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Synthesis, Characterization and Antimicrobial Evaluation of Novel Imidazole Ureas / Carboxamides Containing Dioxaphospholanes

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Abstract: *New novel derivatives of 1-((6-(4-chlorophenoxy) / (4-bromophenoxy) / (4-nitrophenoxy)-6-oxido-4, 8-dihydro-1H-[1, 3, 2]dioxaphosphepino[5, 6-d]imidazole-1-yl) methyl)-3-phenyl / (p-tolyl) / (4-methoxy phenyl) / (4-chloro phenyl) urea* ***(7a-l as per Scheme-1)*** *and were prepared by condensation of phenyl phosphordichloridates* ***6(a-c)*** *with 1-((4, 5-bis (hydroxyl methyl)-1H-imidazole-1-yl) methyl)-3-phenyl / (p-tolyl) / (4-methoxy phenyl) / (4-chlorophenyl) urea* ***5(a-d).*** *The Synthons* ***5(a-d)*** *were obtained by deprotection of isopropylidene 1-(6, 6-dimethyl-4, 8-dihydro-1H-[1, 3] dioxepino[5, 6-d] imidazole-1-yl) methyl)-3-phenyl / (p-tolyl) / (4-methoxy phenyl) / (4-chlorophenyl) ureas* ***4(a-d).*** *The Synthons* ***4(a-d)*** *were obtained by the condensation of aniline / p-toluidine / 4-methoxyaniline / 4-chloroaniline* ***3(a-d)*** *and 1-(isocyanato methyl)-6, 6 - dimethyl-4, 8 – dihydro - 1H - [1, 3] dioxepino [5, 6-d] imidazole* ***(2).*** *The synthon* ***(2)*** *was obtained from synthon* ***(1).*** *The similar procedure was adapted to prepare N-((6 - (4-chlorophenoxy) / (4-bromophenoxy) / (4-nitrophenoxy) - 6 - oxido - 4, 8-dihyro - 1H - [1, 3, 2] dioxaphophepino [5, 6-d] imidazole-1-yl-) methyl) morpholine - 4 – carboxamide / piperidine - 1 – carboxamide / 4-methyl piperazine - 1 – carboxamide (****11a-i as per Scheme-2).*** *The products were characterized by IR, ^{1}H NMR, ^{13}C NMR, ^{31}P NMR and elemental analyses. The newly synthesized compounds were subjected to various biological activities viz., antimicrobial.*

Keywords: *Antibacterial, Antifungal, deprotection, imidazole, phenyl phosphorodichloridates.*

I. Introduction

Imidazole derivetives possess a broad spectrum of pharmalogical activities such as anticonvulsant,

Antiparkinson , monoamine oxidase (MAO) inihibitory activity, anti-bacterial, anti-fungul activity, it also function as dyestuff, catalyst, polymerizing agents, drugs, herbicides and fungicides [1-3]. Imidazole derivatives are valuable vasodialating and vasoconstructing drugs.

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. 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. Some organophosphorus compounds have been described in the literature as inhibitors of bacterial, herbicides, insecticides, pesticides, anti-fungal agents, anti-HIV, anti-cancer, anti-viral and anti-inflammatory [4-10].

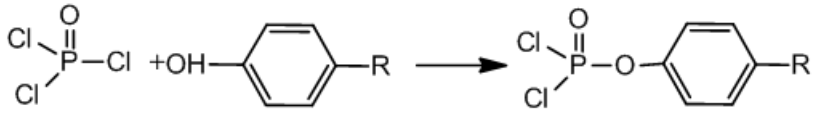
A good deal of importance was given to dioxaphosphepino ureas / carboxamides and their derivatives in the field of organophosphorus heterocyclic chemistry due to their unique biological applications [11]. In view of the above observations, we synthesized Imidazole possessing dioxaphosphepino ureas / carboxamides and screening for possible biological and pharmacological activities.

II. 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 60F254, 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 1H 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). Elemental analysis was recorded on a Carlo Erba 1108 elemental Analyzer, Central Drug Research Institute, Lucknow, India.

Preparation of Intermediates:

1.1 Synthesis of phenyl phosphorodichloridates 6(a-c) [12]:



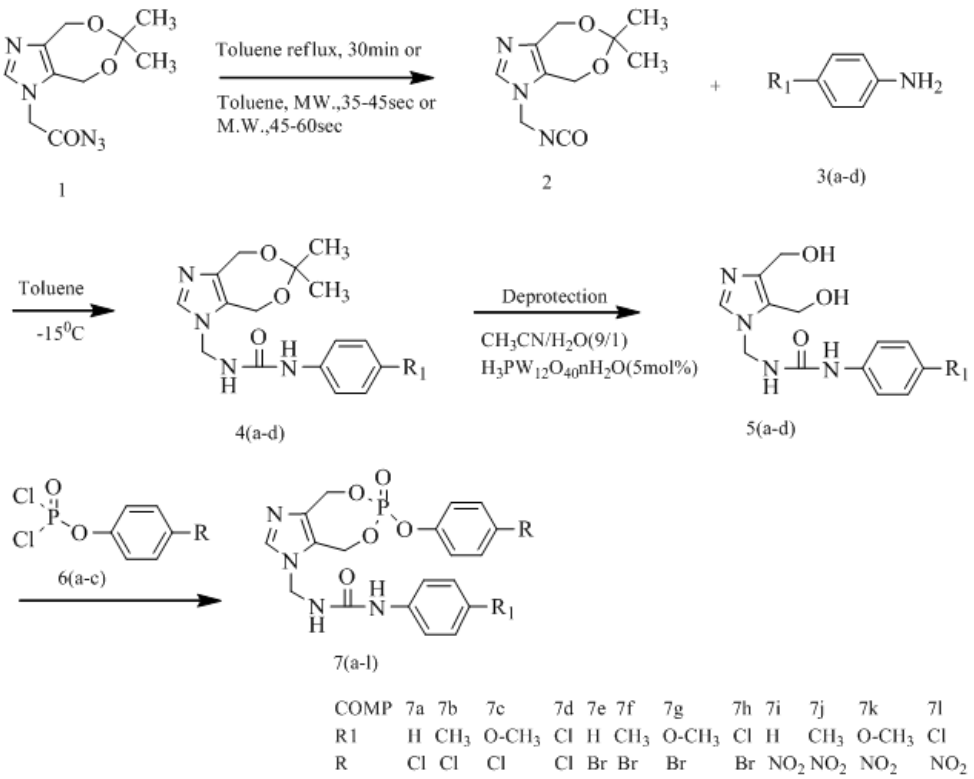
6(a-c)

Phosphorus oxychloride (15.3 gr, 0.1mole) in dry benzene (60 ml) was taken into 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 mole) 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 mole) 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 **6(a-c)** were prepared by the same procedure [13] by reacting equimolar quantities of phosophorous oxychloride and respective substituted phenols in benzene in the presence of tri ethylamine. The data of these aryl phosphorodichloridates are given in **Table -1.**

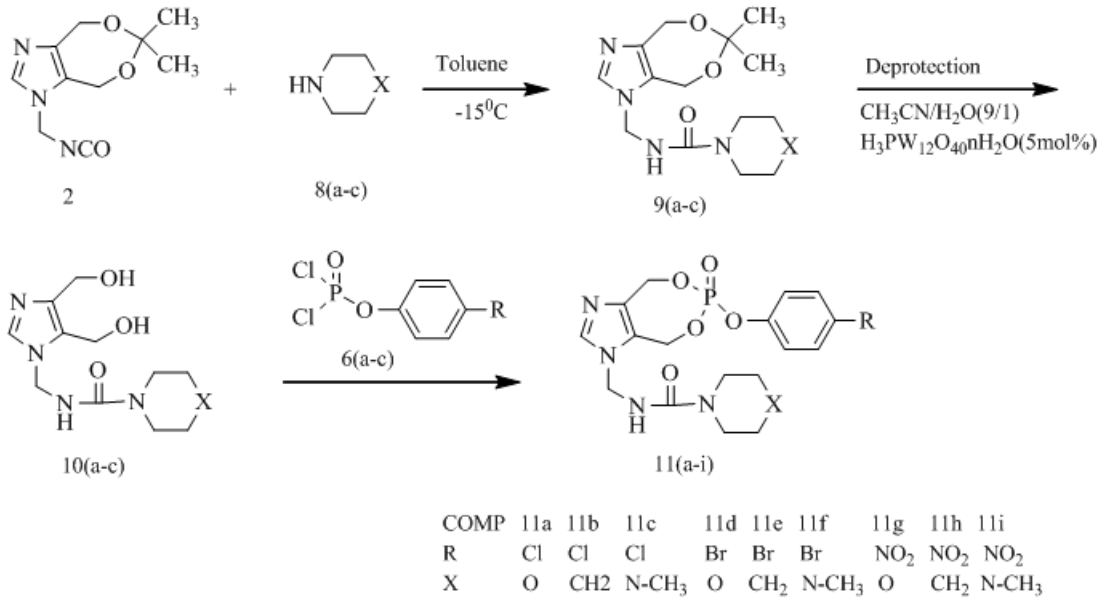
Table-1.1: **Phenyl phosphorodichloridate 6(a-c):**

COMP	NAME OF THE DICHLORIDATE	REACTION TIME (hrs)	Bp (^{0}C/mm)	YIELD (%)
6a	4- chloro Phenyl phosphorodichloridate	9	142-145/	35
6b	4-bromo Phenyl phosphorodichloridate	9	145-148/8	33
6c	4-nitro Phenyl phosphorodichloridate	10	134-136/6	33



1 2 3(a-d) 4(a-d) 5(a-d) 7(a-l)

Scheme-I: Synthesis of 1-((6-(4-chlorophenoxy) / (4-bromophenoxy) / (4-nitrophenoxy)-6-oxido-4, 8-dihydro-1H-[1, 3, 2]dioxaphosphepino[5, 6-d]imidazole-1-yl) methyl)-3-phenyl / (p-tolyl) / (4-methoxy phenyl) / (4-chloro phenyl) urea 7(a-l)



Scheme-2: Synthesis of N-((6 - (4-chlorophenoxy) / (4-bromophenoxy) / (4-nitrophenoxy) - 6 - oxido - 4, 8-dihyro - 1H - [1, 3, 2] dioxaphophepino [5, 6-d] imidazole-1-yl-) methyl) morpholine - 4 – carboxamide / piperidine - 1 – carboxamide / 4-methyl piperazine - 1 – carboxamide 11(a-i).

III. Results And Discussion

1.2. Synthesis of 1-(isocyanato methyl)-6, 6 - dimethyl-4, 8 – dihydro - 1H - [1, 3] dioxepino [5, 6-d] imidazole (2) [14]:

The 2-(6, 6-dimethyl-4, 8-dihydro-1H-[1, 3] dioxepino[5, 6-d]imidazole-1-yl) acetyl azide **(1)** (1mmol) dissolved in toluene (10mL) was refluxed for 30min at 65^{o}C under nitrogen atmosphere. After the completion of the reactionas indicated by TLC, the solvent was removed under reduced pressure to get crude 1-(isocyanato methyl) - 6, 6 - dimethyl-4, 8 – dihydro - 1H - [1, 3] dioxepino [5, 6-d] imidazole **(2).** The crude product was purified by column chromatography (60-120 mesh silica gel, eluent: 10 % EtoAc-pet ether), which was recrystallized using dichloromethane and n-hexane, mp 139-141^{o}C, yield 70%.

1.3. Synthesis of 1-(6, 6-dimethyl-4, 8-dihydro-1H-[1, 3] dioxepino [5, 6-d] imidazole-1-yl) methyl) – 3 - phenyl / (p-tolyl) / (4-methoxy phenyl) / (4-chlorophenyl) urea 4(a-d):

To the solution of isocyanate **(2)** (1eq), in aniline **(3a)** (10 times) dissolved in toluene (10mL) was stirred -15^{o}C was refluxed for 16 hours. After completion of the reaction as indicated by TLC, solvent was evaporated under vacuum to give crude residue, purified by column chromatography (60-120 mesh silica gel, eluent: 30% EtoAc-pet ether). Finally the product compound 1-(6, 6-dimethyl-4, 8-dihydro-1H-[1, 3] dioxepino [5, 6-d] imidazole-1-yl) methyl) – 3 - phenyl urea **(4a)** was purified from aqueous dimethyl formamide with m p 166-168^{o}C, yield 65%.

The similar procedure was adopted to synthesise **4(b-d)** by condensing 1-(isocyanato methyl)-6, 6 - dimethyl-4, 8 – dihydro - 1H - [1, 3] dioxepino [5, 6-d] imidazole **(2)** with p-toluidine **(3b)**, 4-methoxyaniline **(3c)** and 4-chloroaniline **(3d)** respectively.

1.4. Synthesis of 1-((4, 5 - bis (hydroxyl methyl) -1H- imidazole-1-yl) methyl) – 3 -phenyl / (p-tolyl) / (4-methoxy phenyl) / (4-chlorophenyl) urea 5(a-d):

The isopropylidenation of 1, 2-diols was carried out by a procedure as reported in the literature [15]. A suspension of the 1-(6, 6-dimethyl-4, 8-dihydro-1H-[1, 3] dioxepino [5, 6-d] imidazole-1-yl) methyl) -3- phenyl urea **(4a)** (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 mobile phase. 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 30% ethyl acetate in cyclohexane as an eluent. The m p of **(5a)** was 182-184^{o}C with yield of 74%.

The similar procedure was adopted to synthesise **5(b-d)** from **4(b-d)**.

1.5. Synthesis of 1-((6-(4-chlorophenoxy) / (4-bromophenoxy) / (4-nitrophenoxy)-6-oxido-4, 8-dihydro-1H-[1, 3, 2] dioxaphosphepino [5, 6-d] imidazole-1-yl) methyl)-3-phenyl / (p-tolyl) / (4-methoxy phenyl) / (4-chloro phenyl) urea 7(a-l):

A solution of 4-chlorophenyl phosphorodichloridate **(6a)** (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-((4, 5-bis (hydroxyl methyl)-1H-imidazole-1-yl) methyl)-3-phenyl urea **(5a)** (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^OC 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 1-((6-(4-chlorophenoxy) - 6 -oxido - 4, 8 – dihydro - 1H - [1, 3, 2] dioxaphosphepino [5, 6-d] imidazole-1-yl) methyl)-3-phenyl urea **(7a)**, yield 70%, m p 142-144^{0}C.

The similar procedure was adopted to synthesise **7(b-l)** by the reaction between **5(b-d)** with 4 - chlorophenyl phosphorodichloridate **(6a),** 4 - bromophenyl phosphorodichloridate **(6b)** and 4 - nitrophenyl phosphorodichloridate **(6c).** The structures of newly synthesised of compounds **7(a-l)** were established by IR, ^{1}H-NMR, ^{13}C-NMR, ^{31}P-NMR and elemental analysis. The IR, ^{1}H-NMR, ^{13}C-NMR, ^{31}P-NMR and analytical data was shown in the **Table 1.2-1.6.**

1.6. Synthesis of N-((6, 6-dimethyl-4, 8-dihydro-1H-[1, 3] dioxepino [5, 6-d] imidazole-1-yl) methyl) morpholine-4-carboxamide / piperidine-1-carboxamide / 4 - methyl piperazine-1-carboxamide 9(a-c):

To the solution of isocyanate **(2)** (1eq), in morpholine **(8a)** (10 times) dissolved in toluene (10mL) was added and heated -15^{o}C, the reaction mixture was refluxed for 16 hours. After completion of reaction as indicated by TLC solvent was evaporated under vacuum to give crude residue, purified by column chromatography (60-120 mesh silica gel, eluent: 30% EtoAc-pet ether) solvent was used as an eluent. Finally the product N-((6, 6 – dimethyl - 4, 8 – dihydro - 1H - [1, 3] dioxepino [5, 6-d] imidazole-1-yl) methyl) morpholine – 4 - carboxamide **(9a)** was purified from aqueous dimethyl formamide. Yield 65%, m p 139-142^{0}C. The similar procedure was adopted to synthesise **9(b-c)** by condensing 1-(isocyanato methyl) - 6, 6 – dimethyl - 4, 8 – dihydro - 1H - [1, 3] dioxepino [5, 6-d] imidazole **(2)** with piperidine **(8b)** and 1-methylpiperazine **(8c)** respectively.

1.7. Synthesis of N-((4, 5-bis (hydroxyl methyl)-1H -imidazole-1-yl) methyl) morpholine-4-carboxamide / piperidine-1-carboxamide / 4 - methyl piperazine-1-carboxamide 10(a-c):

The isopropylidenation of 1, 2-diols was carried out by a procedure as reported in the literature[27]. A suspension of the N-((6, 6-dimethyl-4, 8-dihydro-1H-[1, 3] dioxepino [5, 6-d] imidazole-1-yl) methyl) morpholine-4-carboxamide **(9a)** (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 a mobile phase. 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 30% ethyl acetate in cyclohexane as an eluent. The m p of **(10a)** was 123-126^{0}C with yield of 65 %.

The similar procedure was adopted to synthesise **10(b-c)** from **8(b-c)**.

1.8. Synthesis of N-((6 - (4-chlorophenoxy) / (4-bromophenoxy) / (4-nitrophenoxy) - 6 - oxido - 4, 8-dihyro - 1H - [1, 3, 2] dioxaphophepino [5, 6-d] imidazole-1-yl-) methyl) morpholine - 4 – carboxamide / piperidine - 1 – carboxamide / 4-methyl piperazine - 1 – carboxamide 11(a-i):

A solution of 4-chlorophenyl phosphorodichloridate **(6a)** (0.002 mole) in 25 ml of dry toluene was added drop wise over a period of 20 minutes to a stirred solution of N-((4, 5-bis (hydroxyl methyl)-1H - imidazole-1-yl) methyl) morpholine-4-carboxamide **(10a)** (0.002mole) and triethylamine (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. Triethyl amine hydrochloride was filtered from reaction 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 N-((6 - (4-chlorophenoxy) - 6 - oxido - 4, 8-dihyro - 1H - [1, 3, 2] dioxaphophepino [5, 6-d] imidazole-1-yl-) methyl) morpholine - 4 - carboxamide **(11a)**, yield 70%, m p 152-155^{0}C.

The similar procedure was adopted to synthesise **11(b-i)** by the reaction between **10(b-c)** with 4 - chlorophenyl phosphorodichloridate **(6a),** 4 - bromophenyl phosphorodichloridate **(6b)** and 4 - nitrophenyl phosphorodichloridate **(6c).** The structures of newly synthesised compounds 11**(a-i)** were established by IR, ^{1}H-NMR, ^{13}C-NMR, ^{31}P-NMR and elemental analysis. The IR, ^{1}H-NMR, ^{13}C-NMR, ^{31}P-NMR and analytical data was shown in the **Table 1.7-1.11.**

Spectral, Physical and analytical data for the compounds:

Table I.2: The IR (KBr) spectra of 1-((6-(4-chlorophenoxy) / (4-bromophenoxy) / (4-nitrophenoxy)-6-oxido-4, 8-dihydro-1H-[1, 3, 2]dioxaphosphepino [5, 6-d] imidazole-1-yl) methyl)-3-phenyl / (p-tolyl) / (4-methoxy phenyl) / (4-chloro phenyl) urea 7(a-l) ($\bar{\upsilon}$ / δ, cm^{-1}):

COMP	R_1	R	N-H	Ar-H	C=N	C=O	C-N	C-O	P=O	P-O-$C_{(arom)}$
7a	H	Cl	3418-3384	3100	1716	1650	1416	1320	1250	950
7b	CH_3	Cl	3420-3386	3104	1718	1654	1418	1324	1250	950
7c	OCH_3	Cl	3420-3388	3110	1720	1660	1420	1328	1250	950
7d	Cl	Cl	3422-3390	3120	1722	1655	1424	1326	1250	950
7e	H	Br	3418-3384	3125	1716	1664	1410	1322	1250	950
7f	CH_3	Br	3420-3386	3127	1718	1660	1415	1327	1250	950
7g	OCH_3	Br	3420-3388	3129	1720	1667	1426	1323	1250	950
7h	Cl	Br	3422-3390	3130	1722	1659	1417	1329	1250	950
7i	H	NO_2	3418-3384	3129	1720	1653	1419	1320	1250	950
7j	CH_3	NO_2	3420-3386	3130	1722	1656	1423	1328	1250	950
7k	OCH_3	NO_2	3420-3388	3129	1720	1660	1427	1325	1250	950
7l	Cl	NO_2	3422-3390	3130	1722	1669	1423	1327	1250	950

Table1.3: The ^{1}H NMR (400MHz) spectra of 1-((6-(4-chlorophenoxy) / (4-bromophenoxy) / (4-nitrophenoxy)-6-oxido-4, 8-dihydro-1H-[1, 3, 2] dioxaphosphepino [5, 6-d]imidazole-1-yl) methyl)-3-phenyl / (p-tolyl) / (4-methoxy phenyl) / (4-chloro phenyl) urea 7(a-l) (δ_{PPM}):

COMP	R_1	R	^{1}H-NMR(DMSO-d_6) **(δ_{PPM})**
7a	H	Cl	5.23 (s, 4H, two CH_2 groups attached to phosphorus moiety), 5.60 (s, 2H, N-CH_2), 6.0 (t, 1H, NH of urea), 6.1 (s, 1H, NH of urea), 6.89-7.32 (m, 5H of phenyl group), 7.57 (s, 1H, CH of imidazole ring) and 7.19-7.61 (m, 4H of 4-chlorophenoxy ring).
7b	CH_3	Cl	2.34 (s, 3H, CH_3 group attached to phenylurea moiety), 5.23 (s, 4H, two CH_2 groups attached to phosphorus moiety), 5.60 (s, 2H, N-CH_2), 6.0 (t, 1H, NH of urea), 6.1 (s, 1H, NH of urea), 6.90-7.2 (m, 4H of p-tolyl group), 7.20-7.50 (m, 4H of 4-chlorophenoxy ring) and 7.57 (s, 1H, CH of imidazole ring).
7c	OCH_3	Cl	3.80 (s, 3H, CH_3 group attached to phenylurea moiety), 5.23 (s, 4H, two CH_2 groups attached to phosphorus moiety), 5.60 (s, 2H, N-CH_2), 6.0 (t, 1H, NH of urea), 6.1 (s, 1H, NH of urea), 6.90-7.10 (m, 4H of 4-methoxyphenyl group), 6.2-7.5 (m, 4H of 4-chlorophenoxy ring) and 7.57 (s, 1H, CH of imidazole ring).
7d	Cl	Cl	5.23 (s, 4H, two CH_2 groups attached to phosphorus moiety), 5.60 (s, 2H, N-CH_2), 6.0 (t, 1H, NH of urea), 6.1 (s, 1H, NH of urea), 7.1-7.3 (m, 4H of 4-chlorophenyl group), 7.57 (s, 1H, CH of imidazole ring) and 7.40-7.70 (m, 4H of 4-chlorophenoxy ring).
7e	H	Br	5.23 (s, 4H, two CH_2 groups attached to phosphorus moiety), 5.60 (d, 2H, N-CH_2), 6.0 (t, 1H, NH of urea), 6.1 (s, 1H, NH of urea), 6.89-7.32 (m, 5H of phenyl group), 7.57 (s, 1H, CH of imidazole ring) and 7.30-7.60 (m, 4H of 4-bromophenoxy ring).
7f	CH_3	Br	2.34 (s, 3H, CH_3 group attached to phenylurea moiety), 5.23 (s, 4H, two CH_2 groups attached to phosphorus moiety), 5.60 (d, 2H, N-CH_2), 6.0 (t, 1H, NH of urea), 6.1 (s, 1H, NH of urea), 6.90-7.20 (m, 4H of p-tolyl group), 7.30-7.56 (m, 4H of 4-bromophenoxy ring) and 7.57 (s, 1H, CH of imidazole ring).
7g	OCH_3	Br	3.80 (s, 3H, CH_3 group attached to phenylurea moiety), 5.23 (s, 4H, two CH_2 groups attached to phosphorus moiety), 5.60 (d, 2H, N-CH_2), 6.0 (t, 1H, NH of urea), 6.1 (s, 1H, NH of urea), 6.84-7.43 (m, 4H of 4-methoxyphenyl group), 7.30-7.54 (m, 4H of 4-bromophenoxy ring) and 7.57 (s, 1H, CH of imidazole ring).
7h	Cl	Br	5.23 (s, 4H, two CH_2 groups attached to phosphorus moiety), 5.60 (d, 2H, N-CH_2), 6.0 (t, 1H, NH of urea), 6.1 (s, 1H, NH of urea), 7.1-7.3 (m, 4H of 4-chlorophenyl group), 7.57 (s, 1H, CH of imidazole ring) and 7.30-7.56 (m, 4H of 4-bromophenoxy ring).
7i	H	NO_2	5.23 (s, 4H, two CH_2 groups attached to phosphorus moiety), 5.60 (d, 2H, N-CH_2), 6.0 (t, 1H, NH of urea), 6.1 (s, 1H, NH of urea), 7.57 (s, 1H, CH of imidazole ring), 6.90-7.30 (m, 5H of phenyl ring) and 7.36-7.70 (m, 4H of 4-nitrophenoxy group).
7j	CH_3	NO_2	2.34 (s, 3H, CH_3 group attached to phenylurea moiety), 5.23 (s, 4H, two CH_2 groups attached to phosphorus moiety), 5.60 (d, 2H, N-CH_2), 6.0 (t, 1H, NH of urea), 6.1 (s, 1H, NH of urea), 6.9-7.2 (m, 4H of p-tolyl ring), 7.57 (s, 1H, CH of imidazole ring) and 7.35-7.70 (m, 4H of 4-nitrophenoxy group).
7k	OCH_3	NO_2	3.80 (s, 3H, CH_3 group attached to phenylurea moiety), 5.23 (s, 4H, two CH_2 groups attached to phosphorus moiety), 5.60 (d, 2H, N-CH_2), 6.0 (t, 1H, NH of urea), 6.1 (s, 1H, NH of urea), 6.90-7.10 (m, 4H of 4-methoxyphenyl ring), 7.57 (s, 1H, CH of imidazole ring) and 7.34-7.72 (m, 4H of 4-nitrophenoxy group).
7l	Cl	NO_2	5.23 (s, 4H, two CH_2 groups attached to phosphorus moiety), 5.60 (d, 2H, N-CH_2), 6.0 (t, 1H, NH of urea), 6.1 (s, 1H, NH of urea), 7.57 (s, 1H, CH of imidazole ring), 7.10-7.30 (m, 4H of 4-chlorophenyl ring) and 7.34-7.70 (m, 4H of 4-nitrophenoxy group).

Table 1.4: The ^{13}C NMR (75MHz) spectra of 1-((6-(4-chlorophenoxy) / (4-bromophenoxy) / (4-nitrophenoxy) – 6 - oxido - 4, 8 - dihydro -1H- [1, 3, 2] dioxaphosphepino [5, 6-d] imidazole-1-yl) methyl) -3- phenyl / (p-tolyl) / (4-methoxy phenyl) / (4-chloro phenyl) urea 7(a-l) (δ_{PPM}):

COMP	R_1	R	^{13}C-NMR(DMSO-d_6)(δ_{PPM})
7a	H	Cl	137.3, 132.9, 127.7, 63.0, 60.2, 62.4, 154.3, 139.4, 121.6, 128.9, 128.0, 121.6, 148.9, 125.7, 131.3 and 126.9 corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9 & C_{13}, C_{10} & C_{12}, C_{11}, C_{14}, C_{18}, C_{15} & C_{19}, C_{16} & C_{18} and C_{17}.
7b	CH_3	Cl	137.3, 132.9, 127.7, 63.0, 60.2, 62.4, 154.3, 136.4, 121.5, 129.2, 136.8, 21.3, 148.3 and 126.9, corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9 & C_{13}, C_{10} & C_{12}, C_{11}, C_{14}, C_{15}, C_{16} & C_{20}, C_{17} & C_{19} and C_{18}.
7c	OCH_3	Cl	137.3, 132.9, 127.7, 63.0, 60.2, 62.4, 154.3, 131.7, 119.8, 114.5, 158.9, 55.8, 148.3, 125.7, 131.3 and 126.9 corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9 & C_{13}, C_{10} & C_{12}, C_{11}, C_{14}, C_{15}, C_{16} & C_{20}, C_{17} & C_{19} and C_{18}.
7d	Cl	Cl	137.3, 132.9, 127.7, 63.0, 60.2, 62.4, 154.3, 137.5, 120.8, 129.0, 133.3, 148.3, 125.7, 131.3 and 126.9 corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10} & C_{12}, C_{11}, C_{13}, C_{14}, C_{18}, C_{15} & C_{19}, C_{16} & C_{18} and C_{17}.
7e	H	Br	137.3, 132.9, 127.7, 63.0, 60.2, 62.4, 154.3, 139.4, 121.6, 128.9, 128.0, 149.2, 123.0, 133.0 and 115.7 corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10} & C_{12}, C_{11}, C_{13}, C_{14}, C_{18}, C_{15} & C_{19}, C_{16} & C_{18} and C_{17}.
7f	CH_3	Br	137.3, 132.9, 127.7, 63.0, 60.2, 62.4, 154.3, 136.4, 121.5, 129.2, 136.8, 21.3, 149.2, 123.0, 133.0 and 115.7 corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9 & C_{13}, C_{10} & C_{12}, C_{11}, C_{14}, C_{15}, C_{16} & C_{20}, C_{17} & C_{19} and C_{18}.
7g	OCH_3	Br	137.3, 132.9, 127.7, 63.0, 60.2, 62.4, 154.3, 131.7, 119.8, 114.5, 158.9, 55.8, 149.2, 123.0, 133.0 and 115.7 corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9 & C_{13}, C_{10} & C_{12}, C_{11}, C_{14}, C_{15}, C_{16} & C_{20}, C_{17} & C_{19} and C_{18}.
7h	Cl	Br	137.3, 132.9, 127.7, 63.0, 60.2, 62.4, 154.3, 137.5, 120.8, 129.0, 133.3, 149.2, 123.0, 133.0 and 115.7 corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10} & C_{12}, C_{11}, C_{13}, C_{14}, C_{18}, C_{15} & C_{19}, C_{16} & C_{18} and C_{17}.
7i	H	NO_2	137.3, 132.9, 127.7, 63.0, 60.2, 62.4, 154.3, 139.4, 121.6, 128.9, 128.0, , 156.3, 121.9, 126.3 and 140.5 corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10} & C_{12}, C_{11}, C_{13}, C_{14}, C_{18}, C_{15} & C_{19}, C_{16} & C_{18} and C_{17}.
7j	CH_3	NO_2	137.3, 132.9, 127.7, 63.0, 60.2, 62.4, 154.3, 136.4, 121.5, 129.2, 136.8, 129.2, 121.5, 21.3, 156.3, 121.9, 126.3 and 140.5 corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9 & C_{13}, C_{10} & C_{12}, C_{11}, C_{14}, C_{15}, C_{16} & C_{20}, C_{17} & C_{19} and C_{18}.
7k	OCH_3	NO_2	137.3, 132.9, 127.7, 63.0, 60.2, 62.4, 154.3, 131.7, 119.8, 114.5, 158.9, 55.8, 156.3, 121.9, 126.3 and 140.5, corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9 & C_{13}, C_{10} & C_{12}, C_{11}, C_{14}, C_{15}, C_{16} & C_{20}, C_{17} & C_{19} and C_{18}.
7l	Cl	NO_2	137.3, 132.9, 127.7, 63.0, 60.2, 62.4, 154.3, 137.5, 120.8, 129.0, 133.3, 156.3, 121.9, 126.3 and 140.5 corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10} & C_{12}, C_{11}, C_{13}, C_{14}, C_{18}, C_{15} & C_{19}, C_{16} & C_{18} and C_{17}.

Table 1.5: The ^{31}P NMR (161.89MHz) spectra of 1-((6-(4-chlorophenoxy) / (4-bromophenoxy) / (4-nitrophenoxy) – 6 - oxido - 4, 8 - dihydro -1H- [1, 3, 2] dioxaphosphepino [5, 6-d] imidazole-1-yl) methyl) -3-phenyl / (4-chloro phenyl) urea (7a, 7d, 7e, 7h, 7i and 7l) (δ_{PPM}):

COMP	R_1	R	^{31}P-NMR(DMSO-d_6)(δ_{PPM})
7a	H	Cl	-7.60 and -11.20
7d	Cl	Cl	-7.40
7e	H	Br	-7.90 and -11.50
7h	Cl	Br	-7.70
7i	H	NO_2	-7.20 and -10.50
7l	Cl	NO_2	-7.10

Table 1.6: Pysical and Analytical data of 1-((6-(4-chlorophenoxy) / (4-bromophenoxy) / (4-nitrophenoxy)-6-oxido-4, 8-dihydro-1H-[1, 3, 2]dioxaphosphepino [5, 6-d] imidazole-1-yl) methyl)-3-phenyl / (p-tolyl) / (4-methoxy phenyl) / (4-chloro phenyl) urea 7(a-l):

COMP	MOLECULAR FORMULA	MP(^{0}C)	YIELD (%)	ELEMENTAL ANALYSS(%)	
				FOUND	CALC
7a	$C_{19}H_{18}ClN_4O_5P$	142-144	70	C 50.05, H 3.54, Cl 7.10, N 11.88, P 6.20.	C 50.85, H 4.04, Cl 7.90, N 12.48, P 6.90.
7b	$C_{20}H_{20}ClN_4O_5P$	163-165	70	C 51.10, H 3.86, Cl 6.86, N 11.41, P 5.99.	C 51.90, H 4.36, Cl 7.66, N 12.11, P 6.69.
7c	$C_{20}H_{20}ClN_4O_6P$	179-181	75	C 49.37, H 3.71,	C 50.17, H 4.21,

				Cl 6.60, N 11.10, P 5.77.	Cl 7.40, N 11.70, P 6.47.
7d	$C_{19}H_{17}Cl_2N_4O_5P$	160-162	72	C 46.42, H 3.05, Cl 13.87, N 10.99, P 5.71.	C 47.22, H 3.55, Cl 14.67, N 11.59, P 6.41.
7e	$C_{19}H_{18}BrN_4O_5P$	161-163	70	C 45.47, H 3.18, Br 15.60, N 10.76, P 5.58.	C 46.27, H 3.68, Br 16.20, N 11.36, P 6.28.
7f	$C_{20}H_{20}BrN_4O_5P$	157-159	65	C 46.55, H 3.47, Br 15.15, N 10.44, P 5.41.	C 47.35, H 3.97, Br 15.75, N 11.04, P 6.11.
7g	$C_{20}H_{20}BrN_4O_6P$	178-180	60	C 45.11, H 3.35, Br 14.67, N 10.11, P 5.22.	C 45.91, H 3.85, Br 15.27, N 10.71, P 5.92.
7h	$C_{19}H_{17}BrClN_4O_5P$	185-187	64	C 42.45, H 2.75, Br 14.54, Cl 5.92, N 10.02, P 5.17.	C 43.25, H 3.25, Br 15.14, Cl 6.72, N 10.62, P 5.87.
7i	$C_{19}H_{18}N_5O_7P$	173-175	60	C 48.88, H 3.45, N 14.65, P 6.04.	C 49.68, H 3.95, N 15.25, P 6.74.
7j	$C_{20}H_{20}N_5O_7P$	165-167	65	C 49.94, H 4.11, N 14.19, P 5.94.	C 50.74, H 4.61, N 14.79, P 6.54.
7k	$C_{20}H_{20}N_5O_8P$	193-195	65	C 48.29, H 3.62, N 13.71, P 5.63.	C 49.09, H 4.12, N 14.31, P 6.33.
7l	$C_{19}H_{17}ClN_5O_7P$	207-209	70	C 45.41, H 2.97, Cl 6.38, N 13.58, P 5.67.	C 46.21, H 3.47, Cl 7.18, N 14.18, P 6.27.

Table 1.7: The IR (KBr) spectra of N-((6 -(4-chlorophenoxy) / (4-bromophenoxy) / (4-nitrophenoxy)-6-oxido-4, 8-dihyro-1H-[1, 3, 2] dioxaphophepino [5, 6-d] imidazole-1-yl-) methyl) morpholine - 4 – carboxamide / piperidine - 1 – carboxamide / 4-methyl piperazine - 1 – carboxamide 11(a-i) ($\bar{\upsilon}$ / δ, cm^{-1}):

COMP	R	X	N-H	C=O	C=N	C-N	C-O	P=O	P-O-$C_{(arom)}$
11a	Cl	O	3418	1650	1616	1416	1320	1250	950
11b	Cl	CH_2	3420	1655	1618	1418	1325	1245	955
11c	Cl	N-CH_3	3420	1656	1620	1420	1323	1240	960
11d	Br	O	3422	1653	1622	1423	1326	1255	954
11e	Br	CH_2	3418	1657	1616	1414	1328	1260	940
11f	Br	N-CH_3	3420	1660	1618	1419	1327	1259	948
11g	NO_2	O	3420	1665	1620	1420	1315	1264	958
11h	NO_2	CH_2	3422	1663	1622	1424	1319	1269	963
11i	NO_2	N-CH_3	3418	1664	1624	1425	1323	1254	968

Table 1.8: The ^{1}H NMR (400MHz) spectra of N-((6 - (4-chlorophenoxy) / (4-bromophenoxy) / (4-nitrophenoxy) - 6 - oxido - 4, 8-dihyro - 1H - [1, 3, 2] dioxaphophepino [5, 6-d] imidazole-1-yl-) methyl) morpholine - 4 – carboxamide / piperidine - 1 – carboxamide / 4-methyl piperazine - 1 – carboxamide 11(a-i) (δ_{PPM}):

COMP	R	X	^{1}H-NMR(DMSO-d_6)(δ_{PPM})
11a	Cl	O	3.31 (t, 4H, N-CH_2 of morpholine ring), 3.65 (t, 4H, -CH_2-O of morpholine ring), 5.23 (s, 4H, two CH_2 groups attached to phosphorus moiety), 5.60 (d, 2H, N-CH_2), 6.0 (s, 1H, NH-of carboxamide moiety), 6.89-7.32 (m, 4H, of phenoxy group) and 7.57(s, 1H of imidazole ring).
11b	Cl	CH_2	1.53-1.59 (m, 6H, CH_2 piperidine of carboxamide), 3.77 (t, 4H, N-CH_2 piperidine of carboxamide), 5.23 (s, 4H, two CH_2 groups attached to phosphorus moiety), 5.60 (d, 2H, N-CH_2), 6.0 (s, 1H, NH-of carboxamide moiety), 6.89-7.32 (m, 4H, of phenoxy group) and 7.57(s, 1H of imidazole ring).
11c	Cl	N-CH_3	2.10 (s, 3H, N-CH_3), 2.27 (t, 4H, CH_2-N piperazine of carboxamide), 3.40 (t, 4H, N-CH_2 piperazine of carboxamide), 5.23 (s, 4H, two CH_2 groups attached to phosphorus moiety), 5.60 (d, 2H, N-CH_2), 6.0 (s, 1H, NH-of carboxamide moiety), 6.89-7.32 (m, 4H, of phenoxy group) and 7.57(s, 1H of imidazole ring).
11d	Br	O	3.31 (t, 4H, N-CH_2 of morpholine ring), 3.65 (t, 4H, -CH_2-O of morpholine ring), 5.23 (s, 4H, two CH_2 groups attached to phosphorus moiety), 5.60 (d, 2H, N-CH_2), 6.0 (s, 1H, NH-of carboxamide moiety), 6.80-7.23 (m, 4H, of phenoxy group) and 7.57(s, 1H of imidazole ring).
11e	Br	CH_2	1.53-1.59 (m, 6H, CH_2 piperidine of carboxamide), 3.77 (t, 4H, N-CH_2 piperidine of carboxamide), 5.23 (s, 4H, two CH_2 groups attached to phosphorus moiety), 5.60 (d, 2H, N-CH_2), 6.0 (s, 1H, NH-of carboxamide moiety), 6.80-7.23 (m, 4H, of phenoxy group) and 7.57(s, 1H of imidazole ring).
11f	Br	N-CH_3	2.10 (s, 3H, N-CH_3), 2.27 (t, 4H, CH_2-N piperazine of carboxamide), 3.40 (t, 4H, N-CH_2 piperazine of carboxamide), 5.23 (s, 4H, two CH_2 groups attached to phosphorus moiety), 5.60 (d, 2H, N-CH_2), 6.0 (s, 1H, NH-of carboxamide moiety), 6.80-7.23 (m, 4H, of phenoxy group) and 7.57(s, 1H of imidazole ring).
11g	NO_2	O	3.31 (t, 4H, N-CH_2 of morpholine ring), 3.65 (t, 4H, -CH_2-O of morpholine ring), 5.23 (s, 4H, two CH_2 groups attached to phosphorus moiety), 5.60 (d, 2H, N-CH_2), 6.0 (s, 1H, NH-of carboxamide moiety), 7.57 (s, 1H of imidazole ring) and 7.34-8.09 (m, 4H, of phenoxy group).
11h	NO_2	CH_2	1.53-1.59 (m, 6H, CH_2 piperidine of carboxamide), 3.77 (t, 4H, N-CH_2 piperidine of carboxamide), 5.23 (s, 4H, two CH_2 groups attached to phosphorus moiety), 5.60 (d, 2H, N-CH_2), 6.0 (s, 1H, NH-of carboxamide moiety), 7.57 (s, 1H of imidazole ring) and 7.34-8.09 (m, 4H, of phenoxy group).
11i	NO_2	N-CH_3	2.10 (s, 3H, N-CH_3), 2.27 (t, 4H, CH_2-N piperazine of carboxamide), 3.40 (t, 4H, N-CH_2 piperazine of carboxamide), 5.23 (s, 4H, two CH_2 groups attached to phosphorus moiety), 5.60 (d, 2H, N-CH_2), 6.0 (s, 1H, NH-of carboxamide moiety), 7.57 (s, 1H of imidazole ring) and 7.34-8.09 (m, 4H, of phenoxy group).

Table 1.9: The ^{13}C NMR (75MHz) spectra of N-((6 - (4-chlorophenoxy) / (4-bromophenoxy) / (4-nitrophenoxy) - 6 - oxido - 4, 8-dihyro - 1H - [1, 3, 2] dioxaphophepino [5, 6-d] imidazole-1-yl-) methyl) morpholine - 4 – carboxamide / piperidine - 1 – carboxamide / 4-methyl piperazine - 1 – carboxamide 11(a-i) (δ_{PPM}):

COMP	R	X	^{13}C-NMR(DMSO-d_6)(δ_{PPM})
11a	Cl	O	137.3, 132.9, 127.7, 63.0, 60.2, 62.7, 157.7, 46.6, 65.7, 148.3, 125.7, 131.3 and 126.9 corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8 & C_{11}, C_9 & C_{10}, , C_{12}, C_{13} & C_{17}, C_{14} & C_{16} and C_{15}.
11b	Cl	CH_2	137.3, 132.9, 127.7, 63.0, 60.2, 62.7, 157.7, 49.3, 24.9, 23.8, 148.3, 125.7, 131.3 and 126.9 corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8 & C_{12}, C_9 & C_{11}, C_{10}, C_{13}, C_{14} & C_{18}, C_{15} & C_{17} and C_{16}.
11c	Cl	N-CH_3	137.3, 132.9, 127.7, 63.0, 60.2, 62.7, 157.7, 51.7, 51.0, 46.6, 148.3, 125.7, 131.3 and 126.9 corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8 & C_{11}, C_9 & C_{10}, , C_{12}, C_{13} C_{14} & C_{18}, C_{15} & C_{17} and C_{16}.
11d	Br	O	137.3, 132.9, 127.7, 63.0, 60.2, 62.7, 157.7, 46.6, 65.7, 149.2, 123.0, 133.3 and 115.7 corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8 & C_{11}, C_9 & C_{10}, , C_{12}, C_{13} & C_{17}, C_{14} & C_{16} and C_{15}.
11e	Br	CH_2	137.3, 132.9, 127.7, 63.0, 60.2, 62.7, 157.7, 49.3, 24.9, 23.8, 149.2, 123.0, 133.3 and 115.7 corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8 & C_{12}, C_9 & C_{11}, , C_{10}, C_{13} C_{14} & C_{18}, C_{15} & C_{17} and C_{16}.
11f	Br	N-CH_3	137.3, 132.9, 127.7, 63.0, 60.2, 62.7, 157.7, 51.7, 51.0, 46.6, 149.2, 123.0, 133.3 and 115.7 corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8 & C_{11}, C_9 & C_{10}, , C_{12}, C_{13} C_{14} & C_{18}, C_{15} & C_{17} and C_{16}.
11g	NO_2	O	137.3, 132.9, 127.7, 63.0, 60.2, 62.7, 157.7, 46.6, 65.7, 156.3, 121.9, 126.3 and 140.5corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8 & C_{11}, C_9 & C_{10}, , C_{12}, C_{13} & C_{17}, C_{14} & C_{16} and C_{15}.
11h	NO_2	CH_2	137.3, 132.9, 127.7, 63.0, 60.2, 62.7, 157.7, 49.3, 24.9, 23.8, 156.3, 121.9, 126.3 and 140.5 corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8 & C_{12}, C_9 & C_{11}, , C_{10}, C_{13} C_{14} & C_{18}, C_{15} & C_{17} and C_{16}.
11i	NO_2	N-CH_3	137.3, 132.9, 127.7, 63.0, 60.2, 62.7, 157.7, 51.7, 51.0, 46.6, 156.3, 121.9, 126.3 and 140.5 corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8 & C_{11}, C_9 & C_{10}, , C_{12}, C_{13} C_{14} & C_{18}, C_{15} & C_{17} and C_{16}.

Table 1.10: The ^{31}P NMR (161.89MHz) spectra of N-((6 - (4-chlorophenoxy) / (4-bromophenoxy) / (4-nitrophenoxy) - 6 - oxido - 4, 8-dihyro - 1H - [1, 3, 2] dioxaphophepino [5, 6-d] imidazole-1-yl-) methyl) morpholine - 4 – carboxamide / 4-methyl piperazine - 1 – carboxamide (11a, 11c, 11d, 11f, 11g and 11i) (δ_{PPM}):

COMP	R	X	^{31}P-NMR(DMSO-d_6)(δ $_{PPM}$)
11a	Cl	O	-7.30 and -11.10
11c	Cl	N-CH_3	-7.50
11d	Br	O	-7.70 and -11.40
11f	Br	O	-7.80
11g	NO_2	O	-6.90 and -10.80
11i	NO_2	N-CH_3	-7.20

Table 1.11: Pysical and Analytical data of N-((6 - (4-chlorophenoxy) / (4-bromophenoxy) / (4-nitrophenoxy) - 6 - oxido - 4, 8-dihyro - 1H - [1, 3, 2] dioxaphophepino [5, 6-d] imidazole-1-yl-) methyl) morpholine - 4 – carboxamide / piperidine - 1 – carboxamide / 4-methyl piperazine - 1 – carboxamide 11(a-i):

COMP	MOLECULAR FORMULA	MP(^{0}C)	YIELD (%)	ELEMENTAL ANALYSS(%)	
				FOUND	CALC
11a	$C_{17}H_{20}ClN_4O_6P$	152-155	70	C 45.31, H 4.05, Cl 7.21, N 12.05, P 6.30.	C 46.11, H 4.55, Cl 8.01, N 12.65, P 7.00.
11b	$C_{18}H_{22}ClN_4O_5P$	133-136	67	C 48.24, H 4.53, Cl 7.24, N 12.11, P 6.33.	C 49.04, H 5.03, Cl 8.04, N 12.71, P 7.03.
11c	$C_{18}H_{23}ClN_5O_5P$	172-175	65	C 46.63, H 4.59, Cl 6.98, N 14.76, P 6.09.	C 47.43, H 5.09, Cl 7.78, N 15.36, P 6.79.
11d	$C_{17}H_{20}BrN_4O_6P$	146-149	75	C 49.11, H 3.64, Br 15.80, N 10.90, P 5.66.	C 49.91, H 4.14, Br 16.40, N 11.50, P 6.36.
11e	$C_{18}H_{22}BrN_4O_5P$	165-168	70	C 43.75, H 4.07, Br 587, N 10.95, P 5.68.	C 44.55, H 4.57, Br 16.47, N 11.55, P 6.38.
11f	$C_{18}H_{23}BrN_5O_5P$	189-192	68	C 42.41, H 4.13, Br 15.37, N 13.40, P 5.49.	C 43.21, H 4.63, Br 15.97, N 14.00, P 6.19.
11g	$C_{17}H_{20}N_5O_8P$	180-183	65	C 44.24, H 3.95, N 14.85, P 6.13.	C 45.04, H 4.45, N 15.45, P 6.83.
11h	$C_{18}H_{22}N_5O_7P$	177-180	60	C 47.10, H 4.41, N 14.92, P 6.16.	C 47.90, H 4.91, N 15.52, P 6.86.
11i	$C_{18}H_{23}N_6O_7P$	206-209	68	C 45.55, H 4.47, N 17.42, P 5.94.	C 46.35, H 4.97, N 18.02, P 6.64.

Biological activity

The antimicrobial activity [16] of these newly synthesized compounds was performed according to disc diffusion method, as recommended by the National Committee for Clinical Laboratory. The synthesised compounds were used at the concentration of 250µg/ml DMF as a solvent [17].

Anti-bacterial activity

The antibacterial activity of Imidazole Ureas / Carboxamides containing Dioxaphospholanes **7(a-l)** and **11(a-i)** were screened against the ***Staphylococcus aureus*** and ***Bacillus cerus*** (gram positive) and ***Escherichia coli, Pseudomonasaeruginosa*** (gram negative) organisms. Most of the compounds exhibited good antibacterial

activity against both bacteria. The presence of nitro **(7j, 7k)** and **(11g, 11i)**, chloro **(7c, 7d)** and **(11a, 11c)** and bromo **(7h, 11d)** were showed more activity than other substituted compounds. Here Amoxicillin is tested as reference compound to compare the activity. The anti-bacterial activity was shown in the **Table 1.12**

Table I.12: Anti-bacterial activity (Diameter zone of Inhibition in mm) of compounds of 7(a-l) and 11(a-i) (250 µg/ml):

S.NO	**COMP NO**	**Zone of inhibition(mm)**			
		Staphylococcus aureus **NCCS 2079 250 (µg/disc)**	***Bacillus cereus*** **NCCS 2106 250(µg/disc)**	***Escherichia coli*** **NCCS 2065 250(µg/dis)**	***Pseudomonas aeruginosa*** **NCCS 2200 250 (µg/ disc)**
1	7a	12	16	15	14
2	7b	13	17	16	15
3	7c	15	19	18	17
4	7d	16	20	19	18
5	7e	09	13	12	11
6	7f	10	14	13	12
7	7g	12	16	15	14
13	11a	15	19	18	17
14	11b	11	15	14	13
15	11c	14	18	17	16
16	11d	12	16	15	14
17	11e	09	13	12	11
18	11f	10	14	13	12
19	11g	16	20	19	18
20	11h	13	17	16	15
21	11i	14	18	17	16
Amoxiciilin		21	27	24	22

Anti-fungal activity

Antifungal activity of Imidazole Ureas / Carboxamides containing Dioxaphospholanes **7(a-l)** and **11(a-i)** were screened against ***Aspergillus niger*** and ***Candida albicans***. Most of the compounds exhibit good antifungal activity against both fungai. Most of the compounds exhibit good antifungal activity against both fungai. The presence of nitro **(7j,7k)** and **(11g, 11i)** chloro **(7c, 7d)** and **(11a, 11c)** and bromo **(7h, 11d)** were showed more activity than other substituted compounds. Here Ketoconazole is tested as reference compound to compare the activity. The anti-fungalactivity was shown in the **Table 1.13.**

Table I.13: Anti-bacterial activity (Diameter zone of Inhibition in mm) of compounds of 7(a-l) and 11(a-i) (250 µg/ml):

S.NO	COMP NO	Zone of inhibition(mm)	
		Aspergillus niger NCCS 1196 250(µg/disc)	*Candida albicans* NCCS 3471 250(µg/disc)
1	7a	09	07
2	7b	10	08
3	7c	12	10
4	7d	16	14
5	7e	08	06
6	7f	10	08
7	7g	12	10
8	7h	14	12
9	7i	13	11
10	7j	15	13
11	7k	17	15
12	7l	19	17
13	11a	17	15
14	11b	12	10
15	11c	15	13
16	11d	14	12
17	11e	09	07
18	11f	12	10
19	11g	20	18
20	11h	16	14
21	11i	18	16
Ketoconazole		22	25

IV. Conclusions

The newly synthesized compounds Imidazole Ureas / Carboxamides containing Dioxaphospholanes derivatives 7(a-l) and 11(a-i) were found to be active in the study of anti-bacterial and anti-fungal activity. It can be concluded that this class of compounds certainly holds great promise towards the pursuit to discover novel classes of antimicrobial agents.

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