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Synthesis Characterization And Antimicrobial Activity Of 6-Oxido-1- ((5 -5- (5 -Pyridine-3-Yl)- 1H-Terazol -1- Yl) - 1,3,4 - Thiadiazol -2- Yl)Ethyl)- 4,8- Dihydro-1H-[1,3,2] Dioxa Phosphepino [5,6-C] Pyrazol-6-Yl) Carbamates

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Abstract: *The newly synthesized Cyclopropyl /cyclohexyl /terahydro - 2H - pyran - 4 - yl / tetrahydro - 2H - thiopyran - 4 -yl / perfluorophenyl (6 - oxido -1- ((5 -5 - (5 -pyridine - 3 - yl) -1H-tetrazol - 1 - yl) -1,3,4 - thiadiazol - 2 - yl)methyl) - 4,8 - dihydro - 1H - [1,3,2]dioxaphosphepino[5,6 - c]pyrazol - 6 -yl)carbamates(**7a-e**) were obtained by condensation reaction of substituted dichlorophosphoryl carbamates **(6a - e)** and 1 - ((5 - (5 - (pyridine - 3 - y)l - 1H - tetrazol - 1 - yl) - 1,3,4 - thiadiazol- 2-yl)methyl) - 1H-pyrazole - 4,5 - diyl)dimethanol**(5).** The synthon **(5)** was prepaired by deprotection of 6,6 - dimethyl -1 - ((5 - (5 - (pyridine -3 - y)l - 1H- tetrazol - 1 - yl) -1,3,4 - thiadiazol - 2 - yl) methyl - 4,8-dihydro - 1H - [1,3]dioxepino[5,6 - c]pyrazole **(4).**Which in turn was obtained by treatment of 5 - ((6,6 - dimethyl - 4,8-dihydro - 1H - [1, 3] dioxepino [5, 6 - c] pyrazol -1 -yl) methyl) - N - (pyridine - 3 - yl methylene) - 1, 3, 4 - thiadiazol - 2 - amine **(3)** with $POCl_3$ on NaN_3 / THF conditions under the temperature 100^oC The synthon **(3)** was obtained by condensation reaction between nicotinaldehyde **(2)** and 5 - ((6, 6 - dimethyl - 4, 8 - dihydro - 1H - [1, 3]dioxepino [5, 6 - c] pyrazol - 1 - yl) methyl - 1, 3, 4 - thiadiazol -2 - amine **(1)**. The products were characterized by spectral analysis (IR, ^{1}H- NMR, ^{13}C- NMR, ^{31}P- NMR and elemental analysis). The newly synthesized compounds were subjected to various biological activities viz., antimicrobial.*

Key Words: *Antibacterial; Antifungal; deprotection; dichloro phosphoryl carbamates; Pyrazole.*

I. Introduction

Carbamates of hetero cyclic compounds are important intermediates in the synthesis of compounds in pharmaceuitical, medicinal, agrochemical and polymer chemistry, which possess biologically potent properties such as inhibitor of HIV, anti convulsants, anti bacterials, antiepileptics and enzyme inhibitors [**1-3]**.

Organo phosphorus compounds consisting with 1, 3, 4- Thiadiazole are versatile pharmacophores. These widely used as diuretic agents, CNS depressant, hypoglycemic agent, anti-inflammatory agent and anti microbial agent [**4-8]**.

1H- terazole and its derivatives are associated with a variety biological activities such as anti fungal, anti nociceptive, anti convulsant, anti diabetic, cyclo oxygenase inhibitors,

hypo glycaemic, anti bacterial and anti inflammatory [**9-11]**.

In support of our study pyrazoles and derivatives function as dyestuff, catalyst, polymerizing agents, drugs , herbicides and fungicides [**12**].they also possess various pharmacological activities such as anti-fungal activity [**13**], monoamineoxidase (MAO) inhibitory activity [**14,15**], antiparkinson [**16**], anticonvulsant[**17**]. Pyrazole derivatives are valuable vasodialating and vasoconstructing drugs.

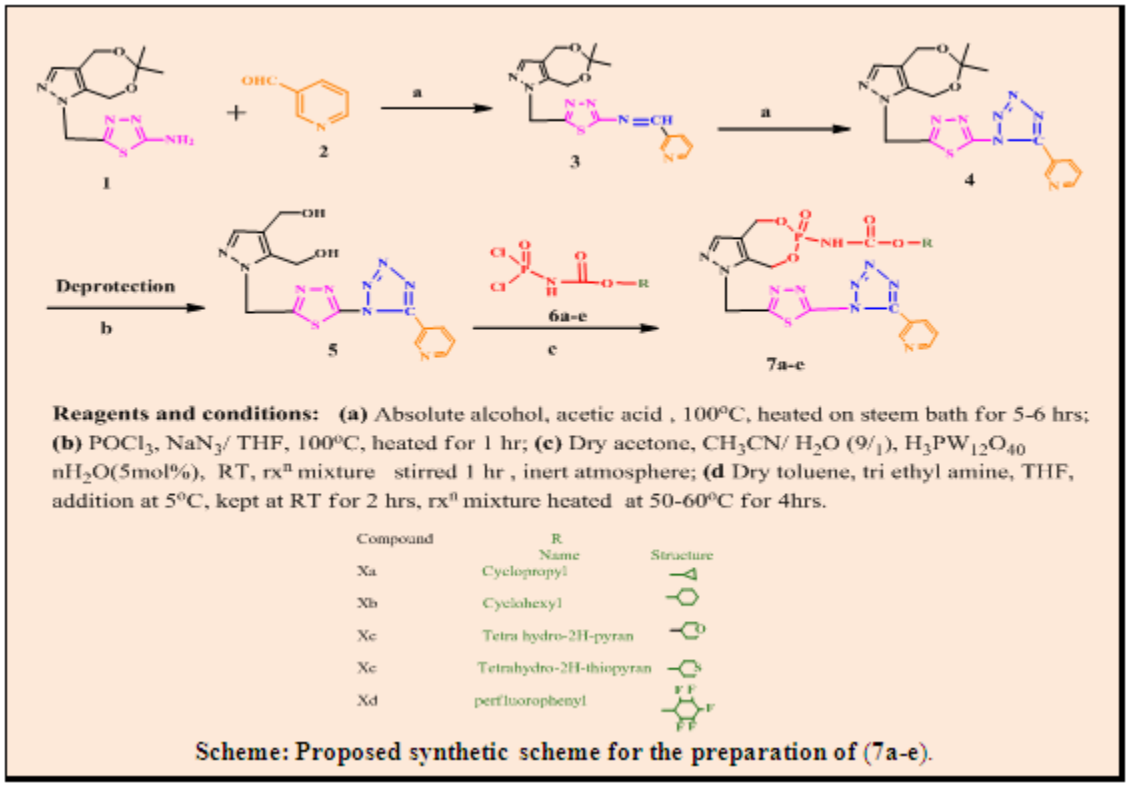
In view of the numerous commercial applications of organophosphorus compounds, we synthesized dichloro phosphoryl carbamates derivatives possesing Pyrazole moiety besides Azetidin-2-one, 1H- terazole and Thiazolidinone derivatives, also they screening for possible biological and pharmacological activities.

II. Experimental Section

Meterials And Methods

All the chemicals used in the present investigation were purchased from Sigma-Aldrich Chemicals company, Inc. USA. And used without further purification. TLC was performed on aluminum sheet of silica gel $60F_{254}$, E-Merk, Germany using iodine as visualizing agent. Melting point was determined in open capillary tubes on Mel-Temp apparatus and is 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 H^1 and C^{13}-NMR spectra were recorded on a Varian XL-300 spectrometer operating at 400MHz for H^1-NMR and 75 MHz for C^{13}-NMR. P^{31}-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 (H^1 and C^{13}-NMR) and 85% H_3PO_4 (P^{31}-NMR). Mass spectral data was recorded on FAB-MS instrument at 70ev with direct inlet system. Elemental analysis was recorded on a Carlo Erba 1108 elemental Analyzer, Central Drug Research Institute, Lucknow, India.

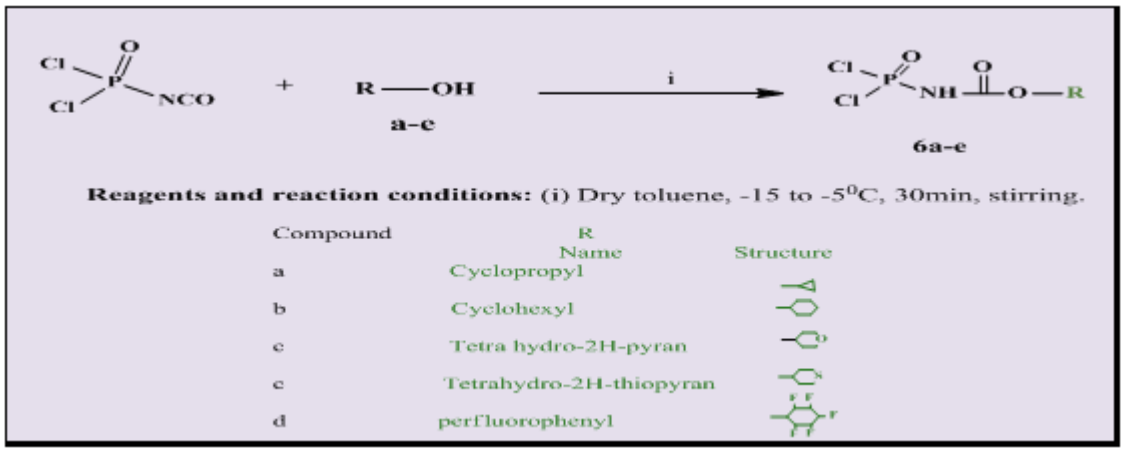


Reagents and conditions: **(a)** Absolute alcohol, acetic acid , 100°C, heated on steem bath for 5-6 hrs; **(b)** $POCl_3$, NaN_3/ THF, 100°C, heated for 1 hr; **(c)** Dry acetone, CH_3CN/ H_2O (9/1), $H_3PW_{12}O_{40}$ nH_2O(5mol%), RT, rx^n mixture stirred 1 hr , inert atmosphere; **(d** Dry toluene, tri ethyl amine, THF, addition at 5°C, kept at RT for 2 hrs, rx^n mixture heated at 50-60°C for 4hrs.

Compound	R Name	Structure
Xa	Cyclopropyl	
Xb	Cyclohexyl	
Xc	Tetra hydro-2H-pyran	
Xc	Tetrahydro-2H-thiopyran	
Xd	perfluorophenyl	

Scheme: Proposed synthetic scheme for the preparation of (7a-e).

Preparation of Intermediates: [**18,19**]



Reagents and reaction conditions: (i) Dry toluene, -15 to -5°C, 30min, stirring.

Compound	R Name	Structure
a	Cyclopropyl	
b	Cyclohexyl	
c	Tetra hydro-2H-pyran	
c	Tetrahydro-2H-thiopyran	
d	perfluorophenyl	

A solution of cyclopropyl alcohol (0.51g, 0.004mole) in dry toluene (25ml) was added drop wise to Phosphorisocyanatidic dichloride (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^{0}c for 30 minutes. Later the temperature of the mixture was raised to room temperature, with stirring for 30 minutes. Dichlorophosphorylcarbamate being insoluble in toluene was separated out .It was collected by filtration and dried under reduced pressure

Similar treatment of Cyclohexyl alcohol/ Terahydro-2H-pyran-4-yl alcohol / Tetrahydro-2H-thiopyran-4-ylalcohol/ 2,3,4,5,6-pentaflurophenol with Phosphorisocyanatidic dichloride in presence of dry toluene at -15 to -5^{0}c for 30 minutes offered the respective derivatives of Cyclohexyl/ Terahydro-2H-pyran-4-yl/ Tetrahydro-2H-thiopyran-4-yl/.Perflurophenyl dichlorophosphoryl carbamates.

The structure of newly synthesized dichlorophosphoryl carbamates **(6a-e)** were established by IR, ^{1}HNMR and elemental analysis.

III. Result And Discussion

1. Synthesis of 5-((6,6-dimethyl-4,8-dihydro-1H-[1,3]dioxepino[5,6-c]pyrazol-1-yl)methyl)-N-(pyridin-3-ylmethylene)-1,3,4-thiadiazol-2-amine (3):[20]

The synthesis and characterization of 5-((6,6-dimethyl-4,8-dihydro-1H-[1,3] dioxepino[5,6-c] pyrazol-1-yl)methyl)-1,3,4-thiadiazol-2-amine **(1)**was reported in literature[**21,22**]

Equimolar quantity of 5-**((**6,6-dimethyl-4,8-dihydro-1H-[1,3]dioxepino [5,6-c]pyrazol-1-yl**)** methyl**)** -1,3,4-thiazol-2-amine **(1)** and Nicotinaldehydes **(2)** were dissolved in absolute alcohol, to this one a drop of acetic acid was added, then heated on a steam bath for 5-6 h at 100^{o}C. After standing for 24 h at room temperature. The progress of the reaction was monitored by TLC using cyclohexane and ethyl acetate (9:1) solvent mixture as an eluent. At the end of reaction product 5-((6,6-dimethyl - 4,8 - dihydro -1H-[1,3] dioxepino[5,6-c]pyrazol-1-yl)methyl)-N-(pyridin-3-ylmethylene)-1,3,4-thiadiazol-2-amine **(3)** was dried and recrystalised from warm absolute alcohol, mp136-138^{0}C and yield 65. %. The structure of **(3)** was established by IR, ^{1}H-NMR and elemental analysis.

2. Synthesis of 6,6-dimethyl-1-((5-(5-(pyridin-3-y)l-1H-tetrazol-1-yl)-1,3,4-thiadiazol-2-yl)methyl-4,8-dihydro-1H-[1,3]dioxepino[5,6-c]pyrazole(4)[23]

Schiff base (**3**) (0.004mol) and PCl_5 (0.004mol) was heated at 100^{o}C for 1h. When the evolution of HCl ceased, excess of PCl_3 was removed under reduced pressure and the residual imidoyl chloride was treated with an ice -cold solution of Sodium azide (0.0075 mol) and excess of Sodium acetate in water (25mol) and acetone (30 ml) with stirring . Stirring was continued for overnight. 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 acetone was removed under reduced pressure. The remaining aqueous portion was extracted with Chloroform and dried. The yield of 6,6-dimethyl-1-((5-(5-(pyridin-3-y)l-1H-tetrazol-1-yl)-1,3,4-thiadiazol-2-yl)methyl-4,8-dihydro-1H-[1,3]dioxepino [5,6-c]pyrazole **(4)** was 65 % with mp 144-149^{o}C.

3. Synthesis of 1 ((5-(5- (pyridine-3-yl) l-1H-tetrazol-1-yl) -1, 3, 4-thiadiazol-2-yl) -methyl) 1H-pyrazole-4, 5-diyl) dimethanol (5)

The isopropylidenation of 1, 2-diols was carried out by a procedure as reported in the literature **[24]**. A suspension of the 6,6-dimethyl-1-((5-(5-(pyridin-3-y)l-1H-tetrazol-1-yl)-1,3,4-thiadiazol-2-yl)methyl-4,8-dihydro-1H-[1,3]dioxepino[5,6-c]pyrazole **(4)** (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 mobilephase. After completion of the reaction, the solvent was removed under reduced pressure. The residue was extracted with dichloromethane (3×20 ml) and water, 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 m p of **(5)** was 167-169^{0}C with yield of...%. The structure of **(5)** was established by IR, ^{1}H-NMR and elemental analysis.

4. Synthesis of Cyclopropyl/cyclohexyl/ terahydro - 2H - pyran - 4 - yl/tetrahydro - 2H-thiopyran -4 - yl/ perfluorophenyl(6-oxido-1-((5-5-(5-pyridin-3-yl)-1H- tetrazol -1-yl)-1,3,4-thiadiazol-2-yl)methyl)-4,8-dihydro-1H-[1,3,2]dioxaphosphepino[5,6-c] pyrazol -6-yl)carbamates(7a-e)

A solution of Cyclopropyl dichlorophosphoryl carbamate **(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 of 1 ((5-(5- (pyridine-3-yl) l-1H-tetrazol-1-yl) -1, 3, 4-thiadiazol-2-yl) -methyl) 1H-pyrazole-4, 5-diyl) dimethanol **(5)** (0.002mole) and triethylamine (0.004mole) in 30 ml of dry toluene and 10ml of tetrahydrofuran at 5^{0}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 recrystalized from aqueous 2-propanol to get pure compound of cyclopropyl(6-oxido-1-((5-(5-(pyridin-3-yl)1H-tetrazol-1-yl)-1,3,4-thiadiazol-2-yl)methyl)-4,8 - dihydro - 1H - [1,3,2]dioxaphosphepino [5,6 - c] pyrazol - 6 - yl)carbamate **(7a)**, yield 178-180% and mp 70^{O}C.

The similar procedure was adopted to synthesize **7b-e** by the reaction between **(5)**with Cyclohexyl alcohol**(6b)**Terahydro-2H-pyran-4-yl alcohol **(6c)** Tetrahydro-2H-thiopyran-4-yl alcohol**(6d)** 2,3,4,5,6-pentaflurophenol**(6e)** respectively. The Structures of **7a-e** were established by IR, ^{1}H-NMR, ^{13}C-NMR, and elemental analysis.

Spectral, Physical and analytical data for the compounds 7a-e:

Table .1: IR (KBr)) spectral data of Cyclopropyl / cyclohexyl / terahydro-2H -pyran -4-yl/tetrahydro-2H-thiopyran-4-yl/ perfluorophenyl(6- oxido- 1- ((5 - (5 -prydin-3-yl)-1H-Terazol -1- yl) - 1,3,4 - thiadiazol -2-yl) methyl)- 4,8- dihydro-1H-[1,3,2]dioxaphosphepino [5,6-c] pyrazol-6-yl)carbamates (7a-e)

COMPOUND (7)	R	$\bar{\nu}/\delta$, cm^{-1}						
		P-NH	P=O	Azide	Carbamate carbonyl	Pyrazole	Terazolre	P-O-C
7a	Cyclopropyl	3325	1240	2120	1680	1375-1487	1157	1190
7b	Cyclohexyl	3323	1245	2130	1675	1370-1485	1156	1185
7c	Tetrahydro -2H-pyran	3320	1248	2127	1673	1375-1490	1145	1191
7d	Tetrahydro-2H-thiopyran	3328	1243	2119	1670	1380-1495	1155	1194
7	Perfluorophenyl	3315	1230	2125	1690	1385-1495	1160	1197

Table.2:^{1}H-NMR spectral data of Cyclopropyl / cyclohexyl / terahydro-2H -pyran -4- yl/tetrahydro-2H-thiopyran-4-yl/ perfluorophenyl(6- oxido-1- ((5 - (5 -prydin-3-yl)- 1H-Terazol -1- yl) - 1,3,4 - thiadiazol -2-yl)ethyl)- 4,8- dihydro-1H-1,3,2] dioxa phosphepino [5,6-c] pyrazol-6-yl)Carbamates (7a-e):

Comp	R	^{1}H – NMR (DMSO – d_6)(δ_{ppm})
7a	Cyclopropyl	0.34- 0.58 (m, 4H, –CH_2 – of cyclopropyl) 2.69(m,1H,-CH- of cyclopropyl ring attached to carbamate moiety), 4.99(s,2H,–CH2- flanked between pyrazole and 1,3,4-thiadiazole), 5.29 (s, 4H, two CH_2 group of acetal), , 7.30 (s, 1H, of pyrazole ring) 7.57-9.24 (m, 4H, CH of pyridine) and 8.0(s,1H,-NH- of carbamate moiety).
7b	Cyclohexyl	1.47 –1.55 (m, 10H, CH_2 of cyclohexyl),3.91 (m, 1H, -CH- of cyclohexyl attached to carbamate moiety) ,4.99(s,2H,–CH_2- flanked between pyrazole and 1,3,4-thiadiazole), 5.29 (s, 4H, two CH_2 group of acetal), 7.30 (s, 1H, of pyrazole ring) 7.57-9.24 (m, 4H, -CH- of pyridine) and 8.10(s,1H,-NH- of carbamate moiety.
7c	Tetrahydro -2H-pyran	1.97 - 1.72 (m, 4H, -CH_2- of tetrahydro-2H-pyran), 3.65 (t, 4H, CH_2-O-CH_2 of tetrahydro-2H-pyran, J=3.60Hz H-2^{I} and H-3^{I}),4.07 (m, 1H, -CH - of tetrahydro-2H-pyran attached to carbamate moiety) , 4.99(s,2H,-CH_2- flanked between pyrazole and 1,3,4-thiadiazole),5.29 (s, 4H, two CH_2 group of acetal), 7.30 (s, 1H, of pyrazole ring) 7.57-9.24 (m, 4H, CH of pyridine) and 8.15(s,1H,-NH- of carbamate moiety).
7d	Tetrahydro -2H-thiopyran	2.06 - 1.81 (m, 4H, CH_2 of terahydro-2H-thiopyran),2.57 (t, 4H, CH_2-S-CH_2 of tetrahydro-2H-thiopyran, J=2.52Hz H-2^{I} and H-3^{I}),4.17 (m, 1H, -CH-oftetrahydro-2H- thiopyran attached to carbamate),4.99(s,2H,-CH_2- flanked between pyrazole and 1,3,4-thiadiazole), 5.29 (s, 4H, two CH_2 group of acetal), 7.30 (s, 1H, of pyrazole ring) 7.57-9.24 (m, 4H, CH of pyridine) and 8.07(s,1H,-NH- of carbamate moiety).
7e	Perfluorophenyl	4.99(s, 2H,-CH_2- flanked between pyrazole and 1, 3,4-thiadiazole), 5.29 (s, 4H, two -CH_2- group of acetal),7.30 (s, 1H, of pyrazole ring) 7357-9.24 (m, 4H, -CH- of pyridine) and 8.15(s,1H,-NH- of carbamate moiety).

Table.3:^{13}C-NMR spectral data of Cyclopropyl / cyclohexyl / terahydro-2H -pyran -4- yl/tetrahydro-2H-thiopyran-4-yl/ perfluorophenyl(6- oxido-1- ((5 - (5 -prydin-3-yl)- 1H-Terazol -1- yl) - 1,3,4 - thiadiazol -2-yl)ethyl)- 4,8- dihydro-1H-1,3,2] dioxa phosphepino [5,6-c] pyrazol-6-yl)Carbamates (7a-e):

Comp	structure	^{13}C NMR (DMSO – d_6)(δ_{ppm})
7a	Cyclopropyl	135.2 , 118.0 ,141.0 , 62.2 , 61.1 , 47.6 , 168.0 , 162.7 , 163.5 , 132.9 , 135.4 , 124.0 , 147.9 , 155.1, 157.6, 43.0 and 3.7 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_{18}, C_{15} , and C_{17}&C_{18}.
7b	Cyclohexyl	135.2 , 118.0 ,141.0 , 62.2 , 61.1 , 47.6 , 168.0 , 162.7 , 163.5 , 132.9 , 135.4,124.0, 147.9 , 155.1, 157.6, 76.5, 30.82, 24.1 and 25.7corresponding 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_{18}, C_{15} , C_{16} , C_{17}&C_{21}, C_{18}&C_{20} and C_{19}.
7c	Tetrahydro -2H-pyran	135.2 , 118.0 ,141.0 , 62.2 , 61.1 , 47.6 , 168.0 , 162.7 , 163.5 , 132.9 , 135.4 , 124.0 , 147.9 , 155.1, 157.6, 72.2, 33.4 and 63.2corresponding 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_{16}, C_{17}&C_{20} and C_{18}&C_{19}.
7d	Tetrahydro -2H-thiopyran	135.2 , 118.0 ,141.0 , 62.2 , 61.1 , 47.6 , 168.0 , 162.7 , 163.5 , 132.9 , 135.4 , 124.0 , 147.9 , 155.1, 157.6, 69.3, 32.2 and 25.5 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_{16}, C_{17}&C_{20} and C_{18}&C_{19}.
7e	Perfluorophenyl	135.2 , 118.0 ,141.0 , 62.2 , 61.1 , 47.6 , 168.0 , 162.7 , 163.5 , 132.9 , 135.4 , 124.0 , 147.9 , 155.1, 157.6, 142.0, 139.3, 142.4 and 140.1 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_{16} , C_{17}&C_{21}, C_{18}&C_{20} and C_{19}.

Table.4:^{31}P-NMR spectra spectral data of Cyclopropyl / cyclohexyl / terahydro-2H -pyran -4-yl/tetrahydro-2H-thiopyran-4-yl/ perfluorophenyl(6- oxido-1- ((5 - (5 -prydin-3-yl)- 1H-Terazol -1- yl) - 1,3,4 - thiadiazol -2- yl)ethyl)- 4,8- dihydro-1H-1,3,2] dioxa phosphepino [5,6-c] pyrazol-6-yl)Carbamates (7a-e):

COMP (7)	STRUCTURE	^{31}P – NMR (DMSO – d_6) (δ_{PPM})
7a	Cyclopropyl	-9.30, 0.70
7b	Cyclohexyl	-10.70, 0.60
7c	Tetrahydro-2H-pyran	-9.60, 075
7d	Tetrahydro-2H-thiopyran	-9.65, 0.65
7e	Perfluorophenyl	-8.90, 0.80

Table.5 Physical and Analytical data of compounds synthesized as per the scheme

COMPOUND	MOLECULAR FORMULA	mp (^{O}C)	YIELD (%)	ELEMENTAL ANALYSIS	
				FOUND	CALCULATED
3	$C_{17}H_{18}N_6O_2S$	136-138^{O}C	65%	C:54.62% H:4.40% N: 22.09%. S:8.46%	C:55.12% H:4.90% N: 22.69%. S:8.66%
4	$C_{17}H_{17}N_9O_2S$	144-146 ^{O}C	65%	C:47.83% H:4.11% N: 30.04%. S:7.59%	C:49.63% H:4.61% N: 30.64%. S:7.79%
9	$C_{14}H_{13}N_9O_2S$	167-169 ^{O}C	70%	C:4.48% H :3.03% N:33.34% S:8.43%	C:45.28% H :3.53% N:33.94% S:8.63%
7a	$C_{18}H_{17}N_{10}O_5PS$	178-180 ^{O}C	70%	C:41.06% H :2.82% N :26.55% P : 5.30% S:6.01%	C:41.86% H :3.32% N :27.15% P : 6.00% S:6.21%
7b	$C_{21}H_{23}N_{10}O_5PS$	157-159 ^{O}C	60%	C :44.36% H :3.65% N :24.48% P : 4.85% S:5.54%	C :45.16% H :4.15% N :25.08% P : 5.55% S:5.74%
7c	$C_{20}H_{21}N_{10}O_6PS$	173-175 ^{O}C	69%	C:42.06% H :3.28% N :24.39% P : 4.93% S:5.52%	C:42.86% H :3.78% N :24.99% P : 5.53% S:5.72%
7d	$C_{20}H_{21}N_{10}O_5PS_2$	165-167 ^{O}C	65%	C:40.86% H :3.17% N :23.69% P : 4.77% S:10.92%	C:41.66% H :3.67% N :24.29% P : 5.37% S:11.12%
7e	$C_{21}H_{12}F_5N_{10}O_5PS$	204-206 ^{O}C	75%	C :38.52% H :1.38% F: 13.99% N :21.20% P : 4.12% S:4.79%	C :39.32% H :1.88% F: 14.79% N :21.80% P : 4.82% S:4.99%

Biological activity:

The antimicrobial activity [**25**] of chemical compound is influenced by physical and biological characteristics [**26**].It has been well established that physiological activity is a function of the chemical structure of compound [**27**].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[**28**].

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

Antibacterial activity:

Organo phosphorus Pyrazole Carbamates containing 1H-terazoles (7a-e) reported in respectively were offered average antimicrobial activity against the Staphylococcus aureus NCCS 2079, BacillusCerus NCCS 2106, Escherichia coli NCCS 2065 and Pseudomonas aeruginosa NCCS 2200 at the concentration of

250µg/disc. Organo phosphorus pyazole carbamate of Tetrahydro-2H-pyran (**7c,)** and Tetrahydro-2H-thiopyran (**7d)** were exhibited more activity than other compounds of the series.

Antibacterial activity of Cyclopropyl / cyclohexyl / terahydro-2H -pyran -4- yl/tetrahydro-2H-thiopyran-4-yl/ perfluorophenyl(6- oxido-1- ((5 - (5 -prydin-3-yl)- 1H-Terazol -1- yl) - 1,3,4 - thiadiazol -2- yl)ethyl)-4,8- dihydro-1H-1,3,2] dioxa phosphepino [5,6-c] pyrazol-6-yl)Carbamates (7a-e):
Antifungal activity

COMPOUND	R	Zone of inhibition (mm)			
		Staphylococus aureus NCCS2079 250(µg/ml)	Bacillus Cerus NCCS2106 250(µg/ml	Escherichia Coli NCCS2065 250(µg/ml)	Pseudomonas aeruginosa NCCS2200 250(µg/ml)
7a	Cyclopropyl	10	13	12	11
7b	Cyclohexyl	13	16	15	14
7c	Tetrahydro-2H-pyran	17	20	19	18
7d	Tetrahydro-2H-thiopyran	15	18	17	16
7e	Perfluorophenyl	12	15	14	13
Amoxicillin		21	27	24	22

Organo phosphorus Pyrazole Carbamates containing 1H-terazoles **(7a-e)** as synthesized in **section** respectively of were offered average antifungal activity against the Aspergillus niger NCCS1196 and Candida albicans NCCS 3471 at the concentration of 250µg/disc. Organo phosphorus pyrazole carbamate system consisting of penta fluoro benzene (**7e**,**)** Tetrahydro-2H-thiopyran (**7d) and** Tetrahydro-2H-pyran(**7c**,**)** were exhibited more activity than other compounds of the series

Antifungal activity of Cyclopropyl / cyclohexyl / terahydro-2H -pyran -4- yl/tetrahydro-2H-thiopyran-4-yl/ perfluorophenyl(6- oxido-1- ((5 - (5 -prydin-3-yl)- 1H-Terazol -1- yl) - 1,3,4 - thiadiazol -2- yl)ethyl)-4,8- dihydro-1H-1,3,2] dioxa phosphepino [5,6-c] pyrazol-6-yl)Carbamates (7a-e):

COMPOUND	R	Zone of inhibition (mm)	
		Aspergillus niger NCCS 1196 250(µg/ml)	Canadida albicans NCCS 3471 250(µg/ml)
7a	Cyclopropyl	12	15
7b	Cyclohexyl	14	17
7c	Tetrahydro-2H-pyran	15	18
7d	Tetrahydro-2H-thiopyran	16	19
7e	Perfluorophenyl	17	20
Ketoconazole		22	25

IV. Conclusions

The newly synthesized compounds of Cyclopropyl / cyclohexyl / terahydro-2H -pyran -4-yl/tetrahydro-2H-thiopyran-4-yl/ perfluorophenyl(6- oxido-1- ((5 - (5 -prydin-3-yl)- 1H-Terazol -1- yl) - 1,3,4 - thiadiazol -2- yl)ethyl)- 4,8- dihydro-1H-1,3,2] dioxa phosphepino [5,6-c] pyrazol-6-yl)Carbamates (**7a-e**) 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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