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Short Communication

Antifungal Activity of Some Synthesized 1,3,4-oxadiazole Derivatives

Ashwini Kumar*[1], Shiv Shankar Sharma[2], Balmukund Tiwari[3] and Kumar Kaushik Azad[4]

[1-4] P. G. Department of Chemistry, Magadh University of Bodh-Gaya - 824 234, Bihar, India

***Key words*:** 1,3,4- oxadiazole, Aryloxy acetyl, Antifungal activities

Five membered heterocyclic compounds with Nitrogen and Oxygen i.e, 1,3,4- oxadiazole [1-2] and 1,3,4- thiadiazole [3-4] or Sulphur atoms are potential compounds for the development of antifungal agents. The physicochemical characteristics and biological activity of prospective compounds gradually alter as a result of molecular modification [5]. These findings let to the conclusion that it would be beneficial to synthesize some substituted 1,3,4-oxadiazole derivatives and assess their antifungal activity.

Experimental section

The melting points were established in open capillaries may be uncorrected. The ^1H NMR spectra in $CDCl_3$ were obtained on a varian EM-360 (200 MHz) spectrometer using TMS as internal reference, while the IR spectra in KBr were obtained as a perkin- Elmer 881 Infrared spectrophotometer (cm^{-1})

Synthesis of N-[5-(2-hydroxy phenyl)-1,3,4-oxadiazol-2-yl]-2-phenoxy acetamide [4a-e]

2-Amino-5-(2-hydroxy phenyl)-1,3,4- oxadiazole (3a-e)

These were prepared according to following method.

Typical procedure for 3a

O-hydroxy benzoic acid (1gm) (1) and triturated semi carbazide (1gm) (2) were dissolved in ethanol (50ml). The concentrated H_2SO_4 (5ml) was added dropwise over the time while the mixture was kept cold between 2-5°C. To eliminate unreacted H_2SO_4 the entire reaction mixture was refluxed with cold water. The product was recrystallized from ethanol.

N-[5-(2-hydroxy phenyl)-1,3,4-oxadiazol-2-yl]-2-phenoxy acetamide [4a-e]

Typical procedure for 4a

2-amino -5-(2-hydroxy phenyl)-1,3,4-oxadiazole (3) was dissolved in aq. KOH with stirring till yellow solution was obtained and filtered to remove suspended impurities. Then various Aryloxy acetyl chloride was added in small portion with constant shaking at 50-60 °C for 4 to 5 hours the reaction mixture was kept overnight. The precipitate was filtered and washed with cold water to remove excess aq. KOH and recrystallized from ethanol. The yields, melting points and elemental analysis of the various synthesized compounds [4a-e] are recorded in (Table 1).

Antifungal screening

Using standard dithane M-45 (a commercial fungicide). the fungicidal activity was assessed against two fungal species *Collectorichum falcatum* and *fusarium oxysporum* by standard agar-plate methods at 1000, 100 and 10 ppm concentrations. There were three replications in each case. The diameter of the fungal growth zone was determined after 96 hrs. By comparing the results to growth under control, the findings were reported as a percentage growth inhibition.

Thus,

$$\% \text{ inhibition} = (C - T) / 100$$

Where;

C = In control plate, diameter of the fungal colony (in mm)

T = In treated plate, diameter of the fungal colony (in mm)

According to the fungicidal results all of the tested compounds shown strong to moderate activity. It is remarkable to note from antifungal data of all the tested compounds [4a-e] exhibit strong antifungal activity against both *Collectorichum falcatum* and *Fusarium oxysporum* at 1000 ppm, while their activity diminishes at lower doses i.e., 100 ppm and 10ppm. It is significant to note that the antifungal activities of all the title compounds are enhanced by the addition of more electronegative oxophores (Cl and NO_2). These substances disrupt the fungal cell wall, which affects the metabolic process of the fungi.

The title compounds [4a-e] were synthesized as per scheme 1 with the yield of 58-72%.

All the compounds [4a-e] were identified by elemental analysis and one compound 4e by IR and ^1H NMR analysis.

All the compounds [4a-e] have been evaluated for their antifungal activity mentioned in (Table 2). From this screening data it is cleared that most of the compounds showed significant antifungal activities at 1000 ppm concentration against two fungal species i.e., *Collectorichum falcatum* and *Fusarium oxysporum*. On the basis of antifungal screening data, it

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Correspondence to: Ashwini Kumar, P. G. Department of Chemistry, Magadh University of Bodh-Gaya - 824 234, Bihar, India; E-mail: kumarashwini121178@gmail.com

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indicated that the compounds having Cl or NO_2 group are more fungitoxic.

SUMMARY

The present manuscript explains the synthesis of some novel 1,3,4- oxadiazole derivatives and assessment of their antifungal activity. In this study the semi carbazide (2) were cyclized with o-hydroxy aromatic acid (1) in presence of H_2SO_4 and ethanol to give 2-Amino-5-[2-hydroxy phenyl] - 1,3,4-oxadiazole (3), then the compound (3) reacted with aryloxy acetyl chloride to give corresponding N-[5-(2-hydroxyphenyl)-1,3,4- oxadiazol-2-yl]-2-phenoxy acetamide [4a-e].The structure of synthesized compounds were confirmed by IR, ^{1}H NMR spectra and elemental analysis. These molecules were evaluated for antifungal activities.

Scheme 1

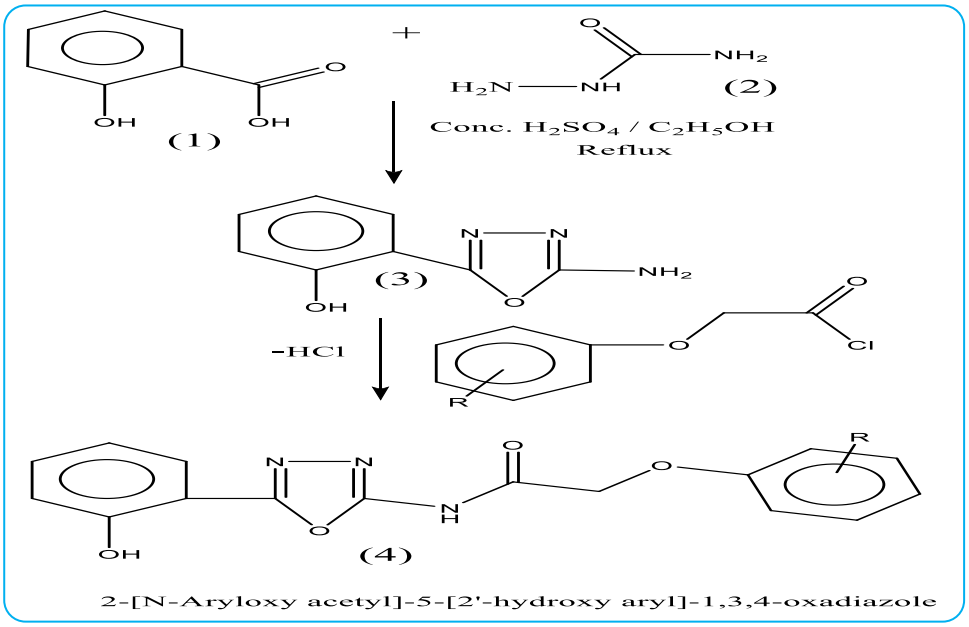

Table 1 Physical and spectral data of the title compounds

Compound	R	Yield (%)	M.P.	C Experimental (Calculated)	H Experimental (Calculated)	N Experimental (Calculated)
4a	H	72	172	59.57 (61.73)	3.89 (4.21)	12.97 (13.50)
4b	2-Cl	68	183	54.52 (55.58)	2.85 (3.50)	11.62 (12.15)
4c	2,4- Cl_2	65	188	49.97 (50.55)	2.13 (2.92)	10.11 (11.05)
4d	2-NO_2	62	193	47.80 (53.94)	2.78 (3.39)	14.67 (15.73)
4e*	2-CH_3	58	179	61.87 (62.76)	4.11 (4.65)	12.11 (12.92)

*1H NMR (DMSO-d6) ;2.10(s,3H, CH3), 4.59(S,2H, CH2), 6.81-7.10(m,4H, Ar-H), 6.90-7.16(m,4H, Ar-H), 9.57-(s,H,N-H), 9.31(s,H,-OH)
*IR(KBr) (cm^{-1} 3362(Ar-OH); 1690(C=O), 3016(N-H)

Table 2 Fungicidal screening data of N-[5-(2-hydroxy phenyl)-1,3,4-oxadiazol-2-yl]-2-Phenoxy acetamide [4a-e]

Compound No.	Average % inhibition against					
	Collectorichum falcatum			*Fusarium oxysporum*		
	1000 ppm	100 ppm	10 ppm	1000 ppm	100 ppm	10 ppm
4a	63	34	26	61	36	29
4b	89	72	56	90	69	55
4c	93	79	61	91	74	59
4d	86	73	58	87	69	57
4e	66	36	29	68	41	33
Dithane M-45	100	86	70	100	85	66

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