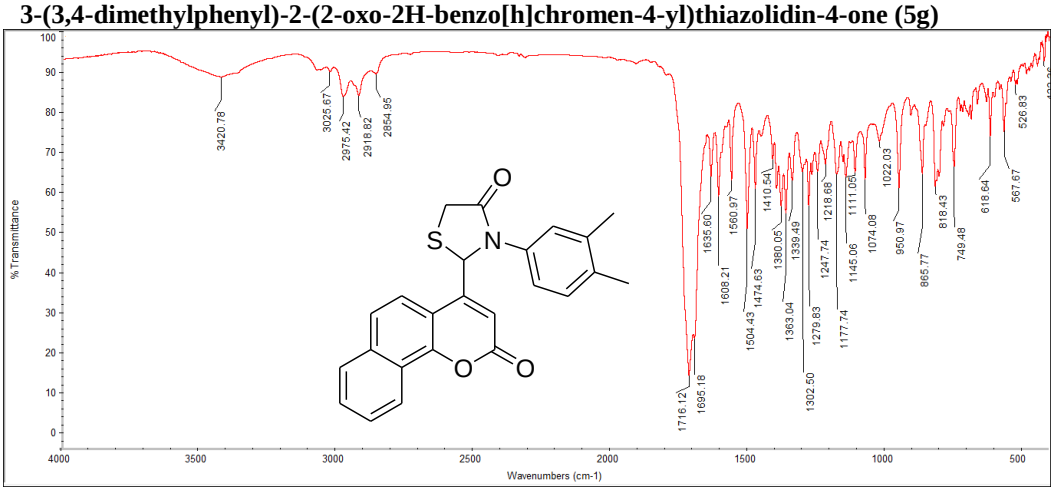


Spectrum-18: ^{1}H NMR spectrum of compound **5f**

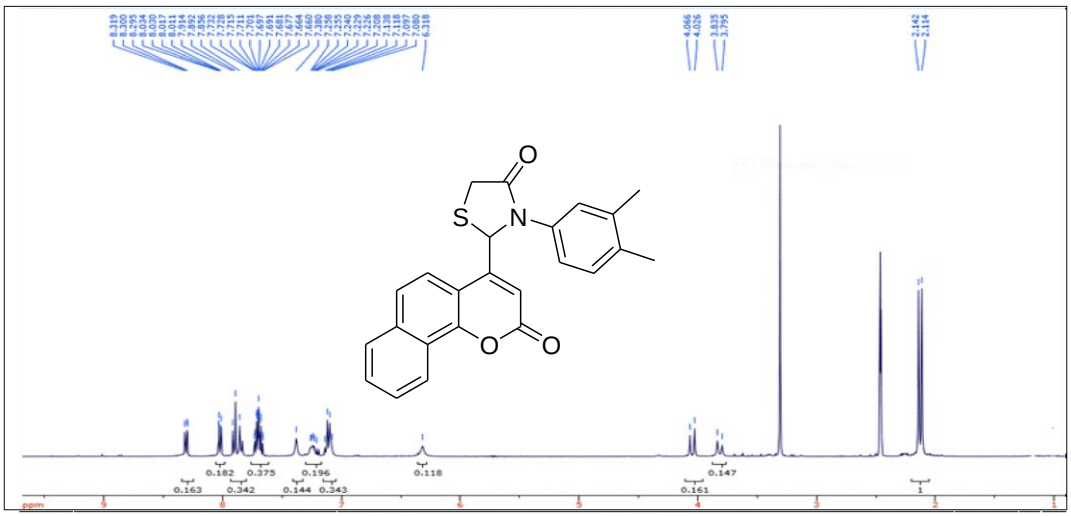


Spectrum-19: ^{13}C NMR spectrum of compound **5f**

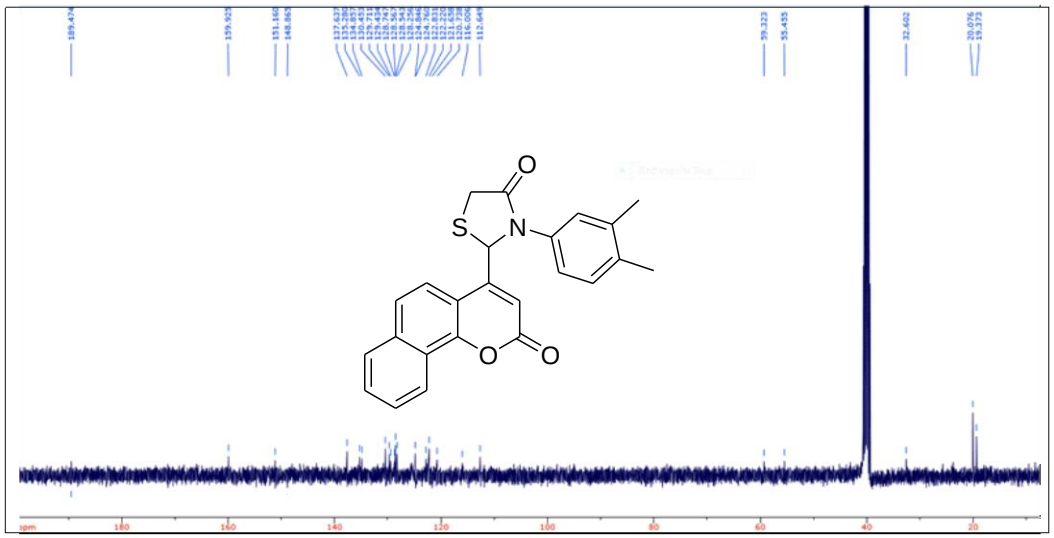
3-(3,4-dimethylphenyl)-2-(2-oxo-2H-benzo[h]chromen-4-yl)thiazolidin-4-one (5g)



Spectrum-20: IR spectrum of compound **5g**

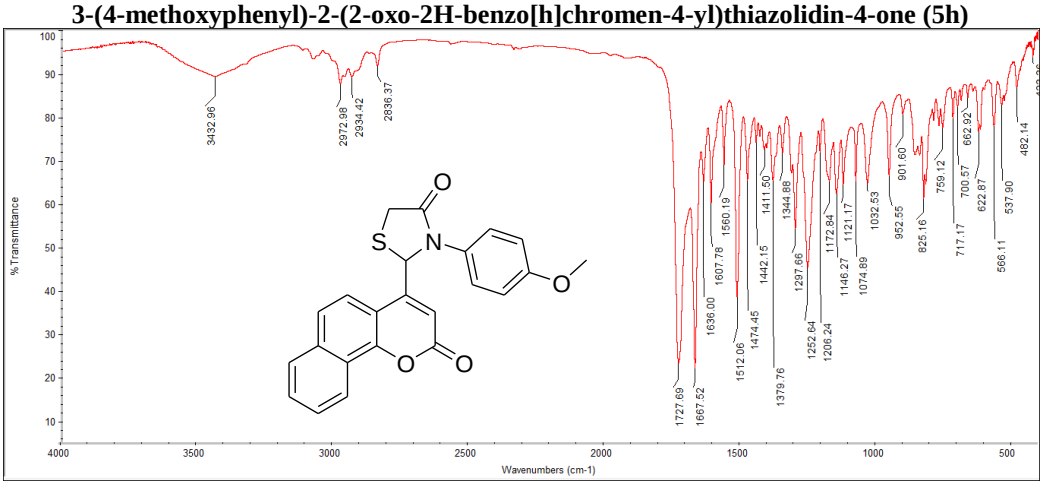


Spectrum-21: ^{1}H NMR spectrum of compound **5g**

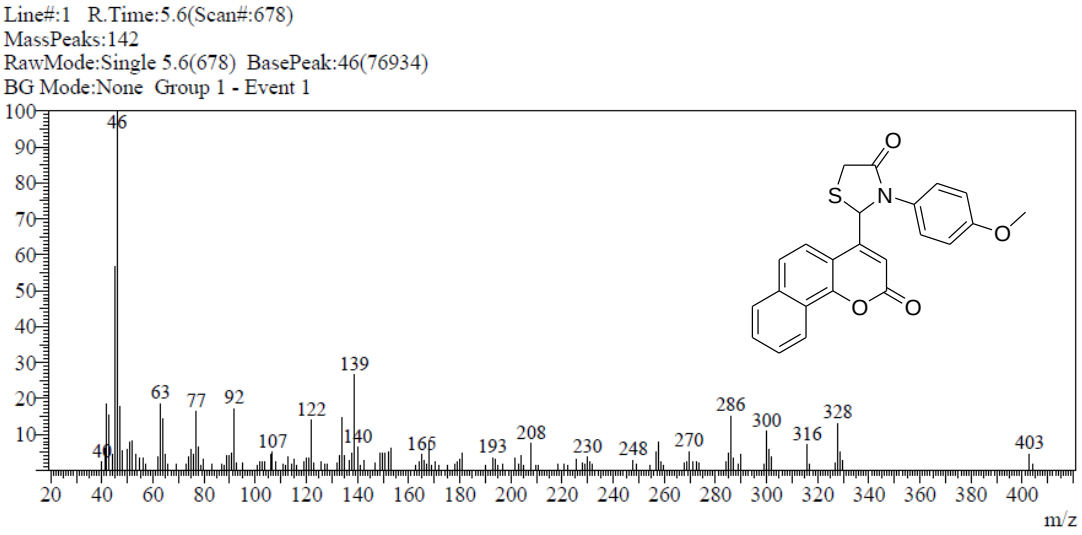


Spectrum-22: ^{13}C NMR spectrum of compound **5g**

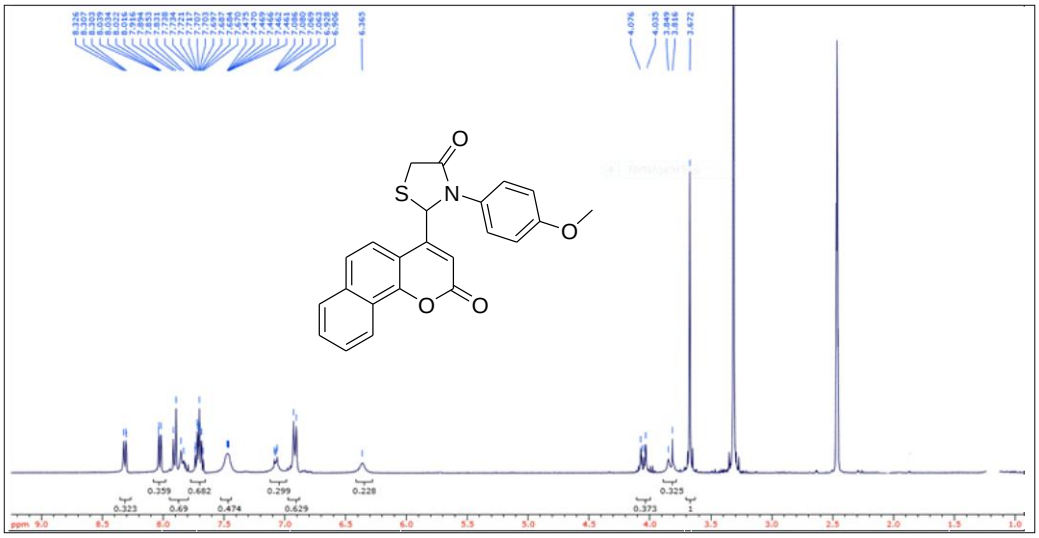
3-(4-methoxyphenyl)-2-(2-oxo-2H-benzo[h]chromen-4-yl)thiazolidin-4-one (5h)



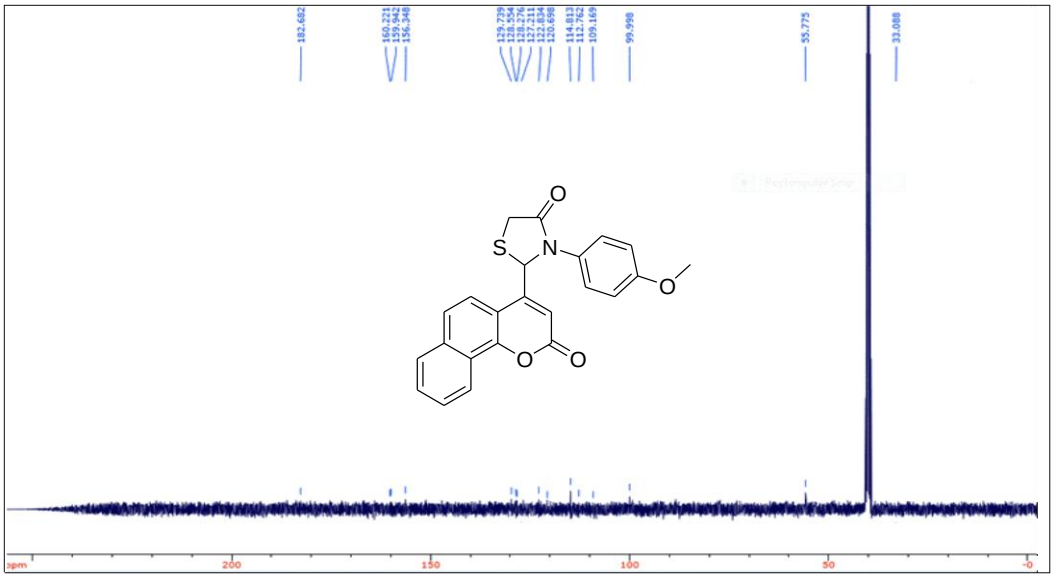
Spectrum-23: IR spectrum of compound **5h**



Spectrum-24: GC-MS spectrum of compound **5h**

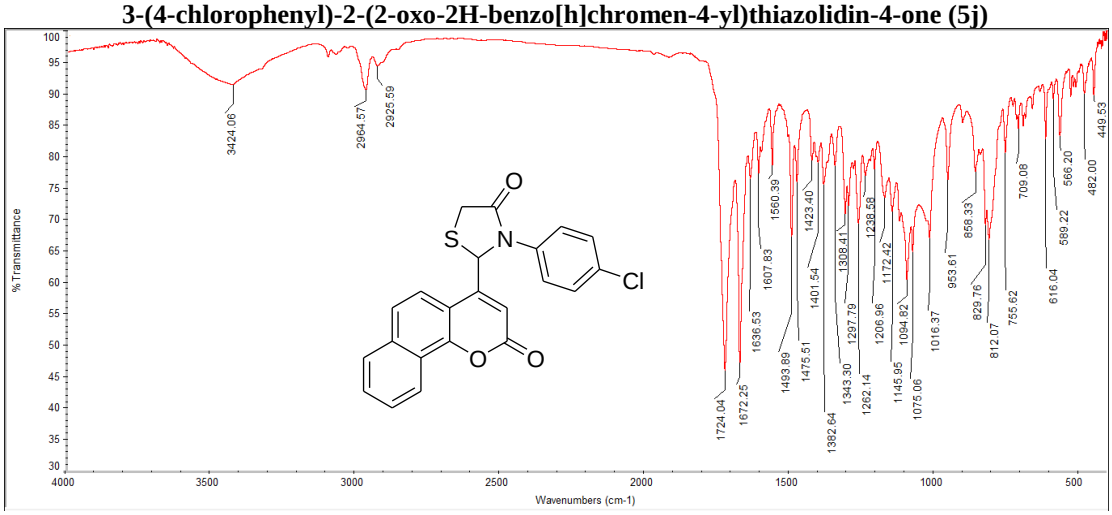


Spectrum-25: ^{1}H NMR spectrum of compound **5h**

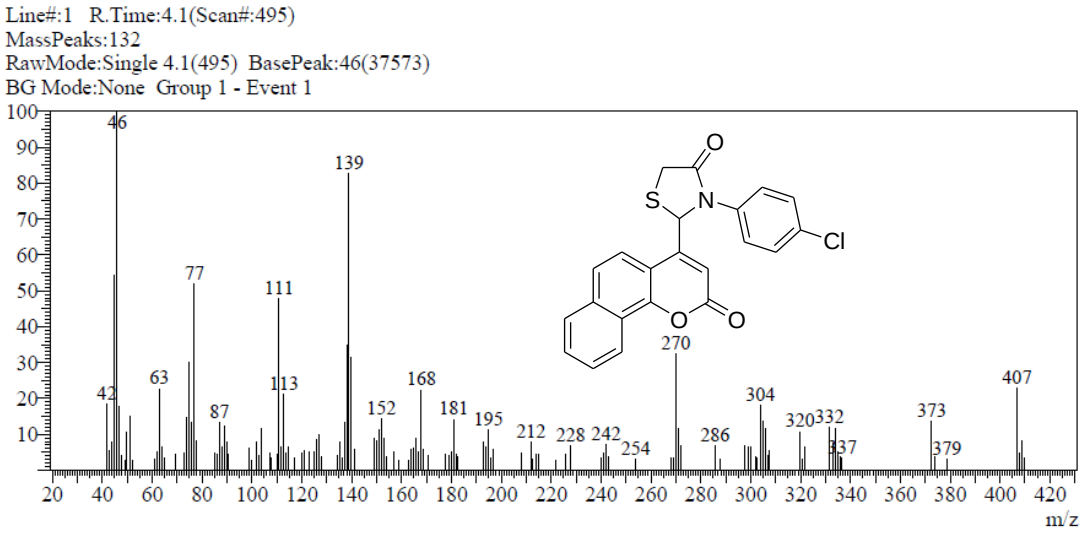


Spectrum-26: ^{13}C NMR spectrum of compound **5h**

3-(4-chlorophenyl)-2-(2-oxo-2H-benzo[h]chromen-4-yl)thiazolidin-4-one (5j)

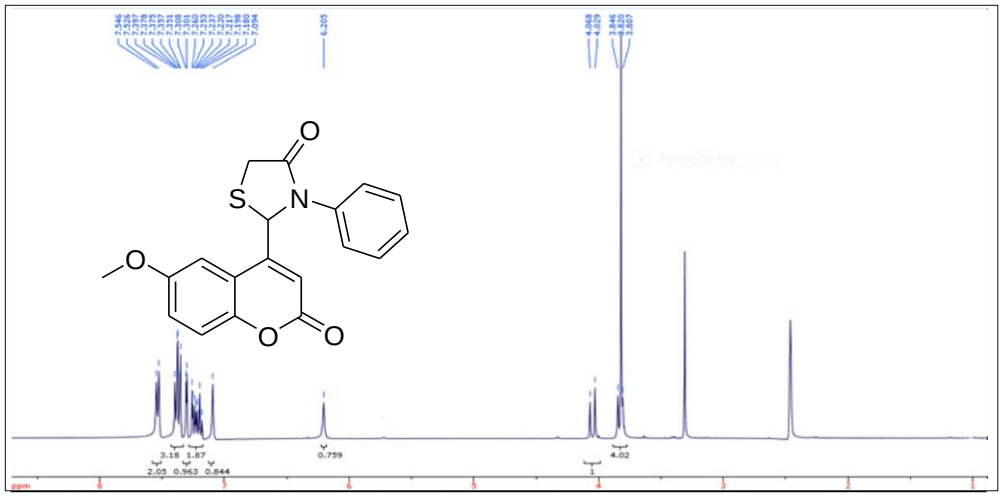


Spectrum-27: IR spectrum of compound **5j**

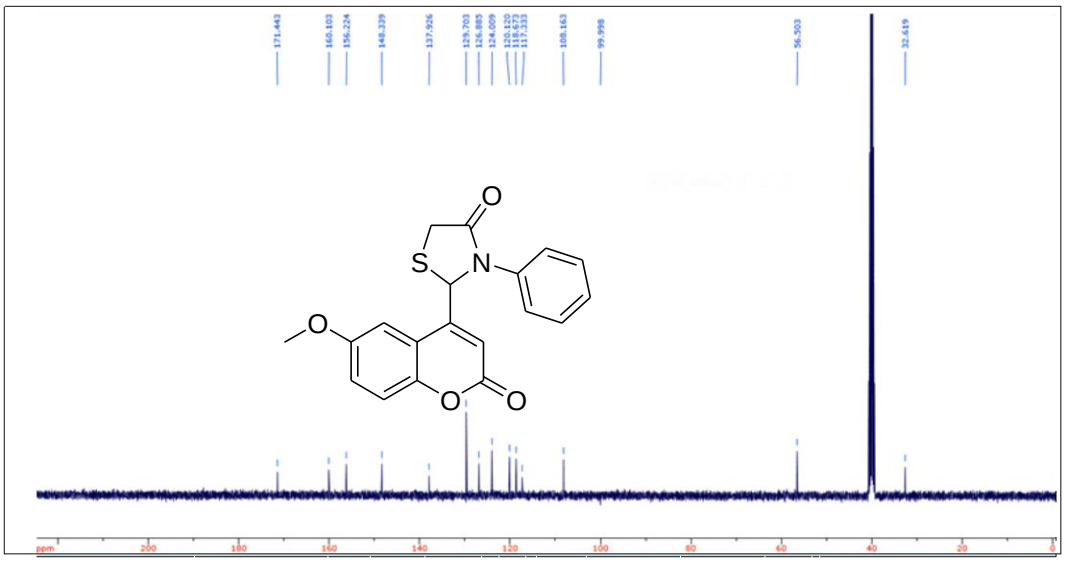


Spectrum-28: GC-MS spectrum of compound **5j**

2-(6-methoxy-2-oxo-2H-chromen-4-yl)-3-phenylthiazolidin-4-one(5k)

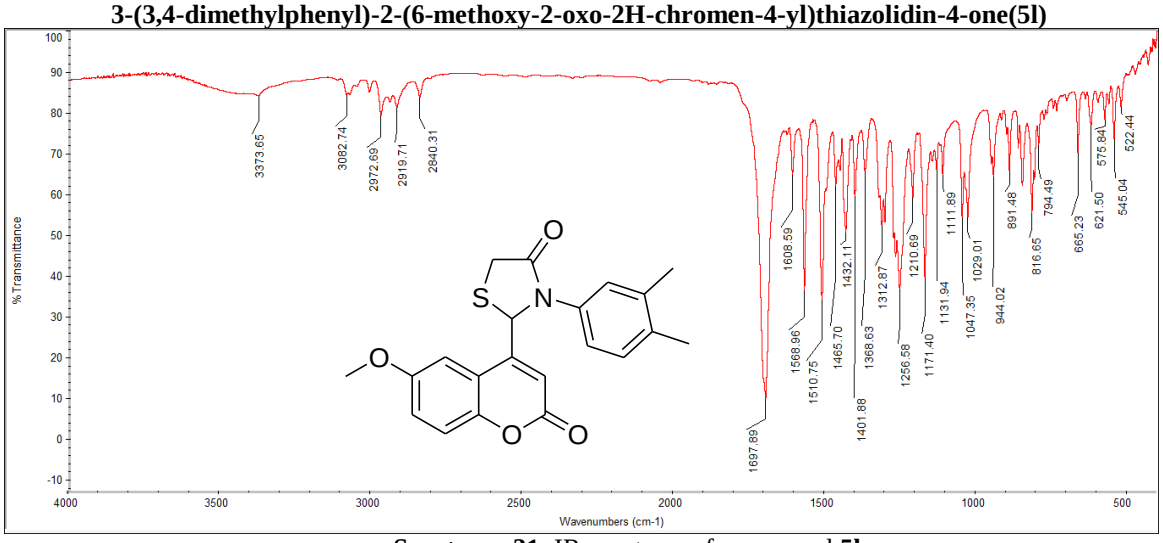


Spectrum-29: ^{1}H NMR spectrum of compound **5k**

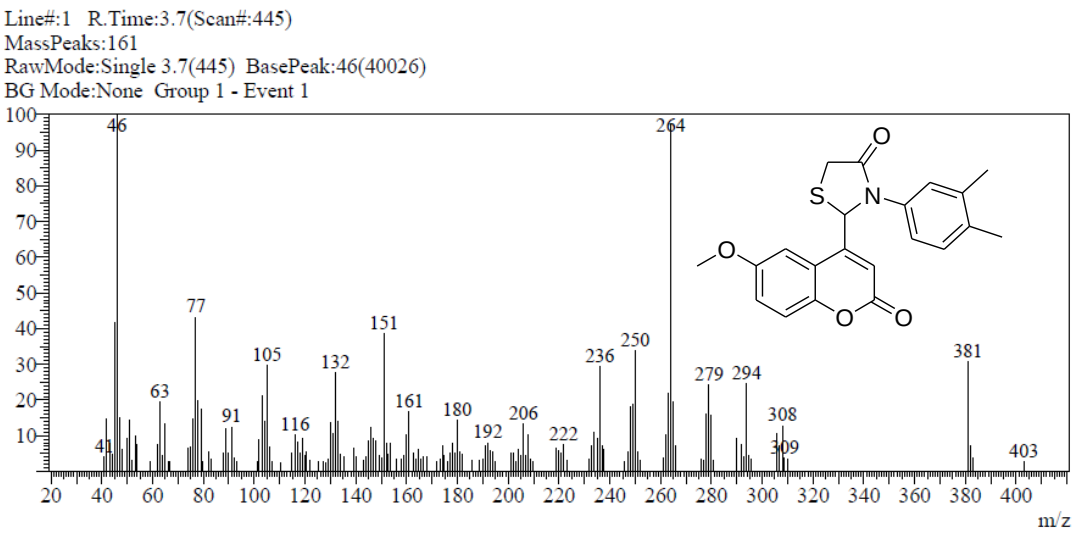


Spectrum-30: ^{13}C NMR spectrum of compound **5k**

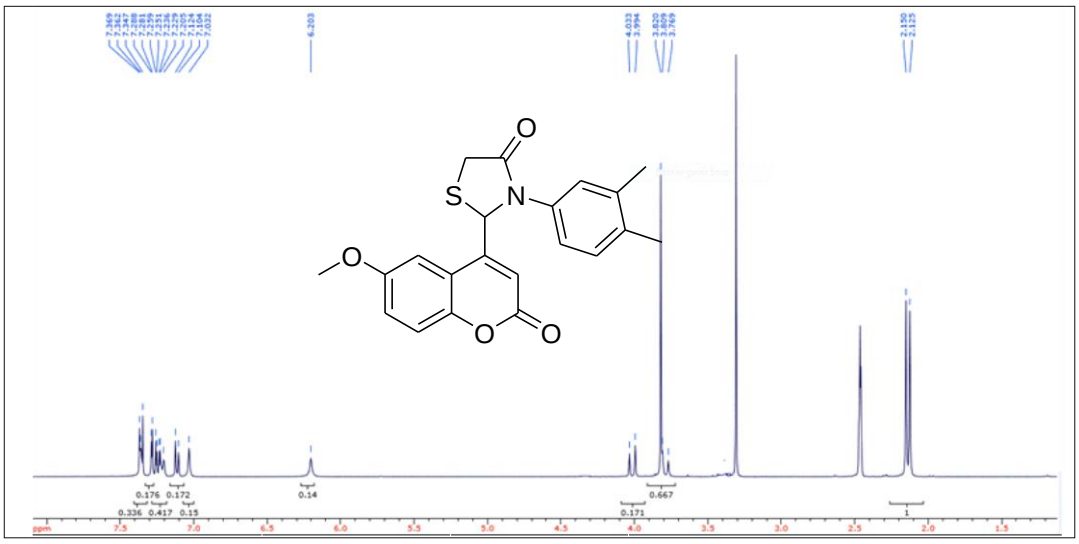
3-(3,4-dimethylphenyl)-2-(6-methoxy-2-oxo-2H-chromen-4-yl)thiazolidin-4-one(5l)



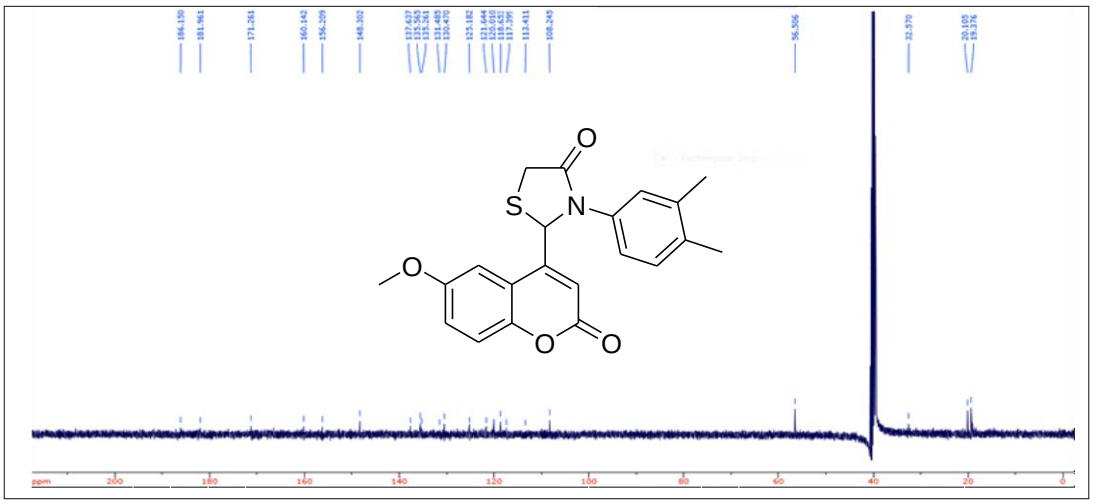
Spectrum-31: IR spectrum of compound **5l**



Spectrum-32: GC-MS spectrum of compound **5l**

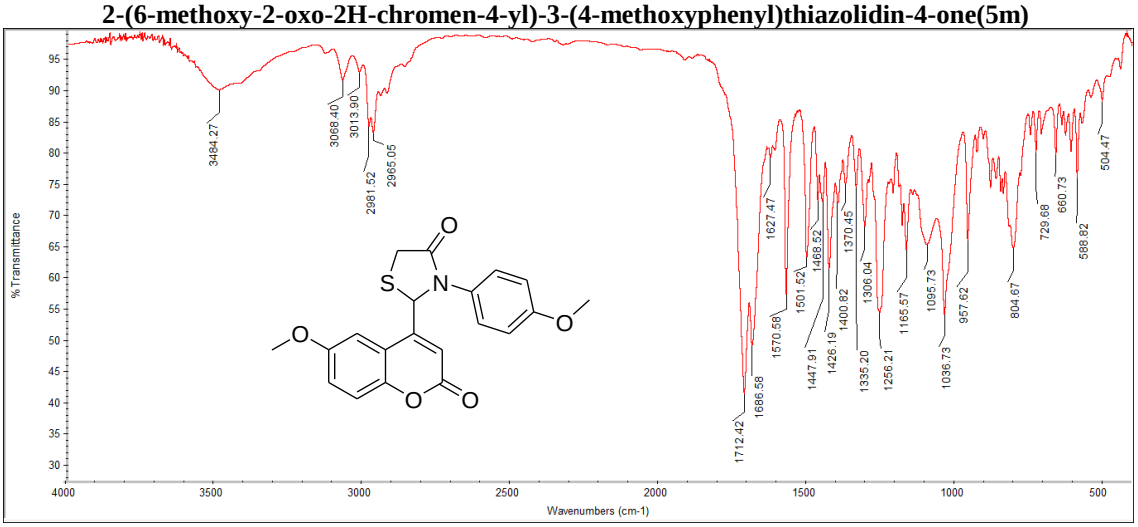


Spectrum-33: ^{1}H NMR spectrum of compound **5l**

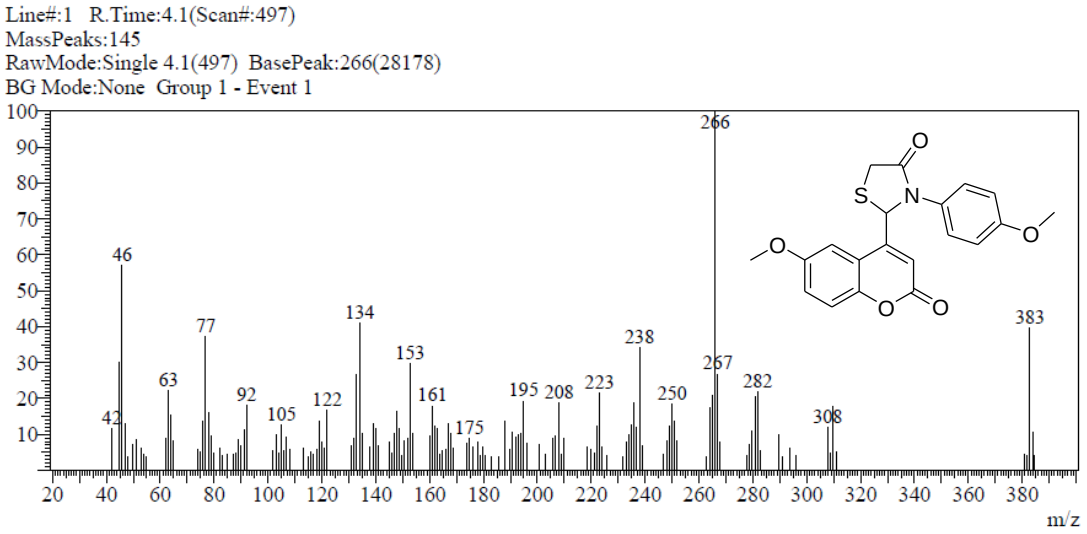


Spectrum-34: ^{13}C NMR spectrum of compound **5l**

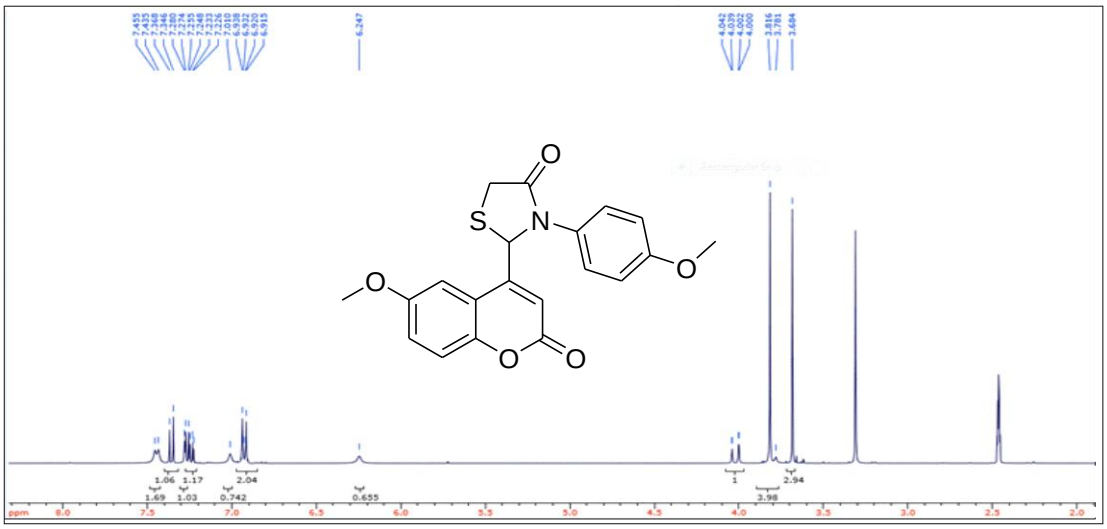
2-(6-methoxy-2-oxo-2H-chromen-4-yl)-3-(4-methoxyphenyl)thiazolidin-4-one(5m)



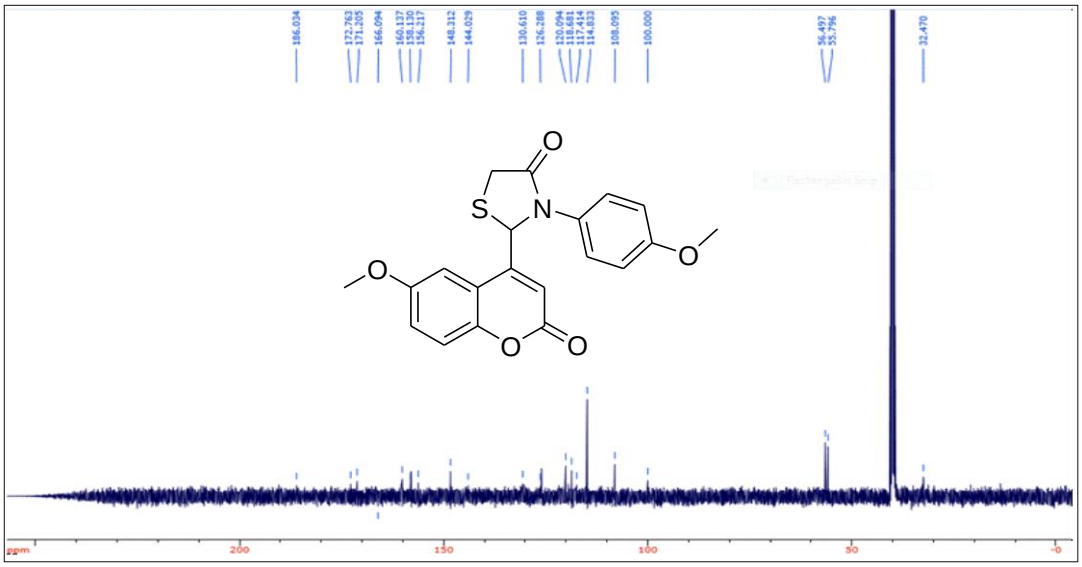
Spectrum-35: IR spectrum of compound **5m**



Spectrum-36: GC-MS spectrum of compound **5m**



Spectrum-37: ^{1}H NMR spectrum of compound **5m**

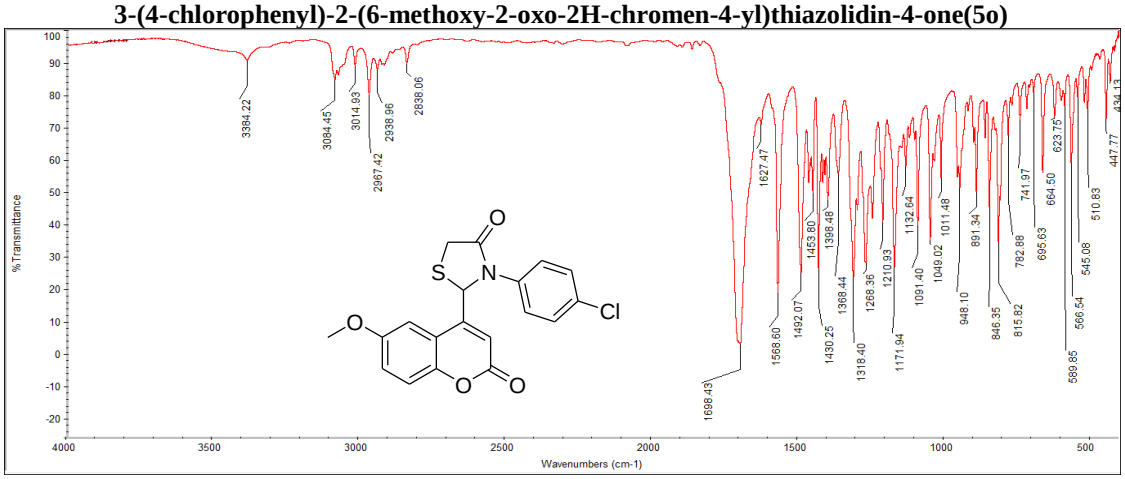


Spectrum-38: ^{13}C NMR spectrum of compound **5m**

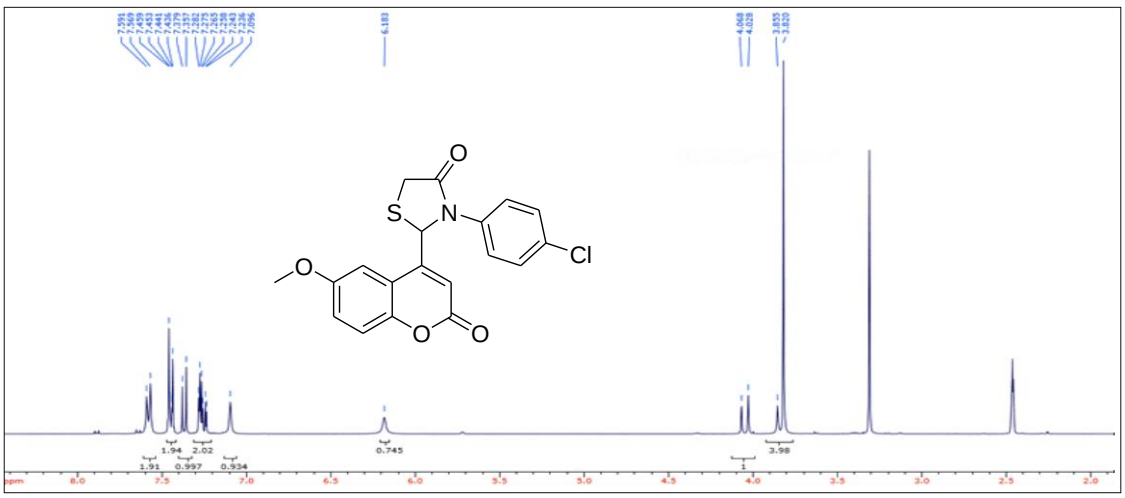
3-(4-methoxy-2-nitrophenyl)-2-(6-methoxy-2-oxo-2H-chromen-4-yl)thiazolidin-4-one(5n)

Spectrum-39: ^{1}H NMR spectrum of compound **5n**

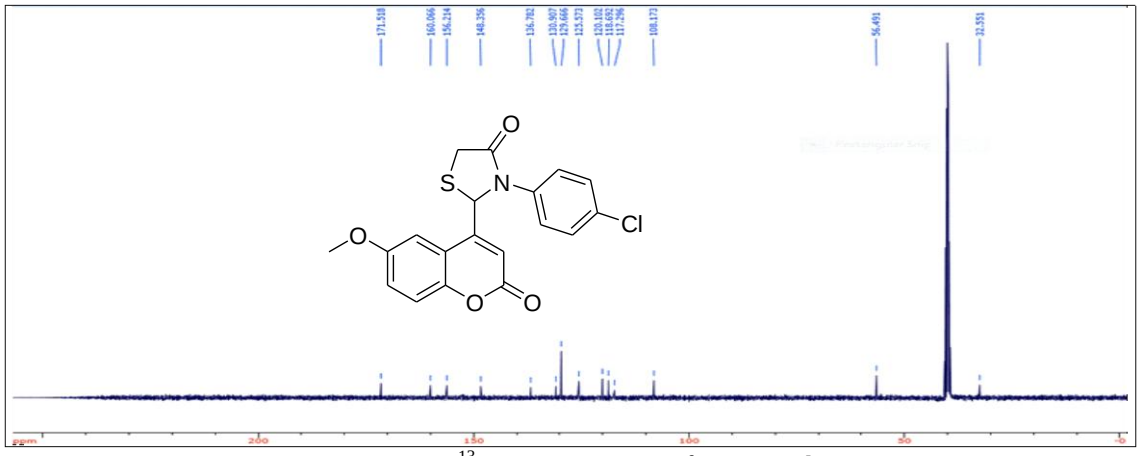
3-(4-chlorophenyl)-2-(6-methoxy-2-oxo-2H-chromen-4-yl)thiazolidin-4-one(5o)



Spectrum-40: IR spectrum of compound **5o**



Spectrum-41: ^{1}H NMR spectrum of compound **5o**



Spectrum-42: ^{13}C NMR spectrum of compound **5o**

Lokesh A. Shastri Synthesis and characterization of coumarin-4-thiazolidinone scaffolds as new class of anti-tuberculosis and antibacterial agentsIOSR Journal of Applied Chemistry (IOSR-JAC) 11.7 (2018): 77-101.