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SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL ACTIVITY OF SOME NEW ORGANOPHOSPHORUS COMPOUNDS

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Abstract

A series of biologically active organophosphorus compounds have been synthesized by the reactions of Phenylphosphonic dichloride/ 4-Chlorophenyl dichlorophosphate *with 5-substituted -2-mercapto-1,3,4-oxadiazole ligands. The compounds have been characterized on the basis of elemental analyses and spectral (IR, ^{1}H NMR ^{31}P NMR) data. All the compounds were screened for their antimicrobial activity .They were found to possess significant anti-microbial activity.*

***Keywords**: Organophosphorus, oxadiazole, IR, NMR, anti-microbial activity.*

1. Introduction

Heterocyclic compounds containing the five-membered nucleus possess a diversity of useful biological effects. The 1,3,4-oxadiazole derivatives are useful targets in the search for antimicrobial as they have been associated with many types of biological properties such as anti-inflammatory(Malladi et al., 2014; Amir and Kumar, 2007; Narayana et al., 2005; Omar et al. 1996) antibacterial, antifungal activities(Ali and Yar, 2007; Zarghi et al., 2005; Kumar, 2011) and inhibit HIV replication(Tan et al., 2006). 2, 5-Disubstituted-1,3,4-oxadiazole were disclosed as a broad-spectrum insecticide and acaricide having potential agriculture use(Lanza, 1998). Some examples of compounds containing the 1,3,4-oxadiazole unit currently used in clinical medicine are Raltegravir as an antiretroviral drug and Zibotentan as an anticancer agent(C.Shukla et al., 2015). In contrast to traditional pesticides, they mainly control the growth and development process of insects by interfering with chitin biosynthesis (Goankar et al., 2006). On the other hand the chemistry of organophosphorus heterocyclic compounds has always attracted much attention because of their unique potential biological properties. A few recent studies (Sengupta et al., 1998, 2002, 2003) have shown that on the basis of suitable logic organic molecules, incorporating phosphorus may be designed such that they may be less dangerous in use without losing their value as effective pesticides. The

discovery of the mechanism of action (Wang et al., 1998) of organophosphorus compounds made it possible to develop the fundamental principles of the directed synthesis of new substances and to establish the cause of their selective action on an organism. Studies on organophosphorus derivatives could constitute a new and promising field of application in the national economy. The present communication includes the reactions of Phenylphosphonic dichloride/4-Chlorophenyl dichlorophosphate with substituted mercaptooxadiazole ligands. In addition the anti-microbial activities of these newly synthesized organophosphorus compounds against various important bacterial and fungal pathogens were also evaluated.

2. Materials and methods

Melting points of the newly synthesized compounds were determined in open capillary tubes and are uncorrected. FTIR spectra (cm^{-1}) were recorded on a Thermo Nicolet, Avator 370 spectrophotometer by making KBr pellets. ^{1}H NMR and ^{31}P NMR spectra were recorded on a Bruker Avance III 400 MHz spectrometer operating at 400 MHz for ^{1}H and 161.9 MHz for ^{31}P NMR using DMSO -d_6 as solvent .All chemical shifts values were referenced from TMS (^{1}H). All ^{31}P NMR data were taken on similar solutions and referenced to 85% H_3PO_4 (^{31}P, δ ppm). CHN analysis was carried out on a Vario-EL (Elementar-III) model. Homogeneity of the compounds was checked by TLC on silica-gel plates.

The reactions of Phenylphosphonic dichloride/4-Chlorophenyl dichlorophosphate with 5-substituted -2-mercapto-1,3,4-oxadiazole ligands were carried out under inert atmosphere and anhydrous conditions. Special precautions were taken to exclude moisture from the apparatus and the starting materials Phenylphosphonic dichloride / 4-Chlorophenyl dichlorophosphate as reactions were susceptible to hydrolysis. Glass apparatus with interchangeable joints were used throughout the work. All the organic solvents used were of analytical reagent grade. The solvents were purified and dried using the method described in the literature (Chaturvedi, 1995) [19]. Phenylphosphonic dichloride/4-Chlorophenyl dichlorophosphate was procured from Aldrich Chemical Company, Inc. USA and was used without further purification. Substituted benzoic acid hydrazides were synthesized according to method described in the literature (Efimovsky and Rumpt, 1954; Teriunobu, 1969). The details of analysis and physical measurements were the same as reported earlier (Schrader, 1947).

3. Experimental

3.1 General procedure for the synthesis of 5-(phenyl/substituted phenyl)-1,3,4-oxadiazole-2-thiol

5-(phenyl/substituted phenyl)-1,3,4-oxadiazole-2-thiol were prepared by the reported method (Maff et al 1959). To a solution containing 400 mL of 95% ethanol and (0.1 mol, 5.6 g) of potassium hydroxide (dissolved in 15 mL of water), (0.1 mol) of the appropriate hydrazide was added, (0.1 mol ,6.6 mL) of carbon disulfide was added and the mixture was refluxed for 3 h. The solution was concentrated to a small volume and the residue was dissolved in water. A precipitate was obtained by adding the solution to ice containing hydrochloric acid. The solid was filtered off, dried and re-crystallized from ethanol. The IR spectra showed a weak S-H stretching absorption at 2767-2773 cm^{-1}.

3.2 General procedure for the synthesis of organophosphorus compounds (I-XII):

The Organphosphorus compounds were prepared by mixing Phenylphosphonic dichloride/4-Chlorophenyl dichlorophosphate (1 mol) and the appropriate ligand 5-(phenyl/substituted phenyl)-1,3,4-oxadiazole-2-thiol (2 mol) in benzene (30 mL) in presence of pyridine (2 mol) with continuous stirring .Stirring was continued at room temperature over a period of 7-10 h under anhydrous conditions. After completion of reaction, the reaction mixture was put into a beaker containing crushed ice. A solid was obtained. It was collected and re-crystallised from acetone .For the sake of brevity, the details of the individual reactions along the physical characterization are given in Table 1.

3.2.1 S,S-bis(5-phenyl-1,3,4-oxadiazol-2-yl) phenylphosphonodithioate (I) : Mp 208-209°C, IR (KBr,cm^{-1}): 3054 (C–H $_{aro,str.}$), 742 (C-H $_{aro.oop.}$), 1620 (C=N) , 670 (C-S), 1237 (C-O-C $_{asy}$) , 1174 (C-O-C $_{sym}$), 1290 (P=O), 981 (P-$C_{aro.}$), 610 (P-S-C). ^{1}H NMR (DMSO-d_6 ,δ) : 7.41-7.77 (m ,11H, Ar-H), 8.05 (d, 4H, Ar-H). ^{31}P NMR (DMSO-d_6 ,δ): 12.63 . Anal. Found (Calcd)% for $C_{22}H_{15}O_3N_4S_2P$: C, 55.0(55.2); H, 3.0(3.1); N, 11.5(11.7); S, 13.2(13.4).

3.2.2 S,S-bis[5-(3-nitrophenyl)-1,3,4-oxadiazol-2-yl] phenylphosphonodithioate (II): Mp 140-142°C, IR (KBr,cm^{-1}): 3065 (C–H $_{aro,str}$), 725 (C-H $_{aro.oop.}$), 1622 (C=N) , 660 (C-S), 1247 (C-O-C $_{asy}$), 1184 (C-O-C $_{sym}$), 1295 (P=O), 985 (P-$C_{aro.}$), 1570 (NO_2-$C_{aro.asy\ str.}$), 1320 (NO_2-$C_{aro.sym\ str.}$), 612 (P-S-C). ^{1}H NMR (DMSO-d_6 ,δ) : 7.45-7.77 (m ,7H, Ar-H), 8.22-8.44 (m, 4H, Ar-H), 8.65 (s ,2H, Ar-H), ^{31}P NMR (DMSO-d_6 ,δ): 12.65. Anal. Found (Calcd)% for $C_{22}H_{13}O_7N_6S_2P$: C, 46.2 (46.4); H, 2.0(2.2); N, 14.5(14.7); S, 11.0(11.2).

3.2.3 S,S-bis[5-(4-nitrophenyl)-1,3,4-oxadiazol-2-yl] phenylphosphonodithioate (III) : Mp 137-138°C, IR (KBr, cm^{-1}): 3060 (C–H $_{aro,str}$), 782 (C-H $_{aro.oop.}$), 1624 (C=N), 665 (C-S), 1260 (C-O-C $_{asy}$) , 1186 (C-O-C $_{sym}$), 1298 (P=O), 990 (P-$C_{aro.}$), 1565 (NO_2-$C_{aro.asy\ str.}$), 1340 (NO_2-$C_{aro.sy\ str.}$), 614 (P-S-C). ^{1}H NMR (DMSO-d_6 ,δ) : 7.45-7.77 (m, 5H, Ar-H), 8.23-8.32 (m, 4H, Ar-H), ^{31}P NMR (DMSO-d_6, δ): 12.62. Anal. Found (Calcd)% for $C_{22}H_{13}O_7N_6S_2P$: C, 46.2 (46.4); H, 2.0(2.2); N, 14.5(14.7); S, 11.0(11.2).

3.2.4 S,S-bis[5-(4-aminophenyl)-1,3,4-oxadiazol-2-yl] phenylphosphonodithioate (IV) : Mp 173-175°C, IR (KBr,cm^{-1}): 3070 (C–H $_{aro,str}$), 780 (C-H $_{aro.oop.}$), 1623 (C=N), 667 (C-S), 1262 (C-O-C $_{asy}$) , 1190 (C-O-C $_{sym}$), 1300 (P=O), 990 (P-$C_{aro.}$), 3400 ($C_{aro,st}$-.NH_2), 612 (P-S-C). ^{1}H NMR (DMSO-d_6 ,δ) :7.45-7.77 (m, 9H, Ar-H), 6.58 (d, 4H, Ar-H), 6.27(s, 4H,-NH_2); ^{31}P NMR (DMSO-d_6, δ): 12.64. Anal. Found (Calcd)% for $C_{22}H_{17}O_3N_6S_2P$: C, 51.7 (51.9); H, 3.0(3.3); N, 16.4(16.5); S, 12.5(12.6).

3.2.5 S,S-bis[5-(4-hydroxyphenyl)-1,3,4-oxadiazol-2-yl] phenylphosphonodithioate (V) : Mp 132-135°C, IR (KBr,cm^{-1}): 3080 (C–H $_{aro,str}$), 782 (C-H $_{aro.oop.}$), 1626 (C=N), 675 (C-S), 1264 (C-O-C $_{asy}$), 1192 (C-O-C $_{sym}$), 1297 (P=O), 985 (P-$C_{aro.}$), 3400 (C_{aro}-OH_{st}), 618 (P-S-C). ^{1}H NMR (DMSO-d_6 ,δ) :7.45(d, 3H, Ar-H), 7.77-7.96 (m, 6H, Ar-H), 6.86 (d, 4H, Ar-H), 5.35(s, 2H,aro.OH); ^{31}P NMR (DMSO-d_6 ,δ): 12.63 . Anal. Found (Calcd)% for : $C_{22}H_{15}O_5N_4S_2P$: C, 51.7 (51.9); H, 2.7(2.9); N, 10.7(10.9); S, 14.4(14.5).

3.2.6 S,S-bis[5-(2,4-dichlorophenyl)-1,3,4-oxadiazol-2-yl] phenylphosphonodithioate (VI) : Mp 145-147°C, IR (KBr,cm^{-1}): 3085 (C–H $_{aro,str}$), 778 (C-H $_{aro.oop.}$), 1628 (C=N), 678 (C-S), 1265 (C-O-C $_{asy}$) , 1195 (C-O-C $_{sym}$), 1305 (P=O), 992 (P-$C_{aro.}$), 1040 (C-Cl_{ortho}), 1090 (C-Cl_{para}), 618 (P-S-C). ^{1}H NMR (DMSO-d_6 ,δ) : 7.43-7.45 (m, 5H, Ar-H), 7.67-7.77(m, 6H, Ar-H); ^{31}P NMR (DMSO-d_6 ,δ): 12.64. Anal. Found(Calcd)% for $C_{22}H_{11}O_3N_4S_2PCl_4$: C, 42.6 (42.8); H, 1.6(1.7); N, 8.8(9.0); S, 10.2(10.4); Cl, 22.8(23.0).

3.2.7 O-4-chlorophenyl S,S-bis(5-phenyl-1,3,4-oxadiazol-2-yl) phosphorodithioate (VII) : Mp 215-217°C, IR (KBr,cm^{-1}): 3054 (C–H $_{aro,str.}$), 740 (C-H $_{aro.oop.}$), 1622 (C=N), 668 (C-S), 1240 (C-O-C $_{asy}$), 1178 (C-O-C $_{sym}$), 1294 (P=O), 1165 (P-O-$C_{aro.}$), 1190 (C-$Cl_{aro,str)}$, 614 (P-S-C). ^{1}H NMR (DMSO-d_6 ,δ) :6.89 (d, 2H, Ar-H), 7.32-7.51 (m, 8H, Ar-H), 8.05 (d ,4H, Ar-H), ^{31}P NMR (DMSO-d_6 ,δ): -18.28, -6.33. Anal. Found (Calcd)% for $C_{22}H_{14}O_4N_4S_2PCl$: C, 49.7(49.9); H, 2.4(2.6); N, 10.4(10.6); S, 12.0(12.2); Cl,6.5(6.7)

3.2.8 O-4-chlorophenyl S,S-bis[5-(3-nitrophenyl)-1,3,4-oxadiazol-2-yl] phosphorodithioate (VIII) : Mp 160-162°C, IR (KBr,cm^{-1}): 3068 (C–H $_{aro,str}$), 727 (C-H

$_{aro.oop.}$), 1622 (C=N) , 665 (C-S), 1250 (C-O-C $_{asy}$) , 1185 (C-O-C $_{sym}$), 1298 (P=O), 1168 (P-O-$C_{aro.}$), 1572 (NO_2-$C_{aro.asy\ str.}$), 1322 (NO_2-$C_{aro.sy\ str.}$), 620 (P-S-C). ^{1}H NMR (DMSO-d_6 ,δ) : 6.89 (d, 2H, Ar-H), 7.32 (t, 2H, Ar-H), 7.77 (t, 2H, Ar-H), 8.22 (d ,2H, Ar-H), 8.44-8.65 (m ,4H, Ar-H), ^{31}P NMR (DMSO-d_6 ,δ): -18.28, -6.33. Anal. Found (Calcd)% for : $C_{22}H_{12}O_8N_6S_2PCl$: C, 42.4(42.6); H, 1.8(2.0); N, 13.6(14.7); S, 10.2(10.4); Cl, 5.5(5.7).

3.2.9 O-4-chlorophenyl S,S-bis[5-(4-nitrophenyl)-1,3,4-oxadiazol-2-yl] phosphorodithioate (IX) : Mp 153-155°C, IR (KBr,cm^{-1}): 3064 (C–H $_{aro,str}$), 782 (C-$H_{aro.oop.}$), 1627 (C=N) , 670 (C-S), 1264 (C-O-C $_{asy}$), 1187 (C-O-C $_{sym}$), 1302 (P=O), 1172 (P-O-$C_{aro.}$), 1565 (NO_2-$C_{aro.asy\ str.}$), 1340 (NO_2-$C_{aro.sy\ str.}$), 612 (P-S-C). ^{1}H NMR (DMSO-d_6 ,δ) :6.89 (d, 2H, Ar-H), 7.32 (d, 2H, Ar-H), 8.23-8.32 (m, 8H, Ar-H), ^{31}P NMR (DMSO-d_6, δ): -18.28, -6.33. Anal. Found(Calcd)% for $C_{22}H_{12}O_8N_6S_2PCl$: C, 42.6(42.6); H, 1.8(2.0); N, 13.6(14.7); S, 10.2(10.4); Cl, 5.5(5.7).

3.2.10 O-4-chlorophenyl S,S-bis[5-(4-aminophenyl)-1,3,4-oxadiazol-2-yl] phosphorodithioate (X) : Mp 170-172°C, IR (KBr,cm^{-1}): 3070 (C–H $_{aro,str}$), 780 (C-H $_{aro.oop.}$), 1623 (C=N) , 667 (C-S), 1262 (C-O-C $_{asy}$), 1190 (C-O-C $_{sym}$), 1300 (P=O), 1170 (P-O-$C_{aro.}$), 3410 ($C_{aro,st}$-NH_2), 618 (P-S-C). ^{1}H NMR (DMSO-d_6 ,δ) : 6.27(s, 4H,-NH_2), 6.58-6.89 (m, 6H, Ar-H), 7.32 -7.54 (m, 6H, Ar-H); ^{31}P NMR (DMSO-d_6 ,δ): -18.28, -6.33. Anal. Found(Calcd)% for $C_{22}H_{16}O_4N_6S_2PCl$: C, 47.0 (47.2); H, 2.6(2.8); N, 14.8(15.0); S, 11.2(11.4); Cl, 6.2(6.4).

3.2.11 O-4-chlorophenyl S,S-bis[5-(4-hydroxyphenyl)-1,3,4-oxadiazol-2-yl] phosphorodithioate (XI) : Mp 152-155°C, IR (KBr,cm^{-1}) : 3088 (C–H $_{aro,str}$), 790 (C-H $_{aro.oop.}$), 1632 (C=N) , 678 (C-S), 1265 (C-O-C $_{asy}$), 1195 (C-O-C $_{sym}$), 1310 (P=O), 1180 (P-O-$C_{aro.}$), 3410 (C_{aro}-OH_{st}), 614 (P-S-C).^{1}H NMR (DMSO-d_6 ,δ) : 7.32(d, 2H, Ar-H), 7.96 (d, 4H, Ar-H), 6.86-6.89 (m, 6H, Ar-H), 5.35(s, 2H,aro.OH); ^{31}P NMR (DMSO-d_6 ,δ): -18.28, -6.33. Anal. Found(Calcd)% for : $C_{22}H_{16}O_4N_6S_2PCl$: C, 46.8 (47.0); H, 2.2(2.4); N, 9.8(9.9); S, 11.3(11.5); Cl, 6.2(6.4).

3.2.12 O-4-chlorophenyl S,S-bis[5-(2,4-dichlorophenyl)-1,3,4-oxadiazol-2-yl] phosphorodithioate (XII) : Mp 164-166°C, IR (KBr,cm^{-1}) : 3090 (C–H $_{aro,str}$), 778 (C-H $_{aro.oop.}$), 1636 (C=N), 685 (C-S), 1257 (C-O-C $_{asy}$), 1198 (C-O-C $_{sym}$), 1302 (P=O), 1182 (P-O-$C_{aro.}$), 1038 (C-Cl_{ortho}), 1090 (C-Cl_{para}), 618 (P-S-C). ^{1}H NMR (DMSO-d_6 ,δ) : 6.89 (d, 2H, Ar-H), 7.32-7.75 (m, 8H, Ar-H); ^{31}P NMR (DMSO-d_6, δ): -18.28, -6.33. Anal. Found

(Calcd)% for $C_{22}H_{10}O_4N_4S_2PCl_5$: C, 39.4 (39.5); H, 1.2(1.4); N, 8.1(8.3); S, 9.4(9.6); Cl, 24.6(24.8).

3.3 Antimicrobial Activity

Antimicrobial test was performed on two bacteria (*Staphylococcus aureus* and *Escherichia coli*) and three fungi (*Aspergillus niger, Aspergillus ochraceus* and *Fusarium oxyporum*). The media used were prepared by dissolving separately 2g of the nutrient broth powder and 38g of the Mueller Hinton agar powder in 250mL and 1L of deionized water, respectively. The two media were sterilized in an autoclave at 121ºC for 15 min. and then stored overnight in a refrigerator after cooling. Cultures of the microorganisms were prepared in sterile nutrient broth and incubated for 24 h at 37ºC for the bacteria and 27ºC for the fungi. 0.1mL of each of the overnight cultures in sterile test tubes with caps were made upto 10mL with 9.9mL of sterile deionised water. The technique used for the study was agar-well diffusion.

Solutions of concentrations 250, 500 and 1000 ppm were made in methanol. Methanol was also used as the negative control. The positive controls for bacteria and fungi were discs of commercial antibiotics Streptomycin and Griseofulvin respectively dissolved in methanol. The discs were carefully placed on the inoculated media with the aid of sterile forceps. The plates inoculated with bacteria were incubated at 37ºC for 24 h and those inoculated with fungi were incubated at 27ºC for 72 h. Afterwards, the zones of inhibition of microbial growth that appeared around the wells of the compounds were examined and the diameters measured and recorded in millimetres (mm). Antimicrobial activities of all newly synthesized organophosphorus compounds were evaluated in vitro against Gram positive bacteria- *Staphylococcus aureus* and Gram negative bacteria- *Escherichia coli* (Table 2).The majority of the compounds (I-XII) exhibited moderate to good activity against both the bacteria. The same compounds were screened for their antifungal activity (Table 3) against *A. niger, A. ochraceus* and *F. oxyporum* species. It is gratifying to observe that the majority of the compounds (I-XII) exhibited moderate to good antifungal activity when compared with the Griseofulvin in reference.

4. **Results and Discussion**

Reactions of Phenylphosphonic dichloride / 4-Chlorophenyl dichlorophosphate with 5-(phenyl/substituted phenyl)-1,3,4-oxadiazole-2-thiol ligands have been carried out in benzene in the presence of pyridine and a variety of organophosphorus derivatives have been

isolated according to Eqs.(1), and (2)**.** The methods used for the preparation and isolation of these compounds gave materials of good purity as supported by their analyses and TLC. Physical properties of the organophosphorus compounds are given in Table 1. All compounds are quite stable in air. The organophosphorus derivatives are found to be soluble in dimethylformamide, tetrahydrofuran and dimethylsulfoxide. All of these compounds are cream to yellow in colour. The compounds melt in the temperature range of 132-215°C.

4.1 Infrared spectra

The mercaptooxadiazole ligand has one oxadiazole ring and one mercapto group resulting in the presence of four donor sites (two nitrogen, one oxygen and one sulphur atom). The infrared spectra of mercapto oxadiazoles show one weak band at ca. 2767-2773 cm^{-1} due to S-H stretching (Gaber, 2004). However, in the spectra of organophosphorus derivatives, this band disappear which confirm the formation of bond between sulphur and phosphorus. This is further supported by the appearance of band at ca.620-610 cm^{-1} assignable to ν(P-S-C). The IR spectrum showed the bands at 1620,1253 and 670 cm^{-1} assigned to stretching absorptions of C=N,C-O-C and C-S groups, respectively(Chaturvedi, 1995) strong-medium bands at 1237-1267 cm-1 and 1174-1200 cm-1 which are characteristic for C-O-C asymmetric and symmetric stretching of oxadiazole ring(Ainsworth, 1955), respectively. Medium-weak absorption band at 3054-3137 cm^{-1} and strong-medium band at 725-790 cm^{-1} which are characteristic of aromatic C-H stretching and bending, respectively are obtained.

The position of infrared bands due to phenyl and oxadiazole ring (C-O-C) does not change in the complexes indicating the non- coordination of oxygen atom. The above observations indicate that possibly the bonding in organophosphorus derivatives is through thiol sulphur.

In addition all organophosphorus derivatives derivatives show bands at ca.1290-1310 cm^{-1} assignable to *ν*(P=O)(Bradley and Gitlitz, 1969; Ewald et al., 1969) vibrations. Organophosphorus derivatives (I, II, III, IV, V. VI) show bands at ca. 998-981 cm^{-1} due to ν(P-C) aromatic. Organophosphorus derivatives (VII, VIII, IX, X, XI, XII) show bands at ca. 960 cm^{-1} and 1240 cm^{-1} assignable to ν (P-O) and ν (O-C) aromatic respectively.

4.2 Nuclear Magnetic Resonance Spectra

The ^{1}H NMR spectra were recorded on a Bruker Avance III, 400MHz spectrometer operating at 400 MHz to ^{1}H and 161.9 MHz for ^{31}P NMR using DMSO-d_6 as solvent. In

general, a slight shift to lower field in the position of the resonance signals of various protons in the organophosphorus derivatives was observed due to a change in the electronic-environment (de-shielding) around protons in the oxadiazoles. Of course, the protons of R groups in the mercapto 3-oxadiazoles are affected very little due to the remote positions of these protons from the phosphorus atom. The signals due to aromatic ring protons appear in region *ca*. δ 6.58-8.65. The signals due to –SH protons appears at about *ca*. δ 13.05 in the spectra of all mercaptooxadiazoles ligands which disappears in their corresponding organophosphorus derivatives indicating the deprotonation of S–H proton and formation of bond between sulphur and phosphorus.

^{31}P NMR chemical shifts of the compounds (I, II, III, IV, V, VI) appeared in the region-12.63 ppm whereas in the compounds (VII, VIII, IX, X, XI, XII) signals appear in the region -6.22 to -18.21ppm. Presence of O atom in between the P atom and C atom increases the deshielding of phosphorus in the compounds (VII, VIII, IX, X, XI, XII).

5. Conclusions

A series of novel organophosphorus compounds were synthesized by the reactions of Phenylphosphonic dichloride / 4-Chlorophenyl dichlorophosphate with 5-(phenyl/substituted phenyl)-1,3,4-oxadiazole-2-thiol ligands with the aim to develop better antimicrobial agent. The results of biological tests make both oxadiazole and phosphorus interesting lead molecules for further synthetic and biological evaluation. It can be concluded that this class of compound certainly hold great promise for discovering safer antimicrobial agents.

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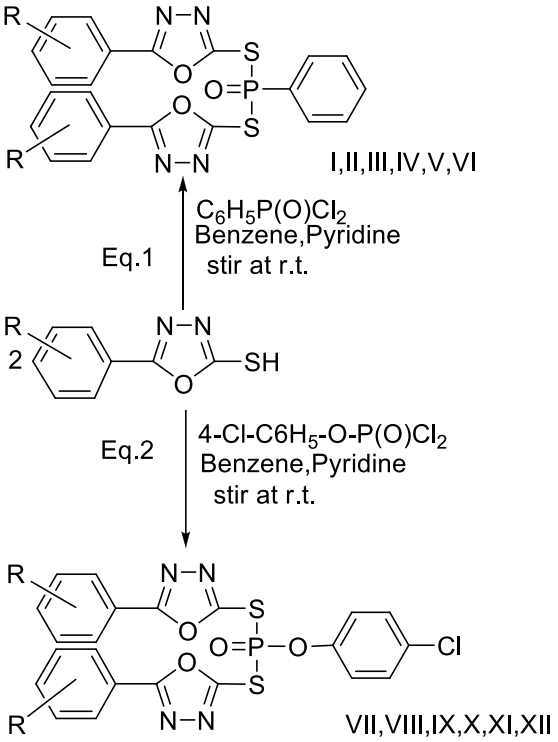

Where, in Compounds

(I and VII), R= H, (II and VIII), R=3-NO_2, (III and IX), R=4-NO_2,

(IV and X), R=4-NH_2, (V and IX), R=4-OH, (VI and XII), R=2,4-Cl_2,

Comps.	Reactants Taken		Molar Ratio	Stirring Time (h)	Product	Colour	Yield (%)
	$(C_6H_5)POCl_2$/ $(ClC_6H_5O)POCl_2$ (mL)	Ligands (g)					
I	1.4	3.5(L1)	1:2	8	$C_{22}H_{15}O_3N_4S_2P$	White	56
II	1.4	4.4(L2)	1:2	10	$C_{22}H_{13}O_7N_6S_2P$	Light Brown	58
III	1.4	4.4(L3)	1:2	12	$C_{22}H_{13}O_7N_6S_2P$	Dark Yellow	63
IV	1.4	3.8(L4)	1:2	7	$C_{22}H_{17}O_3N_6S_2P$	Light Yellow	55
V	1.4	3.8(L5)	1:2	9	$C_{22}H_{15}O_5N_4S_2P$	Yellow	61
VI	1.4	4.9(L6)	1:2	14	$C_{22}H_{11}O_3N_4S_2PCl_4$	White	70
VII	1.6	3.5(L1)	1:2	12	$C_{22}H_{14}O_4N_4S_2PCl$	White	59
VIII	1.6	4.4(L2)	1:2	10	$C_{22}H_{12}O_8N_6S_2PCl$	Yellow	61
IX	1.6	4.4(L3)	1:2	8	$C_{22}H_{12}O_8N_6S_2PCl$	Yellow	69
X	1.6	3.8(L4)	1:2	7	$C_{22}H_{16}O_4N_6S_2PCl$	Yellow	62
XI	1.6	3.8(L5)	1:2	12	$C_{22}H_{14}O_6N_4S_2PCl$	Creamish	55
XII	1.6	4.9(L6)	1:2	11	$C_{22}H_{10}O_4N_4S_2PCl_5$	White	56

L1 = 5-(phenyl)-1,3,4-oxadiazole-2-thiol, L2 = 5-(3-nitro phenyl)-1,3,4-oxadiazole-2-thiol, L3 = 5-(4-nitro phenyl)-1,3,4-oxadiazole-2-thiol, L4 = 5-(4-amino phenyl)-1,3,4-oxadiazole-2-thiol., L5 = 5-(4-hydroxy phenyl)-1,3,4-oxadiazole-2-thiol, L6 = 5-(2,4-dichloro phenyl)-1,3,4-oxadiazole-2-thiol

Table 1: Reactions of of Phenylphosphonic dichloride / 4-Chlorophenyl dichlorophosphate with 1,3,4-oxadiazole-2-thiol ligands

Compounds	*Escherichia coli*			*Staphylococcus aureus*		
	250ppm	**500ppm**	**1000ppm**	**250ppm**	**500ppm**	**1000ppm**
I	8.0	9.0	10.3	8.3	9.6	11.3
II	8.0	9.3	10.6	8.0	9.3	10.6
III	8.3	9.3	10.6	8.3	10.6	11.6
IV	8.6	10.3	11.3	8.6	9.6	12.3
V	9.3	10.6	12.0	8.0	9.3	10.6
VI	7.3	7.6	10.0	7.6	9.0	10.6
VII	8.6	9.3	11.0	8.6	10.6	11.3
VIII	8.6	10.6	12.3	9.0	10.0	11.6
IX	7.0	7.6	10.0	7.6	8.3	10.6
X	8.3	10.6	11.3	8.6	10.6	12.6
XI	8.0	8.6	11.3	8.6	10.3	11.3
XII	8.3	9.3	12.0	8.3	9.3	11.3
Streptomycin	12.6	15.3	20.0	14.0	17.3	21.3

Table 2: Antibactirial screening data of organophosphorus compounds (zone of inhibition in mm)

Compounds	***Aspergillus niger***			***Aspergillus ochraceus***			***Fusarium oxyporum***		
	250 ppm	**500 ppm**	**1000 ppm**	**250 ppm**	**500 ppm**	**1000 ppm**	**250 ppm**	**500 ppm**	**1000 ppm**
I	14.9	17.0	19.0	8.0	10.0	13.3	12.3	13.0	14.3
II	8.6	10.0	11.3	8.6	10.0	12.6	12.3	14.0	16.6
III	10.3	11.3	14.0	12.0	14.3	16.6	10.0	12.6	15.3
IV	10.6	11.3	12.6	12.0	14.0	16.3	8.6	9.3	12.0
V	12.3	15.0	17.3	10.0	12.3	14.3	13.6	15.6	19.3
VI	12.6	16.3	18.6	10.0	11.3	13.0	10.6	12.0	14.0
VII	12.0	15.6	17.3	7.3	9.3	12.0	9.3	11.3	14.0
VIII	10.6	15.3	18.6	9.3	11.3	13.6	11.3	13.0	17.6
IX	8.6	10.6	12.0	12.6	15.6	17.0	10.0	10.6	12.6
X	10.0	11.3	12.6	11.3	15.3	16.6	9.3	12.0	13.3
XI	12.3	15.3	17.3	8.6	11.3	12.6	12.3	15.3	17.6
XII	12.6	15.0	18.0	8.6	10.0	11.3	11.3	12.3	14.3
Griseofulvin	15.3	18.0	20.6	13.6	15.6	17.0	15.0	17.6	20.3

Table 3 : Antifungal screening data of organophosphorus compounds (zone of inhibition in mm)