Synthesis and Acaricidal Activity of *N*-(1,3,4-Thiadiazol-2-yl)carboxamides

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INTRODUCTION

Some herbicidal N-(1,3,4-thiadiazol-2-yl)carboxamides have been reported, 1,2) but little is known about their acaricidal activity. In this investigation into the development of a new acaricide, we identified a new class of N-(1,3,4-thiadiazol-2-yl)carboxamides with high acaricidal activity. 3) This paper describes the synthesis and acaricidal activities of N-(1,3,4-thiadiazol-2-yl)carboxamides.

MATERIALS AND METHODS

1. Synthesis of Compounds

Melting points were uncorrected. The structures of compounds were confirmed by 'H NMR and IR spectra. 'H NMR spectra were measured on a Varian UNITY 300 spectrometer at 300 MHz using tetramethylsilane as an internal standard. IR spectra were measured on a JASCO IR-810 spectrometer.

N-(1,3,4-Thiadiazol-2-yl)carboxamides were synthesized by the reaction of acid chlorides and 2-amino-1,3,4-thiadiazoles in the presence of a base (Fig. 1). 2-Amino-5-substituted-1,3,4-thiadiazoles were purchased from commercial sources or synthesized according to the reported procedure.^{4,5)} Acid chlorides were purchased from commercial sources or synthesized according to the reported procedure.⁶⁾ 2,2-Dibromo-3,3-dimethylbutanoyl chloride was synthesized by bromination of 3,3-dimethylbutanoyl chloride (Fig. 2).

1.1. 2,2-Dibromo-3,3-dimethylbutanoyl chloride

A mixture of 3,3-dimethylbutanoyl chloride (21.4 g, 159 mmol) and bromine (64.0 g, 400 mmol) was refluxed for 9 hr. Excess bromine was removed, and the residue was distilled

Fig. 1. Synthetic route of *N*-(1,3,4-thiadiazol-2-yl)carboxamides.

Fig. 2. Synthetic route of 2,2-dibromo-3,3-dimethylbutanoyl chloride.

under reduced pressure to give 18.6 g (40%) of the title compound. bp: 71^-72° C (0.6 mmHg); 1 H NMR (CDCl₃) δ (ppm): 1.41 (9H, s); IR (NaCl) cm $^{-1}$: 2984, 1783, 1464, 1398, 1367, 1041, 1000, 875, 796, 750, 695, 665, 572.

1.2. 2, 2-Dibromo - 3, 3 - dimethyl - N - (5-pentafluoroethyl-1, 3, 4-thiadiazol-2-yl)butanamide (23)

A mixture of 2,2-dibromo-3,3-dimethylbutanoyl chloride (8.78 g, 30 mmol), 2-amino-5-pentafluoroethyl-1,3,4-thiadiazole (6.57 g, 30 mmol) and potassium carbonate (4.14 g, 30 mmol) in toluene (100 ml) was refluxed for 6 hr. After cooling to room temperature, the mixture was poured into water (200 ml), acidified with hydrochloric acid and extracted with ethyl acetate. The organic layer was washed with water and saturated aqueous sodium chloride, then dried over sodium sulfate. The solvent was removed under reduced pressure and the resulting solid was washed by hexane to give **23** (9.98 g, 70%). mp: 152–154°C; 1 H NMR (CDCl₃) δ (ppm): 1.33 (9H, s), 11.2 (1H, br).

2. Biological Tests

Test species of mite (*Tetranychus urticae*) and the method used were the same as preciously reported.⁷⁾

The activity rating was expressed as indices of 0 to 3, corresponding to 0-29, 30-79, 80-99 and 100% mortality, respectively.

RESULTS AND DISCUSSION

Table 1 shows the effect of substituent (R) of the acid moiety. Only tert- and sec-alky analogs showed a high activity against T. urticae. Among these, the tert-butyl analog (9) showed activity at 50 ppm. Introduction of a bulkier tert-amyl group (10) resulted in reduced activity. The hydrogen (1), normal-alkyl (2-4 and 6) and cycloalkyl (11 and 12) analogs showed little or no activity.

Table 2 shows the effect of halogen atoms at 2-positon of carbonyl moiety. Halogen atom is essential for acaricidal activity because the nonhalogenated compound (13) did not show any activity at 500 ppm. The dibromo (14) and monochloro (15) analogs were as active as the monobromo analog (9).

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Table 1. Effect of substituent R on activity against Tetranychus urticae

$$\mathsf{R} \underset{\mathsf{Br}}{\underbrace{\hspace{0.1cm} \bigcap_{\mathsf{N}^{-}\mathsf{N}}}} \underset{\mathsf{S}}{\underbrace{\hspace{0.1cm} \bigcap_{\mathsf{N}^{-}\mathsf{N}}}} \mathsf{CF}_{3}$$

			Activ	ity rating	(Tetran	ychus urticae)
No.	R	mp (°C)	500	200	50	12.5 (ppm)
1	Н	150-152	0	_a)	-	•
2	CH ₃	138-140	0	-	-	-
3	C_2H_5	124-125	0	-	-	-
4	<i>n</i> -C ₃ H ₇	124-126	1	0	-	-
5	i-C ₃ H ₇	131-132	3	1	-	-
6	n-C ₄ H ₉	102-104	0	-	-	-
7	i-C ₄ H ₉	117-119	0	•	-	-
8	s-C ₄ H ₉	108-110	3	3	2	1
9	t-C ₄ H ₉	151-153	3	3	3	1
10	t-C ₅ H ₁₁	155-156	2	2	1	0
11	cyclo-C ₅ H ₉	130-132	1	0	-	-
12	cyclo-C ₆ H ₁₁	148-150	1	0	-	-

a) Not tested.

Table 2. Effect of substituents X1 and X2 on activity against Tetranychus urticae

No.	X^1	X ²	mp (°C)	Activity rating (Tetranychus urticae)					
				500	200	50	12.5 (ppm)		
13	Н	Н	117-119	0	_a)	-	-		
9	Br	Н	151-153	3	3	3	1		
14	Br	Br	147-149	3	3	3	1		
15	Cl	Н	162-163	3	3	3	1		

a) Not tested.

Tables 3 and 4 show the effect of substituent (Y) at 5-position of thiadiazole ring. Unsubstituted (20) and alkyl analogs (21,22) did not show any activity at 500 ppm (Table 3). In the case of monobromo analogs, the trifluoromethyl analog (9) showed the highest activity (Table 3). However, in the case of the dibromo analogs, the pentafluoroethyl (23), heptafluoropropyl (24) and nonafluorobutyl (25) analogs also showed high activity (Table 4). Among these, 2,2-dibromo-3,3-dimethyl-N-(5-pentafluoroethyl-1,3,4-thiadiazol-2-yl)butanamide (23) showed the highest activity.

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Table 3. Effect of substituent Y on activity against Tetranychus urticae

No.	Y	mp (°C)	Activity rating (Tetranychus urticae)					
			500	200	50	12.5	(ppm)	
9	CF ₃	151-153	3	3	3	1		
16	CF ₂ CF ₃	201-203	3	2	2	1		
17	$(CF_2)_2CF_3$	201-202	2	1	1	1		
18	$(CF_2)_3CF_3$	196-197	0	- ^{a)}	-	-		
19	$(CF_2)_4CF_3$	166-167	0	-	-	-		
20	Н	212-213	0	-	-	-		
21	CH ₃	217-219	0	-	-	-		
22	C_2H_5	190-192	0	-	-	-		

a) Not tested.

Table 4. Effect of substituent Y on activity against Tetranychus urticae

No.	Y	mp (°C)	Activity rating (Tetranychus urticae)						
			500	200	50	12.5	3.13	(ppm)	
14	CF ₃	147-149	3	3	3	1	_a)		
23	CF ₂ CF ₃	152-154	3 .	3	3	2	1		
24	$(CF_2)_2CF_3$	142-143	3	3	2	0	-		
25	$(CF_2)_3CF_3$	89-91	3	3	3	1	-		

a) Not tested.

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