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NOTE

Microwave Synthesis and Biological Activity of 2-Phenyl-5-aryl-1,3,4-oxadiazoles

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The reaction of substituted aryl hydrazides with benzoic acid in the presence of dehydrating agent $POCl_3$, affords a series of 2,5-aryl-1,3,4-oxadiazoles under microwave irradiation (MWI). 2,5-Disubstituted-1,3,4-oxadiazoles have attracted much attention due to their diverse biological activities. Compared with classical methods, this method has the advantages of high yields, short reaction time, easy preparation. The preliminary biological test showed that the synthesized compound has weak activity to *G. zeae* Petch, *B. cinerea* Pers, *Phytophthora infestans* (Mont.) de Bary, *Botryosphaeria berengeriana* f. sp. *piricola* (Nose) koganezawa et Sakuma, *Fusarium oxysporum* f.sp. *cucumerinum* and *Cercospora arachidicola*. The structures of compounds were characterized by melting points, ^{1}H NMR and IR.

Key Words: Microwave irradiation, Antibacterial, 2,5-Substituted-1,3,4-oxadiazoles.

Substituted 1,3,4-oxadiazoles are heterocyclic compounds which are widely used in biological derivatives; *e.g.*, they are used as anticancer[1], antiinflammatory[2], pesticides and insecticidal[3], herbicide[4] and plant growth agents[5]. The conventional methods of the synthesis of 1,3,4-oxadiazloes are as follows: the cyclization of 1,4-disubstituted thiosemicarbazide in the presence of $POCl_3$ and the condensation of acid hydrazide with aromatic acids under a severe condition. These methods are inconvenient as they require heating of the reactants for an extended period of time. Moreover, the yield is frequently only moderate or low.

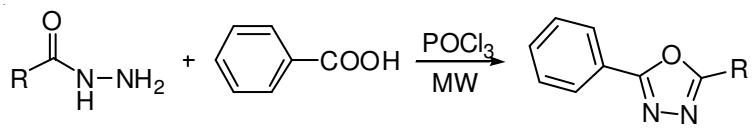
In continuation of our work in the synthesis of biological important molecules[6], it is reported here the microwave-assisted synthesis of 2,5-disubstituted-1,3,4-oxadiazole. Conventionally, synthesis of this class of compounds have been achieved[7-9] in 4-9 h (Table-1).

Melting points were determined using a Yanaco MP-241 apparatus and are uncorrected. Infrared spectra were recorded on a Bruker Equinox55 spectrophotometer as potassium bromide tablets. ^{1}H NMR spectra were measured on a Bruker AC-P500 instrument (300 MHz) using tetramethylsilane as an internal standard and dimethyl sulfoxide-d_6 as solvent. Elemental analyses were performed on a Yanaco MT-3CHN elemental analyzer.

TABLE-1
COMPARISON BETWEEN MICROWAVE-ASSISTED AND CONVENTIONAL METHOD OF SYNTHESIS OF 2,5-DISUBSTITUTED-1,3,4-OXADIAZOLE

No.	R	Microwave		Conventional	
		Time (min)	Yield (%)	Time (h)	Yield (%)
A	C_6H_5	12	91	4	89
B	*o*-FC_6H_5	12	87	5	86
C	*o*-$OCH_3C_6H_5$	12	84	7	79
D	*o*-ClC_6H_5	12	84	9	73
E	*o*-$CH_3C_6H_5$	12	82	7	79
F	*m*-$CH_3C_6H_5$	12	84	9	75
G	*p*-ClC_6H_5	12	87	5	84
H	*p*-$NO_2C_6H_5$	15	93	4	86
I	*p*-$OCH_3C_6H_5$	12	89	6	80
J	2,4-$Cl_2C_6H_5$	15	87	5	81
K	3,4-$Cl_2C_6H_5$	15	88	5	78
L	C_5H_5N	12	91	6	81

Hydrazides which are producted according to the references were treated with different carboxylic acids (**2A-L**) in the presence of phosphorous oxychloride to afford 2,5-disubstituted-1,3,4-oxadiazoles (**3A-L**) (**Scheme-I**). The reaction was found to proceed smoothly under microwave irradiation within 12-15 min whereas under reflux conditions, 4-9 h were required (Table-1). The products were isolated by simple cold aqueous work-up followed by either solvent extraction or precipitation and were finally purified by column chromatography wherever necessary, to afford pure 2,5-disubstituted-1,3,4-oxadiazole.



Scheme-I

Bioassay of fungicidal activities

Fungicidal activities of the title compounds against *G. zeae* Petch, *Phytophthora infestans* (Mont.) de Bary, *Botryosphaeria berengeriana* f. sp. *piricola* (Nose) koganezawa et Sakuma, *Fusarium oxysporum* f.sp. *cucumerinum* and *Cercospora arachidicola* were evaluated using the mycelium growth rate test at 50 ppm. The culture media, with known concentration of the test compounds. The blank test was made using acetone. The culture was carried out at 24 ± 0.5ºC. Three replicates were performed.

Primary bioassay (Table-2) showed that the tested compounds has weak fungicidal activity against *G. zeae* Petch, *B. cinerea* Pers, *Phytophthora infestans* (Mont.) de Bary, *Botryosphaeria berengeriana* f. sp. *piricola* (Nose) koganezawa et Sakuma, *Fusarium oxysporum* f.sp. *cucumerinum* and *Cercospora arachidicola*. The compound **L** showed against *Phytophthora infestans* (Mont.) de Bary and *Fusarium oxysporum* f.sp. *cucumerinum* of 69.2 and 64.4 %. All of the results in this paper will be useful for later research.

TABLE-2
FUNGICIDAL ACTIVITY OF TESTED COMPOUNDS AT 50 ppm

No	R	*G. zeae* Petch	*Phytophthora infestans* (Mont.) de Bary	*Botryosphaeria berengeriana* f. sp. *iricola* (Nose) koganezawa et Sakuma	*Fusarium oxysporum* f.sp. *cucumerinum*	*Cercospora arachidicola*
A	C_6H_5	11.8	15.4	21.7	0.0	0.0
B	*o*-FC_6H_5	28.9	11.5	31.7	35.6	35.7
C	*o*-$OCH_3C_6H_5$	23.6	30.8	17.6	48.9	40.7
D	*o*-ClC_6H_5	0.0	11.5	41.7	15.6	17.9
E	*o*-$CH_3C_6H_5$	23.3	32.1	0.0	0.0	17.9
F	*m*-$CH_3C_6H_5$	0.0	23.9	23.5	40.0	21.4
G	*p*-ClC_6H_5	0.0	56.4	23.5	46.7	51.4
H	*p*-$NO_2C_6H_5$	19.0	23.1	17.6	24.4	0.0
I	*p*-$OCH_3C_6H_5$	0.0	38.5	0.0	28.9	28.5
J	2,4-$Cl_2C_6H_5$	14.3	15.4	17.8	35.1	17.9
K	3,4-$Cl_2C_6H_5$	33.3	32.1	29.4	33.3	16.7
L	C_5H_5N	38.1	69.2	35.3	64.4	39.3

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