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Journal of Chemical and Pharmaceutical Research, 2017, 9(10):34-42

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Synthesis, Characterization and Antimicrobial Evaluation of Novel Compounds of 3-((benzo[d]oxazol-2-ylmethyl) Amino)-1-(2,5-difluorobenzoyl)-4-(2-phenyl hydrazono)-1H-Pyrazol-5(4H)-one

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ABSTRACT

New novel derivatives of 3-((benzo[d]oxazol-2-ylmethyl)amino)-1-(2,5-difluorobenzoyl)-4-(2-(4-(substituted)phenyl)hydrazono)-1H-pyrazol-5(4H)-one (5a-g) were prepared by refluxing a mixture of ethyl 2-(4-(2-(4-subtituted methyl)phenyl)hydrazono)-1-(2,5-difluoro benzoyl)-4,5-dihydro-5-oxo-1H-pyrazol-3-yl)amino Carboxylic acid. (4a-g) and 2- amino phenol, polyphosphoric acd, dichloro methane and cyclo hexane. The synthone 4a-g were synthesized by refluxing a mixture of 2 a-g and tetra hydro furan. The newly synthesized compounds were characterized by IR, 1H-NMR, 13C-NMR, mass spectra and elemental analysis. The newly synthesized compounds were screened for their Biological activity.

Keywords: Benzoxazole; 2-amino phenol; Antibacterial; Antifungal activity; Spectral data

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INTRODUCTION

Benzoxazole

Biologically potent benzoxazole derivatives have been known for long time, since they are the isosters of naturally occuring cyclic nucleotides and they may easily interact with the biopolymers of the organisms [1].

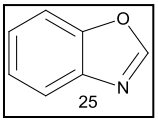
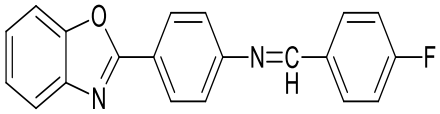
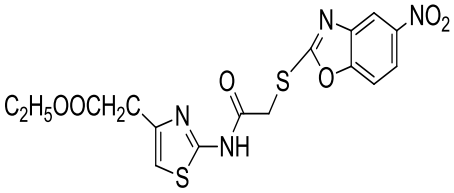
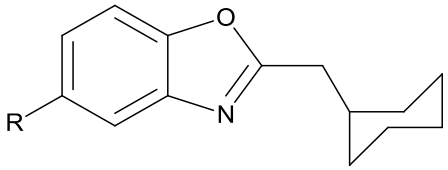
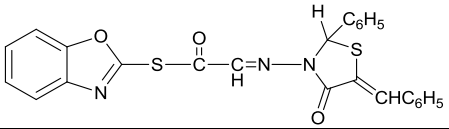
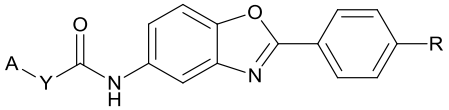
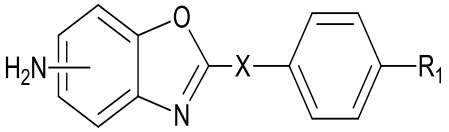
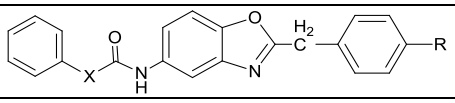
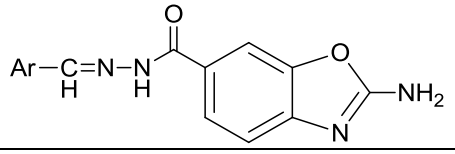


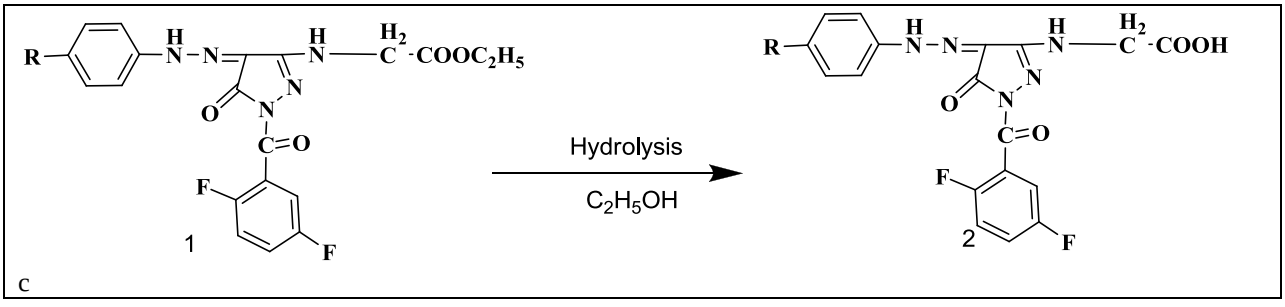
Figure 1: Benzoxazole

Literature survey of benzoxazoles revealed that they possess most remarkable and a wide range of biological activities [2]. The substituted benzoxazoles were found to exhibit insecticidal [2], antitumor [3], antihistaminic, antiparasitic, herbicidal, antiallergic, antihelmintic [4], COX-2 inhibitory [5], antitubercular, antibacterial, anticancer, antifungal, anticonvulsant [6], diarrhea-predominant irritable bowel syndrome [7], hypoglycaemic [8], HIV-1 reverse transcriptase inhibitor [9] activities (Scheme 1). It has also been found to have binding affinity to Aβ42 fibrils [10]. The review of literatures describes that the benzoxazole derivatives possess a variety of biological activities [11-18]. The synthetic route was depicted in Scheme 1. The title compounds 4 (a-g) were synthesised in four sequential steps using different reagents and reaction conditions, the 4(a-g) were obtained in moderate yields.

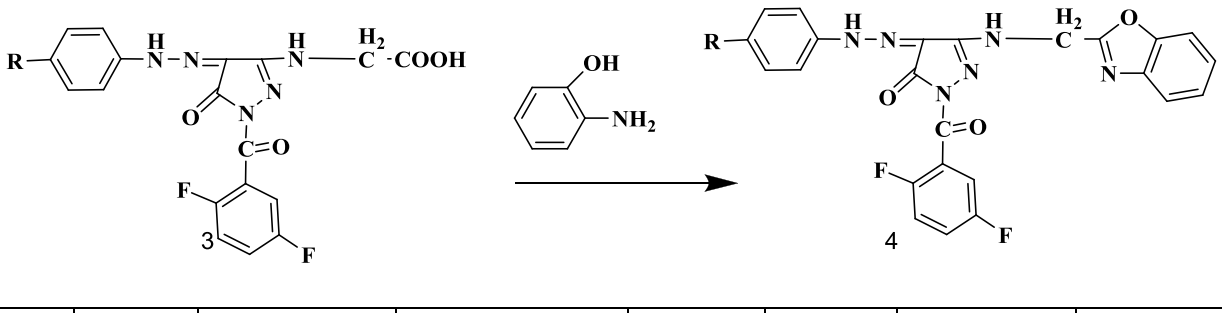
The structure were established by spectral (IR, ^{1}HNMR, ^{13}CNMR and mass) and analytical data (Figure 1 and Table 1).

Table 1: Biologically active benzoxazole derivatives

S.No	Compound	Activity	Reference
1		Antimicrobial	SK Saraf, et al. [1]
2		Antibacterial and antifungal	ZA Kaplancikli, et al. [2]
3		Antibacterial and anti-fungal	I Yalcin, et al. [3]
4		Antimicrobial	P Kohli, et al. [4]
5		Microbiological	EA Sener, et al. [5]
6		Antibacterial and antifungal	I Yildiz, et al. [6]
7		Antibacterial	IY Oren, et al. [7]
8		COX-2 inhibitory	S Garrepalli, et al. [8]



c



R	-H	-CH3	-OCH_3	-Cl	Br	NO_2	CF_3

Scheme 1: Reagents and reaction conditions: (a) ester tetra hydro furan/MeOH/H_2O, NaOH, reflx 4-6 hr, washed with EtOA, 1 N HCl, anhydrous Na_2SO_4 (b) rflex 2h, 6N HCl, ((9:1) cyclo hexane, ethyl acetate, $NaHCO_3$, coloumn chromatography, chloroform (c) reflx 2 hr at ortho phenylene diamine cyclo hexane, ethyl acetate, dichloro methane, aq NaOH (1N), evopareted by RE, unhydrous Na_2SO_4, chloroform

EXPERIMENTAL SECTION

Materials and Methods

All the chemicals used in the present investigation were purchased from Sigma-Aldrich Chemicals Company, Inc., USA and used without further purification. TLC was performed on aluminum sheet of silica gel 60F254, E-Merk,Germany using iodine as visualizing agent. Melting point was determined in open capillary tubes on Mel-Tempapparatus and is uncorrected. Column chromatography was performed on silica gel with different solvent systemsas eluents to afford the pure compound. The IR Spectra were recorded as KBr pellets on Perkin-Elmer 1000 units, instruments. All 1H and 13C-NMR spectra were recorded on a Varian XL-300 spectrometer operating at 400 MHz for 1H -NMR and 75 MHz for ^{13}C-NMR were recorded on a Varian XL-spectrometer operating at161.89 MHz. The compounds were dissolved in DMSO-d6 and Chemical shifts were referenced to TMS (1H and^{13}C-NMR). Mass spectral data were recorded on FAB-MS instrument at 70 ev with direct inlet system. Elemental analysis was recorded on a Carlo Erba 1108 elemental analyzer at Central Drug Research Institute, Lucknow, India.

RESULTS AND DISCUSSION

Synthesis of Ethyl 2-(4-(2-(4-subtituted methyl) phenyl)hydrazono)-1-(2,5-difluoro benzoyl)-4,5-dihydro-5-oxo-1H-pyrazol-3-yl)amino Carboxylic Acid

To a solution of ester (2a,1eq) in tetra hydro furan/MeOH/H_2O(1:1:1) ratio aq NaOH(2 N) was added and stirred (room temp) or reflux for 4-6 hrs. After completion of the reaction as indicated by TLC using mobile phase as cyclohexane and ethyl acetate (7:3) the a residue was washed with EtOA(removing impurities). The solvent was evaporated under vaccum to affored 3a-g. After the residue was acidified with 1N HCl up to PH-2 to give solid suspension, which filtered extracted with EtOAc (2×30 ml) twice. The organic layer was collected washed with water brain dried over anhydrous Na_2SO_4 filtered and evaporated under vacuum to give the crude acid product (4-(2-(4-substituted) phenyl) hydrazono)-1-(2,5-difluorobenzoyl)-4,5-dihydro-5-thioxo-1H-pyrazole-3-yl)amino carboxylic acid(3a).

Synthesis of 3-(((1H-benzo[d]imidazol-2-yl) methyl) amino)-1-(2, 5-difluorobenzoyl)-4-(2-(4-Substituted) phenyl) hydrazono)-1H-pyrazol-5(4H)-one (5a-g)

A mixture of (4-(2-(4-phenyl)hydrazono)-1-(2,5-difluoro benzoyl)-4,5-dihydro-5-oxo-1H-pyrazol-3-yl)amino Carboxylic acid (3a) and ortho phenylene diamine in 1:1 eqivalent ratio was refluxed for 2 h at 100°C in presence of 6 N HCl. The progress of the reaction was monitored by TLC using 9:1 hexane and ethyl acetate solvent mixture as mobile phase. After completion of the reaction, the reaction mixture was neutralized by $NaHCO_3$. The crude product 3-(((1H-benzo[d]imidazol-2-yl)methyl)amino)-1-(2,5-difluorobenzoyl)-4-(2-(Phenylhydrazono)-1H-pyrazol-5(4H)-one(4a) was purified by using silica gel 60-120 mesh and Chloroform was used as an elutent. The yield of 4a was found to 70%, mp 160-162°C. The similar procedure was adopted to synthesize 4 b-g from 3 b-g and O-phenyldiamine.

Physical, Analytical and Spectral Data for the Compounds

3-((benzo[d]oxazol-2-ylmethyl) amino)-1-(2,5-difluorobenzoyl)-4-(2-phenylhydrazono)-1H-pyrazol-5(4H)-one (5a):

Yield 70%, mp: 160-162°C. **IR (KBr):** 3381(-NH str.), 3040(Ar-Hstr.), 1694(exocyclic >C=O), 1654(>C=O of pyrazoline-5-one), 1617 cm^{-1} (>C=N- group) and 1100 cm^{-1}(C-F str.). ^{1}H-NMR (400 MH_Z DMSO-d6):) δppm 2.0(s, H, NH attached to pyrazoline-5-one ring), 3.91(t, 2H, -CH2 of 1H benzo [d] imidazole group), 5.0(s,^{1}H,-NH of imidazole group), 10.15(s,1H,Ar-NH-N= Group) and 6.81-7.59(m,12H C_6H_5 C_6H_4 and C_6H_3) respectively.

^{13}CNMR(75MHz, DMSO-d6): 143.0, 113.9, 129.5, 122.4, 136.8, 162.1, 142.7, 170.2, 126.7, 154.9, 118.7, 120.5, 158.6, 113.9, 120.9, 117.5, 37.5, 141.5, 123, 115.2 and 123.7 corresponding to C_1, C_2&C_6, C_3&C_5, C_4, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{15}, C_{16}, C_{17}, C_{18}, C_{19}&C_{24}, C_{20}&C_{23} and C_{21}&C_{22} respectively. Anal calcd for $C_{24}H_{17}F_2N_7O_2$ C 57.72%, H 2.25% and N14.39%. Found: C 57.42%, H 1.93% and N 14.02%.

3-((benzo[d]oxazol-2-ylmethyl) amino)-1-(2,5-difluorobenzoyl)-4-(2-(4-(trifluoromethyl) phenyl)hydrazono)-1H-pyrazol-5(4H)-one (5b):

Yield 72%, mp: 163-165°C. **IR (KBr):** 3381(-NH str.), 3040(Ar-Hstr.), 1694(exocyclic >C=O), 1654(>C=O of pyrazoline-5-one), 1617 cm^{-1} (>C=N- group) and 1100 cm^{-1}(C-F str.). ^{1}H-NMR (400 MH_Z DMSO-d6) δppm 2.0(s, H, NH attached to pyrazoline-5-one ring), 3.91(t, 2H, -CH2 of 1H benzo [d] imidazole group), 5.0(s,^{1}H,-NH of imidazole group) 10.15(s,1H,Ar-NH-N= Group) and 6.81-7.59(m,12H C_6H_5 C_6H_4 and C_6H_3), respectively.

^{13}CNMR(75MHz,DMSO-d6): 143.0, 113.9, 129.5, 122.4, 136.8, 162.1, 142.7, 170.2, 126.7, 154.9, 118.7, 120.5, 158.6, 113.9, 120.9, 117.5, 37.5, 141.5, 123, 115.2 and 123.7 corresponding to C_1, C_2&C_6, C_3&C_5, C_4, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{15}, C_{16}, C_{17}, C_{18}, C_{19}&C_{24}, C_{20}&C_{23} and C_{21}&C_{22} respectively. Anal calcd for $C_{24}H_{17}F_2N_7O_2$ C 57.72%, H 2.25% and N14.39%. Found: C 57.42%, H 1.93% and N 14.02%.

3-((benzo[d]oxazol-2-ylmethyl) amino)-1-(2,5-difluorobenzoyl)-4-(2-(4-methoxyphenyl)hydrazono)-1H-pyrazol-5(4H)-one (5c):

Yield 73%. mp: 165-167°C. **IR (KBr)**: 3381(-NH str.), 3040(Ar-Hstr.), 1694(exocyclic >C=O), 1654(>C=O of pyrazoline-5-one), 1617 cm^{-1} (>C=N- group) and 1100 cm^{-1} (C-F str.)^{1}H-NMR (400 MH_Z DMSO-d6) δppm 2.0(s, H, NH attached to pyrazoline-5-one ring), 3.91(t,2H, -CH2 of 1H benzo [d] imidazole group), 5.0(s,^{1}H,-NH of imidazole group), 10.15(s,1H,Ar-NH-N= Group) and 6.81-7.59(m,12H C_6H_5 C_6H_4 and C_6H_3), respectively.

^{13}CNMR(75MHz,DMSO-d6): 143.0, 113.9, 129.5, 122.4, 136.8, 162.1, 142.7, 170.2, 126.7, 154.9, 118.7, 120.5, 158.6, 113.9, 120.9, 117.5, 37.5, 141.5, 123, 115.2 and 123.7 corresponding to C_1, C_2&C_6, C_3&C_5, C_4, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{15}, C_{16}, C_{17}, C_{18}, C_{19}&C_{24}, C_{20}&C_{23} and C_{21}&C_{22} respectively. Anal calcd for $C_{24}H_{17}F_2N_7O_2$ C 57.72%, H 2.25% and N14.39%. Found: C 57.42%, H 1.93% and N 14.02%.

3-((benzo[d]oxazol-2-ylmethyl) amino)-4-(2-(4-bromophenyl)hydrazono)-1-(2,5-difluoro benzoyl)-1H-pyrazol-5(4H)-one (5d):

Yield 70%, mp: 160-162°C. **IR (KBr):** 3381(-NH str.) 3040(Ar-Hstr.), 1694(exocyclic >C=O), 1654(>C=O of pyrazoline-5-one), 1617 cm^{-1} (>C=N- group) and 1100 cm^{-1} (C-F str.). ^{1}H-NMR (400 MH_Z DMSO-d6) δppm 2.0(s, H, NH attached to pyrazoline-5-one ring), 3.91(t,2H, -CH2 of 1H benzo [d] imidazole group), 5.0(s,^{1}H,-NH of imidazole group), 10.15(s,1H,Ar-NH-N= Group) and 6.81-7.59(m,12H C_6H_5 C_6H_4 and C_6H_3) respectively.

^{13}CNMR(75MHz,DMSO-d6): 143.0, 113.9, 129.5, 122.4, 136.8, 162.1, 142.7, 170.2, 126.7, 154.9, 118.7, 120.5, 158.6, 113.9, 120.9, 117.5, 37.5, 141.5, 123, 115.2 and 123.7 corresponding to C_1, C_2&C_6, C_3&C_5, C_4, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{15}, C_{16}, C_{17}, C_{18}, C_{19}&C_{24}, C_{20}&C_{23} and C_{21}&C_{22} respectively. Anal calcd for $C_{24}H_{17}F_2N_7O_2$ C 57.72%, H 2.25% and N14.39%. Found: C 57.42%, H 1.93% and N 14.02%.

3-((benzo[d]oxazol-2-ylmethyl) amino)-4-(2-(4-chlorophenyl) hydrazono)-1-(2,5-difluoro benzoyl)-1H-pyrazol-5(4H)-one(5e):

Yield 70%, mp: 160-162°C. **IR (KBr):** 3381(-NH str.), 3040(Ar-Hstr.), 1694(exocyclic >C=O), 1654(>C=O of pyrazoline-5-one), 1617 cm^{-1} (>C=N- group) and 1100 cm^{-1} (C-F str.). ^{1}H-NMR (400 MH_Z DMSO-d6) δppm 2.0(s, H, NH attached to pyrazoline-5-one ring), 3.91(t,2H, -CH2 of 1H benzo [d] imidazole group), 5.0(s,^{1}H,-NH of imidazole group), 10.15(s,1H,Ar-NH-N= Group) and 6.81-7.59(m,12H C_6H_5 C_6H_4 and C_6H_3), respectively.

^{13}CNMR(75MHz,DMSO-d6): 143.0, 113.9, 129.5, 122.4, 136.8, 162.1, 142.7, 170.2, 126.7, 154.9, 118.7, 120.5, 158.6, 113.9, 120.9, 117.5, 37.5, 141.5, 123, 115.2 and 123.7 corresponding to C_1, C_2&C_6, C_3&C_5, C_4, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{15}, C_{16}, C_{17}, C_{18}, C_{19}&C_{24}, C_{20}&C_{23} and C_{21}&C_{22} respectively. Anal calcd for $C_{24}H_{17}F_2N_7O_2$ C 57.72% , H 2.25% and N14.39%. Found: C 57.42%, H 1.93% and N 14.02%.

3-((benzo[d]oxazol-2-ylmethyl)amino)-1-(2,5-difluorobenzoyl)-4-(2-(4-nitrophenyl) hydrazono)-1H-pyrazol-5(4H)-one(5f):

Yield 69%, mp: 161-162°C. **IR (KBr):** 3381(-NH str.), 3040(Ar-Hstr.), 1694(exocyclic >C=O), 1654(>C=O of pyrazoline-5-one), 1617 cm^{-1} (>C=N- group) and 1100 cm^{-1} (C-F str.). ^{1}H-NMR (400 MH_Z DMSO-d6) δppm 2.0(s, H, NH attached to pyrazoline-5-one ring), 3.91(t, 2H, -CH2 of 1H benzo [d] imidazole group), 5.0(s, ^{1}H, -NH of imidazole group), 10.15 (s, 1H, Ar-NH-N= Group) and 6.81-7.59(m, 12H C_6H_5 C_6H_4 and C_6H_3) respectively.

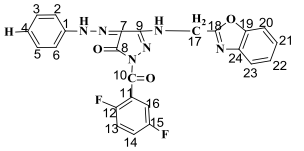
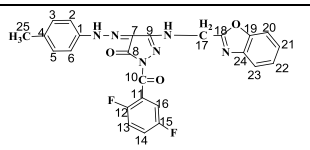
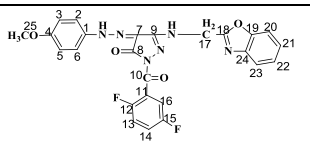
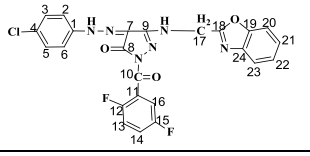
^{13}CNMR (75MHz,DMSO-d6): 143.0, 113.9, 129.5, 122.4, 136.8, 162.1, 142.7, 170.2, 126.7, 154.9, 118.7, 120.5, 158.6, 113.9, 120.9, 117.5, 37.5, 141.5, 123, 115.2 and 123.7 corresponding to C_1, C_2&C_6, C_3&C_5, C_4, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{15}, C_{16}, C_{17}, C_{18}, C_{19}&C_{24}, C_{20}&C_{23} and C_{21}&C_{22} respectively. Anal calcd for $C_{24}H_{17}F_2N_7O_2$ C 57.72%, H 2.25% and N14.39%. Found: C 57.42%, H 1.93% and N 14.02%.

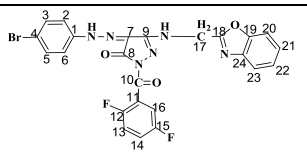
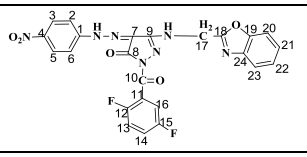
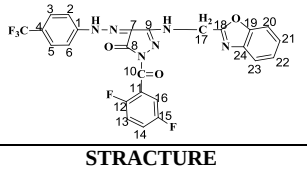
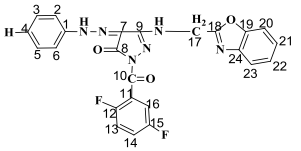
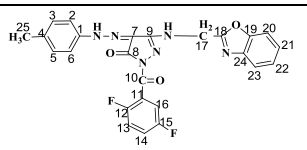
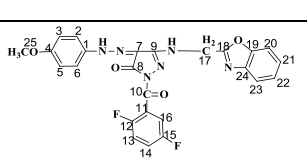
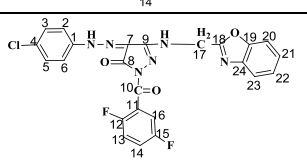
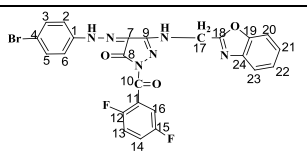
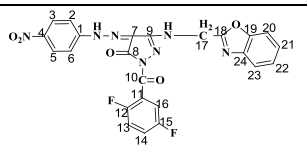
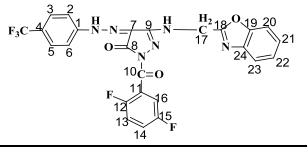
3-((benzo[d]oxazol-2-ylmethyl) amino)-1-(2,5-difluorobenzoyl)-4-(2-(4-(trifluoromethyl) phenyl) hydrazono)-1H-pyrazol-5(4H)-one (5g):

Yield 70%, mp: 160-162°C. **IR (KBr):** 3381(-NH str.), 3040(Ar-Hstr.), 1694(exocyclic >C=O), 1654(>C=O of pyrazoline-5-one), 1617 cm^{-1} (>C=N- group) and 1100 cm^{-1} (C-F str.). ^{1}H-NMR (400 MH_Z DMSO-d6) δppm 2.0(s, H, NH attached to pyrazoline-5-one ring), 3.91(t,2H, -CH2 of 1H benzo [d] imidazole group), 5.0(s,^{1}H,-NH of imidazole group), 10.15(s,1H,Ar-NH-N= Group) and 6.81-7.59(m,12H C_6H_5 C_6H_4 and C_6H_3) respectively.

^{13}CNMR(75MHz,DMSOd6): 143.0, 113.9, 129.5, 122.4, 136.8, 162.1, 142.7, 170.2, 126.7, 154.9, 118.7, 120.5, 158.6, 113.9, 120.9, 117.5, 37.5, 141.5, 123, 115.2 and 123.7 corresponding to C_1, C_2&C_6, C_3&C_5, C_4, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{15}, C_{16}, C_{17}, C_{18}, C_{19}&C_{24}, C_{20}&C_{23} and C_{21}&C_{22} respectively (Table 2). Anal calcd for *$C_{24}H_{17}F_2N_7O_2$ C 57.72%, H 2.25% and N14.39%. Found: C 57.42%, H 1.93% and* N 14.02%.

Table 2: 13NMR massspectra

S.No	R	STRACTURE	^{13}C-NMR SPECTRA (DMSO-d6(δ,ppm),
4a	**H**		143.0, 113.9, 129.5, 122.4, 136.8, 162.1, 142.7, 170.2, 126.7, 154.9, 118.7, 120.5, 158.6, 113. 9, 43.3, 152.6, 150.0, 110.6, 123.8, 119.1, 141.5 Corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{15}, C_{16}, C_{17}, C_{18}, C_{19}, C_{20}, C_{21}, C_{22} , C_{23}, C_{24}.
4b	**CH_3**		140.0, 116.2, 129.8, 131.2, 136.8, 162.1, 142.7, 170.2, 126.7, 154.9, 118.7, 120.5, 158.6, 113.9, 43.3, 152.6, 150.0, 110.6, 123.8, 119.1, 141.5 Corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{15}, C_{16}, C_{17}, C_{18}, C_{19}, C_{20}, C_{21}, C_{22}, C_{23}, C_{24}, C_{25},
4c	**OCH_3**		124.6, 117.3, 115.1, 153.3, 136.8, 162.1, 142.7, 170.2, 126.7, 154.9, 118.7, 120.5, 158.6, 113.9, 43.3, 152.6, 150.0, 110.6, 123.8, 119.1, 141.5 Corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{15}, C_{16}, C_{17}, C_{18}, C_{19}, C_{20}, C_{21}, C_{22}, C_{23}, C_{24}, C_{25}
4d	**Cl**		141.1, 117.7, 129.6, 127.7, 136.8, 162.1, 142.7, 170.2, 126.7, 154.9, 118.7, 120.5, 158.6, 113.9, 43.3, 152.6, 150.0, 110.6, 123.8, 119.1, 141.5 Corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8 , C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{15}, C_{16}, C_{17}, C_{18}, C_{19}, C_{20}, C_{21}, C_{22}, C_{23}, C_{24}.

4e	**Br**		142.0, 117.0, 132.4, 116.7, 136.8, 162.1, 142.7, 170.2, 126.7, 154.9, 118.7, 120.5, 158.6, 113.9 , 43.3, 152.6, 150.0, 110.6, 123.8, 119.1, 141.5, Corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{15}, C_{16}, C_{17}, C_{18}, C_{19}, C_{20}, C_{21} , C_{22}, C_{23}, C_{24}.
4f	**NO_2**		149.1, 113.2, 124.7, 137.9, 136.8, 162.1, 142.7, 170.2, 126.7, 154.9, 118.7, 120.5, 158.6, 113.9, 43.3, 152.6, 150.0, 110.6, 123.8, 119.1, 141.5 Corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7 , C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{15}, C_{16}, C_{17}, C_{18}, C_{19}, C_{20}, C_{21}, C_{22}, C_{23}, C_{24}.
4g	**CF_3**		146.3, 116.6, 120.3, 126.5, 136.8, 162.1, 142.7, 170.2, 126.7, 154.9, 118.7, 120.5, 158.6, 113.9, 43.3, 152.6, 150.0, 110.6, 123.8, 119.1, 141.5 Corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{15}, C_{16}, C_{17}, C_{18}, C_{19}, C_{20}, C_{21}, C_{22} , C_{23}, C_{24}, C_{25}.l
S.No	**R**	**STRACTURE**	**^{13}C-NMR SPECTRA (DMSO-d6(δ, ppm)**
4a	**H**		143.0, 113.9, 129.5, 122.4, 136.8, 162.1, 142.7, 170.2, 126.7, 154.9, 118.7, 120.5, 158.6, 11 3.9, 43.3, 152.6, 150.0, 110.6, 123.8, 119.1, 141.5 Corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{15}, C_{16}, C_{17}, C_{18}, C_{19}, C_{20}, C_{21}, C_{22} , C_{23}, C_{24}.
4b	**CH_3**		140.0, 116.2, 129.8, 131.2, 136.8, 162.1, 142.7, 170.2, 126.7, 154.9, 118.7, 120.5, 158.6, 113.9, 43.3, 152.6, 150.0, 110.6, 123.8, 119.1, 141.5 Corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{15}, C_{16}, C_{17}, C_{18}, C_{19}, C_{20}, C_{21}, C_{22}, C_{23}, C_{24}.C_{25},
4c	**OCH_3**		124.6, 117.3, 115.1, 153.3, 136.8, 162.1, 142.7, 170.2, 126.7, 154.9, 118.7, 120.5, 158.6, 113.9, 43.3, 152.6, 150.0, 110.6, 123.8, 119.1, 141.5 Corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{15}, C_{16}, C_{17}, C_{18}, C_{19}, C_{20}, C_{21}, C_{22} , C_{23}, C_{24}.C_{25},
4d	**Cl**		141.1, 117.7, 129.6, 127.7, 136.8, 162.1, 142.7, 170.2, 126.7, 154.9, 118.7, 120.5, 158.6, 113.9, 43.3, 152.6, 150.0, 110.6, 123.8, 119.1, 141.5 Corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8 , C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{15}, C_{16}, C_{17}, C_{18}, C_{19}, C_{20}, C_{21}, C_{22}, C_{23}, C_{24}.
4e	**Br**		142.0, 117.0, 132.4, 116.7, 136.8, 162.1, 142.7, 170.2, 126.7, 154.9, 118.7, 120.5, 158.6, 113.9 , 43.3, 152.6, 150.0, 110.6, 123.8, 119.1, 141.5, Corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{15}, C_{16}, C_{17}, C_{18}, C_{19}, C_{20}, C_{21} , C_{22}, C_{23}, C_{24}.
4f	**NO_2**		149.1, 113.2, 124.7, 137.9, 136.8, 162.1, 142.7, 170.2, 126.7, 154.9, 118.7, 120.5, 158.6, 113.9, 43.3, 152.6, 150.0, 110.6, 123.8, 119.1, 141.5Corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7 , C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{15}, C_{16}, C_{17}, C_{18}, C_{19}, C_{20}, C_{21}, C_{22}, C_{23}, C_{24}.
4g	**CF_3**		146.3, 116.6, 120.3, 126.5, 136.8, 162.1, 142.7, 170.2, 126.7, 154.9, 118.7, 120.5, 158.6, 113.9, 43.3, 152.6, 150.0, 110.6, 123.8, 119.1, 141.5, Corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14}, C_{15}, C_{16}, C_{17}, C_{18}, C_{19}, C_{20}, C_{21}, C_{22} , C_{23}, C_{24}.C_{25},

Mass Spectra

The electron impact mass spectrum of 3-((benzo[d]oxazol-2-ylmethyl) amino)-1-(2, 5-difluorobenzoyl)-4-(2-(4-(trifluoromethyl)phenyl)hydrazono)-1H-pyrazol-5(4H)-one(5a) was recorded and interpreted. The mass spectral data of compound (5a) showed the molecular ion [M^+] ion peak at m/z=473.10(100%) it appeared as a base peak and

indicates the presence of odd number of nitrogen atoms. The molecular ion signal was obeying nitrogen rule, but primary fragmented ions derived from molecular ion may or may not obeying nitrogen rule (Table 3).

Table 3: Mass spectral data of primary fragmented ions for 3-((benzo[d]oxazol-2-ylmethyl)amino)-1-(2, 5-difluorobenzoyl)-4-(2-(4-(trifluoromethyl)phenyl)hydrazono)-1H-pyrazol-5(4H)-one(5a)

Molecular ion	Lost radical	Primary fragmented ion	m/z values	Relative abundance (R.A) (%)
$C_{24}H_{16}F_2N_6O_3$ m/z=472.13 (100%)	$C_{18}H_{13}N_6O_3$ •	$C_6H_3F_2^+$ (II)	114.02	6.5
	$C_6H_3F_2$ •	$C_{18}H_{13}N_6O_3^+$ (III)	378.09	19.7
	$C_{17}H_{14}N_6O2$ •	$C_7H_3F_2O^+$ (IV)	142.02	7.6
	$C_7H_3F_2O$ •	$C_{17}H_{14}N_7O2^+$ (V)	351.10	20.7
	C_6H_6N •	$C_{18}H_{11}F_2N_5O_3^+$ (VI)	400.06	19.7
	$C_{18}H_{11}F_2N_5O_3$ •	$C_6H_6NO^+$ (VII)	93.05	6.9
	$C_{16}H_{10}F_2N_5O_2$ •	$C_8H_6NS^+$ (VIII)	149.03	8.8
	C_8H_6NO •	$C_{16}H_{10}F_2N_5O_3^+$ (IX)	343.08	19.2
	$C_{17}H_{12}F_2N_5O_2$ •	$C_7H_4NO^+$ (X)	135.01	8.3
	C_7H_4NO •	$C_{17}H_{12}F_2N_5O_2^+$ (XI)	114.02	6.5

Biological Activity

The atimicrobial profile of 3-(((1H-benzo[d]oxazol-2-yl) methyl) amino)-1-(2, 5-difluorobenzoyl)-4-(2-phenylhydrazono)-1H-pyrazol-5(4H)-one (5a-g):

The synthesis and characterization of Aryl hydrazono-Pyrazoline-5-ones bearing benzo[d]imidazol-2-yl) methyl) moiety the antibacterial and antifungal activity of 5(a-g) were studied and incorporated. The experimental results pertaining to the zone of Inhibition (mm) of 5(a-g) were shown below. Each well contains 25 and 50 µg of compounds; Ch=Chloromphenicol 5 µg/mL, Ketocanazole 50 µg/mL (Figure 2 and Table 4).

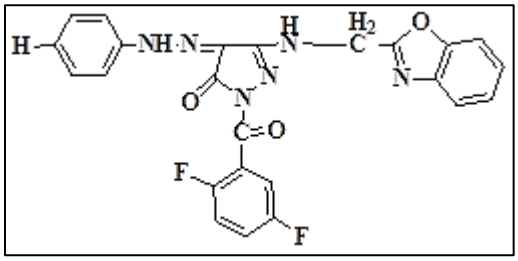


Figure 2: Aryl hydrazono-Pyrazoline-5-one

Table 4: Parameters of bacteria and fungi

Entry	Bacteria						Fungi			
	Staphylococcus aureus NCCS2079		*Bacillus cereus* NCCS 2106		*Escherichia coli* NCCS2065		*Aspergillus niger* NCCS 1196		*Candida albicans* NCCS 2106	
	25	50	25	50	25	50	25		25	50
5a	-	9	-	8	-	7	-		-	11
5b	-	7	-	7	-	6	-		-	10
5c	-	8	-	10	-	9	-		-	12
5d	6	10	9	10	4	8	6		8	9
5e	10		10		7		8	13	7	
5f	9		10		6		7	12	6	
5g	13		13		10		11	16	12	
Chloromphenicol (5)	-		-		-		-	-	-	
Ketocanazole -50	-		-		-		-	22	-	

The antibacterial activity of 3-(((1H-benzo[d]oxazol-2-yl)methyl)amino)-1-(2, 5-difluorobenzoyl)-4-(2-phenylhydrazono)-1H-pyrazol-5(4H)-one (5a-g) was screend against the gram-positive bacteria *Staphylococcus aureus* NCCS 2079 and *Bacillus cereus* NCCS 2106. The gram negative bacteria used was *Escherichia coli* 2065. The antibacterial results reveal that most of the compounds exhibit good antibacterial activity against both bacteria at the concentration of 50 µg/mL. The presence of nitro (5f), tri fluoro methyl (5g), Chloro (5d) and Bromo (5e) were showed more activity than other substituted compounds. Chloromphenicol was used as reference compound to compare the activity. The anti-fungal activity of 3-(((1H-benzo[d]oxazol-2-yl) methyl)amino)-1-(2, 5-difluorobenzoyl)-4-(2-phenylhydrazono)-1H-pyrazol-5(4H)-one (5a-g) was screened against the *Aspergillus niger* NCCS1196 and *Candida albicans* NCCS 2106. The antifungal results reveal that most of the compounds exhibit good anti-fungal activity against both fungi at the concentration of 50 µg/mL. The presence of nitro (5f), tri fluoro methyl (5g), Chloro (5d) and Bromo (5e) were showed more activity than other substituted compounds. Here Ketocanazole was used as reference compound to compare the activity. The order of anti-microbial activity (50 µg/mL) 5f>5g >5d>5e>5c>5a>5b.

CONCLUSION

Hetero cyclic compound containing Benzoxazol nucleus plays most important role in biological systems. Benzoxazole and its derivatives are used for biological activities. Such as antiviral, antibacterial, antifungal and antitubercular. Vast number of benzimidazole derivative compounds have been synthesized and evaluated for their biological activity

ACKNOWLEDGEMENT

The author is very thankful to UGC authorities, New Delhi for providing UGC BSR SAP fellowship to carry out present research work and also thankful to IICT, Hyderabad and CDRI to get spectral data. The author expresses sincere thanks to Dept. of Chemistry, Sri Krishna Deveraya University for carrying out research work.

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