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Synthesis, characterization and biological evaluation of pyrazolones containing multi substituted thiazolidinones and oxadizoles

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ABSTRACT

A series of novel Pyrazolone Schiff bases bearing thiazolidinone and oxadiazoles systems were prepared from ethyl-2-(4-formyl-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)acetate (4) and substituted amines. All pyrazolone schiff bases were refluxed with mercapto acetic acid in presence of anhydrous zinc chloride and solvent N,N-dimethyl formamide to afforded novel series of Ethyl-2-(4-(3-(4-substitutedphenyl)-4-oxothiazolidin-2-yl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)acetate [5a-f]. Novel moieties 2-(1-((4-acetyl-5-(4-substituted phenyl)-5-methyl-4,5-dihydro-1,3,4-oxadiazol-2-yl) methyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-(4-substituted phenyl) thiazolidin-4-one were synthesized by the condensation of (E)-2-(4-(3-(4-substitutedphenyl)-4-oxothiazolidin-2-yl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)-N'-(1-(4-substitutedphenyl)ethylidene)acetohydrazide (6a-f) and substituted ketones (7a-e) afford corresponding (E)-2-(4-(3-(4-substitutedphenyl)-4-oxothiazolidin-2-yl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)-N'-(1-(4-substitutedphenyl) ethylidene)acetohydrazide (8a-f). This was subjected to cyclization with excess of acetic anhydride to give corresponding congeners 2-(1-((4-acetyl-5-(4-substitutedphenyl)-5-methyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-(4-substitutedphenyl) thiazolidin-4-one (9a-j) in excellent yields. The structures of these newly synthesized compounds were characterized by ^{1}H-NMR, ^{13}C-NMR, Mass, IR and elemental analysis. The prepared compounds have been screened on some strains of bacteria and fungi.

Keywords: Thiazolidinones, pyrazalones, Oxadiazoles, Anti-microbial activity

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INTRODUCTION

Thiazolidinone, a saturated form of thiazole with carbonyl group on fourth carbon posses almost all types of biological activities. This diversity in the biological response profile has attracted the attention of many researchers to explore this skeleton to its multiple potential against several activities. Among pharmacologically important heterocyclic compounds, 4-thiazolidinone derivatives have been known to possess a wide range of biological properties such as antimicrobial[1-7,21-25] anticonvulsant [9], anti-HIV [10], antifungal [11], antibacterial agents[12], anti-inflammatory, analgesic[2] cytotoxic[8]. Oxadiazole is a cyclic compound containing one oxygen and two nitrogen atoms in a five member ring[13]. Oxadiazoles have occupied a unique place in the field of medicinal chemistry due to its wide range of activities[14].From the literature survey Oxadiazole nucleus has been found to posses antimicrobial[15], anti fungal[16], anti inflammatory[17], anti convulsent[18], antioxidant,analgesic[19],and mutagenic activity[20].

The derivatives of pyrazolone are important class of antipyretic and analgesic Compounds.Some substituted pyrazoline derivatives are used as antitumor[25], anti bacterial, antifungal, antiviral, anti parasitic, anti-tubercular

and insecticidal agents[26-34], some of these compounds have also anti-inflammatory, anti-diabetic, and anesthetic properties[35-39].

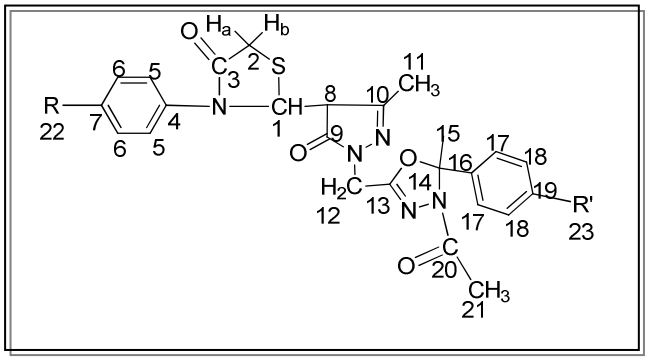
Hence it was thought worthwhile to synthesise some new Pyrazolone heterocyclics by incorporating the thiazolidin-4-one and 1,3,4-Oxadiazole moieties in a single molecular frame work. The present work deals with the synthesis of the title compounds using the synthon 3-methyl-5-oxo-4,5-dihydro-1H-pyrazole-4-carbaldehyde followed by their antimicrobial screening.

MATERIALS AND METHODS

Melting points were determined on open capillaries using a cintex melting point apparatus. T.L.C analyses were performed on precoated silicagel (E-Merck Kieselgel $60F_{254}$) plates and visualisation was done by exposing to iodine vapour. Solvents were purified by standard procedures before use. Column chromatography was conducted by using silica gel with different solvent systems as elutes. IR Spectra were recorded in KBr on Perkin-Elmer Spectrum BX series FT-IR spectrometer. ^{1}H-NMR spectrum were recorded on Varian Gemini 300MHz spectrometers using TMS as internal standard (chemical shifts in δ ppm). 13C-NMR Spectra were recorded on a Brucker 75MHz spectrometer. Mass spectra were scanned on a varian MATCH-7 and Jeol JMSD-300 mass spectrometer at 70ev. Elemental analyses were carried out on a carloerba 106 and Perkin-Elmer Analyser. All the chemicals used in the present investigation were purchased from Aldrich chemicals.

RESULTS AND DISCUSSION

3-methyl-5-oxo-4,5-dihydro-1H-pyrazole-4-carbaldehyde on reaction with chloro ethyl acetate and DMF yielded ethyl-2-(4-formyl-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)acetate (2). Compound-2 on treatment with substituted amines afford a Ethyl-2-(3-methyl-4-((phenyl imino)methyl)-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)acetate (4) with yield of 58%. Compound (1) on reaction with chloroethyl acetate yielded compound-2 with 50% yield**.** Compound-4 on reaction with mercaptoacetic acid afford a Ethyl-2-(4-(3-(4-substitutedphenyl)-4-oxothiazolidin-2-yl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)acetate (5a-f). Compound 5 on refluxion with hydrazine hydrate afford 2-(4-(3-(4-substitutedphenyl)-4-oxothiazolidin-2-yl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl) aceto hydrazide (6). The condensation reaction of compound-6 with 4-substituted acetophenone (7) yielded (E)-2-(4-(3-(4-substitutedphenyl)-4-oxothiazolidin-2-yl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)-N'-(1-(4-substitutedphenyl) ethylidene)acetohydrazide (8). Compounds (8a-f) on reaction with on cyclisation with excess of acetic anhydride resulted 2-(1-((4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-phenylthiazolidin-4-one (9a-f). These reactions are summarised in the scheme-I**.** Yields were moderate to fair (40-70%). The purity of the compounds was monitored by TLC.



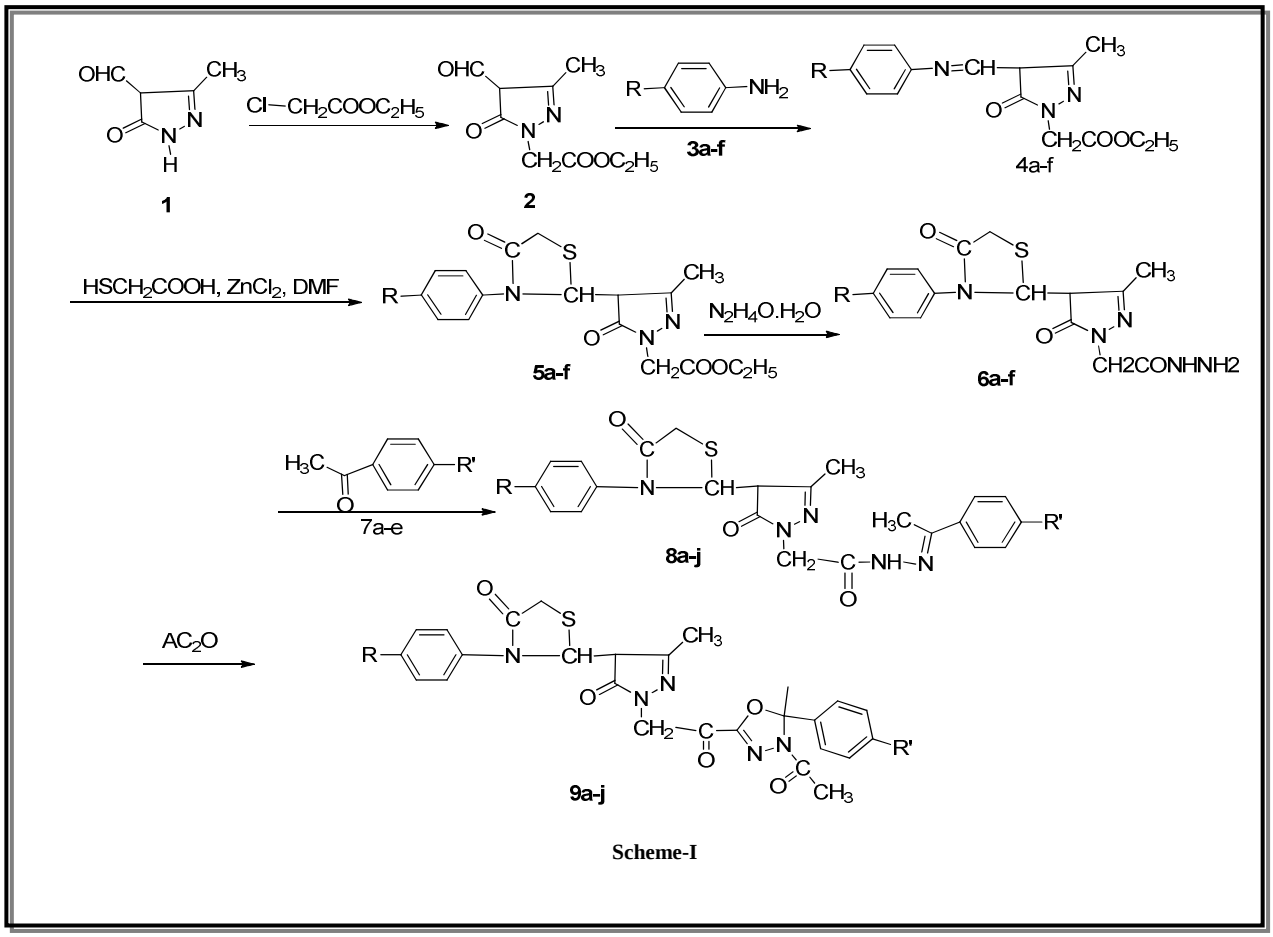
The newly synthesised compounds (9a-j) were characterized by IR, H^1 NMR, Massdata and elemental analysis. In IR spectra compound (9a), strong bands are noticed in the region of 3042, 1619, 1693, 1720,cm^{-1} and a weak band at 1186 cm^{-1} indicating the presence of characteristic peaks for Ar-H, C=N , Cyclic C=O, Acyclic C=O and –C-S groups respectively. In ^{1}H-NMR ($(CD_3)_2SO$) the compounds (9a) showd the signals at δ: 1.78(s, 3H, -CH_3 of oxadiazole), 1.94(s, 3H, -CH_3 of pyrazolone), 2.02(s, 3H, -CO-CH_3), 2.22(d,1H, -CH of pyrazolone), 3.86(d,1H, -CH_b of CH2 of thiazolidinone), 3.99(d d,1H, -CH_a of CH_2 of thiazolidinone), 6.08(d, 1H, -CH of thiazolidinone), 4.12 (s, 2H, N–CH_2–CO), 6.73–7.7 (m, 10H, C_6H_5 and C_6H_5). The ^{13}C-NMR spectrum of ($CDCl_3$) shown δ: showed the following signals at 53.5, 33.2, 170.9, 141.7, 127.5, 129.0, 128.0, 50.5, 175.9, 155.6, 19.6, 52.8, 158.2, 90.2, 28.0, 142.5,127,128.5, 126.7, 170.0 and 24.2 and these signals are due to C_1, C_2,C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{16}, C_{17}, C_{18}, C_{19},C_{20} & C_{21}. Mass spectrum of 6a was recorded by ESI-MS technique showed the molecular ion signal at 519.16. The spectral values are in good agreement with the structure of the compound (9a).

3.1. Anti- Bacterial Activity

The anti-bacterial activity of 9a-j was determined by the disc diffusion method with Cefaclor (100µg/ml) as the reference antibiotic [40]. The newly synthesised compounds were examined, respectively against *Staphylococcus aureus*, *Bacillus cereus*, *Escherichia c-oli* and *Pseudomonas aeruginosa* bacteria. The test results presented in the table-2, suggest that, -Chloro(9g), –Bromo(9h) –trifluoromethyl(9i) and –Nitro (9j) derivatives exhibit high activity against the tested bacteria, the rest of the compounds were found to be either slightly active or inactive against the tested microorganisms.

3.2. Antifungal Activity

The antifungal activity of 9a-j were tested against two different fungi such as *Asperigillus flavus* and *Candida albicans* by disc diffusion method [40] with Clotrimazole as standard(100µg/ml). The test results presented in the table-3, suggest that -Chloro(9g), –Bromo(9h) –trifluoromethyl(9i) and –Nitro (9j) derivatives exhibit high activity against the fungi species tested, the rest of the compounds were found to be either slightly active or inactive against the fungi species tested.



Scheme-I

Comp	9a	9b	9c	9d	9e	9f	9g	9h	9i	9j
R	H	CH_3	OCH_3	OC_2H_5	Cl	Br	Cl	Cl	Cl	Cl
R'	H	H	H	H	H	H	Cl	Br	CF_3	NO_2

3.3. Synthesis of Ethyl-2-(3-methyl-4-(((4-substitutedphenyl)imino)methyl)-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)acetate (4)

A mixture of 3-methyl-5-oxo-4,5-dihydro-1H-pyrazole-4-carbaldehyde (1) (0.01mol), anhydrous K_2CO_3, chloro ethyl acetate and DMF were stirred at room temperature for 8 hours. The reaction mixture was diluted with ice cold water. The separated solid was identified as ethyl-2-(4-formyl-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)acetate (2).

Equimolar quantity of4-substituted amines(3a-f) and ethyl-2-(4-formyl-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)acetate (2) were dissolved in absolute alcohol, to this three drops of acetic acid is added then heated on a steam

bath for 5-6h at 100^0C. After standing for 24h at room temperature, the product was dried and recrystallised from warm absolute alcohol. The separated solid was identified as Ethyl-2-(3-methyl-4-((phenyl imino)methyl)-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)acetate (4a). Similar procedure was adopted to synthesise (4b-f) from (3b-f).

3.4. Synthesis of Ethyl-2-(4-(3-(4-substitutedphenyl)-4-oxothiazolidin-2-yl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)acetate (5a-f)

A mixture of Schiff base (4a) (0.01mol)and mercaptoacetic acid(0.01mol) were dissolved in dioxane(20ml), anhydrous zinc chloride(0.5mg) was added and refluxed for 8 hrs. The reaction was cooled and the resulting solid was washed with sodium bicarbonate solution and recrystalised from absolute alcohol to afford ethyl 2-(3-methyl-5-oxo-4-(4-oxo-3-phenylthiazolidin-2-yl)-4,5-dihydro-1H-pyrazol-1-yl)acetate (5a).Other compounds of the series were similarly prepared (5b-f).

3.5. Synthesis of 2-(4-(3-(4-substitutedphenyl)-4-oxothiazolidin-2-yl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)acetohydrazide (6a-f).

A solution of ethyl 2-(3-methyl-5-oxo-4-(4-oxo-3-phenylthiazolidin-2-yl)-4,5-dihydro-1H-pyrazol-1-yl)acetate (5a) (0.01mol) and hydrazine hydrate (0.015mol) in ethanol was refluxed for 5 hours. The reaction mixture was cooled and poured on to ice cold water with stirring. The separated solid was filtered, washed with water and recrystallized from ethanol to afford 2-(3-methyl-5-oxo-4-(4-oxo-3-phenylthiazolidin-2-yl)-4,5-dihydro-1H-pyrazol-1-yl) acetohydrazide (6a). The similar procedure was extended to synthesise 6b-f from 5b-f. In each and every step of the reaction, the reaction was monitored by T.L.C.

The structures of these newly synthesized compounds (6a-f) were characterized by their elemental analysis and spectral data (^{1}HNMR, and IR).

3.5.1. 2-(4-(3-(phenyl)-4-oxothiazolidin-2-yl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)acetohydrazide (6a)

IR(KBr): 1616(-C=N), 1688(-C=O), 3207(-NH), 3492,3418(-NH_2),3042(Ar-H), s1188cm^{-1}(C-S). ^{1}HNMR(DMSO – d_6) (δ ppm): δ= 1.95(s, 3H, -CH_3), 2.24(d,1H, -CH of pyrazolone), 3.86(d,1H, -CHa of CH_2 of thiazolidinone), 3.99(d,1H, -CH_b of CH_2 of thiazolidinone), 4.31(s, 2H, NH_2), 6.08(d, 1H, -CH of thiazolidinone), 6.82-7.93 (m, 5H, C_6H_5), 3.65 (s, 2H, N – CH_2 – CO), 9.60 (s, 1H, NH-CO-).

3.5.2. 2-(4-(3-(4-methylphenyl)-4-oxothiazolidin-2-yl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)aceto hydrazide (6b)

IR(KBr): 1618(-C=N), 1684(-C=O), 3208(-NH), 3492,3410(-NH_2), 3040(Ar-H), 1149cm^{-1} (C-S). ^{1}HNMR(DMSO–d_6) (δ ppm)**:** δ= 1.96(s, 3H, -CH_3), 2.23(d,1H, -CH of pyrazolone), 3.86(d,1H, -Ha of CH_2 of thiazolidinone), 3.99(d,1H,-H_b of CH_2 of thiazolidinone), 3.14 (s, 3H, Ar – CH_3), 4.35 (s, 2H, NH_2), 6.06(d, 1H, -CH of thiazolidinone), 6.80-7.98 (m, 4H, C_6H_4), 3.62 (s, 2H, N–CH_2 –CO), 9.62 (s, 1H, NH-CO-).

3.5.3. 2-(4-(3-(4-methoxyphenyl)-4-oxothiazolidin-2-yl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)aceto hydrazide (6c)

IR(KBr): 1620(-C=N), 1686(-C=O), 3206(-NH), 3498,3416(-NH_2), 3040(Ar-H), 1156cm^{-1} (C-S). ^{1}HNMR(DMSO – d_6) (δ ppm)**:** δ1.97(s, 3H, -CH_3), 2.24(d,1H, -CH of pyrazolone), 3.86(d,1H, -H_b of CH_2 of thiazolidinone), 3.99(d,1H, -H_a of CH_2 of thiazolidinone), 3.25 (s, 3H, OCH_3), 4.36 (s, 2H, NH_2), 6.83-7.96 (m, 4H, C_6H_4), 3.64 (s, 2H, N – CH_2 – CO), 6.08(d, 1H, -CH of thiazolidinone), 9.65 (s, 1H, NH-CO-).

3.5.4. 2-(4-(3-(4-ethoxyphenyl)-4-oxothiazolidin-2-yl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)aceto hydrazide (6d)

IR(KBr): 1621(-C=N), 1682(-C=O), 3212(-NH), 3495,3413(-NH_2), 3042(Ar-H), 1185cm^{-1} (C-S^{1}HNMR(DMSO – d_6) (δ ppm**):** δ= 1.34 (t, 3H, CH_3), 1.95(s, 3H, -CH_3), 2.22 (d,1H, -CH of pyrazolone), 3.86(d,1H, -Ha of CH_2 of thiazolidinone), 3.99(d,1H,-Hb of CH_2 of thiazolidinone), 4.12 (q, 2H, O – CH_2), 4.32(s, 2H, NH_2), 6.81-7.90 (m, 4H, C_6H_4), 3.67 (s, 2H, N – CH_2 – CO), 6.10(d, 1H, -CH of thiazolidinone), 9.59 (s, 1H,NH-CO-)

3.5.5. 2-(4-(3-(4-Chlorophenyl)-4-oxothiazolidin-2-yl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)aceto hydrazide (6e)

IR(KBr): 1622(-C=N), 1685(-C=O), 3210(-NH), 3494,3412(-NH_2), 3040(Ar-H), 1138cm^{-1} (C-S). ^{1}HNMR(DMSO–d_6) (δ ppm)**:** δ= 1.96(s, 3H, -CH_3), 2.18(d,1H, -CH of pyrazolone), 3.86(d,1H, -H_b of CH_2 of thiazolidinone), 3.99(d,1H, -H_a of CH_2 of thiazolidinone),4.35 (s, 2H, NH_2), 6.80-7.98 (m, 4H, C_6H_4), 3.68 (s, 2H, N – CH_2 – CO), 6.10(d, 1H, -CH of thiazolidinone), 9.66 (s, 1H,NH-CO-).

3.5.6. 2-(4-(3-(4-Bromophenyl)-4-oxothiazolidin-2-yl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)aceto hydrazide (6f)
IR(KBr): 1615(-C=N), 1690(-C=O), 3212(-NH), 3498,3415(-NH_2), 3042(Ar-H), 1149cm^{-1} (C-S). ^{1}HNMR(DMSO–d_6) (δ ppm)**:** δ= 1.96(s, 3H, -CH_3), 2.22(d,1H, -CH of pyrazolone), 3.86(d,1H, -Ha of CH_2 of thiazolidinone), 3.99(d,1H, -CH_b of CH_2 of thiazolidinone), 4.34 (s, 2H, NH_2), 6.80-7.96 (m, 4H, C_6H_4), 3.66 (s, 2H, N – CH_2 – CO), 6.10(d, 1H, -CH of thiazolidinone),, 9.64 (s, 1H, NH-CO-).

3.6. Synthesis of (E)-2-(4-(3-(4-substituted phenyl)-4-oxothiazolidin-2-yl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)-N'-(1-(4-substitutedphenyl)ethylidene) acetohydrazide (8a-j)
A mixture of 2-(4-(3-(4-substituted phenyl)-4-oxothiazolidin-2-yl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)acetohydrazide(6a-f)(0.0mol) in hot methanol(25ml) and 4-substitutedacetophenone (7a) (0.01mol) and a drop of glacial acetic acid were added. The solid that separated on refluxing for 3 hours filtered wash with cold methanol and recrystalised from methanol to give (E)-2-(4-(3-(4-substitutedphenyl)-4-oxothiazolidin-2-yl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)-N'-(1-(4-substitutedphenyl) ethylidene) acetohydrazide **(8a-j).** The analytical data of 8a-j was shown in **Table -1.**

The course of the reaction was monitored by T.L.C.The structures of these newly synthesized compounds (8a-j) were established on the basis of elemental analysis and spectral data (1H-NMR, IR).

3.6.1. (E)-2-(4-(3-(phenyl)-4-oxothiazolidin-2-yl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)-N'-(1-(4-substituted phenyl) ethylidene)acetohydrazide (8a)
IR(KBr): 1615(-C=N), 1188(C-S), 1670(NH-C=O), 1690(Thiazolidinone-C=O), 3042 (Ar-H str). ^{1}HNMR(DMSO–d_6) (δ ppm): δ1.95(s,3H,-CH_3 of pyrazolone),2.24(d,1H,-CH of pyrazolone), 2.32(s, 3H, -CH_3), 3.86(d,1H, -H_a of CH_2 of thiazolidinone), 3.99(d,1H, -H_b of CH_2 of thiazolidinone),6.08(d, 1H, -CH of thiazolidinone), 6.58-7.8 (m, 10H, C_6H_5 and C_6H_5 of two phenyl groups), 4.01 (s, 2H, N – CH2 – CO), 9.62(s,1H, NH-CO-).

3.6.2. (E)-2-(4-(3-(4-methylphenyl)-4-oxothiazolidin-2-yl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)-N'-(1-(4-substitutedphenyl)ethylidene)acetohydrazide (8b)
IR(KBr): 1618(-C=N), 1189(C-S), 1677(NH-C=O), 1688(Thiazolidinone-C=O), 3040cm^{-1} (Ar-H str). ^{1}HNMR(DMSO–d_6) (δ ppm) : δ= 1.96 (s, 3H, - CH_3 of pyrazolone), 2.22(d,1H, -CH of pyrazolone), 2.32(s, 3H, -CH_3),3.88(d,1H, -H_a of CH_2 of thiazolidinone), 3.96(d,1H, -H_b of CH_2 of thiazolidinone), 6.08(d, 1H, -CH of thiazolidinone), 3.12 (s,3H, Ar – CH_3), 6.54-7.5 (m, 9H, C_6H_4 and C_6H_5 of two phenyl groups), 4.05 (s, 2H, N – CH_2 – CO), 9.64(s,1H, NH-CO-).

3.6.3. (E)-2-(4-(3-(4-methoxyphenyl)-4-oxothiazolidin-2-yl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)-N'-(1-(4-substitutedphenyl)ethylidene)acetohydrazide (8c)
IR(KBr): 1620(-C=N), 1186(C-S), 1675(NH-C=O), 1685(Thiazolidinone-C=O), 3040cm^{-1} (Ar-H str^{1}HNMR(DMSO–d_6) (δ ppm)**:** δ= 1.94(s,3H,-$CH_3$of pyrazolone), 2.24(d,1H, -CH of pyrazolone), 2.30(s, 3H, -CH_3),3.86(d,1H, -H_a of CH_2 of thiazolidinone), 3.97(d,1H, -H_b of CH_2 of thiazolidinone), 6.08(d, 1H, -CH of thiazolidinone), 3.83 (s, O – CH_3), 6.56-7.7 (m, 9H, C_6H_4 and C_6H_5 of two phenyl groups), 4.03 (s, 2H, N – CH_2 – CO), 9.63 (s, 1H, NH-CO-).

3.6.4. (E)-2-(4-(3-(4-ethoxyphenyl)-4-oxothiazolidin-2-yl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)-N'-(1-(4-substitutedphenyl)ethylidene)acetohydrazide (8d)
IR(KBr): 1615(-C=N), 1185(C-S), 1673(NH-C=O), 1685(Thiazolidinone-C=O), 3042cm^{-1} (Ar-H str). ^{1}HNMR(DMSO–d_6) (δ ppm): δ= 1.8 (t, 3H, CH_3), 1.96(s, 3H, - $CH_3$of pyrazolone), 2.24(d,1H, -CH of pyrazolone), 2.32(s, 3H, -CH_3), 3.89(d,1H, -H_a of CH_2 of thiazolidinone), 3.98(d,1H, -H_b of CH_2 of thiazolidinone),6.08(d, 1H, -CH of thiazolidinone),3.16 (q,2H,O– CH_2), 6.56-7.8 (m, 9H, , C_6H_4 and C_6H_5 of two phenyl groups), 4.10 (s, 2H, N – CH_2 – CO), 9.66 (s, 1H, NH-CO-).

3.6.5. (E)-2-(4-(3-(4-chlorophenyl)-4-oxothiazolidin-2-yl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)-N'-(1-(4-substitutedphenyl)ethylidene)acetohydrazide (8e)
IR(KBr): 1618(-C=N), 1188(C-S), 1675(NH-C=O), 1695(Thiazolidinone-C=O), 3040cm^{-1} (Ar-H str). ^{1}HNMR(DMSO – d_6) (δ ppm) : δ= 1.96(s,3H,- $CH_3$of pyrazolone), 2.22(d,1H, -CH of pyrazolone), , 2.32(s, 3H, -CH_3), 3.88(d,1H, -H_a of CH_2 of thiazolidinone), 3.97(d,1H, -H_b of CH_2 of thiazolidinone),6.08(d, 1H, -CH of thiazolidinone),6.56-7.90 (m, 9H, C_6H_4 and C_6H_5 of two phenyl groups), 4.02 (s, 2H, N – CH_2 – CO), 9.63(s, 1H, NH-CO-).

3.6.6. (E)-2-(4-(3-(4-bromophenyl)-4-oxothiazolidin-2-yl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)-N'-(1-(4-substitutedphenyl)ethylidene)acetohydrazide (8f)

IR(KBr): 1620(-C=N), 1189(C-S), 1677(NH-C=O), 1692(Thiazolidinone-C=O), 3042cm^{-1} (Ar-H str). ^{1}HNMR(DMSO – d_6) (δ ppm): δ= 1.96(s,3H,-$CH_3$of pyrazolone), 2.20(d,1H,-CH of pyrazolone), 2.32(s, 3H, -CH_3), 3.84(d,1H, -H_a of CH_2 of thiazolidinone), 3.96(d,1H, -H_b of CH_2 of thiazolidinone), 6.08(d, 1H, -CH of thiazolidinone), 6.55-7.9 (m, 9H, C_6H_4 and C_6H_5 of two phenyl groups), 4.04 (s, 2H, N –CH_2–CO), 9.68(s,1H, NH-CO-).

3.6.7. (E)-2-(4-(3-(4-chlorophenyl)-4-oxothiazolidin-2-yl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)-N'-(1-(4-chlorophenyl)ethylidene)acetohydrazide (8g)

IR(KBr): 1622(-C=N), 1181(C-S), 1672(NH-C=O), 1688(Thiazolidinone-C=O), 3044cm^{-1} (Ar-H str). ^{1}HNMR(DMSO – d_6) (δ ppm): δ= 1.98 (s, 3H, - $CH_3$of pyrazolone), 2.22(d,1H, -CH of pyrazolone), 2.32(s, 3H, -CH_3),3.86(d,1H, -H_a of CH_2 of thiazolidinone), 3.99(d,1H, -H_b of CH_2 of thiazolidinone), 6.08(d, 1H, -CH of thiazolidinone), 7.01-7.8 (m, 8H, C_6H_4 and C_6H_4 of two phenyl groups), 4.05 (s, 2H, N – CH_2 – CO), 9.64(s,1H, NH-CO-).

3.6.8. (E)-2-(4-(3-(4-chlorophenyl)-4-oxothiazolidin-2-yl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)-N'-(1-(4-bromophenyl)ethylidene)acetohydrazide (8h)

IR(KBr): 1624(-C=N), 1184(C-S), 1673(NH-C=O), 1685(Thiazolidinone-C=O), 3046cm^{-1} (Ar-H str). ^{1}HNMR(DMSO – d_6) (δ ppm): δ= 1.96(s,3H,- $CH_3$of pyrazolone), 2.22(d,1H, -CH of pyrazolone), , 2.32(s, 3H, -CH_3), 3.88(d,1H, -H_a of CH_2 of thiazolidinone), 3.97(d,1H, -H_b of CH_2 of thiazolidinone),6.08(d, 1H, -CH of thiazolidinone), 6.9-7.7 (m, 8H, C_6H_4 and C_6H_4 of two phenyl groups), 4.02 (s, 2H, N – CH_2 – CO), 9.63(s, 1H, NH-CO-).

3.6.9. (E)-2-(4-(3-(4-Chlorophenyl)-4-oxothiazolidin-2-yl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)-N'-(1-(4-trifloromethylphenyl)ethylidene)acetohydrazide (8i)

IR(KBr): 1620(-C=N), 1182(C-S), 1674(NH-C=O), 1692(Thiazolidinone-C=O), 3040cm^{-1} (Ar-H str). ^{1}HNMR(DMSO–d_6) (δ ppm): δ= 1.94(s,3H,-$CH_3$of pyrazolone), 2.24(d,1H, -CH of pyrazolone), 2.30(s, 3H, -CH_3),3.86(d,1H, -H_a of CH_2 of thiazolidinone), 3.97(d,1H, -H_b of CH_2 of thiazolidinone), 6.08(d, 1H, -CH of thiazolidinone), 7.15-7.8 (m, 8H, C_6H_4 and C_6H_4 of two phenyl groups), 4.03 (s, 2H, N – CH_2 – CO), 9.63 (s, 1H, NH-CO-).

3.6.10. (E)-2-(4-(3-(4-Chlorophenyl)-4-oxothiazolidin-2-yl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-1-yl)-N'-(1-(4-Nitrophenyl)ethylidene)acetohydrazide (8j)

IR(KBr): 1624(-C=N), 1184(C-S), 1676(NH-C=O), 1690 (Thiazolidinone-C=O), 3042cm^{-1} (Ar-H str). ^{1}HNMR(DMSO – d_6) (δ ppm): δ= 1.94(s,3H,-CH_3 of pyrazolone), 2.24(d,1H, -CH of pyrazolone), 2.30(s, 3H, -CH_3),3.8(d,1H, -H_a of CH_2 of thiazolidinone), 3.97(d,1H, -H_b of CH_2 of thiazolidinone), 6.08(d, 1H, -CH of thiazolidinone), 7.2-7.9 (m, 8H, for C_6H_4 and C_6H_5 of two phenyl groups), 4.03 (s, 2H, N – CH_2 – CO), 9.63 (s, 1H, NH-CO-).

3.7. Synthesis of 2-(1-((4-acetyl-5-(4-substitutedphenyl)-5-methyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-(4-Substitutedphenyl) thiazolidin-4-one (9a-j)

A mixture of (E)-2-(3-methyl-5-oxo-4-(4-oxo-3-phenylthiazolidin-2-yl)-4,5-dihydro-1H-pyrazol-1-yl)-N'-(1-phenylethylidene) acetohydrazide (8a) on cyclisation with excess of acetic anhydride resulted 2-(1-((4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-phenyl thiazolidin-4-one (9a). The reaction procedure leading to (9a) was then extended to the syntheses of 9b-j from 8b-J.

The course of the reaction was monitored by T.L.C.The structures of these newly synthesized compounds **(9a-j)** were characterized by their elemental analysis and spectral data (^{1}H-NMR, ^{13}C-NMR, IR).

3.7.1. 2-(1-(2-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-2-oxoethyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-phenylthiazolidin-4-one (9a)

IR (KBr): 1613(-C=N), 1698 (Thiazolidinone-C=O), 1710(CO-NH), 1188(C-S), 3040 (Ar-H str), 3190cm^{-1} (NH). ^{1}HNMR(DMSO–d_6) (δ ppm): δ 1.78(s, 3H, -CH_3 of oxadiazole), 1.94(s, 3H, -CH_3 of pyrazolone), 2.02(s, 3H, -CO-CH_3), 2.22(d,1H, -CH of pyrazolone), 3.86(d,1H, -H_a of CH_2 of thiazolidinone), 3.99(d,1H, -H_b of CH_2 of thiazolidinone),6.08(d, 1H, -CH of thiazolidinone), 4.12 (s, 2H, N–CH_2–CO), 6.73 – 7.7 (m, 10H, C_6H_5 and C_6H_5)^{13}CNMR(75 MHz,$CDCl_3$,TMS)δ: 53.5, 33.2, 170.9, 141.7, 127.5, 129.0, 128.0, 50.5, 175.9, 155.6, 19.6, 52.8, 158.2, 90.2,28.0,142.5,127,128.5,126.7,170.0 & 24.2 and these signals are due to C_1, C_2,C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{16}, C_{17}, C_{18}, C_{19},C_{20} & C_{21}.

3.7.2 2-(1-((4-acetyl-5-(phenyl)-5-methyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-(4-methylphenyl) thiazolidin-4-one (9b)

IR (KBr): 1604(-C=N), 1696 (Thiazolidinone-C=O), 1702(CO-NH), 1179(C-S), 3041 (Ar-H str), 3189cm^{-1}(NH). ^{1}HNMR (DMSO–d_6) (δ ppm): δ 1.76(s, 3H, -CH_3 of oxadiazole), 1.96(s, 3H, -CH_3 of pyrazolone), 2.04(s, 3H, -CO-CH_3), 2.24(d,1H, -CH of pyrazolone), 3.21 (s,3H, Ar –CH_3 of pyrazolone), 3.84(d,1H,-H_a of CH_2 of thiazolidinone), 3.97(d,1H, -H_b of CH_2 of thiazolidinone), 6.10(d, 1H, -CH of thiazolidinone), 4.08 (s, 2H, N–CH_2–CO), 6.6 – 7.6 (m, 9H, C_6H_4andC_6H_5). ^{13}CNMR(75MHz,$CDCl_3$,TMS)δ: 53.6, 33.4, 170.9, 138.7, 133.4, 129.2, 136.8, 50.7, 175.7, 155.6, 19.6,53.2,158.4,90.2, 27.8,142.5,127,128.4,126.7,170.0,24.2,21.3 and these signals are due to C_1, C_2,C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{16}, $C_{17,}$ C_{18}, C_{19},C_{20} , C_{21} & C_{22}.

3.7.3. 2-(1-((4-acetyl-5-(phenyl)-5-methyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-(4-methoxyphenyl) thiazolidin-4-one (9c)

IR (KBr): 1609(-C=N), 1697 (Thiazolidinone-C=O), 1696(CO-NH), 1166(C-S), 3040 (Ar-H str), 3180cm^{-1} (NH). ^{1}HNMR(DMSO – d_6) (δ ppm): δ 1.81(s, 3H, -CH_3 of oxadiazole), 1.98(s, 3H, -CH_3 of pyrazolone), 2.06(s, 3H, -CO-CH_3), 2.20(d,1H, -CH of pyrazolone), 3.52(s, O–CH_3), 3.88(d,1H, -H_a of CH_2 of thiazolidinone), 4.02(d,1H, -H_b of CH_2 of thiazolidinone),6.05(d, 1H, -CH of thiazolidinone), 4.10 (s, 2H, N–CH_2–CO), 6.76 – 7.6 (m, 9H, C_6H_4 and C_6H_5). ^{13}C NMR(75MHz,$CDCl_3$,TMS) δ:53.4,33.2,170.6,134.0,122.6,114.8,159,50.6,175.7,155.6,19.6,52.7, 158.4,90.2,27.9,142.6,127,128.6,126.7,170.2,24.0,55.8 and these signals are due to C_1, C_2,C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{16}, $C_{17,}$ C_{18}, C_{19},C_{20} ,C_{21}& C_{22}.

3.7.4. 2-(1-((4-acetyl-5-(4-substitutedphenyl)-5-methyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-(4-ethoxyphenyl)thiazolidin-4-one (9d)

IR (KBr): 1602(-C=N), 1692(Thiazolidinone-C=O), 1704(CO-NH), 1179(C-S), 3042 (Ar-H str), 3185cm^{-1} (NH). ^{1}HNMR(DMSO – d_6) (δ ppm): 1.8(t, 3H,CH_3),3.16(q,2H,O-CH_2), 1.79(s, 3H, -CH_3 of oxadiazole), 1.94(s, 3H, -CH_3 of pyrazolone), 2.04(s, 3H, -CO-CH_3), 2.20(d,1H, -CH of pyrazolone), 3.84(d,1H, -H_a of CH_2 of thiazolidinone), 3.92(d,1H, -H_b of CH_2 of thiazolidinone), 6.08(d, 1H, -CH of thiazolidinone), 4.08 (s, 2H, N–CH_2–CO), 6.6 – 7.5 (m, 9H, C_6H_4 and C_6H_5). ^{13}CNMR(75MHz,$CDCl_3$,TMS)δ: 53.5, 33.0, 170.9, 133.3, 122.2, 114.6, 157.6, 50.4, 175.6, 155.6, 19.6,52.6,158.2,90.2,27.9,142.5,127,128.7,126.5,170.1,24.0,64.6,14.8 and these signals are due to C_1, C_2,C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{16}, $C_{17,}$ C_{18}, C_{19},C_{20} , C_{21}& C_{22}.

3.7.5. 2-(1-((4-acetyl-5-(phenyl)-5-methyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-(4-chlorophenyl) thiazolidin-4-one (9e)

IR (KBr): 1600(-C=N), 1694(Thiazolidinone-C=O), 1710(CO-NH), 1168(C-S), 3040 (Ar-H str), 3178cm^{-1} (NH). ^{1}HNMR(DMSO – d_6) (δ ppm): δ 1.82(s, 3H, -CH_3 of oxadiazole), 1.96(s, 3H, -CH_3 of pyrazolone), 2.04(s, 3H, -CO-CH_3), 2.20(d,1H, -CH of pyrazolone), 3.84(d,1H, -H_a of CH_2 of thiazolidinone), 3.97(d,1H, -H_b of CH_2 of thiazolidinone),6.10(d, 1H, -CH of thiazolidinone), 4.10 (s, 2H, N–CH_2–CO), 6.83 – 7.3 (m, 9H, C_6H_4 and C_6H_5). ^{13}CNMR (75 MHz,$CDCl_3$,TMS)δ: 53.7, 33.1, 170.6, 139.8, 125.6, 129, 133, 50.3, 175.6, 155.6, 19.6, 52.5, 158.4, 90.2, 27.8,142.5,127, 128.5, 126.5,170.0,24.4 and these signals are due to C_1, C_2,C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{16}, $C_{17,}$ C_{18}, C_{19},C_{20} & C_{21}.

3.7.6. 2-(1-((4-acetyl-5-(phenyl)-5-methyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-(4-bromophenyl) thiazolidin-4-one (9f)

IR (KBr): 1600(-C=N), 1692(Thiazolidinone-C=O), 1724(CO-NH), 1169(C-S), 3040 (Ar-H str), 3186cm^{-1} (NH). ^{1}HNMR(DMSO – d_6) (δ ppm): δ 1.75(s, 3H, -CH_3 of oxadiazole), 1.95(s, 3H, -CH_3 of pyrazolone), 2.09(s, 3H, -CO-CH_3), 2.24(d,1H, -CH of pyrazolone), 3.87(d,1H, -H_a of CH_2 of thiazolidinone), 3.94(d,1H, -H_b of CH_2 of thiazolidinone),6.12(d, 1H, -CH of thiazolidinone), 4.10 (s, 2H, N–CH_2–CO), 6.79 – 7.5 (m, 9H, C_6H_4 and C_6H_5). ^{13}C NMR (75 MHz,$CDCl_3$,TMS)δ: 53.6, 33.2, 170.8, 140.7, 136.7, 131.8, 122.3, 50.4, 175.6, 155.6, 19.6, 52.6, 158.2, 90.2,28.0,142.5,127,128.6,126.7,170.4,24.2 and these signals are due to C_1, C_2,C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{16}, $C_{17,}$ C_{18}, C_{19},C_{20} & C_{21}.

3.7.7. 2-(1-((4-acetyl-5-(4-chlorophenyl)-5-methyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-(4-chlorophenyl) thiazolidin-4-one (9g)

IR (KBr): 1604(-C=N), 1692(Thiazolidinone-C=O), 1694(CO-NH), 1185(C-S), 3042(Ar-H str), 3183cm^{-1} (NH). ^{1}HNMR(DMSO – d_6) (δ ppm): δ 1.86(s, 3H, -CH_3 of oxadiazole), 1.96(s, 3H, -CH_3 of pyrazolone), 2.04(s, 3H, -CO-CH_3), 2.24(d,1H, -CH of pyrazolone), 3.84(d,1H, -H_a of CH_2 of thiazolidinone), 3.97(d,1H, -H_b of CH_2 of thiazolidinone), 6.10(d, 1H, -CH of thiazolidinone), 4.08 (s, 2H, –CH_2 attached to oxadiazole), 7.0-7.7 (m, 8H, C_6H_4 and C_6H_4). ^{13}C NMR(75MHz,$CDCl_3$,TMS)δ: 53.5, 33.2, 170.6, 141.7, 127.5, 129.0, 128.0, 50.5, 175.9, 155.6, 19.6, 52.5, 158.2,90.2, 28,139.6,126.8,129,136.4,170.2,24.2 and these signals are due to C_1, C_2,C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{16}, $C_{17,}$ C_{18}, C_{19},C_{20} & C_{21}.

3.7.8. 2-(1-((4-acetyl-5-(4-bromophenyl)-5-methyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-(4-chlorophenyl) thiazolidin-4-one (9h)

IR (KBr): 1618(-C=N), 1694(Thiazolidinone-C=O), 1698(CO-NH), 1168(C-S), 3040(Ar-H str), 3188cm^{-1} (NH). ^{1}HNMR(DMSO – d_6) (δ ppm): δ 1.82(s, 3H, -CH_3 of oxadiazole), 1.96(s, 3H, -CH_3 of pyrazolone), 2.04(s, 3H, -CO-CH_3), 2.20(d,1H, -CH of pyrazolone), 3.84(d,1H, -H_a of CH_2 of thiazolidinone), 3.97(d,1H, -H_b of CH_2 of thiazolidinone),6.10(d, 1H, -CH of thiazolidinone), 4.10 (s, 2H, –CH_2 attached to oxadiazole), 6.83 – 7.1-7.7 (m, 8H, C_6H_4 and C_6H_4). ^{13}CNMR(75MHz,$CDCl_3$,TMS)δ:53.5,33.2,170.8,141.7,127.5,129.0,128.0,50.5,175.9, 155.6,19.6,52.5,158.8, 90.2,27.8,140.7,125.6,128.6,132.3,170.0,24.2 and these signals are due to C_1, C_2,C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{16}, $C_{17,}$ C_{18}, C_{19},C_{20} & C_{21}.

3.7.9. 2-(1-((4-acetyl-5-(4-triflourophenyl)-5-methyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-(4-chlorophenyl) thiazolidin-4-one (9i)

IR (KBr): 1600(-C=N), 1692(Thiazolidinone-C=O), 1724(CO-NH), 1169(C-S), 3040 (Ar-H str), 3186cm^{-1} (NH). ^{1}HNMR(DMSO – d_6) (δ ppm): δ 1.87(s, 3H, -CH_3 of oxadiazole), 1.98(s, 3H, -CH_3 of pyrazolone), 2.06(s, 3H, -CO-CH_3), 2.20(d,1H, -CH of pyrazolone), 3.88(d,1H, -H_a of CH_2 of thiazolidinone), 4.02(d,1H, -H_b of CH_2 of thiazolidinone),6.05(d, 1H, -CH of thiazolidinone), 4.10 (s,2H,–CH_2 attached to oxadiazole), 7.15-7.8 (m, 8H, C_6H_4 and C_6H_4). ^{13}CNMR(75MHz,$CDCl_3$,TMS)δ:53.5,33.2,170.9,141.7,127.5,129.0,128.0,50.5,176.2,155.6,19.4,52.5,158.4,90.2,27.8,141.6,129,131.4,121.0,170.0,24.2,-,124.1, and these signals are due to C_1, C_2,C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{16}, $C_{17,}$ C_{18}, C_{19},C_{20} , C_{21} & C_{23}.

3.7.10. 2-(1-((4-acetyl-5-(4-Nitrophenyl)-5-methyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)methyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-(4-chlorophenyl) thiazolidin-4-one (9j)

IR (KBr): 1600(-C=N), 1692(Thiazolidinone-C=O), 1724(CO-NH), 1169(C-S), 3040 (Ar-H str), 3186cm^{-1} (NH). ^{1}HNMR(DMSO – d_6) (δ ppm): δ 1.88(s, 3H, -CH_3 of oxadiazole), 1.98(s, 3H,-CH_3 of pyrazolone), 2.06(s, 3H, -CO-CH_3), 2.20(d,1H, -CH of pyrazolone), 3.88(d,1H, -H_a of CH_2 of thiazolidinone), 4.02(d,1H, -H_b of CH_2 of thiazolidinone),6.05(d, 1H, -CH of thiazolidinone), 4.10 (s, 2H, –CH_2 attached to oxadiazole), 7.2 – 7.9 (m, 8H, C_6H_4 and C_6H_4). ^{13}C NMR(75MHz,$CDCl_3$,TMS)δ:53.6,33.2,170.9,141.7,127.5,129.0,128.0,50.5,175.7,155.6,19.6, 52.5,158.2,90.2,27.9,148.7,128,124,146,170.0,24.2 and these signals are due to C_1, C_2,C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{16}, $C_{17,}$ C_{18}, C_{19},C_{20} & C_{21}.

Table 1. Analytical data of the compounds 6a-f, 8a-jand 9a-j

Compound	Moleular formula	Yield (%)	M.P.* (^{0}C)	% Analysis					
				C		H		N	
				Cald	Found	Cald	Found	Cald	Found
6a	$C_{15}H_{17}N_5O_3S$	60	162-3	51.86	51.71	4.93	4.84	20.16	19.98
6b	$C_{16}H_{19}N_5O_3S$	55	144-5	53.17	53.08	5.30	5.18	19.38	19.26
6c	$C_{16}H_{19}N_5O_4S$	60	152-3	50.92	50.68	5.07	4.92	18.56	18.37
6d	$C_{17}H_{21}N_5O_4S$	58	173-4	52.16	52.02	5.41	5.32	17.89	17.72
6e	$C_{15}H_{16}ClN_5O_3S$	65	185-6	47.18	47.06	4.22	4.17	18.34	18.25
6f	$C_{15}H_{16}BrN_5O_3S$	65	188-9	42.26	42.12	3.78	3.71	16.43	16.36
8a	$C_{23}H_{23}N_5O_3S$	65	175-6	61.45	61.32	5.16	5.07	15.58	15.49
8b	$C_{24}H_{25}N_5O_3S$	70	161-2	62.18	62.02	5.44	5.32	15.11	15.04
8c	$C_{24}H_{25}N_5O_4S$	65	172-3	60.11	59.92	5.25	5.16	14.60	14.42
8d	$C_{25}H_{27}N_5O_4S$	70	188-9	60.83	60.68	5.51	5.38	14.19	14.07
8e	$C_{23}H_{22}ClN_5O_3S$	75	194-5	57.08	56.96	4.58	4.45	14.47	14.36
8f	$C_{23}H_{22}BrN_5O_3S$	70	207-8	52.28	49.49	4.20	3.18	13.25	13.17
8g	$C_{23}H_{21}Cl_2N_5O_3S$	67	223-4	53.29	53.14	4.08	4.01	13.51	13.48
8h	$C_{23}H_{21}BrClN_5O_3S$	70	207-8	49.08	48.97	3.76	3.63	12.44	12.32
8i	$C_{24}H_{21}ClF_3N_5O_3S$	64	232-3	52.22	52.14	3.83	3.74	12.69	12.51
8j	$C_{23}H_{21}ClN_6O_5S$	70	194-5	52.22	52.09	4.00	3.87	15.89	15.76
9a	$C_{25}H_{25}N_5O_4S$	65	160-1	61.08	60.98	5.13	5.11	14.25	14.05
9b	$C_{26}H_{27}N_5O_4S$	60	148-9	61.77	61.58	5.38	5.16	13.85	13.72
9c	$C_{26}H_{27}N_5O_5S$	55	185-6	59.87	59.32	5.22	5.08	13.43	13.38
9d	$C_{27}H_{29}N_5O_5S$	58	174-5	60.55	59.96	5.46	5.32	13.08	12.98
9e	$C_{25}H_{24}ClN_5O_4S$	70	204-5	57.08	56.94	4.60	4.45	13.31	13.12
9f	$C_{25}H_{24}BrClN_5O_4S$	70	192-3	52.64	52.51	4.24	4.17	12.28	12.13
9g	$C_{25}H_{23}Cl_2N_5O_4S$	75	202-3	53.58	53.49	4.14	4.08	12.50	12.36
9h	$C_{25}H_{23}BrClN_5O_4S$	69	221-2	49.64	49.52	3.83	3.74	11.58	11.46
9i	$C_{26}H_{23}ClF_3N_5O_4S$	70	190-1	52.57	52.49	3.90	3.82	11.79	11.67
9j	$C_{25}H_{23}ClN_6O_6S$	70	227-8	52.59	52.46	4.06	3.98	14.72	14.65

Table 2.Antibacterial Activity by the disc diffusion method

S.No	Compound	Zone of Inhibition			
		Staphylococcus aureus	*Bacillus Cereus*	*Escherichia Coli*	*Pseudomonas aeruginosa*
1	2-(1-(2-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-2-oxoethyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-phenylthiazolidin-4-one (9a)	7	6	6	7
2	2-(1-(2-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-2-oxoethyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-(p-tolyl)thiazolidin-4-one (9b)	6	7	7	6
3	2-(1-(2-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-2-oxoethyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-(4-methoxyphenyl)thiazolidin-4-one (9c)	8	6	6	6
4	2-(1-(2-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-2-oxoethyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-(4-ethoxyphenyl)thiazolidin-4-one (9d)	6	7	7	7
5	2-(1-(2-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-2-oxoethyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-(4-chlorophenyl)thiazolidin-4-one (9e)	7	7	7	7
6	2-(1-(2-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-2-oxoethyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-(4-bromophenyl)thiazolidin-4-one (9f)	6	8	7	6
7	2-(1-(2-(4-acetyl-5-(4-chlorophenyl)-5-methyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-2-oxoethyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-(4-chlorophenyl)thiazolidin-4-one (9g)	13	14	12	13
8	2-(1-(2-(4-acetyl-5-(4-bromophenyl)-5-methyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-2-oxoethyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-(4-chlorophenyl)thiazolidin-4-one. (9h)	11	13	11	12
9	2-(1-(2-(4-acetyl-5-methyl-5-(4-(trifluoromethyl)phenyl)-4,5-dihydro-1,3,4-oxadiazol-2-yl)-2-oxoethyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-(4-chlorophenyl)thiazolidin-4-one (9i)	14	15	13	14
10	2-(1-(2-(4-acetyl-5-methyl-5-(4-nitrophenyl)-4,5-dihydro-1,3,4-oxadiazol-2-yl)-2-oxoethyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-(4-chlorophenyl)thiazolidin-4-one (9k)	12	13	12	13
11	Cefaclor	19	22	19	20

**Figures indicate diameter of inhibition in mm.*

Table 3. Antifungal Activity by the disc diffusion method

S.No	Compound	Zone of Inhibition	
		Asperigillus flavus	*Candida albicans*
1	2-(1-(2-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-2-oxoethyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-phenylthiazolidin-4-one (9a)	7	6
2	2-(1-(2-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-2-oxoethyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-(p-tolyl)thiazolidin-4-one (9b)	6	6
3	2-(1-(2-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-2-oxoethyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-(4-methoxyphenyl)thiazolidin-4-one (9c)	8	7
4	2-(1-(2-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-2-oxoethyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-(4-ethoxyphenyl)thiazolidin-4-one (9d)	7	6
5	2-(1-(2-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-2-oxoethyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-(4-chlorophenyl)thiazolidin-4-one (9e)	7	7
6	2-(1-(2-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-2-oxoethyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-(4-bromophenyl)thiazolidin-4-one (9f)	7	6
7	2-(1-(2-(4-acetyl-5-(4-chlorophenyl)-5-methyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-2-oxoethyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-(4-chlorophenyl)thiazolidin-4-one (9g)	13	12
8	2-(1-(2-(4-acetyl-5-(4-bromophenyl)-5-methyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-2-oxoethyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-(4-chlorophenyl)thiazolidin-4-one (9h)	11	10
9	2-(1-(2-(4-acetyl-5-methyl-5-(4-(trifluoromethyl)phenyl)-4,5-dihydro-1,3,4-oxadiazol-2-yl)-2-oxoethyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-(4-chlorophenyl)thiazolidin-4-one (9i)	14	15
10	2-(1-(2-(4-acetyl-5-methyl-5-(4-nitrophenyl)-4,5-dihydro-1,3,4-oxadiazol-2-yl)-2-oxoethyl)-3-methyl-5-oxo-4,5-dihydro-1H-pyrazol-4-yl)-3-(4-chlorophenyl)thiazolidin-4-one (9j)	12	11
11	Clotrimazole	20	21

**data indicate diameter of inhibition in mm.*

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