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SYNTHESIS AND ANTIBACTERIAL SCREENING OF IMIDAZOLE ANCHORED PYRAZOLINES, BENZODIAZEPINES AND CHROMONES

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ABSTRACT
Imidazole anchored chalcones were converted into pyrazolines, benzodiazepines, chromones, chlorochromones and hydroxychromones. 3-*O*-alkylated-6-(4-fluorophenyl)chromones were synthesized from 3-*O*-alkylated-6-bromochromonesby Suzuki-Miyaura Reaction. Formation of the target compounds was confirmed by spectral tools like IR, ^{1}H NMR and mass spectrometry. The newly synthesized compounds were studied for their antibacterial potential using bacterial strains *Bacillus Subtilis* and *Escherichia Coli*.

KEYWORDS: Suzuki-Miyaura Reaction, pyrazolines, benzodiazepines, chromones, chlorochromones and hydroxychromones.

INTRODUCTION
Imidazole ring system is important biological building-block present in hormones such as histidine and the related hormone histamine. Many drugs contain an imidazole ring having antifungal[i], antibiotic[ii], anticancer[iii], andantiepilepsy[iv] properties. Some important marketed drugs which contain imidazole ring are Ketoconazole (antifungal), Miconazole (antifungal), Losartan (antihypertension) and Ondansetron (nausea).
Pyrazoline and imidazole are five membered heterocyclic compounds having high importance in synthetic chemistry due to their pharmacological activity and less toxicity. Pyrazolines have shown biological activities like antidepressant[v], anticonvulsant[vi], antimicrobial[vii], analgesic[viii] and anticancer[ix].
The importance of benzodiazepines has been increased in medicinal chemistry because of their wide range of biological activity, easily available raw material and high yield. In all benzodiazepines, 1,5-benzodiazepines and their derivatives are important because of their wide spectrum of biological and pharmacological activity. 1, 5-Benzodiazepines are known to have antimicrobial[x], antiHIV[xi] and antidepressive[xii] activities.

Chromones have shown biological activities such as anticancer[xiii], antibacterial[xiv], antiHIV[xv], antioxidant[xvi] and anti-inflammatory[xvii] activities. One of the prominent and medicinally most useful property of many chromones and their derivatives is their ability to scavenge free radicals[xviii]. The health promoting effects of chromones and their derivatives may make interactions with key enzymes, signaling cascade mechanism as involving cytokines and transcription factor[xix].

Literature survey shows that incorporation of halogen in heterocyclic compounds increases their activities. Several synthetic organic chemists have synthesized halogenated heterocycles and evaluated them for biological screening. Several commercially available drugs also contain chlorinated and fluorinated heterocyclic compounds such as Sitagliptin phosphate, Clotrimazole, Econazole and Fluoxetine.

Considering the biological importance of fluorine, chlorine and imidazole nucleus, it was planned to incorporate them in some heterocycles such as pyrazolines, benzodiazepines and chromones.

EXPERIMENTAL

Physical constants of all synthesized compounds were determined in open capillary tubes in liquid paraffin bath and are uncorrected. The IR spectra were recorded on Perkin Elmer spectrophotometer using potassium bromide discs. The NMR spectra were recorded on Varian NMR 400 MHz spectrometer (Varian Inc., Switzerland) and chemical shifts are given in δppm relative to TMS using deuterated DMSO and deuterated chloroform as solvents. Mass spectra were recorded on Water's Acquity Ultra Performance TQ Detector Mass Spectrometer.

Preparation of 2-(5-(1-((4-(2,2,2-trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-4,5-dihydro-1*H*-pyrazol-3-yl)phenol (2).

Chalcone**1**(1mmol) was dissolved in 10 mL ethanol in 50 mL round bottom flask. To this solution hydrazine hydrate (8 mmol) was added. Reaction mixture was stirred for 1h at 40^0C. Progress of reaction was monitored by TLC (10% Methanol + 80% Dichloromethane). After completion of reaction, contents were cooled to get solidified product. Then it was filtered and recrystallized from ethanol to afford pure compound**2**.The compounds synthesized by above experimental procedure are listed in Table **1**.

2-(5-(1-((4-(2,2,2-Trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-4,5-dihydro-1H-pyrazol-3-yl)phenol (2a). ir (KBr, cm^{-1}): 1120 (Ar-Cl), 1260(-CF_3), 1465&1588 (C=C), 1635 (C=N); ^{1}H nmr(DMSO-d_6), δ: 0.78 (t, J= 7.6 Hz, 3H, -CH_3), 1.26 (m, 2H, -CH_2), 1.48 (m, 2H, -CH_2), 1.94 (s, 3H, -CH_3), 2.42 (m, 2H, -CH_2), 2.75 (m, 1H, -CH), 3.27 (m, 1H, -CH), 4.52 (m, 1H, -CH), 4.76 (m, 1H, -CH), 4.93 (m, 1H, -CH), 5.26 (d, J= 18.3 Hz, 1H, -CH), 5.39 (d, J= 18.3Hz, 1H, -CH), 6.75 (t, J=7.2Hz,1H, Ar-H), 6.84 (d, J=8.4Hz, 1H, Ar-H), 6.89 (m, 1H, Ar-H), 7.17 (s, 1H, Ar-H), 7.22 (d, 1H, Ar-H), 7.65 (s, 1H, -NH), 8.22 (d, J= 5.6 Hz, 1H, Ar-H), 10.91 (s, 1H, -OH);ms: m/z 522.23 (M+1) with (M+2), (M+4) &(M+6) peaks.

2-(5-(1-((4-(2,2,2-Trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-4,5-dihydro-1H-pyrazol-3-yl)-5-methylphenol (2b). ir (KBr, cm^{-1}): 1090 (Ar-Cl), 1245 (-CF_3), 1465& 1590 (C=C), 1639 (C=N); ^{1}H nmr (DMSO-d_6), δ: 0.79(t, J= 7.6Hz, 3H, -CH_3), 1.26 (m, 2H, -CH_2), 1.50 (m, 2H, -CH_2), 1.93 (s, 3H, -CH_3), 2.22 (s, 3H, -CH_3), 2.35 (m, 2H, -CH_2), 2.66 (dd, J= 8.8& 11.9 Hz, 1H, -CH), 3.28 (dd, J= 8.8& 12.0 Hz,1H, -CH), 4.47 (q, 1H, -CH), 4.79 (m, 1H, -CH), 4.92 (m, 1H, -CH), 5.22 (d, J= 16.0Hz, 1H, -CH), 5.41 (d, J= 16.0 Hz, 1H, -CH), 6.57 (d, J= 8.4Hz, 1H, Ar-H), 6.64 (m, 2H, Ar-H), 6.97 (d, J=5.6 Hz, 1H, Ar-H), 7.57 (s, 1H, -NH), 8.22 (d, J= 5.6 Hz,1H, Ar-H), 10.86 (s, 1H, -OH); ms: m/z 536.4 (M+1) with (M+2), (M+4) &(M+6) peaks.

2-(5-(1-((4-(2,2,2-Trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-4,5-dihydro-1H-pyrazol-3-yl)-4-methylphenol (2c).ir (KBr, cm^{-1}): 1101 (Ar-Cl), 1250 (-CF_3), 1460 &1580 (C=C), 1625 (C=N); ^{1}H nmr (DMSO-d_6), δ: 0.80 (t, J= 7.6Hz, 3H, -CH_3), 1.24 (m, 2H, -CH_2), 1.50 (m, 2H, -CH_2), 1.93 (s, 3H, -CH_3), 2.23 (s, 3H, -CH_3), 2.36 (m, 2H, -CH_2), 2.66 (dd, J= 8.8& 11.6 Hz, 1H, -CH), 3.27 (dd, J= 8.8& 11.6 Hz,1H, -CH), 4.46 (q, 1H, -CH), 4.73 (m, 1H, -CH), 4.87 (m, 1H, -CH), 5.28 (q, 2H, -CH_2), 6.54 (d, 1H, Ar-H), 6.71 (d, J=8.4Hz, 1H, Ar-H), 6.94 (d, J=8.4Hz, 1H, Ar-H), 6.95 (d, J=5.6 Hz, 1H, Ar-H), 7.59 (s, 1H, -NH), 8.21 (d, J= 5.6 Hz,1H, Ar-H), 10.67 (s, 1H, -OH), ms: m/z 536.4 (M+1) with (M+2), (M+4) & (M+6) peaks.

2-(5-(1-((4-(2,2,2-Trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-4,5-dihydro-1H-pyrazol-3-yl)-4-chlorophenol (2d).ir (KBr, cm^{-1}): 1102 (Ar-Cl), 1255 (-CF_3), 1450 &1586 (C=C), 1630 (C=N); ^{1}H nmr (DMSO-d_6), δ:0.80 (t, J=7.6Hz, 3H, -CH_3), 1.26 (m, 2H, -CH_2), 1.51 (m, 2H, -CH_2), 1.91 (s, 3H, -CH_3), 2.43 (m, 2H, -CH_2), 2.71 (dd, J=8.8& 11.4 Hz, 1H, -CH), 3.31 (dd, J=8.8& 11.4 Hz, 1H, -CH), 4.54 (q, 1H, -CH), 4.83 (m, 1H, -CH), 4.97 (m, 1H, -CH), 5.28 (q, 2H, -CH_2), 6.74 (m, J=2.4Hz, 1H, Ar-H), 6.87 (d, J=8.8Hz, 1H, Ar-H), 6.97 (d, J=5.6 Hz, 1H, Ar-H),7.18 (dd, J=2.4 & 8.8Hz, 1H, Ar-H), 7.82(s, 1H, -NH), 8.24 (d, J= 5.6 Hz,1H, Ar-H), 10.96 (s, 1H, -OH); ms: m/z 556.3 (M+1) with (M+2), (M+4) & (M+6) peaks.

2-(5-(1-((4-(2,2,2-Trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-4,5-dihydro-1H-pyrazol-3-yl)-4-chloro-5-methylphenol (2e).ir (KBr, cm^{-1}): 1116 (Ar-Cl), 1253 (-CF_3), 1462& 1581 (C=C), 1629 (C=N); ^{1}H nmr (DMSO-d_6), δ:0.80 (t, J=7.2Hz, 3H, -CH_3); 1.26 (m, 2H, -CH_2); 1.52 (m, 2H, -CH_2); 1.90 (s, 3H, -CH_3); 2.23 (s, 3H, -CH_3); 2.32-2.50 (m, 2H, -CH_2); 2.65 (dd, 1H, J= 8.4& 11.2 Hz, -CH); 3.28 (m, 1H -CH); 4.46 (q, J= 8.4 & 11.2 Hz,1H -CH); 4.82 (q, J= 8.4 Hz, 1H -CH); 4.96 (q, J= 8.4 Hz,1H, -CH); 5.28 (q, J=7.2 Hz, 2H, -CH_2); 6.68 (s, 1H, Ar-H); 6.85 (s, 1H, Ar-H); 6.97 (d, J=5.6Hz, 1H, Ar-H); 7.74 (s, 1H, N-H); 8.25 (d, J= 5.6Hz, 1H, Ar-H); 10.85 (s, 1H, -OH); ms: m/z 571.40 (M+1)with (M+2), (M+4) & (M+6) peaks.

2-(5-(1-((4-(2,2,2-Trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-4,5-dihydro-1H-pyrazol-3-yl)-4,6-dichlorophenol (2f). ir (KBr, cm^{-1}): 1109 (Ar-Cl), 1250 (-CF_3), 1475 & 1599 (C=C), 1633 (C=N); ^{1}H nmr (DMSO-d_6), δ: 0.81 (t, 3H, -CH_3), 1.30 (m, 2H, -CH_2), 1.51 (m, 2H, -CH_2), 1.83 (m, 2H, -CH_2), 2.22 (s, 3H, -CH_3), 3.57 (m, 1H, -CH),4.10 (q, J= 8.8 Hz, 1H, -CH), 4.87 (q, J= 8.8 Hz, 1H, -CH); 5.26 (q, J=17.6 Hz, 2H, -CH_2); 6.79 (m, 1H, Ar-H), 7.02 (m, J= 5.6Hz, 1H, Ar-H), 7.52 (s, 1H, Ar-H), 7.68 (s, 1H, N-H), 8.21 (d, 1H, J= 5.6 Hz, Ar-H), 11.78 (s, 1H, -OH); ms: m/z 590.30 (M+1), (M+1) with (M+2), (M+4) & (M+6) peaks.

Preparation of 2-((E)-2-(1-((4-(2,2,2-trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-2,3-dihydro-1H-benzo[b][1,4]diazepin-4-yl)phenol (3).

To the solution of chalcone **1** (1.0 mmol) and 10 mL methanol was added 1,2-diaminobenzene (1.5 mmol) in 50 mL round bottom flask. Reaction mixture was refluxed for 5h at 65^0C. Progress of reaction was monitored by TLC (10% Methanol + 80% Dichloromethane). After completion of reaction, contents were cooled and solid crude product obtained was filtered.It was recrystallized from ethanol to afford pure benzodiazepines **3**.

2-((E)-2-(1-((4-(2,2,2-Trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-2,3-dihydro-1H-benzo[b][1,4]diazepin-4-yl)phenol (3a).ir (KBr, cm^{-1}): 1110 (Ar-Cl), 1265 (-CF_3), 1485 & 1587 (C=C), 1605 (C=N), 3279 (N-H); ^{1}H nmr (400 MHz, DMSO-d_6), δ: 0.78 (t, J= 7.6Hz, 3H, -CH_3), 1.24 (m, 2H, -CH_2), 1.44 (m, 2H, -CH_2), 2.08 (s, 3H, -CH_3), 2.44 (m, 2H, -CH_2), 3.05 (t, J= 12.4Hz, 1H, -CH), 3.25 (d, J= 13.2Hz, 1H, -CH), 4.93 (q, 2H, -CH_2), 5.05 (d, J= 12.4Hz, 1H, -CH), 5.37 (q, J= 18.4 Hz, 2H, -CH), 5.99 (s, 1H, -NH), 6.62 (t, J= 7.6Hz, 1H, Ar-H), 6.85 (m, 2H, Ar-H), 6.93 (d, J= 8.4Hz, 2H, Ar-H), 7.04 (t

,J= 8.4Hz, 2H, Ar-H), 7.12 (d, J= 6.0Hz, 1H, Ar-H), 7.29 (t, J= 7.6 Hz, 1H, Ar-H), 8.35 (d, J=5.6Hz, 1H, Ar-H), 15.21 (s, 1H, -OH), ms: m/z 598.4 (M+1) with (M+2), (M+4) &(M+6) peaks.

2-((E)-2-(1-((4-(2,2,2-Trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-2,3-dihydro-1H-benzo[b][1,4]diazepin-4-yl)-5-methylphenol (3b).ir (KBr, cm^{-1}): 1095 (Ar-Cl), 1255(-CF_3), 1466& 1585 (C=C), 1598 (C=N), 3275 (N-H); ^{1}H nmr (DMSO-d_6),δ: 0.79 (t, J=7.6Hz, 3H, -CH_3), 1.24 (m, 2H, -CH_2), 1.44 (m, 2H, -CH_2), 2.07 (s, 3H, -CH_3), 2.24 (s, 3H, -CH_3), 2.45 (m, 2H, -CH_2), 2.99 (t, J = 11.2 Hz, 1H,-CH), 3.16 (d, J= 13.6Hz, 1H, -CH), 4.91 (m, 2H, -CH_2), 5.04 (d,J = 11.2Hz, 1H, -CH), 5.37 (q, J= 18.4Hz, 2H, -CH_2), 5.96 (s, 1H, -NH), 6.43 (d, J= 8.4Hz, 1H, Ar-H), 6.69 (s, 1H, Ar-H), 6.81-6.88 (m, 2H, Ar-H), 6.92 (d, J= 8.0Hz, 1H, Ar-H), 7.02 (t, J= 7.2 Hz, 1H, Ar-H), 7.10 (m, 1H, Ar-H), 7.15 (d, J= 5.6 Hz, 1H, Ar-H), 8.34 (d, J= 5.6 Hz, 1H, Ar-H), 15.23 (s, 1H, -OH); ms: m/z 613.08 (M+1) with (M+2), (M+4) &(M+6) peaks.

2-((E)-2-(1-((4-(2,2,2-Trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-2,3-dihydro-1H-benzo[b][1,4]diazepin-4-yl)-4-methylphenol (3c).ir(KBr, cm^{-1}): 1107 (Ar-Cl), 1260 (-CF_3), 1455 & 1582 (C=C), 1605 (C=N), 3265 (N-H); ^{1}H nmr (DMSO-d_6), δ: 0.78 (t, J=7.6Hz, 3H, -CH_3), 1.24 (m, 2H, -CH_2), 1.45 (m, 2H, -CH_2), 2.07 (s, 3H, -CH_3), 2.25 (s, 3H, -CH_3), 2.44 (m, 2H, -CH_2), 2.97 (t, J = 11.2 Hz, 1H,-CH), 3.17 (d, J= 13.6Hz, 1H, -CH), 4.92 (m, 2H, -CH_2), 5.03 (d, J = 11.2Hz, 1H, -CH), 5.36 (q, J= 18.4Hz, 2H, -CH_2), 5.96 (s, 1H, -NH), 6.45 (d, J= 8.4Hz, 1H, Ar-H), 6.70 (s, 1H, Ar-H), 6.83-6.88 (m, 2H, Ar-H), 6.91 (d, J= 8.0Hz, 1H, Ar-H), 7.03 (t, J= 7.2 Hz, 1H, Ar-H), 7.10 (m, J= 7.6Hz, 1H, Ar-H), 7.15 (d, J= 5.6 Hz, 1H, Ar-H), 8.34 (d, J= 5.6 Hz, 1H, Ar-H), 15.23 (s, 1H, -OH); ms: m/z 613.08 (M+1) with (M+2), (M+4) & (M+6) peaks.

2-((E)-2-(1-((4-(2,2,2-Trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-2,3-dihydro-1H-benzo[b][1,4]diazepin-4-yl)-4-chlorophenol (3d).ir (KBr, cm^{-1}): 1095 (Ar-Cl), 1262 (-CF_3), 1466& 1580 (C=C), 1607 (C=N), 3280 (N-H); ^{1}H nmr (DMSO-d_6), δ: 0.76 (t, J=7.2Hz, 3H, -CH_3), 1.24 (m, 2H, -CH_2), 1.41 (m, 2H, -CH_2), 2.10 (s, 3H, -CH_3), 2.42 (t, J= 7.2Hz, 2H, -CH_2), 2.64 (t, J = 7.2 Hz, 1H,-CH), 3.13 (d, J= 13.3Hz, 1H, -CH), 4.87 (m, 2H, -CH_2), 5.11 (d, J = 8.8Hz, 1H, -CH), 5.36 (q, J= 18.4Hz, 2H, -CH_2), 6.06 (s, 1H, -NH), 6.87 (m, 2H, Ar-H), 6.97-7.09 (m, 2H, Ar-H), 7.15 (d, J=7.6Hz, 1H, Ar-H), 7.34 (d, J=8.8Hz, 1H, Ar-H), 7.44-7.52 (m, 2H, Ar-H), 8.33 (d, J= 5.6 Hz, 1H, Ar-H), 15.45 (s, 1H, -OH); ms: m/z 633.3 (M+1) with (M+2), (M+4) &(M+6) peaks.

2-((E)-2-(1-((4-(2,2,2-Trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-2,3-dihydro-1H-benzo[b**][1,4]diazepin-4-yl)-4-chloro-5-methylphenol (3e).**ir (KBr, cm^{-1}): 1114 (Ar-Cl), 1259 (-CF_3), 1462 & 1581 (C=C), 1602 (C=N), 3271 (N-H); ^{1}H nmr (DMSO-d_6), δ: 0.76 (t, J=7.2Hz, 3H, -CH_3), 1.20 (m, 2H, -CH_2), 1.40 (m, 2H, -CH_2), 2.08 (s, 3H, -CH_3), 2.27 (s, 3H, -CH_3), 2.42 (t, J= 7.2Hz, 2H, -CH_2), 3.10 (dd, 1H,-CH), 3.27 (m, 1H, -CH), 4.87 (q, J= 8.8Hz, 2H, -CH_2), 5.10 (d, J = 8.4Hz, 1H, -CH), 5.36 (q, J= 18 Hz, 2H, -CH_2), 6.01 (s, 1H, -NH), 6.9 (m, 3H, Ar-H), 7.05 (m, 3H, Ar-H), 7.40 (s, 1H, Ar-H), 8.33 (d, J= 5.6 Hz, 1H, Ar-H), 15.34 (s, 1H, -OH); ms: m/z 646.3 (M+1) with (M+2), (M+4) &(M+6) peaks.

2-((E)-2-(1-((4-(2,2,2-Trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-2,3-dihydro-1H-benzo[b][1,4]diazepin-4-yl)-4,6-dichlorophenol (3f).ir (KBr, cm^{-1}): 1110 (Ar-Cl), 1255 (-CF_3), 1465& 1590 (C=C), 1600 (C=N), 3300 (N-H); ^{1}H nmr (DMSO-d_6), δ: 0.76 (t, J=7.2Hz, 3H, -CH_3), 1.20 (m, 2H, -CH_2), 1.40 (m, 2H, -CH_2), 2.13 (s, 3H, -CH_3), 2.43 (t, J= 7.2Hz, 2H, -CH_2), 3.24 (dd, 7.2 & 13.3 Hz, 1H,-CH), 3.43 (d, J= 13.3Hz, 1H, -CH), 4.88 (m, 2H, -CH_2), 5.08 (d, J = 8.0Hz, 1H, -CH), 5.36 (s, 2H, -CH_2), 6.26 (s, 1H, -NH), 6.86 (d, J= 8.0Hz, 1H, Ar-H), 6.92 (d, J= 8.4Hz, 1H, Ar-H), 7.09 (m, 2H, Ar-H), 7.21 (d, J=8.0Hz, 1H, Ar-H), 7.47 (s, 1H, Ar-H), 7.62 (d, J= 2.0Hz, 1H, Ar-H), 8.33 (d, J= 5.6

Hz, 1H, Ar-H), 17.40 (s, 1H, -OH); ms: m/z 667.3 (M+1) with (M+2), (M+4) & (M+6) peaks.

Preparation of 2-(2-butyl-4-chloro-1H-imidazol-5-yl)-4H-chromen-4-one (4).

Chalcone **1**(1 mmol) was dissolved in 10 mL of dimethylsulfoxide in 100 mL round bottom flask. To this reaction mixture, catalytic amount of iodine was added. Contents were heated at 110^0C for 5 h. Progress of reaction was monitored by TLC. After completion, reaction mixture was cooled to 10^0C. To this reaction mixture 50 mL icecoldwater was added and the separated product was filtered and washed with dilute sodium thiosulfate (10%) for several times. Again it was washed with cold water and recrystallized from isopropyl alcohol to afford chromone **4**.

2-(2-Butyl-4-chloro-1H-imidazol-5-yl)-4H-chromen-4-one (4a).ir (KBr, cm^{-1}): 1105 (Ar-Cl), 1460& 1589 (C=C), 1640 (C=O), 3170 (N-H); ^{1}H nmr ($CDCl_3$-d_3), δ: 0.96 (t, J=7.2 Hz 3H, -CH_3), 1.23 (m, 2H, -CH_2), 1.44 (m, 2H, -CH_2), 2.83 (m, 2H, -CH_2), 6.70 (s, 1H, Chromone), 7.09 (s, 1H, Ar-H), 7.72 (d, 2H, Ar-H), 8.04 (d, 1H, Ar-H), 13.01 (s, 1H, -NH); ms: m/z 303.14 (M+1) with (M+2) peak.

2-(2-Butyl-4-chloro-1H-imidazol-5-yl)-6-methyl-4H-chromen-4-one (4b). ir (KBr, cm^{-1}): 1098 (Ar-Cl), 1460 & 1580 (C=C), 1655 (C=O), 3259 (N-H); ^{1}H nmr ($CDCl_3$-d_3), δ: 0.92 (t, J=7.6 Hz, 3H, -CH_3), 1.34 (m, 2H, -CH_2), 1.65 (m, 2H, -CH_2), 2.54 (s, 3H, -CH_3), 2.70 (t, J=7.6 Hz, 2H, -CH_2), 6.72 (s, 1H, chromone), 7.68 (d, 1H, Ar-H), 7.93 (s, 1H, Ar-H), 8.21 (d, 1H, Ar-H), 13.08 (s, 1H, -NH);ms: m/z 317.2 (M+1) with (M+2) peak.

2-(2-Butyl-4-chloro-1H-imidazol-5-yl)-7-methyl-4H-chromen-4-one (4c).ir (KBr, cm^{-1}): 1090 (Ar-Cl), 1429 & 1595 (C=C), 1645 (C=O), 3247 (N-H); ^{1}H nmr ($CDCl_3$-d_3), δ: 0.91 (t, J= 7.2 Hz, 3H, -CH_3), 1.33 (m, 2H, -CH_2), 1.67 (m, 2H, -CH_2), 2.54 (s, 3H, -CH_3), 2.69 (m, 2H, -CH_2), 6.71 (s, 1H, chromone), 7.21 (d, J= 8.0 Hz, 1H, Ar-H), 7.29 (d, 1H, Ar-H), 7.9 (d, J= 8.0 Hz, 1H, Ar-H), 13.05 (s, 1H, -NH); ms: m/z 317.2 (M+1) with (M+2) peak.

2-(2-Butyl-4-chloro-1H-imidazol-5-yl)-6-chloro-4H-chromen-4-one (4d).ir (KBr, cm^{-1}): 1105 (Ar-Cl), 1450 & 1575 (C=C), 1638 (C=O), 3250 (N-H); ^{1}H nmr ($CDCl_3$-d_3), δ: 0.86(t, J=7.6Hz, 3H, -CH_3), 1.34 (m, 2H, -CH_2), 1.63 (m, 2H, -CH_2), 2.66 (m, 2H, -CH_2), 6.73 (s, 1H, chromone), 7.02 (d, 2H, Ar-H), 7.81 (d, 1H, Ar-H), 13.08 (s, 1H, -NH); ms: m/z 338.3 (M+1) with (M+2)&(M+4) peaks.

2-(2-Butyl-4-chloro-1H-imidazol-5-yl)-6-chloro-7-methyl-4H-chromen-4-one (4e).ir (KBr, cm^{-1}): 1109 (Ar-Cl), 1452 & 1583 (C=C), 1654 (C=O), 3255 (N-H); ^{1}H nmr ($CDCl_3$-d_3), δ: 0.91 (t, 3H, J= 7.6 Hz, -CH_3), 1.33 (m, 2H, -CH_2), 1.67 (m, 2H, -CH_2), 2.42 (s, 3H, -CH_3), 2.69 (t, 2H, J= 7.2, -CH_2), 6.70 (s, 1H, Chromone), 7.65 (s, 1H, Ar-H), 7.92 (s, 1H, Ar-H), 13.08 (s, 1H, -NH); ms: m/z 351.4 (M+1) with (M+2)& (M+4) peaks.

2-(2-Butyl-4-chloro-1H-imidazol-5-yl)-6,8-dichloro-4H-chromen-4-one (4f). ir (KBr, cm^{-1}): 1115 (Ar-Cl), 1458 & 1589 (C=C), 1659 (C=O), 3265 (N-H); ^{1}H nmr ($CDCl_3$-d_3), δ: 0.96 (t, J= 7.2Hz, 3H, -CH_3), 1.24 (m, 2H, -CH_2), 1.44 (m, 2H, -CH_2), 2.62 (t, J=7.2Hz, 2H, -CH_2), 7.09 (s, 1H, Chromone), 7.72 (s, 1H, Ar-H), 8.04 (d, 1H, Ar-H), 13.09 (s, 1H, -NH); ms: m/z 371.3 (M+1) with (M+2), (M+4) & (M+6) peaks.

Preparation of 2-(2-Butyl-4-chloro-1H-imidazol-5-yl)-3-chloro-4H-chromen-4-one (5).

Chalcone **1**(1.0 mmol) was dissolved in 5 mL of dimethylsulfoxide in 100 mL round bottom flask. To this reaction mixture, cuprous chloride (1.4 mmol) was added. Contents were heated at 110^0C for 5 h and kept overnight. To this reaction mixture 50 mL ice cold water was added and the separated solid product was filtered and washed with cold water and recrystallized from isopropyl alcohol to afford 3-chlorochromone **5**.

2-(2-Butyl-4-chloro-1H-imidazol-5-yl)-3-chloro-4H-chromen-4-one (5a).ir (KBr, cm^{-1}): 1100 (Ar-Cl), 1450 & 1590 (C=C), 1640 (C=O); ^{1}H nmr ($CDCl_3$-d_3), δ: 0.88 (t, J=7.4Hz, 3H, -CH_3), 1.23 (m, 2H, -CH_2), 1.52 (m, 2H, -CH_2), 2.43 (t, J=7.4Hz, 2H, -CH_2), 7.01 (m, 2H, Ar-H), 8.04 (m, 2H, Ar-H), 13.08 (s, 1H, -NH), ms: m/z 338.3 (M+1) with (M+2) &(M+4)peaks.

2-(2-Butyl-4-chloro-1H-imidazol-5-yl)-3-chloro-6-methyl-4H-chromen-4-one (5b). ir

(KBr, cm^{-1}): 1095 (Ar-Cl), 1439 & 1580 (C=C), 1620 (C=O); ^{1}H nmr ($CDCl_3$-d_3), δ: 0.88 (t, J=7.5 Hz, 3H, -CH_3), 1.23 (m, 2H, -CH_2), 1.45 (m, 2H, -CH_2), 2.26 (s, 3H, -CH_3), 2.40 (t, J=7.4 Hz, 2H, -CH_2), 6.55 (s, 1H, Ar-H), 7.0 (d, J=8.0 Hz, 1H, Ar-H), 7.65 (d, J=8.0 Hz, 1H, Ar-H), 13.10 (s, 1H, -NH), ms: m/z 352.2 (M+1) with (M+2)& (M+4) peaks.

2-(2-Butyl-4-chloro-1H-imidazol-5-yl)-3-chloro-7-methyl-4H-chromen-4-one (5c).ir (KBr, cm^{-1}): 1120 (Ar-Cl), 1465 & 1580 (C=C), 1630 (C=O); ^{1}H nmr ($CDCl_3$-d_3), δ: 0.75 (t, J= 7.6 Hz, 3H, -CH_3), 1.20 (m, 2H, -CH_2), 1.44 (m, 2H, -CH_2), 2.22 (s, 3H, -CH_3), 2.40 (t, J= 7.6Hz, 2H, -CH_2), 6.52 (s, 1H, Ar-H), 7.04 (d, J= 5.6Hz, 1H, Ar-H), 7.57 (d, J= 5.6Hz, 1H, Ar-H), 13.19 (s, 1H, -NH); ms: m/z 352.23 (M+1) with (M+2)&(M+4) peaks.

2-(2-Butyl-4-chloro-1H-imidazol-5-yl)-3,6-dichloro-4H-chromen-4-one (5d). ir (KBr, cm^{-1}): 1101 (Ar-Cl), 1455& 1583 (C=C), 1630 (C=O); ^{1}H nmr ($CDCl_3$-d_3), δ: 0.86 (t, J= 7.4Hz, 3H, -CH_3), 1.34 (m, 2H, -CH_2), 1.63 (m, 2H, -CH_2), 2.66 (t, J= 7.4Hz, 2H, -CH_2), 6.99 (d, J=5.6Hz, 1H, Ar-H), 7.02 (d, J= 7.2Hz, 1H, Ar-H), 7.8 (dd, J= 5.6 & 7.2Hz, 1H, Ar-H), 13.10 (s, 1H, -NH); ms: m/z 372.5 (M+1) with (M+2), (M+4) & (M+6) peaks.

2-(2-Butyl-4-chloro-1H-imidazol-5-yl)-3,6-dichloro-7-methyl-4H-chromen-4-one (5e). ir(KBr, cm^{-1}): 1109 (Ar-Cl), 1454& 1583 (C=C), 1635 (C=O); ^{1}H nmr ($CDCl_3$-d_3), δ: 0.89 (t, J= 7.2 Hz, 3H, -CH_3), 1.33 (m, 2H, -CH_2), 1.66 (m, 2H, -CH_2), 2.31 (s, 3H, -CH_3), 2.70 (t, J= 7.2 Hz, 2H, -CH_2), 7.0 (s, 1H, Ar-H), 8.02 (s, 1H, Ar-H), 12.95 (s, 1H, -NH); ms: m/z 385.3 (M+1) with (M+2), (M+4) & (M+6) peaks.

2-(2-Butyl-4-chloro-1H-imidazol-5-yl)-3,6,8-trichloro- H 4-chromen-4-one (5f). ir (KBr, cm^{-1}): 1106 (Ar-Cl), 1445 & 1580 (C=C), 1639 (C=O); ^{1}H nmr ($CDCl_3$-d_3), δ:1.01 (t, J= 7.5Hz, 3H, -CH_3), 1.25 (m, 2H, -CH_2), 1.50 (m, 2H, -CH_2), 2.36 (t,J= 7.6Hz, 2H, -CH_2), 7.82 (d, 1H, Ar-H), 8.14 (d, 1H, Ar-H), 13.08 (s, 1H, -NH), ms: m/z 407.10 (M+1) with (M+2), (M+4), (M+6) & (M+8) peaks.

Preparation of 2-(1-((4-(2,2,2-trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-3-hydroxy-4H-chromen-4-one (6).

Chalcone**1**(1 mmol) was dissolved in 20 mL methanol and 10% sodium hydroxide was added in it. To this reaction mixture, 50% hydrogen peroxide (10 mL) was added slowly at 10°C. Contents were stirred at room temperature for 2 h. Progress of reaction was monitored by TLC. After completion, reaction mixture was poured in 100 mL water and extracted with ethyl acetate. Product was isolated by removing solvent under vacuum. The solid obtained was recrystallized fromdiisopropyl ether to afford 3-hydroxychromones **6**.

2-(1-((4-(2,2,2-trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-6-bromo-3-hydroxy-4H-chromen-4-one (6a). ir (KBr, cm^{-1}): 1100 (Ar-Cl), 1250 (-CF_3), 1450 & 1600 (C=C), 1642 (C=O); ^{1}H nmr ($CDCl_3$-d_3),δ: 0.91 (t, J= 7.6Hz, 3H,-CH_3), 1.39 (m, 2H, -CH_2), 1.74 (m, 2H, -CH_2), 2.04 (s, 3H, -CH_3), 2.68 (t, J= 7.6Hz, 2H, -CH_2), 4.44 (q, J= 8.8Hz, 2H, -OCH_2), 5.42 (s, 2H, N-CH_2), 6.88 (d, 1H, J=5.6, Ar-H), 7.30-8.17 (m, 4H, Ar-H), 8.25 (d, 1H, J=5.6Hz, Ar-H), 9.73 (s, 1H, -OH); MS: m/z = 570 (M+1) with (M+2peak.

2-(1-((4-(2,2,2-Trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-3-hydroxy-4H-chromen-4-one (6b). ir (KBr, cm^{-1}): 1095 (Ar-Cl), 1255 (-CF_3), 1440& 1609(C=C), 1640 (C=O); ^{1}H nmr ($CDCl_3$-d_3), δ: 0.93 (t, J= 7.6Hz, 3H, -CH_3), 1.43 (m, 2H, -CH_2), 1.80 (m, 2H, -CH_2), 1.98 (s, 3H, -CH_3), 2.49 (s, 3H, -CH_3),2.88 (t, 2H, J= 7.6Hz, -CH_2), 4.50 (m, 2H, -OCH_2), 5.75 (s, 2H, -NCH_2), 7.06 (d, J=5.5Hz, 1H, Ar-H), 7.39 (m, 1H, Ar-H), 7.54 (m, 1H, Ar-H), 8.09 (d, J= 2.2Hz, 1H, Ar-H), 8.19 (d, 1H, J=5.5Hz, Ar-H), 9.72 (s, 1H, -OH), MS: m/z = 536 (M+1); ms: m/z 536 (M+1) with (M+2) peak.

2-(1-((4-(2,2,2-Trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-3-hydroxy-6-methyl-4H-chromen-4-one(6c).ir (KBr, cm^{-1}): 1098 (Ar-Cl), 1246 (-CF_3), 1465 & 1601 (C=C), 1642 (C=O); ^{1}H nmr ($CDCl_3$-d_3), δ: 0.94 (t, J= 7.2Hz, 3H,

-CH_3), 1.43 (m, 2H, -CH_2), 1.80 (m, 2H, -CH_2), 1.98 (s, 3H, -CH_3), 2.49 (s, 3H, -CH_3), 2.81 (t, J=7.2Hz, 2H, -CH_2), 4.46 (q, J= 7.6 Hz, 2H, -OCH_2), 5.63 (s, 2H, -NCH_2), 6.94 (d, J=5.4Hz 1H, Ar-H), 7.20 (m, 1H, Ar-H), 7.29 (m, 1H, Ar-H), 7.99 (d, J=2.4Hz, 1H, Ar-H), 8.19 (d, J=5.4Hz, 1H, Ar-H), 9.75 (s, 1H, -OH), ms: m/z 536.3 (M+1) with (M+2) peak.

2-(1-((4-(2,2,2-Trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-3-hydroxy-7-methyl-4H-chromen-4-one (**6d).**ir (KBr, cm^{-1}): 1105 (Ar-Cl), 1253 (-CF_3), 1458&1608 (C=C), 1639 (C=O); ^{1}H nmr ($CDCl_3$-d_3), δ: δ, 0.94 (t, J= 7.6Hz, 3H, -CH_3), 1.44 (m, 2H, -CH_2), 1.81 (m, 2H, -CH_2), 1.97 (s, 3H, -CH_3), 2.48 (s, 3H, -CH_3), 2.82 (t, J=7.2Hz, 2H, -CH_2), 4.48 (q, J= 7.6 Hz, 2H, OCH_2), 5.62 (s, 2H, -NCH_2), 6.94 (s, 1H, Ar-H), 7.19 (d, J= 8.4Hz, 1H, Ar-H), 7.26 (s, 1H, Ar-H), 8.05 (d, J=8.4Hz, 1H, Ar-H), 8.20 (d, J=5.6 Hz, 1H, Ar-H), 9.70 (s, 1H, -OH); ms: m/z 536.3 (M+1) with (M+2), (M+4) & (M+6) peaks.

2-(1-((4-(2,2,2-Trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-6-chloro-3-hydroxy-4H-chromen-4-one (**6e).**ir (KBr, cm^{-1}): 1107 (Ar-Cl), 1253 (-CF_3), 1465 & 1610 (C=C), 1635 (C=O); ^{1}H nmr ($CDCl_3$-d_3), δ: 0.87 (t, J= 7.2Hz, 3H, -CH_3), 1.34 (m, 2H, -CH_2), 1.64 (m, 2H, -CH_2), 1.95 (s, 3H, -CH_3), 2.38 (s, 3H, -CH_3) 2.67 (t, J= 7.2Hz, 2H, -CH_2), 4.82 (q, J = 16Hz, 2H, -OCH_2), 5.32 (s, 2H, -NCH_2), 7.0 (d, J=5.6 Hz, 1H, Ar-H), 7.5 (s, 1H, Ar-H), 7.95 (s, 1H, Ar-H), 8.17 (d, J= 5.6 Hz, 1H, Ar-H), 9.76 (s, 1H, -OH); ms: m/z 556.2 (M+1) with (M+2) &(M+4) peaks.

2-(1-((4-(2,2,2-Trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-6-chloro-3-hydroxy-7-methyl-4H-chromen-4-one (**6f).** ir (KBr, cm^{-1}): 1105 (Ar-Cl), 1255 (-CF_3), 1456 & 1605 (C=C), 1645 (C=O); ^{1}H nmr (DMSO-d_6) δ: 0.91 (q, 3H, J= 7.4 Hz, -CH_3), 1.40 (m, 2H, -CH_2), 1.78 (m, 2H, -CH_2), 2.12 (s, 3H, -CH_3), 2.81 (t, 2H, J= 7.4 Hz, -CH_2), 4.72 (q, J= 16.0Hz 2H, -OCH_2), 5.73 (s, 2H, N-CH_2), 7.40 (d, J= 5.6 Hz, 1H, Ar-H), 7.80 (s, 1H, Ar-H), 7.95 (s, 1H, Ar-H), 8.17 (d, J= 5.6 Hz, 1H, Ar-H), 9.76 (s, 1H, -OH); ms: m/z 570.2 (M+1) with (M+2), (M+4) & (M+6) peaks.

2-(1-((4-(2,2,2-Trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-6,8-dichloro-3-hydroxy-4H-chromen-4-one (**6g).**ir (KBr, cm^{-1}): 1106 (Ar-Cl), 1255 (-CF_3), 1456& 1587 (C=C), 1629 (C=O); ^{1}H nmr ($CDCl_3$-d_3), δ: 0.86 (t, J= 7.6 Hz, 3H, -CH_3), 1.34 (m, 2H, -CH_2), 1.63 (m, 2H, -CH_2), 1.94 (s, 3H, -CH_3), 2.66 (t, J= 7.6Hz, 2H, -CH_2), 4.82 (q, J= 16.0Hz, 2H, -CH_2), 5.33 (s, 2H, -CH_2), 7.0 (m, 2H, Ar-H), 7.81 (dd, 1H, Ar-H), 8.12 (d, J= 2.8Hz, 1H, Ar-H), 8.17 (d, J= 5.6Hz, 1H, Ar-H), 9.82 (s, 1H, -OH);ms: m/z 600 (M+1) with (M+2) & (M+4) peaks.

Preparation of 2-(1-((4-(2,2,2-trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-6-bromo-3-methoxy-4H-chromen-4-one (7).

To the solution of 2-(1-((4-(2,2,2-trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-6-bromo-3-hydroxy-4H-chromen-4-one **6** (1 mmol) in N,N'-dimethylformamide (4.0 mL), potassium carbonate (1.6 mmol) and 4-(2,2,2-trifluoroethoxy)-2-(chloromethyl)-3-methylpyridine hydrochloride alkyl/aryl halide (1 mmol) was added at 0°C. The reaction mixture was stirred at 10°C. Progress of the reaction was monitored by TLC. After completion of reaction, it was poured in ice cold water. The solid obtained was separated by filtration and purified by recrystallization with diethyl ether to afford **7a-g**.

2-(1-((4-(2,2,2-Trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-6-bromo-3-methoxy-4H-chromen-4-one (7a).ir (KBr, cm^{-1}): 1103 (Ar-Cl), 1256 (-CF_3), 1465 & 1585 (C=C), 1645 (C=O); ^{1}H nmr ($CDCl_3$-d_3), δ: 0.96 (q, J= 7.2 Hz, 3H,CH_3), 1.44 (m, 2H, CH_2), 1.81 (m, 2H, CH_2), 1.99 (s, 3H, CH_3), 2.76 (t, 2H,J= 7.2 Hz,CH_2), 3.80 (s, 3H, -OCH_3), 4.41 (q, J= 7.6 Hz, 2H, -OCH_2), 5.48 (s, 2H, -NCH_2), 6.66 (m,1H, Ar-H), 7.25 (m, 1H,Ar-H), 7.75 (m, 1H, Ar-H), 7.95 (dd, J= 2.4 & 8.8 Hz,1H, Ar-H), 8.25 (m , 1H, Ar-H); ms: m/z = 616.3 (M+1) with (M+2)& (M+4) peaks.

2-(1-((4-(2,2,2-Trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-6-bromo-3-propoxy-4H-chromen-4-one (7b).ir (KBr, cm^{-1}): 1102 (Ar-Cl), 1245 (-CF_3), 1460& 1587 (C=C), 1646 (C=O); ^{1}H nmr ($CDCl_3$-d_3), δ: 0.82 (t, J= 7.2 Hz,3H,CH_3), 0.96 (t, 3H, J= 7.6 Hz, CH_3), 1.47 (m, 2H, CH_2), 1.58 (m, 2H, CH_2), 1.84 (m, 2H, CH_2), 2.05 (m, 2H, CH_2), 2.81 (t, 2H, J= 7.2 & 7.6 Hz, CH_2), 3.98 (m, 2H, OCH_2), 4.41 (q, 2H, OCH_2), 5.60 (s, 2H, N-CH_2), 6.82 (d, J= 7.2 Hz, 1H, Ar-H), 7.51 (m, 1H, Ar-H), 7.77 (m, 2H, Ar-H), 8.20 (m , 1H, Ar-H);ms: m/z = 644.3(M+1) with (M+2)& (M+4) peaks.

2-(1-((4-(2,2,2-Trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-6-bromo-4-oxo-4H-chromen-3-yl acetate (7c).ir (KBr, cm^{-1}): 1095 (Ar-Cl), 1255 (-CF_3), 1470& 1590 (C=C), 1650 (C=O); ^{1}H nmr ($CDCl_3$-d_3), δ: 0.81 (t, 3H,J= 7.2 Hz,CH_3), 1.35 (m, 2H,CH_2), 1.74 (m, 2H, CH_2), 1.89 (s, 3H, CH_3), 2.15 (s, 3H, CH_3), 2.64 (t, 2H, CH_2), 4.35 (q, 2H, J= 8.8Hz, OCH_2), 5.20 (s, 2H, N-CH_2), 6.58 (d,1H, J= 8.4 Hz, Ar-H), 6.92 (d, 1H, J= 8.4Hz, Ar-H), 7.64 (d,1H, J= 8.0Hz, Ar-H), 8.01 (d, J= 8.0 Hz, 1H, Ar-H), 8.20 (m, 1H, Ar-H), ms: m/z = 642.2 (M+1) with (M+2)& (M+4) peaks.

2-(1-((4-(2,2,2-Trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-3-(allyloxy)-6-bromo-4H-chromen-4-one (7d).ir (KBr, cm^{-1}): 1115 (Ar-Cl), 1260 (-CF_3), 1467 & 1578 (C=C), 1645 (C=O); ^{1}H nmr ($CDCl_3$-d_3), δ: 0.85 (t, 3H, J= 7.2 Hz, CH_3), 1.34 (m, 2H, CH_2), 1.70 (m, 2H,CH_2), 1.97 (s, 3H, CH_3), 2.27 (m, 2H, CH_2), 2.62 (t, 2H, J= 7.2 Hz, CH_2), 4.25 (q, 2H, OCH_2), 5.18 (s, 2H, N-CH_2), 6.48 (d, 2H,), 6.59 (m, 1H,), 6.76 (d, 1H, Ar-H), 7.49 (m, 1H, Ar-H), 7.62 (m, 1H, Ar-H), 7.99 (d, 1H, Ar-H), 8.22 (m , 1H, Ar-H);ms: m/z = 642.3 (M+1) with (M+2)&(M+4) peaks.

2-(2-(1-((4-(2,2,2-Trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-6-bromo-4-oxo-4H-chromen-3-yloxy)acetonitrile (7e).ir (KBr, cm^{-1}): 1105 (Ar-Cl), 1254 (-CF_3), 1461& 1587 (C=C), 1640 (C=O); ^{1}H nmr ($CDCl_3$-d_3), δ:0.90 (t, 3H, J= 7.2 Hz,CH_3), 1.43 (m, 2H, CH_2), 1.81 (m, 2H, CH_2), 2.02 (s, 3H, CH_3), 2.72 (t,2H, J= 7.2 Hz, CH_2), 4.44 (q,2H, OCH_2), 4.90 (s, 2H, OCH_2), 5.36 (s, 2H, N-CH_2), 6.71 (d, 1H, J=4.8 Hz, Ar-H), 7.14 (d, 1H, Ar-H), 7.73 (dd, 1H, J= 2.4 & 8 Hz, Ar-H), 8.12 (d, J= 5.2 Hz, 1H, Ar-H), 8.28 (m, J= 2.4 Hz, 1H, Ar-H);ms: m/z = 639.2 (M+1) with (M+2)& (M+4) peaks.

2-(1-((4-(2,2,2-Trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-3-(benzyloxy)-6-bromo-4H-chromen-4-one (7f).ir (KBr, cm^{-1}): 1093 (Ar-Cl), 1240 (-CF_3), 1460& 1577 (C=C), 1638 (C=O); ^{1}H nmr ($CDCl_3$-d_3), δ: 0.94 (t, 3H, J= 7.2 Hz,CH_3), 1.40 (m, 2H, CH_2), 1.58 (m, 2H,CH_2), 1.94 (s, 3H, CH_3), 2.66 (t, 2H, J= 7.2 Hz, CH_2), 4.30 (q, 2H, 2H, OCH_2), 5.05 (s, 2H, OCH_2), 5.08 (s, 2H, N-CH_2), 6.58 (d, 1H, J= 5.6 Hz,Ar-H), 7.11 (m, 1H, Ar-H), 7.14 (dd, 2H, J= 1.6 & 8.31 Hz, Ar-H), 7.25-7.28 (m, 3H, Ar-H), 7.68 (dd, 1H, J= 2.4 & 9.2 Hz, Ar-H), 8.07 (d, 1H, J= 5.6 Hz, Ar-H), 8.31 (d, 1H, J= 2.4 Hz, Ar-H), ms: m/z = 690.2 (M+1) with (M+2)&(M+4) peaks.

3-((4-(2,2,2-Trifluoroethoxy)-3-methylpyridin-2-yl)methoxy)-2-(1-((4-(2,2,2-trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-6-bromo-4H-chromen-4-one (7g).ir (KBr, cm^{-1}): 1111 (Ar-Cl), 1253 (-CF_3), 1463& 1577 (C=C), 1639 (C=O); ^{1}H nmr ($CDCl_3$-d_3), δ: 0.88 (q, 3H, J= 7.6 Hz,CH_3), 1.35 (m, 2H,CH_2), 1.66 (m, 2H, CH_2), 2.06 (s, 3H, CH_3), 2.10 (s, 3H, CH_3), 2.57 (t, 2H, J= 7.6 Hz,CH_2), 4.29 (q,2H, J= 15.6Hz, OCH_2), 4.40 (q,2H, J= 15.6 Hz, OCH_2), 5.15 (s, 2H, -NCH_2), 5.24 (s,2H, -NCH_2), 6.49 (d, 1H, J=5.6Hz,Ar-H), 6.63 (d, 1H, J=5.6Hz,Ar-H), 7.13 (d, 1H, J=8.8Hz,Ar-H), 7.68 (dd, 1H, J= 2.4 & 8.8 Hz, Ar-H), 8.09 (d, 1H, J=5.6Hz,Ar-H), 8.20 (d, 1H, J=5.6Hz,Ar-H), 8.35 (d, 1H, J= 2.4Hz,Ar-H);ms: m/z = 805.30 (M+1) with (M+2)&(M+4) peaks.

Preparation of 2-(1-((4-(2,2,2-trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-6-(4-fluorophenyl)-3-methoxy-4H-chromen-4-one (8).

Compound **7**(0.0006 mol) was dissolved in 4 mL N,N'-dimethylformamide. To this reaction mixture 4-fluorophenylboronic acid (0.0006 mol), potassium acetate (0.0023 mol) and

tetrakis(triphenylphosphine)palladium(0) (0.00009mol) was added under inert atmosphere at room temperature. Reaction mixture was stirred for 2 h at 80^0C. Progress of reaction was monitored by TLC. After completion of reaction, catalyst was filtered and reaction mixture was poured in 10 mL water and product was extracted in diethyl ether. Solid product was isolated by removing solvent under vacuum. The solid obtained was recrystallized from diisopropyl ether to afford compound **8**.

2-(1-((4-(2,2,2-Trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-6-(4-fluorophenyl)-3-methoxy-4H-chromen-4-one (8a).ir (KBr, cm^{-1}): 1101 (Ar-Cl), 1260 (-CF_3), 1620 (C=O); ^{1}H nmr ($CDCl_3$-d_3), δ: 0.96 (t, 3H, J= 7.2 Hz,CH_3), 1.43 (m, 2H, CH_2), 1.82 (m, 2H, CH_2), 2.0 (s, 3H, CH_3), 2.78 (t, 2H, CH_2), 3.88 (s, 3H, OCH_3), 4.44 (q, 2H, OCH_2), 5.48 (s, 2H, N-CH_2), 6.69 (m, 1H, Ar-H), 7.0 (d, J= 5.6 Hz, 1H, Ar-H), 7.18 (m, 2H, Ar-H), 7.44 (m,2H, Ar-H), 7.66 (m, 1H, Ar-H), 7.90 (m, 1H, Ar-H), 8.26 (d, 1H, J=5.6Hz,Ar-H);ms: m/z = 631.05 (M+1) with (M+2) peaks.

2-(1-((4-(2,2,2-Trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-6-(4-fluorophenyl)-3-propoxy-4H-chromen-4-one (8b.)ir (KBr, cm^{-1}): 1095 (Ar-Cl), 1252 (-CF_3), 1640 (C=O); ^{1}H nmr ($CDCl_3$-d_3), δ: 0.82 (t, 3H, J= 7.2 Hz,CH_3), 0.97 (m, 3H, CH_3), 1.47 (m, 2H, CH_2), 1.59 (m, 2H, CH_2), 1.84 (m, 2H, CH_2), 2.05 (m, 2H, CH_2), 2.81 (t, 2H, CH_2), 3.98 (t, 2H, CH_2), 4.45 (q, 2H, OCH_2), 5.60 (s, 2H, N-CH_2), 6.91 (m, 1H, Ar-H), 7.05 (m, 1H, Ar-H), 7.19 (m, 2H, Ar-H), 7.46 (m,2H, Ar-H), 7.65 (m, 1H, Ar-H), 7.89 (m, 1H, Ar-H), 8.27 (d , 1H, J= 5.6 Hz, Ar-H);ms: m/z = 658.3(M+1) with (M+2)peak.

2-(1-((4-(2,2,2-Trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-3-(benzyloxy)-6-(4-fluorophenyl)-4H-chromen-4-one (8c).ir (KBr, cm^{-1}): 1115 (Ar-Cl), 1258 (-CF_3), 1651 (C=O); ^{1}H nmr ($CDCl_3$-d_3), δ: 0.81 (t, 3H, J= 7.2 Hz,CH_3), 1.33 (m, 2H, CH_2), 1.68 (m, 2H, CH_2), 1.88 (s, 3H, CH_3), 2.61(t, 2H, J= 7.2 Hz, CH_2), 4.15 (q, 2H, OCH_2), 5.02 (s, 2H, N-CH_2), 5.23 (s,2H,O-CH_2), 6.72 (d, 1H, J=8.4Hz,Ar-H), 6.81 (m, 1H, Ar-H), 7.07 (m, 3H, Ar-H), 7.25 (m,2H, Ar-H), 7.45 (m, 2H, Ar-H), 7.59 (m,2H, Ar-H), 7.75 (d, 1H, J=8.8 Hz,Ar-H), 8.02 (m, 1H, Ar-H),8.28 (d, 1H, J=5.6Hz,Ar-H);ms: m/z = 706.4 (M+1) with (M+2) peak.

3-((4-(2,2,2-Trifluoroethoxy)-3-methylpyridin-2-yl)methoxy)-2-(1-((4-(2,2,2-trifluoroethoxy)-3-methylpyridin-2-yl)methyl)-2-butyl-4-chloro-1H-imidazol-5-yl)-6-(4-fluorophenyl)-4H-chromen-4-one (8d).ir (KBr, cm^{-1}): 1109 (Ar-Cl), 1255 (-CF_3), 1580 & 1616 (C=C), 1647 (C=O); ^{1}H nmr ($CDCl_3$-d_3), δ: 0.88 (t, 3H, J= 7.2 Hz,CH_3), 1.35 (m,2H,CH_2), 1.64 (m, 2H, CH_2), 2.07 (s, 3H, CH_3), 2.11 (s, 3H, CH_3), 2.58 (t, 2H, J= 7.2 Hz,CH_2), 4.28 (q, 2H, OCH_2), 4.40 (q, 2H, OCH_2), 5.17 (s, 2H, N-CH_2), 5.28(s,2H,CH_2), 6.50 (d, 1H, J=5.6Hz,Ar-H), 6.63 (d, 1H, J=5.6Hz,Ar-H), 7.09-7.18 (m, 1H, Ar-H), 7.30 (d, 1H, J=8.8Hz,Ar-H), 7.45-7.50 (m, 2H, Ar-H), 7.64-7.69 (m, 2H, Ar-H), 7.79 (d,1H, Ar-H), 8.12 (d, 1H, J= 5.6Hz, Ar-H),8.21 (d, 1H, J=5.6 Hz,Ar-H), ms: m/z = 819.50(M+1) with (M+2), peak.

RESULTS AND DISCUSSION

All the newly synthesized compounds were characterized by spectral techniques which confirm their formation. The antibacterial activity of some of the newly synthesized compounds was by using two bacterial species were chosen for the study, one was Gram Positive Bacillus Subtilis and another was Gram Negative Escherichia Coli. Ampicillin was used as a standard drug for this study.

The activity was tested by agar well diffusion method. The bacteria were cultured on nutrient agar. The concentration of the compounds taken was 10mg/mL of which 0.1mL was used in this assay. Ampicillin was used as a standard drug and its final concentration used was 1mg. The zone of antibacterial activity was measured in mm and the results were produced as an

average of three repeated assays. The result of this assay is given in **Table 3**. It was found that the compounds **5b**, **6b**, **6e**, and **6f** have shown moderate activity towards both bacterial species.

CONCLUSION

The main objective of this research work, was to synthesize imidazole anchored pyrazolines, benzodiazepines and chromones followed by their antibacterial activities. The new synthesized compounds were characterized with the help of spectral techniques. Some of the compounds showed moderate activity towards bacterial species when compared to standard Ampicillin.

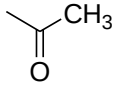
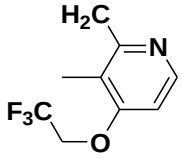
Table 1

Physical data of the synthesized compounds(scheme1)

Compd	R_1	R_2	R_3	mp (°C)	Yield (%)	Compd	R_1	R_2	R_3	mp (°C)	Yield (%)
2a	H	H	H	140	90	**4e**	H	CH_3	Cl	220	82
2b	H	H	CH_3	170	91	**4f**	Cl	H	Cl	260	81
2c	H	CH_3	H	163	91	**5a**	H	H	H	210	85
2d	H	H	Cl	180	89	**5b**	H	H	CH_3	230	82
2e	H	CH_3	Cl	176	93	**5c**	H	CH_3	H	220	86
2f	Cl	H	Cl	169	91	**5d**	H	H	Cl	226	83
3a	H	H	H	130	92	**5e**	H	CH_3	Cl	240	85
3b	H	H	CH_3	187	90	**5f**	Cl	H	Cl	235	86
3c	H	CH_3	H	180	93	**6a**	H	H	H	191	92
3d	H	H	Cl	184	89	**6b**	H	H	CH_3	204	94
3e	H	CH_3	Cl	186	90	**6c**	H	CH_3	H	205	91
3f	Cl	H	Cl	220	92	**6d**	H	H	Cl	207	95
4a	H	H	H	209	80	**6e**	H	CH_3	Cl	209	94
4b	H	H	CH_3	220	81	**6f**	Cl	H	Cl	212	90
4c	H	CH_3	H	210	82	**6g**	H	H	Br	183	90
4d	H	H	Cl	235	79						

Table 2

Physical data of the synthesized compounds (scheme 2)

Compd	R’	mp (°C)	Yield (%)
7a	$-CH_3$	208	93
7b	$-C_3H_7$	155	90
7c		142	92
7d	$-CH_2-CH=CH_2$	144	90
7e	$-CH_2-CN$	135	91
7f	$-CH_2-Ph$	151	92
7g		135	93
8a	$-CH_3$	109	85

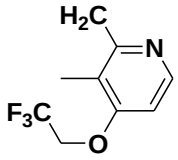
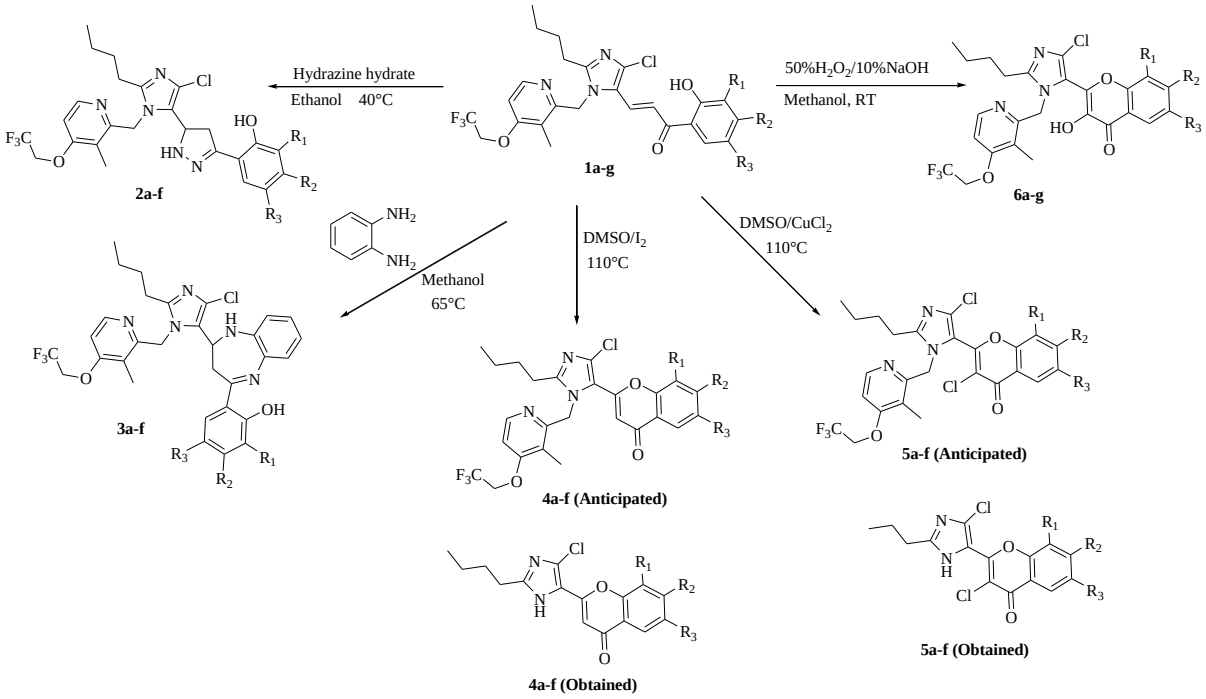
8b	-C_3H_7	113	80
8c	-CH_2-Ph	131	82
8d		126	83

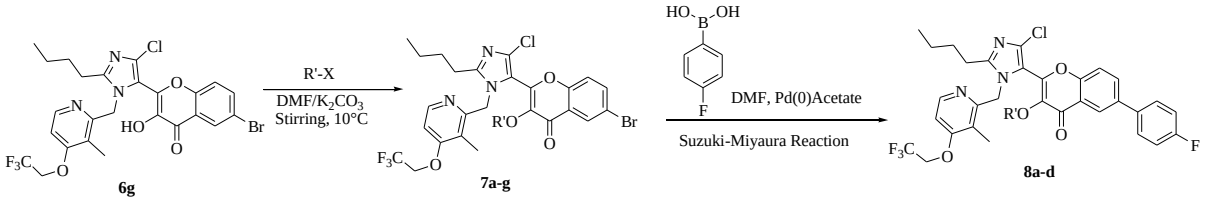
Table 3

Antibacterial Screening of synthesized compounds

Compound	**E. Coli**	**B. Subtilis**	**Compound**	**E. Coli**	**B. Subtilis**
2a	14	13	**6d**	11	16
2b	10	10	**6e**	**15**	**16**
2c	12	16	**6f**	**15**	**14**
2d	10	15	**5a**	11	16
2e	9	14	**5b**	**15**	**15**
2f	8	15	**5c**	13	14
3a	12	9	**5d**	11	16
3b	13	9	**5e**	12	15
3c	12	14	**5f**	12	13
3d	11	9	**4a**	14	16
3e	13	10	**4b**	11	18
3f	12	9	**4c**	13	13
6a	9	13	**4d**	12	14
6b	**14**	**15**	**4e**	11	15
6c	10	16	**4f**	12	14
Standard drug: Ampicillin				**16**	**17**



SCHEME 1



SCHEME 2

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