Note

Biological Activity of Some 2-Arylamino-4-aryloxyacetyl- Δ^2 -1,3,4-thiadiazolidine Derivatives

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INTRODUCTION

A 1,3,4-thiadiazole nucleus is associated with a broad spectrum of biocidal activities possibly by virtue of incorporating a >N-C-S- moiety.^{1,2)} The derivatives of 1,3,4-thiadiazolidine have been

found to display a variety of biological activities *e.g.* insecticidal³⁾ and herbicidal.^{4,5)}

Since the aryloxy moiety forms the structural unit of a number of pesticidal agents⁶⁾ including well known herbicidal aryloxy and hetero-aryloxy alkanoic acids,⁷⁾ a molecule of type (2) and (3) including thiadiazolidine ring and aryloxy moiety may be effective pesticide. With this background the title compounds (2) and (3) have been synthesized.

The starting materials arylthiosemicarbazides (1) were synthesized according to the method reported.⁸⁾ Reaction of arylthiosemicarbazide with acid chloride and carbonyl compounds, such as benzaldehyde and acetone in pyridine furnished the title compounds (2) and (3), respectively (Fig. 1).

MATERIALS AND METHODS

All the melting points were taken in open

Fig. 1 Synthetic scheme of some 2-arylamino-4-aryloxyacetyl-5-phenyl- Δ^2 -1,3,4-thiadiazolidines (2) and 2-arylamino-4-aryloxyacetyl-5,5-dimethyl- Δ^2 -1,3,4-thiadiazolidines (3).

capillaries and are uncorrected. IR spectra were recorded on a Perkin Elmer Spectrophotometer (model 557) in KBr disk and PMR spectra were recorded on a varian EM 360 Spectrometer at 60 MHz in DMSO- d_6 .

1. Arylthiosemicarbazides (1a-d)

These thiosemicarbazides were prepared according to the method of Kazakov & Postovskii.⁸⁾

2. 2-(4-Methylphenylamino)-4-(2-chlorophenoxyacetyl)-5-phenyl- Δ^2 -1,3,4-thiadiazolidine (2c)

A mixture of 4-(4-methylphenyl)-3-thiosemicarbazide (1.8 g), 2-chlorophenoxyacetyl chloride (2 ml) and benzaldehyde (1 ml) in pyridine (2 ml)

was stirred for five min. The reaction mixture was poured into water. The solid deposited was obtained by filtration and recrystallized from methanol to give the desired compounds (2c) in 86% yield as a solid. The yields and melting points of the compounds (2) thus prepared are recorded in Table 1.

3. 2-(4-Methylphenylamino)-4-(2-chlorophenoxyacetyl)-5, 5-dimethyl- Δ^2 -1, 3, 4-thiadiazolidine (3g)

A mixture of 4-(4-methylphenyl)-3-thiosemicarbazides (1.86 g), 2-chlorophenoxyacetyl chloride (2 ml) and acetone (1 ml) in pyridine (2 ml) was stirred for five min. The reaction mix-

Table 1 Yield and melting point of 2-arylamino-4-aryloxyacetyl- Δ^2 -1, 3, 4-thiadiazolidine (2, 3).

2	R	R ¹	Yield (%)	mp (°C)	3	R	R ¹	Yield (%)	mp (°C)
a	H	2-Cl	71	82-84	a	H	4-Cl	56	104-106
b	4-Cl	2-Cl	76	164-165	b	H	2-Cl	60	96-97
c	4-CH ₃	2-Cl	86	100-101	c	4-Cl	2-Cl	80	68-69
d	4-OCH ₃	2-Cl	74	172-173	d	4-Cl	3-CH ₃	69	120-122
e	H	3-CH ₃	79	123-125	e	4-CH ₃	3-CH ₃	74	182-185
f	4-Cl	3-CH ₃	81	136-139	f	4-OCH ₃	3-CH ₃	78	150-153
g	4-CH ₃	3-CH ₃	78	151-153	g	4-CH ₃	2-Cl	69	108-109
h	4-OCH ₃	3-CH ₃	77	104-105	h	4-OCH ₃	2-Cl	65	125-127

Table 2 Herbicidal activity (post-emergent activity).

Compound ^{b)} No.	Herbicidal activity ^{a)}				
	Wheat	Johnson grass	Barnyard grass	Velvet leaf	Foxtail green
2a	20	60	50	50	50
2b	25	40	60	50	60
2c	30	60	50	40	50
2d	10	90	100	100	100
2e	0	60	60	60	60
2f	15	60	60	50	50
2g	10	50	30	60	20
2h	10	100	100	100	100
3a	0	60	50	40	40
3b	20	70	60	40	50
3c	10	30	50	40	50
3d	10	60	50	40	50
3e	15	50	60	30	20
3f	10	100	100	100	100
3g	30	50	20	50	50
3h	10	100	100	100	100

^{a)} Herbicidal activity: 100=completely killed.

^{b)} The compounds were sprayed at a concentration of 6 kg/ha.

ture was poured into water. The solid thus separated was filtered and recrystallized from ethanol to give the desired product (**3g**) in 69% yield as a solid. The yields and melting points of the compounds (**3**) thus prepared are recorded in Table 1.

4. Herbicidal Activity

All the compounds were subjected to primary pre- and post-emergent evaluations at the rate of 6.0 kg/ha. The test species were wheat, Johnson grass, barnyard grass, velvet leaf and foxtail green. The activity data are recorded in Table 2.

5. Fungicidal Screening

The fungicidal activities of these compounds were evaluated by agar growth technique.⁹⁾ Two species of fungi viz. *Aspergillus niger* and *Helminthosporium oryzae* were used for testing at three different concentrations of 1000, 100 and 10 ppm. The number of replications in each case were three. The inhibitory activities were compared with Dithane M-45 tested under similar conditions. The activity data are recorded in Table 3.

The percentage inhibition after the incubation for 96 hr was calculated by following equation:

$$\% \text{ Inhibition} = \frac{(C - T)}{C} \times 100$$

where,

C = Diameter of the mycelial colony (in mm) on the control plate.

T = Diameter of the mycelial colony (in mm) on the treated plate.

RESULTS AND DISCUSSION

A perusal of herbicidal data indicates that all the compounds in this investigation are strong to moderately toxic to all the test species (Table 2). Especially, 5-phenyl derivatives, **2d** and **2h**, were found to be promising herbicides. Both of them showed 90–100% activity at 6.0 kg/ha on all the test weeds with only 10% activity on wheat. Similar results were also obtained with 5,5-dimethyl derivatives, **3f** and **3h**.

These results notably indicated that more active compounds (**2d**, **2h**, **3f** and **3h**) have an electron-donating methoxy group as the R substituent with addition to a chloro atom or methyl group as the R¹ substituent. From these data it can be concluded that the presence of the 4-methoxyphenylamino moiety along with 2-chloro or 3-methylphenoxyacetyl moiety on the thiadiazolidine ring imparts much towards herbicidal activity in this series of compounds.

A perusal of fungicidal data indicates that all the compounds under this investigation were moderately toxic to both the species of fungi but their activity decreases considerably with dilu-

Table 3 Fungicidal activity.

Compound No.	Fungi conc. (ppm)	Percentage inhibition after % hr					
		<i>A. niger</i>			<i>H. oryzae</i>		
		1000	100	10	1000	100	10
2a		92	82	77	90	80	75
2b		92	83	78	92	80	78
2c		65	52	43	60	50	39
2d		65	59	44	63	58	44
2e		67	54	38	61	49	39
2f		62	49	40	58	48	38
2g		70	62	47	68	61	46
2h		74	67	51	72	65	50
3a		78	69	45	76	67	59
3b		56	44	51	52	42	31
3c		62	50	49	58	48	39
3d		63	54	48	59	47	38
3e		75	68	54	71	63	48
3f		69	58	43	65	54	36
3g		63	52	49	56	44	32
3h		65	56	37	60	53	31
Dithane M-45		100	98	95	100	97	95

tion (Table 3). It is also notable that the activity of the test compounds on *A. niger* is more effective than on *H. oryzae*.

The compounds (**2a** and **2b**) have comparable activity with the commercial fungicide Dithane M-45, tested under similar conditions. Further investigation of the activity of these two compounds on wide varieties of fungi as well as at higher dilution is in process.

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要 約

2-アリールアミノ-4-アリールオキシアセチル- Δ^2 -1, 3,4-チアジアゾリジン誘導体の生物活性

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殺虫, 殺菌, 除草など幅広い生物活性を有するチアジアゾリジンを母核とした 2-アリールアミノ-4-アリールオキシアセチル-5-フェニル- Δ^2 -1,3,4-チアジアゾリジン (1) および 2-アリールアミノ-4-アリールオキシアセチル-5,5-ジメチル- Δ^2 -1,3,4-チアジアゾリジン (2) のそれぞれ 8 種類の誘導体を合成した。これら誘導体の殺草活性および殺菌活性について検討した結果, 除草活性には (1), (2) 化合物ともにチアジアゾリジン環に対する 2-クロロあるいは 3-メチルフェノキシアセチル部分と 4-メトキシフェニルアミノ部分の存在が重要であることが認められた。また, 殺菌活性では 2-クロロフェノキシアセチル部分を有する (1) 化合物が高い活性を示した。