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Synthesis of 2,3,5-Trisubstituted 1,3,4-Oxadiazole Via Cyclization of 5-Fused Heteryl Pyrazole-3-Carbohydrazone having Quinolin-3-yl Moiety and their Antibacterial Activity

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ABSTRACT

In the undertaken research, 5-(5-H/Br benzofuran-2-yl)-N'-((-2-(p-tolyloxy) substituted quinolin-3-yl)methylene)-1-phenyl-1H-pyrazole-3-carbohydrazide **(3a-h)** on treatment with acetic anhydride afforded novel 1-(5-(5-(5-H/Br benzofuran-2-yl)-1-phenyl-1H-pyrazol-3-yl)-2-(-2-(p-tolyloxy)substitutedquinolin-3-yl)-1,3,4-oxadiazol-3(2H)-yl)ethanone derivatives **(4a-h)**. 5-fused heteryl pyrazole-3-carbohydrazone **(3a-h)** needed for the synthesis of **4a-h** were synthesized by reaction of 2-(p-tolyloxy) substituted quinoline-3-carbaldehyde **(2a-h)** with 5-(5-H/Br benzofuran-2-yl)-1-phenyl-1*H*-pyrazole-3-carbohydrazides **(1a-b)** in ethanol as solvent. The structures of the newly synthesized compounds were identified on the basis of elemental analysis and spectral studies like IR, ^{1}H NMR and Mass spectra. The *in-vitro* antibacterial screening of these synthesized compounds against *E. coli, S. aureus, E. areogenes* and *B. thurengienesis* relative to the reference standard Chloramphenicol have been found to possesses good to moderate inhibitory activity.

Keywords: 1,3,4-Oxadiazole,Quinoline carbaldehyde, fused heteryl pyrazole-3-carbohydrazone

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INTRODUCTION

The advantage of heterocyclic hybrid compound through the arrangement of different pharmacophores may provide compounds with good biological activities[1]. It is not surprising that quinoline is a more importance class of heterocycles. The quinoline ring system is an important structural unit in naturally occurring quinoline alkaloids, have been shown to possess useful pharmacological activities, for example, Primaquine is an antimalarial agent, Dibucaine hydrochloride is an anaesthetic, Apomorphine is antiparkinsonian and Oxamniquine is schistosomicidal. Also synthetically substituted quinoline derivatives possess a broad range of bioactivities such as antmicrobial[2], antimalarial[3], antibacterial[4], antitumor[5] and antiviral[6]. Recently, substituted quinolines have also been reported to act as antagonists for endothelin[7], $5HT_3$[8], NK-3[9] and leukotriene D4 receptor[10]. They also function as inhibitors of gastric (H^+/K^+)-ATPase[11], dihydroorotate dehydrogenase[12] and 5-lipoxygenase[13]. Furthermore, these compounds find applications in coordination chemistry for synthesis Lanthanide complexes[14].

From last two decades the synthesis of novel 1,3,4-Oxadiazole derivatives and investigation of their chemical properties and biological behavior has accelerated. In recent years the number of scientific studies with these compounds has increased considerably. Among heterocyclic compounds, 1,3,4-Oxadiazole has become an important construction design for the development of new drugs. Oxadiazole nucleus containing drug are commercially available in market like Furamizole as an antibiotic[15], Tiodazosin[16] and Nesapidil[17] as a antihypertensive agents. Compounds containing 1,3,4-Oxadiazole cores have a broad spectrum of biological activities such as antibacterial, antifungal[18,19], anti-inflammatory and antihypertensive[20], anticonvulsant[21], anticancer[22], antioxidant[23], analgesic[24], antitubercular[25].

Many researchers have used aryl/heteryl carbohydrazone for the synthesis of 1,3,4- Oxadiazoles by using different oxidizing agents such as Br_2, HgO, $KMnO_4$ and , acetic anhydride[26]. Other milder oxidizing agents like cerium ammonium nitrate (CAN) in dichloromethane solvent[27], Cu(OTf)2 as catalyst[28], chloramine-T[29] trichloroisocyanuric acid[30] 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU)[31], Dess-Martin periodinane[32] etc.

Prompted by the above observations and as a part of our work on development of novel antibacterial agent we have attempted to synthesize 2,3,5-trisubtituted-1,3,4-Oxadiazoles by the reaction of 5-fused heteryl pyrazole-3-carbohydrazone derivatives with acetic anhydride and explore the possibility of generation of any antibacterial activities.

MATERIALS AND METHOD

Chemicals used for the synthesis were of AR grade of Merck, S.D. Fine and Aldrich. The reactions were monitored by E. Merck TLC aluminum sheet silica $gel_{60}F_{254}$ and visualizing the spot in UV Cabinet and iodine chamber. The melting points were recorded in open capillary in paraffin bath and are uncorrected. ^{1}H NMR spectra are recorded on a Bruker AM 400 instrument (400 MHz) using tetramethylsilane (TMS) as an internal reference and DMSO-d_6 as solvent. Chemical shifts are given in parts per million (ppm). IR spectra were recorded on a Shimadzu IR Spectrophotometer (KBr, v max in cm^{-1}). Positive-ion Electro Spray Ionization (ESI) mass spectra were obtained with a Waters Micromass Q–TOF Micro, Mass Spectrophotometer. Elemental (CHN) analysis was done using Thermo Scientific (Flash-2000). The compounds were analyzed for carbon, hydrogen, nitrogen and the results obtained are in good agreement with the calculated values.

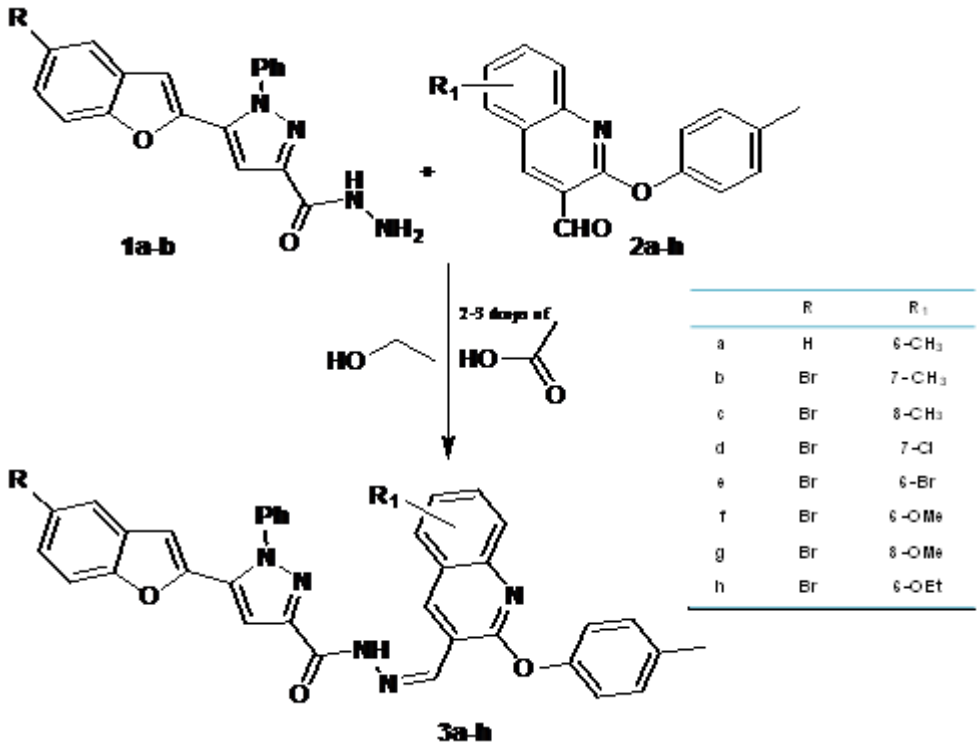
Experimental Procedure

Procedure for the synthesis of 5-(benzofuran-2-yl)-N'-((6-methyl-2-(p-tolyloxy) quinolin-3-yl)methylene)-1-phenyl-1H-pyrazole-3-carbohydrazide (3a) To a mixture of 6-methyl-2-(p-tolyloxy)quinoline-3-carbaldehyde **2a** (1.39 g, 0.005mol) and 5-(benzofuran-2-yl)-1-phenyl-1H-pyrazole-3-carbohydrazide **1a** (0.1.59 g, 0.005mol) in ethanol (25mL) , 2-3 drops of acetic acid was added as a catalyst, the reaction contents were refluxed for 2h. Resulting mass was allow to cool, filtered and the product was recrystallized from 1,4-Dioxane to get **3a** (Scheme **1**).

Similarly, **3b-h** were synthesized from **1b** and **2b-h** by following the same procedure followed for **3a.**

5-(benzofuran-2-yl)-N'-((6-methyl-2-(p-tolyloxy)quinolin-3-yl)methylene)-1-phenyl-1H-pyrazole-3-carbohydrazide (3a): White crystalline solid; mp,272-274°C; yield, 87%; M. F. $C_{36}H_{27}N_5O_3$. IR: 3407, 3145 (NH), 3057 (ArH), 2913, 2889, 2956, 2854 (-CH_3 group), 1585 (C=C), 1239,1210, 1034 (C-O-C) ,1687 (C=O), 1506 (C=N in pyrazole). ^{1}H NMR: 2.35 (s, 3H, CH_3 attached to Ar. ring), 2.46 (s, 3H, CH_3 attached to quinoline ring), 6.62 (s, 1H, C_4 of pyrazole ring), 7.88 (s, 1H, N=CH), 8.79 (s, 1H, C_8 position of quinoline ring), 9.08 (s, 1H, C_4 position of quinoline) 12.28 (s, 1H, NH of amide group), 7.16-7.65 (m, 16H, ArH + quinoline proton)MS: *m/z* 578 $[M+H]^+$, 600 $[M+Na]^+$, 601 $[(M+H)+Na]^+$. Elemental Anal. Calcd. for $C_{36}H_{27}N_5O_3$ required: C, 74.85; H, 4.71; N, 12.12 Found: C, 74.56; H, 4.64; N, 12.37

Reaction Scheme 1:



	R	R_1
a	H	6-CH_3
b	Br	7-CH_3
c	Br	8-CH_3
d	Br	7-Cl
e	Br	6-Br
f	Br	6-OMe
g	Br	8-OMe
h	Br	6-OEt

5-(5-bromobenzofuran-2-yl)-N'-((7-methyl-2-(p-tolyloxy)quinolin-3-yl)methylene)-1-phenyl-1H-pyrazole-3-carbohydrazide (3b): White crystalline solid; Recrystallization solvent, 1,4-Dioxane; mp, 160-162°C; yield, 83%; M. F. $C_{36}H_{26}BrN_5O_3$. IR: 3413, 3248 (NH), 3057, 3034 (ArH), 2946, 2878 (-CH_3 group), 1585, 1560 (C=C), 1234, 1222, 1018 (C-O-C), 1676 (C=O), 1502 (C=N in pyrazole).

5-(5-bromobenzofuran-2-yl)-N'-((8-methyl-2-(p-tolyloxy)quinolin-3-yl)methylene)-1-phenyl-1H-pyrazole-3-carbohydrazide (3c): White crystalline solid; Recrystallization solvent, 1,4-Dioxane; mp, 280-282°C; yield, 82%; M. F. $C_{36}H_{26}BrN_5O_3$. IR: 3402, 3254 (NH), 3057, 3034, 3012 (ArH), 2933, 2917, 2830 (-CH_3 group), 1560, 1528 (C=C), 1229, 1033 (C-O-C), 1680 (C=O), 1495 (C=N in pyrazole).

5-(5-bromobenzofuran-2-yl)-N'-((7-chloro-2-(p-tolyloxy)quinolin-3-yl)methylene)-1-phenyl-1H-pyrazole-3-carbohydrazide(3d): White crystalline solid; Recrystallization solvent, 1,4-Dioxane; mp, 278-280°C; yield, 83%; M. F. $C_{35}H_{23}BrClN_5O_3$. IR: 3433, 3224 (NH), 3057, 3042, 3034 (ArH), 2926, 2912, 2887 (-CH_3 group), 1543 (C=C), 1227, 1048 (C-O-C), 1670 (C=O), 1506 (C=N in pyrazole).

N'-((7-bromo-2-(p-tolyloxy)quinolin-3-yl)methylene)-5-(5-bromobenzofuran-2-yl)-1-phenyl-1H-pyrazole-3-carbohydrazide (3e): White crystalline solid; Recrystallization solvent, 1,4-Dioxane; mp,188-190°C; yield, 80%; M. F. $C_{35}H_{23}Br_2N_5O_3$. IR: 3411, 3260 (NH), 3045, 3037

(ArH), 2946, 2923, 2844 (-CH_3 group), 1566, 1560 (C=C), 1214, 1202, 1047 (C-O-C), 1673 (C=O), 1497 (C=N in pyrazole).

5-(5-bromobenzofuran-2-yl)-N'-((6-methoxy-2-(p-tolyloxy)quinolin-3-yl)methylene)-1-phenyl-1H-pyrazole-3-carbohydrazide (3f): White crystalline solid; Recrystallization solvent, 1,4-Dioxane; mp, 302-305°C; yield, 86%; M. F. $C_{36}H_{26}BrN_5O_4$. IR: 3427, 3238 (NH), 3034, 3024 (ArH), 2922, 2874 (-CH_3 group), 1545, 1530 (C=C), 1223, 1212, 1048 (C-O-C), 1669 (C=O), 1504 (C=N in pyrazole).

5-(5-bromobenzofuran-2-yl)-N'-((8-methoxy-2-(p-tolyloxy)quinolin-3-yl)methylene)-1-phenyl-1H-pyrazole-3-carbohydrazide (3g): White crystalline solid; Recrystallization solvent, 1,4-Dioxane; mp, 172-174°C; yield, 83%; M. F. $C_{36}H_{26}BrN_5O_4$. IR: 3417, 3223 (NH), 3044, 3020 (ArH), 2952, 2919, 2834 (-CH_3 group), 1534, 1528 (C=C), 1243, 1207, 1047 (C-O-C), 1667 (C=O), 1490 (C=N in pyrazole).

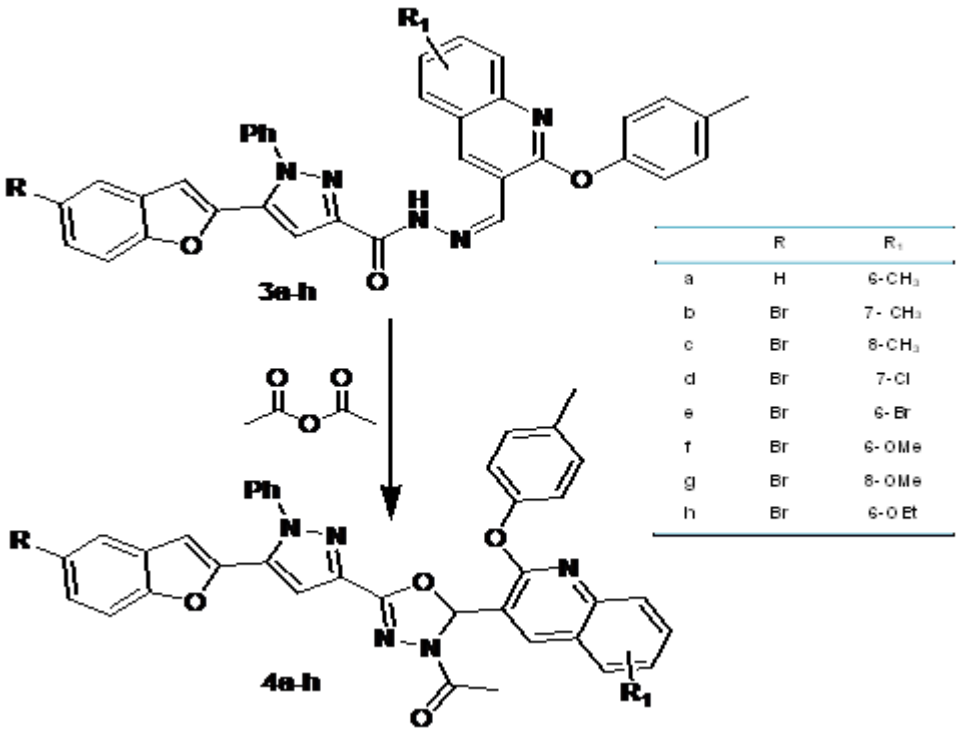
5-(5-bromobenzofuran-2-yl)-N'-((6-ethoxy-2-(p-tolyloxy)quinolin-3-yl)methylene)-1-phenyl-1H-pyrazole-3-carbohydrazide (3h): White crystalline solid; Recrystallization solvent, 1,4-Dioxane; mp, 238-240°C; yield, 80%; M. F. $C_{37}H_{28}BrN_5O_4$. IR: 3453, 3263 (NH), 3044, 3032, 3023 (ArH), 2942, 2916, 2864 (-CH_3 group), 1556, 1536 (C=C), 1254, 1212, 1048 (C-O-C), 1669 (C=O), 1510 (C=N in pyrazole).

Procedure for the synthesis of 1-(5-(5-(benzofuran-2-yl)-1-phenyl-1H-pyrazol-3-yl)-2-(6-methyl-2-(p-tolyloxy)quinolin-3-yl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (4a): 5-(benzofuran-2-yl)-1-phenyl-N'-((2-(p-tolyloxy)quinolin-3-yl)methylene)-1H-pyrazole-3-carbohydrazide **3a** (2.885 gm, 0.005mol) were taken in acetic anhydride (20mL). The reaction mixture was reflux for 6h, allowed to cool and poured on crushed ice, reaction content kept for overnight, product obtained was filtered, washed, dried and recrystallized from 1,4-Dioxane to get **4a**.(Scheme **2**).

Similarly, **4b-h were** synthesized from **3b-h** by following the same procedure for **4a.**

1-(5-(5-(benzofuran-2-yl)-1-phenyl-1H-pyrazol-3-yl)-2-(6-methyl-2-(p-tolyloxy)quinolin-3-yl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (4a) : White crystalline solid; mp, 230-232°C; yield, 85%; M. F. $C_{38}H_{29}N_5O_4$. IR: 3061, 3034 (ArH), 2919, 2856 (-CH_3 group), 1410 (C=C), 1221, 1078 (C-O-C), 1660 (C=O), 1505 (C=N in pyrazole). ^{1}H NMR: 2.30 (s, 3H, CH_3 attached to Ar. ring), 2.31 (s, 3H, CH_3 attached to quinoline ring), 2.47 (s, 3H, NHCOC$\underline{H}_3$), 6.68 (s, 1H, C_4 of pyrazole ring), 7.84 (s, 1H, C_2 of oxadiazole ring), 8.50 (s, 1H, C_4 of quinoline ring), 7.05-7.64 (m, 17H, ArH + quinoline ring) MS: *m/z* 620 $[M+H]^+$, 621 $[M+2]^+$, 622 $[M+3]^+$, 642 $[M+Na]^+$, 643 $[(M+H)+Na]^+$. Elemental Anal. Calcd. for $C_{38}H_{29}N_5O_4$ required: C, 73.65; H, 4.72; N, 11.30 Found: C, 73.16; H, 4.15; N, 11.03.

Reaction Scheme 2:



	R	R_1
a	H	6-CH_3
b	Br	7- CH_3
c	Br	8-CH_3
d	Br	7-Cl
e	Br	6-Br
f	Br	6-OMe
g	Br	8-OMe
h	Br	6-OEt

1-(5-(5-(5-bromobenzofuran-2-yl)-1-phenyl-1H-pyrazol-3-yl)-2-(7-methyl-2-(p-tolyloxy) quinolin-3-yl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (4b): White crystalline solid; recrystallization solvent, 1,4-Dioxane; mp,182-184°C; yield, 90%; M. F. $C_{38}H_{28}BrN_5O_4$. IR: 3052, 3032 (ArH), 2917, 2875 (-CH_3 group), 1470, 1422 (C=C), 1260, 1108 (C-O-C), 1664 (C=O), 1508 (C=N in pyrazole).

1-(5-(5-(5-bromobenzofuran-2-yl)-1-phenyl-1H-pyrazol-3-yl)-2-(8-methyl-2-(p-tolyloxy) quinolin-3-yl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (4c): White crystalline solid; Recrystallization solvent, 1,4-Dioxane; mp,190-192°C; yield, 83%; M. F. $C_{38}H_{28}BrN_5O_4$. IR: 3066, 3054, 3022 (ArH), 2907, 2862 (-CH_3 group), 1475, 1427 (C=C), 1224, 1087 (C-O-C), 1660 (C=O), 1499 (C=N in pyrazole).

1-(5-(5-(5-bromobenzofuran-2-yl)-1-phenyl-1H-pyrazol-3-yl)-2-(7-chloro-2-(p-tolyloxy) quinolin-3-yl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (4d): White crystalline solid; Recrystallization solvent, 1,4-Dioxane; mp, 234-236°C; yield, 85%; M. F. $C_{37}H_{25}BrClN_5O_4$. IR: 3051, 3030 (ArH), 2913, 2875 (-CH_3 group), 1470,1482 (C=C), 1230, 1057 (C-O-C, 1660 (C=O), 1502 (C=N in pyrazole).

1-(2-(6-bromo-2-(p-tolyloxy)quinolin-3-yl)-5-(5-(5-bromobenzofuran-2-yl)-1-phenyl-1H-pyrazol-3-yl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (4e): White crystalline solid; Recrystallization solvent, 1,4-Dioxane; mp,167-169°C; yield, 83%; M. F. $C_{37}H_{25}Br_2N_5O_4$. IR: 3043, 3024 (ArH),

2919, 2860 (-CH_3 group), 1462 (C=C), 1211, 1068 (C-O-C), 1667 (C=O), 1506 (C=N in pyrazole).

1-(5-(5-(5-bromobenzofuran-2-yl)-1-phenyl-1H-pyrazol-3-yl)-2-(6-methoxy-2-(p-tolyloxy)quinolin-3-yl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (4f): White crystalline solid; Recrystallization solvent, 1,4-Dioxane; mp,189-190°C; yield, 80%; M. F. $C_{38}H_{28}BrN_5O_5$. IR: 3054, 3043, 3027 (ArH), 2937, 2823 (-CH_3 group), 1457, 1472 (C=C), 1227, 1080 (C-O-C), 1670 (C=O), 1490 (C=N in pyrazole).

1-(5-(5-(5-bromobenzofuran-2-yl)-1-phenyl-1H-pyrazol-3-yl)-2-(8-methoxy-2-(p-tolyloxy)quinolin-3-yl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (4g): White crystalline solid; Recrystallization solvent, 1,4-Dioxane; mp,172-174°C; yield, 83%; M. F. $C_{38}H_{28}BrN_5O_5$. IR: 3062, 3047, 3034 (ArH), 2906, 2868 (-CH_3 group), 1460 (C=C), 1218, 1067 (C-O-C), 1667 (C=O), 1502 (C=N in pyrazole).

1-(5-(5-(5-bromobenzofuran-2-yl)-1-phenyl-1H-pyrazol-3-yl)-2-(6-ethoxy-2-(p-tolyloxy) quinolin-3-yl)-1,3,4-oxadiazol-3(2H)-yl)ethanone (4h): White crystalline solid; Recrystallization solvent, 1,4-Dioxane; mp,172-174°C; yield, 83%; M. F. $C_{39}H30BrN_5O_5$. IR: 3055, 3037 (ArH), 2915, 2889 (-CH_3 group), 1495, 1506 (C=C), 1212, 1038 (C-O-C), 1664 (C=O), 1510 (C=N in pyrazole).

Antibacterial activity

The novel synthesized heterocyclic compounds were screened for their *in vitro* antimicrobial activity using cup plate agar disc-diffusion method against two Gram positive bacterial strains, *B. thurengienesis* and *S. aureus* and two Gram negative strains, *E. coli* and *E. aerugenes.* Chloramphenicol was used as standard drug for bacteria.

General procedure: Determination of zone of inhibition by agar disc-diffusion method:

Test solutions were prepared with known weight of compound in DMSO and half diluted suitably to give the resultant concentration of 31-1000µg/mL. Whatmann no. 1 sterile filter paper discs (6 mm) were impregnated with solution and allowed to dry at room temperature. *In vitro* antibacterial activity was determined by using Mueller Hinton Agar obtained from Himedia Ltd., Mumbai. Petri plates were prepared by pouring 10 mL of Mueller Hinton Agar for bacteria containing microbial culture was allowed to solidify. The discs were then applied and the plates were incubated at 37°C for 24h (bacteria) and the inhibition zone was measured in mm in four directions and expressed as mean. The results were compared using Chloramphenicol as a standard antibacterial drug.

RESULTS AND DISCUSSION

The present work contributes the synthesis, characterization and biological evaluation of the of 5-

fused heteryl pyrazole-3-carbohydrazone and trisubstituted 1,3,4-Oxadiazole derivatives. The synthesis of the novel compound **3a-h** and **4a-h** is designated in the reaction schemes **1** and **2**. At every stage purity of the compounds were monitored by TLC technique. The synthesized compounds were confirmed structurally by means of their spectral such as IR, ^{1}H-NMR, and mass spectra (MS) and elemental analysis. The spectral and analytical data are in good agreement with their structures. The synthesis of the starting compound, 5-(5-H/Br benzofuran-2-yl)-1-phenyl-1*H*-pyrazole-3-carbohydrazides **(1a-b)** achieved in quantitative yields by the reference method[33]. In the first step, **1a-b** reacted with 2-(p-tolyloxy) substituted quinoline-3-carbaldehyde **(2a-h)** using ethanol as a solvent to furnish heteryl carbohydrazone as an intermediate **3a-h.** The percentage yield of all the synthesized compounds **3a-h** was found to be in the range of 80-87%.

The IR spectrum of the **3a** showed -NH stretch at 3407 cm^{-1} and C=O stretching in amide group at 1687 cm^{-1}. The ^{1}H NMR spectrum showed singlet at δ 2.35 ppm for (–CH_3 attached to Ar. Ring), also singlet at δ 2.46 ppm for (–CH_3 attached to quinoline ring), hence it confirms that substituted 2-(p-tolyloxy) quinoline-3-carbaldehyde has condensed with 5-(5-H/Br benzofuran-2-yl)-1-phenyl-1*H*-pyrazole-3-carbohydrazide to afford (Z)-5-(5-H/Br benzofuran-2-yl)-N'-((-2-(p-tolyloxy)substituted quinolin-3-yl)methylene)-1-phenyl-1H-pyrazole-3-carbohydrazide (**3a-h).** In elemental analysis, the compound 3a was found to contain C, 74.56; H, 4.64; N, 12.37 and these results are in good agreement with the calculated values. The mass spectra of the products revealed a molecular ion peak at *m/z* 578 $[M+H]^+$ which is consistent with the molecular formula $C_{36}H_{27}N_5O$.

5-(5-bromobenzofuran-2-yl)-N'-((-2-(p-tolyloxy)substituted quinolin-3-yl)methylene)-1-phenyl-1H-pyrazole-3-carbohydrazide **(3a-h)** was reacted with acetic anhydride to yield 1-(5-(5-(5-H/Br benzofuran-2-yl)-1-phenyl-1H-pyrazol-3-yl)-2-(-2-(p-tolyloxy)substituted quinolin -3-yl)-1,3,4-oxadiazol-3(2H)-yl)ethanone derivatives **(4a-h).** The IR spectrum of **4a** reveals that C=O stretching in amide group has disappeared and C-O-C stretch has appeared at 1078 cm^{-1}. This was further confirmed from its ^{1}H NMR spectrum which showed expected signals for aromatic and aliphatic proton. Disappearance of a singlet at δ 12.28 ppm for -N<u>H</u> proton, as obtained in heteryl-3- carbohydrazone confirms that cyclization has occurred to get the target molecule. Its mass spectrum shows a molecular ion peak at *m/z* 620 $[M+H]^+$ matches with the molecular formula $C_{38}H_{29}N_5O_4$.

Antibacterial activity

Antimicrobial screening data showed that the test compound **3a** and **4a** possessed antibacterial activity against all the test organisms at each concentration. In case of Gram positive bacteria,

compound **3a** at a conc. 63 µg/mL showed high activity than the standard drug against *B. thurengienesis* while **3a** and **4a** at rest of conc. showed good activity against *B. thurengienesis* and moderate activity against *S. aureus.* Similarly, in case of Gram negative bacteria,**4a** showed high activity than the standard drug at a conc. 250 µg/mL against *E. coli* while **3a** and **4a** at rest of conc. showed good to moderate activity against against *E. coli* and *E. Areogenes* The results of antibacterial activities of the synthesized compounds are tabulated in Table **1**.

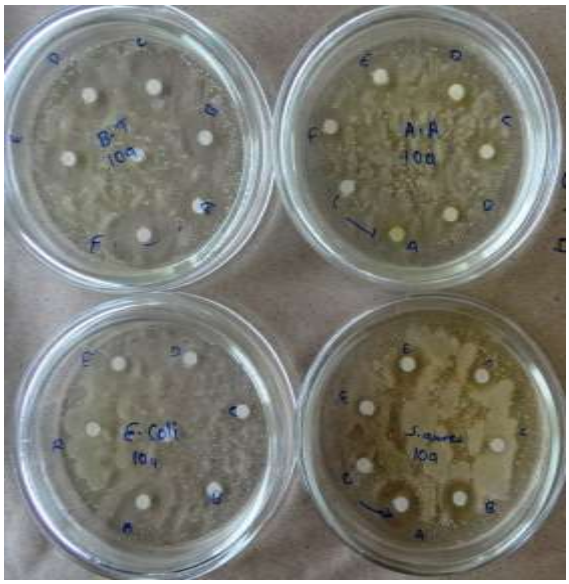


Figure 1: 3a

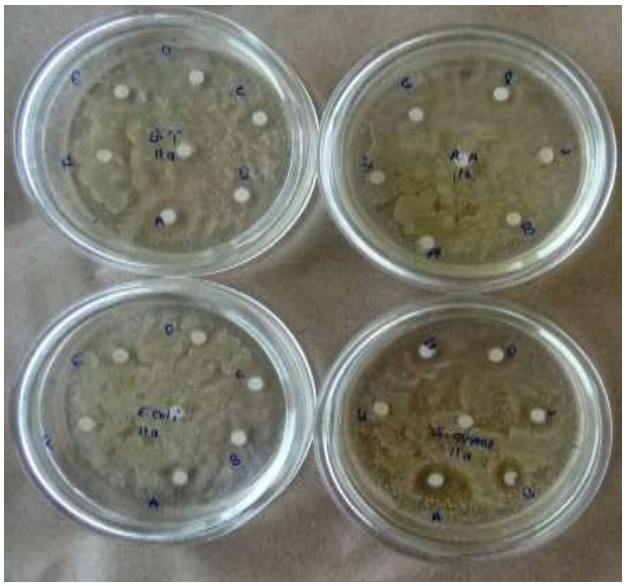


Figure 2: 4a

Table 1: Antibacterial Activity of 3a and 4a:

Sr. No.	**Conc. (µg/mL)**	***Zone of Inhibition in mm***			
		Gram +ve		Gram -ve	
		B. thurengienesis	*S. aureus*	*E. coli*	*E. areogenesis*
3a					
1.	1000	15	18	14	12
2.	500	18	12	10	10
3.	250	20	07	08	15
4.	125	15	08	06	10
5.	63	16	10	10	12
6.	31	12	08	05	12
4a					
1.	1000	15	20	12	08
2.	500	14	10	14	13
3.	250	10	15	**20**	05
4.	125	08	10	10	06
5.	63	10	12	08	10
6.	31	06	08	05	08
Standard Chloramphenicol					
1.	1000	22	26	24	16
2.	500	20	30	20	16

3.	250	21	27	18	17
4.	125	16	21	17	16
5.	63	15	18	17	15
6.	31	16	20	21	15

CONCLUSION

The target derivatives, trisubstituted 1,3,4-Oxadiazoles **(4a-h)** and heteryl-3-carbohydrazone **(3a-h)** were successfully synthesized in good yields. Their purity and confirmation was checked by physical, analytical and spectral data. Antibacterial screening of these compounds was found to possess good to moderate activity against selected strains of bacteria.

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