EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 2
Issue: 7
293-302
Year: 2015

SYNTHESIS, CHARACTERIZATION, ANTIMICROBIAL EVALUATION AND DOCKING STUDIES OF NOVEL 1, 2, 3 TRIAZOLE HETERO CYCLIC COMPOUNDS CONTAINING DIOXAPHOSPHOLANE DERIVATIVES

***D. Rajesh, G. Govindu, B. Saritha, L. K. Ravindranath**

Department of Chemistry, S. K. University, Anantapuramu, A.P, India.

***Author for Correspondence: D. Rajesh**
Department of Chemistry, S. K. University, Anantapuramu, A.P, India.

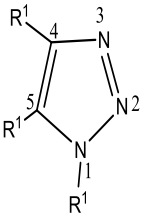
Article Received on 29/09/2015 **Article Revised on 22/10/2015** **Article Accepted on 16/11/2015**

ABSTRACT

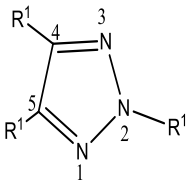
Novel derivatives of (Z)-N'-(1-((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)(-5-chloro/ bromo)-2-oxoindolin-3-ylidene)-2-(4- methyl/ methoxy/ trifluoro/ nitro) cyclohexa-1,3-dien-1-yloxy)benzo[d] [1,3,2]dioxaphosphole-5-carbohydrazide 2-oxide 9(a-o) as per scheme-1 were Synthesized by condensation reaction of (Z)-N'-(1-((1-benzyl-1H-1, 2, 3-triazol-4-yl) methyl) (5-chloro/bromo)-2-oxoindolin-3-ylidene)-3, 4-dihydroxybenzo hydrazide 7(a-c) and (Phenyl) phosphorodichloridates 8(a-g). The synthon 7(a-c) was obtained by condensation reaction between (Z)-3, 4-dihydroxy-N'-(5- chloro / bromo)2-oxo-1-(prop-2-yn-1-yl) indolin-3-ylidene) benzohydrazide 5(a-c) (azidomethyl) benzene(6) and $CUSO_4$-Cu turnings. The synthon 5(a-c) was obtained by reaction between 3, 4-dihydroxybenzohydrazide (3) with N-Propargyl Isatin. The synthon (3) was obtained by condensation reaction between of ethyl 3,4dihydroxybenzoate and hyrazinehydrate. The structures of newly synthesized compounds were established by IR, ^{1}HNMR, ^{13}C-NMR, ^{31}P-NMR and elemental analysis. The newly synthesized compounds were subjected to various biological activities and docking studies.

KEY WORDS: 1, 2, 3 triazole, Propargyl isatin, (Phenyl) phosphorodichloridates, antimicrobial and Docking studies.

INTRODUCTION: 1, 2, 3-Triazole compounds are important of heterocyclic compounds.



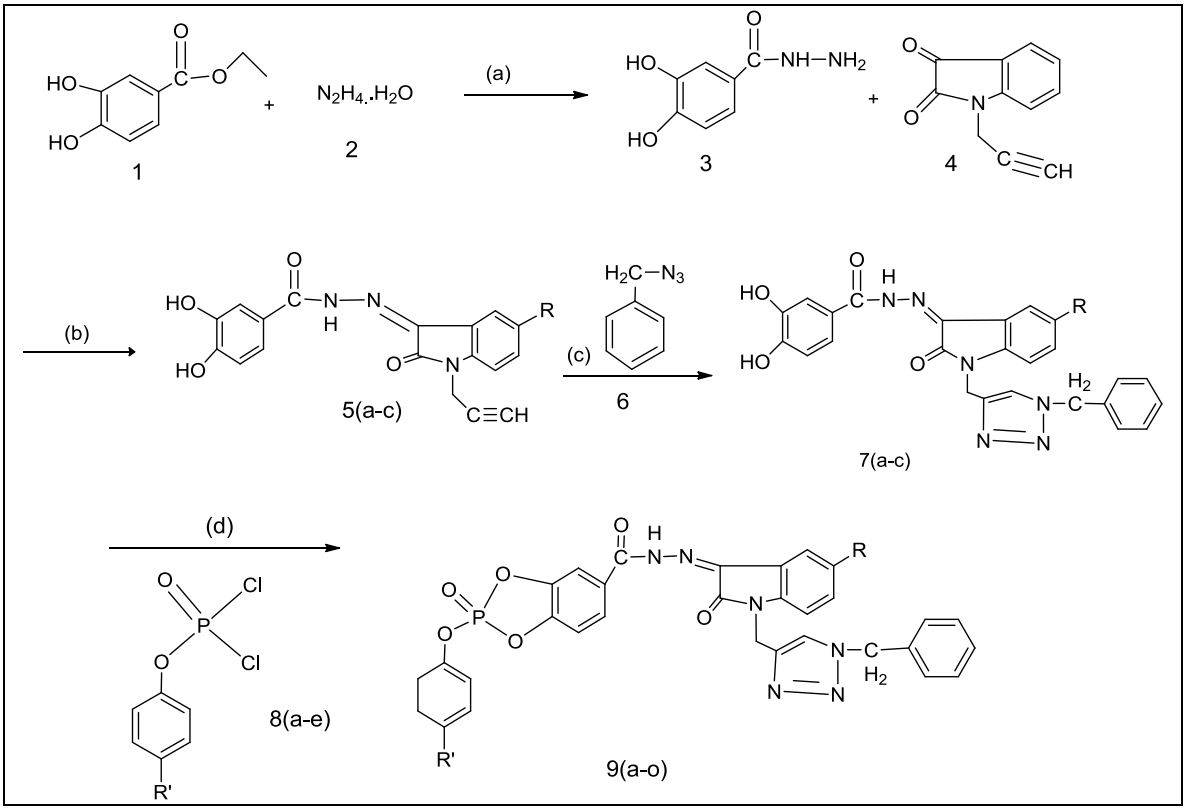
Structures of 1H-1,2,3 Triazole



2H-1,2,3-Triazole

They find numerous applications in industry, namely as dyestuffs, fluorescent whiteners, photo stabilizers of polymers, optical brightening agents, corrosion inhibitors and as photo graphic photoreceptors.[1, 2] Also due to their extensive biological activities, they find successful applications in medicine blood-sugar-lowering drug[3], Anti tubercular agent[4], an anticancer[5], Anti viral activity[6], multivalent antibiotic[7] and some agrochemical applications are Staphylococcus aureus Klebsiella pneumoniae and Bacillussubstilis[8], Antibacterial activity.[9]

In the preparation of 1, 2, 3 triazole compounds azides undergo addition to acetylene and to symmetrically substituted alkynes to give only one 1-substituted 1*H*-1, 2, 3-triazole, which simplifies the purification step. This is a general method for the preparation of triazoles and in some cases the yields are excellent. Addition of phenyl azide[10], aryl methyl azides[11-13] or other alkyl azides[11] to acetylene yields the corresponding 4, 5-unsubstituted triazoles. This method has also been used for the preparation of dendimers containing various 1, 2, 3-triazole rings.[14]



Scheme-I.1*:* (Z)-N'-(1-((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)(-5-chloro/ bromo)-2-oxoindolin-3-ylidene)-2-(4-methyl/ methoxy/ trifluoro/ nitro) cyclohexa-1,3-dien-1-yloxy)benzo[d] [1,3,2]dioxaphosphole-5-carbohydrazide 2-oxide 9(a-o)

Comp	5a	5b	5c
R	7a	7b	7c
	H	Cl	Br

Comp	9a	9b	9c	9d	9e	9f	9g	9h	9i
R	H	H	H	H	H	Cl	Cl	Cl	Cl
R'	H	CH_3	OCH_3	CF_3	NO_2	H	CH_3	OCH_3	CF_3

Comp	9j	9k	9l	9m	9n	9o
R	Cl	Br	Br	Br	Br	Br
R'	NO_2	H	CH_3	OCH_3	CF_3	NO_2

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 aluminium sheet of silica gel 60F254. E-mark Germany using iodine as visualizing agent. Melting points were determined in open capillary tubes on Mel-Temp apparatus and 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 units, instruments. All ^{1}H and ^{13}C-NMR spectra were recorded on a Varin XL-300 spectrometer operating at 400MHz for ^{1}H-NMR and 75 MHz for ^{13}C-NMR, ^{31}P-NMR spectra were recorded on a Varin XL-spectrometer operating at 161.89MHz .The compounds were dissolved in DEMSO-d_6 and chemical shifts were referenced to TMS (^{1}H-NMR and ^{13}C-NMR) and 85% H_3PO_4 (^{31}P-NMR). Mass spectral data was recorded on FAB-MS instrument at 70ev with direct inlet system. Elemental analyses were recorded on a Cario Erba 1108 elemental analyser. Central Drug Research Institute, Lucknow, India. Docking studies were carried out using GOLD soft ware in Bio-chemistry applications institute, Hyderabad.

Preparation of Intermidiates

4-Substiteted phenyl phosphorodichloridates 8(a-g) [15,16]: Phosphorus oxy chloride (15.3gr, 0.1mole) in dry benzene (60 ml) was taken in to three-necked flask (500 ml) 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. The dry tri ethyl amine (10.1 gm, 0.1 mole) and dry benzene (50 ml) were added into the flask slowly while stirring. To this mixture, freshly distilled phenol (9.4 gr, 0.1 mole) in dry benzene (60 ml) was added drop wise through the dropping funnel. The addition took

about thirty minutes and whole reaction mixture was refluxed with vigorous stirring for 10 hours. The reaction mixture was cooled and the solid tri ethylamine - hydrochloride was filtered off. The solvent from the filtrate was removed under reduced pressure in a rota evaporator. The dark brown liquid remained, was subjected to fractional distillation and the major product distilling at 118-124^0 C / 11(mm) was collected as colorless glassy viscous liquid (8.3 gr, 40%).

The other substituted phenyl phosphorodichlorates **8(a-g)** were prepared by the same procedure[17-20] by reacting equimolar quantities of phosphorous oxychloride and respective substituted phenols in benzene in the presence of tri ethylamine.

RESULTS AND DISCUSSION

Typical procedure for Synthesis of 3, 4 – dihydroxybenzohydrazide (3)

A mixture of ethyl 3,4dihydroxybenzoate and hyrazinehydrate dissloved in ethanol was refluxed for 5 hours .The progress of the reaction was monitored by (TLC) with hexane: ethyl acetate (7:3) as mobile phase. The reaction mixture was cooled and poured into ice-cooled water with stirring. The separated solid was filtered, washed with water and recrystalized from ethanol to afford to 3, 4–Dihydroxybenzohydrazide. The structure of compound is characterized by spectral data IR, ^{1}H-NMR, and elemental analysis.

Physical, analytical and spectral data for 3, 4 – dihydroxybenzohydrazide (3)

Yield: 71%; M. P: 132-134^0 C; IR (KBr): (ν/ δ, cm^{-1}) 3350 (γ -OH, interamolecular-OH bending), 3460 & 3440 (NH_2- stretching of acid hydrazide), 1676 (C=O,), 3410 (NH-Stretching of acid hydrazide); ^{1}H-NMR (400MHz, DMSO-d6) 2.0 (d, 2H, hydrazine of NH_2), 5.35(s, 2H, vicinal OH of Ar-OH),7.16-7.42(m, 3H, benzene ring), 8.10(t, 1H, NH of amide group); Anal. calcd(%) for $C_7H_8N_2O_3$: C:50.00%, H:4.80%, N:16.66% and O:28.54%. Found: C: 49.20%, H: 4.20%, N: 16.06% and O: 27.74%.

Typical procedure for Synthesis of Z)-3, 4-dihydroxy-N'- (5-chloro-/5-bromo) 2-oxo -1- (prop-2-yn-1-yl) indolin-3-ylidene) benzo hydrazide 5(a-c)

An equimolar quantities of N-Isatinpropargyl and 3,4 dihyroxybenzohydrazed were dissolved in warm ethanol 35ml containing D.M.F (0.5ml).The reaction mixture was refluxed for 4 hours and kept room temperature overnight .The progress of the reaction was monitored by TLC with hexane and ethyl acetate (7:3) as mobile phase .The resulted solid compound was washed with ethanol and dried. The compound was recrystalized with ethanol to afford compound 3, 4-dihydroxy-N'-(2-oxo-1-(prop-2-ynyl) indoline-3-ylidene)benzohydrazide. The compound was characterized by spectral data IR, ^{1}H- NMR and elemental analysis. The similar procedure was employed for the synthesis of Z)-3, 4-dihydroxy-N'- (5-Chloro/5-bromo)2-oxo -1- (prop-2-yn-1-yl) indolin-3-ylidene)benzohydrazide **5(b-c)**, by condensing 3,4–Dihydroxybenzo hydrazide **(3)** with N-Isatinpropargyl. The structure of **5(b-c)** was established by IR, ^{1}H-NMR and elemental analysis.

Physical, analytical and spectral data for 3, 4-dihydroxy-N'-(2-oxo-1-(prop-2-ynyl) indoline-3-ylidene) benzohydrazide 5(a).

Yield: 62%; M. P: 128-130^0 C; IR (KBr): (ν/ δ,, cm^{-1}) 3350 (γ -OH, interamolecular-OH bending),1676 (C=O), 2251(-C≡CH), 3410 (NH-Stretching of acid hydrazide);1656 (C=O,Isatin), 1625(C=N); ^{1}H-NMR (400MHz, DMSO-d6) 3.70 (s, 2H, -CH_2 attached to Isatin), 3.80(s,1H, acetylene group), 5.35(s, 2H,-OHgroups attached to benzene ring), 8.10 (s,1H, NH-amide), 7.10-7.46 (m,7H, Aromatic protons); Anal. Calcd (%) for $C_{18}H_{13}N_3O_4$; C: 64.47%, H: 3.91%, N: 12.53% and O: 19.09%. Found: C: 63.77%, H: 3.31%, N: 11.93% and O: 18.29%.

Physical, analytical and spectral data for Z)-3, 4-dihydroxy-N'- (5-chloro) 2-oxo -1- (prop-2-yn-1-yl) indolin-3-ylidene) benzo hydrazide 5(b).

Yield: 68%; M. P: 135-137^0 C; IR (KBr): (ν/ δ,, cm^{-1}) 3358(γ-OH), 3415 (NH-), 2254(-C≡CH,), 1660(C=O), 1629, 1610 (C=N),730(C-Cl) ; ^{1}H-NMR (400MHz, DMSO-d6) 3.70 (s, 2H, -CH_2 attached to Isatin), 3.80(s,1H, acetylene group), 5.35(s, 2H, 2OH), 8.10 (s,1H, NH-), 7.30-7.60 (m,6H,Aromatic protons) ; Anal. Calcd (%) for $C_{18}H_{12}ClN_3O_4$; C:58.47%, H:3.27%, Cl:9.59%, N:11.36% and O:17.31. Found: C: 57.67 %, H: 2.77%, Cl:8.89%, N:10.86% and O:16.61%.

Physical, analytical and spectral data for Z)-3, 4-dihydroxy-N'- (5-bromo) 2-oxo -1- (prop-2-yn-1-yl) indolin-3-ylidene) benzo hydrazide 5(c).

Yield: 65%; M. P: 133-135^0 C; IR (KBr): (ν/ δ,, cm^{-1}) 3354(γ-OH,), 3409 (NH- stretching), 2251(-C≡CH, stretching), 1658(C=O, Isatin), 1604 (C=N), 650(C-Br); ^{1}H-NMR (400MHz, DMSO-d6); 3.70 (s,2H, CH_2), 3.80 (s,1H,acetylene group), 5.35 (s, 2H, vicinal 2 OH), 8.10 (s,1H, NH), 7.20-7.50 (m,6H, Aromatic protans) ; Anal. Calcd (%) for $C_{18}H_{12}BrN_3O_4$; C: 52.19%, H: 2.92%, Br: 19.29%, N: 10.14% and O: 15.45%. Found: C: 51.69%, H: 2.32%, Br: 18.69%, N: 9.54% and O: 14.65%.

Typical procedure for Synthesis of (Z) -N'-(1- ((1 -benzyl-1H-1, 2, 3-triazol-4-yl) methyl) -5-chloro /bromo -2-oxoindolin -3-ylidene)-3, 4-dihydroxy benzohydrazide 7(a-c)

In the procedure a mixture of Z)-3, 4-dihydroxy-N'- (2-oxo -1- (prop-2-yn-1-yl) indolin-3-ylidene) benzo hydrazide (5a) (0.01 mol) and benzylazide (0.01 mol) are added in ethanol 10 ml ,saturated copper sulphate solution(0.3mL ,1M) and cupper turnings (12 grams) was added. The contents are refluxed for 8 hours, after

completion of the reaction (monitored by TLC); the reaction mixture was filtered through celite. The progress of the reaction was monitored by TLC with hexane and ethyl acetate (7:3) as mobile phase. The compound washed with ethanol and dried. The compound was recrystalized with ethanol to afford compound (Z)-N'-(1-((1-benzyl-1H-1, 2, 3-triazol-4-yl) methyl)-2-oxoindolin-3-ylidene)-3, 4-dihydroxybenzo hydrazide. The compound was characterized by spectral data IR, ^{1}H-NMR, and elemental analysis.

The similar procedure was employed for the synthesis of (Z)-N'-(1-((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)-5-chloro/bromo-2-oxoindolin-3-ylidene)-3,4-dihydroxy benzohydrazide **7 (b-c)** by condensing Z)-3, 4-dihydroxy-N'- (5-chloro-/5-bromo) 2-oxo -1- (prop-2-yn-1-yl) indolin-3-ylidene) benzo hydrazide **5(b-c)** with benzylazide in presence of saturated copper sulphate solution and Cu-turnings in ethanol. The structure of **7(b-c)** was established by IR, ^{1}H-NMR and elemental analysis.

Physical, analytical and spectral data for (Z) -N'-(1-((1 -benzyl-1H-1, 2, 3-triazol-4-yl) methyl) -5-chloro -2-oxoindolin -3-ylidene)-3, 4-dihydroxy benzohydrazide 7(a).

Yield: 65%; M. P: 130-132^{0} C; IR (KBr): (ν/ δ,, cm^{-1}) 3350 (γ -OH, interamolecular-OH bending),1676 (C=O), 2251(-C≡CH), 3410 (NH-Stretching of acid hydrazide);1656 (C=O,Isatin), 1625(C=N), 1456&1355 (characteristics of triazole); ^{1}H-NMR (400MHz, DMSO-d6); 4.22 (s, 2H, CH_2 attached to phenyl ring), 5.35(s, 2H, 2 visional OH), 3.90.48(s, 2H, CH_2 flanked between isatin and triazole), 8.10(s,1H, NH-amide), 7.10-7.46(m,12, aromatic protons), 7.63(s,1H, CH in triazole ring). Anal. Calcd (%) for $C_{25}H_{20}N_6O_4$; C:64.10%, H:4.30%, N:17.94% and O:13.66%;Found; C:63.30%,H:3.70%, N:17.44% and O:13.16%

Physical, analytical and spectral data for (Z) -N'-(1- ((1 -benzyl-1H-1, 2, 3-triazol-4-yl) methyl) -5-chloro -2-oxoindolin -3-ylidene)-3, 4-dihydroxy benzohydrazide 7(b).

Yield: 60%; M.P: 125-127^{0} C; IR (KBr): (ν/ δ,, cm^{-1}). 3358(γ-OH), 3415 (NH-), 2254(-C≡CH,), 1660(C=O), 1629, 1610 (C=N), 1458& 1357 (characteristic of triazole),730(C-Cl) ^{1}H-NMR (400MHz, DMSO-d6); 4.22 (s, 2H ,CH_2 attached to Isatin), 5.35(s, 2H, 2OH-Ar), 5.48(s, 2H,CH_2-Ar) 8.10(s, 1H, NH), 7.16-7.42(m, 11 H, aromatic protons),7.63(s, 1H, CH in triazole ring). Anal. Calcd (%) for $C_{25}H_{19}ClN_6O_4$; C:59.71%, H:3.81%, Cl:7.05%, N:16.71% and O:12.73%; Found: C:58.91%, H:3.31%, Cl:6.25%, N:16.11% and O:11.93%

Physical, analytical and spectral data for (Z) -N'-(1- ((1 -benzyl-1H-1, 2, 3-triazol-4-yl) methyl) -5-bromo-2-oxoindolin -3-ylidene)-3, 4-dihydroxy benzohydrazide 7(c). Yield: 57%; M.P:118-120^{0} C; IR (KBr): (ν/ δ,, cm^{-1}) 3354(γ-OH,), 3409 (NH- stretching), 2251(-C≡CH, stretching), 1658(C=O, Isatin), 1604 (C=N), 1457& 1356 (characteristic of triazole. 650(C-Br),.^{1}H-NMR (400MHz, DMSO-d6); 4.22 (s,2H, CH_2 attached to Isatin), 5.35(s,2H, 2OH-Ar),), 5.48(s,2H, CH_2- Ar) 8.10(s,1H, NH),7.20-7.50(m,11 H, aromatic protans), 7.63(s,1H, CH of triazole ring). Anal. Calcd (%) for $C_{25}H_{19}BrN_6O_4$; C:54.86%,H:3.50%, Br:14.60%,N:15.35% and O:11.69%, Found; C:54.26%, H:2.90%, Br:14.00%,N:14.75% and O:10.89%

Typical procedure for Synthesis of Synthesis of (Z)-N'-(1-((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)(-5-chloro/bromo)-2-oxoindolin-3-ylidene)-2-(4-methyl /methoxy/ trifluoro/ nitro) cyclohexa-1,3-dien-1-yloxy)benzo[d] [1,3,2]dioxaphosphole-5-carbohydrazide 2-oxide 9(a-o)

A solution of phenylphosphorodichloridate **8(a)** (0.002 mol) in 25 ml of dry toluene was added drop wise over a period of 20 minutes to a stirred solution of (Z)-N'-(1-((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)-2-oxoindolin-3-ylidene)-3,4-dihydroxybenzohydrazide **(7a)** (0.002 mole) and triethylamine (0.004mole) in 30 ml of dry toluene and 10ml of tetrahydrofuran a 5^{0} C. After the addition, the temperature of the reaction mixture was slowly raised to room temperature and stirred for 2 hours. Later the reaction mixture was heated at 50-60^{0} C for 4 hours with stirring. The completion of the reaction was monitored by TLC analysis. Tri ethyl amine hydrochloride was filtered from mixture and solvent was removed under reduced pressure. The residue was washed with water, which was further purified by column chromatography over silicagel (60-120mesh),hexane and ethyl acetate (7:3) was used as an eluent to afford the compound (Z)-N'-(1-((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)-2-oxoindolin-3-ylidene)-2-(cyclohexa-1,3-dien-1-yloxy) benzo[d] [1,3,2] dioxaphosphole-5-carbohydrazide 2-oxide **(9a).**The compound was characterized by spectral data IR, ^{1}H-NMR, ^{13}C-NMR, ^{31}P-NMR and elemental analysis.

The similar reaction procedure was adopted to synthesis of (Z)-N'-(1-((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)(-5-chloro/bromo)-2-oxoindolin-3-ylidene)-2-(4-methyl /methoxy/ trifluoro/ nitro)cyclohexa-1,3-dien-1-yloxy)benzo[d] [1,3,2] dioxa phosphole-5-carbohydrazide 2-oxide 9(a-o), by the reaction between (Z)-N'-(1-((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)-(5-chloro/bromo) 2-oxoindolin-3-ylidene)-3,4-dihydroxybenzo hydrazide 7(a-c) with 4-methylphenyl phosphorodichloridate 8(b), methoxyphenyl phosphorodichloridate 8(c), 4-p(trifluoro phenyl phosphorodichloridate 8(d), 4-chlorophenyl phosphorodichloridate 8(e), 4-bromophenyl phosphorodichloridate 8(f) and nitrophenyl Phosphorodichloridate 8(g), respectively. The structures of 9(a-o) were established by IR, ^{1}H-NMR, ^{13}C-NMR, ^{31}P-NMR and elemental analysis.

Physical, analytical and spectral data for (Z)-N'-(1-((1-benzyl-1H-1, 2, 3-triazol-4-yl)methyl)-2-oxoindolin-3-

ylidene)-2-(cyclohexa-1,3-dien-1-yloxy)benzo[d] [1,3,2] dioxaphosphole-5-carbohydrazide 2-oxide (9a).

Yield: 65%; M.P: 130-132^0 C; IR (KBr): (ν/ δ,, cm^{-1}), 3410 (NH-Stretching of acid hydrazide) 1676 (Carbinyl of acid hydrazide), 1656 (C=O,Isatin), 1625(C=N), 1456 & 1355(Characteristics of tiazole), 1250(P=O), 950 (P-O-$C_{(Ar-c)}$). ^{1}H-NMR (400MHz, DMSO-d6); 3.90 (s,2H -CH_2 flanked between isatin triazole), 3.60(s,2H, CH_2 group attached to phenyl ring) 8.10(s,1H, NH-amide),7.63(s, 1H, CH in triazole ring),7.10-7.46(m,17H,aromatic protons).^{13}C-NMR(75MHz, DMSO-d6); δ, ppm.114.6, 145.3, 148.6, 117.4, 121.5, 128.2, 163.2, 129.4, 124.4, 131.2, 122.9, 147.3, 117.7, 163.5, 131.5, 52.1, 130.7, 115.8, 57.3, 133.7, 127.6, 128.6, 125.7, 128.6, 127.6, 150.2, 120.3, 130.1, 121.3, 130.1, and 120.3 Corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14} ,C_{15} ,C_{16}, C_{17}, C_{18}, C_{19}, C_{20} , C_{21}, C_{22}, C_{23}, C_{24}, C_{25}, C_{26}, C_{27}, C_{28}, C_{29}, C_{30}, and C_{31}.^{31}P-NMR (161.89MHz, DMSO-d6)-5.90 and -5.53ppm. Anal. Calcd (%) for $C_{31}H_{25}N_6O_6P$; C: 61.94%, H: 4.06%, N: 13.54%, O: 15.47% and P: 4.99%. Found; C: 61.24%, H: 5.46%, N: 12.94%, O: 14.57% and P: 4.39%

Physical, analytical and spectral data for (Z)-N'-(1-((1-benzyl-1H-1, 2, 3-triazol-4-yl)methyl)-2oxoindolin-3-ylidene)-2-((4methylcyclohexa-1,3-dien-1-yl)oxy)benzo[d][1,3,2] dioxaphosphole-5-carbohydrazide 2-oxide 9(b)

Yield: 73%; M.P: 138-140^0 C; IR (KBr): (ν/ δ,, cm^{-1}) 3416 (NH-Stretching of acid hydrazide) 1678 (Carbinyl of acid hydrazide), 1659 (C=O,Isatin), 1627(C=N), 1456 & 1355(Characteristics of tiazole), 1253(P=O), 950 (P-O-$C_{(Ar-c)}$). ^{1}H-NMR (400MHz, DMSO-d6); 2.54(s,3H,$\underline{CH_3}$-Ar), 3.90 (s,2H -CH_2 flanked between isatin triazole), 3.60(s,2H, CH_2 group attached to phenyl ring) 8.10(s,1H, NH-amide), 7.64(s, 1H, CH in triazole ring), 7.10-7.46(m,16H,aromatic protons).^{13}C-NMR(75MHz, DMSO-d6); δ, ppm. 114.6, 145.3, 148.6, 117.4, 121.5, 128.2, 163.2, 129.4, 124.4, 131.2, 122.9, 147.3, 117.7, 163.5, 131.5, 52.1, 130.7, 115.8, 57.3, 133.7, 127.6, 128.6, 125.7, 128.6, 127.6, 147.2, 118.2, 130.1, 121.3, 130.1, 120.3 and 21.3 Corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14} ,C_{15} ,C_{16}, C_{17}, C_{18}, C_{19}, C_{20} , C_{21}, C_{22}, C_{23}, C_{24}, C_{25}, C_{26}, C_{27}, C_{28}, C_{29}, C_{30}, C_{31} and C_{32} . ^{31}P-NMR (161.89MHz, DMSO-d6)-6.40 and -5.48 ppm. Anal. Calcd (%) for $C_{32}H_{25}N_6O_6P$; C: 61.94%, H: 4.06%, N: 13.54%, O: 15.47% and P: 4.99%.Found; C: 61.34%, H: 5.56%, N: 12.94%, O: 14.87% and P: 4.49%

Physical, analytical and spectral data for (Z)-N'-(1-((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)-2oxoindolin-3-ylidene)-2-((4methoxyCyclohexa-1,3-dien-1yl)oxy)benzo[d] [1,3,2] dioxa phosphole-5-carbohydrazide 2-oxide 9(c).

Yield: 58%; M.P: 120-122^0 C; IR (KBr): (ν/ δ,, cm^{-1}) 3418 (NH-Stretching of acid hydrazide) 1678 (Carbinyl of acid hydrazide), 1657 (C=O,Isatin), 1628(C=N), 1456 & 1355(Characteristics of tiazole), 1253(P=O), 950 (P-O-$C_{(Ar-c)}$). ^{1}H-NMR (400MHz, DMSO-d6); 3.25(s, 3H OCH_3 attached to phenyl ring), 3.90 (s, 2H -CH_2 flanked between isatin triazole), 3.60(s,2H, CH_2 group attached to phenyl ring) 8.14(s,1H, NH-amide), 7.63(s, 1H, CH in triazole ring), 7.12-7.46 (m,16H,aromatic protons). ^{13}C-NMR (75MHz, DMSO-d6); δ, ppm. 114.6, 145.3, 148.6, 117.4, 121.5, 128.2, 163.2, 129.4, 124.4, 131.2, 122.9, 147.3, 117.7, 163.5, 131.5, 52.1, 130.7, 115.8, 57.3, 133.7, 127.6, 128.6, 125.7, 128.6, 127.6, 145.2, 116.9, 115.7, 153.2, 115.7, 116.9 and 55.8 Corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14} ,C_{15} ,C_{16}, C_{17}, C_{18}, C_{19}, C_{20} , C_{21}, C_{22}, C_{23}, C_{24}, C_{25}, C_{26}, C_{27}, C_{28}, C_{29}, C_{30}, C_{31} and C_{32} .^{31}P-NMR (161.89MHz, DMSO-d6) -10.09 and -5.16ppm. Anal. Calcd (%) for $C_{32}H_{25}N_6O_7P$; C: 60.38%, H: 3.96%, N: 13.20%,O:17.59% and P: 4.87%.Found; C:59.58%, H:3.46%, N:12.60%, O:16.79% and P:4.17%

Physical, analytical and spectral data for Z)-N'-(1-((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)-2oxoindolin-3-ylidene)-2-((4-(trifluoromethyl) cyclohexa-1,3-dien-1-yl)oxy) benzo[d][1,3,2] dioxaphosphole-5-carbohydrazide2-oxide 9(d).

Yield: 73%; M.P: 130-132^0 C; IR (KBr): (ν/ δ,, cm^{-1}) (ν/ δ,, cm^{-1}) 3420 (NH-Stretching of acid hydrazide) 1676 (Carbinyl of acid hydrazide), 1656 (C=O,Isatin), 1625(C=N), 1456 & 1355(Characteristics of tiazole), 1252(P=O), 950 (P-O-$C_{(Ar-c)}$). ^{1}H-NMR (400MHz, DMSO-d6); 3.90 (s,2H -CH_2 flanked between isatin triazole), 3.60(s,2H, CH_2 group attached to phenyl ring) 8.10(s,1H, NH-amide), 7.63(s, 1H, CH in triazole ring), 7.10-7.46 (m,16H,aromatic protons) .^{13}C-NMR (75MHz, DMSO-d6); δ, ppm 114.6, 145.3, 148.6, 117.4, 121.5, 128.2, 163.2, 129.4, 124.4, 131.2, 122.9, 147.3, 117.7, 163.5, 131.5, 52.1, 130.7, 115.8, 57.3, 133.7, 127.6, 128.6, 125.7, 128.6, 127.6, 153.5, 118.6, 128.6, 123.6,128.6, 118.6 and 124.1 Corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14} ,C_{15} ,C_{16}, C_{17}, C_{18}, C_{19}, C_{20} , C_{21}, C_{22}, C_{23}, C_{24}, C_{25}, C_{26}, C_{27}, C_{28}, C_{29}, C_{30}, C_{31} and $C_{32.}$ ^{31}P-NMR (161.89MHz, DMSO-d6)-11.03ppm. Anal. Calcd (%) for $C_{32}H_{22}F_3N_6O_6P$; C: 56.98%, H: 3.29%, F: 8.45%, N: 12.46%, O: 14.23% and P: 4.59%. Found; C: 56.28%, H: 2.69%, F: 7.75%, N: 11.86%, O: 13.53% and P: 3.89%.

Physical, analytical and spectral data for Z)-N'-(1-((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)-2 oxoindolin-3-ylidene)-2-((4-nitrocyclohexa-1,3-dien-1-yl)oxy)benzo[d][1,3,2] dioxaphosphole-5-carbohydrazide 2-oxide 9(e).

Yield: 62%; M.P: 128-130^0 C; IR (KBr): 3417 (NH-Stretching of acid hydrazide) 1675 (Carbinyl of acid hydrazide), 1656 (C=O,Isatin), 1625(C=N), 1456 & 1355(Characteristics of tiazole), 1254(P=O), 950 (P-O-

$C_{(Ar-c)}$). ^{1}H-NMR (400MHz, DMSO-d6); 3.90 (s,2H -CH_2 flanked between isatin triazole), 3.60(s,2H, CH_2 group attached to phenyl ring) 8.10(s,1H, NH-amide), 7.63(s, 1H, CH in triazole ring), 7.10-7.46 (m,16H,aromatic protons) . ^{13}C-NMR (75MHz, DMSO-d6); δ, ppm 114.6, 145.3, 148.6, 117.4, 121.5, 128.2, 163.2, 129.4, 124.4, 131.2, 122.9, 147.3, 117.7, 163.5, 131.5, 52.1, 130.7, 115.8, 57.3, 133.7, 127.6, 128.6, 125.7, 128.6, 127.6, 150.2, 120.3, 130.1, 121.3, 130.1, and 120.3 Corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14} ,C_{15} ,C_{16}, C_{17}, C_{18}, C_{19}, C_{20} , C_{21}, C_{22}, C_{23}, C_{24}, C_{25}, C_{26}, C_{27}, C_{28}, C_{29}, C_{30}, and C_{31}. ^{31}P-NMR (161.89MHz, DMSO-d6) -11.40 and -5.85ppm. Anal. Calcd (%) for $C_{31}H_{22}N_7O_8P$; C: 57.15%, H: 3.40%, N: 15.05%, O: 19.65% and P: 4.75%. Found; C: 56.35%, H: 2.90%, N: 14.55%, O: 18.85% and P: 4.15%.

Physical, analytical and spectral data for (Z)-N'-(1-((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)-5-chloro-2-oxoindolin-3-ylidene)-2-(cyclohexa-1,3-dien-1yloxy)benzo[d][1,3,2]dioxaphosphole-5-carbohydrazide 2-oxide 9(f)

Yield: 68%; M.P: 136-138^0 C; IR (KBr): (ν/ δ,, cm^{-1}) 3414 (NH-Stretching of acid hydrazide) 1678 (Carbinyl of acid hydrazide), 1657 (C=O,Isatin), 1626(C=N), 1456 & 1355(Characteristics of tiazole), 1250(P=O),,950 (P-O-$C_{(Ar-c)}$). ^{1}H-NMR (400MHz, DMSO-d6); 3.90 (s,2H -CH_2 flanked between isatin triazole), 3.60(s,2H, CH_2 group attached to phenyl ring) 8.10(s,1H, NH-amide), 7.63(s, 1H, CH in triazole ring), 7.30-7.56 (m,16H,aromatic protons). ^{13}C-NMR (75MHz, DMSO-d6); δ,ppm. 114.6, 145.3, 148.6, 117.4, 121.5, 128.2, 163.2, 129.4, 130.0, 131.3, 122.9, 145.5, 119.1, 163.5, 151.1, 52.1, 130.7, 115.8, 57.3, 133.7, 127.6, 128.6, 125.7, 128.6, 127.6, 150.2, 120.3, 130.1, 121.3, 130.1, and 120.3 Corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14} ,C_{15} ,C_{16}, C_{17}, C_{18}, C_{19}, C_{20} , C_{21}, C_{22}, C_{23}, C_{24}, C_{25}, C_{26}, C_{27}, C_{28}, C_{29}, C_{30}, and C_{31}. ^{31}P-NMR (161.89MHz, DMSO-d6)-6.87 and -5.06ppm. Anal. Calcd (%) for $C_{31}H_{22}ClN_6O_6P$; C: 58.09%, H: 3.46%, Cl: 5.53%, N: 13.11%, O: 14.98% and P: 4.83%. Found; C: 57.29%, H: 2.96%, Cl: 4.73%, N: 12.51%, O: 14.18 %and P: 4.13%.

Physical, analytical and spectral data for Z)-N'-(1-((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)-5-chloro-2-oxoindolin-3-ylidene)-2-(p-tolyloxy)benzo[d][1,3,2] dioxaphosphole-5-carbohydrazide 2-oxide 9(g).

Yield: 56%; M.P: 118-120^0 C; IR (KBr): (ν/ δ,, cm^{-1}3415 (NH-Stretching of acid hydrazide) 1677 (Carbinyl of acid hydrazide), 165 (C=O,Isatin), 1628(C=N), 1456 & 1355(Characteristics of tiazole), 1253(P=O),, 950 (P-O-$C_{(Ar-c)}$). ^{1}H-NMR (400MHz, DMSO-d6); 3.90 (s,2H -CH_2 flanked between isatin triazole), 3.60(s,2H, CH_2 group attached to phenyl ring) 8.10(s,1H, NH-amide), 7.63(s, 1H, CH in triazole ring), 7.31-7.56 (m,15 H,aromatic protons). ^{13}C-NMR (75MHz, DMSO-d6); δ, ppm 114.6, 145.3, 148.6, 117.4, 121.5, 128.2, 163.2, 129.4, 130.0, 131.3, 122.9, 145.5, 119.1, 163.5, 151.1, , 52.1, 130.7, 115.8, 57.3, 133.7, 127.6, 128.6, 125.7, 128.6, 127.6, 147.2, 118.2, 130.1, 121.3, 130.1, 120.3 and 21.3 Corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14} ,C_{15} ,C_{16}, C_{17}, C_{18}, C_{19}, C_{20} , C_{21}, C_{22}, C_{23}, C_{24}, C_{25}, C_{26}, C_{27}, C_{28}, C_{29}, C_{30}, C_{31} and C_{32} .^{31}P-NMR (161.89MHz, DMSO-d6)-7.60 and ppm. Anal. Calcd (%) for $C_{32}H_{24}ClN_6O_6P$; C: 58.68%, H: 3.69%, Cl: 5.41%, N: 12.83%, O: 14.66% and P: 4.73%. Found; C: 57.98%, H: 3.09%, Cl: 4.61%, N: 12.13%, O: 14.06% and P: 4.03%.

Physical, analytical and spectral data for (Z)-N'-(1-((1-benzyl-1H-1, 2, 3-triazol-4-yl)methyl)-5-chloro-2-oxoindolin-3-ylidene)-2-(4-methoxyphenoxy)benzo[d] [1,3,2] dioxaphosphole-5- carbohydrazide 2-oxide 9(h)

Yield: 60%; M.P: 125-127^0 C; IR (KBr): (ν/ δ,, cm^{-1}) 3418 (NH-Stretching of acid hydrazide) 1679 (Carbinyl of acid hydrazide), 1658 (C=O,Isatin), 1627(C=N), 1456 & 1355(Characteristics of tiazole), 1254(P=O),, 950 (P-O-$C_{(Ar-c)}$). ^{1}H-NMR (400MHz, DMSO-d6); 3.90 (s, 2H -CH_2 flanked between isatin triazole), 3.60(s,2H, CH_2 group attached to phenyl ring) 8.10(s,1H, NH-amide), 7.63(s, 1H, CH in triazole ring), 7.31-7.56 (m,15 H,aromatic protons). ^{13}C-NMR (75MHz, DMSO-d6); δ, ppm 114.6, 145.3, 148.6, 117.4, 121.5, 128.2, 163.2, 129.4, 130.0, 131.3, 122.9, 145.5, 119.1, 163.5, 151.1, 52.1, 130.7, 115.8, 57.3, 133.7, 127.6, 128.6, 125.7, 128.6, 127.6, 153.5, 118.6, 128.6, 123.6,128.6, 118.6 and 124.1 Corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14} ,C_{15} ,C_{16}, C_{17}, C_{18}, C_{19}, C_{20} , C_{21}, C_{22}, C_{23}, C_{24}, C_{25}, C_{26}, C_{27}, C_{28}, C_{29}, C_{30}, C_{31} and C_{32} .^{31}P-NMR (161.89MHz, DMSO-d6)-10.37 and 5.47ppm. Anal. Calcd (%) for $C_{32}H_{24}ClN_6O_7P$; C: 57.28%, H: 3.61%, Cl: 5.28%, N: 12.52%, O: 16.69% and P: 4.62%. Found; C: 56.48%, H: 3.11%, Cl: 4.48%, N: 11.92%, O: 15.89% and P: 3.92%.

Physical, analytical and spectral data for (Z)-N'-(1-((1-benzyl-1H-1, 2, 3-triazol-4-yl)methyl)-5-chloro-2-oxoindolin-3 -ylidene) -2(4(trifluoromethyl) phenoxy)benzo[d] [1,3,2] dioxaphosphole -5-carbohydrazide 2-oxide 9(i)

Yield: 64%; M.P: 132-133^0 C; IR (KBr): ν/ δ,, cm^{-1}) 3410 (NH-Stretching of acid hydrazide) 1676 (Carbinyl of acid hydrazide), 1656 (C=O, Isatin), 1625(C=N), 1456 & 1355(Characteristics of tiazole), 1256(P=O), 950 (P-O-$C_{(Ar-c)}$). ^{1}H-NMR (400MHz, DMSO-d6); 3.90 (s, 2H -CH_2 flanked between isatin triazole), 3.60(s, 2H, CH_2 group attached to phenyl ring) 8.10(s,1H, NH-amide), 7.63(s, 1H, CH in triazole ring), 7.10-7.46 (m,15 H,aromatic protons). ^{13}C-NMR (75MHz, DMSO-d6); δ, ppm 114.6, 145.3, 148.6, 117.4, 121.5, 128.2, 163.2, 129.4, 130.0, 131.3, 122.9, 145.5, 119.1, 163.5, 151.1, , 52.1, 130.7, 115.8, 57.3, 133.7, 127.6, 128.6, 125.7, 128.6, 127.6, 153.5, 118.6, 128.6, 123.6, 128.6, 118.6

and 124.1 Corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14} ,C_{15} ,C_{16}, C_{17}, C_{18}, C_{19}, C_{20} , C_{21}, C_{22}, C_{23}, C_{24}, C_{25}, C_{26}, C_{27}, C_{28}, C_{29}, C_{30}, C_{31} and C_{32}. ^{31}P-NMR (161.89MHz, DMSO-d6ppm) -11.05. Anal. Calcd (%) for $C_{32}H_{21}ClF_3N_6O_6P$; C: 54.21%, H: 2.99%, Cl: 5.00%, F: 78.04%, N: 12.85%, O: 13.54% andP: 4.37%. Found; C: 53.71%, H: 2.39%, Cl: 4.20, F: 77.34%, N: 11.35%, O: 12.84%and P: 3.67%.

Physical, analytical and spectral data for (Z)-N'-(1-((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)-5-chloro-2-oxoindolin-3-ylidene)-2-(4-nitrophenoxy)benzo [d][1,3,2]dioxaphosphole-5 carbohydrazide 2-oxide 9(j).

Yield: 60%; M.P: 126-128^0 C; IR (KBr): (ν/ δ,, cm^{-1}) 3420 (NH-Stretching of acid hydrazide) 1680 (Carbinyl of acid hydrazide), 1662 (C=O,Isatin), 1629(C=N), 1456 & 1355(Characteristics of tiazole), 1254(P=O),, 950 (P-O-$C_{(Ar-c)}$). ^{1}H-NMR (400MHz, DMSO-d6); 3.90 (s,2H - CH_2 flanked between isatin triazole), 3.60(s,2H, CH_2 group attached to phenyl ring) 8.10(s,1H, NH-amide), 7.63(s, 1H, CH in triazole ring), 7.38-7.56 (m,15 H,aromatic protons). ^{13}C-NMR (75MHz, DMSO-d6); δ, ppm 114.6, 145.3, 148.6, 117.4, 121.5, 128.2, 163.2, 129.4, 130.0, 131.3, 122.9, 145.5, 119.1, 163.5, 151.1, 52.1, 130.7, 115.8, 57.3, 133.7, 127.6, 128.6, 125.7, 128.6, 127.6, 153.5, 118.6, 128.6, 123.6, 128.6, 118.6 and 124.1 Corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14} ,C_{15} ,C_{16}, C_{17}, C_{18}, C_{19}, C_{20} , C_{21}, C_{22}, C_{23}, C_{24}, C_{25}, C_{26}, C_{27}, C_{28}, C_{29}, C_{30}, C_{31} and C_{32} . ^{31}P-NMR (161.89MHz, DMSO-d6) -8.86ppm. Anal. Calcd (%) for; C: 54.28%, H: 3.09%, Cl: 5.17%, N: 14.29%, O: 18.66% and P: 4.52%. Found; C: 53.48%, H: 2.59%, Cl: 4.37%, N: 13.59%, O: 17.86% and P: 3.82%.

Physical, analytical and spectral data for (Z)-N'-(1-((1-benzyl-1H-1, 2, 3-triazol-4-yl)methyl)-5-bromo-2-oxoindolin-3-ylidene)-2-phenoxy benzo[d][1,3,2 dioxaphosphole-5-carbohydrazide 2-oxide 9(k).

Yield: 68%; M.P: 140-142^0 C; IR (KBr): (ν/ δ,, cm^{-1}) 3416 (NH-Stretching of acid hydrazide) 1679 (Carbinyl of acid hydrazide), 1657 (C=O,Isatin), 1625(C=N), 1456 & 1355(Characteristics of tiazole), 1252(P=O),, 950 (P-O-$C_{(Ar-c)}$). ^{1}H-NMR (400MHz, DMSO-d6); 3.90 (s, 2H - CH_2 flanked between isatin triazole), 3.60(s,2H, CH_2 group attached to phenyl ring) 8.21(s,1H, NH-amide), 7.63(s, 1H, CH in triazole ring), 7.10-7.40 (m,16 H,aromatic protons). ^{13}C-NMR (75MHz, DMSO-d6); 114.6, 145.3, 148.6, 117.4, 121.5, 128.2, 163.2, 132.9, 118.8, 141.8, 117.9, 146.4, 119.9 163.5, 131.5, 52.1, 130.7, 115.8, 57.3, 133.7, 127.6, 128.6, 125.7, 128.6, 127.6, 150.2, 120.3, 130.1, 121.3, 130.1, and 120.3 Corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14} ,C_{15} ,C_{16}, C_{17}, C_{18}, C_{19}, C_{20} , C_{21}, C_{22}, C_{23}, C_{24}, C_{25}, C_{26}, C_{27}, C_{28}, C_{29}, C_{30}, and C_{31}. ^{31}P-NMR (161.89MHz, DMSO-d6)-7.72 and 6.57ppm. Anal. Calcd (%) for; $C_{31}H_{22}BrN_6O_6P$; C: 54.32%, H: 3.24%, Br: 11.66%, N: 12.26%, O: 14.01% and P: 4.52%. Found; C: 53.92%, H: 2.74%, Br:11.56%, N:11.66%, O:13.21% and P:4.02%. Physical, analytical and spectral data for (Z)-N'-(1-((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)-5-bromo-2-oxoindolin-3-ylidene)-2-(p-tolyloxy)benzo[d] [1,3,2]dioxaphosphole-5 carbohydrazide 2-oxide 9(l)

Yield: 63%; M.P: 130-132^0 C; IR (KBr): (ν/ δ, cm^{-1}) 3418 (NH-Stretching of acid hydrazide) 1680 (Carbinyl of acid hydrazide), 1671 (C=O,Isatin), 1627(C=N), 1456 & 1355(Characteristics of tiazole), 1250(P=O),, 950 (P-O-$C_{(Ar-c)}$). ^{1}H-NMR (400MHz, DMSO-d6); 3.90 (s,2H - CH_2 flanked between isatin triazole), 3.60(s,2H, CH_2 group attached to phenyl ring) 8.14(s,1H, NH-amide), 7.63(s, 1H, CH in triazole ring), 7.12-7.43 (m,15H ,aromatic protons). ^{13}C-NMR (75MHz, DMSO-d6); 114.6, 145.3, 148.6, 117.4, 121.5, 128.2, 163.2, 132.9, 118.8, 141.8, 117.9, 146.4, 119.9 163.5, 131.5, 52.1, 130.7, 115.8, 57.3, 133.7, 127.6, 128.6, 125.7, 128.6, 127.6, 147.2, 118.2, 130.1, 121.3, 130.1, 120.3 and 21.3 Corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14} ,C_{15} ,C_{16}, C_{17}, C_{18}, C_{19}, C_{20} , C_{21}, C_{22}, C_{23}, C_{24}, C_{25}, C_{26}, C_{27}, C_{28}, C_{29}, C_{30}, C_{31} and C_{32}. ^{31}P-NMR (161.89MHz, DMSO-d6)-6.02ppm. Anal. Calcd (%) for; $C_{32}H_{24}BrN_6O_6P$; C: 54.95%, H: 3.46%, Br: 11.42%, N: 12.02%, O: 13.72% and P: 4.43%. Found; C: 54.35%, H: 2.96%, Br: 10.82%, N: 11.42%, O: 13.02% and P: 3.83%.

Physical, analytical and spectral data for (Z)-N'-(1-((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)-5-bromo-2-oxoindolin-3-ylidene)-2-(4 methoxyphenoxy)benzo[d] [1,3,2] dioxaphosphole-5-carbohydrazide 2-oxide 9(m).

Yield: 70%; M.P: 145-147^0 C; IR (KBr): (ν/ δ,, cm^{-1}) 3420 (NH-Stretching of acid hydrazide) 1682 (Carbinyl of acid hydrazide), 1661 (C=O,Isatin), 1634(C=N), 1456 & 1355(Characteristics of tiazole), 1252(P=O),, 950 (P-O-$C_{(Ar-c)}$). ^{1}H-NMR (400MHz, DMSO-d6); 3.90 (s,2H - CH_2 flanked between isatin triazole), 3.60(s,2H, CH_2 group attached to phenyl ring) 8.25(s,1H, NH-amide), 7.63(s, 1H, CH in triazole ring), 7.16-7.43 (m,15 H,aromatic protons). ^{13}C-NMR (75MHz, DMSO-d6); 114.6, 145.3, 148.6, 117.4, 121.5, 128.2, 163.2, 132.9, 118.8, 141.8, 117.9, 146.4, 119.9 163.5, 131.5, 52.1, 130.7, 115.8, 57.3, 133.7, 127.6, 128.6, 125.7, 128.6, 127.6, 153.5, 118.6, 128.6, 123.6,128.6, 118.6 and 124.1 Corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14} ,C_{15} ,C_{16}, C_{17}, C_{18}, C_{19}, C_{20} , C_{21}, C_{22}, C_{23}, C_{24}, C_{25}, C_{26}, C_{27}, C_{28}, C_{29}, C_{30}, C_{31} and C_{32} . ^{31}P-NMR (161.89MHz, DMSO-d6)-7.29ppm. Anal. Calcd (%) for; $C_{32}H_{24}BrN_6O_7P$; C: 53.72%, H: 3.38%, Br: 11.17%, N: 11.75%, O: 15.65% and P: 4.33% Found; C: 53.02%, H: 2.68%, Br: 10.47%, N: 11.25%, O: 14.85% and P: 3.63%. Physical, analytical and spectral data for (Z)-N'-(1-((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)-5-bromo-2-oxoindolin-3-ylidene)-2-(4-(trifluoromethyl)phenoxy) benzo[d][1,3,2] dioxa phosphole-5-carbohydrazide 2-oxide 9(n). Yield: 73%; M.P: 152-154^0 C; IR (KBr): (ν/ δ,, cm^{-1}) 3418 (NH-Stretching of acid hydrazide) 1678 (Carbinyl of acid

hydrazide), 1659 (C=O,Isatin), 1627(C=N), 1456 & 1355(Characteristics of tiazole), 1258(P=O),, 956 (P-O-$C_{(Ar-c)}$). ^{1}H-NMR (400MHz, DMSO-d6); 3.94 (s,2H -CH_2 flanked between isatin triazole), 3.80(s,2H, CH_2 group attached to phenyl ring) 8.40(s,1H, NH-amide), 7.93(s, 1H, CH in triazole ring), 7.19-7.46 (m,15 H,aromatic protons). ^{13}C-NMR (75MHz, DMSO-d6); 114.6, 145.3, 148.6, 117.4, 121.5, 128.2, 163.2, 132.9, 118.8, 141.8, 117.9, 146.4, 119.9 163.5, 131.5, 52.1, 130.7, 115.8, 57.3, 133.7, 127.6, 128.6, 125.7, 128.6, 127.6, 153.5, 118.6, 128.6, 123.6, 128.6, 118.6 and 124.1 Corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14} ,C_{15} ,C_{16}, C_{17}, C_{18}, C_{19}, C_{20} , C_{21}, C_{22}, C_{23}, C_{24}, C_{25}, C_{26}, C_{27}, C_{28}, C_{29}, C_{30}, C_{31} and C_{32} . ^{31}P-NMR (161.89MHz, DMSO-d6)-11.82ppm. Anal. Calcd (%) for; $C_{31}H_{21}BrN_7O_8P$; C: 50.98%, H: 2.90%, Br: 10.94%, N: 13.42%, O: 17.52% and P: 4.24%. Found; C:50.48%, H:2.20%, Br:10.44%, N:12.82%, O:16.72 and P:3.54%. Physical, analytical and spectral data for (Z)-N'-(1-((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)-5-bromo-2-oxoindolin-3-ylidene)-2-(4-nitrophenoxy)benzo [d][1,3,2] dioxaphosphole-5 carbohydrazide 2-oxide 9(o)

Yield: 56%; M.P: 135-137^0 C; IR (KBr): (ν/ δ,, cm^{-1}) 3410 (NH-Stretching of acid hydrazide) 1676 (Carbinyl of acid hydrazide), 1656 (C=O,Isatin), 1625(C=N), 1456 & 1355(Characteristics of tiazole), 1254(P=O),, 952 (P-O-$C_{(Ar-c)}$). ^{1}H-NMR (400MHz, DMSO-d6); 3.90 (s, 2H -CH_2 flanked between isatin triazole), 3.60(s,2H, CH_2 group attached to phenyl ring) 8.10(s,1H, NH-amide), 7.63(s, 1H, CH in triazole ring), 7.10-7.46 (m,15 H,aromatic protons). ^{13}C-NMR (75MHz, DMSO-d6); 114.6, 145.3, 148.6, 117.4, 121.5, 128.2, 163.2, 132.9, 118.8, 141.8, 117.9, 146.4, 119.9 163.5, 131.5, 52.1, 130.7, 115.8, 57.3, 133.7, 127.6, 128.6, 125.7, 128.6, 127.6, 151.3, 121.9, 126.3, 140.5, 126.3 and 121.9 Corresponding to C_1, C_2, C_3, C_4, C_5, C_6, C_7, C_8, C_9, C_{10}, C_{11}, C_{12}, C_{13}, C_{14} ,C_{15} ,C_{16}, C_{17}, C_{18}, C_{19}, C_{20} , C_{21}, C_{22}, C_{23}, C_{24}, C_{25}, C_{26}, C_{27}, C_{28}, C_{29}, C_{30} and C_{31} . ^{31}P-NMR (161.89MHz, DMSO-d6)-9.37ppm. Anal. Calcd (%) for; $C_{31}H_{21}BrN_7O_8P$; C: 50.98%, H: 2.90%, Br: 10.94%, N: 13.42%, O: 17.52% and P: 4.24%. Found; C: 50.18%, H: 2.40%, Br: 10.34%, N: 12.82%, O: 16.72% and P: 3.54%.

Biological activity

The antimicrobial activity[21] of these newly synthesized compounds was performed according to disc diffusion method as recommended by the National Committee for Clinical Laboratory.[22] The synthesized compounds were used as the concentration of 250µg/ml DMF as a solvent.[23]

Antibacterial activity

The antibacterial activity[24] 1, 2, 3 Triazole containing Dioxaphospholanes 9(a-o) were screened against the Staphyloccus aureus and Bacillus cerus (gram positive) and Escherichia coli, Pseudomonas aeruginosa (gram negative) organisms. Most of the compounds exhibited good antibacterial activity against both bacteria. Here Amoxicillin is tested as reference compound to compare the activity. The anti-bacterial activity was shown in the table: 1.1

Table-1.1: Antibacterial activity (Diameter zone of inhibition in mm) of Compounds 9(a-o)

S.NO	COMP	Zone of inhibition(mm)			
		Staphylococcus Aureus NCCS 2079 250 µg/disc	Bacillus cereus NCCS 2106 250 µg/disc	Escherichia coli NCCS2065 250µg/disc	Pseudomonas aeruginosa NCCS 2200 250µg/disc
1	9a	06	03	04	05
2	9b	07	04	05	06
3	9c	08	05	06	07
4	9d	09	06	07	09
5	9e	11	07	09	10
6	9f	13	08	10	11
7	9g	15	09	11	12
8	9h	16	11	12	14
9	9i	17	12	13	16
10	9j	19	14	15	17
11	9k	07	04	05	06
12	9l	08	05	06	07
13	9m	09	06	07	08
14	9n	11	07	09	10
15	9o	12	09	10	11
Amoxicillin		21	27	24	22

The chloro substituted compounds (9f-9j) showed more antimicrobial activity than bromo substituted compound [9k-9(o)], which interned showed high antibacterial activity than unsubstituted compounds (9a-9e) containing same substituents .The order of activities are Unsubstituted: Chloro Substituted; Bromo Substituted: 9j>9i>9h>9g>9f>,; 9(o)>9n>9m>9l>9k, 9e>9d>9c> 9b>9a,

Anti-fungal activity

Anti fungal activity 1.2.3 triazole containing Dioxaphospholanes 9(a-l) were screened against Aspergillus Niger and Candida albicans. Most of the compounds exhibit well anti fungal activity against both fungi. The most of the compounds exhibit good antifungal activity against both fungai. Here Ketoconazole is tested as reference[25, 26] compounds to compare the activity. The anti-fungal activity was shown in the table: 1.2

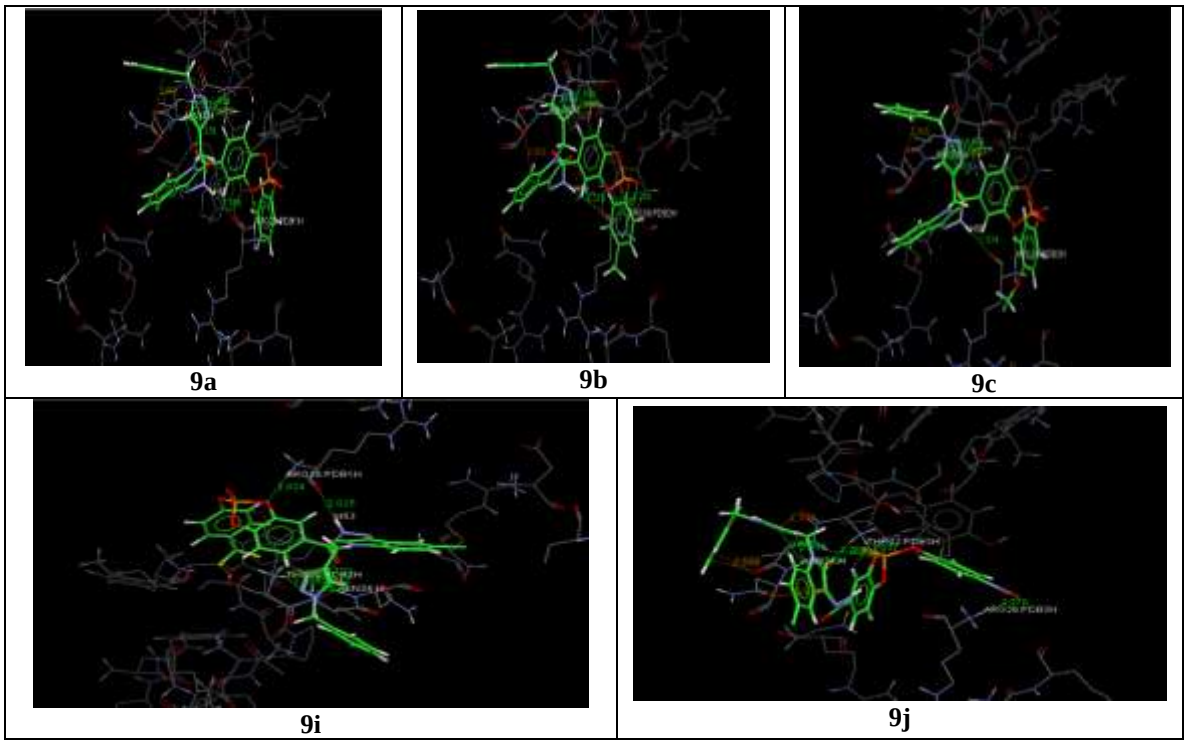
Table-1.2: Antifungal activity (Diameter zone of inhibition in mm) of Compounds 9(a-o)

S.NO	COMP	Zone of inhibition (mm)	
		Aspergillus niger NCCS 1196 250 µg/disc	Candida albicans NCCS 3471 250 µg/disc
1	9a	09	08
2	9b	10	09
3	9c	12	10
4	9d	14	11
5	9e	16	13
6	9f	14	09
7	9g	15	11
8	9h	17	12
9	9i	19	14
10	9j	20	16
11	9k	12	10
12	9l	13	11
13	9m	14	13
14	9n	16	14
15	9o	18	15
Ketoconazole		22	25

The substituted compounds (9j-9f) showed more antifungal activity than compounds [9k-9(o)] compounds, which interned showed high antibacterial activity than unsubstituted compounds (9a-9e).The reactivity order of the compounds: 9(o)>9n>9m>9l>9k, 9j>9i>9h>9g>9f>, 9e>9d>9c> 9b>9a.

Docking studies

Computational methodologies have become a crucial module of many new drug discovery programs, from his identification to lead optimization and beyond[27] and approaches such as ligand[28] or structure based virtual screening techniques[29] are widely used in many discovery efforts. One key methodology is docking of a small molecule to protein binding site was pioneered during the early 1980s, and became a highly active area of drug research. Furthermore, docking can also contribute to the analysis of drug metabolism using structures such as cytochrome P450 isoforms. Docking was carried out using GOLD (Genetic Optimization of Ligand Docking) which is based on genetic algorithm (G. A) .This method allows as partial flexibility of protein and full flexibility of ligand. The compounds are docked to the active site of proteins. After Docking, The individual binding possess of each ligand were observed and their interactions with the protein were studied. The synthesis of Organo phosphorus containing 1,2,3 triazole compounds 9(a-o).The Docking studies of 9a, 9b, 9c, 9i and 9j were carried out as model compounds on C_2H_2 zinc finger protein to study the anti-Cancer activity of 1,2,3 triazole compounds.



"**Fifure-1": Docking images of compounds 9(a-e) with C_2H_2 zinc finger protein**

Table-1.3: Docking results of 9(a-o) on C_2H_2 zinc finger protein

Comp	R	R'	Fitness	S(hb_ext)	S(vdw_ext)	S(hb_int)	S(vdw_int)
9a	H	H	51.40	15.05	31.84	0.00	-7.44
9b	H	CH_3	50.34	12.97	33.40	0.00	-8.55
9c	OMe	H	48.86	14.81	31.80	0.00	-9.67
9i	Cl	CF_3	50.57	14.78	31.07	0.00	-6.94
9j	Cl	NO_2	53.23	15.30	33.75	0.00	-8.48

Table-1.4: Hydrogen bonding interactions of compounds 9(a-o) with C_2H_2 zinc finger protein

Comp No	R	R'	Number of Hydrogen bonds	Comp		Bond Length (A^0)	Fitness
				Protein	Atom		
9a	H	H	2	ARG26:PDB1H ASN34H	-	1.938 2.320	51.40
9b	H	CH_3	2	ARG26:PDB2H ASN 2H	H=49	2.236 2.645	50.34
9c	OCH_3	H	2	ARG26:PDB2H ASN34H	H=50	1.851 2.703	40.86
9i	Cl	CF_3	3	ARG26:PDB1H ASN 34H THR32:PDB2H	-	2.024 2.53 2.782	50.57
9j	Cl	NO_2	3	ARG26:PDB3H ASN 34H THR32:PDB3H	-	2.270 2.609 2.037	53.23

Based on protein–ligand interaction gold score fitness was evaluated and the 1, 2, 3 triazole having high gold score fitness exhibits high anti-Cancer activity based on Docking studies is 9j>9a>9i>9b>9c.

CONCLUSION

The newly synthesis compounds 1,2,3triazole containing Dioxaphopolanes derivatives 9(a-o) were found to be active in the study of anti-bacterial, anti-fungal and anti-cancer activity of Docking studies .It can be concluded that this class of compounds certainly holds great promise towards the pursuit to discover novel classes of anticancer agents.

ACKNOWLEDGEMENT

One of the author D. Rajesh is thankful to S. K. University for providing facilities to my research work.

REFERENCE

1. Wamhoff, H., In Comprehensive Heterocyclic Chemistry, Katritzky, A. R.; Rees, C. W., Eds.; Pergamon: Oxford, 1984; 5 Part 4A: 669.
2. Fan, W.-Q.; Katritzky, A. R., In Comprehensive Heterocyclic Chemistry II, Katritzky, A. R.; Rees, C. W.; Scriven, E. F. V., Eds.; Elsevier: Oxford, 1996; 4, p 1.
3. F. Pagliai, T. Pirali, E. Del Grosso, R. Di Brisco, G. C. Tron,G. Sorba, A. A. Genazzani, J. Med. Chem., 2006; 49: 467–470.
4. Yempala T, Sridevi JP, Yogeeswari P, Sriram D, Kantevari S. Rational design and synthesis of novel dibenzo[b,d]furan-1,2,3-triazole conjugates as potent inhibitors of Mycobacterium tuberculosis. Eur J Med Chem., 2014; 71: 160-167.
5. Duan YC, Ma YC, Zhang En, Shi XJ, Wang MM, Ye XW, et al. Design and synthesis of novel 1,2,3-triazole-dithiocarbamate hybrids as potential anticancer agents. Eur J Med Chem., 2013; 62: 11-19.
6. Piotrowska DG, Balzarini J, Glowacka IE. Design, synthesis, antiviral and cytostatic evaluation of novel isoxazolidine nucleotide analogues with a 1, 2, 3-triazole linker. Eur J Med Chem., 2012; 47: 501-509.
7. C. G. Wermuth, in: The Practice of Medicinal Chemistry, Academic Press, New York, 2003.
8. Stefania-felicia Barbuceanu, Gabriela Laura Almajan. New heterocyclic Rev. Chim., 2011; 62: 308-12.
9. A SAGAR NARALA1*, VENKATESHWAR RAO JUPALLY1 AND BHUJANGA RAO A.K.S.2 sian J Pharm Clin Res, 2012; 5(1): 889-943.
10. Dimorth, O; Fester,G., Chem.Ber., 1910.
11. Gold,H.,Justus Liebigs Amm.Chem., 1973; 38: 2708.
12. Hubert,A.J.,Bull.Soc.Chim .Belg., 1970; 79: 195.
13. FOURNIER,J.O.;Miller, J.B.S. Hetero Cycl. Chem., 1965; 2: 488.
14. Wuytswinkel, G. V. ; Verheyde, B; Compernolle, F. ;Toppet, W., J. Chem Soc. Perkin Trans., 2000; 1: 1337.
15. I K Rubtsova and R D Zhilina, ZhurPrikladKhim, 1959, 32, 2604,ChemAbstr, 1960; 54: 8683.
16. P. Jagadeeswra Rao; K.S.Bhavani Aishwarya; D.Ishrath Begum and L.K.Ravindranath, Scholar Research Library, Der pharma Chemica, 2012; 4(5): 1934-1945.

17. E. C Briton; U S pat, 2033918; Chem Abstr, 1936; 30: 2988.
18. X Francis, FX Markley and CJ Worrel, U S Pat, 3153081; Chem Abstr, 1965; 62: 483.
19. W Autenrieth and E Bolli, Ber, 1925; 58: 2144.
20. V V Korshak; I A Gribova and MA Andreeva ;Izvest; Akad Nauk SSSR Octdel KhimNauk, 1958, 880, Chem Abstr, 1959; 53: 1220b.
21. N. Bakthavatchala Reddy; B. Siva Kumar; N. J. Reddy, P. Santhipriya and C. Suresh Reddy, J.Chem.Pharm.Res., 2010; 2(2): 405-410.
22. G. Nagalakshmi; Indian Journal of Pharmaceutical Science, 2008; plaintiff.49-55.
23. A. Balakrishna' S. Annar; M. Veerenarayana Reddy, G. Chendrasekar Reddy, C. Suresh Reddy, S.K.Nayak; J.Chem.Phrma.Res., 2009; 1(1): 256.
24. H.M Hassan and Farrag, J. Chem. Pharm. Res, 2011; 3(2): 776-785.
25. V. Esther Rani, CH Lakshmi Praveena, Y. N. Spoorthi and L. K. Ravindranth. Der Pharma Chemica, 2013; 5(3): 169-178.
26. H J Benson, Microbiological Aapplicatioons, W M C Brown Publication, USA, 1990; 5th ed , 134.
27. Bajorath, J. Integration of virtual and high-throughput screening. Nature Rev. Drug Discov., 2002; 1: 882–894.
28. Walters, W. P., Stahl, M. T. & Murcko, M. A. Virtual screening an overview. Drug Discov., 1998; Today 3: 160–178.
29. Gohlke, H. & Klebe, G.; Angew. Chem. Int. Ed., 2002; 41: 2644–2676.