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Synthesis, characterization and antimicrobial evaluation of novel compounds 1(-benzo[d]oxazol/thiazol-2-yl)-methyl-6-phenoxy-4,8-dihydro-1*H*-[1,3,2] dioxaphosphepino[5,6-d]imidazole-6-oxide

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ABSTRACT

New novel derivatives of 1-(5/6-mono substituted or 5,6-disubstituted benzo [d] oxazol-2-yl) methyl)-6-(4-substituted phenoxy)-4,8-dihydro-1H-[1,3,2] dioxaphosphepino [5,6-d] imidazole-6-oxide ***(8a-f as per Scheme-1)*** *were prepared by condensation of 4-substituted phenyl phosphorodichloridates* ***(7a-f)*** *with 1-(5/6-mono substituted or 5,6-disubstituted benzo [d] oxazol-2-yl)methyl) -1H-imidazole-4,5-diyl) dimethanol* ***(6a-f).*** *The synthons* ***(6a-f)*** *obtained by deprotection of isopropylidene of 1-(5/6-mono substituted or 5,6-disubstituted benzo [d] oxazol-2-yl) methyl)-6,6-dimethyl-4,8-dihydro-1H-[1,3]- dioxepino [5,6-d] imidazole* ***(5a-f)****. The synthons* ***(5a-f)*** *were obtained by the reaction of 2-(6, 6-dimethyl-4,8-dihydro-1H-[1,3] dioxepino[5,6-d] imidazole-1-yl) acetic acid* ***(3)*** *with 4/5-mono substituted or 4,5-di substituted 2-amino phenols* ***(4a-f)****. Similar procedure was adapted to prepare 1-(benzo [d] thiazol-2-yl) methyl) -6-(4-substituted phenoxy)-4,8-dihydro-1H-[1,3,2] dioxaphosphepino [5,6-d] imidazole-6-oxide* ***(12a-f according to Scheme-2).***

Key words: Benzodioxaphospholes, imidazole, cyclization, deprotection, Antibacterial and Antifungal activity.

INTRODUCTION

The chemistry of phosphorus heterocyclic compounds containing nitrogen plays an important role in the development of new pharmaceutical materials with novel properties [1, 2]. The chemistry of organophosphorus compounds and their derivatives were found to be the highlight of study in lead compound discovery and biological screening and study of their various biological activities including its application in the field of Agriculture, medicine and industry [3, 4]. Organophosphorus compounds occupied a unique position in biological activities such as anti-bacterial [5], herbicides, insecticides, pesticides [6, 7], anti-fungal agents [8], anti-HIV [9], anti-cancer [10], anti-viral and anti-inflammatory [11].

Benzoxazole and benzthiazoles nuclei are constituent of many of the bioactive heterocyclic compounds that exhibit antiangial, antiischaemic, vasodilator, anti-diabetic, anti-microbial, cardiovascular, tranquilizer and virucidal activities [12-21].

In support of our study, imidazoles are also an interesting group of compounds, many of which possess anti-fungal activity [22], anti-bacterial, monoamine oxidase (MAO) inhibitory activity [23], antiparkinson [24], anticonvulsant [25], it also function as dyestuff, catalyst, polymerizing agents, drugs, herbicides and fungicides [26]. Imidazole derivatives are valuable vasodialating and vasoconstructing drugs.

A good deal of importance was given to 1, 3, 2-Dioxaphosphorinane and dioxaphospholane derivatives [27] in the field of organophosphorus heterocyclic chemistry due to their unique stereo chemical futures and diverse potential biological applications [28]. In view of the above observations, we have synthesized imidazole derivatives

possessing Benzoxazole / Benzthiazole moiety besides 1, 3, 2-Dioxaphosphorinane and dioxaphospholanes and screening for possible biological and pharmacological activities.

EXPERIMENTAL SECTION

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 $60F_{254}$, E-Merk, Germany using iodine as visualizing agent. Melting point were determined in open capillary tubes on Mel-Temp apparatus and are uncorrected. Column 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 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 75 MHz for ^{13}C-NMR. ^{31}P-NMR spectra were 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). Mass spectral data was recorded on FAB-MS instrument at 70ev with direct inlet system. Elemental analysis were recorded on a Carlo Erba 1108 elemental Analyser, Central Drug Research Institute, Lucknow, India.

Preparation of Intermediates:

4-substituted phenyl phosphorodichloridates (7a-f) [29, 30]:

Phosphorus oxy chloride (15.3 gr, 0.1mole) in dry benzene (60 ml) was taken in to three-necked flask (500 ml) equipped with dropping funnel and reflux condenser fitted with a calcium chloride guard tube. The flask was heated and stirred by means of hot plate –cum –magnetic stirrer. To this dry triethyl amine (10.1 gr, 0.1 moles) and dry benzene (50 ml) were added slowly and the reaction mixture was stirred for 30 minutes. To this mixture, freshly distilled phenol (9.4 gr, 0.1 moles) in dry benzene (60 ml) was added drop wise through the dropping funnel. The addition took about thirty minutes and whole reaction mixture was refluxed with vigorous stirring for 10 hours. The reaction mixture was cooled and the solid tri ethylamine -hydrochloride was filtered off. The solvent from the filtrate was removed under reduced pressure in a rota evaporator. The dark brown liquid remained, was subjected to fractional distillation and the major product distilling at 118-124^{0}C / 11mm was collected as colourless glassy viscous liquid (8.3 gr, 40%).

Other substituted phenyl phosphorodichlorates **(7a-f)** were prepared by the same procedure [31-34] by reacting equimolar quantities of phosophorousoxychloride and respective substituted phenols in benzene in the presence of tri ethylamine.

RESULT AND DISCUSSION

Typical procedure for the synthesis of 2-(6, 6-dimethyl-4,8-dihydro -1H-[1,3] dioxepino [5,6-d] imidazole-1-yl) acetic acid (3) :

A suspension of 1-H-Imidazole-4, 5-dimethanol (1Mmole) 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-Imidazole-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)** [35], which was recrystallized by dissolving in boiling ether(5ml/g), cooling and then adding hexane(5ml/g) to give the pure product **(2)**. The structure of **(2)** was established by IR, ^{1}H- NMR and elemental analysis

A mixture of 6, 6-dimethyl-4, 8-dihydro-1H-[1, 3] dioxepino [5, 6-d] imidazole **(2)**, anhydrous K_2CO_3 chloroacetic 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 2-(6, 6-dimethyl-4,8-dihydro-1H-[1,3] dioxepino [5,6-d] imidazole-1-yl) acetic acid **(3)**. This was collected by filtration and recrystallized from ethanol. The structure of **(3)** was established by IR, $^{1,}H$-NMR and elemental analysis.

Typical procedure for 1- (5/6- mono substituted or 5,6-di substituted benzo[d] oxazol-2-yl-methyl)-6,6-dimethyl-4,8-dihydro -1H-[1,3] dioxepino [5,6-d] imidazol [36-38](5a-f) :

A mixture of 0.1 mole 2-(6,6-dimethyl-4,8-dihydro-1H-[1,3] dioxepino[5,6-d] imidazole-1-yl) acetic acid **(1)** and 0.1 mole of 2-aminophenol **(4a)** was heated under reflux for 1.5 hours with stirring at 140^{o}C. The progress of the

reaction was monitered by TLC using cyclohexane and ethylacetate (7:3) solvent mixture as an elutent. At the end of the reaction, the mixture was taken in a 30 ml dichloromethane and neutralized with 50 ml 1N NaOH solution. The organic layer was separated and aqueous solution extracted with CH_2Cl_2 (3×25 ml). The combined extracted were 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 1-(benzo [d] oxazol-2-yl-methyl)-6,6-dimethyl-4,8-dihydro-1H-[1,3]- dioxepino [5,6-d] imidazole **(5a)** was recrystalised from aqueous dimethyl formamide.

The similar procedure was employed for the synthesis of 1-(5/6- mono substituted or 5,6-di substituted benzo [d] oxazol-2-yl-methyl)-6,6-dimethyl-4,8-dihydro-1H-[1,3]- dioxepino [5,6-d] imidazole **(5b-f),** by condensing 2-(6,6-dimethyl-4,8-dihydro-1H-[1,3] dioxepino[5,6-d] imidazole-1-yl) acetic acid **(3)** with 5-nitro aminophenol **(4b)** / 6-nitro aminophenol **(4c)** / 5,6-dinitro aminophenol **(4d)** / 5-chloro aminophenol **(4e)** / 5-chloro,6-nitro aminophenol **(4f)**. The structure of **(5a-f)** was established by IR, ^{1}H-NMR and elemental analysis.

Typical procedure for the synthesis of 1-(5/6- mono substituted or 5, 6-di substituted -1H-benzo [d] oxazol-2-yl) methyl) -1H-imidazole-4, 5-diyl) dimethanol (6a-f):

The isopropylidenation of 1, 2-diols was carried out by a procedure as reported in the literature [39]. A suspension of the 1-((1H-benzo[d] oxazol-2-yl) methyl)-6, 6-dimethyl-4, 8-dihydro-1H-[1, 3]-dioxepino [5, 6-d] imidazole **(5a)** (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 **(6a).** 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 (**6b-f)** from **(5b-f)**. The structure of **(6a-f)** was established by IR, ^{1}H-NMR and elemental analysis.

Typical procedure for the synthesis of 1(5/6- mono substituted or 5,6-di substituted benzo [d] oxazol-2-yl - methyl)- 6-(4-substituted-phenoxy)-4,8-dihydro-1H-[1,3,2] dioxaphosphepino [5,6-d] imidazole-6-oxide (8a-f) :

A solution of phenylphosphorodichloridate **(7a)**(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-(benzo [d] oxazol-2-yl) methyl) -1H- imidazole-4,5-diyl) dimethanol **(6a)** (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. After completion of the reaction the Triethyl amine hydrochloric acid was filtered from mixture and solvent was removed under reduced pressure. The residue was washed with water and then recrystalized from aqueous 2-propanol to get pure compound [40] of 1(benzo [d] oxazol-2-yl - methyl) - 6- phenoxy-4,8-dihydro-1H-[1,3,2] dioxaphosphepino [5,6-d] imidazole-6-oxide **(6a)**

The similar procedure was adopted to synthesise **(8b-f)** by the reaction between **(6b-f)** with 4-methyl phenyl phosphorodichloridate **(7b),** 4-methoxy phenyl phosphorodichloridate **(7c),** 4-chloro phenyl phosphorodichloridate **(7d),** 4-bromo phenyl phosphorodichloridate **(7e),** 4-nitro phenyl phosphorodichloridate **(7f).**

The structures of these newly synthesized compounds **(8a-f)** were characterized by their elemental analysis and spectral data (IR, ^{1}H-NMR, ^{13}C-NMR, ^{31}P-NMR and Mass).

Typical procedure for the synthesis of 1- (benzo[d] thiazol-2-yl-methyl)-6,6-dimethyl-4,8-dihydro -1H-[1,3] dioxepino [5,6-d] imidazol (10)

A mixture of 0.1 mole 2-(6, 6-dimethyl-4, 8-dihydro-1H-[1, 3] dioxepino[5,6-d] imidazole-1-yl) acetic acid **(3)** and 0.1 mole of 2-aminobenzenethiol **(9)** was heated under reflux for 1.5 hours with stirring at 140^{o}C. 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. The organic layer was separated and aqueous solution extracted with CH_2Cl_2 (3×25 ml). The combined extracted were dried on Na_2SO_4. After filtration, the solvent was removed with rotary 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 1-(benzo [d] thiazol-2-yl-methyl)-6, 6-dimethyl-4,8-dihydro-1H-[1,3]- dioxepino [5,6-d] imidazole **(10) [**36-

38] was recrystallized from aqueous dimethyl formamide. The structure of **(10)** was established by IR, 1H-NMR and elemental analysis.

Typical procedure for the synthesis of 1-(benzo [d] thiazol-2-yl) methyl) -1H-imidazole-4,5-diyl) dimethanol (11) :

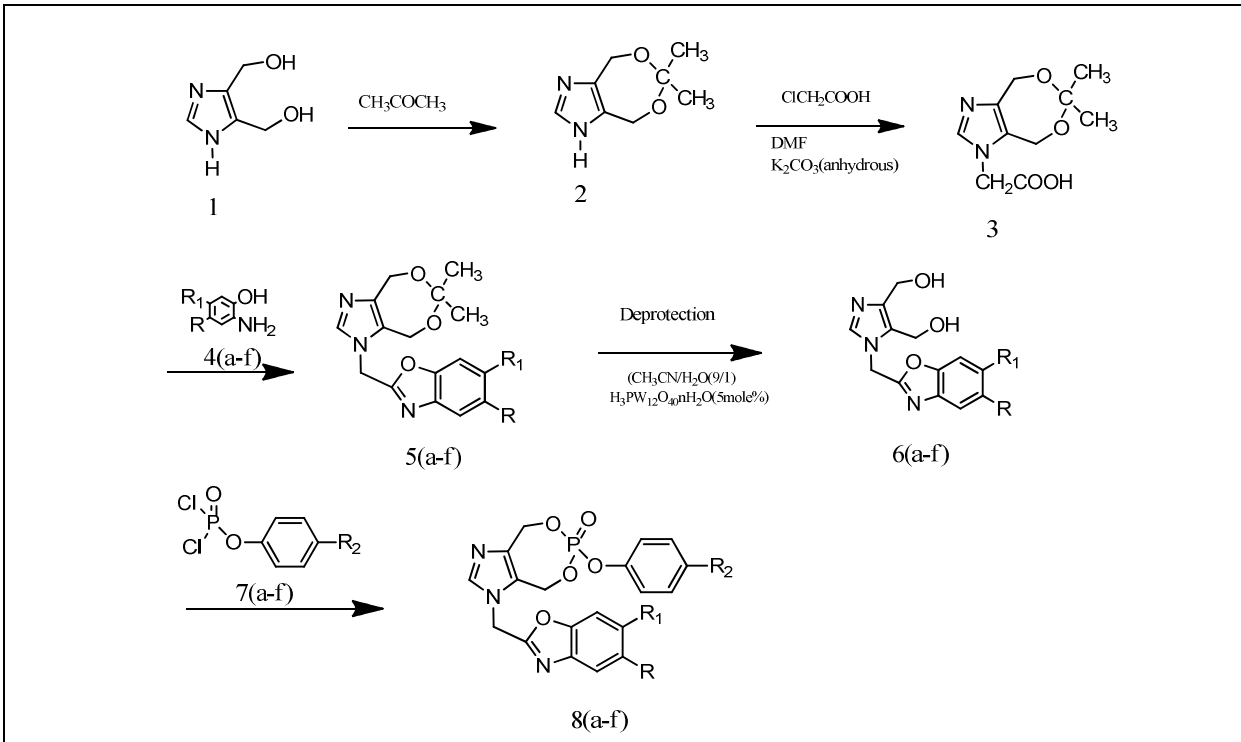
The isopropylidenation of 1, 2-diols was carried out by a procedure as reported in the literature [39]. A suspension of the 1-(benzo[d] thiazol-2-yl) methyl)-6,6-dimethyl-4,8-dihydro-1H-[1,3]-dioxepino [5,6-d] imidazole **(10)** (1 m mol) in dry acetone and to this 5 mol % of phosphotungstic acid was 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 structure of **(11)** was established by IR, ^{1}H-NMR and elemental analysis.

Typical procedure for the synthesis of 1(benzo [d] thiazol-2-yl - methyl) - 6-(4-substituted-phenoxy)-4, 8-dihydro-1H-[1, 3, 2] dioxaphosphepino [5, 6-d] imidazole-6-oxide (12a-f):

A solution of phenylphosphorodichloridate **(7a)**(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-(benzo [d] thiazol-2-yl) methyl) -1H- imidazole-4,5-diyl) dimethanol **(11),** (0.002mole) and triethylamine (0.004mole) in 30 ml of dry toluene and 10ml of tetrahydrofuranat 5^{o}C. 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(benzo [d] thiazol-2-yl - methyl) - 6-(4-substituted) phenoxy-4,8-dihydro-1H-[1,3,2] dioxaphosphepino [5,6-d] imidazole-6-oxide **(12a)** [40].

The similar procedure was adopted to synthesise **(12b-f)** by the reaction between **(11)** with 4-methyl phenyl phosphorodichloridate **(7b),** 4-methoxy phenyl phosphorodichloridate **(7c),** 4-chloro phenyl phosphorodichloridate **(7d),** 4-bromo phenyl phosphorodichloridate **(7e),** 4-nitro phenyl phosphorodichloridate **(7f).**

The structures of these newly synthesized compounds **(12a-f)** were characterized by their elemental analysis and spectral data (IR, ^{1}H-NMR, ^{13}C-NMR, ^{31}P-NMR and Mass).

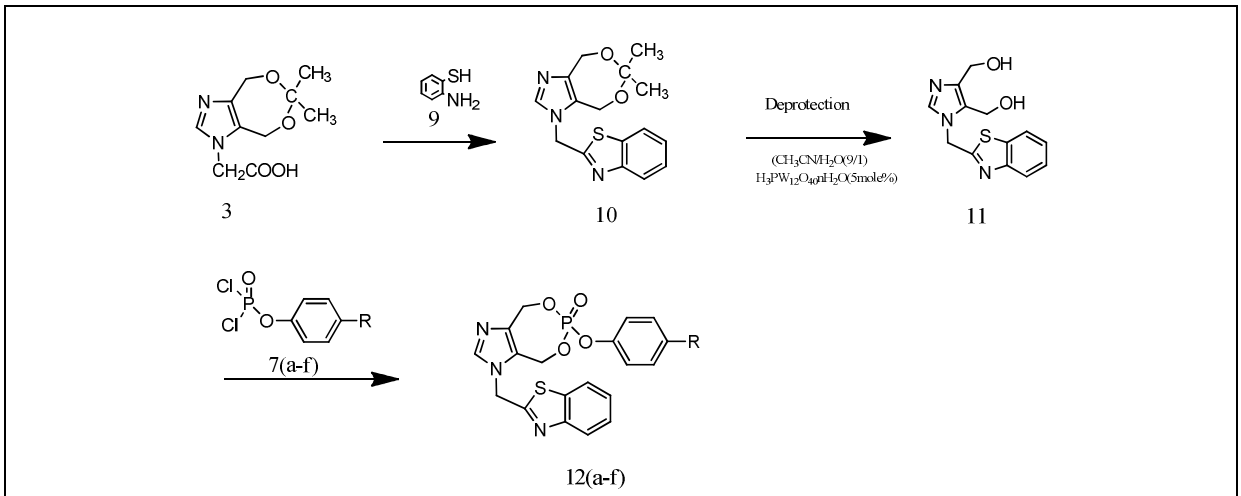


Scheme-1: Synthesis of 1-(5/6-mono substituted or 5,6-disubstituted benzo [d] imidazol-2-yl) methyl)-6-(4-substituted phenoxy) - 4,8-dihydro - 1H - [1,3,2] dioxaphosphepino [5,6-d] imidazole-6-oxide (8a-f)

COMPOUND (5)	5a	5b	5c	5d	5e	5f
R	H	H	NO_2	NO_2	Cl	Cl
R_1	H	NO_2	H	NO_2	H	NO_2

COMPOUND (6)	6a	6b	6c	6d	6e	6f
R	H	H	NO_2	NO_2	Cl	Cl
R_1	H	NO_2	H	NO_2	H	NO_2

COMPOUND (8)	8a	8b	8c	8d	8e	8f
R	H	H	NO_2	NO_2	Cl	Cl
R_1	H	NO_2	H	NO_2	H	NO_2
R_2	H	CH_3	OCH_3	Cl	Br	NO_2



Scheme-2: Synthesis of 1(benzo [d] thiazol-2-yl - methyl)- 6-(4-substituted phenoxy)-4,8-dihydro-1H-[1,3,2] dioxaphosphepino [5,6-d] imidazole-6-oxide (12a-f)

COMPOUND (12)	12a	12b	12c	12d	12e	12f
R	H	CH_3	OCH_3	Cl	Br	NO_2

Physical, analytical and spectral data for the compounds:

2-(6, 6-dimethyl-4, 8-dihydro-1H-[1, 3] dioxepino [5, 6-d] imidazole-1-yl) acetic acid (3):

Yield: 78%; M p: 174^{0}C; IR (KBr): 2950 (OH stretching of COOH), 2940 and 2895 (CH_2 and CH_3 aliphatic –CH stretching), 1690 (carbonyl group of COOH), 1478 & 1366 (characteristic of imidazole ring), 1360 & 1380 (bending vibration of C $(CH_3)_2$) and 1140 cm^{1} (C-O, stretching vibrations). ^{1}H NMR (400MHz, DMSO-d6): δ 1.27 (s, 6H, two geminial CH_3 groups), 4.57 (s, 2H, two CH_2 groups of acetals), 4.67 (s, 2H, CH_2 of –CH_2COOH group), 7.57 (s, 1H of imidazole ring) and 11.0 (s, 1H, -COOH group). Anal.Calcd.For $C_{10}H_{14}N_2O_4$: C 56.68%, H 7.13% and N 11.02%; Found: C 55.88%, H 6.63% and N 10.42%.

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

Yield: 70%; M p: 158-160^{0}C; IR (KBr): 3052 (Ar-H stretching), 2940 & 2895 (CH2 and CH_3 aliphatic C-H stretching), 1478 & 1366 (bending vibrations, characteristic of imidazole ring), 1455 & 1390 (bending vibrations, characteristic of benzoxazole), 1360 & 1380 (bending vibration of C $(CH_3)_2$) and 1140 cm^{1} (C-O stretching). ^{1}H NMR (400MHz, DMSO-d6): δ 1.27 (s, 6H, two geminial CH_3 groups), 4.57 (s, 4H, two CH_2 groups of acetals), 4.99 (s, 2H, N-CH_2-benzoxazole), 7.57 (s, 1H of imidazole ring) and 7.39-7.74 (m, 4H of benzoxazole ring). Anal.Calcd.For $C_{16}H_{17}N_3O_3$: C 64.24%, H 5.7% and N 14.04%; Found: C 63.44%, H 5.2% and N 13.44%.

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

Yield: 75%; M p: 182-184^{0}C; IR (KBr): 3020 (Ar-H stretching), 2940 & 2895 (CH_2 and CH_3 aliphatic C-H stretching), 1470 & 1360 (bending vibrations, characteristic of imidazole ring), 1455 & 1390 (bending vibrations, characteristic of benzoxazole), 1360 & 1380 (bending vibration of C $(CH_3)_2$), 1355-1330 (NO_2 stretching) and 1145 cm^{1} (C-O stretching). ^{1}H NMR (400MHz, DMSO-d6): δ 1.27 (s, 6H, two geminial CH_3 groups), 4.57 (s, 2H, two CH_2 groups of acetals), 4.99 (s, 2H, N-CH_2-benzoxazole), 7.57 (s, 1H of imidazole ring) and 7.88-8.43 (m, 3H of benzoxazole ring). Anal.Calcd.For $C_{16}H_{16}N_4O_5$: C 55.81%, H 4.6% and N 16.27% Found; C 55.01%, H 4.1% and N 15.67%.

6, 6-dimethyl-1-((5-nitro benzo [d] oxazol-2-yl) methyl) -4, 8-dihydro-1H-[1, 3] - doxepino [5, 6-d] imidazole (5c):
Yield: 75%; M p: 174-176^{0}C; IR (KBr): 3035 (Ar-H stretching), 2940 & 2895 (CH_2 and CH_3 aliphatic C-H stretching), 1472 & 1365(bending vibrations, characteristic of imidazole ring), 1455 & 1390 (bending vibrations, characteristic of benzoxazole), 1360 & 1380 (bending vibration of C $(CH_3)_2$), 1355-1330 (NO_2 stretching) and 1145 cm^1 (C-O stretching). ^{1}H NMR (400MHz, DMSO-d6): δ 1.27 (s, 6H, two geminial CH_3 groups), 4.57 (s, 2H, two CH_2 groups of acetals), 4.99 (s, 2H, N-CH_2-benzoxazole), 7.57 (s, 1H of imidazole ring) and 8.05-8.26(m, 3H of benzoxazole ring). Anal.Calcd.For $C_{16}H_{16}N_4O_5$: C 55.81%, H 4.6% and N 16.27% Found; C 55.01%, H 4.1% and N 15.67%.

6, 6-dimethyl-1-((5, 6-dinitro benzo [d] oxazol-2-yl) methyl) -4, 8-dihydro-1H-[1,3]- dioxepino [5,6-d] imidazole (5d):
Yield: 80%; M p: 204-206^{0}C; IR (KBr): 3045 (Ar-H stretching), 2940 & 2895 (CH_2 and CH_3 aliphatic C-H stretching), 1488 & 1375(bending vibrations, characteristic of imidazole ring), 1455 & 1390 (bending vibrations, characteristic of benzoxazole), 1360 & 1380 (bending vibration of C $(CH_3)_2$), 1355-1330 (NO_2 stretching) and 1148 cm^1 (C-O stretching). ^{1}H NMR (400MHz, DMSO-d6): δ 1.27 (s, 6H, two geminial CH_3 groups), 4.57 (s, 2H, two CH_2 groups of acetals), 4.99 (s, 2H, N-CH_2-benzoxazole), 7.57 (s, 1H of imidazole ring) and 8.35-8.45 (m, 2H of benzoxazole ring). Anal.Calcd.For $C_{16}H_{15}N_5O_7$: C 49.36%, H 3.8% and N 17.99% Found; C 48.56%, H 3.3% and N 17.39%.

6, 6-dimethyl-1-((5-chloro benzo [d] oxazol-2-yl) methyl) -4, 8-dihydro-1H-[1, 3] - dioxepino [5, 6-d] imidazole (5e):
Yield: 70%; M p: 140-142^{0}C; IR (KBr): 3035(Ar-H stretching), 2940 & 2895 (CH_2 and CH_3 aliphatic C-H stretching), 1472& 1365 (bending vibrations, characteristic of imidazole ring), 1455 & 1390 (bending vibrations, characteristic of benzoxazole), 1360 & 1380 (bending vibration of C $(CH_3)_2$), 1146 (C-O stretching) and 725 cm^1 (Cl stretching). ^{1}H NMR (400MHz, DMSO-d6): δ 1.27 (s, 6H, two geminial CH_3 groups), 4.57 (s, 2H, two CH_2 groups of acetals), 4.99 (s, 2H, N-CH_2-benzoxazole), 7.57 (s, 1H of imidazole ring) and 7.49-7.81 (m, 3H of benzoxazole ring). Anal.Calcd.For $C_{16}H_{16}ClN_3O_3$: C 57.58%, H 4.8%, Cl 10.62%, and N 12% Found; C 56.78%, H 4.3% and Cl 9.62.

6, 6-dimethyl-1-((5-chloro 6-nitro benzo [d] oxazol-2-yl) methyl) -4, 8-dihydro-1H-[1, 3] - dioxepino [5, 6-d] imidazole (5f):
Yield: 75%; M p: 158-160^{0}C; IR (KBr): 3045(Ar-H stretching), 2940 & 2895 (CH_2 and CH_3 aliphatic C-H stretching), 1488 & 1375 (bending vibrations, characteristic of imidazole ring), 1455 & 1390 (bending vibrations, characteristic of benzoxazole), 1360 & 1380 (bending vibration of C $(CH_3)_2$), 1355 & 1330 (NO_2 stretching), 1145 (C-O stretching) and 725 cm^1 (Cl stretching). ^{1}H NMR (400MHz, DMSO-d6): δ 1.27 (s, 6H, two geminial CH_3 groups), 4.57 (s, 2H, two CH_2 groups of acetals), 4.99 (s, 2H, N-CH_2-benzoxazole), 7.57 (s, 1H of imidazolering) and 8.07-8.13(m, 2H of benzoxazole ring). Anal.Calcd.For $C_{16}H_{15}ClN_4O_5$: C 50.74%, H 3.9%, Cl 9.36% and N 14.7% Found; C 49.9% Cl 8.56% and N 14.1%.

(1-benzo [d] oxazol-2-yl methyl)-1H-imidazole-4, 5-diyl) dimethanol (6a):
Yield: 70%; M p: 178-180^{0}C; IR (KBr): 3520 (ν_{O-H}, intramolecular H-bonding), 3052 (Ar-H stretching), 2940 & 2895 (CH_2 aliphatic C-H stretching), 1478 & 1366 (bending vibrations, characteristic of imidazole ring), 1455 & 1390 (bending vibrations, characteristic of benzoxazole ring) and 1140 cm^{-1} (C-O stretching). ^{1}H NMR (400MHz, DMSO-d6): δ 3.65 (s, 2H, two –OH groups having Intramolecular H-bonding) 4.73 (s, 4H, two CH_2 groups of dimethanols), 4.99 (s, 2H, N-CH_2-benzoxazole), 7.57 (s, 1H of imidazole ring) and, 7.89-8.43 (m, 3H of benzoxazole ring). Anal.Calcd.For $C_{13}H_{12}N_4O_5$: C 60.22%, H 5.0% and N 16.21% Found; C 59.82%, H 4.4% and N 15.61%.

(1-((6-nitro benzo [d] oxazol-2-yl) methyl)-1H-imidazole-4, 5-diyl) dimethanol (6b):
Yield: 75%; M p: 183-185^{0}C; IR (KBr): 3515 (ν_{O-H}, intramolecular H-bonding), 3015 (Ar-H stretching), 2940 & 2895 (CH_2 aliphatic C-H stretching), 1470 & 1360 (bending vibrations, characteristic of imidazole ring), 1455 & 1390 (bending vibrations, characteristic of benzoxazole ring), 1355 & 1330 (NO_2 stretching) and 1145cm^{-1} (C-O stretching). ^{1}H NMR (400MHz, DMSO-d6): δ 3.65 (s, 2H, two –OH groups having Intramolecular H-bonding) 4.73 (s, 4H, two CH_2 groups of dimethanols), 4.99 (s, 2H, N-CH_2-benzoxazole), 7.57 (s, 1H, of imidazole ring) and 7.89-8.43 (m, 3H of benzoxazole ring). Anal.Calcd.For $C_{13}H_{12}N_4O_5$: C 51.2%, H 3.98% and N 18.41% Found; C 50.4%, H 3.48% and N 17.81%.

(1-((5-nitro benzo [d] oxazol-2-yl) methyl)-1H-imidazole-4, 5-diyl) dimethanol (6c):
Yield: 75%; M p: 172-174^{0}C; IR (KBr): 3525 (ν_{O-H}, intramolecular H-bonding), 3030 (Ar-H stretching), 2940 & 2895 (CH_2 aliphatic C-H stretching), 1473 & 1365 (bending vibrations, characterstic of imidazole ring), 1455 &

1390 (bending vibrations,charecterstic of benzoxazole ring), 1355 & 1330 (NO_2 stretching) and 1145cm^{-1} (C-O stretching). ^{1}H NMR (400MHz, DMSO-d6): δ 3.65 (s, 2H, two –OH groups having Intramolecular H-bonding) 4.73 (s, 4H, two CH_2 groups of dimethanols), 4.99 (s, 2H, N-CH_2-benzoxazole), 7.57 (s, 1H of imidazole ring) and 8.05-8.26 (m, 3H of benzoxazole ring). Anal.Calcd.For $C_{13}H_{12}N_4O_5$: C 51.2%, H 3.98% and N 18.41% Found; C 50.4%, H 3.48% and N 17.81%.

(1-((5, 6-dinitro benzo [d] oxazol-2-yl) methyl)-1H-imidazole-4, 5-diyl) dimethanol (6d):
Yield: 70%; M p: 194-196^{0}C; IR (KBr): 3530 (ν_{O-H}, intramolecular H-bonding), 3040 (Ar-H stretching), 2940 & 2895 (CH_2 aliphatic C-H stretching), 1488 & 1375 (bending vibrations, characteristic of imidazole ring), 1455 & 1390 (bending vibrations, characteristic of benzoxazole ring), 1355 & 1330 (NO_2 stretching) and 1148cm^{-1} (C-O stretching). ^{1}H NMR (400MHz, DMSO-d6): δ 3.65 (s, 2H, two –OH groups having Intramolecular H-bonding) 4.73 (s, 4H, two CH_2 groups of dimethanols), 4.99 (s, 2H, N-CH_2-benzoxazole), 7.57 (s, 1H of imidazole ring) and 8.35-8.45 (m, 2H of benzoxazole ring). Anal.Calcd.For $C_{13}H_{11}N_5O_{7:}$ C 44.71%, H 3.1% and N 20.05% Found; C 43.91%, H: 2.6% and N 19.45%.

(1-((5-chloro benzo [d] oxazol-2-yl) methyl)-1H-imidazole-4, 5-diyl) dimethanol (6e):
Yield: 65%; M p: 165-167^{0}C; IR (KBr): 3525 (ν_{O-H}, intramolecular H-bonding), 3030 (Ar-H stretching), 2940 & 2895 (CH_2 aliphatic C-H stretching), 1473 & 1365 (bending vibrations, characteristic of imidazole ring), 1455 & 1390 (bending vibrations, characteristic of benzoxazole ring), 1148 (C-O stretching) and 725 cm^{-1} (Cl stretching). ^{1}H NMR (400MHz, DMSO-d6): δ 3.65 (s, 2H, two –OH groups having Intramolecular H-bonding) 4.73 (s, 4H, two CH_2 groups of dimethanols), 4.99 (s, 2H, N-CH_2-benzoxazole), 7.57 (s, 1H of imidazole ring) and 7.49-7.81 (m, 3H of benzoxazole ring). Anal.Calcd.For $C_{13}H_{12}ClN_3O_3$: C 53.16%, H 4.1%, Cl 12.07% and N 14.4% Found; C 52.36%, H 3.6%, Cl 11.27% and N 15.0%.

(1-((5-chloro 6-nitro benzo [d] oxazol-2-yl) methyl)-1H-imidazole-4, 5-diyl) dimethanol (6f):
Yield: 70%; M p: 173-175^{0}C; IR (KBr): 3530 (ν_{O-H}, intramolecular H-bonding), 3040 (Ar-H stretching), 2940 & 2895 (CH_2 aliphatic C-H stretching), 1488 & 1375 (bending vibrations, characteristic of imidazole ring), 1455 & 1390 (bending vibrations,charecterstic of benzoxazole ring) 1355 & 1330 (NO_2 stretching), 1145 (C-O stretching) and 725 cm^{-1} (Cl stretching). ^{1}H NMR (400MHz, DMSO-d6): δ 3.65 (s, 2H, two –OH groups having Intramolecular H-bonding), 4.73 (s, 4H, two CH_2 groups of dimethanols), 4.99 (s, 2H, N-CH_2-benzoxazole), 7.57 (s, 1H, of imidazole ring) and 8.07-8.13 (m, 2H, of benzoxazole ring). Anal.Calcd.For $C_{13}H_{11}ClN_4O_5$: C 46.10%, H 3.27%, Cl 10.47% and N 16.4% Found; C 45.30%, H 2.7%, Cl 9.67% and N 15.9%.

1-(benzo [d] oxazol-2-yl)methyl)- 6- phenoxy-4,8-dihydro-1H-[1,3,2] dioxaphosphepino [5,6-d] imidazole-6-oxide (8a):
Yield: 70; M p: 138-140^{0}C;IR (KBr): 3052 (Ar-H stretching), 2940 & 2895 (CH_2 aliphatic C-H stretching), 1478 & 1366 (bending vibrations, characteristic of imidazole ring), 1455 & 1390 (bending vibrations, characteristic of benzoxazole ring) , 1300 (γ_{C-O} / δ_{C-O}), 1250 ($\gamma_{P=O}$) and 954 cm^1($\gamma_{P-O-C(arom)}$).^{1}H NMR (400MHz, DMSO-d6): δ 4.99 (s, 2H, -N-CH_2-benzoxazole), 5.23 (s, 4H, two CH_2 groups attached to phpsphorus moiety), 7.18-7.28 (m, 5H of phenoxy group), 7.57(s, 1H, CH of imidazole ring) and 7.39-7.74(m, 4H of benzoxazol ring). Anal.Calcd.For $C_{19}H_{16}N_3O_5P$: C 56.64%, H 3.55%, N 9.98% and P 6.38% Found; C 57.44%, H 4.0%, N 10.58% and P 7.0%.

1-(benzo [d] oxazol-2-yl) methyl)-6- phenoxy-4,8-dihydro-1H-[1,3,2] dioxaphosphepino [5,6-d] imidazole-6-oxide (8b):
Yield: 75%; M p: 155-157^{0}C; IR (KBr): 3052 (Ar-H stretching), 2940 & 2895 (CH_2 aliphatic C-H stretching), 1475& 1360 (bending vibrations,characteristic of imidazole ring), 1455 & 1390 (bending vibrations, characteristic of benzoxazole ring), 1550 &1330 (NO_2 stretching), 1305 (γ_{C-O} / δ_{C-O}), 1245 ($\gamma_{P=O}$) and 950 cm^1($\gamma_{P-O-C(arom)}$).^{1}H NMR (400MHz, DMSO-d6): δ 2.34 (s,1H,CH_3 of tolyloxy), 4.99 (s,2H,-N-CH_2-benzoxazole), 5.23 (s,4H,two CH_2 groups attached to phosphorus moiety), 6.83-7.06 (m, 4H,of phenoxy group), 7.57 (s,1H,CH of imidazole ring) and 7.88-8.34 (m, 3H of benzoxazole ring). Anal.Calcd.For $C_{20}H_{17}N_4O_7P$: C 51.84%, H: 3.25%, N 11.68% and P 6.09% Found; C 52.64, H 3.75%, N 12.28% and P 6.7%.

1-((6-nitro benzo [d] oxazol-2-yl) methyl) - 6- (p-tolyloxy)-4, 8-dihydro-1H-[1, 3, 2] dioxaphosphepino [5, 6-d] imidazole-6-oxide (8c):
Yield: 75%; M p: 142-144^{0}C; IR (KBr): 3065 (Ar-H stretching), 2940 & 2895 (CH_2 aliphatic C-H stretching), 1478 & 1371(bending vibrations,characterstic of imidazole ring), 1455 & 1390 (bending vibrations, charecterstic of benzoxazole ring), 1550 &1330 (NO_2 stretching), 1310 (γ_{C-O} / δ_{C-O}), 1254 ($\gamma_{P=O}$) and 958 cm^1($\gamma_{P-O-C(arom)}$).^{1}H NMR (400MHz, DMSO-d6): δ 3.83 (s,1H,CH_3 of methoxy phenoxy), 4.99 (s,2H,-N-CH_2-benzoxazole), 5.23 (s,4H,two CH_2 groups attached to phosphorus moiety), 6.82-6.84 (m, 4H,of phenoxy group), 7.57 (s,1H,CH of imidazole ring)

and 8.05-8.26 (m, 3H of benzoxazole ring). Anal.Calcd.For $C_{20}H_{17}N_4O_8P$: C 50.06%, H 3.13%, N 11.26% and P 5.86% Found; C 50.86%, H 3.6%, N 11.86% and P 6.5%.

6-(4-chloro phenoxy)-1-((5,6-dinitro benzo [d] oxazol-2-yl)methyl)-4,8-dihydro-1H-[1,3,2] dioxaphosphepino [5,6-d] imidazole-6-oxide (8d):
Yield: 70%; M p: 174-176^{0}C; IR (KBr): 3067 (Ar-H stretching), 2940 & 2895 (CH_2 aliphatic C-H stretching), 1483& 1370 (bending vibrations,characterstic of imidazole ring), 1455 & 1390 (bending vibrations, charecterstic of benzoxazole ring), 1550 &1330 (NO_2 stretching), 1315 (γ_{C-O} / δ_{C-O}), 1259 ($\gamma_{P=O}$), 959 ($\gamma_{P-O-C(arom)}$) and 725 cm^1 (Cl stretching). ^{1}H NMR (400MHz, DMSO-d6): δ 4.99 (s, 2H,-N-CH_2-benzoxazole), 5.23 (s, 4H, two CH_2 groups attached to phosphorus moiety), 6.89-7.32 (m, 4H of phenoxy group), 7.57 (s, 1H, CH of imidazole ring) and 8.35-8.45 (m, 2H, of benzoxazole ring). Anal.Calcd.For $C_{19}H_{13}ClN_5O_9P$: C 42.94%, H 2.01%, Cl 5.99%, N 12.7% and P 5.24% Found; C 43.74%, H 2.5%, Cl 6.79%, N 13.4% and P 5.94%.

6-(4-bromo phenoxy)-1-((5-chloro benzo [d] oxazol-2-yl) methyl)-4, 8-dihydro-1H-[1, 3, 2] dioxaphosphepino [5, 6-d] imidazole-6-oxide (8e):
Yield: 65%; M p: 125-127^{0}C;IR (KBr): 3051 (Ar-H stretching), 2940 & 2895 (CH_2 aliphatic C-H stretching), 1480 & 1369 (bending vibrations,characterstic of imidazole ring), 1455 & 1390 (bending vibrations, characteristic of benzoxazole ring), 1310 (γ_{C-O} / δ_{C-O}), 1241($\gamma_{P=O}$), 946 ($\gamma_{P-O-C(arom)}$), 725 (Cl stretching) and 600 cm^1 (Br stretching).^{1}H NMR (400MHz, DMSO-d6): δ 4.99 (s,2H,-N-CH_2-benzoxazole), 5.23 (s,4H,two CH_2 groups attached to phosphorus moiety), 6.89-7.43 (m, 4H of phenoxy group), 7.57 (s,1H,CH of imidazole ring) and 7.49-7.81 (m, 2H of benzoxazole ring). Anal.Calcd.For $C_{19}H_{14}ClBrN_3O_5P$: C 43.89%,H 2.26%, Br 15.45%, Cl 6.1%, N 7.63% and P 5.37% Found; C 44.69%, H 2.7%, Br 15.65%, Cl 6.9%, N 8.23% and P 6.07%.

1-((5-chloro-6-nitro benzo [d] oxazol-2-yl) methyl)-6-(4-nitrophenoxy)-4, 8-dihydro-1H-[1, 3, 2] dioxaphosphepino [5, 6-d] imidazole-6-oxide (8f):
Yield: 70%; M p: 153-155^{0}C; IR (KBr): 3068 (Ar-H stretching), 2940 & 2895 (CH_2 aliphatic C-H stretching), 1471& 1356 (bending vibrations,characterstic of imidazole ring), 1455 & 1390 (bending vibrations, charecterstic of benzoxazole ring),1550 & 1330 (NO_2 stretching), 1310 (γ_{C-O} / δ_{C-O}), 1257($\gamma_{P=O}$), 961 ($\gamma_{P-O-C(arom)}$) and 725 cm^1 (Cl stretching). ^{1}H NMR (400MHz, DMSO-d6): δ 44.99 (s, 2H,-N-CH_2-benzoxazole), 5.23 (s, 4H, two CH_2 groups attached to phosphorus moiety), 7.34-8.09 (m, 4H of phenoxy group), 7.57 (s, 1H, CH of imidazole ring) and 8.07-8.1 (m, 2H of benzoxazole ring). Anal.Calcd.For $C_{19}H_{13}ClN_5O_9P$: C 42.94%, H 2.07%, Cl 5.99%, N 12.8% and P 5.24% Found; C 43.74%, H 2.51%, Cl 6.79%, N 13.42% and P 5.94%.

1-(benzo [d] thiazol-2-yl) methyl)-6,6-dimethyl-4,8-dihydro-1H-[1,3]- dioxepino [5,6-d] imidazole (10):
Yield: 70%; M p 132-134^{0}C; IR (KBr): 3052 (Ar-H stretching), 2940 & 2895 (CH_2 and CH_3 aliphatic C-H stretching), 1478 & 1366 (bending vibrations, characteristic of imidazole ring), 1474, 1344, 715 & 620 (bending vibrations, characteristic of benzothizole) , 1360 & 1380 (bending vibration of $C(CH_3)_2$), and 1140 cm^1 (C-O stretching). ^{1}H NMR (400MHz, DMSO-d6): δ 1.27 (s, 6H, two geminial CH_3 groups), 4.57 (s, 4H, two CH_2 groups of acetals), 4.99 (s, 2H, N-CH_2-benzthiazole), 7.57 (s, 1H of imidazole ring) and 7.53-8.18 (m, 4H of benzthiazole ring). Anal.Calcd.For $C_{16}H_{17}N_3O_2S$: C 60.93%, H 5.43%, N 13.32% and S 10.1% Found; C 60.13%, H 4.93%, N 12.72% and S 9.97%.

(1-(benzo [d] thiazol-2-yl) methyl) -1H-imidazole-4, 5-diyl) dimethanol (11):
Yield: 70%; M p 155-157^{0}C; IR (KBr): 3520 (ν_{O-H}, intramolecular H-bonding), 3052 (Ar-H stretching), 2940 & 2895(CH_2 aliphatic C-H stretching), 1478 & 1366 (bending vibrations, characteristic of imidazole ring), 1474 , 1344, 715 & 620 (bending vibrations, characteristic of benzothizole) and 1140 cm^{-1} (C-O stretching). ^{1}H NMR (400MHz, DMSO-d6): δ 3.65 (s, 2H, two –OH groups having Intramolecular H-bonding), 4.73 (s, 4H, two CH_2 groups of dimethanols), 4.99 (s, 2H, -NCH_2-benzthiazole), 7.57 (s, 1H of imidazole) and, 7.53-8.18 (m, 4H of benzthiazole). Anal.Calcd.For $C_{13}H_{13}N_3O_2S$: C 56.71%, H 4.76%, N 15.26% and S 11.6% Found: C 55.91%, H 4.26%, N14.66% and S11.45%.

1-(benzo [d] thiazol-2-yl) methyl) -6-phenoxy-4, 8-dihydro-1H-[1, 3, 2] dioxaphosphepino [5, 6-d] imidazole-6-oxide (12a):
Yield: 70%; M p 144-146^{0}C; IR (KBr): around 3052 (Ar-H stretching), 2940 & 2895 (CH_2 aliphatic C-H stretching), 1478 & 1366 (bending vibrations,characterstic of imidazole ring), 1474 , 1344, 715 & 620 (bending vibrations, characteristic of benzthiazole) , 1300 (γ_{C-O} / δ_{C-O}), 1250 ($\gamma_{P=O}$) and 954 cm^{-1} ($\gamma_{P-O-C(arom)}$). ^{1}H NMR (400MHz, DMSO-d6): δ 4.99 (s, 2H, -N-CH_2-benzthiazole), 5.23 (s, 4H, two CH_2 groups attached to phosphorus moiety), 7.18-7.28 (m, 5H of phenoxy group), 7.57(s, 1H, CH of imidazole) and 7.53-8.18 (m, 4H of benzthiazol).

Anal.Calcd.For $C_{19}H_{16}N_3O_4PS$: C 55.20%, H 3.90%, N 10.16%, P 7.49% and S 7.76% Found; C 54.40%, H 3.40%, N 9.56%, P 6.79% and S 7.56%.

1-(benzo [d] thiazol-2-yl) methyl) -6-(p-tolyloxy)-4, 8-dihydro-1H-[1, 3, 2] dioxaphosphepino [5, 6-d] imidazole-6-oxide (12b):
Yield: 60%; M p 223-224^{0}C; IR (KBr): around 3055 (Ar-H stretching), 2940 & 2895 (CH_2 aliphatic C-H stretching), 1475 & 1360 (bending vibrations,characteristic of imidazole ring), 1474 , 1344, 715 & 620 (bending vibrations, characteristic of benzthiazole) , 1300 (γ_{C-O} / δ_{C-O}), 1245 ($\gamma_{P=O}$) and 950cm^{-1} ($\gamma_{P-O-C(arom)}$). ^{1}H NMR (400MHz, DMSO-d6): δ 2.34 (s, 3H, CH_3 of tolyloxy), 4.99 (s, 2H, N-CH_2-benzthiazole), 5.23 (s, 4H, two CH_2 groups attached to phosphorus moiety), 6.83-7.06 (m, 4H of phenoxy group), 7.57(s, 1H, CH of imidazole ring) and 7.53-8.18 (m, 4H of benzthiazol). Anal.Calcd.For $C_{20}H_{18}N_3O_4PS$: C 56.20%, H: 4.24%, N 9.83%, P 7.25% and S 7.50% Found; C 55.40%, H 3.74%, N 9.23%, P 6.55% and S 7.30%.

1-(benzo [d] thiazol-2-yl) methyl) -6-(4-methoxyphenoxy)-4, 8-dihydro-1H-[1,3,2] dioxaphosphepino [5,6-d] imidazole-6-oxide (12c):
Yield: 60%; M p 167-168^{0}C; IR (KBr): around 3065 (Ar-H stretching), 2940 & 2895 (CH_2 aliphatic C-H stretching), 1478& 1371 (bending vibrations,characterstic of imidazole ring), 1474 , 1344, 715 & 620 (bending vibrations, charecterstic of benzthiazole) , 1300 (γ_{C-O} / δ_{C-O}), 1254($\gamma_{P=O}$) and 958cm^{-1} ($\gamma_{P-O-C(arom)}$). ^{1}H NMR (400MHz, DMSO-d6): δ 3.83 (s, 3H, CH_3 of methoxy phenoxy), 4.99 (s, 2H, N-CH_2-benzthiazole), 5.23 (s, 4H, two CH_2 groups attached to phosphorus moiety), 6.82-6.84 (m, 4H of phenoxy group), 7.57(s, 1H, CH of imidazole ring) and 7.53-8.18(m, 4H of benzthiazol). Anal.Calcd.For $C_{20}H_{18}N_3O_5PS$: C 54.17%, H 4.09%, N 9.49%, P 6.99% and S 7.23% Found; C 53.37%, H 3.59%, N 8.89%, P 6.29% and S 7.03%.

1-(benzo [d] thiazol-2-yl) methyl) -6-(4-chlorophenoxy)-4, 8-dihydro-1H-[1, 3, 2] dioxaphosphepino [5, 6-d] imidazole-6-oxide (12d):
Yield: 70%; M p 196-197^{0}C; IR (KBr): around 3067 (Ar-H stretching), 2940 & 2895 (CH_2 aliphatic C-H stretching), 1483 & 1370 (bending vibrations, characteristic of imidazole ring), 1474 , 1344, 715 & 620 (bending vibrations, characteristic of benzthiazole) , 1300 (γ_{C-O} / δ_{C-O}), 1259($\gamma_{P=O}$) , 959 ($\gamma_{P-O-C(arom)}$) and 725 cm^{-1} (Cl stretching). ^{1}H NMR (400MHz, DMSO-d6): δ 4.99 (s, 2H, N-CH_2-benzthiazole), 5.23 (s, 4H, two CH_2 groups attached to phosphorus moiety), 6.89-7.32 (m, 4H of phenoxy group), 7.57(s, 1H, CH of imidazole ring) and 7.53-8.18(m, 4H of benzthiazol). Anal.Calcd.For $C_{19}H_{15}ClN_3O_4PS$: C 50.96%, H 3.38%, Cl 7.92%, N 9.38%, P 6.92% and S 7.16% Found; C 50.16%, H 2.88%, Cl 7.12%, N 8.78%, P 6.22% and S 6.96%.

1-(benzo [d] thiazol-2-yl) methyl) -6-(4-bromophenoxy)-4, 8-dihydro-1H-[1, 3, 2] dioxaphosphepino [5, 6-d] imidazole-6-oxide (12e):
Yield: 65%; M p 157-158^{0}C; IR (KBr): around 3051(Ar-H stretching), 2940 & 2895 (CH_2 aliphatic C-H stretching), 1480 & 1369 (bending vibrations,characterstic of imidazole ring), 1474 , 1344, 715 & 620 (bending vibrations, characteristic of benzthiazole) , 1300 (γ_{C-O} / δ_{C-O}), 1241($\gamma_{P=O}$) , 946 ($\gamma_{P-O-C(arom)}$) and 600 cm^{-1} (Br stretching). ^{1}H NMR (400MHz, DMSO-d6): δ 4.99 (s, 2H, N-CH_2-benzthiazole), 5.23 (s, 4H, two CH_2 groups attached to phosphorus moiety), 6.84-7.43 (m, 4H of phenoxy group), 7.57(s, 1H, CH of imidazole) and 7.53-8.18(m, 4H, of benzthiazol). Anal.Calcd.For $C_{19}H_{15}BrN_3O_4PS$: C 46.36%, H 3.07%, Br 16.23%, N 8.54%, P 6.29% and S 6.51% Found; C 45.56%, H 2.57%, Br 15.63%, N 7.94%, P 5.59% and S 6.31%.

1-(benzo [d] thiazol-2-yl) methyl) -6-(4-nitrophenoxy)-4,8-dihydro-1H-[1,3,2] dioxaphosphepino [5,6-d] imidazole-6-oxide (12f):
Yield: 65%; M p 124-126^{0}C; IR (KBr): around 3068 (Ar-H stretching), 2940 & 2895 (CH_2 aliphatic C-H stretching), 1471 & 1356 (bending vibrations,characterstic of imidazole ring), 1474 , 1344, 715 & 620 (bending vibrations, charecterstic of benzthiazole), 1550 &1330 (NO2 stretching), 1300 (γ_{C-O} / δ_{C-O}), 1257($\gamma_{P=O}$) and 961 cm^{-1}($\gamma_{P-O-C(arom)}$) . ^{1}H NMR (400MHz, DMSO-d6): δ 4.99 (s, 2H, N-CH_2-benzthiazole), 5.23 (s, 4H, two CH_2 groups attached to phosphorus moiety), 7.57(s, 1H, CH of imidazole ring), 7.34-8.09 (m, 4H of phenoxy group) and 7.53-8.18(m, 4H of benzthiazol). Anal.Calcd.For $C_{19}H_{15}N_4O_6PS$: C 49.78%, H 3.30%, N 12.22%, P 5.94% and S 7.00% Found; C 48.98%, H 2.80%, N 11.62%, P 5.24% and S 6.80%.

Biological activity
The antimicrobial activity [41] of these newly synthesized compounds was performed according to disc diffusion method, as recommended by the National Committee for Clinical Laboratory [42]. The synthesised compounds were used at the concentration of 250µg/ml DMF as a solvent [43].

Antibacterial activity

The antibacterial activity [44] of 1(5/6- mono substituted or 5,6-di substituted benzo [d] oxazol-2-yl - methyl)- 6-(4-substituted-phenoxy)-4,8-dihydro-1H-[1,3,2] dioxaphosphepino [5,6-d] imidazole-6-oxide **(8a-f)** were screened against the Staphylococcus aureus (gram positive), Bacillus cereus, Escherichia coli (gram negative) and Pseudomonas aeruginosa organisms. The benzo[d]-oxazoles **(8d-f)** shown more activity, while **(8a-c)** exhibited low activity. The antibacterial activity of **(8a-f)** was shown in the **(Table 1)**.

The similar results were also noticed with the benzo[d]-thiazole possessing chloro **(12d)**, bromo **(12e)** and nitro **(12f)** exhibit high anti-bacterial activity, when compared to compounds **(12a-c)**. Here Amoxicillin and Cefaclor are tested as reference compounds to compare the activity. The antibacterial activity of benzo[d]-thiazole **(12a-f)** was shown in the **(Table 2)**.

Table 1: Antibacterial activity of 1- (5/6 - mono substituted or 5, 6-disubstituted benzo [d] oxazol-2-yl) methyl) - 6-(4-substitutedphenoxy)-4, 8-dihydro-1H-[1, 3, 2] dioxaphosphepino [5, 6-d] imidazole-6-oxide (8a-f)

S.NO	COMPOUND	R	R_1	R_2	Zone of inhibition (mm)			
					Staphylococcus aureus NCCS 2079 250 (µg/ disc)	*Bacillus cereus NCCS 2106 250(µg/ disc)*	*Escherichia coli NCCS 2065 250(µg/ disc)*	*Pseudomonas aeruginosa NCCS 2200 250(µg/ disc)*
1	8a	H	H	H	8	7	9	10
2	8b	H	NO_2	CH_3	9	6	7	8
3	8c	NO_2	H	OCH_3	7	5	6	7
4	8d	NO_2	NO_2	Cl	17	18	17	17
5	8e	Cl	H	Br	15	14	15	14
6	8f	Cl	NO_2	NO_2	16	15	16	15
7	Amoxicillin				21	27	24	22
8	Cefaclor				19	22	19	20

Table 2: Antibacterial activity of 1-(benzo [d] thiazol-2-yl) methyl) -6-(4-substituted phenoxy)-4, 8-dihydro-1H-[1, 3, 2] dioxaphosphepino [5, 6-d] imidazole-6-oxide (12a-f)

S.NO	COMPOUND	R	Zone of inhibition (mm)			
			Staphylococcus aureus NCCS 2079 250 µg/ disc	*Bacillus cereus NCCS 2106 250(µg/ disc)*	*Escherichia coli NCCS 2065 250(µg/ disc0*	*Pseudomonas aeruginosa NCCS 2200 250 (µg/ disc)*
1	12a	H	9	8	10	11
2	12b	CH_3	10	7	8	9
3	12c	OCH_3	8	6	7	8
4	12d	Cl	18	19	18	18
5	12e	Br	16	15	16	15
6	12f	NO_2	17	16	17	16
7	Amoxicillin		21	27	24	22
8	Cefaclor		19	22	19	20

Antifungal activity

Antifungal activity of final compounds 1-(5/6-mono substituted or 5,6-disubstituted benzo [d] oxazol-2-yl) methyl)- 6-(4-substituted phenoxy)-4,8-dihydro-1H-[1,3,2] dioxaphosphepino [5,6-d] imidazole-6-oxide **(8a-f)** were screened against Aspergillus niger, Helminthosporium Oryzae. The compounds **(8d-f)** showed more fungal activity, while **(8a-c)** exhibited low activity. The fungal activity of benzo[d]-oxazole **(8a-f)** was shown in the **(Table 3)**. The similar results were also noticed with 1-(benzo [d] thiazol-2-yl) methyl) -6-(4-substituted phenoxy)-4,8-dihydro-1H-[1,3,2] dioxaphosphepino [5,6-d] imidazole-6-oxide **(12a-f)** under given experimental conditions. The fungal activity of **(12a-f)** was shown in the **(Table 4)**. Here Griseofulvin [45-47] is tested as reference compound to compare the activity.

Table 3: Antifungal activity of 1-(5/ 6-mono substituted or 5, 6-disubstituted benzo [d] oxazol-2-yl) methyl)- 6-(4-substituted phenoxy)-4,8-dihydro-1H-[1,3,2] dioxaphosphepino [5,6-d] imidazole-6-oxide (8a-f).

S.NO	COMPOUND	R	R1	R_2	Zone of inhibition (mm)	
					Aspergillus niger NCCS 1196 250(µg/disc)	*Helminthosporium Oryzae 250(µg/disc)*
1	8a	H	H	H	9	8
2	8b	H	NO_2	CH_3	10	9
3	8c	NO_2	H	OCH_3	8	6
4	8d	NO_2	NO_2	Cl	18	19
5	8e	Cl	H	Br	16	17
6	8f	Cl	NO_2	NO_2	17	18
7	Griseofulvin				28	26

Table 4: Antifungal activity of 1-(benzo [d] thiazol-2-yl) methyl) -6-(4-substituted phenoxy)-4, 8-dihydro-1H-[1, 3, 2] dioxaphosphepino [5, 6-d] imidazole-6-oxide (12a-f)

S.NO	COMPOUND	R	Zone of inhibition (mm)	
			Aspergillus niger NCCS 1196 250(µg/disc)	*Helminthosporium Oryzae 250(µg/disc)*
1	12a	H	10	9
2	12b	CH_3	8	8
3	12c	OCH_3	9	7
4	12d	Cl	19	20
5	12e	Br	17	17
6	12f	NO_2	18	19
7	Griseofulvin		28	26

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