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Synthesis of Some New Organophosphorus Compounds as Potent Antimicrobial Agents.

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ABSTRACT

A series of biologically active organophosphorus compounds have been synthesized by the reactions of chlorodiphenylphosphine 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.

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INTRODUCTION

Infectious diseases are one of the leading causes of death worldwide. During the past few decades, new infectious diseases have appeared and old ones previously thought to be controlled have re-emerged [1]. Despite the critical need for new antimicrobial agents, the development of these agents is declining. Solutions encouraging and facilitating the development of new antimicrobial agents are needed. 1,3,4-oxadiazoles constitute an important family of heterocyclic compounds as they have attracted significant interest in medicinal chemistry, pesticide chemistry and polymer science [2-4]. Since many of 1,3,4-oxadiazoles display a remarkable biological activity [5, 6], their synthesis and transformations have been receiving particular interest for a long time [7]. Most of the marketed antihypertensive agents such as Tiodazosin [8] and Nesapidil [9] as well as antibiotics such as Furamizole [10] contain oxadiazole nucleus. During the past years, considerable evidences have accumulated to demonstrate the efficacy of 1,3,4-oxadiazole including antimicrobial [5], anti-inflammatory, analgesic [6], anti-HIV [11], antimycobacterial [12], cathepsin K inhibitors [13], tyrosinase inhibitors [14], monoamine oxidase (MAO) inhibitors [15] and anticonvulsant [16] properties. 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 [17-19] 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 [20] 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 chlorodiphenylphosphine 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.

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 (31P, δ ppm). C,H,N 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 chlorodiphenylphosphine 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 chlorodiphenylphosphine 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 [21]. Chlorodiphenylphosphine 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 [22, 23]. The details of analysis and physical measurements were the same as reported earlier [24].

EXPERIMENTAL

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 [25]. To a solution containing 400 mL of 95% ethanol and potassium hydroxide (0.1 mol, 5.6 g dissolved in 15 mL of water), was added (0.1 mol) of the appropriate hydrazide and (0.1 mol ,6.6 mL) of carbon disulfide. Then the mixture was refluxed for 3 h or until most of the hydrogen sulphide had been evolved. The solution was concentrated to a small volume and the residue was dissolved in water. A precipitate was obtained by pouring 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}.

General procedure for the synthesis of organophosphorus compounds (I-VII)

The organophosphorus compounds were prepared by mixing chlorodiphenylphosphine (1 mol) and the appropriate ligand 5-(phenyl/substituted phenyl)-1,3,4-oxadiazole-2-thiol (1 mol) in benzene (30 mL) in presence of pyridine (1 mol) with continuous stirring .Stirring was continued at room temperature over a period of 7-14 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.

2-(diphenylphosphinothio)-5-phenyl-1,3,4-oxadiazole (I)

Mp 233-235°C, IR (KBr,cm^{-1}): 3058 (C–$H_{aro,str.}$), 744(C-$H_{aro.oop.}$), 16210 (C=N) , 672 (C-S), 1240 (C-O-C_{asy}) , 1184 (C-O-C_{sym}), 988 (P-$C_{aro.}$), 610 (P-S-C). ^{1}H NMR (DMSO-d_6 ,δ) : 7.38-7.51 (m ,13H, Ar-H), 8.05 (d, 2H, Ar-H, J=8Hz). ^{31}P NMR (DMSO-d_6 ,δ): -12.6 . Anal. Found (Calcd)% for $C_{20}H_{15}ON_2SP$: C, 66.0(66.2); H, 4.0(4.1); N, 7.5(7.7); S, 8.6(8.8).

2-(diphenylphosphinothio)-5-(3-nitrophenyl)-1,3,4-oxadiazole (II)

Mp 161-163°C, IR (KBr,cm^{-1}): 3068 (C–$H_{aro,str}$), 750 (C-$H_{aro.oop.}$), 1624 (C=N) , 668 (C-S), 1249 (C-O-C_{asy}), 1186 (C-O-C_{sym}), 988 (P-$C_{aro.}$), 1500 (NO_2-$C_{aro.asy\ str.}$), 1320 (NO_2-$C_{aro.sym\ str.}$), 618 (P-S-C). ^{1}H NMR (DMSO-d_6 ,δ) : 7.38-7.77 (m ,11H, Ar-H), 8.22(s, 1H, Ar-H),8.44 (s, 1H, Ar-H), 8.65 (s ,1H, Ar-H), ^{31}P NMR (DMSO-d_6 ,δ): -12.5. Anal. Found (Calcd)% for $C_{20}H_{14}O_3N_3SP$: C, 58.7(58.9); H, 3.2(3.4); N, 10.0(10.3); S, 7.6(7.8).

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2-(diphenylphosphinothio)-5-(4-nitrophenyl)-1,3,4-oxadiazole (III)

Mp 166-168°C, IR (KBr, cm^{-1}): 3070 (C–H $_{aro,str}$), 762 (C-H $_{aro.oop.}$), 1628 (C=N), 670 (C-S), 1262 (C-O-C $_{asy}$) , 1182 (C-O-C $_{sym}$), 992 (P-$C_{aro.}$), 1525 (NO_2-$C_{aro.asy\ str.}$), 1342 (NO_2-$C_{aro.sy\ str.}$), 616 (P-S-C). ^{1}H NMR (DMSO-d_6 ,δ) : 7.38-7.75 (m, 10H, Ar-H), 8.23-8.32 (m, 4H, Ar-H), ^{31}P NMR (DMSO-d_6, δ): -12.4. Anal. Found (Calcd)% for $C_{20}H_{14}O_3N_3SP$: C, 58.6(58.9); H, 3.1(3.4); N, 10.1(10.3); S, 7.6(7.8).

2-(diphenylphosphinothio)-5-(4-aminophenyl)-1,3,4-oxadiazole (IV)

Mp 196-198 °C, IR (KBr,cm^{-1}): 3085 (C–H $_{aro,str}$), 782 (C-H $_{aro.oop.}$), 1628 (C=N), 678 (C-S), 1258 (C-O-C $_{asy}$) , 1192 (C-O-C $_{sym}$), 990 (P-$C_{aro.}$), 3450 ($C_{aro,st}$-.NH_2), 612 (P-S-C). ^{1}H NMR (DMSO-d_6 ,δ) :7.38-7.58 (m, 14H, Ar-H), 6.27(s, 2H,-NH_2); ^{31}P NMR (DMSO-d_6, δ): -12.8. Anal. Found (Calcd)% for $C_{20}H_{16}ON_3SP$: C, 63.4(63.6); H, 4.0(4.2); N, 11.0(11.1) ; S, 8.3(8.5).

2-(diphenylphosphinothio)-5-(4-hydroxyphenyl)-1,3,4-oxadiazole (V)

Mp 200-202°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 $_{asy}$), 1196 (C-O-C $_{sym}$), 990 (P-$C_{aro.}$), 3500 (C_{aro}-OH_{st}), 615 (P-S-C). ^{1}H NMR (DMSO-d_6 ,δ) : 7.38-7.96 (m, 12H, Ar-H), 6.86 (d, 2H, Ar-H), 5.35(s, 1H,-OH); ^{31}P NMR (DMSO-d_6 ,δ): -12.6 . Anal. Found (Calcd)% for $C_{20}H_{15}O_2N_2SP$: C, 63.2(63.4); H, 3.7(3.9); N, 7.2(7.4); S, 8.2(8.4).

2-(diphenylphosphinothio)-5-(2,4-dichlorophenyl)-1,3,4-oxadiazole (VI)

Mp 142-145°C, IR (KBr,cm^{-1}): 3073 (C–H $_{aro,str}$), 775 (C-H $_{aro.oop.}$), 1622 (C=N), 676 (C-S), 1266 (C-O-C $_{asy}$) , 1198 (C-O-C $_{sym}$), 994 (P-$C_{aro.}$), 1042 (C-Cl_{ortho}), 1088 (C-Cl_{para}), 618 (P-S-C). ^{1}H NMR (DMSO-d_6 ,δ) : 7.38-7.75 (m, 13H, Ar-H) ; ^{31}P NMR (DMSO-d_6 ,δ): -12.4. Anal. Found(Calcd)% for $C_{20}H_{13}ON_2SPCl_2$: C, 55.4(55.6); H, 2.8(3.0)1.6(1.7); N, 6.2(6.4); S, 7.2(7.4); Cl, 16.2(16.4).

2-(diphenylphosphinothio)-5-(2-bromophenyl)-1,3,4-oxadiazole (VII)

Mp 171--173°C, IR (KBr,cm^{-1}): 3082 (C–H $_{aro,str.}$), 776(C-H $_{aro.oop.}$), 1624 (C=N) , 674 (C-S), 1250 (C-O-C $_{asy}$) , 1188 (C-O-C $_{sym}$), 990 (P-$C_{aro.}$), 612 (P-S-C). ^{1}H NMR (DMSO-d_6 ,δ) : 7.38-7.61 (m ,14H, Ar-H); ^{31}P NMR (DMSO-d_6 ,δ): -12.6 . Anal. Found (Calcd)% for $C_{20}H_{14}ON_2SPBr$: C, 54.1(54.4); H, 3.0(3.1); N, 6.1(6.3); S, 7.0(7.2).

Antimicrobial Activity

Antimicrobial test was performed on two bacterias (*Staphylococcus aureus* and *Escherichia coli*) and three fungus (*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 deionized 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 newly synthesized all organophosphorus compounds was evaluated in vitro against Gram positive bacteria- *Staphylococcus aureus* and Gram negative bacteria- *Escherichia coli.* The majority of the compounds (I-VII) exhibited moderate to good against both the bacteria.The same compounds were screened for their antifungal activity (Table 4) against *A.niger, A.ochraceus* and *F.oxyporum* species. It is gratifying to observe that the majority of the compounds (I-VII) exhibited moderate to good antifungal activity when compared with the Griseofulvin in reference.

Reactions of chlorodiphenylphosphine 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 scheme. 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.

Table 1: Reactions of chlorodiphenylphosphine with 1,3,4-oxadiazole-2-thiol ligands.

Comps.	Reactants Taken		Molar Ratio	StirringTime (h)	Product	Colour	Yield (%)
	$(C_6H_5)_2PCl$ (mL)	Ligands (g)					
I	1.7	1.7(L1)	1:1	10	$C_{20}H_{15}ON_2SP$	White	56
II	1.7	2.2(L2)	1:1	8	$C_{20}H_{14}O_3N_3SP$	Light Brown	58
III	1.7	2.2(L3)	1:1	14	$C_{20}H_{14}O_3N_3SP$	Dark Yellow	63
IV	1.7	1.9(L4)	1:1	11	$C_{20}H_{16}ON_3SP$	Light Yellow	55
V	1.7	1.9(L5)	1:1	9	$C_{20}H_{15}O_2N_2SP$	Yellow	61
VI	1.7	2.4(L6)	1:1	12	$C_{20}H_{13}ON_2SPCl_2$	White	70
VII	1.7	2.6(L7)	1:1	12	$C_{20}H_{14}ON_2SPBr$	White	59

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, L7 = 5-(2-bromo phenyl)-1,3,4-oxadiazole-2-thiol

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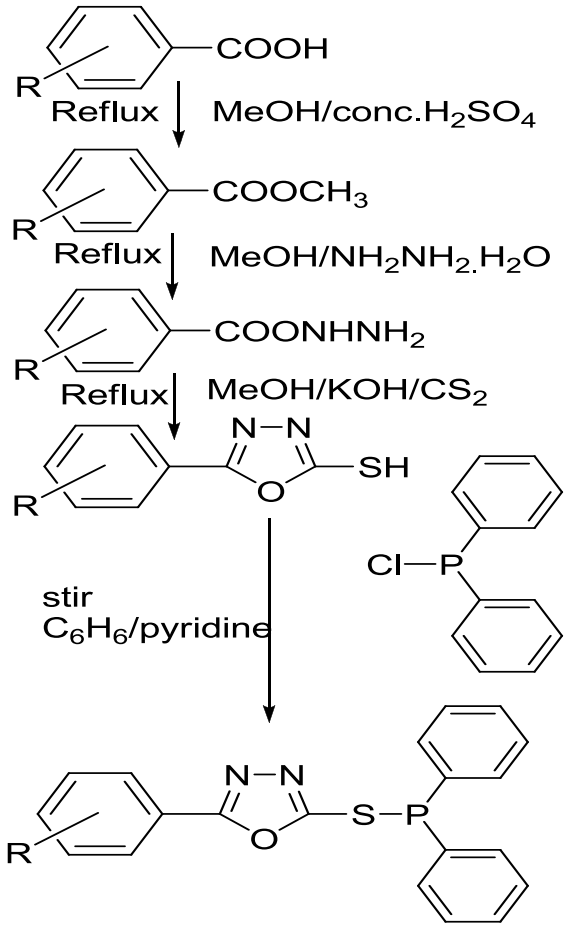

Scheme: Synthetic route of 2-(diphenylphosphinothio)-5-(substituted phenyl)-1,3,4-oxadiazole

Where,

R=H (comp.I), 3-NO_2 (comp.II), 4-NO_2 (comp.III), 4-NH_2 (comp. IV), 4-OH (comp. V), 2,4.Cl_2 (comp. VI), 2-Br (comp. VII).

Table 2: Antibacterial activities, zone of inhibition(in mm)

Compounds	Escherichia coli			Staphylococcus aureus		
	250ppm	500ppm	1000ppm	250ppm	500ppm	1000ppm
I	10.3	12.3	13.6	8.6	12.0	13.6
II	10.3	12.0	13.0	8.6	10.6	12.0
III	8.3	10.3	11.3	9.0	11.0	12.3
IV	9.0	10.3	12.0	10.3	12.0	13.3
V	9.3	11.0	12.3	8.3	10.3	12.0
VI	7.0	8.0	10.6	7.3	8.3	10.3
VII	8.6	10.6	11.6	9.3	11.6	13.0
Streptomycin	12.6	15.3	20.0	14.0	17.3	21.3

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Table 3: Antifungal activities, 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	13.0	15.3	18.0	10.3	12.6	15.6	12.0	14.3	17.3
II	12.6	16.0	19.3	10.3	12.3	14.6	12.6	16.0	18.0
III	10.6	13.0	15.3	13.0	16.0	18.6	11.3	13.3	16.6
IV	9.6	11.6	13.0	12.3	15.3	18.3	9.0	11.6	13.3
V	13.3	16.0	18.6	10.6	13.0	14.3	12.6	14.6	16.6
VI	13.3	16.3	18.6	10.0	11.3	12.6	11.0	12.3	15.0
VII	12.3	14.3	17.3	10.6	\11.6	13.6	11.6	14.3	15.6
Griseofulvin	15.3	18.0	20.6	13.6	15.6	17.0	15.0	17.6	20.3

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[17]. 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 670cm^{-1} assigned to stretching absorptions of C=N,C-O-C and C-S groups, respectively[8]. 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[16], respectively. Medium-weak absorption band at 3054-3073 cm^{-1} and strong-medium band at 690--742 cm^{-1} which are characteristic of aromatic C-H stretching and bending, respectively.

The position of infrared bands due to phenyl and oxadiazole ring (C-O-C) do 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.
All organophosphorus derivatives show bands at ca. 998-988 cm^{-1} due to ν (P-C) aromatic.

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 mercapto3-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 mercapto oxadiazoles 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 appeared in the region ca. δ -12.6 ppm

ANTIMICROBIAL ACTIVITY

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-VII) exhibited moderate to excellent 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-VII) exhibited moderate to excellent antifungal activity when compared with the Griseofulvin in reference.

CONCLUSIONS

A series of novel organophosphorus compounds were synthesized by the reactions of chlorodiphenylphosphine 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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REFERENCES

[1] Sharma PC, Jain S. Acta Pharm Sci 2008; 50: 35–40.
[2] Bostrom J, Hogner A, Llinas A, Wellner E, Plowright AT. J Med Chem 2012; 55: 1817–1830.
[3] Mohan TP, Vishalakshi B, Bhat KS, Rao KS, Kendappa GN. Indian J Chem Sect B 2004; 43: 1798–1801.
[4] Schulz B, Kaminorz Y, Brehmer L. Synth Met 1997; 84: 449–450.
[5] Zoumpoulakis P, Camoutsis Ch, Pairas G, Sokovic M, Glamoclija J, Potamitis C, Pitsas A. Bioorg Med Chem 2012; 20: 1569–1583.
[6] Ingale N, Maddi V, Palkar M, Ronad P, Mamledesai S, Vishwanathswamy AHM, Satyanarayana D. Med Chem Res 2012; 21: 16–26.
[7] Bondock S, Adel S, Etman HA, Badria FA. Eur J Med Chem 2012; 48: 192–199.

[8] Vardan S, Smulyan H, Mookherjee S, Eich R. Clin Pharmacol Ther 1983; 34: 290–296.
[9] Schlecker R, Thieme PC. Tetrahedron 1988; 44: 3289–3294.
[10] Ogata I, Atobe H, Kushida H, Yamamoto K. J Antibiot 1971; 24: 443–451.
[11] Sriram D, Banerjee D, Yogeeswari P. J Enzyme Inhib Med Chem 2009; 24: 1–5.
[12] Macaev F, Rusu G, Pogrebnoi S, Gudima A, Stingaci E, Vlad L, Shvets N, Kandemirli F, Dimoglo A, Reynolds R. Bioorg Med Chem 2005; 13: 4842–4850.
[13] Palmer JT, Hirschbein BL, Cheung H, McCarte RJ, Janc JW, Yu ZW, Wesolowski G. Bioorg Med Chem Lett 2006; 16: 2909–2914.
[14] Khan MTH, Choudhary MI, Khan KM, Rani M, Attaur Rahman. Bioorg Med Chem 2005; 13: 3385–3395.
[15] Ke S, Li Z, Qian X. Bioorg Med Chem 2008; 16: 7565–7572.
[16] Almasirad A, Tabatabai SA, Faizi M, Kebriaeezadeh A, Mehrabi N, Dalvandi A, Shafiee A. Bioorg Med Chem Lett 2004; 14: 6057–6059.
[17] Sengupta SK, Pandey OP, Rao GP, Shahi SP and Jaiswal AK. Sugarcane 1998; 4: 17.
[18] Sengupta SK, Pandey OP, Rao GP and Singh P. Metal Based Drugs 2002; 8: 293.
[19] Sengupta SK, Pandey OP, Rao GP, Dwivedi A and Vishen P. Phosphorus Sulphur Silicon 2003; 178: 839.
[20] Wang S, Zheng S, Meng H and Hua W. Synth. Metals 1998; 93: 181.
[21] Chaturvedi, K, Jaiswal AK, Pandey OP and Sengupta SK. Synth React Inorg Org Chem 1995; 25(10): 1581-1595.
[22] Efimovsky and Rumpt, P. Bull Soc Chim Fr 1954; 648.
[23] Teriunobu U, Tohihike S and Honda I. Kogyo Kagaku Zasahi 1969; 72: 2661.
[24] Schrader G. Bios Final Rep 1947; 714: 1095.
[25] Maffii G, Testa E and Ettorre R. Chem Abstr 1959; 53: 2211.