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Synthesis of a Novel products of 1, 3, 4 - Oxadiazole Contain in Thiozolid-4-one Derivatives

Ramakrishna Vellalacheruvu[1, 2]* R. Sai Leela[3] Dr L. K. Ravindranath[4],
[1]Department in Chemistry, S.K. University, Anantapur, Andhra Pradesh, India
[2]GVK Bio Science Pvt. Ltd., IDA, Nacharam, Secundrabad, Telangana, India
[3] S.K Universities. College of Pharmacy, Anantapur, Andrapradesh, India
[4]. Prof, S.K University, Chemistry department, Andhra Pradesh, India

Abstract:

8-(benzyloxy) quinoline-5-carbaldehyde **(1)** was converted into 2-(8-(benzyloxy) quinolin-5-yl)-3-(4-(trifluoro-methyl) phenyl) thiazolidin-4-one **(3)** by using conventional methods of schiff's base and cyclised using mercapto acetic acid and anhydrous $ZnCl_2$ in 1,4 Diaoxane. These intermediate (**3)** was converted to 2-((5-(4-oxo-3-(4-(trifluoromethyl) phenyl) thiazolidin-2-yl) quinolin-8-yl) oxy) acetohydrazide **(6)** by using hydrogenolysis and treated with Ethyl bromo acetate and hydrazine hydrate. The intermediate **(6)** was converted into thiozolidine attached 1,3,4 oxa diazole derivatives **(7a-h)** was synthesized using benzaldehyde analogs and I_2 / K_2CO_3 .and scaffolds were thoroughly characterized. The thiozoldine attached benzimidazole and benzthiozole, benzoxazole derivatives were synthesized using PPA and characterized.

Keywords: 1,3,4, Oxadiazole; Quinolines; Thiozolidine-4- One Nucleus; Dry $Zncl_2$; Dry Solvents;Combi-Flash Chromatography.

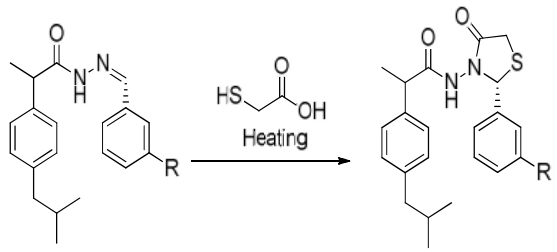
INTRODUCTION:

Quinoline ring attached heterocyclic drug candidates played a vital role in treating for human diagnosis diseases. Quinoline attached heterocyclic compounds act as a Anti Biotic activity such as leavofloxacin, moxiflaxacin, garenoxaicn etc. Quinoline derivatives shows vital diagnosis activity against Gram-negative, gram – positive and and anerobic bacteria. These drugs used for urinary infections and sexually transmitted diseases and prostatis. Thiozolidine 4-one and 1,3,4 oxadiazole condensed hetero cyclic compounds shows antimicrobial activity and using for type II Diabetic receptor drugs. By keeping attention of pharmaco dynamic activity of quionline condensed thiozolidine- 4-one derivatives, we were synthesized Quinoline containing thiozolidine -4-one, 1, 34 oxadiazole derivatives process was developed and characterized. Many research chemists has been focused on synthesis of thiozolidine-4-one derivatives because of their biological interest.

Thiazolidine-4-one moiety is a heterocycle that has received more attention in the last years due its important biological properties. Many effects have been found, including anti-inflammatoryand analgesic, antitubercular, antimicrobial and antifungal, antiviral, especially as anti-HIV agents, anticancer, antioxidants, anticonvulsants and antidiabetic activity.

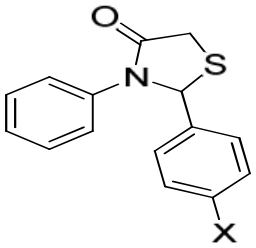
Ioana Mirela vasincu at al [1] and co- workers synthesized 1, 3-Thiazolidine-4-one.

Derivatives of 2-(4-Isobutylphenyl) propionic Acid. (Ibruprofen derivatives) and tested their biological evolution. The favorable influence of thiazolidin-4-one scaffolds shows greater antioxidant potential.



Anti oxident pottential tagets

Tribhuvan Singh* at al [13] synthesize and biological evolution of thiozolidine 4-one derivatives. These compounds show anti bacterial analogies.



Anti bacterial activity nature

On keeping the biological importance, in this research work we gave priority in synthesis thiozolidine-4-one derivatives

MATERIALS AND METHODES:

All reagents were procured from commercial sources and all solvents were thoroughly dried before use. The new compounds were fully characterized. The melting points were recorded using on a WRS-1A or a WRS-1B Digital Melting Point Apparatus without correction. Infrared spectra were taken using an AVATAR 370 FT-IR spectrometer. ^{1}HNMR, ^{13}CNMR spectra were recorded with a Bruker spectrometer operating at 400MHz used as a Trimethyl silane reference and values recorded in ppm. Mass spectra and high resolution mass spectra were recorded with an (Agilent) Electron impact (EI) ESI) techniques. 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.

Objective of this research:

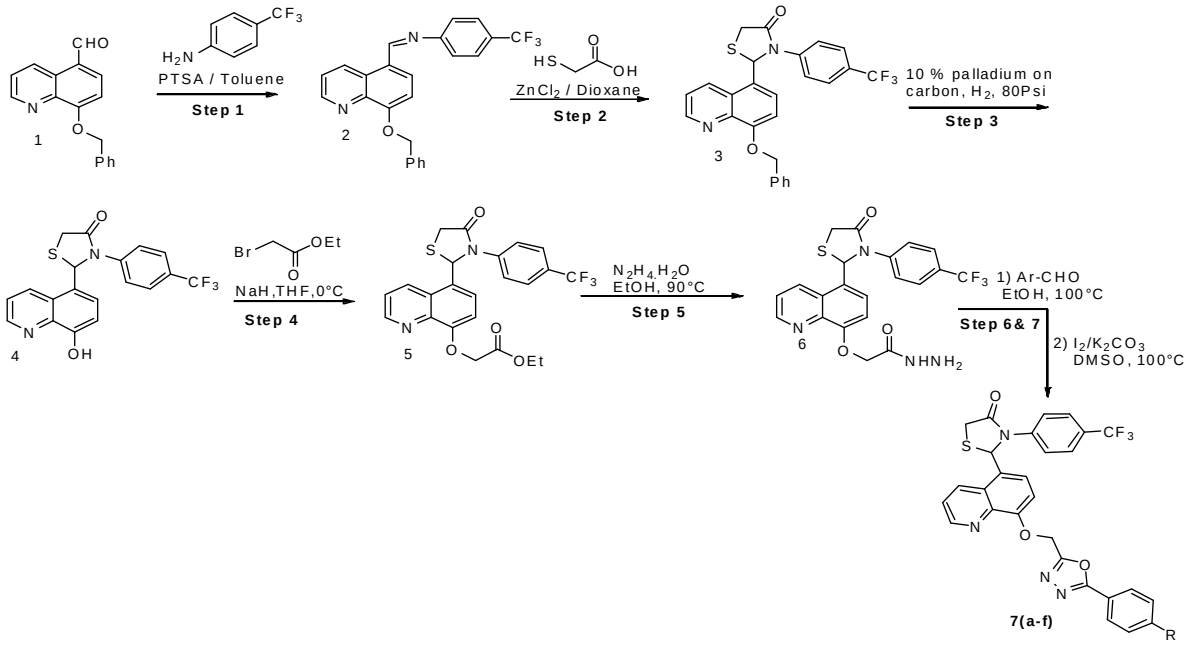
Present work is related to develop new synthetic route for preparation of the quinoline containing thiozolidin-4-one attached 1,3, 4 oxa diazole nucleus and thiazolidin-4-one attached benz imidazole and benz thiozole and benzoxazole derivatives and thoroughly characterized. The scaffolds of 2-(8-((5-(4-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

EXPERIMENTAL METHODS

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

- **Step-1:** (Z)-N-((8-(benzyloxy)quinolin-5-yl)methylene)-4-(trifluoromethyl)aniline **(2)**
- **Step-2** 2-(8-(benzyloxy) quinolin-5-yl)-3-(4-(trifluoromethyl) phenyl) thiazolidin-4-one **(3)**.
- **Step-3:** 2-(8-hydroxyquinolin-5-yl)-3-(4-(trifluoromethyl) phenyl) thiazolidin-4-one **(4).**
- **Step-4:** 2-((5-(4-oxo-3-(4-(trifluoromethyl) phenyl) thiazolidin-2-yl) quinolin-8-yl) oxy) acetate **(5).**
- **Step-5:** 2-((5-(4-oxo-3-(4-(trifluoromethyl) phenyl) thiazolidin-2-yl) quinolin-8-yl) oxy) acetohydrazide **(6).**
- **Step-6&7:** 2-(8-((5-(4- substituted phenyl)-1, 3, 4-oxadiazol-2-yl) methoxy) quinolin-5-yl)-3-(4-(trifluoromethyl) phenyl) thiazolidin-4-one **(7a-f).**
- **Step 8:** 2-(8-((1H-benzo[d]imidazol-2-yl) methoxy) quinolin-5-yl)-3-(4-(trifluoromethyl) phenyl) thiazolidin-4-one **(8).**
- **Step 9:** 2-(8-(benzo[d]oxazol-2-ylmethoxy) quinolin-5-yl)-3-(4-(trifluoromethyl) phenyl) thiazolidin-4-one **(9).**
- **Step 10:** 2-(8-(benzo[d]thiazol-2-ylmethoxy) quinolin-5-yl)-3-(4-(trifluoromethyl) phenyl) thiazolidin-4-one **(10).**

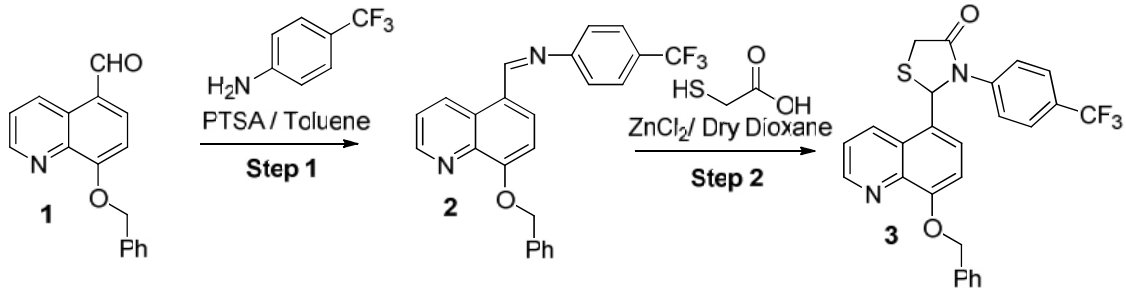
Scheme 1:



Reaction conditions: Step 1 : PTSA, toluene, 110 °C, Dean-stark condenser, 10 h, **Step 2:** Mercapto acetic acid, $ZnCl_2$/1,4 Dioxane, 80°C, 8 h, **Step 3:** 10% palladium on carbon, H_2, 80Psi **Step 4** : NaH/DMF, Ethyl bromo acetate, 0°C, **Step 5:** $N_2H_4.H_2O$, EtOH, Reflux , **Step 6 &7:** 1) Ar-CHO, EtOH, 100 °C, 2) I_2 (1.5 eq), K_2CO_3 (3 eq) DMSO, 100 °C, **Step 8, 9& 10:** PPA, 120 °C, 6 h.

Experimental Procedure:

Step 1 & 2: 2-(8-(benzyloxy) quinolin-5-yl)-3-(4-(trifluoromethyl) phen yl) thiazolidin-4-one (3):



Step 1:

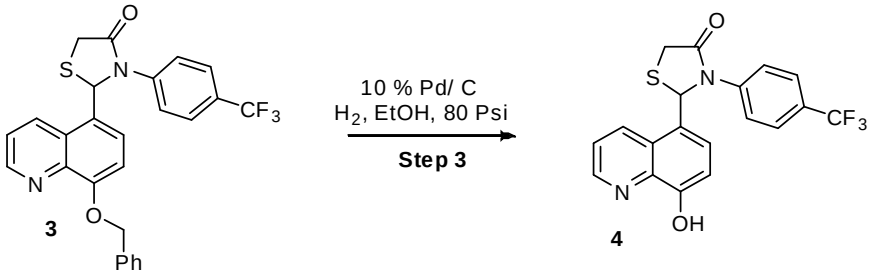
8-(benzyloxy)quinoline-5-carbaldehyde (10 g, 0.038 mol), 4-(trifluoromethyl) aniline (6.5 g, 0.039 mol) in dry toluene (100 mL) was added para-toluene sulfonic acid (1 g, cat) and refluxed under dean- stark condenser (removing water) for 10 h. The progress of reaction was monitored by TLC. After consumption of starting material, toluene was evaporated under vacuum to gave crude residue of compound- 2 (15 g). The crude was carried to next step.

Step 2:

A mixture of Schiff's base (15g) was dissolve in dry 1,4 Dioxane (150 mL) and cooled to 0 °C. Anhydrous zinc chloride () was added portion wise and stirred for 10 min. A solution of Mercapto acetic acid (3.5 g, 0.038 mol) in 1, 4 Dioxane (25 mL) was added drop wise with dropping funnel under argon atm. The reaction mixture was heated at 80 °C for 8 hrs. The pogress of reaction was monitored by TLC. After completion, reaction mixture was cooled to room temperature and poured in ice cold water (100 mL) and stirred for 10 min to get solid suspension. The obtained solid was filtered and and dried under vacuum. The solid was dissolve in EtOH (100 mL) and heated at 100 °C for 1h and left to room temperature. The obtained crystals were collected in Buchner-funnel and dried to get 2-(8-(benzyloxy) quinolin-5-yl)-3-(4-(trifluoromethyl) phenyl) thiazolidin-4-one (3) (10 g) as a solid (pale yellow colour). M.p. 185-188 °C. IR (KBr, cm–

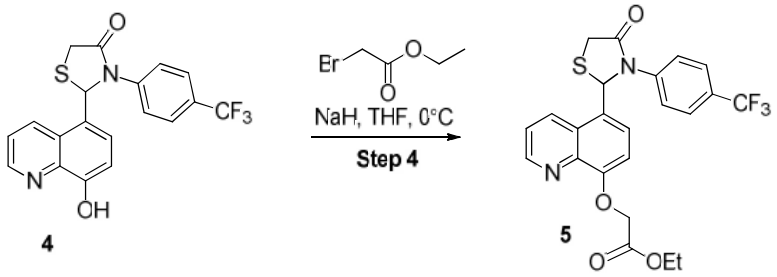
1): 3010, 3050, 1725, 1640, 1500, 1005, 691, 644. **^{1}HNMR (d_6-DMSO, 400 mHz) :** 3.87 (d, 1H), 3.95 (d, 1H,) 4.56 (s, 2H), 6.38 (s, 1H), 6.7-7.0 (m, 3H), 7.4-7.8 (m, 9H), 8.35(d, 1H), 8.9 (d, 1H).

Step 3: 2-(8-hydroxyquinolin-5-yl)-3-(4-(trifluoromethyl)phenyl)thiazolidin-4-one.



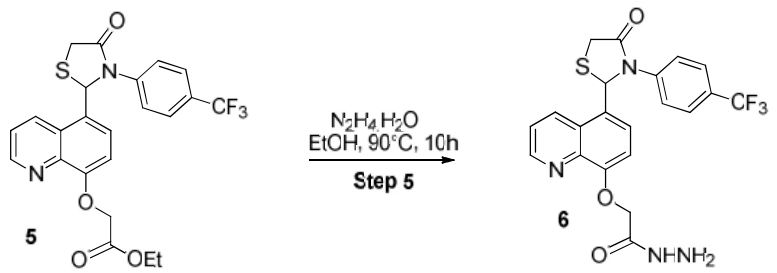
2-(8-(benzyloxy)quinolin-5-yl)-3-(4-(trifluoromethyl)phenyl) thiazolidin-4-one (3) (10 g, 0.02 mol) in EtOH (100 mL) was added 10% Palladium on carbon (2 g, cat) and hydrozinated at 80 Psi under parsheker for 8h at room temperature. The pogress of reaction was monitored by TLC. After completion, reaction mixture was filtered on cellite bed and thoroughly washed with EtOH (2 x 25 mL). The EtOH layer were collected and dried under vaccum to gave 2-(8-hydroxy quinolin-5-yl)-3-(4-(trifluoromethyl) phenyl) thiazolidin-4-one (4)(7g, yield : 86%) 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) :** 3.7 (d, 1H, 3.8 (d, 1H,), 6.15 (s, 1H), 6.8 (d, 2H), 7.1 (d, 1H), 7.2 (d, 1H), 7.6-7.7 (m, 3H), 8.3(d, 1H), 8.7 (d, 1H).

Step 4: ethyl 2-((5-(4-oxo-3-(4-(trifluoromethyl)phenyl)thiazolidin-2-yl)quinolin-8-yl)oxy)acetate (5):



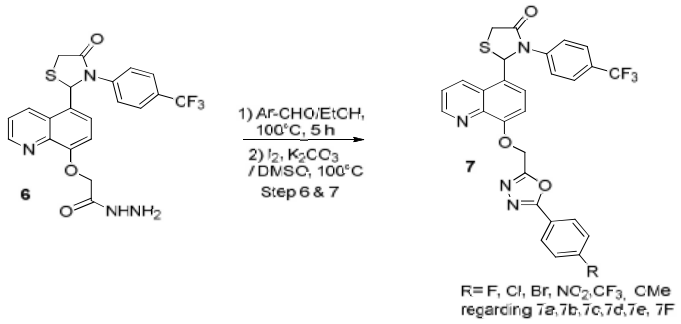
2-(8-hydroxyquinolin-5-yl)-3-(4-(trifluoromethyl)phenyl)thiazolidin-4-one (4) (7 g , 0.017 mol) was taken in dry THF (100 mL) and cooled to 0°C, then added sodium hydride (2.15g, 3 eq, 0.051 mol) portion wise and stirred for 10 min. A solution of 2-Bromo ethyl acetate (3.12 g, 0.0187 mol) in THF was added drop wise with dropping funnel under nitrogen atm and stirred for 5h. The progress of reaction was monitored by TLC. After collection, Reaction mixture was poured in ice cold water (100 mL) and basified with Aq sat $NaHCO_3$ solution up to P^H -8 and extracted with Ethyl acetate (3 x 100 mL). The organic layer were collected and washed with water (100 mL) and brine solution (100 mL).The EtOAc layer was collected and evaporated under vacuum using rota- vapour to gave 6 g of crude compound. The crude was purified by column chromatography (100-200 mesh silica, Eluent: 80% EtOAc-Pet ether) and isolated ethyl 2-((5-(4-oxo-3-(4-(trifluoromethyl)phenyl) thiazolidin-2-yl)quinolin-8-yl)oxy)acetate (5) (6.5 g yield : 74%) as a solid (milk white). M.p. 170-175°C. IR (KBr, cm–1): 3010 , 1735, 1610, 1520, 1050, 700, 654.**^{1}HNMR (DMSO, 400 mHz) :** 1.4 (t, 3H)**,** 3.7 (d, 1H,), 3.8 (d, 1H),4.2 (q, 2H), 5.1 (s, 2H), 6.2 (s, 1H), 6.8(m, 3H), 7.5-7.6 (m, 4H), 8.3(d, 1H, , 8.7 (d, 1H).

Step 5 : 2-((5-(4-oxo-3-(4-(trifluoromethyl)phenyl)thiazolidin-2-yl)quinolin-8-yl)oxy) acetohydrazide (6).



Ethyl 2-((5-(4-oxo-3-(4-(trifluoromethyl) phenyl) thiazolidin-2-yl) quinolin-8-yl) oxy) acetate (5) (6.5 g, 0.013 mol) in EtOH (70 mL) was cooled to 0°C. To that hydrazine hydrate (3 eq) was added and warm to room temperature. The reaction mixture was heated at 90°C for 10 h. The progress of reaction was monitored by TLC. After completion, reaction mixture was evaporated under vaccum to gave crude residue. The residue was co-distilled with EtOH (20 mL) and washed with water (50 mL) and filtered and dried to to gave 2-((5-(4-oxo-3-(4-(trifluoromethyl)phenyl) thiazolidin-2-yl)quinolin-8-yl)oxy)acetohydrazide **(6)**(5g, yield: 79%, white colour)) as a solid. M.p. 250-255°C. IR (KBr, cm–1): 3502 , 3400, 1740, 1650, 1520, 1050, 710, 690.**^{1}HNMR (d_6-DMSO, 400 mHz) :** 3.7 (d, 1H), 3.8 (d, 1H,), 5.1 (s, 2H,), 5.2 (br s, 2H), 6.2 (s, 1H,), 6.8(m, 3H), 7.5-7.6 (m, 4H),8.0 (brs, 1H), 8.3(d, 1H), 8. (d, 1H).

Step 6 &7 : 2-(8-((5-(4-substituted-phenyl)1,3,4-oxadiazol-2-yl)methoxy)quinolin-5-yl)-3-(4-(trifluoromethyl) phenyl)thiazolidin-4-one (7a-f):

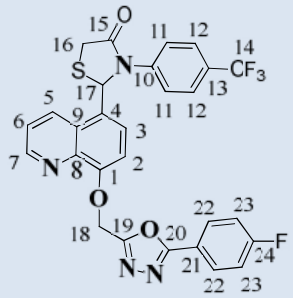
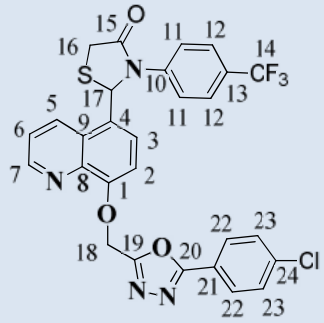


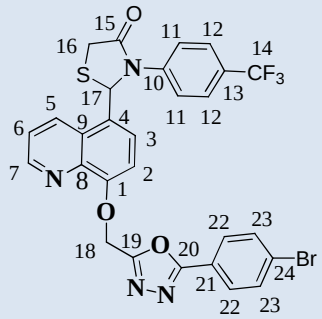
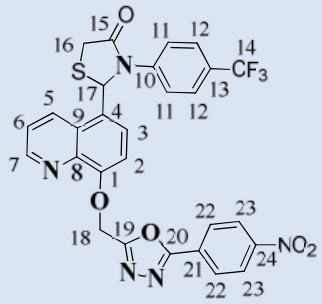
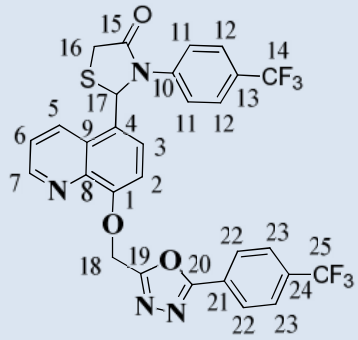
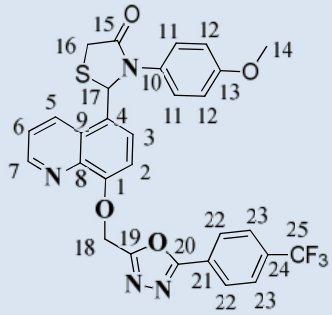
2-((5-(4-oxo-3-(4-(trifluoromethyl)phenyl)thiazolidin-2-yl)quinolin-8-yl)oxy) acetohydrazide (6) (500 mg, 1.08 mmol) in EtOH (10 mL)was added 4- fluoro benzaldehyde (134 mg, 1.08 mmol)and heated at 80°C for 5h. The pogress of reaction was monitored by TLC. After completion, reaction mixture was evaporated under vaccum to gave crude product. The crude was dissolve in Dry DMSO (10 mL) and cooled to 0°C. Then added dried K_2CO_3 (436 mg, 3.28 mmol) and iodine (163 mg, 1.29 mmol) and warm to room temperature. The reaction mixture was heated at 100°C for 10 h. The progress of reaction was monitored by TLC. The reaction mixture was cooled to room temperature and poured in ice cold water (30 mL). The reaction mixture was basified with sat aq $NaHCO_3$ solution and and extracted with 10% MeOH-$CHCl_3$ (3 x 25 mL). The organic layer were collected and washed with brine and dried over anhydrous Na_2SO_4, filtered and evaporated under vacuum to gave crude residue. The residue was purified by Combi-flash chromatography (230-400 mesh silica) isolated 2-(8-((5-(4-fluorophenyl)-1, 3, 4-oxadiazol-2-yl) methoxy) quinolin-5-yl)-3-(4-(trifluoromethyl) phenyl) thiazolidin-4-one (7a) (300 mg, Yield: 49%). The fallowing scaffold reaction time and melting point details and yield was mentioned in Table-1.

Table -1 : The fallowing scaffolds were synthesized using same protocol.

S.NO	R = substituent	Time	Yield	Melting point	Colour
7a	F	6h	55%	220-225°C	White
7b	Cl	8h	50%	210-215°C	Pale pink
7c	Br	4 h	60%	212-215°C	reddish
7d	NO_2	8 h	30%	230-233°C	Yellow
7e	CF_3	10 h	40%	210-215°C	white
7f	OMe	3h	60%	200-205°C	Milk white

Table-2: The ^{1}HNMR of scaffolds was recorded in 400 mHz Bruckner instrument was mentioned below.	
Comp	**^{1}HNMR (DMSO-d_6) (δ ppm)**
7a	3.87 (d, 1H), 3.99 (d, 1H), 5.21 (s, 2H), 6.44 (s, 1H), 6.8-6.9 (m, 3H), 7.3-7.45 (m, 3H), 7.6-7.7 (m, 3H), 8.3 (dd, 2H), 8.5 (d, 1H), 8.85 (d, 1H).
7b	3.88 (d, 1H), 3.99 (d, 1H), 5.21(s, 2H), 6.44 (s, 1H), 6.85 (m, 3H), 7.4-7.7 (m, 8H), 8.51 (d, 1H), 8.85 (d, 1H).
7c	3.88(d, 1H,-CH_2 of Thiazolidinone),3.99(d, 1H, -CH_2 of Thiazolidinone), 5.23(s, 2H, -O-CH_2), 6.44(s, 1H,-CH of Thiazolidin attached to phenyl ring), 6.85-6.9 (m, 3H), 7.4-7.7 (m, 8H), 8.51 (d, 1H), 8.85 (d, 1H, quinoline ring).
7d	3.88(d, 1H,-CH_2 of Thiazolidinone),3.99(d, 1H, -CH_2 of Thiazolidinone), 5.23(s, 2H, -O-CH_2), 6.44(s, 1H,-CH of Thiazolidin attached to phenyl ring), 6.85-6.9 (m, 3H), 7.4-7.8 (m, 4H), 8.2-8.4 (m, 5H), 8.86 (d, 1H, quinoline ring).
7e	3.88(d, 1H,-CH_2 of Thiazolidinone),3.99(d, 1H, -CH_2 of Thiazolidinone), 5.23(s, 2H, -O-CH_2), 6.44(s, 1H,-CH of Thiazolidin attached to phenyl ring), 6.85-6.9 (m, 3H), 7.4-7.8 (m, 6H), 8.1 (d, 2H),8.4 (d, 1H), 8.87 (d, 1H, quinoline ring).
7f	3.88(d, 1H,-CH_2 of Thiazolidinone),3.99(d, 1H, -CH_2 of Thiazolidinone), 4.2 (s, 3H, -O-Me), 5.23(s, 2H, -O-CH_2), 6.44(s, 1H,-CH of Thiazolidin attached to phenyl ring), 6.85-6.9 (m, 3H), 7.4-7.8 (m, 6H), 8.1 (d, 2H),8.4 (d, 1H), 8.87 (d, 1H, quinoline ring).

Table–3: ^{13}C NMR spectral data of 2-(8-((5-(4-substitutedphenyl)-1,3,4-oxadiazol-2-yl) methoxy) quinolin-5-yl)-3-(4-(trifluoromethyl) phenyl)thiazolidin-4-one (7a-f).		
Table	**2: The ^{1}HNMR of scaffolds was recorded in 400 mHz Bruckner instrument was mentioned below.**	**Table**
7a		**146,107,116,133,130,121,139,142,129,126, 171,33,74,72,163,165,162 and the signals are ascribed to C1&7,C2,C3&23,C4,C5,C6,9&21,C8, C10,C11,12,13,14&22,C12,C15,C16,C17,C18,C19,C20and C24 respectively.**
7b		**147,107,116,133,130,120,139,142,129,125,171,33,74,72,163,165 ,135 and the signals are ascribed to C1&7,C2,C3,C4,C5,C6&9,C7,C8,C10,C11&13,22&23,C12,14 &21,C15,C16,C17,C18,C19,C20 and C24, respectively.**

7c		**146,107,116,133,130,121,139,142,129,126,171,33, 74,72,163,165,125,132,123 and the signals are ascribed to C1&7,C2,C3,C4,C5,C6&9,C8,C10,C11,13&22,C12&14,C15, C16,C17,C18, C19,C20,C21,C23, C24, and C25 respectively.**
7d		**146,107,116,133,130,120,139,142,129,125,171,33,74,72,163,165 ,132,131,147 and the signals are ascribed to C1&7,C2,C3, C4, C5,C6&9,C7,C8,C9,C10,C11,13&23,C12&14,C15,C16,C17,C 18,C19,C20,C21,C22 and C24, respectively**
7e		**146,107,116,133,130,120,139,142,** **129,126,171,33,74,72,163,165,128,131 and the signals are ascribed to C1&7,C2,C3, C4, C5,C6 & 9,C8,C10, C11&13,C12,14,23&25,C15,C16,C17, C18,C19,C20, C21, C22 and C24 respectively.**
7f		**146,107,116,133,130,120,139,142,** **114,120,171,33,74,74,163,168,128, 75 and the signals are ascribed to C1&7,C2,C3, C4, C5,C6 & 9,C8,C10, C11&13,C12,14,23&25,C15,C16,C17, C18,C19,C20, C21, C22 and C24 respectively.**

IR Spectra

The IR (KBr) spectra of 2-(8-((5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl)methoxy)quinolin-5-yl)-3-phenylthiazolidin-4-one **(7a)** exhibitedcharacteristic bands around 3190 (-NH-str), 3048(Ar-H str), 1698 (-C=O), 1613(-C=N), 1188 (-C-S), 1160(C-O-C), 1145(N-N) supports thestructural formation of 7a. The IR data of (7a-f) were shown in the **table 4**.

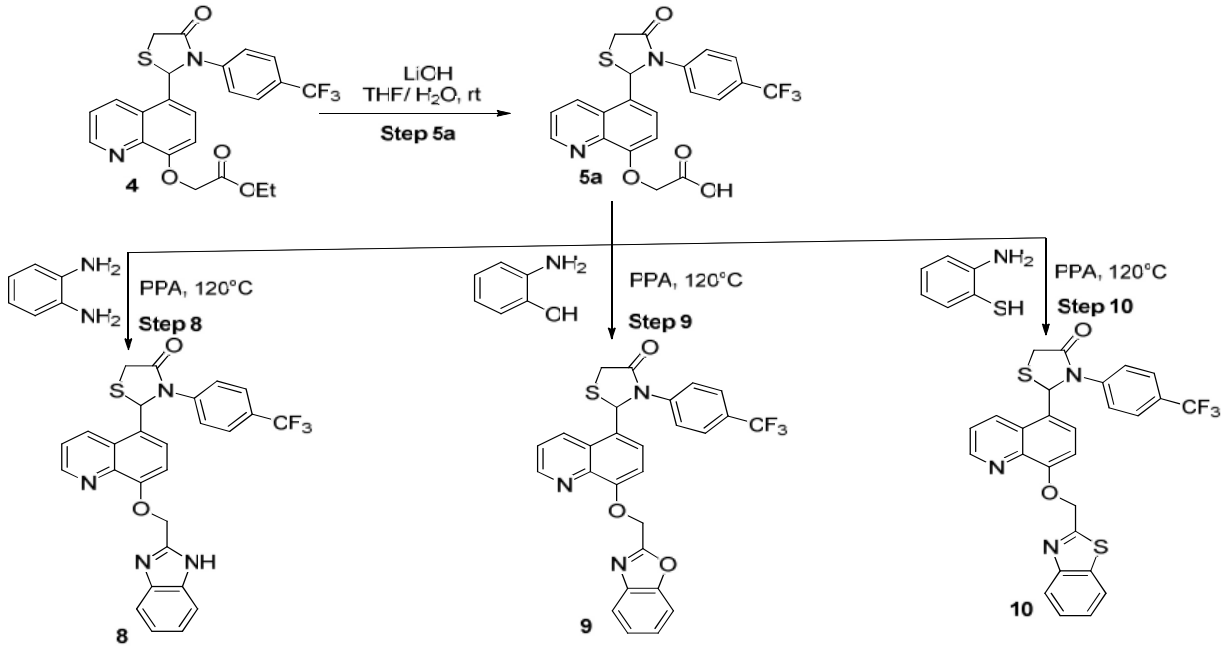
Table 4.

Co	R	*v*max in cm^{-1}					
		Ar-H	C=O	C=N	C-S	C-O-C	N-N
7a	F	3048	1698	1613	1188	1160	1145
7b	Cl	3045	1696	1614	1179	1164	1147
7c	Br	3046	1697	1619	1166	1162	1141
7d	NO_2	3042	1692	1612	1179	1158	1145
7e	CF_3	3040	1694	1610	1178	1166	1147
7f	OMe	3010	1610	1600	1170	1160	1138

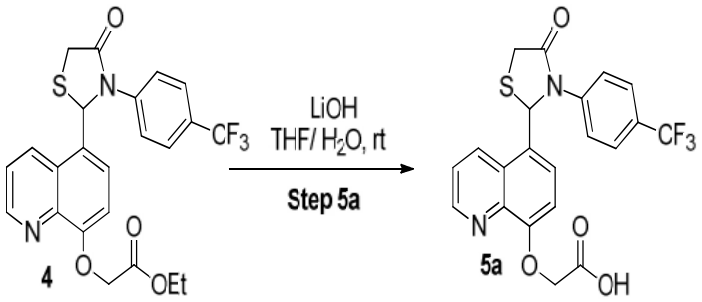
Table– 5: The primary fragmented mass spectral data of 2-(8-((5-(4-fluorophenyl)-1,3,4-oxadiazol-2-yl)methoxy)quinolin-5-yl)-3-phenylthiazolidin-4-one (7a).

Molecular Ion	**Lost free radical**	**Primary fragmented ion**	**m/z**	**Intensity %**
C28H18F4N3 M^+ : 566.10	$C6H4F^{\bullet}$	$C22H14F3N4O3S^+$ (A)	471.07	15.1
	$C7H4F3^{\bullet}$	$C21H14FN4O3S^+$ (B)	421.08	18.9
	$C8H4FN2O^{\bullet}$	$C20H14F3N2O2S^+$(C)	403.07	11.2
	$C9H6FN2O^{\bullet}$	$C19H12F3N2O2S^+$ (D)	389.06	84.4
	$C10H7F3NOS^{\bullet}$	$C18H11FN3O2^+$(E)	320.08	100
	$C18H11FN3O2^{\bullet}$	$C10H7F3NOS^+$ (F)	246.02	55.1
	$C19H11ClF3N2O2^{\bullet}$	$C9H6FN2O^+$ (G)	177.04	9.9
	$C20H14F3N2O2S^{\bullet}$	$C8H4FN2O^+$ (H)	163.03	12.8
	$C21H13FN4O3S^{\bullet}$	$C7H4F3^+$ (I)	145.02	25.4
	$C22H14F3N4O3S^{\bullet}$	$C6H4F^+$ (J)	95.03	23.3

Scheme-2:

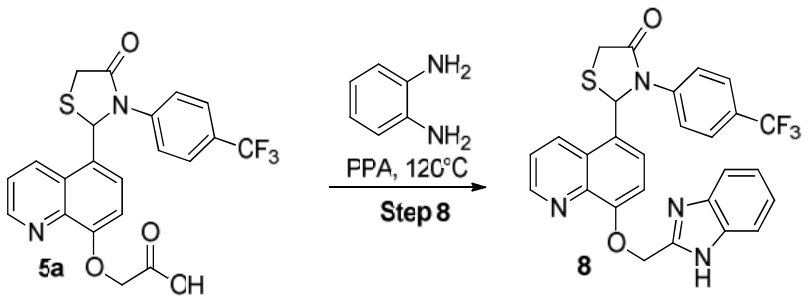


Step 5A: 2-((5-(4-oxo-3-(4-(trifluoromethyl) phenyl) thiazolidin-2-yl) quinolin-8-yl) oxy) acetic acid (5a):

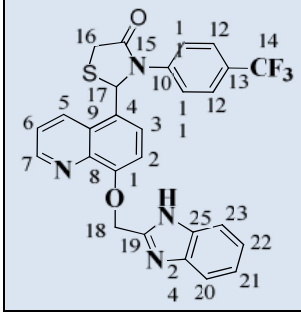


Ethyl 2-((5-(4-oxo-3-(4-(trifluoromethyl) phenyl) thiazolidin-2-yl) quinolin-8-yl) oxy) acetate (3 g, 6.3 mmol) in THF / H_2O (30 ml/10 mL) was added LiOH (600mg, 24 mmol) and stirred at room temperature for 10 h. The progress of reaction was monitored by TLC. After completion, reaction mixture was poured in ice cold water (100 mL) and acidified with saturated sodium by sulphate upto P^{H-} 4 and extracted with 10% MeOH-$CHCl_3$ (3 x 25 mL). The organic layer were collected and and washed with brine (30 mL), and dried over anhydrous Na_2SO_4, filtered and evaporated under vacuum to gave 2.8 g of crude product. The crude was purified by Combi-flash chromatography (230-400 mesh silica, Eluent : 6% MeOH-$CHCl_3$) isolated 2-((5-(4-oxo-3-(4-(trifluoromethyl)phenyl)thiazolidin-2-yl)quinolin-8-yl)oxy)acetic acid (5a) (2g, 71%) as a white colour solid. M.p. 250-253 °C. IR (KBr, cm–1): 3500, 3010 , 1735, 1655, 1610, 1520, 1050, 700, 654.**^{1}HNMR (DMSO, 400 mHz) :** 3.75 (d, 1H,), 3.8 (d, 1H), 4.8 (s, 2H), 6.3(s, 1H), 6.8 (m, 3H), 7.5 (d, 1H), 7.6-7.7 (m, 3H), 8.5(d, 1H), 8.8 (d, 1H).

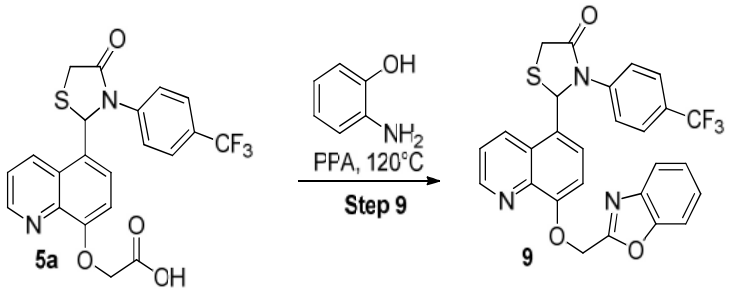
Step8: 2-(8-((1H-benzo[d]imidazol-2-yl) methoxy) quinolin-5-yl)-3-(4-(trifluoromethyl) phenyl) thiazolidin -4-one (8):



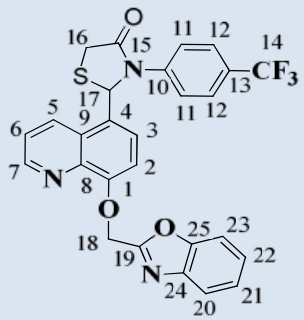
To a mixture of 2-((5-(4-oxo-3-(4-(trifluoromethyl)phenyl)thiazolidin-2-yl)quinolin-8-yl)oxy)acetic acid (5a) (500 mg, 1.1 mmol), benzene-1,2-diamine (120 mg, 1.1 mmol) was added poly phosphoric acid (500 mg) and thoroughly mix up and heated at 120°C for 10h. The progress of reaction was monitored by TLC. After completion, reaction mixture was poured in ice cold water (100 mL) and basified with saturated sodium bicarbonate up to P^{H-} 8 and extracted with 10% MeOH-$CHCl_3$ (3 x 25 mL). The organic layer were collected and and washed with brine (30 mL), and dried over anhydrous Na_2SO_4, filtered and evaporated under vacuum to gave 1 g of crude product. The crude was purified by Combi-flash chromatography (230-400 mesh silica, Eluent: 10% MeOH-$CHCl_3$) isolated 2-(8-((1H-benzo[d]imidazol-2-yl) methoxy) quinolin-5-yl)-3-(4-(trifluoromethyl) phenyl) thiazolidin-4-one **(8)** (400 mg, 71%) as a pale white solid. M.p. 205-208°C. IR (KBr, cm–1): 3200, 3010 , 1735, 1610, 1520, 1150, 700, .**^{1}HNMR (DMSO- d_6, 400 mHz) :** 3.9 (d, 1H,), 3.85 (d, 1H), 5.2(s, 2H), 6.3 (s, 1H), 6.5 (brs, 1H), 6.8(m, 3H), 7.3 (d, 2H), 7.41 (d, 1H), 7.5-7.7 (m, 5H), 8.5(d, 1H) , 8.82 (d, 1H).

Comp	^{13}CNMR (DMSO-d_6) (δ ppm)
	146,107,116,133,130,120,139,142,129,171,33,75,72,141 and these signals are ascribed to C1&7,C2,C3,20&23,C4,C5,C6&9,C8,24&25,C10,C11,12,13,14,21&22,C 15,C16,C17,C18,C19 respectively.

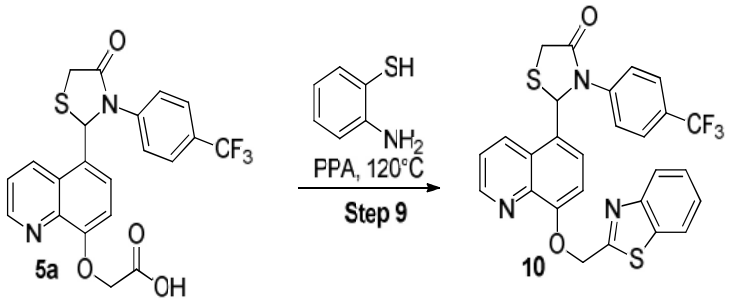
Step 9: 2-(8-(benzo[d]oxazol-2-ylmethoxy)quinolin-5-yl)-3-(4-(trifluoromethyl)phenyl) thiazolidin-4-one (9):



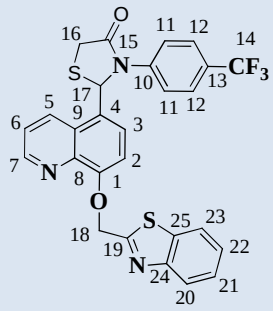
To a mixture of 2-((5-(4-oxo-3-(4-(trifluoromethyl)phenyl)thiazolidin-2-yl)quinolin-8-yl)oxy)acetic acid (5a) (500 mg, 1.1 mmol), 2-Amino phenol (120 mg, 1.1 mmol) was added poly phosphoric acid (500 mg) and thoroughly mix up and heated at 120°C for 10 h. The progress of reaction was monitored by TLC. After completion, reaction mixture was poured in ice cold water (100 mL) and basified with saturated sodium bicarbonate up to P^{H-} 8 and extracted with 10% MeOH-$CHCl_3$ (3 x 25 mL). The organic layer were collected and and washed with brine (30 mL), and dried over anhydrous Na_2SO_4, filtered and evaporated under vacuum to gave 800mg of crude product. The crude was purified by Combi-flash chromatography (230-400 mesh silica, Eluent: 8 % MeOH-$CHCl_3$) isolated 2-(8-(benzo[d]oxazol-2-ylmethoxy) quinolin-5-yl)-3-(4-(trifluoromethyl) phenyl) thiazolidin-4-one (9) (300 mg, 51%) as a white solid. M.p. 195-198°C. IR (KBr, cm–1): 3200, 3010 , 1735, 1610, 1520, 1150, 700, .**^{1}HNMR (DMSO, 400 mHz) :** 3.9 (d, 1H,), 3.85 (d, 1H), 5.2 (s, 2H), 6.35 (s, 1H), 6.8 (m, 3H), 7.3-7.8 (m, 8H), 8.5(d, 1H, , 8.8 (d, 1H).

Comp	^{13}CNMR ($CDCl_3$) (δ ppm)
	146,107,116,133,130,120,139,142,129,171,33,75,72,141 and these signals are ascribed to 1&7,C_2,$C_{3,20\&23}$,C_4,C_5,$C_{6\&9}$,$C_{8,24\&25}$,$C_{10,}C_{11,12,13,14,21\&22}$,$C_{15,}C_{16}$,$C_{17}$,$C_{18,}C_{19}$ respectively.

Step 10: 2-(8-(benzo[d]thiazol-2-ylmethoxy)quinolin-5-yl)-3-(4-(trifluoromethyl)phenyl) thiazolidin-4-one (10):



To a mixture of 2-((5-(4-oxo-3-(4-(trifluoromethyl)phenyl)thiazolidin-2-yl)quinolin-8-yl)oxy)acetic acid (5a) (500 mg, 1.1 mmol), 2-aminobenzenethiol(120 mg, 1.1 mmol) was added poly phosphoric acid (500 mg) and thoroughly mix up and heated at 120°C for 12 h. The progress of reaction was monitored by TLC. After completion, reaction mixture was poured in ice cold water (100 mL) and basified with saturated sodium bicarbonate up to P^{H-} 8 and extracted with 10% MeOH-$CHCl_3$ (3 x 30 mL). The organic layer were collected and and washed with brine (30 mL), and dried over anhydrous Na_2SO_4, filtered and evaporated under vacuum to gave 1g of crude product. The crude was purified by Combi-flash chromatography (230-400 mesh silica, Eluent: 12 % MeOH-$CHCl_3$) isolated 2-(8-(benzo[d]thiazol-2-ylmethoxy) quinolin-5-yl)-3-(4-(trifluoromethyl) phenyl) thiazolidin-4-one (10) (400 mg, 66 %) as a solid. M.p. 198-200 °C. IR (KBr, cm–1): 3200, 3010 , 1735, 1610, 1520, 1150, 700, .**^{1}HNMR (DMSO-d_6 400 mHz) :** 3.95 (d, 1H,), 3.88 (d, 1H), 5.18 (s, 2H), 6.4 (s, 1H), 6.8-6.9 (m, 3H), 7.5-7.7 (m, 5H), 8.0 (d, 1H), 8.3(d, 1H), 8.46 (d, 1H, , 8.8 (d, 1H).

Comp	^{13}CNMR (DMSO-d_6) (δ ppm)
	146,107,116,133,130,119,139,122,142,129,125,171,33,75,67,168,121,152 ,135 and these signals are ascribed toC1&7,C2,C3,C4,C5,C6,C8,C9,C10,C11&13,C12,14,21&22,C15,C16,C 17,C18,C19,C20&23,C24,C25 respectively.

CONCLUSION

In this research work we successfully synthesized and characterized of quinoline containing thiozolidine 4-one attached 1, 3, 4 oxa diazole ring of benzoxazole, bezimidazole and Benz thiozole derivatives. We are planning to these derivatives check for biological evolution. The biological evolution details will include next journal.

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