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Novel Route for Synthesis of Anti - Hyperglycaemic Activity of Thiazolidine 2,4-Dione Derivatives As A Mannich Bases

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Abstract

The mannish bases of Thiozolidine 2,4 -dione derivatives has come to lime light due to their multi functional biological activities. Thiazolidine-2,4-dione is an extensively explored hetero cyclic nucleus for designing of novel agents implicated for a wide variety of pathophysiological conditions, that is, diabetes, diabetic complications ,cancer, arthritis, inflammation, microbial infection, and melanoma. Present work, synthesise quinoline attached imidozoline derivative using (3 +2) cycloaddition via imine of quinoline and TOSMIC. These derivatives were converted to mannich bases of thiozolidine 2,4 one using knoevenagel condensation. The sulfonyl derivatives of thiozolidine 2, 4 -dione were also synthesized and characterized by using alkylation conditions.

Keywords: Imidazole derivatives; Thiozolidine 2,4 one nucleus; TOSMIC; Combi- flash Chromatography

Introduction

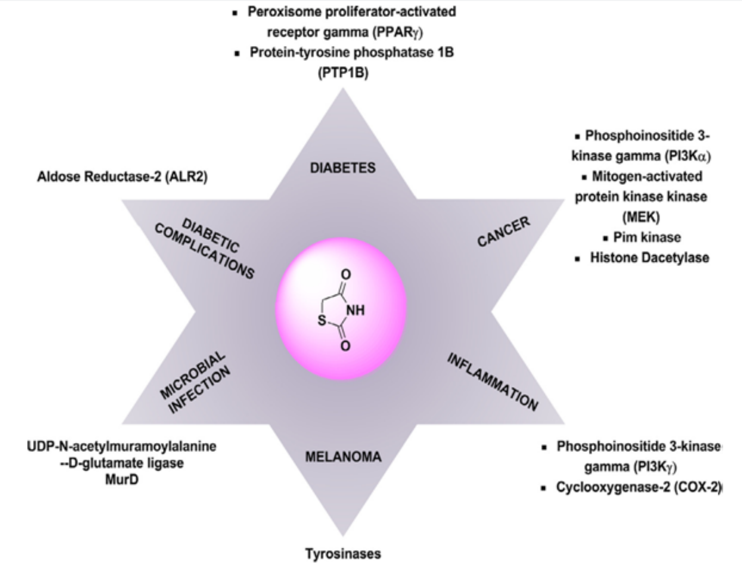

Figure 1

Thiazolidine 2,4 dione (TZD) is a vital nucleolus in heterocyclic chemistry. TZD shows multidirectional phamocodynamical activities such as Anti-hyperglycemic (glitazone drugs), anti-cancer, anti microbial, anti-arthritic. Due to multidirectional pathological actions, huge explored research work has been attempted and still efforts under progress for drug candidates. The metabolic disorder of diabetic is now a day's shows major impact on human beings throughout world. The Thiazolidine 2,4-dione (TZD) derivatives act as a drug candidates such as rosiglitagone, pioglitazone, lobigli tazone, enaglitazone, netoglitazone, ozoline, daragletazone, troglitazone etc. TZD derivatives not only confine for treatment of metabolic disorder diabetic, it o shows as an inflammatory agents, and anti- cancer and for treatment of melanoma. Due to importance of TZD, derivatives many scientists have been developed various routes for synthesis. Om silakari et al. developed different TZD derivatives and evolutes their biological activity (Figure 1). Ivanildo Mangueira, da Silva and co workers [1] developed TZD derivatives using Knoevenagel condensation (Figure 2). Boja Poojary and co workers [2] synthesized and characterization of Antimicrobial activity of novel derivatives (Figure 3). Archana Kapoor and Neha Khare [3] synthesized various mannich bases of Antibacterial and antifungal activity of 2,4-thiazolidinedione and rhodanine (Figure 4). Many routes has been developed for synthesis of 2,4thiozolidinone. The Thiazolidine 2,4 dione having many active sites. Thiazolidine 2,4,dione nucleus numbering is given as fallows (Figure 5).

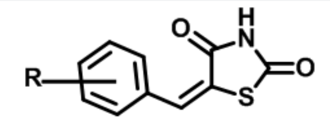

Figure 2: TZD derivatives using Knoevenagel condensation.

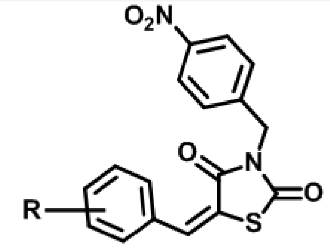

Figure 3: Synthesized and characterization of Antimicrobial activity of novel derivatives.

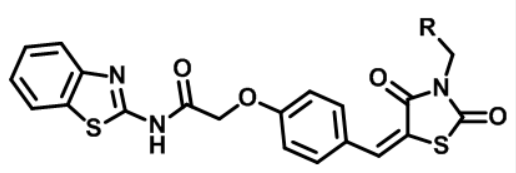

Figure 4: synthesized various mannich bases of Antibacterial and antifungal activity of 2,4-thiazolidinedione and rhodanine.

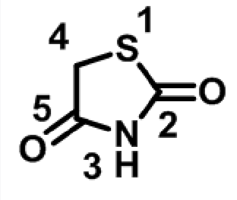

Figure 5: Thiazolidine 2,4, dione nucleus numbering

Materials and Methods

All reagents and starting material were procured from commercial sources (Aldrich, Alfa Aesar). Solvents were thoroughly dried before use. THF and toluene were dried using sodium metal and benzophenone.DMF was dried using CaH. The new compounds were fully characterized using Analytical methods like IR, NMR (Bruker). The melting points were recorded using on a (WRS-1A) Digital Melting Point Apparatus without correction. Infrared spectra were taken using an AVATAR 370 FT-IR spectrometer. HNMR, CNMR spectra were recorded with a Bruker spectrometer operating at 400MHz used as a Trimethyl silane reference and values recorded in ppm. The progress of reaction was monitored using TLC system and I_2 spray and $KMnO_4$ TLC strain. The crude compounds were purified using column chromatography (100-200 mesh silica) and Combi-flash chromatography. The hydrogenolysis process was carried out using parr shaker [4-19].

Objective of this Research

Present work is related to develop new synthetic route for preparation of the quinoline containing thiozolidin-4-one attached 1,3, 4 oxa diazole nucleus and thiazolidin-4-one attached benz imidazole and benz thiozole and benzoxazole derivatives and thoroughly characterized. The scaffolds of 2-(8-((5-(4- substituted phenyl)-1,3,4-oxadiazol-2-yl)methoxy) quinolin-5-yl)-3-(4-(trifluoromethyl)phenyl)thiazolidin-4-one(7a-h)weresynthesized and characterized.

Experimental Methods

In this research work, we prepared below compounds and mentioned in step wise manner.

a) **Step-1:** (Z)-N-((8-(benzyloxy)quinolin-5-yl)methylene)-4-(trifluoromethyl)aniline **(2)**

b) **Step-2:** 8-(benzyloxy)-5-(1-(4-(trifluoromethyl) phenyl)-1H-imidazol-5-yl) quinoline **(3).**

c) **Step-3:** 5-(1-(4-(trifluoromethyl) phenyl)-1H-imidazol-5-yl) quinolin-8-ol **(4).**

d) **Step-4:** 2-((5-(1-(4-(trifluoromethyl) phenyl)-1H-imidazol-5-yl) quinolin-8-yl) oxy) acetaldehyde **(5).**

e) **Step-5:** 5-(5-(1-(4-(trifluoromethyl)phenyl)-1H-imidazol-5-yl)quinolin-8-oxy)methylene)thiazolidine-2,4-dione **(6).**

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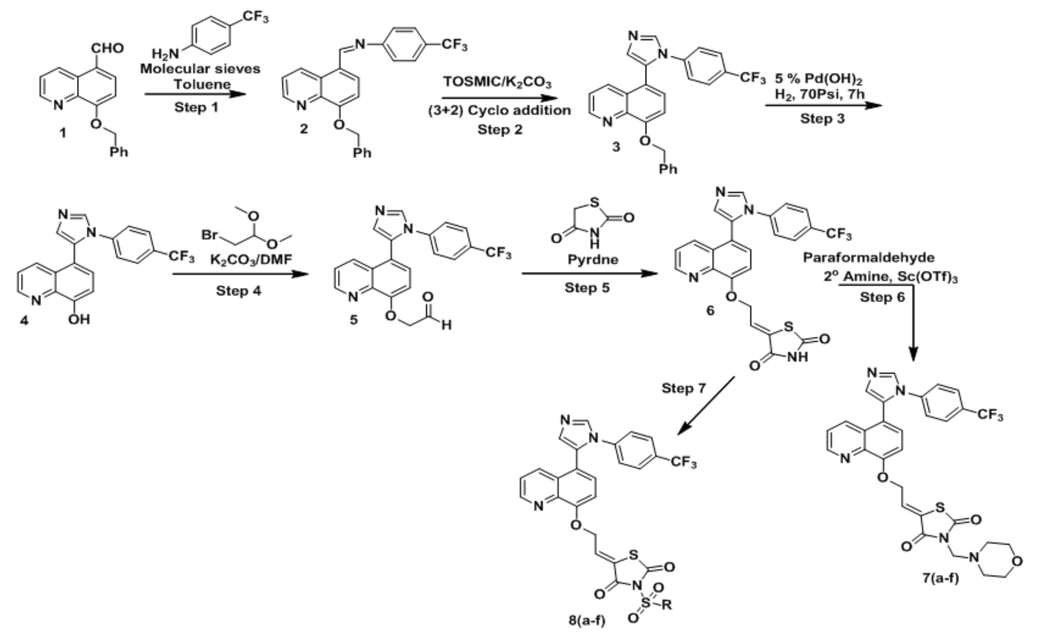
f) Step-6: 3-(Amine substituted methyl)-5-(2-((5-(1-(4-(trifluoromethyl) phenyl)-1H-imidazol-5-yl)quinolin-8-yl)oxy) ethylidene)thiazolidine-2,4-dione **(7a-f).**

g) Step-7: 3-(sulfonyl-derivatives)-5-(2-((5-(1-(4-(trifluoromethyl) phenyl)-1H-imidazol-5-yl) quinolin-8-yl)oxy)ethylidene)thiazolidine-2,4-dione (8a-f) (Figure 6).



Reaction Conditions: Step 1) Molecular sieves, Toluene, 100 °C, 10 h, **Step 2)** TOSMIC /K_2CO_3, 0 °C, 16 h, **Step 3)** 5% $Pd(OH)_2$, H_2, 70Psi, 3 h, **Step 4)** 2-bromo-1,1-dimethoxy ethane, K_2CO_3/DMF, 5h, **Step 5)** thiazolidine-2,4-dione, Piperdine, 90°C, 6h, **Step 6)** Para formaldehyde /2o Amine, $Sc(OTf)_3$ EtOH, 90 °C, 8 h.

Figure 6: Scheme:

Reaction mechanism for Step 2 (Figure 7)

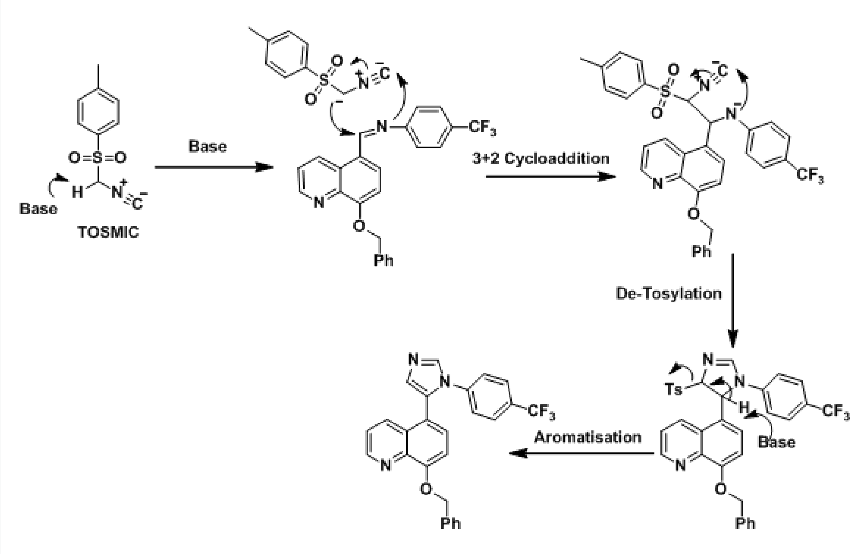


Figure 7: Reaction mechanism for Step 2

Step 1: (Z)-N-((8-(benzyloxy) quinolin-5-yl) methylene)-4-(trifluoromethyl) aniline(2)

8-(benzyloxy) quinoline-5-carbaldehyde (10 g, 0.038 mol), 4-(trifluoromethyl) aniline (6.5 g, 0.039 mol) in dry toluene (100 mL) was added freshly dried molecular sieves and refluxed for 10 h under N_2 atm. The progress of reaction was monitored by TLC. After completion of starting material, toluene was evaporated under vacuum to gave crude residue of Compound- 2

(15 g) as a solid (white colour). The crude was carried to next step (Figure 8).

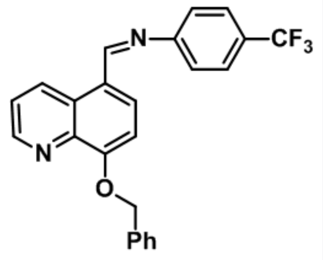


Figure 8: (Z)-N-((8-(benzyloxy) quinolin-5-yl)methylene)-4-(trifluoromethyl) aniline(2)

Step 2 : 8-(benzyloxy)-5-(1-(4-(trifluoromethyl) phenyl)-1H-imidazol-5-yl)quinoline(3)

(Z)-N-((8-(benzyloxy) quinolin-5-yl)methylene)-4-(trifluoromethyl) aniline(2) (15 g, 0.036 mol)was dissolved in Dry DMF (80 mL) and cooled to 0 °C. To that dried K_2CO_3 (15 g. 108 mol) and Toluene methyl isocyanide (7.02 g, 0.036 mol) was added and warm to room temperature and stirred for 16h. The progress of reaction was monitored by TLC. After completion, reaction mixture was poured in ice cold water (100 mL) and extracted with EtOAc (3 x 100 mL). The organic layer was separated and washed with brine solution, dried over anhydrous Na_2SO_4, filtered and evaporated under vacuum to give crude residue. The obtained crude product was purified by column chromatography (100-200 mesh silica, Eluent: 80% EtOAc-Pet Ether) isolated 8-(benzyloxy)-5-(1-(4-(trifluoromethyl) phenyl)-1H-imidazol-5-yl)quinoline(3) (10 g, yield: 64%) as a solid (Pale yellow colour). M.p. 252-255 °C. IR (KBr, cm−1): 3030, 1440, 1520, 1005, 691, 655. **HNMR (d_6-DMSO, 400 mHz): 5.2** (s, 1H, -CH_2), 7.1 (m, 3H), 7.3-7.5 (m, 7H), 7.6-7.7 (m, 4H), 7.85(d, 1H), 8.36(d, 1H), 8.85(d, 1H) (Figure 9).

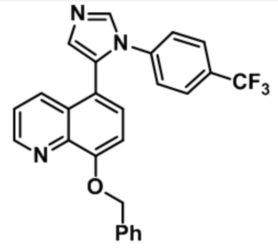


Figure 9: 8-(benzyloxy)-5-(1-(4-(trifluoromethyl)phenyl)-1H-imidazol-5-yl)quinoline(3)

Step 3 : 5-(1-(4-(trifluoromethyl)phenyl)-1H-imidazol-5-yl)quinolin-8-ol (4)

8-(benzyloxy)-5-(1-(4-(trifluoromethyl)phenyl)-1H-imidazol-5-yl)quinoline(3) (10 g, 0.022 mol) in MeOH (100 mL) was added 5% Palladium hydroxide on carbon (1 g, cat) and hydrozinated at 70 Psi under parr shaker for 3 h at room temperature. The progress of reaction was monitored by TLC. After completion, reaction mixture was filtered on cellite bed and thoroughly washed with MeOH (2 x 75 mL). The MeOH layer were collected and evaperated under vaccum to gave 5-(1-(4-(trifluoromethyl)phenyl)-1H-imidazol-5-yl)quinolin-8-ol (4)(7g, yield : 86%) as a solid (white colour)). M.p. 280-285 °C. IR (KBr, cm−1): 3620, 3014, , 1525, 1050, 691, 620 .^{1}**HNMR (d_6-DMSO, 400 mHz) :** 6.5 (brs, 1H),7.1 (m, 2H), 7.3 (d, 2H), 7.63 (m, 4H),7.8(d,1H), 8.35(d, 1H), 8.8(d, 1H) (Figure 10).

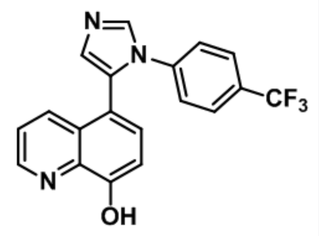


Figure 10: 5-(1-(4-(trifluoromethyl)phenyl)-1H-imidazol-5-yl) quinolin-8-ol (4)

Step 4 : 2-((5-(1-(4-(trifluoromethyl)phenyl)-1H-imidazol-5-yl)quinolin-8-l)oxy)acetaldehyde (5)

5-(1-(4-(trifluoromethyl) phenyl)-1H-imidazol-5-yl) quinolin-8-ol (4) (7 g, 0.017 mol) in Dry DMF (70 mL) was added K_2CO_3 (9.7 g, 0.07 mol, 4 eq) and stirred at rt for 30 min. To that a solution of 2-bromo-1,1-dimethoxy ethane(1.2 eq) in DMF (20 mL) was added drop wise at 0°C and stirred for 5h. The progress of reaction was monitored by TLC. After completion, reaction mixture was filtered on cellite bed and washed with DMF (10 mL). The Reaction mixture was poured in ice cold water (200 mL) and stirred for 20 min. The reaction mixture was acidified aq $NaHSO_3$ solution up to P^H-5 and extracted with EtOAc (2 x 200 mL). The aqueous layer was collected and basified up to P^H-8 with sat aq $NaHCO_3$ sol. The aqueous layer was extracted with EtOAc (3 x 100 mL). The organic layer were collected and dried over anhydrous Na_2SO_4, filtered and evaporated under vacuum to gave 2-((5-(1-(4-(trifluoromethyl)phenyl)-1H-imidazol-5-yl)quinolin-8-yl)oxy) acetaldehyde (5) (5g) as a solid(white colour). M.p. 200-205 °C. IR (KBr, cm−1): 3602, 3014, 1712, 1646, 1503, 1050, 691, 644.^{1}**HNMR (d_6-DMSO, 400 mHz) :** 5.2 (s, 2H), 7.1 (m, 2H), 7.3(d, 2H),7.9(d, 1H), 8.36(d, 1H), 8.82(d, 1H), 9.6(s, 1H) (Figure 11).

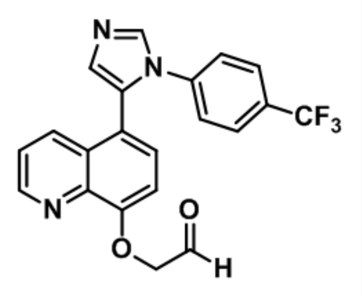


Figure 11: 2-((5-(1-(4-(trifluoromethyl)phenyl)-1H-imidazol-5-yl)quinolin-8-yl)oxy) acetal dehyde (5)

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Step 5: 5-(2-((5-(1-(4-(trifluoromethyl)phenyl)-1H-imidazol-5-yl)quinolin-8-yl)oxy) ethylidene) thiazolidine-2,4-dione (5)

To a mixture of 2-((5-(1-(4-(trifluoromethyl)phenyl)-1H-imidazol-5-yl)quinolin-8-yl)oxy) acetaldehyde (5) (5g, 0.012 mol), thiazolidine-2,4-dione (1.62 g, 0.013 mol) in EtOH (50 mL) was added piperdine (2 mL) and heated at 90 °C for 6 h. The progress of reaction was monitored by TLC. After completion, Reaction mixture was evaporated under vacuum to gave crude residue. The residue was diisolve in water(100 mL) and filtered under vaccum and dried to gave (Z)-5-(2-((5-(1-(4-(trifluoromethyl) phenyl)-1H-imidazol-5-yl)quinolin-8-yl)oxy) ethylidene) thiazolidine-2,4-dione (6) (5.5 g, Yield: 88%) as a solid (brown colour).M.p:240-243 °C. IR (KBr, cm–1): 3050, 1725, 1650, 1503, 1050, 691, 644.**^{1}HNMR (d_6-DMSO, 400 mHz) : 4.6** (dd, 1H), 4.61(dd, 1H), 6.15 (dd, 1H), 7.12 (m, 2H), 7.3 (d, 2H), 7.6-7.65 (m, 4H), 7.9(d, 1H), 8.4(d, 1H), 8.6 (brs, 1H), 8.87 (d, 1H) (Figure 12).

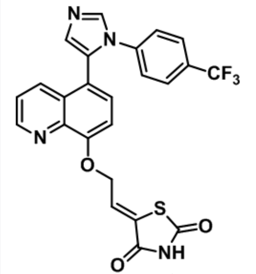
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Figure 12: 5-(2-((5-(1-(4-(trifluoromethyl)phenyl)-1H-imidazol-5-yl)quinolin-8-yl)oxy) ethylidene) thiazolidine-2,4-dione (5)

Step 6 : 3-(Amino substituted methyl)-5-(2-((5-(1-(4-(trifluoromethyl)phenyl)-1H-imidazol-5-yl)quinolin-8-yl)oxy)ethylidene)thiazolidine-2,4-dione &7(a-f)

To a mixture of (Z)-5-(2-((5-(1-(4-(trifluoromethyl) phenyl)-1H-imidazol-5-yl)quinolin-8-yl)oxy)ethylidene) thiazolidine-2,4-dione (6) (500 mg,), 2o Amine (1.1 eq), Para formal dehyde (3 eq) in EtOH (50 mL) was added $Sc(OTf)_3$ (0.1 eq) and heated for 8 h. The progress of reaction was monitored by TLC. After completion, EtOH was evaporated under vaccum to give crude product. The crude was purified by reverse-phase column chromatography (C18 silica, Eluent: 30% ACN-MeOH-H_2O, 0.01% TFA) isolated (Z)-3-(Amino substituted methyl)-5-(2-((5-(1-(4-(trifluoromethyl)phenyl)-1H-imidazol-5-yl)quinolin-8-yl) oxy)ethylidene) thiazolidine-2,4-dione &7(a-f). 1H NMR spectra of 7(a-f) was given below Table 1 & Figure 13.

Table 1: 1H NMR spectra.

Comp	7a	7b	7c	7d	7e	7f
X	C=O	N-Me	N-Boc	N-Et	O	S

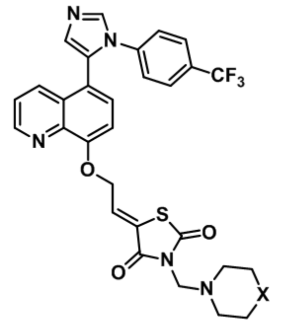

Figure 13: 3-(Amino substituted methyl)-5-(2-((5-(1-(4-(trifluoromethyl)phenyl)-1H-imidazol-5-yl)quinolin-8-yl)oxy) ethylidene)thiazolidine-2,4-dione &7(a-f)

a) 3-((4-oxopiperidin-1-yl)methyl)-5-(2-((5-(1-(4-(trifluoromethyl)phenyl)-1H-imidazol-5-yl)quinolin-8-yl) oxy)ethylidene)thiazolidine-2,4-dione (7a): M.p. 280-283 °C. IR (KBr, cm–1): 3050, 3010, 1720, 1655, 1600, 1320,770, 620,.**^{1}HNMR (d_6-DMSO, 400 mHz) :** 2.4 (t, 4H), 2.8 (t, 4H), 4.65 (s, 2H,), 4. 68(dd,2H), 4.7 (dd,1H), 5.1(d, 2H), 6.8 (dd, 1H), 7.1 (m, 1H), 7.3 (d, 2H), 7.6 (m, 4H), 8.0 (d, 1H), 8.43 (d, 1H), 8.81(d, 1H). **^{13}CNMR (d_6-DMSO, 400 mHz) :** 45, 53, 65, 108, 120, 122, 124, 124.5, 131, 135, 139, 145,150,164, 173, 190.

b) 3-((4-methylpiperazin-1-yl)methyl)-5-(2-((5-(1-(4-(trifluoromethyl)phenyl)-1H-imidazol-5-yl)quinolin-8-yl) oxy)ethylidene)thiazolidine-2,4-dione (7b): M.p. 290-292 °C. IR (KBr, cm–1): 3350, 3050, 1660,1610, 1320,750, 625,**^{1}HNMR (d_6-DMSO, 400 mHz) :** 2.3 (s, 3H), 2.4 (d, 4H), 2.45 (d, 4H), 4.63 (s, 2H,), 4.66 (dd, 1H),4.67 (dd,1H), 6.81 (dd, 1H), 7.1 (m, 2H), 7.32 (d, 2H), 7.6 (m, 4H), 8.03 (d, 1H), 8.44 (d, 1H), 8.81(d, 1H). **C-NMR (d_6-DMSO, 400 mHz) :** 47, 53, 58, 65, 107, 121, 122, 124, 124.5, 127, 130, 134, 138, 145,150,163, 174.

c) tert-butyl4-((2,4-dioxo-5-(2-((5-(1-(4-(trifluoromethyl)phenyl)-1H-imidazol-5-yl)quinolin-8-yl) oxy)ethylidene)thiazolidin-3-yl)methyl)piperazine-1-carboxylate (7c): M.p. 260-2262 °C. IR (KBr, cm–1): , 3014, 1713, 1650, 1620, 1505, 1310, 1050, 698, 655, **HNMR (d_6-DMSO, 400 mHz) :** 1.4 (s, 9H), 2.5 (t, 4H), 3.1(t, 4H), 2.45 (d, 4H), 4.5 (s, 2H,), 4.68 (dd, 1H),4.69 (dd,1H), 6.83 (dd, 1H), 7.1 (m, 2H), 7.32 (d, 2H), 7.62 (m, 4H),7.9 (d, 1H), 8.42 (d, 1H), 8.82(d, 1H). **^{13}C-NMR (d_6-DMSO, 400 mHz) :** 31, 44, 52, 65, 78, 107, 121, 124, 127, 130, 132, 139, 145,154,162, 174.

d) 3-((4-ethylpiperazin-1-yl)methyl)-5-(2-((5-(1-(4-(trifluoromethyl)phenyl)-1H-imidazol-5-yl)quinolin-8-yl) oxy)ethylidene)thiazolidine-2,4-dione (7d): M.p. 290-292 °C. IR (KBr, cm–1): 3350, 3020, 1680,1620, 1330,750, 625,**^{1}HNMR (d6-DMSO, 400 mHz) :** 1.2 (t, 3H), 2.5 (m, 10H), 4.5 (s, 2H,), 4.67(d, 1H), 4.68(d, 1H), 6.80 (dd, 1H), 7.1 (m, 2H), 7.3(d, 2H), 7.62 (m, 4H),7.8 (d, 1H), 8.42 (d, 1H), 8.82(d, 1H). **C-NMR (d_6-DMSO, 400 mHz) :** 14, 50, 53,58,65, 108, 122, 124, 125, 130, 132, 145,149,165, 174.

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e) 3-(morpholinomethyl)-5-(2-((5-(1-(4-(trifluoromethyl)phenyl)-1H-imidazol-5-yl)quinolin-8-yl)oxy)ethylidene)thiazolidine-2,4-dione (7e): M.p. 280-282 °C. IR (KBr, cm–1): 3016, 1720, 1650, 1503, 1300, 1050, 695, 650.^{1}**HNMR (d_6-DMSO, 400 mHz) :** 2.6 (t, 4H), 3.7 (t, 4H), 4.5 (s, 2H,), 4.68 (dd, 1H), 4.69 (dd,1H), 6.80 (dd, 1H), 7.15 (m, 2H), 7.25(d, 2H), 7.62 (m, 4H),7.9(d, 1H), 8.38 (d, 1H), 8.89(d, 1H). **C-NMR (d_6-DMSO, 400 mHz) :** 53,65, 66,107, 123, 124, 125, 130, 132, 139, 145,149,164, 178.

f) 3-(thiomorpholinomethyl)-5-(2-((5-(1-(4-(trifluoromethyl)phenyl)-1H-imidazol-5-yl)quinolin-8-yl)oxy)ethylidene)thiazolidine-2,4-dione (7f): M.p. 272-275 °C. IR (KBr, cm–1): 3080, 1730, 1645, 1520, 1310, 1125, 670, 660, ^{1}**HNMR (d_6-DMSO, 400 mHz) :** 2.6 (t, 4H), 2.8(t, 4H), 4.51 (s, 2H,), 4.66 (dd, 1H),4.67 (dd, 1H), 6.81 (dd, 1H), 7.15 (m, 2H), 7.25(d, 2H), 7.62 (m, 4H),7.9(d, 1H), 8.37 (d, 1H), 8.86(d, 1H). **C-NMR (d_6-DMSO, 400 mHz) :** 27,58,63, 106, 122,123, 124, 125, 130, 131, 135,139,145,149,164, 174.

Step 7: General procedure for -3-(sulfonyl derivative)-5-(2-((5-(1-(4-trifluoromethyl)phenyl)-1H-imidazol-5-yl)quinolin-8-yl)oxy)ethylidene)thiazolidine-2,4-dione (8a-f)

5-(2-((5-(1-(4-(trifluoromethyl)phenyl)-1H-imidazol-5-yl) quinolin-8-yl)oxy)ethylidene) thiazolidine-2,4-dione (500 mg, 1.08 mmol) in Dry DMF(5 mL) was added NaH (3 eq) at 0 °C under N_2 atm and stirred for 1h. To that sulfonyl chloride (1.1 eq) was added and stirred for 5h.The pogress of reaction was monitored by TLC. The reaction mixture was poured in aq sat $NaHCO_3$ and stirred for 15 min. The aq layer was extracted with 10% MeOH-$CHCl_3$ (3x 25 ml) and dried over anhydrous Na_2SO_4, filtered and evaporated under vaccum to gave crude product. The crude product was purified by Column chromatography (100-200 mesh silica) isolated 3-(sulfonyl derivative)-5-(2-((5-(1-(4-(trifluoromethyl) phenyl)-1H-imidazol-5-yl)quinolin-8-yl) oxy) ethylidene) thiazolidine-2,4-dione (8a-f) (Figure 14 and Table 2).

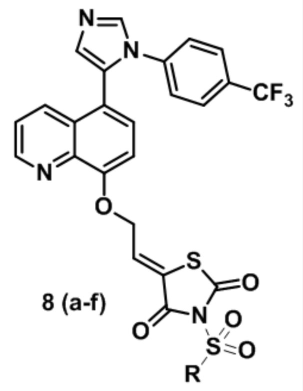

Figure 14: General procedure for -3-(sulfonyl derivative)-5-(2-((5-(1-(4-(trifluoromethyl)phenyl)-1H-imidazol-5-yl)quinolin-8-yl)oxy)ethylidene)thiazolidine-2,4-dione (8a-f).

Table 2:

Comp	**8a**	**8b**	**8c**	**8d**	**8e**	**8f**
R	Me	Et	P-Tolyl	4-Cl-C_6H_4	4-Br-`	4-NO_2-C_6H_4

i. 3-(methylsulfonyl)-5-(2-((5-(1-(4-(trifluoromethyl)phenyl)-1H-imidazol-5-yl)quinolin-8-yl)oxy)ethylidene)thiazolidine-2,4-dione(8a): M.p.280-283°C. IR (KBr, cm–1): 3040, 3025, 1730, 1645, 1600, 1320, 1070, 770, 715 620,.^{1}**HNMR (d^6-DMSO, 400 mHz) :** 2.8 (s, 3H), 4.67 (dd, 1H), 4.68 (dd,1H), 6.8 (dd, 1H), 7.1 (m, 2H), 7.3(d, 2H), 7.6 (m, 4H), 7.8 (d, 1H), 8.4 (d, 1H), 8.81(d, 1H). **CNMR (d^6-DMSO, 400 mHz) :** 42, 64, 106, 121, 122, 124, 124.5, 126,130, 135, 138,139, 145, 148, 164, 173.

ii. 3-(ethylsulfonyl)-5-(2-((5-(1-(4-(trifluoromethyl)phenyl)-1H-imidazol-5-yl)quinolin-8-yl)oxy)ethylidene)thiazolidine-2,4-dione(8b): M.p.:88-290 °C. **IR (KBr, cm–1):** 3040, 3025, 1730, 1645,1603, 1325, 1075,772,715 620,.^{1}**HNMR (d_6-DMSO, 400 mHz) :** 1.3 (t, 3H), 3.45 (q, 2H), 4.65 (dd, 1H),4.67 (dd,1H), 6.8 (dd, 1H), 7.13 (m, 2H), 7.32(d, 2H), 7.65 (m, 4H), 7.8 (d, 1H), 8.41 (d, 1H), 8.82(d, 1H). ^{13}**CNMR (d^6-DMSO, 400 mHz) :** 10, 52, 63, 106, 121, 122, 124, 124.5, 126,130, 135, 138,139, 145, 148, 164, 173.

iii. 3-tosyl-5-(2-((5-(1-(4-(trifluoromethyl)phenyl)-1H-imidazol-5-yl)quinolin-8-yl)oxy) ethylidene) thiazolidine-2,4-dione(8c): M.p. 300-302 °C. IR (KBr, cm–1): 3050, 3030, 1735, 1640,1603, 1325, 1075,770,715 620.^{1}**HNMR (d_6-DMSO, 400 mHz) :** 2.3 (s, 3H), 4.68 (dd, 1H), 4.69 (dd, 1H), 6.8 (dd, 1H), 7.13 (m, 2H), 7.32(d, 2H),7.4 (d, 2H), 7.65 (m, 4H),7.7 (d, 2H), 7.8 (d, 1H), 8.42 (d, 1H), 8.85(d, 1H). ^{13}**CNMR (d^6-DMSO, 400 mHz) :** 20, 64, 107, 121, 122, 123, 124, 124.5, 126,128, 130,132, 133 135, 138,139, 145, 148, 155, 165, 175.

iv. 3-((4-chlorophenyl)sulfonyl)-5-(2-((5-(1-(4-(trifluoromethyl)phenyl)-1H-imidazol-5-yl)quinolin-8-yl)oxy)ethylidene)thiazolidine-2,4-dione (8d): M.p. 290-292 °C. **IR (KBr, cm–1):** 3070, 3020, 1720, 1620,1530,1325, 1080,770,720, 655.^{1}**HNMR (d_6-DMSO, 400 mHz) :** 4.68(dd, H), 4.69 (dd, 1H), 6.85 (dd, 1H), 7.15 (m, 2H), 7.28(d, 2H),7.4(d, 2H), 7.63(m, 6H),7.8(d, 2H), 7.95(d, 1H), 8.5 (d, 1H), 8.87(d, 1H). ^{13}**CNMR (d_6-DMSO, 400 mHz) :** 64, 108, 121, 122, 123, 124, 124.5, 126,128, 130,132, 133 135, 139, 145, 149, 155, 162, 173.

v. 3-((4-bromophenyl)sulfonyl)-5-(2-((5-(1-(4-(trifluoromethyl)phenyl)-1H-imidazol-5-yl)quinolin-8-yl)oxy)ethylidene)thiazolidine-2,4-dione (8e): M.p. 298-300 °C. **IR (KBr, cm–1):** 3080, 3025, 1720, 1623,1530,1325, 1085,770,725, 655.^{1}**HNMR (d^6-DMSO, 400 mHz) :** 4.68(dd, 1H), 4.69 (dd,1H), 6.87 (dd, 1H), 7.18 (m, 2H), 7.28(d, 2H),7.6(m, 4H), 7.88(m, 5H), 8.4 (d, 1H), 8.8(d, 1H). ^{13}**CNMR (d^6-DMSO, 400 mHz):** 64.2, 107, 121, 122, 123, 124, 124.5, 126,128, 130,132, 134, 136, 139, 146, 149, 155, 163, 174.

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vi. 3-((4-nitrophenyl)sulfonyl)-5-(2-((5-(1-(4-(trifluoromethyl)phenyl)-1H-imidazol-5-yl)quinolin-8-yl)oxy)ethylidene)thiazolidine-2,4-dione(8f): M.p. 305-308 °C. **IR (KBr, cm–1):** 3070, 3028, 1720, 1623,1535, 1400, 1328, 1085,770,730, 655.^{1}**HNMR (d_6-DMSO, 400 mHz) :** 4.68(dd, 1H),4.6 9(dd, 1H), 6.87 (dd, 1H), 7.18 (m, 2H), 7.28(d, 2H),7.6(m, 4H), 7.8(d, 1H), 8.12 (d, 2H), 8.4 (m, 3H), 8.85(d, 1H). ^{13}**CNMR (d_6-DMSO, 400 mHz) :** 64.2, 107, 121, 122, 123, 124, 124.5, 126,128, 130,132, 134, 136, 139, 142, 146, 149, 151155, 164, 174.5.

Conclusion

In this research work we successfully synthesized and characterization, mannich bases of quinoline attached imidazoline thiozolidine 2,4-one derivatives . We are planning to these derivatives check for biological evolution. The biological evolution details will include next journal.

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