Available online www.jocpr.com

Journal of Chemical and Pharmaceutical Research, 2013, 5(5):280-292

Research Article

ISSN : 0975-7384
CODEN(USA) : JCPRC5

Synthesis characterization and antimicrobial activity of 6-nitro-1*H*-benzo[*d*]imidazole-2-yl) methyl)-6-oxido-4,8-dihydro-1*H*-[1, 3, 2] dioxaphosphepino [*5,6-c*] pyrazole-6-yl) ureas/carboxamides-Mannich bases

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ABSTRACT

New mannich bases of 1(-(1-((1-(morpholinomethyl/piperidin-1-ylmethyl/(4-methyl piperazine-1-yl)methyl))-6-nitro-1H-benzo[d]imidazole-2-yl)methyl)-6-oxido-4,8-dihydro-1H-[1,3,2] dioxaphosphepino [5,6-c] pyrazole-6-yl)-3-(phenyl/p-tolyl/4-methoxy phenyl/4-chloro phenyl) ureas ***9(a-j)*** *were prepared by condensation reaction between1-((1-(piperidin-1-ylmethyl)/(1-morpholino methyl)/(4-methyl piperazin-1-ylmethyl)-6-nitro-1H-benzo [d] imidazol-2-yl) methyl)-1H-pyrazole-4, 5-diyl) dimethanol* ***7(a-c)*** *and (phenyl carbamoyl) phosphoric acid dichlorides* ***8(a-g).****The synthon 7(a-c) was obtained by deprotection of isopropilidine group of 6,6-dimethyl-1-((6-nitro-1-((1-(piperidin-1-ylmethyl)/ (1-morpholinomethyl)/ (4-methyl piperazin-1-ylmethyl)-1H-benzo[d]imidazol-2-yl)methyl)-4,8-dihydro-1H-[1,3]- dioxepIno [5,6-c] pyrazole* ***6(a-c).****The synthon* ***6(a-c)*** *was obtained by mannich reaction of 6, 6-dimethyl-1-((6-nitro-1H-benzo[d]imidazol-2-yl) methyl-4, 8-dihydro-1H-[1, 3] - dioxepino [5, 6-c] pyrazole* ***(5)*** *with different secondary amines having hetero atom in cyclic ring and HCHO in presence of DMF.The synthon* ***5*** *obtained by condensation reaction between 2-(6, 6-dimethyl-4, 8-dihydro-1H-[1, 3] dioxepino [5, 6-c] pyrazole-1-yl) acetic acid* ***3*** *and 4-nitro benzene 1,2-amine. Similar procedure was adapted to prepare N-(1-((1-morpholinomethyl)-1H-benzo[d]imidazol-2-yl)methyl)-6-oxido-4,8-dihydro-1H-[1,3,2]dioxaphosphepino[5,6-c]pyrazol-6-yl)morpholine piperadine/4-methylpiperazine carboxamides* ***(9k-m)****.*

Key words: (phenyl carbamoyl) phosphoric acid dichlorides, Pyrazole, Cyclizaton, Deprotection, Antibacterial and Antifungal activity.

INTRODUCTION

Pyrazole derivatives possess a broad spectrum of pharmalogical activities such as anticonvulsant p[1], antiparkinson [2] , monoamine oxidase (MAO) inhibitory activity [3], anti-bacterial, anti-fungal activity [4] , it also function as dyestuff, catalyst, polymerizing agents, drugs, herbicides and fungicides [5]. Pyrazole derivatives are valuable vasodialating and vasoconstructing drugs.

Benzimidazoles, benzoxazole and benzthiazoles nuclei are constituent of many of the bioactive heterocyclic compounds that exhibit antianginal, antiischaemic, vasodilator, anti-diabetic, anti-microbial, cardiovascular, tranquilizer and virucidal activities [6-14].

The chemistry of phosphorus heterocyclic compounds containing nitrogen has pioneered the application of combinatorial techniques to the development of new pharmaceutical materials with novel properties [15, 16].

Organophosphorus compounds possess significant biological activity against broad spectrum of bacteria, pets, virus, fungicides and plant growth regulators. The organophosphorus heterocyclic compounds chemistry received much attention of chemists in past two decades due to their wide range of applications in the field of the Agriculture, medicine and industry [17, 18]. Some organophosphorus compounds have been described in the literature as inhibitors of bacterial [19], herbicides, insecticides, pesticides [20,21], anti-fungal agents [22], anti-HIV [23] , anti-cancer [24], anti-viral and anti-inflammatory [25] .

A good deal of importance was given to 1, 3, 2-Dioxaphosphorinane and dioxaphospholane derivatives in the field of organophosphorus heterocyclic chemistry due to their unique stereochemical futures and diverse potential biological applications [26, 27]. In view of the numerous commercial applications of organophosphorus compounds. It appeared of interest to synthesize pyrazole derivatives possessing Benzazole moiety besides 1, 3, 2-Dioxaphosphorinane and dioxaphospholanes.

EXPRIMENTAL SECTION

All the chemicals used in the present investigation were purchased from Sigma-Aldrich Chemical Company, inc.USA. and used without further purification. TLC was performed on aluminum sheet of silica gel $60F_{254}$, E-Merk, Germany using iodine as visualizing agent .Melting points were determined in open capillary tubes on Mel-Temp apparatus and are uncorrected. Colum chromatography was performed on silica gel with different solvent systems as eluents to afford the pure compound. The IR spectra were recorded as KBr pellets on Perkin-Elmer 1000 unit, Instrument. All H^1 and C^{13} –NMR .P^{31} -NMR spectra were recorded on a Varian XL-300MHz for H^1-NMR and 75.46MHZ for C^{13}-NMR. P^{31}-NMR spectra were recorded ona Varian XL-spectrometer operating at 161.89MHz.The compounds were dissolved in DMSO-d6 and Chemical shifts were referenced to TMS (H^1 and C^{13}-NMR) and 85%H_3PO_4(p31-NMR). Mass spectral data was recorded on FAB-MS instrument at 70ev with direct inlet system. Elemental analyses were recorded on Carlo Erba 1108 Elemental Analyses, Central Drug Research Institute, Lucknow, India.

Prepration of Intermediates:

(Phenyl carbamoyl) phosphoric acid dichloride (*8a-g*)[28, 29]:

A solution of aniline (0.51g, 0.004mole) in dry toluene (25ml) was added drop wise to phosphide oxide (6, 0.64g, 0.004 mole) in dry toluene (30ml). After the addition, the temperature of the reaction mixture was maintained between -15 to - 5^0c for 30 minutes. Later the temperature of the mixture was raised to room temperature, with stirring for 30 minutes .Phenyl carbomido phosphoric acid dichloride being insoluble in toluene was separated out .It was collected by filtration and dried under reduced pressure.

Similar treatment of 4-substituted Anilines / morpholine/piperidine/ N-methyl piperazine with dichloro isocyanato phosphine oxide in presence of dry toluene at -15 to -5^0c for 30 minutes offered the respective derivatives of 4-substituted Phenyl /marphonylyl /piperidinyl/ N–methyl piperazenyl carbamido phosphoric acid dichloride.

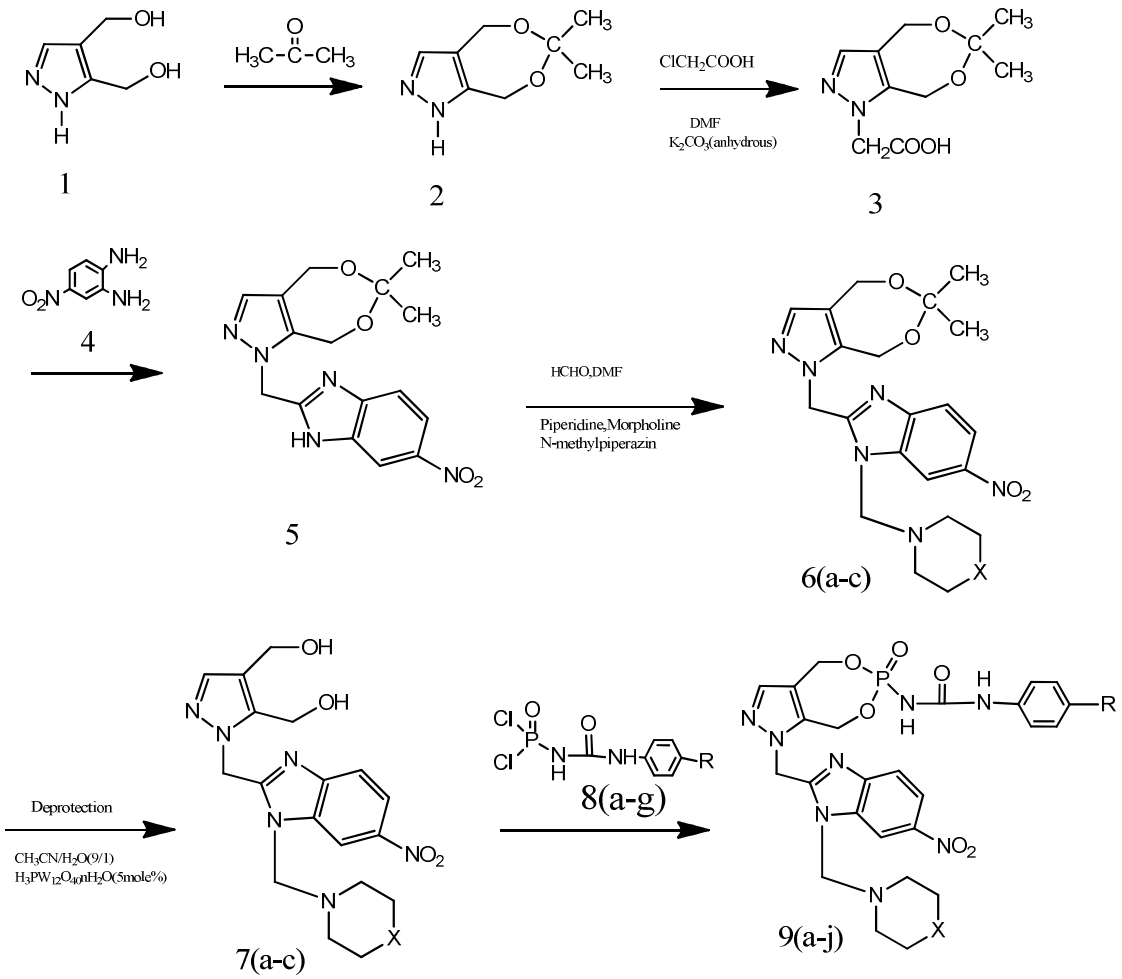
RESULTS AND DISCUSSION

Typical Procedure for Synthesis of 2-(6, 6-dimethyl-4, and 8-dihydro-1H-[1, 3] dioxepino [5, 6-c] pyrazole-1-yl) acetic acid *3:*

A suspension of 1-H-pyrazole-4, 5-dimethanol (1Mmole) (1) was dissolved in acetone (5ml) and 2, 2-dimethoxy propane (DMP, 2Mmole) solvent mixture. To the reaction mixture phosphotungstic acid (PTA, 5mole %) was added. The reaction mixture was stirred at room temperature for 4 hours under argon atmosphere until the 1-H-pyrazole-4; 5-dimethanol **(*1*)** had dissolved. The progress of the reaction was monitored by TLC using cyclohexane and ethyl acetate (9:1) solvent mixture as an eluent. After completion of the reaction, it was observed that the catalyst forms a gummy mass to stick on the wall inside the reaction flask. The solvent was decanted, dried under reduced pressure and the dried mass was re dissolved in dichloromethane (DCM). The dichloromethane solution was washed with water, dried with Na_2SO_4 and evaporated to get the crude product **(*2*)**, which was recrystallized by dissolving in boiling ether (5ml/g), cooling and then adding hexane (5ml/g) to give the pure product **(*2*)** [30]

A mixture of 6, 6-dimethyl-4, 8-dihydro-1H-[1, 3] dioxepino [5, 6-c] pyrazole **(*2*)**, anhydrous K_2CO_3 chloro acetic acid and dimethyl formamide (DMF) was stirred at room temperature for 8 hours. The progress of the reaction was monitored by TLC using cyclohexane and ethyl acetate (7:3) solvent mixture as an eluent. The reaction mixture was

diluted with ice cold water. The separated solid was identified as **(*3*)**. This was collected by filtration and recrystallized from ethanol.

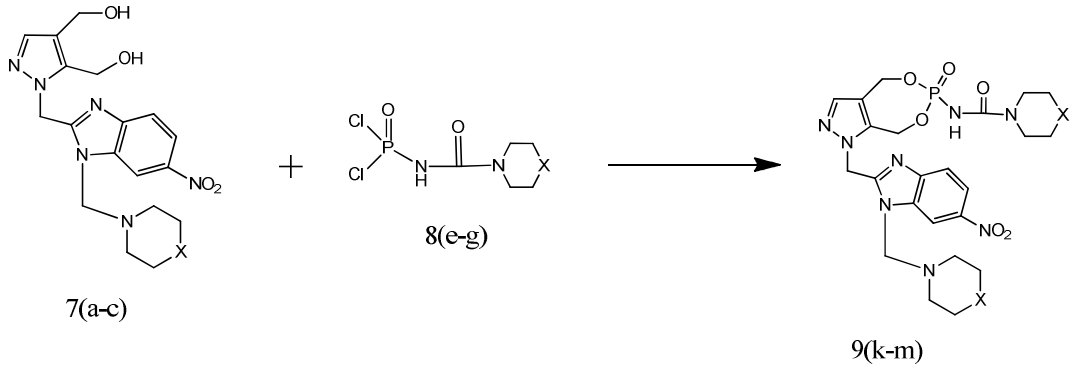


Scheme:1:synthetic route of 1(-(1-((1-(morpholinomethyl/piperidin-1-ylmethyl/(4-methyl piperazine-1-yl) methyl))-6-nitro-1H-benzo[d]imidazole-2-yl)methyl)-6-oxido-4,8-dihydro-1H-[1,3,2]dioxaphosphepino[5,6-c]pyrazole-6-yl)-3-(phenyl/p-tolyl/4-methoxy phenyl / 4-chloro phenyl) ureas (9a-j)

Compound *9*	*9a*	*9b*	*9c*	*9d*	*9e*	*9f*	*9g*	*9h*	*9i*	*9j*
R	-H	$-CH_3$	$-OCH_3$	-Cl	-H	$-CH_3$	-Cl	-H	$-CH_3$	-Cl
X	O	O	O	O	-CH2	-CH2	-CH2	$-N-CH_3$	$-N-CH_3$	$-N-CH_3$

Physical, analytical and spectral data for 2-(6, 6-dimethyl-4, 8-dihydro-1H-[1, 3] dioxepino [5, 6-c] pyrazole-1-yl) acetic acid *3:*

Yield:78%; M.p: 166-168^{O}C; IR(KBr): 2950cm^{-1}(-OH), 2940 and 2895 cm^{-1}(Aliphatic γ_{C-H}), 1690 cm^{-1} (>C=O) , 1375-1487 cm^{-1} (pyrazole ring); H^{1}-NMR(300Hz, DMSO-d6): δ 1.27 (s, 6H, two geminial CH_3 groups), 4.63(s, 2H, two CH_2 groups of acetals), 5.10 (s, 2H, -CH_2 of –CH_2COOH group), 7.30(s, 1H, of pyrazole ring) and 11.0 (s, 1H, -COOH group); Anal. calcd(%) for $C_{10}H_{14}N_2O_4$: C 53.09%, H 6.24% and N 12.38%. Found: C 52.29%, H 5.74% and N 11.78%.



Scheme:2: Synthetic route of N-(1-((1-morpholinomethyl)-1H-benzo[d]imidazol-2- yl)methyl)-6-oxido-4,8-dihydro-1H-[1,3,2]dioxaphosphepino[5,6-c]pyrazol-6-yl) morpholine/ piperadine/4-methyl piperazine carboxamides (9k-m)

Compound *9*	*9k*	*9l*	*9m*
X	O	$-CH_2$	$-N-CH_3$

Typical Procedure for Synthesis of 6, 6-dimethyl-1-((6-nitro-1H-benzo[d]imidazol-2-yl) methyl-4, 8-dihydro-1H-[1, 3]-dioxepino [5, 6-c] pyrazole (*5*) [31, 32] :

A mixture of 0.1 mole 2-(6, 6-dimethyl-4, 8-dihydro-1H-[1, 3] dioxepino [5, 6-c] pyrazole-1-yl) acetic acid **(*3*)** and 0.1 mole 4-nitrobenzene1, 2-diamine **(*4*)** was heated under reflux for 1.5 hours with stirring at 130^oC. The progress of the reaction was monitored by TLC using cyclohexane and ethyl acetate (7:3) solvent mixture as an eluent. At the end of the reaction period, the mixture was taken in a 30 ml dichloromethane and neutralized with 50 ml 1N NaOH solution, after neutralization the mixture was extracted with CH_2Cl_2 (3×25 ml). The combined extract was dried on Na_2SO_4 . After filtration, the solvent was removed with rotary evaporator. The residue was purified by column chromatography, using 60 mesh silica and $CHCl_3$ solvent was used as an eluent. Finally the product 6, 6-dimethyl-1-((6-nitro-1H-benzo [d] imidazol-2-yl) methyl-4, 8-dihydro-1H-[1, 3]-dioxepino [5, 6-c] pyrazole **(*5*)** was purified from aqueous dimethyl formamide.

Physical, analytical and spectral data for 6, 6-dimethyl-1-((6-nitro-1H-benzo[d]imidazol-2-yl) methyl-4, 8-dihydro-1H-[1, 3]-dioxepino [5, 6-c] pyrazole (*5*) :

Yield:70%; M.p: 152-154^OC;IR(KBr):3460 cm^{-1} (-NH-), 3052 cm^{-1} (Ar-H), 2940 & 2895 cm^{-1} (Aliphatic γ_{C-H}), 1390 & 1365 cm^{-1} (benzimidazole ring),1375-1487 cm^{-1} (pyrazole ring) , 1360 & 1380 cm^{-1} ($-C(CH_3)_2$) 1355 & 1330 cm^{-1} ($-NO_2$) and 1140 cm^1 (-C-O); H^1-NMR(300Hz,DMSO-d6): δ 1.27 (s, 6H, two geminial CH_3 groups), 4.63 (s, 2H, two CH_2 groups of acetals), 4.99 (s, 2H, $-CH_2-$ group flanked between pyrazole and benzimidazole ring), 5.0 (s, 1H, NH of benzimidazole ring), 7.30 (s, 1H, of pyrazole ring) and 7.66-8.39 (m, 3H, of benzimidazole ring); Anal.calcd(%) for $C_{16}H_{17}N_5O_4$: C 55.97% , H 4.99% and N 20.40% . Found: C 55.17%, H 4.49% and N 19.80%.

Typical Procedure for Synthesis of 6, 6-dimethyl-1-((6-nitro-1-((1-(piperidin-1-ylmethyl)/ (morpholino methyl) / (4-meth yl piperazin-1-ylmethyl)-1H-benzo[d]imidazol-2-yl) methyl)-4, 8-dihydro-1H-[1, 3] dioxepino [5, 6-c] pyrazole *6(a-c)* :

A mixture of 0.1 mole 6, 6-dimethyl-1-((6-nitro-1H-benzo[d]imidazol-2-yl) methyl-4, 8-dihydro-1H-[1, 3]-dioxepino [5, 6-c] pyrazole **(*5*)**, piperidine (0.15 mol) and water 20 ml was stirred to obtained a clear solution. To this solution, HCHO (0.05 mol) and DMF were added in ice cold condition and stirred for 2 hours in an ice bath and left over night at room temperature. The progress of the reaction was monitored by TLC using cyclohexane and ethyl acetate (7:3) solvent mixture as an eluent. At the end of the reaction, the mixture was taken in a 30 ml dichloromethane and neutralized with 50 ml 1N NaOH solution, after neutralization the mixture was extracted with CH_2Cl_2 (3×25 ml). The combined extract was dried on Na_2SO_4 . After filtration, the solvent was removed with rota evaporator. The residue was purified by column chromatography, using 60-120 mesh silica and $CHCl_3$ solvent was used as an eluent. Finally the product compound 6,6- dimethyl-1- ((6-nitro-1-((1-(piperidin-1-ylmethy) l-1H-benzo [d] imidazol-2-yl) methyl)-4,8-dihydro-1H-[1,3]-dioxepino[5,6-c] pyrazole **(*6a*)** was purified from aqueous dimethyl formamide. The similar procedure was adopted to synthesize ***6(b - c)*** by condensing **(*5*)** with morpholine and N-methyl piperazine respectively. The compounds thus obtained were charecterised by their elemental analysis and spectral data (IR,H^1-NMR).

Physical, analytical and spectral data for the compounds *6(a-c)*:

6,6-dimethyl-1-((1-(morpholinomethyl)6-nitro-1H-benzo[d]imidazole-2-yl)methyl-4,8dihydro-1H-[1,3] dioxepino [5,6-c]pyrazole6(a):

Yield:75%; M.p: 160-162^{O}C; IR(KBr): 3040(γ_{Ar-H}), 2940 & 2895 (Aliphatic γ_{C-H}), 1390 & 1365 (benzimidazole ring), 1375-1487(pyrazole ring), 1355 & 1330 (–NO_2) and 1145 cm^{1} (γ_{C-O}). H^{1}-NMR(300Hz,DMSO-d6): δ 1.27 (s, 6H, two geminial CH_3 groups) ,2.50 (t, 4H, -CH_2-N-CH_2 of morpholine ring J=7.5 Hz H-2^{I} and H-3^{I}), 3.65 (t, 4H, -CH_2-O-CH_2 of morpholine ring J=7.5 Hz H-3^{I} and H-2^{I}), 4.63 (s, 4H, two CH_2 groups of acetals), 4.80 (s, 2H, -N-CH_2-N- of morpholine ring), 4.99 (s, 2H, -N-CH_2-benz Imidazole ring), 7.30 (s, 1H, of pyrazole ring) and 7.66 - 8.19 (m, 3H, of benzimidazole ring); Anal.calcd(%) for $C_{21}H_{26}N_6O_5$: C 57.00%,H 5.92%,N 18.99%.Found: C 56.20%,H 5.42%,N 18.39%.

6,6-dimethyl-1-((6-nitro-1-(piperidine-1-ylmethyl)-1H-benzo[d]imidazole-2-yl)methyl-4,8dihydro-1H-[1,3] dioxepino[5,6-c]pyrazole(b):

Yield:70%; M.p: 173-175^{O}C;IR(KBr):3052 cm^{1}(γ_{Ar-H}), 2940 & 2895 cm^{1} (Aliphatic γ_{C-H}), 1395& 1365 cm^{1} (benzimidazole ring), 1375-1487 cm^{1} (pyrazole ring), 1355 & 1330 cm^{1}(γ_{-NO2}), 1140 cm^{1} (γ_{C-O}); H^{1}-NMR(300Hz,DMSO-d6):δ 1.27 (s, 6H, two geminial CH_3 groups) ,1.53-2.45 (m, 10H, $(CH_2)_5$ of piperidine ring), 4.63 (s, 4H, two CH_2 groups of acetals)

4.80 (s, 2H, -N-CH_2-N- flanked between Benzimidazole and piperidine ring), 4.99 (s, 2H, -CH_2- group flanked between pyrazole and benzimidazole ring), 7.30 (s, 1H, of pyrazole ring) and 7.66 -8.19 (m, 3H, of benzimidazole ring);); Anal.calcd(%) for $C_{22}H_{28}N_6O_4$: C 59.99% , H 6.41% ,N 19.08% . Found: C: 59.19%, H: 5.91% N: 18.68%.

6,6-dimethyl-1-((1-(morpholinomethyl)6-nitro-1H-benzo[d]imidazole-2-yl)methyl-4,8dihydro-1H-[1,3]dioxepino [5,6-c]pyrazole6(c):

Yield:70%; M.p: 185-187^{O}C;IR(KBr): 3035 cm^{1}(γ_{Ar-H}),2940 & 2895 cm^{1} (Aliphatic γ_{C-H}), 1398& 1370cm^{1} (benzimidazole ring),1375-1487 cm^{1} (pyrazole ring),1355 & 1330 cm^{1} (γ_{-NO2}), 1148 cm^{1} (γ_{C-O}); H^{1}-NMR(300Hz,DMSO-d6): δ 1.27 (s, 6H, two geminial CH_3 groups) , 2.26 (s, 3H, CH_3 group attached to piperazine ring), 2.35 (m, 8H, $(CH_2)_4$ of piperazine ring), 4.63 (s, 4H, two CH_2 groups of acetals), 4.80 (s, 2H, -N-CH_2-N- flanked between Benzimidazole and N-methyl piperazine ring), 4.99 (s, 2H, -CH_2- group flanked between pyrazole and benzimidazole ring), , 7.30(s, 1H, of pyrazole ring) and 7.66 -8.19 (m, 3H, of benzimidazole ring); Anal.calcd(%) for $C_{22}H_{29}N_7O_4$: C 58.01%,H 6.42%, N 21.52%. Found: C 57.21%,H 5.92%,N 20.92%.

Typical Procedure for Synthesis of1-((1- (piperidin-1-ylmethyl) / (1-morpholinomethyl) / (4-methylpiperazin-1-yl methyl)-6 -nitro-1H-benzo[d]imidazol-2-yl) methyl)-1H-pyrazole-4, 5-diyl) dimethanol *7(a-c)*:

The isopropylidenation of 1, 2-diols was carried out by a procedure as reported in the literature[29]. A suspension of the 6,6- dimethyl-1- ((6-nitro-1-((1-(piperidin-1-ylmethy) l-1H-benzo [d] imidazol-2-yl) methyl)-4,8-dihydro-1H-[1,3]-dioxepino[5,6-c] pyrazole ***(6a)*** (1 m mol) in dry acetone and to this 5 mol % of phosphotungstic acid was added and the reaction mixture was stirred at room temperature under nitrogen atmosphere for 1 hour The progress of the reaction was monitored by TLC using cyclohexane and ethyl acetate (7:3) solvent mixture as an eluent. After completion of the reaction, the solvent was removed under reduced pressure. The residue was extracted with dichloromethane (3×20 ml) and water and the combined organic layer was dried with Na_2SO_4 and concentrated in vacuum to give the crude product. The crude product was purified by column chromatography on silica gel (60-120 mesh) with 15-30% ethyl acetate in cyclohexane as an eluent. The similar procedure was adopted to synthesise ***7b*** & ***7c*** from ***6b*** & ***6c.*** The compounds thus obtained were charecterised by their elemental analysis and spectral data (IR,H^{1}-NMR).

Physical, analytical and spectral data for the compounds *7(a-c):*

1-((1-morpholinomethyl)-6-nitro-1H-benzo[d]imidazol-2-yl)methyl)-1H-pyrazole-4,5-diyl) dimethanol(7a):

Yield:65%; M.p: 149-151^{O}C;IR(KBr): 3520(γ_{O-H}), 3040(γ_{Ar-H} **),** 2940 & 2895(Aliphatic γ_{C-H} **),** 1385 & 1365(Benzimidazolering), 1375-1487(pyrazole ring), 1355 & 1330(γ_{-NO2} **) ,** 1145 (γ_{C-O}); H^{1}-NMR(300Hz,DMSO-d6): δ 2.50 (t, 4H, -CH_2-N-CH_2 of morpholine ring J=7.2 Hz H-2^{I} and H-3^{I}), 3.65 (t, 4H, -CH_2-O-CH_2 of morpholine ring J=7.2 Hz H-3^{I} and H-2^{I}), 3.65 (s, 2H, two –OH groups having Intramolecular H-bonding), 4.61 (s, 2H, - CH_2 group of dimethanol),4.79(s,2H,-CH_2 group of dimethanol), 4.80 (s, 2H, -N-CH_2-N- flanked between Benzimidazole and morpholine ring), 4.99 (s, 2H, -CH_2- group flanked between pyrazole and benzimidazole ring),

7.30 (s, 1H, of pyrazole ring) and 7.66 -8.19 (m, 3H, of benzimidazole ring); Anal.calcd(%) for $C_{18}H_{22}N_6O_5$:C 53.73% ,H 5.51%, N 20.88%. Found: C 52.93%, H 5.01%, and N 20.28%.

1-((6-nitro-1-(piperidine-1-ylmethyl)-1H-benzo[d]imidazole-2-yl)methyl)-1H-pyrazole-4,5-diyl)dimethanol7(b):
Yield:75%; M.p: 162-164^{O}C; IR(KBr): 3520(γ_{O-H}), 3040(γ_{Ar-H}), 2940 & 2895(Aliphatic γ_{C-H}), 1385 & 1365 (Benzimidazolering), 1375-1487(pyrazole ring), 1355 & 1330(γ_{-NO2}) , 1145 (γ_{C-O}); H^1-NMR(300Hz,DMSO-d6): δ 1.53-2.45 (m, 10H, $(CH_2)_5$ of piperidine ring), 3.65 (s, 2H, two –OH groups having Intramolecular H-bonding), 4.61 (s, 2H, - CH_2 group of dimethanol),4.79(s,2H,-CH_2 group of dimethanol), 4.80 (s, 2H, -N-CH_2-N- flanked between Benzimidazole and piperidine ring), 4.99 (s, 2H, -CH_2- group flanked between pyrazole and benzimidazole ring), 7.30 (s, 1H, of pyrazole ring) and 7.66 -8.19 (m, 3H, of benzimidazole ring); Anal.calcd(%) for $C_{18}H_{22}N_6O_5$: C 56.99%, H 6.04% ,N 20.99.Found : C 56.18%, H 5.54% N 20.39%.

(1-((1-((4-methylpiperazin-1-yl)methyl)-6-nitro-1H-benzo[d]imidazole-2-yl)methyl-1H-pyrazole-4,5-diyl)dimethanol7(c):
Yield:70%; M.p:166-168^{O}C;IR(KBr):3520(γ_{O-H}), 3035(γ_{Ar-H}), 2940 & 2895(Aliphatic γ_{C-H}), 1385 & 1365 (Benzimidazolering), 1375-1487(pyrazole ring), 1355 & 1330(γ_{-NO2}) , 1148(γ_{C-O}); H^1-NMR(300Hz,DMSO-d6): δ 2.26 (s,3H,-CH_3 group attached to piperazine ring),2.35 (m, 8H, $(CH_2)_4$ of piperazine ring), 3.65 (s, 2H, two –OH groups having Intramolecular H-bonding), 4.61 (s, 2H, - CH_2 group of dimethanol),4.79(s,2H,-CH_2 group of dimethanol), 4.80 (s, 2H, -N-CH_2-N- flanked between Benzimidazole and N-methyl piperazine ring), 4.99 (s, 2H, -CH_2- group flanked between pyrazole and benzimidazole ring), 7.30 (s, 1H, of pyrazole ring) and 7.66 -8.19 (m, 3H, of benzimidazole ring; Anal.calcd(%) for $C_{19}H_{25}N_7O_4$: C 54.93%,H 6.07%,N 23.60%.

Typical Procedure for Synthesis of 1(-(1-((1-(morpholinomethyl/piperidin-1-ylmethyl/(4-methyl piperazine-1-yl)methyl))-6-nitro-1H-benzo[d]imidazole-2-yl)methyl)-6-oxido-4,8-dihydro-1H-[1,3,2] dioxaphosphepino[5,6-c] pyrazole-6-yl)-3-(phenyl/p-tolyl/4-methoxy phenyl / 4-chloro phenyl) ureas (*9a-j*):
A solution of (phenylcarbamoyl)phosphoramidic dichloride(8a) (0.002 mole) in 25 ml of dry toluene was added drop wise over a period of 20 minutes to a stirred solution of 1-((1-morpholinomethyl)-6-nitro-1H-benzo[d]imidazol-2-yl)methyl)-1H-pyrazole-4,5-diyl)dimethanol **(*7a*)** (0.002mole) and triethylamine (0.004mole) in 30 ml of dry toluene and 10ml of tetrahydrofuran at 5^0c. After completion of the addition, the temperature of the reaction mixture was slowly raised to room temperature and stirred for 2 hours. Later the reaction mixture was heated to 50-60^{O}C and maintained for 4 hours with stirring. The completion of the reaction was monitored by TLC analysis. Triethyl amine 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 1-1-((1-(morpholino methyl)-6-nitro-1H-bezo[d] imidazole-2-yl)-6-oxido-4,8-dihydro-1H-[1,3,2]dioxaphosphepino[5,6-c]pyrazol-6-yl)-3-phenylurea **(*9a*)** .The similar procedure was adopted to synthesise 9b-d by the reaction between 7a with p-tolyl carbamoyl phosphoramidic dichloride **(*8b*)**, 4-methoxy phenyl carbamoyl phosphoramidic dichloride **(*8c*)**, and 4-chloro phenyl carbamoyl phosphoramidic dichloride **(*8 d*)**.

The reaction between 7b with phenylcarbamoyl) phosphoramidic dichloride **(*8a*)**, p-tolyl carbamoyl phosphoramidic dichloride **(*8b*)** and 4-chloro phenyl carbamoyl phosphoramidic dichloride **(*8d*)** afforded ***9e-g***. The similar procedure was adapted to synthesis ***9h-j*** from ***7c*** and ***8a/8b/8d*** respectively.. The compounds thus obtained were charecterised by their elemental analysis and spectral data (IR,H^1-NMR, P^{31}-NMR,C^{13}-NMR and Mass).

Physical, analytical and spectral data for the compounds *9(a-j):*
1-(1-((1-morpholinomethyl)-6-nitro-1H-benzo[d]imidazol-2-yl)methyl)-6-oxido-4,8-dihyro-1H-[1,3,2]dioxaphos pheno[5,6-c]pyrazol-6-yl)-3-phenylurea9(a):
Yield:65%; M.p:168-17^{O}C;IR(KBr): 3317(γp-NH),3052(Ar-H), 2940&2895(Aliphatic C-H), 1656 (NH-CO) 1390&1365 (Benzimidazole), 1375-1487(pyrazole), 1355&1330 (-NO_2), 1300 (C-O), 1250(P=O), 954(P-O); H^1-NMR(300Hz,DMSO-d6): δ 2.50 (t, 4H, -CH_2- attached to nitrogen of morpholine ring, J=7.1 Hz, H-2^I and H-3^I), 3.65 (t, 4H, -CH_2- attached to oxygen of morpholine ring, J=7.1 Hz H-3^I and H-2^I), 4.80 (s, 2H, -N-CH_2-N- flanked between Benzimidazole and morpholine ring), 4.99 (s, 2H, pyrazole and between pyrazole and benzimidazole ring), 5.29 (s, 4H, two CH_2 groups attached to phosphorus moiety), 6.15(s,2H,-NH- of urea moiety), 7.30 (s, 1H, of pyrazole ring), 7.19-7.61 (m, 5H, C_6H_5 attached to urea moiety) and 7.66 -8.19 (m, 3H, of benzimidazole ring);C^{13}-NMR (75.46NHz , DMSo-d6): δ 135.2 , 118.0 , 141.0 , 61.8 , 60.7 , 48.9 , 145.9 , 116.1 , 118.6, 144.3 , 106.7 , 135.1 , 148.3 ,75.7 , 53.5 , 66.4 , 152.0 , 139.4, 121.6 , 128.9 and 128.0corresponding 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_{18} , C_{16} & C_{17}, C_{19} , C_{20} , C_{21} & C_{25} , C_{22} & C_{24} and C_{23} ;

^{31}PNMR(161.89MHz,DMSO-d6): δ 11.20, 1.36; Anal.calcd(%) $C_{25}H_{27}N_8O_7P$: C 51.55% , H 4.67% , N 19.24%, P 5.32%.Found: C:50.75% , H 4.17%, N 18.84, P 4.62%.

1-(1-((1-morpholinomethyl)-6-nitro-1H-benzo[d]imidazol-2-yl)methyl)-6-oxido-4,8-dihyro-1H-[1,3,2]dioxaphos pheno[5,6-c]pyrazol-6-yl)-3-(p-tolyl)urea9(b):

Yield:70%; M.p:146-148^{O}C;IR(KBr): 3320 (γp-NH), 3055 (Ar-H)**,** 2940&2895(Aliphatic C-H), 1660 (NH-CO**)** 1390&1365 (Benzimidazole), 1375-1487(pyrazole), 1355 &1330 (-NO_2), 1300 (C-O), 1245 (P=O), 950 (P-O); H^1-NMR(300Hz,DMSO-d6): δ 2.34 (s, 3H ,CH_3 group attached to phenyl urea), 2.50 (t, 4H, -CH_2- attached to nitrogen of morpholine ring, J=7.1 Hz,H-2^I and H-3^I), 3.65 (t, 4H, -CH_2- attached to oxygen of morpholine ring, J=7.1 Hz H-3^I and H-2^I), 4.80 (s, 2H, -N-CH_2-N- flanked between Benzimidazole and morpholine ring), 4.99 (s, 2H, -CH_2- group flanked between pyrazole and benzimidazole ring), 5.29 (s, 4H, two CH_2 groups attached to phosphorus moiety), 6.15(s, 2H,-NH- of urea moiety), 7.21-7.56 (m, 4H, C_6H_4 attached to urea moiety), 7.30 (s, 1H, of pyrazole ring) and 7.66 -8.19 (m, 3H, of benzimidazole ring); C^{13}-NMR (75.46NHz , DMSo-d6): δ 135.2 , 118.0 , 141.0 , 61.8 , 60.7 , 48.9 , 145.9 , 116.1 , 118.6 , 144.3 , 106.7 , 135.1 , 148.3 ,75.7 , 53.5 , 66.4 , 152.0 , 136.4 , 121.5 , 129.2 , 136.8 and 21.3 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_{18} , C $_{16}$ & C_{17}, C_{19} , C_{20} , C_{21} & C_{25} , C_{22} & C_{24} , C_{23} and C_{26} ; ^{31}PNMR(161.89MHz,DMSO-d6): δ -11.53; Anal.calcd(%)$C_{26}H_{29}N_8O_7P$ for : C:52.35% ,H :4.90%, N 18.7,P 5.9%. Found: C: 51.55%, H: 4.40%, N 18.18, P 6.49%.

1-(4-methoxyphenyl)-3-(1-((1-morpholinomethyl)-6-nitro-1H-benzo[d] imidazol-2-yl)methyl)-6-oxido-4,8-dihyro-1H-[1,3,2]dioxaphospheno[5,6-c]pyrazol-6-yl)-urea9(C):

Yield:70%; M.p: 154-156^{O}C;IR(KBr): 3325 (γp-NH), 3065 (Ar-H)**,** 2940&2895(Aliphatic C-H), 1665 (NH-CO**)** 1390&1365 (Benzimidazole), 1375-1487(pyrazole), 1355 &1330 (-NO_2), 1300 (C-O), 1254 (P=O), 958 (P-O); H^1-NMR(300Hz,DMSO-d6): δ 3.83 (s, 3H , methoxy group), 2.50 (t, 4H, -CH_2- attached to nitrogen of morpholine ring, J=7.1 Hz,H-2^I and H-3^I), 3.65 (t, 4H, -CH_2- attached to oxygen of morpholine ring, J=7.1 Hz H-3^I and H-2^I), 4.80 (s,2H,-N-CH_2-N- flanked between Benzimidazole and morpholine ring) , 4.99 (s, 2H, -CH_2- group flanked between pyrazole and benzimidazole ring) , 5.29 (s, 4H, two CH_2 groups attached to phosphorus moiety), 6.15(s,2H,-NH- of urea moiety), 6.97-7.51 (m, 4H, C_6H_4 attached to urea moiety), 7.30 (s, 1H, of pyrazole ring) and 7.66 -8.19 (m, 3H, of benzimidazole ring); C^{13}-NMR (75.46NHz , DMSo-d6): δ 135.2 , 118.0, 141.0 , 61.8 , 60.7 , 48.9, 145.9, 116.1, 118.6, 144.3, 106.7, 135.1, 148.3,75.7, 53.5, 66.4, 152.0, 131.7, 119.8, 114.5, 158.9, and 55.8 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_{18}, C $_{16}$ & C_{17}, , C_{19}, C_{20}, C_{21} & C_{25} , C $_{22}$ & C_{24}, C_{23}, and C_{26};^{31}PNMR(161.89MHz,DMSO-d6): δ -11.48 ; Anal.calcd(%)$C_{26}H_{29}N_8O_8P$: C:50.98% ,H :4.77%,N 18.29%, P 5.06%.

1-(4-chlorophenyl)-3-(1-((1-morpholinomethyl)-6-nitro-1H-benzo[d]imidazol-2-yl)methyl)-6-oxido-4,8-dihyro-1H-[1,3,2]dioxaphospheno[5,6-c]pyrazol-6-yl)-urea9(d) :

Yield:70%; M.p: 172-174^{O}C;IR(KBr): 3330 (γp-NH), 3067 (Ar-H)**,** 2940&2895(Aliphatic C-H), 1670 (NH-CO**)** 1390&1365 (Benzimidazole), 1375-1487(pyrazole), 1355 &1330 (-NO_2), 1300 (C-O), 1256 (P=O), 956 (P-O); H^1-NMR(300Hz,DMSO-d6): δ 2.50 (t, 4H, -CH_2- attached to nitrogen of morpholine ring, J=7.1 Hz,H-2^I and H-3^I), 3.65 (t, 4H, -CH_2- attached to oxygen of morpholine ring, J=7.1 Hz H-3^I and H-2^I), 4.80(s,2H, -N-CH_2-N- flanked between Benzimidazole and morpholine ring), 4.99 (s, 2H, -CH_2- group flanked between pyrazole and benzimidazole ring), 5.29(s, 4H, two CH_2 groups attached to phosphorus moiety), 6.15(s,2H,-NH- of urea moiety), 7.30 (s, 1H, of pyrazole ring), 7.47-7.75 (m, 4H, C_6H_4 attached to urea moiety) and 7.66 -8.19 (m, 3H, of benzimidazole ring); C^{13}-NMR (75.46NHz , DMSo-d6): δ 135.2 , 118.0 , 141.0 , 61.8 , 60.7 , 48.9 , 145.9 , 116.1 , 118.6 , 144.3 , 106.7 , 135.1 , 148.3 ,75.7 , 53.5 , 66.4 , 152.0 , 137.5 , 120.8 , 129.0 and 133.3 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_{18}, C $_{16}$ & C_{17} , C_{19}, C_{20}, C_{21} & C_{25} , C $_{22}$ & C_{24} and C_{23} ; ^{31}PNMR(161.89MHz,DMSO-d6): δ -9.23,; Anal.calcd(%)$C_{26}H_{29}N_8O_8P$ C 48.67%, H 4.25%, Cl 5.75%,N 18.16%, P 5.02%.Found: C 47.87%,H 3.75%, Cl 5.05%, N 17.56%,P 4.32%.

1-(1-((6-nitro-1-(piperidine-1-ylmethyl)-1H-benzo[d]imidazol-2-yl)methyl)-6-oxido-4,8-dihyro-1H-[1,3,2]dioxa phospheno[5,6-c]pyrazol-6-yl)-3-phenylurea9(e):

Yield:70%; M.p: 139-141^{O}C;IR(KBr): 3315 (γp-NH), 3069 (Ar-H)**,** 2940&2895(Aliphatic C-H), 1655 (NH-CO**)** 1390&1365 (Benzimidazole), 1375-487(pyrazole), 1355 &1330 (-NO_2), 1300 (C-O), 1259 (P=O), 961 (P-O); H^1-NMR(300Hz,DMSO-d6): δ 1.53-2.45(m,10H,-$(CH_2)_5$ of piperidine ring), 4.80 (s, 2H, -N-CH_2-N- flanked between

Benzimidazole and piperidine ring), 4.99 (s, 2H, -CH_2- group flanked between pyrazole and benzimidazole ring), 5.29 (s, 4H, two CH_2 groups attached to phosphorus moiety), 6.15(s,2H,-NH- of urea moiety), 7.19-7.61(m,5H, C_6H_5 attached to urea moiety),7.30 (s, 1H, of pyrazole ring), 7.66-8.19(m, 3H, of benzimidazole ring; C^{13}-NMR (75.46NHz , DMSo-d6): δ 135.2 , 118.0 , 141.0 , 61.8 , 60.7 , 48.9 , 145.9 , 116.1 , 118.6 , 144.3 , 106.7 , 135.1 , 148.3 ,75.7 , 54.5 , 25.6 , 24.5 , 150.2 , 139.4 , 121.6 , 128.9 and 128.0 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_{19} , C_{16} & C_{18}, , C_{17} , C_{20} , C_{21} , C_{22} & C_{26} , C_{23} & C_{25} , and C_{24} ; ^{31}PNMR(161.89MHz,DMSO-d6): δ -11.50, 1.45; Anal.calcd(%)$C_{26}H_{29}N_8O_6P$: C 53.79% ,H 5.04%, N 19.30%, P 5.34%.Found: C 52.99% ,H 4.54% ,N 18.70%,P 4.64%.

1-(1-((6-nitro-1-(piperidine-1-ylmethyl)-1H-benzo[d]imidazol-2-yl)methyl)-6-oxido-4,8-dihyro-1H-[1,3,2]dioxa phospheno[5,6-c]pyrazol-6-yl)-3-(p-tolyl)urea9(f):

Yield:70%; M.p: 158-160^{O}C;IR(KBr): 3324 (γp-NH), 3070 (Ar-H)**,** 2940&2895(Aliphatic C-H), 1658 (NH-CO**)** 1390&1365 (Benzimidazole), 1375-1487(pyrazole), 1355 &1330 (-NO_2), 1300 (C-O), 1256 (P=O), 964 (P-O); H^1-NMR(300Hz,DMSO-d6): δ 1.53-2.45(m,10H,-$(CH_2)_5$ of piperidine ring), 2.34 (s, 3H ,CH_3 group attached to phenyl urea), 4.80 (s, 2H, -N-CH_2-N- flanked between Benzimidazole and piperidine ring), 4.99 (s, 2H, -CH_2- group flanked between pyrazole and benzimidazole ring), 5.29 (s, 4H, two CH_2 groups attached to phosphorus moiety), 6.15(s,2H,-NH- of urea moiety), 7.30 (s, 1H, of pyrazole ring),7.21-7.56(m,4H, C_6H_4 attached to urea moiety),7.66-8.19(m, 3H, of benzimidazole ring); C^{13}-NMR (75.46NHz , DMSo-d6): δ 135.2 , 118.0 , 141.0 , 61.8 , 60.7 , 48.9 , 145.9 , 116.1 , 118.6 , 144.3 , 106.7, 135.1 , 148.3 ,75.7 , 54.5 , 25.6 , 24.5 , 150.2 , 136.4 , 121.5 , 129.5 , 136.8 and 21.3 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_{19} , C_{16} & C_{18} , C_{17} , C_{20} , C_{21} , C_{22} & C_{26} , C_{23} & C_{25} , C^{24} and C_{27}; ^{31}PNMR(161.89MHz,DMSO-d6): -11.75; Anal.calcd(%)$C_{27}H_{31}N_8O_6P$: C 54.54% ,H 5.26%,N 18.85%, P 5.21%. Found:C 53.74% , H 4.76%, N 18.25%, P 4.51%.

1-(4-chlorophenyl)-3-(1-((6-nitro-1-(piperidine-1-ylmethyl)-1H-benzo[d]imidazol-2-yl)methyl)-6-oxido-4,8-dihyro-1H-[1,3,2]dioxaphospheno[5,6-c]pyrazol-6-yl)urea9(g):

Yield: 75%; M.p: 183-18^{O}C;IR(KBr): 3328 (γp-NH), 3075 (Ar-H)**,** 2940&2895(Aliphatic C-H), 1668 (NH-CO**)** 1390&1365 (Benzimidazole), 1375-1487(pyrazole), 1355 -1330 (-NO_2), 1300 (C-O), 1258 (P=O), 966 (P-O); H^1-NMR(300Hz,DMSO-d6): δ 1.53-2.45(m,10H,-$(CH_2)_5$ of piperidine ring), 4.80 (s, 2H, -N-CH_2-N- flanked between Benzimidazole and piperidine ring),4.99 (s,2H,-C H_2 - group flanked between pyrazole and benzimidazole ring), 5.29 (s, 4H, two CH_2 groups attached to phosphorus moiety), 6.15(s,2H,-NH- of urea moiety), 7.30 (s, 1H, of pyrazole ring),7.47-7.75(m,4H, C_6H_4 attached to urea moiety),7.66-8.19(m, 3H, of benzimidazole ring); C^{13}-NMR (75.46NHz , DMSo-d6): δ 135.2 , 118.0 , 141.0 , 61.8 , 60.7 , 48.9 , 145.9 , 116.1 , 118.6 , 144.3 , 106.7 , 135.1 , 148.3 ,75.7 , 54.5 , 25.6 , 24.5 , 150.2 , 137.5 , 120.8 , 129.0 and 133.3 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_{19} , C_{16} & C_{18} , C_{17} , C_{20} , C_{21} , C_{22} & C_{26} , C_{23} & C_{25} and C_{24} ; ^{31}PNMR(161.89MHz,DMSO-d6): -10.52; Anal.calcd(%)$C_{26}H_{28}ClN_8O_6P$: C 50.78%, H 4.59%, Cl 5.76%, N 18.22%,P 5.04%.Found: C 49.98% ,H 4.09%, Cl 5.06%,N 17.62%, P 4.34%.

1-(1-((1-((4-methylpiperazin-1-yl)methyl)-6-nitro-1H-benzo[d]imidazol-2-yl)methyl)-6-oxido-4,8-dihyro-1H-[1,3,2] dioxaphospheno[5,6-c]pyrazol-6-yl)-3-phenylurea9(h):

Yield: 75%; M.p: 170-17^{O}C;IR(KBr): 3320 (γp-NH), 3062 (Ar-H)**,** 2940&2895(Aliphatic C-H), 1656 (NH-CO**)** 1390&1365 (Benzimidazole), 1375-1487(pyrazole), 1355 &1330 (-NO_2), 1300 (C-O), 1254 (P=O), 968 (P-O); H^1-NMR(300Hz,DMSO-d6): δ 2.26 (s, 3H, CH_3 attached to piperazine ring),2.35(m,8H,-(CH2)4 of piperazine ring), 4.80(s,2H,-N-CH_2-N- flanked between Benzimidazole and N-methyl piperazine ring,), 4.99 (s, 2H, -CH_2- group flanked between pyrazole and benzimidazole ring), 5.29 (s, 4H, two CH_2 groups attached to phosphorus moiety), 6.15(s,2H,-NH- of urea moiety), 7.19-7.61(m,5H, C_6H_5 attached to urea moiety),7.30 (s, 1H, of pyrazole ring),7.19-7.61(m,5H, C_6H_5 attached to urea moiety),7.66-8.19(m,3H,of benzimidazole ring); C^{13}-NMR (75.46NHz , DMSo-d6): δ 135.2 , 118.0 , 141.0 , 61.8 , 60.7 , 48.9 , 145.9 , 116.1 , 118.6 , 144.3 , 106.7 , 135.1 , 148.3 ,75.4 , 52.5 ,57.3 ,46.6 ,150.2 ,139.4 , 121.6 , 128.9 and 128.0 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_{18} , C_{16} & C_{17} , C_{19} , C_{20} , C_{21} , C_{22} & C_{26} , C_{23} & C_{25} and C_{24} ; ^{31}PNMR(161.89MHz,DMSO-d6): -12.15, 1.65;Anal.calcd(%) $C_{27}H_{31}N_8O_6P$: C 52.44%,H 5.08%,N 21.17%, P 5.20% .Found: C 51.84%, H 4.58%,N 20.57%, P 4.50%.

1-(1-((1-((4-methylpiperazin-1-yl)methyl)-6-nitro-1H-benzo[d]imidazol-2-yl)methyl)-6-oxido-4,8-dihyro-1H-[1,3,2] dioxaphospheno[5,6-c]pyrazol-6-yl)-3-(p-tolyl)urea9(i):

Yield: 70%; M.p: 162-164^{O}C;IR(KBr):3318(γp-NH), 3050 (Ar-H)**,** 2940&2895(Aliphatic C-H), 1658 (NH-CO**)** 1390&1365 (Benzimidazole), 1375-1487(pyrazole), 1355 &1330 (-NO_2), 1300 (C-O), 1250(P=O), 963 (P-O); H^1-NMR(300Hz,DMSO-d6): δ 2.26 (s, 3H, CH_3 attached to piperazine ring), 2.34 (s, 3H ,CH_3 group attached to phenyl urea),2.35(m,8H,-(CH2)4 of piperazine ring),4.80 (s, 2H, -N-CH_2-N- flanked between Benzimidazole and N-methyl piperazine ring), 4.99 (s, 2H, -CH_2- group flanked between pyrazole and benzimidazole ring), 5.29(s, 4H, two CH_2 groups attached to phosphorus moiety), 6.15(s,2H,-NH- of urea moiety), 7.21-7.51(m,4H, C_6H_4 attached to urea moiety),7.30 (s, 1H, of pyrazole ring), 7.66-8.19(m, 3H, of benzimidazole ring); C^{13}-NMR (75.46NHz , DMSo-d6): δ 135.2 , 118.0 , 141.0 , 61.8 , 60.7 , 48.9 , 145.9 , 116.1 , 118.6 , 144.3 , 106.7 , 135.1 , 148.3 ,75.4 , 52.5 ,57.3 ,46.6 ,150.2 , 136.4 , 121.5 , 129.5 , 136.8 and 21.3 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_{18} , C_{16} & C_{17} , C_{19} , C_{20} , C_{21} , C_{22} & C_{26} , C_{23} & C_{25} , C_{24} and C_{27} ; ^{31}PNMR(161.89MHz,DMSO-d6): -10.75; Anal.calcd(%) $C_{27}H_{32}N_9O_6P$: C 53.20%, H 5.29%, N 20.68%, p 5.08 .Found: C 52.40% ,H 4.79% ,N 20.08%, P 4.38%.

1-(4-chlorophenyl)-3-(1-((1-((4-methylpiperazin-1-yl)methyl)-6-nitro-1H-benzo[d]imidazol-2-yl)methyl)-6-oxido-4,8-dihyro-1H-[1,3,2]dioxaphospheno[5,6-c]pyrazol-6-yl)urea9(J) :

Yield: 75%; M.p: 158-160^{O}C;IR(KBr): 3328 (γp-NH), 3055 (Ar-H)**,** 2940&2895(Aliphatic C-H), 1665 (NH-CO**)** 1390&1365 (Benzimidazole), 1375-1487(pyrazole), 1355 &1330 (-NO_2), 1300 (C-O), 1256 (P=O), 967 (P-O); H^1-NMR(300Hz,DMSO-d6): δ 2.26 (s, 3H, CH_3 attached to piperazine ring), 2.35(m,8H,-(CH2)4 of piperazine ring), 4.80 (s, 2H, -N-CH_2-N- flanked between Benzimidazole and N-methyl piperazine ring), 4.99 (s, 2H, -CH_2- group flanked between pyrazole and benzimidazole ring), 5.29 (s, 4H, two CH_2 groups attached toPhosphorus moiety), 6.15(s,2H,-NH- of urea moiety), 7.30 (s, 1H, of pyrazole ring),7.47-7.75(m,4H, C_6H_4 attached to urea moiety) ,7.66-8.19 (m, 3H, of benzimidazole ring);C^{13}-NMR (75.46NHz , DMSo-d6): δ 135.2 , 118.0 , 141.0 , 61.8 , 60.7 , 48.9 , 145.9 , 116.1 , 118.6 , 144.3 , 106.7 , 135.1 , 148.3 , 75.4 , 52.5 , 57.3 , 46.6 , 150.2 , 137.5 , 120.8 , 129.0 and 133.3 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_{18} , C_{16} & C_{17} , C_{19} , C_{20} , C_{21} , C_{22} & C_{26} , C_{23} & C_{25} and C_{24} ; ^{31}PNMR(161.89MHz,DMSO-d6): -10.75; Anal.calcd(%)$C_{26}H_{29}ClN_9O_6P$: C 49.57%, H 4.64%, Cl 5.63%, N 20.01%, P 4.92% . Found: C 48.77%, H 4.14%, Cl 4.93%, N 19.41%, P 4.22%.

Typical Procedure for Synthesis of N-(1-((1-morpholinomethyl)-1H-benzo[d]imidazol-2-yl)methyl)-6-oxido- , 8-dihydro-1H-[1,3,2]dioxaphosphepino[5,6-c]pyrazol-6-yl)morpholine/piperadine/4-methylpiperazine carboxamides(*9k-m*):

A solution of Morpholino carbamoyl phosphoramidic dichloride(8e) (0.002 mole) in 25 ml of dry toluene was added drop wise over a period of 20 minutes to a stirred solution of 1-((1-morpholino methyl)-6-nitro -1H-benzo[d]imidazol-2-yl)methyl)-1H-pyrazole-4,5-diyl) dimethanol***7(a)***(0.002mole)andtriethylamine(0.004 mole) in 30 ml of dry toluene and 10ml of tetrahydrofuran at 5^0c. After completion of the addition, the temperature of the reaction mixture was slowly raised to room temperature and stirred for 2 hours. Later the reaction mixture was heated to 50-60^{O}C and maintained for 4 hours with stirring. The completion of the reaction was monitored by TLC analysis. Trimethyl amine 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 N-(1-((1-(morpholino methyl)-6-nitro-1H-bezo[d]imidazol-2-yl)methyl)-6-oxido-4,8-dihydro-1H-[1,3,2]dioxaphosphepino[5,6-c]pyrazol-6-ylmorpholine-4-carboxamide **(*9k*)**.

The similar procedure was adopted to synthesize 9l and 9m by the reaction between ***7b*** and ***7c*** with (piperidine-1-carbonyl) phosphoramidic dichloride ***8(f)*** and 4-methyl piperazine-1-carbamoyl phosphoramidic dichloride ***8(g)*** respectively. The structures of 9l-m were established by IR, ^{1}H-NMR, ^{13}C-NMR, mass data and elemental analysis. The compounds thus obtained were charecterised by their elemental analysis and spectral data (IR, H^1-NMR, P^{31}-NMR, C^{13}-NMR and Mass).

Physical, analytical and spectral data for the compounds *9(k-m):*

N-1-((1-(morpholinomethyl)-6-nitro-1H-benzo[d]imidazol-2-yl)-6-oxido-4,8-dihydro-1H-[1,3,2] dioxaphosphepino [5,6-c]pyrazol-6-yl)morpholine-4-carboxamide9(K):

Yield: 70%; M.p: 184-186^{O}C;IR(KBr): 3317 (γp-NH), 3052 (Ar-H)**,** 2940&2895(Aliphatic C-H), 1656 (-CO-N<**)** 1390&1365 (Benzimidazole), 1375-1487(pyrazole), 1355 &1330 (-NO_2), 1300 (C-O), 1250 (P=O), 954 (P-O); H^1-

NMR(300Hz,DMSO-d6): δ 2.50 (t, 4H, -CH_2-N-CH_2 of morpholine ring attached to benzimidazole ring, J=7.1 Hz,H-2^I and H-3^I),3.31(t,4H, -CH_2- N-CH_2- of morpholine ring attached to carbamido moiety, J=7.1Hz, H-2^I and H-3^I),(3.65 (t, 8H, -CH_2-O-CH2- group of two morpholine rings , J=7.1 Hz H-3^I and H-2^I), 4.80 (s, 2H, -N-CH_2-N flanked between Benzimidazole and morpholine ring), 4.99 (s, 2H, -CH_2- group flanked between pyrazole and benzimidazole ring), 5.29 (s, 4H, two CH_2 groups attached to phosphorus moiety), 6.15(s,1H,-NH- of urea moiety), 7.30 (s, 1H, of pyrazole ring), and 7.66 -8.19 (m, 3H, of benzimidazole ring); C^{13}-NMR (75.46NHz , DMSo-d6): δ 135.2 , 118.0 , 141.0 , 61.8 , 60.7 , 48.9 , 145.9 ,116.1 , 118.6 , 144.3 ,106.7 , 135.1 , 148.3 ,75.7 , 53.5 , 66.4 , 158.5 ,46.3 and 65.7 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_{18} , C_{16} & C_{17} , C_{19} , C_{20}& C_{23} and C_{21}& C_{22} ;^{31}PNMR(161.89MHz,DMSO-d6): -7.15; Anal.calcd(%)$C_{23}H_{29}N_8O_8P$: C 47.92% , H 5.07%, N 19.44%, P 5.37%. Found: C 47.12%, H 4.57%, N 18.84%, and P 4.67%.

N-(1-((6-nitro-1-(piperidine-1-ylmethyl)-1H-benzo[d]imidazol-2-yl)-6-oxido-4,8-dihydro-1H-[1,3,2]dioxaphos phepino[5,6-c]pyrazol-6-yl)piperidine-1-carboxamide9(l):

Yield: 70%; M.p: 172-174^{O}C;IR(KBr): 3315 (γp-NH), 3055 (Ar-H)**,** 2940&2895(Aliphatic C-H), 1655 (-CO-N<**)** 1390&1365 (Benzimidazole), 1375-1487(pyrazole), 1355 &1330 (-NO_2), 1300 (C-O), 1245 (P=O), 950 (P-O); H^1-NMR(300Hz,DMSO-d6): δ 1.53-1.592(m,12H,3-(CH2)- groups of two piperidine rings)2.45 (t,4H,-CH_2-N-CH_2 of piperidine ring attached to Benzimidazole , J=7.1Hz H-2^I and H-3^I), 3.77(t,4H,CH2-N-CH2 of piperidine ring attached to carbamido moiety , J=7.1Hz H-2^I and H-3^I), 4.80 (s, 2H, -N-CH_2-N- flanked between Benzimidazole and piperidine ring), 4.99 (s, 2H, -CH_2- group flanked between pyrazole and benzimidazole ring), 5.29 (s, 4H, two CH_2 groups attached to phosphorus moiety), 6.15(s,2H,-NH- of urea moiety), 7.30 (s, 1H, of pyrazole ring), 7.66-8.19(m, 3H, of benzimidazole ring); C^{13}-NMR (75.46NHz , DMSo-d6): δ 135.2 , 118.0 , 141.0 , 61.8 , 60.7 , 48.9 , 145.9 , 116.1 , 118.6 , 144.3 , 106.7 , 135.1 , 148.3 , 75.7 , 54.5 , 25.6 , 24.5 , 156.5 , 49.0 , 24.9 and 23.9 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_{19} , C_{16} & C_{18} , C_{17} , C_{20} , C_{21} & C_{24} and C_{22} & C_{24} , C_{23} ; ^{31}PNMR(161.89MHz,DMSO-d6): -5.23; Anal.calcd(%)$C_{25}H_{33}N_8O_6P$: C 52.44% ,H 5.81% , N 19.57% , P 5.41% . Found: C 51.64%, H 5.31%, N 18.97%, and P 4.71%.

4-methyl-N-(1-((1-((4-methylpiperazin-1-yl)methyl)-6-oxido-4,8-dihydro-1H-[1,3,2]dioxaphosphepino[5,6-c] pyrazol-6-yl)piperazine-1-carboxamide9(m):

Yield: 75%%; M.p: 194-196^{O}C;IR(KBr): 3320 (γp-NH), 3065 (Ar-H)**,** 2940&2895(Aliphatic C-H), 1658 (-CO-N<**)** 1390&1365 (Benzimidazole), 1375-1487(pyrazole), 1355 &1330 (-NO_2), 1300 (C-O), 1254 (P=O), 958 (P-O); H^1-NMR(300Hz,DMSO-d6): δ 2.26(s,6H,-CH_3 group of two N-methyl piperazine rings) ,2.27(t,4H, -CH_2-N(CH_3)-CH_2- of piperazine attached to carbamido moiety),2.35(s,8H,-CH2-N-CH20 of piperazine ring attached to Benzimidazole ring),3.40(t,4H,-CH2-N-CH2- of piperazine ring attached to carbmido moiety=7.1Hz , H-2I and H-3I) , 4.80 (s, 2H, -N-CH_2-N- flanked between Benzimidazole and N-methyl piperazine ring), 4.99 (s, 2H, -CH_2- group flanked between pyrazole and benzimidazole ring), 5.29 (s, 4H, two CH_2 groups attached to phosphorus moiety), 6.15(s,1H,-NH- of urea moiety), 7.30 (s, 1H, of pyrazole ring),7.19-7.61(m,5H, C_6H_5 attached to urea moiety),7.66-8.19(m, 3H, of benzimidazole ring); C^{13}-NMR (75.46NHz , DMSo-d6): δ 135.2 , 118.0 , 141.0 , 61.8 , 60.7 , 48.9 , 145.9 , 116.1 , 118.6 , 144.3 , 106.7 , 135.1 , 148.3 , 75.4 , 52.5 , 57.3 , 46.6 , 158.5 , 51.4 , 51.0 and 46.6 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_{18} , C_{16} & C_{17} , C_{19} , C_{20} , C_{21} & C_{24} , C_{22} & C_{23} , and C_{25} ; ^{31}PNMR(161.89MHz,DMSO-d6): -8.23; Anal.calcd(%)$C_{25}H_{35}N_{10}O_6P$: C 9.83% , H 5.85% , N 23.24% , P 5.14% .

Biological activity:

The antimicrobial activity [33] of chemical compound is influenced by physical and biological characteristics [34].It has been well established that physiological activity is a function of the chemical structure of compound [35].Heterocyclic organic compounds containing phosphorus, oxygen, nitrogen or sulfur in the ring system are expected to be more active due to the presence of hetero atoms [36,37,38].

In view of this, the synthesized new organophosphorus heterocyclic compounds have been tested for their antimicrobial activity.

Antibacterial activity:

The antibacterial activity [39] of 1(-(1-((1-(morpholinomethyl/piperidin-1-ylmethyl/(4-methyl piperazine-1-yl) methyl))-6-nitro-1H-benzo[d] imidazole-2-yl)methyl)-6-oxido-4,8-dihydro-1H-[1,3,2]dioxaphos phepino[5,6-c]

pyrazole-6-yl)-3-(phenyl/p-tolyl/4-methoxyphenyl/4-chloro phenyl)ureas(*9a-j*) and N-(1-((1-morpholinomethyl)-1H-benzo[d] imidazol-2yl)methyl)-6-oxido-4,8-dihydro-1H-[1,3,2]dioxaphos phepino[5,6-c]pyrazol-6-yl) morpholine/piperadine/4-methyl piperazine carboxamides(*9k-m*) were screened against the Staphylococcus aureus (gram positive), BacillusCerus **,** Escherichia coli (gram negative) and Pseudomonas aeruginosa organism . Most of the compounds exhibited moderate antibacterial activity against bacteria. The presence of chloro group in the structure has shown increased effect on their antibacterial activity. Amoxicillin and Cefaclor are tested as reference compounds to compare the activity.

Antibacterial activity of 1(-(1-((1-(morpholinomethyl/piperidin-1-ylmethyl/(4-methyl piperazine-1-yl)methyl))-6-nitro-1H-benzo[d]imidazole-2-yl)methyl)-6-oxido-4,8-dihydro-1H-[1,3,2] dioxaphosphepino [5,6-c]pyrazole-6-yl)-3-(phenyl/p-tolyl/4-methoxy phenyl / 4-chloro phenyl) ureas (*9a-j*) and N-(1-((1-(morpholinomethyl)-1H-benzo [d] imidazol-2yl) methyl)-6-oxido-4, 8-dihydro -1H- [1, 3, 2] dioxaphosphepino [5,6-c] pyrazol-6-yl)morpholine/ piperidine /4-methyl piperazine carboxamides(*9k-m*)

COMPOUND (*9*)	R	X	Zone of inhibition (mm)			
			Staphylococcus aureus NCCS2079 250(µg/disc)	*Bacillus Cerus* NCCS2106 250(µg/disc)	*EscherichiaColi* NCCS2065 250(µg/disc)	*Pseudomonas aeruginosa* NCCS2200 250(µg/disc)
9a	-H	O	6	4	5	3
9b	$-CH_3$	O	4	-	3	2
9c	$-OCH_3$	O	2	-	-	2
9d	-Cl	O	16	13	15	17
9e	-H	$-CH_2$	4	2	3	3
9f	$-CH_3$	$-CH_2$	2	-	-	-
9g	-Cl	$-CH_2$	12	11	10	13
9h	-H	$-N-CH_3$	7	5	5	4
9i	$-CH_3$	$-N-CH_3$	5	3	3	2
9j	-Cl	$-N-CH_3$	14	14	13	15
9k	-	O	17	14	15	13
9l	-	$-CH_2$	11	9	11	12
9m	-	$-N-CH_3$	14	11	13	12
9n	Amoxicillin	-	21	27	24	22
9o	Cefaclor	-	19	22	19	20

"_" indicates no activity

Antifungal activity of 1(-(1-((1-(morpholInomethyl / piperidin-1-yl methyl/(4-methyl piperazine-1-yl)methyl))-6- nitro-1H-benzo[d]imidazole-2-yl)methyl)-6-oxido-4,8-dihydro-1H-[1,3,2] dioxaphosphepino [5,6-c]pyrazole-6-yl)- 3-(phenyl/p-tolyl/4-methoxy phenyl / 4-chloro phenyl) ureas (*9a-j*) and N-(1-((1-(morpholino methyl)-1H- benzo[d]imidazol-2yl) methyl)-6-oxido-4, 8-dihydro -1H-[1, 3, 2] dioxaphosphepino [5, 6-c] pyrazol-6-yl) morpholine / piperidine/4-methyl piperazine carboxamides (*9k-m*)

COMPOUND(*9*)	R	X	Zone of inhibition (mm)	
			Aspergillus niger NCCS 1196 250(µg/dsic)	*Canadida albicans* NCCS 3471 250(µg/dsic)
9a	-H	O	03	02
9b	$-CH_3$	O	02	-
9c	$-OCH_3$	O	02	-
9d	-Cl	O	12	11
9e	-H	$-CH_2$	07	05
9f	$-CH_3$	$-CH_2$	05	03
9g	-Cl	$-CH_2$	13	14
9h	-H	$-N-CH_3$	07	06
9i	$-CH_3$	$-N-CH_3$	08	05
9j	-Cl	$-N-CH_3$	14	13
9k	-	O	16	14
9l	-	$-CH_2$	10	9
9m	-	$-N-CH_3$	13	11
9n	Ketoconazole	-	22	25

"_" indicates no activity

Antifungal activity

The antifugal activity of 1(-(1-((1-(morpholinomethyl/piperidin-1-ylmethyl/(4-methyl piperazine-1-yl)methyl))-6-nitro-1H-benzo[d]imidazole-2-yl)methyl)-6-oxido-4,8-dihydro-1H-[1,3,2]dioxaphosphepino[5,6-c]pyrazole-6-yl)-3-(phenyl/p-tolyl/4-methoxyphenyl/4-chlorophenyl)ureas(*9a-j*)andN-(1-((1-morpholinomethyl)-1H-benzo[d] imidazol -2-yl)methyl)-6-oxido-4,8-dihydro-1H-[1,3,2]dioxaphosphepino[5,6-c]pyrazol-6-yl)morpholine/ piperadine /4-

methylpiperazinecarboxamides(*9k-m*) were screened against Aspergillus niger , Canadida albicans. Ketoconazole and Griseofulvinis are useful references [40, 41]. Here Ketoconazole is tested as reference compound to compare the activity.

Acknowledgements
The authors (CHLP and VER) thanks to UGC-SAP and UGC-BSR, New Delhi for financial assistance. They are also thankful to Sri Krishnadevaraya University-Anantapur; IICT, Hyderabad and CDRI Lucknow for spectral and analytical data.

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