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Synthesis, characterization and antimicrobial evaluation of novel compounds containing 2- phenoxy-1, 3, 2-benzodioxa phosphole-2-oxide and 1, 3, 4 -oxadiazole system

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ABSTRACT

New novel derivatives of 2-(4-substituted phenoxy)-1, 3, 2-benzodioxa phosphole-2-oxide with 1, 3, 4 -oxadiazole System were prepared by the reaction between 2-(4-substituted phenoxy)-1,3,2-benzodioxaphosphole-4-carbohydrazide-2-oxides 3(a-e) with p-substituted acetophenone (4) yielded the corresponding 2-(4-substituted phenoxy)-N'-(1-(4-substituted phenyl) ethylidene)-1,3,2-benzodioxaphosphole-4-carbohydrazide-2-oxide 5(a-t). These were allowed to undergo cyclization to develop 2-aryl-3-acetyl-1,3,4-oxadiazole system in the presence of aceticanhydride to give corresponding final products 1-(2-(4-substituted phenyl)-5-(2-(4-substituted phenoxy)-1,3,2-benzodioxa phosphole-4-yl-2-oxide)-2-methyl-1,3,4-oxadiazole-3(2H)-yl) ethanone 6(a-t). The chemical structures of these newly synthesized compounds were characterized by ^{1}H-NMR, Mass, IR, C^{13}-NMR and P^{31}-NMR Spectral data. These newly synthesized compounds 6(a-t) were screened for their antibacterial and antifungal activity.

Keywords: Benzodioxaphospholes, cyclization, 1,3,4-Oxadiazoles, Antibacterial and Antifungal activity.

INTRODUCTION

The Organophosphorous heterocyclic compounds chemistry received much attention of chemists in past two decades due to their wide range of applications in the field of agriculture, medicine and industry [1, 2]. Some organophosphorus compounds have been described in the literature as inhibitors of bacterial [3], herbicides, insecticides, pesticides [4, 5], antifungal agents [6], anti-HIV [7], anti-cancer [8], antiviral and anti-inflammatory [9]. An important group of this class is 1, 3, 2-benzodioxaphospholes which have been used in many reactions and synthesis of new organic compounds.

1,3,4-Oxadiazole system belongs to the group of heterocycles that exhibit antibacterial [10], anticonvulsant [11], anticancer activities and are used to fight infections involving AIDS. For instance, 2-amino-1, 3, 4-Oxadiazoles act as muscle relaxants and show antimitotic activity. Analgesic, anti-inflammatory [12, 13], anticonvulsive, diuretic and antiemetic properties are exhibited by 5-aryl-2-hydroxymethyl-1,3,4-Oxadiazole derivatives [14,15]. 2-hydroxyphenyl-1,3,4-Oxadiazole acts as a hypnotic and as a sedative. 1,3,4-Oxadiazoles containing phosphorous ester moiety exhibit insecticidal and pesticidal property.

In view of these observations, it appeared of interest to synthesis some novel 2- phenoxy-1, 3, 2-benzodioxa phosphole-2-oxide derivatives with 1, 3, 4 -oxadiazole System.

MATERIALS 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 alluminium sheet of silica gel $60F_{254,}$ E-Merk, Germany using iodine as visualizing agent. Melting points 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 unit, Instrument. All H^1 and C^{13}-NMR spectra were recorded on a Varian XL-300 spectrometer operating at 300MHz for H^1-NMR and 75.46 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-d6 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 analyses were recorded on a Carlo Erba 1108 Elemental Analyser, Central Drug Research Institute, Lucknow, India.

Preparation of Intermediates:

4- substituted phenyl phosphorodichloridates :

Phosphorous oxychloride (0.1mole) in dry benzene (60ml) was taken into a three necked flask (500ml) 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. Dry trimethyl amine (0.1mol) and dry benzene (50ml) were added into the flask slowly while stirring. To this mixture, freshly distilled phenol (0.1mol) in dry benzene (60ml) was added drop wise through the dropping funnel. The addition took about 30 minutes and the whole reaction mixture was refluxed with vigorous stirring for 10 hours. The reaction mixture was cooled and the solid triethylamine hydrochloride was filtered off. The solvent from the filtrate was removed under reduced pressure in a rotaevaporator. The dark brown liquid remained was subjected to fractional distillation and the major product distilling at 118-124^{0}C / 11mm was collected as colorless glassy viscous liquid [16].

Other substituted phenyl phosphorodichloridates **1(a-e)** were prepared by the same procedure [17-20] by treating equimolar quantities of phosphorousoxychloride and respective substituted phenols in benzene in the presence of triethylamine.

2-(4-substitutedphenoxy)-1, 3, 2-benzodioxa phosphole-4-carbohydrazide-2-oxides 3(a-e)

The cyclization of 2, 3-dihydroxy ethyl benzoate with various aryl phosphoro dichloridates **1(a-e)** occurred smoothly under heating and stirring conditions in dry toluene- tetra hydro furan (THF) mixture in the presence of triethyl amine in 6hrs [21] and yields Ethyl 2-(4-substituted phenoxy)-1, 3, 2-benzodioxa phosphole-4- carboxylate-2-oxides **2(a-e).** A solution of **2(a-e)** (0.01mole) and hydrazine hydrate in absolute ethanol- tetrahydrofuran (THF) (1:1) mixture was refluxed for 5 hours [22, 23]. The course of progress of the reaction was monitored by TLC. After completion of the reaction the solvent was removed in rotaevaporator. The crude products 2-(4-substitutedphenoxy)-1, 3, 2-benzodioxa phosphole-4-carbohydrazide-2-oxides **3(a-e)** were obtained as brown gummy solids. Fairly pure and stable products are obtained from these gums with 2-propanol [24]. The compounds thus obtained were characterized by their elemental analysis and spectral data (IR, H^1-NMR, P^{31}-NMR).

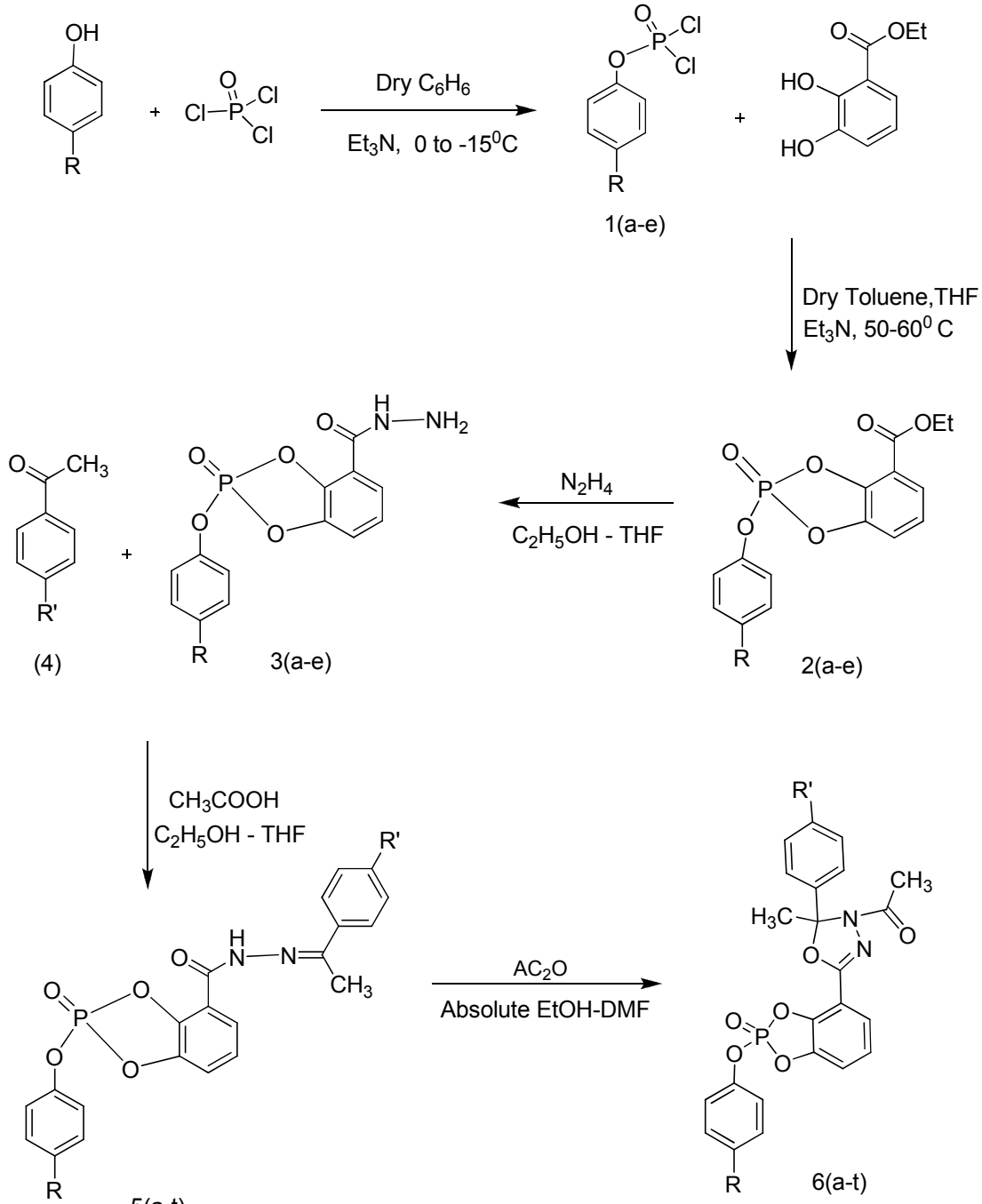
Physical, analytical and spectral data for the compounds 3(a-e):

2-(phenoxy)-1, 3, 2-benzodioxa phosphole-4-carbohydrazide-2-oxide **3(a):**

Yield: 60%; M.p: 76-78ºC; IR (KBr): 3457, 3413(-NH_2), 3220 (-NH), 1690(C=O), 1258 (P=O), 954, 1196 (P-O-C) cm^{-1}; ^{1}HNMR (300MHz, DMSO-*d6*): δ 4.21(s, 2H, NH_2), 8.75(s,1H, NH), 6.73 -7.34(m, 8H, C_6H_5 ring A and C_6H_3 of ring B); ^{31}PNMR (161.89 MHz, DMSO-*d6*): δ -9.12 ppm. Anal. Calcd.(%) for $C_{13}H_{11}N_2O_5P$: C 50.99, H 3.62, N 9.15; Found: C 50.92, H 3.58, N 9.07.

2-(4-methyl phenoxy)-1, 3, 2-benzodioxa phosphole-4-carbohydrazide-2-oxide **3(b):**

Yield: 55%; M.p: 69-71ºC; IR (KBr): 3452, 3439(-NH_2), 3206 (-NH), 1685(C=O), 1252 (P=O), 949, 1190 (P-O-C) cm^{-1}; ^{1}HNMR (300MHz, DMSO-*d6*): δ 4.19(S, 2H, NH_2), 8.75(S, 1H, NH), 6.61-7.34 (m, 7H, C_6H_4 ring A and C_6H_3 ring B), 3.10 ppm(S,3H,Ar-CH_3); ^{31}PNMR (161.89 MHz, DMSO-*d6*): δ -7.25ppm. Anal. Calcd.(%) for $C_{14}H_{13}N_2O_5P$: C 52.51, H 4.09, N 8.75; Found: C 52.43, H 4.02, N 8.69.



Comp	6a	6b	6c	6d	6e	6f	6g	6h	6i	6j
R	H	CH_3	Cl	Br	NO_2	H	CH_3	Cl	Br	NO_2
R'	- H	- H	- H	- H	- H	p - Cl	p - Cl	p - Cl	p - Cl	p - Cl

Comp	6k	6l	6m	6n	6o	6p	6q	6r	6s	6t
R	H	CH_3	Cl	Br	NO_2	H	CH_3	Cl	Br	NO_2
R'	p-Br	p-Br	p-Br	p-Br	p-Br	p-NO_2	p-NO_2	p-NO_2	p-NO_2	p-NO_2

2-(4-chloro phenoxy)-1, 3, 2-benzodioxa phosphole-4-carbohydrazide-2-oxides **3(c):**
Yield: 50%; M.p: 86-88ºC; IR (KBr): 3464, 3454(-NH_2), 3209 (-NH), 1689(C=O), 1254 (P=O), 952, 1192 (P-O-C) cm^{-1}; ^{1}HNMR (300MHz, DMSO-*d6*): δ 4.25(S, 2H, NH_2), 8.78(S, 1H, NH), 6.67-7.34(m, 7H, C_6H_4 ring A and C_6H_3 ring B).; ^{31}PNMR (161.89 MHz, DMSO-*d6*): δ -9.42 ppm. Anal. Calcd.(%) for $C_{13}H_{10}N_2O_5PCl$: C 45.83, H 2.96, N 8.22; Found: C 45.76, H 2.87, N 8.15.

2-(4-bromo phenoxy)-1, 3, 2-benzodioxa phosphole-4-carbohydrazide-2-oxides **3(d):**
Yield: 50%; M.p: 92-94ºC; IR (KBr): 3464, 3454(-NH_2), 3210 (-NH), 1685(C=O), 1260 (P=O), 954, 1194 (P-O-C) cm^{-1}; ^{1}HNMR (300MHz, DMSO-*d6*): δ 4.28(S, 2H, NH_2), 8.78(S, 1H, NH), 6.62-7.34(m, 7H, C_6H_4 ring A and C_6H_3 ring B); ^{31}PNMR (161.89 MHz, DMSO-*d6*): δ -8.76 ppm. Anal. Calcd.(%) for $C_{13}H_{10}N_2O_5PBr$: C 40.54, H 2.62, N 7.27; Found: C 40.49, H 2.57, N 7.18.

2-(4-nitro phenoxy)-1, 3, 2-benzodioxa phosphole-4-carbohydrazide-2-oxides **3(e):**
Yield: 64%; M.p: 104-106ºC; IR (KBr): 3468, 3455(-NH_2), 3214(-NH), 1684(C=O), 1268 (P=O), 960, 1204 (P-O-C) cm^{-1}; ^{1}HNMR (300MHz, DMSO-*d6*): δ 4.27(S.2H, NH_2), 8.80(S, 1H, NH), 6.99-8.02(m, 7H, C_6H_4 ring A and C_6H_3 ring B); ^{31}PNMR (161.89 MHz, DMSO-*d6*): δ -8.87 ppm. Anal. Calcd.(%) for $C_{13}H_{10}N_3O_7P$: C 44.46, H 2.87, N 11.96; Found: C 44.35, H 2.74, N 11.89.

RESULTS AND DISCUSSION

Typical procedure for the synthesis of 2-(4-substituted phenoxy)-N'-(1-(4-substituted phenyl) ethylidene)-1,3,2-benzodioxaphosphole-4-carbohydrazide-2-oxide 5(a-t).
A mixture of 2- phenoxy-1,3,2-benzodioxa phosphole-4-carbohydrazide-2-oxides **(3a)** and acetophenone was refluxed [10,13] in absolute ethanol- tetrahydrofuran (1:1) solvent mixture containing a catalytic amount of glacial acetic acid for 4 hours. The course of progress of the reaction was monitored by TLC. After completion of the reaction the solvent was removed in rotaevaporator. The crude product was obtained as a reddish brown gummy solid. Fairly pure and stable products are obtained from these gums with 2-propanol and petroleum ether (60-80^{0}C) solvent mixture to afford 2-phenoxy-N'-(1-(phenyl) ethylidene) - 1,3,2-benzodioxaphosphole-4-carbohydrazide-2-oxide (5a). Similar procedure was adopted to synthesize 5(b-e) from 5(b-e)

The above reaction of **(5a)** with acetophenone has been extended to p–chloro acetophenone, p-bromo acetophenone and p–nitro acetophenone.
Synthesis of 1-(2-(4-substituted phenyl)-5-(2-(4-substituted phenoxy)-1,3,2-benzodioxa phosphole-4-yl-2-oxide)-2-methyl-1,3,4-oxadiazole-3(2H)-yl) ethanone 6(a-t)
In a typical procedure a mixture of hydrazone **(5a)** and excess of acetic anhydride were dissolved in absolute ethanol-DMF solvent mixture [25, 26]. Reaction mixture was refluxed for 3 hours and then kept at room temperature overnight. The progress of the reaction was monitered by TLC. After completion of the reaction the solvent was removed in rotaevaporator. The gummy brown solid was recrystalised from 2-propanol-petroleum ether (60-80^{0}C) solvent mixture to afford 1-(2-(phenyl)-5-(2-phenoxy)-1,3,2-benzo dioxa phosphole-4-yl-2-oxide)-2-methyl-1,3,4-oxadiazole-3(2H)-yl) ethanone **(6a)** in 55% yield.

The cyclization reaction was extended to other hydrazones **5(b–t)** and in each case the respective substituted acetophenones were used to get **6(b-t)** in moderate yields (56-44%).

The structures of these newly synthesized compounds **6(a–t)** were characterized by their elemental analysis and spectral data (IR, ^{1}H-NMR, C^{13}-NMR, P^{31}-NMR and Mass).

Physical, analytical and spectral data for the compounds 6(a-t):
1-(2-(phenyl)-5-(2-(phenoxy)-1,3,2-benzodioxaphosphole-4-yl-2-oxide)-2-methyl-1,3,4-oxadiazole-3(2H)-yl) ethanone 6(a):
Yield: 40%; M.p: 138-140ºC; IR (KBr): 1690(C=O), 1620(C=N), 1267 (P=O), 963, 1197(P-O-C) cm^{-1}; ^{1}HNMR (300MHz, DMSO-*d6*): δ 2.04 (s, 3H, $COCH_3$), 1.83 (s, 3H, CH_3 of oxadiazole ring), 6.81-7.38 (m, 13H, for C_6H_5, C_6H_3 and C_6H_5 of three phenyl groups); C^{13}-NMR (75.46 MHz, DMSO-*d6*): δ 150.3(C-1),120.3(C-2&6),130.1 (C-3&5), 121.3(C-4) of ringA, 128.5(C-4'), 123.2(C-5'), 122.8(C-6'), 114.5(C-7'), 145.3(C-8'), 145.0(C-9') of ring B, 142.2(C-1"), 126.8(C-2"&6"), 128.4(C-3"&5"),126.5(C-4") of ring C (phenyl group attached to Oxadiazole) and 90.1(C-2), 157.0(C-5), 27.9(-CH_3 of oxadiazole), 168.5(-CO-), 23.7(-CH_3 of –CO-CH_3) of ring D(oxadiazole);

^{31}PNMR (161.89 MHz, DMSO-*d6*): δ -8.51 ppm. Anal. Calcd.(%) for $C_{23}H_{19}N_2O_6P$: C 61.34, H 4.25, N 6.22; Found: C 61.27, H 4.19, N 6.18.

1-(2-(phenyl)-5-(2-(4-methyl phenoxy)-1,3,2-benzodioxa phosphole-4-yl-2-oxide)-2-methyl-1,3,4-oxadiazole-3(2H)-yl) ethanone 6(b):
Yield: 45%; M.p: 152-154ºC; IR (KBr): 1685(C=O), 1622(C=N), 1276 (P=O), 965, 1194(P-O-C) cm^{-1}; ^{1}HNMR (300MHz, DMSO-*d6*): 2.03 (s, 3H, $COCH_3$), 1.83 (s, 3H, CH_3 of oxadiazole ring), 3.10(s, 3H, Ar-CH_3), 6.81-7.38 (m, 12H, for C_6H_5, C_6H_3 and C_6H_4 of three phenyl groups); C^{13}-NMR (75.46 MHz, DMSO-*d6*): δ 147.2(C-1),118.2(C-2&6),130.4 (C-3&5), 131.0(C-4), 21.3(-CH_3) of ringA, 128.3(C-4'), 123.7(C-5'), 122.5(C-6'), 114.3(C-7'), 145.7(C-8'), 145.0(C-9') of ring B, 142.5(C-1"), 126.5(C-2"&6"), 128.3(C-3"&5"),126.9(C-4") of ring C (phenyl group attached to Oxadiazole) and 90.2(C-2), 157.0(C-5), 27.7(-CH_3 of oxadiazole), 168.6(-CO-), 23.8(-CH_3 of –CO-CH_3) of ring D(oxadiazole); ^{31}PNMR (161.89 MHz, DMSO-*d6*): δ -8.45 ppm. Anal. Calcd.(%) for $C_{24}H_{21}N_2O_6P$: C 62.07, H 4.56, N 6.03; Found: C 62.01, H 4.48, N 5.98.

1-(2-(phenyl)-5-(2-(4-chloro phenoxy)-1,3,2-benzodioxa phosphole-4-yl-2-oxide)-2-methyl-1,3,4-oxadiazole-3(2H)-yl) ethanone 6(c):
Yield: 50%; M.p: 159-161ºC; IR (KBr): 1678(C=O), 1629(C=N), 1264 (P=O), 960, 1195(P-O-C) cm^{-1}; ^{1}HNMR (300MHz, DMSO-*d6*): δ 2.07 (s, 3H, $COCH_3$), 1.83 (s, 3H, CH_3 of oxadiazole ring), 6.81-7.38 (m, 12H, for C_6H_5, C_6H_3 and C_6H_4 of three phenyl groups); C^{13}-NMR (75.46 MHz, DMSO-*d6*): δ 148.3(C-1),125.7(C-2&6),131.3 (C-3&5), 126.9(C-4) of ringA, 128.5(C-4'), 123.2(C-5'), 122.8(C-6'), 114.5(C-7'), 145.3(C-8'), 145.0(C-9') of ring B, 142.2(C-1"), 126.8(C-2"&6"), 128.4(C-3"&5"),126.5(C-4") of ring C (phenyl group attached to Oxadiazole) and 90.1(C-2), 157.0(C-5), 27.9(-CH_3 of oxadiazole), 168.5(-CO-), 23.7(-CH_3 of –CO-CH_3) of ring D(oxadiazole); ^{31}PNMR (161.89 MHz, DMSO-*d6*): δ -9.07 ppm. Anal. Calcd.(%) for $C_{23}H_{18}N_2O_6PCl$: C 56.98, H 3.74, N 5.78; Found: C 56.92, H 3.67, N 5.73.

1-(2-(phenyl)-5-(2-(4-bromo phenoxy)-1,3,2-benzodioxa phosphole-4-yl-2-oxide)-2-methyl-1,3,4-oxadiazole-3(2H)-yl) ethanone 6(d):
Yield: 45%; M.p: 174-176ºC; IR (KBr): 1686(C=O), 1630(C=N), 1269 (P=O), 962, 1195(P-O-C) cm^{-1}; ^{1}HNMR (300MHz, DMSO-*d6*): δ 2.05 (s, 3H, $COCH_3$), 1.83 (s, 3H, CH_3 of oxadiazole ring), 6.81-7.43(m, 12H, for C_6H_5, C_6H_3 and C_6H_4 of three phenyl groups); C^{13}-NMR (75.46 MHz, DMSO-*d6*): δ 149.2(C-1),123.3(C-2&6),133.0 (C-3&5), 115.7(C-4) of ring A, 128.5(C-4'), 123.2(C-5'), 122.8(C-6'), 114.5(C-7'), 145.3(C-8'), 145.0(C-9') of ring B, 142.2(C-1"), 126.8(C-2"&6"), 128.4(C-3"&5"),126.5(C-4") of ring C (phenyl group attached to Oxadiazole) and 90.1(C-2), 157.0(C-5), 27.9(-CH_3 of oxadiazole), 168.5(-CO-), 23.7(-CH_3 of –CO-CH_3) of ring D(oxadiazole); ^{31}PNMR (161.89 MHz, DMSO-*d6*): δ -9.12 ppm. Anal. Calcd.(%) for $C_{23}H_{18}N_2O_6PBr$: C 52.19, H 3.43, N 5.26; Found: C 52.14, H 3.36, N 5.21.

1-(2-(phenyl)-5-(2-(4-nitro phenoxy)-1,3,2-benzodioxa phosphole-4-yl-2-oxide)-2-methyl-1,3,4-oxadiazole-3(2H)-yl) ethanone 6(e):
Yield: 45%; M.p: 167-169ºC; IR (KBr): 1690(C=O), 1620(C=N), 1267 (P=O), 963, 1197(P-O-C) cm^{-1}; ^{1}HNMR (300MHz, DMSO-*d6*): δ 2.06 (s, 3H, $COCH_3$), 1.83 (s, 3H, CH_3 of oxadiazole ring), 6.81-8.09(m, 12H, for C_6H_5, C_6H_3 and C_6H_4 of three phenyl groups)**;** C^{13}-NMR (75.46 MHz, DMSO-*d6*): δ 156.3(C-1),121.9(C-2&6),126.3 (C-3&5), 140.5(C-4) of ringA, 128.5(C-4'), 123.2(C-5'), 122.8(C-6'), 114.5(C-7'), 145.3(C-8'), 145.0(C-9') of ring B, 142.2(C-1"), 126.8(C-2"&6"), 128.4(C-3"&5"),126.5(C-4") of ring C (phenyl group attached to Oxadiazole) and 90.1(C-2), 157.0(C-5), 27.9(-CH_3 of oxadiazole), 168.5(-CO-), 23.7(-CH_3 of –CO-CH_3) of ring D(oxadiazole); ^{31}PNMR (161.89 MHz, DMSO-*d6*): δ -9.16 ppm. Anal. Calcd.(%) for $C_{23}H_{18}N_3O_8P$: C 55.76, H 3.66, N 8.48; Found: C 55.70, H 3.58, N 8.39.

1-(2-(4-chloro phenyl)-5-(2-(phenoxy)-1,3,2-benzodioxa phosphole-4-yl-2-oxide)-2-methyl-1,3,4-oxadiazole-3(2H)-yl) ethanone 6(f):
Yield: 45%; M.p: 165-167ºC; IR (KBr): 1695(C=O), 1626(C=N), 1265 (P=O), 964, 1195(P-O-C) cm^{-1}; ^{1}HNMR (300MHz, DMSO-*d6*): δ 2.04 (s, 3H, $COCH_3$), 1.83 (s, 3H, CH_3 of oxadiazole ring), 6.81-7.42 (m, 12H, for C_6H_5, C_6H_3 and C_6H_4 of three phenyl groups); C^{13}-NMR (75.46 MHz, DMSO-*d6*): δ 150.3(C-1),120.3(C-2&6),130.1 (C-3&5), 121.3(C-4) of ringA, 128.5(C-4'), 123.2(C-5'), 122.8(C-6'), 114.5(C-7'), 145.3(C-8'), 145.0(C-9') of ring B, 140.7(C-1"), 125.4(C-2"&6"), 128.6(C-3"&5"),132.3(C-4") of ring C (phenyl group attached to Oxadiazole) and 90.1(C-2), 157.0(C-5), 27.9(-CH_3 of oxadiazole), 168.5(-CO-), 23.7(-CH_3 of –CO-CH_3) of ring D(oxadiazole);

^{31}PNMR (161.89 MHz, DMSO-*d6*): δ -8.91 ppm. Anal. Calcd.(%) for $C_{23}H_{18}N_2O_6PCl$: C 56.98, H 3.74, N 5.78; Found: C 56.85, H 3.68, N 5.63.

1-(2-(4-chloro phenyl)-5-(2-(4-methyl phenoxy)-1,3,2-benzodioxa phosphole-4-yl-2-oxide)-2-methyl-1,3,4-oxadiazole-3(2H)-yl) ethanone 6(g):
Yield: 40%; M.p: 183-185ºC; IR (KBr): 1692(C=O), 1623(C=N), 1273 (P=O), 967, 1197(P-O-C) cm^{-1}; ^{1}HNMR (300MHz, DMSO-*d6*): 2.08 (s, 3H, $COCH_3$), 1.83 (s, 3H, CH_3 of oxadiazole ring), 3.10 (s, 3H, Ar-CH_3), 6.81-7.43(m, 11H, for C_6H_4, C_6H_3 and C_6H_4 of three phenyl groups); C^{13}-NMR (75.46 MHz, DMSO-*d6*): δ 147.2(C-1),118.2(C-2&6),130.4 (C-3&5), 131.0(C-4), 21.3(-CH_3) of ringA, 128.3(C-4'), 123.7(C-5'), 122.5(C-6'), 114.3(C-7'), 145.7(C-8'), 145.0(C-9') of ring B, 140.5(C-1"), 125.5(C-2"&6"), 128.6(C-3"&5"),132.3(C-4") of ring C (phenyl group attached to Oxadiazole) and 90.2(C-2), 157.0(C-5), 27.7(-CH_3 of oxadiazole), 168.6(-CO-), 23.8(-CH_3 of –CO-CH_3) of ring D(oxadiazole); ^{31}PNMR (161.89 MHz, DMSO-*d6*): δ -8.55 ppm. Anal. Calcd.(%) for $C_{24}H_{20}N_2O_6PCl$: C 57.78, H 4.04, N 5.62; Found: C 57.65, H 3.95, N 5.55.

1-(2-(4-chloro phenyl)-5-(2-(4-chloro phenoxy)-1,3,2-benzodioxa phosphole-4-yl-2-oxide)-2-methyl-1,3,4-oxadiazole-3(2H)-yl) ethanone 6(h):
Yield: 45%; M.p: 194-196ºC; IR (KBr): 1697(C=O), 1620(C=N), 1262 (P=O), 968, 1194(P-O-C) cm^{-1}; ^{1}HNMR (300MHz, DMSO-*d6*): δ 2.09 (s, 3H, $COCH_3$), 1.83 (s, 3H, CH_3 of oxadiazole ring), 6.81-7.43(m, 11H, for C_6H_4, C_6H_3 and C_6H_4 of three phenyl groups); C^{13}-NMR (75.46 MHz, DMSO-*d6*): δ 148.3(C-1),125.7(C-2&6),131.3 (C-3&5), 126.9(C-4) of ringA, 128.5(C-4'), 123.2(C-5'), 122.8(C-6'), 114.5(C-7'), 145.3(C-8'), 145.0(C-9') of ring B, 140.5(C-1"), 125.4(C-2"&6"), 128.6(C-3"&5"),132.3(C-4") of ring C (phenyl group attached to Oxadiazole) and 90.1(C-2), 157.0(C-5), 27.9(-CH_3 of oxadiazole), 168.5(-CO-), 23.7(-CH_3 of –CO-CH_3) of ring D(oxadiazole); ^{31}PNMR (161.89 MHz, DMSO-*d6*): δ -9.09 ppm. Anal. Calcd.(%) for $C_{23}H_{17}N_2O_6PCl_2$: C 53.20, H 3.30, N 5.39; Found: C 53.07, H 3.21, N 5.28.

1-(2-(4-chloro phenyl)-5-(2-(4-bromo phenoxy)-1,3,2-benzodioxa phosphole-4-yl-2-oxide)-2-methyl-1,3,4-oxadiazole-3(2H)-yl) ethanone 6(i):
Yield: 45%; M.p: 155-157ºC; IR (KBr): 1693(C=O), 1625(C=N), 1267 (P=O), 965, 1196(P-O-C) cm^{-1}; ^{1}HNMR (300MHz, DMSO-*d6*): δ 2.05 (s, 3H, $COCH_3$), 1.83 (s, 3H, CH_3 of oxadiazole ring), 6.81-7.43(m, 11H, for C_6H_4, C_6H_3 and C_6H_4 of three phenyl groups); C^{13}-NMR (75.46 MHz, DMSO-*d6*): δ 149.2(C-1),123.3(C-2&6),133.0 (C-3&5), 115.7(C-4) of ring A, 128.5(C-4'), 123.2(C-5'), 122.8(C-6'), 114.5(C-7'), 145.3(C-8'), 145.0(C-9') of ring B, 140.5(C-1"), 125.4(C-2"&6"), 128.6(C-3"&5"),132.3(C-4") of ring C (phenyl group attached to Oxadiazole) and 90.1(C-2), 157.0(C-5), 27.9(-CH_3 of oxadiazole), 168.5(-CO-), 23.7(-CH_3 of –CO-CH_3) of ring D(oxadiazole); ^{31}PNMR (161.89 MHz, DMSO-*d6*): δ -9.15 ppm. Anal. Calcd.(%) for $C_{23}H_{17}N_2O_6PClBr$: C 49.00, H 3.04, N 4.97; Found: C 48.91, H 2.98, N 4.83.

1-(2-(4-chloro phenyl)-5-(2-(4-nitro phenoxy)-1,3,2-benzodioxa phosphole-4-yl-2-oxide)-2-methyl-1,3,4-oxadiazole-3(2H)-yl) ethanone 6(j):
Yield: 50%; M.p: 187-189ºC; IR (KBr): 1696(C=O), 1622(C=N), 1275 (P=O), 963, 1198(P-O-C) cm^{-1}; ^{1}HNMR (300MHz, DMSO-*d6*): δ 2.02 (s, 3H, $COCH_3$), 1.83 (s, 3H, CH_3 of oxadiazole ring), 6.81-8.09(m, 11H, for C_6H_4, C_6H_3 and C_6H_4 of three phenyl groups)**;** C^{13}-NMR (75.46 MHz, DMSO-*d6*): δ 156.3(C-1),121.9(C-2&6),126.3 (C-3&5), 140.5(C-4) of ringA, 128.5(C-4'), 123.2(C-5'), 122.8(C-6'), 114.5(C-7'), 145.3(C-8'), 145.0(C-9') of ring B, 140.5(C-1"), 125.4(C-2"&6"), 128.6(C-3"&5"),132.3(C-4") of ring C (phenyl group attached to Oxadiazole) and 90.1(C-2), 157.0(C-5), 27.9(-CH_3 of oxadiazole), 168.5(-CO-), 23.7(-CH_3 of –CO-CH_3) of ring D(oxadiazole); ^{31}PNMR (161.89 MHz, DMSO-*d6*): δ -9.25 ppm. Anal. Calcd.(%) for $C_{23}H_{17}N_3O_8PCl$: C 52.14, H 3.23, N 7.93; Found: C 52.03, H 3.17, N 7.85.

1-(2-(4-bromo phenyl)-5-(2-(phenoxy)-1,3,2-benzodioxa phosphole-4-yl-2-oxide)-2-methyl-1,3,4-oxadiazole-3(2H)-yl) ethanone 6(k):
Yield: 40%; M.p: 178-180ºC; IR (KBr): 1698(C=O), 1614(C=N), 1269 (P=O), 969, 1195(P-O-C) cm^{-1}; ^{1}HNMR (300MHz, DMSO-*d6*): δ 2.07 (s, 3H, $COCH_3$), 1.83 (s, 3H, CH_3 of oxadiazole ring), 6.81-7.90 (m, 12H, for C_6H_5, C_6H_3 and C_6H_4 of three phenyl groups); C^{13}-NMR (75.46 MHz, DMSO-*d6*): δ 150.3(C-1),120.3(C-2&6),130.1 (C-3&5), 121.3(C-4) of ringA, 128.5(C-4'), 123.2(C-5'), 122.8(C-6'), 114.5(C-7'), 145.3(C-8'), 145.0(C-9') of ring B, 141.6(C-1"), 129.1(C-2"&6"), 131.4(C-3"&5"), 121.1(C-4") of ring C (phenyl group attached to Oxadiazole) and 90.1(C-2), 157.0(C-5), 27.9(-CH_3 of oxadiazole), 168.5(-CO-), 23.7(-CH_3 of –CO-CH_3) of ring D(oxadiazole);

^{31}PNMR (161.89 MHz, DMSO-*d6*): δ -8.52 ppm. Anal. Calcd.(%) for $C_{23}H_{18}N_2O_6PBr$: C 52.15, H 3.43, N 5.29; Found: C 52.04, H 3.37, N 5.17.

1-(2-(4- bromo phenyl)-5-(2-(4-methyl phenoxy)-1,3,2-benzodioxa phosphole-4-yl-2-oxide)-2-methyl-1,3,4-oxadiazole-3(2H)-yl) ethanone 6(l):
Yield: 40%; M.p: 190-192ºC; IR (KBr): 1694(C=O), 1617(C=N), 1271 (P=O), 964, 1194(P-O-C) cm^{-1}; ^{1}HNMR (300MHz, DMSO-*d6*): 2.03 (s, 3H, $COCH_3$), 1.83 (s, 3H, CH_3 of oxadiazole ring), 3.10(s, 3H, Ar-CH_3), 6.81-7.38 (m, 12H, for C_6H_5, C_6H_3 and C_6H_4 of three phenyl groups); C^{13}-NMR (75.46 MHz, DMSO-*d6*): δ 147.2(C-1),118.2(C-2&6),130.4 (C-3&5), 131.0(C-4), 21.3(-CH_3) of ringA, 128.3(C-4'), 123.7(C-5'), 122.5(C-6'), 114.3(C-7'), 145.7(C-8'), 145.0(C-9') of ring B, 141.6(C-1"), 129.1(C-2"&6"), 131.4(C-3"&5"), 121.1(C-4") of ring C (phenyl group attached to Oxadiazole) and 90.2(C-2), 157.0(C-5), 27.7(-CH_3 of oxadiazole), 168.6(-CO-), 23.8(-CH_3 of –CO-CH_3) of ring D(oxadiazole); ^{31}PNMR (161.89 MHz, DMSO-*d6*): δ -8.45 ppm. Anal. Calcd.(%) for $C_{24}H_{20}N_2O_6PBr$: C 53.06, H 3.71, N 5.16; Found: C 52.95, H 3.57, N 5.05.

1-(2-(4- bromo phenyl)-5-(2-(4-chloro phenoxy)-1,3,2-benzodioxa phosphole-4-yl-2-oxide)-2-methyl-1,3,4-oxadiazole-3(2H)-yl) ethanone 6(m):
Yield: 45%; M.p: 196-198ºC; IR (KBr): 1697(C=O), 1611(C=N), 1266 (P=O), 961, 1197(P-O-C) cm^{-1}; ^{1}HNMR (300MHz, DMSO-*d6*): δ 2.05 (s, 3H, $COCH_3$), 1.83 (s, 3H, CH_3 of oxadiazole ring), 6.81-7.90(m, 11H, for C_6H_4, C_6H_3 and C_6H_4 of three phenyl groups); C^{13}-NMR (75.46 MHz, DMSO-*d6*): δ 148.3(C-1),125.7(C-2&6),131.3 (C-3&5), 126.9(C-4) of ringA, 128.5(C-4'), 123.2(C-5'), 122.8(C-6'), 114.5(C-7'), 145.3(C-8'), 145.0(C-9') of ring B, 141.6(C-1"), 129.1(C-2"&6"), 131.4(C-3"&5"), 121.1(C-4") of ring C (phenyl group attached to Oxadiazole) and 90.1(C-2), 157.0(C-5), 27.9(-CH_3 of oxadiazole), 168.5(-CO-), 23.7(-CH_3 of –CO-CH_3) of ring D(oxadiazole); ^{31}PNMR (161.89 MHz, DMSO-*d6*): δ -9.18 ppm. Anal. Calcd.(%) for $C_{23}H_{17}N_2O_6PClBr$: C 49.00, H 3.04, N 4.97; Found: C 48.87, H 2.97, N 4.83.

1-(2-(4- bromo phenyl)-5-(2-(4-bromo phenoxy)-1,3,2-benzodioxa phosphole-4-yl-2-oxide)-2-methyl-1,3,4-oxadiazole-3(2H)-yl) ethanone 6(n):
Yield: 45%; M.p: 168-170ºC; IR (KBr): 1696(C=O), 1614(C=N), 1273 (P=O), 965, 1194(P-O-C) cm^{-1}; ^{1}HNMR (300MHz, DMSO-*d6*): δ 2.08 (s, 3H, $COCH_3$), 1.83 (s, 3H, CH_3 of oxadiazole ring), 6.81-7.90(m, 11H, for C_6H_4, C_6H_3 and C_6H_4 of three phenyl groups); C^{13}-NMR (75.46 MHz, DMSO-*d6*): δ 149.2(C-1),123.3(C-2&6),133.0 (C-3&5), 115.7(C-4) of ring A, 128.5(C-4'), 123.2(C-5'), 122.8(C-6'), 114.5(C-7'), 145.3(C-8'), 145.0(C-9') of ring B, 141.6(C-1"), 129.1(C-2"&6"), 131.4(C-3"&5"), 121.1(C-4") of ring C (phenyl group attached to Oxadiazole) and 90.1(C-2), 157.0(C-5), 27.9(-CH_3 of oxadiazole), 168.5(-CO-), 23.7(-CH_3 of –CO-CH_3) of ring D(oxadiazole); ^{31}PNMR (161.89 MHz, DMSO-*d6*): δ -9.14 ppm. Anal. Calcd.(%) for $C_{23}H_{17}N_2O_6PBr_2$: C 45.42, H 2.82, N 4.61; Found: C 45.28, H 2.71, N 4.49.

1-(2-(4- bromo phenyl)-5-(2-(4-nitro phenoxy)-1,3,2-benzodioxa phosphole-4-yl-2-oxide)-2-methyl-1,3,4-oxadiazole-3(2H)-yl) ethanone 6(o):
Yield: 50%; M.p: 191-193ºC; IR (KBr): 1693(C=O), 1613(C=N), 1277 (P=O), 967, 1191(P-O-C) cm^{-1}; ^{1}HNMR (300MHz, DMSO-*d6*): δ 2.09 (s, 3H, $COCH_3$), 1.83 (s, 3H, CH_3 of oxadiazole ring), 6.81-8.09(m, 11H, for C_6H_4, C_6H_3 and C_6H_4 of three phenyl groups)**;** C^{13}-NMR (75.46 MHz, DMSO-*d6*): δ 156.3(C-1),121.9(C-2&6),126.3 (C-3&5), 140.5(C-4) of ringA, 128.5(C-4'), 123.2(C-5'), 122.8(C-6'), 114.5(C-7'), 145.3(C-8'), 145.0(C-9') of ring B, 141.6(C-1"), 129.1(C-2"&6"), 131.4(C-3"&5"), 121.1(C-4") of ring C (phenyl group attached to Oxadiazole) and 90.1(C-2), 157.0(C-5), 27.9(-CH_3 of oxadiazole), 168.5(-CO-), 23.7(-CH_3 of –CO-CH_3) of ring D(oxadiazole); ^{31}PNMR (161.89 MHz, DMSO-*d6*): δ -9.25 ppm. Anal. Calcd.(%) for $C_{23}H_{17}N_3O_8PBr$: C 48.10, H 2.98, N 7.32; Found: C 47.95, H 2.85, N 7.21.

1-(2-(4-nitro phenyl)-5-(2-(phenoxy)-1,3,2-benzodioxa phosphole-4-yl-2-oxide)-2-methyl-1,3,4-oxadiazole-3(2H)-yl) ethanone 6(p):
Yield: 45%; M.p: 197-199ºC; IR (KBr): 1698(C=O), 1618(C=N), 1268 (P=O), 963, 1195(P-O-C) cm^{-1}; ^{1}HNMR (300MHz, DMSO-*d6*): δ 2.05 (s, 3H, $COCH_3$), 1.83 (s, 3H, CH_3 of oxadiazole ring), 6.81-8.19 (m, 12H, for C_6H_5, C_6H_3 and C_6H_4 of three phenyl groups); C^{13}-NMR (75.46 MHz, DMSO-*d6*): δ 150.2(C-1),120.3(C-2&6),130.1 (C-3&5), 121.3(C-4) of ringA, 128.5(C-4'), 123.2(C-5'), 122.8(C-6'), 114.5(C-7'), 145.3(C-8'), 145.0(C-9') of ring B, 143.7(C-1"), 127.8(C-2"&6"), 123.7(C-3"&5"), 145.9(C-4") of ring C (phenyl group attached to Oxadiazole) and 90.1(C-2), 157.0(C-5), 27.9(-CH_3 of oxadiazole), 168.5(-CO-), 23.7(-CH_3 of –CO-CH_3) of ring D(oxadiazole);

^{31}PNMR (161.89 MHz, DMSO-*d6*): δ -8.52 ppm. Anal. Calcd.(%) for $C_{23}H_{18}N_3O_8P$: C 55.76, H 3.66, N 8.48; Found: C 55.64, H 3.57, N 8.31.

1-(2-(4-nitro phenyl)-5-(2-(4-methyl phenoxy)-1,3,2-benzodioxa phosphole-4-yl-2-oxide)-2-methyl-1,3,4-oxadiazole-3(2H)-yl) ethanone 6(q):
Yield: 45%; M.p: 203-205ºC; IR (KBr): 1697(C=O), 1611(C=N), 1273 (P=O), 965, 1191(P-O-C) cm^{-1}; ^{1}HNMR (300MHz, DMSO-*d6*): 2.03 (s, 3H, $COCH_3$), 1.83 (s, 3H, CH_3 of oxadiazole ring), 3.10 (s, 3H, Ar-CH_3), 6.81-8.19(m, 11H, for C_6H_4, C_6H_3 and C_6H_4 of three phenyl groups); C^{13}-NMR (75.46 MHz, DMSO-*d6*): δ 147.2(C-1),118.2(C-2&6),130.4 (C-3&5), 131.0(C-4), 21.3(-CH_3) of ringA, 128.3(C-4'), 123.7(C-5'), 122.5(C-6'), 114.3(C-7'), 145.7(C-8'), 145.0(C-9') of ring B, 143.7(C-1"), 127.8(C-2"&6"), 123.7(C-3"&5"), 145.9(C-4") of ring C (phenyl group attached to Oxadiazole) and 90.2(C-2), 157.0(C-5), 27.7(-CH_3 of oxadiazole), 168.6(-CO-), 23.8(-CH_3 of –CO-CH_3) of ring D(oxadiazole); ^{31}PNMR (161.89 MHz, DMSO-*d6*): δ -8.42 ppm. Anal. Calcd.(%) for $C_{24}H_{20}N_3O_8P$: C 56.59, H 3.96, N 8.25; Found: C 56.46, H 3.82, N 8.18.

1-(2-(4-nitro phenyl)-5-(2-(4-chloro phenoxy)-1,3,2-benzodioxa phosphole-4-yl-2-oxide)-2-methyl-1,3,4-oxadiazole-3(2H)-yl) ethanone 6(r):
Yield: 55%; M.p: 187-189ºC; IR (KBr): 1692(C=O), 1617(C=N), 1264 (P=O), 967, 1193(P-O-C) cm^{-1}; ^{1}HNMR (300MHz, DMSO-*d6*): δ 2.06 (s, 3H, $COCH_3$), 1.83 (s, 3H, CH_3 of oxadiazole ring), 6.81-8.19(m, 11H, for C_6H_4, C_6H_3 and C_6H_4 of three phenyl groups); C^{13}-NMR (75.46 MHz, DMSO-*d6*): δ 148.3(C-1),125.7(C-2&6),131.3 (C-3&5), 126.9(C-4) of ringA, 128.5(C-4'), 123.2(C-5'), 122.8(C-6'), 114.5(C-7'), 145.3(C-8'), 145.0(C-9') of ring B, 143.7(C-1"), 127.8(C-2"&6"), 123.7(C-3"&5"), 145.9(C-4") of ring C (phenyl group attached to Oxadiazole) and 90.1(C-2), 157.0(C-5), 27.9(-CH_3 of oxadiazole), 168.5(-CO-), 23.7(-CH_3 of –CO-CH_3) of ring D(oxadiazole); ^{31}PNMR (161.89 MHz, DMSO-*d6*): δ -9.17 ppm. Anal. Calcd.(%) for $C_{23}H_{17}N_3O_8PCl$: C 52.14, H 3.23, N 7.93; Found: C 51.99, H 3.14, N 7.85.

1-(2-(4-nitro phenyl)-5-(2-(4-bromo phenoxy)-1,3,2-benzodioxa phosphole-4-yl-2-oxide)-2-methyl-1,3,4-oxadiazole-3(2H)-yl) ethanone 6(s):
Yield: 50%; M.p: 171-173ºC; IR (KBr): 1694(C=O), 1610(C=N), 1270 (P=O), 967, 1193(P-O-C) cm^{-1}; ^{1}HNMR (300MHz, DMSO-*d6*): δ 2.09 (s, 3H, $COCH_3$), 1.83 (s, 3H, CH_3 of oxadiazole ring), 6.81-8.19(m, 11H, for C_6H_4, C_6H_3 and C_6H_4 of three phenyl groups); C^{13}-NMR (75.46 MHz, DMSO-*d6*): δ 149.2(C-1),123.3(C-2&6),133.0 (C-3&5), 115.7(C-4) of ring A, 128.5(C-4'), 123.2(C-5'), 122.8(C-6'), 114.5(C-7'), 145.3(C-8'), 145.0(C-9') of ring B, 143.7(C-1"), 127.8(C-2"&6"), 123.7(C-3"&5"), 145.9(C-4") of ring C (phenyl group attached to Oxadiazole) and 90.1(C-2), 157.0(C-5), 27.9(-CH_3 of oxadiazole), 168.5(-CO-), 23.7(-CH_3 of –CO-CH_3) of ring D(oxadiazole); ^{31}PNMR (161.89 MHz, DMSO-*d6*): δ -9.23ppm. Anal. Calcd.(%) for $C_{23}H_{17}N_3O_8PBr$: C 48.10, H 2.98, N 7.32; Found: C 47.94, H 2.83, N 7.18.

1-(2-(4-nitro phenyl)-5-(2-(4-nitro phenoxy)-1,3,2-benzodioxa phosphole-4-yl-2-oxide)-2-methyl-1,3,4-oxadiazole-3(2H)-yl) ethanone 6(t):
Yield: 55%; M.p: 185-187ºC; IR (KBr): 1698(C=O), 1615(C=N), 1278 (P=O), 969, 1197(P-O-C) cm^{-1}; ^{1}HNMR (300MHz, DMSO-*d6*): δ 2.07 (s, 3H, $COCH_3$), 1.83 (s, 3H, CH_3 of oxadiazole ring), 6.81-8.19(m, 11H, for C_6H_4, C_6H_3 and C_6H_4 of three phenyl groups)**;** C^{13}-NMR (75.46 MHz, DMSO-*d6*): δ 156.3(C-1),121.9(C-2&6),126.3 (C-3&5), 140.5(C-4) of ringA, 128.5(C-4'), 123.2(C-5'), 122.8(C-6'), 114.5(C-7'), 145.3(C-8'), 145.0(C-9') of ring B, 143.7(C-1"), 127.8(C-2"&6"), 123.7(C-3"&5"), 145.9(C-4") of ring C (phenyl group attached to Oxadiazole) and 90.1(C-2), 157.0(C-5), 27.9(-CH_3 of oxadiazole), 168.5(-CO-), 23.7(-CH_3 of –CO-CH_3) of ring D(oxadiazole); ^{31}PNMR (161.89 MHz, DMSO-*d6*): δ -9.20 ppm. Anal. Calcd.(%) for $C_{23}H_{17}N_4O_{10}P$: C 51.12, H 3.17, N 10.37; Found: C 51.03, H 3.06, N 10.21.

Biological activity
The antimicrobial activity [27, 28] of these newly synthesized compounds was performed according to disk diffusion method, as recommended by the National Committee for Clinical Laboratory [29]. The synthesized compounds were used at the concentration of 250µ g/ml and 500µ g/ml Using DMF as a solvent [30].

Antibacterial activity
The antibacterial activity of 1-(2-(4-substituted phenyl)-5-(2-(4-substituted phenoxy)-1,3,2-benzodioxa phosphole-4-yl-2-oxide)-2-methyl-1,3,4-oxadiazole-3(2H)-yl) ethanone (8a-t) were screened against the *Staphylococcus aureus* (gram positive) and *Escherichia coli* (gram negative) organisms. Most of the compounds exhibited good

antibacterial activity against both bacteria. The presence of chloro and nitro group in the structure has shown increased effect on their antibacterial activity. Penicillin and Streptomycin are tested as reference compounds to compare the activity [31, 32].

Antibacterial activity of 1-(2-(4-substituted phenyl)-5-(2-(4-substituted phenoxy)-1,3,2-benzodioxa phosphole-4-yl-2-oxide)-2-methyl-1,3,4-oxadiazole-3(2H)-yl) ethanone (8a-t)

Comp	R	R^1	Zone of inhibition (mm)			
			Staphylococcus aureus		*Escherichia coli*	
			250 (µg/disc)	500 (µg/disc)	250 (µg/disc)	500 (µg/disc)
8a	H	-H	8	10	8	9
8b	CH_3	-H	7	9	6	8
8c	Cl	-H	14	16	14	15
8d	Br	-H	13	14	11	13
8e	NO_2	-H	14	15	12	14
8f	H	4-Cl	12	14	10	12
8g	CH_3	4-Cl	11	13	9	11
8h	Cl	4-Cl	16	18	15	17
8i	Br	4-Cl	13	15	12	14
8j	NO_2	4-Cl	14	17	13	15
8k	H	4-Br	11	13	9	11
8l	CH_3	4-Br	10	12	8	10
8m	Cl	4-Br	14	16	12	13
8n	Br	4-Br	12	15	11	14
8o	NO_2	4-Br	13	16	12	14
8p	H	4-NO_2	12	14	10	12
8q	CH_3	4-NO_2	10	12	9	11
8r	Cl	4-NO_2	16	17	13	15
8s	Br	4-NO_2	13	14	12	14
8t	NO_2	4-NO_2	15	16	14	15
Penicillin			22	25	21	22
Streptomycin			27	29	25	27

Comp	R	R^1	Zone of inhibition (mm)			
			Aspergillus niger		*Candida albicans*	
			250 (µg/disc)	500 (µg/disc)	250 (µg/disc)	500 (µg/disc)
8a	H	-H	12	15	14	10
8b	CH_3	-H	8	11	9	11
8c	Cl	-H	15	18	14	16
8d	Br	-H	13	16	11	13
8e	NO_2	-H	12	15	13	15
8f	H	4-Cl	10	13	9	11
8g	CH_3	4-Cl	11	14	10	12
8h	Cl	4-Cl	16	19	15	18
8i	Br	4-Cl	14	15	13	14
8j	NO_2	4-Cl	15	17	14	16
8k	H	4-Br	12	14	11	13
8l	CH_3	4-Br	11	13	10	12
8m	Cl	4-Br	14	16	13	15
8n	Br	4-Br	12	14	11	13
8o	NO_2	4-Br	13	15	12	15
8p	H	4-NO_2	14	16	13	14
8q	CH_3	4-NO_2	13	15	11	13
8r	Cl	4-NO_2	15	17	14	16
8s	Br	4-NO_2	14	16	13	15
8t	NO_2	4-NO_2	16	18	15	17
Griseofulvin			28	22	26	24

Antifungal activity

The antifungal activity of 1-(2-(4-substituted phenyl)-5-(2-(4-substituted phenoxy)-1,3,2-benzodioxa phosphole-4-yl-2-oxide)-2-methyl-1,3,4-oxadiazole-3(2H)-yl) ethanone (8a-t) were screened against *Aspergillus niger, Candida albicans.* Griseofulvin is used as reference compound and exhibited 28 mm, 26 mm inhibition for both fungi at 250 µg / disc and 22mm, 24mm inhibition at 500 µg / disc. [33].

Antifungal activity of 1-(2-(4-substituted phenyl)-5-(2-(4-substituted phenoxy)-1,3,2-benzodioxa phosphole-4-yl-2-oxide)-2-methyl-1,3,4-oxadiazole-3(2H)-yl) ethanone (8a-t)

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