Available online at www.derpharmachemica.com

Scholars Research Library

Der Pharma Chemica, 2011, 3(3): 382-388
(http://derpharmachemica.com/archive.html)

ISSN 0975-413X
CODEN (USA): PCHHAX

Synthesis and bioassay of 2-substituted-1, 3, 2- oxazaphosphole 2-ones

K. Reddi Mohan Naidu, C. Bhupendra Reddy, S. Rasheed, C. Naga raju*

Department of Chemistry, Sri Venkateswara University, Tirupati, India

---

ABSTRACT

A series of new phosphorus heterocycles has been synthesized by the condensation of octahydro-1H-indol(3aS,7aS)-2-yl(2S) methanol (1) with phosphorus oxychloride in the presence of triethylamine in dry tetrahydrofuran, followed by the reaction with various phenols and aminoacidester hydrochlorides. All the title compounds were characterized by elemental and spectral analyses. Their antimicrobial activity was also evaluated.

Key words: 1,3,2-Oxaza Phosphole 2-ones, Octahydro-1*H*-indol(3aS,7aS)-2-yl(2S) methanol, antimicrobial activity.

INTRODUCTION

Heterocyclic molecules containing a phosphorus linked to an oxygen or nitrogen atom are common to a diverse array of important biological molecules [1]. Cyclic organophosphorus compounds have been employed for the generation of novel biocatalysts [2]. The cyclic phosphonate has been successfully used to generate antibodies that catalyse the enantioselective aminolysis of lactones [3]. The attachment of an amino acid group to the phosphate moiety is expected to increase cellular uptake and thus enhance chemotherapeutic properties. Organophosphorus compounds are used as insecticides, agricultural and horticultural pesticides and veterinary medicines. They are also used in human medicines and in various public hygiene products for use both by professional operators and the general public. Pesticides in soil have far reaching consequences as they disturb the delicate equilibrium between microorganisms and their environment [4]. Bioremediation is a promising area which holds potential for eco-restoration of pesticide contaminated soil. Several microorganisms are able to degrade a large variety of compounds [5]. At the outset a wide range of pesticides, insecticides and antibiotics emanated from phosphorus compounds [6]. Specifically organophosphorus heterocycles bearing the P-N functionality exhibited anti-tumor, pesticidal and medicinal activity [7-9]. Optically active organophosphorus compounds possessing a chiral centre at phosphorus are known to

exhibit a variety of unique biological activities and hence they have a potential use as agricultural chemicals [10]. The synthesis of multi–ring phosphorus heterocycles were accomplished much importance as they find applications in medicine and industry [11]. Simillarly proline-based phosphorylated derivatives were used for borane mediated reduction of prochiral α-halo ketones to α-halo alcohols [12]. In view of the above applications of phosphorus compounds, we herein report the synthesis of novel 2-substtituted-1,3,2-oxazaphosphole 2-ones containing three chiral centres in the heterocycle.

MATERIALS AND METHODS

Experimental section

Chemicals were obtained from Sigma-Aldrich, Lancaster used as such without further purification. All solvents (AR or Extra pure grade) used for spectroscopic and other physical studies were further purified by reported methods [17]. All operations were performed under nitrogen atmosphere using standard glassware. Melting points were determined in open capillary tubes on a Mel-Temp apparatus and are uncorrected. Optical rotations were recorded using Perkin-Elmer model 343 in methanol. IR spectra were recorded as KBr pellets on a FT-IR 200 double beam spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded as solutions in DMSO-d_6 on a Bruker AMX 400 MHz spectrometer operating at 400 MHz for ^{1}H, 100 MHz for ^{13}C and 161.5 MHz for ^{31}P. The ^{1}H and ^{13}C chemical shifts were referenced to tetramethylsilane and ^{31}P chemical shifts to 85% H_3PO_4. APCI and LC-MS mass spectra were recorded on a Jeol SX 102 DA/600 Mass spectrometer.

Synthetic procedure for the title compounds (3a-j).

A solution of phosphoryl chloride (0.002 mol) in 15 mL of dry THF was added dropwise over a period of 15 min to a stirred solution of octahydro-1H-indol(3aS,7aS)-2-yl(2S) methanol (**1**) (0.002 mol) and triethylamine (0.004 mol) in 10 mL of THF at 0-5 ºC. After stirring for 1 hour at room temperature, formation of intermediate monochloride **2** was ascertained by TLC analysis run in 3:7 mixture of ethyl acetate and hexane, TEA hydrochloride was removed from the reaction mixture by filtration. The filtrate containing **2** was used for the next step of the reaction without further purification.

To a stirred solution of various phenols and amino acid ester hydrochlorides in dry THF (10 mL) and TEA (0.002 mol), the intermediate monochloride (**2**) in dry THF was added dropwise at 0 ºC. After the addition, the temperature was slowly raised to 40-45 ºC and stirred for 2 h. The completion of reaction was ascertained by TLC conducted on 3:7 mixture of ethylacetate and hexane with an average R_f value 0.53. The reaction mixture was filtered to remove TEA hydrochloride and the solvent from the filtrate was removed in a rotaevaporator to obtained the crude product. It was further purified by column chromatography on silica gel (60-120 mesh) with ethyl acetate: hexane mixture (1:9) as an eluent. The afforded pure compounds were characterized by IR, ^{1}H, ^{13}C, ^{31}P-NMR and mass spectral analyses.

2-Phenoxy perhydro-2λ^5 –[1,3,2] oxaza phospholo[3,4-a] indol 2-one **(3a)**: Yield 75%; semisolid; $[\alpha]_D^{31}$ (CH_3-OH): -0.7; ^{1}H NMR (DMSO-d_6): δ 7.62-6.19 (m, 5H, Ar-H), 4.23-3.80 (m, 2H, OCH_2), 3.50-3.0 (2H, m, N-CH), 1.90-0.80(11H, m, -(CH),-$(CH_2)_5$); ^{13}CNMR data: 151.2 (C-1$'$), 129.3 (C-3$'$, C-5$'$), 124.0 (C-4$'$), 115.2 (C-2$'$, C-6$'$), 69.1 (C-9), 44.4 (C-3a), 41.2 (C-8a),

34.6 (C-7a), 29.9 (C-8), 30.5 (C-4), 30.7 (C-7), 28.0 (C-6), 23.4 (C-5); ^{31}P NMR data: δ 22.1; IR(KBr): 1260 (P=O), 1220, 950 (P-O-C_{aryl}) cm^{-1}; LC-MS m/z 294 [60, M +1]$^{+}$, Anal. Calcd for $C_{15}H_{20}NO_3P$: C, 61.43, H, 6.87, N, 4.78. Found. C, 61.36, H, 6.80, N, 4.72.

2-(2-Chlorophenoxy)- perhydro-2λ^5 –[1,3,2] oxaza phospholo[3,4-a] indol 2-one (**3b**): Yield 73%; m.p.127-29 ºC; $[\alpha]_D^{31}$ (CH_3-OH): -1.0; ^{1}H NMR (DMSO-d_6): δ 7.50-6.20 (m, 4H, Ar-H), 4.30-3.50 (m, 2H, -OCH_2), 3.45-2.95 (2H, m, N-CH), 2.10-0.94 (11H, m, -(CH),-$(CH_2)_5$); ^{13}C NMR data: 146.1 (C-1'), 129.1(C-3'),128.3 (C-5') 123.0 (C-4'), 124.6 (C-2'), 118.5 (C-6'), 68.6 (C-9), 45.2 (C-3a), 41.6 (C-8a), 33.2 (C-7a), 31.2 (C-4), 30.2 (C-7), 28.3 (C-6), 28.1 (C-8), 23.6 (C-5); ^{31}P NMR data: δ 22.6; IR(KBr): 1270 (P=O), 1210, 940 (P-O-C_{aryl}) cm^{-1}; Anal. Calcd for $C_{15}H_{19}NO_3ClP$: C, 54.97, H, 5.84, N, 4.27. Found. C, 54.93, H, 5.77, N, 4.18.

2-(4-Chlorophenoxy)- perhydro-2λ^5 –[1,3,2] oxaza phospholo[3,4-a] indol 2-one (**3c**):Yield 70%; m.p.127-29 ºC; $[\alpha]_D^{31}$ (CH_3-OH): -0.2; ^{1}H NMR ($CDCl_3$): δ 7.41 (2H, d, *J*=7.8 Hz, Ar-H), 7.29 (2H, d, *J*=7.4 Hz, Ar-H), 4.34-3.52 (m, 2H, -OCH_2), 3.48-2.93 (2H, m, N-CH), 2.06-0.96 (11H, m, -(CH),-$(CH_2)_5$); ^{13}C NMR data: 151.5 (C-1'), 128.2 (C-3', C-5'), 125.4 (C-4'), 114.0 (C-2', C-6'), 69.9 (C-9), 44.8 (C-3a), 44.3 (C-8a), 34.2 (C-7a), 31.9 (C-7), 30.3 (C-4), 29.6 (C-8), 28.9 (C-6), 23.4 (C-5); ^{31}P NMR data: δ 23.0; IR(KBr): 1270 (P=O), 1210, 936 (P-O-C_{aryl}) cm^{-1}; LC-MS m/z 327 [M^{+}], 329 [32, M+2] Anal. Calcd for $C_{15}H_{19}NO_3ClP$: C, 54.97, H, 5.84, N, 4.27. Found. C, 54.94, H, 5.78, N, 4.21.

2-(4-Nitrophenoxy)- perhydro-2λ^5 –[1,3,2] oxaza phospholo[3,4-a] indol 2-one (**3d**): Yield 71%; m.p.124-26 ºC; $[\alpha]_D^{31}$ (CH_3-OH): - 2.0; ^{1}H NMR (DMSO-d_6): δ 8.11 (2H, d, *J*=9.0 Hz, Ar-H), 6.92 (2H, d, *J*=9.0 Hz, Ar-H), 4.30-3.52 (m, 2H, -OCH_2), 3.43-2.91 (2H, m, N-CH), 2.10-0.91 (11H, m, -(CH),-$(CH_2)_5$); ^{13}C NMR data: 153.5 (C-1'), 128.2 (C-3', C-5'), 141.2 (C-4'), 116.0 (C-2', C-6'), 68.9 (C-9), 44.4 (C-3a), 44.1 (C-8a), 33.9 (C-7a), 31.5 (C-7), 30.2 (C-4), 29.9 (C-8), 28.5 (C-6), 23.8 (C-5); ^{31}P NMR data: δ 19.5; IR(KBr): 1270 (P=O), 1220, 935 (P-O-C_{aryl}) cm^{-1}; APCI- MS 339 [70, M +1] $^{+}$ Anal. Calcd for $C_{15}H_{19}N_2O_5P$: C, 53.26, H, 5.66, N, 8.28. Found. C, 53.20, H, 5.59, N, 8.21

2-(3-Pyridyloxy) - perhydro-2λ^5 –[1,3,2] oxaza phospholo[3,4-a] indol 2-one **(3e):** Yield 71%; m.p.124-26 ºC; $[\alpha]_D^{31}$ (CH_3-OH): - 1.7; ^{1}H NMR (DMSO-d_6): 7.35-7.05 (m, 4H, Ar-H), 4.30-3.52 (m, 2H, -OCH_2), 3.43-2.91 (2H, m, N-CH), 2.10-0.91 (11H, m, -(CH),-$(CH_2)_5$); ^{31}P NMR data: δ 21.6; IR(KBr): 1265 (P=O), 1225, 945 (P-O-C_{aryl}) cm^{-1}; Anal. Calcd for $C_{14}H_{19}N_2O_3P$: C, 57.14, H, 6.51, N, 9.52. Found. C, 57.10, H, 6.45, N, 9.46.

Ethyl 3-[(2-oxoperhydro-2λ^5 –[1,3,2] oxaza phospholo[3,4-a] indol-2-ylamino]3- phenylacetate (**3f):** Yield 72% ; viscous liquid, $[\alpha]_D^{31}$ (CH_3-OH): - 0.9; ^{1}H NMR (DMSO-d_6): δ 7.29-6.31 (5H, m, Ar-H), 4.39-4.24 (2H, m, -OCH_2),3.92-3.85 (1H, NH-CH), 3.32-3.26 (2H, m, N-CH), 2.55 (1H, s, NH), 2.45-1.82 (11H, m, -(CH),-$(CH_2)_5$),1.15 (3H, t, *J*=7.5 Hz, -CH_3); ^{13}C-NMR data: 169.4 (C-8'), 133.2 (C-2'), 128.2 (C-3', C-7'), 127.9 (C-4', C-6'), 125.2 (C-5'), 61.7 (C-9ª, C-9'), 51.4 (C-1'), 44.2 (C-3a), 44.6 (C-8a), 33.5 (C-7a), 31.1 (C-7), 30.4 (C-4), 29.2 (C-8), 28.8 (C-6), 23.2 (C-5); 16.6(C-10'); ^{31}P NMR data: δ 14.53 ; IR(KBr): 3410 (-NH), 1728 (C=O), 1237 (P=O)

cm^{-1} ; APCI -MS m/z(%) 378 [66 M] $^+$ 379 [25 M+1] $^+$ 380 [10 M+2] $^+$ Anal. Calcd for $C_{19}H_{27}N_2O_4P$: C, 60.31, H, 7.19, N, 7.40. Found. C, 60.25, H, 7.16, N, 7.36.

Ethyl 3-(4-hydroxyphenyl)3-[(2-oxoperhydro-2λ^5 –[1,3,2] oxaza phospholo[3,4-a] indol-2-ylamino]acetate **(3g):** Yield 74 %; viscous liquid; $[\alpha]_D^{31}$ (CH_3-OH): -0.5; ^{1}HNMR (DMSO-d_6): δ 9.90 (1H, s, Ar-OH), 7.12 (2H, d, *J*=9.0 Hz, Ar-H), 6.76 (2H, d, *J*=9.0 Hz, Ar-H), 4.50-4.32 (4H, m, -OCH_2), 3.89-3.74 (1H, m, NH-CH), 3.47-3.30 (2H, m, N-CH), 2.95 (1H, s, -NH) 2.63-1.90 (11H, m, -(CH),-$(CH_2)_5$),1.12 (3H, t, *J*=7.0 Hz, -CH_3); ^{13}C-NMR data: 167.8 (C-8'), 151.7 (C-5'), 128.5 (C-3', C-7'), 127.2 (C-2'), 115.2 (C-4', C-6'), 62.2 (C-9ª, C-9'), 51.8 (C-1'), 44.3 (C-3a), 44.0 (C-8a), 33.6 (C-7a), 31.2 (C-7), 30.5 (C-4), 29.4 (C-8), 28.1 (C-6), 23.2 (C-5), 16.2 (C-10'); ^{31}P NMR data: δ 23.02 ; IR(KBr): 3514(-OH), 3326 (-NH), 1738 (C=O),1265 (P=O) cm^{-1} ; LC-MS 395 [650, M +1] $^+$ Anal. Calcd for $C_{19}H_{27}N_2O_5P$: C, 57.86, H, 6.90, N, 7.10. Found. C, 57.83, H, 6.85, N, 7.06.

Methyl 4-(4-hydroxyphenyl)-3-[(2-oxoperhydro-2λ^5 –[1,3,2] oxaza phospholo[3,4-a] indol-2-ylaminoamino]propanoate **(3h):** Yield 70% ; viscous liquid, $[\alpha]_D^{31}$ (CH_3-OH): - 0.6; ^{1}H NMR (DMSO-d_6): δ 10.10 (1H, s, Ar-OH), 7.29-6.31 (4H, m, Ar-H), 4.30-4.21 (2H, m, -OCH_2), 3.32-3.26 (3H, m, N-CH), 2.38-1.76 (11H, m, -(CH),-$(CH_2)_5$),1.59-1.38 (2H, m, -N-CH-CH_2)1.10 (3H, t, *J*=7.5 Hz, -CH_3); ^{31}P NMR data: δ 13.0; IR(KBr): 3415 (-OH),1728 (C=O), 1237 (P=O), 3319 (-NH) cm^{-1} ; Anal. Calcd for $C_{19}H_{27}N_2O_5P$: C, 57.86, H, 6.90, N, 7.10. Found. C, 57.82, H, 6.93, N, 7.13.

Ethyl 3-[(2-oxoperhydro-2λ^5 –[1,3,2] oxaza phospholo[3,4-a] indol-1-yl]-1-isoindoline carboxylate **(3i).** Yield 76% ; viscous liquid, $[\alpha]_D^{31}$ (CH_3-OH): - 0.8; ^{1}H NMR (DMSO-d_6): δ 7.81 - 6.92 (4H, m, Ar-H), 4.34-4.19 (2H, m, -OCH_2) 3.82 (3H, s, -OCH_3),3.72-3.64 (1H, m, NH-CH-CO), 3.52-3.45 (2H, m, N-CH), 3.37 (1H, s, NH), 2.6 (2H, d, J=6.6 Hz, Ar-CH_2-CH-), 1.89-0.96 (11H, -(CH),-$(CH_2)_5$); ^{31}P NMR data: δ 14.53; IR(KBr): 1746 (C=O), 1214 (P=O) cm^{-1}; Anal. Calcd for $C_{20}H_{27}N_2O_4P$: C, 61.53, H, 6.97, N, 7.18. Found. C, 61.59, H, 6.94, N, 7.12.

Methyl 4-(1H-3-indolyl)-3-[(2-oxoperhydro-2λ^5 –[1,3,2] oxaza phospholo[3,4-a] indol-2-ylamino]propanoate (**3j):** Yield 73% ; viscous liquid; $[\alpha]_D^{31}$ (CH_3-OH): - 0.7; ^{1}H NMR (DMSO-d_6): δ 10.15 (1H, s, -NH), 7.81 - 6.92 (4H, m, Ar-H), 6.12 (1H, s, -CH) 4.34-4.19 (2H, m, -OCH_2) 3.78 (3H, s, -OCH_3),3.72-3.64 (1H, m, NH-CH-CO), 3.52-3.45 (2H, m, N-CH), 3.37 (1H, s, NH), 2.6 (2H, d, J=6.6 Hz, Ar-CH_2-CH-), 1.89-0.96 (11H, -(CH),-$(CH_2)_5$); ^{31}P NMR data: δ13.5 ; IR(KBr): 3326 (-NH), 1746 (C=O), 1214 (P=O) cm^{-1}; LC-MS m/z(%) 417 [80 M+1] $^+$ Anal. Calcd for $C_{21}H_{28}N_3O_4P$: C, 60.42, H, 6.76, N, 10.07. Found. C, 60.36, H, 6.70, N, 10.02.

RESULTS AND DISCUSSION

The synthesis of substituted 1,3,2-oxazaphosphole 2-ones (**3a-j)** is accomplished in a two-step process (Scheme 1). The synthetic route involves the condensation of octahydro-1H-indol(3aS,7aS)-2-yl(2S) methanol (**1**) with phosphoryl chloride in dry tetrahydrofuran (THF) in the presence of triethylamine (TEA) at 0-20 ºC to afford the corresponding monochloride

intermediate, 2-chloro-perhydro-2λ^5- [1,3,2] oxazaphospholo [3,4a] indol 2-one **(2)**. In the second step the intermediate (**2**) was reacted with various phenols and amino acid ester hydrochlorides in dry THF in the presence of TEA to obtain the title compounds **3a-l** in high yields. The second step of the reaction was completed in 2-3 h at 40-45 ºC with stirring. Progress of the reaction was monitored by TLC (3:7 ethyl acetate: hexane). The cyclised products **3a-j** were isolated by filtration to remove TEA hydrochloride, followed by evaporation of the filtrate in a rotaevaporator. Further purification was carried out by washing the residue with hexane followed by column chromatography using hexane-ethyl acetate (4:2) mixture as an eluent.

The compounds **3a-j** exhibited IR absorption bands for P=O, C=O and P-NH in the regions 1269-1214, 1746-1721 and 3410-3326 cm^{-1} [13] respectively. The –NH proton gave a singlet at δ 3.55-2.42, the C-9 methyleneoxy hydrogens resonated as multiplets at δ 4.40-3.90. The N-CH proton gave a multiplet at δ 3.68-2.92. In the ^{13}C-NMR spectra, C-9 resonated at δ 68.3-66.8. The chemical shifts of the α-carbon of the amino acid ester group appeared at δ 59.8-52.6 [14]. The remaining carbon resonances are observed in the expected region. ^{31}P-NMR chemical shifts were observed in the region 22.19-15.94 ppm [15]. The LC-MS and APCI-MS data of **3a-j** showed their protonated molecular ions.

Table 1. Antibacterial activity of compounds 3a-j.

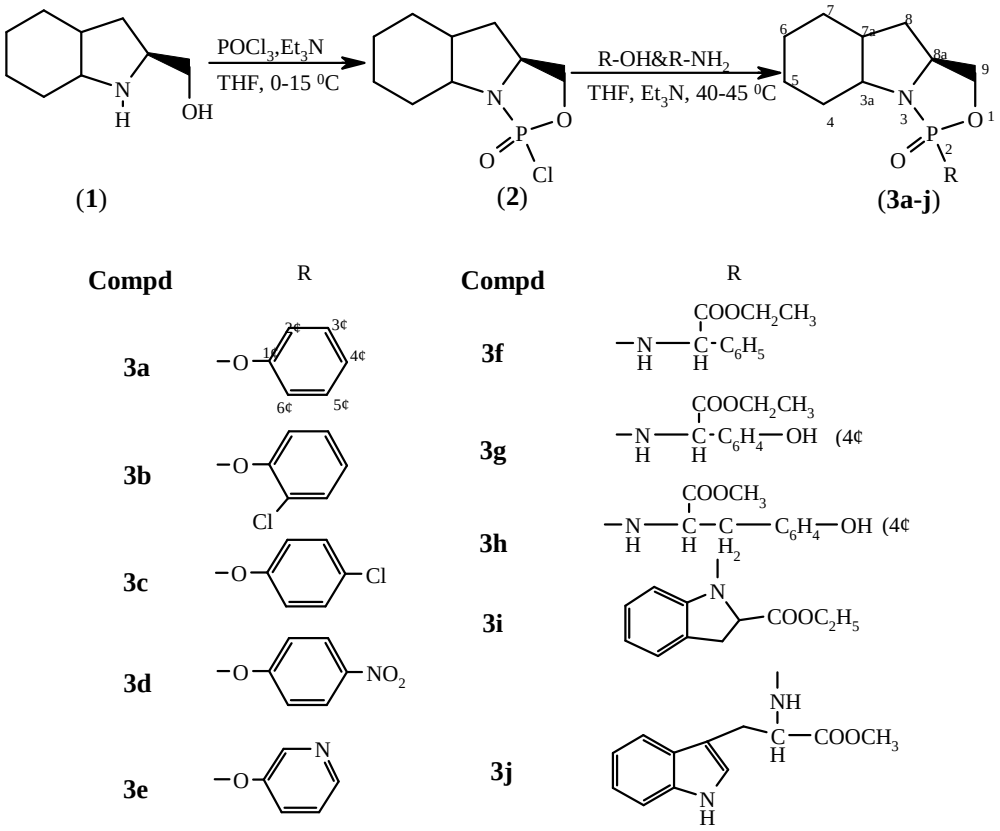
Compd.	*Staphylococcus aureus*			*Bacillus subtilis*			*Escherichia coli*			*Klebsiella pneumoniae*		
	100 µg/mL	200 µg/mL	300 µg/mL	100 µg/mL	200 µg/mL	300 µg/mL	100 µg/mL	200 µg/mL	300 µg/mL	100 µg/mL	200 µg/mL	300 µg/mL
3a	6.8	7.2	8.6	5.3	6.9	8.3	5.9	7.3	8.9	5.2	6.7	8.5
3b	10.0	11.2	13.1	8.0	10.2	11.1	9.6	10.2	11.6	10.1	11.2	13.0
3c	13.6	14.2	15.9	10.1	12.4	15.0	12.3	13.0	13.6	11.0	13.2	18.1
3d	14.2	14.9	15.6	13.2	14.5	16.0	12.9	13.6	14.5	11.0	12.2	15.0
3e	16.2	17.1	18.3	15.3	16.7	17.2	13.2	14.4	16.0	13.1	16.0	19.2
3f	10.2	13.2	15.2	12.1	13.6	14.0	11.5	12.0	13.1	11.0	12.8	14.1
3g	12.2	14.1	15.1	11.3	12.6	13.2	12.0	13.1	15.2	12.6	12.9	13.5
3h	10.0	11.1	13.2	8.2	10.2	11.2	5.0	6.2	8.1	7.4	8.2	10.0
3i	14.0	15.1	17.0	10.1	12.0	13.2	12.1	14.2	17.0	12.0	12.5	15.3
3j	12.1	15.2	19.0	9.3	13.0	15.8	8.2	12.3	14.0	9.5	15.0	16.0
Gentamycin	19.0			18.0			19.0			18.0		

Table 2. Antifungal activity of compounds 3a-j.

Compd.	Zone of inhibition (mm)			
	Colletotrichum gloeosporioides		*Sclerotium rolfsii*	
	250 µg/mL	500 µg/mL	250 µg/mL	500 µg/mL
3a	10	10.2	9.6	9.8
3b	11.2	13.0	10.6	12.0
3c	12.6	13.3	14.1	14.6
3d	14.2	14.9	13.2	14.3
3e	12.6	13.0	11.0	12.4
3f	13.2	13.9	12.5	13.1
3g	11.2	12.3	12.0	12.9
3h	13.6	14.5	12.9	14.6
3i	12.8	14.2	13.2	15.6
3j	13.2	14.6	12.4	12.3
Carbendazim	18.0	19.5	18.0	19.3

Antimicrobial activity

All the compounds (**3a-j**) were screened for their antibacterial activity against *Staphylococcus aureus, Klebsiella pneumoniae, Escherichia coli* and *Bacillus subtils*. The *in vitro* anti bacterial activity of the compounds was tested by disc diffusion method [16] in nutrient agar medium at three different concentrations (100, 200, 300 µg/mL) in DMSO. The solutions were added to each filter disc, and the plates were incubated at 36 °C and examined for zone of bacterial inhibition around each disc after 24 h. Results were compared with the activity of the standard antibiotic Gentamycin. The *in vitro* antifungal activity of the compounds were tested by disc diffusion method [16] against *Colletotrichum gloeosporioides*, *Sclerotium rolfsii* at two different concentrations (250, 500 µg/mL) in DMSO. Fungal cultures were grown on potato dextrose agar at 25 °C and spore suspension was adjusted to 10^5 spores/mL. Results were compared with the activity of the standard anti fungal Carbendazim. All the title compounds showed moderate activity against both bacteria and fungai and these results are presented in **Table 1** and **Table 2**.



Scheme 1

CONCLUSION

An elegant synthesis of novel 5-membered phosphorus heterocycles containing N, O, P and three chiral centers with high yields is accomplished and their antimicrobial activity was evaluated. They exhibited promising antimicrobial activity.

Acknowledgement
The authors thank UGC (F.No. 34-356/2008(SR), New Delhi, India for providing financial assistance.

REFERENCES

[1] Hetherington, L.; Greedy, B.; Gouverneur, V. *Tetrahedron* **2000,** *56,* 2053.
[2] Bartlett, P .A.; Hanson, J. E.; Gannousis, P. P. *J. Org. Chem*. **1990,** *55,* 6268.
[3] Stewart, J. D.; Liotta, L. J.; Benkovic, S. J. *Acc. Chem. Res*. **1993,** *26,* 396.
[4] Rynk, R. *Compost Sci. Util*. **2000,** *8,* 1.
[5] Kumar, S.; Mukerji, K. G.; Lal, R. *Crit. Rev. Microbiol*. **1996,** *22,* 1.
[6] Fest, C.; Schmidt, K. J. 1982 *The Chemistry of Organophosphorus Pesticides.* Springer-Verlag, Berlin **12.**
[7] Venugopal, M.; Sankar Reddy, B.; Devendranath Reddy, C.; Berlin, K. D. *J. Heterocycl. Chem.* **2001**, *38,* 275.
[8] Katrizky, A. R.; Ress, C. W.; Scriven, E. F. V. *Comprehensive Heterocyclic Chemistry II*; Pergamon Press: Oxford, U.K.. **1996.**
[9] Reddy, P. V. G.; Babu, Y. H.; Reddy, C. S.; Srinivasulu, D. *Heteroatom Chem.* **2002,** ***13***, 340.
[10] Weil, E. D. *Handbook of Organophosphorus Chemistry*. Engel R., ed.; Marcel Dekker Inc.: New York, **1992**.
[11] Srinivasulu, K.; Kumar, M. A.; Raju, C. N.; Reddy, C. S. *Arkivoc*. **2007**, *xiv,* 100.
[12] Basavaiah, D.; Reddy, G. J.; Chandrashekar, V. *Tetrahedron: Asymmetry*. **2001**, *12***,** 685.
[13] Silverstein, R. M.; Webster, F. X. *Spectrometric Identification of Organic Compounds*, 5th Edition, John Wiley & Sons, New York, **1998**.
[14] Anil Kumar, M.; Suresh Kumar, K.; Devendranath Reddy, C.; Naga Raju, C.; Suresh Reddy, C.; Hari Krishna, P.; *S.Afr. J. Chem*. **2009,** *62,* 26.
[15] Quin, L. D.; Verkade, J. G. *Phosphorus-31 NMR Spectral Properties Compound Characterization and Structural Analysis*, VCH Publishers: New York, **1994.**
[16] Benson, J. *Microbiological Applications*.5th edn., Brown W C Publications, Boston, **1990.**
[17] Armarego, W. L. F.; Perrin, D. D. *Purification of Laboratory Chemicals*, 4th Edn. (Butterworth, Heinemann, Oxford) OX2 8DP, **1997**.