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SYNTHESIS, CHARACTERISATION, MOLECULAR DOCKING AND ANTI-MICROBIAL EVALUATION OF NOVEL 2-(4-SUBSTITUTED PHENOXY-1,3,2-BENZODIOXA PHOSPHOLE-2-OXIDE DERIVATIVES CONTAINING 1,3,4-OXADIAZOLE-4-THIAZOLIDINONE

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ABSTRACT

The reaction of pyrazole derivative (3) with mono chloro ethyl formate in presence or triethyl amine as base resulted ethyl-4-(((3,4-dimethoxyphenyl)imino)methyl-5-oxo-3-(trifluoro methyl)-4,5-dihydro-1H-pyrazole-1-carboxylate (4) which on further with mercapto acetic acid and catalytic amount of znic chloride in 1,4- dioxane affords the ethyl-4-(3-(3,4-dimethoxyphenyl)-4-oxothiazolidin-2-yl)-5-oxo-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazole-1-carboxylate (5). The synthon (5) reacts with hydrazine hydrate followed by acetophenone forms 4-(3-(3,4-dimethoxyphenyl)-4-oxothiazolidin-2-yl)-5-oxo-N'-(1-phenylethylidene)-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazole-1-carbo hydrazide (8). Acetylation of hydazone derivative (8) followed by internal rearrangement gives analogue(9) which on hydrolysis affords 2-(1-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-5-oxo-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazol-4-yl)-3-(3,4-dihydroxy phenyl)thiazolidin-4-one (10)A new series of 2-(1-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-5-oxo-3(trifluoro methyl)-4,5-dihydro-1H-pyrazol-4-yl)-3-(2-oxido-2-(4-substituted phenoxy) benzo[d] [1,3,2]dioxaphosphol-5-yl)thiazolidin-4-one (12a-f) were synthesized from 2-(1-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-5-oxo-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazol-4-yl)-3-(3,4-dihydroxy phenyl)thiazolidin-4-one (10) by condensing with 4-substituted phenyl phosphoro dichloridates (11a-f). The structures of these analogues (12a-f) have been established by ^{1}H NMR, IR, Mass spectral data and elemental analysis.

KEYWORDS: Monochloroethylformate, mercapto acetic acid, hydrazine hydrate, acetophenone, acetic anhydride, substituted phenylphosphorodichloridate, methoxy quinolone, thiazolidinone, oxadiazole.

INTRODUCTION

Oxadiazoles and its derivatives are associated with a variety of biological activities such as anti convulsent, anti depressant and antianxiety activities,[1] antibacterial activity,[2] antifungal activity,[3] herbicide,[4] Anti-inflammatory activity,[5-6] Thiazolidinones moiety is also associated with broad spectrum of biological activities including antibacterial.[7-8] antifungal.[9] anti-inflammatory,[10-12] hypnotic, anticonvulsant, antitubercular,[13] antiviral,[14-15] antihistaminic16, anthelmintic, cardio vascular and anticancer.[17]

Pyrazolone moiety have also been shown to possess high biological activities such as anticancer,[18] antifungal,[19] antipyretic,[20] antitubercular,[21] antihypertensive,[22] and antiviral.[23] The derivatives of pyrazolones are an important class of antipyretic and analgesic compounds.

Prompted by the above observations, a research project was undertaken to synthesize a series of organophosphorous heterocycles baring thiazolidinone moiety, pyrazolone moiety and 1,3,4-oxadiazole moiety in the same carbon skeleton structure.

Thus different 2-(1-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-5-oxo-3(trifluoromethyl)-4,5-dihydro-1H-pyrazol-4-yl)-3-(2-oxido-2-(4-substi tuted phenoxy)benzo[d][1,3,2]dioxaphosphol-5-yl)thiazolidin-4-one (12a-f) were synthesized. The structures of these analogues have been established by Mass, NMR, IR studies, elemental analysis and synthesis.

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 aluminium sheet of silica gel 60F254, E-Merk, Germany using iodine as visualizing agent. Melting points were determined in open capillary tubes on Mel-Temp apparatus and are uncorrected.The IR

spectra were recorded as KBr pellets on PERKIN-Elmer 1000 units, instruments. All ^{1}H and ^{13}C-NMR spectra were recorded on a Varian XL-300 spectrometer operating at 400MHz for ^{1}H-NMR and 75MHz for ^{13}C-NMR respectively. ^{31}P-NMR spectrum was recorded on a Varian XL-spectrometer operating at 161.89MHz. The compounds were dissolved in DMSO-d_6 and chemical shifts were referenced to TMS (^{1}H and ^{13}C-NMR) and 85% H_3PO_4 (^{31}P-NMR). Elemental analysis was recorded on a Carlo Erba 1108 elemental Analyzer, Central Drug Research Institute, Lucknow, India.

Synthesis of ethyl-4-(((3,4-dimethoxyphenyl)imino)methyl-5-oxo-3-(trifluoro methyl)-4,5-dihydro-1H-pyrazole-1-carboxylate (4).

A mixture of 4-(((3,4-dimethoxyphenyl)imino)methyl)-3-(trifluoromethyl)-1-1H–pyrazol-5-(4H)-one (3,4.1grms, 0.013moles), K2CO3, Monochloroethylformate (1.62grms, 0.015moles) and triethylamine were stirred at room temperature for 8hrs. The reaction mixture was diluted with ice cold water. The progress of the reaction was monitored by TLC with hexane:ethylacetate (7:3) as mobile phase. The separated solid was identified as ethyl-4-(((3,4-dimethoxyphenyl)imino)methyl-5-oxo-3-(trifluoro methyl)-4,5-dihydro-1H-pyrazole-1-carboxylate (4,5.4grms, 0.014moles). This was recrystallized from 2-propanol.

The structure of ethyl-4-(((3,4-dimethoxyphenyl)imino)methyl-5-oxo-3-(trifluoro methyl)-4,5-dihydro-1H-pyrazole-1-carboxylate **(4)** was established by spectral analysis (IR and ^{1}H NMR) and elemental analysis.

Yield (70.00%). IR (KBr pellet), ν, cm^{-1}: 3040cm^{-1} (Ar-H str.),1710cm^{-1}(>C=O of ester group),1657cm^{-1}(>C=O str. of pyrazoline-5-one), 1620cm^{-1}(exoazomethine >C=N-H str),1500,1430,1375cm^{-1}(str. characteristics of pyrazoline-5-one ring), 1340cm^{-1}(C-F str band of CF_3) and 1240cm^{-1}(Ar-O-CH_3 str), 1150cm^{-1}(-C-O stretching of ester group). $^{1}HNMR$ (DMSO-d_6), δ, ppm 1.25(t,3H,J=12Hz,-CH_3 of ethyl group), 2.20(d,1H,J=7.50,-CH of pyrazoline -5-one ring), 3.40(s,6H, two –OCH_3 groups),4.20(q,2H,J=12Hz,-OCH_2 of ethyl group), 6.9-7.2(m,3H of aromatic ring) and 8.4(d,1H,J=7.50,>CH=N- exocyclic)., mp 134-136^{o}C. The elemental analysis of $C_{16}H_{16}F_3N_3O_5$ found %C,48.9, %H,3.99, %N,10.48, agreed well with the calculated %C,49.6,%H,4.1,%N,10.8.

Synthesis of ethyl-4-(3-(3,4-dimethoxyphenyl)-4-oxothiazolidin-2-yl)-5-oxo-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazole-1-carboxylate (5).

A mixture of ethyl-4-(((3,4-dimethoxyphenyl) imino)methyl-5-oxo-3-(trifluoro methyl)-4,5-dihydro-1H-pyrazole-1-carboxylate (4) (5.4grms,0.014moles) and mercapto acetic acid (0.01mol) were dissolved in dry 1,4-dioxane (20ml). A pinch of anhydrous zinc chloride was added and then refluxed for 8hrs. The progress of the reaction was monitored by TLC using n-hexane – ethyl acetate (7:3) as an eluent. After completion of the reaction the solvent was removed under reduced pressure in rota evaporator to give solid. The residue was then treated by solution of sodium bicarbonate to remove excess of mercapto acetic acid. The compound obtained was recrystallized from 2-propanal and petroleum ether (60-80℃) solvent mixture to afford ethyl-4-(3-(3,4-dimethoxyphenyl)-4-oxothiazolidin-2-yl)-5-oxo-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazole-1-carboxy late (5).

Yield (75.00%). IR (KBr pellet), ν, cm^{-1}: 3040cm^{-1} (Ar-H str.),1675cm^{-1}(>C=O of thiozolidine ring),1710cm^{-1}(>C=O of ester group),1657cm^{-1}(>C=O str. of pyrazoline-5-one), 1500,1430,1375cm^{-1}(str. characteristics of pyrazoline-5-one ring),1340cm^{-1}(C-F str band of CF_3),1240cm^{-1}(Ar-O-CH_3 str),1150cm^{-1}(-C-O stretching of ester group),619cm^{-1}(C-S, str. of thiazolidinone ring). $^{1}HNMR$ (DMSO-d_6), δ, ppm (J, Hz): 1.25(t,3H,J=12Hz, -CH_3 of ethyl group), 2.20 (d, 1H,J=14Hz,-CH of pyrazoline -5-one ring), 3.40 (s, 6H, two –OCH_3 groups), 3.80(d,1H,Ha of –CH_2 of thiazolidinone ring),3.90 (d, 1H,Hb of –CH_2 of thiazolidinone ring),4.20(q,2H,J=12Hz,-OCH_2 of ethyl group), 5.93(s,1H,J=14Hz,-CH- of thiazolidone ring), mp 154-166^{o}C. The elemental analysis of $C_{18}H_{18}F_3N_3O_6S$ found %C,46.3,%H,3.8,%N,8.87, agreed well with the calculated %C,46.8,%H,3.9,%N,9.1.

Synthesis 4-(3-(3,4-dimethoxyphenyl)-4-oxothiazolidin-2-yl)-5-oxo-3-(trifluoro methyl)-4,5-dihydro-1H-pyrazole-1-carbohydrazide (6).

A mixture of ethyl-4-(3-(3,4-dimethoxyphenyl)-4-oxothiazolidin-2-yl)-5-oxo-3-(trifluoro methyl)-4,5-dihydro-1H-pyrazole-1-carboxylate (5, 6.9grms,0.015 moles,) and hydrazine hydrate in ethanol was refluxed for 5hrs. The progress of the reaction was monitored by TLC with n-hexane: ethyl acetate (7:3) as mobile phase. The reaction mixture was cooled and poured on to ice cold water with stirring. The separated solid was filtered, washed with water and recrystallized from 2-propanol to afford 4-(3-(3,4-dimethoxyphenyl)-4-oxo thiazolidin-2-yl)-5-oxo-3-(trifluoromethyl)- 4,5-dihydro-1H-pyrazole-1-carbohydrazide (6).

Yield (5.00%). IR (KBr pellet), ν, cm^{-1}: 3457,3443cm^{-1}(NH_2 group of acid azide), 3220cm^{-1}(-NH- group of acid azide),3040cm^{-1} (Ar-H str.),1675cm^{-1}(>C=O of thiazolidinone ring),1690cm^{-1}(>C=O acid azide group),1657cm^{-1}(>C=O str. of pyrazoline-5-one),1500,1430,1375cm^{-1}(str. characteris tics of pyrazoline-5-one ring),1340cm^{-1}(C-F str band of CF_3), 1240cm^{-1}(Ar-O-CH_3 str),619cm^{-1}(C-S of thiazolidinone ring). $^{1}HNMR$ (DMSO-d_6), δ, ppm (J, Hz): 2.20(d,1H,J=14Hz,-CH of pyrazoline-5-one ring),3.40 (s,6H, two –OCH_3 groups),3.80(d,1H,Ha of –CH_2 of thiazolidinone ring), 3.90(d, 1H, Hb of –CH_2 of thiazolidinone ring),4.20(s,2H,-NH_2 of acid azide),5.93(s,1H,J=14Hz, CH- of thiazolidone ring),6.9-7.2(m,3H of aromatic ring) and 8.70(s,1H,-NH- of acid

azide), mp 147-149°C. The elemental analysis of $C_{16}H_{16}F_3N_5O_5S$
found %C,41.8.,%H,3.59.,%N,15.19...agreed well with the calculated %C, 42.9,%H,3.5,%N,15.6.

Synthesis of 4-(3-(3,4-dimethoxyphenyl)-4-oxothiazolidin-2-yl)-5-oxo-N'-(1-phenyl ethylidene)-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazole-1-carbo hydrazide (8).
In a typical procedure a mixture of 4-(3-(3,4-dimethoxyphenyl)-4-oxothiazolidin-2-yl)-5-oxo-3-(trifluoromethyl)-4,5 -dihydro-1H-pyrazole-1-carbohydrazide (6,5.8grms,0.013 moles) and acetophenone were refluxed in methanol containing a catalytic amount of glacial acetic acid for 4hrs. After usual workup the synthon (8) was obtained.

Yield (70.00%). IR (KBr pellet), ν, cm^{-1}: 3195cm^{-1}(-NH of acid hydrazone),3040cm^{-1} (Ar-H str.),1620cm^{-1}(>C=N of hydrazone),1340cm^{-1} (C-F str band of CF_3) and 1240cm^{-1}(Ar-O-CH_3 str),1675cm^{-1}(>C=O of thiazolidinone),1690cm^{-1}(>C=O acid azide group),1657cm^{-1} (>C=O str. of pyrazolin-5-one),1500,1430,1375cm^{-1}(str. characteristics of pyrazoline-5-one ring),619cm^{-1}(C-S of thiazolidinone ring). ^{1}HNMR (DMSO-d_6), δ, ppm (J, Hz): 2.20(d,1H,J=14Hz,-CH of pyrazoline -5-one ring),2.40(s,3H,-CH_3) 3.40(s,6H, two –OCH_3 groups),3.80(d,1H,Ha of –CH_2 of thiazolidinone ring), 3.90(d,1H,Hb of –CH_2 of thiazolidinone ring), 5.93(s,1H,J=14Hz,-CH-Ar of thiazolidone ring), 7.0-7.2(m,8H,C_6H_3 and C_6H_5 rings), 8.5(s,1H,-CO-NH-N=)., mp 170-172°C. The elemental analysis of $C_{24}H_{22}F_3N_5O_5S$ found %C,51.8, %H,3.89, %N,12.15, agreed well with the calculated %C,52.4,%H,4.0,%N,12.7.

Synthesis of 2-(1-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-5-oxo-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazol-4-yl)-3-(3,4-dimethoxy phenyl) thiazolidin-4-one(9)
In a typical procedure a mixture of hydrazone (8,7.6grms,0.014moles) and excess of acetic anhydride were dissolved in absolute ethanol-DMF solvent mixture. Reaction mixture was refluxed for 3 hours and then kept at room temperature overnight. The progress of the reaction was monitored by TLC using n-hexane + ethylacetate (7:3) as mobile phase. After completion of the reaction the solvent was removed in rotaevaporator. The gummy brown solid was recrystalised from 2-propanol-petroleum ether (60-80℃) solvent mixture to afford 2-(1-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-5-oxo-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazol-4-yl)-3-(3,4-dimethoxyphenyl) thiazolidin-4-one(9).

Yield (65.00%). IR (KBr pellet), ν, cm^{-1}: 3040cm^{-1} (Ar-H str.),1675cm^{-1}(>C=O str. of thiazolidinone ring),1657cm^{-1}(>C=O str. of pyrazoline-5-one),1500,1430, 1375cm^{-1} (str. characteristics of pyrazoline-5-one ring), 1340cm^{-1}(C-F str band of CF_3) and 1240cm^{-1} (Ar-O-CH_3 str),1690cm^{-1}(str. -C=O- of –N-C=O-CH_3 group),1626,1218cm^{-1}(1,3,4-oxadizole ring). ^{1}HNMR (DMSO-d_6), δ, ppm (J, Hz): 1.80(s,3H,-CH_3 of oxadiazole ring),2.10(s,3H,CO-CH_3),2.20(d,1H, J=14Hz,-CH of pyrazoline-5-one ring),3.40(s,6H, two –OCH_3 groups),3.80(d,1H,Ha of –CH_2 of thiazolidinone ring),3.90(d,1H,Hb of –CH_2 of thiazolidinone ring),5.93(s,1H,J=14Hz,-CH-Ar of thiazolidone ring),7-7.2(m,8H,C_6H_3 and C_6H_5 rings), mp 157-159°C. The elemental analysis of $C_{26}H_{24}F_3N_5O_6S$ found %C,51.7, %H,3.89, %N,11.3, agreed well with the calculated %C,52.7,%H,4.0,%N,11.8.

Synthesis of 2-(1-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-5-oxo-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazol-4-yl)-3-(3,4-dihydroxy phenyl)thiazolidin-4-one (10).
A mixture of synthon (9), methoxy quinolone as solvent and hydroiodic acid (5%) were refluxed in glass joined apparatus for 4hrs. The phenolic synthon 2-(1-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-5-oxo-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazol-4-yl)-3-(3,4-di hydroxyphenyl)thiazolidin-4-one (10) was liberated from the viscous hydroiodic acid by adding approximately the calculated amount of sodium carbonate solution, after neutralization, the reaction mixture was distilled under reduced pressure to afford crystallised product 2-(1-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-5-oxo-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazol-4-yl)-3-(3,4-dihydroxyphenyl) thiazolidin-4-one (10).

Yield (65.00%). IR (KBr pellet), ν, cm^{-1}: 3040cm^{-1} (Ar-H str.),1675cm^{-1}(>C=O of thiozolidine ring),1710cm^{-1}(>C=O of ester group),1657cm^{-1}(>C=O str. of pyrazoline-5-one), 1500,1430,1375cm^{-1}(str. characteristics of pyrazoline-5-one ring),1340cm^{-1}(C-F str band of CF_3), 1240cm^{-1}(Ar-O-CH_3 str),1150cm^{-1}(-C-O stretching of ester group),619cm^{-1}(C-S, str. of thiazolidinone ring). ^{1}HNMR (DMSO-d_6), δ, ppm (J, Hz): 1.25(t,3H,J=12Hz, -CH_3 of ethyl group), 2.20 (d, 1H,J=14Hz,-CH of pyrazoline -5-one ring), 3.40 (s, 6H, two –OCH_3 groups), 3.80(d,1H,Ha of –CH_2 of thiazolidinone ring),3.90 (d, 1H,Hb of –CH_2 of thiazolidinone ring),4.20(q,2H,J=12Hz,-OCH_2 of ethyl group), 5.93(s,1H,J=14Hz,-CH- of thiazolidone ring), mp 140-142°C. The elemental analysis of $C_{24}H_{20}F_3N_5O_6S$ found %C, 49.89, %H,3.39, %N,11.98, agreed well with the calculated %C,51.1, %H,3.5, %N,12.4.

Synthesis of 4-substituted phenyl phosphorodichloridates (11a-f):-
4-substituted phenyl phosphoro dichloridates (11a-f) were prepared as per literature peocedure.

Synthesis of 2-(1-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-5-oxo-3(trifluoromethyl)-4,5-dihydro-1H-pyrazol-4-yl)-3-(2-

oxido-2-(4-substit uted phenoxy)benzo[d][1,3,2]dioxaphosphol-5-yl)thiazolidin-4-one (12a-f).

A solution of phenylphosphorodichloridate (11a) in 25ml of dry toluene was added dropwise over a period of 20 mins to a stirred solution 2-(1-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-5-oxo-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazol-4-yl)-3-(3,4-di hydroxyphenyl)thiazolidin-4-one (10) and triethylamine in 30ml of dry toluene and 10ml of tetrahydrofuran at 5˚c,after completion of the addition, the temperature of the reaction mixture was slowly raised to room temperature and stirred for 2hrs.The reaction mixture was later heated to 50˚-60˚c and maintained for 4hrs with stirring. The completion of the reaction was monitored by TLC analysis using n-hexane and ethylacetate (7:3) as a mobile phase. Triethylamine hydrochloric acid was filtered from mixture and solvent was removed under reduced pressure. The residue was washed with water and then recrystallized from aqueous 2-propanol to get pure compound of 2-(1-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazole-2-yl)-5-oxo-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazol-4-yl)-3-(2-oxido-2 phenoxybenzo[d][1,3,2]dioxaphosphol-5-yl)thiazo lidin-4-one (12a).

The similar procedure was adopted to synthesis (12a-f) by the reaction of synthon (10) with (4-substituted phenyl) phosphorodichloridate (11a-f).

Physical,analytical and spectral data for the analogues (12a-f)

12a: Yield: 55.00%; IR (KBr pellet), ν, cm^{-1}: 3040cm^{-1} (Ar-H str.),1690cm^{-1}(>C=O group str. –N-C=O-CH_3),1657cm^{-1}(>C=O str. of pyrazoline-5-one),1626,1218cm^{-1}(1,3,4-oxadiazole ring),1500,1430,1375cm^{-1}(str of characteristic of pyrazoline-5-one ring),1675cm^{-1}(>C=O group of thiazolidinone ring) 1340cm^{-1}(C-F str band of CF_3),1255cm^{-1}(P=O str vibrations),1196cm^{-1} ($C_{aromatic}$-O str vibrations of $C_{aromatic}$-O-P group),954cm^{-1}(P-O str vibration of P-O-C aromatic ring).^{1}HNMR (DMSO-d_6), δ, ppm (J, Hz): 1.80(s,3H,-CH_3 of oxadiazole ring),2.10(s,3H,CO-CH_3), 2.20 (d,1H,J=14Hz,-CH of pyrazoline -5-one ring),3.80 (d,1H, Ha of –CH_2 of thiazolidinone ring),3.90(d,1H,H b of –CH_2 of thiazolidinone ring),5.93(s,1H,J=14Hz,-CH-Ar of thiazolidone ring), 6.9-7.4(m,13H for C_6H_5,C_6H_5,C_6H_3). ^{13}C-NMR (75MH_Z)(DMSO-d_6),δ,ppm:155.6,30.5,207.6,53.2,33.2,170.9,135.7,107.7, 145.4,140.8,117.5,115.6,148.8,87.6,142.6, 126.9,128.5,126.7,128.5,126.9,150.2,120.3,130.1,121.3,130.1,120.3,27.6,168.5,23.7, 124.8 and the signals are ascribed as 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},C_{26},C_{27}, C_{28}, C_{29},C_{30} carbon atoms respectively. ^{31}P-NMR(δ, ppm): -8.3; Mass: 701 (M+1), mp 143-145^{o}C. Elemental Analysis found for $C_{30}H_{23}F_3N_5O_8PS$ is C: 50.65, H: 3.18, N: 9.58.

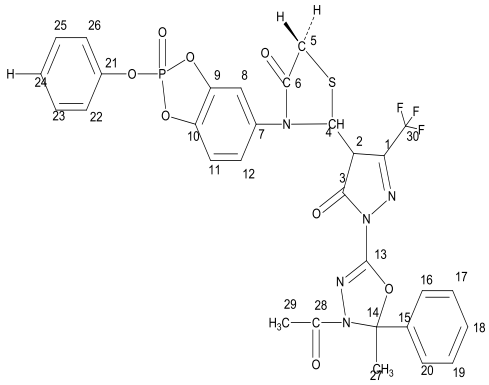


Fig. 1: Structure of 12a.

12b: Yield: 60.00%; IR (KBr pellet), ν, cm^{-1}: 2958 cm^{-1} (Ar-H str.), 1652cm^{-1}(>C=O str. of pyrazoline-5-one),1621,1213cm^{-1}(1,3,4-oxadiazole ring),1495,1425,1370cm^{-1}(str of characteristic of pyrazoline-5-one ring),1698cm^{-1}(>C=O group of thiazolidinone ring),1267cm^{-1}(P=O str vibrations),1193cm^{-1} ($C_{aromatic}$-O str vibrations of $C_{aromatic}$-O-P group),965cm^{-1}(P-O str vibration of P-O-C aromatic ring); ^{1}HNMR (DMSO-d_6), δ, ppm (J, Hz): 1.80(s,3H,-CH_3 of oxadiazole ring),2.10(s,3H,CO-CH_3), 2.20(d,1H,J=14Hz,-CH of pyrazoline -5-one ring), 3.10(s,3H, Ar-CH_3),3.80(d,1H,Ha of –CH_2 of thiazolidinone ring), 3.90(d, 1H,H_b of –CH_2 of thiazolidinone ring),5.93(s,1H,J=14Hz,-CH-Ar of thiazolidone ring),6.8-7.4(m,12H for C_6H_5,C_6H_4,C_6H_3) ^{31}P-NMR(δ, ppm): -7.9; Mass: 715(M+1), mp 81-83^{o}C. Elemental Analysis found for $C_{31}H_{25}F_3N_5O_8PS$ is C: 51.50, H: 3.39, N: 9.40.

12c: Yield: 60.00%; IR (KBr pellet), ν, cm^{-1}: 2955 cm^{-1} (Ar-H str.),1649cm^{-1}(>C=O str. of pyrazoline-5-one),1618,1200cm^{-1}(1,3,4-oxadiazole ring),1492,1422,1367cm^{-1}(str of characteristic of pyrazoline-5-one ring),1695cm^{-1}(>C=O group of thiazolidinone ring), 1260cm^{-1}(P=O str vibrations),1190cm^{-1} ($C_{aromatic}$-O str vibrations of $C_{aromatic}$-O-P group),960cm^{-1}(P-O str vibration of P-O-C aromatic ring); ^{1}HNMR (DMSO-d_6), δ, ppm (J, Hz): 1.80(s,3H,-CH_3 of oxadiazole ring),2.10(s,3H,CO-CH_3), 2.20(d,1H,J=14Hz,-CH of pyrazoline -5-one ring),3.4(s,3H,Ar-OCH_3),3.80(d,1H,Ha of –CH_2 of thiazolidinone ring), 3.90(d, 1H,H_b of –CH_2 of thiazolidinone ring),5.93(s,1H,-CH-Ar of thiazolidone ring),6.9-7.3(m,12H for C_6H_5,C_6H_4,C_6H_3); ^{31}P-NMR(δ, ppm): -8.2; Mass: 731 (M+1), mp 89-91^{o}C. Elemental Analysis found for $C_{31}H_{25}F_3N_5O_9PS$ is C: 49.80, H: 3.34, N: 9.20.

12d: Yield: 65.00%; IR (KBr pellet), ν, cm^{-1}: 2968 cm^{-1} (Ar-H str.),1662cm^{-1}(>C=O str. of pyrazoline-5-one),1631,1223cm^{-1}(1,3,4-oxadiazole ring),1505,1435,1380cm^{-1}(str of characteristic of pyrazoline-5-one ring),1703cm^{-1}(>C=O group of thiazolidinone ring), 1280cm^{-1}(P=O str vibrations),1202cm^{-1} ($C_{aromatic}$-O str vibrations of $C_{aromatic}$-O-P group),968cm^{-1}(P-O str vibration of P-O-C

aromatic ring); ^{1}HNMR (DMSO-d_6), δ, ppm (J, Hz): 1.80(s,3H,-CH_3 of oxadiazole ring),2.10(s,3H,CO-CH_3), 2.20 (d,1H,J=14Hz,-CH of pyrazoline -5-one ring),3.80(d,1H,Ha of –CH_2 of thiazolidinone ring),3.90(d,1H,H_b of –CH_2 of thiazolidinone ring),5.93(s,1H,J=14Hz,-CH-Ar of thiazolidone ring),7-7.4(m,12H for C_6H_5,C_6H_4,C_6H_3); ^{31}P-NMR(δ, ppm): -7.3; Mass: 735 (M+1), mp 110-112^{o}C. Elemental Analysis found for $C_{30}H_{22}ClF_3N_5O_8PS$ is C: 47.80, H: 2.89,N: 9.15.

12e: Yield: 60.00%; IR (KBr pellet), ν, cm^{-1}: 2966 cm^{-1} (Ar-H str.),1660cm^{-1}(>C=O str. of pyrazoline-5-one),1629,1221cm^{-1}(1,3,4-oxadiazole ring),1503,1433,1378cm^{-1}(str of characteristic of pyrazoline-5-one ring),1706cm^{-1}(>C=O group of thiazolidinone ring), 1277cm^{-1}(P=O str vibrations),1198cm^{-1} ($C_{aromatic}$-O str vibrations of $C_{aromatic}$-O-P group),965cm^{-1}(P-O str vibration of P-O-C aromatic ring); ^{1}HNMR (DMSO-d_6), δ, ppm (J, Hz): 1.80(s,3H,-CH_3 of oxadiazole ring),2.10(s,3H,CO-CH_3), 2.20 (d,1H,J=14Hz,-CH of pyrazoline -5-one ring),3.80 (d,1H,Ha of –CH_2 of thiazolidinone ring),3.90(d,1H,H_b of –CH_2 of thiazoli dinone ring),5.93(s,1H,-CH-Ar of thiazolidone ring),6.9-7.4 (m,12H for C_6H_5,C_6H_4,C_6H_3); ^{31}P-NMR(δ, ppm): -7.7; Mass: 779(M+1), mp 123-125^{o}C. Elemental Analysis found for $C_{30}H_{22}BrF_3N_5O_8PS$ is C: 45.70, H: 2.76, N: 8.65.

12f: Yield: 70.00%; IR (KBr pellet), ν, cm^{-1}: 2971cm^{-1} (Ar-H str.),1666cm^{-1}(>C=O str. of pyrazoline-5-one),1634,1226cm^{-1}(1,3,4-oxadiazole ring),1508,1438,1383cm^{-1}(str of characteristic of pyrazoline-5-one ring),1705cm^{-1}(>C=O group of thiazolidinone ring), 1283cm^{-1}(P=O str vibrations),1205cm^{-1} ($C_{aromatic}$-O str vibrations of $C_{aromatic}$-O-P group),971cm^{-1}(P-O str vibration of P-O-C aromatic ring); ^{1}HNMR (DMSO-d_6), δ, ppm (J, Hz): δ_{ppm}: 1.80(s,3H,-CH_3 of oxadiazole ring),2.10(s,3H,CO-CH_3), 2.20 (d,1H,J=14Hz,-CH of pyrazoline -5-one ring),3.80(d,1H,Ha of –CH_2 of thiazolidinone ring),3.90(d,1H,H_b of –CH_2 of thiazoli dinone ring),5.93(s,1H,J=14Hz,-CH-Ar of thiazolidone ring),7-7.50(m,12H for C_6H_5,C_6H_4,C_6H_3); ^{31}P-NMR(δ, ppm): -7.4; Mass: 769 (M+1), mp 113-115^{o}C. Elemental Analysis found for $C_{31}H_{22}F_6N_5O_8PS$ is C: 47.16, H: 2.77, N: 8.90.

RESULTS AND DISCUSSION

The synthetic route followed for the synthesis of 2-(4-substituted phenoxy-1,3,2-benzodioxa phosphole-2-oxide derivatives containing 1,3,4-oxadiazole-4-thiazolidinone is presented in scheme-1.

4-(((3,4-dimethoxyphenyl)imino) methyl)-3-(trifluoromethyl)-1H-pyrazol -5(4H)-one (3) was prepared by reacting 5-oxo-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazol-4-carbaldehyde with 3,4-dimethoxyaniline in presence of catalytic amount of acetic acid in ethanol at reflux temperature (100°C).

Ethyl-4-(((3,4-dimethoxy phenyl) imino)methyl-5-oxo-3-(trifluoro methyl)-4,5-dihydro-1H-pyrazole-1-carboxylate (4) was prepared by reacting 4-(((3,4-dimethoxyphenyl)imino) methyl)-3-(trifluoromethyl)-1H-pyrazol -5(4H)-one (3) with mono ethyl chloro formate in presence of TEA at RT. Further the Ethyl-4-(((3,4-dimethoxy phenyl) imino)methyl-5-oxo-3-(trifluoro methyl)-4,5-dihydro-1H-pyrazole-1-carboxylate (4) reacts with mercapto acetic acid in dry 1,4-dioxane in presence of catalytic amount of anhydrous zinc chloride affords ethyl-4-(3-(3,4-dimethoxyphenyl)-4-oxothiazolidin-2-yl)-5-oxo-3-(trifluoro methyl)-4,5-dihydro-1H-pyrazole-1-carboxylate (5). The IR spectra of (5) exhibited bands around 1675cm^{-1}(>C=O of thiozolidine ring),619cm^{-1}(C-S, str. of thiazolidinone ring) which is supporting the structure of (5). ^{1}H NMR of (5) showed one dublet at δ 3.80(d,1H,Ha of –CH_2 of thiazolidinone ring), another dublet at δ 3.90 (d, 1H,Hb of –CH_2 of thiazolidinone ring) and one singlet at δ 5.93(s,1H,J=14Hz,-CH- of thiazolidone ring) confirming the structure of compound (5).

4-(3-(3,4-dimethoxyphenyl)-4-oxo thiazolidin-2-yl)-5-oxo-3-(trifluoro methyl)-4,5-dihydro-1H-pyrazole-1-carbohydrazide (6) was synthesized by reaction of ethyl-4-(3-(3,4-dimethoxyphenyl)-4-oxothiazolidin-2-yl)-5-oxo-3-(trifluoro methyl)-4,5-dihydro-1H-pyrazole-1-carboxylate (5) with hydrazine hydrate using ethanol as solvent. The IR spectra of 4-(3-(3,4-dimethoxyphenyl)-4-oxo thiazolidin-2-yl)-5-oxo-3-(trifluoro methyl)-4,5-dihydro-1H-pyrazole-1-carbohydrazide (6) exhibited bands around 3457,3443cm^{-1}(NH_2 group of acid azide), 3220cm^{-1}(-NH- group of acid azide). ^{1}H NMR showed one singlet at δ 4.20(s,2H,-NH_2 of acid azide) and 8.70(s,1H,-NH- of acid azide) confirming the structure of 4-(3-(3,4-dimethoxyphenyl)-4-oxo thiazolidin-2-yl)-5-oxo-3-(trifluoro methyl)-4,5-dihydro-1H-pyrazole-1-carbohydrazide (6).

4-(3-(3,4-dimethoxyphenyl)-4-oxothiazolidin-2-yl)-5-oxo-N-(1-phenylethylidene)-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazole-1-carbo hydrazide (8) was synthesized by reaction of 4-(3-(3,4-dimethoxyphenyl)-4-oxo thiazolidin-2-yl)-5-oxo-3-(trifluoro methyl)-4,5-dihydro-1H-pyrazole-1-carbohydrazide (6) with acetophenone in refluxing methanol in presence of catalytic amount of glacial acetic acid. The IR spectra of 4-(3-(3,4-dimethoxyphenyl)-4-oxothiazolidin-2-yl)-5-oxo-N-(1-phenylethylidene)-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazole-1-carbo hydrazide (8) exhibited bands around 3195cm^{-1}(-NH of acid hydrazone),3040cm^{-1} (Ar-H str.),1620cm^{-1}(>C=N of hydrazone). ^{1}H NMR showed absence of one singlet at δ 4.20(s,2H,-NH_2 of acid azide) and presence of 8.5(s,1H,-CO-NH-N=) along with aromatic protons 7.0-7.2(m,8H,C_6H_3 and C_6H_5 rings) confirming the structure of 4-(3-(3,4-dimethoxyphenyl)-4-oxothiazolidin-2-yl)-5-oxo-N-(1-

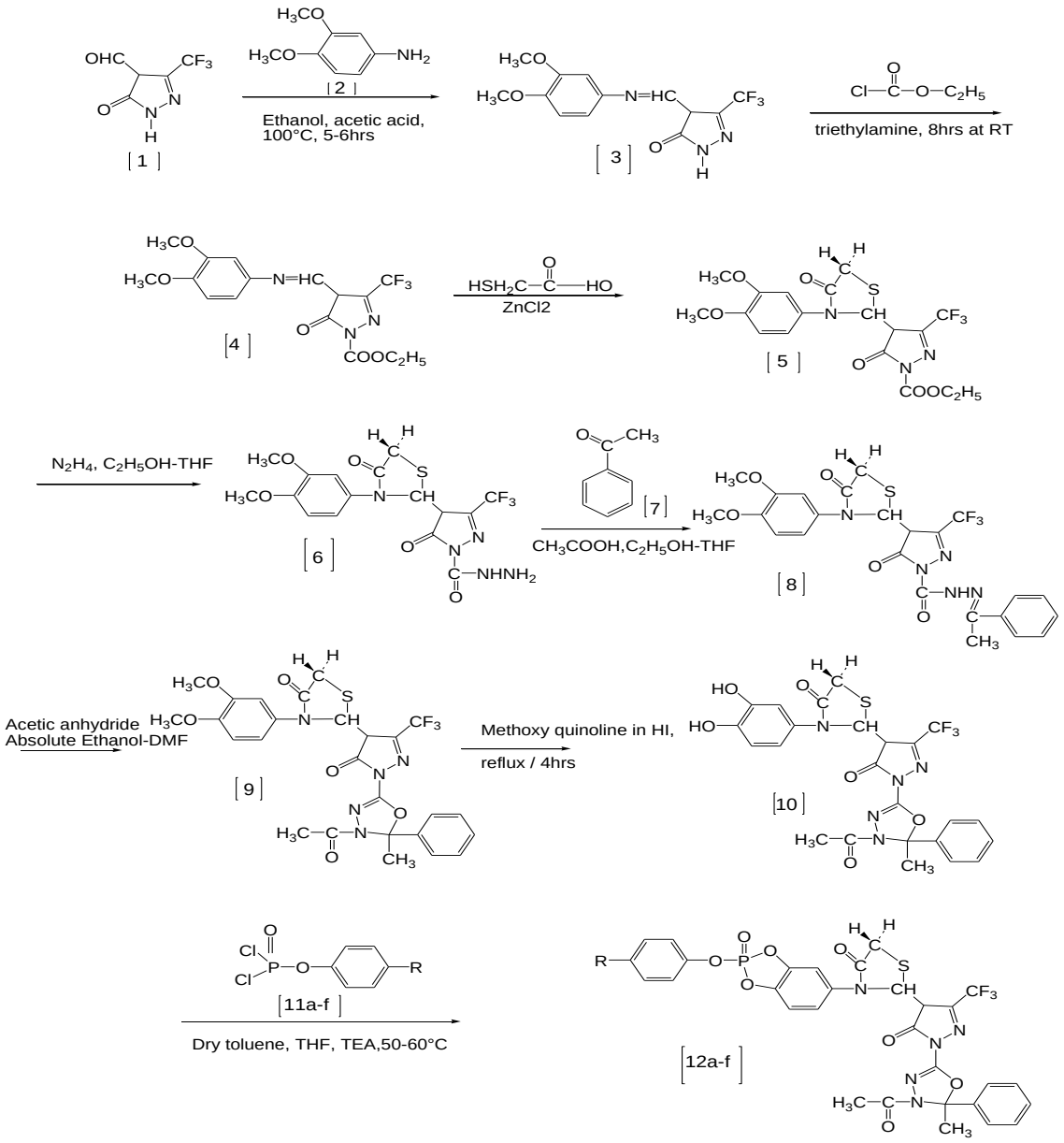
phenylethylidene)-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazole-1-carbo hydrazide (8).

2-(1-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-5-oxo-3-(trifluoro methyl)-4,5-dihydro-1H-pyrazol-4-yl)-3-(3,4-dimethoxyphenyl) thiazoli din-4-one(9) was by acetylation followed by cyclization of 4-(3-(3,4-dimethoxyphenyl)-4-oxothiazolidin-2-yl)-5-oxo-N-(1-phenylethylidene)-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazole-1-carbo hydrazide (8) using acetic anhydride and absolute ethanol-DMF solvent mixture at reflux condition. The IR spectra of 2-(1-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-5-oxo-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazol-4-yl)-3-(3,4-dimethoxyphenyl) thiazoli din-4-one(9) exhibited bands around 1626,1218cm^{-1}(1,3,4-oxadizole ring). ^{1}H NMR showed 1.80(s,3H,-CH_3 of oxadiazole ring),2.10(s,3H,CO-CH_3) conforming the structure of 2-(1-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-5-oxo-3-(trifluoro methyl)-4,5-dihydro-1H-pyrazol-4-yl)-3-(3,4-dimethoxyphenyl) thiazoli din-4-one(9).

2-(1-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-5-oxo-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazol-4-yl)-3-(3,4-di hydroxyphenyl)thiazolidin-4-one (10) was obtained by hydrolysis of 2-(1-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-5-oxo-3-(trifluoro methyl)-4,5-dihydro-1H-pyrazol-4-yl)-3-(3,4-dimethoxyphenyl) thiazoli din-4-one(9) using hydro iodic acid at reflux condition in methoxy quinolone as solvent. The IR spectra of 2-(1-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-5-oxo-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazol-4-yl)-3-(3,4-di hydroxyphenyl)thiazolidin-4-one (10) exhibited bands around 3350cm^{-1}(str. intramolecular –OH bond) . ^{1}H NMR showed one singlet at 4.6(s,2H, two phenolic –OH groups) conforming the structure of 2-(1-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-5-oxo-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazol-4-yl)-3-(3,4-di hydroxyphenyl)thiazolidin-4-one (10).

2-(1-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-5-oxo-3(trifluoro methyl)-4,5-dihydro-1H-pyrazol-4-yl)-3-(2-oxido-2-(4-substituted phenoxy) benzo[d] [1,3,2]dioxaphosphol-5-yl)thiazolidin-4-ones (12a-f) (12a-f) were prepared by condensing 2-(1-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazol-2-yl)-5-oxo-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazol-4-yl)-3-(3,4-di hydroxyphenyl)thiazolidin-4-one (10) with 4-substituted phenyl phosphoro dichloridates (11a-f) in presence of tri ethyl amine as base and dry toluene, THF mixture as solvent at 50-60°C. The IR spectra of 2-(1-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazole-2-yl)-5-oxo-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazol-4-yl)-3-(2-oxido-2-phenoxybenzo[d][1,3,2] dioxaphosphol-5-yl) thiazolidin-4-one (12a) exhibited bands around 1255cm^{-1}(P=O str vibrations),1196cm^{-1} ($C_{aromatic}$-O str vibrations of $C_{aromatic}$-O-P group),954cm^{-1}(P-O str vibration of P-O-C aromatic ring). ^{1}H NMR showed multiplet at δ 6.9-7.4(m,13H for C_6H_5,C_6H_5,C_6H_3) confirming the structure of 2-(1-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxadiazole-2-yl)-5-oxo-3-(trifluoromethyl)-4,5-dihydro-1H-pyrazol-4-yl)-3-(2-oxido-2-phenoxybenzo[d][1,3,2]dioxaphosphol-5-yl) thiazolidin-4-one (12a)

Similarly remaining analogues (12b-f) were prepared.



Scheme-1:- Reaction path way for the preparation of 2-(4-substituted phenoxy-1,3,2-benzodioxa phosphole-2-oxide derivatives containing 1,3,4-oxadiazole-4-thiazolidinone derivatives.

Biological activity: The antimicrobial activity of newly synthesized compounds was performed according to disc diffusion method, as recommended by the National Committee for Clinical Laboratory. The synthesized compounds were used at the concentration of 250µg/ml DMSO as a solvent.

Antibacterial activity: The antibacterial activity of 2-(1-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxa diazol-2-yl)-5-oxo-3(trifluoromethyl)-4,5-dihydro-1H-pyrazol-4-yl)-3-(2-oxido-2-(4-substitu ted)benzo[d][1,3,2]dioxaphosphol-5-yl)thiazolidin-4-one **(12a-f)** were screened against the gram-positive bacterial screened were staphylococcus aureus NCCS 2079 and Bacillus cereus NCCS 2106 and The gram negative bacterial screened were Escherichia coli NCCS2065 and Pseudomonas aeruginosa NCC2200. The presence of $-CF_3$ (12f), chloro (-Cl,12d) and bromo (-Br,12e) showed more activity than other substituted compounds. The antibacterial activity of **(12a-f)** was shown in the **Table-1.** The synthesized compounds were used at the concentration of 250 µg/ml and 500 µg/ml using DMSO as a solvent. The amoxycillin was used as a standard. (Hi-media laboratories limited, Mumbai).

Table-1: Antibacterial activity (Diameter zone of inhibition in mm) of Compounds (12a-f) (250µg/ml).

S. no.	Compound	Zone of inhibition(mm)			
		Antibacterial activity			
		Gram +ve		Gram -ve	
		SA	BC	EC	PA
1	12a(-H)	13	15	12	10
2	12b(-CH_3)	10	12	9	9
3	12c(-OCH_3)	9	11	8	8
4	12d(-Cl)	15	17	14	14
5	12e(-Br)	14	16	13	13
6	12f(-CF_3)	17	19	16	16
Amoxicillin		22	25	25	27

Antifungal activity: The antifungal activity of 2-(1-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxa diazol-2-yl)-5-oxo-3(trifluoromethyl)-4,5-dihydro-1H-pyrazol-4-yl)-3-(2-oxido-2-(4-substitu ted)benzo[d][1,3,2]dioxaphosphol-5-yl)thiazolidin-4-one (12a-f) were screened against the Aspergillus niger NCCS 1196 (AN) and Candied albicans NCCS 3471(CA) organisms. Most of the compounds exhibit moderate antifungal activity against both fungi. The presence of -CF_3 (12f), chloro (-Cl,12d) and bromo (-Br,12e) showed more activity than other substituted compounds. Here Ketaconazole was used as reference compound to compare the activity.

The antifungal activity of **(12a-f)** was shown in the **Table-2.**

Table-2: Antifungal activity ((Diameter zone of inhibition in mm) of compounds (9a-g)(250µg/ml).

S. No.	Comp	Zone of inhibition (mm)	
		Aspergillius niger NCCS 1196	Candida albicans NCCS 3471
1	12a	11	9
2	12b	10	8
3	12c	9	7
4	12d	15	13
5	12e	14	12
6	12f	17	15
Ketoconazole		**22**	**25**

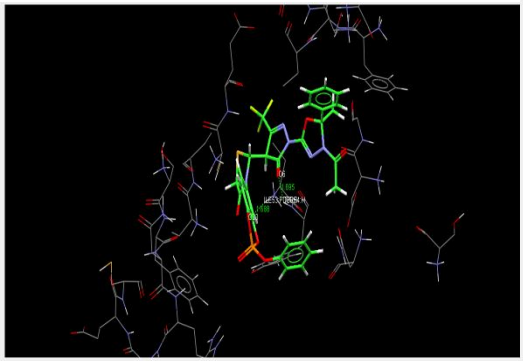
Docking Studies of the compounds (12a-f)

The docking studies of 12a,12b,12c,12d.12e,12f were carried out as model compounds on sortase-A enzyme. The docking ligands were found to have some interactions between an oxygen atom of the ligands and sortase-A enzyme. The results pertaining to Docking studies were shown in the Table **3** and fig **2 and** fig **3.** Moreover, these docked conformations form hydrogen bond interactions with the active site of the enzyme. The common hydrogen bonding interactions were formed between all the docked ligands and ILE53PDBCD, TYR54H, PHE76CD, TYR54O, THR77H, ILE53:PDB2H, ILE53:PDB3H, ILE53:PDB1H. The order of enzyme-ligand hydrogen bond energy (S(Hb_ext)) is 12e>12a>12c>12d>12f>12b. The vanderwaals interactions between ligand-enzyme were also noticed. The order of enzyme-ligand vanderwaals score of interaction was found to be 12f>12b>12d>12a>12c>12e. However the ligands fail to exhibit intramolecular hydrogen bonding with the enzyme. The ligands exhibit minimum intramolecular strain. Finally, all the ligands exhibit moderate to good antibacterial activity with Sortase-A enzyme. The order of gold score fitness value of the ligands is 12e>12d>12f>12a>12b>12c. According to gold score fitness value ligand 12e exhibits high binding activity with the enzyme and ligand 12c showed leads binding activity with the enzyme.

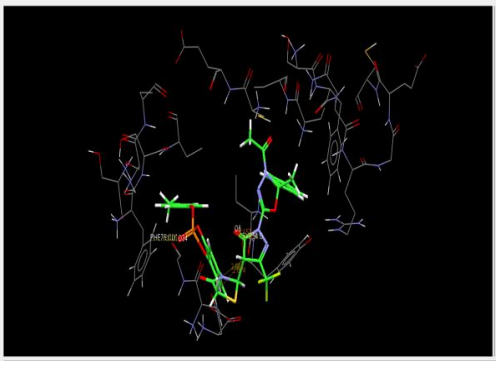
Table-3: Docking results of ligands (12a-f) with Sortase A enzyme.

Comp	R	Fitness	S(Hb_ex)	S(vdw_et)	S(Hb_in)	S(vdw_it)
12a	H	43.33	6.28	33.03	0.00	-8.37
12b	CH_3	40.88	0.00	34.59	0.00	-6.69
12c	OCH_3	37.46	6.18	32.92	0.00	-13.98
12d	Cl	45.84	6.00	33.53	0.00	-6.25
12e	-Br	46.16	7.16	32.64	0.00	-5.88
12f	-CF_3	43.48	4.43	34.72	0.00	-8.69

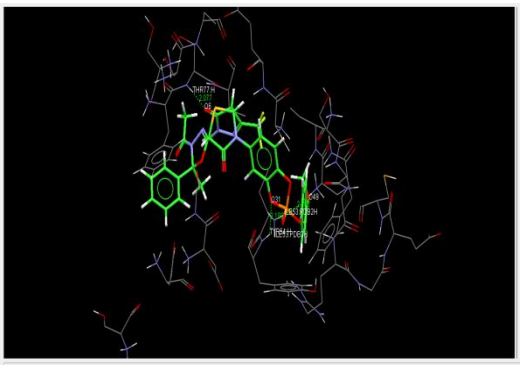
Comp No	R	No of 'H' bonds	Compounds		Bond Length (A°)	Fitness
			Protein	Atoms		
12a	-H	2	ILE53:PDBCD TYR54:H	O:33 O:6	1.688 1.695	43.33
12b	$-CH_3$	4	PHE76CD TYR54:O	O:34 O:6	2.670 2.157	40.88
12c	$-OCH_3$	3	THR77:H TYR54:H ILE53:PDB2H	O:6 O:31 O:49	2.077 2.180 2.162	37.46
12d	-Cl	3	ILE53:PDB3H ILE53:PDB3H TYR54:H	O:34 O:33 O:6	2.647 1.820 1.844	45.84
12e	-Br	2	THR77:H ILE53:PDB1H	O:44 O:31	2.560 1.701	46.16
12f	$-CF_3$	2	ILE53:PDB1H TYR54:H	O:34 O:22	2.046 1.919	43.48



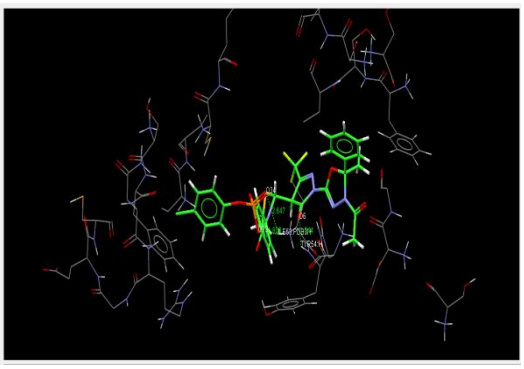
12a



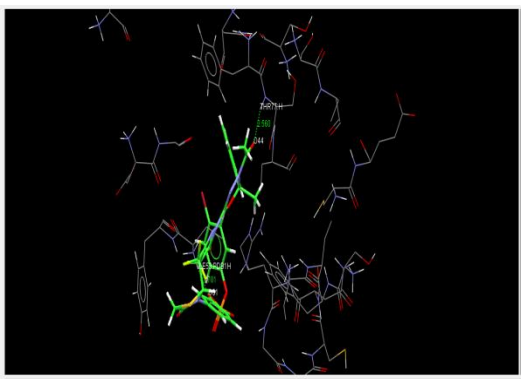
12b



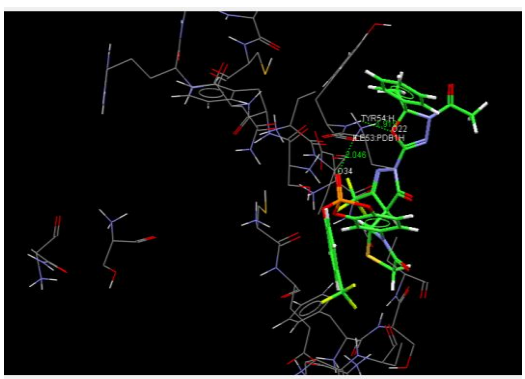
12c



12d



12e



12f

Fig. 2: docking images of thiazolidine-4-one with Sortase-A.

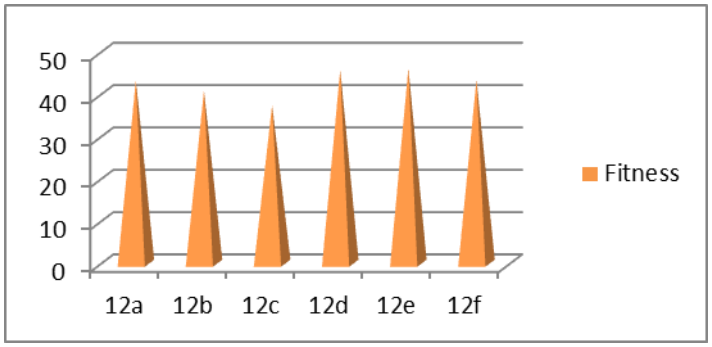


Fig: 3: Comparative Gold score fitness values for compounds (12a-f).

The results of docking study of newly synthesized 2-(1-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxa diazol-2-yl)-5-oxo-3(trifluoromethyl)-4,5-dihydro-1H-pyrazol-4-yl)-3-(2-oxido-2-(4-substitu ted)benzo[d][1,3,2]dioxaphosphol-5-yl)thiazolidin-4-one reveals that all the compounds are having good interaction in favourable pose of Sortase-A. Among six 2-(1-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxa diazol-2-yl)-5-oxo-3(trifluoromethyl)-4,5-dihydro-1H-pyrazol-4-yl)-3-(2-oxido-2-(4-substitu ted)benzo[d][1,3,2]dioxaphosphol-5-yl)thiazolidin-4-one, three derivatives (12f, 12e &12d) showed better activity.

CONCLUSION

In current research work, few analogues of 2-(1-(4-acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxa diazol-2-yl)-5-oxo-3(trifluoromethyl)-4,5-dihydro-1H-pyrazol-4-yl)-3-(2-oxido-2-(4-substitu ted)benzo[d][1,3,2]dioxaphosphol-5-yl)thiazolidin-4-one were successfully prepared and characterized. Biological activity and docking studies of these compounds were also conducted. Among six analogues three derivatives shown better activity and these can be taken as lead compounds for further development in future.

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