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Synthesis and Characterization of Novel Thiazole Anchored Pyrazolyl Benzoxazoles

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ABSTRACT

3-Formylchromone 1 was treated with 1-(4-(4-bromophenyl)thiazol-2-yl)hydrazine 2 to get (1-(4-(4-bromophenyl)thiazol-2-yl)-1H-pyrazol-4-yl)(2-hydroxyphenyl)methanone --------(3a-e). Compound 3 on treatment with NH_2OH/HCl gavethe compound 2-[(*E*)-{1-[4-(4-bromophenyl)-1,3-thiazol-2-yl]-1*H*-pyrazol-4-yl}(hydroxyimino)methyl]phenol (4a-e). Compound 4 on treatment with $POCl_3$ gave 2-(1-(4-(4-bromophenyl)thiazol-2-yl)-1*H*-pyrazol-4-yl)benzo[*d*]oxazole (5a-e). The synthesized compounds have been characterized with the help of spectral techniques.

Key words: Benzo[d]oxazole, Thiazole, Pyrazole, 3-Formylchromone.

INTRODUCTION

Heterocyclic compounds are pharmacologically and medicinally very important because most of the drugs present in the market today are containing heterocyclic scaffolds. Benzoxazole derivatives exhibits anthelmintic[1], antiulcer[2], antitumor[3], antimicrobial[4,5] andanticancer[6] activities. Benzoxazole containing compounds are also acts as RSK2 inhibitor[7] and α_1-AR antagonist[8].

Thiazole scaffold containing compounds are associated with anti-inflammatory[9], cyclooxygenase-2 inhibitor[10], analgesic[11], monoamine oxidases[12] and immunosuppressive[13] activities. Pyrazole is one of the most important pharmacologically active heterocyclic compound. Pyrazole and its derivatives are associated with fungicidal[14], anti-angiogenic[15], antidiabetic[16], antiparasitic[17], antitubercular[18], antimicrobial[19] and antioxidant[19] activities.

3-Formylchromoneis one of the class of chromone family. Chromone derivatives are known to have acetylcholinesterase inhibitor[20],antitumor[21], breast cancer resistance protein ABCG2 inhibition[22]activities.

The various pharmacological activities associated with benzoxazole, thiazole and pyrazole prompted us to synthesizesome novel thiazole anchored pyrazolyl benzoxazole derivatives.

EXPERIMENTAL

(1-(4-(4-Bromophenyl)thiazol-2-yl)-1*H*-pyrazol-4-yl)(2-hydroxyphenyl)methanone 3a-e

3-Formylchromone **1** (0.012 mol) was dissolved in 25 mL of ethanol with thiazolyl hydrazine **2** (0.012 mol). The reaction mixture heated under reflux for 40 min to get corresponding hydrazone. To the same reaction mixture 1.2 g KOH in 10 mL H_2O was added and heating was continued for 4 hr. After completion of reaction the contents were cooled to room temperature and poured into crushed ice. The resulting solution was neutralized with conc. HCl. The solid obtained was separated by filtration and crystallized from ethanol to affordcompound **3**.

3a: IR (KBr):3085 (O-H), 1656 (C=O), 1612 (C=N), 1109 (Ar-Cl), 1218 (C-O) cm^{-1}; ^1H NMR (DMSO-d_6): δ 7.40-7.82 (m, 7H, Ar-H), 8.21 & 8.97 (s, 2H, Pyrazole), 12.40 (s, 1H, O-H); MS: *m/z*:[M^+] 493;Elem. Anal. Calcd.: C, 46.09; H, 2.04; N, 8.49; found: C, 46.12; H, 2.08; N, 8.53 %.

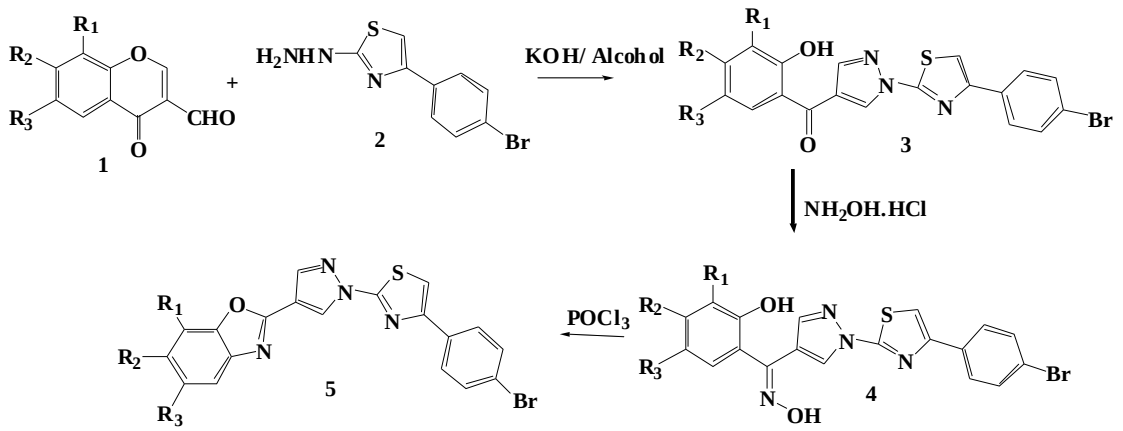
2-[(*E*)-{1-[4-(4-Bromophenyl)-1,3-thiazol-2-yl]-1*H*-pyrazol-4-yl}(hydroxyimino)methyl]phenol 4a-e

Compound **3** (0.055 mol) was dissolved in 20 mL of ethanol in 150 mL conical flask. To this 10 mL of 20% KOH was added with constant stirring at 4^{0}C, and to this hydroxylamine hydrochloride (1.1 mol) was added in portion wise. Further stirring was continued for 3-4 h at room temperature. Then reaction mixture was poured into crushed ice and acidified with acetic acid. The product obtained was separated by filtration and crystallized from ethanol to afford compound **4**.

4a: IR (KBr): 3185 (OH), 1630 (C=N), 1113 (Ar-Cl) cm^{-1}; ^1H NMR (DMSO-d_6): 7.27-7.97 (m, 7H, Ar-H), 8.05-8.89 (s, 2H, pyrazole), 9.90 (s, 1H, -OH of

Table 1: Characterization data of synthesized compounds

Compd	R1	R2	R3	M.P.(^{0}C)	Yield (%)
3a	Cl	H	Cl	202	69
3b	H	Me	Cl	248	64
3c	H	H	Cl	208	67
3d	H	H	Br	205	61
3e	H	H	Me	196	59
4a	Cl	H	Cl	256	57
4b	H	Me	Cl	254	60
4c	H	H	Cl	244	53
4d	H	H	Br	222	58
4e	H	H	Me	204	48
5a	Cl	H	Cl	268	51
5b	H	Me	Cl	290	57
5c	H	H	Cl	240	55
5d	H	H	Br	250	59
5e	H	H	Me	232	46



Scheme 1:

oxime), 11.97 (s,1H, Ar-OH); MS: *m/z*:[M+] 508;Elem. Anal. Calcd.: C, 44.73; H, 2.17; N, 10.98; found: C, 44.77; H, 2.21; N, 11.02 %.

2-(1-(4-(4-Bromophenyl)thiazol-2-yl)-1*H*-pyrazol-4-yl)benzo[*d*]oxazole 5a-e

Compound **4** (0.055 mol) were dissolved in 15 mL of $POCl_3$ in 50 mL RBF and the contents were heated under reflux for 2.5 h. After completion of reaction the contents were cooled to room temperature and poured into crushed ice, and neutralized by adding sodium acetate. The solid thus obtained was separated by filtration and crystallized from ethanol gave compound **5**.

5a

IR (KBr): 1586&1539 (C=N), 1239 (C-OC), 1114 (Ar-Cl) cm^{-1}; ^1H NMR (DMSO-d_6): δ 7.35-7.83 (m, 7H, Ar-H), 8.36&9.11 (s, 2H, Pyrazole); MS: *m/z*:[M+] 490;Elem. Anal. Calcd.: C, 46.37; H, 1.84; N, 11.38; found: C, 46.41; H, 1.88; N, 11.42 %.

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