ABSTRACT

Amongst different heterocyclic systems, the chemistry of fused heterocycles with one heteroatom has gained importance because many of them exhibit pronounced bioactive nature. Specifically, those containing the organophosphorus pyrazole 5-one moiety. Specifically, those containing the pyrazole 5-one nucleus have been shown to possess biological activities such as tranquilizing, muscle relaxant, psycho analeptic, anticonvulsant, antihypertensive, antidepressant activities. The derivatives of pyrazolone are important class of antipyretic and analgesic compounds. Besides antituberculosis antineoplastic, antidiabetic, anti fertility and antithyroid activity.

In view of high biopotency of pyrazole 5-one ring. The target molecules are synthesized with pyrazole 5-one ring as basic unit and it is coupled with Isatine mannich bases/1,3,4-oxadiazole/thiazolidine/1,2,4-triazoles and sulfones/ pyrimidines /1,3,4-thiadiazole sulfonamides. Posses' very good biological activities like anti microbial, pesticidal, antitumor, antitubercular, anticancer and cytotoxic activities.

A novel mannich bases Ethyl2-(5-oxo-4-(phenyl/4-methoxy/4 triflouro-methyl/4-nitrophenylilmino) methyl)-3-(tri fluoromethyl)-4, 5 dihydro-1H-pyrazol-1-yl-condensed to (R)-2-(5-oxo-4-(phenyl/4-methoxy/4-triflouro methyl/ nitrophenyl imino)methyl)-3-(triflouro methyl)-4,5 dihydro-1H-Pyrazole-yiaceto hydrazide Condensation of 6 with isatin afforded (R)-2-(5-oxo-4-(phenyl/4-methoxy/4-triflouro methyl/4-nitrophenyl imino) methyl)-3-(triflouro methyl)-4,5 dihydro-1H-Pyrazole-yln-(2-oxoindoline-3-yldene)condition(R)-N-(1-Morpholine/thiomorpholino methyl)-2-Oxindoline-3-yldine)-2-(5-oxo-4-(phenyl/4-methoxy/4-nitro/4-triflouro methyl phenylilmino) methyl-3-(triflouro methyl)-4,5 dihydro-1H-pyrazol-1-yl)-aceto hydrazide diethyle phosphate condensed 2((4R)-4-(diethylphosphoryl)(phenyl/4-meth oxy / 4-triflouro methyl/ 4-nitrophenyl imino) methyl)-5-oxo-3-(triflouro methyl)-4,5 dihydro-1H-pyrazol-1-yl)-N-(1-morpholine/thiazomorpholino methyl)-2-oxoindolin-3-yldine) aceto hydrazide in excellent yields.

Synthesis of (R) -2-(5-oxo-4-(phenyl/4-methoxy/4-triflouro methyl/ 4-nitrophenyl- imino)methyl)-3-(triflouro methyl)-4,5 dihydro-1H-Pyrazole-ylaeto hydrazide aceto phenone condensed 2-(5-oxo-4-(phenyl/4-methoxy/4-triflouro methyl/ 4-nitrophenyl amino)methyl)-3-(triflouro methyl)-4,5 dihydro-1H-pyrazol-1-yl)-N-(1-phenyl ethyl idene) aceto hydrazide acetic anhydride condensed (1-(4acetyl-5-methyl-5-phenyl-4,5 dihydro-1,3,4-
oxadiazole-2-yl)methyl)-4-(phenyl/4-methoxy/4-trifluromethyl/4-nitrophenyl imino) methyl-3-(tri flouro methyl)-1H-pyrazol-5(4H)-one. Diethyl phosphate, Diethyl(1-(4acetyl-5-methyl-5-phenyl-4,5-dihydro-1,3,4-oxa diazole-2-yl) methyl)-5-oxo-3-(trifluromethyl)-4,5-dihydro-1H-pyrazol-4-yl)(phenyl/ 4-methoxy/4-trifluromethyl/4-nitrophenyl imino) methyl phosphate.

Synthesis of Ethyl2-(5-oxo-4-(phenyl/4-methoxy/4-trifluromethyl/ nitro phenyl imino)methyl)-3-(tri fluoromethyl) -4, 5 dihydro-1H-pyrazol-1-yl) acetate mercaptoacetic acid condensed ethyl2-(4-3-(phenyl/4-methoxy/4-trifluromethyl/4-nitrophenylthiazolidine)-4-oxo thiazolidine-2-yl) - 5- oxo-3-(trifuromethyl)-4,5-dihydro-1H-pyrazol-1yl)acetate. Hydrazine hydrate in 2-(4-3-(phenyl/4-methoxy/4-trifluromethyl/4-nitrophenyl)-4-oxothiazolidine-2-yl)-5-oxo-3- (trifluromethyl)4, 5dihydro-1H-pyrazol-1-yl)acetoxyhydrazide acetophenone was refluxed in methanol containing a catalitic amount of glacial acitic acid for 4hrs. 2-(4-(3-(phenyl/4-methoxy/4-trifluromethyl/4-nitro phenyl)-4-oxothiazolidine-2-yl)-5-oxo-3-(trifuromethyl)-4,5-dihydro-1H-pyrazol-1-yl)-N\(^1\)-(1-(4-nitrophenyl) ethlidene) aceto hydrazide. acetic anhydride reflux for 2hrs Synthesis of 2-(1-(4-acetyl-5-methyl-5-(4-nitrophenyl)-4,5-dihydro-1,3,4-oxadiazole-2-yl)methyl)-5-oxo-3-trifluoro-methyl)-4,5-dihydro-1H-pyrazole-4-yl)-3-phenyl/4-methoxy/4-trifluromethyl/4-nitrophenyl thiazolidine-4-one 5(a-d).

Synthesis of (R)-2-(2-(5-oxo-3-(trifuromethyl)-4-((4-(trifluromethyl) phenylimino)methyl)-4,5-dihydro-1H-Pyrazol-1-yl)acetyl) condensed (R) -1-((5-thioxo-4,5-dihydro-1H-1,2,4-triazol-3-yl)methyl)-3-(trifuromethyl)-4-(4-(trifuromethyl) phenylamino)methyl-1H-Pyrazol-5(4H)-one (3) condensed (R) -1-((5-(phenyl/4-methyl/4methoxy/4-nitro/4-chloro/4-bromo/4-fluorobenzylthio)-4H-1,2,4-triazol -3 –yl) methyl) -3 – (trifuromethyl)-4-((4-(trifuromethyl) phenylimino) methyl-1H-pyrazol -5(4H)- One (4a - g). morpholine and water condensed (R) -1-((5-(phenyl/4-methyl/4-methoxy/4-nitro/4-chloro/4bromo/4-fluorobenzylthio)-4-(morpholinomethyl)-4H-1,2,4-triazol-3 –yl) methyl) -3 – (trifuromethyl)-4-((4-(trifuromethyl) phenylimino) methyl-1H-pyrazol -5(4H)-One glacial acetic acid 30% (R) -1-((5-(phenyl/4-methyl/4-methoxy/ 4-nitro/4-chloro/4-bromo/4-fluorobenzyl sulfonyl) -4-(morpholinomethyl)-4H-1,2,4-triazol -3 –yl) methyl) -3 –(trifuromethyl)-4-((4-(trifuromethyl) phenylimino) methyl-1H-pyrazol -5(4H)-One (6a-g) Diethyl phosphate Anhydrous toluene, diethyl (R)-1-((5-(phenyl/4-methyl/4-methoxy/4-nitro/4-chloro/4-bromo/4fluorobenzylsulfonyl)-4-(morpholinomethyl)-4H-1,2,4-triazol-3-yl)methyl)-5-oxo-3-
A solution of 1(a-hydrazine hydrate in ethanol was refluxed for 5hrs Synthesis of 4-(4-diethylamino/4-pyrrolidine/4-pyron phenyl) 2(oxo/thiones/imines) 1,2,3,4-tetrahydropyrimidine-5-carbohydrate(2a-i). Ethyl4-trifluoro-3-oxobutanate condensed to 1-(4(4-diethylamino/4-pyrrolidine/4-pyron phenyl)-2(oxo/thiones/ imines) 1,2,3,4-tetrahydropyrimidine-5-carbonyl)-3-(trifluoromethyl)-1H-pyrazol-5(4H)-one (3a-i).

Synthesis of Ethyl 2-(4-formyl-5-oxo-3-(tri fluoromethyl)-4,5-dihydro-1H-pyrazol-1-yl)acetate(2)-phenylamine
Ethyl2-(5-oxo-3-(trifluoromethyl)-4-(4-trifluoromethyl)phenylimino)methyl)-4,5-dihydro-1H-pyrazol-1-yl)acetic acid(4). 1-(5-amino-1,3,4-thiadiazol-2-yl)methyl)-3-(tri fluoro methyl)-4-(4-(trifluoromethyl)phenylimino)methyl)-1H-pyrazol-5(4H)-one (5) con densation to give methyl(cyclopropyl/2,3,4,5 pentfluoro phenyl /4-tri fluoro methyl phenyl /4-nitro phenyl /4-bromo phenyl/4-methoxy phenyl /4-methyl phenyl /phenyl)sulfonyl carbamates(6a-h) to get N-(5-(5-oxo-3-(trifluoromethyl)-4-((4-(trifluoro methyl) phenylimino)methyl)-4,5-dihydro-1H-pyrazol-1-yl)methyl)-1,3,4-thiadiazol-2-ylcarbamoyl)cyclopropane/(2,3,4,5,6-penta fluoro/4-trifluoro methyl/ 4-nitro/ 4-bromo/ 4-methoxy/ 4-methyl benzene sulfonamides(7a-h) condencedto give Diethyl(1-((5-(3-(cyclopropane/(2,3,4,5,6-pentafluor04-trifluoromethyl/4-nitro/4-bromo/ 4-methoxy/ 4-methyl benzene)phenyl sulfonyl)ureido))-1,3,4-thiadiazol-2-yl)methyl)-5-oxo-3-(trifluoro-methyl)-4,5-dihydro-1H-pyrazol-4-yl(4-(trifluoro methyl)phenylimino) methylphosphonate (8a-h).

Chromatographic techniques such as thin layer chromatography and solvent extraction were used for purification of active ingredients. Structural elucidation of the compounds synthesized were carried out using Infrared, ¹H-NMR, ¹³C-NMR, ³¹P-NMR elemental analyzer and Mass Spectrometry.

All the synthesized compounds were screened for antibacterial and antifungal activities (in vitro); which exhibited different activities depending on the nature of the heterocyclic moiety present.

All the synthesized compounds were screened for docking studies; which exhibited binding interactions depending on the nature of the heterocyclic moiety present. We have
reported docking studies in pertaining to the newly synthsised pyrazole phosphrous heterocycles on sortaseA staphylococcus (PDB ID: 1T2P).