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Synthesis, antimicrobial properties of novel mannich bases containing 2- phenoxy-1, 3, 2-benzodioxa phosphole and Indole systems

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ABSTRACT

New novel mannich bases of 2-phenoxy-1,3,2-benzodioxaphosphole derivatives 2 - (4-substituted phenoxy) - N'-[2-oxo-1, 2-dihydro-1-(piperidine-1-ylmethyl) / (morpholino methyl) / (4 - methyl piperazine - 1 – yl methyl) indole – 3 - ylidene] - 1, 3, 2 -benzodioxaphosphole-4-carbohydrazide-2-oxide 6(a-g) were prepared by the condensation reaction between 2-(4-substituted phenoxy)-1,3,2-benzodioxaphosphole-4-carbohydrazide-2-oxides (3) with Isatin (4) yielded the corresponding 2-(4-substitutedphenoxy)-N'-(-2-oxo-1,2-dihydro-3H-indol-3-ylidene)-1,3,2-benzodioxa- phosphole -4-carbohydrazide-2-oxide (5). This was allowed to undergo the Mannich reaction with different Secondary Amines namely: piperidine, morpholine and N-methyl piperazine in the presence of formaldehyde in DMF to give corresponding hydrazides 6(a-g). 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-g) were screened for their antibacterial and antifungal activity.

Keywords: Benzodioxaphospholes, Isatin, Mannich bases, Antibacterial and Antifungal activity.

INTRODUCTION

The Organophosphorous heterocyclic compounds chemistry received much attention of chemists in past two decades due to their pharmaceutical importance [1] and extensive applications in organic synthesis [2]. Hence a good deal of importance is given to phosphorus derivatives [3]. Indole system and related heterocyclic compounds possess various types of biological activities. It is due to their wide use in medicinal chemistry and some of them possess antimicrobial [4], antiviral [5, 6], anti tumor [7] and anti hypertensive activities [8]. The anti bacterial activity of Mannich bases has been well established [9-13]. In view of these observations, it appeared of interest to synthesis some novel mannich bases baring phosphorus moiety and indole moieties.

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[14].

Other substituted phenyl phosphorodichloridates **1(a-e)** were prepared by the same procedure [15-18] 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 [19] 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 [20, 21]. 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. 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, -9.47. 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.

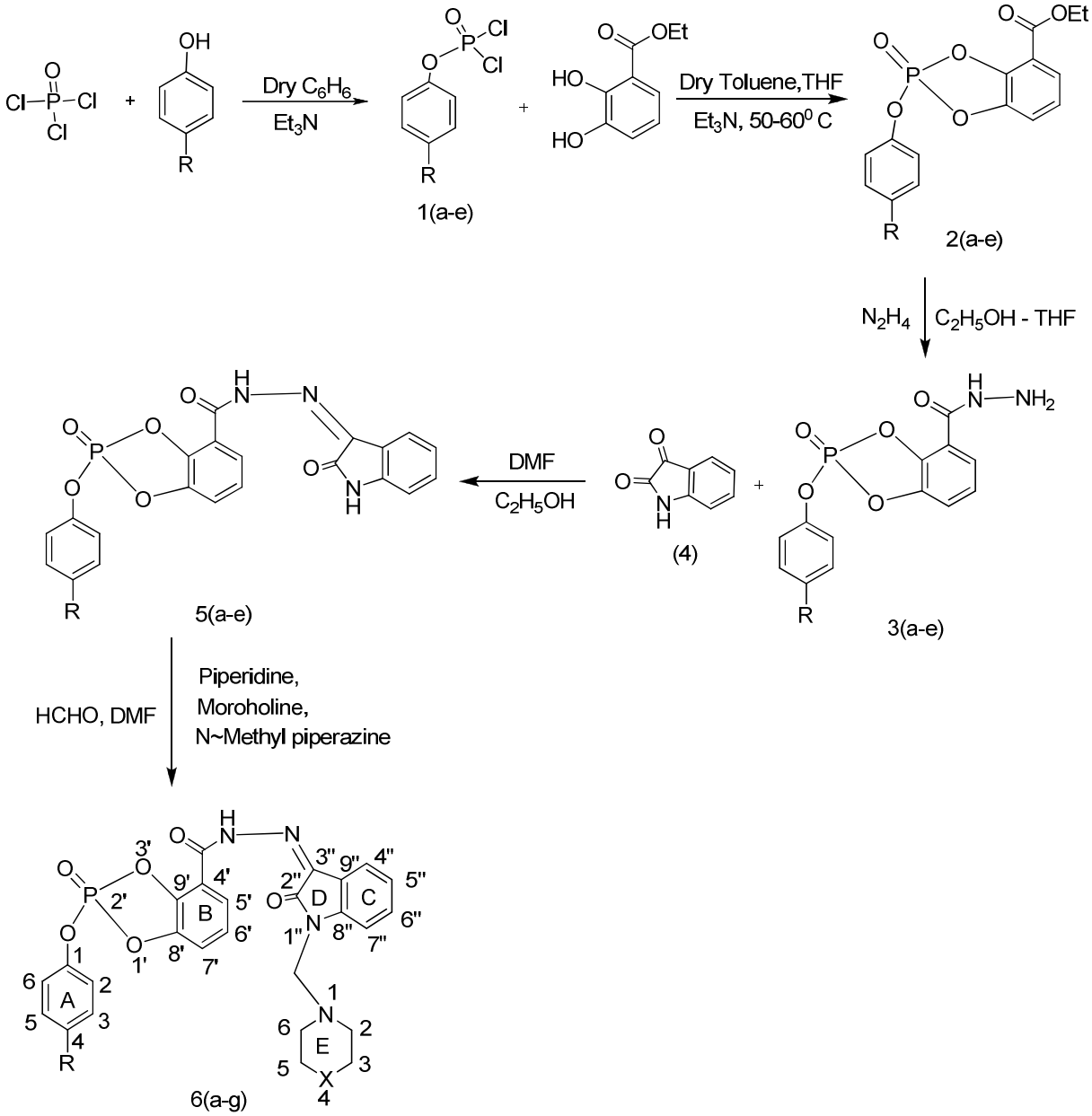
2-(4-methyl phenoxy)-1, 3, 2-benzodioxa phosphole-4-carbohydrazide-2-oxide **3(b):**

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 -7.25, -7.79 ppm. 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.

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, -9.80. 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.

Scheme-I



Compounds	6a	6b	6c	6d	6e	6f	6g
R	4-H	4-CH_3	4-Cl	4-Br	4-NO_2	4-H	4-H
X	CH_2	CH_2	CH_2	CH_2	CH_2	O	N-CH_3

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, -9.11. 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, -9.28. 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-substitutedphenoxy)-N'-[-2-oxo-1, 2-dihydro-1-(piperidine-1-ylmethyl) / (morpholinomethyl) / (4-methylpiperazine-1-ylmethyl) indole-3-ylidene]-1, 3, 2-benzodioxaphosphole-4-carbohydrazide-2-oxide (6a-g)

Equimolar quantities (0.01mol) of Isatin **(4)** [22] and the corresponding hydrazide **3(a-e)** were dissolved in absolute ethanol – DMF solvent mixture. The reaction mixture was refluxed for 1-4 hours and then kept at room temperature overnight. The course of the progress of the reaction was monitored by TLC. After completion of the reaction the solvent was removed in rotaevaporator. The solid was recrystallized from 2-propanol and petroleum ether (60-80^{0}C) solvent mixture to afford **5(a-e).** A mixture of **5(a)** (0.1 mol), piperidine (0.15 mol) and dimethyl formamide (DMF) was stirred to obtain a clear solution. To this solution, HCHO (0.05 mol) and DMF were added in ice-cold condition and stirred for 6 hours in an ice-bath and left overnight at room temperature. The obtained solid was isolated and recrystallized from 2-propanol and petroleum ether (60-80^{0}C) solvent mixture to give Compound **6(a).** The reaction procedure [23, 24] leading to synthesize **6(a)** was then extended to the syntheses of **6(b-e)**.

The reaction procedure is repeated with Morpholine / N-methyl piperazine to afford **6(f and g).** These reactions are summarized in the scheme-I. Yields were moderate to fair (45-60%). The purity of the compounds was monitored by TLC. All the structures of the synthesized compounds 6(**a-g**) were established [25, 26] by elemental analysis, IR, ^{1}H- NMR, ^{13}C-NMR, ^{31}P- NMR spectroscopy and Mass spectrometry.

Physical, analytical and spectral data for the compounds 6(a-g):

*2-phenoxy-N'-[2-oxo-1,2-dihydro-1-(piperidine-1-ylmethyl)indole-3-ylidene]- 1,3,2-benzodioxa phosphole-4-carbohydrazide-2-oxide**(6a):***

Yield: 60%; M.p: 92-94ºC; IR (KBr): 1760(Indole C=O), 1652 (CO-NH), 2920(CH_2), 1250 (P=O), 954, 1196 (P-O-C) cm^{-1}; ^{1}HNMR (300MHz, DMSO-*d6*): δ 1.53–1.59 [m, 6H $(CH_2)_3$ of piperidine ring E], 2.45 (t, 4H, –CH_2–N–CH_2 of piperidine ring E), 4.03 (s, 2H, –N–CH_2–N–), 8.75 (s, 1H, CO-NH), 7.03-7.86 (m, 12H, for C_6H_5 of ring A, C_6H_3 of ring B and C_6H_4 of ring C); C^{13}-NMR (75.46 MHz, DMSO-*d6*): δ 150.3(C-1),115.9(C-2&6),130.2(C-3&5), 121.4(C-4) of ringA, 121.3(C-4'), 121.5(C-5'), 122.9(C-6'), 120.7(C-7'), 145.3(C-8'), 143.3(C-9'), 163.0(CO-NH) of ring B, 163.5(C-2"), 132.8(C-3"), 129.4(C-4"), 124.5(C-5"), 131.3(C-6"), 121.7(C-7"), 147.4(C-8"), 117.8(C-9"), 70.4(N-CH_2-N) of ring C&D and 52.0(C-2&6), 25.6(C-3&5), 25.9(C-4) ring E . ^{31}PNMR (161.89 MHz, DMSO-*d6*): δ -9.23, -9.59. Anal. Calcd.(%) for $C_{27}H_{25}N_4O_6P$: C 60.90, H 4.73, N 10.52; Found: C 60.81, H 4.67, N 10.44.

*2-(4-methyl phenoxy)-N'-[-2-oxo-1, 2-dihydro-1-(piperidine-1-ylmethyl) indole-3-ylidene]-1, 3, 2-benzodioxaphosphole-4-carbohydrazide-2-oxide **(6b):***

Yield: 50%; M.p: 89-91ºC; IR (KBr): 1758 (Indole C=O), 1650 (CO-NH), 2910(CH_2), 1279 (P=O) and 960, 1190 (P-O-C) cm^{-1}; ^{1}HNMR (300MHz, DMSO-*d6*): 1.53–1.59 [m, 6H $(CH_2)_3$ of piperidine ring E], 2.45 (t, 4H, –CH_2–N–CH_2 of piperidine ring E), 4.03 (s, 2H, –N–CH_2–N–), 8.70 (s, 1H, CO-NH), 6.83-7.86 (m, 11H, for C_6H_4 of ring A C_6H_3 of ring B and C_6H_4 of ring C), and 3.15 (S,3H,Ar-CH_3); C^{13}-NMR (75.46 MHz, DMSO-*d6*): δ 147.3(C-1),115.8(C-2&6),130.5(C-3&5), 131.0(C-4), 24.3 (Ar-CH_3) of ringA, 121.3(C-4'), 121.5(C-5'), 122.9(C-6'), 120.7(C-7'), 145.3(C-8'), 143.3(C-9'), 163.0(CO-NH) of ring B, 163.5(C-2"), 132.8(C-3"), 129.4(C-4"), 124.5(C-5"), 131.3(C-6"), 121.7(C-7"), 147.4(C-8"), 117.8(C-9"), 70.4(N-CH_2-N) of ring C&D and 52.0(C-2&6), 25.6(C-3&5), 25.9(C-4) ring E . ^{31}PNMR (161.89 MHz, DMSO-*d6*): δ -9.34, -9.48. Anal. Calcd.(%) for $C_{28}H_{27}N_4O_6P$: C 61.54, H 4.98, N 10.25; Found: C 61.43, H 4.89, N 10.25.

*2-(4-chloro phenoxy)-N'-[-2-oxo-1, 2-dihydro-1-(piperidine-1-ylmethyl) indole-3-ylidene]-1, 3, 2-benzodioxaphosphole-4-carbohydrazide-2-oxide **(6c):***

Yield: 50%; M.p: 104-106ºC; IR (KBr): 1759(Indole C=O), 1650 (CO-NH), 2905(CH_2), 1254 (P=O), 952, 1192 (P-O-C) cm^{-1}; ^{1}HNMR (300MHz, DMSO-*d6*): δ 1.53–1.59 [m, 6H $(CH_2)_3$ of piperidine ring E], 2.45 (t, 4H, –CH_2–N–CH_2 of piperidine ring E), 4.03 (s, 2H, –N–CH_2–N–), 8.78 (s, 1H, CO-NH), 6.89-7.86 (m, 11H, for C_6H_4 of ring A C_6H_3 of ring B and C_6H_4 of ring C); C^{13}-NMR (75.46 MHz, DMSO-*d6*): δ 148.4(C-1),175.3(C-2&6),130.3(C-3&5),

126.9(C-4) of ringA, 121.3(C-4'), 121.5(C-5'), 122.9(C-6'), 120.7(C-7'), 145.3(C-8'), 143.3(C-9'), 163.0(CO-NH) of ring B, 163.5(C-2"), 132.8(C-3"), 129.4(C-4"), 124.5(C-5"), 131.3(C-6"), 121.7(C-7"), 147.4(C-8"), 117.8(C-9"), 70.4(N-CH_2-N) of ring C&D and 52.0(C-2&6), 25.6(C-3&5), 25.9(C-4) ring E . ^{31}PNMR (161.89 MHz, DMSO-*d6*): δ -9.54, -9.92. Anal. Calcd.(%) for $C_{27}H_{24}N_4O_6PCl$: C 57.20, H 4.27, N 9.88; Found: C 57.15, H 4.1, N 9.76.

2-(4-bromo phenoxy)-N'-[-2-oxo-1, 2-dihydro-1-(piperidine-1-ylmethyl) indole-3-ylidene]-1, 3, 2-benzodioxaphosphole-4-carbohydrazide-2-oxide ***(6d):***
Yield: 45%; M.p: 110-112ºC; IR (KBr): 1759(Indole C=O), 1650 (CO-NH), 2912(CH_2), 1260 (P=O), 954, 1194 (P-O-C) cm^{-1}; ^{1}HNMR (300MHz, DMSO-*d6*): δ 1.53–1.59 [m, 6H $(CH_2)_3$ of piperidine ring E], 2.45 (t, 4H, –CH_2–N–CH_2 of piperidine ring E), 4.03 (s, 2H, –N–CH_2–N–), 8.72 (s, 1H, CO-NH), 6.84-7.86 (m, 11H, for C_6H_4 of ring A C_6H_3 of ring B and C_6H_4 of ring C)C^{13}-NMR (75.46 MHz, DMSO-*d6*): δ 149.3(C-1), 118.1(C-2&6),133.2(C-3&5), 126.9(C-4) of ringA, 121.3(C-4'), 121.5(C-5'), 122.9(C-6'), 120.7(C-7'), 145.3(C-8'), 143.3(C-9'), 163.0(CO-NH) of ring B, 163.5(C-2"), 132.8(C-3"), 129.4(C-4"), 124.5(C-5"), 131.3(C-6"), 121.7(C-7"), 147.4(C-8"), 117.8(C-9"), 70.4(N-CH_2-N) of ring C&D and 52.0(C-2&6), 25.6(C-3&5), 25.9(C-4) ring E . ^{31}PNMR (161.89 MHz, DMSO-*d6*): δ -8.84, -9.21. Anal. Calcd.(%) for $C_{27}H_{24}N_4O_6PBr$: C 53.04, H 3.96, N 9.16; Found: C 52.97, H 3.89, N 9.07.

2-(4-nitro phenoxy)-N'-[-2-oxo-1, 2-dihydro-1-(piperidine-1-ylmethyl) indole-3-ylidene]-1, 3, 2-benzodioxaphosphole-4-carbohydrazide-2-oxide ***(6e):***
Yield: 50%; M.p: 122-124ºC; IR (KBr): 1773(Indole C=O), 1650 (CO-NH), 2905(CH_2), 1262 (P=O), 956, 1196 (P-O-C) cm^{-1}; ^{1}HNMR (300MHz, DMSO-*d6*): δ 1.53–1.59 [m, 6H $(CH_2)_3$ of piperidine ring E), 2.45 (t, 4H, –CH_2–N–CH_2 of piperidine ring E), 4.03 (s, 2H, –N–CH_2–N–), 8.70 (s, 1H, CO-NH), 7.03-8.09 (m, 11H, for C_6H_4 of ring A C_6H_3 of ring B and C_6H_4 of ring C); C^{13}-NMR (75.46 MHz, DMSO-*d6*): δ 156.4(C-1),116.8(C-2&6),122.5(C-3&5), 141.0(C-4) of ringA, 121.3(C-4'), 121.5(C-5'), 122.9(C-6'), 120.7(C-7'), 145.3(C-8'), 143.3(C-9'), 163.0(CO-NH) of ring B, 163.5(C-2"), 132.8(C-3"), 129.4(C-4"), 124.5(C-5"), 131.3(C-6"), 121.7(C-7"), 147.4(C-8"), 117.8(C-9"), 70.4(N-CH_2-N) of ring C&D and 52.0(C-2&6), 25.6(C-3&5), 25.9(C-4) ring E . ^{31}PNMR (161.89 MHz, DMSO-*d6*): δ -8.87, -9.28. Anal. Calcd.(%) for $C_{27}H_{24}N_5O_8P$: C 56.16, H 4.19, N 12.13; Found: C 56.09, H 4.11, N 12.05.

2-(phenoxy)-N'-[-2-oxo-1,2-dihydro-1-(morpholinomethyl)indole-3-ylidene]-1,3,2-benzodioxa phosphole-4-carbohydrazide-2-oxide ***(6f)****:*
Yield: 50%; M.p: 126-128ºC; IR (KBr): 1756 (Indole C=O), 1654 (CO-NH), 2925(CH_2), 1258 (P=O), 954, 1195 (P-O-C) cm^{-1}; ^{1}HNMR (300MHz, DMSO-*d6*): δ 3.65 (t, 4H, –CH_2–O–CH_2 of morpholine ring E)**,** 2.50 (t, 4H, –CH_2–N–CH_2 of morpholine ring E), 4.03 (s, 2H, –N–CH_2–N–), 8.76 (s, 1H, CO-NH), 7.03-7.86 (m, 12H, for C_6H_5 of ring A, C_6H_3 of ring B and C_6H_4 of ring C); C^{13}-NMR (75.46 MHz, DMSO-*d6*): δ 150.3(C-1),115.9(C-2&6),130.2(C-3&5), 121.4(C-4) of ringA, 121.3(C-4'), 121.5(C-5'), 122.9(C-6'), 120.7(C-7'), 145.3(C-8'), 143.3(C-9'), 163.0(CO-NH) of ring B, 163.5(C-2"), 132.8(C-3"), 129.4(C-4"), 124.5(C-5"), 131.3(C-6"), 121.7(C-7"), 147.4(C-8"), 117.8(C-9"), 70.4(N-CH_2-N) of ring C&D and 51.1(C-2&6), 66.5(C-3&5) ring E . ^{31}PNMR (161.89 MHz, DMSO-*d6*): δ -9.21, -9.57. Anal. Calcd.(%) for $C_{26}H_{23}N_4O_7P$: C58.43, H 4.34, N 10.48; Found: C 58.32, H 4.27, N 10.37.

2-(phenoxy)-N'-[-2-oxo-1, 2-dihydro-1 (4-methylpiperazine-1-ylmethyl) indole-3-ylidene]-1, 3, 2-benzodioxaphosphole-4-carbohydrazide-2-oxide ***(6g)****:*
Yield: 50%; M.p: 132-134ºC; IR (KBr): 1759 (Indole C=O), 1652 (CO-NH), 2918(CH_2), 1260 (P=O), 958, 1196 (P-O-C) cm^{-1}; ^{1}HNMR (300MHz, DMSO-*d6*): δ 2.26 (s, 3H, N–CH_3), 2.35 (s, 8H, –CH_2–N–CH_2 of piperazine ring E), 4.03 (s, 2H, –N–CH_2–N–), 8.73 (s, 1H, CONH), 7.08-7.86 (m, 12H, for C_6H_5 of ring A, C_6H_3 of ring B and C_6H_4 of ring C); C^{13}-NMR (75.46 MHz, DMSO-*d6*): δ 150.3(C-1),115.9(C-2&6),130.2(C-3&5), 121.4(C-4) of ringA, 121.3(C-4'), 121.5(C-5'), 122.9(C-6'), 120.7(C-7'), 145.3(C-8'), 143.3(C-9'), 163.0(CO-NH) of ring B, 163.5(C-2"), 132.8(C-3"), 129.4(C-4"), 124.5(C-5"), 131.3(C-6"), 121.7(C-7"), 147.4(C-8"), 117.8(C-9"), 70.4(N-CH_2-N) of ring C&D and 50.1(C-2&6), 54.9(C-3&5), 43.1(N–CH_3). ^{31}PNMR (161.89 MHz, DMSO-*d6*): δ -9.29, -9.65. Anal. Calcd.(%) for $C_{27}H_{26}N_5O_6P$: C 59.23, H 4.79, N 12.79; Found: C 59.14, H 4.68, N 12.68.

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

Heterocyclic organic compounds containing phosphorous, oxygen, nitrogen or sulfur in the ring system are expected to be more active due to the presence of hetero atoms [29, 3].

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

Antibacterial activity

The antibacterial activity of 2-(4-substitutedphenoxy)-N'-[-2-oxo-1, 2-dihydro-1-(piperidine-1-ylmethyl) / (morpholinomethyl) / (4-methylpiperazine-1-ylmethyl) indole-3-ylidene]-1, 3, 2-benzodioxaphosphole-4-carbohydrazide-2-oxide (6a-g) 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 chlorogroup in the structure has shown increased effect on their antibacterial activity. Penicillin and Streptomycin are tested as reference compounds to compare the activity [30].

Antibacterial activity of 2-(4-substitutedphenoxy)-N'-[-2-oxo-1, 2-di hydro-1-(piperidine-1-ylmethyl) / (morpholinomethyl) / (4-methylpiperazine-1-ylmethyl) indole-3-ylidene]-1, 3, 2-benzodioxaphosphole-4-carbohydrazide-2-oxide (6a-g)

Compound	R	X	Zone of inhibition (mm)			
			Staphylococcus aureus		*Escherichia coli*	
			250 (µg/disc)	500 (µg/disc)	250 (µg/disc)	500 (µg/disc)
6a	4-H	CH_2	9	10	8	9
6b	4-CH_3	CH_2	7	9	5	7
6c	4-Cl	CH_2	15	16	14	15
6d	4-Br	CH_2	13	14	11	12
6e	4-NO_2	CH_2	14	15	12	13
6f	4-H	O	12	14	10	12
6g	4-H	N-CH_3	10	11	9	10
Penicillin			22	25	21	22
Streptomycin			27	29	25	27

Antifungal activity

The antifungal activity of 2-(4-substitutedphenoxy)-N'-[-2-oxo-1, 2-dihydro-1-(piperidine-1-ylmethyl) / (morpholinomethyl) / (4-methylpiperazine-1-ylmethyl) indole-3-ylidene]-1, 3, 2-benzodioxaphosphole-4-carbohydrazide-2-oxide (6a-g) were screened against *Aspergillus niger*, *Helminthosporium oryzae*. Griseofulvin is used as reference compound and exhibited 28 mm and 26 mm inhibition for both fungi at 250 µg / disc [31].

Antifungal activity of 2-(4-substitutedphenoxy)-N'-[-2-oxo-1, 2-di hydro-1-(piperidine-1-ylmethyl) / (morpholinomethyl) / (4-methylpiperazine-1-ylmethyl) indole-3-ylidene]-1, 3, 2-benzodioxaphosphole-4-carbohydrazide-2-oxide (6a-g)

Compound	R	X	Zone of inhibition (mm)			
			Aspergillus niger		*Helminthosporium oryzae*	
			250 (µg/disc)	500 (µg/disc)	250 (µg/disc)	500 (µg/disc)
6a	4-H	CH_2	9	12	8	10
6b	4-CH_3	CH_2	8	11	9	11
6c	4-Cl	CH_2	15	18	14	16
6d	4-Br	CH_2	13	16	11	13
6e	4-NO_2	CH_2	12	15	13	15
6f	4-H	O	10	13	9	11
6g	4-H	N-CH_3	11	14	10	12
Griseofulvin			28	22	26	23

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