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RESEARCH ARTICLE

NOVEL SYNTHESIS OF SEVERAL SUBSTITUTED N-[2,4,5-TRIPHENYLOXOZOLE-3*(2H)*-YL]BENZAMIDE AND N-[(2-FURYL)-4,5,-DIPHENYLOXAZOLE-3*(2H)*-YL]BENZAMIDE AS POTENTIAL PESTICIDES

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ABSTRACT

Several N-[2,4,5-triphenyloxazole-3*(2H)*-yl]benzamide and N-[(2-furyl)4,5-diphenyloxazole-3*(2H)*-yl]benzamide have been synthesized by refluxing N^1-aroyl-N^2-arylidenehydrazines / N^1-aroyl-N^2-furylidenehydrazines with equimolar of benzoin and triethylamine few drops in ethanol for six hours and screened for their herbicidal activities against *Echinochloa oryzicola, Echinochloa crus-galli, Oryza sativa, Glycine max* and antifungal activities against *Aspergillus niger, Pyricularia oryzae* whereas antibacterial activities against *Salmonella typhi, Escherichia coli, Klebsiella pneumonia, Bacillus subtilis* and *Bacillus pumilus* of the title compounds.

INTRODUCTION

The design, synthesis and structure–activity relationships of a series of oxazole-benzamide derivatives constitute an important class of heterocyclic compounds for their antibacterial and pesticidal activities (Tiwari *et al.,*1997; Tiwari *et al.,*2014; Stokes *et al.,*2014; Hisano *et al.,*1982; Prudhomme *et al.,*1986; Ersan *et al.,*1997; Sener *et al.,*1991; Sener *et al.,*1997; Oren *et al.,* 1997; Temiz *et al.,*1998; Yalcin *et al.,* 1992; Sener *et al.,* 2000). Benzamide derivatives that are the possible metabolites of oxazoles exhibites various types of biological activities. Such as anthelmenthic, antihistaminic, antifungal and antibacterial (Mrozik *et al.,*1969; Japan Patent, 1974; Braz Pedido, 1981; White, 1989; Yalcin *et al.,*1997; Pradhan *et al.,* 1999; Oren *et al.,* 2004). Guided by these observations and in continuation of our work on fused heterocyclic system, we synthesized the title compounds. The structure of these compounds was established by the IR, ^{1}HNMR spectral data and elemental analysis. The results of the elemental analysis (C, H, N) were within ± 0.4% of the calculated amounts.

Aims and objectives

- To screened herbicidal activity
- To screened pesticidal activity
- To screened antibacterial activity

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MATERIALS AND METHODS

Melting points were taken in open capillary tubes and are uncorrected. IR spectra were recorded in KBr on a Perkin-Elmer-881 spectrophotometer and ^{1}HNMR spectra on a Perkin-Elmer R-32 spectrometer at 60MHz. Procedure for on typical case for each step has been described.

Experimental

N^1-aroyl-N^2-arylidenehydrazines (R=4-Cl)

It was prepared according to the known method (Kumar *et al.,* 1991). A mixture of 4-chlorobenzohydrazide (0.02 mole) and benzaldehyde (0.02 mole) was refluxed in methanol using gl. CH_3COOH as a catalyst for 3-4 hours. The mixture was cooled and poured in to water. The solid product was obtained, which was filtered, washed and recrystallized from aq. ethanol.

Substituted-N-[2,4,5-triphenyloxazol-3*(2H)*-yl]benzamide (3b) R=4-OCH_3

It was prepared by refluxing N^1-4-methoxybenzoyl-N^2-benzylidenehydrazine schiff's base (0.01 mole) with benzoin (0.01 mole) and triethyl amine (0.01 mole) in ethanol (40.0 ml) for four-hours. Excess solvent was removed and then poured into water. The Compound thus obtained was filtered, washed, dried and recrystallized from aq. ethanol m.p. 195 ^{0}C, yield 72%, IR (KBr); 2950 (Ar-H), 1729 (>C=O); 1585, 1500, 1440

(aromatic C–C); 1230 (-CN) and 1160 cm^{-1} (C-O-C). ^{1}HNMR (DMSO-d): δ 11.5 (s, NH); 7.2–7.9 (m, Ar–H); 5.9 (s, CH); 3.0 (s, CH_3).

N^1-aroyl-N^2-furylidenehydrazines (R=4-Cl)

It was prepared by the known method (Kumar *et al.,* 1991). A mixture of 4-chlorobenzohydrazide (0.02 mole) and furfuraldehyde (0.02 mole) was refluxed in methanol using gl. CH_3COOH as catalyst for 3-4 hours. The mixture was cooled and poured in to water. The solid product was obtained which was filtered washed and recrystallized from aq. ethanol.

Substituted-N-[(2-furyl)-4,5-diphenyloxazole-3*(2H)*-yl]benzamide (5e) R=4-Cl

It was prepared by refluxing N^1-4-cholorobenzoyl-N^2-furylidenehydrazine i.e. schiff's base (0.01 mole) with benzoin (0.01 mole) and triethyl amine (0.01 mole) in ethanol (40.0 ml) for four hours. Excess solvent was removed and then poured in to water; the compound thus obtained was filtered, washed dried and recrystallised from aq. ethanol m.p. 158^{0}C yield 80%. IR (KBr) 2970 (Ar-H), 1730(>C=0), 1580, 1500, 1450 (aromatic C–C), 1235 (-CN) and 1180 cm^{-1} (C–O–C). ^{1}HNMR (DMSO-d): δ 11.5 (s, NH) ; 7.1–7.7 (m, Ar – H) ; 5.8 (s, CH). Other such compounds were also prepared in a similar way and their characterization data are given in Table 1.

Table 1. Characterization data of Compounds 3 a-g and 5 a-g

Compounds	M.P (ºC)	Yield (%)	Mol Formula	Found (%) (Caled.)		
				C	H	N
3a	108		$C_{28}H_{22}N_2O_2$	80.36 (80.54	5.30 (5.42)	6.69 (6.81)
3b	192		$C_{29}H_{24}N_2O_3$	77.78 (77.66)	5.52 (5.39)	6.35 (6.25)
3c	80		$C_{28}H_{22}N_2O_3$	77.53 (77.40)	5.25 (5.10)	6.61 (6.45)
3d	78		$C_{28}H_{22}N_2O_3$	77.32 (77.40)	5.24 (5.10)	6.62 (6.45)
3e	207		$C_{28}H_{21}ClN_2O_2$	75.27 (74.25)	4.80 (4.67)	6.28 (6.18)
3f	201		$C_{28}H_{21}ClN_2O_2$	75.28 (74.25)	4.83 (4.67)	6.27 (6.18)
3g	246		$C_{28}H_{21}N_3O_4$	7276 (72.56)	4.77 (4.57)	9.27 (9.07)
5a	82		$C_{26}H_{20}N_2O_3$	74.75 (74.45)	5.14 (4.94)	7.16 (6.86)
5b	74		$C_{27}H_{22}N_2O_4$	74.16 (73.96)	5.26 (5.06)	6.59 (6.39)
5c	90		$C_{26}H_{20}N_2O_4$	73.34 (73.57	4.95 (4.75)	6.83 (6.60)
5d	85		$C_{26}H_{20}N_2O_4$	73.36 (73.57)	4.93 (4.75)	6.86 (6.60)
5e	158		$C_{26}H_{19}ClN_2O_3$	70.71 (70.51)	4.62 (4.32)	6.67 (6.33)
5f	151		$C_{26}H_{19}ClN_2O_3$	70.73 (70.51)	4.64 (4.32)	6.69 (6.33)
5g	212		$C_{26}H_{19}N_3O_5$	69.07 (68.87)	4.62 (4.22)	9.47 (9.27)

Biological activity

Antibacterial Studies

The synthesized oxazole and benzamide derivatives were screened for the antibacterial activity against two gram-positive bacteria viz. *Bacillus subtilis* and *Bacillus pumilus* and three Gram-negative bacteria viz. *Salmonella typhi, Escherichia coli* and *Klebsiella pneumonia* by using the cup plate method. Streptomycin was used as reference standard for comparing the results. The antibacterial activity of the benzamide derivatives are shown in Fig. 1 for plates 1-5 and the zone of inhibition values are given Table 2. The clustered column showed that oxazole and benzamide derivatives of compounds 3a-g and 5a-g possess significant activity in which compounds 3e, 3g, 5e, 5g almost having equipotent with standard streptomycin against Gram +ve and Gram –ve pathogenic organism. Thus the substituents place a vital role in imparting enhanced anti-bacterial activity to the compounds. The screening results indicate that compound 3e and 5e was found to be active against *S. typhi* and *K. pneumonia* compounds 3g and 5g were found to be active against *S. typhi, E.coli, K.pneumonia, B.subtilis* and *B. pumilus* where as compounds 3b, 3c, 5b, 5c were found to be inactive be active against *B. pumilus.*

The minimum inhibitory concentrations of the strongly active compounds were also measured. The antimicrobial activity of the synthesized benzamide derivatives by the agar cup diffusion methods (In; Microbiological assays and tests, 1996; Barry, 1976). In the present study DMSO is used as control while streptomycin are used as standards for bacterial strain.

Antibacterial activity of all active synthesized benzamide derivatives was measured by serial dilution method and the MICs are presented in Table 2.

Table 2. Antimicrobial activity of the synthesized compounds which is biologically active. Cup diameter = 0.5 cm

Compound No.	Gram-positive bacteria		Gram-negative bacteria		
	B.subtilis	*B.pumilus*	*S.typhi*	*E.coli*	*K.pneumonia*
3b	–	05	–	–	–
3c	–	15	–	–	–
3e	–	–	25	–	15
3g	25	35	35	45	65
5b	–	05	–	–	–
5c	–	15	–	–	–
5e	–	–	25	–	15
5g	25	35	35	45	65
Streptomycin	Δ	Δ	Δ	Δ	Δ

Less active 1-1.5 cm; moderately active; 1.5-2 cm; highly active 2-3 cm; very high active = Δ = 3 – 4.5 cm^{-1}

Herbicidal activity

The compounds 3b, 3c, 3e, 5b, 5c and 5e were subjected to primary post and pre emergent herbicidal evaluation (Tiwari *et al.,* 2013; Tiwari and Ahamad, 2013; Tiwari, 2013) at rate of 8.0, 4.0, 1.0 and 0.5 Kg/ha. The test species are *Echinochloa oryzicola, Echinochloa crus-galli, Oryza sativa* and *Glycine max*. The detailed data on title compounds having promising herbicidal activity are given in Table 3.

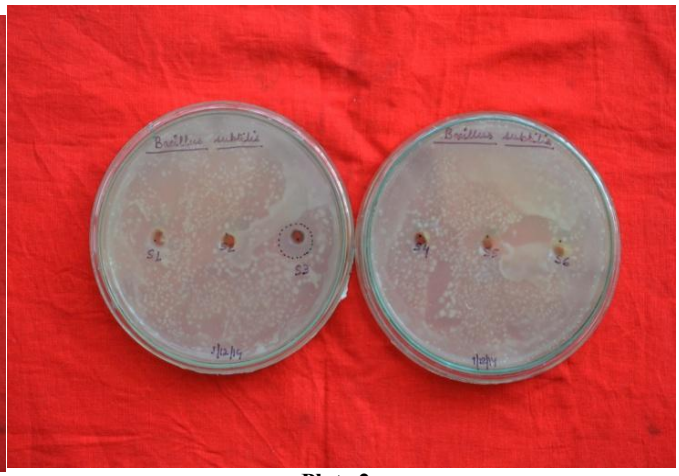
Fungicidal Activity

All the compounds were screened for their anti-fungal activity by agar growth technique (Lorenz *et al.,* 1975) against *Aspergillus niger* and *Pyricularia oryzae* at 1000 ppm, 100 ppm and 10 ppm concentrations respectively. Amongst the tested compounds the most active compounds 3c, 3e, 5c and 5e showed activity nearly comparable (90% at 1000 ppm) to that

the carbendazim (98% at 1000 ppm). Other compounds were found to be moderate to poorly active.

The results of further investigation on compound 3c, 3e, 5c and 5e on wider range of fungi as well as at higher dilution was not encouraging.

Plate 1



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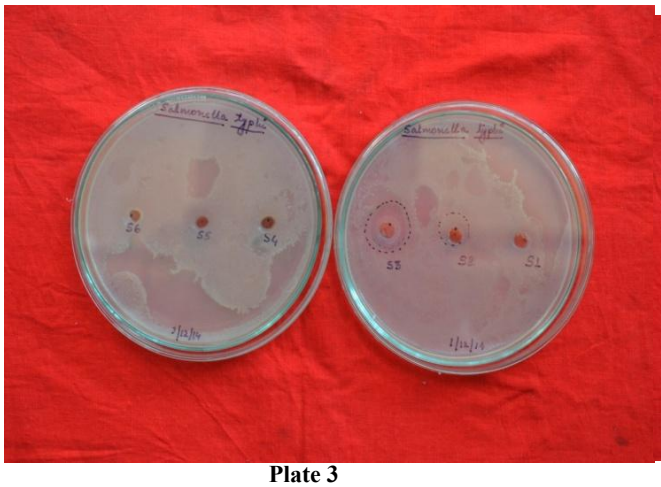


Plate 3

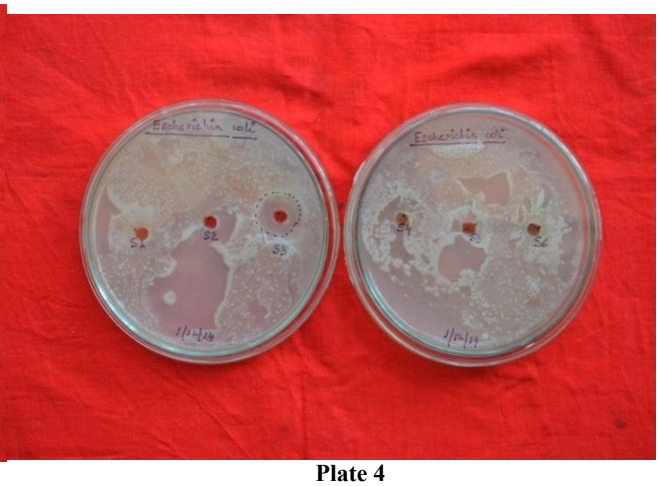


Plate 4

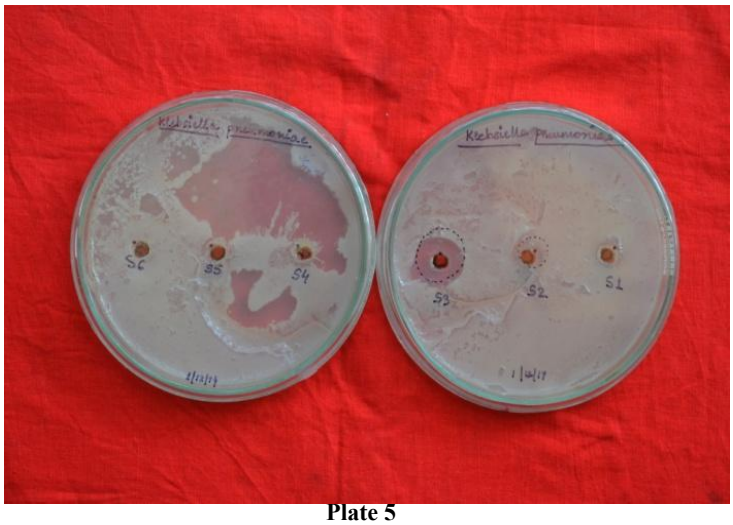


Plate 5

Figure 1-5. Compound S_1-S_6 showing antibacterial activity against *B. subtilis, B. pumilus, S. typhi,. E. coli,* and *K. pneumonia* in which compound S_3 = 3gis most active than other

Table 3. Herbicidal activity of compounds 3b, 3c, 3e, 5b, 5c and 5e

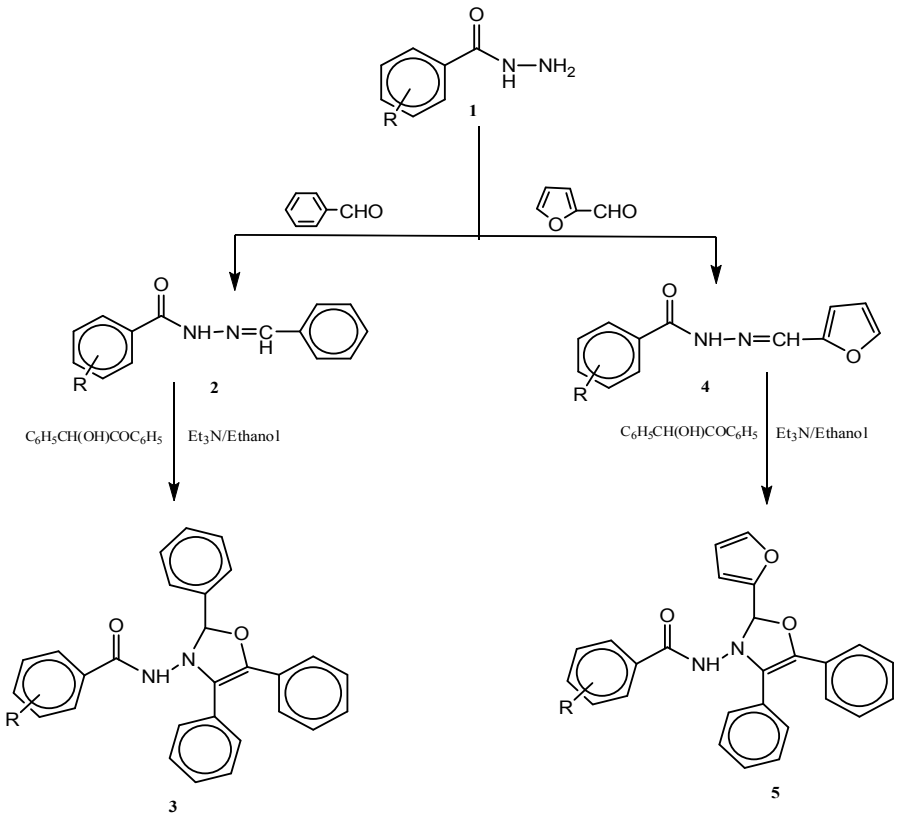
Compound no.	Application rate Kg/ha	Post-emergence species				Pre-emergence species			
		E. or	*E. cr*	*O. sa*	*G. max*	*E. or*	*E. cr*	*O. sa*	*G. max*
3b	8.0	4	5	5	4	5	4	4	5
	4.0	5	4	4	4	5	4	5	4
	1.0	3	2	2	3	2	2	3	3
	0.5	1	2	1	1	2	2	1	1
3e	8.0	5	5	5	5	5	5	5	5
	4.0	4	5	4	5	5	4	4	4
	1.0	4	4	4	3	4	4	4	4
	0.5	4	3	3	3	4	3	4	4
3e	8.0	5	5	5	4	5	5	5	5
	4.0	4	4	4	4	4	4	4	4
	1.0	4	3	2	1	3	2	2	2
	0.5	1	1	1	1	1	1	1	1
5b	8.0	4	4	5	4	4	5	5	4
	4.0	4	5	5	5	4	5	4	4
	1.0	2	3	3	2	3	3	2	2
	0.5	1	2	1	2	2	2	2	1
5c	8.0	5	5	5	5	5	5	5	5
	4.0	4	5	5	4	4	4	4	5
	1.0	4	4	4	3	4	4	4	4
	0.5	4	3	3	3	4	3	4	4
5e	8.0	4	5	4	5	4	4	4	5
	4.0	4	4	4	4	4	4	4	4
	1.0	2	3	3	2	3	3	2	2
	0.5	1	2	1	2	2	2	2	1

RESULTS AND DISCUSSION

Compounds 3a-g and 5a-g were screened for their herbicidal activity against *Echinochloa oryzicola, Echinochloa crus-galli, Oryzae sativa* and *Glycine max* fungicidal activity against *Aspergillus niger and Pyricularia oryzae* where as antibacterial activity against *Bacillus subtitlis, Bucillus pumilus* (Gram +ve) *Salmonella typhi, Escherichia coli, and Klebsiella pneumonia* (Gram -ve). Amongs these the most active compounds are 3b, 3c, 3e, 5b, 5c and 5e for herbicidal as well as fungicidal activity where as compound 3e, 5e, 3g and 5g showed highly antibacterial activity.

Applications

We have synthesized several substituted-N-(2,4,5-triphenyloxazol-3*(2H)*-yl)benzamide / substituted-N-[(2-furyl)-4,5-diphenyloxazol-3*(2H)*-yl)benzamide. All these compounds have been assayed for their pesticidal activities. Some of them have shown excellent pesticidal activity.



3a R=H	5a R=H
3b R=4-OCH_3	5b R=4-OCH_3
3c R=4-OH	5c R=4-OH
3d R=2OH	5d R=2OH
3e R=4Cl	5e R=4Cl
3f R=2Cl	5f R=2Cl
3g R=4-NO_2	5g R=4-NO_2

Fig 2. Scheme

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